Ch.3 Biomolecules

Basic Questions

- What kinds of molecules are present in cells?
- What are the structures of these molecules?
- What forces stabilize their structure?
- What are their chemical properties? How reactive are they?
- How do they interact?

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Concepts for review

- Bonding of carbon with itself & other elements
- Functional groups in organic and biological molecules
- 3D structure and stereochemistry
- Effect of structure on reactivity
- Common classes of chemical reactions which occur in living organisms

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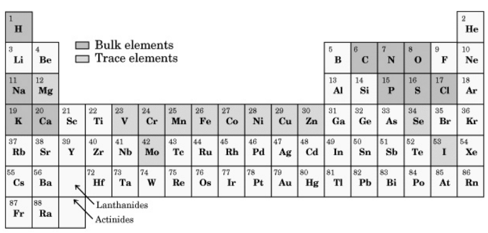
~ 30 out of 90 elements essential for life



- low atomic weight
- > 99% H,O,N & C

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Biomolecules (amino acids, sugars, lipids, etc.) constructed primarily from a few simple compounds

Element	Mol. Wt.	No. bonds
Carbon	12	1, 2, 3 or 4
Hydrogen	1	1
Nitrogen	14	3
Oxygen	16	2

The lightest elements capable of forming 1, 2, 3 or 4 bonds

In general, the lightest elements form the strongest bonds

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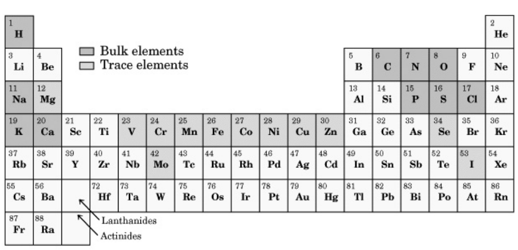

Trace elements (Mg, Fe, Cu, Zn, etc.) essential for function of certain enzymes

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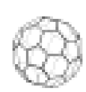
Biochemistry is organized around Carbon

- Carbon can form single, double, and triple bonds
- Carbon-carbon bonds are particularly stable
- No other element can match carbon for the diversity of structures it is able to form

- Linear chains CH_3-CH_2-CH_3
- Branched chains CH_3-CH_2-CH(OH)–CH_3
- Cyclic, or cage-like structures 

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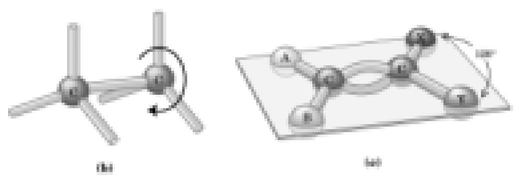
Free rotation about C-C single bonds



Double bonds are shorter, and allow little rotation about the bond axis

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Functional groups determine chemical properties

Most biomolecules are derivatives of <u>hydrocarbons</u>

- Carbon backbones bonded to H atoms
- Very stable
- Unreactive
- Replacement of H atoms with functional groups changes chemical properties

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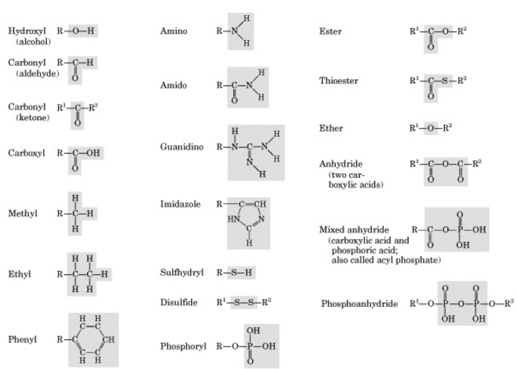

Reactions result from interactions between <u>functional groups</u>

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Functional groups

- replace H atoms in hydrocarbons
- alter electron distribution and geometry, making molecules more reactive
- often either <u>nucleophiles</u> or <u>electrophiles</u>
- Nucleophiles are rich in electrons
  - (O, N, S)
- Electrophiles are electron-deficient
  - (carbonyl carbon, amino groups, etc.)

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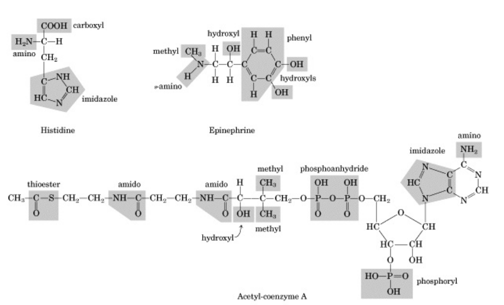
Many biomolecules contain two or more groups



Chemical characteristics (solubility, reactivity, etc.) determined by chemistry and 3-D position of <u>functional groups</u>

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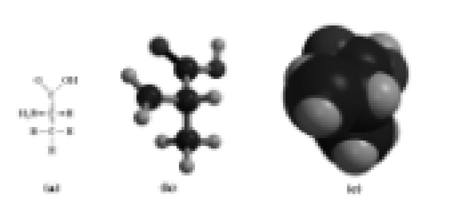
3-dimensional structure also critical to function



Perspective | Ball and Stick (bond angles and lengths) | Space filling (van der Waals radii)

Models help visualize molecular structures

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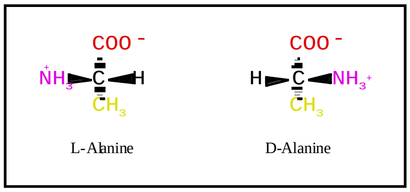
Biomolecules commonly exist as <u>Stereoisomers</u>



Bonding the same, spatial relationship different

In most cases, only one forms is biologically active (stereospecificity)

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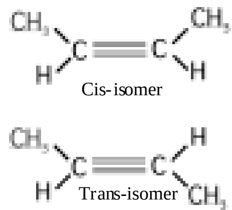
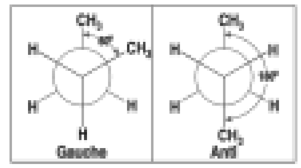
Stereochemistry : <u>configuration</u> and <u>conformation</u>





Configuration = spatial arrangement around <u>double bonds</u> and <u>chiral centers</u>

Conformation = spatial arrangement around <u>freely rotating groups</u>

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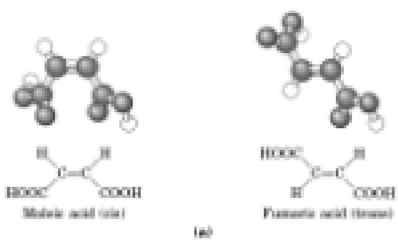
Configurational isomers can't be interchanged without breaking a covalent bond



Cis-Trans isomers: arrangement with respect to non-rotating double bond

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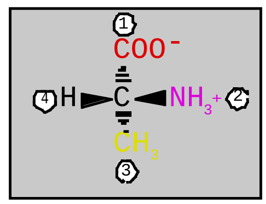
Carbons bonded to 4 <u>different</u> substituents are <u>asymmetric</u>



Asymmetric carbons are called <u>chiral centers</u>

Most biomolecules are asymmetric

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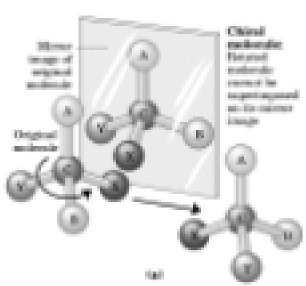
Chiral Centers may be arranged in 2 (configurations), yielding 2 <u>stereoisomers</u>



Some stereoisomers are mirror images of one another - "enantiomers" - which are non-superimposable

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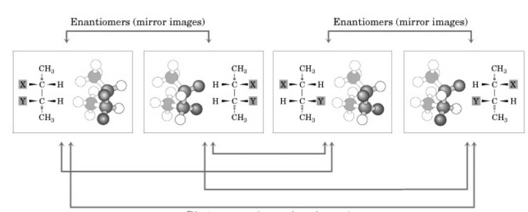
Enantiomers have nearly identical chemical properties



Stereoisomers not mirror images of each other = <u>diastereoisomers</u>

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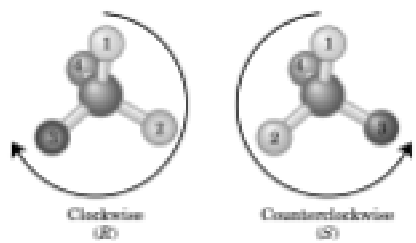
Biological interactions are stereospecific - stereochemical identification must be unambiguous



RS nomenclature useful for compounds with > 1 chiral center

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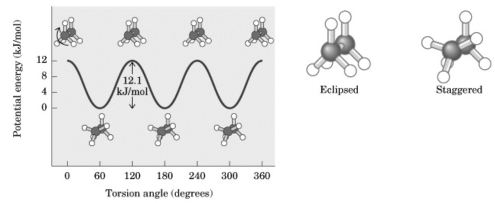
Conformation - arrangement of freely rotating groups



Many conformations are possible

Functional groups may limit the number of <u>stable</u> ones

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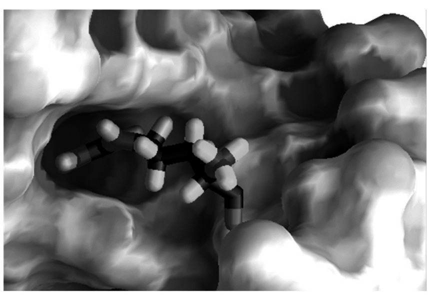
Interactions between biomolecules are <u>stereospecific</u>



Enzymes distinguish between sterioisomers - binding sites complementary to only <u>one</u> chiral form

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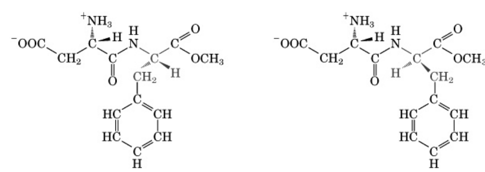
Example - receptors for taste



L-Aspartyl-L-phenylalanine methyl ester (aspartame) (sweet)

L-Aspartyl-D-phenylalanine methyl ester (bitter)

(b)

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<u>Chemical Reactivity</u>

Biochemical reactions not fundamentally different from other chemical reactions

Functional groups alter the electron distribution and geometry of neighboring atoms

Most cellular reactions are of only a few general types

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Bond strength depends on electronegativity - the relative affinity of an element for its electrons

table 3–2

The Electronegativities of Some Elements

Element	Electronegativity*
F	4.0
O	3.5
Cl	3.0
N	3.0
Br	2.8
S	2.5
C	2.5
I	2.5
Se	2.4
P	2.1
H	2.1
Cu	1.9
Fe	1.8
Co	1.8
Ni	1.8
Mo	1.8
Zn	1.6
Mn	1.5
Mg	1.2
Ca	1.0
Li	1.0
Na	0.9
K	0.8

*The higher the number, the more electronegative (the greater the electron affinity of) the element.

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Number of shared electrons also influences bond strength

table 3–3

Strengths of Bonds Common in Biomolecules

Type of bond	Bond dissociation energy* (kJ/mol)	Type of bond	Bond dissociation energy (kJ/mol)
Single bonds		Double bonds	
O—H	461	C=O	712
H—H	435	C=N	615
P—O	419	C=C	611
C—H	414	P=O	502
N—H	389		
C—O	352	Triple bonds	
C—C	348	C≡C	816
S—H	339	N≡N	930
C—N	293		
C—S	260		
N—O	222		
S—S	214		

*The greater the energy required for bond dissociation (breakage), the stronger the bond.

Bond energy - energy required to break a bond

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Difference between energy required to break a bond and energy released upon formation of new bond = enthalpy change (ΔH)

Net heat absorption = endothermic (ΔH+)
Net heat loss = exothermic (ΔH-)

Enthalpy, Temperature (T) and Entropy (S) determine free energy change

$$\Delta G = \Delta H - T \bullet (\Delta S)$$

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Biochemical transformations

5 general types:

(1) Oxidation-Reduction

(2) Cleavage/formation of Carbon-Carbon bonds

(3) Internal rearrangements

(4) Group transfers

(5) Condensations reactions (monomers to polymers)

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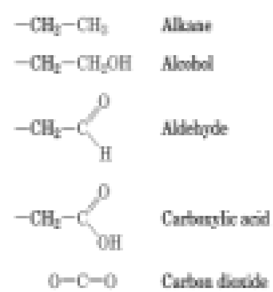
Oxidation states of Carbon in biomolecules



Going from lower to higher oxidation state involves loss of electrons - generally exergonic (energy-releasing)

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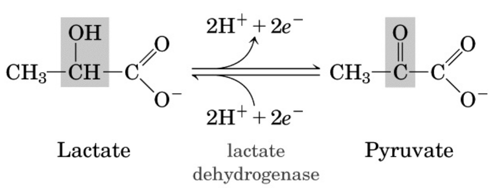
(1) Oxidation - Reduction Reactions

Every oxidation must be accompanied by a reduction



Reduction reactions transfer electrons to e⁻ acceptors (finally to $O_2 \rightarrow H_2O$)

In many oxidation-reduction reactions 2 e⁻'s and 2 H⁺'s lost (Dehydrogenation)

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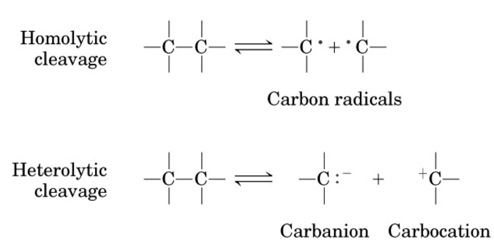
(2) Cleavage/Formation of Carbon-Carbon bonds



- Breakage of covalent bonds
  - Homolytic cleavage - carbon radicals (rare)
  - Heterolytic cleavage - anions and cations

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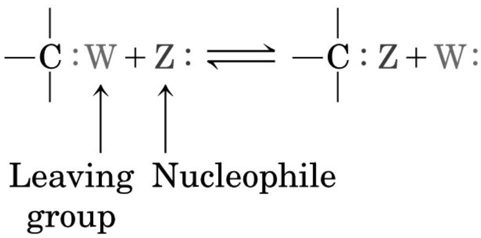
Nucleophilic substitution



Second e^--rich group replaces the departing carbanion

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Many biochemical reactions involve interactions between nucleophiles and electrophiles

Nucleophiles: functional groups with Oxygen, Nitrogen or Sulfur

Electrophiles: H^+, Metal ions

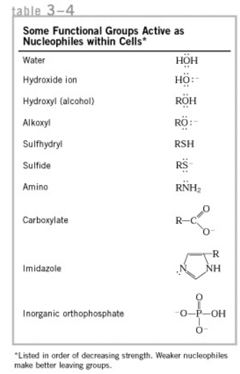
table 3–4

Some Functional Groups Active as Nucleophiles within Cells*

Water	HÖH
Hydroxide ion	HÖ:⁻
Hydroxyl (alcohol)	RÖH
Alkoxyl	RÖ:⁻
Sulfhydryl	RSH
Sulfide	RS⁻
Amino	RNH$_2$
Carboxylate	R–COO⁻
Imidazole	
Inorganic orthophosphate	⁻O–P(O)(O⁻)–OH

*Listed in order of decreasing strength. Weaker nucleophiles make better leaving groups.

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(3) Internal Rearrangement Reactions

Redistribution of e^-'s results in :

- Isomerization
- transposition of double bonds
- cis-trans rearrangements of double bonds

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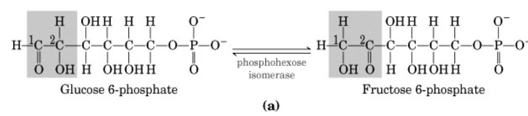
Isomerization example:

- C_1 reduced (aldehyde converted to alchohol)
- C_2 oxidized (alchohol coverted to ketone)



Transposition and cis-trans rearrangements of double bonds frequently occur during metabolism of fatty acids (lipids)

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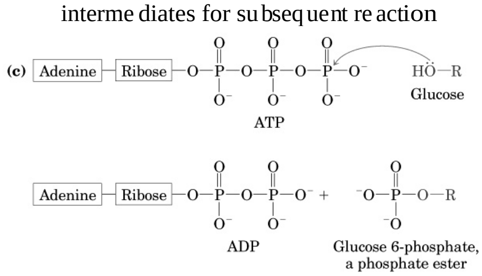
(4) Group transfer reactions

Common theme - "Activation" of metabolic intermediates for subsequent reaction



Attachment of a phosphoryl group makes hydroxyl (-OH) substituent a much better leaving group

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Phosphoryl groups not only activators of this type:

- Sulfur
  - (Thiols, Thioesters)
- Nucleotides
  - (ADP-glucose, CDP-diacylglycerol)
- tRNA (protein synthesis)
- Biotin (CO_2 activation)

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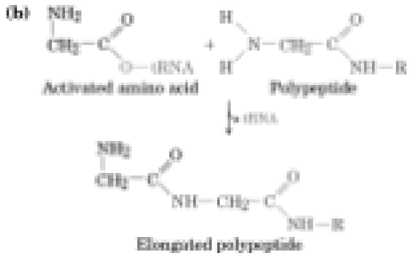
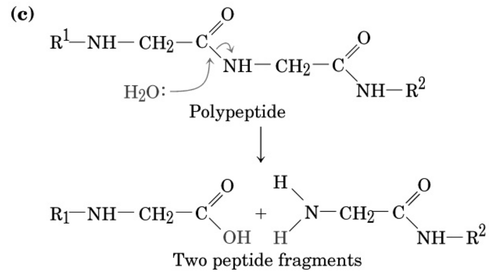
(5) Condensation reactions - Formation of Biopolymers



Monomeric subunits →proteins, nucleic acids, polysaccharides

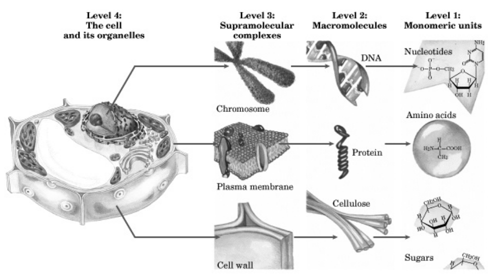
joined by nucleophillic displacement reactions 37

Macromolecules broken down by <u>hydrolysis</u> reactions - H_2O is the attacking nucleophile



Enzymatically catalyzed by <u>Hydrolases</u> 38

<u>Macromolecules and their Monomeric Subunits</u>



Synthesis of macromolecules is a major energy-consuming activity of cells 39

<u>Classes of macromolecules</u>

Proteins
- Polymers of amino acids
- Largest fraction of cell constituents after water
- Enzymes, structural elements, signal receptors, etc.

Nucleic Acids
- Polymers of nucleotides
- Store (DNA) and transmit (RNA) genetic information
- Structural roles in macromolecular complexes (rRNA, tRNA

Polysaccharides
- Polymers of monosaccharides (simple sugars - glucose)
- Energy-yielding fuel stores (glycogen, starch)
- Extracellular structural elements (cellulose)

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<u>Classes of macromolecules</u>

Lipids
- Oily hydrocarbon derivatives
- Structural elements of membranes (fatty acids, phospholipids)
- Energy-rich food stores (triacylglerols "fat")
- Pigments and intracelluar signals (retinal, phosphoinositol)

Macromolecules are synthesized through <u>Condensation Reactions</u>

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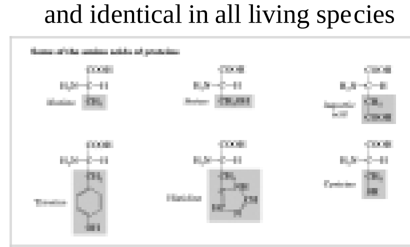
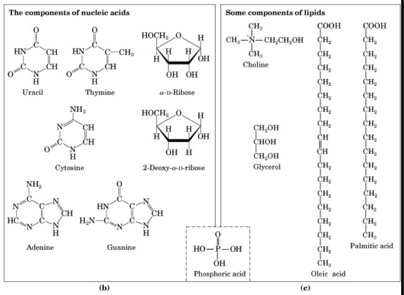
The monomeric subunits are few in number and identical in all living species



Amino Acids
- 20 total
- Amino group, Carboxyl group on alpha-Carbon
- Unique side chains (acidic, basic, hydrophobic, hydrophillic) 42

Nucleotides



3 Components

(1) Nitrogeneous base (Adenine, Guanine, Cytosine, Thymine (DNA), Uracil (RNA)
(2) 5-Carbon sugar: Deoxyribose (DNA) or Ribose (RNA)
(3) Phosphate group

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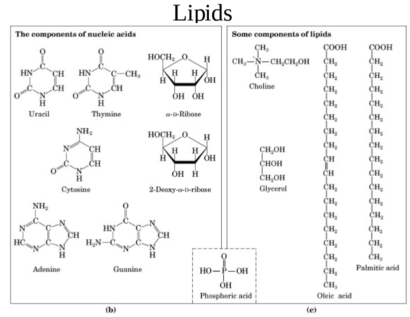
Lipids



- 1 or more long chain fatty acids
- Many contain 1 or more -OH groups (e.g. gylcerol)
- Some contain phosphate or nitrogeneous groups

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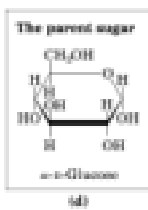
Polysaccharides



- Primarily glucose monomers
- Starch, glycogen, cellulose
- Fuel stores and structural elements
- Other polymers contain chemically modified monomers (chitin, peptidoglycans, etc.)

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~ 36 organic molecules form the bulk of biomolecules

- 20 amino acids
- 8 Nucleotides (4 deoxyribo-, 4 ribonucleotides)
  - 5 nitrogeneous bases/2 5-carbon sugars
- Glucose
- ~ 5 fatty acids
  - (stearic, palmitic, oleic, linoleic, linolenic)
- Glycerol
- Phosphoric Acid

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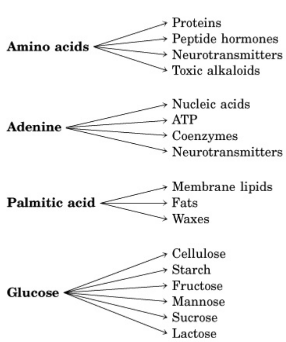
Each compound is a precursor of many other kinds of biomolecules



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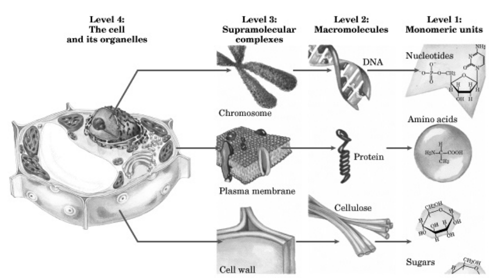
Macromolecular synthesis and free energy (G)



Subunit condensation creates order and requires energy

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Free energy change: $\Delta G = \Delta H - T \bullet (\Delta S)$

- H = enthalpy : number and kinds of bonds broken and re-formed
- S = entropy : randomness of system components
- T = absolute Temperature (K°)
  Reactions spontaneous if G < 0

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Macromolecular synthesis increases order - free energy must be supplied

Synthesis coupled to exergonic reactions:

- hydrolysis of ATP
- " tRNA-amino acid linkages
- " ADP-glucose linkages
- etc.

Net G change in coupled reactions is <0

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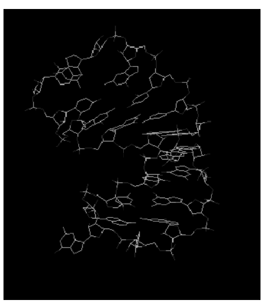
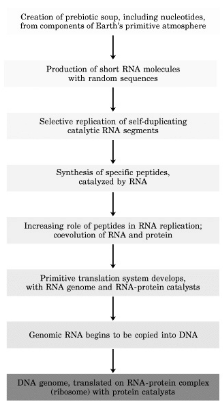
Pre-biotic evolution - "RNA World" Hypothesis





Summary

- Living matter - low atomic weight elements (H,O,N,C,S,P)
- Bonding versatility of Carbon - most important element in biochemistry
- Most biomolecules are derivatives of hydrocarbons with a variety of attached functional groups
- Biochemistry is three-dimensional - configuration and conformation play a crucial role in function

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- Most biomolecules are asymmetric - one chiral form found in nature
- Biochemical reactions fundamentally similar to other chemical reactions
  - Bond energy- size and electronegativity of elements
- 5 general types of chemical transformations
  - Oxidation-Reduction (e^- transfer)
  - Breakage and Formation of Carbon-Carbon bonds
  - Rearrangements (isomerization, double bonds)
  - Group transfers ("activation")
  - Condensation (macromolecule synthesis/breakdown)

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- Macromolecules are the major consituents of cells
  - Proteins, Nucleic acids, polysaccharides, lipids (membranes)
  - Composed of small monomeric sub units
    - Amino acids
    - Nucleotides
    - Monosaccharides
    - Fatty acids
- Synthesis creates order and requires energy
  - Couplingexergonic reactions tosynthesis
  - (ATP , tRNA hydrolysis, etc.)
- First macromolecules - RNA?

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