Contrasting the role of I_h and I_{CaT} currents in post-inhibitory rebound mechanisms in reciprocal-inhibitory networks

Julie Dethier¹, Guillaume Drion¹, and Rodolphe Sepulchre^{1, 2}

¹Department of Electrical Engineering and Computer Science, Systmod Research Unit, University of Liege, Belgium ²Department of Engineering, University of Cambridge, Cambridge CB2 1PZ, UK

Models with reciprocal inhibition are ubiquitous in the literature. For instance, common rhythmic motor behaviors produced by central pattern generators (CPGs) involve half-center oscillators, which consist of two inhibitory neurons that are not endogenous oscillators, but produce rhythmic outputs when reciprocally connected (Marder & Calabrese 1996). Models of thalamocortical spindle oscillations also suggest that the rhythm originates from the thalamic reticular nucleus, which consists in interacting inhibitory nonoscillatory neurons (Wang & Rinzel 1992).

Rhythms arise from reciprocal inhibition between nonoscillatory neurons if these neurons exhibit the property of post-inhibitory rebound (PIR), a transient depolarization evoked by a prior hyperpolarizing stimulus (Perkel & Mulloney 1974). The ionic mechanism for PIR can come from several currents including hyperpolarization-activated cation current, I_h (Ansgstad *et al.* 2005), or low-threshold T-type calcium current, I_{CaT} (Steriade *et al.* 1990).

We study the different role those two currents play in PIR. I_h produces a transient increase in excitation in the neuron but is slow restorative (in the sense defined by the authors in previous work). The neuron remains memoryless/monostable at any time. The transient increase in excitation results in a rebound-burst mechanism with restorative firing. By contrast, I_{CaT} brings slow regenerativity to the neuron. This current is a source of transient increase in excitation and in slow regenerativity. The neuron acquires memory/bistability and produces regenerative firing activity during the rebound.

The cellular regenerativity has a major impact on the robustness and modulation properties of the network. We compare a network with slow cellular restorativity with a model with slow cellular regenerativity: we investigate how the two networks respond to heterogeneity in the connections (maximal conductances and kinetics) and in the neuron intrinsic properties, as well as how modulation can affect the networks. We also explore the entrainability of the two networks by an external source.

Our study shows that oscillations are endogenous/robust in the regenerative case and exogenous/entrainable in the restorative case. The properties of I_h and I_{CaT} suggest a drastically different role for the two currents, with I_h more prominent in networks with major sensory feedbacks, to deal with environmental perturbations for instance, and I_{CaT} more prominent in networks with a very strong endogenous rhythm, much less responsive to external inputs.