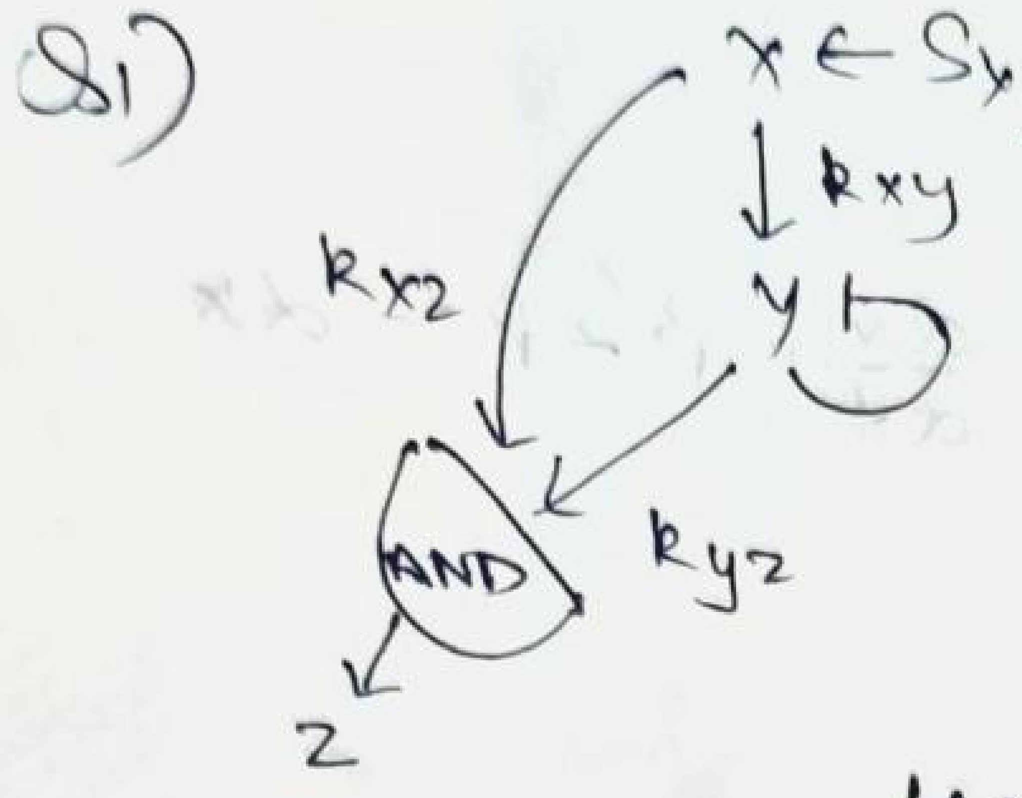
Q1)



→ we are assuming a step func for X.

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the rate for y will have 3 terms

production due to x ($\Theta(x > k_{xy})$)

repression due to itself (hill func type $\frac{k_{yy}^n}{y^n + k_{yy}^n}$)

degradation ($-\alpha y$)

$$\therefore \boxed{\frac{dy}{dt} = \beta_1 \Theta(x > k_{xy}) \frac{k_{yy}^n}{k_{yy}^n + y^n} - \alpha y}$$

for a simple FFL with no negative autoregulation

$$\boxed{\frac{dy}{dt} = \beta_2 \Theta(x > k_{xy}) - \alpha y}$$

↳ the rate of z will have 3 terms

production from x ($\Theta(x > k_{xz})$)

production from y ($\Theta(y > k_{yz})$)

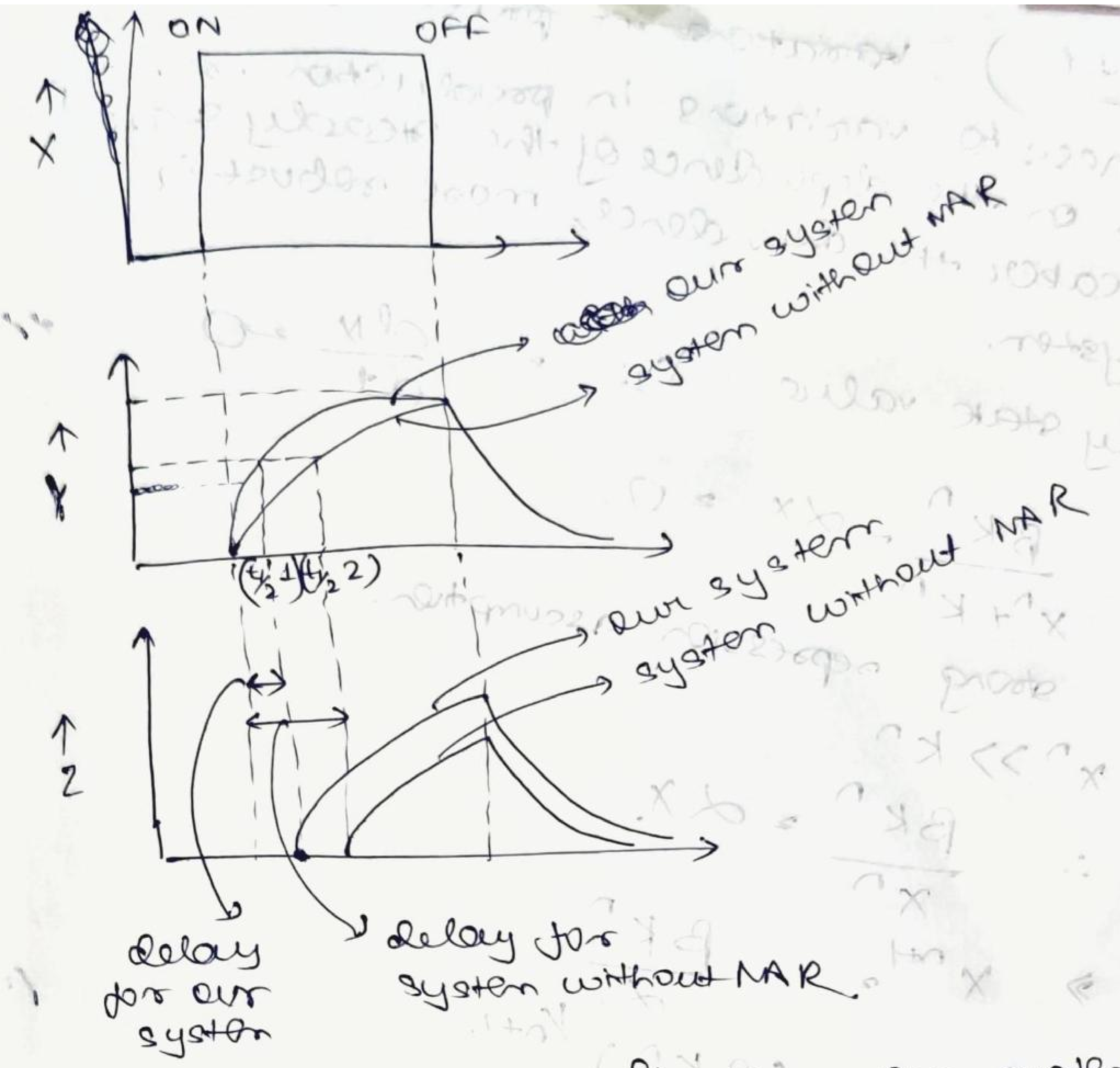
degradation ($-\alpha z$)

as we have an AND gate

$$\boxed{\frac{dz}{dt} = \beta_3 \Theta(x > k_{xz}) \Theta(y > k_{yz}) - \alpha_z}$$

↳ same for one with no NAR on y

now if we draw graphs for them.



As we can see from the figures, our system (with NAR on y) ~~reaches~~ has a quicker response time hence ~~crosses~~ crosses the limit $\theta(y > k_{y2})$ faster than the one without NAR.

As we have a $\boxed{\text{AND}}$ gate implemented the production of z begins only when both input signals are 1. ∴ There is a delay as it takes some time for y to be produced $> k_{y2}$. Note that there is no delay for OFF as if either one $\theta(x > k_{x2})$ or $\theta(y > k_{y2})$ is 0 then the func. switches off.

∴ NAR on y reduces transient delay in production of z and also allows more z to be produced as they switch off together.

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Q2) Show that the response time can vary with n.

Sol) for a NAR system.

$$\frac{dx}{dt} = \beta \frac{K^n}{x^n + K^n} - \alpha x$$

assumption for strong autorepression:

$$\left(\frac{x}{K}\right)^n >> 1 \quad \text{or} \quad x^n >> K^n$$

$$\frac{dx}{dt} = \beta \frac{K^n}{x^n} - \alpha x.$$

$$\Rightarrow \frac{dx}{dt} = \frac{\beta K^n - \alpha x^{n+1}}{x^n}$$

$$\Rightarrow \int_{x_0}^{x} \frac{x^n dx}{\beta K^n - \alpha x^{n+1}} = \int_0^t dt$$

taking $\beta K^n - \alpha x^{n+1} = a$

$$\therefore -\alpha(n+1)x^n dx = da$$

~~limits e fo~~

$$\int_{a_1}^{a_2} \frac{-da}{\alpha(n+1)(a)} = \int_0^t dt$$

$$\therefore \ln(a_2/a_1) = -\alpha(n+1)t$$

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$a_2 = a_1 e^{-\alpha(n+1)t}$

taking $x_0 = 0$

$a_2 = \beta K^n - \alpha x^{n+1}$ $\quad a_1 = \beta K^n$

$\beta K^n - \alpha x^{n+1} = \beta K^n e^{-\alpha(n+1)t}$

$x^{n+1} = \frac{\beta}{\alpha} K^n \left(1 - e^{-\alpha(n+1)t}\right)$

$\therefore x = \left(\frac{\beta K^n}{\alpha}\right)^{1/n+1} \left(1 - e^{-\alpha(n+1)t}\right)^{1/n+1}$

calculating $t_{1/2}$ we

at t_∞ $x = x_{st} = \left(\frac{\beta K^n}{\alpha}\right)^{1/n+1}$

$\therefore$ at $t_{1/2}$ $x = \frac{x_{st}}{2}$

$\frac{x_{st}}{2} = x_{st} \left(1 - e^{-\alpha(n+1)t}\right)^{1/n+1}$

$\therefore \left(\frac{1}{2}\right)^{n+1} = 1 - e^{-\alpha(n+1)t}$

$e^{-\alpha(n+1)t} = 1 - (1/2)^{n+1}$

$-\alpha(n+1)t = \log_e\left(1 - \frac{1}{2^{n+1}}\right)$

$t = \frac{1}{\alpha(n+1)} \log_e\left(\frac{2^{n+1}-1}{2^{n+1}}\right)^{-1}$

$$\therefore \boxed{t_{1/2} = \frac{1}{(n+1)\alpha} \log_e\left(\frac{2^{n+1}}{2^{n+1}-1}\right)}$$

response time

we can rewrite as $t_{1/2} = \frac{1}{(n+1)\alpha} \log_e\left(\frac{1}{1 - \frac{1}{2^{n+1}}}\right)$

on increasing $n \uparrow$ $\quad$ this term decreases $\quad$ this term decreases

$\frac{1}{(n+1)\alpha}$ decreases

also $\frac{1}{1 - \frac{1}{2^{n+1}}}$ decreases $\quad \therefore t_{1/2}$ decreases on increasing n.

$\therefore$ response time decreases with increasing n

Q2 contd) ~~variations in production rates~~

Robustness to variations in production rates (β) depends on the dependence of the steady state on β. weaker the dependence, more robust is our system.

steady state value X_{st} : $\frac{dx}{dt} = 0$

$$\therefore \frac{\beta K^n}{x^n + K^n} - \alpha x = 0.$$

using strong repression assumption.

$$x^n >> K^n$$

$$\therefore \frac{\beta K^n}{x^n} = \alpha x.$$

$$\Rightarrow x^{n+1} = \frac{\beta K^n}{\alpha}.$$

$$\therefore X_{st} = \left(\frac{\beta K^n}{\alpha}\right)^{1/n+1}.$$

$$\text{or } X_{st} = \left(\beta^{1/n+1}\right)\left(\frac{K^n}{\alpha}\right)^{1/n+1}.$$

as n increases dependence of X_{st} on β reduc

[for $n = \infty$ X_{st} is independent of β]

$\therefore$ as $n \uparrow$ robustness to variations in production rates (β) $\uparrow$.

Q3) $\frac{dx}{dt} = \beta' + \beta x - \alpha x$

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$\Rightarrow \frac{dx}{dt} = \beta' + (\beta - \alpha) x$

$$\int_0^x \frac{dx}{\beta' + (\beta-\alpha)x} = \int_0^t dt$$

$\beta' + (\beta - \alpha) x = a$

$(\beta - \alpha) dx = da$

$$\int_{a_1}^{a_2} \frac{da}{(\beta-\alpha) a} = \int_0^t dt$$

$\ln(a_2/a_1) = (\beta-\alpha) t \Rightarrow a_2 = a_1 e^{(\beta-\alpha)t}$

$a_2 = \beta' + (\beta-\alpha) x$

$a_1 = \beta'$

$\therefore$ $\Rightarrow \beta' + (\beta-\alpha) x = \beta' e^{(\beta-\alpha)t}$

$\Rightarrow \left(\beta' - \beta' e^{-(\alpha-\beta)t}\right) = (\alpha-\beta) x$

$$\Rightarrow \boxed{x = \frac{\beta'}{(\alpha-\beta)}\left(1 - e^{-(\alpha-\beta)t}\right)}$$

for steady state $\frac{dx}{dt} = 0$

$\therefore \beta' + \beta x_{st} - \alpha x_{st} = 0$

$$\therefore \boxed{x_{st} = \frac{\beta'}{(\alpha-\beta)}}$$

$\therefore$ at $t_{1/2} \Rightarrow x = \frac{x_{st}}{2} = \frac{\beta'}{2(\alpha-\beta)}$

$$\frac{1}{2}\frac{\cancel{\beta'}}{\cancel{(\alpha-\beta)}} = \frac{\cancel{\beta'}}{\cancel{(\alpha-\beta)}}\left(1 - e^{-(\alpha-\beta)t_{1/2}}\right)$$

$\Rightarrow -(\alpha-\beta)\, t_{1/2} = \log_e 1/2$

$\Rightarrow \boxed{t_{1/2} = \dfrac{\log_e 2}{(\alpha-\beta)}} \longrightarrow$ for $\dfrac{dx}{dt} = \beta' + \beta x - \alpha x$

↳ In a simple system

$\dfrac{dx}{dt} = b - ax$

$x = \dfrac{b}{a}\left(1 - e^{-at}\right)$

at steady state $dx/dt = 0$ ∴ $x_{st} = b/a$

at $t_{1/2} \Rightarrow x = \dfrac{x_{st}}{2} = b/2a$

$\therefore \dfrac{1\beta}{2\alpha} = \dfrac{\beta}{\alpha}\left(1 - e^{-at}\right)$

$\Rightarrow t_{1/2} = \dfrac{\log_e 2}{a} \longrightarrow$ for simple system $\dfrac{dx}{dt} = \beta - \alpha x$

↳ so we can say that our system is just like a simple system with $b = \beta'$ and $a = \alpha - \beta$.

↳ if we are comparing a simple system with $a = \alpha$ then our response time than a simple system is lesser than a simple system.