CHEM-4301.001 Biochemistry

Tuesday, Thursday 11-12:15, CCH 118

Dr. Patrick Larkin
Office -CS 206
plarkin@falcon.tamucc.edu
ph. 825-3258

Office Hours: M 9-11am, T,R 12:30-1:30 pm, W 1-3 pm

Course Outline

I. Foundations of Biochemistry

Chapter 1	The molecular logic of Life
Chapter 2	Organisms, Tissues, Cells and Organelles
Chapter 3	Biomolecules; Composition, Structure and Reactivity
Chapter 4	The importance of Water

II. Protein Structure, Enzymes and Catalysis

Chapter 5	Amino Acids, Peptides and Proteins
Chapter 6	The Three-dimensional Structure of Proteins
Chapter 7	Protein Function
Chapter 8	Enzymes

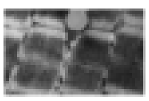
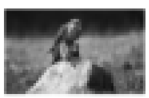
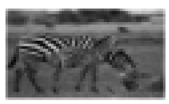
III. Membranes and Transport

Chapter 9	Carbohyrdates and Glycobiology
Chapter 11	Lipids
Chapter 12	Biological Membranes and Transport
Chapter 13	Biosignalling

IV. The Flow of Genetic Information

Ch. 10	Nucleotides and Nucleic Acids
Handout	Flow of genetic information

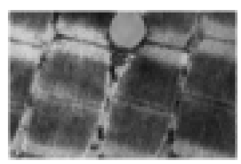
The molecular logic of Life

Why do we study biochemistry ?

- What distinguishes living matter from inanimate ?
- How do living organisms survive in their environment ?
- How do they produce copies of themselves ?

Living matter is structurally complicated and organized



plants, animals, fungi, etc.
↑
organs
↑
cells
↑
organelles
(mitochondria, chloroplasts, etc.)
↑
Macromolecules
(proteins, DNA, RNA, etc.)
↑
Biomolecules
(Amino acids, glucose, dNTP's)
↑
C, H, N, O, S, P

What distinguishes living matter from inanimate?

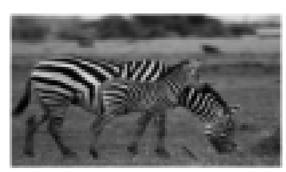
- Living matter extracts, transforms and utilizes energy from its environment

Inanimate matter decays to a state of equilibrium with its surroundings

---

What distinguishes living matter from inanimate?

Living matter : self-assembly and replication



Inanimate matter formed from elements combined under physical forces such as pressure and heat.

Biochemistry - processes of life in chemical terms

By isolating the components of living matter from cells and organelles

- Chromosomal DNA and proteins from the cell nucleus
- Enzymes involved in metabolic reactions
- Protein complexes involved in gene expression, membranes

By studying their structure and function

- Amino acid, nucleic acid sequence
- 3D structure of proteins, nucleic acids, membranes

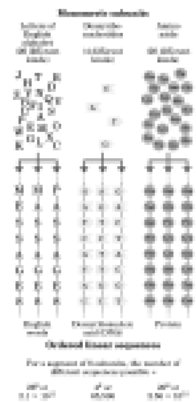
By elucidating the physical and chemical means by which such reactions and interactions take place

- Catalytic mechanisms (enzymes)
- Protein-protein, protein-nucleic acid interactions

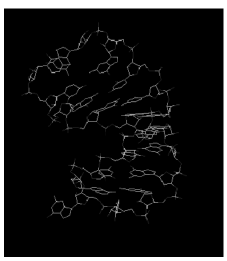
All macromolecules are constructed from a few "simple" compounds

- Amino Acids
- Nucleotides
- Monosaccharides

MW < ~ 500



The functional groups of monomers react with each other to form new covalent bonds



The <u>polymerization</u> of these <u>monomeric units</u> results in the creation of larger, macromolecular structures such as proteins, DNA, and cellulose

<u>Most monomeric subunits serve more than one function</u>

- Nucleotides: DNA, RNA, energy carriers (ATP)
- Amino Acids: Proteins, Hormones, neurotransmitters, pigments
- Carbohydrates: Energy stores, communication
- Lipids: Energy stores, membranes, vitamins, hormones

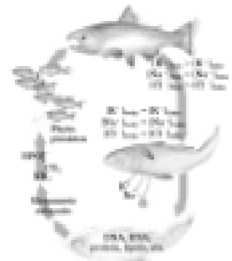
Principles of Molecular Logic

- All living organisms build molecules from same kinds of <u>monomeric units</u> (starting materials)
- The <u>structure</u> of a <u>macromolecule</u> determines its specific <u>biological function</u>
- Each genus and species is defined by its distinctive set of macromolecules

<u>Energy Production and Consumption</u>

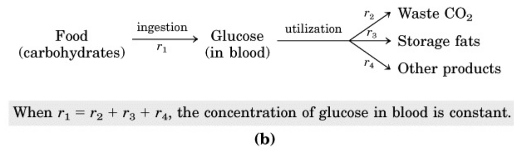
- Nature's tendency: systems decay to lowest energy state
- Energy requirements:
  - Storage and expession of genetic information
  - Biosynthesis (proteins, nucleic acids, starch)
  - Motion (muscle contraction)
  - Structural integrity (ion pumping)
  - Chemical reactions (neuron firing)

Organisms are never at equilibrium with their surroundings



- Mineral concentrations differ (Na^+, K^+, Cl^-, etc.)
- Amino acids, proteins, nucleic acids (DNA, RNA) virtually absent outside of cells
- Energy expenditure is required to maintain balance with surroundings

Biological composition reflects a <u>dynamic steady state</u>



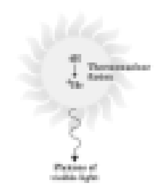
- Fats, carbohydrates, proteins, etc. continuously broken down to release energy and synthesize other compounds
- Constant flux of mass and energy through organism ("system")

Organisms transform energy and matter from their surroundings into cellular "parts" and chemical energy (ATP)

- Synthesis of DNA, RNA, proteins, lipids, membranes, etc.
- Accumulation and retention of salts, ions (K^+, H^+), etc. against a concentration gradient.
- Contraction of muscle, operation of cytoskeleton to move organisms, and contents within cells.

Biochemistry studies how energy is extracted, converted and consumed

2 General Strategies



- Organism extracts energy from sunlight (photosynthesis)
- Organism takes up chemical energy ("food") and extracts energy via oxidation (removal of electrons)

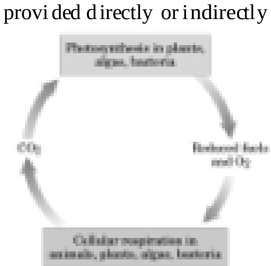
Living organisms maintain their complex, orderly structures using energy from sunlight or chemical fuels

Cells have evolved highly efficient mechanisms for capturing energy from sunlight or fuel molecules (food)

Photosynthesis: energy of sunlight is used to drive electrons from "fuel" molecules (H_2O, H_2S) to "acceptor" molecules (CO_2), with the concomittant synthesis of Adenosine Triphosphate (ATP), a short term store of chemical energy used in an abundant number biochemical reactions.

Oxidation: electrons are removed ("oxidized") from fuel molecules such as fats, carbohydrates, and proteins. The electrons flow in an energetically downward path to O_2, releasing energy used to drive the synthesis of ATP.

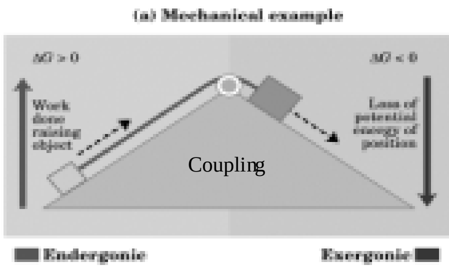
Most energy needs for biological organisms are ultimately provided directly or indirectly by sunlight



Plants use solar energy to drive electrons from H_2O to CO_2
(CO_2 → glucose → starch)

Non-photosynthetic cells obtain energy by removing electrons from food sources (starch → glucose → CO_2)

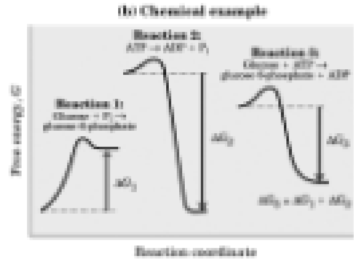
Energy coupling links reactions in Biology



Energy releasing chemical reactions are coupled to energy-requiring reactions through shared intermediates

---

Adenosine Triphosphate (ATP) is a high-energy compound which often serves as a source of a shared intermediate (P_i)



Catalyzing a direct reaction between glucose and ATP provides the energy to convert glucose to glucose-6-phosphate

---

The amount of energy required depends on the reaction and how far the system is from equilibrium (i.e. concentration of products and reactants)

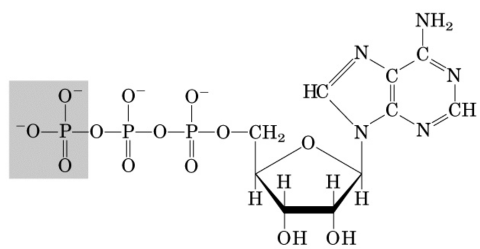
Glucose + P_i $\rightleftharpoons$ glucose-6-phosphate ΔG= +14 kJ/mole

ATP $\rightleftharpoons$ ADP + P_i ΔG= -32 kJ/mole

Glucose + ATP $\rightleftharpoons$ Glucose-6-phosphate +ADP ΔG= -18 kJ/mole

Spontaneous reactions release free energy (ΔG-, exergonic)
Non-spontaneous reactions require free energy (ΔG+, endergonic)

The Breakdown of ATP drives many cellular reactions



The removal of the terminal phosphoryl group is highly exergonic

---

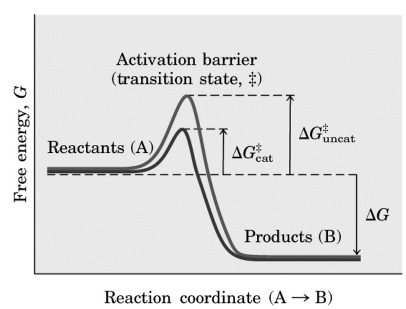
Enzymes promote sequences of chemical reactions

Reactions that proceed spontaneously (ΔG-) don't necessarily proceed rapidly

- Chemical reactants must be in proper position relative to each other
- Reactants must have sufficient kinetic energy to combine
- Concentration of reactants must be sufficient for interactions to occur

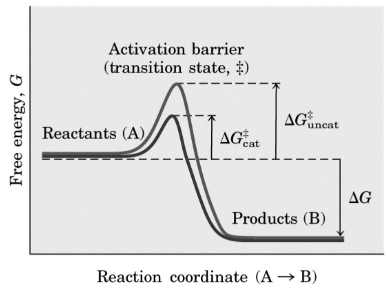
---

Paths from reactants to products often have an energy barrier



Enzymes lower the activation energy barrier

Converting A to B requires breaking existing bonds and forming new ones



Distortion of existing bonds creates a transition state that Has a higher free energy than either A or B

Enzymes lower the activation energy barrier by binding reactants in close proximity in the correct orientation

- Increases the <u>effective</u> concentration of reactants (proximity)
- Provides proper orientation for reaction to occur
- "bends" reactants until they mimic the transition state (highly reactive intermediate)

Combination of effects increases rate of reaction by a factor of 10^{14} compared to uncatalyzed reaction.

Chemical reactions in cells occur at measurable rates because of the presence of enzymes

- The concentration of many reactants is very low
- At physiological temperature (37° C) most reactants lack sufficient kinetic energy
- Orientation between reactants must be precise

Enzymes are <u>biocatalysts</u> - they greatly enhance the rate of <u>specific</u> chemical reactions, without becoming used up in the process

A particular enzyme catalyzes a <u>specific</u> reaction. Each reaction in a cell is catalyzed by a different enzyme

$A \xrightarrow{\text{enzyme 1}} B \xrightarrow{\text{enzyme 2}} C \xrightarrow{\text{enzyme 3}} D \xrightarrow{\text{enzyme 4}} E \xrightarrow{\text{enzyme 5}} F$

Chemical reactions in the cell are often organized into sequences of reaction pathways -

the product of one reaction becomes the reactant in the next

Pathways which convert smaller, precursor molecules to larger, more complex molecules are known as <u>anabolic</u> pathways

<u>Catabolic</u> pathways break down larger, more complex molecules into simpler ones (example : proteins to amino acids)

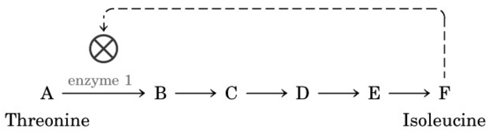
The network of anabolic and catabolic pathways is know as <u>metabolism</u>

ATP is the major connecting link (<u>shared intermediate)</u> linking anabolism and catabolism

ATP is <u>made</u> during catoblism and "<u>spent</u>" in anabolic pathways

ATP is the universal carrier of biological, chemical (metabolic) energy

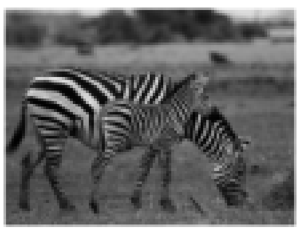
Metabolism is regulated to achieve balance and economy



- Key enzymes in each pathway are regulated so that precisely the amount of product required is made
- Often accomplished via "feedback" inhibition - high concentrations of final product can inhibit the catalytic activity of the key enzyme in the pathway.
- Cells may also regulate the amount of enzyme made

These self adjusting mechanisms allow cells to maintain themselves in a dynamic steady state, despite fluctuations in the environment (nutrient concentration, etc.)

Biological Information Transfer



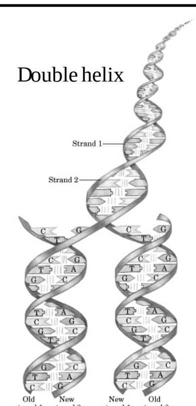
The continued existence of a species requires that its genetic information be maintained in a stable form, and be transmitted and expressed with very few errors

DNA (Deoxyribonucleic acid) is a linear polymer of nucleotides with the instructions for forming all other cellular components

...AGTTCGAGAGATTCCTGCGT…
…TCAAGCTCTCTAAGGACGCA..

DNA provides a template for the production of identical DNA molecules to be distributed to progeny

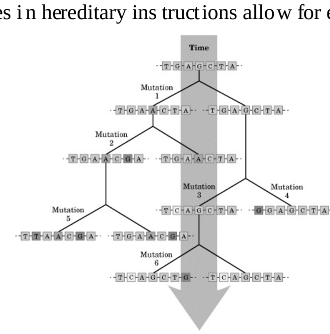
The structure of DNA allows for its repair and replication with near-perfect fidelity



DNA is a linear polymer of four different monomer subunits: A,T,G,C

Arranged in a precise linear sequence

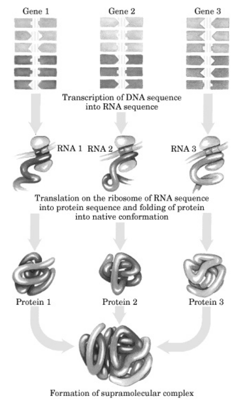
Changes in hereditary instructions allow for evolution



Mistakes in the DNA replication or repair process can introduce mutations

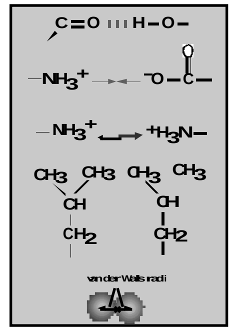
The linear, one-dimensional sequence in DNA encodes proteins with three-dimensional structure

DNA codes (through the intermediary RNA) for proteins, which fold into 3D structures, determined by their amino acid sequence

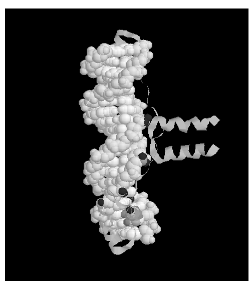


Weak, non-covalent interactions stabilize the three-dimensional structures of biomolecules

1. Hydrogen bonds
2. Ionic bonds
   - Attraction
   - Repulsion
3. Hydrophobic interactions
4. van der Waals interactions



The weak, transient nature of these non-covalent interactions allows for the flexibility found in proteins, DNA, and RNA



The multiple number of interactions ensures stability - very unlikely all would be broken at any one instant

Summary

- Living organisms differ from inanimate matter by their chemical complexity and organization
- All organisms are remarkably alike at the cellular level
- Living organisms are constructed from a few simple compounds (amino acids, nucleotides, lipids, carbohydrates)
- Energy coupling links unfavorable (energy requiring) to favorable (energy releasing) reactions
- Enzymes catalyze cellular reactions by binding to reactants and lowering activation energy barriers

Summary (continued)

- Enyme-catalyzed reactions are organized into highly regulated, pathways, conserving nutrients and energy
- Genetic information is contained in DNA molecules
- The unique double-helical structure of DNA allows for its efficient replication and repair
- The linear, 1D sequence of DNA encodes for RNA and proteins with 3D structure
- Noncovalent interactions dictate the 3D conformation of DNA, RNA and proteins, as well as supramolecular complexes (chromosomes, ribosomes, membranes, etc.)