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

Dear Professor Brun,

I wish to be considered for the tenure-track faculty position in Computational Systems Biology at Indiana University as advertised in Science.

Currently, I am a post-doctoral fellow in the laboratory of Dr. George Church in the Genetics Department at Harvard Medical School. One of my major research topics supported by the Alfred P. Sloan and U.S. DOE Postdoctoral Fellowship is to study principles underlying transcriptional regulatory networks in yeast *S. cerevisiae*. I have developed the first deterministic mathematical method, the Motif Expression Decomposition (or MED) method, which provides framework for deciphering principles of transcription regulation at the single gene level of resolution. My work, which has been provisionally accepted for publication in *Nature/EMBO Molecular Systems Biology*, has led to the identification of four classes of regulatory principles in yeast *S. cerevisiae*, all of which were validated by expression data. In addition, my research has discovered a novel mechanism that evolution has employed for amplifying gene expression levels in lieu of motif-motif functional interactions.

Prior to my post-doctoral work, I obtained a Ph.D. degree in theoretical chemistry and a M.S. degree in computer science from the University of California-Davis in the laboratory of Dr. William H. Fink. During that period, I was also a pre-doctoral fellow in computational science at the Lawrence Livermore National Laboratory, working in the laboratory of Dr. Michael E. Colvin. One of my dissertation topics was the theoretical study of principles underlying physical interactions and the molecular biomechanics of packing of small organic molecules by the RNA aptamer, which has recently been used to build biological switches for controlling gene expression.

In the future, my laboratory will seek to address two fundamental questions in molecular biology: (1) how evolution has designed and selected regulatory principles across species from prokaryotes such as *E. coli* to eukaryotes such as yeast *S. cerevisiae* and *S. pombe* by cataloging transcriptional regulatory principles in each species and comparing them, and (2) how transcription factors interpret genome's transcriptional programs via interactions with cis-regulatory elements, and how such interpretation is affected by protein post-translational modifications, such as phosphorylation or co-factors. I foresee that the outcomes of my proposed research will be useful to the synthetic biology community by providing them with detailed quantitative knowledge of the transcriptional process—e.g., the exact motif's sequence and geometry in the gene promoter for a given desirable level of gene expression—for constructing complex biological systems with desired properties. Furthermore, quantitative knowledge learned from my proposed research will be essential not only for understanding how genomes encode properties of organisms, but also for the dynamical study of transcriptional genetic circuits for explaining cellular physiology.

I believe that my expertise in a wide range aspect of theoretical/computational molecular systems biology and biophysics could strongly contribute to the overall goals of your department. Enclosed, you will find a copy of my curriculum vitae, research statement, teaching philosophy, and copies of my pending manuscripts. Please let me know if I can provide any additional materials. Thank you very much for your consideration.

Sincerely yours,

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Dat H. Nguyen

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Teaching Philosophy

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Fortunately many great teachers and mentors have entered my life, and they have fascinated me with science and inspired me to be a teacher myself. They came with different personalities and varied talents. I have realized, however, and now firmly believe that a good teacher should be an effective facilitator for students to realize their own potentials, and for stimulating their enthusiasm and curiosity about the subject materials they learn. To this end, I concur with George Bernard Shaw, a well-known philosopher, a writer, and a Nobel Laureate in literature of the last century, who simply put it: "I'm not a teacher: only a fellow traveler of whom you asked the way. I pointed ahead, ahead of myself as well as you."

This teaching philosophy of mine has solidified in my role as a teaching assistant of both physical chemistry and computer science for many years. I have learned how important it is to use simple and clear language to explain a complex theoretical concept to students who are not in the realm of theoretical science. As a result, I have learned that the key to being effective in teaching includes the passion for teaching a younger generation; the development of well-organized materials with logical flow; the formulation of homework problems and projects designed to engender curiosity, creative thinking and problem-solving skills; and the use of the modern visual aids for presenting complex ideas with excitement in an interactive classroom setting. As a teacher, I develop each of my lectures in a narrative form, showing students a big picture of the subject matter, how ideas and theories are discovered and developed, and from that, details of each topic to be explored. In my view, this teaching strategy can be extremely valuable to students because it helps them track where they are on their learning path so that they can easily integrate new materials into their existing knowledge base and be left with an appetite for what would happen next. In addition, I consider teaching as a forum for the introduction of new progress in research in the context of the course objective so that students can be aware of where the frontiers of science lie. This, in principle, can help to shape their academic goals more effectively and prepare them well for whatever career path they choose to pursue.

As a result of my previous experiences in mentoring both undergraduate and graduate students with varied backgrounds, ethnics and genders in their research, I realize that good mentoring requires both a good understanding of a student's background and interests and a dedication to their success. To this effect, I guide my students by matching their academic background and interests with projects appropriate to their potential, while ensuring that they have both the opportunity and freedom to pursue their own research, and providing them with necessary advice they need for the successful completion of their research projects. In my view, such mentoring strategy will lead them to the path of being independent scientists, who are confident with their potential, inspired in their thoughts, and productive in their work.

As a professor, I would like to involve in teaching both undergraduate and graduate curricula in computational biology defined broadly enough to cover genetics, proteomics, and systems biology. I am also well prepared to teach chemistry, computer science, and biophysics. From my research experience, I could also contribute to special topic courses such as gene regulation, computational genetics, metabolic network modeling using Flux Balance Analysis, energy landscape, protein/RNA folding, and parallel scientific computing. Certainly, I would adapt and expand my capacity to meet teaching needs of your department as long as they are within the realms of my expertise.