CHEME 7770-Alexus Locke

Problem 1

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```
In[4]:= Solve[{0 == -kf*L*Rs + kr*Rsa - ke*Rs + Vs + krec*Ri,
     0 == kf*L*Rs - kr*Rsa - kea*Rsa + krec*Ria,
      0 == ke*Rs - kdeg*Ri - krec*Ri, 0 == kea*Rsa - kdeg*Ria - krec*Ria},
     {Rs, Rsa, Ri, Ria}] // FullSimplify
```

Out[4]=

$$\left\{\left\{Rs \to \frac{(kdeg + krec)\ (kdeg\ (kea + kr) + kr\ krec)\ Vs}{kdeg\ ke\ (kdeg\ (kea + kr) + kr\ krec) + kdeg\ kea\ kf\ (kdeg + krec)\ L},\right.\right.$$

$$Rsa \to \frac{kf\ (kdeg + krec)^2\ L\ Vs}{kdeg\ ke\ (kdeg\ (kea + kr) + kr\ krec) + kdeg\ kea\ kf\ (kdeg + krec)\ L},$$

$$Ri \to \frac{ke\ (kdeg\ (kea + kr) + kr\ krec)\ Vs}{kdeg\ ke\ (kdeg\ (kea + kr) + kr\ krec) + kdeg\ kea\ kf\ (kdeg + krec)\ L},$$

$$\left.\left.Ria \to \frac{kea\ kf\ (kdeg + krec)\ L\ Vs}{kdeg\ ke\ (kdeg\ (kea + kr) + kr\ krec) + kdeg\ kea\ kf\ (kdeg + krec)\ L}\right\}\right\}$$

```
In[5]:= Rtot = kf (kdeg + krec)^2 L Vs / (kdeg ke (kdeg (kea + kr) + kr krec) + kdeg kea kf (kdeg + krec) L) +
     kea kf (kdeg + krec) L Vs / (kdeg ke (kdeg (kea + kr) + kr krec) + kdeg kea kf (kdeg + krec) L) // FullSimplify
```

Out[5]=

$$\frac{kf\ (kdeg + krec)\ (kdeg + kea + krec)\ L\ Vs}{kdeg\ ke\ (kdeg\ (kea + kr) + kr\ krec) + kdeg\ kea\ kf\ (kdeg + krec)\ L}$$

```
In[7]:= MaxConca =
    Limit[(kf (kdeg + krec) (kdeg + kea + krec) L Vs / (kdeg ke (kdeg (kea + kr) + kr krec) + kdeg kea kf (kdeg + krec) L)),
     L -> Infinity] // FullSimplify
```

Out[7]=

$$\frac{(kdeg + kea + krec)\ Vs}{kdeg\ kea}$$

For comparison of maximum concentration of active receptors, I repeated the process for the process done in class without the recycling step:

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```
In[8]:= Solve[{0 == -kf*L*Rs + kr*Rsa - ke*Rs + Vs,
     0 == kf*L*Rs - kr*Rsa - kea*Rsa, 0 == ke*Rs - kdeg*Ri, 0 == kea*Rsa - kdeg*Ria},
    {Rs, Rsa, Ri, Ria}] // FullSimplify
```

Out[8]=

$$\left\{\left\{Rs \to \frac{(kea + kr)\ Vs}{ke\ (kea + kr) + kea\ kf\ L},\ Rsa \to \frac{kf\ L\ Vs}{ke\ (kea + kr) + kea\ kf\ L},\right.\right.$$

$$\left.\left.Ri \to \frac{ke\ (kea + kr)\ Vs}{kdeg\ ke\ (kea + kr) + kdeg\ kea\ kf\ L},\ Ria \to \frac{kea\ kf\ L\ Vs}{kdeg\ ke\ (kea + kr) + kdeg\ kea\ kf\ L}\right\}\right\}$$

```
In[9]:= Rtot = kf L Vs / (ke (kea + kr) + kea kf L) + kea kf L Vs / (kdeg ke (kea + kr) + kdeg kea kf L) // FullSimplify
```

Out[9]=

$$\frac{(kdeg + kea)\ kf\ L\ Vs}{kdeg\ ke\ (kea + kr) + kdeg\ kea\ kf\ L}$$

```
In[10]:= MaxConca = Limit[((kdeg + kea) kf L Vs / (kdeg ke (kea + kr) + kdeg kea kf L)), L -> Infinity]
```

Out[10]=

$$\frac{kdeg\ kf\ Vs + kea\ kf\ Vs}{kdeg\ kea\ kf}$$

The addition of the recycling step seems to increase the maximum concentration.

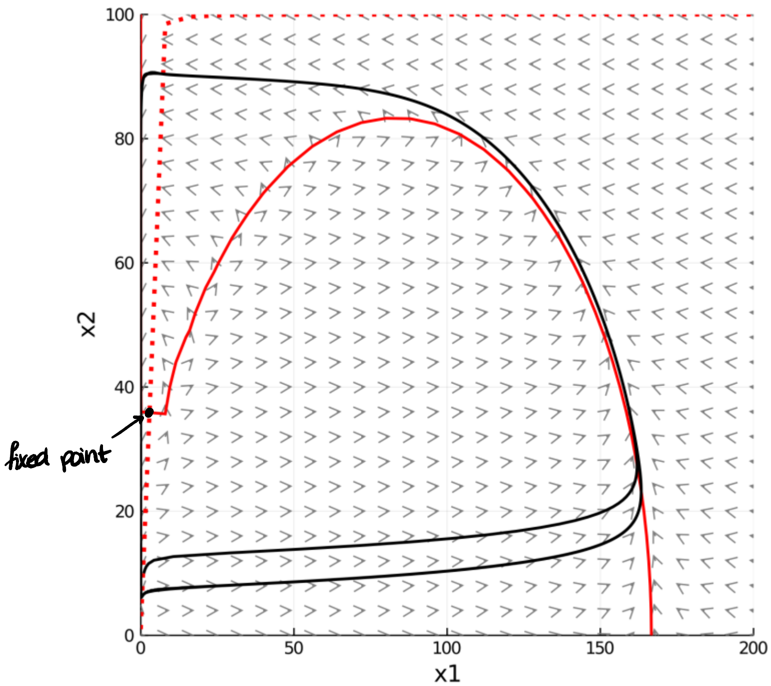
Problem 2

a)

- A is an activator of both R and A
- R is an inhibitor of A and has no effect on R
- Da describes the kinetics of degradation
- The basal rates:
  $\frac{dc_a}{dt} = r_{oa}$ *and* $\frac{dc_r}{dt} = r_{or}$
- The maximum rates:
- $\frac{dc_a}{dt} = r_a$ *and* $\frac{dc_r}{dt} = r_r$

b) The fixed point is unstable because vectors point away. See part c for nullclines.

c)



d)
At small values, there's a big increase in cr and a slow increase of ca. As we increase about halfway in cr, ca starts to decrease. Above the curve, while ca is decrease, there is no changes in concentration of cr.

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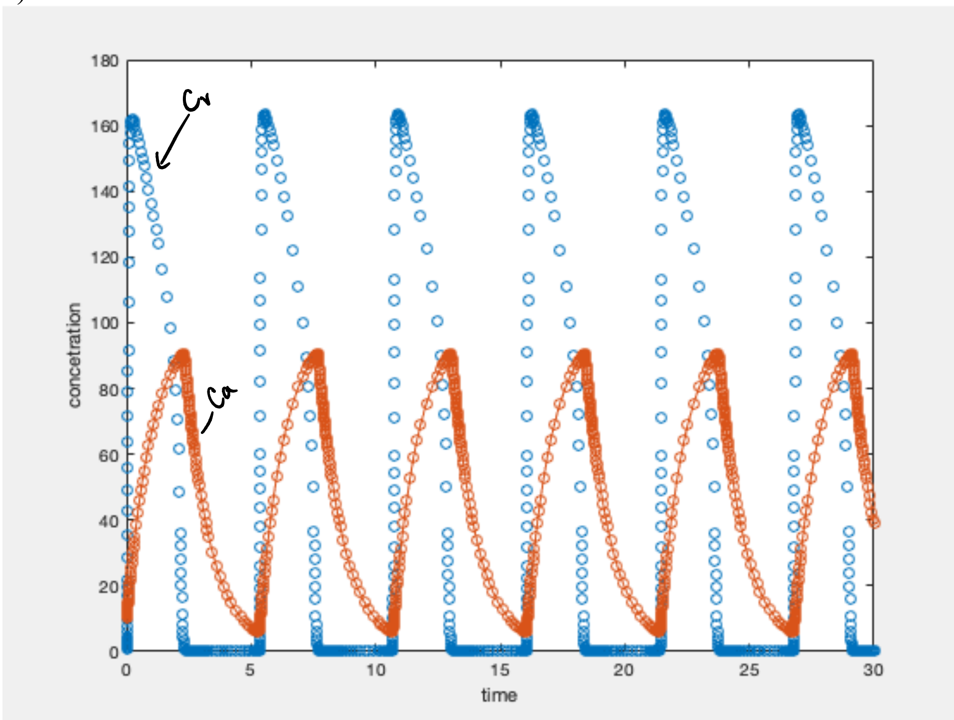
e)



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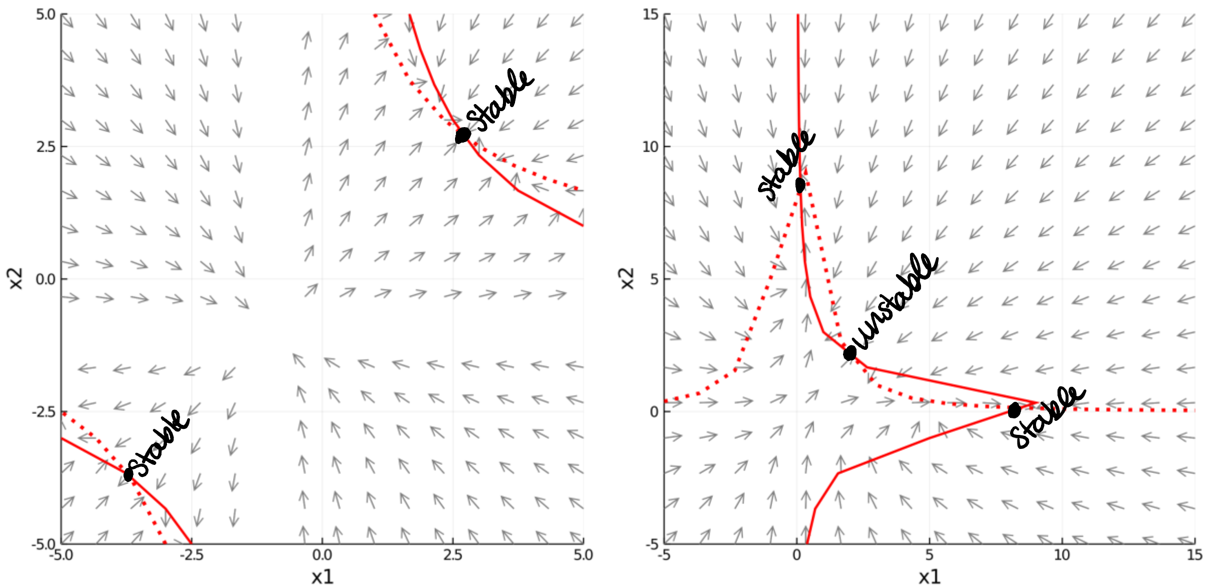
Problem 3)

a)
u &v = Concentration of a repressor of gene expression (there are two repressors)
α = 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
n = Cooperativity of repression
1 = Degradation rate constant for repressor

b)
As n increases the number of steady states increase. For n=1 there are 2 S.S., and for n=2 there are 3 S.S. Nullclines in part C.

c)



For n = 1: both steady states are stable
For n = 2: the steady state at around (2,2) is unstable because only some of the vectors point toward it. The others are stable steady states.

Once again, as cooperativity increases the number of steady states increase for both unstable and stable.

d)

```
syms u v a n

dydt1 = -u + a/(1+v^n)
```

dydt1 =

$$\frac{a}{v^n+1} - u$$

```
dydt2 = -v + a/(1+u^n)
```

dydt2 =

$$\frac{a}{u^n+1} - v$$

(code also provided)

```
jacobian([dydt1, dydt2], [u v])
```

ans =

$$\begin{pmatrix} -1 & -\frac{a\,n\,v^{n-1}}{(v^n+1)^2} \\ -\frac{a\,n\,u^{n-1}}{(u^n+1)^2} & -1 \end{pmatrix}$$

Steady States = Stable if eigenvalues have real, negative plots

e)

```
eig(A)
```

ans =

$$\begin{pmatrix} -\frac{u^n+v^n+\sigma_1+a\,n\,\sqrt{\frac{\sigma_1}{u\,v}}+1}{u^n+v^n+\sigma_1+1} \\ -\frac{u^n+v^n+\sigma_1-a\,n\,\sqrt{\frac{\sigma_1}{u\,v}}+1}{u^n+v^n+\sigma_1+1} \end{pmatrix}$$

where

$$\sigma_1 = u^n\,v^n$$

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```
In[25]:= n = 1;
a = 10;
LPLUS = -(u^n + v^n + u^n*v^n + a*n*((u^n*v^n)/(u*v))^(1/2) + 1)/
    (u^n + v^n + u^n*v^n + 1);
LMINUS = -(u^n + v^n + u^n*v^n - a*n*((u^n*v^n)/(u*v))^(1/2) + 1)/
    (u^n + v^n + u^n*v^n + 1);


Solve[0 == a/(1 + u^n) - u, u] // N
Out[29]= {{u → -3.70156}, {u → 2.70156}}

LPLUS /. {u → 2.70156, v → 2.70156}

Out[30]= -1.72984

In[31]:= LMINUS /. {u → 2.7015621187164243`, v → 2.7015621187164243`}
Out[31]= -0.270156
```

Stable

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```
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In[32]:= n = 2;
         a = 10;
         LPLUS = - (u^n + v^n + u^n*v^n + a*n*((u^n*v^n) / (u*v)) ^ (1/2) + 1) /
            (u^n + v^n + u^n*v^n + 1);
         LMINUS = - (u^n + v^n + u^n*v^n - a*n*((u^n*v^n) / (u*v)) ^ (1/2) + 1) /
            (u^n + v^n + u^n*v^n + 1);


         Solve[0 == a / (1 + u^n) - u, u] // N

Out[36]= {{u → -1. - 2. i}, {u → -1. + 2. i}, {u → 2.}}

In[37]:= LPLUS /. {u → 2., v → 2.}
```

stable

```
Out[37]= -2.6

In[38]:= LMINUS /. {u → 2.`, v → 2.`}
```

unstable

```
Out[38]= 0.6

In[41]:= u = -1.` + 2.` i;
         v = -1.` - 2.` i;
         solve[- (u^n + v^n + u^n*v^n + a*n*((u^n*v^n) / (u*v)) ^ (1/2) + 1) /
           (u^n + v^n + u^n*v^n + 1)]

Out[43]= solve[-3.23607 + 0. i]

In[44]:= u = -1.` - 2.` i;
         v = -1.` + 2.` i;
         solve[- (u^n + v^n + u^n*v^n + a*n*((u^n*v^n) / (u*v)) ^ (1/2) + 1) /
           (u^n + v^n + u^n*v^n + 1)]
```

unstable

```
Out[46]= solve[-3.23607 + 0. i]
```

As n increases, number of SS increase

f)

$$\frac{dR_i^*}{dt} = k_f L R_i - k_r R_i^*$$

$$\frac{dN_i^*}{dt} = k_f^{ND} N_i D_j - k_r^{ND} N_i^*$$

$$\frac{dD_i}{dt} = k_D R_i^* - \gamma_D D_i$$

$$\frac{dR_i}{dt} = \frac{\beta^N}{K^n + [N_i^*]^n} - \gamma_R R_i$$

Set dR_i^*, dN_i^*, and $dD_i = 0$

we get $N_i^* = \dfrac{k_f^{ND} N_i D_j}{k_r^{ND}}$

$$R_i^* = \frac{k_f L R_i}{k_r}$$

$$D_i = \frac{k_D R_i^*}{\gamma_D}$$

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

$$\frac{dR_1}{dt} = \frac{\beta^n}{K^n + \left[\dfrac{k_f^{ND} N_1 k_D k_f L R_1}{k_r^{ND} k_r \gamma_D}\right]^n} \qquad \frac{dR_2}{dt} = \frac{\beta^n}{K^n + \left[\dfrac{k_f^{ND} N_2 k_D k_f L R_2}{k_r^{ND} k_r \gamma_D}\right]^n}$$

b) dimensionless variables : $u = \frac{R_1}{K}$ $v = \frac{R_2}{K}$ $\tau = \gamma_R t$

$$K \gamma_R \frac{du}{d\tau} = \frac{\beta^n}{K^n + \left[\frac{K_f^{NO} N_1 K_O K_f L}{K_r^{NO} K_r \gamma_D}\right]^n v^n K^n} - \gamma_R u K$$

$$K \gamma_R \frac{dv}{d\tau} = \frac{\beta^n}{K^n + \left[\frac{K_f^{NO} N_2 K_O K_f L}{K_r^{NO} K_r \gamma_D}\right]^n u^n K^n} - \gamma_R v K$$

divide by K and γ_R to get

$$\frac{du}{d\tau} = \frac{\left[\frac{\beta^n}{\gamma_R K^{n+1}}\right]}{1 + \left[\frac{K_f^{NO} N_1 K_O K_f L}{K_r^{NO} K_r K_O}\right]^n v^n} - u$$

$$\frac{dv}{dt} = \frac{\left[\frac{\beta^n}{\gamma_R K^{n+1}}\right]}{1 + \left[\frac{K_f^{NO} N_2 K_O K_f L}{K_r^{NO} K_r K_O}\right] u^n} - v$$

$$\alpha = \left[\frac{\beta^n}{\gamma_R K^{n+1}}\right] \qquad \theta_i = \frac{K_f^{NO} N_2 K_O K_f L}{K_r^{NO} K_r K_O}$$

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