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ELEC436 HW#5

Q1) (25 points) The following questions from the textbook: 5, 6, 11, 15, 21 .

~ ELEC436 HW5 ~

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Q1)

5) R, C → ~secs
   a → ~A/cm2

$$I_{min}^{2nd} = \frac{\alpha}{\left(1-\exp\left(\frac{-500}{RC}\right)\right)}$$ ← 0.5 msec → 500 μsec

6) In the end of stimulus produced transmembrane voltage is W mV.

11) For lower stimulus current, at the end of stimulus produced transmembrane voltage was 20 mV, Thus $\underline{\text{rheobase} = 20\,mV}$
↓ Rheobase equivalent for all currents.

15) $$I_{th} = \frac{I_R}{1-e^{-kt}}$$

$$i(t) = \frac{dq(t)}{dt}$$

duration required for Vt. ← $\left(\int_0^T i(t)\,dt = \int_0^T dq(t)\right) \rightarrow \int_0^T \frac{I_R}{1-e^{-kT}} \cdot dt = Q_{total}$

$$Q_{total} = \frac{I_R \cdot T}{1-e^{k \cdot T}}$$

21) a) $r = \sqrt{(x-e)^2 + h^2}$ so $P(x) = \frac{5}{\sqrt{(x-e)^2+h^2}}$

b) $$A(x) = \frac{\partial^2 P(x)}{\partial x^2} = 5\left(\frac{(x-e)^2 \cdot 3}{\left(\sqrt{(x-e)^2+h^2}\right)^5} - \frac{1}{\left(\sqrt{(x-e)^2+h^2}\right)^3}\right)$$

$$A(x) = 5\left(\frac{3(x-e)^2}{r^5} - \frac{1}{r^3}\right)$$

c) $x=0$: $A(x=0) = 5\left(\frac{3e^2}{r^5} - \frac{1}{r^3}\right)$

$e=0$: $A(x=0) = -\frac{5}{r^3}$

$h=1$: $r = \sqrt{(0-0)^2+1^2} = 1 \Big\} \rightarrow A(x=0)\Big|_{h=1,\, e=0} = -5$

Q2) (14 points) Calculate the relation for extracellular axial current. In other words, you need to calculate Ie(x). What is the Ie(x) for x=0 and x→∞.

Q2) From the chapter 7.4 :

$$I_0 = I_e + I_i$$

$$I_e = \frac{I_e \cdot r_i}{(r_e + r_i)}$$

$$I_i = \frac{I_0 \cdot r_e}{(r_e + r_i)}$$

$$I_i(x) = \frac{r_e}{r_e + r_i} \cdot I_0 + \int_x^{\infty} i_m \, dx$$

$$I_e(x) = \frac{r_i}{r_i + r_e} \cdot I_0 - \int_x^{\infty} i_m \, dx$$

$\hookrightarrow i_m = \frac{v_m}{r_m} \rightarrow \quad v_m = r_i \underbrace{I_0}_{\text{total currents in } +x \text{ direction}} \lambda e^{-\frac{|x|}{\lambda}}$

$$I_e(x) = \frac{r_i}{r_i + r_e} \cdot I_0 - \int_x^{\infty} \frac{I_0 \lambda r_i}{r_m} \cdot e^{-x/\lambda} \, dx \qquad 0 < x < \infty$$

$$\frac{r_i}{r_i + r_e} \cdot I_0 - \frac{r_i \cdot I_0}{r_e + r_i} \cdot e^{-x/\lambda} = \frac{r_i}{r_e + r_i} \cdot I_0 (1 - e^{-x/\lambda})$$

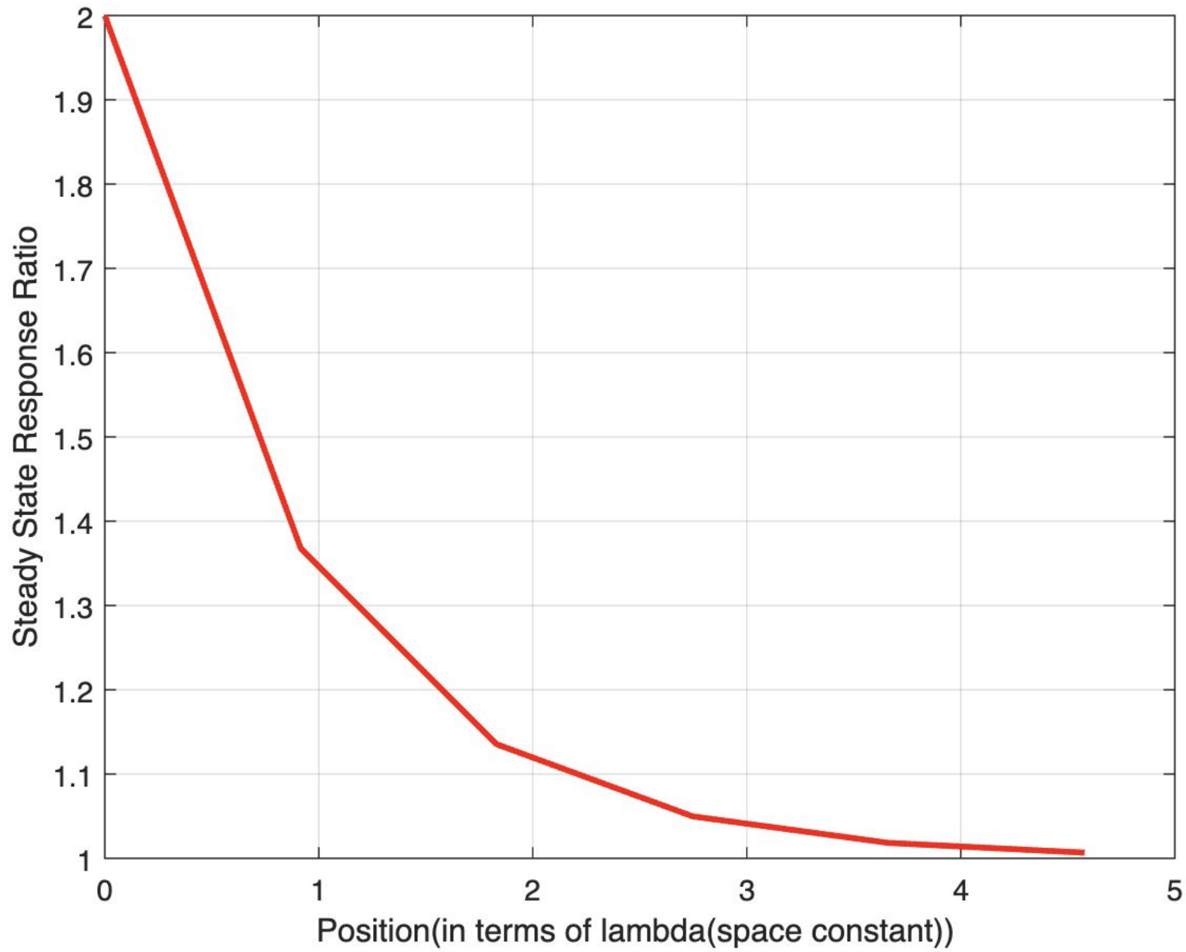
$$I_e(x \to \infty) = \frac{r_i}{r_i + r_e} \cdot I_0 \quad , \quad I_e(x \to 0) = 0 .$$

$$I_i(x) = \frac{r_e}{r_i + r_e} \cdot I_0 + \int_x^{\infty} \frac{I_0 \lambda r_i}{r_m} \cdot e^{-x/\lambda} \, dx \qquad 0 < x < \infty$$

$$\hookrightarrow \frac{r_e}{r_i + r_e} I_0 \left(\frac{r_i}{r_e} e^{-x/\lambda} + 1 \right)$$

Q3) (14 points) In equation (7.54), we derived the extracellular axial current. Consider as α=1, which is the case for muscle bundles and cardiac tissue. Calculate and discuss how the ratio of the position and spatial steady-state response ratio changes for different space constants. Draw this ratio (e.g., by using MATLAB) in terms of space constant.

As position in terms of space constant increases, steady state response ratio decreases exponentially. This implies that for larger position in terms of space constant, amount of time needed for steady state will be increased.



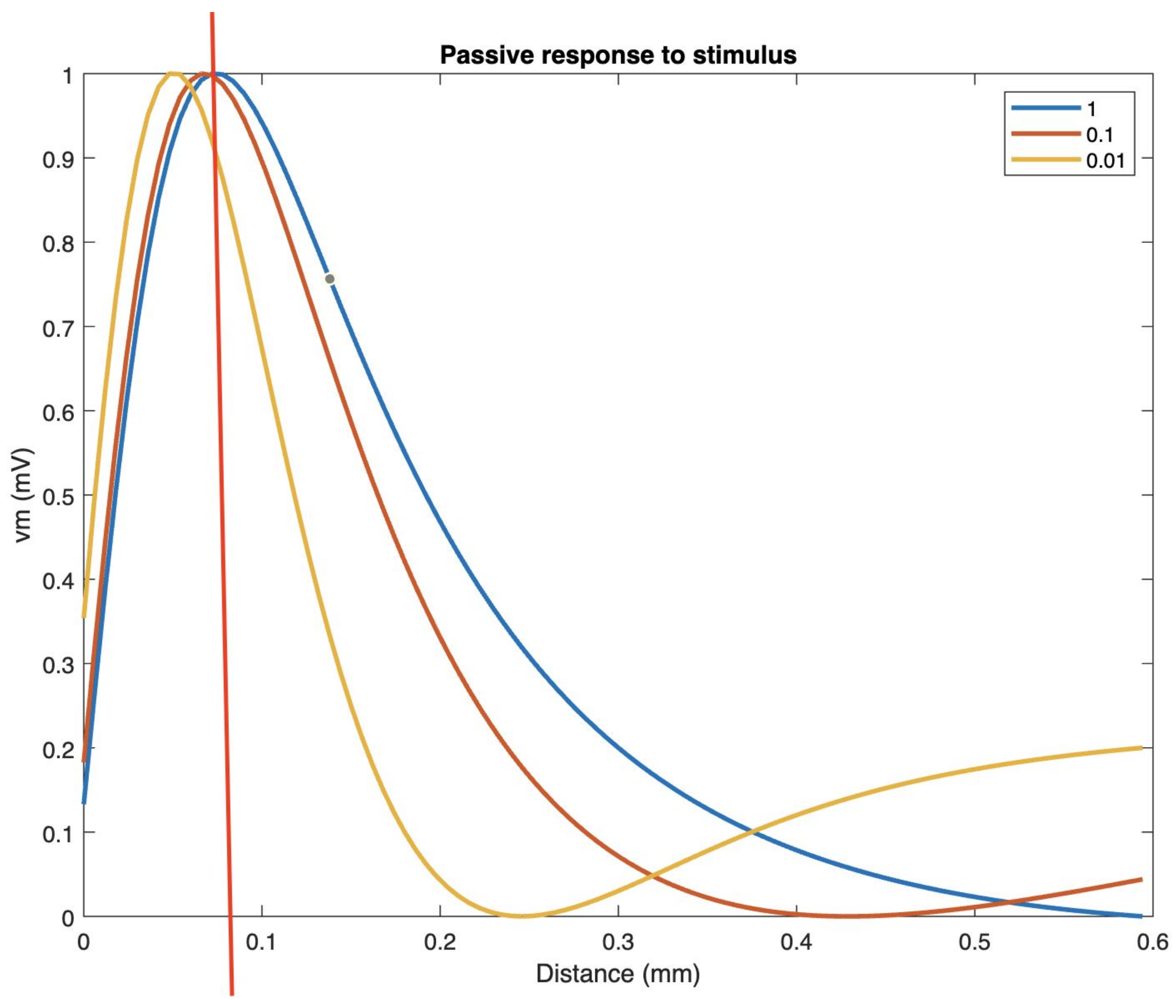
Matlab Code:

```
%% Parameters
lambda=rand(); % arbitrary value, will be used x/lambda
x = 0:lambda:(5*lambda); % in terms of lambda(space constant)
alfa = 1;
r_e = rand(); % arbitrary value, since alfa is 1, r_e will be equal to
r_i.(assumption made)
r_i = r_e*alfa;
cons = r_e/(r_i+r_e); %(re/(ri+re))
```

```
I_0 = rand() ;  % arbitrary value, will be used I_i/I_inf
%% Steady State Response Ratio
I_i = cons*I_0*(1+exp(-x/lambda));
I_inf = cons*I_0;
steady_state_response_ratio = I_i/I_inf;
%% Plot
figure()
plot(x,steady_state_response_ratio,'r', 'Linewidth', 2)
ylabel('Steady State Response Ratio')
xlabel('Position(in terms of lambda(space constant)) ')
grid on
```

slm

Q4) (12 points) Reproduce Figure 7.6 in the book. Use equation 7.75 for isolated single fiber and a point current source and following constants: h = 0.01 cm, λ = 0.086 cm, dz = λ/14.33, ri = 200 Ohm.cm, σ = 33.3 mS/cm, I = -0.44 mA, τ = 1.5 msec.



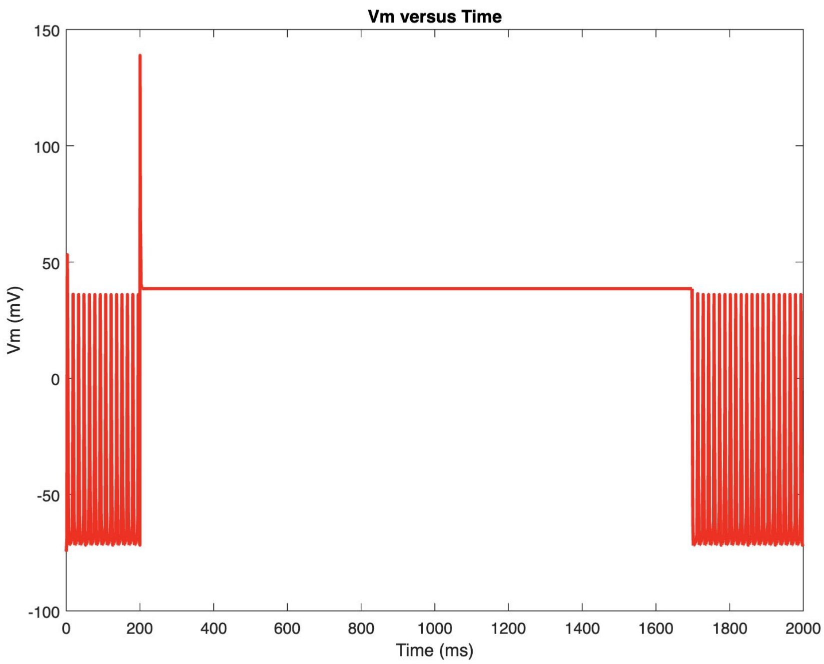
The output looks similar trend given book figure 7.6 after vertical red line.
I added code for Q4 as appendix.

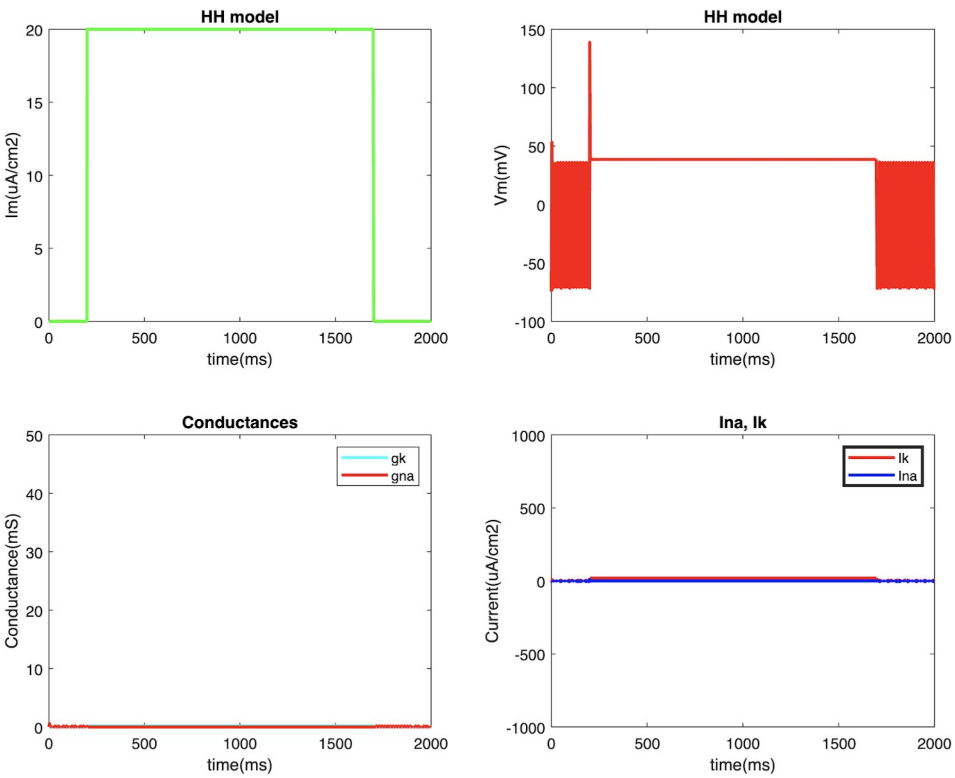
Q5) (35 points) Potassium Induced Repetitive Firing in Neurons The Hodgkin-Huxley model includes a single potassium current and for long pulses it is unrealistic. Connor and Stevens [1] developed a better model of the neuron using the same approach of HodgkinHuxley. This model will respond with realistic repetitive action potentials in response to a long pulse stimulus current using second potassium current which regulates the firing rate. In addition to HH model, Connor and Stevens model has additional repetitive activation gate (a) and repetitive inactivation gate (b) Modify the Hodgkin-Huxley scripts to implement the Connor model. Use simulation time of 2000 msec and step time of 0.005 msec. The stimulus current is 0.3 μA/cm applied from 200 msec to 1700 msec (pulse width of 1500 msec). Use the HH model and apply the stimulus current as 20 μA/cm2 from 200 msec to 1700 msec (pulse width of 1500 msec). Compare old HH model and Connor and Stevens HH model. Generate plots of the membrane potential, currents, and gates (for gates a and b, use a_∞ and b_∞). Plot the time constants for the m, h, and n gates versus Vm. Currents are given in μA/cm2 , conductances in mS/cm2 , and potentials in mV. Note that l'Hoˆpital's rule must be applied to some of the opening rates.
$J_{ion} = J_{Na} + J_K + J_A + J_{leak}$ ion current
$J_{Na} = g_{Na} \cdot m^3 \cdot h \cdot (V_m - E_{Na})$ Na+ current
$J_K = g_K \cdot n^4 \cdot (V_m - E_K)$ K + current
$J_A = g_A \cdot a^3 \cdot b \cdot (V_m - E_A)$ repetitive K+ current
$J_{leak} = g_L \cdot (V_m - E_L)$ leak current
Gates n, m, and h are governed by the opening and closing rates (in $msec^{-1}$):
Gates a and b are calculated using their steady-state value (x_∞) and time constant (τ_x)
Parameters and initial conditions: ENa = +55, gNa =1.2, EK = −72, gK =0.2, EA = −75, gA = 0.477, EL = −70, gL =0.003, Cm = 0.01 μF/cm2 , Vm = −74.5, n =0.0977, m = 0.0043, a =0.5079, h = 0.9869, b=0.4332

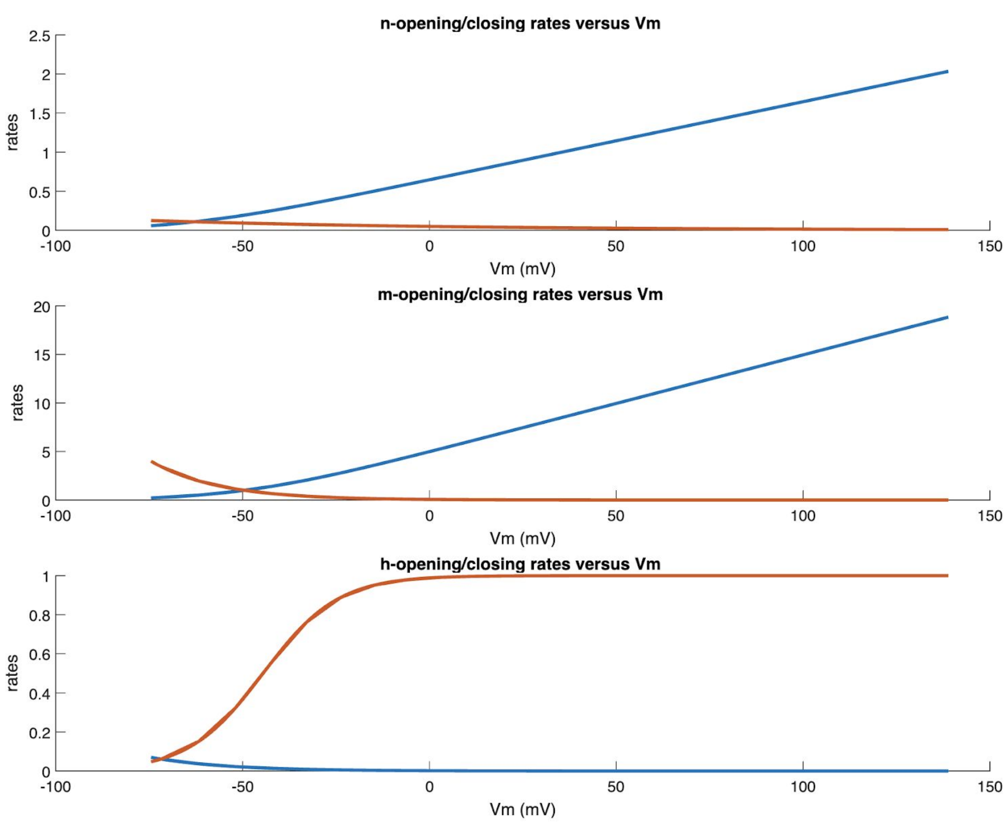
Connor and Stevens model can simulate potassium repetitive firing of neurons and is realistic. Because of having a single potassium current HH model fails to simulate the potassium induced repetitive firing of neurons. Hudgkin-Huxley model is also fails to give realistic currents for larger pulses.

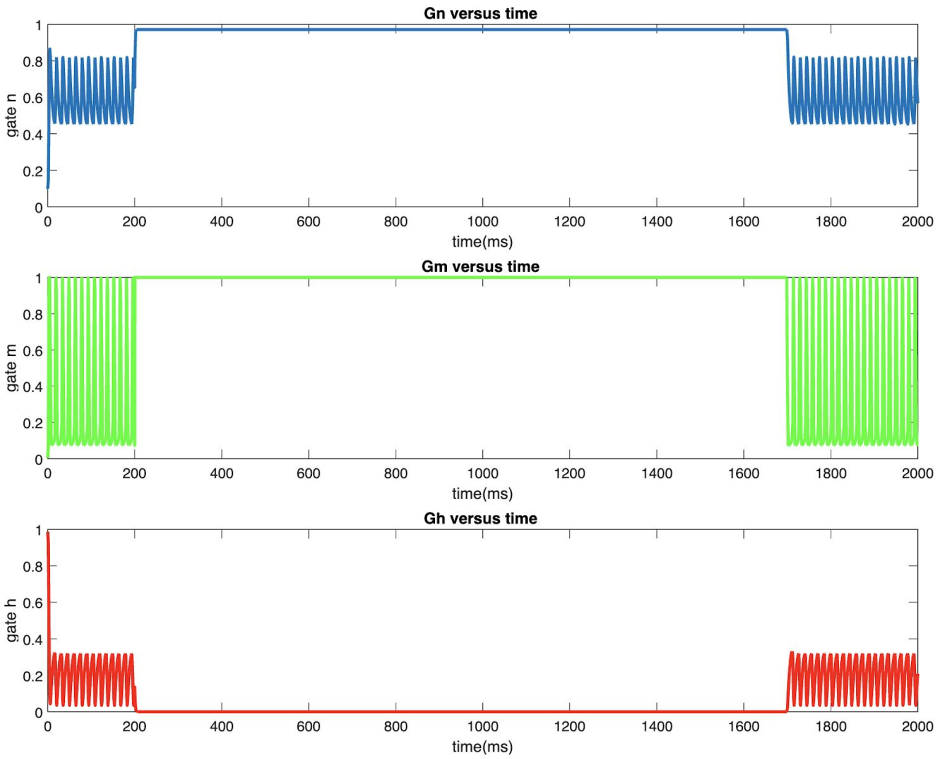
The plots for both Hudgkin Huxley and Connor and Stevens model is given below.

Hudgkin Huxley

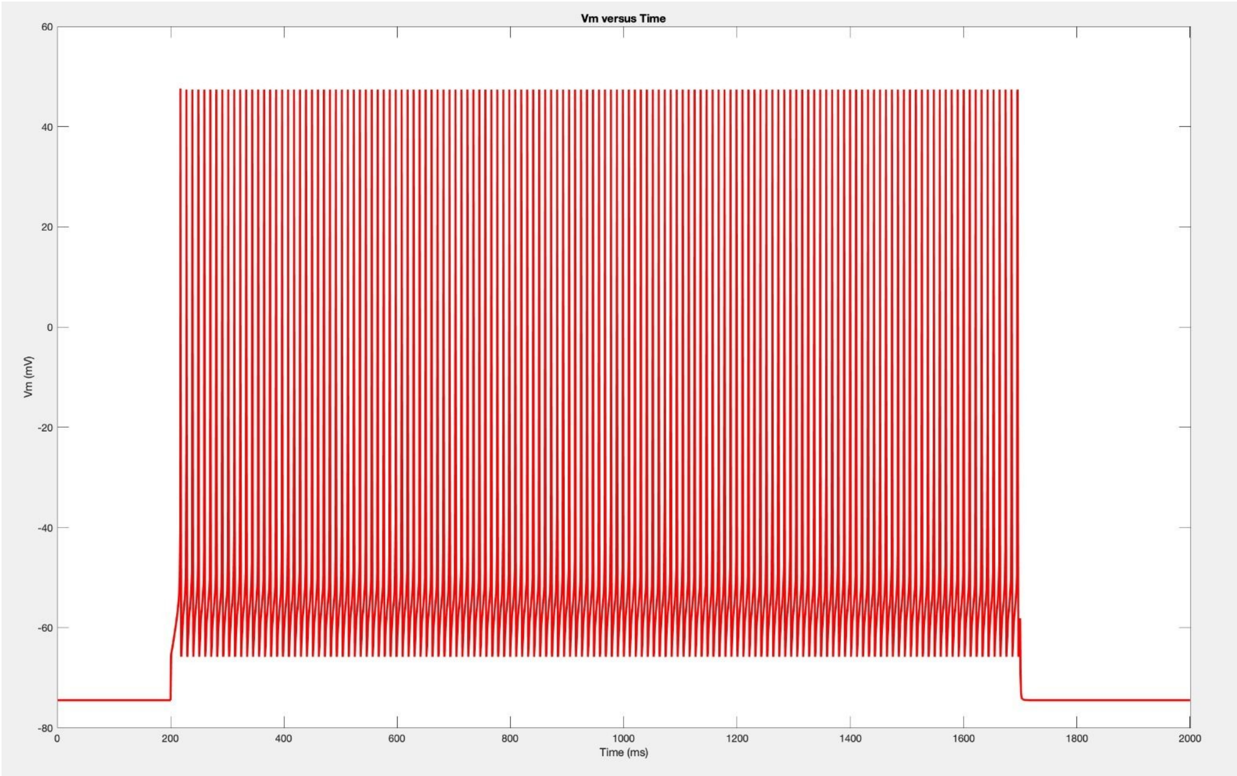


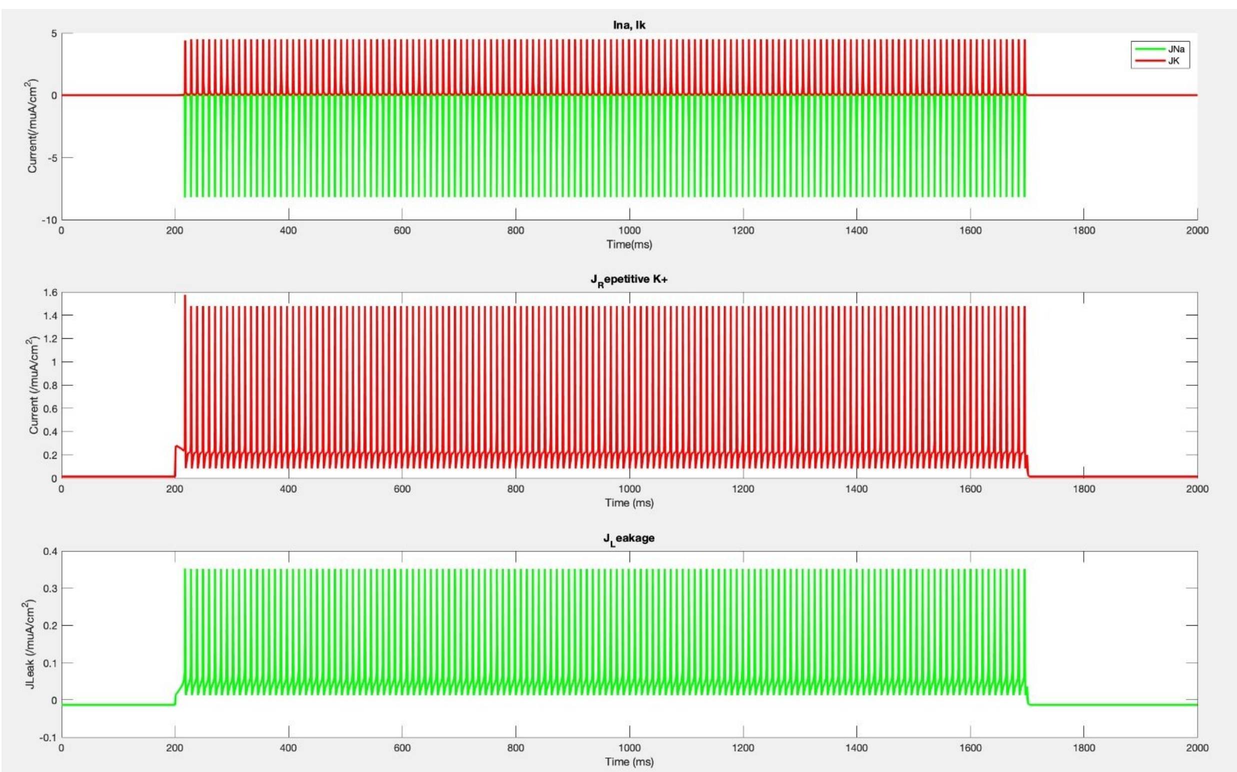

HH model
Im(uA/cm2)
time(ms)
HH model
Vm(mV)
time(ms)
Conductances
gk
gna
Conductance(mS)
time(ms)
Ina, Ik
Ik
Ina
Current(uA/cm2)
time(ms)

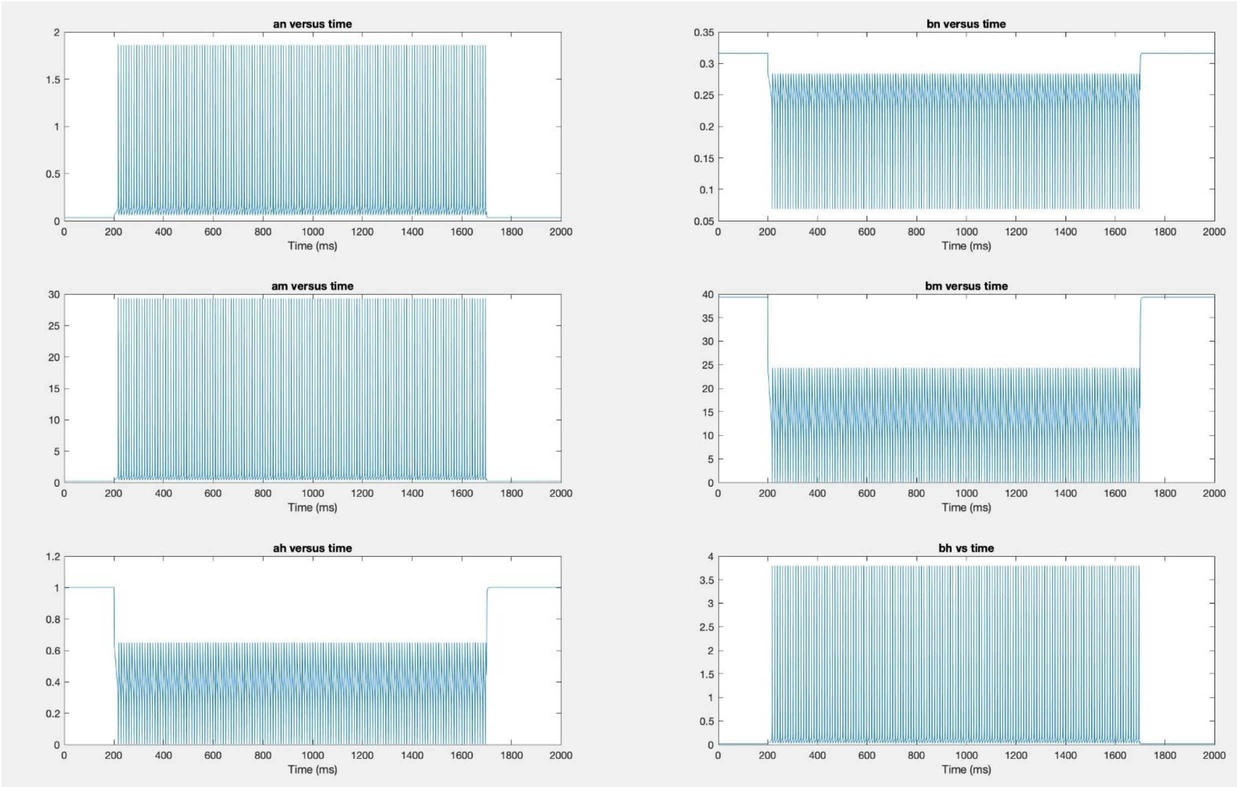

n-opening/closing rates versus Vm
rates
Vm (mV)
m-opening/closing rates versus Vm
rates
Vm (mV)
h-opening/closing rates versus Vm
rates
Vm (mV)

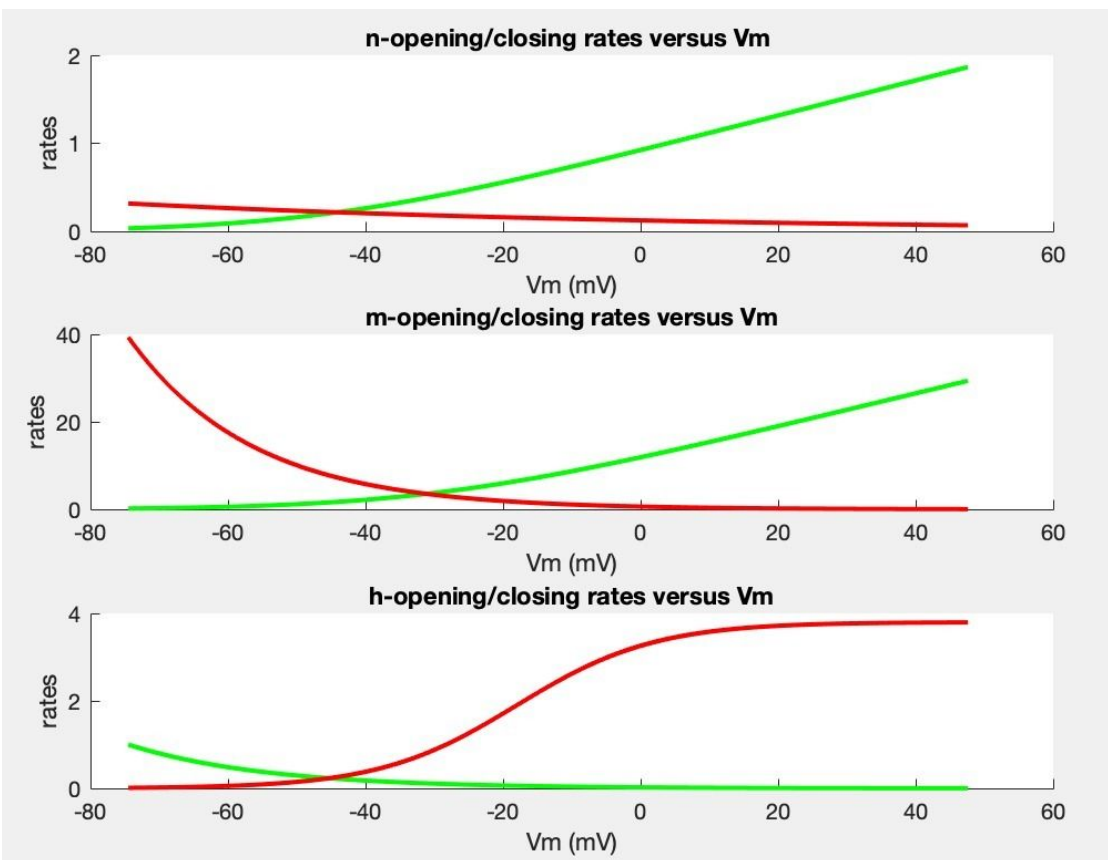


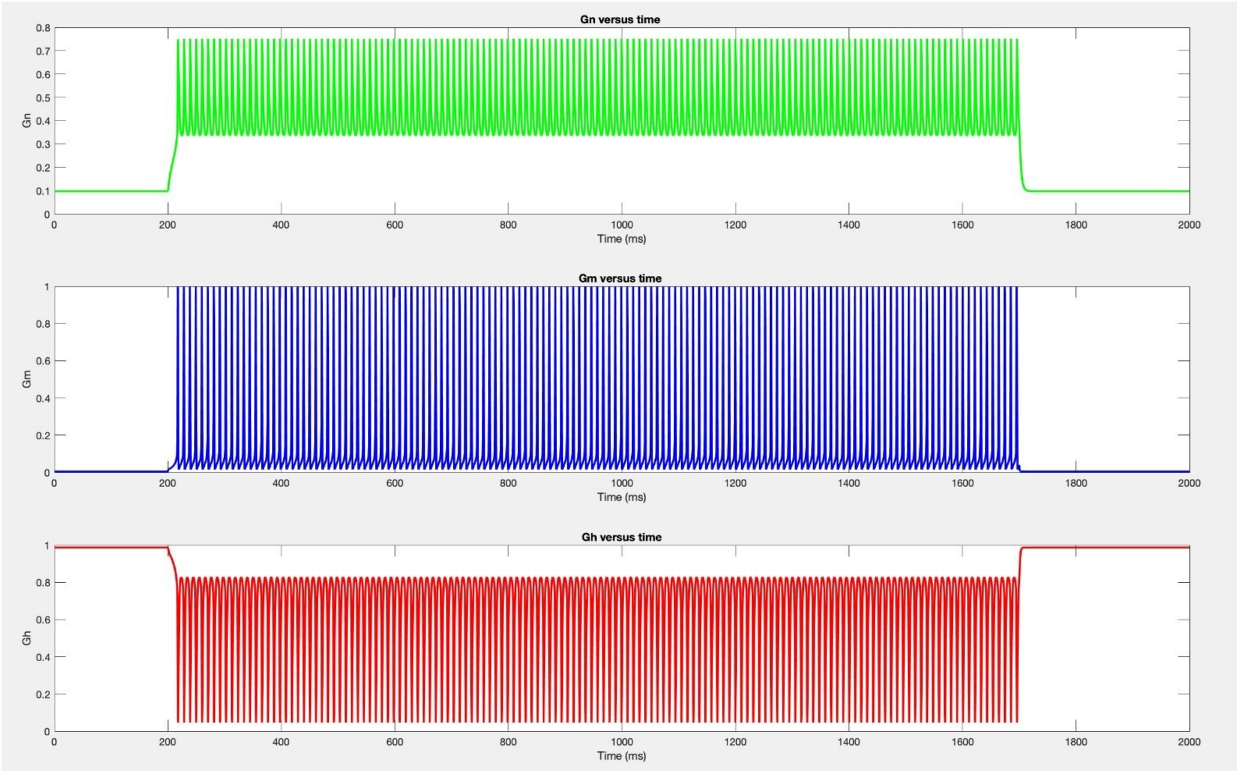
Connor and Stevens

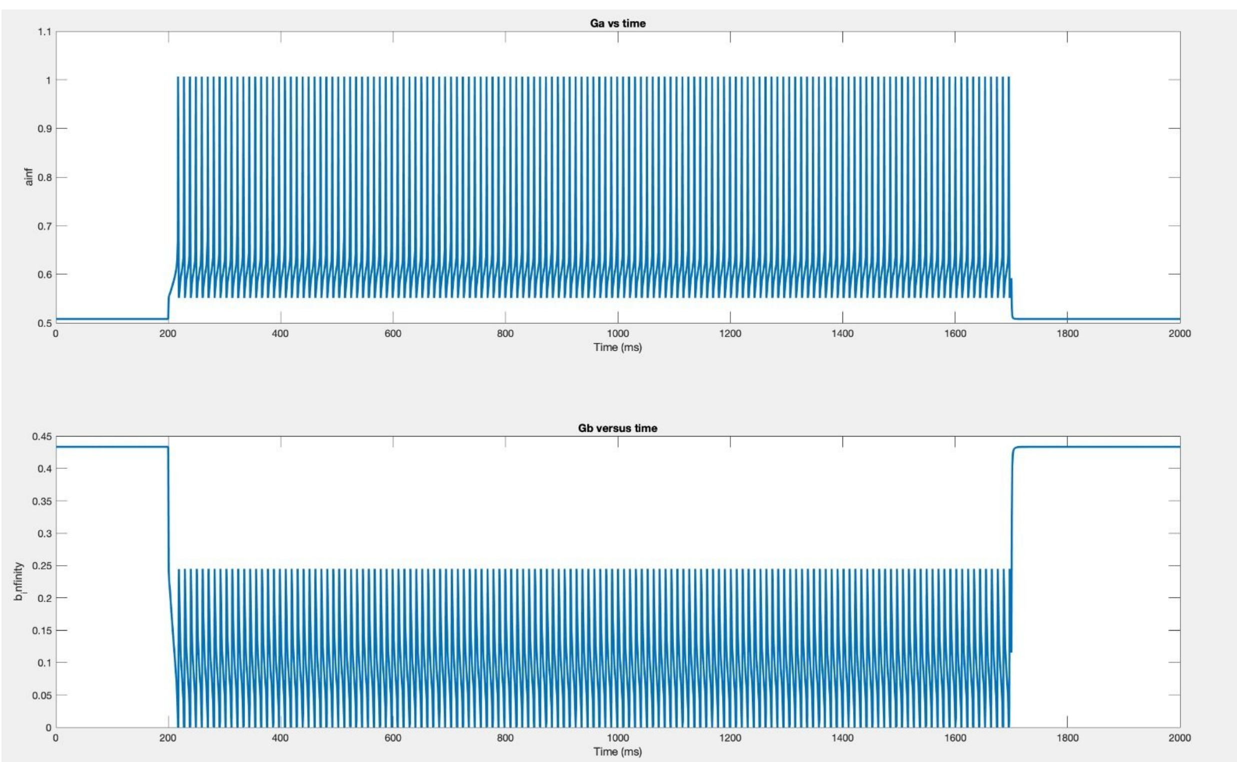

Vm versus Time
Vm (mV)
60
40
20
0
-20
-40
-60
-80
0
200
400
600
800
1000
1200
1400
1600
1800
2000
Time (ms)


Ina, Ik
JNa
JK
Current(/muA/cm^2)
5
0
-5
-10
0
200
400
600
800
1000
1200
1400
1600
1800
2000
Time(ms)
J$_R$epetitive K+
Current (/muA/cm^2)
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
200
400
600
800
1000
1200
1400
1600
1800
2000
Time (ms)
J$_L$eakage
JLeak (/muA/cm^2)
0.4
0.3
0.2
0.1
0
-0.1
0
200
400
600
800
1000
1200
1400
1600
1800
2000
Time (ms)


an versus time
bn versus time
am versus time
bm versus time
ah versus time
bh vs time
Time (ms)


n-opening/closing rates versus Vm
m-opening/closing rates versus Vm
h-opening/closing rates versus Vm
rates
Vm (mV)


Gn versus time
Gn
Time (ms)
Gm versus time
Gm
Time (ms)
Gh versus time
Gh
Time (ms)


Ga vs time
ainf
Time (ms)
Gb versus time
binfinity
Time (ms)

APPENDIX

Code for Q4

```
close all
clc
clear all

h = 0.01;
lambda = 0.086;
dz = lambda / 14.33;
ri = 200;
sigma = 33.3;
I = -0.44;
tau = 1.5;

H = h / lambda;
xmax = 0.6;
X = 0:dz:xmax;
T = [1.00, 0.1, 0.01];
T = T/tau;


t = T(1);
t = sqrt(t);
vm = (lambda/ri) * ifft((I / (16*pi*sigma*lambda)) * fft((2*X.^2-H^2)./(H^2 +
X.^2).^(5/2)) .* fft(exp(-X).*(1 - erf(X./(2*t) - t)) - exp(X).*(1 -
erf(X./(2*t) + t))));
figure()
plot(X,normalize(vm,'range'), 'Linewidth', 2)
hold on


t = T(2);
t = sqrt(t);
vm = (lambda/ri) * ifft((I / (16*pi*sigma*lambda)) * fft((2*X.^2-H^2)./(H^2 +
X.^2).^(5/2)) .* fft(exp(-X).*(1 - erf(X./(2*t) - t)) - exp(X).*(1 -
erf(X./(2*t) + t))));
plot(X,normalize(vm,'range'), 'Linewidth', 2)
hold on


t = T(3);
t = sqrt(t);
vm = (lambda/ri) * ifft((I / (16*pi*sigma*lambda)) * fft((2*X.^2-H^2)./(H^2 +
X.^2).^(5/2)) .* fft(exp(-X).*(1 - erf(X./(2*t) - t)) - exp(X).*(1 -
erf(X./(2*t) + t))));
plot(X,normalize(vm,'range'), 'Linewidth', 2)
```

```
  hold off
  title('Passive response to stimulus')
  legend('1', '0.1', '0.01')
  xlabel('Distance (mm)')
  ylabel('vm (mV)')
```

Code for Q5
Connor&Stevens

```
close all
clc
clear all

%% Constants

Vm = -74.5;
Cm = 0.01;

El = -70;
Ena = +55;
Ek = -72;
Ea = -75;


gl = 0.003;
gna = 1.2;
gk = 0.2;
ga = 0.477;


h0 = 0.9869;
a0 = 0.5079;
m0 = 0.0043;
b0 = 0.4332;
n0 = 0.0977;


I = 0.3;
sstart = 200;
send = 1700;

dt = 0.005;
final_t = 2000;
t = 0:dt:final_t;

Im = zeros(1, length(t));
```

```
Im((sstart / dt) : (send/dt)) = I;

%% Calculation

for k = 1:length(t)
Ina(k) = gna * m0(k)^3 * h0(k) * (Vm(k) - Ena);
Ik(k) = gk * n0(k)^4 * (Vm(k) - Ek);
Ia(k) = ga * a0(k)^3 * b0(k) * (Vm(k) - Ea);
Ileak(k) = gl * (Vm(k) - El);
Iion(k) = Ina(k) + Ik(k) + Ia(k) + Ileak(k);
deltaVm(k) = (dt/Cm) * (Im(k) - Iion(k));
if (-45.71 < Vm(k)) && (Vm(k) < -45.69)
an(k) = 0.02 / (1/10 * exp(-(Vm(k) + 45.7)/10));
else
an(k) = 0.02*(Vm(k) + 45.7) / (1 - exp(-(Vm(k) + 45.7)/10));
end
bn(k) = 0.25 * exp(-(Vm(k) + 55.7) / 80);
if (-29.71 < Vm(k)) && (Vm(k) < -29.69)
am(k) = 0.38 / (1/10 * exp(-(Vm(k)+29.7)/10));
else
am(k) = 0.38*(Vm(k)+29.7) / (1- exp(-(Vm(k)+29.7)/10));
end
tau_a(k) = 0.3632 + 1.158 / (1 + exp(0.0497*(Vm(k)+55.96)));
tau_b(k) = 1.24 + 2.678 / (1 + exp(0.0624*(Vm(k) + 50)));
a_inf(k) = ((0.0761*exp(0.0314*(Vm(k)+94.22))) /
(1+exp(0.0346*(Vm(k)+1.17))))^(1/3);
b_inf(k) = (1+exp(0.0688*(Vm(k)+53.3)))^(-4);
bm(k) = 15.2 * exp(-0.0556 * (Vm(k) + 57.4));
ah(k) = 0.266 * exp(-(Vm(k) + 48)/20);
bh(k) = 3.8 / (1 + exp(-(Vm(k)+18)/10));
Vm(k+1) = Vm(k) + deltaVm(k);
n0(k+1) = n0(k) + dt * (an(k)*(1-n0(k)) - bn(k)*n0(k));
m0(k+1) = m0(k) + dt * (am(k)*(1-m0(k)) - bm(k)*m0(k));
h0(k+1) = h0(k) + dt * (ah(k)*(1-h0(k)) - bh(k)*h0(k));
a0(k+1) = a0(k) + dt * (a_inf(k) - a0(k)) / tau_a(k);
b0(k+1) = b0(k) + dt * (b_inf(k) - b0(k)) / tau_b(k);
end

t1 = 0:dt:final_t+dt;

figure()
plot(t1, Vm, 'r', 'Linewidth', 2)
title('Vm versus Time')
xlim([0 (final_t+1)])
ylabel('Vm (mV)')
xlabel('Time (ms)')
```

```
figure()
subplot(3,1,1)
plot(t1, n0,'g', 'Linewidth', 2)

title('Gn versus time ')
xlim([0 2000])
ylabel('Gn')
xlabel('Time (ms)')

subplot(3,1,2)
plot(t1, m0,'b', 'Linewidth', 2)
title('Gm versus time ')
xlim([0 2000])
ylabel('Gm')
xlabel('Time (ms)')

subplot(3,1,3)
plot(t1, h0, 'r', 'Linewidth', 2)
title('Gh versus time')
ylabel('Gh')
xlim([0 2000])
xlabel('Time (ms)')


figure()
subplot(3,1,1)
hold on
plot(t, Ina, 'g', 'Linewidth', 2)
plot(t, Ik, 'r','Linewidth', 2)
title('Ina, Ik');
ylabel('Current(/muA/cm^2)')
xlabel('Time(ms)')
legend('JNa','JK')

subplot(3,1,2)
plot(t, Ia, 'r', 'Linewidth', 2)
title('J_Repetitive K+');

  ylabel('Current (/muA/cm^2)')
  xlabel('Time (ms)')

  subplot(3,1,3)
  plot(t, Ileak,'g', 'Linewidth', 2)
  title('J_Leakage');
  ylabel('JLeak (/muA/cm^2)')
  xlabel('Time (ms)')
```

```
figure()
subplot(2,1,1)
plot(t, a_inf, 'Linewidth', 2)
title('Ga vs time - CSHH')
xlabel('Time (ms)')
ylabel('ainf')

subplot(2,1,2)
plot(t, b_inf, 'Linewidth', 2)
title('Gb versus time')
ylabel('b_infinity')
xlabel('Time (ms)')


figure()
subplot(3,1,1)
hold on
plot(Vm(1:end-1), an,'g' ,'Linewidth', 2)
plot(Vm(1:end-1), bn,'r', 'Linewidth', 2)
title('n-opening/closing rates versus Vm ')
xlabel('Vm (mV)')
ylabel('rates')

subplot(3,1,2)
hold on
plot(Vm(1:end-1), am,'g', 'Linewidth', 2)
plot(Vm(1:end-1), bm,'r', 'Linewidth', 2)
title('m-opening/closing rates versus Vm')
xlabel('Vm (mV)')
ylabel('rates')

subplot(3,1,3)
hold on
plot(Vm(1:end-1), ah,'g', 'Linewidth', 2)
plot(Vm(1:end-1), bh,'r', 'Linewidth', 2)
title('h-opening/closing rates versus Vm')
xlabel('Vm (mV)')
ylabel('rates')



figure()
subplot(3,2,1)
plot(t, an)
title('an versus time')
xlabel('Time (ms)')
```

```
  subplot(3,2,2)
  plot(t, bn)
  title('bn versus time')
  xlabel('Time (ms)')

  subplot(3,2,3)
  plot(t, am)
  title('am versus time')
  xlabel('Time (ms)')

  subplot(3,2,4)
  plot(t, bm)
  title('bm versus time')
  xlabel('Time (ms)')

  subplot(3,2,5)
  plot(t, ah)
  title('ah versus time')
  xlabel('Time (ms)')

  subplot(3,2,6)
  plot(t, bh)
  title('bh vs time')
  xlabel('Time (ms)')
```

Hudgkin&Huxley

```
clear all
clc
close all

dt=0.005;
t=0:dt:2000;

Im = zeros(size(t));

m(1)=0.0043;
h(1)=0.9869;
n(1)=0.0977;

Temp=6.3;
gl=0.003;
gkk=0.2;
gnana=1.2;
```

```
El=-70;
Ek = -72;
Ena = 55;
Cm=0.01;

Is=20;
sim_start = 200;
sim_end = 1700;

Im((sim_start/dt):(sim_end/dt)) = Is;


Vrest=-74.5;
Vm(1)=Vrest;
vm(1)=0;
for j=1:length(t)
gk(j) = gkk*n(j)^4;
gna(j) = gnana*m(j)^3*h(j);
Ik(j) = gk(j)*(Vm(j)-Ek);
Ina(j) = gna(j)*(Vm(j)-Ena);
Il(j) = gl*(Vm(j)-El);
I(j)=Im(j)-Ik(j)-Ina(j)-Il(j);
vm(j)=Vm(j)-Vrest;
dVm(j) = dt*(Im(j)-Ik(j)-Ina(j)-Il(j))/Cm;
an(j) = 0.01*(10-vm(j))/((exp((10-vm(j))/10))-1);
bn(j) = 0.125*exp(-vm(j)/80);
bh(j) = 1/((exp((30-vm(j))/10))+1);
ah(j) = 0.07*exp(-vm(j)/20);
am(j) = 0.1*(25-vm(j))/((exp((25-vm(j))/10))-1);
bm(j) = 4*exp(-vm(j)/18);
deln(j) = dt*(an(j)*(1-n(j))-bn(j)*n(j));
delh(j) = dt*(ah(j)*(1-h(j))-bh(j)*h(j));
delm(j) = dt*(am(j)*(1-m(j))-bm(j)*m(j));
Vm(j+1) = Vm(j) + dVm(j);
n(j+1) = n(j) + deln(j);
m(j+1) = m(j) + delm(j);
h(j+1) = h(j) + delh(j);

end

t1=0:dt:2000+dt;


figure()
plot(t1, Vm, 'r', 'Linewidth', 2)
title('Vm versus Time')
xlim([0 (1999+1)])
```

```
ylabel('Vm (mV)')
xlabel('Time (ms)')


figure()
subplot(2,2,1)
  plot(t,Im,'g', 'Linewidth', 2)
  title('HH model')
  xlim([0 2000])
  xlabel('time(ms)')
  ylabel('Im(uA/cm2)')

  subplot(2,2,2)
  plot(t1,Vm,'r', 'Linewidth', 2)
  title('HH model')
  xlim([0 2000])
  xlabel('time(ms)')
  ylabel('Vm(mV)')

  subplot(2,2,3)
  plot(t,gk,'c', 'Linewidth', 2)
  title('Conductances')
  xlim([0 2000])
  hold on
  plot(t,gna,'r', 'Linewidth', 2)
  xlim([0 2000])
  legend('gk','gna')
  ylim([0 50])
  xlabel('time(ms)')
  ylabel('Conductance(mS)')

  subplot(2,2,4)
  plot(t,Ik, 'r','Linewidth', 2)
  hold on
  plot(t,Ina,'b', 'Linewidth', 2)
  title('Ina, Ik')
  xlim([0 2000])
  legend('Ik','Ina','c', 'Linewidth', 2)
  ylim([-1000 1000])
  xlabel('time(ms)')
  ylabel('Current(uA/cm2)')


  figure()
  subplot(3,1,1)
  hold on
  plot(Vm(1:end-1), an, 'Linewidth', 2)
```

```
plot(Vm(1:end-1), bn, 'Linewidth', 2)
title('n-opening/closing rates versus Vm ')
xlabel('Vm (mV)')
ylabel('rates')

subplot(3,1,2)
hold on
plot(Vm(1:end-1), am, 'Linewidth', 2)
plot(Vm(1:end-1), bm, 'Linewidth', 2)
title('m-opening/closing rates versus Vm ')
xlabel('Vm (mV)')
ylabel('rates')

subplot(3,1,3)
hold on
plot(Vm(1:end-1), ah, 'Linewidth', 2)
plot(Vm(1:end-1), bh, 'Linewidth', 2)
title('h-opening/closing rates versus Vm ')
xlabel('Vm (mV)')
ylabel('rates')

figure()
subplot(3,1,1)
plot(t1,n, 'Linewidth', 2)
xlim([0 2000])
title('Gn versus time ')
xlabel('time(ms)')
ylabel('gate n')

subplot(3,1,2)
plot(t1,m,'g', 'Linewidth', 2)
xlim([0 2000])
title('Gm versus time ')
xlabel('time(ms)')
ylabel('gate m')

subplot(3,1,3)
plot(t1,h,'r', 'Linewidth', 2)
xlim([0 2000])
title('Gh versus time ')
xlabel('time(ms)')
ylabel('gate h')
```