

Variability, Compensation, Modulation, and Homeostasis in a Rhythmic Neuronal Network

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Neurons and networks must constantly rebuild themselves in response to the continual and ongoing turnover of all of the ion channels and receptors that are necessary for neuronal signaling. A good deal of work argues that stable neuronal and network function arises from homeostatic negative feedback mechanisms. Nonetheless, while these mechanisms can produce a target activity or performance, they are also consistent with a good deal of recent theoretical and experimental work that shows that similar circuit outputs can be produced with highly variable circuit parameters. This work argues that the nervous system of each healthy individual has found a set of different solutions that give “good enough” circuit performance. I will describe a new theoretical model for cellular homeostasis that gives insight into a variety of experimental observations.

Experimental work on the crustacean stomatogastric ganglion (STG) has revealed a 2-6 fold variability in many of the parameters that are important for circuit dynamics. These include the strength of the same synapse across animals, as well as the conductance densities of many membrane currents and the copy numbers of the mRNA that encode those currents (Goaillard et al., Nat Neuroscience. 2009). At the same time, a body of theoretical work shows that the similar network performance can arise from diverse underlying parameter sets (Prinz et al., Nat Neuroscience 2004; Gutierrez and Marder, 2013). Together, these lines of evidence suggest that each individual animal has found a different solution to producing “good enough” motor patterns for healthy performance in the world. These findings raise the question of the extent to which animals with different sets of underlying circuit parameters can respond reliably and robustly to perturbations. Consequently, we studied the effects of temperature and neuromodulation on the pyloric rhythm of crabs. Temperature is a global perturbation that influences every membrane current differently. Nonetheless, we find that all animals respond reliably and robustly to changes in temperature that mimic those the animals ordinarily encounter in their environment (Tang et al PLoS Biol 2010), but more extreme temperature perturbations “crash” the network, resulting in a loss of rhythmic activity (Tang et al, 2012; Rinberg et al., 2013). Each individual “crashes” in different ways, consistent with the underlying variability in parameter structure.