What is Biochemistry?
What is Biochemistry?

Chemistry of biological molecules
Study of the chemistry of life

Structure of biological molecules
Specificity and molecular interactions
Synthesis and degradation of molecules
Energy transduction and storage
Control of molecular activities
Information, storage and retrieval
What are the properties of a living organism?

Chemical complexity and organization
   (thousands of different molecules)

Extract, transform and use energy from environment
   (we need chemical nutrients, plants need sunlight)
   (need energy to do mechanical, chemical, osmotic work)

Self-replicate and self-assemble
   (keep the population alive)

Sense and respond to environmental changes

Each component has a specific function
   (lungs vs. heart)
   (nucleus of cell vs. membrane)

Evolutionary change
   (changes made to survive)

***Organisms a lot alike at cellular and chemical level
Cellular foundations

Chemical foundations

Physical foundations

Genetic foundations

Evolutionary foundations
Cellular Foundation

Cells
Structural and functional units of living organisms

Nucleus (eukaryotes) or nucleoid (bacteria)
Contains genetic material—DNA and associated proteins. Nucleus is membrane-bounded.

Plasma membrane
Tough, flexible lipid bilayer. Selectively permeable to polar substances. Includes membrane proteins that function in transport, in signal reception, and as enzymes.

Cytoplasm
Aqueous cell contents and suspended particles and organelles.
Chemical foundations - Macromolecules

Made of simple monomeric units

Besides water, major macromolecules in cell are:

Proteins  long polymers of amino acids
catalytic enzymes, structural, signal receptors, transporters
size = M.W. 5000 - 1,000,000

Nucleic Acids  polymers of nucleotides to make DNA or RNA
store/transmit genetic information
size = M.W. up to 1,000,000,000
monomers act as energy source - ATP!!

Polysaccharides  polymers of simple sugars
energy-yielding fuel stores
extracellular structural elements
size = up to 1,000,000 (starch)

Lipids  greasy hydrocarbons
structural components of membranes, energy-rich
fuel stores, pigments, intracellular signals
size = M.W. 750 - 1500 (NOT MACRO)

CARBON CARBON EVERYWHERE!!!!
Monomers of macromolecules

- **Amino acids**
  - Proteins
  - Peptide hormones
  - Neurotransmitters
  - Toxic alkaloids

- **Adenine**
  - Nucleic acids
  - ATP
  - Coenzymes
  - Neurotransmitters

- **Palmitic acid**
  - Membrane lipids
  - Fats
  - Waxes

- **Glucose**
  - Cellulose
  - Starch
  - Fructose
  - Mannose
  - Sucrose
  - Lactose
Physical foundations

Potential energy
- Nutrients in environment (complex molecules such as sugars, fats)
- Sunlight

Energy transductions accomplish work

Chemical transformations within cells
- Cellular work:
  - chemical synthesis
  - mechanical work
  - osmotic and electrical gradients
  - light production
  - genetic information transfer

Heat

Increased randomness (entropy) in the surroundings

Metabolism produces compounds simpler than the initial fuel molecules: $\text{CO}_2$, $\text{NH}_3$, $\text{H}_2\text{O}$, $\text{HPO}_4^{2-}$

Decreased randomness (entropy) in the system

Simple compounds polymerize to form information-rich macromolecules: DNA, RNA, proteins
Metabolism

Metabolism = Anabolism + Catabolism

ATP is the carrier of metabolic energy, linking catabolism to anabolism.
ATP - adenosine triphosphate
Physical foundations
Energy Coupling in Chemical Reactions

(b) Chemical example

\[
\text{Reaction 1:}
\quad \text{Glucose} + P_i \rightarrow \text{glucose 6-phosphate}
\]

\[
\text{Reaction 2:}
\quad \text{ATP} \rightarrow \text{ADP} + P_i
\]

\[
\Delta G_1
\]

\[
\text{Reaction 3:}
\quad \text{Glucose} + \text{ATP} \rightarrow \text{glucose 6-phosphate} + \text{ADP}
\]

\[
\Delta G_3 = \Delta G_1 + \Delta G_2
\]

Reaction coordinate

\[\text{enzyme}\]

Glucose + ATP \rightarrow \text{Glucose 6-phosphate} + \text{ADP}
Thermodynamics

Life obeys the laws of thermodynamics

System vs. surroundings
Normal cell activities demand energy

1st Law of Thermodynamics
• energy is conserved (cannot be created or destroyed)

2nd Law of Thermodynamics
• spontaneous processes are characterized by conversion of order to disorder
Thermodynamics

Review:

**Enthalpy (H)**
reflects numbers and kinds of bonds

**Entropy (S)**
Randomness (measure of disorder) of a system
**Free Energy**

Spontaneity of process cannot be predicted by entropy alone

True criteria for spontaneity = Gibbs free energy \((G)\)

\[
\Delta G = \Delta H - T\Delta S \quad \text{(constant pressure and temp)}
\]

Spontaneous --> \(-\Delta G\) (exergonic)
Nonspontaneous --> \(+\Delta G\) (endergonic)

---

Variation of reaction spontaneity (sign of \(\Delta G\)) with the signs of \(\Delta H\) and \(\Delta S\)

<table>
<thead>
<tr>
<th>(\Delta H)</th>
<th>(\Delta S)</th>
<th>(\Delta G)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(-)</td>
<td>(+)</td>
<td>Spontaneous at all temperatures</td>
</tr>
<tr>
<td>(-)</td>
<td>(-)</td>
<td>Spontaneous at low temperatures</td>
</tr>
<tr>
<td>(+)</td>
<td>(+)</td>
<td>Spontaneous at high temperatures</td>
</tr>
<tr>
<td>(+)</td>
<td>(-)</td>
<td>Nonspontaneous at all temperatures</td>
</tr>
</tbody>
</table>
Free Energy and Equilibrium constants

\[ A + B + C \rightleftharpoons D + E + F \]

\[ \Delta G = RT \ln Q + \Delta G^\circ \]

\[ Q = \frac{[D][E][F]}{[A][B][C]} \]

\[ \Delta G < 0 \text{ reaction goes to products} \]
\[ \Delta G > 0 \text{ reaction goes to reactants} \]
\[ \Delta G = 0 \text{ at equilibrium} \]

At equilibrium, \( \Delta G = 0 \), so

\[ 0 = RT \ln K + \Delta G^\circ \]

\[ \Delta G^\circ = -RT \ln K \]
Enzymes promote chemical reactions

Transition state has a free energy higher than either reactant or product
Cellular chemical reactions occur at a fast enough rate because of enzymes (proteins)
Enzymes lower the energy barrier between reactant and product
Enzymes promote chemical reactions

Enzyme-catalyzed reactions proceed at rates up to $10^{10}$ to $10^{14}$ times faster than uncatalyzed reactions.
Genetic foundations

Central Dogma of Biochemistry

informational molecules

DNA

Reverse Transcription

Transcription

RNA

Translation

Protein

functional molecules

DNA Replication
# Genetic information

## TABLE 1-4  Some Organisms Whose Genomes Have Been Completely Sequenced

<table>
<thead>
<tr>
<th>Organism</th>
<th>Genome size (millions of nucleotide pairs)</th>
<th>Biological interest</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td>0.8</td>
<td>Causes pneumonia</td>
</tr>
<tr>
<td><em>Treponema pallidum</em></td>
<td>1.1</td>
<td>Causes syphilis</td>
</tr>
<tr>
<td><em>Borrelia burgdorferi</em></td>
<td>1.3</td>
<td>Causes Lyme disease</td>
</tr>
<tr>
<td><em>Helicobacter pylori</em></td>
<td>1.7</td>
<td>Causes gastric ulcers</td>
</tr>
<tr>
<td><em>Methanococcus jannaschii</em></td>
<td>1.7</td>
<td>Grows at 85 °C!</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>1.8</td>
<td>Causes bacterial influenza</td>
</tr>
<tr>
<td><em>Methanobacterium thermoautotrophicum</em></td>
<td>1.8</td>
<td>Member of the Archaea</td>
</tr>
<tr>
<td><em>Archaeoglobus fulgidus</em></td>
<td>2.2</td>
<td>High-temperature methanogen</td>
</tr>
<tr>
<td><em>Synechocystis sp.</em></td>
<td>3.6</td>
<td>Cyanobacterium</td>
</tr>
<tr>
<td><em>Bacillus subtilis</em></td>
<td>4.2</td>
<td>Common soil bacterium</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>4.6</td>
<td>Some strains cause toxic shock syndrome</td>
</tr>
<tr>
<td><em>Saccharomyces cerevisiae</em></td>
<td>12.1</td>
<td>Unicellular eukaryote</td>
</tr>
<tr>
<td><em>Plasmodium falciparum</em></td>
<td>23</td>
<td>Causes human malaria</td>
</tr>
<tr>
<td><em>Caenorhabditis elegans</em></td>
<td>97.1</td>
<td>Multicellular roundworm</td>
</tr>
<tr>
<td><em>Anopheles gambiae</em></td>
<td>278</td>
<td>Malaria vector</td>
</tr>
<tr>
<td><em>Mus musculus domesticus</em></td>
<td>(2.5 \times 10^3)</td>
<td>Laboratory mouse</td>
</tr>
<tr>
<td><em>Homo sapiens</em></td>
<td>(2.9 \times 10^3)</td>
<td>Human</td>
</tr>
</tbody>
</table>
Linear DNA encodes proteins with complex 3D structures
Evolutionary foundations
Changes in genetic information - evolution

Time

Mutation 1

TGAGCTA

Mutation 2

TGAACTA

Mutation 3

TGAACTA

Mutation 4

TCAGCTA

Mutation 5

TTAACGA

Mutation 6

TCAGCTA

TCAGCTG

GGAAGCTA
Changes in genetic information - evolution

1. Gene duplication leads to a superfluous copy of gene 1


3. Mutations in many genes lead to evolution of a new species.

Homologous genes 1 and 1* are orthologs, encoding proteins of the same function in different species.

Homologous genes 1 and 2 are paralogs, related in sequence but encoding proteins of different function in the same species.


**Chemical evolution simulated in the lab**

Yields from Sparking a Mixture of CH₄, NH₃, H₂O, and H₂

<table>
<thead>
<tr>
<th>Compound</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formic acid</td>
<td>4.0</td>
</tr>
<tr>
<td>Glycine (Amino acid)</td>
<td>2.1</td>
</tr>
<tr>
<td>Glycolic acid</td>
<td>1.9</td>
</tr>
<tr>
<td>Alanine (Amino acid)</td>
<td>1.7</td>
</tr>
<tr>
<td>Lactic acid</td>
<td>1.6</td>
</tr>
<tr>
<td>β-alanine</td>
<td>0.76</td>
</tr>
<tr>
<td>Propionic acid</td>
<td>0.66</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>0.51</td>
</tr>
<tr>
<td>Iminodiacetic acid</td>
<td>0.37</td>
</tr>
<tr>
<td>α-Amino-n-butyric acid</td>
<td>0.34</td>
</tr>
<tr>
<td>α-Hydroxybutyric acid</td>
<td>0.34</td>
</tr>
<tr>
<td>Succinic acid</td>
<td>0.27</td>
</tr>
<tr>
<td>Sarcosine</td>
<td>0.25</td>
</tr>
<tr>
<td>Iminoaeticpropionic acid</td>
<td>0.13</td>
</tr>
<tr>
<td>N-Methylalanine</td>
<td>0.07</td>
</tr>
<tr>
<td>Glutamic acid (Amino acid)</td>
<td>0.051</td>
</tr>
<tr>
<td>N-Methylurea</td>
<td>0.051</td>
</tr>
<tr>
<td>Urea</td>
<td>0.034</td>
</tr>
<tr>
<td>Aspartic acid (Amino acid)</td>
<td>0.024</td>
</tr>
<tr>
<td>α-Aminoisobutyric acid</td>
<td>0.007</td>
</tr>
</tbody>
</table>

RNA WORLD

Creation of prebiotic soup, including nucleotides, from components of Earth’s primitive atmosphere

Production of short RNA molecules with random sequences

Selective replication of self-duplicating catalytic RNA segments

Synthesis of specific peptides, catalyzed by RNA

Increasing role of peptides in RNA replication; coevolution of RNA and protein

Primitive translation system develops, with RNA genome and RNA-protein catalysts

Genomic RNA begins to be copied into DNA

DNA genome, translated on RNA-protein complex (ribosome) with protein catalysts

Crick

Rich!!

Orgel

Watson

RNA tie club - 1955