BIOE60024 – Modelling in Biology

Coursework 1

Hongyu Rui
CID: 02069033
December 26, 2023

Question1

1(a)

As for G1

$$\frac{d[G_1]}{dt} = \alpha[G_1] + \beta[G_4] - \gamma[G_1][G_2]$$

$$d[G_1] = \frac{\alpha^2}{\beta\delta} dg_1,$$

$$dt = \frac{1}{\alpha} d\tau,$$

$$\frac{d[G1]}{dt} = \frac{\alpha^2}{\beta\delta} \cdot \alpha \cdot \frac{dg_1}{d\tau} = \frac{\alpha^3}{\beta\delta} \frac{dg_1}{d\tau}.$$

$$\therefore \frac{\alpha^3}{\beta\delta} \frac{dg_1}{d\tau} = \frac{\alpha^3}{\beta\delta} g_1 + \frac{\alpha^3}{\beta^2\delta} \cdot \beta \cdot g_4 - \gamma \left(\frac{\alpha^2}{\beta\delta}\right)^2 g_1 g_2,$$

$$\frac{dg_1}{d\tau} = g_1 + g_4 - \gamma \cdot \frac{\alpha^4}{\beta^2\delta^2} \cdot \frac{\beta\delta}{\alpha^3} g_1 g_2$$

$$= g_1 + g_4 - \gamma \cdot \frac{\alpha}{\beta \cdot \delta} g_1 g_2$$

$$= g_1 + g_4 - \mu g_1 g_2,$$

where $\mu = \gamma \cdot \dfrac{\alpha}{\beta \cdot \delta}$

For G2

$$\frac{d[G_2]}{dt} = \alpha[G_2] + \beta[G_3] - \gamma[G_1][G_2]$$

$$d[G_2] = \frac{\alpha^2}{\beta\delta} dg_2,$$

$$dt = \frac{1}{\alpha} d\tau,$$

$$\frac{d[G_2]}{dt} = \frac{\alpha^3}{\beta\delta} \frac{dg_2}{d\tau}.$$

$$\frac{\alpha^3}{\beta\delta} \frac{dg_2}{d\tau} = \frac{\alpha^3}{\beta\delta} g_2 + \frac{\alpha^3}{\beta\delta} g_3 - \gamma \left(\frac{\alpha^2}{\beta\delta}\right)^2 g_1 g_2,$$

$$\frac{dg_2}{d\tau} = g_2 + g_3 - \gamma \cdot \frac{\alpha^4}{\beta^2\delta^2} \cdot \frac{\beta\delta}{\alpha^3} g_1 g_2$$

$$= g_2 + g_3 - \gamma \cdot \frac{\alpha}{\beta\delta} g_1 g_2$$

$$= g_2 + g_3 - \mu g_1 g_2$$

where $\mu = \gamma \cdot \dfrac{\alpha}{\beta\delta}$

For G3

$$
\begin{aligned}
\frac{d[G_3]}{dt} &= \delta([G_1]-[G_2])^2 - \epsilon[G_1][G_2] \\
d[G_3] &= \frac{\alpha^3}{\beta^2\delta} dg_3, \\
dt &= \frac{1}{\alpha} d\tau. \\
\frac{d[G_3]}{dt} &= \frac{\alpha^4}{\beta^2\delta}\frac{dg_3}{d\tau} \\
\frac{\alpha^4}{\beta^2\delta}\frac{dg_3}{d\tau} &= \delta \cdot \frac{\alpha^4}{\beta^2\delta^2}(g_1-g_2)^2 - \epsilon\left(\frac{\alpha^3}{\beta^2\delta}\right)^2 g_3g_4 \\
\frac{dg_3}{d\tau} &= (g_1-g_2)^2 - \epsilon \cdot \frac{\alpha^6}{\beta^4\delta^2} \cdot \frac{\beta^2\delta}{\alpha^4} g_3g_4 \\
&= (g_1-g_2)^2 - \epsilon \cdot \frac{\alpha^2}{\beta^2\delta} g_3g_4 \\
\text{where } v &= \epsilon \cdot \frac{\alpha^2}{\beta^2\delta} \\
&= (g_1-g_2)^2 - vg_3g_4.
\end{aligned}
$$

For G4

$$
\begin{aligned}
\frac{d[G_4]}{dt} &= \eta - \epsilon[G_3][G_4] \\
d[G_4] &= \frac{\alpha^3}{\beta^2\delta} dg_4. \\
dt &= \frac{1}{\alpha} d\tau, \\
\frac{d[G_4]}{dt} &= \frac{\alpha^4}{\beta^2\delta}\frac{dg_4}{d\tau}. \\
\frac{\alpha^4}{\beta^2\delta}\frac{dg_4}{d\tau} &= \eta - \epsilon\left(\frac{\alpha^3}{\beta^2\delta}\right)^2 g_3g_4 \\
\frac{dg_4}{d\tau} &= \eta \cdot \frac{\beta^2\delta}{\alpha^4} - \epsilon \cdot \frac{\alpha^6}{\beta^4\delta^2} \cdot \frac{\beta^2\delta}{\alpha^4} g_3g_4 \\
&= \eta \cdot \frac{\beta^2\delta}{\alpha^4} - \epsilon \cdot \frac{\alpha^2}{\beta^2\delta} g_3g_4 \\
\text{where } v &= \epsilon \cdot \frac{\alpha^2}{\beta^2\delta}, \quad \rho = \eta \cdot \frac{\beta^2\delta}{\alpha^4} \\
&= \rho - vg_3g_4.
\end{aligned}
$$

1(b)

$$
\begin{aligned}
\dot{x} &= \dot{g}_1 - \dot{g}_2 \\
&= g_1 + g_4 - \sigma g_1 g_2 - g_2 - g_3 + \mu g_1 g_2 \\
&= (g_1 - g_2) - (g_3 - g_4) \\
\because x &= g_1 - g_2 \\
y &= g_3 - g_4 \\
\therefore \dot{x} &= x - y \\
\dot{y} &= \dot{g}_3 - \dot{g}_4 \\
&= (g_1 - g_2)^2 - \nu g_3 g_4 - \rho + \nu g_3 g_4 \\
&= x^2 - \rho
\end{aligned}
$$

1(C)

Find x^* and y^*

$$
\begin{aligned}
&\dot{x} = 0 \\
&\dot{y} = 0 \\
&x - y = 0 \\
&x^2 - \rho = 0 \\
&\because \rho > 0 \\
&\therefore x^* = \pm\sqrt{\rho} \\
&x^* = y^* = \pm\sqrt{\rho}
\end{aligned}
$$

1(d)

The eigenvalues of the Jacobian matrix is found for the two fixed point, the calculation is in the next page. For fixed point $x = y = \sqrt{\rho}$,

$\lambda = \dfrac{1 \pm \sqrt{1 - 8\sqrt{\rho}}}{2}$, if $1 - 8\sqrt{\rho} > 0$, both eigenvalues always have positive real part, which make this fixed point unstable. If $1 - 8\sqrt{\rho} < 0$ both eigenvalues will also have real positive part, which make the point unstable.

For fixed point $x = y = -\sqrt{\rho}$, $\lambda = \dfrac{1 \pm \sqrt{1 + 8\sqrt{\rho}}}{2}$, $1 + 8\sqrt{\rho} > 0$, because $\rho > 0$. It gonna make one eigenvalue have real positive part and the other have negative. The fixed point is a Saddle point.

$$
\begin{aligned}
\text{Make } x_1 &= x, \quad x_2 = y, \\
X &= \begin{bmatrix} x_1 \\ x_2 \end{bmatrix}, \\
\dot{x}_1 &= f_1(\mathbf{x}) = x_1 - x_2, \\
\dot{x}_2 &= f_2(\mathbf{x}) = x_1^2 - \rho, \\
J(X^*) &= \begin{bmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} \end{bmatrix} = \begin{bmatrix} 1 & -1 \\ 2x_1 & 0 \end{bmatrix}, \\
\text{For } x_1 &= x_2 = \sqrt{\rho}, \\
J(X^*) &= \begin{bmatrix} 1 & -1 \\ 2\sqrt{\rho} & 0 \end{bmatrix}, \\
\det(\lambda I - J) &= 0, \quad \lambda = \ ? \\
\det \begin{bmatrix} \lambda - 1 & 1 \\ -2\sqrt{\rho} & \lambda \end{bmatrix} &= 0, \\
(\lambda - 1)\lambda + 2\sqrt{\rho} &= 0, \\
\lambda^2 - \lambda + 2\sqrt{\rho} &= 0, \\
\lambda &= \frac{1 \pm \sqrt{1 - 8\sqrt{\rho}}}{2}, \\
\lambda_1 &= \frac{1}{2} + \frac{\sqrt{1 - 8\sqrt{\rho}}}{2}, \\
\lambda_2 &= \frac{1}{2} - \frac{\sqrt{1 - 8\sqrt{\rho}}}{2}, \\
\text{For } x_1 &= x_2 = -\sqrt{\rho}, \\
J(X^*) &= \begin{bmatrix} 1 & -1 \\ -2\sqrt{\rho} & 0 \end{bmatrix}, \\
\det(\lambda I - J) &= 0, \quad \lambda = \ ? \\
\det \begin{bmatrix} \lambda - 1 & 1 \\ 2\sqrt{\rho} & \lambda \end{bmatrix} &= 0, \\
(\lambda - 1)\lambda - 2\sqrt{\rho} &= 0, \\
\lambda &= \frac{1 \pm \sqrt{1 + 8\sqrt{\rho}}}{2}, \\
\lambda_1 &= \frac{1}{2} + \frac{\sqrt{1 + 8\sqrt{\rho}}}{2}, \\
\lambda_2 &= \frac{1}{2} - \frac{\sqrt{1 + 8\sqrt{\rho}}}{2},
\end{aligned}
$$

1(e)

Fixed points: $(1,1), (-1,-1)$.

Nullclines: $\dot{x} = x - y = 0 \Rightarrow y = x$

$\dot{y} = x^2 - 1 = 0 \Rightarrow x = \pm 1$

For $(1,1)$:

$1 - 8\sqrt{\rho} = 1 - 8 = -7 < 0$

$\sqrt{-7} = \sqrt{7}i$

unstable, spiral.

Plug point near

$x = 1.5$

$y = 1.$

$\dot{y} = 1.25$

anti-clockwise.

For $(-1,-1)$:

$1 + 8\sqrt{\rho} = 9 > 0$

saddle point.

$$J = \begin{pmatrix} 1 & -1 \\ -2 & 0 \end{pmatrix}$$

$\lambda_1 = 2, \quad \lambda_2 = -1$

Eigenvector of J:

$$\begin{pmatrix} 2-1 & 1 \\ 2 & 2 \end{pmatrix} \mathbf{v}_1 = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

$$\mathbf{v}_1 = \begin{pmatrix} 1 \\ -1 \end{pmatrix} \cdot t$$

$$\begin{pmatrix} -1-1 & -1 \\ -2 & -1 \end{pmatrix} \mathbf{v}_2 = \begin{pmatrix} 0 \\ 0 \end{pmatrix},$$

$$\mathbf{v}_2 = \begin{pmatrix} 1 \\ 2 \end{pmatrix} t.$$

$t \in \mathbb{R}$

$\because |\lambda_1| > |\lambda_2|$

$|2| > |-1|$

$\therefore$ the divergence along V1 is faster than the convergence along V2.

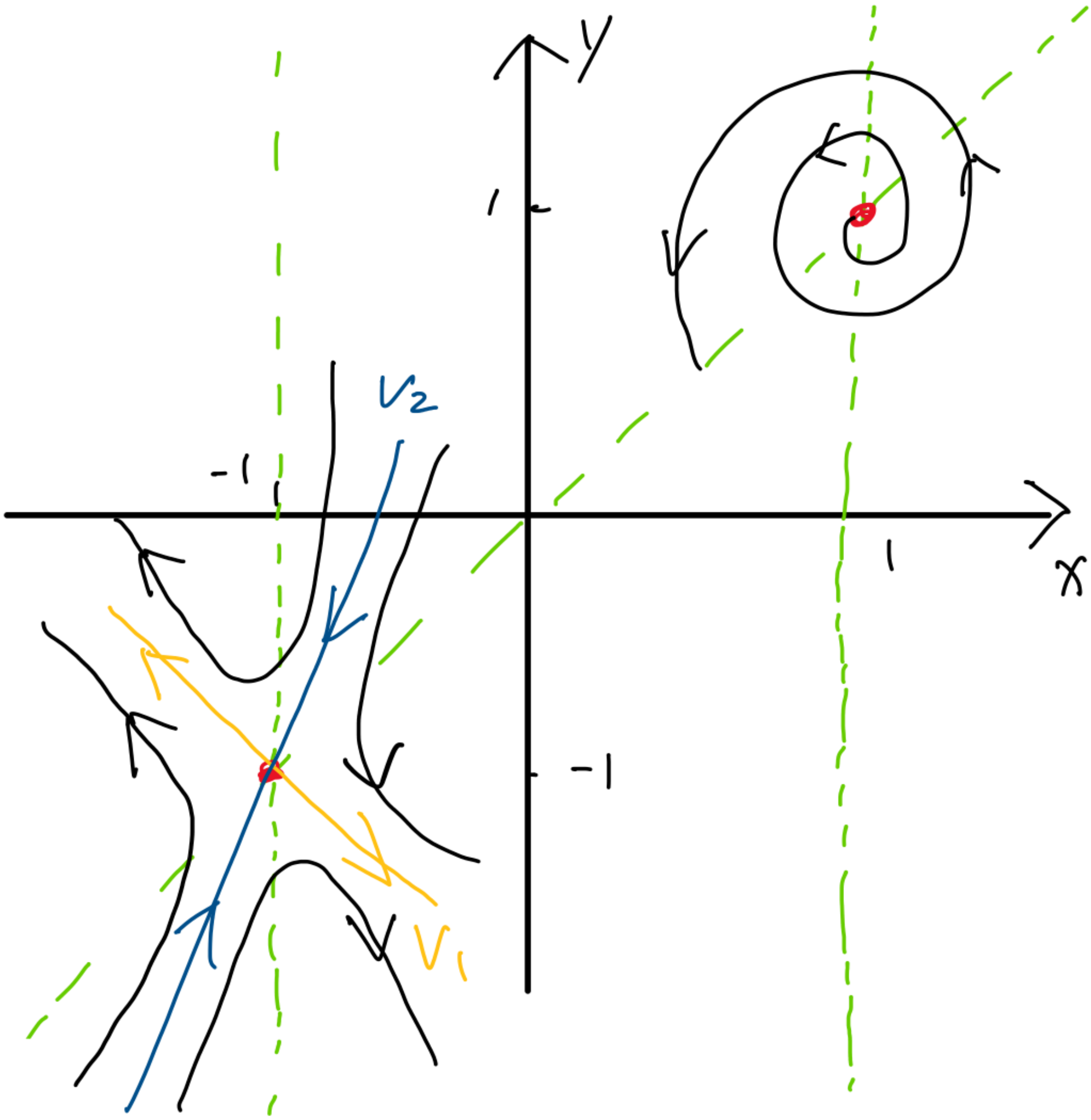

Figure1

Figure1 is the sketch of the phase-plane (x-y), nullclines is indicated with green dotted lines and fixed point is indicated by red points.

1(f)

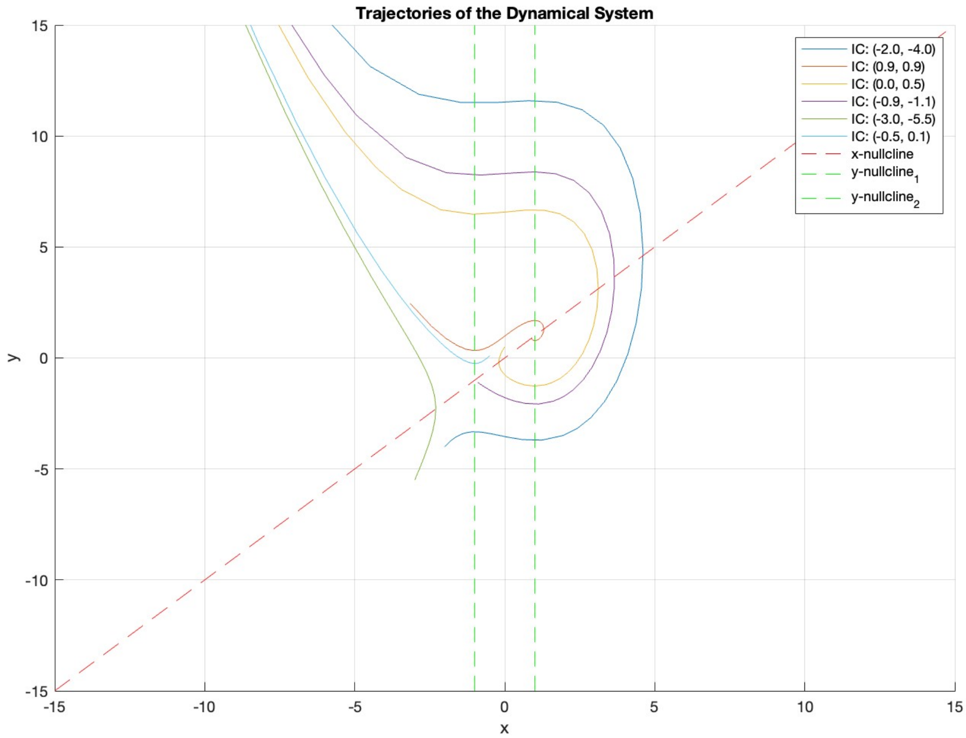

Figure2

The evolution of trajectories over the time is shown is Figure2, more detailed Matlab code can be find in Appendix A in the very end of the document.

1(g)

The model is designed to simulate the concentrations of four different genes: G1, G2, G3, and G4. Ultimately, either G1 and G4 dominate, or G2 and G3 dominate, as indicated in the question. This outcome is represented by the transformation of variables into x and y. Consequently, a scenario where x is positive and y is negative, or vice versa, is expected. Figure 2 illustrates the latter scenario, aligning with real-world observations. Additionally, the system balances simplicity and accuracy. For instance, the transcription factors and mutually destructive factors are related to the environment. Instead of modelling these as variables within a subsystem, the system treats them as parameters. This approach may sacrifice some accuracy but enhances the system's simplicity, making it more user-friendly. Overall, it is a good model.

Question 2

2(a)

Make $\dot{v} = 0, \dot{w} = 0$. Get $v = 5, w = 26$

2(b)

Find $J(v^*, w^*)$:

$$J = \begin{pmatrix} \frac{\partial \dot{v}}{\partial v} & \frac{\partial \dot{v}}{\partial w} \\ \frac{\partial \dot{w}}{\partial v} & \frac{\partial \dot{w}}{\partial w} \end{pmatrix}$$

$$= \begin{pmatrix} -1 - \frac{4w(1-v^2)}{(1+v^2)^2} & -\frac{4v}{1+v^2} \\ b \cdot \frac{v^2 w - w}{(v^2+1)^2} + 1 & -\frac{bv}{1+v^2} \end{pmatrix}$$

With $v^* = 5,\ w^* = 26$:

$$J = \begin{pmatrix} \frac{35}{13} & -\frac{10}{13} \\ \frac{25b}{13} & -\frac{5b}{26} \end{pmatrix}$$

For $\det(\lambda I - J) = 0$:

$$\det \begin{pmatrix} \lambda - \frac{35}{13}, & \frac{10}{13} \\ -\frac{25b}{13}, & \lambda + \frac{5b}{26} \end{pmatrix} = 0$$

$$\lambda = -\frac{5b}{52} + \frac{35}{26} \pm \frac{5 \cdot \sqrt{b^2 - 132b + 196}}{52}$$

make sure $-\frac{5b}{13} + \frac{35}{26} < 0$

$$-5b + 35 \times 2 < 0$$
$$-b + 14 < 0$$
$$-b < -14$$
$$b > 14$$

2(c)

To proof there is a limit circle in certain area, need to find that area not contain any fixed point and being attractive (The Poincare-Bendixson

Theorem). Considering the lines defined in the question, the phase plane visualise it is shown in Figure3, only need to make sure the outer red box's each edge flow inside and the little green circle around the fixed point flow outside, which will make the area between red box and green circle attractive without a fixed point inside.

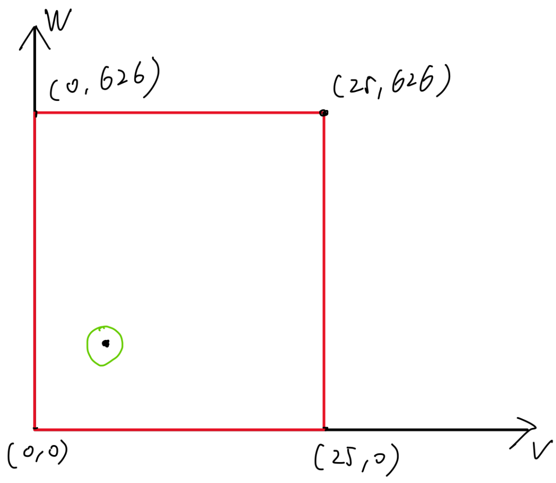

Figure3

As for the outer red box to make sure it only flow inside, it need to satisfy those a few conditions:

$$v = 0, \dot{v} > 0; w = 0, \dot{w} > 0; v = 25, \dot{v} < 0; w = 626, \dot{w} < 0$$

For v = 0:

$$\begin{aligned} \dot{v} &= 25 \\ \dot{w} &= 0 \\ \dot{v} &> 0 \end{aligned}$$

For w = 0:

$$\begin{aligned} \dot{v} &= 25 - v \\ \dot{w} &= bV(1 - s) = bV \\ \because 25 &> v > 0 \\ \therefore bv &> 0 \\ \dot{w} &> 0 \end{aligned}$$

For v = 25:

$$\begin{aligned} \dot{v} &= 25 - 25 - \frac{4 \cdot 25 \cdot w}{1 + 25^2} \\ &= -\frac{100}{626}w \\ \dot{w} &= b \cdot 25 \cdot \left(1 - \frac{w}{1 + 25^2}\right) \\ &= b \cdot 25 \cdot \left(1 - \frac{w}{626}\right), \\ &= b \cdot 25 \cdot \frac{626 - w}{626}. \\ \because 626 &> w > 0, \\ \therefore -\frac{100}{626}w &< 0, \\ \dot{v} &< 0. \end{aligned}$$

For w = 626:

$$
\begin{aligned}
\dot{v} &= 25 - v - \frac{4 \cdot v \cdot 626}{1 + v^2} \\
\dot{w} &= bV\left(1 - \frac{626}{1 + fV^2}\right) \\
&\because 0 < v < 25, b > 0 \\
&\therefore 1 + v^2 < 626 \\
&\frac{626}{1 + v^2} > 1 \\
&1 - \frac{626}{1 + v^2} < 0 \\
&bv\left(1 - \frac{626}{1 + v^2}\right) < 0 \\
&\dot{w} < 0
\end{aligned}
$$

The four conditions for the outer red box(Figure3) is satisfied without any extra constrain on b. However, as for the little green circle(Figure3), when $b > 14$ the fixed point is going to be an attractive point, which would not make the region between red box and green circle attractive. Only when $b < 14$, it is not an attractive point anymore, the flow will come out of the circle and make the defined area be attractive.
Therefore, there is a unit circle inside the region between the red box and green circle when $b < 14$.

2(d)

The Hopf bifurcation happens when $b = 14$. The v and w represents concentration as stated in the question, as b decrease, the system go though the Hopf bifurcation the limit cycle will occur and it means the v and w will oscillate. In the chemical system what can be observed is the concentration that v and w represent oscillate in certain range. As the b decrease further, the limit cycle will get bigger, which means the observed concentration oscillated in a wider range.

Appendix A

```
% Main script
rho = 1;  % Value of rho
tspan = [0 6];  % Time interval

% Initial conditions
init_conditions = [-2 -4; 0.9 0.9; 0 0.5; -0.9 -1.1; -3 -5.5; -0.5 0.1];


% Solve the system for each set of initial conditions
for i = 1:size(init_conditions, 1)
    % Solve the differential equation
    [t, y] = ode45(@dynamical_system, tspan, init_conditions(i, :));

    % Plot the results
    figure(1);
    hold on;
    plot(y(:,1), y(:,2),'DisplayName',sprintf('IC: (%.1f, %.1f)', init_conditions(i,:)));
end
xlabel('x');
ylabel('y');
% Plot the nullclines
x_nullcline = linspace(-15, 15, 400);
y_nullcline = x_nullcline;
plot(x_nullcline, y_nullcline, 'r--', 'DisplayName', 'x-nullcline');
plot([sqrt(rho), sqrt(rho)], [-15, 15], 'g--', 'DisplayName', 'y-nullcline_1');
plot([-sqrt(rho), -sqrt(rho)], [-15, 15], 'g--', 'DisplayName', 'y-nullcline_2');
title('Trajectories of the Dynamical System');
grid on;
hold off;
xlim([-15,15]);
ylim([-15,15]);
legend

function dydt = dynamical_system(t, y)
    dydt = [y(1) - y(2); y(1)^2 - 1];
end
```