Role of A-current in Lamprey Locomotor Network Neurons

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Abstract

A compartmental model of lamprey central pattern generator neurons was built in order to examine the effects of a fast, transient, high-voltage-activated potassium current (A-current) found experimentally. The model consisted of a soma, a compartment corresponding to the axon initial segment, and a (passive) dendritic tree. The simulation showed that the A-current was necessary for repeated spiking in the neuron following current injection. With only the delayed rectifier present, the neuron fires one initial spike. This corresponds well with in vitro experimental results.

Summary

Transient A-type K^+ channels can act as a control mechanism for neuronal excitability. A transient A-type potassium current has recently been characterized in lamprey locomotor network neurons [3]. This current is high-voltage-activated and promotes repetitive firing in lamprey neurons by facilitating Na^+ channel recovery from inactivation. On a higher anatomical level, the A-current seems to stabilize the lamprey swimming motor pattern by keeping the cycle duration fairly constant [3].

A compartmental model of a lamprey neuron has been developed to investigate the effect of transient A-type K^+ channels on the neurons' firing characteristics. The model was implemented in the GENESIS simulation environment [1] and included Na^+, K^+ delayed rectifier, transient A-type K^+, calcium-dependent K^+, Ca^{2+}, and NMDA channels. The intracellular Ca^{2+} that activates calcium-dependent K^+ (K_{Ca}) channels was modeled using two different intracellular pools, Ca_{AP} and Ca_{NMDA}. They activate separate K_{Ca} channels, K_{CaAP} and K_{CaNMDA} channels respectively [2]. The simulated neuron's morphology consisted of a 32 μm diameter soma and two primary dendrites, each of which had two branches. The primary dendrites were of length 90 μm and diameter 2.5 μm, the secondary dendrites of length 148 μm and diameter 1.5 μm and the tertiary dendrites were of length 240 μm and diameter 0.75 μm. An alternative model consisted of a large (length 100 μm, diameter 65 μm), "naked" soma. Both models included a special compartment corresponding to the initial segment of the axon. In both models, the morphology was chosen in such a way that the resulting input resistance och input capacitance would be reasonably close to the experimentally measured values (177$\pm$109 MΩ for the resistance and 400-500 pF for the capacitance). The model that included dendrites had another additional constraint: the total area of the dendritic segments should be an order of magnitude larger than the area of the soma. In practice, the ratio between the areas ended up at around 8:1. The input resistance in this model was 158 MΩ and the input capacitance 253 pF.

Only the soma and initial segment were equipped with active ion channels. The kinetics of most ion channels were based on previous lamprey models [2], although some parameters were changed as a result of new experimental data. Gating properties of the sodium current were modified to allow the firing of a single spike when the A-current was blocked and the cell was depolarized by a pulse of current. More precisely, the inactivation curve was shifted -7 mV (so that $V_{1/2}$=-51.5 mV). Recording of the Na+ current on isolated lamprey spinal neurons with the patch clamp technique supported this modification but also showed that the lamprey sodium current is faster than the one implemented previously [2]. The A-type potassium current was modelled as a Hodgkin-Huxley type current with three activation gates and one inactivation gate. The half-activation potential was set to -1.0 mV and the half-inactivation potential to -9.3 mV, with slope factors of

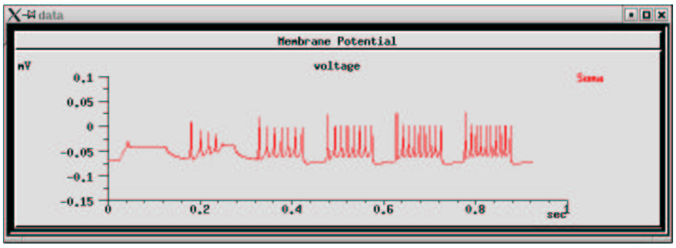

Figure 1: Response to increasing current steps, both with A-type potassium and delayed rectifier present.

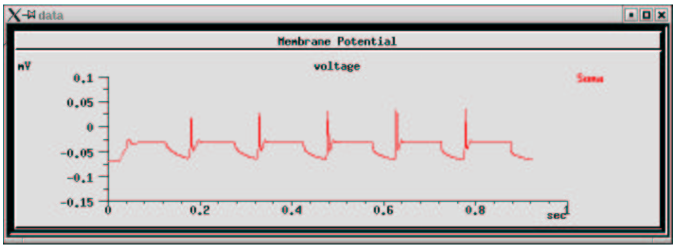

Figure 2: Response to increasing current steps, with only delayed rectifier present.

10.6 mV for the activation and -11.7 mV for the inactivation [3]. The simulated A-current was able to produce the effects found experimentally: it gave rise to faster (narrower) action potentials and sustained repetitive firing. With just the delayed rectifier, the simulated cell was unable to fire repetitively. Further investigation is required in order to find out whether adding the A-current also stabilizes the locomotor patterns in a simulated lamprey locomotor network. We also intend to add active channels, including A-type potassium channels, to the dendrites and explore how this affects the behaviour both on the single-cell and network levels.

References

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[3] Dietmar Hess and Abdeljabbar El Manira. Characterization of a high-voltage-activated I_A current with a role in spike timing and locomotor pattern generation. *PNAS*, 98:5276, 2001.