November 17, 2004

Biocomplexity Faculty Search Committee c/o Prof. Rob de Ruyter van Steveninck Department of Physics Swain Hall West 117 Indiana University Bloomington, IN 47405-7105

Dear Search Committee,

I am writing to support the candidacy of Chin-lin Guo for a faculty position at your institution.

Chin-lin is an amazing person, as even a short glance at his resume will reveal. He has both an M.D. degree and a Ph.D. in physics, with an engineering master's degree thrown in for good measure. He is absolutely driven to understand the functioning of complex biological systems and correctly ignores traditional boundaries in his quest to do so.

So far, Chin-lin has worked on two major research topics: collective behavior in molecular and cellular biophysics, for his Ph.D. at UCSD (under my supervision), and the spatiotemporal dynamics of polarity formation and chemotropism in yeast during his postdoc at Harvard. At UCSD, Chin-lin defined his own problems (receptor clustering as a way of sharpening signal transduction, cooperative beta-sheet formation as a general mechanism that could lead to protein aggregation) and needed only small amounts of guidance to carry out the theoretical research. In addition to his published papers, he contributed a great deal by organizing student/postdoc reading groups, by being the most lucid local source on a whole variety of biomedical phenomena, and by just helping stimulate everybody's thinking by participating in all manner of discussions. My impression is that he continues to function the same way at Harvard: in my one visit there since Chin-lin's arrival, he was the one who coherently explained to me the various experiments on evolution that were going on at the genomics center, although he had not been working in this area.

Rather than taking a "safe" postdoctoral position from the many offered to him by biophysics groups, Chin-lin decided he needed to broaden his experimental capabilities in the area of cell biology. He went to a leading laboratory and started a multi-faceted look at the problem of yeast chemotropism. As a word of background, most of the work on "systems biology" makes the assumption that the reaction networks in cells act on bulk concentrations; i.e. the gradients across the cells and the obvious compartmentalization of many reactions are completely ignored. For the problem of chemotropism (and the related problem of eukaryotic chemotaxis that I work on), spatial structure is everything

as the cell must choose a direction based on external cues translated into internal gradients. This makes the relevant models into stochastic PDE's instead of ODE's, makes the internal structure a relevant degree of freedom and tremendously complicates both the experiments and their interpretation via theoretical models. Chin-lin has devoted himself to this system in an almost inhuman fashion, producing a whole variety of exciting new measurements (using modern tools of fluorescence microscopy, microfluidic devices etc.) and an innovative new set of conceptual ideas. I myself am still trying to absorb all this work, and exactly how far he has gotten towards fully "cracking" the problem is impossible for anyone to say. But the sheer boldness of the attempt is staggering and the sheer volume of new data is breathtaking.

Often, junior faculty are expected to be conservative, as they learn to teach, apply for grants and become comfortable in their new surroundings. This would not happen with Chin-lin. He will always attempt to push right at the edges of our knowledge and capabilities, perhaps a risky approach, but perhaps what we all should do more of. If you are looking for a potential scientific leader, you should definitely consider Chin-lin.

Sincerely,

Herbert Levine, Professor of Physics and Co-Director Center for Theoretical Biological Physics

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