Mini Course: Neuronal behaviors

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1. Neurons are nonlinear circuits: the heritage of Hodgkin and Huxley (R. Sepulchre)

The foundation of today's computational neuroscience is the 1952 paper of Hodgkin and Huxley. This paper is a model of behavioral modeling. It uses an exquisite combination of parsimonious experiments, biophysical principles, and curve fitting, to reduce the mechanism of the action potential to an elementary switching RC circuit. Yet the default textbook presentation of Hodgkin Huxley model is an obscure set of four nonlinear differential equations that produce oscillations for a well chosen set of parameters. The talk will review the basics of this historical model and emphasizes the importance of regarding this model as a behavior, that is, an open system, regulated by elementary but fundamental feedback principles.

2. Detailed and reduced models of neurons (G. Drion)

Mammalian neurons exhibit a great diversity in the morphology of their membrane and its regulated permeability to different ions. Nevertheless, the modeling principles of Hodgkin Huxley apply to any neuron, leading to high-dimensional compartmental models with several hundreds of states and parameters as quantitative knowledge accumulates for specific families of neurons. Those models have a remarkable predictive power but an overwhelming complexity. Moreover, many of their parameters have a broad range of variability, making the relevance of detailed simulations questionable. Model reduction is therefore essential to address behavioral questions such as modulation, robustness, and sensitivity. Starting from the reduction of the Hodgkin-Huxley model proposed by FitzHugh in 1961, the talk will describe how the complexity of any arbitrary conductance-based model can be reduced while retaining the physiological interpretation of parameters and variables in the reduced model.

3. Organizing singularities (A. Franci)

Neuronal behaviors are inherently nonlinear and linearized models fail to capture their organizing principles. Nevertheless, the highly constrained nature of their architecture can be exploited to unfold their nonlinear behavior from a static analysis. Furthermore, their static analysis can be localized around specific points in the space of parameters and variables. Exploiting this remarkable feature, wse show how singularity theory offers a systematic methodology to relate circuit architectures to nonlinear static behaviors. Those static nonlinear behaviors are then turned into dynamic nonlinear behaviors with the help of elementary linear filters. We illustrate this approach on spiking and bursting, two fundamental neuronal behaviors. We use recent work to illustrate the excellent match between the few modulation parameters predicted by singularity theory and their physiological counterpart in neuronal architectures.

4. Modulation and robustness of neuronal firing (G. Drion)

Neuronal behaviors are tightly regulated. For instance, thalamocortical cells are able to switch from tonic firing to bursting and this switch is a critical component of the transitions between wakefulness and sleep. On the other hand, neuronal behaviors are also robust against large uncertainties. For instance, a particular maximal conductance parameter can routinely vary by an order of magnitude without affecting the neuronal behavior. The talk will illustrate the mechanisms underlying this impressive combination of modulation and robustness properties both in large-scale detailed conductance-based models and in reduced models. The fundamental role of neuromodulators naturally enters the scene at this point since they can drastically modulate the behavior of the cell without impairing its robustness.

5. Neuronal interconnections (J. Dethier)

Neuronal behaviors determine brain function only when considered in large network interconnections rather than in isolation. Early attempts to understand the organizing principles of neuronal networks led to the theory of artificial neural networks and eventually to machine learning theory. In this talk we will emphasize how the principles of Hodgkin and Huxley model extend to synaptic and electrical interconnections of neurons. This suggests that many organizing principles of neuronal networks behaviors can be studied in the same way as those of isolated neuronal behaviors. In other words, the interconnection theory that Hodgkin and Huxley paper sets for single neuron conductance based models extends to neuronal networks. The talk will illustrate this principle by showing how the action potential mechanism can be transferred from the single cell to the network level.

References:

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