University of Moratuwa, Sri Lanka

Department of Electronic & Telecommunication Engineering

Assignment 4
Properties of the Hodgkin-Huxley equations

Pirathishanth.A
220480P

Submitted in partial fulfillment of the requirements for the module
BM 2102 Modeling and Analysis of Physiological Systems

Contents

1 Introduction

The Hodgkin-Huxley model, introduced by Alan Hodgkin and Andrew Huxley in 1952 through their work on the squid giant axon, provides a crucial mathematical framework for understanding how neurons generate and transmit action potentials. It uses nonlinear differential equations to represent the voltage-dependent behavior of ion channels. In this report, MATLAB simulations are used to investigate key aspects of neuronal excitability, such as threshold levels, refractory behavior, sustained firing patterns, and how these processes are influenced by temperature. By modifying input stimuli and observing resulting changes in membrane voltage and ionic currents, we gain a deeper understanding of the fundamental mechanisms driving neural signal transmission.

2 Threshold

The **threshold** refers to the minimum level of membrane depolarization necessary to initiate an action potential in a neuron. It marks the point at which voltage-gated sodium (Na^+) channels begin to open, allowing a rapid entry of Na^+ ions that drives a self-amplifying electrical response.

When the membrane potential fails to reach this threshold, the neuron remains inactive, and the disturbance fades without consequence. Therefore, the threshold serves as a critical decision boundary in neuronal signaling—only stimuli that exceed this level can initiate a full action potential and transmit signals along the nerve.

```
hhconst
```

Start the simulation by delivering a brief current pulse—both sub-threshold and supra-threshold—using the default parameters of the Hodgkin-Huxley model. This will allow observation of the neuron's response to stimuli below and above the firing threshold.

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

Because action potentials (AP) are absent at amplitude A_1 and present at amplitude A_2, the threshold is expected to fall between A_1 and A_2.

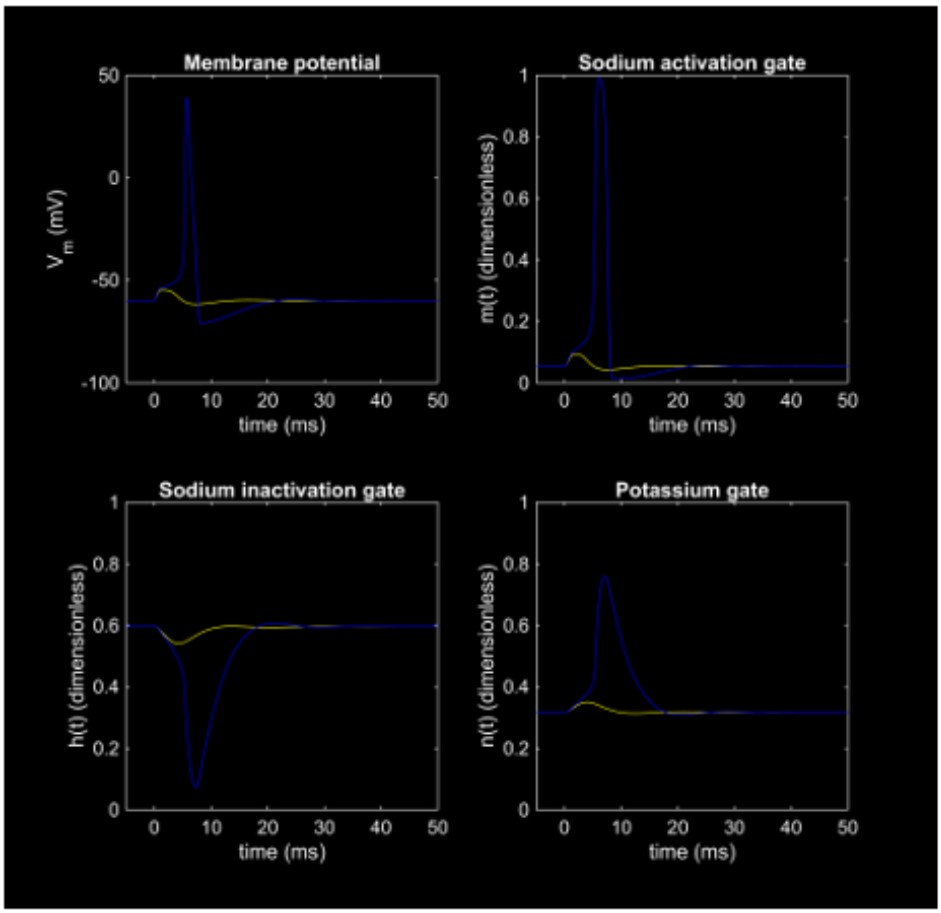

Figure 1: Response to a short-duration sub-threshold and supra-threshold current pulse to the Hodgkin-Huxley equations

2.1 Question 1

```
pause on;
hhconst;

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

i = 1;
while i <= 10
    amp1 = amp1 + 0.1;
    hhmplot(0, 50, i);
    pause(1);
    i = i + 1;
end
```

As there are no action potentials (AP) when the amplitude is 6.9,
but there are APs when the amplitude is 7.0, the threshold should lie between 6.9 and 7.0.
Since the amplitude was increased by 0.1 and only one action potential was observed at

the 10th step,
the last subthreshold amplitude was $6 + 0.9 = 6.9$.
Therefore, the threshold lies in the interval $[6.9\,\mu\text{A/cm}^2,\ 7.0\,\mu\text{A/cm}^2]$.

```
1
2  pause on;
3  hhconst;
4
5  amp1 = 6.90;
6  width1 = 1;
7
8  hhmplot(0, 50, 0);
9
10 i = 1;
11 while i <= 10
12     amp1 = amp1 + 0.01;
13     hhmplot(0, 50, i);
14     pause(1);
15     i = i + 1;
16 end
```

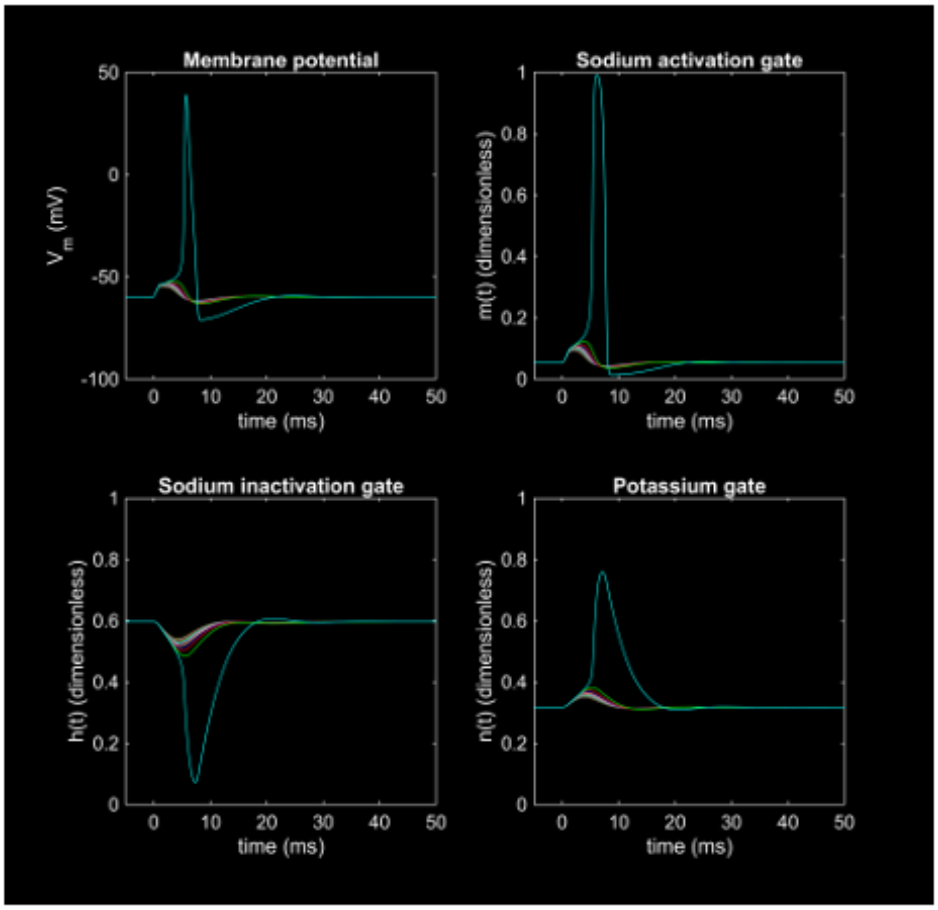

Figure 2: Results at the threshold simulating current

In the action potential plot, 5 color bands indicate possible action potentials at amplitudes:

7, 6.99, 6.98, 6.97, and 6.96.
The minimum of these values is $6.96\,\mu\text{A/cm}^2$, which is considered the threshold amplitude.

2.2 Question 2

If the integration time interval $[t_0, t_f]$ includes only a single action potential—as shown in the examples above—then running the following command for any given stimulation amplitude will yield the corresponding response.

```
[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

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

$$\int_{t_0}^{t_f} \sum_k J_k(t)\,dt = q_{Na} + q_K + q_L \quad \text{(expected total charge from individual ion currents)}$$

The computed results are $6.96\,\mu\text{A/cm}^2$ and $6.9620\,\mu\text{A/cm}^2$.

Due to minor numerical errors, these values are not exactly equal. However, they are theoretically equal as expected.

2.2.1 When Amplitude is Lower than the Threshold

```
clf;
amp1 = 6.96;
[qna,qk,ql]=hhsplot(0,50);
qna+qk+ql
```

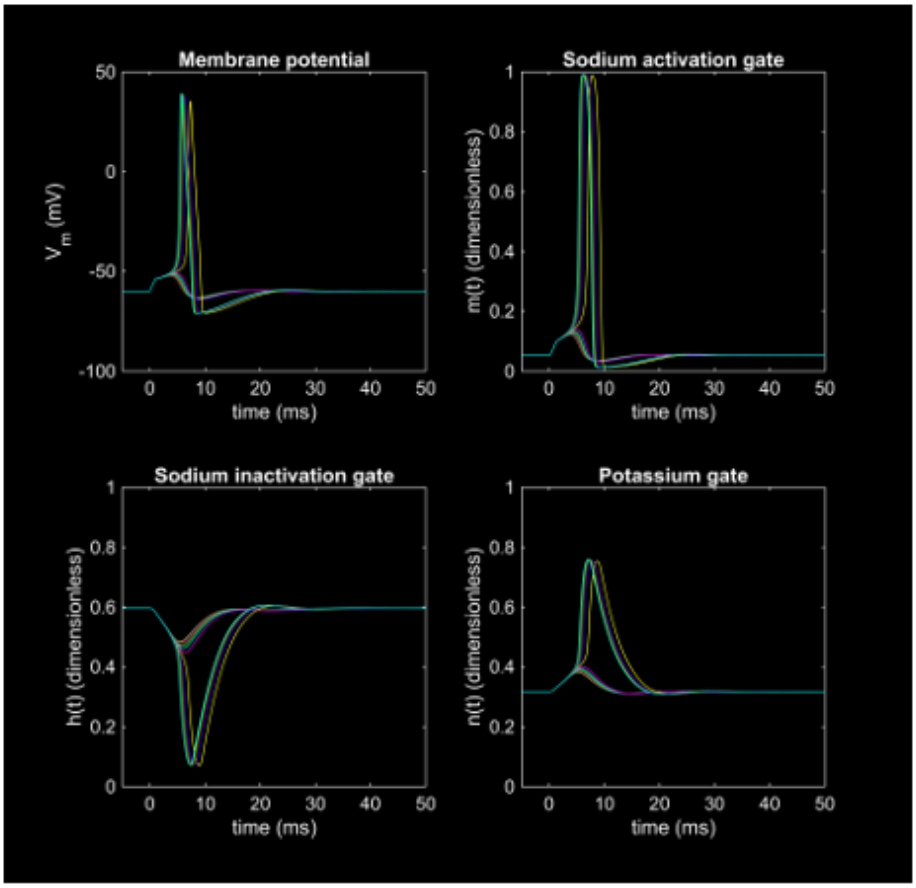

Figure 3: Results when Amplitude is Lower than Threshold

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 the 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:

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

3 Refractoriness

Refractoriness is the temporary change in a neuron's excitability following an action potential. It consists of two distinct phases: the absolute refractory period, during which a second action potential cannot occur regardless of stimulus intensity, and the relative refractory period, where only a stimulus stronger than usual can trigger another spike. These phases are crucial for maintaining proper signal timing, preventing overlapping impulses, and ensuring that action potentials travel in one direction along the axon. The Hodgkin-Huxley model effectively explains the biophysical basis of refractoriness by modeling the dynamics of ion channel activity that influence neuronal responsiveness over time.

To demonstrate the characteristics of the absolute and relative refractory periods, apply two successive current pulses to the model axon, adjusting the time interval between them. Start by configuring the following parameters and then run the hhmplot function to visualize the response.

```
amp1 = 27.4;
width1 = 0.5;
delay2 = 25;
amp2 = 13.4;
width2 = 0.5;
hhsplot(0,40);
```

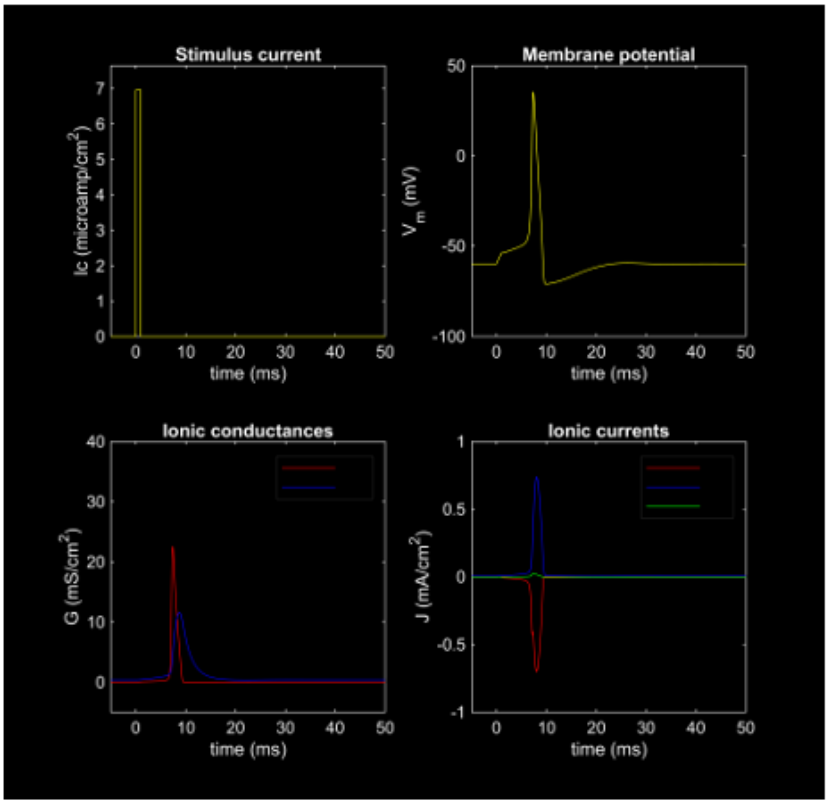

Figure 4: Results when Amplitude is Greater than Threshold

3.1 Question 3

Gradually reduce `delay2` to values of 25, 20, 18, 16, 14, 12, 10, 8, and 6 ms. For each interval, adjust `amp2` with a precision of 0.1 µA cm^{-2} to determine the minimum amplitude required to trigger a second action potential. The resulting amplitude, denoted as $I_{2\text{th}}$, represents the threshold current for eliciting a second spike as a function of the inter-stimulus interval.

3.1.1 Delay of 25 ms

```
close;
amp2=13.4;
```

```
amp1 = 26.8;
width1 = 0.5;
delay2 = 25;
width2 = 0.5;
for i = 1:6
 hhmplot(0,35,i);
 amp2 = amp2+0.1;
end
```

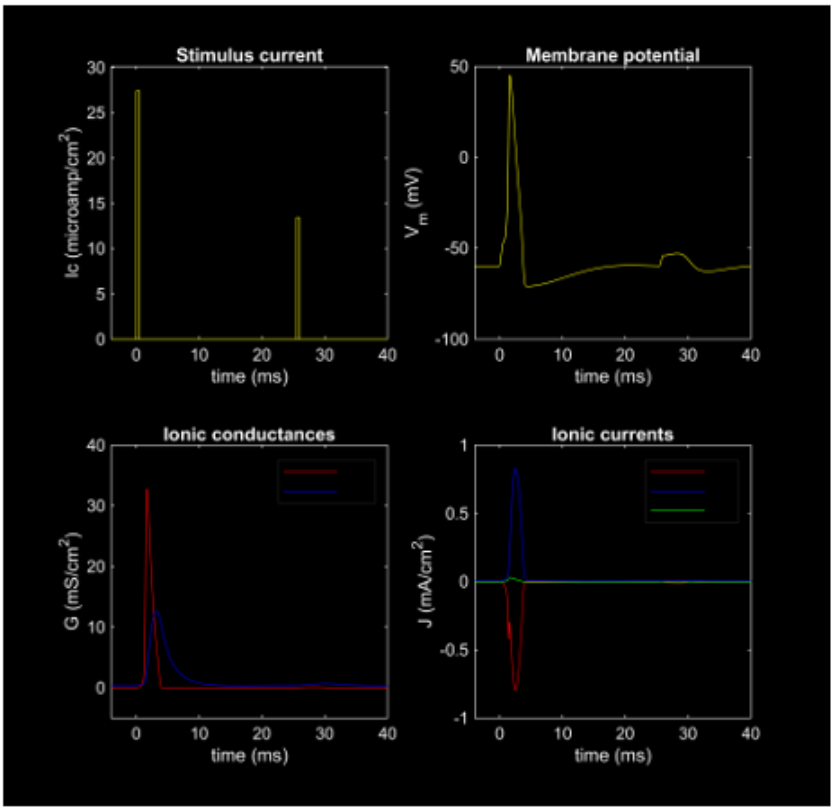

Figure 5: Results for stimulating the model axon with two current pulses separated by varying time intervals

An action potential is triggered at 13.7 µA/cm^2.

3.1.2 Delay of 20 ms

```
close;
amp1 = 26.8;
width1 = 0.5;
delay2 = 20;
amp2 = 11.4;
width2 = 0.5;
for i = 1:6
 hhmplot(0,35,i);
 amp2 = amp2+0.1;
end
```

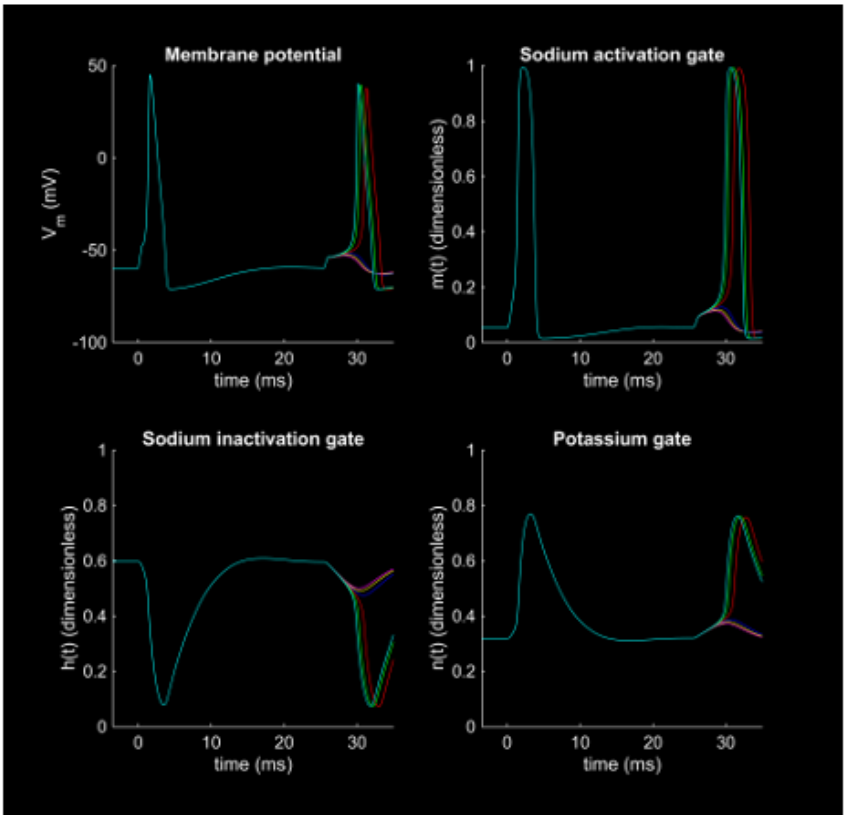

Figure 6: Spikes for a Delay of 20 ms

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

3.1.3 Delay of 18 ms

```
close;
amp1 = 26.8;
width1 = 0.5;
delay2 = 18;
amp2 = 11;
width2 = 0.5;
for i = 1:6
 hhmplot(0,35,i);
 amp2 = amp2+0.1;
end
```

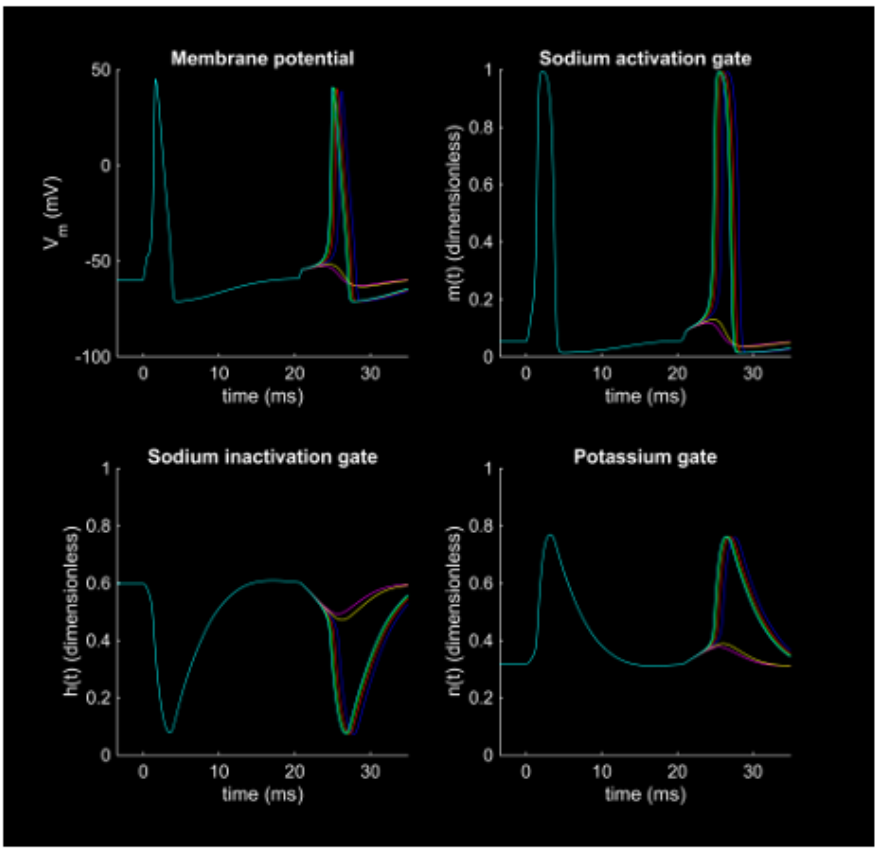

Figure 7: Spikes for a Delay of 18 ms

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

3.1.4 Delay of 16 ms

```
close;
amp1 = 26.8;
width1 = 0.5;
delay2 = 16;
amp2 = 12.2;
width2 = 0.5;
for i = 1:6
 hhmplot(0,35,i);
 amp2 = amp2+0.1;
end
```

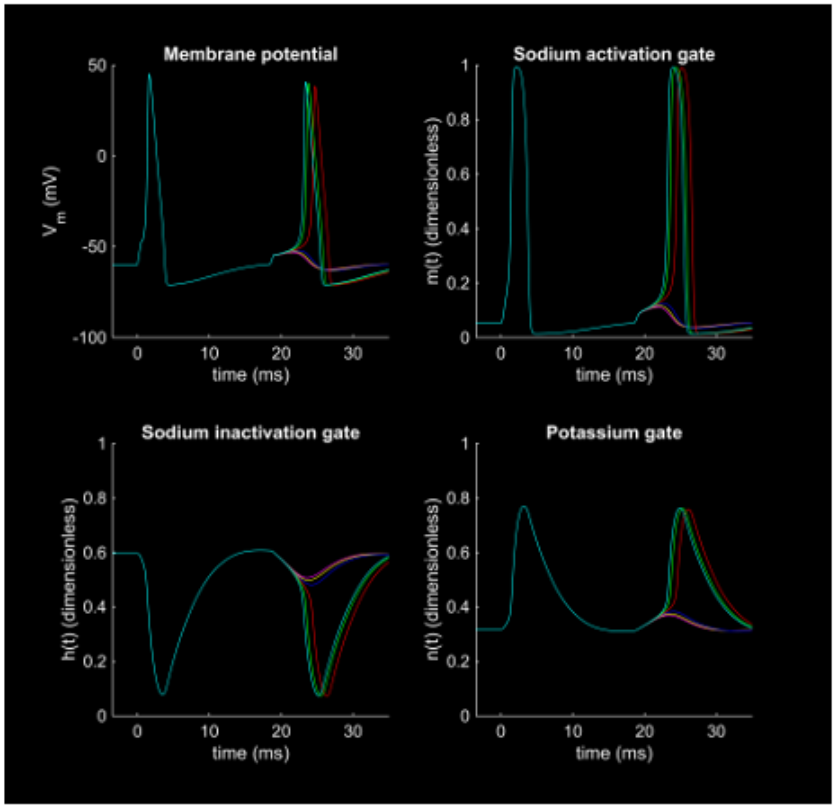

Figure 8: Spikes for a Delay of 16 ms

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

3.1.5 Delay of 14 ms

```
close;
amp1 = 26.8;
width1 = 0.5;
delay2 = 14;
amp2 = 16.5;
width2 = 0.5;
for i = 1:6
 hhmplot(0,35,i);
 amp2 = amp2+0.1;
end
```

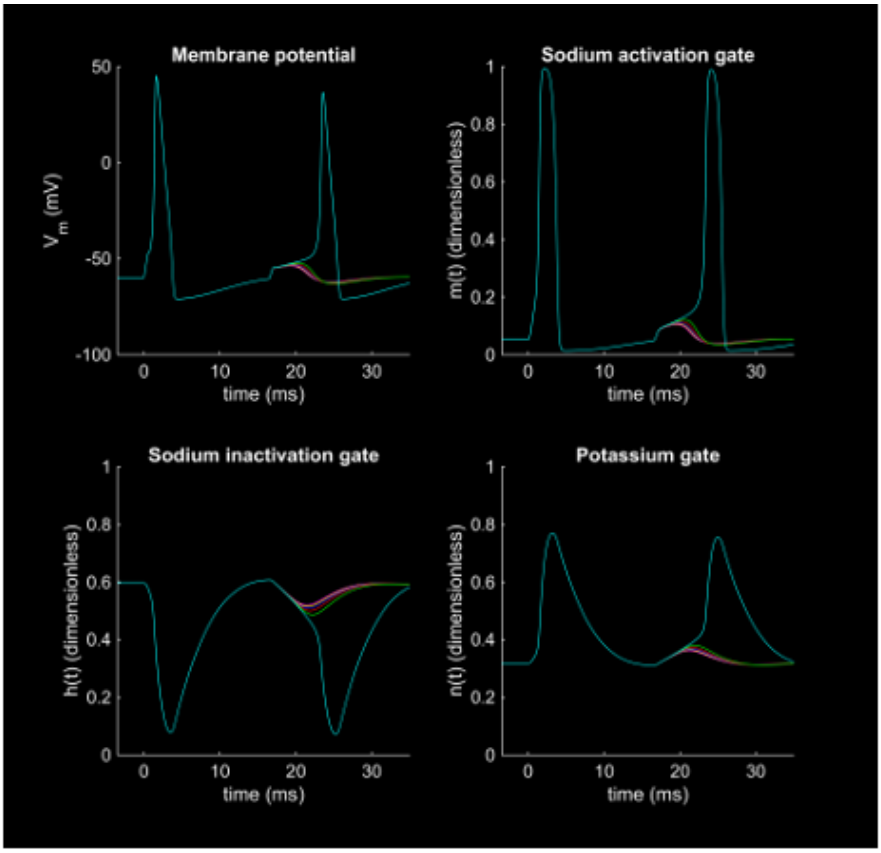

Figure 9: Spikes for a Delay of 14 ms

An action potential is triggered at 17 µA/cm^2.

3.1.6 Delay of 12 ms

```
close;
amp1 = 26.8;
width1 = 0.5;
delay2 = 12;
amp2 = 25;
width2 = 0.5;
for i = 1:6
 hhmplot(0,35,i);
 amp2 = amp2+0.1;
end
```

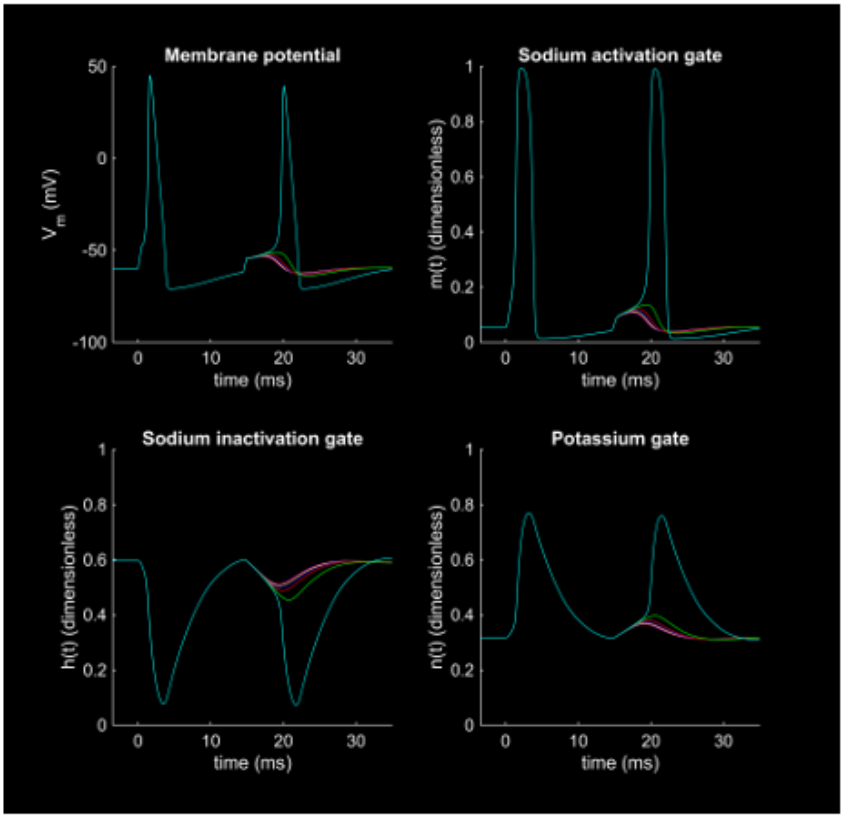

Figure 10: Spikes for a delay of 12 ms

An action potential is triggered at 25.5 µA/cm^2.

3.1.7 Delay of 10 ms

```
close;
amp1 = 26.8;
width1 = 0.5;
delay2 = 10;
amp2 = 40.3;
width2 = 0.5;
for i = 1:6
 hhmplot(0,35,i);
 amp2 = amp2+0.1;
end
```

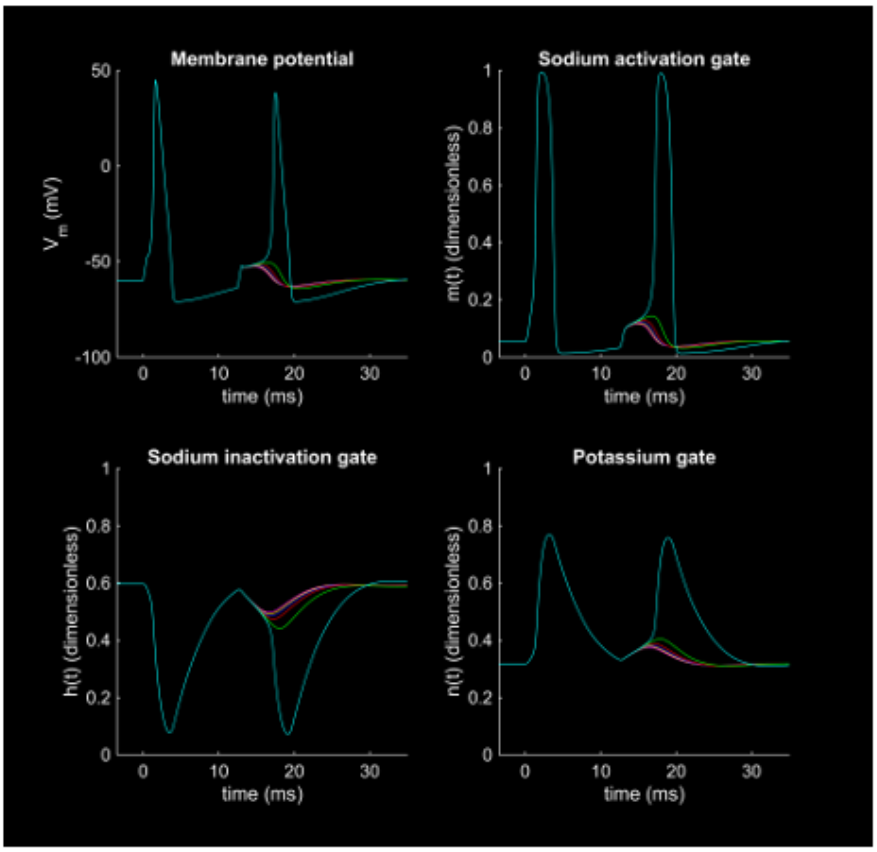

Figure 11: Spikes for a Delay of 10 ms

An action potential is triggered at $40.6\,\mu A/cm^2$.

3.1.8 Delay of 8 ms

```
close;
amp1 = 26.8;
width1 = 0.5;
delay2 = 8;
amp2 = 70.1;
width2 = 0.5;
for i = 1:6
 hhmplot(0,35,i);
 amp2 = amp2+0.1;
end
```

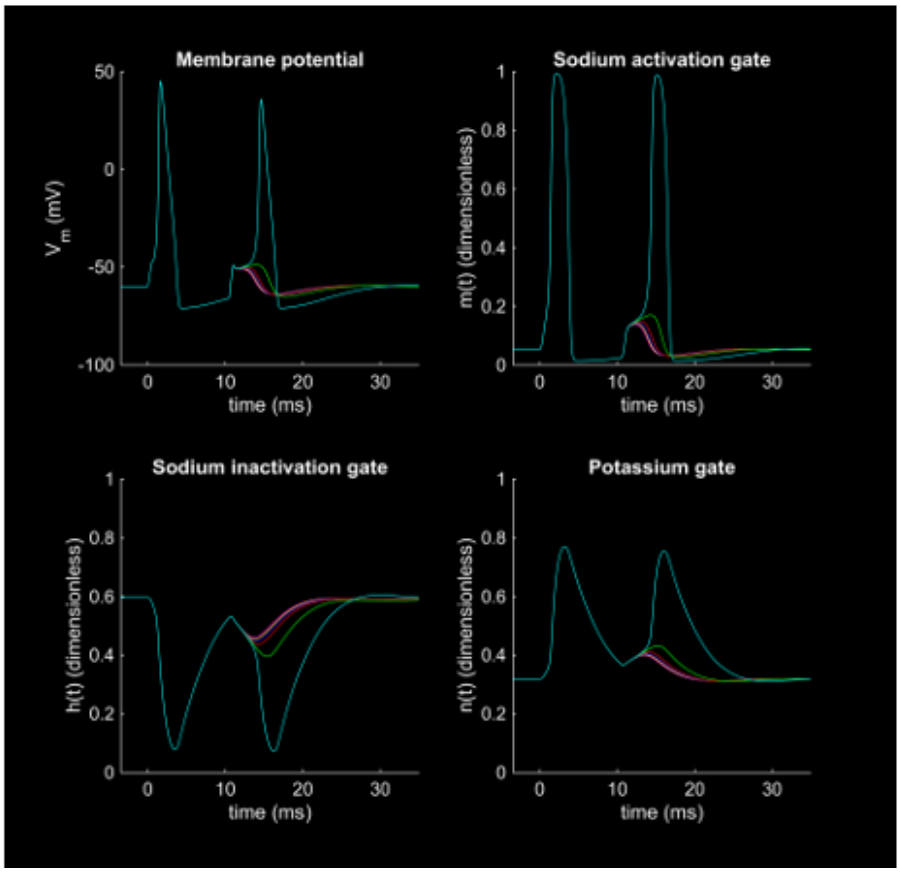

Figure 12: Spikes for a Delay of 8 ms

An action potential is triggered at 70.1 µA/cm^2.

3.1.9 Delay of 6 ms

```
close;
amp1 = 26.8;
width1 = 0.5;
delay2 = 6;
amp2 = 145.1;
width2 = 0.5;
for i = 1:6
 hhmplot(0,35,i);
 amp2 = amp2+0.1;
end
```

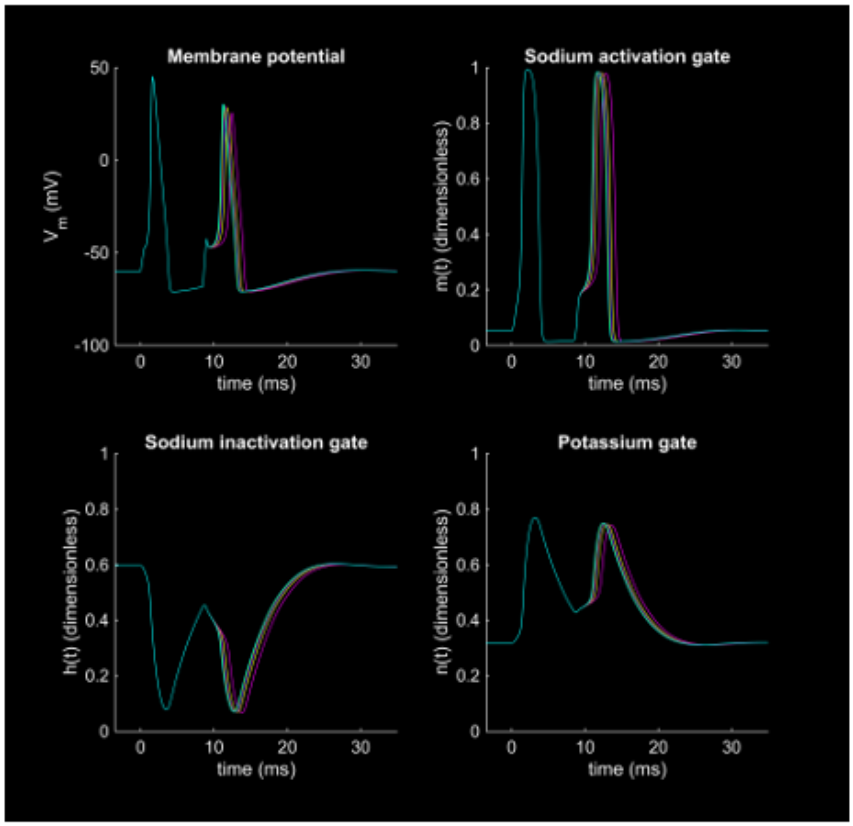

Figure 13: Spikes for a Delay of 6 ms

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

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.

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

The code to obtain the graph is as follows:

```
 close;
 I2 = [145.2, 70.1, 40.8, 25.5, 17.0, 12.7, 11.3, 11.6, 13.7];
 I1 = 26.8;
 ratio= I2 / I1;
 delay_ms = [6, 8, 10, 12, 14, 16, 18, 20, 25];
 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');
```

The resulting graph was as follows:

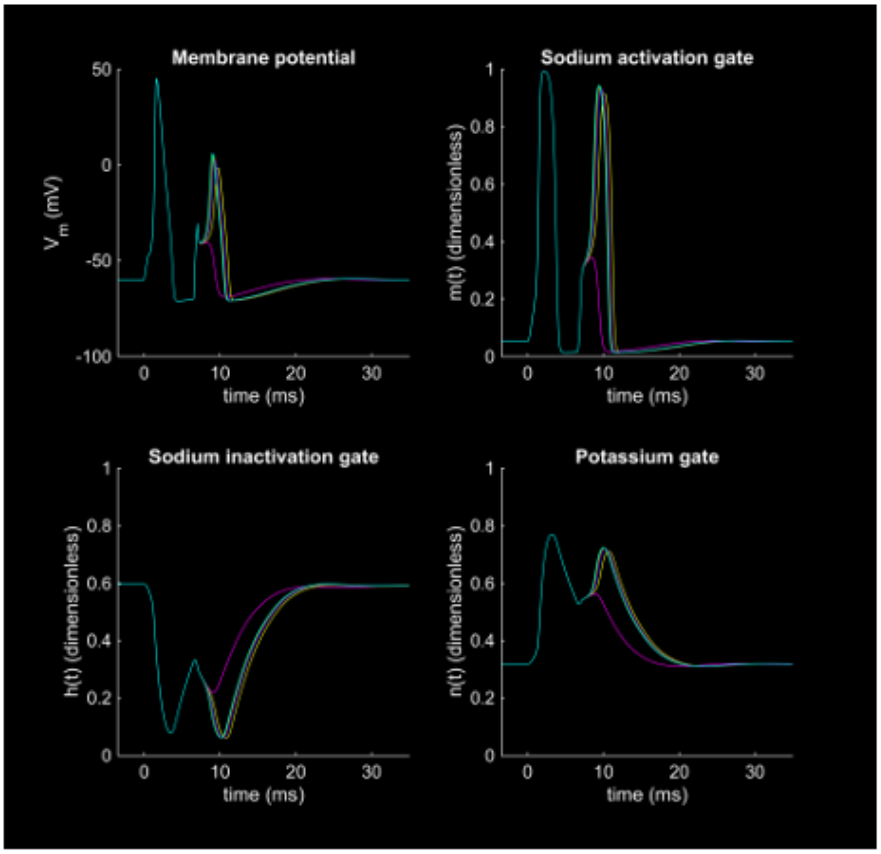

Figure 14: Relative Threshold Current vs. Inter-pulse Interval

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

The code for the analysis is provided 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');
```

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

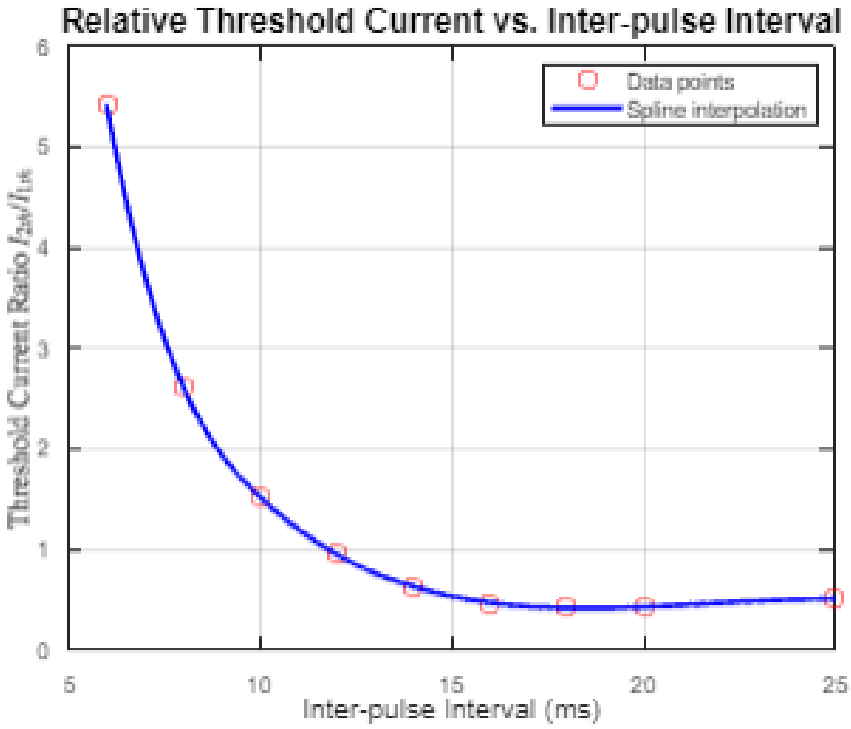

Figure 15: Finding the Absolute and Relative Refractory Periods

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 describes the generation of multiple action potentials in response to a prolonged, supra-threshold stimulus. Instead of producing a single spike, a neuron subjected to sustained depolarization from a sufficiently strong current emits a continuous series of action potentials. This pattern demonstrates how neurons translate ongoing stimuli into repetitive electrical signals. Within the Hodgkin-Huxley framework, repetitive firing arises when the membrane potential repeatedly recovers and surpasses the threshold, reflecting the interplay between sodium and potassium channel conductances during extended excitation.

4.1 Question 5

Using either `hhsplot` or `hhmplot`, estimate the firing rate (number of action potentials per second) by applying single stimulus currents of 80 ms duration at amplitudes of 5,

10, 20, 30, 50, 70, and 100 µA cm^{-2}. Then, plot the frequency of action potentials as a function of the stimulus 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 5 µA/cm^2

```
% Plot for amp1 = 5
close;
amp1=5;
width1 = 80;
delay2 = 0;
amp2 = 0;
width2 = 0;
amp2 = 0;
hhmplot(0,100,0);
```

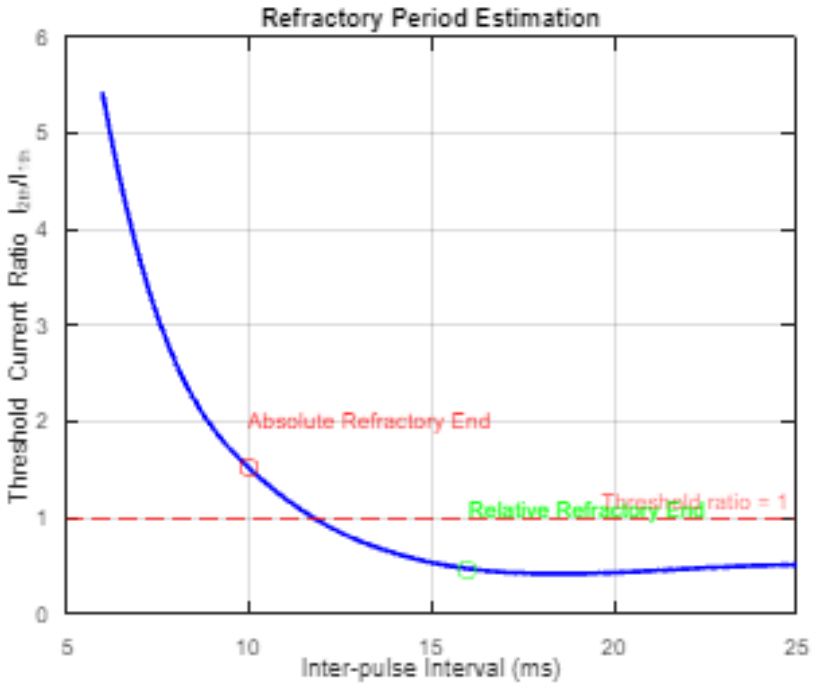

Figure 16: Spikes for Stimulus Current of 5 µA/cm^2

4.1.2 Stimulus Current of 10 µA/cm^2

```
% Plot for amp1 = 10
close;
amp1 = 10;
width1 = 80;
delay2 = 0;
amp2 = 0;
```

```
width2 = 0;
hhmplot(0, 100, 0);
```

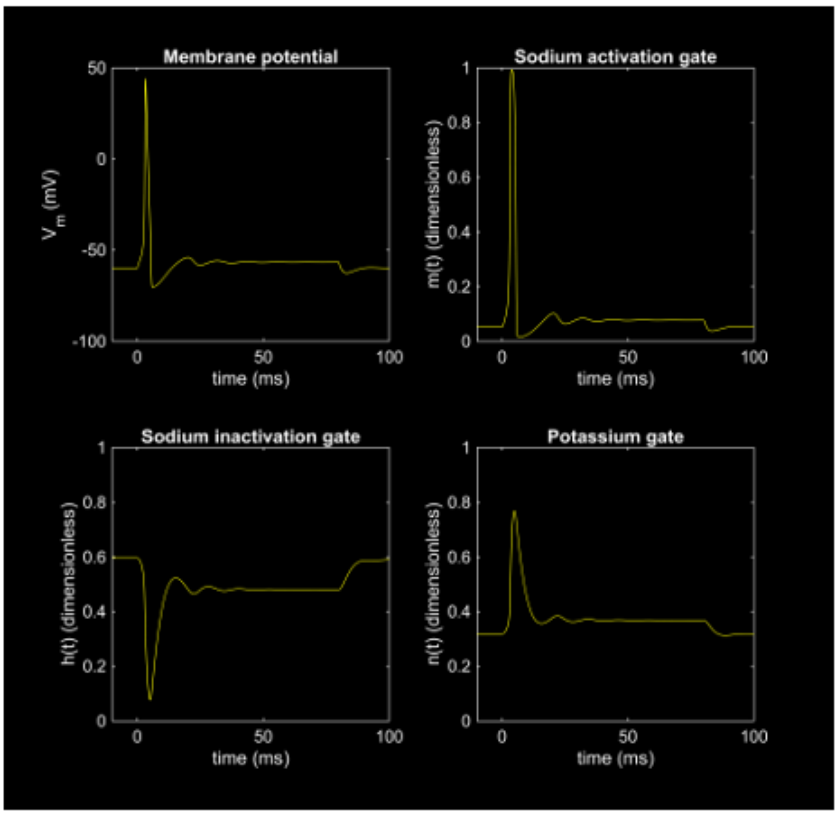

Figure 17: Spikes for Stimulus Current of $10\,\mu A/cm^2$

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

```

% Plot for amp1 = 20
close;
amp1 = 20;
width1 = 80;
delay2 = 0;
amp2 = 0;
width2 = 0;
hhmplot(0, 100, 0);
```

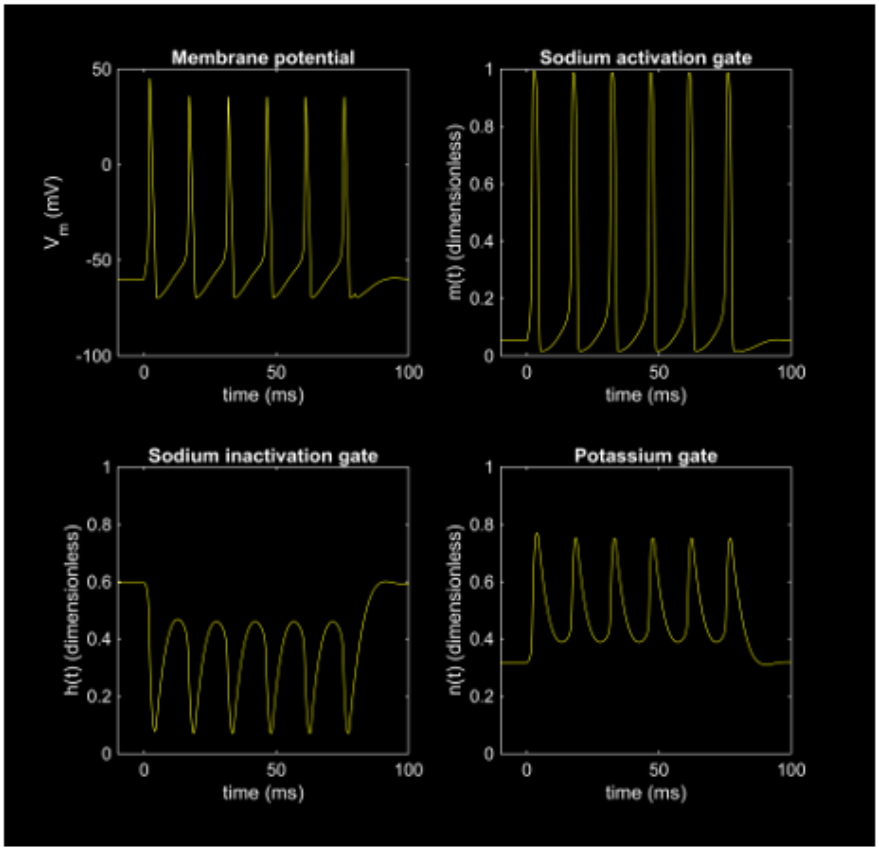

Figure 18: Spikes for Stimulus Current of $20\,\mu A/cm^2$

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

```
1
2 % Plot for amp1 = 30
3 close;
4 amp1 = 30;
5 width1 = 80;
6 delay2 = 0;
7 amp2 = 0;
8 width2 = 0;
9 hhmplot(0, 100, 0);
```

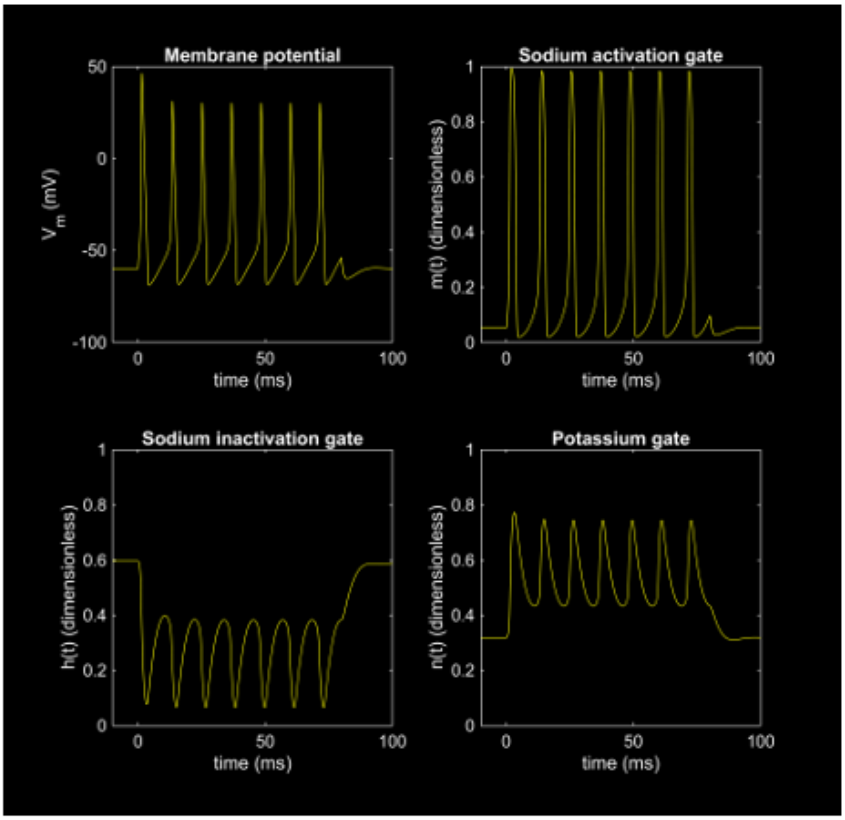

Figure 19: Spikes for Stimulus Current of $30\,\mu A/cm^2$

4.1.5 Stimulus Current of $50\,\mu A/cm^2$

```
1
2  pause on
3  % Plot for amp1 = 50
4  close;
5  amp1 = 50;
6  width1 = 80;
7  delay2 = 0;
8  amp2 = 0;
9  width2 = 0;
10 hhmplot(0, 100, 0);
```

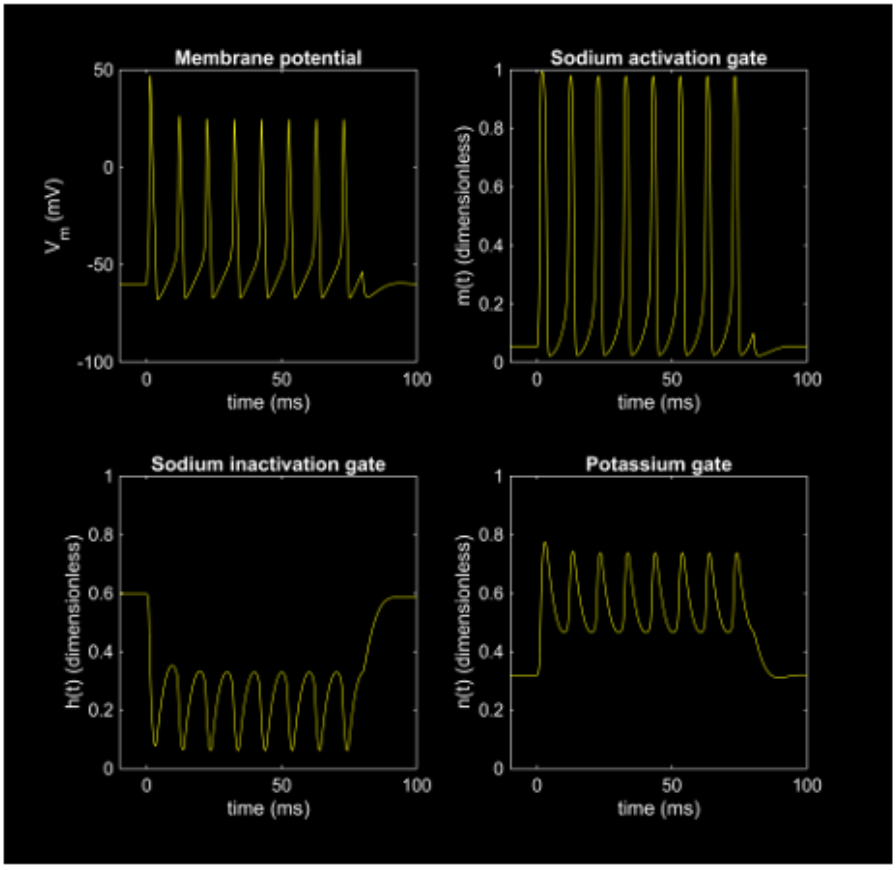

Figure 20: Spikes for Stimulus Current of $50\,\mu A/cm^2$

4.1.6 Stimulus Current of $70\,\mu A/cm^2$

```
1
2 % Plot for amp1 = 70
3 close;
4 amp1 = 70;
5 width1 = 80;
6 delay2 = 0;
7 amp2 = 0;
8 width2 = 0;
9 hhmplot(0, 100, 0);
```

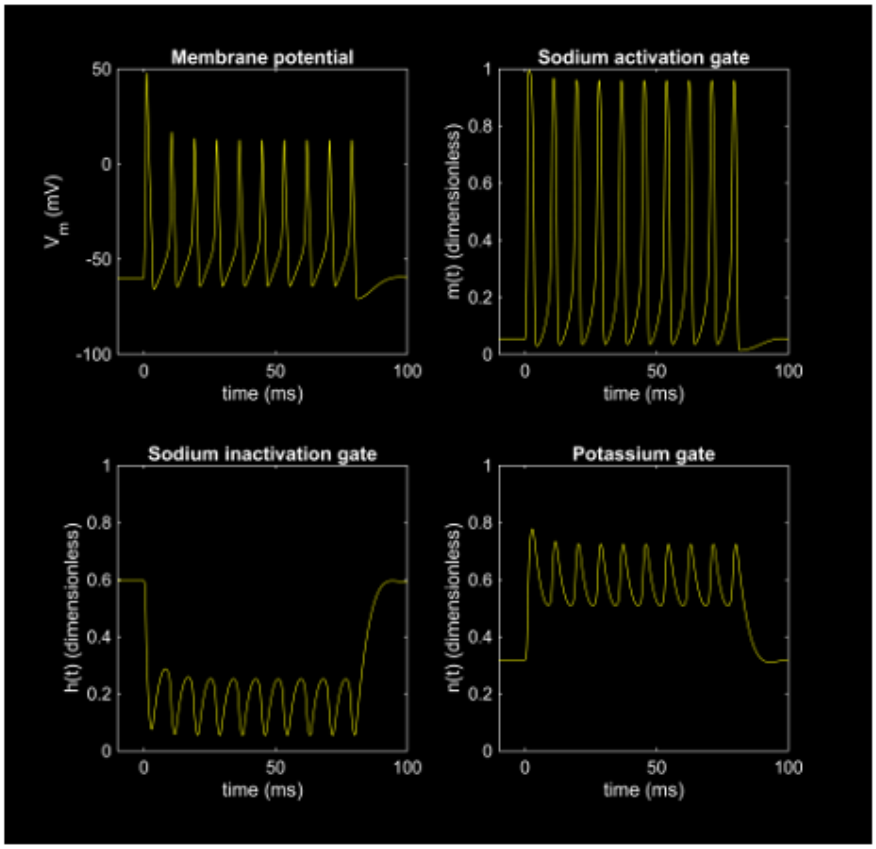

Figure 21: Spikes for Stimulus Current of $70\,\mu A/cm^2$

4.1.7 Stimulus Current of $100\,\mu A/cm^2$

```
1
2 % Plot for amp1 = 100
3 close;
4 amp1 = 100;
5 width1 = 80;
6 delay2 = 0;
7 amp2 = 0;
8 width2 = 0;
9 hhmplot(0, 100, 0);
```

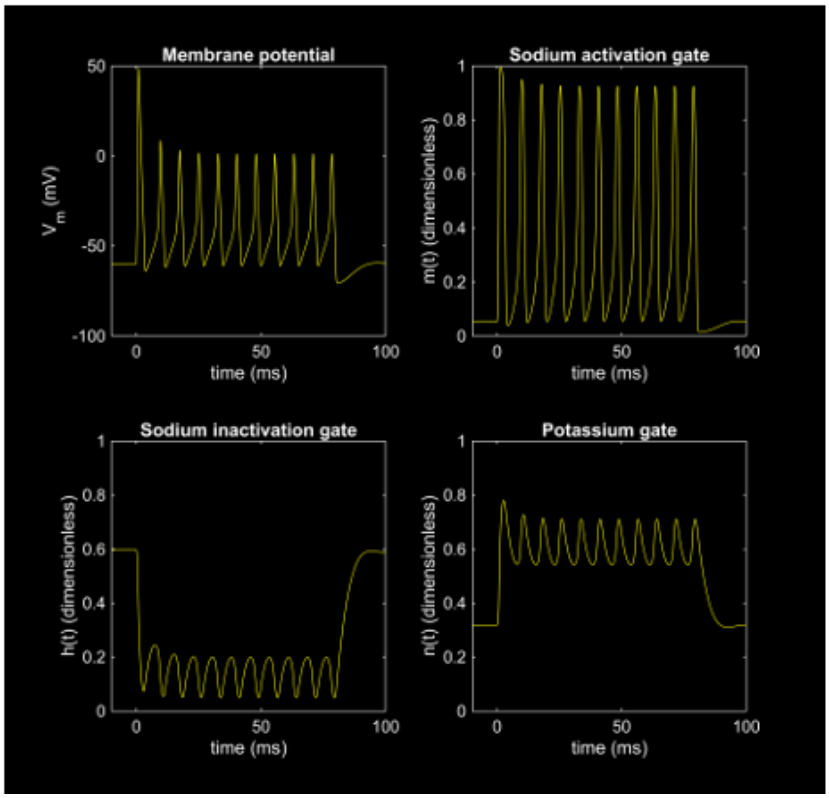

Figure 22: Spikes for Stimulus Current of 100 µA/cm^2

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

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

```
1
2  pause on
3  close;
4  amp = [5,10,20,30,50,70,100];
5  freq = [1,6,7,8,10,11,12];
6  x_values = linspace(0, 105, 1000); % Points to evaluate the
       smooth curve
7  fx = spline(amp, freq, x_values);
8  plot(x_values, fx);
9  xlabel('Amplitude');
10 ylabel('Frequency');
```

```
grid on;
```

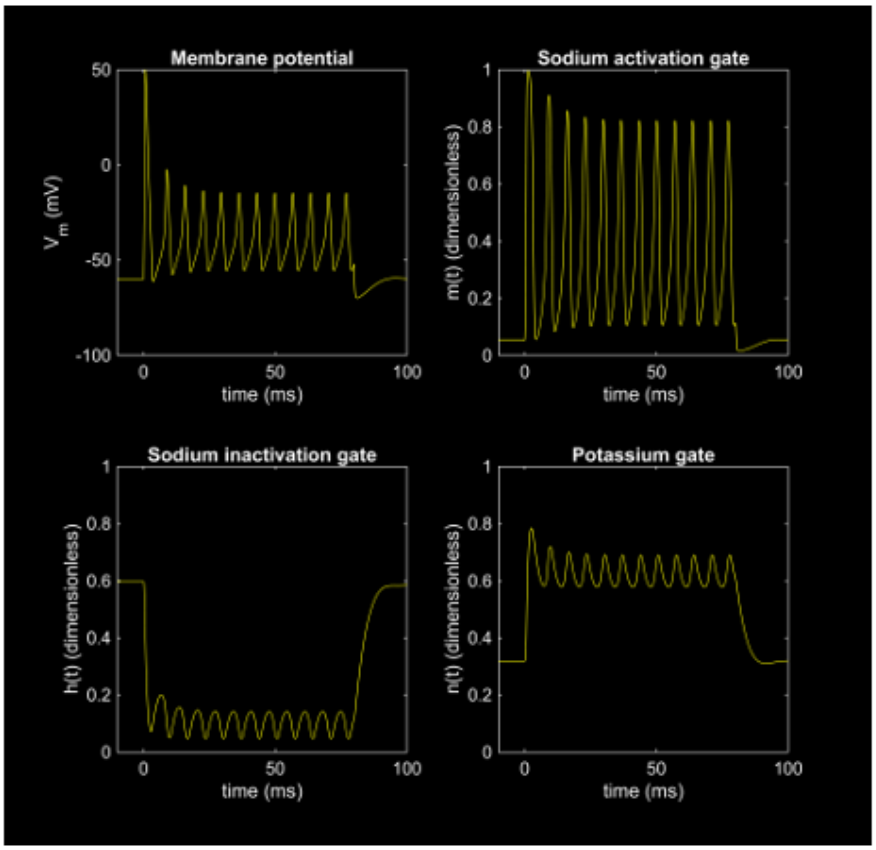

Figure 23: Action potential frequency vs. stimulating current amplitude

The frequency increases with the amplitude. Initially, there is a rapid increase at small amplitudes,
followed by a gradual slowing in the rate of increase. However, as the frequency continues to rise,
the amplitude of the stimulus intensity decreases.

4.2 Question 6

```
 close all;
[amp1, width1, delay2, amp2, width2] = deal(200, 80, 0, 0, 0);
hhmplot(0, 100, 0);
```

The obtained graphs are given below.

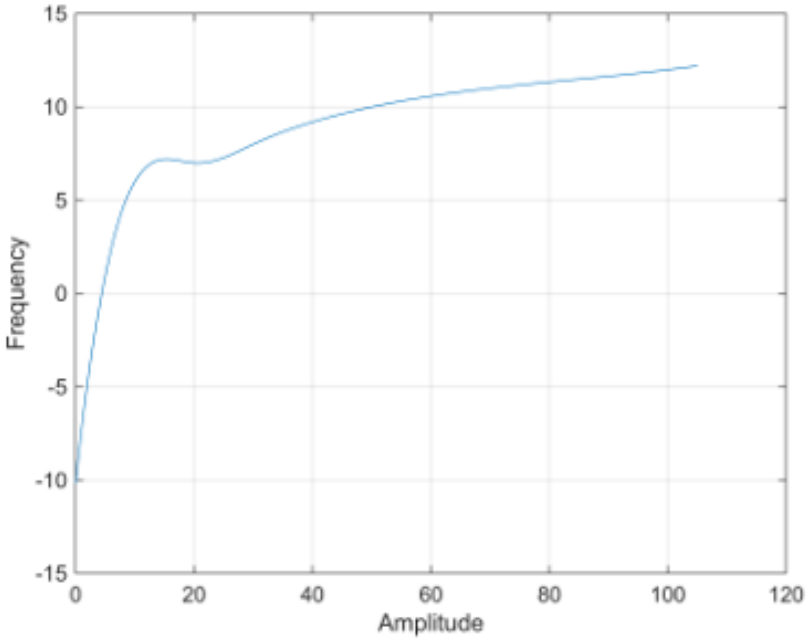

Figure 24: Plots at stimulating current amplitude to $200\,\mu A/cm^2$

When the stimulating current is set to $200\,\mu A\,cm^{-2}$, the neuron initially fires one or two action potentials but then ceases firing despite continued stimulation. This phenomenon is called a *depolarization block*.

A depolarization block occurs because a sustained, strong depolarizing current holds the membrane potential at a high level, preventing the initiation of further spikes.

Although one might expect that higher current leads to more firing, the opposite occurs due to the behavior of the Hodgkin-Huxley voltage-dependent gating variables—m, h, and n.

The m gate, which activates Na^+ channels, responds rapidly and remains elevated during depolarization. Meanwhile, the h gate, responsible for inactivating Na^+ channels, gradually decreases, causing sodium channels to become inactivated and unable to reopen.

Because h is low, new spikes cannot be generated. At the same time, the n gate activates K^+ channels slowly, leading to more potassium channels opening and preventing proper repolarization.

With high m, low h, and elevated n values, the membrane stays in a depolarized, non-excitable state, resulting in the depolarization block.

5 Temperature Dependence

Temperature dependence in the Hodgkin-Huxley model describes how variations in temperature influence the kinetics of ion channels and overall membrane excitability. Higher temperatures increase the speed at which sodium and potassium channels open and close, as reflected in the gating variables m, h, and n, due to enhanced molecular activity. This results in faster action potentials, reduced spike durations, and increased firing rates.

The model accounts for these effects by applying a Q_{10} factor, which adjusts the rate constants according to temperature changes.

5.1 Question 7

Using a single current pulse of intensity $20\,\mu A\,cm^{-2}$ with a pulse width of 0.5 ms, we examine how varying temperatures—0, 5, 10, 15, 20, 24, 25, 26, and 30 °C—affect the duration and amplitude of the resulting action potential.

Generally, increasing temperature leads to faster ion channel kinetics, which shortens the action potential duration and can slightly increase the peak amplitude due to more rapid sodium channel activation.

The action potential graphs at these different temperatures were generated 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
```

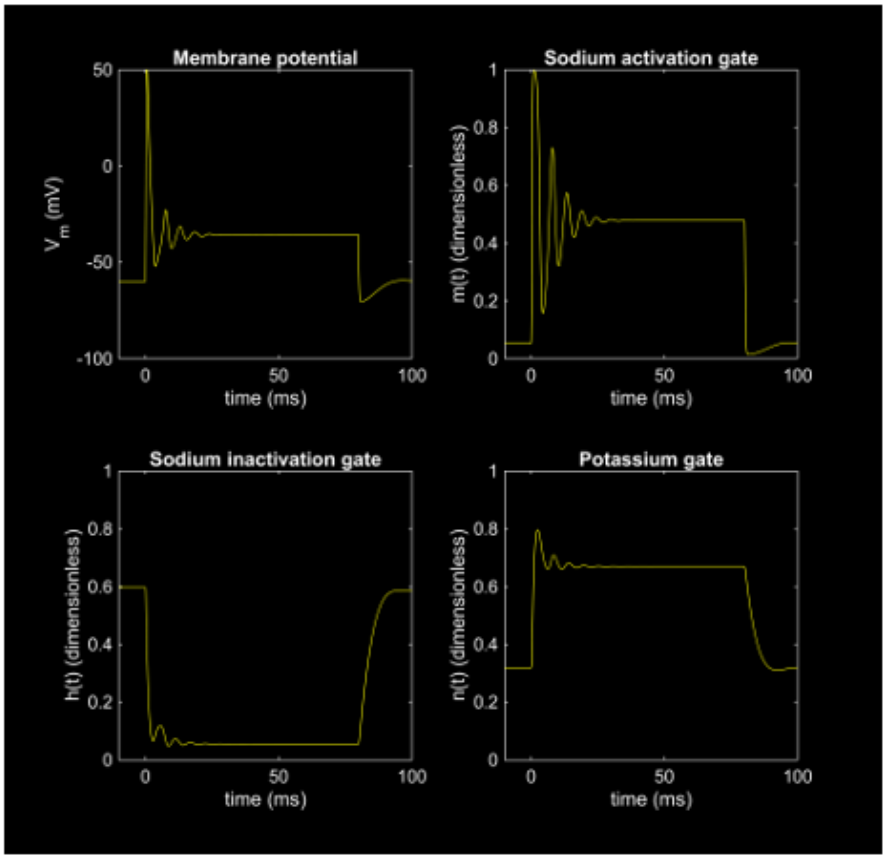

Figure 25: Plots at Different Temperatures

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

1. As temperature rises, the action potential duration decreases, resulting in quicker spikes. This happens because the ion channels open and close more rapidly at elevated temperatures.

2. The peak amplitude of the action potential can increase somewhat due to the faster activation of sodium channels. Nevertheless, at very high temperatures, the amplitude might reduce because of increased channel inactivation or other physiological effects.

In summary, higher temperatures produce action potentials that are briefer and often more pronounced, reflecting the accelerated behavior of ionic channel dynamics.

6 Conclusion

This study employed the Hodgkin-Huxley model to explore fundamental features of neuronal excitability. We determined the threshold current necessary to trigger action potentials, characterized both absolute and relative refractory periods, and analyzed how increasing stimulus strength results in repetitive firing. At very high stimulus intensities, a depolarization block occurred, caused by prolonged sodium channel inactivation. Additionally, we investigated temperature effects, which enhanced firing frequency by speeding up ion channel kinetics. Together, these simulations highlight how neuronal responses emerge from the complex interaction of stimulus parameters, timing, and intrinsic biophysical mechanisms such as voltage- and temperature-sensitive 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`