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function []=addition_of_conotoxin()
clc;
clear;
close all;

[V,t] = hodgkinHuxleyMembranePotential();
conc = cationConcentrations(V);
%membranePotentialPlot(t,V,conc);
%cationTimePlot(t,conc);
concentration_matrix = potassiumSodiumConcentration(t,V,conc);
potassiumSodiumTimePlot(t,concentration_matrix,V);
end

function [V,t] = hodgkinHuxleyMembranePotential()
    %Constants set for all Methods
    Cm=0.01; % Membrane Capacitance uF/cm^2
    dt=0.01;% Time Step ms
    tmax = 35;
    t=0:dt:tmax; %Time Array ms

    I=0.4; %External Current Applied
    ENa=55.17; % mv Na reversal potential
    EK=-72.14; % mv K reversal potential
    El=-49.42; % mv Leakage reversal potential
    gbarNa=1.2; % mS/cm^2 Na conductance
    gbarK=0.36; % mS/cm^2 K conductance
    gbarl=0.003; % mS/cm^2 Leakage conductance
    V(1)=-60; % Initial Membrane voltage
    m(1)=am(V(1))/(am(V(1))+bm(V(1))); % Initial m-value
    n(1)=an(V(1))/(an(V(1))+bn(V(1))); % Initial n-value
    h(1)=ah(V(1))/(ah(V(1))+bh(V(1))); % Initial h-value
    for i=1:length(t)-1
        %Euler method to find the next m/n/h value
        m(i+1)=m(i)+dt*((am(V(i))*(1-m(i)))-(bm(V(i))*m(i)));
        n(i+1)=n(i)+dt*((an(V(i))*(1-n(i)))-(bn(V(i))*n(i)));
        h(i+1)=h(i)+dt*((ah(V(i))*(1-h(i)))-(bh(V(i))*h(i)));
        gNa=gbarNa*m(i)^3*h(i);
        gK=gbarK*n(i)^4;
        gl=gbarl;

        INa=gNa*(V(i)-ENa);
        IK=gK*(V(i)-EK);
        Il=gl*(V(i)-El);

        %Euler method to find the next voltage value
        V(i+1)=V(i)+(dt)*((1/Cm)*(I-(INa+IK+Il)));
    end
end

function [conc] = cationConcentrations(V)
    % Finding the total concentration of cations

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cellvol = .67; %E.coli volume \mum^3
cellvol = cellvol * (1/(1e+6))^3 * (1000/1);
%           \mum^3 * (1m/1e6\mum)^3 * (L/m^3)
%cellcol = cellvol*1000
%           m^3 * (L/m^3)
cellsurfacearea = .77911; %\mum^2
p = 1.6e-19; %charge of single +1 ion
C = 1*(1/(1e6))*(100)^2*cellsurfacearea*(1/1e6)^2; %Capacitance per unit length
%1\muF/cm^2*(1F/1e6\muF)*(100cm/m)^2*(\mum^2)*(1m/1e6\mum)^2
nions = C.*V.*10^3/p; %Unitless
N = 6.02e23; %Avogadro's Number
nmols = nions/N;
I_o = 190+20; %Initial intracellular concentration of positive ions in E. Coli
conc = (nmols./cellvol)+I_o; %Concentration change per voltage change
end

function[] = membranePotentialPlot(t,V,conc)
%Plotting the membrane potential and cation concentration v. time
figure
yyaxis left
plot(t,V,'b')
ylabel('Membrane Potential(mV)');
yyaxis right
plot(t,conc,'r')
ylim([290,310])
ylabel('Concentration of positive ions (mM)')
legend('Membrane potential(mV)','Concentration')
xlabel('Time (\mu s)');
title('Membrane potential and Cation Concentration')
title('Membrane potential for Hodgkin-Huxley Model')
end

function [] = cationTimePlot(t,conc)
%Plotting the concentrations of cations v. time
figure
plot(t,conc,'r')
title('Intracellular Cation Concentration Due To Change In Voltage')
legend('Concentration of positive ions (mM)')
xlabel('Time ( \mu s)')
ylabel('Concentration (mM)')
end

function [concentration_matrix] = potassiumSodiumConcentration(t,V,conc)
% Determine the concentrations of Potassium and Sodium
%based on the total concentration of cations
%Initial intracellular concentration of Potassium
Kinitial = 190;% mM

%Initial intracellular concentration of Sodium
Nainitial = conc(1)-Kinitial;

%Vector of initial concentrations
initial_concentration = [Kinitial; Nainitial];

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%Initialize a matrix where first row is K concentration, second row is Na
%concentration, each column is time step corresponding to the Euler's
%method time step for determining membrane potential

%Series of if-statements which determine which channel/pump is relevant
%given the voltage and time.

%Numerical derivative of concentration wrt time
dC = diff(conc);
concentration_matrix = zeros(2,length(dC));
concentration_matrix(:,1) = initial_concentration;
%Initialize a matrix to represent which channel is open:
% [Na channel; Na/K pump; K channel]
channelopen = zeros(4,length(dC));
channelopen(1,:) = t(1:length(t)-1);
thresholdpotential = -38.0389; %mV

disp(['The threshold potential for the opening of sodium voltage'...,
' gated ion channel in E. coli is predicted to be ',...
num2str(thresholdpotential),' millivolts']);
for n = 2:length(conc)-1
%Determine which pump is open based on changing concentrations
if dC(n-1) > 0 %ie, if cation concentration is rising
    if V(n-1)> thresholdpotential %mV, the approximate threshold for Na ch
        channelopen(2,n) = 1;
        concentration_matrix(:,n) = sodium_channel(dC(n),...
            concentration_matrix(:,n-1));
    else %If the threshold has not been meet, the change is due to
        %the Na/K pumps
        concentration_matrix(:,n) = sodium_potassium_pump(dC(n),...
            concentration_matrix(:,n-1));
        channelopen(3,n) = 1;
    end
else %if the cation concentration is decreasing, it is due to a opening
    %of K chanel
    channelopen(4,n)=1;
    concentration_matrix(:,n) = potassium_channel(dC(n),...
        concentration_matrix(:,n-1));
end
end
end

function []= potassiumSodiumTimePlot(t,concentration_matrix,V)
%Plot concentrations of both ions v. time
figure
plotyy(t(1:length(t)-1),concentration_matrix(1,:),t(1:length(t)-1),...
    concentration_matrix(2,:))
grid minor
ylabel('Concentration (mM)')
xlabel('Time (\mus)')
legend('K^{+}', 'Na^{+}')
title('Concentrations of individual intracellular cations')
end

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function [V] = goldmanhogkinkatz(t,concentration_matrix)
%Assume extracellular concentration remains fixed
R = 8.3144598;
T = 310;
F = 96485;
Kin = concentration_matrix(1,:);
Kout = 10.455;
Nain = concentration_matrix(2,:);
Naout = 481.75;
p_k = 1;
p_na = 0.05;

numerator = Kout*p_k+Naout*p_na;
denominator = (Kin*p_k+Nain*p_na);
for n = 1:length(t)-1
    V(n) = -R*T/F * log(numerator/denominator(n));
end

figure
plot(t(1:length(t)-1),V)
end

function [out] = potassium_channel(dC,Cin)
    out = Cin + dC*[1;0];
end

function [out] = sodium_channel(dC,Cin)
    out = Cin + dC*[0;1];
end

function [out] = sodium_potassium_pump(dC,Cin)
    out = Cin + dC*[3;-2];
end

function [a] = am(v) %Alpha for Variable m
    a = 0.1*(v+35)/(1-exp(-(v+35)/10));
end

function [b] = bm(v) %Beta for variable m
    b = 4.0*exp(-0.0556*(v+60));
end

function [a] = an(v) %Alpha for variable n
    a = .01*(v+50)/(1-exp(-(v+50)/10));
end

function [b] = bn(v) %Beta for variable n
    b = 0.125*exp(-(v+60)/80);
end

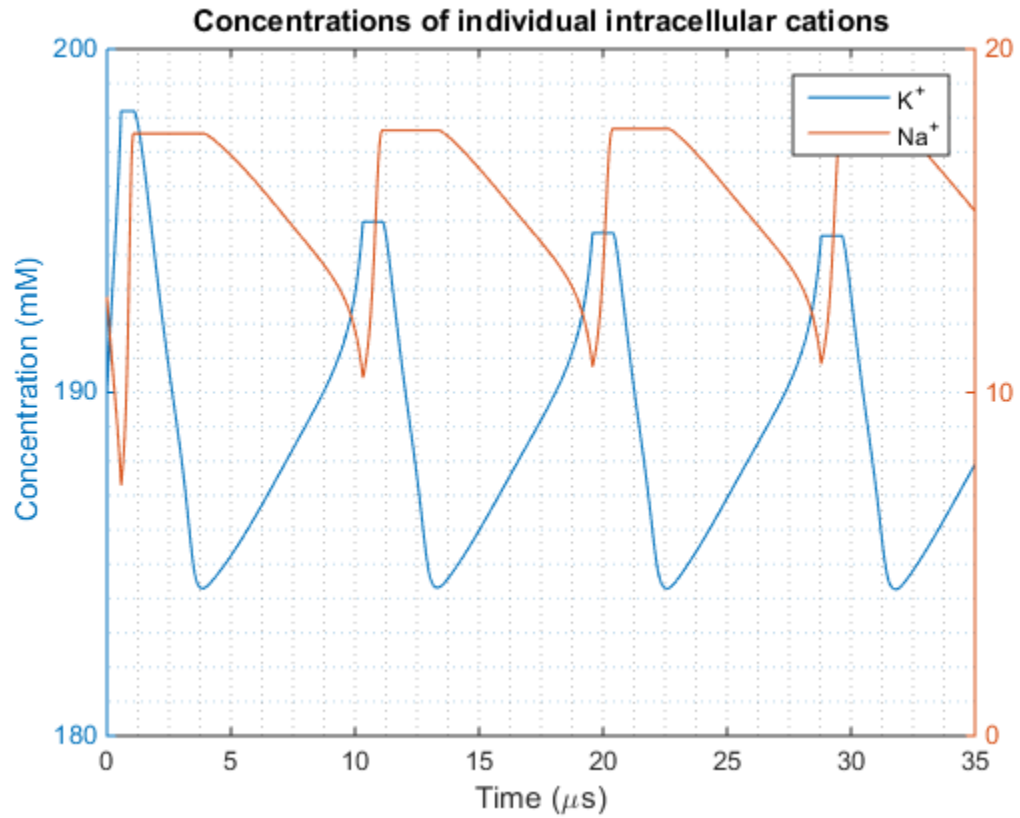
function [a] = ah(v) %Alpha value forr variable h
    a = 0.07*exp(-0.05*(v+60));
end

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function [b] = bh(v) % beta value for variable h
    b = 1/(1+exp(-(0.1)*(v+30)));
end
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The threshold potential for the opening of sodium voltage gated ion channel in E.



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