

COMPUTATIONAL MODELS OF INTRACORTICAL AUGMENTING RESPONSES. A.R. Houweling<sup>1\*</sup>, M. Bazhenov<sup>1</sup>, I. Timofeev<sup>2</sup>, M. Steriade<sup>2</sup> and T.J. Sejnowski<sup>1</sup>. <sup>1</sup>The Salk Institute, PO Box 85800, San Diego, CA 92186 and <sup>2</sup>Lab. of Neurophysiology, School of Medicine, Laval University, Québec, Canada G1K 7P4.

Augmenting responses in cortical pyramidal cells can be elicited by 10 Hz repetitive stimulation *in vivo* and *in vitro*. One of the underlying mechanisms is intrinsic to the thalamus because such augmenting responses may be elicited in decorticated animals. Stimulation of the white matter or corpus callosum in thalamically lesioned animals also results in augmenting responses, however, with different features. A realistic network model of cortical regular spiking or bursting pyramidal (PY) cells and fast spiking interneurons (IN) was developed to explore possible intracortical mechanisms. Two-compartment models of PY and IN cells included voltage-dependent currents described by Hodgkin-Huxley type kinetics. Synaptic currents were described by kinetic models of AMPA and GABA<sub>A</sub> receptors together with a simple model of short-term depression for both types of synapses. We found that the simplest network model demonstrating augmenting responses during repetitive stimulation is a set of coupled PY and IN cells. Repetitive stimulation of thalamocortical synaptic inputs produced postsynaptic potentials in the PY cell that grew in size carrying an increasing number of action potentials from disinhibition through short-term depression of inhibitory (IN-PY) synapses at frequencies greater than 3-5 Hz. In a one-dimensional chain of PY-IN pairs additional strong, fast recovering depression of lateral excitatory synapses between PY cells and thalamocortical afferents led to a reduction of augmenting responses at frequencies greater than 15-20 Hz. Thus, short-term depression of intracortical and thalamocortical synapses during repetitive stimulation may explain the main features of intracortical augmenting responses. Supported by the Howard Hughes Medical Institute, Sloan Foundation, MRC of Canada, Human Frontier Science Program and Savoy Foundation.