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Re: Reference letter for Boris Shakhnovich

11.09.2005

Dear Dr Bennett,

It gives me great pleasure to enthusiastically recommend Dr. Boris Shakhnovich for the Assistant Professor position that is open in your Department. I believe that Boris is an outstanding young scientist in the fields of Systems Biology and Computational Biology. I know him for approximately 5 years since the time he was a first year graduate student. I had the pleasure to be a member of his defense committee and also had an opportunity to read in detail many of his manuscripts and engage in extensive discussions with him, which makes me intimately familiar with his work. Speaking formally, it is, of course, highly unusual that Boris managed to finish and defend his PhD thesis in ~2.5 yrs, publishing in the process 12 papers in top journals. Much more importantly, however, the research he has already done qualifies as a series of significant achievements and shows that he has an unlimited potential. Boris' PhD thesis was, quite simply, the most substantial and ambitious work of that kind I have ever seen or heard of. It is not every day or even every year that a graduate student defends a thesis entitled "Toward a comprehensive theory of molecular evolution". It also might seem extremely arrogant but I believe that Boris had results justifying this sort of title. I think that the work done by Boris and his coworkers at the interface of protein structure comparison, regulatory network analysis and exploration of the space of protein functions is, more or less, without precedent in recent years in Computational Biology, in terms of originality combined with rigor and scrupulous attention to detail. For example, in one of their striking papers, Boris and his co-authors ventured to uncover the hierarchical structure of the protein Universe and develop a mathematical model describing its evolution and very origin. They claim to have deduced that evolution of proteins started with a biological "Biological Big Bang" and proceeded to yield a scale-free organization of the protein Universe. I must confess that, after seeing the title of this paper, I was originally skeptical as to the validity and meaning of these grand claims. However, after examining this work in every detail, I have come to the conclusion that their discovery of scale-free structure is quite reliable and the evidence supporting a "Big Bang" model of protein evolution is strong. Furthermore, Boris has already made remarkable inroads in the study of protein designability and its links to biological properties of organisms and in understanding how protein functions are connected to mathematical properties of biological networks. His latest

interest Most important, I think, is the general approach: Boris and his collaborators strive to investigate problems of biological evolution and function the way physical theory is built, i.e., by formulating fully defined models and testing them against the available body of empirical data. It is a steep road, but I think it is the road to be taken, and they have already reached considerable heights. Certainly, as of today, "toward" is a critical word to characterize Boris' research because the theory as such is not there yet. However, I think that Boris has a good chance to stake the actual theory long before the end of his career.

On a more personal level, Boris is an excellent colleague, always ready to share his ideas and technical expertise, and a wonderful human being with an always positive outlook at life and a remarkable sense of humor.

In summary, I believe that Boris Shakhnovich is a truly outstanding young, independent researcher in the fields of Systems Biology, Computational Biology and Genome Evolution. He should be a very strong contender for a tenure-track position in one of the top universities.

Yours sincerely,

A handwritten signature in blue ink, appearing to read "Eugene V. Koonin". The signature is fluid and cursive, with a large initial "E" and a long, sweeping underline.

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