Functional Relevance of Homeostatic Intrinsic Plasticity in Neurons and Networks

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Abstract

Maintaining the intrinsic excitability of neurons is crucial for stable brain activity. This can be achieved by the homeostatic regulation of membrane ion channel conductances, although it is not well understood how these processes influence broader aspects of neuron and network function. One of the many mechanisms which contribute towards this task is the modulation of potassium channel conductances by activity-dependent nitric oxide signalling. Here, we first investigate this mechanism in a conductance-based neuron model. By fitting the model to experimental data we find that nitric oxide signalling improves synaptic transmission fidelity at high firing rates, but that there is an increase in the metabolic cost of action potentials associated with this improvement. Although the improvement in function had been observed previously in experiment, the metabolic constraint was unknown. This additional constraint provides a plausible explanation for the selective activation of nitric oxide signalling only at high firing rates. In addition to mediating homeostatic control of intrinsic excitability, nitric oxide can diffuse freely across cell membranes, providing a unique mechanism for neurons to communicate within a network, independent of synaptic connectivity. We next conduct a theoretical investigation of the distinguishing roles of diffusive homeostasis mediated by nitric oxide in comparison with canonical non-diffusive homeostasis in cortical networks. We find that both forms of homeostasis robustly maintain stable activity. However, the resulting networks differ, with diffusive homeostasis maintaining substantial heterogeneity in activity levels of individual neurons, a feature disrupted in networks with non-diffusive homeostasis. This results in networks capable of representing input heterogeneity, and linearly responding over a broader range of inputs than those undergoing non-diffusive homeostasis. We further show that diffusive homeostasis interferes less than non-diffusive homeostasis in the synaptic weight dynamics of networks undergoing Hebbian plasticity. Overall, these results suggest a novel homeostatic mechanism for maintaining stable network activity while simultaneously minimising metabolic cost and conserving network functionality.