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Prof. Rob de Ruyter van Steveninck
Biocomplexity Faculty Search Committee
Biocomplexity Institute
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Dear Faculty Search Committee:

Dr. Zhisong Wang (Nargate, as he is called) has asked me to provide you with a letter of reference on his behalf, which I am most happy to do. Nargate is a bright, creative and productive scientist who has the diverse and requisite skills required to succeed as an academic scientist. I am sure he will go far.

My interactions with Nargate started two years ago when I began a collaborative project with his advisor, Dima Makarov at Austin. Our experimental SAXS studies of the dimensions of chemically denatured proteins had turned up the rather unexpected observation that the highly helical unfolded states induced by alcohols exhibit dimensions that are indistinguishable from those observed for the random coil denatured state induced by urea. I approached Dima asking him to consider a simulations study aimed at understanding the mechanisms underlying this coincidence and he responded with enthusiasm. I now realize that this enthusiastic response was because of Nargate; the project would require the development of highly efficient code for Monte Carlo simulations of excluded volume denatured ensembles. Historically this has been an overwhelmingly difficult task because the ensembles need to be large in order for the averages to converge and yet the rejection rate (due to steric clashes) is normally quite high. It turned out that Nargate had, in the short time he had been at Austin, already developed what is probably the most efficient code to date for running these demanding simulations. Nargate jumped on the project with ease and enthusiasm and quickly generated large, nicely converged and highly detailed models of the various denatured states. Furthermore, with no guidance from me and, I believe, little guidance from his advisor, Nargate distilled his ensembles into a compelling explanation of the coincident dimensions of these otherwise extremely different denatured states. Moreover, in generating the ensembles he used in order to define the properties of the random coil state, Nargate argued that the radius of gyration of a truly random-coil polypeptide would scale as $\langle R_g^2 \rangle = 4.58 \cdot N^{1.21}$. This result is *absolutely* astonishing as Nargate produced *unaware* that we have just characterized this relationship experimentally and found the pre-exponential and exponentials to be $3.92 \pm 0.44 \text{ \AA}^2$ and 1.19 ± 0.04 respectively. I think the extraordinary coincidence between the results of Nargate's (truly, honestly *blind*) simulations and that of our experiments

is both astonishing and a testament to Nargate's skill as a simulator and his ability to pick simulatable problems.

Based on a number of such interactions with Nargate, I have, in the past year, begun to consider him a willing and extremely able collaborator. For example, my laboratory has quite recently begun FRET-based measurements of pairwise distances in a highly unfolded protein. Given as FRET scales with distance to the sixth power, I was curious as to how FRET signals would change with increasing N for a random coil state. Just last week I turned to Nargate to answer this question. He quickly derived a first principles, analytical solution for the problem (R^6 proportional to $N^{18/5} = N^{3.6}$) and then reanalyzed his unfolded ensembles to come up with the simulations-based estimate of $N \sim 3.8$.

On the less directly scientific fronts, Nargate is splendid fellow and a fine communicator. His English is excellent and his ability to craft and compellingly express a scientific "story" is as good as almost any postdoc I have worked with. Moreover, Nargate is not only an effective and productive scientist, he is also extremely enthusiastic. While I have never seen him in a traditional educational environment, I am sure this enthusiasm would be amply evident and exceedingly effective in the classroom. On a personal note Nargate is a charming, outgoing and communicative fellow. His enthusiasm for the science really rubs off and thus it is an unqualified pleasure to work with him. In short, I think he would make a fine colleague and I thus strongly encourage you to consider favorably his candidacy.

With very best wishes,

A handwritten signature in black ink, appearing to read "Kevin Plaxco". The signature is fluid and cursive, with a large, stylized initial "K" and "P".

Kevin W. Plaxco