IMO II Exam 1
Source code

Ana Milena Forero Pinto

February 17th, 2022

1 Question 1

```matlab
%-------------------------------------------------------------
%-------------------------------------------------------------
%                          Data
%-------------------------------------------------------------
%-------------------------------------------------------------
warning off
path = '/Users/ana/Desktop/Exam1_IMO2/';
df = readtable(strcat(path,'Data.csv'), 'Delimiter',',');
df1 = table2array(df);
con = df1(:,1);
uptake_data = df1(:,2);


%-------------------------------------------------------------
%-------------------------------------------------------------
%                          Main
%-------------------------------------------------------------
%-------------------------------------------------------------

params_guess = [0.5,0.5];
lb = [0,0];
ub = [1,1];
[solution,resnorm,residual,exitflag,output,lambda,jacobian] =
    lsqcurvefit(@(params,x) Model(params,x),params_guess,con,
    uptake_data, lb, ub)

% %Plots
%Plot for fit
f1 = figure(1);
plot(con,uptake_data,'bo', con, Model(solution,con),'g--', 'MarkerSize
    ',10, 'LineWidth',3);
set(gca,'fontsize',18)
xlabel('\textbf{Concentration [$\mu g/ \mu m^3$]}', 'Interpreter','
    latex');
ylabel('\textbf{Uptake rate per cell [$\mu g/ \mu m^3 s$]}', '
    Interpreter','latex');
legend({'Data','Fit'}, 'Location','best', 'Position',[0.65 0.25 0.2
    0.15],'Interpreter','latex','FontSize',14); %[left bottom width
    height]
grid on
exportgraphics(f1,'fit.pdf','BackgroundColor','none');
```

```matlab
% Plot for L parameter behavior
L_1 = [1.3, 1, 0.8];
k_1 = 0.5;
con1 = 0:200;

f2 = figure(2);
plot(con1,Model([L_1(1),k_1], con1),'b-', con1, Model([L_1(2),k_1],
    con1),'g-',con1, Model([L_1(3),k_1],con1),'m-', 'MarkerSize',10, '
    LineWidth',3);
title('$\kappa = 0.5$','Interpreter','latex')
xlabel('\textbf{Concentration [$\mu g/ \mu m^3$]}', 'Interpreter','
    latex');
ylabel('\textbf{Uptake rate per cell [$\mu g/ \mu m^3 s$]}', '
    Interpreter','latex');
legend({'$\mathcal{L} = 1.3$','$\mathcal{L} =1.0$','$\mathcal{L} =
    0.8$'}, 'Location','best', 'Position',[0.65 0.25 0.2 0.15],'
    Interpreter','latex','FontSize',14);
set(gca,'fontsize',18)
grid on
exportgraphics(f2,'kconst.pdf','BackgroundColor','none');


%Plot for k parameter behavior
L_2 = 0.5;
k_2 = [1, 0.3, 0.1];

f3 = figure(3);
plot(con1,Model([L_2,k_2(1)], con1),'r-', con1, Model([L_2,k_2(2)],
    con1),'k-',con1, Model([L_2,k_2(3)],con1),'c-', 'MarkerSize',10, '
    LineWidth',3);
title('$\mathcal{L} = 0.5$','Interpreter','latex')
legend({'$\kappa = 1$','$\kappa = 0.3$','$\kappa =0.1$'}, 'Location','
    best', 'Position',[0.65 0.25 0.2 0.15],'Interpreter','latex','
    FontSize',14);
set(gca,'fontsize',18)
xlabel('\textbf{Concentration [$\mu g/ \mu m^3$]}', 'Interpreter','
    latex');
ylabel('\textbf{Uptake rate per cell [$\mu g/ \mu m^3 s$]}', '
    Interpreter','latex');
grid on
exportgraphics(f3,'Lconst.pdf','BackgroundColor','none');


% %------------------------------------------------------------------
% %------------------------------------------------------------------
% %                          Functions
% %------------------------------------------------------------------
% %------------------------------------------------------------------


function y = Model(params,x)
    L = params(1);
    k = params(2);
    y = L./(1+exp(-k*(x - 50)));
end
```

2 Questions 3 and 4, ABM

```matlab
concentration = [1, 10, 25, 50, 75, 100, 200, 300, 400, 500];      % [
    micrograms/micrometer^2]
export = [];

for g = 1:size(concentration,2)
rng(7)
%----------- COMPUTATIONAL DOMAIN ------------------%

xmin = -500; xmax = 500; ymin = xmin; ymax = xmax;
hg = 6;                                          % width of the grid
[xx,yy] = meshgrid(xmin:hg:xmax,ymin:hg:ymax);
[Ngy, Ngx] = size(xx);
area = (Ngx-1)*(Ngy-1);                          % area of the lattice

%----------- PARAMETERS------------------%

time = 2;                                         % [h]
dt = 0.6;                                         % time step [s]
Niter = round(time*3600/dt);                      % number of iterations
diff  =10;                                        % diffusion
    coefficient
stability = diff*dt/(hg^2);                       % stability condition
Rcell= hg;                                        % cell radius [
    micrometer]
areacell = pi*Rcell^2;                            % cell area [
    micrometer]
Ncells = round(0.35*area/areacell);               % number of cells
cellMaturation = 20*3600;                         % maturation age (20 h
    ) [s]
ageMat = ones(Ncells,1)*cellMaturation;           % maturation age for
    each cell
maxNeigh = 6;                                     % number of neighbours
     needed before division can happen
nu = 120;                                         % medium viscosity
L = 0.0201;                                       % [micrograms/s]
kappa = 0.0937;                                   % [micrometer^2/
    microgram]
stif = 100;                                       % tumor cell springs
    stiffness
step = 1+floor(Rcell/hg);
uptake_cond = 1;                                  % if 0, min(L*dt,
    biomark(Ny+iy+1,Nx+ix+1)). If 1, L*dt/(1+exp(-kappa*(biomark(x,y) -
    50)))
to_save = 0;                                      % if 1, save csv. if 0
     not to save.

%----------- INITIAL CONDITIONS ---------%

cells = 2*(xmax-2*Rcell)*(rand(Ncells,2) - 0.5);    % cells'
    coordinates
age = rand(Ncells,1)*cellMaturation;              % initialize ages
cell_biomark = zeros(Ncells,1);                   % biomarker
    concentration inside cell
gamma0 = concentration(g);                        % Initial value of
```

```matlab
    biomarker [micrograms]
biomark = gamma0*ones(Ngy,Ngx);

% set zero value of biomarker inside cells
for ii = 1:Ncells
        angle = linspace(0,2*pi,50);
        xc = cells(ii,1)+(Rcell*cos(angle));
        yc = cells(ii,2)+(Rcell*sin(angle));
        in = inpolygon(xx,yy,xc,yc);
        biomark(in) = 0; %This works because "in" is a logical array
end

%-------------IF VISUALIZATION-----------------%

plot = 1; %1 to plot, 0 to not plot.
concentration_cond = 75; %choose the concentration you want to plot
if (plot == 1 && gamma0 == concentration_cond)
    figure
end

%-------------SIMULATION-----------------------%


for iter = 0:Niter

    age = age + dt; % tumor cell age

    %%%%%%%%%%%%%%%%%%%%%%%
    % tumor cell neighbours
    %%%%%%%%%%%%%%%%%%%%%%%

    cellNeigh = zeros(Ncells,1);

    for ii = 1:Ncells
       for jj = 1:Ncells
         dx = cells(ii,1)-cells(jj,1);
         dy = cells(ii,2)-cells(jj,2);
         dxy = sqrt(dx^2+dy^2);
         if (dxy <= 3.5*Rcell) && (dxy > 0)
           cellNeigh(ii) = cellNeigh(ii) + 1;
         end
       end
    end

    %%%%%%%%%%%%%%%%%%%%%%%
    % tumor cell division
    %%%%%%%%%%%%%%%%%%%%%%%

    for cc = 1:Ncells
         if (age(cc) > ageMat(cc)) && (cellNeigh(cc) < maxNeigh)
           biom_mother = cell_biomark(cc);
           Ncells = Ncells + 1;  % cell division
           theta = rand*2*pi;
           cells(Ncells,1:2) = cells(cc,1:2)+0.5*Rcell*[cos(theta),
               sin(theta)];
           age(Ncells) = 0;
```

```matlab
                age(cc) = 0;
                ageMat(Ncells) = ageMat(cc)+2*(rand-0.5)*0.2*ageMat(cc);
                %Division of biomarker:
                cell_biomark(Ncells) = 0.5*biom_mother;
                cell_biomark(cc) = 0.5*biom_mother;
            end
        end


        %%%%%%%%%%%%%%%%%%%%%
        % Forces
        %%%%%%%%%%%%%%%%%%%%%%
        % tumor cell-tumor cell repulsive and adhesive forces
        RepForce = zeros(Ncells,2); %Respulsive force
        for ii = 1:Ncells-1
            for jj = ii+1:Ncells
                dx = cells(ii,1)-cells(jj,1);
                dy = cells(ii,2)-cells(jj,2);
                dxy = sqrt(dx^2+dy^2);
                if (dxy<2*Rcell)&&(dxy>0)
                    RepForce(ii,1:2)=RepForce(ii,1:2)+stif*(2*Rcell-dxy)*[
                        dx,dy]/dxy;
                    RepForce(jj,1:2)=RepForce(jj,1:2)-stif*(2*Rcell-dxy)*[
                        dx,dy]/dxy;
                end

            end
        end
        cells = cells+dt*RepForce/nu;

        % clean up
        % check outside tumor cells
        ind = find((cells(:,1)>xmin)&(cells(:,1)<xmax)&...
                (cells(:,2)>ymin)&(cells(:,2)<ymax));
        cells = cells(ind,:);
        Ncells = size(cells,1);
        RepForce = RepForce(ind,:);
        age = age(ind,:);
        ageMat = ageMat(ind,:);
        cell_biomark = cell_biomark(ind,:);

        %%%%%%%%%%%%%%%%%%%%%
        % Biomarker diffussion
        %%%%%%%%%%%%%%%%%%%%%%%
        % Neumann boundary condition in a central difference approximation
            .

        biomark(1,:) = biomark(2,:);
        biomark(Ngy,:) = biomark(Ngy-1,:);
        biomark(:,1) = biomark(:,2);
        biomark(:,Ngx) = biomark(:,Ngx-1);


        % biomarker diffusion
        biomarkL = biomark(1:Ngy-2,2:Ngx-1);  % diffusion from left
        biomarkR = biomark(3:Ngy,2:Ngx-1);  % diffusion from right
        biomarkT = biomark(2:Ngy-1,3:Ngx);  % diffusion from top
```

```matlab
        biomarkB = biomark(2:Ngy-1,1:Ngx-2);  % diffusion from bottom

        biomark(2:Ngy-1,2:Ngx-1) = biomark(2:Ngy-1,2:Ngx-1) +(diff*dt/(hg*
            hg))*...
                              (biomarkL+biomarkR+biomarkT+biomarkB-4*
                                 biomark(2:Ngy-1,2:Ngx-1));

    %%%%%%%%%%%%%%%%%%%%%%%
    % Biomarker uptake
    %%%%%%%%%%%%%%%%%%%%%%%
     for ii = 1:Ncells %Iterate over cells
       Nx = 1+floor((cells(ii,1)-xmin)/hg); % closest grid point to
           the cell
       Ny = 1+floor((cells(ii,2)-ymin)/hg);

       for ix = -step:step  %Iterate over grid points near the cell
        for iy = -step:step
           if (Nx+ix>0)&&(Nx+ix<=Ngx)&&(Ny+iy>0)&&(Ny+iy<=Ngy)
               ixy = sqrt((cells(ii,1)-(xmin+(Nx+ix)*hg))^2+(cells(ii
                   ,2)-(ymin+(Ny+iy)*hg))^2);
               if (ixy<Rcell) %If grid point is inside cell
                   if uptake_cond == 0
                       uptake = min(L*dt, biomark(Ny+iy+1,Nx+ix+1));
                       biomark(Ny+iy+1,Nx+ix+1) = max(0, biomark(Ny+
                           iy+1,Nx+ix+1) - uptake);
                   elseif uptake_cond == 1
                       uptake = L*dt/(1+exp(-kappa*(biomark(Ny+iy+1,
                           Nx+ix+1) - 50))) ;
                       biomark(Ny+iy+1,Nx+ix+1) = max(0, biomark(Ny+
                           iy+1,Nx+ix+1) - uptake);
                   end

                    %Store cell biomark uptake per each cell
                    cell_biomark(ii) = cell_biomark(ii) + uptake;
               end

           end
        end
       end
     end


    %%%%%%%%%%%%%%%%%%%%%%%
    % Plot
    %%%%%%%%%%%%%%%%%%%%%%%
    if (plot == 1 && gamma0 == concentration_cond)
        if (mod(iter,100) == 0)
            clf
            ax1 = axes;
            contourf(ax1,xx,yy,biomark,'edgecolor','none');
            axis equal
            ax2 = axes;
            %plot cells
            for ii = 1:Ncells
                angle = linspace(0,2*pi,50);
                xc = cells(ii,1)+(Rcell*cos(angle));
```

```matlab
                yc = cells(ii,2)+(Rcell*sin(angle));
                patch(ax2,xc,yc,cell_biomark(ii))
            end
            axis equal
            axis([xmin-0.5,xmax+0.5,ymin-0.5,ymax+0.5])

            % Hide the top axes
            ax2.Visible = 'off';
            ax2.XTick = [];
            ax2.YTick = [];
            colormap(ax1,"cool")
            colormap(ax2,flipud(hot))


            % colorbars
            cb1 = colorbar(ax1,'Position',[0.1 0.1 0.05 0.815]); %
                Position [left bottom width height]
            cb2 = colorbar(ax2,'Position',[0.85 0.1 0.05 0.815]);
            cb1.Label.String = 'Biomarker concentration';
            cb2.Label.String = 'Uptake concentration';
            cb1.Label.FontSize = 14;
            cb2.Label.FontSize = 14;
            cb1.Label.FontWeight = 'bold';
            cb2.Label.FontWeight = 'bold';
            title(ax1, ['Iteration=',num2str(iter),'    Time=',num2str(
                round(iter*dt/3600,2)),' [h]' ,'    Ncells=',num2str(
                Ncells) ], "FontSize",14)

        pause(0.1)
        end
    end
end
disp(strcat('Concentration: ',num2str(gamma0), ' done'))
export = [export, cell_biomark];
end

if to_save == 1
    to_csv = array2table(export);
    to_csv.Properties.VariableNames(1:size(concentration,2)) = {'con_1
        ', 'con_10', 'con_25', 'con_50', 'con_75', 'con_100', 'con_200'
        , 'con_300', 'con_400', 'con_500'};
    writetable(to_csv, strcat('uptake_condition_',num2str(uptake_cond)
        ,'.csv'))
end
```

3 Questions 3 and 4, histogram and bar plots

```matlab
warning off
path = '/Users/ana/Desktop/Exam1_IMO2/';

dfa = readtable(strcat(path,'uptake_condition_0.csv'), 'Delimiter',','
    ); % min(L*dt, biomark(Ny+iy+1,Nx+ix+1))
df1 = table2array(dfa);
total_cells_0 = size(df1,1);
```

```matlab
dfb = readtable(strcat(path,'uptake_condition_1.csv'), 'Delimiter',','
    ); % L*dt/(1+exp(-kappa*(biomark(x,y) - 50)))
df2 = table2array(dfb);
total_cells_1 = size(df2,1);

percentage = @(con, total_cells) sum(con >= 200.0)*100/total_cells; %
    con is the concentration of biomarker inside cell

percentage_0 = [];
percentage_1 = [];
for i = 1:size(df1,2)
    percentage_0 = [percentage_0, percentage(df1(:,i), total_cells_0)
        ];
    percentage_1 = [percentage_1, percentage(df2(:,i), total_cells_1)
        ];
end

y = [percentage_0;percentage_1];

%Plots
figure(1)
histogram(df2(:,4),10, 'FaceColor','#EDB120');
title('\textbf{Initial concentration: $50$}','Interpreter','latex')
xlabel('\textbf{Concentration inside cell [$\mu g/ \mu m^2$]}', '
    Interpreter','latex');
ylabel('\textbf{Number of cells}', 'Interpreter','latex');
set(gca,'fontsize',17)

figure(2)
histogram(df2(:,5),10, 'FaceColor','#D95319');
title('\textbf{Initial concentration: $75$}','Interpreter','latex')
xlabel('\textbf{Concentration inside cell [$\mu g/ \mu m^2$]}', '
    Interpreter','latex');
ylabel('\textbf{Number of cells}', 'Interpreter','latex');
set(gca,'fontsize',17)

figure(4)
histogram(df1(:,1),10, 'FaceColor','#A2142F');
title('\textbf{Initial concentration: $1$}','Interpreter','latex')
xlabel('\textbf{Concentration inside cell [$\mu g/ \mu m^2$]}', '
    Interpreter','latex');
ylabel('\textbf{Number of cells}', 'Interpreter','latex');
set(gca,'fontsize',17)

figure(3)
h = bar(1:size(df1,2), y, 1);
set(h(1),'FaceColor','#7E2F8E')
set(h(2),'FaceColor','#77AC30')
hold on
plot(0:size(df1,2)+1,75*ones(size(df1,2)+2,1), 'k--', 'LineWidth',2)
axis([0, size(df1,2)+1, 0, 110])
ylabel('\textbf{\% of cells with concentration inside $\ge 200$}', '
    Interpreter','latex');
xlabel('\textbf{Initial concentration}', 'Interpreter','latex');
set(gca,'xticklabel',{'1', '10', '25', '50', '75', '100', '200', '300'
```

```
    , '400', '500'}, 'fontsize',13)
leg = legend({'\textbf{constant: $\mathcal{L}$}','$\mathcal{L}/[1+e
    ^{-\kappa(\gamma(\textbf{x},t) - 50)}]$'}, ...
                      'Interpreter','latex','Location','northeastoutside
                      ','EdgeColor','none');
t = title(leg,'\textbf{\underline{Uptake rates}}', 'Interpreter','
    latex');
```