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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 Search Committee Chair,

It is with great pleasure that I write this letter of reference for Dr. Youping Xiao. Dr Xiao was recruited to our graduate program in 1992 and joined my laboratory in 1993. Youping had an excellent background for neuroscience, having majored in electrical engineering as an undergraduate and having completed a Masters degree in the neurophysiology of the cerebellum. In addition, he had outstanding scores on the Graduate Record Examination. Once enrolled in the Doctoral program, Youping excelled in all of his classes as well as in his research program.

Dr. Xiao's doctoral work involved physiological and anatomical studies of areas V2 and V4 in macaque monkey visual cortex. When he joined my laboratory, we were just starting our studies of optical recording of intrinsic cortical signals. Youping was primarily responsible for the development of this technique in our laboratory. Rather than purchasing a turnkey optical recording system, we developed our own system based upon a Photometrics camera hosted by a Macintosh computer running Biological Detection System's Image software. Youping was critically involved in the programming of this BDS system (Macintosh C programming) as well as in the development of visual stimulus protocols on a Silicon Graphics workstation (Indigo<sup>2</sup> High Impact and O<sub>2</sub>). A third computer running Discovery from DataWave Inc sequenced the experiments. Youping also programmed this data acquisition environment to trigger image acquisition or microelectrode recording based upon respiration signals. This system has been the mainstay of our laboratory by providing functional imaging data upon which anatomical pathway tracing and microelectrode recording experiments are based.

Dr. Xiao developed a large number of anatomical techniques that have proven to be critical in our research program. He quickly mastered a variety of immunocytochemical techniques and combined them with traditional histochemical and fluorescent tracer methods. Our work requires precise localization of labeled cells and axons and the analysis of their locations with respect to cytochrome oxidase defined compartments in V1 and V2. To achieve this goal, the locations of labeled cells are recorded using a computer-interfaced microscope and these data are imported to a Silicon Graphics workstation for three-dimensional reconstruction and overlay onto images of cytochrome oxidase stained sections. Youping used this system and developed a variety of analytical methods to characterize the spatial relationships among labeled

axon populations in area V4 (Matlab) and between labeled cells and cytochrome oxidase compartments in V1 and V2. His work in areas V2 and V4 has led to three publications, the second of which directly stems from his thesis work. His thesis demonstrates for the first time, that the parallel visual processing that is so prominent in areas V1 and V2 is maintained along the cortical hierarchy to area V4. In this work, optical recording was used to define the functional compartments in area V2 and to guide the placement of anterograde tracer injections. The axon terminals were then reconstructed in area V4 and formed segregated projections in V4. The resulting paper was well received after its publication in the *Journal of Neuroscience*. Subsequently, Youping turned his attention to determining the specific pattern of inputs that V2 thin and interstripes receive from area V1. This work, published in the *Proceedings of the National Academy of Science*, provided a revision of some long held beliefs about the nature of parallel processing between V1 and V2 in primate visual cortex. Specifically, he determined that the projections from V1 blobs and interblobs to V2 thin stripes and interstripes are not strictly segregated. Rather, V1 blobs project to both V2 stripe types, while V1 interblobs only project to V2 interstripes. Youping's work on the intrinsic connections of V2 compartments is also very important. His results indicate that a highly specific pattern of long-range intrinsic connections is observed in V2 when tracers are directed at functionally defined compartments. This result is different than previous studies of short range and long range connections in V2 that used blind injections into V2 that were later correlated with cytochrome oxidase architecture. These results support the view that V2 thin stripe chromatic modules have highly specific patterns of long-range intrinsic connections. Ongoing work will determine whether other portions of V2 thin stripes have similar patterns of intrinsic and extrinsic connections.

Dr. Xiao finished his thesis in February of 1999 and remained in the laboratory as a postdoctoral fellow until May of 2001. During that time he postulated that the thin cytochrome oxidase stripes of V2 were functionally heterogeneous and might contain a systematic representation of color. He then designed and executed a difficult series of experiments that examined the internal organization of V2 thin stripes. He found that individual thin stripes contain sub-domains that contain systematic representations of color. A full color map was found to occupy a linear to nearly circular domain that extended roughly .4 x 1.2 mm. Within that domain, individual color had peak regions of activation that extended roughly .3 mm across. These color maps were organized in the order of perceptual colors and thus might provide the physiological substrate for color perception. This work, published in *Nature*, demonstrated the first, spatially organized representation of color in the primate visual cortex. While maps for other stimulus attributes have been found in V1 and V2, a systematic representation of color has not been found in any cortical area. Furthermore, his work suggests that the perception of color is coded by the spatial location of activations in the cortex. Furthermore, Dr. Xiao performed a series of microelectrode recording experiments to determine the relationships between the maps of color, revealed through functional imaging, to the properties of single cells and cell clusters within specific loci within those maps.

During Youping's analysis of the color maps within V2 thin stripes, he and others demonstrated a functional heterogeneity that suggested that thin stripes contain segregated compartments that prefer achromatic, luminance modulation. This research project, conducted in collaboration with another postdoctoral fellow in the laboratory, Yi Wang, demonstrated spatially segregated cell populations that encoded the magnitude and direction of relative achromatic luminance change. This functional imaging project and its associated microelectrode recordings are currently being prepared for publication.

In addition to his own research work, Dr. Xiao has been indispensable in the training of the Research Assistant in immunocytochemical methods and in the training of a new postdoctoral fellow in the physiological and anatomical methods necessary to continue this research program.

Dr. Xiao is very interested in the relationships between cortical structure, function, and perception. In the future, he plans to continue his work on color processing and to more directly relate the color maps to perception. In the discussions that we have had, he indicated that he would combine both optical and microelectrode recording in awake animals with psychophysical methods to explore the neural bases of hue, saturation, and brightness perception. Dr. Xiao certainly has the technical skills and intellectual capacity to solve these cutting-edge problems.

In summary, Dr. Youping Xiao has been an outstanding student and he has a very promising future. He is a very dedicated scientist who is undeterred in the development and application of new techniques to solve important scientific problems. He has a keen insight into current scientific problems and understands how to apply scientific methods to solve them. Furthermore, he is an excellent team player who has been an absolute pleasure to work with. Based upon my experience with other students and postdoctoral fellows in this and other programs, including the California Institute of Technology, I would rate Dr. Xiao among the top 5%. He possess both the necessary technical and analytical skills to succeed as a first rate scientist. He is well read and often brings articles to me to discuss. His verbal communication skills are excellent and his written skills are quite good and continue to improve as he writes additional papers. Based upon these characteristics as well as his wonderful personality, I highly recommend Dr. Youping Xiao for an Assistant Professor position in your department.

If I can be of further assistance, please do not hesitate to call or email.

Sincerely,



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