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Yves Brun,  
Systems Biology/Microbiology Faculty Search,  
Department of Biology,  
Indiana University,  
Jordan Hall 142, 1001 E 3rd St,  
Bloomington IN 47405-7005

Dear Dr. Brun,

I am writing in support of Dr. Boris Shakhnovich's candidacy for a tenure track position. Borya entered the Bioinformatics Program at Boston University in September 2001, immediately after receiving his undergraduate degree in Biophysics from the University of Illinois, Urbana-Champaign. He joined my laboratory in his second semester, and in the next two years wrote a series of ten papers on molecular evolution, rooted in structural principles, leading to a PhD in something under three years. His introduction of graph theoretic principles to describe the structural evolution of protein domains is especially noteworthy. Among other things it enabled inclusion of contextual information for improving the precision of functional annotation from structure alignment. His papers, published in leading journals including JMB, PNAS and PLOS, are striking for their creativity and for displaying a conceptual sophistication that is extremely uncommon in someone so young.

During his second year Borya wrote an NIH R01 proposal which was ranked, but unfunded. It was revised and resubmitted, and funded with a score that placed it in the 11<sup>th</sup> percentile. Boris works independently, and since I tend to devote my time to students who need guidance, he received essentially no help from me, either with his papers or with the grant submission, although my name and his father's (Professor Eugene Shakhnovich, Harvard Chemistry) appear as co-PIs on the grant, and on some of his papers.

Two years ago Boris and another graduate student, Joseph Mellor, developed and taught a graduate seminar course which received excellent evaluations, and for which they received a certificate of merit. I approved this course as an experiment, and attendance was strictly voluntary. Nevertheless a core of 20 students attended all lectures, with some lectures having as many as 30 participants. This fall, Boris is teaching our Bioinformatics Applications course. The course had been taught for five years and needed to be updated. Borya undertook the revision and teaching with his typical passion. Borya's presence at

the head of the class was initially met by disbelief and a measure of bemusement by some students, since he looks younger than most of the class. His breadth of knowledge and scientific insight, and the extensiveness of his notes, quickly removed any doubt about the appropriateness of his presence. By the time this course is over, I expect he will have made a substantial impact on our curriculum

Borya is currently Research Assistant Professor of Bioinformatics. In addition to teaching, he is supervising several undergraduates, and one of our outstanding PhD students, Tim Reddy. Boris and Tim developed a new unsupervised method for discovery of regulatory protein binding sites, which appears to be very promising. The method was used to analyze the upstream sequences of GABA receptor genes that are being studied by my colleague, Professor Shelley Russek, in the Department of Pharmacology. Tim and Borya predicted 15 binding, six of which have been tested in the Russek Lab, and all six appear to bind. A manuscript detailing results from this study is currently in preparation.

Borya is extremely quick, scientifically astute, and writes with a facility that I have rarely encountered. As a result he has been able to make a number of valuable contributions to projects both within and outside the laboratory. Among them are his contributions to the development of the gene fusion concept (in preparation) for the purpose of rooting evolutionary trees, and phylogenetic profiling (published in PLOS).

At a personal level Borya is congenial, pleasant and interactive. This, coupled to an unusual scientific acumen bodes well for a stellar career. I'm sure that you will find him a stimulating and valuable colleague.

Sincerely,

A handwritten signature in blue ink that reads "Charles DeLisi". The signature is written in a cursive, slightly slanted style.

Charles DeLisi