We now have a prescription for handling any biochemical reaction network. But what about the rates? How do we physically understand the origins of $k_u + k_b$?

Task: relate transitions between states to energies of those states. (non-trivial!)

First step: survey possible energy scales of bonds in biology

Physics references:
- energy to remove electron from H atom = 13.6 eV
  ground state
  \[ 1 \text{eV} = 1.6 \times 10^{-19} J \]
  \[ 1 \text{eV/particle} = 96 \text{kJ/mol} \]
- requires extreme UV photon $\Rightarrow$ huge energy by biological standards
- typical energy provided by thermal agitation (heat bath at room temp.) $\Rightarrow 298 \text{K}$
  \[ k_B T = 0.026 \text{ eV} = 2.5 \text{ kJ/mol} \]
  (we will discuss this further in a few lectures)

Biological bonds (in increasing scale of energy)

1) London dispersion (a type of van der Waals interaction)

neutral atoms far apart
(symmetric clouds of electrons)
induced dipole-dipole attraction at close distances

strongest at 0.2 - 0.4 nm separation (depending on atom sizes)
strength: $\approx 0.003 - 0.009$ eV

$0.25 - 0.8$ kJ/mol

$0.1 - 0.3$ keV

Tiny! But it exists for any pair of atoms, irrespective of type, and orientation.

This is a good, promiscuous weak interaction to keep $k_u$ (combining drifting away after collision) smaller.

Bigger surface area of contact $\Rightarrow$

more possible dispersion interactions

importance of shape complementarity

maximizing area of contact

Need at least $\approx 10$ atom-atom contacts to survive thermal agitation.

For typical protein-DNA contact at specific target $\Rightarrow \frac{2}{3}$ of surface area at interface involves just dispersion interactions

$\Rightarrow \frac{1}{3}$ hydrogen bonding (direct, w/ water), etc.

2) Hydrogen bonding

water-water

Permanent dipole

(O end of molecule more negative than H ends)
"Bond" formed by dipole-dipole attraction, but stronger because dipoles are permanent. Typical distance ≈ 0.3 - 0.4 nm (0.28 nm for water-water)

These can form between H + O or H + N in biological contexts. (partner molecules do not have to be water)

Because dipoles are permanent, strength is larger ≈ 4 - 23 kJ/mol in biology
0.04 - 0.2 eV
1.6 - 9 kBT

In water, r ≈ 0.28 nm, energy ≤ 23 kJ/mol

Molecules with charged groups or dipolar O or N which can interact and form H bonds with water are hydrophilic.

Opposite: hydrophobic.

Hydrogen bonds are stronger than dispersion interactions, but they are directional; need specific orientation of dipoles.

3) Ion-dipole interactions

\[ \text{Strength} \approx 50 \text{ kJ/mol} \]

= 20 kBT

in vacuum:

4) Ion-ion interactions

\[ \text{Na}^+ \text{Na}^+ \text{Cl}^- \text{Cl}^- \]

140 kJ/mol ≈ 56 kBT
5. Intramolecular bonds

Covalent and ionic bonds that form the backbone of molecular structure

\[ \approx 10^2 - 10^3 \text{ KJ/mole} \]

and directional

\[ 40 - 400 \text{ K}_B T \]

Generally, strength of interaction comes at the cost of requiring directionality.

Ion-ion continued:

In water interaction much weaker:

At 1 nm separation

\[ \approx 1.8 \text{ KJ/mole} \]

or 0.7 K_BT

(80 times weaker than in vacuum)

\[ E = \frac{1}{4\pi \varepsilon_0} \frac{q_1 q_2}{r} \frac{1}{\varepsilon} \]

\( \varepsilon \approx 80 \) for water