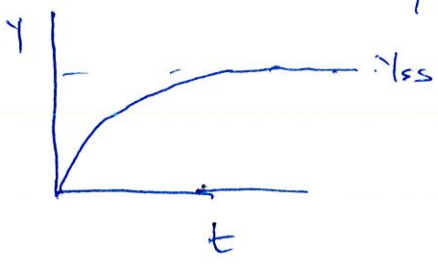
NETWORK MOTIFS & SYSTEM DYNAMICS

9/18/2018

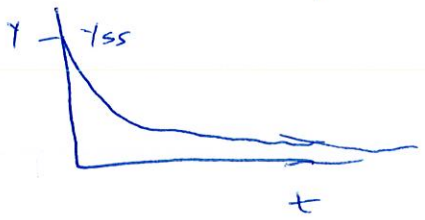
Recall $X \rightarrow Y$

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



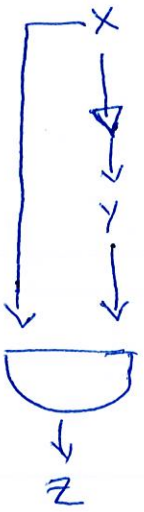
$X \dashv Y$

$Y = Y_{ss} e^{-\alpha t}$



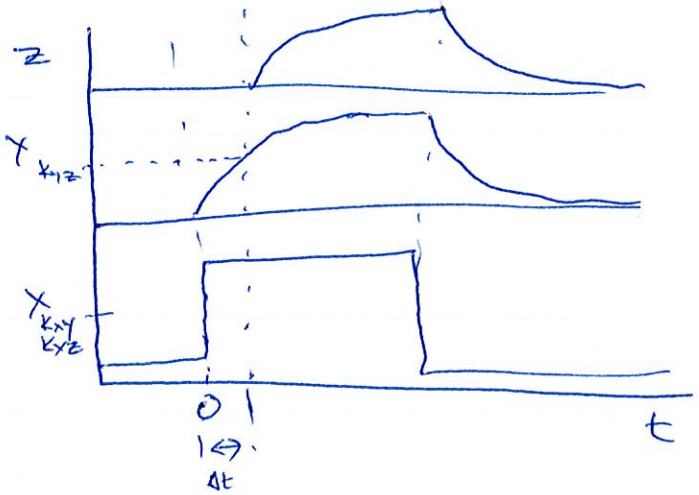
FFL - feedforward motifs have **two** parallel (one direct & one indirect) to regulate a gene from 1 input

e.g.



coherent
(same signal)

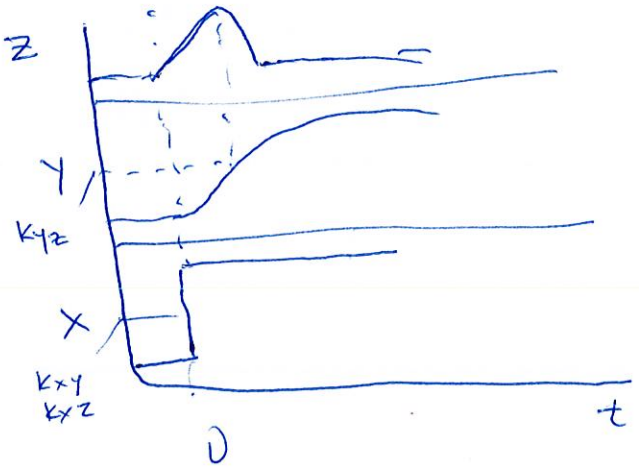
X **AND** Y must be **ON** to activate Z



- sign sensitive delay
  - ↳ ON signal has a delay but OFF doesn't

Coherent FFL w/ OR logic
- ↳ ON has no delay but OFF does

incoherent FFL
(conflicting signals)



Z expressed only in brief window when X on & Y low (Pulse generator)

Biology gives rise to interesting behavior due to dynamics & connectivity

- $X \longrightarrow Y$ $\quad X \dashv Y$

  Response time $= \frac{\ln 2}{\alpha}$

  Steady state proportional to K, n, [redacted], u, kd, β

- Cascade $\quad X \longrightarrow Y \longrightarrow Z$

  Amplify gain, increase steepness / binary

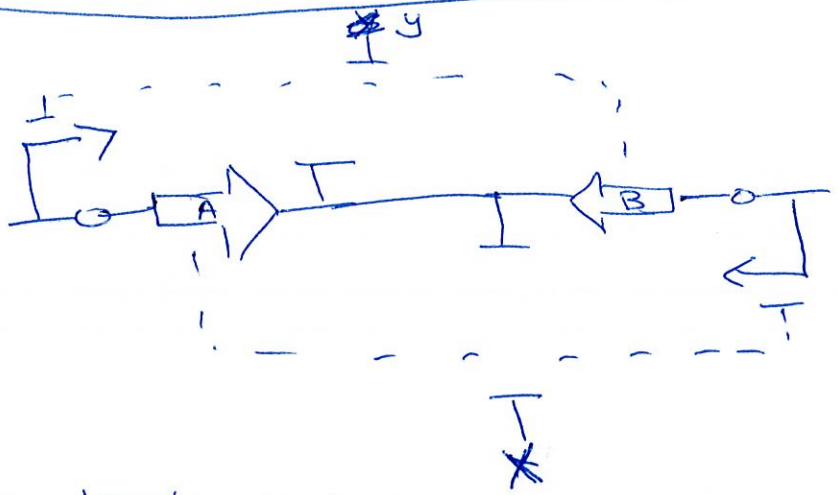
  - make decisions, definitively determine fates.
  - used in developmental & signal transduction pathways

- Negative autoregulation (−f(x))
  - faster response time
  - increased robustness [$S = \frac{1}{n+1}$ vs 1]

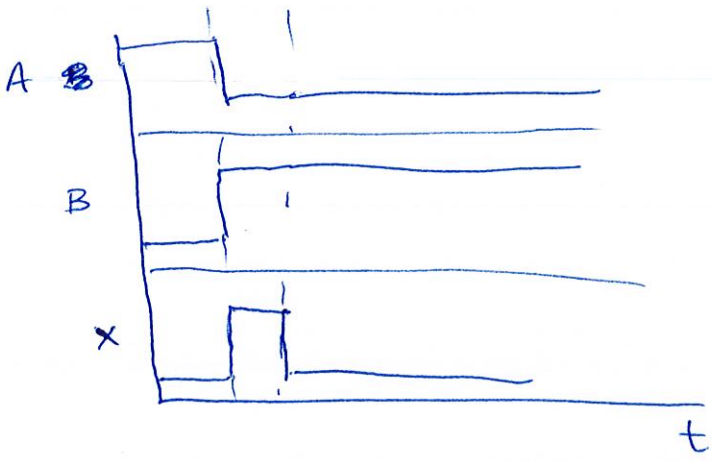
- FFL
  - sign sensitive delay, filters out noise in input
    - ↳ ON filter AND logic
    - ↳ OFF filter OR logic

    } Coherent

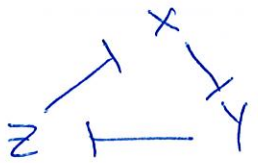
  - incoherent FFL → pulse generator for transient signal

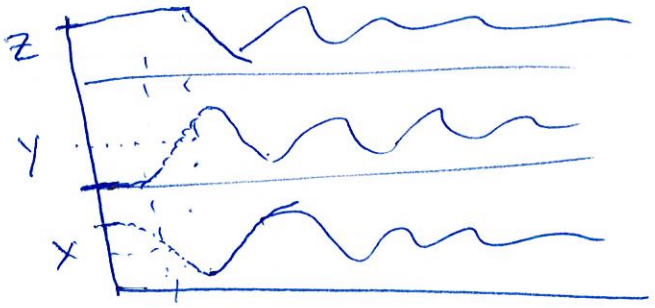


Genetic toggle switch or memory



under the right param. values memory fails



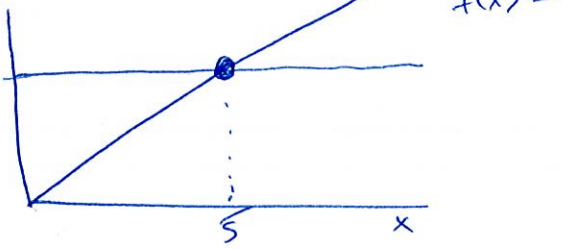


Basic design requirements for oscillation

1. negative feedback - prevents system from growing to ∞ or collapsing to zero
2. feedback has sufficient time delay
3. kinetic rate laws must be sufficiently non-linear

$$\frac{dy}{dt} = \overbrace{x}^{\text{prod.}} - 5$$

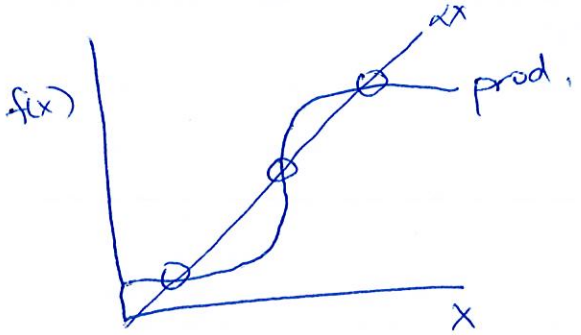
$$f(x) = \frac{dy}{dt}$$



$\Leftrightarrow$ $\overset{f)}{x}$

$x \dashv\vdash y \Rightarrow \overset{f)}{x}$

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



(4) rate of events must be on appropriate timescales relative to each other