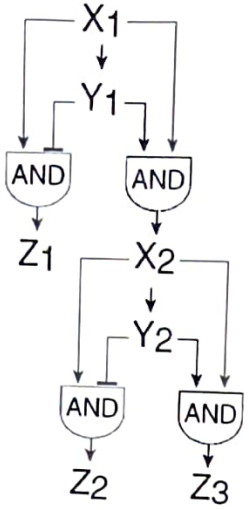
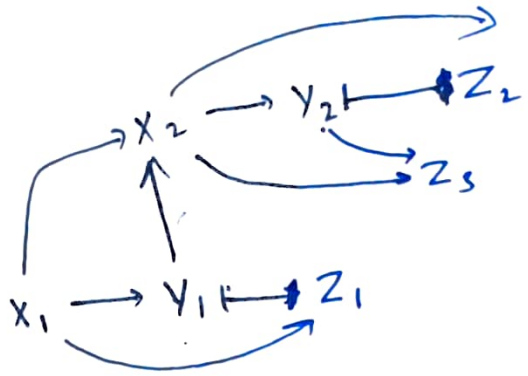
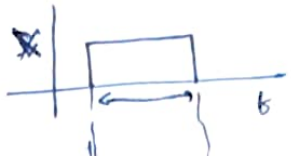
1. Draw the profile of Z1, Z2 and Z3. **[2 marks]**



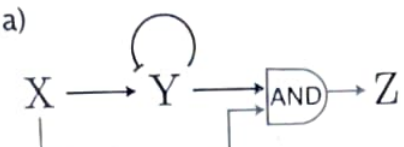


2. Design a gene circuit to filter out short, noisy inputs while responding to a sustained signal. What is the minimum pulse duration of signal is required to activate the response? **[2 marks]**

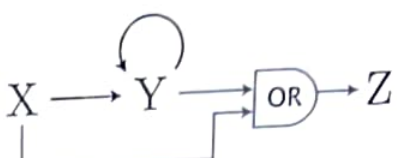


3. (a) The regulator Y in FFLs in transcription networks is often negatively autoregulated. How does this affect the dynamics of the circuit, assuming that it has an AND input function at the Z promoter? (b) The *Y* regulator in an OR gate FFL is often positively autoregulated. How does this affect the dynamics of the circuit? **[3 marks]**

a)



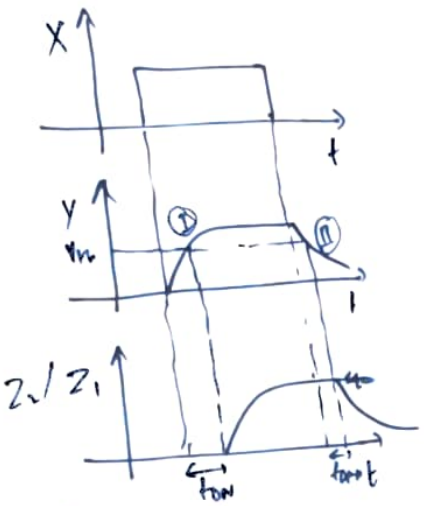
b)

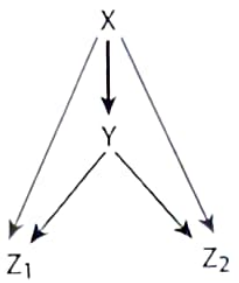


$$\frac{dY}{dt} = \beta \cdot \frac{K^n}{Y^n + K^n} - \alpha_y Y$$

$$\frac{dY}{dt} = \beta \frac{Y^n}{K^n + Y^n} - \alpha_y Y$$

4. What is the temporal order of turn ON and turn OFF in a multi-output coherent feedforward where all genes are regulated by AND gates? Which thresholds determine the ON and OFF orders of Z_1 and Z_2? Can one obtain FIFO (first in and first out) orders? For example, Z_1 appears and disappears first with increase and decrease in X, respectively.
[3 marks]





if $Y_{th_1} < Y_{th_2}$
Z_1 appears first (turns ON)
Z_2 disappears first (turns OFF)

we can't obtain FIFO as decay rate for Y is same in both cases & lower thresholds will appear faster but disappear slower (takes time to decay from steady state to threshold value)

(I) $Y(t) = Y_{ss}(1 - e^{-\alpha t})$

Z_1 : $Y_{th_1} = Y_{ss}(1 - e^{-\alpha t_{ON_1}})$

Z_2 : $Y_{th_2} = Y_{ss}(1 - e^{-\alpha t_{ON_2}})$

$$\frac{\ln\left(1 - \frac{Y_{th}}{Y_{ss}}\right)}{-\alpha} = t_{ON}$$

(II) $Y(t) = Y_{ss} e^{-\beta t}$

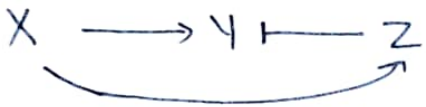
$Y_{th_1} = Y_{ss} e^{-\beta t_{OFF_1}}$

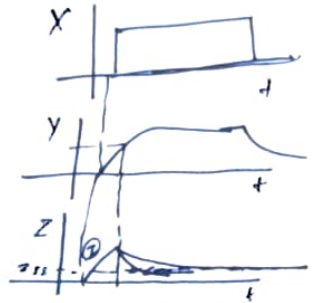
$Y_{th_2} = Y_{ss} e^{-\beta t_{OFF_2}}$

$$\frac{\ln\left(\frac{Y_{th}}{Y_{ss}}\right)}{-\beta} = t_{OFF}$$

∴ output with least threshold for Y appears first
output with highest threshold for Y disappears first
output thresholds for Y determine the t_{ON} & t_{OFF} for each out put
First In First out cant be obtained

5. Calculate the response time for incoherent feed forward loop and compare it with simple regulation. What is the condition for adaptation? [3 marks]





$$\frac{dz}{dt} = \alpha_z X - \frac{\beta_z \beta_y K^n}{X^n + K^n}$$

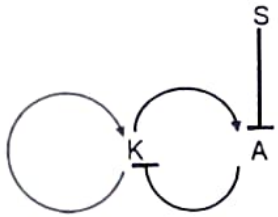
↳ steady state $\frac{dz}{dt} = 0 = \alpha_z X - \beta_z \beta_y$

6. Define nullclines. Use nullclines to show that mutual inhibition between X and Y proteins can give rise to bistable characteristics. Write the relevant equations. Show how trajectories cross nullclines? If signal S activates X independently, sketch how the steady state of X changes with S. **[5 marks]**

(4)

(1)

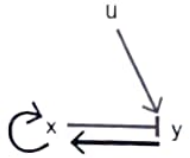
7. Explain the difference between fold change detection (FCD) and adaptation? What is the relationship between these two characteristics. Show that the given circuit exhibit FCD. **[5 marks]**

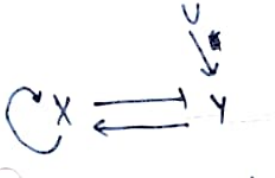


every system that does fold change detection is adaptive

3·025

8. Write the equation for the given system. Demonstrate that the system can exhibit oscillatory characteristics by drawing the phase plane. Comment about the characteristics of the oscillations. Discuss how the system can exhibit excitable characteristics by modifying the parameters or structure of the phase plane. [**5 marks**]





9. A biochemical reaction involves binding of a substrate (S) to enzyme (E) forming modified substrate (Sp). [**5 marks**]

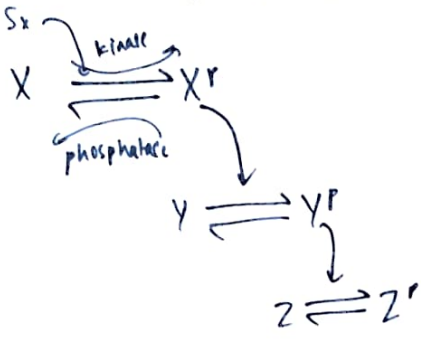
$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E + Sp$$

Write the rate expression for the formation of the modified substrate (Sp). Explain the role of different parameters in the reaction. Illustrate how varying these parameters affects the rate using appropriate plots.

$$\frac{d[ES]}{dt} = k_1[E][S] - k_{-1}[ES] - k_2[ES]$$

steady state $\rightarrow \frac{d[ES]}{dt} = 0$

10. Describe how a protein modification, such as phosphorylation by a kinase and dephosphorylation by a phosphatase, contributes to signal propagation within a cell. **[2 marks]**



X, Y, Z here are intracellular proteins which pass on the signal

Sx is the external signal which activates X by adding a phosphate group

If forms a stable complex [Sx X] which dissociates into Sx & Xp (activated form of X).

Xp further activates Y & so on

this is how a signal is propagated within a cell.

regular X can't interact with Y

Why Y with Z

so activation is necessary

2