Designing optimal stimuli to control neuronal spike timing

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We develop fast computational methods for optimally designing a natural or artificial stimulus to make a neuron emit a desired spike train. We consider three specific examples of artificial stimulation methods: extracellular electrical stimulation (Salzman et al. 1990), two-photon uncaging of caged neurotransmitters (Nikolenko et al., 2008), and optical activation of genetically implanted light-sensitive ion channels (Han et al. 2007). We also consider the case of optimizing a sensory stimulus (e.g., the spatiotemporal modulation of visual contrast) for this purpose.

We adopt a model based approach, using relatively simple biophysical models which describe how, in the case of each stimulation method, the input affects the spiking activity of the neuron. For example, in the case of photo-stimulation of light-sensitive ion channels, we model how laser light interacts with the ion channels in a neuron and how the latter affect its membrane potential and hence its spiking activity. Depending on the type of the neuron in question, we have used both a conductance based leaky integrator model, and a resonator model inspired by a certain linearization of the Hodgkin-Huxley equations, to describe the membrane potential dynamics. Finally, in the case of sensory stimuli, we use a generalized linear model to effectively capture how the whole upstream sensory network encodes the stimulus in the spike train of the neuron in question.

Based on these models, we solve the reverse problem of finding the best time-dependent modulation of the input that makes the neuron emit a spike train which with highest probability will be close to a target spike train. However, this problem as stated is ill-posed: for example, if we can inject any arbitrary current into a cell, we can simply make the cell fire any desired pattern. Instead, we need to impose constraints on the set of allowed stimuli, as there are limitations on the stimuli we can safely apply in any physiological preparation without damaging the cells or causing other unwanted results. Thus, the task becomes a constrained convex optimization problem. We have developed fast methods for solving such optimization problems (Paninski et al. 2009). These methods can be implemented in real time and are also potentially generalizable to the case of many cells without losing tractability. This makes them suitable for neural prosthesis applications.

Our simulations show that our methods provide an automatic, fast, and stable way of constructing the best possible input. These simulations can also be used to gauge how precisely spike trains can be induced in practice, given realistic values for the constraints such as the maximum allowed magnitude of current, light intensity, etc. We are in the process of experimentally testing these methods on neurons in cortical slices.

Our work is motivated by several possible applications in neuroscience. As an example, our method can be used to produce desired spike trains in a number of selected neurons in some network. Observing the effect of the produced spikes on the subsequent activity in the whole network can then help study its connectivity patterns.