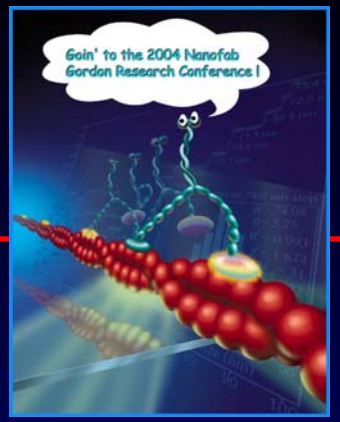
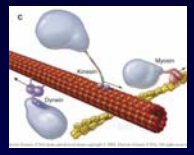
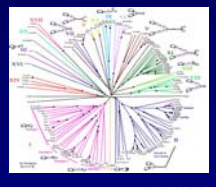
University of Pennsylvania

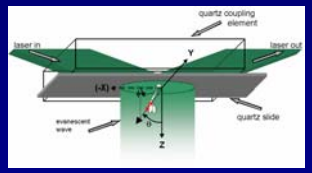
APS Workshop on Biology March 12, 2006

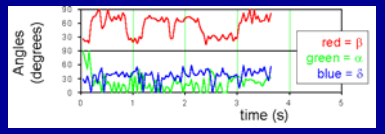


goldmany@mail.med.upenn.edu







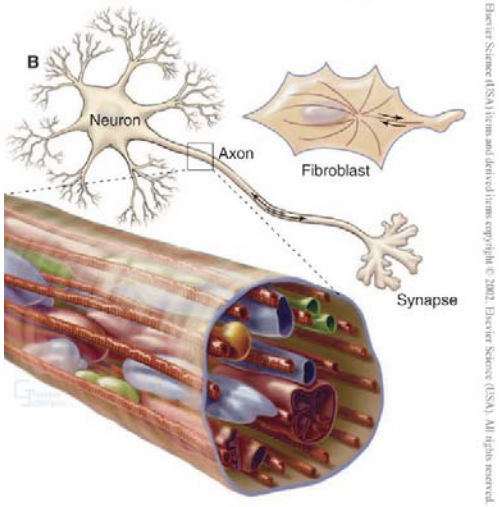


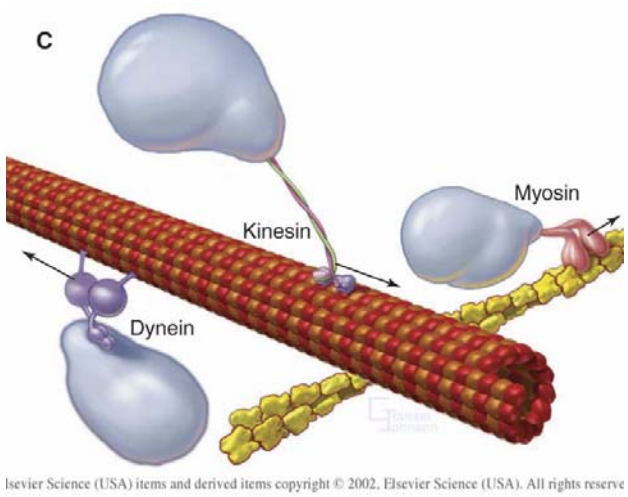
- Molecular Motors
- Muscle Energetics and Strain Dependence
- Unconventional Myosins – Myosin V
- Single-Molecule Fluorescence Polarization

FIONA

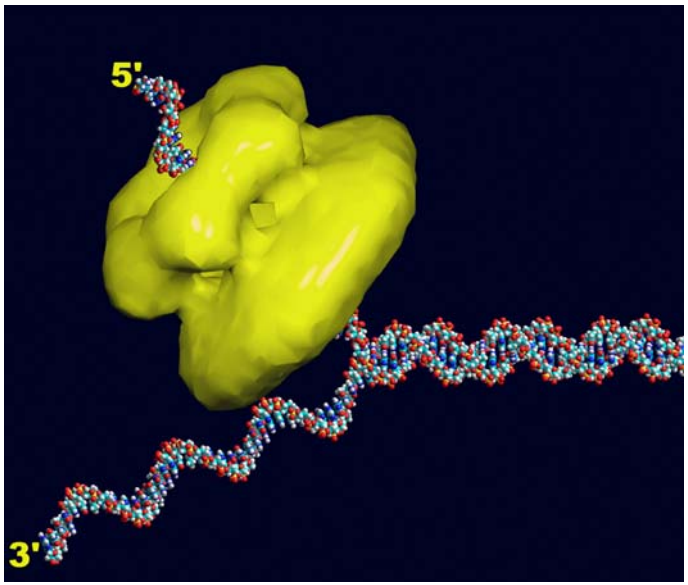
- Fluorescence Imaging at 1 – 2 nm
- Defocussed Orientation and Positional Imaging
- Challenges in Molecular Motor Research

(Classic) Molecular Motors

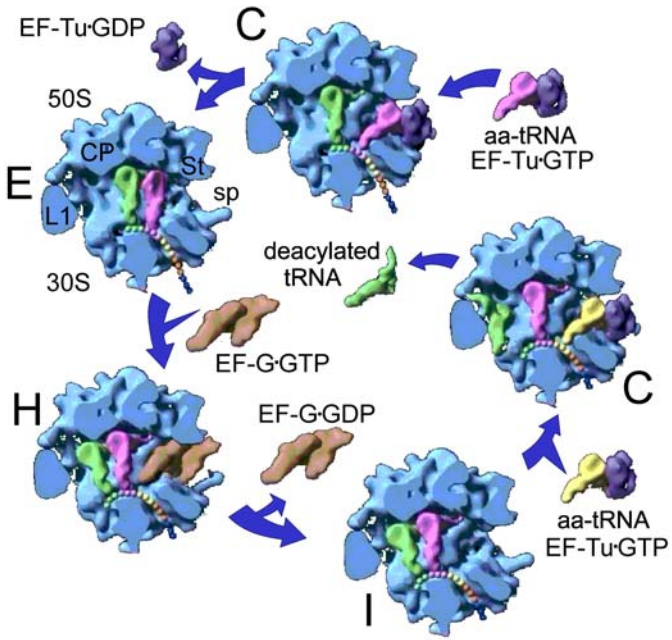




Helicase Unwinds DNA

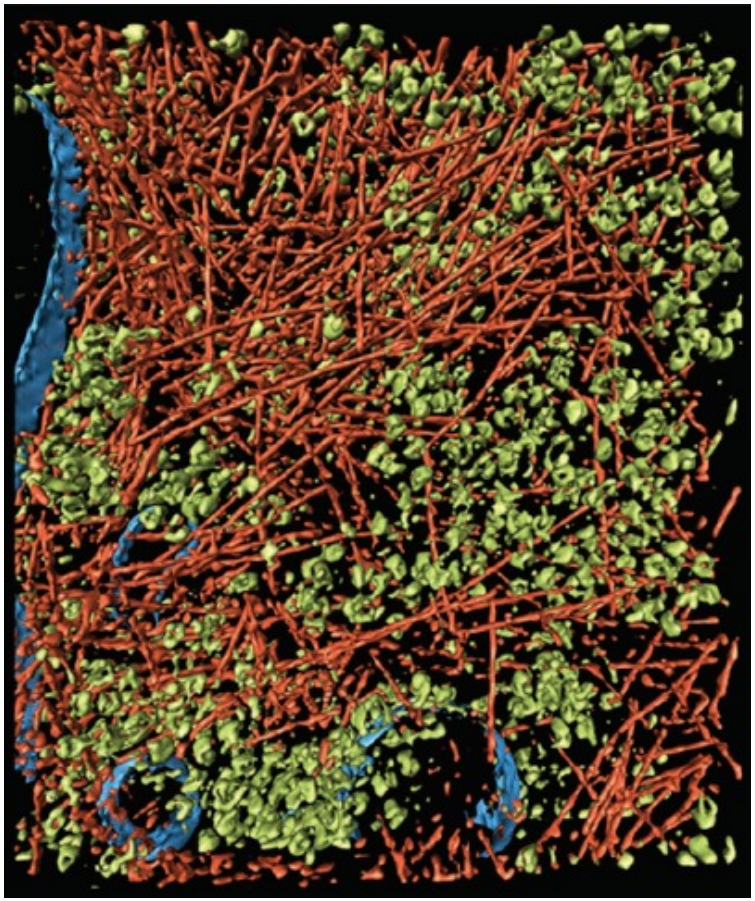


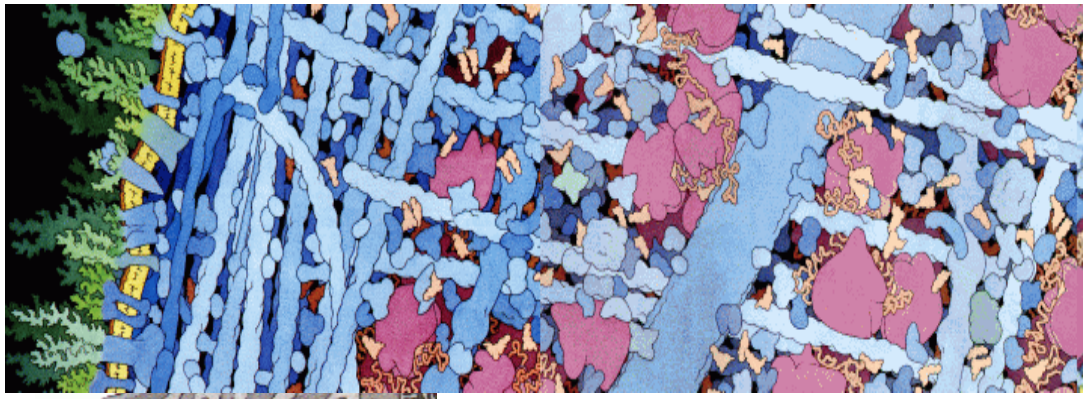
Ribosome Synthesizes Proteins

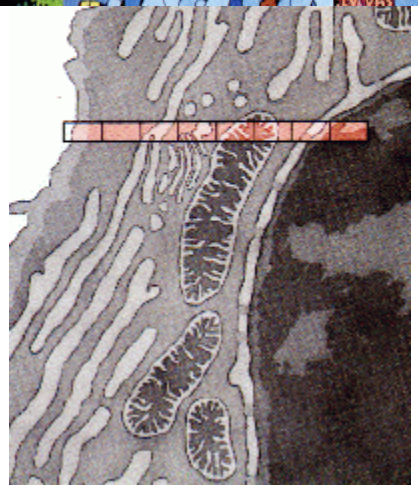


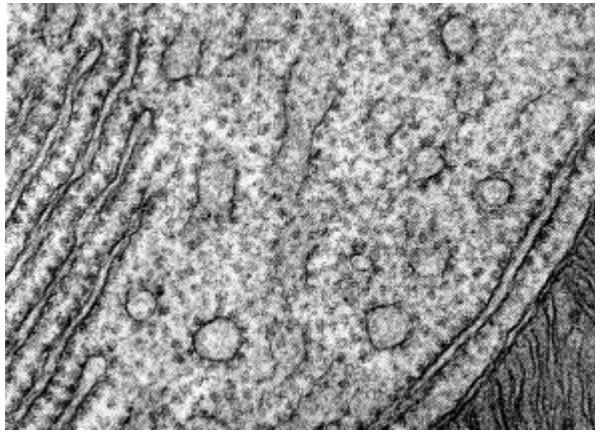
Cryo-EM of Cell

Artist's Imagination





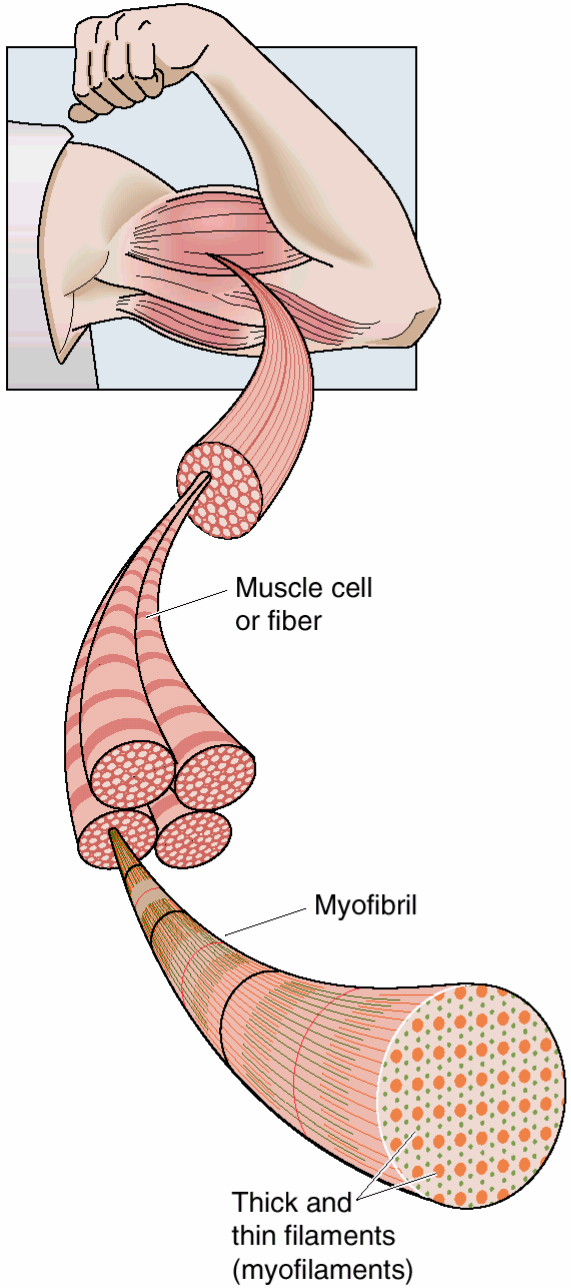




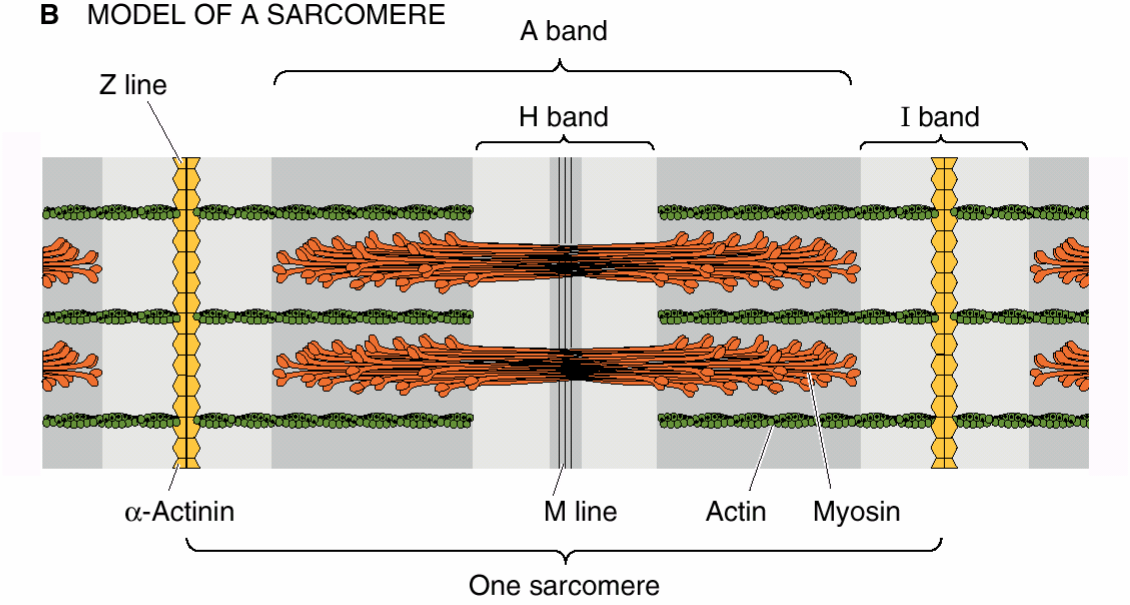
Medalia et al. 2002 *Science*. 298:1209-13.

David C. Goodsell

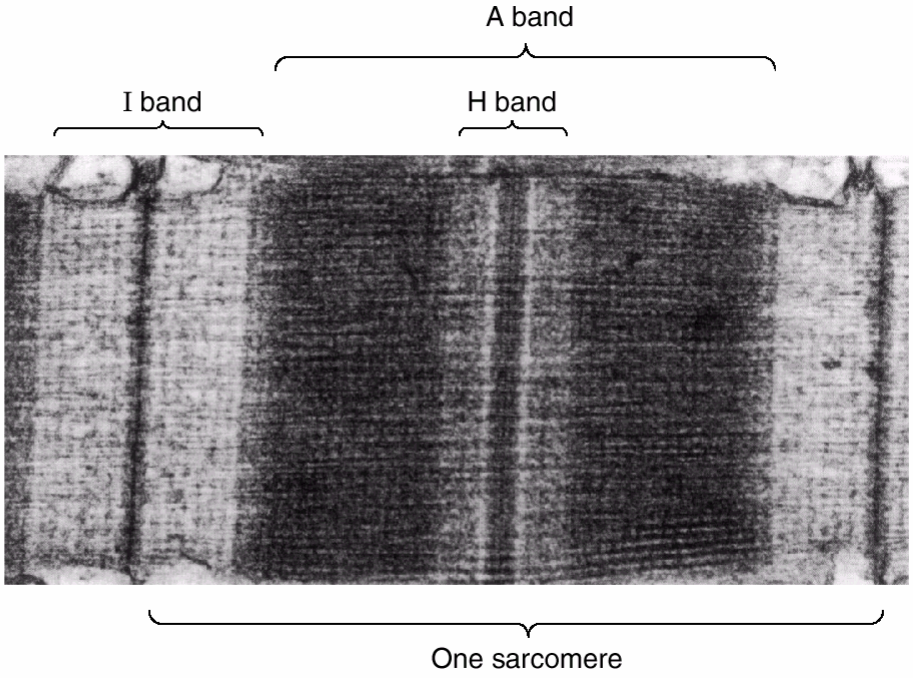
A FROM MUSCLE TO MYOFILAMENTS



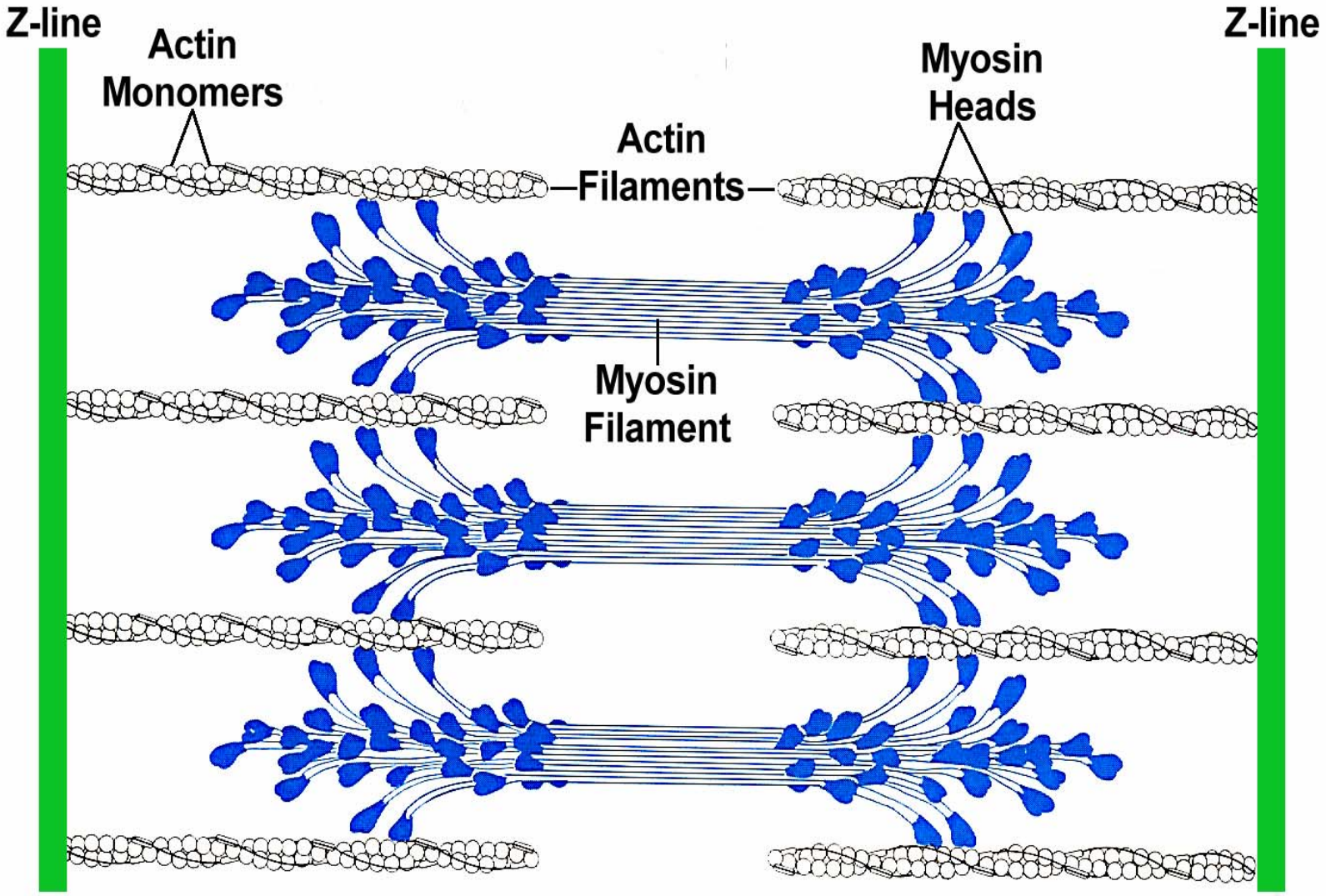
B MODEL OF A SARCOMERE



C ELECTRON MICROGRAPH OF SARCOMERE

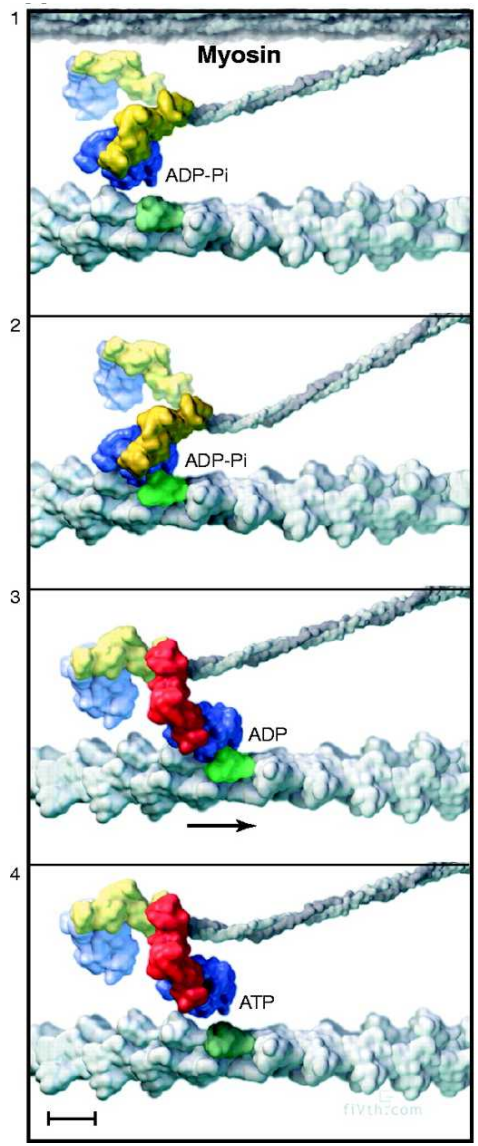


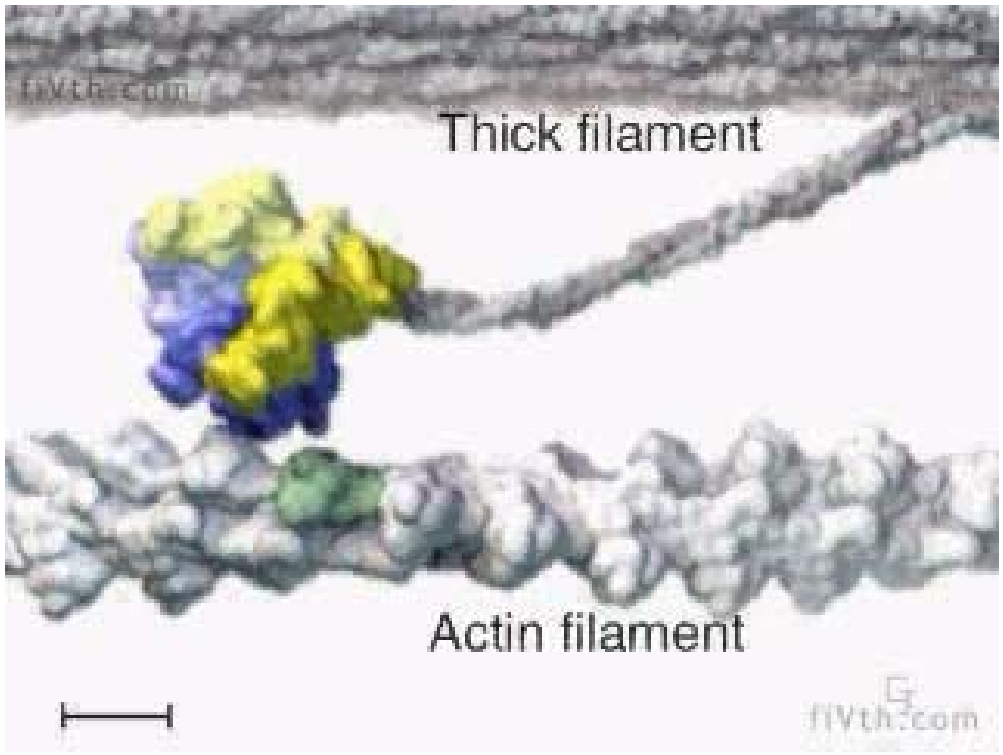
Sarcomere Structure



from Rhoades & Pflanzer, Human Physiology

The Actin-Myosin Cycle

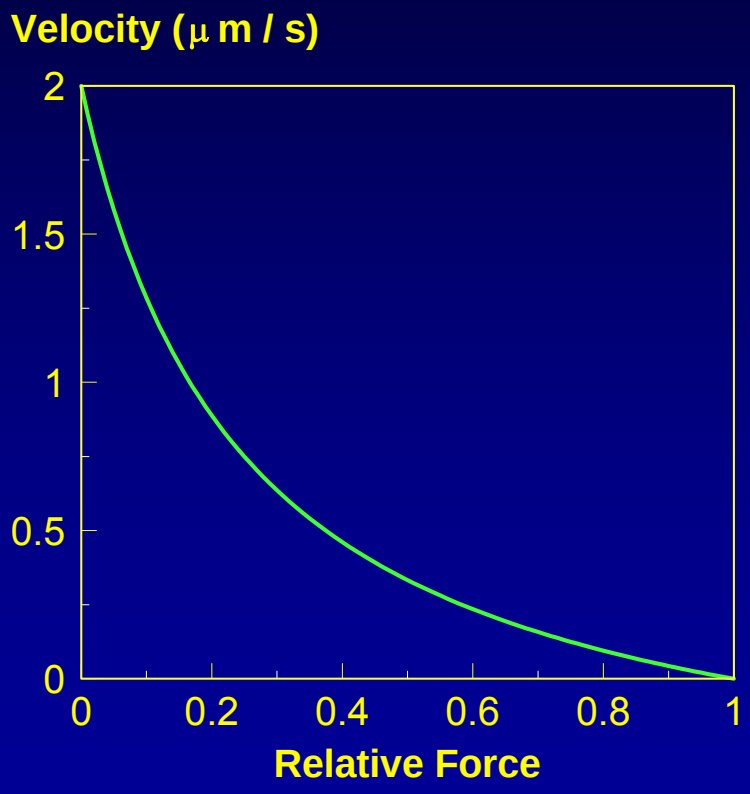


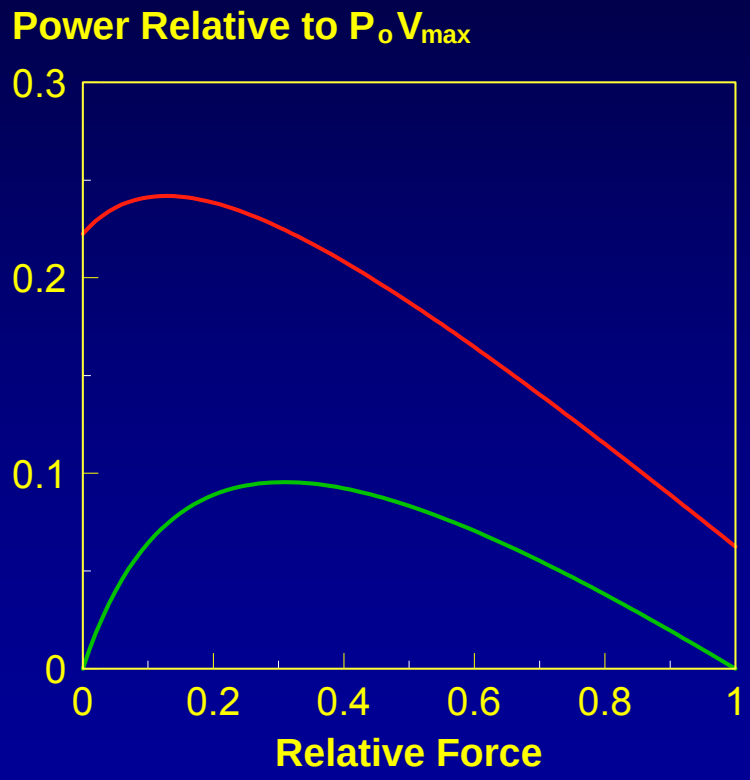


Deterministic Tilting Motion

Force-Velocity, Power and Energy Utilization

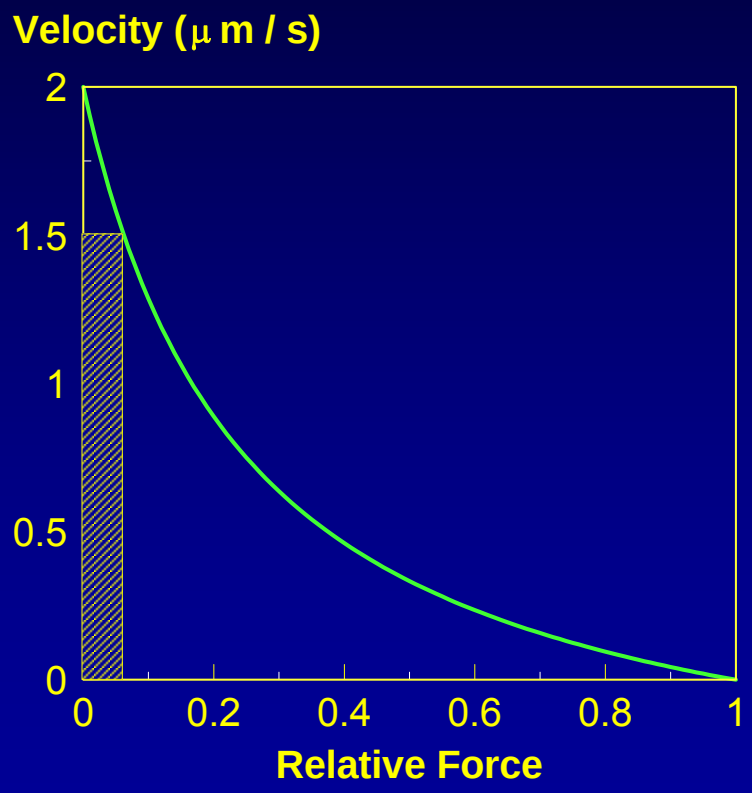
Penn

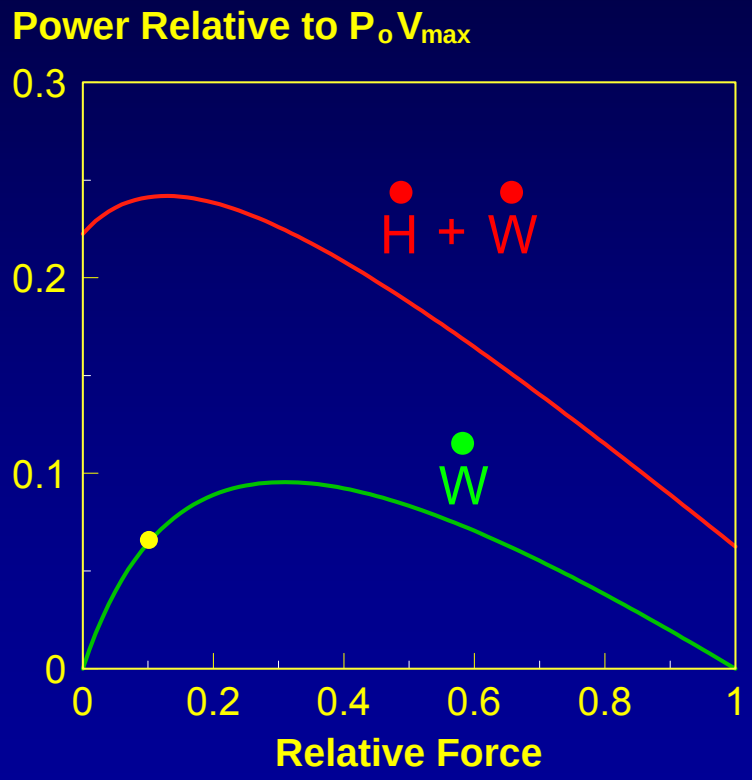




Fenn and Hill, *J. Physiol.* 1932

Force-Velocity, Power and Energy Utilization



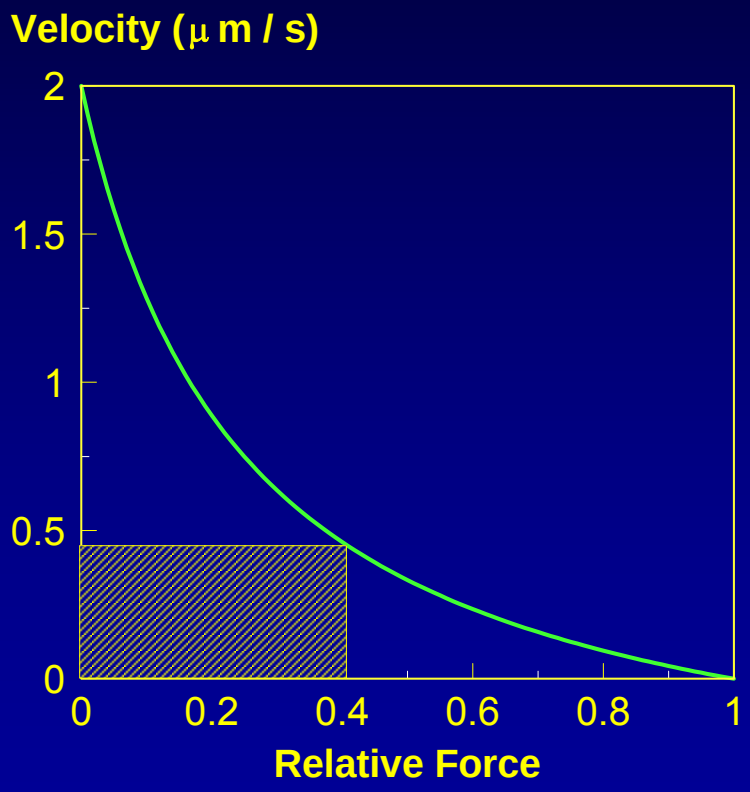


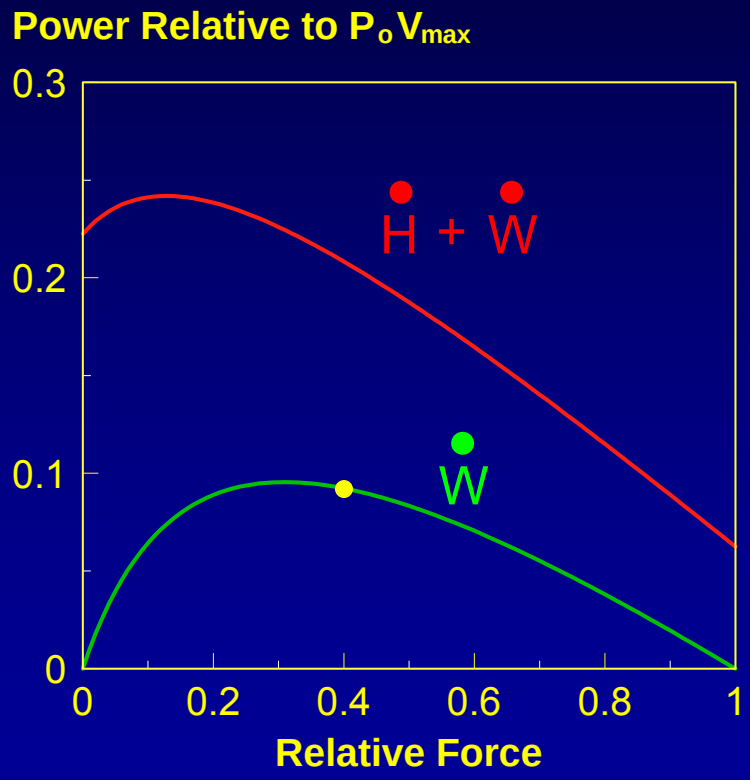
Fenn and Hill, *J. Physiol.* 1932

$\dot{W}$ = Power = F dx/dt = F · V

Force-Velocity, Power and Energy Utilization

Penn





Fenn and Hill, *J. Physiol.* 1932

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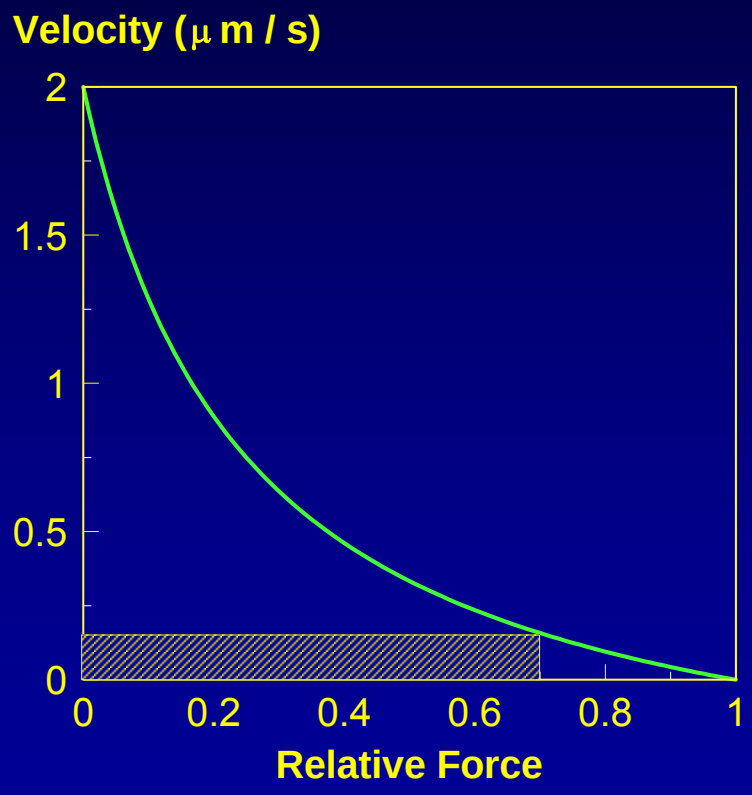
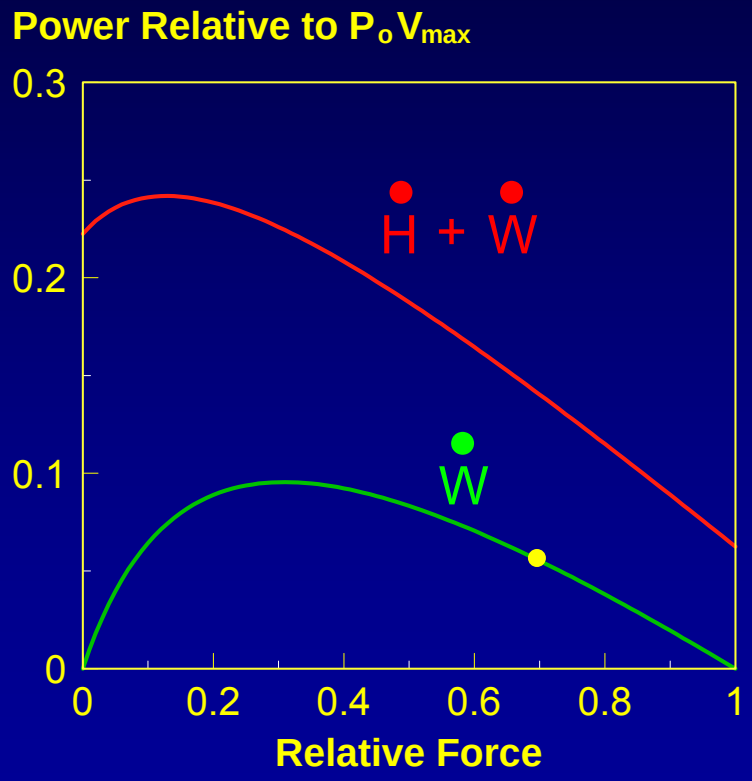
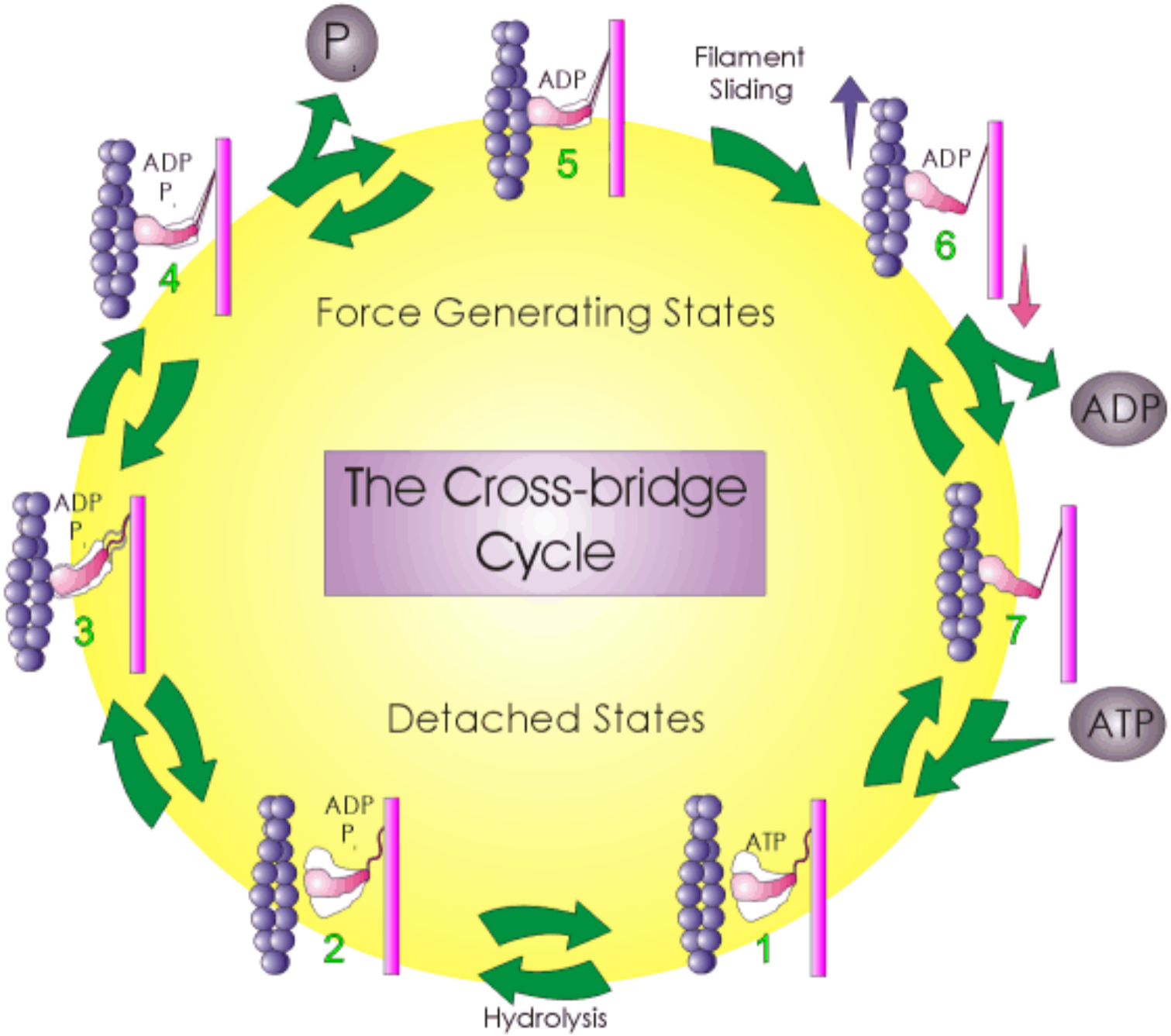
Force-Velocity, Power and Energy Utilization





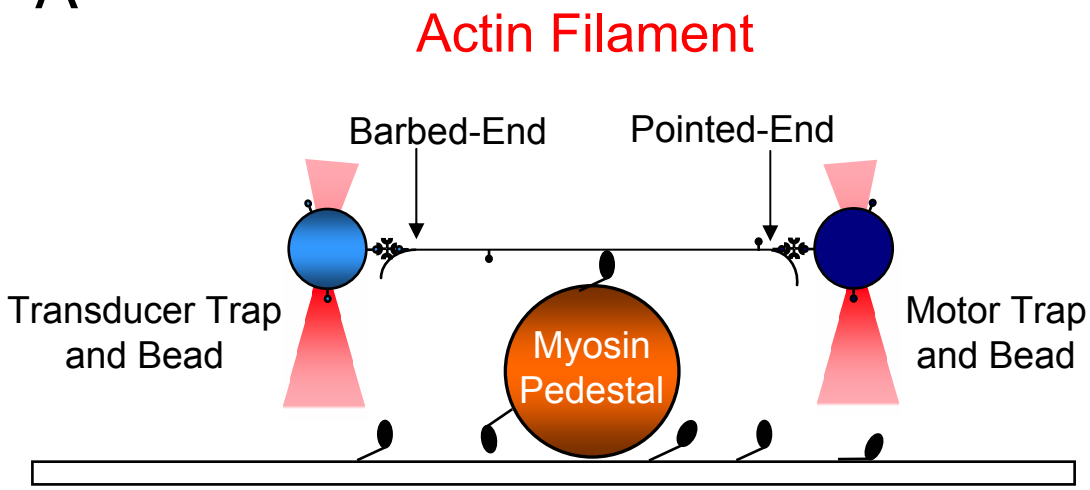
Fenn and Hill, *J. Physiol.* 1932

$\dot{W}$ = Power = F dx/dt = F · V

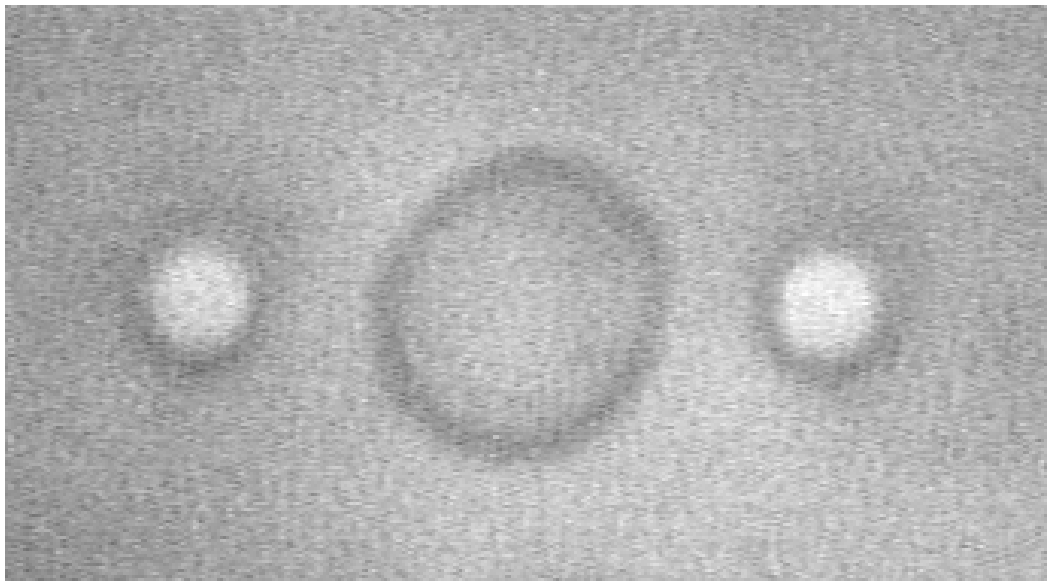

P
ADP
5
Filament
Sliding
ADP
6
ADP
4
Force Generating States
ADP
The Cross-bridge
Cycle
ADP
3
7
ATP
Detached States
ADP
ATP
2
1
Hydrolysis

Isometric Three-Bead Assay

A



B

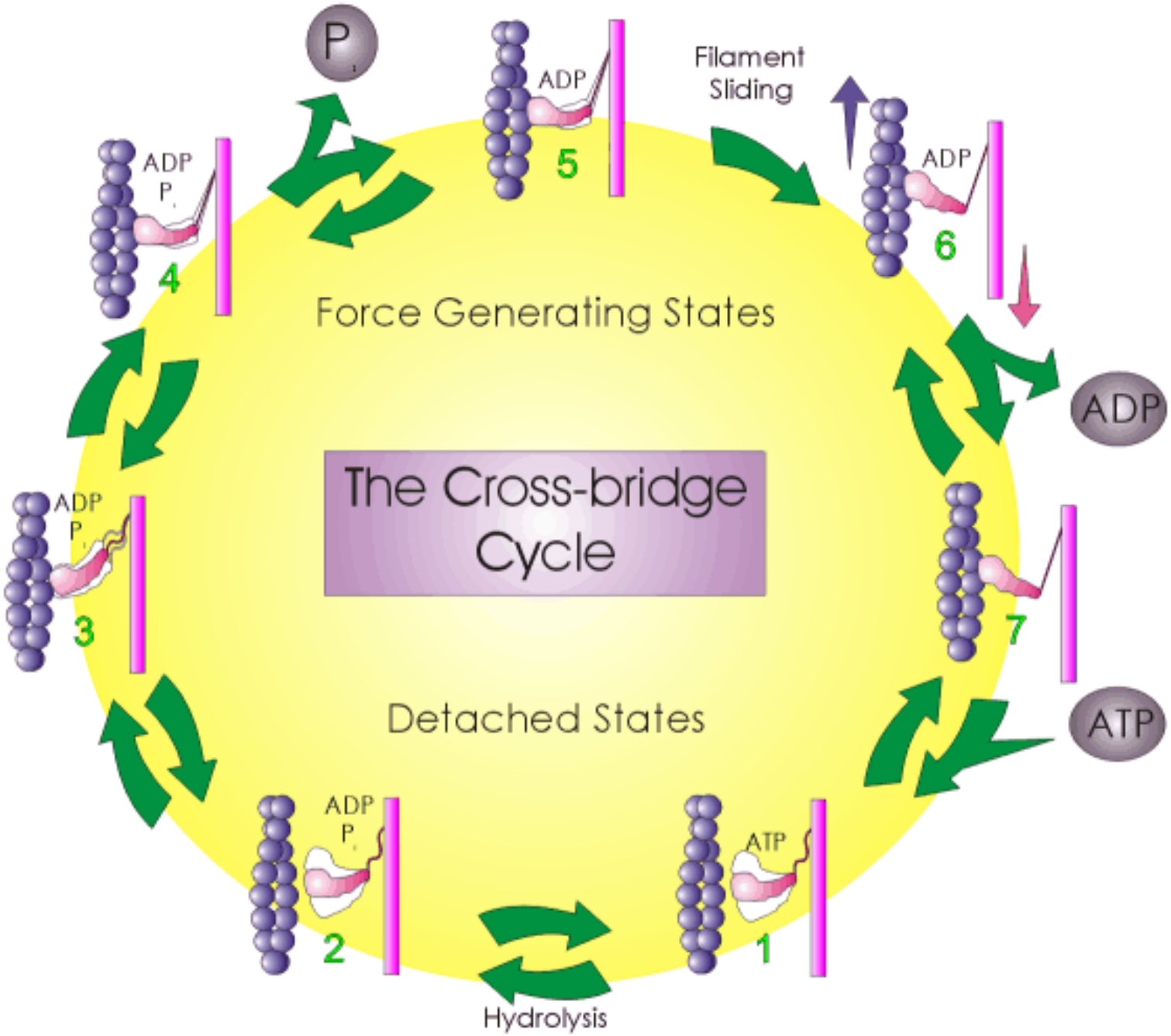


Force = ~10 picoNewtons

Displacement
= ~10 nanometers

$W = \frac{1}{2} F \cdot D$
= ~50 x 10^{-21} Joules
= ~50 zepto Joules

ΔG_{ATP}
= ~100 zepto Joules


P
ADP
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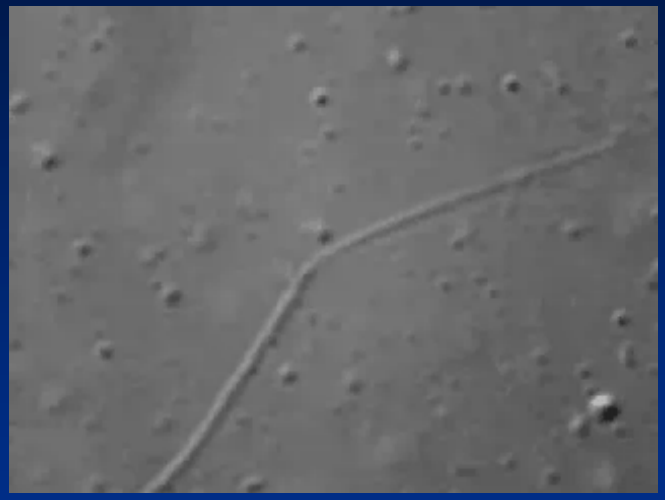
4
Force Generating States
ADP
The Cross-bridge
Cycle
ADP
3
7
ATP
Detached States
ADP
ATP
2
1
Hydrolysis

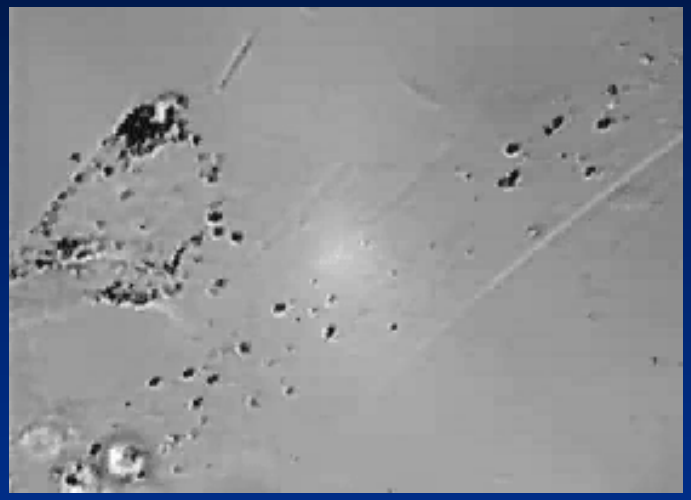
Molecular Motors in Non-Muscle Cells

University of Pennsylvania



Vesicle Movement in Cell Extract

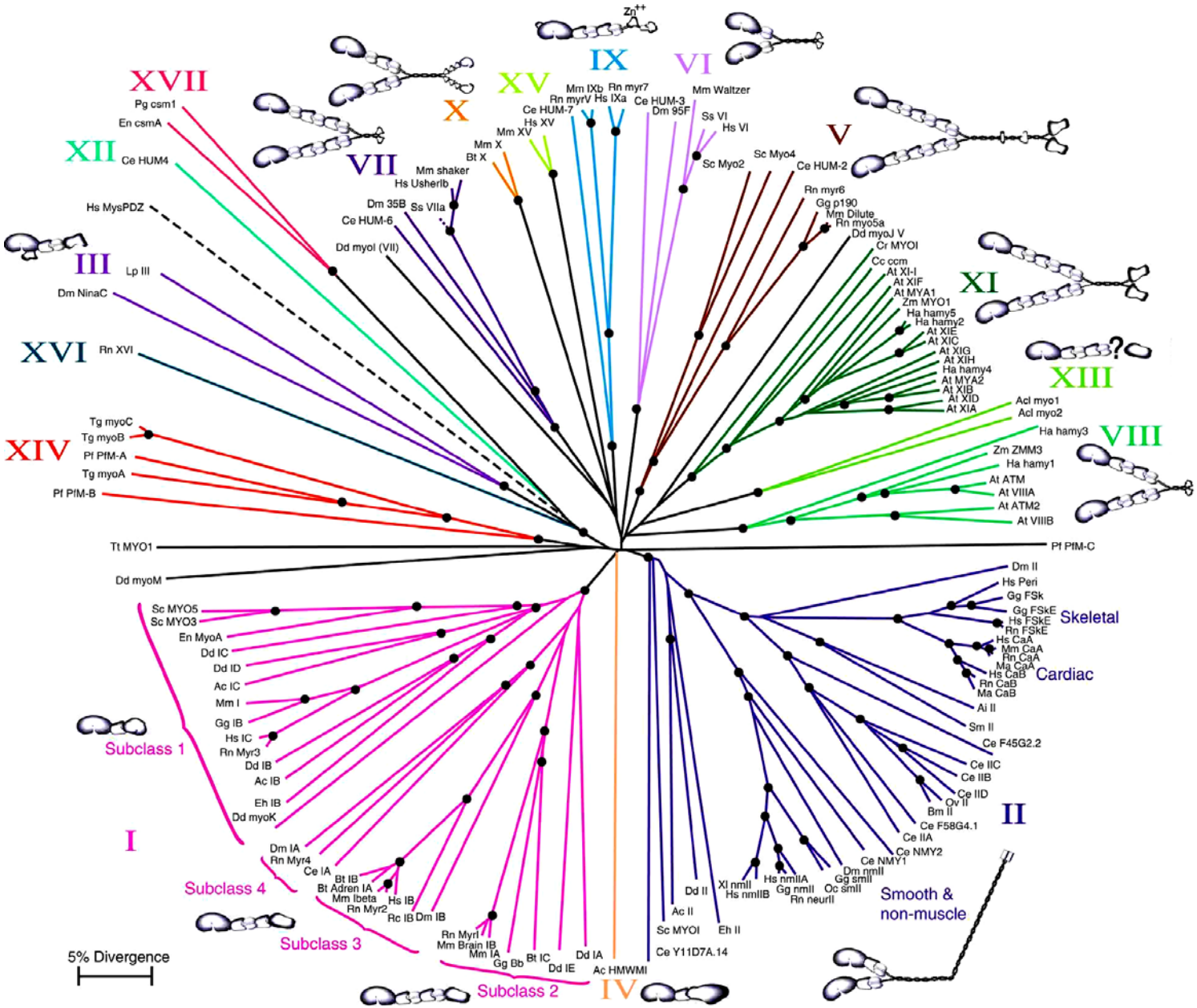
Nira Pollack & Ron D. Vale, UCSF
From: Molecular Biology of the Cell, 4th ed.



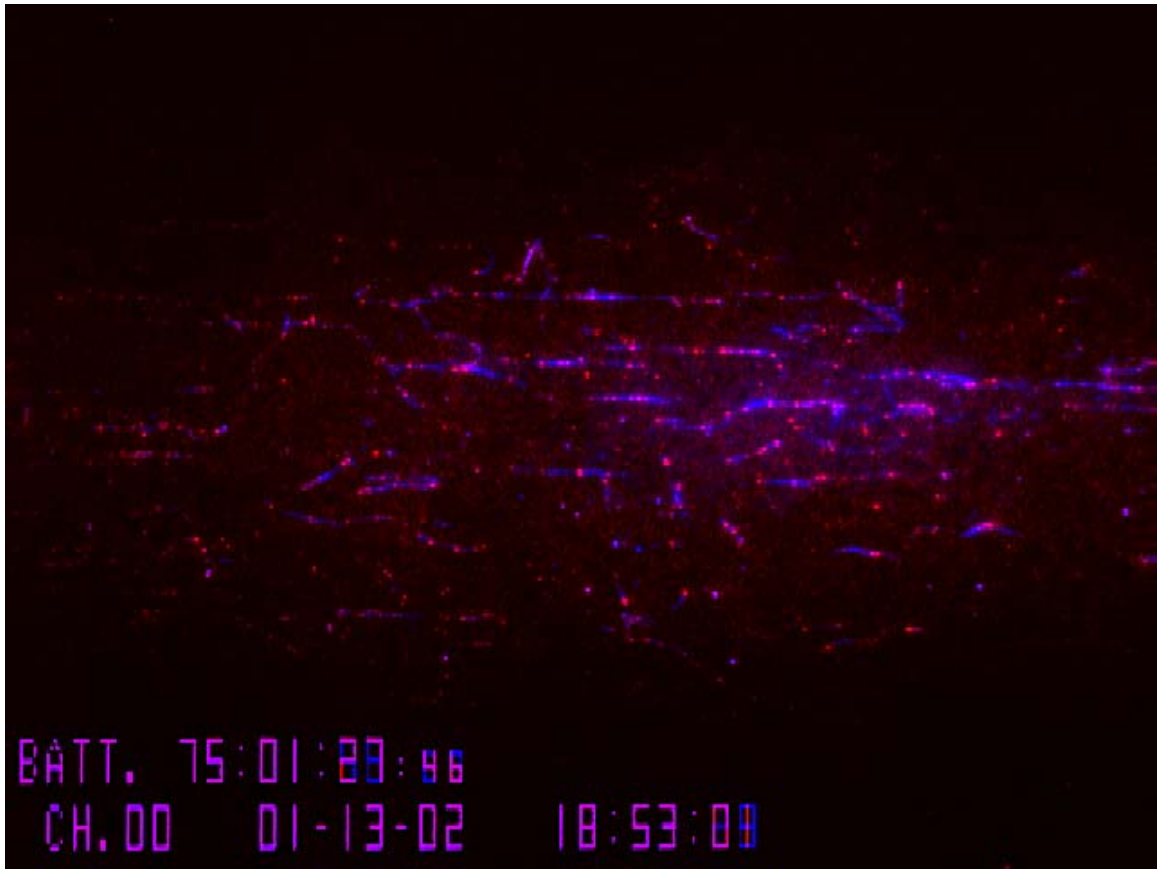
Melanosome Movement

John A. Hammer, III, NIH

Myosin Family Tree



Myosin V Processivity



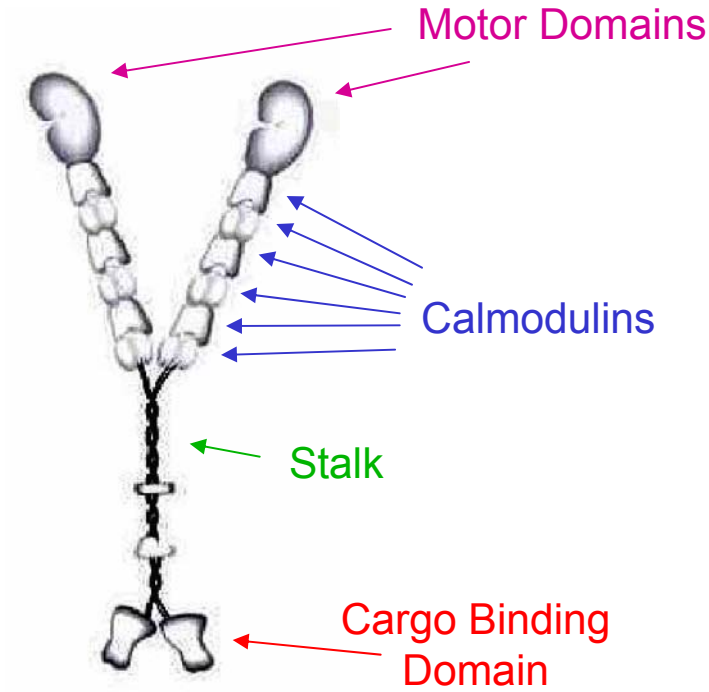
20,000 nm

10x speed

Actin Filament

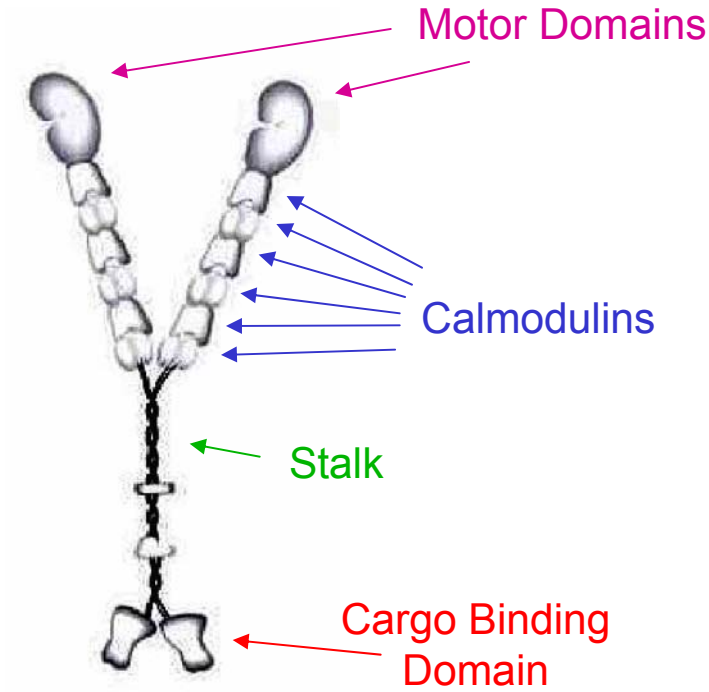
37 nanometers

Myosin V

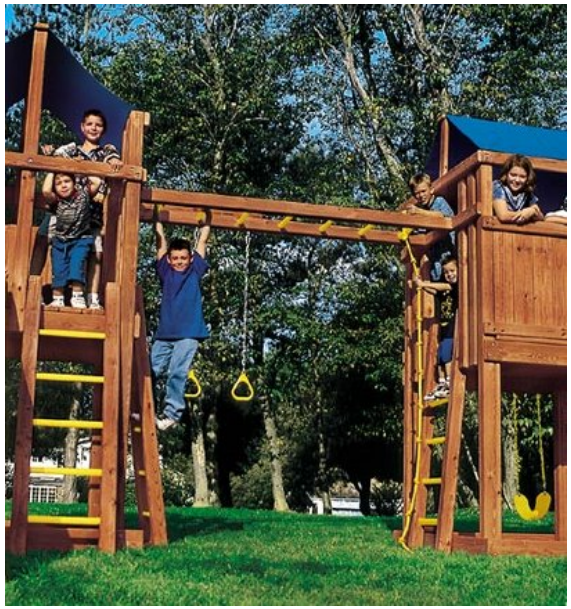


Actin Filament

Myosin V



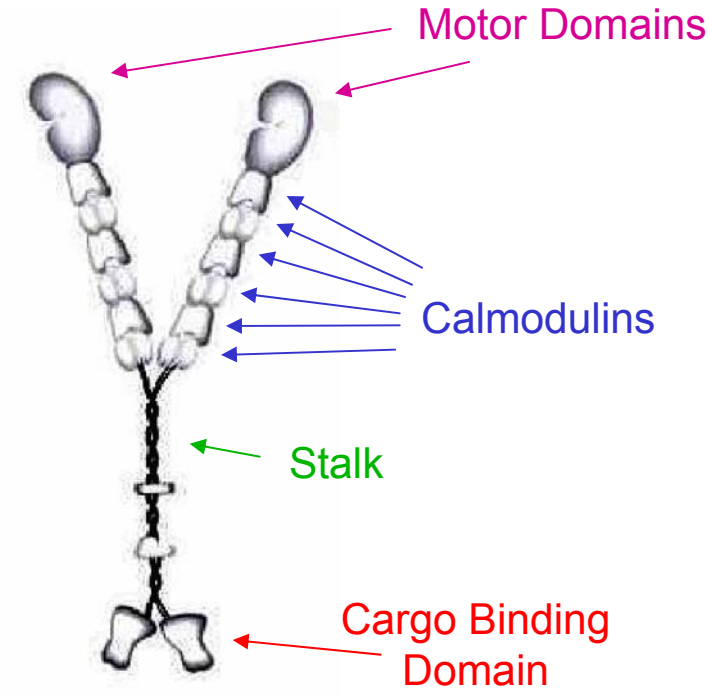
Monkey Bars



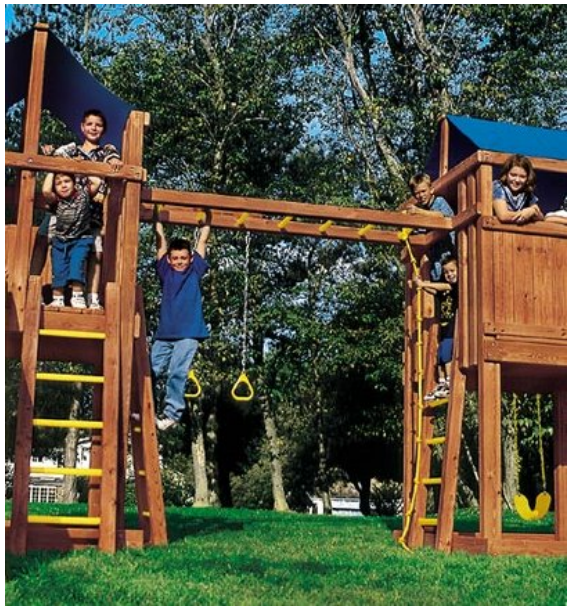
Actin Filament

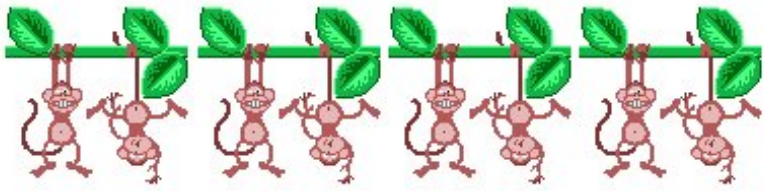
37 nanometers

Myosin V

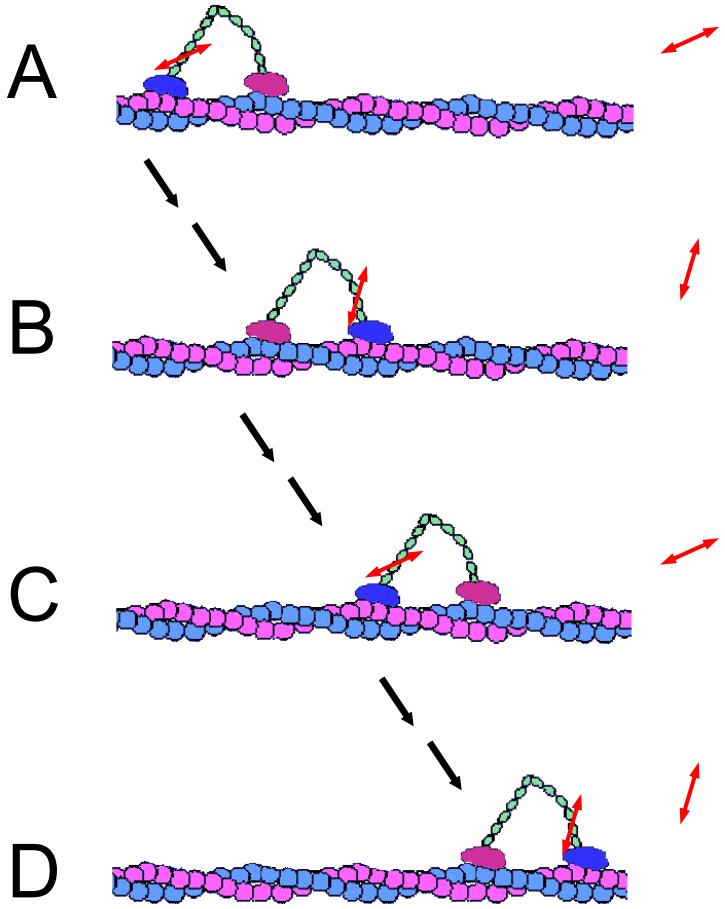


Monkey Bars

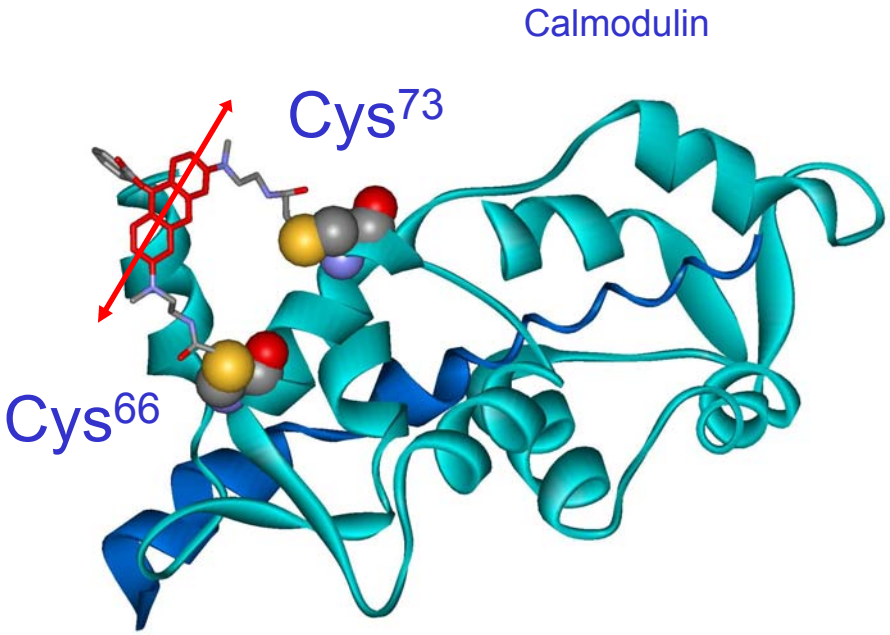


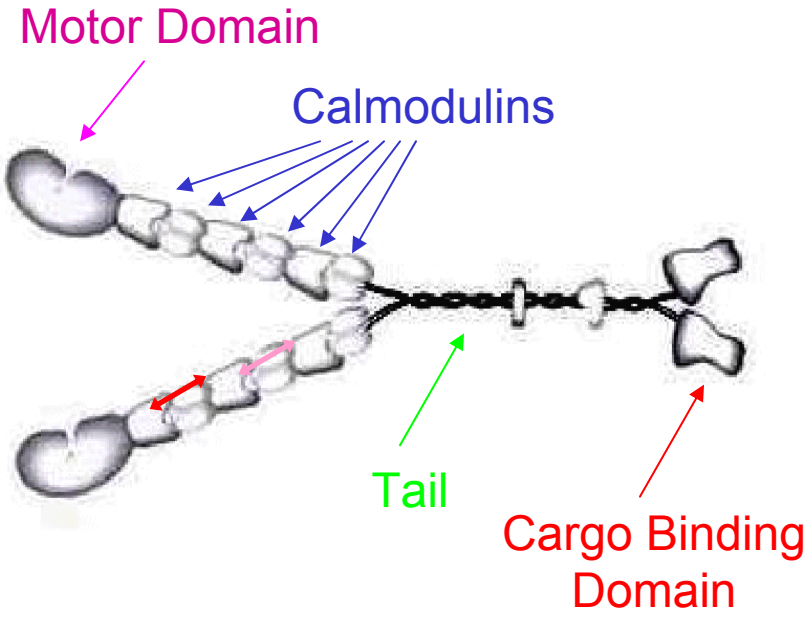


Hand-Over-Hand Model of Processive Transport



Bifunctionally Labeled Calmodulin on Myosin V

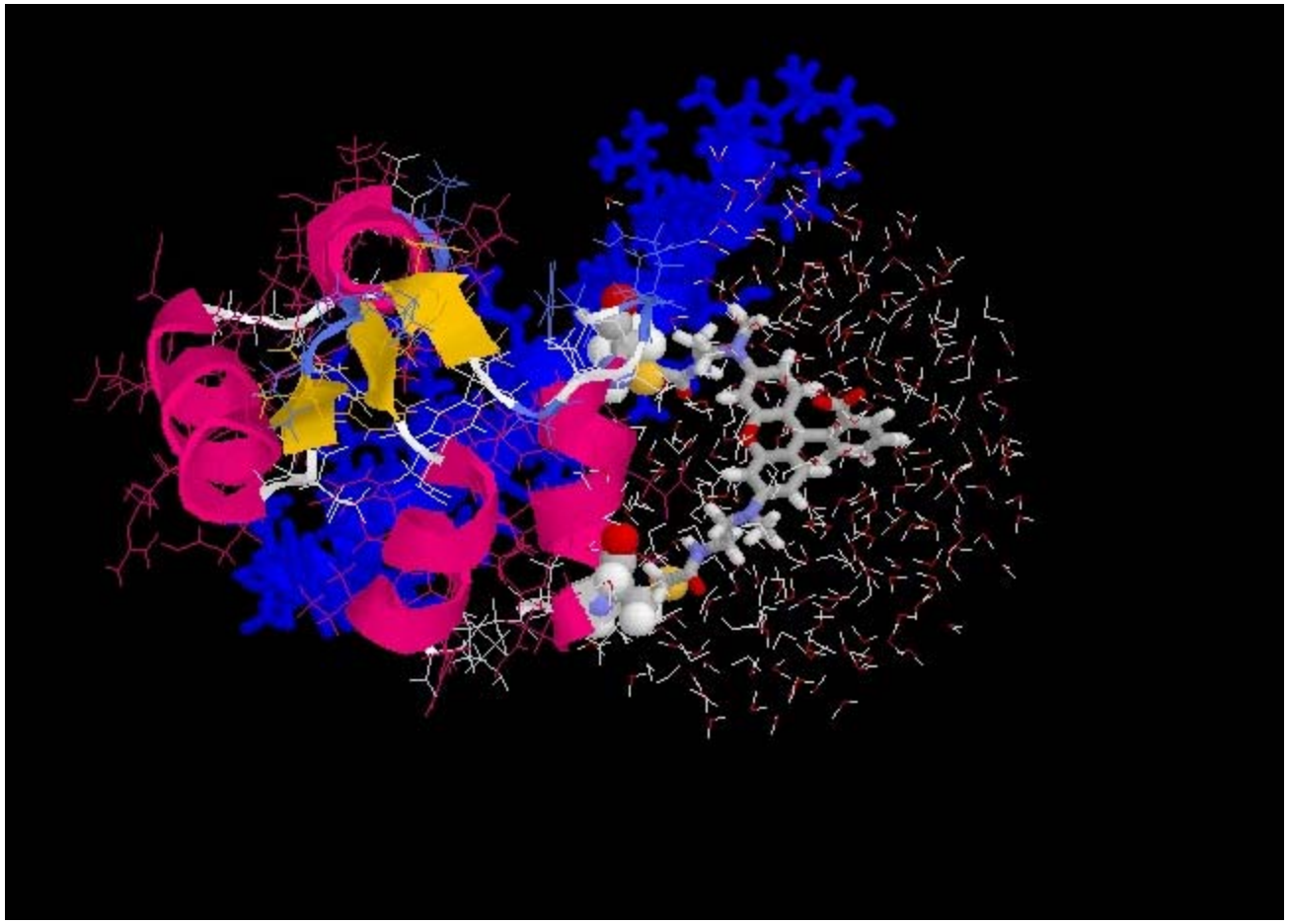




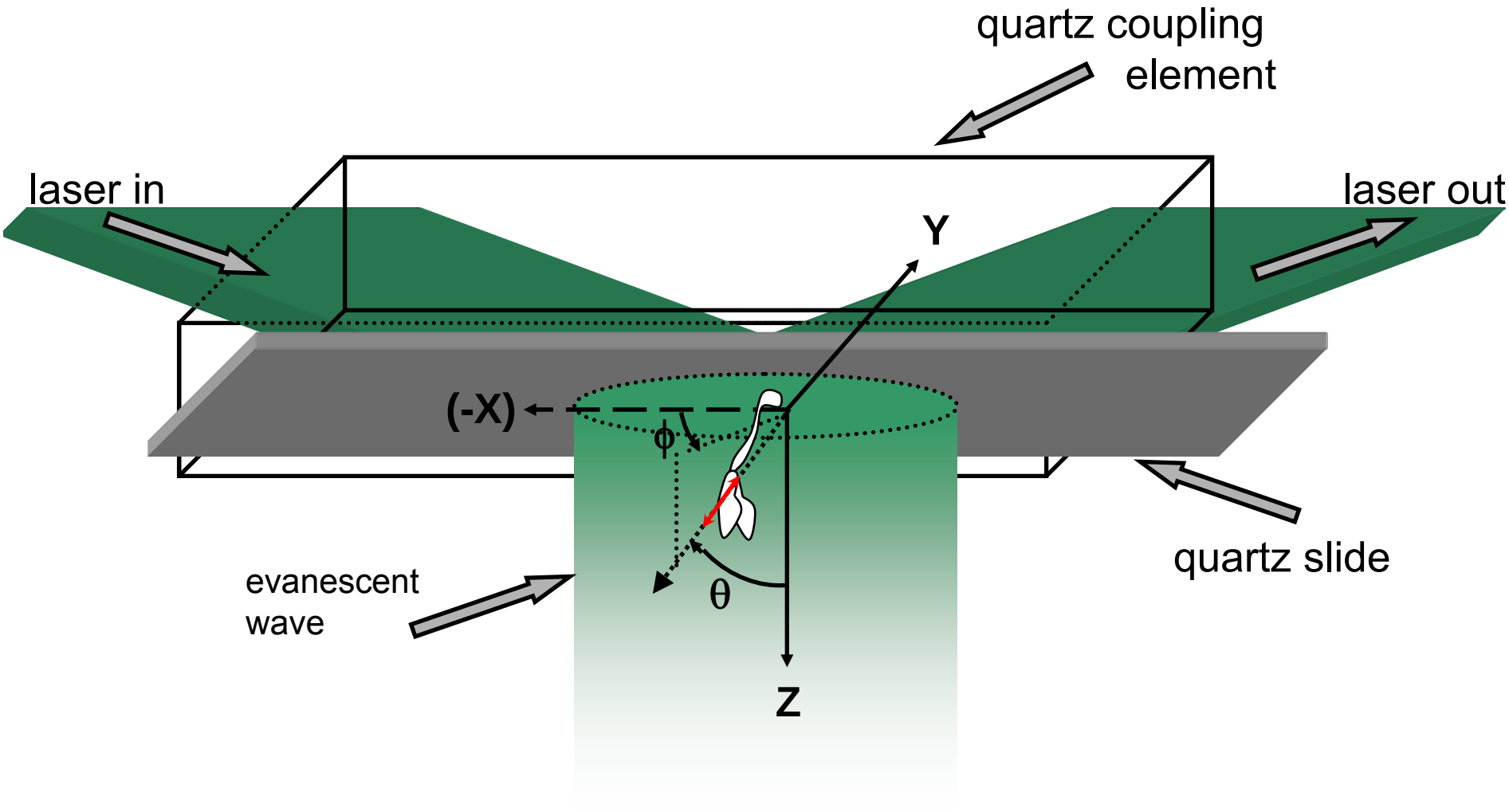
Stoichoimetry, Specificity and Cross-linking:

- HPLC
- Mass spectrometry
- Tryptic digestion

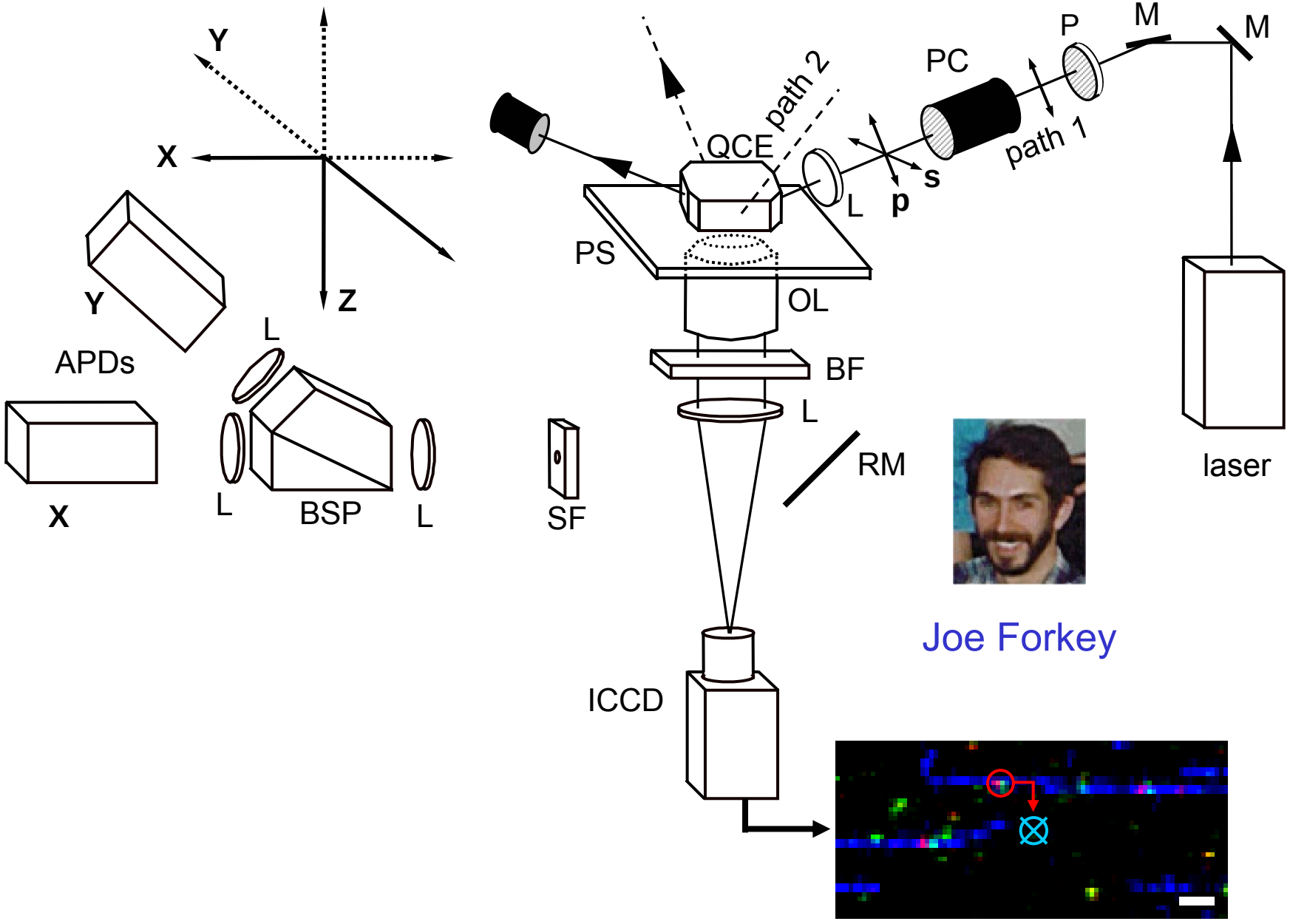
Bifunctional Rhodamine on Myosin Regulatory Light Chain



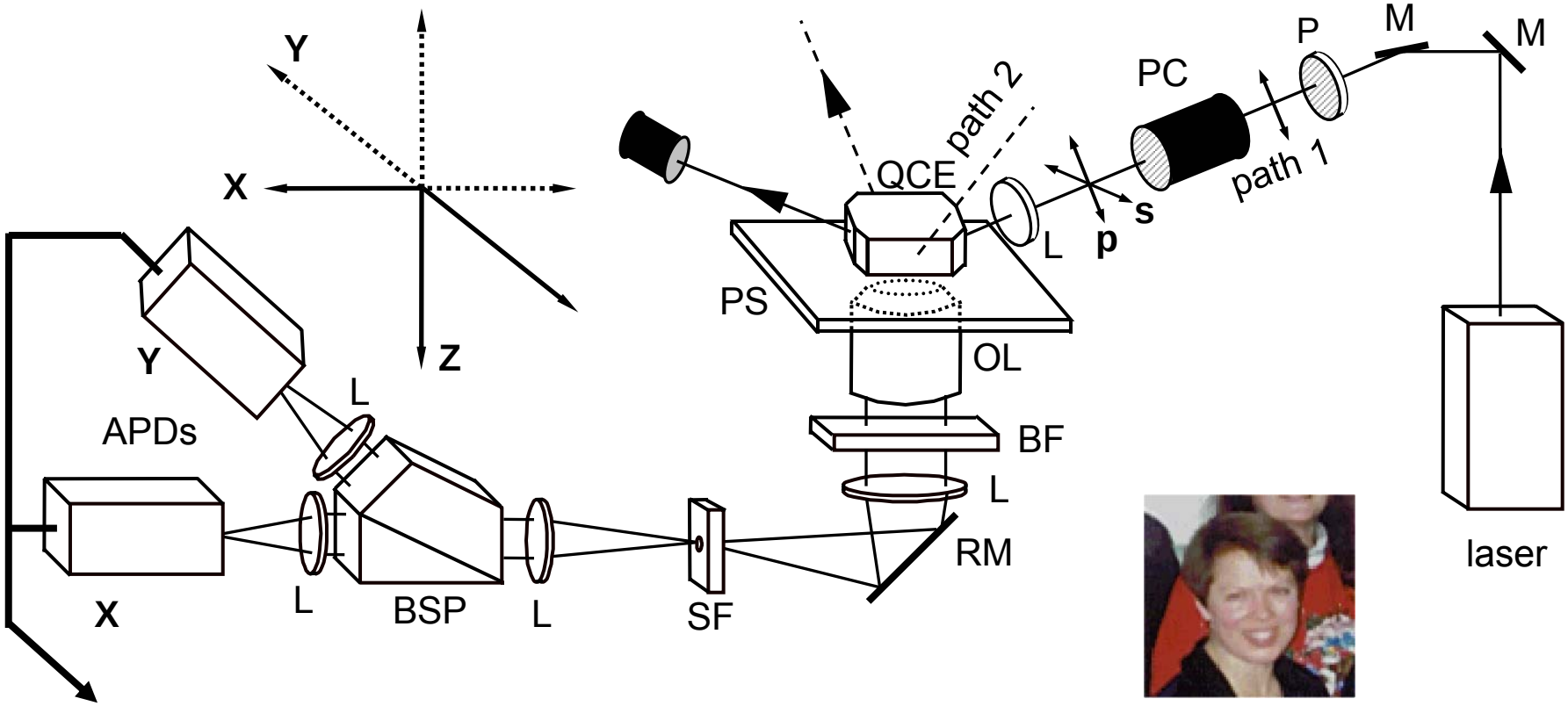
bwiggle.avi


quartz coupling
element
laser in
laser out
Y
(-X)
ϕ
θ
evanescent
wave
quartz slide
Z

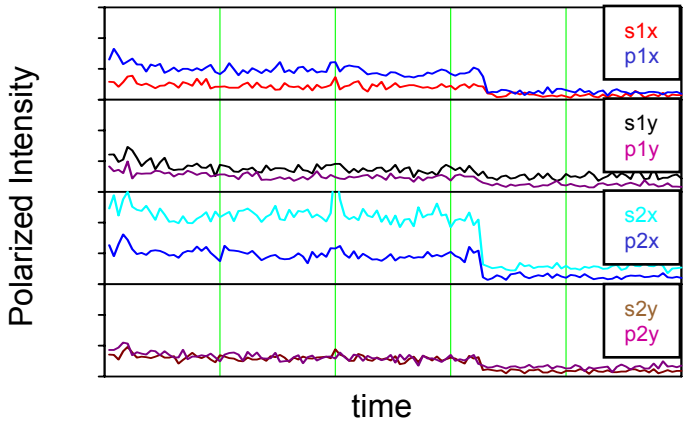
Experimental Apparatus

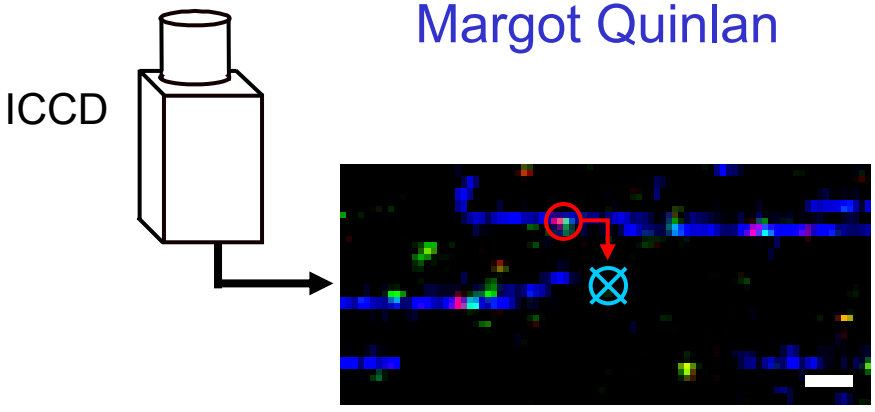


Experimental Apparatus

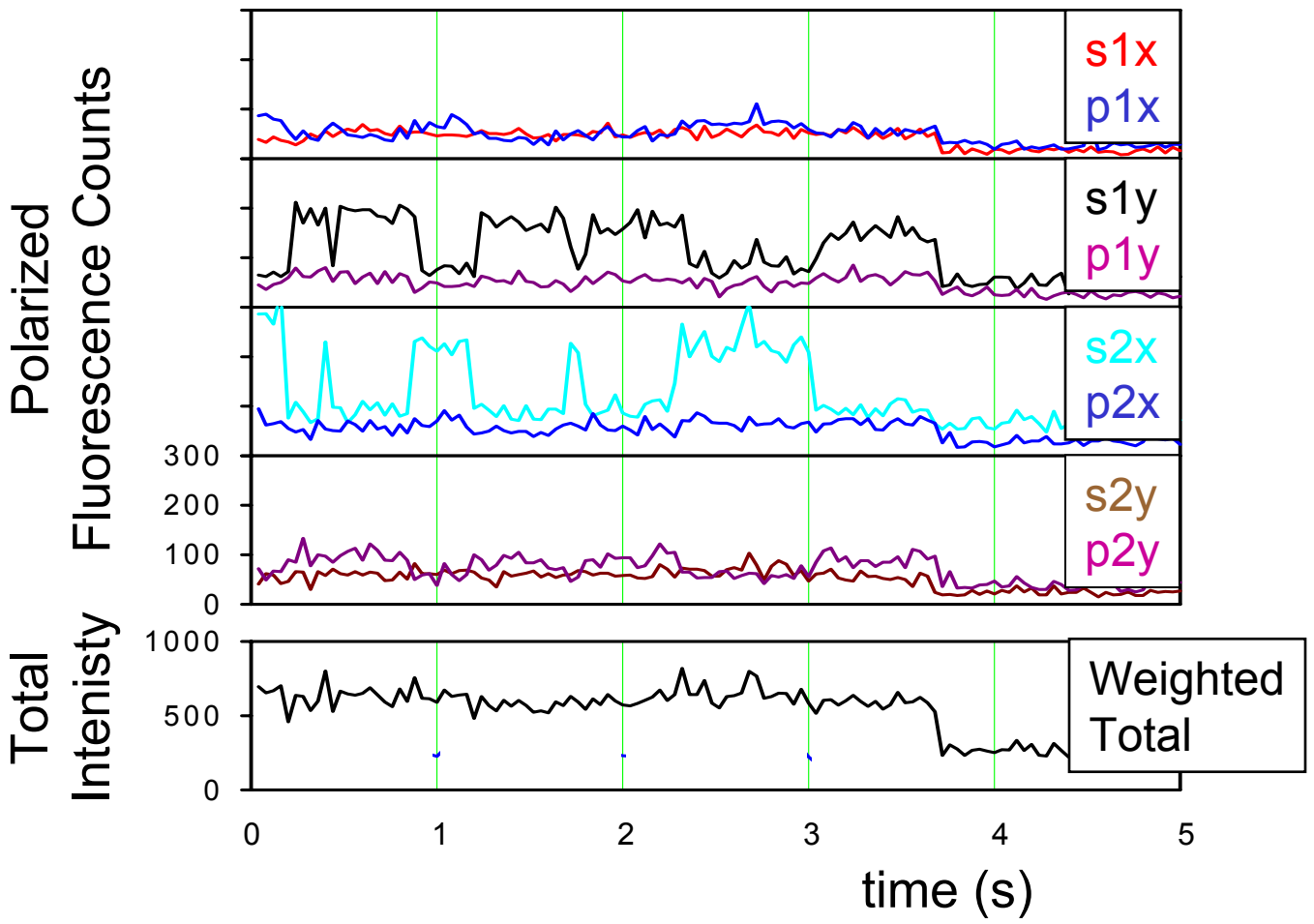


Margot Quinlan

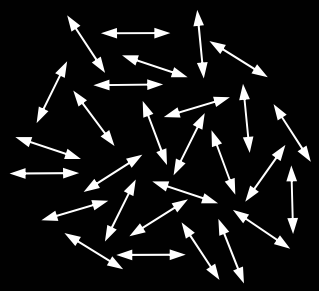


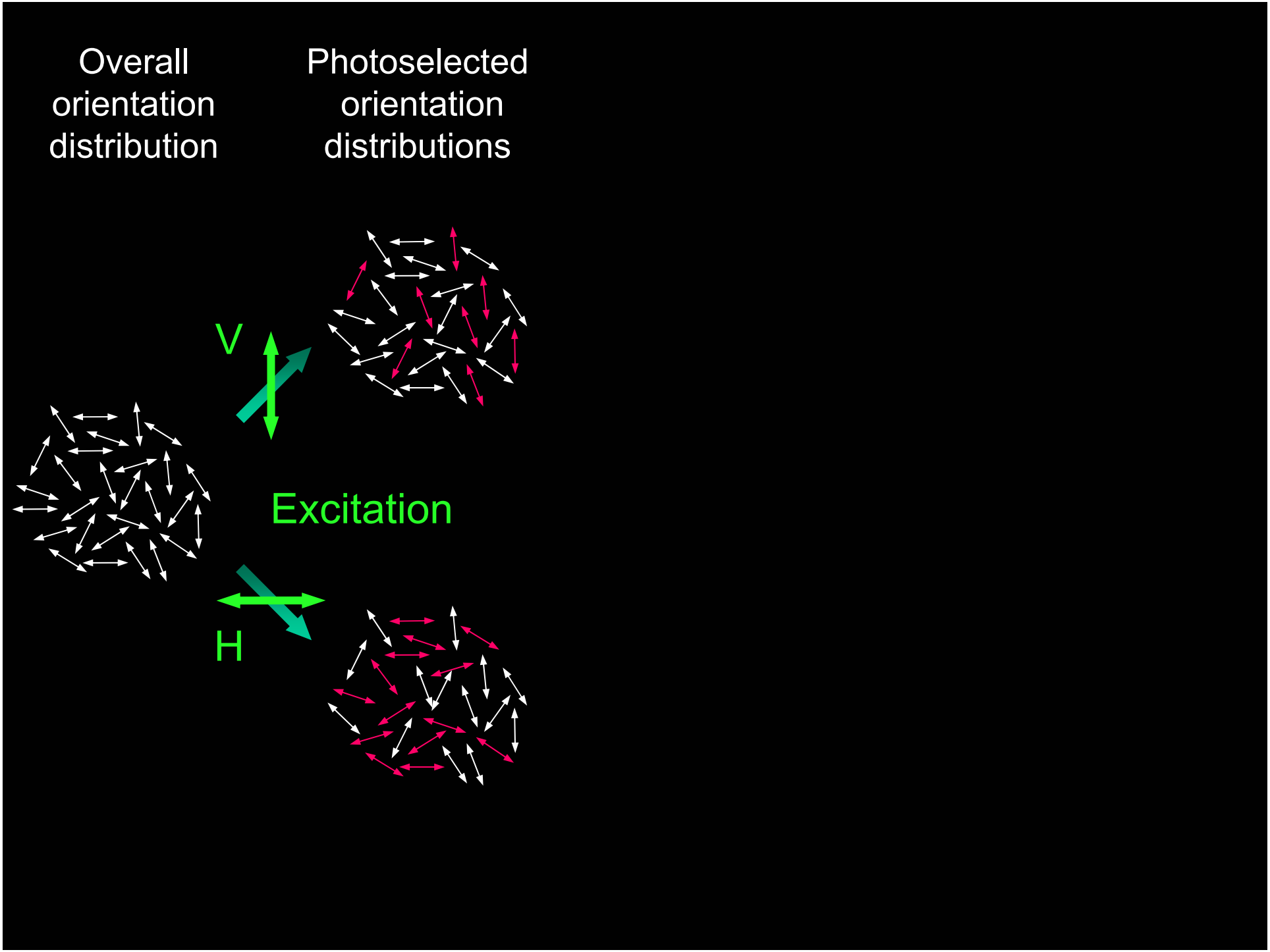


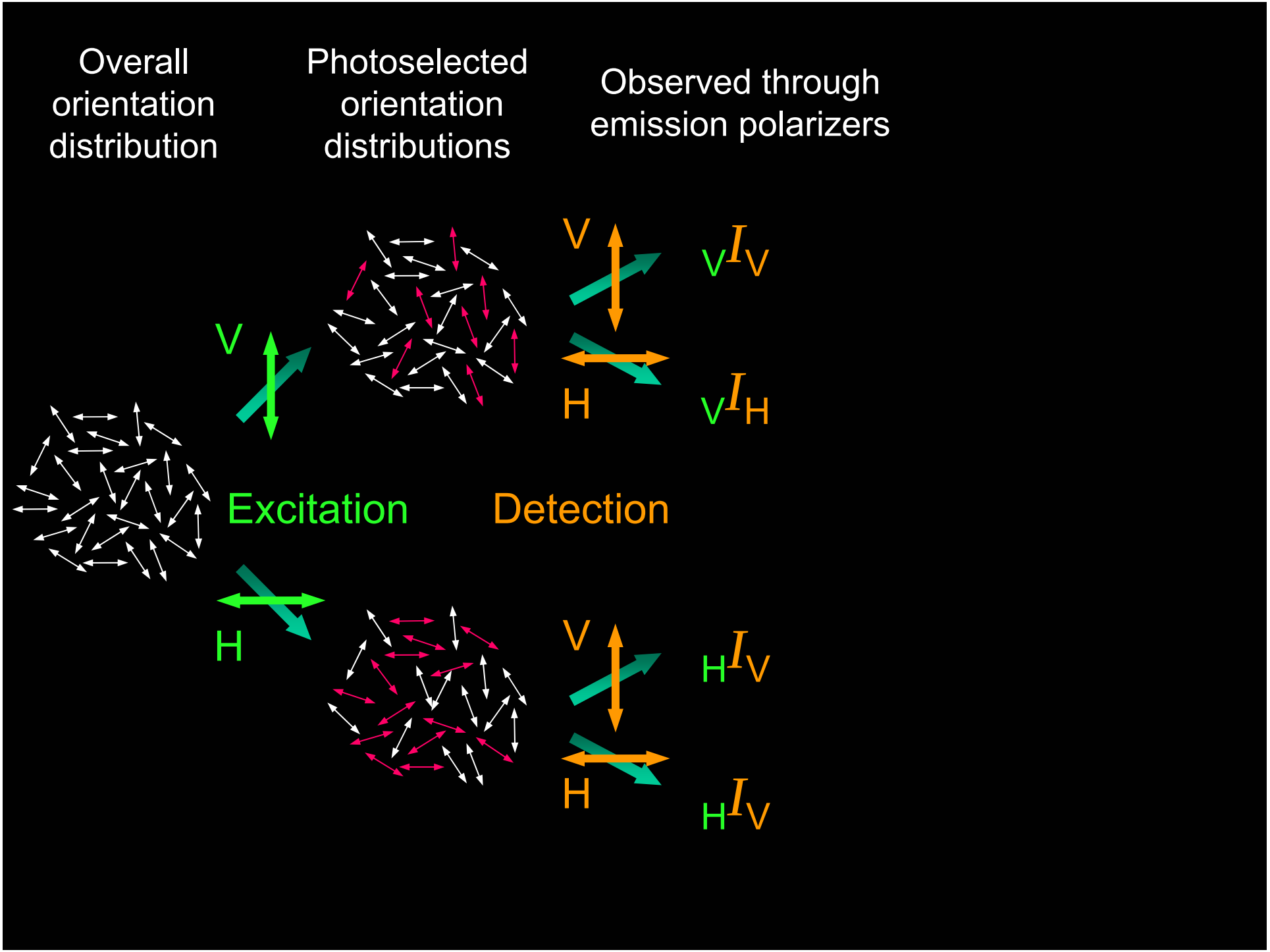
Myosin V - 5μM ATP

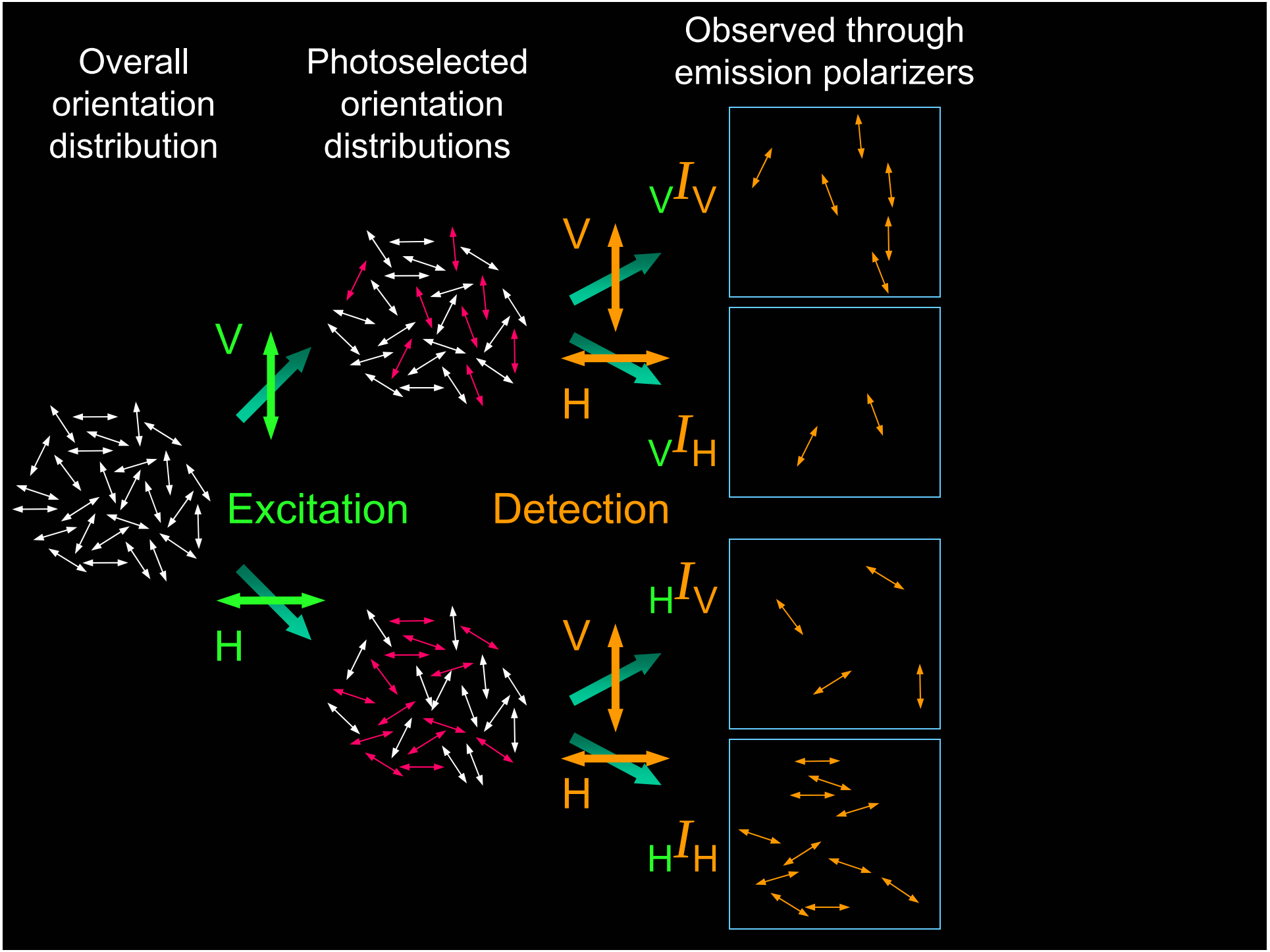


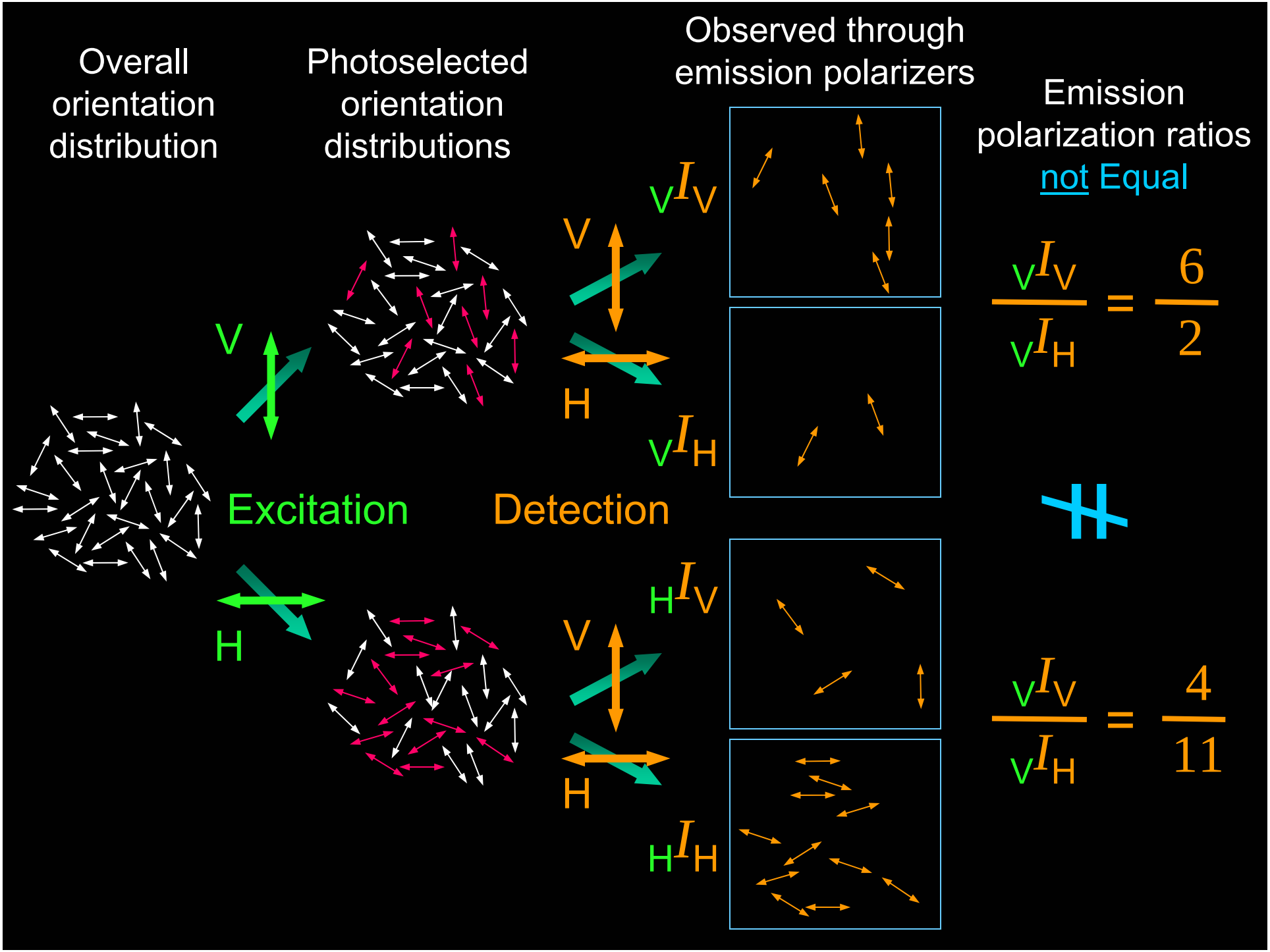
Probe
orientation
distribution

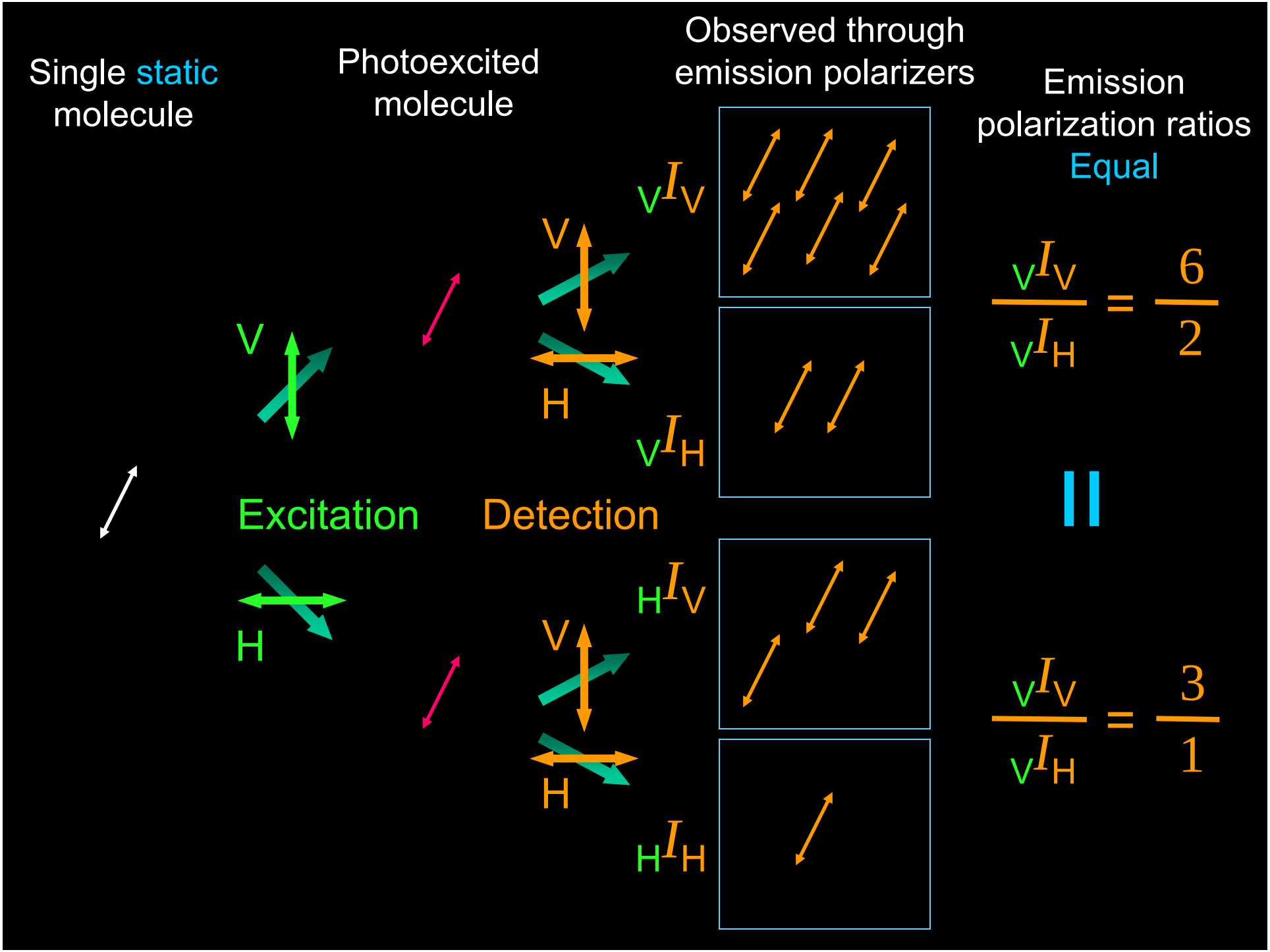


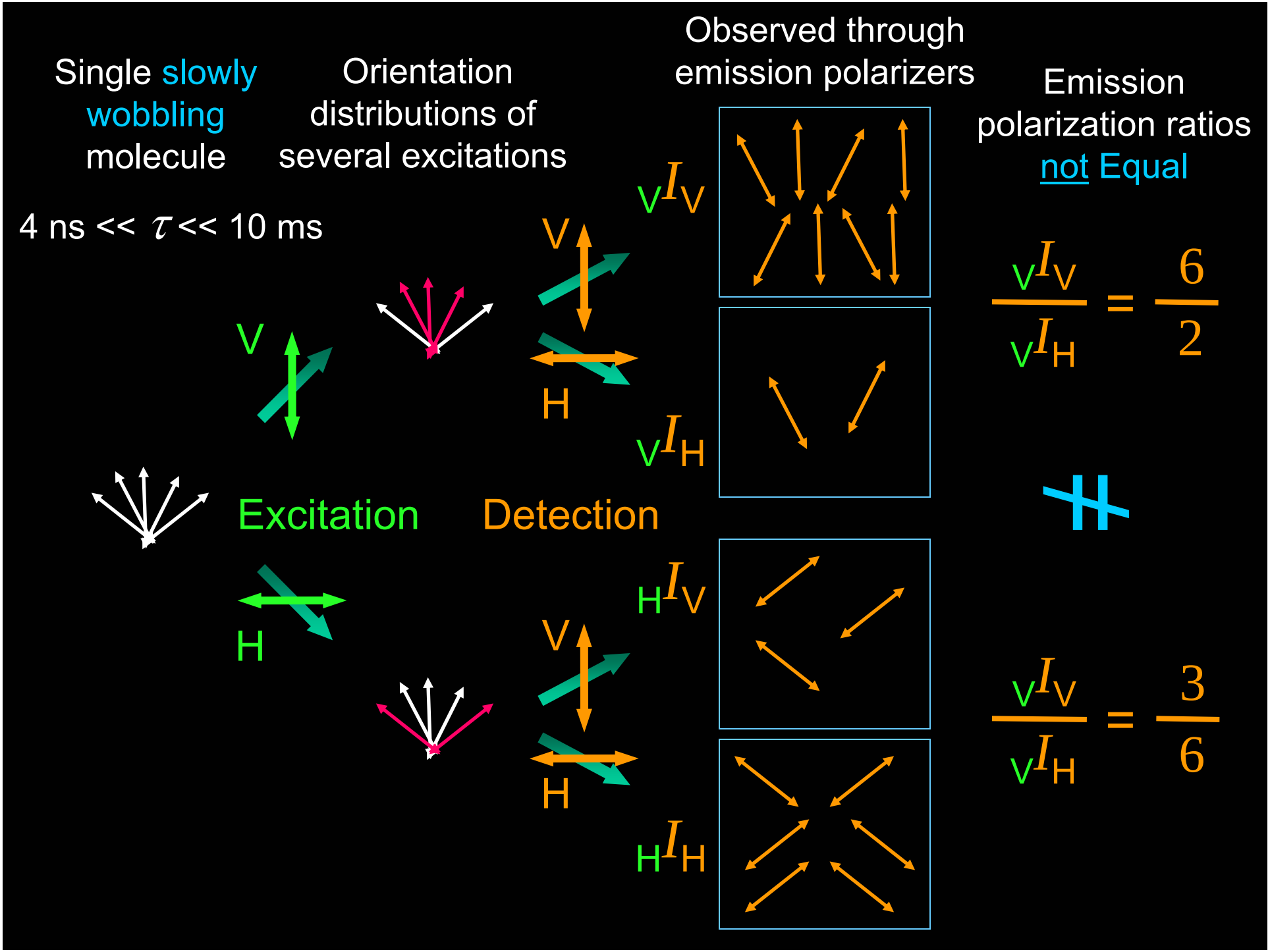

Overall orientation distribution
Photoselected orientation distributions
V
Excitation
H

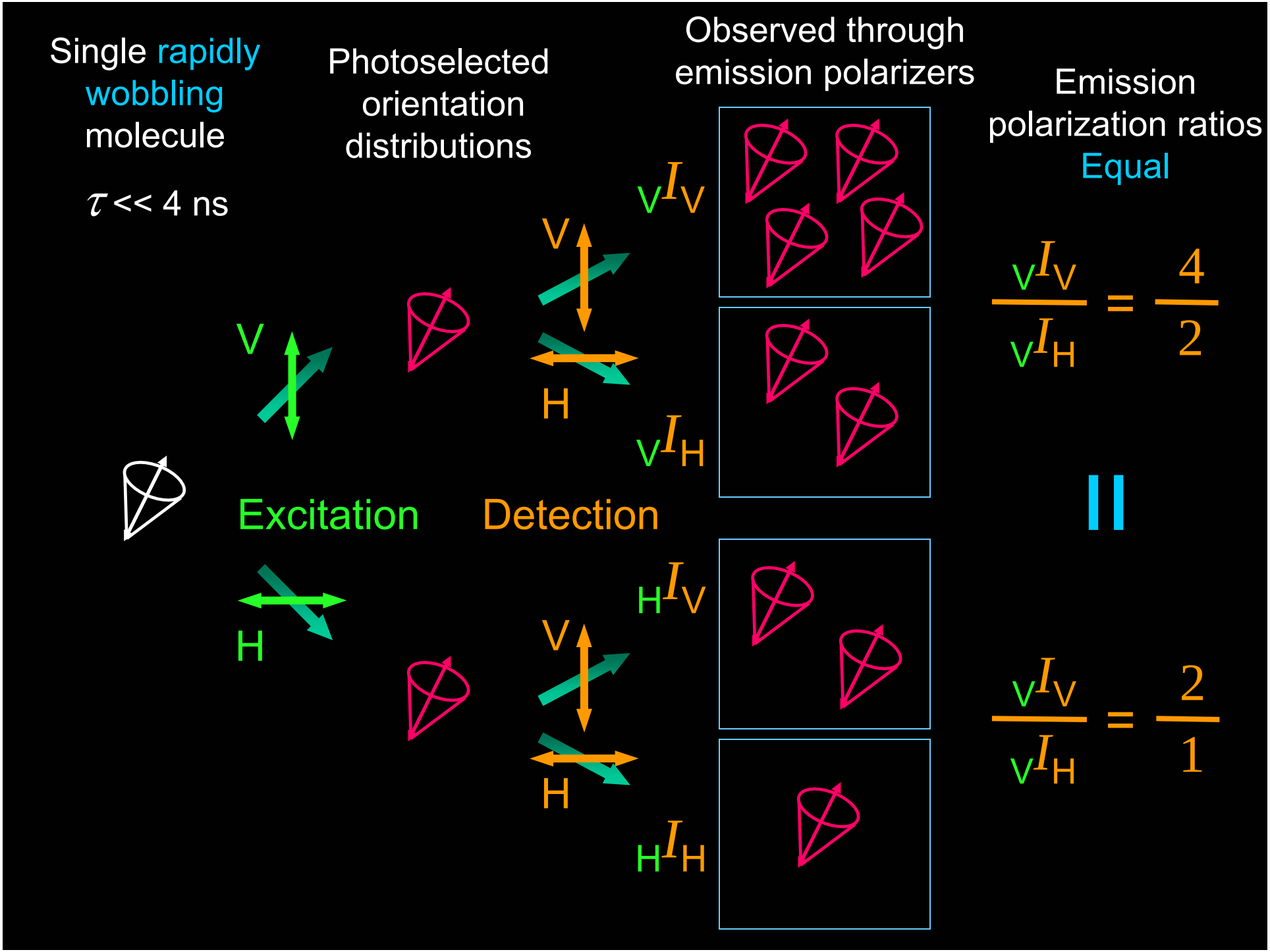

Overall orientation distribution
Photoselected orientation distributions
Observed through emission polarizers
V
H
Excitation
Detection
V
H
$_{V}I_{V}$
$_{V}I_{H}$
V
H
$_{H}I_{V}$
$_{H}I_{V}$


Overall orientation distribution
Photoselected orientation distributions
Observed through emission polarizers
V
H
Excitation
Detection
V
H
VIV
VIH
HIV
HIH


Overall orientation distribution
Photoselected orientation distributions
Observed through emission polarizers
Emission polarization ratios not Equal
V
H
Excitation
Detection
$_{V}I_{V}$
$_{V}I_{H}$
$_{H}I_{V}$
$_{H}I_{H}$
$\frac{_{V}I_{V}}{_{V}I_{H}} = \frac{6}{2}$
$\neq$
$\frac{_{V}I_{V}}{_{V}I_{H}} = \frac{4}{11}$


Single static molecule
Photoexcited molecule
Observed through emission polarizers
Emission polarization ratios Equal
V
H
Excitation
Detection
$_{V}I_{V}$
$_{V}I_{H}$
$_{H}I_{V}$
$_{H}I_{H}$
$\frac{_{V}I_{V}}{_{V}I_{H}} = \frac{6}{2}$
II
$\frac{_{V}I_{V}}{_{V}I_{H}} = \frac{3}{1}$


Single slowly wobbling molecule
Orientation distributions of several excitations
Observed through emission polarizers
Emission polarization ratios not Equal
4 ns << τ << 10 ms
V
H
Excitation
Detection
$_{V}I_{V}$
$_{V}I_{H}$
$_{H}I_{V}$
$_{H}I_{H}$
$\frac{_{V}I_{V}}{_{V}I_{H}} = \frac{6}{2}$
$\neq$
$\frac{_{V}I_{V}}{_{V}I_{H}} = \frac{3}{6}$


Single rapidly wobbling molecule
τ << 4 ns
Photoselected orientation distributions
Observed through emission polarizers
Emission polarization ratios Equal
V
H
Excitation
Detection
$_{V}I_{V}$
$_{V}I_{H}$
$_{H}I_{V}$
$_{H}I_{H}$
$\frac{_{V}I_{V}}{_{V}I_{H}} = \frac{4}{2}$
II
$\frac{_{V}I_{V}}{_{V}I_{H}} = \frac{2}{1}$

Expressions for Data Analysis

General Expression

$$ {}_{\varepsilon}I_{\alpha} = K \int_0^{\infty} \iint \rho(\theta_{\mathrm{a}},\, \phi_{\mathrm{a}},\, \theta_{\mathrm{e}},\, \phi_{\mathrm{e}},\, t)(1/\tau)\mathrm{e}^{-(t/\tau)} P_{\mathrm{a}}(\theta_{\mathrm{a}},\, \phi_{\mathrm{a}},\, \hat{\varepsilon}) P_{\mathrm{e}}(\theta_{\mathrm{e}},\, \phi_{\mathrm{e}},\, \hat{\alpha})\, \mathrm{d}\Omega_{\mathrm{a}}\, \mathrm{d}\Omega_{\mathrm{e}}\, \mathrm{d}t $$

Fast Wobble $\tau_c << \tau_f$

$$ {}_{\varepsilon}I_{\alpha} = K \left[\int \rho_{\mathrm{fa}}(\theta_{\mathrm{a}},\, \phi_{\mathrm{a}}) P_{\mathrm{a}}(\theta_{\mathrm{a}},\, \phi_{\mathrm{a}},\, \hat{\varepsilon}) \mathrm{d}\Omega_{\mathrm{a}} \right] \left[\int \rho_{\mathrm{fe}}(\theta_{\mathrm{e}},\, \phi_{\mathrm{e}}) P_{\mathrm{e}}(\theta_{\mathrm{e}},\, \phi_{\mathrm{e}},\, \hat{\alpha}) \mathrm{d}\Omega_{\mathrm{e}} \right] $$

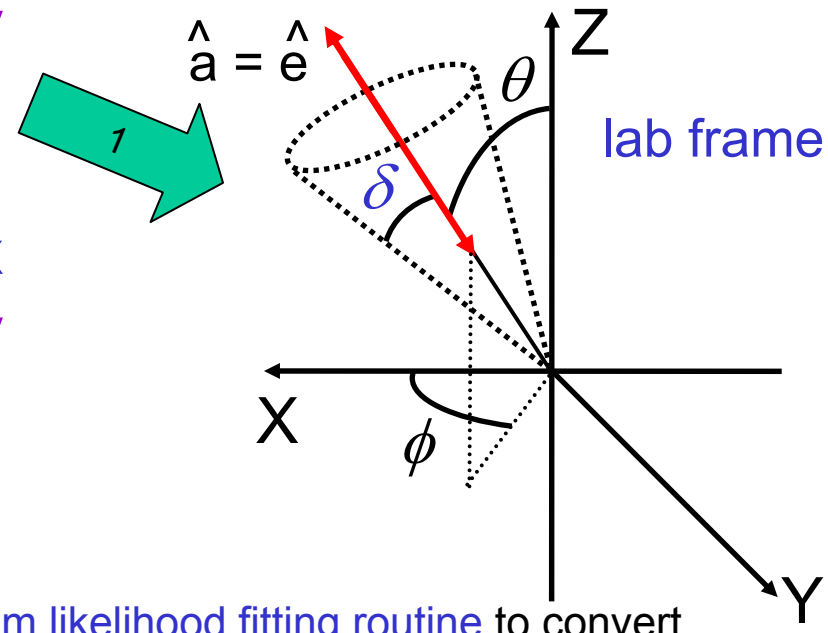
Slow Wobble $\tau_f << \tau_c << \tau_g$

$$ {}_{\varepsilon}I_{\alpha} = K \iint \rho_{\mathrm{s}}(\theta_{\mathrm{a}},\, \phi_{\mathrm{a}},\, \theta_{\mathrm{e}},\, \phi_{\mathrm{e}}) P_{\mathrm{a}}(\theta_{\mathrm{a}},\, \phi_{\mathrm{a}},\, \hat{\varepsilon}) P_{\mathrm{e}}(\theta_{\mathrm{e}},\, \phi_{\mathrm{e}},\, \hat{\alpha}) \mathrm{d}\Omega_{\mathrm{a}} \mathrm{d}\Omega_{\mathrm{e}} $$

Data Analysis

polarized intensities

s1x
s1y
p1x
p1y
s2x
s2y
p2x
p2y



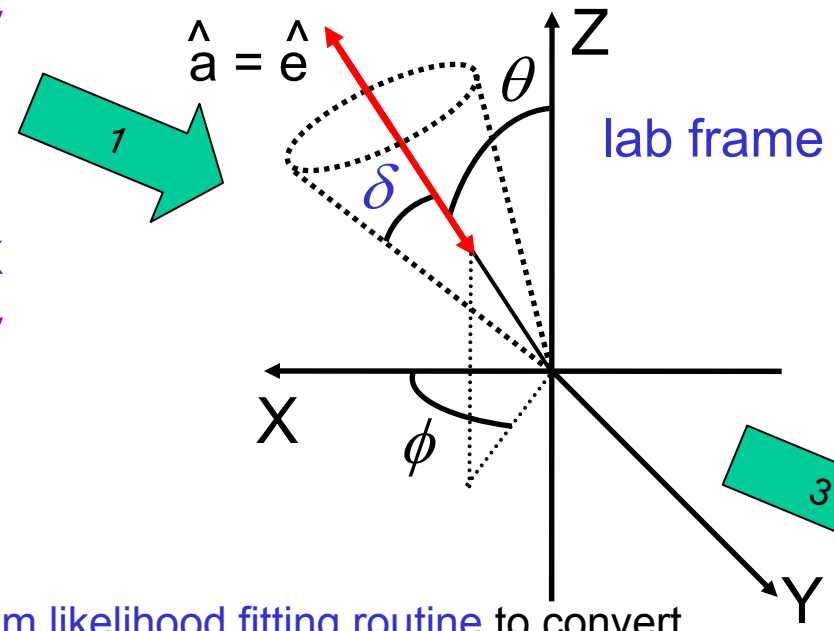
1) Maximum likelihood fitting routine to convert measured intensities to 3-D orientation: θ,ϕ,δ
Considerations include:
- colinear absorption and emission dipoles
- evanescent wave polarization
- high numerical aperture objective lens
- fast and slow motion

2) Verification of method
- Single and multi-molecule polarization of labeled actin
- Single and multi-molecule polarization of RLC-labeled myosin II

Data Analysis

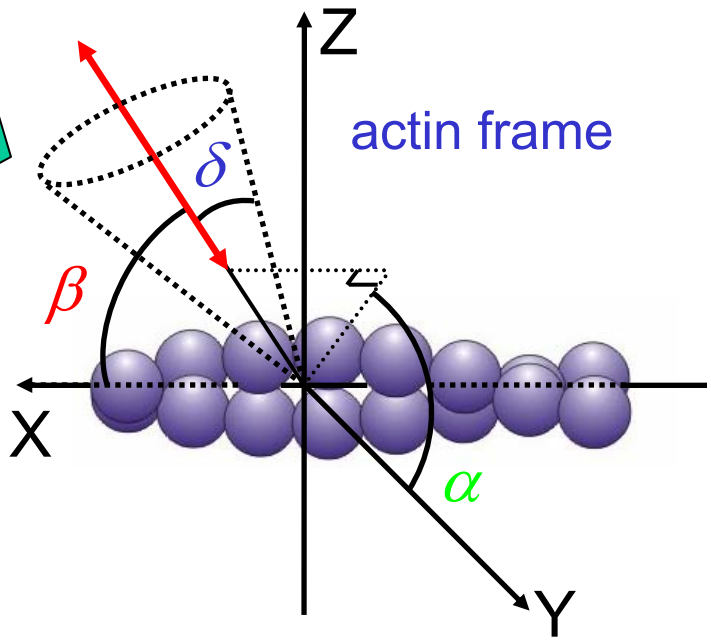
polarized intensities

s1x
s1y
p1x
p1y
s2x
s2y
p2x
p2y

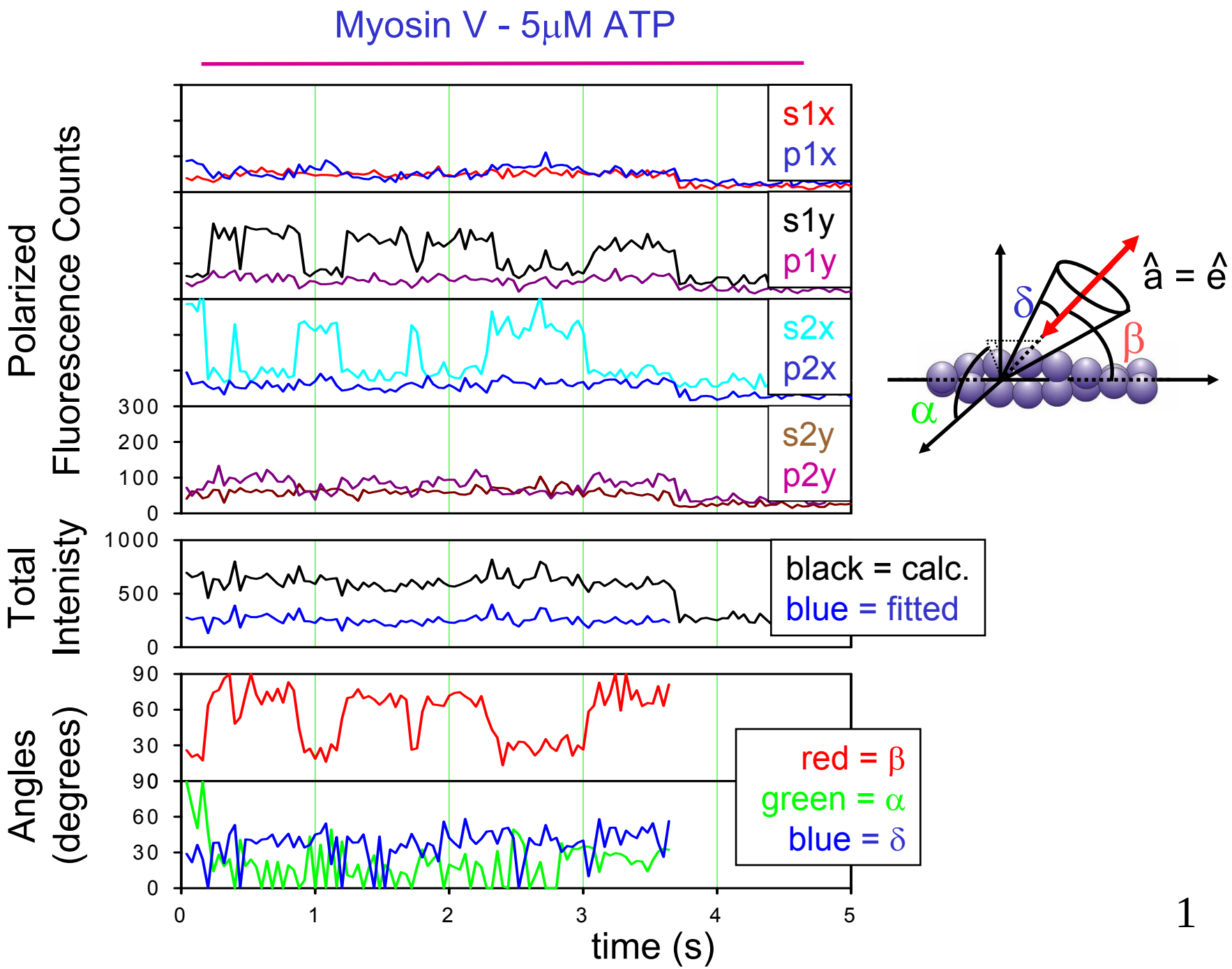


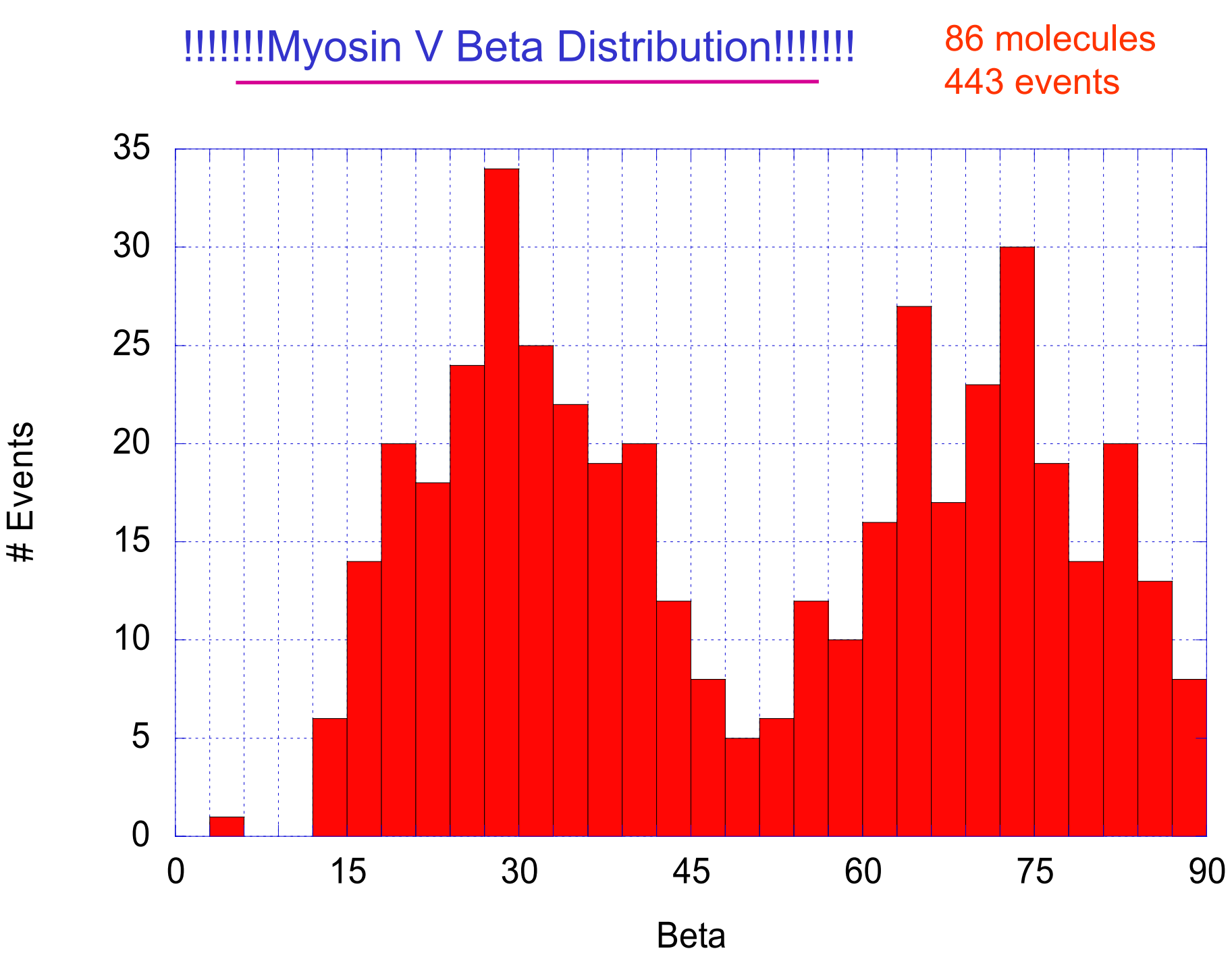
2) Verification of method

3) Euler angle transformation

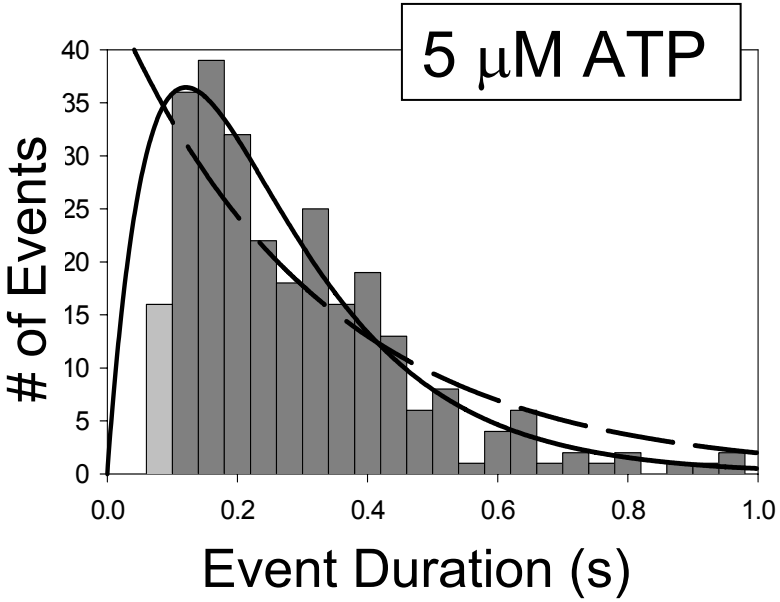


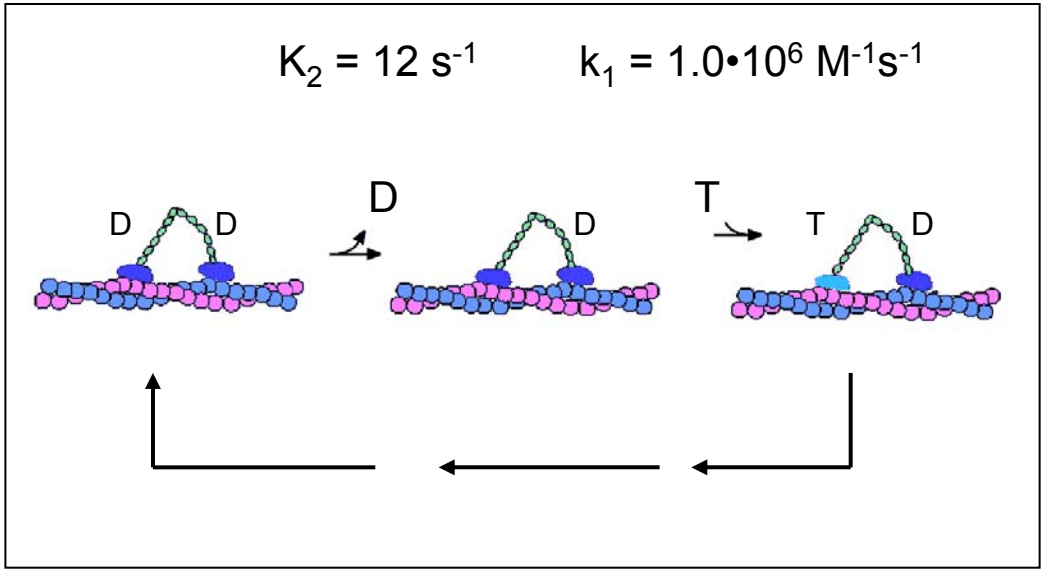
1) Maximum likelihood fitting routine to convert measured intensities to 3-D orientation: θ,ϕ,δ
Considerations include:
- colinear absorption and emission dipoles
- evanescent wave polarization
- high numerical aperture objective lens
- fast and slow motion

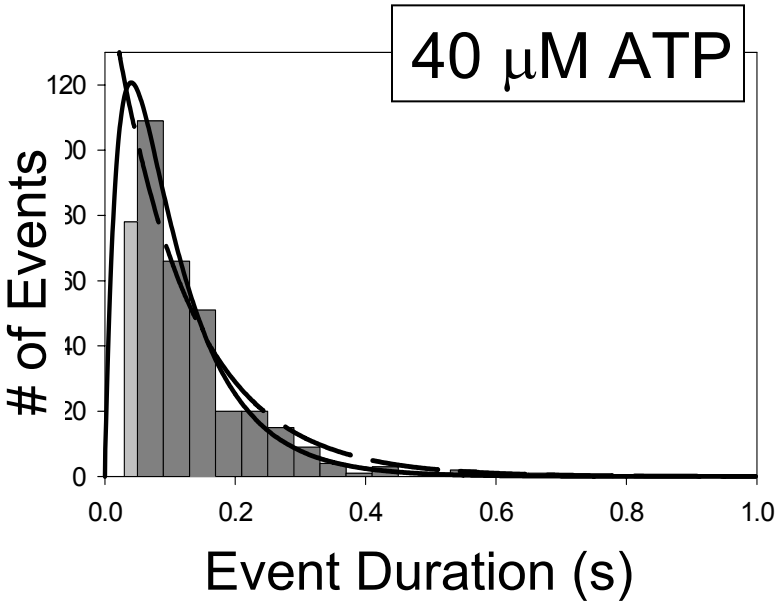

Myosin V - 5μM ATP
Polarized Fluorescence Counts
s1x
p1x
s1y
p1y
s2x
p2x
s2y
p2y
300
200
100
0
Total Intenisty
1000
500
0
black = calc.
blue = fitted
Angles (degrees)
90
60
30
90
60
30
0
red = β
green = α
blue = δ
0
1
2
3
4
5
time (s)
δ
β
α
â = ê


!!!!!!!Myosin V Beta Distribution!!!!!!!
86 molecules
443 events
Events
Beta
0
5
10
15
20
25
30
35
0
15
30
45
60
75
90

Event Time Histograms



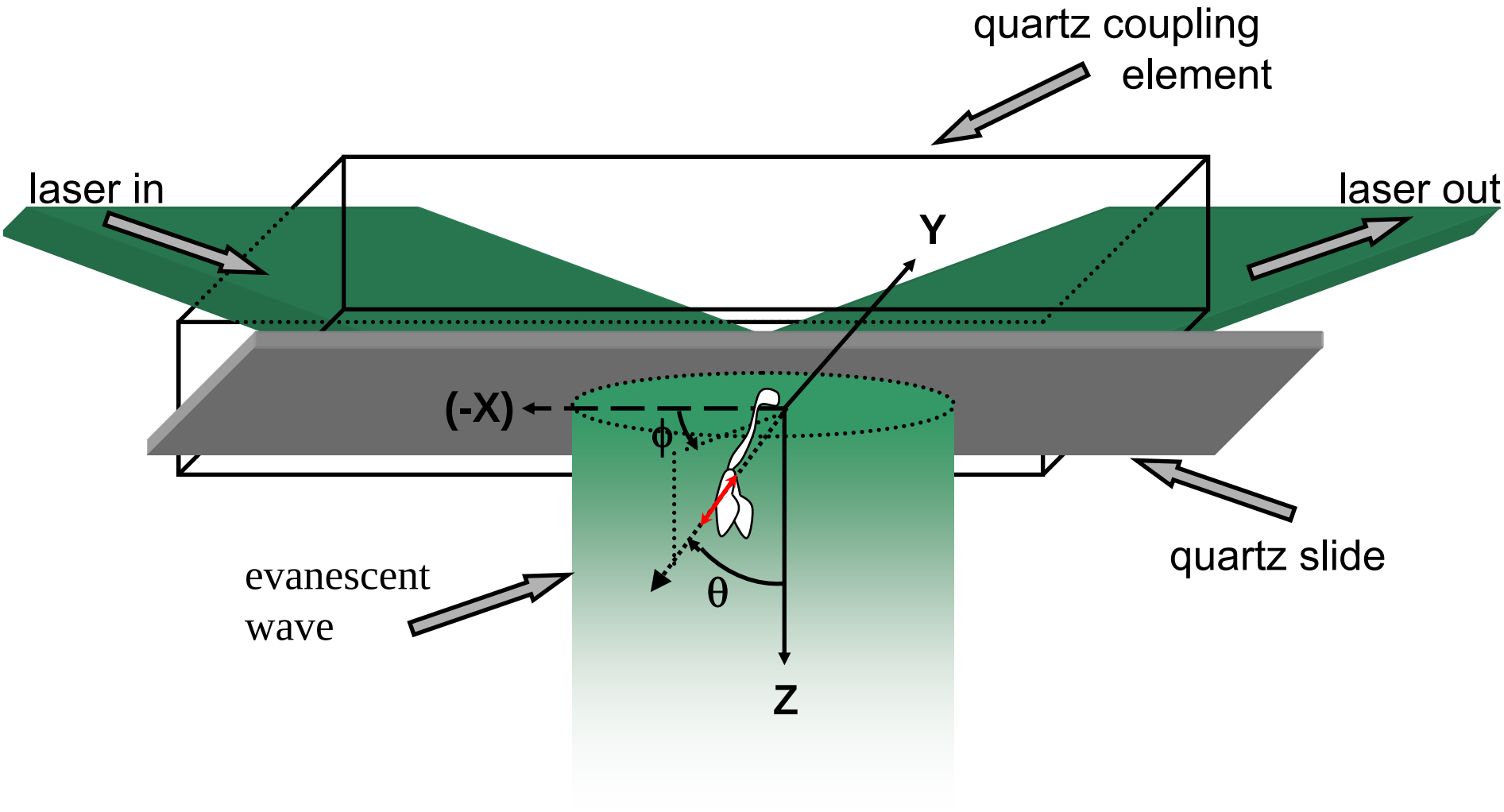




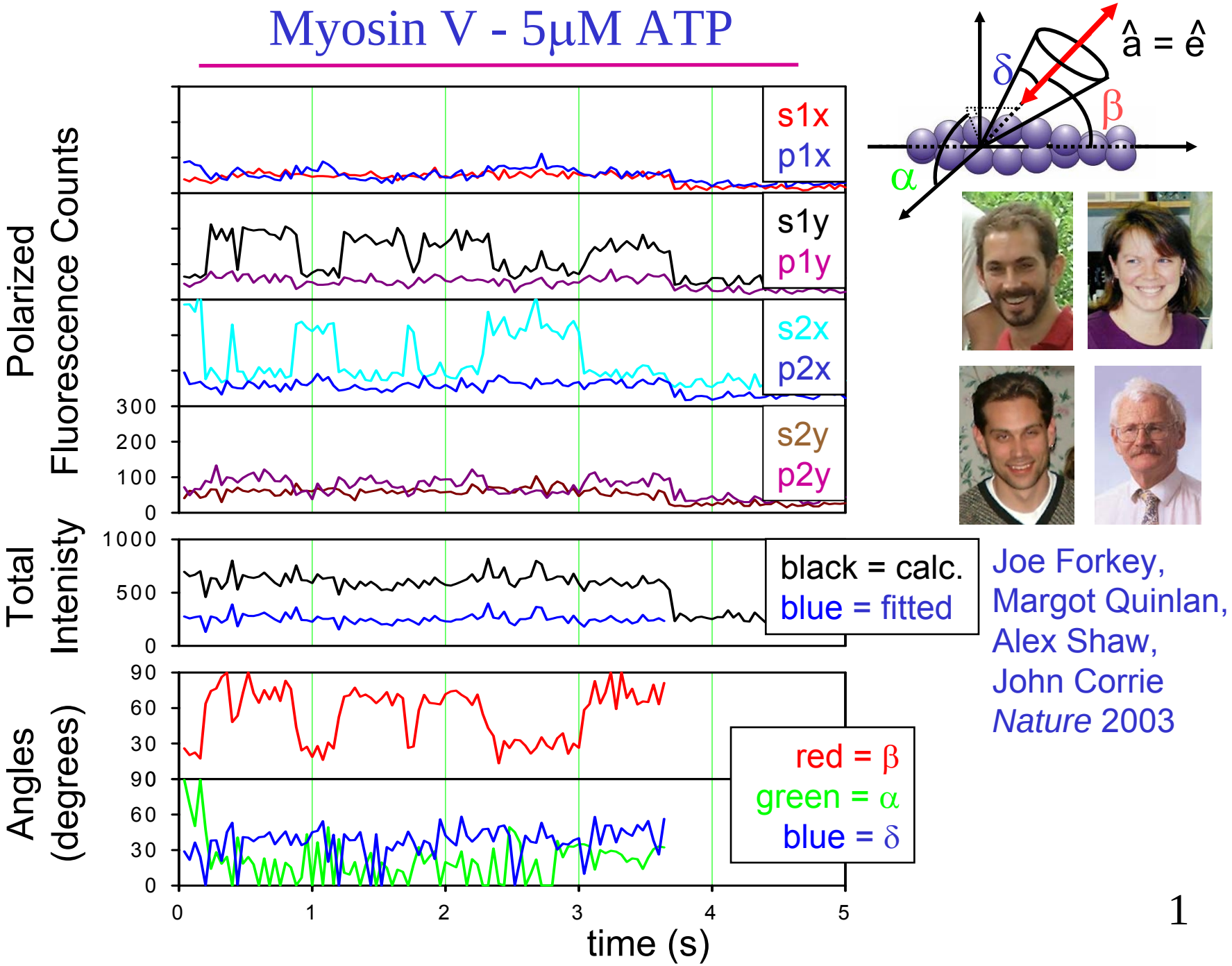
$$\text{velocity} \times \left(\frac{1}{k_1[ATP]} + \frac{1}{k_2} \right) = \text{Translation / Tilt}$$

[ATP] (μM)	Velocity (nm/s)	Dwell time (ms)	Step (nm)
5	138 ± 3	264 ± 26	36.4 ± 4
40	354 ± 5	107 ± 9	38.1 ± 3.5

Evanescent Wave (TIRF) Microscopy



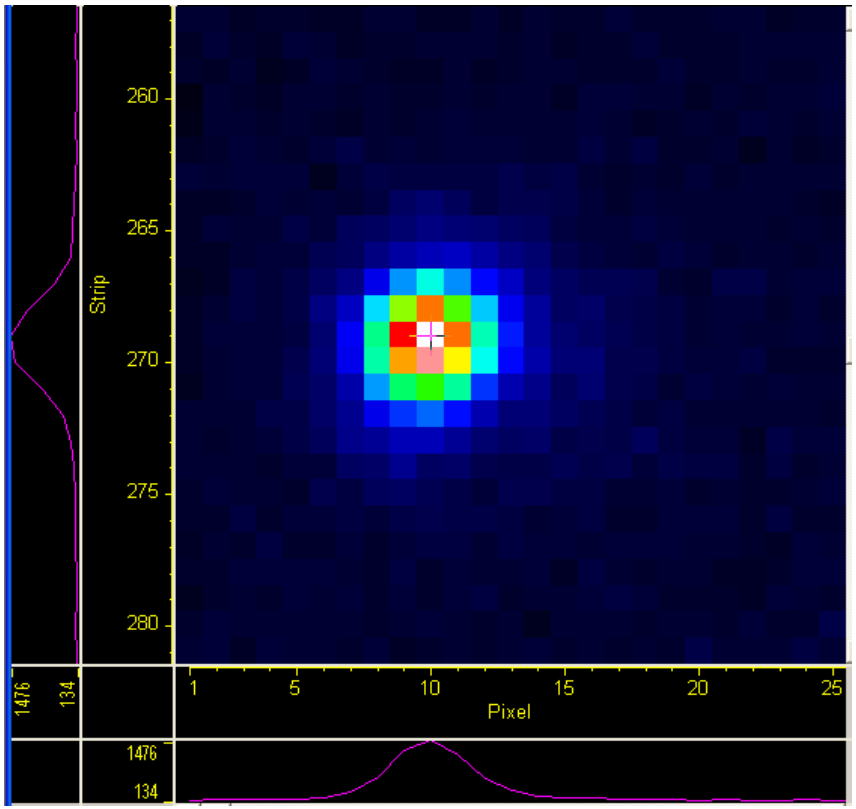
Myosin V - 5μM ATP

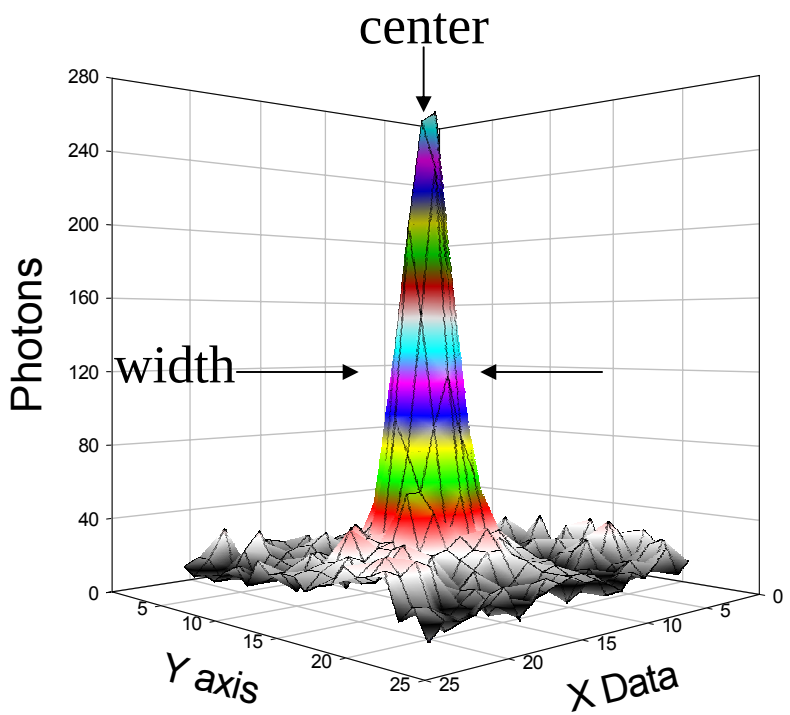


Joe Forkey,
Margot Quinlan,
Alex Shaw,
John Corrie
Nature 2003

Diffraction limited spot

Width of $\lambda/2 \approx 250$ nm



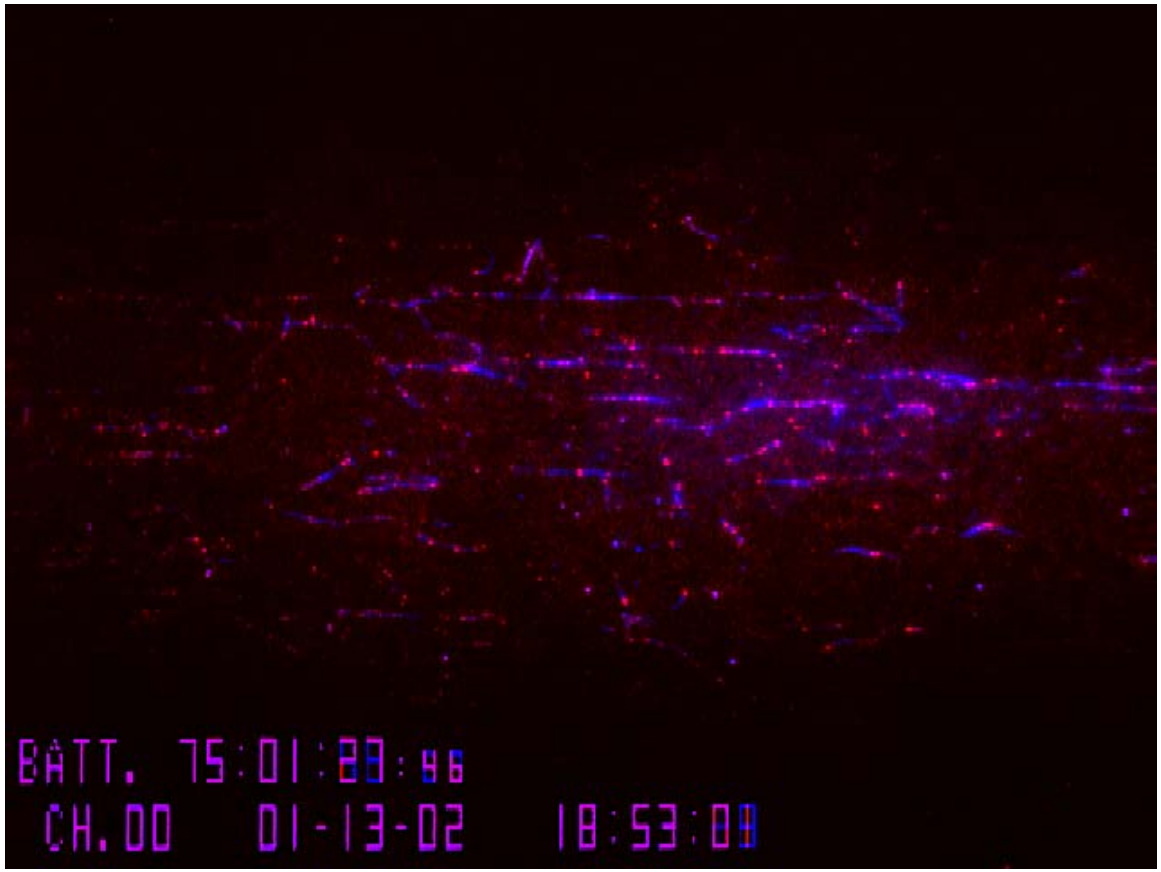


With enough photons (signal to noise) …

Center can be determined to ≈ 1 nm.

Center represents (under appropriate conditions) position of dye.

Myosin V Processivity



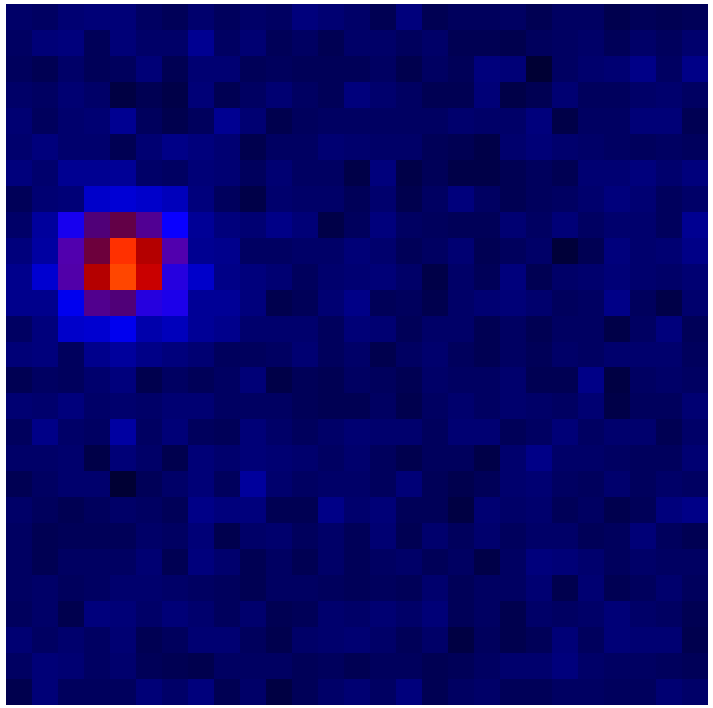
20,000 nm

10x speed

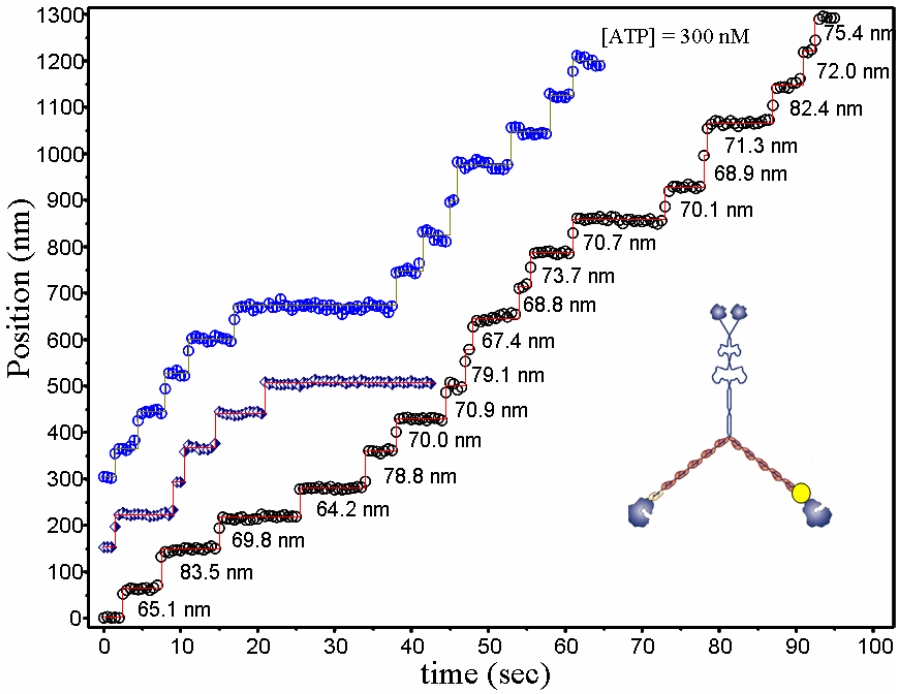
FIONA

The Movie

Fluorescence Imaging at One Nanometer Accuracy

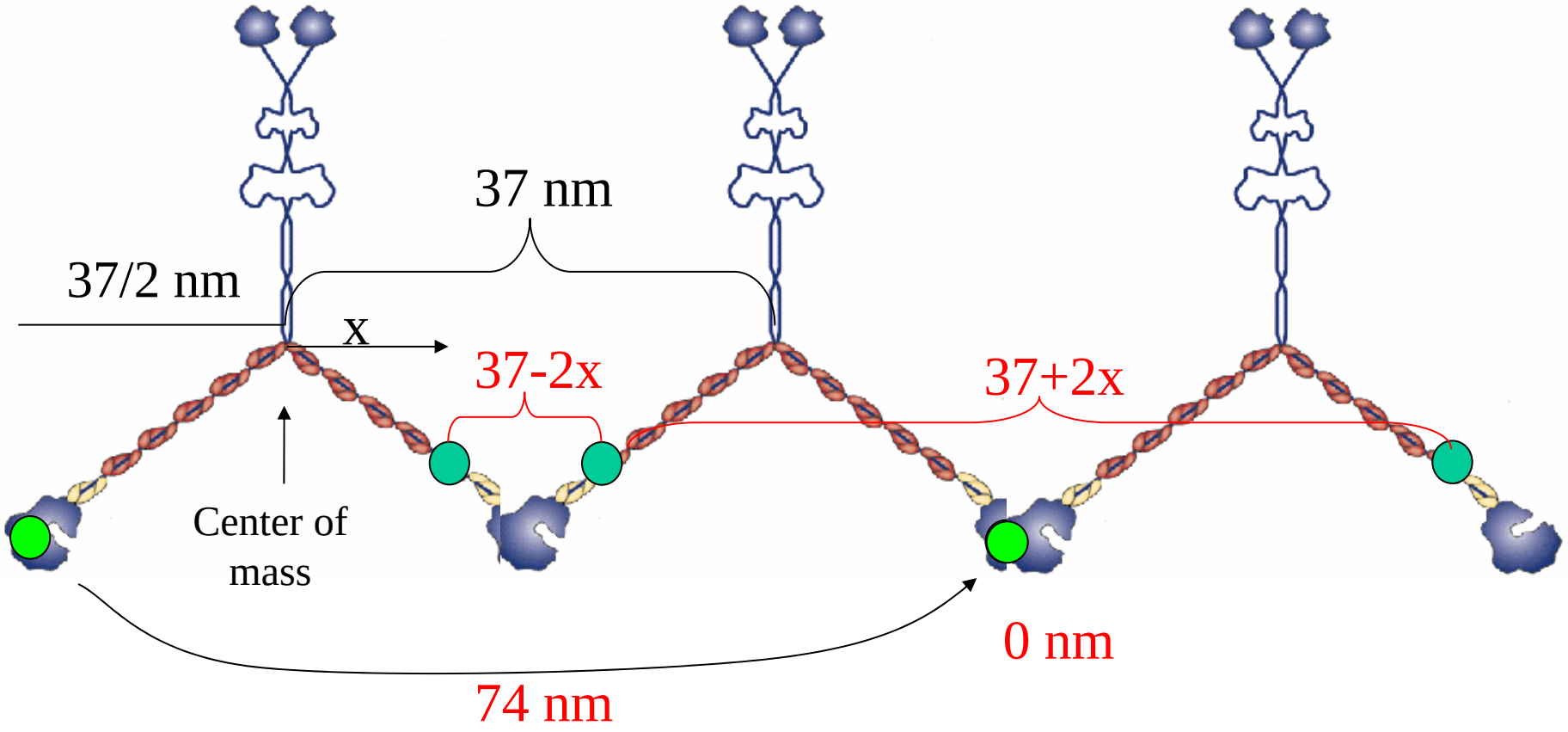


1000 nm



Paul Selvin, Taekjip Ha
and colleagues
University of Illinois

Myosin V Labeling on Light Chain: Expected Step Sizes



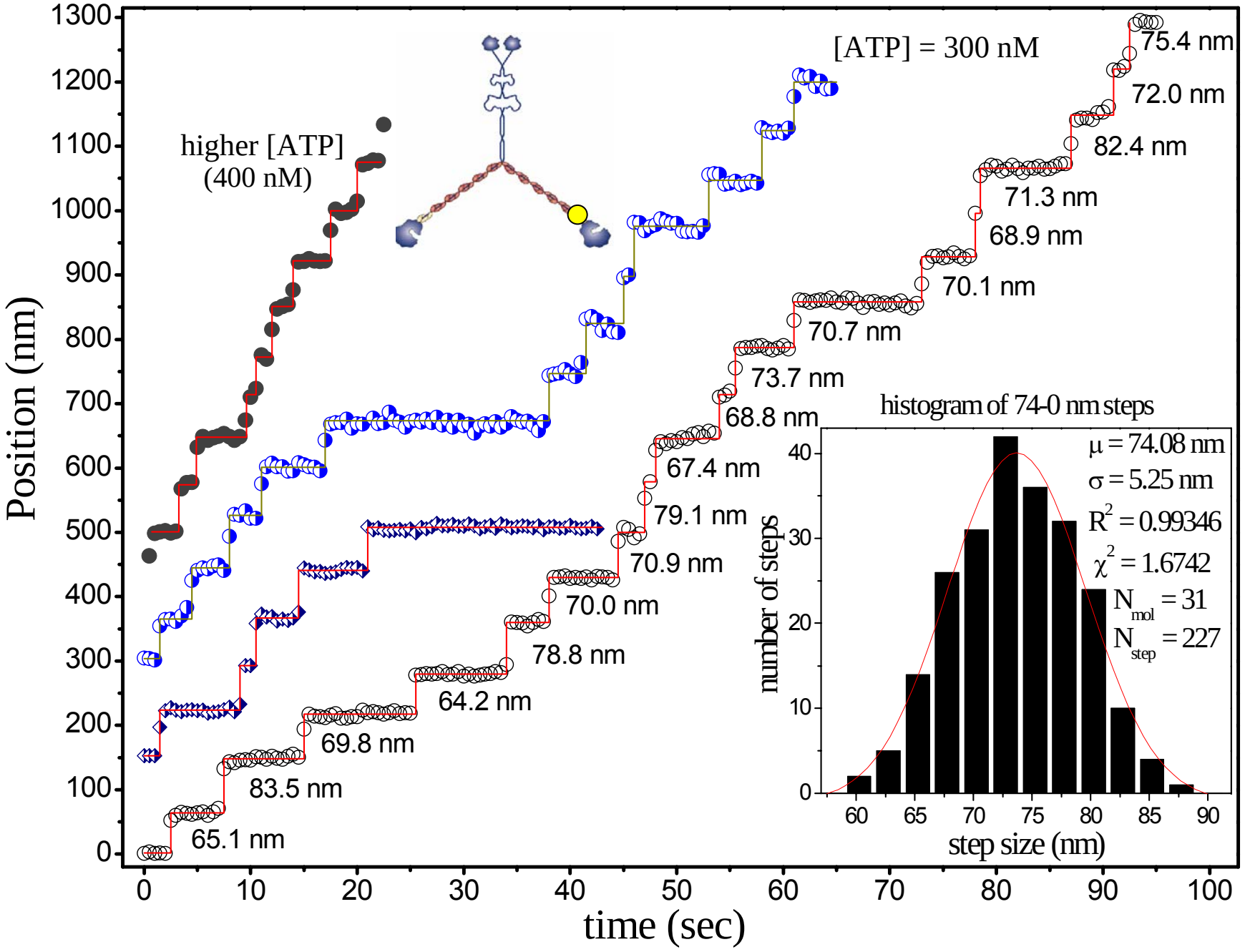
Expected step size

Hand-over-hand:

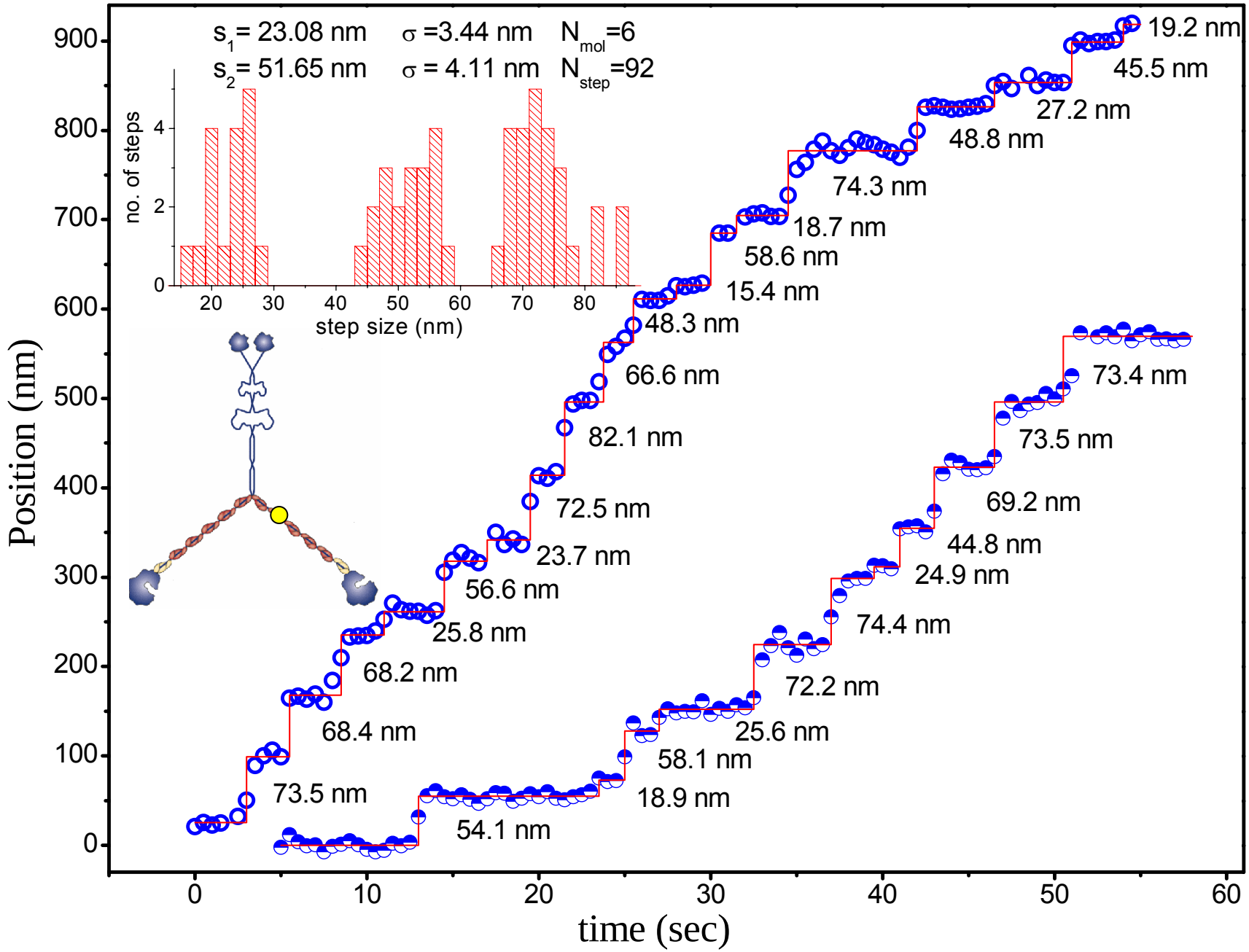
Head = 2 x 37 nm= 74, 0, 74 nm

CaM-Dye: 37-2x, 37+2x, …

Myosin V steps: 74 nm +/- 5nm

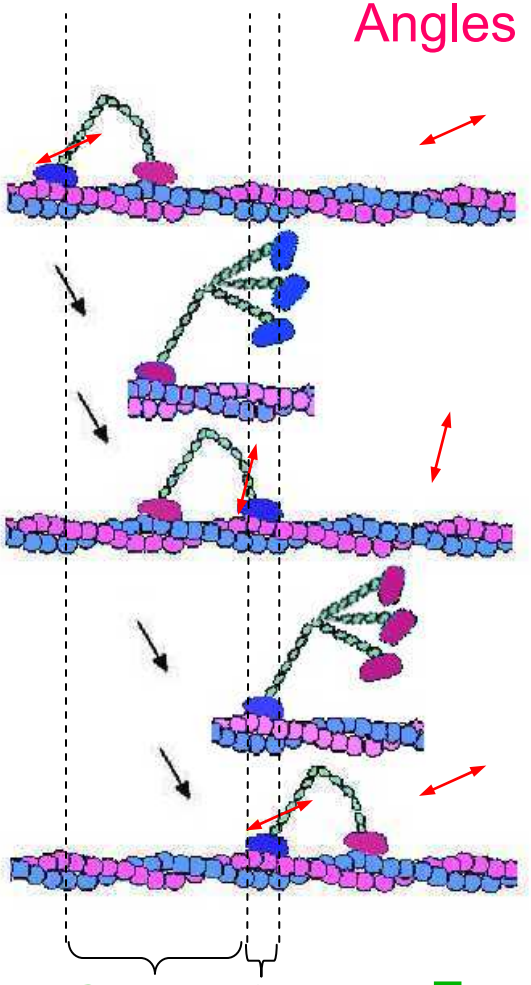


52-23 nm steps

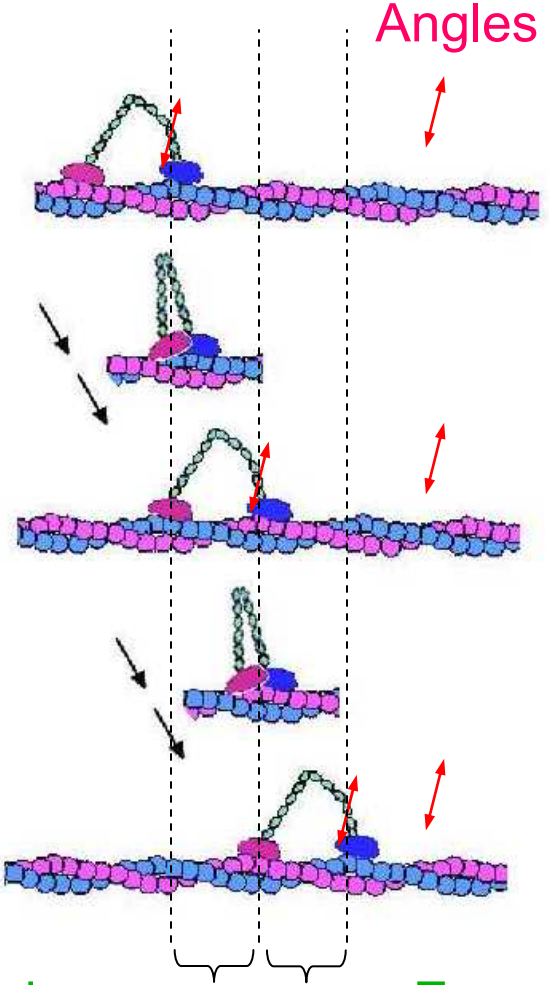


Models for Myosin V Processivity

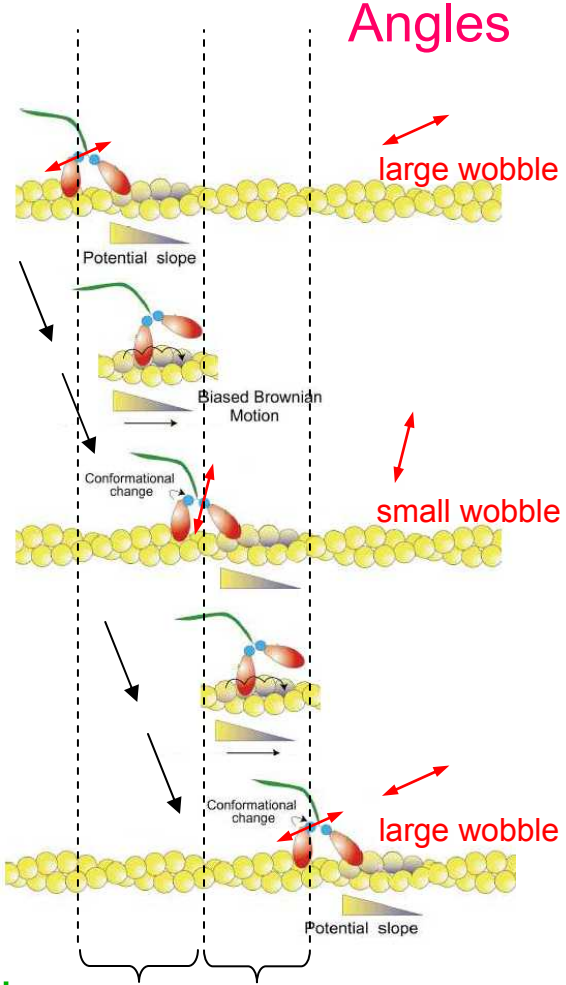
A. Hand Over Hand



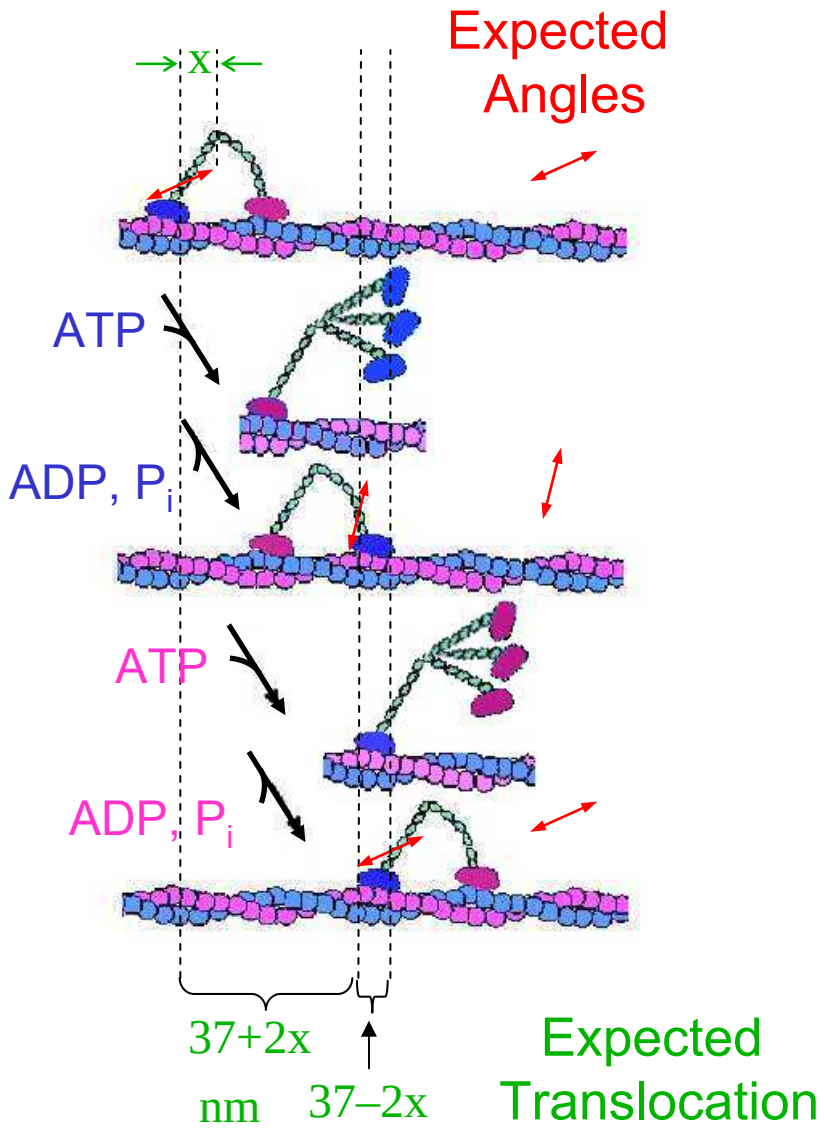
B. Inch Worm



C. Hot Spot



Hand over Hand Model for Myosin V Processivity



Coworkers and Collaborators on Single Molecule Fluorescence and Mechanics

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Yasuharu Takagi
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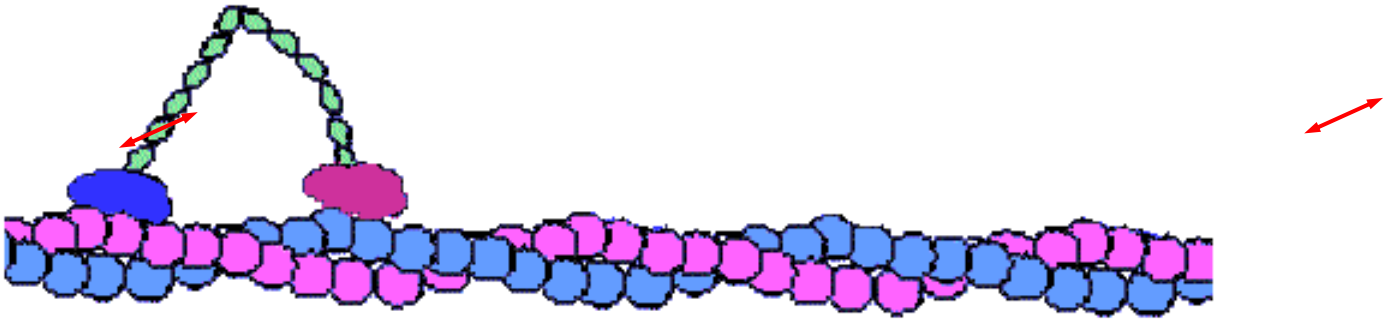
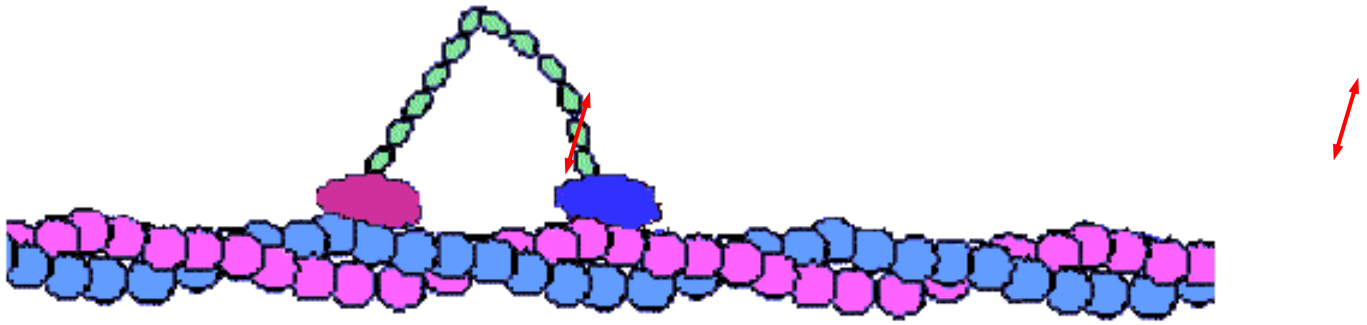
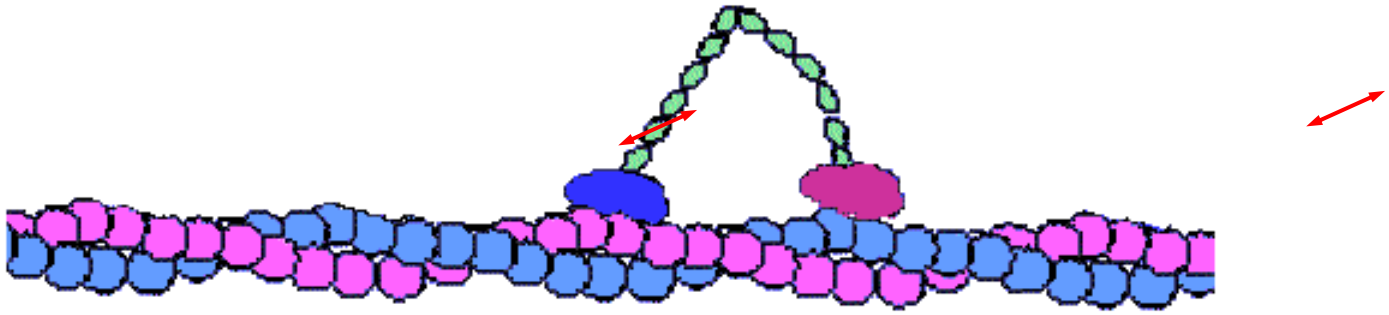
Myosin V Processivity 1



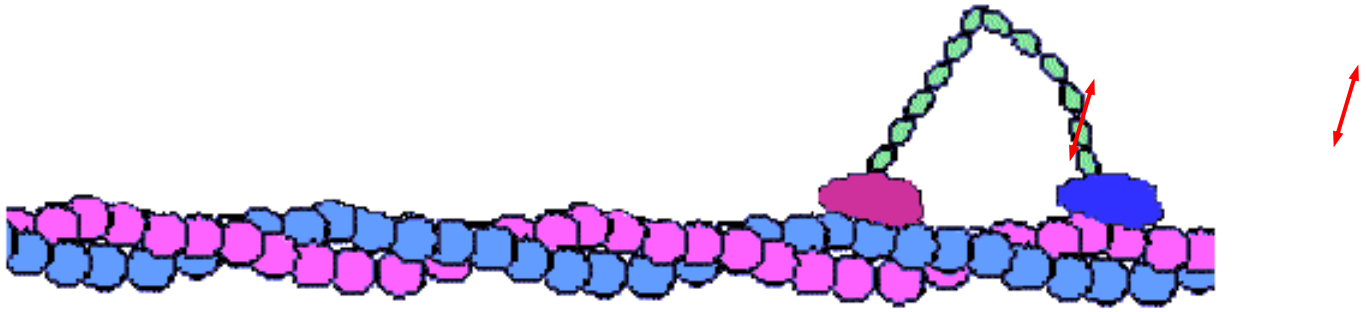
Myosin V Processivity 2

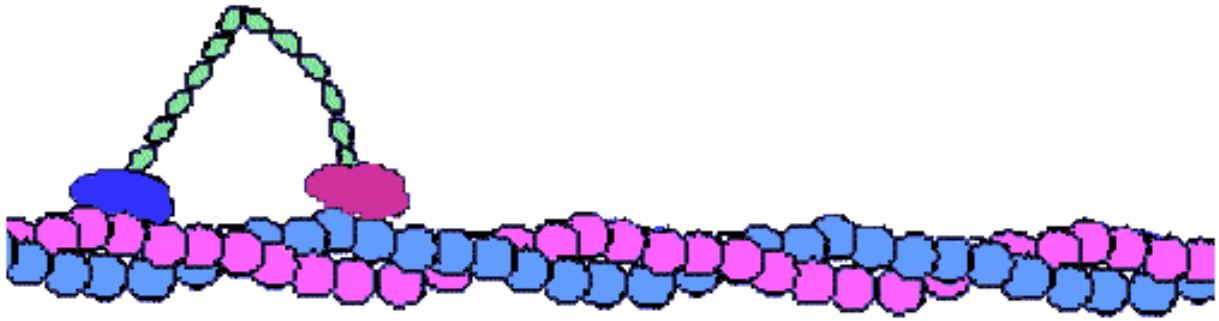


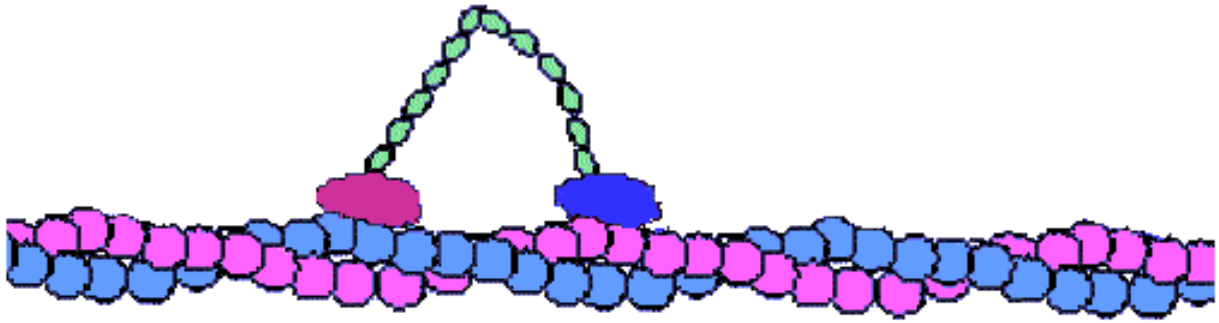
Myosin V Processivity 3

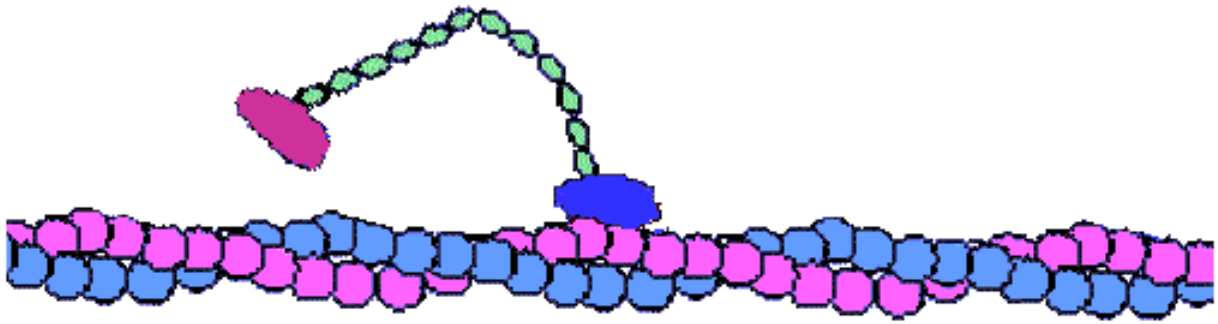


Myosin V Processivity 4

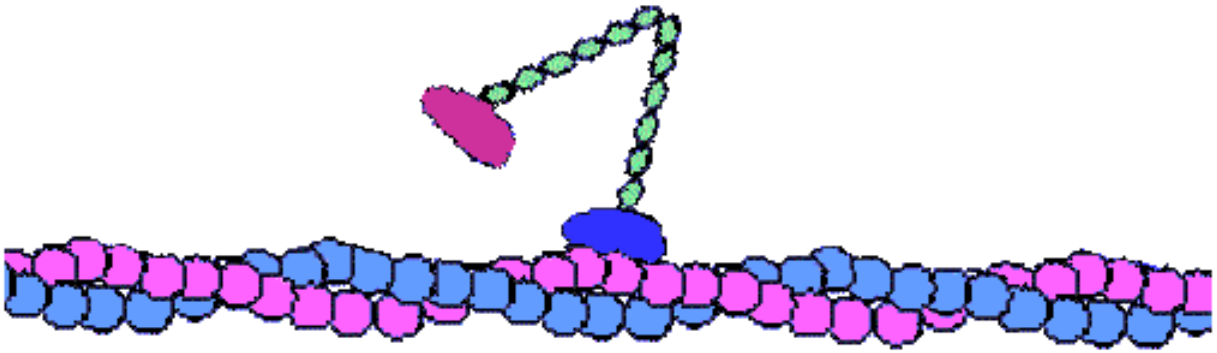




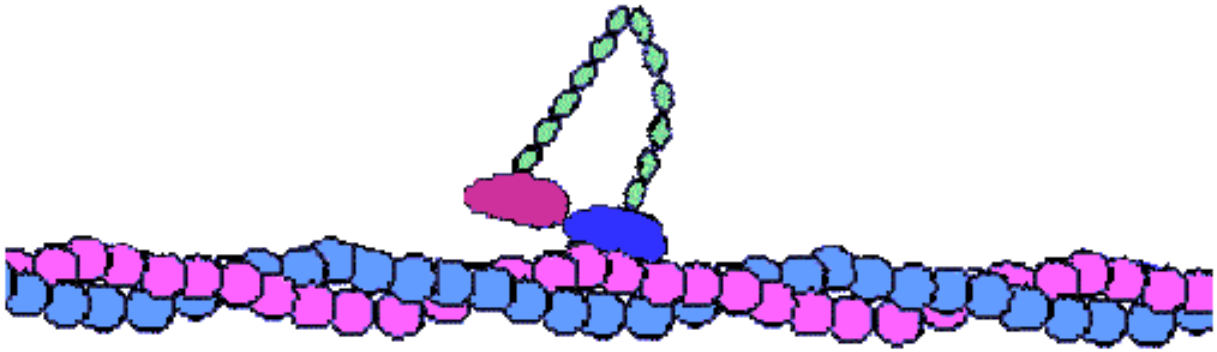


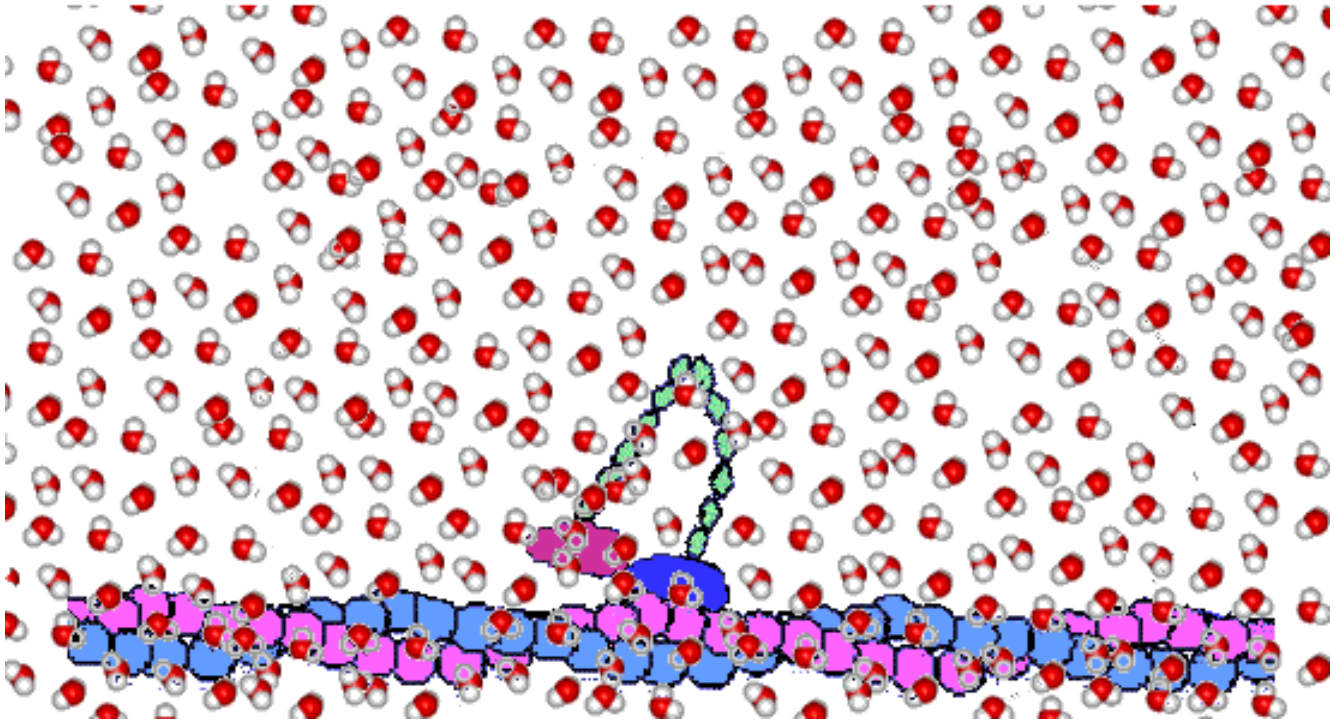


Deterministic Working Stroke

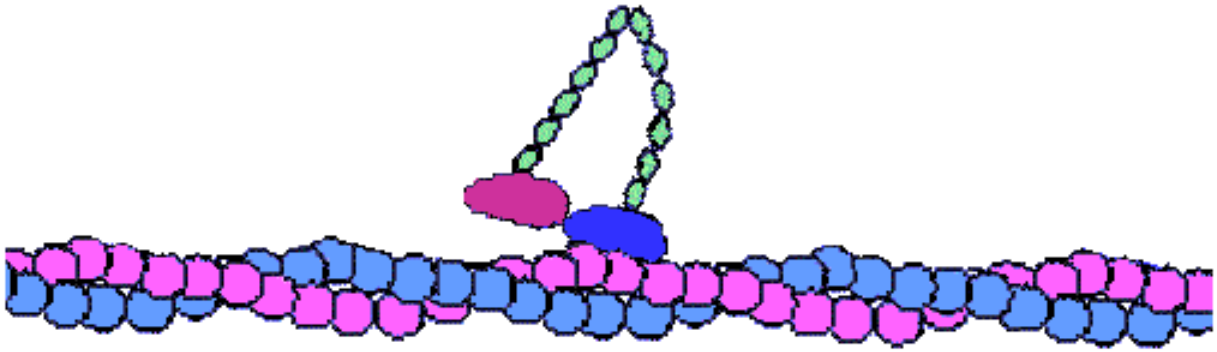


Thermal Motions

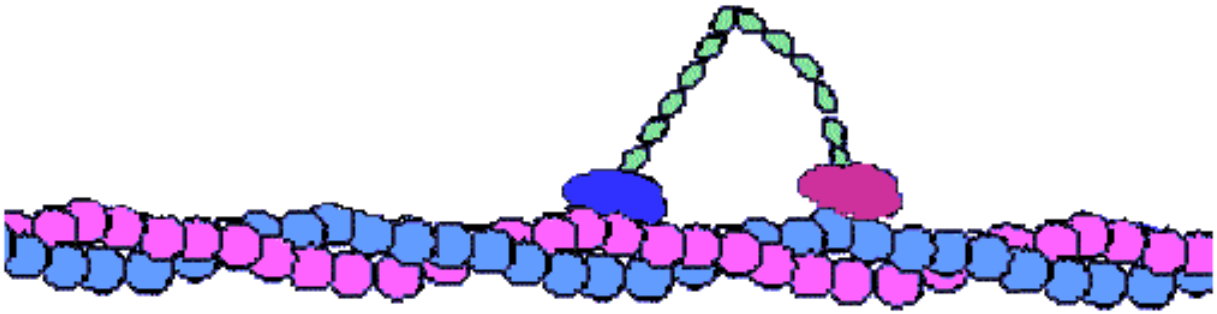


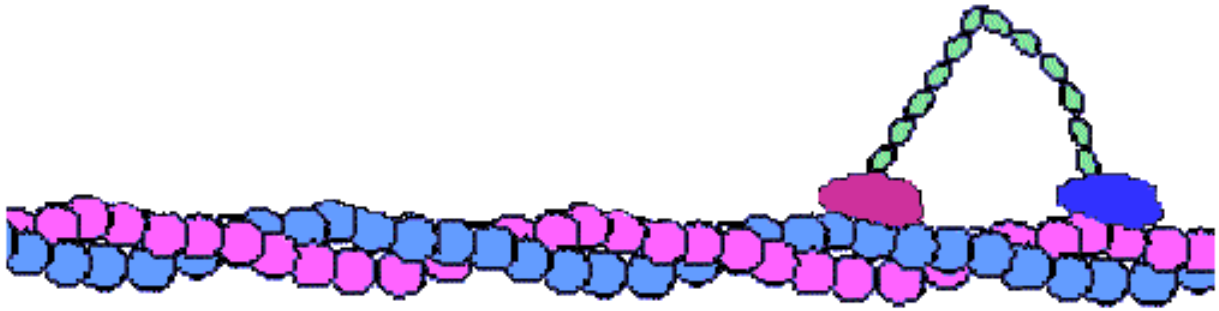


Thermal Motions

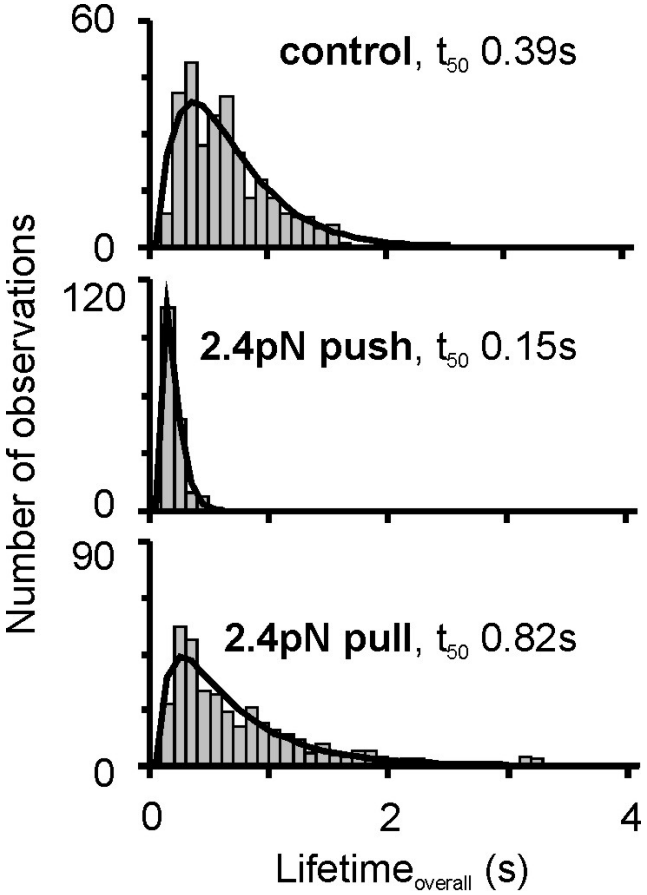


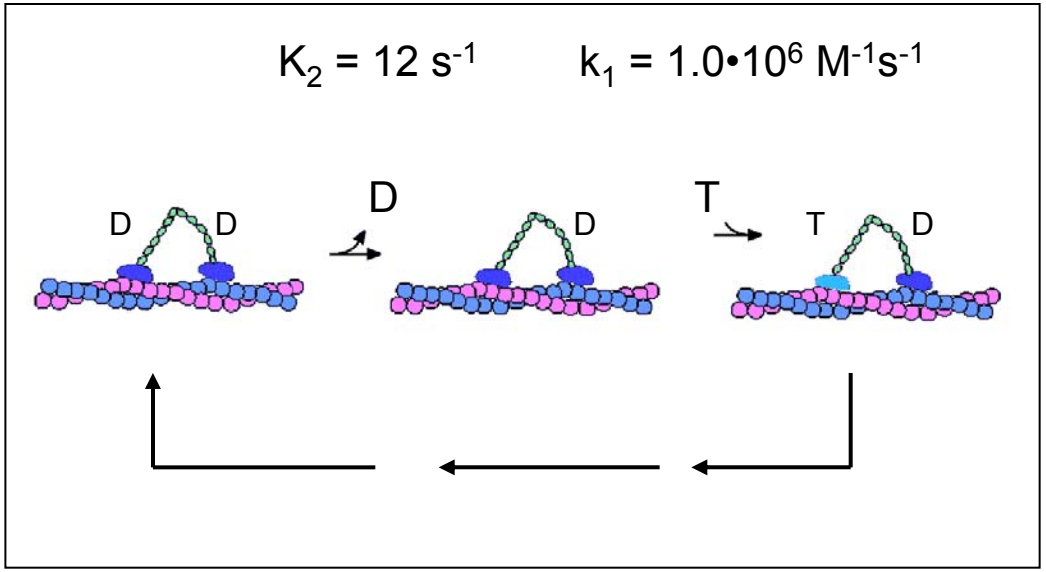
Completion of Step

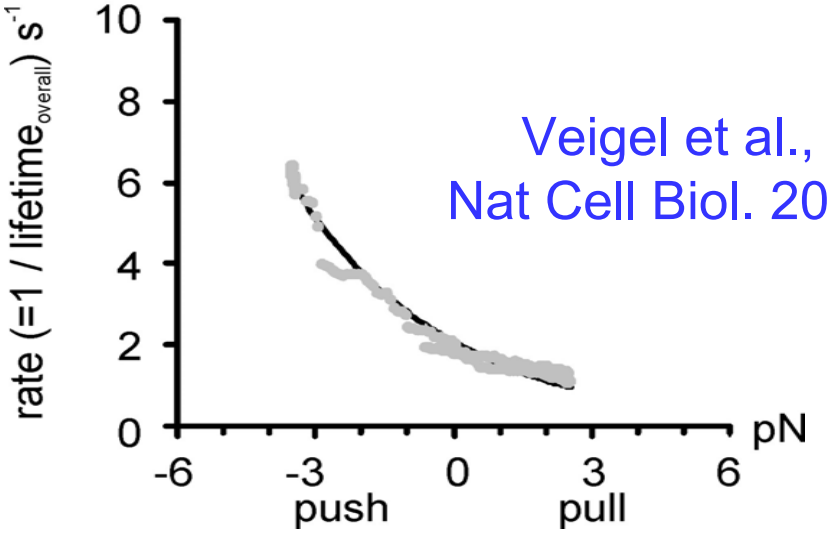




Lifetime of Myo V S1 Attachments

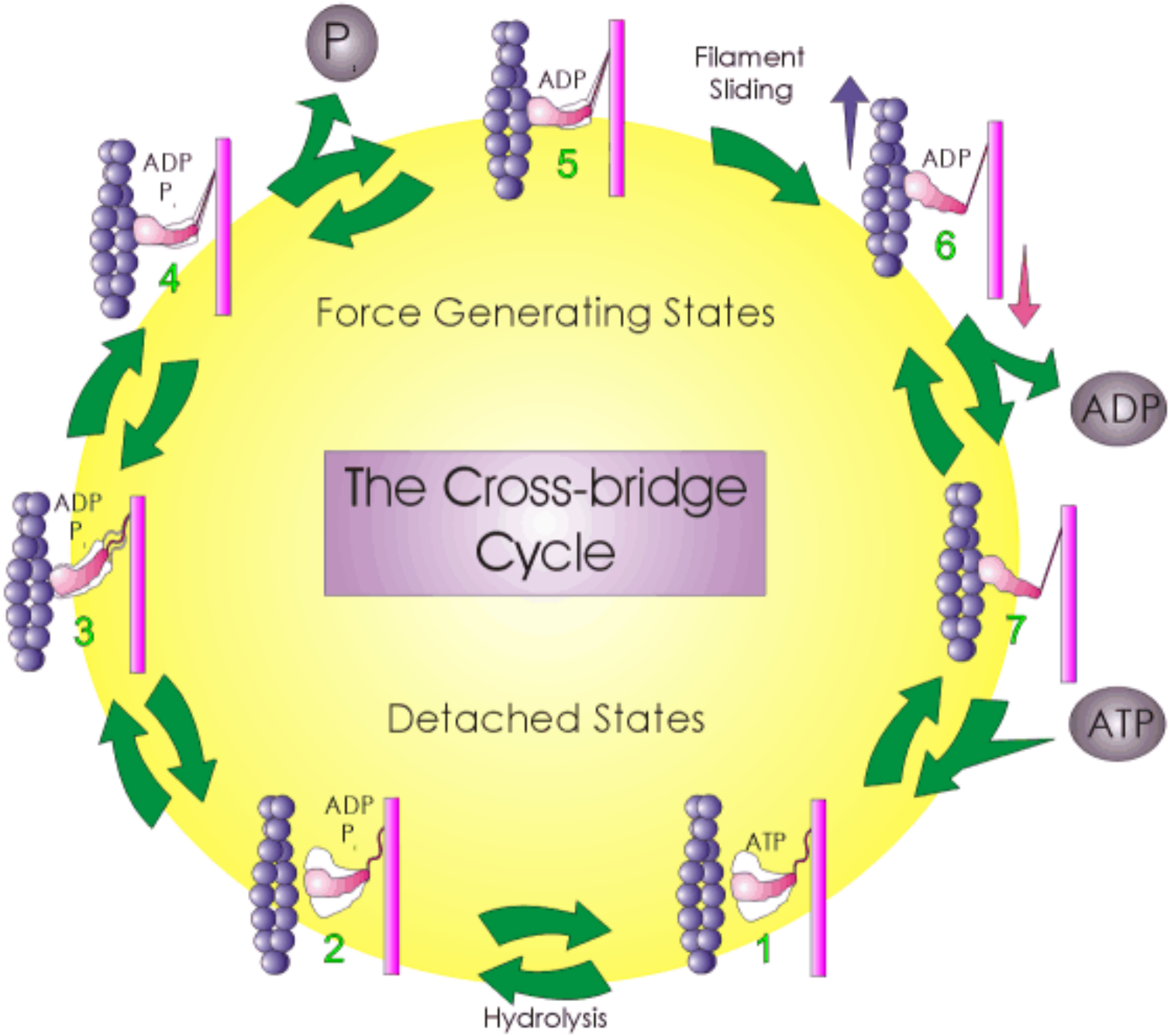


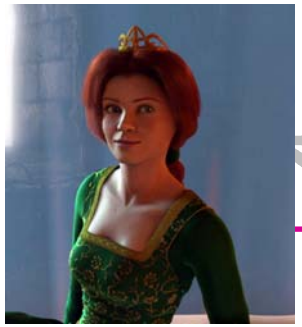




Veigel et al.,
Nat Cell Biol. 2005

$r = r_0 \exp(- W / kT)$

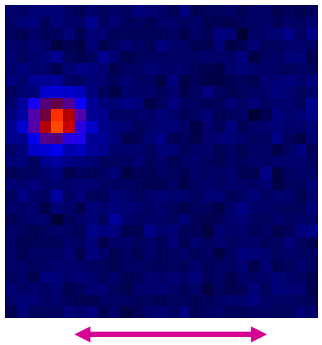

P
ADP
5
Filament
Sliding
ADP
6
ADP
4
Force Generating States
ADP
The Cross-bridge
Cycle
ADP
3
7
ATP
Detached States
ADP
ATP
2
1
Hydrolysis



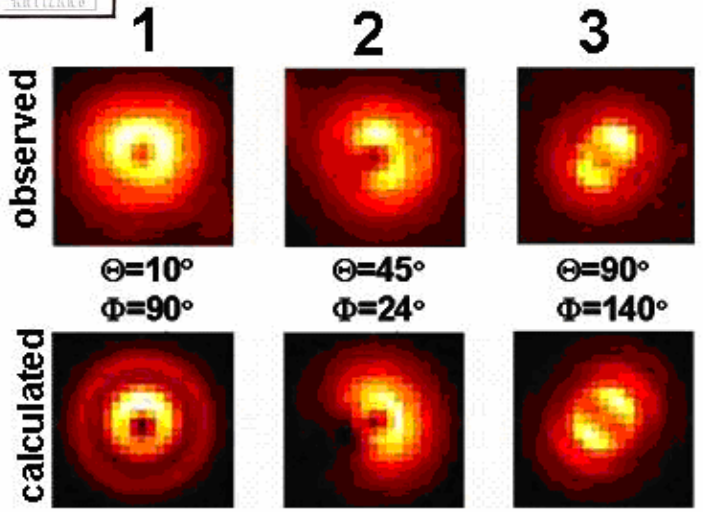
FIONA

DOPI

The Movie



Fluorescence
Imaging at
One
Nanometer
Accuracy

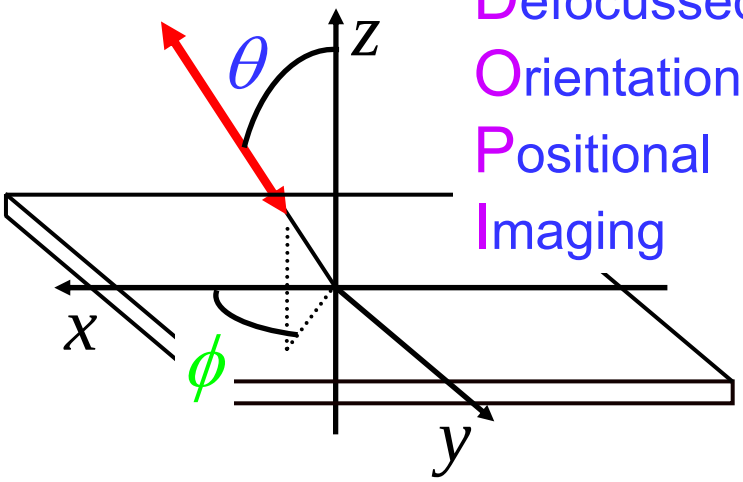


Ahmet
Yildiz

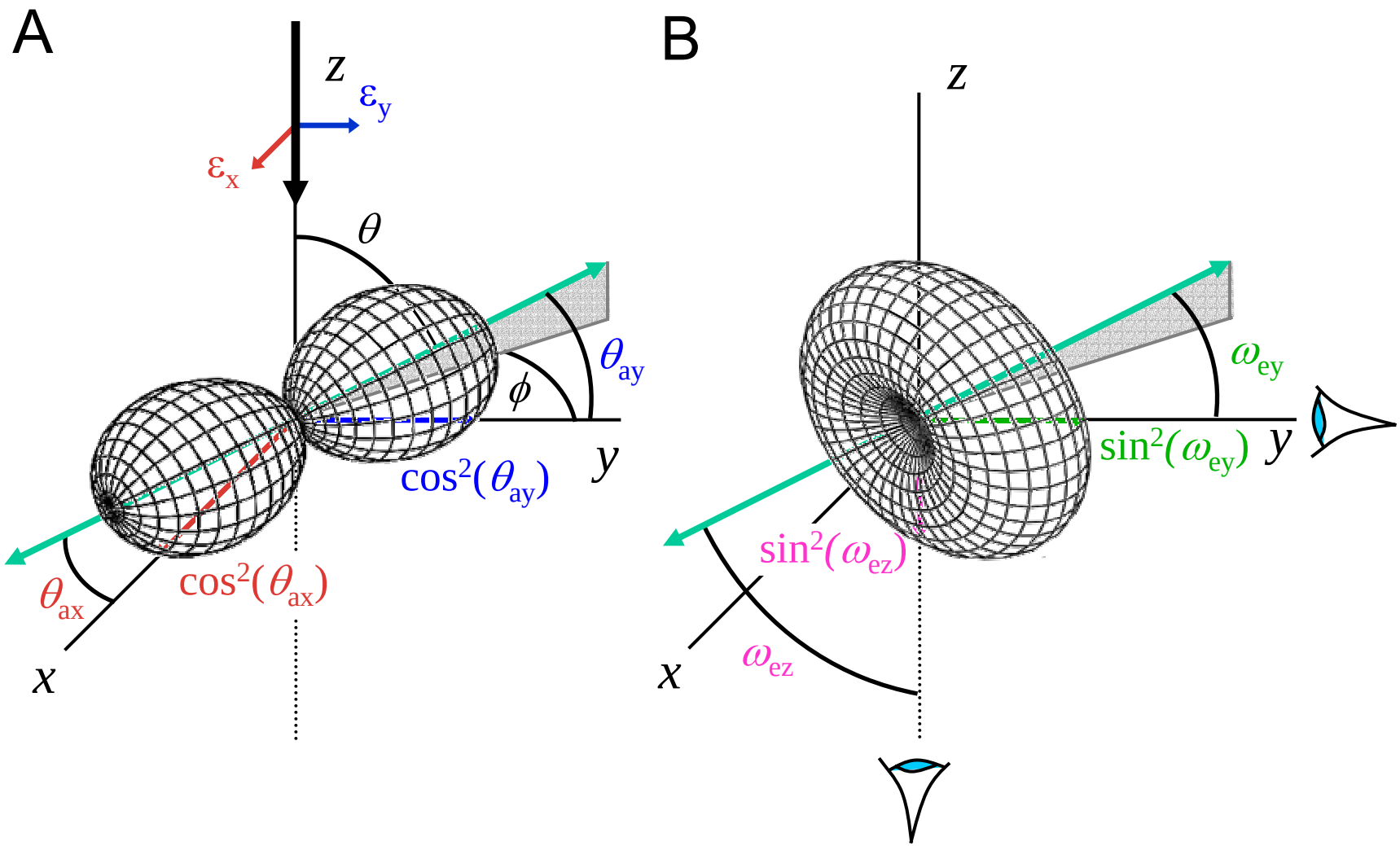
Taekjip
Ha

Paul
Selvin

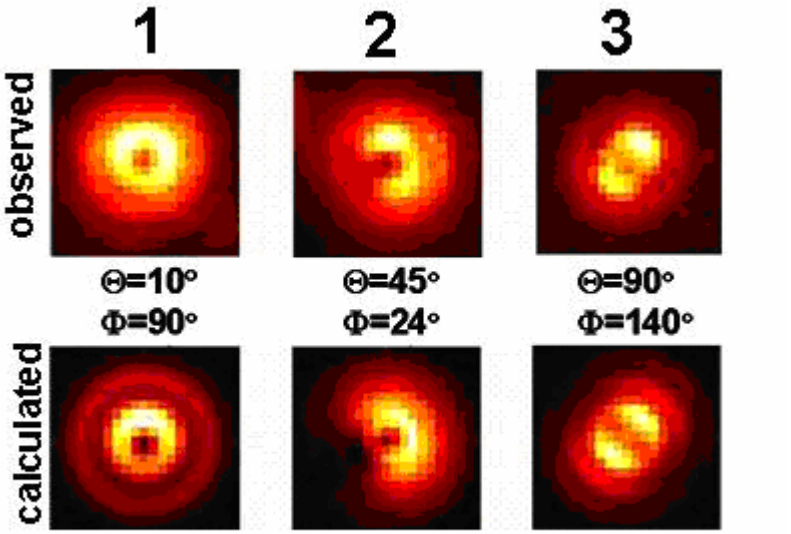
Erdal
Toprak

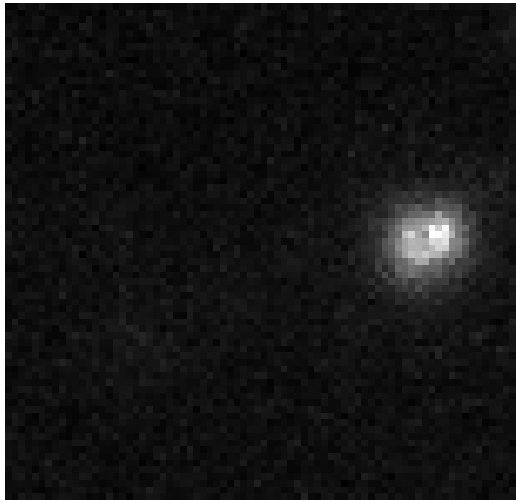


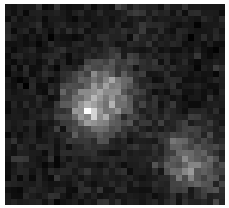
Defocussed
Orientation and
Positional
Imaging


A
z
ε_y
ε_x
θ
θ_{ay}
ϕ
y
$\cos^2(\theta_{ay})$
θ_{ax}
$\cos^2(\theta_{ax})$
x
B
z
ω_{ey}
$\sin^2(\omega_{ey})$
y
$\sin^2(\omega_{ez})$
ω_{ez}
x

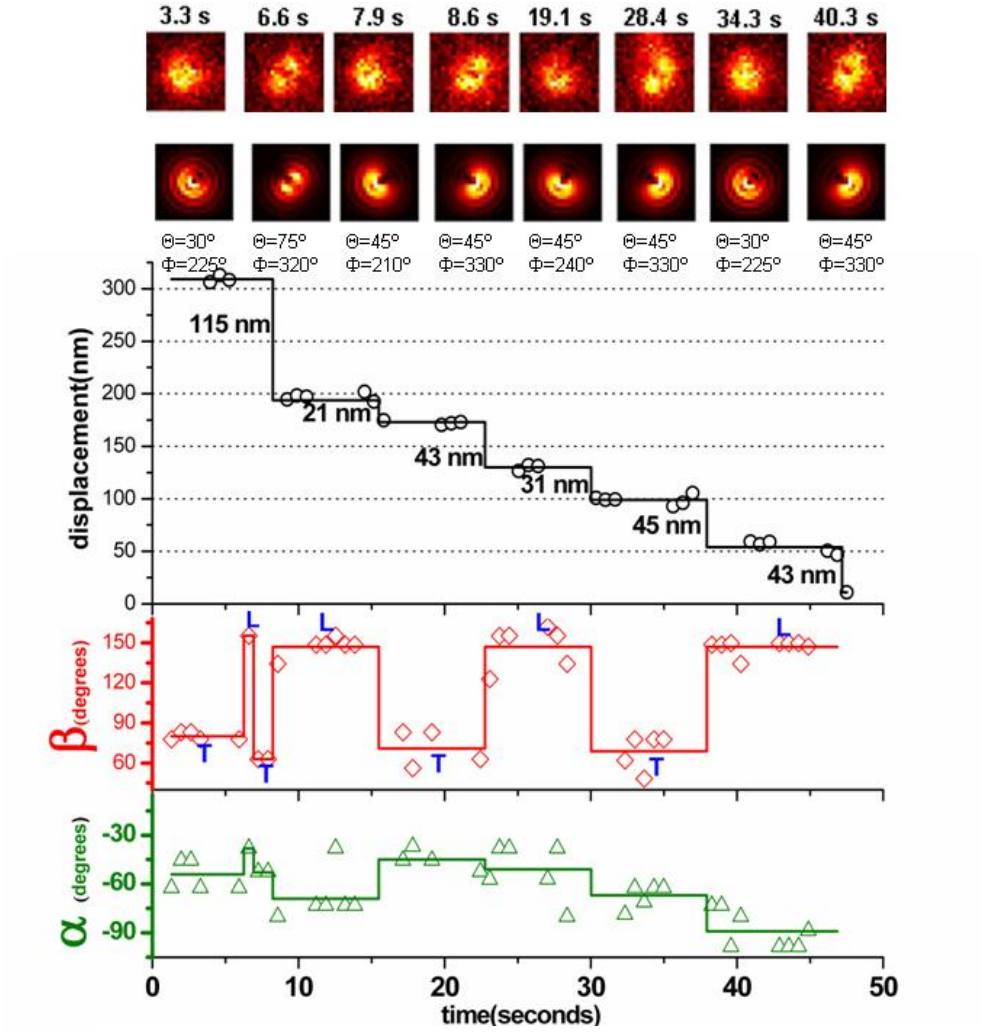
DOPI



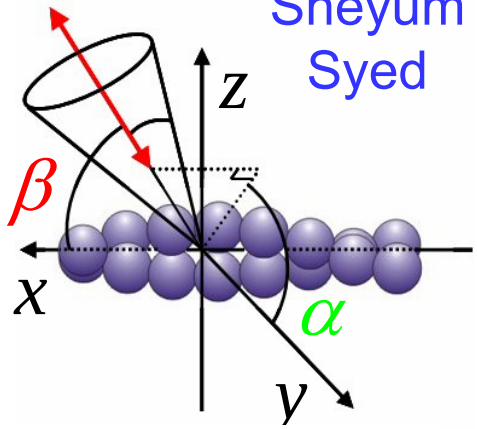


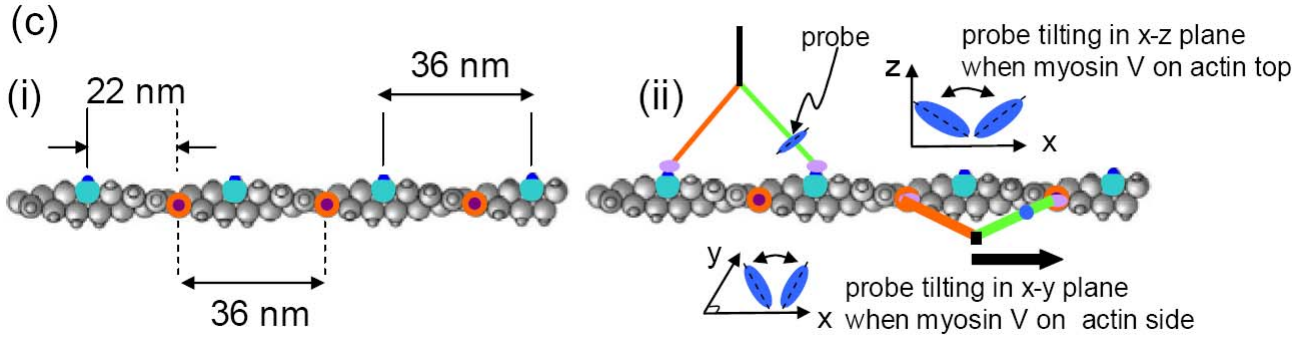


70 nm pixels; 2 frames/s

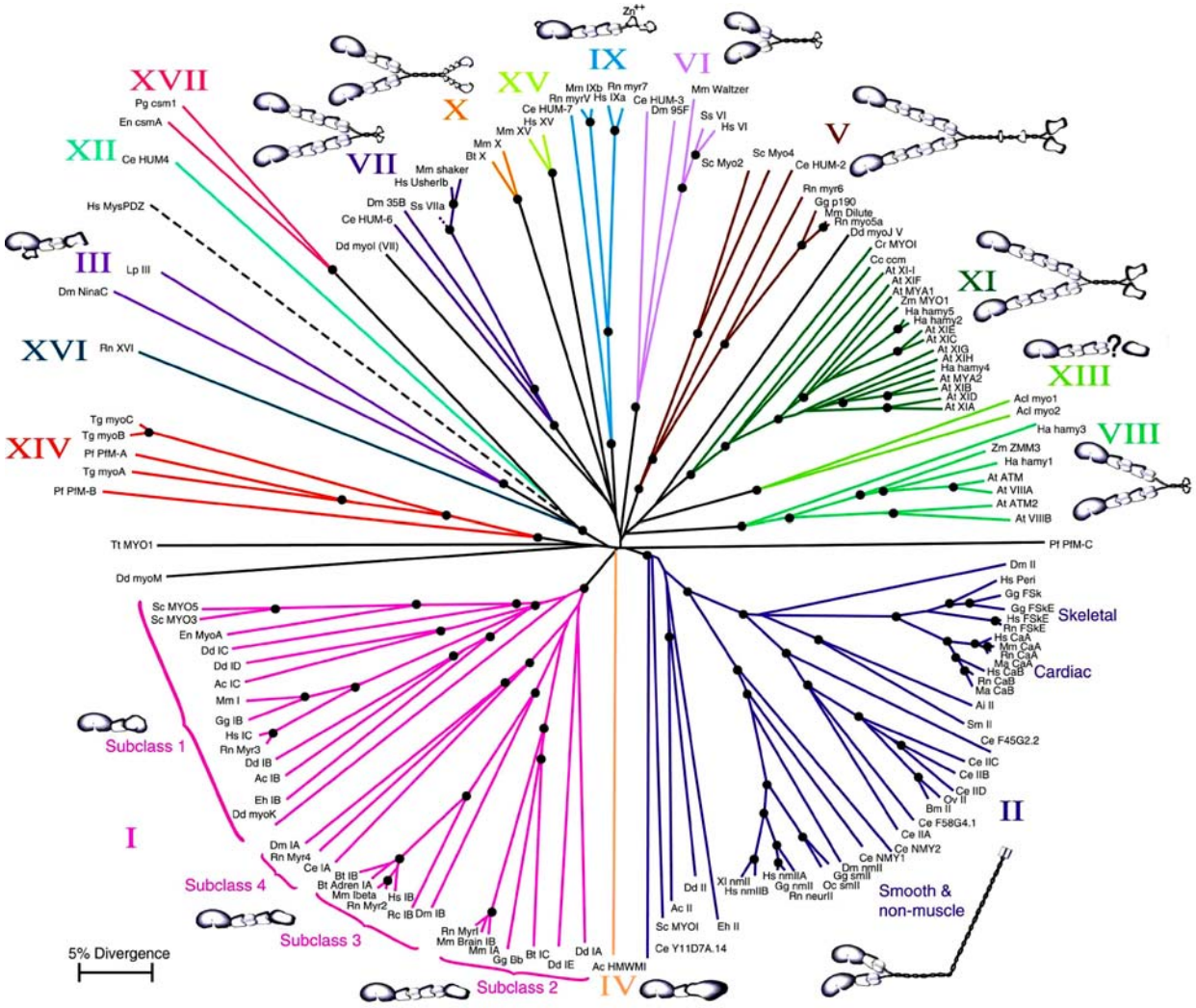

3.3 s
6.6 s
7.9 s
8.6 s
19.1 s
28.4 s
34.3 s
40.3 s
Θ=30° Φ=225°
Θ=75° Φ=320°
Θ=45° Φ=210°
Θ=45° Φ=330°
Θ=45° Φ=240°
Θ=45° Φ=330°
Θ=30° Φ=225°
Θ=45° Φ=330°
displacement(nm)
115 nm
21 nm
43 nm
31 nm
45 nm
43 nm
β(degrees)
α (degrees)
time(seconds)

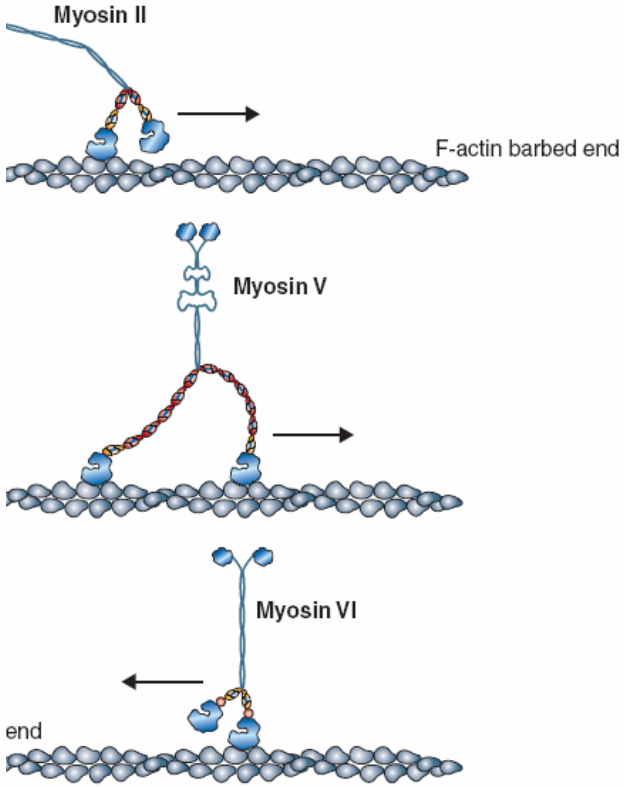
Sheyum Syed

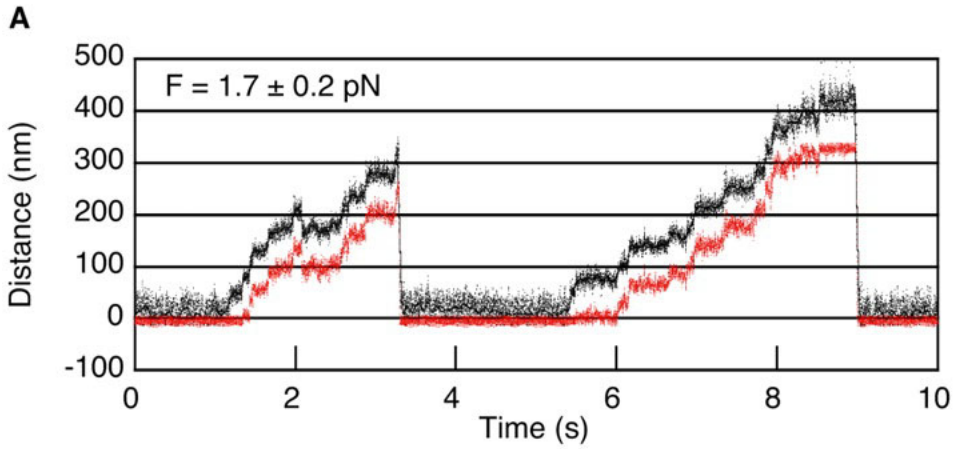

z
β
x
α
y

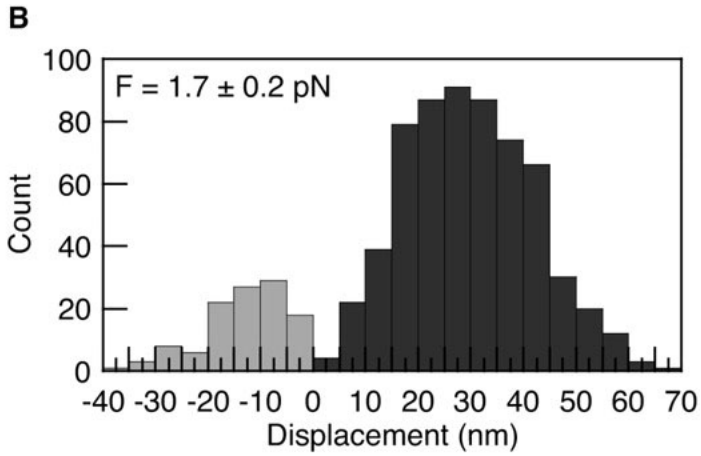

(c)
(i)
22 nm
36 nm
36 nm
(ii)
probe
probe tilting in x-z plane
when myosin V on actin top
z
x
y
x
probe tilting in x-y plane
when myosin V on actin side

Myosin Family Tree









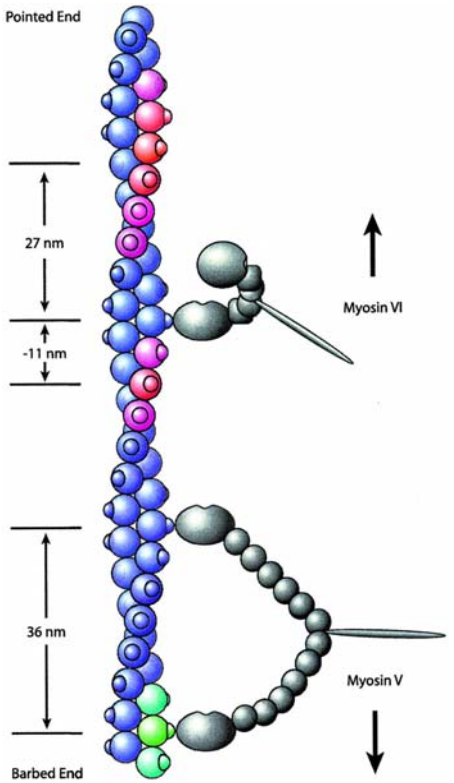
Myosin VI is a processive motor with a large step size

Ronald S. Rock*, Sarah E. Rice*, Amber L. Wells†, Thomas J. Purcell*, James A. Spudich*‡, and H. Lee Sweeney†

PNAS | November 20, 2001 | vol. 98 | no. 24 | 13655–13659

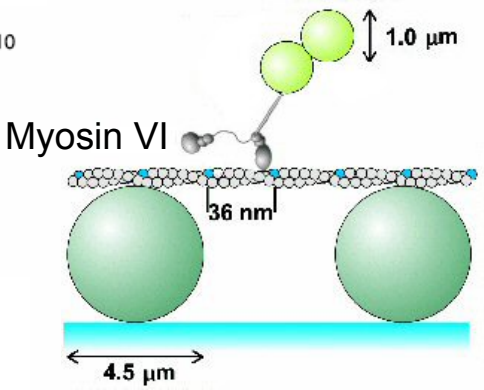
- Myosin-VI is a processive motor that takes frequent backward steps.

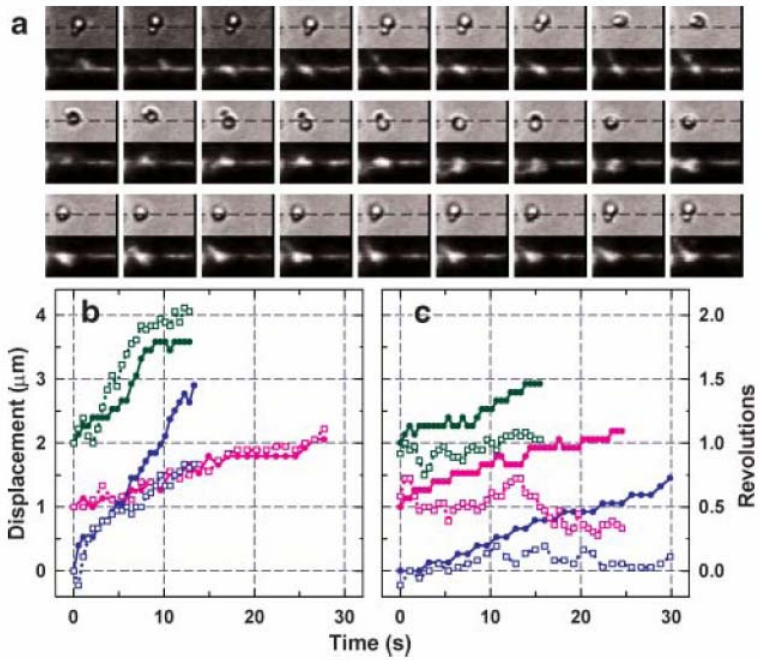
- The step size of myosin-VI is much larger than expected, based on the length of the putative lever arm.

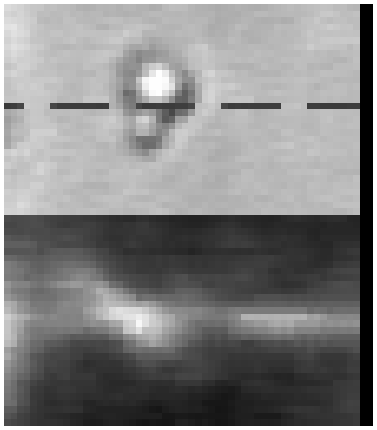


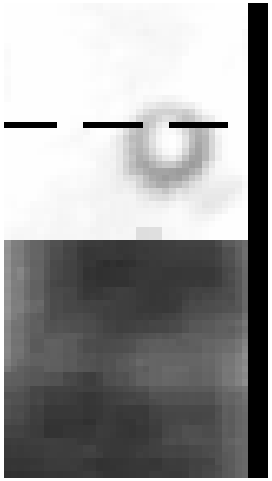
Unconstrained Steps of Myosin VI Appear Longest among Known Molecular Motors

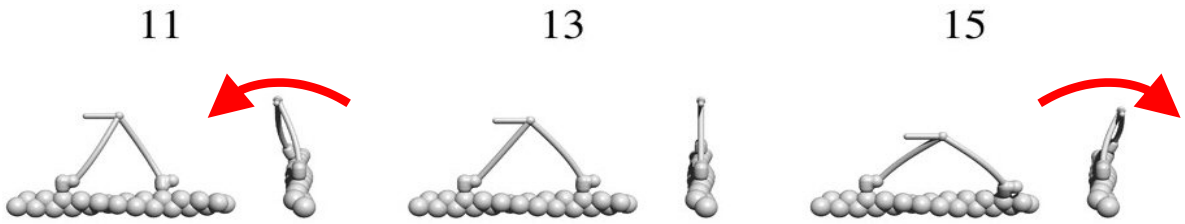
M. Yusuf Ali,*† Kazuaki Homma,‡ Atsuko Hikikoshi Iwane,§ Kengo Adachi,* Hiroyasu Itoh,¶‖ Kazuhiko Kinosita Jr.,* Toshio Yanagida,§ and Mitsuo Ikebe‡









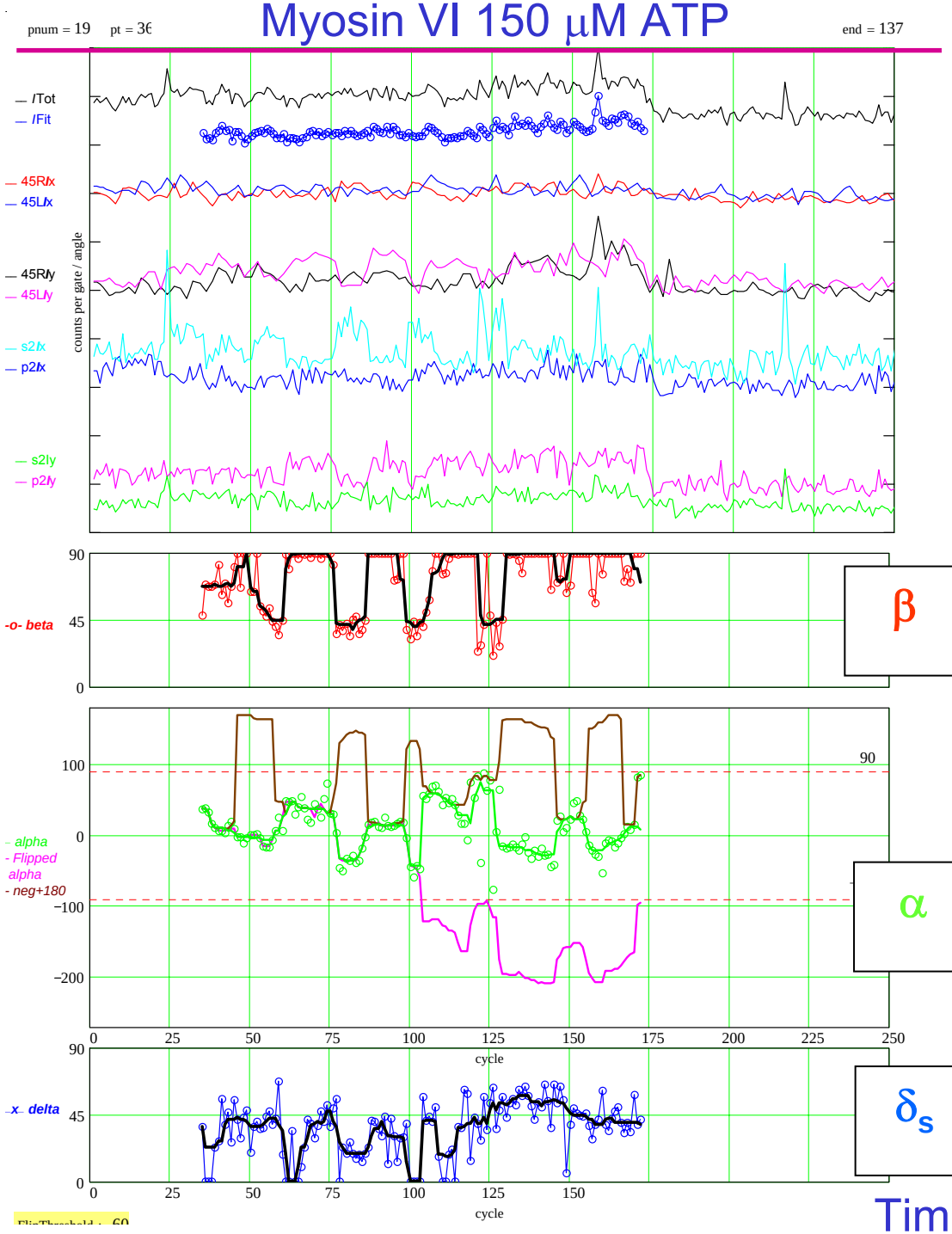


MORE Complicated SMFP Experimental Setup:

John Beausang

Harry Trey Schroeder

Myosin VI 150 μM ATP



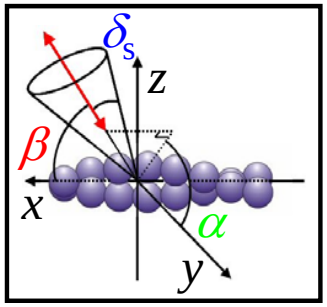
I_{TOT}
I_{FIT}

$45R I_x$
$45L I_x$

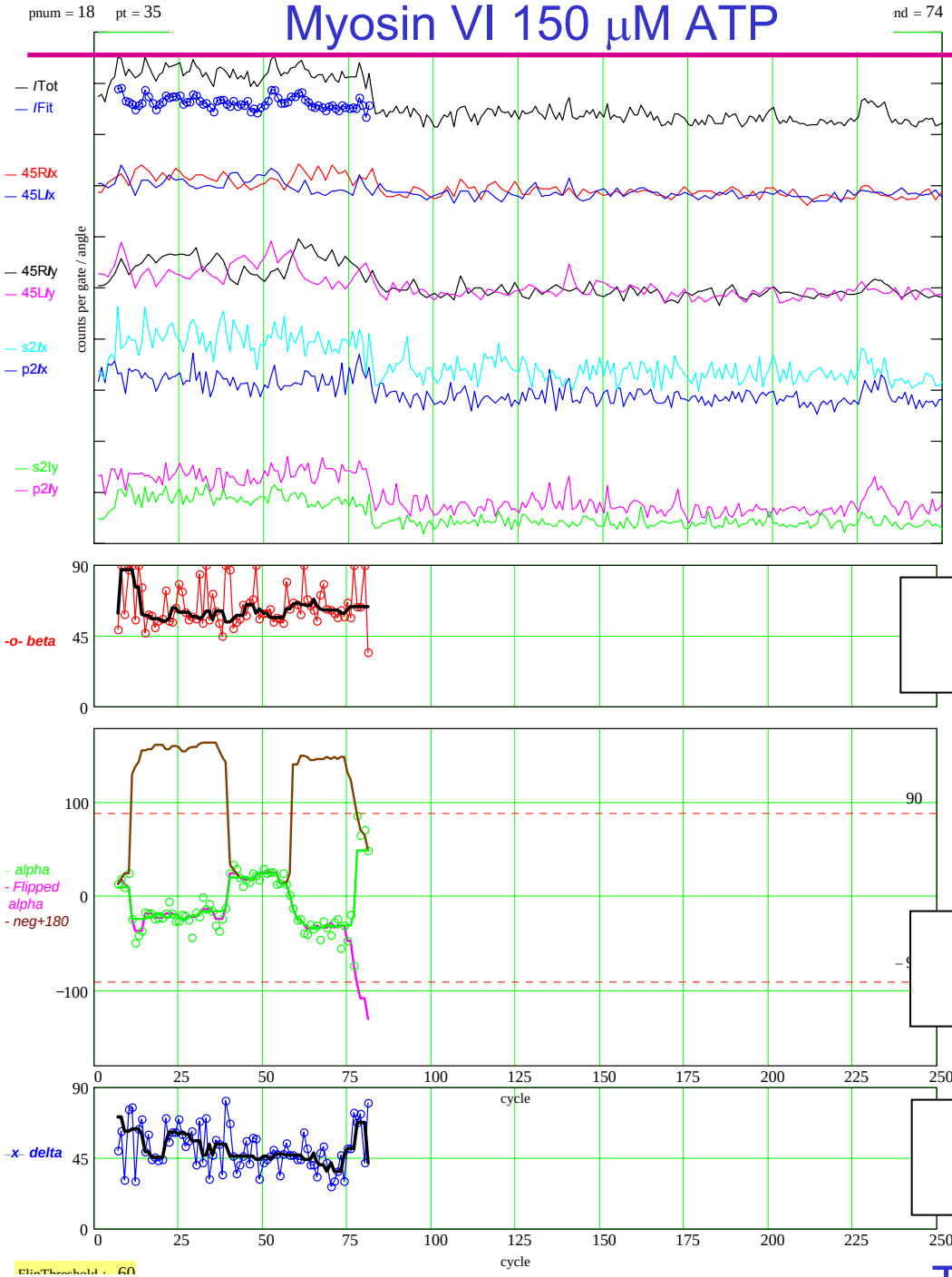
$45R I_y$
$45L I_y$

$s2 I_x$
$p2 I_x$

$s2 I_y$
$p2 I_y$



Myosin VI 150 μM ATP



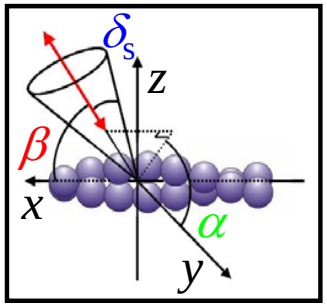
I_{TOT}
I_{FIT}

$45R I_x$
$45L I_x$

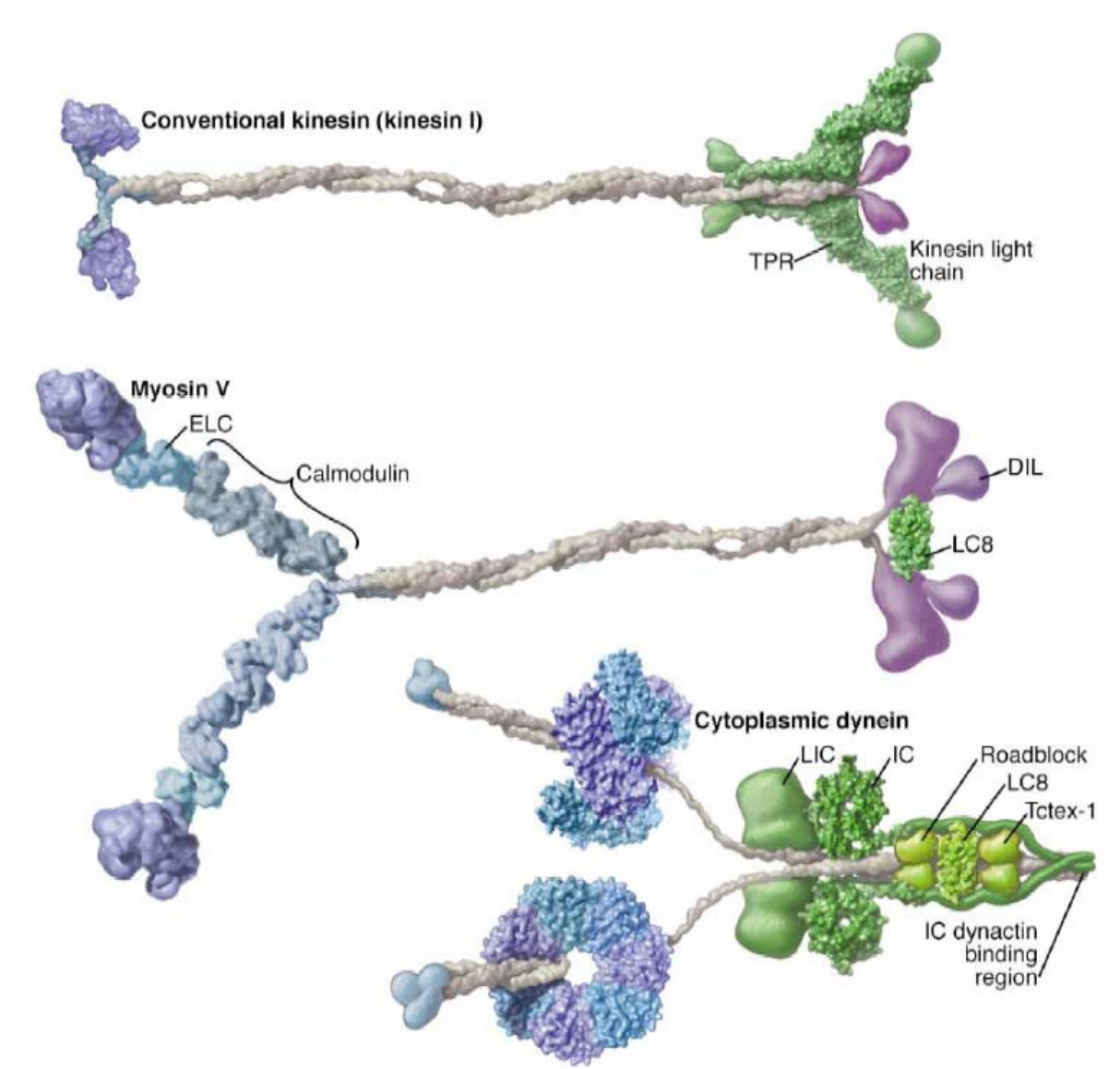
$45R I_y$
$45L I_y$

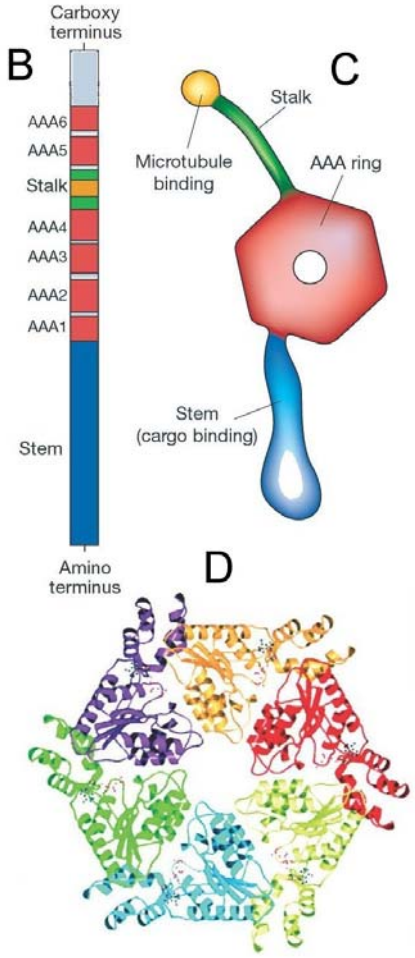
$s2 I_x$
$p2 I_x$

$s2 I_y$
$p2 I_y$

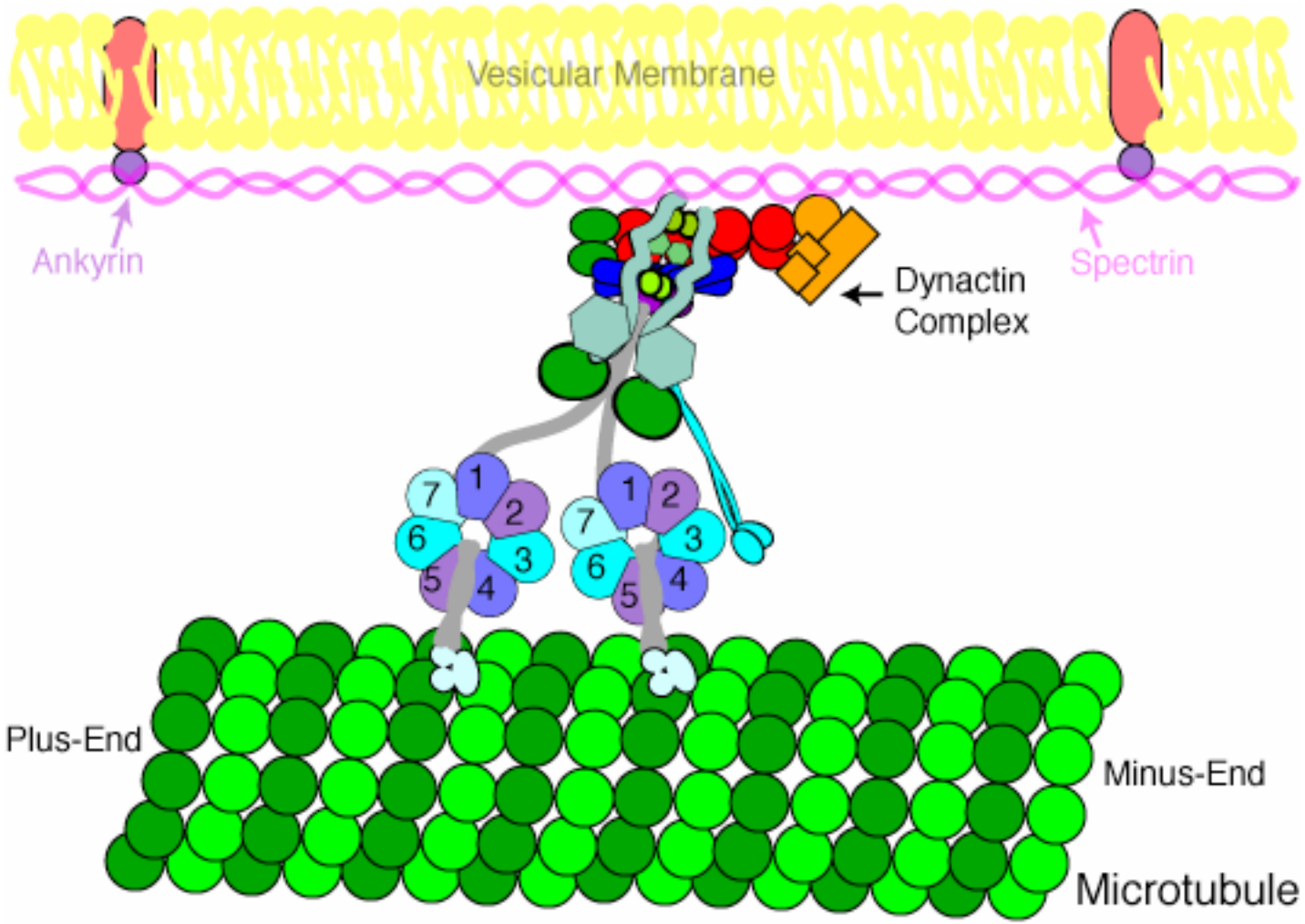


Molecular Motor Toolbox





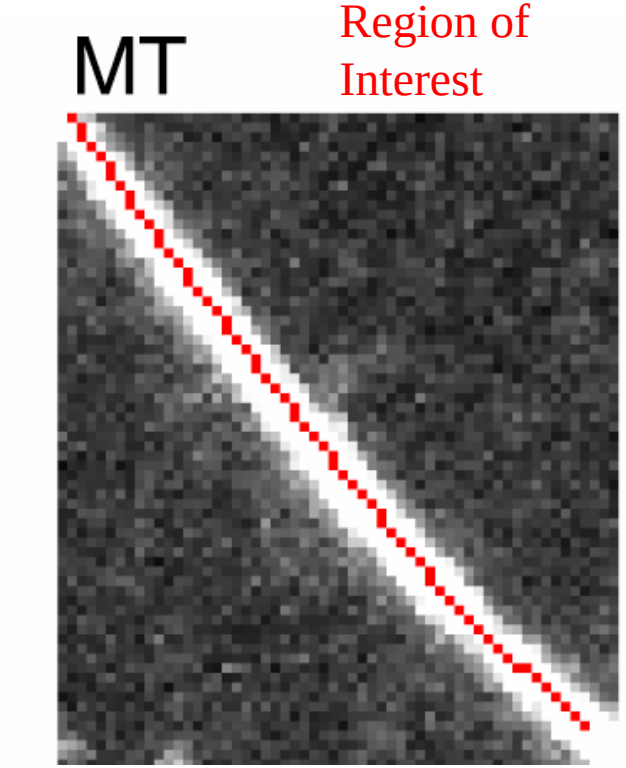
Dynein and Dynactin Complex for Cargo Binding



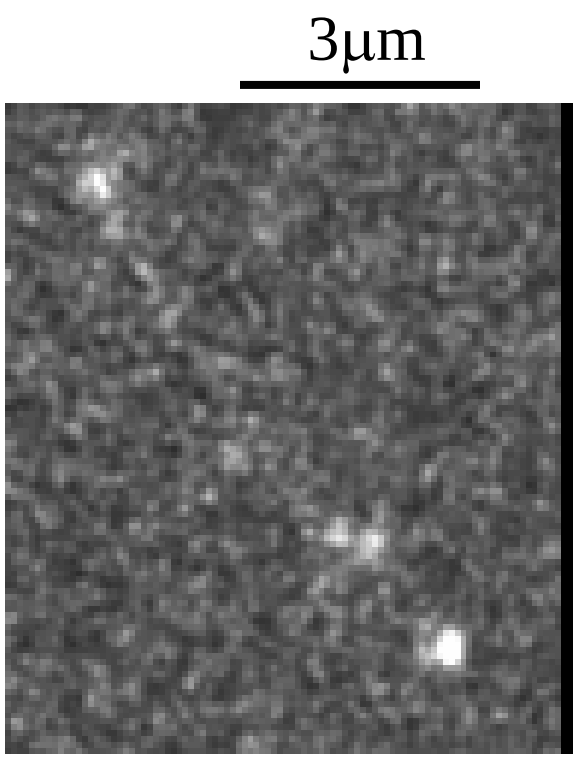
Single Molecule Symposium

April 21, 2005

Single Molecules of GFP-Dynactin/Dynein Walk Along Microtubules Bi-directionally



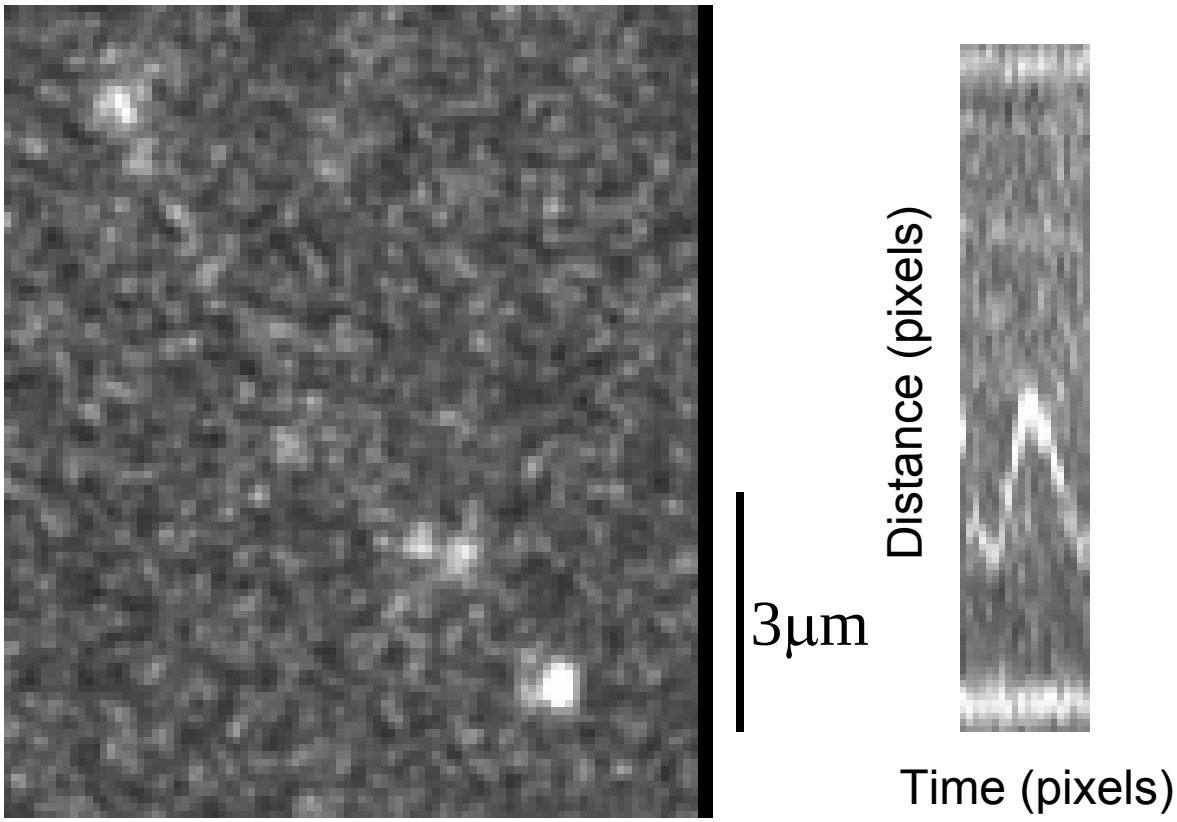
Rhodamine Microtubules in epi-fluorescence



Processive GFP-dynactin/dynein visualized by total internal reflection fluorescence (TIRF) microscopy.

Δt = 100 ms

Analysis using Kymographs of Single Microtubules



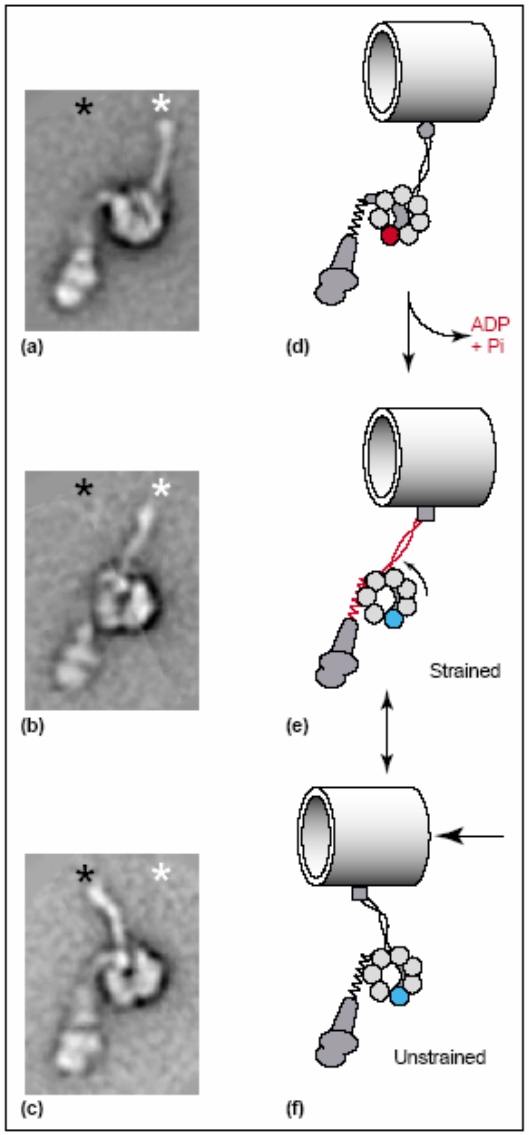
Angle, θ, relates to velocity in pixels/frame by: $\tan(\theta) = \frac{\Delta x(\,pixels)}{\Delta t(\,frames)}$

Is the dynein motor a winch?

Stan A Burgess and Peter J Knight*

Astbury Centre for Structural Molecular Biology & School of Biomedical Sciences, University of Leeds, Leeds LS2 9JT, UK
*e-mail: p.j.knight@leeds.ac.uk

2004, 14:138–146
Current Opinion in Structural Biology

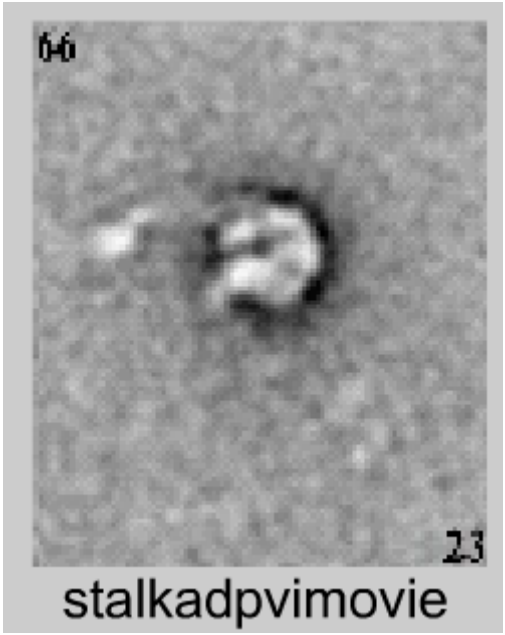


Dynein structure and power stroke

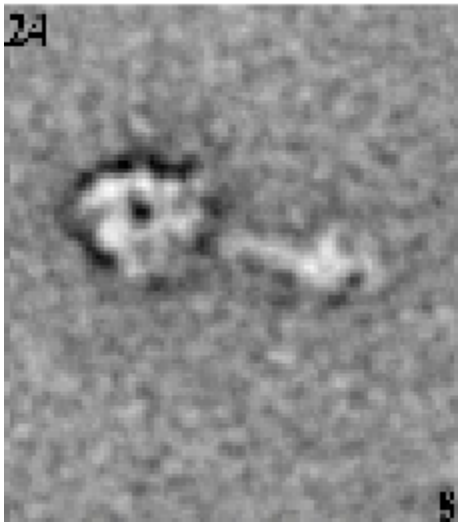
Stan A. Burgess*, Matt L. Walker*, Hitoshi Sakakibara†, Peter J. Knight* & Kazuhiro Oiwa†

*Astbury Centre for Structural Molecular Biology & School of Biomedical Sciences, University of Leeds, Leeds, LS2 9JT, UK
†Kansai Advanced Research Centre, Communications Research Laboratory, Kobe, 651-2492, Japan

NATURE | VOL 421 | 13 FEBRUARY 2003 | www.nature.com/nature



stalkadpvimovie



Conclusion: Dynein Bi-Directionality Caused by Flexible Structure

First direct observation of dynein motility via fluorescence

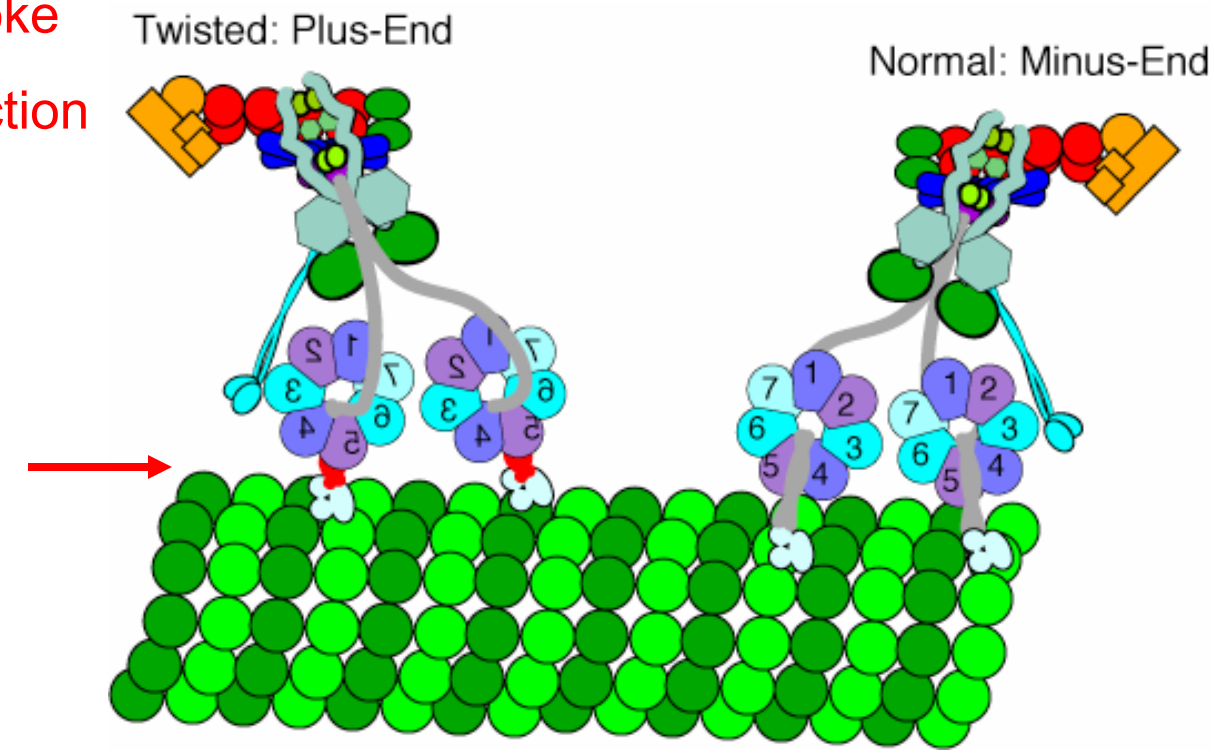
Dynein AAA motor head could function as a gear

Dynein appear bi-directional: How?

Over-rotation of coiled-coil flexible linkers?

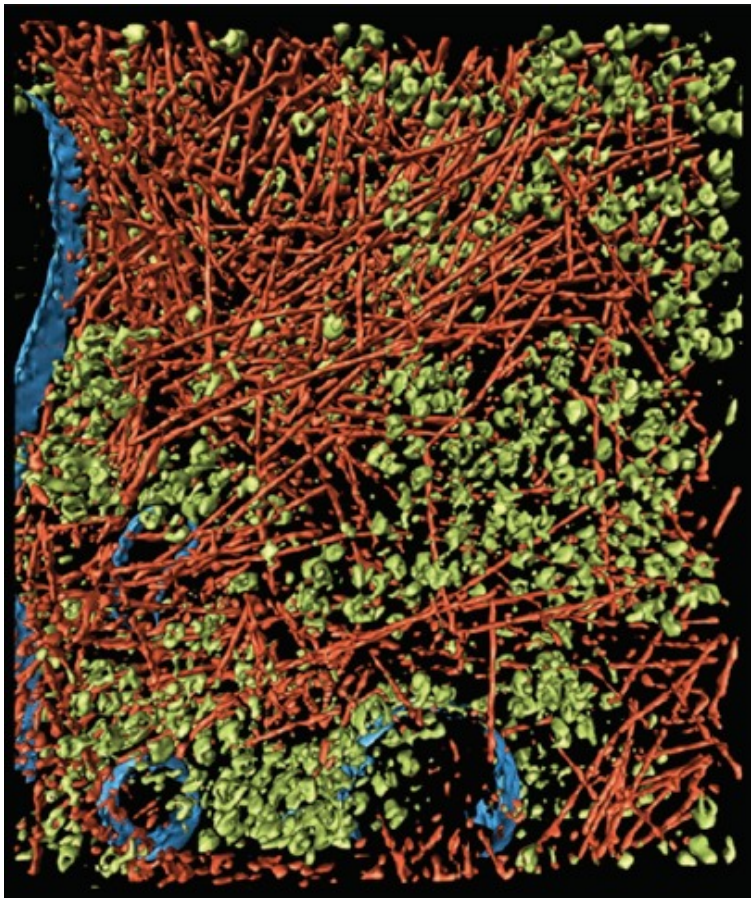
Continues to powerstroke

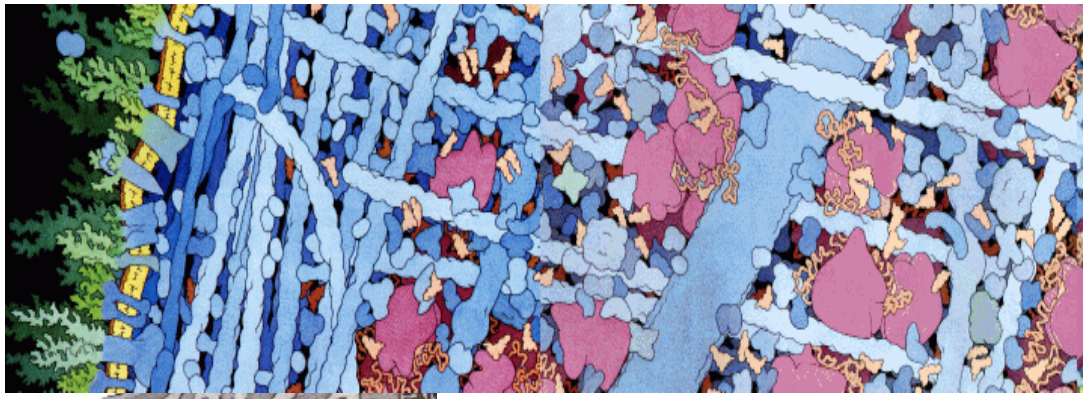
Walks in opposite direction

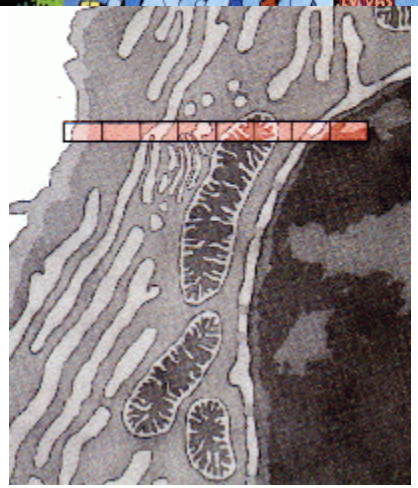


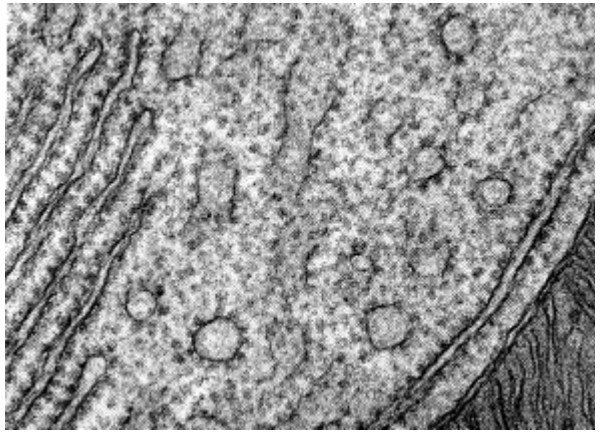
Cryo-EM of Cell

Artist's Imagination







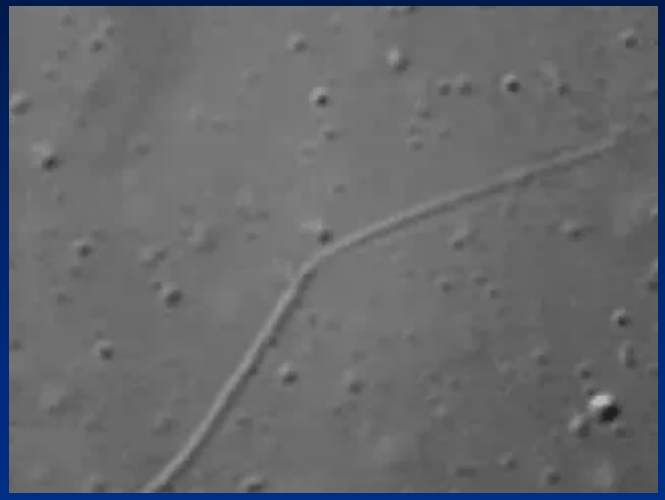


Medalia et al. 2002 *Science*. 298:1209-13.

David C. Goodsell

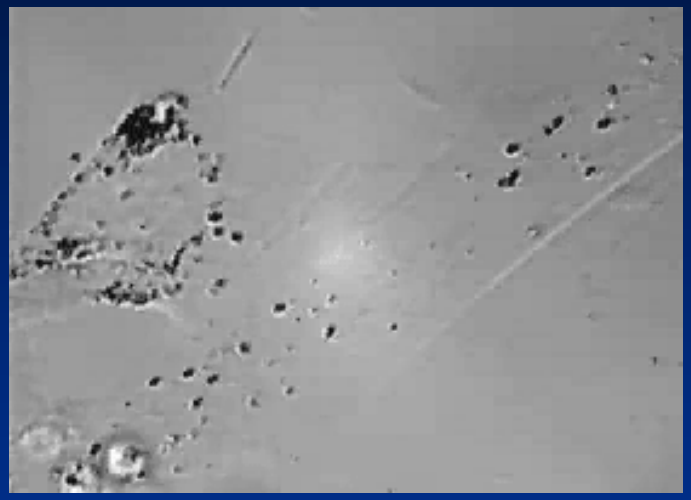
Molecular Motors in Non-Muscle Cells

University of Pennsylvania



Vesicle Movement in Cell Extract

Nira Pollack & Ron D. Vale, UCSF
From: Molecular Biology of the Cell, 4th ed.

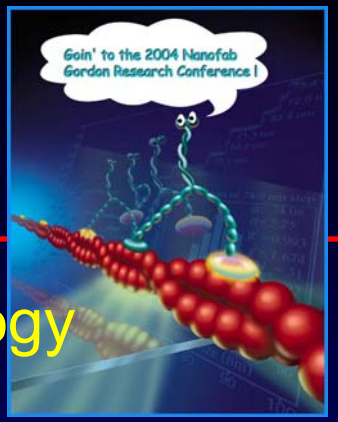


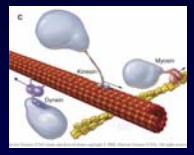
Melanosome Movement

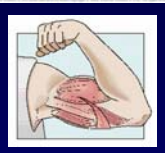
John A. Hammer, III, NIH

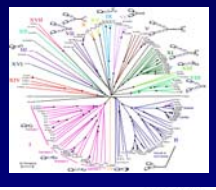
University of Pennsylvania

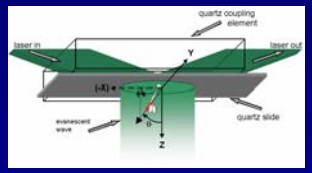
Challenges and Opportunities

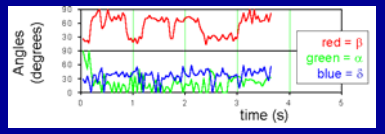












- Improvement of experimental technology
- Functional modulation the rate constants
- Controlled assembly of secondary structure?
- Mechanisms of the other motors
- Specificity of cargo binding
- Targeting of cargo destination
- Integration with other events (cell division, signal transduction, etc)

Acknowledgements

NIAMS
National Institute of Arthritis and Musculoskeletal and Skin Diseases

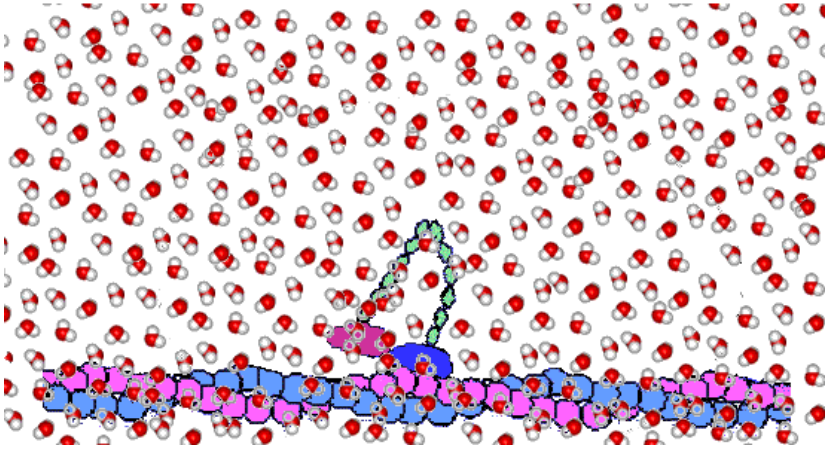
NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES
NIGMS 40 years of discovery
NATIONAL INSTITUTES OF HEALTH

National Science Foundation
WHERE DISCOVERIES BEGIN

HFSP Human Frontier Science Program

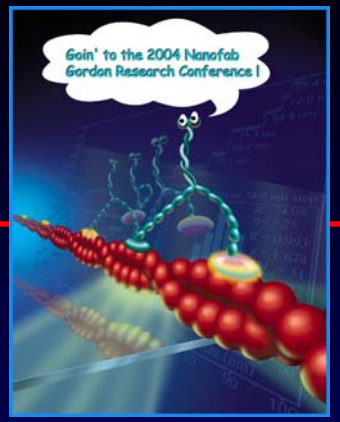
Joe Forkey
Margot Quinlan
Stephanie Rosenberg
John Beausang
Harry (Trey) Schroeder

Myosin's Thermal Search

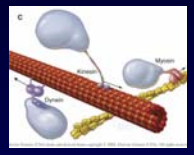


University of Pennsylvania

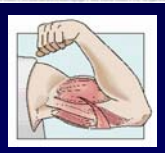
APS Workshop on Biology March 12, 2006



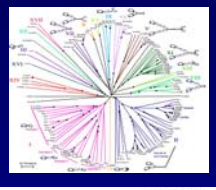
goldmany@mail.med.upenn.edu



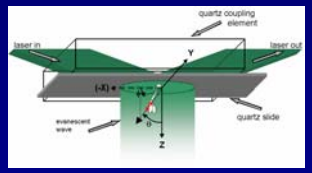
- Molecular Motors



- Muscle Energetics and Strain Dependence



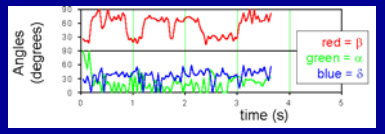
- Unconventional Myosins – Myosin V



- Single-Molecule Fluorescence Polarization

- FIONA

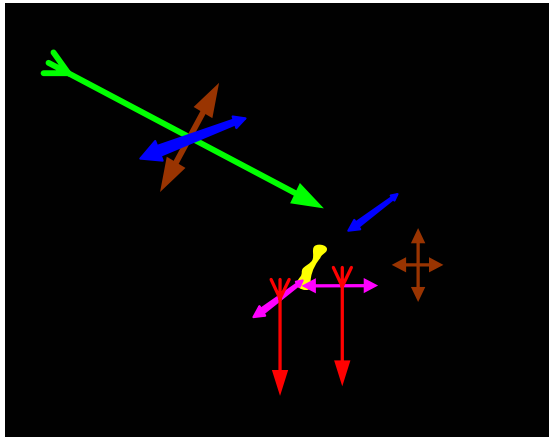
- DOPI

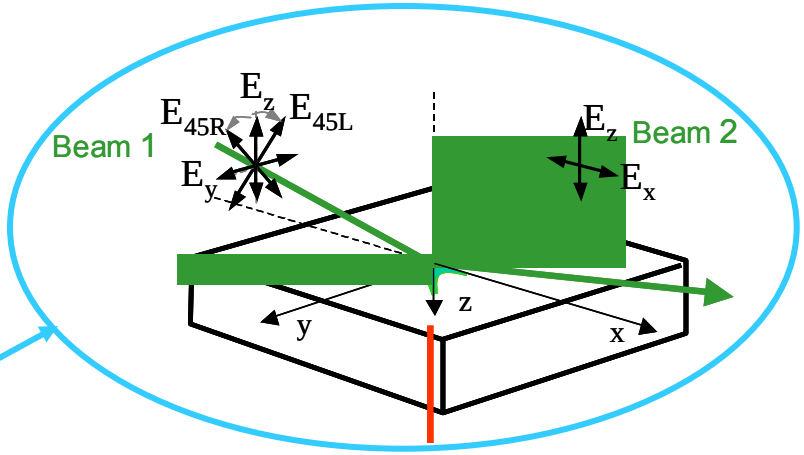


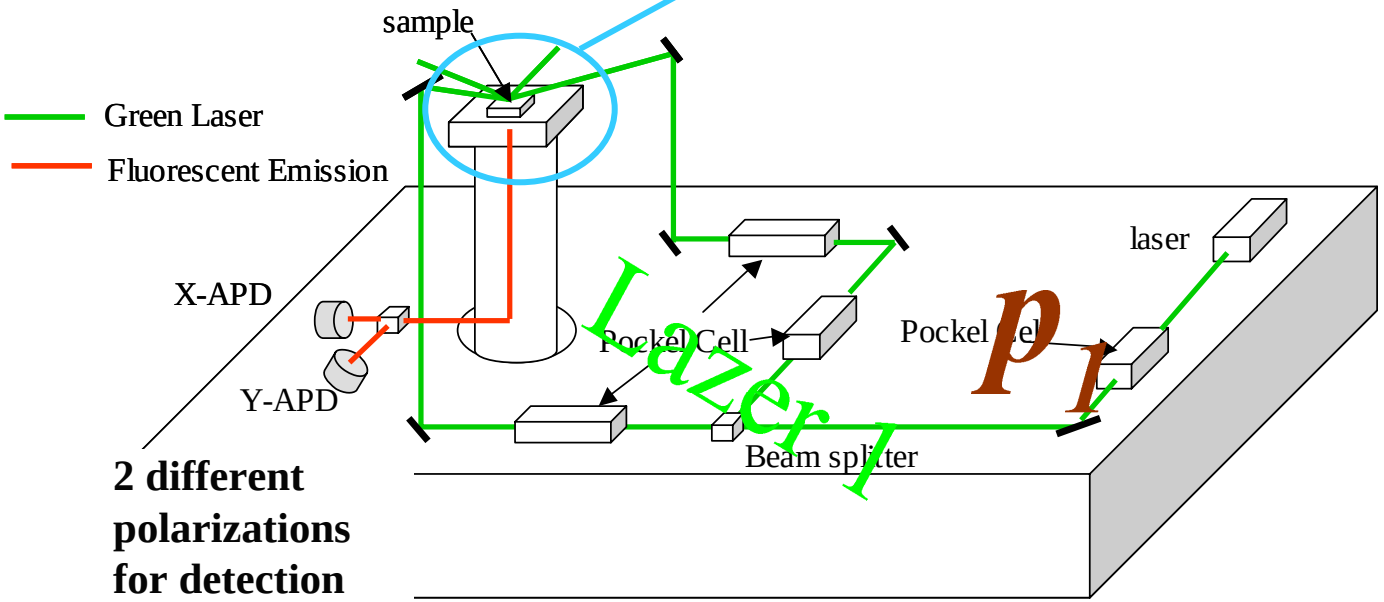
- Challenges

❖ SMFP Experimental Setup:

6 different polarizations for excitation







2 different polarizations for detection

Totally eight measured intensities along x and y direction obtained within 40 ms

$s1_x$ ($45L1_x$) $s2_x$

$s1_y$ ($45R1_y$) $s2_y$

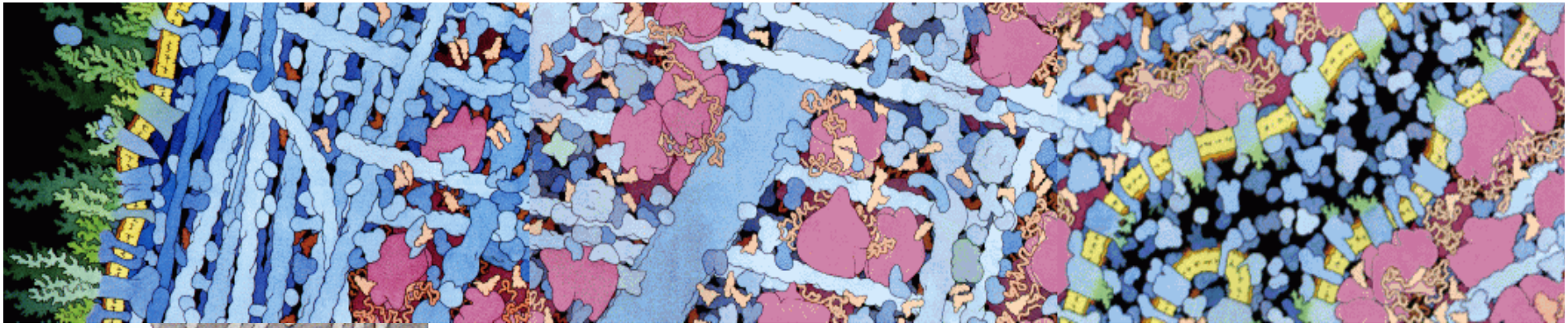
$p1_x$ ($45L1_x$) $p2_x$

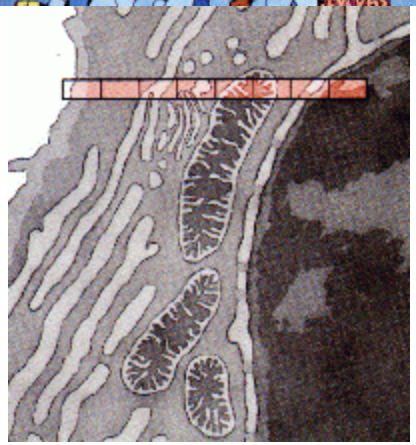
$p1_y$ ($45R1_y$) $p2_y$

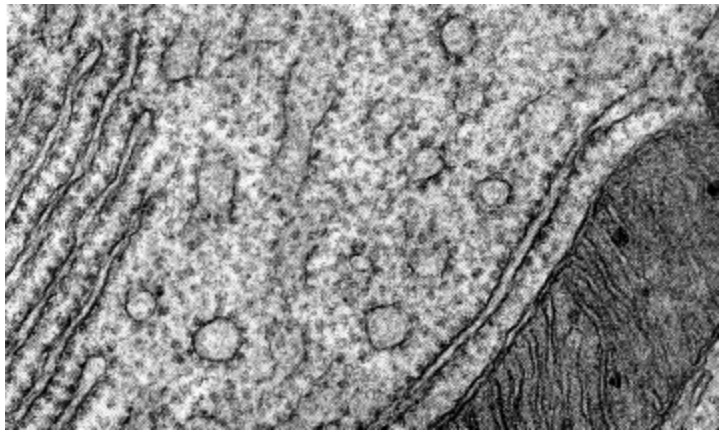
Use polarized light for excitation and detection to determine orientation of probe

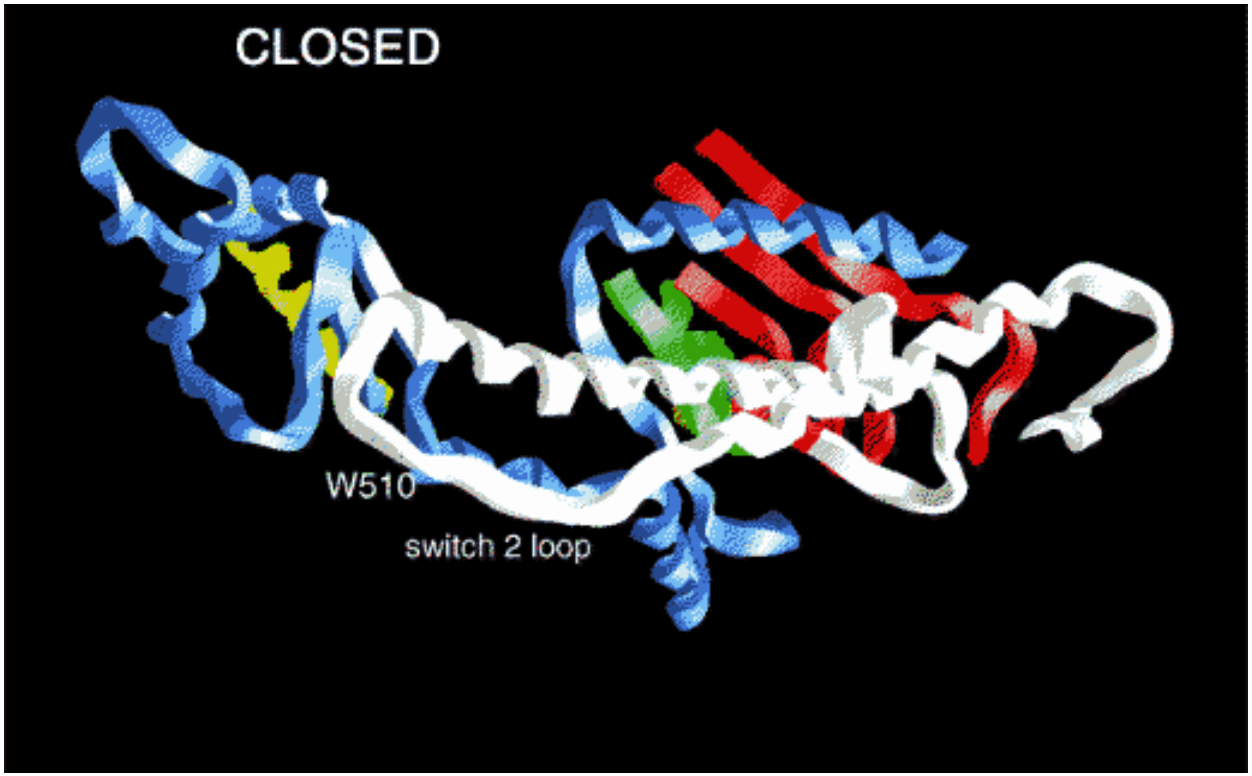
s_1 X s_1

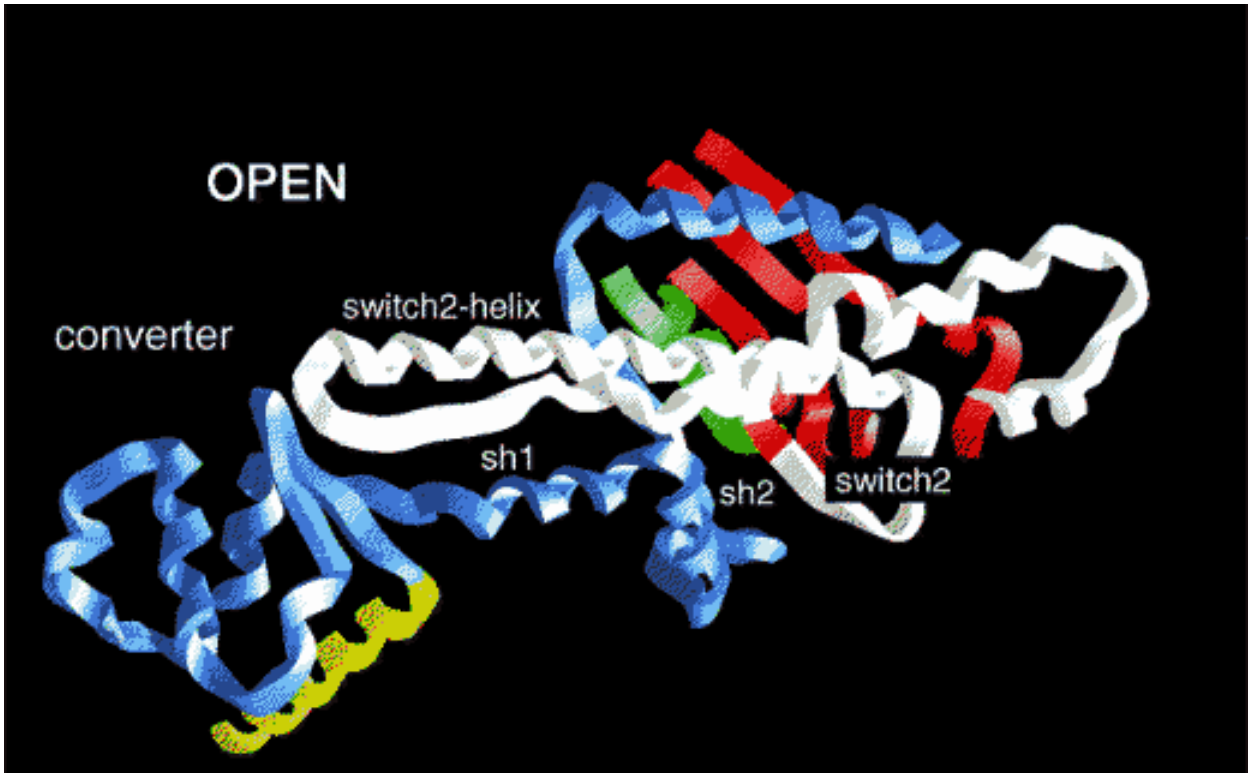
The image below is a panoramic view of the interior of a eukaryotic cell, such as a cell from your own body. The area covered is shown in the schematic map to the right. The panorama starts at the cell surface, passes through an area of cytoplasm, then follows the synthesis of proteins from the endoplasmic reticulum, through the Golgi, and into a coated vesicle. At the center of the panorama is a mitochondrion, generating energy for the cell. The final region passes into nucleus. All macromolecules are shown, with proteins in blue, DNA and RNA in red and orange, lipids in yellow, and carbohydrates in green. Ribosomes, composed of RNA and protein, are colored magenta. In a real cell, the spaces between each macromolecule are filled with small molecules, ions and water.



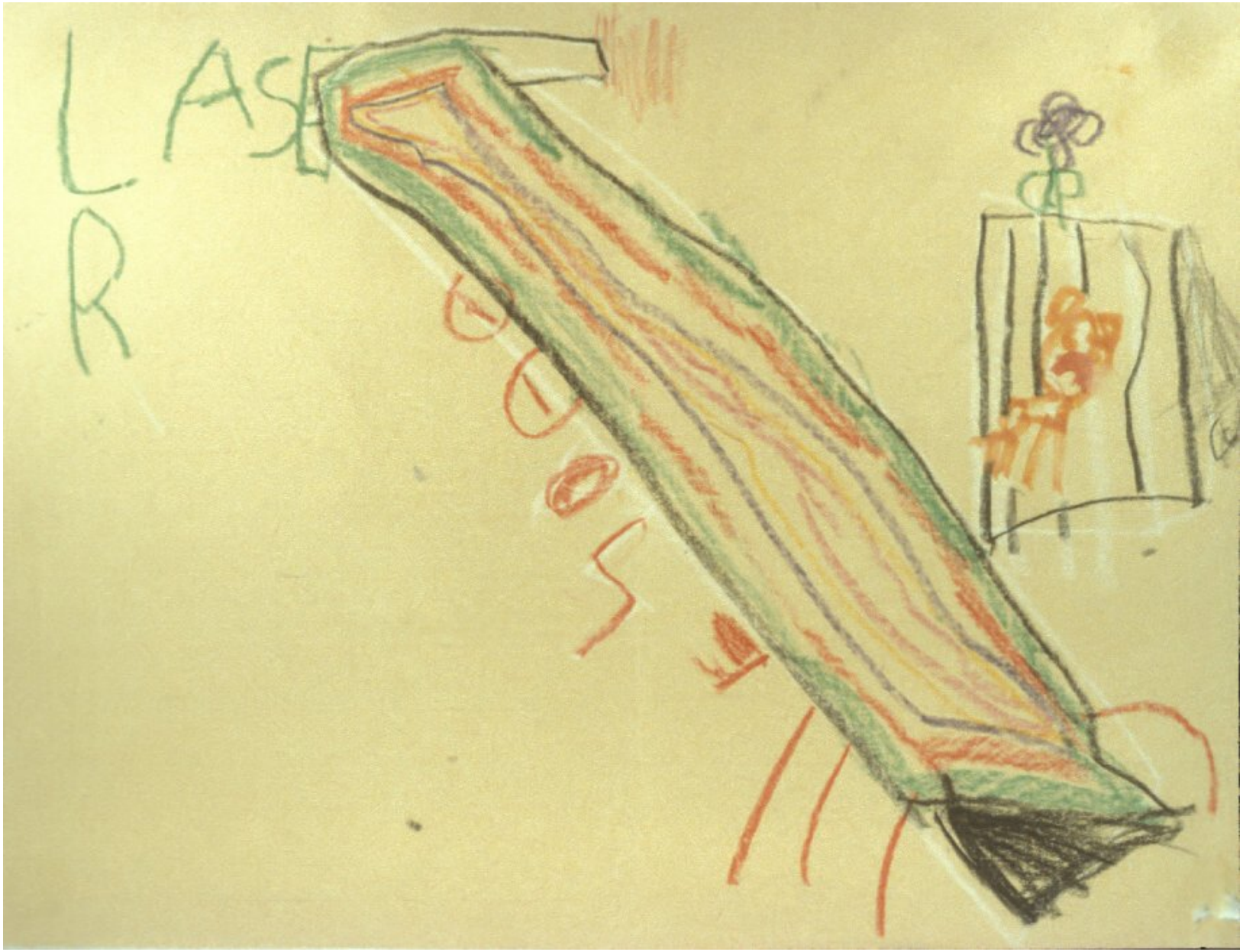




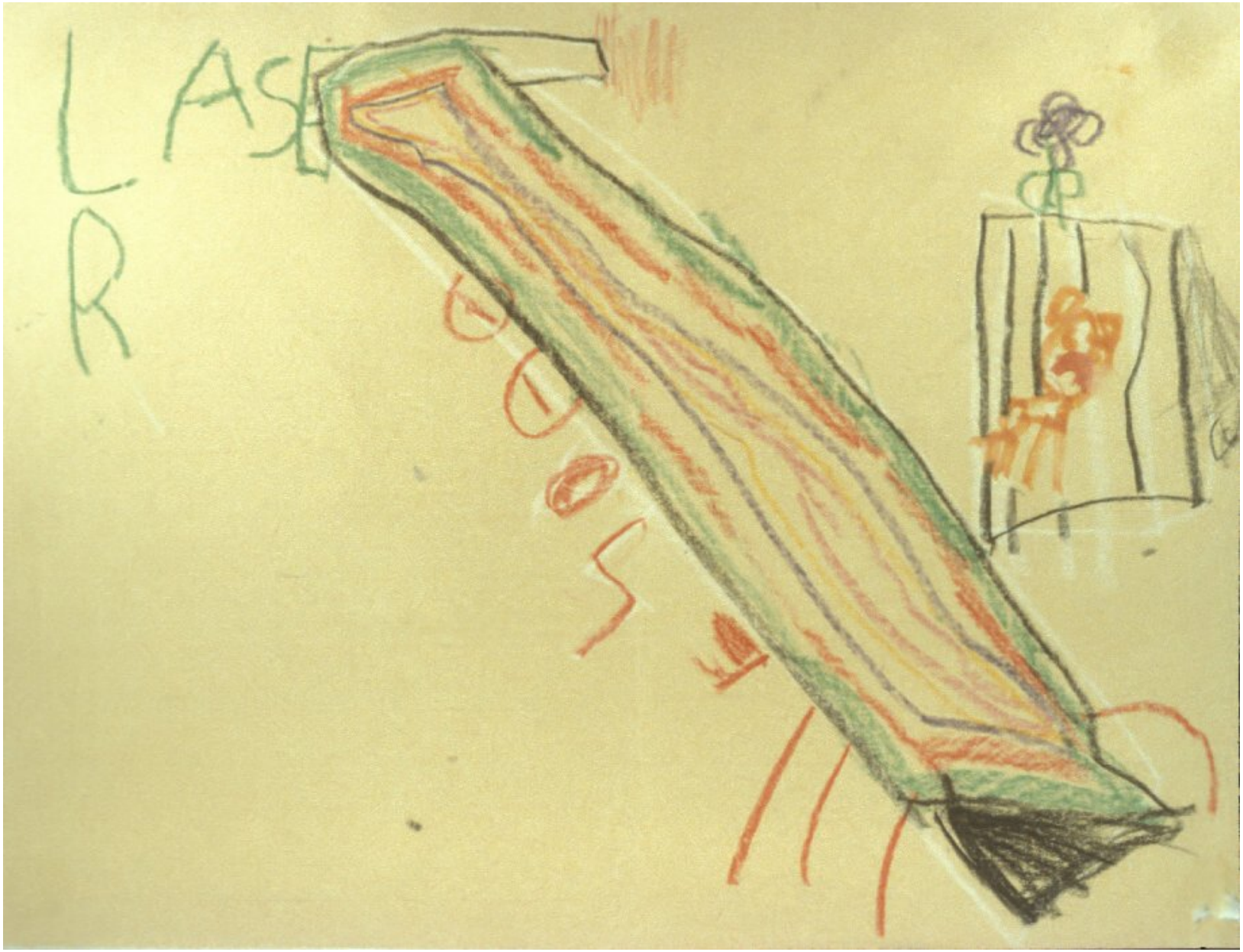

CLOSED
W510
switch 2 loop


OPEN
converter
switch2-helix
sh1
sh2
switch2

Roger Goldman, *PGFR USA*, 1984



Roger Goldman, *Proc. Gold. Fam. Refrig.*, 1984



Acknowledgements

NIAMS
National Institute of Arthritis and Musculoskeletal and Skin Diseases

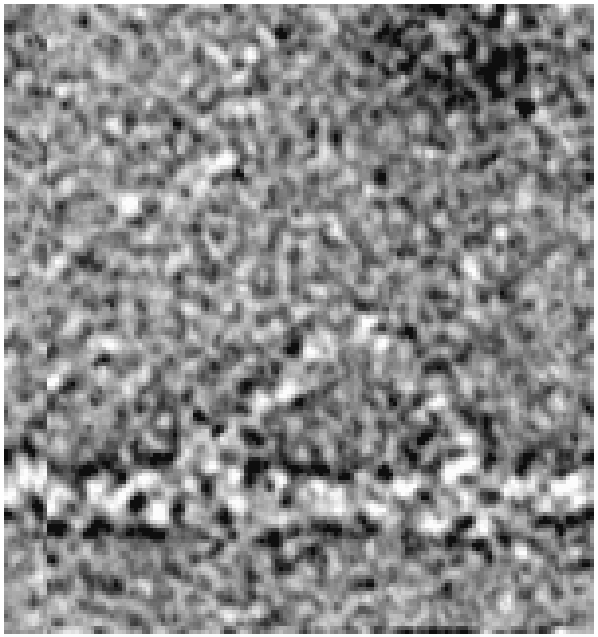
NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES
NIGMS 40 years of discovery
NATIONAL INSTITUTES OF HEALTH

National Science Foundation
WHERE DISCOVERIES BEGIN

HFSP Human Frontier Science Program

Joe Forkey
Margot Quinlan
Stephanie Rosenberg
Henry Shuman
Barry S. Cooperman

Myosin V Strolling



The Muscle Group, Leeds 2000

Rate and Equilibrium Constants Depend on Mechanical Strain

$$\mu_1(x) = \mu_0 + \int F(x)\,dx$$

$$K = e^{[\mu_1(x) - \mu_2]/k_B T}$$

$$k_- = k_+ / K = e^{[\mu_2 - \mu_1(x)]/k_B T}$$