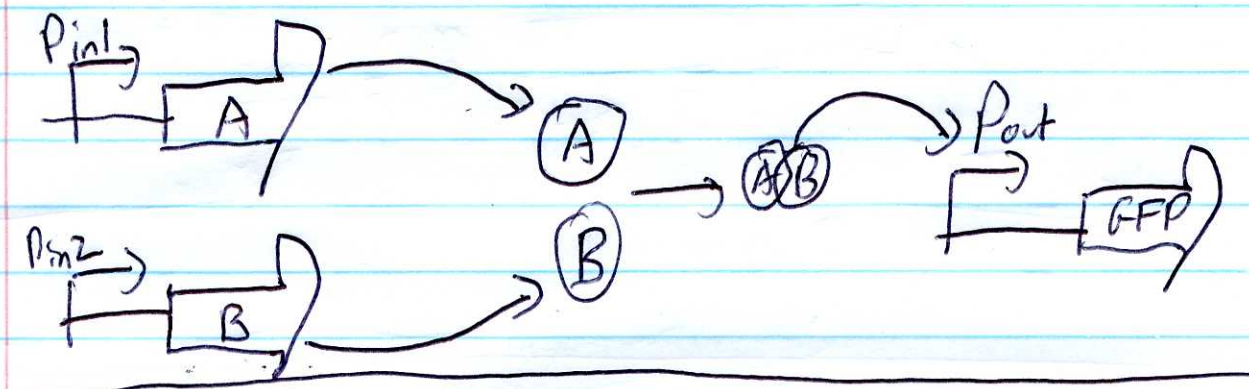
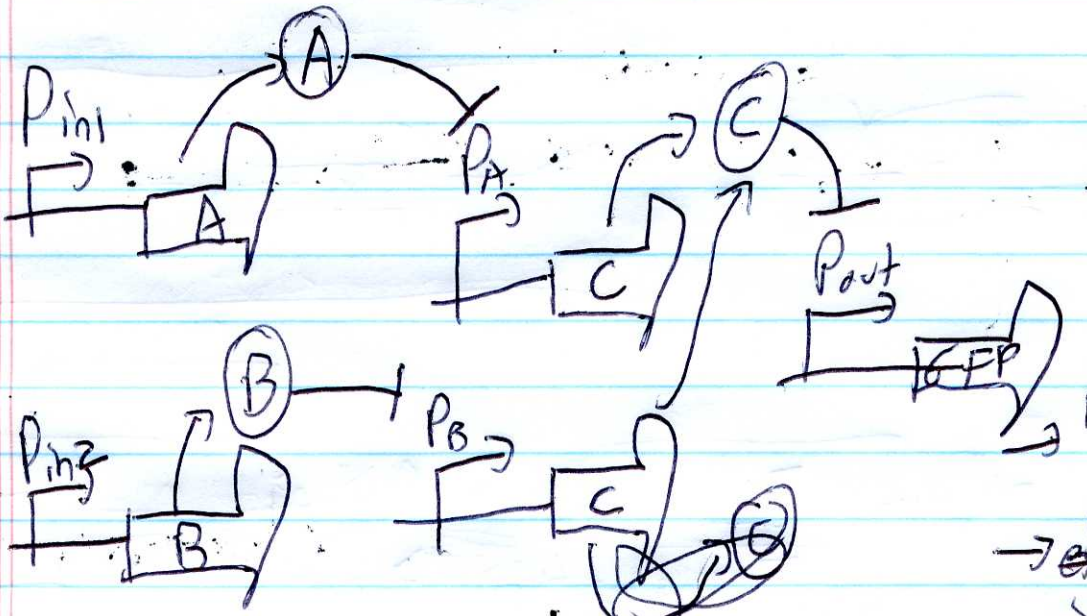
Ex from start:





mutation analysis by inspection limits → ~~extreme~~ states identical

Pin1	Pin2	Pout
0	0	0
0	1	0
1	0	0
1	1	1

→ both "work" under binary conditions

→ not same at intermediary states

1) Protein degrading over time
2) In vitro translation
3) Constitutive expression
4) Repression
5) Activation
6) Steady States; activation & repression

i) Use to model a device that has been constructed already
2) Use to compare 2 designs → ex at end
3) Design w/ parameters

Promoter: $\frac{dP}{dt} = k_p \cdot \frac{[I]^h}{K_m^h + [I]^h} - \gamma P$

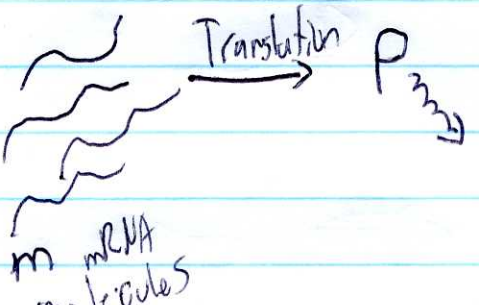
$P \rightarrow$ (transcription & translation)

$\frac{dP}{dt} = -\gamma P$

$P(t) = P_0 e^{-\gamma t}$

"Stable then" $\equiv 0 = -\gamma P$

$P = 0$



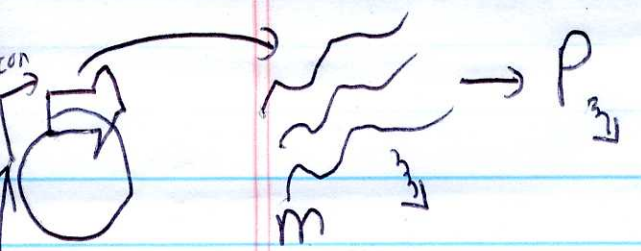
$\frac{dP}{dt} = \beta \cdot m - \gamma P \equiv 0$

$\beta m = \gamma P$

$P = \frac{\beta m}{\gamma}$

Stability Analysis

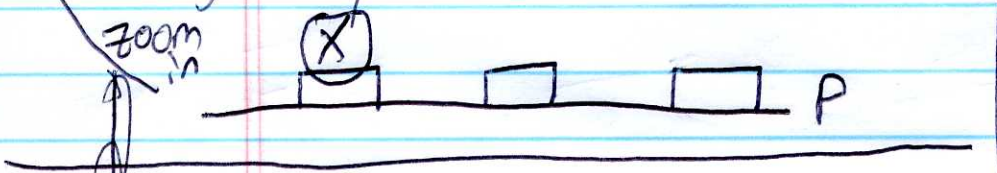
$\frac{dP}{dt}$



$$\frac{dP}{dt} = \beta m - \gamma_p P \equiv 0$$

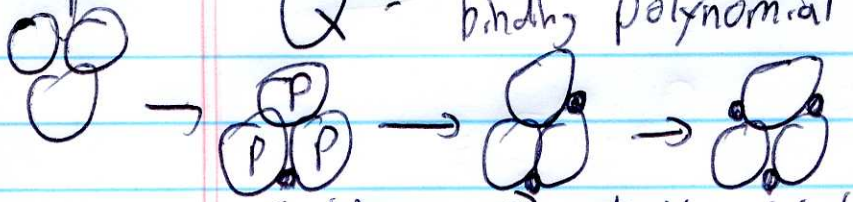
$$\frac{dm}{dt} = k - \gamma_m m \equiv 0$$

Binding Polynomials



"What fraction of promoter population has an activator/repressor bound"

Q = "binding polynomial"



↑ trimer ⇒ indistinguishable, independent

$$\beta_m = \gamma_p P$$

$$k = \gamma_m m$$

$$\Downarrow$$

$$m = \frac{k}{\gamma_m}$$

$$\gamma_p P = \frac{\beta K}{\gamma_m}$$

$$P = \frac{\beta K}{\gamma_m \gamma_p}$$

$$P + X \underset{}{\overset{K_1}{\rightleftharpoons}} PX_1$$

$$P + 2X \overset{K_2}{\rightleftharpoons} PX_2$$

$$P + 3X \overset{K_3}{\rightleftharpoons} PX_3$$

$$Q[P] = [P] + [PX_1] + [PX_2] + [PX_3]$$

$Q[P]$ = "Total Protein"; each microstate

$$K_i = \frac{[PX_i]}{[P][X]^i} \qquad [PX_i] = [P] * K_i[X]^i$$

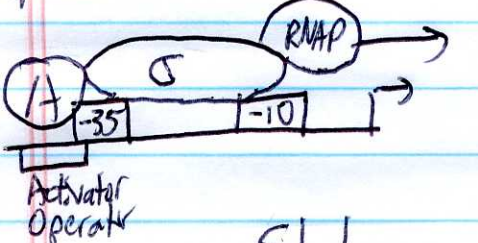
$$Q[P] = [P](1 + K_1 X + K_2 X^2 + K_3 X^3)$$

$$Q = 1 + K_1 X + K_2 X^2 + K_3 X^3$$

$$f_i = \frac{K_i X^i}{Q}, \text{ so } f_3 = \frac{K_3 X^3}{1 + K_1 X + K_2 X^2 + K_3 X^3}$$

"fraction w/ 3 bound"

Activators



States

0 DNA bare
1 DNA + σ
2 DNA + A
* 3 DNA + σ + A Active

$$Q\,[DNA] = [DNA] + [DNA\cdot\sigma] + [DNA\cdot A] + [DNA\cdot A\cdot\sigma]$$

$$f_3 = \frac{K_3\,[A][\sigma]}{Q}$$

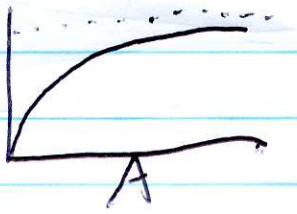
$$Q\,[DNA] = [DNA] + K_1\,[DNA][\sigma] + K_2\,[DNA][A] + K_3\,[A][\sigma]\,[DNA]$$

Simplification

→ Eliminate σ_{70} term (assume it is always constant and never consumed)

0
*1 (A)

$$f_A = \frac{K_A A}{1 + K_A A}$$



→ Reduce states (dimers)

0
1 (A)
2 (A)
*3 (A)(A)

$$f_3 = \frac{K_3 A^2}{1 + K_1 A + K_2 A + K_3 A^2} = \frac{K_3 A^2}{1 + K_3 A^2}$$

minor

Hill → 2

Repressors

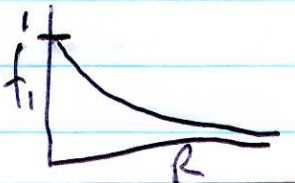
0 (negligible)
*1 (σ)
2 (R)

$$Q = 1 + K_1\,[RNAP] + K_2\,[R]$$

$$f_1 = \frac{K_1\,[\sigma]}{1 + K_1\,[\sigma] + K_2\,[R]}$$

⇓ simplify

$$f_1 = \frac{1}{1 + K_2\,[R]}$$



Shea Ackers

"Applying Binding Polynomials to operator binding in gene expression"

$$\frac{dm}{dt} = \beta f_0 - \gamma m$$

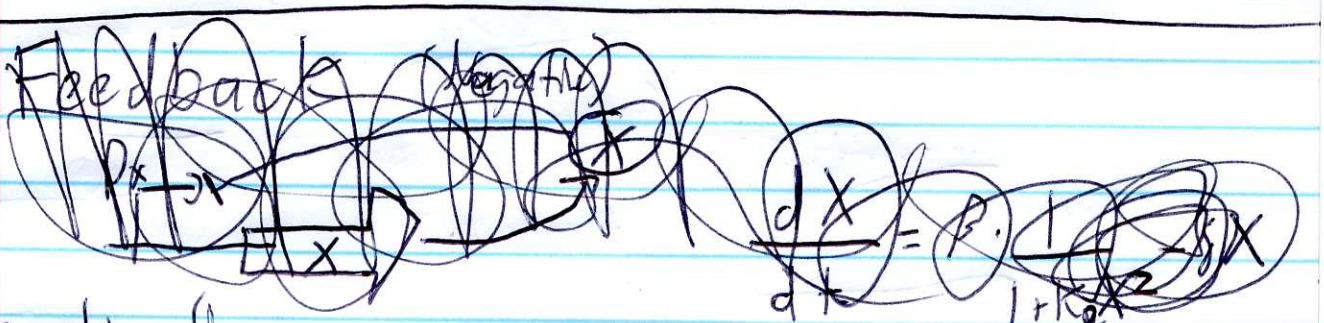
f_0 → fraction in active states

Activator $$\frac{dm}{dt} = \frac{\beta K_A A}{1 + K_A A} - \gamma m$$

PMID: 15797194
Chart of f's

Repressor $$\frac{dm}{dt} = \beta \cdot \frac{1}{1 + K_2 R} - \gamma m$$

What if have only 1 DNA?



Complications

Activation: basal transcription

0 ——

1 * ⑥ ——

$$\frac{dm}{dt} = \frac{\beta_0 K_0 + \beta_3 K_3 A \cdot \sigma}{1 + K_1 \sigma + K_2 A + K_3 A \cdot \sigma} - \gamma m$$

2 Ⓐ ——

3 * ⑤Ⓐ ——

Degradation: sometimes it's ~~Zeroth~~ order

$$\frac{dP}{dt} = \beta m - \delta P$$

$$\Downarrow$$

$$\frac{dP}{dt} = \beta m - \delta$$