Phys-301
Biophysics: Physics of the Cell

Prof. Suliana Manley
TAs: Santiago Rodriguez and Nick Mahtani

exercisos (problems)

journal articles

Overall course goals

- Understand the **organization of the cell** and its components
- Examine **universal** features/processes of cells
- Model features/processes using **physical concepts**

Note: This course is taken by students from PH, SV, GM …

Biophysics overview

Key physical concepts behind most biophysical models:

1. Simple numerical estimates
2. Elasticity theory (1D, 2D, 3D)
3. Statistical mechanics models
4. Diffusion and random walks
5. Circuit/network theory
6. Fluid mechanics (Newtonian, Navier-Stokes) (BA5, Ramirez-San Juan)
7. Information theory, dynamical systems (MA1/3, PHYS-302, Rahi)
8. Biopolymers (MA2, PHYS-441, De Los Rios)
9. Charges in solution (Poisson-Boltzmann)
10. Rate equation models of chemical kinetics

Course content

Topics (lectures)**:**

1. **Introduction to the cell** (1-3)
2. **Biological membranes** (4-5)
3. **Proteins** (6-7)
4. **Dynamics** (8-9)
5. **Genomes** (10-13)

Course components:

1. **Introduction to systems and concepts**
2. **Description of observations and measurements**
3. **Estimates of relevant numbers / development of quantitative models**
4. **Analysis of research articles**

Why is the course designed this way?

Introduce fundamental topics in cellular biophysics
Develop skills in model building
Practice reading to find information, provide context
Consider uncertainties of unsolved problems

Course structure

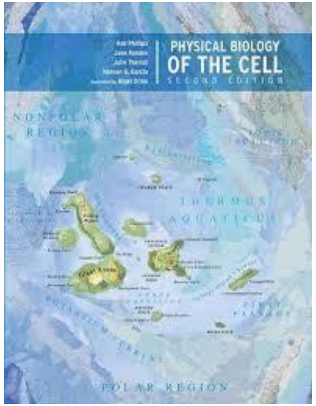
- One lecture and one exercise session per week.
  - (C) Mon, 13:15-15:00 (SM).
  - (E) Mon, 15:15-16:00 (SR or NM)
- Your role:
  - Read weekly before the course from PBOC (~1-2 hours)
  - Attempt the exercises/article before the exercises (~1-2 hours)
- Lectures will introduce and develop topics
- Exercises: problem solving or analyzing journal articles
- Written final exam

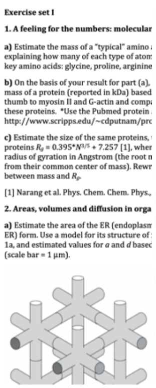
Resources:

- Moodle
- Lecture slides (TAKE NOTES)
- Bionumbers website https://bionumbers.hms.harvard.edu/search.aspx
- Physical Biology of the Cell by Rob Phillips, Jane Kondev and Julie Theriot.
- Selected journal articles

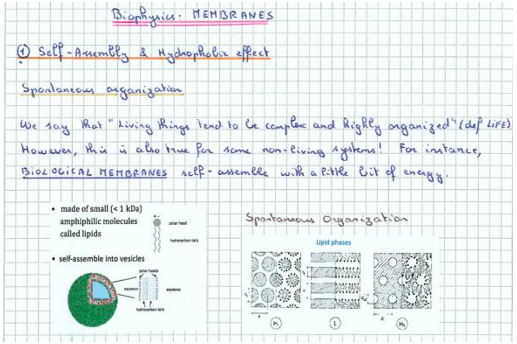
Your roles

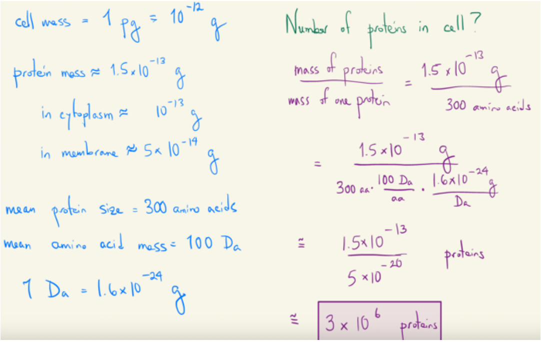
1. Before class: read PBoC, glossary, attempt weekly assignment





2. During lecture: take notes, do in-class exercises





3. After lecture: participate in exercise session, complete weekly assignment, compare with posted solutions (Wednesday each week)

Lecture 1 outline

Today's goal: Introductions

- Physical biology of the cell
- The stuff of life
- Model building in biology
- Quantitative models and the power of idealization

PBOC Chapter 1

atoms / molecules

electrical / mechanical

philosophy / approach

components: biomolecules

physical models for different components

examples

Physical biology of the cell

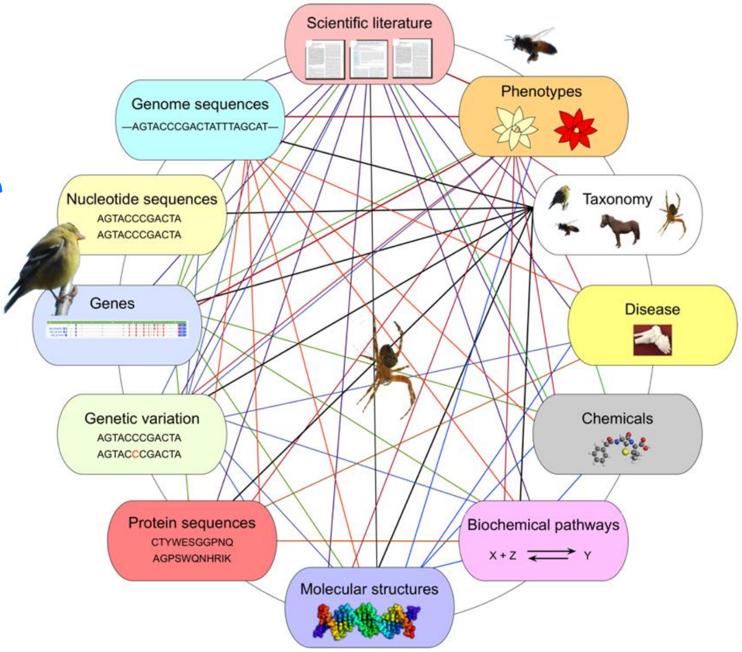
… all observation must be for or against some view if it is to be of any service!

Darwin

lots of data!

lists of constituents: "ome"

- genome (genetic sequences)
- proteome (proteins)
- biome (organisms)



Good models overlook some of the details, while keeping enough to make useful predictions.

The stuff of life

What is life?

- grow
- move
- reproduce
- consume energy
- die
- respond to stimuli

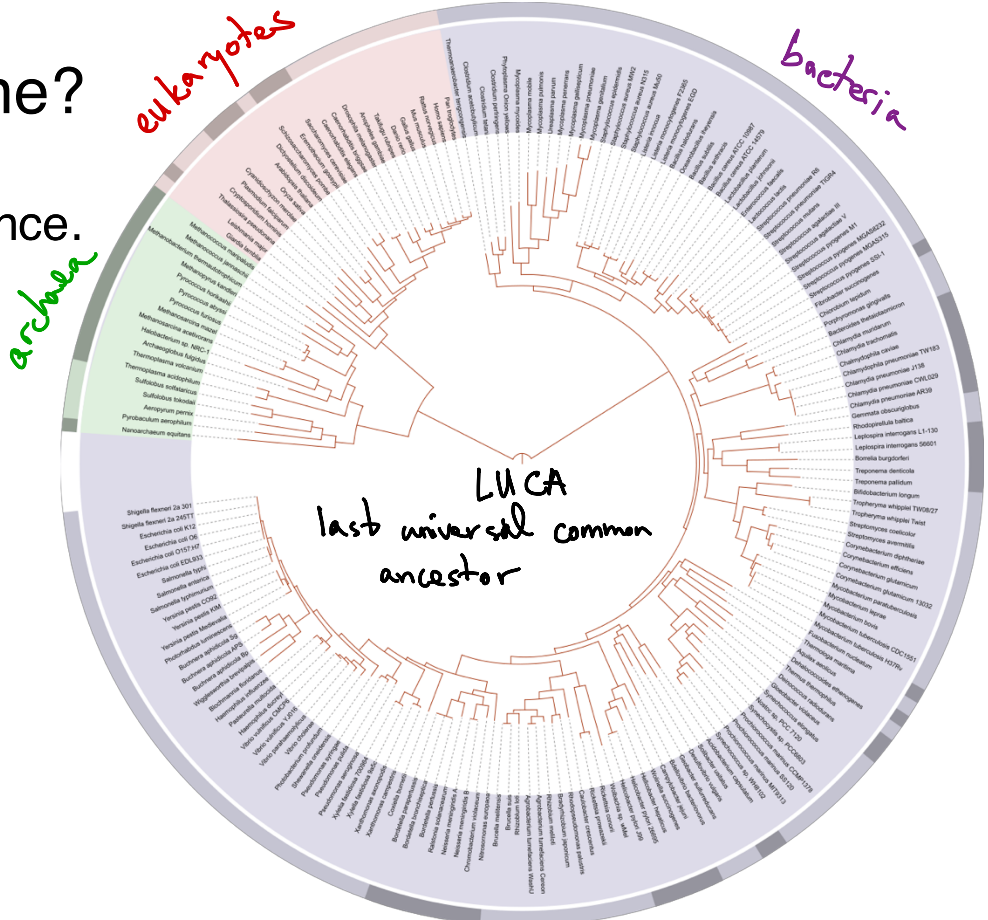
The stuff of life

Why is it so difficult to define?

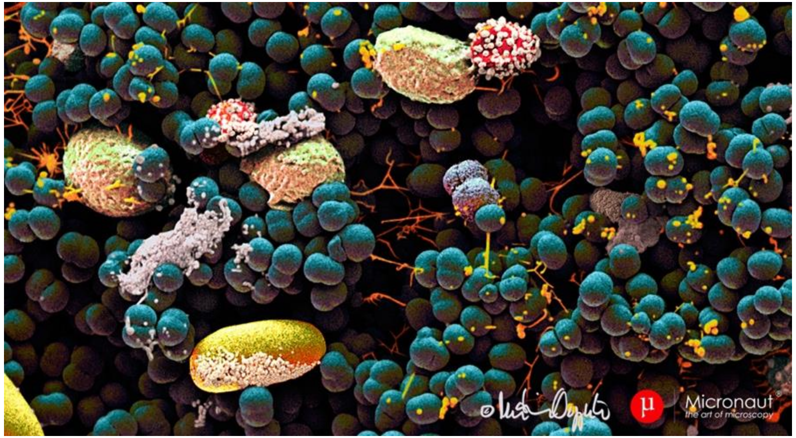
Life is a process, not a pure substance.
A great diversity of life exists.

phylogenetic classification: evolutionary history, encoded in genes

NASA: life is a self-sustaining chemical system capable of Darwinian evolution



LIFE ADAPTS / EVOLVES TO ENVIRONMENTAL NICHE



The stuff of life


WHAT IS LIFE?

The Physical Aspect of the Living Cell

BY

ERWIN SCHRÖDINGER

4339

CAMBRIDGE

AT THE UNIVERSITY PRESS

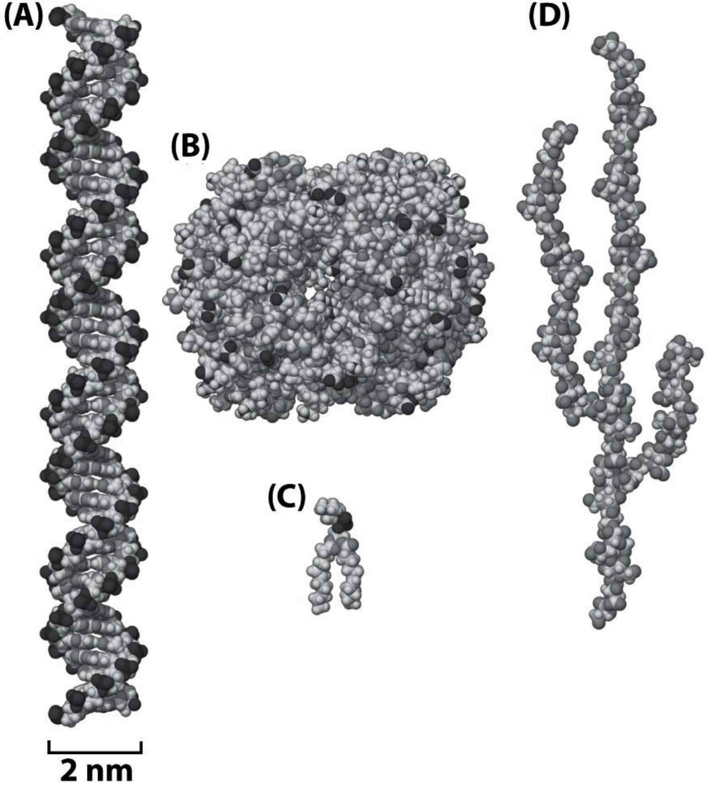
When is a piece of matter said to be alive? When it goes on "**doing something**," … for a much longer period than we would expect an inanimate piece of matter to "keep going" under similar circumstances. When a system that is not alive is isolated or placed in a uniform environment, all motion usually comes to a standstill very soon as a result of various kinds of friction; differences of electric or chemical potential are equalized, substances which tend to form a chemical compound do so, temperature becomes uniform by heat conduction. After that the whole system fades away into a dead, inert lump of matter. A permanent state is reached, in which no observable events occur. *The physicist calls this the state of thermodynamical equilibrium, or of "maximum entropy."*

“What is life”, 1944, Schrödinger

The stuff of life

What macromolecules are cells made of?

four main
bio- macromolecules



Name the molecule
What are its parts?
What are its units?
What is it used for?

The stuff of life

What macromolecules are cells made of?

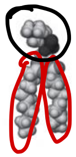
Name the molecule
What are its parts?
What are its units?
What is it used for?

lipid (phospholipid)

hydrophilic / hydrophobic

chain length, saturation of bonds in chains

cell membrane, compartmentalize (cell, organelles)



polar head : hydrophilic

fatty acid chains } hydrophobic

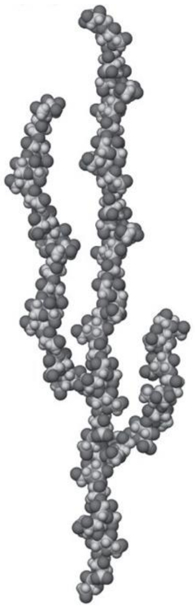
hydrocarbon chains

The stuff of life

What macromolecules are cells made of?

(we aren't going to study this one)

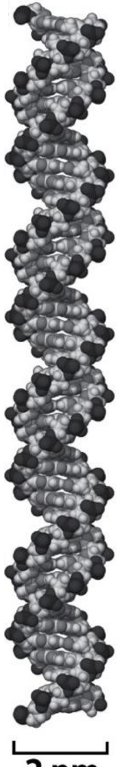
Name the molecule — carbohydrate
What are its parts? — carbon, hydrogen, oxygen
What are its units? — $(C_mH_2O)_n$ chain length n
What is it used for? — energy storage, cell surface selectivity, cell walls



The stuff of life

What macromolecules are cells made of?

Name the molecule
What are its parts?
What are its units?
What is it used for?



DNA

bases / nucleotides (A, T, G, C)

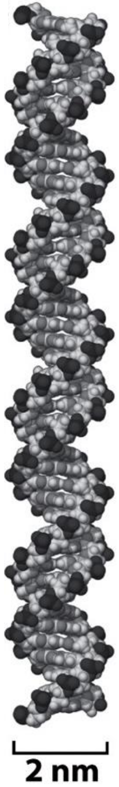
base pairs

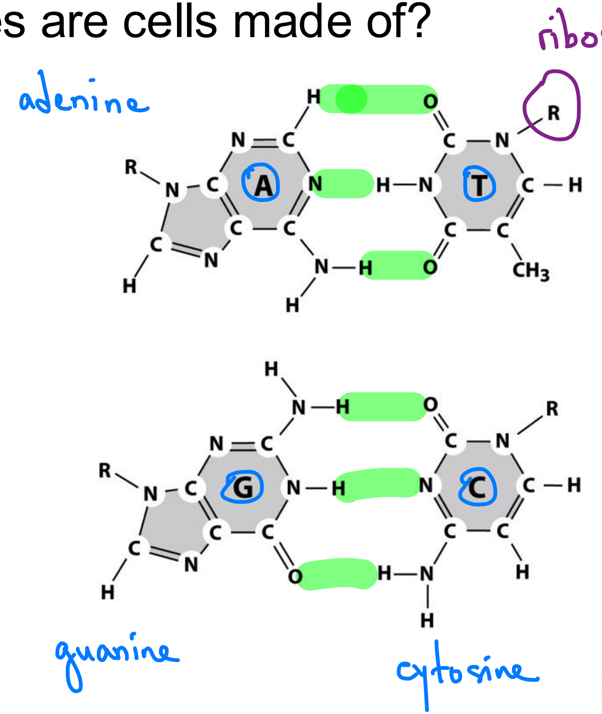
encoding genetic information

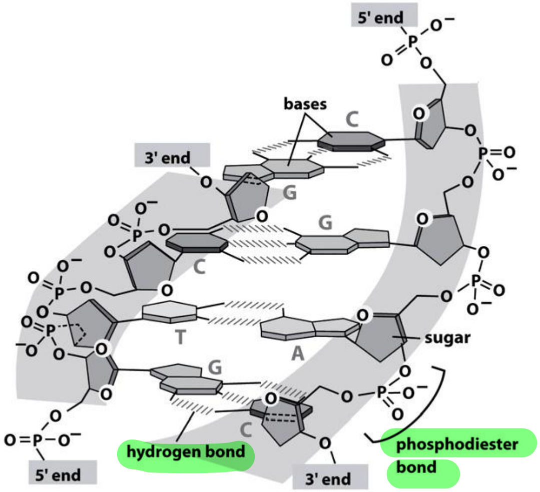
The stuff of life

What macromolecules are cells made of?

Name the molecule
What are its parts?
What are its units?
What is it used for?



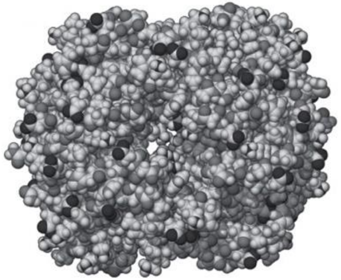




The stuff of life

What macromolecules are cells made of?

Name the molecule
What are its parts?
What are its units?
What is it used for?



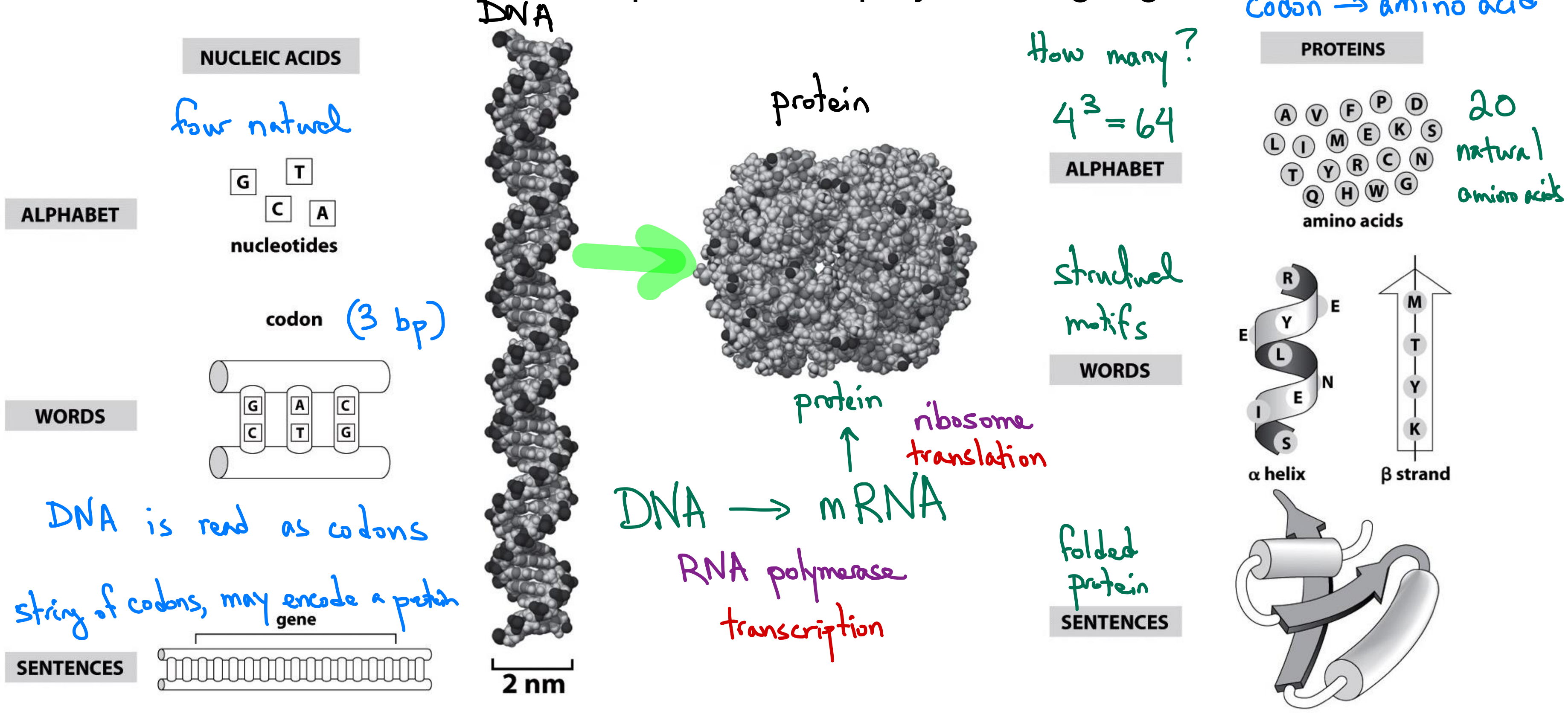
protein (hemoglobin)
amino acids
Daltons (unified atomic mass unit)
1/12 mass of C_{12} atom

enzymes (catalyze processes) or
structural (mechanical properties)
bind ligands/ions (sensors, carriers)

structural motifs: alpha helices, beta sheets

The stuff of life

Nucleic acids and proteins are polymer languages

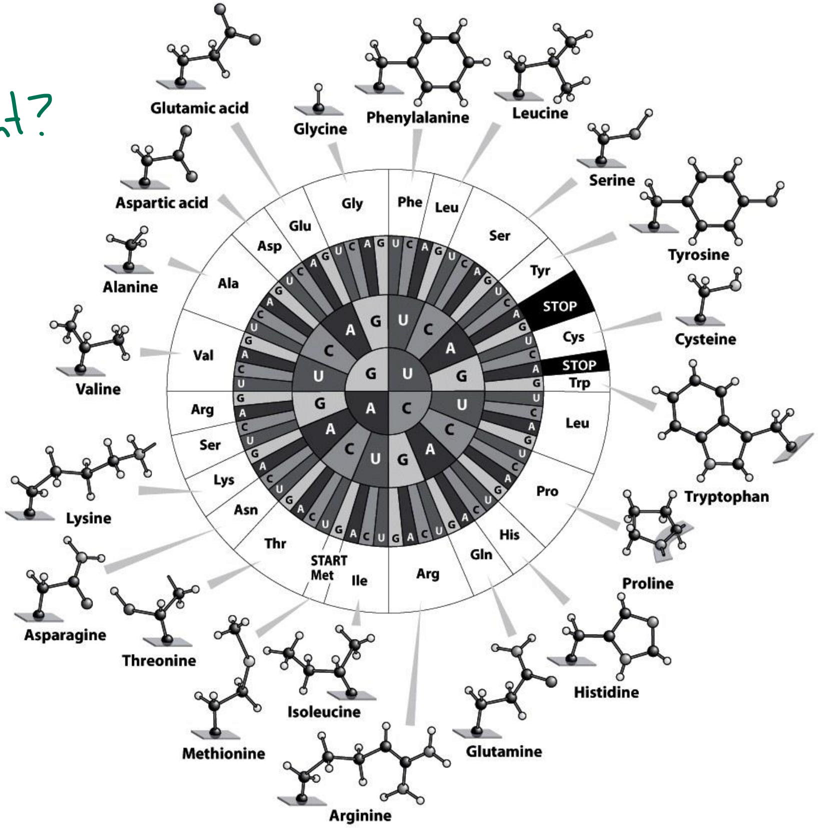


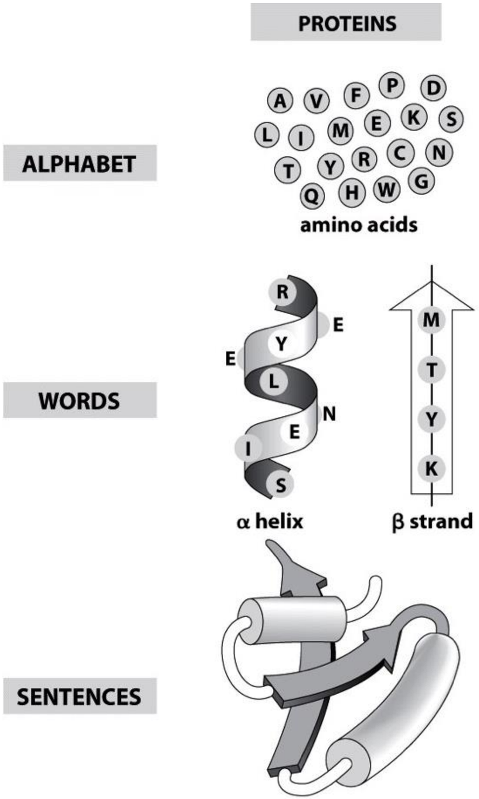
The stuff of life

What macromolecules are cells made of?

Why redundant?

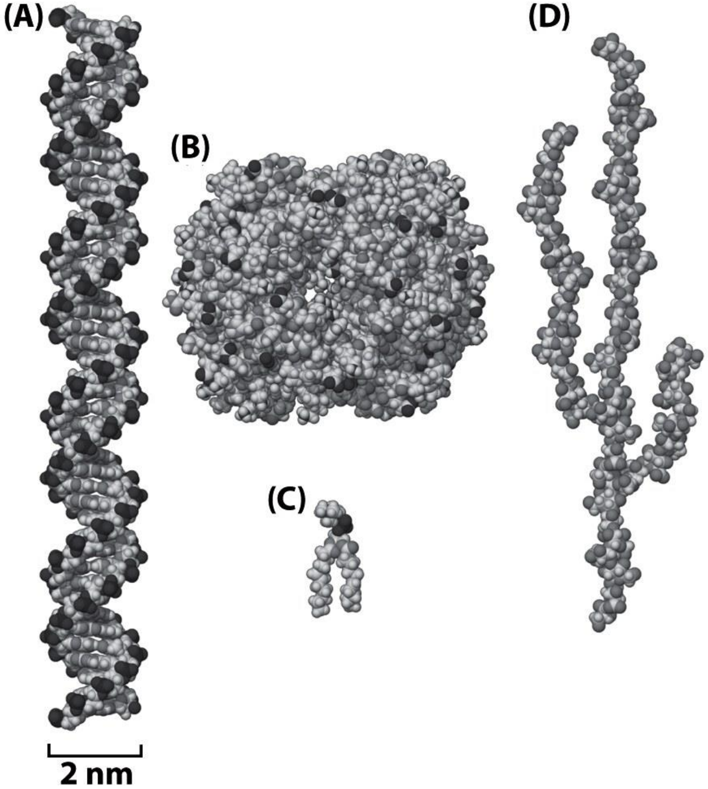
Robustness





The stuff of life

What macromolecules are cells made of?



Advantages:

- Each class can be assembled by the cell from a small set of simpler subunits
- Combinatorial assembly gives rise to diversity
- Limited repertoire of chemical reactions needed
- Facilitates existence of food chain

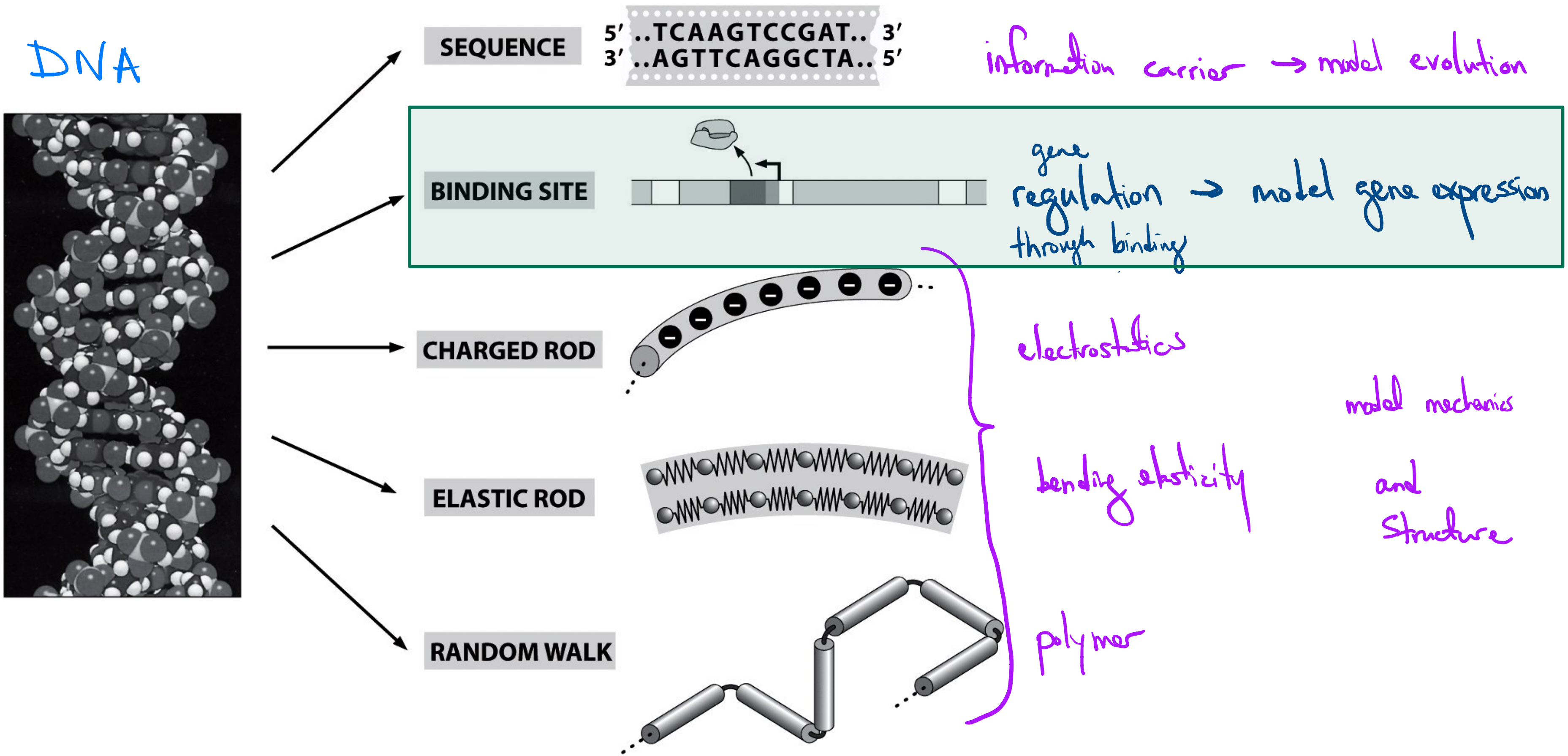
Model building

What is a model?

- Overlook / coarse grain some details, keep enough to make prediction
- Explain / capture existing phenomena → extrapolable to predict

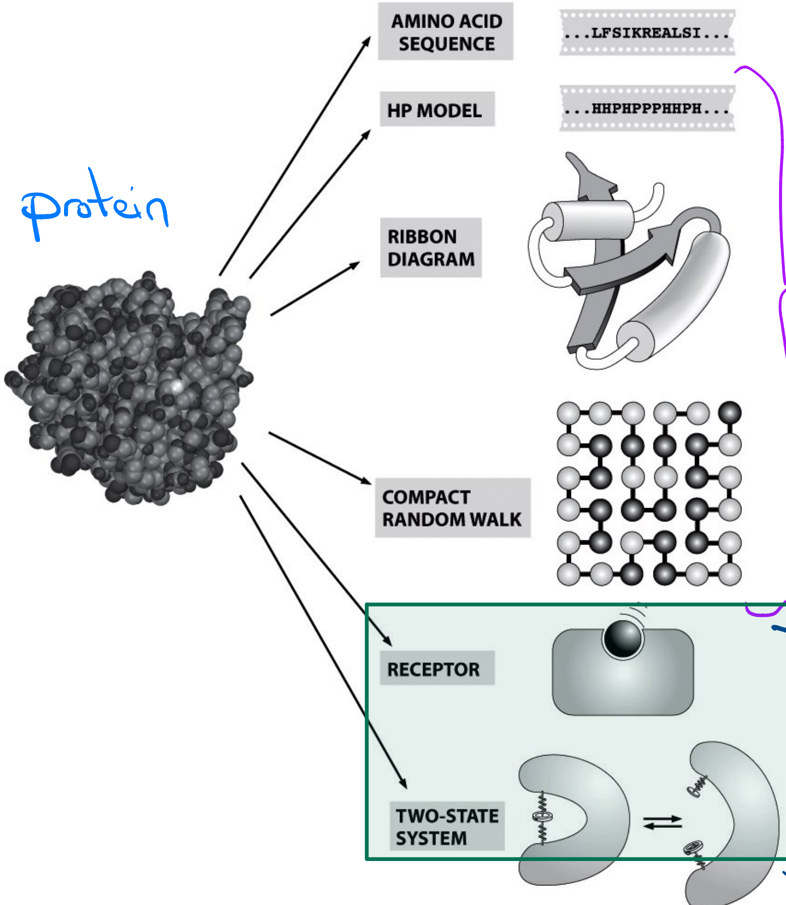
Main challenge: what to simplify, what to keep complex

Model building



Model building

protein



information → model mutations, diversification & evolution of species

3D folded shape of protein gives it function.

HP: H = hydrophobic P = polar

coarse-grain structure

random walk

→ model folding.

functional models, ignore internal structure.

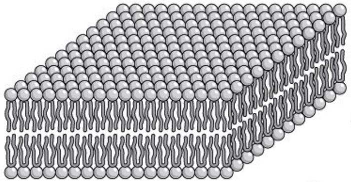
receptor binding ligand.

conformational change: active/inactive enzyme.

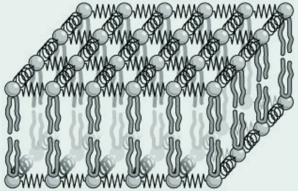
model cellular response

Model building

lipid bilayer membrane

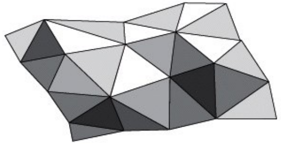


ARRAY OF SPRINGS



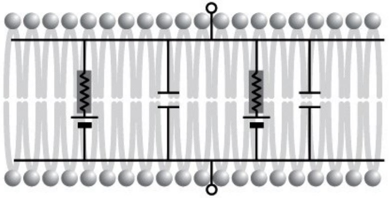
mechanics. → model deformations under applied force, energy to create different shapes

RANDOM SURFACE



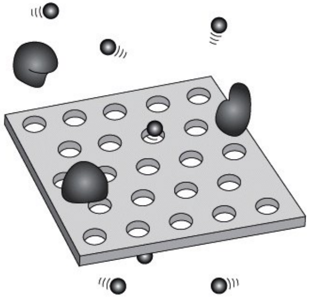
interaction surface. → model binding

RC CIRCUIT



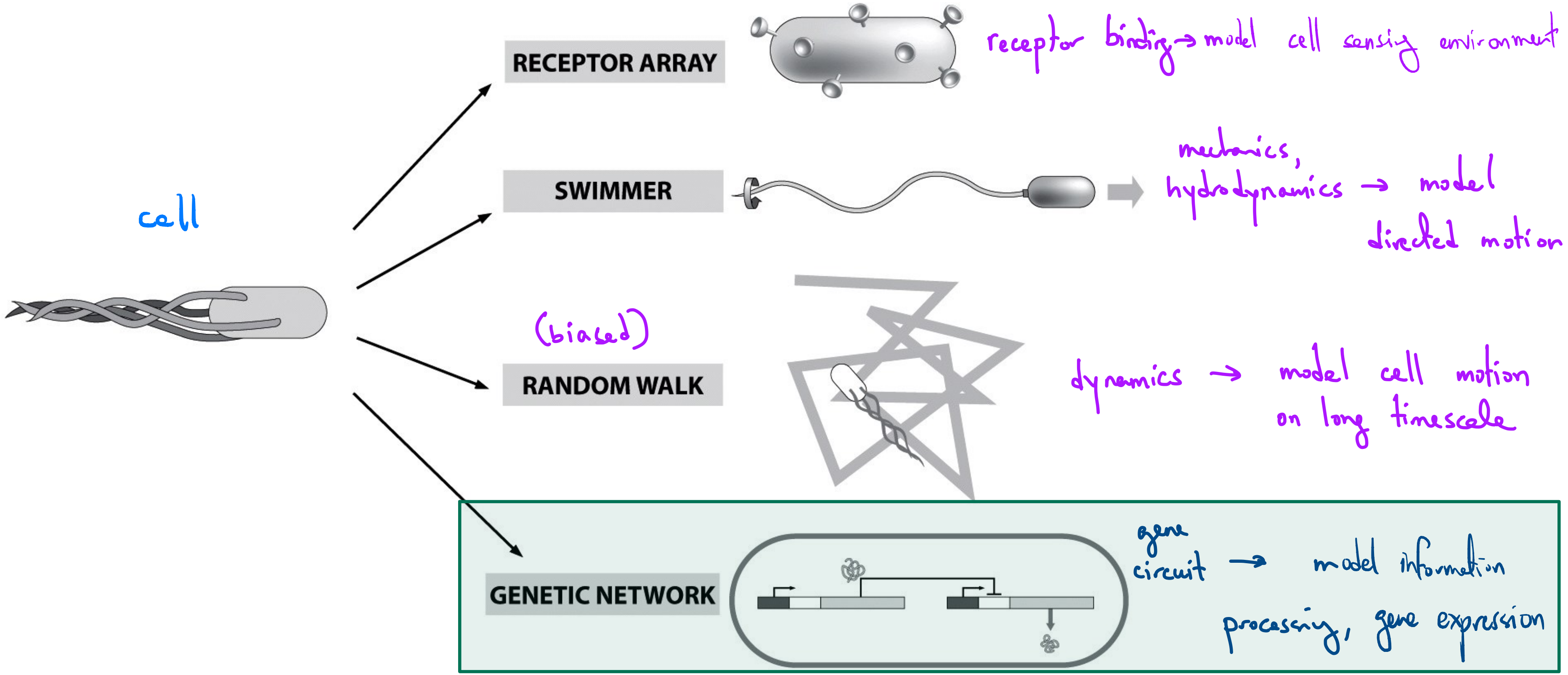
electrical properties. → model voltage across membrane.

SEMI-PERMEABLE BARRIER



transport properties → model transport of material (ions, molecules)

Model building



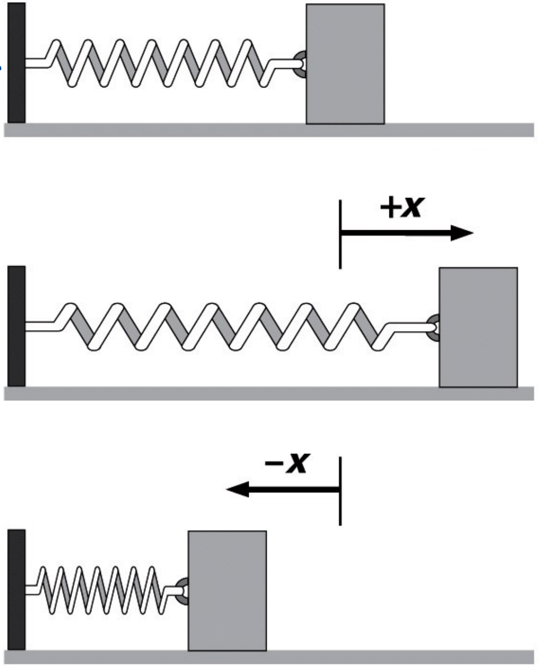
Quantitative models and the power of idealization

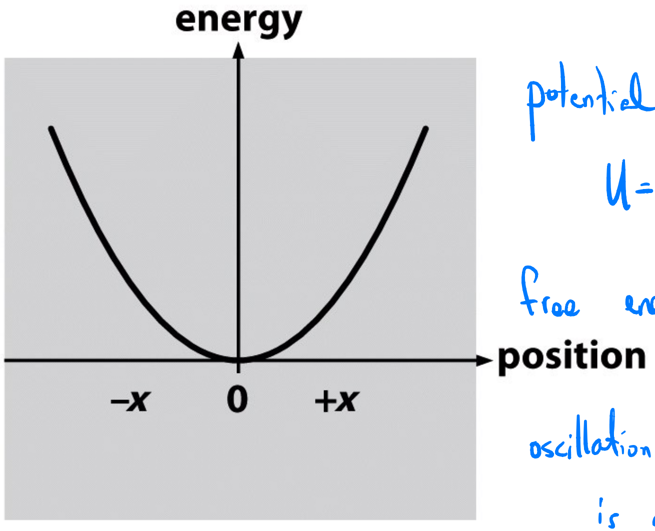
Example: Potential energy landscape

Simple spring model

linear force-displacement

$F = -kx$





potential energy

$U = \frac{1}{2} kx^2$

free energy minimization

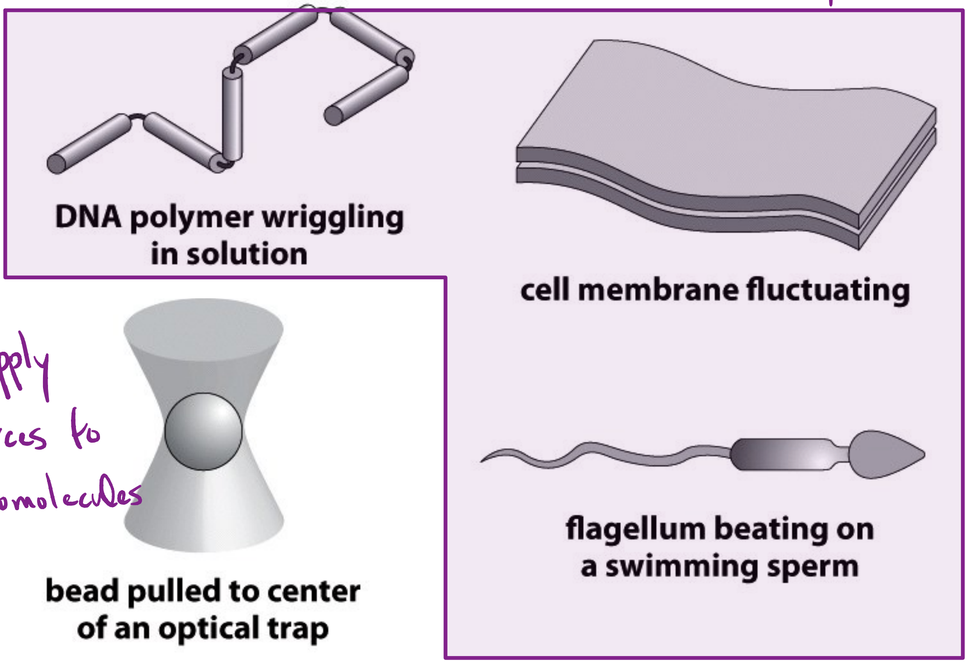
oscillation when energy is added

Quantitative models and the power of idealization

Analogs in biophysics

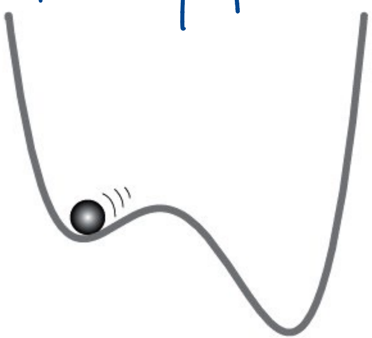
Example: Potential energy landscape

measure mechanics of biological systems



apply forces to biomolecules

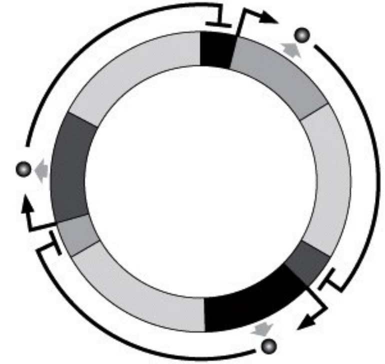
probability $p(E)$



molecules in an energy landscape

dynamics

$c_1(t), c_2(t), c_3(t)$



genetic network changing expression levels over time

oscillatory solutions to differential eqn's

Quantitative models and the power of idealization

Numerical estimates

Phillips Numbers SnapShot

BioNumbers website

	Quantity of interest	Symbol	Rule of thumb
E. coli	Cell volume	$V_{E.\ coli}$	$\approx 1\ \mu m^3$
	Cell mass	$m_{E.\ coli}$	≈ 1 pg
	Cell cycle time	$t_{E.\ coli}$	≈ 3000 s
	Cell surface area	$A_{E.\ coli}$	$\approx 6\ \mu m^2$
	Genome length	$N_{bp}^{E.\ coli}$	$\approx 5 \times 10^6$ bp
	Swimming speed	$v_{E.\ coli}$	$\approx 20\ \mu m/s$
Yeast	Volume of cell	V_{yeast}	$\approx 60\ \mu m^3$
	Mass of cell	m_{yeast}	≈ 60 pg
	Diameter of cell	d_{yeast}	$\approx 5\ \mu m$
	Cell cycle time	t_{yeast}	≈ 200 min
	Genome length	N_{bp}^{yeast}	$\approx 10^7$ bp
Organelles	Diameter of nucleus	$d_{nucleus}$	$\approx 5\ \mu m$
	Length of mitochondrion	l_{mito}	$\approx 2\ \mu m$
	Diameter of transport vesicles	$d_{vesicle}$	≈ 50 nm
Water	Volume of molecule	V_{H_2O}	$\approx 10^{-2}\ nm^3$
	Density of water	ρ	$1\ g/cm^3$
	Viscosity of water	η	≈ 1 centipoise (10^{-2} g/(cm s))
	Hydrophobic embedding energy	$\approx E_{hydr}$	25 cal/(mol $Å^2$)

DNA	Length per base pair	l_{bp}	$\approx 1/3$ nm
	Volume per base pair	V_{bp}	$\approx 1\ nm^3$
	Charge density	λ_{DNA}	2 e/0.34 nm
	Persistence length	ξ_P	50 nm
Amino acids and proteins	Radius of "average" protein	$r_{protein}$	≈ 2 nm
	Volume of "average" protein	$V_{protein}$	$\approx 25\ nm^3$
	Mass of "average" amino acid	M_{aa}	≈ 100 Da
	Mass of "average" protein	$M_{protein}$	$\approx 30{,}000$ Da
	Protein concentration in cytoplasm	$c_{protein}$	≈ 300 mg/mL
	Characteristic force of protein motor	F_{motor}	≈ 5 pN
	Characteristic speed of protein motor	v_{motor}	≈ 200 nm/s
	Diffusion constant of "average" protein	$D_{protein}$	$\approx 100\ \mu m^2/s$
Lipid bilayers	Thickness of lipid bilayer	d	≈ 5 nm
	Area per molecule	A_{lipid}	$\approx \frac{1}{2}\ nm^2$
	Mass of lipid molecule	m_{lipid}	≈ 800 Da

Lecture 2 outline

Goal: Size and contents of cells

- An ode to E. coli
- Cells and the structures within them

PBOC Chapter 2.1, 2.2