16.01.2020

ELL 707

TODAY

(1)

A → B means $\frac{dB}{dt} = \alpha_0' + \frac{\alpha A^n}{A^n + K^n} - rB$

A ⊣ B means $\frac{dB}{dt} = \alpha_0 + \frac{\alpha K^n}{A^n + K^n} - rB$

— ok / secure feeling

underlying derivation?

— unit of B → concentration (M, μM, nM)

μM → 10^{-6}, nM → 10^{-9}

Questions

—

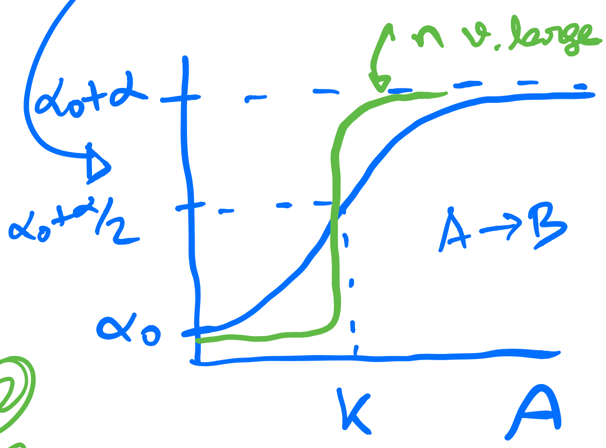
$$\frac{dB}{dt} = \begin{pmatrix}\text{production} \\ \text{term}\end{pmatrix} - \begin{pmatrix}\text{degradation} \\ \text{term}\end{pmatrix}$$

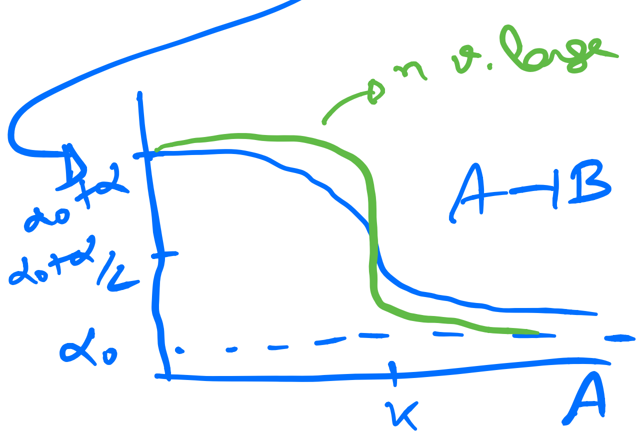
degradation term: recall radioactive decay → gives a time constant

production term:

$\alpha_0 + \frac{\alpha A^n}{K^n + A^n}$

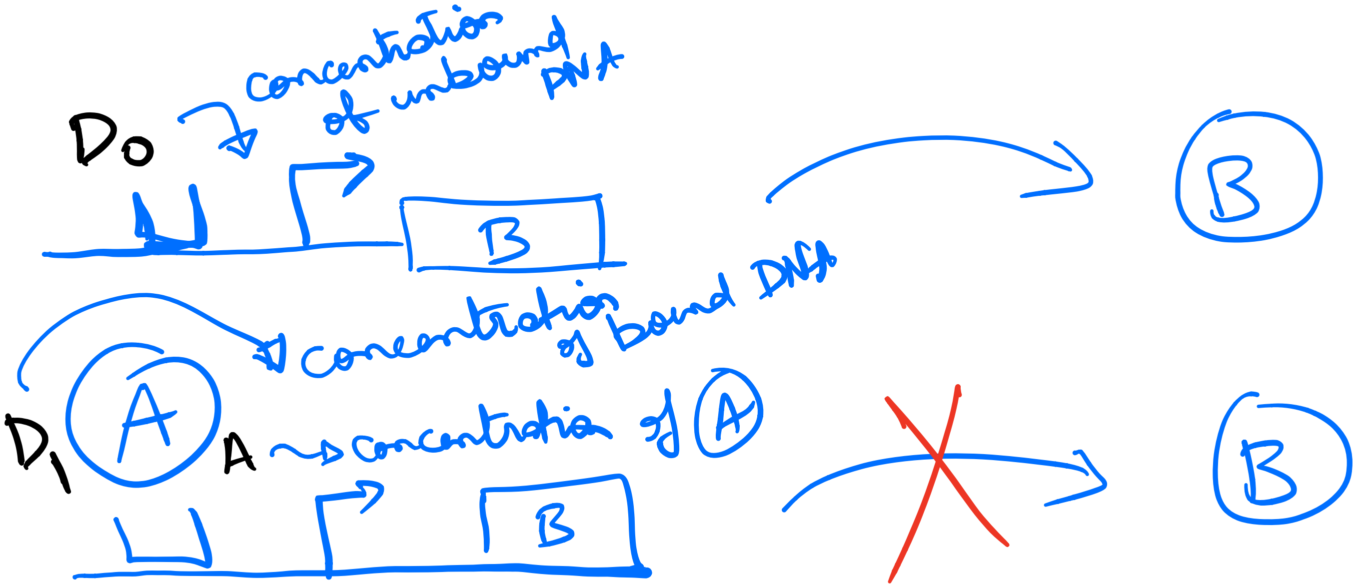
$\alpha_0 + \frac{\alpha K^n}{K^n + A^n}$





How to get functions of the form $\frac{K^n}{K^n + A^n}$?

Consider $A \dashv B$

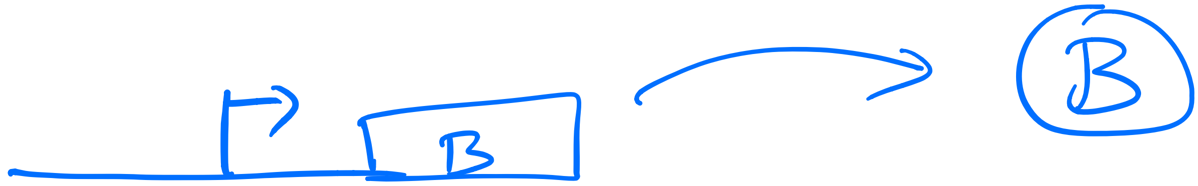


We have D_0, D_1, A

$$D_0 + A \rightleftharpoons D_1$$

(pause)

B is constitutively produced (independent of A)



D : concentration of DNA

$$\frac{dB}{dt} = k D - r B$$

Model (useful or not)

k : proportionality constant

$$D_0 + A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} D_1$$

$\rightarrow$, $\rightleftharpoons$, $\leftrightharpoons$, $\leftarrow$? different possibilities

$$\frac{dB}{dt} = k D_0 - r B$$

how much D_0 is there?

$$D = D_0 + D_1$$

$$\frac{dD_0}{dt} = k_2 D_1 - k_1 A D_0$$

$$\frac{dD_1}{dt} = -(\quad)$$

Law of mass action
rate of a reaction $\propto$ product of reactants

At steady-state, $\frac{dD_1}{dt} = 0 = \frac{dD_0}{dt}$

$$\Rightarrow \quad k_2 D_1 - k_1 A D_0 = 0$$

$D_1 \downarrow$ as $D_0 + D_1 = D$

$$\Rightarrow \quad k_2 (D - D_0) - k_1 A D_0 = 0$$

$$\Rightarrow \quad D_0 = \frac{k_2 D}{k_2 + k_1 A} = D \cdot \frac{k_2/k_1}{k_2/k_1 + A}$$

$$\frac{dB}{dt} = kD \, \frac{k_2/k_1}{(k_2/k_1) + A} - \gamma B$$

$kD \rightarrow \alpha$, $k_2/k_1 \rightarrow K$

$$\frac{dB}{dt} = \alpha \cdot \frac{K}{K + A} - \gamma B$$

↑ production term obtained

$$\alpha_0 + \frac{\alpha K^n}{A^n + K^n}$$

← production term desired.

Differences

- n could be due to $A^n D_0$ instead of $A D_0$

or $D_0 \underset{k_2}{\overset{k_1 A}{\rightleftharpoons}} D_1 \underset{k_2}{\overset{k_1 A}{\rightleftharpoons}} D_2^{(n=2)}$ and only $D_2 \rightarrow B$.

$\Rightarrow$ n (2) binding events required. "Co-operativity"

- α_0 could come due to leaky expression of B from D_0 and D_1.