Department of Electronic and Telecommunication Engineering
University of Moratuwa

BM2101 – Analysis of Physiological Systems

Assignment 3

Properties of Hodgkin-Huxley equations

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This is submitted as a partial fulfillment for the module BM2101: Analysis of Physiological Systems
Department of Electronic and Telecommunication Engineering,
University of Moratuwa
February 22, 2021

Contents

1 Question 1

Using the suggested bisection method, the amplitude interval of the sub-threshold and the supra-threshold is analyzed in order to estimate the threshold stimulating current amplitude in accuracy to two decimal places.

$$The\ initial\ limits\ of\ the\ amplitude\ interval = 6\mu Acm^{-2}\ and\ 7\mu Acm^{-2}$$

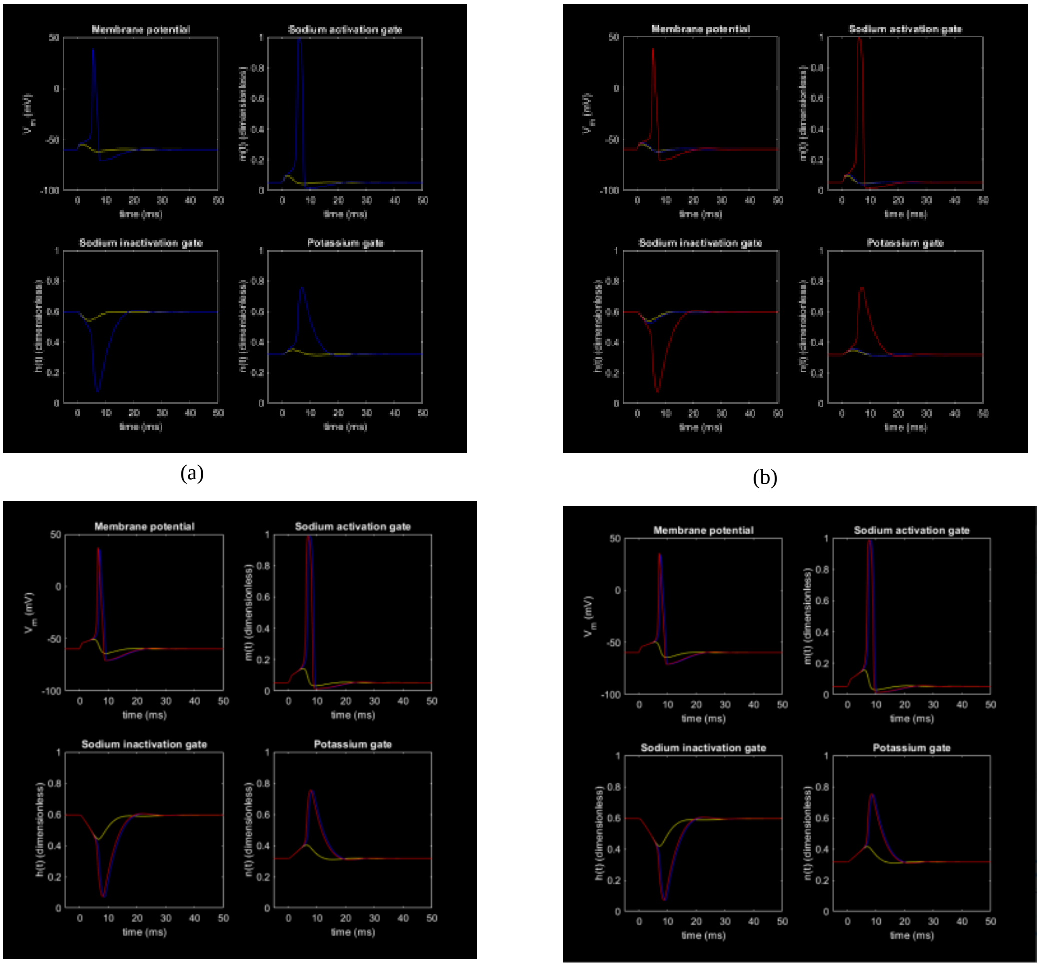
$$Obtained\ bisect\ points$$
$$= [6.5, 6.75, 6.875, 6.9375, 6.953125, 6.9609375, 6.95703125, 6.958984375]\mu Acm^{-2}$$

Therefore,

$$Threshold\ stimulating\ current\ amplitude\ (estimated\ to\ two\ decimal\ places) = 6.96\mu Acm^{-2}$$

This is the obtained supra-threshold value for eliciting action potentials.
Further, thus, it could also approximated the value of sub-threshold as,

$$Sub - threshold\ value\ (estimated\ to\ two\ decimated\ places) = 6.95\mu Acm^{-2}$$



(a) (b) (c) (d)

Figure 1: MATLAB based action potential plots (a): amplitudes 6 (yellow) and 7 (blue)μAcm^{-2}, (b): bisect point 6.5 μAcm^{-2}, (c): bisect point: 6.95703125 μAcm^{-2}, (d): bisect point: 6.958984375 μAcm^{-2}

2 Question 2

By analyzing the obtained simulation results and calculated values (by considering outward as positive),

J ($\boldsymbol{\mu Acm^{-2}}$)	**Width** ($\boldsymbol{ms}$)	$\int_{t_0}^{t_f} \boldsymbol{J_{ei}}$	$\boldsymbol{Q_{Na}}$	$\boldsymbol{Q_K}$	$\boldsymbol{Q_L}$	$\boldsymbol{\sum Q_k = Q_{Na} + Q_K + Q_L}$
5	1	**5**	-66.4728	231.8038	-160.3311	**4.9998**
6	1	**6**	-71.2768	236.8179	-159.5414	**5.9997**
6.96	1	**6.96**	-1320	1455.5	-127.9376	**6.9620**
7	1	**7**	-1362.7	1500.3	-130.5537	**7.0014**
6.96	2	**13.92**	-1435.8	1583.8	-134.0003	**13.9203**
7	2	**14**	-1436	1584	-134.0070	**14.0000**
8	3	**24**	-1434.4	1592.5	-134.1122	**23.9990**
10	10	**50**	-1439.8	1623.6	-133.8179	**49.9990**

Table 1: The resulting values from MATLAB simulations/computations and manual calculations for the comparison of the stimulating current and the net inward current

Since,

$$Net\ inward\ current = \sum currents\ through\ ionic\ gates$$

$$\int_{t_0}^{t_f} \sum J_k = Q_{Na} + Q_K + Q_L$$

From the above table, it could be concluded that (by comparing 3rd and 7th columns),

$$\int_{t_0}^{t_f} \sum J_k \approx \int_{t_0}^{t_f} J_{ei}$$

Further, since some (relatively small) numerical error is allowed, the relationship between the stimulating current and the net inward current could be developed as,

$$\int_{t_0}^{t_f} \sum J_k = \int_{t_0}^{t_f} J_{ei}$$

3 Question 3

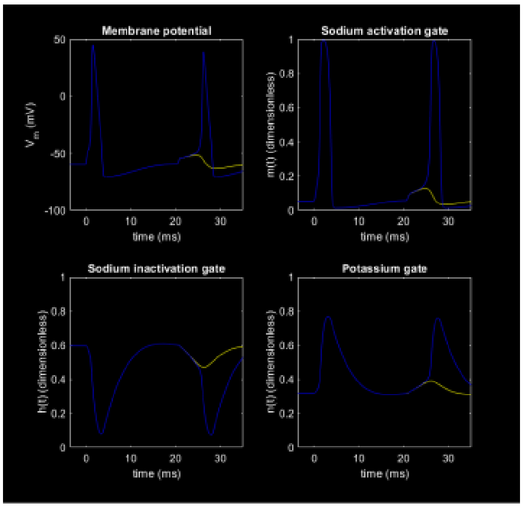
By defining the following parameters as given,

$$amp1 = 26.8\mu Acm^{-2}, width1 = width2 = 0.5ms, I_{1th} = 13.4\mu Acm^{-2}$$
$$where\ I_{1th} = \ The\ threshold\ for\ a\ single\ pulse$$

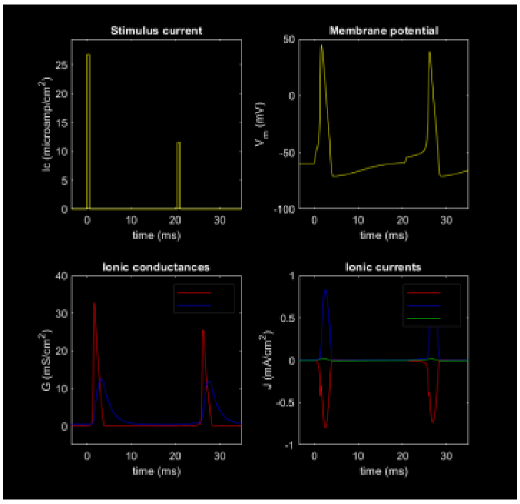
The threshold amplitude values for a second pulse for a given inter-stimulus interval (I_{2th}) could be estimated using simulations as follows:

Delay (ms)	25	20	18	16	14	12	10	8	6
I_{2th} (μAcm^{-2})	13.7	11.6	11.3	12.7	17.0	25.5	40.8	70.1	145.2

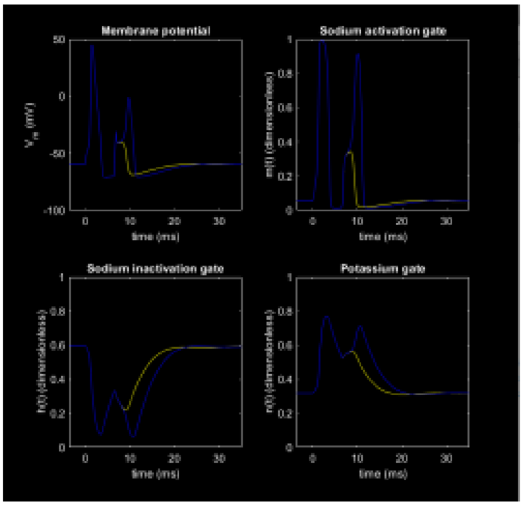
Table 2: The estimated values for the second impulse threshold amplitude (for one decimal place accuracy) against the corresponding inter-stimulus interval



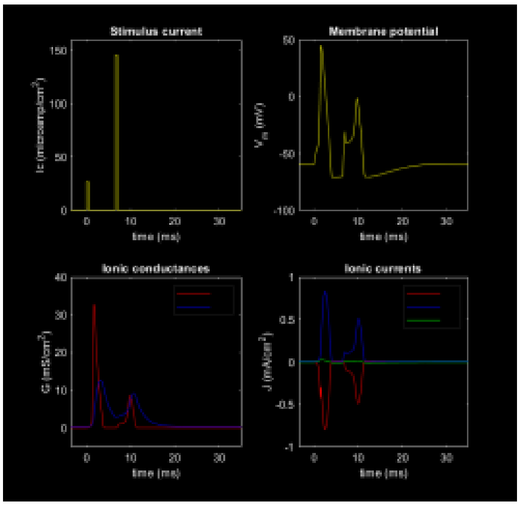
(a)



(b)



(c)



(d)

Figure 3: MATLAB based action potential plots with inter-stimulus intervals (a): delay 20ms hhmplot, (b) delay 20ms hhsplot, (c): delay 6ms hhmplot, (d): delay 6ms hhsplot

4 Question 4

As obtained from the Table 2, the ratio between the considered threshold amplitudes could be calculated as follows:

Delay (ms)	25	20	18	16	14	12	10	8	6
I_{2th}/I_{1th}	1.022	0.866	0.843	0.948	1.269	1.903	3.045	5.231	10.836

Table 3: The calculated values for the ratio of I_{2th}/I_{1th} against the corresponding delay

Hence,

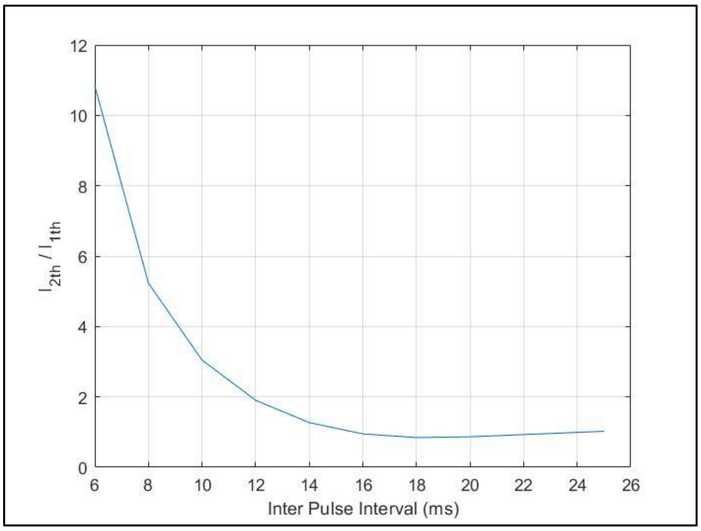


Figure 4(a): I_{2th}/I_{1th} against inter-pulse interval

By considering the Table 3 and Figure 4(a), it is applicable to plot a best fit line for the above curve using MATLAB built-in function for curve fitting: cftool.

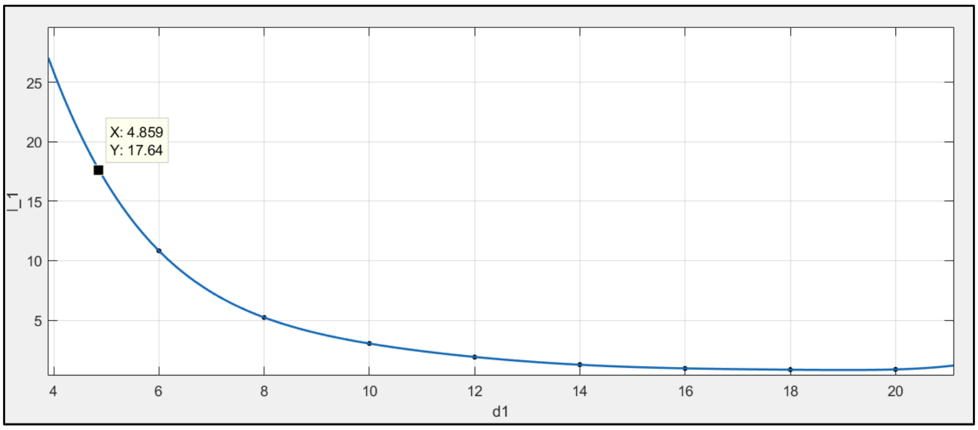


Figure 4(b): The best fitted plot using MATLAB for I_{2th}/I_{1th} against inter-pulse interval (d1 in ms) (6^{th} order polynomial fitting with LAR robustness)

Since in the time interval of absolute refractory period (which is immediately after an action potential), no second action potential can be elicited regardless of how intense the stimulus, it is intuitive to say that I_{2th}/I_{1th} value must be infinite in theory. As in the figures 4(a) and 4(b), the previous immediate conclusion is indirectly proven since both of these figures convey an exponential decay. Howsoever, since of data limitation, it is impossible to assign a finite value for exact inter-pulse delay in which the decay initiates. Howsoever, it is observable to state that, when the inter-pulse delay is 6ms, the exponential decay is visible (with a finite partial gradient) and thus, the absolute refractory period must be less than 6ms. By considering best fitted curve in Figure 4(b), it could be estimated that the absolute refractory period is more close to 4ms.

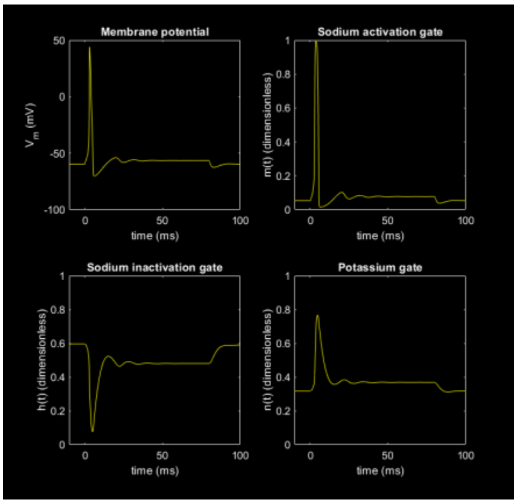
Therefore,

$$Absolute\ Refractory\ Period\ \approx 4ms$$

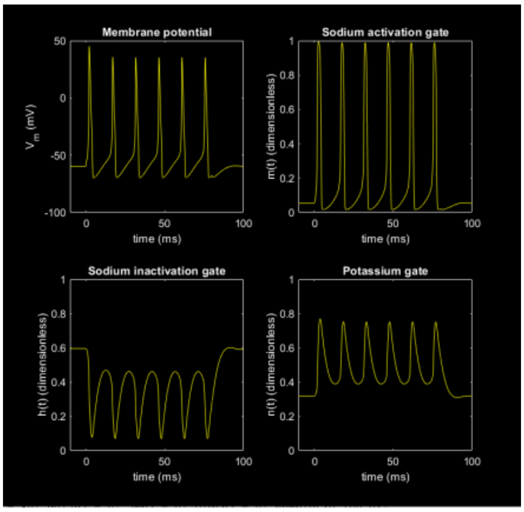
In the relative refractory period, a second action potential can be elicited for current strengths greater than the initial supra-threshold stimulus (since, the relative refractory period is characterized by a progressively increasing threshold the closer one gets to the end of the absolute refractory period) which suggest the $(I_{2th}/I_{1th})>1$ in intuitively. This is visible between the inter-pulse intervals of 14ms and 16ms (by referring Table 3) and thus, could be estimated as,

$$Relative\ Refractory\ Period\ \approx (15-4)ms = 11ms$$

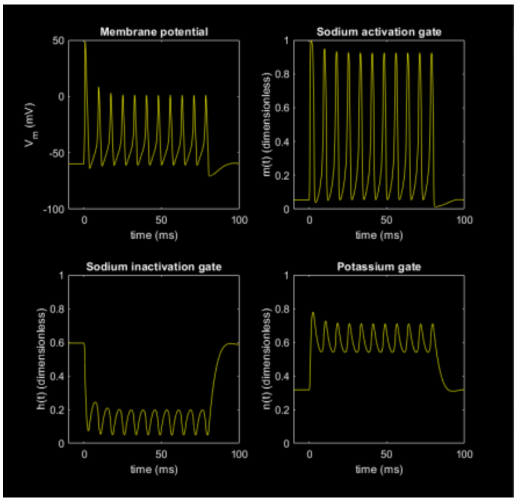
5 Question 5



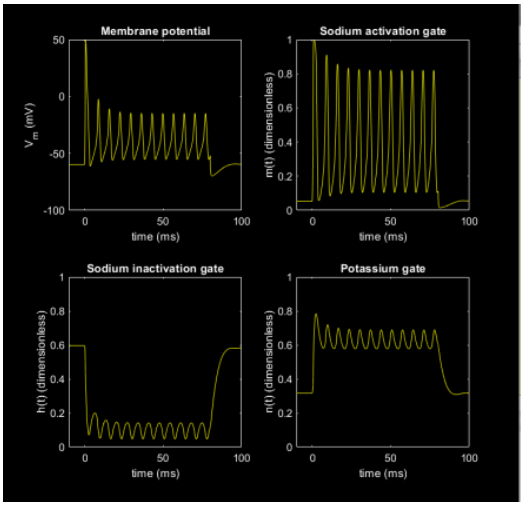
(a)



(b)



(c)



(d)

Figure 5: MATLAB based action potential plots (hhmplot) with increasing stimulating currents (a): stimulating current 5 μAcm^{-2}, (b) stimulating current 10 μAcm^{-2}, (c): stimulating current 70 μAcm^{-2}, (d): stimulating current 100 μAcm^{-2}

As per the MATLAB simulations,

Simulating current amplitude (μAcm^{-2})	5	10	20	30	50	70	100
Action Potential frequency (Hz)	10	60	70	80	100	110	120

Table 4: Action potential occurring frequency vs simulating current amplitude

By utilizing the values from Table 4,

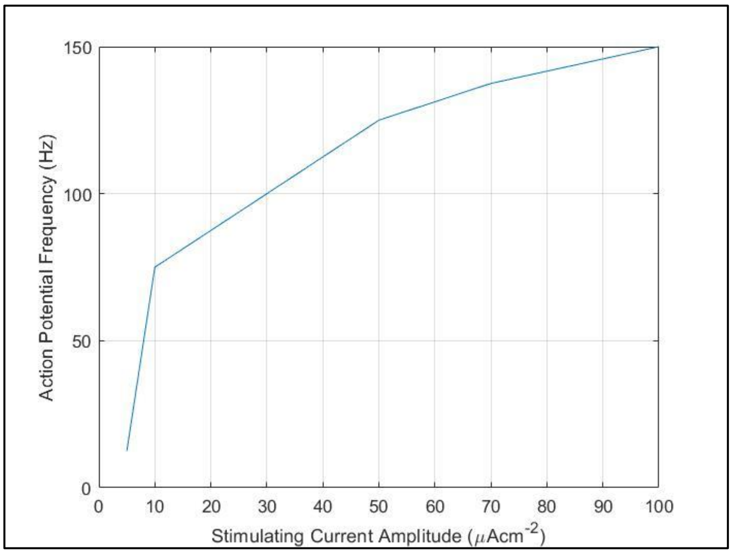


Figure 5: Simulating current amplitude against the action potential occurring frequency

The corresponding graph and the table show that the action potential occurring frequency is obviously increasing when the stimulating current is increased. Howsoever, the MATLAB plots of action potentials in each instance also suggest that with the increment of frequency, the amplitude of each action potential also decreases in a unique manner. As an example, when the stimulating current is 100 μAcm^{-2}, there is only one significant peak amplitude action potential exists which is the first elicited one. Even though, the amplitudes of the other action potentials are less, they appear to be with comparatively same amplitude value.

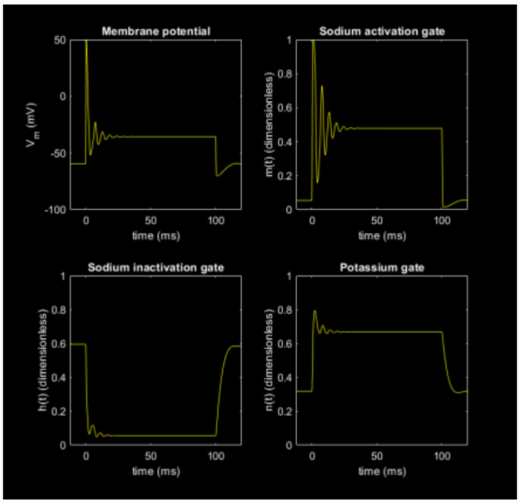
6 Question 6

The observation is that the action potential response to the stimulus current 200 μAcm^{-2} does not show any repetitive behavior rather an under-damped behavior where the response vanishes rapidly.

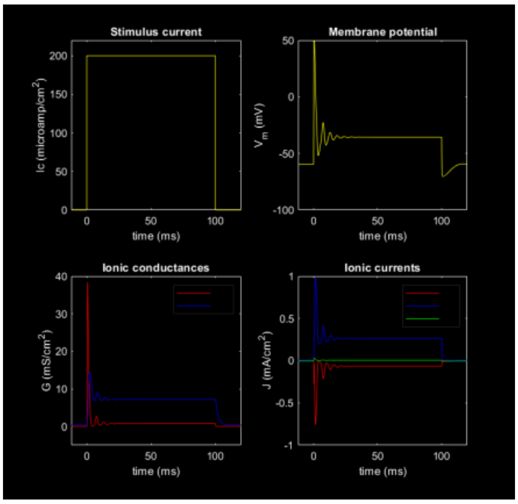
$$\frac{1}{2\pi a v^2(r_o + r_i)v^2}\frac{d^2Vm(z,t)}{dt^2} = C_m\frac{dv}{dt} + \overline{G_{K+}}\boldsymbol{n^4}(V - V_{K+}) + \overline{G_{Na+}}m^3(V - V_{Na+})\boldsymbol{h}(V - V_{Na+}) + \overline{G_L}(V - V_L)$$

As per the ordinary differential equation of Hodgkin-Huxley model, n and h are voltage dependent parameters. The initial under-damping effect was observed in question (5) in which the increment of stimulus current suggested a decrement in action potential amplitude. Howsoever, this reduction in amplitudes over time increases with the stimulating current amplitude in a more considerate manner. When the stimulating current amplitude is set to $200\mu Acm^{-2}$, this under-damping effect becomes much noticeable due to which the amplitudes of action potentials get reduced significantly with time and thus not all action potentials are visible.

This could be intuitively addressed since the degree of effect of h and n are 1 and 4 respectively in the Hodgkin Huxley equation above. When stimulus intensity amplitude increases, the damping effect of n is significant than the incremental effect of h. Therefore when the Stimulus Intensity Amplitude is $200\mu Acm^{-2}$, the damping effect is high and due to that the action potentials are less visible.



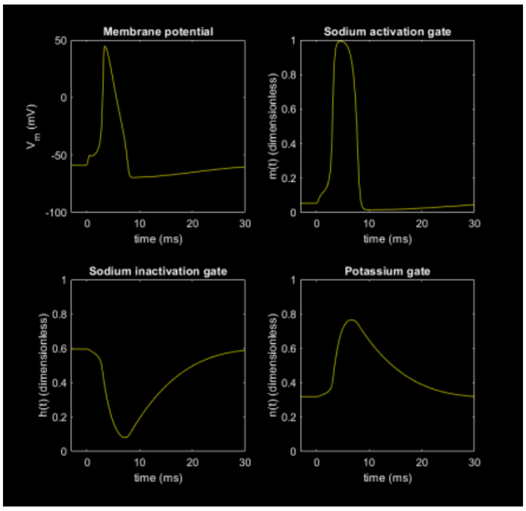
(a)



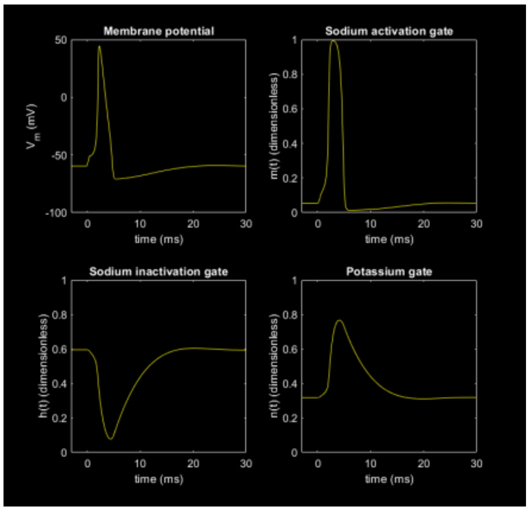
(b)

Figure 5: MATLAB based action potential plots with stimulating current 200 μAcm^{-2} (a): hhmplot (b) hhsplot

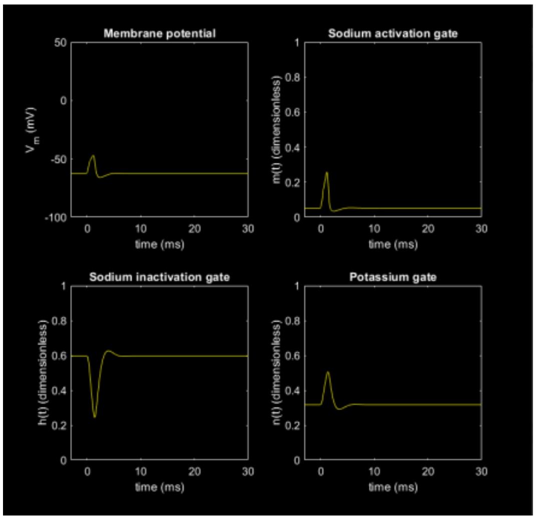
7 Question 7



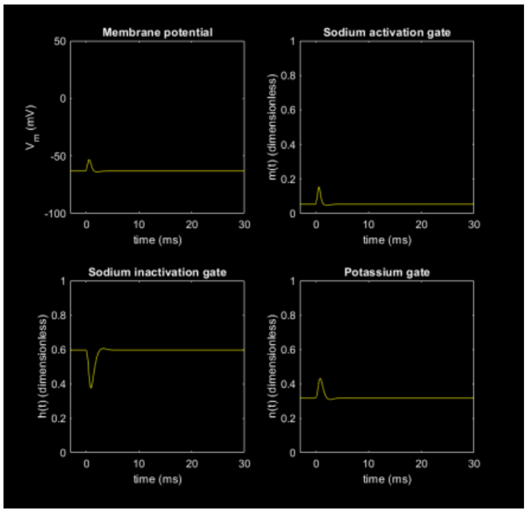
(a)



(b)



(c)



(d)

Figure 7: MATLAB based action potential plots (hhmplot) with increasing stimulating temperature (a): temperature 0 Celsius, (b) temperature 5 Celsius, (c): temperature 26 Celsius, (d): temperature 30 Celsius

When the temperature is increased, three significant changes are observed as follows:

1. Duration of the action potential is reduced. Therefore, both Relative Refractory Period and Absolute Refractory Period get reduced with increase in temperature. As a result, frequency of the action potential occurring also gets increased.
2. Amplitude of the action potential is reduced.
3. After 26^0C action potential does not elicit with the same stimulating current amplitude. This is because of that the maximum membrane potential is lower than the threshold membrane voltage needed to generate an action potential which suggests that the threshold stimulating current amplitude increases with the increment in temperature.

8 Appendix

Question 1:

```
>> clc;
>> close all;
>> hhconst
>> amp1 = 6; width1 = 1; hhmplot(0,50,0); amp1 = 7; hhmplot(0,50,1);
>> amp1 = 6; width1 = 1; hhmplot(0,50,0); amp1 = 6.5; hhmplot(0,50,1); amp1
= 7; hhmplot(0,50,1);
>> amp1 = 6.5; width1 = 1; hhmplot(0,50,0); amp1 = 6.75; hhmplot(0,50,1);
amp1 = 7; hhmplot(0,50,1);
>> amp1 = 6.75; width1 = 1; hhmplot(0,50,0); amp1 = 6.875; hhmplot(0,50,1);
amp1 = 7; hhmplot(0,50,1);
>> amp1 = 6.875; width1 = 1; hhmplot(0,50,0); amp1 = 6.9375;
hhmplot(0,50,1); amp1 = 7; hhmplot(0,50,1);
>> amp1 = 6.9375; width1 = 1; hhmplot(0,50,0); amp1 = 6.96875;
hhmplot(0,50,1); amp1 = 7; hhmplot(0,50,1);
>> amp1 = 6.9375; width1 = 1; hhmplot(0,50,0); amp1 = 6.953125;
hhmplot(0,50,1); amp1 = 6.96875; hhmplot(0,50,1);
>> amp1 = 6.953125; width1 = 1; hhmplot(0,50,0); amp1 = 6.9609375;
hhmplot(0,50,1); amp1 = 6.96875; hhmplot(0,50,1);
>> amp1 = 6.953125; width1 = 1; hhmplot(0,50,0); amp1 = 6.95703125;
hhmplot(0,50,1); amp1 = 6.9609375; hhmplot(0,50,1);
>> amp1 = 6.95703125; width1 = 1; hhmplot(0,50,0); amp1 = 6.958984375;
hhmplot(0,50,1); amp1 = 6.9609375; hhmplot(0,50,1);
```

Question 2:

```
>> amp1 = 6; width1 = 1; [qna,qk,ql]=hhsplot(0,50)
>> amp1 = 6.96; width1 = 1; [qna,qk,ql]=hhsplot(0,50)
>> amp1 = 7; width1 = 1; [qna,qk,ql]=hhsplot(0,50)
>> amp1 = 6.96; width1 = 2; [qna,qk,ql]=hhsplot(0,50)
>> amp1 = 7; width1 = 2; [qna,qk,ql]=hhsplot(0,50)
>> amp1 = 8; width1 = 3; [qna,qk,ql]=hhsplot(0,50)
>> amp1 = 10; width1 = 5; [qna,qk,ql]=hhsplot(0,50)
```

Question 3:

```
>> amp1 = 26.8; width1 = 0.5; delay2 = 25; amp2 = 13.6; width2 = 0.5;
hhmplot(0,35, 0);hhsplot(0,35);amp2 = 13.7; hhmplot(0,35,1);hhsplot(0,35)
>> amp1 = 26.8; width1 = 0.5; delay2 = 20; amp2 = 11.5; width2 = 0.5;
hhmplot(0,35, 0);hhsplot(0,35);amp2 = 11.6; hhmplot(0,35,1);hhsplot(0,35);
>> amp1 = 26.8; width1 = 0.5; delay2 = 18; amp2 = 11.2; width2 = 0.5;
hhmplot(0,35, 0);hhsplot(0,35);amp2 = 11.3; hhmplot(0,35,1);hhsplot(0,35);
>> amp1 = 26.8; width1 = 0.5; delay2 = 16; amp2 = 12.6; width2 = 0.5;
hhmplot(0,35, 0);hhsplot(0,35);amp2 = 12.7; hhmplot(0,35,1);hhsplot(0,35);
>> amp1 = 26.8; width1 = 0.5; delay2 = 14; amp2 = 16.9; width2 = 0.5;
hhmplot(0,35, 0);hhsplot(0,35);amp2 = 17.0; hhmplot(0,35,1);hhsplot(0,35);
>> amp1 = 26.8; width1 = 0.5; delay2 = 12; amp2 = 25.4; width2 = 0.5;
hhmplot(0,35, 0);hhsplot(0,35);amp2 = 25.5; hhmplot(0,35,1);hhsplot(0,35);
>> amp1 = 26.8; width1 = 0.5; delay2 = 10; amp2 = 40.7; width2 = 0.5;
hhmplot(0,35, 0);hhsplot(0,35);amp2 = 40.8; hhmplot(0,35,1);hhsplot(0,35);
>> amp1 = 26.8; width1 = 0.5; delay2 = 8; amp2 = 70.0; width2 = 0.5;
hhmplot(0,35, 0);hhsplot(0,35);amp2 = 70.1; hhmplot(0,35,1);hhsplot(0,35);
>> amp1 = 26.8; width1 = 0.5; delay2 = 6; amp2 = 145.1; width2 = 0.5;
hhmplot(0,35, 0);hhsplot(0,35);amp2 = 145.2; hhmplot(0,35,1);hhsplot(0,35);
```

Question 4:

```
>> I2 = [13.7,11.6,11.3,12.7,17,25.5,40.8,70.1,145.2];
>> I1 = 13.4;
```

```
>> I = I2./I1;
>> d = [25,20,18,16,14,12,10,8,6];
>> plot(d,I);grid on ; xlabel("Inter Pulse Interval") ; ylabel("I_2_t_h / I_1_t_h");
>> cftool(d,I);
```

Question 5:

```
>> amp1 = 5; width1 = 80; delay2 = 0; amp2 = 0; width2 = 0; hhmplot(0,100,0);
>> amp1 = 10; width1 = 80; delay2 = 0; amp2 = 0; width2 = 0; hhmplot(0,100,0);
>> amp1 = 20; width1 = 80; delay2 = 0; amp2 = 0; width2 = 0; hhmplot(0,100,0);
>> amp1 = 30; width1 = 80; delay2 = 0; amp2 = 0; width2 = 0; hhmplot(0,100,0);
>> amp1 = 50; width1 = 80; delay2 = 0; amp2 = 0; width2 = 0; hhmplot(0,100,0);
>> amp1 = 70; width1 = 80; delay2 = 0; amp2 = 0; width2 = 0; hhmplot(0,100,0);
>> amp1 = 100; width1 = 80; delay2 = 0; amp2 = 0; width2 = 0; hhmplot(0,100,0);
>> J = [5,10,20,30,50,70,100];
>> f = [12.5,75,87.5,100,125,137.5,150];
>> plot(J,f); grid on ; xlabel("Stimulating Current Amplitude (\muAcm^-^2)") ; ylabel("Action Potential Frequency (Hz)") ;
```

Question 6:

```
>> amp1 = 200; width1 = 100; delay2 = 0; amp2 = 0; width2 = 0; hhmplot(0,120,0);
>> amp1 = 200; width1 = 100; delay2 = 0; amp2 = 0; width2 = 0; hhsplot(0,120);
```

Question 7:

```
>> vclamp = 0; amp1 = 20; width1 = 0.5; tempc = 0; hhmplot(0,30,0); hhsplot(0,30);
>>  tempc = 5; hhmplot(0,30,0); hhsplot(0,30);
>> tempc = 10; hhmplot(0,30,0); hhsplot(0,30);
>> tempc = 15; hhmplot(0,30,0); hhsplot(0,30);
>>  tempc = 20; hhmplot(0,30,0); hhsplot(0,30);
>>  tempc = 24; hhmplot(0,30,0); hhsplot(0,30);
>> tempc = 25; hhmplot(0,30,0); hhsplot(0,30);
>> tempc = 26; hhmplot(0,30,0); hhsplot(0,30);
>> tempc = 30; hhmplot(0,30,0); hhsplot(0,30);
```