Bio & Nano Machines
Figure 29.11  Kinesin walking is driven by the hydrolysis of ATP.
Kinesin: Fit 1

\[ K_1 = 17800 \]
\[ K_2 = 800. \]
\[ K_{-2} = 365. \]
Kinesin: Fit 1

\[ K_1 = 766. \]
\[ K_2 = 40060 \]
\[ K_{-2} = 9.78 \]
Oxygen binding to hemoglobin

- Hemoglobin is a protein having 4 subunits.
- So, start by assuming 4 independent sites:

\[ Q = (1 + Kx)^4 = 1 + 4Kx + 6(Kx)^2 + 4(Kx)^3 + (Kx)^4 \]

- This model uses your knowledge that you have 4 subunits.
- This model uses only a single parameter \( K \).
- But, it doesn’t fit data very well.

- Let’s improve it. But let’s add the fewest possible added parameters.
- \( f = e^{\frac{-E}{RT}} \) is an equilibrium constant when subunits are tetrahedral neighbors:

\[ Q = 1 + 4Kx + 6(Kx)^2f + 4(Kx)^3f^3 + (Kx)^4f^4 \]

This Pauling model works better. And, it uses only 2 parameters, \( K \) and \( f \).
Table 29.1  In the Pauling model, the four subunits of hemoglobin are assumed to have a tetrahedral arrangement. Each sphere represents one bound ligand molecule. Nearest-neighbor ligand interactions are indicated by continuous lines. The table shows the count of nearest-neighbor interactions.

<table>
<thead>
<tr>
<th>Number of Ligands Bound</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Pairwise Interactions</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>6</td>
</tr>
</tbody>
</table>
Inhibitors compete with other ligands

Suppose $X$ binds to $P$. Suppose $Y$ binds too:

\[ X + P \xrightarrow{K} PX \quad K = \frac{[PX]}{[P][X]} \]

\[ Y + P \xrightarrow{R} PY \quad R = \frac{[PY]}{[P][Y]} \]

Y is a competitive inhibitor of X.

- If $Y$ is present, it can reduce the binding of $X$ to $P.$
Binding polynomial $Q = 1 + K_x + R_y$ (unbound or $X$ bound or $Y$ bound)

$$v_x = \frac{\text{fraction of } P \text{ sites occupied by } X}{\ln x} = \frac{\partial \ln Q}{\partial \ln x} = \frac{K_x}{1 + K_x + R_y}$$

- Adding $Y$ reduces the amount of $X$ bound to $P$. 
Figure 29.4  Types of inhibitors. (a) Competitive inhibitor $Y$ competes for the site where $X$ binds to $P$.
(b) Uncompetitive inhibitor $Y$ does not bind unless a ligand $X$ also binds.
(c) Noncompetitive inhibitor $Y$ has no effect on the binding of $X$ to $P$, for example, because it binds at an independent site. $Y$ affects $P$ in some other way than through the process of binding $X$. 
Another type of modulation mechanism

\[ X + P \xrightarrow{K} PX \]

\[ X + Y + P \xrightarrow{KR} PX + Y \]

\[
\begin{align*}
X & \quad \rightarrow \quad \text{+} \quad \rightarrow \quad \text{?} \\
\text{binding polynomial } G & = 1 + Kx + KRxy
\end{align*}
\]

\[
\text{Amount of } X \text{ bound } = \frac{Kx + KRxy}{1 + Kx + KRxy}
\]

\( Y \) is an activator if \( Ry > 1 \). \( Y \) helps \( X \) bind.

\( Y \) is an uncompetitive inhibitor if \( Ry < 1 \).
Figure 29.6 Fractional binding of oxygen to hemoglobin. Different pH values shift the oxygen binding, indicating a coupling of the binding of oxygen and protons to hemoglobin. The pH values are 6.95 (●), 7.71 (○), and 7.91 (□). Source: J Wyman and SJ Gill, Binding and Linkage: Functional Chemistry of Biological Macromolecules, University Science Books, Mill Valley, CA, 1990.
Figure 29.9  (a) Protein $P$ converts $X$ to $Y$, or pumps material up a concentration gradient from $X$ to $Y$ in a cyclic process driven by the hydrolysis of ATP. (b) A structure-based mechanism for this process in the F1-ATPase motor protein. (1) Protein takes up a proton $H^+$ from above the membrane. (2) Protein then also binds ATP. (3) ATP hydrolyzes to ADP, rotating the motor by a partial turn, positioning the proton to flow from inside (above) to outside (below) the membrane. (4) Proton crosses the membrane through the motor. (5) ADP is released. Ready to start again.
Coupled binding is key to energy flow & transduction

- Biology uses motors, pumps, signals & transducers.

- How does ATP → ADP drive $X \rightarrow Y$ uphill energetically?
- Here’s a thermo cycle:

- $P$ is the protein
- $PX, PY =$ protein bound to $X$ or $Y$
- $PTX =$ protein bound to $X$ and to ATP.

Binding polynomial for all states of $P$:

$$Q = 1 + K_i x + K_i R_i T x + K_2 R_2 D y + K_2 y$$

$T =$ ATP concentration, etc.
The motor spins if it has enough ATP.

- Suppose the slow step is ATP hydrolysis to ADP.
- All other steps are in equilibrium.

- Spin rate (per protein molecule) is:

\[
\frac{J}{[P]} = \frac{k [PTX] - b [PDY]}{[P] - Q}
\]

\[
= \frac{k K R T x - b K R D y}{Q}
\]

So, you can pump uphill from concentration \( x \) to \( y \) if:

\[
\frac{K R_T}{b K_R} \left( \frac{I}{D} \right) > \frac{y}{x}
\]

- Equilibrium is when \( J = 0 \) (if ATP = ADP = 0).

In \( F_1 \)-ATPase, the cycle reverses. Gradients of \( H^+ \) convert ADP → ATP in mitochondria, recharging the cell’s chemical “batteries”.
Figure 29.10 A model of signal transduction. As the concentration of signal molecule $X$ increases, it drives protein $P$ to convert a protein from state $A$ to $B$, for example by phosphorylating or activating it.
Figure 29.8  Logic of the lac operon. (1) (+G, +L) does not activate the DNA, so no $BG$ enzyme. (2) (+G, −L) represses the DNA, so no $BG$ enzyme. (3) (−G, −L) activates, but also represses the DNA, so no $BG$ enzyme. (4) (−G, +L) activates and no repressor binds, so the $BG$ enzyme is made.