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Biocomplexity Faculty Search Committee
c/o Prof. Rob de Ruyter van Steveninck
Department of Physics
Indiana University
Swain Hall West 117
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Dear Search Committee Members:

It is my pleasure to recommend **Dr. Roya Zandi**. Dr. Zandi completed her Ph.D. under my supervision. She impressed me as a student with extraordinary potential. After graduation, both as a post-doc and as a University of California Presidential Fellow, she has continued to collaborate with me. This subsequent experience confirmed my earlier strong assessment of her qualities. Dr. Zandi is now a mature researcher. She is well on her way to becoming a leading scientist, and already has a history of accomplishment that belies her relative "youth" in research. Below, I will review my experiences with Dr. Zandi, describing the projects on which we have worked and presenting my assessment of the contributions of Dr. Zandi to those projects. In this way, I hope to make it clear exactly why I have such a high opinion of her.

Our first project together was the continuation of a program of research into the mechanical and topological influences that control the behavior of supercoiled DNA. At the core of this work is an investigation of the action of histone spools in the so-called nucleosome configuration. Dr. Zandi and I worked out a mathematical description of the way in which histones constrain the possible distortions of DNA that is wrapped around them. In particular, we were able to describe and quantify a minimal set of constraints that serve to stabilize the DNA strand wrapped around it. As a first step in this calculation, Dr. Zandi determined the equilibrium shape of a length of supercoiled DNA in the absence of stabilizing influences. She then determined the nature of the mechanical instability of unconstrained supercoiled DNA. Next, she performed an analytical and numerical analysis of the way in which mathematical constraints on the supercoiling act to stabilize these equilibrium configurations. In particular, she characterized the constraints that suffice to stabilize the double loop of DNA wrapped around a histone.

Finally, she identified source of the constraints in terms of the grooves that have been identified on the surface of histones.

Note that in the above paragraph, I attributed what might look like all the significant progress in this calculation to Dr. Zandi. In fact, this was the case. The idea of the calculation was mine, and I did do what I consider to be important background work. However, the realization of the goals that I set for the project is due entirely to Dr. Zandi's conceptual and calculational breakthroughs. The paper that resulted from this work was published Physical Review E.

The next project on which Dr. Zandi and I embarked arose from our interest in the effect of electrostatic interactions on the configurational properties of long, stiff polymers. This interest was stimulated by our realization that the depiction of DNA as an uncharged elastic rod – which forms the basis of our histone calculation – is not accurate, in that the backbone carries a substantial amount of charge. DNA is, in fact, a polyelectrolyte. As a first step in the direction of understanding the effect of charging on the conformations of DNA, Dr. Zandi and I set out to determine the statistical distribution of the end-to-end distance of a short segment of a stiff polyelectrolyte, modeled as charged Worm-Like-Chain. This calculation built on one already in the literature, in which the distribution was calculated for a neutral Worm-Like-Chain. The general strategy was straightforward – to add electrostatic repulsion to the bending energy of this chain, and carry through an extension of a previously performed computation. The actual implementation of the strategy was far from elementary, as the electrostatic interaction adds a significant layer of difficulty to the problem. The efforts that Dr. Zandi expended to extract results were substantial. However, the information gained was also considerable. We were able to critically assess approximations for the persistence length of polyelectrolytes that have appeared in the literature over the past several years, and to identify the one published form that most accurately represents the statistical mechanics of short, stiff polyelectrolytes. In addition, Dr. Zandi discovered that an unexpected, and as yet unexplained, scaling form describes the persistence length in regimes in which no formula now in the literature is accurate.

The above work led to some extensions. We were able to calculate the equilibrium shape of a polyelectroyte under the influence of external torques. We also obtained new and interesting results and on the buckling of one as the result of compressional stresses. There was a third collaborator in this project, Dr. Ramin Golestanian, who is an expert on polyelectrolytes. He provided general knowledge of the field and creative insight. I provided critical commentary and a few useful suggestions. Dr. Zandi was the workhorse of the group, and the intellectual driving force of the collaboration. She was the linchpin of all discussions, and she performed every significant calculation on which the research was based. As a research advisor, I found myself increasingly impressed by both the speed with which she completed difficult analytical and numerical computations, but also the consistent quality of her results. To first approximation, she never made a mistake.

The results if this project made up the second half of her Ph.D. dissertation. It also led to four published papers.

It should be noted that the participation of Dr. Golestanian in the collaboration was due almost entirely to Dr. Zandi. Drs. Zandi and Golestanian were unacquainted previous to their scientific interaction. I do not recall who initiated the communications between the two of them, which came about because of overlapping research interests. I do know that Roya plays the central role in this three-way interaction.

Since her graduation, Dr. Zandi and I have collaborated on three additional projects. The first project was an investigation of the mechanisms that drive translocation through a pore. This is an extensively studied phenomenon with relevance to a number of important biological processes. Among the explanations for translocation on finds the influential model of rectified Brownian motion, or the Brownian ratchet. At first blush, this is the model that one might expect to apply to the system studied by Dr. Zandi, in collaboration with Professor William Gelbart, Dr. David Reguera and me. This system consists of a stiff rod, which is allowed to move through a hole into an enclosed volume containing a number of particles that can attach to the rod as the result of a short-range attraction. However, simulations carried out by Dr. Zandi clearly established that a more reasonable explanation over a large parameter range is that the rod is effectively pulled into the volume by the particles, and that the force exerted by the particles can be quantified in terms of an effective free energy gradient with dynamical modifications, representing the attenuating effect of time delays associated with the requirement that the particles diffuse to the rod and make room for each other once attached. These results were genuinely unexpected. The article describing them has been published in the Proceedings of the National Academy of Sciences. Once again, Dr. Zandi was the central member of the collaboration. She performed all numerical work of major significance. She also participated fully in all discussions having to do with interpretation of results.

The second project is a study of the sources of icosahedral symmetry in viruses. Here, the collaboration was wider, consisting of Drs. Zandi and Reguera as well as Professors Bruinsma, Gelbart and me. However, the most recent key calculations are, in essence, entirely the consequence of the efforts of Drs. Zandi and Reguera. Two papers has already been published, the first in Physical Review Letters, describing preliminary results, and the second in Proceedings of the National Academy of Sciences, reporting the outcome of a more searching calculation. This second paper earned a commentary by Zlotnick in the same issue of PNAS that carried it, and a short article on this work based largely on an interview with Dr. Zandi will appear in the forthcoming issue of Physics Today.

Finally, I have been working with Dr. Zandi and Professor Mehran Kardar of MIT the Casimir force in Helium film as it is manifested in the dependence on temperature of the thickness of an unsaturated film in the vicinity of the superfluid transition. This research has been stimulated by the remarkable experiments of Garcia and Chan. The Casimir force is propagated via fluctuations of the superfluid order parameter. We have managed to provide a proposal for the mechanism that underlies thinning of the film reasonably well below the transition. This mechanism invokes fluctuations in the phase of the complex wave function associated with the velocity field that is generated by local fluctuations in film thickness. In this collaboration, the three members have acted essentially as equals. A paper describing our results has just appeared in Physical Review Letters. Dr. Zandi's collaboration with Professor Kardar goes beyond this project, as she has initiated a formal arrangement with him that involves her visiting him at his home institution, MIT, on a regular basis. We are now in the process of looking more closely at the unusually large Casimir force that is generated by critical fluctuations.

As noted in the above paragraphs, Dr. Zandi is extraordinarily adept at carrying out both analytical and numerical calculations. Once she has defined a problem and fixed on the computations necessary to generate a solution, she is exceptionally efficient at implementing those computations. In this regard she ranks among the best young physicists I have known. I am now certain that she will be a major player in science.

I recommend Dr. Zandi for this position in the strongest possible terms.

Sincerely,

Joseph Rudnick
Professor of Physics
Chair, Department of Physics and Astronomy