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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 Sir/Madam

Re: Dr. Wonpil Im

I first met Wonpil Im at the Gordon Research Conference in 2000, held at Tilton, New Hampshire. He gave a poster on a novel method of implementing stochastic dynamics simulations. Throughout the course of the meeting, we had many discussions about various aspects of modelling biological ion channels, advantages and disadvantages of different approaches and some of the problems both our groups face in carrying out large-scale computer simulations. Since then, we have been corresponding regularly, and I have reviewed many of his papers submitted to various journals, including *Biophysical Journal*, *Journal of Chemical Physics* and *Journal of Molecular Biology*. I am familiar with all of the papers he published in collaboration with Benoit Roux. I have the highest opinion of him as a young research scientist. He is a pleasant young man, very dedicated, conscientious, imaginative and diligent. I unreservedly recommend him for a faculty position in your Department.

The main research aim of Wonpil is to link the macroscopically observable properties of membrane ion channels, such as the magnitude of currents flowing across them, to their atomic structures through the fundamental processes operating in electrolyte solutions. As all electrical activities in the brain, including communication between cells and the influence of hormones and drugs on cell function, are regulated by opening and closing of ion channels, understanding the mechanisms of how ion channels operate at the molecular level is a fundamental problem in biology. Thus, experimental and theoretical studies on membrane ion channel have been, and still is, one of the most active research areas in biology.

Of the many papers Wonpil published with Benoit Roux, two stand out and will undoubtedly have a large impact in the field of computational biophysics in the years to

come. The first of these is the computational algorithm Wonpil devised based on grand canonical Monte Carlo and Brownian dynamics. Of the two common approaches used to model biological ion channels, molecular dynamics calculations are incapable of analysing ion permeation for periods long enough to measure channel conductance. To determine currents flowing across the channel, biophysicists have been making use of 3-dimensional stochastic dynamics simulations. In these simulations, the water is treated, not explicitly, but as a continuum, and all the atoms forming the channel are assumed to be rigid. One of the major difficulties in implementing this computational method has been the correct treatment of the boundary conditions. A non-equilibrium simulation algorithm developed by Wonpil with Benoit effectively removed this difficulty (Im *et al.*, *Biophys. J.* **79**, 788-801, 2000). With this new algorithm, it has now become possible to simulate certain experimental conditions that were not amenable to analysis previously.

The correct treatment of induced image charges is prohibitively expensive computationally. To avoid this problem, my colleagues and I have been making use of an interpolation method and a set of large look-up tables to store a discretized representation of the Green's function of the system. Because of the large memory requirement, simulations of biological ion channels based on this method can only be run effectively on supercomputers. In one of the papers published by Wonpil and Benoit Roux (Im and Roux, *J. Chem. Phys.* **115**, 4850-4861, 2001), a scheme for computing the electrostatic reaction field in Brownian dynamics simulations is proposed. Here, the reaction field Green's function is expressed as a multipolar basis-set expansion, and the reaction field matrix is pre-calculated and stored before the simulations. Clearly, we expect that the simplifications inherent in the method will introduce errors in a many-body potential of mean force, the magnitude of which will depend of the dimensions of the system under investigation. Nevertheless, this computationally inexpensive way of computing reaction field will enable the simulation technique accessible to many biophysicists.

Wonpil has a strong background in chemistry, computational physics, statistical mechanics and classical electrodynamics. He appears to be familiar with the field of biophysics and understand the biological implications of his research projects. He is a perfectionist and resists the temptation of 'cutting the corners.' His approach to a problem, I found, is thorough and methodical. I also noticed that he has the ability to explain complex ideas in simple terms in such a way that biologists who have little background in physics and biophysics can readily understand. I know of no other young scientist who is better qualified for the position in your Department. My high opinion of Wonpil is shared by many of my colleagues. If the position is offered to him, your Department will have gained a remarkable young scientist.

Yours sincerely.

Shin-Ho Chung
Head, Biophysics Group