3.

a)

i) U and V are the concentrations of the repressors.

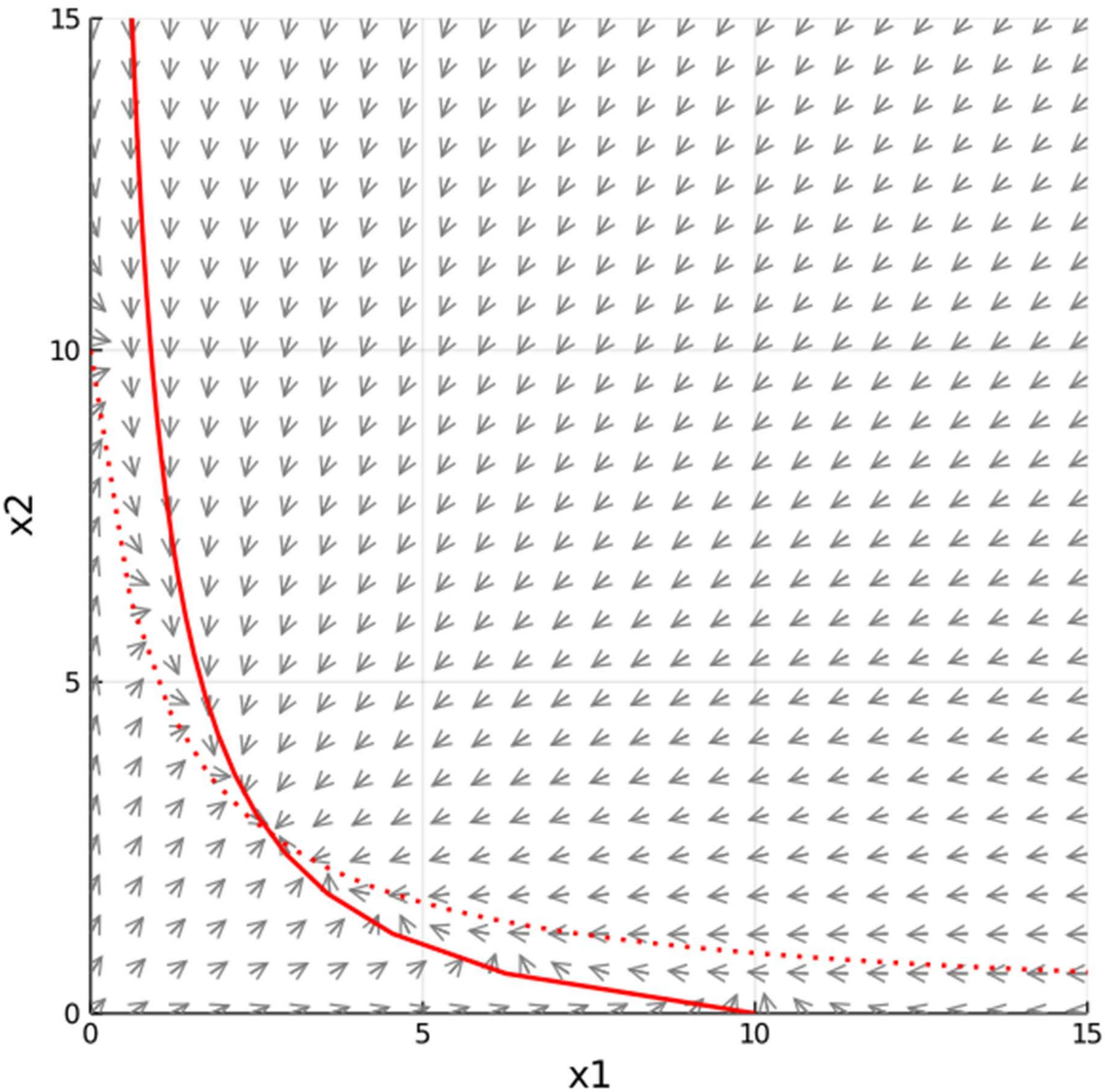
ii) Alpha is the effective rate of synthesis of repressor; lumped parameter that describes the net effect of RNA polymerase binding, open-complex formation, transcript elongation, transcript termination, repressor binding, ribosome binding, and polypeptide elongation.

iii) n is the cooperativity of repression

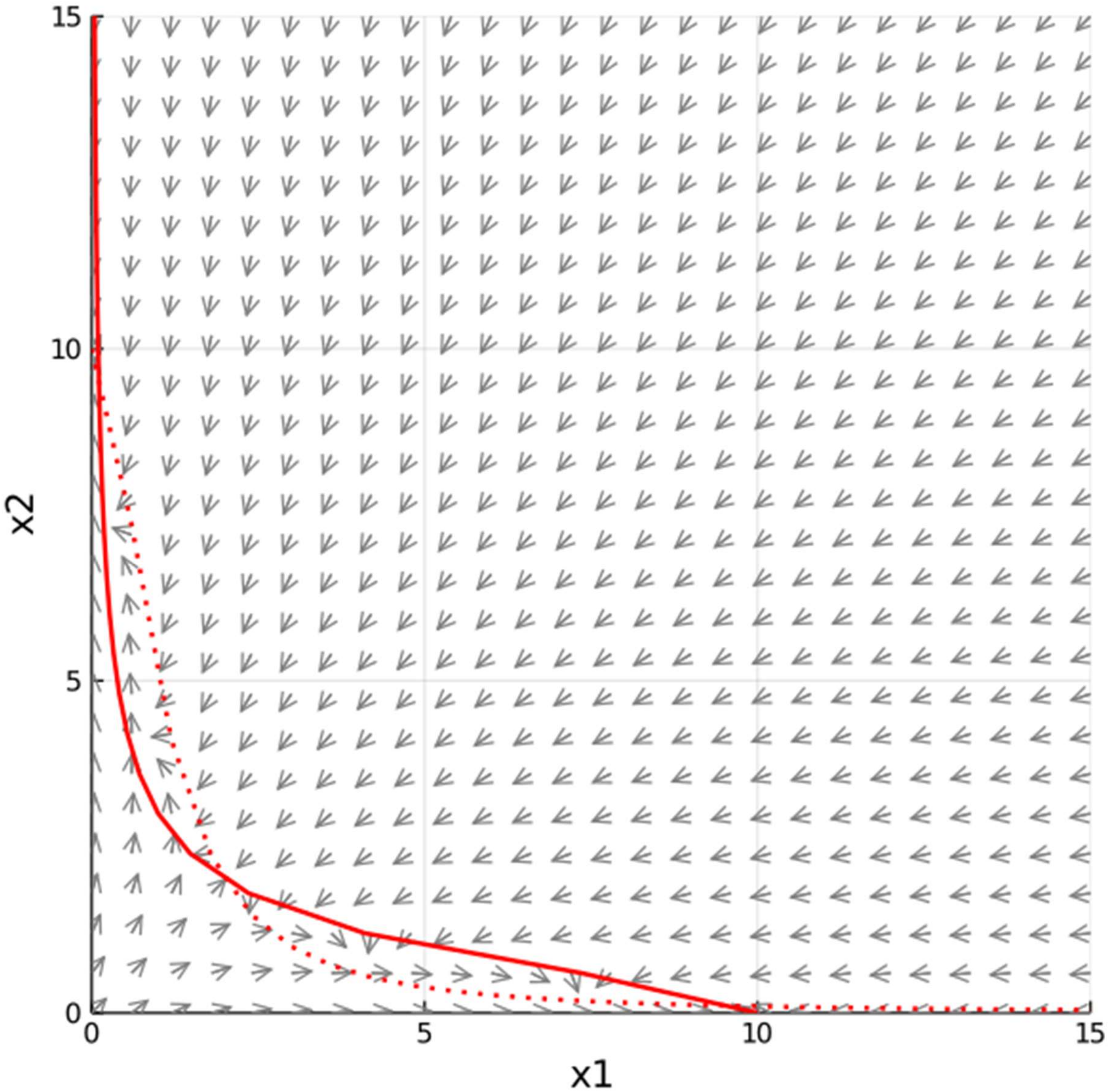
iv) the degradation rate constant for repressor U is 1, and the degradation rate constant for repressor V is 1.

b)

For n = 1:



For n = 2:



For n = 1 there is only 1 steady state (one fixed point).

For n = 2 there are 3 steady states (3 fixed points). Thus, as cooperativity increases the number of steady states also increases.

c)

For n = 1 the single steady state is a stable steady state as when the fixed point is looked at closely on the phase plot all the vectors around it point toward it.

For n = 2 the fixed point at around (2,2) is unstable as when the fixed point is looked at closely on the phase plot only some of the vectors around it point toward it while others point away. However, for the fixed points at approx. (1,10) and (10,1) when looked at closely on the phase plot all the vectors around them point toward them. Thus, they are stable steady states.

Overall, as cooperativity increases the number of stable and unstable states also increases.

$\boxed{3d}$ $\frac{du}{dt} = \frac{\alpha}{1+v^n} - u = f, \; \frac{dv}{dt} = \frac{\alpha}{1+u^n} - v = g$

$$\frac{du}{dt} = \frac{\partial f}{\partial u}\Big|_{u_s, v_s} + \frac{\partial f}{\partial v}\Big|_{u_s, v_s}$$

$$\frac{\partial f}{\partial u}\Big|_{u_s, v_s} = -1 \quad , \frac{\partial f}{\partial v}\Big|_{u_s, v_s} = \alpha \quad v^{n-1}(-n)(1)$$

$$\hookrightarrow = \frac{-n\alpha v_s^{n-1}}{(1+v_s^n)^2}$$

$$\frac{dv}{dt} = \frac{\partial g}{\partial u}\Big|_{u_s, v_s} + \frac{\partial g}{\partial v}\Big|_{u_s, v_s}$$

$$\frac{\partial g}{\partial v}\Big|_{u_s, v_s} = -1 \quad , \frac{\partial g}{\partial u}\Big|_{u_s, v_s} = \frac{-n\alpha u_s^{n-1}}{(1+u_s^n)^2}$$

$\therefore$

$$\overleftrightarrow{J} = \text{Jacobian} = \begin{bmatrix} -1 & \frac{-n\alpha v_s^{n-1}}{(1+v_s^n)^2} \\ \frac{-n\alpha u_s^{n-1}}{(1+u_s^n)^2} & -1 \end{bmatrix}$$

$$\mathrm{Tr}(\overleftrightarrow{J}) = -1 + -1 = -2$$

$$\det(\overleftrightarrow{J}) = 1 - \frac{n^2\alpha^2 u_s^{n-1} v_s^{n-1}}{(1+u_s^n)^2(1+v_s^n)^2}$$

$$\lambda_\pm = \frac{tr(J) \pm \sqrt{tr(J)^2 - 4det(J)}}{2}$$

$$\lambda_\pm = \frac{-2 \pm \sqrt{4 - 4\left(1 - \frac{n^2\alpha^2 u_s^{n-1} V_s^{n-1}}{(1+u_s^n)^2(1+V_s^n)^2}\right)}}{2}$$

$$\lambda_\pm = -1 \pm \sqrt{1 - 1 + \frac{n^2\alpha^2 u_s^{n-1} V_s^{n-1}}{(1+u_s^n)^2(1+V_s^n)^2}}$$

$$\lambda_\pm = -1 \pm \sqrt{\frac{n^2\alpha^2 u_s^{n-1} V_s^{n-1}}{(1+u_s^n)^2(1+V_s^n)^2}}$$

$$\lambda_\pm = -1 \pm \frac{n\alpha}{(1+u_s^n)(1+V_s^n)} \sqrt{u_s^{n-1} V_s^{n-1}}$$

for stability

$$\lambda_\pm < 0$$

$$0 > -1 \pm \frac{n\alpha}{(1+u_s^n)(1+V_s^n)} \sqrt{u_s^{n-1} V_s^{n-1}}$$

$$1 > \pm \frac{n\alpha}{(1+u_s^n)(1+V_s^n)} \sqrt{u_s^{n-1} V_s^{n-1}}$$

By their nature: $\alpha > 0$, $(1+u_s^n) > 0$, $(1+V_s^n) > 0$, $\sqrt{u_s^{n-1} V_s^{n-1}} > 0$

$\therefore$ for stability,

$$\boxed{1 > \left(\frac{n\alpha}{(1+u_s^n)(1+V_s^n)}\right)^2 \left(u_s^{n-1} V_s^{n-1}\right)}$$

as n increases the denominator grows faster than the numerator $\therefore$ as n grows stability increases.

$\downarrow$ $\boxed{\text{For the center steady state}}$

(for $U=V$)

$$1 > \left(\frac{n\alpha}{((1+u_s)^n)^2}\right)^2 \left(u_s^{n-1}\right)^2$$

$$1 > \frac{n^2\alpha^2}{(1+u_s)^{2n}} (u_s)^{2n-2}$$

For cooperativity, : for this steady state as n increases stability increases.

For rate of synthesis : rate of synthesis $\rho = \dfrac{\alpha}{1+u^n}$

$\therefore$ as the rate of synthesis increases stability decreases.

3e)

In[1]:=
$$\lambda plus = \frac{-2 + \sqrt{4 - 4\left(1 - \frac{\alpha^2 * n^2 * u^{n-1} * v^{n-1}}{(1+u^n)^2\ (1+v^n)^2}\right)}}{2};$$

In[2]:=
$$\lambda minus = \frac{-2 - \sqrt{4 - 4\left(1 - \frac{\alpha^2 * n^2 * u^{n-1} * v^{n-1}}{(1+u^n)^2\ (1+v^n)^2}\right)}}{2};$$

In[3]:= n = 1;
α = 10;

In[5]:=
$$\text{Solve}\left[0 == \frac{\alpha}{1 + us^n} - us, us\right] \text{ // N}$$

Out[5]= {{us → -3.70156}, {us → 2.70156}}

```
In[6]:= λplus /. {u -> 2.7015621187164243`, v -> 2.7015621187164243`}
```

Out[6]= -0.270156

```
In[7]:= λminus /. {u -> 2.7015621187164243`, v -> 2.7015621187164243`}
```

Out[7]= -1.72984

In[8]:= n = 2;

In[9]:=
$$\text{Solve}\left[0 == \frac{\alpha}{1 + us^n} - us, us\right] \text{ // N}$$

Out[9]= {{us → -1. - 2. ⅈ}, {us → -1. + 2. ⅈ}, {us → 2.}}

```
In[10]:= λplus /. {u -> 2.`, v -> 2.`}
```

Out[10]= 0.6

```
In[11]:= λminus /. {u -> 2.`, v -> 2.`}
```

Out[11]= -2.6

In[12]:=

Part F.)

i.)

Starting from the given equations in the problem:

$$\frac{dR_i^*}{dt} = k_f L R_i - k_r R_i^* \qquad (3)$$
$$\frac{dN_i^*}{dt} = k_f^{ND} N_i D_j - k_r^{ND} N_i^* \qquad (4)$$
$$\frac{dD_i}{dt} = k_D R_i^* - \gamma_D D_i \qquad (5)$$
$$\frac{dR_i}{dt} = \frac{\beta^n}{K^n + [N_i^*]^n} - \gamma_R R_i \qquad (6)$$

From here, in fast equilibrium we expect the derivatives in equations (3-5) go to zero. Thus, we generate:

$$k_f L R_i = k_r R_i^*$$
$$k_f^{ND} N_i D_j = k_r^{ND} N_i^*$$
$$k_D R_i^* = \gamma_D D_i$$

From here, we substitutde in for N_i^* from (6) using the modified equation (4), then substitute the resulting D_j using the modified equation (5), and substitute that equation finally in with R_i^* into the modified equation (3). This results in the following eqpressions:

$$\frac{dR_1}{dt} = \frac{\beta^n}{K^n + [(\frac{k_f^{ND} k_D k_f N_1 L}{k_r^{ND} k_r \gamma_D}) * R_2]^n} - \gamma_R R_1$$
$$\frac{dR_2}{dt} = \frac{\beta^n}{K^n + [(\frac{k_f^{ND} k_D k_f N_2 L}{k_r^{ND} k_r \gamma_D}) * R_1]^n} - \gamma_R R_2$$

ii.)

To nondimensionalize the results from i.) we first substitute in for the given dimensionless variables,

$$K\gamma_R \frac{du}{d\tau} = \frac{\beta^n}{K^n + (\frac{k_f^{ND} k_D k_f N_1 L}{k_r^{ND} k_r \gamma_D})^n v^n K^n} - \gamma_R u K$$
$$K\gamma_R \frac{dv}{d\tau} = \frac{\beta^n}{K^n + (\frac{k_f^{ND} k_D k_f N_2 L}{k_r^{ND} k_r \gamma_D})^n u^n K^n} - \gamma_R v K$$

further rearranging terms:

$$\frac{du}{d\tau} = \frac{(\beta^n/(\gamma_R K^{n+1}))}{1 + (\frac{k_f^{ND} k_D k_f N_1 L}{k_r^{ND} k_r \gamma_D})^n v^n} - u$$
$$\frac{dv}{d\tau} = \frac{(\beta^n/(\gamma_R K^{n+1}))}{1 + (\frac{k_f^{ND} k_D k_f N_2 L}{k_r^{ND} k_r \gamma_D})^n u^n} - v$$

We define the dimensionless parameters $\alpha = (\beta^n/(\gamma_R K^{n+1}))$ and $\theta_i = \frac{k_f^{ND} k_D k_f N_i L}{k_r^{ND} k_r \gamma_D}$

$$\frac{du}{d\tau} = \frac{\alpha}{1 + \theta_1^n v^n} - u$$
$$\frac{dv}{d\tau} = \frac{\alpha}{1 + \theta_2^n u^n} - v$$