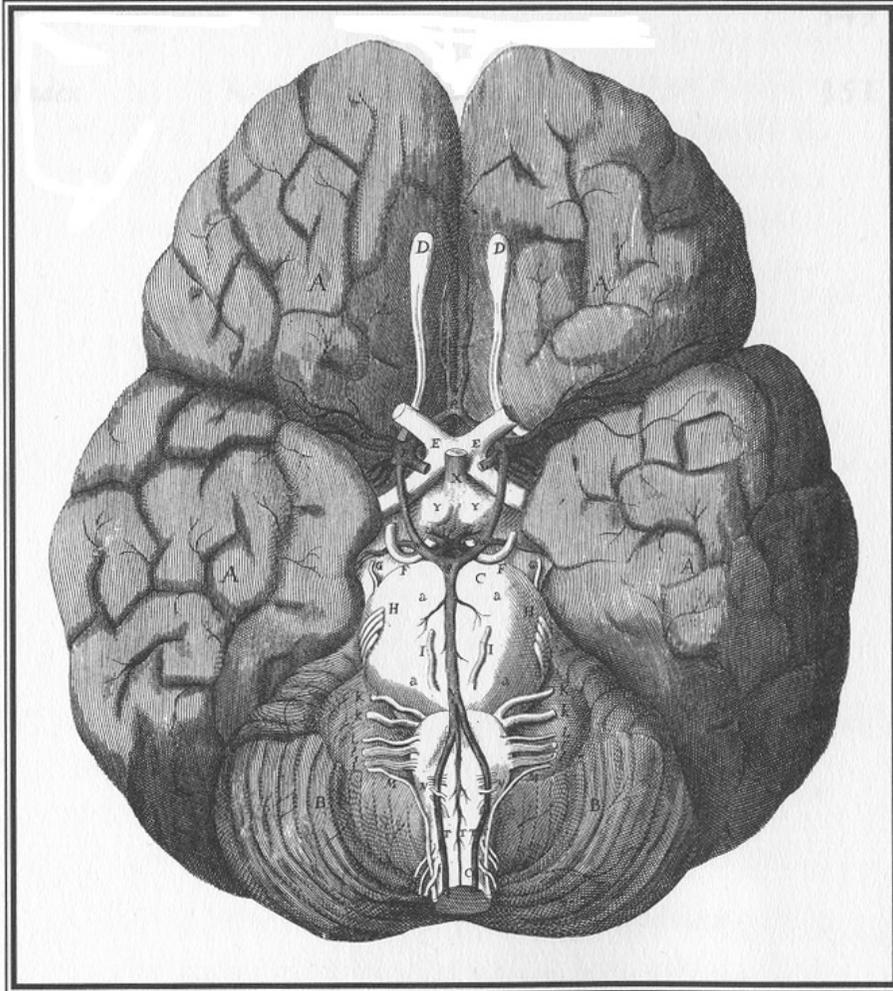


The Interdisciplinary Studies Program in Neuroscience Presents:

The Neuroscience Fall Symposium...

A Tradition of Scientific Discovery



A FULL HUMAN BRAIN, DRAWN BY CHRISTOPHER WREN AND INCLUDED IN
THE ANATOMY OF THE BRAIN AND NERVES.

* from the Soul Made Flesh by Carl Zimmer

The Neurocentric Age of research was begun within the walls of Oxford's Beam Hall, by men like Thomas Willis and Christopher Wren. These presentations show that those traditions of scientific discovery and collaboration continue today at William and Mary.

Keynote Address:

**"Thermoregulation &
Exercise - Heat Stress"**

Speaker:

Michael Sawka, Ph.D.
Thermal & Mountain Medicine Div.
**U.S. Army Research Institute of
Environmental Medicine**

Thursday, November 4th, 2004

University Student Center, Chesapeake A & B

Featuring:

Student Poster Presentations: 2:30 - 3:00pm & 5:00 - 5:30pm

Student Oral Presentations: 3:00 - 3:45pm

Keynote Address: 4:00 - 5:00pm

Also Supported by: The Borgenicht Program for Aging Studies and Exercise Science

Student Symposium Presentations

3:00 – 3:45pm

3:00-3:15pm SPECIFICATION OF GABAERGIC CELLS IN EARLY VERTEBRATE

EMBRYOGENESIS. **Ryan Fame and Margaret Saha.** Department of Biology, The College of William and Mary, Williamsburg, VA 23187-8795.

During embryonic development, regulation of cell differentiation in the zygote may occur through intrinsic cell-lineage fate determination or it may occur through extrinsic cell-cell signaling; I am studying the influence of the latter signaling type on the GABAergic (those neurons that use Gamma aminobutyric acid (GABA) as their neurotransmitter) neural phenotype expression in *Xenopus laevis*. Embryos' presumptive neural tissue can be removed, dissociated in $\text{Ca}^{++}/\text{Mg}^{++}$ -free medium, and dispersed for maturation on cell culture plates to eliminate cell-cell interaction and thus stop the influences of those signals on the differentiating cells. These treatments can be time specific, that is done at different stages in development or they can be spatially specific, that is certain sections of the presumptive neural tissue are plated separately. Using *in situ* hybridization and immunocytochemistry, the presence of either the xGAT1 gene or the GABA molecule itself can be detected. Such manipulations have preliminarily revealed that the number of GABAergic cells decreases as the cell-cell interactions are allowed to continue for longer periods of time, perhaps suggesting that the use of GABA as a neurotransmitter is somewhat of a default state. Studies of the spatial differences have shown that there is differential expression between the anterior, medial, and posterior sections of the neural plate but further studies are required to draw conclusions about the identity of this pattern.

3:15-3:30pm EFFECTS OF FEEDBACK INHIBITION ON RETINOGENICULATE

TRANSMISSION. **Jeffrey R. Groff and Gregory D. Smith.** Department of Applied Science, The College of William and Mary, Williamsburg, VA 23187-8795.

All visual sensory information from the retina passes through the dorsal lateral geniculate nucleus (dLGN) in thalamus on its way to cortex. However, afferents from retinal ganglion cells (RGCs) account for only 10-15% of the synapses on thalamocortical (TC) relay cells in the dLGN (Van Horn et al. 2000). Other sources of dLGN synaptic innervation are layer VI of visual cortex, the reticular (RE) neurons of the perigeniculate nucleus (PGN), local inhibitory interneurons, and subcortical areas. This diversity of synaptic origins suggests that the dLGN may act as a state dependent dynamic filter of visual information rather than as a passive relay. Our research is specifically concerned with the effects of feedback inhibition from RE cells on TC relay cell output. We constructed a minimal TC/RE network where individual neurons are modeled using the integrate fire or burst (IFB) formalism (Smith et al. 2000). The IFB model includes I-T, a low-voltage activated calcium current, in both the TC and RE cells types allowing for state dependent bursting. The network is stimulated with a modulated second-order gamma process representing RGC input. The TC neuron response is gathered, and network throughput properties are studied using temporal frequency analysis. Our results show that modulated RGC input can recruit bursts in TC cells significantly modifying network throughput.

3:30-3:45pm NETWORK PROPERTIES AND RHYTHM GENERATION IN THE RESPIRATORY KERNEL CALLED THE PRE-BÖTZINGER COMPLEX. **John A. Hayes and Christopher A. Del Negro.** Department of Applied Science, The College of William and Mary, Williamsburg, VA 23187-8795.

Breathing originates as a rhythm of neural activity in the brainstem pre-Bötzinger complex, but the neural mechanisms that generate the rhythm remain largely unknown. One leading hypothesis posits that bursting pacemaker neurons generate the inspiratory rhythm for breathing, i.e., the "pacemaker hypothesis". Here we show that the pacemaker hypothesis is incomplete and cannot explain rhythm generation. Instead we use mathematical models and experimental tests of model predictions to show that rhythmically active networks depend critically on (1) the connectivity properties between constituent neurons, (2) neuronal refractoriness (not burst-generation), and (3) sufficient global levels of excitability in the network. We propose that these emergent network properties model respiratory rhythmogenesis in the respiratory pre-Bötzinger complex.

Student Poster Presentations

2:30-3:30pm & 5:00-5:30pm

1. COMPUTATIONAL APPROACHES TO NEUROCHEMISTRY: BIOCHEMICAL STUDIES OF G PROTEIN-COUPLED RECEPTORS VIA SIMULATION AND MODELING. **K. Mendoza, J. Taylor, S. Oakes, and R.A. Coleman.** Department of Chemistry, The College of William and Mary, Williamsburg, VA 23187-8795.

We have established a computational laboratory dedicated to the exploration of G Protein-coupled Receptors (GPCRs) and the metabolism associated with receptor-triggered events. The two neuronal cell types of immediate simulation interest use Gamma-Amino Butyric Acid receptors of type B (GABA_B) and metabotropic Glutamate receptors (mGluRs). These cells are fascinating in their complexity and differences in the many metabolic pathways that may be activated by the docking of a simple ligand to the GPCR. We plan to use these simulation models as an *in silico* workbench environment in which to explore the ramifications of variations in parameters associated with the biochemical activity of the cells. As an outcome, we hope and expect to be able to report findings on emergent properties growing out of these experiments and fully expect to discover findings that are counterintuitive to our present understanding of how these complex systems function. Finally, in the later stages of this research effort, we plan to initiate a research program that studies the pharmacology of these target GPCRs using a physical organic chemistry approach to study ligand-receptor interactions in our simulation environment.

2. MORPHOLOGICAL CHARACTERISTICS OF THERMOSENSITIVE AND TEMPERATURE INSENSITIVE NEURONS IN THE ANTERIOR REGIONS OF THE RAT HYPOTHALAMUS. **Bethany Schaffer, Elizabeth M. Wallis, and John D. Griffin.** Department of Biology, The College of William and Mary, Williamsburg, VA 23187-8795.

Although physiological and anatomical evidence suggests that the ventromedial preoptic area (VMPO) of the hypothalamus is important in the generation of a fever, little is known about the functional morphology of thermally classified neurons in this region. Within the anterior hypothalamus, previous work has shown that warm sensitive neurons have medial-lateral dendritic projections, while temperature insensitive neurons have

dorsal-ventral dendritic projections. We hypothesized that similar differences would be characterized within VMPO. We also hypothesized that some thermally classified neurons in the anterior hypothalamus are GABAergic, suggesting that they provide inhibitory input to other neurons in the thermoregulatory network. Using a tissue slice preparation, whole-cell recordings were made from VMPO neurons. Intracellular perfusion of Lucifer Yellow and Biocytin occurred passively while each neuron was classified as either warm sensitive or temperature insensitive. Tissue slices were then histochemically processed for Biocytin or Glutamic Acid Decarboxylase (GAD). Photo reconstructions were made of each neuron to determine soma location and dendritic morphology or if a neuron was GAD positive. Temperature insensitive neurons in the dorsal VMPO and warm sensitive neurons throughout VMPO showed similar dendritic patterns to thermally classified neurons in other regions of the anterior hypothalamus. However, insensitive neurons in the ventral VMPO showed medial-lateral dendritic projections, suggesting a different functional role for these neurons in thermoregulation and fever. Only temperature insensitive neurons have been identified as GAD positive. (Supported by NSF: IBN-9983624, and in part by a Howard Hughes Medical Institute grant through the Undergraduate Biological Sciences Program to the College of William and Mary.)

3. THE EFFECTS OF LEPTIN ON THE FIRING RATES OF THERMOSENSITIVE AND TEMPERATURE INSENSITIVE NEURONS IN THE ANTERIOR HYPOTHALAMUS. **L.M. Hack, J.L. Wright, and J.D. Griffin.** Department of Biology, The College of William and Mary, Williamsburg, VA 23187-8795.

Leptin, a hormone produced by adipocytes, is found in the circulation at concentrations relative to the amount of body fat and has been shown to reduce feeding behavior through direct effects on the hypothalamus. Evidence also suggests that this response is temperature dependent and that lesions of the hypothalamic preoptic area impair both feeding behavior and thermoregulation. Therefore, we have hypothesized that neurons in the anterior hypothalamus will show a correlation between thermosensitivity and firing rate responses to leptin. Using a hypothalamic tissue slice preparation, neuronal single-unit recordings were made of firing rate activity. Based on the slope of firing rate as a function of temperature, neurons were classified as either warm sensitive or temperature insensitive. Tissue slices were then perfused with the active portion of the leptin hormone (100 nM). Temperature insensitive neurons did not show a correlated response to leptin, with some neurons increasing or decreasing their firing rates, and others showing little or no change in firing rate activity. However, warm sensitive neurons consistently decreased their firing rates in response to leptin. This data suggests that a direct effect of leptin on the activity of warm sensitive neurons in the hypothalamus may be responsible for leptin's ability to influence thermoregulation as well as feeding behavior. (Supported by NSF: IBN-9983624, and in part by a Howard Hughes Medical Institute grant through the Undergraduate Biological Sciences Program to the College of William and Mary.)

4. THE EFFECTS OF CALCITONIN GENE-RELATED PEPTIDE ON THE FIRING RATES OF THERMOSENSITIVE AND TEMPERATURE INSENSITIVE NEURONS IN THE ANTERIOR HYPOTHALAMUS OF THE RAT. **E.M. Deegan, E.R. Grimm, D.C. Braasch, and J.D. Griffin.** Department of Biology, The College of William and Mary, Williamsburg, VA 23187-8795.

For women following the onset of menopause and men during the treatment of prostate cancer, a "hot flash" can become a frequent occurrence. This transient hyperthermic shift in temperature has been linked to calcitonin gene-related peptide (CGRP), which acts peripherally to increase vasodilation and centrally to increase sympathetic activation, including metabolic heat production. Recent studies have demonstrated that these centrally mediated responses may result from CGRP dependent changes in the activity of thermoregulatory neurons. Using a tissue slice preparation, we recorded the extracellular single-unit activity of anterior hypothalamic neurons from the adult male rat, in response to temperature and CGRP (10 nM). Based on the slope of firing rate as a function of temperature, neurons were classified as either warm sensitive ($m > 0.8$

impulses/sec/degree C) or temperature insensitive. The majority of warm sensitive neurons responded to the microdrop application CGRP with a significant decrease in firing rate. While CGRP did not affect the majority of temperature insensitive neurons, responsive neurons showed increases in firing rate. This suggests that both warm sensitive and temperature insensitive neurons in the anterior hypothalamus may play critical and contrasting roles in producing these transient hyperthermic shifts in body temperature. (Supported by NSF: IBN-9983624, The Borgenicht Program for Aging Studies & Exercise, and in part by a Howard Hughes Medical Institute grant through the Undergraduate Biological Sciences Program to the College of William and Mary.)

5. **EFFECTS OF INCREASED OR DECREASED ACTIVITY ON THE NEUROMUSCULAR JUNCTION. Kelly A. Tenny and Michael R. Deschenes.** Department of Kinesiology, The College of William and Mary, Williamsburg, Virginia 23187-8795.

The objective of this study was to directly compare the effects of increased or decreased activity on neuromuscular junction (NMJ) morphology. Twenty-four young (7 wks old) male Sprague-Dawley rats were randomly assigned to one of three treatment groups (N=8/group). Rats assigned to the increased activity group performed treadmill running 5 days per week for 10 weeks. Animals assigned to the decreased activity group were subjected to muscle unloading for 10 wks. Control rats lived freely in their cages for the same 10-week period. At the end of the 10-week intervention, all animals were euthanized before soleus muscles were dissected out and quickly frozen at resting length. To visualize NMJs, 50-um-thick longitudinal muscle sections were stained with rhodamine conjugated bungarotoxin and fluorescein labeled RT97 antibody. Bungarotoxin binds specifically to post-synaptic acetylcholine receptors, and RT97 recognizes pre-synaptic nerve terminals.

Images of NMJs were collected and analyzed with a confocal microscope. One-way ANOVA was used to compare data from the three groups. Results indicate that in both fast- and slow-twitch myofibers, exercise training significantly ($P<0.05$) amplified pre-synaptic nerve terminal branching without altering post-synaptic structure of the NMJ. In contrast, muscle unloading resulted in diminished ($P<0.05$) post-synaptic endplate dimensions without affecting nerve terminal characteristics. These data suggest that although both increased and decreased activity elicited significant synaptic remodeling, the mechanisms involved appear to be activity specific.

6. **NMDA RECEPTOR ANTAGONISTS IMPAIR ATTENTION IN RATS. Lindsay A. Dow, Matthew D. Harrington, Kimberly A. Palmer, Kathryn Henwood, and Joshua A. Burk.** Department of Psychology, The College of William and Mary, Williamsburg, VA 23187-8795.

Hypoactivity of the glutamatergic system may underlie attention deficits thought to contribute to the symptoms of schizophrenia. NMDA receptor antagonists have proven to be a useful model of the changes in the glutamatergic system in this neuropsychiatric disease. The present study assessed the effects of acute administration of a noncompetitive NMDA receptor antagonist, MK-801, on performance in a sustained attention task in rats. Twelve male Long-Evans rats were trained to perform a sustained attention task that involved detection of visual signals (500, 100, or 25 ms illumination of a central panel light) and non-signals (no illumination of the panel light). After reaching asymptotic task performance, rats were administered 0.0 (saline), 0.005, 0.1, or 0.2 mg/kg MK-801 IP in a counterbalanced order prior to task performance. Administration of MK-801 decreased accurate detection of signals and non-signals in a dose-dependent manner. These data suggest that MK-801, at the doses tested, produces a severe decline in performance in this task and that the deficit may extend beyond attention processing. A follow-up study is being conducted to assess whether nicotine administration can attenuate the attention deficits induced by NMDA receptor blockade. (Supported by a Young Investigator Award from NARSAD to JAB and a summer grant from the Howard Hughes Medical Institute to the College of William and Mary.)

7. **ESCALATING AMPHETAMINE TRANSIENTLY INCREASES FALSE ALARMS IN A SUSTAINED ATTENTION TASK IN RATS. Robyn L. Kondrad and Joshua A. Burk.** Department of Psychology, The College of William and Mary, Williamsburg, VA 23187-8795.

Alterations of attention processing are thought to contribute to the positive symptoms in schizophrenia. Sensitization of the mesolimbic dopaminergic system has been hypothesized to underlie many of the cognitive deficits in schizophrenia. The present study tested the effects of administration of an escalating amphetamine regimen (1.0-5.0 mg/kg) in a sustained attention task. Rats were trained to perform a two-lever sustained attention task involving discrimination of brief visual signals and non-signals. Attention performance was assessed following administration of an escalating amphetamine regimen, following challenge amphetamine administration (1.0 mg/kg), and for three days after the challenge session. Finally, a dose-response experiment was conducted to test the appropriateness of the drug dose for the challenge session. Amphetamine-pretreatment increased errors on non-signal trials (an increase in the false alarm rate) following escalating amphetamine administration. Administration of a challenge amphetamine dose did not differentially affect accuracy compared with sessions immediately prior the challenge administration. The latency to press a lever was decreased during and after challenge amphetamine administration. During the final three days of behavioral testing, there were no differences in accuracy between amphetamine-pretreated and saline-pretreated animals. The dose-response study revealed no differences between saline and 1.0 mg/kg amphetamine on any measures of task performance. Doses higher than 1.0 mg/kg amphetamine increased the omission rate. In summary, prior escalating amphetamine administration transiently disrupted attention, increasing incorrect claims for a signal on trials when no signal was presented. The present data support the use of escalating amphetamine regimens to model the attention deficits in schizophrenia. (Supported by a Young Investigator Award from NARSAD to JAB and a summer grant from the Howard Hughes Medical Institute to the College of William and Mary.)

8. **EFFECTS OF ADOLESCENT ADMINISTRATION OF ALCOHOL AND NICOTINE ON TRACE AND DELAY FEAR CONDITIONING IN RATS. R. T. Johnson, E. Yttri, D. Mason, C. Carron, R. Dieckmann, R. C. Barnett, P. S. Hunt, and J. A. Burk.** Dept. of Psychology, College of William & Mary, Williamsburg VA 23187-8795.

The relative scarcity of studies concerning the cognitive consequences of adolescent administration of alcohol and nicotine is surprising given that this age is typically when use of these drugs begins. The present experiments were designed to assess the effects of adolescent alcohol or nicotine on trace and delay fear conditioning. Hippocampal lesions are known to disrupt acquisition of trace, but not delay conditioning, and thus, these tasks were chosen to assess the impact of these drugs on hippocampus-dependent non-spatial learning. In Experiment 1, rats were given binge administration of ethanol, receiving 0, 1.5, 2.5, or 4.5 g/kg/day on PD 28, 30, 32, and 34. Trace conditioning on PD 40 was disrupted by administration of 2.5 and 4.5 g/kg/day while delay conditioning was not affected by any dose. In Experiment 2, rats were assigned to receive access to 10% ethanol or water via drinking tubes from postnatal days (PD) 22-70. There were no differences in trace or delay conditioning as a function of ethanol exposure. In Experiment 3, rats were implanted subcutaneously from PD 22-70 with minipumps that delivered 3.0 mg/kg/day nicotine or saline and another group of rats was not implanted. Preliminary data indicate that, relative to the saline-treated and un-implanted animals, adolescent nicotine administration disrupts trace but not delay conditioning. We conclude that adolescent administration of alcohol or nicotine can impair hippocampus-dependent task performance, but the parameters of the administration regimen and age of testing may be factors that contribute to the presence of a deficit. (Research supported by the Virginia Youth Tobacco Project and NIAAA.)

9. **NEONATAL CHOLINE SUPPLEMENTATION PROMOTES THE DEVELOPMENT OF HIPPOCAMPAL-DEPENDENT MEMORY.** **Alison F. Wagner, Nicole A. Thomas, and Pamela S. Hunt.** Department of Psychology, The College of William and Mary, Williamsburg, VA 23187-8795.

Choline is a constituent of several biological systems and processes, including being the precursor to the neurotransmitter acetylcholine. Several recent studies have shown that choline supplementation during neonatal development can promote memory functions that are subserved by acetylcholine and can reduce age-dependent memory decline. Hippocampal-dependent memory tasks that rely on the septohippocampal cholinergic system seem especially sensitive to early choline administration. In this experiment, we targeted the potential use of choline to promote the development of memory early in life. One hippocampus-dependent memory task that exhibits a relatively late ontogenetic emergence is trace conditioning. In a typical trace conditioning procedure, an unconditioned stimulus (footshock) is presented some time after the offset of a conditioned stimulus (a flashing light), and learning is assessed by measuring the change in activity elicited by the light (called freezing behavior). Damage, inactivation, immaturity or aging of the hippocampus all result in poor trace conditioned performance. In this experiment, neonatal rats were administered choline chloride or saline subcutaneously from P4 through P20. On P25, an age that normally displays poor trace conditioning, pups were given 10 pairings of a flashing light with footshock, and the gap between offset of the light and onset of the shock was 10 sec. Subjects were tested on P26 for freezing to the light. Results indicate that pups injected with choline showed a significantly higher level of light-elicited freezing than those that were injected with saline, indicating improved learning. These results extend the research implicating early choline supplementation on the development of function of the hippocampal memory system. (Research supported by NIAAA.)

10. **THE EFFECT OF FEEDBACK INHIBITION IN NETWORK SIMULATIONS OF RETINOGENICULATE TRANSMISSION.** **Marco Huertas and Gregory D. Smith.** Department of Applied Science, The College of William and Mary, Williamsburg, VA 23187-8795.

The effect of feedback inhibition from thalamic reticular (RE) cells on retinogeniculate transmission by thalamocortical (TC) neurons of the dLGN is analyzed using a minimal integrate-and-fire-or-burst (IFB) network model. The network includes spatially non-local synaptic coupling, alpha-function postsynaptic conductances, and a gamma process representation of spontaneous or visually driven retinal ganglion cell activity. Potassium leakage conductances control the neuromodulatory state of the network and can eliminate rhythmic bursting in the presence of spontaneous input (i.e. wake the network). During oscillatory full-field stimulation the response of the aroused network depends on average input rate, contrast level, and temporal frequency of modulation.

11. **ANALYSIS OF THE EFFECT OF RESIDUAL CALCIUM ON THE GATING OF CALCIUM-REGULATED CALCIUM CHANNELS.** **Borbala Mazzag, Christopher J. Tignanelli, and Gregory D. Smith.** Department of Applied Science, The College of William and Mary, Williamsburg, VA 23187-8795.

Single channel models of type 1 and 2 IP₃ receptors (IP₃R_s) often assume that Ca²⁺-dependent transitions are mediated by background [Ca²⁺] as opposed to a dynamic localized Ca²⁺ domain. We study the effect of so-called 'residual calcium' on the stochastic gating of minimal (two-state) and realistic (De Young-Keizer-like) IP₃R models when coupled to an ordinary differential equation (ODE) describing a dynamic Ca²⁺ domain. Using both Monte-Carlo simulation and numerical solution of Fokker-Planck-type equation, we show that the equilibrium open probability (P_{open}) of such models depends on the time constant for Ca²⁺ domain formation and collapse (tau_{domain}) compared to the dwell times for the various Ca²⁺ channel states (tau_{channel}). For

Ca²⁺-activated channels (type 2), P_{open} increases as tau_{domain} becomes large compared to tau_{channel}, that is, residual Ca²⁺ from previous openings activates the channel. For channels involving Ca²⁺-inactivation, we find that P_{open} also increases when tau_{domain} > tau_{channel} and the comparatively slower formation of the Ca²⁺-domain results in less domain Ca²⁺-mediated inactivation. The P_{open} of an extended DeYoung-Keizer-like IP3R model that includes both domain Ca²⁺-mediated activation and inactivation is also elevated by residual Ca²⁺ when tau_{domain} > tau_{channel}. We show how our numerical approach can be used for any value of tau_{domain} and arbitrarily complex channel models and further provide analytical estimates for P_{open} in the tau_{domain} << tau_{channel} and tau_{domain} >> tau_{channel} limits. Our results do not change qualitatively when the ODE for a dynamic Ca²⁺ domain is replaced by a partial differential equation for the buffered diffusion of intercellular Ca²⁺. These results suggest that both type 1 and type 2 IP3Rs will exhibit elevated P_{open} when endogenous or exogenous Ca²⁺ buffers lead to formation and collapse of the localized Ca²⁺ domain that is slow compared to channel gating.

12. DIRECT CALCULATION OF PUFF STATISTICS FROM STOCHASTIC AUTOMATA NETWORK MODELS OF INSTANTANEOUSLY COUPLED INTRACELLULAR CALCIUM CHANNELS. **Jie Zhang, Vien D. Nguyen, and Gregory D. Smith.** Department of Applied Science, The College of William and Mary, Williamsburg, VA 23187-8795.

Although there is consensus that Ca²⁺ puffs arise from the cooperative action of multiple IP3 receptors (IP3Rs), the precise relationship between single-channel kinetics and the collective phenomena of stochastic Ca²⁺ excitability is not well understood. Here we present a memory-efficient method by which mathematical models for IP3-sensitive Ca²⁺ release sites can be derived from Markov models of IP3R single-channel gating that include Ca²⁺ activation (IP3R-2 like), Ca²⁺ inactivation, or both (IP3R-1 like). Such models are essentially stochastic automata networks (SANs) that involve a large number of so-called 'functional transitions,' that is, the transition probabilities of the infinitesimal generator matrix (or Q-matrix) of one automata (i.e., an individual channel) may depend on the local [Ca²⁺] and thus the state of the other channels. Simulation and analysis of the SAN descriptors that represent homogeneous clusters of type 1 and 2 IP3Rs show that 1) Ca²⁺-inactivation is not a requirement for Ca²⁺ puffs; 2) the bell-shaped equilibrium open probability curve of the IP3R-1 does not necessarily lead to release site activity that is biphasically related to release site density; 3) Ca²⁺ buffers can either increase or decrease the stochastic excitability of a release site. In addition to these equilibrium open probability results, we present hitting time calculations that directly calculate various puff statistics (e.g., puff duration and inter-puff-interval) from the SAN descriptor. Beginning with a small number of DeYoung-Keizer-like IP3R-1 models, we find that simulated puff duration is shorter when the affinity of an IP3 receptor agonist is higher. This is in agreement with experimental observations of the kinetics of Ca²⁺ puffs evoked in *Xenopus* oocytes by different IP3R agonists (Marchant and Parker, *Biochem. J.*, 334, 505-509, 1998).

Keynote Address:

4:00-5:00pm

Thermoregulation & Exercise – Heat Stress

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Dr. Michael N. Sawka is Chief, Thermal and Mountain Medicine Division at the U.S. Army Research Institute of Environmental Medicine. Dr. Sawka's research interests are environmental (heat, cold, altitude) and exercise physiology, fluid / electrolyte balance and rehabilitation medicine. He has published over 280 full-length scientific papers as well as a graduate textbook on environmental physiology and a graduate textbook on exercise physiology. He has presented over 60 invited Symposia and Keynote Lectures at scientific meetings. Dr. Sawka is a member of several editorial boards including *American Journal of Physiology*, *Journal of Applied Physiology*, *Medicine and Science in Sports and Exercise*, *International Journal of Sports Medicine*. He served on many scientific panels and professional committees such as those for the Institute of Medicine, National Academy of Sciences; National Institutes of Health; US Anti-Doping Agency; multiple Olympic Scientific Committees. He is active within the American Physiological Society and the American College of Sports Medicine. He is frequently cited and interviewed by the press.

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