The most important issues in contemporary biology are interdisciplinary, spanning multiple levels of analysis from genes and molecules to the complex properties of networks. Nowhere is the interdisciplinary nature of modern-day life sciences more relevant than in neuroscience. Brain function underlies the vast repertoire of human behaviors and dysfunction of the brain and central nervous system causes many of society's most serious health problems.

I am Professor Christopher A. Del Negro and my Systems Neuroscience laboratory in the Department of Applied Science provides a unique environment for neuroscience research and training at the graduate and postdoctoral level. My team and I have assembled state-of-the-art experimental workstations for intracellular and patch-clamp electrophysiology combined with in vitro live-cell videomicroscopy and fluorescence imaging. We also have a vigorous computational neuroscience branch; we support parallel computing facilities for modeling and simulation. Our strategy to elucidate new knowledge in neuroscience blends theory and experiment: we use modeling to generate testable predictions, which are systematically evaluated via hypothesis-driven experimental studies.

The masters and doctoral degree programs in Applied Science offer flexible curricula that are individually tailored by students, in consultation with their faculty advisors, to accomplish each student's unique and often interdisciplinary educational goals.

Research: The Neural Origins of Breathing

Breathing behavior in mammals begins in utero and continues without lapse for the entire lifespan of the animal, which in humans can last up to, or exceed, 100 years. Diseases that affect the neural control of breathing can strike at any age, but newborns and premature babies are particularly susceptible to various forms of apnea and SIDS. We aim to provide new knowledge about how the neurons, synapses and networks of the brain stem assemble the rhythm-generating systems that drive breathing movements and control respiratory physiology.

Breathing is an especially advantageous model system for this type of analysis because it is a behavior that can be studied under controlled conditions in vitro, using reduced brain stem 'slice' preparations. Our 'breathing slices' retain functional respiratory networks and generate spontaneous motor output during the inspiratory phase of the respiratory cycle.

In mammals, the rhythm for breathing originates in the brain stem nucleus called the preBotzinger Complex (preBötC). We isolate the preBötC and...
multi-photon imaging to measure calcium dynamics. Calcium imaging represents a convenient way to monitor the activity of many neurons simultaneously, which helps reveal network properties such as connectivity (Fig. 3).

Figure 4. Voltage-clamp analysis of preBötC neuron sensitivity to neuropeptides such as substance P.

Our efforts to unravel the neural basis for respiratory rhythm also emphasize mathematical modeling (Fig. 5). We are developing biophysically realistic models of preBötC neurons that account for morphology, the known complement of ion channels in preBötC neurons, as well as the novel biochemical signaling pathways that integrate synaptic and transmembrane calcium fluxes to evoke the burst-generating current $I_{CAN}$. Modeling at the cellular level forms the basis for network simulations that explore the role of connectivity: both the strength of coupling and the pattern of synaptic interconnections in the preBötC.

This intrinsic current ($I_{CAN}$) amplifies synaptic excitation and allows for the creation of robust inspiratory bursts via a positive feedback process often called recurrent excitation, which is a form of self-organized behavior in biology. Inspiratory bursts end once all of the preBötC neurons have become fully excited: this extinguishes recurrent excitation, deactivates $I_{CAN}$, and leads to burst termination. Some preBötC neurons spike tonically at low rates and subsequently restart the cycle, leading to network rhythmicity (Fig. 6). Our overall goal is to evaluate the group-pacemaker hypothesis by determining its key mechanisms at the cellular and synaptic level, and then use mathematical models to test and refine our understanding.

**Selected Recent Publications**


**Applied Science at William and Mary**

The College of William and Mary is the second oldest institution of higher education in the nation and has been repeatedly honored for its excellence by annual rankings in *US News & World Report*. The Department of Applied Science is at the forefront of interdisciplinary research and its graduate students enjoy a flexible curriculum and yearly stipends of $20,040 plus tuition and health insurance. Finally, William & Mary is located in the town of Williamsburg, with its historic Colonial village and nearby tourist attractions like the Chesapeake bay and Atlantic beaches.

**Contact**

Christopher A. Del Negro, Ph.D.
Department of Applied Science
The College of William and Mary
Williamsburg, VA 23185
757-221-7808
cadeln@wm.edu
http://people.wm.edu/~cadeln/