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Properties of the Hodgkin-Huxley equations

by:

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BM2102 Modelling and Analysis of Physiological Systems

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Contents

1 Introduction

This assignment investigates the electrical behavior of excitable cells through the simulation of the Hodgkin-Huxley (HH) model, a foundational mathematical framework that describes the ionic mechanisms underlying action potential generation in neurons. Originally developed from experiments on the squid giant axon, the HH model captures the dynamics of voltage-gated sodium and potassium channels and their roles in membrane excitability.
The focus of the assignment is to explore four key physiological phenomena exhibited by the HH model under space-clamp conditions: threshold behavior, refractoriness (both absolute and relative), repetitive firing in response to sustained stimuli, and the effects of temperature on action potential characteristics. These properties were studied using a series of MATLAB simulations with predefined scripts and parameters, enabling the controlled application of stimulus currents and temperature variations.
Threshold analysis revealed the narrow amplitude range between sub-threshold and supra-threshold stimuli, demonstrating the model's high sensitivity to input. Refractoriness was examined by applying dual pulses at varying intervals to determine the absolute and relative refractory periods. Repetitive activity was observed by using long-duration stimuli of different amplitudes, allowing the estimation of spike frequency as a function of stimulus strength. Temperature dependence was explored by altering simulation temperature and observing changes in action potential amplitude and duration.
The assignment offers valuable insight into how membrane excitability arises from the interplay of ionic conductances, and demonstrates the relevance of the Hodgkin-Huxley equations in modeling real neuronal behavior.

2 Threshold

2.1 Sub-threshold and Supra-threshold Stimulation

A brief stimulus pulse of 1 ms duration was applied to observe threshold behavior in the Hodgkin-Huxley model. At an amplitude of 6 μA/cm^2, no action potential was observed, indicating a sub-threshold response. Increasing the amplitude to 7 μA/cm^2 resulted in the generation of a full action potential. This demonstrates the model's sharp transition from sub-threshold to supra-threshold behavior, consistent with the all-or-none nature of neuronal firing.
The MATLAB code below was used to create the plots associated with this question.

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

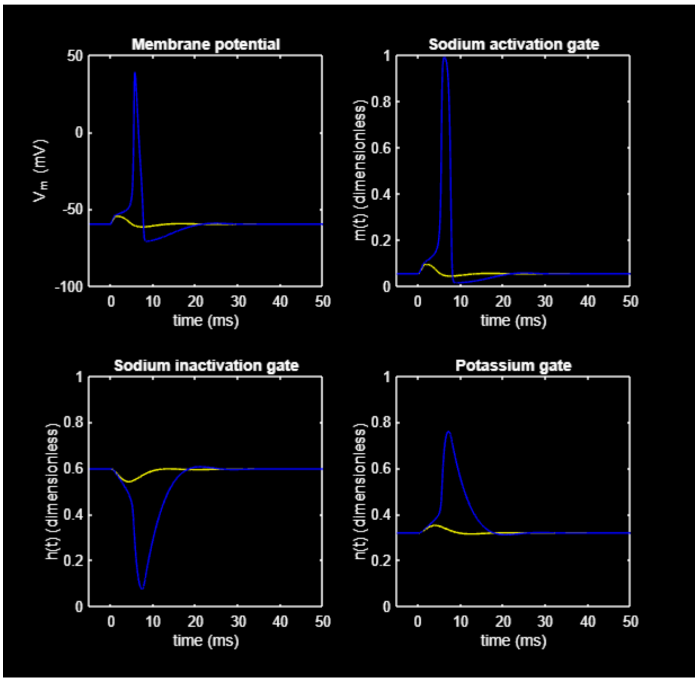

Figure 1: Sub-threshold and Supra-threshold Stimulation

2.2 Question 01

To determine the threshold stimulating current amplitude, the interval between 6 and 7 μA/cm^2 was initially tested using the `hhmplot` function. An action potential was observed at 7 μA/cm^2 but not at 6 μA/cm^2, confirming that the threshold lies within this range.

The amplitude was then incremented by 0.1 units, and it was found that the threshold is between 6.9 and 7. The MATLAB code below was used to create the plots associated with this.

```
hhconst;
amp1 = 6.0;  %Initial stimulus
width1 = 1;
hhmplot(0,50,0);

for i = 1:10
    display(amp1)
    amp1 = 6 + 0.1 * i; % Increment stimulus by 0.1
    hhmplot(0,50,1);
end
```

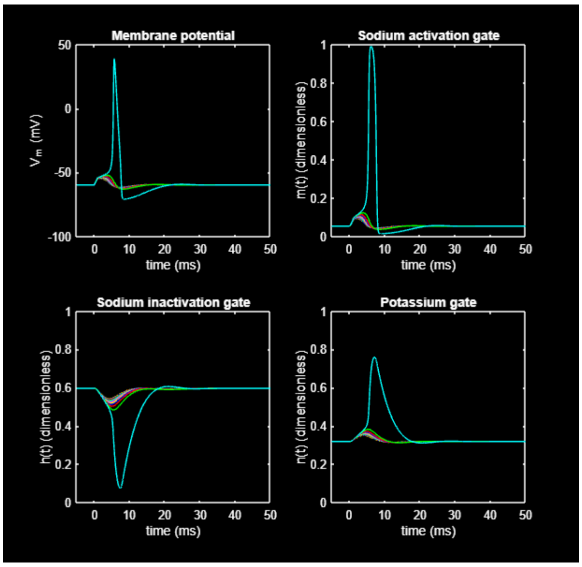

Figure 2: 0.1 increment

A finer search with 0.01 increments revealed that a **full action potential is first triggered at 6.95 μA/cm^2,** which was identified as the threshold current amplitude to two decimal places. The MATLAB code below was used to create the plots associated with this.

```
hhconst;
amp1 = 6.9;
width1 = 1;
hhmplot(0,50,0);

for i = 1:10
    display(amp1)
    amp1 = 6.9 + 0.01 * i; % Increment stimulus by 0.01
    hhmplot(0,50,i);
end
```

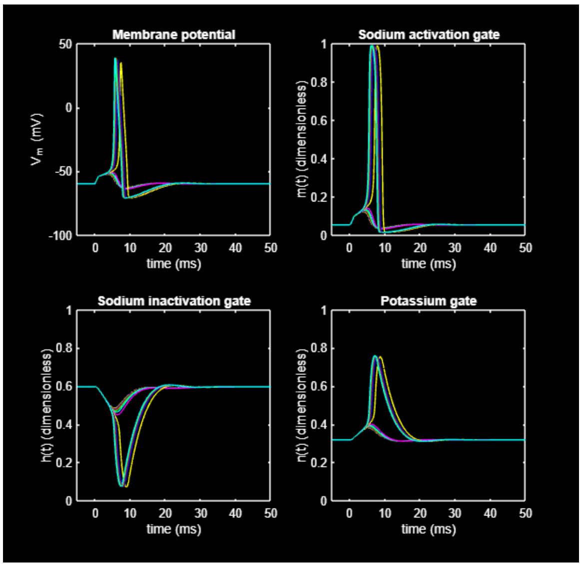

Figure 3: 0.01 increment

2.3 Question 02

To analyze the relationship between the total ionic currents and the external stimulus current, the command `[qna, qk, ql] = hhsplot(0,50);` was used to calculate the time-integrated sodium, potassium, and leak currents over the interval $[t_o, t_f] = [0, 50]$ ms. Simulations were performed for three cases: when the stimulus amplitude was sub-threshold, threshold-level, and supra-threshold.

2.3.1 Case 1: amplitude >threshold

```
hhconst;
amp1 = 7.00; % Choose intensity greater than threshold
width1 = 1;
[qna,qk,ql]=hhsplot(0,50);

sum_Jk = qna + qk + ql % Check the sum
```

A small, non-spiking membrane response was observed. The sum of the integrated ionic currents $(q_{Na} + q_K + q_L)$ was approximately equal to the total external stimulus current input, allowing for minor numerical discrepancies.

$$\text{sum\_}J_k = 7.0014 \approx 7$$

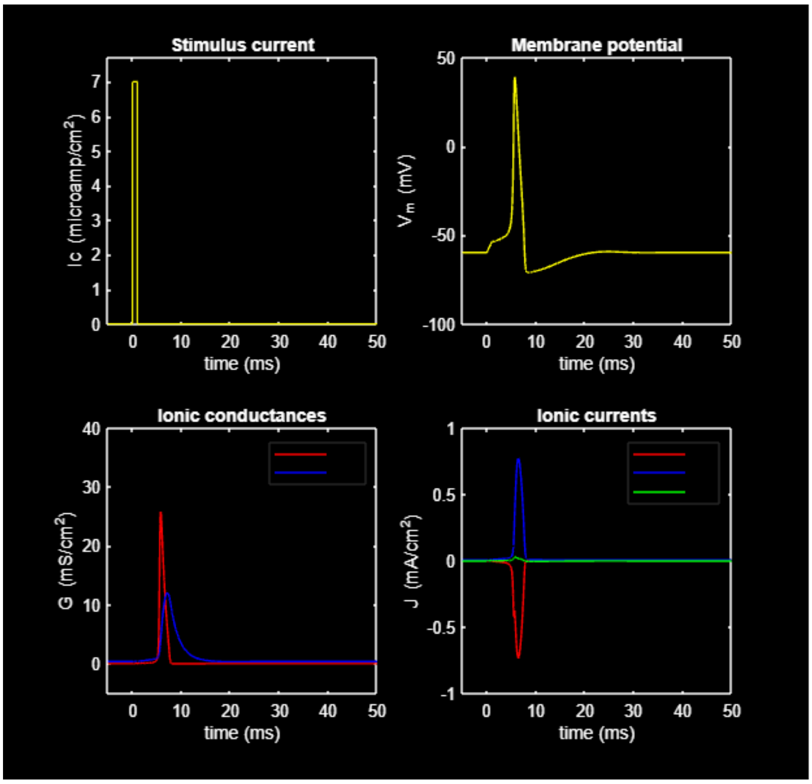

Figure 4: Membrane response for supra-threshold stimulus ($amp1 = 7$)

2.3.2 Case 2: amplitude<threshold

```
hhconst;
amp1 = 6.90; % Choose intensity lesser than threshold
width1 = 1;
[qna,qk,ql]=hhsplot(0,50);

sum_Jk = qna + qk + ql % Check the sum
```

An action potential was clearly observed. The integrated ionic current sum again closely matched the integral of the external input current over the duration of the pulse, confirming that the Hodgkin-Huxley model obeys charge conservation within acceptable numerical error.

$$\text{sum\_}J_k = 6.8998 \approx 6.9$$

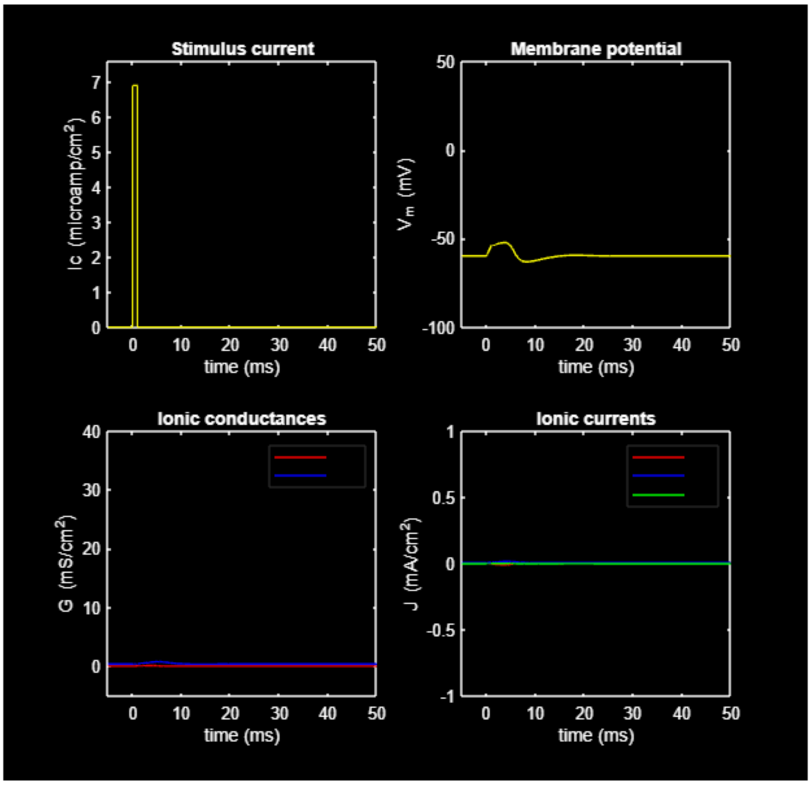

Figure 5: Membrane response for sub-threshold stimulus ($amp1 = 6.9$)

2.3.3 Case 3: amplitude=threshold

```
hhconst;
amp1 = 6.95;
width1 = 1;
[qna,qk,ql]=hhsplot(0,50);

sum_Jk = qna + qk + ql % Check the sum
```

At this finely tuned amplitude, a single action potential occurred. The total ionic current again balanced the external current injection, supporting the expected equivalence:

$$\int_{t_o}^{t_f} (J_{Na}(t) + J_K(t) + J_L(t))dt \approx \int_{t_o}^{t_f} J_e(t)dt$$

$$\text{sum\_}J_k = 6.9500$$

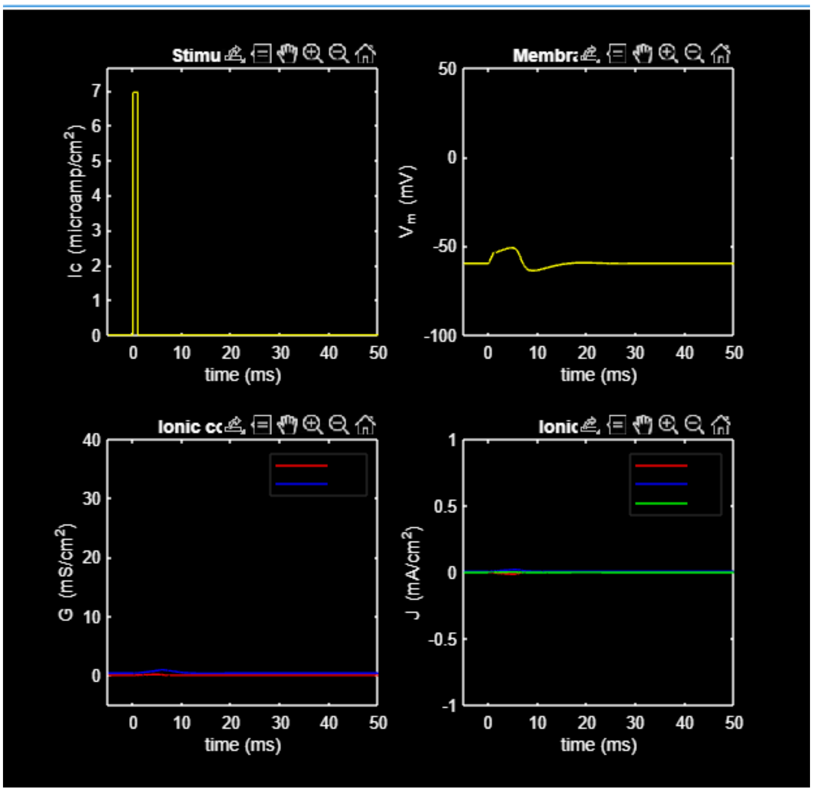

Figure 6: Membrane response at threshold stimulus ($amp1 = 6.95$)

2.3.4 Conclusion

In all three cases, the numerical results support the theoretical expectation that the time integral of the total ionic current is approximately equal to the integral of the externally applied current. Minor differences are attributed to numerical approximations inherent in the simulation process.

3 Refractoriness

3.1 Absolute and Relative Refractory Periods

The refractory period was investigated by applying two stimulus pulses with a fixed duration of 0.5 ms and varying the inter-pulse interval. The amplitude of the first pulse was set to 27.4 μA/cm^2, which is twice the threshold value for a single action potential, and the second pulse amplitude was set to 13.7 μA/cm^2. When the second pulse was applied with a sufficient delay (e.g., 25 ms), two distinct action potentials were observed. This confirms that the Hodgkin-Huxley model demonstrates both absolute and relative refractory periods similar to those seen in real neurons.
The MATLAB code below was used to create the plots associated with this.

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

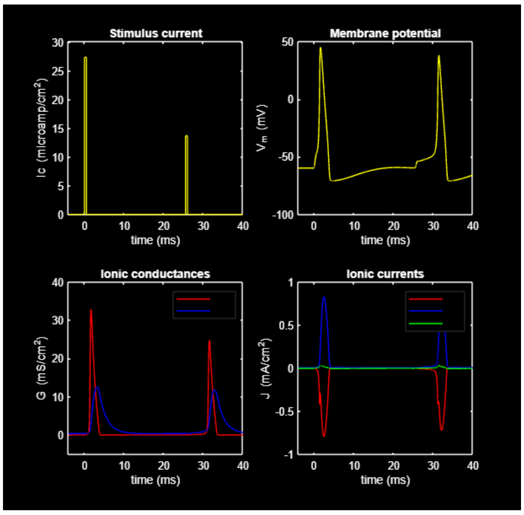

Figure 7: Absolute and Relative Refractory Periods

3.2 Question 03

3.2.1 Delay=20ms

The MATLAB code below was used to create the plots associated with this.

```
amp1 = 27.4;
width1 = 0.5;
amp2 = 10.0; % Start from this value and increment
delay2 = 20; % Set delay to 20 ms
width2 = 0.5;
hhmplot(0,30,0);

for j = 1:6 % Increment for 6 rounds
    amp2 = amp2+0.1; % Increment amp2 by 0.1 each iteration
    hhmplot(0,30,1);
end
```

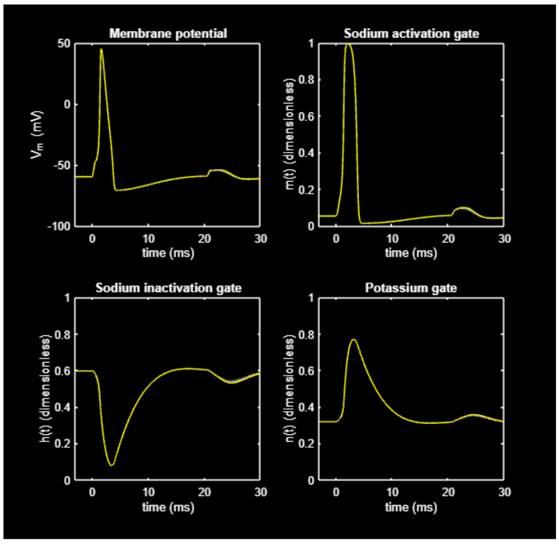

Figure 8: amp2=10.0

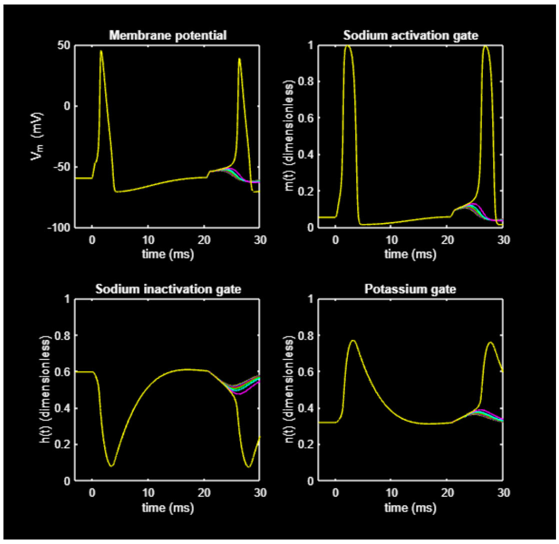

Figure 9: amp2=11.6

An action potential was successfully elicited when the amplitude of the second pulse reached $I_{2\text{th}} = 11.6\ \mu\text{A}/\text{cm}^2$, indicating that this value represents the threshold for the second stimulus under the given conditions.

3.2.2 Delay=18ms

The MATLAB code below was used to create the plots associated with this.

```
amp1 = 27.4;
width1 = 0.5;
amp2 = 10.0; % Start from this value and increment
delay2 = 18; % Set delay to 18 ms
width2 = 0.5;
hhmplot(0,30,0);

for j = 1:6 % Increment for 6 rounds
    amp2 = amp2+0.1; % Increment amp2 by 0.1 each iteration
    hhmplot(0,30,1);
end
```

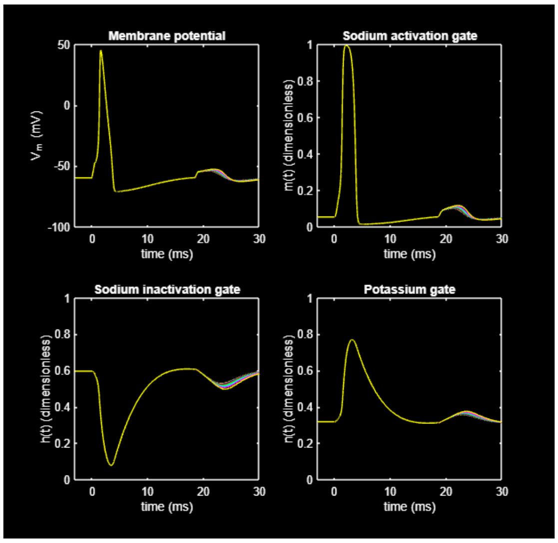

Figure 10: amp2=10.3

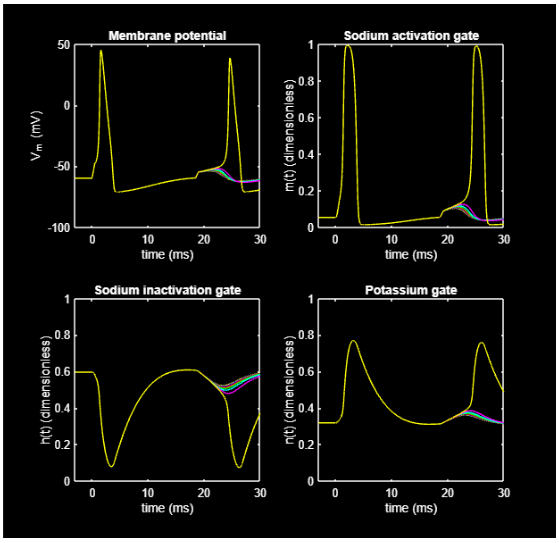

Figure 11: amp2=10.7

An action potential was successfully elicited when the amplitude of the second pulse reached $I_{2\text{th}} = 11.3\ \mu\text{A}/\text{cm}^2$, indicating that this value represents the threshold for the second stimulus under the given conditions.

3.2.3 Delay=16ms

The MATLAB code below was used to create the plots associated with this.

```
amp1 = 27.4;
width1 = 0.5;
amp2 = 11.5; % Start from this value and increment
delay2 = 16; % Set delay to 16 ms
width2 = 0.5;
hhmplot(0,30,0);

for j = 1:6 % Increment for 6 rounds
    amp2 = amp2+0.1; % Increment amp2 by 0.1 each iteration
    hhmplot(0,30,1);
end
```

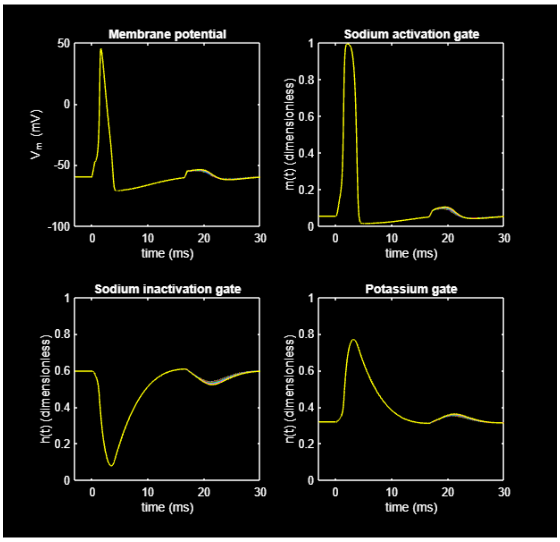

Figure 12: amp2=11.5

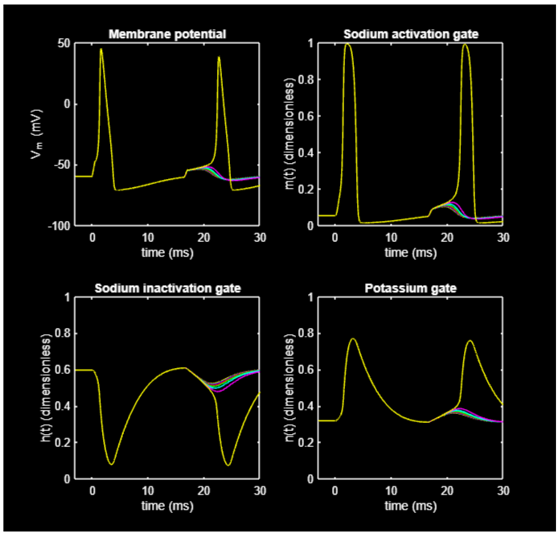

Figure 13: amp2=12.1

An action potential was successfully elicited when the amplitude of the second pulse reached $I_{2\text{th}} = 12.7\ \mu\text{A/cm}^2$, indicating that this value represents the threshold for the second stimulus under the given conditions.

3.2.4 Delay=14ms

The MATLAB code below was used to create the plots associated with this.

```
amp1 = 27.4;
width1 = 0.5;
amp2 = 16.0; % Start from this value and increment
delay2 = 14; % Set delay to 14 ms
width2 = 0.5;
hhmplot(0,30,0);

for j = 1:6 % Increment for 6 rounds
    amp2 = amp2+0.1; % Increment amp2 by 0.1 each iteration
    hhmplot(0,30,1);
end
```

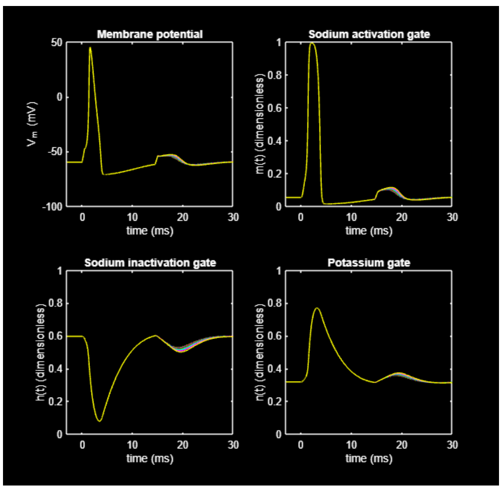

Figure 14: amp2=16.0

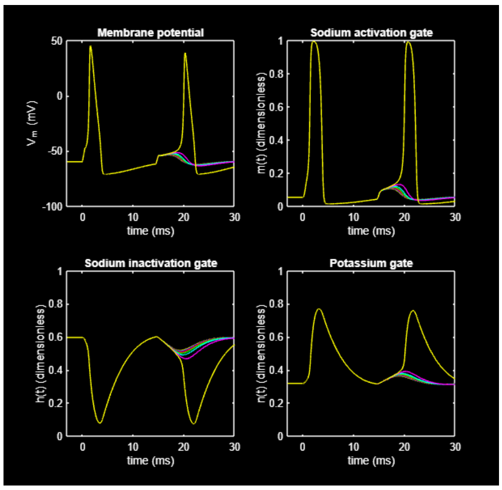

Figure 15: amp2=16.3

An action potential was successfully elicited when the amplitude of the second pulse reached $I_{2\mathrm{th}} = 16.9\ \mu\mathrm{A/cm}^2$, indicating that this value represents the threshold for the second stimulus under the given conditions.

3.2.5 Delay=12ms

The MATLAB code below was used to create the plots associated with this.

```
amp1 = 27.4;
width1 = 0.5;
amp2 = 24.5; % Start from this value and increment
delay2 = 12; % Set delay to 12 ms
width2 = 0.5;
hhmplot(0,30,0);

for j = 1:6 % Increment for 6 rounds
    amp2 = amp2+0.1; % Increment amp2 by 0.1 each iteration
    hhmplot(0,30,1);
end
```

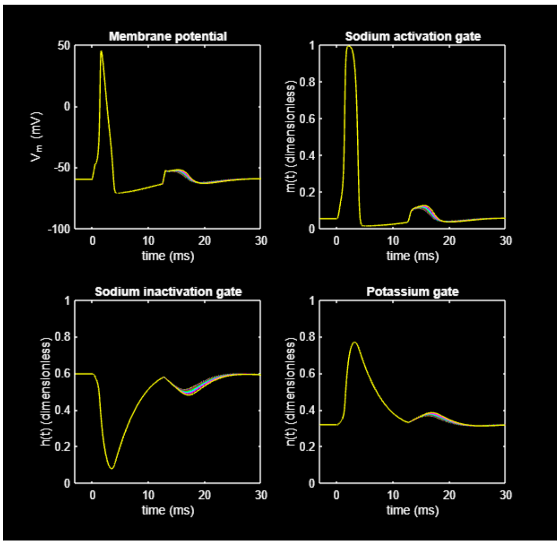

Figure 16: amp2=24.5

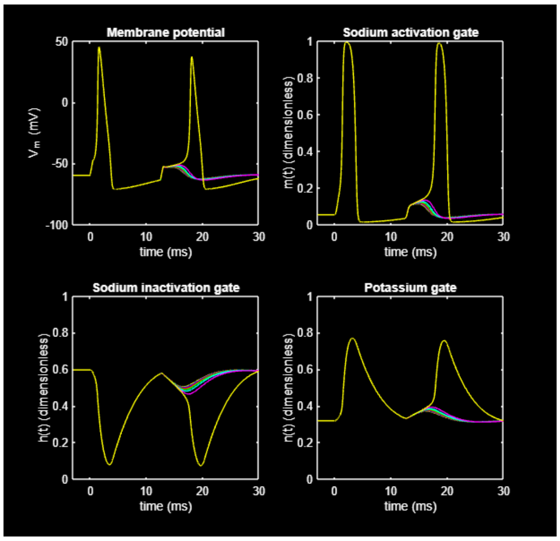

Figure 17: amp2=24.7

An action potential was successfully elicited when the amplitude of the second pulse reached $I_{2\mathrm{th}} = 25.3\ \mu\mathrm{A/cm}^2$, indicating that this value represents the threshold for the second stimulus under the given conditions.

3.2.6 Delay=10ms

The MATLAB code below was used to create the plots associated with this.

```
amp1 = 27.4;
width1 = 0.5;
amp2 = 39.5; % Start from this value and increment
delay2 = 10; % Set delay to 10 ms
width2 = 0.5;
hhmplot(0,30,0);

for j = 1:6 % Increment for 6 rounds
    amp2 = amp2+0.1; % Increment amp2 by 0.1 each iteration
    hhmplot(0,30,1);
end
```

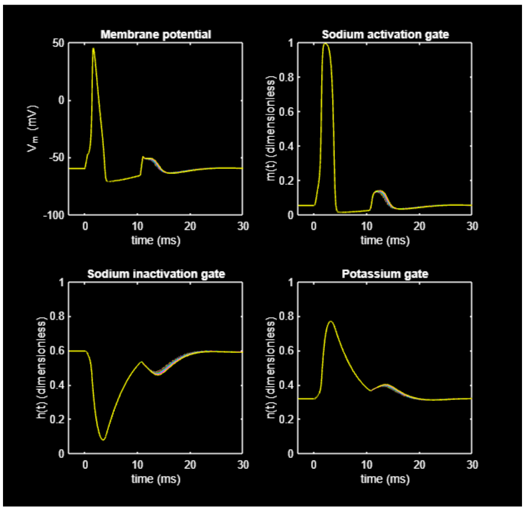

Figure 18: amp2=39.5

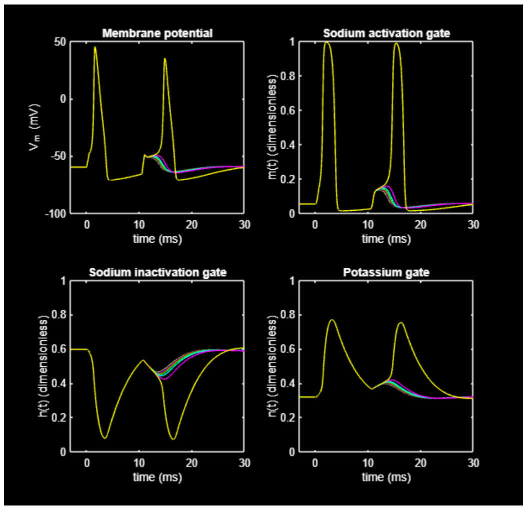

Figure 19: amp2=39.9

An action potential was successfully elicited when the amplitude of the second pulse reached $I_{2\text{th}} = 40.5\ \mu\text{A}/\text{cm}^2$, indicating that this value represents the threshold for the second stimulus under the given conditions.

3.2.7 Delay=8ms

The MATLAB code below was used to create the plots associated with this.

```
amp1 = 27.4;
width1 = 0.5;
amp2 = 68.5; % Start from this value and increment
delay2 = 8; % Set delay to 8 ms
width2 = 0.5;
hhmplot(0,30,0);

for j = 1:6 % Increment for 6 rounds
    amp2 = amp2+0.1; % Increment amp2 by 0.1 each iteration
    hhmplot(0,30,1);
end
```

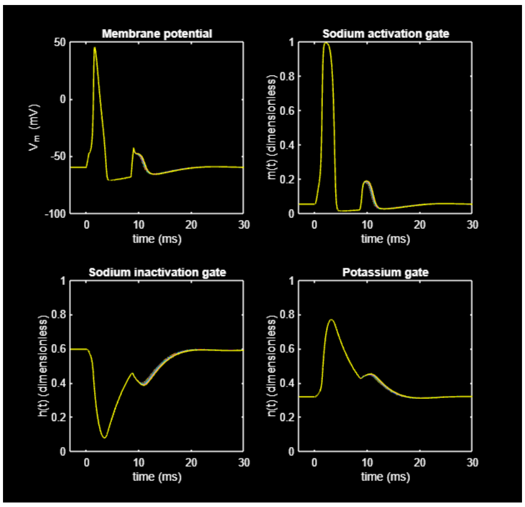

Figure 20: amp2=68.5

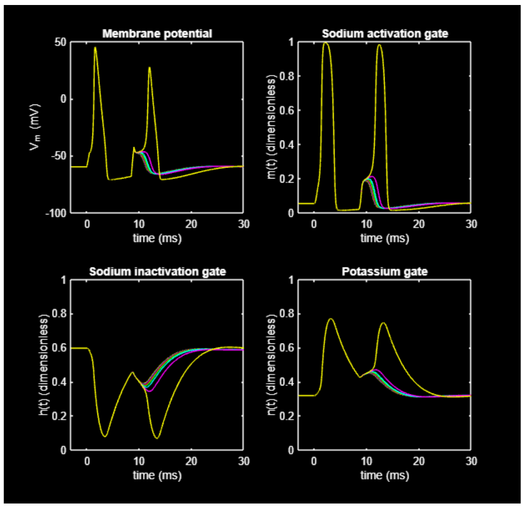

Figure 21: amp2=69.0

An action potential was successfully elicited when the amplitude of the second pulse reached $I_{2\text{th}} = 69.6\ \mu\text{A/cm}^2$, indicating that this value represents the threshold for the second stimulus under the given conditions.

3.2.8 Delay=6ms

The MATLAB code below was used to create the plots associated with this.

```
amp1 = 27.4;
width1 = 0.5;
amp2 = 142.5; % Start from this value and increment
delay2 = 6; % Set delay to 6 ms
width2 = 0.5;
hhmplot(0,30,0);

for j = 1:6 % Increment for 6 rounds
    amp2 = amp2+0.1; % Increment amp2 by 0.1 each iteration
    hhmplot(0,30,1);
end
```

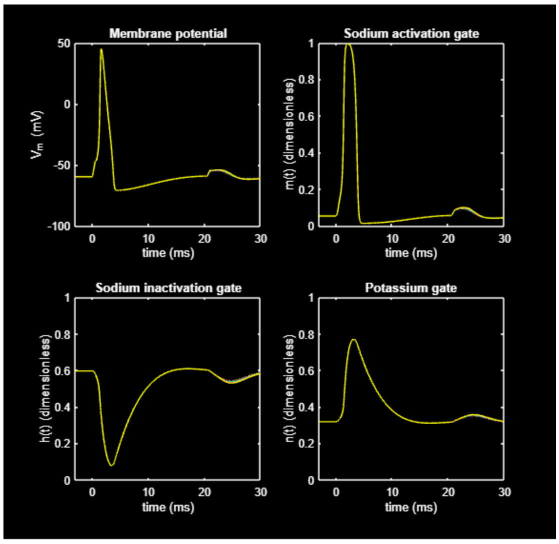

Figure 22: amp2=142.5

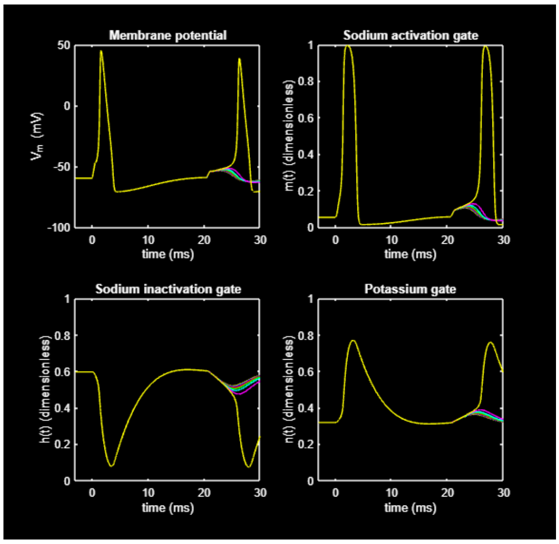

Figure 23: amp2=142.9

An action potential was successfully elicited when the amplitude of the second pulse reached $I_{2\text{th}} = 143.5\ \mu\text{A/cm}^2$, indicating that this value represents the threshold for the second stimulus under the given conditions.

3.3 Question 04

To estimate the absolute and relative refractory periods, the ratio $I_{2\text{th}}/I_{1\text{th}}$ was plotted as a function of the inter-pulse interval. Here, $I_{1\text{th}}$ was set to 27.4 μA/cm^2, and the corresponding $I_{2\text{th}}$ values were obtained experimentally for delays ranging from 6 ms to 25 ms.
The MATLAB code below was used to create the plots associated with this question.

```
% Define data
delays = [6 8 10 12 14 16 18 20 25]; % Interstimulus delays (ms)
I2ths = [143.5 69.6 40.5 25.3 16.9 12.7 11.3 11.6 13.7]; % Threshold amplitudes ( A /
    cm )
ratios = I2ths / 27.4; % Ratios relative to I1 = 27.4  A / cm

% Interpolate and plot
figure; % Create new figure
t = linspace(6, 25, 1000); % Delay space within data range
f = spline(delays, ratios, t); % Spline interpolation
plot(t, f, 'LineWidth', 2);
hold on;
yline(1, 'r--', 'LineWidth', 1); % Red dashed line at y=1
grid on;
xlabel('Delay␣(ms)');
ylabel('Ratio');
title('I2/I1␣Ratio␣Against␣Delay');

% Save plot for LaTeX
exportgraphics(gcf, 'ratio_plot.png', 'Resolution', 300);
```

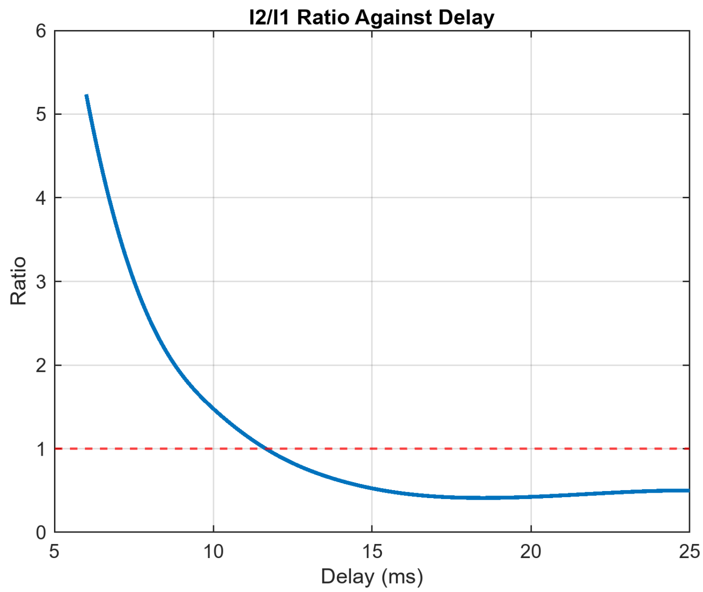

Figure 24: $\frac{I_{2th}}{I_{1th}}$ vs. Delay

For delays below 6 ms, the membrane is unresponsive to normal levels of stimulation during this period, and thus the absolute refractory period can be estimated as 0-6 ms.
For delays beyond 12 ms, the required amplitude of the second stimulus drops below the threshold of the first stimulus. The ratio $I_{2\text{th}}/I_{1\text{th}}$ falls below 1, indicating that the membrane has regained most of its excitability. Therefore, the relative refractory period is estimated to lie between 6 ms and 12 ms.

4 Repetitive Activity

4.1 Question 05

4.1.1 Intensity = 5 μA/cm^2

The MATLAB code below was used to create the plots associated with this question.

```
amp1 = 5; % stimulus amplitude is 5
width1 = 80; % wdith is 80 ms
delay2 = 0;
amp2 = 0;
width2 = 0;
amp2 = 0;
hhmplot(0,100,0);
```

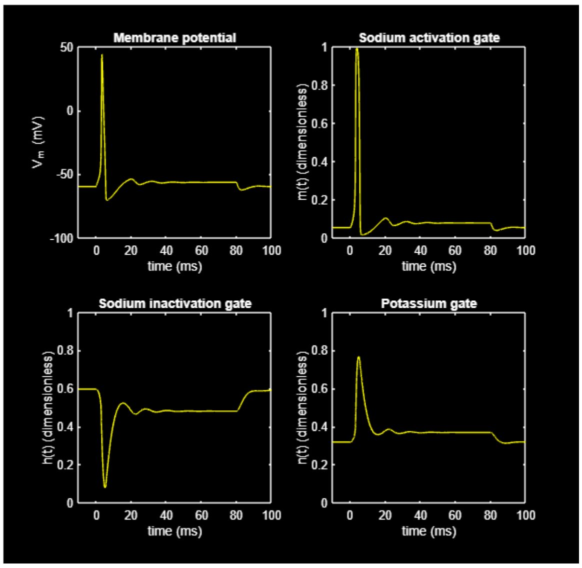

Figure 25: Intensity = 5 μA/cm^2

One action potential was generated in response to a stimulus of 5 μA/cm^2.

4.1.2 Intensity = 10 μA/cm^2

The MATLAB code below was used to create the plots associated with this question.

```
amp1 = 10; % stimulus amplitude is 10
width1 = 80; % wdith is 80 ms
delay2 = 0;
amp2 = 0;
width2 = 0;
amp2 = 0;
hhmplot(0,100,0);
```

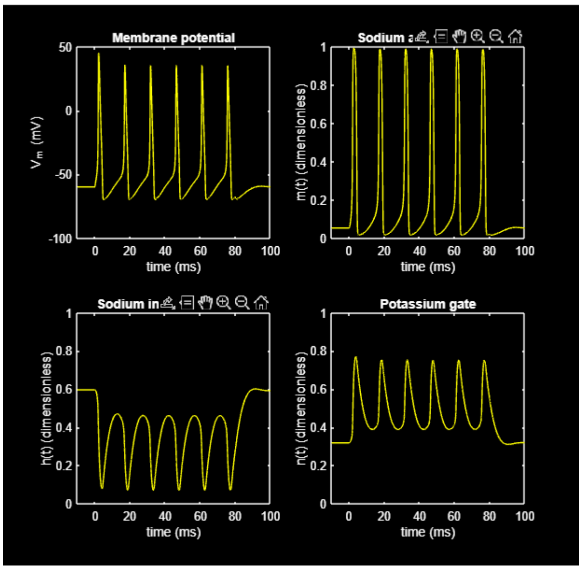

Figure 26: Intensity = 10 μA/cm^2

A total of six action potentials were generated in response to a stimulus of 10 μA/cm^2.

4.1.3 Intensity = 20 μA/cm^2

The MATLAB code below was used to create the plots associated with this question.

```
amp1 = 20; % stimulus amplitude is 20
width1 = 80; % wdith is 80 ms
delay2 = 0;
amp2 = 0;
width2 = 0;
amp2 = 0;
hhmplot(0,100,0);
```

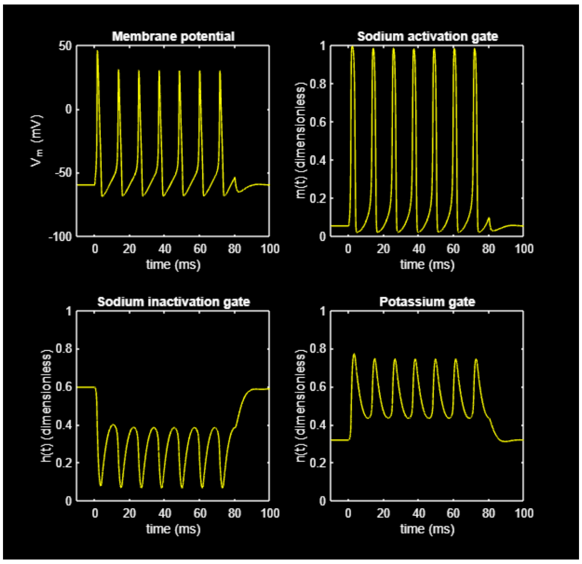

Figure 27: Intensity = 20 μA/cm^2

A total of seven action potentials were generated in response to a stimulus of 20 μA/cm^2.

4.1.4 Intensity = 30 μA/cm^2

The MATLAB code below was used to create the plots associated with this question.

```
amp1 = 30; % stimulus amplitude is 30
width1 = 80; % wdith is 80 ms
delay2 = 0;
amp2 = 0;
width2 = 0;
amp2 = 0;
hhmplot(0,100,0);
```

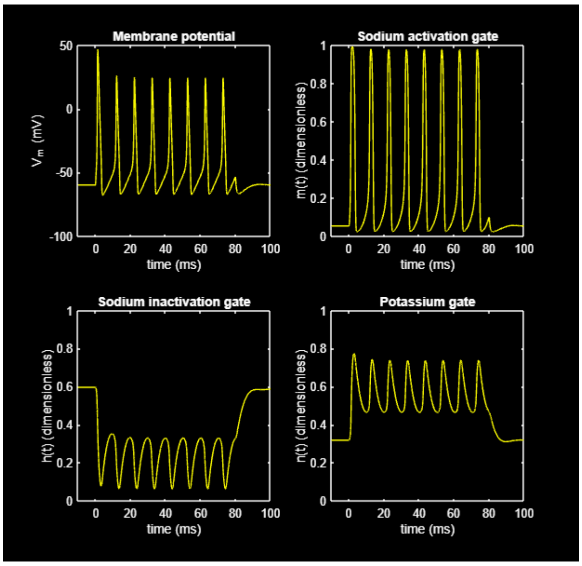

Figure 28: Intensity = 30 μA/cm^2

A total of eight action potentials were generated in response to a stimulus of 10 μA/cm^2.

4.1.5 Intensity = 50 μA/cm^2

The MATLAB code below was used to create the plots associated with this question.

```
amp1 = 50; % stimulus amplitude is 50
width1 = 80; % wdith is 80 ms
delay2 = 0;
amp2 = 0;
width2 = 0;
amp2 = 0;
hhmplot(0,100,0);
```

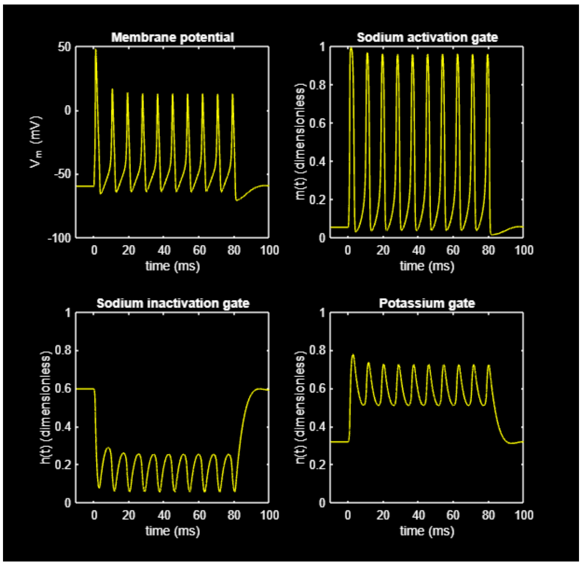

Figure 29: Intensity = 50 μA/cm^2

A total of 10 action potentials were generated in response to a stimulus of 10 μA/cm^2.

4.1.6 Intensity = 70 μA/cm^2

The MATLAB code below was used to create the plots associated with this question.

```
amp1 = 100; % stimulus amplitude is 100
width1 = 80; % wdith is 80 ms
delay2 = 0;
amp2 = 0;
width2 = 0;
amp2 = 0;
hhmplot(0,100,0);
```

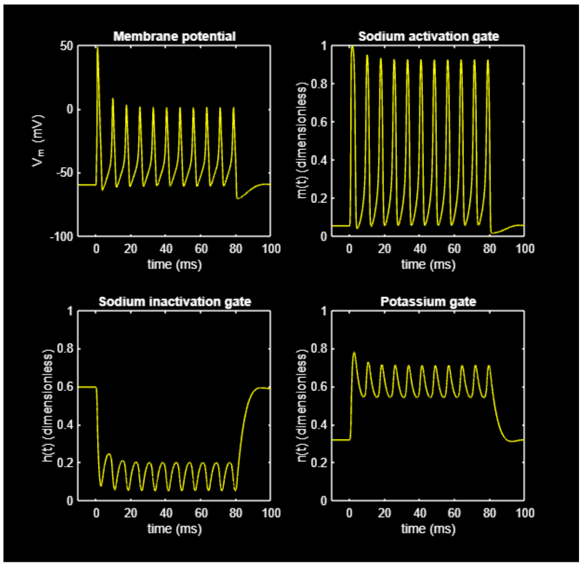

Figure 30: Intensity = 70 μA/cm^2

A total of 11 action potentials were generated in response to a stimulus of 10 μA/cm^2.

4.1.7 Intensity = 100 μA/cm^2

The MATLAB code below was used to create the plots associated with this question.

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

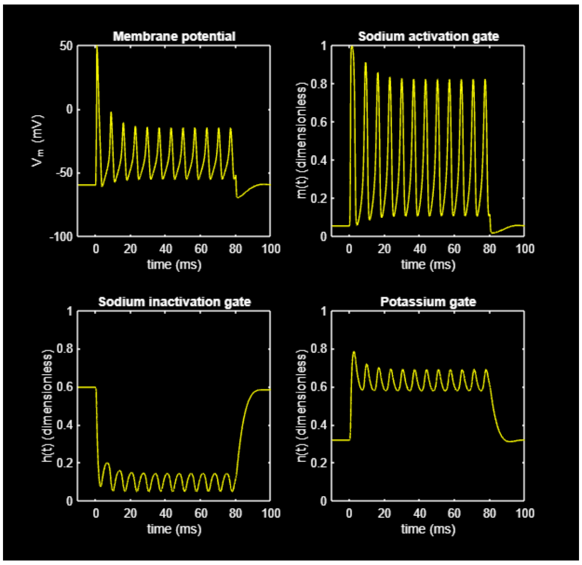

Figure 31: Intensity = 100 μA/cm^2

A total of 12 action potentials were generated in response to a stimulus of 10 μA/cm^2.

4.1.8 Frequency of Action Potentials vs Stimulus Current Amplitude

The code below was utilized to generate a plot of action potential frequency as a function of stimulus amplitude.

```
% Define data
amplitudes = [5 10 20 30 50 70 100]; % Stimulus amplitudes
frequencies = [1 6 7 8 10 11 12]; % Number of action potentials triggered

% Interpolate
x = linspace(0, 105, 1000); % Amplitude range
f = spline(amplitudes, frequencies, x); % Spline interpolation

% Plot
figure; % Create new figure
plot(x, f, 'LineWidth', 2); % Interpolated curve
hold on;
plot(amplitudes, frequencies, 'ro', 'MarkerSize', 8, 'LineWidth', 2); % Data points
xlabel('Amplitude (\muA/cm^2)');
ylabel('Frequency (No. of APs triggered)');
ylim([0 15]);
grid on;
title('Frequency of Action Potentials vs. Amplitude');

% Save plot for LaTeX
exportgraphics(gcf, 'frequency_plot.png', 'Resolution', 300);
```

The following graph was obtained as a result.

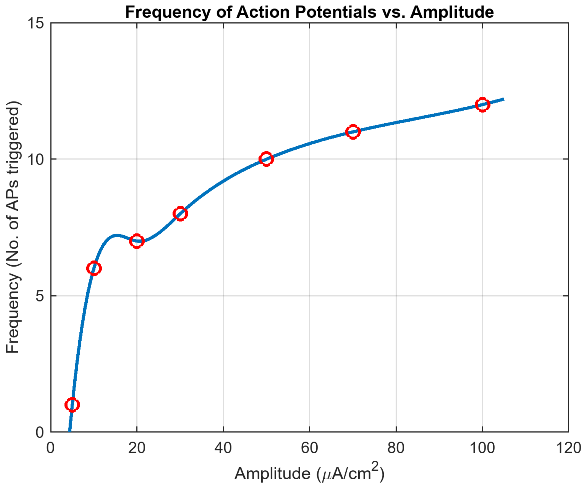

Figure 32: Frequency of Action Potentials vs Stimulus Current Amplitude

As the stimulus amplitude increases, the frequency of triggered action potentials rises sharply at lower amplitudes and then continues to increase with a reduced slope at higher values. This indicates a nonlinear relationship where the neuron becomes increasingly responsive to stronger stimuli initially, followed by a saturation-like behavior as the intensity continues to rise.

4.2 Question 06

The MATLAB code below was used to create the plots associated with this question.

```
amp1 = 200; % stimulus amplitude is 200
width1 = 80; % wdith is 80 ms
delay2 = 0;
amp2 = 0;
width2 = 0;
amp2 = 0;
hhmplot(0,100,0);
```

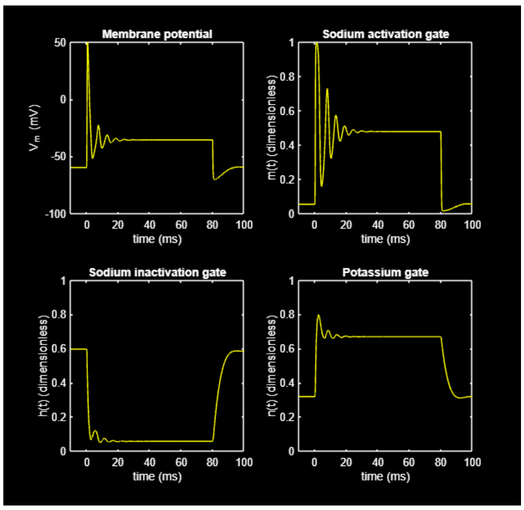

Figure 33: Intensity = 200 μA/cm^2

At a stimulus amplitude of 200 μA/cm^2, the action potentials exhibit diminished amplitude and evolve into a high-frequency oscillatory pattern, consistent with depolarisation block. This phenomenon arises from the voltage-dependent dynamics of the gating variables in the Hodgkin-Huxley model. The activation variable m and inactivation variable h for sodium channels respond to depolarisation by increasing Na^+ conductance.
However, sustained high depolarisation leads to inactivation of Na^+ channels (via h) and insufficient recovery, thereby suppressing full spike generation. Concurrently, the potassium activation variable n increases, promoting K^+ efflux, which can overpower the sodium influx. The imbalance in channel dynamics at excessive depolarisation levels ultimately disrupts normal spike formation, leading to reduced action potential amplitude and repetitive, dampened oscillations.

5 Temperature Dependence

5.1 Question 07

The MATLAB code below was used to create the plots associated with this question.

```
clear all; close all;
hhconst;

vclamp = 0;
amp1 = 20;
width1 = 0.5;

temps=[0, 5, 10, 15, 20, 24, 25, 26, 30]; % Testing temperatures

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

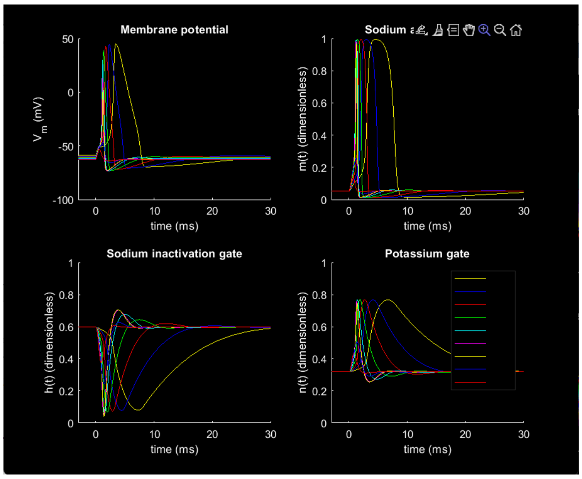

Figure 34: Temperature Dependance

As temperature increases, the action potential becomes shorter in duration, indicating accelerated membrane dynamics. The peak amplitude of the membrane potential shows a slight reduction, and both absolute and relative refractory periods are noticeably shortened. These changes reflect faster ion channel kinetics, which contribute to increased neuronal firing efficiency and faster signal transmission at elevated temperatures.