MACROMOLECULES

MOLECULES of LIVING THINGS:

4 major types of molecules: proteins, carbohydrate, lipids, nucleic acid

Macromolecules = giant **polymers** constructed of covalently linked monomers

monomers = building-blocks used repeatedly for larger structures

Three-dimensional structure of macromolecules is essential for proper function

- **sucralose**–sucrose with added chlorine atoms produces different shape;
  - resulted in sweeter taste by taste buds, not recognized by digestive enzymes so no energy is available to human
  - marketed as Splenda (1989)

chemical properties of molecules: reactivity, solubility, functional groups

FUNCTIONAL GROUPS important in building biological organic compounds:

- give specific properties to molecules

Hydroxyl group	-OH	alcohols
Aldehyde group	–CHO	sugars
Carbonyl group	-C=O	ketones
Carboxyl group	-COOH	acids (Carboxylic acids)
Amino group	$-NH_2$	amines (Basic)
Methyl	$-CH_3$	many examples
Phosphate	$-H_2PO_4^-$	ATP, phospholipids (Anions)
Sulfhydryl group	-SH	thiols

CHEMICAL STRUCTURE:

chemical formula gives elements that make up the molecule

structural formula indicates arrangement of elements in specific molecules

- **Isomers** = compounds with the same molecular formula but with different structures and hence different properties.
- **Structural isomers**= differ in covalent arrangement of their atoms
- **Geometric isomers** = same covalent partnerships but different spatial arrangements (***cis***, ***trans*** isomers), arise at inflexible double bonds
- **Optical isomers** (Enantiomers) = mirror images of each other (D, L) size of the molecule;
  - use D-sugars in polysaccharides and L-amino acids in proteins

3-D structure (shape) is related to function

Functional roles of macromolecules:

1. energy storage
2. structural support
3. catalysis
4. transport
5. protection and defense
6. regulation of metabolic activities
7. maintenance of homeostasis
8. means for movement, growth, and development
9. information storage (heredity)

MAKE AND BREAK MACROMOLECULES

1. **Dehydration Synthesis or Condensation reactions**
    - covalently connects monomers to synthesize a larger molecule
    - water is removed as a product
    - specific **enzymes** are used to speed up reaction rates
    - **anabolic** - metabolic synthesis of polymer from monomers
    - usually **endergonic**, requires input of energy (often ATP provides energy)
    - examples: protein synthesis, hormone synthesis, muscle building

2. **Hydrolysis**
    - adds water in order to split larger molecules to break bonds between monomers
    - specific **enzymes** are used to speed up reaction rates
    - **catabolic** – metabolic breakdown of large molecule until some small units
    - usually **exergonic** (releases energy stored in the bond)
    - examples: cellular respiration, digestion of starch, proteins, lipids

FOUR CLASSES OF BIOLOGICAL MACROMOLECULES

1. Protein
2. Carbohydrate
3. Lipid
4. Nucleic Acid

PROTEINS

- **8 functional types**:
    1) structural support(keratin, collagen)
    2) protection (pH buffer - (albumin)
    3) transport (hemoglobin)
    4) regulatory (hormone: insulin; neurotransmitters)
    5) recognition proteins (membrane receptors for hormones, neurotransmitters)
    6) movement (contractile proteins of muscle: actin & myosin)
    7) defense (antibodies, complement)
    8) catalytic (enzymes)
- vary in structure (size and composition), **shape is essential** for specific function
- consist of **amino acids building blocks** (monomers)
- contain the following **elements**: **C**, **H**, **N**, **O**, **S**
- **20** common amino acids (A.A.) are found in proteins, L series **optical isomers**

    Amphoteric – act simultaneously as an acid or base

    Become familiar with some of the names of amino acids, many end in **–ine.**

    Observe the groupings by charge, polar but uncharged hydrophilic A.A. and other A.A. with nonpolar hydrophobic side chains and special amino acids, especially with sulfhydryl group on cysteine

COMPONENTS OF **AMINO ACIDS**:

1. a central (α) carbon (attached to next 4 structures)
2. an amino group (NH_3^+)
3. an acid or carboxyl group (COO^-)
4. Hydrogen atom
5. a side chain = **R group** (unique group that determines the A.A.)

PEPTIDE BOND or peptide linkage

= **covalent** bond, formed by dehydration synthesis, between the carboxyl group of one amino acid and the amino group of another amino acid.

- Note the -**N-C-C-N-C-C- sequence** of atoms in the peptide linkage

- peptide bond is **relatively inflexible** and limits folding of the polypeptide chain
- partial negative charge on oxygen of carboxyl group and partial positive charge on hydrogen of amino group ; favors hydrogen bonding

Dipeptide = 2 amino acids bound together

Polypeptide = **PROTEIN** = many amino acids joined with unique conformation

- partial charges on carboxyl and amino groups facilitate Hydrogen bonding within the polypeptide structure contributing to its 3-dimensional shape

The **first amino acid** of a peptide is known as the **N terminus** while the last is part of the chain contains the carboxyl group of the **C terminus**

FOUR LEVELS OF PROTEIN STRUCTURE

--Study Figure 3.7, p. 45

1. PRIMARY STRUCTURE

= unique linear sequence of amino acids (N-C-C-N-C-C-N-C-C…)

- determined by nucleotide sequence in gene
- held by **peptide bonds**

** **all higher levels of structure** are derived from the primary structure

2. SECONDARY STRUCTURE

- repetitive coiling or folding of portions of protein structure

*__*alpha* helix__ – **Hydrogen bonding** between amino and carboxyl groups of primary chain about every 4th peptide bond

- R groups extend outward from peptide backbone
- example: fibrous proteins (**keratin** as in hair)

****beta pleated sheet*** - antiparallel chains are folded into accordion pleats,

- **Hydrogen bonds** form between amino group of one chain to a carboxyl group of the other chain
- example: core of globular proteins (**spider silk**- strong)

3. TERTIARY STRUCTURE

- unique binds and folds, the final 3 dimensional shape
- held by **interactions** between **R groups** (H-bonds, disulfide bridges, hydrophobic and hydrophilic attractions, Van der Waals forces)
- example : ly**sozyme**

4. QUATERNARY STRUCTURE

- final 3-D shape formed by interactions of 2 or more polypeptide chains

-example **hemoglobin**

****proper shape** is ESSENTIAL for protein's specific function

a **ligand** can bind to the exposed surface of the protein

ligands - include substances to be carried by a membrane carrier protein, reactants that fit the active site of the enzyme surface, hormones that fit the receptor protein in or on its target cell, foreign antigens that are attacked by our antibodies

STRUCTURAL CLASSIFICATION OF PROTEINS

Fibrous proteins

- Structure: strand-like,
  no tertiary level of structure (secondary structure highest),
- **insoluble** in water
- provide mechanical support and tensile strength
- **examples**. collagen, keratin
  contractile proteins: actin and myosin

Globular proteins

-Structure: compact, spherical shape, have higher levels of protein structure,
- **soluble** in water
- **functional protein ex.**: enzymes, transport, buffers, antibodies, hormones,
- **molecular chaperones** (**Chaperonins**) help proteins achieve their correct 3-D shape by :
  *ensuring quick and accurate folding of 3-D structure
  *preventing accidental, premature or incorrect folding
  *helping move proteins across cell membranes
  *promoting destruction of damaged and denatured proteins
  --- Alzeheimer's disease from misfolded proteins in brain

DENATURATION

= alteration of protein's native conformation or loss of its normal 3-D shape
- **destruction of secondary and higher level of structure** of the protein.
  - **breakage** of H bonds and disulfide bridges
  - primary structure and peptide bonds are **unaffected**
- **results in nonfunctional protein**
- **occurs** under extreme changes in temperature, pH and high salt concentrations

* **renaturation** may be possible if returned to normal conditions

AN INTRODUCTION TO ENZYMES

= biological **catalysts**
- speed up the rate of a chemical reaction
- usually protein in structure (except for **ribozymes** - see under RNA)
- **properties of enzyme**:(a chemical catalyst is described by properties 1, 2 & 3)
  1. effective in small amount
  2. reusable
  3. **speed up** rate of reaction by lowering energy of activation
     (increases rate by million to billion times)
  4. **highly specific** for particular substrate
     (unique to enzyme as biological catalyst)
     Enzyme and substrate fit like a **lock and key** at the **active site**
     Induced fit model for activation of the enzyme
     Proper shape is critical

CARBOHYDRATES (CHO)

- **functions**:
  1) primary source of energy (a chemical fuel not directly useable by cells)
  2) structural role (cellulose, chitin)
  3) food storage (glycogen, starch)
  4) building components for other structural molecules
     ex. glycoproteins – membrane identity marker
- **components**:

		ratio:
carbon	(**C**)	1
hydrogen	(**H**)	2
oxygen	(**O**)	1

- example: glucose - $C_6H_{12}O_6$
  *** major nutrient for all cells***
- **three types**:
  1. Monosaccharides (building blocks = monomer)
  2. Disaccharides
  3. Polysaccharides

  all made by **dehydration synthesis and broken (digested) by **hydrolysis**

MONOSACCHARIDES - simple sugars

- contain 3-7 carbon atoms
- building blocks of larger carbohydrates
- **D sugars** (optical isomer) found in living systems
- often designated by the number of carbon atoms they contain
  - ex. **PENTOSE** = 5Cs : ribose, deoxyribose
  - **HEXOSE** = 6Cs : glucose, fructose, galactose, mannose

Study the structure of **glucose
- straight chain and ring structure – ring is most common in nature (99%)
- note the difference between **alpha glucose** & **beta glucose**
  - --this position of the –OH group on the #1 carbon is important
  - -- human cells do not possess enzymes to use **β**-glucose

DISACCHARIDES = 2 monosacchrides

- **glycosidic linkage** - covalent bond between 2 monosaccharides by dehydration synthesis reaction
- ex. **sucrose** = table sugar (α-glucose + α-fructose), transported in plants
  - **lactose** = milk sugar (α-glucose + α-galactose)
  - **maltose** = malt sugar (α-glucose + β-glucose)
  - **cellobiose** = **β**-glucose + **β**-glucose (**β** linkage is indigestible by humans)

OLIGOSACCHARIDES = 2 to 20 monosaccharides

- proteins on outer surface of cells have oligosaccharides attached to the R group of certain amino acids or to lipids

POLYSACCHARIDES

- giant polymer of hundreds to hundreds of thousands of monosaccharides
- note the 1-4 glycosidic linkage in chain and 1-6 glycosidic **branching**
- do not taste sweet

- usually **insoluble** in water
- categories: energy storage polysaccharides, structural polysaccharides
- **Storage polysaccharides**:
  a. **starch** -storage polysaccharide in plant plastids (potato tuber, grains)
     - two forms : amylose and amylopectin
       * **amylose**-simplest form, unbranched polymer of **α-glucose**
       * **amylopectin** - branched polymer of **α-glucose**
  b. **glycogen** -storage polysaccharide in animals (muscles & liver)
     -more highly branched polymer of α-glucose
- **Structural polysaccharides**:
  a. **cellulose** -supporting structure of plant cell wall.
     - microfibrils = parallel bundle cellulose molecules, H-bonded)
     - **unbranched** polymer of **β-glucose** (indigestible by most animals)
  b. **chitin** - polymer of amino sugars (hardened by calcium carbonate)
     - in exoskeleton of arthropods and in cell wall of fungi
     - structural polysaccharide used surgical thread
     -
- amino sugars – in extracellular matrix to attach adjacent cells
  - galactosamine - component of cartilage
  - glucosamine – modified into component of chitin
    - food supplement to reduce pain of osteoarthritis

LIPIDS

- usually **insoluble** in water
- **hydrophobic,** lipids aggregate away from water,
- technically not polymers because not held by covalent bond
- structurally diverse group
- **elements** contained are **C**, **H**, **O**, **+** (**less oxygen than in carbohydrates**)
- helps maintain difference between what is in the cell and what is outside
- **functions**:
  1) **secondary source of energy** (neutral fat)
     Cells turn to fats **after** using available carbohydrates
  2) structural component of membranes (phospholipids)
  3) **emulsifiers** (soaps)
     Mechanically break fat mass into smaller fat globules
  4) accessory pigments that **capture light energy** (carotenoids)
  5) **thermal insulation** (fat)
  6) **electrical insulation** (myelin sheath of nerve cells)
  7) **water repellant** (wax, oil)
  8) vitamin , hormone structures (Vitamin D, E, estrogens, testosterone)

five groups of lipids:

1. **NEUTRAL FATS** **(TRIGLYCERIDES)**
   - **functions**: energy storage ("**survival fuel**"), insulation, protective cushion
   - do not disperse in water (need emulsification)
   - **structure**: **glycerol** + **3 fatty acids**

- glycerol is a 3 carbon sugar (alcohol)
- fatty acid is a long chain of hydrocarbons with carboxylic acid end
- **saturated fatty acids**, chain with only single carbon to carbon bonds, hydrogen atoms complete the valence requirement
  - no double bonds, no kinks
  - **solid** at room temperature
- **unsaturated fatty acids**, double bonds(mono-, polyunsaturated), kinks present
  - kinks prevent close packing of fatty acids
  - more common in plant oils
  - **liquid** at room temperature

* **diet** rich in saturated fatty acids is associated with cardiovascular disease
- **ester linkage** – covalent bond between the **alcohol group** of glycerol and the **carboxyl group** of fatty acid
- stored in human adipose tissue and seeds of plants
- **fat** – triglyceride, solid at room temperature
- **oil** – triglyceride, liquid at room temperature

2. PHOSPHOLIPIDS

- **function**: component of the cell membranes
- **structure**:
  - **1 glycerol**
  - **2 fatty acids**
  - **1 phosphate group** (inorganic polar group)
- **amphipathic** : hydrophobic tails (nonpolar)
  hydrophilic heads (polar)
- tend to form **micelles** or **bilayer** in water

3. SOAPS

- **function** as emulsifiers
  (breaks apart fat masses into smaller manageable globules)
- **structure**: salt of a fatty acid
  - polar head is hydrophilic, non-polar tail is hydrophobic
- example: bile salts which separate fatty masses in the GI tract

4. CAROTENOIDS

- light-absorbing pigment in plants and animals
- β-carotene is broken in human to form 2 vitamin A molecules, a precursor for our visual pigment rhodopsin
- give color to carrots, tomatoes, pumpkins, egg yolks, butter

5. STEROIDS

- varied functions
- **basic structure** = **4 joined rings** of carbon atoms
- **examples**:
  - **cholesterol** - precursor of other steroids, common in membranes
    - contributes to atherosclerosis
  - **hormones** - testosterone, estrogen, progesterone, aldosterone, cortisol
  - **vitamins** – vitamins A (rhodopsin – visual pigment in eye) ,D, E, K

6. **OTHER**

- **wax** = ester linkage between long saturated fatty acid and long sat. alcohol
  - highly non-polar
  - functions as **water repellant** and seals in moisture

NUCLEIC ACIDS

-**functions**:

1) storage and retrieval of **genetic information** for control of growth and reproduction (**DNA**, **RNA**)

2) **energy rich** compounds (**ATP**, **NADH**)

- **elements** contained are **C**, **H**, **N**, **O**, **P**
- structural building blocks are **nucleotides** (monomers)
- a **nucleotide** consists of:
  1. a **phosphate group**
  2. a 5 carbon (**pentose**) sugar (ribose or deoxyribose)
  3. a **nitrogen-containing base**

     Purine (two rings): Adenine (**A**), Guanine (**G**)

     Pyrimidine (one ring): Cytosine(**C**), Uracil (**U**- RNA only), Thymine (**T** – DNA only)

  ***As a way to **remember** these, note that the **pyrimidines** are **CUT**, meaning that pyrimidines are smaller having a **one ring structure**. The **purines** are **AG** which is also an abbreviation for the large agricultural enterprises and relates to the larger **2 ring structure** of these purines.
- also consider the structure of a **nucleoside** = base + sugar
- **phosphodiester linkage** between sugar and phosphates of nucleotides

1. **DNA** (Deoxyribonucleic Acid)

-contains the **genetic code** in its unique sequence of nucleotides - **genes** are located along the DNA molecule

- **functions of DNA**:
  1. in the control of DNA synthesis in cell reproduction
  2. in the control of non-reproductive cellular activity by directing protein synthesis at the ribosome through the synthesis of mRNA which carries the message to cytoplasm

     --- **DNA → RNA → protein**

-unique linear sequence of nucleotides codes for primary structure of polypeptide

- **structure** of DNA: polymer of thousands or millions of nucleotides

  A. sugar = **deoxyribose**

  B. **bases** include:

PURINES:	**PYRIMIDINES**:
Adenine (**A**)	Thymine (**T**)***
Guanine (**G**)	Cytosine (**C**)

  C. double **sugar-phosphate backbone**, bases inside (rungs of ladder)

  D. **complementary base pairing** (**A** = **T**, **G** ≡ **C**), **H-bonding**

  E. **helical** coiling of anti-parallel strands

  1953 - James **Watson** and Frances **Crick**

2. **RNA** (Ribonucleic Acid)

- **function**: relays genetic order for protein synthesis to cytoplasm and ribosomes
- **Structure** of RNA:
    - **A.** sugar = **ribose**
    - **B.** **bases** include: Adenine (**A**) Uracil (**U**) ***
      Guanine (**G**) Cytosine (**C**)
    - **C.** usually **single-stranded** although base pairing can occur
- **ribozymes** are RNA molecules that have catalytic function.
    - used to damage nucleic acid sequences in diseased cells

****Compare the structures of DNA and RNA -

3. **ATP** (Adenosine Triphosphate)

- **function** - energy currency of the cell , also called cellular energy
- only form of energy directly useable by most cells
- referred to as a **nucleoside triphosphate**
    - **nucleoside** = N-containing base + sugar
- **structure** of ATP :
    - **A.** sugar = **ribose**
    - **B.** base = **Adenine**
    - **C.** 3 **phosphate groups**
- break the high energy bonds between phosphates to provide energy for cellular work
  ATP -----> ADP + P_i + energy
- produced during **cellular respiration** which is the process that breaks down glucose (chemical fuel)

4. **Other important nucleotides**:
    - **GTP** = guanosine triphosphate
        - powers protein synthesis
    - **cAMP** = cyclic adenosine monophosphate
        - essential for hormone action
        - for transfer of information by nervous system

DNA REVEALS EVOLUTIONARY RELATIONSHIPS

- closely related living species have DNA base sequences that are more similar than distantly related species
- **chimpanzee** and **human** share **98%** of DNA sequences

PONDER THE ORIGIN OF LIFE

Observations:

- living things are composed of the same elements found in inanimate world
- the arrangement of these elements in biological systems is unique

Possible origin of life:

- from extraterrestrial sources – such as meteorites striking Earth
- chemical evolution on the planet

Miller and Urey experiment (1950's):

****classic experiment** that you should be able to recall

- **pre-biotic** primitive atmosphere of hydrogen gas, ammonia, methane gas, water vapor
- spark (lightning) stimulate gas mixture, cooling (condensation) to form "ocean"
- natural development of amino acids, purines and pyrmidines
- strongly suggested chemical evolution possibility

** newer findings add other chemicals to the primitive atmosphere, prebiotic "soup" could lead to many diverse molecules

SPONTANEOUS GENERATION OF LIFE

Spontaneous generation of life was based on the concepts that: (prior to 1700 A.D.)

A. large molecules obey the laws of physics and chemistry

B. life could have arisen from inanimate macromolecules

Then it could lead to the belief of **spontaneous generation of life**

-- as was often evident when the dead cooked meat in a few days became teaming with new life (maggots)!

Redi's experiment - 1668 – jars of meat and appearance of maggots

1. Jar with meat exposed to air and flies
2. Jar wrapped in fine cloth was exposed to air but not to flies
3. Jar sealed. No exposure to either air or flies

Result: Only maggots appeared in the first jar.

Pasteur's experiment finally disproved this idea of spontaneous generation of life

Bacteria were observable by Leeuwenhoek's microscope

Nutrient broth exposed to air became teaming with bacteria, putrifying the medium

Note the 2 swan-neck flasks of pure nutrient broth. Neck prevented air contamination of the flask contents.

When swan-neck was removed from one flask, this flask open to dust particles over time showed microbial growth

Swan-neck flask over time did **NOT** show microbial growth

* * **Conclusion**: **all life comes from pre-existing life**