Model of intermittently bursting stretch sensors in the stomatogastric nervous system

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Abstract:

Bursting neurons play important roles in both vertebrate and invertebrate systems. In recent years, two groups of stretch-sensitive neurons in the crustacean stomatogastric nervous system, the gastropyloric receptors (GPRs) and the anterior gastric receptor (AGR), have been observed to operate both in a non-bursting and a bursting mode. In this paper we present experimental measurements of the GPR bursting mode and a mathematical model that shows how a single conductance can act as a "switch" between bursting and non-bursting states.

Summary:

GPR cells and the AGR cell are stretch receptors that innervate muscles of the gastric mill region of the crustacean foregut. Both types of cells respond to either passive or nerve-evoked stretches of the innervated muscles. Each of the stretch receptors has been observed to operate both in a non-bursting and a bursting mode mode (Katz et al., 1989, Birmingham et al., 1999, Combes et al., 1997). In the non-bursting mode, GPR or AGR is quiescent or fires at a low rate in the absence of stretch. During muscle stretch the firing rate increases but returns to baseline at the completion of the stretch (Katz et al., 1989, Birmingham et al., 1999, Combes et al., 1997). The bursting mode is very different. In the absence of any muscle stimulation, the stretch receptors generate bursts of action potentials. In the case of AGR these burst are typically 400 ms in duration with a period of 1 s (Combes et al., 1997). The GPR bursts are more unusual. Burst periods ranging from 12 to 101 seconds have been reported, and the burst duration can be 20 seconds or longer (Birmingham et al., 1999). When either stretch receptor is in the bursting mode, muscle stretch results in more frequent, shorter bursts (Combes et al., 1997, Birmingham et al., 1999). Bursting in GPR is a property of the neuron itself. Neither ablation of muscles nor isolation of the GPR neuron from the rest of the nervous system eliminates the bursting behavior (Katz et al., 1989).

In naïve AGR and GPR preparations in which the muscles have not been manipulated, both types of behavior are observed, although the non-bursting mode is more common. In both cases, neurons that are not initially bursting can be driven into the bursting mode. This can be done in AGR through bath application of micromolar concentrations of the F1 peptide (TNRNFLRFamide) to AGR dendrites (Combes et al., 1997). Bursting in GPR is induced through repeated stretch of the innervated muscles (Birmingham et al., 1999). Whether the switch of GPR into the bursting mode is due to the release of some as yet unidentified neuromodulator or results from some other activity-dependent process is not yet understood.

There have been no biophysical measurements of the ionic conductances present in the stretch receptors, but we assume that they are similar to those found in other neurons in stomatogastric nervous system. In this spirit, we have adopted a variant of the model of Zheng et al. (1998) to describe mathematically the stretch receptors. This model has been used specifically to model stomatogastric ganglion neurons. It is a two-compartment conductance-based model that has the unique feature of possessing maximal conductances that are dynamical variables, instead of being constants. These maximal conductances are regulated by several Ca-dependent pathways in an activity-dependent manner, and these regulatory processes allow for a model neuron that exhibits

a very rich and wide variety of quasi-stable firing patterns on a number of different time scales. The existence of this Ca-modulation and the interplay between the two compartments in the model provide a mechanism that allows, for example, firing patterns with long bursts in which the inter-burst interval can be extremely long and the intraburst firing frequency very low. Keys to this behavior are the weak intercompartmental coupling, A-current dynamics, and fast transient and slow Ca currents (I_{CaT} and I_{CaS}). For example, I_{CaS} is instrumental in maintaining a long duration burst, while I_{CaT} is important for burst initiation. The existence of many time scales in the model and the feedback mechanisms provided by the dynamical Ca regulation permit the neuron to be entrained relatively easily to sufficiently strong periodic external inputs (stretches) as has been observed experimentally.

Without intracellular measurements, we can only speculate on what conductance constitutes the "switch" and whether the switch used in both AGR and GPR is the same. The AGR experiments suggest that a conductance modulated by the F1 peptide may be responsible. Swensen et al. (2000), recently showed that bath application of many peptides, including the F1 peptide, activates an inward current in stomatogastric neurons. Alternatively, calcium and calcium-dependent processes could be responsible. We present modeling analysis of a few possible candidates, in each case focusing on the robustness of the regimes obtained, entrainment, and precise timing relationships. Future experiments will provide more concrete answers. An important general result of our modeling work is the observation that typical ionic conductances, when combined with weak coupling, can generate very unusual behavior such as slow bursting and very slow intraburst firing.

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