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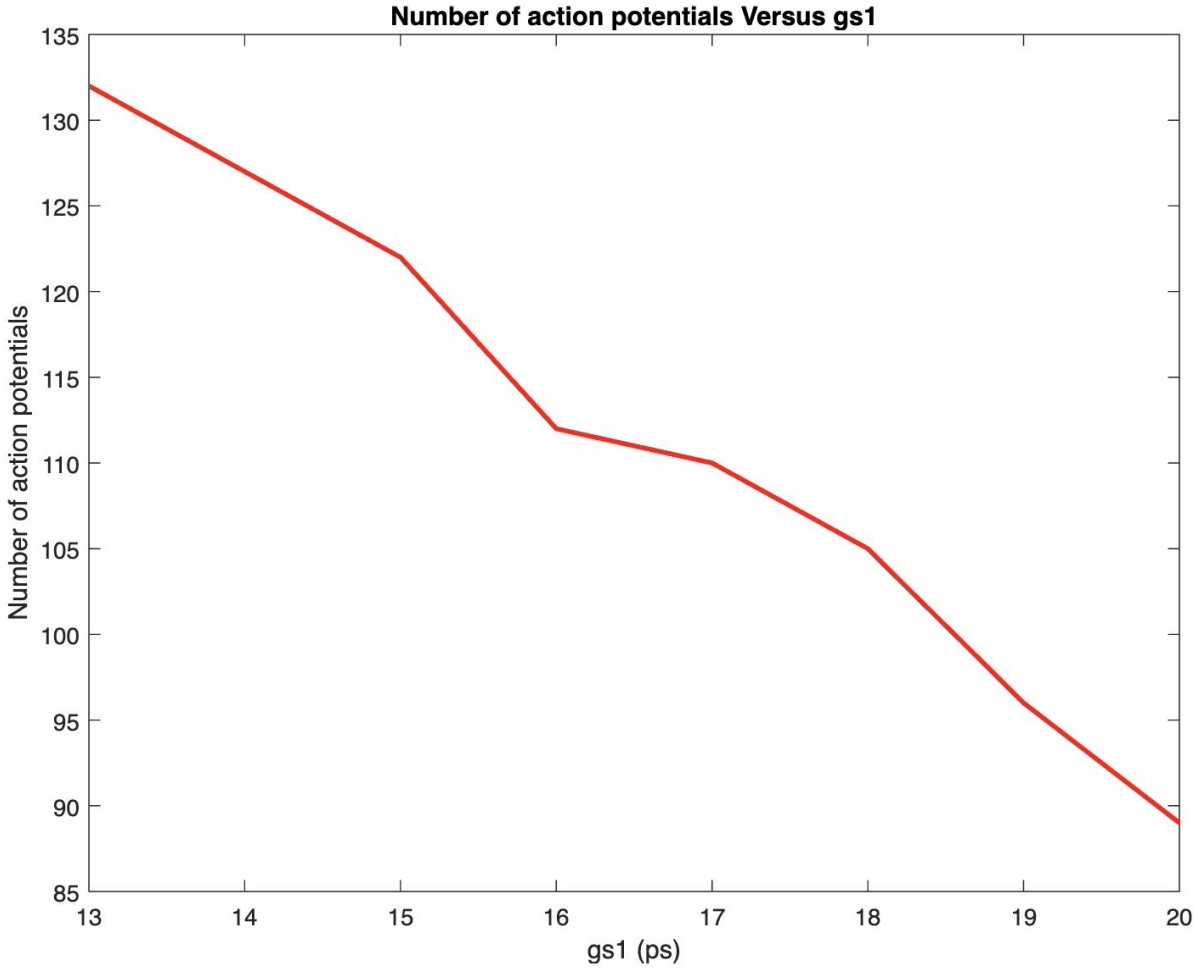
08.05.2020

ELEC436 HW#6

Q1) Bursting Action Potential in Pancreatic β-Cells (Bertram 2000)

Read the following paper [1]. Reproduce Figure 2 in the paper. The parameters given in Table 1 and equations in methods section. Vary the maximum calcium activated potassium conductance gs1 from 13 to 20 pS/cm2 and plot number of action potentials versus gs1. Simulation time should cover 6000 ms. [1] R Bertram, J Previte, A Sherman, TA Kinard, and LS Satin. The phantom burster model for pancreatic beta-cells. Biophysical Journal, 79(6):2880–2892, December 2000.

I changed simulation time to 30ms which is given from the paper's plots. Also, in PS we increased simulation time to see exact graphs in variance of gs1 from 13 to 20 pS/cm2



Q2) The following questions from the textbook: 1-5,14-17,23-24 (pages 478-486 in 3rdEdition of the text book.)

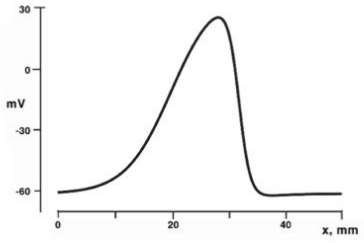


Figure 13.7. Action potential as a function of distance x along the fiber. The triangle was made by overlaying the action potential with three lines, one for the baseline and the other two at peak activation and repolarization slope.

Exercises 1–6 involve $V_m(t)$ and $V_m(x)$. These exercises compare the one to the other in several ways, and also allow practice in manipulating the tabulated data of each. Completing these exercises requires a computer system to tabulate the function and make the plots.

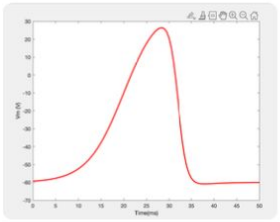
1. Inspect $V_m(x)$ in Figure 13.7. This figure plots the function defined in the prologue. For what time t does this plot result? Estimate by looking at the equations in the prologue and verify by making a confirming plot.

2. Plot $V_m(t)$ at $x = 24$ millimeters. Make the horizontal axis extend from zero to 20 milliseconds.

3. In a few sentences, explain the differences seen in the wave shape of $V_m(x)$ as compared to that of $V_m(t)$, as plotted.

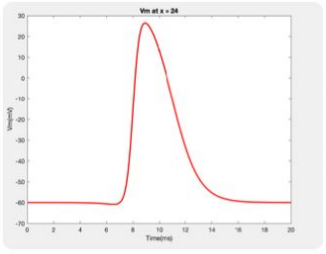
4. Plot $\dot{V}_m(t) = dV_m(t)/dt$ at $x = 24$ millimeters, from zero to 20 milliseconds, and give the number value for $\dot{V}_m^{\max}$, the peak value of the time derivative. (The use of the dot notation for time derivatives is customary in electrophysiology.)

1) t does this plot result at t=10 miliseconds.



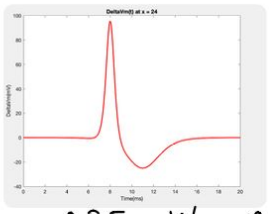
Mid point of upstroke at about 32 mm. The action potential happens about 8 msec after the one at x=0 dividing by velocity (4mm/sec). Parameter t1 adds a 2msec time delay to the upstroke.

2)



3) Activation phase always come first in an action potential. The fast upstroke is on the lower time. The activation phase is on the higher x on an action potential waveform travelling toward higher x because activation is moving to right. Our action potentials seems largely the same, though real action potentials may show more subtle differences.

4)



V_{mmax} = 95.5 mV/ms. Measured transmembrane potentials from healthy tissue usually have V_{mmax} 100 – 200 mV/ms, for comparison, as abnormalities inevitably leads to lower value. The action potential is also on slow side.

5. The location and magnitude of monopolar or dipolar lumped sources as given in the text of the chapter depends on idealizing the action potential into a triangulated shape. That requires determining straight lines matching the maximum activation slope and recovery slope, and matching the baseline. Often these lines are determined graphically; however, with $V_m(x,t)$ given here as a noise-free mathematical function, the lines also can be determined from tabulated data for $V_m(x)$. Each straight line can be expressed in the standard form $y = ax + b$. Consider $V_m(x)$ as shown in Figure 13.7 and do the following:

a. Create a list of values of x and $V_m(x)$. From these data determine the point of greatest slope of the $V_m(x)$ curve during activation. For this point, give the x position at which it occurs, the value of V_m, and the value of dV_m/dt.

b. Find the linear equation that fits the data of part a.

c. Find the same data as in a, for the point of greatest slope during recovery.

d. Find the linear equation that fits the data of part c.

e. Find the point of intersection of the two lines. Specifically, find the x and V_m coordinates of the point of crossing.

f. Find the x coordinates of the points where the activation line and the recovery line cross the baseline (–60 mV).

You may be able to answer these questions with purely analytical methods instead of numerical ones.

a) va = -14.9093 value of Vm at that point.
i = 640
Amax = 23.87083 magnitude of slope at that point.
xa = 32.0070 } x coordinate of point of max. slope.

b) $V_m = -A_{max}(x - x_a)$

c) Bmax = 6.2494
xr = 19.9950
Vr = -10.0319
i = 400

d) $V_m = B_{max}(x - x_r) + V_r$

e) Vm(roi) = 48.4 mV,
x(roi) = 29.35 mm

f) Recovery crossing at x = 12.0 mm
Activation " " x = 33.9 mm.

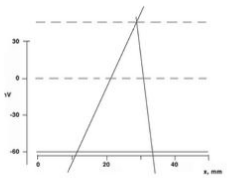


Figure 13.8. Action potential as a function of distance x along the fiber. The action potential was constructed using the template function. This figure is a triangulation of Figure 13.7.

14. Carefully examine the triangulated action potential as shown in Figure 13.8 and give a value for each of the following quantities, with units. As these values are used in subsequent exercises, you may wish to enlarge the figure so as to measure it more precisely. [Because there is a template function for V_m, another possibility for answering each part is to examine the data for a digitized version of the action potential, to locate the points of maximum slope during the activation and recovery phases, and to find the points of intersection of the lines thereby defined. (See Ex. 5 above.) The figure then can be used to check the answers obtained analytically.]

a. Activation slope A_{max}.

b. Recovery slope B_{max}.

Crossing point → Vm = 48.4 mV, x = 29.35 mm
Intersection with -60 line → x = 33.9 mm } $A_{max} = -\frac{60 + 48.4}{(-29.35 + 33.9)} = -23.83$
Intersection with -60 line → x = 12.0 mm } $B_{max} = -\frac{-(-60) + 48.4}{-12.0 + 29.35} = 6.2494$

c. Peak-to-peak voltage of triangularized AP, V_{pp}.

$V_m = -(-60) + 48.4 = 108.4$ mV

d. Width w_a.

$w_a = -29.35 + 33.9 = 4.55$ mm

e. Width w_r.

$w_r = -12.0 + 29.35 = 17.35$ mm

f. Points of intersection x_1, x_2, x_3.

$x_3 = 33.9$ mm, $x_2 = 29.35$ mm, $x_1 = 12.0$ mm

15. Determine the strength and location of each of the three monopole lumped sources. Be sure to include the location (x coordinate) magnitude, sign, and units of each one.

16. Computations of extracellular potentials from membrane currents can be placed into a matrix format:

$$[P_e] = [H][I_m] \tag{13.7}$$

Here matrix $[I_m]$ is a column vector containing the values of lumped sources 1 to 3 for time t. Matrix $[H]$ is set of coefficients by which each source must be multiplied to find

15) It is 0 outside of corner points because lumped source values are found using $\frac{\partial^2 V_m}{\partial x}$. 3 lumped source at $x_1 = 12.0$ mm → $M_1 = \pi a^2 \sigma_i \cdot B_{max}$
$x_2 = 29.35$ mm → $M_2 = -\pi a^2 \sigma_i \cdot (A_{max} + B_{max})$
$x_3 = 33.9$ mm → $M_3 = \pi a^2 \sigma_i \cdot A_{max}$

$A_{max} = -23.83$ mV/mm

$B_{max} = 6.2494$ mV/mm

$\sigma_i = 10^{-3}\ 1/(\Omega\,mm) = 1/R_i$

$a = 50$ μm

$M_1 = \pi \cdot (50\times10^{-3}\,mm)^2 \times (10^{-3}\cdot(\Omega\,mm)^{-1}) \times (6.2494\ mV/mm) = 0.0491\ nA$

$M_2 = -0.138\ nA$

$M_3 = 0.187\ nA$

one of the extracellular potentials. $[P_e]$ is a column vector giving the set of extracellular potentials. Matrices $[H]$ and $[P_e]$ have one row for each extracellular potential to be found. Suppose there are three extracellular potentials to be found, at three field points. The three field points have x positions 30, 31, and 32 mm. They are located at a distance h away from the fiber axis.

a. Define each of the 9 elements of $[H]$ defined in terms of r_{ij}, where r_{ij} is the distance from field point i to monopolar source j.

b. Find matrix $[H]$ (numerical values) for $h = 100$ micrometers.

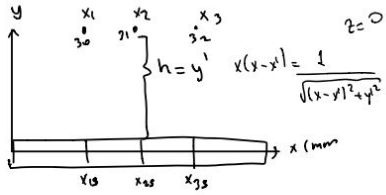
c. If the monopole sources have values of 3, −4, and 1 mA, respectively, what are the values of the extracellular potentials at each of the 3 field points?

17. Plot $\Phi_e(x)$ along a line parallel to the x axis at distance $y = h$ with $z = 0$ (i.e., plot $\Phi_e(x)$, as it is generated at distance h away from the fiber axis, from the three lumped monopole sources). Let the horizontal axis extend from $x = 0$ to $x = 50$ millimeters. Calibrate the vertical axis, and make each plot large enough that the magnitudes of the peaks can be read from the graph. Compare to the plots for $\Phi_e(x)$ as determined from the distributed sources, as in Ex. 11. Make plots for:

a. $h = 100$ micrometers.

b. $h = 1000$ micrometers.

c. $h = 10000$ micrometers.



$x(y-y') = \dfrac{1}{\sqrt{(x-y')^2+y^2}}$ 3 rows

a)

$$H = \begin{bmatrix} \frac{1}{\sqrt{(x_{13}-y_1)^2+h^2}} & \frac{1}{\sqrt{(x_{23}-y_1)^2+h^2}} & \frac{1}{\sqrt{(x_{33}-y_1)^2+h^2}} \\ \frac{1}{\sqrt{(x_{13}-y_2)^2+h^2}} & \frac{1}{\sqrt{(x_{23}-y_2)^2+h^2}} & \frac{1}{\sqrt{(x_{33}-y_2)^2+h^2}} \\ \frac{1}{\sqrt{(x_{13}-y_3)^2+h^2}} & \frac{1}{\sqrt{(x_{23}-y_3)^2+h^2}} & \frac{1}{\sqrt{(x_{33}-y_3)^2+h^2}} \end{bmatrix}$$

$h = 100$ micrometer $= 0.1$ mm

$P_{3\times1} = H_{3\times3} \cdot [I_{m\,(3\times1)}]$ only diagonal

b)

$$H = \begin{bmatrix} \frac{1}{h} & \frac{1}{\sqrt{1+h^2}} & \frac{1}{\sqrt{2+h^2}} \\ \frac{1}{\sqrt{1+h^2}} & \frac{1}{h} & \frac{1}{\sqrt{1+h^2}} \\ \frac{1}{\sqrt{2+h^2}} & \frac{1}{\sqrt{1+h^2}} & \frac{1}{h} \end{bmatrix}$$

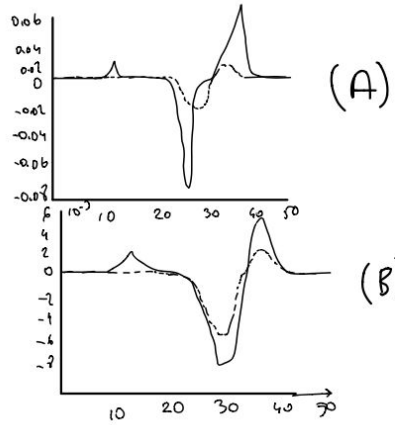
$$P_e = \begin{bmatrix} 10 & 0.99504 & 0.70535 \\ 0.99504 & 10 & 0.99504 \\ 0.70535 & 0.99504 & 10 \end{bmatrix} \cdot \begin{bmatrix} 3 \\ -4 \\ 1 \end{bmatrix}$$

c) $P_e = \begin{bmatrix} 26.7252 \\ -36.0198 \\ 8.1359 \end{bmatrix}$ //

$$H = \begin{bmatrix} 10 & 0.99504 & 0.70535 \\ 0.99504 & 10 & 0.99504 \\ 0.70535 & 0.99504 & 10 \end{bmatrix}$$

17)

Each panel shows the potential that arises from the lumped monopolar sources and the potential that arises from the continous sources. Panels A, B, C are for distances h of 0.1, 1, 10 milimeters. All plots are for time $t = 10$ msec. When h is small, as in panel A, the approximation of the continous by lumped sources is poor, so lumping is striking. Conversely, as h increases to 1 milimeter, the potentials generated by lumped sources are smoother. At 10 milimeters, the lumped solution becomes similar to those from the continous sources, although distance h still is less than distance btw sources m_1, m_3.



23. Examine Figure 13.10. What is the corresponding plot of $\Phi_e(x)$ at a distance of 1 mm from the axis of this fiber? Assume the fiber parameters (though not the action potential) are those given in the prologue.

24. Examine Figure 13.11. Assume the peak of this fiber is at $x = -100$ mm at $t = 0$ ms.
a. Plot $\Phi_e(t)$ at $x = 0$ mm at a distance of 1 mm from the axis of the fiber.

b. Make a table that shows the magnitude and timing of every extrema (positive or negative peak) of the waveform plotted in part A.

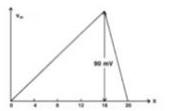


Figure 13.10. A monophasic action potential is approximated as triangular; the latter is described above. Along the horizontal axis, x is given in millimeters. The fiber extends well beyond the region shown and is cylindrical with a radius of 50 micrometers. The intracellular and extracellular resistivities are 90 and 30 Ω/cm, respectively. The action potential is propagating along the fiber with a velocity of 4 m/sec.

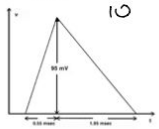
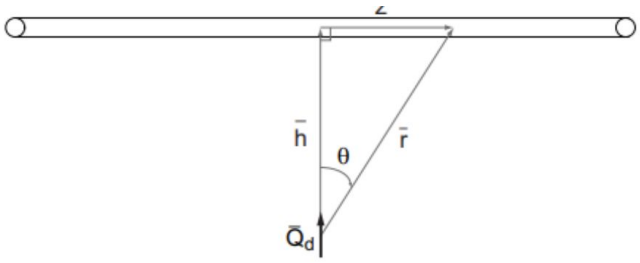


Figure 13.11. This propagating action potential is approximated with a triangular waveform, as shown. The axon on which it is propagating has a diameter of 10 μm. Propagation is in the $+x$ direction with a velocity of 5 m/sec. The extracellular conductivity $\sigma_e = 0.01$ S/cm, while the intracellular conductivity is $\sigma_i = 0.01$ S/cm. (The extracellular medium is unbounded.) Assume that the value $V_m(t)$ occurs at every position, albeit in time.

Q3) Consider the case of four extracellular stimulating electrodes that are well approximated by an idealized quadrupole source Qd that is pointing toward to a fiber, as depicted below.



The extracellular potential that is created by the idealized quadrupole source is:

$$\phi_e = \frac{Q_d}{4\pi\sigma_e}\left(\frac{3\cos^2(\theta)-1}{r^3}\right),$$

a) Find φe (z).

b) Find the activating function $\frac{\partial^2 \varphi_e}{\partial z^2}$

c) When this quadrupole source is turned on, is the membrane initially depolarized or hyperpolarized at position z = 0 ?

a) $r = \sqrt{h^2+z^2}$

$\cos\theta = h/r$

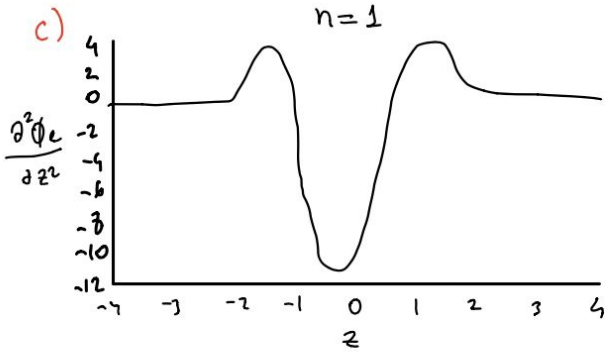
$$\phi_e = \frac{Q_d}{4\pi\sigma_e}\left(\frac{3\cos^2(\theta)-1}{r^3}\right) = \frac{Q_d}{4\pi\sigma_e}\left(\frac{3(h/r)^2-1}{r^3}\right) = \frac{Q_d}{4\pi\sigma_e}\left(\frac{3h^2-r^2}{r^5}\right) = \frac{Q_d}{4\pi\sigma_e}\left(\frac{3h^2-(h^2+z^2)}{(h^2+z^2)^{5/2}}\right)$$

$$= \frac{Q_d}{4\pi\sigma_e}\left(\frac{2h^2-z^2}{(h^2+z^2)^{5/2}}\right)$$

b) $$\frac{\partial \phi_e}{\partial z} = \frac{Q_d}{4\pi\sigma_e}\left(\frac{-2z}{(h^2+z^2)^{5/2}} + \frac{-5z(2h^2-z^2)}{(h^2+z^2)^{7/2}}\right) = \frac{Q_d}{4\pi\sigma_e}\left(\frac{3z(-4h^2+z^2)}{(h^2+z^2)^{7/2}}\right)$$

$$\frac{\partial^2 \phi_e}{\partial z^2} = \frac{Q_d}{4\pi\sigma_e}\left(\frac{3(-4h^2+z^2)}{(h^2+z^2)^{7/2}} + \frac{6z^2}{(h^2+z^2)^{7/2}} - \frac{21z^2(-4h^2+z^2)}{(h^2+z^2)^{9/2}}\right) = \frac{Q_d}{4\pi\sigma_e}\left(\frac{-3(4h^4-27z^2h^2+4z^4)}{(h^2+z^2)^{9/2}}\right)$$

c)



Evaluating activation function at $z=0$ gives:

$$\left.\frac{\partial^2 \phi_e}{\partial z^2}\right|_{z=0} = \frac{Q_d}{4\pi\sigma_e}\left[\frac{-3(4h^4-0+0)}{(h^2+0)^{9/2}}\right] = \frac{Q_d}{4\pi\sigma_e}\left[\frac{-12h^4}{h^9}\right] = \frac{-Q_d}{4\pi\sigma_e}\cdot\frac{12}{h^5}$$

Both h and Q_d are magnitudes, so the activating function is negative at $z=0$. Consequently, the membrane will initially hyperpolarize at $z=0$.

APPENDIX

1)

```
clear all
clc
close all
dt=0.01;
tf = 30000;
t=0:dt:tf;


gl=25;
gkk=1300;
gca = 280;
%gs1 = 20;
g = 13:20;
gs2=32;
Vl=-40;
Vk = -80;
Vca = 100;
Cm=4524;
taus1 = 1000;
taus2=120000;
Vrest = -43.4;
N=zeros(1,length(g))
Vm(1)=Vrest;
for i=1:length(g)
   gs1 = g(i);
   n(1)=0.03244;
   s1(1) = 0.64195;
   s2(1) = 0.43931;
   Vm(1)=Vrest;
   for j=1:length(t)
       minf(j) = 1/(1+exp((-22-Vm(j))/7.5));
       taun(j) = 8.3/(1+exp((9+Vm(j))/10));

       Ica(j)=gca*minf(j)*(Vm(j)-Vca);
       Ik(j)=gkk*n(j)*(Vm(j)-Vk);
       Is1(j)=gs1*s1(j)*(Vm(j)-Vk);
       Is2(j)=gs2*s2(j)*(Vm(j)-Vk);
       Il(j)=gl*(Vm(j)-Vl);
       dVm(j) = (dt/Cm)*(-Ica(j)-Ik(j)-Is1(j)-Is2(j)-Il(j));

       deln(j) = (dt/taun(j))*((1/(1+exp((-9-Vm(j))/10)))-n(j));
       dels1(j) = (dt/taus1)*((1/(1+exp((-40-Vm(j))/0.5)))-s1(j));
       dels2(j) = (dt/taus2)*((1/(1+exp((-42-Vm(j))/0.4)))-s2(j));
```

```
        Vm(j+1) = Vm(j) + dVm(j);
        n(j+1) = n(j) + deln(j);
        s1(j+1) = s1(j) + dels1(j);
        s2(j+1) = s2(j) + dels2(j);

    end
    %[N(i), out1] = spike_times(Vm,(Vrest+15));
    [pks,locs] = findpeaks(Vm, 'MinPeakDistance',5);
    N(i) = length(pks(pks > -25));
end


figure()
plot(g, N, 'r', 'Linewidth', 2)
title('Number of action potentials Versus gs1')
ylabel('Number of action potentials')
xlabel('gs1 (ps)')
%disp('Time interval from start of stimulus to the peak of subsequent action
potential length for stimulus current with amplitude 50:')
%disp(t(out1));
%disp(N);
t1=0:dt:tf+dt;



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

2-

1.

```
close all
clear all
clc

%constants
s1 = 2;
s2 = 0.5;
t= 10;
x = 0:0.5:50;
a  = 50;
b = -60;
t1 = 2;
t2 = 5;
x0 = 0;
```

```
teta = 4;

for i=1:length(x)

  Vm(i) = b + a * (tanh(s1 * ((t - t1) - (x(i) - x0)/teta)) - tanh(s2 * ((t - t2) - (x(i) - x0)/teta)));

end

figure()
plot(x,Vm,'r', 'Linewidth',2)
xlabel('Time(ms)')
ylabel('Vm (V)')
```

2.

```
close all
clear all
clc

%constants
t1 = 2;
t2 = 5;
x0 = 0;
teta = 4;
s1 = 2;
s2 = 0.5;
a  = 50;
b = -60;

t= 0:0.1:20;

x = 24;

for i=1:length(t)
    Vm(i) = b + a * (tanh(s1 * ((t(i) - t1) - (x - x0)/teta)) - tanh(s2 * ((t(i) - t2) - (x - x0)/teta)));

end

figure()
plot(t,Vm, 'r','LineWidth', 2)
title(['Vm at x = ' num2str(x)])
ylabel('Vm(mV)')
xlabel('Time(ms)')
```

4.

```
close all
clear all
clc

%constants
teta = 4;
s1 = 2;
s2 = 0.5;
a  = 50;
dt = 0.01;
t= 0:dt:20;
x = 24;
b = -60;
t1 = 2;
t2 = 5;
x0 = 0;
```

```
dVm(1) = 0;
for i=1:length(t)
   Vm(i) = b + a * (tanh(s1 * ((t(i) - t1) - (x - x0)/teta)) - tanh(s2 * ((t(i) - t2) - (x - x0)/teta)));

   if i ~= 1
      dVm(i) = (Vm(i) - Vm(i-1)) / dt;
   end

end

figure()
plot(t,dVm, 'r','LineWidth', 2)
title(['DeltaVm(t) at x = ' num2str(x)])
ylabel('DeltaVm(mV)')
xlabel('Time(ms)')


max_value = max(dVm)
```