ODE Simulation: Hodgkin-Huxley Action Potential Model

MATH 7205-Fall 2020

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Presentation Outline

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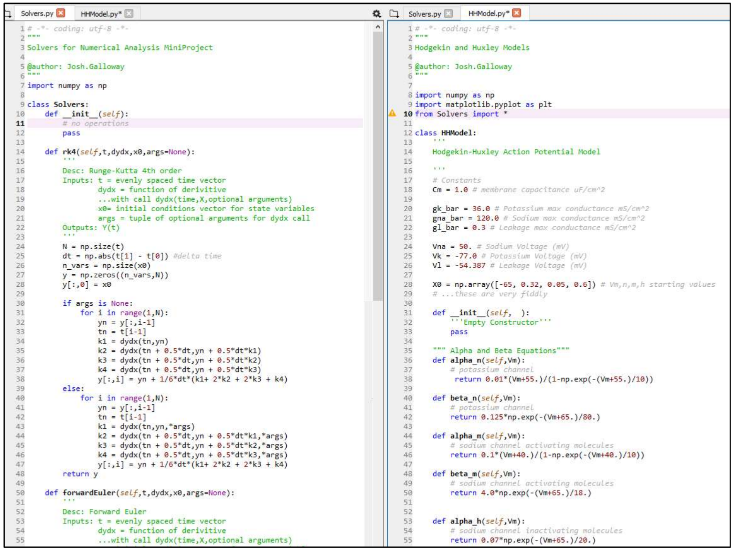
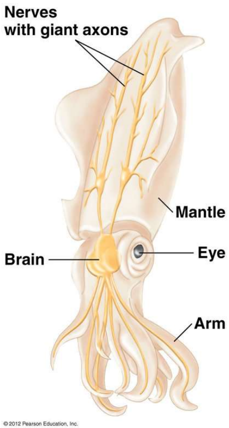
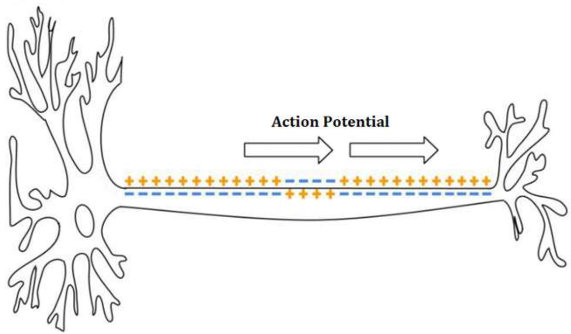


Introduction

Hodgkin-Huxley Model:

- Created in 1952 to explain the ionic mechanisms underlying the initiation and propagation of action potentials in the squid giant axon
- Received the Nobel Prize in Physiology and Medicine for this work in 1963
- Electrical model of action potentials in neurons created from experiments on squid giant axons
- Set of 4 non-linear Autonomous ODE‘s





References: [1], [2], [3]

Model

System of Equations

Nonlinear ODE's

$$I = C_m \frac{dV_m}{dt} + \bar{g}_K n^4 \left(V_m - V_K\right) + \bar{g}_{Na} m^3 h \left(V_m - V_{Na}\right) + \bar{g}_L \left(V_m - V_L\right)$$

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

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

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

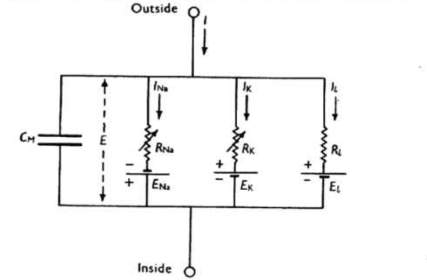


Fig. 1. Electrical circuit representing membrane. $R_{Na} = 1/g_{Na}$; $R_K = 1/g_K$; $R_l = 1/\bar{g}_l$. R_{Na} and R_K vary with time and membrane potential; the other components are constant.

PDE

$$\frac{a}{2R_2} \frac{\partial^2 V_m}{\partial x^2} = C_m \frac{dV_m}{dt} + \bar{g}_K n^4 \left(V_m - V_K\right) + \bar{g}_{Na} m^3 h \left(V_m - V_{Na}\right) + \bar{g}_L \left(V_m - V_L\right)$$

where,

- Na, K, L are sodium, potassium and leakage channel subscripts (i-th ion channel)
- I total current density, I_i channel current density for the i-th ion channel
- C_m membrane capacitance
- V_m voltage across membrane, V_i channel voltage for the i-th ion channel
- α_i and β_i are rate constants for the i-th ion channel
- $\bar{g}_i$ is the maximal value of the conductance for the i-th ion channel
- n, m, and h are dimensionless quantities between 0 and 1 that are associated with potassium channel activation, sodium channel activation, and sodium channel inactivation, respectively
- a axon fibre radius
- R_2 axoplasm specific resistance

 [1]

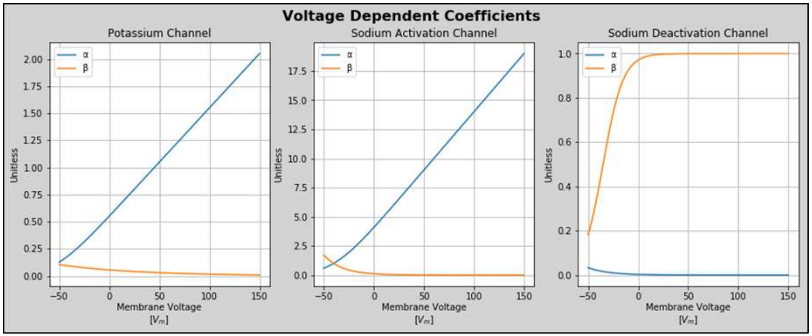
Model (continued)

Functions α and β Voltage Dependant Coefficients

$$\alpha_n(V_m) = \frac{0.01 \cdot (V_m + 55)}{1 - exp(\frac{V_m+55}{10})} \qquad \beta_n(V_m) = 0.125 \cdot exp\left(\frac{-(V_m+65)}{80}\right)$$

$$\alpha_m(V_m) = \frac{0.1 \cdot (V_m + 40)}{1 - exp(\frac{-(V_m+40)}{10})} \qquad \beta_m(V_m) = 4 \cdot exp\left(\frac{-(V_m+65)}{18}\right)$$

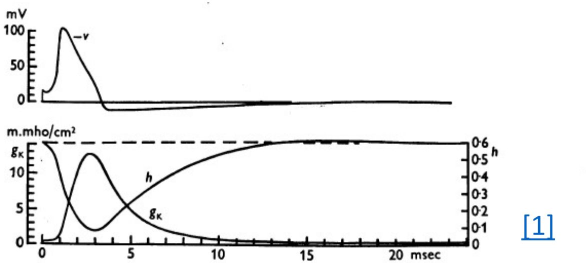
$$\alpha_h(V_m) = 0.07 \cdot exp\left(\frac{-(V_m+65)}{20}\right) \qquad \beta_h(V_m) = \left(1 + exp(\frac{-(V_m+35)}{10})\right)^{(-1)}$$



Parameters Used	Capacitance [uF/cm^2]	V_i [mV]	$\bar{g}_i$ [mS/cm^2]	Initial Values
Membrane	1.0	--	--	$V_m = -65$
Potassium Channel	--	-77.0	0.5	$n = 0.32$
Sodium Activation	--	50.0	120.0	$m = 0.05$
Sodium Deactivation	--	50.0	120.0	$h = 0.6$
Leakage Channel	--	-54.387	0.3	--

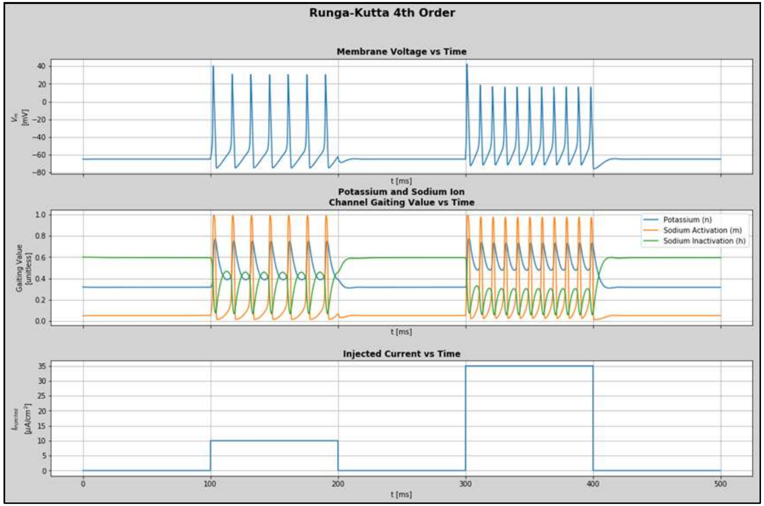
Simulation

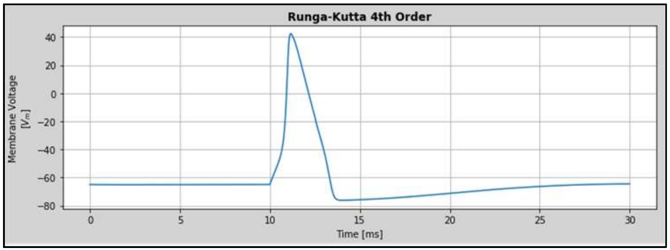
- Forward Euler, Huen's Method, and 4th Order Runga-Kutta Implemented from Scratch in Python using Numpy

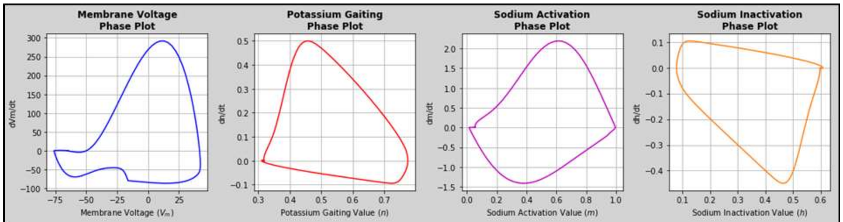


[1]

Fig. 19. Numerical solution of eqn. (26) for initial depolarization of 15 mV and temperature of 6° C. Upper curve: membrane potential, as in Fig. 13. Lower curves show time course of g_K and h during action potential and refractory period.

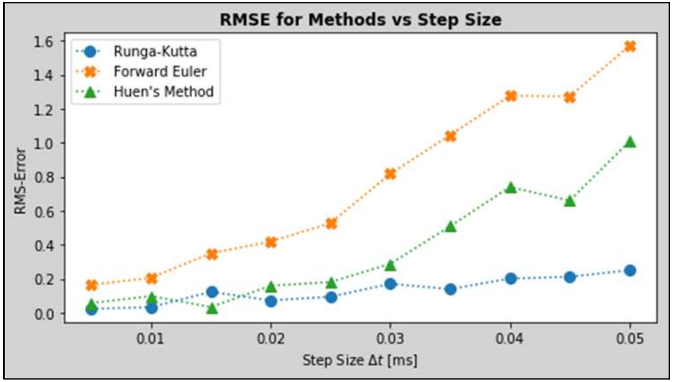


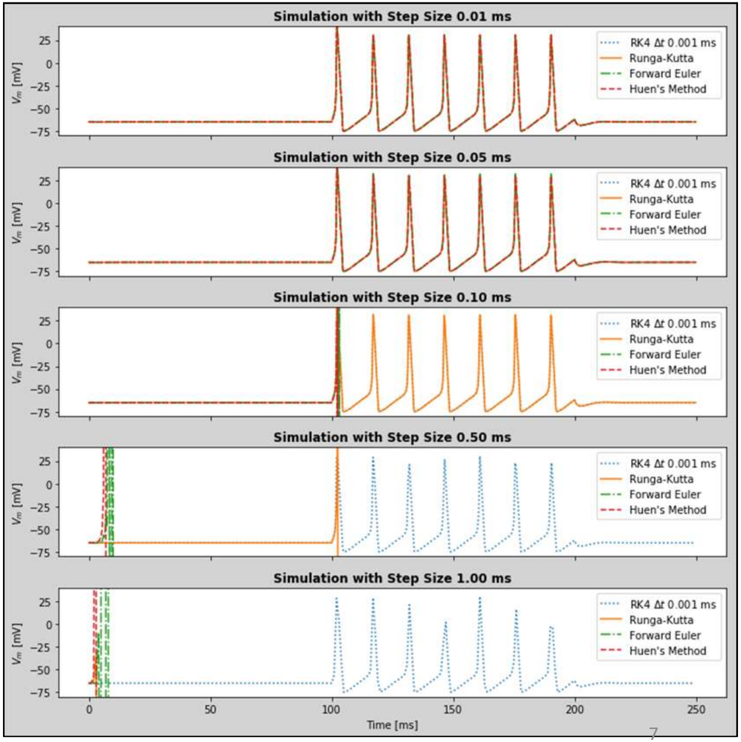




Stability and Accuracy

- Vary Step Size for Simulation and Observe when the Methods become Unstable
- Compare Each Simulation to a Benchmark of Runga-Kutta 4th Order with a Step Size of 0.001 ms
- Calculate the Root Mean Squared Error for Step Sizes in [0.005,0.05] and Compare Against the Benchmark





Conclusion

We Saw…

Model

- Electrical Circuit, Model Equations

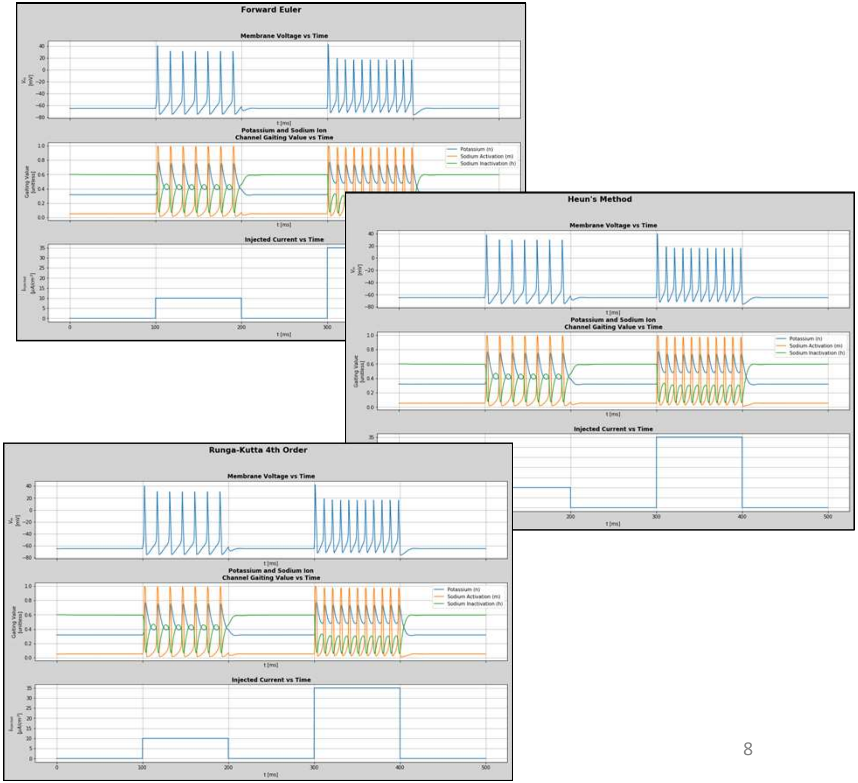
Simulation

- Forward Euler, Huen’s Method, Runga-Kutta 4^{th} Order
- Simulations all Matched the Original Paper with Proper Parameter Selection

Stability and Accuracy

- Runga-Kutta Performed Best in both Stability and Accuracy followed by Huen’s Method then Forward Euler as would be Expected

Questions?....



References

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