Lecture 1:
The Scope and Topics of Biophysics

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BIRTH OF BIOPHYSICS

- **Advanced interdisciplinary science involving:**
  - **physics, biology, chemistry, mathematics;**
- **New, 60-100 years old discipline:**
  - **-1892: Karl Pearson (missing link between biology and physics => name biophysics)**
  - **-1943: Erwin Schrodinger (Nobel Prize, 1933) lecture series: *What is Life***
  - **-1946: *Biophysics Research Unit*, King's College, London, hire physicists to work on questions of biological significance; Maurice Wilkins, Rosalind Franklin: X-ray diffraction of DNA**
  - **-1953: Francis Crick (particle physicist turned into biophysicist at Cambridge) and James Watson (biologist): double helix structure of DNA**
  - **-1957: *The Biophysical Society* founded**

BIOPHYSICAL TOPICS

- **Biophysical topics based on relative size of the subject:**
  - **molecular and subcellular biophysics**
  - **physiological and anatomical biophysics**
  - **environmental biophysics**

- **Biophysical techniques and applications:**
  - **general biophysical techniques**
  - **imaging biophysics**
  - **medical biophysics**

Molecular and Subcellular Biophysics

- The Structure and Conformation of Biological Molecules
- Structure Function Relationships
- Conformational Transitions
- Ligand Binding and Intermolecular Binding
- Diffusion and Molecular Transport
- Membrane Biophysics
- DNA and Nucleic Acid Biophysics
- Protein Biophysics
- Energy Flow and Bioenergetics
- Thermodynamics
- Statistical Mechanics
- Kinetics
- Molecular Machines
- Allosterics

Biophysical Techniques and Applications

- ***Ultracentrifugation*** **to separate molecules of different sizes based on the sedimentation principle, up to 10^6 g;**
- ***Electrophoresis*** **to separate molecules of different molecular mass/size based on the sedimentation principle; electric field acts on the charged molecules;** ***gel electrophoresis***
- ***Size Exclusion Chromatography (SEC)*** **uses tightly packed gel beads and sedimentation based on gravity (and sometimes pressure) to trap small molecules and allow larger molecules to pass through the gel faster than small molecules;**
- ***Spectroscopy*** **mostly with incident EM radiation and measuring the intensity/direction/polarization of the emitted radiation (originally only the visible spectrum 380-750 nm was used; now also UV and IR); in addition to** ***EM also electron and mass spectroscopy;***
- ***Absorption Spectroscopy*** **to find e.g. the concentration of molecules in the solution by using EM of a particular λ to shine on the sample and measure the intensity that comes out OR absorbance versus λ to identify the type of molecules;**

- ➔ ***Fluorescence Spectroscopy*** **to characterize molecules and to follow conformational transitions; caused by absorption at a one wavelength and emission at a longer wavelength (electrons drop from their excited energy state emitting light;**
- ➔ ***Mass Spectrometry*** **to measure mass or molecular weight of molecules; molecules are ionized in a vacuum, then passed through a magnetic field;**
- ➔ ***X-Ray Crystallography*** **to determine the relative positions of atoms within a crystal by using diffraction on a 3D crystal lattice; high resolution of structural details but the molecules need to be in a crystalline phase;**
- ➔ ***Nuclear Magnetic Resonance Spectroscopy (NMR)*** **to obtain structural information about molecules of the highest resolution using EM of a radio frequency, which interacts with nuclear spins of atoms in a large magnetic field, causing them to jump between the spin states and emit at different λ depending on the local structure around the atom;**
- ➔ ***Electron Microscopy*** **to view objects 1,000-2,500 smaller than those seen by light microscopes (electrons of a small wavelength are used instead of EM);** ***transmission EM (TEM) and scanning electron microscopy (SEM)*****;**

- ***Atomic Force Microscopy (AFM)*** **with resolution similar to TEM, 3D features like SEM; a mechanical probe (a tip) moves along the surface of the scanned object to obtain 3D information;**
- ***Optical Tweezers*** **to hold and manipulate microscopic particles even single molecules or atoms using focused laser beams to create forces of the order of pN = 10^{-12} N (0.1 nm to 10,000 nm size objects) and measure forces needed to bend or break DNA, for example;**
- ***Voltage Clamp*** **is used in electrophysiology to determine electric currents in cells, in particular neurons; a fine microelectrode is inserted into the cell with another in contact with the surrounding fluid while the voltage is clamped (held constant) by a feedback that generates a counter-current to that generated by the cell;**
- ***Current Clamp*** **is analogous to voltage clamp; the current is clamped (held constant) and the voltage change induced by the cell measured;**
- ***Patch Clamp*** **is alternative to voltage/current clamp; the electrode is placed inside a micropipette with electrolyte solution and the micropipette combined with a gentle suction electrically isolates a small patch on the membrane; enables to study a single ion channel within the membrane;**
- ***Calorimetry*** **measures C_P or C_V versus T: transitions or ligand binding.**

Four Classes of Macromolecules:

(A) DNA in a B form
(B) Protein (hemoglobin)
(C) Lipid molecule (phosphatidylcholine)
(D) Branched complex carbohydrate

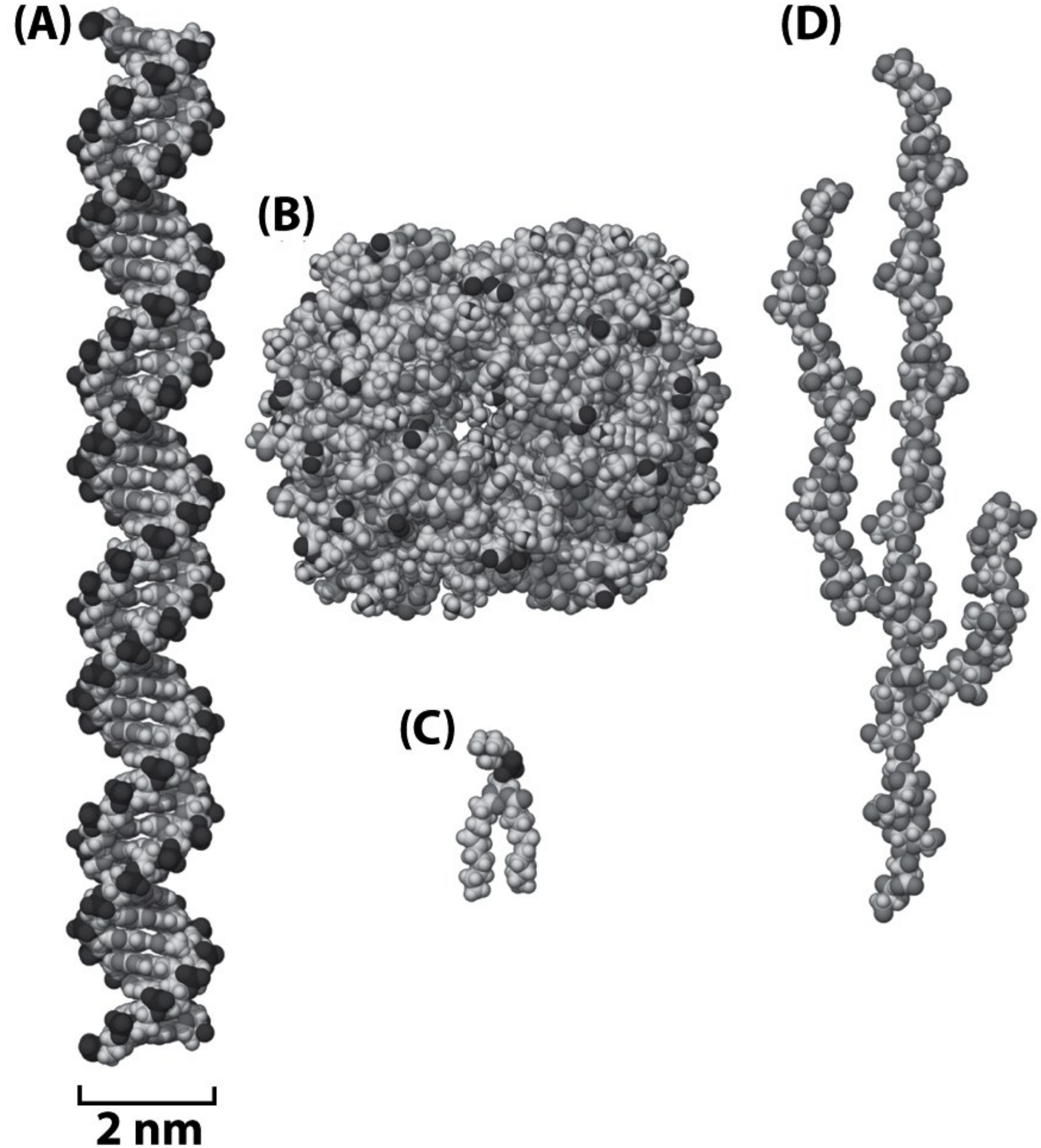


Figure 1.1 Physical Biology of the Cell (© Garland Science 2009)

Polymer Nature of Macromolecules:

(1) DNA and RNA molecules: made of nucleic acids
(2) proteins: made of amino acids

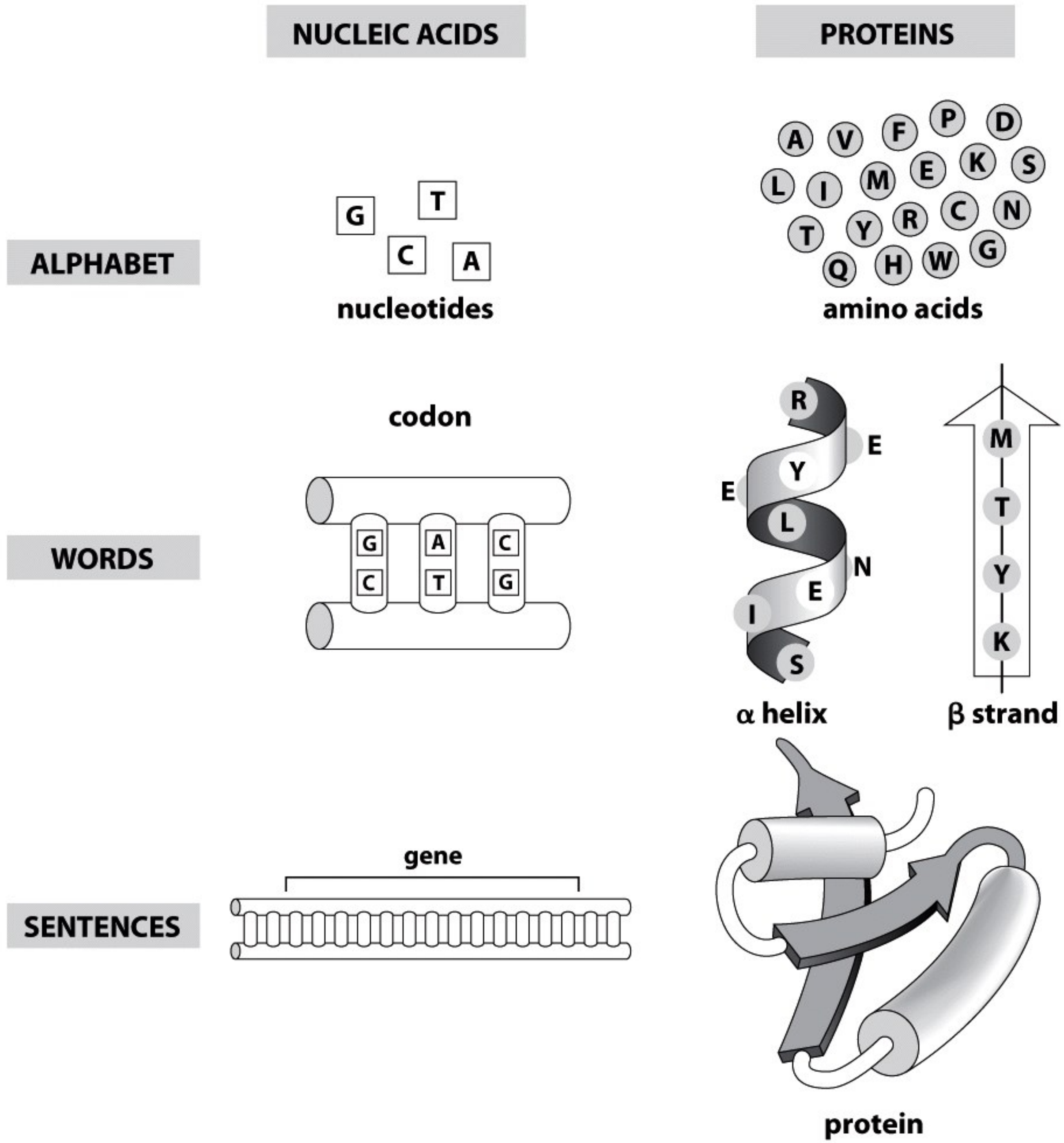
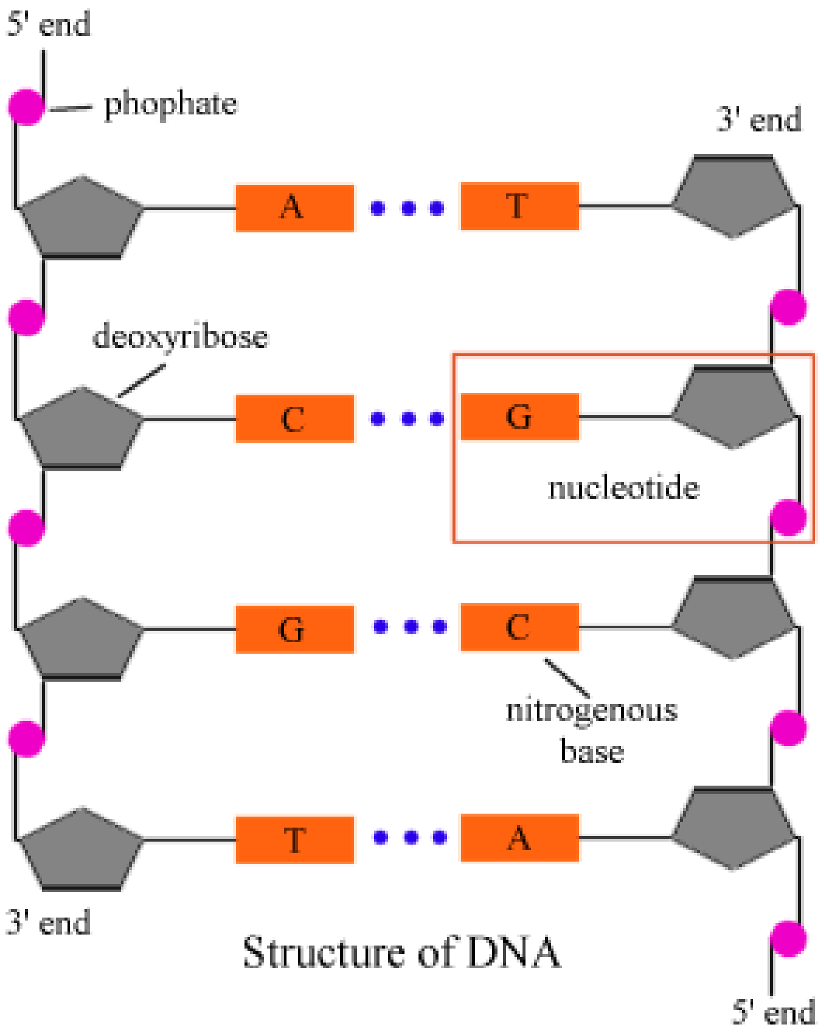
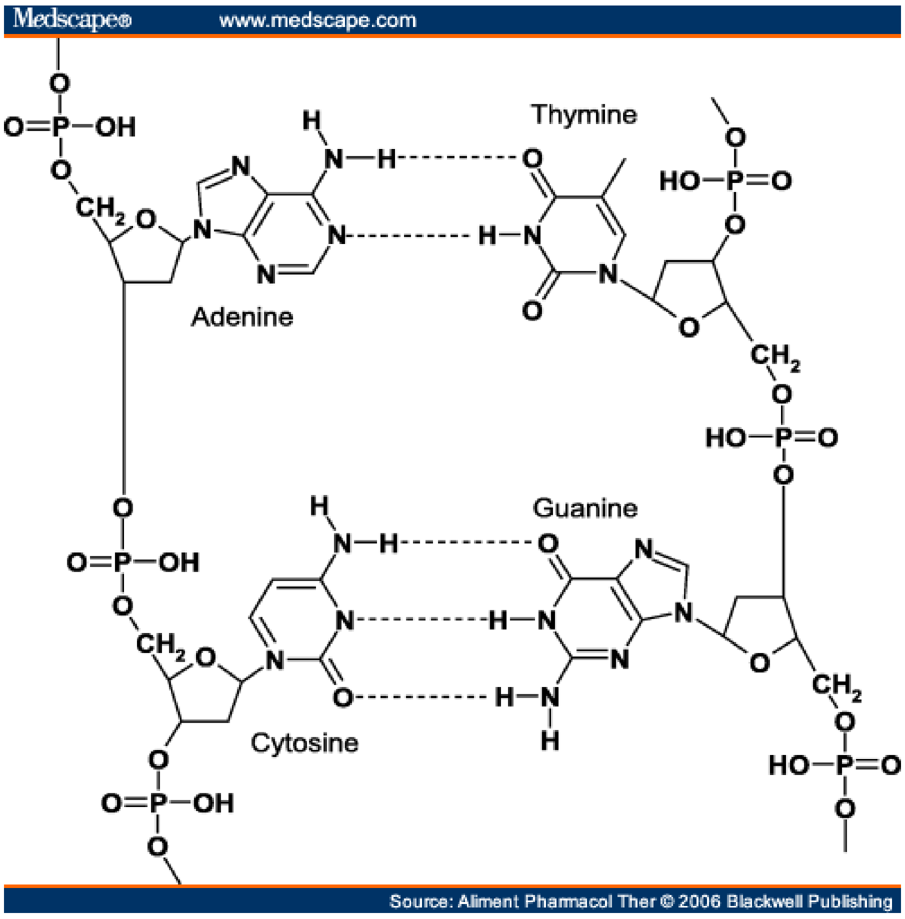


Figure 1.2 Physical Biology of the Cell (© Garland Science 2009)

DNA cartoon and detailed chemical structure





Each DNA molecule is polymers of four nucleic acids:

A, T, G, C

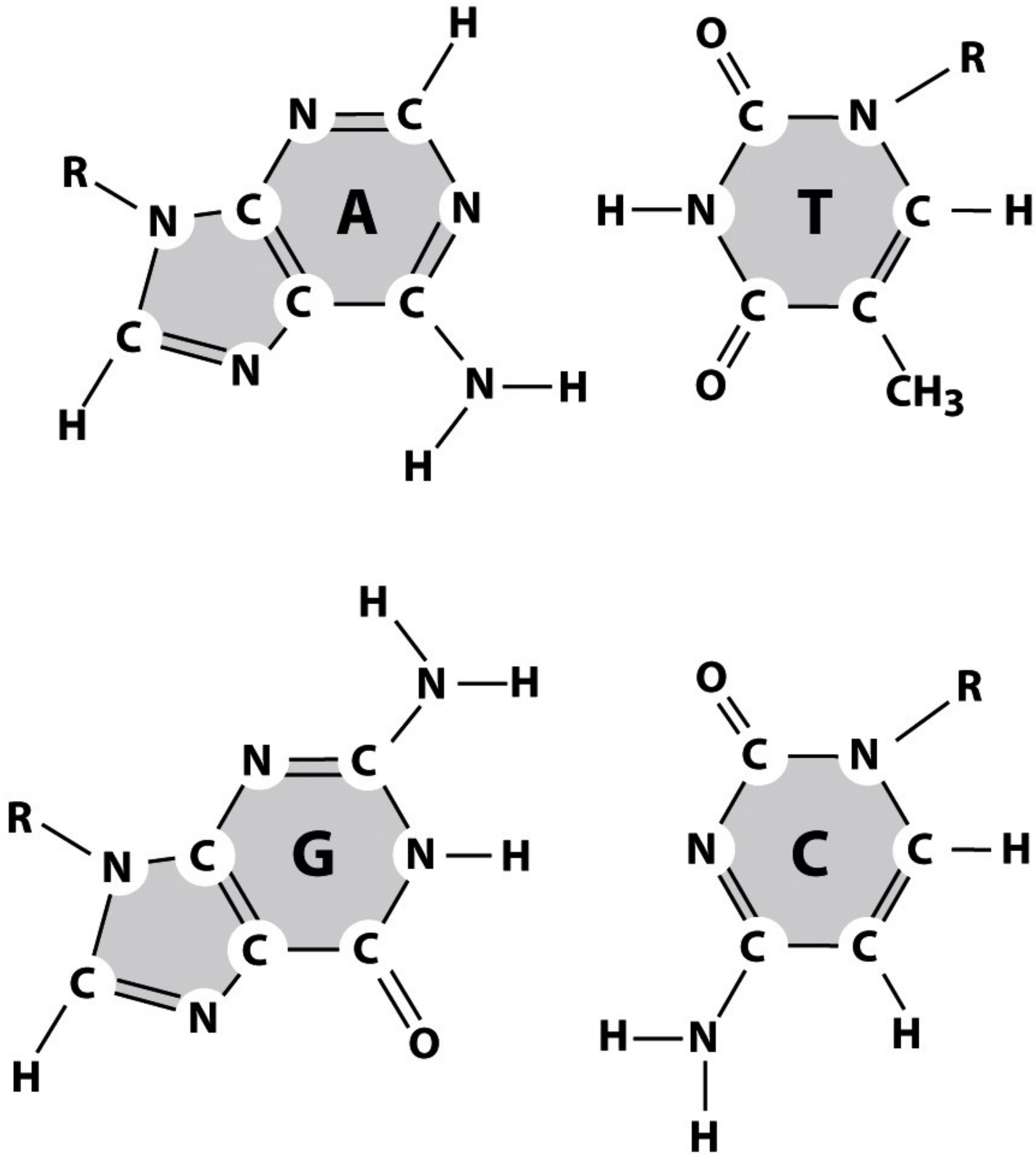


Figure 1.3a Physical Biology of the Cell (© Garland Science 2009)

Nucleic acids within a double-strand DNA:

Backbone groups:

- -deoxyribose
- -phosphate

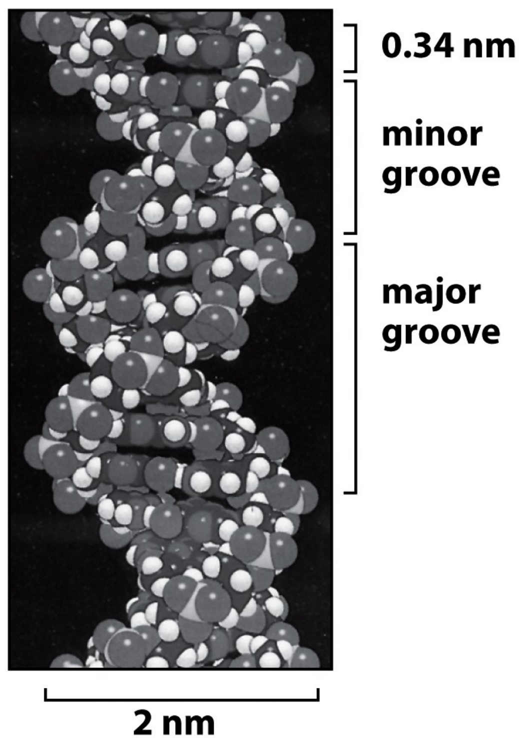


Figure 1.3c Physical Biology of the Cell (© Garland Science 2009)

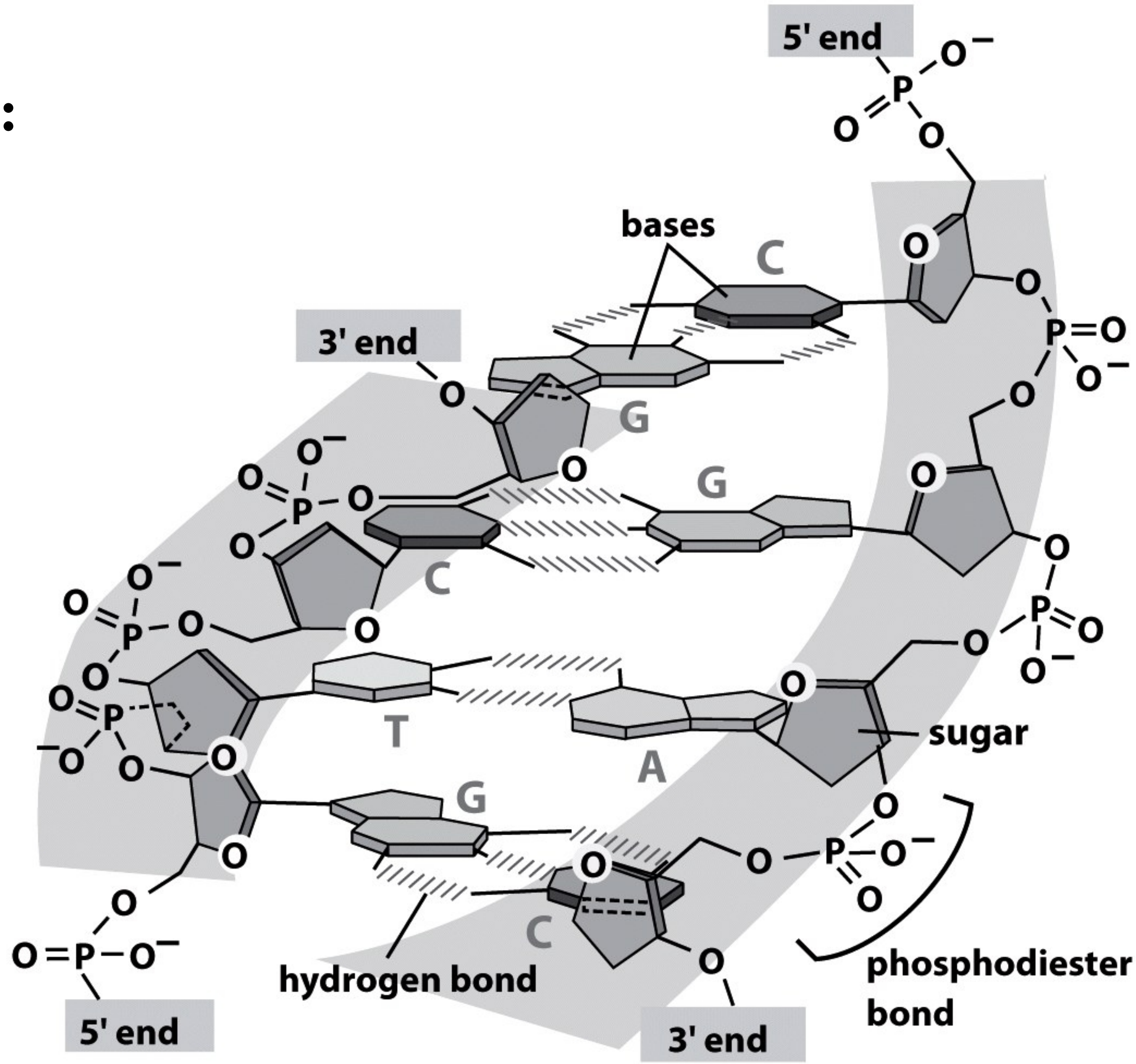


Figure 1.3b Physical Biology of the Cell (© Garland Science 2009)

mRNA encodes Proteins:

nucleotide to amino acid sequences

Uracil (instead of Thymine)

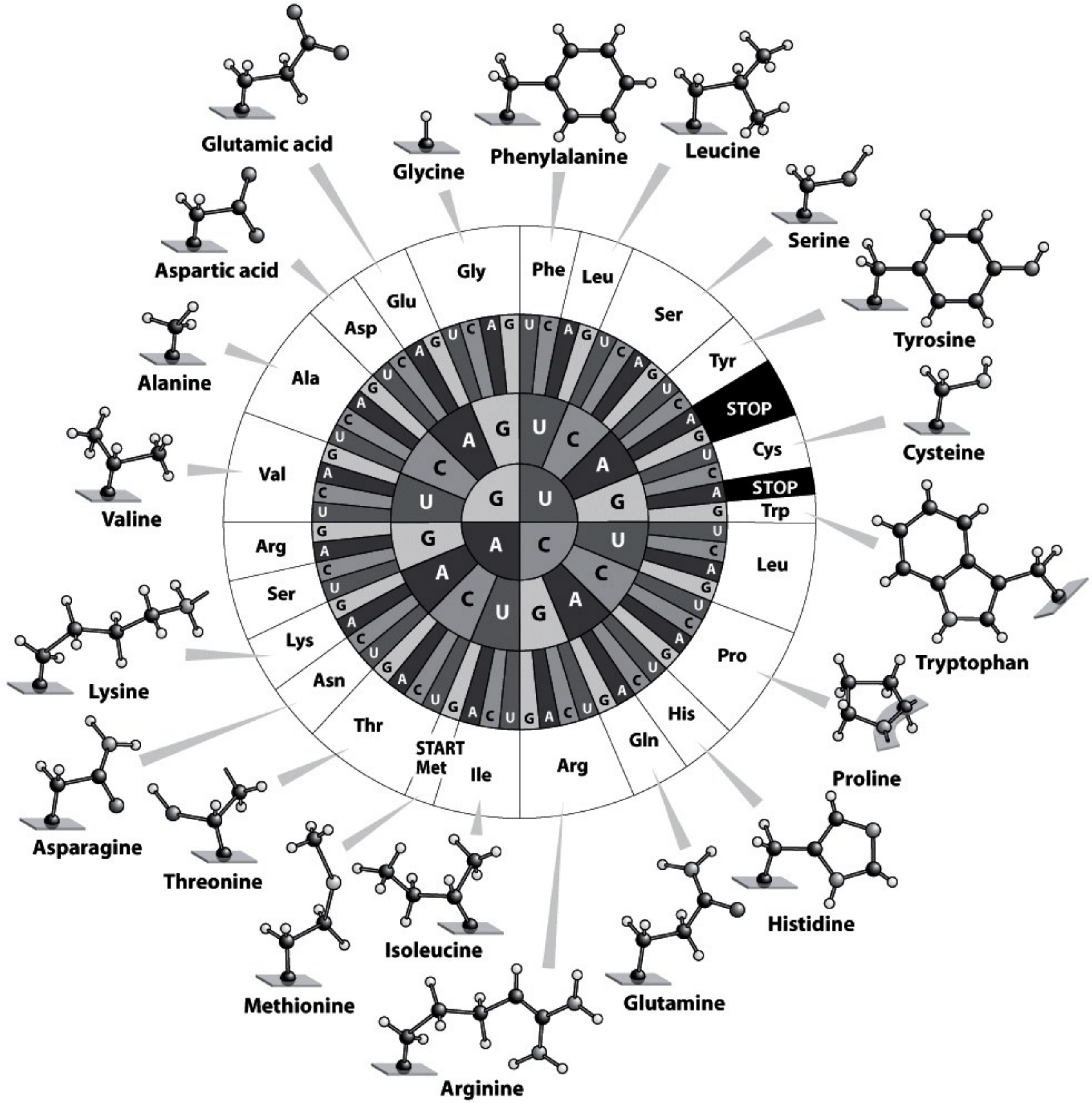
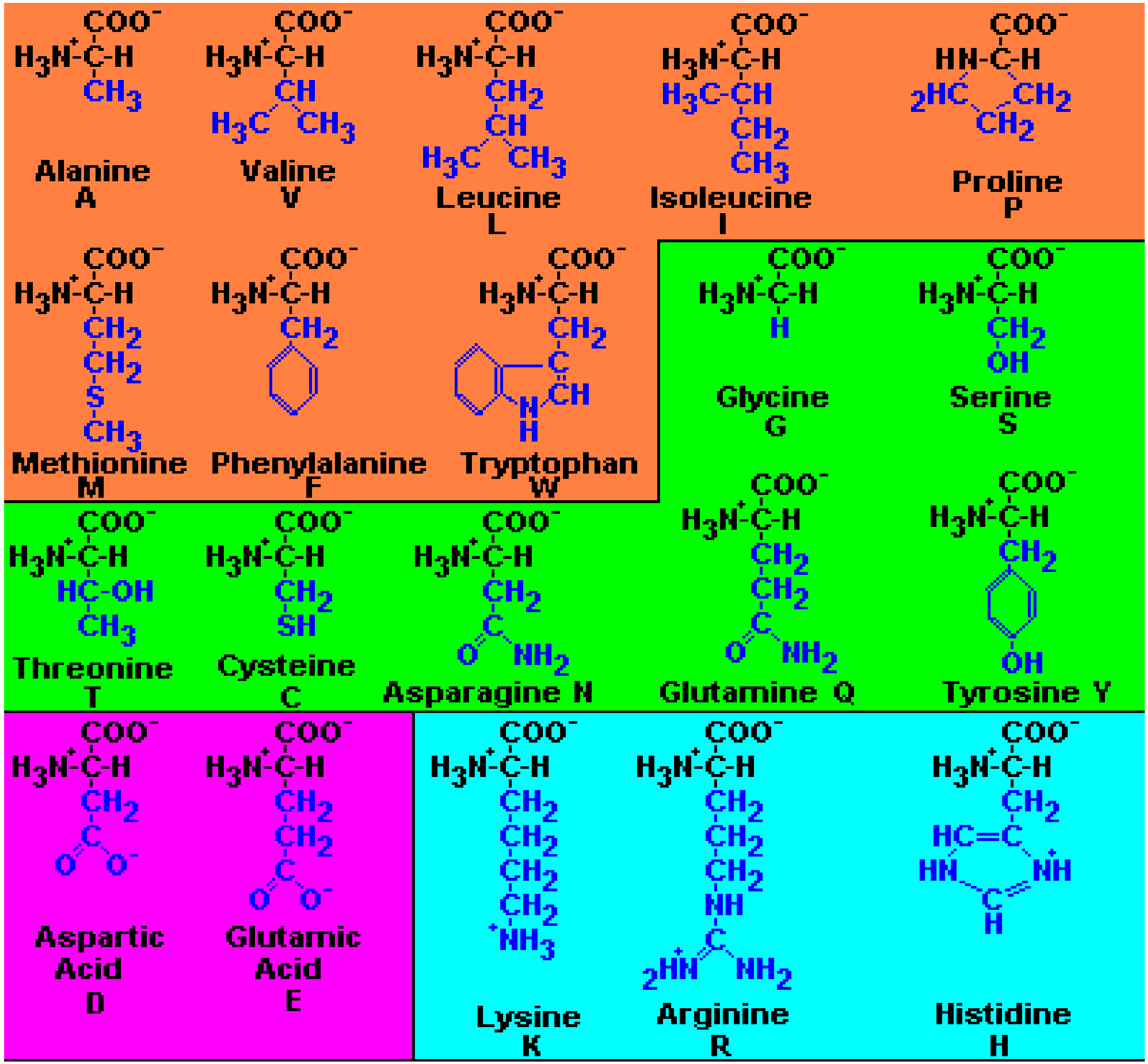


Figure 1.4 Physical Biology of the Cell (© Garland Science 2009)

20 natural amino acids

hydrophobic (“hate” water)

hydrophilic (“love” water)



Most common chemical groups found in proteins:

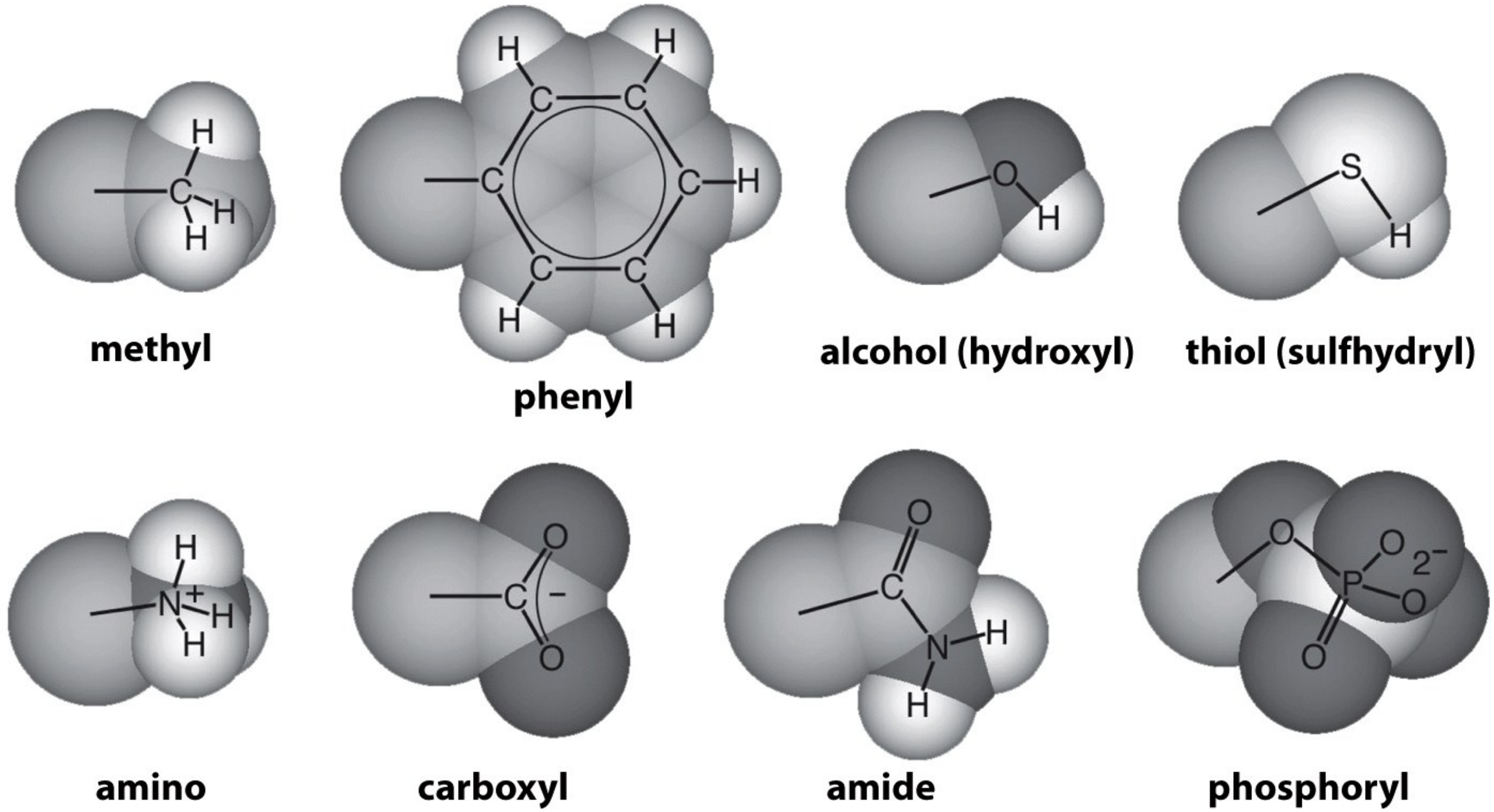
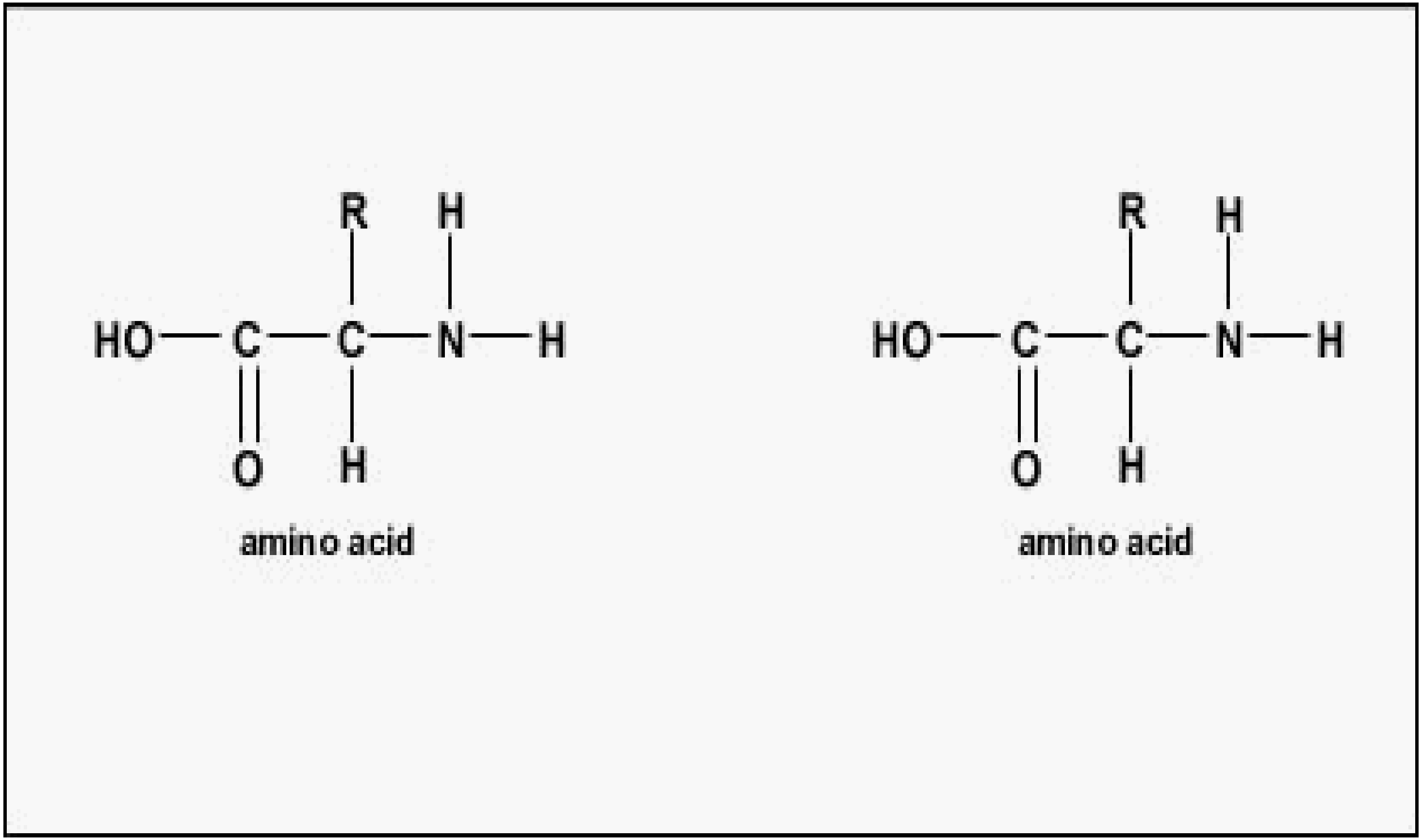


Figure 2.24 Physical Biology of the Cell (© Garland Science 2009)

CHNOPS acronym: elements most commonly found in cells (accounts for about 98% of all atoms)

Two Amino acids   Form a Peptide Bond



Membrane is a lipid bilayer.

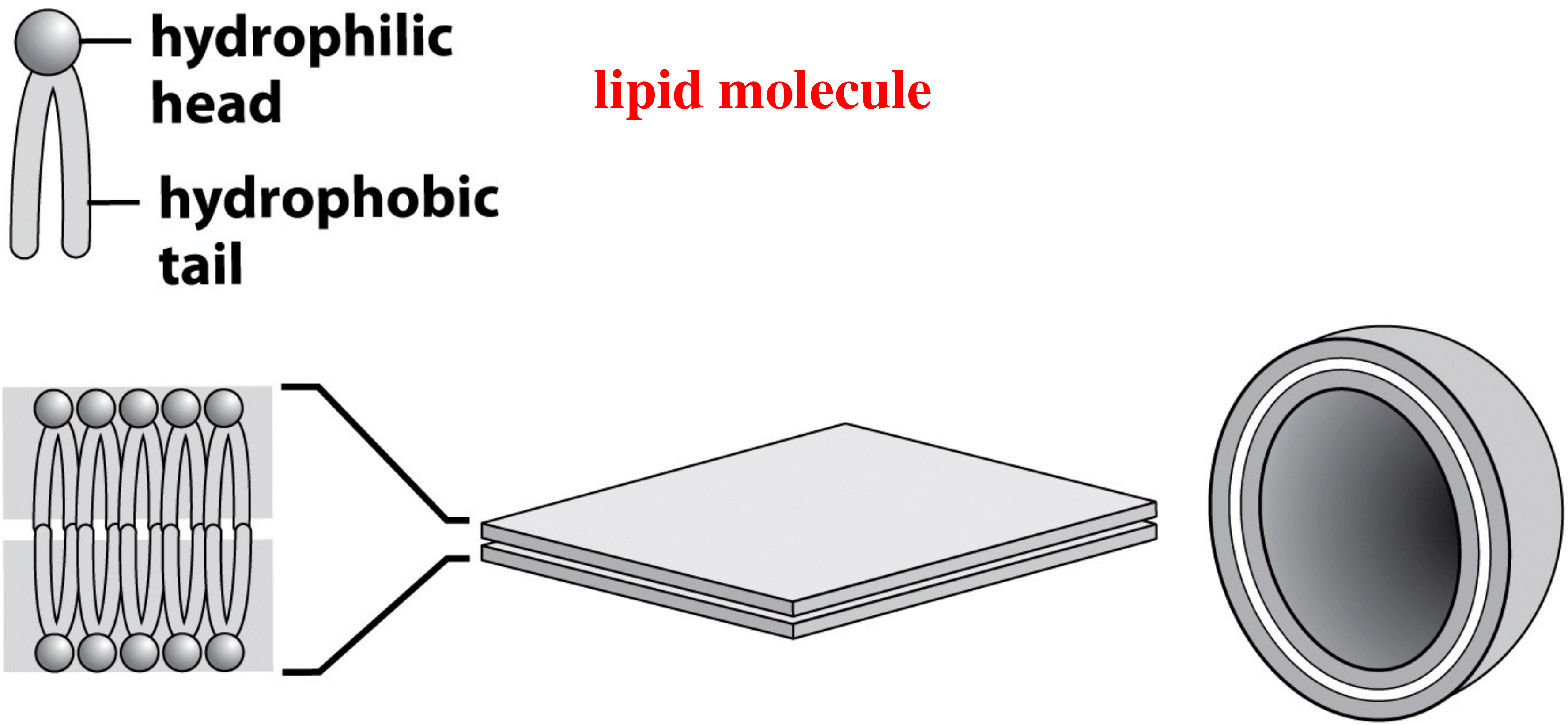
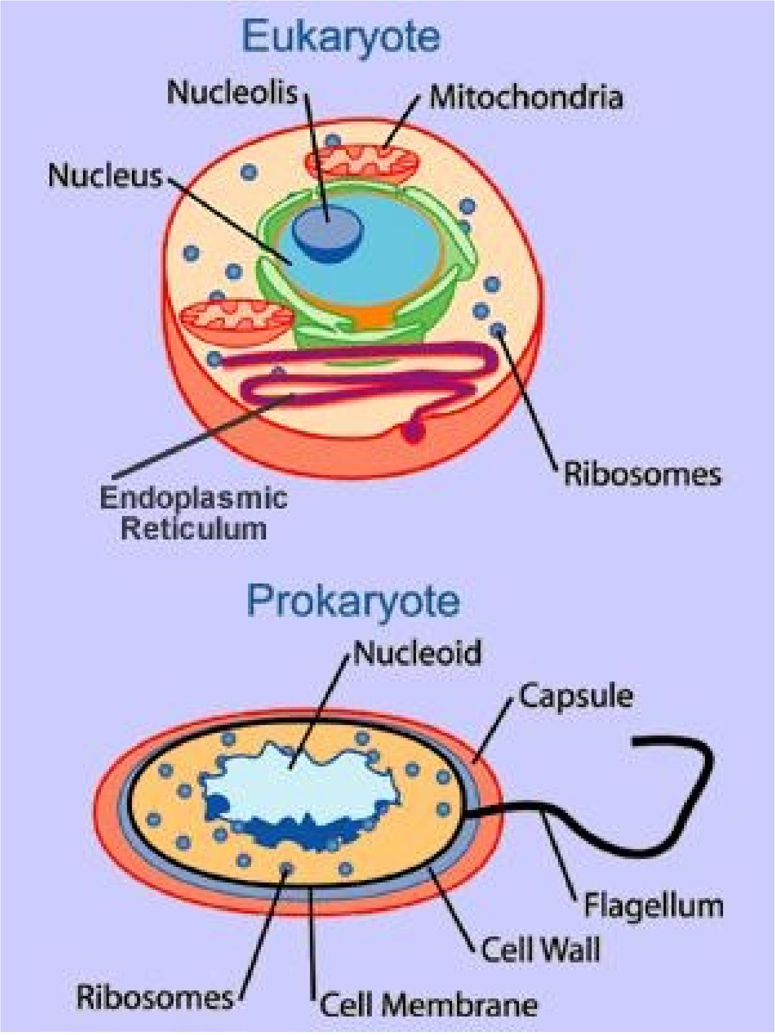
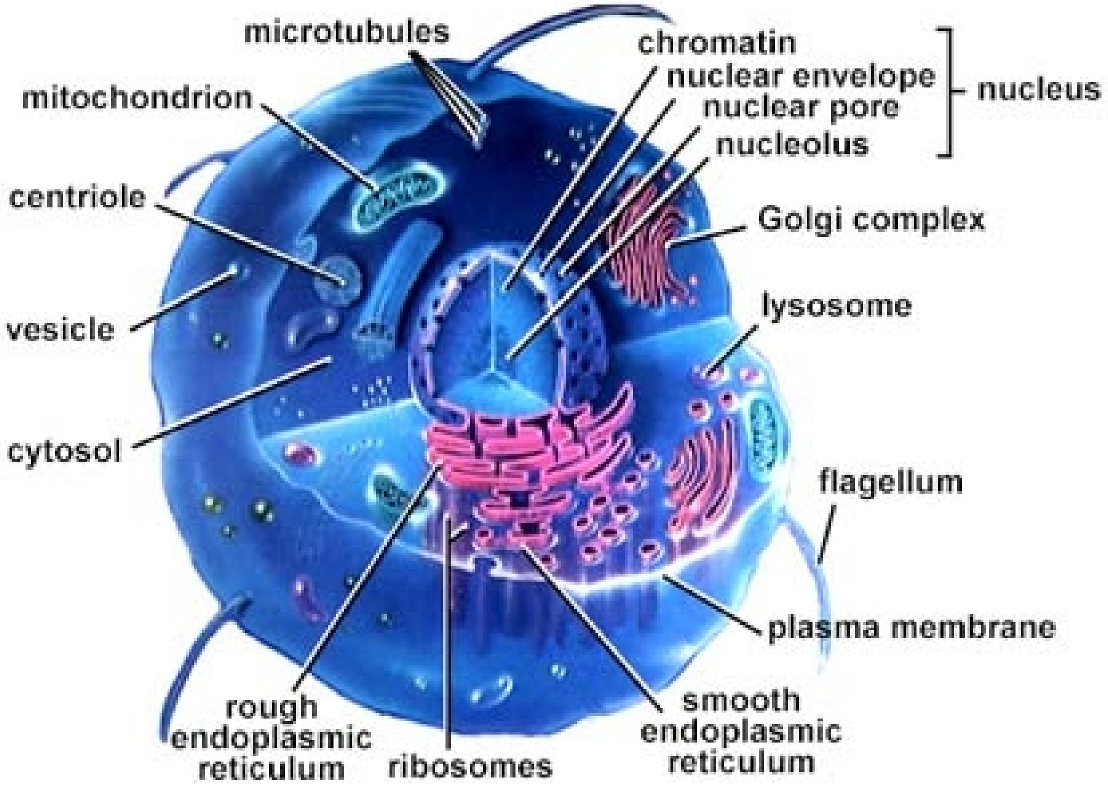


Figure 11.1a Physical Biology of the Cell (© Garland Science 2009)

Structure of a Cell

plants, animals (mostly multicelullar; also amoeba)





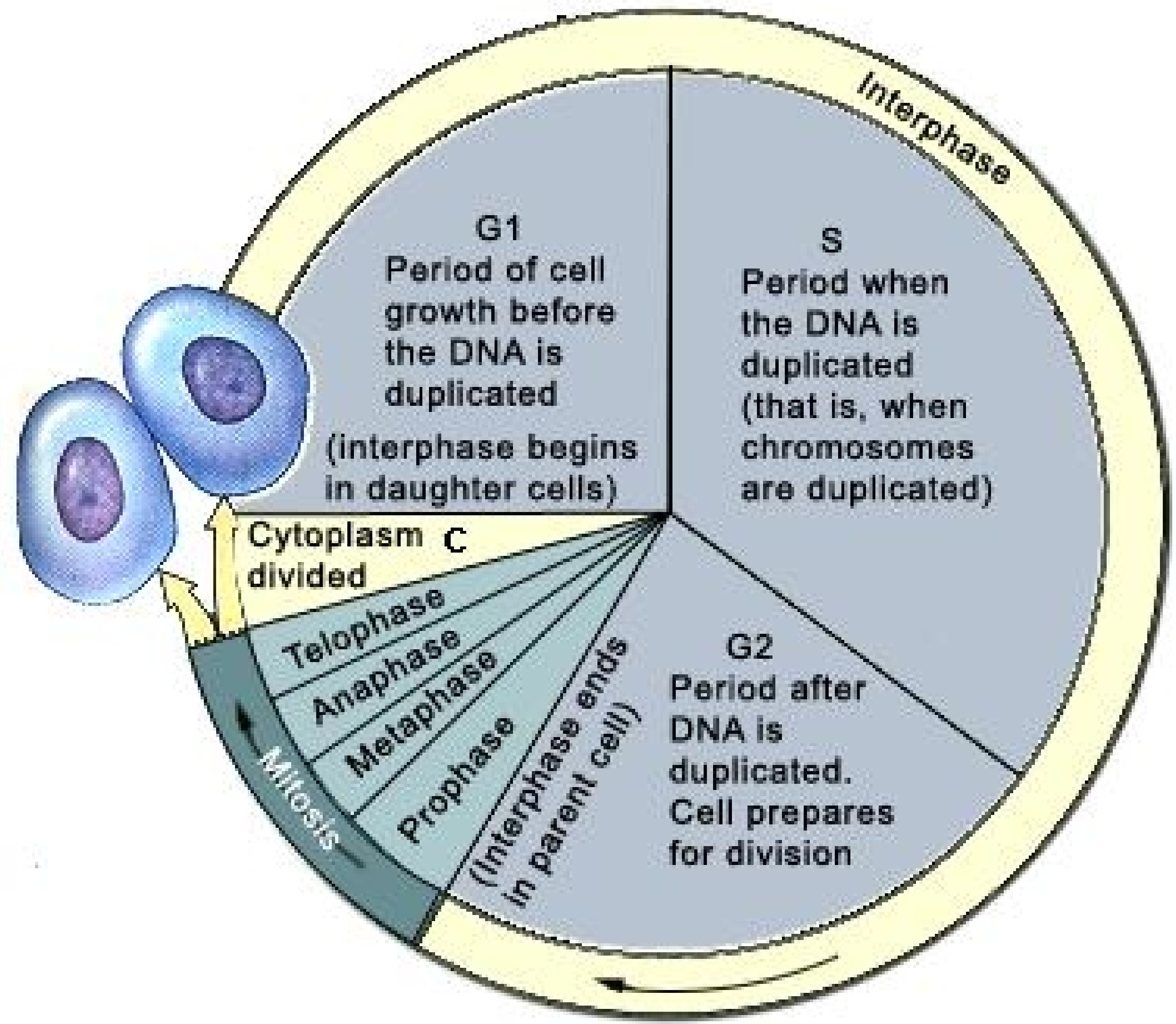
bacteria, archaea (unicellular organisms)

Major Cell Compartments

- ***nucleus*: approximately spherical membrane-bound organelle near the center of a cell; contains almost all of cell's genome; functions: gene expression (transcription of DNA to RNA to make proteins), DNA replication prior to cell division; surrounded by a double membrane called *nuclear envelope (membrane);* the outer membrane connected to rough ER;**
- ***endoplasmic reticulum (ER)*: is a network of folded membranes with large surface to facilitate processes; *rough ER* hosts ribosomes, where the synthesis of proteins occurs; *smooth ER* contains lipid vesicles and is involved in lipid and steroid synthesis; ER also involved in adding carbohydrates to proteins, splicing and folding peptides, and packaging proteins into lipid vesicles for transport to other parts of the cell;**
- ***Golgi apparatus*: similar to smooth ER (folded membrane); functions: processing and packaging of lipids and proteins, breakdown of carbohydrates and lipids;**
- ***vesicles*: small spherical bilayer containers, they fuse with or bud from the plasma membrane; *lysosomes*: vesicles with enzymes lysozymes to break down or digest larger molecules; *peroxisomes*: vesicles that break down long chain fatty acids;**

- ***vacuoles*****: giant vesicles without a particular shape; functions: isolate harmful objects and waste products, help maintain correct hydrostatic pressure;**
- ***ribosomes*****: large complex of proteins, enzymes, and ribosomal RNA (rRNA) found in both prokaryotes and eukaryotes; function: protein synthesis according to the sequence of messenger RNA (mRNA);**
- ***mitohondria*****: membrane-bound organelles, also contain DNA (*****mtDNA*****); function: ATP (adenine triphosphate) synthesis, convert energy stored in food into high energy phosphate bonds of ATP;**
- ***chloroplasts*****: organelles mostly found in plant cells (green parts), carry out photosynthesis (capture light and convert it into chemical bond energy of carbohydrates and ATP);**
- ***cytoskeleton*****: interconnected tube- or rope-like fibrous structures made of proteins; function: to support, transmit, or apply forces, to preserve the shape of the cell and anchor various organelles in place; three types: *****microtubules, intermediate filaments, and microfilaments*****;**
- ***DNA*****: most significant structure inside the cell with genetic material organized in *****chromosomes*****: each chromosome is a single DNA molecule; sometimes DNA is organized into complexes with proteins; all chromosomes in a cell = *****cell's genome*****.**

Life Cycle of an Eukaryotic Cell



What is the goal of biophysics?

(1) Create simplified models of biological systems
(2) Make quantitative predictions
(3) Experimentally test quantitative predictions

DNA models:

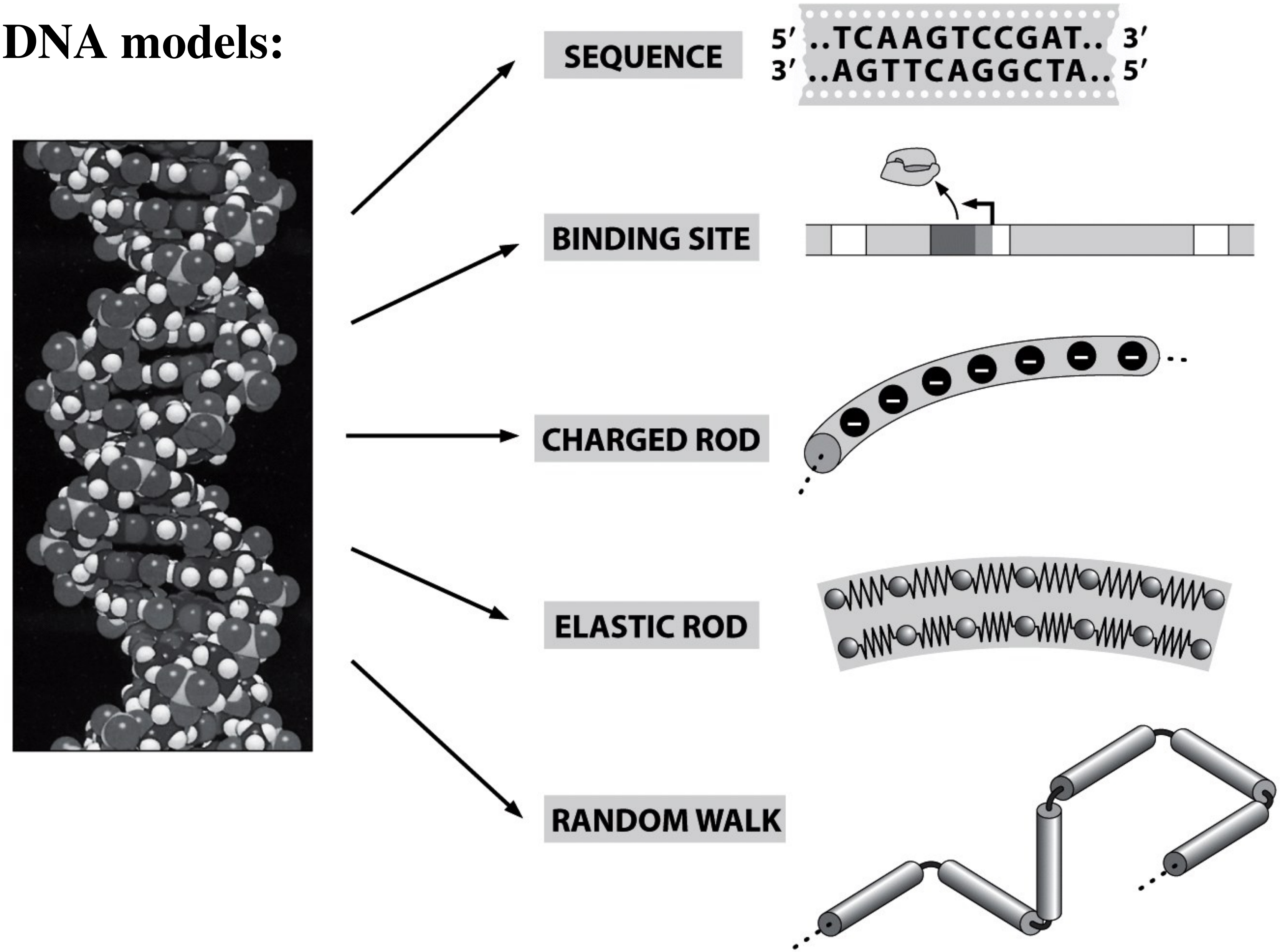


Figure 1.5 Physical Biology of the Cell (© Garland Science 2009)

Protein models:

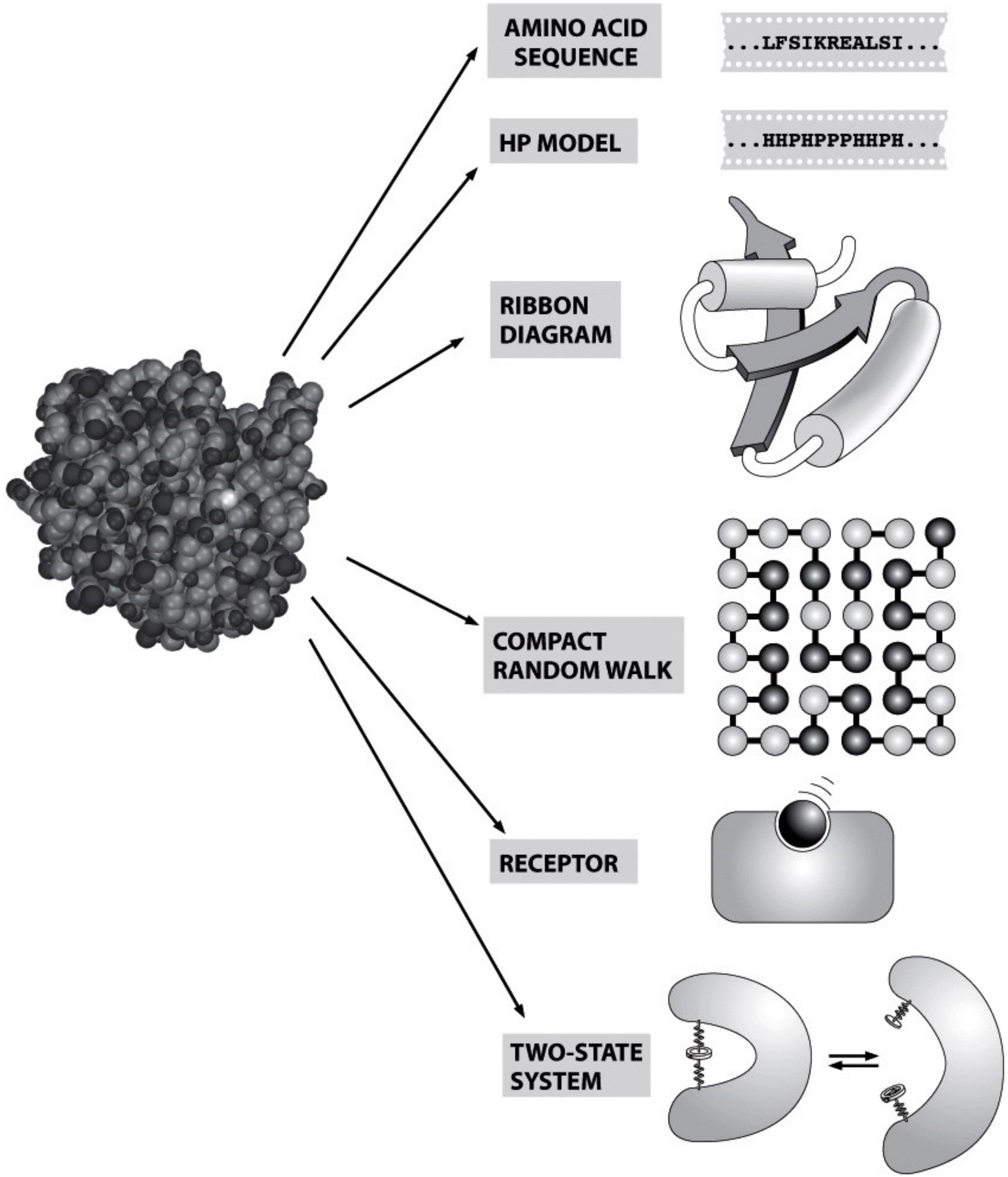


Figure 1.6 Physical Biology of the Cell (© Garland Science 2009)

Membrane models:

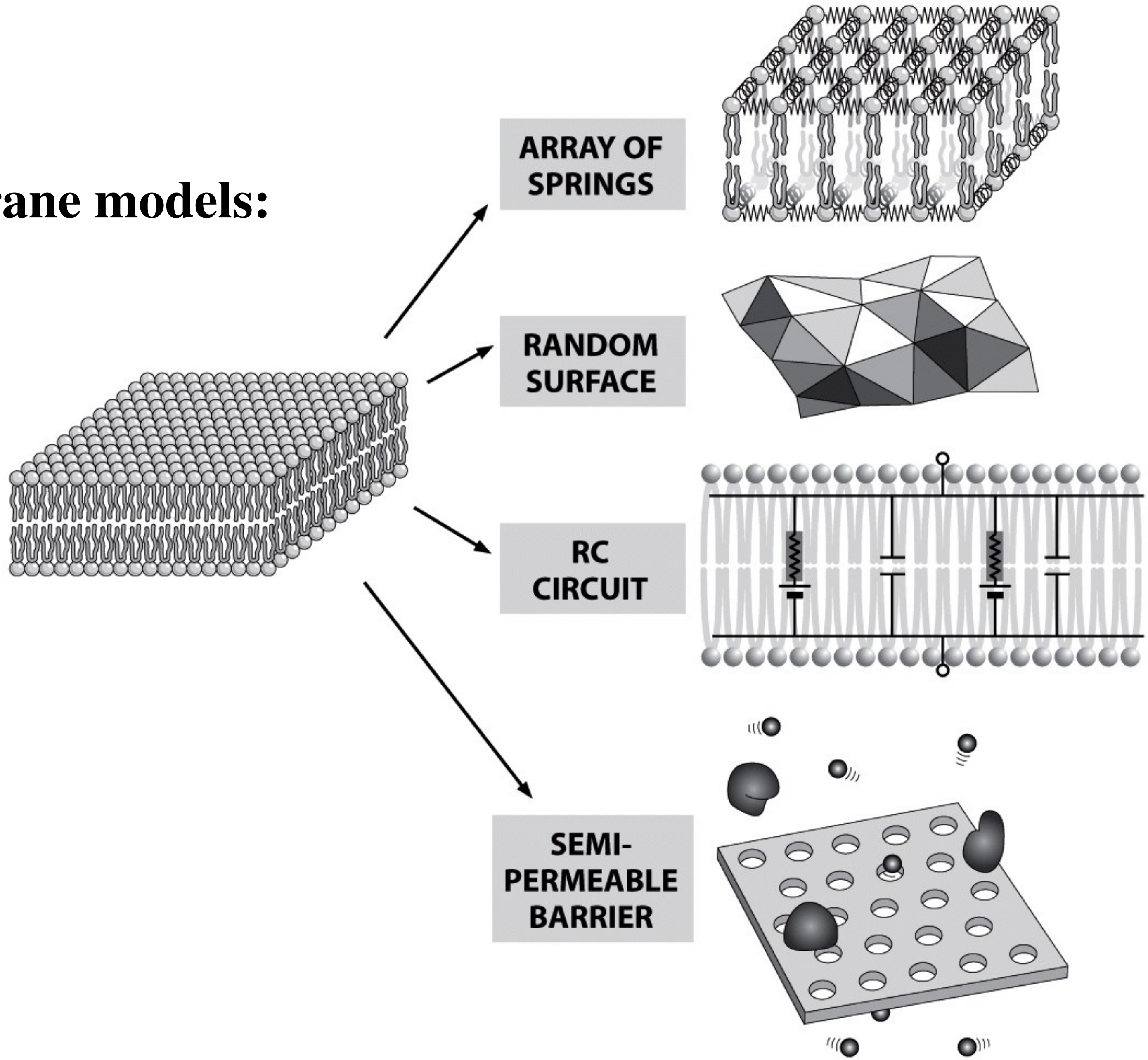


Figure 1.7 Physical Biology of the Cell (© Garland Science 2009)