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Biocomplexity Faculty Search Committee
In Care of Professor Rob de Ruyter van Steveninck
Department of Physics
Indiana University
Swain Hall West 117
Bloomington, IN 47405-7105

Dear Faculty Search Committee:

It is with the greatest of pleasure and enthusiasm that I write in support of Dr. Emadeddin Tajkhorshid's application for an Assistant Professorship in Biophysics at your university. In my capacity both as a Professor of Chemistry with a theoretical group active in the field of protein folding and physical bioinformatics and as a member of the National Institute of Health (NIH) Resource for Macromolecular Modeling and Bioinformatics where Dr. Tajkhorshid is the Assistant Director of Research, I have become well acquainted with his outstanding research and teaching achievements in the area of the function and simulations of membrane proteins. Furthermore, we have collaborated on two research projects.

As is clear from Dr. Tajkhorshid's resume, he is an active and prolific scientist. He received most of his professional training both in the USA and Germany, and with his unique background in Biophysics, Pharmaceutical and Medicinal Chemistry, he has been able to have an impact on modern research at the interface of several different disciplines. I first became aware of Dr Tajkhorshid's expertise after he joined the NIH Resource here at the University of Illinois and published a series of papers in *PNAS* and *Science* on the transport (SMD simulations) of small molecules through membrane proteins. While membrane proteins constitute approximately one-quarter of all the proteins in any genome, they have been difficult to study both experimentally and computationally because of their size and low solubility in water. The computational approaches and techniques developed in the NIH Resource have allowed researchers throughout the world to simulate large protein complexes and assemblies in membranes.

Emad is clearly one of the leading computational biophysicists in the world working on membrane proteins. His recent research has focused on water channels (aquaporins), which play very important physiological roles in many human organs, such as the kidneys, the eye, and the central nervous system. Dr. Tajkhorshid's results also provided new insights into properties of the channel which determine their selectivity and to the discovery of an absolutely novel mechanism of selectivity against charged particles (protons). A movie based on Emad's simulations of the functioning water channel was shown by the Director of the National Science Foundation already in 2003 to an international audience as an outstanding achievement in bringing the computational power of the US supercomputers to investigate biological processes. Many colleagues have told me that they use the movie in teaching their biophysics classes, and it is used in classrooms around the world to explain the action of this system. A figure from this movie recently won the NSF Award for Best Science and Engineering Visualization and appeared in *Science*.

The techniques that the Resource colleagues developed to analyze the conduction profile in water channels were instrumental for my own research on calculating the free-energy landscape for the channeling of ammonia between active sites in the biosynthesis of histidine *(PNAS*, 2003). During this collaboration, I came to deeply appreciate his great talent for molecular modeling which includes both thoughtful applications of quantum chemistry calculations and molecular dynamics simulations. In connection with my grant, "*Merging Bioinformatics and Molecular Simulations: Investigating the Function and Docking of Complexes*" we again collaborated to develop classical force fields parameters for cytochrome c2 which my group then applied to study the transient docking of the small redox protein to the photosynthetic reaction center (*J. Comput. Chem, 2004 and J. Phys. Chem. 2004*).

As both a collaborator and as instructor of the course, "Biophysics of Membrane Proteins", Bioph490M, Emad has helped to train our biophysics graduate students at UIUC. His course (www.ks.uiuc.edu/Services/Class/BIOPHYS490M/) focused on structure-function relationships of membrane proteins. Emad has also participated in developing lectures and tutorials for the joint NSF/NIH Summer School on Theoretical and Computational Biophysics (www.ks.uiuc.edu/Training/SumSchool03/) at the Beckman Institute (BI) and for other computational biology workshops. The BI summer school was attended by over 90 participants from all parts of the US and several other countries, and his class on computer simulations of channel proteins was much appreciated. The clarity and generosity of his teaching are remarkable.

In closing I would like to emphasize that with his outstanding background in pharmacology and experience in applying physical models and computational methodologies to simulate the function of receptors and channel proteins, Dr. Tajkhorshid is uniquely qualified to build a bridge between the physical and medical sciences and advance the field of computational molecular biology. His interests in understanding the biology and resulting physiology of large integrated systems like membrane channels and G-protein coupled receptors involved in signal transduction will resonant well with colleagues in either Biophysics or Biomedical Engineering. While his strength is not in developing new algorithms for molecular dynamics (MD) simulations like a young Charlie Brooks (Computational Biophysics, Scripps) or Ron Elber (Computer Science and Biomedical Engineering, Cornell), his considerable strengths are in applying MD to important biological problems, analyzing the results, and teaching. His scientific capabilities and history of good citizenship in the area of computational biology make him more similar to in spirit to Eric Jacobsson (Biophysics, UIUC) and Alex MacKerell (School of Pharmacy, Maryland). It is with the greatest of enthusiasm that I re-iterate my support for his application, and I am confident he would be an excellent colleague in any department with a strong interest in Computational Biology.

Sincerely yours,

Zaida (Zan) Luthey-Schulten