Parallel Computing of Action Potentials in the Hodgkin-Huxley Model via the Parareal Algorithm

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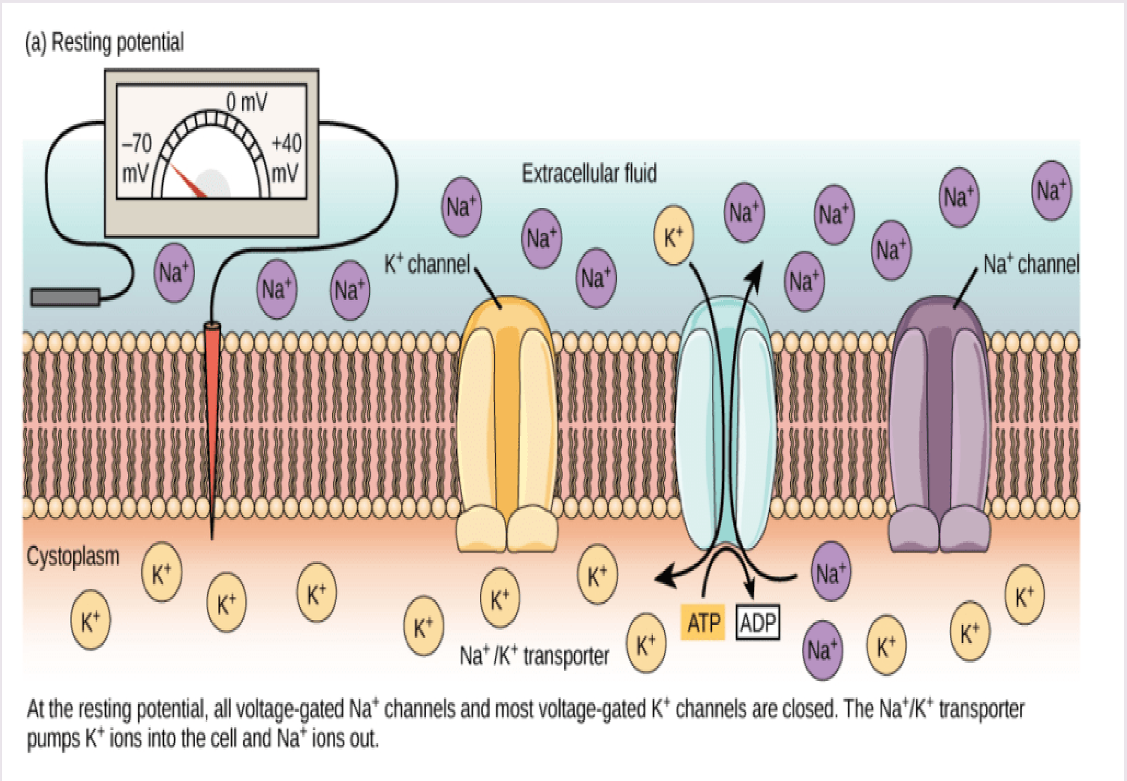
Abstract

The Hodgkin-Huxley model [2] is a system of differential equations that describe the membrane voltage of an axon as it fires the basic signal of the nervous system: the action potential. When charge-carrying ions such as sodium and potassium are enabled to cross a selectively permeable membrane, the resulting current propagates along the length of the axon as a wave of altered voltage. However, the degree to which the membrane is permeable to sodium and potassium is itself gated by voltage; therefore, voltage depends on permeability and permeability depends on voltage.

Hodgkin-Huxley Model



https://jackwestin.com/resources/mcat-content/plasma-membrane/membrane-potential

Voltage-gated channels can open or close and allow a surge of Sodium and Potassium ions to pass through. Voltage and current in the system are caused by charged ions moving across the membrane.

$$\frac{dV}{dt} = \frac{(\bar{g}_{K^+})n^4(V-V_K)+(\bar{g}_{Na^+})m^3h(V-V_{Na})+\bar{g}_l(V-V_l)}{-C_m} \quad (1)$$

$$\frac{dm}{dt} = \alpha_m(1-m) - \beta_m m \quad (2)$$

$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n \quad (3)$$

$$\frac{dh}{dt} = \alpha_h(1-h) - \beta_h h \quad (4)$$

i	$\alpha_i(V)$	$\beta_i(V)$
m	$\frac{2.5+0.1V}{e^{2.5+0.1V}-1}$	$4e^{\frac{V}{18}}$
n	$\frac{0.1+0.01V}{e^{1+0.1V}-1}$	$0.125e^{\frac{V}{80}}$
h	$0.07e^{\frac{V}{20}}$	$\frac{1}{1+e^{3-0.1V}}$

I: Total membrane current density (inward current positive) ($\mu A/cm^2$)
$\mathbf{I}_i$: Ionic current density (inward current positive) ($\mu A/cm^2$)
V: Displacement of the membrane potential from its resting value (depolarization negative) (mV)
C_M: Membrane capacity per unit area (assumed constant) ($\mu F/cm^2$)
t: Time (ms)
α_i and β_i: Rate constants for the *i*-th ion channel

Na^+: Sodium
K^+: Potassium
l: Leak
g: Conduction ($m.mho/cm^2$)
$\bar{\mathbf{g}}$: Maximal value of the conductance ($m.mho/cm^2$)
n, m, and h: Dimensionless quantities between 0 and 1 (i.e. proportions) that are associated with Potassium channel activation, Sodium channel activation, and Sodium channel inactivation

Computational Methods

Forward Euler Method [1] - *Fast, but inaccurate*

$x_{i+1} = x_i + [\alpha_{x_i} * (1 - x_i) - \beta_{x_i} * x_i] * dt$ for $x = m, n, h$

$V_{i+1} = V_i + \left[I_i * \frac{1}{C_M}\right] * dt$

For $I_i = (I_{Total})_i - (\bar{g}_{Na^+})(m_i^3)(h_i)(V_i - V_{Na}) - (\bar{g}_{K^+})(n_i^4)(V_i - V_K) - \bar{g}_l(V_i - V_L)$

RK4 Method [1] - *Accurate, but more expensive*

$x_{i+1} = x_i + [k_{1x_i} + 2k_{2x_i} + 2k_{3x_i} + k_{4x_i}] * \frac{1}{6} * dt \;\; for\, x = m, n, h, V$

With k_{jx_i} $For\ j = 1,2,3,4\ and\ x = m, n, h, V$ are calculated as:

$k_{jx_i} = [\alpha_{x_i} * (1 - (x_{now})_i) - \beta_{x_i}(x_{now})_i]$ for $x = m, n, h.$

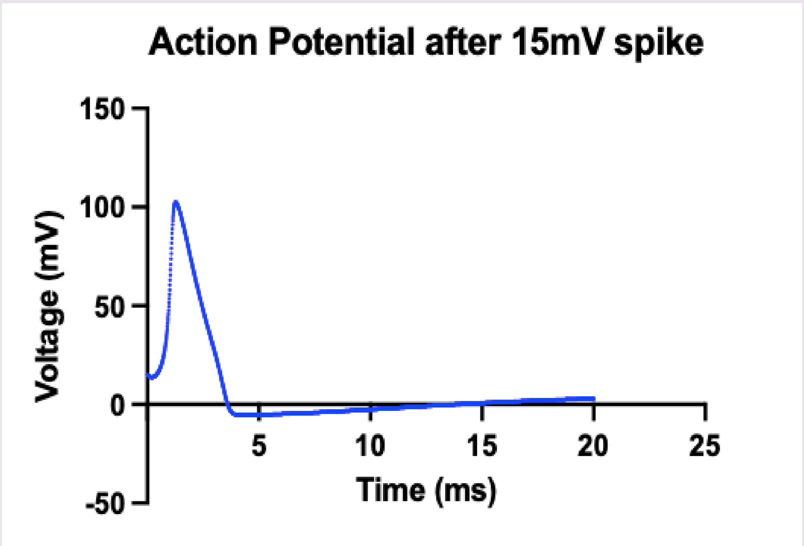
$k_{jx_i} = \left[I_i * \frac{1}{C_M}\right]$ $for\, x = V.\ We\ have\ I_i$ are calculated as:

$I_i = (I_{Total})_i - (\bar{g}_{Na^+})(m_{now}^3)_i(h_{now})_i((V_{now})_i - V_{Na}) - (\bar{g}_{K^+})(n_{now}^4)_i((V_{now})_i - V_K) - \bar{g}_l((V_{now})_i - V_L)$

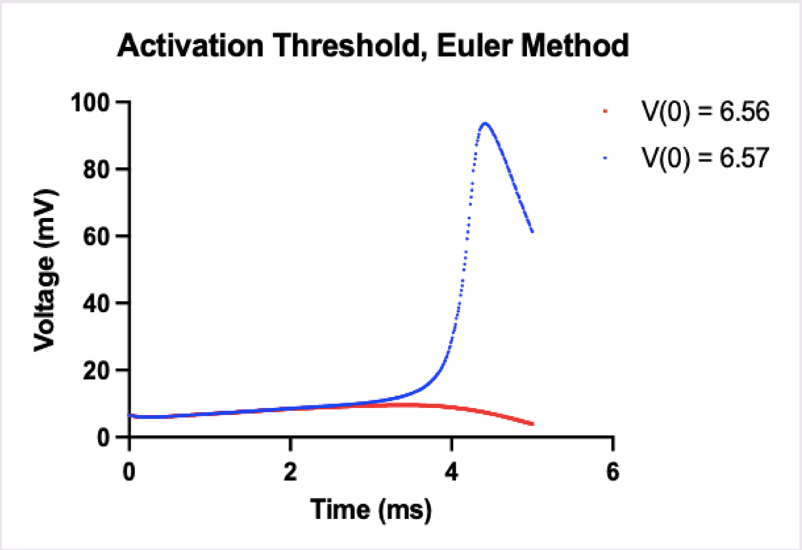
Table of $(x_{now})_i$. For $x = m, n, h, V.$

$j=1$	$(V_{now})_i = V_i$	$(m_{now})_i = m_i$	$(n_{now})_i = n_i$	$(h_{now})_i = h_i$
$j=2$	$(V_{now})_i = V_i + 0.5k_{1V_i}$	$(m_{now})_i = m_i + 0.5k_{1m_i}$	$(n_{now})_i = n_i + 0.5k_{1n_i}$	$(h_{now})_i = h_i + 0.5k_{1h_i}$
$j=3$	$(V_{now})_i = V_i + 0.5k_{2V_i}$	$(m_{now})_i = m_i + 0.5k_{2m_i}$	$(n_{now})_i = n_i + 0.5k_{2n_i}$	$(h_{now})_i = h_i + 0.5k_{2h_i}$
$j=4$	$(V_{now})_i = V_i + k_{3V_i}$	$(m_{now})_i = m_i + k_{3m_i}$	$(n_{now})_i = n_i + k_{3n_i}$	$(h_{now})_i = h_i + k_{3h_i}$

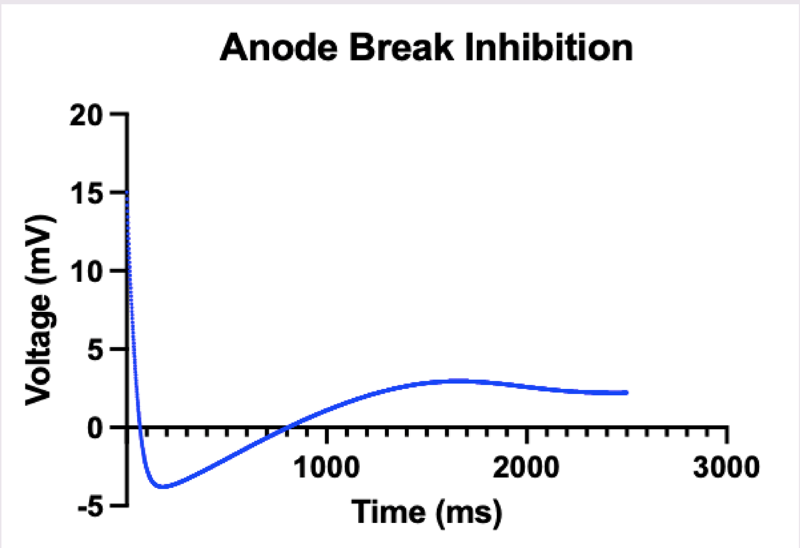
Numerical Experiments



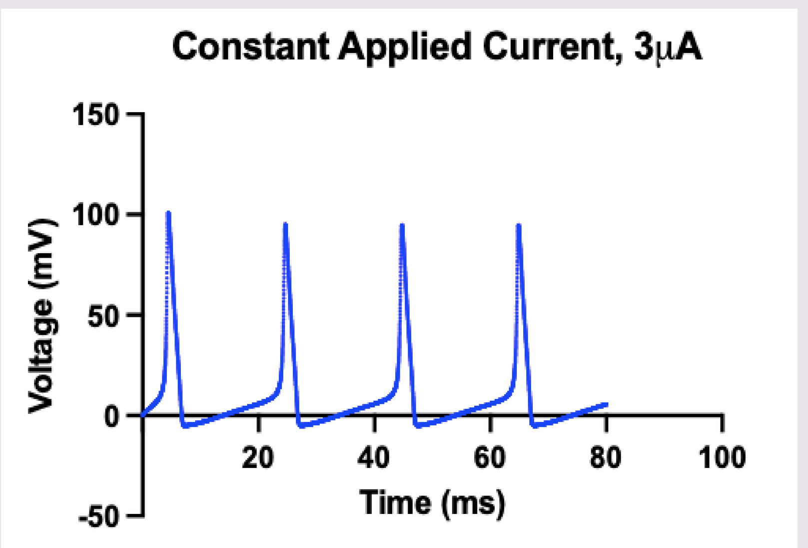
Numerical approximation of an action potential in the Hodgkin-Huxley model after a millisecond-long depolarization of 15mV.



Initial depolarizations below the excitation threshold return to rest without activation. For the same initial parameters, the threshold for the RK4 method falls between 6.61mV and 6.62mV.



Produced by holding the voltage at 15mV for an indefinite time and then releasing it. Holding voltage above the steady state value causes the excitation value to shift upward such that voltages normally above the threshold may return to rest without activation. Similarly, holding the voltage below rest shifts the activation threshold below rest.



Constant current can often be used to model the input for biological systems. Repeated activations show the minimum time between action potentials due to a refractory period in which no additional activity can occur. Additionally, the voltage peak for the first activation is slightly higher than subsequent values.

Parareal Algorithm

The Parareal Algorithm is a unique parallel-in-time algorithm, developed by Lions, Maday, and Turinici in 2001 [3]. It uses sequential numerical methods running at different time discretizations. The algorithm converges to the result obtained by the sequential method, but can achieve significant time savings [4].

- Achieves time savings by solving sections at the same time using multiple CPUs.
- Utilizes two temporal discretizations – one coarse, running in sequential; and one fine, running in parallel, to solve the problem.
- Predictor-corrector algorithm generates reasonable starting values for parallel computing carried out on all time slices simultaneously.
- Converges to a solution over multiple iterations with lower overall running time than an equivalent sequential computation.

Tolerance (mV)	Iterations (47 max)
10^{-5}	3
10^{-6}	4
10^{-7}	4
10^{-8}	5

- Preliminary estimations for a 48-CPU system.
- At 47 iterations time savings is negative compared to sequential calculations, but the Parareal algorithm finishes well before then.
- At massively increased CPU counts (100, 200, etc.), iteration count seems to fall around ~1/100th at this tolerance level.

Conclusion

In conclusion, our numerical methods show high agreement with Hodgkin and Huxley's findings. It shows a number of behaviors dependent on starting conditions that appear consistent with biological reality. The threshold of activation that we found using the Hodgkin-Huxley model does line up with Hodgkin and Huxley's calculated results, but does not line up with the biological experimentally based results. Even though there are values for which the model deviates from biological behaviors, the model has reasonable predicted value for a variety of starting values.

References

[1] Burden, Richard L., and J. Douglas Faires. *Numerical Analysis*. Thomson Brooks/Cole, 2005.
[2] Hodgkin, A L, and A F Huxley. "A Quantitative Description of Membrane Current and Its Application to Conduction and Excitation in Nerve." *Bulletin of Mathematical Biology*, vol. 52, no. 1-2, 1990, pp. 500–544., doi:10.1016/s0092-8240(05)80004-7.
[3] Jacques-Louis Lions, Yvon Maday, Gabriel Turinici. Résolution d'EDP par un schéma en temps <pararéel >. Comptes rendus de l'Académie des sciences. Série I, Mathématique, Elsevier, 2001, 332(7), pp.661-668. hal-00798372
[4] Staff, Gunnar A. *The Parareal Algorithm*, 2003, pp. 3–25.