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FOUNDATION

LERNER RESEARCH INSTITUTE

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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

Dear Committee Members,

It is my pleasure to have the opportunity to apply for the joint faculty position in biocomplexity at your esteemed university (as advertised on *APS Career Center*). Enclosed please find my curriculum vitae with a list of publications, statements of my research and teaching interests, and a list of the references.

I obtained my Ph.D. degree in physics with a biomedical concentration from Case Western Reserve University in May 2000. Since then I have been a project staff (~ research assistant professor) in the Biomedical Engineering Department, Lerner Research Institute, Cleveland Clinic Foundation. More recently I have become an instructor in the newly opened Cleveland Clinic Lerner College of Medicine. I have maintained close collaboration with researchers at Case Western Reserve University and serves there as an adjunct assistant professor. I have been advising graduate and undergraduate students from the nearby Case Western Reserve University and Cleveland State University.

My major research interests are to study human brain and the neuromuscular system using multi-modality approaches. Underlying this theme I am carrying out research in three closely dependent categories: experimental studies using the existing state-of-the-art neuroimaging tools including MRI, fMRI, EEG and MEG; theoretical approaches including biophysical modeling; improvement of current techniques/methods and development of new ones for the study. I have been a major co-investigator in a number of NIH, DOD and VA grants, and am actively seeking external funds to become a financially independent researcher.

It is my goal to pursue a successful career in research and education. I strongly believe that my expertise and experience will be a valuable asset to your prestigious institute if I have the privilege to join your highly respected team of faculty, and I also believe such an opportunity will greatly facilitate the accomplishment of my goal.

If you need further information, please don't hesitate to contact me.

Sincerely,

Jingzhi Liu, Ph.D.
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Research Interests and Plans

Jingzhi Liu, Ph.D.

My major research interests are to study human brain and the neuromuscular system using multi-modality approaches. Underlying this theme I am carrying out research in three closely dependent categories: experimental studies using the existing state-of-the-art neuroimaging tools including magnetic resonance imaging (MRI), functional MRI (fMRI), electroencephalography (EEG) and magnetoencephalography (MEG); theoretical approaches including biophysical modeling; improvement of current techniques/methods and development of new ones for the study. My strong background in both modern physics and biomedical engineering has put me in a unique position to carry out such a multidisciplinary research program. Below I will briefly describe the current projects that I will continue to work on and the new directions that I will open in the near future.

1. Cortical motor control and muscle fatigue

In the past several years, I have focused my main effort on motor control, especially the issue of muscle fatigue, a phenomenon that has been investigated for over a century. Using fMRI and EEG, I have been able to carry out various studies to examine the role of the brain in modulating fatiguing muscles. We have quantified the cortical activation levels (including fMRI-measured hemodynamic responses in blood and EEG-measured movement-related cortical electrical potentials) in maximal- and submaximal-force fatigue tasks. The results have shed light on the underlying mechanisms in both peripheral and central fatigue. I plan to further the study by applying even more advanced data-processing methods and exploring several important aspects of the problem. The coherence (EEG) and functional connectivity (fMRI) among different cortical areas and between the brain and muscle will be investigated. The nonlinear dynamic characteristics (fractal, chaos, etc) in the signals will be explored. Inverse problem, an important and highly interested approach in EEG, will be solved to locate the neural sources that generate the signals; and this may be done by taking advantage of the excellent spatial resolution of fMRI (~mm) and excellent temporal resolution of EEG (~ms) that are supplementary to each other. Some other advanced data-processing approaches may also benefit the inverse problem as well as providing other dimensions to extract information from the data. They include ICA (independent component analysis) and PCA (principle component analysis). Strange attractor, an approach of chaos, may sometimes be an even more “attractive” concept to quantify the nonlinear dynamic aspect of the signal. Other imaging modalities may also be applied; for example, collaborations have recently been sought to include MEG and transcranial magnetic stimulation (TMS) in the study. Further biophysical modeling of this problem will also be carried out. (Several aforementioned aspects are also discussed in the following topics.) Some of these studies have been done partially and I will continue this multi-modality study of motor control of fatigue in the future.

2. Brain dynamics and biophysical modeling of the neuromuscular system

Many physiological processes regarding the functioning of the brain and the neuromuscular system are biophysical in essence. These fundamental problems are not understood well yet, and it is rewarding to apply physical and mathematical methods to study them. Recently I have developed a dynamic model that describes muscle activation, fatigue and recovery under voluntary brain effort. This model can explain many neuromuscular issues in terms of force generation; for example, it clarifies the long-standing question about why human cannot maximally activate a muscle solely by voluntary effort. It also bears potential in clinical applications, and this will be explored in future proposals. I will continue my research on the biophysics direction in which I can well utilize my extensive knowledge on modern physics. Some of interesting and fundamental biophysical problems that I plan to investigate are briefly described as follows. (1) Nonlinear behaviors in neural and muscular electromagnetic (EEG, MEG and electromyogram [EMG]) activities. Brain, as a dynamic and nonlinear system, is a perfect object to be studied by various physics methods such as chaos and fractals. Brain dynamics is one of my favorite topics that always intrigue me highly. Recently, we have measured the fractal dimensions in EEG signals at different physiological periods of a motor task and determined the relationship between fractal dimension and force level under condition of no fatigue effect. We plan to further apply the concept of fractal and chaos (including strange attractor) to quantify the fatigue and clinical data. The endeavor is to find appropriate and sensitive indices for quantifying physiological signals so that indexing of physiological condition changes and even predications of diseases can be made based on them. (2) Relationships between neural activities at different levels such as measured by fMRI and EEG. Such relationships are important for rendering a whole picture of the brain and its functioning; and it requires substantial biophysical modeling to achieve this. (3) Neural electrical oscillations and their origin. The EEG signals are typically represented by characteristic oscillations of different frequencies such as alpha, beta and gamma. These oscillations are the overall effect of the firing of neuron aggregates; however, the exact mechanisms of their formation are not clearly understood. A better understanding, especially better biophysical modeling, of this problem will solve many fundamental issues remaining in the EEG interpretation and provide new ways of clinical usage of EEG. The interactions among these frequency components are also of high interest and deeper examination of them may render new views about EEG. (4) Consciousness and its origin. This is, by any means, a very confusing and fundamental problem. I am, to satisfy my long-lasting curiosity, endeavoring to develop a theory that can explain it. I believe I have found some of the basic elements to piece up the whole puzzle. There are also other high-end possibilities for my future research, and time will gradually unfold them to the world. In practice I am also interested in applying the knowledge rendered from fundamental research to clinical and engineering problems.

3. Structural organization of the brain and the underlying principles

Since MR images provide excellent resolution (~mm) in anatomical structures, there is great interest in obtaining information about the brain from MRI data. Recently we have developed an automated brain segmentation and volume measurement algorithm based on histogram analysis of T1-weighted 3D MR head images. This algorithm can measure the brain volume with an error of 1.5%, one of the most accurate methods currently available. We have also developed an automated method to identify several major cortical landmarks and segment the two hemispheres and the frontal lobe based on fuzzy-logic encoded knowledge about the brain structures. Using these methods, we quantified the aging effects on the cortical volumes and found gender-related left-right asymmetry in atrophy of the frontal lobe. We are trying to improve the algorithms so that they can be used to segment other cortical and even sub-cortical structures. Another interesting project is to study the fractal structures in the anatomical brain. Fractal dimension can serve as an index of complexity of a structure being examined, and thus, it can be applied to study neurological development and degeneration due to factors such as aging, diseases, and even evolution. We have recently quantified the fractal dimensions of brain white matter in both healthy young and elderly people, as well as in pediatric brain tumor (medulloblastoma) survivors. Aging and disease/therapy related effects on fractal dimension were detected. We are currently developing more advanced image-processing algorithms to make more accurate measurement of fractal dimensions of structures of interest in both the cerebrum and cerebellum. The structures of interest include the white matter skeletons, the interface of the white matter and gray matter, the cortical surface, etc. A more exciting and fundamental direction that I have been pursuing is to find the underlying principles that govern the formation of the brain structures. I believe that the brain must have an *intrinsic* coordinate underlying its apparent high complexity; such a coordinate governs all its structural arrangement in terms of functioning. The finding of such a coordinate will advance brain research tremendously, and in practical it will eliminate most of the pains-taking efforts currently undergone in processing the brain structural/functional data.

4. Brain plasticity in aging and neurological disorders

Besides my interest in investigating normal healthy condition of the neuromuscular system, I also have strong interest in probing physiological states in dynamic changes due to factors such as development, aging, or diseases because examining these dynamic or abnormal conditions often gives us more opportunities to peek into the mechanisms that underlie both normal functioning and disorders. For this reason, I have particular interest in studying the effects of aging (including development and degeneration) and diseases (such as stroke) on the neuromuscular system. I have performed in collaboration with my colleagues various studies in this direction, including studies of aging effects on cortical volume and fractal dimension, treatment/rehabilitation related recovery in stroke and hydrocephalus patients, a longitudinal study of white matter changes in a population of pediatric brain tumor survivors, etc. I will continue this type of research and will also try to transfer the findings to clinical usages.

5. Development of new techniques/methods for studying the neuromuscular system

Scientific breakthroughs often bring about technical advancements, and vice versa, technical advancements often pave the way for scientific leaps. I believe that more and better techniques are needed for the maturity and prosperity of the next-stage brain research at the time of quantitative biology that has just started. For this reason, I am keeping alert of technical advancements and am also interested in developing new techniques and methods to facilitate the study of the brain. Recently we have developed a data-acquisition system that allows us to record muscle force and EMG simultaneously with fMRI data. This system is the first of its type and has facilitated sophisticated studies of the brain, muscle, and their interactions in motor-related tasks. In the future, I am strongly interested in exploring more exciting ideas. For example, I have a strong desire to invent a machine or device that can visualize the transmission of neural signal in real time. Imagine you can see a neural signal propagating from the brain to the peripheral or from one part of the brain to another! Another interesting possibility is to utilize the MR in some unique, novel and unconventional ways that have the potential to open up completely new approaches for research and medicine. I have gained some preliminary clues for these novel directions, and believe that given time, wills and interests will become reality!

Overall, my research interests include both current down-to-the-earth mainstream topics and future ground-breaking directions that have potential to change our life and thinking permanently. As a self-positioning, I am determined to achieve distinction in science. To make important scientific achievements is the inner pulse pushing me forward and the basis for social and personal fulfillment. In fact, it has been a habit for me to keep thinking over fundamental problems in science and novel developments in technology; and I believe such a habit is critical to hatch breakthroughs. I believe that I have the ability to achieve the goals and I also believe that my participation in your respected team will greatly facilitate my progress toward the goals, and meanwhile, adding strength and value to your already prestigious institute.

Statement of Teaching Interests

Jingzhi Liu, Ph.D.

I am interested in teaching any courses that are related to my research, e.g., physics of MRI, functional imaging (fMRI and EEG), applications of these tools in biomedical sciences, and biophysics. I have particular interest in teaching a neuroimaging course that includes the introduction to the principles of the modern imaging modalities (such as MRI, fMRI, EEG, MEG, TMS, PET, CT, ultrasound, etc) and their applications in research and medicine. Practically I can teach any fundamental and more advanced physics courses such as mechanics, electromagnetism, electrodynamics, quantum mechanics, thermodynamics, atomic and particle physics, etc because I have an excellent background in physics (note that my PhD is in Physics!). I can also teach applied mathematics courses such as calculus, differential geometry, differential equations, etc, especially their applications in biomedical problems since I had studied theoretical physics before I entered the multi-disciplinary biomedical physics area and had a thorough learning of many advanced mathematics courses.

My philosophy in teaching is to try to stimulate each individual student's maximal potential of learning and performing. This could be achieved based on observation of each student's own characteristics, both personality and intelligence potential. I am a strong proponent of active learning, in which an extremely effective way is to involve students in research projects and let them feel that they are important along the way. I have been raised in an educational rich environment --- both of my parents are teachers and I had been edified with educational nutrition along my growth and am familiar with educational strategies and techniques. Luckily, my Ph.D. adviser, Prof. Robert W. Brown, is also an excellent teacher besides his excellence in research. He has carried out effective teaching by heavily involving both undergraduate and graduate students in research activities and by introducing new methods into teaching. He has been awarded numerous honors in teaching, and I have learned a lot along my participation in both his research and teaching. Therefore, I am very confident in my ability to teach effectively. In practice, I have gained significant experience in the past years by serving as teaching assistant and instructor, giving lectures and presentations, and advising a number of graduate and undergraduate students (see the teaching experience part in my CV). The interactions between the students and me have benefited both the education and the research; along the way I have had opportunities to improve my educating skills. I believe that I can create a learning-conducive environment for our students and inspire them to learn and explore effectively.