Activity-Dependent Homeostatic Plasticity Maintains Circuit-Level Dynamic Properties with Local Activity Information | Lindsay Stolting

Neural circuits are remarkably robust to perturbations that threaten their function, like changing cellular environments and the constant turnover of membrane proteins which dictate their electrical properties. Nowhere is this robustness more evident than in the motor circuits which direct rhythmic behaviors, such as the crustacean stomatogastric ganglion (STG). Not only must STG neurons rhythmically burst, but they must burst in a specific order for the animal's pyloric muscles to function properly in a digestive rhythm. Amazingly, they continue to do so despite various challenges, like temperature change and pharmacological manipulation. Research has attributed this resilience to activity-dependent homeostatic plasticity (ADHP), which prevents the chronic over- or under-activation of individual neurons by up- or down-regulating their ionic currents. Previous work has suggested how such a mechanism, operating on information about single-neuron activity levels, might improve circuit-wide signal propagation and encourage rhythmic bursting by calibrating each neuron's activation function to the magnitude of inputs it receives. But how could such a mechanism maintain other properties that are less directly connected to the average activity of individual neurons, such as burst order? We explored this question in a computational model of the pyloric pattern generator. First, we developed a set of criteria to measure the pyloric character of a pattern generator. We used this measure to optimize a set of pyloric models. Finally, we optimized ADHP mechanisms for these models that could maintain their pyloric character in the face of various parameter perturbations. This proved a relatively easy task for many of our models, suggesting that local information about neural activity levels can indeed be used to maintain circuit-level dynamic properties. We then used our model to more closely examine what makes this possible. Neural activity levels are not necessarily related to pyloric ordering characteristics (i.e. correctly ordered rhythms may have a variety of average activity levels and a given average activity level may occur either for a pyloric rhythm or non-pyloric dynamics). However, in subsets of network parameter space this is not always true. In other words, when only some fraction of possible circuit configurations are considered, there exist average neural activity levels which occur only among pyloric pattern generators and never among non-pyloric ones. ADHP which targets these neural activity levels will therefore be assured to restore pyloricness from a subset of possible perturbations, despite lacking any direct

information about this circuit-level characteristic. This highlights the importance of considering what perturbations homeostatic mechanisms are expected to contend with, and may explain ADHP's success at maintaining functional properties for which individual neural activity is unlikely to be a direct proxy.

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