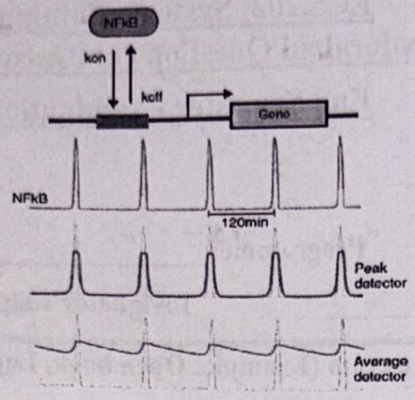
1. NFkB (shown in orange) is a transcriptional factor activating gene G (shown in green). Under what parametric condition, there will be peak detection and average detection. **[2 marks]**



$k_{on} > k_{off}$ → Average detector

$k_{off} > k_{on}$ → Peak detector

2. Name the process: **[1.5 marks]**
(a) DNA to mRNA: ....Transcription....
(b) mRNA to Protein: ....Translation....
(c) DNA to DNA: ....Replication....

3. Which of the following forms of human communication are similar to paracrine, endocrine, and synaptic signaling by cells? **[1.5 marks]**
(a) A telephone conversation: ....Synaptic....
(b) Talking to people at a cocktail party: ....~~endocrine~~.... paracrine
(c) A radio announcement: ....endocrine....

4. Why NAR is robust compared to a simple system. [2 marks]

$X \qquad X_{ss} = K \Leftarrow \frac{dx}{dt} = \beta \cdot \frac{K^n}{K^n + x^n} - \alpha . X$

K is fixed for the system and it does not change (hardwire)

β, α are Variable/noisy

5. A dynamic system is represented by the differential equation [3 marks]

$$\tau \frac{dy(t)}{dt} + y(t) = r(t)$$

The system is given the sinusoidal input r(t) = sinωt. The value of ω at which magnitude of the output y(t) is $1/\sqrt{2}$ at steady state, is given by (in terms of τ) $\Rightarrow y(t) = |G(j\omega)| \cdot \sin(\omega t + \phi)$

$\tau s y(s) + y(s) = r(s)$

$= \frac{1}{\sqrt{2}} \sin(\omega t + \phi)$

$G(s) = \frac{y(s)}{r(s)} = \frac{1}{\tau s + 1}$

$G(j\omega) = \frac{1}{\tau j\omega + 1}$

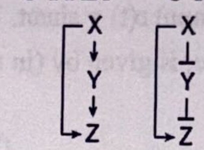
$|G(j\omega)| = \frac{1}{\sqrt{\tau^2 \omega^2 + 1}}$

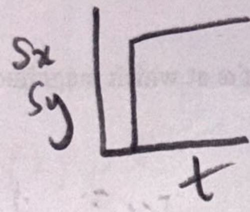
$\boxed{\omega = \frac{1}{\tau}} \Leftarrow$ Ans

$|G(j\omega)| = \frac{1}{\sqrt{2}}$

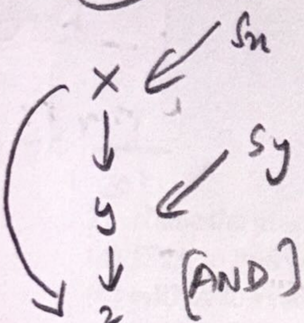
6. What might explain the difference in occurrence of C-FFL1 vs C-FFL2 in transcription networks? Draw and explain using Sx and Sy as inputs to the motif. [4 marks]

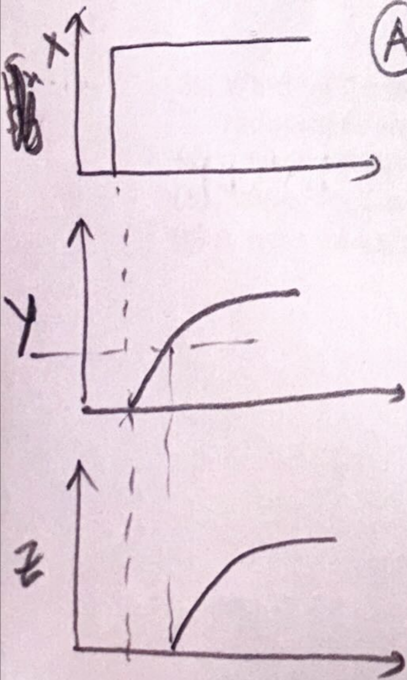
A B





A

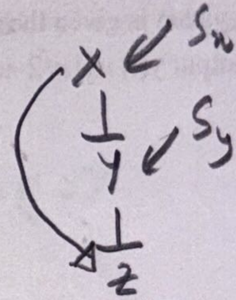


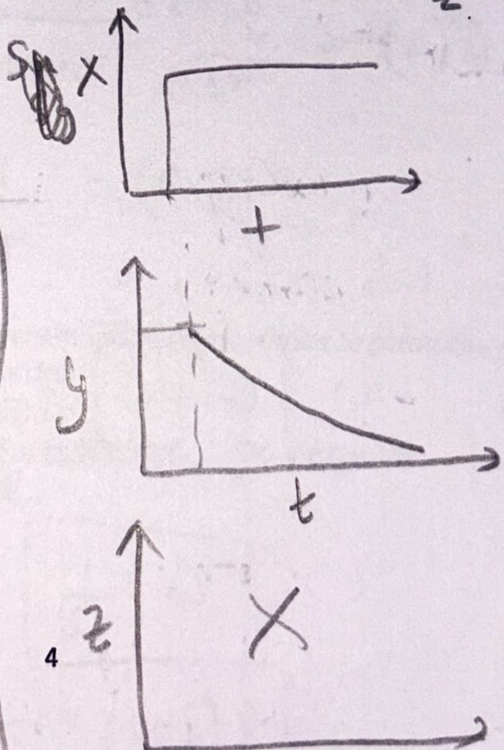


A is responsive

$\boxed{S_x \wedge S_y}$

in B

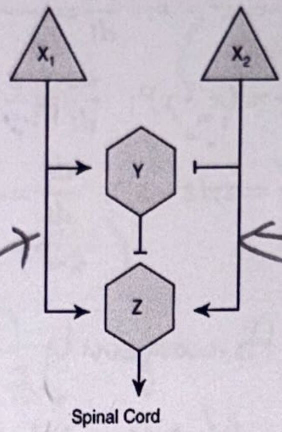




in B, S_y cannot act on y since y disappears wit x increase (S_x)

Essentially, not responding to multiple inputs ($S_x \wedge S_y$)

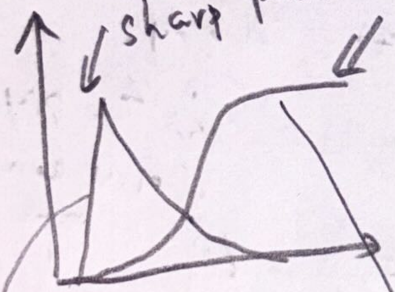
7. Multi-input circuit occurs in the neurons for human pain sensation (X1, X2, Y, Z are neurons). Identify the circuit. This circuit explains why there are two types of pain (say after an insect bite). Explain how the pain works based on the circuit. **[4 marks]**



Coherent FFL

Incoherent FFL

Circuit explain two types of Pain



Think what you feel when Something bites/or similar situation.

I-FFL (driven by neuron X_1) (plus generator)

C-FFL (driven by neuron X_2) (sign sensitive delay)

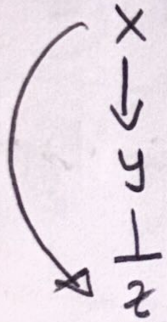
8. What is the homogeneity condition that you can use to check equations for fold change detection (FCD) property? Which circuits (equation given below) have FCD? The input is x, the internal variable is y and the output is z. Draw each model circuit diagram and comment about it. **[6 marks]**

i. $\dfrac{dy}{dt} = x^2 - y; \quad \dfrac{dz}{dt} = \dfrac{x}{y} - z$

ii. $\dfrac{dy}{dt} = (x-y)^2; \quad \dfrac{dz}{dt} = \dfrac{x}{y} - z$

iii. $\dfrac{dy}{dt} = zy(z - z_o); \quad \dfrac{dz}{dt} = \dfrac{x}{y} - z$

i.



I-FFL

Homogenity Condition for FCD

$f(\lambda x, \lambda y, z) = \lambda f(x, y, z)$ — ①

$g(\lambda x, \lambda y, z) = g(x, y, z)$ — ②

$\cancel{f(x,y,z) = x^2} - y \quad f(x, y, z) = x^2 - y$

$\dfrac{dy}{dt} = f(x, y, z)$

$f(\lambda x, \lambda y, z) = \lambda^2 x^2 - \lambda y$ ① ✗

(First condition not satisfied

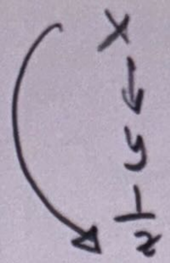
$\dfrac{dz}{dt} = g(x, y, z)$

$g(x, y, z) = \dfrac{x}{y} - z$

$g(\lambda x, \lambda y, z) = \dfrac{\cancel{\lambda} x}{\cancel{\lambda} y} - z = g(x, y, z)$

Not a FCD Circuit since ① is not satisfied ii $f(x,y,z) = (x-y)^2$

$g(x,y,z) = \frac{x}{y} - z$



I - FFL

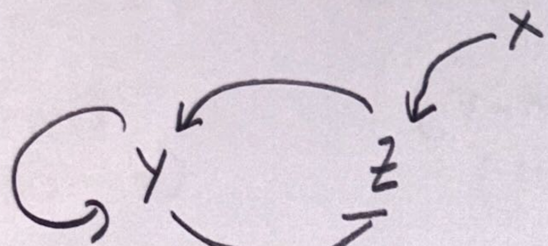
$f(\lambda x, \lambda y, z) = (\lambda x - \lambda y)^2$ (1 is not Satified)

$g(\lambda x, \lambda y, z) = \frac{\lambda x}{\lambda y} - z = g(x,y,z)$

(2 is statified)

$\boxed{\text{Not FCD}}$

(iii)



Amplified Negative feedback loop

(positive feedback / PAR + Negative feedback)

$f(x,y,z) = zy(z - z_0)$

$g(x,y,z) = \frac{x}{y} - z$

$f(\lambda x, \lambda y, z) = \lambda zy(z - z_0) = \lambda f(x,y,z)$ ✓

$g(\lambda x, \lambda y, z) = \frac{\cancel{\lambda} x}{\cancel{\lambda} y} - z = g(x,y,z)$ ✓

FCD Condition Statisfied

9. Show that the model given below exhibit periodic behaviour. [8 marks]

$$\frac{dU}{dt} = U(1 - V)$$

$$\frac{dV}{dt} = \alpha V(U - 1)$$

α is a kinetic parameter (analyze the eigen values). Draw the circuit and phase plane. Why this model shows periodic behaviour? How this circuit can be modified to do FCD with respect to S input (no FFL strategy)?

9

$$J = \begin{bmatrix} \frac{\partial f}{\partial u} & \frac{\partial f}{\partial v} \\ \frac{\partial g}{\partial u} & \frac{\partial g}{\partial v} \end{bmatrix} = \begin{bmatrix} 1-v & -u \\ \alpha v & \alpha u - \alpha \end{bmatrix}$$

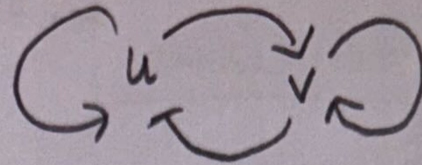
$$[u, v]_{ss} = [1, 1] \qquad = \begin{bmatrix} 0 & -1 \\ \alpha & 0 \end{bmatrix}_{[1,1]} \qquad \begin{bmatrix} a & b \\ c & d \end{bmatrix}$$

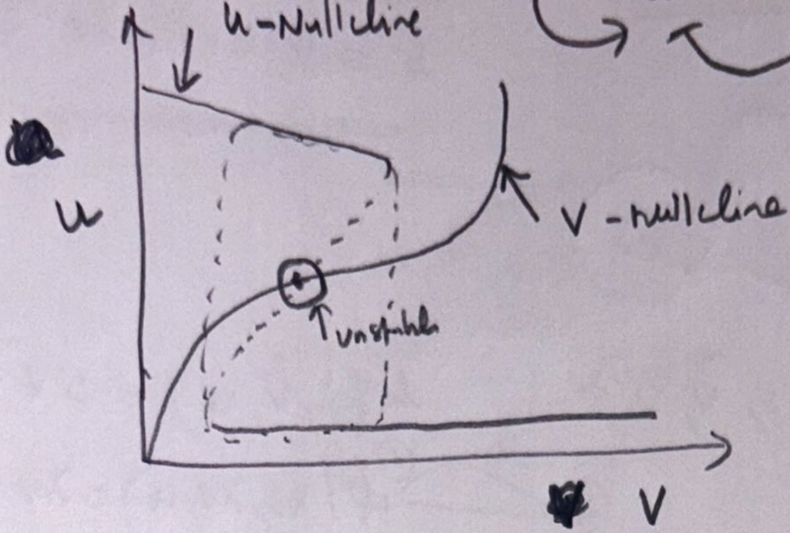
(eigen values)

$$\lambda_g = \frac{a+d \pm \sqrt{(a+d)^2 - 4(ad-bc)}}{2} = \frac{0 \pm \sqrt{0 - 4(0-(-\alpha))}}{2} = \frac{\sqrt{-4\alpha}}{2}$$

Eigen values are imaginary
So periodic $(\alpha > 0)$

(b) Phase plane





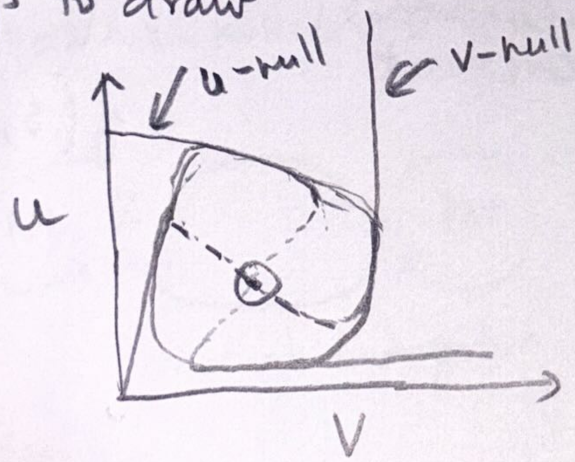
u ⊣ v

(u-null)
(Bistable)

u → v

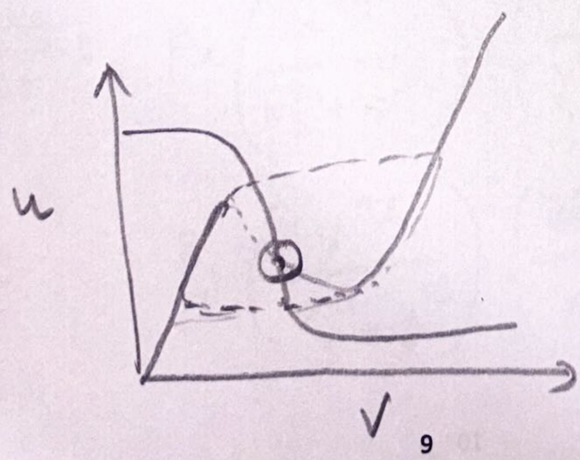
(v-null)
(switch-like)

other ways to draw



u-null
(bistable)

v-null
(Bistable



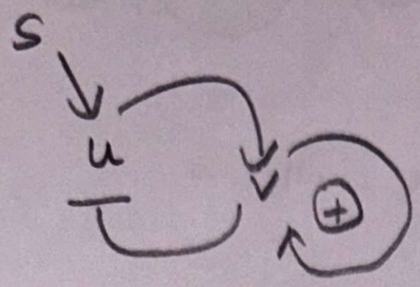
u-null
(Switch)

v-null
(Bistable)

Check → They may have changed x-axis ~~/~~ y-axis ⇒ So phase plane will be tilted accordingly

Ⓒ Modifications for FCD

· Remove NAR from u
s will activate u



$$\frac{dv}{dt} = f(s, v, u) \qquad f(s, v, u) = \alpha v (u-1)$$

$$f(\lambda s, \lambda v, u) = \lambda v \cdot \alpha (u-1)$$

$$= \lambda f(s, v, u)$$

$$\frac{du}{dt} = g(s, v, u)$$

$$g(s, v, u) = \frac{s}{v}(1-u)$$

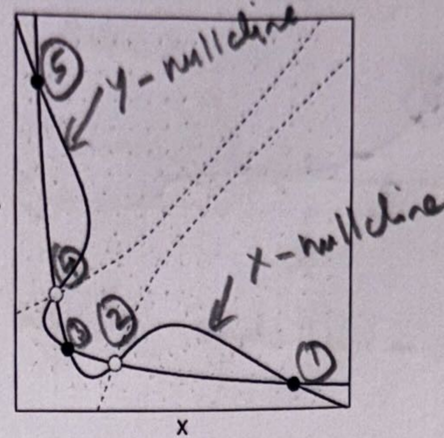
$$= \frac{\lambda s}{\lambda V} = (1-u)$$

$$= g(s, v, u)$$

This eqn is Changed accordingly from the given equation otherwise no FCD

FCD Conditions are met

10. A phase-plane diagram is given below. **[8 marks]**



(a) Mark the x and y nullclines. Comment about the shape of the nullclines, steady states and the phase plane.
(b) Design a circuit (interactions involving X and Y) that can give rise to this phase plane.
(c) Write the equations for this circuit.
(d) How can we change the phase plane to obtain only three stable steady states?

(a) 1, 3, 5 stable, 2, 4 unstable

Both x-nullcline & y-nullcline are bistable

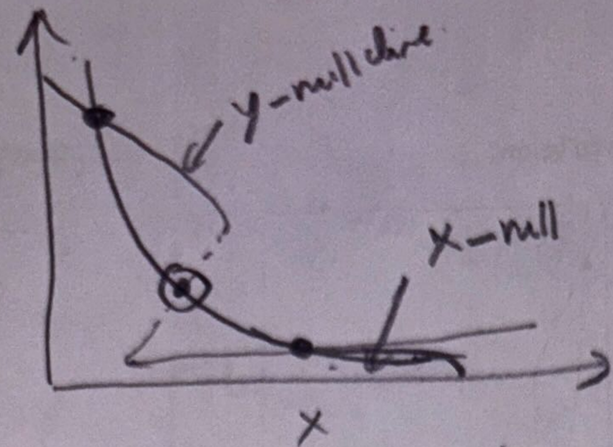
(b)

Mutual antagonism.

(c)
$$\frac{dx}{dt} = \beta_x \left(\frac{x^{n_1}}{K_x^{n_1} + x^{n_1}}\right) \cdot \left(\frac{K_{ix}^{n_2}}{y^{n_2} + K_{ix}^{n_2}}\right) - \alpha_x \cdot x$$

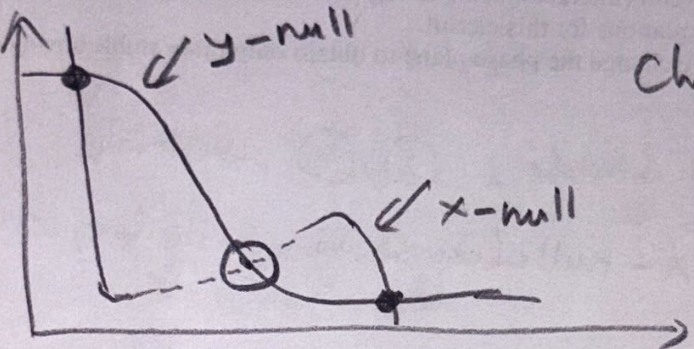
$$\frac{dy}{dt} = \beta_y \left(\frac{y^{n_3}}{K_y^{n_3} + y^{n_3}}\right) \left(\frac{K_{iy}^{n_4}}{x^{n_4} + K_{iy}^{n_4}}\right) - \alpha_y \cdot y$$

(d) =



changing x-nullcline Shape

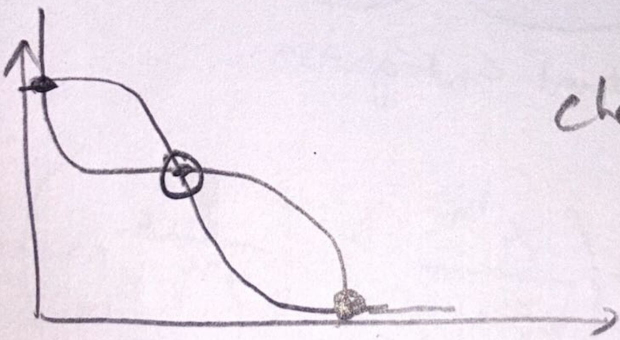
OR



Change y-nullcline Shape

$\boxed{\text{Anyone is fine}}$

OR



changing both x & y nullclines Shape