

THE UNIVERSITY OF BRITISH COLUMBIA



Steven Plotkin

Department of Physics and Astronomy

6224 Agricultural Road

Vancouver, B.C. Canada V6T 1Z1

Tel: (604) 822-3853

Fax: (604) 822-5324

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To the Search Committee,

This is a letter in support of Dr. Reza Ejtehadi's application for a faculty position in biophysics theory at your university.

I first heard of Reza through my colleagues Richard Goldstein and Hue Sun Chan, who may also have useful opinions on his earlier work. They were particularly impressed by his early research on protein design, where for some idealized models he was able to make very general analytical statements on the form of the distribution of the number of sequences that fold to a given geometrical structure. These statements cleared up a controversy in the literature, where researchers (Hao Li, Richard Goldstein and others) had found inconsistencies in the form of this distribution. However they were using less general computational techniques- within Reza's framework he was able to show as special cases of his Hamiltonian under what conditions these different distributions would occur.

It struck me as particularly noteworthy that this work was carried out by Reza as a graduate student in near isolation in Iran, without any interaction between Reza and outside researchers, and essentially without even a Ph.D. supervisor- It turned out his co-authors were actually undergraduates that he was supervising!

Reza then joined the group of Ralf Everaers in Mainz as a post-doc, where he developed computational models of DNA interactions. Here he applied some ideas regarding Gay-Berne potentials often used in liquid crystal simulations to account for van der Waals and excluded volume interactions between the disk-like bases in DNA, which Dr. Everaers can speak to better than I.

Reza has been in my group as a post-doc for the last 14 months, working mostly on elucidating the effects of many-body interactions in protein folding. While in my group Reza has undertaken several responsibilities in addition to his research. He organized a bi-weekly Biophysics seminar that has significantly boosted the interactions between the researchers here. Through his own decision he has also been teaching tutorial sections for undergraduate students as well. UBC requires a research thesis for an undergraduate degree in honors physics, and right now I have taken on two students in this capacity. However they are essentially Reza's students, as he has gravitated naturally to supervising them, as well as having a significant part in the direction of their research projects.

Reza has been very active in his own research in spite of taking on these extra responsibilities. Although he has not yet submitted a paper with me, he has already made several significant discoveries through a computational investigation of three-body interactions in folding that are important and publishable: An explicit 3-body contribution to the energy of about 20% gives a curve of folding rate vs. contact order (a property of the folded geometry of the protein) spanning the same orders of magnitude ($\sim 10^7$) as experimental proteins. The experimental trend was discovered by Baker,

Plaxco and coworkers, and up to now, simulations of model proteins had failed to show the wide range of folding rates present in laboratory proteins, spanning only 2 orders of magnitude at most. Perhaps more importantly, when about the same amount of 3-body energy is present in the Hamiltonian, the agreement between experimental and simulated ϕ -values (a measure of an amino-acid's importance for folding) increases dramatically, strongly suggesting a role of many-body interactions in determining the way a protein folds. At the same time he has also been involved in a collaboration with one of his former undergraduate students, Mehdi Vahyanejad, now a graduate student at MIT working jointly under Christopher Burge in Biology and Mehran Kardar in Physics. My understanding is that they are near to submitting another paper. While all these undertakings have probably spread Reza's time to focus a bit thin, it shows he is willing and able to work simultaneously on several research projects, and contribute substantially to each.

To give an honest appraisal of his abilities, I would rate his computational proficiency as slightly beneath Joan Shea's (UCSB) or Cecilia Clementi's (Rice) who I both know well. However I would rate his analytical skills above theirs, as evidenced by his work on protein design. He has a very even-keel, mature and relaxed personality, yet he is very active- the most active- in my group discussions. Presently he is clearly the strongest in my group, as well as being the easiest to talk to. I strongly support his candidacy for a faculty position in your department.

Sincerely,

A handwritten signature in black ink, appearing to read "Steven Plotkin". The signature is fluid and cursive, with a large, sweeping initial "S".

Steven Plotkin
Tel: (604) 822-8813
Fax: (604) 822-5324
E-mail: steve@physics.ubc.ca