



College of Engineering

**5th Annual BME
Symposium in Quantitative
Biology and Physiology**

Friday, January 16, 2009
School of Management Auditorium



Time	Presenter	Presentation Title
1:00pm	BME Chair Solomon Eisenberg	<i>Opening Remarks</i>
1:10pm	Corin Williams	<i>Altered structure across multiple length scales can explain changes in tissue-level mechanical function in decellularized rabbit carotid arteries</i>
1:30pm	Patrick Allen	<i>Using human vascular progenitor cells to create engineered microvascular networks</i>
1:50pm	Todd Jennings	<i>An improved inferior colliculus cell model for interaural time difference analysis</i>
2:10pm	Rapeechai Navawongse	<i>Responses of the dorsal cochlear nucleus in awake gerbil</i>
2:30pm		<i>Break and Snacks</i>
3:00pm	Keynote J. Anthony Movshon	<i>Brain mechanisms of visual motion perception</i>
4:30pm	Finnegan Calabro	<i>Depth segmentation during motion perception: psychophysics and computational physiology</i>
4:50pm	Kyle Lillis	<i>Two-photon imaging of cell-type specific firing patterns and neuronal network correlations during epileptiform activity in hippocampal slices</i>
5:10pm	BME Chair Solomon Eisenberg	<i>Closing Remarks</i>

Corin Williams

Altered structure across multiple length scales can explain changes in tissue-level mechanical function in decellularized rabbit carotid arteries

1:10pm

Recently, major achievements in creating decellularized tissue scaffolds have drawn considerable attention to decellularization as a promising approach for tissue engineering. Although decellularized tissues are expected to have mechanical strength and structure similar to their corresponding native tissues, numerous studies have shown that mechanical properties change after decellularization. In this study, we investigated changes in tissue structure across multiple length scales in order to determine the relationship to altered mechanical behavior at the tissue level using decellularized rabbit carotid arteries as a model system. By histology, native and decellularized arteries appeared morphologically similar; however, uniaxial tests and opening angle measurements revealed that decellularized arteries had significantly increased stiffness, decreased extensibility, and decreased residual stress compared with native arteries. Transmission electron microscopy showed that proteoglycans (PG) were preserved after decellularization, but there was loss of PG density and increased spacing between collagen fibrils. Scanning electron microscopy showed that collagen in the adventitia of decellularized arteries was less crimped compared to native. Finally, small angle light scattering revealed that fibers had increased mobility and that structural integrity was compromised in decellularized arteries, likely due to increased porosity and disrupted ECM network interactions that occurred with the removal of cells. Together, these structural changes can explain altered mechanical behavior in decellularized arteries. Further studies are warranted to determine the specific effects of different decellularization methods on structure-function relationships in decellularized arteries, and will be valuable for predicting and improving the performance of decellularized scaffolds used as vascular grafts.

Patrick Allen

Using human vascular progenitor cells to create engineered microvascular networks

1:30pm

The field of tissue engineering (TE) strives to create various artificial organs for therapeutic purposes. By necessity, such organs will be large and metabolically demanding, yet the length scale of oxygen diffusion through tissues is measured in fractions of a millimeter. To address this challenge, we have developed a method of tissue vascularization using human endothelial progenitor cells (EPCs) and mesenchymal progenitor cells (MPCs) to form robust microvascular networks *in vivo*. In this method, EPCs from blood and MPCs from bone marrow are suspended together in a solubilized ECM material, Matrigel, then subcutaneously injected into immunosuppressed mice. Within seven days, these cells form blood-perfused vessel networks composed of EPCs, many with MPCs associated on their abluminal surface as pericytes. Because future TE applications will require vascularization in a variety of matrix materials, we tested whether EPCs and MPCs could form a vessel network in type I collagen, fibrin, and an engineered peptide hydrogel, PuraMatrix. We found that 1) perfused blood vessels develop in all three types of ECM in 7 days or less, and 2) vascular density differed in the various matrices, and in the case of collagen could be further modulated by varying protein concentration; vascular density was maximized in 5 mg/mL collagen gels. This suggests the possibility of tailoring the vascular supply to the requirements of a given TE application. To explore the role of matrix physical properties on *in vivo* vascularization, rheological properties of collagen, fibrin, and Matrigel were evaluated. Among the different matrices, compliance and elasticity varied widely, yet EPCs and MPCs were capable of vascularizing matrices having dissimilar properties. We propose that progenitor cell-mediated vascularization is a versatile enabling technology which can overcome the limits of oxygen diffusion to facilitate development of metabolically demanding, dynamic, and functional organs.

Todd Jennings

An improved inferior colliculus cell model for interaural time difference analysis

1:50pm

The inferior colliculus (IC) is a key structure in the auditory brainstem. This project focuses on IC processing of interaural time difference (ITD), an important sound localization cue to which many types of cells in the IC show sensitivity. To better understand this processing, a versatile, physiologically-based IC cell model was developed. Specifically, the model includes both neuron membrane properties and a structural description of neural interconnections. The inputs to the IC model incorporate inputs from models of lower-level neurons that are sensitive to ITD, namely the medial superior olive (MSO) and the lateral superior olive (LSO), as well as monaural inputs from a cochlear nucleus (CN) model. Various parameters of the model neurons were varied systematically and their impact on the IC model's response was determined and compared.

Rapeechai Navawongse

Responses of the dorsal cochlear nucleus in awake gerbil

2:10pm

Most dorsal cochlear nucleus (DCN) units to date have been recorded from either anesthetized or decerebrate preparations instead of awake preparations because of technical difficulties. There are, however, drawbacks in these preparation techniques. The neural activity was suppressed by anesthesia. Decerebration cuts off feedback pathways from rostral auditory and possibly somatosensory centers to the DCN. These drawbacks bring up a question about the validity of the recording obtained from these preparations. Our experiment in the awake gerbils ensures that the feedback pathways intact and gerbils are closest to a natural state possible. By combining techniques of survival surgery, conditioning, and restraining, we could record the responses of DCN units in the awake gerbils. We investigated response maps (RMs) and post-stimulus time histograms (PSTHs). Some aspects of the units' responses were compared to those from previous experiments in anesthetized and decerebrate gerbil preparations. Of 102 units, we found all the RM types that have been observed in decerebrate gerbil, except type IV units. Type III units were still the most common recorded gerbil DCN. We found, however, that the spontaneous rates of the units in the awake gerbils were lower compared with those in decerebrate gerbils. Other properties such as thresholds to best frequency tones and tunings of RMs showed no significant differences in results from awake and decerebrate gerbil preparations. All four complex-spiking units recorded in the awake gerbils responded strongly to the sound, and their best frequency can be clearly located. We speculate that DCN neurons are more inhibited in awake gerbils in comparison to decerebrate gerbils.

J. Anthony Movshon

**Professor of Neural Science and Psychology,
New York University**

Brain mechanisms of visual motion perception

3:00pm

Practically everything of interest in the world moves, and even the retinal images of stationary objects move because the eyes are never entirely still. It is therefore not a surprise that the mammalian visual system has evolved a pathway that seems to be devoted to processing visual motion information. In monkeys, neurons in area MT (V5) of the extrastriate visual cortex are all direction-selective, and signal the true motion of complex visual patterns, a response pattern not seen in earlier visual areas. For this and other reasons, MT is thought to have a special role in visual motion processing. Surprisingly, this complex neuronal behavior can be accurately captured by a linear feed-forward model that operates on the outputs of nonlinear directionally-selective V1 cells. This model reveals that the complex response properties of MT cells do not result only from the action of circuits in MT, but depend critically on computations that take place in earlier visual areas such as V1. This suggests that a relatively simple and experimentally tractable architecture may account for the complex transformations of visual information that take place beyond the primary visual cortex, but that evaluating this kind of architecture requires a good understanding of both cortical networks and their inputs. An incidental finding arising from tests of this model suggests, unexpectedly, that despite its central role in visual motion processing, there are important situations in which MT does not contribute to our experience of visual motion.

Finnegan Calabro

Depth segmentation during motion perception: psychophysics and computational physiology

4:30pm

We tested normal observers with a motion discrimination task in which signal and noise dots were presented with different binocular disparities giving the appearance of two planes in depth. By varying the depth separation between the two planes, we found that observers were more impaired in the presence of near-disparity noise than far-disparity noise. Two control experiments suggested that the near-far differences could not be accounted for by attention or surface completion processes. Therefore, we sought an explanation at the physiological hardware level, and developed a physiologically constrained model of neurons in the middle temporal area (MT)—a cortical area known to significantly contribute to motion processing. Results of simulations with the model showed that when population anisotropies, like those reported by DeAngelis et al (2003), are included, the model predicts the near-far disparity skew we observed in the human psychophysical task. We will show that our psychophysical results can be explained by the model, and suggest that disparity tuning properties of MT are sufficient for producing depth segmentation of the motion signals.

Kyle Lillis

Two-photon imaging of cell-type specific firing patterns and neuronal network correlations during epileptiform activity in hippocampal slices.

4:50pm

A recently developed laser-scanning strategy allows the simultaneous measurement from many neurons distributed across a large area with high spatial and temporal resolution. Here we use this technique, Targeted Path Scanning (TPS), in conjunction with two-photon excitation of bath-applied, calcium-sensitive dyes, Calcium Green-1 AM or Indo-1 AM, to image epileptiform activity in the hippocampal formation. With TPS, user-selected neurons separated by a distance of $>2\text{mm}$ could be sampled at rates exceeding 100Hz without sacrificing single cell resolution. In this study, TPS was employed to record up to four minutes of 4-AP-induced epileptiform activity. Dozens of cells in the entorhinal cortex (EC) and CA1 were sampled at a rate of 30-50 Hz. The resulting data provided an independent calcium signal for each cell. GAD67-GFP mice were used in these experiments to permit visual discrimination of a subset of inhibitory neurons. To better understand the role these cells play in neuronal network dynamics, multidimensional correlation analyses were performed. Cross-correlations were calculated between calcium signals recorded from each pair of cells during seizure-like events (SLEs) and used to establish graph representations of the data. In these graphs, each cell was represented as a node, and edges were drawn between sufficiently coupled pairs of nodes (i.e., strongly correlated pairs of cells). To analyze the complicated topological properties of the graphs determined during SLE, techniques from network analysis were implemented. Two measures of network connectivity were calculated for each node: in-degree, the sum of correlations for which other cells lead the node (as determined by peak correlation); and out-degree, the sum of correlations for which the node leads other cells. These statistics provide a means to determine which cells, or populations of cells, are “leading” activity in the neural circuit being imaged. Preliminary results show that inhibitory (GAD67-GFP+) neurons tend to strongly lead the other cells just before the end of SLEs, suggesting that populations of interneurons play a role in seizure termination.

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