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October 17, 2003

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

Dear Mr. Teterina,

     This letter is written to lend my strong support to **Dr Wonpil Im** in his application for the position of Assistant Professor at the Department of Physics at **Indiana University**. Wonpil is an extremely bright and hard working young scientist who has a bright future as an independent researcher; additionally, he is a pleasure to interact with as a postdoctoral collaborator. I highly recommend him for a position in your institution.

     Wonpil joined my group a last year after finishing his Ph.D. studies with Benoit Roux at the University of Montreal and Cornell University. He came highly recommended by Benoit as possessing the necessary elements to be a very successful scientist. Benoit was on the mark as far as his recommendation went. Most of my students and postdocs work relatively independently, interacting with me and other students and postdocs in the group as scientific collaborators. Dr Im found this sort of arrangement very comfortable and quickly identified an area of research that sparked his interest, and allowed him to exploit some of the ideas he had worked on as a grad student. This was in the extension of the generalized Born (GB) continuum solvent representation of aqueous environment. At the time there were two other postdocs in the group (Mike Lee and Michael Feig) who were investigating this class of models and consequently I was a little skeptical about Wonpil also working here. However, he very quickly learned the basic formalism and extensions that had been proposed by Mike Lee, and extended these ideas to provide a smooth representation of the solute/solvent interface, thus mimicking ideas he had developed as a grad student for numerical Poisson-Boltzmann (PB) methodologies and permitting the direct comparison of forces from the numerical PB solutions and the GB model.

Charles L. Brooks III
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This initial work was published in the *Journal of Computational Chemistry* earlier this year. It represents a solid extension of the related work on the GB models and methods from our group during the past several years.

In addition to his initial work on the GB model, Wonpil collaborated with other postdocs and students in a number of areas exploring the application and assessment of these new GB approaches to problems of protein structure refinement from *ab initio* folding, the development of protein structural models from NMR data and peptide folding. Some of these collaborative efforts are soon to be published in the *Journal of Chemical Physics, Journal of Computational Chemistry* and elsewhere while others are still ongoing. Wonpil is a highly interactive member of my group and contributes positively to many problems.

As a student Wonpil was involved in investigations of membrane bound ion channels, as this was a main theme in Roux's research program. These interests motivated him to explore the extension of his newly formulated GB model to include the implicit treatment of a membrane as a low dielectric region within the context of a GB representation of aqueous solvent. The development of such a model, the implicit membrane GB theory, is an important and timely development. Wonpil demonstrated that this model was semi-quantitative in its representation of the equivalent continuum models with PB. More importantly, he demonstrated that when this analytic implicit solvent and membrane theory was coupled with the advanced sampling methods, replica exchange in particular, (developed in our group by Michael Feig) that he could fold and assemble atomically detailed models of trans-membrane helical peptides de novo. This work was published recently in the *Biophysical Journal* and represents a really significant advance for the modeling of integral membrane peptides and proteins.

Following on his initial work on membrane peptides, he worked to establish connections with the solid state NMR group of Stan Opella at UCSD to gain insight into the NMR related issues associated with solving structural problems via solid state NMR. To this end, he has explored the de novo folding of the fd coat protein and characterized the success of his models in reproducing the properties of this peptide by direct comparison with both the structural model from NMR and the NMR spectral properties (^{15}N chemical shift tensor and ^{15}N-^{1}H dipolar coupling). Stan has also "challenged" him with a number of yet-to-be-determined sequences of peptides his group is working on, and Wonpil has been exploring the de novo folding of these membrane bound peptides. Finally, in this area Wonpil has initiated collaborative efforts with Tim Baker from Purdue University, on exploring the conformations of and predicting structures of trans-membrane domains of E and M proteins from dengue virus in conjunction with Baker's electron microscopy efforts, and Hartmut Luecke from UC-Irvine on modeling G-protein coupled receptors.

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It is clear that Wonpil is a hard-working and creative young scientist. He has many ongoing projects that could develop into long-term research problems to help him launch his independent career. However, he is still working through many of these and would likely benefit from more "sheltered" experience before jumping into the game of teaching, seeking funding and directing graduate students and postdocs. At the current point he is an excellent candidate for a faculty position, in another year he will be an outstanding candidate who will have a well-defined direction and objectives to pursue as an independent scientist.

If you have any questions or would like to discuss Wonpil's potential directly, please call.

Sincerely,

Charles L. Brooks III
Professor and Member
The Scripps Research Institute