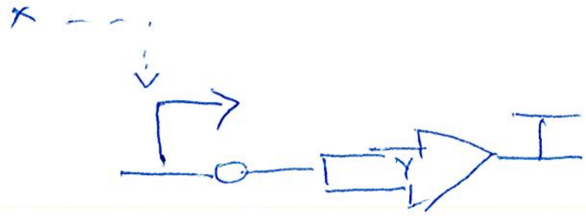
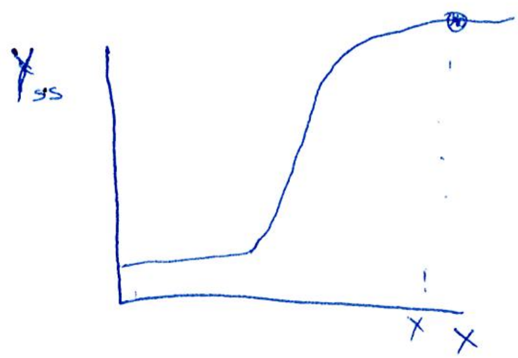
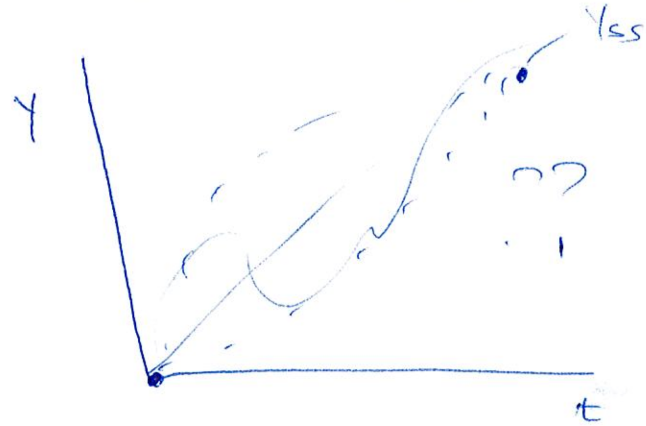
SYSTEM DYNAMICS & NETWORK MOTIFS 9/13/2018







$$\frac{dY}{dt} = am - \overset{\mu + k_d}{\overset{\shortparallel}{\alpha}} Y$$

$$= \alpha + \frac{Bx^n}{K^n + x^n} - \alpha Y$$

0 no leaky expression

Assume $x >> K$

$$\Rightarrow \frac{dY}{dt} \approx \frac{Bx^n}{x^n} - \alpha Y$$

$$\frac{dy}{dt} = B - \alpha y \qquad Y(0) = 0$$

$$\int_0^y \frac{dy}{B - \alpha y} = \int_0^t dt$$

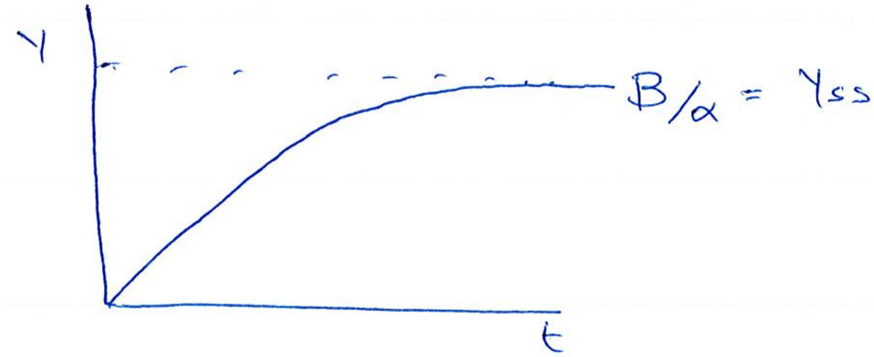
$$-\frac{1}{\alpha} \ln(B - \alpha y)\Big|_0^y = t\Big|_0^t$$

$$-\frac{1}{\alpha} \ln\left(\frac{B - \alpha y}{B}\right) = t - 0$$

$$\ln\left(\frac{B - \alpha y}{B}\right) = -\alpha t$$

$$\frac{B - \alpha y}{B} = e^{-\alpha t}$$

$$\boxed{Y = \frac{B}{\alpha}\left(1 - e^{-\alpha t}\right)}$$



define ~~half life~~ response time as time to reach $\frac{1}{2} Y_{ss}$ ($T_{1/2}$)

$$Y_{ss} = \frac{B}{\alpha}$$

$$Y(T_{1/2}) = \frac{Y_{ss}}{2} = \frac{B}{2\alpha}$$

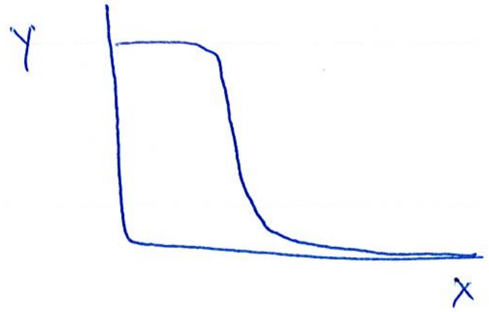
$$\frac{\cancel{B}}{2\cancel{\alpha}} = \frac{\cancel{B}}{\cancel{\alpha}}\left(1 - e^{-\alpha T_{1/2}}\right)$$

$$\frac{1}{2} = 1 - e^{-\alpha T_{1/2}}$$

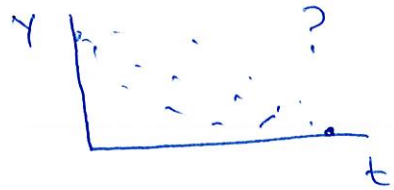
$$\frac{1}{2} = e^{-\alpha T_{1/2}}$$

$$-\ln 2 = -\alpha T_{1/2}$$

$$\boxed{T_{1/2} = \frac{\ln 2}{\alpha}}$$



$X \dashv Y$



$Y(t) = ?$

$T_{1/2} = ?$

$Y(0) = Y_{ss}$

$= \frac{B}{\alpha}$

$$\frac{dY}{dt} = am - \alpha Y$$

$$= A + \frac{BK^n}{x^n + K^n} - \alpha y$$

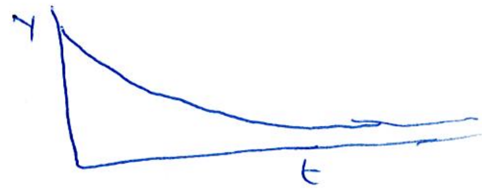
Assume no leaky exp. $A \to 0$

$X \gg K$

$$\frac{dY}{dt} = -\alpha y$$

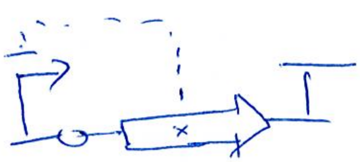
$$\Rightarrow Y = Y_{ss} e^{-\alpha t}$$

$$= \frac{B}{\alpha} e^{-\alpha t}$$



$$\boxed{T_{1/2} = \frac{\ln 2}{\alpha}}$$

Negative autoregulation



Assume no leaky expression

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

$$= \frac{B}{1 + \left(\frac{X}{K}\right)^n} - \alpha X$$

Assume $\frac{X}{K} \gg 1$

$$\frac{dx}{dt} \approx \frac{B}{\left(\frac{x}{K}\right)^n} - \alpha X$$

$$X^n \frac{dX}{dt} = BK^n - \alpha X^{n+1}$$

$x(0) = 0$
$\Rightarrow u(0) = 0$

let $u = X^{n+1}$

subs $\left\{ \frac{du}{dt} = (n+1) X^n \frac{dX}{dt} \Rightarrow \frac{dx}{dt} = \frac{1}{n+1} \cdot \frac{1}{x^n} \cdot \frac{du}{dt} \right.$

$$\frac{1}{n+1} \frac{du}{dt} = BK^n - \alpha u$$

$$\frac{1}{n+1} \int_0^u \frac{du}{BK^n - \alpha u} = \int_0^t dt$$

$$-\frac{1}{\alpha(n+1)} \ln\left[\frac{BK^n - \alpha u}{BK^n}\right] = t$$

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

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

$$\boxed{X = \underbrace{\left(\frac{BK^n}{\alpha}\right)^{\frac{1}{n+1}}}_{X^{ss}} \left(1 - e^{-\alpha(n+1)t}\right)^{\frac{1}{n+1}}}$$

Response Time : $T_{1/2}$?

$$\frac{\cancel{X_{ss}}}{2} = \cancel{X_{ss}} \left[1 - e^{-\alpha(n+1) T_{1/2}} \right]^{\frac{1}{n+1}}$$

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

$$\frac{\ln\left(1 - \left(\frac{1}{2}\right)^{n+1}\right)}{-\alpha(n+1)} = T_{1/2}$$

$$\frac{\ln\left(\frac{2^{n+1} - 1}{2^{n+1}}\right)}{-\alpha(n+1)} = T_{1/2}$$

$$\boxed{T_{1/2} = \frac{\ln\left(\frac{2^{n+1}}{2^{n+1} - 1}\right)}{\alpha(n+1)}} < \frac{\ln 2}{\alpha} \quad \text{for } n > 1$$

For any real system, negative feedback has a faster response time

Negative feedback also makes systems more robust

↳ β, k_d, μ can fluctuate from cell to cell
- leads to variability in SS.

↳ if $X < K$, trxn ↑, return to SS
$X > K$, trxn ↓, return to SS