

OAK RIDGE NATIONAL LABORATORY

MANAGED BY UT-BATTHELL FOR THE DEPARTMENT OF ENERGY

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November 1, 2004

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

To the Search Committee Chair:

I am writing to express my strongest support for Dr. Xiefeng Wan's application for a junior faculty position in Biocomplexity at Indiana University. I worked closely with Dr. Wan during his postdoctoral tenure in the Environmental Sciences Division at Oak Ridge National Laboratory (ORNL) before he joined Dr. Dong Xu's group at the University of Missouri. Dr. Jizhong Zhou and I co-supervised Dr. Wan during his postdoctoral training at ORNL. I have worked with Dr. Wan on a number of research projects and thus am very familiar with his background and potential as a research scientist. I think I am qualified to highly recommend Dr. Wan for a tenure-track faculty position in bioinformatics based on the strength of his abilities as a scientist.

During his postdoctoral training at ORNL, Dr. Wan worked on a Genomes to Life (GTL) project funded by the U.S. Department of Energy (DOE), entitled "Rapid Deduction of Stress Response Pathways in Metal-Radionuclide Reducing Bacteria," for which I served as a co-PI. *Shewanella oneidensis* MR-1 (formerly, *S. putrefaciens* MR-1), a gram-negative facultatively anaerobic bacterium, is capable of coupling the generation of energy to the reduction of insoluble ferric iron (Fe^3+), as well as other compounds (e.g., manganese, uranium, nitrate, fumarate, and dimethyl sulfoxide) in the absence of O_2 . Thus, this bacterium is of particular interest to the DOE because of its potential for remediating various metal and radionuclide contaminants found at numerous DOE field sites. Dr. Wan's roles were to construct the regulatory network for *Shewanella*. Dr. Wan successfully defined the regulatory networks (regulons) controlled by the major global regulatory protein Fur in *Shewanella*. Among his findings, it is worth mentioning that Dr. Wan discovered that the transcriptional binding motif for the Fur regulator can be a 21-mer palindromic DNA sequence, which is different from the canonical recognition element discovered in the model organism *Escherichia coli*. His findings elucidating the *far* regulon has recently been accepted for publication in the *Journal of Bacteriology*. The papers describing the *arsA*, *uraA*, and *crp* regulons are currently in preparation and will be submitted to high-quality journals. In addition to these research accomplishments, Dr. Wan developed a novel design for regulatory network construction using a multiple mutation strategy. Ultimately, this technology will allow biological scientists to combine different microarray datasets to retrieve regulatory elements and thus construct the regulatory network *in silico*.

Because of his strong background and broad knowledge in computational biology and bioinformatics, Dr. Wan was involved in all the major research projects in our laboratory and served as an incredibly valuable contributor. Dr. Wan also participated as a co-PI on a number of grant proposals.

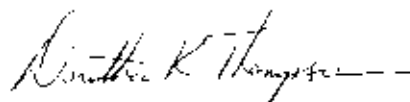
one of which was entitled "Development and Validation of Computational Tools for Theoretical Modeling of Gene Regulatory Networks in (Metal-Reducing) Bacteria". Dr. Wan managed to complete independently more than one third of this proposal. Although this proposal was not funded for other reasons, his novel thinking, broad knowledge, and writing skills were very impressive.

Dr. Wan's achievements to date in his research have demonstrated his dedication to difficult scientific challenges in the discovery of gene regulatory elements in both *Shewanella* and *Synochococcus*. His knowledge in computational biology, molecular biology, and environmental science is quite good and clearly gives him the ability to make connections and to solve problems that interface different disciplines. Based upon my knowledge of Dr. Wan and his scientific achievements, it is my opinion that Dr. Wan is capable of rising to the top of his field in computational biology.

I must also emphasize that Dr. Wan works in an extremely technical field and is highly motivated. As the leading scientist of a research group, I am keenly aware of how much the research of my group relies on talented and creative computational biologists like Dr. Wan. Such researchers are rare and the numbers of people with comparable credentials are in shortage. More importantly, computational prediction of regulatory motifs, of which Dr. Wan is an expert, is almost an art form. An advanced degree and years of experience do not necessarily enable a researcher to be skillful in this field, as I have learned from experience. A relatively small percentage of researchers in the field become highly creative and skilled experimentalists. Dr. Wan's work in developing a novel algorithm for RNA local secondary structure prediction and its application to *rho*-independent terminator prediction is significant enough to place him well above an average young researcher in the field. His track record and proven skills justify a confident prediction that he will benefit the Biocomplexity Institute and the university in general.

Thus, I express my strong support for Dr. Wan's application for a faculty position at Indiana University. Please feel free to contact me if you need more information concerning Dr. Wan.

Sincerely,



Dorothea K. Thompson, Ph.D.
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