Lecture 3: Mechanical and chemical equilibrium

Goal: Energy minimization models

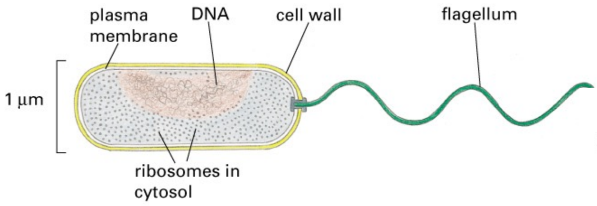
- Biological systems as minimizers
- Entropy and hydrophobicity

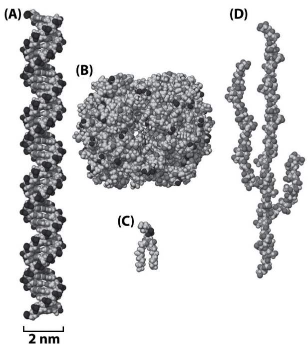
PBOC Chapter 5.2, 5.5.1

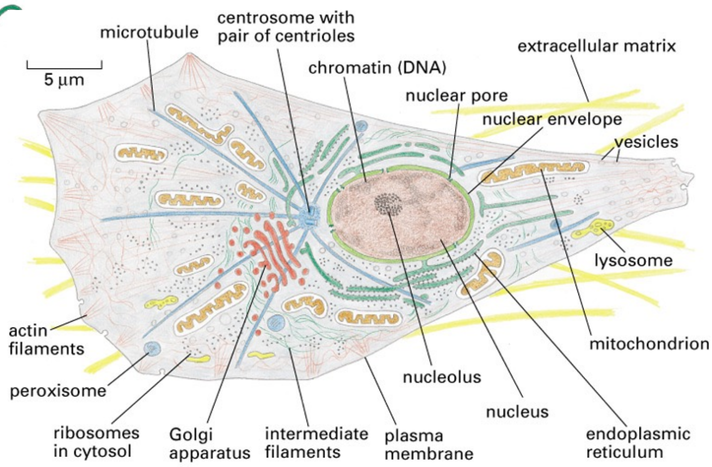
Announcement: Video-recorded lecture next week.

Basic facts about cells

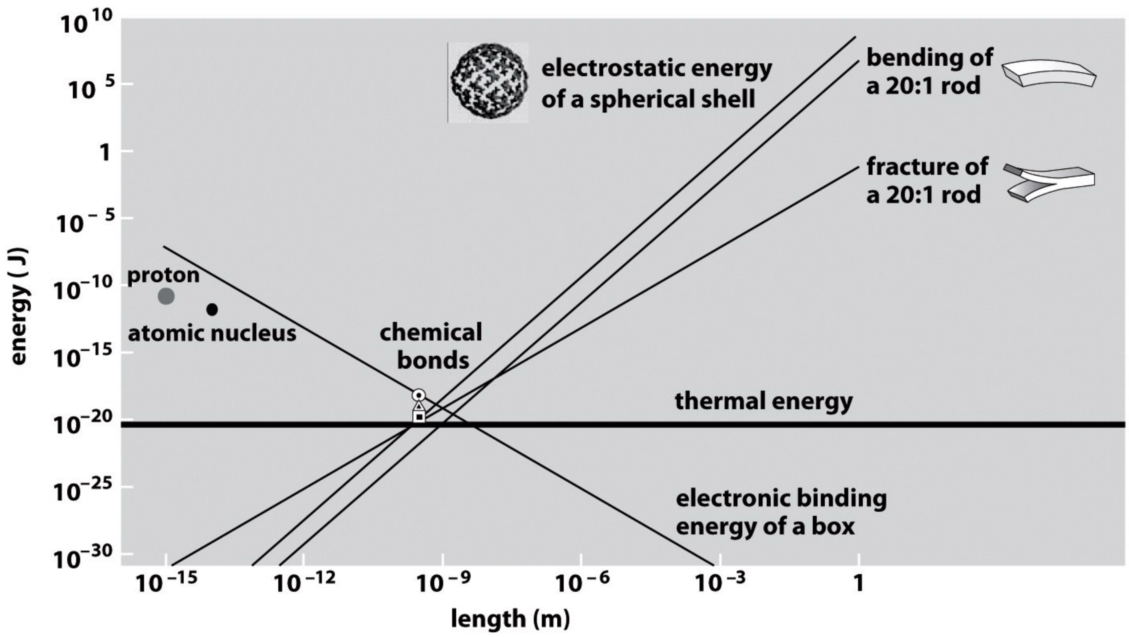
Previously: *Prokaryotes and Eukaryotes*







Energy in the cell



Energy in the cell

Active vs passive processes

Biological systems as minimizers

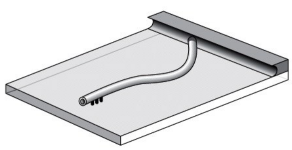
- What determines the shape of a red blood cell?
- Given a particular oxygen partial pressure in the lungs, what is the fractional binding occupancy of the hemoglobin within red blood cells?
- How much force is required to package the DNA within the capsid of a bacteriophage?
- What fraction of Lac repressor molecules in an E. coli cell are bound to DNA and what is the probability that one such molecule is bound specifically?

Useful simplification: many chemical and mechanical systems can be treated as if they are close to an equilibrium state.

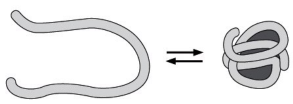
Biological systems as minimizers

Proteins as minimizers

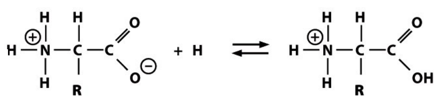
chemical bonds contribute to energy



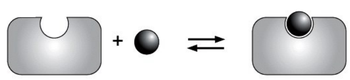
microtubule growing against a barrier



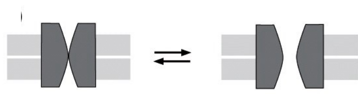
protein folding and unfolding



carboxylic acid group becoming protonated and deprotonated



ligand binding and unbinding to receptor



ion channel opening and closing

deformation contributes to energy

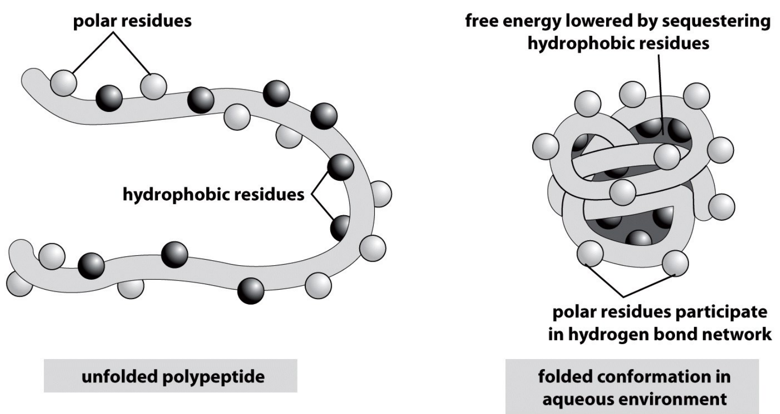
Biological systems as minimizers

How to find minimum energy states? Probabilities?

1. Identify the states.
2. Determine free energy of each state.

Biological systems as minimizers

Protein folding



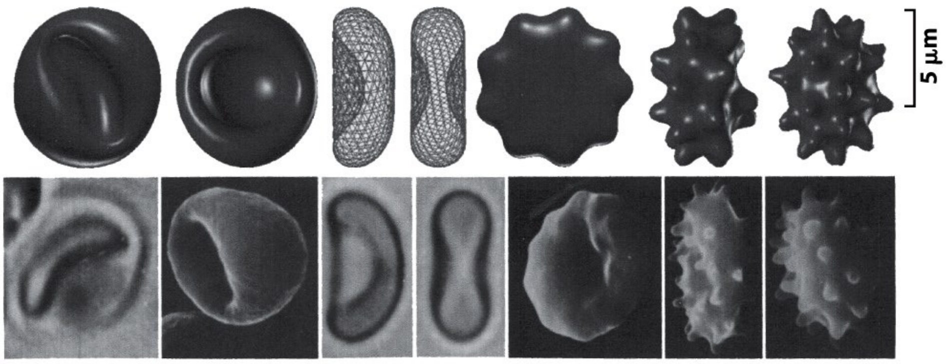
Number of possible 3D conformations is so large that a random search would take a long time:

100-monomer chain
$6^{100} = 6.5 \times 10^{77}$

One structure per femtosecond
2×10^{55} years
Age of universe ~10^{10} years

Biological systems as minimizers

Cells as minimizers

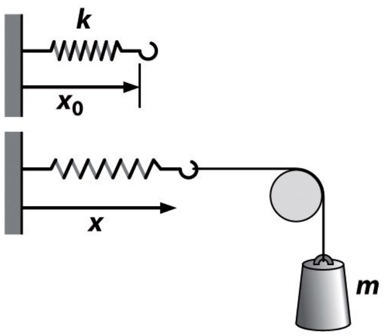


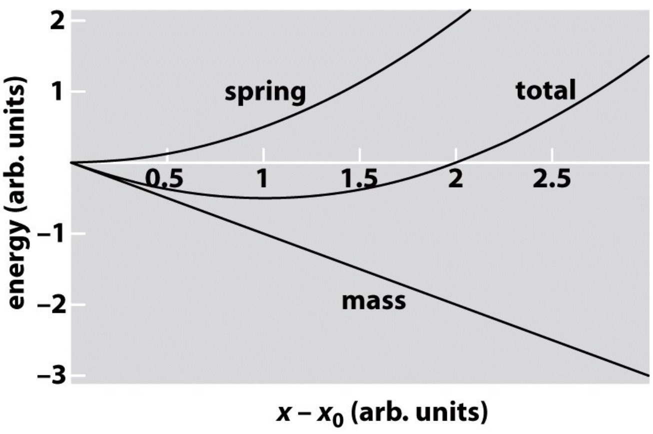
changes in area difference between two leaflets of bilayer

states: membrane shapes satisfying geometric constraints (constant area, constant volume)
energy: mechanical (elastic) energy of deformation

Biological systems as minimizers

Deformation energy: Macroscopic spring-mass system

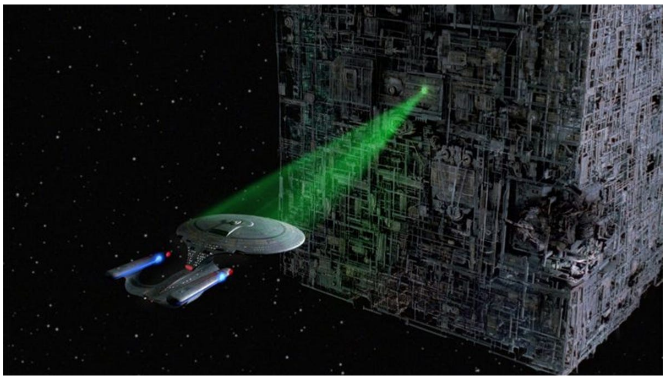




$$U(x) = \underbrace{\frac{1}{2}k(x - x_0)^2}_{\text{PE of spring}} - \underbrace{mg(x - x_0)}_{\text{PE of weight}}$$

Biological systems as minimizers

How do we know? Force-extension mechanics

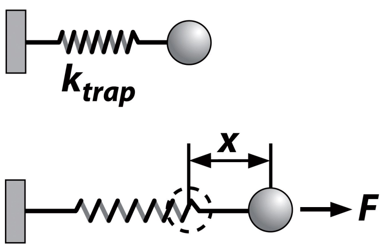


Tractor beam

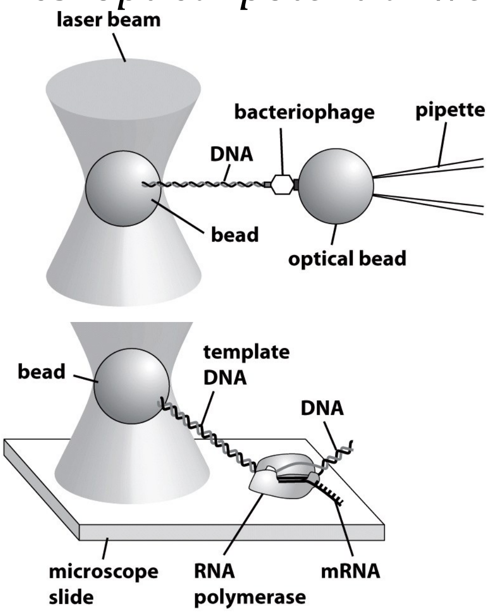
Optical tweezers

Biological systems as minimizers

Biopolymer mechanics: optical potential well

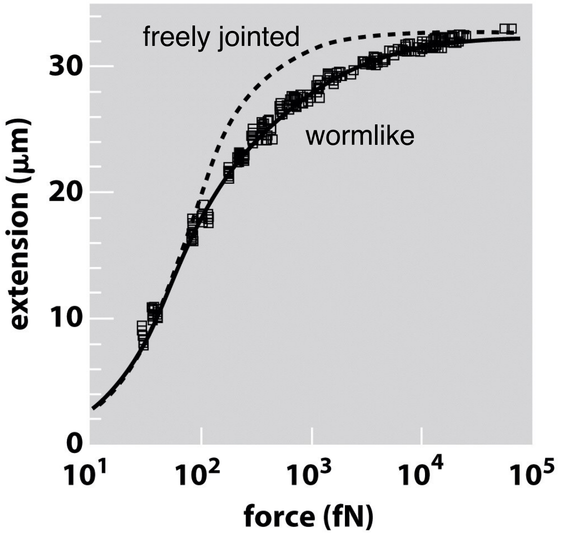


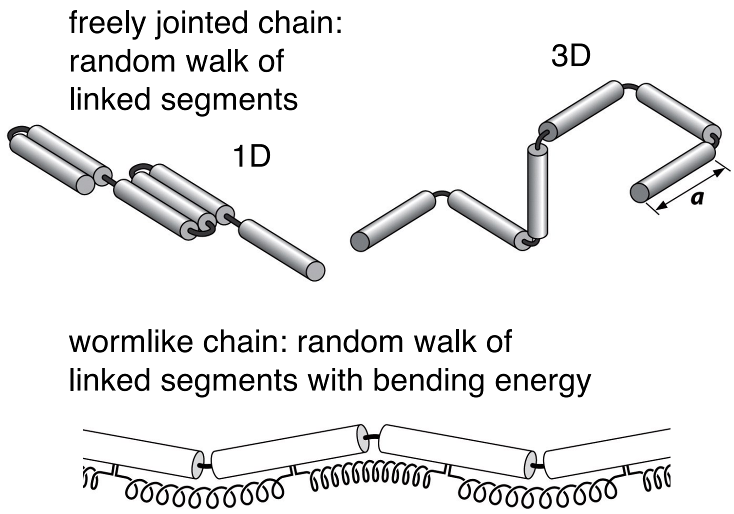
$$U(x) = \frac{1}{2}k_{trap}x^2 - Fx$$



Biological systems as minimizers

Biopolymer mechanics: optical potential well





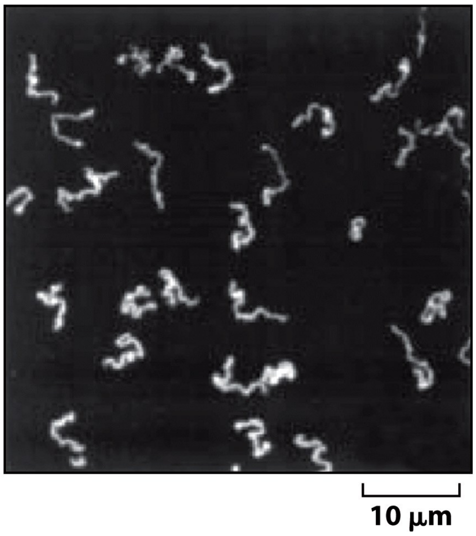
Including entropy

Thermal fluctuations

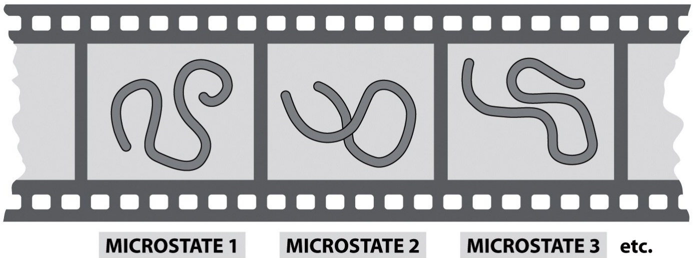
the equilibrium state of a system is the one out of all states available to the system that minimizes the free energy

Including entropy

System microstates

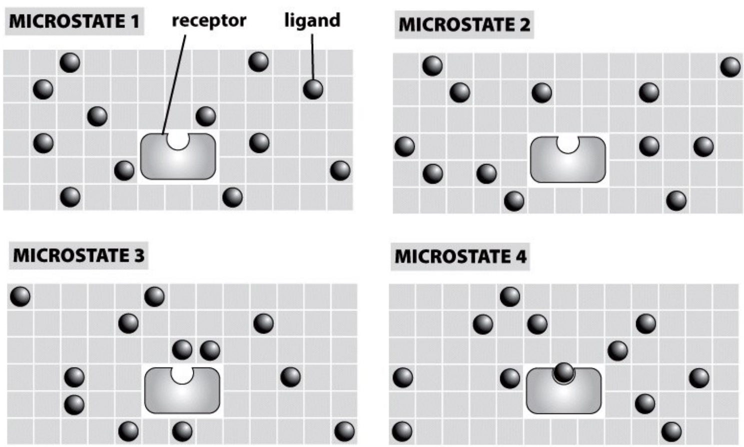


DNA conformations



Including entropy

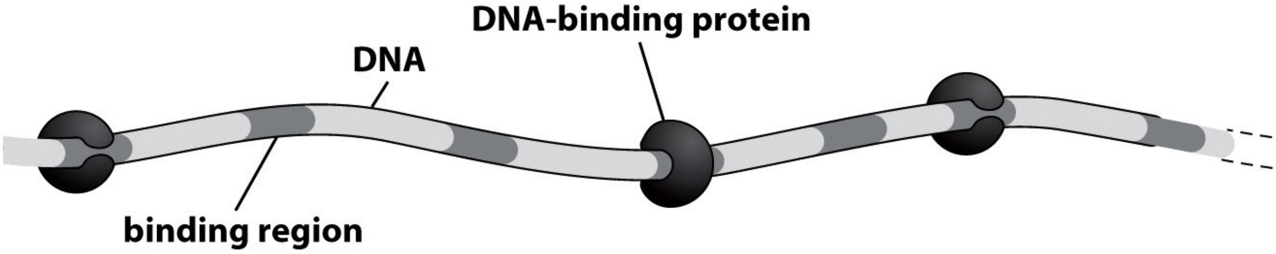
System microstates

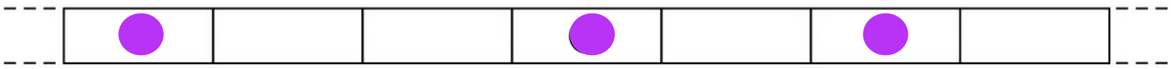


ligand binding to receptor protein

Including entropy

System microstates



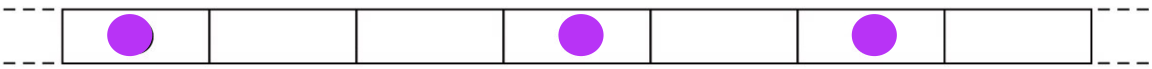


lattice model of DNA/protein complexes

protein binding to DNA

Including entropy

System microstates



lattice model of DNA/protein complexes

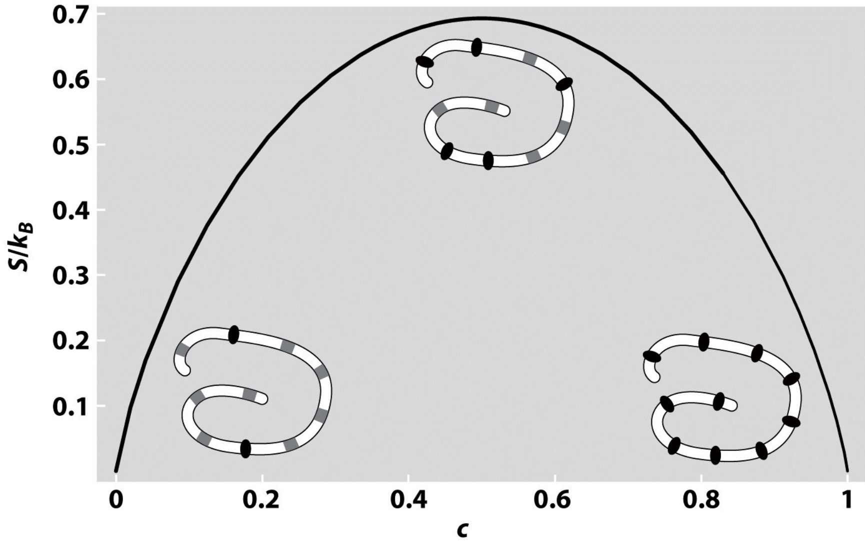
N boxes, N_P proteins (indistinguishable)

How many accessible states?

protein binding to DNA

Including entropy

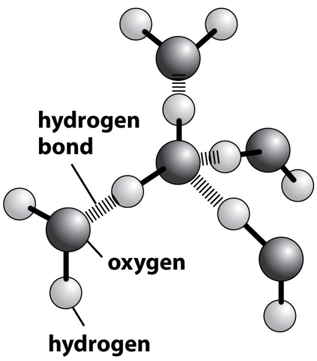
System microstates

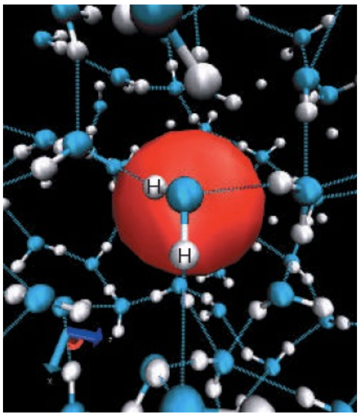


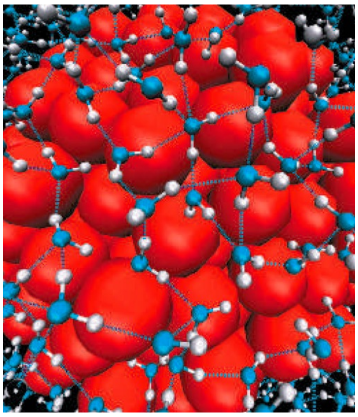
protein binding to DNA

Including entropy

Hydrophobicity: Toy model





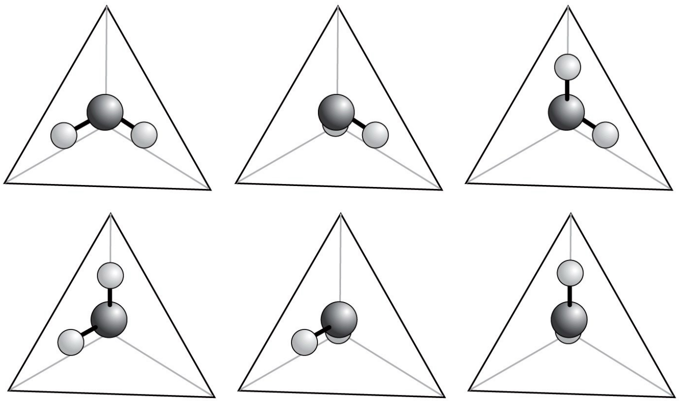


a hydrophobic molecule prevents water molecules from hydrogen bonding

Including entropy

Hydrophobicity: Toy model

What is the free energy cost?

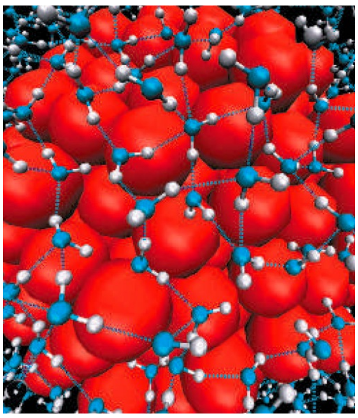


a hydrophobic molecule prevents water molecules from hydrogen bonding

Including entropy

Hydrophobicity: Toy model

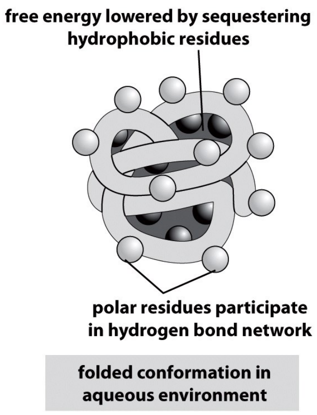
What is the free energy cost?

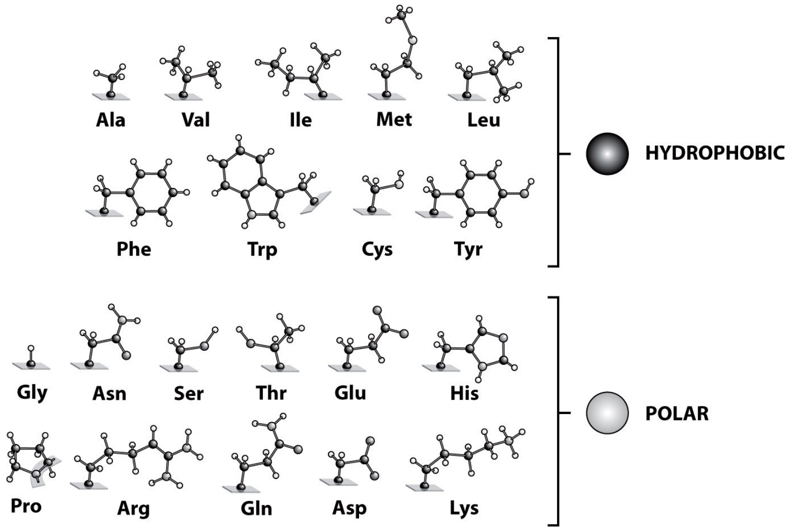


a hydrophobic molecule prevents water molecules from hydrogen bonding

Biological systems as minimizers

Protein folding: HP model





coarse-grained model

Biological systems as minimizers

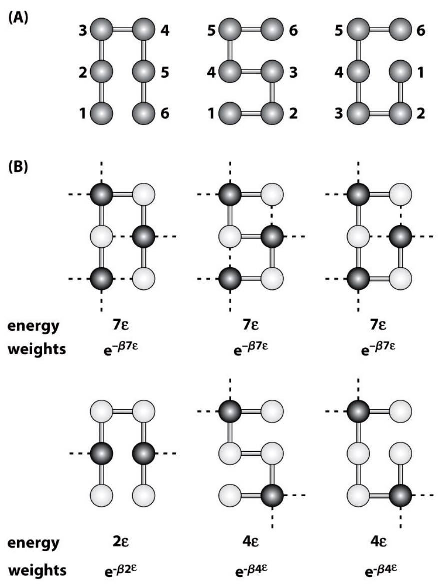
Protein folding: HP model

toy HP model:
6 monomers on a 3x2 lattice

sequences: $2^6 = 64$

sequence HPHPHP

sequence PHPPHP



states
number of unique structures: 3

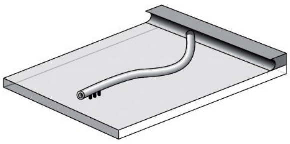
interaction model: assign **energy** penalty for H-P or H-solvent interactions (---)

Given an HP sequence, which of the possible structures minimizes the total free energy?

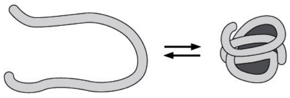
Biological systems as minimizers

Proteins as minimizers

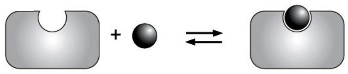
chemical bonds contribute to energy



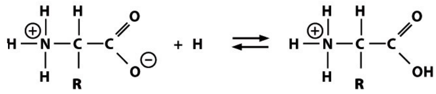
microtubule growing against a barrier



protein folding and unfolding



ligand binding and unbinding to receptor



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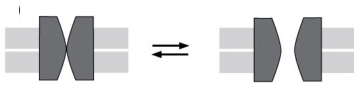

ion channel opening and closing

deformation contributes to energy

Lecture 3: Mechanical and chemical equilibrium

Many processes can be modeled using free energy minimization

- hydrophobic effect
- protein folding
- protein-ligand binding
- protein-DNA binding
- polymer (1D) or membrane (2D) bending

Model ingredients: energies associated with states, number of states

Lecture 4: Biological membrane elasticity

Goal: Calculate energy cost for bending membranes away from their equilibrium configurations

- The nature of biological membranes
- Springiness of membranes

PBOC Chapter 11.1, 11.2