Michael P. Sceniak, Ph.D.
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Feb. 25, 2012

Dear Faculty Search Committee,

I am writing to apply for the recently advertised faculty position in your department.

Currently I am a Senior Research Associate in the department of pharmacology at Case Western Reserve University Medical Center. My work here focuses on synaptic physiology of excitatory and inhibitory neurons of the visual cortex. Prior to my move to Case Western Reserve University I was a postdoctoral fellow in the Stanford University Medical Center, Department of Anesthesia. I received my doctoral degree from New York University's Center for Neural Science under the guidance of Robert Shapley. I received a B.S.Eng degree from Northwestern University, School of Engineering. As a graduate student and postdoc I have studied the visual system at the systems level both *in vivo* and *in vitro*, as well as through human psychophysics.

My primary research interest is the micro-circuitry of the visual cortex. I am interested in pursuing this larger goal at the synaptic physiological, and intrinsic cellular mechanistic level. In addition, my work aims to address the functional circuitry and computation interactions that lead to cortical information processing. My training in biomedical engineering as an undergraduate student and neural science as a graduate student has prepared me to explore these issues from the cellular to the psychophysical level. The postdoctoral training that I have received at Stanford University has allowed me to expand my range of techniques to include whole-cell patch clamp recording *in vitro*, *in vivo* pharmacological manipulations, and single cell labeling *in vitro* and *in vivo*.

My training has prepared me well to lead a productive research group. In my current position, I am working independently and have designed and assembled the experimental system from the ground up, including the linux-based dynamic clamp system. I have the technical knowledge and quantitative background required to carry out the experiments that I am proposing. During my postdoctoral experiences I independently introduced new experimental techniques and approaches and have developed novel analysis and protocols. These are necessary skills to establish an independent research program. I have been able to closely observe and participate in the establishment of new labs from their earliest stages. Importantly, during my training, I have gained invaluable experience with mentoring students and managing and coordinating the work of fellow researchers.

I hope that you will consider my application for your job opening. My research goals complement those already established at your department, while adding a new perspective in the study of systems neurophysiology. Dr. Robert M. Shapley, Dr. Michael J. Hawken, Dr. M. Bruce MacIver and Dr. Shasta Sabo will serve as primary references. Their contact information, my curriculum vitae and a summary of my current and future research goals are attached. Thank you for your time and consideration.

Sincerely,

Michael P. Sceniak

Brief Research Statement —Michael P. Sceniak

The overall goal of my research plan is to determine the circuitry and cellular mechanisms that mediate visual information processing. Specifically, I am interested in synaptic integration and the effects of the excitatory (E) to inhibitory (I) balance. It has been shown that the balance between E and I is important in maintaining network excitability. EI interactions have also been shown to be essential to normal receptive field formation. Treatment of visual developmental disorders, such as amblyopia, and prolonged loss of vision will require an understanding of how EI balance affects neuronal function. Understanding the effects of EI interaction for visual cortical function serves as a model for cortical function in general. Alterations of the cortical EI balance have been linked to disease states such as epilepsy, schizophrenia and autism. Therefore, knowledge of EI interactions has widespread importance in neuroscience and medicine.

Synaptic background noise has been shown to modulate the firing rate properties of neocortical neurons, and the degree of modulation depends on the balance of excitation to inhibition. The role of EI temporal statistical interactions in firing rate modulation from background synaptic activity has not been explored. My hypothesis is that neurons are sensitive not only to the amplitudes of synaptic E and I but also the temporal interactions of E and I which make up the background synaptic activity. This hypothesis will be tested using whole-cell patch-clamp recordings and the dynamic clamp technique *in vitro*.

In addition, the effects of EI balance on EPSP to spike (E-S) encoding will be examined. The E-S transformation is the relationship between the probability of firing an action potential to the EPSP amplitude evoked through extracellular stimulation. The dynamic-clamp technique will be used to determine spike encoding mechanisms in response to simulated synaptic inputs, while the E-S transformation is a measure of synaptic modulation driving spikes. The effects of EI balance on the E-S transformation will be explored by altering the EI balance using the dynamic-clamp system. Synaptic inhibition will be blocked and recreated electronically through a dynamic clamp model.

Estimates of both spike encoding and E-S transformation will be performed *in vivo* as well. Whole-cell patch clamp recordings will be combined with extracellular electrical stimulation in order to determine the effects of synaptic activity driven by natural inputs in the intact system. Network activity will be driven through visual stimulation in order to determine the modulatory effects on spike encoding and E-S transformation. The dynamic-clamp will also be utilized in vivo in order to determine the effects of shift the EI balance on both spike encoding and E-S transformation.

Curriculum Vitae
Michael P. Sceniak

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Education

1994-2000	Ph.D. New York University Center for Neural Science. Advisors: Robert Shapley and Michael Hawken.
1990-1994	BS Eng from Northwestern University, with a major in Biomedical Engineering

Awards

2004-2007	Stanford University Anesthesia Department Fellowship
2005	Anesthesia Department Research Award, Stanford University Medical Center, Dept. of Anesthesia
2001-2003	Ruth L. Kirschstein National Research Service Award Fellowship
2000-2001	Hoffman Foundation Fellowship, Salk Institute
1998	NYU, Deans's Travel Award

Positions

2007-present	Senior Research Associate, Dept. of Pharmacology, Case Western Reserve University.
2004-2007	Postdoctoral fellow in the laboratory of M. Bruce MacIver at Stanford University School of Medicine, Department of Anesthesia.
2001-2003	Postdoctoral research associate in the laboratory of Marty Usrey at the University of California, Davis.
2000-2001	Visiting postdoctoral fellow in the laboratory of Edward M. Callaway at the Salk Institute, La Jolla, CA.
1994-2000	Doctoral research under the guidance of Prof. Robert Shapley and Michael J. Hawken at the Center for Neural Science at New York University. Dissertation: Spatial summation and surround suppression in primate V1 neurons: contrast effects.
1992-1994	Undergraduate research in the laboratory of Prof. David Ferster, Northwestern University.

Teaching Experience

2010	(EBME 328) Case Western Reserve University, Biomedical Engineering Research Methods
2001-present	Mentoring graduate students and technicians in laboratory procedures and scientific project design.
1995,1997	Teaching Assistant for Lab in Neural Science I, graduate level laboratory course on neuroanatomy and biophysics.

Scientific Community Activities

2011	Reviewer for Journal of Neurophysiology, Experimental Brain Research and Bio Essays
2010	Reviewer for Journal of Neurophysiology and Experimental Brain Research
2008	Invited speaker, Case Western Reserve University, Dept. Biomedical Engineering
2007	Reviewer for Medical Research Council, Council's Triage: Neurosciences and Mental Health Board (t-NMHB), United Kingdom
2006	Reviewer for Journal of Neurophysiology, Anesthesiology and Journal of Neuroscience
2006	Grant reviewer for NIH SAT study section.

2004 Invited speaker, Northwestern University, Dept. of Physiology

2004 Invited speaker, Stanford University Medical Center, Dept. of Neurology

2003 Grant reviewer for National Science Foundation Learning Information Systems (LIS).

2001 Invited Speaker at Smith Kettlewell Eye Research Institute.

1998 ARVO 1998, Oral Presentation: Michael P. Sceniak, Dario L. Ringach, Michael J. Hawken and Robert Shapley. Spatial Summation in Macaque V1 Neurons Depends on Stimulus Contrast.

1998 Society for Neuroscience 1998, Oral Presentation: Michael P. Sceniak, Dario L. Ringach, Michael J. Hawken and Robert Shapley. Contrast-Dependent Area Summation in Macaque V1 Neurons.

Publications

Sceniak, M.P., Berry C.T. and Sabo S.L. (2012). Facilitation of neocortical presynaptic terminal development by NMDA receptor activation. Neural Dev. Feb. 16; 7(1):8. Epub

Sceniak, M.P. and Sabo SL (2010). Modulation of firing rate by background synaptic noise statistics in rat visual cortical neurons. J Neurophysiol. Nov; 104(5):2792-805. Epub 2010 Aug 25.

Sceniak, M.P. and MacIver M.B. (2008) Slow GABA(A) mediated synaptic transmission in rat primary visual cortex. *BMC Neurosci*. Jan 16; 9:8.

Sabo, S.L. and **Sceniak M.P.** (2006) SOM diversity in the inhibitory population. *J Neurosci*. Jul 19;26(29):7545-6 (review).

Sceniak, M.P. Chatterjee, S. and Callaway, E.M. (2006) VisualSpatial Summation in Macaque Geniculocortical Afferents. *J Neurophysiol*. Dec; 96(6): 3474-84. Epub 2006 Aug 23.

Sceniak, M.P. and MacIver M.B. (2006) Anesthesia *in silico*. *Anesthesiology*. Mar;104(3):400-2.

Sceniak, M.P. and MacIver, M.B., (2006) Cellular actions of urethane on rat visual cortical neurons *in vitro*. *J Neurophysiol*. Jun; 95(6): 3865-74. Epub 2006 Mar 1.

Usrey W.M., **Sceniak, M.P.** and Chapman, B. (2003) Receptive Fields and Response Properties of Neurons in Layer 4 of Ferret Visual Cortex. *J. Neurophysiolog*, 89(2):100315.

Sceniak, M.P., Hawken, M.J. and Shapley, R. (2002) Contrast-dependent changes in spatial frequency tuning of Macaque V1 neurons: effects of a changing receptive field size. *J Neurophysiolog*, 88(3):1363-73.

Mareschal, I. **Sceniak, M.P.**, and Shapley, R. (2001). Contextual influences on orientation discrimination: binding local and global cues. *Vision Res* 41(15): 1915-1930.

Hawken, M.J., Shapley R.M., **Sceniak, M.P.,** Ringach DL & Johnson EN (2000) "Contrast gain, Area summation and temporal tuning in the primate visual cortex. In Vision and Attention, ed LR Harris and M Jenkin, Springer-Verlag, NY.

Sceniak, M.P., Hawken, M.J. and Shapley, R. (2001). Visual Spatial Characterization of Macaque V1 Neurons. *J Neurophysiolog* 85(5): 1873-87.

Sceniak, M.P., Ringach, D.L., Hawken, M.J. and Shapley, R. (1999). Contrast's Effect on Spatial Summation by Macaque V1 Neurons. *Nature Neuroscience* 2(8): 733-739.

Abstracts

Patel C.,**Sceniak, M.P.,** Sabo, S.L. (2009) Regulation of excitatory synapse development between cerebral cortical neurons by vesicular release of glutamate. Program No. 609.12/B30. 2009 *Neuroscience Meeting Planner.* Chicago, IL: Society for Neuroscience, 2009. Online.

Sceniak, M.P. and Sabo S.L., (2009) Sensitivity to higher-order statistical properties of excitation and inhibition in rat visual cortical neurons. Program No. 525.1/G9. 2009 *Neuroscience Meeting Planner.* Chicago, IL: Society for Neuroscience, 2009. Online.

Sceniak, M.P. and MacIver M.B., (2007) GABAa slow synaptic responses in rat visual cortex. *Program No. 358.10. Abstract Viewer/Itinerary Planner.* San Diego, CA: Society for Neuroscience, 2007. Online.

Sceniak, M.P. and MacIver M.B., (2006) $GABA_A$ slow synaptic responses in rat visual cortex. *Program No. 730.3*. *Abstract Viewer/Itinerary Planner.* Atlanta, GA: Society for Neuroscience, 2006. Online.

Sceniak, M.P. and MacIver M.B., (2005) Urethane Anesthesia: A Novel and Specific Mechanism Of Action*. Anesthesiology*; 103: A141

Sceniak, M.P., MacIver, M.B., (2005) Cellular actions of urethane on rat primary visual cortical Neurons *In Vitro*. *Program No. 736.8*. *Abstract Viewer/Itinerary Planner.* Washington, DC: Society for Neuroscience.

Sceniak, M.P., and Usrey W.M. (2003). Frequency Dependence of Spike-Rate Encoding in Ferret Primary Visual Cortical Neurons in vitro. *Soc. Neurosci. Abstr*., **29**: 485.15.

Sceniak, M.P., Chatterjee, S., and Callaway, E.M. (2001). Spatial Analysis of Geniculocortical Afferents in Macaque V1. *Soc. Neurosci. Abstr*., **27**: 619.44.

Mareschal, I., **Sceniak, M.P**., Shapley, R. (2000). Contextual influences on orientation judgments. *Invest Ophth Vis Sci. Suppl. S* 41(4): 188B188.

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Sceniak, M.P., Ringach, D.L., Hawken, M.J. and Shapley, R. (1998). Spatial Summation in Macaque V1 Neurons Depends on Stimulus Contrast. *Invest. Opthal. Vis. Sci.,* Suppl. **39**, 1091.

Sceniak, M.P., Ringach, D.L. Hawken, M.J. and Shapley, R. (1998). Contrast-Dependent Area Summation in Macaque V1 Neurons. *Soc. Neurosci. Abstr*., **24**:789.5.

Hawken, M.J., Shapley, R., Ringach, D.L., **Sceniak, M.P**., and Johnson, E.N. (1998). Direction Selective Neurons in Macaque V1: Response as a Function of Temporal Frequency. *Soc. Neurosci. Abstr*., **24**:789.4.

Hawken, M.J., Shapley, R., Ringach, D.L., **Sceniak, M.P**. and Johnson, E.N. (1998). Influence of Temporal Frequency on Direction Selectivity of Macaque V1 Neurons. *Invest. Opthal. Vis. Sci*., Suppl. **39**, 1089.

Hawken, M.J., Shapley, R., Mechler, F.M., Ringach, D.L., **Sceniak, M.P**., and Johnson, E.N. (1997). Temporal Tuning for Color and Luminance in Macaque V1*. Soc. Neurosci. Abstr*. **23**:405.6.

Research Statement —Michael P. Sceniak

The neocortex is the brain region responsible for high level cognition and perception. Understanding the cellular mechanisms and anatomical circuitry that makes up the neocortex is a necessary step to ultimately understanding information processing that gives rise to perception and cognition. As a graduate student I worked on receptive field properties of the visual cortex. During that time I helped expand the view that the neurons in the neocortex are highly dependent on the network state and the connections within the visual cortex. Visual cortical neurons are no longer viewed as passive spatially isolated linear filters. Instead, the properties of the receptive fields of visual cortical neurons depend on the nature of the stimulus as well as the degree of feedback recurrent input within the network. My goal as an independent investigator is to expand on my graduate work as well as my post doctoral work in cellular properties of visual cortical neurons. The goal is to determine how network activity gates individual neuronal responses and what cellular mechanisms are responsible for this response modulation. Ultimately these mechanisms will help us understand cortical processing in normal and disease states such as schizophrenia, autism and drug addiction. Therefore, knowledge of cortical information processing and dendritic integration has widespread importance in neuroscience and medicine.

It has been shown that even *in vitro*, synaptic background noise can modulate the firing rate properties of neocortical neurons, and the degree of modulation depends on the balance of excitation to inhibition. Recently I have demonstrated that the temporal interactions of the background synaptic noise critically influence the degree of synaptic summation and spike encoding. The subthreshold signals embedded within the synaptic background noise that enhance firing rates contain distinct oscillation frequencies consistent with gamma band activity. It has been shown that these signals exist in vivo and have been linked to perceptual linking across the cortical network. Therefore, neurons are sensitive not only to the amplitudes of synaptic E and I but also the temporal interactions of E and I which make up the background synaptic activity. It remains to be studied what other higher order EI interactions affect spike encoding both *in vitro* and *in vivo*.

Much work has been done to show that synapses display plasticity. However, less work has been done to show how this plasticity effects spike encoding. Spiking or action potentials are the primary means of transmitting information through the cortex. Much work still needs to be done to determine EPSP to spike (E-S) encoding throughout the layers of the visual cortex. The E-S transformation is the ratio of the EPSP amplitude evoked through extracellular stimulation to the probability of firing an action potential. The in vitro preparation offers the best preparation in which to study the effects of network activity on E-S transformation. The dynamic-clamp technique can be used to determine spike encoding mechanisms in response to simulated synaptic inputs. The E-S transformation is a measure of synaptic modulation driving spikes. The effects of EI balance on the E-S transformation will be explored by altering the EI balance using the dynamic-clamp system. Synaptic inhibition will be blocked and recreated electronically through a dynamic clamp model. This offers the most controlled environment to probe the intrinsic properties of neocortical circuits. Optogenetic tools will also be used to identify particular cell types and cortical layers.

Ultimately, the activity from natural *in vivo* inputs will be tested in the intact system. Estimates of both spike encoding and E-S transformation will be performed *in vivo*. Whole-cell patch clamp recordings will be combined with extracellular electrical stimulation in order to determine the effects of synaptic activity driven by natural inputs in the intact system. Network activity will be driven through visual stimulation in order to determine the modulatory effects on spike encoding and E-S transformation. The dynamic-clamp will also be utilized *in vivo* in order to determine the effects of shifting the EI balance on both spike encoding and E-S transformation.

Research Plans as an Independent Investigator

As a primary investigator, I plan to use my expertise with *in vivo* recording and intracellular techniques *in vitro* to understand better the microcircuits and biophysical mechanisms that contribute to modulation of response properties of neocortical circuits.

Three general approaches will be employed. Whole-cell patch clamp recordings *in vitro* combined with conductance injections obtained through the dynamic–clamp system. The dynamic-clamp system will be used to simulate synaptic network activity as synaptic conductances that will be injected into neurons in current-clamp mode. In addition, *in vitro* whole cell recordings will be combined with extracellular synaptic stimulation. *In vivo* whole-cell patch-clamp recordings combined with extracellular stimulation will be conducted to investigate the intrinsic response properties of the intact system. Visual stimulation will be paired with *in vivo* recordings to record spiking activity and evoked synaptic response in the presence of natural visually evoked synaptic activity.

Objective 1: Test the hypothesis that EI latency modulates the degree of spike encoding in response to EI background synaptic activity. While it has been shown that background synaptic activity can modulate the firing rate responses of individual neurons, it is not known what role the temporal interactions between excitation and inhibition contribute to firing rate modulation. To address the effects of EI latency on firing response, we will use whole cell patch clamp recording and the dynamic clamp system to systematically alter the EI correlation and the EI delay of simulated synaptic background noise conductances. A stochastic model will be used to simulate E and I synaptic noise activity with independent control of the mean and standard deviation of each component.

Objective 2: To determine the extent to which EI balance modulates the encoding of action potentials initiated from synaptic stimulation. Theoretical modeling studies have shown that excitatory synaptic strength controls E-S threshold while inhibitory synaptic strength alters the E-S threshold and gain. However, it has not been shown how the relative timing of E to I alters the E-S

threshold and gain. In addition, although it has been shown that EI balance affects E-S estimates, actual biological estimates have been limited to control vs. complete block of inhibition. We propose to examine the effects of EI amplitude and temporal interactions using simulated IPSPs through the dynamic clamp system. After pharmacologically blocking ISPS, evoked EPSPs will be pared with simulated IPSPs to estimate the relative contribution of timing and strength to the E-S measure. In Aim 1, we used simulated synaptic noise to determine the EI interactions which effect spike encoding. In this aim, we use direct measures of EPSP to spike induction to determine the effects of EI interactions on the E-S estimate.

Objective 3: Determine the extent to which the EI balance of synaptic activity from visual stimulation *in vivo* modulates spike encoding. In order to determine the effects of background synaptic activity from natural sources of synaptic input, we will measure E-S transfer in visual cortical neurons of anesthetized paralyzed rats. Whole cell patch-clamp recordings combined with extracellular stimulation will be used to determine the EPSP to spike transfer function under visual stimulation. E-S transfer estimates will be compared for conditions with and without visual stimulation, Calculations of the E and I synaptic components will be made based the intracellular voltage records to visual stimulation vs. control. In addition, the dynamic clamp system will be used to inject simulated inhibitory synaptic inputs to determine the effects of EI balance on spiking and receptive field structure *in vivo*.

Background synaptic activity is a global measure of the network activity state carried within the sub-threshold membrane potential. Visual cortical neurons respond not only to the feedforward synaptic inputs, but are also sensitive to the cortical feedback inputs that signal the state of the cortical network. The intrinsic connections of the cortex and the EI balance establish the background synaptic activity. Sensitivity to the statistics of the background synaptic activity is a possible mechanism for altered visual perception in disease states as well.

Teaching Statement — Michael P. Sceniak

A commitment to teaching is an important component to success as a professor. My undergraduate experience at Northwestern University emphasized the importance of a strong understanding of the fundamentals in science and mathematics. Teaching not only benefits the student, but also the professor. As we advance in our investigations of cutting edge science, it is important to be aware of this work as it relates to the big picture of the field. Teaching forces the professor to be aware of different perspectives and more fundamental issues in science.

During my graduate training at New York University's Center for Neural Science, I was a teaching assistant for the laboratory component of the core course in neural science twice. The course ran for one semester and consisted of a section on neuroanatomy, both gross and cellular, as well as a section on biophysics. I assisted the students in learning neuroanatomy by answering questions and designing and administering exams. The course covered human, sheep, cat, monkey and rat neuroanatomy. We also covered basic methods of anatomical preparation including rat perfusion, histology and microscope techniques. The latter portion of the course covered biophysics. During the course I gave lectures and assisted in the experiments. The students were required to perform intracellular recording of leech and frog neurons. I assisted the students in making the preparations and explaining and assisting in the actual recording. This included extensive explanation of the computer controlled data acquisition system.

As a research associate at Case Western, I taught a hands-on biomedical engineering course in biomedical research methods. This course requires me to design a curriculum that is composed of laboratory exercises, quantitative homework sets in electrophysiology, physical chemistry and electronic instrumentation. In addition, the course covers basic data collection and experimental design principles.

My graduate and undergraduate experience has exposed me to subjects ranging from basic science and engineering to advanced subjects in neuroscience and psychology. I feel confident teaching courses ranging from biophysics and neuroanatomy to specialized courses within visual neurophysiology and psychophysics. I also have experience explaining and teaching others computational methods and analysis.

During my time as a graduate student and as a postdoc, I have given many public lectures on my work. I have given talks and poster presentations at the annual meeting for the Society of Neuroscience and the ARVO annual meeting. I was also an invited speaker at the Smith Kettlewell Eye Research Institute and Department of Physiology at Northwestern University. Recently I have given presentations at departmental seminars including the Biomedical Engineering Department at Case Western Reserve University. These experiences have given me exposure to lecturing in front of large audiences, teaching and seminar format lectures.

The success of any academic department ultimately depends both on the quality of its research and the quality of its teaching. As a Professor, I look forward to the challenges and rewards of research and teaching.

Teaching Experience:

2010	Instructor	Biomedical Engineerin (EBME 328) Biomedical Research Methods
2008-2010		Synapse Development and Physiology Journal Club Organizer, Case Western Reserve University Pharmacology Dept.
1995	TA	Neural Science I — laboratory in neuroanatomy and biophysics
1997	TA	Neural Science I — laboratory in neuroanatomy and biophysics

Reference List — Michael P. Sceniak

Robert M. Shapley
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New York, NY 10003
(212) 998-7798
shapely@cns.nyu.edu

Michael J. Hawken
Center for Neural Science
New York University
4 Washington Place, Room 809
New York, NY 10003
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Stanford University Medical Center
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