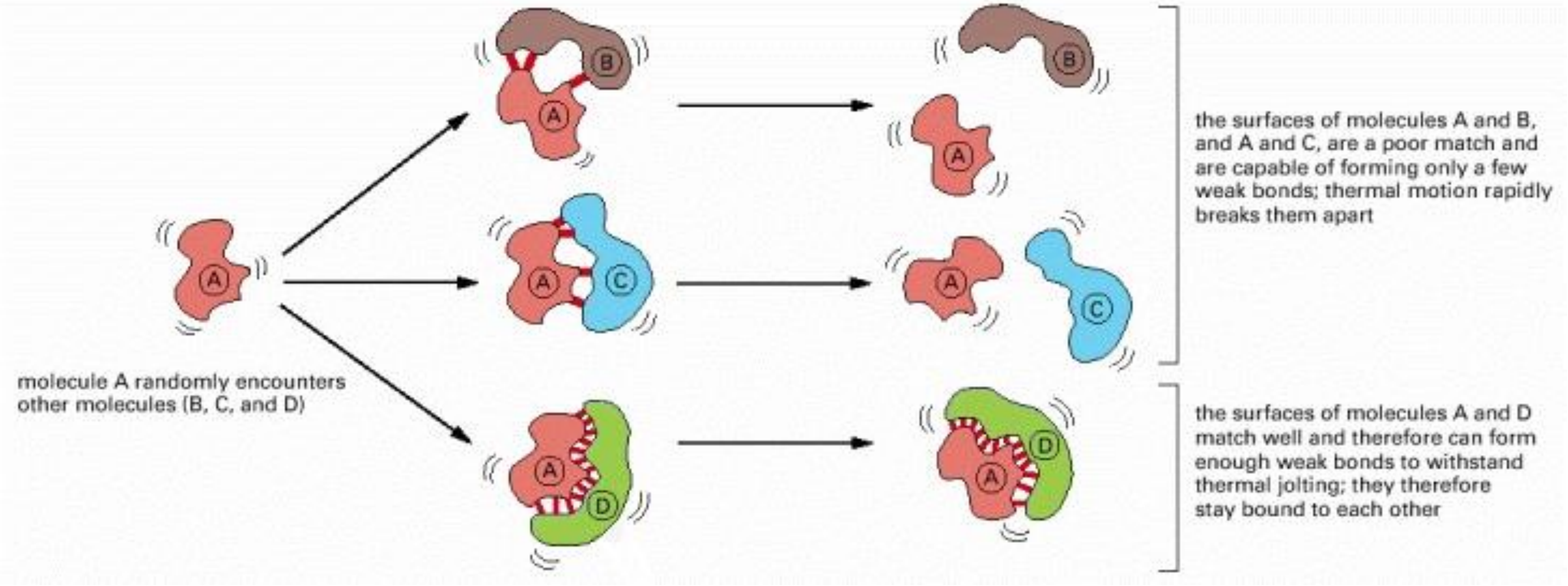
Cell and Tissue Engineering

Kinetic Equations

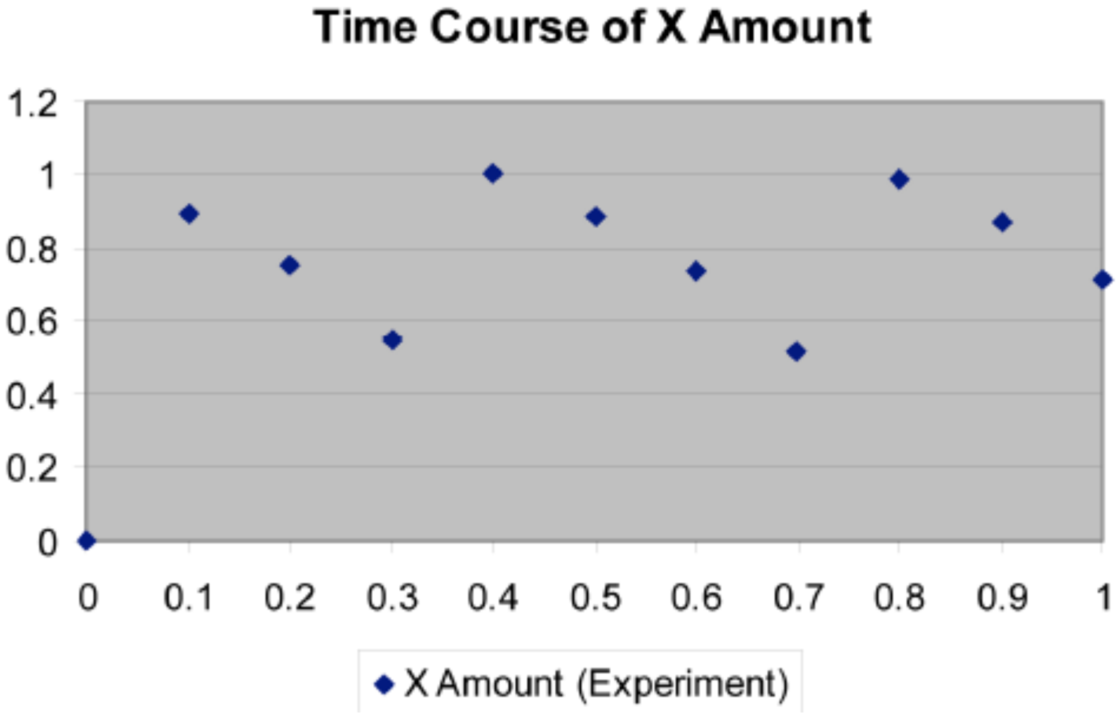
Johns Hopkins Whiting School of Engineering

Protein dynamics: binding and unbinding



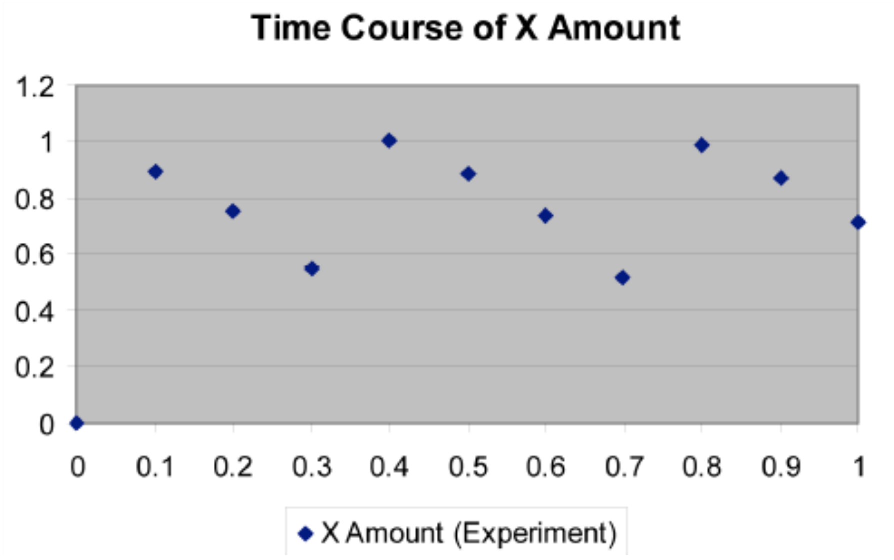
Molecular Biology of the Cell, 4th edition

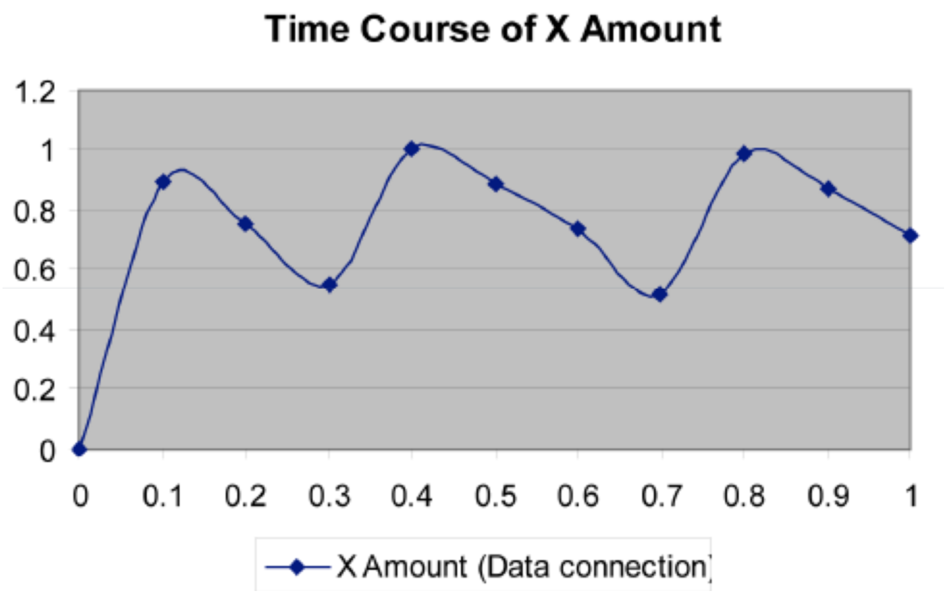
Protein Dynamics: Modeling



Molecular Biology of the Cell, 4th edition

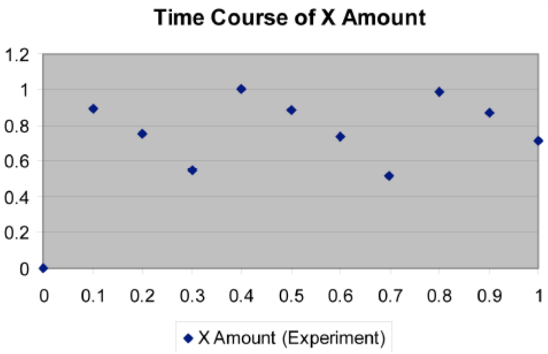
Protein Dynamics: Modeling (cont.)

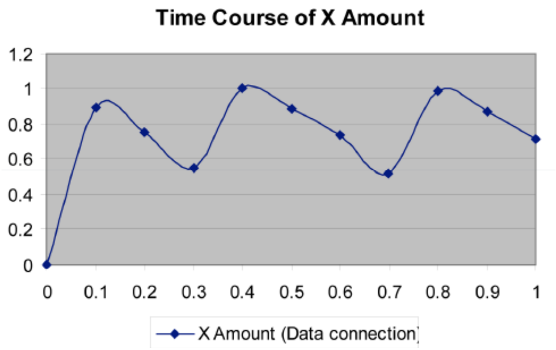


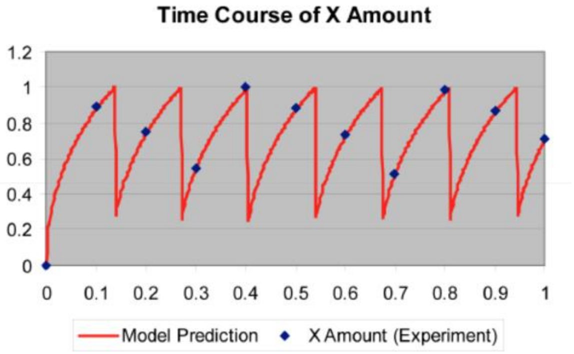


Molecular Biology of the Cell, 4th edition

Protein Dynamics: Modeling (cont.)







http://edoc.hu-berlin.de/

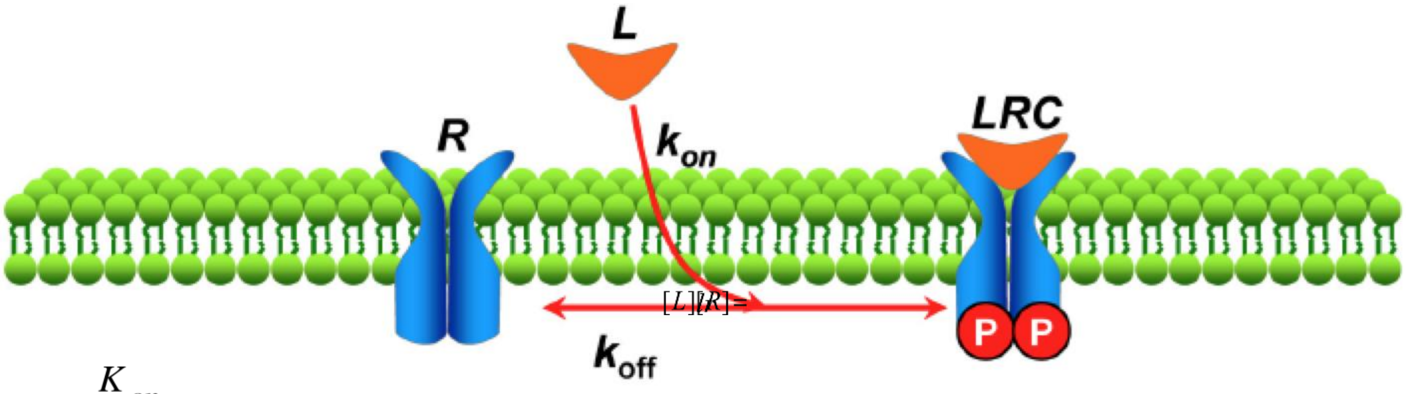
Protein Dynamics: Modeling (cont.)

$$\frac{d[C_i]}{dt} = \sum v_{production} - \sum v_{consumption}$$

<u>Production</u>
Newly made protein
Dissociated from a complex
Activated
…

<u>Consumption</u>
Degradation
Association with a complex
Deactivation
…

Protein Dynamics: Law Of Mass Action



$$L + R \underset{K_{off}}{\overset{K_{on}}{\Longleftrightarrow}} LRC$$

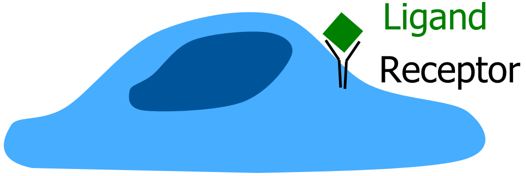
$$\frac{[L][R]}{[LRC]} = \frac{k_{off}}{k_{on}} = K_d = \frac{1}{K_a}$$

k_{on} – forward rate constant
k_{off} – reverse rate constant
K_d – dissociation equilibrium constant
K_a – association equilibrium constant

Protein Dynamics: Law Of Mass Action (cont.)

$$\frac{d[C_i]}{dt} = \sum v_{production} - \sum v_{consumption}$$

$$L + R \underset{K_{off}}{\overset{K_{on}}{\Longleftrightarrow}} LRC$$



$$\frac{d[L]}{dt} = k_{off}[LRC] - k_{on}[L][R]$$

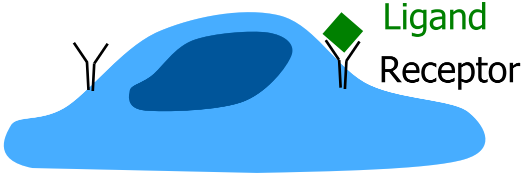
$$\frac{d[R]}{dt} = k_{off}[LRC] - k_{on}[L][R]$$

$$\frac{d[LRC]}{dt} = k_{on}[L][R] - k_{off}[LRC]$$

Protein Dynamics: Law Of Mass Action (cont.)

$$L + R \underset{K_{off}}{\overset{K_{on}}{\Longleftrightarrow}} LRC$$

$$\frac{d[LRC]}{dt} = k_{on}[L][R] - k_{off}[LRC]$$



$$R_T = R + LRC$$

$$\frac{d[LRC]}{dt} = k_{on}\left(R_T - [LRC]\right)\left[L_0\right] - k_{off}[LRC]$$

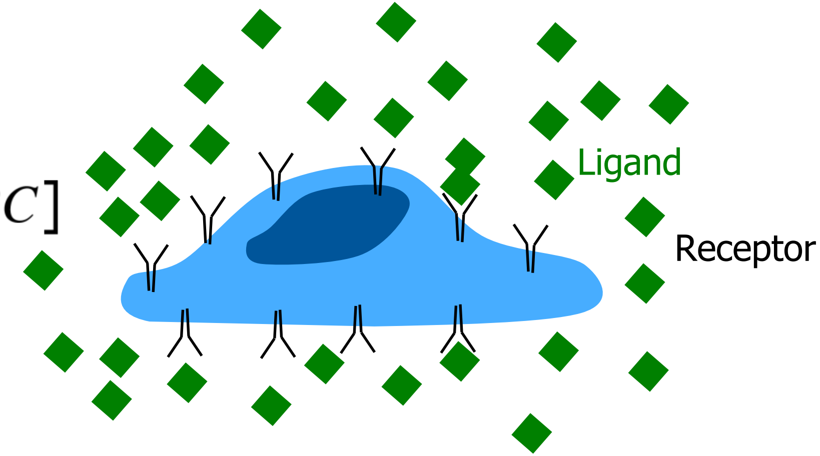
Protein Dynamics: Law Of Mass Action(cont.)

$$L + R \underset{K_{off}}{\overset{K_{on}}{\Longleftrightarrow}} LRC$$

$$\frac{d[LRC]}{dt} = k_{on}[L][R] - k_{off}[LRC]$$

$$R_T = R + LRC$$

$$\frac{d[LRC]}{dt} = k_{on}\left(R_T - [LRC]\right)\left[L_0\right] - k_{off}[LRC]$$



Protein Dynamics: Law Of Mass Action (cont.)

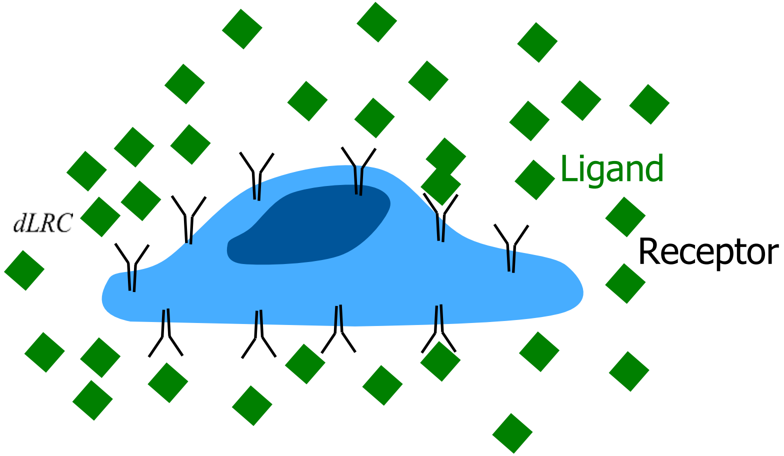
$$L + R \underset{K_{off}}{\overset{K_{on}}{\Longleftrightarrow}} LRC$$

$$\frac{d[LRC]}{dt} = k_{on}[L][R] - k_{off}[LRC]$$

$$R_T = R + LRC$$

$$\frac{d[LRC]}{dt} = k_{on}\left(R_T - [LRC]\right)\left[L_0\right] - k_{off}[LRC]$$

$$[LRC](t) = \frac{k_{on}R_T\left[L_0\right]}{k_{on}\left[L_0\right] + k_{off}}\left(1 - exp\left(-\left(k_{on}\left[L_0\right] - k_{off}\right)t\right)\right)$$



Protein Dynamics: Law Of Mass Action (cont.)

$$L + R \underset{K_{off}}{\overset{K_{on}}{\Longleftrightarrow}} LRC$$

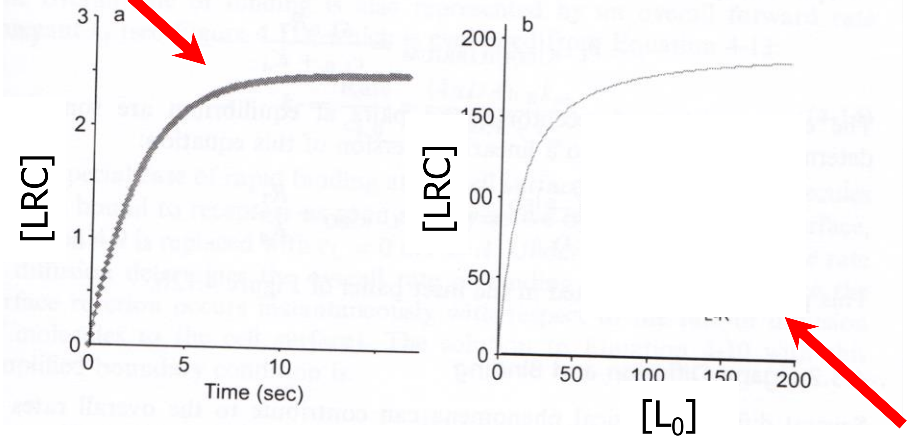
$$[LRC](t) = \frac{k_{on} R_T [L_0]}{k_{on}[L_0] + k_{off}} \left(1 - exp\left(-\left(k_{on}[L_0] - k_{off} \right) t \right) \right)$$

After a while…. the model reaches equilibrium

$$[LRC]\Big|_{equilibrium} = \frac{R_T [L_0]}{[L_0] + k_d}$$

Protein Dynamics: Law of Mass Action (cont.)

$$[LRC](t) = \frac{k_{on} R_T [L_0]}{k_{on}[L_0] + k_{off}} \left(1 - exp\left(-\left(k_{on}[L_0] - k_{off}\right) t\right)\right)$$

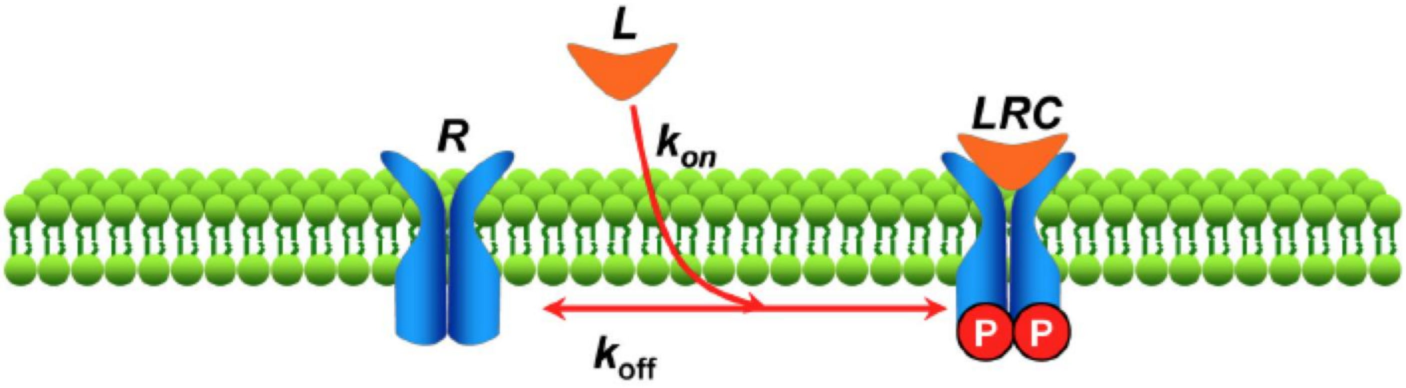


$$[LRC]\big|_{equilibrium} = \frac{R_T [L_0]}{[L_0] + k_d}$$

Diffusion-reaction kinetic graphs show equilibrium and saturation based on our assumptions:

1. Constant ligand concentration
2. Constant and limited receptor number

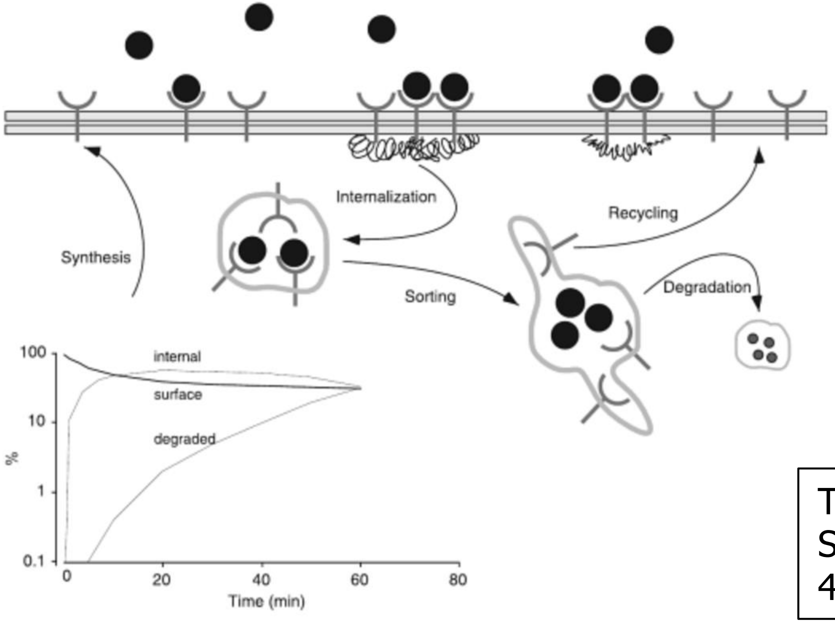
What can ligands do?

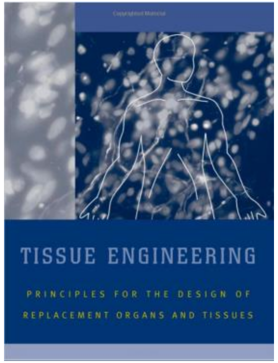


<u>LIGAND</u>
Agonist
Neutral agonist
Inverse agonist

<u>RECEPTOR</u>
Monomer, dimer, tetramer…
Outside-in or inside-out

Protein Dynamics: Law of Mass Action (conclusion)





Tissue Engineering, Saltzman
4.3.1 – 4.4

JOHNS HOPKINS

WHITING SCHOOL of ENGINEERING