Simulation of the Hodgkin-Huxley Model

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Introduction

This assignment is a simulation of the Hodgkin-Huxley Model, which is an electrical RC circuit modelling the action potential in a neuron, more specifically, the giant squid axon, which Hodgkin and Huxley worked on, in their research paper. Hence, the constant values used in the code, pertain to the above-mentioned research paper.

Simulation Method

While the Hodgkin-Huxley model is a first-order differential equation that resembles an RC circuit, the fact that the conductance of the sodium and potassium channels vary with the voltage across the cell membrane in a rather sigmoid manner means that this equation cannot be analytically solved. Hence, this assignment solves the differential equation numerically by using the **Exponential Euler Rule**, given that the functions dealt with in this model are exponential decaying functions.

Exponential Euler Rule

The exponential Euler rule states that, given a first order differential equation of the form

$$\frac{dy}{dx} = A - By$$

We can use the following recurrence relation to numerically approximate the solution for the differential equation

$$y_{i+1} = y_i e^{-\Delta x} + \frac{A}{B}(1 - e^{-B\Delta x})$$

where Δx is the timestep of the simulation, and A and B are functions of the independent variable.

The given set of differential equations may look complex, but upon expansion, they appear to fit the above form of differential equation.

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

$$= \alpha_n(V) - (\alpha_n(V) + \beta_n(V))n$$

Here, $A = \alpha_n(V)$ and $B = \alpha_n(V) + \beta_n(V) = \frac{1}{\tau_n}$

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

$$= \alpha_h(V) - (\alpha_h(V) + \beta_h(V))h$$

Here, $A = \alpha_h(V)$ and $B = \alpha_h(V) + \beta_h(V) = \frac{1}{\tau_h}$

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

$$= \alpha_m(V) - (\alpha_m(V) + \beta_m(V))m$$

Here, $A = \alpha_m(V)$ and $B = \alpha_m(V) + \beta_m(V) = \frac{1}{\tau_m}$

The actual differential equation

$$C_m\frac{dV}{dt} = \bar{G}_{Na}m^3h(E_{Na} - V) + \bar{G}_K n^4(E_K - V) + G_m(V_{rest} - V) + I_{inj}(t)$$

can be rewritten as

$$\frac{dV}{dt} = (\frac{\bar{G}_{Na}m^3hE_{Na} + \bar{G}_K n^4 E_K + G_m V_{rest}}{C_m}) - (\frac{\bar{G}_{Na}m^3h + \bar{G}_K n^4 + G_m}{C_m})V$$

Here, $A = \frac{\bar{G}_{Na}m^3hE_{Na} + \bar{G}_K n^4 E_K + G_m V_{rest}}{C_m}$ and $B = \frac{\bar{G}_{Na}m^3h + \bar{G}_K n^4 + G_m}{C_m}$

The timestamp chosen in the simulation is $0.1ms$ and the duration of the simulation is $100ms$, hence there are $\frac{100ms}{0.1ms} = 1000$ iterations in the simulation.

Estimation of Quantities

The rheobase and superthreshold were empirically determined from the simulation by varying the input current and observing the peak(s) of the action potential.

Rheobase

The rheobase was observed to be $2.2459\mu A$ for an area of $1cm^2$ (from the code). From this, the current density is $2.2459\mu A/cm^2$. Hence, for a patch of area $900\pi\mu m^2$, the rheobase comes out to be $2.2459\mu A/cm^2 \times 900\pi(10^{-4}cm)^2 = 0.0635nA$. This is close to the rheobase given in the reading material on the Hodgkin-Huxley model ($0.065nA$). The corresponding plot can be found under the Relevant Plots section.

Superthreshold

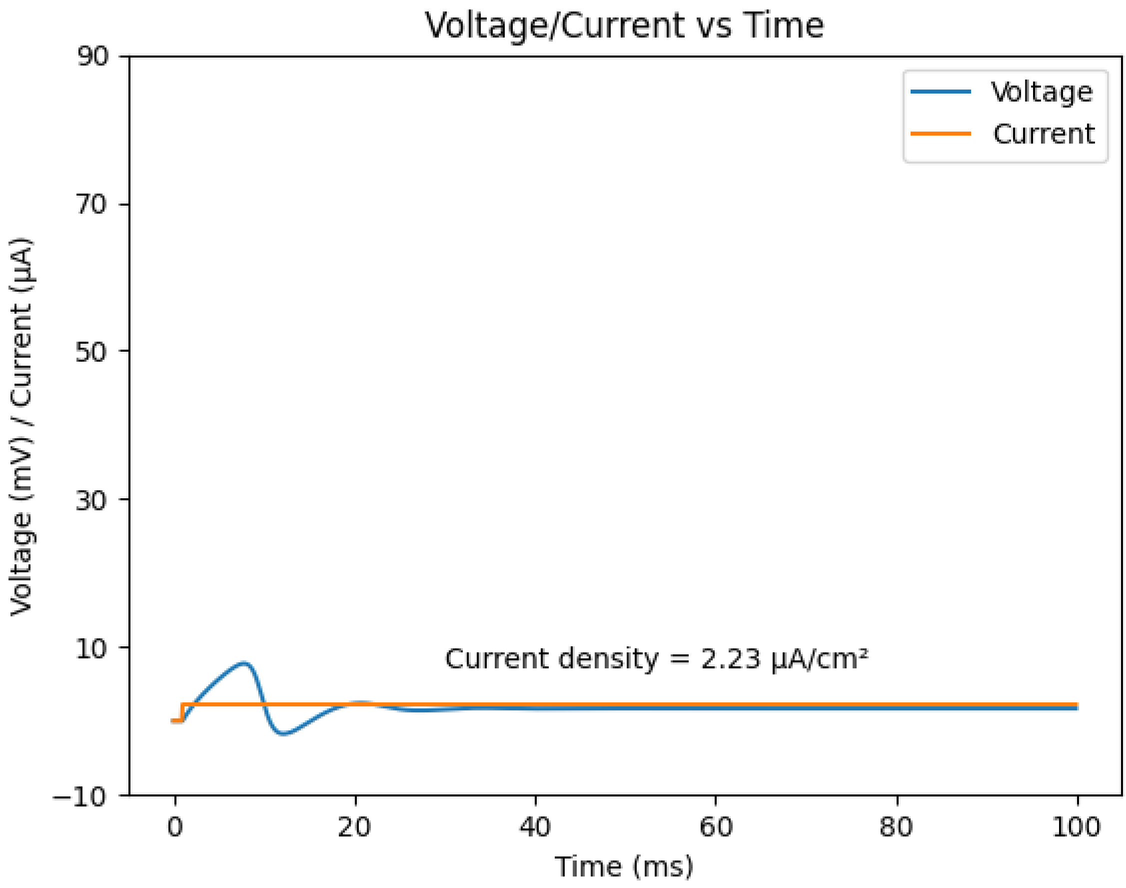
The superthreshold current was observed to be $6.2495\mu A$ for an area of $1cm^2$ (from the code). From this, the current density is $6.2495\mu A/cm^2$. Hence, for a patch of area $900\pi\mu m^2$, the rheobase comes out to be $2.2459\mu A/cm^2 \times 900\pi(10^{-4}cm)^2 = 0.1767nA$. The corresponding plot can be found under the Relevant Plots section.

f-I curve

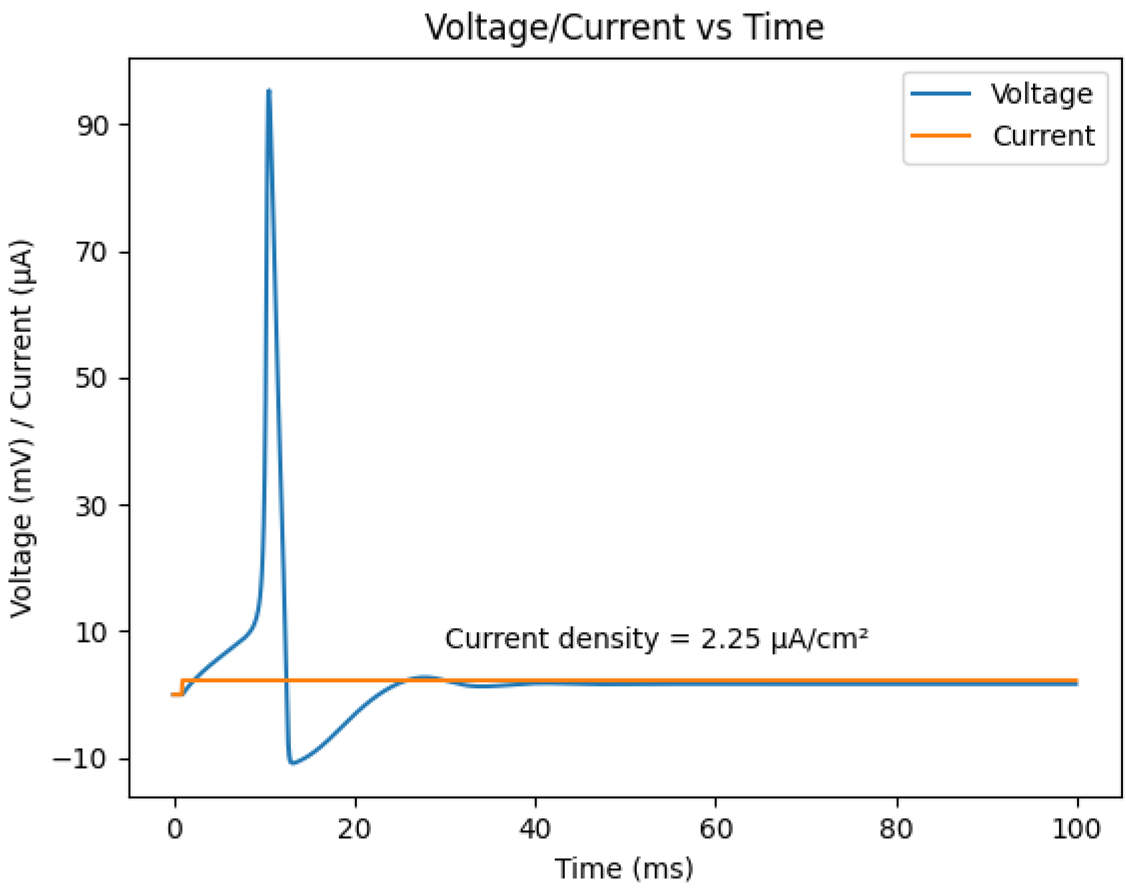
The f-I curve was empirically arrived at by varying the current (density) and manually finding out the (average) time period between two action potentials, then plotting a graph with the resulting data. The corresponding plot can be found under the Relevant Plots section.

Relevant Plots

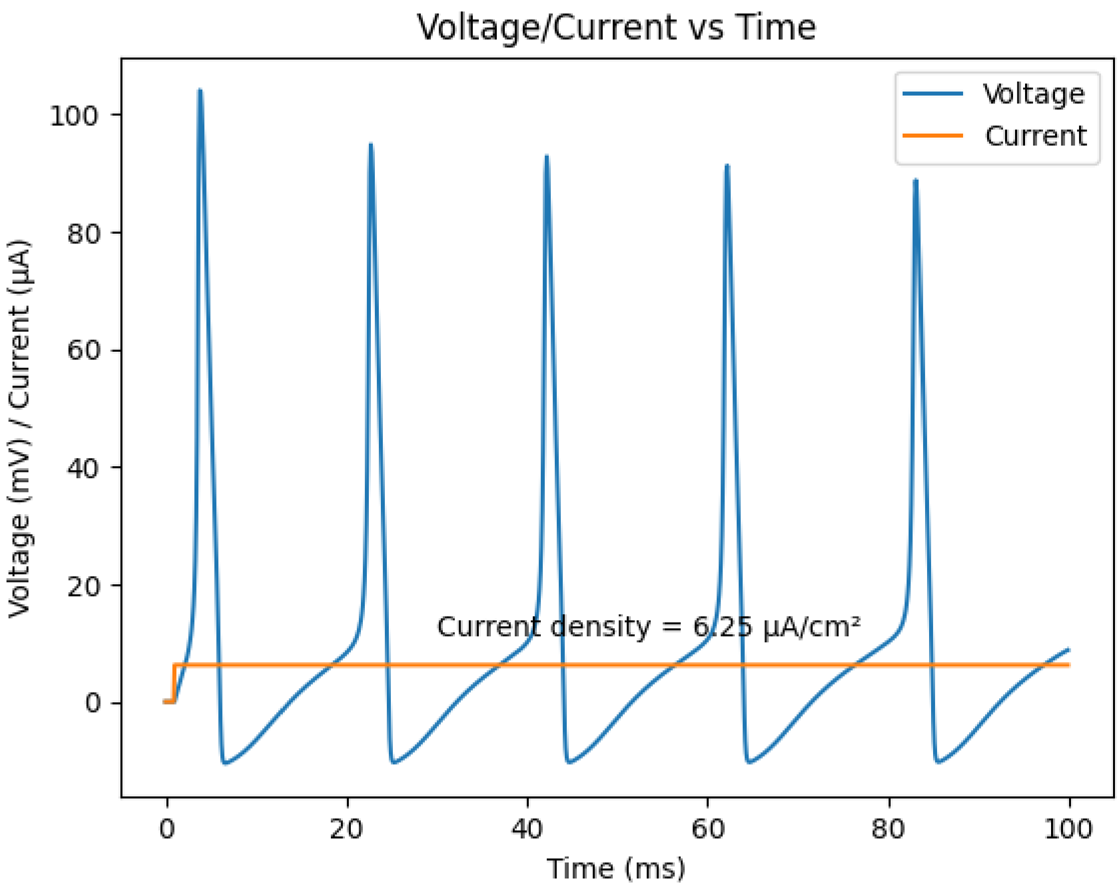
Subthreshold



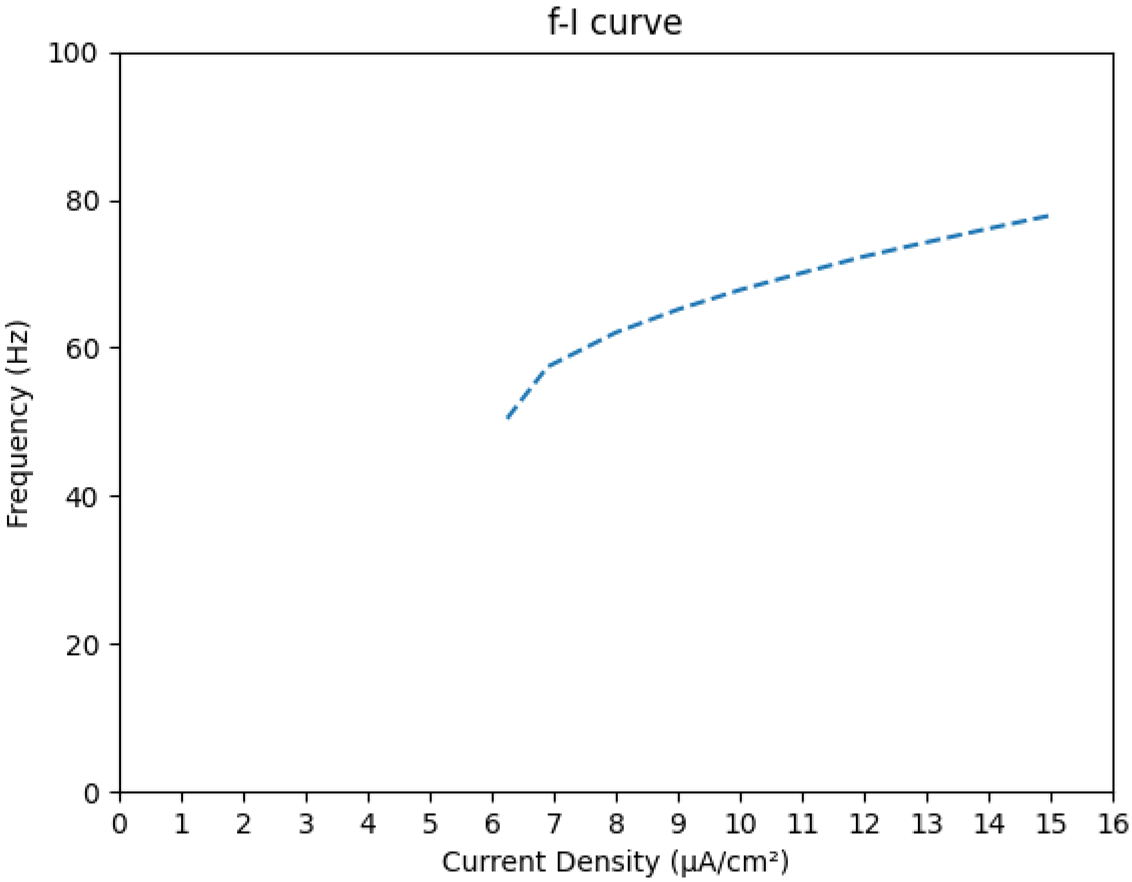
Rheobase



Superthreshold



f-I curve



Code

```
import matplotlib.pyplot as plt  # matplotlib for plotting graphs
import numpy as np  # numpy for mathematical functions and handling arrays

A = 1.0  # area of the patch (in cm²)
C_m = 1.0  # Membrance Capacitance (in μF)
G_Na_bar = 120  # maximal sodium conductance (in mS/cm²)
G_K_bar = 36  # maximal potassium conductance (in mS/cm²)
G_m = 0.3  # voltage independent "leak" conductance (in mS/cm²)
E_Na = 115  # sodium reverse potential (in mV)
E_K = -12  # potassium reverse potential (in mV)
V_rest = 10.613  # reverse potential (in mV)
dt = 0.1  # timestep of the simulation
t_start = 0  # start time of the simulation (in ms)
t_end = 100  # end time of the simulation (in ms)
p_start = 1  # start of the pulse current (in ms)
p_dur = 99  # duration of the pulse current (in ms)
p_end = p_start + p_dur  # end time of the pulse current (in ms)
I_inj = ((0.0635 * 1e-3) / (900 * np.pi * (1e-4) ** 2)) * A  # current
injected (in μA)


def alpha_n(V):
```

```
    return (10 - V) / (100 * (np.exp((10 - V) / 10) - 1))


def beta_n(V):
    return 0.125 * np.exp(-V / 80)


def alpha_m(V):
    return (25 - V) / (10 * (np.exp(-((V - 25) / 10)) - 1))


def beta_m(V):
    return 4 * np.exp(-V / 18)


def alpha_h(V):
    return 0.07 * np.exp(-V / 20)


def beta_h(V):
    return 1 / (np.exp((30 - V) / 10) + 1)


def tau_n(V):
    return 1 / (alpha_n(V) + beta_n(V))


def tau_m(V):
    return 1 / (alpha_m(V) + beta_m(V))


def tau_h(V):
    return 1 / (alpha_h(V) + beta_h(V))


def n_inf(V):
    return alpha_n(V) * tau_n(V)


def m_inf(V):
    return alpha_m(V) * tau_m(V)


def h_inf(V):
    return alpha_h(V) * tau_h(V)


t = np.arange(t_start, t_end, dt)
n = np.zeros(len(t))
m = np.zeros(len(t))
h = np.zeros(len(t))
V = np.zeros(len(t))
I = np.zeros(len(t))
```

```
m[0] = m_inf(V[0])
h[0] = h_inf(V[0])
n[0] = n_inf(V[0])

for i in range(int(p_start / dt), int(p_end / dt)):
    I[i] = I_inj  # setting the current

for i in range(len(t) - 1):
    n[i + 1] = n_inf(V[i]) + (n[i] - n_inf(V[i])) * np.exp(-dt /
tau_n(V[i]))
    m[i + 1] = m_inf(V[i]) + (m[i] - m_inf(V[i])) * np.exp(-dt /
tau_m(V[i]))
    h[i + 1] = h_inf(V[i]) + (h[i] - h_inf(V[i])) * np.exp(-dt /
tau_h(V[i]))
    G_Na = G_Na_bar * (m[i + 1] ** 3) * h[i + 1]  # sodium channel
conductance
    G_K = G_K_bar * (n[i + 1] ** 4)  # potassium channel conductance
    G_eff = G_Na + G_K + G_m  # 1/R = 1/R1 + 1/R2 + 1/R3 = G1 + G2 + G3 = G
    I_Na = G_Na * E_Na  # I = V/R = VG
    I_K = G_K * E_K
    I_leak = G_m * V_rest
    I_eff = I_Na + I_K + I_leak
    V_inf = (I_eff + (I[i] / A)) / G_eff
    tau_V = C_m / G_eff  # τ = RC = C/G
    V[i + 1] = V_inf + (V[i] - V_inf) * np.exp(
        -dt / tau_V
    )  # Using Exponential Euler rule

plt.plot(t, V)  # Plot voltage varying with time
plt.plot(t, I)  # Plot current varying with time
plt.title("Voltage/Current vs Time")
plt.legend(["Voltage", "Current"])
plt.xlabel("Time (ms)")
plt.ylabel("Voltage (mV) / Current (µA)")
plt.annotate(
    "Current density = {:.2f} µA/cm²".format(round(I_inj, 2)),
    xy=(50, 10),
    xytext=(30, I_inj + 5),
)
plt.show()  # Show plot
```