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Assignment 4
Properties of the Hodgkin-Huxley equations

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BM 2102 Modeling and Analysis of Physiological Systems

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Contents

1 Introduction

The Hodgkin-Huxley model is a foundational mathematical framework that describes the initiation and propagation of action potentials in neurons. Developed by Alan Hodgkin and Andrew Huxley in 1952 based on experiments with the squid giant axon, the model captures the dynamic behavior of ion channels and membrane voltage using a set of nonlinear differential equations. This report explores the core properties of neuronal excitability through MATLAB simulations, focusing on threshold determination, refractory periods, repetitive firing, and temperature dependence. We gain insight into the fundamental electro-physiological mechanisms that govern nerve signal transmission by adjusting stimulus parameters and analyzing voltage and current responses.

2 Threshold

The threshold is the critical level of membrane depolarization that must be reached for a neuron to fire an action potential. It represents the minimum stimulus intensity required to trigger the opening of voltage-gated sodium channels, leading to a rapid influx of Na^+ ions and a self-sustaining electrical impulse. If the membrane potential does not reach this threshold, the neuron will not fire, and the electrical disturbance will dissipate. Thus, the threshold acts as a key decision point in neuronal signaling, distinguishing between sub-threshold stimuli with no lasting effect and supra-threshold stimuli that initiate nerve communication.

Load the default equation and stimulus parameters of the Hodgkin-Huxley Model.

```
hhconst;
```

Begin by applying a short-duration sub-threshold and supra-threshold current pulse to the Hodgkin-Huxley equations using the default parameters that have already been loaded.

```
amp1 = 6;
width1 = 1;
hhmplot(0,50,0);
amp1 = 7;
hhmplot(0,50,1);
```

The graphs are as follows:

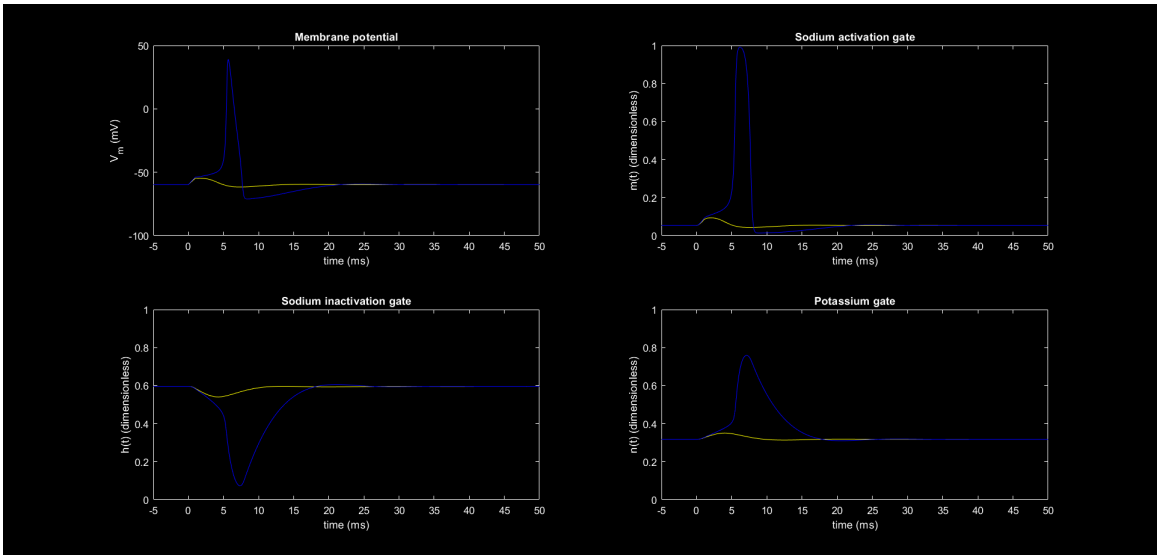

Figure 1: Response to a short-duration sub-threshold and supra-threshold current pulse to the Hodgkin-Huxley equations

2.1 Question 1

Continue to bisect the amplitude interval for sub-threshold and supra-threshold stimulating currents and obtain an estimate of the threshold stimulating current amplitude to two decimal places.

To estimate the threshold stimulus for action potential generation, a bisection method was employed between a known sub-threshold current of $6.00\,\mu\text{A/cm}^2$ and a supra-threshold current of $7.00\,\mu\text{A/cm}^2$. By repeatedly halving the interval and observing whether a spike occurred using the `hhmplot` function, the method converged to a threshold value with a precision of $0.01\,\mu\text{A/cm}^2$. Then the minimum current required to trigger an action potential was identified, approximately $6.96\,\mu\text{A/cm}^2$.

```
hhconst;

lower = 6.00;      % Known sub-threshold
upper = 7.00;      % Known supra-threshold
width1 = 1;
delay = 5;

threshold = 0;
tol = 0.01;

while (upper - lower) > tol
    amp1 = (upper + lower) / 2;
    fprintf('Testing amplitude: %.2f\n', amp1);

    hhmplot(0, 50, 0);

    % Wait for user input to classify response
    reply = input('Did it spike? (y/n): ', 's');

    if strcmpi(reply, 'y')  % If user observed a spike
        upper = amp1;
```

```
    else                        % No spike observed
        lower = amp1;
    end
end

threshold = (upper + lower) / 2;
fprintf('Estimated threshold current: %.2f \x03bcA/cm^2\n', threshold);
```

The results got for the threshold current $6.96\,\mu\text{A/cm}^2$ are as follows:

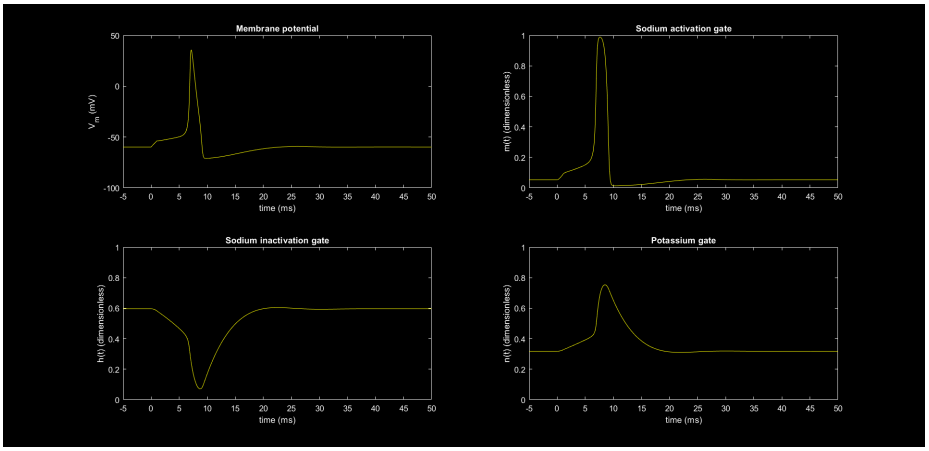

Figure 2: Results at the threshold simulating current

2.2 Question 2

If the integration time interval $[t_o, t_f]$ contains only one action potential, as in the above examples, by executing the following command for any amplitude of the stimulating current,

```
[qna, qk, ql] = hhsplot(0, 50);
```

what, in general, will be the relationship between

$$\int_{t_o}^{t_f} \sum J_k(t)\,dt$$

and

$$\int_{t_o}^{t_f} J_{ei}(t)\,dt$$

(for some numerical error)?

2.2.1 When Amplitude is Lower than Threshold

```
hhconst;
amp1 = 6.6;
width1 = 1;
[qna, qk, ql] = hhsplot(0, 50);
sum_Jion = qna + k + ql
```

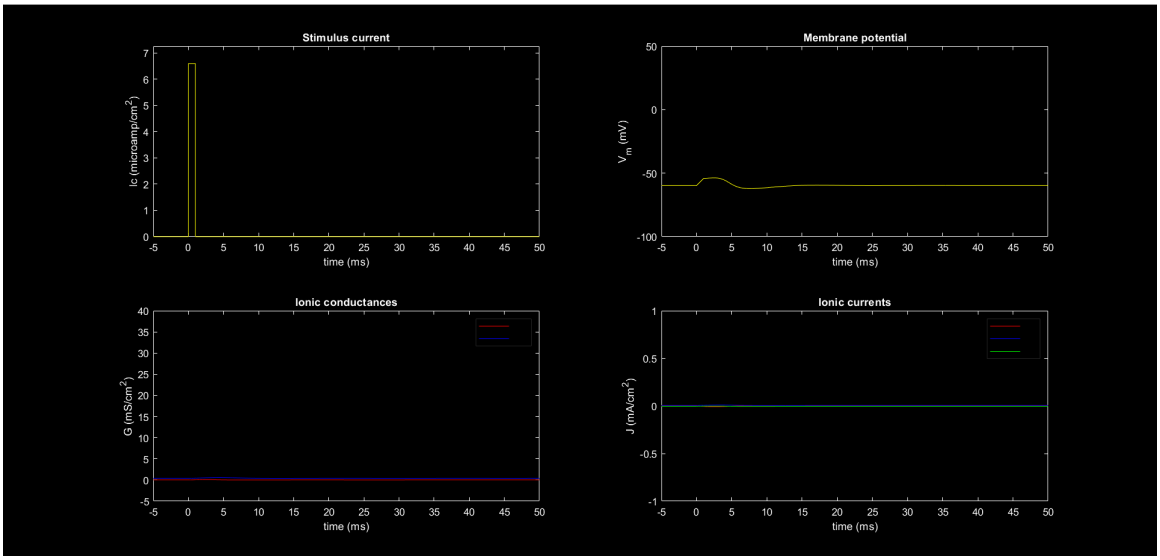

Figure 3: Results when Amplitude is Lower than Threshold

As it turns out, the sum is 6.5996, approximately equal to the stimulus amplitude $6.6\,\mu\text{A/cm}^2$.

2.2.2 When Amplitude is Greater than Threshold

```
hhconst;
amp1 = 7.2;
width1 = 1;
delay1 = 5;
[qna, qk, ql] = hhsplot(0, 50);
sum_Jion = qna + qk + ql
```

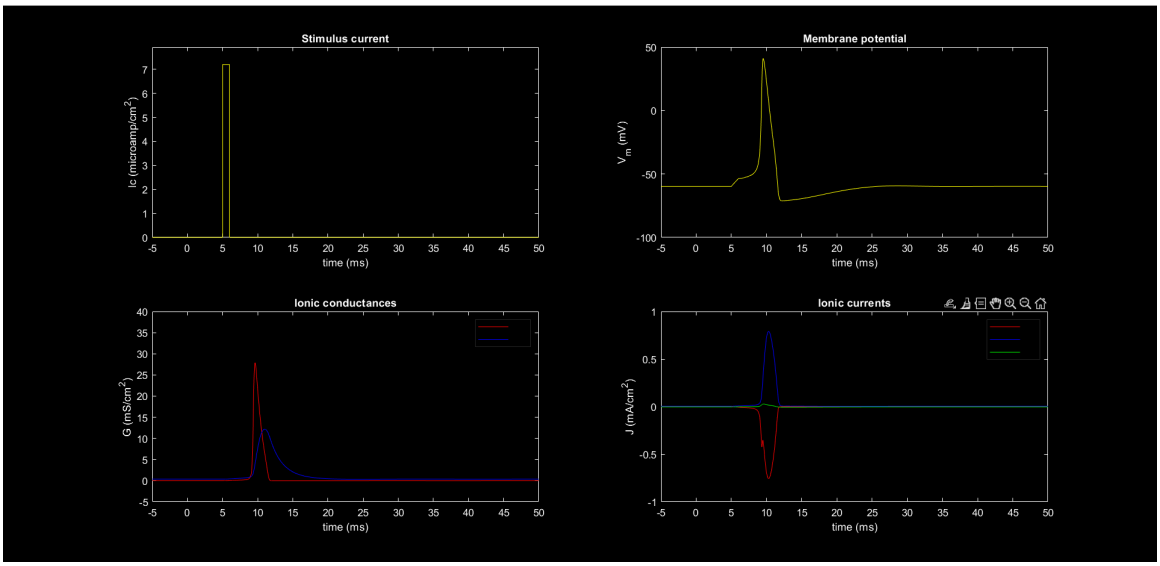

Figure 4: Results when Amplitude is Greater than Threshold

As it turns out, the sum is 7.2009, approximately equal to the stimulus amplitude $7.2\,\mu\text{A/cm}^2$.

This confirms the result:

$$\int_{t_0}^{t_f} \sum_k J_k(t)\,dt = \int_{t_0}^{t_f} J_{ei}(t)\,dt$$

3 Refractoriness

Refractoriness refers to a period following an action potential during which a neuron's ability to generate a subsequent action potential is temporarily altered. This period is divided into two phases: the absolute refractory period, during which no new action potential can be initiated regardless of stimulus strength, and the relative refractory period, where a stronger-than-normal stimulus is required to elicit another action potential. These refractory phases are essential for regulating the timing and frequency of nerve impulses, preventing the overlap of signals, and ensuring unidirectional propagation along the axon. The biophysical basis of refractoriness is well described by the Hodgkin-Huxley model, which captures the ionic mechanisms underlying these time-dependent changes in neuronal excitability.

To illustrate the features of the absolute and relative refractory periods, stimulate the model axon with two current pulses separated by varying time intervals. Begin by setting the following parameters and executing hhmplot.

```
amp1 = 27.4;
width1 = 0.5;
delay2 = 25;
amp2 = 13.7;
width2 = 0.5;
hhsplot(0,40);
```

The resulting graphs are as follows:

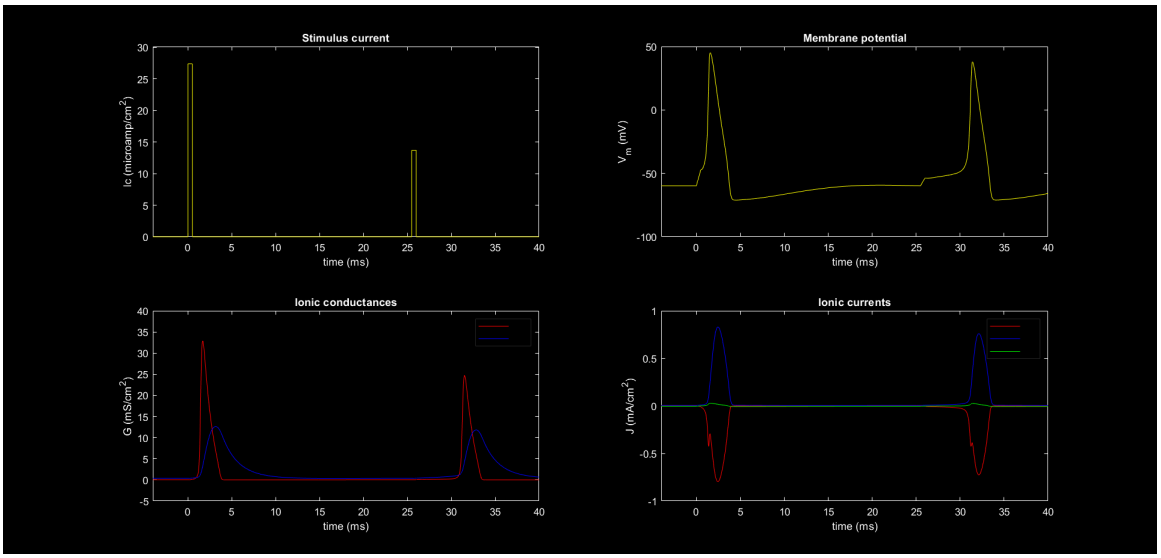

Figure 5: Results for stimulating the model axon with two current pulses separated by varying time intervals

The simulation shows that the neuron can fire twice if the pulses are spaced far enough apart, demonstrating the absolute and relative refractory periods in action.

3.1 Question 3

By setting delay2 successively to 20, 18, 16, 14, 12, 10, 8, and 6 ms, adjust amp2 to an accuracy of 0.1 μA/cm^2 to elicit an action potential. The amplitude obtained, $I_{2\text{th}}$, will correspond to the current threshold amplitude for a second pulse as a function of the inter-stimulus interval.

3.1.1 Delay of 20 ms

```
amp1 = 26.8;
width1 = 0.5;
amp2 = 11.0;
delay2 = 20;
width2 = 0.5;
hhmplot(0, 30, 0);

for j = 1:6
    amp2 = amp2 + 0.1;
    hhmplot(0, 30, 1);
end
```

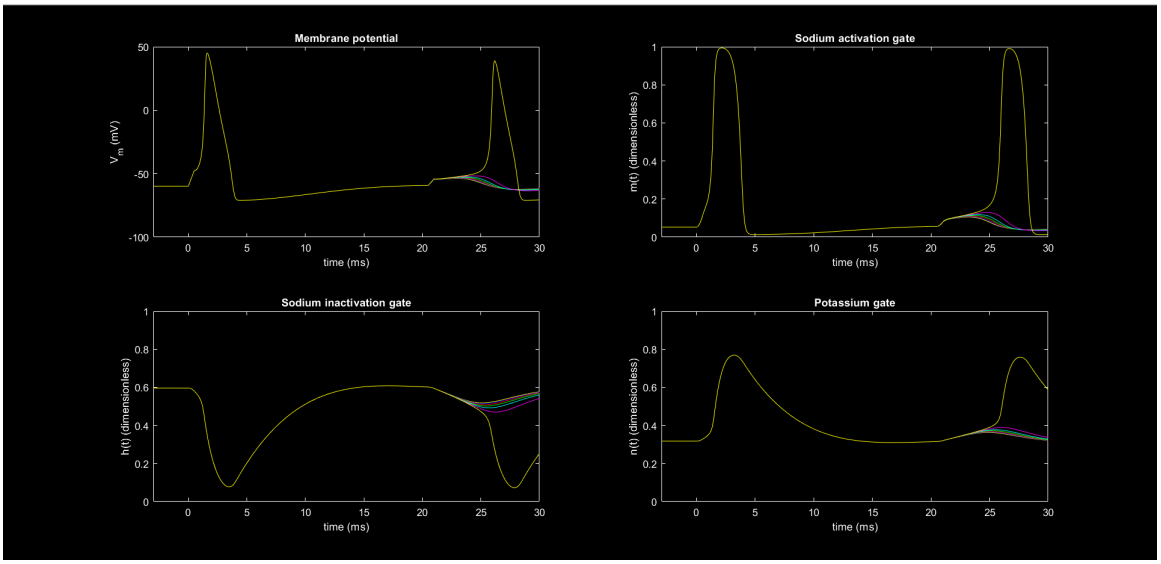

Figure 6: Spikes for a Delay of 20 ms

An action potential is triggered at 11.6μA/cm^2.

3.1.2 Delay of 18 ms

```
amp1 = 26.8;
width1 = 0.5;
amp2 = 11.0;
delay2 = 18;
width2 = 0.5;
hhmplot(0, 30, 0);

for j = 1:6
    amp2 = amp2 + 0.1;
    hhmplot(0, 30, 1);
end
```

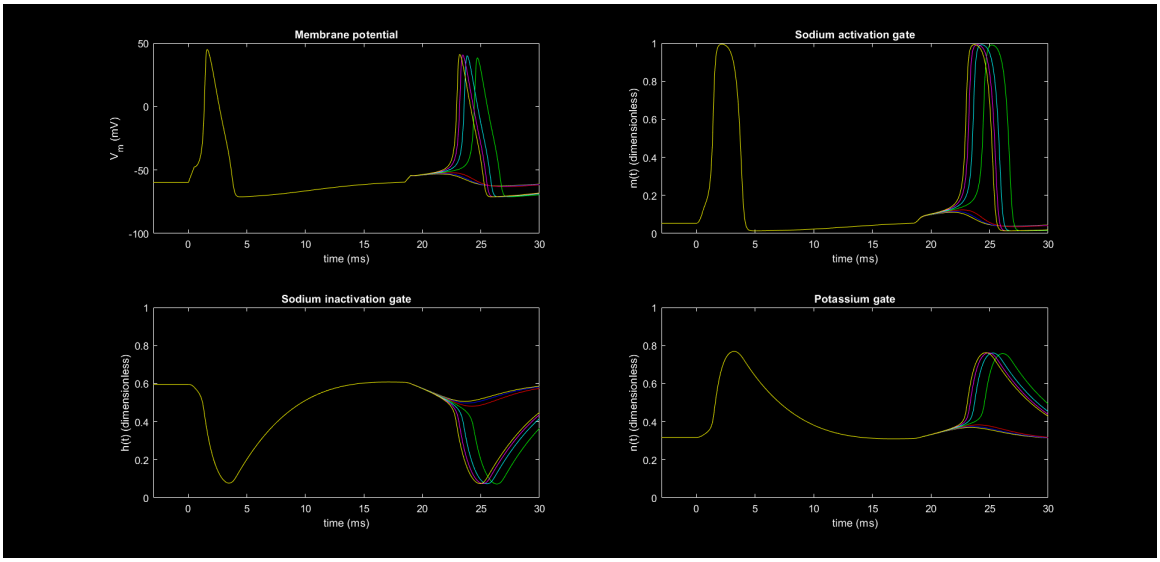

Figure 7: Spikes for a Delay of 18 ms

An action potential is triggered at $11.3\mu\text{A/cm}^2$.

3.1.3 Delay of 16 ms

```
amp1 = 26.8;
width1 = 0.5;
amp2 = 12.0;
delay2 = 16;
width2 = 0.5;
hhmplot(0, 30, 0);

for j = 1:10
    amp2 = amp2 + 0.1;
    hhmplot(0, 30, 1);
end
```

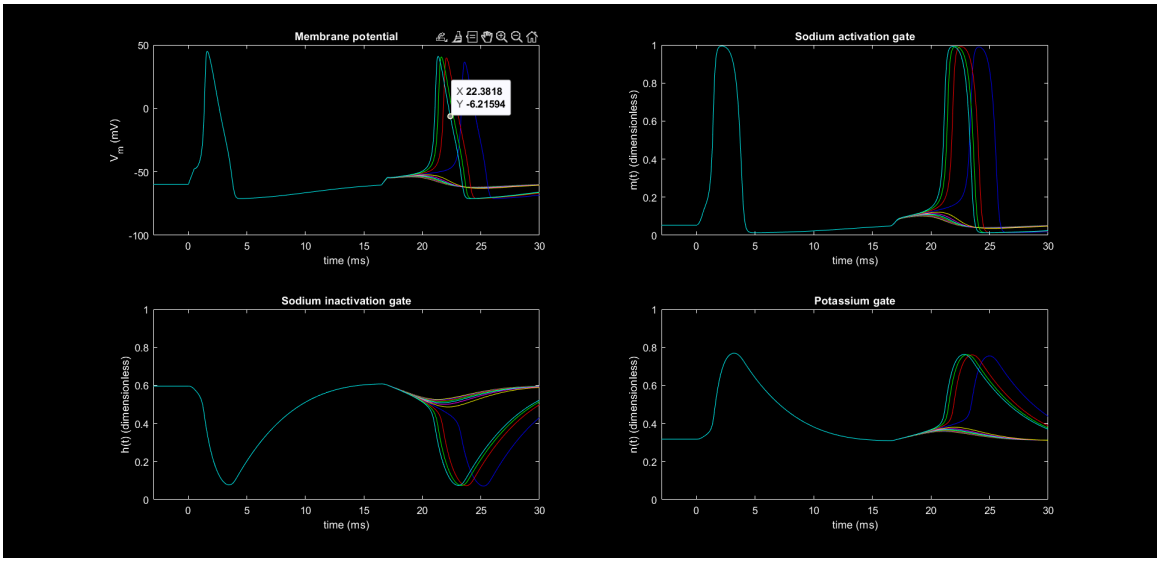

Figure 8: Spikes for a Delay of 16 ms

An action potential is triggered at $12.7\mu\text{A/cm}^2$.

3.1.4 Delay of 14 ms

```
amp1 = 26.8;
width1 = 0.5;
amp2 = 16.5;
delay2 = 14;
width2 = 0.5;
hhmplot(0, 30, 0);

for j = 1:8
    amp2 = amp2 + 0.1;
    hhmplot(0, 30, 1);
end
```

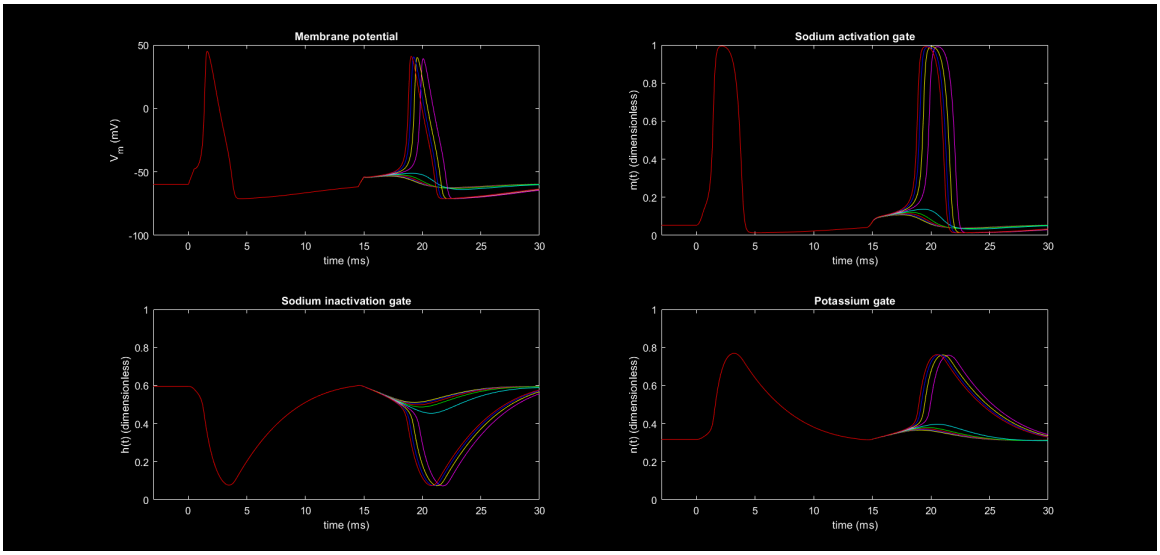

Figure 9: Spikes for a Delay of 14 ms

An action potential is triggered at $17.1\mu\text{A/cm}^2$.

3.1.5 Delay of 12 ms

```
amp1 = 26.8;
width1 = 0.5;
amp2 = 25.0;
delay2 = 12;
width2 = 0.5;
hhmplot(0, 30, 0);

for j = 1:6
    amp2 = amp2 + 0.1;
    hhmplot(0, 30, 1);
end
```

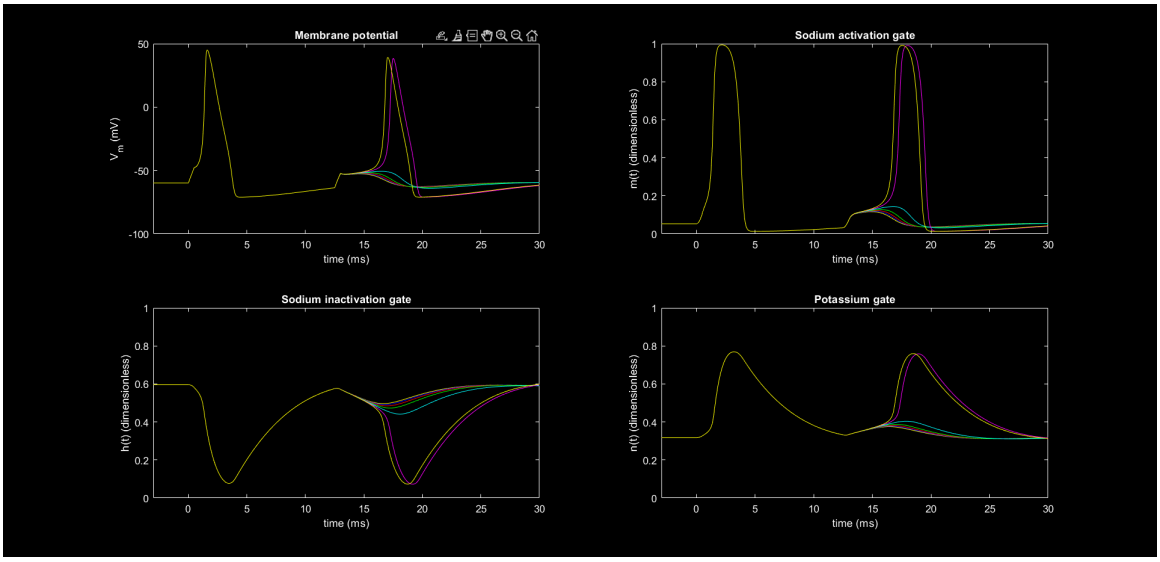

Figure 10: Spikes for a Delay of 12 ms

An action potential is triggered at $31.1\mu\text{A/cm}^2$.

3.1.6 Delay of 10 ms

```
amp1 = 26.8;
width1 = 0.5;
amp2 = 40.0;
delay2 = 10;
width2 = 0.5;
hhmplot(0, 30, 0);

for j = 1:8
    amp2 = amp2 + 0.1;
    hhmplot(0, 30, 1);
end
```

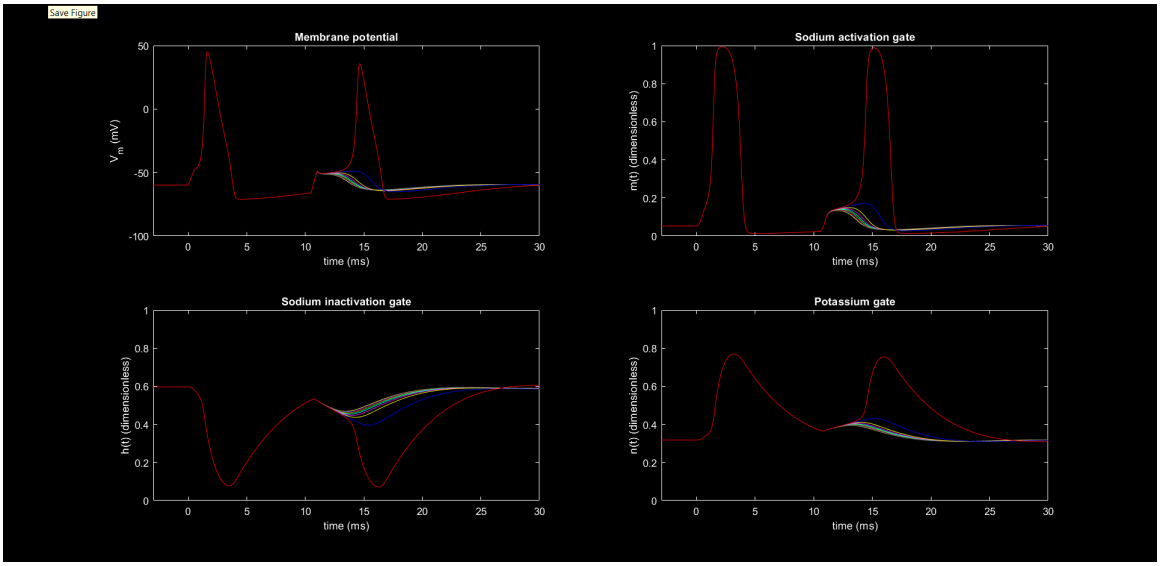

Figure 11: Spikes for a Delay of 10 ms

An action potential is triggered at $40.8\mu\text{A/cm}^2$.

3.1.7 Delay of 8 ms

```
amp1 = 26.8;
width1 = 0.5;
amp2 = 70.0;
delay2 = 8;
width2 = 0.5;
hhmplot(0, 30, 0);

for j = 1:6
    amp2 = amp2 + 0.1;
    hhmplot(0, 30, 1);
end
```

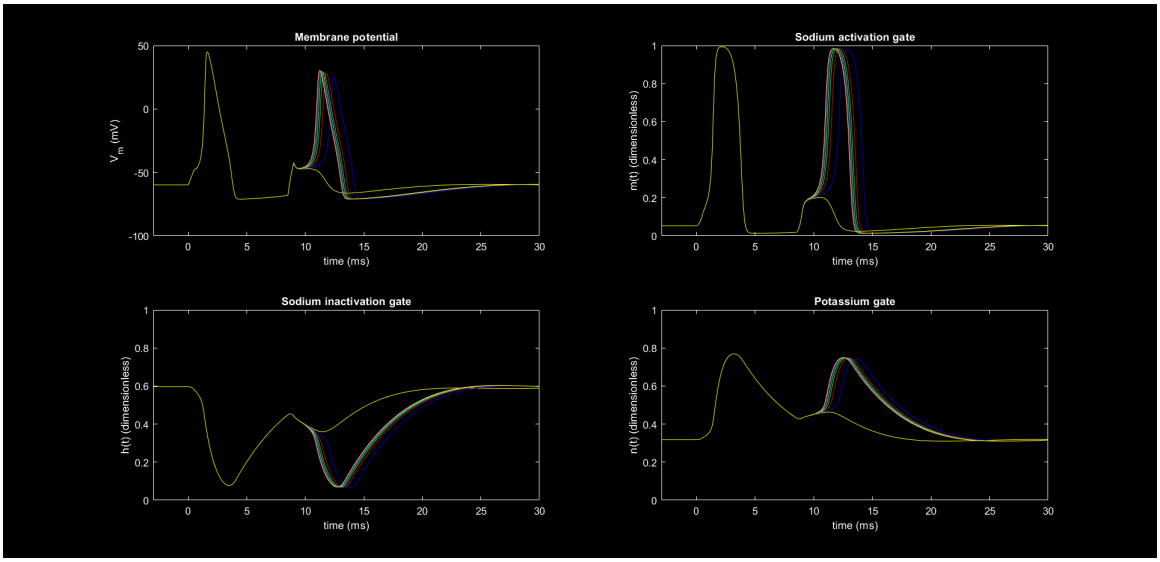

Figure 12: Spikes for a Delay of 8 ms

An action potential is triggered at $70.1\mu\text{A/cm}^2$.

3.1.8 Delay of 6 ms

```
amp1 = 26.8;
width1 = 0.5;
amp2 = 145.0;
delay2 = 6;
width2 = 0.5;
hhmplot(0, 30, 0);

for j = 1:6
    amp2 = amp2 + 0.1;
    hhmplot(0, 30, 1);
end
```

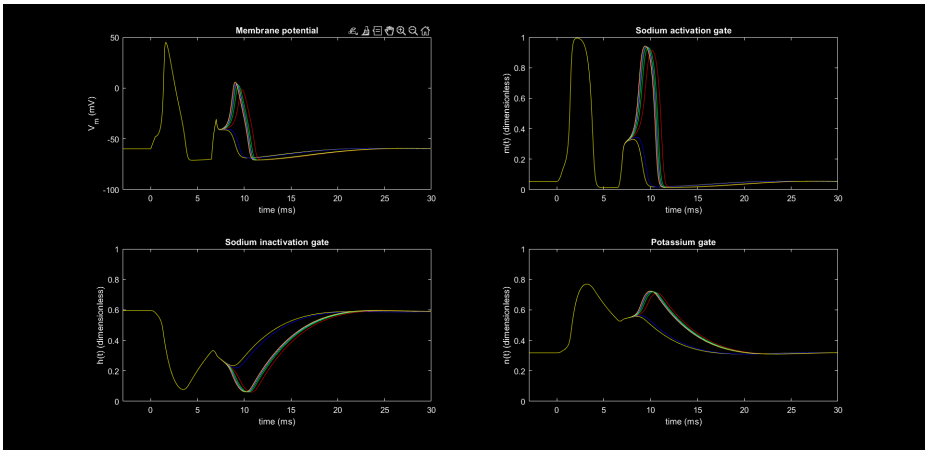

Figure 13: Spikes for a Delay of 6 ms

An action potential is triggered at $145.2\mu\text{A/cm}^2$.

3.2 Question 4

By plotting the ratio $\frac{I_{2th}}{I_{1th}}$ as a function of the inter-pulse interval, estimate the absolute and relative refractory periods.

Inter-pulse Interval (ms)	I_{2th} $(\mu A/cm^2)$	I_{2th}/I_{1th}
6	145.2	5.418
8	70.1	2.616
10	40.8	1.522
12	31.1	1.160
14	17.1	0.638
16	12.7	0.474
18	11.3	0.422
20	11.6	0.433

Table 1: Threshold current amplitude for the second pulse as a function of inter-pulse interval

A graph was obtained by plotting the Relative Threshold Current vs. Inter-pulse Interval.

The code to obtain the graph is as follows:

```
delay_ms = [6, 8, 10, 12, 14, 16, 18, 20];
ratio = [5.418, 2.616, 1.522, 1.160, 0.638, 0.474, 0.422, 0.433];

delay_fine = linspace(min(delay_ms), max(delay_ms), 200);

%ratio_smooth = interp1(delay_ms, ratio, delay_fine, 'spline');

figure;
plot(delay_ms, ratio, 'ro', 'MarkerSize', 8, 'DisplayName', 'Data points');
    ↪ hold on;
plot(delay_fine, ratio_smooth, 'b-', 'LineWidth', 2, 'DisplayName', 'Spline
    ↪ interpolation');
grid on;
xlabel('Inter-pulse Interval (ms)', 'FontSize', 12);
ylabel('Threshold Current Ratio $I_{2th}/I_{1th}$', 'Interpreter', 'latex',
    ↪ 'FontSize', 12);
title('Relative Threshold Current vs. Inter-pulse Interval', 'FontSize', 14)
    ↪ ;
legend('Location', 'northeast');
```

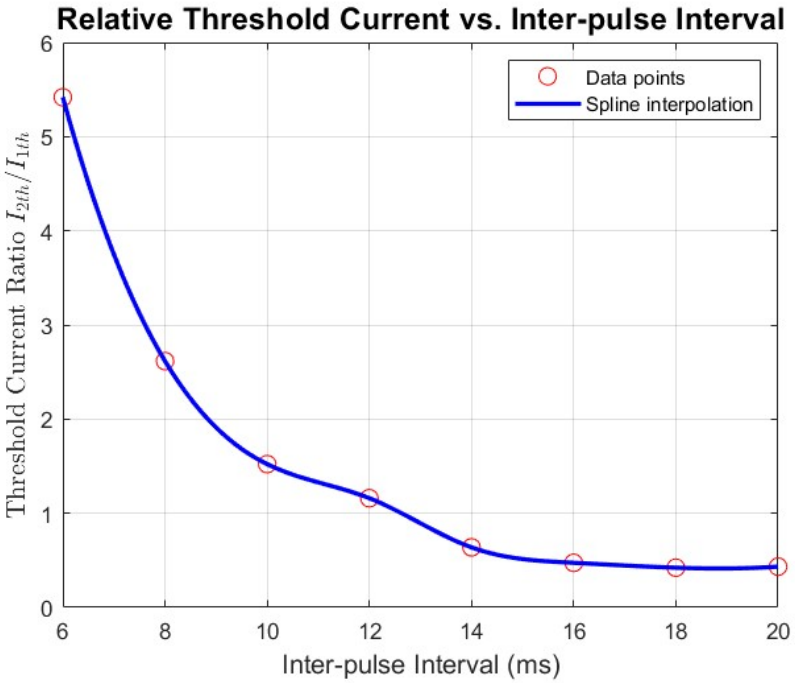

Figure 14: Relative Threshold Current vs. Inter-pulse Interval

The absolute and relative refractory periods can be obtained by analyzing the above graph.

The code to do the analysis is given below.

```
figure;
plot(delay_fine, ratio_smooth, 'b-', 'LineWidth', 2); hold on;
yline(1, 'r--', 'Threshold ratio = 1');
xlabel('Inter-pulse Interval (ms)');
ylabel('Threshold Current Ratio I_{2th}/I_{1th}');
title('Refractory Period Estimation');
grid on;

abs_refrac_end = 10; % example value, find exact from plot
rel_refrac_end = 16; % example value, find exact from plot

plot(abs_refrac_end, interp1(delay_fine, ratio_smooth, abs_refrac_end), 'ro'
    ↪ , 'MarkerSize', 8);
text(abs_refrac_end, 2, 'Absolute Refractory End', 'Color', 'r');

plot(rel_refrac_end, interp1(delay_fine, ratio_smooth, rel_refrac_end), 'go'
    ↪ , 'MarkerSize', 8);
text(rel_refrac_end, 1.1, 'Relative Refractory End', 'Color', 'g');
```

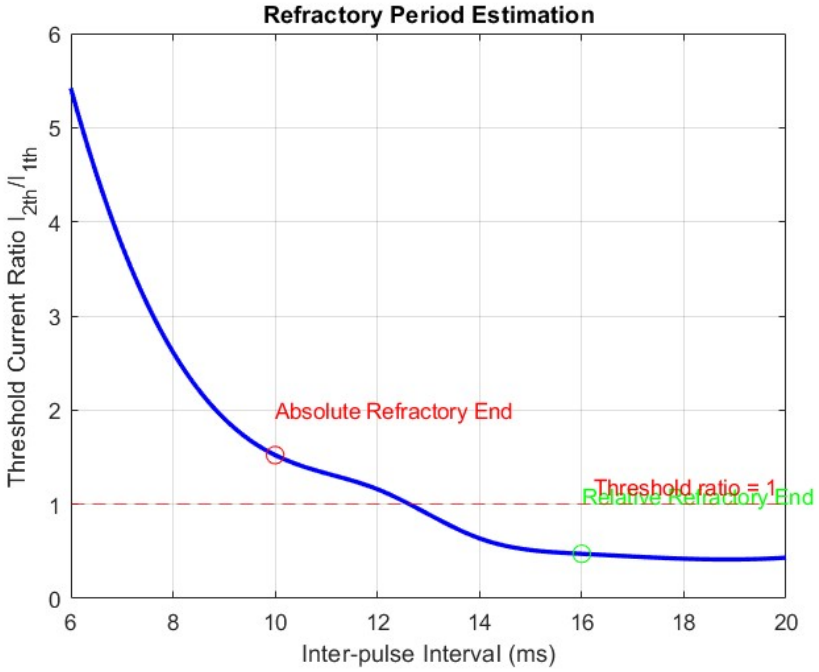

Figure 15: Finding the Absolute and Relative Refractory Periods

According to the graph,

- The absolute refractory period is 0 - 10 ms.
- The relative refractory period is 10 - 16 ms.

4 Repetitive Activity

Repetitive activity refers to generating multiple action potentials in response to a long-duration, supra-threshold stimulus. When a neuron is continuously depolarized by a strong enough current over an extended period, it does not fire a single spike but instead emits a train of action potentials. This behavior reflects the neuron's ability to encode sustained stimuli into repeated electrical signals. In the Hodgkin-Huxley model, repetitive firing occurs as long as the membrane potential is periodically able to recover and re-cross the threshold, highlighting the dynamic balance between sodium and potassium conductance during prolonged excitation.

4.1 Question 5

By using either hhsplot or hhmplot, estimate the number of action potentials per second by applying single 80-ms-wide stimulus currents of 5, 10, 20, 30, 50, 70, and 100μA/cm^2. Plot action potential frequency as a function of stimulating current amplitude.

What changes do you notice in the amplitude of the action potentials as a function of stimulus intensity?

4.1.1 Stimulus Current of 5μA/cm^2

```
hhconst;
amp1 = 5;
```

```
width1 = 80;
amp2 = 0; width2 = 0; delay2 = 0;
hhmplot(0, 100, 0);
```

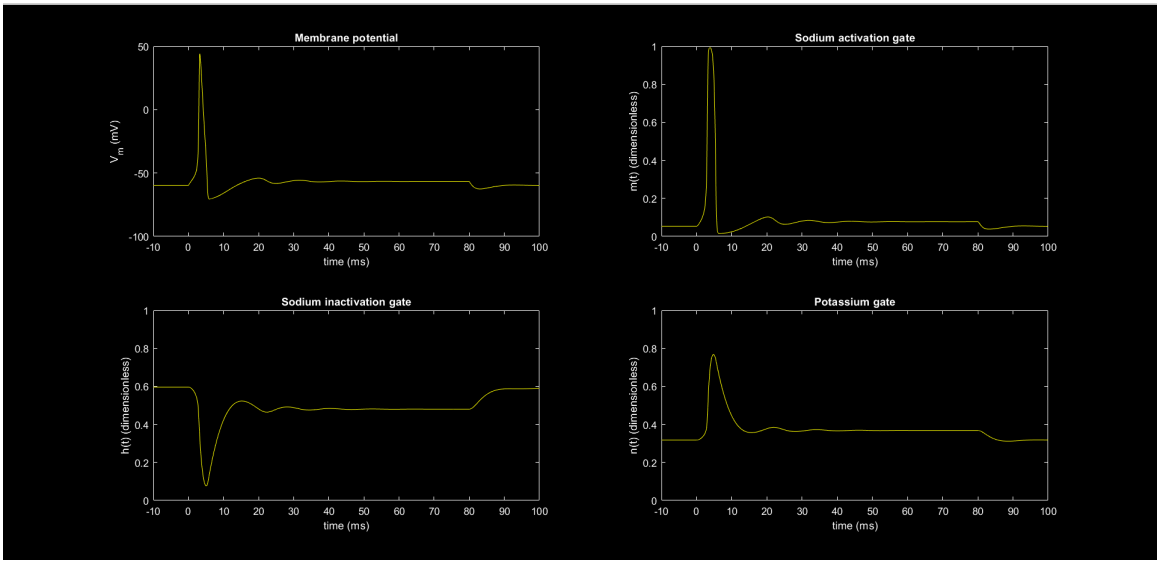

Figure 16: Spikes for Stimulus Current of $5\mu\text{A/cm}^2$

4.1.2 Stimulus Current of $10\mu\text{A/cm}^2$

```
hhconst;
amp1 = 10;
width1 = 80;
amp2 = 0; width2 = 0; delay2 = 0;
hhmplot(0, 100, 0);
```

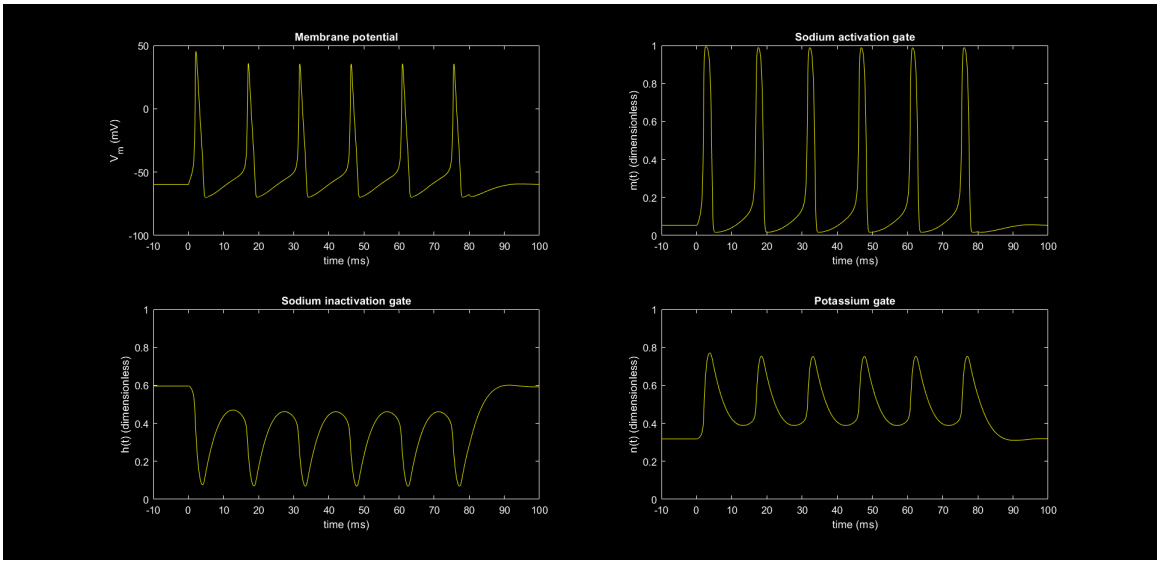

Figure 17: Spikes for Stimulus Current of $10\mu\text{A/cm}^2$

4.1.3 Stimulus Current of $20\mu A/cm^2$

```
hhconst;
amp1 = 20;
width1 = 80;
amp2 = 0; width2 = 0; delay2 = 0;
hhmplot(0, 100, 0);
```

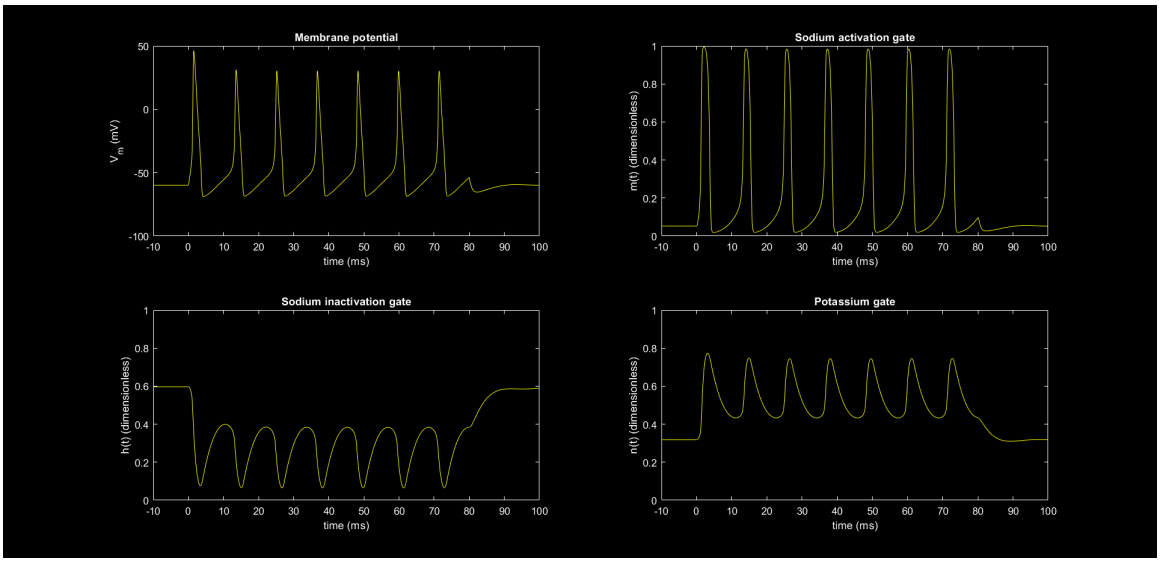

Figure 18: Spikes for Stimulus Current of $20\mu A/cm^2$

4.1.4 Stimulus Current of $30\mu A/cm^2$

```
hhconst;
amp1 = 30;
width1 = 80;
amp2 = 0; width2 = 0; delay2 = 0;
hhmplot(0, 100, 0);
```

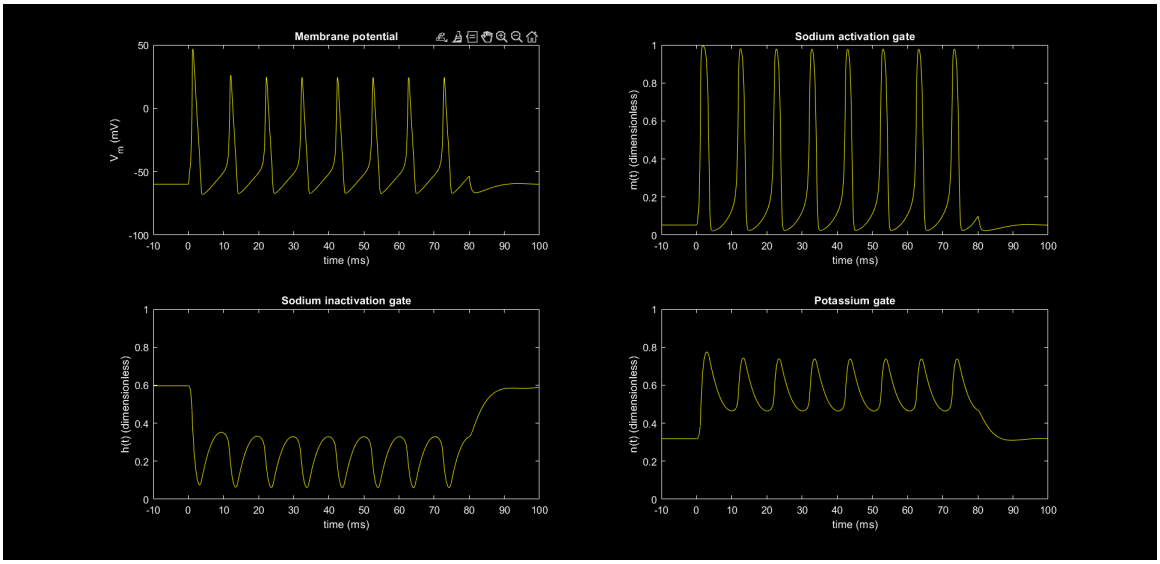

Figure 19: Spikes for Stimulus Current of $30\mu\text{A/cm}^2$

4.1.5 Stimulus Current of $50\mu\text{A/cm}^2$

```
hhconst;
amp1 = 50;
width1 = 80;
amp2 = 0; width2 = 0; delay2 = 0;
hhmplot(0, 100, 0);
```

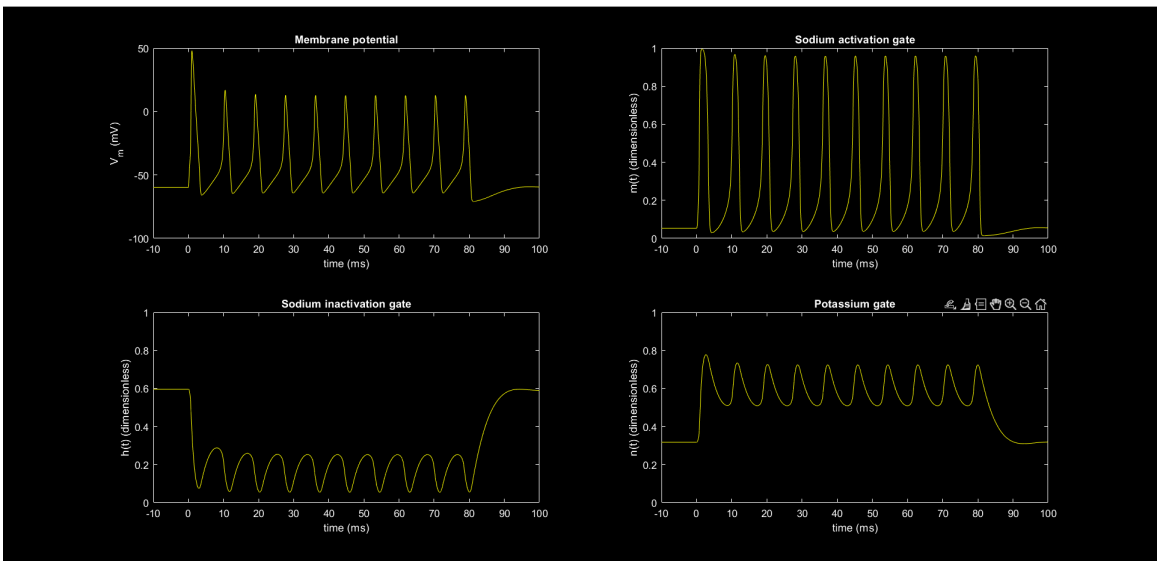

Figure 20: Spikes for Stimulus Current of $70\mu\text{A/cm}^2$

4.1.6 Stimulus Current of $70\mu\text{A/cm}^2$

```
hhconst;
amp1 = 70;
```

```
width1 = 80;
amp2 = 0; width2 = 0; delay2 = 0;
hhmplot(0, 100, 0);
```

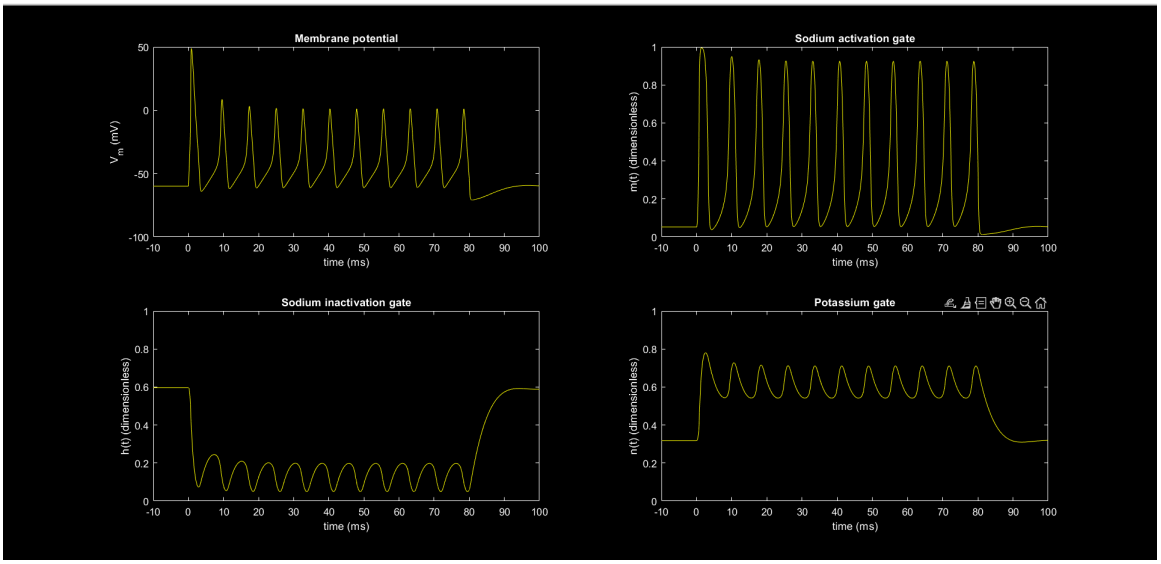

Figure 21: Spikes for Stimulus Current of $80\mu\text{A/cm}^2$

4.1.7 Stimulus Current of $100\mu\text{A/cm}^2$

```
hhconst;
amp1 = 100;
width1 = 80;
amp2 = 0; width2 = 0; delay2 = 0;
hhmplot(0, 100, 0);
```

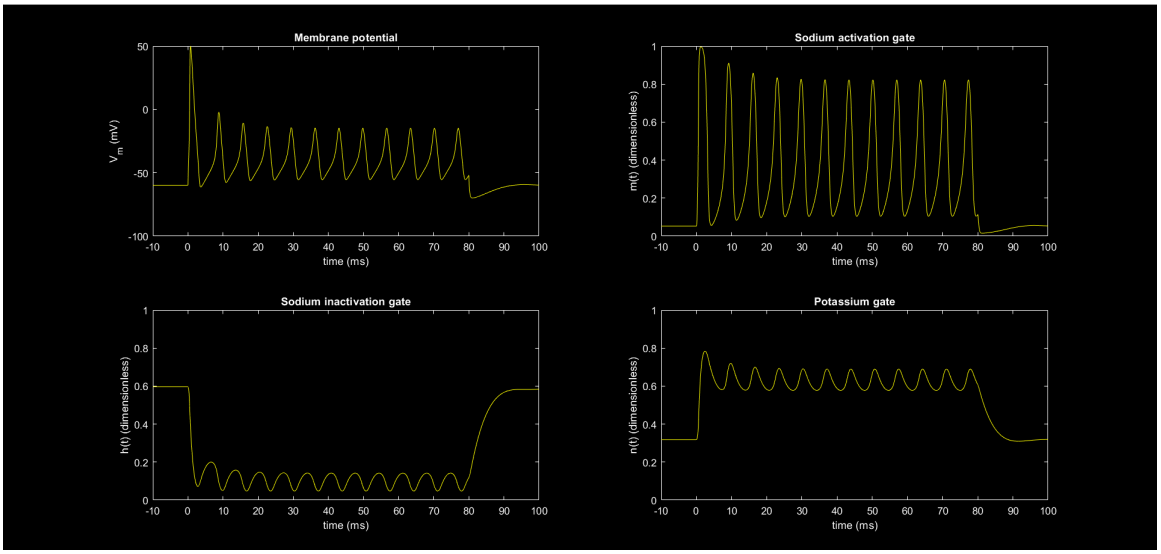

Figure 22: Spikes for Stimulus Current of $100\mu\text{A/cm}^2$

Stimulating Current Amplitude ($\mu A/cm^2$)	No. of Spikes in 80 ms
5	1
10	6
20	7
30	8
50	10
70	11
100	12

Table 2: Threshold current amplitude for the second pulse as a function of inter-pulse interval

The above values are plotted using the following code.

```
amplitudes = [5, 10, 20, 30, 50, 70, 100];
spikes = [1, 6, 7, 8, 10, 11, 12];

xq = linspace(min(amplitudes), max(amplitudes), 200);
spikes_smooth = interp1(amplitudes, spikes, xq, 'spline');

figure;
plot(amplitudes, spikes, 'o', 'MarkerSize', 6, 'MarkerFaceColor', 'b');
hold on;
plot(xq, spikes_smooth, 'r-', 'LineWidth', 2);
xlabel('Stimulating Current Amplitude (\muA/cm^2)', 'FontSize', 12);
ylabel('Number of Spikes in 80 ms', 'FontSize', 12);
title('Repetitive Firing vs Stimulus Intensity', 'FontSize', 14);
legend('Data points', 'Spline interpolation', 'Location', 'NorthWest');
```

The resulting plot is as follows:

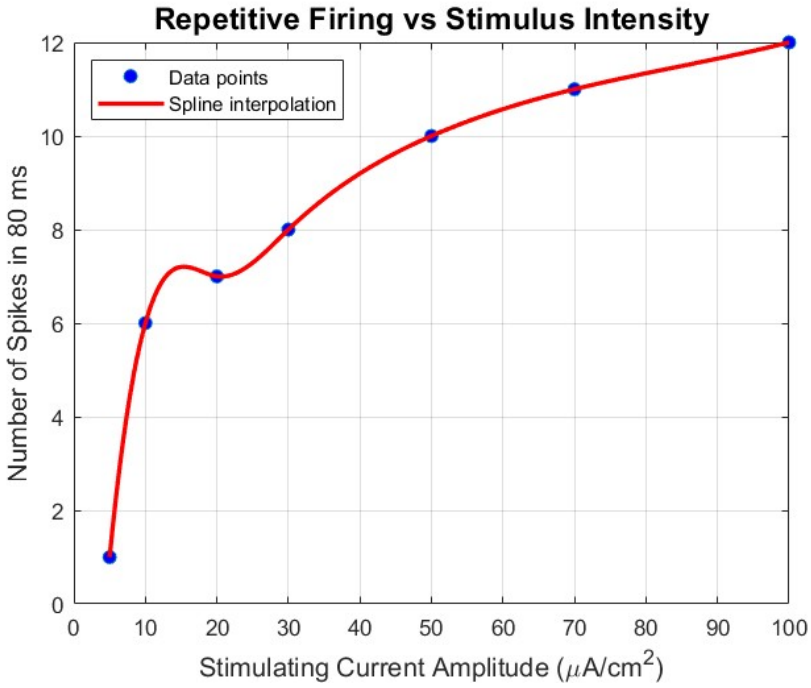

Figure 23: Action potential frequency vs. stimulating current amplitude

When the strength of the stimulus gets bigger, the nerve fires more action potentials. At first, even a small increase in stimulus causes a big jump in how often the nerve fires. As the stimulus

gets very strong, the increase in firing rate slows down and levels off because the nerve can't fire any faster.

4.2 Question 6

Set the stimulating current amplitude to $200\mu A/cm^2$. What do you notice? This result is known as a depolarization block. Can you think of an explanation of the results of Question 5 and Question 6 in terms of the voltage dependence of the m, h, and n factors of the Hodgkin-Huxley equations?

The code to get the graphs at stimulating current amplitude to $200\mu A/cm^2$ is as follows:

```
hhconst;
amp1 = 200;
width1 = 80;
delay1 = 5;
amp2 = 0;
width2 = 0;
delay2 = 0;
[qna, qk, ql] = hhsplot(0, 100);
```

The obtained graphs are given below.

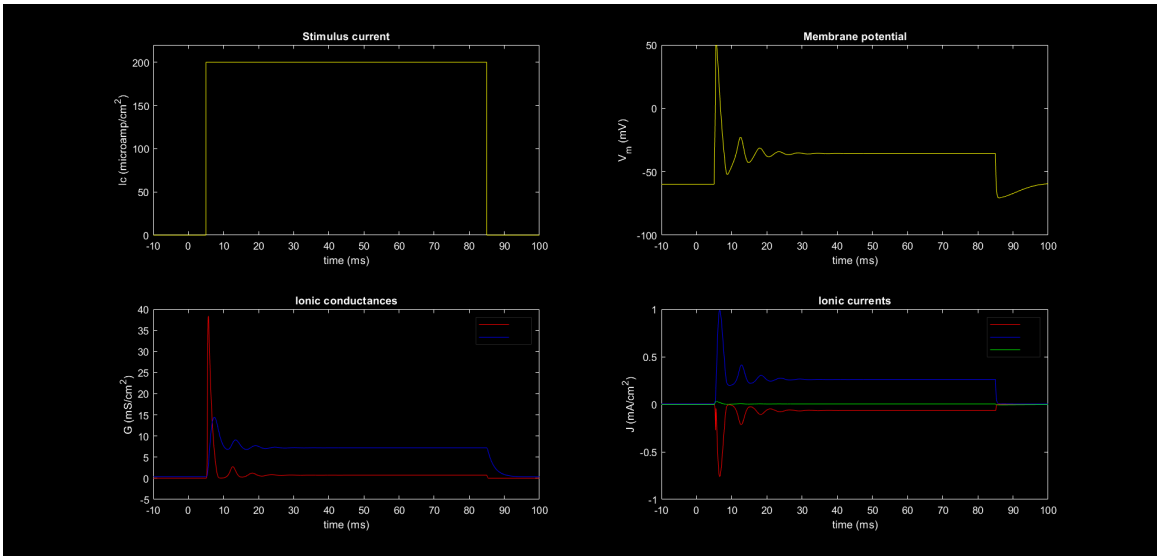

Figure 24: Plots at stimulating current amplitude to $200\mu A/cm^2$

In Question 5, as the stimulating current amplitude increased, the neuron fired more action potentials over time. Initially, lower currents resulted in fewer spikes, but higher currents caused more frequent firing as the membrane potential reached the threshold faster. However, at a certain point, the increase in spike frequency slowed, indicating a limit to how quickly the neuron can reset and fire again.

In Question 6, increasing the current amplitude to $200\mu A/cm^2$ caused the neuron to stop firing after an initial spike, a phenomenon known as depolarization block. This strong depolarization inactivated sodium channels (h-gate closed) and kept potassium channels open (n-gate open), preventing the neuron from recovering and generating new spikes. Essentially, the membrane becomes "stuck" in a depolarized state, illustrating how the Hodgkin-Huxley model's variables control action potential firing and neural excitability limits.

5 Temperature Dependence

Temperature dependence in the Hodgkin-Huxley model refers to how temperature changes affect the speed of ion channel kinetics and membrane excitability. As temperature increases, the opening and closing rates of sodium and potassium channels (controlled by the m, h, and n variables) become faster due to increased molecular activity. This leads to quicker action potentials, shorter durations, and higher firing frequencies. The model typically incorporates this through a Q10 factor, which scales rate constants based on temperature.

5.1 Question 7

By using a single current pulse of intensity 20 $\mu A/cm^2$ and 0.5 ms in width, observe the effects of the following temperatures on the duration and amplitude of the resulting action potential: 0, 5, 10, 15, 20, 24, 25, 26, and 30°C.

In general, what features of the action potential are affected by increasing temperature?

The graphs at different temperatures were obtained using the following code.

```
vclamp = 0;
amp1 = 20;
width1 = 0.5;
temps = [0, 5, 10, 15, 20, 24, 25, 26, 30];

for i = 1:length(temps)
    tempc = temps(i);
    hhmplot(0, 30, 1);
end
```

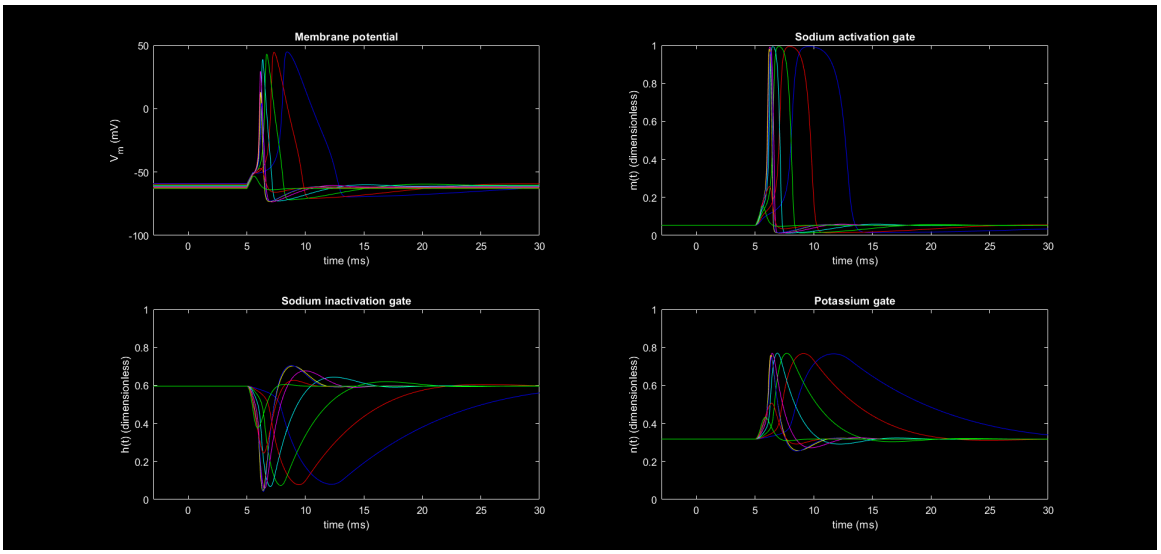

Figure 25: Plots at Different Temperatures

As the temperature increases, several features of the action potential change noticeably.

First, the duration of the action potential becomes shorter, meaning the spike happens more quickly. This occurs because the ionic channel kinetics (activation and inactivation) speed up with temperature.

Second, the amplitude of the action potential can increase slightly due to faster sodium channel activation. But at very high temperatures, it may decrease because of channel inactivation or metabolic effects.

Overall, higher temperatures cause the action potentials to become briefer and often sharper, reflecting faster underlying ionic processes.

6 Conclusion

This study used the Hodgkin-Huxley model to investigate key aspects of neuronal excitability. We estimated the threshold current for spike initiation, identified absolute and relative refractory periods, and examined how increasing stimulus amplitude leads to repetitive firing. Depolarization block was observed at high intensities, due to sustained inactivation of sodium channels. Finally, we studied the effect of temperature, which increased firing rates by accelerating the kinetics of ion channels. Overall, these simulations demonstrate how neuronal behavior arises from the interplay of stimulus strength, timing, and biophysical properties like voltage- and temperature-dependent gating.

References

[1] "Hodgkin–Huxley model," Wikipedia, The Free Encyclopedia. Available: `https://en.wikipedia.org/wiki/Hodgkin%E2%80%93Huxley_model`

[2] Gerstner, W., Kistler, W. M., Naud, R., Paninski, L. (2014). *Neuronal Dynamics: From single neurons to networks and models of cognition*, Chapter 2, Section 2. Available: `https://neuronaldynamics.epfl.ch/online/Ch2.S2.html`