CORNELL
UNIVERSITY

Joan and Sanford I. Weill
Medical College and
Graduate School of Medical Sciences

Department of Biochemistry
1300 York Avenue
New York, NY 10021-4896

October 29, 2003

Ms. Yana Teterina
Biocomplexity Faculty Search
Department of Physics
Indiana University
727 East 3rd Street
Swain Hall West 117
Bloomington, IN 47405-7105

Subject: Letter of recommendation for Wonpil Im

Dear Members of the Search Committee,

The object of this letter is to recommend Wonpil Im for the position of Assistant Professor that has been advertised. I have known Wonpil Im since the mid-nineties, when he joined my lab at the University of Montreal to do a Ph.D. in Chemistry. I moved to the Biochemistry Department of the Weill Medical College of Cornell University in 2000 and Wonpil transferred to this department to complete his degree.

As soon as Wonpil started to do a first research project, I could tell he was in a class of his own. His first project was to implement analytical derivatives in finite-difference Poisson-Boltzmann continuum electrostatics, a difficult problem that had been previously worked on by Kim Sharp, Mike Gilson and Andy McCammon. Immediately, Wonpil started to make progress and in less than a few months had worked out a very elegant method, which was published in Computer Physics Communication. The method is implemented in the program CHARMM. Although Wonpil was then only a beginning graduate student, his performance during this first project far exceeded that of many postdocs that had previously worked in my lab. Since then, Nathan Baker and Andy McCammon have adopted this elegant method for computing analytical forces from Poisson-Botlzmann as a standard for their most recent developments on electrostatics.

A second project consisted in generalizing a treatment of reaction field and solvent boundaries for simulating a small "active" region part of a large molecular system. This became the Generalized Solvent Boundary Potential (GSBP) method, which is now implemented in CHARMM. The description of the method and initial tests were reported in two papers published in the Journal of Chemical Physics. An important part of our current activities is to compute the free energy of ligands in binding sites of proteins and the GSBP method is at the heart of our calculations.

His third and main project was to perform a comprehensive study of the role of electrostatics on ion permeation through the OmpF porin. To this end, Wonpil generated a molecular

dynamics trajectory of this channel in a membrane, including all solvent and lipids explicitly (published in The Journal of Molecular Biology). He also developed and tested a sophisticated Grand Canonical Monte Carlo Brownian dynamics (GCMC/BD) algorithm for simulating ion flow through this large channel under various non-equilibrium conditions of ion concentration (published in Biophysical Journal). For the GCMC/BD, Wonpil had to expanded considerably the treatment of the reaction field of GSBP to account for the irregular geometries of these molecular pores. Solving that particular problem took almost two years of discouraging efforts, and it is through this period that he demonstrated the full strength of his character. Many would have given up. He ended up solving this extremely difficult problem completely on his own, using a singular matrix decomposition (published in The Journal of Chemical Physics). Finally, the complete results from MD, GCMC/BD and three-dimensional Poisson-Nernst-Planck electro diffusion (a method he implemented and programed in a couple of weeks!) were extensively compared in a culminating paper published in The Journal of Molecular Biology. To my opinion, this work on OmpF is one of the most comprehensive studies of ion permeation. I should also mention collaboration with Andreas Engel and Daniel Mueller, where Wonpil obtained a quantitative agreement between the forces calculated with continuum electrostatics and the results from atomic force microscopy measurements with OmpF (published in Biophysical Journal).

During all the time that he spent working in my lab, Wonpil kept developing and implementing novel elegant methods as well as aiming at applying these methods to significant biophysical questions. His command of electrostatics in biological systems is outstanding, going from multi-ion Brownian dynamics, Poisson-Boltzmann theory, Poisson-Nernst-Planck electro diffusion, and reaction fields, Generalized Born. Wonpil carried out also a very interesting study of dielectric decrement in aqueous salt solution and the manuscript is in currently in preparation. He is probably one of the foremost international experts in the field of electrostatics for biomolecular systems by now. Wonpil possesses the imagination to formulate important biological questions, the passion to pursue them, and the motivation and the technical abilities to realize and implement them. One rarely meets such maturity and commanding knowledge of the available tools in theoretical biophysics in a young scientist.

Lastly, Wonpil is a very well balanced person who is a pleasure to work with. He is very cooperative and can work well within a team. His communications skills are above average. I have no doubts in his ability to build and manage a productive research group. In my opinion, Wonpil is one of the most promising young scientists in the field of theoretical biophysics at the present time. Please let me know if you need further information.

With my best regards,

Benoit Roux, Ph.D.
Professor of Biochemistry