Energy/Length Scales in Biology:

Amino Acids Review:
Non-polar side groups: Glycine (gly), Alanine (ala), Valine (val), Leucine (leu), Isoleucine (ile), Methionine (met), Phenylalaline (phe), Proline (pro), Tryptophan (trp)
Uncharged polar side groups: Serine (ser), Threonine (thr), Asparagine (asn), Cysteine (cys), Glutamine (gln), Tyrosine (tyr)
Acidic side groups: Aspartic Acid (asp), Glutamic Acid (glu)
Basic side groups: Lysine (lys), Arginine (arg), Histidine (his)
Useful amino acids: Cys (not very reactive and rare – 1.7% abundant), Gly (small, mobile, 7% abundant), Leu (most abundant – 9%), Tryptophan (least abundant – 1.3%, best for spectroscopy)

Protein Review:
Primary structure – the sequence of the amino acids.
Secondary structure – local 3D structure formed due to H-bonds. The most common are alpha helices and beta sheets.
Alpha helix – 3.6 residues/turn, 1.5A/residue, linear distance = 3.6n A
Beta sheet – 3.4A/residue
Tertiary structure – the 3D structure of the entire protein
Quarternary structure – arrangement of multiple polymer subunits

Interactions
Covalent: shared electrons. Need to know the wave function to treat properly.
Electrostatic:

$$E = \frac{1}{4\pi\varepsilon}\left(\frac{q_1 q_2}{r}\right)$$

q = electron charge = 1.6 x 10^{-19} C
r = separation distance
ε = relative permittivity (=80 for water)
ε_0= vacuum permittivity = 8.85 x 10^{-12} C^2/Jm

Energy between a dipole and a point charge: $E = \frac{1}{4\pi\varepsilon_0}\left(\frac{-q_1 q_2 l}{r^2}\right)$

Energy between a dipole and dipole: $E \propto \frac{1}{r^3}$

H-bonds
Van der Waal
Hydrophobic

Useful Equations and Relations

Diffusion: $< x^2 >= 2Dt$
Einstein-Smulchowski: $Df_{drag} = k_B T$
Reynolds Number: $\mathrm{Re} = \frac{\rho L v}{\mu} = \frac{F_{inertial}}{F_{viscous}}$ (note: for many biological systems, viscous forces dominate)
Energy kBT = 4.1 pN nm
ATP = 20 kBT
Glucose = 30 ATP
Typical protein: 300 aa, 30 kDa, 34.8 nm^3, 4.8 x 10^{-23} kg, 1.38 x 10^3 kg/m^3, radius ~ 2nm
Typical stall forces:

Myosin: 1-2 pN	Biotin: 200 pN	Migrating cell: 10 nN
Kinesin: 5-6 pN	RNAp: 25 pN	E. Coli drag force: 0.5 pN

Random Walk Model

Chain with N segments of length b
Contour length (total length of the chain) $L_c = Nb$
r_i is the vector to point i: $b = r_i - r_{i-1}$
R is the end-to-end length of the chain: $\vec{R} = \sum \vec{r}_i$

Average end-to-end distance: $< \vec{R} >= 0$

Distribution: $< \vec{R}^2 >= Nb^2$

Radius of gyration: $< \vec{R}^2 >^{1/2} = R = b\sqrt{N}$

Probability of finding the ends of polymer of size N at distance R:

$p(R,N) \approx p_{Gaussian} = \left(\frac{d}{2\pi Nb^2}\right)^{d/2} \exp\left(\frac{-dR^2}{2Nb^2}\right)$; d = dimensionality

Using entropy ($S = k_B \ln p$) and energy ($G=H-TS$), modeling as a spring, and neglecting some constants and higher order terms: $F = \frac{3k_BT}{Nb^2}R \Rightarrow$ model breaks down at high R!

Freely Jointed Chain

Similar to random walk, but segments can freely rotate about the joints.

At low force: $F = \frac{3k_BT}{Nb^2}R$ (same as Gaussian/Random Walk)

At high force: $F \to \infty$

Interpolated at medium forces.

Worm-Like Chain Model

Continuous rope that is flexible everywhere, not only at discrete junctions.
Good for modeling double stranded DNA, RNA, and **unfolded** proteins.
Persistence length l_p is the distance over which a polymer is relatively "straight":

$$l_p = \frac{b}{2} = \frac{EI}{k_BT}$$ = rigidity/thermal energy

E = Young's Modulus = stress/strain; I = moment of inertia

$$F \approx \frac{k_BT}{l_p}\left[\frac{1}{4(1-\frac{x}{L_c})^2} + \frac{x}{L_c} - \frac{1}{4}\right]$$

Useful Constants

Boltzmann's constant = k_b =1.38 E -23 J/K

Planck's constant = h= 6.62 E -34 J·s

η_{water} = 0.001 Pa·s

Thermodynamics and Statistical Mechanics

S = $k_b \ln W$; W = # of microstates = $\frac{n!}{(n-k)!k!}$ n = # positions, k = # of things.

$W_{state\ 1\ combined\ w/state\ 2} = W_{state\ 1} \cdot W_{state\ 2}$; $S_{state\ 1\ combined\ w/state\ 2} = S_{state\ 1} + S_{state\ 2}$

Partition Function $Q = \sum_j e^{-\varepsilon_j / k_b T}$; ε_j = ΔG = Energy of the microstate

w_j = density of states = # of microstates in a given macrostate

Probability a molecule is in a given microstate $P_i = \frac{e^{-\varepsilon_i / k_b T}}{\sum_j e^{-\varepsilon_j / k_b T}}$

or multiply by w_i to get probability a molecule is in a given macrostate

Energy Landscapes

Rate = $A \exp\left(-\Delta G / k_b T\right)$; A= frequency factor $\Delta G = \Delta G_0 - F\Delta x$

$[E_1]$ → avg duration of structural state 1 = $1/k_{on}$ → $k_{on} = A \exp\left(-\Delta G / k_b T\right) = k_{on}^0 \exp\left(F\Delta x / k_b T\right)$

$\frac{[E_1]}{[E_2]} = \frac{k_{1\ \text{or on}}}{k_{-1\ \text{or off}}} = K_{EQ} \cdot \exp\left(\frac{F\Delta x}{k_b T}\right)$

Eyring:	*Kramers:*
protein **relaxes** into new state after fast local changes	protein goes through **global** diffusion into new state
$A = \frac{k_b T}{h} = 6E12$ 1/s	A = $\varepsilon_1 / \pi\tau_1$; $\tau_1 = \gamma / \kappa$ =frictional drag/stiffness

Instrumentation

AFM:
2 major uses:
(1) imaging
(2) material properties (know force and indentation, can find Young's modulus)

Optical trap:
3 ways to calibrate:
(1) Lorentzian roll-off (shifts L for weaker trap)
(2) Equipartition
(3) Stokes drag & $F = k\Delta x$

Molecular Motors and Single Molecule Measurements

Types: Rotary (ATP synthase, flagella), linear motors (actin/myosin, kinesin/dynein, RNA polymerase, ribosome)
Assays: Kinesin force clamp, stepping, tethered bead assay, paired optical traps

Polymerization

$F_{EQ} = \frac{k_b T}{\delta} \ln\left(\frac{[A]}{K_D}\right)$; [A]= k_{off} / k_{on} = $K_D \exp\left(\frac{F\delta}{k_b T}\right)$; [A] = monomer concentration

Actin Polymerization: $C_c = \frac{k_{off}^{ADP}}{k_{on}^{ATP}} = \frac{1}{K_{EQ}}$

Brownian ratchet: inhibitor diffuses away from filament end to allow chemical reaction