Text S1. Supplement to "Optimal stimulus shapes for neuronal excitation"

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Calculus of variations for endogenously applied currents

A neuron in the brain is embedded within a network of neurons that are interconnected synaptically. In this section we determine optimal waveforms for stimulating a neuron by requiring that $I_{stim}(t)$ be given by $g_{syn}(t)$ $(V(t) - E_{syn})$, where $g_{syn}(t)$ is a particular type of synaptic conductance, either excitatory or inhibitory, and E_{syn} is the reversal potential of the conductance [1]. As noted in the text, $I_{stim}(t)$ can have both positive and negative phases when it is unconstrained to provide the optimal pathway to spike threshold - exogenous stimulation (Results in text). When $I_{stim}(t)$ is constrained to be given by PSCs, one requirement of the analysis is that $g_{syn}(t)$ cannot be less than 0. We restricted $g_{syn}(t)$ to nonnegative values by using the factor $\exp(g_{syn}(t)\ z)/(1+\exp(g_{syn}(t)\ z))$, where z is a constant having units of $k\Omega\cdot cm^2$. (Conductance in the Hodgkin & Huxley model has units of mS/cm^2). This factor is near zero when $g_{syn}(t)$ is below zero and is sufficiently smooth as a function of time to allow it to be numerically tractable [2]. Any potentially negative portion of the signal is minimized by choosing z to be relatively large. We used $z = 50\ k\Omega\cdot cm^2$. Applying the Euler equations yields

$$2g_{syn}(t) = dI_{stim}(t)/dg_{syn}(t), \quad \text{(S1)}$$

$$g_{syn}(t) = (I_V(E_{syn} - V(t)))\exp(z\, g_{syn}(t))(1 + \exp(z\, g_{syn}(t)) + z\, g_{syn}(t))/(1 + \exp(z\, g_{syn}(t)))^2. \qquad \text{(S2)}$$

The above equations were solved by Newton's method with an initial guess of $(I_V(E_{syn} - V(t))/2)$ where we required a relative error of less than e^{-6}. The rest of the Euler equations are a before (Methods in text) except for the following

$$dI_V/dt = I_V(120\, m^3 h + 0.3 + \exp(g_{syn}(t)z)/(1+\exp(g_{syn}(t)z)) - I_m(d\alpha_m(V)(1-m) - d\beta_m(V)m) - I_n(d\alpha_n(V)(1-n) - d\beta_n(V)n) - I_h(d\alpha_h(V)(1-h) - d\beta_h(V)h). \qquad \text{(S3)}$$

Calculations were carried out to determine optimal signals to bring the model to V = 7.2 mV, m = 0.112, n = 0.3485, and h = 0.5435 for E_{syn} = 25 mV, and V = -3 mV, m = 0.035, n = 0.270, and h = 0.68 for E_{syn} = -25 mV. The results are shown in Figures S1 and S2. For each condition the results are compared with the corresponding $I_{stim}(t)$ obtained for exogenous stimulation as described in Figure 2 of the main text. These two contrasting approaches yield waveforms for the optimal stimulus for eliciting a spike that do not differ substantially, especially for excitatory PSCs (Figure S1).

REFERENCES

1. Destexhe A, Mainen ZF, Sejnowski TJ (1994) Synthesis of models for excitable membranes, synaptic transmission and neuromodulation using a common kinetic formalism. J Comp Neurosci 1:195-230.
2. Forger DB, Paydarfar D (2004) Starting, stopping, and resetting biological oscillators: In search of optimum perturbations. J Theor Biol 230:521-532.