Dear Dr. de Ruyter van Steveninck:

I am writing to apply for the position of "Assistant Professor of Biocomplexity, Modeling & Imaging" that was advertised on the Physics Today web page.

My Ph.D. degree is in Biophysics with emphasis in MR Imaging and Pharmacokinetics. The title of my dissertation is "Mathematical and Pharmacokinetics Modeling of MRI Contrast Agents' Transport into the Intervertebral Discs". I had 2 years of Graduate School Courses in Medical Physics from the Medical College of Ohio @ Toledo. I have an M.S. degree in Physical Chemistry from the University of California, Davis Campus. I believe neurological diseases can be studied with MR & PET Imaging, as a derangement of transport phenomena in cells/tissues, which are dependent on membrane's viability. I also believe that my training and experience in medicine & biophysics will greatly compliment the research direction and mission of your department.

I have also completed a 2-year postdoctoral research in Brain Aging & Alzheimer's Disease research at the University of California @ Irvine. In addition, my M.D. degree program was completed in December of 2002 and graduation in June of 2003.

Please, find attached, a copy of my Curriculum Vitae, statement of research interests, publication list, and list of references & recommendations. Please don't hesitate to contact me if you need more information.

Thank you for your cooperation and consideration.

Sincerely,

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Michael A. Ibrahim, M.D., Ph.D.

STATEMENT OF RESEARCH INTERESTS

There are two main mechanisms by which cells of human and animal tissues or organs receive nutrients and other vital substances: (1.) Perfusion(bulk flow or convection), and (2.) Diffusion(passive & active). Perfusion is the main route of supply to tissues and organs, whereas diffusion processes occur mostly at the cellular level. Convection or bulk flow at the cellular level is akin to perfusion at the tissue or organ level.

There are known mathematical and pharmacokinetics equations that can be written for these processes in simple systems. However, obtaining the equations that govern these processes and applying them to the transport of substances in human tissues and organs are difficult to achieve. In my research, I have devised two mathematical equations that can model the transport mechanisms in the brain and intervertebral discs. The analytic solution of the equation governing transport process in the intervertebral discs had been developed and applied in my dissertation work. I am now working on developing an analytical solution governing transport processes in the brain. ***In vivo***, dynamic MR Imaging with contrast agents is being used in my work to clearly define and elucidate these processes.

Intervertebral Discs:

Intervertebral disc is the largest ***avascular*** structure in the human body. Nutrients reach the disc exclusively by diffusion through the ***end-plates*** and the ***annulus fibrosus***. Bulk flow, and convection play an insignificant role. Mathematical equation governing this process is that of diffusion***(Fick's 2nd Law)*** in a finite geometry. When dynamic MR Imaging with contrast agents are performed, the images obtained, in conjunction with my modeling equation, can be processed to give a map of diffusion and diffusion parameters throughout the tissue. Abnormality of diffusion parameters, such as diffusion coefficient can be used to assess the viability of the discs. Degeneration may be initiated by a decrease in the rate of diffusion into the disc. Therefore, changes in diffusion may be an early marker of disc degeneration and or trauma (herniation, prolapse etc.).

The Brain:

Transport of nutrients and substances into the brain is by perfusion and diffusion processes. Unlike the intervertebral discs, brain is a highly vascularized and perfused organ. Therefore, mathematical modeling equation that describes the transport mechanisms of the brain must include diffusion and perfusion processes explicitly. Analytical solution of this kind of non-linear, combined equation has not been solved. One can use numerical integration methods to obtain a solution. But, there are several disadvantages to this approach, one of which is that generalization and global extensions of the parameters are not advisable. The ultimate goal is to develop an analytic equation that can be applied to dynamic MR Images with contrast agents, and obtain transport parameters that can define transport mechanisms of the brain in detail. Once, these parameters are obtained, the problem of transport abnormalities in neurological diseases, such as Alzheimer's disease, dementias, stroke, and trauma can be fully characterized.

In summary, my short term goals are to investigate ***in vivo***, the mechanisms controlling transport of nutrients and other biological molecules into the brain and intervertebral discs with MR Imaging. This goal can be achieved with mathematical and pharmacokinetics modeling. My long-term goal is to translate the findings of this research into early diagnosis and treatment of diseases, such as Alzheimer's disease, other dementias, and intervertebral discs degeneration. Although, there is no funding mechanism for these projects at this time, the potential of being funded is very strong, and certainly be enhanced by joining efforts with an interdisciplinary scientific community.