

THE BIOLOGICAL PHYSICIST

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

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As the academic year starts,
THE BIOLOGICAL PHYSICIST
once again brings you a blockbuster issue! In addition to our
regular features like PRE Highlights, and DBP updates from
Peter Jung and Shirley Chan, we bring you the results of a
survey of DBP members conducted jointly by PRE and
DBP. And, we bring you a profile of pioneering biochemist
Jane Richardson.

■ SB

Results from Survey of Members of the Division of Biological Physics

by Margaret Foster,
Senior Assistant Editor, Physical Review E

In June 2003, editors of Physical Review E and the chair of the Division of Biological Physics sent a survey to members of the APS Division of Biological Physics. The questions were intended to ascertain how well the section of Biological Physics serves the community and to solicit suggestions for enhancing the quality and usefulness of the section. Seventy-nine responses were received, and we would like to thank all who participated. We present here results from selected questions, as well as some information concerning submissions during 2003. All responses were tabulated, although respondents did not always answer all questions.

We asked how important various considerations were when members were selecting a journal for submitting their work on biological physics. We found interesting that respondents rated a fair review as somewhat more important than a timely review. The readership and the prestige of the journal were also rated as important. (See Fig. 1)

When asked where they had submitted work in the past 3 years, respondents listed 77 different journals. The Biophysical Journal and PNAS topped the list, with Physical Review Letters and Physica Review E following closely behind. Nature and Science were next, followed by Macromolecules, Journal of Neuroscience, Journal of Theoretical Biology, and Journal of Chemical Physics. (See Fig. 2)

When asked about their research interests in biological physics, DBP members indicated a large interest in theory, followed by interests in biomolecules, subcellular and cellular structures and processes, and multicellular phenomena. There was interest also in bioinformatics, properties of higher organisms, and ecology and evolution. (See Fig. 3)

Topics of papers submitted in 2003 to the Biological Physics Section in Physical Review E may be seen in Fig. 4. The papers were characterized by their principal PACS number. The largest number of papers were submitted on biomolecules, followed by properties of higher organisms, theory, and subcellular and cellular structure and processes. Bioinformatics does not explicitly appear, since there is no corresponding PACS number. Otherwise, submission topics may be compared to research interests of the respondents in the survey.

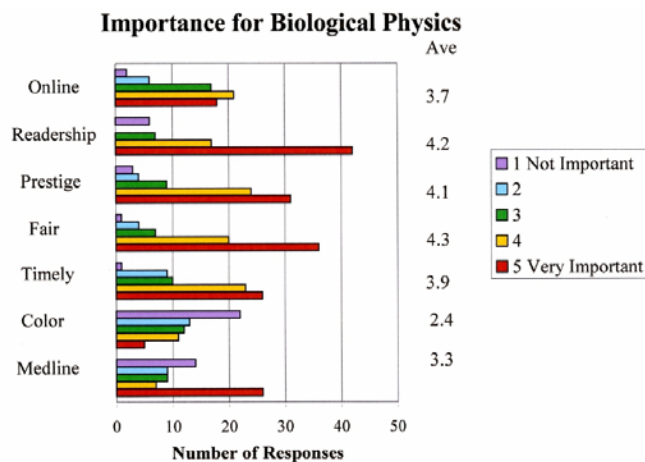


Fig. 1. Results for survey question: Please rate on a scale of 1-5 (1: not important, 5: very important) the importance of the following criteria when selecting a journal for submission of biological physics articles:

- indexing in MEDLINE
- Color online
- timely reviews
- fair and helpful reviews
- prestige of journal
- readership of journal
- availability of online journal

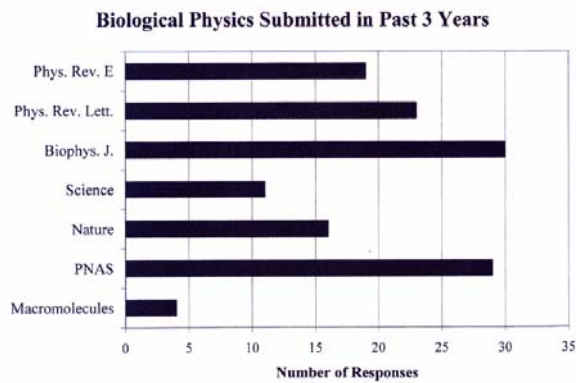


Fig. 2. Results for survey question: In the past three years, where have you submitted your work in biological physics? Please check all that apply:

- Physical Review E
- Physical Review Letters
- Biophysical Journal
- Science
- Nature
- PNAS
- Macromolecules
- Other (please specify)

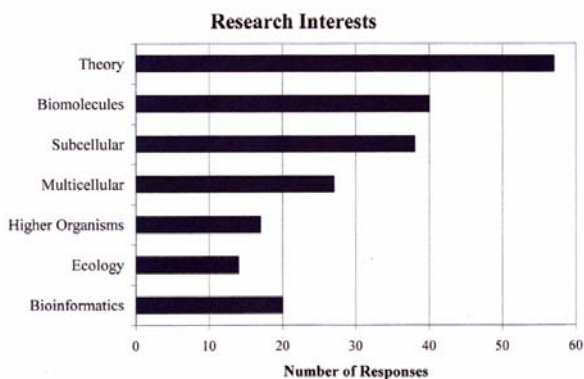


Fig. 3. Results for survey question: Please indicate your research interests in biological physics (check all that apply)

- theoretical and mathematical aspects of biological physics
- biomolecules
- subcellular and cellular structure and processes
- multicellular phenomena
- properties of higher organisms
- ecology and evolution
- bioinformatics
- other (please specify)

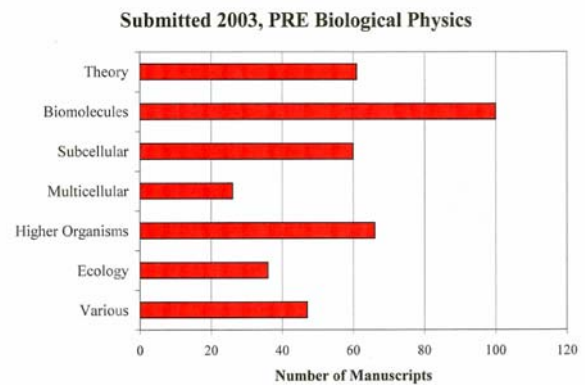


Fig. 4. Topics of papers submitted in 2003 to the Biological Physics Section in Physical Review E. Papers were characterized by the topic indicated by their principal PACS numbers

Average Time from Receipt to Acceptance Published 2003 Direct Submissions

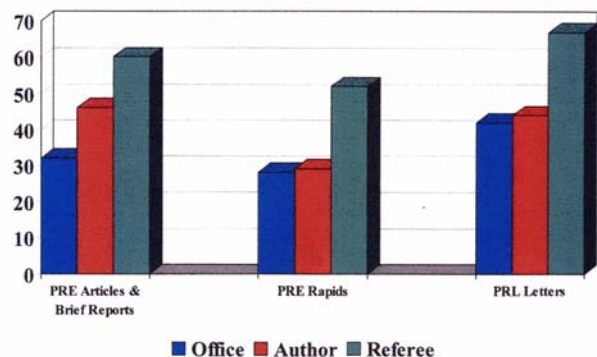


Fig. 5. Average times, in days, from receipt to acceptance, for manuscripts to reside in the office, with authors, and with referees, for papers submitted directly to Physical Review E and to Physical Review Letters and published in these journals in 2003.

We consider it a strength that the Biological Physics Section of Physical Review E does not restrict topics for submission and publication. The section welcomes submissions of biologically inspired physics papers reporting new results. Guidelines are given in the memo "Biological Physics papers in Physical Review E," available from <http://forms.aps.org/author.html>. The new results may involve any of the following:

- advances in fundamental physical understanding of biological systems.
- new physical phenomena in a biological system.
- better theoretical and experimental methods for physical analysis of biological data.

(iv) new physical instrumentation relevant to biology.

Within these guidelines, we are trying to improve the quality of papers published in the Biological Physics

section. We thank the referees for sharing their expertise. Average times from receipt to acceptance for manuscripts published in 2003 in PRE and PRL are indicated in Fig. 5.

Last Call for Symposium Proposals from Program Chair and Chair-Elect Peter Jung

There is still time to submit a proposal for an invited symposium at the APS March meeting. The deadline is September 1. When you put one together, please follow the instructions below. I am looking forward to your ideas!

Instructions for submission of proposals for DBP symposia at the 2005 March meeting in LA

A. Symposium Title: Please don't forget that we would like to attract a large audience to each symposium and that we compete with many parallel events. If a title is too technical – as grand as the content of the symposium may be – it is likely that we will not attract a large audience.

B. Organizer:

Name:
Affiliation:
Phone:
Email:
Postal Address:

C. Description of Symposium:

This description is the basis upon which the program committee will select proposals.

Please describe the symposium in non technical terms (so that the committee members with a diverse background can understand the relevance). Write it like you write the proposal summary of an NSF

proposal. Describe the role of each speaker and what she/he will present and how it complements the other speakers. In other word, we would like to see an overall plan and coherence between the speakers. Like an NSF summary, please stay within 1 page.

D. For each speaker:

Name:
Affiliation:
Phone:
Email:
Postal Address:

E. Session chair: It is very important that a session chair is selected at the time of proposal submission. The organizer can be session chair. The chair needs to be absolutely committed to attend the March meeting and chair the session.

Name:
Affiliation:
Phone:
Email:
Postal Address:

The DBP program committee (6 members of the executive committee) will select proposals for invited sessions. Submit by email to the program-chair by 09/01 to: Peter Jung, jung@helios.phy.ohiou.edu.

Ribbon Diagrams and Protein Taxonomy: a profile of Jane S. Richardson by S. Bahar

“I was an amateur astronomer all through elementary and high school,” recalls Jane Richardson, “counting meteors, building a telescope, traveling to eclipses, and calculating the orbit of Sputnik from my own observations to earn a Science Talent Search Award.” When she enrolled at Swarthmore College, near Philadelphia, she began in mathematics, physics and astronomy, but then switched to philosophy, keeping a math/physics minor. When she began graduate studies in philosophy at Harvard, however, she quickly realized that the most active research areas in philosophy were those she liked least: modern philosophy, rather than the classics.

Meanwhile, Richardson explains, she had enrolled in “several excellent courses in plant taxonomy and evolution in the Harvard botany department, [which was] very gracious to an interested outsider. I then tried high school teaching, which didn’t work because when I concentrated on something I became completely oblivious to anything else. Then I joined, as a technician, the chemistry lab at MIT where my husband, David, was working on a PhD.”

David Richardson, who had met Jane at Swarthmore, had become fascinated with the recently determined crystal structures of myoglobin and hemoglobin during his senior year, and, as a beginning graduate student, was researching protein structure in Al Cotton’s laboratory at MIT. “Soon”, says Jane Richardson, “I became hooked as well, and we’ve worked together on various aspects of 3D molecular structure ever since. Protein crystallography appealed to Dave’s talent for making machinery (and, later, software) work right, and it appealed to my love of complex primary data and what is essentially a new kind of natural history.”

It was the beginning of a remarkable collaboration that would spark a revolution in our understanding of protein structure. In 1963,

future Nobel Laureate Chris Anfinsen was looking for someone to determine the crystal structure of Staphylococcal nuclease, which he thought would serve as a powerful model system for the study of protein folding. Dave Richardson took the project on for his doctoral thesis, collaborating with postdoc Ted Hazen, a protein chemist who worked on protein purification and crystal growth.

With one master’s degree in philosophy and another in teaching, Jane Richardson played for a

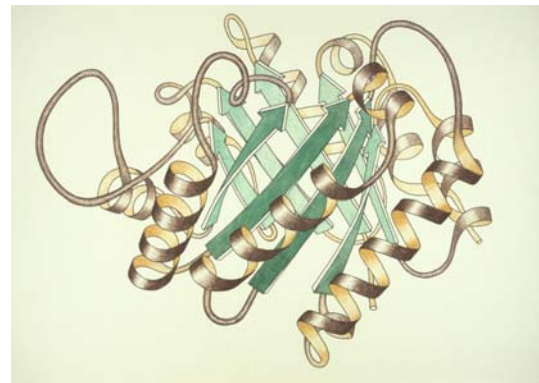


Figure 1. One of Jane Richardson’s early hand-drawn ribbon schematics: a side view of triose phosphate isomerase (the classic “TIM barrel” structure) with a twisted cylinder of 8 green beta strands in the center ringed by 8 brown alpha-helices), colored with pastels.

time what she describes as “the role of a relatively invisible hanger-on”. But that didn’t last long. Her studies of taxonomy and evolution resonated in the protein structure studies she, her husband, and their colleagues were publishing in the late 1960s and early 70s [1-4]. She soon realized that the recurring structural motifs they kept finding in their crystallographic studies could fit into a general classification scheme for protein structure. She was driven, she says, by an

approach of “exhaustively *looking*, in detail, at each beautifully quirky and illuminating piece of data with a receptive mind and eye, as opposed to the more masculine strategy of framing an initial hypothesis, writing a computer program to scan the reams of data, and obtaining an objective and quantitative answer to that one question while missing the more significant answers which are suggested only by entirely unexpected patterns in those endless details.” One can gain fruitful insights through “the inherent charm of close acquaintance with the phenomena”. Painstakingly, Richardson began to construct an almost Linnean taxonomy of protein structure. During this process, she realized that she had to learn to draw the structures she wanted to classify. “I spent two years,” she says, “learning how to make drawings that captured the simplicity and elegance I found in those structures.” [5]

In Richardson’s careful sketches, a remarkable array of structural motifs and rules



Figure 2. A ribbon drawing produced by David Richardson’s Mage program: four subunits of Cu,Zn superoxide dismutase (shown as they pack in the crystal). The structure of this protein was solved in the Richardson laboratory.

emerged. She described these in a seminal *Nature* paper, “ β -sheet topology and the relatedness of proteins”, in 1977 [6], focusing on the topological classification of β -sheets. The article, which also had the cover picture, a

powerful illustration of a “Greek key” structure in the polypeptide backbone of prealbumin, juxtaposed with a photograph of a Greek key structure along the edge of a 450 B.C. Greek amphora, solidified Richardson’s reputation. And it also revolutionized biophysicists’ understanding of protein structure. Combining observations of taxonomy from earlier papers, and adding many new insights, Richardson presented a table of schematic diagrams for all the topologically distinct β -pleated sheets found in protein structures which had been crystallized up to that time. From her careful observations, she was able to postulate general rules, most of which still appear valid today.

Richardson found that there were two possible types of backbone connections between β strands: “hairpin” connections, in which the backbone chain re-enters the same end of the β sheet it left, and “crossover” connections, where the chain loops around and re-enters the sheet from the opposite end. Crossover connections, she found, were always right-handed [4]. Parallel β structures occurred in large sheets, protected from the solvent by α helices. In contrast, anti-parallel β structures were found as partially unprotected twisted ribbons of two strands. Moreover, all observed β topologies could be described as a relatively limited subset of all possible combinations of connections (hairpins and crossovers). These observations led Richardson to speculate on the energetic landscapes that could lead to such a subset of possible structures. She proposed that

...it may be that one reason that these structures are favourable is because they can fold correctly by many alternative pathways and therefore tend to fold rapidly and reliably. The idea that some broad features of protein structure are determined by essentially kinetic factors during folding (such as the dominance of near-neighbor strand interactions) is not incompatible with the requirement that the stable native conformation of a protein should be in the global free energy minimum. During its evolution, once a protein finds a reasonably stable, kinetically accessible, minimum energy conformation, it is then subject to natural selection for its stability. Selection will dig that particular local energy minimum as deep as possible by adjusting the amino acid sequence to approach optimal fit for the native conformation, and

at the same time probably will raise all the other local energy minima whose stability is not being selected for. The result is very likely to be a genuine global energy minimum, in spite of the influence of kinetic requirements. [6]

The stage was set for a new generation of biophysicists and structural biochemists to investigate the energetics and evolution of protein folding. Furthermore, a new picture of protein topology had entered the scientific canon: the ribbon diagram. Elegant and simple, ribbon diagrams (also called Richardson diagrams) convey the basic outlines of molecular structure in a powerful and immediate visual form (Figure 1). Richardson still expresses amazement that she has “a whole generation of scientists see[ing] protein structure through my eyes”.

In the years that followed, Jane and Dave Richardson, working at Duke University Medical Center expanded their studies to include other

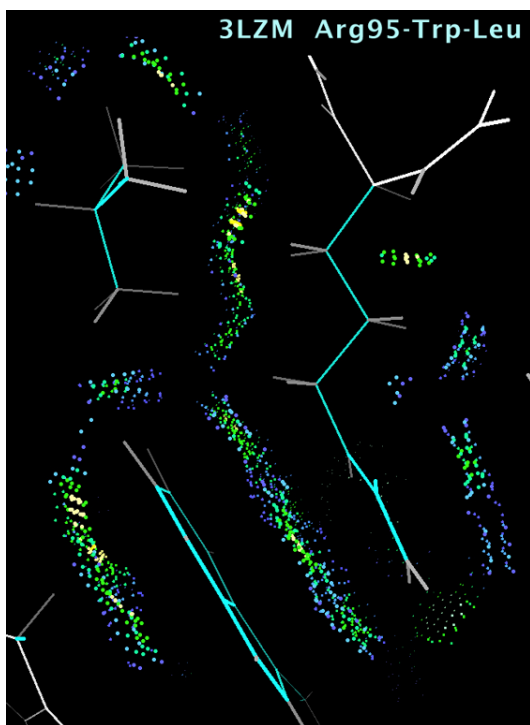


Figure 3. An example of the Richardsons' current all-atom contact analysis for the packing of three sidechains in T4 lysozyme, where the dot surfaces outline the places where two atoms are in contact.

aspects of 3D protein structure. In addition to looking for broad structural motifs, they were led to investigate de novo protein design, as a method of testing theoretical predictions about the determinants of protein folding [7]. De novo design, explains Richardson, is “sort of like doing prediction backwards. Instead of working from natural structures, we look at whole categories of structures to find one that is relatively simple, that we think we understand, and that we can try to isolate as a sort of simplest-case paradigm structure. We then use that structure to design a sequence of amino acids that is not related to any natural structures. And then we actually try to make the new structure, either by direct chemical synthesis or by cloning and expression. At that point, you are able to see if it does actually fold up into something that resembles what you expected.” [8]

The Richardsons have also become pioneers of developing software methods for the representation of protein and nucleic acid structures. They develop software in order, as they write on their lab's website, “to fill what we see as unmet needs, most notably **kinemages** (molecular graphics optimized for the communication of specific ideas in 3D) and the associated Mage and KiNG display programs, free software on Mac, PC and Unix, widely used for teaching, textbooks, journals, and databases as well as for research.” For more details on these software packages, visit <http://kinemage.biochem.duke.edu>.

Most recently they have developed a method for studying the detailed contacts where atoms touch (Figure 3; [9]). It is used to study the packing inside and between molecules and also to find and correct errors in the experimental models of protein [10] and nucleic acid [11] structures.

Twenty one years ago, Jane Richardson wrote that she “never got a PhD, and I don't have tenure and probably never will.” Today, she is a James B. Duke Professor of Biochemistry. “I think”, she says, “that you can be intensely ambitious in science on very non-establishment terms that have nothing at all to do with running your own lab, with getting tenure and lots of grant money, or even with getting explicit recognition for your ideas. The first big reward is the excitement of attaining a new insight, independent of whether it is shared with anyone else. But if later work proves you right and if everyone else eventually ends up adopting and using your ideas, then that is *success*, and it can

in some ways add to the fun if they don't always realize who started it. I want immortality from both my biological and my intellectual children, but I don't think they would be as much worth procreating and nurturing if they were always busy thinking of me as their source."

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PRE HIGHLIGHTS

**Biological Physics Articles
from Physical Review E**
(Statistical, Nonlinear, and Soft Matter
Physics)

**June 2004
Volume 69, Number 6, Articles
(06xxxx)**

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Sorting mesoscopic objects with periodic potential landscapes: Optical fractionation

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010902(R)

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Stochastic model for the species abundance problem in an ecological community

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[Marek Cieplak](#), [Trinh Xuan Hoang](#), and [Mark O. Robbins](#)

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BRIEF REPORTS

Spreading of families in cyclic predator-prey models

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[M. Martinis](#), [A. Knežević](#), [G. Krstačić](#), and [E. Vargović](#)

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012903

COMMENTS

Comment on "Theory of high-force DNA stretching and overstretching"

[Pui-Man Lam](#)

Published 2 July 2004 (2 pages)
013901

Reply to "Comment on 'Theory of high-force DNA stretching and overstretching' "

[Cornelis Storm](#) and [Philip Nelson](#)

Published 2 July 2004 (2 pages)
013902

CONFERENCE ANNOUNCEMENT

The 2004 fall meeting of the Ohio Section of the American Physical Society will be held Oct 15-16, 2004 at Oakland University in Rochester, Michigan. One of the themes of the meeting will be

"Physics in Medicine",

and we will have a special symposium to celebrate the 2003 Nobel Prize in Physiology or Medicine for the development of Magnetic Resonance Imaging. For more information about the meeting, see

<http://www.oakland.edu/~roth/OSAPS-MIAAPT.htm> or contact

Brad Roth (roth@oakland.edu).

The abstract deadline is Sept. 24.

CONFERENCE ANNOUNCEMENT

The 24th annual Dynamics Days conference (Dynamics Days 2005)
will be held

Jan. 7 - 10, 2005 in Long Beach, CA.

The meeting will be hosted by

U. C. Irvine. Dynamics Days is an annual conference organized to gather a
variety of researchers with overlapping interests in nonlinear dynamics.

Participants span the fields of mathematics, physics,
biology, chemistry, ecology, engineering, and geology. For more
information and registration, please see the conference website:

<http://www.physics.uci.edu/dynamicsdays2005/>.

(Dynamics Days is not a DBP or APS event.)

DBP Leadership Update From Secretary-Treasurer Shirley Chan

Current members of DBP's election nominating committee:

Raymond Goldstein, as the Chair, one-year term, expires in March 2005,

Herbert Levine, two-year term, expires in March 2005.

Ned Wingreen, two-year term, expires in March 2005.

Andre Longtin, two-year term, expires in March 2006.

Aihua Xie, APS Council-appointee, one-year term, expires in March 2005.