MATLAB Implementation of Action Potential Propagation

Muhammed Saadeddin Koçak
Electrical & Electronics Enginnering Department
Middle East Technical University
Ankara,Turkey
e223234@metu.edu.tr

***Abstract*—Biological characteristics of excitable cell are quite complex and interesting. Understanding these characteristics is fundamental to study on cell structure and its properties. Therefore, it was always an important issue to interpret and simulate excitable cell behavior. Hodgkin Huxley core conductor model is an accurate and easy to understand model which gives insights about propagation behavior of excitable cell. In this documentation a simulation of Hodgkin Huxley core conductor model is presented. Main goal was to observe action potential propagation phenomena however, reader might use the simulation to explore other characteristics of cell membrane. Using the simulation, responses to different stimuli is observed and action potential properties and theory is verified. Such simulations of excitable cell may be used for research much earlier than clinical trials.**

Keywords—excitable cell, Hodgkin Huxley model, action potential propagation, stimuli, MATLAB, core-conductor model, cable equations,

I. Introduction

Quantitative modeling of excitable cell membrane has always been an interest of researchers. The main reason behind it is with quantitative modeling, characteristics of excitable cell could be better understood. Such interpretation allows researchers to develop better diagnosis, monitoring, and treatment tools. Therefore, Hodgkin Huxley model, which demonstrates the mathematical model of excitable cell membrane, remain as a precious tool is still being used.

Hodgkin Huxley model describe the membrane characteristics with some constants and equations which examined in second section. These formulas model a patch of cell membrane. However, to understand the propagation of electrical stimulus through cell membrane subthreshold and transthreshold models must have been developed rather than only a patch model. Core-conductor model is the remedy for propagation model. Being closely related with cable equations, core-conductor model treats membrane as very small patches of Hodgkin Huxley patch models. It is based on some assumptions, described in second section, that are very reasonable and appropriate with the real case.

In this paper, implementation of core-conductor model is described, supported with mathematical background. After implementation propagation of action potential is shown revealing some characteristics of cell membrane. Such implementation may allow reader to simulate propagation and analyze the results for his or her work.

II. Theory and Algorithm

In this section, mathematical equations and implementation process will be presented. Mathematical model is based on core-conductor model and all equations derived from the book Bioelectricity A Quantitative Approach. Required equation will be presented whenever necessary during description of algorithm.

Before moving onto algorithm, assumptions od core-conductor model must be discussed. According to core conductor model axial symmetry is assumed. Having a cylindrical cell and very small radius, calculations are generally made in only axial directions allowing us to have linear core-conductor model. Examining physiology of nerve and muscle cells, where action potential propagation is interesting, such assumption is quite valid. Secondly, it is assumed that external path carries axial current only allowing us to set extracellular resistivity to zero. By this way, external potential variation can easily be observed. Thirdly, internal conductive path is assumed to have only axial current flow appropriate with the small diameter of cell. And lastly, for subthreshold conditions membrane is simply modeled with only resistance and capacitance.

Fundamental approach while developing the algorithm was to use very small time and distance intervals which gives small mesh ratio. For each interval variables were calculated from previous interval. Finding each variable was quite straightforward since only mathematical description was to be coded.

1. Determining Membrane Current

Initialization of all variables is required before determining membrane current. This initialization also increases speed of code by memory allocation. I_s is initialized according to stimulus properties. To find membrane current equation (1) is used.

$$I_m^{i,j} = \frac{a}{2R_i}\frac{V_m^{i,j-1} - 2V_m^{i,j} + V_m^{i,j+1}}{\Delta x^2} \tag{1}$$

where a is axon radius, R_i is intracellular resistivity, $I_m^{i,j}$ is membrane current, and $V_m^{i,j}$ membrane voltage. Note that i is the time and j is the position parameters.

This step is the most complicated of all because of special cases that arise at boundaries. At the extreme ends the differentiation is not possible since there is no $V_m^{i,j-1}$ or $V_m^{i,j+1}$. In this implementation calculation of membrane current is avoided at the boundaries and it is assumed zero. In addition, impulse is applied from second position index rather than first.

Determining membrane current with position relations is quite critical since this step is the only one that relates one position with the next one.

2. Calculating Ionic Currents

According to Hodgkin Huxley Model to calculate ionic currents some constants must be found. Using the equations (2), (3), and (4) ionic currents are found.

$$\begin{aligned} I_K &= g_K(V_m - E_K) \\ I_{Na} &= g_{Na}(V_m - E_{Na}) \\ I_L &= g_L(V_m - E_L) \end{aligned} \tag{2}$$

where the conductivities are

$$\begin{aligned} g_K &= g_{K,max} n^4 \\ g_{Na} &= g_{Na,max} m^3 h \\ g_L &= g_{L,max} \end{aligned} \tag{3}$$

Here, initial values of n, m, and h are found using

$$\begin{aligned} n_0 &= a_n/(a_n + b_n) \\ m_0 &= a_m/(a_m + b_m) \\ h_0 &= a_h/(a_h + b_h) \end{aligned} \tag{4}$$

The values of a and b for all n, m, and h can be found in the book Bioelectricity A Quantitative Approach. It is crucial here to note that, all above values are calculated for time instant i for all j positions. The time instants correspond to small time intervals, 10 usec and position corresponds to small intervals of 100um for this implementation.

3. Estimating Mebrane Voltage Changes

Sensitive calculations are needed in this step since membrane voltage variations are highly dependent on ionic currents. Membrane voltage change can be discretized as in equation (5). Specifically, ΔV_m is calculated with equation (6).

$$\frac{dV_m}{dt} \approx \frac{\Delta V_m}{\Delta t} \tag{5}$$

$$\Delta V_m = \Delta t(I_m - I_K - I_{Na} - I_L)/C_m \tag{6}$$

4. Estimating Model Parameter Changes

In this step, changes in n, m, and h are calculated. These calculations are done using current values of a and b. For each cycle a and b values are recalculated using the equations from the book Bioelectricity A Quantitative Approach. While changes are calculating, similar estimation to (5) is utilized.

$$\begin{aligned} \Delta n &= \Delta t(a_n(1-n) - b_n n) \\ \Delta m &= \Delta t(a_m(1-m) - b_m m) \\ \Delta h &= \Delta t(a_h(1-h) - b_h h) \end{aligned} \tag{7}$$

It must be stressed that again these parameters are calculated for each time instant at each position. Otherwise, simulation of propagation is not possible.

5. Advancing Through Time

After calculating the changes, next step is to calculate new values for all variables. To do this, changes are added to previous values for $n, m, h,$ and V_m. Accordingly, new values for conductance's and ionic currents are recalculated.

III. Results

Here results to various stimulus amplitude and duration combinations are presented. Specifically, membrane voltage and model parameters are displayed. Response of cell membrane to consecutive impulses is observed. In addition, propagation of action potential through cell membrane is analyzed to find stimulus speed.

It is best to visualize the results with real-time plots since propagation is a dynamic process. However, since it is not possible to implement a dynamic plot to this paper position of impulse at various times and impulse pattern in various positions along the fiber is displayed.

In Fig. 1 it can be seen that at 0.2 cm action potential appears the first and at 0.8 cm action potential appears last. The reason is the propagation is not instant and takes time. Another aspect can be seen in Fig. 2, at 30 msec action potential has not yet reached to 0.4 cm of fiber. These figures confirm each other and present propagation of action potential.

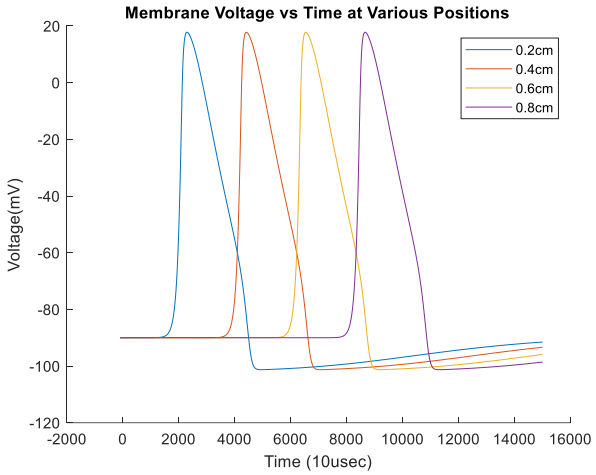

Figure 1: Membrane voltage vs time at various positions for one stimulus with amplitude 500 uA/cm^2 and duration 200 usec

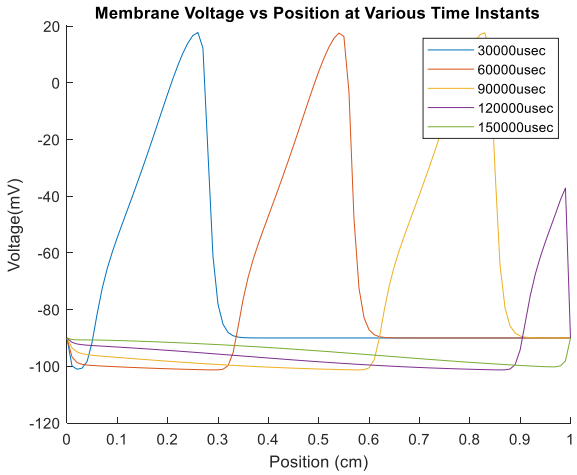

Figure 2: Membrane voltage vs position at various time instants for one stimulus with amplitude 500 uA/cm^2 and duration 200 usec

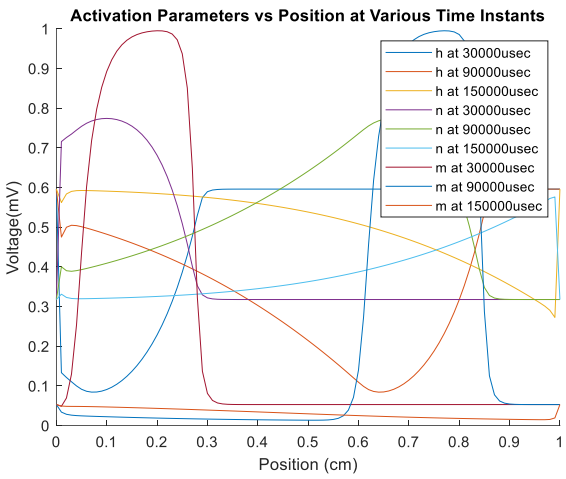

Figure 3: Activation parameters vs position at various time instants for one stimulus with amplitude 500 uA/cm^2 and duration 200 usec

Fig. 3 is rather complicated but explanatory when a researcher familiar with Hodgkin Huxley model examines. Activation parameters closely related with ionic mechanics of membrane gives intuition about action potentials. Properties of action potential such as refractory period can be interpreted by examining activation parameters. For better understanding two consecutive impulses with various delays in between can be observed.

When two stimuli applied consecutively with proper interval in between two action potentials may be observed. Looking at Fig. 4 and 5 it is clear that two action potentials were successfully generated and propagated through fiber. In Fig. 5 from yellow line, it can be interpreted that second stimulus was fired around 80 msec. Green line may be deceptive but at 150 msec first stimulus is out of picture because of stimulated part of fiber is limited.

Furthermore, speed analyses can be easily done from Fig. 5. One can find the distance between two peaks of first action potential and divide it to time difference. Doing so speed is found to be 9.33 cm/sec.

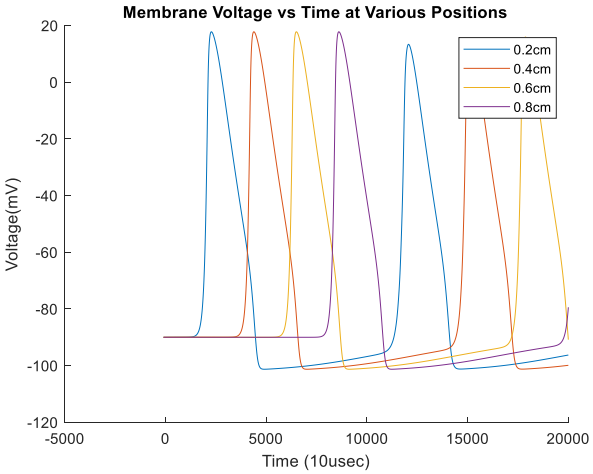

Figure 4: Membrane voltage vs time at various positions for two stimuli with amplitude 500 uA/cm^2, duration 200 usec and 80 msec delay

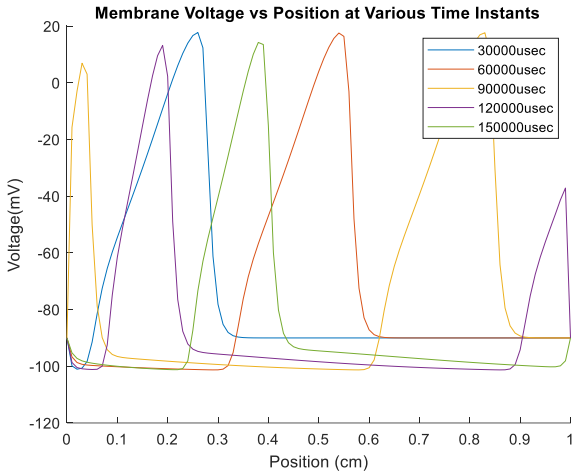

Figure 5: Membrane voltage vs position at various time instants for two stimuli with amplitude 500 uA/cm^2, duration 200 usec and 80 msec delay

Another interesting observation may be done by examining Fig. 6. Again, looking too complex for untrained eyes, for a specialist, activation parameters explain the morphological variance of second stimulus. m follows a pattern parallel to membrane voltage, but spatial relaxation of n and h takes much longer. Therefore, when simulation is done with high precision morphological changes and reasons behind can be deeply understood.

In Fig. 7 membrane voltage vs time characteristics of a fiber with a radius ten times bigger than that in Fig.1 to 6. With increasing radius propagation speed is expected to increase[1]. On the other hand, higher stimulus amplitude is needed probably due to the size. When speed is calculated it is found to be 56.73 cm/sec.

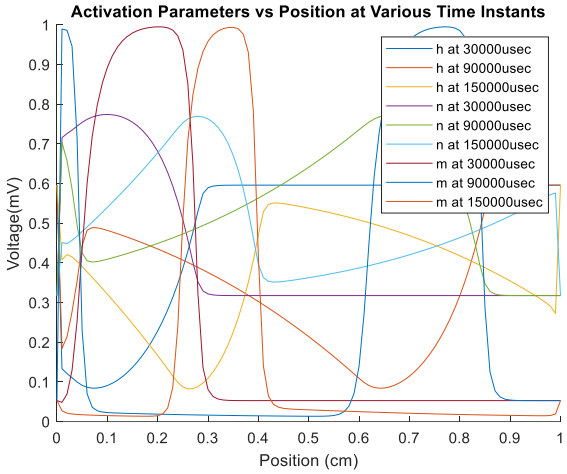

Figure 6: Activation parameters vs position at various time instants for two stimuli with amplitude 500 uA/cm^2, duration 200 usec and 80 msec delay

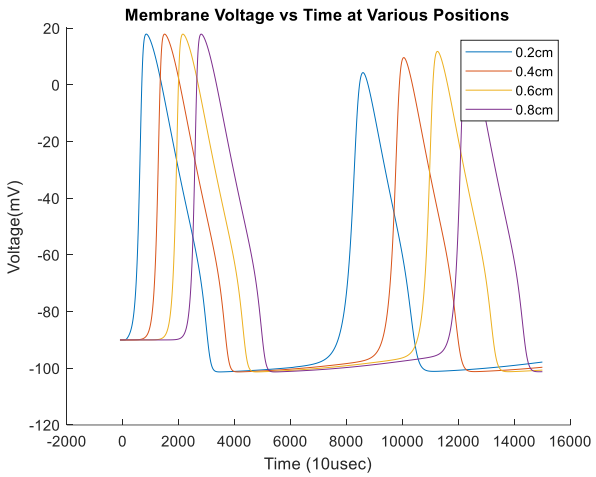

Figure 7: Membrane voltage vs time at various positions for two stimuli with amplitude 5000 uA/cm^2, duration 200 usec and 80 msec delay for increased radius

IV. Discussion and Conclusion

Quantitative modeling of excitable cell reveals some of the most important characteristics of action potential propagation. While single cell simulations yield results for only one cell, because of the interaction between neighbor cells such results give broader perspective. Consequently, one may be able to derive wide range of results both in microscopic and macroscopic scale. In this section, reaction of the cell membrane to various stimuli will be discussed.

Firstly, basis of action potential propagation relies on equation (1), because only this equation relates spatial distribution. Stimulation of a membrane at one end triggers whole membrane by stimulating the action potential just next to the stimulation point and so on. Here, of course, action potential generation requirements such as correct polarization, amplitude, and duration still holds. Unless these requirements are satisfied even small disturbances are suppressed and action potential is not created so propagated. Although requirements are not met, incorrect simulation intervals may cause mesh ratio to have a value higher than 1 and in this case results diverge reflecting incorrect membrane behavior[1].

Examining Fig. 1 to 3 a correct action potential propagation with satisfactory impulse characteristics is seen. There several ways of showing the result and both methods used in this paper allow reader to analyze desired characteristic. In addition, code provided in Appendix display real-time propagation dynamically.

Fig. 3 to 6 shows results of two stimuli with correct delay. When delay time is smaller, second response is not observed due to refractory period. In this period, membrane is insensitive to any stimulus. The reason of applying two proper stimulus is to easily observe speed of propagation. By correct analysis done in third section speed values were found. Here an interesting point is the value of speed, 9.33 cm/sec is not typical in human structure. Indeed, the values used belong to squid axon. In human conduction velocities range from 0.5 m/sec to 100 m/sec. Such variance is due to various radius and existence of myelination. The speed, 9.33 cm/sec, would probably be unacceptable for human and cause illness but it may be satisfactory for squid. Small and relatively less evolved structure of squid may be the reason of such slow speeds.

In Fig. 7 radius is increased theoretically to observe speed characteristics. In this case, stimulus current amplitude must also be increased probably due to bigger size. As can be seen, speed is significantly increased to 56.73 cm/sec.

One important point during implementation is efficiency of algorithm. In this work, optimization was partially done with memory allocation and such, but further improvement of code may allow better temporal and spatial resolution. Though, while changing delta values mesh ratio must always be considered.

To sum it all up, remarkable mathematical model of excitable cell from Hodgkin and Huxley reveals important properties of action potential propagation. Mathematical implementation is quite straightforward, and results are very much relatable with behavior of cell in microscopic scale and behavior of living in macroscopic scale. Simulation of cell membrane may provide accessibility to research even in early stages of work.

References

[1] R. Plonsey and R. C. Barr, Bioelectricity: a quantitative approach. New York, NY: Springer, 2014.K. K. Shung, M. Smith, and B. M. W. Tsui, *Principles of Medical Imaging*. Burlington: Elsevier Science, 2012.

APPENDIX

SIMULATION CODE

```
%% Muhammed Saadeddin Koçak
%% Clear
clear
%% Initialization
%Remember to update variables according to project description
%Need further variable definitions
a=0.03;%axon radius,cm
Ri=94;%intracellular resistivity,ohmcm
ri=Ri/(pi*a^2);%intracellular resistance per unit length,ohm/cm
Re=20;%extracellular resistivity,ohmcm
re=Re/(pi*a^2);%extracellular resistance per unit length,ohm/cm
Cm=1;%uF/cm^2
EK=-102;%mV
ENa=25;%mV
EL=-79.387;%mV
gKmax=36;%mS/cm^2
gNamax=120;%mS/cm^2
gLmax=0.3;%mS/cm^2
t=linspace(-99,15000,15100);%usec
l=linspace(0,1,101);%cm
n=zeros(length(t),length(l));
m=zeros(length(t),length(l));
h=zeros(length(t),length(l));
an=zeros(length(t),length(l));
bn=zeros(length(t),length(l));
am=zeros(length(t),length(l));
bm=zeros(length(t),length(l));
ah=zeros(length(t),length(l));
bh=zeros(length(t),length(l));
Vm=zeros(length(t),length(l));
gK=zeros(length(t),length(l));
gNa=zeros(length(t),length(l));
Is=zeros(length(t),length(l));
% gK(:,1)=gKmax*(n(:,1).^4);
% gNa(:,1)=gNamax*(m(:,1).^3).*(h(:,1));
%
Vr=(EL*gLmax+EK*gNa(1,1)+EK*gK(1,1))/(gLmax+gNa(1,1)+gK(1,1));%S
ee pg. 176
Vr=-90;%mV
Vm(1:100,:)=Vr;%mV
vm=zeros(length(t),length(l));
Im=zeros(length(t),length(l));
impulseduration=200;%usec
numberofconsecutivestimuli=1;
timedelaybetweenstimuli=8000;%usec
impulseamplitude=500;%uA/cm^2
```

```
%% Loops
figure;
for i=100:length(t)
    for j=1:length(l)
            if t(i)>-1 && t(i)<=impulseduration
                Is(i,2)=impulseamplitude;%uA/cm^2
            else
                Is(i,2)=0;
            end
            %For the second stimuli
            if numberofconsecutivestimuli~=1
            if t(i)>timedelaybetweenstimuli &&
t(i)<=timedelaybetweenstimuli+impulseduration
                Is(i,2)=impulseamplitude;%uA/cm^2
            end
            end
%          Im(i,j)=(((Vm(i,j-1)-2*Vm(i,j)+Vm(i,j+1))-
re*Is(i,j))/(2*pi*a*(ri+re)))+Is(i,j);%According
        %to book description
        if j~=1 && j~=length(l)
        Im(i,j)=((Vm(i,j-1)-
2*Vm(i,j)+Vm(i,j+1))*a/((2*Ri)*(0.01^2)))+Is(i,j);
        end
        %Calculating ionic currents
        an(i,j)=((0.01*(10-vm(i,j)))/(exp((10-vm(i,j))/10)-
1))/1000;%1/usec
        bn(i,j)=(0.125*exp((-vm(i,j))/80))/1000;%1/usec
        am(i,j)=((0.1*(25-vm(i,j)))/(exp(0.1*(25-vm(i,j)))-
1))/1000;%1/usec
        bm(i,j)=(4*exp((-vm(i,j))/18))/1000;%1/usec
        ah(i,j)=(0.07*exp((-vm(i,j))/20))/1000;%1/usec
        bh(i,j)=(1/(exp((30-vm(i,j))/10)+1))/1000;%1/usec
        n(100,j)=an(100,j)/(an(100,j)+bn(100,j));
        m(100,j)=am(100,j)/(am(100,j)+bm(100,j));
        h(100,j)=ah(100,j)/(ah(100,j)+bh(100,j));
        gK(i,j)=gKmax*(n(i,j).^4);%mS/cm^2
        gNa(i,j)=gNamax*(m(i,j).^3)*h(i,j);%mS/cm^2
        IK(i,j)=gK(i,j)*(Vm(i,j)-EK);%uA/cm^2
        INa(i,j)=gNa(i,j)*(Vm(i,j)-ENa);%uA/cm^2
        IL(i,j)=gLmax*(Vm(i,j)-EL);%uA/cm^2
        deltan(i,j)=(an(i,j)*(1-n(i,j)))-(bn(i,j)*n(i,j));
        deltam(i,j)=(am(i,j)*(1-m(i,j)))-(bm(i,j)*m(i,j));
        deltah(i,j)=(ah(i,j)*(1-h(i,j)))-(bh(i,j)*h(i,j));
        deltaVm(i,j)=(Im(i,j)-IK(i,j)-INa(i,j)-
IL(i,j))*10/(Cm*1000);%mV
        n(i+1,j)=n(i,j)+deltan(i,j);
        m(i+1,j)=m(i,j)+deltam(i,j);
        h(i+1,j)=h(i,j)+deltah(i,j);
```

```
        Vm(i+1,j)=Vm(i,j)+deltaVm(i,j);
        vm(i+1,j)=vm(i,j)+deltaVm(i,j);
    end
    plot(l,Vm(i,1:length(l)));
    title('Position vs Membrane Voltage');
    xlabel('Position (cm)');
    ylabel('Voltage(mV)');
    drawnow;
end
%% Results
% plot(t,Vm(1:length(t),21));
% title('Membrane Voltage vs Time at 0.2cm');
% xlabel('Time (usec)');
% ylabel('Voltage(mV)');
figure
hold on
plot(t,Vm(1:length(t),21));
plot(t,Vm(1:length(t),41));
plot(t,Vm(1:length(t),61));
plot(t,Vm(1:length(t),81));
legend({'0.2cm','0.4cm','0.6cm','0.8cm'});
title('Membrane Voltage vs Time at Various Positions');
xlabel('Time (10usec)');
ylabel('Voltage(mV)');
hold off


% figure
% plot(l,Vm(1000,1:length(l)));
% title('Position vs Membrane Voltage at t=10000us');
% xlabel('Position (cm)');
% ylabel('Voltage(mV)');
figure
hold on
plot(l,Vm(3000,1:length(l)));
plot(l,Vm(6000,1:length(l)));
plot(l,Vm(9000,1:length(l)));
plot(l,Vm(12000,1:length(l)));
plot(l,Vm(15000,1:length(l)));
legend({'30000usec','60000usec','90000usec','120000usec','150000
usec'});
title('Membrane Voltage vs Position at Various Time Instants');
xlabel('Position (cm)');
ylabel('Voltage(mV)');
hold off

figure
hold on
```

```
plot(l,h(3000,1:length(l)));
plot(l,h(9000,1:length(l)));
plot(l,h(15000,1:length(l)));
plot(l,n(3000,1:length(l)));
plot(l,n(9000,1:length(l)));
plot(l,n(15000,1:length(l)));
plot(l,m(3000,1:length(l)));
plot(l,m(9000,1:length(l)));
plot(l,m(15000,1:length(l)));

legend({'h at 30000usec','h at 90000usec','h at 150000usec','n
at 30000usec','n at 90000usec','n at 150000usec','m at
30000usec','m at 90000usec','m at 150000usec'});
title('Activation Parameters vs Position at Various Time
Instants');
xlabel('Position (cm)');
ylabel('Voltage(mV)');
hold off
```