Duke University

DEPARTMENT OF COMPUTER SCIENCE
LEVINE SCIENCE RESEARCH CENTER
DURHAM, NORTH CAROLINA 27708-0129

TELEPHONE (919) 660-6500
FACSIMILE (919) 660-6519
WWW.CS.DUKE.EDU

Biocomplexity Faculty Search Committee
c/o Prof. Rob de Ruyter van Steveninck
Department of Physics
Indiana University
Swain Hall West 117
Bloomington, IN 47405-7105

16 November 2004

Dear Biocomplexity Faculty Search Committee:

It is with distinct pleasure that I write this letter in support of Victoria Anne Smith's application for a faculty position at the Biocomplexity Institute of Indiana University. By way of introduction, I am an Assistant Professor of Computer Science at Duke University, having completed my doctorate from the Massachusetts Institute of Technology under the supervision of Professors David Gifford in the Laboratory for Computer Science, Tommi Jaakkola in the Artificial Intelligence Laboratory, and Richard Young in the Whitehead Institute for Biomedical Research. I am also closely affiliated with the Center for Bioinformatics and Computational Biology here, one of five centers in Duke University's Institute for Genome Sciences and Policy.

My research for the past eight years has been at the intersection of biology and computer science. The area I explored in my dissertation—and one of the areas I continue to explore today as part of a collaboration with Anne—is the development of principled computational, statistical, and mathematical methods for the understanding of complex biological systems, with a particular application focus on networks of regulation and control. I have been significantly involved in this area, having published often in conferences and journals, and having been invited to give a number of talks and serve on various conference program committees. I mention all this only to provide you some perspective on my degree of familiarity with the area in which Anne proposes to begin her faculty career.

I have known Anne for the past two and a half years in the context of a significant research collaboration, and also as a student in one of my classes on Computational Functional Genomics. Anne is a postdoctoral research associate that I have been co-supervising with Professor Erich Jarvis in the Department of Neurobiology; I have been working closely with her and with Erich to develop effective computational methods for inferring the functional networks governing learned vocal communication in songbirds from gene expression and neural electrophysiological activity data. Learning from data gathered at multiple levels of biological organization is not a trivial task, and indeed, pushes the limits of our current ability to think in systems biology terms, but recent work with Anne and Erich suggests that we may be able to make progress in this area

using some of the methods developed in my dissertation. I am very excited about the work we have been doing and am enthusiastic in my support of Anne.

In the time that I have been working with her, I have become extremely impressed by Anne's initiative, work ethic, and productivity, not to mention her immense scientific and technical abilities. Her initiative in this area first drew me into this collaboration. She had thoroughly researched various methods for automatic inference of functional networks and arranged to meet me because she was interested in comparing various methods, including my own, to determine which would be best for the work she and Erich had set out to do. I was amazed by the amount she had read in the field and her level of preparation, even before our first meeting. In the time since that first meeting, she has exhibited tremendous energy and a strong work ethic, usually doing twice what I have come to expect students to do in a similar amount of time. She never seems to need low-level guidance, always understanding the details well enough to discuss matters at a high and intuitive level. In addition to her significant expertise in songbird behavior and vertebrate biology, she has impressed me by writing software in C++, and compiling and porting code between different operating systems, displaying a level of comfort with advanced technical issues that is rare for someone so well trained in her area of biology.

Anne, Erich, and I submitted our first paper to the premier conference in computational biology, Intelligent Systems in Molecular Biology (ISMB), a fully peer-reviewed conference with an acceptance rate of under 20% and attendance of over 1500. Anne worked diligently on the paper, and her ability to quickly synthesize our work and tie off all the loose ends resulted in a paper that was reviewed unanimously favorably and accepted for oral presentation at the conference, in addition to publication in *Bioinformatics*, the flagship journal of the International Society for Computational Biology (ISCB). Other papers were accepted at the International Conference on Systems Biology (ICSB) in December 2002, the Pacific Symposium on Biocomputing (PSB) in January 2003, and again in the journal *Bioinformatics* in 2004. We are also preparing a fifth paper that we plan to submit to a very high quality neuroscience journal. This latter paper is especially interesting because we apply our Bayesian network inference algorithm to electrophysiological data collected from live songbirds exposed to various auditory stimuli (songs, white noise). As far as we can tell, this is the first paper to attempt to recover an entire network of (nonlinear) neural information flow in an active brain; others have looked at (linear) information flow between pairs of electrodes, but we are unaware of anyone else who has considered higher-order nonlinear network interactions all at once.

Beyond her research credentials and years of experience in the area of computational systems biology, I should also mention that Anne has contributed to the preparation of a number of grants during her time here, both for herself and for our collaboration. She is quite adept at conveying the direction and promise of the proposed research and in pulling these grants together, so I suspect she would have no problem securing funding for her research. In addition, she has been working closely with a graduate student named Jing Yu, and has provided quite effective guidance and supervision for her, so mentoring students will not be a new challenge for Anne when she takes up a faculty position.

I am very proud of Anne's work in this area and am extremely pleased at how productive this collaboration has been. Anne will make an excellent faculty member in computational biology

or bioinformatics—she is well-versed in both the biological and computational sides of the problem; she both conducts experiments and codes up software; she is an excellent writer and communicator of ideas, which I feel is significantly underappreciated in scientific circles; she has experience with grant-writing and advising; she is dedicated to her work; and she is very pleasant and easy-going. I am convinced she will be a fantastic colleague for her peers and mentor for her students.

If you require any additional information, please do not hesitate to contact me. I wish you all the best in the deliberation process.

Sincerely,

A. Hartemink

Alexander J. Hartemink
Assistant Professor of Computer Science