What's in a cell

What are cells?

Basic, most fundamental unit of life

Diversity and characteristics

- size: micrometers (bacterial) to millimeter (egg cells)
- shape: spherical (bacteria), highly extended (human nerve), hairy (paramecium), tailed (bacteria)

What's in common:

- DNA – genetic information, recipes
  - **genome** is the information
  - **evolution** acts upon the information through mutations of DNA to create new species and species diversity
- RNA – copies of recipes sent to protein factories
- proteins – the "worker" molecules that accomplish many biomolecular functions

Basic categories of cells:

- prokaryotes – no nucleus
  - bacteria – most familiar
  - archea – hostile environments (acidic, high temperature)
- eukaryotes – has nucleus, typically bigger in size
  - plants, animals, fungi

How is a cell similar to or different from chemical processing?

Similar:

- unit operations = specialized molecules, processes, compartments, organelles that are reused again and again

- master control = DNA
- energy optimization
- many steps often required to accomplish simple cell behavior
- limited by same laws of physics: thermodynamics, kinetics, transport

Different:

- much smaller; interfacial interactions can play very important roles
- very robust redundancies and error-correction for chemical processes
- highly heterogeneous, crowded mixtures
- most processes happen in much smaller molecular copy numbers → need to consider molecular behavior that is often different from bulk → random fluctuations can be significant [ex: concentration profile]

Interactions

All cellular molecular building blocks are governed by the same kinds of interactions and physiochemical processes that dictate the properties of nonliving things in nature and in synthetic chemicals and materials.

A critical challenge is identifying how these interactions result in much more complex behavior in living systems than in synthetic ones.

At a fundamental level, all interactions are described by electrostatics due to electron clouds interacting with nuclei. A quantum description is ultimately required, but we can find simple common ways that the quantum behavior manifests.

Here we will take a simple picture in understanding what interactions between two atoms entail. It will be important to consider their pairwise separation distance r:

- **at large separation distances** – energy should be zero (normalization condition)
- **attractive** – negative, decreasing interaction energy when atoms come close
- **repulsive** – positive, increasing interaction energy when atoms come close

Covalent bonds

One of the strongest chemical interactions between atoms. Involves sharing electrons and emerges from the quantum mechanical solution.

Magnitude is typically 100 kcal/mol

van der Waals interactions

Also called London or dispersion forces.

Generic attractive interaction between all atoms due to instantaneous alignment of electronic charge distribution (e.g., dipoles). In other words, electrons in neighboring atoms close by dance in sync.

Interaction potential energy decays as r^{-6}.

Typical form is the Lennard Jones potential,

$$u(r) = 4\epsilon\left[\left(\frac{r}{\sigma}\right)^{-12} - \left(\frac{r}{\sigma}\right)^{-6}\right]$$

where parameters a different for different pairs of atom types. {Plot out the LJ potential.}

Magnitude of the order 0.5 kcal/mol.

electrostatic interactions (p 261 Nelson)

Bonded atoms can donate electrons (ionic) or share them in uneven ways (covalent). For ionic bonds, each atom attains a nonzero **formal charge**. For covalent bonds, we can have an effective charge on each atom that is nonzero that we think of as a **partial charge**.

Effective interaction potential energy between two atoms then follows Coulomb's law:

$$u(r) = \frac{q_1 q_2}{4\pi\epsilon\epsilon_0 r}$$

Can be attractive or repulsive for opposite or like charges.

In addition to vdW interactions for charged or partially-charged atoms.

Magnitude in ionic bonds in a solid salt – ~200 kcal/mol

Magnitude between two ions in water – less due to screening by water (dielectric constant 80 times that of vacuum)

Hydrogen bonds

Hydrogen bonds are particularly strong, attractive, directional interactions between hydrogen atoms and electronegative atoms.

Examples: O-H…O , O-H…N , N-H…O , N-H…N

Typically the hydrogen atom is also bonded to an electronegative atom, so that it has a partial positive charge.

Cannot be described by simply Coulombic, electrostatic interactions – requires a more detailed treatment of the quantum mechanical solution that we won't cover here.

Magnitude:

- O-H…O 5 kcal/mol
- O-H…N 7 kcal/mol
- N-H…O 2 kcal/mol

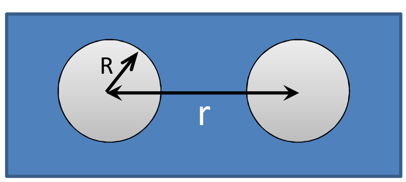
The hydrophobic interaction (p 273 Nelson)

Arguably the most important interaction in biology. About ~70% of cells are water; therefore, most other molecules behave as if they are solvated in liquid water.

Drives the separation of oil and water. In general, drives the separation of **nonpolar hydrophobic** groups (low charge, low dipole, oily, carbon-based) with **polar hydrophilic** ones (high charge or dipole, hydrogen-bonding, involves many electronegative atoms like N or O).

Not one of the basic interactions per se, but an emergent effective interaction that arises due to complex van der Waals, electrostatic, and hydrogen bonding interactions in bulk liquid water.

Basic model is association of hydrophobic solutes:



What causes these solutes to want to associate? Remember in thermodynamics, the free energy tends towards a minimum. Therefore, the associated state must be a lower free energy than the separated state.

Water can form tetrahedral networks via hydrogen bonding.

In the associated state, there is less solute surface area interacting with water. Water at the surface of a nonpolar solute retracts and becomes more "ordered" by forming more tetrahedrally-ordered arrangements. This results in a decrease in the entropy of the water. By associating, molecules minimize the amount of surface area water and thus increase the entropy.

Specificity in interactions

Biology accomplishes complex tasks by having very specific interactions:

- selective catalysis
- selective transport
- binding and recognition

How can molecular interactions be specific?

Imagine that we want molecule A to bind selectively to B, but not C, D, or E. We can use to properties to make A recognize B:

- **geometry** – shape complementarity between A and B
- **multiple interactions** – use many kinds of interactions (vdW, hydrophobic, hbond, electrostatic) that each are relatively weak, but when complemented by a binding partner, result in a net strong interaction

Requires two components:

- molecules that have **well-defined and varied shapes**
- **diversity of building blocks** to achieve different kinds of interactions

What's kinds of molecules are necessary for life?

- programmable – can carry lots of different kinds of information
- replication – copies can be made
- specificity – able to do things selectively, interact with specific other molecules
- reactions can occur at ambient conditions, but not spontaneously (enzymes)

Molecular building blocks

Small molecules

- water - ~70% by weight
- ions
- misc inorganics and small molecules

Small building block molecules can be bonded together in long chains to form various macromolecules

- nucleotides → DNA, RNA
- amino acids → proteins
- sugars → polysaccharides
- fatty acids → lipids

What's important?

- **synthesis** – cells can make many molecules from "scratch" after breaking down ingested ones; however, others are "essential" [e.g., amino acids]
- **chirality** – molecules can have L or D forms, often times only one is biologically active/relevant [question: Why?]
- **precision** – cells make molecules with precise control over chemistry, chirality, sequence, etc
- **polymers and sequence is critical** – long chain molecules can spontaneously adopt unique, collapsed shapes that enable them to accomplish specificity by way of geometry. Different sequences result in different shapes.
- **toolkit** – cells have evolved to use certain molecules over and over again to perform important tasks [e.g., energy storage]. In many cases, the same molecules can have more than one role in the body.

Sugars and polysaccharides

Role: energy sources, storage, structural support, recognition properties on cell surfaces

Basic sugar unit: monosaccharide

Example: glucose

Monosaccharides can be linked together covalently to form di-, tri-saccharides, and on up.

Condensation versus hydrolysis reactions

Polysaccharides can be very long, up to thousands of linked monosaccharides, and can be branched in complicated ways due to different OH groups on each. This allows biology to create different branched structures that have distinct mechanical properties, just like polymers.

Oligosaccharides = small polysaccharides (e.g. up to 50 monomers)

Cellulose = polysaccharide of glucose.

- Very important to structural support in plants.
- Most abundant organic molecule on earth
- Difficult to break down, digest (human's can't →fiber) due to dense, tightly bound structure

Oligosaccharides can be added to lipids (**glycolipids**) and proteins (**glycoproteins**) to alter their function and/or serve as "markers" that are recognized by other molecules [e.g., immune system]

Fatty acids and phospholipids

Role: major building blocks of cell membranes, long-term storage of energy

Hydrophilic carboxyl head group plus a hydrophobic carbon tail

Phospholipids are typically two fatty acids bonded to a glycerol, then to a phosphate group, then to a polar group. This makes the molecule very **ampipathic.**

Very important behavior: self-assembly into micelles and vesicles. Similar to surfactants (e.g., soap)

Form phospholipid bilayer, or membrane. Essential to compartmentalization and specialization in cells.

Saturation of carbon bonds affects tail flexibility; fully saturated means very flexible, unsaturated has double bonds that introduce kinks. Cells can vary in order to tune membrane properties

Nucleotides, DNA, RNA

Role: central information storage and transmission, energy transport (batteries)

Three parts make up a single nucleotide:

- base – two categories:
  - pyrimidines (cytosine, thymine, uracil) have six-membered ring
  - purines (guanine, adenine) have a second five-membered ring
- sugar: ribose or deoxyribose
- phosphate group

Nucleotides provide life's "batteries". Adenosine triphosphate (ATP) is the most common energy carrier. The phosphate groups store tremendous energy and dephosphorylation is used to drive many normally thermodynamically unfavorable reactions [more on this later].

Nucleotides can be bonded into long polymers at the phosphate group. Importantly, the tri- and di-phosphate nucleotides can carry the energy needed to be polymerized into polymers.

These long polymers are the basis of information storage in living systems. Different sequences of the polymerized nucleotides encode different sets of information. Sequence contains information like a bar code.

DNA is the source of genetic information; one DNA per cell. Called deoxyribonucleic acid (deoxyribose sugar). In humans, the sequence is ~3 billion nucleotides long.

Four kinds of nucleotides possible at each junction.

Information in biology has error-protection built in because DNA exists in complementary strands. Hydrogen bonding ensures that a adenine always hydrogen-bonds to thymine (two h-bonds) and guanine to cytosine (three h-bonds).

RNA is used to make copies of DNA for processing by cellular chemistry. Called ribonucleic acid, since the sugar is ribose.

Amino acids and proteins

ROLE: Proteins are arguably the most important molecules in cells: tremendously versatile. Responsible for structure, catalysis, signaling, transport, motion, detection (receptor), many other processes.

Made of long strings of amino acids joined together in polymer fashion, typically 50-500 long.

Twenty natural kinds of amino acids of varying chemistry. Most important distinction is hydrophobic versus hydrophilic.

All amino acids have an NCC structure with an amine group and a carbonyl group.

A peptide bond is formed when two amino acids are joined together.

Proteins to collapse into a dense, “folded” structure. The structure is specific to the sequence, and different proteins fold to different structures. Driving this process is the desire by the protein to shield its hydrophobic amino acids from water by burial in the protein core.

We will discuss proteins in much greater depth later on.

Summary of macromolecules

DNA, RNA, sugars, lipids, and proteins are all macromolecules stitched together from a basic set of fundamental parts

Most common reaction to form macromolecules is a **dehydrolysis** reaction

Macromolecules can come together to form large functional complexes

Macromolecules constitute most of the non-water mass inside cells

Basic dogma of biology

DNA contains instructions (recipes) for making many different kinds of proteins

The instructions for a protein are first copied by making an RNA strand with the same sequence

The RNA then is used as instructions in protein-making molecular machines (called ribosomes)

Proteins then accomplish many critical tasks inside the cells, including making other proteins, RNA, and copies of DNA (during cell division)

The unit operations: Components, organelles, compartments

Cells have specialized structures and compartments responsible for different processes

Compartments must be separated from one another → membranes, typically very, very thin

Membranes are not simply containers, they contain many functional molecules: proteins, carbohydrates, anchors for structural units that connect to other membranes or parts of the cell

Membranes are typically made of phospholipid bilayers

Many membranes in the cell constantly change. A common mechanism for sending components from one part of the cell to another is to pinch off part of the membrane into a small vesicle that then joins with another membrane, releasing the components into the other compartment

Basic structure

Plasma membrane – separates inside from outside of cell

Cell wall – often present in prokaryotes, plants, fungi → an extra, tough layer outside of the plasma membrane that provides structural rigidity

The inside is called the **cytoplasm,** except for the nucleus

Everything in the cytoplasm that is not inside a special membrane-enclosed sac (e.g., in an organelle) is called the **cytosol**

Outside is the **extracellular matrix**, a dense region connecting cells in tissues made of strong protein fibers and a sugar (polysaccharide) gel

The inside of a cell contains many structural fibers and "beams" that hold the cell together, cause it to change shape, facilitate cell division, and allow the cell to move → called the **cytoskeleton**

The cytoskeleton is like the frame structure of a house, only in cells it is constantly changing → fibers are continuously forming and falling apart to support the cells needs

These fibers and struts also serve as highways along which motor proteins can shuttle vesicles filled with functional molecules very fast from one side of the cell or compartment to another

Nucleus

Eukaryotes have these – contains the all-important genetic material, DNA

Here, instructions for making proteins are copied into RNA transcripts

Nuclear envelope is a double-layer membrane surrounding the nucleus; this extra-special care is used to separate the genetic information from the rest of the cell activities

Prokaryotes lack a nucleus. Their DNA simply exists inside the single cytoplasmic compartment inside the plasma membrane

Endoplasmic reticulum (ER)

Membrane-enclosed, maze-like structure

Location of the synthesis of lipids and many proteins

The membrane of the ER forms the outer part of the nuclear envelope, such that the ER is always in close contact with the nucleus. This is important because the ER gets its synthesis instructions from the genetic information

Many **ribosomes** are attached to the membranes of the ER. These are large, molecular machines that read RNA recipes and spit out proteins. So-called "free" ribosomes can also roam about the cytosol.

Golgi apparatus

Flattened membrane-enclosed sacs next to the ER

Where synthesized components from the ER are finally processed and chemically modified

Chemical modification serves to **sort** these components for selective transport to other parts of the cell

Somes (compartments)

X-somes are typically special membrane-enclosed sacs in which special processing can be isolated from the rest of the cell

These can grow, shrink, or divide as needed by the cell

Lysosomes are where digestion occurs, breaking down big molecules and releasing small components for their later use

Peroxisomes are compartments where chemical reactions that require the generation and degradation of peroxides are performed

Endosomes are holding stages for material captured from outside the cell, places where small compartments of material are deposited from places where the cell wall buds inwards

In these cases, reactions or materials that would normally be dangerous to the cell can be isolated from the important functional components

Mitochondria

Look like small sausages

Enclosed by two membranes; the inner one folds back and forth inside

The source of the huge energy needs for the cell → produce ATP from food molecules (e.g., sugars), consume oxygen, and release CO2

Have their own DNA and divide, replicate separately from the rest of the cell

Evidence that early prokaryotes "swallowed" small bacterial cells that eventually became mitochondria → symbiotic relationship

Chloroplasts

In plant cells, capture sunlight to build energy-rich sugars

Sugars then exported to mitochondria to provide energy

Like mitochondria, contain their own DNA and reproduce on their own → suggests these two used to be early eukaryotes that swallowed small photosynthetic bacteria

How do we know what we know about cells?

Model organisms

- simple bacteria and basic prokaryote – E. coli, lives in the gut, easily cultured
- brewer's yeast, model fungus and basic eukaryote – S. cerevesai
- model plant – Arabidopsis thaliana, grows fast and easily indoors
- model animals –
    - Drosophila melanogaster (fruit fly) – many generations grow fast
    - C. elegans – very precise development (Exactly 959 cells)
    - mouse – model mammal, many similar systems to humans