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Professor Robert de Ruyter van Steveninck
Biocomplexity Institute
Indiana University
Swain Hall West 117
Bloomington, IN 47405-7105

Dear Professor de Ruyter van Steveninck:

I hereby apply for a faculty position in theoretical biophysics at the Biocomplexity Institute starting Fall 2004.

In summer of 2001, I received a PhD in physics from Michigan State University, with specialization in theoretical condensed matter physics. My thesis work was devoted to the theory of tunneling in a magnetic field. The obtained semiclassical solution allowed us to obtain qualitative and quantitative agreement, without any adjustable parameters, with experimental data on electron tunneling from a strongly correlated 2D electron system in the presence of a magnetic field perpendicular to the layer.

Since then I have switched my research focus to biological systems and during the past two years have been working in collaboration with Professors William Bialek and Kenneth D. Miller on problems in neuroscience. The main result of this work was the development of a method for calculating receptive fields from neural responses to correlated, non-Gaussian stimuli. In particular, it will allow the use of natural movies in physiological measurements, where previously only correlated Gaussian noise ensembles could be used to study the filter properties of neurons, aside from a strictly linear model. In the future I would like to continue to work at the interface between neuroscience and physics, and believe that interdisciplinary environment would be most beneficial for my scientific growth.

Even though I have been trained as a theorist, I carried out a series of experiments in Professor Miller's laboratory. The research plan I propose has a large experimental component, which I plan to pursue either in my group or through collaborations with other groups at Indiana University.

I appreciate your consideration of my application for the faculty position. Enclosed please find my curriculum vitae, statement of research interests, and a teaching prospectus.

Yours sincerely,

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Statement of Research Plans

Given my background, I would like to work at the interface between physics and neuroscience, and use methods from condensed matter and statistical physics to study neurobiological systems. My current work has relied on information theory to design a method of analyzing neural responses which does not depend on the particular properties of the stimulus ensemble and can be applied to correlated non-Gaussian stimuli. The method is based on calculating how well projections on a set of filters (whose output is nonlinearly combined to generate the response, otherwise if the model is strictly linear, then there is only one filter) can explain an observed sequence of responses from a neuron, and try to look for those filters that recover as much as possible of the Shannon information conveyed by the sequence of responses as a whole. Shannon information provides a convenient and quantitative way to compare probability distributions of signals globally, and not just with respect to a given number of moments, thus allowing us to go beyond the case of Gaussian stimuli. One of the most interesting applications of such a distribution-free method is to probe neural responses with natural stimuli, such as those to which an animal is constantly exposed and which are thus the most biologically relevant. Natural stimuli have been shown to have strong spatiotemporal correlations with large deviations from a Gaussian distribution. It is possible to use this method to find stimulus features relevant to not just a single response, but to a temporal sequence of responses. The number of filters that could be reliably estimated depends on the size and quality of a particular data set available for the neuron under investigation. For one filter, the method gives errors which are comparable to those of the reverse correlation method, which is well established and used to find one filter from neural responses to Gaussian noise ensembles. Overall, the possibility to study neurons with natural stimuli opens a series of questions, some of which I list below and hope to pursue in the near future.

Adaptation to stimulus ensemble. Neurons at the first few stages of processing of sensory signals respond to both natural stimuli and Gaussian noise ensembles. Therefore it is possible to use both types of stimulus ensembles to study the same neuron and ask whether its characteristics change with the stimulus ensemble, which would be an indication that the adaptation process took place during the course of an experiment. We will also be able to correlate changes in the neuron's filters with the Shannon information transmitted by the neuron about the stimulus ensemble and ask how much of information would have been transmitted in the absence of adaptation, i.e. if we use a white noise filter to account for responses to natural scenes and vice versa.

On a theory side, we could hypothesize that a set of neurons has been designed with the goal of maximizing information transmission about the incoming signals, and derive the appropriate neurons' characteristics from this assumption given the constraints of metabolic costs per response. It would be interesting to derive these properties optimal from the view of information transmission given what we know about the statistics of natural signals and compare with those optimal for transmitting white noise signals. These predictions could then be compared with the results of the above-mentioned experiments. I plan to first consider properties of retinal ganglion cells, since it is the first spiking layer of visual signal processing and a lot is known about the anatomical and physiological classes of retinal cells.

Formation of invariant neural responses. At successive stages of sensory signal processing, neurons become increasingly less responsive to noise ensembles, but continue to respond to natural stimuli. The increasing complexity of features in the stimulus that are most relevant for generating neuron's responses is accompanied by the increasing degree of invariance with respect to certain continuous transformations, such as translation, scaling or rotation in the case of visual neurons. These two factors combined make it difficult to systematically analyze filter characteristics of neurons at the stages beyond the primary visual cortex. The method that I have been working on during the past two years assumes that the number of filters describing the neuron's response is small, and it is difficult to reliably find more than several filters. To analyze responses of a neuron with a substantial degree of tolerance with respect to object position would require finding a large numbers of filters, all of which represent transformed versions of each other. Therefore I want to design a method that would find the main template or filter of the neurons assuming *a priori* that the neural response is invariant with respect to a known continuous symmetry. It is an approximation, of course, but I expect that for neurons at higher stages of signal processing it will be a better approximation than to assume that the overall number of relevant filters is small. The long-term goal will be to apply this invariant version of the method to systematically study feature selectivity of neurons in areas V2, V4, and the inferotemporal cortex.

It is also unknown how the invariant representations are actually being formed in the brain, while still allowing stimuli not related to each other by continuous transformations to be distinguished. One of the current hypotheses is that it involves the integration of responses from neurons that correspond to different values of the group transformation of interest, while simultaneously keeping track of a relative temporal pattern of activation in a group of neurons describing stimuli at the same value of the transformation parameter. For example, in the case of translation within the visual field, the responses of neurons will be summed across all retinotopic positions, while keeping track of the relative timing of neurons of nearby orientations and positions. To verify this hypothesis, I plan to study feature selectivity with respect to different temporal spike sequences of neurons in the primary visual cortex, as they provide input to subsequent areas V2, V4, and the inferotemporal cortex where the invariant object recognition is thought to develop. It would very interesting to see the deviations between filters conditional on a temporal sequence of responses, and a linear combination of filters conditional on single spikes comprising the temporal pattern.

Information-theoretic criterion for classifying neurons in primary visual cortex. Originally two different classes of neurons were observed and defined by Hubel and Wiesel in the primary visual cortex. The cell was termed "simple" if light intensities could be linearly combined across space to predict the cell's firing rate, or termed "complex" if otherwise. The currently acceptable criterion to classify a cell as simple or complex is based on the degree of linearity in the cell's responses to moving sinusoidal gratings. However, even in the case of a simple cell, its response could represent a strongly nonlinear function of a single linear combination of light intensities. I would like to know if cells could be separated into simple and complex according to how well a single linear combination of light intensities can predict the cell's responses, where "how well" is quantified in information-theoretic terms. Such a classification would not depend on the use of moving gratings, would more closely capture the classic qualitative definition of Hubel and Wiesel, and would not be confused by nonlinearities associated with the conversion of input voltages to the cell to its output responses.

Statement of Teaching Interests

I am well versed in and prepared to teach all of the general physics courses at undergraduate and graduate level. I will also enjoy teaching canonical graduate courses such as quantum mechanics, electrodynamics and magnetism, classical mechanics, statistical physics, quantum electrodynamics, as well as a range of specialized condensed matter courses on transport phenomena, magnetism, nonlinear dynamics, application of Green's function to many-body problems. Given my experience in neuroscience, I would be able to teach cross-disciplinary courses emphasizing the techniques in condensed matter theory and statistical physics that are most readily applicable to neurobiological problems and supplementing illustrations from physics with those from biology. Having worked at the junction of these disciplines, I am in the unique position of being able to demonstrate the direct usage of physics related problem solving skills and methods directly to areas beyond those traditional in physics. I am computer literate in both Windows and various UNIX platforms and would willingly incorporate education software and technology in general into my lesson plans.

I believe in style of teaching that worked best for me which includes regular quizzes and homeworks in undergraduate courses and regular homeworks in graduate courses; projects to be accomplished at the end of advanced graduate courses, which ideally would lead to publications. I have a commitment to being accessible to students as much as possible given my obligations to research and preparatory work for teaching, since I have found myself that personal consultations by professors were most helpful.

I have been a teaching assistant for undergraduate courses and gave substitution lectures in a graduate course on quantum mechanics. I have also supervised a high-school student through "High-School Honors Science Program" at Michigan State University. The student, David Farber, has been selected for this project among the semi-finalists in the 58th Intel Science Talent Search competition.