Modeling Neuronal Bursting and Stable Low Frequency Firing

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Overview

1. Hodgkin-Huxley Model
2. Modeling Ion Currents
    a. Calcium-gated K^+ Channels & Bursting Activity
3. Works Cited

The Hodgkin-Huxley Model

- Based on observed data
- Used voltage-clamp to measure voltage sensitivity and kinetics of activation and inactivation of voltage-gated Na^+ channels
- Generated a series of differential equations that describe the generation of an action potential
- Only had access to a mechanical calculator

$$I = C_m \frac{\mathrm{d}V_m}{\mathrm{d}t} + \bar{g}_{\mathrm{K}} n^4 (V_m - V_K) + \bar{g}_{\mathrm{Na}} m^3 h (V_m - V_{Na}) + \bar{g}_l (V_m - V_l),$$

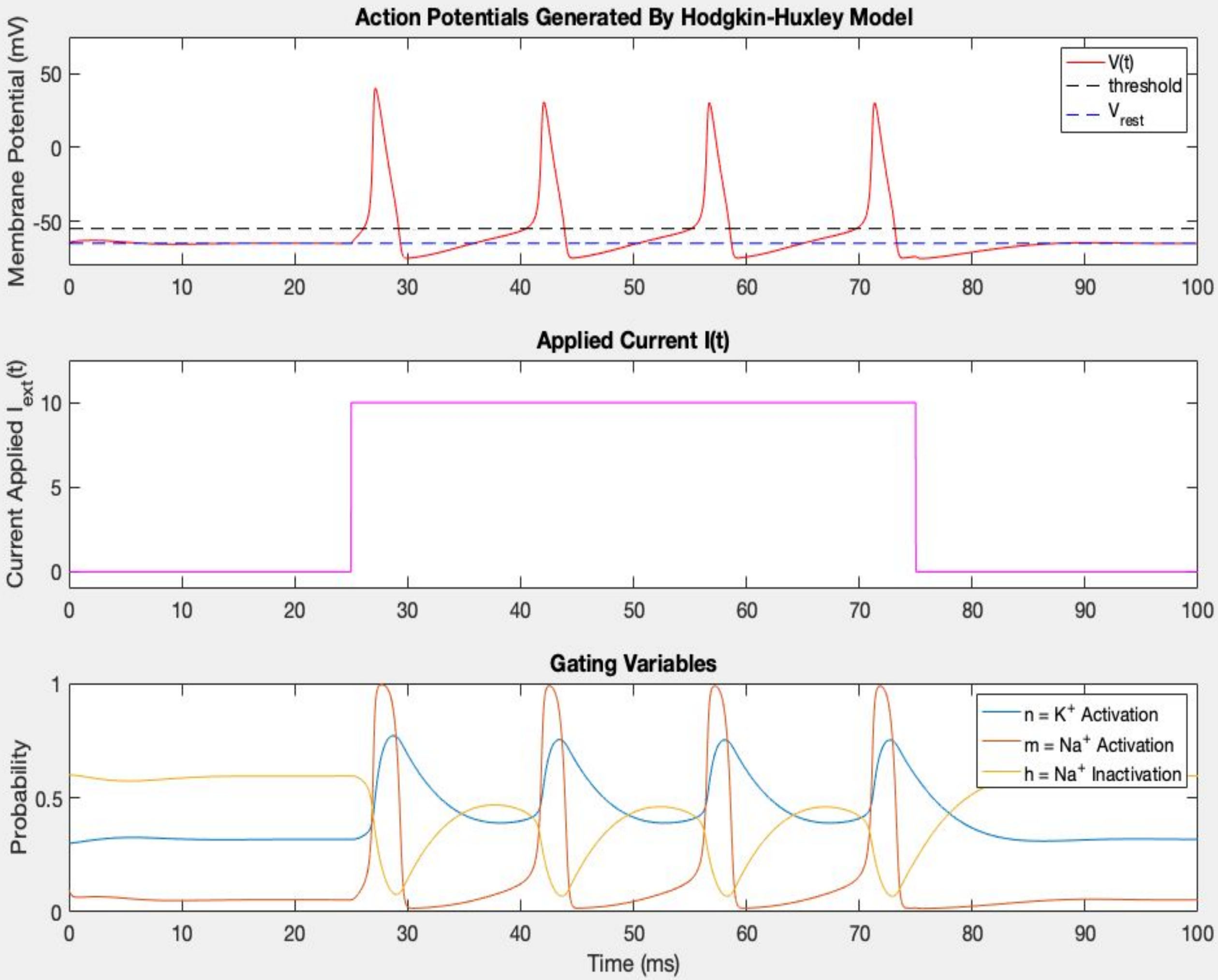
$$\frac{dn}{dt} = \alpha_n(V_m)(1 - n) - \beta_n(V_m)n$$

$$\frac{dm}{dt} = \alpha_m(V_m)(1 - m) - \beta_m(V_m)m$$

$$\frac{dh}{dt} = \alpha_h(V_m)(1 - h) - \beta_h(V_m)h$$

$$\alpha_p(V_m) = p_\infty(V_m)/\tau_p$$

$$\beta_p(V_m) = (1 - p_\infty(V_m))/\tau_p.$$



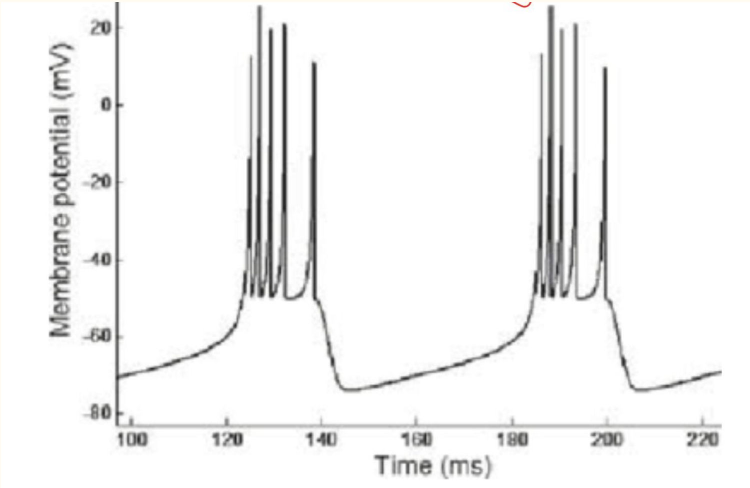
Comments

- Stimulating current of 10nA applied at 25ms and removed at 75ms
- 4 action potentials generated
- Gating activity plotted below

Ca^{2+} Gated K^{+} Channels and Bursting Activity

Mechanism:

- Action potentials reach pre-synaptic terminal
- V-Ca^{2+} channels open, calcium flows into cell, eventually accumulates
- High Ca^{2+} activates calmodulin, subsequently stimulates K^{+} channel
- K^{+} current hyperpolarizes cell and prevents membrane potential from reaching threshold



Modeling Ca^{2+} Gated K^{+} Channels

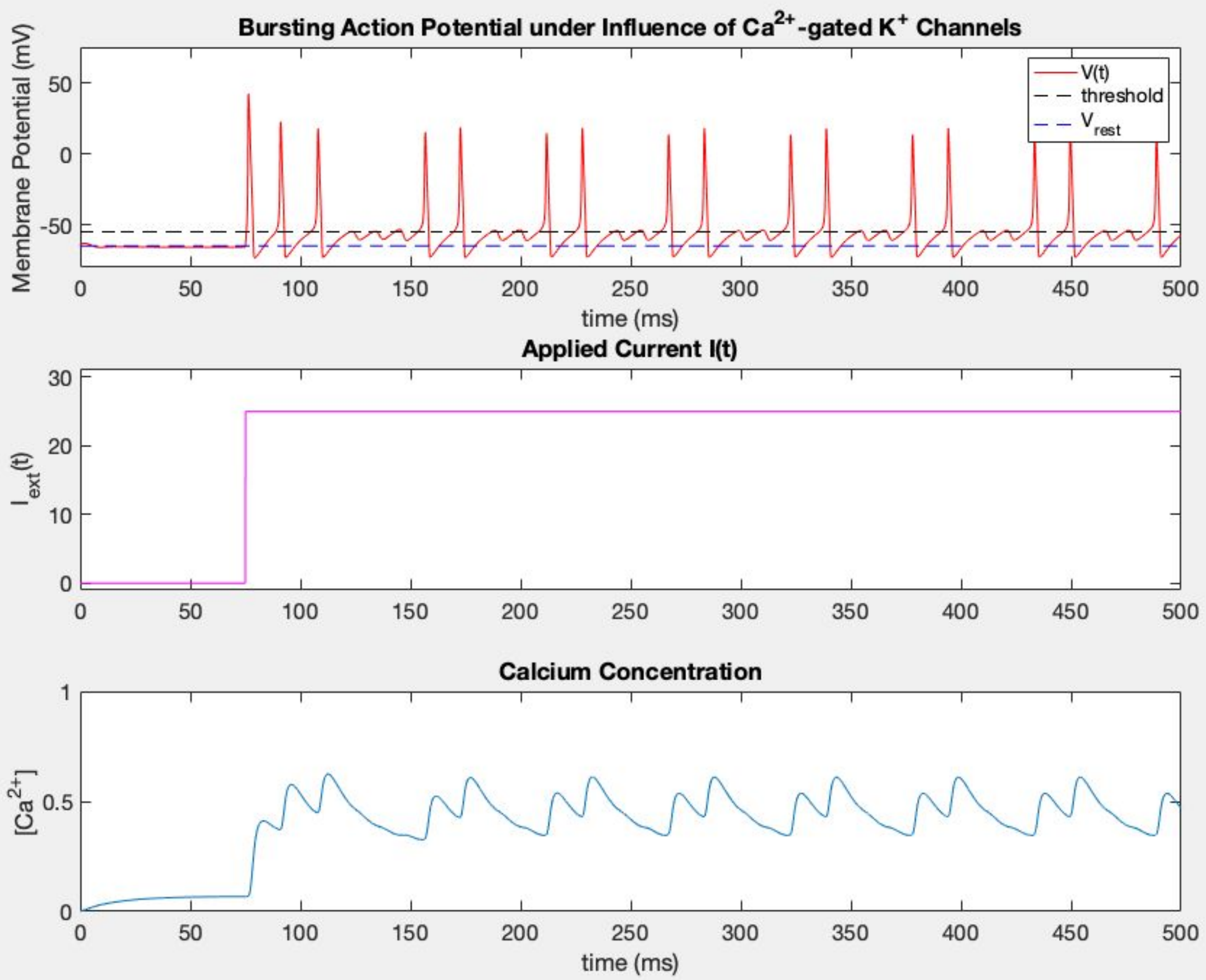
- Assumptions
  - V-gated Ca^{2+} channels behave similarly to V-gated K^{+}; slow inactivation
  - Ca^{2+} entry proportional to Ca^{2+} current
  - Ca^{2+} removal follows exponential decay

$$\frac{d[Ca^{2+}]}{dt} = k * n^4 \bar{g}_{Ca}(V_{Ca} - V_m) - \frac{1}{\tau_{Ca}} * [Ca^{2+}]$$

V-K^{+} gating variable

Max Ca^{2+} conductance

Rate (time constant) for Ca^{2+} removal


Bursting Action Potential under Influence of Ca2+-gated K+ Channels
Membrane Potential (mV)
V(t)
threshold
Vrest
time (ms)
Applied Current I(t)
Iext(t)
Calcium Concentration
[Ca2+]
time (ms)

Comments

Works Cited

Amberg, Gregory C., et al. "A-Type Potassium Currents in Smooth Muscle." *American Journal of Physiology-Cell Physiology*, vol. 284, no. 3, 1 Mar. 2003, doi:10.1152/ajpcell.00301.2002.

McCormick, David A. "Hodgkin-Huxley Model." *Hodgkin-Huxley Model - an Overview* | *ScienceDirect Topics*, 2014, www.sciencedirect.com/topics/neuroscience/hodgkin-huxley-model.

Miller, Paul. *An Introductory Course in Computational Neuroscience.* The MIT Press, 2018.

Xia, X.-M., et al. "Mechanism of Calcium Gating in Small-Conductance Calcium-Activated Potassium Channels." *Nature News*, Nature Publishing Group, 1 Oct. 1998, www.nature.com/articles/26758.