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Practice 6: Final Project.

Departamento de Ingeniería Eléctrica y Electrónica, Ingeniería Biomédica

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Table of Contents

Información general

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Objetive

In this study, we present a dynamical systems model designed to describe the progression of **metastatic melanoma**, an aggressive form of skin cancer characterized by rapid proliferation, tissue invasion, and immune system evasion. The model is formulated using a **three-population system**, represented by three first-order ordinary differential equations, which describe the temporal evolution of key biological populations within the tumor microenvironment.

Specifically, the model considers the interactions between:

$$\dot{x} = p_1 xy\dot{z} + p_2 xy^2$$

$$\dot{y} = p_3 y - p_4 xy$$

$$\dot{z} = p_5 z - p_6 xz$$

Populations

- *x(t)* — the population of **melanoma tumor cells**
- *y(t)* — the population of **healthy skin tissue cells**
- *z(t)* — the population of **effector immune cells**, such as **$CD8^+$ cytotoxic T lymphocytes** and **natural killer (NK) cells**

Interpretation

$p_1xyz =$ tumor cell growth enhanced by the simultaneous presence of healthy tissue and immune cells (reflecting inflammatory microenvironment and immune evasion mechanisms).

$p_2xy^2 =$ aggressive tumor proliferation fueled by the availability of abundant healthy tissue (early-stage expansion).

$p_3y =$ physiological regeneration of healthy skin tissue.

$-p_4xy =$ destruction of healthy tissue due to tumor invasion and local damage.

$p_5z =$ activation and proliferation of effector immune cells in response to tumor presence.

$-p_6xz =$ tumor-induced immune suppression (e.g., via PD-L1 expression, TGF-β secretion).

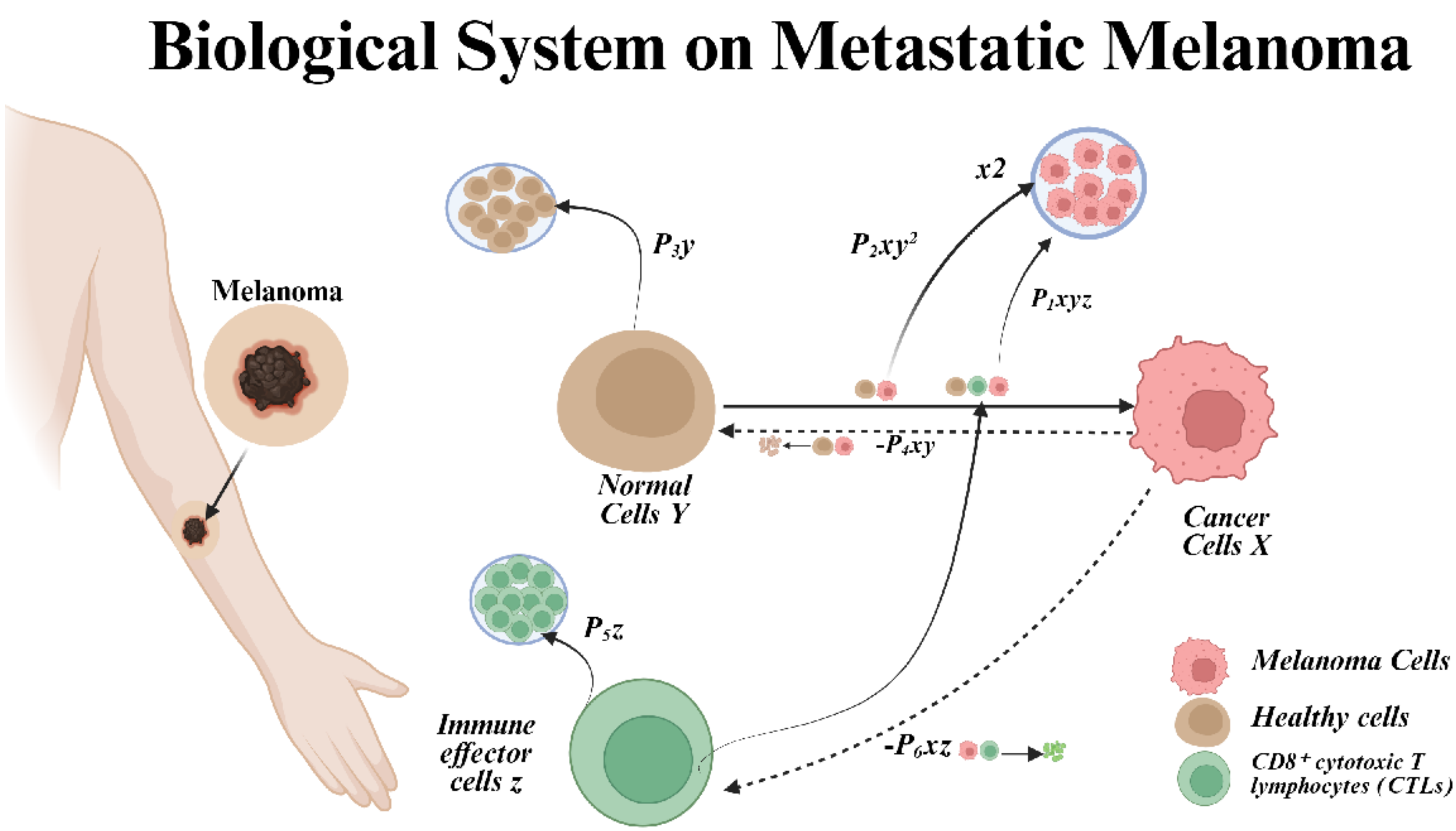


Figure. Diagram of the biological three-population system, where *x(t)* represents pathogenic (tumor) cells, *y(t)* represents healthy tissue cells, and *z(t)* represents effector immune cells. *The diagram was created using BioRender.*

Simulation data

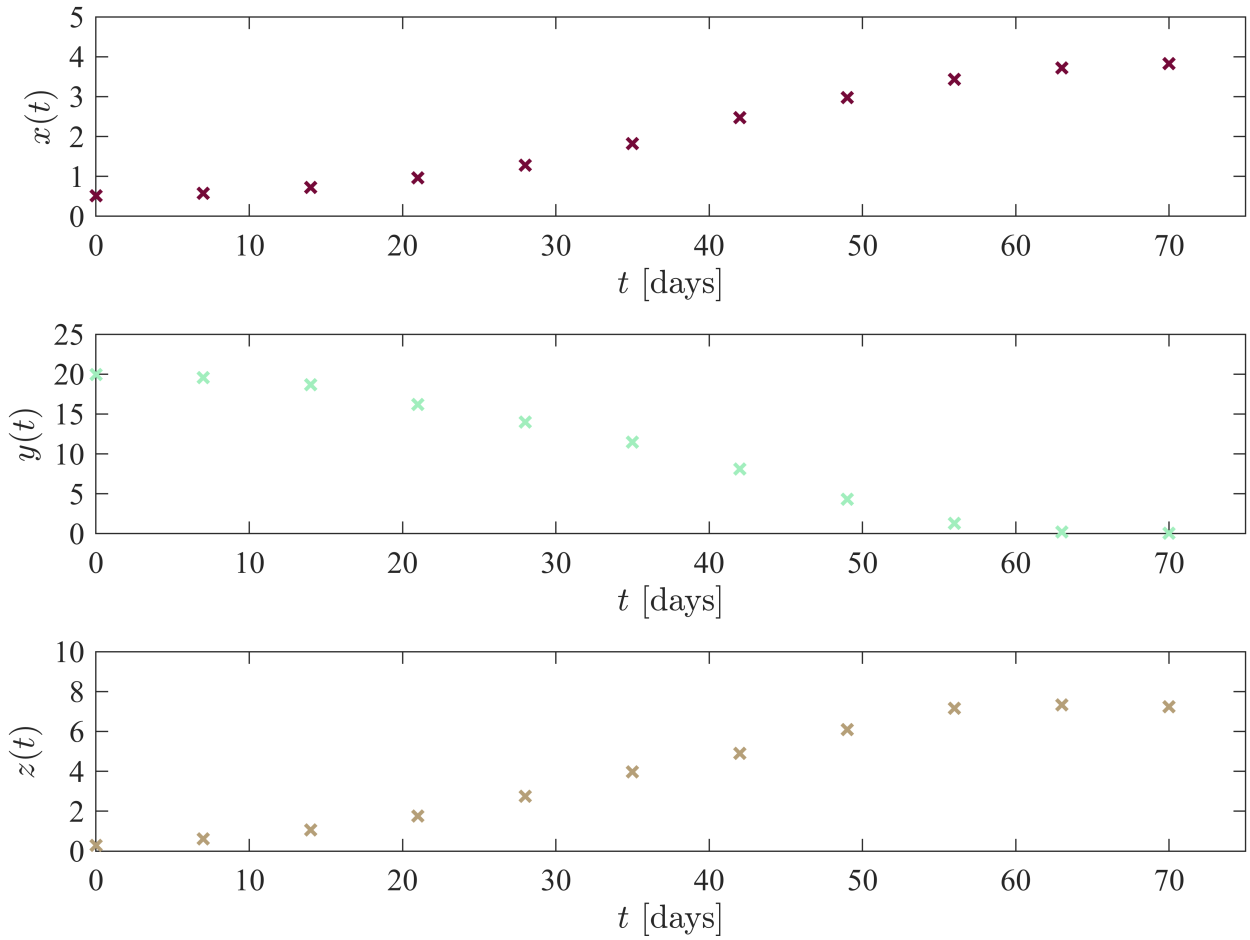
```
clc; clear; close all; warning('off','all')
filename = 'data2.csv';
sys = readmatrix(filename);
t = sys(:,1);
x1 = sys(:,2);
y1= sys(:,3);
z1 = sys(:,4);
T = array2table([t, x1, y1, z1], 'VariableNames', {'Time', 'x(t)', 'y(t)', 'z(t)'});

disp(T); plotEDOsxd(t,x1,y1,z1); %ttl = ' system';
sgtitle(ttl,'Interpreter','Latex')
```

Time	x(t)	y(t)	z(t)
0	0.517	19.939	0.281

```
 7      0.58    19.578    0.609
14     0.726    18.678    1.063
21     0.965    16.215    1.758
28     1.282    14.005    2.752
35     1.825    11.467    3.975
42     2.473     8.096    4.895
49     2.974     4.327    6.096
56      3.43     1.287    7.152
63     3.717     0.194    7.328
70     3.829     0.056    7.232
```

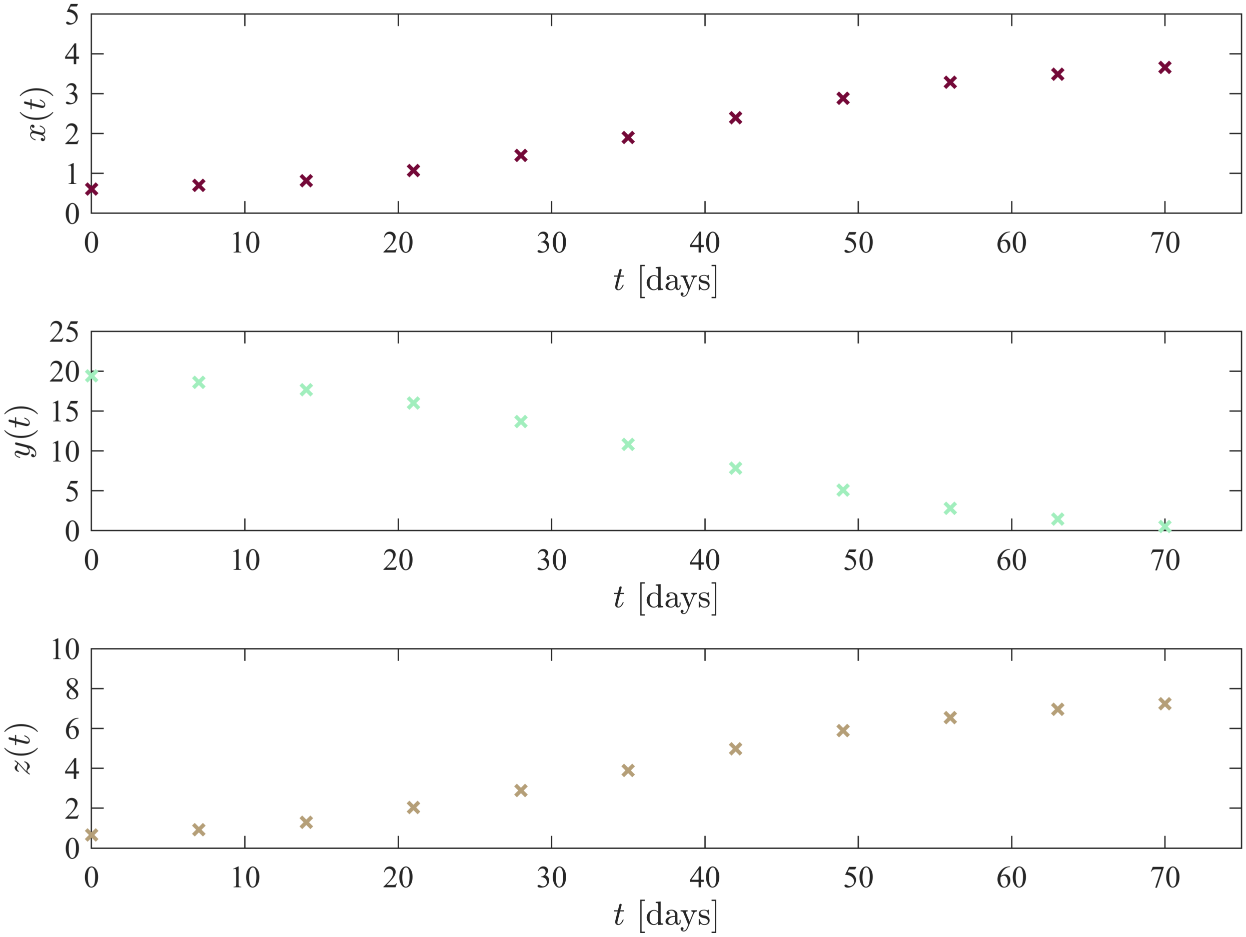
```
exportgraphics(gcf,'data.pdf','ContentType','vector')
```



Smoothing

```
x1s = smoothdata(x1);
y1s = smoothdata(y1);
z1s = smoothdata(z1);

plotEDOs2(t,x1s,y1s,z1s); %ttl = ' system'; sgtitle(ttl,'Interpreter','Latex')
exportgraphics(gcf,'Smoothdata.pdf','ContentType','vector')
```




```
T1 = array2table([t, x1s, y1s, z1s], 'VariableNames', {'Time', 'x1(t)', 'y1(t)',
'z1(t)'});
writetable(T1,'Smooth_data2.csv');
```

Linear Regression

```
% Leer el archivo correctamente
filename = 'Smooth_data2.csv';
sys = readmatrix(filename);
t = sys(:,1);
x = sys(:,2);
y= sys(:,3);
```

```
z = sys(:,4);


P0x = [0.000761528747328915, 5.40193151929626e-5];
P0y = [0.0139506931568651, 0.0288201962071527];
P0z = [0.0741556526131045, 0.0192439855016189];

P0 = [P0x, P0y, P0z];

mdl = ModelXYZ(t, x, y, z, P0x, P0y, P0z);
```

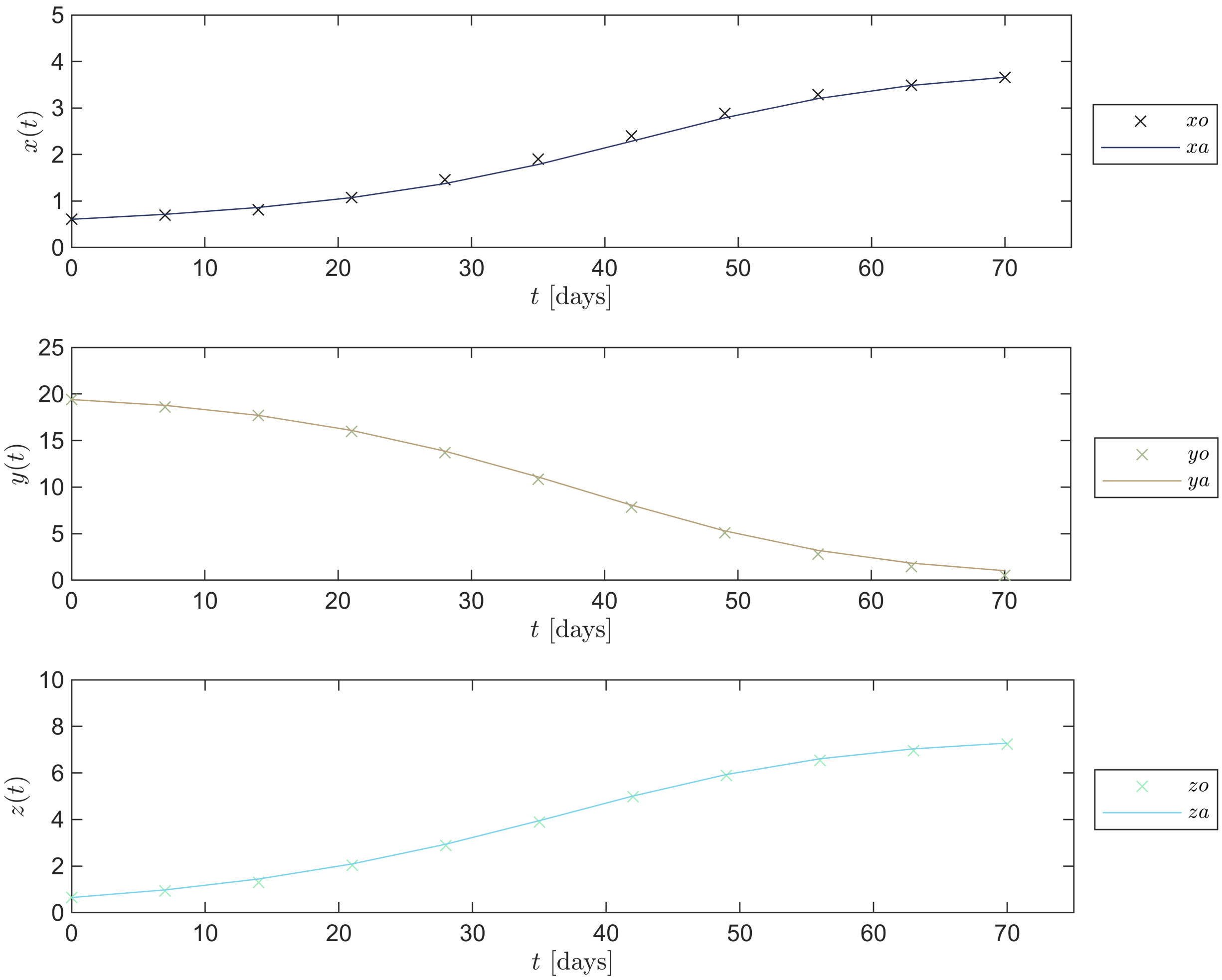
```
--- XYZ Model Fitting ---
Sample size: 11
Fitted parameters: 6
Degrees of freedom: 24
Adjusted R^2: 0.9954
Corrected AIC: 84.3921
```

Parameter	Estimate	StdError	MoE	CI95		PValue
"p1"	0.00077525	6.6718e-05	0.0001377	0.00063755	0.00091295	2.4268e-11
"p2"	3.0776e-05	9.7428e-06	2.0108e-05	1.0667e-05	5.0884e-05	0.0042427
"p3"	0.015219	0.0016395	0.0033838	0.011835	0.018602	2.062e-09
"p4"	0.030408	0.002845	0.0058717	0.024536	0.03628	1.3188e-10
"p5"	0.071353	0.0020469	0.0042246	0.067129	0.075578	4.5322e-22
"p6"	0.018398	0.0016367	0.003378	0.01502	0.021776	4.7772e-11

```
Pest = table2array(mdl.Coefficients(:,1));

[~, x_fit, y_fit, z_fit] = simulateXYZ(t, x(1), y(1), z(1), Pest);

plotXYZResults(t, [x, x_fit], [y, y_fit], [z, z_fit]);
%ttl = ' Linear Regression'; sgtitle(ttl,'Interpreter','Latex')
exportgraphics(gcf,'Linear Regression.pdf','ContentType','vector')
```



Equilibrium points and jacobian matrix

```
clc; clear; close all; warning('off','all')

syms x y z
p = sym('p', [1 6]);  % Define un vector simbólico p(1) a p(7)

   dx = p(1)*x*y*z + p(2)*x*y^2;
   dy = p(3)*y - p(4)*x*y;
   dz = p(5)*z - p(6)*x*z;
J = jacobian([dx, dy, dz], [x, y, z]);
fprintf('Jacobian matrix of the system:\n');disp(J)
```

```
Jacobian matrix of the system:
```

$$\begin{pmatrix} p_2\,y^2+p_1\,z\,y & 2\,p_2\,x\,y+p_1\,x\,z & p_1\,x\,y \\ -p_4\,y & p_3-p_4\,x & 0 \\ -p_6\,z & 0 & p_5-p_6\,x \end{pmatrix}$$

```
eq1 = dx == 0;
eq2 = dy == 0;
eq3 = dz == 0;
edos = solve([eq1, eq2, eq3], [x, y, z]);

n = length(edos.x);
fprintf('Equilibrium Points of the system:\n');fprintf('The system has %d
equilibrium point(s).\n\n', n);
```

```
Equilibrium Points of the system:
The system has 2 equilibrium point(s).
```

```
for i = 1:min(2,n)
    X = edos.x(i);
    Y = edos.y(i);
    Z = edos.z(i);
    syms x y z
    fprintf('Equilibrium point %d:\n', i);
    disp([x y z X Y Z])
end
```

```
Equilibrium point 1:
```

$$\begin{pmatrix} x & y & z & \frac{p_5}{p_6} & 0 & 0 \end{pmatrix}$$

```
Equilibrium point 2:
```

$$\begin{pmatrix} x & y & z & 0 & 0 & 0 \end{pmatrix}$$

Local stability

```
clc; clear; close all; warning('off','all')

% Parámetros
p1 = 0.000761528747328915;
p2 = 5.40193151929626e-5;
p3 = 0.0139506931568651;
p4 = 0.0288201962071527;
p5 = 0.0741556526131045;
p6 = 0.0192439855016189;

x1 = 0; y1 = 0; z1 = 0;
x2 = p5 / p6;
y2 = 0;
z2 = 0;

x = [x1; x2];
```

```
y = [y1; y2];
z = [z1; z2];
var = {'(x0,y0,z0)'; '(x1,y1,z1)'};

Equilibria = table(x, y, z, 'RowNames', var);
Equilibria.Properties.VariableNames = {'xe','ye','ze'};
fprintf('Equilibrium points of the  system:\n');disp(Equilibria)
```

```
Equilibrium points of the  system:
                   xe      ye    ze
                 ______    __    __

    (x0,y0,z0)        0    0     0
    (x1,y1,z1)   3.8534    0     0
```

```
syms xs ys zs
J = [ p2*ys^2 + p1*zs*ys,   2*p2*xs*ys + p1*xs*zs,   p1*xs*ys;
     -p4*ys,               p3 - p4*xs,              0;
     -p6*zs,               0,                      p5 - p6*xs ];



L = zeros(2,3);
for i = 1:2
    Ji = double(subs(J, {xs, ys, zs}, {x(i), y(i), z(i)}));
    L(i,:) = sort(eig(Ji), 'descend');
end

% Tabla de autovalores
L1 = L(:,1); L2 = L(:,2); L3 = L(:,3);
Lambdas = table(L1, L2, L3, 'RowNames', var);
disp('Eigenvalues of the Jacobian matrix evaluated at each equilibrium
point:');disp(Lambdas)
```

```
Eigenvalues of the Jacobian matrix evaluated at each equilibrium point:
                    L1            L2            L3
                 ________    ___________    _________

    (x0,y0,z0)   0.074156       0.013951            0
    (x1,y1,z1)          0    -1.9761e-18    -0.097106
```

2t prediction

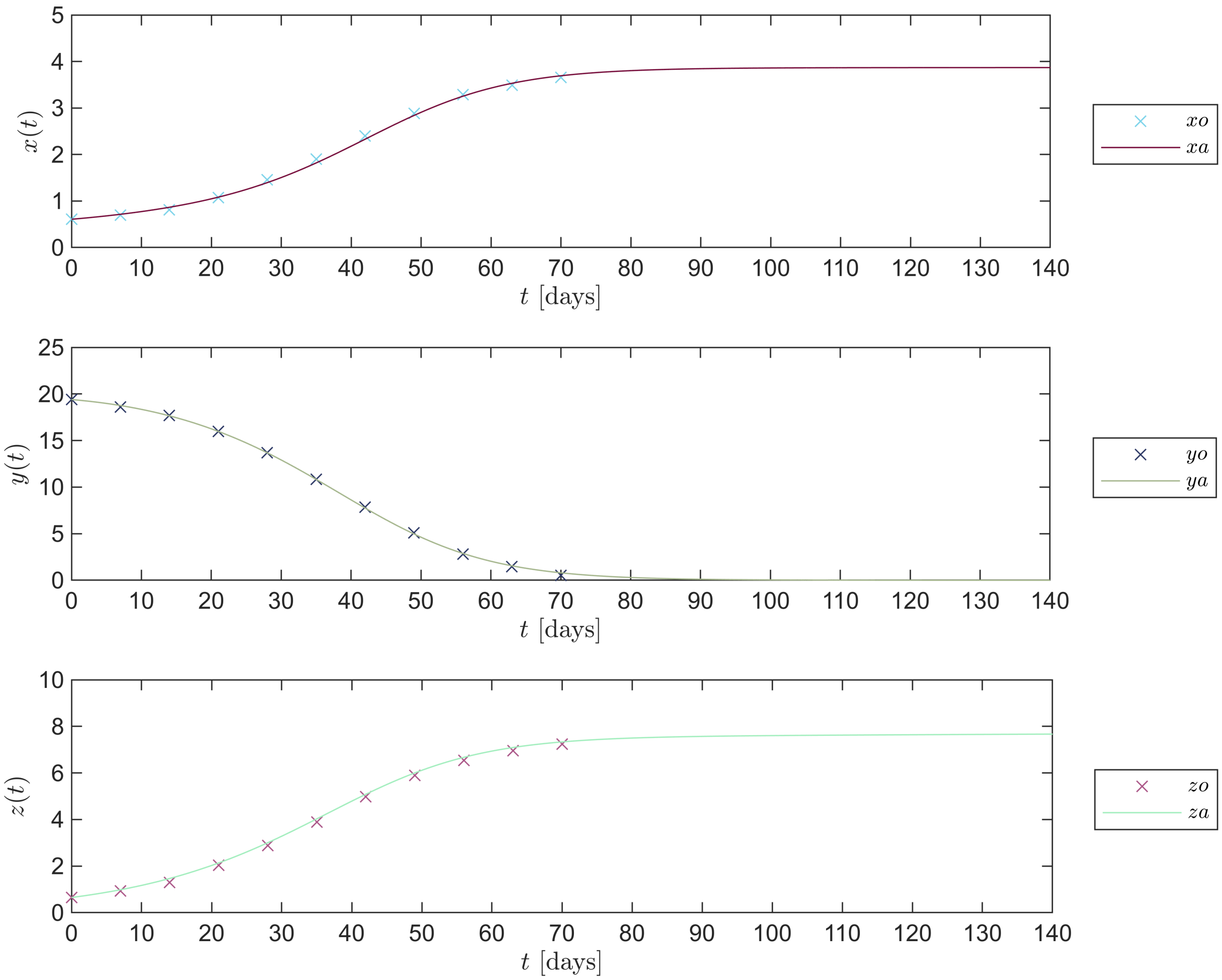
```
filename = 'Smooth_data2.csv';
sys = readmatrix(filename);
t = sys(:,1);
x = sys(:,2);
y= sys(:,3);
z = sys(:,4);
```

```
P0x = [0.000761528747328915, 5.40193151929626e-5];
P0y = [0.0139506931568651, 0.0288201962071527];
P0z = [0.0741556526131045, 0.0192439855016189];
P0 = [P0x, P0y, P0z];  % Vector total de parámetros
mdl = ModelXYZ(t, x, y, z, P0x, P0y, P0z);
```

```
--- XYZ Model Fitting ---
Sample size: 11
Fitted parameters: 6
Degrees of freedom: 24
Adjusted R^2: 0.9954
Corrected AIC: 84.3921
```

Parameter	Estimate	StdError	MoE	CI95		PValue
"p1"	0.00077525	6.6718e-05	0.0001377	0.00063755	0.00091295	2.4268e-11
"p2"	3.0776e-05	9.7428e-06	2.0108e-05	1.0667e-05	5.0884e-05	0.0042427
"p3"	0.015219	0.0016395	0.0033838	0.011835	0.018602	2.062e-09
"p4"	0.030408	0.002845	0.0058717	0.024536	0.03628	1.3188e-10
"p5"	0.071353	0.0020469	0.0042246	0.067129	0.075578	4.5322e-22
"p6"	0.018398	0.0016367	0.003378	0.01502	0.021776	4.7772e-11

```
P = table2array(mdl.Coefficients(:,1));
dt = 1E-2;
tend = 1000;
[tp, xp, yp, zp] = Predict(x(1), y(1), z(1), dt, tend, P);
plotXYZPredict(t, x, y, z, tp, xp, yp, zp);
%ttl = ' 2T prediction'; sgtitle(ttl,'Interpreter','Latex')
exportgraphics(gcf,' 2t prediction.pdf','ContentType','vector')
```



Conclusion

English

The analyzed dynamic system models the interaction between tumor cells, healthy tissue, and immune effector cells using a set of nonlinear differential equations. Based on parameter estimation and stability analysis, the system exhibits no biologically stable equilibrium where all three populations coexist. Instead, equilibrium points either correspond to total cell absence or dominance of tumor cells in the absence of immune response and healthy tissue. This reflects an aggressive disease progression scenario, such as metastatic melanoma, where the tumor proliferates uncontrollably while suppressing the immune system and destroying surrounding tissue. Numerical simulations support this behavior, showing rapid tumor growth, immune stagnation, and tissue collapse. Overall, the system effectively captures a pathological, unstable biological environment and may serve as a foundation for exploring therapeutic strategies like immunotherapy in future studies.

MDL

```
function mdl = ModelXYZ(t, x, y, z, P0x, P0y, P0z)
    dt = 1E-1;
    fo = [diff(x)/dt; diff(y)/dt; diff(z)/dt];
    to = [t(2:end); t(2:end); t(2:end)];

    t_base = t;

    function f_pred = model(p, ~)
        [~, x_, y_, z_] = simulateXYZ(t_base, x(1), y(1), z(1), p);
        dxdt_ = diff(x_) / dt;
        dydt_ = diff(y_) / dt;
        dzdt_ = diff(z_) / dt;
        f_pred = [dxdt_; dydt_; dzdt_];
    end

       P0 = [P0x, P0y, P0z];
    mdl = fitnlm(to, fo, @model, P0);

    Estimate = table2array(mdl.Coefficients(:,1));
    SE = table2array(mdl.Coefficients(:,2));
    Pvalue = table2array(mdl.Coefficients(:,4));
    CI95 = coefCI(mdl, 0.05);
    MoE = SE .* tinv(0.975, mdl.DFE);
    param_names = compose("p%d", 1:length(P0));
    Results = table(param_names', Estimate, SE, MoE, CI95, Pvalue, ...
        'VariableNames', {'Parameter', 'Estimate', 'StdError', 'MoE', 'CI95',
'PValue'});

    fprintf('\n--- XYZ Model Fitting ---\n')
fprintf('Sample size: %d\n', length(x))
fprintf('Fitted parameters: %d\n', length(P0))
fprintf('Degrees of freedom: %d\n', mdl.DFE)
fprintf('Adjusted R^2: %.4f\n', mdl.Rsquared.Adjusted)
fprintf('Corrected AIC: %.4f\n\n', mdl.ModelCriterion.AICc)
disp(Results)

end


function [dx, dy, dz] = dynamics(x, y, z, p)


    dx = p(1)*x*y*z + p(2)*x*y^2;


    dy = p(3)*y - p(4)*x*y;

   dz = p(5)*z - p(6)*x*z;
```

```
end


function [t_, x_, y_, z_] = simulateXYZ(t, x0, y0, z0, p)
    dt = mean(diff(t));
    t_ = (0:dt:max(t))';
    n = length(t_) - 1;

    x_ = zeros(n+1,1); x_(1) = x0;
    y_ = zeros(n+1,1); y_(1) = y0;
    z_ = zeros(n+1,1); z_(1) = z0;

    for i = 1:n
        [dx1, dy1, dz1] = dynamics(x_(i), y_(i), z_(i), p);
        [dx2, dy2, dz2] = dynamics(x_(i)+dx1*dt, y_(i)+dy1*dt, z_(i)+dz1*dt, p);
        x_(i+1) = x_(i) + 0.5*(dx1 + dx2)*dt;
        y_(i+1) = y_(i) + 0.5*(dy1 + dy2)*dt;
        z_(i+1) = z_(i) + 0.5*(dz1 + dz2)*dt;
    end

    x_ = interp1(t_, x_, t);
    y_ = interp1(t_, y_, t);
    z_ = interp1(t_, z_, t);
end
```

Functions

Graphics

```
function plotEDOsxd(t, x1, y1, z1)
    c1 = [116, 9, 56] / 255;
    c2 = [161, 238, 189] / 255;
    c3 = [181, 159, 120] / 255;

    figure('Color', 'w', 'Units', 'centimeters', 'Position', [2, 2, 28, 20]);

    % Subplot 1: x(t)
    subplot(3, 1, 1)
    set(gca, 'FontName', 'Times New Roman', 'FontSize', 12);
    hold on; box on; grid off;
    plot(t, x1, 'x', 'LineWidth', 1.5, 'Color', c1)
    xlabel('$t$ [days]', 'Interpreter', 'latex', 'FontSize', 13)
    ylabel('$x(t)$', 'Interpreter', 'latex', 'FontSize', 13)
    xlim([0 75]); xticks(0:10:75)
    ylim([0 5]); yticks(0:1:5)
    %legend('$x(t)$', 'Interpreter', 'latex', 'FontSize', 12, 'Location',
'NorthEast')
```

```
    % Subplot 2: y(t)
    subplot(3, 1, 2)
    set(gca, 'FontName', 'Times New Roman', 'FontSize', 12);
    hold on; box on; grid off;
    plot(t, y1, 'x', 'LineWidth', 1.5, 'Color', c2)
    xlabel('$t$ [days]', 'Interpreter', 'latex', 'FontSize', 13)
    ylabel('$y(t)$', 'Interpreter', 'latex', 'FontSize', 13)
    xlim([0 75]); xticks(0:10:75)
    ylim([0 25]); yticks(0:5:25)
    %legend('$y(t)$', 'Interpreter', 'latex', 'FontSize', 12, 'Location',
'NorthEast')

    % Subplot 3: z(t)
    subplot(3, 1, 3)
    set(gca, 'FontName', 'Times New Roman', 'FontSize', 12);
    hold on; box on; grid off;
    plot(t, z1, 'x', 'LineWidth', 1.5, 'Color', c3)
    xlabel('$t$ [days]', 'Interpreter', 'latex', 'FontSize', 13)
    ylabel('$z(t)$', 'Interpreter', 'latex', 'FontSize', 13)
    xlim([0 75]); xticks(0:10:75)
    ylim([0 10]); yticks(0:2:10)
    %legend('$z(t)$', 'Interpreter', 'latex', 'FontSize', 12, 'Location',
'NorthEast')
end


function plotEDOs2(t, x1s, y1s, z1s)
    c1 = [116, 9, 56] / 255;
    c2 = [161, 238, 189] / 255;
    c3 = [181, 159, 120] / 255;

    figure('Color', 'w', 'Units', 'centimeters', 'Position', [2, 2, 28, 20]);

    % Subplot 1: x(t)
    subplot(3, 1, 1)
    set(gca, 'FontName', 'Times New Roman', 'FontSize', 12);
    hold on; box on; grid off;
    plot(t, x1s, 'x', 'LineWidth', 1.5, 'Color', c1)
    xlabel('$t$ [days]', 'Interpreter', 'latex', 'FontSize', 13)
    ylabel('$x(t)$', 'Interpreter', 'latex', 'FontSize', 13)
    xlim([0 75]); xticks(0:10:75)
    ylim([0 5]); yticks(0:1:5)
    %legend('$x(t)$', 'Interpreter', 'latex', 'FontSize', 12, 'Location',
'NorthEast')

    % Subplot 2: y(t)
    subplot(3, 1, 2)
    set(gca, 'FontName', 'Times New Roman', 'FontSize', 12);
    hold on; box on; grid off;
    plot(t, y1s, 'x', 'LineWidth', 1.5, 'Color', c2)
```

```
    xlabel('$t$ [days]', 'Interpreter', 'latex', 'FontSize', 13)
    ylabel('$y(t)$', 'Interpreter', 'latex', 'FontSize', 13)
    xlim([0 75]); xticks(0:10:75)
    ylim([0 25]); yticks(0:5:25)
    %legend('$y(t)$', 'Interpreter', 'latex', 'FontSize', 12, 'Location',
'NorthEast')

    % Subplot 3: z(t)
    subplot(3, 1, 3)
    set(gca, 'FontName', 'Times New Roman', 'FontSize', 12);
    hold on; box on; grid off;
    plot(t, z1s, 'x', 'LineWidth', 1.5, 'Color', c3)
    xlabel('$t$ [days]', 'Interpreter', 'latex', 'FontSize', 13)
    ylabel('$z(t)$', 'Interpreter', 'latex', 'FontSize', 13)
    xlim([0 75]); xticks(0:10:75)
    ylim([0 10]); yticks(0:2:10)
    %legend('$z(t)$', 'Interpreter', 'latex', 'FontSize', 12, 'Location',
'NorthEast')
end

function plotXYZPredict(to, xo, yo, zo, tp, xp, yp, zp)
    % Definición fija de colores similar al segundo código
    colores = [116, 9, 56;
               161, 238, 189;
               170, 84, 134;
               255, 101, 0;
               123, 211, 234;
               181, 159, 120;
               42,  54,  99;
               26,  26,  29;
               254, 236, 55;
               165, 182, 141] / 255;

    % Selección fija de colores para obs y mod (6 colores al azar sin repetir)
    rng('shuffle');
    indices = randperm(size(colores,1),6);
    c1_obs = colores(indices(1), :);
    c1_mod = colores(indices(2), :);
    c2_obs = colores(indices(3), :);
    c2_mod = colores(indices(4), :);
    c3_obs = colores(indices(5), :);
    c3_mod = colores(indices(6), :);

    figure(); set(gcf,'Color','w')
    set(gcf,'Units','Centimeters','Position',[2,2,20,15])
    set(gca,'FontName','Times New Roman')
    fontsize(12,'points')

    % Subplot X
    subplot(3,1,1); hold on; box on;
```

```
    plot(to, xo, 'x', 'Color', c1_obs)
    plot(tp, xp, '-', 'Color', c1_mod)
    ylabel('$x(t)$','Interpreter','latex')
    xlabel('$t\ \mathrm{[days]}$', 'Interpreter','latex')  % ← Corregido
    legend({'$xo$','$xa$'}, 'Interpreter','latex', 'Location',
'eastoutside','Box','on')
    xticks(0:10:140); xlim([0 140]);
     ylim([0 5]); yticks(0:1:5)

    % Subplot Y
    subplot(3,1,2); hold on; box on;
    plot(to, yo, 'x', 'Color', c2_obs)
    plot(tp, yp, '-', 'Color', c2_mod)
    ylabel('$y(t)$','Interpreter','latex')
    xlabel('$t\ \mathrm{[days]}$', 'Interpreter','latex')  % ← Corregido
    legend({'$yo$','$ya$'}, 'Interpreter','latex', 'Location',
'eastoutside','Box','on')
    xticks(0:10:140); xlim([0 140]);
    ylim([0 25]); yticks(0:5:25)

    % Subplot Z
    subplot(3,1,3); hold on; box on;
    plot(to, zo, 'x', 'Color', c3_obs)
    plot(tp, zp, '-', 'Color', c3_mod)
    xlabel('$t\ \mathrm{[days]}$', 'Interpreter','latex')  % ← Corregido
    ylabel('$z(t)$','Interpreter','latex')
    legend({'$zo$','$za$'}, 'Interpreter','latex', 'Location',
'eastoutside','Box','on')
    xticks(0:10:140); xlim([0 140]);
    ylim([0 10]); yticks(0:2:10)
end




function plotXYZPredict2(to, xo, yo, zo, tp, xp, yp, zp)
    % Definición fija de colores similar al segundo código
    colores = [116, 9, 56;
               161, 238, 189;
               170, 84, 134;
               255, 101, 0;
               123, 211, 234;
               181, 159, 120;
               42,  54,  99;
               26,  26,  29;
               254, 236, 55;
               165, 182, 141] / 255;

    % Selección fija de colores para obs y mod (6 colores al azar sin repetir)
```

```
    rng('shuffle');
    indices = randperm(size(colores,1),6);
    c1_obs = colores(indices(1), :);
    c1_mod = colores(indices(2), :);
    c2_obs = colores(indices(3), :);
    c2_mod = colores(indices(4), :);
    c3_obs = colores(indices(5), :);
    c3_mod = colores(indices(6), :);

    figure(); set(gcf,'Color','w')
    set(gcf,'Units','Centimeters','Position',[2,2,20,15])
    set(gca,'FontName','Times New Roman')
    fontsize(12,'points')

    % Subplot X
    subplot(3,1,1); hold on; box on;
    plot(to, xo, 'x', 'Color', c1_obs)
    plot(tp, xp, '-', 'Color', c1_mod)
    ylabel('$x(t)$','Interpreter','latex')
    legend({'$x_{obs}$','$x_{2T}$'}, 'Interpreter','latex', 'Location',
'eastoutside','Box','on')
   xticks(0:100:1000); xlim([0 1000]);
     ylim([0 6]); yticks(0:1:6)

    % Subplot Y
    subplot(3,1,2); hold on; box on;
    plot(to, yo, 'x', 'Color', c2_obs)
    plot(tp, yp, '-', 'Color', c2_mod)
    ylabel('$y(t)$','Interpreter','latex')
    legend({'$y_{obs}$','$y_{2T}$'}, 'Interpreter','latex', 'Location',
'eastoutside','Box','on')
    xticks(0:100:1000); xlim([0 1000]);
    ylim([0 25]); yticks(0:5:25)

    % Subplot Z
    subplot(3,1,3); hold on; box on;
    plot(to, zo, 'x', 'Color', c3_obs)
    plot(tp, zp, '-', 'Color', c3_mod)
    xlabel('$t\ \text{[días]}$','Interpreter','latex')
    ylabel('$z(t)$','Interpreter','latex')
    legend({'$z_{obs}$','$z_{2T}$'}, 'Interpreter','latex', 'Location',
'eastoutside','Box','on')
    xticks(0:100:1000); xlim([0 1000]);
    ylim([0 10]); yticks(0:2:10)
end
```

```
```

Plot mdl

```
function plotXYZResults(t, X, Y, Z)

    colores = [116, 9, 56;
               161, 238, 189;
               170, 84, 134;
               255, 101, 0;
               123, 211, 234;
               181, 159, 120;
               42,  54,  99;
               26,  26,  29;
               254, 236, 55;
               165, 182, 141] / 255;


    rng('shuffle');
    indices = randperm(size(colores,1), 6);
    c1_obs = colores(indices(1), :);
    c1_mod = colores(indices(2), :);
    c2_obs = colores(indices(3), :);
    c2_mod = colores(indices(4), :);
    c3_obs = colores(indices(5), :);
    c3_mod = colores(indices(6), :);

    set(figure(),'Color','w')
    set(gcf,'Units','Centimeters','Position',[2,2,20,15])
    set(gca,'FontName','Times New Roman')
    fontsize(12,'points')

    % Subplot X
    subplot(3,1,1)
    hold on; box on;
    plot(t, X(:,1), 'x', 'Color', c1_obs)
    plot(t, X(:,2), '-', 'Color', c1_mod)
    ylabel('$x(t)$','Interpreter','latex')
    xlabel('$t\ \mathrm{[days]}$', 'Interpreter','latex')  % ← Corregido
    legend({'$xo$','$xa$'}, 'Interpreter','latex', 'Location',
'eastoutside','Box','on')
    xlim([0 75]); xticks(0:10:75)
    ylim([0 5]); yticks(0:1:5)

    % Subplot Y
    subplot(3,1,2)
    hold on; box on;
    plot(t, Y(:,1), 'x', 'Color', c2_obs)
    plot(t, Y(:,2), '-', 'Color', c2_mod)
    ylabel('$y(t)$','Interpreter','latex')
```

```
    xlabel('$t\ \mathrm{[days]}$', 'Interpreter','latex')  % ← Corregido
    legend({'$yo$','$ya$'}, 'Interpreter','latex', 'Location',
'eastoutside','Box','on')
    xlim([0 75]); xticks(0:10:75)
    ylim([0 25]); yticks(0:5:25)

    % Subplot Z
    subplot(3,1,3)
    hold on; box on;
    plot(t, Z(:,1), 'x', 'Color', c3_obs)
    plot(t, Z(:,2), '-', 'Color', c3_mod)
    xlabel('$t\ \mathrm{[days]}$', 'Interpreter','latex')  % ← Corregido
    ylabel('$z(t)$','Interpreter','latex')
    legend({'$zo$','$za$'}, 'Interpreter','latex', 'Location',
'eastoutside','Box','on')
    xlim([0 75]); xticks(0:10:75)
    ylim([0 10]); yticks(0:2:10)
end
```

2t Predict

```
function [t, x, y, z] = Predict(x0, y0, z0, dt, tend, P)

    rho1 = P(1);
    rho2 = P(2);
    rho3 = P(3);
    rho4 = P(4);
    rho5 = P(5);
    rho6 = P(6);
    %rho7 = P(7);


    t = (0:dt:tend)';
    N = length(t);
    x = zeros(N, 1); x(1) = x0;
    y = zeros(N, 1); y(1) = y0;
    z = zeros(N, 1); z(1) = z0;


    for i = 1:N-1
        [fx, fy, fz] = f(x(i), y(i), z(i));
        xn = x(i) + fx * dt;
        yn = y(i) + fy * dt;
        zn = z(i) + fz * dt;
        [fxn, fyn, fzn] = f(xn, yn, zn);

        x(i+1) = x(i) + (fx + fxn) * dt / 2;
```

```
        y(i+1) = y(i) + (fy + fyn) * dt / 2;
        z(i+1) = z(i) + (fz + fzn) * dt / 2;
    end


    function [dx, dy, dz] = f(x, y, z)
         dx = rho1 * x * y * z + rho2 * x * y^2;
         dy = rho3 * y - rho4 * x * y;
         dz = rho5 * z - rho6 * x * z;
    end
end
```