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

November 23, 2003

Dear Prof. de Ruyter van Steveninck,

In response to your advertisement I would like to apply for the junior faculty position in Biocomplexity.

I obtained my basic education in Physics and specialization in Laser Physics and Optics at Moscow Engineering Physics Institute and at Saratov State University (Russia). Since 1997 I have been a postdoc at the University of Illinois at Urbana-Champaign, where I have been working in Tissue Optics, Biophysics, and MR imaging. I have developed and validated methods for real-time near-infrared monitoring of the hemodynamic and neural processes in the human brain. Currently I am a Senior Research Scientist at the Biomedical Imaging Center. I am studying the biochemical and biophysical nature of functional MR signals, developing a combined optical – MR brain imaging system, and performing theoretical biophysical modeling of brain function. I am a Co-Principal Investigator on the NIH-funded grant, which I submitted under the advisory of Prof. A. G. Webb.

I have publications in both physical journals, such as Physical Review A and E, and Medical Physics, and in biomedical journals, such as Neuroimage (impact factor 7.879). According to Science Citation Index, my papers have been repeatedly cited by other authors, one of them – more than 20 times ("On-line optical imaging of the human brain with 160-ms temporal resolution", *Optics Express 6*(3), 49-57, 2000).

I enclose the application materials required in your advertisement. I asked the following persons to forward their recommendation letters to you:

Prof. Enrico Gratton, Department of Physics, University of Illinois at Urbana-Champaign, 1110 West Green Street, Urbana, Illinois, USA, 61801-3080
e-mail: enrico@scs.uiuc.edu Telephone: 217/244-5620 Telefax: 217/244-7187

Prof. Andrew Webb, Department of Electrical and Computer Engineering, 4221 Beckman Institute, 405 N.Mathews, Urbana. IL 61801
Telephone: 217-333-7480. Fax: 217-244-0105, Email: a-webb2@uiuc.edu
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Prof. Sergio Fantini, Department of Electrical Engineering and Computer Science , Tufts University, 4 Colby Street, Medford, MA 02155-6013
Phone: (617) 627-4356 , Fax: (617) 627-3151, e-mail: sergio.fantini@tufts.edu

Please, do not hesitate to contact me if more information is needed.

Sincerely,

Vladislav Toronov
Beckman Institute for Advanced Science and Technology
University of Illinois at Urbana-Champaign
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Vladislav Y. Toronov
Statement of Research Interests and Plans

My research interests include optical imaging of biological tissues, the physics and biochemistry of functional magnetic resonance imaging, and the biophysics and biochemistry of brain function.

Optical Imaging of Biological Tissues

Human tissue is relatively transparent to near-infrared light in the band between 700 and 1000 nm, so that light can penetrate into tissue to a depth of up to several centimeters depending on the type of tissue. This property can be used to obtain physiological information, for example to detect tumors or to measure hemodynamic changes in tissue. The method is called near-infrared spectro-imaging (NIRSI). The main advantages of NIRSI are the high biochemical specificity, high temporal resolution (of the order of milliseconds), ability to directly access neuronal activity, and complete non-invasiveness. However, to fully benefit from these exciting opportunities it is necessary to overcome certain challenging physical and engineering problems.

The most fundamental problem is the extremely high scattering of light by tissue, which brings the description of light transport beyond the capabilities of approaches based on geometric optics or macroscopic Maxwell electrodynamics, and also fundamentally complicates the inverse problem of local optical characterization of tissue from measurements on its surface. This requires development of new experimental techniques, accurate theoretical models of light transport, and efficient algorithms for the solution of the inverse problem. Other problems include optimization of light sources and detectors, development of optical sensors, and reduction of biological noise in optical signals.

My research in NIRSI has been focused on the development of new frequency-domain experimental techniques and methods of signal processing for detection and measurement of functional hemodynamic and neuronal changes in the human brain.

Physics and Biochemistry of Functional Magnetic Resonance Imaging

Although the high spatial resolution and non-invasiveness of MRI has made it one of the most important clinical and research techniques, magnetic resonance in biological tissue is a complex biophysical phenomenon. Theoretically, there are many physiological factors that can affect the MR signal. In case of functional MRI based on the blood oxygen level dependent (BOLD) effect these factors include cerebral blood volume, oxygenation, and architecture of the vascular network. Several biophysical models of the BOLD effect have been proposed; however understanding of the phenomenon is far from being complete. The biochemical specificity of NIRSI makes it a unique tool for better understanding factors contributing to functional MR signals. Therefore, one of the directions of my research is the development and validation of the biophysical models of fMRI signals using simultaneously acquired optical data.

Biophysics and Biochemistry of Brain Function

Advances in techniques for measuring functional changes in the brain have stimulated growing interest in the biophysical mechanisms of brain function. The aim of the biophysical approach to this problem is to develop mathematical models describing the roles of different physiological factors in a dynamic manner. The objective of my research is the development of the mathematical model describing the dynamic interconnection between neural activation and oxygen transport to brain tissue. This model involves such variables as cerebral blood volume, oxygenation, flow, oxygen metabolic rate, and others. As the Ariadne's thread I use the NIRSI and fMRI data obtained on humans during functional activation.

Proposed Initial Research

I plan to establish a research program which will embrace my research interests and will be compatible with the department research resources and environment.

In the area of the *Optical Imaging of Biological Tissue* the primary goal will be to develop a fast imaging method allowing localization and accurate measurement of cerebral hemodynamic changes and neuronal signals. Since events occurring in neuronal membranes and volume changes of cellular compartments can influence light scattering, NIRSI has a potential to measure directly the neuronal activity. This can make NIRSI a unique neuroimaging tool, because two other existing methods to measure neuronal activity directly, EEG and MEG, have a very poor spatial resolution due to the fundamental physical reasons. The spatial resolution of NIRSI can theoretically be increased to the order of a few millimeters, which is significantly better than that of EEG and MEG. In particular, I plan to integrate NIRSI with structural (anatomical) MRI, because such integration promises significant progress in mathematical algorithms for reconstructing optical properties of tissues. This research will include the development of experimental techniques and imaging algorithms, and *in-vivo* experimental data collection. I have contacts with one of the leading companies that developed near-infrared biomedical instrumentation (ISS, Champaign, IL), who are willing to collaborate with me to further develop their instruments.

In the area of the *Physics and Biochemistry of Functional MRI* I plan to establish research aimed at increasing the biochemical specificity of fMRI. Currently fMRI is mostly used to locate neuronal processes rather than to obtain biochemical information. I expect that understanding biophysical and biochemical nature of fMRI signals will allow developing fMRI methods to obtain biochemical information. For this I will continue to develop models of MR signals. Although several potentially good models of BOLD effect have been proposed, only the Buxton's model has been evaluated up to date. This model, however, may be inaccurate in the case of magnetic fields higher than 1.5 T. The models which potentially can be used at high fields still need to be further developed and verified. I will use NIRSI for validation of MR signal models.

In the area of *Biophysics and Biochemistry of Brain Function* I will continue the development and analysis of biophysical models of biochemical and neuronal processes in the brain. This will be essentially theoretical work, but it will be based on experimental data obtained within my other projects. The aim will be to develop realistic models describing neuronal and metabolic responses to functional activations, such as motor, visual, and mental ones. These models will be non-linear, and therefore I will use methods of non-linear dynamics to analyze them. This project should result in the understanding of fundamental mechanisms of cognition at the biophysical level.

My research can accommodate both graduate and undergraduate assistants, and also postdocs. Students will learn how to apply principles of optics and electromagnetism to obtain information about biochemical processes in tissue. They will obtain practical experience in optical and MR engineering, biophysics, scientific programming, and signal processing. Postdocs will be in charge of particular directions, such as optical imaging, or brain modeling.

I plan to submit grant applications covering each of the research directions to such funding agencies as National Institutes of Health and National Science Foundation.