BIOENGINEERING
Spring 2021 Seminar

Date: **Thursday, April 15, 2021**
Time: **12:00 pm - 1:00pm**
Location: **Virtual**
Join Zoom Meeting
https://gmu.zoom.us/j/98805494005?pwd=M1A2R1BaSEdqa2hhOUltTE5YeWxtdz09

Meeting ID: 988 0549 4005 Passcode: 454698

Carmen Canavier, Ph.D.

Biography: Dr. Canavier is a theoretical and computational neuroscientist who is interested in nonlinear neuronal dynamics and synchronization of pulse coupled oscillators. She works on delineating the biophysical basis for diversity in subpopulations of midbrain dopamine neurons, on mechanisms of hippocampal gamma oscillations, and on neuromodulation of intrinsic dynamics. She received her PhD in electrical and computer engineering from Rice University and did her postdoctoral research at the University of Texas Health Sciences Center at Houston. She is the Mullins Professor and Interim Head of the Department of Cell Biology and Anatomy at LSU Health Sciences Center in New Orleans.

Title: Responses of CA1 pyramidal neurons and midbrain dopamine neurons to sustained depolarization

Abstract: Area CA1 of the hippocampus is thought to play a key role in learning and memory, specifically episodic memories, sequential order and trace conditioning. In behaving rodents, CA1 pyramidal neurons receive spatially-tuned depolarizing synaptic input while traversing a specific location within an environment called its place. Midbrain dopamine neurons participate in reinforcement learning, and bursts of action potentials riding a depolarizing wave of synaptic input signal rewards and reward expectation. Interestingly, slice electrophysiology *in vitro* shows that both types of cells exhibit a pronounced reduction in firing rate (adaptation) and even cessation of firing during sustained depolarization. In response to a temporally symmetric current ramp, the firing rate adapts so that the neuron fires substantially less on the down ramp compared to the up ramp. Such adaptation is likely to affect the dependence of the firing rate of CA1 neurons on position within the place field. Our experiments in vitro show that adaptation in these neurons in response to a symmetric current ramp is more pronounced in the apical dendrite than in the soma. Our simulations of a biophysically and morphologically detailed pyramidal neuron were calibrated using data from the literature that shows slow inactivation of the sodium current increases with distance along the apical trunk. A five state Markov model of NaV1.6 suggests that slow inactivation of this channel is responsible for this adaptation, consistent with our experimental data showing that the SK, M and ERG potassium channels are not major contributors to this adaptation. Our experimental data shows that the cholinergic agonist CCh reverses the adaptation and produces acceleration of the firing rate on the down ramp instead. Both FFA and a specific TRPM blocker largely occlude the effects of CCh. We implemented a detailed model of calcium handling including calcium-induced calcium release co-localized with the TRPM channel, and simulate the effect of CCh primarily via an increase in IP3 in order to capture the acceleration on the down ramp. We also present recent data showing the differential contribution of slow inactivation in two subpopulations of midbrain dopamine neurons accounts for their different dynamic range, as assessed by their responses to similar depolarizing ramps. These results suggest slow inactivation of the sodium channel is a general mechanism for adaptation.