Research overview

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I am generally interested in studying phenomena that depend on processes occurring in different temporal and spatial scales. In particular, the complex and adaptive nature of physiological systems is of outmost interest to me. In brief, I like learning about the physiology underlying different aspects of behavior. For instance, the nervous system binds information from different levels and different physiological systems while coordinating different behaviors. Overt behavior occurs over seconds to hours, and is produced by muscle contractions. In turn, muscles are controlled by motor neurons that integrate and process sensory feedback and other inputs from elsewhere in the nervous system. Decisions and processing that occurs within the nervous system depend on already stored information, and the current state of the participating cells. At the next level, neurons produce fast signals called action potentials that occur in sub-millisecond to millisecond time scales, and serve to transmit messages to cells located potentially far from the originating neuron. My work is aimed to establish connections between physiological processes as those just mentioned. To do so, I combine mathematical modeling and data analysis with single- and multiple-cell recordings from neurons.

From a more general perspective, I would like to contribute to broadening the involvement of mathematics in studying biological sciences.

Training

I have Ph.D. training in two different fields, Physiology and Mathematics. I obtained a Ph.D. in Physiological Sciences in August, 2008 and will earn a second Ph.D. degree in Mathematics during the Spring of 2010, both from the University of Arizona.

My dissertation in Physiological Sciences is about the relationship between nearly-coincident spiking and common excitatory synaptic input in motor neurons (Herrera-Valdez and Fuglevand, 2010). One of the interesting aspects of this research effort was that it combined modeling constrained by physiological data with theory of dynamical systems under random perturbations to deduce possible schemes of synaptic input to motor neurons. This work was supervised and supported by Dr. Andrew J. Fuglevand from the Physiology Department at the University of Arizona.

My dissertation in Mathematics is about the dynamics of minimal biophysical models of excitability (Herrera-Valdez and Lega, 2010a,b). This research involved the study of membrane biophysics through systems of equations derived from first principles of electrodiffusion, dimensional reduction of multidimensional systems and bifurcation analysis. This work is being directed by Dr. Joceline Lega from the Mathematics Department at the University of Arizona.

While in graduate school I had intense and extensive training doing multiunit recordings in whole-animal preparations, both in insects and in freely moving rodents. I also had some experience doing single cell patch recordings in reduced preparations, and electrophysiology and behavior in primates. On the mathematical side, my initial training was in pure mathematics, with emphasis on probability theory and stochastic processes. During the later stages of my graduate studies my training was mainly on dynamical systems and computation. At some point in between I acquired expertise in using symbolic and numerical software (python, matlab, neurons) and programming languages (c/c++) to tackle computational aspects of my research questions.

Since October 2008, I joined the Mathematical, Computational and Modeling Sciences Center (MCMSC) in Arizona State University. Since I arrived to Tempe, I have been conducting an intense research program that includes the topics mentioned above, some in collaboration with colleagues from other universities, but most of it directly related to the research groups of Sharon Crook and Carlos Castillo-Chavez.

Ongoing research

So far, I have been learning about biophysical properties of excitable cells, and how these properties influence network activity. In doing so, I have combined single-cell and multiunit recordings with mathematical analysis and modeling to tackle various specific research questions. My ultimate goal is to develop a deep understanding about general principles governing physiological function at different levels.

At the *cellular level*, I am currently studying relationships between cell morphology, channel expression, and neuronal function. To do so, I am building whole-cell neuron models based on electrophysiological and anatomical data. One part of the project is aimed at investigating the differential contributions of ion channels to membrane excitability Herrera-Valdez et al. (2010a). The second part of this project involves large-scale to simulations of how dendritic integration and neural excitability change with the morphology and gene expression in neurons. A holometabolous insect like the moth *Manduca Sexta* was chosen as our animal model because the behavior of the animal, and by extension, its neurons, changes during development (Herrera-Valdez et al., 2010b).

At the *network level*, I am studying how different behavioral states and learning are reflected by, and influence the dynamics of neural populations. I have done some analytical work to connect large scale models of networks formed by single cells and population models (Radulescu and Herrera-Valdez, 2010).

In a related path, I am analyzing data collected simultaneously from several neurons while learning occurs with the intention of establishing guidelines to constrain my models. The main idea here is that the changes in network dynamics can be ultimately related to changes in single cells. The general principles that I am studying apply to different systems. I plan to use data from simultaneous recordings of large neural populations to constrain my network and population models. Two ongoing projects are aimed to pursue this goal.

On one hand, I collected data by simultaneously recording the activity of rat neurons in the hippocampus and the midbrain during wakefulness and sleep. The findings from those hippocampus-midbrain recordings will complemented with patterns of early gene expression and neuromodulation triggered by learning in rats (Satvat et al., 2009). This is an ongoing collaboration Diano Marrone from W. Laurer University, in Canada. On the other hand, I am currently analyzing data recorded from olfactory neurons (Strube-Bloss et al., 2009, 2010) during a learning protocol. One of the goals from this olfaction study is to characterize the macroscopic changes that occur in single cells during learning at two different sensory processing stages. This is a collaboration with Martin Stube and Brian Smith in ASU.

Extension research. Recently, my interest in dynamical systems and networks prompted me to collaborate with epidemiologists at MCMSC studying the spread of AH1N1 influenza in Mexico. The modeling work I have done in this area incorporates some of my background from neurophysiology and networks to study the role played by the historical architechture of local transportation, school closures, and social distancing in explaining and capturing the three waves of AH1N1 influenza observed in Mexico during 2009 (Herrera-Valdez et al., 2010c,d). My involvement in this project includes supervising the work of two doctoral students. We used mathematical, computational, and modeling approaches to construct a model that builds from a single city, to a network of strongly and weakly connected cities, that has helped to understand the role of mass transportation in the spread of influenza. As a result, we found that the combination of local dynamics of contact within each city with the transportation between cities explains the epidemic waves observed in Mexico during the last pandemic.

Some of the research mentioned above has been submitted for peer review publications. I am currently preparing articles reporting the research mentioned above, which I expect to submit during the current academic year (see References section).

Research program

As explained above, I am using my dual background into developing a unique research program that crosses the traditional boundaries between mathematics and biology. This way, I am contributing to address scientific challenges that require both theoretical and experimental approaches.

In the latter months I have had the fortune to interact with faculty and mentor graduate students at MCMSC and therefore broaden my participation in the mathematical sciences. I plan to continue doing so, as my research and mentoring can only benefit from diversifying my knowledge and expanding my expertise to other areas of science.

I plan to use preliminary findings from the projects mentioned above to seek financial support from granting agencies. In the future, I want to push my current approach a bit further and establish links between biophysical and biochemical aspects of cellular function, population activity, and behavior by combining experiments and modeling. It is my intention to continue doing cross-disciplinary research and eventually conduct a unique research program that combines experimentation and theory. This will require using animal models in which behavior can be recorded from cellular to whole-animal levels in combination with theoretical approaches that allow synthesis and abstraction of experimental data to describe general principles of organization in time and space.

References

Marco Arieli Herrera-Valdez and Andrew J. Fuglevand. Nearly-coincident spiking and coherence in motoneurones receiving common cortico-spinal input. *PhD Dissertation, University of Arizona*, 2010.

Marco Arieli Herrera-Valdez and Joceline Lega. A reduced model for the pacemaker dynamics of cardiac cells. *Submitted to Journal of Theoretical Biology. Preprint available upon request*, 2010a.

Marco Arieli Herrera-Valdez and Joceline Lega. Minimal biophysical models of excitability. *In preparation*, 2010b.

Marco Arieli Herrera-Valdez, Sandra D. Berger, Carsten Duch, and Sharon Crook. Contribution of potassium currents to the membrane excitability in *Drosophila* neurons. *Submitting to PLOS Computational Biology, March 2010. Preprint available upon request*, 2010a.

Marco Arieli Herrera-Valdez, Sandra D. Berger, Carsten Duch, and Sharon Crook. Dendritic integration in *Manduca* motor neurons during development. *In preparation*, 2010b.

Marco Arieli Herrera-Valdez, Maytee Cruz-Aponte, and Carlos Castillo-Chavez. Multiple waves during an influenza epidemic explained by local transportation and behavioural changes. *Submitted to PLOS ONE, Preprint available upon request*, 2010c.

Marco Arieli Herrera-Valdez, Maytee Cruz-Aponte, Jose Vega-Guzman, Gerardo Chowell-Puente, and Carlos Castillo-Chavez. The role of transportation, social distance, and delayed vaccination in the time course of influenza epidemics. *Submitted to BMC, Preprint available upon request*, 2010d.

Anca R. Radulescu and Marco Arieli Herrera-Valdez. Mechanisms explaining transitions between tonic and phasic firing in neuronal populations as predicted by a low dimensional firing rate model. *Submitted to PLOS Computational Biology, December 2010. Preprint available upon request*, 2010.

E. Satvat, Marco Arieli Herrera-Valdez, A. Gheidi, A.A. Adams, A. Hertel, and Diano Fabio Marone. D1 receptor activation is not required for place cell-related arc expression. *Society for Neuroscience Annual Meeting, Chicago*, October 2009.

Martin Strube-Bloss, Marco Arieli Herrera-Valdez, and Brian H. Smith. Poster: Representation of single odors and their mixture at the input and output stages of the honey bee mushroom body. *Society for Neuroscience Annual Meeting, Chicago*, October 2009.

Martin Strube-Bloss, Marco Arieli Herrera-Valdez, and Brian H. Smith. Representation of single odors and their mixture at the input and output stages of the honey bee mushroom body. *Submitting to Nature Neuroscience, February*, 2010.