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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

December 7, 2004

Dear Search Committee,

I would be very excited to be considered for the position of Assistant Professor at Indiana University. In all honesty, the position, as described, is exactly the sort of career announcement that I was hoping to find.

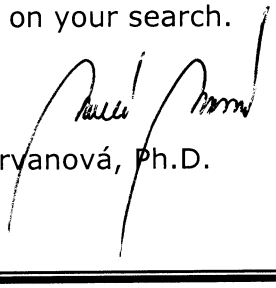
My first Ph.D. is in Pharmacology from the University of Kuopio (Finland) and the second Ph.D. is in Pharmacy/Biochemistry from Charles University (Czech Republic). I am currently a Medical Research Fellow at Vanderbilt University in Nashville working primarily with the nematode, *C. elegans*, as a model organism for the study of neurodegeneration, specifically Parkinson's disease.

*C. elegans* as a study model is eminently familiar to me, including its biology, and something that I would bring with me to the department. A relatively simple and inexpensive model, it is very easy to maintain and can be utilized for many biological and pharmacological investigations. This animal model is also appropriate for different behavioral tests as well as for pharmacological/toxicological assays *in vivo*. I have a solid background in biotechnology, genomics, neurobiology and neuropharmacology, but am informed on and comfortable with the much wider range of general biological science. I am experienced and interested in teaching both classes and laboratory practicals, and I am equally prepared for the instruction and scientific mentoring of undergraduate/graduate students.

I am a very enthusiastic researcher and teacher and would very much like the opportunity to discuss with you and the search committee my qualifications and motivations for seeking an Assistant Professorship at Indiana University. I am available, at your convenience, to schedule an interview by phone or in person, and would look forward learning more about the department's needs and how I might meet them.

Best wishes on your search.

Yours truly,



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# TEACHING STATEMENT

## Introduction

Teaching is great. The process both the instructor and learner go through during the a lecture or course or semester or academic care abound with new possibilities and challenges and difficulties, for both parties. An academic career is something to which I aspire, but more and more I am convinced that teaching is where the greatest joy for me lies. Research is where new ideas are developed, but unless they are taught effectively by people with a passion for teaching, they will not flourish. This is what is great about teaching.

## Teaching

During 2002-2003, I had the opportunity to taken an active teaching and organizing role in the courses organized by the Laboratory of Function Genomics and Bioinformatics of the University of Kuopio in Finland. These courses were for upper division undergraduate students (3rd, 4th, and 5th year in Finland) as well as post-graduate (doctoral) students from the bioscience faculties from Finland. Class size averaged about 20-30 students per session. My responsibilities, among the topics covered, were to teach:

1) Comparative genomics
2) Introduction to nematode and non-human primates
3) SNPs and microarray technology for SNPs analysis
4) Molecular biology of ESTs
5) Non-human primates models in biomedical research
6) General microarray and chip analysis

Most lecture sessions were immediately followed by a practical 'hands-on' component of several hours time. This lecture-lab format worked well and was excellent at providing students the opportunity to experience first-hand the lecture topics previously presented. Included were practical applications of theoretical and methodological perspectives including use of the new tools and methods. Students were the required to complete a graded written-lab assignment and later, a final course exam.

In 2002, I participated in the delivery of an international microarray course and workshop. That course was sponsored by the Nordic Academy for Advanced Study (NorFA) and was open to 100 students from any of the Baltic states. My function was as director the laboratory workshop covering microarray hybridization and data analysis. Each student conducted their own guided experiments utilizing their own research materials. In this way the course was very useful for participants, teaching them new concepts and methodologies, and allowing them to use these new methods on their own research samples in a controlled and closely supervised environment. The most challenging yet most rewarding part of this experience was that the course and workshops were offered primarily to biologists with no prior knowledge about

microarray technology and bioinformatics analysis. This mandated that to teach these difficult materials effectively, one needed to present complex, advanced information and techniques in a clear and easy-to-understand manner.

**Research Mentoring**

My teaching experiences are not only limited to teaching formal courses and labs. During my post-graduate studies, under the tutelage of Dr. Garry Wong, I had the extraordinary opportunity to both co-ordinate and supervise efforts teach the "genomic, bioinformatic and microarray approach" to different labs across the country. During the few years of involvement with this, I was the primary person responsible for helping researchers with their microarray hybridization and data analysis. This was in conjunction with my role as a lab member of the Genomic Core group of University of Kuopio in Finland.

While a post-doc fellow at Vanderbilt University, I was fortunate enough to be able to supervise two summer undergraduate students in the biological sciences during their 3-month summer work-study projects. I introduced them to the concepts and problematic of *C. elegans*. Because of their unfamiliarity with the professional lab environment, it was also necessary that I instruct them in basic laboratory work protocol as well as principles of instrument handling. From the beginning, I tried to a very inter- and pro-active environment (I always encourage students to ask questions and to work creatively to find solutions to problem-solving in the lab). This resulted in the students rapidly becoming active contributors to the laboratory, with only a moderate level of supervision required. They were able, during the short stint in our lab, to produce high-quality results that have been presented in poster format. And their materials have provided for the preparation of one manuscript as well grant application supporting material. I found it very satisfying to work closely with undergraduate students helping them build a solid foundation for research work. In many ways, it is easier than teaching more advanced students, not because of the level of the material, but undergraduates often have less to "unlearn" and are less concerned with impressing you with their skills. I am also currently responsible for teaching and supervising new rotation (Vanderbilt graduate students go through "rotations" in three labs before selecting their resident lab) and resident graduate students as well as working with research collaborators. The supervision of one graduate student in our lab is ongoing and her project has thus far generated important data for a large grant application, and will result in a publication.

**Teaching Philosophy**

Teaching is not an easy task. It requires commitment and diligence at a level not seen in other career paths. I understand that every individual has different strengths and weaknesses as an instructor, just as every individual has different strengths and weaknesses as a learner. While there is no fool-proof method one can employ or philosophy one can espouse in teaching, there are things that are the cornerstone of success. First, one must work very hard. Second, one must be knowledgeable. Third, one must be open. Fourth, one must be flexible. And finally, one must love to teach. I possess all of these qualities, but I am not so self-possessed that I cannot admit that I must also seek to continually improve my abilities on all points mentioned above. To sum my philosophy up in one sentence: Teaching is a privilege.

I have a wide variety of teaching interests (I would love to delve further into large mammal study/teaching, particularly primates). I can effectively teach both general undergraduate classes and specialty undergraduate and graduate courses in my area of expertise. Supervision of thesis research would also be something that I would relish. I look forward to giving back the

knowledge I acquired through my years of study. I firmly believe that my academic and research experience, as well as my tested ability to interact with and teach students and researchers from a wide range of national, ethnic, and cultural backgrounds, has left me well-prepared to teach effectively and enthusiastically at any undergraduate or graduate institution.

**Course Coverage**

I would be pleased to participate in the teaching of undergraduate, graduate and special courses in the following categories:

- General biology
- Molecular biology
- Cellular biology
- Pharmacology
- Neurobiology
- Function genomics
- Scientific/Laboratory methods

And, as part of a departmental team at a university, I would be willing to learn/master whatever necessary in order to supplement the departmental offerings as needs change over time. I have wide-ranging interests and will rise to any challenge presented in the way of new courses to be developed.

**Summary**

Teaching the biological sciences is intrinsically challenging because the science and the technology are still rapidly changing, with no abatement in sight. In order to keep the material stimulating and relevant, one must constantly evaluate, reevaluate and update course content. As an active researcher in this field, I do this with great pleasure and look forward to hearing and advancing the ideas brought forward by students and researchers alike.

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## RESEARCH STATEMENT

My research interests and contributions are in the areas of neurobiology and neuropharmacology, applying both molecular and genomic approaches.

My doctoral work was based in the use of novel genomic technology and different animal models, including rats, nonhuman primates and *C. elegans*, in the neurobiological and neuropharmacological fields [1,2]. Research involved the identification of potential molecular mechanisms that are involved in the effects of neuroprotective drugs (NMDA receptor antagonists) in mammalian brains using the tools of genomic and molecular biology [2,3,4,5,6]. Also of interest was the utilization of affymetrix technology to carry out cross-species hybridization. The goal was to map gene expression within different brain regions of biomedically-utilized non-human primates [2,7,8]. Moreover, I mapped gene expression of 150 unknown genes, sequenced in the rat genome project. The function and anatomical location in the brain were previously undetermined [1,4,9]. I also used *C. elegans* for behavioral and pharmacological assays to study the effects of neuroactive drugs [1].

In my current postdoctoral position, I have been embarked upon a new research direction. It involves using *C. elegans* as an animal model to explore novel pathways of neurodegeneration and therapy for Parkinson's disease. Currently and significantly, *C. elegans* is a powerful tool with a multitude of exiting possible uses in neuroscience, but with the possibility of broader applications to other research subfields in the biological sciences. The strength of this organism in such research is very impressive.

To these ends, new pharmacogenetic model systems (6-hydroxydopamine induced dopamine neurodegeneration using a transgenic worm line expressing GFP under dat-1 promoter) as well as other *C. elegans* transgenic models overexpressing molecules involved in human neurodegenerative disorders (parkin, $\alpha$-synuclein) have been developed. The overarching research goals are to utilize these systems in order to: 1) evaluate dopamine (DA) neurodegeneration *in vivo*, 2) identify and characterize the molecular components involved in DA neuronal cell death, 3) screen for compounds that inhibit or enhance dopamine neuronal degeneration in *C. elegans*, and 4) screen for genetic inducers and suppressors of neuroprotection and 6-OHDA and $\alpha$-synuclein toxicity.

To progress towards these goals, I am utilizing 3 different but related approaches:

1. Genetic approach (genetic manipulation, mutagenesis, RNA interference)
2. Pharmacological approach (drug treatment and exposure, DA uptake assays)
3. Genomic and molecular biology approach (microarrays, RT-PCR, western blot, single worm PCR)

As a postdoctoral fellow, working with Prof. Richard Nass, I have recently completed a research project (manuscript in preparation) which was begun in January 2004. This work focused on identification of novel compounds that protect dopamine neurons against 6-OHDA induced cell death. In developing the screen and subsequent secondary assays we have identified three different compounds that protect against 6-OHDA induced degeneration in *C. elegans*. In this study we show that these compounds, which have known molecular targets in mammals and do not inhibit the dopamine transporter (dat-1), confer dopamine neuroprotection against 6-OHDA in *C. elegans in vivo*. Using genetic and pharmacological approaches, we characterized the receptor system that is responsible for their neuroprotective effect *in vivo*. We also show that these compounds confer neuroprotection in rat primary mesencephalic neurons following exposure to 6-OHDA [10,11].

More recently, we have developed several different transgenic lines of *C. elegans* which over express human parkin and $\alpha$-synuclein genes in dopamine neurons. These genes are known to be associated with familial PD. It was suggested that different mutations of parkin and alpha synuclein genes might play role in the selective degeneration of dopaminergic neurons in PD. Transgenic worms carrying different mutations of these proteins are capable of explaining these proteins' roles in physiological but also pathological stage of PD. We are trying to develop a construct enabling us to better understand selective degeneration of dopaminergic neurons which might contribute to cell death of dopaminergic neurons in sporadic and also familial form of PD. The data from these experiments would lead to better understanding of the cell death process of dopaminergic neurons and thus towards better characterization of new treatment targets for neurodegenerative diseases, such as PD. It is important that the ideas played out in this simple animal model be verified and further explored in higher organisms such as rodents and non-human primates.

Another project, involving study of genetic factors, including parkin and $\alpha$-synuclein in familial form of PD, has progressed very well and within several months the manuscript will be complete [12,13].

Other ongoing projects involve the toxicological study of heavy metals and pesticides. These will culminate in June 2005, and show promise for interesting findings [13]. I also took advantage of high-throughput gene expression technologies such as DNA microarrays to profile different time points of 6-OHDA treated animals. This enabled me to observe more global gene expression profiles after treatment. Gene expression data revealed several new gene targets as well as several interesting synexpression groups regulated after treatment [10].

**Closing Remarks:**

As evident from the summary of my research interests, I strive take a very interdisciplinary approach to the biological sciences, integrating neuropharmacological, genomic and molecular biological theories and methods in my work. The effectiveness of the integration of genomics and bioinformatics, pharmacological and molecular tools and different model systems (animal and cell cultures) is very exciting. And I am very committed to further research in neuropharmacology and model problems in neurological disorders.

I am keenly interested in the development of grant proposals that would enable me to expand hands-on, multidisciplinary research opportunities for both undergraduate and graduate researchers. The end goal being to better increase the number of persons who pursue advanced degrees in the areas listed above through the provision of exciting opportunities for research and scholarship, but also realizing that there are many paths to success, and research

is a process by which students might find their way forward, thereby adding my strengths and the strengths of the student body to that of the biology department.

I am a very hardworking person and apply this ethic to any endeavor I undertake. My future goals include establishing an academic career undergraduate and post-graduate science education, building expertise through research and teaching to advance students, staff, and department, thereby making my own small contribution to science.


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