THE BIOLOGICAL PHYSICIST

The Newsletter of the Division of Biological Physics of the American Physical Society

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In this Issue

MARCH MEETING SPECIAL EDITION!

This special March Meeting edition of the DBP newsletter brings you PRE and PRL Highlights, and a handy compilation of all the DBP sessions at the March Meeting, as well as a map of downtown Denver and full details about the Opportunities in Biological Physics Workshop. Find more March Meeting details, including the Program Scheduler & the "Epitome", at

http://www.aps.org/meetings/march/index.cfm.

Don't forget to attend the DBP Business Meeting on Tuesday March 6th at 5:45 pm in Room 405 of the Colorado Convention Center!

See you in Denver!

-- SB

PRL HIGHLIGHTS

Soft Matter, Biological, &
Inter-disciplinary Physics Articles from
Physical Review Letters

1 December 2006
Vol 97, Number 22, Articles (22xxxx)
Articles published 25 Nov - 1 Dec 2006
http://scitation.aip.org/dbt/dbt.jsp?KEY=PRLTAO&Volume=97&Issue=22

Director-Configurational Transitions around Microbubbles of Hydrostatically Regulated Size in Liquid Crystals
C. Völtz, Y. Maeda, Y. Tabe, and H. Yokoyama
Published 30 November 2006
227801

Failure of Viral Shells
William S. Klug, Robijn F. Bruinsma, Jean-Philippe Michel, Charles M. Knobler, Irena L. Ivanovska, Christoph F. Schmidt, and Gijs J. L. Wuite
Published 27 November 2006
228101

Dynamic Broadening of the Crystal-Fluid Interface of Colloidal Hard Spheres
Roel P. A. Dullens, Dirk G. A. L. Aarts, and Willem K. Kegel
Published 29 November 2006
228301

Realizing Colloidal Artificial Ice on Arrays of Optical Traps
A. Libál, C. Reichhardt, and C. J. Olson Reichhardt
Published 30 November 2006
228302

8 December 2006
Vol 97, Number 23, Articles (23xxxx)
Articles published 2 Dec - 8 Dec 2006
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Entropy-Driven Formation of the Gyroid Cubic Phase
L. J. Ellison, D. J. Michel, F. Barmes, and D. J. Cleaver
Published 8 December 2006
237801

Modifications of the Mesoscopic Structure of Cellulose in Paper Degradation
Mauro Missori, Claudia Mondelli, Marco De Spirito, Carlo Castellano, Marina Bicchieri, Ralf Schweins, Giuseppe Arcovito, Massimiliano Papi, and Agostina Congiu Castellano
Published 6 December 2006
238001

Double Coherence Resonance in Neuron Models Driven by Discrete Correlated Noise
Thomas Kreuz, Stefano Luccioli, and Alessandro Torcini
Published 6 December 2006
238101

Transient Ordered Domains in Single-Component Phospholipid Bilayers
Teemu Murtola, Tomasz Róg, Emma Falck, Mikko Karttunen, and Ilpo Vattulainen
Published 7 December 2006
238102

Hierarchical Organization Unveiled by Functional Connectivity in Complex Brain Networks
Changsong Zhou, Lucia Zemanová, Gorka Zamora, Claus C. Hilgetag, and Jürgen Kurths
Published 8 December 2006
238103

Origin of the Slow Dynamics and the Aging of a Soft Glass
Sylvain Mazoyer, Luca Cipelletti, and Laurence Ramos

Published 4 December 2006
238301

Space-Time Clustering and Correlations of Major Earthquakes
James R. Holliday, John B. Rundle, Donald L. Turcotte, William Klein, Kristy F. Tiampo, and Andrea Donnellan
Published 6 December 2006
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Anomalous Behavior of Proton Zero Point Motion in Water Confined in Carbon Nanotubes
G. Reiter, C. Burnham, D. Homouz, P. M. Platzman, J. Mayers, T. Abdul-Redah, A. P. Moravsky, J. C. Li, C.-K. Loong, and A. I. Kolesnikov
Published 14 December 2006
247801

Confinement Effects in Polymer Crystal Nucleation from the Bulk to Few-Chain Systems
Michael V. Massa, Jessica L. Carvalho, and Kari Dalnoki-Veress
Published 14 December 2006
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Charles W. Wolgemuth and Sean X. Sun
Published 15 December 2006
248101

Direct Observation of Hydrodynamic Rotation-Translation Coupling between Two Colloidal Spheres
S. Martin, M. Reichert, H. Stark, and T. Gisler
Published 15 December 2006
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Critical Scaling in Linear Response of Frictionless Granular Packings near Jamming
Wouter G. Ellenbroek, Ellák Somfai, Martin van Hecke, and Wim van Saarloos
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Diffusion and Segmental Dynamics of Double-Stranded DNA
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Hydra Molecular Network Reaches Criticality at the Symmetry-Breaking Axis-Defining Moment
Jordi Soriano, Cyril Colombo, and Albrecht Ott
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Coevolution of Strategy and Structure in Complex Networks with Dynamical Linking
Jorge M. Pacheco, Arne Traulsen, and Martin A. Nowak
Published 19 December 2006
258103

Bistable Bacterial Growth Rate in Response to Antibiotics with Low Membrane Permeability
Johan Elf, Karin Nilsson, Tanel Tenson, and Måns Ehrenberg
Published 19 December 2006
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Mechanisms of Molecular Response in the Optimal Control of Photoisomerization
Benjamin Dietzek, Ben Brüggemann, Torbjörn Pascher, and Arkady Yartsev
Published 20 December 2006
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Nonlinear Screening and Gas-Liquid Separation in Suspensions of Charged Colloids
Bas Zoetekouw and René van Roij
Published 20 December 2006

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Collective Rearrangement at the Onset of Flow of a Polycrystalline Hexagonal Columnar Phase
Teresa Bauer, Julian Oberdisse, and Laurence Ramos
Published 21 December 2006
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Atomistic Simulations of a Thermotropic Biaxial Liquid Crystal
Jorge Peláez and Mark R. Wilson
Published 26 December 2006
267801

Rheology of Active Filament Solutions
T. B. Liverpool and M. C. Marchetti
Published 29 December 2006
268101

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Articles published 1 Jan - 5 Jan 2007
http://scitation.aip.org/dbt/dbt.jsp?KEY=PRLTAO&Volume=98&Issue=1

Molecular Scale Imaging of F-Actin Assemblies Immobilized on a Photopolymer Surface
Taiji Ikawa, Fumihiko Hoshino, Osamu Watanabe, Youli Li, Philip Pincus, and Cyrus R. Safinya
Published 3 January 2007
018101

Force Balance and Membrane Shedding at the Red-Blood-Cell Surface
Pierre Sens and Nir Gov
Published 4 January 2007
018102

Critical Fluctuations of Tense Fluid Membrane Tubules
Jean-Baptiste Fournier and Paolo Galatola
Published 5 January 2007
018103

Refraction of Shear Zones in Granular Materials
Tamás Unger
Published 2 January 2007
018301

Phase Behavior and Charge Regulation of Weak Polyelectrolyte Grafted Layers
Peng Gong, Jan Genzer, and I. Szleifer
Published 5 January 2007
018302

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Articles published 6 Jan - 12 Jan 2007
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Effect of Particle Shape on the Stress Dip Under a Sandpile
I. Zuriguel, T. Mullin, and J. M. Rotter
Published 11 January 2007
028001

Controlled Manipulation of Atoms in Insulating Surfaces with the Virtual Atomic Force Microscope
T. Trevethan, M. Watkins, L. N. Kantorovich, and A. L. Shluger
Published 8 January 2007
028101

How Complex Is the Dynamics of Peptide Folding?
Rainer Hegger, Alexandros Altis, Phuong H. Nguyen, and Gerhard Stock
Published 12 January 2007
028102

Viscoelasticity of Dynamically Self-Assembled Paramagnetic Colloidal Clusters
Pietro Tierno, Ramanathan Muruganathan, and Thomas M. Fischer
Published 9 January 2007
028301

Mechanism of Thermal Transport in Dilute Nanocolloids
Jacob Eapen, Ju Li, and Sidney Yip
Published 10 January 2007
028302

Length-Scale-Dependent Relaxation in Colloidal Gels
Emanuela Del Gado and Walter Kob
Published 10 January 2007
028303

Atom-By-Atom Extraction Using the Scanning Tunneling Microscope Tip-Cluster Interaction
A. Deshpande, H. Yildirim, A. Kara, D. P. Acharya, J. Vaughn, T. S. Rahman, and S.-W. Hla
Published 11 January 2007
028304

No-Slip Hydrodynamic Boundary Condition for Hydrophilic Particles
Christopher D. F. Honig and William A. Ducker
Published 11 January 2007
028305

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Articles published 13 Jan - 19 Jan 2007
http://scitation.aip.org/dbt/dbt.jsp?KEY=PRLTAO&Volume=98&Issue=3

Evidence of Early Stage Precursors of Polymer Crystals by Dielectric Spectroscopy
M. Soccio, A. Nogales, N. Lotti, A. Munari, and T. A. Ezquerra
Published 17 January 2007
037801

Optical Activity Produced by Layer Chirality in Bent-Core Liquid Crystals
Loren E. Hough, Chenhui Zhu, Michi Nakata, Nattaporn Chattham, Gert Dantlgraber, Carsten Tschierske, and Noel A. Clark
Published 19 January 2007
037802

Could Humans Recognize Odor by Phonon Assisted Tunneling?
Jennifer C. Brookes, Filio Hartoutsiou, A. P. Horsfield, and A. M. Stoneham
Published 16 January 2007
038101

Network Formation of Tissue Cells via Preferential Attraction to Elongated Structures
Andras Szabo, Erica D. Perryn, and Andras Czirok
Published 18 January 2007
038102

Loop Dynamics in DNA Denaturation
A. Bar, Y. Kafri, and D. Mukamel
Published 17 January 2007
038103

Noncentral Forces in Crystals of Charged Colloids
D. Reinke, H. Stark, H.-H. von Grünberg, Andrew B. Schofield, G. Maret, and U. Gasser
Published 19 January 2007
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Articles published 20 Jan - 26 Jan 2007
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Two-Dimensional Dynamics of Metal Nanoparticles on the Surface of Thin Polymer Films Studied with Coherent X Rays
S. Streit, C. Gutt, V. Chamard, A. Robert, M. Sprung, H. Sternemann, and M. Tolan
Published 24 January 2007
047801

Electronic Excitation Energy Transfer between Two Single Molecules Embedded in a Polymer Host
Rémi Métivier, Fabian Nolde, Klaus Müllen, and Thomas Basché
Published 25 January 2007
047802

Does Changing the Pulling Direction Give Better Insight into Biomolecules?
Sanjay Kumar and Debaprasad Giri
Published 23 January 2007
048101

Anharmonicity and Self-Similarity of the Free Energy Landscape of Protein G
F. Pontiggia, G. Colombo, C. Micheletti, and H. Orland
Published 24 January 2007
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Two-State Folding, Folding through Intermediates, and Metastability in a Minimalistic Hydrophobic-Polar Model for Proteins
Stefan Schnabel, Michael Bachmann, and Wolfhard Janke
Published 25 January 2007
048103

Dynamically Maintained Spike Timing Sequences in Networks of Pulse-Coupled Oscillators with Delays
Pulin Gong and Cees van Leeuwen
Published 25 January 2007
048104

Channel-Facilitated Molecular Transport across Membranes: Attraction, Repulsion, and Asymmetry
Anatoly B. Kolomeisky
Published 26 January 2007
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Production of Ball-Lightning-Like Luminous Balls by Electrical Discharges in Silicon
Gerson Silva Paiva, Antonio Carlos Pavão, Elder Alpes de Vasconcelos, Odim Mendes, Jr., and Eronides Felisberto da Silva, Jr.
Published 24 January 2007
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PRE HIGHLIGHTS

Biological Physics Articles from

Physical Review E

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Equilibration of experimentally determined protein structures for molecular dynamics simulation
Emily B. Walton and Krystyn J. VanVliet
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061901

Transition from long- to short-lived transient pores in giant vesicles in an aqueous medium
Nicolas Rodriguez, Sophie Cribier, and Frédéric Pincet
Published 8 December 2006 (10 pages)
061902

Nonperturbative retrieval of the scattering strength in one-dimensional media
K. D. Lamb, S. Menon, Q. Su, and R. Grobe
Published 8 December 2006 (9 pages)
061903

Dynamics of spiral pairs induced by unidirectional propagating pulses
A. Rabinovitch, M. Gutman, Y. Biton, I. Aviram, and D. S. Rosenbaum
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Calcium dynamics on a stochastic reaction-diffusion lattice model
Nara Guisoni and Mário J. de Oliveira
Published 18 December 2006 (6 pages)
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Periodicity and chaos in electrically coupled Hindmarsh-Rose neurons
R. Erichsen, Jr., M. S. Mainieri, and L. G. Brunnet
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Effect of supercoiling on formation of protein-mediated DNA loops
P. K. Purohit and P. C. Nelson
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061907

Phase transition in the collective migration of tissue cells: Experiment and model
B. Szabó, G. J. Szöllösi, B. Gönci, Zs. Jurányi, D. Selmeczi, and Tamás Vicsek
Published 22 December 2006 (5 pages)
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Light scattering regimes along the optical axis in turbid media
S. D. Campbell, A. K. O'Connell, S. Menon, Q. Su, and R. Grobe
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Episodic synchronization in dynamically driven neurons
Pablo Balenzuela, Javier M. Buldú, Marcos Casanova, and Jordi García-Ojalvo
Published 26 December 2006 (8 pages)
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Protein fluctuations and breakdown of time-scale separation in rate theories
Jianhua Xing and K. S. Kim
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Internal protein dynamics shifts the distance to the mechanical transition state
Daniel K. West, Emanuele Paci, and Peter D. Olmsted
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Hydrodynamics of isotropic and liquid crystalline active polymer solutions
Aphrodite Ahmadi, M. C. Marchetti, and T. B. Liverpool
Published 29 December 2006 (23 pages)
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How to determine local elastic properties of lipid bilayer membranes from atomic-force-microscope measurements: A theoretical analysis
Davood Norouzi, Martin Michael Müller, and Markus Deserno
Published 29 December 2006 (12 pages)

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Morphogen transport in epithelia
T. Bollenbach, K. Kruse, P. Pantazis, M. González-Gaitán, and F. Jülicher
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Separation of long DNA chains using a nonuniform electric field: A numerical study
Shin-ichiro Nagahiro, Satoyuki Kawano, and Hidetoshi Kotera
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Dielectric relaxation of α-tocopherol acetate (vitamin E)
K. Kaminski, S. Maslanka, J. Ziolo, M. Paluch, K. J. McGrath, and C. M. Roland
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Inferring DNA sequences from mechanical unzipping data: the large-bandwidth case
V. Baldazzi, S. Bradde, S. Cocco, E. Marinari, and R. Monasson
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Universal laws in the force-induced unraveling of biological bonds
Yuriy V. Pereverzev and Oleg V. Prezhdo
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Synchronization in coupled cells with activator-inhibitor pathways
S. Rajesh, Sudeshna Sinha, and Somdata Sinha
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Nanosecond molecular relaxations in lipid bilayers studied by high energy-resolution neutron scattering and in situ diffraction
Maikel C. Rheinstädter, Tilo Seydel, and Tim Salditt
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Generalization of coupled spiking models and effects of the width of an action potential on synchronization phenomena
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Dielectric dispersion of short single-stranded DNA in aqueous solutions with and without added salt
Yoichi Katsumoto, Shinji Omori, Daisuke Yamamoto, Akio Yasuda, and Koji Asami
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Structural network heterogeneities and network dynamics: A possible dynamical mechanism for hippocampal memory reactivation
Piotr Jablonski, Gina R. Poe, and Michal Zochowski
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Equation of state of looped DNA
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Vivek Thakur, Rajeev K. Azad, and Ram Ramaswamy
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Lateral tension increases the line tension between two domains in a lipid bilayer membrane
Sergey A. Akimov, Peter I. Kuzmin, Joshua Zimmerberg, and Fredric S. Cohen
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Amino acid hydrophobicity and accessible surface area
M. A. Moret and G. F. Zebende
Published 19 January 2007 (4 pages)
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BRIEF REPORTS

4th APS Workshop on Opportunities in Biological Physics

Sunday, March 4, 2007
Denver Convention Center
Denver, Colorado

Division of Biological Physics

Abstract: Modern Biomedicine provides a host of research and employment opportunities for physicists. New techniques for monitoring and manipulating complex biological processes at the molecular level promise to revolutionize our ability to understand and control normal and disease states. This workshop will introduce some of the most exciting recent and prospective areas of this rapidly expanding field. Topics will include tissue mechanics, tissue engineering, regenerative medicine, microfluidics and micro-optics. Speakers from academia and industry will provide extensive tutorial overviews, accessible to non-specialists. Breaks and a lunch with speakers will allow ample time for participants to discuss their current and future scientific and career directions with the speakers. The workshop is aimed at all physicists who are curious about the interface between physics and biology, especially graduate students and post-docs who are eager to apply their expertise in novel ways in the life sciences.

The workshop will start at 8:00 AM and run until approximately 7:30PM.

SPEAKERS:

• Chris Chen	Stem Cell Engineering	University of Pennsylvania
• Andrea Chow	Microfluidics	CaliperLS Corporation
• Lance Davidson	Tissue Mechanics	University of Pittsburgh
• Bogdan Dragnea	Micro-Optics	Indiana University Bloomington
• Russell Higbee	Tissue Engineering	VaxDesign Corporation
• ChihMing Ho	Bioengineering	University of California Los Angeles
• Bob Jones	Microfluidics	Fluidigm Corporation
• Darren Link	Microfluidics	Raindance Technologies, Inc.
• David Stocum	Regenerative Medicine	Indiana U. Purdue U. Indianapolis
• Jennifer West	Tissue Engineering	Rice University

Steering Committee:
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For more information, see: http://www.aps.org/units/dbp/meetings.cfm
For information on past workshops, see:
http://www.aps.org/units/dbp/links/index.cfm

Workshop Schedule

8:00AM-8:40AM Registration and Snacks

Part I— Morning Panel—Regeneration and Tissue Engineering (Rm 203/205)

8:40AM-9:20AM David Stocum—Opportunities for Physicists in Regeneration Research
9:20AM-10:00AM Lance Davidson—Challenges in Morphogenesis and Tissue Engineering
10:00AM-10:10AM Break
10:10AM-10:50AM Russell Higbee—Finding the Sweet Spot in Tissue Engineering: *In Vitro* Model Systems
10:50AM-11:30AM Jennifer West—Engineering Living Tissues
11:30AM-12:10PM Chris Chen—Multidisciplinary Approaches to Stem Cell Biology

12:20AM-2:00PM Lunch—Box Lunches—Speakers will sit at designated tables to facilitate discussion (Rm 207)

Part II—Afternoon Panel—Microfluidics and Microsensors (Rm 203/205)

2:00PM-2:40PM ChihMing Ho—Challenges of Studying Biological Flows in Microsystems
2:40PM-3:20PM Robert Jones—The Promise of Complex Microfluidic Circuitry
3:20PM-3:30PM Break
3:30PM-4:10PM Andrea Chow—Lab-on-a-Chip: Challenges in R&D and Commercialization
4:10PM-4:50PM Darren Link—The Science and Potential of Droplet Encapsulation Microfluidics
4:50PM-5:30PM Bogdan Dragnea— Physical Aspects in the Self-Assembly of Biological Complexes

5:30PM-7:30PM Networking/Reception with Snacks (Rm 207)

Abstracts

Multidisciplinary Approaches to Stem Cell Biology

Chris Chen
Stem Cell Engineering
University of Pennsylvania

Abstract: Like people, the behavior of cells is regulated by cooperative interactions between genetics and environment. And like a city, these behaviors in turn govern emergent properties of the multicellular community. My group seeks to understand the fundamental laws that govern how cells coordinate to form functional organs or devolve into pathologic tissues, and to use this knowledge to understand how to engineer tissues and organs in the laboratory. The binding interactions between cell surface receptors and local bioactive ligands serve as the principal mechanism by which cells survey their microenvironment and accordingly modulate their behaviors, such as proliferation, differentiation, migration, and suicide. I will discuss how traditional and innovative tools are being used to investigate the complex interactions between signals from extracellular matrix adhesions, growth factors, intercellular adhesions, and mechanical forces in regulating cell function. It will become evident that multi-disciplinary approaches provide our only hope to achieve practical understandings of some of the most important biomedical problems we face today – cancer, heart disease, obesity, mental health.

Christopher S. Chen, M.D., Ph.D., is the Skirkanich Associate Professor of Innovation at the University of Pennsylvania Department of Bioengineering, a faculty member of the Cell Biology and Physiology Program and Cell Growth and Cancer Program, and Director of the Tissue Microfabrication Laboratory. The goal of Dr. Chen's research is to identify the underlying mechanisms by which cells interact with materials and coordinate with each other to build tissues, and to apply this knowledge in the biology of stem cells, wound healing, tissue vascularization and cancer. In recognition of his work, Dr. Chen has received numerous honors, including the Presidential Early Career Award for Scientists and Engineers, the Angiogenesis Foundation Fellowship, the Office of Naval Research Young Investigator Award, the Mary Hulman George Award for Biomedical Research, and the Herbert W. Dickerman Award For Outstanding Contribution to Science. He serves as a member of the Faculty of 1000 Biology, the Board of Trustees for the Society for BioMEMS and Biomedical Nanotechnology, Editor for the *Journal of Biomedical Microdevices*, and *Molecular and Cellular Biomechanics*, and as a Fellow for the Defense Science Research Council, an advisory board serving the Defense Advanced Research Projects Agency. He received his A.B. in Biochemistry from Harvard, M.S. in Mechanical Engineering from M.I.T., and Ph.D. in Medical Engineering and Medical Physics from the Harvard-M.I.T. Health Sciences and Technology Program. He earned his M.D. from the Harvard Medical School. He was Assistant Professor in Biomedical Engineering and in Oncology at Johns Hopkins University prior to his current appointment.

Lab-on-a-Chip: Challenges in R&D and Commercialization

Andrea W. Chow
Vice President,
Microfluidics R&D
Caliper Life Sciences, Inc.

Abstract: Microfluidics lab-on-a-chip technology promises to fundamentally transform the way laboratory processes are performed through miniaturization, integration and automation. Microfluidics is often compared to integrated circuits, which have transformed the world by enabling increased speed in personal computing, information access, and global communication. Has the technology fulfilled its promise so far? I will provide a retrospective view on research, development, and commercialization challenges to the development of microfluidic products for applications in drug discovery, genomics, proteomics, and diagnostics. I will also discuss my views on exciting new applications and near-term development opportunities.

Dr. Andrea W. Chow is Vice President of Microfluidics R&D at Caliper Life Sciences. Since joining Caliper in 1997, she has been involved in microfluidics research, chip design, assay development, system integration, and product development for many lab-on-the-chip applications, including drug discovery, genomics and proteomics analysis, and diagnostics. Dr. Chow received her B.S. in Chemical Engineering from the University of Southern California, and her M.S. and Ph.D. degrees in Chemical Engineering from Stanford University. She is a Board Member of the Association for Laboratory Automation and an Editorial Board Member of *Biomicrofluidics*. She has also served on the Board on Chemical Sciences and Technology of the National Academy of Sciences, and on the Editorial Board of *Lab-on-a-Chip*.

Challenges in Morphogenesis and Tissue Engineering

Lance Davidson
Tissue Mechanics
University of Pittsburgh

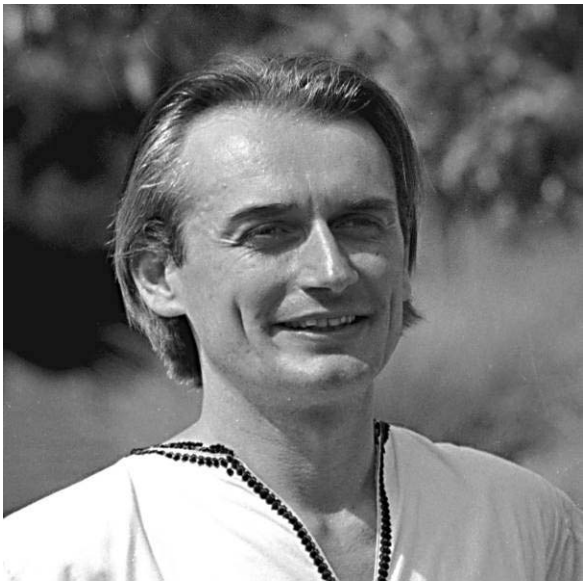
Abstract: One of the great challenges facing modern biology is understanding how the molecular information coded in the genome translates into organic form and function. At the same time, tissue engineers face a similar challenge in their attempts to construct functional tissues and organs. Both challenges abound with opportunities for collaborations between physicists and biologists, *e.g.* in imaging and image analysis, computational simulations and experimental biomechanics. Advanced imaging techniques, which allow the visualization of molecular dynamics, protein-protein interactions, novel structures and tissue movements, require sophisticated image analysis techniques. The ability to observe novel dynamic structures at the molecular level demands more complex theories that bridge multiple scales and incorporate multiple physical principles. The next phase of modern biological research on morphogenesis and tissue engineering will draw on the talents of multidisciplinary teams capable of solving these complex tasks.

Dr. Lance Davidson is Assistant Professor in the Department of Bioengineering at the University of Pittsburgh (2006); PhD in Biophysics at the University of California at Berkeley; Postdoctoral fellowship in Biology and Cell Biology at the University of Virginia in Charlottesville (1996-2004); American Cancer Society Postdoctoral Fellow (1999-2002); Research Assistant Professor in Biology at University of Virginia in Charlottesville (2005).

Dr. Davidson's research integrates cell biology of adhesion and cell motility with tissue architecture and mechanics in order to understand the role of mechanics in morphogenesis: how forces are patterned, generated, and transmitted to bring about formation of tissues in the early developing embryo. Dr. Davidson has pioneered techniques using microsurgery, high resolution time-lapse confocal microscopy, and a variety of biomechanical test apparatus to observe and measure cells and tissues during morphogenesis in the frog embryo.

Ongoing projects in the lab involve: 1) Measuring forces generated either internally by cells and tissue explants or after applied strain, 2) Observing and learning to modulate cellular responses to a heterogeneous tissue environment, and 3) Investigating the role of cell signaling, the cytoskeleton, and the extracellular matrix during morphogenesis.

Physical Aspects in the Self-Assembly of Biological Complexes



Abstract: Functional subcellular biological units are often composed of subunits that spontaneously associate to form a unique quaternary structure encoded in the sequence of the participating molecular building blocks. This association into well-defined multimolecular complexes is known as *self-assembly*. While self-assembly is ubiquitous in the organization of the microscopic living world, very few methods enabling its study in real-time are available at present. In reviewing the state of the field and identifying new opportunities for physical measurements, I will focus on one example: the physical aspects of virus self-assembly.

Bogdan Dragnea
Micro-Optics
Chemistry Department
and Physics Department
Indiana University Bloomington

Dr. Bogdan Dragnea is an Assistant Professor of Chemistry at Indiana University at Bloomington. He has a Diploma in Physics from University of Bucharest, Romania and a PhD in Physics from University of Paris XI at Orsay, France. After three years of training in chemical imaging and near-field microscopy as a postdoctoral fellow at JILA in Boulder, CO, he moved to his current faculty position in 2001. Dragnea was the recipient of the 1997 Aguirre-Basualdo Award for a PhD in Sciences, at Sorbonne, France, of a French Government Graduate scholarship (1993-1997), and of a SPIE fellowship (2001). Dragnea has 27 publications and a patent and is member of two editorial boards.

Finding the Sweet Spot in Tissue Engineering: *In Vitro* Model Systems

Russell Higbee
Tissue Engineering
VaxDesign Corporation

Abstract: We all remember the mid-1970's science-fiction television series *The Six Million Dollar Man*. The opening monologue (following the star's spectacular crash) captured the imagination: "We can rebuild him. We have the technology. … Better than he was before: better… stronger… faster." The superhuman capabilities of the fictional Steve Austin were the result of replacing normal body parts with supercharged *mechanical* substitutes. Today's mechanical hearts and kidney-dialysis machines are poor substitutes for natural organs. Medical science has not yet been able match Hollywood's vision in either cost or function. Biological systems can assemble and repair themselves. If a person cuts his finger, his body knows how to repair the cut. The goal of Tissue Engineering (*TE*) research is to replace lost body parts with new, living ones, and to cure disease as the body cures disease. As an example, we can imagine a cure for diabetes where a vascularized, cellular network, in a controlled microenvironment, provides a platform for islet cells to proliferate and regenerate in the pancreas. TE's potential to build precise, three-dimensional biological structures means that investigators can now identify and reproduce natural mechanisms for growth and repair of human tissues. Can this be a profitable industrial venture? Tissue engineering companies have brought products to market, but most have gone bankrupt. Why? *In vitro* tissue-engineered systems face substantially lower costs and hurdles, *e.g.* an *in vitro* surrogate immune model to test adjuvants, vaccines and chemicals, an *in vitro* liver to test drug toxicity, mucosal tissue models (lung, gut, skin) to examine drug delivery and pathogen interactions, and engineered disease models (cancer, tuberculosis, *etc.*) to provide clinically relevant information early in the development of disease-related immunotherapies.

Dr. Russell Higbee, D.V.M., is Professor of Biomolecular Sciences at the University of Central Florida and Senior Scientist at VaxDesign Corporation. He has over 25 years of combined teaching and research experience in the departments of Cell Biology and Anatomy (The Pennsylvania State University School of Medicine in Hershey, PA), Ophthalmology and Pediatric Neurosurgery (Northwestern University School of Medicine, Chicago, IL) and Veterinary Laser Surgery (Oklahoma State University College of Veterinary Medicine, Clinical Veterinary Sciences). He has over 80 peer reviewed publications, two patents, and three patents pending.

Challenges of Studying Biological Flows in Microsystems

ChihMing Ho

Center for Cell Control
Institute for Cell Mimetic Space Exploration (CMISE)
Henry Samueli School of Engineering and Applied Science
University of California Los Angeles

Abstract: Micro-Electro-Mechanical-Systems (*MEMS*) technology enables us to design and fabricate miniature sensors and actuators which can directly manipulate microscale objects. Many recently developed transducers further extend their range of applications to nano scales. With these micro/nano modalities, we can interrogate and manipulate cells and bio-molecules. Moving, stopping, mixing and separation of fluids and particles are the basic processes in medical diagnoses and drug development. In these applications, complex macromolecules in bio-fluid flows present many challenges, which do not exist in simple fluid flows. *E.g.*, the interactions of macromolecules with solid boundaries make micro/nano fluidics an extremely rich research field. In bio-medical applications, target collection, sample preparation and bio-marker detection involve flows ranging from macro to nano scales. The nature of the dominating force changes through the flow range. Understanding and controlling these complex interactions are significant biological physics challenges and opportunities.

Dr. Chih-Ming Ho is Ben Rich-Lockheed Martin Chair Professor in School of Engineering. He is the Director of the NIH Center for Cell Control (http://CenterForCellControl.org) and of the NASA Institute for Cell Mimetic Space Exploration (http://www.cmise.org). After receiving his Ph.D. from Johns Hopkins, Dr. Ho started his career at the University of Southern California. In 1991 he moved to the University of California, Los Angeles to establish a program in micro-electro-mechanical-system (MEMS) and to serve as the founding Director of the Center for Micro Systems. UCLA MEMS research is now recognized as one of the top three programs in the world. He served as UCLA Associate Vice Chancellor for Research from 2001 to 2005.

Dr. Ho is an internationally renowned researcher in bio-nano technology, micro/nano fluidics, and turbulence. He was ranked by ISI as one of the top 250 most cited researchers in all engineering around the world. He is a member of the National Academy of Engineering, a Fellow of the American Physical Society and the American Institute of Aeronautics and Astronautics, an Academician of Academia Sinica and holds five honorary professorships. He has published 260 papers and 10 patents. He has presented over 100 keynote talks at international conferences and has chaired and organized numerous international conferences on high technology topics. He served as the Chair of the APS Division of Fluid Dynamics in 1995. He has served on advisory panels for many countries and regions, including France, China, United Kingdom, Israel, Thailand, Taiwan, and Japan, on the development of nano/micro technologies.

The Promise of Complex Microfluidic Circuitry

Robert C. Jones
Fluidigm
Corporation

Abstract: Just as electronic integrated circuits dramatically reduced the size of electronic equipment, integrated fluidics circuits (IFCs) are uniquely suited to do the same for life science. In these devices, liquid and control channels are molded into polydimethylsiloxane (PDMS) layers using patterns of photoresist on silicon wafers. Pressure is used to control valves and drive liquids to perform desired reactions. A very wide variety of devices, including valves, pumps, mixers, reaction chambers, separation columns and detection cells, can be fabricated at very high density to work together in a single chip. These products reliably perform thousands of biological reactions in a 3cm x 3cm device. To make these devices, research and development teams have addressed challenges across the fields of molecular biology, chemistry, optics, fluidics, materials science, engineering, and software. Due to the highly interdisciplinary nature of this work, scientists with physics training are needed to drive the technology forward. As devices for single cell and single molecule analysis are developed, challenges at the interface between biology and physics offer unique opportunities for physicists to make quantitative contributions to biology.

Robert C. Jones is Executive Vice President of Research & Development at Fluidigm, leading the R&D team, including development of the BioMark product from alpha prototype to commercial sales. He has 20 years R&D and business experience from Applied Biosystems, including 10 years at the executive staff level. As Senior Vice President of Product Research and Development, he directed product development for all genomic, proteomics and informatics platforms. He brings to Fluidigm the ability to create a high performing R&D team to meet business needs across multiple product lines. Bob has demonstrated success bringing new products to new markets, for example, the real-time PCR business was created under his leadership. He contributed directly to development of the automated DNA sequencer, designing the operating software and leading the engineering team. Prior to Applied Biosystems, he developed thermal printers at Hewlett Packard as a manufacturing engineer and firmware engineer. Mr. Jones holds a BSEE and MSEE in Computer Engineering from University of Washington.

The Science and Potential of Droplet Encapsulation Microfluidics

Darren Link
Microfluidics
Raindance Technologies, Inc.

Abstract: Encapsulating chemical and biological samples in micron-sized droplets suspended in air or a hydrophobic medium on a microfluidic chip (*NanoReactor*s) allows enormous increases in throughput and precision over continuous flow microfluidics techniques. The manipulation of individual droplets in microchannels to perform basic operations such as adding reagents, combining droplets, splitting samples, interrogating reaction products and sorting of reagents or objects based on their optical characteristics, offers novel ways to control fluid flow, mixing, distribution and characterization. Because droplets are small, reagent usage is much reduced, making possible much less expensive experiments. Encapsulation makes each droplet equivalent to a well in a microtiter plate and allows sample processing at rates up to 10,000 droplets per second, enabling new approaches and new science in genomics, proteomics, diagnostics and drug discovery.

We will introduce the basic physics and engineering of this method and illustrate its applications for high-speed electric-field-based control of droplets for applications in biomaterials processing of pico-liter to nano-liter aliquots of reagents.

Dr. Darren R. Link is Vice President, Microfluidics Engineering at RainDance Technologies, Inc., holds a B.Sci. degree in Physics from Montana State University (Bozeman, MT), and a Ph.D. in Physics from the University of Colorado (Boulder, CO). Prior to RDT, he spent two years at Harvard University as a postdoctoral scientist studying soft materials physics in the department of physics and division of engineering and applied sciences. Previous to joining the group at Harvard, Dr. Link spent two years at Tokyo Institute of Technology as a postdoctoral scientist studying liquid crystalline materials. He has co-authored more than 40 peer-reviewed articles and 10 patent applications.

Opportunities for Physicists in Regeneration Research

David L. Stocum
Regenerative Medicine
Indiana U. Purdue U. Indianapolis

Abstract: I will attempt show how physicists can interface with biologists and chemists to define the mechanisms by which tissue patterning and morphogenesis take place to reproduce perfect structural and functional copies of damaged tissues, organs and appendages. Among the questions asked will be (1) Can we generate a quantitative description of regeneration that can explain what we see? (2) What physical constraints might operate to allow appendage regeneration only in small organisms? (3) How might gradients of morphogens be measured in the regenerating tissues of living animals?

Dr. David L. Stocum graduated in 1961 with a BA from Susquehanna University, where he majored in Biology and Psychology. He earned his PhD degree in Biology from the University of Pennsylvania in 1968. That year, he became Assistant Professor in the School of Life Sciences at the University of Illinois Urbana-Champaign, becoming Full Professor in 1981. He also served terms as Director of the Honors Biology Program (1974-1976) and Acting Head of Anatomical Sciences (1984-1986). In 1989, he was appointed Dean of the School of Science at Indiana University-Purdue University Indianapolis. Dr. Stocum became Dean Emeritus in 2004 and is now Professor of Biology and Director of the Center for Regenerative Biology and Medicine at IUPUI.

Dr. Stocum's research interests focus on the mechanisms of limb regeneration in salamanders. He is best known for his work on the mechanisms of tissue differentiation patterns in the limb-regeneration blastema. Major contributions have been to show that (1) the blastema is a self-organizing system that does not depend on signals from adjacent differentiated tissues for structural patterning, (2) the local interactions between blastema cells are mediated by axially-graded cell surface properties and that these properties are re-programmed by retinoic acid, and (3) the apical wound epidermis may play an important role in the proximo-distal patterning of the blastema. Dr. Stocum has written extensively on mammalian regenerative biology and medicine. His book *Regenerative Biology and Medicine* was published by Elsevier in fall 2006.

Engineering Living Tissues

Jennifer West
Tissue Engineering
Rice University

Abstract: Tissue engineering seeks to address the shortage of donor tissues for transplantation. Small diameter vascular graft applications could particularly benefit from tissue engineering. Most approaches have used small samples of cells from the patient that are expanded in culture then seeded onto a scaffold material that defines the size and shape of the new tissue and provides mechanical support for the cells as they divide and synthesize new extracellular matrix (ECM). Scaffolds include both synthetic polymers such as polylactic acid or ECM proteins such as collagen. Synthetic polymers offer better control and manipulation of material properties, ease of processing and safety. Unfortunately, cell-material interactions are based on protein adsorption and thus largely uncontrolled and somewhat variable. ECM proteins have very specific cellular interactions that can facilitate tissue formation. My laboratory develops bioactive scaffolds that can mimic ECM functions, including proteolytic degradation, biospecific cell adhesion and presentation of growth factors. Genetic modification of the cells used to form the engineered tissues provides additional improvements. For example, vascular smooth muscle cells transfected to express endothelial nitric oxide synthase improve thromboresistance while lysyl oxidase improves tissue-mechanical properties. Culturing in pulsatile flow bioreactors mimicking *in vivo* mechanical conditions further improves tissue quality.

Dr. Jennifer West is the Cameron Professor of Bioengineering and the Director of the Institute of Biosciences and Bioengineering at Rice University. Professor West was one of the founding members of the Department of Bioengineering, building it to a top ten program over the past ten years. Her research focuses on the development of novel biofunctional materials, including development of synthetic polymers that mimic many of the functions of the extracellular matrix, for use as scaffolds in tissue engineering to support and guide cell growth and migration.

In 2000, Professor West founded Nanospectra Biosciences, Inc. to commercialize nanoparticle-assisted photothermal ablation technology, now called AuroLase. Nanospectra Biosciences, Inc., located in Houston, TX, is the recipient of a NIST ATP Award. Professor West is a director of the company. She has received numerous accolades for her work. In 2006, she was named one of 20 Howard Hughes Medical Institute Professors, recognizing integration of world class research and teaching. She has been listed by MIT Technology Review as one of the 100 most innovative young scientists and engineers world-wide. Other recognitions include the Christopher Columbus Foundation Frank Annunzio Award for scientific innovation, Nanotechnology Now's Best Discovery of 2003, Small Times Magazine's Researchers of the Year in 2004, and the Society for Biomaterials Outstanding Young Investigator Award.

Downtown Denver Accommodations

American Physical Society

March 5 - 9, 2007

1. Adam's Mark
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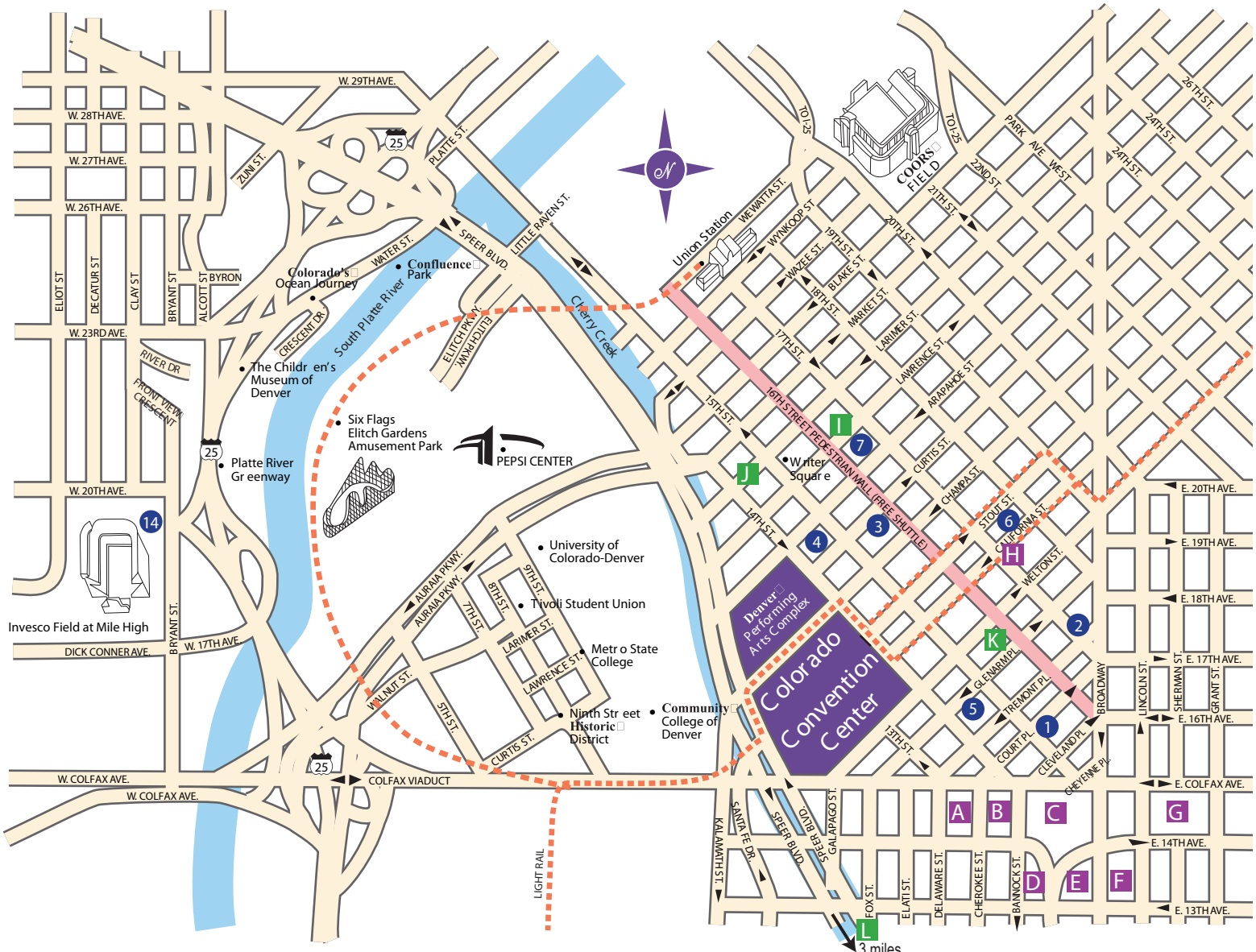
4. The Curtis
5. Holiday Inn
6. Marriott City Center
7. Westin Tabor Center



- A U.S. Mint
- B Denver City & County Building
- C Civic Center Park
- D Denver Art Museum
- E Denver Public Library
- F Colorado History Museum
- G Colorado State Capitol Building
- H DMCVB Visitor Information Center
- I Tabor Center Shopping
- J Larimer Square Shopping
- K Pavilions Shopping
- L Cherry Creek Shopping

Monday, March 5, 2007 8:00AM - 10:24AM –

Session A5 DBP: Mechanisms and Landscapes of Cellular Networks Colorado Convention Center Korbel 1A-1B

8:00AM A5.00001 JOHN TYSON, Virginia Tech — No abstract available.

8:36AM A5.00002 , LUCY SHAPIRO, Stanford — No abstract available.

9:12AM A5.00003 Some physics problems in biological networks , WILLIAM BIALEK, Princeton University — Most of the interesting things that happen in living organisms require interactions among many components, and it is convenient to think of these as a "network" of interactions. We use this language at the level of single molecules (the network of interactions among amino acids that determine protein structure), single cells (the network of protein-DNA interactions responsible for the regulation of gene expression) and complex multicellular organisms (the networks of neurons in our brain). In this talk I'll try to look at two very different kinds of theoretical physics problems that arise in thinking about such networks. The first problems are phenomenological: Given what our experimentalists friends can measure, can we generate a global view of network function and dynamics? I'll argue that maximum entropy methods can be useful here, and show how such methods have been used in very recent work on networks of neurons, enzymes, genes and (in disguise) amino acids. In this line of reasoning there are of course interesting connections to statistical mechanics, and we'll see that natural statistical mechanics questions about the underlying models actually teach us something about how the real biological system works, in ways that will be tested through new experiments. In the second half of the talk I'll ask if there are principles from which we might actually be able to predict the structure and dynamics of biological networks. I'll focus on optimization principles, in particular the optimization of information flow in transcriptional regulation. Even setting up these arguments forces us to think critically about our understanding of the signals, specificity and noise in these systems, all current topics of research. Although we don't know if we have the right principles, trying to work out the consequences of such optimization again suggests new experiments.

9:48AM A5.00004 Yeast cell cycle experiments , FREDERICK CROSS, Rockefeller — No abstract available.

Monday, March 5, 2007 8:00AM - 11:00AM –

Session A26 DCP DBP: Focus Session: Protein Folding: Theory and Simulations I Colorado Convention Center 205

8:00AM A26.00001 Exploring The Folding Energy Landscape–Triumphs and Tribulations , PETER G. WOLYNES, University of California, San Diego — The folding process has become one of the best understood transformations of condensed matter,owing to the minimal frustration principle and the collective nature of the key bottlenecks in the folding process. I will discuss the limits of models based on topology alone and also highlight the effects of residual frustration and co-factors in some puzzling examples that challenge the funnel paradigm.

8:36AM A26.00002 Simulating protein folding and aggregation on the 10 second timescale , VIJAY PANDE, Stanford University — Understanding how proteins self-assemble or "fold" is a fundamental problem in biophysics. Moreover, the ability to understand and quantitatively predict folding kinetics would have many implications, especially in the area of diseases related to protein misfolding, such as Alzheimer's Disease. However, there are many challenges to simulating folding, most notably the great computational challenges of simulating protein folding with models with sufficient accuracy to make quantitative predictions of experiments. In my talk, I will discuss our recent work to combine distributed computing with a new theoretical technique (Markov State Models) in order to simulate folding on long timescales as well as the direct and quantitative experimental tests of these methods. I will conclude with the application of these methods to the study of the Abeta peptide, whose aggregation has been directly implicated as the toxic element in Alzheimer's Disease.

9:12AM A26.00003 Understanding ensemble protein folding at atomic detail.[1] , EUGENE SHAKHNOVICH, Harvard University — Here we present a new all-atom model and development of simple potential functions (inspired by discoveries of general principles of protein folding) that allow to fold small proteins from sequence to near native structure at an atomic level of detail. Availability of numerous successful all-atom folding trajectories and their novel graph theoretical analysis, makes it possible to gain a detailed atomic level understanding of folding pathways/intermediates/transition states for engrailed homeodomain - a small alpha-helical protein that has been recently studied experimentally.

[1]In collaboration with Isaac Hubner, Eric Deeds, and Jae Shick Yang, Harvard University.

9:48AM A26.00004 Investigating the Disordered States of Two Proteins Using Intramolecular Contact Formation , VIJAY SINGH, MICHAELA KOPKA, YUJIE CHEN, WILLIAM WEDEMEYER, LISA LAPIDUS, Michigan State University — Using the quenching of the triplet state of tryptophan by cysteine, we investigate the unfolded states of two structurally similar but sequentially non-homologous proteins, the IgG binding domain of proteins L and G, under a range of denaturing conditions. These proteins show remarkably similar dynamics of intramolecular diffusion marked by a decrease in contact formation at denaturant conditions that favor folding. A reaction limited rate and the diffusion limited rate are obtained by measuring the viscosity dependence of the intramolecular contact rate. To further investigate the polymer dynamics of the unfolded state under folding conditions, we modeled the proteins as a worm-like chain with excluded volume using Szabo, Schulten and Schulten (SSS) theory to estimate the effective persistence length and intramolecular diffusion constant at various concentrations of GdnHCl. The results reveal an unfolded state under folding conditions that is significantly more compact and less diffusive than the fully denatured state.

10:00AM A26.00005 Thermodynamics of the Beta-hairpin to Coil Transition using a Distance Constraint Model[1] , OLEG VOROV, DONALD JACOBS, DENNIS LIVESAY, University of North Caroline, Charlotte — The configuration partition function is calculated exactly [1] for a distance constraint protein model that describes the beta-hairpin to coil transition. The model employs a Gaussian backbone chain of N atoms in which bonds may form to crosslink pairs of atoms in close proximity along the chain, represented by fluctuating distance constraints. Each distinct pattern of cross-linking bonds defines a constant energy over all atomic geometries that are consistent with the constraint topology. This geometrical degeneracy factor is directly calculated from configuration space integrals for each accessible constraint topology. All constraint topologies consistent with no pair of bonds that link two backbone atoms are themselves crossed are enumerated, leading to an analytical closed form expression for the configuration partition function. The phase diagram for the beta-hairpin to coil transition as a function of chain length has been studied.
[1] O.K.Vorov, D.J.Jacobs, D.R.Livesay, subm. to Phys.Rev.Lett., 2006, in preparation.

[1]NIH Grant N R01 GM073082-01A1

10:12AM A26.00006 Computational studies of the structural properties of the monomer and dimer of Aβ(1-28)[1] , XIAO DONG, WEI CHEN, NORMAND MOUSSEAU, Departement de physique and RQMP, Universite de Montreal, Montreal (QC), Cananda, PHILIPPE DERREUMAUX, Laboratoire de Biochimie Theorique, UPR 9080 CNRS, IBPC, Universite Paris 7-Denis Diderot, Paris, France — Neurodegenerative diseases are linked with the self-assembly of normally soluble proteins into amyloid fibrils. In this work, *in silico* characterization of the structures of the monomer and dimer of Aβ(1-28) are studied with the coarse-grained OPEP model using the activation-relaxation technique (ART nouveau). We find a dominant anti-parallel β-sheet structure present for both the monomer and dimer. While the monomer does not adopt a stable conformation, it fluctuates around a well-defined structure: starting from the end point, the monomer wraps a first time around, producing a β-hairpin and returns on the other side of the N-terminal, forming a three-strand β-sheet. The dimer assembles in a similar fashion, but with the two strands interlocking. The thermodynamics of the molecular assemblies and various folding path-ways are further studied using molecular dynamics.

[1]This work is supported in part by the Alzheimer Society of Canada, NSERC and the Canada Research Chair Foundation. We thank the RQCHP for a generous allocation of computer ressources.

10:24AM A26.00007 Lattice Model Investigations of Protein Aggregation , YANXIN LIU, PREM CHAPAGAIN, JOSE PARRA, BERNARD GERSTMAN, Department of Physics, Florida International University, Miami, FL 33199 — Protein aggregation is known to be important in a variety of diseases. We have expanded a well-known 3-dimensional protein folding computer lattice model with explicit side-chains in order to investigate the thermodynamics and statistical mechanics of protein aggregation between two chains. The modeling of a two-chain system presents technical and physics issues in addition to those found when modeling only a single chain. We report on preliminary results of the simulations.

10:36AM A26.00008 Effective potentials for Folding Proteins , CHUNG-YU MOU, National Tsing Hua University, Taiwan, NAN-YOW CHEN, Academic Sinica, Taiwan, ZHENG-YAO SU, National Center for High-Performance Computing, Taiwan — A coarse-grained off-lattice model that is not biased in any way to the native state is proposed to fold proteins. To predict the native structure in a reasonable time, the model has included the essential effects of water in an effective potential. Two new ingredients, the dipole-dipole interaction and the local hydrophobic interaction, are introduced and are shown to be as crucial as the hydrogen bonding. The model allows successful folding of the wild-type sequence of protein G and may have provided important hints to the study of protein folding.

10:48AM A26.00009 Forced Unfolding of the Coiled-Coils of Fibrinogen by Single-Molecule AFM , ANDRE BROWN, RUSTEM LITVINOV, DENNIS DISCHER, JOHN WEISEL, University of Pennsylvania — A blood clot needs to have the right degree of stiffness and plasticity for hemostasis, but the origin of these mechanical properties is unknown. Here we report the first measurements using single molecule atomic force microscopy (AFM) to study the forced unfolding of fibrinogen to begin addressing this problem. To generate longer reproducible curves than are possible using monomer, factor XIIIa cross-linked, single chain fibrinogen oligomers were used. When extended under force, these oligomers showed sawtooth shaped force-extension patterns characteristic of unfolding proteins with a peak-to-peak separation of approximately 26 nm, consistent with the independent unfolding of the coiled-coils. These results were then reproduced using a Monte Carlo simulation with parameters in the same range as those previously used for unfolding globular domains. In particular, we found that the refolding time was negligible on experimental time and force scales in contrast to previous work on simpler coiled-coils. We suggest that this difference may be due to fibrinogen's structurally and topologically more complex coiled-coils and that an interaction between the alpha C and central domains may be involved. These results suggest a new functional property of fibrinogen and that the coiled-coil is more than a passive structural element of this molecule.

Monday, March 5, 2007 11:15AM - 1:39PM –

Session B5 DBP: Adaptation in Biological Systems Colorado Convention Center Korbel 1A-1B

11:15AM B5.00001 Precise Adaptation in Bacterial Chemotaxis through "Assistance Neighborhoods"[1] , ROBERT ENDRES, Princeton University — The chemotaxis network in *Escherichia coli* is remarkable for its sensitivity to small relative changes in the concentrations of multiple chemical signals over a broad range of ambient concentrations. Key to this sensitivity is an adaptation system that relies on methylation and demethylation (or deamidation) of specific modification sites of the chemoreceptors by the enzymes CheR and CheB, respectively. It was recently discovered that these enzymes can access five to seven receptors when tethered to a particular receptor. We show that these "assistance neighborhoods" (ANs) are necessary for precise and robust adaptation in a model for signaling by clusters of chemoreceptors: (1) ANs suppress fluctuations of the receptor methylation level; (2) ANs lead to robustness with respect to biochemical parameters. We predict two limits of precise adaptation at large attractant concentrations: either receptors reach full methylation and turn off, or receptors become saturated and cease to respond to attractant but retain their adapted activity.

[1]Funding from HFSP

11:51AM B5.00002 Adaptation in neural processing , ADRIENNE FAIRHALL, University of Washington — No abstract available.

12:27PM B5.00003 Adaptation by Plasticity of Genetic Regulatory Networks , NAAMA BRENNER, Technion - Israel Institute of Technology — Genetic regulatory networks have an essential role in adaptation and evolution of cell populations. This role is strongly related to their dynamic properties over intermediate-to-long time scales. We have used the budding yeast as a model Eukaryote to study the long-term dynamics of the genetic regulatory system and its significance in evolution. A continuous cell growth technique (chemostat) allows us to monitor these systems over long times under controlled condition, enabling a quantitative characterization of dynamics: steady states and their stability, transients and relaxation. First, we have demonstrated adaptive dynamics in the *GAL* system, a classic model for a Eukaryotic genetic switch, induced and repressed by different carbon sources in the environment. We found that both induction and repression are only transient responses; over several generations, the system converges to a single robust steady state, independent of external conditions. Second, we explored the functional significance of such plasticity of the genetic regulatory network in evolution. We used genetic engineering to mimic the natural process of gene recruitment, placing the gene *HIS3* under the regulation of the *GAL* system. Such genetic rewiring events are important in the evolution of gene regulation, but little is known about the physiological processes supporting them and the dynamics of their assimilation in a cell population. We have shown that cells carrying the rewired genome adapted to a demanding change of environment and stabilized a population, maintaining the adaptive state for hundreds of generations. Using genome-wide expression arrays we showed that underlying the observed adaptation is a global transcriptional programming that allowed tuning expression of the recruited gene to demands. Our results suggest that non-specific properties reflecting the natural plasticity of the regulatory network support adaptation of cells to novel challenges and enhance their evolvability.

1:03PM B5.00004 How Large Asexual Populations Adapt , MICHAEL DESAI, Princeton University — We often think of beneficial mutations as being rare, and of adaptation as a sequence of selected substitutions: a beneficial mutation occurs, spreads through a population in a selective sweep, then later another beneficial mutation occurs, and so on. This simple picture is the basis for much of our intuition about adaptive evolution, and underlies a number of practical techniques for analyzing sequence data. Yet many large and mostly asexual populations – including a wide variety of unicellular organisms and viruses – live in a very different world. In these populations, beneficial mutations are common, and frequently interfere or cooperate with one another as they all attempt to sweep simultaneously. This radically changes the way these populations adapt: rather than an orderly sequence of selective sweeps, evolution is a constant swarm of competing and interfering mutations. I will describe some aspects of these dynamics, including why large asexual populations cannot evolve very quickly and the character of the diversity they maintain. I will explain how this changes our expectations of sequence data, how sex can help a population adapt, and the potential role of "mutator" phenotypes with abnormally high mutation rates. Finally, I will discuss comparisons of these predictions with evolution experiments in laboratory yeast populations.

Monday, March 5, 2007 11:15AM - 2:15PM –

Session B26 DCP DBP: Focus Session: Protein Folding: Theory and Simulations II Colorado Convention Center 205

11:15AM B26.00001 , DEVARAJAN THIRUMALAI, University of Maryland — No abstract available.

11:51AM B26.00002 Protein folding and dynamics from simulations of coarse protein models.[1] , GERHARD HUMMER, Laboratory of Chemical Physics, NIDDK, National Institutes of Health — The dynamics and folding transitions of proteins are studied by computer simulations of coarse-grained models. The simulations are related to experimental studies of the unfolding of proteins under mechanical force, and the effects of mutations on the folding rates using phi-value analysis. Coarse protein models have also been useful in studies of slow conformational transitions. Applications to the helix-to-sheet transition of an arc repressor mutant, and the open-to-closed transition of the calmodulin C-terminal domain indicate that local unfolding events can contribute significantly to the slow dynamics of these proteins.

[1]co-authors: Robert B. Best and Yng-Gwei Chen.

12:27PM B26.00003 , HENRI ORLAND, Service de Physique Theorique — No abstract available.

1:03PM B26.00004 The folding of an "average" beta trefoil protein. , SHACHI GOSAVI, PAT JENNINGS, JOSE ONUCHIC, UCSD — The beta-trefoil fold is characterized by twelve beta strands folded into three similar beta-beta-beta-loop-beta (trefoil) units. The overall fold has pseudo-threefold symmetry and consists of a six stranded-barrel, capped by a triangular hairpin triplet. The loops connecting the beta-strands vary in length and structure. It is these loops that give the fold its varied binding capability and the binding sites lie in different parts of the fold. The beta-trefoil proteins have little sequence similarity (sometimes less than 17%) and bind a range of molecules, including other proteins, DNA, membranes and carbohydrates. Protein folding experiments have been performed on four of the beta trefoils, namely, interleukin-1 (IL1B), acidic and basic fibroblast growth factors (FGF-1 and FGF-2) and hisactophilin (HIS). These experiments indicate that the proteins fold by different routes. Folding simulations of the proteins identify the possible folding routes and also show that the shapes of the barriers are different for the different proteins. In this work, we design a model protein which contains only the core fold elements of the beta-trefoil fold. We compare the folding of this "average" protein to the folding of His, FGF and IL1B and make some connections with function.

1:15PM B26.00005 Life in a Crowd: Macromolecular Crowding and Confinement Effects on Protein Interactions in Living Systems , MARGARET CHEUNG, Department of Physics, University of Houston — Biological polymers carry out their functions in living systems where the environment is very concentrated or crowded by macromolecules. Physically, the composition of a cell is more than "a sack of water"; its consistency is closer to Jell-O. Experiments suggests that, because of this macromolecular crowding effect that confines polymeric dynamics, the kinetics and thermodynamics of protein folding and the association rate constants of protein-protein interactions in a cell (in vivo) are very different from that ina diluted test tube (in vitro). In order to quantitatively understand macromolecular crowding and confinement effects on protein dynamics, we used coarse-grained models that physically captured interactions between crowders and a protein. The folding rates of a model protein nonmonotonically increased with the volume fraction of the crowders. At lower volume fractions, depletion-induced attractions from crowders could be mapped according to the spherical confinement model. A result of spherical confinement was the destabilization of denatured states by disallowing extended configurations that were longer than the pore size. However, at higher volume fractions, conformational fluctuations of a protein were susceptible to the shape of the confining condition. Thus, an approximation of the spherical confinement to mimic crowding effects was no longer effective.

1:27PM B26.00006 2D IR Spectroscopy of Ubiquitin Unfolding Dynamics , ZIAD GANIM, HOI SUNG CHUNG, ANDREI TOKMAKOFF, Department of Chemistry, Massachusetts Institute of Technology — The unfolding dynamics of ubiquitin have been studied using a combination of amide I 2D IR spectroscopy and spectral calculations drawing on structures from molecular dynamics simulations. Equilibrium temperature-dependent 2D IR spectra and transient 2D IR spectra following a nanosecond temperature jump are used to follow the unfolding of ubiquitin's β-sheet. The equilibrium 2D IR spectra show two features that arise from delocalized β-sheet vibrations of which differ by whether C=O oscillators vibrate parallel or perpendicular to its strands. Spectral changes in the transient difference spectrum start with an abrupt blue shift of the perpendicular diagonal region, which corresponds to the disruption of hydrogen bonds between water and solvent-exposed peptide groups. This change is followed over μs to ms time scales by a blue shift of the perpendicular region and disappearance of a cross peak, which reflect the gradual unfolding of the β-sheet of the protein. The experiments are compared with 2D IR spectra calculated from molecular dynamics trajectories of ubiquitin unfolding using a structure-based model for protein amide I spectroscopy.

1:39PM B26.00007 Generalization of distance to higher dimensional objects, and applications to biopolymer folding[1] , STEVEN PLOTKIN, Department of Physics, University of British Columbia, Vancouver — The measurement of distance between two objects is generalized to the case where the objects are no longer points but are one-dimensional (strings) or many-dimensional (differential manifolds). Applications to biopolymer folding will be discussed.

[1]Support from the NSERC and the A.P. Sloan Foundation is gratefully acknowledged

1:51PM B26.00008 Collapse transition for self-avoiding random walks with hydrophobic interaction on a 2 dimensional lattice , MATHIEU GAUDREAULT, JORGE VINALS, Department of Physics, McGill University, Canada — We study the collapse transition of a protein model with an explicit coarse-grained model of solvent hydrophobicity using Monte Carlo simulation. The protein is modelled as self- avoiding random walk with nearest neighbour interaction on a two dimensional lattice by using the pivot algorithm. Without the solvent, universal quantities of the chain around the transition temperature are well known. Hydrophobicity is modelled through a lattice of solvent molecules in which each molecule can have q states, depending of an orientation variable. Only one state is energetically favoured, when two neighbouring solvent molecules are both in the same state of orientation. The monomers are placed in interstitial position of the solvent lattice, and are only allowed to occupy sites surrounded by solvent cells of the same orientation. The potential of mean force between two interstitial solute molecules is calculated, showing that the strength of attraction increases by increasing the free energy of H-bond formation while its range decreases. We also show that the temperature of the collapse transition is shifted in the presence of solvent, while the universal quantities of the protein transition are conserved.

2:03PM B26.00009 Monte Carlo simulations on a Rubik's cube model , CHI-LUN LEE, National Central University — We perform Monte Carlo simulations on a Rubik's cube model. In particular we derive thermodynamic and kinetic information of the Rubik cube with assigned energy functions. Through simulation studies one can gain information on its energy landscape. The similarity between the current model and several well-known protein-folding simulation models will be discussed.

Monday, March 5, 2007 11:15AM - 2:15PM –

Session B38 GIMS DBP: Focus Session: Bioinstrumentation and Biophotonic Technologies

Colorado Convention Center 501

11:15AM B38.00001 Fourier-Domain Biophotoacoustic Sub-surface Depth Selective Amplitude and Phase Imaging of Turbid Phantoms and Biological Tissue[1] , SERGEY TELENKOV, Imaging Diagnostic Systems, Inc. — A novel photothermoacoustic imaging modality utilizing a frequency-swept (chirped) intensity-modulated laser source and coherent frequency domain signal processing ("biophotoacoustics") was introduced for non-invasive imaging of biological tissues. The developed frequency-domain imaging system takes advantage of linear frequency modulation waveforms to relate depth of tissue chromophores to the frequency spectrum of the detected acoustic response and of a narrow signal detection bandwidth to improve signal-to-noise ratio (SNR). Application of frequency-domain photothermoacoustic (FD-PTA) imaging was demonstrated using turbid phantoms and ex-vivo specimens of chicken breast with embedded absorbing inclusions simulating tumors.

[1]This work was done in collaboration with Andreas Mandelis.

11:51AM B38.00002 An application of fast response Polarized Light Microscopy , DEEPENDRA KANTHA, DAVID VAN WINKLE, Department of Physics, Florida State University and MARTECH — A fast response polarized light microscope was designed based on the algorithm by Shribak et. al (Applied Optics, vol. 42, 3009-3017). A pulsed laser beam was passed through two Pockels cells aligned at different angles with respect to optical axis. The retardance of the Pockels cell was controlled by external switches and power supplies. The electronics circuit in the system allows change of the retardance of the Pockels cell each millisecond for four milliseconds. In four milliseconds, four images of a birefringent sample, formed by different states of polarized light are recorded. The images are added appropriately to calculate retardence amplitude and phase by using codes written in imageJ software. The microscope was used to show the retardance and phase of a rabbit muscle fiber. Recordings were also taken of the contraction of Vorticella convallaria but the changes were too fast to yield retardance images. This type of microscope can be used to study different kinds of biological functions that change on a timescale slower than four milliseconds but faster than two seconds.

12:03PM B38.00003 Evaluation of optical excitation conditions for ruthenium complex for biosensor optodes , SEAN PIEPER, Elec. and Comp. Engr. Dept. CSU, ZHONG ZHONG, Chemical Engineering Dept. CSU, KEVIN L. LEAR, Elec. and Comp. Engr. Dept. CSU, KEN REARDON, Chemical Engineering Dept. CSU — Development of a fiber optic biosensor incorporating genetically engineered enzymes which catalyze chlorinated ethenes in an oxygen-consuming reaction for in situ monitoring of groundwater contaminants motivates optimization of optode excitation conditions. These conditions affect the sensitivity, signal-to-noise, and optode service life impacting the quality of the overall biosensor. Optodes are generally comprised of a fluorophore conjugated with a polymer as a substrate cross linked at the distal end of a fiber optic. We investigate the excitation conditions of tris(4,7-diphenyl-1,10-phenanthroline) ruthenium(II) chloride (Ru(dpp)3) conjugated with poly(vinyl alcohol) (PVOH) as an optode. A reported advantage of Ru(dpp)3 is that it has no emission spectral shift occurring under varying chemical and environmental conditions. Photostability degradation due to photobleaching of Ru(dpp)3 with PVOH as a substrate is explored by varying the optical irradiance of the fluorophore containing optode. Other issues relating to practical implementation of Ru(dpp)3 as oxygen sensitive biosensors will be discussed.

12:15PM B38.00004 Two-Photon Microscope with Spectral Resolution , RUSSELL FUNG, MIKE MELNICHUK, ANURAG CHATURVEDI, DEVIN GILLMAN, VALERICA RAICU, Department of Physics and Department of Biological Sciences, University of Wisconsin, Milwaukee — Two-photon microscopy has many distinct advantages over other types of microscopy: it is faster, there is no out-of-plane photobleaching, and using near-infrared laser light (to produce visible fluorescence signal) allows deeper penetration into thick samples. We have built a two-photon microscope based on a novel design that uses a diffractive optic, a nondescanned detection scheme and an EM-CCD camera to produce spectrally resolved fluorescence images of samples after only one full scan of the sample and with relatively high speed. Our design is readily extended to incorporate control in the excitation channel through pulse shaping using spatial filtering in the frequency domain. This microscope, in conjunction with Fluorescence Resonance Energy Transfer (FRET) between fluorescent tags, has been used to detect interactions between proteins in various systems including yeast (Saccharomyces cerevisiae) cells. Also, its exquisite sensitivity makes it suitable to spectrally resolve signals from single quantum dots and single molecules.

12:27PM B38.00005 Exploration of detection sensitivity of biomarker acetone in aqueous samples using cavity ringdown spectroscopy , ARMSTRONG MBI, CHUJI WANG[1], Department of Physics and Astronomy, Mississippi State University — Breath acetone is a biomarker for diabetes (Type 1). Currently, high sensitivity breath gas analysis is mainly performed by gas chromatography-mass spectrometry (GC-MC). We are developing a potable ringdown spectrometer for diabetes diagnostics using non-invasive breath gas analysis. The ringdown spectrometer consists of a compact Nd: YAG laser source operating at 266 nm, a atmospheric gas cell of 43 cm in length, a miniature detector, and a data processing section. In this work, the exploration of detection sensitivity of acetone in aqueous samples using cavity ringdown spectroscopy is presented. Pure acetone is diluted in distilled water in different concentrations ranging from 0.5 drop/liter to 8 drops/liter, or 730 ppbv - 12 ppmv in gas phase. The instrument performance using two sampling methods is evaluated. With the mirror reflectivity of 99.98%, the spectrometer demonstrates a detection limit of acetone of 450 ppbv (based on 1-σ), which is slightly lower than the threshold number of acetone concentration in normal human breath. Preliminary results from actual breath gases are also presented.

[1](Author to whom correspondence should be made)

12:39PM B38.00006 Optofluidic intracavity spectroscopy of single cells in a passive Fabry-Perot resonator , HUA SHAO, WEINA WANG, Electrical and Computer Engineering Department, Colorado State University, SUSAN LANA, Animal Cancer Center, Colorado State University, KEVIN LEAR, Electrical and Computer Engineering Department, Colorado State University — Considerable effort has been devoted to analyzing complex biological systems such as living cells by combining photonic and microfluidic techniques. Cells in biocavity lasers developed by Gourley et al produced rich multimode spectra that multivariate analysis correlated with the cell type. Optofluidic intracavity spectroscopy (OFIS) reported here operates on a similar principles but does not require gain media. It measures transmission spectra of individual cells in a passive Fabry-Perot (FP) cavity. Non-normal incidence identified the relative order of the various transverse modes to verify the applicability of different simplified models of the cavity modes. Distinctive spectral features, including transverse mode spacing and the number of modes were used to differentiate red and white human blood cells, for example. OFIS measurements of canine lymphoma cells produced repeatable transmission spectra. Continuing investigations on the capability of OFIS to distinguish cancer cells will be reported.

12:51PM B38.00007 Magnetically Directed Cell Co-Localization , EDWARD FELTON, DANIEL REICH, Johns Hopkins University, YOOJIN AN, CHRISTOPHER CHEN, University of Pennsylvania — The ability to control the movement and location of biological cells has led to novel approaches to several areas of interest, from tissue engineering to the study of cell-cell interactions. We have introduced ferromagnetic nanowires as a tool for applying forces to cells; their high remanent magnetization allows cells bound to nanowires to be manipulated in low-strength magnetic fields. Micropatterned magnetic structures generate magnetic fields that can precisely guide cells into predetermined positions on substrates in culture, and cells can be restricted to localized areas through chemical functionalization of the substrate. We have used these directed cell assembly techniques to organize cells into a variety of patterns with a single cell type, and have extended its utility to include two cell types. We have created regular arrays of cells in which heterotypic cells pairs are magnetically trapped at each array site. This method of producing large numbers of isolated heterotypic cell pairs is potentially useful in studies of cell-cell interactions between different cell types.

1:03PM B38.00008 Detection of cancer protein using Spectroscopic Ellipsometry as Surface Plasmon Resonance Mode , YUNBOG KIM, DONGRYUL JEON, Seoul National University, Department of Physics Education and Nano Systems Institute, Seoul 151-748, Korea, MIN-AH WOO, MYUNGHAING CHO, Seoul National University, College of Veterinary Medicine and Nano Systems Institute, Seoul 151-748, Korea — Since the first application of surface plasmon resonance (SPR) for biosensing almost two decades ago, SPR has made great strides in terms of both the instrumentation and the application. We used spectroscopic ellipsometry as an SPR sensor to detect the reaction of HER2 protein of SKBR3 cancer cells with its antibody. Since the Psi value of ellipsometry is related to the reflectivity of P wave, the surface plasmon signal can be measured using spectroscopic ellipsometry. A glass plate coated with 50 nm-thick gold film was dipped in HER2 antibody solution for 1 hour. The substrate was then dipped in a soup containing broken SKBR3 cells to induce HER2 antibody-antigen reaction. The pure gold film exhibited a SPR peak at 2.04 eV. After the adsorption of HER2 antibody, the peak shifted to 1.99eV. After dipping in the soup of SKBR3 cells, the peak shifted to 1.96 eV. We believe this shift is due to the change in surface plasmon caused by binding of HER2 protein and antibody. The AFM images of the samples supported our conclusion. Our result adds an example to the possibility of using spectroscopic ellipsometry as an SPR mode for detecting cancer cells.

1:15PM B38.00009 Holography with Low Energy Electrons[1] , TATIANA LATYCHEVSKAIA, GREGORY STEVENS, ANDREAS PLUECKTHUN, HANS-WERNER FINK, Physics Institute, University of Zurich — Coherent low energy electrons of 60-200 eV kinetic energy and sub-nanometer wavelength provide a tool to record holograms of individual bio-molecules, such as DNA or viruses. From the recorded holograms, the three-dimensional shape of the molecules can numerically be reconstructed. The experimental setup as well as the numerical reconstruction of low energy electron holograms from individual bio-molecules shall be discussed. Since most biological objects are transparent for electrons they introduce only a phase shift to the incident electron wave. We present a method to not only retrieve the absorbing (as most known methods do) but also the phase properties of the object wave. Finally, we present a general solution of the long-standing twin image problem in holography. It is applicable to any type of holography independent of the wavelength used and the nature of the wave, be it light, electrons, x-rays or any other coherent radiation.

[1]The work is part of the Project SIBMAR within the frame of the "New and Emerging Science and Technology" European Programme.

1:27PM B38.00010 In-line Phase Contrast Imaging of Soft Tissue in the Mammalian Cochlea , LIXIN FAN, Northwestern University Feinberg School of Medicine, 200 E. Superior St., Chicago, IL, 60611, C. RAU, Advanced Photon Source, Argonne National Lab, 9700 S. Cass Ave. , Argonne, IL 60439, I. ROBINSON, Frederick Seitz Materials Research Laboratory, University of Illinois at Urbana-Champaign, 104 S. Goodwin Ave., Urbana, IL61801, C.-P. RICHTER, Northwestern University Feinberg School of Medicine, 200 E. Superior St., Chicago, IL, 60611 — Soft tissue has been visualized in a mammalian cochlea with hard X-rays in-line phase contrast imaging at the UNICAT beamline 34 ID-C, APS. The sensation of hearing results from a series of complex events that transform acoustic pressure waves into the perception of sound. During the normal hearing process, sound energy is converted to mechanical energy by the middle ear, which then is converted to motions in the structures of the cochlea. To date, many aspects of the sound induced vibrations are still unclear. Firstly, mechanics of the cochlea are likely to changes by the manipulations, and secondly, cochlear micromechanics are unexplored for the cochlear middle section. Therefore, our objective is to measure the motion patterns of cochlear tissues in a closed cochlea. Thick mammalian cochlear slices have been imaged and were compared with those obtained by light microscopy. Furthermore, intact cochleae have been imaged to identify the soft tissue structures involved in the hearing process.

1:39PM B38.00011 Dental Photothermal Radiometry: Theoretical Analysis. , ANNA MATVIENKO, RAYMOND JEON, ANDREAS MANDELIS, Center for Advanced Diffusion Wave Technologies, University of Toronto, Canada, STEPHEN ABRAMS, Four Cell Consulting, Toronto, Canada — Dental enamel demineralization in its early stages is very difficult to detect with conventional x-rays or visual examination. High-resolution techniques, such as scanning electron microscopy, usually require destruction of the tooth. Photothermal Radiomety (PTR) was recently applied as a safe, non-destructive, and highly sensitive tool for the detection of early dental demineralization, artificially created on the enamel surface. The experiments showed very high sensitivity of the measured signal to incipient changes in the surface structure, emphasizing the clinical capabilities of the method. In order to analyze the biothermophotonic phenomena in a tooth sample during the photothermal excitation, a theoretical model featuring coupled diffuse-photon-density-wave and thermal-wave fields was developed. Numerical simulations identified the effects on the PTR signal of changes in optical and thermal properties of enamel and dentin as a result of demineralization. The model predictions and experimental results will be compared and discussed.

1:51PM B38.00012 ABSTRACT HAS BEEN MOVED TO J21.00010 –

2:03PM B38.00013 ABSTRACT HAS BEEN MOVED TO J21.00009 –

Monday, March 5, 2007 2:30PM - 5:30PM –

Session D26 DCP DBP: Focus Session: Protein Folding: Theory and Simulations III Colorado Convention Center 205

2:30PM D26.00001 Mechanisms of Protein Assembly and Folding: Lessons from Minimalist Models[1] , JOSE ONUCHIC, CTBP - UCSD — Globally the energy landscape of a folding protein resembles a partially rough funnel. The local roughness of the funnel reflects transient trapping of the protein configurations in local free energy minima. The overall funnel shape of the landscape, superimposed on this roughness, arises because the interactions present in the native structure of natural proteins conflict with each other much less than expected if there were no constraints of evolutionary design to achieve reliable and relatively fast folding (minimal energetic frustration). A consequence of minimizing energetic frustration is that the topology of the native fold also plays a major role in the folding mechanism. Topological effects go beyond the structure of the TSE. The overall structure of the on-route and off-route (traps) intermediates for the folding of more complex proteins is also strongly influenced by topology. Going beyond folding, the power of reduced models to study the physics of protein assembly will be discussed. Since energetic frustration is sufficiently small, native topology-based models have shown that binding mechanisms are robust and governed primarily by the protein's native topology. These models impressively capture many of the binding characteristics found in experiments and highlight the fundamental role of flexibility in binding.

[1]Supported by the NSF

3:06PM D26.00002 Direct application of a simple model to the quantitative analysis of experiments on an ultrafast folding protein , ERIC HENRY, National Institutes of Health — A simple Ising-like statistical-mechanical model for protein folding (Henry and Eaton, *Chem. Phys.* **307**, 163-185, 2004) is used to analyze a broad set of experimental data on the ultrafast folding villin subdomain. In this model each residue in the protein sequence can adopt one of two possible microscopic states corresponding to native and non-native conformations; model protein states are identified with distinct sequences of native/non-native residues. The folding properties of the protein are determined entirely by the map of inter-residue contacts in the native structure. To compute partition functions by complete enumeration of all protein states, only those states are included that contain at most two contiguous sequences of native residues. Native contacts are only permitted between residues lying in such contiguous sequences. The stability of any state of the chain is determined by the offsetting effects of the stabilizing native contacts and the destabilizing entropy losses associated with fixing residues in the native conformation and with closing loops of nonnative residues created by contacts between distinct native sequences. In a least-squares fitting analysis, the temperature-dependent populations predicted by the model for all the protein states, combined with a simple description of the spectroscopic properties of individual states, are used to model the results of spectroscopic and thermodynamic experiments. The model reproduces the temperature dependence of the excess heat capacity, tryptophan fluorescence quantum yield, circular dichroism, and relaxation rates and amplitudes, as well as the effects of site-directed mutants on the folding rates and equilibrium constants.

3:42PM D26.00003 Desolvation effects and topology-dependent protein folding , ALLISON FERGUSON, ZHIRONG LIU, HUE SUN CHAN, Dept. of Biochemistry, Faculty of Medicine, University of Toronto — As a protein folds, water molecules must be excluded from the hydrophobic core, and thus desolvation barriers between the protein's constituents must be crossed in order to reach the final folded state. Previous research on continuum G$\bar{o}$-like protein models has demonstrated that pairwise-additive desolvation potentials lead to more thermodynamically and kinetically cooperative folding/unfolding transitions (Z. Liu and H. S. Chan, Phys. Biol. **2**, S75-S85, *2005*). The present work focuses on the role of this elementary desolvation potential in improving predictions of the well-known topology-folding rate relationship (K. W. Plaxco *et al*, J. Mol. Biol. **277**, 985-994, *1998*) of small single-domain proteins. Recent computational studies without desolvation barriers have shown (S. Wallin and H. S. Chan, J. Phys.: Condens. Matt. **18**, S307-S328, *2006*) that the observed correlation between topological parameters and folding rates is because these parameters may be proxies for rate-determining properties of the transition state, such as the activation free energy $\Delta G^{\ddagger}$ and activation conformational entropy $\Delta S^{\ddagger}$. Including the desolvation barrier in the model results in stronger correlations between measures of topology and simulated folding rates / transition state properties, reinforcing the theory that even simple representations of the desolvation effect are important for understanding crucial features of protein folding.

3:54PM D26.00004 Networks in Protein Folding , ERZSÉBET RAVASZ REGAN, Beth Israel Deaconess Medical Center, Harvard Medical School, ZOLTÁN TOROCZKAI, University of Notre Dame, Physics Department, G. GNANAKARAN, Los Alamos National Laboratory, T-10 — We take a networks approach to protein folding by identifying different protein conformations with nodes, while an elementary step of the system (rotation around a bond) that takes one configuration to another is defined as a link. The energies of configurations are scalar quantities associated with each node. Using this approach we can show that the scale-free nature of the observed protein conformation networks can be explained by simple results obtained on gradient networks.

4:06PM D26.00005 Intramolecular Vibrational Preparation of the Unfolding Transition State of Zn^{II}-substituted Cytochrome *c*: Picosecond Time-Resolved Fluorescence and Dynamic Stokes Shift Studies[1] , WARREN F. BECK, SANELA LAMPA-PASTIRK, Department of Chemistry, Michigan State University — We show that an intramolecular vibrational excitation provided by the radiationless decay of a covalently bound electronic chromophore can be exploited to drive a protein from its native folded state to the transition state for unfolding. Using this approach, we examine the effect of the polarity and viscosity of the solvent medium on the unfolding and refolding reactions of Zn^{II}-substituted cytochrome *c* at room temperature. The dynamic Stokes shift of the S_1-state Zn^{II}–porphyrin is monitored using picosecond time-resolved fluorescence spectroscopy as a probe of the protein and solvent dynamics that are associated with the crossing of the unfolding transition state and with the subsequent unfolding and refolding trajectories. The results show that the solvent polarity controls the activation energy for the unfolding and refolding reactions; the solvent viscosity further controls the rate by frictionally hindering the moving polypeptide. These findings suggest an important role for the solvent in the kinetic control of protein-folding trajectories on the energy landscape.

[1]Supported by grants MCB-0091210 and MCB-0520002 from the NSF Molecular Biophysics program

4:18PM D26.00006 Single Mutation Effect on Lysozyme Stability and Misfolding , RUHONG ZHOU, IBM Thomas J. Watson Research Center — We propose a mechanism, based on an unprecedended 10+ microsecond molecular dynamics simulation, for the surprising misfolding of hen lysozyme caused by a single mutation (W62G). Our simulations of the wild-type and the mutant lysozyme in 8M urea solution at biological temperature (with both pH = 2 and pH = 7) reveal that the mutant structure is much less stable than the wild-type, with the mutant showing larger fluctuations and less native-like contacts. Analysis of local contacts reveals that the Trp62 residue is the key to a cooperative long-range interaction within the wild-type where it acts like a bridge between two neighboring basic residues. A native-like cluster or nucleation site can thus form near these residues in the wild-type, but not in the mutant. These findings, while supporting the general conclusions of a recent experimental study by Dobson and coworkers, provide a detailed but different molecular picture of the misfolding mechanism.

4:30PM D26.00007 On the Mechanism of Protein Unfolding by Pressure A Molecular Dynamics Simulation Study , J. RAUL GRIGERA[1], ANDRES MCCARTHY , CARLOS FERRARA, IFLYSIB — Proteins are denaturized at high pressure and the mechanism of such a denaturation is still on debate. We have studied lyzozyme and apomyoglobin, under pressure up to 0.3GPa using molecular dynamics simulation. Lysozyme shows more stability, although it cannot retain the native structure. On the other hand apomyoglobin shows a continuing unfolding process during the 180 ns simulation time. The analysis of the hydrophilic and hydrophobic proteins Solvent Accessed Surface clearly shows the increment of the hydrophobic exposed area in the formation of crevices and in the appearing of hydrophobic 'spikes' around the overall surface. The observation of the final state, within the simulation time, shows a clear effect on the conformational state of the proteins. Comparing the behavior of the proteins with de aggregation state of simple non-polar solutes at different pressures we have been able to conclude that the driving force of the denaturation is the change in the hydrophobic contribution to the native folding due to the changes of water structure under pressure, which have been shown both experimental and by computer simulation.

[1]CONICET-UNLP-CIC

4:42PM D26.00008 Free Energy Landscape - Settlements of Key Residues. , SVETLANA AROUTIOUNIAN, Dillard University — FEL perspective in studies of protein folding transitions reflects notion that since there are $\sim 10^N$ conformations to scan in search of lowest free energy state, random search is beyond biological timescale. Protein folding must follow certain fel pathways and folding kinetics of evolutionary selected proteins dominates kinetic traps. Good model for functional robustness of natural proteins - coarse-grained model protein is not very accurate but affords bringing simulations closer to biological realm; Go-like potential secures the fel funnel shape; biochemical contacts signify the funnel bottleneck. Boltzmann-weighted ensemble of protein conformations and histogram method are used to obtain from MC sampling of protein conformational space the approximate probability distribution. The fel is F(*rmsd*) = -1/β•Ln[Hist(*rmsd*)], β=k_BT and *rmsd* is root-mean-square-deviation from native conformation. The sperm whale myoglobin has rich dynamic behavior, is small and large - on computational scale, has a symmetry in architecture and unusual sextet of residue pairs. Main idea: there is a mathematical relation between protein fel and a key residues set providing stability to folding transition. Is the set evolutionary conserved also for functional reasons? Hypothesis: primary sequence determines the key residues positions conserved as stabilizers and the fel is the battlefield for the folding stability. Preliminary results: primary sequence - not the architecture, is the rule settler, indeed.

4:54PM D26.00009 Interplay between secondary and tertiary structure formation in a lattice model alpha helical hairpin peptide , PREM CHAPAGAIN, Department of Physicss, Florida International University, BERNARD GERSTMAN, Department of Physics, Florida International University, THEORETICAL BIOPHYSICS GROUP TEAM — We present results from Monte Carlo simulations of folding dynamics of a model alpha helical hairpin peptide. The dynamics shows that the peptide chain folds in a two step fashion that involves the formation of partial helical segments followed by the formation of a stable tertiary structure by joining these semi-stable helical segments. The interplay between the formation of secondary and tertiary structures during the folding process was investigated by calculating the heat capacity and other thermodynamic quantities at various simulation temperatures. In addition to a sharp peak in the heat capacity curve for the transition between unfolded state and folded native state, the helix-random coil transition in the unfolded state is also cooperative.

5:06PM D26.00010 Impact of solvent pH on buried charge formation and protein quake of photoactive yellow protein , AIHUA XIE, SANDIP KALEDHONKAR, LORAND KELEMEN, WOUTER D. HOFF, ANUPAMA THUBAGERE, Oklahoma State University — Embedding a charge group inside a protein in a low dielectric environment is energetically unfavorable. Therefore, most charged groups are solvent exposed. We have developed a hypothesis that a new buried charge transiently formed in a non-polar environment serves as an electrostatic epicenter that drives protein quake (protein conformational changes). Here we report an experimental study on the effects of solvent pH on the protonation states of buried ionizable groups, and their correlation with protein quakes. Time-resolved Fourier transfer infrared (FTIR) difference absorbance spectroscopy is the major experimental technique for simultaneous detection of the proton transfer event (to generate a new buried charge) and the protein quake event. The results are expected to provide insight into the impact of solvent pH on protein structural dynamics in general.

5:18PM D26.00011 First Principles Study of the Reaction Mechanism for Intein C-terminal Cleavage , PHILIP SHEMELLA, SAROJ NAYAK, Department of Physics, Applied Physics & Astronomy, BRIAN PEREIRA, SHEKHAR GARDE, GEORGES BELFORT, Department of Chemical & Biological Engineering. Rensselaer Polytechnic Institute. Troy, NY — Protein splicing, consisting of the excision and ligation of two flanking sequences (the exteins), is auto-catalyzed by the internal sequence (the intein). It has been shown experimentally that by mutating the critical first residue of the intein, the first step of splicing is inhibited, although intein C-terminal cleavage can still occur independently. Using a tripeptide model system with QM methods, we have investigated the effect of different mutants in order to provide an atomic level understanding of this mechanism. We find that the reaction energy barrier for asparagine cyclization can be controlled by mutation of non-essential residues: specifically we found that the barrier with a methionine mutant is larger than to the barrier for cysteine, resulting in slower C-terminal cleavage in agreement with experiment. The accuracy of our model system is further confirmed by comparing results with that of a combined quantum mechanics and molecular mechanics (QM/MM) approach. These results suggest that certain mutations in inteins could be used to control the reaction rate without affecting the overall reaction mechanism and could exploited for many applications including molecular switches, sensors and controlled drug delivery.

Monday, March 5, 2007 2:30PM - 5:30PM –

Session D34 DBP: Cell Level Patterning During Embryonic Development Colorado Convention Center 404

2:30PM D34.00001 The *de novo* formation of a vascular network, in warm-blooded embryos, occurs via a self-assembly process that spans multiple length and time scales , CHARLES D. LITTLE, University of Kansas Medical Center — Taking advantage of wide-field, time-lapse microscopy we examined the assembly of vascular polygonal networks in whole bird embryos and in explanted embryonic mouse tissue (allantois). Primary vasculogenesis assembly steps range from cellular (1-10 μm) to tissue (100μm-1mm) level events: Individual vascular endothelial cells extend protrusions and move with respect to the extracellular matrix/surrounding tissue. Consequently, long-range, tissue-level, deformations directly influence the vascular pattern. Experimental perturbation of endothelial-specific cell-cell adhesions (VE-cadherin), during mouse vasculogenesis, permitted dissection of the cellular motion required for sprout formation. In particular, cells are shown to move actively onto vascular cords *that are subject to strain via tissue deformations*. Based on the empirical data we propose a simple model of preferential migration along stretched cells. Numerical simulations reveal that the model evolves into a quasi-stationary pattern containing linear segments, which interconnect above a critical volume fraction. In the quasi-stationary state the generation of new branches offsets the coarsening driven by surface tension. In agreement with empirical data, the characteristic size of the resulting polygonal pattern is density-independent within a wide range of volume fractions. These data underscore the potential of combining physical studies with experimental embryology as a means of studying complex morphogenetic systems.
In collaboration with Brenda J. Rongish[1], András Czirók[1,2], Erica D. Perryn[1], Cheng Cui[1], and Evan A. Zamir[1]

[1]Department of Anatomy and Cell Biology, the University of Kansas Medical Center, Kansas City, KS
[2]Department of Biological Physics, Eötvös Loránd University, Budapest, Hungary.

3:06PM D34.00002 Physical Mechanisms of Patterning Instabilities in the Formation of Vascular Network , ABBAS SHIRINIFARD, JAMES GLAZIER, The Biocomplexity Institute, Department of Physics, Indiana University, SHANTIA YARAHMADIAN, Mathematics Department, Indiana University — Endothelial cells, which line the inner walls of blood vessels, self-organize into network structures in vitro and in vivo. The physical mechanisms of network formation are a current subject of debate may be important during development, wound heeling, and tumor growth. Using Glazier and Graner's Cellular Potts Model (CPM) to model chemotactically migrating cells, we studied the patterning instabilities and scaling properties of the network in two and three-dimensions. We ran our simulations in Compucell3D, an open-source software environment based on CPM (http://simtk.org/home/compucell3d). The average characteristics of the network structure are independent of the initial configuration of cells and scale with the diffusion parameters of the chemoattractant. We have also developed an analytical PDE model to study nature of patterning instabilities.

3:18PM D34.00003 Physical Mechanisms of Pattern Formation in the Early Chick Embryo[1] , ARIEL BALTER, JAMES GLAZIER, BENJI ZAITLEN, Indiana University, MARK CHAPLAIN, CORNELIS WEIJER, University of Dundee, BIOCOMPLEXITY INSITTUTE COLLABORATION, UNIVERSITY OF DUNDEE COLLABORATION, UNIVERSITY OF DUNDEE COLLABORATION — Gastrulation marks a critical step in early embryogenesis when the first recognizable patterns are laid down. Although the genome maintains ultimate responsibility for this pattern formation, it cannot actually control the organization of individual cells. The robustness of embryogenic pattern formation suggests that a few simple, physical mechanisms are unleashed and that self-organization results. We perform numerical simulations of early chick gastrulation using an agent based method in which individual cells interact via a handful of behaviors including adhesivity, secretion and chemotaxis. Through these simulations we have identified certain behaviors as being important for various stages and morphological events. For instance, experimental results on primitive streak formation are best reproduced by a model in which the Kohler's Sickle secretes a chemo repellant for streak tip cells, and cell polarization appears to be important for initiating *polonaise* motion during streak elongation.

[1]Biocomplexity Institute

3:30PM D34.00004 Interface Instabilities and Fingering in a Simulated Growing Tumor , NIKODEM POPLAWSKI, MACIEJ SWAT, JAMES GLAZIER, Indiana University, Department of Physics and Biocomplexity Institute, ALEXANDER ANDERSON, University of Dundee, Division of Mathematics — We study the physical origin of interface instabilities, which may lead to metastasis in medical contexts, during the invasion of healthy tissue by a solid tumor. We use Glazier and Graner's Cellular Potts Model (CPM), a lattice-based stochastic framework designed to simulate cell interactions and movement. This model reduces the large molecular complexity of living cells to a few basic processes: cell-cell adhesion, cell growth, division, differentiation and death, secretion and absorption of materials, chemotaxis, and cellular deformation. We run our simulations in CompuCell3D, an open-source software environment based on the CPM (https://simtk.org/home/compucell3d). We show that cells adhesivity and growth, and rate per unit nutrient consumed, determine whether the growing tumor has a flat or fingered interface. Our results differ from those reported by Anderson (A. R. A. Anderson, Math. Med. Biol. (2005) 22:163) using a continuum model. This difference shows the importance of explicit modeling of spatially extended cells to understanding the morphologies of developing tissues.

3:42PM D34.00005 Pattern formation of glioma cells: effects of adhesion , EVGENIY KHAIN, Department of Physics, the University of Michigan, Ann Arbor, MI 48109, MICHAL O. NOWICKI, E. ANTONIO CHIOCCA, SEAN E. LAWLER, Department of Neurological Surgery, The Ohio State University Medical Center, Columbus, OH 43210, LEONARD M. SANDER, Department of Physics, the University of Michigan, Ann Arbor, MI 48109 — *Glioblastoma multiforme* is a highly malignant brain tumor. We investigate the mechanism of clustering of glioma cells *in vitro*; this may shed light on clustering in the brain. Recent experiments with tumor spheroids growing in a transparent gel showed that one cell line formed clusters in a region where invasion occurs, whereas a very similar cell line does not cluster significantly. Using stochastic discrete modeling of motile adhesive and proliferative cells, we identified two important mechanisms which may lead to clustering. First, there is a critical value of the strength of cell-cell adhesion; above the threshold, large clusters grow from a homogeneous suspension of cells; below it the system remains homogeneous. Second, when several single cells form a small cluster, they may switch their phenotype from "invasive" to "proliferative," increasing their division rate. The theoretical predictions were tested in an experiment in which we followed the clustering dynamics of glioma cells on a surface. We have successfully reproduced the experimental findings and found that both mechanisms are crucial for cluster formation and growth.

3:54PM D34.00006 Role of viscosity and surface tension of zebrafish embryonic tissues in tissue flows during gastrulation. , E.M. SCHOETZ, MPI-CBG/-PKS, T. BACARIAN, UCI, M.S. STEINBERG, R.D. BURDINE, W. BIALEK, Princeton University, C.P. HEISENBERG, MPI-CBG, R.A. FOTY, UMDNJ, F. JULICHER, MPI-PKS — At the onset of gastrulation in zebrafish, complex flows and cell movements occur, which are not well understood. Here, we study the material properties of zebrafish embryonic tissues which are important for the tissue dynamics. We found that these tissues behave viscoelastic and exhibit liquid-like properties on long time scales. They relax internal stress caused by compressive forces or, in the absence of external forces, round up and fuse into spheres to minimize their free surface. Quantitative differences in the adhesivity between different types of tissues result in their immiscibility and sorting behavior analogous to that of ordinary immiscible liquids. When mixed, cells segregate into discrete phases, and the position adopted correlates with differences in the aggregate surface tensions for these phases. Surface tensions were measured with a tissue surface tensiometer. Aggregates were compressed and their force response and shape were recorded as a function of time. From the analysis of the force-relaxation curves, we determined the surface tensions, relaxation times, tissue viscosities and shear moduli. Furthermore, by 4D-cell tracking, we measured kinetic parameters such as cell speed, directionality and persistence of cell movement.

4:06PM D34.00007 Stochastic model of cell rearrangements in convergent extension of ascidian notochord[1] , SHARON LUBKIN, North Carolina State University, TRACY BACKES, Harvey Mudd College, RUSSELL LATTERMAN, Arizona State University, STEPHEN SMALL, Norfolk State University — We present a discrete stochastic cell based model of convergent extension of the ascidian notochord. Our work derives from research that clarifies the coupling of invagination and convergent extension in ascidian notochord morphogenesis (Odell and Munro, 2002). We have tested the roles of cell-cell adhesion, cell-extracellular matrix adhesion, random motion, and extension of individual cells, as well as the presence or absence of various tissue types, and determined which factors are necessary and/or sufficient for convergent extension.

[1]This work was partially supported by the National Science Foundation

4:18PM D34.00008 Time markers for Drosophila morphogenesis based on cell-pattern topology. , RICHARD ZALLEN, Department of Physics, Virginia Tech, JENNIFER A. ZALLEN, Developmental Biology Program, Sloan-Kettering Institute — Recent work on convergent extension in Drosophila has shown that the accumulation of actin-myosin networks at specific cell interfaces initiates planar polarity and the formation of multicellular rosette structures that contribute to elongation of the body axis [1]. This cell-rearrangement process takes place within a one-cell-thick layer, and the changing two-dimensional cell pattern can be characterized using topological measures such as cell-shape statistics [2]. We find that the timeline for the process contains a well-defined marker corresponding to a sharp increase in the slope of the time dependence of the variance of the cell-shape (number-of-sides) distribution. A rosette in this context is a cluster of cells enclosing high-order vertices at which 4 or 5 or more cells meet. While the cell-shape variance climbs steadily during axis elongation, the frequency of high-order vertices and large rosettes plateaus after 10 and 13 minutes, respectively. These time markers calibrate the conventional timeline descriptors referred to as stages 7 and 8 of embryonic development [3]. [1] J.T. Blankenship et al., Developmental Cell 11, 459 (2006); [2] J.A. Zallen and R. Zallen, J. Phys.: Condensed Matter 16, S5073 (2004); [3] J.A. Campos-Ortega and V. Hartenstein, The embryonic development of Drosophila melanogaster (1985).

4:30PM D34.00009 Different Strategies for Aggregation in Social Amoeba Colonies , CARL FRANCK, RYAN MONAGHAN, ALBERT BAE, DUANE LOH, Cornell University, EBERHARD BODENSCHATZ, Cornell University and MPI Dynamics and Self-Organization, Goettingen, Germany — When confronted by starvation, collections of the amoeba Dictyostelium discoideum seek to aggregate in order to form genome-preserving stalk and spore structures. We have been interested in the means by which individual cells unite for this purpose. It has long been recognized that communication by means of diffusion of small molecules affords one such strategy: periodic chemical wave signaling can direct individual cells to an aggregation site. By employing thin layer substrates that presumably alter the propagation characteristics of such waves, we have shifted the colonial aggregation strategies to modes that rely on adhesive interactions for initial stages of multicellular assembly. Besides relentless aggregation of individual cells into large scale streams, these substrates reveal remarkable structures composed of only a few cells which we call "squads" that search for each other in order to achieve sufficient aggregation mass in sparse populations.

4:42PM D34.00010 Optimal Foraging by Zooplankton , RICARDO GARCIA, FRANK MOSS, University of Missouri at St. Louis — We describe experiments with several species of the zooplankton, *Daphnia,* while foraging for food. They move in sequences: *hop-pause-turn-hop* etc. While we have recorded hop lengths, hop times, pause times and turning angles, our focus is on histograms representing the distributions of the turning angles. We find that different species, including adults and juveniles, move with similar turning angle distributions described by exponential functions. Random walk simulations and a theory based on active Brownian particles indicate a maximum in food gathering efficiency at an optimal width of the turning angle distribution. Foraging takes place within a fixed size food patch during a fixed time. We hypothesize that the exponential distributions were selected for survival over evolutionary time scales.

4:54PM D34.00011 Precision and Reproducibility in Biological Patterning , THOMAS GREGOR, ERIC F. WIESCHAUS, WILLIAM BIALEK, DAVID W. TANK, Princeton University — During embryonic development, information about spatial location is represented by the concentration of various morphogen molecules. The reproducibility and precision of biological pattern formation thus is limited by the accuracy with which these concentration profiles can be established and "read out" by their target pathways. We consider four measures of precision for the Bicoid morphogen in the Drosophila embryo: The concentration differences that distinguish neighboring cells, the limits set by the random arrival of Bcd molecules at their targets (which depends on the absolute concentration), the noise in readout of Bcd by the activation of Hunchback, and the reproducibility of Bcd concentration at corresponding positions in multiple embryos. We show, through a combination of different experiments, that all of these quantities are $\sim$10%. This agreement among different measures of accuracy, which depend on very different molecular mechanisms, indicates that the embryo is not faced with sloppy input signals and noisy readout mechanisms; rather we have to understand how the embryo exerts precise control over absolute concentrations and responds reliably to small changes in these concentrations, down to the limits set by basic physical principles.

5:06PM D34.00012 A lattice model of parasite-host population dynamics[1] , BRIAN SKINNER, BEATE SCHMITTMANN, ROYCE ZIA, Virginia Tech — The study of simple parasite-host population models may help us advance fundamental understanding of nonequilibrium steady-states and provide insight into potential applications for controlling epidemics. Using Monte Carlo techniques, we investigate a model of interacting parasite-host populations in which parasites must come into contact with a host in order to reproduce. We treat the parasites and hosts as random walkers on a two-dimensional lattice with reflecting boundary conditions and vary the parasite death rate and the relative diffusion rates of the two species. For low death rates and slow host diffusion, steady state populations can exist and the resulting non-trivial spatial distributions are measured. We also explore the consequences of allowing the hosts to respond to local gradients in the parasite concentration. If the hosts are biased to move away from regions of high parasite concentration, an effective repulsion between hosts emerges. Both the population levels and the spatial distributions are observed to depend sensitively on the details of this response. Some aspects of these phenomena can be understood analytically.

[1]supported by NSF-DMR-0414122

5:18PM D34.00013 Cell Assisted Cell Growth Experiments with Dictyostelium discoideum , ALBERT BAE, WUI IP, CARL FRANCK, Cornell University — In eukaryotic cell culture, it is routinely recommended to keep the cells above a minimum cell density to maintain vigorous growth. We are investigating the basis for this prescription by viewing cell growth as a social behavior facilitated by cell-cell communication. Employing Dictyostelium discoideum, we find good evidence for a slow-fast transition in the cell growth rate vs. density in well mixed, 25 ml, cell cultures. We also use low height microfluidic chambers (four orders of magnitude smaller in volume) to find similar behavior even though the system is not well mixed and the cells are confined to substrates. A preliminary measurement at a flow rate that should strongly perturb cell-cell communication by means of diffusing signal molecules suggests that cell communication essential for growth is not accomplished by such means but possibly via direct contacts.

Monday, March 5, 2007 2:30PM - 5:42PM –

Session D35 DBP: Focus Session: Biological Networks Colorado Convention Center 405

2:30PM D35.00001 Synthetic Gene Networks: *De novo constructs – in numero* descriptions , JEFF HASTY, Department of Bioengineering, University of California, San Diego — Uncovering the structure and function of gene regulatory networks has become one of the central challenges of the post-genomic era. Theoretical models of protein-DNA feedback loops and gene regulatory networks have long been proposed, and recently, certain qualitative features of such models have been experimentally corroborated. This talk will focus on model and experimental results that demonstrate how a naturally occurring gene network can be used as a "parts list" for synthetic network design. The model formulation leads to computational and analytical approaches relevant to nonlinear dynamics and statistical physics, and the utility of such a formulation will be demonstrated through the consideration of specific design criteria for several novel genetic devices. Fluctuations originating from small molecule-number effects will be discussed in the context of model predictions, and the experimental validation of these stochastic effects underscores the importance of internal noise in gene expression. The underlying methodology highlights the utility of engineering-based methods in the design of synthetic gene regulatory networks.

3:06PM D35.00002 Origin of Modularity in Recombination Evolution , JUN SUN, MICHAEL DEEM, Rice University — Modularity is a well-known phenomenon in biology. Modularity implies a hierarchical character, and is manifested in both phenotypic and genotypic levels. A module is defined, in general, as a component which operates relatively independently of other components of the system. The independence is in both the structural and functional levels. How does modularity originate? Evolvability is a selectable trait and modularity enhances evolvability. Thus, under conditions that select for evolvability, we expect to see the emergence of modularity. We used a spin-glass model to simulate the evolution of genomes. This model captures the interactions between amino acids or epistasis between genes. The evolutions include both sequence evolution and structure evolution. The environment changes and recombination plays an important role in evolution. We will present our result of the emergence of modularity, a symmetry breaking of the system. We will present the dependence of modularity on the amplitude and frequency of environment changing. The crucial role of recombination in the emergence of modularity will be discussed as well.

3:18PM D35.00003 Dynamic network analysis of protein interactions[1] , EIVIND ALMAAS, Lawrence Livermore Natl Lab, JOYA DERI, Lawrence Livermore Natl Lab and Stanford University — Network approaches have recently become a popular tool to study complex systems such as cellular metabolism and protein interactions. A substantial number of analyses of the protein interaction network (PIN) of the yeast *Saccharomyces cerevisiae* have considered this network as a static entity, not taking the network's dynamic nature into account. Here, we examine the time-variation of gene regulation superimposed on the PIN by defining mRNA expression profiles throughout the cell cycle as node weights. To characterize these network dynamics, we have both developed a set of novel network measures as well as studied previously published measures for weighted networks. We expect that our approach will provide a deeper understanding of protein regulation during the cell cycle.

[1]LDRD 06-ERD-061

3:30PM D35.00004 Growth induced instability in metabolic networks[1] , SIDHARTHA GOYAL, Joseph Henry Laboratories of Physics, Princeton University, NED S. WINGREEN, Department of Molecular Biology, Princeton University — Networks of molecular interactions are essential for mass, energy, and information transport into and within cells. Thus, understanding the emergent physical properties of various network architectures is of fundamental interest in biology. One such architecture, product-feedback inhibition is widely used in the regulation of biosynthetic pathways of all organisms. Importantly, these biosynthetic pathways are often coupled both by the use of a common substrate and by stoichiometric utilization of their products for cell growth. We analyze networks having the following three essential features: all branches start from a common substrate, the product of each branch inhibits the first dedicated step towards its synthesis, and all products are essential for growth. We show that such a coupled network can have at most one steady state. However, the network may be unstable about this steady state, even if the branches are individually stable. In the unstable region, the network exhibits limit-cycle oscillations which arise via a Hopf bifurcation. In the oscillating regime, a two-branch coupled network can be mapped to a three-species frustrated system. Our results highlight new design principles essential for realizing robust biosynthetic pathways.

[1]SG acknowledges the generous support from Burroughs Wellcome Fund.

3:42PM D35.00005 Emergent Criticality from Co-evolution in Random Boolean Networks[1] , MIN LIU, KEVIN E. BASSLER, Department of Physics, University of Houston — The co-evolution of network topology and dynamics is studied in an evolutionary Boolean network model that is a "coarse-grained" model of a gene regulatory network. We find that a critical state emerges spontaneously from the interplay between topology and dynamics when the network is updated by a rule that rewires its internal connections based on the activities of nodes and changes the dynamical functions. The final evolved state is shown to be critical and independent of initial conditions. The network appears to be driven to a random Boolean network with uniform in-degree of 2 in the large network limit. However, for biologically realized network sizes, significant finite-size effects are observed including a broad in-degree distribution and an average in-degree connection between 2 and 3. These results may be important for explaining the formation of heterogeneous topology in real gene regulatory networks. Detailed work is discussed in the paper Phys. Rev. E **74**, 041910 (2006).

[1]Acknowledge the support by NSF Grant No. DMR-0427538. Min Liu is thankful for Santa Fe Institute 2005 Complex Systems Summer School.

3:54PM D35.00006 Protein-Protein interaction networks: why static MpK model works and preferential attachment does not , JINGSHAN ZHANG, EUGENE SHAKHNOVICH, Harvard University — Various approaches have been proposed to explain the observed scale free structure $p(k) \sim k^{-\gamma}$ of protein-protein interaction networks. We argue that the preferential attachment coming from gene duplication[1] is questionable. A static "MpK" model produces the scale free structure via computer simulations[2] for unexplained reasons. On the other hand, it was analytically proved[3] that deterministic threshold models produce scale free networks (with $\gamma \equiv 2$) if fitness distributions are exponential. We study the static MpK model further and find the above analytical proof applicable with extensions, and γ dependent on the threshold parameter. This work not only predicts the dependence of γ on protein concentrations, but also provides a generic mechanism of scale free networks. The clustering coefficient distribution in the model is interpreted by a simple picture.

[1] A.-L. Barabási and Z. N. Oltvai, Nature Reviews Genetics **5**, 101 (2004).
[2] E. J. Deeds, O. Ashenberg, E. I. Shakhnovich, Proc. Natl. Acad. Sci. USA **103**, 311 (2006).
[3] G. Caldarelli, A. Capocci, P. De Los Rios, and M. A. Muñoz, Phys. Rev. Lett. **89**, 258702 (2002).

4:06PM D35.00007 A closer look at activity in metabolic networks , NATALI GULBAHCE, Los Alamos National Laboratory, TAKASHI NISHIKAWA, Southern Methodist University, ADILSON E. MOTTER, Northwestern University — Single-cell organisms are assumed to optimize growth under specific conditions. Using flux balance analysis, it is possible to estimate the number of reactions that are utilized (active) by the metabolism in random and optimal metabolic states. Here we investigate the mechanisms that determine the number of active reactions mathematically and compare them to those of real organisms.

4:18PM D35.00008 Stochastic Chemical Kinetics in Biochemical Reaction Networks. , GAREGIN PAPOIAN, YUEHENG LAN, The University of North Carolina at Chapel Hill — We used various analytic and numerical methods to elucidate complex dynamics in stochastic signal transduction. We demonstrate that the commonly used linear noise approximation to solving the chemical master equation fails when the number of proteins becomes too low. Consequently, we developed a new analytical approximation to the solution of the master equation, based on the generating function approach, which works in a much wider range of protein number fluctuations. We show that in a linear signaling pathway, a reaction rate at a node could be tuned so the node acts either as a noise amplifier or as a noise filter. For more complex cascades, we mapped the stochastic chemical kinetics master equation into a quantum field theoretical problem, which we solved using the variational principle. We demonstrate stochastic resonance in signal transmission in enzymatic cascades with and without feedback loops.

4:30PM D35.00009 Noise propagation in combined cellular control motifs[1] , CHEOL-MIN GHIM, EIVIND ALMAAS, Lawrence Livermore Natl Lab — A cell's ability to respond robustly to noisy stimuli critically depends on the structure of its regulation and control circuitry, as well as kinetic parameters. While kinetic parameters take a wide range of values, there is markedly less variation in the basic network building blocks. We have explored the functional implications of several motif-combinations, investigating their information processing properties. Adopting a spectral-analysis approach, we study how circuit topology affects the propagation or attenuation of intrinsic and extrinsic noise. Finally, we discuss possible fitness benefits of the different circuit topologies, relating design principles to evolutionary selection.

[1]LDRD 06-ERD-061

4:42PM D35.00010 Stochastic effects in reaction networks , ARYEH WARMFLASH, AARON DINNER, University of Chicago — Experiments that yield information about single cells make clear that intrinsic noise in reactions involving low copy numbers of molecules can have important functional consequences. Although it is typically assumed that noise introduces isotropic fluctuations about a mean, this need not be the case. Within the Langevin framework, we develop "rules of thumb" for understanding the impact of noise on systems of reactions. We show analytically how increases in either the magnitude or correlation time of fluctuations can give rise to amplifications and bifurcations. As an example, we consider the enzymatic cycle studied by Goldbeter and Koshland. Fluctuations in the total number of enzyme for the forward reaction have been shown to amplify the concentration of the modified substrate and can even create additional peaks in its distribution. We show how our results lead to a transparent physical interpretation of these observations, and we clarify how ultrasensitivity, amplification, bifurcation, and stochastic focusing relate to each other.

4:54PM D35.00011 Universal patterns in the behavior of complex systems: from relaxation in fractal networks to distribution of income , VALERICA RAICU, MICHAEL STONEMAN, RUSSELL FUNG, University of Wisconsin-Milwaukee — The study of relaxation is an active area of research in the fields of dielectric, mechanical and optical spectroscopy, which is insufficiently developed for the case of complex systems. It has been established that the relaxation of many systems deviates markedly from classical Debye dispersion function (in the frequency domain) or from pure exponential decay (in the time domain), but the exact ways in which these deviations occur and their significance are still debated issues. Here we propose that a fractal-tree network appropriately describes the relaxation pathway in a variety of complex systems and predicts coupled (or hierarchical) as well as uncoupled (parallel) relaxation processes. This approach has been originally introduced for description of dielectric relaxation in Cantorian trees in biology. Upon adequate generalization this approach sheds new light on a variety of processes, ranging from kinetics of protein-ligand rebinding through distribution of income in populations of humans.

5:06PM D35.00012 Understanding Dynamic Patterns of NF-κB Signaling: Derivation and Analysis of a Minimal Model through Sensitivity Analysis , JAEWOOK JOO, STEVE PLIMPTON, SHAWN MARTIN, LAURA SWILER, Sandia National Laboratories, JEAN-LOUP FAULON, Sandia National Laboratoris — Understanding the pleiotropism of NF-κB signal transduction is a challenge of clear medical importance and systems biology. Current mathematical modeling frameworks for NF-κB signal transduction, though limited to a small signaling module located in a downstream of IKK, heavily rely on the parameterizations and the numerical studies of ODE models and doubtless lack intuitive explanations about underlying mechanisms of the dynamic patterns of the NF-κB signaling. Here we present a systematic way to derive a minimal model from an up-to-dated and detailed NF-κB signaling network by means of sensitivity analysis. Using analysis of the minimal model, we predict a dose-response curve shape, existence of Hopf-bifurcation, and underlying mechanisms of all possible dynamic patterns of NF-κB signaling. Simulating the detailed ODE model for NF-κB signaling network with large sets of the parameter values that are sampled from the biologically feasible parameter space, we present an ensemble of all possible dynamic patterns of NF-κB signaling and verify the predictions from the minimal model.

5:18PM D35.00013 Sloppy systems biology: tight predictions with loose parameters , JAMES SETHNA, RYAN GUTENKUNST, JOSHUA WATERFALL, Laboratory of Atomic and Solid State Physics, Cornell University, FERGAL CASEY, Center for Applied Mathematics, Cornell University, KEVIN BROWN, Department of Molecular and Cellular Biology, Harvard University, CHRISTOPHER MYERS, Cornell Theory Center, Cornell University — Directly measuring the parameters involved in dynamical models of cellular processes is typically very difficult, and collectively fitting such parameters to other data often yields large parameter uncertainties. Nonetheless, a collective fit which only weakly constrains model parameters may strongly constrain model *predictions*, if the model is ill-conditioned: much more sensitive to some directions in parameter space than others. In the quadratic approximation, the model sensitivities are proportional to the inverse square roots of the hessian matrix eigenvalues. Using a collection of 14 models from the systems biology literature, we show that for large systems the eigenvalue spectra are universally *sloppy*; they span huge ranges ($> 10^6$) and have approximately constant logarithmic spacing. Thus the models are ill-conditioned and have no well-defined cutoff between important and unimportant parameter combinations. This universal sloppiness suggests that collective fits will often poorly constrain parameters but usefully constrain many predictions.

5:30PM D35.00014 A Physical Theory of the Competition that Allows HIV to Escape from the Immune System , MICHAEL DEEM, Rice University — Competition within the immune system may degrade immune control of viral infections. We formalize the evolution that occurs in both HIV-1 and the immune system quasispecies [1]. Inclusion of competition in the immune system leads to a novel balance between the immune response and HIV-1, in which the eventual outcome is HIV-1 escape rather than control. The analytical model reproduces the three stages of HIV-1 infection. We propose a vaccine regimen that may be able to reduce competition between T cells, potentially eliminating the third stage of HIV-1. 1) G. Wang and M. W. Deem, Phys. Rev. Lett. 97 (2006) 188106.

Tuesday, March 6, 2007 8:00AM - 11:00AM –

Session H18 DPOLY DBP: De Novo Designed Peptides as Building Nanostructural Blocks

Colorado Convention Center 103

8:00AM H18.00001 BREAK –

8:36AM H18.00002 Responsive Polypeptide-based Block Copolymer Assemblies , DANIEL A. SAVIN, GOPAL VENKATACHALAM, SANDEEP S. NAIK, KAY E. GEBHARDT, University of Vermont — Amphiphilic block copolymers of poly(butadiene) and poly(L- lysine) (PB-P(Lys)) as well as poly(propylene oxide) and P(Lys) (PPO-P(Lys)) were synthesized and their solution properties studied using dynamic light scattering and transmission electron microscopy. We exploit secondary structure changes that occur in the P(Lys) chain to observe changes in solution morphology as a function of solution conditions. At high pH, the P(Lys) chain assumes either an α-helical or a β-sheet conformation depending on temperature, while at lower pH the side chains become protonated, resulting in an expanded coil configuration. In these studies, we explore the pH and temperature responsiveness for a series of block copolymers with varying morphology.

8:48AM H18.00003 Early Stages of De Novo Designed Beta-Hairpin Peptide Self-Assembly , TUNA YUCEL, Department of Materials Science and Engineering, Delaware Biotechnology Institute, University of Delaware, Newark, DE 19716, JOEL P. SCHNEIDER, Department of Chemistry and Biochemistry, University of Delaware, Newark, DE 19716, DARRIN J. POCHAN, Department of Materials Science and Engineering, Delaware Biotechnology Institute, University of Delaware, Newark, DE 19716 — In aqueous solution, MAX 1 peptide is unfolded and does not self-assemble. The peptide intramolecularly folds into a beta-hairpin when the electrostatic interactions between charged residues are screened through increasing the ionic strength at neutral pH. Beta-hairpin molecules supramolecularly assemble via hydrophobic collapse and hydrogen bonding into a 3-D hydrogel network. By combining the results of CD, cryo-TEM, DLS, and oscillatory rheology, we understand that the self-assembly proceeds by nucleation of monodisperse (3 nm wide) beta-sheet fibrils, which elongate, branch and cross-link to form clusters of fibrils. Assembly kinetics at this early stage indicates power law growth with assembly time. Eventually, clusters of fibrils interpenetrate to form a percolated network, as evidenced by the increasing network rigidity. The early stage assembly process will be discussed and compared to published gelation models.

9:00AM H18.00004 Effect of Strand Symmetry on the Nanostructure and Material Properties in Beta-Hairpin Peptide Hydrogels , ROHAN HULE, DARRIN POCHAN, Department of Materials Science and Engineering and Delaware Biotechnology Institute, University of Delaware, RADHIKA NAGARKAR, JOEL SCHNEIDER, Department of Chemistry and Biochemistry — Hydrogels have been established as promising biomaterials for applications such as scaffolds for tissue engineering, controlled drug delivery and cell encapsulation. De novo designed beta hairpin peptides, capable of undergoing self assembly and hydrogel formation, were investigated that contain asymmetric beta strand arms surrounding a turn sequence. The stimuli responsive self assembly of the hydrogels occurs via an intramolecular folding and strand interdigitation mechanism. CD and FTIR indicate a beta sheet secondary structure. WAXS shows a fibril structure reminiscent of the cross beta spine. SANS has been employed to globally quantify the local structure as being rod-like. Modification of the strand registry results in fibrils with non-twisting, laminated vs. twisted nanostructure. Fibril dimensions as measured by TEM and AFM corroborate the interdigitated assembly. Bulk material properties of these hydrogels studied using oscillatory rheology vary significantly for the different morphologies. Differences in the peptide registry that drive hydrogel nanostructure and the consequent material properties can be potentially utilized for usage in specific biomaterial applications.

9:12AM H18.00005 Self-assembling, bioactive protein hydrogels via engineered coiled-coil aggregation. , JAMES HARDEN, University of Ottawa, STEPHEN FISCHER, Johns Hopkins University, LIXIN MI, Georgetown University — We describe associating triblock proteins with that self-assemble into reversible, nanostructured hydrogels with a regular network structure and specific biofunctional attributes. These fibrilar, telechelic designs consist of a hydrophilic random coil (denoted R) flanked by associating coiled-coil end domains (denoted A, B, C). The central R domain also encodes specific cell binding and signaling functions of extracellular matrix (ECM) constituents. We will discuss a series of proteins with complimentary associating end blocks that preferentially form heterotrimer aggregates of A, B, and C domains. Mixtures of symmetric triblocks ARA, BRB, and CRC in aqueous solution self assemble into reversible viscoelastic network structures, which we characterize using microscopy, light scattering techniques and computer simulations. Supporting circular dichroism and analytical ultracentrifugation studies of the secondary structure and association behavior of the A, B, C domains will also be presented. Through the use of microscopic and cell proliferation assays, we also show that these hydrogels are capable of inducing biomimetic responses of ECM constituents in cell culture experiments.

9:24AM H18.00006 Planar peptide processing , KIRK BALDWIN, ROBERT WILLETT, Bell Laboratories, Lucent Technologies — Spatial manipulation on small length scales of biological materials, in particular peptide based substances, is important both for implementing assays and for exploiting the properties of the materials set. In this talk we describe methods for patterning peptides in planar manipulations much as is exercised with materials in semiconductor processing: Controlled deposition into small length-scale patterns is accomplished through selective adhesion to patterned substrates or deposition through patterned masks, and removal of peptide films can be achieved through wet or dry etching techniques. These methods are shown to be applicable to at least the micron scale, and this technique summary presents an elemental tool-box for planar processing of this set of biological films. Collectively these techniques provide a "toolbox" of methods to accomplish rudimentary planar processing with peptides.

9:36AM H18.00007 Self-Assembling Octa-peptides , ALINE MILLER, ANTONIOS KONSTANTOPOLOUS, LAURENT CARON, ALBERTO SAIANI, University of Manchester — In this work we have focused on examining systematically the effect of hydrophobicity, charge distribution and size of amino acid on the self assembly behavior of a series of octa-peptides that have been synthesized in our laboratory: AEAEAKAK, AEAKAEAK, FEFKFEFK. FEFKFEFK, FDFDFRFR, FDFRFDFR, FDFDFKFK, FDFKFDFK, FKFDFDFK and FDFKFKFD. The structure of our systems have been elucidated using a combination of Fourier transform infra-red spectroscopy, atomic force microscopy and small angle neutron scattering. This work has shown that the peptides form beta-sheet rich fibrils that have circa 4-6 nm in diameter, and these can associate further along their length scales depending on the amino acid sequence. In some cases these fibrils, or thicker fibers, then become physically entangled to give rise to a 3-dimensional fibrillar hydrogel that does not flow upon inversion of the sample vial. The mechanical properties of all resulting hydrogels have been explored using oscillatory rheometry and results related back to hydrogel structure across the length scales. Here we will present phases diagrams, propose a generalized gelation mechanism and link molecular structure to macroscopic properties.

9:48AM H18.00008 Sequence Dependent Peptide Self-Assembly and Beta-Sheet Fibrils as Templates for Inorganic Material , MATTHEW LAMM, DARRIN POCHAN, Materials Science and Engineering, JOEL SCHNEIDER, Chemistry and Biochemistry, University of Delaware — Synthetic peptides have been designed to self-assemble into beta-sheet fibrils of varying morphology depending on the peptide sequence. Incorporation of a diproline sequence between two beta-sheet forming strands is used to affect peptide conformation and thus the self-assembly mechanism and resulting fibrillar morphology (e.g. twisted vs. untwisted). Peptide length, proline stereochemistry, diproline sequence position, and assembly kinetics are shown to significantly affect fibril morphology. Furthermore, fibrils of varying morphology are employed as templates for inorganic material such as amorphous silica. In addition, metal nanoparticles were synthesized and functionalized to interact with the fibrils resulting in laterally spaced, linear particle arrays.

10:00AM H18.00009 Incorporation of Designed Extended Chromophores into Amphiphilic 4-helix Bundle Peptides for Biomolecular Materials , TING XU, University of Pennsylvania, JIAYU WANG, JOE STRZALKA, University of Pennsylvania, THOMAS RUSSELL, University of Massachusetts, Amherst, MICHAEL THERIEN, J. KENT BLASIE, Univesity of Pennsylvania, UNIVERSITY OF PENNSYLVANIA COLLABORATION, UNIVERSITY OF MASSACHUSETTS, AMHERST COLLABORATION — De novo designed peptides, together with synthetic non-biological cofactors, could lead to peptide-based systems with novel properties not exhibited by biological systems. Extended chromophores can be designed and tailored, with appropriate donors, acceptors and constituents, to exhibit selected nonlinear optical responses and light-induced electron transport and/or proton translocation over large distances. Designed extended chromophores can be incorporated into the amphiphilic 4-helix bundle peptides via bis-histidyl ligation. Amphiphilic 4-helix bundle peptide monolayer, both the apo- and holo-form, can be oriented vectorially at the air/water interface. Nanoporous thin films made from diblock copolymers are ideal templates to assemble the artificial proteins with laterally hexagonal order. We will also discuss the efforts on re-designing the artificial proteins and incorporate them into block copolymer based nanoporous templates.

10:12AM H18.00010 Turning protein into room temperature molecular magnet[1] , CHIA-CHING CHANG, Dept. Bio.Sci.Tech., Natl. Chiao Tung Univ., SHANG-FAN LEE, Inst. Phys., Academia Sinica, KIEN-WEN SUN, Inst.Mol.Sci.Dept Appl.Chem., Natl. Chiao Tung Univ., LOU-SING KAN, Inst. Chem., Academia Sinica — Metallothionein-2 (MT-2) is a cysteine-rich protein that binds seven divalent transition metal ions avidly via its metal-thiol linkages. A magnetic MT-2 containing two Mn and five Cd (Mn,Cd-MT-2) has been synthesized by protein refolding process. No trace of Fe was detected by ICP mass spectroscopy. The uniform size distribution, tested by dynamic light scattering, indicated that each Mn,Cd-MT-2 molecule is a single molecular magnet. Its coercive field of ferromagnetic signals changed slightly from 50 to 300K, but dropped rapidly when the temperature rose from 330 to 395 K. The blocking temperature T_B is around 410K, in powder form. These results indicated that the un-paired electron of both Mn^{2+} might be aligned by electron hoping of the bridging sulfurs in the β-metal binding cluster of MT-2 and when the protein deformed at 410K the ferromagnetic signals disappear correspondingly. This engineered molecule exhibits both molecular magnetization and bio-compatibility. These features make Mn,Cd-MT-2, a good candidate for biological applications and sensing sources of new nano-devices.

[1]This study was supported in part by grants NSC 95-2112-M-009-019

10:24AM H18.00011 Interaction of the synthetic polypeptide poly(FFDD) with single-walled carbon nanotubes , YACHIN COHEN, MERAV GRANITE, AMRAM MOR, Technion, Israel, WIM PYCKHOUT-HINTZEN, Fz. Juelich, Germany — Dispersion of bulk-synthesized single-walled carbon nanotubes (SWCNT) and their subsequent assembly into beneficial structures, especially in aqueous medium, requires the interaction of amphiphilic moieties. Among these, proteins as well as *de-novo* polypeptides have been found to provide useful functional SWCNT dispersions. The synthetic polypeptides reported so far have rather elaborate sequences, which are deemed necessary for the specific conformations that successfully interact with the SWCNT surface. We have sought to study simple oligo-peptides and their basic interactions with SWCNTs in water. An oligo-peptide: poly(FFDD) [F=phenyl alanine, D = aspartic acid] with 30 amino-acid units, exhibiting and alternating hydrophobic/hydrophilic motif, was synthesized and used successfully to disperse SWCNTS. Small-angle neutron scattering (SANS) measurements with contrast variations were performed in different D_2O/H_2O mixtures. The SANS patterns show that poly(FFDD) alone in water assembles into a complex structure. However, an open conformation which is loosely attached to the SWCNT surface is indicated by SANS.

10:36AM H18.00012 Investigating the specificity of adsorption of onto gold by gold-binding peptides using molecular dynamics simulations[1] , ANA VILA VERDE, JANNA MARANAS, The Pennsylvania State University, Department of Chemical Engineering — It is possible to engineer artificial peptide sequences showing high specificity of adsorption for surfaces like gold, platinum or other solid materials. However, the reasons behind that high specificity are not clear. We investigate the adsorption of a genetically engineered peptide with high gold specificity using all-atom molecular dynamics simulations. Accurate Lennard-Jones parameters describing the interactions of gold with both water and amino acids are not currently available, so thus we discuss assignment of appropriate values. Two sets of simulations are presented: one using peptides made of a gold-binding motif (MHGKTQATSGTIQS) and another using peptides made of a non gold-binding motif (AIRRDVNCIGASMH). Adsorption onto the (111) and the (100) crystalline faces of gold is investigated. We discuss our results in light of the features of the peptide (sequence, charge, structure, nature of the amino acids) that may be responsible for the specificity of the gold-binding motif for gold.

[1]A. V. V acknowledges support from the Portuguese FCT through fellowship SFRH/BPD/20555/2004/0GVL

10:48AM H18.00013 Direct Assembly of Periplasmic Binding Proteins on Gold Surfaces , CRISTIAN STAII, Department of Chemistry, Princeton University, DAVID WOOD, Department of Chemical Engineering and Department of Molecular Biology, Princeton University, GIACINTO SCOLES, Department of Chemistry, Princeton University and Scuola Internazionale Superiore di Studi Avanzati (SISSA), Trieste, Italy — We present a new and very promising approach to protein based biosensor design, which uses a technique called nanografting to immobilize proteins at addressable locations on Au surfaces. In nanografting, an Atomic Force Microscope (AFM) tip is used to disrupt a preexisting monolayer of alkanethiol molecules on a gold surface, thereby facilitating exchange with alternative thiol-linked proteins from the surrounding solution. This technique opens the possibility of preparing highly ordered, nanometer size protein arrays that can be patterned at different addressable locations on the surface. We also use the AFM to monitor the ligand-induced conformational changes of periplasmic binding proteins nanografted on Au substrates.

Tuesday, March 6, 2007 8:00AM - 10:48AM –

Session H25 DBP: Focus Session: Medical Radiation Biology Colorado Convention Center 203

8:00AM H25.00001 Proteomic determination of the biological sequelae of electron irradiation. , RICHARD BRITTEN, Eastern Virginia Medical School — Radiobiological-based treatment planning, where radiation dose is varied according to the regional biological variations in tumor tissue e.g. hypoxia, is becoming increasingly available and represents a radically different approach to improving the radiocurability of tumors. However, many of the current algorithms are based upon radiobiological phenomenon that have been studied for decades, e.g., the oxygen effect, and few utilize recent information on biological parameters that influence radiation response, e.g. EGFR status. With regard to electron treatment planning, there is a paucity of studies that have looked at the biological consequence of exposure to electrons of differing energies. The assumption is that there is a uniform cell killing per unit dose within the treatment volume. We have recently applied proteomic analysis to determine the impact that exposure to low and high-energy electrons have on the proteome of tumor cells; preliminary data suggests that a completely different spectrum of proteins are expressed 24 hours after exposure to 50 cGy of high versus low LET electrons. Changes in the cellular proteome provide an indication of the different cellular responses elicited in response to damage induced by high and low energy electrons. Should these protein changes reflect a different high versus low energy electron mediated cell inactivation, then algorithms may have to be developed that take into account the energy distribution within the dose field. A new technique called MALDI-imaging is capable of resolving proteomic differences at various sites in a tissue slice, thus allowing for a spatial determination of proteins within an irradiated tumor volume. In the future it may thus be feasible to determine the exact dose distribution with an irradiated field and determine the efficacy with which radiation kills tumor or normal cells.

8:36AM H25.00002 Energy Spectra Reconstruction from Beta Emitters: A Study of the 90SR/90Y Case , ARIANO MUNDEN, PAUL GUEYE, CYNTHIA KEPPEL, CHRIS SOARES — Reconstruction of individual electron energies from a 25μCi ^{90}Sr/^{90}Y radioactive source was performed using a dipole magnet and a scintillating fiber based detector. The dipole was constructed from two 5.08x5.08x2.54cm permanent magnets separated by a distance of 2 cm and having a maximum field of about 5kG. The electron beam leaving the source has a 2.28MeV maximum energy and was collimated within a 1cm at the entrance face of the magnet. Mapping of the magnetic field was done using a hall probe with an accuracy of about 2G. An electron detector consisted of blue shifted scintillating fibers with thicknesses of 1mm was used to detect the particles exiting the magnet. The data was compared with the ICRU energy distribution data for 90Sr, 90Y, and the composite 90Sr/90Y sources. The comparison was performed using a chi squared test. The setup provides an energy resolution less than 10%. Such system could be used to reconstruct the energy distribution of any beta emitter for various types of calibrations as used in experimental physics (nuclear/high energy, medical, material sciences etc.). .

8:48AM H25.00003 Validity Of the Low Energy Electromagnetic Physics As Implemented Using the Geant4 Toolkit Using A Sr^{90}/Y^{90}Beta Emitter Source , RACHEL BLACK, PAUL GUEYE, Hampton University — Calibration procedures in experimental physics (nuclear physics, material sciences, medical physics etc.) usually require the use of a low activity radioactive source. A model of the setup is most often performed to understand and optimize system performances. We have investigated the validity of the low energy electromagnetic physics models up to a 2.3 MeV as implemented in the Geant4 simulation toolkit. For this, a set of experiments was done using a beta emitter source consisting of a Sr^{90}/Y^{90} in secular equilibrium. The electrons enter a permanent dipole magnet made of two 5.08x5.08x2.54 cm^3 blocks of Neodymium Iron Boron encased within an iron support frame and separated by a distance of 2cm. The measured Gaussian-like magnetic field separates the energies of the beta particles exiting the magnet. These electrons were then collected on an array made from sixteen 1mm thick scintillating fibers. The experimental data were compared against the ICRU database. The Geant4 simulation was developed to understand the energy loss and spectra obtained during the actual experiment. Forward (backward) simulation were done to generate (reconstruct) the (secondary) primary energy distribution of the source. Preliminary results of this study will be discussed.

9:00AM H25.00004 Comparison of Fluid Attenuated Inversion Recovery Sequence with Spin Echo T_2 Weighted MRI for Characterization of Brain Pathology , INDRA SAHU, SUNY Albany, SHESHKANT ARYAL, Tribhuvan University, SHANTA SHRESTHA, Tribhuvan University, Institute of Medicine, RAM GHIMIRE, Tribhuvan University,Institute of Medicine, KEITH EARLE, SUNY Albany — Twenty cases of different brain pathology have been studied via MRI using an open resistive magnet with magnetic field strength of 0.2 Tesla. The relative signal intensity with respect to the repetition time (TR) at fixed echo time (TE) 0.11 sec. has been studied. It was found that the signal intensity saturates for most lesions beyond a certain TR$\sim$6 sec in the T_2 - weighted image. The signal intensity differs with respect to the inversion time (TI) for fat and cerebrospinal fluid (CSF). It was found that the intensity is nulled for CSF at TI $\sim$1.5 sec. and for Fat at TI $\sim$ 0.10 sec in the FLAIR imaging sequence. Thus the intensity of the lesions is qualitatively different for the two sequences. From the radiological diagnostic point of view, it was concluded that the FLAIR sequence is more useful for the detection of lesions compared to T_2 sequences.

9:12AM H25.00005 Experimental test of specific predictions of a model for the oscillatory response of p53 to DNA damage. , GUSTAVO STOLOVITZKY, IBM T.J. Watson Research Center, Yorktown Heights, New York;, JOHN WAGNER, J. JEREMY RICE, IBM T.J. Watson Research Center, Yorktown Heights, New York, LAN MA, The Univ. of Texas Southwestern Medical Center, Dallas, Texas, WENWEI HU, ZHAOHUI FENG, Cancer Inst of New Jersey, Univ. of Med and Dent. NJ, New Brunswick, New Jersey, ARNOLD LEVINE, School of Natural Sciences, Institute for Advanced study, Princeton, New Jersey — We have proposed a model for radiation-induced oscillations of the p53-mdm2 system that makes specific predictions about the range of both p53 and mdm2 transcription rates that support oscillation. Our model predicts that in cells with a polymorphism in the mdm2 gene (SNP309) that enhances mdm2 transcription levels, oscillations disappear. The kinetics of the p53 and Mdm2 levels measured in cells with different genotype at the SNP309 locus show that oscillations of p53 and Mdm2 are observed in the cells wild type for mdm2 SNP309 but not in cells homozygous for mdm2 SNP309. By using H1299 cell line expressing wild-type p53 under a tetracycline-regulated promoter we found that only when p53 levels are in a certain range, oscillation can be observed after stress. This study provides evidence that proper range of the p53 and Mdm2 levels are required for the coordinated p53-Mdm2 oscillation upon stress.

9:24AM H25.00006 Impedance Analysis of Ovarian Cancer Cells upon Challenge with C-terminal Clostridium Perfringens Enterotoxin[1] , GEOFFREY GORDON, CHUN-MIN LO, University of South Florida — Both in vitro and animal studies in breast, prostate, and ovarian cancers have shown that clostridium perfringens enterotoxin (CPE), which binds to CLDN4, may have an important therapeutic benefit, as it is rapidly cytotoxic in tissues overexpressing CLDN4. This study sought to evaluate the ability of C-terminal clostridium perfringens enterotoxin (C-CPE), a CLDN4-targetting molecule, to disrupt tight junction barrier function. Electric cell-substrate impedance sensing (ECIS) was used to measure both junctional resistance and average cell-substrate separation of ovarian cancer cell lines after exposure to C-CPE. A total of 14 ovarian cancer cell lines were used, and included cell lines derived from serous, mucinous, and clear cells. Our results showed that junctional resistance increases as CLDN4 expression increases. In addition, C-CPE is non-cytotoxic in ovarian cancer cells expressing CLDN4. However, exposure to C-CPE results in a significant ($p<0.05$) dose- and CLDN4-dependent decrease in junctional resistance and an increase in cell-substrate separation. Treatment of ovarian cancer cell lines with C-CPE disrupts tight junction barrier function.

[1]Support: Florida Space Grant Consortium.

9:36AM H25.00007 Understanding Radiotherapy-Induced Second Cancers , DAVID BRENNER, Columbia University — There is increasing concern regarding radiation-related second-cancer risks in long-term radiotherapy survivors, and a corresponding need to be able to predict cancer risks at high radiation doses. While cancer risks at moderately low radiation doses are reasonably understood from A-bomb survivor studies, there is much more uncertainty at the high doses used in radiotherapy. It has generally been assumed that cancer induction decreases rapidly at high doses due to cell killing. However, most recent studies of radiation-induced second cancers in the lung and breast, covering a very wide range of doses, contradict this assumption. A likely resolution of this disagreement comes from considering cellular repopulation during and after radiation exposure. Repopulation / proliferation with a significant number radiation-induced pre-malignant cells, tends to counteract the effect of cell killing, and keeps the induced cancer risks higher at high doses. We describe and apply a biologically based, minimally parameterized model of dose-dependent cancer risks, incorporating carcinogenic effects, cell killing and, additionally, proliferation / repopulation effects. The situation is somewhat different for radiation-induced leukemia, as repopulation via the blood stream tends to be with cells that originated father away from the treatment volume than is the case for solid second cancers, thus containing a smaller proportion of radiation-damaged cells. The model predictions agree well with recent data on second cancer risks, both for radiation-induced solid cancers and for radiation-induced leukemias. Incorporating repopulation effects provides both a mechanistic understanding of cancer risks at high doses, as well as providing a practical methodology for predicting, and therefore potentially minimizing, cancer risks in organs exposed to high radiation doses during radiotherapy.

10:12AM H25.00008 Photoelectric Effect, Bremsstrahlung, and Compton Effect Formulas Should Contain Rotational and Vibrational Energies , STEWART BREKKE, Northeastern Illinois University (former grad student) — The kinetic energy element in the Photoelectric Effect, Bremsstrahlung and Compton Effect formulas should also include besides the linear kinetic energy element rotational (spin) and vibrational kinetic energy elements. In the photoelectric effect the formula should be $[h\nu = 1/2mv^2 + 1/2I\omega_r^2 + (n+1/2)\hbar\omega_v + \phi]$ where ω_r is the rotational angular velocity and ω_v is the vibrational angular frequency. Similarly, in Bremsstrahlung the kinetic energy lost to photon creation at total braking shoudl be $[1/2mv^2 + 1/2I\omega_r^2 + (n+1/2)\hbar\omega_v = eV = h\nu_{max}]$. The resulting kinetic energy of a recoil particle in the Compton Effect should be $[1/2mv^2 + 1/2I\omega_r^2 + (n+1/2)\hbar\omega_v = (h\nu)\Delta\lambda/(\lambda + \Delta\lambda)]$. Also, in pair production and annhiliation the kinetic energies of the annhiliated pair and created pair should include the spin and vibrational energies.

10:24AM H25.00009 Exploring the Role of Calcium in Cardiac Cell Dynamics[1] , CAROLYN BERGER, SALIM IDRISS, NED ROUZE, DAVID HALL, DANIEL GAUTHIER, Duke University — Bifurcations in the electrical response of cardiac tissue can destabilize spatio-temporal waves of electrochemical activity in the heart, leading to tachycardia or even fibrillation. Therefore, it is important to understand the mechanisms that cause instabilities in cardiac tissue.Traditionally, researchers have focused on understanding how the transmembrane voltage is altered in response to an increase in pacing rate, i.e. a shorter time interval between propagating electrochemical waves. However, the dynamics of the transmembrane voltage are coupled to the activity of several ions that traverse the membrane. Therefore, to fully understand the mechanisms that drive these bifurcations, we must include an investigation of the ionic behavior. We will present our recent investigation of the role of intracellular calcium in an experimental testbed of frog ventricle. Calcium and voltage are measured simultaneously, allowing for the previous research regarding voltage to guide our understanding of the calcium dynamics.

[1]NSF Grants PHY-0549259 and PHY-0243584

10:36AM H25.00010 Biological Response of Cancer and Normal Cells on Irradiation from Electrons with Energies up to 200 keV. , YURIY PRILEPSKIY, Hampton University, JLAB, CAMI COLLABORATION, HAMPTON UNIVERSITY COLLABORATION — This paper presents continuation data of the series of experiments with the electron gun of the CEBAF machine at Jefferson Lab (Newport News, VA), which is capable of delivering electrons with energies up to 200 keV. This 1.5 GHz beam permits to generate cellular damage within minutes. We have performed irradiation of cancer and normal cells with different electron energies and currents to investigate cell biological responses. The biological response is measured through proteomics analysis before and after irradiation. The living cells are encased in special air containers allowing proper positioning in vacuum where the electrons are present. The containers receive the irradiation from the mono energetic electrons with energy up to 120 keV, resulting in an irradiation from both electrons and a small number of photons from the original beam passing through the thin container window. This window allows approximately half of the beam to come through. The study will permit to address the physical processes involved in the RBE and LET at a level that supersedes current data listed in the literature. We will discuss the experimental setup and the second stage of data collected with the new more developed system. This research is part of a global program to provide detailed information for the understanding of radiation based cancer treatments.

Tuesday, March 6, 2007 8:00AM - 11:00AM –

Session H34 DBP: DNA and Protein Analysis with Nanofluidics Colorado Convention Center 404

8:00AM H34.00001 Single Molecule Manipulation and Analysis in Nanofluidic Systems , HAROLD CRAIGHEAD, Cornell Univeristy — We have used simple small-scale structures to isolate and manipulate individual biomolecules in order to observe there activity and identity. Nanofluidic devices with dimensions, smaller than a relevant molecular length scale, have been used to sort or control the confirmation of long biopolymers such as DNA. Structurally-derived entropic and frictional forces balanced against the forces resulting from applied fields can elongate and controllably move a selected molecule. This can be used for measuring the length of the DNA or presenting it in an oriented manner for analysis. We have also employed metallic apertures a few tens of nanometers in diameter to confine a region of optical excitation to a volume on the order of 10^{-20} liters, which allows the observation of single molecule motion and binding activity at meaningful rates and concentrations. This approach enables measuring the motility of proteins and binding of individual molecules in lipid layers and cell membranes. Small fluid channels have also been used to isolate individual optically detected molecules for evaluation in flowing systems. The measurement of mobility and detection of discrete molecular binding events can be done at the individual molecule level in such fluid systems.

8:36AM H34.00002 Single-molecule manipulation of genomic DNA in extensional flow for haplotyping applications , REBECCA DYLLA-SPEARS, LYDIA SOHN, SUSAN MULLER, University of California, Berkeley — We have developed a method amenable to haplotyping and manipulation of single molecules of double-stranded genomic DNA. Fluorescent polystyrene beads that are surface-functionalized with site-specific probes are incubated with fluorescently labeled double-stranded lambda-DNA. The solution is introduced into a microfluidic cross slot where the DNA molecules are trapped and elongated at the stagnation point of the planar extensional flow. The degree of elongation can be controlled using the flow strength in the device, as demonstrated by Perkins, Smith, and Chu (Science 1997). Beads bound along the stretched DNA may be directly observed and their locations along the backbone determined using fluorescence microscopy.

8:48AM H34.00003 A Single–Step Photolithographic Interface for Cell-Free Gene Circuits and Active Biochips , AMNON BUXBOIM, MAYA BAR-DAGAN, VERONICA FRYDMAN, DAVID ZBAIDA, MARGHERITA MORPURGO, ROY BAR-ZIV, Weizmann Institute of Science — We developed a biochip platform technology suitable for controlled cell-free gene expression at the micron scale. A new hybrid molecule, "daisy," was designed and synthesized to form in a single step a bio-compatible lithographic interface on silicon dioxide. A protocol was formulated for immobilization of linear DNA molecules thousands of base pairs long on daisy-coated surfaces to submicron spatial resolution and up to high densities. On-chip protein synthesis can be obtained with dynamic range of up to four orders of magnitude and minimal nonspecific activity. En route to on-chip artificial gene circuits, a simple two-stage gene cascade was built in which the protein synthesized at the first location diffuses to regulate the synthesis of another protein at a second location. The current approach opens possibilities for laboratories not proficient in surface chemistry to design active biochips based on cell-free gene expression with applications in artificial systems and synthetic biology.

9:00AM H34.00004 Mode Transition of RNA Trap by Electric and Hydraulic Force Field in Microfluidic Taper Shape Channel , YUZURU TAKAMURA, Jpn. Adv. Inst. of Sci. and Tech. (JAIST) and PRESTO/JST, KUNIMITSU UENO, WAKO NAGASAKA, YUICHI TOMIZAWA, EIICHI TAMIYA, Jpn. Adv. Inst. of Sci. and Tech. (JAIST) — We have discovered a phenomenon of accumulation of DNA near the constricted position of a microfluidic chip with taper shaped channel when both hydro pressure and electric field are applied in opposite directions. However, RNA has not been able to trap so far, unlike huge and uniformly double stranded DNA molecules, RNAs are smaller in size and single stranded with complicated conformation like blocks in lysed cell solution. In this paper, we will report not only large but also small RNA (100∼10b) are successfully trapped in relatively large microfluidic taper shape channel (width >10um). RNA are trapped in circular motion near the constricted position of taper shape channel, and the position and shape of the trapped RNA are controlled and make mode transition by changing the hydraulic and the electric force. Using this technique, smaller size molecule can be trapped in larger micro fluidic structure compared to the trap using dielectrophoresis. This technique is expected to establish easy and practical device as a direct total RNA extraction tool from living cells or tissues.

9:12AM H34.00005 The Physics of Nanoconfined DNA: Varying Temperature and Ionic Conditions , WALTER REISNER[1], ANDERS KRISTENSEN, Danish Technical University, JONAS TEGENFELDT, Dept of Physics Lund University, HENRIK FLYVBJERG, NIELS B. LARSEN, RISØ National Laboratory — Top-down approaches to nanotechnology have the potential to revolutionize biology by making possible the construction of chip-based devices with nanoscale features that can not only detect, separate and analyze single DNA molecules by size but also–it is hoped in the future–actually sequence at the single molecule level. Using electron beam lithography we have fabricated nanochannel devices in fused silica with dimensions on order of 100x100nm and lengths of 100s of micrometers. Both dsDNA and ssDNA molecules, imaged via fluorescence microscopy, are observed to stretch out in these effectively one dimensional systems. We present measurements of the DNA extension as a function of ionic strength. We also demonstrate how the DNA melting transition can be probed in real time by heating the nanochannel extended DNA.

[1]Alternative affiliation: RISØ National Laboratory

9:24AM H34.00006 Modeling DNA Separation in Entropic Trap Device , ALEX VAUGHN, YONGMEI WANG[1], University of Memphis — DNA electrophoresis in the entropic trap device fabricated by Craighead and coworkers has some interesting properties that allow long chains to be separated; moreover, their results showed that long chains had higher mobility than short chains, a counter-intuitive result. The mechanism by which the device works is not well understood. This study seeks therefore to understand the device's mechanism more thoroughly with a desire to provide the knowledge necessary to optimize the separation of long chains of DNA. The study uses dynamic Monte Carlo simulations on a simple-cubic lattice to model the separation of DNA. The simulation algorithm was first tested by confirming the chain length independence of the electrophoretic mobility of DNA in bulk solution, a well-known experimental fact. When DNA chains are constrained in a slit channel, the electrophoretic mobility is still independent of chain length. If DNA-wall interactions are added to the model, then the mobility decreases with the chain length for short chains and reaches a plateau for long chains. In a channel with entropic traps, the mobility is found to increase with the chain length, consistent with experimental results by Craighead and coworkers. We also found that a better separation was achieved when the trap was made deeper.

[1]Department of Chemistry

9:36AM H34.00007 Imaging Biological Systems using Dielectric Near-Field Microscopy , KEITH BROWN, DAVID ISSADORE, TOM HUNT, ROBERT WESTERVELT, Harvard University, WESTERVELT GROUP TEAM — We have developed a dielectric spectrometer for use on biological systems. The spectrum of dielectric response to RF electric fields is analogous to color as an optical response. Measurement of the dielectric spectrum from $\sim$ 10 kHz to $\sim$ 3 GHz will reveal information about the structure and conditions of protein solutions, protein crystals and biological tissues. We designed and built a system to test biological samples in a microfluidic chamber mounted on a circuit board. The apparatus measures the RF dielectric spectrum directly, or by analyzing the pulse response in the time domain. We have constructed several versions of the hardware for sensitive capacitive measurements, including two types of capacitive bridges, and a transmission line, incorporating precision electronics and local generation of pulses. A goal is to scale the system down and implement many dielectric spectrometers as an array of pixels on a CMOS chip for dielectric near-field microscopy of biological samples. This work made possible by NSEC NSF grant PHY-0117795 and the NCI MIT-Harvard CCNE.

9:48AM H34.00008 Fundamental limits of detection with nanowire FET chem/bio sensors in subthreshold and linear regimes , XUAN GAO, Harvard University, GENGFENG ZHENG, CHARLES LIEBER — Nanowire field effect transistors (NW-FETs) have been demonstrated to be powerful sensors for the detection of biological and chemical species, and thus understanding and pushing their intrinsic sensitivity limits could have a significant impact on a broad-range of applications of these devices. We report studies of the response of silicon-NW-FET sensors as the devices are tuned from linear to subthreshold regimes by electrochemical gating. Conductance versus solution pH data show that operation in the subthreshold regime can increase both the percentage change in conductance and the signal to noise ratio of the device by over ten times compared to the linear regime. We also demonstrate that operating in the subthreshold regime yields improvement in the detection limit for the cancer marker protein PSA with detection down to $\sim$1.5 fM for a device with $\sim$0.75 pM detection limit in the linear regime. Analysis of these results shows that the sensitivity improvement is due to the more effective surface charge gating resulting from the reduced screening by carriers. In addition, the effect of NW diameters and the intrinsic charge detection limit for using NW-FET devices will be described. Our work shows that optimization of NW-FET structure and operating conditions can provide a significant enhancement as well as a fundamental understanding of the sensitivity limits for nano-FET sensors.

10:00AM H34.00009 Modeling PCR in Natural Convection Systems[1] , KEVIN DORFMAN, University of Minnesota, EHUD YARIV, GUY BEN DOV, Technion, Israel — Polymerase chain reaction (PCR) is a biochemical protocol for making many copies of a DNA template by thermal cycling between a hot temperature (where the strands are separated) and a cool temperature (where primers are annealed). In natural convection PCR, the requisite thermal cycling is provided by a buoyancy-driven circulating flow of the carrying buffer between a lower hot plate (at the denaturing temperature) and an upper cold plate (at the annealing temperature). We present a multi-component convection-diffusion-reaction model for natural convection-driven PCR when both primers and PCR enzyme are in excess. The evolution of the DNA population achieves a stationary state, wherein the problem is recast as an eigenvalue problem for computing the exponential amplification rate. With a realistic choice of parameters, the model predicts a doubling time on the order of two minutes, in agreement with experiments and much slower than the fluid cycling time. In contrast to what might be expected, the doubling time increases monotonically with the diffusion coefficient.

[1]Supported by the Human Frontier Science Program.

10:12AM H34.00010 Tethered DNA molecules stretched by an electric field: A Molecular Dynamics Study. , GARY SLATER, MARTIN BERTRAND, University of Ottawa — It has been predicted by Long, Ajdari and Viovy (Phys. Rev. Lett., 1996, 76:3858) that the mechanical force necessary to stall a DNA molecule during electrophoresis is substantially smaller than the sum of the electrical forces applied on all of its monomers. In fact, it should be proportional to its hydrodynamic friction coefficient, which may vary with the molecular conformation. We have tested this prediction using coarse-grained Molecular Dynamics simulations in which we explicitly included the polymer, the solvent, the counterions and the salt. Our results show that the above prediction is indeed valid. In fact, our data demonstrate that there is a universal linear relationship between the stall force and the product of the electrical field and the radius of gyration of the polyelectrolyte. This remarkable relationship holds even when the electric forces stretch the DNA molecule near full extension. We thus conclude that an electrophoretic field is equivalent to a fluid flow, as suggested by Long, Ajdari and Viovy. This has profound implications for the development of a theoretical framework that can explain the electrophoresis of hybrid DNA-protein molecules.

10:24AM H34.00011 Electrical Noise Characterization of Noble Gas Ion Beam Fabricated Nanopore Detectors , RYAN ROLLINGS, BRADLEY LEDDEN, ERIC KRUEGER, GREG SALAMO, JIALI LI, University of Arkansas, JOHN CHERVINSKY, JENE GOLOVCHENKO, Harvard University — Nanopores fabricated with low energy noble gas ion beams in a silicon nitride membrane can be employed as the fundamental element of single biomolecule detection and characterization devices. The effect of morphology, annealing, and physical surface treatments are systematically studied to determine their effect on the electrical noise characteristics of the nanopore when used as part of a nanofluidic detector. Atomic Force Microscopy (AFM) is used to measure the morphology of the region near the pore, while X-ray Photoelectron Spectroscopy (XPS) and Rutherford Backscattering (RBS) are used to measure the change in the surface composition with annealing as well as initial depth profiles of imbedded ions. We qualitatively discuss the underlying physical processes that contribute to the electrical noise characteristics of the pore in comparison with our measurements and present optimized conditions for fabricating the quietest pores.

10:36AM H34.00012 Self-trapping and stretching of DNA using single nano-height micropillar , PO-KENG LIN, Department of Physics, National Taiwan University, Taipei, Taiwan, CHI-CHENG FU, Institute of Atomic and Molecular Science, Academia Sinica, Taipei, Taiwan, Y.-L. CHEN, Institute of physics and Applied Sciences, Academia Sinica, Taipei, Taiwan, W. S. FANN, Institute of Atomic and Molecular Science, Academia Sinica, Taipei, Taiwan — We propose a novel method to trapping ds-DNA molecules in 30-100nm slit-like nanochannel with single micropillar. In this environment the DNA molecules unusually extend around obstacles such as pillars or walls. The DNA molecules appear to have quasi-one dimensional dynamics even though the confinement is quasi-two dimensional. The trapping process can occur only when the channel height below the Kuhn length of ds-DNA. We experimentally observe the Brownian motions of the DNA using wide-field fluorescence microscopy. The static and dynamic scaling with DNA length (9.4$\sim$166 kbps) and channel height (30$\sim$240nm) have been analyzed and compared with the experimental results of DNA confined in the square nanochannels in the literatures (W. Reisner et al., Phys. Rev. Lett. 94 196101 (2005)). This micro/nano fluidic device can be applied to study the multi-step biochemical reactions in confinements such as DNA folding induced by protein and restriction mapping of DNA in the future.

10:48AM H34.00013 Spatial Detection of Submicron Particles with Integrated Circuit Charge Sensors[1] , DAVID ISSADORE, TOM HUNT, ROBERT WESTERVELT, Harvard University — Using a standard MOSIS 0.35 micron Integrated Circuit process, we have built a position sensor for use in all-electrical feedback traps for submicron particles. The device has four transistors in a square, with floating gates that capacitively detect a charged particle in a microfluidic chamber above. The four transistors form the front ends of two independent differential amplifiers that report the x and y position of the particle. Future work towards integration of dielectrophoretic feedback forces for an all-electrical "Anti-Brownian motion" trap will be discussed.

[1]NSEC NSF grant PHY-0117795 and the NCI MIT-Harvard CCNE.

Tuesday, March 6, 2007 8:00AM - 11:00AM –
Session H35 DBP DCP: Emerging Spectroscopic Techniques Colorado Convention Center 405

8:00AM H35.00001 BREAK –

9:48AM H35.00002 Real-time detection of multiple biomolecular reactions on a functionalized glass surface using a scanning oblique-incidence optical reflectivity difference (an ellipsometric technique).[1] , YUNG-SHIN SUN, JAMES P. LANDRY, XIANGDONG ZHU, Dept. of Physics, Univ. of California at Davis — One of the enabling platforms in proteomic research is parallel (high-throughput) detection of multiple biomolecular interactions on a microarray. To keep conformational and in turn functional integrity of protein molecules, label-free detection is desirable. We have developed an oblique-incidence optical reflectivity difference (OI-RD) technique for label-free measurements of protein reactions with molecular targets in microarray format immobilized on functionalized glass surface. As an ellipsometric technique, OI-RD measures changes in thickness and/or optical dielectric response instead of fluorescence. By incorporating total internal refection geometry and a multi-element photodiode array detector, we demonstrate how such the OI-RD technique can be efficiently used to measure multiple protein reactions in real time with surface-immobilized molecules or molecular groups on a glass substrate.

[1]This work is supported by NSF Center for Biophotonics Science and Technology, UC-GREAT, and NIH.

10:00AM H35.00003 In Situ X-ray Reflectivity Studies of Protein Adsorption onto Functionalized Surfaces[1] , ANDREW RICHTER, Valparaiso University — The adsorption of protein films onto solid surfaces, both artificial and naturally occurring, have been widely studied using a variety of techniques due to their importance in medicine, biomedical applications, and the general understanding of protein structure and function. What have yet to be performed are in situ, time-resolved, high-resolution structural studies of these systems. We have begun a project that uses the technique of in situ x-ray reflectivity to obtain highly resolved structural information with time resolution on the order of minutes. This talk will present our first findings of serum albumin and immunoglobulin G films on hydrophobic self-assembled monolayers. The protein films are readily observable, showing extensive denaturing after adsorption with a slow decay of density into the aqueous solution. Additionally, a thin low-density region that occurs between the hydrophobic film and the solution persists after protein deposition. Comparisons to films that are removed from solution, the influence of solution concentration, the effects of x-ray damage, and the time scales for protein film formation and evolution will also be discussed.

[1]This work is supported by an award from Research Corporation, CC6924

10:12AM H35.00004 Mid-IR spectra of the bio-related molecules in the gas phase , YONGJUN HU, ELLIOT R. BENSTEIN, Department of Chemistry, Colorado State Univ. — Mid-IR spectra of gas phase bio-related molecules R-OH, R-COOH and simple non-aromatic amino acids, such as glycine and valine, detected by vacuum ultraviolet (VUV), 10.5 eV single photon ionization of supersonically expanded and cooled samples, are presented and discussed. Molecules and their fragment species, generated by a proton transfer reaction following ionization, are identified by time of flight mass spectroscopy. The fundamentals and overtones of the CH and OH stretches and some combination bands are identified in the spectra. Rotational resolution for the OH mode and its first overtone yield an estimate of ∼50 K for the methanol monomer in the supersonic beam. Two neutral C_2H_5OH conformers can be identified by high sensitivity IR plus VUV nonresonant ionization and fragmentation detected (NRIFD-IR) vibrational spectroscopy. Free OH and NH stretches are missing in the spectrum of glycine and valine, indicating that the strong intra-molecular hydrogen bonds are formed in these gas phase species.

10:24AM H35.00005 Single Quantum Dots Imaged with Resonance Rayleigh Scattering Do Not Blink , DAVID W. WARD, WEI MIN, ETHAN S. KARP, XIAOLIANG SUNNEY XIE, Harvard University, Department of Chemistry and Chemical Biology — Semiconductor quantum dots have become a robust fluorescent marker for the life sciences. Two key issues limit the broad use of quantum dots as fluorescent markers: heterogeneous emission and non-radiant dark populations. All bright quantum dots blink stochastically, have considerable heterogeneity in their emission, and have fluctuations in their fluorescence lifetimes, limiting their utility as single particle trackers by introducing potentially large interruptions in particle trajectories. Further, a significant fraction does not fluoresce at all, undermining biophysical studies such as immuno-fluorescence. We present an alternative or complement to fluorescent imaging of quantum dots. We have developed a new technique, resonant Rayleigh scattering (RRS) microscopy, for imaging single quantum dots which does not exhibit blinking. Detection of individual quantum dots, both surface immobilized and freely diffusing in aqueous solution, is demonstrated. Non-fluorescent populations of quantum dots are visible through RRS microscopy. Though other non-fluorescence detection techniques exist they are significantly more complicated than our technique, which requires minimal alteration of a conventional confocal fluorescence microscope.

10:36AM H35.00006 Development of 0.24 THz pulsed electron paramagnetic resonance to "film" proteins in action with the UCSB free electron laser , SUSUMU TAKAHASHI, DAN G. ALLEN, KIYOTAKA AKABORI, MELISSA ANHOLM, HIEU NGUYEN, SANGWOO KIM, MARK S. SHERWIN, University of California Santa Barbara, JOHAN VAN TOL, LOUIS-CLAUDE BRUNEL, National High Magnetic Field Laboratory — Pulsed electron paramagnetic resonance (EPR) is extremely useful to study the fast dynamics of molecules. Currently, most high-power pulsed EPR experiments are performed near 10 GHz, with a time resolution of 100 ns. The spin dephasing times of spin labels on proteins in aqueous solution are tens of ns. Thus, conventional pulsed EPR measurements of proteins are performed on frozen samples. There exist instruments which operate at 95 GHz with time resolution shorter than 100 ns. We present the development of a 0.24 THz pulsed EPR system which is expected to have sub-ns time resolution, enabling the EPR study of proteins in solution. The system uses the UCSB free electron laser (FEL) to produce kW-level pulses at 240 GHz. A "pulse-slicer" shortens the FEL's microsecond pulses to the ns range. Sequences of two or three pulses separated by up to 25 ns will be made using a home-made delay line. A superheterodyne detection system is being fabricated to be sensitive enough to detect 1nW signals and also protected from kW FEL inputs.

10:48AM H35.00007 Three-Dimensional Imaging of Single Large Macromolecules Using Equally Sloped Tomography[1] , E. LEE, B. FAHIMIAN, J. MA, University of California at Los Angeles, C. IANCU, C. SULOWAY, E. WRIGHT, G. JENSEN, California Institute of Technology, J. MIAO, University of California at Los Angeles, UNIVERSITY OF CALIFORNIA AT LOS ANGELES TEAM, CALIFORNIA INSTITUTE OF TECHNOLOGY COLLABORATION — We report the development of equally sloped tomography for the reconstruction of the 3D structure of single large macromolecules. In a combination of pseudo-polar fast Fourier transform and the oversampling method with an iterative algorithm, equally sloped tomography makes superior 3D reconstruction to conventional tomography which has an intrinsic drawback due to the use of equally angled 2D projections. By employing equally sloped tomography and cryo electron microscopy, we have obtained the 3D structure of single hemocyanin protein molecules and HIV viruses at $\sim$ 5 nanometer resolution. Preliminary analysis based on cross- correlation has indicated that the 3D images using equally sloped tomography are superior to those of the conventional method. We believe this general approach will find broad applications in high-resolution 3D imaging of large macromolecules.

[1]NSF, DOE

Tuesday, March 6, 2007 11:15AM - 2:03PM –

Session J21 DBP: Medical Physics: Approaches to Cancer Treatment Colorado Convention Center 106

11:15AM J21.00001 The use of Monte Carlo methods in heavy charged particle radiation therapy.[1] , HARALD PAGANETTI, Massachusetts General Hospital — This presentation will demonstrate the importance of Monte Carlo (MC) simulations in proton therapy. MC applications will be shown which aim at 1. Modeling of the beam delivery system. MC can be used for quality assurance verification in order to understand the sensitivity of beam characteristics and how these influence the dose delivered. 2. Patient treatment dose verification. The capability of reading CT information has to be implemented into the MC code. Simulating the ionization chamber reading in the treatment head allows the dose to be specified for treatment plan verification. 3. 4D dose calculation. The patient geometry may be time dependent due to respiratory or cardiac motion. To consider this, patient specific 4D CT data can be used in combination with MC simulations. 4. Simulating positron emission. Positron emitters are produced via nuclear interactions along the beam path penetration and can be detected after treatment. Comparison between measured and MC simulated PET images can provide feedback on the intended dose in the patient. 5. Studies on radiation induced cancer risk. MC calculations based on computational anthropomorphic phantoms allow the estimation of organ dose and particle energy distributions everywhere in the patient.

[1]Supported by NCI grants: PO1 CA21239; RO1 CA111590; RO1 CA116743

11:51AM J21.00002 Simulating the migration of multiple cancer cells in the bloodstream , KENG-HWEE CHIAM, Institute of High Performance Computing, Singapore — We model the migration of cancer cells that have broken away from a tumor and are circulating in the bloodstream. Using the immersed boundary method and culling from literature the material properties of cancer cells, we solve for the deformation of the cells represented as "immersed boundaries" being advected by the shear flow of the bloodstream. We solve for the magnitude of the deformation as a function of the flow magnitude as well as the adhesive properties between the cancer cells and the endothelial cells of the bloodstream. We also simulate the migration characteristics as a function of the migrating cell density. From these, we calculate rough approximations of the metastatic rate and efficiency.

12:03PM J21.00003 Multicatheter Device for Brachytherapy Treatment , CARLOS VELASCO, PAUL GUEYE, CYNTHIA KEPPEL, Hampton University, CAMI TEAM — Low dose rate brachytherapy treatment for prostate cancer encompasses the delivery of capsules containing radioactive material into the prostate's cancerous tissue via injection through needles. High dose rate brachytherapy treatment for prostate cancer follows the same concept with the difference that the radioactive source has a higher activity and it is placed temporarily into the patient. For this reason, the source is driven by an afterloading device that moves the source into the catheters and back into a shielded container. From both HDR and LDR brachytherapy, two issues remain unaddressed: homogeneity and localization. Sources not being homogeneous result in a delivered dose that does not correspond to the treatment plan. In the case of HDR, the afterloader not always places the source where it should within the catheter. This results in undertreatment of the cancerous tissue as well as damage to healthy tissue. To address both issues we have placed scintillating fiber into brachytherapy needles. If placed geometrically around the radioactive seeds we are able to check for homogeneity in the sources. At the same time, by analyzing the detected signals we are trying to determine the exact physical position of the seeds within the catheter. Using a radioactive source, we have taken measurements to calibrate the device and measurements under water to simulate living tissue environment. Results are discussed.

12:15PM J21.00004 Calibration Of An Active Mammosite Using A Low Activity Sr-90 Radioactive Source , JACQUELYN WINSTON, Morgan State University, CAMI COLLABORATION — The latest involvement of the Brachytherapy research group of the medical physics program at Hampton University is in the development of a scintillating fiber based detector for the breast cancer specific Mammosite (balloon device) from Cytyc Inc. Recent data were acquired at a local hospital to evaluate the possibility of measuring the dose distribution during breast Brachytherapy cancer treatments with this device. Since sub-millimeter accuracy in position is required, precision of the device relies on the accurate calibration of the scintillating fiber element. As part of a collaboration work, data were acquired for that purpose at Hampton University and subsequently analyzed at Morgan State University. An 8 mm diameter strontium-90 radioactive field source with a low activity of 25 μCi was used along with a dedicated LabView data acquisition system. We will discuss the data collected and address some of the features of this novel system.

12:27PM J21.00005 Brachytherapy with an improved MammoSite Radiation Therapy System , NANDA KARTHIK, CYNTHIA KEPPEL, VAHAGN NAZARYAN, Hampton University — Accelerated partial breast irradiation treatment utilizing the MammoSite Radiation Therapy System (MRTS) is becoming increasingly popular. Clinical studies show excellent results for disease control and localization, as well as for cosmesis. Several Phase I, II, and III clinical trials have found significant association between skin spacing and cosmetic results after treatment with MRTS. As a result, patients with skin spacing less then 7 mm are not recommended to undergo this treatment. We have developed a practical innovation to the MammoSite brachytherapy methodology that is directed to overcome the skin spacing problem. The idea is to partially shield the radiation dose to the skin where the skin spacing is less then 7 mm, thereby protecting the skin from radiation damage. Our innovation to the MRTS will allow better cosmetic outcome in breast conserving therapy (BCT), and will furthermore allow more women to take advantage of BCT. Reduction in skin radiation exposure is particularly important for patients also undergoing adjuvant chemotherapy. We will present the method and preliminary laboratory and Monte Carlo simulation results.

12:39PM J21.00006 Recent advances in radiation cancer therapy , C.-M. CHARLIE MA, Fox Chase Cancer Center — This paper presents the recent advances in radiation therapy techniques for the treatment of cancer. Significant improvement has been made in imaging techniques such as CT, MRI, MRS, PET, ultrasound, etc. that have brought marked advances in tumor target and critical structure delineation for treatment planning and patient setup and target localization for accurate dose delivery in radiation therapy of cancer. Recent developments of novel treatment modalities including intensity-modulated x-ray therapy (IMXT), energy- and intensity modulated electron therapy (MERT) and intensity modulated proton therapy (IMPT) together with the use of advanced image guidance have enabled precise dose delivery for dose escalation and hypofractionation studies that may result in better local control and quality of life. Particle acceleration using laser-induced plasmas has great potential for new cost-effective radiation sources that may have a great impact on the management of cancer using radiation therapy.

1:15PM J21.00007 An Active MammoSite© for Breast Cancer Treatment , ALICE QUAN, Hampton University, CAMI COLLABORATION — Breast brachytherapy using the MammoSite© balloon catheter is one of the latest developments in breast cancer treatment and is the most performed method of brachytherapy. A high activity ^{192}Ir radioactive source is pushed inside the shaft of the device until it reaches the center of the balloon. The latest involvement of the Brachytherapy research group of the medical physics program at Hampton University is in the development of a scintillating fiber based detector for the breast cancer specific MammoSite© balloon catheter from Cytyc, Inc. During the summer 2006, data were acquired at a local hospital (Bon Secours DePaul Medical Center) to evaluate the possibility of measuring the source location and dose distribution during breast brachytherapy cancer treatments with this device. Two 0.5 mm^2 and 1.0 mm^2 scintillating fibers were used for these experiments. We used two modified MammoSite© devices, each housing an extra tubing within which the fibers were inserted. The results from these runs confirm the possibility of an active MammoSite© to monitor the location of the source as well its dose distribution during patient treatment. We will describe the experimental setup and discuss the data.

1:27PM J21.00008 Optical Interferometric Response of Living Tissue to Cytoskeletal Anticancer Drugs , DAVID NOLTE, KWAN JEONG, JOHN TUREK, Purdue University — Living tissue illuminated by short-coherence light can be optically sectioned in three dimensions using coherent detection such as interferometry. We have developed full-field coherence-gated imaging of tissue using digital holography. Two-dimensional image sections from a fixed depth are recorded as interference fringes with a CCD camera located at the optical Fourier plane. Fast Fourier transform of the digital hologram yields the depth-selected image. When the tissue is living, highly dynamic speckle is observed as fluctuating pixel intensities. The temporal autocorrelation functions are directly related to the degree of motility at depth. We have applied the cytoskeletal drugs nocodazole and colchicine to osteogenic sarcoma multicellular spheroids and observed the response holographically. Colchicine is an anticancer drug that inhibits microtubule polymerization and hence prevents spindle formation during mitosis. Nocodazole, on the other hand, depolymerizes microtubules. Both drugs preferentially inhibit rapidly-dividing cancer cells. We observe dose-response using motility as an effective contrast agent. This work opens the possibility for studies of three-dimensional motility as a multiplexed assay for drug discovery.

1:39PM J21.00009 Characterization and modeling of relative efficiency of optically stimulated luminescence Al_2O_3:C detectors exposed to heavy charged particles , GABRIEL SAWAKUCHI, EDUARDO YUKIHARA, Department of Physics, Oklahoma State University — Medical dosimetry of heavy charged particles (HCPs) and personnel space dosimetry are becoming important areas with the development of new facilities for cancer therapy of heavy ions and the increase of human activities in space. In particular, the measurement of dose in the space radiation field is one of the most challenging problems in personnel dosimetry due to the presence of a mixture of different particles with a wide range of energies. HCP creates a pattern of energy deposition around its path which is a characteristic of the type of particle and its energy. Due to different spatial distribution of dose around the HCP path, the response of the dosimeter can be significantly different for different types of particles and energies. This work characterizes the optically stimulated luminescence (OSL) response of Al_2O_3:C personnel dosimeter to different HCPs and energies. Also, a model based on track structure theory to predict the OSL response of the dosimeter is presented.

1:51PM J21.00010 Computed Tomography Measurements Using Optically Stimulated Luminescence of KBr:Eu In Real-Time. , DAVID KLEIN, Dept. of Physics, Oklahoma State University, DAVID PEAKHEART, Oklahoma University Health Sciences Center, RAZVAN GAZA, X. JOHN RONG, UT MD Anderson Cancer Center, STEPHEN MCKEEVER, Dept. of Physics, Okla. State Univ. — Increasing complexity in modern scanning geometries invalidates the concept of computed tomography dose index (CTDI) for CT dosimetry. A real-time dosimetry system using optically stimulated luminescence (OSL) of KBr:Eu is evaluated in comparison with a pencil ionization chamber for CT dosimetry in this study. CT scans were measured over a relevant range of energies and tube currents using a GE LightSpeed Ultra scanner. Complete OSL signals were obtained before, during, and after the CT scans at a rate of 10Hz. Performance was determined in part by normalizing both the initial OSL intensity and the background-subtracted integral OSL to exposure reported by an ionization chamber. OSL response normalized to exposure shows good correlation with coefficients of variation of $\sim$%5 or less. Results show that this OSL dosimetry system possesses great potential for faster, higher-resolution CT characterization and may prove a valuable alternative to CTDI.

Tuesday, March 6, 2007 11:15AM - 2:03PM –

Session J27 DMP DBP: Focus Session: DNA Translocation / Nanopores - Experiments Colorado Convention Center 301

11:15AM J27.00001 A tunable DNA spring in a nanochannel , ROBERT RIEHN, RORY STAUNTON, SHUANG FANG LIM, Dept. of Physics, NC State University, ROBIJN BRUINSMA, Department of Physics, UC Los Angeles, WALTER REISNER, Technical University of Denmark, ROBERT AUSTIN, Dept. of Physics, Princeton University — dsDNA becomes linearized when it is confined to nanofluidic channels with a cross-section of (100 nm)^2 or less, which has made them interesting for genomic DNA analyses. DNA is typically manipulated by means of electric fields. We have found that DNA undergoes a phase transition to a condensed state if an a.c. electric field is applied along the channel direction. The molecule collapses to about 1/4 of it's initial contour length. We will discuss how the effect depends on parameters such as frequency, field strength, channel dimensions, and will discuss the origin of the effect. Interestingly, DNA behaves like an artifical muscle that can be triggered by an a.c. electric field. Since the interaction is expected to hold for any solubilized polyelectrolyte, we speculate that the mechanism may lead to a new class of polymer-based mechanical actuators. These would not suffer from depolarization like piezo transducers.

11:27AM J27.00002 dsDNA and nanobubble studies using solid-state nanopores , RALPH SMEETS, Kavli Institute of Nanoscience Delft, ULRICH KEYSER, Universität Leipzig, DIEGO KRAPF, MENG-YUE WU, NYNKE DEKKER, CEES DEKKER, Kavli Institute of Nanoscience Delft — DNA transport through fabricated solid-state nanopores is studied at various salt concentrations. dsDNA translocation at 1M KCl results in current blokkades, whereas by contrast current enhancements are observed at low salt concentrations. These current changes can be understood by taking both the volume and the counter ions of the molecule into account. Nanopore conductance and noise is studied as a nanopore is moved through a laser beam. The resulting conductance profiles show strong variations in the magnitude of the conductance and the low-frequency noise. In addition, we measure an unexpected double-peak conductance profile. A nanometer-sized gaseous bubble (nanobubble) explains this profile. Our data suggest that such nanobubbles act as the dominant source of low-frequency noise and conductance variability. Currently, translocation of RecA-coated DNA is employed to detect local protein structures and test translocation models. We will report on the latest status of these experiments.

11:39AM J27.00003 Protein translocating as unfolded chains through solid-state nanopores , THOMAS AREF, ALEXEY BEZRYADIN, UIUC — We have detected translocation of the protein shrimp alkaline phosphatase (SAP) through a solid-state nanopore. The nanopores were fabricated in a silicon nitride membrane using a highly focused electron beam in a transmission electron microscope. Once formed, the nanopore was wet with an electrolytic solution and current was driven through it by application of an electric potential. When introduced to the negative side of the nanopore, the negatively charged SAP produced current blockages as the protein molecules were driven through the pore by the electric field. No current blockages occurred when protein had not been added to the electrolytic solution nor when polarity of the applied electric field was reversed. Furthermore, this globular protein does not appear to translocate as a sphere as might be expected, but rather goes through as an unfolded chain. Our current blockage events are similar to signals produced by lambda DNA translocating through a nanopore significantly larger than the DNA's diameter. This has implications for future experiments using nanopores to probe proteins.

11:51AM J27.00004 Fabrication of sealed nanofluidic channels with single wall carbon nanotube electrodes for electronic DNA detection and analysis , CHIH-KUAN TUNG, Dept. of Physics, Princeton Univ., ROBERT RIEHN, Princeton Univ. / NC State Univ., LUKAS URBAN, Univ. of Illinois, Urbana-Champaign, ALI YAZDANI, ROBERT AUSTIN, Dept. of Physics, Princeton Univ. — Detection of entropically elongated polymer molecules such as DNA in nanotubes by electronic means is a challenging task. SWCNT's are attractive nanoelectrode detection elements but cannot withstand many nanofabrication techniques commonly used in making nanochannels, such as dry etching. We have used near room temperature parylene deposition to create self-sealed nanochannels which pass over SWCNTs on the substrate surface. The process is totally e-beam compatible, and therefore allows us great flexibility in addressing problems and opportunities in nanoscale electronics. We will demonstrate applications such as electronic length measurement of elongated dsDNA molecules in the sealed nanochannels.

12:03PM J27.00005 Capturing and Expulsion Processes of DNA Translocations in Solid-State Nanopores , JAMES UPLINGER, DANIEL FOLOGEA, BRIAN THOMAS, RYAN ROLLINGS, JOHN WANG, JIALI LI, University of Arkansas, Physics Department — We study the DNA translocation dynamics through voltage biased solid-state nanopores. Our study examines the capturing and expulsion process of translocation events at various conditions, and compares them to artificial events. For events with translocation time on the order of 100 μs a significant portion of the translocation event corresponds to the transitory process of the DNA entering and exiting the nanopore, which is normally included in the overall translocation time. Our study reveals that DNA enter the nanopore with a higher speed than on exit. The limitations of the electronic response of the measurement system will also be discussed.

12:15PM J27.00006 Manipulating DNA molecules inside nanopores using magnetic tweezers[1] , HONGBO PENG, SEAN LING, Brown University — There has been intense interest recently in using solid-state nanopores for DNA sequencing. A key to this goal is to develop the capability to control the motion or translocation of DNA molecules through the pore. Magnetic tweezers provide the possibility for manipulating multiple DNA molecules through addressable nanopore arrays. We will report our experimental design as well as the preliminary results on manipulating DNA molecules inside nanopores using magnetic tweezers.

[1]This work was supported by NSF-NIRT.

12:27PM J27.00007 Controlling DNA translocation through nanopores using optical tweezers[1] , SHANSHAN WU, XINSHENG SEAN LING, Brown University — One of the key questions regarding DNA translocation studies is the ultimate limit to the spatial resolution of using ionic conductance measurement. We propose a method to improve on the spatial resolution by holding DNA under tension during translocation using optical tweezers. We will discuss the experimental setup and preliminary results.

[1]This work is supported by an NSF-NIRT (Nanoscale Interdisciplinary Research Team) grant.

12:39PM J27.00008 Metastability and capillary condensation hysteresis in nearly ideal cylindrical alumina nanopores[1] , FELIX CASANOVA, CASEY E. CHIANG, CHANG-PENG LI, IGOR V. ROSHCHIN, Physics Dept., ANNE M. RUMINSKI, MICHAEL J. SAILOR, Dept. Chemistry and Biochemistry, IVAN K. SCHULLER, Physics Dept., University of California San Diego — Nanoporous materials can be used as chemical and biological sensors. Anodized alumina, in which ordered cylindrical nanopores can be tuned in size, is a nearly ideal system to study gas adsorption and capillary condensation occurring in mesopores. Porous alumina with tunable pore diameters in the 10 to 60 nm range and a narrow distribution (<20%) were dosed with several organic vapors. Capillary **evaporation** occurs at equilibrium pressure for all pore sizes and gases, as predicted by the Kelvin equation. On the other hand, capillary **condensation** occurs within a range of metastability of the gas phase, in agreement with theoretical models. Such a hysteresis in the condensation-evaporation process is a signature of metastability and depends on the gas adsorbed. Isopropanol (with stronger surface interactions) always condenses at the same pressure, whereas for toluene (with weaker interactions), the condensation pressure is less reproducible.

[1]Supported by AFOSR and MEC-Fulbright

12:51PM J27.00009 Natural Gas Storage on Nanoporous Carbon.[1] , JACOB BURRESS, MIKAEL WOOD, SARAH BARKER, JOHN FLAVIN, CINTIA LAPILLI, Dept. of Physics, University of Missouri, Columbia, MO 65211, PARAG SHAH, GALEN SUPPES, Dept. of Chem. Engineering, University of Missouri, Columbia, MO 65211, PETER PFEIFER, Dept. of Physics, University of Missouri, Columbia, MO 65211 — Powdered and monolithic activated carbons have been made that have a large methane storage capacity (Alliance for Collaborative Research in Alternative Fuel Technology, http://all-craft.missouri.edu). The current best performer stores 115-119 grams methane per liter carbon at ambient temperature and 34 bar, compared to the DOE target of 118 g/L. Results are reported for the structure of the pore space (small angle x-ray scattering, nitrogen adsorption isotherms, methane adsorption isotherms, scanning and transmission electron microscopy), the methane binding energy (methane adsorption isotherms), and computer simulations of pore formation (probabilistic cellular automata). Most pores are centered about a width of 1.1 nm. At length scales larger than 100 nm, the samples are surface fractals with fractal dimension 2.4-2.6.

[1]NSF (EEC-0438469), University of Missouri, Midwest Research Institute, ED (GAANN), and DOE (W-31-109-Eng-38)

1:03PM J27.00010 Structure of Alkali Metals in Silica Gel Nanopores: New Materials for Chemical Reductions and Hydrogen Production[1] , MOUATH SHATNAWI, GIANLUCA PAGLIA, JAMES DYE, KEVIN CRAM, Michigan State University, MICHAEL LEFENFELD, SiGNa Chemistry, SIMON BILLINGE, Michigan State University — Alkali metals and their alloys can be protected from spontaneous reaction with dry air by intercalation into the pores of silica gel (SG). The resulting powders are new convenient materials for the chemical reduction and the production of clean hydrogen. The pair distribution function was used to examine their structures. Na-K alloys added to silica gel at room temperature (stage 0) or heated to 150°C (stage I) as well as stage I Na-SG, retain the overall pattern of pure silica gel with fraction of the added alkali metals remain in the pores as nanoscale metal clusters. ^{23}Na-MAS NMR studies confirm the presence of Na^0 and demonstrate that Na^+ ions are formed as well. Na-SG I when heated to 400°C (stage II) yields a dual-phase product that consists of Na_4Si_4 and Na_2SiO_3.

[1]This work was supported in part by the National Science Foundation (NSF)/CHE-0211029/, and in part by SiGNa Chemistry, LLC

1:15PM J27.00011 Anisotropy of photoluminescence from dye molecules and zeolite-dye composites , HYUNJIN LIM, HYEONSIK CHEONG, Dept. of Physics, Sogang Univ., JIN SEOK LEE, KYUNG BYUNG YOON, Dept. of Chemistry, Sogang Univ. — The dynamics of photoluminescence from dye molecules in solvents and dye-containing zeolite rods were studied using polarized photoluminescence spectroscopy. We used nanoporous zeolites and pyronine dyes as the host and guest materials, respectively. The effects of concentration of dye molecules and zeolite-dye composites in various solvent were studied systematically. The anisotropy value ($\sim$2.8) reached the theoretical value ($\sim$3.0) in a highly viscous solvent (glycerol), whereas the anisotropy value is $\sim$1 in a low viscosity solvent (DMSO). The PL peak also shows a blue-shift in strongly polar solvents. In the case of zeolite-dye composites, we obtained a lower anisotropy value ($\sim$2.2) in glycerol. This result is interpreted in terms of energy transfer from dye molecules inside the zeolite pores to dye molecules on the surface of zeolite crystals. We also prepared a more advanced system, dye-containing zeolite rods in uniform orientations, using pyronine B and Y and zeolite L. The polarized PL spectra from vertically oriented monolayer of zeolite rods containing dye molecules show that the anisotropy ratio is $\sim$9 when the polarization direction of excitation light and the c-axis of zeolite rods are parallel.

1:27PM J27.00012 How conductive polymer/nano-conductive filler composites can be? , SUPING LYU, DARREL UNTEREKER, JAMES SCHLEY, Medtronic Corporate Science and Technology — How conductive can polymer/filler composites be? It was thought the conductivity of composites could be increased by reducing the sizes of the fillers or increasing their aspect ratios, for example, by using carbon nanotubes. Invention of numerous conductive nanomaterials provides opportunity to verify this idea and to achieve higher conductivity. However, the highest conductivity of composites achieved was just a few percents of that of bulk materials of the fillers, regardless whether the filler was silver micron particles, platinum nano particles, carbon nano particles, or carbon nano tubes. The conductivity of filler-based composite is intrinsically limited by the micro-contact between the conductive fillers. Reducing the filler size or increasing aspect ratio did not yield significant improvements in conductivity although percolation may occur earlier.

1:39PM J27.00013 Free-volume anomaly in confined glycerol. , DUNCAN KILBURN, Indiana University Cyclotron Facility, VICTORIA GARCIA-SAKAI, NIST Center for Neutron Research and University of Maryland, ASHRAF ALAM, Bristol University, PAUL SOKOL, Indiana University Cyclotron Facility — Glycerol is a small molecule glass-former which exhibits relatively high viscosity due to its extensive hydrogen bonding. Here we report the first measurements of local free volume and local mobility of glycerol confined in Vycor: a mesoporous silica glass with pores 70 Angstroms in diameter. We find that the lower molecular mobility in confinement (measured here using quasi-elastic neutron scattering) is accompanied by a higher mean free-volume size between molecules (as measured using positron annihilation lifetime spectroscopy). The strong wetting between glycerol and the glass surface appears to perturb the glycerol to such an extent that the normally observed free-volume/mobility relationship is reversed. Previous studies have come to similar conclusions (high glass transition temperature, low density) but this is the first to show that these effects originate locally. This is expected to have significant ramifications for the study of hydrogen-bonding liquids in confinement, for example water – a topic of much current interest due to its application in hydration water in biological material.

1:51PM J27.00014 Induced Thermal Dynamics in Aerosil Dispersed Glass Forming Liquid , DIPTI SHARMA, GERMANO IANNACCHIONE, Worcester Polytechnic Institute — A high-resolution calorimetric spectroscopy study has been performed on pure glycerol and colloidal dispersions of an aerosil gel in glycerol covering a wide range of temperatures from 300 to 380 K, deep in the liquid phase of glycerol. The colloidal glycerol+aerosil samples with 0.07, 0.14, and 0.32 grams of silica per cm^3 of glycerol reveal activated energy (thermal) dynamics at temperatures well above the T_g of the pure glycerol. The onset of these dynamics appears to be due to the frustration or pinning imposed by the silica gel on the glycerol liquid. Since this behavior occurs at relatively low silica density (large mean-void length compared to the size of a glycerol molecule), this induced dynamics is likely due to a cooperative mode of glycerol molecules with the aerosil gel via mutual hydrogen-bonding. However, the exact nature of these energy dynamics is not known. The study of such frustrated colloids may provide a unique avenue for illuminating the physics of glasses.

Tuesday, March 6, 2007 11:15AM - 2:15PM –

Session J34 DBP: In vivo Imaging and Biomolecular Fibrils Colorado Convention Center 404

11:15AM J34.00001 Crystallographic Properties of Physiological Hydroxyapatite as a Function of Age[1] , TH. LEVENTOURI, R. VENTURELLI, A. KYRIACOU, Florida Atlantic University — Hydroxyapatite with 4-6 wt % B-type carbonate substitution is the major mineral component in our teeth and bones. Crystal structure properties of human teeth as a function of age between 17 and 91 years are investigated. X-ray powder diffraction reveals a partial phase transition from the hexagonal $Ca_5(PO_4)_3OH$ (Hydroxyapatite) to the triclinic $Ca_4H(PO_4)_3.2H_2O$ (Calcium Hydrogen Phosphate Hydrate) at the 70 year old tooth. This phase becomes predominant in the diffraction pattern of a 91 year old tooth. Correlation of such transition with physical properties of synthetic hydroxyapatite could provide useful insights in dentistry and medicine.

[1]Support from the Cancer Institute at the FAU Research Park is acknowledged.

11:27AM J34.00002 Single fluorescent nanodiamond as a cellular biomarker , HSU-YANG LEE, HUAN-CHENG CHANG, WUNSHAIN FANN, Institute of Atomic and Molecular Sciences, Academia Sinica, Taipei 106, Taiwan — Type Ib diamonds emit bright fluorescence at 550–800 nm from nitrogen-vacancy point defects, (N-V)0 and (N-V)-, by high-energy ion beam irradiation and subsequent thermal annealing. The absence of fluorescence intermittency and photobleaching in addition to its non-cytotoxicity and the easiness of surface functionalization make the fluorescent nano-sized diamonds (FND) a promising fluorescent probe for single-particle tracking in heterogeneous environments. We investigated the basic photophysical properties of surface-functionalized single FND particles with average diameter of 35-nm using single-photon and two-photon excitation. The application of tracking single FNDs in HeLa cells was also demonstrated. We found that the photostability of FNDs is not deteriorated by the surface treatment and the brightness of the fluorescence emitted by FNDs is much higher than typical organic dyes. The absorption and emission wavelength of FND, which are well separated from that of the intracellular components, further ensures the good signal to noise ratio for its application as a cellular biomarker.

11:39AM J34.00003 Intracellular Osmolyte Distributions Assessed by ^{1}H and ^{23}Na Magnetic Resonance Microscopy , SAMUEL GRANT, The Florida State University — Recently, Magnetic Resonance Microscopy (MRM) has been applied to the high resolution imaging and localized spectroscopy of isolated cells[1,2]. With resolutions $<$40 μm, these efforts have demonstrated the diverse intracellular environments that can be probed by proton MRM to provide insight into the compartmental diffusion and relaxation of intracellular water and metabolites. In this study, the intracellular distribution of the inorganic osmolyte sodium in isolated single neurons is assessed by MRM through the acquisition of three-dimensional (3D) microimages by direct observation of ^{23}Na. These efforts are made possible through (a) the use of a specially constructed, double-tuned Radio Frequency (RF) microcoil and (b) the application of a unique, ultra-widebore 21.1-T magnet. Results show an increased sodium signal in the nucleus of the L7 neuron of *aplysia Californica*. These ^{23}Na findings are compared with MR data that display a heterogeneous distribution of the organic osmolyte betaine, which appears to be localized at high concentrations to the cytoplasm. The link between the intracellular distributions of sodium and other osmolytes in this single neuron model may shed light on intracellular osmoregulatory processes, particularly in response to toxic or pathological perturbations. [1]S.C.Grant, *et al.*, Magn. Reson. Med. 2000. [2]S.C.Grant, *et al.,* Magn. Reson. Med. 2001.

11:51AM J34.00004 Harmonic Generation Spectroscopy of Enzymatic Activity in Live Organisms , JIE FANG, GUSTAVO CARDENAS, SHIH-YING HSU, WILLIAM WIDGE, JOHN MILLER, University of Houston — We report on measurements of harmonics generated by whole cells, chloroplasts, and whole plants in response to applied sinusoidal electric fields. The frequency- and amplitude-dependence of the induced harmonics exhibit features that correlate with physiological processes. In particular, we find that harmonics generated by whole plants and suspensions of chloroplasts are dramatically increased by the presence of light. Systematic studies of the second and third harmonic generation spectra of chloroplast suspensions indicate the following: 1) a broad peak, centered around 10 kHz applied frequency (20 kHz for the second harmonic) appears when the photosynthetic electron transport chain is activated by light in the presence of a suitable electron acceptor, such as ferricyanide; changes observed in the time-dependent harmonic response for fixed frequency are correlated to the presence of light activation of photosynthetic election transport activity. 2) This feature correlates with oxygen evolution activity of photosynthesis. In whole plants, multiple peaks in the light-activated harmonic generation spectra suggest that the method may be able to selectively probe specific photosynthetic activity in plants.

12:03PM J34.00005 Near-Infrared Fluorescence of the NBT/BCIP Chromogenic Stain[1] , M. D. MCCUTCHEN, L. A. BUMM, Homer L. Dodge Department of Physics and Astronomy, University of Oklahoma, Norman, OK, D. W. MCCAULEY, Department of Zoology, University of Oklahoma, Norman, OK, L. A. TRINH, M. BONNER-FRASER, S. E. FRASER, Division of Biology, California Institute of Technology, Pasadena, CA — We demonstrate the previously unreported near infrared (NIR) fluorescence of the dark purple stain formed from 5-bromo-4-chloro-3-indolyl phosphate (BCIP) and nitro blue tetrazolium (NBT). Although the product is a solid with strong optical absorption, its fluorescence enables high cellular resolution imaging of gene expression. We use spectrofluorometry to identify NBT diformazan as the component of the stain that is the fluorophore exhibiting the strong fluorescence signal. The fluorescence shows an intense emission signal (780-910 nm) that is well separated from excitation (645-685 nm). The NBT diformazan fluorescence is also photostable. Because NBT/BCIP is a widely used chromogenic stain, existing staining protocols can also be applied to fluorescence imaging techniques to increase the resolution of gene expression patterns.

[1]This work has been supported by NSF CAREER grant No. CHE-0239803 and NSF MRSEC No. DMR-0080054, and AFSRO FA9550-06-1-0365.

12:15PM J34.00006 Development of a 'Protein Microscope' to Map Peptide Distributions in Cells , J.A. HOFFMANN, M.E. REEVES, Department of Physics, George Washington University — We report on the development of a new instrument, dubbed a 'Protein Microscope,' that uses near-field optical techniques to increase the spatial resolution of atmospheric pressure matrix-assisted laser desorption and ionization (AP-MALDI). This functions as a novel front-end for time-of-flight mass spectrometry. Standard protein identification techniques involve homogenization of a tissue sample, which destroys all spatial and temporal information about the expressed proteins. Our new NSOM-based instrument will allow the identification and mapping of proteins expressed in intact cells and tissues, which is of great interest as protein expression connects genomic information with the functioning of an organism.

12:27PM J34.00007 The fate of cells in skin: from clonal analysis to cell kinetics , ALLON M. KLEIN, DAVID P. DOUPE, DOUGLAS J. WINTON, PHIL H. JONES, BENJAMIN D. SIMONS, Department of Physics, Cavendish Laboratory, J J Thomson Avenue, Cambridge CB3 0HE, UK — Biologists are keen to understand the mechanisms of development and maintenance of tissues in mammals. As well as its intrinsic scientific interest, an understanding of the kinetics of cell division has important implications for mechanisms of aging and cancer development. Analysis of cell populations (clones) resulting from progenitor cells provides indirect access to the laws governing cell division and fate. Yet, until recently, the quality of clonal fate data acquired *in vivo* has inhibited reliable quantitative analysis. By addressing a recent, detailed, and extensive experimental study of mammalian skin, we develop a general theoretical framework which shows that the wide range of clonal fate data are consistent with a remarkably simple cell kinetic model. As well as overturning the accepted paradigm for skin maintenance, the analysis introduces a general framework for analysing clone fate data in future experiments. We now have a robust platform to study the effect of drug treatments and the influence of cell mutations on the epidermis.

12:39PM J34.00008 Photo-ionization Potential Threshold of Single Human Fibrinogen Molecule Absorbed onto Silicon Surfaces , XIANHUA KONG, JACOB GAUGUILO, ROBERT NEMANICH, Department of Physics, North Carolina State University — Human Plasma Fibrinogen (HPF), which is a protein involved in haemostasis and thrombosis, is known to readily adsorb onto artificial surfaces. Therefore, understanding the absorption process for specific surfaces is critical to establish biocompatibility. In this study, the photo-ionization potential of single HPF molecules adsorbed onto oxidized p-type silicon substrates was studied by photoelectron emission microscopy (PEEM). PEEM, using the spontaneous emission output of the Duke OK-4 free electron laser (FEL), were illuminated at tunable wavelengths between 248 and 310 nm. The photo-ionization potential threshold for single HPF molecules was found to be 4.6 $\pm$ 0.2 eV. The electronic states of the molecule were related to the electronic states of the oxidized Si surfaces. The deduced alignment of the electronic states is consistent with negative charge transfer from the adsorbed fibrinogen to the p-type silicon substrates which would proceed by tunneling through the thin oxidized layer.

12:51PM J34.00009 In vitro, interaction of homotrimers with heterotrimers of type I collagen , SEJIN HAN, WOLFGANG LOSERT, University of Maryland, SERGEY LEIKIN, NIH — The dominant mutations in type I collagen cause a group of diseases, often termed collagen, or connective tissue, diseases: for example, Osteogenesis Imperfecta (OI) characterized by bone fragility and skeletal deformity. The mechanism in which collagen mutations affect on the diseases is still unknown. To understand the fibril assembly and their interactions might provide a key to approaching the cause of the collagen diseases. This study demonstrates that the self-assembly, termed fibrillogenesis, of type I collagen homozygous mutations revealed substantial differences in the kinetics with the absence of lag time and in the morphology of 3D fibril network structure. The heterotrimers (normal) and homotrimers (mutant) in mixtures were segregated within the same fibrils during fibrillogenesis, in correspondence between confocal microscopy and thermodynamic measurements. The efficiency for self-assembly of the homotrimers into fibrils was markedly reduced, while that of the heterotrimers was not affected by the presence of homotrimers with no change in solubility.

1:03PM J34.00010 Determining Beta Sheet Crystallinity in Fibrous Proteins by Thermal Analysis and Infrared Spectroscopy[1] , XIAO HU, DAVID KAPLAN, PEGGY CEBE, Tufts University — We report a study of self-assembled beta pleated sheets in *Bombyx mori* silk fibroin films using thermal analysis and infrared spectroscopy. Crystallization of beta pleated sheets was effected either by heating the films above the glass transition temperature (Tg) and holding isothermally, or by exposure to methanol. The fractions of secondary structural components including random coils, alpha helices, beta pleated sheets, turns, and side chains, were evaluated using Fourier self-deconvolution (FSD) of the infrared absorbance spectra. As crystalline beta sheets form, the heat capacity increment from the TMDSC trace at Tg is systematically decreased and is linearly well correlated with beta sheet content determined from FSD. This analysis of beta sheet content can serve as an alternative to X-ray methods and may have wide applicability to other crystalline beta sheet forming proteins.

[1]The authors thank the National Science Foundation Division of Materials Research, Polymers Program, for support of this research through grant DMR-0402849.

1:15PM J34.00011 Resonance Effects in the Ultraviolet Raman Spectroscopy of Collagen in Mineralized Tissues , J. W. AGER III, Lawrence Berkeley National Laboratory, M. PUGACH, S. HABELITZ, University of California San Francisco, G. BALOOCH, Lawrence Berkeley National Laboratory, J. H. KINNEY, Lawrence Livermore National Laboratory, G. W. MARSHALL, University of California San Francisco, R. O. RITCHIE, Lawrence Berkeley National Laboratory — Ultraviolet resonance Raman spectroscopy (UVRRS) was used to investigate type I collagen in solid tissues including tendon, dentin, and bone. With 244 nm excitation, spectral features from both the amide backbone (amide I, II, and III) and resonance-enhanced side-chain vibrations (Y8a, tyrosine) were observed. This contrasts with reported Raman spectra of proteins in solution excited with similar UV wavelengths, where side chain vibrations, but not strong amide features, are observed. The height of the dominant amide I feature in teeth and bone can be reversibly increased/decreased in dentin by dehydration/rehydration cycles. Also, the amide I peak is relatively stronger in both human bone and dentin from older donors. The strong intensity of the amide I UVRRS feature in these mineralized tissues is attributed to an increase in the width of the $\pi \rightarrow \pi^*$ amide resonance in collagen compared to the solution phase. These findings suggest that UVRRS can be used as a specific probe of the collagen environment in bone and dentin.

1:27PM J34.00012 Surface modification of cotton and silk fabrics by SF_6 plasma[1] , SATREERAT HODAK, THIDARAT SUPASAI, Department of Physics, Faculty of Science, Chulalongkorn University, VARONG PAVARAJARN, Chemical Engineering Department, Faculty of Engineering, Chulalongkorn University, BOONCHOAT PAOSAWATYANYONG, Department of Physics, Faculty of Science, Chulalongkorn University — Hydrophobic properties are of the interest in fabric and textile manufacturers. We have used SF_6 plasma to modify the surface of cotton and silk fabrics. We have found that SF_6 plasma enhances the hydrophobic property of both types of fabrics. The water contact angle of SF_6-treated fabrics increased from 20 degrees up to 140 degrees. The measured absorption time was found to depend upon the treatment time and RF power, only at the low SF_6 pressure of 0.005 and 0.05 torr. At higher pressure, all samples achieved high absorption time of about 200 min, regardless of the RF power and treatment time. The morphology changes of fabrics after plasma treatment were characterized by scanning electron microscopy and atomic force microscopy. After plasma treatment, the rms surface roughness of the fibre increased from about 20 nm to 40 nm. From X-ray photoelectron microscopy analysis, we found that the higher the F/C atomic ratio leads to the longer the absorption time or the improved hydrophocity of the fabric.

[1]National Research Council of Thailand (NCRT)

1:39PM J34.00013 Fundamental Investigations of the Extracellular Proteins Fibrin and Collagen in Microchannel Devices[1] , HEATHER M. EVANS, SARAH KOESTER, THOMAS PFOHL, Max Planck Institute for Dynamics and Selforganization, Goettingen, Germany — Microfluidic structures are particularly amenable to controlled investigations of protein bundle and network formation. Hydrodynamic focusing is utilized to create a diffusion-controlled gradient of reactants, enabling non-equilibrium investigations. We present studies of the blood clotting protein fibrin, a three-dimensional network formed from the enzymatic cleavage of fibrinogen monomers by the protein thrombin. Fibrin is a vital component of blood clots, and has been implicated in a variety of diseases. Real-time fluorescence microscopy and x-ray micro-diffraction are used to quantify supramolecular assembly and provide snapshots of the evolution of fibrin network formation. We also show that collagen, a ubiquitous extracellular protein, can be bundled in situ through the use of a pH gradient. An outlook toward artificial blood vessels arises from the insight that both fibrin and collagen can easily be used to coat microchannel structures. The resulting mesh forms an ideal environment for red blood cells and other cell types.

[1]H. Evans acknowledges a postdoctoral fellowship from the Alexander von Humboldt Foundation.

1:51PM J34.00014 Biomolecule surface patterning by aqueous polymer nanografting (APN) , ROBERT DAVIS, KATHERINE BARNETT, JODI KNOEBEL, MATTHEW LINFORD, Brigham Young University — We have demonstrated a method to chemically pattern aqueous polymer layers on the nanoscale. An atomic force microscope (AFM) was used to mechanically remove positively charged polymers from silica and mica surfaces with submicron resolution in liquid. Polyallyl amine (PAA) and polylysine were both been patterned creating 10 and 20 micron boxes with nanometer scale edge transition lengths. These patterns can serve as templates for patterning lipid and protein layers in buffer environments where pH and concentration can be controlled.

2:03PM J34.00015 Mechanical Single Molecule Investigations of SNARE Protein Interactions , WEI LIU, VEDRANA MONTANA, VLADIMIR PARPURA, UMAR MOHIDEEN, Department of Physics, UC Riverside, Riverside, CA — We used an Atomic Force Microscope (AFM) to perform single molecule investigations of the SNARE (soluble N-ethyl maleimide-sensitive fusion protein attachment protein receptors) proteins, syntaxin, synaptobrevin and SNAP 25. These proteins are involved in the docking and release of neurotransmitters. The rupture force and extension of the interactions were measured. Chemical reaction rate theory was applied to obtain the energy barrier width and lifetime. Their temperature dependence was also explored.

Tuesday, March 6, 2007 11:15AM - 2:03PM –

Session J35 DBP DCP DCOMP: Protein Water Interactions Colorado Convention Center 405

11:15AM J35.00001 Oscillatory Growth of Ice Crystals Observed in a Solution of Antifreeze Glycoprotein , YOSHINORI FURUKAWA, YOSHIHIRO NISHIMURA, SALVADOR ZEPEDA, HIROYUKI NAKAYA, ILTS, Hokkaido University, ETSURO YOKOYAMA, Gakushuin University — One-directional growth experiments of ice crystals in an aqueous solution of antifreeze glycoprotein (AFGP) were carried out using a growth cell made of thin glass capillaries. When the interface tips of ice crystals were constructed by prismatic planes, the interface position changed periodically with time. These phenomena were not observed for the growth of basal planes in the AFGP solution or for the growth of ice crystals in pure water. We first observed the oscillatory growth of ice crystals in the AFGP solution. Fluorescent labeled AFGP molecules were also used to observe the diffusion, incorporation, and segregation of the solute at the interface, in the solid and in solution. The periodic incorporation of AFGP molecules were clearly observed in conjunction with the growth rate changes.

11:27AM J35.00002 A model of self-oscillatory growth of ice crystals in antifreeze glycoprotein solutions , ETSURO YOKOYAMA, Gakushuin University, YOSHINORI FURUKAWA, ILTS, Hokkaido University — We discuss that an oscillatory crystal growth is observed not only in the growth of an ice crystal from AFGP solution but also in the motion of steps on the surface of ice crystals in the presence of AFGP molecules. Our model of the oscillatory growth of crystals accounts for two elementary processes relevant to the growth: 1) an interface kinetic processes for transformation into a crystalline phase at the interface, and 2) a diffusion process for the transport of latent heat liberated at the growing interface. In this talk, we propose the hypothesis of a hysteresis behavior of growth rate to explain the formation of periodic structures of a growing crystal without a change of external conditions. The self-oscillatory growth in the presence of AFGP adsorbed molecules can occur because of the coupling of interface kinetics to the transport of latent heat under constant growth conditions.

11:39AM J35.00003 Antifreeze Protein (AFP) and Antifreeze Glycoprotein (AFGP) Kinetics at the Ice/Solution Interface , SALVADOR ZEPEDA, HIROYUKI NAKAYA, YUKIHIRO UDA, Hokkaido University, ETSURO YOKOYAMA, Gakushuin University, YOSHINORI FURUKAWA, Hokkaido University — AFPs and AFGPs found in some fish, plants and insects are a necessary tool for surviving sub-freezing environments. They occur in a wide range of compositions and structure, but to some extent they all accomplish the same functions: they suppress the freezing temperature, inhibit recrystallization, and modify ice crystal growth. Here, we observe the exact location of AFGPs, Type I and Type III AFPs by 1-directional growth experiments using fluorescence and phase contrast microscopy as well as free growth experiments using 3-d confocal microscopy. In all cases, the proteins clearly adsorb at the interface. By comparing the fluorescent image with the corresponding phase contrast image we find that AFGPs incorporate only into the solid in veins and not into the ice lattice structure. Type I AFPs show similar behavior as AFGPs, but type III AFPs adsorb to specific planes within the ice lattice. We have also calculated the diffusion constants and the surface adsorption concentration from both types of experiments. Our results indicated that the different types of AFPs or AFGPs accomplish essentially the same function in slightly different ways and that it is not necessary for the protein adsorption to the ice interface to be as rigid as once thought.

11:51AM J35.00004 Protein slaving to the solvent and the relation to hydrodynamics , P. W. FENIMORE, GUO CHEN, B. H. MCMAHON, Los Alamos National Lab — Protein motions can be categorized by the nature of their coupling to solvent dynamics. Some protein motions, including the final ligand binding process in myoglobin (Mb), are largely independent of solvent fluctuations. Others, such as entry and exit of ligands from Mb require Debye-like α fluctuations in the solvent to proceed. A third class of motions, including the r. m. s. displacments of atoms are controlled by solvent β fluctuations. We show that a slaving picture of protein dynamics, $k_{\rm protein} = k_\alpha/n$, where n is a nearly T-independent factor, known to be as large as 10^5, is consistent with an essentially hydrodynamic picture of α-slaved protein motions. Consistency with hydrodynamics (i. e. the Stokes-Einstein equation) can be demonstrated by considering changes to protein stability caused by ordinary experimental protocols for measuring viscosity- and T-dependent protein dynamics data. The decomposition of protein dynamics into several discrete classes suggests modelling techniques to simplify the simulation of protein dynamics.

12:03PM J35.00005 Dynamics of Lysozyme in a Glycerol-Water system , PAVAN GHATTY, GUSTAVO CARRI, The University of Akron — Bio-preservation of proteins is of great commercial and academic interest. A variety of sugars have been found to be effective in preserving the structure of proteins. This has been attributed and in some cases proved to their ability to form strong hydrogen bonds with proteins thus restricting their motion. The work presented here explores the hypothesis that glycerol, a tri-alcohol curbs the motion of protein.
We have carried out a 10ns Molecular Dynamics simulation to study the phenomenon. The structure of Lysozyme (PDB code 193L) has been studied in three solutions of 10, 20 and 30 % by weight of glycerol in water.
Glycerol molecules in all three solutions have shown a tendency to agglomerate around the protein. Strong hydrogen bonding has also been observed between glycerol molecules and the protein. With increasing time, the g(r) of glycerol molecules around proteins shows two peaks with increasing prominence suggesting the movement of glycerol cluster to positions closer to the protein surface.

12:15PM J35.00006 An extended dynamical solvation shell around proteins.[1] , SEUNG JOONG KIM, U. of Illinois (UIUC), SIMON EBBINGHAUS, MATTHIAS HEYDEN, Ruhr-Uni. Bochum, Germany, XIN YU, U. of Nevada, UDO HEUGEN, Ruhr-Uni. Bochum, Germany, MARTIN GRUEBELE, U. of Illinois (UIUC), DAVID LEITNER, U. of Nevada, MARTINA HAVENITH, Ruhr-Uni. Bochum, Germany — Water solvating biomolecules in organisms has different properties from the bulk. Such solvation shells can be characterized by a variety of structural and dynamical measures. The fundamental question of biomolecule hydration is: how far out into the solvent does the influence of the biomolecule reach? We use terahertz absorption spectroscopy of the five helix bundle protein Lambda Repressor 6-85, coupled with molecular dynamics simulations, to show that correlated water motion at a sub-psec time scale persists to distances of at least 20 angstrom. We show this by determining that bulk water, water molecules mainly interacting with a single protein molecule, and water molecules interacting with more than one protein molecule have different absorption signatures in the THz frequency range, leading to an experimentally detectable non-monotonic dependence of the absorption coefficient on protein concentration. This trend is supported in the calculations, which further show that long-distance hydration is a dynamical effect correlating many water molecules, not one that noticeably perturbs the structural distribution of one or a few water molecules from the bulk value.

[1]This work was supported by a grant from the Human Frontiers Science

12:27PM J35.00007 Structural and dynamical properties of water in hydrophobic confinement, as probed by *ab-initio* molecular dynamics. , GIANCARLO CICERO, Politecnico of Torino, Torino, Italy, JEFFREY C. GROSSMAN, Center of Integrated Nanomechanical Systems, University of California, Berkeley, ERIC SCHWEGLER, LLNL, Livermore, CA, GALLI GIULIA, University of California, Davis, CA — Unraveling the microscopic properties of water confined in small channels will help understand fluid flow and transport at the nanoscale, and will shed light on the solvation of biomolecules. To date most of the properties of confined water are poorly understood and, in many cases, controversial. We present a first principles computational study of prototype systems —water confined between graphene sheets and inside carbon nanotubes– which have received widespread experimental attention and for which, however, such basic questions as diffusion at the nanoscale, and characteristics of the hydrogen bonded network remain unanswered. Our simulations show that the liquid density substantially increases at the water/surface interface, and that water diffusion is faster in highly confined structures, due to a decrease of the dipole moment in interfacial water molecules and correspondingly a decrease in H-bond network strength. We propose that many effects attributed to confinement in the past are actually interfacial effects due to subtle electronic structure rearrangements, and that these are amenable to vibrational and x-ray absorption spectroscopy investigations.

12:39PM J35.00008 Basal Plane Affinity of an Insect Antifreeze Protein , N. PERTAYA, Ohio University, S.Y. GAUTHIER, P.L. DAVIES, Queen's University, I. BRASLAVSKY, Ohio University — sbwAFP is a powerful antifreeze protein (AFP) with high thermal hysteresis activity that protects spruce budworm (sbw) from freezing during harsh winters in the spruce and fir forests of USA and Canada. Different types of antifreeze proteins have been found in many other species and have potential applications in cryomedicine and cryopreservation. When an ice crystal is cooled in the presence of AFP below the non-equilibrium freezing point the crystal will suddenly and rapidly grow in specific directions. Hyperactive antifreezes like sbwAFP expand perpendicular to the c-axis (in the plane of the a-axes), whereas moderately active AFPs, like type III from fish, grow in the direction parallel to the c-axis. It has been proposed that the basis for hyperactivity of certain AFPs is that they bind and accumulate on the basal plane to inhibit c-axial growth. By putting fluorescent tags on these two types of AFPs we have been able to directly visualize the binding of different types of AFPs to ice surfaces. We do indeed find that the insect AFP accumulates on the basal plane of an ice crystal while type III AFP does not. Supported by CIHR and BNTI.

12:51PM J35.00009 Study of Hydrogen Bond and Dipolar Interaction in Water-like Fluid with Toy Model , Y.S. JHO, KAIST/UCSB, C.S. CHANG, KAIST/NYU, P.A. PINCUS, UCSB/KAIST, M.W. KIM, KAIST/UCSB — Hydrogen bond and dipolar interaction, which originated from the high polarizability of asymmetric water-like molecules, give rise to anomalous properties. Anionic interface of water-like fluid is understandable as a result of hydrogen bond and excluded interactions of OH^- and H_3O^+. Range of dipolar interaction reaches over several water-like molecule size. And, the interaction between dipole and ion affects on about 20 times longer than the size of water-like molecule. Therefore, the interaction between charged particles within this range shows different behavior compared to interaction in a uniform dielectric medium. Toy model gives physical insights and helps comprehensions to complex phenomena. In this study we give the numerical simulation to investigate these phenomena.

1:03PM J35.00010 Density and Structure of Water under Confinement as Determined using Monte Carlo Simulations , SUMIT SHARMA, SANAT K. KUMAR, Columbia University — The structure and local density of water is thought to play an important role in phenomena such as protein adsorption. These properties of water under confinement between surfaces can be significantly different from those of bulk water. A change in the water's structure, which is coupled to a change in the local density of the confined water in equilibrium with the bulk water, can create an attractive or repulsive force between the planar surfaces. This force itself can dominate the mechanism of adsorption when adsorbing molecules are within close proximity from adsorbent. In order to probe the effects of confinement further, Grand Canonical ensemble Monte Carlo (GCMC) simulations of Single Point Charge Enhanced (SPC/E) water confined between two planar surfaces of differing hydrophobicity, ranging from hydrophobic to hydrophilic, have been performed. The dependence of the water's structure and local density on the hydrophobicity and distance between the two planar surfaces has been determined. Further, the effect of surface curvature will also be examined.

1:15PM J35.00011 The protein hydration transition , YUNFEN HE, JOSEPH KNAB, JING-YIN CHEN, ANDREA MARKELZ, Physics Department, State University of New York at Buffalo — We previously reported the hydration transition in the THz dielectric response for native state hen egg white lysozyme (HEWL). As hydration increases the response slowly increases until at 0.25h (gm water/gm protein) the absorbance and index sharply increase. The hydration level coincides with the filling of the first solvation shell. The THz dielectric response arises from relaxational and resonant vibrational response, where the vibrational response corresponds to delocalized structural motions sensitive to the conformation and the environment. We examine the contribution of low frequency vibrational modes to the hydration transition by calculating the normal mode density as a function of solvent content using CHARMM. We find that the density of low frequency modes increases with the increasing solvent content, but this increase does not show the transition seen experimentally. We discuss that another source for the hydration transition in the THz response may be the hydration dependence of the activation energy for glass-like beta fluctuations that contribute to the relaxational response.

1:27PM J35.00012 Inverted Solubility of the Pro 23 to Val Mutant of Human γD Crystallin– Altered Phase Diagram from a Single Amino Acid Substitution and the Effect of PEG , J.J. MCMANUS, A. LOMAKIN, M. BASAN, O. OGUN, MIT, Department of Physics, CMSE and Materials Processing Centre, A. PANDE, J. PANDE, Dept. of Chemistry, SUNY, Albany., G.B. BENEDEK, MIT, Department of Physics, CMSE and Materials Processing Centre — Many genetic cataracts are the result of single point mutations in the amino acid sequence of lens crystallin proteins. The P23T mutation in human γD-crystallin (HGD) is associated with several different cataract phenotypes. The solubility of the protein shows an inverse temperature dependence. This is in contrast with the native protein. The replacement of Thr23 with a Ser or a Val residue shifts the location of the inverted solubility line to higher concentrations [1]. We describe the phase diagram of the P23V mutant of HGD, which exhibits aggregation, crystallization and liquid-liquid phase separation (LLPS). We have used QLS to probe the interactions of the protein in the soluble region of the phase diagram. We have developed a model to describe the observed retrograde solubility of the protein. Using PEG we introduce a so-called "depletion interaction" to further investigate the origin of the retrograde solubility. [1] A. Pande, O. Anunziata, N. Asherie, O. Ogun, G.B. Benedek, J. Pande, *Biochemistry* **44**, 2491-2500 (2005).

1:39PM J35.00013 Free energy study of uranyl complexes across water-oil and water-oil+tributyl phosphate (TBP) interfaces[1] , MANORI JAYASINGHE, THOMAS L. BECK, University of Cincinnati — Free energy profiles of heavy metal ion complexes, UO_2 $(NO_3)_2$, UO_2 $(NO_3)_2TBP_2$, and TBP, across the water-hexane and water hexane+TBP (50%/50%) interfaces, were calculated from molecular dynamics simulations. These complexes and interfaces are relevant to recently developed heavy-ion separation techniques. The solute complex with TBP, UO_2 $(NO_3)_2TBP_2$, shows strong interfacial activity in contrast to the free energy barrier for UO_2 $(NO_3)_2$ at the water-hexane interface. Increased TBP concentration in the oil phase reduces the interfacial activity and better solvates the ion complexes and their ligands. The solute complex with TBP oriented parallel to the water-hexane+TBP interface binds more strongly to the hexane+TBP phase than to the pure hexane phase. The (un-complexed) TBP orientational probability distribution shows the polar head buried in water, while the nonpolar tails are buried in the oil phase, and hence TBP exhibits interfacial activity. The calculated density profiles at the interface show that TBP acts not only as a carrier for uranyl transport across the interface, but also as an "interface modifier". Our simulation results are in agreement with the recent study of uranyl transport across chemically modified membranes with TBP based metal ion carriers.

[1]National Science Foundation Membrane Applied Science & Technology (MAST) Center grant.

1:51PM J35.00014 Differential Dielectric Spectroscopy of Protein Solutions: Observation of Protein Interactions , BRIAN MAZZEO, ANDREW FLEWITT, Cambridge University — Observation of a protein-protein interaction is illustrated by dielectric measurements on rabbit IgG (190 μg/ml) and Protein A (19 μg/ml) by a homemade dielectric cell and HP 4194A impedance analyzer. Frequency shifts of ratios 2.0 and 1.6 with respect to the individual relaxation characteristics of IgG and Protein A were obtained by dielectric spectroscopy, which has historically been used to determine the properties of solvated biomolecules to measure the hydrodynamic and electrical properties of individual proteins and of solution. Dielectric relaxation theory predicts changes in the dielectric relaxation characteristics of proteins due to protein interactions resulting in larger hydrodynamic volumes. Experimentally, bovine serum albumin, protein A, and rabbit IgG were added sequentially to phosphate buffer and the incremental dielectric changes were measured. The differential dielectric response, as a biophysical technique, gives insight into the interaction of the added protein with biomolecules in solution and can indicate the presence of protein-protein interactions.

Tuesday, March 6, 2007 2:30PM - 5:30PM –

Session L34 DBP: Focus Session: Virus-Inspired Supramolecular Structures Colorado Convention Center 404

2:30PM L34.00001 Size regulation of ss RNA viruses , ROYA ZANDI, University of California, Riverside — Under the right circumstances, single-stranded RNA viruses self assemble spontaneously from aqueous solutions containing the subunit proteins and genome molecules. While a monodisperse size distribution is common for most icosasedral viruses, the size of the spherical viral shells can vary from one type of virus to another. We study the effect of genome length, genome concentration and protein concentration on the size of spherical viral capsids in the absence of spontaneous curvature and bending energy. We find that based on the size of genome, it could be advantageous to have relatively small spherical shells with higher curvature rather than bigger and thus flatter shells. Furthermore, we find that the small ratio of genome to protein concentration could, quite interestingly, result in larger spherical shells. Experimental data on the encapsidation of model genome supports these findings.

3:06PM L34.00002 Synthesis and properties of virus-like particles , BOGDAN DRAGNEA, Indiana University — The principles underlying self-assembly of virus-like particles (VLP), which are composed of an icosahedral virus protein coat encapsulating a nanoparticle core are discussed. Such VLPs have potential practical utility as biomedical imaging and sensing tools, as novel functional materials, and as experimental models for molecular self-assembly of quasi-spherical molecular cages. Moreover, we show that, as a consequence of their regular protein surface, VLPs readily form three-dimensional crystals having optical properties influenced by multipolar plasmonic coupling.

3:18PM L34.00003 Soft modes near the buckling transition of icosahedral shells , MICHAEL WIDOM, Carnegie Mellon University, JACK LIDMAR, Royal Institute of Technology, Sweden, DAVID NELSON, Harvard University — Closed shells comprised of pentamers and hexamers may be smooth and nearly spherical, or sharply faceted and icosahedral, depending on the elastic constants of the shell. We interpret the transition from smooth to faceted as a soft-mode transition. Our analysis is based on the phonon spectrum of a simplified mass-and-spring model of the shell. In contrast to the case of a disclinated planar network, where the transition is sharply defined, the mean curvature of the sphere smooths the transition rather like a magnetic field smears out a ferromagnetic phase transition. We define susceptibilities of the transition as the response to forces applied at vertices, edges and faces of an icosahedron. At the soft-mode transition the vertex susceptibility is largest, but as the shell becomes faceted the edge and face susceptibilities greatly exceed the vertex susceptibility.

3:30PM L34.00004 ABSTRACT WITHDRAWN —

3:42PM L34.00005 A Precise Packing Sequence for Self-Assembled Convex Structures , TING CHEN, ZHENLI ZHANG, SHARON GLOTZER, Department of Chemical Engineering, University of Michigan — We present molecular simulations of the self-assembly of cone-shaped particles with patchy, attractive interactions[1,2]. Upon cooling from random initial conditions, we find that the cones self assemble into clusters and that clusters comprised of particular numbers of cones have a unique and precisely packed structure that is robust over a range of cone angles. These precise clusters form precise packing sequence that for small sizes is identical to that observed in evaporation-driven assembly of colloidal spheres. This sequence is reproduced and extended in simulations of two simple models of spheres self-assembling from random initial conditions subject to convexity constraints, and contains six of the most common virus capsid structures obtained in vivo including large chiral clusters, and a cluster that may correspond to several non- icosahedral, spherical virus capsid structures obtained in vivo. For prolate spheroidal convexity conditions, we demonstrate the formation of several prolate virus structures from self-assembling hard spheres[3].
[1] Chen T, Zhang ZL, Glotzer SC, PNAS, in press (http://xxx.lanl.gov/pdf/cond-mat/ 0608592) [2] Chen T, Zhang ZL, Glotzer SC, http://xxx.lanl.gov/pdf/cond-mat/0608613 [3] Chen T, Glotzer SC http://xxx.lanl.gov/pdf/q-bio.BM/0608040

3:54PM L34.00006 Charge profiles inside sigle-stranded viruses , VLADIMIR BELYI, M. MUTHUKUMAR, UMass — Many single stranded viruses pack their genome using flexible peptide arms of capsid proteins. Genome binding may then be mapped onto interaction between polyelectrolyte and charged brush. In this talk we pursue an electrostatic model of genome binding and address several questions on charge profiles inside capsids.

4:06PM L34.00007 Buckling and Mechanical Failure of Viral Shells , WILLIAM S. KLUG, ROBIJN F. BRUINSMA, JEAN-PHILIPPE MICHEL, CHARLES M. KNOBLER, University of California, Los Angeles, IRENA L. IVANOVSKA, Vrije Universiteit, Amsterdam, CHRISTOPH F. SCHMIDT, Vrije Universiteit, Amsterdam, and Georg-August Universität, Göttingen, GIJS J. L. WUITE, Vrije Universiteit, Amsterdam — We present a combined theoretical and experimental study of the structural failure of viral shells under mechanical stress due to indentation by atomic force microscopy. Modeling the indentation of icosahedral viruses with two-dimensional continuum shell elasticity theory, we find that the fivefold-symmetric disclinations precipitate geometric "buckling" instabilities, leading to structural collapse at indentation loads that are significantly lower than those which buckle perfectly spherical shells. Coincident with these instabilities, discontinuities in the force-indentation curve appear when the so-called Föppl-von Kármán (FvK) number exceeds a critical value. A nano-indentation study of a viral shell subject to a soft-mode instability, where the stiffness of the shell decreases with increasing pH, confirms the predicted onset of failure as a function of the FvK number.

4:18PM L34.00008 Using The Interfaces In Self-Assembled Protein Cage Architectures For Materials Synthesis , TREVOR DOUGLAS, Montana State University — The self-assembled architectures of viral capsids have been used as models for understanding processes of encapsulation of both hard and soft materials. We have explored modifications to the exterior and interior interfaces of viral (and other protein cage architectures) while maintaining the assembly of stable icosahedral capsid particles. This has allowed us to utilize the high symmetry of the viral capsid to engineer unique functionality for highly ordered multivalent presentation for controlled nucleation of hard inorganic materials and packaging of soft organic materials. Of particular interest is the nature of the hard-soft interface in these systems. Through the incorporation of peptides derived from phage display we can direct the nucleation and growth of specific inorganic phases, constrained within the protein cage architecture. The coupled synthesis of cage-constrained ferrimagnetic and antiferromagnetic nanoparticles results in formation of stable composites that exhibit unique exchange bias magnetic coupling. To understand the role of the protein in directing inorganic materials synthesis, we have probed the protein-mineral interface using genetic and chemical modifications, spatially controlled inorganic synthesis, high-resolution transmission electron microscopy, and cryo-electron microscopy and image reconstruction. The role of protein interfaces in these assembled protein cage architectures has been explored to understand and exploit packaging of a wide range of materials as diverse as nucleic acids, drugs, and inorganic nano-materials.

4:54PM L34.00009 Direct measurement of the elastic properties of the Wiseana Iridovirus (WIV) capsid using Brillioun Spectroscopy , STEPHEN WARGACKI, Air Force Research Laboratory, R.D. HARTSCHUH, H. XIONG, J. NEISWINGER, A. KISLIUK, A.P. SOKOLOV, University of Akron, E.L. THOMAS, T GORISHNYY, Massachusetts Institute of Technology, V.K. WARD, University of Otago, New Zealand, R.A. VAIA, Air Force Research Laboratory — Viral capsids are of great interest for their potential as templates or scaffolds to direct the growth of secondary structures for various sensing, energy harvesting, and photonic devices. However, due to their size (10's-100's nms) and complex structure (symmetrically repeating protein subunits); the mechanical properties of viruses and viral films has yet to be directly measured. We measured the phononic spectra of virus capsids assembled on silicon substrates using Brillioun Light Scattering at different scattering wave vectors. The phononic spectrum provides a direct measurement of the mechanical properties of individual viruses as well as that of the collective assemblage. The spectra are analyzed to understand the origins of both the propagating phonons as well as those that remain localized within individual viruses. Understanding the mechanical properties of the viruses is critical for the reliable utilization of viral technologies, as well as contributing to the understanding of the impact of capsid flexibility and rigidity on cellular infection by viruses.

5:06PM L34.00010 Viral Capsid Assembly in a crowded environment , ERCAN KAMBER, Brandeis University, MICHEAL F. HAGAN, University of California, Berkeley, JANE' KONDEV, Brandeis University — While many experimental and all theoretical studies of viral capsid assembly dynamics focus on assembly in dilute solution, viruses replicate in the cell, which presents a crowded environment composed of numerous confining sub-volumes. We examine the effects of crowding and confinement on the formation of T1 capsidlike objects by using Newtonian dynamics simulations[1]. Subunits have excluded volume and asymmetric pairwise bonding interactions between complementary sides [1] and are confined to a three-dimensional box. We address the effects of finite system size on assembly dynamics by varying the system size with a fixed volume fraction of capsid subunits, and by varying the system size with a fixed number of subunits. In both cases, we find a non-monotonic variation in capsid formation times as the system dimensions become comparable with the size of a capsid. By analyzing assembly mechanisms, we probe the nature of assembly in crowded and confined environments. This work is supported by NSF DMR-0403997.
[1] M. Hagan and D. Chandler, Biophys. J. v 91, 2006

5:18PM L34.00011 Microrheology of Viscoelastic Shells: Applications to Viral Capsids , TATIANA KURIABOVA, Department of Physics and Astronomy, University of California, Los Angeles, CA 90095, ALEXANDER LEVINE, Department of Chemistry & Biochemistry, University of California, Los Angeles, CA 90095 — We study the microrheology of nanoparticles shells [cite: Dinsmore et al. Science 298, 1006 (2002)] and viral capsids by computing the fluctuation spectrum of a viscoelastic spherical shell that is permeable to the surrounding solvent. We determine analytically the overdamped dynamics of the shear, bend, and compression modes of the shell coupled to the solvent both inside and outside the sphere in the zero Reynolds number limit. In this talk we identify fundamental length and time scales in the system, and compute the thermal correlation function of displacements of antipodal points on the sphere. We describe how such an antipodal correlation function, which should be measurable in new AFM-based microrheology experiments, can probe the viscoelasticity of these synthetic and biological shells constructed of nanoparticles. We then discuss some of the remaining challenges in interpreting these measurements.

Tuesday, March 6, 2007 5:45PM - 6:45PM –

Session M35 DBP: DBP Business Meeting Colorado Convention Center 405

5:45PM M35.00001 DBP Business Meeting –

Wednesday, March 7, 2007 8:00AM - 11:00AM –

Session N25 DPOLY DBP: Focus Session: Biopolymers I: Mechanical Properties Colorado Convention Center 203

8:00AM N25.00001 Probing Polarization Dynamics and Energy Dissipation in Ferroelectric Polymers on the Nanoscale , SERGEI V. KALININ, Materials Sciences and Technology Division and The Center for Nanophase Materials Sciences, ORNL — Ferroelectric polymers are emerging as prominent materials for ultrasonic actuators, gate materials for non-volatile ferroelectric memories, and energy storage. The nature of ferroelectricity in polymers is significantly different from that in inorganic perovskites, resulting in significant interest to elementary mechanism of switching and the role of local microstructure. In this talk, I briefly delineate Piezoresponse Force Microscopy and Spectroscopy as applied for characterization of Langmuir-Blodgett ferroelectric PVDF polymer films. The slow polarization switching in PVDF can be attributed to the grain-by grain switching mechanism. Recent advances in PFM probing of polarization dynamics and electromechanical energy dissipation are discussed. In particular, switching spectroscopy PFM is used to probe the spatial variability of switching behavior and role of grain boundaries on switching. Local energy dissipation imaging through the changes of the Q-factor of electrically driven cantilever in contact with the surface is developed to study energy losses in the ferroelectric switching processes. In collaboration with Brian J. Rodriguez and Stephen Jesse, Materials Sciences and Technology Division and The Center for Nanophase Materials Sciences, Oak Ridge National Laboratory; Jihee Kim and Steven Ducharme, Department of Physics and Astronomy, Nebraska Center for Materials and Nanoscience University of Nebraska, Lincoln.

Research was supported by the U.S. Department of Energy Office of Basic Energy Sciences Division of Materials Sciences and Engineering (SVK, BJR, and SJ) and user proposal of The Center for Nanophase Materials Sciences (JK and SD) and was performed at Oak Ridge National Laboratory which is operated by UT-Battelle, LLC.

8:36AM N25.00002 Synchrotron X-ray Diffraction Study on the Effect of the Tau protein on the Mechanical Properties of Microtubules , MYUNG CHUL CHOI, UCSB / KAIST, URI RAVIV, UCSB / Univ of Jerusalem Israel, HERBERT MILLER, MICHELLE MASSIE, YOULI LI, LESLIE WILSON, STUART FEINSTEIN, UCSB, MAHN WON KIM, KAIST, CYRUS SAFINYA, UCSB — Microtubules (MTs) are 25 nm protein nanotubes used as tracks for intracellular trafficking of biomolecules, for example, those involved in transmitting signals between neurons. In neurons, MTs are long-lived both in axons and dendrites. A distinct member of microtubule-associated-proteins (MAPs) regulates microtubule assembly, although the mechanisms of regulation resulting from different tau isoforms remains to be fully elucidated. Incorrectly phosphorylated MAP tau is implicated in a large number of neurodegenerative diseases where altered tau-MT interactions and MT depolymerization and tangles of taus lead to detrimental consequences for neuronal survival. We will describe our recent finding on the effect of tau isoforms on the mechanical properties of MTs, probed by synchrotron X-ray diffraction. Supported by NSF DMR-0503347, DOE DE-FG02-06ER46314, and NIH GM59288. M.C.Choi received partial support from the Korean Foundation Grant KRF-2005-2214-C00202.

8:48AM N25.00003 Time-resolved studies of actin organization by multivalent ions and actin-binding proteins , GHEE HWEE LAI, KIRSTIN PURDY, University of Illinois at Urbana-Champaign, JAMES R. BARTLES, Northwestern University, GERARD CHEE LAI WONG, University of Illinois at Urbana-Champaign — Actin is one of the principal components in the eukaryotic cytoskeleton, the architecture of which is highly regulated for a wide range of biological functions. In the presence of multivalent salts or actin-binding proteins, it is known that F-actin can organize into bundles or networks. In this work, we use time-resolved confocal microscopy to study the dynamics of actin bundle growth induced by multivalent ions and by espin, a prototypical actin binding protein that is known to induce bundles. For divalent ion induced bundles, we observe a rapid lateral saturation followed by longitudinal growth of bundles, in sharp contrast to the bundling mechanism of espin, which favors finite length bundles.

9:00AM N25.00004 Elastic Behavior of Composite Actin and Microtubule Networks , YI-CHIA LIN, Harvard University, GIJSJE KOENDERINK, AMOLF, the Institute for Atomic and Molecular Physics, FREDERICK MACKINTOSH, Vrije Universiteit, DAVID WEITZ, Harvard University — We explore the non-linear shearing behavior of composite actin and microtubule networks. Large bending rigid microtubules are used as a probe of the deformation mode of cross-linked actin networks. For a sparsely cross-linked actin network that deforms non-affinely, adding microtubules can drive the system back to affine by suppressing local rearrangements of actin filaments. It applies to both permanently rigid cross-linker, such as scruin, and flexible cross-linker, such as filamin. This experiment also shows that filamin cross-linked actin networks are deforming in an affine manner.

9:12AM N25.00005 Mechanics of actin networks crosslinked with mutant human α-actinin-4[1] , SABINE VOLKMER, MIT, DANIEL BLAIR, KAREN KASZA, DAVID WEITZ, Harvard University — Globular actin can be polymerized *in vitro* to form F-actin in the presence of various binding proteins. These networks often exhibit dramatic nonlinear rheological response to imposed strains. We study the rheological properties of F-actin networks crosslinked with human α-actinin-4. A single genetic mutation of the α-actinin-4 protein is associated with focal and segmented glomerulosclerosis (FSGS), a genetic disorder which leads to renal failure. Mechanically, the mutant crosslinker has an increased binding strength compared to the wild type. We will show that human α-actinin-4, displays a unique stiffening response. Moreover, we also demonstrate that a single point mutation dramatically effects the inherent relaxation time of the crosslinked network.

[1]Funding from the NSF under grant DMR-0602684

9:24AM N25.00006 Viscoelastic properties of Ionomer Melt , MONOJOY GOSWAMI[1], SANAT KUMAR, Columbia University — Viscoelastic prperties of a model telechelic ionomer, i.e., a melt of non-polar polymers with a charge at each chain end along with neutralizing counterions, have been examined using molecular dynamics simulation. Equlibrium calculation of the loss modulus $G''(\omega)$ and storage modulus $G'(\omega)$ shows plateau at lower temperatures when the systems are not relaxed. In this situation the specific heat (C_v) peak corresponds to the self-assembly of the system, at lower temperatures the specific heat begins to plateau. Similarities of the dynamic features found for telechelic melts with those observed in glass-forming liquids and entangled polymers have been shown. Furthremore, using an athermal 'probe', the properties of these materials is being distinctly classified as 'strong' glass or physical gels.

[1]Speaker

9:36AM N25.00007 Controlling the Properties of Thermoreversible Protein Hydrogels[1] , HUI YAN, ALBERTO SAIANI, ALINE MILLER, University of Manchester — In this work we have explored the potential of using self-assembling protein molecules as the basic unit for novel biomaterials for biomedical applications. Here we will show how thermo-reversible fibrillar hydrogels can be formed from an aqueous solution of hen egg white lysozyme by adding the reductant dithiothreitol. The elastic modulus of the hydrogels formed has been examined and micro differential scanning calorimetry experiments confirmed that the hydrogels were thermally reversible and that gelation and melting occurs through a solid-liquid like first order transition. Infra-red and transmission electron microscopy studies of very dilute samples revealed the presence of beta-sheet rich fibrils that were 4–6 nm in diameter and 1micron in length. These fibrils self-assemble along their long axes to form larger fibers that become physically entangled to form the 3D network observed in both cryoSEM and small angle neutron scattering studies. We will also demonstrate that we can control and manipulate gel properties by varying the protein concentration, reductant concentration and ionic strength of the matrix.

[1]We thank EU 6th Framework Marie Curie EST 'ExPERT' programme for financial supprt.

9:48AM N25.00008 Electrospinning of Hyaluronic acid (HA) and HA/Gelatin Blends[1] , AIHUA HE, JUNXING LI, CHARLES HAN, Institute of Chemistry, Chinese Academy of Sciences, DUFEI FANG, BENJAMIN HSIAO, BENJAMIN CHU, StonyBrook Technology and Applied Research, INSTITUTE OF CHEMISTRY, CHINESE ACADEMY OF SCIENCES COLLABORATION, STONYBROOK TECHNOLOGY AND APPLIED RESEARCH COLLABORATION — It was found that the processability of HA solution with high viscosity had been improved greatly by using a DMF-water solvent mixture or/and by adding gelatin(GE) into the HA solution. Nano-fibrous membranes with different average fiber diameters and different HA/GE compositions could be obtained. Measurements on viscosity indicated that the HA solution in DMF-water mixed solvent still showed high viscosity. The decrease in surface tension contributed to the fiber formation of HA and HA/GE by electrospinning. Therefore, this study not only provided a novel and simpler way to electrospin the natural polyanion HA solution, but also provided the fundamental physical insight and solution to this spinning difficulty. The HA-GE nanofibrous membranes at different HA/GE compositions are expected to be useful in the biomedical field as novel scaffolds for many applications.

[1]Supported by the Natural Science Foundation of China.

10:00AM N25.00009 Rheology and lubricity of hyaluronic acid , JING LIANG, WENDY E. KRAUSE, North Carolina State University — The polyelectrolyte hyaluronic acid (HA, hyaluronan) is an important component in synovial fluid ($i.e.$, the fluid that lubricates our freely moving joints). Its presence results in highly viscoelastic solutions. In comparison to healthy synovial fluid, diseased fluid has a reduced viscosity and loss of lubricity. In osteoarthritis the reduction in viscosity results from a decline in both the molecular weight and concentration of HA. In our investigation, we attempt to correlate the rheological properties of HA solutions to changes in lubrication and wear. A nanoindenter will be used to evaluate the coefficient of friction and wear properties between the nanoindenter tip and ultrahigh molecular weight polyethylene in both the presence and absence of a thin film of HA solution.

10:12AM N25.00010 Physical Control of Stem Cells via Matrix Elasticity , FLORIAN REHFELDT, DENNIS DISCHER, University of Pennsylvania — Most of our cells reside in soft tissue, but it has only become clear over the last decade that substrate elasticity exerts a major influence on cell motility, contractility, and overall cell function. The mechanical properties of the matrix can even direct the differentiation of human adult stem cells as reported by our group recently (Engler et al. Cell 2006). Basically, the greater the resistance to matrix deformation, the larger the force with which the cell pulls on the matrix, driving the assembly of cytoskeleton and adhesions. For a deeper understanding of the molecular mechanisms of force generation and transduction, various biophysical and biochemical tools must be combined with well-defined extracellular matrix (ECM) models. Past studies have been conducted mostly with synthetic and uncharged polyacrylamide (PA) gel matrices, motivating more bio-relevant gel models. We have developed such a biocompatible hydrogel system of widely and finely tunable elasticity using hyaluronic acid (HA), which is ubiquitous in development and in particular adult tissues. The effective Young's modulus E of these negatively charged hydrogels measured by AFM can be finely tuned by variation of cross-linker and HA concentration yielding a stiffness of 0.1 kPa to 150 kPa. E scales with the concentration of HA to the power of n=2.6 and is a biphasic function of cross-linker concentration. We will describe the influence of these unique gels on stem cell differentiation.

10:24AM N25.00011 Elasticity of Short DNA Molecules: Quantitative Agreement Between Theory and Experiment , YEONEE SEOL, JINYU LI, University of Colorado, PHILIP NELSON, University of Pennsylvania, THOMAS PERKINS, University of Colorado and JILA, M. D. BETTERTON, University of Colorado — Single-molecule experiments have yielded new insight into the mechanical behavior of individual DNA molecules and protein-DNA interactions. Single-molecule force experiments require a model to deduce the polymer's intrinsic contour length (L) from measurements of force and extension. To date, the worm-like chain model (WLC) provides the best description of DNA elasticity. This theory requires parameters, the contour length L and the persistence length p. Using both theory and experiment, we studied the elasticity of dsDNA as function of L using the classic WLC solution, for L between 632 nm and 7.03 microns. When the elasticity data were analyzed using the classic WLC, the fit value of p depended L. Therefore we developed the finite worm-like chain solution (FWLC) by including the finite length of the chain and bead rotation. After incorporating these two corrections, our FWLC solution was used to predict elasticity curves and to analyze experimental data. The FWLC provides a single theoretical framework in which to analyze single molecule experiments over a broad range of experimentally accessible DNA lengths, including both short and very long molecules.

10:36AM N25.00012 Tube Radius in Entangled Networks of Semiflexible Polymers , HAUKE HINSCH, JAN WILHELM, ERWIN FREY, Arnold Sommerfeld Center for Theoretical Physics and Center for NanoScience, Ludwig-Maximilians-University, Munich, Germany — The mechanical properties of the cytoskeleton play an important role in many cellular functions like locomotion or adhesion. One of the cytoskeleton's dominant constituents is a network structure composed of the semiflexible polymer F-Actin. To connect the single polymer properties to the macroscopic behavior of the network, a single polymer is considered to be constrained to a tube established by neighboring filaments. Here we focus on the tube's diameter in entangled networks. While scaling laws for the tube diameter are well established, the absolute value is still under debate and different theoretical concepts and experimental measurements exist. We present a new approach to the problem and have conducted extensive computer simulations to check the validity of our assumptions. A model of independent rods is used to describe the confinement of a single semi-flexible polymer in the network environment. A self-consistency approach allows us then to derive an absolute tube radius for the network as a function of several parameters and compare our results to experimental measurements.

10:48AM N25.00013 Stretching and bending in cross-linked biopolymer networks , CLAUS HEUSSINGER, ERWIN FREY, Arnold-Sommerfeld Center for theoretical physics, University of Munich — The elastic response of cross-linked biopolymer networks is usually interpreted in terms of affine stretching models, adopted from the theory of rubber-elasticity valid for flexible polymer gels. Unlike flexible polymers, however, stiff polymers have a highly anisotropic elastic response, where the low-energy elastic excitations are actually of bending nature. As a consequence, similar to springs connected in series, one would expect the softer bending mode to dominate the elastic energy rather than the stiff stretching mode. We propose a theory that, unlike recent affine models, properly accounts for the soft bending response of stiff polymers. It allows calculating the macroscopic elastic moduli starting from a microscopic characterization of the (non-affine) deformation field. The calculated scaling properties for the shear modulus are in excellent agreement with the results of recent simulations obtained in simple two-dimensional model networks, and can also be applied to rationalize bulk rheological data in reconstituted actin networks.

Wednesday, March 7, 2007 8:00AM - 11:00AM –

Session N34 DBP: Focus Session: Brownian Motors in Physics, Chemistry, and Biology Colorado Convention Center 404

8:00AM N34.00001 Brownian Heat Engines – from Leidenfrost Droplets to Nanowire Thermoelectrics , HEINER LINKE, University of Oregon — A Brownian heat engine is a system that rectifies the flow of Brownian particles to transform local temperature variations into directed motion (work). In the context of electronics, this is the principle of thermoelectric energy conversion. For a long time it was thought that Brownian heat engines (and thermoelectric devices) are inherently irreversible and would therefore necessarily fall short of the Carnot limit for the energy conversion efficiency. I will introduce the concept of a Brownian heat engine, and will discuss how quantum energy-filtering can in fact be used to design a Carnot efficient, Brownian heat engine [1]. I will then present two experimental systems. The first, heat-propelled Leidenfrost droplets [2], is not really 'Brownian' but nevertheless a very entertaining and illustrative ratchet heat engine. The second is our experimental effort to demonstrate a near-Carnot efficient thermal-to-electric energy converter [3] based on a quantum dot embedded into a heterostructure nanowire [4]. The physics behind this novel thermoelectric system, and the status of experiments will be discussed.
[1] T. E. Humphrey, R. Newbury, R. P. Taylor, H. Linke, *Phys. Rev. Lett.* **89**, 116801 (2002).
[2] H. Linke *et al.*, *Phys. Rev. Lett.* **96**, 154502 (2006).
[3] M. O'Dwyer, T. E. Humphrey, H. Linke, *Nanotechnology* **17**, S338 (2006).
[4] M. T. Björk *et al.*, *Nano Letters* **2**, 87 (2002).

8:36AM N34.00002 Study of single flagellar propulsion with optical tweezers , SUDDHASHIL CHATTOPADHYAY, XIAO-LUN WU, University of Pittsburgh — Various theoretical models predict propulsion by the bacterial flagellum. Use of these models to calculate dynamical quantities of bacterial swimming are commonplace. However, direct verification of the various mathematical approaches has been difficult due to the lack of precise experimental data, which has been challenging to obtain. In this work we perform measurements on swimming bacterium which posses a single polar flagellum. Swimming with a single flagellum allows simpler parametrization as compared to a flagellar bundle. Bacteria are stably trapped in the bulk fluid (away from a surface) and perpendicular to the trapping axis with the aid of an imposed flow. This approach avoids hydrodynamic effects due to wall proximity, which were observed in previous measurements. The optical trap allows all dynamical quantities of a swimming bacterium to be determined. Flagellar dimensions are obtained by fluorescent imaging to obtain all pertinent information, required to put different theoretical models to test.

8:48AM N34.00003 The stochastic dynamics of filopodial growth , YUEHENG LAN, GAREGIN PAPOIAN, Univ. of North Carolina at Chapel Hill — We build stochastic models for filopodial growth and retraction that combine mechanical and spatiotemporal signaling components to elucidate the mechanisms of filopodia dynamics. We explicitly model the tip signaling and diffusion process while the membrane and retrograde flow are modeled implicitly. The results are compared with experiments to verify the model effectivness.

9:00AM N34.00004 Swimming movements of filaments in a linearly viscoelastic medium , HENRY FU, THOMAS POWERS, Brown University, CHARLES WOLGEMUTH, University of Connecticut Health Center — Motivated by the swimming of sperm in the non-Newtonian fluids of the female mammalian reproductive tract, we examine beating filaments in a linearly viscoelastic medium. The forces exerted by the medium are incorporated via a resistive force theory approriate for a Maxwell fluid, in which the force per unit length acting on a filament relaxes to the force per unit length exerted by a purely viscous fluid. We calculate the shapes of beating patterns of filaments with prescribed driving forces in two models: 1) an elastic passive filament forced from one end; 2) a simplified sliding-filament model for sperm flagellum with active internal sliding forces. We note that in a linearly viscoelastic model, for prescribed beating patterns, swimming velocity is the same in viscoelastic and viscous fluids, and there is a simple relation between the power dissipated in each fluid. In contrast, for prescribed driving forces, beating patterns may be different in viscoelastic and viscous fluids leading to changes in swimming velocities and power dissipated.

9:12AM N34.00005 Fusion versus endocytosis: the stochastic entry of enveloped viruses , TOM CHOU, UCLA — Viral infection requires the binding of receptors on the target cell membrane to glycoproteins, or "spikes," on the virus membrane. Fusion peptides that make up part of these spikes on the viral membrane may then be triggered by pH changes or binding of additional coreceptors. Thus, binding of virus envelope proteins to cell surface receptors not only initiates the viral adhesion and the wrapping process necessary for internalization, but also starts the direct fusion process. Both fusion and internalization may be viable pathways for some viruses, under appropriate conditions. We develop a stochastic model for viral entry that incorporates both receptor mediated fusion and endocytosis. The relative probabilities of fusion and endocytosis of a virus particle initially nonspecifically adsorbed on the host cell membrane are computed as functions of receptor concentration, binding strength, and number of spikes. We find the parameter regimes where each pathway is expected to arise and discuss possible experimental tuning of these parameters.

9:24AM N34.00006 Exact results for random deposition-driven ratcheting , MARIA-RITA D'ORSOGNA, TOM CHOU, UCLA — We consider the discrete translocation of a polymer through a pore, across a wall, driven by the irreversible, random sequential adsorption of particles on one side of the pore. Although the kinetics of the wall motion and the deposition are coupled, we find the exact steady state distribution for the gap between the wall and the nearest deposited particle. From this exact result, the mean translocation velocity and variance are constructed. We explicitly show that translocation is faster and less variable when the adsorbing particles are smaller. The relative efficiencies of ratcheting using different sized deposition particles are also defined and compared.

9:36AM N34.00007 Molecular motors driven by asymmetric nucleation , AMIT LAKHANPAL, TOM CHOU, UCLA — We study a one dimensional model of asymmetric nucleation where the phase boundaries are coupled to a load particle. Sites on the one-dimensional lattice are either empty or filled. Empty sites get filled faster if the is a filled site immediately preceding it. This model has applicability to nucleation problems where the substrate is directional. Examples include nucleation of proteins on filamentary substrates such as nucleic acids and microtubules. The hydrolysis of ATP or GTP in microfilaments such as RecA has been proposed as a mechanism of moving Halliday junctions, and can also be described qualitatively by our model. Using Monte Carlo simulations, we find mean velocities and of a load particle as function of the nucleation rates and the asymmetry parameter. Our results are compared with simple mean field approximations.

9:48AM N34.00008 Free boundaries and confinement in driven diffusive systems , PAK-WING FOK, Caltech, SARAH NOWAK, TOM CHOU, UCLA — We study the dynamics of a load wall confining an asymmetric exclusion process with Langmuir kinetics. Results from Monte Carlo simulations and mean field approximations are compared. We find that the mean position of the wall depends not only on the load on the wall and the injection, adsorption, and desorption rates, but also on the intrinsic fluctuations of the wall. Our results are discussed in the context of nonequilirium phases of the system, fluctuating boundary layers, and particle densities in the lab frame versus the frame of the fluctuating wall.

10:00AM N34.00009 Slow axonal transport: Neurofilaments switch between distinct mobile and stationary states during their transport along axons , PETER JUNG, Department of Physics and Astronomy, Ohio University, NIRAJ TRIVEDI, Center for Molecular Neurobiology, Ohio State University, LEI WANG, The Burnham Institute, La Jolla, ANTHONI BROWN, Center for Molecular Neurobiology, Ohio State University — According to the stop-and-go hypothesis of slow axonal transport, cytoskeletal and cytosolic proteins are transported along axons at fast rates but the average velocity of movement is slow because the movements are infrequent and bidirectional. To test whether this hypothesis can explain the kinetics of slow axonal transport in vivo, we have developed a stochastic model of neurofilament (NF) transport in axons based on tracking of single NF molecules. Based on this model, we propose that NFs in vivo move in both, anterograde and retrograde directions along cytoskeletal tracks switching between mobile and a stationary states. To verify the proposed stationary state we have developed a novel pulse-escape fluorescence photoactivation technique. We find that on average, the NFs spent 92% of their time in the stationary state and 97% of their time pausing. We speculate that the relative proportion of the time that NFs spend in the stationary state may be a principal determinant of their transport rate and distribution along axons, and a potential target of mechanisms that lead to abnormal NF accumulations in disease.

10:12AM N34.00010 A Geometric Mechanism for Asymmetric Diffusion and Membrane Rectification , ROBERT SHAW, NORMAN PACKARD, ProtoLife Srl. — Biological membranes commonly conduct ions freely in one direction while clogging in the other. Existing theories emphasize electrostatic binding of blocking ions in pores as a mechanism for rectification. Here we show that rectification can have a purely geometric origin, based on the interaction of shapes of diffusing particles and pore geometry. The two possibilities can be experimentally distinguished. Blocker binding based on confinement in a potential well will have a strong Arrhenius temperature dependence, whereas "geometric binding" will have a much smaller dependence on temperature. We present both Hamiltonian and Brownian-based computer simulations which demonstrate this effect. A rectifying membrane can maintain different concentrations on either side, resulting in a long-lived metastable state. We derive a dynamic equation of state describing the decay of this metastable system.

10:24AM N34.00011 Untying molecular friction knots , SERDAL KIRMIZIALTIN, DMITRII MAKAROV, The University of Texas at Austin — Molecular knots tied in individual polymer strands have fascinated researchers from many fields. Recently, laser tweezers have been used to tie knots in individual DNA and protein molecules and to observe their dynamics. Unlike their macroscopic counterparts, knots in tensioned polymer strands undergo rapid diffusion caused by thermal fluctuations. Here, we use computer simulations to study the dynamics of a "friction knot" joining a pair of polymer strands. While a friction knot splicing two ropes is jammed when the ropes are pulled apart, molecular friction knots eventually become undone by thermal motion. We show that depending on the knot type and on the polymer structure, a friction knot between polymer strands can be strong (the time τ the knot stays tied increases with the force F applied to separate the strands) or weak (τ decreases with increasing F). We further propose a simple model explaining these behaviors.

10:36AM N34.00012 Exact Solutions of Burnt-Bridge Models for Molecular Motor Transport , ALEXANDER MOROZOV, EKATERINA PRONINA, ANATOLY KOLOMEISKY, Department of Chemistry, Rice University, MAXIM ARTYOMOV, Department of Chemistry, MIT — Transport of molecular motors, stimulated by interactions with specific links between consecutive binding sites (called "bridges"), is investigated theoretically by analyzing discrete-state stochastic "burnt-bridge" models. When an unbiased diffusing particle crosses the bridge, the link can be destroyed ("burned") with a probability p, creating a biased directed motion for the particle. It is shown that for probability of burning $p = 1$ the system can be mapped into one-dimensional single-particle hopping model along the periodic infinite lattice that allows one to calculate exactly all dynamic properties. For general case of $p < 1$ a new theoretical method is developed, and dynamic properties are computed explicitly. Discrete-time and continuous-time dynamics, periodic and random distribution of bridges and different burning dynamics are analyzed and compared. Theoretical predictions are supported by extensive Monte Carlo computer simulations. Theoretical results are applied for analysis of the experiments on collagenase motor proteins.

10:48AM N34.00013 Molecular Dynamics simulation of Buttiker-Landauer Refrigerator , RONALD BENJAMIN, RYOICHI KAWAI, University Of Alabama at Birmingham — A position dependent temperature profile in presence of a periodic potential leads to directed current of Brownian particles, commonly known as Buttiker-Landauer ratchet. Onsager symmetry tells us that inhomogeneous temperature profile can be generated by reversing the Buttiker-Landauer ratchet. When Brownian particles driven by a constant external force cross over the potential barrier, they carry heat from one side to the other. Hence, starting with uniform temperature the flow of Brownian particles induces inhomogeneous temperature profile. We investigate this phenomenon using first principles molecular dynamics simulations as well as the phenomenologial Langevin equation.

Wednesday, March 7, 2007 8:00AM - 10:48AM –

Session N35 DBP DCP: Focus Session: Time Resolved Structural Investigations on Protein Folding and Function Colorado Convention Center 405

8:00AM N35.00001 Correlating folding and signaling in a photoreceptor by single molecule measurements and energy landscape calculations[1] , WOUTER HOFF, Dept of Microbiology and Molecular Genetics, Oklahoma State University — Receptor activation is a fundamental process in biological signaling. We study the structural changes during activation of photoactive yellow protein (PYP). This is triggered by photoisomerization of the p-coumaric acid (pCA) chromophore of PYP, which converts the initial pG state into the activated pB state. Mechanical unfolding of Cys-linked PYP multimers probed by atomic force microscopy (AFM) in the presence and absence of illumination reveals that the core of the protein is extended by 3 nm and destabilized by 30 percent in pB. These results establish a generally applicable single molecule approach for mapping functional conformational changes to selected regions of a protein and indicate that stimulus-induced partial protein unfolding can be employed as a signaling mechanism. Comparative measurements, Jarzynski-Hummer-Szabo analysis of the data, and steered MD simulations of two double-Cys PYP mutants reveal strong anisotropy in the unfolding mechanism along the two axes defined by the Cys residues. Unfolding along one axis exhibits a transition-state-like feature where six hydrogen bonds break simultaneously. The other axis displays an unpeaked force profile reflecting a non-cooperative transition, challenging the notion that cooperative unfolding is a universal feature in protein stability. MD simulations with a coarse-grained protein model show that the folding of pG is two-state, consistent with experimental observations. In contrast, the folding free energy surface of a coarse-grained model of pB involves an on-pathway partially unfolded intermediate that closely matches experimental data. The results reveal that interactions between the pCA and its binding pocket can switch the energy landscape for PYP from two- to three-state folding, and show how this can be exploited to trigger large functionally important protein conformational changes.

[1]WDH is supported by NIH grant MG063805

8:36AM N35.00002 Spectroscopic probes of enzyme-ligand interaction dynamics[1] , CHRISTOPHER CHEATUM, JIGAR BANDARIA, SAMRAT DUTTA, SARAH HILL, AMNON KOHEN, University of Iowa, Department of Chemistry — Formate dehydrogenase catalyzes the NAD-dependent oxidation of formate to carbon dioxide. The intrinsic chemical step involves hydride transfer from formate to the nicotinamide ring of NAD. As with several other NAD-dependent dehydrogenases, kinetic measurements suggest that thermal fluctuations of the enzyme are important in the hydride-transfer reaction. We have measured the dynamics of enzyme-inhibitor interactions in binary and ternary complexes of formate dehydrogenase with pseudohalides using infrared photon-echo spectroscopy. The pseudohalides are excellent vibrational chromophores that are known to be sensitive reporters of interactions with their local environments. They are also excellent inhibitors for formate dehydrogenase. Our measurements reveal significant differences in the dynamics of the different binary and ternary complexes. By comparing and contrasting the dynamics for different complexes we gain insight into the active-site components that make the most important contributions to the observed dynamics.

[1]Supported by the Roy J. Carver Charitable Trust

8:48AM N35.00003 Shallow Free Energy Landscapes Remodelled by Ligand Binding[1] , TROY MESSINA, DAVID TALAGA, EMILIO GALLICHIO, RONALD LEVY, Rutgers University, Department of Chemistry and Chemical Biology — Glucose/galactose binding protein (GGBP) functions as part of a larger system of proteins for molecular recognition and signalling in enteric bacteria. Here we report on the thermodynamics of conformational equilibrium distributions of GGBP from both time-resolved fluorescence experiments and computational umbrella sampling molecular dynamics analyzed by the weighted histogram analysis method (WHAM). Three conformations appear at zero glucose concentration and systematically transition to three conformations at high glucose concentration. Fluorescence anisotropy correlations, fluorescent lifetimes, thermodynamics, computational structure minimization and molecular dynamics, and previous work were used to identify the three components as open, closed, and twisted conformations of the protein. The existence of three states at all glucose concentrations indicates that the protein continuously fluctuates about its conformational state space via thermodynamically driven state transitions, and the glucose biases the populations by reorganizing the free energy profile. These results and their implications are discussed in terms specific and non-specific interactions GGBP has with cytoplasmic membrane proteins.

[1]supported by NIH Ruth L. Kirschstein NRSA Post Doctoral Fellowship F32GM072328

9:00AM N35.00004 High-throughput biophysics of functional tuning in photoactive yellow protein[1] , WOUTER HOFF, Dept of Microbiology and Molecular Genetics, Oklahoma State University, ANDREW PHILIP, GEORGE PAPADANTONAKIS, Dept of Biochemistry and Molecular Biology, University of Chicago, OSU TEAM, UOFC TEAM — The relationship between the structure of a protein and its function is a central unresolved problem in biology. We use photoactive yellow protein (PYP) to develop quantitative high-throughput methods to study this problem. PYP is a small bacterial photoreceptor with rhodopsin-like photochemistry based on its p-coumaric acid (pCA) chromophore. The absorbance maximum and pKa of the pCA in the active site of native PYP are shifted from 400 nm and 9.0 in water to 446 nm and 2.8 in the protein. Thus, PYP offers a unique model system to probe protein-ligand interactions. Here we show that high-throughput microscale methods can be used for quantitative biophysical studies of the absorbance spectrum PYP, its fluorescence quantum yield, apparent pKa of the pCA, protein stability against chemical denaturation, and kinetics of the last PYP photocycle step. A wide range of properties was observed among the mutants, and structural features that tune functional properties were identified. These results open the way for high-throughput quantitative biophysical studies of PYP.

[1]WDH is supported by NIH grant MG063805

9:12AM N35.00005 Probing protein dynamics using Fluorescence Resonance Energy Transfer with donors of different lifetimes , WEIQUN PENG, George Washington University, TANIA CHAKRABARTY, University of Chicago, PAUL GOLDBART, University of Illinois at Urbana Champaign, PAUL SELVIN, University of Illinois at Urbana Champaign — Fluorescence resonance energy transfer (FRET), using nanosecond dyes, and its derivative, Lanthanide-based resonance energy transfer (LRET), using millisecond-lifetime lanthanide chelates, are methods to measure distances on the 2-10 nm length-scale. It has been found that in certain systems energy transfer efficiency E for FRET and LRET measurements can be dramatically different [Chakrabarty et al., PNAS, 99: 6011-6016 (2002)]. Here we develop a theoretical model that shows that the dramatic difference can be explained by the presence of intrinsic dynamics of the system. Furthermore, we quantitatively investigate how information about the time-scale and distance-scale associated with the intrinsic dynamics can be inferred, by comparison of FRET and LRET results.

9:24AM N35.00006 Advanced Infrared Spectroscopy for Time-Resolved Structural Investigation of Protein Structure and Function[1] , AIHUA XIE, Department of Physics, Oklahoma State University — The human genome encodes approximately 30,000 different proteins. A single mutation at a critical site of one protein can cause serious diseases, such as cardiac failure and cancer. This illustrates the significant role of protein structures in protein functions. In order to obtain a fundamental understanding of protein structure-function relation, we must develop and employ both physical theories and experimental techniques. In my talk, I will report both experimental and computational studies on vibrational structural markers for advanced infrared spectroscopy, slaved protein structural dynamics, and "electrostatic epicenter" model as a general mechanism for activation of receptor proteins in cell signaling.

[1]In collaboration with Anupama Thubagere, Lorand Kelemen, Beining Nie, Sandip Kaledhonkar, and Edward Manda, Oklahoma State University.

10:00AM N35.00007 Channel noise reduction due to gating charge effects , GERHARD SCHMID, IGOR GOYCHUK, PETER HÄNGGI, University of Augsburg, Germany — We investigate the influence of gating charge effects on the channel noise-induced spontaneous spiking activity of excitable membrane patches [1] within a stochastic Hodgkin-Huxley model [2]. The random switching of the channel gates between an open and a closed configuration is always connected with movement of gating charge within the cell membrane. At the beginning of an action potential the gating current is opposite to the direction of the ion current through the membrane. Therefore, the excitability is expected to become reduced due to the influence of gating current. Our study revealed that while the deterministic modelling with gating charge effects does not differ dramatically from the original Hodgkin-Huxley model for the standard set of parameters, the corresponding stochastic model which takes into account the channel noise – i.e. the fluctuations of the number of open ion channels – does behave very differently for intermediate-to-large membrane patch sizes. A main finding is that spontaneous spiking activity becomes drastically reduced [1].

[1] G. Schmid, I. Goychuk, and P. Hänggi, Phys. Biol., in press (2006); (arXiv:abs/q-bio.NC/0611040).
[2] G. Schmid, I. Goychuk, and P. Hänggi, Europhys. Lett. **56**, 22 (2001)

10:12AM N35.00008 A Molecular Dynamics-Decorated Finite Element Method (MDeFEM) Framework for Simulating the Gating of Mechanosensitive Channels , XI CHEN, YUYE TANG, GUOXIN CAO, JEJOONG YOO, ARUN YETHIRAJ, QIANG CUI, Columbia University — The gating pathways of mechanosensitive channels of large conductance (MscL) are studied using the finite element method. The phenomenological model treats transmembrane helices as elastic rods and the lipid membrane as an elastic sheet of finite thickness. The interactions between various continuum components are derived from atomistic energy calculations. The structural variations along the gating pathway are consistent with previous analyses based on structural models and biased molecular-dynamics simulations. Upon membrane bending, there is notable and nonmonotonic variation in the pore radius. This emphasizes that the gating behavior of MscL depends critically on the form of the mechanical perturbation. Compared to popular all-atom simulations, the MDeFEM framework offers a unique alternative to bridge detailed intermolecular interactions and biological processes occurring at large spatial and timescales. It is envisioned that such a hierarchical multiscale framework will find great value in the study of a variety of biological processes involving complex mechanical deformations such as muscle contraction and mechanotransduction.

10:24AM N35.00009 Develop vibrational structural makers for probing the protonation state and hydrogen bonding interactions of tyrosine in proteins and their functional intermediates , AIHUA XIE, BEINING NIE, EDWARD MANDA, ANUPAMA THUBAGERE, Oklahoma State University — Proteins are dynamic in nature. In order to understand how a protein performs its function based on laws of physics, it is critical to probe and investigate functionally important structural transitions of the protein. Time-resolved infrared spectroscopy offers excellent time resolution (picoseconds to seconds), and contains extensive structural information. The real challenge is how to extract structural information from time-resolved infrared data. We will report computational methods for developing vibrational structural markers of tyrosine. Using density function theory (DFT) based first principle computational studies combined with experimental data, we found that it is possible to unambiguously determine if the phenolic ring in Tyrosine is neutral or negatively charged based on the frequency of one ring vibrational mode. In addition, we show that it possible to determine the number and nature of hydrogen bonding interactions of a phenolic group in proteins using a combination of C-O stretching and O-H stretching frequencies (2D vibrational spectroscopy).

10:36AM N35.00010 Correlated Fluorescence Parameters of Single Molecules , CLAUDIU GRADINARU, University of Toronto, DAVID CHANDLER, CARL HAYDEN, Sandia National Labs — A novel detection system is used in a confocal optical microscope for measuring correlated fluorescence lifetimes and spectra. Fluorescence photons emitted from a sample are imaged through a dispersive optical system onto a time- and position-sensitive detector. For each photon the apparatus records the wavelength, the emission time relative to the laser excitation pulse and the absolute detection time, so that correlations among all the fluorescence properties are maintained. A histogram over many photons can generate a full fluorescence spectrum and a correlated decay plot at every pixel in a fluorescence image. The complex data structure allows mapping the time-dependent distribution of multiple fluorescent species in a sample and enables monitoring the dynamics of single molecules on a time scale that spans from picoseconds to minutes. Unique correlations between intensity, spectrum and lifetime prove useful for tracking changes in the nanoenvironment of fluorescent probes. The detection method also provides a more complete description of the fluorescence resonance energy transfer (FRET) than conventional microscopy techniques, as demonstrated by single-pair FRET experiments between dyes spaced apart by short peptides and by dsDNA chains.

Wednesday, March 7, 2007 11:15AM - 1:39PM –

Session P2 DBP: Nanopore World: from Single-Molecules to Bionanotechnology Prospects

Colorado Convention Center Four Seasons 4

11:15AM P2.00001 Towards DNA Sequencing using Solid-State Nanopores , SEAN LING, Brown University — 10 Years ago John Kasianowicz and coworkers invented the concept of using ionic conductance as a mechanism for scanning a DNA molecule for genetic information. Their proposal has since led to the creation of an exciting field of nanopore biophysics. I will discuss our current effort in combining the SBH (sequencing-by-hybridization) concept and solid-state nanopores for fast DNA sequencing.

11:51AM P2.00002 Entropic springs in single-molecule polymer partitioning into protein nanopores , SERGEY BEZRUKOV, National Institutes of Health — The capture and release of single polyethylene glycol molecules by the alpha-Hemolysin pore are observed as time-resolved reversible steps in ion conductance. The capture on-rate, inferred from the step frequency, decreases monotonically with polymer size. However, the polymer residence time shows a cross-over behavior, first increasing and then decreasing with molecular weight (*Phys. Rev. Lett.*, 2006, **97**:018301). Our interpretation is that in case of polymers which are too large to be accommodated within the pore, the out-of-the-pore part of the molecule pulls on the trapped part thus acting as an entropic spring.

12:27PM P2.00003 Forces on DNA in a solid-state nanopore , ULRICH KEYSER, Institut f. Experimentelle Physik I, Universitaet Leipzig, Germany & Kavli Institute of Nanoscience, Delft University of Technology, The Netherlands — Amongst the variety of roles for nanopores in biology, an important one is enabling polymer transport, for example in gene transfer between bacteria and transport of RNA through the nuclear membrane. Recently, this has inspired the use of protein and solid-state nanopores as single-molecule sensors for the detection and structural analysis of DNA and RNA by voltage-driven translocation. The magnitude of the force involved is of fundamental importance in understanding and exploiting this translocation mechanism. Furthermore, solid-state nanopores can be seen as a model system for biological nanopores. We will discuss the forces acting on single DNA strands electrophoretically driven through a solid-state nanopore. The force was directly measured using optical tweezers [1]. The force depends linearly on the applied voltage for a wide range of salt concentrations (0.02M – 1M KCl) and nanopore diameters (6 nm – 80 nm). Interestingly, we find for small nanopores with a diameter less than 15 nm that the force on the DNA is independent of the salt concentrations. However, the force decreases significantly in the larger nanopores. We will qualitatively discuss our results using the Poisson-Boltzmann and Navier-Stokes equations for a simple geometry. The influence of hydrodynamic coupling between the nanopore walls and the DNA molecule is of crucial importance to understand the force on a DNA molecule in nanopores. [1] U. F. Keyser et al. Nature Physics 2, 473 (2006)

1:03PM P2.00004 Molecular Tweezers: Using the Electric Field in a Synthetic Nanopore to Disrupt Biomolecular Binding Forces[1] , GREGORY TIMP, Beckman Institute, University of Illinois — The forces binding proteins to DNA in an aqueous solution are vital to biology, but inadequately understood. In particular, restriction enzymes like EcoRI are extraordinarily sequence-specific and yet the complex with DNA is very stable. To stringently test these forces, we use the electric field inside a synthetic nanometer-diameter pore in a thin membrane to pull on double-stranded DNA bound to EcoRI and BamHI, introducing a shear between the enzyme and their respective cognate sites in DNA. We observe a sharp threshold near 1nN in the force required to disrupt the binding in the complex, which is in stark contrast with previous measurements of the force (10pN) accomplished by unzipping the DNA molecule at a constant loading rates (1nN/sec). This force, acting over a distance corresponding to the separation between bases, coincidentally corresponds to the free energy of formation for the EcoRI-DNA complex. Using molecular dynamics, we interpret the measurements and elucidate the binding with atomic precision.

[1]This work is supported by a grant from the NIH (R01 HG003713A)

Wednesday, March 7, 2007 11:15AM - 2:15PM –

Session P34 DBP GSNP DPOLY: Focus Session: Cytoskeletal Dynamics and Cell Migration I

Colorado Convention Center 404

11:15AM P34.00001 Integration of actin dynamics and adhesion in cell migration[1] , CLARE WATERMAN-STORER, Scripps Research Institute — Cell migration requires transmission of motion generated in the actin cytoskeleton to the extracellular environment through a complex assembly of proteins in focal adhesions. We developed Correlational Fluorescent Speckle Microscopy to measure the coupling of focal adhesion proteins to actin filaments. Different classes of focal adhesion structural and regulatory molecules exhibited varying degrees of correlated motions with actin filaments, indicating hierarchical transmission of actin motion through focal adhesions. Interactions between vinculin, talin and actin filaments appear to constitute a slippage interface between the cytoskeleton and integrins, generating a molecular clutch that is regulated during the morphodynamic transitions of cell migration.

[1]NIH Director's Pioneer Award Program, DP1-OD000435

11:51AM P34.00002 The Translation of Actin Dynamics into Traction Force via Focal Adhesions in Migrating Cells , MARGARET GARDEL, The Scripps Research Institute, BENEDIKT SABASS, Heidelberg University, LIN JI, The Scripps Research Institute, ULRICH SCHWARZ, Heidelberg University, CLARE WATERMAN, The Scripps Research Institute — Forces are generated in the actin cytoskeleton by myosin-II motors and transmitted to the extracellular matrix (ECM) via dynamic macromolecular assemblies called focal adhesions (FA). To explore how forces are transmitted from the contractile actomyosin network to the ECM, we combine traction force microscopy and fluorescent speckle microscopy (FSM) of FAs and actin cytoskeleton in Ptk1 epithelial cells. We find that the relationship between intracellular actin flow and traction force is spatially segregated within individual focal adhesions. Near the leading edge, actin flow is inversely related to force, while towards the cell center, there is a positive correlation. This change is regulated by small GTPase signal transduction pathways and myosin II motor based contraction. Thus, the FA is a molecular clutch that exhibits regulatory switching between different coupling mechanisms.

12:03PM P34.00003 Modeling and imaging the topography of nascent adhesions. , ERDINC ALTIGAN, DAVID ENTENBERG, BEN OVRYN, Department of Anatomy and Structural Biology, Albert Einstein College of Medicine — We have developed a model to explain the initiation of adhesions on the ventral surface of a cell. An analysis of the energetics of membrane bending and the effects of a composite system of freely diffusing repellers and receptors and a fixed network of ligands on the extracellular matrix demonstrates that a small bundle of actin filaments is able to push the membrane down to the extracellular matrix and nucleate a nascent adhesion. This model is consistent with experiments which demonstrate that cell motility requires cycles of actin polymerization and depolymerization at the leading edge of cell protrusions; the leading lamella adheres to the extracellular matrix and stable focal contacts form which can resist strong contractile forces. Although several of the mechanisms responsible for focal contact formation have been elucidated, the detailed processes leading to the formation of the earliest adhesions have remained elusive. Based upon the energetics of adhesion formation, our model predicts the shape of the membrane at the nucleated adhesion. We have developed a novel form of confocal interference microscopy to measure the distance between the ventral surface of a cell and the substratum with several nanometer precision and we have measured the topography of focal adhesions.

12:15PM P34.00004 Actin-Filamin Networks and Cell Mechanics , KAREN KASZA, Harvard University, FUMIHIKO NAKAMURA, THOMAS STOSSEL, Brigham and Women's Hospital, NING WANG, University of Illinois at Urbana-Champaign, DAVID WEITZ, Harvard University — We seek to elucidate the mechanisms underlying stress dependent stiffening of the cellular cytoskeleton. Filamin A (FLNa) is a protein that cross-links and bundles actin filaments into soft gels that stiffen dramatically with applied mechanical stress. Living cells show similar stiffening behavior, but the underlying physical mechanism is poorly understood. While it is known that FLNa plays an important *biological* role in some very mechanical cellular processes, it is still unclear whether FLNa plays such a dominant *mechanical* role in the cell as it does in simple reconstituted actin networks. Here, we work with a human melanoma cell line deficient in FLNa and a transfected subline expressing FLNa. For both cell lines, we probe cell stiffness measured by magnetic twisting cytometry as we increase the stress supported by the actin cytoskeleton to determine the contribution of FLNa to both the linear and nonlinear material properties of the cell cytoskeleton.

12:27PM P34.00005 Critical state enhances cross-linker denaturation under stress in biopolymer networks , BRIAN DIDONNA, ALEX J. LEVINE, University of California, Los Angeles — We report on the statistical behavior of cross-linker molecules containing numerous unfolding domains when they are used to bind a random semiflexible polymer network. Cross-linkers with unfolding domains are ubiquitous in the F-actin component of the cytoskeleton - examples include filamin and a-actinin. We show, through mean field calculations and simulations, that under tension the cross-linkers naturally organize into a critical state which greatly enhances their propensity to unfold. Unfolding of cross-links could play a role in stress-regulation and mechanotransduction. The critical state is characterized by an exponential or faster growth in the population of cross-linkers as a function of tension up to a characteristic unfolding tension. This critical state should occur at physiologically relevant stress levels in any open random network built with such cross-linkers.

12:39PM P34.00006 Molecular motor-induced instabilities and crosslinkers determine biopolymer organization , DAVID SMITH, University of Leipzig, Institute for Soft Matter Physics, FALKO ZIEBERT, Universitaet Bayreuth, DAVID HUMPHREY, CYNTHIA DUGGAN, University of Texas at Austin, CNLD, WALTER ZIMMERMANN, Universitaet Bayreuth, JOSEF KAES, University of Leipzig, Institute for Soft Matter Physics — All eukaryotic cells rely on the active self-organization of protein filaments to form a responsive intracellular cytoskeleton. The need for motility and reaction to stimuli additionally requires pathways that quickly and reversibly change cytoskeletal organization. While thermally-driven order-disorder transitions are, from the viewpoint of physics, the most obvious method for controlling such organization, the timescales necessary for effective cellular dynamics would require temperatures exceeding the physiologically viable temperature range. We report a mechanism whereby myosin II can cause near-instantaneous order-disorder transitions in reconstituted cytoskeletal actin solutions. When motor-induced filament sliding diminishes, the actin network structure rapidly and reversibly self-organizes into various assemblies. Addition of stable crosslinkers was found to alter the architecture of ordered assemblies. These isothermal transitions between dynamic disorder and self-assembled ordered states illustrate that the interplay between passive crosslinking and molecular motor activity plays a substantial role in dynamic cellular organization.

12:51PM P34.00007 Instabilities in filament-motor solutions with crosslinkers.[1] , FALKO ZIEBERT, Materials Science Division, Argonne National Laboratory, 9700 South Cass Avenue, Argonne, IL 60439, RONNY PETER, WALTER ZIMMERMANN, Theoretical Physics Ia, University of Bayreuth, D-95440 Bayreuth, Germany — Filament-motor systems are in nonequilibrium due to the energy consumption during motor movement (via ATP hydrolysis), and thus display pattern and structure formation. We report on simple mesoscopic modeling based on conservation laws with active filament currents. We discuss instabilities in a recent experiment on actomyosin, where ATP is depleted in the presence of a small amount of crosslinker proteins. In the limit of high density of crosslinkers, we propose a model where transported filaments are coupled to an elastic crosslinked network, leading to oscillatory behavior.
References:
D. Smith, F. Ziebert, D. Humphrey, C. Duggan, W. Zimmermann and J. Kaes, submitted to Biophys. J. ; R. Peter, F. Ziebert and W. Zimmermann, submitted to Europhys. Lett.

[1]supported by the U.S. Department of Energy, grant W-31-109-ENG-38 (IA)

1:03PM P34.00008 Interaction of Semi-flexible Filaments and Molecular Motors[1] , DMITRY KARPEEV, IGOR ARONSON, Argonne National Laboratory, LEV TSIMRING, University of California at San Diego, HANS KAPER, Argonne National Laboratory/National Science Foundation — We consider effects of finite flexibility on interaction of two microtubules with molecular motor. On the basis of numerical solution to nonlinear elasticity equation we show that the flexibility enhances tendency of microtubules to align, which, in turn, favors formation of large-scale structures in the multi-tubules system. Moreover, for much softer filaments, like actin, we observed that the action of the motor may result in formation of multiple loops due to buckling of the filaments.

[1]This work was supported by U.S. DOE grants DE-AC02-06CH11357 (DK,IA,HK) and DE-FG02-04ER46135 (LT)

1:15PM P34.00009 Effective medium theory of semiflexible filamentous networks[1] , MOUMITA DAS[2], Dept of Chemistry and Biochemistry, University of California, Los Angeles., ALEX J. LEVINE, Dept. of Chemistry and Biochemistry, University of California, Los Angeles., F.C. MACKINTOSH, Dept. of Physics, Vrije Universiteit, Amsterdam, The Netherlands. — We develop an effective medium approach to the mechanics of disordered, semiflexible polymer networks such as those forming the cytoskeleton and study their response to both spatially uniform and nonuniform strain. We identify distinct elastic regimes in which the effective filament bending stiffness or stretch modulus vanishes. We also show that our effective medium theory predicts a crossover between affine and non-affine strain, consistent with both prior numerical studies and scaling theory.

[1]MD and AJL acknowledge support from NSF-DMR0354113. FCM acknowledges the hospitality of theUCLA chemistry department.This work was supported in part by the Foundation for Fundamental Research on Matter (FOM).
[2]Affiliation from Jan 2007: Dept. of Physics, Vrije Universiteit, Amsterdam, The Netherlands.

1:27PM P34.00010 Forced shape deformations of interfaces and biopolymer networks , WOLFGANG LOSERT, ANDREW POMERANCE, CORY POOLE, ERIN RERICHA, University of Maryland — What sets the characteristic length and timescale of shape deformations of motile cells? To investigate possible contributions to these scales, we investigate shape deformations of biopolymer networks and lipid bilayers, two key components of motile cells. Controlled deformations are generated with holographic optical tweezers and detected optically. We observe that for small deformation lengths of up to 4 microns (for cage sizes less than one micron) and short time deformations of order seconds, actin networks respond mostly elastically. We see evidence of coupling between two nearby deformation fields in an actin network. Relaxations of directly forced giant unilamellar vesicles reveal that -during free relaxation- apparent membrane stresses remain localized on micron scales.

1:39PM P34.00011 Viscoelasticity and rheology of a suspension of active filaments[1] , M. CRISTINA MARCHETTI, Syracuse University, TANNIEMOLA B. LIVERPOOL, Leeds University, UK — We study the viscoelasticity of an active solution of polar biofilaments and motor proteins under an externally imposed stress. Adapting methods from polymer physics, we derive the constitutive equations for the stress tensor in the isotropic phase and in phases with liquid crystalline order (nematic and polarized). The stress relaxation in the various phases is discussed. Activity is responsible for a strong enhancement (a divergence in 2d) of the viscosity at the isotropic-nematic transition. This behavior is reminiscent of an equilibrium liquid-solid transition rather than a liquid-liquid transition, and is a direct consequence of contractile bundling. A second signature of activity is found in the nematic phase, where the stress tensor acquires a nonequilibrium contribution proportional to ATP (Adenosine Tri-Phosphate) consumption rate that remains finite in the absence of imposed mechanical deformation. The role of boundaries on these phenomena will also be discussed.

[1]Work supported by the NSF grant No. DMR-0305407 and by the Royal Society

1:51PM P34.00012 Dynamics and statistical mechanics of semiflexible polymer bundles , CLAUS HEUSSINGER, MARK BATHE, ERWIN FREY, Arnold-Sommerfeld Center for theoretical physics, University of Munich — Bundles formed from semiflexible polymers are ubiquitous in nature (e.g. filopodia) and many areas of technology (e.g. carbon nanotube bundles). Despite their simple structure, their mechanical and dynamical properties are only poorly understood. We set up an elastic energy functional that allows characterizing the dynamical and statistical mechanical properties of polymer bundles, in much the same way as the standard worm-like chain model (WLC) does for single polymers. The key result of our analysis is that bundles must be characterized by a wave-number dependent persistence length $l_p(q)$ instead of just a single q-independent value. This finding is shown to have dramatic consequences not only on the static and dynamic fluctuation spectrum of an isolated bundle but also on the scaling behaviour of their entangled solutions as well as their cross-linked networks.

2:03PM P34.00013 Dynamic Control of F-actin Polymerization Using Electrical Interfaces , IAN Y. WONG, Materials Science and Engineering, Stanford University, MATTHEW J. FOOTER, Biochemistry, Stanford University, NICHOLAS A. MELOSH, Materials Science and Engineering, Stanford University — The cytoskeletal biopolymer F-actin plays a crucial role in the mechanics and motility of eukaryotic cells and is also a model system for the investigation of the physics of semiflexible polymers. Historically, the polymerization of reconstituted F-actin has been initiated in vitro by increasing the bulk ion concentration from reduced to physiological levels. In this work, nanoscale electrodes are used to achieve spatial and temporal control of F-actin polymerization. The application of a low-frequency AC voltage alternately concentrates divalent cations and negatively charged G-actin monomers at the electrode surface, promoting highly localized polymerization. Unlike bulk polymerization, the kinetics of this electronically activated polymerization are governed by two competing mechanisms: ionic activation through Mg^{2+} binding and nucleation of actin trimers. Additional control can be achieved through the superposition of a high-frequency AC signal to align and trap filaments through dielectrophoresis. This combination of low and high frequency AC voltages may allow for the dynamic assembly of nanostructures with precisely controlled size and registry.

Wednesday, March 7, 2007 11:15AM - 1:51PM –

Session P35 DBP DCP: Focus Session: Protein Motin Vibrations to Conformational Changes

Colorado Convention Center 405

11:15AM P35.00001 Dose and exposure requirements for the protein x-ray serial crystallography. , DMITRI STARODUB, Department of Physics, Arizona State University, Tempe, AZ 85287-1504 — We have proposed spraying proteins (aligned by a laser) across a synchrotron beam to solve proteins which cannot be crystallized.[1] A single-file stream of ice-jacketed proteins is considered. We compute diffraction patterns for the GroEL at the incident x-ray flux predicted for a new coherent scattering beamline at the Advanced Photon Source. Using iterative phasing of the data, we determine the relationship between the count rate at a reconstructed pixel (or 3D voxel) of a given size in the real-space charge-density map and number N of proteins in the 10-μm 2 kV x-ray beam at any instant. A modulation transfer function estimates resolution for various exposure times. With the incident flux of 10^6 photons/s/nm^2 and N=10, over 5,000 counts/s are distributed over the entire diffraction pattern, which is sufficient for a nm resolution with 200 s exposure. We compare the results of this numerical lensless imaging experiment with a simple theoretical treatment of image formation in the dark and bright field phase contrast. Supported by ARO, NSF and co-workers.[1] [1]J. Chem Phys. 123, 244304 .

11:27AM P35.00002 Crystallization media inhibit protein structural dynamics , ANUPAMA THUBAGERE, LORAND KELEMEN, SANDIP KALEDHONKAR, AIHUA XIE, Oklahoma State University — The first role of any crystallization solution is to reduce the solubility of proteins, so that it induces protein precipitation. Most times, protein precipitation does not lead to protein crystallization. Do crystallization solutions play any other roles that are crucial for protein crystallization? Here we report our studies that crystallization solutions suppress or inhibit protein structural dynamics. Photoactive yellow protein (PYP), a bacterial blue light photoreceptor protein, is employed as a model system in our study. We use time-resolved FTIR spectroscopic technique to probe the structural dynamics of proteins, including the proton transfer process and global conformational motions. We found that high concentration crystallization solutions $(NH_4)_2SO_4$ strongly inhibit the structural dynamics of PYP upon blue light excitation. We will examine and discuss the mechanism in which crystallization solutions inhibit protein structural dynamics. The results are expected to provide insights to fundamental understanding of protein crystallization of water-soluble proteins. In addition, the data clearly demonstrates that the structural dynamics observed in crystalline conditions may be far from their natural structural dynamics for studies of protein structure-function relations.

11:39AM P35.00003 ABSTRACT HAS BEEN MOVED TO D26.00011 –

11:51AM P35.00004 Conformational dependence of a protein kinase phosphate transfer reaction , MONTIAGO LABUTE, Theoretical Division, Los Alamos National Laboratory, GRAEME HENKELMAN, Department of Chemistry and Biochemistry, University of Texas, Austin, CHANG-SHUNG TUNG, PAUL FENIMORE, BEN MCMAHON, Theoretical Division, Los Alamos National Laboratory — Atomic motions and energetics for a phosphate transfer reaction catalyzed by the cAMP-dependent protein kinase have been calculated using plane-wave density functional theory, starting from structures of proteins crystallized in both the reactant conformation (RC) and the transition-state conformation (TC). In TC, we calculate that the reactants and products are nearly isoenergetic with a 20-kJ/mol barrier, whereas phosphate transfer is unfavorable by 120 kJ/mol in the RC, with an even higher barrier. Our results demonstrate that the phosphate transfer reaction occurs rapidly and reversibly in a particular conformation of the protein, and that the reaction can be gated by changes of a few tenths of an angstrom in the catalytic site [1]. [1] G.H. Henkelman, M.X. LaBute, C.-S. Tung, P.W. Fenimore, B.H. McMahon, Proc. Natl. Acad. Sci. USA vol. 102, no. 43:15347-15351 (2005).

12:03PM P35.00005 Interaction of Receptors and GTPase-Activating Proteins in a G Protein Signaling Module[1] , MARC TURCOTTE, WEI TANG, ELLIOTT M. ROSS, University of Texas Southwestern Medical Center — We have developed a model of the interactions of proteins involved in G protein signaling using steady-state data from reconstituted vesicles. The model includes receptor, G protein (G), GTPase activating protein (GAP), GTP and GDP. Implementation is done using coupled ordinary differential equations. We performed a global fit to the model parameters against enzymologic and nucleotide-binding data using simulated annealing constrained by thermodynamics. Validation was done using Monte Carlo data. Fit parameters uncertainties were obtained via multiple repeats of stochastic searches. We studied fit parameter correlations near a solution by local thermal sampling of the cost manifold. The best fit parameters agree with values derived from dynamic data not used in our fit. We used our model to study signaling in familiar regimes and to predict new, testable behaviors in others. Signal output is a complex function of the inputs: receptor and GAP at physiologic and experimental concentrations of GTP and GDP. We studied the shape of the activation surface. Its complexity derives from stoichiometric relationships among protein concentrations. Our model predicts signaling pathways and dynamical response in G protein modules.

[1]NIH RO1GM30359, NIH K25GM071957, Welch Foundation I-0982

12:15PM P35.00006 Fast motion of the surface alcohol molecules deduced from sum-frequency vibrational spectroscopy , JAEHO SUNG, Department of Physics, Sogang University, DOSEOK KIM, Department of Physics and Interdisciplinary Program of Integrated Biotechnology, Sogang University — Sum-frequency generation (SFG) vibrational spectroscopy was used to investigate the surface of the homolog series of alcohols from methanol to octanol. It was found that SFG signal strengths from the terminal methyl group of short-chain alcohols cannot be explained by assuming the surface molecules were fixed in time. Introduction of the rotational motion with time scale comparable to the dephasing time of the vibrational mode of the terminal methyl group ($\sim$0.7 picosecond) was able to explain the reduction of the SFG signal by motional averaging effect. This timescale of motion increased with the increase in the molecule size and bulk viscosity. Our result also suggests that surface alcohol molecules move faster as compared to the same molecules in the bulk liquid.

12:27PM P35.00007 Effect of molecular vibrations on charge transfer in polypeptide chains , NIKOLAI SERGUEEV, ALEXANDER DEMKOV, University of Texas at Austin — We present first principles framework suitable for analyzing and understanding the effect of molecular vibrations on charge transfer in polypeptide chains. Our approach is based on density functional theory and Keldysh nonequilibrium Green's function formalism. This method allows us to treat both electrons and molecular vibrations (phonons) on equal footing in a self-consistent manner. The salient feature of our technique is that we consider the vibration of the whole polypeptide bridge. We present a numerical results for a charge transfer through alanine polypeptide chains of the various length and show that the electron tunneling is greatly affected when the interaction between electrons and molecular vibrations is taken into account. We also present a vibrational spectroscopy analysis and identify those vibrational modes of the alanine polypeptides involved into the inelastic charge transfer.

12:39PM P35.00008 No Long-Lived Coherent Oscillations in Proteins at Room Temperature , ROBERT AUSTIN, MICHAEL WHITE, Princeton University — A recent PRL (PRL 95, 253601 (2005)) suggested that proteins could have very narrow holes (Hz wide) burnt into their electronic spectra at 300K, and suggested that "snail-paced" light group velocity light could result. We will show that the authors mistook conformational diffusion phase shifts for narrow lines and show that there are no narrow long-lived holes in a protein spectra at 300 K nor is there any snail-paced light.

12:51PM P35.00009 Slow light with bacteriorhodopsin solutions , CHANDRA YELLESWARAPU, FRANCISCO ARANDA, REJI PHILIP, RAO DEVULAPALLI, University of Massachusetts - Boston — Slow light in gases and solids has been studied in recent years. Various applications are possible depending on the modulation frequency and the amount of delay that can be induced in the traveling wave. Recently we demonstrated ultra slow light in the biological photo-membrane bacteriorhodopsin (bR) polymer film at room temperature [Phy. Rev. Lett., **95**, 2536011, 2005]. By exploiting the photoisomerization property of bR for coherent population oscillation, the group velocity is controlled from about 0.1 mm/sec to the speed of light. But as bR is embedded in a polymer matrix, the isomerization rates are slow and hence limited to low modulation frequencies. On the other hand bacteriorhodopsin solution can be used for obtaining slow light at higher modulation frequencies. Studies in solution also offer the advantage of changing the optical density at ease resulting in longer pulse delays. Detailed results on slow light where the delay is varied with modulation frequency, optical density and all-optical control with a blue laser beam will be presented.

1:03PM P35.00010 Physical basis for membrane-charge selectivity of cationic antimicrobial peptides , BAE-YEUN HA, SATTAR TAHERI-ARAGHI, University of Waterloo — Antimicrobial peptides are known to selectively disrupt (highly-charged) microbial membranes by asymmetrical incorporation into the outer layers. We present a physical basis for membrane-charge selectivity of cationic antimicrobial peptides. In particular, we provide a clear picture of how peptide charge, Q, influences the asymmetrical insertion – one salient feature is the existence of an optimal peptide charge, at which selective insertion is optimized. Our results suggest that large Q is required for antimicrobial selectivity, consistent with experiments.

1:15PM P35.00011 Investigating Potential Surfaces with QM/MM Methods , THOM VREVEN, Gaussian, Inc., 340 Quinnipiac Street, Building 40, Wallingford, CT 06492 — Geometry optimization of large QM/MM systems is not trivial, especially when transition states or higher order saddle points are desired. The optimization can be carried out with a macro/micro scheme, which alternates (internal coordinate) geometry steps in the QM region with full (cartesian) minimizations of the MM region. This significantly reduces the number of QM calculations, and avoids bottlenecks associated with coordinate transformation and Hessian manipulation. This standard macro/micro scheme, however, suffers from numerical instability and compromised convergence behavior. This affects particularly the optimization of transition states, which is therefore not often successful. To address these problems we present extensions to the macro/micro scheme, which have been implemented in the ONIOM framework for hybrid methods. In the standard scheme, the QM and MM regions are coupled only through first order terms. We now include second order coupling using analytical MM contributions, employing linear scaling methods. We show how this improves convergence and allows for the optimization and characterization of saddle points in very large systems. We demonstrate our methods using various examples, such as the hydrogen peroxide reduction by Selenoprotein Glutathione Peroxidase, proton transfer in H-Y zeolite, and thermal isomerization of retinal in Bacteriorhodopsin.

Wednesday, March 7, 2007 2:30PM - 5:30PM –

Session S5 DBP: Quantum Mechanics/Molecular Mechanics: Developments and Applications

Colorado Convention Center Korbel 1A-1B

2:30PM S5.00001 Modeling Enzymatic Reactions in Proteins. , RICHARD FRIESNER, Columbia University — We will discuss application of our density functional (DFT)-based QM/MM methodology to modeling a variety of protein active sites, including methane monooxygenase, myoglobin, and cytochrome P450. In addition to the calculation of intermediates, transition states, and rate constants, we will discuss modeling of reactions requiring protein conformational changes. Our methodology reliably achieves small errors as a result of imposition of the QM/MM boundary. However, the accuracy of DFT methods can vary significantly with the type of system under study. We will discuss a novel approach to the reduction of errors in gradient corrected and hybrid DFT functionals, using empirical localized orbital corrections (DFT-LOC), which addresses this problem effectively. For example, the mean unsigned error in atomization energies for the G3 data set using the B3LYP-LOC model is 0.8 kcal/mole, as compared with 4.8 kcal/mole for B3LYP and 1.0 kcal/mole for G3 theory.

3:06PM S5.00002 Challenges and advances in QM/MM methods for studies of energetics and dynamics of biological systems , ARIEH WARSHEL, University of Southern California — QM/MM approaches have become a popular tool in studies of large systems, yet the use of such approaches in accurate evaluations of reaction rates in proteins and solutions is very challenging. Unfortunately, quantitative studies require a combination of accurate (ab intitio based) potential surfaces and the ability of extensive sampling for proper evaluation of activation free energies and transmission factors. Our strategies for overcoming these problems are based on the use of an EVB potential surface as reference potential for ab initio sampling. The use of this powerful approach for studies of the redox potential of blue copper proteins and related problems, the autoionization of water in water and some enzymatic reactions will be described, emphasizing the requirements of stable and reliable results for biological processes.

3:42PM S5.00003 QM/MM in complex systems using SCC-DFTB and its implementation in Amber. , ADRIAN ROITBERG, University of Florida — We will present our current implementation of SCC-DFTB into the molecular dynamics program Amber. Details of the efficiency and accuracy of the method will be presented. We will also shows some case studies involving conformational searches in peptides, replica exchange simulations in solution, and an application to an enzyme mechanism.

4:18PM S5.00004 Improved QM Methods and Their Application in QM/MM Studies of Enzymatic Reactions[1] , WILLIAM L. JORGENSEN, Dept. of Chemistry, Yale University — Quantum mechanics (QM) and Monte Carlo statistical mechanics (MC) simulations have been used by us since the early 1980s to study reaction mechanisms and the origin of solvent effects on reaction rates. A goal was always to perform the QM and MC/MM calculations simultaneously in order to obtain free-energy surfaces in solution with no geometrical restrictions. This was achieved by 2002 and complete free-energy profiles and surfaces with full sampling of solute and solvent coordinates can now be obtained through one job submission using BOSS [JCC 2005, 26, 1689]. Speed and accuracy demands also led to development of the improved semiempirical QM method, PDDG-PM3 [JCC 1601 (2002); JCTC 817 (2005)]. The combined PDDG-PM3/MC/FEP methodology has provided excellent results for free energies of activation for many reactions in numerous solvents. Recent examples include Cope, Kemp and E1cb eliminations [JACS 8829 (2005), 6141 (2006); JOC 4896 (2006)], as well as enzymatic reactions catalyzed by the putative Diels-Alderase, macrophomate synthase, and fatty-acid amide hydrolase [JACS 3577 (2005); JACS (2006)]. The presentation will focus on the accuracy that is currently achievable in such QM/MM studies and the accuracy of the underlying QM methodology including extensive comparisons of results from PDDG-PM3 and ab initio DFT methods.

[1]Support from the NSF (CHE 0446920) and NIH (GM32136) is gratefully acknowledged.

4:54PM S5.00005 Local and global refinement of electronic and structural properties of proteins via QM/MM , JOSE GASCON, University of Connecticut — This talk presents a new method to incorporate polarization effects in the electrostatic potential of proteins and enzymes, with potential application to even larger biological systems such as ribosomes. Polarization effects are incorporated via an iterative self-consistent point-charge model of the protein electrostatic potential. The method, which scales linearly with the size of the protein, achieves quantitative agreement with full QM calculations in the description of electrostatic potentials of small polypeptides where polarization effects are significant, showing a remarkable improvement relative to the corresponding electrostatic potentials obtained with popular MM force fields. The capabilities of the method will be demonstrated in several applications, including calculations of the electrostatic potential in the potassium channel protein and the description of protein-protein association.

Wednesday, March 7, 2007 2:30PM - 5:30PM –

Session S24 DPOLY DBP: Focus Session: Interaction of Polymers with Biological Structures

Colorado Convention Center 201

2:30PM S24.00001 Theoretical and Numerical Modeling of faceted Ionic crystalline vesicles , MONICA OLVERA DE LA CRUZ, Northwestern University — Icosahedral shape is found in several natural structures including large viruses, large fullerenes and cationic-anionic vesicles. Faceting into icosahedral shape can occur in large crystalline membranes via elasticity theory. Icosahedral symmetry is found in small systems of particles with short-range interactions on a sphere. Dr G. Vernizzi and I show a novel electrostatic-driven mechanism of ionic crystalline shells faceting into icosahedral shapes even for systems with a small number of particles. Icosahedral shape is possible in cationic and anionic molecules adsorbed onto spherical interfaces, such as emulsions or other immiscible liquid droplets because the large concentration of charges at the interface can lead to ionic crystals on the curved interface. Such self-organized ionic structures favors the formation of flat surfaces. We find that these ionic crystalline shells can have lower energy when faceted into icosahedra along particular directions. Indeed, the "ionic" buckling is driven by preferred bending directions of the planar ionic structure, along which is more likely for the icosahedral shape to develop an edge. Since only certain orientations are allowed, rotational symmetry is broken. One can hope to exploit this mechanism to generate functional materials where, for instance, proteins with specific charge groups can orient at specific directions along an icosahedral cationic-anionic vesicle.

3:06PM S24.00002 Microchannels with adhesive posts trap cells with specific mechanical properties , GUANGDONG ZHU, ALEXANDER ALEXEEV, ANNA BALAZS, Chemical Engineering Department, University of Pittsburgh — In order to perform various biological assays and tissue engineering studies, there is a critical need for microfluidic devices that can be used to trap cells with specific mechanical properties. Here, we model cells as fluid filled elastic shells, which also represent polymeric microcapsules. Using a combined approach based on lattice Boltzmann and lattice spring models, we study the motion of cells within a channel with two adhesive posts on the opposite walls. The distance between the posts is comparable to the diameter of the cell. The cells are driven to move through the channel by an imposed pressure gradient. We probe the effect of post compliance and the adhesion strength on the dynamics of the cells. We isolate the conditions at which all cells with shell stiffness lying within a specified range can be trapped in between the posts. Thus, our study can facilitate the design of simple and robust devices for analyzing mechanical properties of biological cells and synthetic microcapsules.

3:18PM S24.00003 Biomimetic Micellar Networks , JOHN ZUPANCICH, MARC HILLMYER, FRANK BATES, University of Minnesota — The self-assembly of amphiphilic block copolymers in dilute aqueous solution has been used to prepare structural analogues of fibrous materials common in physiology. The dependence of aggregate structure on amphiphile composition has been documented for a number of polymeric systems and by controlling the relative extent of hydrophilicity to hydrophobicity, block copolymers can be designed to target specific morphologies. Cell interactions with self-assembled structures can be promoted through conjugation of peptides or other targeting moieties to the constituent amphiphiles. The covalent attachment of RDG-containing peptides to the hydrophilic terminus of poly(ethylene oxide)-b-polybutadiene and the dilute solution behavior of these modified polymeric amphiphiles has been studied. An overall amphiphile composition conducive to worm-like micelle formation was targeted, and cross-linking of the hydrophobic core of these aggregate structures resulted in solution properties akin to fibrillar collagen gels.

3:30PM S24.00004 Post-Functionalized Polymer Brushes for Bio-Separation: Tuning GFP Adsorption via Functional Group Display , STEVE DIAMANTI, Air Force Research Laboratories, SHAFI ARIFUZZAMAN, JAN GENZER, North Carolina State University, RAJESH NAIK, RICHARD VAIA, Air Force Research Laboratories — An inexpensive and robust biosensor platform that can be tuned to separate and/or detect complex mixtures of biomolecules while minimizing reagents would be of great use for military, homeland security, and medical diagnostic applications. Gradient surfaces of poly(2-hydroxyethyl methacrylate) (PHEMA) brushes have been previously shown to spatially localize biomolecule binding, while minimizing non-specific adsorption of the same biomolecule on other regions of the gradient specimen. In order to further improve the specificity and to provide latent functionality for detection of the binding events, post-polymerization modification of PHEMA with various functional groups has been investigated. Using standard succinimide-based coupling, hydroxyl pendants of PHEMA brushes were conjugated to oligo-peptides, alkanes and oligo(ethylene glycol) (OEG) through an alpha-terminus primary amine. Ellipsometry, contact angle, XPS and ER-FTIR spectroscopy indicated that coupling occurred with efficiencies ranging from 10-40%. Post-functionalization of PHEMA with OEG and hexadecane allows manipulation of the hydrophilicity of the surface and thus tuning of Green Fluorescent Protein (GFP) binding.

3:42PM S24.00005 Structure and dynamics of water near the interface with oligo(ethylene oxide) self-assembled monolayers , AHMED E. ISMAIL, GARY S. GREST, MARK J. STEVENS, Sandia National Laboratories — Oligo(ethylene oxide) self-assembled monolayers (OEO SAM's) deposited on Au are the prototypical materials used to study protein resistance. Recently, protein resistance has been shown to vary as a function of surface coverage and to be maximal at about two-thirds coverage, not complete coverage. We use molecular dynamics simulations to study the nature of the interface between water and the OEO SAM for a range of SAM coverages. As SAM coverage decreases, the amount of water within the OEO monolayer increases monotonically; however, the penetration depth of the water shows a maximum near the experimentally-found maximal coverage. As the water content increases, the SAM-water mixture becomes harder to distinguish from bulk water. Since the oxygen atoms of OEO are hydrogen bond acceptors, a hydrogen bond network forms within the SAM-water mixture. The water molecules diffuse freely within the monolayer and exchange with the bulk water. Because the monolayer becomes increasingly like bulk water as the coverage decreases, proteins stay in their bulk soluble conformation and do not adsorb. *Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company, for the United States Department of Energy under Contract No. DE-AC04-94AL85000.*

3:54PM S24.00006 Development of novel antibiofouling materials from natural phenol compounds , RAHUL CHELIKANI, DONG SHIK KIM, The University of Toledo — Biofilms consist of a gelatinous matrix formed on a solid surface by microbial organisms.Biofilm is caused due to the adhesion of microbes to solid surfaces with production of extracellular polymers and the process of the biofilm formation is reffered to as biofouling.Biofouling causes serious problems in chemical, medical and pharmaceutical industries.Although there have been some antibiofouling materials developed over the years,no plausible results have been found yet.Natural polyphenolic compounds like flavanoids,cathechins have strong antioxidant and antimicrobial properties.Recently,apocynin,a phenol derivative,was polymerized to form oligomers,which can regulate intracellular pathways in cancer cells preventing cell proliferation and migration.These natural phenolic compounds have never been applied to solid surfaces to prevent biofouling.It is thought that probably because of the difficulty to crosslink them to form a stable coating.In this study,some novel polyphenolic compounds synthesized using enzymatic technique from cashew nut shell liquid,a cheap and renewable byproduct of the cashew industry are used as coating materials to prevent biofouling.The interaction of these materials with microbes preventing fouling on surfaces and the chemico-physical properties of the materials causing the antibiofouling effect will be discussed.It is critical to understand the antibiofouling mechanism of these materials for better design and application in various fields.

4:06PM S24.00007 Conformation Distributions in Adsorbed Proteins. , CURTIS W. MEUSE, JOSEPH B. HUBBARD, JOHN S. VRETTOS, Biochemical Science Division, National Institute of Standards and Technology, Gaithersburg, MD, 20899, JACKSON R. SMITH, MARCUS T. CICERONE, Polymers Division, National Institute of Standards and Technology, Gaithersburg, MD, 20899 — While the structural basis of protein function is well understood in the biopharmaceutical and biotechnology industries, few methods for the characterization and comparison of protein conformation distributions are available. New methods capable of measuring the stability of protein conformations and the integrity of protein-protein, protein-ligand and protein-surface interactions both in solution and on surfaces are needed to help the development of protein-based products. We are developing infrared spectroscopy methods for the characterization and comparison of molecular conformation distributions in monolayers and in solutions. We have extracted an order parameter describing the orientational and conformational variations of protein functional groups around the average molecular values from a single polarized spectrum. We will discuss the development of these methods and compare them to amide hydrogen/deuterium exchange methods for albumin in solution and on different polymer surfaces to show that our order parameter is related to protein stability.

4:18PM S24.00008 ABSTRACT WITHDRAWN –

4:30PM S24.00009 Strain-stiffening response in organogels assembled using steroidal biomolecules , SHIH-HUANG TUNG, SRINIVASA R. RAGHAVAN, University of Maryland, College Park — The phenomenon of strain-stiffening or strain-hardening refers to an increase in the elastic modulus (stiffness) of a material with increasing strain amplitude. While this response is exhibited by many biological materials, including gels of biopolymers such as actin, it is rarely seen in other types of soft matter. Here, we report strain-stiffening in a new class of self- assembled organogels being studied in our laboratory. These gels are formed in nonpolar organic liquids by combining a lipid (lecithin) or two-tailed surfactant (AOT) with a type of naturally occurring steroidal amphiphile called a bile salt. Based on rheological and scattering data, we deduce that the gel structure comprises a network of semiflexible filaments. Interestingly, gels induced by small organic molecules other than bile salts do not show strain-stiffening. We suggest that the bile salt molecules confer an intrinsic stiffness to the filaments in the gel, which is important for strain-stiffening.

4:42PM S24.00010 Solvent Viscosity at the Protein Surface , SHEILA KHODADADI, MARIAN PALUCH, SEBASTIAN PAWLUS, YOSHIHITO HAYASHI, ALEXEI SOKOLOV, Department of Polymer Science, University of Akron — Biochemical activity of biological macromolecules depends on solvent's viscosity, η, at their surface. The latter might differ from the bulk solvent viscosity due to preferential hydration. In order to estimate η at the protein surface, we studied dielectric relaxation spectra of lysozyme-water-glycerol mixtures. Additional relaxation process that appears in the presence of proteins has been assigned to their rotation. Employing Debye-Stokes-Einstein relationship [$\tau_R = (4\pi R_R^3 \eta/KT)$],and assuming that hydrodynamics radius of protein, R_R, does not change, we estimated η at the protein surface. Analysis of the obtained results indeed reveals a significant difference between bulk solvent's viscosity and the viscosity experienced by a protein. The water concentration appears to be significantly enhanced at the protein surface, in agreement with earlier thermodynamics study. Using the viscosity data, we estimate solvent composition at the protein surface.We expect that the developed approach will help to unravel the role of the solvent and its viscosity in dynamics, stability and biochemical activity of proteins.

4:54PM S24.00011 Correlation of chitosan's rheological properties to its ability to electrospin , WENDY E. KRAUSE, HAILEY A. QUEEN, REBECCA R. KLOSSNER, ANDREW J. COUGHLIN, North Carolina State University — Chitosan, derived from chitin found in the exoskeleton of crustaceans, has been investigated extensively for use in biomedical applications ranging from drug delivery to scaffolds for tissue engineering. Therefore, forming nanofibers of this linear polysaccharide is desirable for use in such applications, because the nanofibers can be tailored to mimic the size and porosity of the extracellular matrix. Electrostatic spinning (electrospinning) is a convenient method to produce nonwoven mats of nanofibers. The ability of the solutions to successfully electospin is closely correlated with the rheological properties of the solutions. Chitosan is challenging to electrospin due to its relatively high viscosity at modest concentrations. Solutions of chitosan blended with poly(ethylene oxide) (PEO) have been electrospun successfully with freshly prepared solutions. If the blended solutions are stored, they do not readily electrospin. Moreover, chitosan/PEO blend solutions show a drastic decrease in zero shear rate viscosity over time, which can be attributed to phase separation. The challenges associated with electrospinning charged biopolymers (chitosan is cationic) will be discussed in terms of their rheological properties. Successes and failures will be highlighted and compared results for readily electrospun neutral polymers.

5:06PM S24.00012 Diblock Copolymer as a Surface Delivery Vehicle for DNA Chip Construction , LU CHEN, CHRIS GRIGORAS, JEFFREY KOBERSTEIN, MONG MARMA, ZENGMIN LI, JINGYUE JU — A generic DNA sensor is made of a substrate, a coupling layer built on the substrate and the DNA attached to the coupling layer. Previously a DNA chip was constructed using a small molecule bi-functional linker via 1,3-dipolar zaide-alkyne cycloaddition coupling chemistry. The reaction efficiency of the cycloaddition coupling chemistry is high but there are some disadvantages such as low DNA coverage and low mobility of DNA due to the use of the small molecule linker. In this paper, a newly synthesized asymmetric diblock copolymer poly(methyl methacrylate-b-tert butyl acrylate) [poly(MMA-b-tBA)] with alkyne functional groups at the end of tBA block will be used as the coupling layer for the DNA chip construction. As will be shown in this paper, the attached DNA will have more mobility and higher surface coverage because of the use of the alkyne-end functionalized diblock copolymer as the coupling layer. More importantly, the areal density of the DNA molecules can be tuned by the thickness of the film simply made by the spin-coating method. The copolymer thin film was characterized by angle-dependent X-ray photoelectron spectroscopy, ellipsometry measurement and contact angle measurement. The thickness of tBA block was estimated using the substrate-overlayer model of ADXPS. The dye-labeled DNA chemically bonded to the surface was characterized by fluorescence measurement.

5:18PM S24.00013 Effect of copolymer microstructure on single chain collapse , ASHOK DASMAHAPATRA, Polymer Division, National Chemical Laboratory, Pune and Department of Chemical Engineering, IIT Bombay, GURUSWAMY KUMARASWAMY, Polymer Division, National Chemical Laboratory, Pune, HEMANT NANAVATI, Department of Chemical Engineering, Indian Institute of Technology Bombay — We present dynamic Monte Carlo simulations of the collapse of copolymers containing sticky comonomers, c. There is a qualitative difference in the transition depending on c content. For c content $>\sim$ 50%, copolymer collapse is qualitatively similar to that observed for homopolymers, when rescaled to account for comonomer solvophobicity. However, collapse of copolymers with $c < \sim$50% is qualitatively steeper than for homopolymers. We show that the change in the nature of collapse is due to the formation of an intermediate structure after the theta-point. The pathway to collapse is also strongly influenced by the distribution of comonomers along the chain. For uniform copolymer chains (viz. equispaced c units), collapse happens at lower temperatures than random copolymers. Further, uniform copolymers, but not random, appear to collapse cooperatively. Our results have relevance to protein folding where specific amino acid sequences lead to collapse and folding to a unique native structure.

Wednesday, March 7, 2007 5:30PM - 7:18PM –

Session T5 DBP: Simplifying Biological Complexity Colorado Convention Center Korbel 1A-1B

5:30PM T5.00001 Statics and dynamics of ecosystems[1] , JAYANTH BANAVAR, Penn State — Understanding an ecological community represents a formidable many-body problem - one has an interacting many-body system with imperfectly known interactions and a wide range of spatial and temporal scales. In tropical forests across the globe, ecologists have been able to measure certain quantities such as the distribution of relative species abundance; the probability that two trees drawn randomly a specified distance apart belong to the same species; and the dynamics of species turnover. A simple analytic framework will be presented for describing the statics and dynamics of ecosystems and its predictions will be benchmarked against observational data.
I. Volkov et al., Nature 424, 1035-1037 (2003); Phys. Rev. Lett. 92, 218703 (2004); Nature 438, 658-661 (2005).
T. Zillio et al., Phys. Rev. Lett. 95, 098101 (2005).
S. Azaele et al., Nature (2006) in press.

[1]Co-author: Amos Maritan (Padova, Italy)

6:06PM T5.00002 Mechanochemical cycles in cells , THOMAS DUKE, University of Cambridge — No abstract available.

6:42PM T5.00003 Stretching to Understand Proteins , MAREK CIEPLAK, Institute of Physics, Polish Academy of Sciences — Mechanical stretching of single proteins has been studied experimentally for about 50 proteins yielding a variety of force patterns and values of the peak forces. We have performed a theoretical survey of 7749 proteins of known native structure and map out the landscape of possible dynamical behaviors unders stretching at constant speed. The model used is constructed based on the native geometry. It is solved by methods of molecular dynamics and validated by comparing the theoretical predictions to experimental results. We characterize the distribution of peak forces and on correlations with the system size and with the structure classification as characterized by the CATH scheme. We identify proteins with the biggest forces and show that they belong to few topology classes. We determine which protein segments act as mechanical clamps and show that, in most cases, they correspond to long stretches of parallel beta-strands, but other mechanisms are also possible. We then consider stretching by fluid flows. We show that unfolding induced by a uniform flow shows a richer behavior than that in the force clamp. The dynamics of unfolding is found to depend strongly on the selection of the amino acid, usually one of the termini, which is anchored. These features offer potentially wider diagnostic tools to investigate structure of proteins compared to experiments based on the atomic force microscopy.

Thursday, March 8, 2007 8:00AM - 11:00AM –

Session U4 DPOLY DBP: Interfaces between Synthetic and Biological Polymers Colorado Convention Center Korbel 2B-3B

8:00AM U4.00001 Design Rules for Thermally Responsive Polymer Brushes[1] , DEBORAH LECKBAND, University of Illinois at Urbana-Champaign — Thermally responsive polymers such as poly(N-isopropylacrylamide) (PNIPAM) are extensively used to thermally tune the interfacial properties of thin polymer films. Above a lower critical solution temperature (LCST) of 32C, PNIPAM becomes insoluble in water and the chains collapse. Below the LCST the polymer chains are swollen. Yet such dramatic changes are not observed in all cases. The molecular weight and grafting density may also influence the phase behavior. This talk describes the systematic investigation of the thermally driven collapse of end-grafted PNIPAM as a function of the chain grafting density, molecular weight, and temperature. The polymer was grafted from the surface of an alkanethiol monolayer on gold containing a brominated alkanethiol initiator. The chains were synthesized by Atom Transfer Radical Polymerization (ATRP). Extensive chain collapse occurred at the highest grafting density and molecular weight, but the change in the film thickness decreased with decreasing density and molecular weight. The LCST was unchanged within 1C for all films. The force profiles measured between the PNIPAM brushes and a second surface at T below the LCST further suggest a one-dimensional phase separation within the polymer brush. These findings are compared with theoretical models of water-soluble polymers. We further discuss design criteria that impact the ability to thermally tune the interfacial properties of grafted PNIPAM films.

[1]NSF BES 0349915

8:36AM U4.00002 Studying Polymer Transport on Soft and Hard Surfaces[1] , SANAT KUMAR, Columbia University — We have employed experiments and simulations to understand the factors controlling the transport of polymers on surfaces. From an experimental viewpoint we have focused on the transport of DNA (single stranded) on lipid bilayers. We show that this behavior is slaved to the mobility of the lipids. More surprisingly, it appears that the transport of molecules adsorbed on surfaces follows the same dependence on lipid mobility as for molecules incorporated into the lipid layer. The ability to control this surface diffusion through the introduction of posts or varying the strength of adsorption (by the use of an AC field normal to the surfaces) will also be studied. Theoretically we have used molecular dynamics simulations of a polymer chain of length N dissolved in explicit solvent and adsorbed as a pancake at the solid-liquid interface to discriminate between respective influences on surface diffusion of hydrodynamics and adsorption energetics. Only for analytically-smooth surfaces do we observe a strong influence of hydrodynamics; the polymer lateral diffusion constant, D, scales as $D \propto 1/N^{3/4}$, more weakly than for implicit solvent. For atomistic surface corrugation with uniform surface chemical makeup, $D \propto 1/N$ instead. This suggests that while we can understand the results for diffusion on lipid surfaces, more recent experimental observations of stronger N dependence for diffusion on hard solid surfaces originate not in hydrodynamic interactions but in spatially patchy energetic interactions.

[1]in collaboration with C. Padala, T. Desai, R. Kane, P. Keblinski (RPI), S. Granick (UIUC)

9:12AM U4.00003 Design of dendrimer-based drug delivery nanodevices with enhanced therapeutic efficacies[1] , RANGARAMANUJAM KANNAN, Wayne State University — Dendrimers and hyperbranched polymers possess highly branched architectures, with a large number of controllable, tailorable, 'peripheral' functionalities. Since the surface chemistry of these materials can be modified with relative ease, these materials have tremendous potential in targeted drug delivery. They have significant potential compared to liposomes and nanoparticles, because of the reduced macrophage update, increased cellular transport, and the ability to modulate the local environment through functional groups. We are developing nanodevices based on dendritic systems for drug delivery, that contain a high drug payload, ligands, and imaging agents, resulting in 'smart' drug delivery devices that can target, deliver, and signal. In collaboration with the Children's Hospital of Michigan, Karmanos Cancer Institute, and College of Pharmacy, we are testing the *in vitro* and *in vivo* response of these nanodevices, by adapting the chemistry for specific clinical applications such as asthma and cancer. These materials are characterized by UV/Vis spectroscopy, flow cytometry, fluorescence/confocal microscopy, and appropriate animal models. Our results suggest that: (1) We can prepare drug-dendrimer conjugates with drug payloads of greater than 50%, for a variety of drugs; (2) The dendritic polymers are capable of transporting and delivering drugs into cells faster than free drugs, with superior therapeutic efficiency. This can be modulated by the surface functionality of the dendrimer; (3) For chemotherapy drugs, the conjugates are a factor of 6-20 times more effective even in drug-resistant cell lines; (4) For corticosteroidal drugs, the dendritic polymers provide higher drug residence times in the lung, allowing for passive targeting. The ability of the drug-dendrimer-ligand conjugates to target specific asthma and cancer cells is currently being explored using *in vitro* and *in vivo* animal models.

[1]Design of dendrimer-based drug delivery nanodevices with enhanced therapeutic efficacies

9:48AM U4.00004 Ligand-receptor binding in the presence of polymeric spacers , IGAL SZLEIFER, Purdue University — Ligand-receptor binding is of fundamental importance in many biological processes. Examples include cell-cell adhesion and cell-surface interactions among others. In several biomimetic materials as well as in some biological systems the ligand is attached to the surface by a spacer. In this talk we address the role that spacers play in ligand-receptor binding. More specifically, we present a series of theoretical studies in which we systematic study the role of polymeric spacers on the efficiency of ligand-receptor binding. The systems of interest correspond to the ligand chemically bound at the free end of polymers tethered to the surface, while the receptor is part of proteins free to move in the solution. Our theoretical approach is based on a molecular theory that has been shown to predict thermodynamic and structural information for tethered polymer layers in excellent agreement with experimental observations. We have generalized the theory to include the equilibrium between the bound and unbound species. We find that the presence of spacers increases the amount of binding as compared to the case in which the ligands are directly on the surface. The maximal binding is obtained at a relatively low surface coverage of spacer and it increases as the spacer chain length increases. The maximal binding is found to correspond to the cases in which the bound proteins can accommodate at different distances from the surface while bound to the ligand. We will show how the binding depends upon the size of the protein, the free energy of binding of the bare ligand-receptor pair, the polymer surface coverage and molecular weight. The predictions of the theory will be compared with recent experimental observations on the interactions between protein coated surfaces and surfaces with ligands at the end of polyethylene oxide spacers. Finally, we will show the use of mixed tethered layers to optimize ligand- receptor binding and at the same time to minimize non-specific adsorption of proteins. Throughout the presentation the interplay between different interactions in determining the binding will be discussed.

10:24AM U4.00005 Using Liquid Crystallinity to Design Interfaces between Synthetic and Biological Materials. , NICHOLAS ABBOTT, University of Wisconsin-Madison — This presentation will discuss the spontaneous assembly of amphiphiles and biological macromolecules at interfaces between thermotropic liquid crystalline phases and aqueous phases. This assembly process gives rise to patterned orientations of the liquid crystals that reflect the spatial and temporal organization of the amphiphiles and macromolecules. Strong and weak specific binding events involving proteins at these interfaces drive the reorganization of phospholipids and trigger orientational transitions in the liquid crystals. Because these interfaces are fluid, processes involving the lateral organization of proteins (e.g., formation of protein and phospholipid-rich domains) are also readily imaged via the orientational response of the liquid crystal, as are stereospecific enzymatic events. These results suggest new principles for designing interfaces between synthetic and biological polymers.

Thursday, March 8, 2007 8:00AM - 11:00AM –

Session U34 DBP: Focus Session: Non-equilibrium Fluctuations in Biomolecules Colorado Convention Center 404

8:00AM U34.00001 Fluctuations in Proteins , HANS FRAUENFELDER, Los Alamos National Laboratory — Proteins are the machines of life. In order to perform their functions, they must move continuously. The motions correspond to equilibrium fluctuations and to non-equilibrium relaxations. At least three different fluctuation processes occur: α- and β-fluctuations and processes that occur even below one Kelvin. The α-fluctuations can be approximated by the Vogel-Tammann-Fulcher relation, while the β-fluctuations appear to follow a conventional Arrhenius law (but may in some cases be better characterized by a Ferry law). Both are usually nonexponential in time. These phenomena are similar in proteins and glasses, but there is a fundamental difference between fluctuations in glasses and proteins: In glasses, they are independent of the environment, in proteins the α-fluctuations are slaved to the α-fluctuations in the solvent surrounding the protein; they follow their rate coefficients but they are entropically slowed. The studies of the protein motions are actually still in their infancy, but we can expect that future work will not only help understanding protein functions, but will also feed back to the physics of glasses.

8:36AM U34.00002 A Tunable Chemical Pattern Filter Constructed by Networks of Reaction Compartments and Tubes , LUDVIG LIZANA, ZORAN KONKOLI, Dept. Applied Physics, Chalmers Univ. Tech., Sweden, OWE ORWAR, Dept. Physical Chemistry, Chalmers Univ. Tech., Sweden — We study numerically the filtering capabilities of nanoscale networks built up of containers and tubes hosting chemical reactions. Spatio-temporal patterns of substrate molecules are injected into the network. The substrate propagates by diffusion and reacts with enzymes distributed in the network prior to the injections. The dimensions of the network are tailored in a way that the transport and reaction rates are comparable in size, a situation in which the overall behavior is highly influenced by the geometry and topology of the network. This property is crucial for the functionality of the pattern filter developed in here. It is demonstrated that input patterns can be classified in a crude way using a simple setup (two micrometer-sized containers joined together by a nanotube) and that the classification can be tuned by changing the geometry of the network (the length of the tube connecting the two containers). The filter device we investigate can also be viewed as a primitive chemistry-based computational element since the information encoded in the input patterns is processed using chemical reactions. In particular it is argued that the filter can be used as a frequency sensor.

8:48AM U34.00003 Effect of Orientation in Translocation of Polymers through Nanopores , STANISLAV KOTSEV, ANATOLY KOLOMEISKY, Rice University — The motion of a polymer with inhomogeneous structure through a nanopore is discussed theoretically. Specifically, we consider the translocation of polymer consisting of one double-stranded and one single-stranded blocks. Since only the single-stranded chain can pass through the nanopore, the double-stranded segment has to unzip before translocating. Utilizing a simple analytical model, translocation times are calculated explicitly for the different polymer orientations - when the single-stranded block enters the pore first and when the double-stranded one enters first. Their dependence on external fields, energy of interaction in the double-stranded segment, total size of the polymer, and the fraction of double-stranded to single-stranded blocks lengths is analyzed. It is found that the order of entrance into the pore has a significant effect on the translocation dynamics.

9:00AM U34.00004 Assisted DNA hairpin retraction from nanopores , MENI WANUNU, Department of Biomedical Engineering, Boston University, Boston, MA 02215, BUDDHAPRIYA CHAKRABARTI, Lyman Laboratory of Physics, Harvard University, Cambridge, MA 02138, JEROME MATHE, Department of Polymeric Materials and Interfaces, Evry University, Evry, France, 91025, DAVID R. NELSON, Lyman Laboratory of Physics, Harvard University, Cambridge, MA 02138, AMIT MELLER, Department of Biomedical Engineering, Boston University, Boston, MA 02215 — We present results from recent experimental and theoretical investigations of DNA hairpin retraction from an α-hemolysin nanopore in the presence of an assisting voltage. By mapping the translocation process to that of biased diffusion of a Brownian particle we compute the probability of the polymer to stay in the pore as a function of time. Using this model we back out the diffusion constant and the drift velocity of the polymer as a function of the assisting voltage. While the drift-diffusion model gives good agreement with experiments at low voltages it fails for high assisting voltages. We discuss possible reasons for this along with the implications of our work.

9:12AM U34.00005 Pharmaceuticals in nanopores - A strategy to manipulate the phase behavior , M. BEINER, G.T. RENGARAJAN, S. PANKAJ, D. ENKE, Martin-Luther-University Halle-Wittenberg, Faculty of Natural Sciences II, D-06099 Halle, Germany — The manipulation of the crystalline state of substances existing in different polymorphic forms is an important issue in many fields of application. In case of pharmaceuticals the stabilization of unstable forms is interesting since solubility and bioavailability are improved. We will show in this presentation that it is possible to manipulate the crystallization behavior of pharmaceuticals and to stabilize unstable crystalline forms by confining the substance in pores with diameters in the range 20-400 nanometers. [1] The crystallization behavior of a pharmaceutical model system in two different types of nanostructured inorganic host systems is studied by DSC and x-ray scattering. The results clearly show that the most unstable crystalline form of this pharmaceutical melts and is stable for long times under confinement which was never observed for bulk samples. This allows to extract the thermodynamic parameters of this crystalline form which have not been reported so far and shows that this is an interesting field of application for nanostructured host-guest systems. The influences of pore geometry and surface interaction are studied and possible explanations for the differences between the crystallization behavior in the bulk and under confinement are discussed.

[1]G.T. Rengarajan et al. *J.Am.Chem.Soc.*, to be published.

9:24AM U34.00006 Thermal fluctuation spectroscopy in histone and nucleosomes during denaturation , ARUP RAYCHAUDHURI, S.N.Bose National Centre for Basic Sciences, K.S. NAGAPRIYA, Indian Institute of Science — Thermal stability of biomolecules is an important issue. We have studied thermal denaturation of histone and nucleosome using precision thermal fluctuation spectroscopy (TFS) . - a problem that we believe has not been studied experimentally before. TFS uses a very sensitive noise calorimeter which can detect thermal fluctuations of micro Kelvin at around room temperature. We find that the thermal denaturation of histones (in particular H1) as well as that of the nucleosome are associated with large fluctuations, which are few orders higher than those away from the denaturation temperature. It involves large energy exchange which can be few tens of kBT0 (T0=300K). It appears that the denaturation occurs in three distinct steps 1. breaking of bonds leading to the cooling jumps, 2. the change in its secondary, tertiary structure leading to slow dynamics and 3. formation of bonds as it is unfolding and in the newly folded high temperature phase which accounts for the heating jumps.

9:36AM U34.00007 Development of High-Resolution Magnetic Tweezers for Single-Molecule Measurements , KIPOM KIM, Materials Department, University of California Santa Barbara, OMAR A. SALEH, Materials Department and BMSE Program, University of California Santa Barbara — Magnetic tweezers can sense single-molecule DNA-protein interactions through optical tracking of the motion of a colloidal particle. This is typically done by relating changes in the colloid's diffraction pattern to its position. While diffraction-tracking is relatively simple to implement, it is intrinsically limited in its resolution. To improve this, we have developed a tracking technique based on Reflection Interference Contrast Microscopy (RICM). RICM relies on interference between light reflected from the colloid and a glass surface. To optimize the interference pattern, the reflecting surfaces of the colloid and the glass substrate were coated with gold and dielectric thin-films, respectively. To maintain the focal position of objective against the defocusing due to a thermal drift, the objective was automatically focused on the glass/water interface using feedback control with a piezo-driven actuator. We evaluated the system's performance by measuring fundamental physical properties of the DNA.

9:48AM U34.00008 Single-biomolecule circuits with carbon nanotube wiring , JOHN CORONEUS, Departments of Molecular Biology and Biochemistry, and Physics and Astronomy, University of California Irvine, Irvine, CA 92697, BRETT R. GOLDSMITH, VAIKUNTH KHALAP, ALEXANDER KANE, GREGORY A. WEISS, PHILIP G. COLLINS — Because of their size and chemistry, carbon nanotubes offer a unique opportunity to couple solid-state electronics with individual proteins or other biomolecules. This talk will describe our success covalently attaching single proteins to functioning, nanotube-based electronic devices. Because the nanotubes are sensitive, one-dimensional conductors, their electrical properties are greatly altered by this attachment, even when only one or two proteins are bound. The single-molecule circuits which result allow the dynamics of molecules to be directly observed without ensemble averaging. This work is partly supported by NSF grant EF-0404057.

10:00AM U34.00009 Probing DNA-Protein Interactions on Surfaces Using Spectral Self-interference Fluorescence Microscopy[1] , MEHMET DOGAN, Boston University Physics Department, PETER DROGE, Nanyang Technological University School of Biological Sciences, Singapore, ANNA K. SWAN, SELIM UNLU, Boston University ECE Department, BENNETT B. GOLDBERG, Boston University Physics Department — We are probing the interactions between double-stranded DNA and integration host factor (IHF) proteins [1] on surfaces using Spectral Self-interference Fluorescence Microscopy (SSFM) [2].The probing technique utilizes the spectral fringes produced by interference of direct and reflected emission from fluorescent molecules. The modified spectrum provides a unique signature of the axial position of the fluorophores. Using the SSFM technique, we probe the average location of the fluorescent markers attached to the DNA molecules to study the conformational changes in double-stranded DNA tethered to SiO_2 surfaces. In the presence of IHF, a DNA bending protein, we observe reduction in the vertical position of fluorescent molecules suggesting the formation of IHF-DNA complex and IHF-induced DNA bending. We also discuss the results with different IHF strains and different binding conditions. [1] Q. Bao et. al., Gene, Vol.343 pp.99-106 (2004) [2] L.A. Moiseev et. al., Journal of Applied Physics, Vol.96, pp. 5311-5315 (2004)

[1]This work has been supported by NSF and NIH grants

10:12AM U34.00010 Dynamics of Single Actin Filaments and Bundles in Flow , DAGMAR STEINHAUSER, SARAH KOESTER, HEATHER M. EVANS, HOLGER STARK, THOMAS PFOHL, Max Planck Institute for Dynamics and Self-organization, Goettingen, Germany — Actin filaments, aside from their biological renown as providing the 'skeleton' of cells, also proffer an ideal platform from which to study – more generally – the properties of semi-flexible polymers. Microfluidic devices made using soft-lithography are easily adapted in dimension and geometry to create well-defined flow environments. Actin filaments are visualized in continuous flow in a microfluidic channel by stroboscopic laser light illumination. A detailed analysis of filament orientation, center-of-mass distribution, and thermal fluctuations as a function of flow rate and channel geometry is reported. In addition, the non-equilibrium bundling behavior of actin in the presence of actin-binding proteins or multivalent ions is studied in microchannel devices using FRET microscopy.

10:24AM U34.00011 Segregation of molecules in self-spreading lipid bilayer at ultra-small metal nano-gaps arrayed on solid surface , KEI MURAKOSHI, HIDEKI NABIKA, MASAHIRO OOWADA, Hokkaido University — Diffusion of target molecules incorporated in the self-spreading lipid bilayer was controlled by the introduction of periodic array of metallic architecture on solid surface. Retardation of the progress of target molecules became significant when the size of gap between small metal architectures was less than a few hundred nm. The self-spreading dynamics of the lipid bilayer depending on the size of the small gap were analyzed semi-quantitatively. Estimated change in the driving force of the spreading layer suggests that highly localized compression of the spreading layer causes selective segregation of molecules. Surface-modified metal nano-architectures were also used to tune the selectivity of the molecules.

10:36AM U34.00012 Calibration of Micromachined Force Sensors by Gravitational Force on Precision Microspheres , STEVEN J. KOCH, University of New Mexico, GAYLE E. THAYER, ALEX D. CORWIN, MAARTEN P. DE BOER, Sandia National Laboratories — To complement the existing tools for applying and measuring piconewton-level forces on biomolecules (e.g. optical tweezers, magnetic tweezers, AFM), we are developing a compliant micromachined spring for simple and direct measurements in an aqueous environment. Accurate calibration of the spring constant is crucial and we will present a gravitational method that uses NIST-traceable size standard microspheres. The method is applicable to calibration of other soft cantilevers of both in-plane and out-of-plane varieties. We affixed two microspheres to the force sensor and measured a deflection per bead of 196 nm $\pm$ 6%. Using a weight of 150 pN $\pm$ 4.8% per microsphere, we obtained a spring constant of 0.76 pN / nm $\pm$ 8%. The method proved simpler and more reliable when compared to two other methods: high resolution SEM and thermal equipartition. The versatility of surface micromachining should enable use of the spring in new platforms for biophysical force measurement, for example on-chip load cells for dynamic DNA stretching.

10:48AM U34.00013 Multimode Analysis of SHG Signal from Complex Biological Systems: Parameterization of Features Using Nearest-Neighbor Analysis and Wavelet Transforms , CLAYTON BRATTON, Department of Physics, University Of California, Davis, KAREN REISER, Department of Neurological Surgery, University of California, Davis, ANDRE KNOESEN, DIEGO YANKELEVICH, Department of Electrical and Computer Engineering, University of California, Davis, ISRAEL ROCHA-MENDOZA, Cardiff School of Biosciences - Cardiff University, Cardiff, Wales, MINGSHI WANG, Department of Electrical and Computer Engineering, University of California, Davis, SHG/SFG SPECTROSCOPY TEAM — We have developed a novel computational approach for quantifying structural disorder in biomolecular lattices with nonlinear susceptibility based on analysis of polarization-modulated second harmonic signal. Transient, regional disorder at the level of molecular organization is identified using a novel signal processing algorithm sufficiently compact for near real-time analysis with a desktop computer. Global disorder within the biostructure is assessed using a two-dimensional wavelet transform of the magnitude and phase of the second harmonic signal. Selection of coefficients and the specific wavelet family is based on topological considerations. Experimental results suggest our signal processing method represents a robust, scaleable tool that allows us to detect both regional and global alterations in signal characteristics of biostructures with a high degree of discrimination.

Thursday, March 8, 2007 8:00AM - 11:00AM –

Session U35 DBP GSNP DPOLY: Focus Session: Cytoskeletal Dynamics and Cell Migration II

Colorado Convention Center 405

8:00AM U35.00001 Modelling cell motility and pathways that signal to the actin cytoskeleton[1] , LEAH EDELSTEIN-KESHET, Dept of Mathematics, UBC — Gradient sensing, polarization, and motility of rapidly moving cells such as neutrophils involves the actin cytoskeleton, and regulatory modules such as membrane bound phosphoinositides (PIs), kinases/phosphatases, and proteins of the Rho family (Rho GTPases). I describe recent work in my group in which we have modeled components of these modules, their interconversions, interactions, and action in the context of protrusive cell motility. By connecting three modules, we find that Rho GTPases work as a spatial switch, and that PIs filter noise, and define the front vs. back. Relatively fast PI diffusion also leads to selection of a unique pattern of Rho distribution from a collection of possible patterns. We use the model to explore the importance of specific hypothesized interactions, to explore mutant phenotypes, and to study the role of actin polymerization in the maintenance of the PI asymmetry. Collaborators on this work include A.T. Dawes, A. Jilkine, and A.F.M. Maree.

[1]We acknowledge a subcontract from NSF (grant # DMS-0240770, to A. Carlsson, Wash U.), NSERC, and MITACS (Canada)

8:36AM U35.00002 Migration of a Model Lamellipodium by Actin Polymerization: A Molecular Dynamics Simulation Approach , JUNHWAN JEON, Department of Chemical Engineering, Vanderbilt University, Nashville, Tennessee 37235, PETER CUMMINGS, Nanomaterials Theory Institute, Center for Nanophase Materials Sciences, Oak Ridge National Laboratory, Oak Ridge, Tennessee 37831 — We performed molecular dynamics simulation of a model lamellipodium with growing F-actin filaments in order to study the effect of stiffness of the F-actin filament, the G-actin monomer concentration, and the number of polymerization sites on lamellipodium motion. The lamellipodium is modeled as a two-end capped cylinder formed by triangulated particles on its surface. It is assumed that F-actin filaments are firmly attached to a lamellipodium surface where polymerization sites are located and actin polymerization takes place by connecting a G-actin monomer to a polymerization site and the first monomer of a growing F-actin filament. It is found that there is an optimal number of polymerization sites for rapid lamellipodium motion. This appearance of the maximum speed is related to the competition between the number of polymerization sites and the number of available G-actin monomers, and the degree of pulling and holding the lamellipodium surface by non-polymerized actin filaments. The model lamellipodium speed distribution is found to be Maxwellian for particles with random motion in two dimensions and is in agreement with experiment.

8:48AM U35.00003 Intracellular dynamics during directional sensing of chemotactic cells , GABRIEL AMSELEM, EBERHARD BODENSCHATZ, CARSTEN BETA, MPI for Dynamics and Self-Organization, Goettingen — We use an experimental approach based on the photo-chemical release of signaling molecules in microfluidic environments to expose chemotactic cells to well controlled chemoattractant stimuli. We apply this technique to study intracellular translocation of fluorescently labeled PH-domain proteins in the social ameba *Dictyostelium discoideum*. Single chemotactic *Dictyostelium* cells are exposed to localized, well defined gradients in the chemoattractant cAMP and their translocation response is quantified as a function of the external gradient.

9:00AM U35.00004 Searching strategies in Dictyostelium , LIANG LI, Department of Physics, Princeton University, EDWARD COX, Department of Molecular Biology, Princeton University — Levy walks are known to be the best strategy for optimizing non-destructive search times, while an intermittent two-state searching process optimizes the destructive case. Here we ask about hunting strategy in Dictyostelium amoebae when they cannot know where their food is. We show that correlated random walks with two typical correlation time scales bias their search, improving the search outcome. Further analysis indicates that cell trajectories consist of runs and turns. Strikingly, amoebae remember the last turn, and have a strong turning preference away from the last turn. Autocorrelation analysis of turn sequences indicates that this tendency does not persist beyond the nth+1 turn. Computer simulations reveal that this bias contributes to the longer of the two correlation times. The search rules are essentially the same when cells are continuously stimulated by cAMP, with different persistence times and lengths. Interestingly, new pseudopods form in an orientation opposite to the following turn. One of the correlation timescales is approximately 30 seconds in all cases, thus indicating a short-lived cellular process, while the other is 9 to 15 minutes suggesting a process sensitive to external signals, perhaps pseudopod extensions during turning.

9:12AM U35.00005 Perturbing Streaming in Dictyostelium Discoideum , COLIN MCCANN, University of Maryland, PAUL KRIEBEL, CAROLE PARENT, National Institutes of Health, ERIN RERICHA, WOLFGANG LOSERT, University of Maryland — Upon starvation the social amoebae *Dictyostelium discoideum* aggregate to form multicellular organisms. During the transition from single cells to full aggregates, cells relay the chemotactic signal, align in a head-to-tail fashion, and follow each other in streams. To gain more insight into streaming behavior we investigated its robustness by perturbing the strength of the relayed chemoattractant. We measured the effects of plating the cells at varying densities, placing them in excess extracellular fluid thereby diluting cell-cell signals, or directly mixing up the local external fluid using ultrasound-induced bubble-driven flow. We compared wild type cells to cells devoid of signal relay and measured how streaming affects cell speed, directionality, and extent of directed migration. Results will be discussed and a model describing our findings will be presented.

9:24AM U35.00006 Traction cytometry applied to chemotacting *Dictyostelium discoideum* , ALBERTO ALISEDA, now at University of Washington, BALDOMERO ALONSO-LATORRE, JUAN CARLOS DEL ALAMO, JAVIER RODRIGUEZ-RODRIGUEZ, now at Universidad Carlos III, RUDOLPH MEILI, RICHARD FIRTEL, JUAN C. LASHERAS, University of California, San Diego — The motion of *Dictyostelium discoideum* cells moving on a elastic substrate has been studied. Joint analysis of time-lapse DIC movies of the cells and UV fluorescence from the beads embedded in the substrate, allows for identification of characteristic time scales of the motion and the quantitative description of the crawling cycle. From the measured displacements of the beads, forces can be computed by analytically solving the elasto-static equation in a finite thickness slab. We found that the finite thickness of the substrate and the distance of the beads to its surface have a substantial effect and that the previous traction cytometry techniques based on the Boussinesq solution effectively low-pass-filtered the force field, reducing the spatial resolution and damping the range of the measured forces by as much as 50%. The improved spatial resolution of this method enables us to determine the spatial extent of the regions where the cells apply force on the substrate and, consequently, the magnitude of the elastic energy spent in its deformation. The measured forces, as well as the elastic energy communicated by the cell to the substrate, will be correlated to the different stages of the crawling cycle for various cell strains.

9:36AM U35.00007 Stem cell cytoskeleton is slaved to active motors , FLORIAN REHFELDT, ANDRE BROWN, ADAM ENGLER, DENNIS DISCHER, University of Pennsylvania — Cells feel their physical microenvironment through their adhesion and respond to it in various ways. Indeed, matrix elasticity can even guide the differentiation of human adult mesenchymal stem cells (MSCs) [Engler et al. *Cell* 2006]. Sparse cultures of MSCs on elastic collagen–coated substrates that are respectively soft, stiff, or extremely stiff were shown to induce neurogenesis, myogenesis, and osteogenesis. Lineage commitment was evaluated by morphological analysis, protein expression profiles, and transcription microarrays. Differentiation could be completely blocked with a specific non-muscle myosin II (NMM II) inhibitor, suggesting that contractile motor activity is essential for the cells to sense matrix elasticity. Current studies by AFM and near-field fluorescence imaging show that NMM II inhibition in stem cells on rigid glass surfaces promotes actin-rich dendritic outgrowth resembling neurite extension. Dynamic cell studies have been conducted to elucidate the complex molecular interplay of the contractile apparatus in response to selected physical and biochemical stimuli. Additional insight is being gained by using AFM to investigate the local elasticity of the cell's cytoskeletal force sensing machinery.

9:48AM U35.00008 The Collective Contractile Dynamics of Confluent Epithelial Cells is Highly Coherent , THOMAS ANGELINI, Harvard University, INEST program, MANUEL MARQUEZ, PMUSA, DAVID WEITZ, Harvard University — We have studied the collective contractile dynamics of confluent Cos-7 epithelial cells in several contexts. We patterned cells in single file lines on confined PDMS 'rubber bands', and quantified substrate deformation by tracking embedded fluorescent particles over the course of approximately 10 hours. Deformations confined to one dimension, well over ten microns in magnitude, correlated over distances exceeding the millimeter scale, were observed. On unpatterened PDMS, collective substrate deformations in two dimensions were over ten times smaller, and exhibited a propagating mechanical excitation. Three dimensional matrix deformation was studied by embedding cells at high density in 1mg/ml collagen. Since collective network deformations are difficult to quantify in the microscope, a dynamic small angle light scattering technique was adapted. With this technique, we have spectrally characterized the three dimensional mechanical network deformations, and observed collective behavior similar to the measurements on compliant surfaces.

10:00AM U35.00009 Membrane fluctuations driven by actin and myosin: waves and quantized division. , NIR GOV, ROIE SHLOMOVITZ, Weizmann Institute of Science — We present a model which couples the membrane with the protrusive forces of actin polymerization and contractile forces of molecular motors, such as myosin. The actin polymerization at the membrane is activated by freely diffusing membrane proteins, that may have a distinct spontaneous curvature. Molecular motors are recruited to the polymerizing actin filaments, from a constant reservoir, and produce a contractile force. All the forces and variables are treated in the linear limit, which allows us to derive analytic solutions. Our results show that for convex membrane proteins the myosin activity gives rise to propagating membrane waves similar to those observed on different cells. For concave membrane proteins the myosin activity gives rise to an unstable contraction, which yields a length-quantization of the mitosis process.

10:12AM U35.00010 Simulation of Actin-Polymerization-Mediated Propulsion[1] , KUN-CHUN LEE, ANDREA LIU, University of Pennsylvania, Department of Physics and Astronomy — An important component of the cellular cytoskeleton is F-actin, a biopolymer whose self-assembly is key to the process of cell crawling. The polymerization and branching of F-actin near the cell membrane is known to drive cell crawling, but the precise mechanism by which these processes lead to the generation of a mechanical force is still controversial. We have constructed a Brownian dynamics simulation of F-actin polymerizing near a surface, which includes all known important processes, including polymerization, depolymerization, branching, severing and capping. Using this model, we are able to simulate the cell movement. We measure the speed as function of concentration of different proteins involved in the process. We find the speed to be non-monotonic, consistent with experimental results [Louis et al. Nature **401** 613 (1999)].

[1]This work is supported by NSF-CHE06-13331 and UPenn MRSEC NSF-DMR05-20020.

10:24AM U35.00011 Symmetry breaking in actin gels - Implications for cellular motility[1] , KARIN JOHN, PHILIPPE PEYLA, CHAOUQI MISBAH, UJF Grenoble, Laboratoire de Spectrométrie Physique — The physical origin of cell motility is not fully understood. Recently minimal model systems have shown, that polymerizing actin itself can produce a motile force, without the help of motor proteins. Pathogens like Shigella or Listeria use actin to propel themselves forward in their host cell. The same process can be mimicked with polystyrene beads covered with the activating protein ActA, which reside in a solution containing actin monomers. ActA induces the growth of an actin gel at the bead surface. Initially the gel grows symmetrically around the bead until a critical size is reached. Subsequently one observes a symmetry breaking and the gel starts to grow asymmetrically around the bead developing a tail of actin at one side. This symmetry breaking is accompanied by a directed movement of the bead, with the actin tail trailing behind the bead. Force generation relies on the combination of two properties: growth and elasticity of the actin gel. We study this phenomenon theoretically within the framework of a linear elasticity theory and linear flux-force relationships for the evolution of an elastic gel around a hard sphere. Conditions for a parity symmetry breaking are identified analytically and illustrated numerically with the help of a phasefield model.

[1]CNES, Humboldt-Foundation

10:36AM U35.00012 A kinematic description of the trajectories of Listeria monocytogenes propelled by actin comet tails , DHANANJAY TAMBE, VIVEK SHENOY, Brown University — The bacterial pathogen Listeria monocytogenes propels itself in the cytoplasm of the infected cells by forming a filamentous comet tail assembled by the polymerization of the cytoskeletal protein, actin. While a great deal is known about the molecular processes that lead to actin based movement, most macroscale aspects of motion, including the nature of the trajectories traced out by the motile bacteria are not well understood. Listeria moving between a glass-slide and cover slip in a Xenopus frog egg extract motility assay is observed to display a number of geometrically fascinating trajectories including sine curves, serpentine shapes, circles, and a variety of spirals. We have developed a dynamic model that provides a unified description of these seemingly unrelated trajectories. A key ingredient of the model is a torque (not included in any microscopic models to date) that arises from the rotation of the propulsive force about the body-axis of the bacterium. The trajectories of bacteria executing both steady and saltatory motion are found to be in excellent agreement with the predictions of our dynamic model. When the constraints that lead to planar motion are removed, our model predicts motion along regular helical trajectories, observed in recent experiments. We discover from the analysis of the trajectories of spherical beads that the comet tail revolves around the bead.

10:48AM U35.00013 Steady-state configurations and dynamics of the MreB helix within bacteria , ANDREW RUTENBERG, JUN ALLARD, Dalhousie University — We present a quantitative model of the actin-like MreB cytoskeleton that is present in many prokaryotes. Individual MreB polymers are bundled into a supra-molecular array to make up helical cables. The cell wall imposes constraint forces through a global elasticity model. With variational techniques and stochastic simulations we obtain relationships between observable quantities such as the pitch of the helix, the total abundance of MreB molecules, and the thickness of the MreB cables. We address changes expected with slow cell growth, as well as turnover dynamics that are relevant to FRAP studies. We also address polarized macromolecular trafficking along the MreB cables without motor proteins.

Thursday, March 8, 2007 11:15AM - 2:15PM –

Session V6 DBP: Cell Motility Colorado Convention Center 207

11:15AM V6.00001 Extremes in motility: actin acrobatics, spasmin spasms and jellyfish jabs , L. MAHADEVAN, Engineering and Applied Sciences, Organismic and Evolutionary Biology, Systems Biology, Harvard University — Fast movements in biology are functionally relevant in the context of avoidance and capture. I will talk about some of the adaptations in biology that lead to speed at the cellular level in a variety of organisms, and then discuss three in some detail: the explosive motility of jellyfish stings, the fast contraction of some pond weeds, and the extrusion of an actin spring. In each case, the morphology and mechano-chemistry come together in unusual ways that are adapted for functionality. This leads to questions of both a comparative and an evolutionary nature, and serve to perhaps move these questions from the realm of stamp collecting to physiology and physics.

11:51AM V6.00002 Natural descriptions of motor behavior: examples from *E. coli* and *C. elegans*. , WILLIAM RYU, Princeton University — *E. coli* has a natural behavioral variable - the direction of rotation of its flagellar rotorary motor. Monitoring this one-dimensional behavioral response in reaction to chemical perturbation has been instrumental in the understanding of how *E. coli* performs chemotaxis at the genetic, physiological, and computational level. Here we apply this experimental strategy to the study of bacterial thermotaxis - a sensory mode that is less well understood. We investigate bacterial thermosensation by studying the motor response of single cells subjected to impulses of heat produced by an IR laser. A simple temperature dependent modification to an existing chemotaxis model can explain the observed temperature response. Higher organisms may have a more complicated behavioral response due to the simple fact that their motions have more degrees of freedom. Here we provide a principled analysis of motor behavior of such an organism – the roundworm *C. elegans*. Using tracking video-microscopy we capture a worm's image and extract the skeleton of the shape as a head-to-tail ordered collection of tangent angles sampled along the curve. Applying principal components analysis we show that the space of shapes is remarkably low dimensional, with four dimensions accounting for $> 95\%$ of the shape variance. We also show that these dimensions align with behaviorally relevant states. As an application of this analysis we study the thermal response of worms stimulated by laser heating. Our quantitative description of *C. elegans* movement should prove useful in a wide variety of contexts, from the linking of motor output with neural circuitry to the genetic basis of adaptive behavior.

12:27PM V6.00003 How Molecular Motors Shape the Flagellar Beat[1] , FRANK JÜLICHER, Max Planck Institute for the Physics of Complex Systems — Cilia and eukaryotic flagella are slender cellular appendages whose regular beating drives fluid flows across epithelia and propels cells and microorganisms through aqueous media. The beat is an oscillating pattern of propagating bends generated by dynein motor proteins that induce sliding between adjacent axonemal microtubules. A key open question is how the activity of the motors is coordinated in space and time to produce the observed regular oscillatory beat pattern. We have developed a physical description of Flagellar dynamics based on the interplay of collective action of dynein motors and relative sliding of microtubules in two and three dimensions. To elucidate the nature of motor coordination, we have inferred the mechanical properties of the motors by analyzing the shape of beating sperm. Steadily beating bull sperm were imaged at a high frame rate and their shapes were measured with high precision using a Fourier averaging technique. We compared our experimental data with theoretical waveforms and found that the observed flagellar beats were in accordance with a model based on sliding controlled motor activity, but not with curvature controlled motor activity. Furthermore, good agreement between observed and calculated waveforms was obtained only if significant sliding between microtubules occurred at the base. This highlights the role of basal sliding in shaping the flagellar waveform. Thus we conclude, that the flagellar beat patterns are determined by an interplay of the basal properties of the axoneme and the collective behavior of sliding controlled dynein motors that are coordinated mechanically via the sliding of adjacent microtubules.

[1]In collaboration with Ingmar Riedel, Max Planck Institute of Molecular Cell Biology and Genetics; Andreas Hilfinger, Max Planck Institute for the Physics of Complex Systems; and Jonathon Howard, Max Planck Institute of Molecular Cell Biology and Genetics.

1:03PM V6.00004 Physical Aspects of Evolutionary Transitions to Multicellularity , RAYMOND E. GOLDSTEIN, DAMTP, University of Cambridge — An important issue in evolutionary biology is the emergence of multicellular organisms from unicellular individuals. The accompanying differentiation from motile totipotent unicellular organisms to multicellular ones having cells specialized into reproductive (germ) and vegetative (soma) functions, such as motility, implies both costs and benefits, the analysis of which involves the physics of buoyancy, diffusion, and mixing. In this talk, I discuss recent results on this transition in a model lineage: the volvocine green algae. Particle Imaging Velocimetry of fluid flows generated by these organisms show that they exist in the regime of very large Peclet numbers, where the scaling of nutrient uptake rates with organism size is highly nontrivial. In concert with metabolic studies of deflagellated colonies, investigations of phenotypic plasticity under nutrient-deprived conditions, and theoretical studies of transport in the high-Peclet number regime, we find that flagella-generated fluid flows enhance the nutrient uptake rate per cell, and thereby provide a driving force for evolutionary transitions to multicellularity. Thus, there is a link between motility, mixing, and multicellularity.

1:39PM V6.00005 Mechanics of actin-based motility , DANIEL A. FLETCHER, University of California, Berkeley — The ability of cells to move is critical for organism evelopment, maintenance, and repair. Growth of actin filament networks drives a variety of cellular and intracellular motions and contributes to the mechanical rigidity of the cell's cytoskeleton. During motility, eukaryotic cells and intracellular pathogens are propelled by dendritic actin networks oriented in the direction of motion and characterized by a branched architecture. Nucleation-promoting factors activated near the cell membrane trigger the formation of nascent filaments from the side of existing filaments in the network. Here we use laser tracking and atomic force microscopy to test models of actin-based motility and actin network elasticity. A Brownian ratchet mechanism has been proposed to couple actin polymerization to cellular movements, whereby thermal motions are rectified by the addition of actin monomers at the end of elongating filaments. By following actin-propelled microspheres using three-dimensional laser tracking, we find that the movement of beads adhered to growing actin networks is consistent with an object-fluctuating Brownian ratchet. Elasticity of actin networks has been shown to arise in part from the resistance of filaments under extension. Using atomic force microscopy, we find that dendritic actin networks exhibit nonlinear stress softening behavior that points to an important role for filaments under compression. Together, these results raise new questions about how actin network architecture is involved in the propulsion and guidance of crawling cells.

Thursday, March 8, 2007 11:15AM - 1:39PM –

Session V15 GSNP DBP: Focus Session: Nonequilibrium Thermodynamics of Small Systems

Colorado Convention Center Korbel 4E

11:15AM V15.00001 The nonequilibrium thermodynamics of small systems , FELIX RITORT, University of Barcelona — Nonequilibrium behavior is widespread and rich in nature. Yet our understanding of the fundamental principles underlying nonequilibrium behavior is still poor as shown by the fact that non-equilibrium theories tend to be ad-hoc and specific (1). Recently there has been a lot of interest in applying single-molecule techniques to scrutinize nonequilibrium theories (2). The use of new micromanipulation tools in the exploration of the behavior of tiny objects (such as biomolecules and motors) embedded in a thermal environment opens the possibility to investigate how these systems exchange energy with their environment. The study of such questions, nowadays referred to as "Nonequilibrium thermodynamics of small systems," is becoming quite popular among statistical physicists who recognize there new aspects of thermodynamics where large Brownian fluctuations are of pivotal importance as compared to fluctuations in macroscopic (or large) systems (3). Nonequilibrium small systems are characterized by large deviations in work/heat distributions that satisfy some relations called fluctuation theorems. In this talk I will discuss single-molecule experiments where some of these fluctuation theorems have been tested (4).

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(2) F. Ritort, Single molecule experiments in biological physics: methods and applications, Journal of Physics C (Condensed Matter),18 (2006) R531-R583;
(3) C. Bustamante, J. Liphardt and F. Ritort, The nonequilibrium thermodynamics of small systems, Physics Today,58 (2005) 43-48;
(4) D. Collin, F. Ritort, C. Jarzynski, S. B. Smith, I. Tinoco Jr and C. Bustamante, Verification of the Crooks fluctuation theorem and recovery of RNA folding free energies, Nature, 437 (2005) 231-234.

11:51AM V15.00002 Activation barrier scaling and crossover for noise-induced switching in a micromechanical parametric oscillator , COREY STAMBAUGH, HO BUN CHAN, University of Florida — We explore fluctuation-induced switching in a parametrically-driven micromechanical torsional oscillator, a system far from thermal equilibrium. Under sufficiently strong parametric modulation of the spring constant, the oscillator possesses one, two or three stable attractors depending on the modulation frequency. Near the bifurcation points where the number of attractors changes, the activation barrier for switching out of a stable state is predicted to display universal, system-independent scaling relationships. We induce the oscillator to switch between the coexisting states by injecting noise in the excitation. By measuring the rate of random transitions as a function of noise intensity, we deduce the activation barrier as a function of frequency. Near both bifurcation points, the activation barriers are found to depend on frequency detuning with critical exponent of 2, consistent with the predicted universal scaling in parametrically driven systems. Away from the immediate vicinity of the bifurcation point, universal scaling relationships for the activation barrier no longer hold. At large detuning, we observe a crossover to a different power law dependence with an exponent that is specific to our device.

12:03PM V15.00003 Scaling crossovers in activated escape of nonequilibrium systems: a resonantly driven oscillator[1] , OLEG KOGAN, California Institute of Technology, IRA SCHWARTZ, Naval Research Laboratory, MARK DYKMAN, Michigan State University — The rate of metastable decay in nonequilibrium systems is expected to display scaling behavior: i.e., the logarithm of the decay rate should scale as a power of the distance to a bifurcation point where themetastable state disappears. Recently such behavior was observed and some of the earlier predicted exponents were found in experiments on several types of systems described by a model of a modulated oscillator. Here we establish the range where different scaling behavior is displayed and show how the crossover between different types of scaling occurs. The analysis is done for a nonlinear oscillator with two coexisting stable states of forced vibrations. We map out the entire parameter range. We find the regions where the scaling exponents are 1 or 3/2, depending on the damping. We also uncover new scaling behavior which extends, numerically, beyond the close vicinity of the bifurcation point. The results of the numerical calculations based on the instanton method are compared with the results of Monte Carlo simulations.

[1]NSF DMR-0314069, ARO W911NF-06-1-0324

12:15PM V15.00004 Spontaneous symmetry breaking in parametrically driven atomic trap and measurement of dynamic critical exponents , WONHO JHE, MYOUNG-SUN HEO, YONGHEE KIM, KIWHAN KIM, Seoul National University, HEUNG-RYOUL NOH, Chonnam National University, SEOUL NATIONAL UNIVERSITY TEAM, CHONNAM NATIONAL UNIVERSITY COLLABORATION — While critical phenomena in equilibrium systems has been well established both in theory and in experiment, experimental studies in non-equilibrium or far-from-equilibrium systems still lack of quantitative investigation and remain as challenging subjects. Here we report on the use of laser cooled and trapped atoms can be a good candidate for such study since one can easily control its temperature and numbers. By parametrically modulating the magneto-optical trap potential we have observed several interesting phenomena such as dynamic double well, Hopf bifurcation and spontaneous symmetry-breaking (SSB). Particularly SSB is identified as the mean-field system exhibiting the Ising-like phase transition. We measured critical exponents relevant to this phase transition, with respect to the control parameter, the size of the system or the total number of atoms. We also have observed the occurrence of SSB as the temperature is changed by illuminating a resonant laser light.

12:27PM V15.00005 Equilibrium theory for a particle pulled by a moving optical trap , RAYMOND DEAN ASTUMIAN, University of Maine — The viscous drag on a colloidal particle pulled through solution by an optical trap is large enough that on experimentally relavant time scales the mechanical force exerted by the trap is equal and opposite the viscous drag force. The rapid mechanical equilibritation allows the system to be modeled using equilibrium theory where the effects of the energy dissipation (*thermodynamic* disequilibrium) show up only in the coordinate transformations that map the system from the laboratory frame of reference, relative to which the particle is moving, to a frame of reference in which the particle is, on average, stationary and on which the stochastic dynamics is governed by a canonical equilibrium distribution function. The simple equations in the stationary frame can be analyzed using the Onsager-Machlup theory for stochastic systems and provide generalizations of equilibrium and near equilibrium concepts such as detailed balance and fluctuation-dissipation relations applicable to a wide range of systems including molecular motors, pumps, and other nano-scale machines.

12:39PM V15.00006 Energy and efficiency optimization of a Brownian heat engine[1] , MULUGETA BEKELE, Department of Physics, Addis Ababa University, Addis Ababa, Ethiopia, YENENEH YALEW, Eindhoven Unversity of Technology, Eindhoven, The Netherlands — A simple Brownian heat engine is modeled as a Brownian particle moving in an external sawtooth potential (with or without) load assisted by the thermal kick it gets from alternately placed hot and cold heat reservoirs along its path. We get closed form expression for its current in terms of the parameters characterizing the model. After analyzing the way it consumes energy to do useful work, we also get closed form expressions for its efficiency as well as for its coefficient of performance when the engine performs as a refrigerator. Recently suggested optimization criteria enables us to exhaustively explore and compare the different operating conditions of the engine.

[1]We would like to thank the International Programme in Physical Sciences, Uppsala University, Sweden for the support in carrying out the research as well as travel support to this APS March Meeting

12:51PM V15.00007 Relationships involving spatial transitions for Brownian particles within a potential-well. , ROSS BRODY, University of Maine — Using an optical tweezer apparatus we have trapped single latex spheres and analyzed their Brownian motion within a potential well. By considering transitions from various initial and final positions within the well, we experimentally show that the ratio of conditional probabilities, $P(x_f, t + \Delta t|x_i, t)/P(x_i, t + \Delta t|x_f, t)$, is independent of Δt. We also show the instanton times corresponding to last-touch-first-touch (LTFT) trajectories obey the equality, LTFT($x_i \rightarrow x_f$)=LTFT($x_f \rightarrow x_i$), shown by Bier et al. [Phys. Rev. E **59**, 6422 (1999)].

1:03PM V15.00008 Analytical calculation of Jarzynski free-energy estimator bias , MATTEO PALASSINI, Department of Fundamental Physics, University of Barcelona, NIKOS SKANTZOS, Instituut voor Theoretische Fysica, Katholieke Universiteit Leuven, FELIX RITORT, Department of Fundamental Physics, University of Barcelona — The Jarzynski equality connects the free-energy difference DF between two equilibrium states A and B of a system to the work done on the system in a non-equilibrium process that takes it from A to B, averaged exponentially over all possible realizations of the process. This provides an estimator for DF given N non-equilibrium experiments, which has been applied in a variety of contexts. Because of the exponential averaging, the Jarzynski estimator suffers a statistical bias for finite N, which can be substantial. Computing this bias is important for estimating correctly the free-energy, and is a notoriously difficult problem for which only results in the large-N limit are known. We propose an analytical method to estimate the bias and test it in the case of a Gaussian work distribution, for which it provides satisfactory estimates both in the large N and small N regimes. Finally, we discuss the applicability of these results to experimental studies on single biomolecules.

1:15PM V15.00009 Exact equality between dissipation and irreversibility , RYOICHI KAWAI, University of Alabama at Birmingham, JUAN M. R. PARRONDO, Universidad Complutense de Madrid, CHRISTIAN VAN DEN BROECK, University of Hasselt — We show, through a reformulation of the Crooks theorem and the Jarzynski equality, that the average dissipation for a system perturbed to go from one equilibrium state to another one, is exactly given by $\langle W \rangle_{diss} = \langle W \rangle - \Delta F = kTD(\rho||\widetilde{\rho}) = kT\langle \ln(\rho/\widetilde{\rho}) \rangle$, where ρ and $\widetilde{\rho}$ are the phase space density of the system measured at the same but otherwise arbitrary intermediate point in time, for the forward and backward process. $D(\rho||\widetilde{\rho})$ is the relative entropy of ρ versus $\widetilde{\rho}$.

1:27PM V15.00010 Free Energy Surface Reconstruction Using Jarzynski's Equality , CHING-HWA KIANG, NOLAN HARRIS, Department of Physics & Astronomy, Rice University — Atomic force microscope was used to manipulate and unfold individual molecules of the muscle protein titin. We reconstructed the free energy surface of stretching and unfolding of titin I27 domain using Jarzynski's equality. An exact formula that relates the nonequilibrium work fluctuations to the molecular free energy was used for the reconstruction. From the free energy surface, the unfolding free energy barrier, i.e. the activation energy, was directly obtained from experimental data for the first time.

Thursday, March 8, 2007 11:15AM - 2:15PM –

Session V34 DBP: Focus Session: Nonlinear Dynamics of Neuronal Systems Colorado Convention Center 404

11:15AM V34.00001 Dynamics and pattern formation of synaptic learning: Why do we profit from slow learning?[1] , J. LEO VAN HEMMEN, Physics Department, TU Munich — Neuronal dynamics is the dynamics of the brain. It is highly nonlinear because neurons are elements responding to a membrane potential that needs to exceed a threshold in order to generate an action potential or 'spike'. Neuronal dynamics occurs on at least two different levels: that of the neurons themselves (on a millisecond timescale) and a much slower one at the synapses, where learning takes place. Synapses are situated on a neuron, receive spikes emitted by other neurons, and are located at the end of an axon transmitting spikes with a finite delay. This talk will concentrate on many fascinating questions such as: What do synaptic representations (maps) of the outside sensory world look like, how do they develop as a consequence of synaptic learning, and is their development compatible with chaos or is it governed by totally different principles? In so doing, we focus on universal principles underlying both the rich diversity of neuronal dynamics of many interacting neurons and the corresponding, adiabatic, learning dynamics at the synapses in conjunction with pattern formation in large systems of synapses. The timescale of the latter is, in general, at least five orders of magnitude slower than that of the neurons. Not only does this "slow" synaptic learning lead to an adiabatic principle and, hence, to analytical insight into the learning process itself but it also allows for robustness of learning as compared to the much more fragile neuronal dynamics.

[1]Supported by BCCN Munich

11:51AM V34.00002 Synchronized dynamics of cortical neurons with time-delay feedback[1] , ALEXANDRA LANDSMAN, IRA SCHWARTZ, Naval Research Laboratory — The dynamics of three mutually delay coupled cortical neurons are explored. When coupled in a line, delays introduce correlations in the time series at the time-scale of the delay. The middle neuron leads the outer ones by the delay time, while the end neurons are synchronized with zero lag times. Synchronization is found to be highly dependent on the synaptic time constant, with faster synapses increasing both the degree of synchronization and the firing rate. Analysis shows that pre-synaptic input during the inter-spike interval stabilizes the synchronous state, even for arbitrarily weak coupling, and independent of the initial phase. The finding may be of significance to synchronization of large groups of cells in the cortex that are spatially distanced from each other.

[1]Office of Naval Research.

12:03PM V34.00003 Eye-Target Synchrony and Attention , R. CONTRERAS, Dept. of Physics and Astronomy and Center for Neurodynamics, Univ. of Missouri - St. Louis (UMSL), R. KOLSTER, Brain Trauma Foundation and Weill Medical College of Cornell, Sackler Institute, Dept. of Psychiatry, S. BASU, Brain Trauma Foundation, H. U. VOSS, Weill Medical College of Cornell, Radiology, J. GHAJAR, M. SUH, Brain Trauma Foundation and Weill Medical College of Cornell, Neurological Surgery, S. BAHAR, Dept. of Physics and Astronomy and Center for Neurodynamics, UMSL — Eye-target synchrony is critical during smooth pursuit. We apply stochastic phase synchronization to human pursuit of a moving target, in both normal and mild traumatic brain injured (TBI) subjects. Smooth pursuit utilizes the same neural networks used by attention. To test whether smooth pursuit is modulated by attention, subjects tracked a target while loaded with tasks involving working memory. Preliminary results suggest that additional cognitive load increases normal subjects' performance, while the effect is reversed in TBI patients. We correlate these results with eye-target synchrony. Additionally, we correlate eye-target synchrony with frequency of target motion, and discuss how the range of frequencies for optimal synchrony depends on the shift from attentional to automatic-response time scales. Synchrony deficits in TBI patients can be correlated with specific regions of brain damage imaged with diffusion tensor imaging (DTI).

12:15PM V34.00004 Complex patterns of synchrony in networks undergoing exogenous drive , JACK WADDELL, Department of Physics, University of Michigan, MICHAL ZOCHOWSKI, Department of Physics & Biophysics Resesarch Division, University of Michgian — It has been established that various exogenous oscillatory drives modulate neural activity (and potentially information processing) in the brain. We explore the effect of an exogenous drive on the spatio-temporal pattern formation of a network of coupled non-identical Rössler oscillators. We investigate the formation and properties of the phase locked states, dependent on the network properties as well as those of the external drive. We have found that such drive has a complex effect on the pattern formation in the network, depending on the coupling strength between the oscillators, drive strength as well as its frequency relative to the oscillators.

12:27PM V34.00005 Measurements of synchronization between interacting networks in a model of focal epilepsy[1] , S. FELDT, Dept. of Phys., Univ. of Michigan, H. OSTERHAGE, Dept. of Epileptology and Helmholtz-Institute for Radiation and Nuclear Phys., Univ. of Bonn, Germany, F. MORMANN, Div. Biol., Caltech., and Dept. of Epileptology, Univ. of Bonn, Germany, K. LEHNERTZ, Dept. of Epileptology, Helmholtz-Institute for Radiation and Nuclear Phys., and Interdisc. Center for Complex Sys., Univ. of Bonn, Germany, M. ZOCHOWSKI, Dept. of Phys.and Biophys., Univ. of Michigan — We use a simple model of two interacting networks of neurons to explain a seemingly paradoxical result observed in epileptic patients indicating that the level of phase synchrony drops below normal levels during the preictal state. We show that the transition from the interictal to preictal and then to ictal state may be divided into separate dynamical regimes: the formation of slow oscillatory activity observed during the normal (interictal) period, structureless activity during the preictal period when the two networks have different properties, and bursting dynamics driven by the network corresponding to the focus. We thus hypothesize that the beginning of the preictal period marks the beginning of the transition of the focal network from normal activity towards seizing and compare our results to measurements of the preictal length in human patients.

[1]Supported by a NSF Grad. Research Fellowship and NIH EB003583

12:39PM V34.00006 Structural network heterogeneities and network dynamics: a possible dynamical mechanism for hippocampal memory reactivation.[1] , PIOTR JABLONSKI, Dept. of Phys. and Biophys. Research Div. University of Michigan, GINA POE, Dept. of Anesthesiology and Dept. of Molecular and Integrative Physiol. University of Michigan Medical School, MICHAL ZOCHOWSKI, Dept. of Phys. and Biophys. Research Div. University of Michigan — The hippocampus has the capacity for reactivating recently acquired memories and it is hypothesized that one of the functions of sleep reactivation is the facilitation of consolidation of novel memory traces. The dynamic and network processes underlying such a reactivation remain, however, unknown. We show that such a reactivation characterized by local, self-sustained activity of a network region may be an inherent property of the recurrent excitatory-inhibitory network with a heterogeneous structure. The entry into the reactivation phase is mediated through a physiologically feasible regulation of global excitability and external input sources, while the reactivated component of the network is formed through induced network heterogeneities during learning. We show that structural changes needed for robust reactivation of a given network region are well within known physiological parameters.

[1]This work was supported by NIH EB003583 (MZ), NIH MH60670 (GP) and by a Fulbright fellowship (PJ).

12:51PM V34.00007 Processing of odor stimuli by neuronal network models of the olfactory bulb[1] , STUART WICK, Northwestern U., MARTIN WIECHERT, MPI for Medical Research, Heidelberg, HERMANN RIECKE, Northwestern U., RAINER FRIEDRICH, MPI for Medical Research, Heidelberg — The space of perceptable odors is high-dimensional and its representation in the various brain structures is still poorly understood. We focus on the olfactory bulb, which constitutes the first processing stage for odor stimuli after they have been sensed by receptor neurons. Experimentally it is found that the correlations between the outputs of the bulb are significantly reduced relative to those of the corresponding inputs, thus enhancing the discriminability of similar odors. We have generated a firing-rate-based network model with parameters derived from experimental data that reproduces decorrelation. Here we use this model to investigate the dependence of stimulus representations on odor concentration. We address the possibility of a change in perceived odor identity with changing concentration and the dependence of odor discriminability on odor concentration. We interpret some of our results within a simple mean-field model for the neural activity.

[1]Supported by NIH 1F33DC8064-1, NSF DMS-9804673, and Humboldt Foundation.

1:03PM V34.00008 The dynamics of temporal ordering in driven integrate-and-fire-neurons. , JAN ENGELBRECHT, RENATO MIROLLO, Boston College — Spike-timing neural codes involve the development of some kind of temporal order (synchrony) between a neuron's spike times and timing features in either the stimulus, local field potentials or the average activity in a population of synchronizing neurons. In order to explore the dynamics of temporal ordering we study an integrate-and-fire neuron with a (small) oscillatory component in its input. Tuning the frustration due to the interplay between the neuron's natural firing time and the oscillatory rhythm's period, leads to a rich structure of asymptotic phase locking patterns and ordering dynamics controlled by a correlation time that diverges at phase boundaries – quite analogous to diverging correlation lengths in equilibrium phase transitions. Our results can be understood in terms on an extension of the theory of circle maps. In addition, they address how fast synchronous behavior can emerge in biological or artificial neural networks.

1:15PM V34.00009 Rocking the boat: Auditory localization of ground-borne vibrations in snakes[1] , J. LEO VAN HEMMEN, Physics Department, TU Munich — Experiments [1] have shown that sand-dwelling desert snakes can localize prey in the absence of visual, chemosensory, and infrared cues. Instead, prey-generated surface waves traveling along the substrate surface provide the necessary information for a snake to estimate the stimulus position. The snake's inner ear is mechanically coupled to the lower jaw through a lever construction. Moreover, the left and right jaws in snakes are only loosely linked, thus providing the possibility of detecting surface vibrations and locating a stimulus through interaural time differences. Using the theory of floating bodies as an approximation of a snake jaw resting on a sandy substrate, we explicitly calculate [2] the response of the lower jaw to incoming surface waves and show that the sensitivity of the snake ear suffices to allow prey localization on the basis of interaural time-of-arrival differences. Refs.: [1] B.A. Young and M. Morain, J. Exp. Biol. **205** (2002) 661; [2] P. Friedel, B.A. Young, and J.L. van Hemmen, TU Munich preprint (2007).

[1]Supported by BCCN Munich & DFG (HE 3252/1-4)

1:27PM V34.00010 Two-dimensional encoding and adaptation in the songbird auditory forebrain , TATYANA SHARPEE, KATHERINE NAGEL, ALLISON DOUPE, University of California, San Francisco — Neural adaptation is crucial for many auditory tasks, such as speech recognition, where robust performance is achieved over a wide range of signal-to-noise ratios and in the presence of 1/f- type noise. While faithful high-rate sampling can work well in the presence of noise which is largely uncorrelated between successive signal samples, alternative strategies might be needed to achieve reliable performance in the presence of strongly correlated noise. We studied how neurons in songbird auditory forebrain region (field L) encode temporal modulations of the amplitude of band-limited sounds using an information- theoretic method for finding relevant stimulus dimensions [1]. We robustly found that neurons in field L perform temporal processing based on simultaneous sampling of locally smoothed values of log-amplitude and its time-derivative. Either one of the two stimulus features could play the dominant role in neural response. We conclude with a theoretical explanation for the optimality of such signal processing strategies in situations where noise and signals have comparable correlation times. [1] T. Sharpee, N.C. Rust, W. Bialek, Neural. Computation 16, 223 (2004).

1:39PM V34.00011 Astrocytes optimize synaptic fidelity[1] , SUHITA NADKARNI, Center for Theoretical Biological Physics, UC SanDiego, PETER JUNG, Dept. of Physics and Astronomy, Ohio University, HERBERT LEVINE, Center for Theoretical Biological Physics, UC SanDiego — Most neuronal synapses in the central nervous system are enwrapped by an astrocytic process. This relation allows the astrocyte to listen to and feed back to the synapse and to regulate synaptic transmission. We combine a tested mathematical model for the Ca^{2+} response of the synaptic astrocyte and presynaptic feedback with a detailed model for vesicle release of neurotransmitter at active zones. The predicted Ca^{2+} dependence of the presynaptic synaptic vesicle release compares favorably for several types of synapses, including the Calyx of Held. We hypothesize that the feedback regulation of the astrocyte onto the presynaptic terminal *optimizes* the fidelity of the synapse in terms of information transmission.

[1]This work was supported by NSF sponsored Center for Theoretical Biological Physics (PHY0216576 and PHY0225630) and NSF Grant No. IBN-0078055

1:51PM V34.00012 Dynamical analysis of Bayesian inference models and its relation to connectionist neural network models for the Eriksen task , YUAN LIU, Department of Physics, Princeton University, ANGELA YU, Center for the Study of Brain, Mind, and Behavior, Princeton University, PHILIP HOLMES, Program in Applied and Computational Mathematics, Princeton University — We analyze Bayesian compatibility bias and spatial uncertainly models for the two-alternative forced choice Eriksen task, in which subjects must correctly identify a central stimulus and disregard flankers that may or may not be compatible with it. We simplify the models, deriving linear, uncoupled, discrete dynamical systems and their continuum limits: stochastic differential equations. Analytical solutions of these allow us to describe how posterior probabilities and psychometric functions depend upon parameters. We compare our results with numerical simulations of original inference models and show that agreement is good enough for them to be useful in parameterizing such models. Our analysis also reveals that Bayesian updating is closely related to a simple drift diffusion process that can be derived from neural network models.

2:03PM V34.00013 Walking at stability's edge , JOHN MILTON, DAVID NICHOLS, ADAM COLEMAN, COURY CLEMENS, ANNIE NGUYENTAT, AMI RADUNSKAYA, The Claremont Colleges — During self-paced human walking, the variability in inter- stride intervals exhibit fractal dynamics characterized by long–range correlations having a power-law decay with exponent α. We used diffusion fluctuation analysis (DFA) to estimate α as a function of the roughness of the walking surface for eight (8) healthy subjects (1200-1400 inter- stride intervals for each walking surface). For each subject the highest α (mean 0.96, range 0.88- 1.10) occured for walking on a running track and α was $15-20\%$ lower for walking on either a relatively smoother (tennis hard court) or a rougher (dirt path) surface. These observations are captured by a stochastic discrete time cubic map: $I_{i+1} = a(\xi_i)I_i - bI_i^3 + \eta_i$, where I_i is the i–th inter–stride time, $a(\xi_i) = a_o(\xi) + \xi_i$ describes parametric, colored noise where $a_0(\xi)$ is a constant that depends on surface roughness and ξ_i is colored noise with mean zero, η_i is low–intensity additive white noise, and b is a constant. As the roughness, and hence $a_0(\xi)$, of the walking surface increases, the fluctuations in the inter–stride interval are predicted to obey a power law whose exponent changes non-monotonically: the highest values of α determined with DFA occur when $a_0(\xi)$ is close to the deterministic stability boundary $a = 1$. Thus the neural control of walking appears to involve a dynamical system tuned close to the edge of stability subjected to the effects of parametric noise.

Thursday, March 8, 2007 11:15AM - 2:15PM –

Session V35 DBP: DNA/RNA in Vitro Colorado Convention Center 405

11:15AM V35.00001 UV exposed electronically activated damage and photoreactivation repair , HENRIK BOHR, Technical University of Denmark, BARY MALIK, Southern Illinois University — An investigation of the possible physics underlying the damage caused to DNA by UV radiation and its subsequent repair via a photoreactivation mechanism is presented in this study. An electronic pathway starting from the initial damage to the final repair process is proposed. UV radiation is absorbed to create a hole-excited thymine or other pyrimidine that subsequently is responsible for the formation of the thymine dimer. The negative-ion of the cofactor riboflavin, FADH-, formed by the exposure of the photolyase protein to visible light interacts with the hole-excited electronic orbital of the thymine dimer inducing a photon-less Auger transition, which restores the two thymines to the ground state, thereby detaching the lesion and repairing the DNA. Due to energy balance, the process has to involve an electronic excited state (s). The mechanism involves the least amount of energy dissipation and is charge neutral. It also avoids radiation damage in the repair process, that is, is a radiationless process.

11:27AM V35.00002 Mean-Field Analysis of Recursive Entropic Segmentation of Biological Sequences , SIEW-ANN CHEONG, Cornell Theory Center, Cornell University, PAUL STODGHILL, DAVID SCHNEIDER, USDA/ARS, Ithaca, CHRISTOPHER MYERS, Cornell Theory Center, Cornell University — Horizontal gene transfer in bacteria results in genomic sequences which are mosaic in nature. An important first step in the analysis of a bacterial genome would thus be to model the statistically nonstationary nucleotide or protein sequence with a collection of P stationary Markov chains, and partition the sequence of length N into M statistically stationary segments/domains. This can be done for Markov chains of order $K = 0$ using a recursive segmentation scheme based on the Jensen-Shannon divergence, where the unknown parameters P and M are estimated from a hypothesis testing/model selection process. In this talk, we describe how the Jensen-Shannon divergence can be generalized to Markov chains of order $K > 0$, as well as an algorithm optimizing the positions of a fixed number of domain walls. We then describe a mean field analysis of the generalized recursive Jensen-Shannon segmentation scheme, and show how most domain walls appear as local maxima in the divergence spectrum of the sequence, before highlighting the main problem associated with the recursive segmentation scheme, i.e. the strengths of the domain walls selected recursively do not decrease monotonically. This problem is especially severe in repetitive sequences, whose statistical signatures we will also discuss.

11:39AM V35.00003 Exploring Threaded Intercalation Using Optical Tweezers , THAYAPARAN PARAMANATHAN, MICAH J. MCCAULEY, Department of Physics, Northeastern University, Boston, USA., FREDRIK WESTERLUND, Department of Chemical and Biological Engineering, Chalmers University of Technology, Gothenburg, Sweden, IOULIA ROUZINA, Department of Biochemistry, Molecular Biology, and Biophysics, University of Minnesota, USA, MARK C. WILLIAMS, Department of Physics, Northeastern University, Boston, USA. — Dumbbell-shaped binuclear ruthenium complexes are of interest due to their potential for use in selective chemotherapy. In bulk experiments, these complexes exhibit extremely slow binding kinetics. In contrast, single molecule studies use optical tweezers to stretch the DNA and induce much more rapid intercalation. The observed DNA force-extension curves clearly indicate an increase in DNA melting force and elongation of the DNA molecule upon drug binding, which is evidence of stabilization of the DNA and intercalation of the binuclear ruthenium complex. Hysteresis in the stretching-relaxation curves implies very slow dissociation of these molecules due to threaded intercalation. The concentration profile suggests unusually strong DNA binding affinity for the binuclear complexes compared to simple intercalators.

11:51AM V35.00004 A simple method to deposit elongated DNA onto fused-silica surfaces for single molecule studies of protein-DNA interactions , YAO ZHANG, Department of Physics, Washington University in St. Louis, KERYN GOLD, Molecular Biophysics Graduate Program, Division of Biology and Biomedical Sciences, Washington University School of Medicine, Y. M. WANG, Department of Physics, Washington University in St. Louis — In order to study facilitated diffusion of proteins along DNA using single molecule fluorescence imaging methods, it is necessary to deposit elongated DNA molecules along fused-silica surfaces [1]. Here we have developed a simple method to deposit elongated DNA molecules onto fused-silica surfaces with high yield. We attached the ends of DNA molecules to streptavidin coated quantum dots and then deposited the end-labeled DNA onto fused-silica surfaces. The flow created by a cover slip is adequate to generate arrays of elongated and suspended DNA anchored by the two ends of each molecule, ideal for protein-DNA interaction studies. Interactions of LacI with these elongated DNA molecules will also be discussed.
[1] Y. M. Wang, E. C. Cox and R. Austin, "Single molecule measurements of repressor proteins 1D diffusion on DNA," Phys. Rev. Lett., 97, 048302, (2006).

12:03PM V35.00005 Strain dependent twist-stretch elasticity in elastic filaments , MONEESH UPMANYU, Colorado School of Mines — Structural chirality (i.e. handedness) often results in large mechanical couplings which modify the conformation and expression of natural and synthetic filamentous aggregates. Twist-stretch elasticity of double stranded DNA is vital during chromatin organization, transcription regulation and protein binding. Engineering such couplings in structurally robust and multifunctional nanowires and nanotubes offers an elegant route for fabrication of nanoscale motors, oscillators and switches. In instances where the device operation relies upon mechanical coupling, twist-stretch elasticity, eliminating the need for an externally actuated rotational degree of freedom. Recent results on single-walled carbon nanotubes and DNA reveal a reversal in the sign of the twist-stretch coupling at large strains. Here, we present a simple non-linear theory that captures the behavior macroscopically. Model simulations reveal that the higher order coefficients are sensitive functions of the microscopic deformation energetics. Such dynamic couplings already exist in nature, a general design principle that remains to be exploited for mechanically coupled self-actuation in nanoscale devices and biomimetic strategies.

12:15PM V35.00006 Condensation of liquid crystals of complementary nDNA duplexes from a solution of mixed oligomers , GIULIANO ZANCHETTA, Universit'à di Milano, TOMMASO BELLINI, Università di Milano, MICHI NAKATA, NOEL CLARK, University of Colorado — We have investigated the phase behavior of concentrated mixtures of: (i) the complementary oligonucleotides CCTCAAAACTCC ("oligoA") + GGAGTTTTGAGG ("oligoB") and (ii) the self complementary oligomer CGCGAAAATTTTCGCG ("oligoSelf") with mixed random 20-22bp non-complementary single stranded oligomers ("oligoMix"). We find that upon cooling from above the duplex unbinding temperature, subpicoliter liquid crystal domains of complementary oligomers condense out from the isotropic mixture of non-complementary sequences. This phenomenon is observed in 300-600 mg/ml oligomer solutions and for mixtures with the ratio of complementary/non-complementary sequences down to [oligoA]/[oligoB] = 1/15 and [oligoSelf]/[oligoMix] = 1/5. Comparison of condensated volumes and complementary/non-complementary weight ratios indicates that the segregation is strong, as also suggested by the columnar ordering on the condensed domains. We interpret these findings in terms of depletion forces acting on mixtures of flexible+rigid solutes. The spontaneous condensation of well paired sequences into microdroplets where the duplexes face each other at their endings opens new possibilities to prebiotic scenarios for the formation of biopolymers. Work was supported by NSF Grant DMR 0606528 and NSF MRSEC Grant No. DMR 0213918.

12:27PM V35.00007 Structural Analysis of D- and L-RNA by UV-Resonance Raman Spectroscopy , S. BINDER, S. BOLIK, B. SCHULZ, M. RUEBHAUSEN, IAP, Univ. of Hamburg, M. PERBANDT, M. KRAMER, C. BETZEL, Biochem., Univ. of Hamburg, V.E. ERDMANN, Biochem., FU Berlin, S. KLUSSMANN, Noxxon Pharma AG, Berlin, N. GENOV, BAS, Bulgaria — Chirality is a fundamental aspect of chemical biology. Nucleic molecules naturally only exist in D- but not in L-configuration. However, the origins of this homochirality are not understood. Here we show that there are differences between the Raman spectra of D-RNA and L-RNA at different photon energies. We have analyzed the L and the D enantiomer of an RNA molecule with the sequence (r(CUGGGCGG).r(CCGCCUGG)) by Raman spectroscopy at different wavelengths. The bases of nucleic acids as well as aromatic amino acids and peptide bonds show electronic transitions in the deep UV. As the oscillation modes depend on conformation and surrounding of a protein, Raman Spectroscopy can be used for structural analysis.When subtracting the Raman spectra of D- and L-RNA from each other, the resulting Raman Difference Spectra indicates that both forms have slightly different Raman tensors. Differences in the D- and L-RNA spectra for different incident photon energies can be explained when assuming that the electronic states in both configurations are slightly shifted with respect to each other. Our results therefore reveal new insights into the nature of chirality in nucleic acids.

12:39PM V35.00008 Anomalous small-angle x-ray scattering (ASAXS) study of multivalent ion-DNA interactions , KURT ANDRESEN, JESSICA LAMB, XIANGYUN QIU, LISA KWOK, HYE YOON PARK, LOIS POLLACK, Cornell University — Multivalent ion-DNA interactions are important for biological function. The condensation and aggregation of DNA by multivalent ions has been extensively studied theoretically and (to a lesser extent) experimentally. We report on the related, but largely unexplored, interactions between DNA and multivalent ions below the critical concentration for condensation/aggregation. Using ASAXS, a technique used for previous studies of monovalent and divalent atmospheres around DNA, we have investigated the competition of monovalent and trivalent ions around the biopolymer. These data should prove vital for modeling DNA-trivalent ion interactions and the mechanisms of DNA condensation and aggregation.

12:51PM V35.00009 Study of Electronic Structures of Nucleobases and Associated Nuclear Quandrupole Interactions for ^{14}N, ^{17}O and ^{2}H in A-DNA and B-DNA , R.H. SCHEICHER, MTU Houghton, DIP N. MAHATO, R.H. PINK, M.B. HUANG, T.P. DAS[1], SUNY Albany, ARCHANA DUBEY, H.P. SAHA, LEE CHOW, UCF Orlando — As part of a research program for first-principles investigation of electronic structures of A-DNA and B-DNA systems we have previously carried out studies of the magnetic hyperfine interactions for the spin-label[1] muonium attached to A-DNA and B-DNA. The present work involves the nuclear quadrupole interactions (NQI) of ^{14}N, ^{17}O and ^{2}H in these two systems. We will present the results of our investigations of the NQI properties using the Hartree-Fock-Roothaan procedure with many-electron correlations included using many-body perturbation theory. For the A-DNA and B-DNA systems we are using available structural data for the four nucleobases. For the free nucleobases, the geometry from the energy optimization procedure is being employed. Comparisons will be made with available experimental NQI data and planned future improvements will be discussed. [1] R.H. Scheicher, E. Torikai, F.L. Pratt, K Nagamine, and T.P. Das, Hyperfine Interactions,158, 53 (2004); Physica B, Physics of Condensed Matter, 374, 448 (2006).

[1]Also UCF Orlando

1:03PM V35.00010 Experimental studies of the relationship between DNA structure and chemical modification, and its charge transport properties , V. SOGHOMONIAN, D. E. DAVIS, A. A. BELAK, J. F. DOWD, J. J. HEREMANS, Virginia Tech, Physics Department — We experimentally investigate the influence of the physico-chemical properties of DNA molecules on its charge transport capabilities. By performing comparative rather than absolute charge transport measurements, we probe the effect of chemical modifications on the electronic properties of the molecule. Modifications include the introduction of phosphodiester bond breaks, and intercalation of metal cations, as probes to ascertain the relationship between DNA structure and electronic properties. Furthermore, we perform comparative measurements between double strand and single strand DNA molecules, to probe the importance of DNA duplex structure on its electronic properties. Our comparative current-voltage measurements yield distinct curves associated with specific modifications to the DNA molecule. We also investigate different lengths of lambda DNA. AFM images confirm the presence of DNA molecules between the lithographic measurement electrodes. (NSF DMR 0103034).

1:15PM V35.00011 Density Functional Analysis of Stabilizing Effects of Stacking Interactions in Nucleic Acid Base Pair Steps , DAVID C. LANGRETH, VALENTINO R. COOPER, TIMO THONHAUSER, AARON PUZDER, Rutgers University, ELSEBETH SCHRÖDER, BENGT I. LUNDQVIST, Chalmers University of Technology — Base pair stacking interactions contribute significantly to the stability of DNA. In addition, numerous studies highlight the stabilizing effect of thymine within DNA. Electrostatic, van der Waals (vdW) and hydrophobic interactions all contribute to these stacking interactions, but their relative contributions are unclear. In this paper, we use the newly developed vdW density functional[1] to investigate the importance of vdW interactions to stacking interactions between Watson-Crick DNA base pairs. Our results indicate that these interactions are essential for defining both the base pair step distance and the helical twist angle of DNA. Furthermore, we show that the stability gained from the presence of thymine is due to vdW interactions between the methyl group of the thymine with neighboring bases.

[1]Dion, Rydberg, Schröder, Langreth, Lundqvist, PRL **92**, 246401 (2004)

1:27PM V35.00012 Molecular Simulations of DNA Hybridization in Solution and in Microarrays. , JUAN ARAQUE, Rice University, ATHANASSIOS PANAGIOTOPOULOS, Princeton University, MARC ROBERT, Rice University — Nucleic acid hybridization describes a thermodynamic transition in which a single-stranded DNA molecule associates with its complementary sequence. A comprehensive understanding of the thermodynamic behavior of this process can be achieved by computer simulation. However, the collective behavior of DNA hybridization in solution and on grafted surfaces exhibits disparate time and length scales that make atomistic simulations technically unfeasible. We propose a coarse-grained model where DNA strands are described by the single-site bond-fluctuation model on a cubic lattice. Our approach incorporates physically relevant features such as the sequence and orientation dependence of base-stacking and base-pairing interactions. We perform parallel tempering Monte Carlo simulations of DNA oligomers in the canonical ensemble. We explore how chain length, interaction heterogeneity, chain stiffness, and surface density alter the location of the melting temperature and the width of the transition. The model allows the determination of the free energy change associated with the grafting of probe chains onto the array surface with respect to the free probes in solution. Overall, the thermodynamic behavior predicted is in qualitative agreement with experimental observations both in solution and in microarrays.

1:39PM V35.00013 Interactions between Counterions and Brushes of ssDNA , D. Y. PETROVYKH, University of Maryland, College Park, MD and Naval Research Laboratory, Washington, DC, A. OPDAHL, University of Wisconsin, La Crosse, WI, XIAOSONG LIU, F. J. HIMPSEL, University of Wisconsin, Madison, WI, L. J. WHITMAN, Naval Research Laboratory, Washington, DC — We investigate interactions between counterions and brushes of single-stranded DNA (ssDNA) using x-ray photoelectron (XPS) and near-edge x-ray absorption fine structure (NEXAFS) spectroscopies. Monolayers of thiol-modified thymine homo-oligonucleotides on gold are convenient model systems because for these ssDNA films the interpretation of the spectroscopic data is simplified and therefore quantitative analysis of the surface density, conformation, and composition is possible. A series of experiments was designed to quantify residual counterions retained in ssDNA brushes after common rinsing procedures. We find that while the residual amount of divalent Ca cations is essentially unaffected by rinsing, the monovalent K cations can be effectively removed by a rinse under flowing deionized water. Our results demonstrate that ex situ surface spectroscopies can be effectively used to systematically investigate interactions between ssDNA and counterions.

1:51PM V35.00014 Single DNA electrophoresis in Pluronic F127 in a real-time fluorescence microscopy , SEUNGYONG YOU, DAVID VAN WINKLE, Dept. of Physics and Center for Materials Research and Technology, Florida State University — Electrophoresis is the separation of bio-molecules in a sieving medium by applying an electric field. The Pluronic F127 gel was introduced as a new sieving medium for electrophoresis. The mobility of DNA in this gel is not fully explained by conventional reptation theories. Here, in our work, the migration of single DNA molecule pre-stained was studied on the gel electrophoresis by real-time fluorescence microscopy. Separations were performed on dsDNA fragments ranging in length from 200 base pairs (bp) to 2500 bp in pluronic gel in various concentrations. Evidence is presented that in some cases DNA fragments electrophorese along gel crystallite grain boundaries and in other cases directly through gel crystallites. This is direct observation of DNA migration through the pluronic gel on a microscopic scale.

2:03PM V35.00015 Shear unzipping of DNA: A semi-microscopic approach , BUDDHAPRIYA CHAKRABARTI, DAVID R. NELSON, Lyman Laboratory of Physics, Harvard University, Cambridge, MA 02138 — The denaturation force of double stranded DNA in shear mode is observed to be much higher than the force required to unzip individual base pairs. We present an analysis of this problem using a nonlinear generalization of a model of shear unzipping first considered by deGennes. We find that the strain on the DNA is localized over a small region on either side of the chain. The nonlinear springs of length κ^{-1} acting in parallel on either side of the chain make the chain stiffer. The competition between this length scale κ^{-1} and the system size L gives rise to a system size dependent rupture force. While for small systems, the force scales as $F_c \approx f_0 L$, where f_0 is the rupture force of a single bond, it saturates to a value $F_c \approx 2\kappa^{-1} f_0$ for large systems. We explore the role of temperature and sequence heterogeneity on the unzipping process and discuss its implications in biology and material science.

Thursday, March 8, 2007 2:30PM - 5:30PM –

Session W2 DBP: Molecular Motors (Biophysical Society Symposium) Colorado Convention Center Four Seasons 4

2:30PM W2.00001 Pathway of Force Production by the Kinesin-Microtubule ATPase[1] , KENNETH JOHNSON, University of Texas at Austin — Kinesin is the smallest of the molecular motors, consisting of a dimer of motor domains that interact with microtubules and ATP to generate motion towards the plus ends of microtubules for fast axonal transport of membranous organelles. It operates via an alternating site ATPase pathway in which the binding of ATP to one motor domain stimulates the release of ADP from the neighboring domain as the motor walks "hand over hand" along the microtubule surface. This alternating site pathway is accomplished in part due to strain that distinguishes the leading from the lagging motor domains when both are bound to the microtubule. This strain leads to a weak nucleotide binding state in the leading motor and a strong nucleotide binding state in the lagging motor. The ATPase activity is linked to alternating weak and strong nucleotide binding states that are coupled to association and dissociation at the microtubule surface to produce a force for forward motion. Strain in the leading motor domain appears to be due to the disruption of the "neck linker" in the leading motor. Release of the trailing motor domain from the microtubule surface is the rate-limiting step and, by relaxing the tension, allows the leading domain to bind ATP and continue the cycle and forward motion. Although many of the rate constants for steps in this pathway are known, details regarding the structural and thermodynamic basis for the coupling of ATP hydrolysis to force production remain to be established. I will review our current understanding and describe some of our early attempts to resolve intermediates during movement using single molecule fluorescence methods.
In collaboration with Tim Scholz and Bernhard Brenner, Hannover Medical School.

[1]Supported by NIH GM26726 and Welch Foundation F1604.

3:06PM W2.00002 , SMITA PATEL, Robert Wood Johnson Medical School — No abstract available.

3:42PM W2.00003 Optical tweezers studies of viral DNA packaging: Motor function and DNA confinement in Bacteriophages phi29, lambda, and T4[1] , DOUGLAS SMITH, University of California, San Diego — In the assembly of many viruses a powerful molecular motor translocates the genome into a pre-assembled capsid. We use optical tweezers to directly measure translocation of a single DNA molecule into the viral capsid. Improved techniques allow us to measure initiation and early stages of packaging. With phi29 the DNA terminal protein was found to cause large variations in the starting point of packaging. Removal of this protein results in terminal initiation, permitting more accurate assessment of motor function and DNA confinement forces. We investigated the role of electrostatic repulsion by varying ionic screening of the DNA. The observed trends are in accord with those theoretically expected considering counter-ion competition; however the forces are larger than expected in comparison with recent theories and DNA ejection measurements. We have recently succeeded in extending our methods to study two other phages: lambda and T4. These systems have unique structural and functional features, presenting an opportunity for comparative studies in this family of molecular motors. Initial measurements show that lambda and T4 translocate DNA several times faster than the phi29 motor, but are more sensitive to applied load.

[1]Supported by Burroughs Wellcome Fund, The Kinship Foundation, The Beckman Foundation, and the NIH.

4:18PM W2.00004 The Viral DNA Packaging Motor of Bacteriophage Lambda[1] , CARLOS E. CATALANO, University of Washington School of Pharmacy — Terminase enzymes are common to both eukaryotic and prokaryotic double-stranded DNA viruses. These enzymes, which serve as molecular motors that selectively "package" viral DNA into a pre-formed procapsid structure, are among the most powerful biological motors characterized to date. Bacteriophage lambda terminase is a heteroligomer composed of gpA and gpNu1 subunits. The smaller gpNu1 subunit is required for specific recognition of viral DNA, a process that is modulated by ATP. The gpA subunit possesses site-specific nuclease and helicase activities that "mature" the viral genome prior to packaging. The subunit further possesses a DNA translocase activity that is central to the packaging motor complex. Discrete ATPase sites in gpA modulate the DNA maturation reactions and fuel the DNA packaging reaction. Kinetic characterization of lambda terminase indicates significant interaction between the multiple catalytic sites of the enzyme and has led to a minimal kinetic model describing the assembly of a catalytically-competent packaging motor complex. Biophysical studies demonstrate that purified lambda terminase forms a homogenous, heterotrimeric structure consisting of one gpA subunit in association with two gpNu1 proteins. Four heterotrimers further assemble into a ring-like structure of sufficient size to encircle duplex DNA. The ensemble of data suggests that the ring tetramer represents the biologically relevant, catalytically-competent motor complex responsible for genome processing and packaging reactions. We present a model for the functional DNA packaging motor complex that finds general utility in our global understanding of the enzymology of virus assembly.

[1]This work was supported by NIH Grant #GM063943-05 and NSF Grant #MCB-0517725

4:54PM W2.00005 Structural dynamics of myosin V: characterization of the one-head bound intermediate , ALEX DUNN, Spudich Lab, Department of Biochemistry, Stanford University School of Medicine — Myosin V transports cargo along actin filaments by walking hand over hand. Although this basic model is supported by numerous studies, little is known about the intermediate that occurs when only one of the two heads is bound to actin. Here we use submillisecond darkfield imaging of gold nanoparticle labeled myosin V to directly observe the free head as it releases from the actin filament, diffuses forward, and rebinds. The released head rotates freely about the lever arm junction, a trait which likely facilitates travel through crowded actin meshworks. Free head rebinding occurs more rapidly when one of the six calmodulins bound to the lever arm is replaced with the light chain LC1sa. Our data suggest that strong rebinding and phosphate release occur rapidly, but that the lever arm swing is thwarted by intramolecular strain. The effect of light chain composition on free head rebinding kinetics suggests a potentially elegant means of modulating filament switching and processivity in a tissue-specific manner.

Thursday, March 8, 2007 2:30PM - 5:30PM –

Session W34 DBP: Biological Physics and Bacterial Behaviors Colorado Convention Center 404

2:30PM W34.00001 Near-Perfect Adaptation in the *E. coli* Chemotaxis Signal Transduction Network , YANG YANG, SIMA SETAYESHGAR, INDIANA UNIVERSITY TEAM — Biochemical reaction networks constitute the computing language of the cell, from converting external stimuli into appropriate intracellular signals to regulating gene expression. Precise adaptation is an important property of many signaling networks, allowing compensation for continued stimulation without saturation. Furthermore, a common feature of intracellular reaction networks is the ability to operate in a noisy environment where concentrations of key components, such as signaling molecules and enzymes controlling reaction rates are typically small and therefore fluctuations in their numbers are significant. In the context of the well- characterized *E. coli* chemotaxis signal transduction network, we present a new computational scheme that explores surfaces in the space of total protein concentrations and reaction rates on which (near-)perfect adaptation holds. The resulting dependencies between parameters provide conditions for (near-)perfect adaptation as well as ranges of numerical values for parameters not reliably known from experiments. We generalize the applicability of this scheme to other signaling networks.

2:42PM W34.00002 Adaptation, Bacteria and Maxwell's Demons , PETER GALAJDA, JUAN E. KEYMER, ROBERT H. AUSTIN, Department of Physics, Princeton University — We propose a method to study the adaptation of bacterial populations with an asymmetric wall of Maxwell Demon openings. A Maxwell Demon opening is a funnel which is easier to enter than to leave. The interaction of swimming cells with such a Maxwell Demon Wall results in a population density separation, in apparent (but not real) violation of the Second Law of Thermodynamics, as we will show. Bacteria can be exposed to spatial challenges in order to move to e. g. higher food levels. The question we address in these experiments is: do the bacteria adapt and overcome the Maxwell Demon Wall?

2:54PM W34.00003 Effects of Noise on Ecological Invasion Processes: Bacteriophage-mediated Competition in Bacteria , JAEWOOK JOO, Sandia National Laboratories, HARVILL ERIC, REKA ALBERT, Pennsylvania State University — Pathogen-mediated competition, through which an invasive species carrying and transmitting a pathogen can be a superior competitor to a more vulnerable resident species, is one of the principle driving forces influencing biodiversity in nature. Using an experimental system of bacteriophage-mediated competition in bacterial populations and a deterministic model, we have shown in [Joo et al 2005] that the competitive advantage conferred by the phage depends only on the relative phage pathology and is independent of the initial phage concentration and other phage and host parameters such as the infection-causing contact rate, the spontaneous and infection-induced lysis rates, and the phage burst size. Here we investigate the effects of stochastic fluctuations on bacterial invasion facilitated by bacteriophage, and examine the validity of the deterministic approach. We use both numerical and analytical methods of stochastic processes to identify the source of noise and assess its magnitude. We show that the conclusions obtained from the deterministic model are robust against stochastic fluctuations, yet deviations become prominently large when the phage are more pathological to the invading bacterial strain.

3:06PM W34.00004 Synchronized Cycles: An allosteric model of the cyanobacterial circadian oscillator , DAVID LUBENSKY, University of Michigan, J.S. VAN ZON, Imperial College, P. ALTENA, P.R. TEN WOLDE, AMOLF (Amsterdam) — In a remarkable experiment, Nakajima et al. [Science, 2005] showed that the 3 cyanobacterial clock proteins KaiA, KaiB, and KaiC are sufficient to generate circadian phosphorylation of KaiC *in vitro*. This system is thus a rare example of a functioning biochemical circuit that can be reconstituted in the test tube. Theoretically, it presents the further challenge that the only reactions driven out of equilibrium are those associated with KaiC phosphorylation and dephosphorylation. Here, we present a model of the Kai system. At its heart is the assumption, motivated by classical models of allostery, that each KaiC hexamer to tends to be phosphorylated in a cyclic manner. For macroscopic oscillations to be possible, however, the cycles of the different hexamers must be synchronized. We propose a novel synchronisation mechanism that allows us to reproduce a wide range of published data, including temperature compensation of the oscillation period, and to make nontrivial predictions about the effects of varying the concentrations of the Kai proteins.

3:18PM W34.00005 Stochasticity in the signalling network of a model microbe , ILKA BISCHOFS, JONATHAN FOLEY, Department of Bioengineering, University of California at Berkeley, CA 94720 , ERIC BATTENBERG, Department of Electrical Engineering and Computer Science, University of California at Berkeley, CA 94720 , LISA FONTAINE-BODIN, GAVIN PRICE, Department of Bioengineering, University of California at Berkeley,CA 94720 , DENISE WOLF, ADAM ARKIN, Biosciences Division, Lawrence Berkeley National Laboratory,CA 94720 — The soil dwelling bacterium *Bacillus subtilis* is an excellent model organism for studying stochastic stress response induction in an isoclonal population. Subjected to the same stressor cells undergo different cell fates, including sporulation, competence, degradative enzyme synthesis and motility. For example, under conditions of nutrient deprivation and high cell density only a portion of the cell population forms an endospore. Here we use a combined experimental and theoretical approach to study stochastic sporulation induction in *Bacillus subtilis*. Using several fluorescent reporter strains we apply time lapse fluorescent microscopy in combination with quantitative image analysis to study cell fate progression on a single cell basis and elucidate key noise generators in the underlying cellular network.

3:30PM W34.00006 The *E. Coli* Response To A Phage Perturbation , EMILY CHAPMAN-MCQUISTON, XIAO-LUN WU, University of Pittsburgh — Bacteria have evolved a variety of defenses against extreme environmental pressure. While a majority of the population dies during times of stress, a portion of the population continues to survive due to the cell's phenotypic state. We study the response of the bacterial system to attack by a particular virus called lambda phage. During times of phage attack bacteria continue to create and lose receptors making the bacteria more or less sensitive to the applied phage concentration. We use experiment and modeling to study how the creation and loss of receptors affects the response and recovery of the bacterial population due to an applied phage pressure.

3:42PM W34.00007 Spatio-Temporal Analysis of Cell-Cell Signaling in a Living Cell Microarray , UTKUR MIRSAIDOV, Beckman Institute, The University of Illinois at Urbana-Champaign, WINSTON TIMP, Whitehead Institute, Massachusetts Institute of Technology, KAETHE TIMP, Beckman Institute, The University of Illinois at Urbana-Champaign, PAUL MATSUDAIRA, Whitehead Institute, Massachusetts Institute of Technology, GREG TIMP, Beckman Institute, The University of Illinois at Urbana-Champaign — Cell-cell signaling plays a central role in biology, enabling individual cells to coordinate their activities. For example, bacteria show evidence of intercellular signaling through *quorum sensing*, a regulatory mechanism that launches a coordinated response, depending on the population density. To explore the spatio-temporal development of cell-to-cell signaling, we have created regular, heterotypic microarrays of living cells in hydrogel using time-multiplexed optical traps for submicron positional control of the cell orientation and location without loss of viability. We studied the *Lux* system for quorum sensing; splitting it into sender and receiver plasmids, which were subsequently introduced into *E. Coli*. Induced by IPTG, the sender cells express a fluorescent reporter (mRFP1) and the *LuxI* enzyme that catalyzes the synthesis of a molecular signal AHL that diffuses through the cell membrane and the extra-cellular scaffold. The receiver cells collect the AHL signal that binds to the *LuxR* regulator and reports it through GFP production. We have measured the time-delay between the onset of mRFP1 and GFP dependence on intercellular spacing in the array.

3:54PM W34.00008 *in silico* simulation and analysis of microbial metabolism.[1] , SHENG HUI[2], SHENGHUA LIANG, LEI-HAN TANG, Department of Physics, Hong Kong Baptist University — Through evolution living organisms have developed an elaborate network of enzyme-facilitated reactions and transport to process and cycle biochemical compounds for cell growth. A majority of these reactions are uni-directional, yet the network allows an organism to live on a variety of carbon sources and synthesize a diverse set of compounds in varying amounts. We found that biosynthesis of the end products can proceed independently. In the three genome-wide *in silico* models examined, the optimal yield for simultaneous synthesis of two compounds is only about 3% higher than what is achievable under separate production of individual compounds. In most cases, the residual correlation can be attributed to the requirement of energy, redox potential, or charge balance. These observations quantify, in the context of cellular metabolism, the bow-tie analogy which has been argued to provide a ubiquitous architecture for multi-input/multi-output networks.

[1]Work supported in part by the RGC of the HKSAR under grant 2016/06P.

[2]Present address: BioMaPS Institute, Rutgers University

4:06PM W34.00009 Study of Signal Detection, Integration, and Propagation in Quorum Sensing at the Single Cell Level , TAO LONG, Department of Physics, BONNIE BASSLER, Department of Molecule Biology, Howard Hughes Medical Institute, NED WINGREEN, Department of Molecule Biology, Princeton University — Bacteria respond to their environment and to each other and accordingly adjust their gene-expression levels. Accurate signal detection, appropriate signal integration, and faithful signal propagation are essential for a cell to make correct adjustments in response to various extracellular cues. To better understand this information processing by living cells, we studied a model system – the quorum-sensing circuit in *Vibrio harveyi*. Quorum sensing is a process in which bacteria communicate with each other by diffusible chemical molecules, termed "autoinducers", to commit to coordinated developmental decisions. Three types of autoinducers are detected coincidently by three parallel receptors. The signals are then integrated into the same signaling pathway and propagated by phosphorylation or dephosphorylation of the pathway components. To quantitatively measure the intracellular response, we applied a fluorescent protein reporter, whose production is regulated by a phosphorylated protein in the pathway. By single-cell microscopy, we can explore features of this information-processing circuit such as coincidence detection, signal integration, noise reduction or filtering, and especially the fidelity in signal processing achieved in the presence of inevitable fluctuations.

4:18PM W34.00010 Evolution of Mutation Rate in Asexual Populations , SCOTT WYLIE, HERBERT LEVINE, Center for Theoretical Biological Physics, UCSD, DAVID KESSLER, Bar-Ilan University — Several evolution experiments with *E. coli* document the spontaneous emergence and eventual fixation of so called "mutator" alleles that increase the genomic mutation rate by the order of 100-fold. Variations in mutation rates are due to polymorphisms in the molecular machinery that copies and checks the genome for errors. These polymorphisms are coded in the genome and thus heritable. Like any heritable trait, elevated mutation rates are subject to natural selection and evolution. However, unlike other traits, mutation rate does not directly affect the rate at which an organism reproduces, i.e. its fitness. Rather, it affects the statistical distribution of the offspring's fitness. This fitness distribution, in turn, leads via "hitchhiking" to a change in the frequency of the mutator allele, i.e. evolution of the mutation rate itself. In our work we simulate a birth-death process that approximates simple asexual populations and we measure the fixation probability of rare mutators. We then develop an approximate analytic model of the population dynamics, the results of which agree reasonably well with simulation. In particular, we are able to analytically predict the "effective fitness" of mutators and the conditions under which they are expected to emerge.

4:30PM W34.00011 Control of growth and adaptation to nutritional shifts for bacteria exposed to amino acid-limiting environments , EDUARD M. MATEESCU, TERENCE HWA, Center for Theoretical Biological Physics, UCSD — In order to grow at the highest rate sustainable by the environment, bacteria turn on different metabolic pathways and utilize a myriad of adaptive strategies. The macromolecular composition (RNA, DNA, protein) and overall cell size (mass) can be very different in different environments. Surprisingly however, these differences appear to depend only on the growth rate and not on the growth medium itself. As the nutritional environment changes in time, the cells quickly adapt their composition to the one corresponding to the new conditions. Here, we propose a phenomenological model of growth and adaptation control for the bacterial cell, based on a simplified formulation of the central dogma and a simplified implementation of the stringent response. The core model contains no free parameters and provides a simple intuitive understanding of cell growth control. The results generated by the model, physiological state of the cell as well as the characteristics of the transition between optimized states of growth, are in qualitative and semi-quantitative agreement (i.e. within a factor of 2) with the experimental observations.

4:42PM W34.00012 Phase Transitions in Bacterial Cultures , HANNA SALMAN, ANTON ZILMAN, ALBERT LIBCHABER, Center for Studies in Physics and Biology, The Rockefeller University, New York, NY, LIBCHABER TEAM — We study how the concentration of bacteria affects their response to temperature changes. The bacteria are grown in a batch mode culture, which affects their physiological state due to nutrient depletion. For bacteria at a constant physiological state, we observe a critical transition in behavior in a one-dimensional temperature gradient as their initial concentration in the sample increases. Above a concentration of 10^8cells/cm^3, an early accumulation near their favored temperature, caused by thermotaxis, develops into a sharp pulse moving at a fast velocity ($\sim$3.5 μm/sec). This mode is the result of a positive feedback mechanism provided by inter-bacterial communication. A theoretical model describing this interaction shows good agreement with the experimental results. For different physiological states, we observe a critical transition in the bacterial response to localized heating by infrared laser. When the bacteria are grown to concentrations below 2x10^8cells/cm^3 they swim towards the heated region; when they are grown beyond this concentration they escape from the heated region. This effect is reversible. Also, mixing populations from different physiological states does not affect the response of either population. A genetic switch controlled by the nutrients' availability seems to be responsible for this behavior.

4:54PM W34.00013 Positioning of receptor clusters along the bacterial cell wall , RANJAN MUKHOPADHYAY, HUI WANG, Clark University, YIGAL MEIR, Ben Gurion University, NED WINGREEN, Princeton University — Chemotaxis receptors in *E. coli* form clusters that are located at the cell poles and also laterally along the cell body, and clustering plays an important role in signal transduction. Recently, experiments using fluorescence imaging, have studied cluster dynamics during cell growth and found that lateral clusters transiently localize at positions approximately periodically spaced along the cell body. We have studied a lattice model of the dynamics of receptor clustering in the presence of cell growth. In this talk we will present results from our model and explore whether lateral cluster positioning could arise spontaneously from receptor clustering dynamics or whether the experimental results indicate the existence of periodically positioned markers along the cell wall that are targeted by the receptors.

5:06PM W34.00014 Genome-scale reconstruction of the metabolic network in *Yersinia pestis* CO92[1] , ALI NAVID, EIVIND ALMAAS, Lawrence Livermore National Laboratory — The gram-negative bacterium *Yersinia pestis* is the causative agent of bubonic plague. Using publicly available genomic, biochemical and physiological data, we have developed a constraint-based flux balance model of metabolism in the CO92 strain (biovar *Orientalis*) of this organism. The metabolic reactions were appropriately compartmentalized, and the model accounts for the exchange of metabolites, as well as the import of nutrients and export of waste products. We have characterized the metabolic capabilities and phenotypes of this organism, after comparing the model predictions with available experimental observations to evaluate accuracy and completeness. We have also begun preliminary studies into how cellular metabolism affects virulence.

[1]LDRD 06-ERD-061

5:18PM W34.00015 Modeling of the Effect of Dynamical Changes of Cell Geometry on MinCDE Oscillations During Cell Division in *E. coli*. , JASON ELLIS, DIANE STROUP, MICHAEL LEE, Kent State University — In the process of cell division in *E. coli*, spatio-temporal oscillations of the MinCDE proteins act to determine the specific site of FtsZ-ring formation which initiates the process of cell separation. The reaction diffusion processes which drive the biochemical oscillations of the MinCDE system have been studied and we have developed a model which incorporates the dynamics of these oscillations while cell division is accomplished through the formation of the peptidoglycan wall at the location of the FtsZ-ring. This model investigates the mechanisms that cause observed protein segregation in the daughter cells as well as the changes in oscillation characteristics observed between early and late stages of cell growth. Simulations of this model are carried out in space and time based on the reaction diffusion dynamics of individual proteins. The model allows the investigation of effects of cell geometry for both the normal cylindrical rod geometry; as well other hypothetical geometries not easily accessible in laboratory cultures.

Thursday, March 8, 2007 2:30PM - 5:30PM –

Session W35 DBP: Dynamic Forces at Cell and Subcell Levels Colorado Convention Center 405

2:30PM W35.00001 Correlation of Force Production with Apoptosis in Tissue Dynamics , YUSUKE TOYAMA, XOMALIN PERALTA, Physics Department, Duke Univ., STEPHANOS VENAKIDES, Mathematics Department, Duke Univ., DANIEL KIEHART, Department of Biology, Duke University, GLENN EDWARDS, Physics Department, Duke Univ. — To understand embryo morphogenesis, it is necessary to know the force distribution in the various tissues. Since cells are largely inaccessible to mechanical probes *in vivo*, measurements of the net forces exerted by cells are challenging. The combination of experimental and theoretical approaches has proven to improve our understanding of these forces. A steerable UV-laser microbeam was used to probe the forces and the resulting kinematics were monitored with confocal microscopy. Dorsal closure is a developmental stage in *Drosophila* embryogenesis, where the dynamics are a consequence of four biological processes [1]. During this stage, cells that have outlived their usefulness undergo apoptosis, a biological process also known as programmed cell death for cells. Apoptotic events were decreased with genetic techniques or increased by irradiation with a UV-C lamp. We present experimental evidence for force generation correlating with apoptosis. This research has been supported by the NIH (GM33830 and GM61240). [1] M. S. Hutson, et al. Science, **300**, 145 (2003).

2:42PM W35.00002 Recoil Dynamics after Laser Ablation of Single Cell Edges in Embryonic Epithelia[1] , XIAOYAN MA, M. SHANE HUTSON, Vanderbilt University — In order to determine the interfacial tensions along cell-cell boundaries in living fruit fly (*Drosophila*) embryos, we have developed a microsurgical method based on laser ablation and laser-scanning confocal microscopy. Following ablation of one cell edge, we follow the recoil dynamics (strain relaxation) of adjacent GFP-labeled cell edges (with time resolution down to 2 ms). The recoils are consistently fit best by a double exponential decay with one time constant around 80 ms and the other around 1.2 s. The initial recoil velocities are in the range of 10-20 μm/s. We observe the same biphasic strain relaxation in multiple (N = 60) embryos at different developmental stages. Both recoil time constants are much longer than either the plasma lifetime or the duration of cavitation.

[1]Supported by NSF Grant #0545679

2:54PM W35.00003 Confounding Effect of Spot-Size on the Wavelength-Dependence of Tissue Ablation Metrics[1] , M. SHANE HUTSON, GILMA ADUNAS, YAOWU XIAO, Vanderbilt University — Tunable free-electron lasers have been used in several previous studies to investigate the mid-IR wavelength-dependence of tissue ablation. These studies gave conflicting results on an important question: do the ablation metrics depend on targeting the laser energy to a water or protein vibration? Here, we investigate the effects of two parameters that varied widely in previous studies – fluence and focused spot-size. We measured ablation threshold, etch depth and collateral damage in porcine corneas for a set of five matched wavelengths – same absorption coefficients, but different primary chromophores. Although the ablation thresholds are similar, the slope of etch depth versus fluence (ablation efficiency) differs by up to a factor of five. These differences are most strongly dependent on the focused spot diameter, not wavelength. When spot sizes are matched, protein-targeting wavelengths still leave less collateral damage, but they remove tissue less efficiently. The confounding roles of fluence and spot size have strong implications for the interpretation of previous wavelength-dependent results.

[1]Supported by grant FA9550-04-1-0045 from the DoD MFEL Program.

3:06PM W35.00004 Nanosecond Infrared Laser for Tissue Ablation , G.S. EDWARDS, R.D. PEARLSTEIN, Duke University, M.L. COPELAND, Northern Rockies Neurosurgeons, M.S. HUTSON, Vanderbilt University, K. LATONE, A. SPIRO, G. PASMANIK, Passat, Inc. — The Mark-III Free-Electron Laser (FEL), operating at the 6.45μm wavelength, has been used successfully in human surgery. Due to the FEL's size and cost, there has been interest in the development of a compact, inexpensive infrared laser for human surgical applications. We have investigated the role of the FEL superpulse, leading to the prediction that nanosecond pulses can satisfy the dynamic criteria for tissue ablation. We have developed a laser based on difference frequency mixing and stimulated Raman scattering with four stages of frequency conversion, emitting at a wavelength of 6.45μm with 3-5ns pulse duration, pulse energies of up to 2mJ, and a pulse repetition rate of 3MHz. The laser system successfully ablated tissue, where collateral thermal damage was limited to several microns. In the future, it will be necessary to increase the pulse repetition rate to achieve an ablation rate acceptable for human surgery. We acknowledge the grant support: R43 RR018435, N00014-99-1-0891, and F49620-00-1-0370.

3:18PM W35.00005 Morphogenic asymmetries in tissue dynamics , XOMALIN G. PERALTA, Y. TOYAMA, Department of Physics, R. MONTAGUE, Department of Biology, S. VENAKIDES, Department of Mathematics, D.P. KIEHART, Department of Biology, G.S. EDWARDS, Department of Physics, Duke University — Structural and kinematic symmetries in living organisms arise from the forces responsible for tissue movements during development. Tissue dynamics during dorsal closure, a stage of *Drosophila* development, provide a model system for cell sheet morphogenesis. It is characterized by tissue movements, driven by four biological processes which are coordinated in space and synchronized in time. Quantifying morphogenic asymmetries is essential for understanding the spatial and temporal differences in the contributing processes, the extent to which they can vary and still result in successful closure. They also provide a basis for understanding dynamic changes that occur to compensate for perturbations. We measured spatial, kinematic and dynamic asymmetries to biophysically characterize natural asymmetries in unperturbed closure, resiliency to laser perturbations and failure of closure in some mutant embryos. We found an asymmetric upregulation of a biological process in response to laser perturbations. In the mutants, there is a reversed asymmetry. Supported by NIH (GM33830 and GM61240).

3:30PM W35.00006 The detection of cancer in living tissue with single-cell precision and the development of a system for targeted drug delivery to cancer , ADAM FIELDS, Jericho High School, SEAN PI, North High School, ALEX RAMEK, HAFTR HIgh School, TAYLOR BERNHEIM, University of Pennsylvania, JESSICA FIELDS, Princeton University, NADINE PERNODET, MIRIAM RAFAILOVICH, SUNY Stony Brook — The development of innovations in the field of cancer diagnostics is imperative to improve the early identification of malignant cells within the human body. Two novel techniques are presented for the detection of cancer cells in living tissue. First, shear modulation force microscopy (SMFM) was employed to measure cell mechanics of normal and cancer cells in separate and mixed tissue cultures. We found that the moduli of normal keratinocytes were twice as high as the moduli of SCC cancerous keratinocytes, and that the cancer cells were unambiguously identifiable from a mixture of both kinds of cells. Second, confocal microscopy and the BIAcore 2000 were used to demonstrate the preferential adhesion of glass micro-beads impregnated with fluorescent dye to the membranes of cancer cells as compared to those of normal cells. In addition to their use as a cancer detection system, these hollow and porous beads present a model system for targeted drug delivery in the treatment of cancer.

3:42PM W35.00007 Characterizing Cell Mechanics with AFM and Microfluidics , N. WALTER, Max-Planck Institute for Metals Research and University of Heidelberg, Germany; Massachusetts Institute of Technology, USA, A. MICOULET, S. SURESH, MIT, J.P. SPATZ, Max-Planck Inst. for Metals Research and Univ. of Heidelberg — Cell mechanical properties and functionality are mainly determined by the cytoskeleton, besides the cell membrane, the nucleus and the cytosol, and depend on various parameters e.g. surface chemistry and rigidity, surface area and time available for cell spreading, nutrients and drugs provided in the culture medium. Human epithelial pancreatic and mammary cancer cells and their keratin intermediate filaments are the main focus of our work. We use Atomic Force Microscopy (AFM) to study cells adhering to substrates and Microfluidic Channels to probe cells in suspension, respectively. Local and global properties are extracted by varying AFM probe tip size and the available adhesion area for cells. Depth-sensing, instrumented indentation tests with AFM show a clear difference in contact stiffness for cells that are spread of controlled substrates and those that are loosely attached. Microfluidic Channels are utilized in parallel to evaluate cell deformation and "flow resistance", which are dependent on channel cross section, flow rate, cell nucleus size and the mechanical properties of cytoskeleton and membrane. The results from the study are used to provide some broad and quantitative assessments of the connections between cellular/subcellular mechanics and biochemical origins of disease states.

3:54PM W35.00008 Measurement of the adhesion and elasticity of single cells using a novel micropipette-based technique , MARIE-JOSEE COLBERT, ADAM N. RAEGEN, CECILE FRADIN, KARI DALNOKI-VERESS, McMaster University — Numerous biological processes have to go through cell adhesion, which makes the fundamental study of the adhesion of cells on solid substrates a key research topic in cellular biophysics. We will present our work on the elasticity and adhesion of a single liposome on a substrate. A vesicle is held at the end of a micropipette mounted on a micromanipulator and put into contact with a surface. We developed a technique to directly measure adhesion using the spring-constant of an L-shaped micropipette when pulling the vesicle from the substrate. The deflection is used to determine the adhesion force of cells as well as a cells elasticity. Since the force applied on the cell is known at every moment of the experiment, this technique enables dynamical measurements. The links between the adhesion strength and the surface tension will also be discussed.

4:06PM W35.00009 Measuring the Interaction between Cell-Surface Markers and Substrate-Coupled Proteins as a Means of Determining Cell Membrane Fluidity , ANDREA CARBONARO, University of California, Berkeley, LUCY A. GODLEY, The University of Chicago, LYDIA L. SOHN, University of California, Berkeley — We have analyzed the detailed interaction between cell-surface markers and substrate-coupled proteins by measuring the transit time of individual cells as they pass through a functionalized pore. Cells that have a specific cell-surface marker will transiently interact with the walls of a pore that are functionalized with a correspondingly specific protein. This interaction results in the cell moving slowly through the pore. In contrast, cells that do not express the specific marker will not interact with the functionalized walls and will pass quickly through the pore. The distribution of transit times measured for interacting cells can be explained in terms of the number of ligand-receptor bonds created between the immobilized proteins on the pore wall and the cell-surface receptors. We will show that this number is a function of both the ligand and receptor densities on the pore and cell membrane, respectively, as well as the fluidity of the cell membrane.

4:18PM W35.00010 Cooperativity of Integrin-mediated Adhesion on Nanopatterned Substrates , CHRISTINE SELHUBER, University of Heidelberg and Max-Planck-Institute for Metals Research, THORSTEN ERDMANN, ULRICH SCHWARZ, University of Heidelberg (BIOMS), HORST KESSLER, Technical University of Munich, JOACHIM SPATZ, University of Heidelberg and Max-Planck-Institute for Metals Research — Surfaces of defined adhesion properties are required for a physical understanding of cell adhesion in vivo. In this work, biofunctional nanopatterns are employed, which allow adhesion ligands to be positioned in a quasi-hexagonal lattice. Such nanopatterns are used to investigate integrin-mediated cell adhesion, which is a highly complex biological process and essential for numerous cell functions. With nanopatterns the distance between adjacent integrin binding sites is precisely defined. Cell culture experiments have revealed that this distance strongly affects cell adhesion and the formation of adhesion clusters, known as focal contacts. To quantify the adhesion cluster formation for different integrin binding site spacings, cell adhesion forces were studied using atomic force microscopy (AFM). The experiments demonstrate that an integrin binding site spacing of 70 nm and more prevents the cooperative formation of early adhesion clusters. In long-term adhesion studies, after several hours of cell adhesion, it turned out that focal contact formation cooperatively increases the local adhesion strength. The obtained results were related to theoretical models on adhesion cluster stability.

4:30PM W35.00011 Dynamics of Cell Migration for cells embedded in Collagen using a multimodal platform of Optical Coherence Tomography, Multi-Photon excitation and Second Harmonic Generation[1] , KANDICE TANNER, SHUO TANG, ENRICO GRATTON, University of California, Irvine, LFD/BLI TEAM — We developed Raster Image Correlation Spectroscopy (RICS) to analyze the dynamics of cell migration from data obtained on a confocal multi-photon microscope. We assembled a microscope that can simultaneously measure the scattering signal from optical coherence tomography (OCT), multi-photon excited emission (TPEF) and second harmonic signals (SHG) with comparable spatial resolution and the same time resolution. We present data here showing the combined 3-D images of the cells embedded in a collagen matrix. The OCT signal adds fine structural information of the cellular morphology and collagen which is enhanced by the SHG image. The RICS analysis of the TPEF signal gives the dynamics of the GFP –style proteins. We show that the cell morphology and the distribution of cell organelles are different in the collagen matrix than what is observed in cells growing on flat surfaces. Using the three modalities of cell imaging we could reach a more realistic interpretation of cell dynamics in tissue.

[1]Supported by NIH PHS 9RO1-EB00559, NTROI-1U54CA105480-01 and PHS 5 P41-RR03155 and by LAMMP-P41RR01192

4:42PM W35.00012 Coordinated Buckling of Microtubule Bundles Produces the Long Wavelength of Microtubule Birefringent Pattern[1] , YONGXING GUO, YIFENG LIU, Physics Department, Brown University, Providence, RI 02912, ALLAN BOWER, Division of Engineering, Brown University, Providence, RI 02912, JAY TANG, JAMES VALLES, Physics Department, Brown University, Providence, RI 02912 — Aligned microtubule (MT) bundles spontaneously form, elongate and buckle in high concentration tubulin solutions that are subjected to a field that initially aligns the microtubules. The nesting of the buckled bundles produces a macroscopic birefringence pattern of stripes. Of interest here is the buckling wavelength, which controls the stripe width. It is shorter than the fundamental wavelength expected in classic Euler buckling and longer than the wavelength expected for the buckling of a single MT bundle within the elastic network formed by the dispersed MTs. We present a mechanical buckling model that accounts for this intermediate wavelength. It shows that the wavelength is shorter than the fundamental one because of the lateral reinforcement by the MT network, and longer than the wavelength expected for a single laterally reinforced bundle due to the coordinated buckling of the neighboring bundles.

[1]Supported by NASA NNA04CC57G and NSF DMR 0405156

4:54PM W35.00013 Cell elasticity as a function of actin expression , CARSTEN STÜBER, JOSEF KÄS — The deformation response to an external force of an eurkaryotic cell mainly depends on its cytoskeletal composition. Theoretical models have been introduced to quantify the concentration dependence of the different cytoskeletal components to the elastic strength of cells. Verifying the models experimentally, the optical stretcher, a two beam optical trap, is used to elongate fibroblast cells. These fibroblasts are transfected with GFP-actin, which leads to an overexpression of actin within the cell and allows to determine the actin concentration using fluorescence image analysis. The dependence of the elasticity on the actin concentration of fibroblasts shows a softening of the cell with increasing number of actin filaments.

5:06PM W35.00014 Measuring mitotic spindle formation through connection graphs , STUART SCHAFFNER, Northeastern University, JORGE JOSE, University at Buffalo and Northeasern University — The mitotic spindle, an important structure formed during biological cell division, consists of a pattern of stiff fibers called microtubules and crosslinking molecular motor complexes. The spindle, consisting of objects interacting through pairwise interactions, is well suited to study via its connection graph. Thermal motion is important in this system; molecular motors attach and detach randomly from the microtubules, but only where the geometry allows. We have found the connection graph approach to be helpful in several ways for analyzing spindle properties. Monitoring the number and size of connected components in the graph allows us to quantify the development of the spindle bipolar pattern. Minimum cut-sets in components measure spindle pole robustness. These computations not only allow us to measure the dynamics of initial pattern formation, but also the structural rearrangements within spindles that have already formed. Our results are compared to known experimental results.

5:18PM W35.00015 ABSTRACT WITHDRAWN –

Friday, March 9, 2007 8:00AM - 11:00AM –

Session X2 DBP: Understanding DNA and RNA machines Colorado Convention Center Four Seasons 4

8:00AM X2.00001 , KOEN VISSCHER, University of Arizona — No abstract available.

8:36AM X2.00002 , VINCENT CROQUETTE, Ecole Normale Superieure — No abstract available.

9:12AM X2.00003 Hexameric DNA-based motor proteins , OMAR A. SALEH, Materials Dept. and BMSE Program, UCSB — Hexameric, ring-shaped motor proteins play important roles in a wide variety of cellular processes. They typically encircle a nucleic acid or protein substrate in order to perform a mechanical activity. Motivated by a desired to understand the advantages and peculiarities of this strikingly symmetric design, we have performed single-molecule measurements of several different DNA-based hexameric motors. I will discuss how, for the bacterial protein FtsK, the hexameric structure causes an anomalous coupling between rotation and linear motion. I will also present recent results in which we exploit the ability of certain hexameric helicases to encircle either single or double-stranded DNA in order to probe their activity in several different ways. Where relevant, I will introduce the novel magnetic-tweezer based measurement techniques we have devised for these experiments.

9:48AM X2.00004 Stretching, Twisting, and Unzipping DNA , MICHELLE WANG, Cornell University — DNA mechanics governs many essential cellular processes. During DNA replication, repair, recombination, and transcription, often a DNA double helix is unwound, its two strands are separated to expose the base sequence, and compensatory supercoils are generated in the remaining DNA. Our lab develops new single molecule optical trapping techniques to probe the mechanics of DNA as it is stretched, twisted, and unzipped. These approaches reveal interesting physical properties as well as permit direct investigation of the mechanisms of enzymes involved in these processes. I will discuss our recent work in these directions.

10:24AM X2.00005 , TAEKJIP HA, Univ. Illinois — No abstract available.

Friday, March 9, 2007 8:00AM - 11:00AM –

Session X5 DBP: Elasticity of Biological Membranes: From Physical Principles to Biological Processes Colorado Convention Center Korbel 1A-1B

8:00AM X5.00001 Biophysical studies of biological membranes , SARAH KELLER, University of Washington — No abstract available.

8:36AM X5.00002 The Beginning of the Ends: A Curvature-Mediated Mechanism for Localization of Lipids to Bacterial Poles[1] , KERWYN HUANG, Princeton University — In the past decade, intracellular fluorescence microscopy has fashioned a new appreciation for the diversity of ways in which proteins organize and segregate on bacterial membranes. Though some targeting anchors are known, cellular symmetry breaking ultimately requires molecular components that self-organize. We propose a novel equilibrium mechanism, based on the two-dimensional curvature of the membrane, for spontaneous lipid targeting to the poles and division site of rod-shaped bacterial cells. If one of the membrane components has a large intrinsic curvature, the geometrical constraint of the plasma membrane by the more rigid bacterial cell wall counteracts the attractive interaction between like lipids and leads to microphase separation. We find that the resulting clusters of high-curvature lipids are large enough to spontaneously and stably localize to the two cell poles and septal regions, and could have similar utility to lipid rafts as a stage for targeting proteins involved in a wide variety of biological processes. Recent evidence of localization of the phospholipid cardiolipin to the poles of bacterial cells suggests that protein targeting may depend on the membrane's heterogeneous lipid content. More generally, aggregates of lipids, proteins, and lipid-protein complexes may localize in response to features of cell geometry incapable of localizing individual molecules.

[1]This work is supported in part by NIH grant number 1K25 GM075000.

9:12AM X5.00003 Fundamental physical mechanisms of membrane phase separation , JAY GROVES, University of California, Berkeley — No abstract available.

9:48AM X5.00004 Membrane mechanics of nuclear division in yeast , GREG HUBER, University of Connecticut Health Center — No abstract available.

10:24AM X5.00005 Fusion, Fission, and Membrane Microdomains , JOSHUA ZIMMERBERG, LCMB, NICHD, NIH — In biology, curvature of intracellular membranes plays a key role in defining compartments to organize the interior of a cell and in creating the optimal shapes of organelles for function. We have studied how membrane curvature plays a crucial role in determining the energetics of membrane fusion in a number of systems. How the proteins that catalyze membrane fusion in cellular secretion and in viral fusion will be discussed in detail. Newer work on the role of proteins in the budding of viruses during assembly will be presented. The assembly of viruses also requires a concentration of viral protein components in the membrane. Recent experiments on cells expressing the influenza hemagglutinin show a clustering of proteins at many length scales. The dependence on cell cholesterol of this clustering (microdomain formation) will also be discussed.

Friday, March 9, 2007 8:00AM - 11:00AM –

Session X6 GSNP DBP: Networks in Genetic Regulation Colorado Convention Center 207

8:00AM X6.00001 Check Point as Fixed point: Analysis of a Yeast Cell-Cycle Model[1] , CHAO TANG, University of California, San Francisco — The cell cycle regulation in the budding yeast *Saccharomyces cerevisiae* is one of the best studied biological systems. Many major players and their interactions have been identified by decades of work in genetics and biochemistry as well as by the more recent effort in high throughput genomics and proteomics. On the other hand, current information about the network is mostly qualitative—while there is a circuit diagram (although it may not be complete) of who regulates whom, there is little quantitative information (e.g. the kinetic constants) about the regulation. Here we construct a model of yeast cell-cycle regulation from the known circuit diagram using ordinary differential equations and focus our attention on the global dynamic property and structural stability of the system. We found that certain qualitative conclusions about the system's behavior are very robust to parameter choices. In particular, each checkpoint can be a global attractor—when a checkpoint is on *all* cell states evolve to the stationary state corresponding to the checkpoint arrest. Furthermore, there is a unique globally attracting trajectory for this dynamic system, which corresponds to the biological pathway of the cell cycle regulation. Substantial changes of certain parameters, especially when several parameters are changed simultaneously, can result in qualitative changes in the system's behavior. Typically, these not-so-robust parameters are associated with transitions between different cell-cycle phases and the corresponding abnormal behavior is often related to the arrest or bypass of a checkpoint. Our results reveal a robust picture of the yeast cell cycle regulation and the mechanisms under which the robustness can be compromised.

[1]Work done in collaboration with F. Li, Y. Lu, M. Zhong, Q. Ouyang.

8:36AM X6.00002 Boolean modeling of cellular regulatory networks[1] , REKA ALBERT, Pennsylvania State University — Interaction between gene products forms the basis of essential processes like signal transduction, cell metabolism or embryonic development. Recent experimental advances helped uncover the structure of many cellular networks, creating a surge of interest in the dynamical description of gene regulation. Traditionally genetic and protein interactions are modeled by differential equations based on reaction kinetics, but these studies are greatly hampered by the sparsity of known kinetic detail. As an alternative, qualitative models assuming a small set of discrete states for gene products, or combinations of discrete and continuous dynamics, are gaining acceptance. Many results also suggest that the interaction topology plays a determining role in the dynamics of regulatory networks and there is significant robustness to changes in kinetic parameters. This presentation will focus on a Boolean model of the signal transduction network regulating drought response in plants. We integrate qualitative and indirect relationships into the simplest network consistent with all experimental observations, and express the regulation of network nodes as logical functions. Our model captures the regulation of more than forty identified network components, and accords well with previous experimental results at both the pathway and whole cell physiological level. We identify the dynamical repertoire of the network by varying process durations and initial conditions and by simulating gene disruptions, and find a remarkable robustness against a significant fraction of possible perturbations. Although qualitative, the model provides a ranking of disruptions and perturbations in the order of their severity. We experimentally test, and validate, the most surprising prediction. The success of this model illuminates the emergent (network-level) functional robustness of cellular regulatory networks.

[1]S. Li, S. M. Assmann, R. Albert, Predicting essential components of signal transduction networks: A dynamic model of guard cell abscisic acid signaling, PLoS Biology 4: e312 (2006).

9:12AM X6.00003 Symmetry and the Self-Organized Evolution of Canalization in Boolean Networks[1] , KEVIN BASSLER, University of Houston — Canalization of genetic regulatory networks have been argued to be favored by evolutionary processes due to the stability that it can confer to phenotype expression. Using an N-K Boolean network model of a genetic regulatory network, we explore whether a significant amount of canalization can arise in purely random networks in the absence of evolutionary pressures. We use a mapping of the Boolean functions in the Kauffman N-K model for genetic regulatory networks onto a k-dimensional Ising hypercube to show that the functions can be divided into different classes strictly due to geometrical constraints. The classes can be counted and their properties determined using results from group theory and isomer chemistry. We demonstrate that partially canalized functions completely dominate all possible Boolean functions, particularly for higher K. This indicates that partial canalization is extremely common, even in randomly chosen networks, and has implications for how much information can be obtained in experiments on native state genetic regulatory networks. Furthermore, we demonstrate that a highly canalized state evolves spontaneously from a competition between the nodes. Network finite-size effects are found to be important to that evolutionary process.

[1]Supported by the NSF through grant #DMR-0427538

9:48AM X6.00004 Quantitative aspects of gene regulation by small RNAs , PANKAJ MEHTA, Princeton University — Small, non-coding RNAs (sRNAs) play an important role as genetic regulators in both prokaryotes and eukaryotes. Many sRNAs act through base-pairing interaction with target messenger RNAs (mRNAs) to regulate transcription, translation, and mRNA stability. sRNAs represent a novel form of genetic regulation distinct from more thoroughly studied protein regulators. This talk addresses quantitative aspectsof sRNA-mediated genetic regulation, focusing on noise, tunability, and feedback. In particular, we compare and contrast sRNA and protein regulators in an attempt to understand the compartive advantages of each form of regulation.

10:24AM X6.00005 Gene regulatory networks: what is still missing? , GABOR BALAZSI, University of Texas M. D. Anderson Cancer Center — Gene regulatory networks have evolved to respond to a changing environment, serving the survival of the biological population. The topology of these networks has been investigated with the hope of gaining insight into their function or identifying the factors shaping their evolution. Recent studies have shown that gene regulatory networks have different in-degree and out-degree distribution, contain network motifs and are organized in a hierarchical set of layers. However, important pieces of information are still needed before the topological features of these networks can be correctly determined and their response to environmental changes can be modeled at increasingly large scale.

Friday, March 9, 2007 8:00AM - 11:00AM –

Session X34 DBP: Shape Changes in Biological Membranes Colorado Convention Center 404

8:00AM X34.00001 Polyunsaturated Fatty Acids in Lipid Bilayers and Tubules , LINDA S. HIRST, Florida State Univ., JING YUAN, YOHANNES PRAMUDYA, LAM T. NGUYEN — Omega-3 polyunsaturated fatty acids (PUFAs) are found in a variety of biological membranes and have been implicated with lipid raft formation and possible function, typical molecules include DHA (Docosahexanoic Acid) and AA (Alphalinoleic Acid) which have been the focus of considerable attention in recent years. We are interested in the phase behavior of these molecules in the lipid bilayer. The addition of lipid molecules with polyunsaturated chains has a clear effect on the fluidity and curvature of the membrane and we investigate the effects the addition of polyunsaturated lipids on bilayer structure and tubule formation. Self-assembled cylindrical lipid tubules have attracted considerable attention because of their interesting structures and potential technological applications. Using x-ray diffraction techniques, Atomic Force Microscopy and confocal fluorescence imaging, both symmetric and mixed chain lipids were incorporated into model membranes and the effects on bilayer structure and tubule formation investigated.

8:12AM X34.00002 Dynamics of Encapsulation and Budding in Lipid Membranes , KURT SMITH, Department of Chemical Engineering, University of Pittsburgh — The behavior of lipid membranes is important in cell biology, as well as in the development of synthetic vesicles for drug delivery and other applications. The fundamental role of the membrane is to control the passage of matter into and out of a cell or vesicle. We have examined two related processes - the encapsulation of a particle by an adhesive membrane (as in endocytosis) and the budding and vesiculation of a phase separated membrane domain. These processes require changes in membrane topology (i.e. pinch-off) which involve molecular-scale rearrangements. Thus they cannot be fully understood through a macroscopic free energy formulation. Using dissipative particle dynamics, we examine the pathway through which pinch-off occurs, and find that it depends upon the nucleation of a pore at the membrane neck. We use simulations to predict the range of conditions under which pinch-off is possible.

8:24AM X34.00003 Lipid tubules Formed by Flow-Controlled Hydration , JING YUAN, LINDA S. HIRST, Florida State Univ. — Self-assembled cylindrical tubules from lipid molecules have attracted considerable attention because of their interesting supramolecular structures and technological applications. Schnur et al. [1] reported the formation of tubular microstructures from a series of diacetylenic phospholipids after liposomes were cooled through their chain melting transition. After that, several methods have been developed to fabricate such unique microstructures mainly by means of deforming preformed Giant unilamellar vesicles. Here we present a simple strategy to construct lipid microtubules through a flow-controlled lipid hydration. Fluorescent microscopy and Confocal Laser Microscopy were used to visualize the formation and the structure of the lipid tubules. Tubules were found to develop following the direction of the dynamic flow with highly parallel alignment. At high flow speeds, partial cross-linking of the lipid tubules was observed. To demonstrate the generality of this method, different types of phospholipids, such as Phosphatidic Acid (PA), Phosphatidylserine (PS), Phosphatidylethanolamine (PE), and Phosphatidylglycerol (PG) were investigated.
[1] J.M. Schnur et al, Science, 264, 945 (1994).

8:36AM X34.00004 Spontaneous Formation of Lipid Nanotubes and Lipid Nanofibers from Giant Charged Dendrimer Lipids , ALEXANDRA ZIDOVSKA, KAI K. EWERT, CYRUS R. SAFINYA, Materials Department, University of California, Santa Barbara, JOEL QUISPE, BRIDGETT CARRAGHER, CLINTON S. POTTER, National Resource for Automated Molecular Microscopy, The Scripps Research Institute, La Jolla — Liposomes have attracted much scientific interest due to their applications in model cells studies and in drug encapsulation. We report on the discovery of new vesicle phases formed in mixtures of MVLBG2, DOPC and water. MVLBG2 is a newly synthesized highly charged (16+) lipid (K. Ewert et al., *JACS,* 2006) with giant dendrimer headgroup thus leading to a high spontaneous curvature of the molecule. In combination with zero-curvature DOPC, MVLBG2 exhibits a rich phase diagram showing novel vesicle morphologies such as bones, lipid nanotubes and nanofibers as revealed by differential contrast microscopy (DIC) and cryo-TEM. At the micron scale DIC reveals a new phase consisting of bone-like vesicles. This novel morphology persists down to the nanometer scale as shown by cryo-TEM. The nanotubes are of diameter 10-50 nm, length $> 1\mu$m and consist of a single lipid bilayer. A surprising new morphology arises resulting from a spontaneous topological transition from tubes to lipid nanorods. Funded by DOE DE-FG-02-06ER46314, NIH GM-59288, NSF DMR-0503347.

8:48AM X34.00005 Hydrodynamic extrusion of membrane nanotubes: the role of the cytoskeleton , KARINE GUEVORKIAN, Curie Institute, NICOLAS BORGHI, Stanford University, SÉBASTIEN KREMER, AXEL BUGUIN, FRANÇOISE BROCHARD, Curie Institute — We have investigated membrane-cytoskeleton adhesion properties by extrusion of tubes from tethered vesicles and cells using hydrodynamic flows. Our experimental results show that impermeable membranes (giant vesicles) act as entropic springs, i.e. the extruded tubes reach a stationary length, whereas porous membranes (vesicles decorated with pores) lead to tubes, which extrude at constant velocity without reaching a stationary length. On the other hand, experiments on red blood cells (RBC) suggest that the dynamics of extruded tubes is dominated by the detachment of the membrane from the cytoskeleton and the flow of lipids through the binding membrane proteins. We have estimated the membrane-cytoskeleton binding energy and the viscosity of the membrane for RBC-s. Tube extrusion from other cell types (S180, MDCK, BON) show phenomena such as healing time for the membrane-cytoskeleton rebinding, and cell aging (breakage of the tube after a few consecutive extrusions). We will discuss how these phenomena depend on the properties of the cytoskeleton and on the presence of cell adhesion molecules.

9:00AM X34.00006 Shape transformations of active tubular membranes , ELNAZ ALIPOUR-ASSIABI, Department of Physics, Brown University, THOMAS POWERS, Division of Engineering, Brown University — Motivated by the action of enzymes that flip lipid molecules from one monolayer to another in a lipid bilayer membrane, we study shape instabilities of a tubular membrane driven by lipid-flipping. We begin with the instability of a tube with a fixed lipid number density distance, determining the relative importance of solvent viscosity, membrane viscosity, and bilayer friction. Then we consider the case of a uniform density of enzymes acting at a fixed rate. Implications for experiments will be discussed.

9:12AM X34.00007 Effective surface tension of red blood cell membranes induced by cytoskeleton meshworks , RUI ZHANG, FRANK BROWN, Department of Chemistry and Biochemistry, University of California, Santa Barbara — The membrane of red blood cell (RBC) consists of a lipid bilayer and a two dimensional cytoskeleton meshwork underneath. Its elastic properties are therefore different from a simple lipid bilayer. We introduced a simple entropic spring model to study the meshwork. In this model, adjacent nodes of the meshwork interact with each other through the link of an entropic spring. We run Monte Carlo and Brownian dynamics simulations, and developed some simple analytical theories to understand the simulation results. For a complete meshwork, we found that the cytoskeleton meshwork produced an effective surface tension to the RBC membrane, as far as the height fluctuation of the membrane is considered. This surface tension depends on the wave length of the fluctuation, and shows a crossover at the wave length of the average mesh size. We also studied the case when a fraction of randomly chosen links are disconnected from the nodes, possibly with the help of ATP. In this case, the surface tension changes with the fraction of connected links. Most interestingly, we found a percolation phase transition of the surface tension at long wave length limit. We discussed the experimental results related to our theory. Our model may improve the understanding of certain functions the RBC membrane related to its elastic properties.

9:24AM X34.00008 Pore formation by antimicrobial peptides: structural tendencies in bulk and quasi-2D membrane systems , VERNITA GORDON, LIHUA YANG, MATTHEW DAVIS, A. SOM, G. TEW, GERARD WONG, Department of Materials Science and Engineering, Dept. of Physics, Dept. of Bioengineering, University of Illinois at Urbana-Champaign — Antimicrobial peptides are cationic, amphiphilic structures that are key components of innate immunity. A prototypical family of synthetic analogs are the phenylene ethynylene antimicrobial oligomers (AMOs), which have hydrophobic alkyl chains connected to cationic hydrophilic regions. Synchrotron small-angle x-ray scattering (SAXS) shows that when AMO is mixed with concentrated model membranes, initially in the form of Small Unilamellar Vesicles, the sample forms the inverted hexagonal phase. This is a 3-dimensional phase characterized by a regular array of size-defined water channels. We demonstrate how this structural tendency is expressed when AMOs interact with dilute model membranes in the form of Giant Unilamellar Vesicles (GUVs). Using confocal microscopy, we see that applying AMO to the GUVs causes small encapsulated molecules to be released while large molecules are retained, indicating that size-defined pores have been created. Examining the partial release of polydisperse intermediately-sized molecules allows a closer measurement of the pore size, and there are indications that this single-vesicle microscopy will allow elucidation of the kinetics of the pore-forming process.

9:36AM X34.00009 Synthetic antimicrobial oligomers induce composition-dependent topological transition in membranes , LIHUA YANG, VERNITA GORDON, ABHIJIT MISHRA, KIRSTIN PURDY, JOHN CRONAN, University of Illinois at Urbana-Champaign, ABHIGYAN SOM, GREGORY TEW, University of Massachusetts, GERARD C.L. WONG, University of Illinois at Urbana-Champaign — Antimicrobial peptides comprise a key component of innate immunity for a wide range of multicellular organisms. Recently, their synthetic analogs have demonstrated broad-spectrum antimicrobial activity via permeating bacterial membranes selectively, although the precise molecular mechanism underlying the activity is still unknown. We systematically investigate interactions and self-assembled structures formed by model bacterial membranes and a prototypical family of phenylene ethynylene-based small molecule antimicrobials with controllable activity and selectivity. Synchrotron small angle x-ray scattering (SAXS) results correlate antibacterial activity and the induced formation of an inverted hexagonal phase, and indicate that the organization of negative curvature lipids such as DOPE are crucially important. Preliminary killing assays of DOPE-deficient mutant bacteria agree with the x-ray results.

9:48AM X34.00010 Role of membrane bending in ASAP1 protein activity , BEATRIZ E. BURROLA GABILONDO, University of Maryland, RUIBAI LUO, National Cancer Institute, WOLFGANG LOSERT, University of Maryland, PAUL A. RANDAZZO, National Cancer Institute — ASAP1 is part of the protein machinery that alters membranes and the actin cytoskeleton in cellular structures, called invadopodia, that mediate invasion of mammary cell carcinoma and uveal melanoma. The molecular mechanism by which ASAP1 contributes to these structures is not well defined. ASAP1 induces the hydrolysis of GTP that is bound to the protein Arf. Another activity is to deform lipid bilayers into tubules. We have set out to test the hypothesis that the enzymatic GAP activity is related to the mechanical activity. We contrast several reaction schemes for GAP activity, including steps that would be sensitive to physical changes in the membrane. We compare the numerical model predictions to data obtained from kinetics experiments. We are also developing assays such as FRET and tools like laser tweezer forcing of vesicle deformations to be used to determine the effect of ASAP1 and mutants with defects in enzymatic activity on the physical state of lipid vesicles. The ramifications of the results to the role of ASAP1 in invadopodia formation will be discussed.

10:00AM X34.00011 Shape transformations of human red blood cells under osmotic deflation-inflation , GERALD LIM, Center for Cell Analysis and Modeling, University of Connecticut Health Center, Farmington, USA, MICHAEL WORTIS, Department of Physics, Simon Fraser University, Burnaby, Canada — We systematically study the mechanics of osmotically driven shape transformations of human red blood cells, based on a computational model we developed earlier that successfully describes the stomatocyte-discocyte-echinocyte shape transformations, which are driven by the bilayer couple mechanism. We obtain a surprisingly complex energy landscape, the prominent feature of which is a tricritical point that gives rise to self-intersection of the main minimum-energy surface in a line and shape transformations exhibiting hysteresis, metastability, and re-entry. These occur in physically accessible regions of parameter space and, thus, can be tested experimentally.

10:12AM X34.00012 Dissipative Particle Dynamics Simulations of Deformable Red Blood Cells in Small Blood Vessels , IGOR PIVKIN, PETER RICHARDSON, GEORGE KARNIADAKIS, Brown University — Explicit simulations of the blood cellular components require computational methods capable of tracking time-varying fluid-solid interface. The Dissipative Particle Dynamics (DPD) is an inherently adaptive method and potentially very effective in simulating complex fluid systems. In DPD, the fluid and solid objects are represented as a collection of interacting points, each representing a group of atoms or molecules. The red blood cell model takes into account bending and in-plane energies as well as constraints of constant surface and volume. We will present results of simulations of the deformable red blood cells in a small blood vessel using DPD.

10:24AM X34.00013 Nucleation of holin domains and holes optimizes lysis timing of *E. coli* by phage λ , GILLIAN RYAN, ANDREW RUTENBERG, Dalhousie University — Holin proteins regulate the precise scheduling of *Escherichia coli* lysis during infection by bacteriophage λ. Inserted into the host bacterium's inner membrane during infection, holins aggregate to form rafts and then holes within those rafts. We present a two-stage nucleation model of holin action, with the nucleation of condensed holin domains followed by the nucleation of holes within these domains. Late nucleation of holin rafts leads to a weak dependence of lysis timing on host cell size, though both nucleation events contribute equally to timing errors. Our simulations recover the accurate scheduling observed experimentally, and also suggest that phage-λ lysis of *E.coli* is optimized.

10:36AM X34.00014 Physiological role of stochastic calcium signaling in subcellar microdomains , YOHANNES SHIFERAW, California Sate University — Calcium (Ca) plays an important role in regulating various cellular processes. In a variety of cell types, Ca signaling occurs within microdomains where Ca channels deliver localized pulses of Ca which activate a nearby collection of Ca sensitive receptors. The small number of channels in these microdomains ensures that the signaling process is stochastic. The aggregate response of several thousand of these micro-domains yields a whole cell response which dictates the observable cell behavior. Here, we study analytically the statistical properties of a population of these micro-domains in response to a trigger signal. We apply these results to understand the relationship between Ca influx and Ca release in cardiac myocytes. In particular, we explain why the global response is graded with respect to total Ca influx, even though Ca response at the micro-domain level is all-or-none.

10:48AM X34.00015 A Systematic Study of Bilayer Failure on Engineered Surfaces , MORGAN MAGER, NICHOLAS MELOSH, Stanford University — Ever since the invention of black lipid membranes, supported lipid bilayers have been an important tool for studying integral membrane proteins as well as fundamental bilayer behavior. In spite of this, these structures have a relatively short lifetime and little is known about their failure mechanisms. By systematically altering the geometry and surface chemistry of microfabricated pores, we are able to isolate the importance of several distinct failure mechanisms. These include pressure fluctuations, unsupported area, surface energy of the pore wall and surface roughness. We will also demonstrate that, even when not actively controlled, these parameters can inadvertently be altered depending in processing conditions.

Friday, March 9, 2007 8:00AM - 11:00AM –

Session X35 DBP: Focus Session: Nucleic Acid Protein Interaction Colorado Convention Center 405

8:00AM X35.00001 Accuracy of Localization Methods for Individual Fluorescent Probes , HENRIK FLYVBJERG, Biosystems Department and Danish Polymer Centre, Risø National Laboratory, Technical University of Denmark — Recent technological developments have made light microscopy of single molecules possible. The limited number of photons available from a single fluorescent molecule makes image analysis a statistical analysis. Consequently, optimal data analysis is as important to experimental resolution as improved experimental conditions, such as photobleaching rates of fluorescent probes. The simple case of *localization accuracy* provides a pertinent example. In theory, conventional lens-based light microscopy can determine the position of a point-like object with an accuracy that increases infinitely with the number of photons producing it. In practice, a finite signal-to-noise ratio limits localization accuracy and so may the choice of statistical estimator. Some estimators are easier to apply than others, but their relative virtues in regards to accuracy is unclear, or only known numerically for specific cases. We analyze three popular estimators under ideal conditions, find exact analytical results for their accuracy, and clear up a confusion in the literature. Next we test our results for accuracies against ideal real data, and find results that change our view of these estimators for practical use.

8:36AM X35.00002 Phenotypic consequences of promoter-mediated transcriptional noise: Experiment and computational modeling , GABOR BALAZSI, WILLIAM BLAKE, MICHAEL KOHANSKI, KEVIN MURPHY, JAMES COLLINS, Center for BioDynamics and Center for Advanced Biotechnology, Boston University, Boston, MA 02215, USA — A more complete understanding of the causes and effects of gene expression noise is needed to elucidate whether the resulting phenotypes are disadvantageous or confer some adaptive advantage. We introduce mutations within the promoter region of an engineered, repressible *Saccharomyces cerevisiae* GAL1 promoter to show that the level of gene expression noise is affected by the sequence of the TATA box. Through computer simulations, we identify transcription scaffold stability as a critical noise-mediating factor. We demonstrate that TATA box-dependent, increased gene expression noise can be beneficial after an acute change in environmental conditions. First, we illustrate computationally how a stable transcription scaffold can enable increased cell-cell variability at steady state. Second, we experimentally verify our computational prediction that the increased gene expression noise enabled by TATA-containing promoters confers a clear benefit in the face of an acute environmental stress.

8:48AM X35.00003 Role of boundary constrains in DNA looping problem. , ALEXEI TKACHENKO, University of Michigan — We present a theoretical study of the effects of boundary constrains on DNA looping. The developed Effective Hamiltonian description enables one to calculate the looping probability density (so called J-factor), in a much simpler way than by traditional methods. Our approach is applicable to a variety of in-vitro and in-vivo problems, ranging from DNA cyclization, to protein-mediated DNA looping. In particular, it will be demonstrated that the existing controversy between various DNA cyclization experiments can be attributed to the variation in the boundary conditions.

9:00AM X35.00004 Kinetic Accessibility of Buried DNA Sites in Nucleosomes , WOLFRAM MÖBIUS, RICHARD A. NEHER, Arnold Sommerfeld Center for Theoretical Physics (ASC) and Center for Nanoscience (CeNS), LMU Munich, ULRICH GERLAND, Institute for Theoretical Physics, University of Cologne — Motivated by recent experiments on nucleosome accessibility [1,2] we study the transient exposure of protein-binding DNA sites within nucleosomes using a theoretical model for spontaneous partial DNA unwrapping from histones. We focus on the functional dependence of the rates for site exposure and re-burial on the site position, which is pertinent to gene regulation. We find the dependence to be roughly described by a random walker model. Close inspection however reveals a surprising dependence of the re-burial rates on the length of unwrapped DNA. We show that this corresponds to a physical effect of flexibility-assisted barrier crossing, which we characterize within a toy model, the *semiflexible Brownian rotor*.
[1] G. Li, M. Levitus, C. Bustamante, and J. Widom, Nat. Struct. Biol. **12**, 46 (2005)
[2] M. Tomschik, H. Zheng, K. van Holde, J. Zlatanova, and S. Leuba, Proc. Natl. Acad. Sci. U.S.A. **102**, 3278 (2005)
[3] W. Möbius, R.A. Neher, and U. Gerland, Phys. Rev. Lett. **97**, 208102 (2006)

9:12AM X35.00005 Coarse-Grained Modeling of Molecular Machines in AAA+ Family , KENJI YOSHIMOTO, CHARLES L. BROOKS III, Department of Molecular Biology, The Scripps Research Institute — We present a new coarse-grained model of the large protein complexes which belong to AAA+ (ATPase associated with diverse cellular activities) family. The AAA+ proteins are highly efficient molecular machines driven by the ATP (adenosine triphosphate) binding and hydrolysis and are involved in various cellular events. While a number of groups are developing various coarse-grained models for different AAA+ proteins, the molecular details of ATP binding and hydrolysis are often neglected. In this study, we provide a robust approach to coarse-graining both the AAA+ protein and the ATP (or ADP) molecules. By imposing the distance restraints between the phosphates of the ATP and the neighboring C_α of the proteins, which are used to conserve a typical motif of ATP binding pocket, we are able to predict large conformational changes of the AAA+ proteins, such as replicative hexameric helicases. In the case of the hexameric LTag (large tumor antigen), the backbone RMSD between the predicted ATP-bound structure and the X-ray structure is 1.2 $\mathring{A}$, and the RMSD between the predicted ADP-bound structure and the X-ray structure is 1.5 $\mathring{A}$. Using the same approach, we also investigate conformational changes in the hexameric E1 protein, whose X-ray structure was recently solved with ssDNA, and give some insights into the molecular mechanisms of DNA translocation.

9:24AM X35.00006 A Simple Model of Nucleosome Localization , DAVID SCHWAB, ROBIJN BRUINSMA, UCLA — It has recently been shown that nucleosomes localize to preferred locations along DNA. This localization is a result of the sequence dependent bending stiffness of dsDNA, which must be wrapped around a histone protein to form a nucleosome. As a simple model of nucleosome localization, we study a one-dimensional hard-core gas in a random potential. We numerically solve for the density profile and other thermodynamic quantities using as input both randomly generated potential profiles and experimental energy landscapes. We compare with the annealed average, inspired by the Random Energy Model, and find that the quenched and annealed averages differ significantly above the localization temperature, implying sequence induced structural organization long before the system has frozen. Although information about the ground state is preserved at higher temperatures, there exist massive structural reorganizations at fixed temperature when the chemical potential is lowered. This offers another perspective on why different cells, with different chemical potentials, have different gene expression.

9:36AM X35.00007 Dynamics of assembly of proteins along a stretched DNA[1] , RANJITH PADINHATEERI, Department of Physics, University of Illinois at Chicago, IL 60607, JOHN MARKO, Department of Physics and Astronomy, and Department of Biochemisty, Molecular Biology and Cell Biology, Northwestern University, Evanston, IL 60208 — We study the dynamics of filling of a one-dimensional lattice by k-site-long hard particles. We show that a model with adsorption, desorption and diffusion of k-mer particles can mimic in vitro experiments involving assembly of proteins along a stretched DNA. We study the dependence of force on the protein assembly dynamics and final filling. We also show that in a regime when adsorption rate is much larger than desorption rate, and no diffusion, one gets a power-law-like filling dynamics soon after jamming.

[1]This research was supported by NSF Grants No. DMR-02030963 and DMR-0605895

9:48AM X35.00008 Hidden Markov Analysis of Tethered Particle Motion , PHIL NELSON, JOHN BEAUSANG, Univ Penn — Tethered particle experiments use light microscopy to measure the position of a micrometer-sized bead tethered to a microscope slide via a micrometer length polymer, in order to learn about the behavior of the invisible polymer. Currently, this method is being used to measure rate constants of DNA loop formation and breakdown mediated by repressor protein that binds to the DNA. We report a new technique for measuring these rates using a modified hidden Markov analysis that directly incorporates the diffusive motion of the bead, which is an inherent complication of tethered particle motion because it occurs on a time scale between the sampling frequency and the looping time. We compare the looping lifetimes found with our method, which are consistent over a range of sampling frequencies, to the lifetimes obtained via the traditional threshold-crossing analysis, which vary depending on how the raw data are filtered. Our method does not involve filtering, and so is able to detect short-lived looping events and sudden changes in looping behavior.

10:00AM X35.00009 Model for the simultaneous evolution of protein sequences and conformations , LONGHUA HU, ALEXANDER GROSBERG, Department of Physics, University of Minnesota — Protein molecule folds because its sequence is quenched while its conformation dynamically evolves governed by the quenched sequence. Sequence design procedures known in the literature usually operate by computationally annealing the sequence on the background of properly quenched conformation. There are suggestions in the literature to invigorate both the sequence design and the computational folding algorithms by considering the simultaneous evolution of both sequence and conformation, assuming that these two sets of degrees of freedom interact with thermostats of two different temperatures. To examine this procedure, we study the model of random walks on the graph in which each vertex represents the state of a protein, including both sequence and conformation. The graph has bonds of two sorts, some represent change of conformation (physical motion), while others represent change of sequence ('mutation'). We show that when sequence and conformation dynamics are governed by different temperatures, there cannot be any equilibrium, and we analyze the stationary currents in the system which are realized by never stopping cascade of sequence rearrangements followed by conformational moves followed by sequence moves and so on, ad infinum.

10:12AM X35.00010 Unwinding of double-stranded DNA and branch migration of Holliday junctions by hexameric motor proteins , NOAH RIBECK, Physics Department, University of California Santa Barbara, OMAR A. SALEH, Materials Department and BMSE Program, University of California Santa Barbara — Ring-shaped hexameric helicases are critical components of the DNA replication machinery in eukaryotes and bacteria. It has been shown that in vitro, certain hexameric helicases such as Mcm4,6,7 from eukaryotes, and DnaB from E. coli can translocate while encircling either single-stranded DNA (while opening a DNA fork in advance of the protein) or while encircling double-stranded DNA. Further, the latter translocation mode can drive branch migration of Holliday junctions. Using magnetic tweezers, we have performed single-molecule measurements of the activity of DnaB and the Mcm complex during both fork-opening and branch migration. We will report on progress of measurements of velocity of these motors in each mode, and relate the results to theoretical models of active and passive unwinding.

10:24AM X35.00011 How cells decide between life and death: predictions from stochastic simulation , SUBHADIP RAYCHAUDHURI, ERIC WILLGOHS, THUC-NGHI NGUYEN, University of California Davis — Recent experiments show that cells experiencing oxidative stress conditions trigger both apoptotic (programmed cell death) and survival pathways. Cross-talk between those two complex signal transduction networks, in turn, crucially decides between life and death of a cell. We have developed a Monte Carlo stochastic simulation method that can predict the outcomes of cellular decision-making (between life and death) under oxidative stress in a probabilistic manner. Even under identical cellular conditions our stochastic simulations can lead to differential cellular response as observed in recent in vitro experiments. Interestingly, our numerical experiments indicate that spatial heterogeneity and localization of signaling molecules, in addition to the structure of the signaling networks, are crucial to such a stochastic outcome of cell signaling. By performing sensitivity analyses under a variety of physiological conditions we are able to identify some of the critical regulators of apoptotic cell death signaling under oxidative stress.

10:36AM X35.00012 Evolution of codes, crosstalk, and sequence niches in biomolecular signaling , CHRISTOPHER MYERS, Cornell University — Signaling and regulation in cellular networks is mediated through biomolecular interactions, which can be somewhat promiscuous, involving the molecular recognition of broad sets of binding targets. This leads to some basic questions concerning crosstalk among similar sets of biomolecules: does it occur, to what extent can it be avoided, how can phenotypic errors due to crosstalk be minimized, and when might crosstalk be advantageous? Beyond biology, questions of this sort have connections to phase transitions in constraint satisfaction problems, and to the theory of message coding in noisy channels. Expanding upon my previous work exploring the nature of the satisfiability (SAT-UNSAT) transition in a simple model of protein-protein interactions, this talk will investigate the role of sequence evolution in shaping high-dimensional sequence niches and biomolecular codes.

10:48AM X35.00013 Transcriptional Interference: A quantitative approach to in vivo dynamics of RNAP on DNA. , KIM SNEPPEN, Niels Bohr Institute — We present a mathematical model for transcriptional interference by RNA polymerase traffic in Escherichia coli. The model deals with the interference between the two promoters pA and pS. The RNAPs are injected onto the DNA through binding and formation of sitting duck complexes at the respective promoters, followed by subsequent formation of elongating complexes. Finally we discuss a combination of modeling and in vivo-experiments can be used to infer the interference-recruitment game that govern the core of the genetic switch in the temperate bacteriophages 186.
K. Sneppen, I.B. Dodd, K.E. Shearwin, A.C. Palmer, R.A. Schubert, B.P. Callen, and J.B. Egan. J. Mol. Biol. 346:399 (2005)

Friday, March 9, 2007 11:15AM - 2:15PM –

Session Y2 DBP: Collective Motions of Living and Nonliving Self-Propelled Particles Colorado Convention Center Four Seasons 4

11:15AM Y2.00001 Swarming by Nature and by Design[1] , ANDREA BERTOZZI, UCLA — The cohesive movement of a biological population is a commonly observed natural phenomenon. With the advent of platforms of unmanned vehicles, this occurrence is attracting renewed interest from the engineering community. This talk will review recent research results on modeling and analysis of biological swarms with some connection to the design ideas for efficient algorithms to control groups of autonomous agents. For biological models we consider two kinds of systems: driven particle systems based on force laws and continuum models based on kinematic and dynamic rules. Both models involve long-rage social attraction and short range dispersal and yield patterns involving clumping, mill vortices, and surface-tension-like effects.

[1]This work is supported by the Army Research Office and the Office of Naval Research.

11:51AM Y2.00002 Direct and Indirect Mechanisms for Collective Behavior in the Spatial Dynamics of Plankton , DANIEL GRUNBAUM, School of Oceanography, University of Washington — Plankton are the dark matter of life in the sea. Though they are poorly understood and usually unseen, plankton dominate the biological dynamics that ultimately determine characteristics important to humans ranging from sustainable fish harvests to rates of carbon sequestration. Through a variety of social, sensory and biophysical mechanisms, plankton display collective behaviors that profoundly alter ecological systems. These collective behaviors include formation of large, coherent social groups (e.g. swarms and schools); alteration of water's mechanical properties (e.g. viscosity) and motion (e.g. bioconvection); and induction of self-organized spatial heterogeneity. In this talk, I will describe recent individual-level observations of collective plankton behaviors. I will develop mathematical descriptions that link some of these behaviors to spatio-temporal patterns in plankton populations. Finally, I will outline some important unsolved problems in plankton ecology that can be addressed using analytical and computational approaches.

12:27PM Y2.00003 Predicting the growth of fractal particle agglomeration networks with graph theoretical methods.[1] , ALFRED HUBLER, University of Illinois at Urbana-Champaign — We study an electromechanical system [J. Jun, A. Hubler, *PNAS* **102**, 536 (2005); J. Jun, Ph.D. thesis, UIUC (2004)], where conducting particles self-organize into dendritic patterns under the influence of an electric field for the purpose of collecting and transporting charge. The system forms stable open-loop networks with many reproducible statistical quantities, such as the number of termini and the number of branch points, but the final topology of the network is sensitive to the initial conditions of the particles. Small differences in the initial configuration may lead to very different stationary states. We present robust and reliable ensemble prediction algorithms for the growth of such fractal charge transportation networks. These predictors may lead to the discovery of common properties and serve a prototype to predict fractal growth in other areas, including neural systems; blood vessel systems, river networks, and dielectric break through.

[1]This work is supported by NSF grant DMS 03-25939 ITR.

1:03PM Y2.00004 Swarming Behavior of Particle-Like Waves in Excitable Media , KENNETH SHOWALTER, West Virginia University — Unstable waves in the photosensitive Belousov-Zhabotinsky reaction are stabilized by global feedback, and the motion of these waves is controlled by imposing excitability gradients that are regulated by a secondary feedback loop. We describe studies of these particle-like waves interacting with one another via realistic excitability potentials. Simulations and experiments with increasing numbers of mutually coupled waves have demonstrated very complex swarming behavior. Measures for characterizing the behavior, such as the average velocity and group size, will be discussed. We will also describe experiments and simulations of stabilized waves navigating excitability landscapes. Of particular interest is the interaction of a swarm with various obstacles as it navigates through the medium. [E. Mihaliuk, T. Sakurai, F. Chirila, and K. Showalter, Phys. Rev. E 65, 65602 (2002); T. Sakurai, E. Mihaliuk, F. Chirila, and K. Showalter, Science 296, 2009-2012 (2002); V. S. Zykov and K. Showalter, Phys. Rev. Lett. 94, 068302 (2005).]

1:39PM Y2.00005 Chemically Powered Nanomotors , RAYMOND KAPRAL[1], University of Toronto — Molecular motors play important roles in transport in biological systems. These molecular machines are powered by chemical energy and operate in the regime of low Reynolds number hydrodynamics. Recently a class of simple inorganic molecular motors has been constructed and studied experimentally [1,2]. These motors are bimetallic rods, one end of which is chemically active. The talk will describe simple mesoscopic models for the motion of such nanomotors. The motor consists of two linked spheres, one of which catalyzes the conversion between two chemical species. The chemical species interact differently with the the two spheres in the dimer. The nano-dimer motor is solvated by a molecules treated at a mesoscopic level whose evolution is governed by multi-particle collision dynamics. The dynamics conserves mass, momentum and energy so that coupling between the nanomotor and the hydrodynamic modes of the solvent is treated correctly. The simulations allow one to explore the mechanisms of the chemically powered motion and the effects of fluctuations on the motor dynamics.
[1] W. F. Paxton, et al., "Catalytic Nanomotors: Autonomous Movement of Striped Nanorods," J. Am. Chem. Soc. (JACS), 126 (41), 13424 (2004).
[2] S. Fournier-Bidoz, et al. "Synthetic Self-Propelled Nanorotors," Chem. Commun., (4), 441 (2005).

[1]work in collaboration with Gunnar Rueckner

Friday, March 9, 2007 11:15AM - 2:15PM –
Session Y7 DBP: Nonequilibrium Thermodynamics Colorado Convention Center Korbel 4A-4B

11:15AM Y7.00001 Exactly solvable models illustrating nonequilibrium work relations , CHRISTOPHER JARZYNSKI, University of Maryland — Nonequilibrium work relations establish a connection between the work performed when driving a system away from thermal equilibrium, and the free energy difference between two equilibrium states of the system. I will discuss several exactly solvable model systems that illustrate these relations. While these examples represent idealized systems, and can be analyzed at the level of undergraduate mechanics, they nevertheless provide insight into subtle and sometimes counter-intuitive aspects of nonequilibrium work relations.

11:51AM Y7.00002 , ATTILA SZABO, National Institutes of Health (NIH) — No abstract available.

12:27PM Y7.00003 , GAVIN CROOKS, LBNL — No abstract available.

1:03PM Y7.00004 Stochastic Thermodynamics: Theory and Experiments , UDO SEIFERT, Universitaet Stuttgart — Stochastic thermodynamics provides a framework for describing small systems embedded in a heat bath and externally driven to non-equilibrium. Examples are colloidal particles in time-dependent optical traps, single biomolecules manipulated by optical tweezers or AFM tips, and motor proteins driven by ATP excess. A first-law like energy balance allows to identify applied work and dissipated heat on the level of a single stochastic trajectory. Total entropy production includes not only this heat but also changes in entropy associated with the state of the small system. Within such a framework, exact results like an integral fluctuation theorem for total entropy production valid for any initial state, any time-dependent driving and any length of trajectories can be proven [1]. These results hold both for mechanically driven systems modelled by over-damped Langevin equations and chemically driven (biochemical) reaction networks [2]. These theoretical predictions have been illustrated and tested with experiments on a colloidal particle pushed by a periodically modulated laser towards a surface [3]. Key elements of this framework like a stochastic entropy can also be applied to athermal systems as experiments on an optically driven defect center in diamond show [4,5]. For mechanically driven non-equilibrium steady states, the violation of the fluctuation-dissipation theorem can be quantified as an additive term directly related to broken detailed balance (rather than a multiplicative effective temperature) [6]. Integrated over time, a generalized Einstein relation appears. If velocities are measured with respect to the local mean velocity, the usual form of the FDT holds even in non-equilibrium. [1] U. Seifert, Phys. Rev. Lett. 95: 040602/1-4, 2005. [2] T. Schmiedl and U. Seifert, cond-mat/0605080. [3] V. Blickle, T. Speck, L. Helden, U. Seifert, and C. Bechinger, Phys. Rev. Lett. 96: 070603/1-4, 2006. [4] S. Schuler, T. Speck, C. Tietz, J. Wrachtrup, and U. Seifert, Phys. Rev. Lett. 94: 180602/1-4, 2005. [5] C. Tietz, S. Schuler, T. Speck, U. Seifert, and J. Wrachtrup, Phys. Rev. Lett. 97: 050602/1-4, 2006. [6] T. Speck and U. Seifert, Europhys. Lett. 74: 391-396, 2006.

1:39PM Y7.00005 , KAY GOTTSCHALK, Ludwig Maximillian University Munich — No abstract available.

Friday, March 9, 2007 11:15AM - 2:15PM –
Session Y34 DBP: Properties of Biological Membranes Colorado Convention Center 404

11:15AM Y34.00001 Bending Elasticity of Bio-Membranes Studied by Neutron Spin-Echo , ZHENG YI, DOBRIN BOSSEV, Indiana University — We have used neutron spin echo (NSE) spectroscopy to study the effects of the unsaturated double bond and the hydrocarbon chain length on the bending elasticity of lipid membranes. The bending elasticity κ of bilayer vesicles made of 1,2-Dioleoyl-*sn*-Glycero-3-phosphocholine(18:1 PC), has been measured in the fluid (L_α) phase in different temperatures. When lipid bilayers made of DOPC are in fluid phase, the temperature effect on bending elasticity is minimal. The bending elasticities of 14:1 PC and 16:1 PC were measured in fluid phase in 30 °C. We found that the lipid bilayers with longer chains have higher bending elasticities. Our data confirms that the stiffening of lipid bilayers increases with increasing chain length of the lipid molecules.

11:27AM Y34.00002 Using Neutron Spectroscopy to Study Collective Dynamics of Biological and Model Membrane Systems , MAIKEL RHEINSTADTER, University of Missouri-Columbia — Only recently, it has become possible to study collective dynamics of planar lipid bilayers using neutron spectroscopy techniques. By combining different neutron scattering techniques, namely three-axis, backscattering and spin-echo spectroscopy, we present measurements of short and long wavelength collective fluctuations in biomimetic and biological membranes in a large range in momentum and energy transfer, covering time scales from about 0.1ps to almost 1μs and length scales from 3Å to about 0.1μm [1-4]. The measurements offer a large window of length and time scales to test and refine theoretical models of dynamics of biomimetic and biological membranes. The objective of this project is to establish dynamics-function relationships in artificial and biological membranes to relate in particular the collective dynamics, i.e., phonons, to key functions of the membranes, as, e.g., transport processes within and across the bilayers. M.C. Rheinstädter, C. Ollinger, G. Fragneto, F. Demmel, T. Salditt, *Phys. Rev. Lett.* **93**, 108107 (2004).[2] Maikel C. Rheinstädter, Tilo Seydel, Franz Demmel, Tim Salditt, *Phys. Rev. E* **71**, 061908 (2005).[3] Maikel C. Rheinstädter, Wolfgang Häußler, Tim Salditt, *Phys. Rev. Lett.* **97**, 048103 (2006).[4] Maikel C. Rheinstädter, Tilo Seydel, Tim Salditt, submitted to PRE, cond-mat/0607514.

11:39AM Y34.00003 Damping of the thermal undulations of bio-membranes , DOBRIN BOSSEV, ZHENG YI, Indiana University — In this work we discuss the damping mechanisms of the thermal undulation of lipid membranes. In the past, we have attempted to determine the bending elasticity of bio membranes by neutron spin-echo spectroscopy (NSE) as a function of the temperature, molecular structure of the phospholipids, ionic strength of the surrounding aqueous environment, and presence of cholesterol. NSE is ideal for studies of the thermal undulations of the biomembranes because it probes the short correlation times (0.01–100 ns) and length scales (10–100 Å) that are characteristic for the biomembrane undulations. The bending modulus of elasticity is obtained through analysis of the intermediate scattering function I(Q,t) using Zilman-Granek theory, which considers the solution viscosity as the only damping mechanism for the thermal undulations. As a result the absolute k values are about an order of magnitude greater than those measured by other methods and predicted by simulations. Here we report measurements in water/glycerol mixtures in attempt to modify the bulk viscosity and to clarify the contribution of the different energy dissipation mechanisms.

11:51AM Y34.00004 Interaction Forces and Mechanics of Cellular Membranes using Novel Atomic Force Microscopy Probes , BENJAMIN ALMQUIST, NICHOLAS MELOSH, Dept. of Materials Science, Stanford University — In order to probe the nature of nanostructure-membrane interfaces, we have developed an AFM probe platform that can quantitatively measure the interaction forces between specifically functionalized layers and the cell membrane. This platform consists of a cantilever with a post-style tip that ends in a hetero-metallic layer. This metallic layer can be selectively functionalized with various molecules of interest. Once functionalized, the layer is inserted into the hydrophobic region of the cell membrane. By varying the molecular species and examining the associated penetration and extraction forces, we will be able to correlate the molecule-membrane interaction forces to the molecular structure. This, in turn, will allow us to determine the role of molecular size, hydrophobicity, and disorder. In addition, the effects of functional layer thickness and post geometry will be examined.

12:03PM Y34.00005 Measuring Surface Potential of Zwitterionic Lipid Bilayers with Atomic Force Microscope , YI YANG, KATHRYN MAYER, JASON HAFNER, Rice University — Electrostatic potential was measured near supported zwitterionic lipid bilayer membrane surfaces with atomic force microscope. In our recent work, two methods were developed to measure the surface charge density of the membrane surface, Fluid electric force microscopy (FEFM) which creates a two- dimensional map of a surface charge density with a corresponding topographic map simultaneously and quantitative measurement method which based on tip-sample force curve analysis.Both FEFM and tip-sample force curve analysis showed that the surface of a DOPC (dioleoylphosphatidylcholine) lipid bilayer carries a negative electrostatic potential.This is an interesting and surprising result, for the head group of DOPC is carrying zero net charge over a broad range of pH where both the choline and phosphate groups are ionized.Two sources are proposed to explain the origin of this negative charge.The bilayers could carry a net charge density due to the counterions from the electrolyte binding to the lipid head groups.Alternatively, the dipole density in the DOPC lipid head group layer could cause an effective surface potential outside the membrane region.To study the source of this negative potential, Charge densities of supported DOPC bilayers under different ion concentrations were measured and compared with both of these two charge mechanisms.

12:15PM Y34.00006 Molecular Organization and Dynamics of Cholesterol Nanodomains in Fluid Lipid Bilayers , KWAN CHENG, BRIAN CANNON, QING ZHU, MARK VAUGHN, JUYANG HUANG, Texas Tech University — The molecular organization and dynamics of cholesterol nanodomains in lipid bilayers containing phospholipid (PL) and cholesterol (CHOL) were examined using FTIR, time-resolved fluorescence and surface-acting cholesterol oxidase enzyme (COD). In binary PL/CHOL system, abrupt changes in the PL C=O frequency, fluorescence lifetime and rotation rate of chain labeled PL, and the rate of cholesterol oxidation by COD were observed at $\sim$ 40 mole% of CHO. For ternary PL_1/PL_2/CHOL system composed of two dissimilar PL's of different chain lengths or headgroup sizes, abrupt changes at PL_1/PL_2 $\sim$ 2 were found. The above critical lipid compositions agree favorably with the theoretical compositions predicted by the lipid superlattice model, suggesting that PL of different structures and CHOL can form regularly distributed, or superlattice-like, nanodomains at the polar headgroup and the acyl chain levels, respectively. The feasibility of the coexistence of headgroup and acyl chain nanodomains was demonstrated by a spacing filling model and MD simulations. We speculate that lipid superlattice domains may play an important role in the regulation of protein/lipid interaction in cells.

12:27PM Y34.00007 Temperature and Composition Dependent Phase Behavior in Two "Raft-Like" Ternary Membrane Mixtures: DPPC/DLPC/Cholesterol and DPPC/DOPC/Cholesterol , JEFFREY BUBOLTZ, Colgate University, GEOFFREY SIEGEL, MATTHEW SCHUTZER, KRYSTLE WILLIAMS, CHARLES BWALYA, SANTIAGO REYES — For the last several years, so-called "lipid-raft" membrane domains have been the subject of intense research activity. As part of this effort, we have been carrying out experiments based on Probe-Partitioning FRET, a technique specifically designed to map out both phase boundaries and tie lines in artificial membrane mixtures. Specifically, we have studied two cholesterol-rich ternary mixtures, DPPC/DLPC/Cholesterol and DPPC/DOPC/Cholesterol, that mimic lipid-raft phase behavior. By studying more than 3000 independently prepared samples, we have gained insight into the general features (i.e., both temperature and composition dependence) that characterize the phase behavior in these two ternary systems. As we work toward extending our studies to other raft-like ternary mixtures, we are also adapting a different, purely thermodynamic technique (Equilibrium Surface Pressure Analysis) for the purpose of corroborating tie line patterns inferred from PP-FRET.

12:39PM Y34.00008 On the interactions between neutral lipid bilayers , OSCAR CALVO, MARIAN MANCIU[1], University of Texas at El Paso, ELI RUCKENSTEIN[2], State University of New York at Buffalo — The stability of many colloids is thought as a balance between attractive van der Waals interactions and double layer repulsive forces. However, the latter does not exist for neutral lipid bilayers, for which the repulsive forces are supposed to be provided by a combination between hydration forces and Helfrich forces, due to the suppression of the thermal undulation, when two bilayers approach each other. Hydration forces are related to the structuring of water near surfaces, which is likely to be decreased by the thermal undulations. Helfrich forces have a longer range than the attractive forces and cannot lead by themselves to a stable minimum. We will show that the polarization model for the hydration forces combined with a statistical treatment for undulating bilayers might explain the interactions between neutral lipid bilayers.

[1]Physics Department
[2]Chemical & Biological Engineering Department

12:51PM Y34.00009 Effect of dipolar moments in domain sizes of lipid bilayers and monolayers[1] , ALEX TRAVESSET, Iowa State University and Ames Lab — Lipid domains are found in systems such as multi-component bilayer membranes and single component monolayers at the air water interface. It was shown by McConnell and collaborators that in monolayers the size of the domains results from balancing the line tension, which favors the formation of a large singular single circular domain, against the electrostatic cost of assembling the dipolar moments of the lipids. In this talk, I will generalize this argument to include effects of ionic strenght, dielectric discontinuities (or image charges) and the polarizability of the dipoles and extend the results to bilayer membranes. I will finish with a discussion on the experimental implications of the calculations.

[1]This work is supported by NDF grant DMR-0426597.

1:03PM Y34.00010 Non-equilibrium dynamics of heterogeneous lipid membranes[1] , MIKKO HAATAJA, JUN FAN, MARIA SAMMALKORPI, Princeton University — Plasma membranes surrounding mammalian cells play a key role in regulating the exchange of information and matter between the cells and their surroundings. The unique properties of these membranes arise from the interactions between amphiphilic lipid molecules, sterols (incl. cholesterol), and proteins. It has been proposed that the plasma membrane displays dynamic heterogeneities (lipid rafts) in the local lipid composition. While such rafts have not yet been observed directly in vivo, there is ample indirect evidence that supports their existence. From a fundamental biophysical perspective, processes which may control the aggregation and stability of these rafts are poorly understood at the moment. Here, we address this issue by introducing a continuum model for the local lipid composition which incorporates non-equilibrium aspects of lipid recycling to and from the membrane. We show that recycling leads to coherent structures with a characteristic size which depends on both the recycling rate and the tendency of the components to phase separate in the absence of recycling. We argue that incorporating non-equilibrium effects is crucial in understanding the biophysical properties of the plasma membrane.

[1]This work has been partially supported by an NSF-DMR Grant No. 0449184.

1:15PM Y34.00011 Mechanisms of protein transduction domains: HIV TAT and ANTP penetratin as prototypical cases , ABHIJIT MISHRA, University of Illinois, Department of Materials Science and Engineering, NATHAN SCHMIDT, University of Illinois, Department of Physics, VERNITA GORDON, University of Illinois, Department of Materials Science and Engineering, GERARD WONG, University of Illinois, Department of Materials Science and Engineering, Department of Physics — Biologically active molecules such as proteins and oligonucleotides can be transduced across cell membranes with high efficiency when covalently linked to a Protein Transduction Domain (PTD), such as the TAT domain in the HIV virus and ANTP from the fruitfly. All PTDs have a high content of basic amino acids resulting in a net positive charge. Electrostatic interactions between cationic PTDs and the negatively charged phospholipids that constitute the plasma membrane are likely to be responsible for peptide uptake, but no detailed structural studies exist. We examined membrane structures induced by the cationic TAT domain and those induced by other cationic polypeptides as a function of membrane composition using synchrotron x-ray scattering. We find that both the TAT PTD and ANTP generate negative Gaussian curvature, which is necessary for pore formation, and produce a bicontinuous Pn3m double diamond cubic phase. A general mechanism is proposed.

1:27PM Y34.00012 Molecular Insights into Phospholipid – NSAID Interactions , MOHAN BABU BOGGARA, RAMANAN KRISHNAMOORTI, Dept of Chemical and Biomolecular Engg., Univ of Houston — Non steroidal anti inflammatory drugs (NSAIDs) e.g. Aspirin and Ibuprofen, with chronic usage cause gastro intestinal (GI) toxicity. It has been shown experimentally that NSAIDs pre-associated with phospholipids reduce the GI toxicity and also increase the therapeutic activity of these drugs compared to the unmodified ones. Using all atomistic simulations and two different methodologies, we studied the partitioning behavior of two model NSAIDs (Aspirin and Ibuprofen) as a function of pH and drug loading. The results from two methodologies are consistent in describing the equilibrium drug distribution in the bilayers. Additionally, the heterogeneity in density and polarity of the bilayer in the normal direction along with the fact that NSAIDs are amphiphilic (all of them have a carboxylic acid group and a non-polar part consisting of aromatic moieties), indicate that the diffusion mechanism in the bilayer is far different compared to the same in a bulk medium. This study summarizes the various effects of NSAIDs and their behavior inside the lipid bilayer both as a function of pH and drug concentration.

1:39PM Y34.00013 Non-equilibrium Lipid Distributions in a Simulated Three-Species Biomembrane , ANDREW P. PARADIS, SUSAN R. MCKAY, SAMUEL T. HESS, University of Maine — Cellular biomembranes are in continual states of flux, yet theoretical models of biomembranes have primarily focused on equilibrium behavior, where constituent species interact but are not driven. This study examines the complex phase behavior of a three-species biomembrane driven out of equilibrium through frequent, simulated endo- and exo-cytosis events. The three species, representing unsaturated lipids, saturated lipids, and cholesterol, move and interact on a two-dimensional triangular lattice, simulated using a Metropolis algorithm. Two types of phase behavior are specifically investigated and discussed: cholesterol super-lattice structures and phase separation of saturated and unsaturated lipids, both as functions of cholesterol mole fraction and temperature.

1:51PM Y34.00014 Simulations of the Pore Structures for a M2GlyR Derived Channel Forming Peptide in Different Membrane Environments , A. AL-RAWI, A. HERRERA, J. TOMICH, Kansas State Univ., T. RAHMAN, Univ. of Central Florida — As part of an effort to develop a peptide-based compound suitable for clinical use as a channel replacement therapeutic for treating channelopathies such as cystic fibrosis, we present a reductionist model that appears to grasp the characteristics of ion channeling peptides. In particular we present the observed changes in the functional characteristics of NK_4-M2GlyR p22 (KKKKPARVGLGITTVLTMTTQS), a M2 GlyR derived channel forming peptide. Starting with a structure determined by multidimensional NMR (800 MHz) in SDS, a potential from CHARMM force-field was used to relax the structure of NK_4-M2GlyR p22. Following the relaxation, numerous pore structures were generated for the symmetric five-helix assembly with geometries varying from cylindrical to conical. As it is difficult *a priori* to assign accurately the orientation of the hydrophilic portion of M2GlyR derived amphipath towards the inside of the pore, we tilted and rotated the helical structure by five different angles about the backbone axis before forming the pore. Energy minimization of the channel was performed in vacuum, in phosphotidylcholine (POPC) membrane, and 60% POPC 30% phosphotidylethanolamine (POPE) in order to determine the effect of the environment surrounding on the structure on its energy minimization. We will present the various pore assemblies, in the different membrane environments, used to predict the most probably membrane bound structure.

2:03PM Y34.00015 The Effects of Polyunsaturated Lipid Components on bilayer Structure , Y. PRAMUDYA, A. KISS, LAM T. NGUYEN, J. YUAN, LINDA S. HIRST, Center for Material Research and Technology, Florida State University — Polyunsaturated fatty acids (PUFAs), such as DHA (Docosahexanoic Acid) and AA (Alphalinoleic Acid) have been the focus of much research attention in recent years, due to their apparent health benefits and effects on cell physiology. They are found in a variety of biological membranes and have been implicated with lipid raft formation and possible function, particularly in the retinal rod cells and the central nervous system. In this work lipid bilayer structure has been investigated in lipid mixtures, incorporating polyunsaturated fatty acid moieties. The structural effects of increasing concentrations of both symmetric and asymmetric PUFA materials on the bilayer structure are investigated via synchrotron x-ray diffraction on solution samples. We observe bilayer spacings to increase with the percentage of unsaturated fatty acid lipid in the membrane, whilst the degree of ordering significantly decreases. In fact above 20% of fatty acid, well defined bilayers are no longer observed to form. Evidence of phase separation can be clearly seen from these x-ray results and in combination with AFM measurements.

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11:15AM Y35.00001 Designability as a Selection Force? An Analysis of the Yeast Cell Cycle Dynamics. , YIGAL NOCHOMOVITZ, SURYA GANGULI, HAO LI, UCSF — The concept of designability may play a role in the evolution of biological phenotypes. We define "designability" generally as the number of genotypes that encode a particular phenotype. For networks, the designability of a dynamical phenotype is the number of topologies that encode a particular ordering of dynamical states. By analyzing ensembles of simplified models of topologies and dynamics (Nochomovitz, Y.D. & Li, H. PNAS 103, 2006.) we have begun to explore the validity of the designability hypothesis at an abstract level. We have discovered from these exploratory studies that certain dynamical signals are highly designable, indicating that some dynamical signals can be realized by many different topological connections. To test the designability hypothesis on a real biological system, we analyze the dynamics of the budding yeast cell cycle. We compute the designability of the yeast cell cycle phenotype and the designabilities of $\sim$ 1000 weakly perturbed variants of the yeast cell cycle phenotype. A comparison of the designability of the true yeast cell cycle phenotype with the designabilities of the pool of perturbed phenotypes reveals that the designability of the budding yeast cell cycle dynamics is near-optimal. This finding provides some evidence for the hypothesis that designability, as an "entropic" force, may couple with the traditional fitness landscape to influence the evolution of biological phenotypes.

11:27AM Y35.00002 Fine tuning by miRNAs in development , PETER MCHALE, EREL LEVINE, HERBERT LEVINE, UCSD — The unique role played by microRNA in a developing embryo is a topic of much current research interest. One possibility is that microRNA diffuse within a developing tissue, acting as communicators between different cells. Here we pursue this possibility in two different contexts. The first case occurs when the transcription profiles of the microRNA and its target are spatially anticorrelated, as for example is the case in the iab4-Ubx system in fly. Conversely, in the second context the two transcription profiles are correlated in space, as may be the case for the mir10-Hoxb4 system in mouse. In each context we identify a major function for a mobile miRNA. In the first, miRNA serve to induce an all-or-nothing response of the mRNA profile to its morphogen by generating a sharp boundary between domains of high and (ultimately) low target expression. In the second, miRNA amplify polarity in the target expression pattern by removing residual mRNAs. Importantly, our model predicts that these two functions require very different type of diffusion. While our results are highly quantitative, we propose ways of realizing them in experiments, taking into account limitations of standard experimental techniques.

11:39AM Y35.00003 Modeling the dynamics of the nucleosome at various levels.[1] , ALEXEY ONUFRIEV, ANDREW FENLEY, JORY ZMUDA-RUSCIO, DAVID ADAMS, Virginia Tech — The primary level of DNA compaction in eukaryotic organisms is the nucleosome, yet details of its dynamics are not fully understood. While the whole nucleosome must be highly stable, protective of its genetic material, at the same time its tightly wrapped DNA should be highly accessible, easily revealing its information content. A combination of atom-level classical molecular dynamics and a course-grained continuum description provide insights into the functioning of the system. In particular, the nucleosomal DNA appears to be considerably more flexible than what can be expected based on its canonical persistence length. A coarse-grained electrostatic model of the nucleosome explains how its stability can be modulated with small environmental changes as well as post-translational modifications. Implications for the nucleosome assembly process in *vivo* are discussed.

[1]This work was supported by NIH grant GM076121

11:51AM Y35.00004 How frog embryos replicate their DNA reliably , JOHN BECHHOEFER, BRANDON MARSHALL, Dept. of Physics, Simon Fraser University — Frog embryos contain three billion base pairs of DNA. In early embryos (cycles 2-12), DNA replication is extremely rapid, about 20 min., and the entire cell cycle lasts only 25 min., meaning that mitosis (cell division) takes place in about 5 min. In this stripped-down cell cycle, there are no efficient checkpoints to prevent the cell from dividing before its DNA has finished replication - a disastrous scenario. Even worse, the many origins of replication are laid down stochastically and are also initiated stochastically throughout the replication process. Despite the very tight time constraints and despite the randomness introduced by origin stochasticity, replication is extremely reliable, with cell division failing no more than once in 10,000 tries. We discuss a recent model of DNA replication that is drawn from condensed-matter theories of 1d nucleation and growth. Using our model, we discuss different strategies of replication: should one initiate all origins as early as possible, or is it better to hold back and initiate some later on? Using concepts from extreme-value statistics, we derive the distribution of replication times given a particular scenario for the initiation of origins. We show that the experimentally observed initiation strategy for frog embryos meets the reliability constraint and is close to the one that requires the fewest resources of a cell.

12:03PM Y35.00005 Modeling the Forced Extension of Nicked DNA , ALEXANDER BALAEFF, STEPHEN CRAIG, DAVID BERATAN, Department of Chemistry, Duke University — The design and study of DNA-based nanodevices has been a topic of considerable interest in the last decade. While the applications of classical continuous DNA structures have been thoroughly studied, nicked DNA structures, i.e., ones that contains breaks ("nicks") in one or both DNA backbone chains, have received much less attention. Recently, Kersey et al. (JACS, 2004) reported the force spectroscopy of long DNA chains with periodic nicks, self-assembled from short DNA oligomers. We attempt to model the experimental force-extension profiles in a series of steered molecular dynamics simulations. The simulated all-atom model of a basic unit of the long self-assembled chain, a 16bp-long DNA segment with a nick in the middle of one strand, is extended by applying either a constant force or a moving harmonic potential to the DNA ends. The computed force-extension profiles are compared to those for a non-nicked DNA; the dynamics of structural changes in the nicked DNA during the forced extension is discussed. A theoretical framework is established to link the extension and rupture in the simulated basic unit to the corresponding events in the long self-assembled chain.

12:15PM Y35.00006 Single-Molecule Studies of the Temperature Dependence of Viral DNA Packaging Motors , MICHAEL WHITE, DORIAN RAYMER, PETER RICKGAUER, DEREK FULLER, University of California, San Diego, SHELLEY GRIMES, PAUL JARDINE, DWIGHT ANDERSON, University of Minnesota, Minneapolis, DOUG SMITH, University of California, San Diego — A key step in the assembly of many viruses is the packaging of dsDNA into a preformed capsid by the action of a portal molecular motor complex. We have developed methods for directly measuring viral DNA translocation at the single molecule level using optical tweezers and applied these methods to study bacteriophages Φ29, lambda, and T4. Our previous measurements with Φ29 were performed at room temperature. Here we report that the rate of DNA translocation is strongly temperature dependent. Preliminary measurements indicate that the motor velocity increases $\sim$2-fold, to $\sim$250-300 bp/s when the temperature is increased from $\sim$20 to 30 degrees C. As the viral packaging motors are enzymes that catalyze ATP hydrolysis, such a trend with increasing temperature is to be expected, at least up to the point where the motor complex is thermally dissociated or denatured. However, the detailed form of the temperature dependence is difficult to quantify using standard bulk assay methods. We have installed a heating/cooling system in our optical tweezers instrument that allows us to precisely control the temperature in our sample chamber. This system allows us to systematically study the temperature dependence of the DNA translocation rate.

12:27PM Y35.00007 Identifying Dyads and their conservation in Drosphila. , DEBASIS DAN, Indiana University, Bloomington — Core promoter regions in Drosophila are enriched with binding sites like TATA, Inr, DPE, MTE, etc. They have very strict spacing between each other in promoters where they occur together. For example, in Drosophila melanogaster TATA-Inr has a spacing of 25-30 bp. Our aim in this work is to identify all such pair of motifs having strict positional constraint in the core promoters of all Drosophila species. We discover how these motifs and the spacing between them evolve within Drosophila species. For this we analyze 700 bp upstream and 300 bp downstream of TSS in D. melanogaster and the corresponding orthologous region in other Drosophila species. For each species, this 1000 bp region is searched for statistically over-represented compound words of the form W1NLW2, where L is the spacing between words W1 and W2. These compound words are systematically clustered for further analysis.

12:39PM Y35.00008 Relating Promoter Sequences to the Proteins that Bind to Them: A Comparison Study. , KIMBERLY GLASS, University of Maryland/National Institute of Health — Chromatin Immunoprecipitation (ChIP-on-ChIP) microarray data reveals that the proteins H3K9dimethyl and RNA-Polymerase II are exclusive regarding their binding to the promoter region of genes. When comparing the base pair sequences of the promoters that bind to Pol2 versus H3K9, striking differences appear. The mononucleotides have fundamentally different behaviors in each group. In addition, motifs that cluster before the transcriptional start site also generally have a strong enrichment in one group compared to the other. Using this knowledge a model can be developed that allows one to calculate a probability that a promoter will bind to either H3K9 or Pol2 based on its base pair sequence.

12:51PM Y35.00009 Studying Codon Usage: From sequence to function[1] , TERRY HWA, STEFAN KLUMPP, Center for Theoretical Biological Physics, UCSD, JIAJIA DONG, Dept. of Physics, Virginia Tech — Protein coding sequences exhibit strong variances in the use of codons. Highly expressed genes such as those encoding ribosomal proteins use codons corresponding to the highly abundant tRNAs ("optimized codons"). High expression of heterologous genes also requires codon optimization, but even the codon usage of very weakly expressed genes tends to be far from random. To understand this biased choice of codon usage, we develop a theory based on the concept of "ribosomal load." Ribosome is the key limiting commodity for rapidly growing organisms so that the use of "non-optimal" codons in any gene prolongs the translational elongation time, thus reducing the effective ribosome concentration. This presents a fitness cost, the magnitude of which depends on the amount of that protein being translated. We formulated and solved an evolution equation based on the above ingredients. This provides a quantitative relation between codon usage and protein abundance, which is found to be in good agreement with the available data for E.coli. This result suggests a convenient way to quantitatively predict protein abundances based on genome sequence data.

[1]Supported by NSF through IGERT (DGE-0504196) and CTBP (PHY-0216576, PHY-0225630) and by DFG (KL 818/1-1).

1:03PM Y35.00010 A Model of Codon Usage Bias , MORTEN KLOSTER, CHAO TANG, UCSF — The genetic code is degenerate; most amino acids can be encoded by from two to as many as six different codons. While one might expect these codons to be used with equal frequency, this turns out not to be the case—not only are some codons favored over others, but their usage can vary significantly between different genes in the same organism. Known causes of codon bias include differences in mutation rates as well as selection pressure related to the expression level of a gene, but the standard analysis methods can explain only a fraction of the observed codon usage variation. We here introduce an explicit model of codon usage bias, inspired by statistical physics. Combining this model with a maximum likelihood approach, we are able to clearly identify up to four different sources of bias in various genomes. We have applied the algorithm to Saccharomyces cerevisiae as well as 325 bacterial genomes, and in most cases our model explains essentially all observed variance.

1:15PM Y35.00011 Single Molecule Study of Metalloregulatory Protein-DNA Interactions , SUSANTA SARKAR, JAIME BENITEZ, ZHENGXI HUANG, QI WANG, PENG CHEN, Cornell University — Control of metal concentrations is essential for living body. Metalloregulatory proteins respond to metal concentrations by regulating transcriptions of metal resistance genes via protein-DNA interactions. It is thus necessary to understand interactions of metalloregulatory proteins with DNA. Ensemble measurements provide average behavior of a vast number of biomolecules. In contrast, single molecule spectroscopy can track single molecules individually and elucidate dynamics of processes of short time scales and intermediate structures not revealed by ensemble measurements. Here we present single molecule study of interactions between PbrR691, a MerR-family metalloregulatory protein and DNA. We presume that the dynamics of protein/DNA conformational changes and interactions are important for the transcription regulation and kinetics of these dynamic processes can provide useful information about the mechanisms of these metalloregulatory proteins.

1:27PM Y35.00012 A plausible model for the digital response of p53 to DNA damage , GUSTAVO STOLOVITZKY, IBM T.J. Watson Research Center, Yorktown Heights, New York, LAN MA, The University of Texas Southwestern Medical Center, Dallas, Texas, JOHN WAGNER, J. JEREMY RICE, IBM T.J. Watson Research Center, Yorktown Heights, New York, HU WENWEI, Cancer Inst of New Jersey, Univ. of Med and Dentistry of NJ, New Brunswick, New Jersey, ARNOLD LEVINE, School of Natural Sciences, Institute for Advanced study, Princeton, New Jersey — The single-cell response of p53 to ionizing radiation (IR) is such that the number of oscillations of p53 shows dependence on the radiation dose. We present a model of this phenomenon. In our model, double strand break (DSB) sites induced by IR interact with a limiting pool of DNA repair proteins, forming complexes that are sensed by ATM, a protein kinase that activates p53 once phosphorylated by DNA damage. The ATM sensing module switches on or off the downstream p53-mdm2 negative feedback loop. Our simulations show that by assuming stochasticity in the initial number of DSBs and the DNA repair process, p53 and Mdm2 exhibit a coordinated oscillatory dynamics upon IR stimulation in single cells, with a stochastic number of oscillations whose mean increases with IR dose.

1:39PM Y35.00013 Transcription factor binding energy vs. biological function[1] , M. DJORDJEVIC, E. GROTEWOLD, The Ohio State University — Transcription factors (TFs) are proteins that bind to DNA and regulate expression of genes. Identification of transcription factor binding sites within the regulatory segments of genomic DNA is an important step towards understanding of gene regulatory networks. Recent theoretical advances that we developed [1,2], allow us to infer TF-DNA interaction parameters from in-vitro selection experiments [3]. We use more than 6000 binding sequences [3], assembled under controlled conditions, to obtain protein-DNA interaction parameters for a mammalian TF with up to now unprecedented accuracy. Can one accurately identify biologically functional TF binding sites (i.e. the binding sites that regulate gene expression), even with the best possible protein-DNA interaction parameters? To address this issue we i) compare our prediction of protein binding with gene expression data, ii) use evolutionary comparison between related mammalian genomes. Our results strongly suggest that in a genome there exists a large number of randomly occurring high energy binding sites that are not biologically functional. [1] M Djordjevic, submitted to *Biomol. Eng.* [2] M. Djordjevic and A. M. Sengupta, *Phys. Biol.* **3:** 13, 2006. [3] E. Roulet et al., *Nature Biotech.* **20**: 831, 2002.

[1]This work is supported by NSF under Agreement No. 0112050 and NSF grant MCB-0418891

1:51PM Y35.00014 Dynamics of DNA bending/unbending in complex with DNA-bending protein IHF , ANJUM ANSARI, PAULA VIVAS, SERGUEI KUZNETSOV, University of Illinois at Chicago — Kinetics of conformational changes in proteins and DNA that lead to precise recognition of specific DNA binding sites are difficult to observe with the limited time-resolution of stop-flow and single-molecule techniques. Here we use a ∼10 ns laser T-jump apparatus to probe the kinetics of a ∼35-bp DNA substrate bound to *E. coli* Integration Host Factor (IHF) and end-labeled with a FRET pair. These T-jump measurements, in combination with stop-flow, provide the first direct observation of the DNA bending/unbending kinetics in a protein-DNA complex (Sugimura and Crothers, PNAS, in press; Kuznetsov et al., PNAS, in press). The rates and activation energy of DNA bending are similar to that of a single A:T base pair opening inside uncomplexed DNA, suggesting that spontaneous thermal disruption in base-pairing nucleated at an A:T site may be sufficient to overcome the free energy barrier needed to partially bend/kink DNA. An unusual salt dependence of the binding affinity observed previously for IHF/DNA complex, and explained in terms of DNA binding coupled with disruption of a network of salt bridges within the protein (Holbrook et al., 2001, JMB, **310**, 379), is reflected in the salt dependence of the observed bending rates. These results suggest that salt-dependent protein conformational changes may be playing a role in the DNA bending process.

2:03PM Y35.00015 HMGB binding to DNA: comparisons between single and double box motifs , MICAH J. MCCAULEY, Department of Physics, Northeastern University, JEFF ZIMMERMAN, L. JAMES MAHER III, Department of Biochemistry and Molecular Biology, Mayo Clinic College of Medicine, MARK C. WILLIAMS, Department of Physics, Northeastern University — High Mobility Group B (HMGB) proteins contain two HMG box domains known to bind non-sequence specifically into the DNA minor groove, slightly intercalating base pairs and producing a strong bend in the DNA backbone. These proteins are believed to alter DNA elasticity, making DNA more accessible for transcription in vivo. To probe the effects of HMG proteins on DNA elasticity, we use optical tweezers to measure the forces required to stretch single DNA molecules, alone and in the presence of HMGB proteins at varying solution conditions. Experiments quantify the binding constant of HMGB to DNA, as well as changes in the flexibility and stability of the double helix. Previous results from a protein fragment containing a single HMG box suggested significant flexibility changes in the double helix but did not show helix stabilization, while a double box protein from rat HMGB–1 appears to significantly stabilize the DNA helix.