Systems Biology

Assignment 2

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Q1) Y gets activated when x > threshold1.

Z gets activated on the satisfaction of 2 conditions:

i) x > threshold1

ii) y < threshold2

If any of them is not true, then Z loses the activation signal and the degradation causes it to eventually reduce in concentration.

Therefore we can model the ODE as follows:

```
y'=alpha1*heav(x-k1)-b1*y
# dy/dt = alpha1 * theta(x>k1) - b1*y
z'=alpha2*heav(x-k1)*heav(k2-y)-b2*z
# dz/dt = alpha2 * theta(x>k1) * theta(y<k2) - b2*z
```

Where k1 is threshold1 and k2 is threshold2.

```
init y=0, z=0
# We start with no initial conc for y and z
param k1=2, k2=0.5, alpha1=1, alpha2=1, b1=1, b2=1
# I used k1 as 2 so that y is activated once x is >=2 which happens after 20 seconds
# I used k2 = 0.5 as max for y was 1 (alpha1/b1). Therefore I kept t_start_repression as t_half for y
```

Initialized y and z to 0. Also, the kept threshold is such that the first threshold (for x) is met once it gets incremented to 5 (which happens after 20 seconds) and the second threshold (for y) is met when it crosses 0.5 which is also the time when it reaches half of its max concentration ($t_{1/2}$). As we had an AND gate implemented as soon as repression starts, the concentration of Z starts to reduce. I simply multiplied k1,k2, and alpha1, alpha2 by 10 to model the second case.

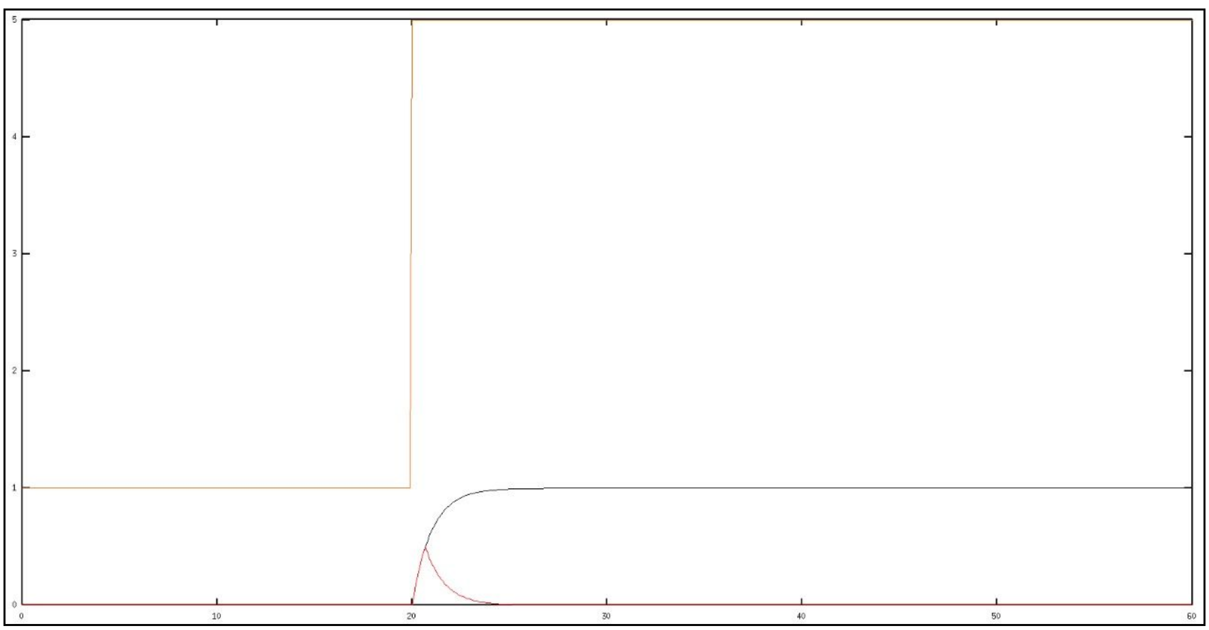
Plotting the ODEs: Orange curve is for x. Black for y. Red for z.

a) Taking X = { 1 : [0,20) and 5: [20,60] }

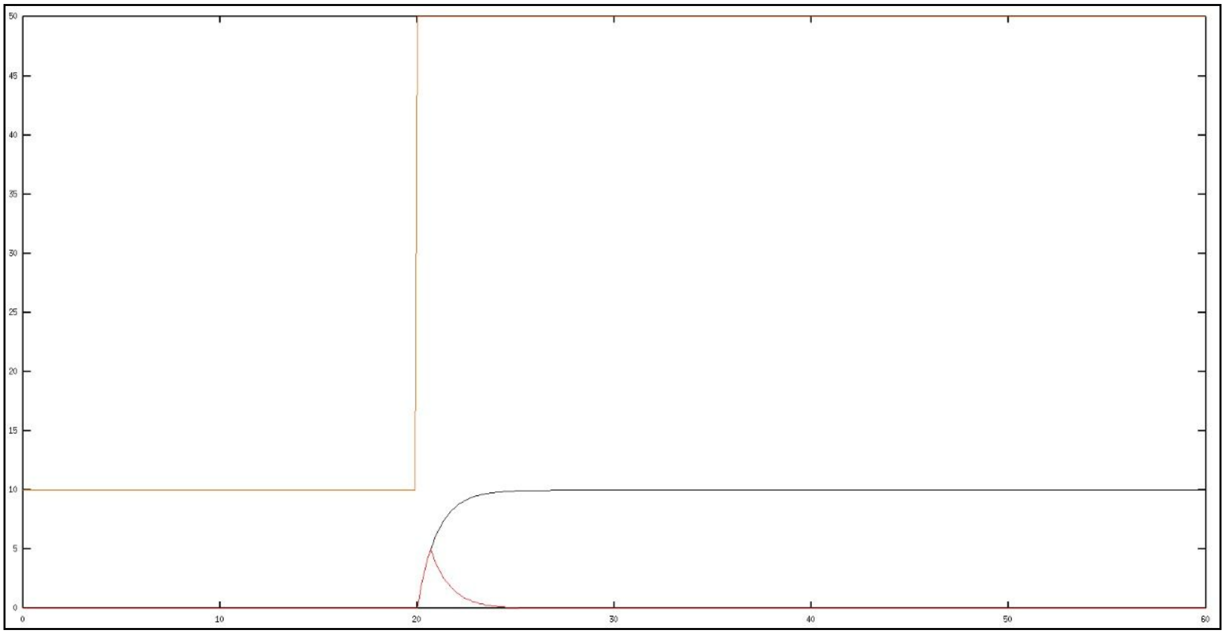
```
x=1+4*heav(t-20)
#signal remains 1 from time 0-20 and then becomes 5
aux signal=x

@ total=60, dt=0.1, method=stiff
@ bounds=1000000
@ NPLOT=3, yp1=y, yp2=z, yp3=signal
@ total=60

done
```



b) Taking X = { 10 : [0,20) and 50: [20,60] }



Q2) In this we had to model different activation profiles of Y by X. We want the Y's to have the same steady-state but different degradation rates. Therefore we need to change (b) while keeping alpha/b the same. Therefore, we scale both alpha and b with the same constants. I plotted 3 variations of the Incoherent FFL problem keeping everything the same except for alpha1 and b1.

```
init y1=0, y2=0, y3=0, z1=0, z2=0, z3=0
# We start with no initial conc for y and z
param k1=2, k2=0.5, alpha11=10, alpha2=1, b11=10, b2=1, alpha12=5, b12=5, alpha13=1, b13=1
# I used k1 as 2 so that y is activated once x is >=2 which happens after 20 seconds
# I used k2 = 0.5 as max for y was 1 (alpha1/b1). Therefore I kept t_start_repression as t_

y1'=alpha11*heav(x-k1)-b11*y1
# dy/dt = alpha1 * theta(x>k1) - b1*y
z1'=alpha2*heav(x-k1)*heav(k2-y1)-b2*z1
# dz/dt = alpha2 * theta(x>k1) * theta(y<k2) - b2*z

y2'=alpha12*heav(x-k1)-b12*y2
z2'=alpha2*heav(x-k1)*heav(k2-y2)-b2*z2

y3'=alpha13*heav(x-k1)-b13*y3
z3'=alpha2*heav(x-k1)*heav(k2-y3)-b2*z3

x=1+4*heav(t-20)
#signal remains 1 from time 0-20 and then becomes 5
aux signal=x

@ total=60, dt=0.05, method=stiff
@ bounds=1000000
@ NPLOT=7, yp1=y1, yp2=z1, yp3=signal, yp4=y2, yp5=y3, yp6=z2, yp7=z3
@ total=60

done
```

The three variations used were:

i) alpha11=10, b11=10

ii) alpha12=5, b12=5

iii) alpha13=1, b13=1

So, the steady states for all the Y's are expected to be the same with the only difference being their time taken to reach half of the steady-state. Therefore Z increases till this time and then starts reducing. As the times took to start repression decrease with an increase in alpha value, we see that the amount of Z that could accumulate (peak of z) also reduces with an increase in alpha value. Below are the 3 plots.

Red is for x

The three curves with peaks around 1 are the plots for Y with the black one with the highest alpha and beta values (10,1) and light orange with the least.

The three curves towards the bottom represent the curves for Z with the red one (lowest peak) being the one for the highest alpha and beta values(10,1) and green for the smallest.