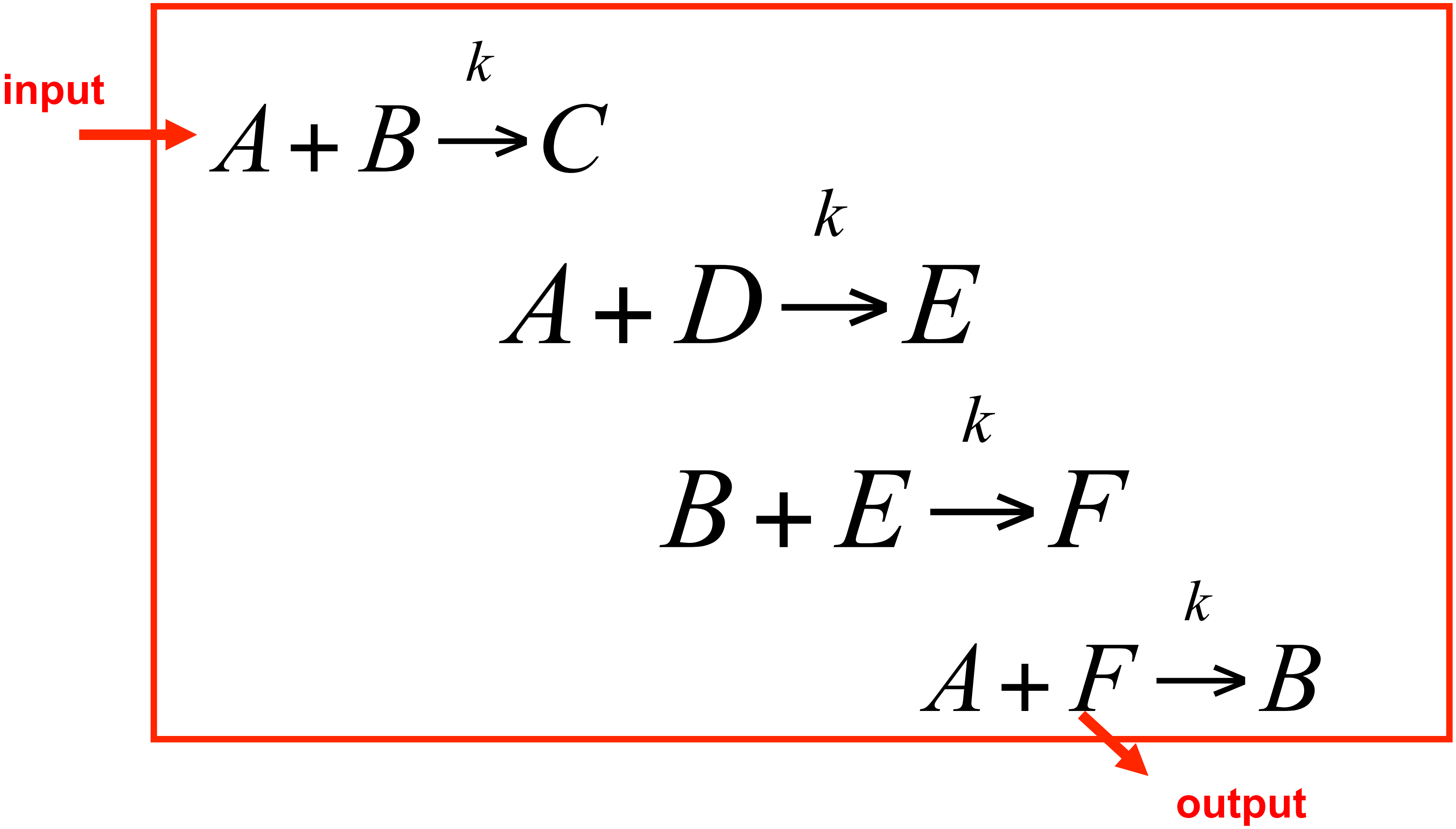
Introduction to Chemical Kinetics and Computational Modeling

Hana El-Samad
Byers Hall (QB3), Rm 403D

Why mathematics in biology?



$$A + B \xrightarrow{k} C$$

$$A + D \xrightarrow{k} E$$

$$B + E \xrightarrow{k} F$$

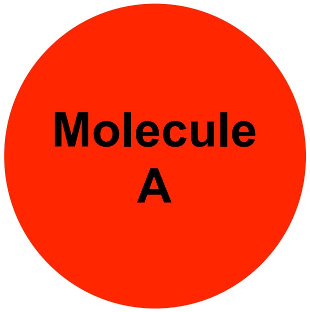
$$A + F \xrightarrow{k} B$$

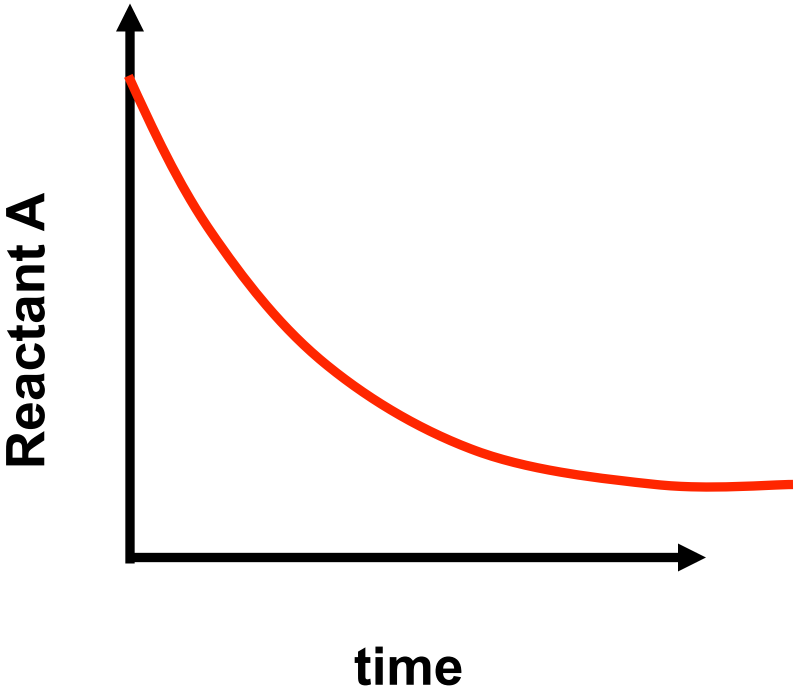
Given some initial concentrations, what is output give some prescribed input?

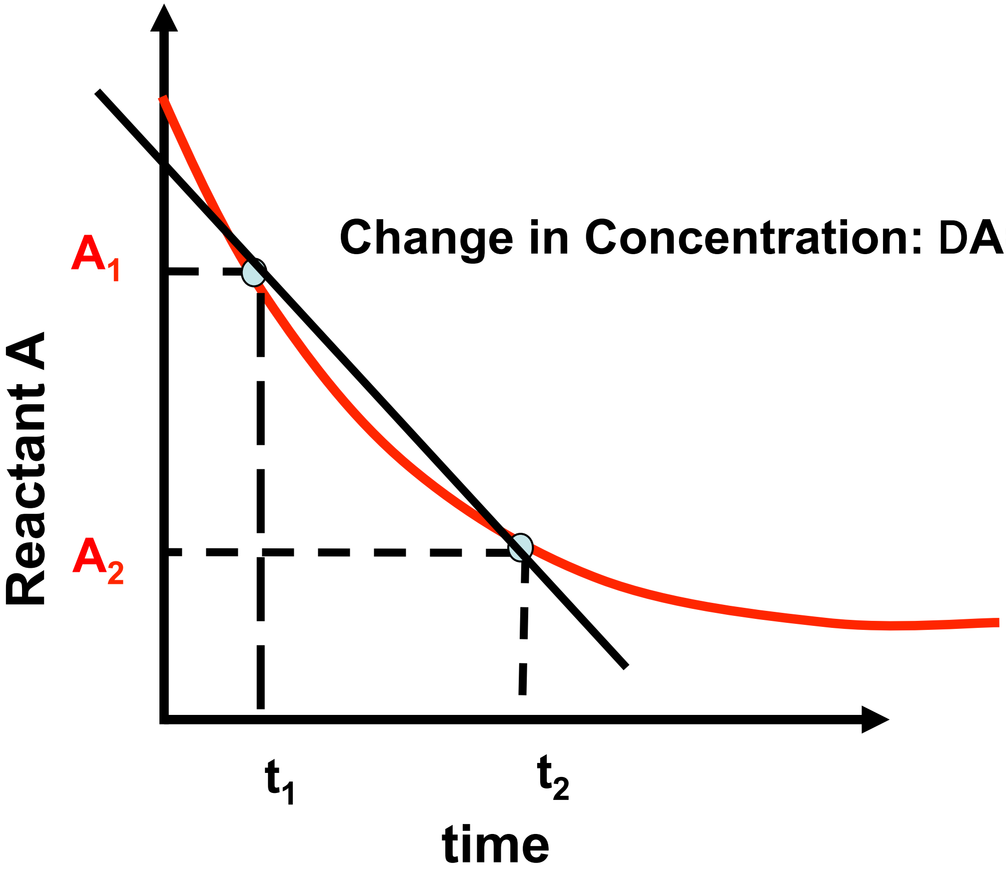
Chemical reactions are collisions of molecules

$$A + B \xrightarrow{k} C$$

$$A \rightarrow \Phi$$



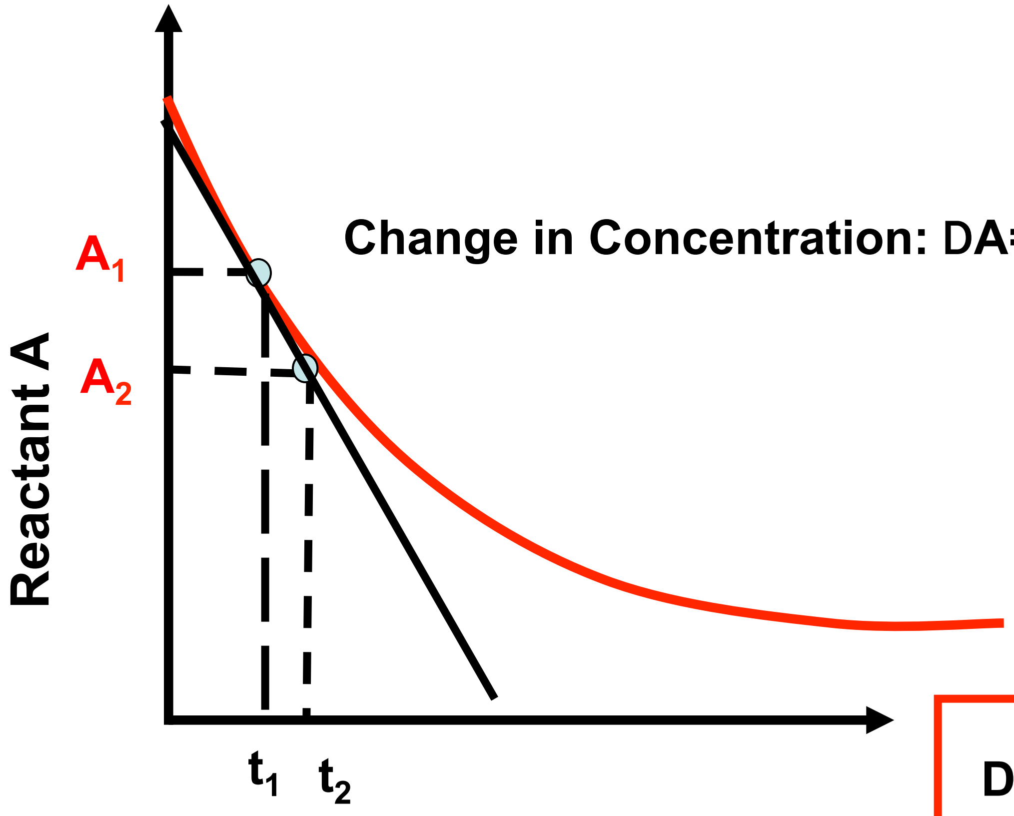




Change in Concentration: DA= A_2-A_1

Change in time: Dt=t_2-t_1

Average rate of change in concentration during time Dt= $$\frac{\Delta A}{\Delta t}$$



Change in Concentration: DA= A_2-A_1

Derivative of A with Respect to time

instantaneous rate of change in concentration during time dt= $\frac{dA}{dt}$

$$A \xrightarrow{\gamma} \Phi$$

$$\frac{dA}{dt} = -\gamma . A$$

Rate of change of A

Concentration of A

Degradation constant

$$D \xrightarrow{k} A \xrightarrow{\gamma} \Phi$$

$$\underbrace{\frac{dA}{dt}}_{\text{Rate of change of A}} = \underbrace{k}_{\text{Production constant}} . \underbrace{D}_{\text{Concentration of D}} - \underbrace{\gamma}_{\text{Degradation constant}} . \underbrace{A}_{\text{Concentration of A}}$$

$$A + B \xrightarrow{k} C$$

$$\frac{dA}{dt} = -k.A.B$$

$$nA + mB \xrightarrow{k} C$$

$$\frac{dA}{dt} = -k.A^n.B^m$$

$$D \xrightarrow{k_1} A \xrightarrow{\gamma} \Phi$$

$$A + B \xrightarrow{k_2} C$$

$$C \xrightarrow{k_{-2}} A + B$$

$$\frac{dA}{dt} = k_1.D - \gamma.A$$

Reaching steady-state (equilibrium)

$$D \xrightarrow{k} A \xrightarrow{\gamma} \Phi$$

$$\frac{dA}{dt} = k.D - \gamma.A$$

Steady-state: No more change in A

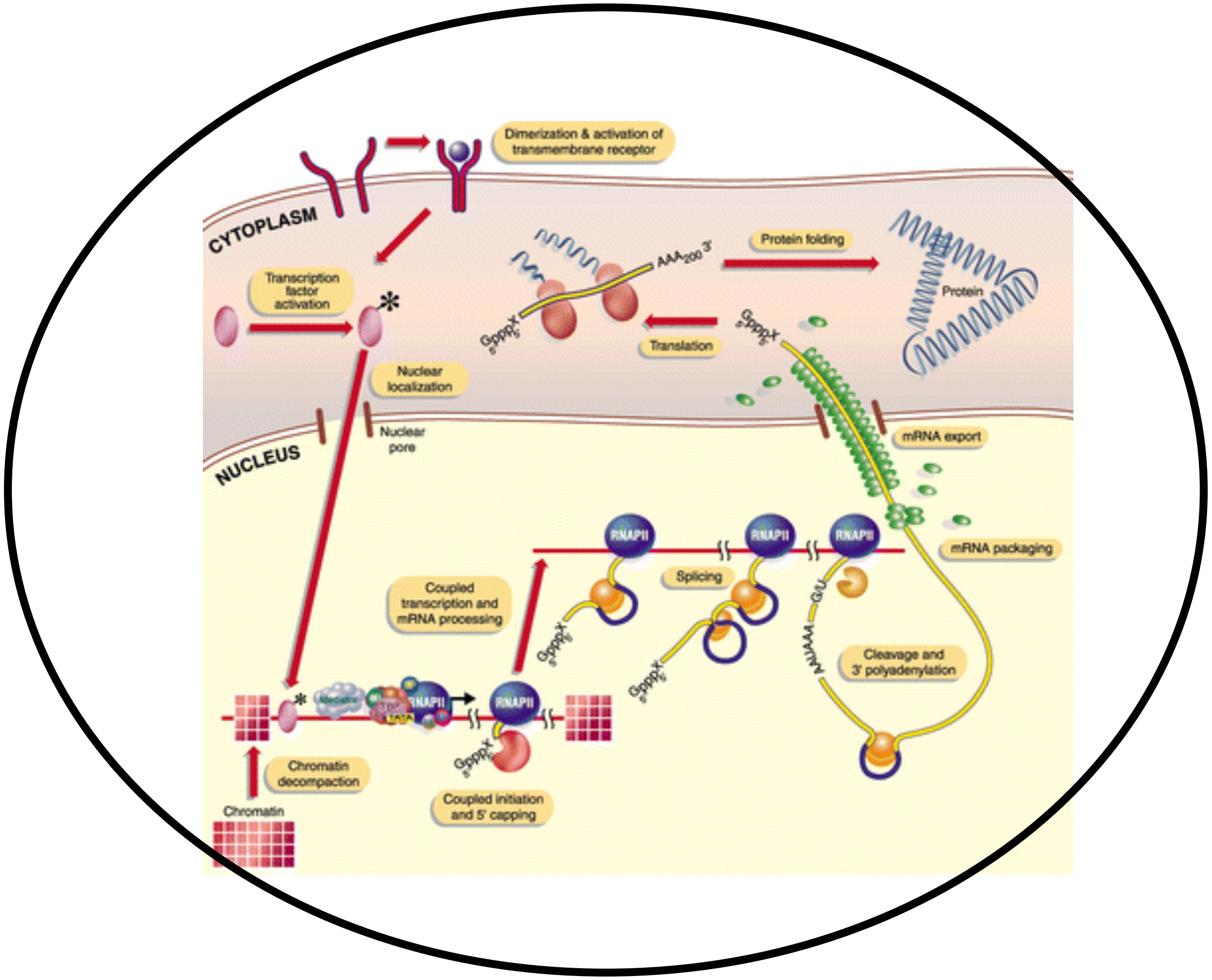
$$\frac{dA}{dt} = 0 \Rightarrow k.D - \gamma.A = 0$$

$$\Downarrow$$

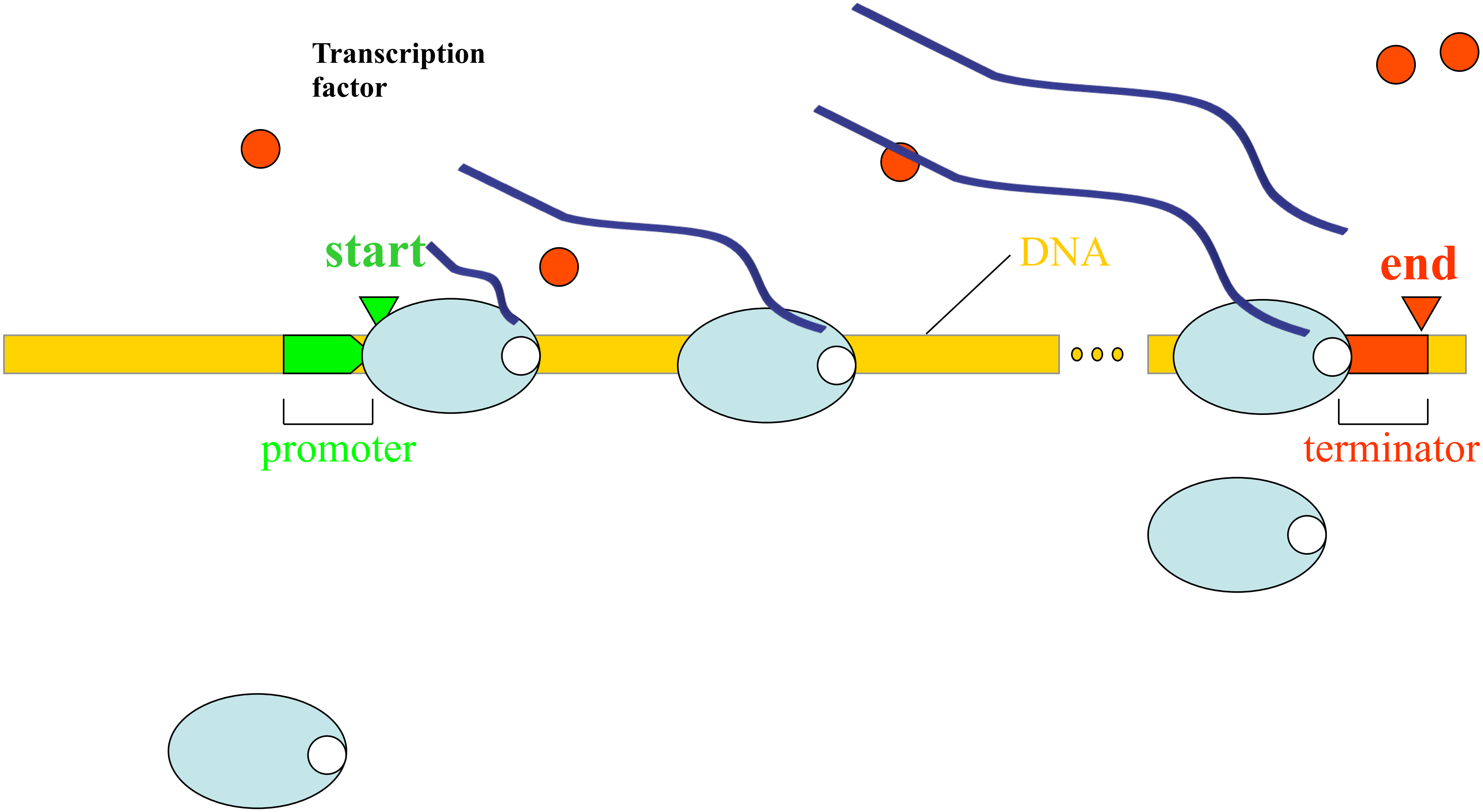
Production of A balances degradation
A is constant $\Leftarrow$ $A = \frac{K.D}{\gamma}$

Chemical Reactions inside the cell

Central Dogma of Molecular Biology



Transcription



Transcription
factor

start

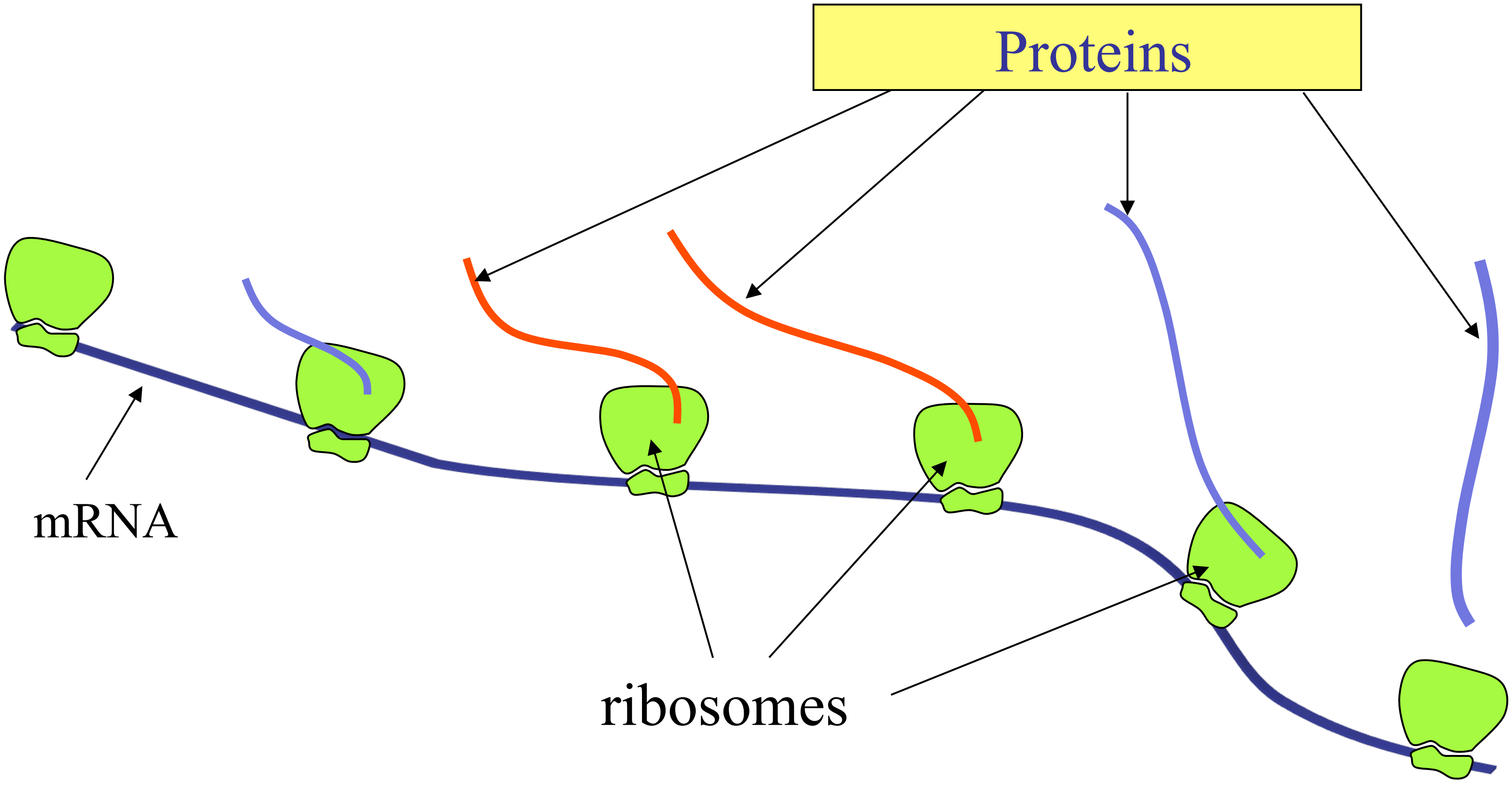
DNA

end

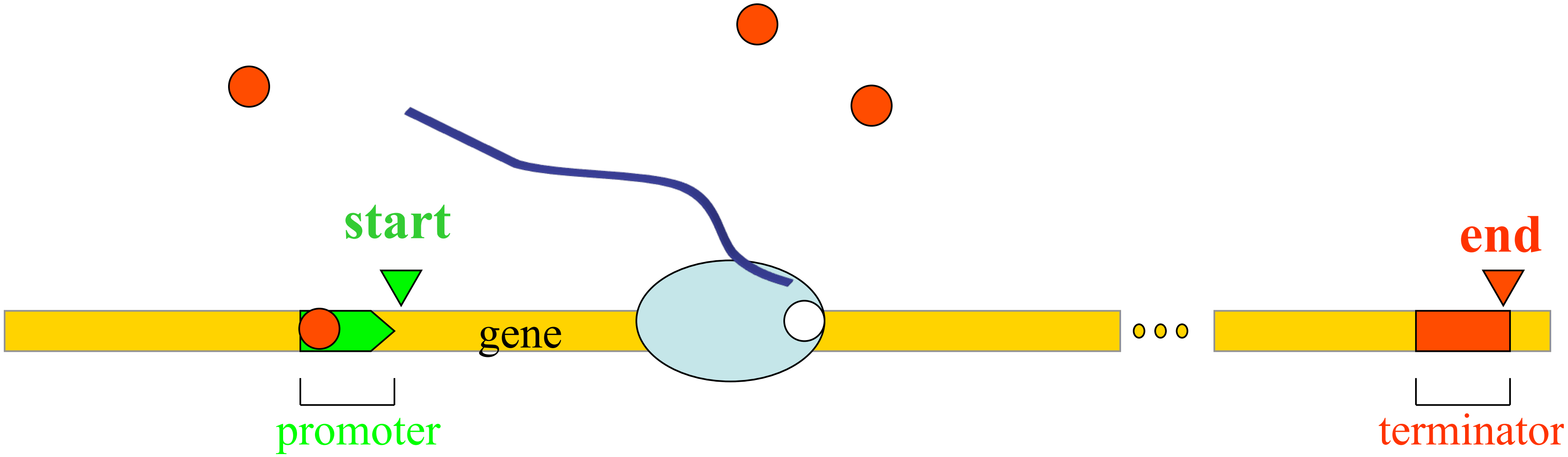
promoter

terminator

mRNA Translation



Modeling activator binding and production of mRNA



$A + DNA \Leftrightarrow A:DNA$ → **Fast**

$A:DNA \xrightarrow{k_2} mRNA + A:DNA$ → **slow**

$A + DNA \Leftrightarrow A : DNA \longrightarrow$ **Fast**

$$\frac{d[A:DNA]}{dt} = \boxed{k_1.A.DNA - k_2.[A:DNA] = 0}$$

$$\swarrow$$

$$k_1.A.DNA = k_2.[A:DNA] \longrightarrow [A:DNA] = \frac{k_1.A.DNA}{k_2}$$

but

$$DNA_{total} = DNA + [A:DNA] = DNA + \frac{k_1.A.DNA}{k_2} = (1 + \frac{k_1.A}{k_2})DNA$$

$$\boxed{DNA = \frac{DNA_{total}}{(1 + \frac{k_1.A}{k_2})}}$$

$$DNA = \frac{DNA_{total}}{(1+\frac{k_1.A}{k_2})}$$

$$[A:DNA] = \frac{k_1.A.DNA}{k_2}$$

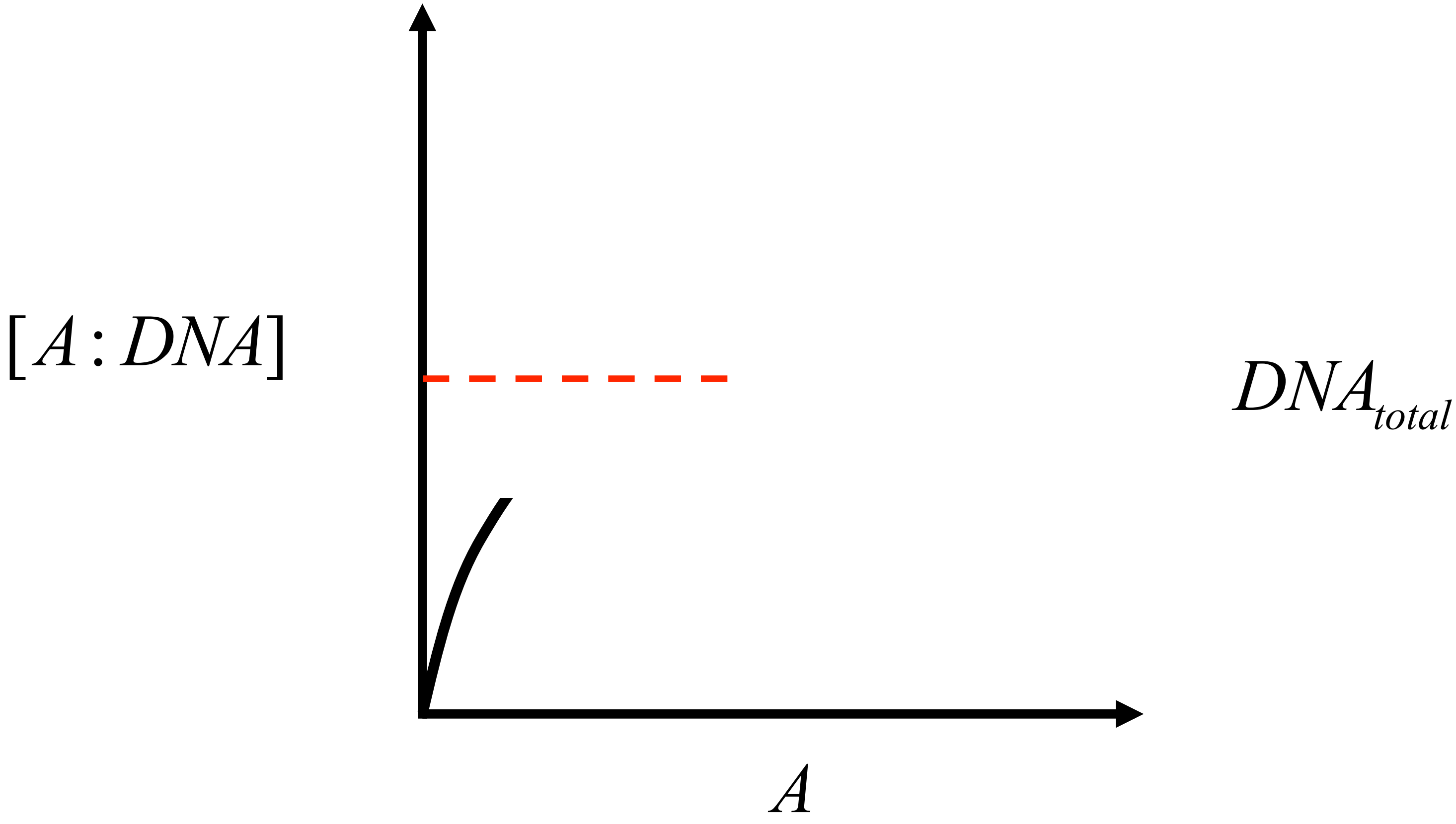
$$[A:DNA] = \frac{\frac{k_1}{k_2}A}{1+\frac{k_1}{k_2}A} DNA_{total}$$

$$\frac{k_2}{k_1} = k_d$$

Dissociation constant

Hill Function

$$\boxed{[A:DNA] = \frac{\dfrac{A}{k_d}}{1+\dfrac{A}{k_d}}\, DNA_{total}}$$



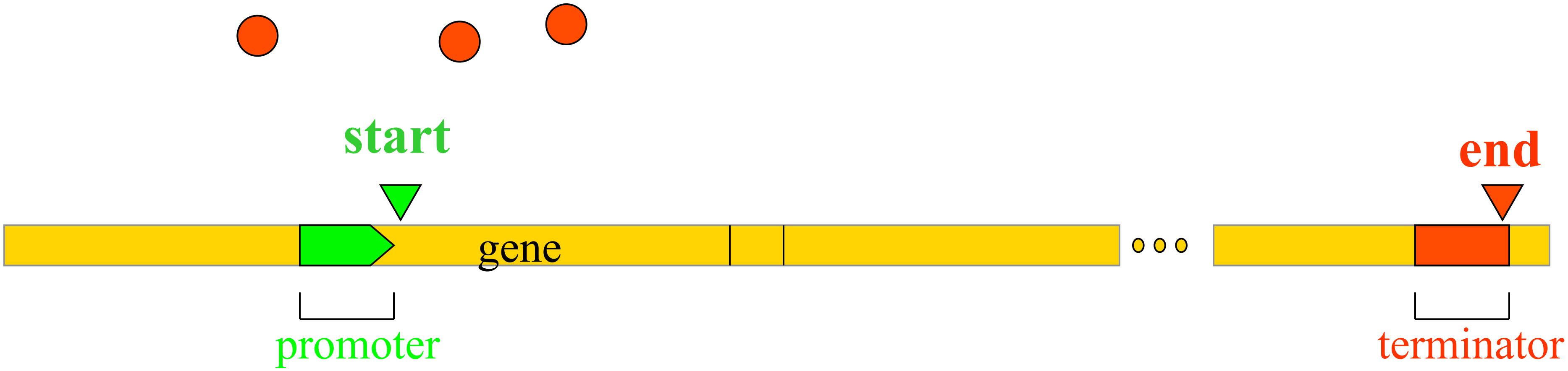
$$A:DNA \xrightarrow{k_2} mRNA + A:DNA$$

$$\frac{dmRNA}{dt} = k_3.[A:DNA] - \gamma_1 mRNA$$

$$\boxed{[A:DNA] = \frac{\frac{A}{k_d}}{1+\frac{A}{k_d}} DNA_{total}}$$

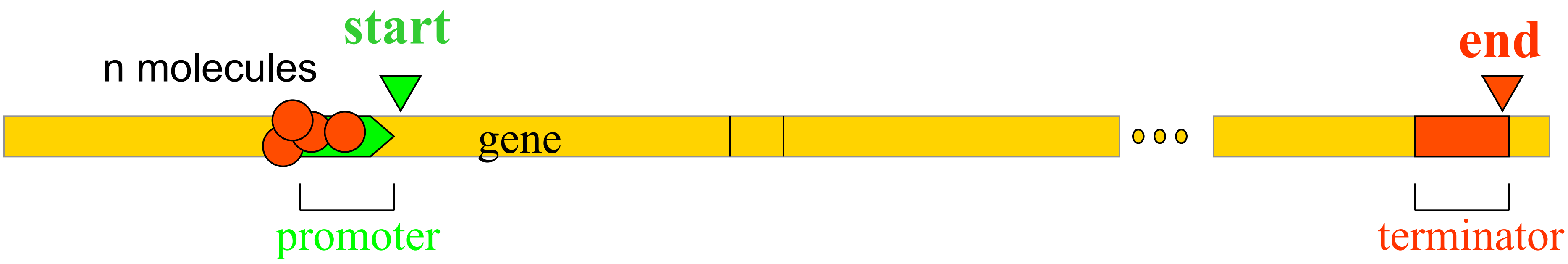
$$\boxed{\frac{dmRNA}{dt} = k_3.\frac{\frac{A}{k_d}}{1+\frac{A}{k_d}} DNA_{total} - \gamma_1 mRNA}$$

Cooperativity

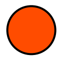


$$\frac{dmRNA}{dt} = k_3 . \frac{\left(\frac{A}{k_d}\right)^3}{1 + \left(\frac{A}{k_d}\right)^3} DNA_{total} - \gamma_1 mRNA$$

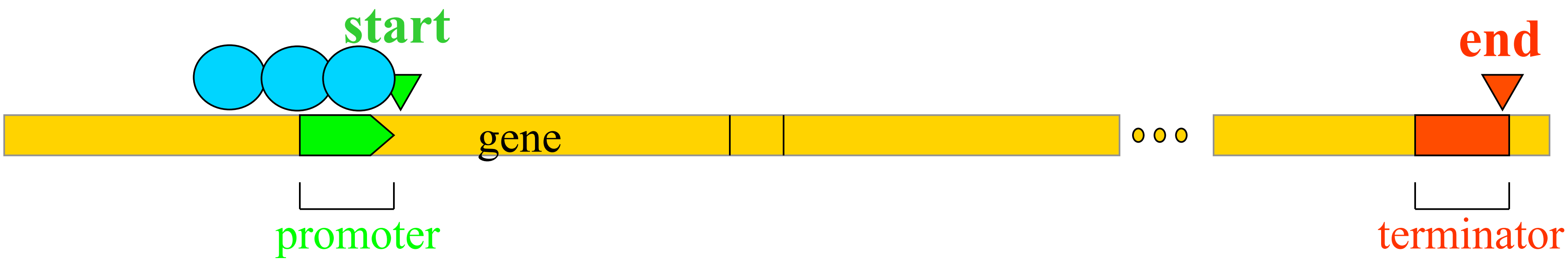
Cooperativity



$$\frac{dmRNA}{dt} = k_3 . \frac{(\frac{A}{k_d}\boxed{)^{n}}}{1+(\frac{A}{k_d}\boxed{)^{n}}} DNA_{total} - \gamma_1 mRNA$$



Repressor



$$\boxed{\frac{dmRNA}{dt} = \boxed{k_3 . \frac{1}{1+(\frac{X}{k_d})^n} DNA_{total}} - \gamma_1 mRNA}$$

$$\boxed{k_3 . \frac{1}{1 + (\frac{X}{k_d})^n} DNA_{total}}$$