

Modeling the Action Potential of Neurons with Stochastic Sodium Channels
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Introduction

The neuron is the core component of the nervous system and is responsible for transmitting information through the body. A key element of the neuron's function is the action potential, which is an electrical pulse that travels along the cell's axon and triggers further cells. The voltage in a neuron is controlled by chemical- and voltage-controlled ion channels, which control the flow of sodium, potassium, and other ions. When the voltage in a neuron rises high enough to open a majority of the voltage-gated ion channels, ions flood into the cell and an action potential is generated.

The nervous system is extremely relevant in current biomedical research. Neurons are known to control motor functions in the body by sending signals from the brain and spinal cord to muscles and other organs. In patients with spinal injuries, neural commands are issued in the brain, but do not reach limbs or other targets. Neural prosthetics hope to read neural commands from the brain in order to command the function of the arm, leg, or other prosthetic devices.

Background

Hodgkin and Huxley wrote the pioneering paper studying action potentials in 1952 and received a Nobel Prize; in it they attempted to write a set of deterministic equations that describe the in-out characteristics of a general neuron based on measurements performed on a giant squid neuron¹. Their equations modeled the action potential well in terms of duration, amplitude, and other parameters but further research found that some action potentials erupted spontaneously and the model does not account for that. The model of a neuron that emerged was a stochastic adaptation of Hodgkin and Huxley's original equations, which involves modeling the conductance of an ion channel as a Markov process.

The first paper employing stochastic methods was by Strassberg and Defelice in 1993³, and in 1997 Fox used an approximation of Hodgkin and Huxley's equations using Langevin's equation⁴. Mino, Rubinstien, and White compared the methods of Strassberg and Defelice, Fox, and several other authors in a paper in 2002².

Objective

The goals of this project are twofold: to animate the time course of the action potential using computational tools, and to verify the results found in Mino et al, namely those of Strassberg and Defelice and Fox. Choosing an algorithm that produces accurate simulation results in a small amount of time is important to current research, since simulating large networks of neurons is computationally intensive.

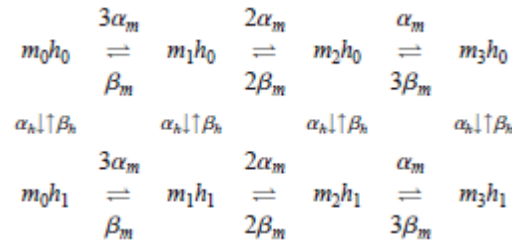
Methods

The current across a membrane is described by

$$C_m \frac{dV_m(t)}{dt} + \frac{V_m(t)}{R_m} + \gamma_{Na} N_{Na}(t) [V_m(t) - E_{Na}] = I_{app}(t)$$

where $I_{app}(t)$ is the applied current, V_m , C_m , and R_m are the voltage, capacitance, and resistance of the membrane, γ_{Na} is the conductance of a sodium channel, and N_{Na} is the number of activated sodium channels. N_{Na} is defined differently for each method.

The Markov process consists of modeling the ion channels as three activating gates with 4 states and one inactivating gate with two states, for a total of 8 states, illustrated in the figure below:



where m's are the states of the three activating gates and h is the state of the inactivating gate. The transition rates α_m , β_m , α_h , and β_h are dependent on membrane voltage, so the current equation and the state transitions are simultaneous equations of voltage. N_{Na} for the Markov process is simply the number of channels in the open state:

$$N_{Na}(t) = N_{m_3h_1}(t)$$

The approximation algorithm takes N_{Na} as

$$N_{Na}(t) = N_{Na}^{max} m^3(t) h(t)$$

where m(t) and h(t) are defined in the differential equations:

$$\begin{aligned}
 \frac{dm(t)}{dt} &= \alpha_m[1 - m(t)] - \beta_m m(t) + g_m(t) \\
 \frac{dh(t)}{dt} &= \alpha_h[1 - h(t)] - \beta_h h(t) + g_h(t)
 \end{aligned}$$

and $g_m(t)$ and $g_h(t)$ are Gaussian random variables.

Simulation of the models involves applying either a small pulse or two-step input to $I_{app}(t)$ in order to trigger an action potential. The output of both models is the number of sodium channels activated and the membrane voltage.

References

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- [4] Fox, R. F. Stochastic versions of the Hodgkin–Huxley equations. Biophys. J. 72:2069–2074, 1997.