

The Energetic Cost of Fast Spiking

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Brains are metabolically expensive: the human brain comprises only two percent of the body's mass, but consumes nearly twenty percent of the body's energy [1]. Much of that energy consumption is believed to be used to recover the ion fluxes associated with action potential generation [2,3]. The hypothesized high cost of action potential generation has inspired a variety of studies on the efficient use of spikes in neural coding and computation. Relatively little work, however, has been done to examine how neurons might efficiently generate spikes in the first place. In particular, the relationships between the kinetics and densities of the active conductances generating the action potential, and the sodium and potassium fluxes during, and thus the metabolic cost of, the action potential, remain largely unknown.

In addition, the biophysics of spike generation are presumably subject to functional, as well as energetic, constraints. For example, in neocortex, fast-spiking interneurons, compared to pyramidal neurons, express faster potassium currents, and thus generate narrower action potentials; they also spontaneously spike at higher rates *in vivo*, can fire faster trains of action potentials, and can follow faster sine-wave stimuli [4], and their distinctive spike response properties are in part due to this difference in spike shape [5]. Similar relationships between speed of spiking and width of action potential waveform are found in a variety of neural structures, prompting us to ask: inasmuch as narrow spikes are required for the fast-spiking phenotype, what are the energetic costs associated with narrow spiking? Are narrow action potentials strictly required for fast spiking, or are there other biophysical strategies to obtain the fast-spiking phenotype that cells might adopt? What are the energetic costs of these strategies?

First, using Hodgkin-Huxley style models, we predict substantial differences in efficacy and energy efficiency between the various strategies for fast spiking. For example, we find that increasing Na⁺ current density increases the model's maximum spike rate but dramatically increases the current fluxes during spikes; speeding Na⁺ current activation permits faster spiking with little effect on current fluxes during spikes; and speeding K⁺ current activation permits faster spiking, but also increases the cost of singly generated spikes. We then validate a subset of these predictions in cortical fast-spiking interneurons *in vitro* by blocking the cells' Na⁺ conductances with TTX, replacing them with high-rate dynamic clamp, and measuring the cost and speed of spiking as a function of the parameters governing the model sodium conductance. Finally, we compare our predictions regarding the energetically favorable strategies for fast spiking to the actual channel properties observed in faster and slower spiking neurons in a variety of neural systems, and find our hypotheses to be well matched by experimental data.

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References

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