BIOL 200 (Section 921)
Lecture # 2
June 20, 2006

Reading for lecture 2: Essential Cell Biology (ECB) 2nd edition. **Chap 2** pp 55-56, 58-64, 74-75; Chap 4, pp. 119-143. Good questions: 4-3, 4-10G, 4-11, 4-14-15, 4-17.

I. MACROMOLECULES [from lecture 1]

II. NUCLEOTIDES, NUCLEIC ACID, DNA [FROM LECTURE 1]

Main Points:

- Nucleotides are the monomers of nucleic acids; nucleic acids are polynucleotides joined by a condensation reaction that maintains a consistent structural polarity throughout the molecule.
- The information content of nucleic acids is provided by the sequence of nucleotides.
- DNA consists of two antiparallel strands with bases that interact via **hydrogen bond formation** and **hydrophobic interactions**.

Base name	nucleoside	nucleoside+phosphate =nucleotides
Adenine	adenosine	adenosine 5'mono/di/triphosphate, eg ATP
Guanine	guanosine	Guanosine 5'mono/di/triphosphate
Cytosine	cytidine	Cytidine 5'mono/di/triphosphate
Thymine	Thymidine	Thymidine 5'mono/di/triphosphate
Uracil	uridine	Uridine 5'mono/di/triphosphate

Secondary structure is determined by the pattern of base pairing, either interstrand (DNA) or intrastrand (RNA).

DNA is the genetic material, ie. DNA carries genetic information. Transformation experiments on page 173-174, Figs. 5-3; 5-4 (Griffith; Avery and co-workers, early 1940's).
(A) Live mutant (non-virulent) bacteria (*Streptococcus pneumoniae*) + heat killed virulent bacteria = virulent bacteria causing pneumonia
control : heat killed virulent bacteria alone do not cause pneumonia
Conclusion: Something in dead cells produces a heritable change in the live cells when they are mixed in a test tube together to produce permanent virulence.
(B) Chemical fractionation of cell-free extracts. Mix various chemical components with live non-virulent bacteria. The big surprise was that DNA and not protein that carried heritable information.
•The sequences of nucleic acids (both RNA and DNA) contain information that can be converted to the sequences of amino acids in proteins.

Structure of DNA
James Watson and Francis Crick (Fig 5-7, p. 175; Fig. 5-8 on page 176)

-based on x-ray diffraction work of Rosalind Franklin who showed double stranded helix
-also on Erwin Chargaff's finding that DNA base composition followed the rules A=T, G=C, and A+T
did not equal C+G (different for each genome).
Watson +Crick (1962 Nobel prize) DNA model features:
• DNA is composed of 2 chains forming a right-handed helix.
• The chains run antiparallel to one another (5' to 3' vs. 3' to 5')
• Sugar phosphate backbone (negatively charged) is hydrophilic, facing solution
• Bases projecting towards the center stacked one on top of the other, form a hydrophobic core
• Rules of base pairing: A pairs with T (or U in RNA); G pairs with C (Fig 5-6 p. 175)
• Purine always hydrogen bonds with pyrimidine (purines=A+G; pyrimidines=T(U)+C)
• Number of hydrogen bonds varies:
-The A::T bond has two hydrogen bonds
-The C:::G bond has three hydrogen bonds
Different numbers of hydrogen bonds between bases is KEY because the number of bonds between the bases influences how strands of DNA will interact with each other.

III. AMINO ACIDS, PEPTIDES AND PROTEINS

Learning Objectives

- Understand how amino acids are joined together via peptide bonds to form a polypeptide. Be able to write out the structure of the reactants and the product.
- Recognize the properties of each of the 20 amino acids, their three letter abbreviations, and how they are linked by peptide bonds.

Main points:

- Amino acids are bifunctional molecules that can combine to form polymers via peptide bond formation.
- The specific chemical properties of the amino acid residue side chains determine the chemical and biological properties of a polypeptide.

20 different amino acids grouped according to the properties of their side chains into 4 families: (Fig. 4-3 and Panel 2-5).
1. BASIC side chains are positively charged at cellular pH of 7.0
2. ACIDIC side chains are negatively charged at cellular pH of 7.0
3. Uncharged, POLAR side chains can interact with water
4. NON-POLAR side chains cannot interact with water. These are also called "hydrophobic" side chains.

Biochemistry of Polypeptide formation:

• The amino group of one amino acid reacts with the carboxyl group of another to form a peptide bond (=amide linkage) with the elimination of a water molecule.
• The polarity of the molecule is retained. The monomers are all joined together in the same orientation. The polypeptide chain has polarity.
• The product of the condensation reaction preserves the reactive group (carboxyl group) at the end of the molecule. This makes it possible for the peptide chain to join to yet another amino acid. The polypeptide contains a free amino group at one end and a free carboxyl group at the other. These ends of the polypeptide chain are referred to as the amino and carboxyl termini (ends) respectively.

IV. PROTEIN STRUCTURE AND FUNCTION

Learning Objectives

- Explain how the interactions and properties of amino acids affect the primary, secondary and tertiary structure of proteins.
- Understand how hydrogen bonding and hydrophobic interactions contribute to formation and stabilization of protein structures.
- Be aware of the functional and structural significance of domains in protein structure.
- Define the quaternary structure of proteins.

Main points

- The chemical properties of specific amino acid residue side chains determine the chemical properties of a polypeptide.
- The main non-covalent forces stabilizing protein structure are hydrogen bonds and hydrophobic interactions.
- Primary structure of proteins consists of the sequence of amino acid residues.
- Secondary structures are stabilized by intra-chain hydrogen bonds usually occurring over relatively short distances (e.g. the alpha helix and the beta pleated sheet)
- Tertiary structure is stabilized primarily by hydrogen bonding between more distantly separated resides within a peptide chain and by hydrophobic interactions of non-polar amino acid residues.
- Quaternary structure is the interaction of multiple polypeptide chains to form a protein composed of multiple subunits. These polypeptides interact by means of the same forces that stabilize tertiary structure.

Problem Solving: Shown in the table below are the sequences of selected amino acids from different types of human hemoglobin (abbreviated Hb). Some forms of hemoglobin are defective, while others are not. From what you know about protein structure, explain why Sickle Cell and Hammersmith Hbs are defective while delta Hb is not.

	Amino acid number
Type of Hemoglobin (Hb)	**3 4 5 6.. 9... 40 41 42 43**
Normal beta Hb	Leu Thr Pro Glu Ser Gln Arg Phe Glu
Sickle Cell Hb (defective)	Leu Thr Pro **Val** Ser Gln Arg Phe Glu
Hammersmith Hb (defective)	Leu Thr Pro Glu Ser Gln Arg **Ser** Glu
Normal delta Hb	Leu Thr Pro Glu **Thr** Gln Arg Phe Glu