$$A + B \xrightarrow{k_1} C \qquad \frac{d}{dt} C = k_1 [A][B]$$

Rapid Equalibrium Assumption

$$A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B \xrightarrow{k_2} \quad \text{if} \quad k_1 + k_{-1} \gg k_2 \quad \Bigg\} \quad \frac{\tilde{b}(t)}{k_1} = \frac{\tilde{a}(t)}{k_{-1}}$$

In equalibrium all the time

$$\tilde{a}(t) + \tilde{b}(t) = \tilde{c}(t)$$

$$\Rightarrow \tilde{a}(t) = \left(\frac{k_{-1}}{k_{-1}+k_1}\right) \tilde{c}(t) \quad \& \quad \tilde{b}(t) = \left(\frac{k_1}{k_{-1}+k_1}\right) \tilde{c}(t)$$

Quasi-Steady State Approximation

$$\emptyset \xrightarrow{k_0} A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B \xrightarrow{k_2} \emptyset \quad , \quad k_1 + k_{-1} \gg k_2$$

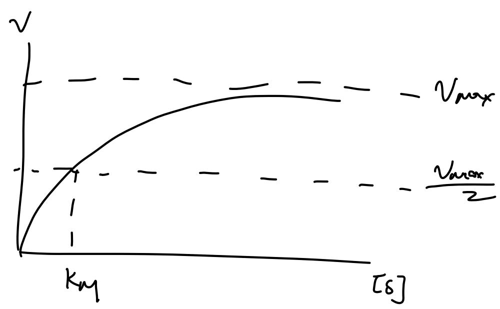
only in fast process

$$0 = k_0 - k_1 a^{qss} + k_{-1} b(t) \longrightarrow \text{reduce } a(t) \text{ to } a^{qss}$$

Michaelis-Menton Kinetics

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C \xrightarrow{k_2} P + E$$

$$\frac{d}{dt} P(t) = \frac{V_{max}[S]}{K_M + [S]}$$



two Substrate:

$$v = \frac{V_{max}[A][B]}{K_{AB} + K_B[A] + K_A[B] + [A][B]}$$

$* \; V_{max} = k_2 e_T$

Activation

Use the signalling molecule as enzyme: $v = \dfrac{k_1 [\text{Signal}][S]}{k_2 + [S]}$

Competitive Inhibition

$$v = \frac{V_{max}[S]}{K_M\left(1+\frac{[I]}{K_i}\right)+[S]}$$

Allosteric Inhibition

$$v = \underbrace{\frac{V_{max}}{1+i/K_i}}_{\text{inhibition}} \; \underbrace{\frac{S}{K_M+S}}_{\text{MM-kinetic}}$$

Cooperativity by Hill Function

$$Y = \frac{[X]^h}{K^h+[X]^h} = \frac{1}{1+\left(\frac{K}{x}\right)^h}$$

$\Rightarrow$ more cooperative for larger h

↳ also more sigmoidal

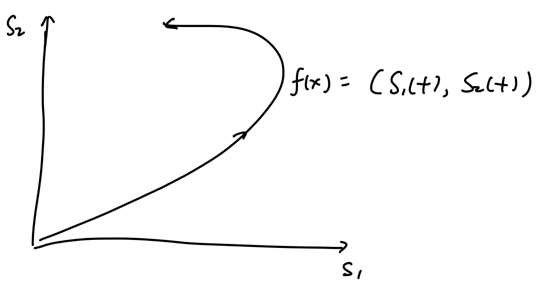
Diffusion

$$v = D([S]_1 - [S]_2)$$

Facilitated Diffusion

$$v = \frac{\alpha_1 [S_1]/K_1 - \alpha_2 [S_2]/K_2}{1+[S_1]/K_1 + [S_2]/K_2}$$

Phase plane



Nullclines

$$\begin{cases} 0 = f(S_1, S_2) = \frac{d}{dt}S_1(t) \\ 0 = g(S_1, S_2) = \frac{d}{dt}S_2(t) \end{cases}$$

↳ seperate entire phase plane

↳ intersections are steady states

↳ stable or unstable

Stability Analysis

For $\begin{cases} \frac{d}{dt}S_1 = f(S_1, S_2) \\ \frac{d}{dt}S_2 = g(S_1, S_2) \end{cases} \Rightarrow J = \begin{bmatrix} \frac{\partial f}{\partial S_1} & \frac{\partial f}{\partial S_2} \\ \frac{\partial g}{\partial S_1} & \frac{\partial g}{\partial S_2} \end{bmatrix}$

If real parts of eigenvalue of J is:

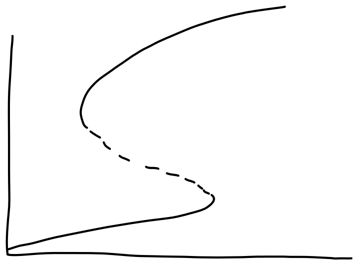
① all negative $\Rightarrow$ stable steady states

② at least one positive $\Rightarrow$ unstable steady states

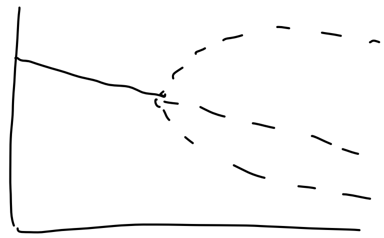
Bifurcation Analysis

Plot: S.S concentration vs. parameter value

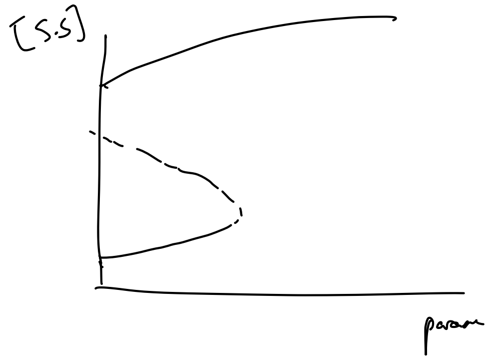
Saddle-node Bifurcation



Hopf Bifurcation



Irreversible switching



Near bifurcation point: fragile ; far from bifurcation point: robust

↳ a hysteretic switching is robust

Local Sensitivity Analysis

absolute local parametric sensitivity:

$$\frac{d[S]}{dp} \approx \frac{S(p+\Delta p) - S(p)}{\Delta p}$$

relative local sensitivity

$$\frac{p}{S}\frac{d[S]}{dp} \approx \left(\frac{p}{S}\right)\frac{S(p+\Delta p) - S(p)}{\Delta p}$$

Flux (J)

- rxn flux: steady state rxn. rate
- pathway flux: S.S rxn rate through an unbranched chain
- flux control coefficient:

$$C_{e_j}^{J_k} = \frac{e_j}{J_k}\frac{\partial J_k}{\partial e_j}$$

Summation Theorem

$$\sum_i C_{e_i}^{J} = 1$$

Ultra sensitivity

10% - 90% activation for < 81-fold increase in input

mRNA Expression Model

$$\frac{d}{dt}p(t) = \frac{k_1 k_0}{\delta_m} - \delta_p\, p(t)$$

Rate of Activated Expression

$$v = \alpha_0 + \alpha \frac{[P]/K}{1+[P]/K}$$

transcription factor

Rate of Repressible Expression

$$v = \alpha_0 + \alpha \frac{1}{1+[P]/K} \; ; \; v = \alpha_0 + \frac{\alpha}{1+[P]^n}$$

for cooperativity

Multiple transcription factors

$$v = \alpha \left(\frac{\text{States with possible transcription}}{\text{total states}} \right)$$

O: $\dfrac{1}{1+\frac{[A]}{K_A}+\frac{[B]}{K_B}+\frac{[A][B]}{K_A K_B}}$

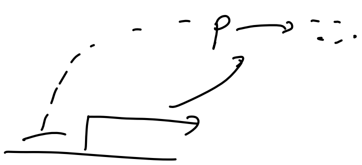
OA: $\frac{[A]}{K_A} / \ldots$

OB: $[B]/K_B \;/ \ldots$

OAB: $[A][B]/(K_A K_B) \;/ \ldots$

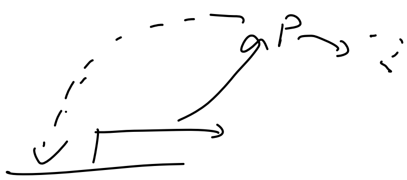
Autoinhibition

$$\frac{d}{dt}p(t) = \alpha \frac{1}{1+p(t)/K} - \delta_p\, p(t)$$



Autoactivation

$$\frac{d}{dt}p(t) = \alpha \frac{p(t)/K}{1+p(t)/K} - \delta_p\, p(t)$$



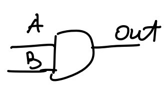
Logic Gates

NOT:

in	out
0	1
1	0

Repressor binding

AND:

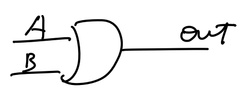


in		out
A	B	
0	0	0
1	0	0
0	1	0
1	1	1

Both activators binding for transcription

(OAB state)

OR:



in		out
A	B	
0	0	0
1	0	1
0	1	1
1	1	1

At least one activator binding for transcription

(OA, OB, OAB)