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To Whom It May Concern:

I am writing to recommend Dr. Zhisong Wang for a position at your Department.

Zhisong has been a postdoctoral associate in my group from March 2001 to June 2003. When he applied for a position in my group, I was impressed by the breadth of his background: After completion of his PhD in nuclear physics, he went to England to work in the area of quantum dynamics in surface science and in quite a short time has written a series of brilliant papers in the field! The approaches he used in his surface science work ranged from full-scale state-of-the-art simulation of time-dependent dynamics of multidimensional quantum systems to the recently developed methods of Bohmian quantum dynamics to the Monte Carlo wavefunction methods for dissipative systems to ingenious simple theoretical models.

While our original intention was to work on quantum dynamics of single molecules, by the time Zhisong arrived in Austin, I had gotten involved in a collaboration with the experimental group of professor Kevin W. Plaxco to study the correlation between the topology of single domain proteins and their folding rates. The entire area of biophysics was totally new for my group. When I told Zhisong about this new topic of research we had, he immediately got excited about this project and decided to start working on it. Having had no previous experience with proteins, he wrote, from scratch, a computer Monte Carlo code to study the properties of denatured proteins, in about 2-3 months (!). He further proceeded to study the mechanical properties of random polypeptide coils (in collaboration with Helen G. Hansma and James B. Thompson from UC Santa Barbara). The results of this work have been published in the *Journal of Chemical Physics* [*J. Chem. Phys.*, **116** (2002) 7760].

In another direction he pursued, he studied the probability of formation of single loops in polypeptides. The formation of loops is believed to determine the "speed limit" of protein folding. The previous theoretical studies of this problem however were in disagreement with experiment: the latter showed that the loop formation probability decreases monotonically with the loop length while theories predicted the existence of a maximum in the loop formation probability. The calculations carried out by Zhisong resolved this controversy and showed that the loop formation rate should decrease monotonically with the loop length, in contrast to the earlier theoretical predictions. This work has been published in *JCP*: [Z. S. Wang and D. E. Makarov,

Rate of intramolecular contact formation in peptides: The loop length dependence, J. Chem. Phys. **117** (2002) 4591].

In his next project, Zhisong has focused on theoretical studies of FRET photoemission statistics in biopolymers. This work has been motivated by the recent experiments, in which FRET photoemission statistics have been measured with high temporal resolution. Our idea was that such measurements may provide detailed information about the conformational dynamics of proteins at a nanosecond time scale. To study the relationship between these dynamics and photoemission signal, Zhisong performed Monte Carlo wavefunction simulations of a FRET model coupled with a Langevin dynamics model for a random polypeptide. This work has resulted in a publication in *J. Phys. Chem* [Z.S. Wang and D.E. Makarov, *Nanosecond dynamics of single polypeptide molecules revealed by photoemission statistics of fluorescence resonance energy transfer: A theoretical study*, *J. Phys. Chem. B* **107** (2003) 5617-5622].

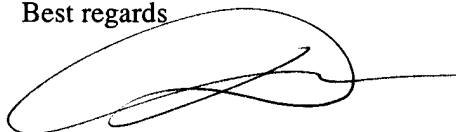
In another direction of his research, Dr. Wang used Monte Carlo simulations to study the effects of residual helical structure on the dimensions of unfolded peptides, with the goal to reconcile the experimental observation of a random coil behavior in most denatured proteins with the observed residual order. This work, which was done in collaboration with Kevin W. Plaxco, was summarized in the manuscript [Zhisong Wang, Kevin W. Plaxco, and Dmitrii E. Makarov, *Influence of local, residual structure on the scaling behavior and dimensions of unfolded proteins: a Monte Carlo study supports the random-coil nature of the chemically denatured state*], which is currently under review.

It is truly impressive that Zhisong Wang has been able to become an expert in the protein folding field and to accomplish so much in a short period of time especially considering the fact that he had had no background in biological sciences when he started. I believe that he will enjoy similar success in any area of physics/chemistry that he chooses to focus on, thanks to his intelligent, creative approach. While having the creativity and the breadth so valuable for a theorist, Zhisong also has a very solid background in computational methods.

On a personal note, Zhisong has a pleasant personality, is fun to work with and to talk to, and would be a welcome addition to any Department.

He is certainly one of the brightest young theoreticians I have met and I have no doubt giving him my *strongest* recommendation. Please contact me if you have any further questions

Best regards



Dmitrii E. Makarov
Assistant Professor of Chemistry