

Functional consequences of presynaptic inhibition in an oscillatory network – a simulation study

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Presynaptic inhibition of synaptic terminals can be a powerful mean of regulating synaptic activity and motor output. In the stomatogastric nervous system of the crab, presynaptic inhibition seems to play an important role in the central pattern generators that drive the pyloric and the gastric mill rhythms (Coleman et al., 1995, *Nature* 387:502-505). The projection neuron MCN1 modulates the pyloric rhythm and excites the two gastric mill half-center cells Int1 and LG (Blitz et. al., 1999, *J. Neurosci.* 19:6774-6783). LG's excitation is mediated by a fast electrical and a slow chemical EPSP. At the same time, the MCN1 axon receives presynaptic inhibition from LG, which causes a decrease in transmitter release on the pyloric and the gastric mill rhythm. Consequently, the timing of the gastric mill rhythm and the speed of the pyloric rhythm are strongly influenced by LG activity (Bartos & Nusbaum, 1997, *J. Neurosci.* 17:2247-2256). The pyloric cycle frequency should thus depend on the strength of the presynaptic inhibition and LG firing frequency.

We are using the network simulator *madSim* to model the neuronal network underlying the generation of the pyloric and gastric mill rhythm of *Cancer pagurus* and to test the impact of presynaptic inhibition on the timing of the gastric mill rhythm and on gastro-pyloric circuit interaction. *MadSim* is a newly developed simulation environment for realistic neural network modeling which adapts and extends the kernel of the unix-based BIOSIM tool (Bergdoll & Koch, 1995, *Neurocomputing* 8:93-112) to WINDOWS. It is capable of creating networks up to several hundreds of neurons. Here, neurons according to the SWIM model (Ekeberg et al., 1991; *Biol. Cybern.* 65, 81-90) were used. For the pyloric rhythm, a network was constructed which consisted of 5 classes of neurons and produced a triphasic pattern with a cycle period of 1.15s. For the gastric mill rhythm, the core pattern generating neurons LG and Int1 were modeled. MCN1 excited both networks and Int1 received inhibition from the pyloric pacemaker neurons PD. Although almost all morphological cell properties are disregarded in *madSim*, we succeeded in modeling the physiological effects of such functional units. Presynaptic inhibition of MCN1, for example, was achieved by connecting the MCN1 axon with an electrical synapse to a nonspiking neuron with graded transmitter release. This 'terminal' then received inhibition from LG which decreased action potential amplitude. To model the different time courses of MCN1's electrical and chemical synapses LG was provided with a fast and a slow dendritic region.

We are currently investigating the effects of changes in LG firing frequency and of changes in the strength of the presynaptic inhibition from LG to Int1 on the pyloric cycle frequency and on the LG burst offset.