

## Biophysical model of acetylcholine modulation in visual cortex

Vinícius Lima<sup>1</sup>, Parviz Ghaderi<sup>2</sup>, Sareh Rostami<sup>2</sup>, Rodrigo Pena<sup>1</sup>, Renan Shimoura<sup>1</sup>, and Antonio C. Roque<sup>1</sup>

<sup>1</sup> Laboratory of Neural Systems, Department of Physics, School of Philosophy, Sciences and Letters of Ribeirão Preto, University of São Paulo, Ribeirão Preto, SP, Brazil

<sup>2</sup> Neuroscience Research Center, Shahid Beheshti University of Medical Science, Tehran, Iran

**Introduction:** Cholinergic inputs from the basal forebrain modulate various visual cortex functions, including visual discrimination, contrast response function, orientation tuning, signal to noise ratio (SNR), and plasticity. Acetylcholine (ACh) has been known to exert its modulatory action via two distinct Acetylcholine receptors (AChR), namely nicotinic ACh receptors (nAChRs) and muscarinic ACh receptors (mAChRs) [1].

**Materials and Methods:** To understand the mechanisms underlying cholinergic neuromodulation in the primary visual cortex (V1), we developed a biophysical model of V1 neurons incorporating both nicotinic and muscarinic neuromodulatory effects. The model allows the study of how the interaction of the different variables contribute to the observed experimental phenomenon. The model was implemented in NEURON and NetPyNe using Python [2]. The cholinergic mAChRs modulation was modeled as the inactivation of  $I_m$  and  $I_{KCa}$  channels which are mainly affected by modulatory effects, and nAChRs as an extra ohmic current [3]. The external stimulus was given by  $I_{ext}(t) = \log_{10}(C + 1)\cos(\theta - \theta_0)$  [4], which enables simulation of grating bars with contrast level  $C$  and orientation  $\theta$ , where  $\theta_0$  is the neuron's preferred orientation. An extra synaptic background input was injected into the neuron to mimic *in vivo* like activity. To study how ACh modulates orientation tuning, first we estimated the orientation selectivity index (OSI) [4] both with and without ACh. The response curves and the measured OSI were compared to our own experimental data. To determine the influence of ACh on the SNR, we computed the coherence function between the membrane voltage time series and the external synaptic input. Finally, to study the influence of ACh modulation in synaptic communication and information flow we computed the Granger causality between coupled neurons.

**Results:** Our results show that synaptic background is fundamental to increase the orientation selectivity in neurons with mAChRs and also nAChRs increases the information capacity of the cell. The comparisons between the response curves generated by the neuron model and experimental response curves showed good agreement.

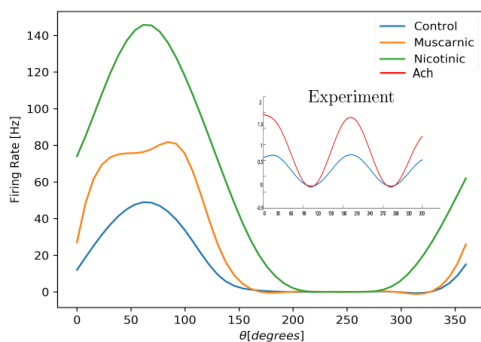


Fig.1: Tuning curves for the neuron model, in the control case (in blue), with mACh (in orange) and nACh (in green). The inset shows the tuning curve recorded in the V1 area of mice (data provided from Shahid Beheshti University of Medical Science) for the control case and with ACh (in red).

**Discussion:** The analyses of our results show the crucial effect of synaptic noise in some modulatory effects. Furthermore, the model also shows significant increase in the information capacity of the cell under nAChRs modulation which suggests the role of this modulator in synaptic communication.

**Conclusion:** In conclusion, our results show how ACh modulation acts on the orientation selectivity, on the response curves, and on the information capacity of the cell. In addition, we show that synaptic background is fundamental in some modulatory effects of ACh.

**References:** [1]doi:10.1007/s00424-002-0999-2;[2]doi:10.1007/s00422-008-0263-8;[3]doi:10.3389/neuro.11.001;[4]doi:10.1523/JNEUROSCI.2831-12.2013;[5]doi:10.1523/JNEUROSCI.6284-11.2012;[6]doi:10.3389/fncir.2015.00042;[7]doi:10.1016/S0306-4522(01)00344-X;[8]doi:10.1523/JNEUROSCI.0863-14.2014.