



Center For Theoretical Biological Physics

CTBP - UC San Diego, MC 0374 - 9500 Gilman Drive - La Jolla, CA 92093-0374
858-822-1296 - 858-534-7697 (fax) - ctbp@ucsd.edu - <http://ctbp.ucsd.edu>

November 29, 2004

Re: Osamu Miyashita's evaluation letter

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, USA

Dear Professor de Ruyter van Steveninck,

It is with great pleasure that I support Dr. Osamu Miyashita for an assistant professorship at your institution. I have been impressed with his scientific abilities and creativity, and I have high hopes he will turn out to be one of the leading scientists in theoretical and computational biology and biophysics. During the last few years I had four outstanding postdoctoral fellows in my group before Osamu has arrived. This quartet has been greatly responsible for our success. They are all currently assistant professors at major places: Joan Shea (UCSB), Nick Socci (Albert Einstein School of Medicine), Cecilia Clementi (Rice) and Steve Plotkin (British Columbia). Osamu Myashita is clearly in the same class. The papers that he has been writing in several different topics will have a major impact in biological physics, biochemistry and molecular biology. If he joins your institution as an Assistant Professor, I am certain that he will perform impressive science since he has already done it as graduate student and has continued to do as a postdoctoral fellow. I really believe you will be very fortunate if you get him as a colleague.

Osamu has all the knowledge needed to perform top interdisciplinary research. He has great mathematical and computational skills that, together with his understanding and creativity for biological problems, make him very unique. He had his undergraduate studies in mathematics and physics and, during his PhD, he has performed research that dealt with electron transfer in biological systems and protein dynamics. His computational skills are superb in programming, simulations and system administration. It is also important to highlight that his PhD advisor is one of the leading scientists in the field of theoretical and computational biology, Prof. N. Go. Following I describe the outstanding scientific contributions produced by Osamu in the last two years (2003 and 2004)

Osamu also enjoys collaborating with experimentalists and he is being very successful interacting with the group of Prof. Mel Okamura in research in electron transfer in the

photosynthetic reaction center and with the group of Prof. Patricia Jennings in investigating how global protein motions affect the function of the Csk kinases (described later). He has published three papers and another one has just been accepted for *PNAS* with Okamura. These papers show results from a joint theoretical and experimental collaboration on electron transfer between the cytochrome c_2 and the photosynthetic reaction center complex. They address the docking of the two proteins and the electron transfer reaction between them. Understanding of the mechanism would be impossible without this theory/experiment collaboration. I had been trying to start theoretical/experimental collaboration with Mel Okamura for many years but we had not been able to locate the appropriate person for this research until Osamu came to UCSD. Okamura's research topic has been a challenging problem in biological electron transfer for many years. Osamu has made this collaboration a reality.

In addition to this work, Osamu has been the catalyst of a new collaboration with Peter Wolynes on an allosteric model for proteins, in particular kinases that are a topic of collaboration with the experimentalists Patricia Jennings and Susan Taylor. The model includes a combination of non-linear elasticity with local unfolding around the transition state ensemble in these reactions. The first manuscript on this topic was just published at *PNAS* and it illustrates this method for the conformational transition of adenylate kinase. This is a complete new idea of how molecular machines work and I believe it will have an enormous impact in the field. A second manuscript extending the approach has just been submitted to *JPC*. Already, as described above, in collaboration with Pat Jennings and Joe Adams, Osamu has a paper published in *JMB* applying this method in combination with experiments to explore the dynamic link between the SH2 domain and the active Site of the COOH Terminal Src Kinase, Csk.

Finally, Osamu has also published a couple papers with Charles Brooks at TSRI on utilizing a normal mode method for flexible fitting of high-resolution structure into low-resolution experimental data from cryo-EM.

As you can see from the description above that he is not your conventional young scientist. It is not only the quality of his work, but also the breath and novelty of it. In conclusion, I believe that Dr. Osamu Miyashita is an outstanding candidate for any top professorial position in computational biology and biophysics. It will be almost impossible to find someone else with his analytical and computational skills, great knowledge of functional and structural molecular biology and biochemistry, ability to collaborate with experimentalists, and at the top of it an amazing creativity. You will be very fortunate if he comes to your institution. I support his application with enormous enthusiasm. Please feel free to contact me if you need any further information.

Sincerely,



José N. Onuchic
Professor of Physics and CTBP co-director