Bimodality of cortical Up states and thalamic modulation of Up state duration: an experimental and computational study

Núria Tort-Colet, UNIC-CNRS
E-mail address: nt0084@gmail.com.

The dynamics of cortical activity during deep stages of sleep and anesthesia consists in a slow alternation of high and low firing rate states of activity (Up and Down states, respectively) (Steriade *et al.*, 1993; Sanchez-Vives and Mattia, 2014). Although this oscillating activity observed in the cortex is also known to be present in the thalamus with a high degree of correlation (Timofeev and Steriade, 1996; Sheroziya and Timofeev, 2014), it is not clear how the two elements of the thalamo-cortical system coordinate to produce such pattern. Here, we investigate the cortical dynamics in the primary visual cortex of ketamine-medetomidine anesthetized rats, in the presence and absence of thalamic activity, in order to separate the contributions of the two elements of the thalamo-cortical system. We found that the statistics of cortical Up state duration change significantly between the two conditions. When the cortex is not receiving input from the thalamus the distribution of Up state duration is unimodal. On the contrary, when the thalamus is active the distribution becomes bimodal, suggesting the presence of two qualitatively different types of Up states. To investigate the possible mechanisms underlying the experimental observations, we used a computational model of a thalamo-cortical network of spiking neurons (Destexhe, 2009). We found that the hyperpolarization-activated Ih current in thalamic cells can account for the bimodal distribution of cortical Up state duration. Indeed, the activation of this current leads to a calcium spike in thalamocortical cells which project to the cortex, occasionally allowing for an elongation of the Up state duration. Such result further supports the hypothesis that the thalamus is not only a relay station of sensory information, as it plays a state-dependent modulatory role of the cortical persistent activity eventually affecting how information is processed and maintained as it has been described for working memory (Guo *et al.*, 2017).

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