Chris Voigt
4/5/4
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Lecture 1

- the advantage of being dimensionless
- simplifying problems by comparing scales
- analyzing steady-state behavior
- ~~requ~~ ~~ational~~ equations for gene regulation
- exhibiting self control ~~a, control one's self~~ : autoregulation

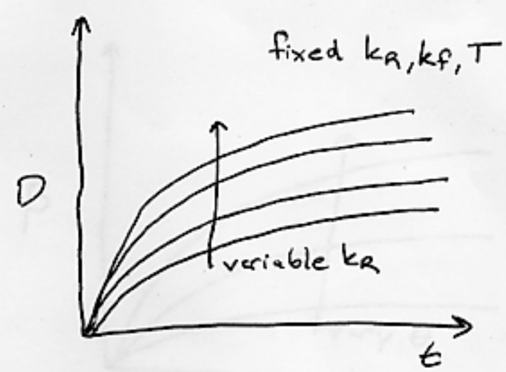
Dimerization

$$2A \underset{k_r}{\overset{k_f}{\rightleftharpoons}} D$$

$$\frac{1}{2}\frac{dA}{dt} = -k_f A^2 + k_r D$$

$$\frac{dD}{dt} = -k_R D + k_F A^2$$

$$T = 2D + A$$



- varying k_R, k_f, T would require a book to convey system behavior
- use intuition to ~~reduce number~~ combine ~~of~~ parameters

STEP 1: Identify all dimensions

$A : c$ $\quad$ $T : c$

$D : c$ $\quad$ $k_R : 1/s$

$t : s$ $\quad$ $k_F : \frac{1}{c\,s}$

BOOKKEEPING: variables (A, D, t) $\quad$ parameters (T, k_R, k_F)

STEP 2: Introduce dimensionless variables

$$\alpha \equiv \frac{A}{T} \qquad \beta \equiv \frac{P}{T} \qquad \tau \equiv t \cdot k_R$$

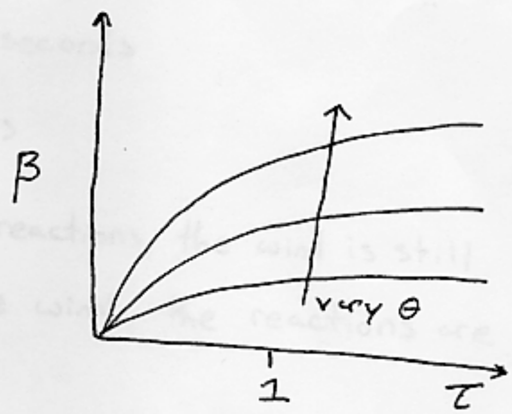
STEP 3: Substitute

$$\frac{dD}{dt} = k_R D - k_F A^2$$

$$k_R T \frac{d\beta}{d\tau} = k_R T \beta - k_F T^2 \alpha^2$$

$$\frac{d\beta}{d\tau} = \beta - \underbrace{\frac{k_F T}{k_R}}_{\theta} \alpha^2$$

$$\boxed{\begin{aligned} \frac{d\beta}{d\tau} &= \beta - \theta\alpha^2 \\ \alpha + \beta &= 1 \end{aligned}}$$



$\tau_{\text{special point}}$

$1 = \tau_s = t_s k_R$

timescale of rxn:

$$t_s = \frac{1}{k_R}$$

if $k_R = 1/s \Rightarrow t \sim$ seconds

$k_R = 0.01/s \Rightarrow t \sim$ minutes

We were lucky, dimerization is relatively easy

more formal definition

$$t_s \sim \frac{f_{max} - f_{min}}{\left|\frac{df}{dt}\right|_{max}}$$

Example: Degradation

$$A \xrightarrow{k} \text{nothing}$$

$$\frac{dA}{dt} = -kA \Rightarrow A(t) = A_0 e^{-kt}$$

BC: @$t=0$, $A=A_0$

$$f_{max} = A_0 \quad f_{min} = 0 \quad \left|\frac{dA}{dt}\right|_{max} = kA_0$$

$$t_s = \frac{A_0 - 0}{kA_0} = \frac{1}{k}$$

Mixing of Reactive Gasses:

Ozone reactions: nanoseconds

Wind: weeks to months

- from the perspective of the reactions, the wind is still
- from the perspective of the wind, the reactions are always over

How can this be used to simplify problems?

Michaelis-Menton Kinetics

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

$$\frac{dS}{dt} = k_{-1}C - k_1 ES$$

$$\frac{dC}{dt} = k_1 ES - k_{-1}C - k_2 C$$

velocity $v = \frac{dP}{dt} = k_2 C$ $\qquad E_0 = E + C$

• common assumption : C is at quasi-steady-state

$$\frac{dC}{dt} = k_1 E_0 S - k_1 C S - k_{-1} C - k_2 C = 0$$

$$= k_1 E_0 S - (k_1 S + k_{-1} + k_2) C$$

$$C = \frac{k_1 E_0 S}{k_{-1} + k_2 + k_1 S} = \frac{E_0 S}{K_m + S} \qquad K_m \equiv \frac{k_{-1} + k_2}{k_1}$$

$$v = \frac{dP}{dt} = \frac{k_2 E_0 S}{K_m + S}$$ familiar form

When is this assumption valid?

wind S — C "sees" constant S (S_0)

ozone C — To S, C is always finished

~~C changes so fast~~

an argument of scale:

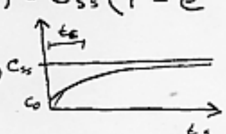
$$t_c \ll t_s$$

– constant $S = S_0$

$$\frac{dC}{dt} = k_1 E_0 S_0 - (k_1 S_0 + k_{-1} + k_2) C$$

form of solution $C(t) = C_{ss}\left(1 - e^{(k_1 S_0 + k_{-1} + k_2) t}\right)$

$$t_c \sim \frac{1}{k_1 S_0 + k_{-1} + k_2} = \frac{1}{k_1 (S_0 + K_m)}$$



– C is always finished $\left(\frac{dS}{dt}\right)_{qss} = -\left(\frac{dP}{dt}\right)_{qss}$ (mass conservation)

$$t_s = \frac{S_0 - 0}{\frac{k_2 E_0 S_0}{K_m + S_0}} = \frac{K_m + S_0}{k_2 E_0} \quad \text{≮} \quad \left|\frac{dS}{dt}\right|_{max, qss} = \frac{k_2 E_0 S_0}{K_m + S_0}$$

Can now state conditions when qss is valid

$$t_c \ll t_s$$

$$\boxed{\frac{1}{k_1(S_0+K_m)} \ll \frac{K_m+S_0}{k_2E_0}}$$

- t_s can be used to dedimensionalize the system

Autocatalysis

eg, Prions, 'RNA world'

$$A + B_o \underset{k_R}{\overset{k_f}{\rightleftharpoons}} 2A$$

Constant B_o

$$\frac{dA}{dt} = k_f A B_o - k_R A^2$$

$$\alpha \equiv \frac{A k_R}{B_o k_F} \qquad \tau \equiv t B_o k_F$$

$$\Downarrow \qquad \qquad \Downarrow$$

$$A = \frac{\alpha B_o k_F}{k_R} \qquad t = \frac{\tau}{B_o k_F}$$

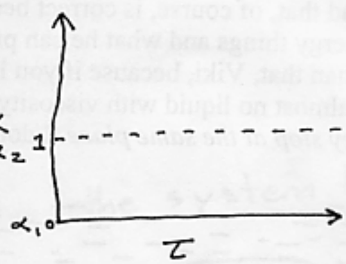
$$\left(\frac{B_o k_F B_o k_F}{k_R}\right)\frac{d\alpha}{d\tau} = \frac{k_F B_o k_F B_o}{k_R}\alpha - \frac{k_R B_o^2 k_F^2}{k_R^2}\alpha^2$$

$$\boxed{\frac{d\alpha}{d\tau} = \alpha - \alpha^2}$$

at steady-state

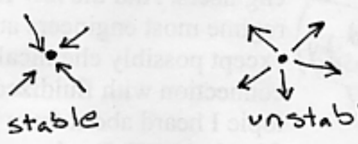
$$0 = \alpha - \alpha^2$$

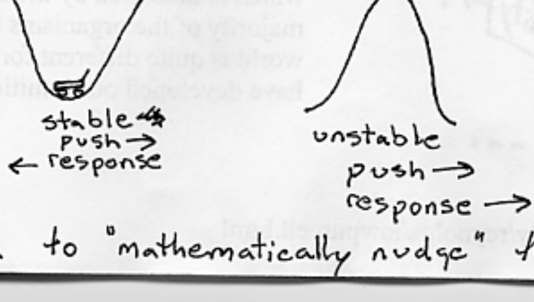
$$\alpha_1 = 0, \quad \alpha_2 = 1$$



- How do the solutions behave around the steady-states?

1-D problem has two options





Need to "mathematically nudge" the system at steady-state "acceleration" of equations

$$\frac{\partial}{\partial\alpha}\left(\frac{d\alpha}{d\tau}\right) = 1 - 2\alpha$$

$@\ \alpha = \alpha_1 = 0$

$$\left.\frac{\partial}{\partial\alpha}\left(\frac{d\alpha}{d\tau}\right)\right|_{\alpha=0} = 1$$

positive, unstable (system responds in the same direction it is pushed)

$@\ \alpha = \alpha_2 = 1$

$$\left.\frac{\partial}{\partial\alpha}\left(\frac{d\alpha}{d\tau}\right)\right|_{\alpha=1} = -1$$

negative, stable (system responds in the opposite direction it is pushed)

timescale of the response

$$t_R \sim \frac{1}{\frac{\partial}{\partial\alpha}\left(\frac{d\alpha}{d\tau}\right)}$$

(the characteristic time for the system to recover)