HARVARD UNIVERSITY

Professor David R. Nelson
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December 10, 2003

R. de Ruyter van Stevenick
Indiana University Bloomington
Department of Physics
727 E. Third Street
Bloomington, IN 47405-7105

Dear Professor van Stevenick:

I write to recommend John Marko for a tenured professorship at Indiana University, Bloomington. I first met Marko during his final year of Ph.D. work at MIT (in 1989) and have since followed his research with some interest. Although I gather that Marko has now started up a laboratory, I also think that John exemplifies new and exciting ways in which theoretical physicists can contribute to biology.

Theoretical analysis has now begun to play an increasing role in problems at the boundaries between physics, biology and materials science. New experiments made possible by fluorescence labeling, genetically engineered production of specific functional units and new techniques from physics like laser tweezers call for increasingly sophisticated theories. Experiments include direct visualization of function in individual cells in neural networks, work on the collective collective behavior of semiflexible filaments like actin, studies of the motion of molecular motors along tubules, as well as manipulation and synthesis of libraries of DNA and protein sequences. Much of John's work has been inspired by direct probes of supercoiling combined with micromanipulations (stretching and twisting) of DNA. An inventory of formidable new theoretical techniques from statistical mechanics, polymer science and "soft" condensed matter physics developed during the past twenty years can be brought to bear on these problems. John is among the most successful "soft condensed matter" physicists attempting to take part in the biological revolution, and he is particularly adept at applying these tools to interesting biological problems.

John is most famous for his theoretical studies (initiated in collaboration with Eric Siggia) of supercoiling in DNA. Synthesis of DNA in biological organisms often leads to plectonemic ("twisted thread") or supercoiled configurations, not unlike the cords on many telephones. Understanding how such a twisted loop behaves when subjected to Brownian motion in a biological solvent involves doing statistical mechanics with a constraint. At finite temperatures the energetically preferred supercoiling is reduced in order to take advantage of entropically favorable configurations available to an untwisted loop. Mathematically, one must study the partition between twist and writhe at fixed linking number as a function of the temperature. Marko and Siggia elegantly analyzed this fascinating problem, and obtained good agreement with measurements of the radius of gyration of a plectoneme as a function of the excess linking number. Subsequent theoretical studies by Marko and others have led to excellent agreement with force vs. extension curves and force vs. twist curves for DNA molecules attached to optical beads.

John is the acknowledged theoretical leader in this field -- he talks frequently to experimentalists, knows all the relevant biological details, and has taking the lead in popularizing important ideas from physics with the biological community. His current work on the packaging of chromosomal DNA's and the binding of various proteins to DNA as a function of the force is extremely interesting. John has now had the courage to start an experimental laboratory, often an important ingredient for achieving credibility with real biologists. I think John is as good or better as Ray Goldstein, recently tenured at the University of Arizona.

His theoretical abilities are not as strong as Phil Nelson and Randall Kamien (tenured at the University of Pennsylvania), but John has better insights into important experimental issues than these theorists.

Sincerely yours,

David R. Nelson
Mallinckrodt Professor of Physics
Professor of Applied Physics
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DAVID A. WEITZ
PROFESSOR OF PHYSICS AND APPLIED PHYSICS

December 13, 2003

Prof. R. de Ruyter van Steveninck
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Dear Sir:

I am writing this letter of recommendation on behalf of John Marko, on your request. I have previously sent a letter on behalf of John to Prof. Glazier in your department, and I am sending essentially the same letter now to you. I have known John for several years, since he worked as a post doc with Tom Witten, and have followed his career as a very interested observer rather than a collaborator. I base my comments on this.

John has followed an unusual, but remarkable, career path. He began his career as a theoretical physicist, doing rather formal work in condensed matter physics. He then did a post doc where he became more versed in soft condensed matter physics, but rather than moving on in that area, he turned to biological physics, and retrained himself first in theoretical biological physics while working with Siggia, and then in both theory and experiment while at Rockefeller in Libchaber's program. Now, I am not even sure exactly what he is, an experimental biophysicist who is excellent with theory, or a theoretical biophysicist who also does experiment. In fact, this ambiguity is exactly what makes John such an excellent scientist. Modern biophysics can not be done exclusively by theorists, and yet experimental work is greatly enhanced by good theoretical input. John is uniquely positioned to offer both, and clearly has a large impact in doing so.

The work of John that I know best is his explanation of the behavior of the force required to stretch DNA. He was clearly the first person to think about the theory of the stretching of DNA and to recognize the crucial interplay between entropic and purely elastic effects. His was the first work to critically analyze the early single molecule experimental data, and, for me, it was John's work that confirmed that all the single molecule experimental work was actually going to make a significant contribution. What I find truly remarkable about John is that to continue with this work he realized that he would have to not only do the theoretical analysis, but would have to contribute to the experimental work as well. As a result, John has set up a significant experimental effort in Chicago. This is a bold move for a theorist, but John has clearly been successful, already attracting funding for his experimental work. Attracting funding is a generally difficult thing to do for a young faculty member; getting funding for an experimental program is all the more difficult if you are a theorist by background. Thus, John's success is clearly a tribute to his abilities and to the quality of his program.

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Albert Libchaber, who has perhaps done more than any other person in training theoretical physicists to work in biophysics with his program in Rockefeller, has said that theoretical physicists make the best experimental biologists. I think he was thinking of John in particular when he said that. A strong testament to his insight, and foresight, is that one of John's post doc advisors has actually followed John and switched from more traditional condensed matter physics to biophysics. There is no question that biophysics is going to play an increasingly central role in the physics of the twenty-first century, and there is no question in my mind that John is going to be a leading participant.

John has clearly built a very impressive program at Chicago. The fact that he is well funded to do experiment, even though his reputation has been as a theorist, is a testament to his ability to identify good problems and to accomplish them. I think that he will only continue to be better funded as his experimental program expands.

I would rank John quite very highly among his peers. For example, he has clearly been more successful so far than some of the other theorists from the Rockefeller program who have switched from theory to experiment as they learned more about biology. For example, I think John has, so far, been more successful than Mark Goulian who moved from the Rockefeller program to UPenn, although I think that Mark has really started to take off in his own right. In addition, although I may be biased as an experimentalist, I think that John will ultimately have far more impact than other theorists who have followed more traditional routes. For example, I think that John will ultimately have more impact than Randy Kamien, who is an excellent soft condensed matter theorist of a similar age to John. More generally, there is a very strong trend for condensed matter physicists to move into biophysics. The very best of these in the US are, in my view, Albert Lichaber, Stan Leibler and Cyrus Safinya, all of whom are having a very large impact, and all of whom are quite a bit more senior than John. After these three, I would rank John as among the best one or two physicists doing biology.

Biophysics is clearly going to be one of the major areas of physics in the coming decade, and John will be one of the leaders. I would strongly urge you to do everything you can to hire him. He would add to any department, and he would be a particular benefit to a department like yours where there is already a growing effort in biophysics.

Yours sincerely,

David Weitz

David A. Weitz

-----Original Message-----
From: Nick Cozzarelli [mailto:ncozzare@socrates.Berkeley.EDU]
Sent: Tuesday, December 16, 2003 1:53 PM
To: De Ruyter, Robert R.
Subject: John Marko

Dear Dr. de Ruyter van Steveninck,

John Marko gets my highest recommendation. John is truly unique. He is someone who has mastered both physics and molecular biology. I can say that about very few others. John is internationally known for his application of physics to biology. He has made particularly important contributions to the structure of DNA and of chromatin. He was the first to show that the new single molecule force extension data on DNA could be beautifully explained by the worm-like chain model. He also had a lovely paper on the kinetics of finding sites in supercoiled DNA. Particularly imaginative was his interpretation of the action of DNA unlinking by topoisomerases in terms of the kinetic proofreading model. His recent work on chromatin structure has been unique in making biophysical measurements essentially in vivo. I found his refutation of scaffold model for chromatin, the long-accepted model in the field, to be compelling. He has also developed a very clever new technology using extremely small magnets which nonetheless exetfar higher forces than previously obtained and allow unique view of DNA for a magnetic tweezer.

When I first met John, he was just breaking into biology and he would ask incessant, difficult, and sometimes a little impolite questions about biology that would give me a headache. The questions were perceptive and revealed how much he knew already in his single-minded quest to master his new field. He is the most original person that I know in the field of biophysics. He's extremely productive because he combines his originality with theoretical and experimental skill and enviable facility in communication.

The field of biophysics is being reborn and I see John as one of the leaders. We are building up biophysics here at Berkeley and in a few years we will have a new building. I have already told people here that I felt that John should be one of the first people to recruit.

Sincerely,
Nicholas Cozzarelli

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Nicholas R. Cozzarelli

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