MACQUARIE University

BMOL2201/6201
Biochemistry: An Introduction

Shoba Ranganathan

Applied Biosciences

T: 02 9850 6262; E: shoba.ranganathan@mq.edu.au

Important messages

Unit Information | Lecture Notes | Practicals and Tutorials | Assessment Outlines | Practice Quizzes

- iLearn.mq.edu.au has all the info you need for this unit.
- Course delivery:
  - 2 lectures each week (recorded)
  - 5 x 3 hr pracs alternating with 5 x 2 hr tutorial (or SGTA): Wed pm, Thu am and Thu pm.
  - Your class number is the same for Prac and SGTA as they run on alternate weeks, starting on the same day at the same time.
- Classes 1, 2 & 3 start with Labs from Academic Week 2 (on 3 & 4 March)
- Classes 4, 5, &6 start with SGTA from Academic Week 2 (on 3 & 4 March)
- **This week: pl. go to the LABS and complete your safety form after watching the safety video, as per the schedule below:**
  - **Wed pm: Class 1: 2 - 2.30 pm & Class 4: 2.30-3 pm**
  - **Thu am: Class 2: 10-10.30 am & Class 5: 10.30-11 am**
  - **Thu pm: Class 3: 2 - 2.30 pm & Class 6: 2.30-3 pm**

What is Biochemistry ?

- **The study of life: chemistry of biomolecules**
  - overlaps other disciplines, including cell and molecular biology, chemistry, genetics, immunology, microbiology, pharmacology, and physiology
- **Key questions**

1. What are the structures of biological molecules?
2. How do biological molecules interact with each other?
3. How does the cell synthesise and degrade biological molecules?
4. How is energy conserved and used by the cell?
5. What are the mechanisms for organizing biological molecules and coordinating their activities?
6. *How is genetic information stored and processed?*

BMOL2201/6201

- Building blocks of key biomolecules
  - nucleic acids,
  - proteins,
  - sugars and
  - lipids
- Biochemical signalling: how does the cell know what to do and when?
- Metabolism: making biomolecules from their building blocks as well as breaking them down
- How do we get energy?
- How are biomolecules organized into teams for coordinating their activities?

Eat healthy and avoid metabolic diseases such as obesity and diabetes!

Learning Objectives of this unit

1. Define the structural and metabolic differences between eukaryotic and prokaryotic cells with emphasis on biochemical energy metabolism, involving the synthesis and breakdown of important biomolecules.
   - ➢ identify the differences in cell structure;
   - ➢ relate the biochemical processes required for growth and energy; and
   - ➢ understand control mechanisms involved in the metabolism of important biomolecules.
2. Define chemical and biochemical principles and apply these to identify the interactions between different metabolic pathways and the biochemical signals.
   - ➢ the key concepts of compartmentation of biochemical processes;
   - ➢ the major biological systems involved in metabolism and energy production pathways in the living cell; and
   - ➢ understand how external changes are communicated to the interior of cells and organelles.

Learning Objectives of this unit - 2

3. Connect protein structure with function:
   - ➢ by defining the protein structure-function paradigm; and
   - ➢ evaluate the relationship between structure and function of proteins.
4. Identify, quantify and separate biomolecules using appropriate experimental methods:
   - ➢ utilize appropriate experimental methods to
     - ❖ characterise,
     - ❖ quantify and
     - ❖ separate different types of biomolecules.

Learning Objectives of this unit - 3

5. Track and measure rates of enzyme reactions and calculate kinetic parameters from the data generated:
   - ➢ understand the thermodynamic principles of enzyme catalysis;
   - ➢ identify the factors influencing the rate of an enzyme-catalysed reaction; and
   - ➢ measure rates of enzyme reactions to determine basic kinetic parameters of an enzyme.
6. Collect experimental data using biochemical techniques and sort, graph, analyze and present the experimental results in a biochemical context
   - ➢ utilize appropriate experimental methods to
     - ❖ characterise,
     - ❖ quantify and
     - ❖ separate different types of biomolecules.

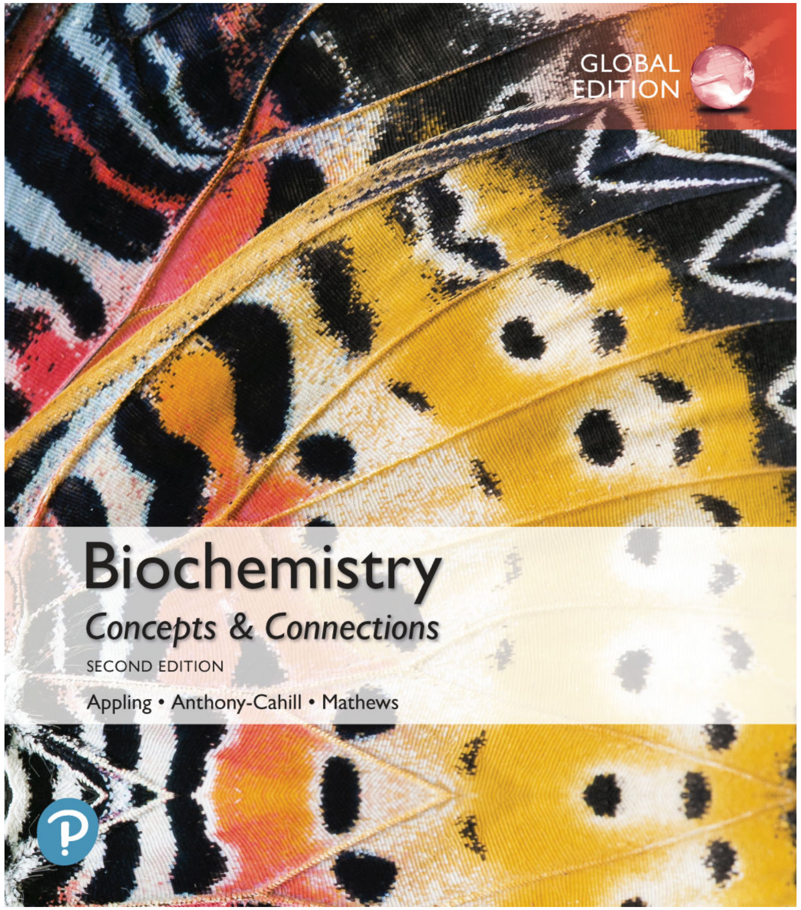
These learning objectives will be delivered *via* **lectures**, **practical exercises** (in the laboratory) and **tutorial questions** (in SGTA sessions).

Content delivery

- **iLearn:** ilearn.mq.edu.au
  - Login: MQ Student ID (8 numbers)
  - Password: your MQ password (OneID)
    - echo360 lecture video recordings
    - Announcements and Discussion Forum
    - Prac and Tutorial materials
    - Link to textbook and assessments.
- **Email:**
  - All emails will be sent to your ***MQ student email***
  - Please setup email forwarding to your favourite email address if you do not regularly look at this

Textbook

Biochemistry: Concepts and Connections



Second Edition, Global Edition

Dean R. Appling
Spencer J. Anthony-Cahill
Christopher K. Mathews
(AAM)

- Link to Textbook resources from iLearn
  - Uses **Mastering Chemistry** adaptive learning approach
  - **eText**
  - Revision exercises
  - Practice exercises
  - Assessment tests
  - Online tutorials.

Where is the e-text?

Student Links

Welcome to MasteringChemistry

Mastering Assignments

More...

Student Links

Welcome to MasteringChemistry

Mastering Assignments

Mastering Scores (for students)

User Settings

Pearson eText

MyLab and Mastering Course Home

Study Area

Pearson Announcements

^ Less

Brushing up your fundamentals

- Revision materials on Textbook Resources
- Check out the review materials at the Pearson Mastering site.

Tips on doing well

- You'll need to work steadily, because new material is based on earlier material.
- You will not be able to leave mastering the content until the last few weeks.
- **Direct correlation between lecture/tutorial attendance and student performance**.

Biochemistry and the Language of Chemistry

- The Science of Biochemistry
- The Elements and Molecules of Living Systems
- Distinguishing Characteristics of Living Systems
- The Unit of Biological Organization: The Cell
- Biochemistry and the Information Explosion

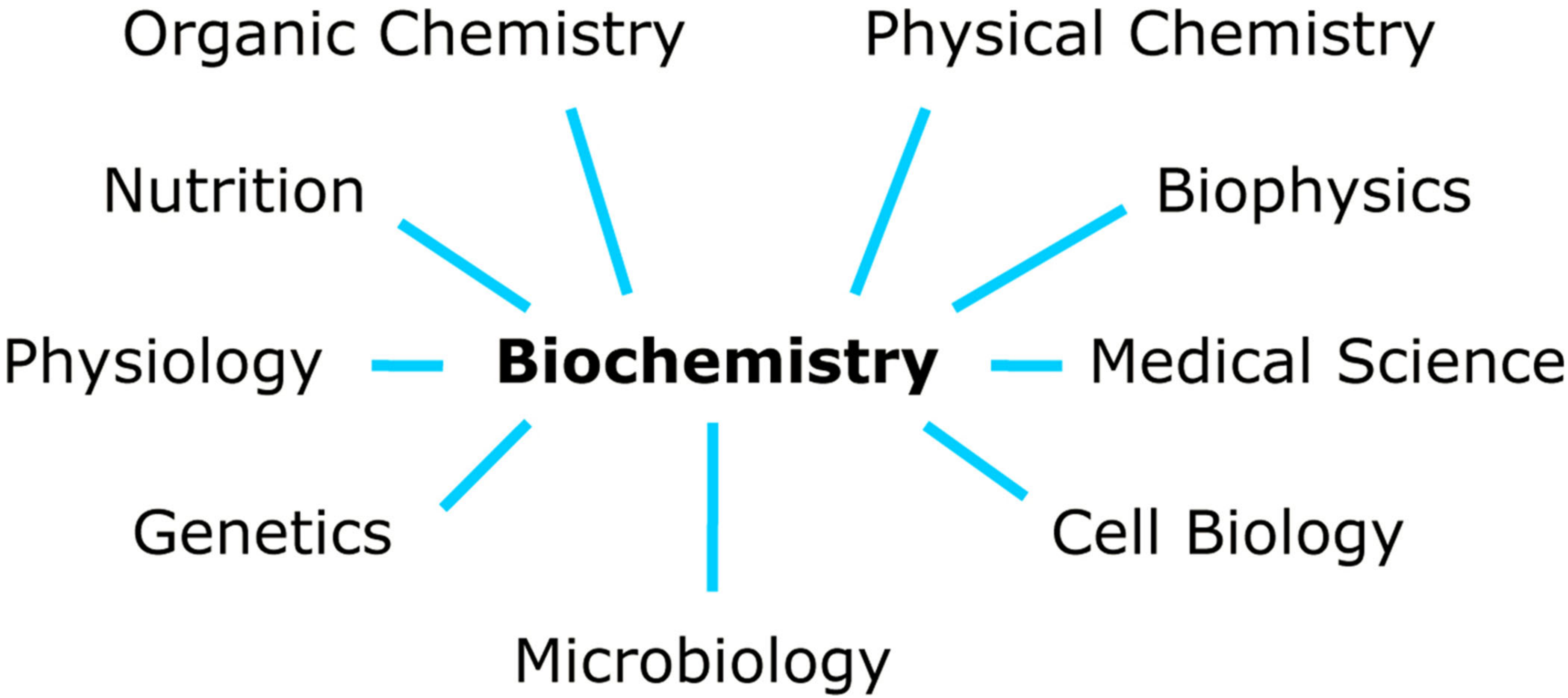
AAM: Chapter 1

The Science of Biochemistry

- **Fermentation**: an ancient application of biochemistry: ~5000 years ago

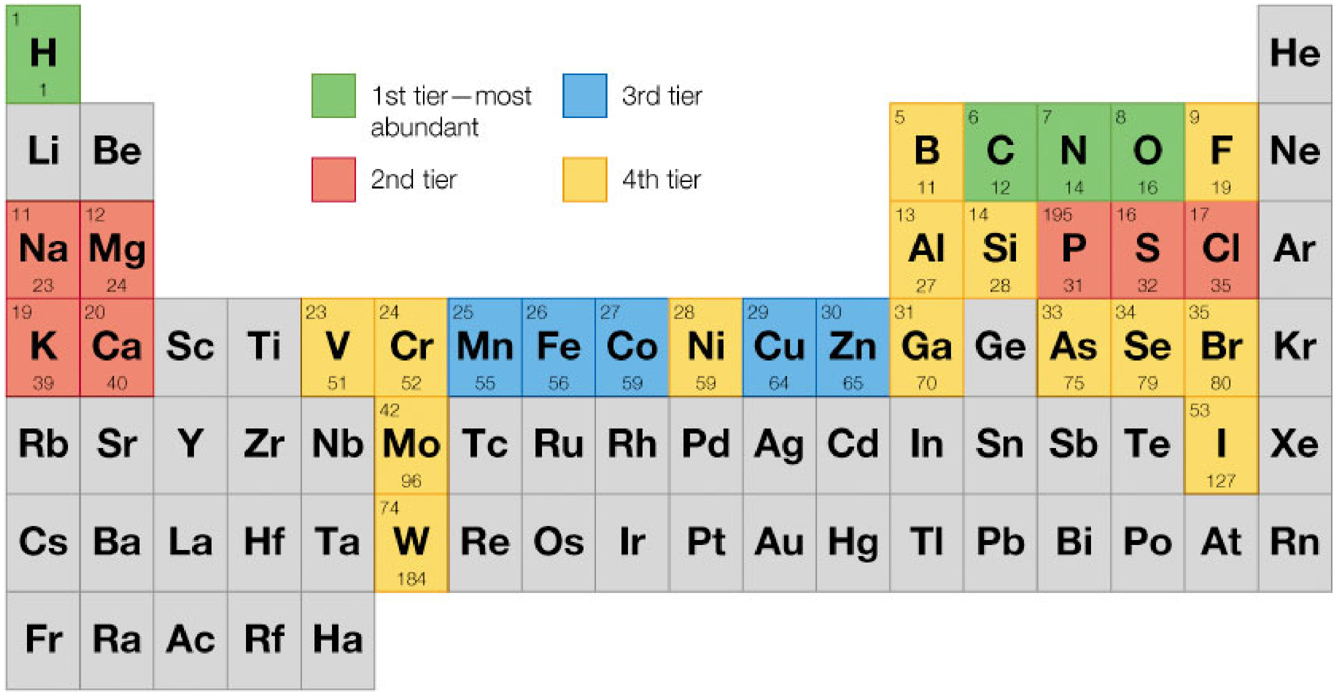
- 1897: Chemists Eduard and Hans Buchner found that **extracts from broken yeast cells** could carry out the entire process of fermentation of sugar into ethanol
- Biological catalysts, known as enzymes, promote biochemical reactions in living systems
- Synthesis of enzymes is controlled by genes
- Genes are the units of hereditary information, encoded in the structure of deoxyribonucleic acid (DNA)
- In 1953, James Watson and Francis Crick described the double-helical structure of DNA

Defining Biochemistry



The elements and molecules of living systems

- Living systems are primarily composed of **carbon** (C), **hydrogen** (H), **oxygen** (O), and **nitrogen** (N)
  - ➢ These are also the most abundant elements
- However, other elements including **sulfur** (S) and **phosphorus** (P) and certain ions, such as **Na^+, K^+, Mg^{2+}, Ca^{2+}, and Cl^-**, are essential for the existence of living systems on Earth as well
- **Trace amounts** of many other elements are also essential



Origin of Living Systems

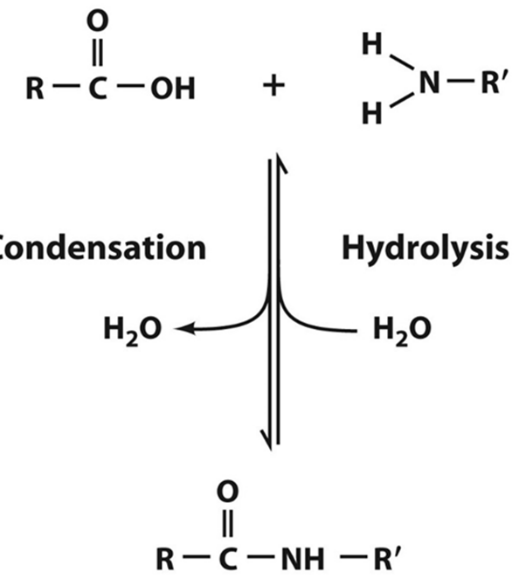
- Stanley Miller's 1953 experiments showed that certain building blocks of complex biomolecules, such as amino acids, could have been produced under early (abiotic) Earth conditions ("Primordial Soup")
- How cells, the basic unit of living systems, may have formed is still unknown
- However, many biochemists believe that ancient cells had already a ribonucleic acid (RNA)-based self-replication mechanism ("RNA World"): here RNA served as both genetic code (currently DNA) as well as enzymes (which are currently carried out by proteins)

Biological macromolecules

- Four major classes are essential for living systems based on cells:
  - A. **Nucleic acids** (DNA and RNA)
  - B. **Proteins**
  - C. **Polysaccharides** (polymeric carbohydrates)
  - D. **Lipids**
- Polymers of smaller organic molecule subunits
- Formed by condensation reactions (reverse reaction is hydrolysis): e.g. carboxylic acid and amine, forming an amide bond

Macromolecule	Monomer	Linkage
Nucleic acids	Nucleotide	Phosphodiester
Protein	Amino acid	Peptide (amide)
Polysaccharide	Monosaccharide	Glycoside (ether)
Lipids* (triacylglycerols)	Fatty acids	Ester

*Lipids are not polymeric, but form large assemblies



Distinguishing Characteristics of Living Systems

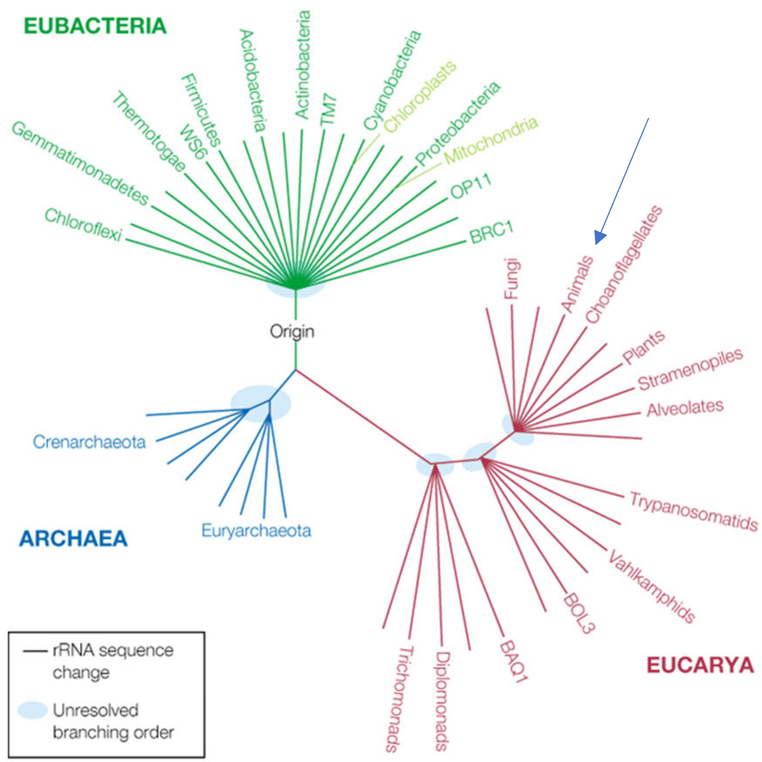
In 2002, Koshland summarized the essential attributes that distinguish living from nonliving things*:

1) **A program** (organized plan for constitution and regeneration; DNA)
2) **Improvisation** (changing the program as surroundings change; evolution)
3) **Compartmentation** (ability to be separate from environment; membranes)
4) **Energy** (ability to maintain order despite overall positive entropy)
5) **Regeneration** (compensation for environmental wear and tear; repair)
6) **Adaptability** (ability to respond to environmental changes)
7) **Seclusion** (operation of processes and pathways in isolation)

*From Koshland, D.E. (2002) **The seven pillars of life**. *Science* 295:2215-2216.

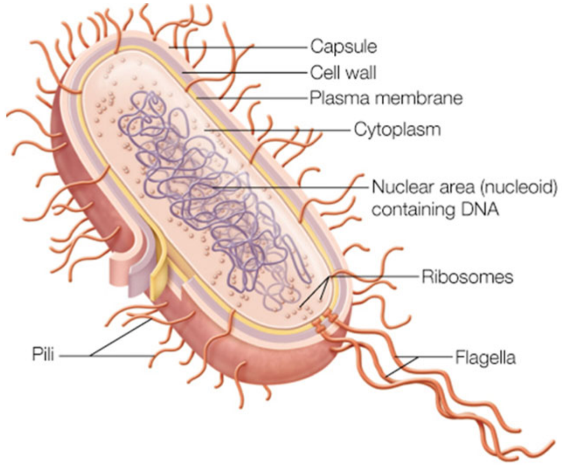
The Unit of Biological Organization: The Cell

- Cells are the universal unit of life
  - ➢bacterial
  - ➢archaeal
  - ➢eukaryotic
- Although distinct in many aspects, bacterial and archaeal cells are summarized as prokaryotic cells
- Cell type correlates with phylogeny ("Molecular Tree of Life")
  - ➢Based on ribosomal RNA sequence comparisons



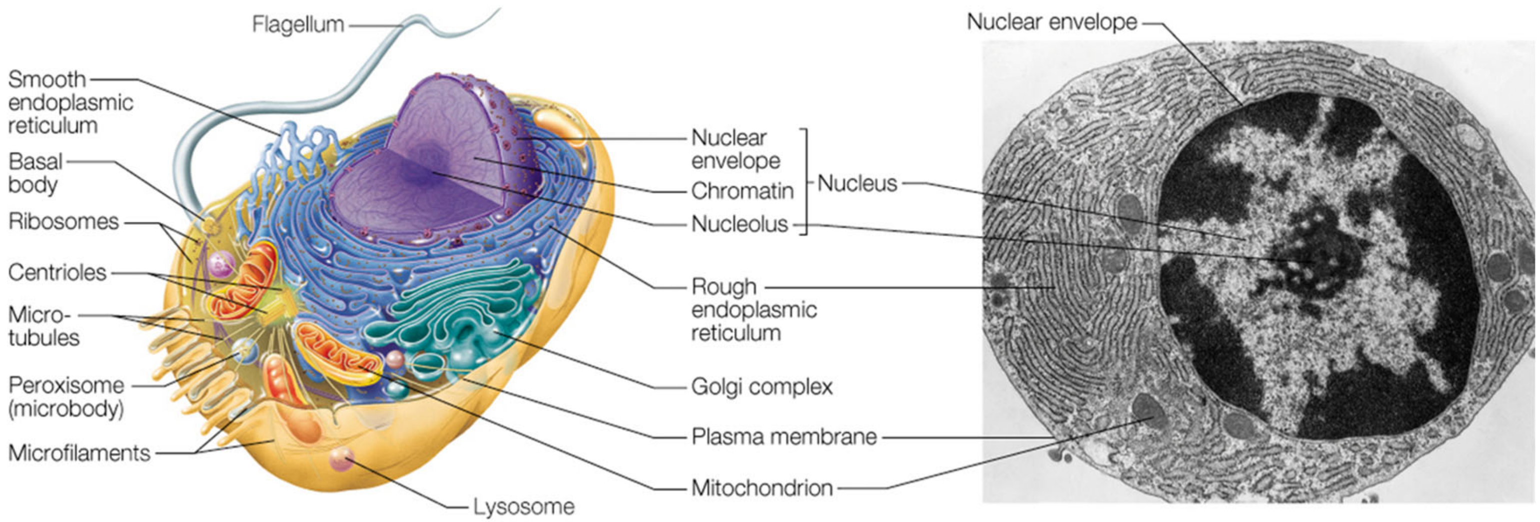
Types of cells

- **Prokaryotic cell**
- **Eukaryotic cells** have membrane-surrounded structures (organelles) within the cellular boundary



(a) Schematic view of a representative bacterial cell. The DNA molecule that constitutes most of the genetic material is coiled up in a region called the nucleoid, which shares the fluid interior of the cell (the cytoplasm) with ribosomes (which synthesize proteins), other particles, and a large variety of dissolved molecules. The cell is bounded by a plasma membrane, outside of which is usually a fairly rigid cell wall. Many bacteria also have a gelatinous outer capsule. Projecting from the surface may be pili, which attach the cell to other cells or surfaces, and one or more flagellae, which enable the cell to swim through a liquid environment.

(b) Scanning electron micrograph of *Salmonella*: rod-shaped Gram-negative enterobacteria that causes typhoid fever, paratyphoid fever, and food-borne illness.



(a) Typical animal cell. The accompanying photograph is an electron micrograph of a representative animal cell, a white blood cell.

MACQUARIE University

New Research Methods in Biochemistry

2015

- Cryo-electron microscopy
- CRISPR-Cas9 technology
- Synthetic biology

2010

- RNA-sequence analysis
- Chromatin immunoprecipitation/ sequencing
- Induced pluripotent cells
- Second generation DNA sequence analysis

2005

- Proteomic analysis with mass spectrometry

2000

- Genetic code expansion
- Gene analysis on microchips
- Single-molecule dynamics

1995

- Targeted gene disruption
- In vivo NMR
- Atomic force microscopy

1990

- Scanning tunneling microscopy

1985

- Pulsed field electrophoresis
- Transgenic animals
- Amplification of DNA: polymerase chain reaction
- Automated oligonucleotide synthesis

1980

- Site-directed mutagenesis of cloned genes
- Automated micro-scale protein sequencing
- Rapid DNA sequence determination
- Monoclonal antibodies

1975

- Southern blotting
- Two-dimensional gel electrophoresis
- Gene cloning

1970

- Restriction cleavage mapping of DNA molecules
- Rapid methods for enzyme kinetics

1965

- High-performance liquid chromatography
- Polyacrylamide gel electrophoresis
- Solution hybridization of nucleic acids

1960

- X-ray crystallographic protein structure determination
- Zone sedimentation velocity centrifugation
- Equilibrium gradient centrifugation
- Liquid scintillation counting

1955

- First determination of the amino acid sequence of a protein
- X-ray diffraction of DNA fibers

1950

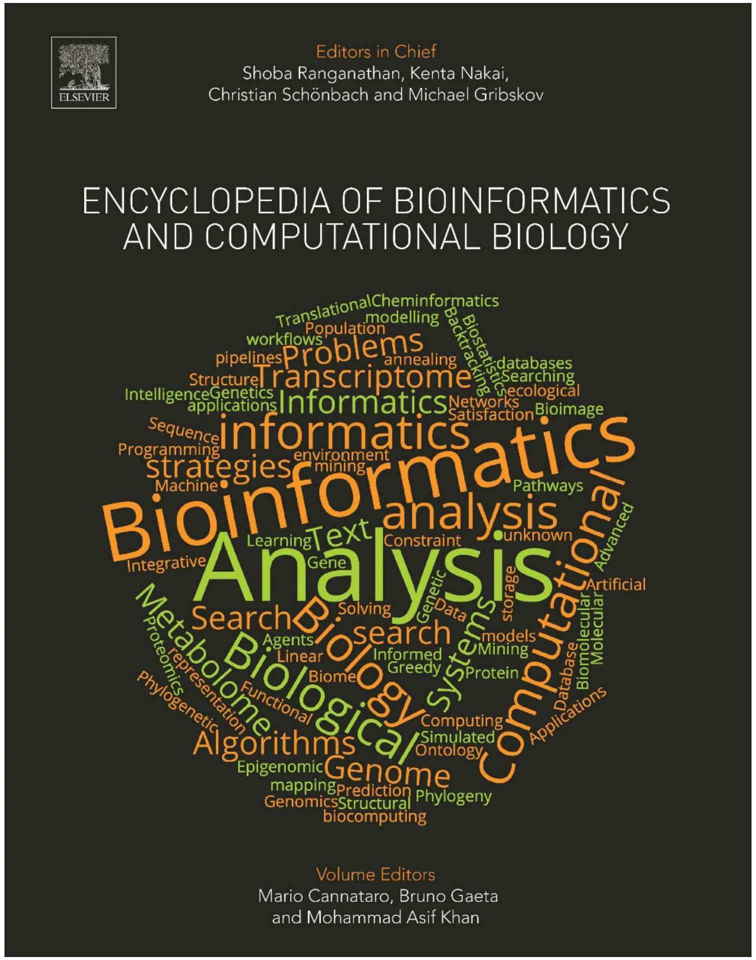
- Radioisotopic tracers used to elucidate reactions

1945

Biochemistry and the Information Explosion

Bioinformatics

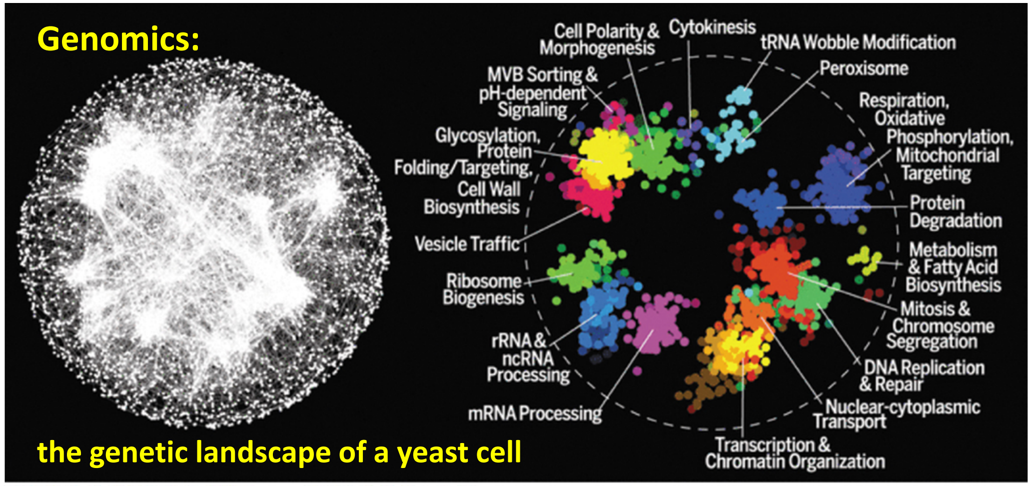
- New scientific tools and techniques can generate and analyze increasing amount of biochemical and molecular biological information
- **Bioinformatics** can be considered as **information science applied to biology**. Examples are
  1) mathematical analysis of DNA sequence data
  2) *in silico* analysis of protein structure and function
  3) computer simulation of metabolic pathways
  4) analysis of potential drug targets (enzymes or receptors) for structure-based drug design

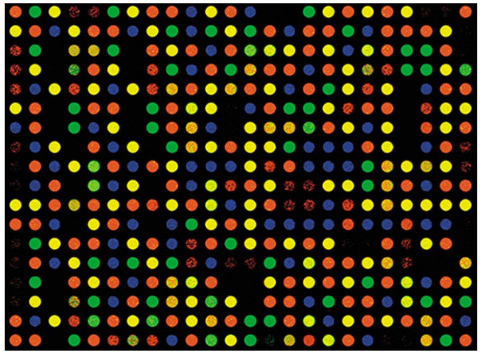


Biochemistry and the Information Explosion - 2

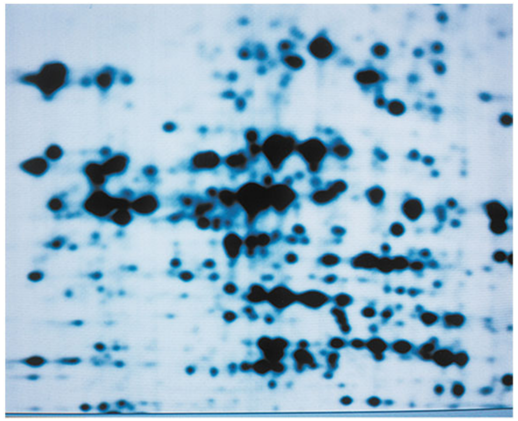
Omics

- **Genetics** concerns itself with the location, expression, and function of individual genes or small groups of genes
- **Genomics** expands the genetics approach and concerns itself with the entire genome, the totality of genetic information in an organism
  - ➢ Some of the broader goals of genomics are to
    1) determine the nucleotide sequence of the whole genome (of an organism)
    2) assess the expression and function of each gene
    3) understand the evolutionary relationships among genes in the same genome and with genomes of different organisms
- Examples of other established "Omics" are **Proteomics**, **Transcriptomics**, **Metabolomics**, and **Interactomics**





Transcriptomics: the abundance of gene-specific mRNAs indicated by microarrays



Proteomics: separation of a large number of proteins from a cellular extract by two-dimensional gel electrophoresis

Biochemistry - Summary

- The aim of biochemistry is to understand and explain living systems in molecular terms
- Biochemistry bridges biological and chemical sciences on the level of molecules present in living systems
- Living systems are composed of cells, which can be divided into three major types: bacterial, archaeal, and eukaryotic
- Biochemistry is an experimental science and uses a variety of different tools and techniques, some of which generate large amount of information

The Chemical Foundation of Life: Weak Interactions in an Aqueous Environment

AAM: Chapter 2

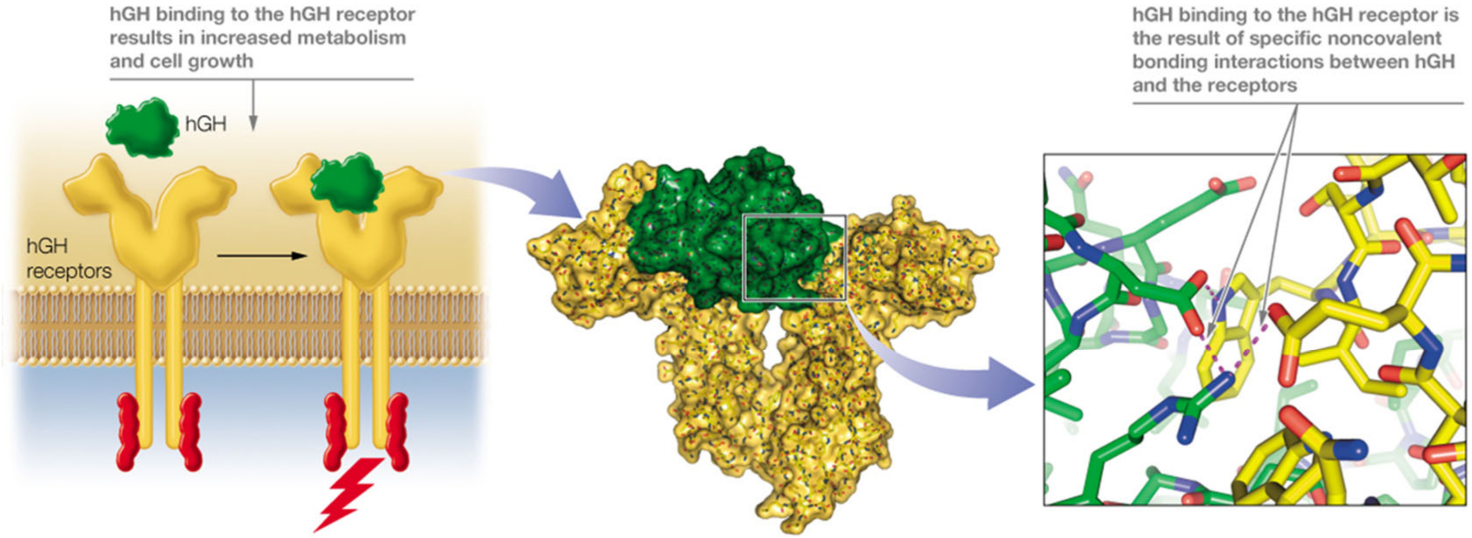
- The Importance of Noncovalent Interactions in Biochemistry
- The Nature of Noncovalent Interactions
- The Role of Water in Biological Processes

Noncovalent Interactions Define the Structure and Function of Biomolecules

a) Binding of hormone to its receptor

b) The binding pocket shows surfaces that complement each other.

c) The binding occurs due to formation of non-covalent bonds.

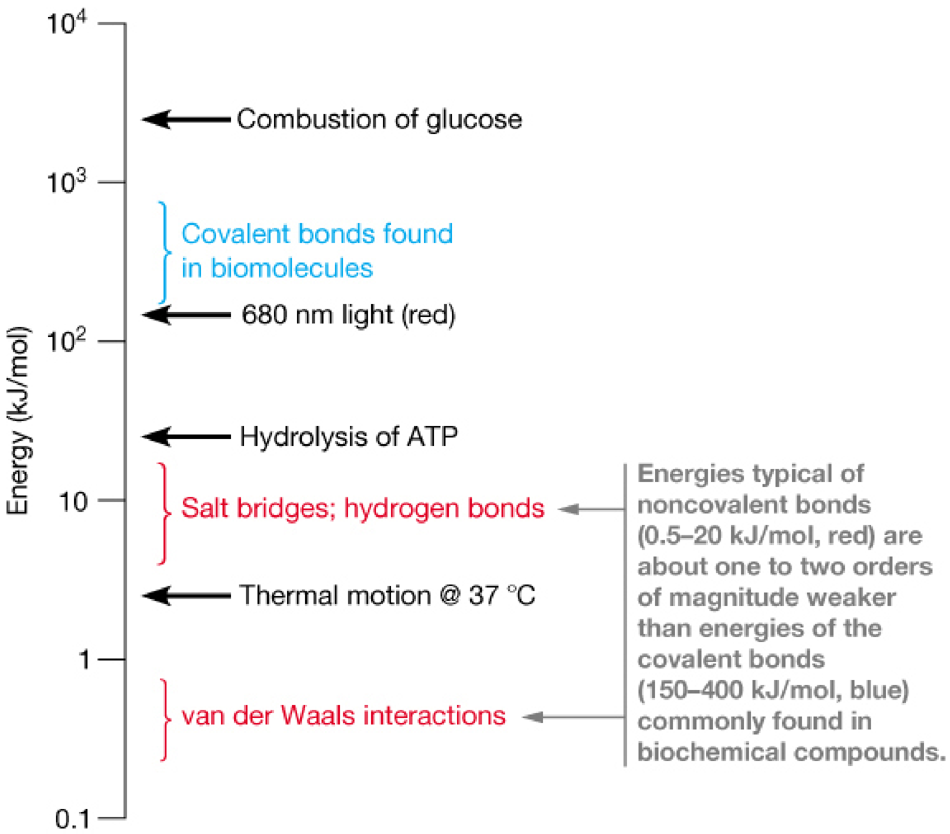


(a) The binding of human growth hormone (hGH) to its receptor transmits a signal across the cell membrane which, in turn, stimulates cell growth (indicated by lightning bolt).

(b) The X-ray crystal structure of the hGH-receptor complex shows the complementary binding surfaces (interfaces) between these proteins.

(c) A zoom into the interface between hGH and the receptor shows highly specific noncovalent bonding interactions (magenta-colored dashed lines). Here, O atoms are colored red, N atoms are blue, and C atoms are either green (on hGH) or yellow (on the receptor).

Noncovalent Bonds vs. Covalent Bonds



- Covalent bonds are strong and not easily broken
- Noncovalent bonds are weak, and thus can be continually broken and reformed

TABLE 2.1 Energies of some noncovalent interactions in biomolecules

Type of Interaction	Approximate Energy (kJ/mol)
Charge–charge	13 to 17
Hydrogen bond	2 to 21
van der Waals	0.4 to 0.8

Source: Data from S. K. Burley and G. A. Petsko, Weakly polar interactions in proteins, *Advances in Protein Chemistry* (1988) 39:125–189.

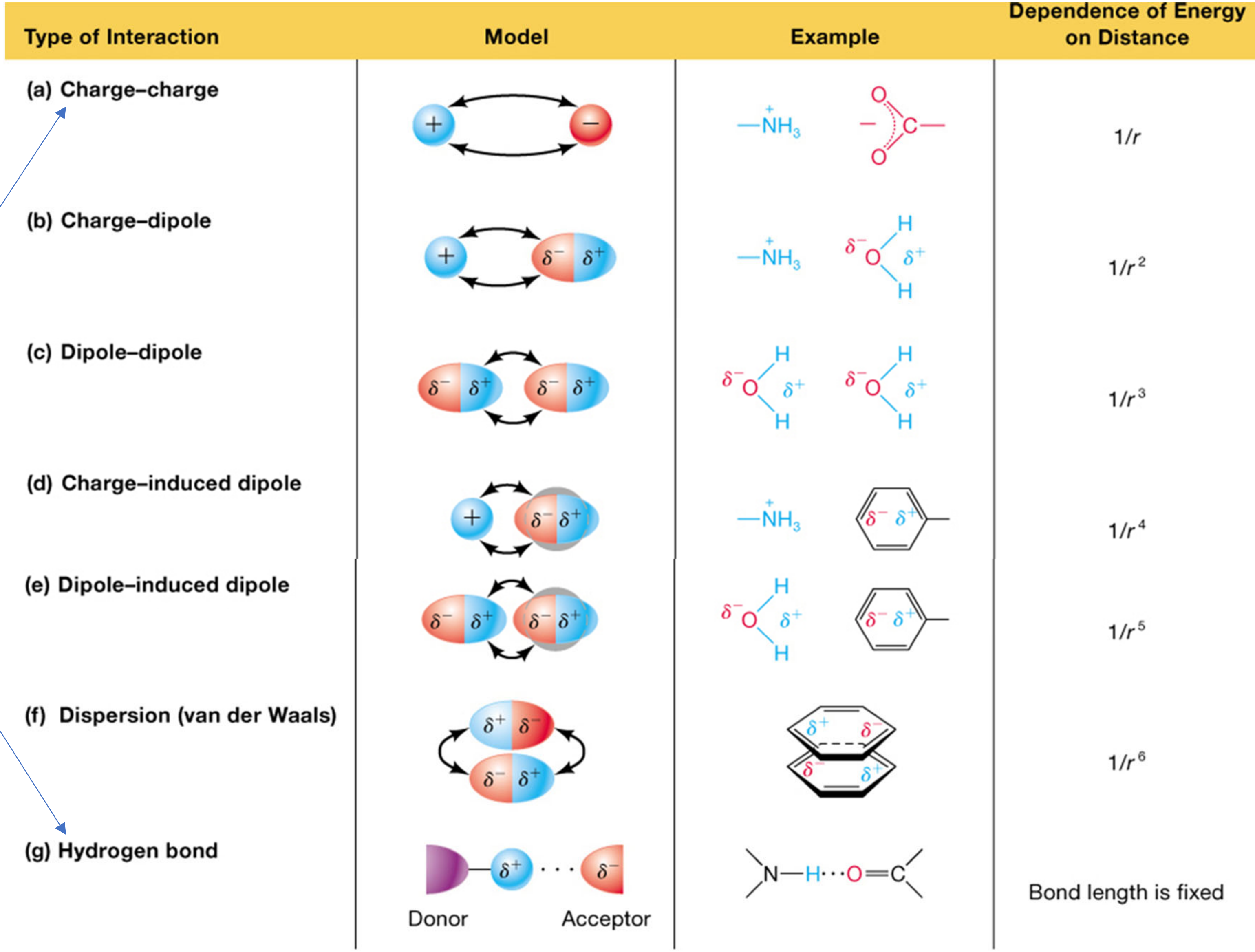
The Nature of Noncovalent Interactions

All noncovalent interactions are electrostatic in nature:

(a) **Charge-charge interactions** between two charged particles – simplest

(g) **Hydrogen bonding** is very important for the structure and properties of biomolecules

- between a hydrogen atom covalently bonded to another atom (e.g., O–H or N–H) and a pair of nonbonded electrons on a separate (e.g., O or N) atom



Hydrogen bonding in biomolecules

- In biomolecules such as proteins
- Known as "bonds of life" – Nobel Laureate Linus Pauling

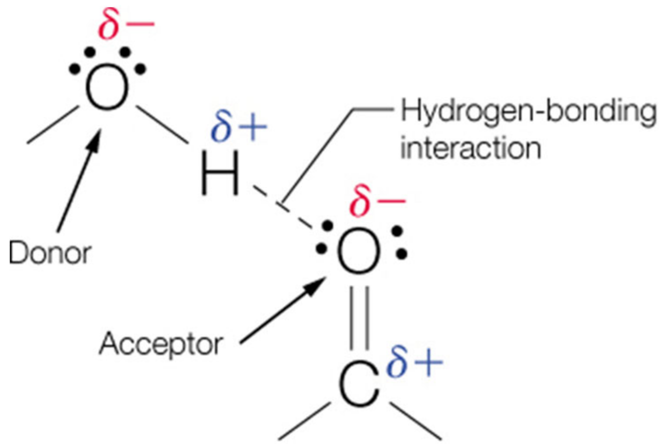
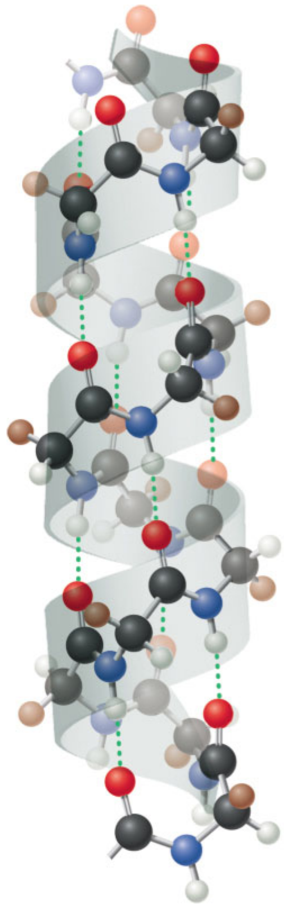
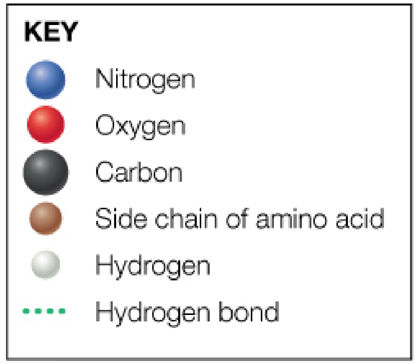


TABLE 2.3 Major types of hydrogen bonds found in biomolecular interactions

Donor . . . Acceptor	Distance between Donor and Acceptor (Å)	Comment
—O—H ··· O(H)	2.8 ± 0.1	H bond formed in water
—O—H ··· O=C	2.8 ± 0.1	Bonding of water to other molecules often involves these
N—H ··· O(H)	2.9 ± 0.1	
N—H ··· O=C	2.9 ± 0.1	Very important in protein and nucleic acid structures
N—H ··· N	3.1 ± 0.2	
N—H ··· S	3.7	Relatively rare; weaker than above

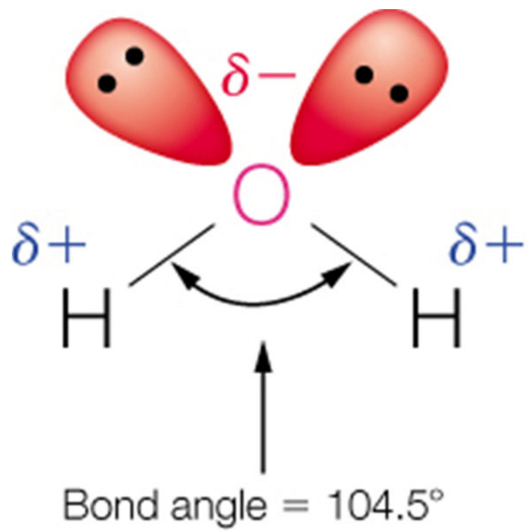




The Role of Water in Biological Processes

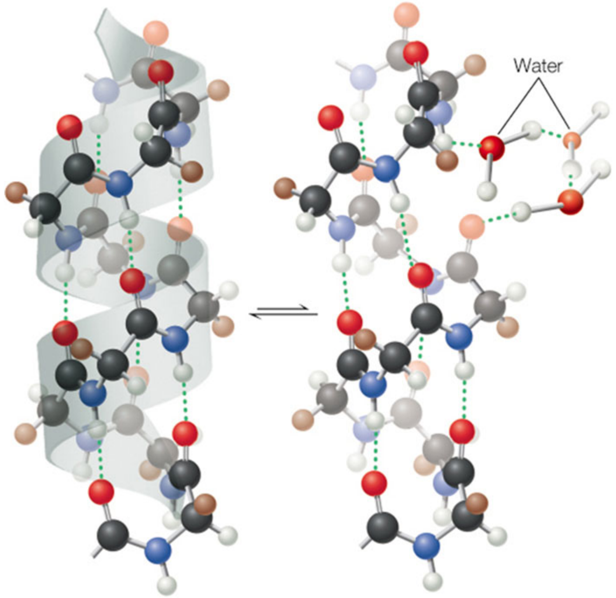
Unique properties of water that make it suitable as the medium of life

- a permanent dipole
  - ➢two H bond donor sites and two H bond acceptor sites
- high heat capacity
- liquid with high density
- relatively high dielectric constant, making it capable of solvating ionic compounds

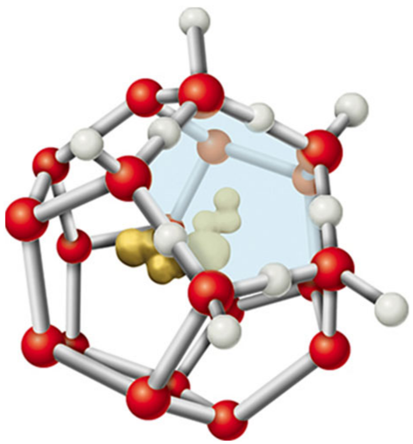


Solvation of hydrophilic, hydrophobic and amphipathic substances

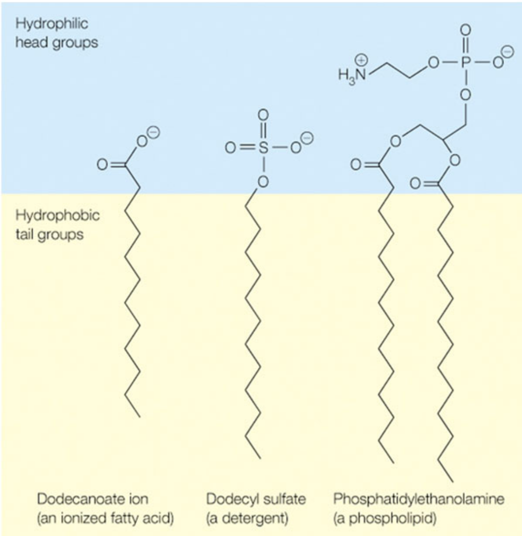
Hydrophilic:
- Solvent can compete with intramolecular H-bond donors/acceptors



Hydrophobic:
- Solvent can form “clathrate”(cage) structures to surround nonpolar surface areas
- “Hydrophobic effect”—stabilizes protein structure by driving apolar groups together



Amphipathic:
- An amphipathic substance has hydrophilic and hydrophobic parts and can form a monolayer, a micelle, or a bilayer.
- Bilayers are typical of biological membranes



Take home message

- Water is essential for all forms of life.
- Every organism is 70-90% water!
- Normal human metabolic activity requires min. 65% water!
- Water is an excellent solvent and is therefore the medium of the majority of biochemical reactions.
- Water causes ionization of polar molecules, critical for the function of:
  - amino acids and proteins
  - nucleotides and nucleic acids
  - even phospholipids and membranes
- Water solvates hydrophilic, hydrophobic and amphipathic molecules.