Science Highlight

A New Mechanism for Fast Regulation of Neuronal Dynamics

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Neuronal spiking activity is the fast and information-dense mode of communication in the nervous system. The timing of spikes carries information, and changes in the patterns of spiking activity can represent changes in information related to memory formation or loss. Traditional mechanisms giving rise to such changes include changes in network connectivity and changes in strength of synapses between neurons. Another, less intensely studied plastic neuronal mechanism is the intrinsic excitability (IE) of neurons, which also is regulated in an activity-dependent manner and can represent a memory. A neuron's IE reflects the complement and magnitude of voltage-gated ionic channels contributing to the subthreshold activity that gives rise to suprathreshold spiking activity.

Birdsong learning is a valuable model system for studying learning and memory, and shares important similarities with speech and language. Both birds and humans monitor their auditory feedback, for example exposure to delayed auditory feedback (DAF) can rapidly induce stuttering in humans and over a longer period of time can induce abnormal syllable morphology and song syntax in songbirds. In both cases these are behaviors with very fast dynamics and a high degree of temporal precision. We have been exploring a new result that gives insight into how the feedback error signal is encoded. Examining the population of "corticostriatal" forebrain neurons known to carry the error signal in zebra finches, we recorded from neurons in a brain slice preparation, so that the activity of neurons is not as dominated by network activity as it is in vivo. Under these conditions, all the neurons from a given bird showed similar neuronal firing patterns to a canonical stimulus, but the firing patterns varied from bird to bird. Similarities between birds, however, were observed in pairs of sibling birds. To refine this result, we observed that the within-bird similarity of neuronal response was disrupted in birds exposed to continuous DAF (cDAF). We also observed that the similarities in firing properties were correlated with similarities in the spike morphology of neurons. For example, in Figure 1, for each of two control birds singing normal songs (top panels), the corticostriatal neurons showed similar spike waveform morphologies, but the morphologies varied between the birds. The spike waveform morphologies were highly disrupted in cDAF birds that experienced singing with abnormal auditory feedback (bottom panels).

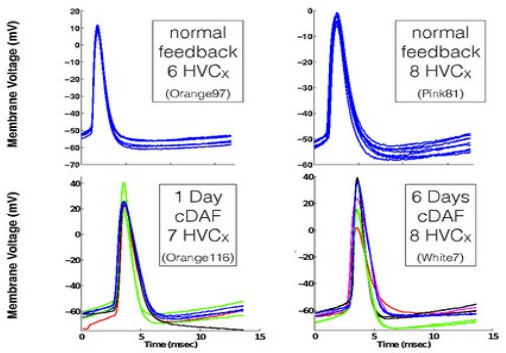

Figure 1. One trace from each corticostriatal neuron recorded from each of four birds. Each trace is the 1st spike emitted in response to 100 pA stimulation. The traces are similar within but differ between each of two control bird (top panels). The cDAF birds, that experienced abnormal auditory feedback during singing, have abnormal spike waveforms and vastly greater variability. Color is to help visualize individual traces.

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Similarities in the IE of neurons from the same bird, and differences in the IE of neurons from the different birds, are likely to underlie the differences in bursting properties and spike waveform morphologies we observed. To gain insight into the mechanisms that give rise to this result, we developed a Hodgkin-Huxley (HH) conductance based model and manually fit the magnitude of five voltage-gated ionic conductances to the spike waveforms for specific values of step currents, achieving good predictions to other step currents and to chaotic current stimuli. Using such HH models to estimate biological parameters is complicated since a range of parameters can appear to reproduce the measured behavior of a neuron. We have therefore been using Beagle to compute the error manifolds for this set of conductances. This massive computation enables us to eliminate potential bias introduced in the labor-intensive manual fitting process. For neurons examined to date, the computations identify global minima (Figure 2). In some cases, the manually determined minimum is near the computed global minimum (Figure 2). In other cases, there is a discrepancy between the two. This arises because manual fitting tends to emphasize shape features of spike morphology whereas the error function used in the error calculations is dominated by the spike heights. Further calculations on Beagle will allow us to explore the sensitivity of the model to different measures of the fitting function.

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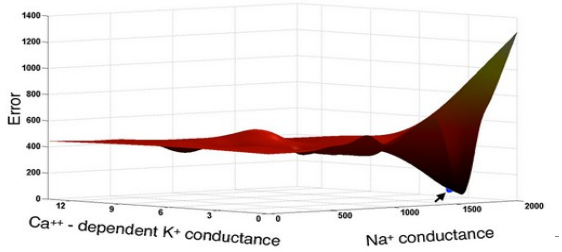

Figure 2. High-resolution error manifold for one neuron. The manually-determined solution (arrow) is near the global minimum.

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