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Classifying functional and non-functional model neurons using the theory of rough sets

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We explored a 12-dimensional parameter space of a 2-compartment model of the AB (anterior burster) neuron, which is one of the two cells that form the pacemaker kernel in the pyloric network in the lobster stomatogastric ganglion (STG). The computational exploration started with a hand-tuned AB model [1] and systematically varied maximal conductances of membrane currents to determine ranges and variation steps that could potentially produce physiologically realistic behavior. We varied the conductances for the following currents in the model: fast sodium I_{Na} and delayed-rectifier potassium I_{Kd} in the axon compartment, and delayed-rectifier I_{Kd}, calcium-dependent I_{KCa}, transient potassium I_A, transient I_{CaT} and persistent I_{CaS} calcium, persistent sodium I_{NaP}, and hyperpolarization-activated inward I_h in the some/neurite (S/N) compartment. To model the descending modulatory inputs, a voltage-gated inward current (such as the one activated by the neuropeptide proctolin) I_{proc} was added to the S/N compartment. Both compartments also contained the leak current I_L.

Every parameter set representing an individual model neuron was simulated and analyzed in terms of its period, burst duration, spike and slow wave amplitude, number of spikes per burst, spike frequency, and afterhyperpolarization potential, as well as the model's responses to neuromodulator deprivation and current injections. All of the above characteristics had to be within limits determined in physiological experiments performed on the AB cell, in order for a model to be classified as functional [2].

In addition to several other data mining and visualization techniques we have previously employed to analyze the parameter space of the "good" models [3], we propose to utilize the theory of rough sets (RS) to investigate the role and importance of the parameters in differentiating between the functional and non-functional models. One of the most useful aspects of the RS theory in these kinds of classification tasks is the concept of a reduct—the smallest possible subset of attributes (*i.e.*, maximal conductances in our model) that preserves the classification accuracy of the full set of attributes [4]. There are usually several such reducts for a given problem, and by extracting the so-called core of the reducts (*i.e.*, the attributes that all the discovered reducts have in common), one can estimate the relative importance of the attributes. For instance, based on the 10 reducts computed from our dataset, we can state that soma *CaT*, *NaP*, *Kd*, *KCa*, and *Proc*, are absolutely necessary for differentiation between the functional and non-functional models (they were included in all 10 reducts), the axon *Na* current is very important (utilized in 9 out of 10 reducts), while the leak currents (both in the soma and the axon) seem to be the least important (they were present in 6 and 7 of the reducts, respectively). Furthermore, based on reducts, one can easily generate *IF-THEN* rules that not only describe how the model's proper behavior depends on its parameters, but also how those parameters (*i.e.*, ionic currents) "cooperate" with one another to assure such activity. For example, one of the most trustworthy rules we discovered (confidence of 78%) describes the following relationship:

IF soma *NaP*$\in$ [2.7μS÷6.4μS) *AND* soma *KCa*$\in$ [3,000μS÷6,000μS) *AND* axon *Na*$\in$ [300μS÷450μS)

THEN "functional AB model,"

where the values in parentheses represent the ranges for the corresponding maximum membrane conductances.

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