Representation of motoneurons by simple input-output functions

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Abstract: We investigated whether a simple model could accurately represent synaptic processing in adult spinal motoneurons with highly active dendrites. Accurate predictions of the net change in rate of firing of action potentials generated by slow muscle stretch could be accurately predicted using just two measured parameters: the net current reaching the soma (measured during voltage clamp) and the gain of the frequency-current function (measured by injecting current into soma of the cell). However, even with this slowly rising inputs, dynamics in the firing rate were not always accurately matched by the changes in synaptic current.

Although computational power is ever increasing, achievement of a relatively simply neuron model that nonetheless accurately represents the neuron's integration of synaptic input and conversion of this input to spike outputs would have a number of advantages. Neuron models that have many ion channels and complicated architectures are now relatively common, but the many parameters needed to specify these models remain a significant problem. Representation of a neuron by a simple set of equations with few parameters that can be directly and easily obtained from experimental measurements would provide a basis for large scale circuit simulations that not only allow for rapid computations but are also biologically realistic and relatively simple to set up.

The adult spinal motoneuron has been extensively studied in terms of input-output processing, which is appropriate given its role in converting both transient and steady inputs into spike outputs that directly drive muscle fibers. Recordings in vivo from the lumbar spinal cord of the cat revealed the existence of a remarkably simple but accurate model of the steady-state input-output processing of the motoneuron. The input to this model is the net synaptic current reaching the soma of the cell (the effective synaptic current, I_N). The output is defined by the neuron's frequency-current (F-I) function. I_N is measured by applying synaptic inputs during voltage clamp of the motoneuron. The F-I function is measured simply by injecting current into the soma of the cell via the microelectrode. This simple I_N/F-I model has been shown to accurately predict the actual firing rates generated by various synaptic inputs (Binder et al. 1996). Systematic measurements of I_N from many sources and F-I functions (along with measurements of conversion of frequency to force in each motoneuron's muscle fibers) have allowed construction of realistic computer simulations of the steady-state input-output function for an entire motoneuron pool and the whole muscle it controls.

A significant problem with this approach is that the studies of I_N and its coupling to the F-I function were largely carried out in preparations where active dendritic currents are suppressed. However, in the presence of the monoamines serotonin and norepinephrine, the dendrites of spinal motoneurons generate a very strong persistent inward current (PIC) that is highly voltage dependent, sometimes resulting in sustained plateau potentials and bistable behavior (Hounsgaard and Kiehn 1993; Lee and Heckman 2000). An L-type calcium current plays a major role in generating this dendritic PIC (Carlin et al. 2000). The dendritic PIC is particularly important for understanding how motoneurons process input in normal motor behavior because the brainstem centers that are the source of the monoamines are tonically active in the waking state and may also modulate their firing rate some motor tasks. Therefore we investigated how this dendritic PIC influenced conversion of synaptic input to rhythmic firing. Our hypothesis was that if I_N is measured at a holding potential that approximates the average level occurring during rhythmic generation of spikes, then the simple I_N/F-I model would still accurately represent steady-state input-output processing.

Methods: A linearly increasing, predominantly excitatory synaptic input was generated in ankle extensor motoneurons by slow stretch (typically lasting 5 s) applied to the Achilles tendon in the decerebrate cat preparation. The firing pattern evoked by stretch was measured by injecting a steady current to depolarize the cell to threshold for firing. The synaptic current generated at the soma of the cell (i.e. effective synaptic current, I_N) by stretch was measured during voltage clamp. Stretch applied at a depolarized holding potential that approximated the average level during rhythmic firing allowed strong activation of the dendritic PIC, enhancing the I_N evoked by stretch (stretch-evoked $I_{N,ACTIVE}$). Stretch applied at a hyperpolarized holding potential minimized the activation of the dendritic PIC and thus estimated stretch-evoked I_N for a passive dendritic tree (stretch-evoked $I_{N,PASS}$). The F-I function was measured by applying a linear, slowly rising injected current. To predict actual stretch-evoked firing rates using I_N/F-I models, both stretch-evoked $I_{N,ACTIVE}$ an $I_{N,PASS}$ were multiplied by the slope of the F-I function. The resulting predicted firing rate modulation was overlaid on the actual firing rate by matching the initial firing levels. These analyses have been applied in 10 cells thus far.

Results: Predictions of actual stretch-evoked firing based on stretch-evoked $I_{N,PASS}$ consistently underestimated the actual firing rate (typically by 30 to 80%). Predictions based on $I_{N,ACTIVE}$ were much closer to the actual firing rates, typically matching the peak firing rates with errors of 10% or less. The time course of firing was also sometimes well predicted. However, in some low input conductance motoneurons, the rate of rise of firing in response to stretch was inconsistent, sometimes being smoothly graded and other times consisting of a rapid surge. Stretch-evoked $I_{N,ACTIVE}$ was always smoothly graded and thus did not predict the presence of the rapid surges.

Conclusions: The results support the proposed hypothesis that I_N and the F-I function accurately represent motoneuron input-output processing even in the presence of a strong dendritic PIC. However, this accuracy only applies for the net change in firing, because the time course of I_N does not always match the time course of the firing pattern. This mismatch may occur because the dynamics of activation of the dendritic PIC during rhythmic firing are different than during voltage clamp.

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