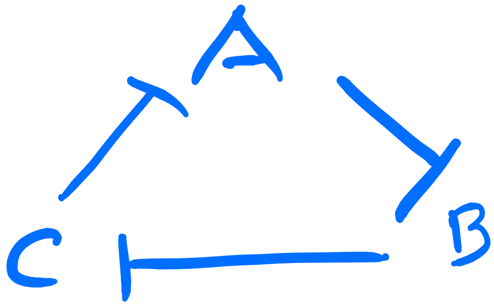
ELL 707

22.01.2020



MODEL →

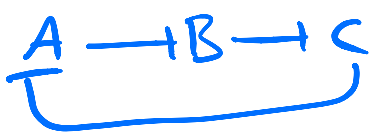
$$\frac{dA}{dt} = f(C) - rA$$

$$\frac{dB}{dt} = f(A) - rB$$

$$\frac{dC}{dt} = f(B) - rC$$

Next what?

→ What is required at biomolecular/systems level for an oscillation to occur?

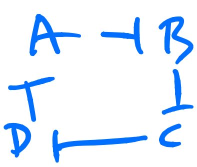
Based on 

, following may be needed

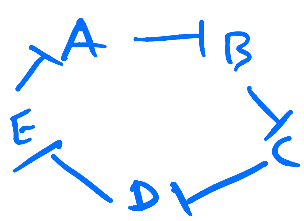
- "there should be a cycle"

  ≡ Feedback

- "product of signs should be negative"



not oscillate



oscillate

≡ ~ Negative

- maybe more . . .

as A doesn't oscillate, maybe a "delay" is required - (think about this in Boolean representation)

Look at a simple(st) circuit that has feedback + "negative".

has stable fixed point.

" Autoregulation"

" Negative autoregulatory circuit"

Does a model of this oscillate?

$$\frac{dA}{dt} = \alpha_0 + \alpha \cdot \frac{K^n}{K^n + A^n} - \gamma A$$

This model does not oscillate.

→ Is it easy to write analytical solution

$A(t) =$ ________ ? ($\alpha_0 = 0$, $n = 1$)

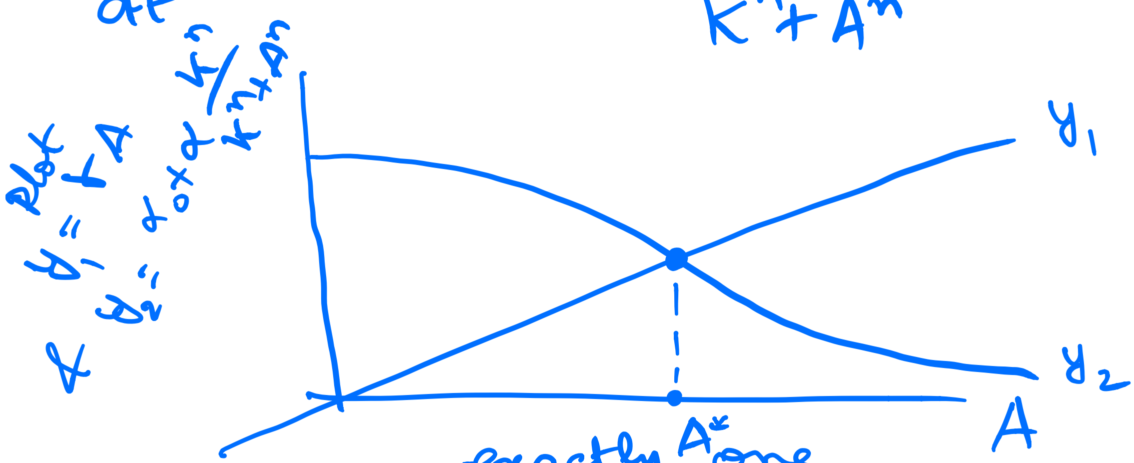
→ Geometric / Qualitative way

- When is $\frac{dA}{dt} = 0$?

(searching for a fixed point ...)

Does it exist? If so, how many?

$$\frac{dA}{dt} = 0 \Rightarrow \alpha_0 + \alpha \cdot \frac{K^n}{K^n + A^n} = \gamma A$$

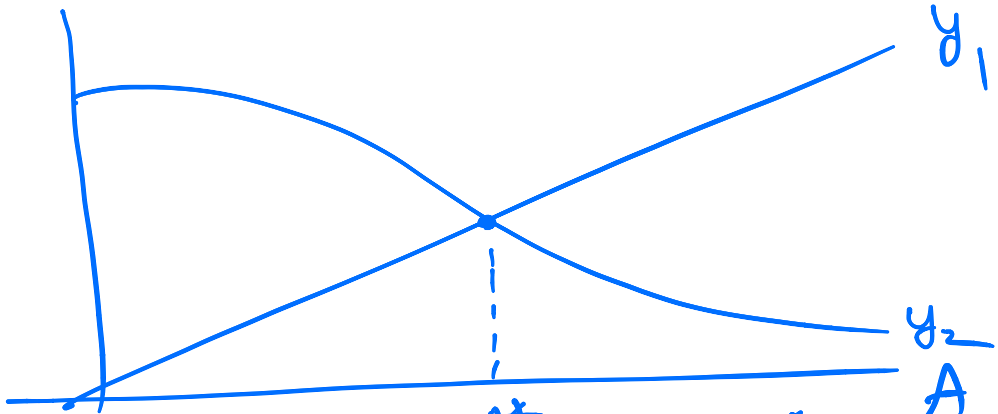


exactly one point of intersection

$\therefore$ If $A(0) = A^* \implies A(t) = A^* \;\; \forall\, t > 0$

Is it stable?

$$\frac{dA}{dt} = \alpha_0 + \frac{\alpha K^n}{K^n + A^n} - rA$$



$A < A^*$ $\implies \frac{dA}{dt} > 0$

$A > A^*$ $\implies \frac{dA}{dt} < 0$

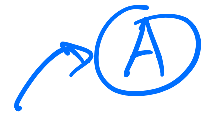
$\therefore$ A is a stable fixed point
{globally $(A \geq 0)$}

This model does not oscillate.
Possibly, no delay?

Point: A model with feedback + negative does not oscillate. $\longrightarrow$ role of delay?

Notion of time scale. (to understand delay)

$$\frac{dA}{dt} = \alpha - rA$$



vs

$$\frac{dA}{dt} = \alpha_0 + \alpha \frac{K^n}{K^n + A^n} - rA$$