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Calcium sensor properties for activity-dependent homeostatic regulation of pyloric network rhythms in the lobster stomatogastric ganglion

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Introduction

Homeostatic regulation has been proposed as a mechanism that can explain the robust behavior of central pattern generating (CPG) neural networks observed experimentally. CPG networks, such as the pyloric network in the stomatogastric ganglion (STG) of the lobster, generate stable patterns of activity in spite of constant molecular turnover and environmental changes. Although the sensing and acting components of regulation are not yet well understood, one likely scenario is that calcium-based activity sensors drive the regulation of intrinsic cellular and synaptic properties.

It has been shown that calcium can help maintain stable activity levels in individual model neurons [1], and pyloric rhythms in one network model [2]. Remaining

questions are: (1) whether calcium sensors work in different network model versions, and (2) what intrinsic properties of calcium sensors are important for distinguishing functional from non-functional activity patterns.

Results

We tested an existing database of about 20 million simplified pyloric networks, constructed by varying the three LP, PY and AB/PD neuron models and their synaptic strengths [3], to see if calcium sensors can distinguish functional pyloric activity. Using a set of three sensors – a fast (F), slow (S) and DC (D) sensor – in each neuron, we reached an 88% success rate. Surprisingly, distinguishing the less restrictive set of pyloric-like networks [3] did not achieve a better rate. Nevertheless, networks with non-pyloric tonically firing neurons were easily distinguished.

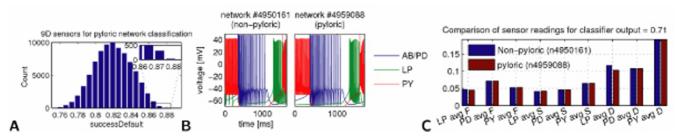


Figure 1 A. Distribution of classification success rates of tested sensor triplets. **B.** Examples of a functional (right) and non-functional (left) model network that were not correctly classified by the activity sensors. **C.** Sensor readings from the undistinguished networks in panel B.

To find properties necessary for these sensors, we constructed a set of 354 sensors with different activation and inactivation rates and sensitivities to calcium. Each of the F, S, D sensors were selected from subsets of these sensors, yielding 85,750 possible F, S, D sensor triplets. Classification performances of pyloric and pyloric-like networks were both normally distributed, reaching a 88.1% success rate (Figure 1A). Incorrect classification was often due to high similarity between pyloric and non-pyloric networks (Figure 1B, C). The slow sensors were found to be most important in distinguishing functional networks: an 83% success rate was reached with one in each neuron. We also determined that the classification performance did not increase with different sensors in each cell compared to identical sensors in each cell. Taken together, our results suggest that activity sensing for homeostatic regulation of the pyloric network can potentially be achieved with relatively few, simple calcium sensors and that the properties of these sensors need not necessarily be adjusted to the particular role of each neuron in the network.

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