MATLAB Implementation of Multiple Activation Wavefront Propagation

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

***Abstract*—Understanding the electrical behavior of action potential propagation is essential to give a meaning to electrical signals measured from the surface of the body. Hodgkin Huxley model explains the action potential propagation in microscopic scale by revealing mechanisms underlying such as ionic currents. However, Hodgkin Huxley model is unable to explain electrical significance and electrical fields arising from action potential propagation. Electromagnetic field solutions are required for such explanation. These field solutions strongly depend on the structure of conductive medium and are not easy to solve. At this point, numerical methods provide quite accurate solutions with proper approximation and assumptions. Double layer source assumption, for instance, sets a basis for developed electrocardiography methods. In this documentation a MATLAB simulation of multiple activation wavefront propagation is presented with theoretical background. Furthermore, relations between electrocardiography and developed model are discussed.**

Keywords—Hodgkin Huxley model, action potential propagation, stimuli, MATLAB, double layer, dipole, wavefront, depolarization, repolarization,

I. Introduction

Electrical measurements from body have been a great interest of biophysicists and physicians. Hodgkin and Huxley are pioneers of such measurements with their voltage-clamp technique. They achieved measurements in a squid axon and with their special technique, explained the behavior of cell membrane voltage variations. They developed a proper cell membrane model thanks to their experiments which reveal underlying mechanisms of action potential. Furthermore, their model explained the propagation behavior with core-conductor model. When it comes to measurements from body with electrodes, either inside or on the surface, some electromagnetic equations are required to be solved.

Human body acts as volume conductor and has complex characteristics in terms of conducting action potentials. With proper assumptions which will be explained in upcoming section, simplified models may provide expected measurements. At this point it is important to differentiate forward and inverse problems. In forward problem it is assumed that researcher has all or almost all information about electrical source within the body. The aim of this problem to guess the measurement values from various sights of the body. On the other hand, in the reverse problem measurements are available and the aim is to figure out the sources and their behavior. Electrocardiography measurements, for example, reveal information about the source which is the heart. Since normal behavior of heart is known by physicians, abnormalities can be detected this way.

The double layer model which was developed mainly by Helmholtz models the electrical behavior of action potential in time[1]. In this model, first single cell is modeled as long thin fiber with narrow action potential wavefront. Then this model is extended to a uniform fiber bundle. An observation point located in some distance see this wavefront as a disk moving in the axial direction. Using solid angle, the potential to be measured from observation point is estimated.

In this paper, implementation of multiple activation wavefront propagation is demonstrated. The development of model and its mathematical background is described in detail. Moreover, after verifying the model, heart in torso is simulated and various measurement are taken from various electrode locations. The correlation of these measurements with electrocardiography signals are discussed. Such implementation may allow reader to simulate multiple activation wavefront propagation and analyze results for his or her own work.

II. Theory and Algorithm

In this section, model development and implementation process will be presented. Mathematical model is based on double layer source model. Required equation will be presented whenever necessary during description of algorithm.

Development of the algorithm is quite straightforward when development of model is interpreted. Electrical behavior of action potential is modelled by following step by step approach. Starting from the concept of double dipole layer, action potential propagation is modelled as a sequence of point dipoles along the source fiber. Then this model is extended to a cylindrical geometry which somehow represents heart and torso.

Fundamental approach while developing the algorithm was to implement integral equation as formula so that MATLAB calculates accurate results. Discrete formulation is tested during development and gave close results however, in the case of real human body structures discrete formulation will cause slight errors. Here is the development of model.

1. Defining the Concept of Double Dipole Layer

Helmholtz stated that potential outside a uniform double layer can be calculated using solid angle, Ω. In the case of fiber cells in human body, dipole moments can be treated as membrane voltage difference. It is important to note here that fields of positive and negative charges cancel each other because solid angle has same value but opposite sign during the calculation. Simply, it can be said that a uniformly polarized double layer surface has zero potential outside if it is closed.

2. Extending the Concept to Membrane of Excitable Cells

After the Helmholtz's development of double layer concept Wilson et al. verified that this model can be used for cell membrane since it has potential difference represented by

negative and positive charge layer inside and outside of membrane. Furthermore, this potential difference is indeed the action potential generated by the cell[1].

In the following steps cell fiber has given a shape of cylinder. Actually, this shape is quite appropriate since both muscle cells and nerve cells, main focus of stimulation observation, has such structure.

3. *Modeling Fiber Membrane as Polarized Disks*

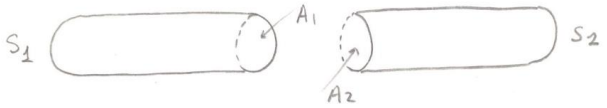

Figure 1: Double Dipole Layer Sources Separation

In the case of uniform and intact fiber potential outside is calculated as zero because of cancellations. To model activation wavefront, it is required to separate the intact fiber into two cylindrical structures and treat the disk which is shown in Fig. 1 as A1 as propagating wavefront. Note that, potential developed by these two structures is still zero outside.

4. *Modeling the Transmembrane Voltage as Double Layer Disks*

Taking separated cylinders as depolarized and resting parts of cell activation wavefront may be represented as discontinuity at the disk position. Here a crucial assumption is being made. The wavefront is not an instant occurrence. It has a time observed in Hodgkin Huxley model. However, when activation duration is compared with propagation velocity and duration, activation wavefront can be assumed as a discontinuity. This way calculation of solid angle simply gives potential created at the observation point due to propagation of activation wavefronts. A more detailed analysis can be done by not assuming wavefront as discontinuity but rather giving a thickness to double layer. This thickness could have characteristics of action potential developed by Hodgkin Huxley model and more realistic measurements can be stimulated. For the sake of simplicity, such detailed modeling is avoided in developed simulation.

The strength of double layer is estimated as summation of resting membrane potential and depolarized membrane potential. Disk is assumed to have uniform dipole layer all over.

5. *Equating Polarized Disk to a Point Dipole*

Potential developed in observation point P is given by equation (1).

$$\varphi(P) = \frac{-\sigma_i}{4\pi\sigma_o}\int_A (V_d + V_r)\frac{a_r.dS}{R^2} \tag{1}$$

In equation (1) σ values represent conductivities, V values represent depolarized and resting voltages, R represent the distance between integration point with observation point, and A is the disk area.

Since

$$a_r.dS = cos\emptyset \tag{2}$$

where $\emptyset$ is the angle between disk surface normal and observation point to integration point, equation (1) takes the form

$$\varphi(P) = \frac{-\sigma_i}{4\pi\sigma_o}\iint_{r,\theta} (V_d + V_r)\frac{cos\emptyset}{R^2} \tag{3}$$

In developed implementation equation (3) is used for calculation of potential fields. integral2 functions is used and this calculation is costly in terms of processing however provide superior results in realistic body structures. On the other hand, if equation is further simplified by assuming very small cross-sectional area of fiber and neglecting integration equation (4) can be obtained.

$$\varphi(P) = \frac{-\sigma_i}{4\pi\sigma_o}A(V_d + V_r)\frac{cos\emptyset}{R^2} \tag{4}$$

6. *Modelling the Action Potential as Sequence of Point Dipoles Distributed along its Spatial Profile*

Proceeding through time, according to the aim of implementation, double layer disk is moved along the z axis. The movement is coordinated by the propagation velocity. Following the activation wavefront propagation, deactivation wavefront follows. By deactivation it is meant the repolarization phase. Because of these phases, at the end a triphasic structure is expected as shown in Fig. 2.

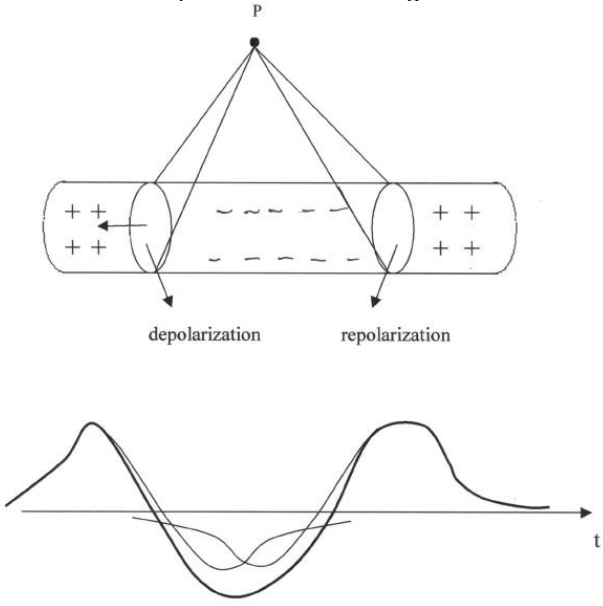

Figure 2: Triphasic Wavefronts

III. Results

First, to confidently use developed model in various body structures it should be verified that correct potentials are being calculated. To achieve this, by taking very long source size it is tried to get the wavefront shown in Fig. 3. In Fig. 4, it can be seen that similar waveform is observed with developed algorithm. To mimic the infinite length fiber, source length is taken 5 m where observation point is in the

middle. Also, distance to source radially is only 30 cm, appropriate with assumptions. Wavefront propagation speed is chosen to be 50 cm/sec according to typical value[2]. It must be stressed that algorithm does not use equation (4), it uses equation (3) for exact integral calculation.

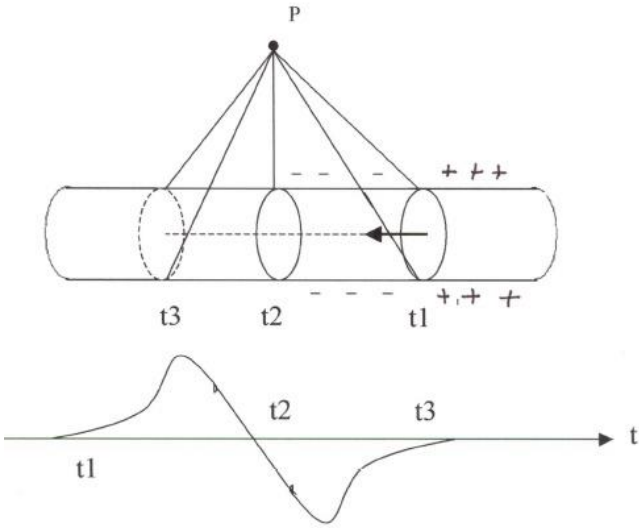

Figure 3: Waveform of Single Activation Wavefront

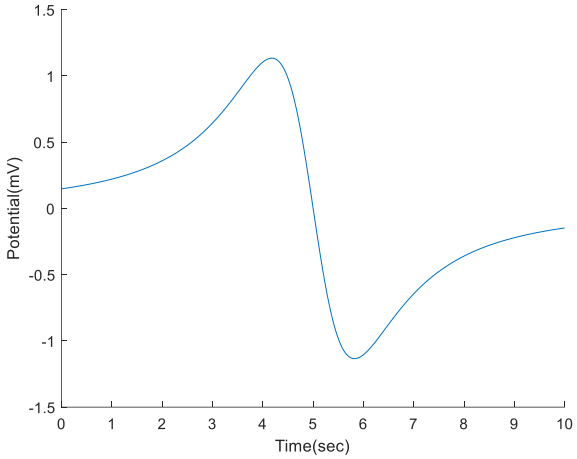

Figure 4: Waveform of Single Activation Wavefront of 5 m Source Observed from 2.5 m

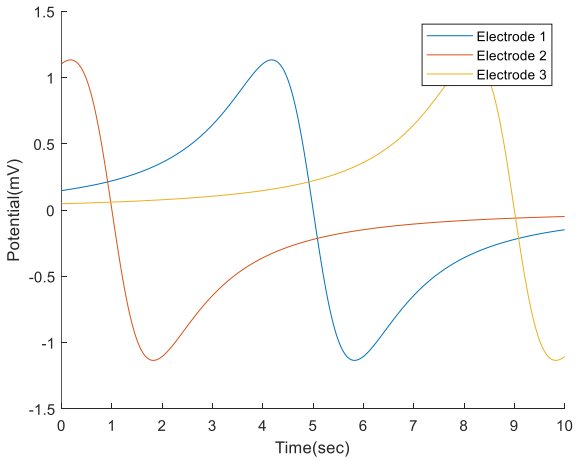

Figure 5: Waveform of Single Activation Wavefront of 5 m Source Observed from 2.5, 0.5, 4.5 m

Fig. 5 shows multiple electrode potentials, and it can be understood form this figure that the wavefront is moving along z axis through right.

Second, model should be verified in case of multiple activation wavefront propagation. To achieve this a depolarizing wavefront is followed by a repolarizing wavefront. Comparing with Fig. 2, Fig. 6 shows triphasic multiple wavefront propagation. To understand the characteristic of waveform in Fig.6, Fig. 7 shows underlying depolarizing and repolarizing wavefronts separately.

In Fig. 8 bipolar measurements are shown when electrodes are located on the same theta and r value, but z is 2.5, 0.5, 4.5 respectively.

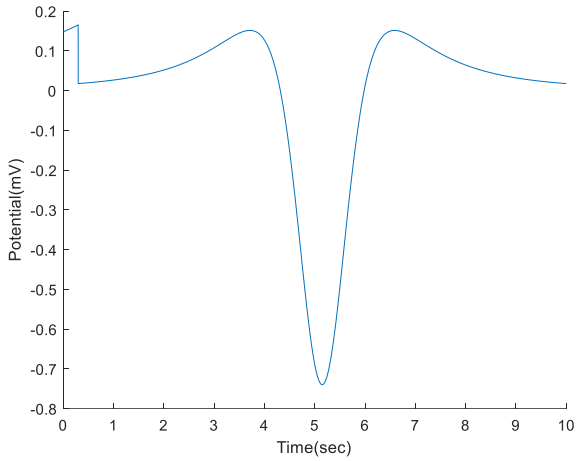

Figure 6: Waveform of Multiple Activation Wavefront of 5 m Source Observed from 2.5 m

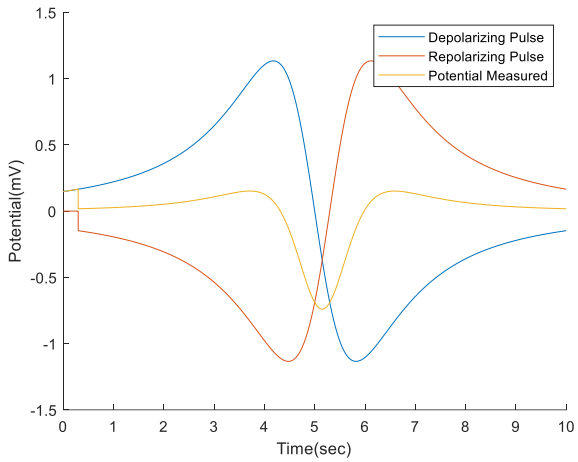

Figure 7: Depolarizing and Repolarizing Waveforms of Multiple Activation Wavefront of 5 m Source Observed from 2.5 m

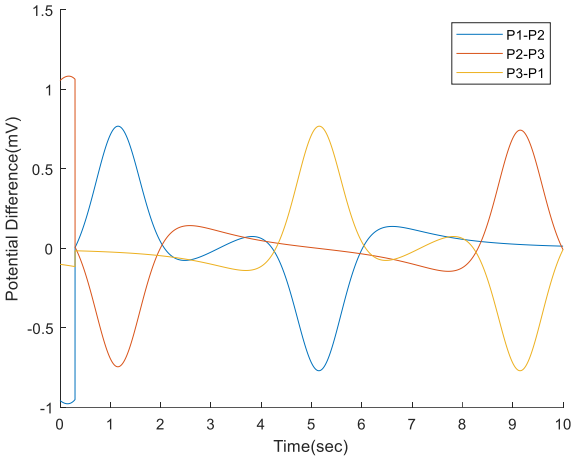

Figure 8: Bipolar Measurements of Multiple Activation Wavefront of 5 m Source Observed from 2.5 m

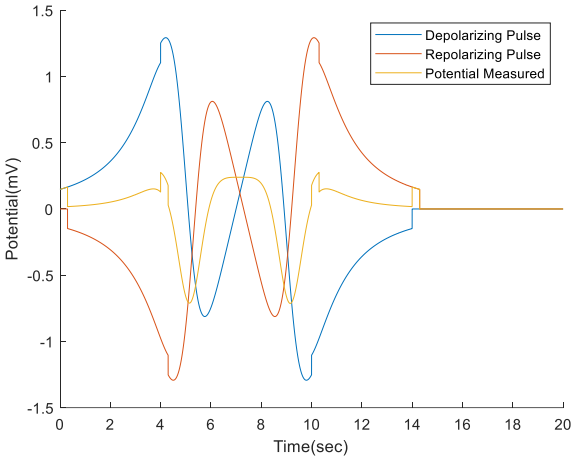

Figure 9: Two Consecutive Depolarizing and Repolarizing Waveforms of Multiple Activation Wavefront of 5 m Source Observed from 2.5 m with 4 sec Delay

In Fig. 9 two consecutive multiple activation wavefront propagation can be observed. To clarify, this is two action potential pulses following each other.

To be able to compare what the time between wavefronts change, Fig. 10 is given in addition to Fig. 7. Moreover, Fig. 11 and Fig. 12 shows measurements when heart is simulated as short source and torso is simulated as cylinder with 0.3 m radius.

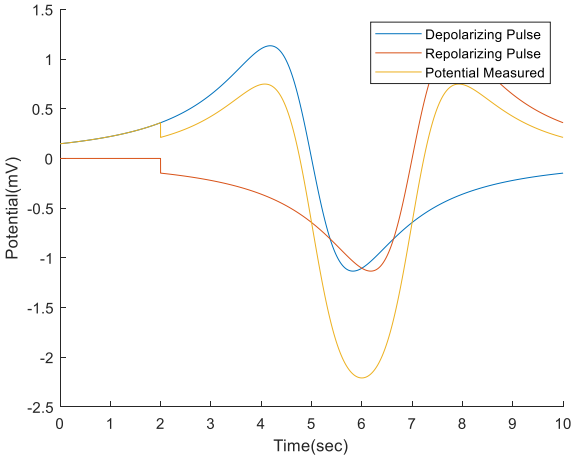

Figure 10: Depolarizing and Repolarizing Waveforms of Multiple Activation Wavefront of 5 m Source Observed from 2.5 m with Increased Delay

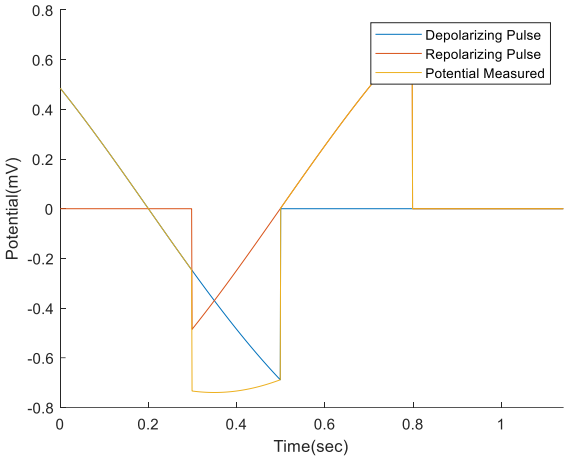

Figure 11: Depolarizing and Repolarizing Waveforms of Multiple Activation Wavefront of 0.25 m Source Observed from 0.5 m

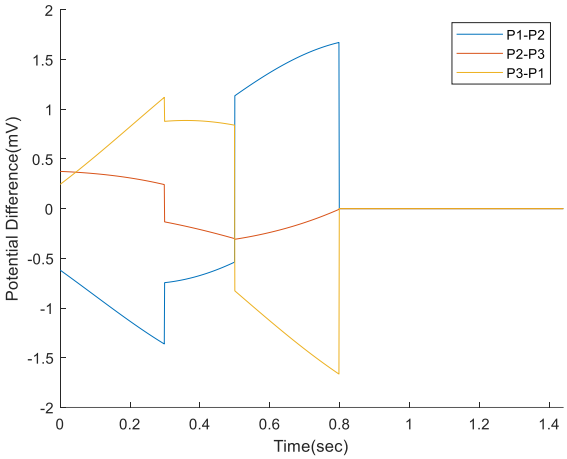

Figure 12: Bipolar Measurements of Waveforms of Multiple Activation Wavefront of 0.25 m Source Observed from 0.5 m

IV. Discussion and Conclusion

Quantitative modeling of multiple activation wavefront propagation is fundamental for electrical behavior analysis. By modeling, both forward and inverse problems are easier to solve. Using the solutions, researchers are able to develop a better understanding of electrical sources in the body. In addition, electrophysiology of various organs like heart is discovered with great detail such that with basic electrocardiography measurements, physicians can diagnose abnormalities.

The model implemented in this study can be examined as follows. Comparing Fig. 3 and Fig. 4, in developed model waveform does not converge to zero at the extremities. This is due to limited source length which is 5 m. As 5 m source length goes to infinity and observation point radius goes to zero, Fig 4 becomes more like ideal case. Similarly, the jumps seen in Fig. 6 and Fig. 7 are all due to limited source length because in these figures repolarizing wave is not initiated at the time zero but at the time 300 msec. The choice of 300 msec is appropriate to refractory period of heart muscle cell.

Looking at Fig. 5 it can be understood that potential measurements depend on location of electrodes, naturally. Fig. 6 is better understood with the help of Fig. 7 since components of measured potential are shown. Repolarization wave is exact opposite of depolarizing wave with a time shift.

This time shift is the activated duration of membrane and as it increases, as can be seen from Fig.10, width of potential minima is increased.

In the case of real-life measurements like electroneurogram, either unipolar or bipolar measurements are used. In Fig. 8 bipolar measurements are shown. It may be possible to utilize these measurements for analysis also.

In Fig. 9 two consecutive action potentials are simulated. As can be seen, second waveform is affected by first one despite having long time difference in between. This is quite natural and troubling at the same time because during real measurements, a single action potential is not present at the source. Rather, multiple action potentials are present and potential measured is affected by all of them. The measurement mostly shows the closest action potential, but the reading is generally multiphasic. This situation presents a great challenge for understanding measurements and signal processing tools are being used. For example, in electrocardiography signal, AV node stimulation, SA node stimulation, Purkinje Fiber stimulation, and many others are added resulting in traditional ECG signal.

Fig. 11 and Fig. 12 shows measurements when source is relatively short. General shape may be obtained from these figures but since approximations and assumption are not as valid as before, measurements are quite discretized. Perhaps, such readings can provide some information however, they are not as useful as previous ones.

In an advanced point of view, using the same approach for modeling, which is described in this paper, further problems like defibrillation problem can be solved. Moreover, if source characteristics can be measured at the same time with internal electrodes, volume conductor characteristics of body can be analyzed and used for detection of anomalies.

REFERENCES

[1] J. Rodriguez-Falces, "Understanding the electrical behavior of the action potential in terms of elementary electrical sources", Advances in Physiology Education, vol. 39, no. 1, pp. 15-26, 2015. Available: 10.1152/advan.00130.2014 [Accessed 17 January 2021].

[2] J. Malmivuo and R. Plonsey, Bioelectromagnetism. New York: Oxford University Press, 1995.

APPENDIX

SIMULATION CODE

```
%Muhammed Saadeddin Koçak 2232346
%% Clarification
clear
clc
close all
%% Parameter Definitions
propagationvelocity=0.5;%m/sec
startingpointofactivation=0;%starting point of activation shifted from the zsource
in z direction
timebetweendepolarisationandrepolarisationwavefronts=0.3;%sec
strength=100;%mV
numberofsuccessivewavefronts=1;
timedelay=6;%sec
sigmai=0.4;
sigmao=1;
t=linspace(0,10,10001);%sec
sourcelength=5;%m
%% Locating Electrodes
E=[2.5 0.3 0.5;0.5 0.3 0.5;4.5 0.3 0.5];%z,r,theta
zsource=0;%m, z coordinate of initial point of source
d=zsource+startingpointofactivation;%location of depolarizing wave
r=zsource+startingpointofactivation;%location of repolarizing wave
%% Calculating Potentials
PD=zeros(length(t),3);
for i=1:length(t)
    for j=1:length(E)
        if d>=zsource+sourcelength
            PD(i,j)=0;
        else
            fun=@(x,y) 1./((sqrt((E(j,1)-d).^2+(E(j,2)-x).^2+(E(j,3)-y).^2)).^3);
            polarfun=@(theta,r) fun(r.*cos(theta),r.*sin(theta));
            q=integral2(polarfun,0,2*pi,0,0.05);
            PD(i,j)=q*sigmai*strength*(E(j,1)-d)/(4*pi*sigmao);
        end
    end
    d=d+propagationvelocity*0.001;
end
PR=zeros(length(t),3);
for i=timebetweendepolarisationandrepolarisationwavefronts*1000:length(t)
    for j=1:length(E)
        if r>=zsource+sourcelength
            PR(i,j)=0;
        else
            fun=@(x,y) 1./((sqrt((E(j,1)-r).^2+(E(j,2)-x).^2+(E(j,3)-y).^2)).^3);
            polarfun=@(theta,r) fun(r.*cos(theta),r.*sin(theta));
            q=integral2(polarfun,0,2*pi,0,0.05);
            PR(i,j)=-q*sigmai*strength*(E(j,1)-r)/(4*pi*sigmao);
        end
    end
    r=r+propagationvelocity*0.001;
end
if numberofsuccessivewavefronts==2
    d=zsource+startingpointofactivation;%location of depolarizing wave
    r=zsource+startingpointofactivation;%location of repolarizing wave
    PD2=zeros(length(t),3);
    for i=timedelay*1000:length(t)
        for j=1:length(E)
            if d>=zsource+sourcelength
                PD2(i,j)=0;
            else
```

```
                fun=@(x,y) 1./((sqrt((E(j,1)-d).^2+(E(j,2)-x).^2+(E(j,3)-
y).^2)).^3);
                polarfun=@(theta,r) fun(r.*cos(theta),r.*sin(theta));
                q=integral2(polarfun,0,2*pi,0,0.05);
                PD2(i,j)=q*sigmai*strength*(E(j,1)-d)/(4*pi*sigmao);
            end
        end
        d=d+propagationvelocity*0.001;
    end
    PD=PD+PD2;
    PR2=zeros(length(t),3);
    for
i=(timebetweendepolarisationandrepolarisationwavefronts+timedelay)*1000:length(t)
        for j=1:length(E)
            if r>=zsource+sourcelength
                PR2(i,j)=0;
            else
                fun=@(x,y) 1./((sqrt((E(j,1)-r).^2+(E(j,2)-x).^2+(E(j,3)-
y).^2)).^3);
                polarfun=@(theta,r) fun(r.*cos(theta),r.*sin(theta));
                q=integral2(polarfun,0,2*pi,0,0.05);
                PR2(i,j)=-q*sigmai*strength*(E(j,1)-r)/(4*pi*sigmao);
            end
        end
        r=r+propagationvelocity*0.001;
    end
    PR=PR+PR2;
end
P=PD+PR;
V1=P(:,1)-P(:,2);
V2=P(:,2)-P(:,3);
V3=P(:,3)-P(:,1);
%% Presenting Results
figure
hold on
plot(t,V1(:,1))
plot(t,V2(:,1))
plot(t,V3(:,1))
xlabel('Time(sec)')
ylabel('Potential Difference(mV)')
legend('P1-P2','P2-P3','P3-P1')

figure
hold on
plot(t,P(:,1))
plot(t,P(:,2))
plot(t,P(:,3))
xlabel('Time(sec)')
ylabel('Potential(mV)')
legend('Electrode 1','Electrode 2','Electrode 3')

figure
hold on
plot(t,PD(:,1))
plot(t,PR(:,1))
plot(t,P(:,1))
xlabel('Time(sec)')
ylabel('Potential(mV)')
legend('Depolarizing Pulse','Repolarizing Pulse','Potential Measured')
% legend('Electrode 1','Electrode 2','Electrode 3')
```