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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  
Bloomington IN, 47405-7105

Dear Members of the Search Committee,

It is a great pleasure to write a letter of recommendation on behalf of Dr. Sergei Noskov who is applying for the position of Assistant Professor that has been advertised. Sergei has been a postdoctoral assistant in my laboratory for the last two years and I know him quite well.

Although we have worked together only for a few months, I had been in touch with him by email for about a year and a half prior to his arrival. Sergei was warmly recommended by his two previous mentors, Dr. Arkadij Kolker from the Russian Academy of Sciences and Dr. Carmay Lim from the Academia Sinica (whom I have known since our days together in the Karplus group at Harvard). Their letters of recommendation are included with this file. The good impression from these letters was largely confirmed by Sergei's performance since last September.

As soon as he arrived, Sergei started to work on several projects focused on the function of ion channels, a new subject for him. His main project was the characterizing of the microscopic factors governing ion flow through the toxin alpha hemolysin using the grand canonical Monte Carlo - Brownian dynamics (GCMC/BD) method. Even though he had been with us only a few months, he succeeded to obtain important results, calculating the conductance and the reversal potential for the wild type and mutant channels. The results are remarkably consistent with the experimental measurements of Hagan Bayley, and we anticipate a close cooperation with the experimental group in the next stages of the project. This work has been published in *Biophysical Journal* (2004). Sergei has also modified the source code of the GCMC/BD computer program to generalize it and make it more user friendly. Since we have had requests from several investigators who are interested in using the GCMC/BD program, the work of Sergei is going to be essential for the dissemination of this methodology. Establishing an accurate computational approach for simulating ion flow through alpha hemolysin at the molecular level will provide an extremely useful investigative tool for future pharmacological studies of such wide toxin pores. The work is expected to have also an impact on the development of biosensors.

A second project that Sergei took on was to characterize the molecular basis of ion selectivity in the narrow pore of potassium channels. The traditional explanation of ion selectivity is based on the idea that potassium ions fit snugly into the narrow pore but that sodium are too small. With incisive clarity, Sergei carried out a series of molecular dynamics free energy calculations showing that selectivity is actually governed by the local electrostatic and dynamic properties of the carbonyl ligands surrounding the cation. This work has been published in Nature (2004).

In addition to his main projects, Sergei has been eager to participate in many of the on-going development of a polarizable force field for biomolecular simulations. He has completed the parametrization of a polarizable model for ethanol in a few weeks and has characterized the thermodynamic properties of water/ethanol mixtures thoroughly. This work was recently submitted to the Journal of Physical Chemistry.

It should be emphasized that performing these computational projects requires very strong analytical skills in mathematics, statistical mechanics, physics and physical chemistry, as well as a broad knowledge of biology and electrophysiology. For example, the complete GCMC/BD method is complex (extending over several papers). With his excellent training in biophysics and his fundamental background in solution chemistry and solvation theory, Sergei grasped all this within a few weeks. He has the ideal background, training creativity and attitude to become one of the prime researcher in the field of theoretical and computational Biophysics.

At the personal level, Sergei is affable and has a very positive attitude, which enables him to interact effectively with his co-workers. He has become a key person in the group, often others with their projects. It is a pleasure to work with him. He is mature and is committed to a career path in science. I anticipate that in a few years, Sergei will have a very fruitful independent academic career.

With my best regards

A handwritten signature in black ink, appearing to read 'Benoît Roux', with a stylized, cursive script.

Benoît Roux