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Professor Robert R. De Ruyter
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Dear Professor De Ruyter:

I have known John Marko since he came to Cornell University as a postdoc. He then became the first fellow in the, then, newly established Center for Studies in Physics and Biology at The Rockefeller University. Throughout that period he displayed a very keen talent in interacting effectively with experimenters, picking relevant problems, and not being seduced by technique. He is in fact quite proficient at technique. Be it Monte Carlo with its panoply of convergence tricks, renormalization group, transfer matrices, or just back of the envelope. I suspect he may be undervalued by the polymer physics community because he has not attacked the more esoteric technical problems that are current. But good science, particularly in biological areas, is more about asking the right question than technical gymnastics. In our joint work, John was a more than equal partner.

While at Rockefeller John began a second career as an experimenter. The idea of examining real chromosomes mechanically did not come from Libchaber, but from John and me, and Chatenay was John's immediate tutor in the lab. (The first author was another theoretical physicist who has not done further work in the chromosome area.) Their paper (48) could never have been written by a cell biologist or a biochemist who would not think of using nonlinear elasticity as a phenotype. Nor would the high tech labs proficient in micromanipulation, such as Block's or Bustamante's, think to work on something as ill defined as an intact chromosome. However, someone familiar with soft condensed matter realizes that complicated objects can have simple phenomological descriptions, and so, they do the experiment. Clearly there is a large niche in biology for those willing to approach complicated systems by phenomological means. It is also essential I feel, for those physicists starting in biology to run a lab (those in bioinformatics might be excused). Pure thought plus the existing data set will only get you so far, as our joint paper on the same subject (paper 51) attests. In biology, as opposed to physics, the experiment you need probably has not been done.

John established his own lab in Chicago, and he is combining the physical manipulation of chromosomes with chemical/biochemical treatments. His projects with Hirano on the SMC's and Heald on xenopus extracts look like particularly promising ways to combine the expertise of

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prominent biochemists with his mechanical measurements. His recent papers (#70, 75 and 76) provide new data on the very controversial subject of protein scaffolds in mitotic chromosomes. Again the questions being asked are physical, what is the nature of the forces condensing DNA, and it's already clear that the results are interesting and would never have occurred to the cell biologists studying chromosome condensation. Chromosome structure is a large area of biology and many biologists enter it and never leave.

There is every indication that Marko is taken very seriously by prominent biologists whose interests touch on kinetics of DNA protein interactions, chromosome dynamics, etc. The paper (#62) with Halford, I believe was initiated by Marko, and comprises a clean test of an important issue of how rapidly DNA binding proteins find their targets. The paper (#65) with the Sadat group is another example where some quantitative analysis was essential to understanding the experiments. The invited presentations at the chromosome Gordon Conference and a CSHL meeting are further evidence of this. His chromosome work has recently been prominently reviewed by N. Kleckner at Harvard, in papers still in preprint form.

It is evident from his CV that John is a well known personage in North America and Europe among biologically oriented physicists and has generated ample grant funds. I think he will do much better in a stronger research university than UIL Chicago, since success in biology more than theoretical physics depends on the caliber of ones group. There are very few people available with strong theoretical physics skills who also run a credible lab. Stan Leibler is one of the few. There is a larger pool of biophysicists with a stronger experimental physics training (e.g. Steve Block and members of his lab, C. Bustamante, etc), but they tend to deal with simpler, better controlled systems than John. Most of biology is not simple, so there is a definite niche for those who have the ability to ask interesting questions by phenomological means about systems ill defined biochemically. His research statement indicates that he is still expanding his circle of biological collaborators and will be quite busy for the foreseeable future.

Best regards,

E Siggia

Professor Eric D. Siggia

EDS:mjl