

Modelling in Biology: Coursework

Part 1: Dynamical systems

Question 1: Diagonalization, in your own words

See written solution

Given the following system of linear ordinary differential equations:

$$\begin{cases} \dot{x}_1 = a_1 x_1 + b_1 x_2 + c_1 x_3 + \dots + z_1 x_n \\ \dot{x}_2 = a_2 x_1 + b_2 x_2 + c_2 x_3 + \dots + z_2 x_n \\ \dot{x}_3 = a_3 x_1 + b_3 x_2 + c_3 x_3 + \dots + z_3 x_n \\ \vdots \\ \dot{x}_n = a_n x_1 + b_n x_2 + c_n x_3 + \dots + z_n x_n \end{cases}$$

Such system can be written in the form $\dot{x} = Ax$ where:

$$\begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \dot{x}_3 \\ \vdots \\ \dot{x}_n \end{bmatrix} = \begin{bmatrix} a_1 & b_1 & c_1 & \dots & z_1 \\ a_2 & b_2 & c_2 & \dots & z_2 \\ a_3 & b_3 & c_3 & \dots & z_3 \\ \vdots & \vdots & \ddots & \ddots & \vdots \\ a_n & b_n & c_n & \dots & z_n \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ \vdots \\ x_n \end{bmatrix} \Leftrightarrow \dot{x} = Ax$$

Column vector
of dimensions
 $n \times 1$

Matrix
 $n \times n$

Column vector of
dimensions $n \times 1$

Now we can workout with the simpler equation

$$\dot{x} = Ax \Leftrightarrow \frac{dx}{dt} = Ax$$

$$\Leftrightarrow \frac{1}{x} dx = Adt$$

$$\Leftrightarrow \int \frac{1}{x} dx = \int Adt$$

$$\Leftrightarrow \ln(x) = At + C_1, \quad C_1 \in \mathbb{R}$$

$$\Leftrightarrow x = e^{At + C_1}$$

$$\Leftrightarrow x = e^{C_1} e^{At}$$

$$\Leftrightarrow x = x(0) e^{At}$$

e^{C_1} can be treated as $x(0)$ at $t=0$
as $e^{At} = 1$ for $t=0$.

~~REMEMBER~~

According to MacLaurin's Theorem:

$$e^{At} = \sum_{k=0}^{\infty} \frac{A^k t}{k}$$

Moreover, according to the spectral theorem:

$$A = V D V^{-1}$$

where, V is a matrix containing the eigenvectors of A as its columns

& D is the diagonal matrix of A which contains A 's eigenvalues in its diagonal.

Combining both theorems:

$$e^{At} = \sum_{k=0}^{\infty} \frac{(VDV^{-1})^k t}{k}$$

It can be shown that $(VDV^{-1})^k = V D^k V^{-1}$

As the multiplication of the eigenvector matrix by its inverted would give the identity matrix all the time.

$$\Rightarrow e^{At} = \sum_{k=0}^{\infty} \frac{V D^k V^{-1} t}{k}$$

$$\Leftrightarrow e^{At} = V \left(\sum_{k=0}^{\infty} \frac{D^k t}{k} \right) V^{-1} \quad \text{as } V \text{ and } V^{-1} \text{ have no dependence on } k$$

$$\Leftrightarrow e^{At} = V e^{Dt} V^{-1}$$

This implies:

$$\boxed{x(t) = V e^{Dt} V^{-1} x(0)}$$

Question 2: Bifurcation analysis

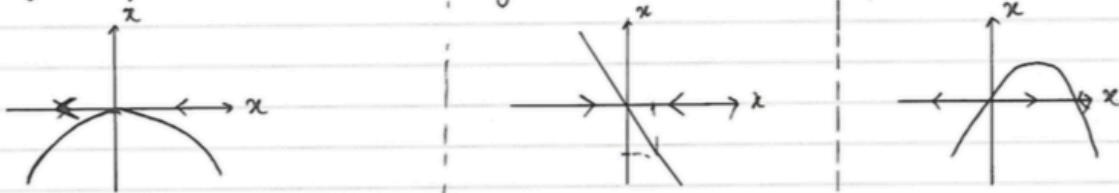
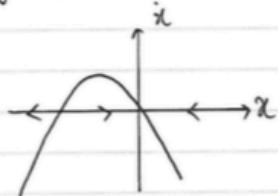
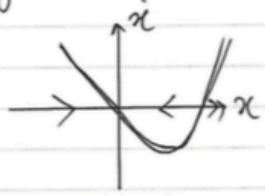
See written solution

SYSTEM 11. System 1

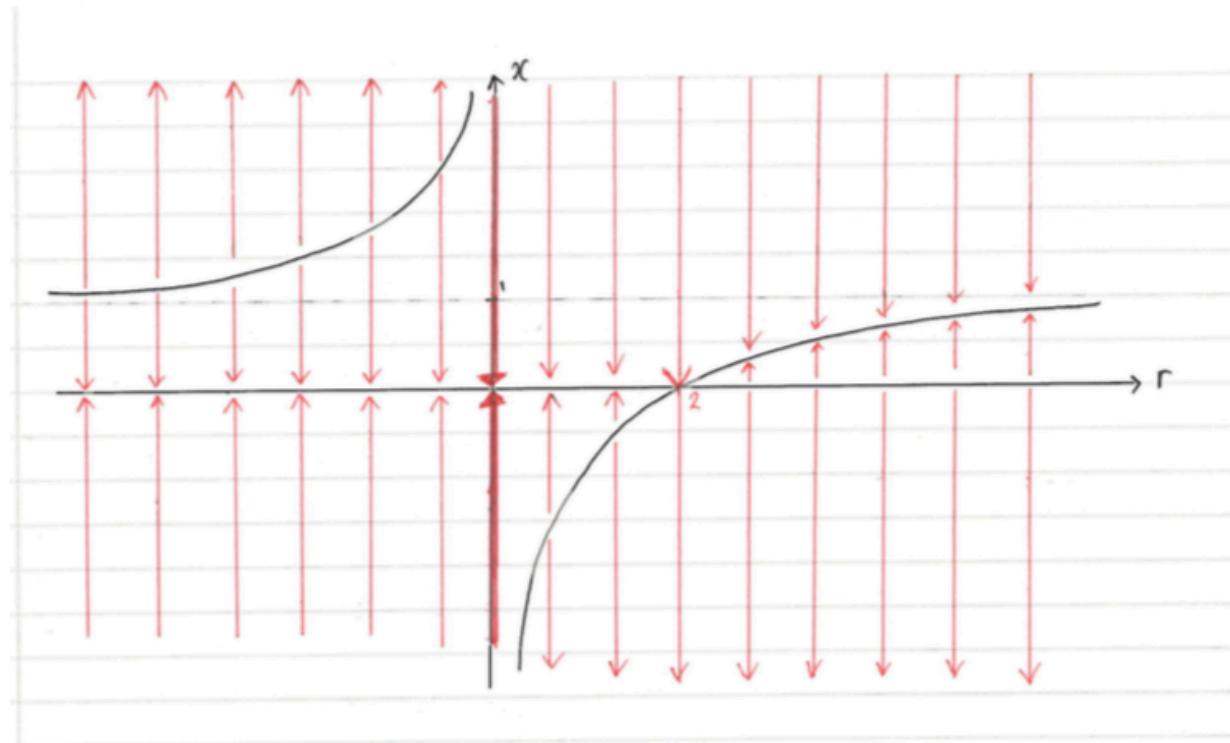
$$\begin{aligned}\dot{x} &= rx(1-x) - 2x \\ \Leftrightarrow \dot{x} &= -rx^2 + x(r-2)\end{aligned}$$

(a) • Fixed points:

$$\begin{aligned}0 &= rx(1-x) - 2x \quad \rightsquigarrow \boxed{x_1^* = 0} \\ \Rightarrow 0 &= r(1-x) - 2 \\ \Rightarrow 2 &= r(1-x) \\ \Rightarrow 1-x &= \frac{2}{r} \Rightarrow \boxed{x_2^* = 1 - \frac{2}{r}}\end{aligned}$$

• Phase portrait & Stability analysisfor $r = 2 \Rightarrow \dot{x} = -2x^2$ | for $r = 0 \Rightarrow \dot{x} = -2x$ | for $r > 2$ for $0 < r < 2$ for $r < 0$ • Bifurcation Diagram (can be seen on the back/next page)

As we can see in the bifurcation diagram at r equal to 2, the stability of the fixed point is reversed. The fixed point $x_1^* = 0$ is stable for values ~~less than~~ of r inferior to 2 and for r greater than 2 this fixed point becomes unstable. The opposite happens with the fixed point $x_2^* = 1 - \frac{2}{r}$.



SYSTEM 2

System 2:

$$\begin{cases} \dot{x}_1 = a + x_1^2 x_2 - (b+1)x_1 & (1) \\ \dot{x}_2 = bx_1 - x_1^2 x_2 \end{cases}$$

$$\begin{cases} \dot{x}_1 = 0 & (3) \\ \dot{x}_2 = 0 & (4) \end{cases} \Rightarrow (3)(4) \quad 0 = a - (b+1)x_1 + bx_1$$

$$\begin{cases} \dot{x}_1 = 0 & (3) \\ \dot{x}_2 = 0 & (4) \end{cases} \Rightarrow (3)(4) \quad 0 = a - (b+1)x_1 + bx_1$$

$$\Rightarrow 0 = a - b x_1 - x_1 + b x_1$$

$$\Rightarrow 0 = a - x_1 \Rightarrow x_1^* = a$$

Now, we plug this solution into equation (4):

$$0 = b a - a^2 x_2^* \Rightarrow \begin{cases} x_2^* = b/a \\ x_2^* = b/a \end{cases}$$

The fixed point has the following coordinates:

$$P = (a; \frac{b}{a})$$

We will first find the Jacobian matrix, and then the Jacobian matrix at the fixed point.

$$J = \begin{pmatrix} \frac{\partial(\dot{x}_1)}{\partial x_1} & \frac{\partial(\dot{x}_1)}{\partial x_2} \\ \frac{\partial(\dot{x}_2)}{\partial x_1} & \frac{\partial(\dot{x}_2)}{\partial x_2} \end{pmatrix}$$

$$\Rightarrow J = \begin{pmatrix} 2x_1 x_2 - (b+1) & x_1^2 \\ b - 2x_1 x_2 & -x_1^2 \end{pmatrix}$$

@ Fixed point

$$J\left(a; \frac{b}{a}\right) = \begin{pmatrix} 2b - b - 1 & a^2 \\ b - 2b & -a^2 \end{pmatrix}$$

$$J(a; \frac{b}{a}) = \begin{pmatrix} b-1 & a^2 \\ -b & -a^2 \end{pmatrix}$$

$$\det |J - \lambda I| = \left| \begin{pmatrix} b-1-\lambda & a^2 \\ -b & -a^2-\lambda \end{pmatrix} \right|$$

$$= -(b-1-\lambda)(a^2+\lambda) + a^2b$$

$$= -[a^2b + b\lambda - a^2 - \lambda - \lambda a^2 - \lambda^2] + a^2b$$

$$= -a^2b \cancel{-b\lambda + a^2 + \lambda + \lambda a^2 + \lambda^2 + a^2b} - b\lambda$$

$$\det(J - \lambda I) = \lambda^2 - \lambda(b - a^2 - 1) + a^2 \quad (3)$$

$$\Rightarrow (3) = 0$$

$$\lambda^2 - \lambda(b - a^2 - 1) + a^2 = 0$$

$$\Leftrightarrow \lambda_{\pm} = \frac{(b-a^2-1) \pm \sqrt{(b-a^2-1)^2 - 4a^2}}{2}$$

The trace γ of J is:

$$\gamma = b - a^2 - 1$$

The determinant Δ of J is:

$$\Delta = a^2$$

We will break this down to different cases (from A to F)

$$\cdot \Delta > 0 \Rightarrow a^2 > 0 \Rightarrow a \in \mathbb{R}$$

The following derivations consider a to be positive.

$$\Rightarrow \gamma > 0$$

$$\Rightarrow b - a^2 - 1 > 0$$

$$\Leftrightarrow b > a^2 + 1$$

$$\text{and } (b - a^2 - 1)^2 - 4a^2 > 0$$

$$\Leftrightarrow (b - a^2 - 1)^2 - (2a)^2 > 0$$

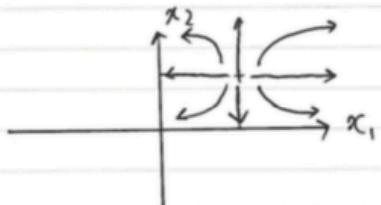
$$\Leftrightarrow (b - a^2 - 1)^2 > (2a)^2$$

$$\Leftrightarrow |b - a^2 - 1| > |2a|$$

$$\Leftrightarrow \text{---} -2a \text{ ---} 0 \text{ ---} 2a \text{ ---} \Rightarrow \begin{cases} b - a^2 - 1 > 2a \\ b - a^2 - 1 < -2a \end{cases}$$

$$\Rightarrow \begin{cases} b > 2a + a^2 + 1 \\ b < -2a + a^2 + 1 \end{cases} \Rightarrow \boxed{\begin{cases} b > (a+1)^2 \\ b < (a-1)^2 \end{cases}}$$

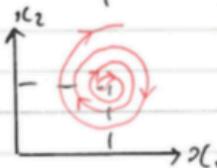
This is case A which corresponds to an unstable node.



Eigenvalues are positive and real.

- and $(b - a^2 - 1)^2 - 4a^2 < 0$
 $\Leftrightarrow (a-1)^2 < b < (a+1)^2$

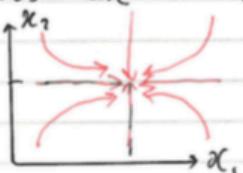
This gives us case B, an unstable spiral.
 Eigenvalues are complex conjugates with positive real parts.



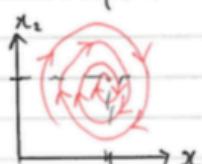
for $\gamma < 0$
 $\Leftrightarrow b - a^2 - 1 < 0$
 $\Leftrightarrow b < a^2 + 1$

- and $(b - a^2 - 1)^2 - 4a^2 > 0$
 $\Leftrightarrow \begin{cases} b > 2a + a^2 + 1 \\ b < -2a + a^2 + 1 \end{cases}$

The fixed point corresponds to a stable node.
 Eigenvalues are real (purely) and negative.



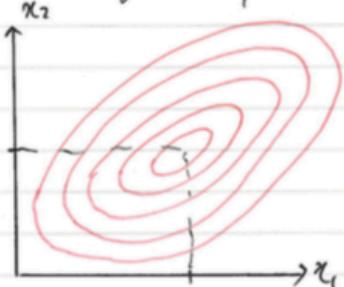
■ and $(a-1)^2 < b < (a+1)^2$
 The fixed point is a stable spiral. The eigenvalues of the Jacobian matrix for the coordinates of this fixed point would be complex conjugates with negative real parts.



$$\rightarrow \text{for } \gamma = 0 \Rightarrow b = a^2 + 1$$

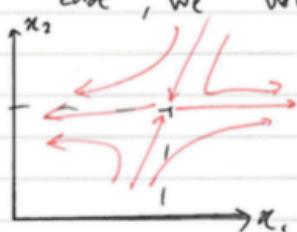
Thus \Rightarrow ~~the~~ a critical point as any slight change from this value of b would change the stability of the system.

In this case both eigenvalues are purely imaginary with opposite values. The fixed point stability is called center.

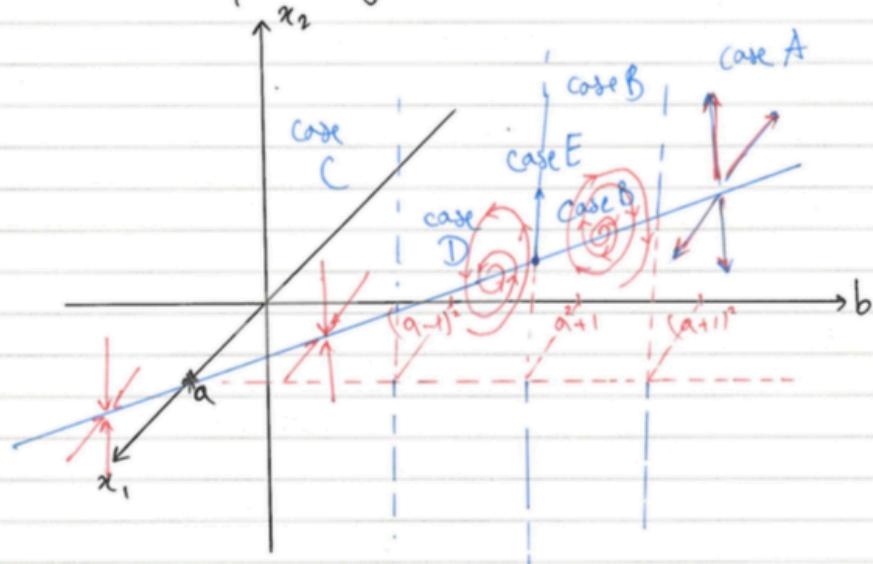


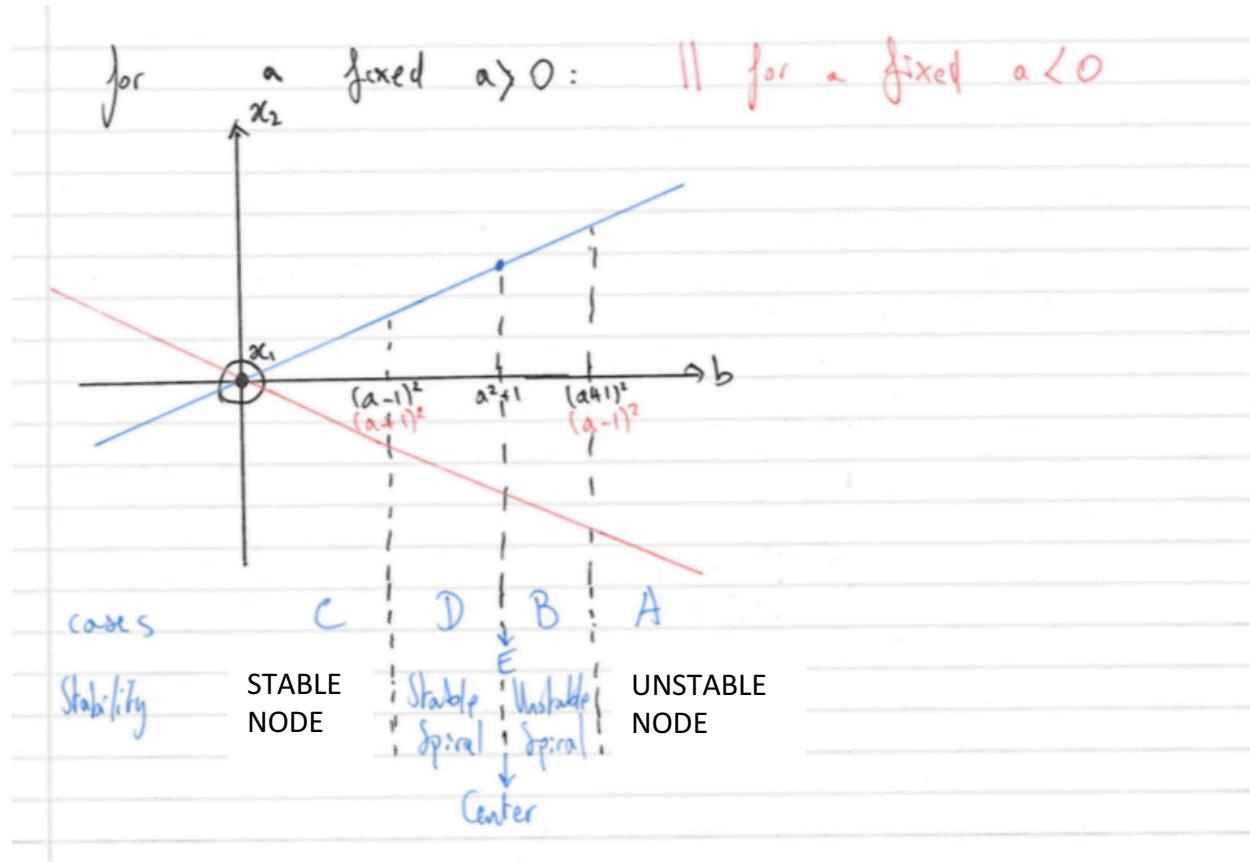
$$\text{if } a^2 < 0 \Rightarrow a \in \mathbb{C} \rightsquigarrow a = ki ; k \in \mathbb{R}$$

in this last case, we will a saddle point.



(b) The plot of system 2 is:





The Hopf bifurcation happens when the system goes from stable to unstable, i.e. when b goes from being less than a^2+1 to being greater than a^2+1 .

Question 3: The Lotka-Volterra equations: Linear analysis around fixed points
 See written solution

$$\begin{cases} \dot{r} = r(3 - 2r - s) & (1) \\ \dot{s} = s(2 - r - s) & (2) \end{cases}$$

(a) The fixed points can be found at the values of r and s equal to 0, mathematically:

$$\begin{array}{l} (1) \\ (2) \end{array} \Rightarrow \begin{cases} r(3 - 2r - s) = 0 \\ s(2 - r - s) = 0 \end{cases}$$

An obvious solution to this system is

$$\begin{cases} r=0 \\ s=0 \end{cases} \quad FP_1 = (0, 0)$$

If we further set r to 0 we can get the following from equation (2):

$$r=0 \Rightarrow (2) \Rightarrow s(2 - 0 - s) = 0$$

As the solution $s=0$ has already been taken:

Our second fixed point is: $FP_2 = (0, 2)$

In a similar for $s=0$:

$$s=0 \rightarrow (1) \Rightarrow r(3 - 2r) = 0$$

Our third fixed point is: $FP_3 = (1.5, 0)$

Finally taking $r, s \neq 0$ and setting (1) and (2) equal:

$$1/3 - 2/3r - s = 1/2 - 1/r - s$$

$\Rightarrow 1 - r = 0 \Rightarrow \boxed{r=1} \rightarrow$ We plug this back onto (1)

$$1 \times (3 - 2 \times 1 - s) = 0 \Rightarrow \frac{1-s}{s=1} = 0$$

Our fourth fixed point is $FP_4 = (1, 1)$

(b) Now we will find the Jacobian matrix for the system, and its eigenvalues for the coordinates of all the fixed points.

$$J = \begin{pmatrix} \frac{\partial(r)}{\partial r} & \frac{\partial(r)}{\partial s} \\ \frac{\partial(s)}{\partial r} & \frac{\partial(s)}{\partial s} \end{pmatrix}$$

$$J = \begin{pmatrix} 3 - 4r - s & -r \\ -s & 2 - r - 2s \end{pmatrix}$$

→ for $FP_1 = (0, 0)$

$$J(FP_1) = \begin{pmatrix} 3 & 0 \\ 0 & 2 \end{pmatrix}$$

Here, the eigenvalues are:

$$\begin{cases} \lambda_{1,1} = 3 \\ \lambda_{1,2} = 2 \end{cases}$$

Both eigenvalues being positive and purely real reveals this fixed point is an unstable node.

→ for $FP_2 = (0, 2)$

$$J(FP_2) = \begin{pmatrix} 3 - 4 \times 0 - 2 & 0 \\ -2 & 2 - 0 - 2 \times 2 \end{pmatrix}$$

$$\Rightarrow J(FP_2) = \begin{pmatrix} 1 & 0 \\ -2 & -2 \end{pmatrix}$$

$$\det [J(FP_2) - \lambda I] = -(1-\lambda)(2+\lambda)$$

$$\begin{cases} \lambda_{2,1} = 1 \\ \lambda_{2,2} = -2 \end{cases}$$

In this case, $\lambda_{2,2} < 0 < \lambda_{2,1}$, which corresponds to a Saddle point.

$$\rightarrow \text{for } FP_3 = (1.5, 0)$$

$$J(FP_3) = \begin{pmatrix} 3-6 & -1.5 \\ 0 & 0.5 \end{pmatrix} = \begin{pmatrix} -3 & -1.5 \\ 0 & 0.5 \end{pmatrix}$$

$$\det(J(FP_3) - \lambda I) = -(3+\lambda)(0.5-\lambda)$$

$$\begin{cases} \lambda_{3,1} = -3 \\ \lambda_{3,2} = 0.5 \end{cases}$$

This again, corresponds to a saddle point.

$$\rightarrow \text{for } FP_4 = (1, 1)$$

$$J(FP_4) = \begin{pmatrix} 3-4-1 & -1 \\ -1 & 2-1-2 \end{pmatrix} = \begin{pmatrix} -2 & -1 \\ -1 & -1 \end{pmatrix}$$

$$\det(J(FP_4) - \lambda I) = (2+\lambda)(1+\lambda) - 1$$

$$\begin{aligned} &= 2 + 3\lambda + \lambda^2 - 1 \\ &= \lambda^2 + 3\lambda + 1 \end{aligned}$$

$$\lambda_{4,1}; \lambda_{4,2} = \frac{-3 \pm \sqrt{9-4}}{2}$$

$$\begin{cases} \lambda_{4,1} = \frac{-3 + \sqrt{5}}{2} < 0 \\ \lambda_{4,2} = \frac{-3 - \sqrt{5}}{2} < 0 \end{cases}$$

Both eigenvalues are negative and purely real, which corresponds to a stable node.

(c) With the previously found eigenvalues we are going to find eigenvectors for all the fixed points:

$$\rightarrow \text{for } FP_1 \quad \begin{cases} \lambda_{1,1} = 3 \\ \lambda_{1,2} = 2 \end{cases}$$

$$A = J(FP_1) - \lambda_{1,1} I = \begin{pmatrix} 0 & 0 \\ 0 & -1 \end{pmatrix}$$

$$A \vec{x} = 0 \Rightarrow \begin{pmatrix} 0 & 0 \\ 0 & -1 \end{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

$$y = 0$$

$$\boxed{v_1 = \begin{pmatrix} 1 \\ 0 \end{pmatrix}}$$

$$B = J(FP_1) - \lambda_{1,1} I = \begin{pmatrix} 1 & 0 \\ 0 & 0 \end{pmatrix}$$

$$B\vec{x} = 0 \Rightarrow x=0$$

$$\boxed{v_2 = \begin{pmatrix} 0 \\ 1 \end{pmatrix}}$$

$$\rightarrow \text{for } FP_2 \quad \left\{ \begin{array}{l} \lambda_{2,1} = 1 \\ \lambda_{2,2} = -2 \end{array} \right.$$

~~$$C = J(FP_2) - \lambda_{2,1} I = \begin{pmatrix} 0 & 0 \\ -2 & -3 \end{pmatrix}$$~~

$$C\vec{x} = 0 \Rightarrow -2x - 3y = 0$$

$$\Rightarrow -2x = 3y \Rightarrow \boxed{v_3 = \begin{pmatrix} -3 \\ 2 \end{pmatrix}}$$

$$D = J(FP_2) - \lambda_{2,2} I = \begin{pmatrix} 3 & 0 \\ -2 & 0 \end{pmatrix}$$

$$D\vec{x} = 0 \Rightarrow 3x = 0 \Rightarrow x=0$$

$$\boxed{v_4 = \begin{pmatrix} 0 \\ 1 \end{pmatrix}}$$

$$\rightarrow \text{for } FP_3 \quad \left\{ \begin{array}{l} \lambda_{3,1} = -3 \\ \lambda_{3,2} = 0.5 \end{array} \right.$$

$$E = J(FP_3) - \lambda_{3,1} I = \begin{pmatrix} 0 & -1.5 \\ 0 & 3.5 \end{pmatrix}$$

$$E\vec{x} = 0 \Rightarrow 3.5y = 0 \Rightarrow y=0$$

$$\boxed{v_5 = \begin{pmatrix} 1 \\ 0 \end{pmatrix}}$$

$$F = J(FP_3) - \lambda_{3,2} I = \begin{pmatrix} -3.5 & -1.5 \\ 0 & 0 \end{pmatrix}$$

$$F\vec{x} = 0 \Rightarrow \begin{pmatrix} -3.5 & -1.5 \\ 0 & 0 \end{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

$$\Rightarrow -3.5x - 1.5y = 0$$

$$\Rightarrow \boxed{\begin{matrix} -3.5x = 1.5y \\ \sqrt{6} = \begin{pmatrix} -3 \\ 7 \end{pmatrix} \end{matrix}}$$

$$\rightarrow \text{for } FP_4 \quad \left\{ \begin{array}{l} \lambda_{4,1} = \frac{-3+\sqrt{5}}{2} \approx -0.382 \\ \lambda_{4,2} = \frac{-3-\sqrt{5}}{2} \approx -2.618 \end{array} \right.$$

$$G = J(FP_4) - \lambda_{4,1} I = \begin{pmatrix} -2 - \left(\frac{-3+\sqrt{5}}{2}\right) & -1 \\ -1 & -1 - \left(\frac{-3+\sqrt{5}}{2}\right) \end{pmatrix}$$

$$= \begin{pmatrix} \frac{-4+3-\sqrt{5}}{2} & -1 \\ -1 & \frac{-2+3-\sqrt{5}}{2} \end{pmatrix}$$

$$G = \begin{pmatrix} \frac{-1-\sqrt{5}}{2} & -1 \\ -1 & \frac{1-\sqrt{5}}{2} \end{pmatrix}$$

$$G\vec{x} = 0 \Rightarrow \begin{pmatrix} \frac{-1-\sqrt{5}}{2} & -1 \\ -1 & \frac{1-\sqrt{5}}{2} \end{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

$$\left\{ \begin{array}{l} \frac{-1-\sqrt{5}}{2}x - y = 0 \\ -x + \frac{1-\sqrt{5}}{2}y = 0 \end{array} \right. \Rightarrow \boxed{x = \frac{1-\sqrt{5}}{2}y}$$

$$\therefore \text{ we set } y = t ; x = \frac{1-\sqrt{5}}{2}t$$

$$\boxed{\sqrt{7} = \begin{pmatrix} 1-\sqrt{5} \\ 2 \end{pmatrix}}$$

$$H = J(FP_4) - \lambda_{4,2} I = \begin{pmatrix} \frac{-1+\sqrt{5}}{2} & -1 \\ -1 & \frac{1+\sqrt{5}}{2} \end{pmatrix}$$

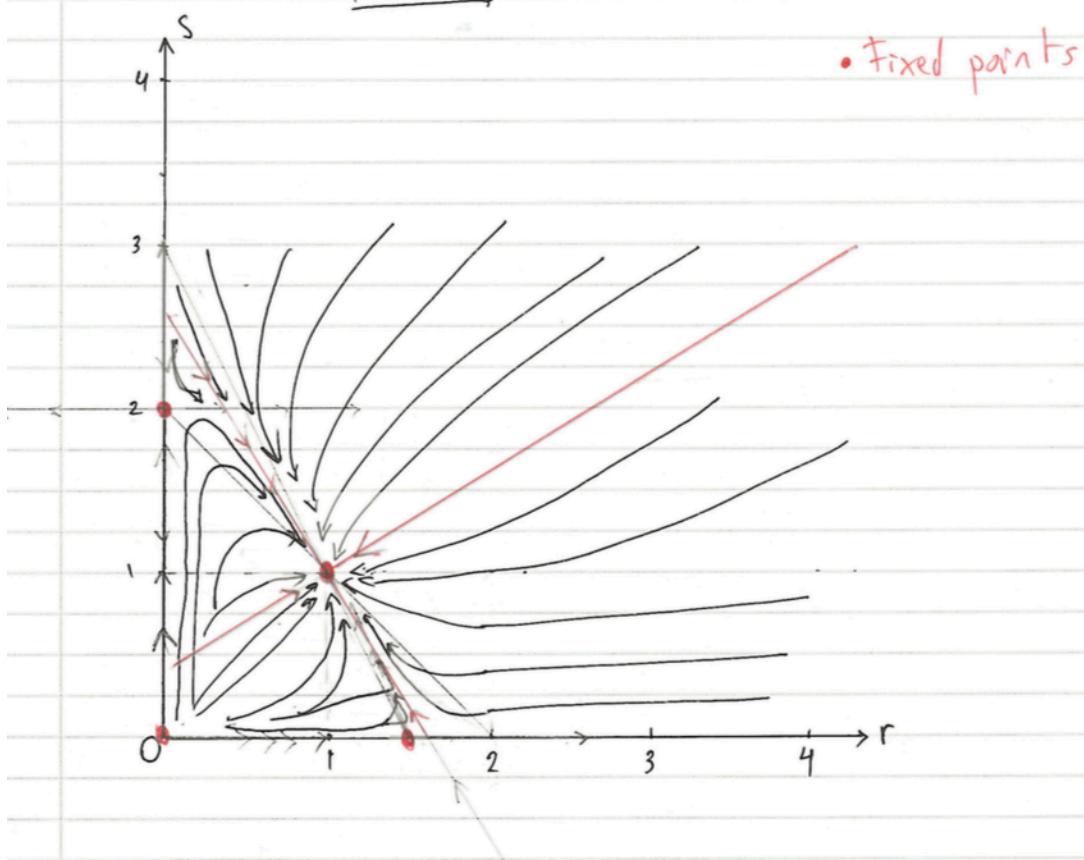
$$H\vec{x} = 0 \Rightarrow \begin{cases} \frac{-1+\sqrt{5}}{2}x - y = 0 \\ -x + \frac{1+\sqrt{5}}{2}y = 0 \end{cases}$$

$$\Rightarrow x = \frac{\frac{1+\sqrt{5}}{2}y}{\frac{-1+\sqrt{5}}{2}} \\ v_8 = \left(\begin{array}{c} 1+\sqrt{5} \\ 2 \end{array} \right)$$

(d) To further help us visualize the global phase portrait we will calculate the equation of the nullclines of the system:

$$N_1: \dot{r} = 0 \\ \Leftrightarrow 3 - 2r - s = 0 \\ \Leftrightarrow s = 3 - 2r$$

$$N_2: \dot{s} = 0 \\ \Leftrightarrow 2 - r - s = 0 \\ \Leftrightarrow s = 2 - r$$

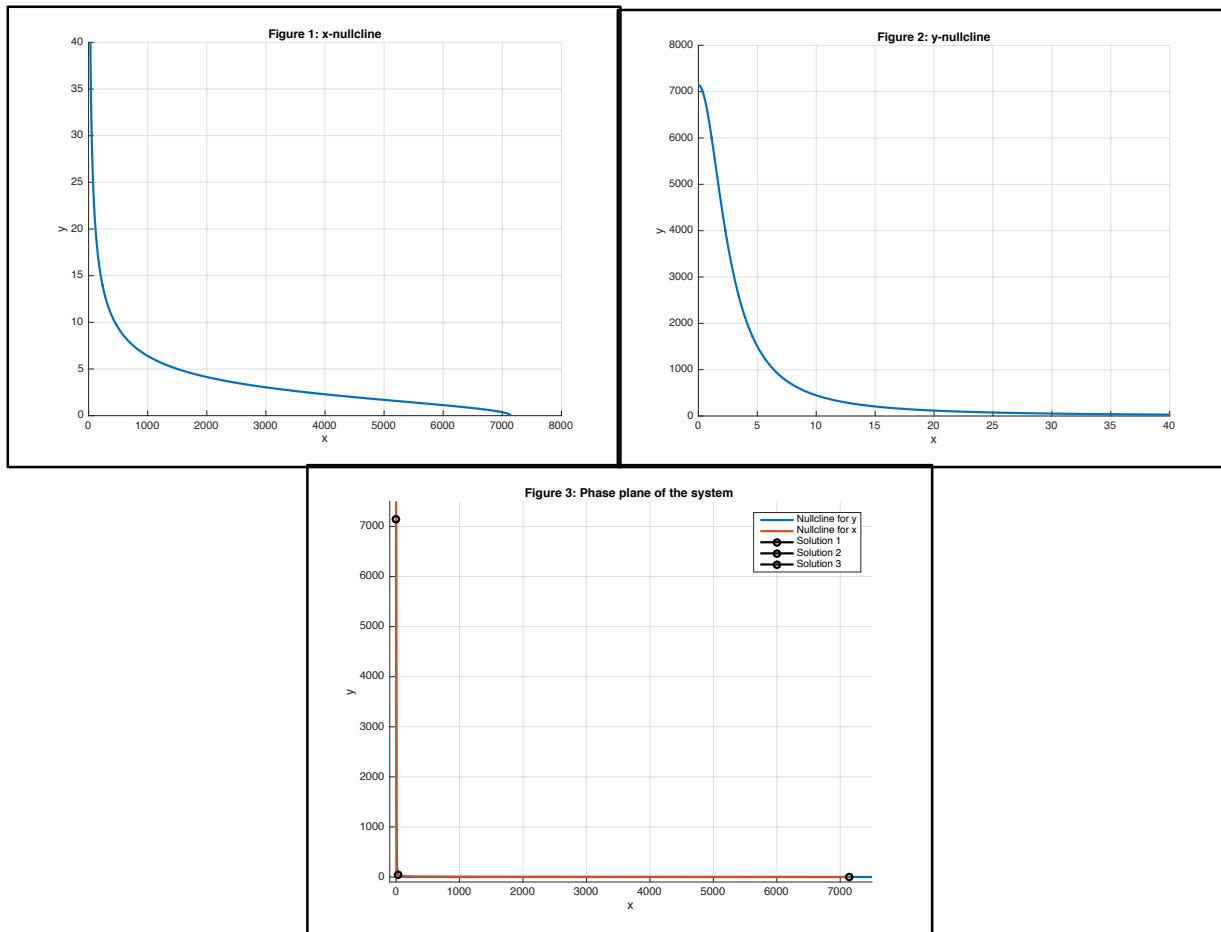


Question 4: A biological switch *The code for this question can be seen after the answer to question 4(c).*

(a) The nullclines of the systems are obtained by setting \dot{x} and \dot{y} to 0. After rearranging the following are found:

$$\begin{aligned} \text{x-nullcline: } x &= \frac{k_x}{k_d} \left(\frac{1}{1+K_1 K_y y^2} \right) \\ \text{y-nullcline: } y &= \frac{k_y}{k_d} \left(\frac{1}{1+K_2 K_x x^2} \right) \end{aligned}$$

The x-nullcline can be visualized on figure 1 and the y-nullcline on figure 2. As commented on the MatLab code attached further on in the answer, an increase from 0 to 40 in x makes y go to about a value of 7000 and vice versa. That is the reason why both nullclines cannot be visualized very well on the same plot. Perhaps, both nullclines can be seen plotted on the same graph on figure 3, although at such a scale the graph is not very representative.



The locations of the fixed points (round to the unit or first decimal place) are the following:

FP1: (36.2; 36.2)

FP2: (0; 7143)

FP3: (7143; 0)

After working out the Jacobian matrix of the system and calculating the eigenvalues of the Jacobian for each fixed point the local stability of each fixed point can be deduced:

eig_FP1 =

-2.0929 This correspond to a saddle node.
0.6929

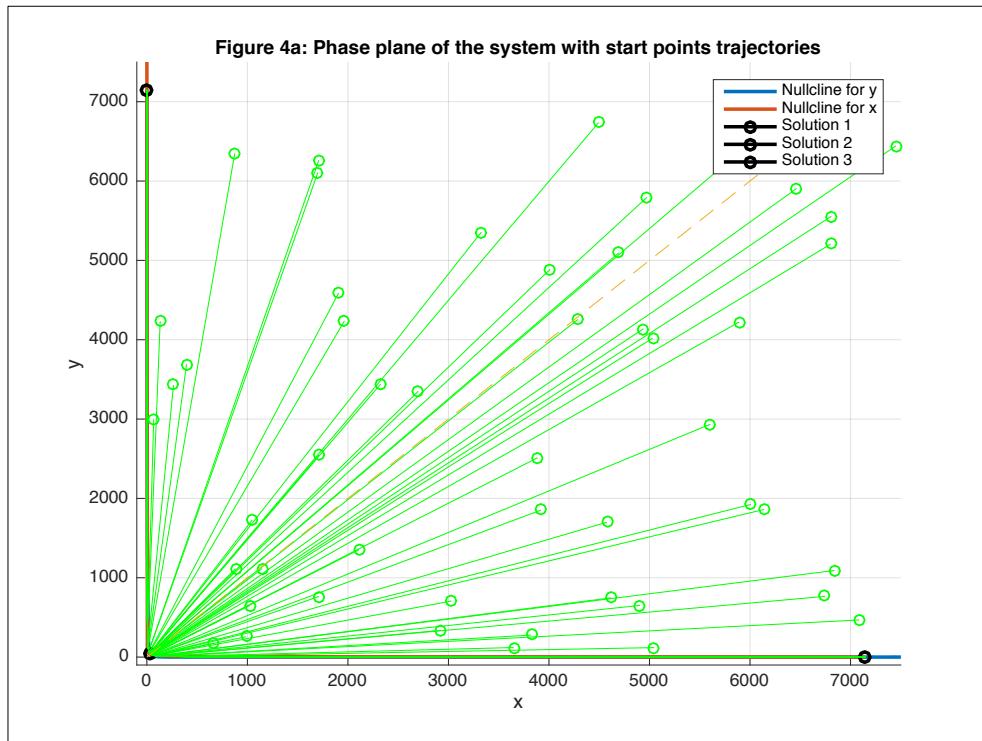
eig_FP2 =

-0.6995 This correspond to a stable node.
-0.7005

eig_FP3 =

-0.6995 This correspond to a stable node.
-0.7005

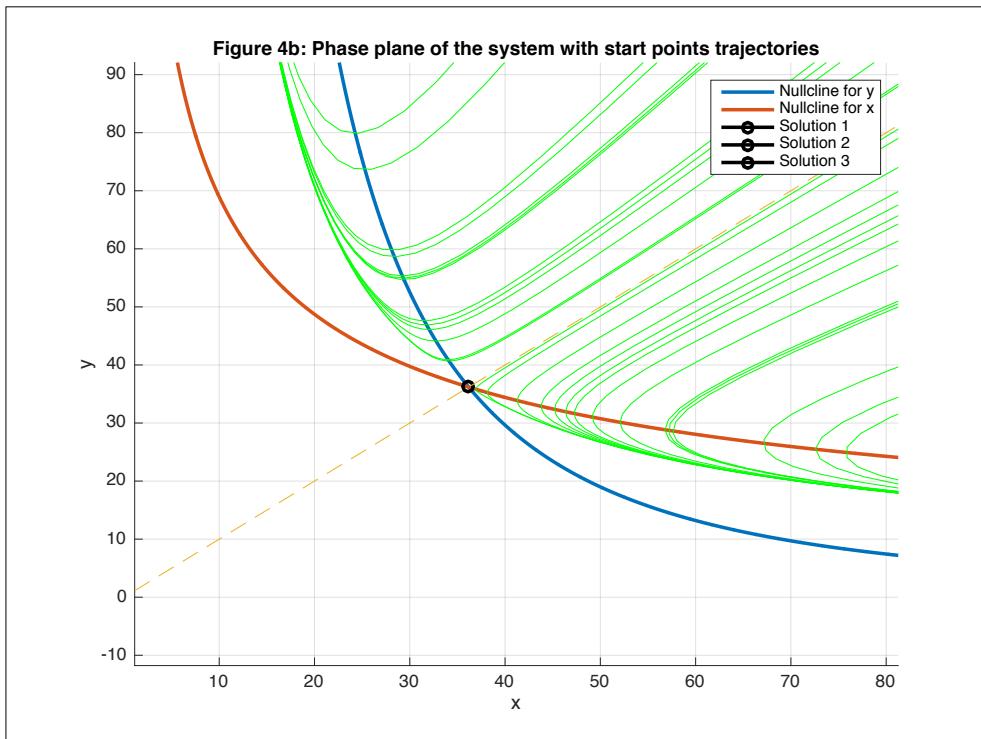
(b) The trajectories of random starting points with coordinates in the range [0; 7500] can be seen on figure 4. All trajectories seem to be directed towards the saddle node fixed point but then are either directed to one of either stable nodes.



(c) When zooming at the saddle node fixed point (Figure 4b) it can be observed how the trajectories of the starting points bend and change their direction towards the stable node fixed points. The dotted line has equation $y = x$ and is technically referred as the separatrix. If a starting point has a coordinate y greater than x then the trajectory of such point will go near the saddle node fixed point and then end up in the fixed point with a greater y coordinate (FP3: (7143;0)). On the other hand, if the starting point has a coordinate x greater than y then the

trajectory of this will finish at the other stable node (FP2: (0; 7142)). In the practically impossible case where concentrations x and y are equal, the optimal equilibrium concentration corresponds to FP1 coordinates (FP1: 36.2; 36.2).

A system of this sort is often referred to as a “biological switch” because by starting above or below the separatrix the system will respectively end up at the fixed point above or below the separatrix.



CODE FOR QUESTION 4

%QUESTION 4

```
%% (a)
%Declaration of parameters
kx = 5000;
ky = 5000;
Kx = 0.5;
Ky = 0.5;
K1 = 0.3;
K2 = 0.3;
kd = 0.7;
%Declaration of variables. Note x = fy and y = fx.
syms x y fx fy
x = 0:0.001:8000;
y = 0:0.001:8000;
%Nullclines by setting x-dot and y-dot to 0 and rearranging
fy = (kx/kd)*(1./(1+K1*Ky*y.^2));%Nullcline for x
fx = (ky/kd)*(1./(1+K2*Kx*x.^2));%Nullcline for y
```

```
%plot of x-nullcline
figure
hold on
grid on
plot(fy,y,'linewidth',2)
xlabel('x')
ylabel('y')
ylim([0 40])
title('Figure 1: x-nullcline')

%plot of y-nullcline
figure
hold on
grid on
plot(x,fx,'linewidth',2)
xlabel('x')
ylabel('y')
xlim([0 40])
title('Figure 2: y-nullcline')

%Plot of both nullclines on the same graph,
%an increase from 0 to 40 in x makes y go
%to about a value of 7000 and vice versa.
% That is the reason why both nullclines cannot be visualized
%very well on the same plot.

figure
hold on
grid on
plot(x,fx,'linewidth',2)
plot(fy,y,'linewidth',2)
xlabel('x')
ylabel('y')
xlim([-100 7500])
ylim([-100 7500])
title('Figure 4: Phase plane of the system with start points
trajectories')

%This section underneath is the computation of the fixed
points and their
%plotting on the graph.
func = @testf2;
sol(1,:) = fsolve(func,[40,40]); %Solution 1
sol(2,:) = fsolve(func,[0,7142]);%Solution 2
sol(3,:) = fsolve(func,[7142,0]);%Solution 3
plot(sol(1,1),sol(1,2),'k-o','linewidth',2); %Solution 1
plot(sol(2,1),sol(2,2),'k-o','linewidth',2); %Solution 2
plot(sol(3,1),sol(3,2),'k-o','linewidth',2); %Solution 3
legend('Nullcline for y', 'Nullcline for x','Solution 1',
'Solution 2','Solution 3','AutoUpdate','off')
```

```
%Jacobian matrix to find stability of each fixed point
%Jacobian for FP1
ddxdx = -kd;%top-left corner
ddxdy= -kx*2*K1*Ky*sol(1,2)*(1+K1*Ky*(sol(1,2))^2)^-2; %top-
right corner
ddydx = -ky*2*K2*Kx*sol(1,1)*(1+K2*Kx*(sol(1,1))^2)^-
2;%bottom-left corner
ddydy = -kd;%bottom-right corner
Jacobian1 = [ddxdx ddxdy;ddydx ddydy]
eig_FP1 = eig(Jacobian1)

%Jacobian for FP2
ddxdx = -kd;%top-left corner
ddxdy= -kx*2*K1*Ky*sol(2,2)*(1+K1*Ky*(sol(2,2))^2)^-2; %top-
right corner
ddydx = -ky*2*K2*Kx*sol(2,1)*(1+K2*Kx*(sol(2,1))^2)^-
2;%bottom-left corner
ddydy = -kd;%bottom-right corner
Jacobian2 = [ddxdx ddxdy;ddydx ddydy]
eig_FP2 = eig(Jacobian2)

%Jacobian for FP3
ddxdx = -kd;%top-left corner
ddxdy= -kx*2*K1*Ky*sol(3,2)*(1+K1*Ky*(sol(3,2))^2)^-2; %top-
right corner
ddydx = -ky*2*K2*Kx*sol(3,1)*(1+K2*Kx*(sol(3,1))^2)^-
2;%bottom-left corner
ddydy = -kd;%bottom-right corner
Jacobian3 = [ddxdx ddxdy;ddydx ddydy]
eig_FP3 = eig(Jacobian3)
```

%% (b)

```
tspan= [0 100];
x0r = 7500*rand([50 2]); %All random values are in the range
[0;7500]

%This for-loop plots the starting position and trajectory of
all random
%starting points.
for i = 1:size(x0r,1)
    [t,v] = ode45(@(t,v) testf2(v),tspan,x0r(i,:));
    plot(v(:,1),v(:,2), 'g','linewidth',0.5);
    plot(v(1,1),v(1,2), 'go','linewidth',0.5);
end

%plot of the separatrix
r = 0:0.01:7000;
p = 0:0.01:7000;
```

```
plot(r,p,'--')
```

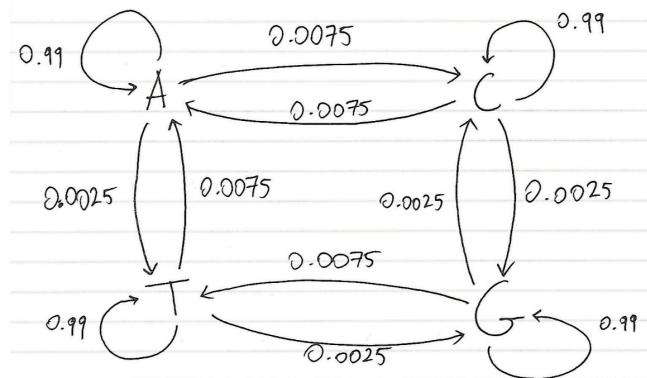
Q4 CODE EXTERNAL FUNCTION:

```
function F = testf2(v)
kx = 5000;
ky = 5000;
Kx = 0.5;
Ky = 0.5;
K1 = 0.3;
K2 = 0.3;
kd = 0.7;
F = [kx*(1/(1+K1*Ky*v(2).^2))-...
kd*v(1);ky*(1/(1+K2*Kx*v(1).^2))-kd*v(2)];
end
```

Part 2: Stochastic processes and networks

Question 5: Evolutionary dynamics of a DNA nucleotide

(a) Such a stochastic process is called a discrete-time Markov chain process. A diagram of this system can be seen on the following sketch:



(b)

Underneath the Matlab code and output with the working out of the stationary distribution can be found. In the transition matrix rows and columns are in the order A,C,T and G.

CODE

```

%% b
%Declaration of Transition Matrix
T = [0.99 0.0075 0 0.0075;0.0075 0.99 0.0025 0;0 0.0025 0.99
0.0025;0.0025 0 0.0075 0.99];
Transition_Matrix = (T)
%Eigenvalues and Eigenvectors of T
[V,D] = eig(T);
Eigen_Vectors = V
Eigen_Values = [D(1,1) D(2,2) D(3,3) D(4,4)]
%Eigenvalue equal to 1
Eigenvalue_of_Interest = D(2,2)
%Corresponding eigenvector
Stationary_Distribution = V(:,2)/sum(V(:,2))
%Flux from A to C
flux_btwn_AC = Stationary_Distribution(1)*T(1,2)-
Stationary_Distribution(2)*T(2,1)
  
```

OUTPUT

Transition_Matrix =

0.9900	0.0075	0	0.0075
0.0075	0.9900	0.0025	0
0	0.0025	0.9900	0.0025
0.0025	0	0.0075	0.9900

Eigen_Vectors =

```
-0.6975 + 0.0000i -0.6975 + 0.0000i -0.0000 - 0.0000i -0.0000 + 0.0000i
 0.5812 + 0.0000i -0.5812 + 0.0000i -0.7071 - 0.0000i -0.7071 + 0.0000i
 -0.2325 + 0.0000i -0.2325 + 0.0000i -0.0000 + 0.0000i -0.0000 - 0.0000i
 0.3487 + 0.0000i -0.3487 + 0.0000i 0.7071 + 0.0000i 0.7071 + 0.0000i
```

Eigen_Values =

```
0.9800 + 0.0000i 1.0000 + 0.0000i 0.9900 + 0.0000i 0.9900 - 0.0000i
Eigenvalue_of_Interest =
```

1.0000

The stationary distribution is the normalised eigenvector for which the eigenvalue of the transition matrix equals 1.

Stationary_Distribution =

```
 $\pi_A = 0.3750$ 
 $\pi_C = 0.3125$ 
 $\pi_G = 0.1250$ 
 $\pi_T = 0.1875$ 
```

flux_btwn_AC =

4.6875e-04

As the flux from A to C is different than 0, this already tell us that this process does not obey detailed balance as all fluxes are 0 in a system that obeys detail balance. *The flux between A and C is worked out by subtracting the product of the stationary distribution of C and the probability of going from A to C to the product of the stationary distribution of A and the probability of going from C to A.*

(c) On average, it takes 534 generations to go to T from a starting point C.

The matrix named U corresponds to a submatrix giving transition probabilities from non-absorbing states to non-absorbing states. R corresponds to a submatrix giving these probabilities from non-absorbing states to absorbing states.

CODE

```
%% C
U = T;
U(:,4) = []; %we take state 4 as absorbing
U(4,:) = [];
W = inv(eye(3) - U); %fundamental matrix
time_to_T_from_C = sum(W(:,2))
```

OUTPUT

time_to_T_from_C =

533.3333

(d)

The probability that a C evolves into T without first having passed through A is found to be 0.2.

CODE:

```
%% d
```

```
U2 = [0.99 0.0025; 0.0025 0.99]
W2 = inv(eye(2)-U2) %fundamental matrix
R = [0 0.0075; 0.0075 0]
```

```
pTbeforeA = R*W2
pTbeforeA_startingC=pTbeforeA(2,2)
```

OUTPUT

U2 =

0.9900	0.0025
0.0025	0.9900

W2 =

106.6667	26.6667
26.6667	106.6667

R =

0	0.0075
0.0075	0

pTbeforeA =

0.2000	0.8000
0.8000	0.2000

pTbeforeA_startingC =

0.2000

(e)

1. This stochastic process matches all binomial distribution requirements:
 - There is a fixed number of observations, in our case N generations.
 - Each generation is independent from the others.
 - Each observation represents one of two outcomes, “success” when a mutation happens and “failure” when a mutation does not happen.
 - The probability of each success is theoretically the same for each outcome.

Therefore $P(M=m)$ can be expressed as:

$$P(M = m) = \binom{n}{m} p^m (1 - p)^{n-m}$$

Where $m = 0, 1, 2, \dots, n$; n is the number of generations your simulations will run for and p is the probability that a mutation happens which is equal to 0.01.

$$\text{And } \binom{n}{m} = \frac{n!}{m!(n-m)!}$$

2. The expectation or mean μ is equal to np . The variance V is equal to $np(1-p)$.

CODE FOR QUESTION 5 AS A WHOLE:

```
%Q5
%% b
%Declaration of Transition Matrix
T = [0.99 0.0075 0 0.0075; 0.0075 0.99 0.0025 0; 0 0.0025 0.99
0.0025; 0.0025 0 0.0075 0.99];
Transition_Matrix = (T)
%Eigenvalues and Eigenvectors of T
[V,D] = eig(T);
Eigen_Vectors = V
Eigen_Values = [D(1,1) D(2,2) D(3,3) D(4,4)]
%Eigenvalue equal to 1
Eigenvalue_of_Interest = D(2,2)
%Corresponding eigenvector
Stationary_Distribution = V(:,2)/sum(V(:,2))
%Flux from A to C
flux_btwn_AC = Stationary_Distribution(1)*T(1,2)-
Stationary_Distribution(2)*T(2,1)

%% c
U = T;
U(:,4) = []; %we take state 4 as absorbing
U(4,:) = [];
W = inv(eye(3) - U); %fundamental matrix
time_to_T_from_C = sum(W(:,2))

%% d
U2 = [0.99 0.0025; 0.0025 0.99]
W2 = inv(eye(2)-U2) %fundamental matrix
R = [0 0.0075; 0.0075 0]

pTbeforeA = R*W2
pTbeforeA_startingC=pTbeforeA(2,2)
```

Question 6: Evolutionary dynamics of a DNA sequence

- (a) After 20 generations, the transition matrix is equal to:

TransitionMatrix_after20steps =

0.8298	0.1246	0.0119	0.1246
0.1245	0.8278	0.0419	0.0099
0.0040	0.0415	0.8219	0.0415
0.0417	0.0060	0.1243	0.8239

CODE:

```
% (a)
T = [0.99 0.0075 0 0.0075; 0.0075 0.99 0.0025 0; 0 0.0025 0.99
0.0025; 0.0025 0 0.0075 0.99];
TransitionMatrix_after20steps = T^20
```

From the starting sequence to the sequence 1 there are three changes: The first nucleotide is now C and it started being A, the fifth nucleotide is now T and it started being and the second to last nucleotide is now A and is started being C.

According to the transition matrix above, the probability of the first event happening is 0.1245, the second event probability is 0.1243 and the probability of the third event is 0.1246. The probability of these two events happening is therefore 0.0019.

From the starting sequence to the sequence 2 there are two changes: The third nucleotide is now T and it started being C and the second to last nucleotide is now T and is started being C.
According to the transition matrix above, the probability of the first event happening is 0.006 and the second 0.006. The probability of these two events happening is therefore 3.6×10^{-4} .

Therefore the most likely sequence after generation is sequence 1.

- (b) After 100,000 simulations the average number of generations until the whole sequence is different from the starting sequence is 1014.

CODE

```
%% Q6
tic
%(a)
T = [0.99 0.0075 0 0.0075; 0.0075 0.99 0.0025 0; 0 0.0025 0.99
0.0025; 0.0025 0 0.0075 0.99];
TransitionMatrix_after20steps = T^20
```

%(b)

```
%Starting sequence
%A is 1, C is 2, G is 3, T is 4
Sequence0 = [1 2 2 4 3 1 2 2 1]
%number of generations
n = 0;

% 10000 simulations
for i=1:100000
```

```
%Declaration of a Sequence that will change after each
generation
Sequence = Sequence0;

%while any of the nucleotides from Sequence is equal to
Sequence0 the
%code will keep running (i.e. another generation will exist)
while Sequence(1)== Sequence0(1) || Sequence(2)== Sequence0(2)
|| Sequence(3)== Sequence0(3) || Sequence(4)== Sequence0(4) ||
Sequence(5)== Sequence0(5) || Sequence(6)== Sequence0(6) ||
Sequence(7)== Sequence0(7) || Sequence(8)== Sequence0(8) ||
Sequence(9)== Sequence0(9)

for a = 1:9

%%check what nucleotide is the initial one
if Sequence(a) == 1
start = 1;
end
if Sequence(a) == 2
start = 2;
end
if Sequence(a) == 3
start = 3;
end
if Sequence(a) == 4
start = 4;
end

eventprob = rand; %random number between 0 and 1
temp = 0; %temporary variable that is going to hold the
increasing probability
reactid = 0;
for c=1:4
%the probability will be chosen from the previously selected
%start column and this for loop will browse through every
%row c
temp = temp+T(c,start); %goes to starting nucleotide column
if temp>=eventprob
%if the chosen rate is not bigger than
%eventprob go to the next one
reactid=c;
break
end
end

%Change nucleotide
if reactid == 1
Sequence(a) = 1;
end
if reactid == 2
Sequence(a) = 2;
```

```
end
if reactid == 3
Sequence(a) = 3;
end
if reactid == 4
Sequence(a) = 4;
end

end
n = n+1; %%adds up for every generation
end

end
%Average number of generation over number of simulations.
avgNumber_of_Generations = n/100000
toc
```

OUTPUT

Sequence0 =

1 2 2 4 3 1 2 2 1

avgNumber_of_Generations =

1.0138e+03

Elapsed time is 125.203772 seconds.