# The Neurophysics of Ion Channels : Merging Cutting-Edge Imaging techniques with Computational Neuroscience to Disclose Ion Channel Functioning in Neurons

Marco Canepari[a,b,c*]

a. Laboratory for Interdisciplinary Physics, UMR 5588 CNRS and Université Grenoble Alpes, 38402 Saint Martin d'Hères, France.
b. Laboratories of Excellence, Ion Channel Science and Therapeutics, France.
c. Institut National de la Santé et Recherche Médicale (INSERM), France.

* marco.canepari@univ-grenoble-alpes.fr

The function of neuron in its multiple compartments is governed by several biophysical parameters including morphology and the expressed proteins in the membranes and in the cytoplasm. These factors determine the generation of action or synaptic potentials and their propagation, as well as the underlying chemical signaling. Yet, dedicated experimental and theoretical methods are necessary to disclose the complexity of electrical and chemical signals and to understand the activity of individual channels cooperating to generate a global function in neuronal compartments. Here I will present a cutting-edge imaging approach, based on combined electrophysiology, membrane potential imaging and ultrafast calcium imaging, which allows tracking the activity of voltage-gated calcium channels in neuronal dendrites from ex-vivo preparations, as well as their biophysical regulation by membrane potential changes [1,2]. I will then show some optical recordings of fast calcium currents, associated with backpropagation of action potentials in the apical dendrite of the CA1 hippocampal pyramidal neuron, and I will illustrate how the resulting calcium signals are finely regulated by the synergy of different types of voltage-gated calcium channels [3]. This pure experimental analysis of calcium currents reveals only a part of the physiological scenario since also other channels, in particular potassium channels, participate to the cooperation that shapes both the membrane potential and the calcium signal. To overcome this limitation we use a computational framework based on NEURON (https://www.neuron.yale.edu/neuron/) to analyse our experimental data and disclose the kinetics of all ion channels underlying a given physiological signal. Thus, I will finally present an unpublished research in which we used this novel approach of combining our advanced imaging methods with computational tools based on NEURON modelling to precisely reconstruct the kinetics of all dendritic calcium and potassium associated with the climbing fibre synaptic potential in the cerebellar Purkinje neuron.

[1] N. Jaafari, M. De Waard, and M. Canepari, Imaging Fast Calcium Currents beyond the Limitations of Electrode Techniques. Biophys. J. **107**,1280-1288 (2014)

[2] N. Jaafari, E. Marret, and M. Canepari, Using simultaneous voltage and calcium imaging to study fast Ca2+ channels. Neurophotonics **2**, 021010 (2015)

[3] N. Jaafari, and M. Canepari, Functional coupling of diverse voltage-gated Ca(2+) channels underlies high fidelity of fast dendritic Ca(2+) signals during burst firing. J. Physiol. **594**, 967-983 (2016)