Apparent neuromodulation-dependent correlation levels in neuron ion channel expression result from a competition between passive and active membrane properties.

Neurons and circuits are subject to significant changes in their firing activity and responsiveness to external inputs via neuromodulation (Marder, 2012). Many nervous system functions depend on reliable neuromodulation, yet the physiological properties of neurons that are targeted by neuromodulators are often highly variable (Grashow et al., 2009 ; Marder et al., 2014). In this work, we use conductance-based neuron models to investigate the mechanisms by which neuromodulation can be reliable in variable neurons by tuning correlations in ion channel expression. We show that the correlations required for reliable neuromodulation depends on the type of variability in neuron intrinsic properties. Variability in neuron passive properties such as input resistance results in correlations whose slope is affected by neuromodulation state. Variability in neuron active properties such as voltage-gated channel densities results in correlations of constant slope that are translated by neuromodulation state. As a result, the global correlation level in neurons that are variables in both passive and active properties will appear strongly correlated when correlations due to both variability types are aligned, i.e. when they are of similar slope, and appear to decorrelate as neuromodulation state varies due to a misalignment of correlation slopes.

References

Grashow R, Brookings T, Marder E (2009) Reliable neuromodulation from circuits with variable underlying structure. Proc Natl Acad Sci U S A. 106:11742-6.

Marder E (2012) Neuromodulation of neuronal circuits: back to the future. Neuron. 76:1-11.

Marder E, O'Leary T, Shruti S (2014) Neuromodulation of circuits with variable parameters: single neurons and small circuits reveal principles of state-dependent and robust neuromodulation. Annu Rev Neurosci. 37:329-46.