MOLECULAR BIOLOGY OF
THE CELL
THIRD EDITION

Bruce Alberts • Dennis Bray
Julian Lewis • Martin Raff • Keith Roberts
James D. Watson

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Bruce Alberts received his Ph.D. from Harvard University and is currently President of the National Academy of Sciences and Professor of Biochemistry and Biophysics at the University of California, San Francisco. *Dennis Bray* received his Ph.D. from the Massachusetts Institute of Technology and is currently a Medical Research Council Fellow in the Department of Zoology, University of Cambridge. *Julian Lewis* received his D.Phil. from the University of Oxford and is currently a Senior Scientist in the Imperial Cancer Research Fund Developmental Biology Unit, University of Oxford. *Martin Raff* received his M.D. from McGill University and is currently a Professor in the MRC Laboratory for Molecular Cell Biology and the Biology Department, University College London. *Keith Roberts* received his Ph.D. from the University of Cambridge and is currently Head of the Department of Cell Biology, the John Innes Institute, Norwich. *James D. Watson* received his Ph.D. from Indiana University and is currently Director of the Cold Spring Harbor Laboratory. He is the author of *Molecular Biology of the Gene* and, with Francis Crick and Maurice Wilkins, won the Nobel Prize in Medicine and Physiology in 1962.

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Front cover: The photograph shows a rat nerve cell in culture. It is labeled (*yellow*) with a fluorescent antibody that stains its cell body and dendritic processes. Nerve terminals (*green*) from other neurons (not visible), which have made synapses on the cell, are labeled with a different antibody. (Courtesy of Olaf Mundigl and Pietro de Camilli.)

Dedication page: Gavin Borden, late president of Garland Publishing, weathered in during his mid-1980s climb near Mount McKinley with MBoC author Bruce Alberts and famous mountaineer guide Mugs Stump (1940–1992).

Back cover: The authors, in alphabetical order, crossing Abbey Road in London on their way to lunch. Much of this third edition was written in a house just around the corner. (Photograph by Richard Olivier.)

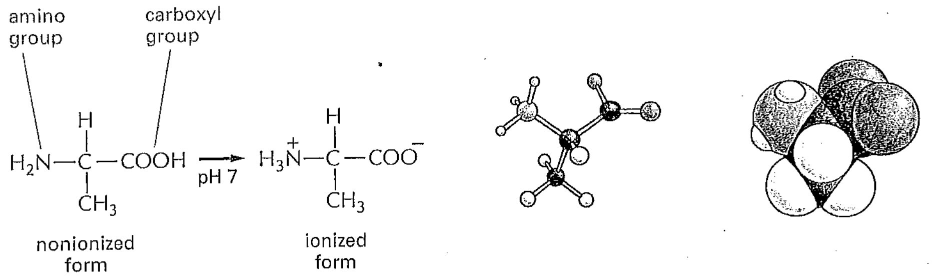


Figure 2–6 The amino acid alanine. In the cell, where the pH is close to 7, the free amino acid exists in its ionized form; but when it is incorporated into a polypeptide chain, the charges on the amino and carboxyl groups disappear. A ball-and-stick model and a space-filling model are shown to the right of the structural formulas. For alanine, the side chain is a $-CH_3$ group.

the hydrophobic tail regions pack together very closely facing the air and the hydrophilic head groups are in contact with the water (Panel 2–4, pp. 54–55). Two such films can combine tail to tail in water to make a phospholipid sandwich, or **lipid bilayer,** an extremely important assembly that is the structural basis of all cell membranes (discussed in Chapter 10).

Amino Acids Are the Subunits of Proteins [5]

The common amino acids are chemically varied, but they all contain a carboxylic acid group and an amino group, both linked to a single carbon atom (called the α-carbon; Figure 2–6). They serve as subunits in the synthesis of **proteins,** which are long linear polymers of amino acids joined head to tail by a *peptide bond* between the carboxylic acid group of one amino acid and the amino group of the next (Figure 2–7). Although there are many different possible amino acids, only 20 are common in proteins, each with a different *side chain* attached to the α-carbon atom (Panel 2–5, pp. 56–57). The same 20 amino acids occur over and over again in all proteins, including those made by bacteria, plants, and animals. Although the choice of these particular 20 amino acids probably occurred by chance in the course of evolution, the chemical versatility they provide is vitally important. For example, 5 of the 20 amino acids have side chains that can carry a charge (Figure 2–8), whereas the others are uncharged but reactive in specific ways (Panel 2–5, pp. 56–57). As we shall see, the properties of the amino acid side chains, in aggregate, determine the properties of the proteins they constitute and underlie all of the diverse and sophisticated functions of proteins.

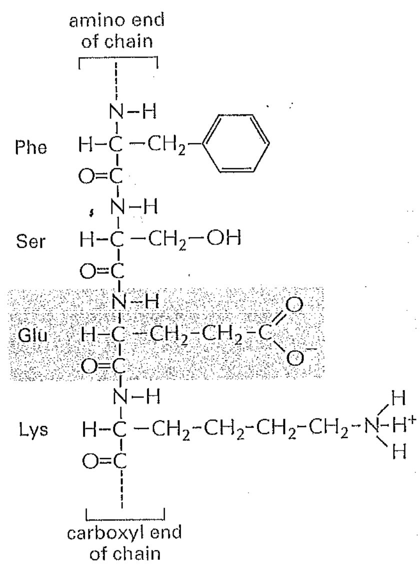


Figure 2–7 A small part of a protein molecule, showing four amino acids. Each amino acid is linked to the next by a covalent *peptide bond*, one of which is shaded *yellow*. A protein is therefore also sometimes referred to as a *polypeptide*. The amino acid *side chains* are shown in *red*, and the atoms of one amino acid (glutamic acid) are outlined by the *gray box*.

Nucleotides Are the Subunits of DNA and RNA [6]

In nucleotides one of several different nitrogen-containing ring compounds (often referred to as *bases* because they can combine with H^+ in acidic solutions) is linked to a five-carbon sugar (either *ribose* or *deoxyribose*) that carries a phosphate group. There is a strong family resemblance between the different nitrogen-containing rings found in nucleotides. *Cytosine* (C), *thymine* (T), and *uracil* (U) are called *pyrimidine* compounds because they are all simple derivatives of a six-membered pyrimidine ring; *guanine* (G) and *adenine* (A) are *purine* compounds, with a second five-membered ring fused to the six-membered ring. Each nucleotide is named by reference to the unique base that it contains (Panel 2–6, pp.58–59).

Nucleotides can act as carriers of chemical energy. The triphosphate ester of adenine, **ATP** (Figure 2–9), above all others, participates in the transfer of energy in hundreds of individual cellular reactions. Its terminal phosphate is added using energy from the oxidation of foodstuffs, and this phosphate can be split off readily by hydrolysis to release energy that drives energetically unfavorable biosynthetic reactions elsewhere in the cell. As we discuss later, other nucleotide derivatives serve as carriers for the transfer of particular chemical groups, such as hydrogen atoms or sugar residues, from one molecule to another. And a cyclic phosphate-

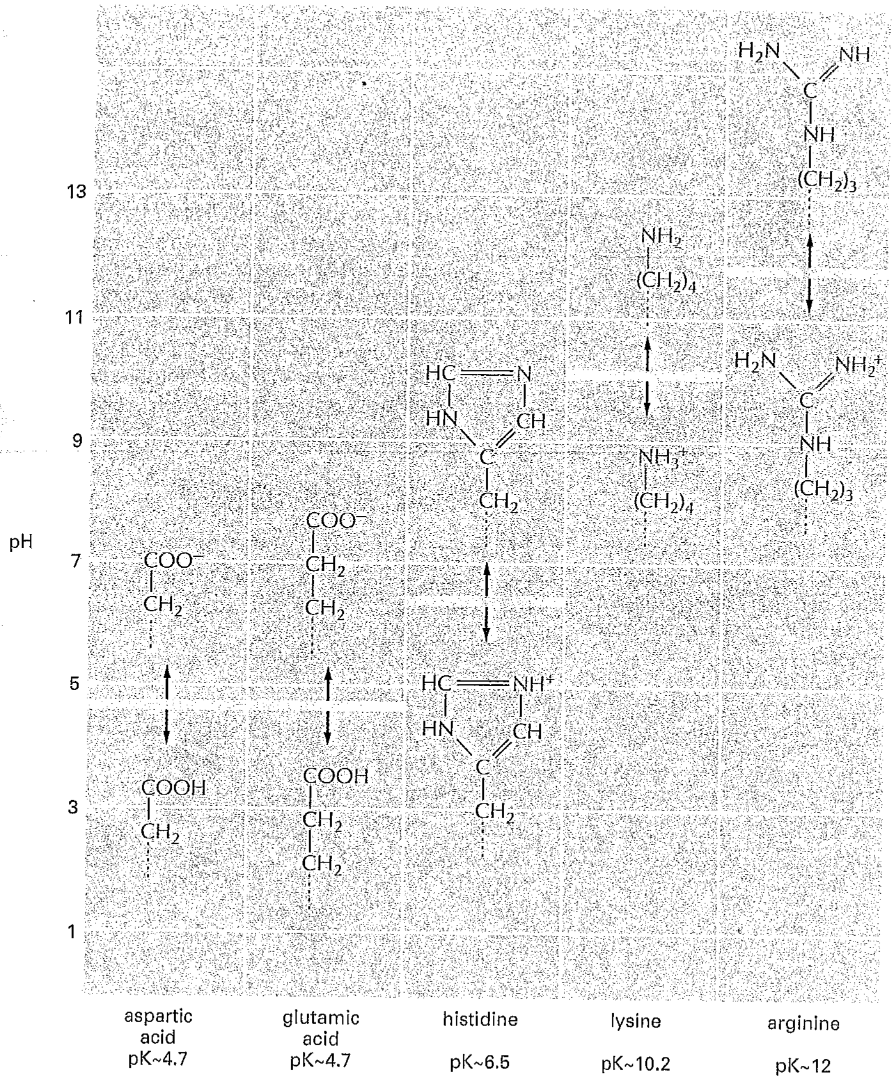


Figure 2–8 The charge on amino acid side chains depends on the pH. Carboxylic acids readily lose H^+ in aqueous solution to form a negatively charged ion, which is denoted by the suffix "-ate," as in aspart*ate* or glutam*ate*. A comparable situation exists for amines, which in aqueous solution take up H^+ to form a positively charged ion (which does not have a special name). These reactions are rapidly reversible, and the amounts of the two forms, charged and uncharged, depend on the pH of the solution. At a high pH, carboxylic acids tend to be charged and amines uncharged. At a low pH, the opposite is true—the carboxylic acids are uncharged and amines are charged. The pH at which exactly *half* of the carboxylic acid or amine residues are charged is known as the pK of that amino acid side chain.

In the cell the pH is close to 7, and almost all carboxylic acids and amines are in their fully charged form.

containing adenine derivative, *cyclic AMP,* serves as a universal signaling molecule within cells.

The special significance of nucleotides is in the storage of biological information. Nucleotides serve as building blocks for the construction of **nucleic acids,** long polymers in which nucleotide subunits are covalently linked by the formation of a phosphate ester between the 3′-hydroxyl group on the sugar residue of one nucleotide and the 5′-phosphate group on the next nucleotide (Fig-

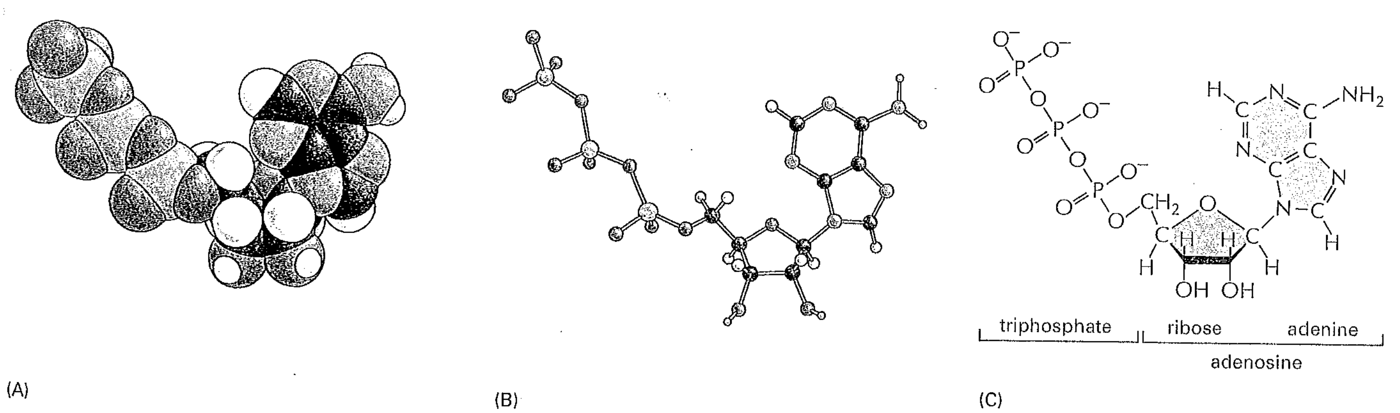
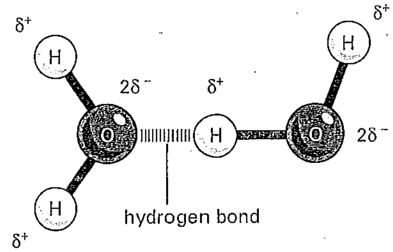


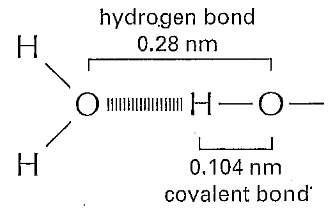
Figure 2–9 Chemical structure of adenosine triphosphate (ATP). A space-filling model (A), a ball-and-stick model (B), and the structural formula (C) are shown. Note the negative charges on each of the three phosphates.

HYDROGEN BONDS

Because they are polarized, two adjacent H_2O molecules can form a linkage known as a hydrogen bond. Hydrogen bonds have only about 1/20 the strength of a covalent bond.



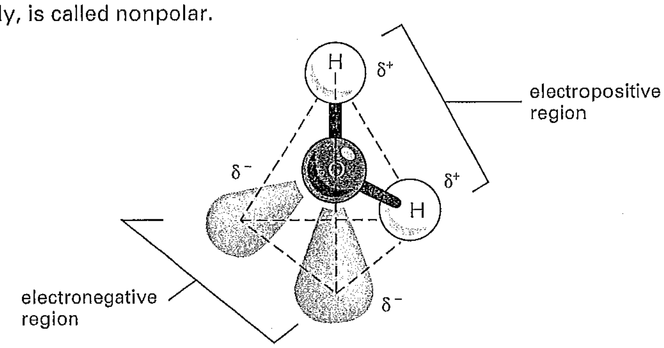
bond lengths



Hydrogen bonds are strongest when the three atoms lie in a straight line.

WATER

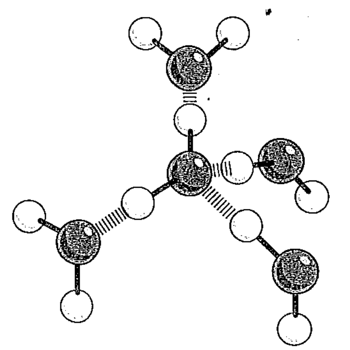
Two atoms, connected by a covalent bond, may exert different attractions for the electrons of the bond. In such cases the bond is dipolar, with one end slightly negatively charged (δ^-) and the other slightly positively charged (δ^+). A bond in which both atoms are the same, or in which they attract electrons equally, is called nonpolar.



Although a water molecule has an overall neutral charge (having the same number of electrons and protons), the electrons are asymmetrically distributed, which makes the molecule polar. The oxygen nucleus draws electrons away from the hydrogen nuclei, leaving these nuclei with a small net positive charge. The excess of electron density on the oxygen atom creates weakly negative regions at the other two corners of an imaginary tetrahedron.

WATER STRUCTURE

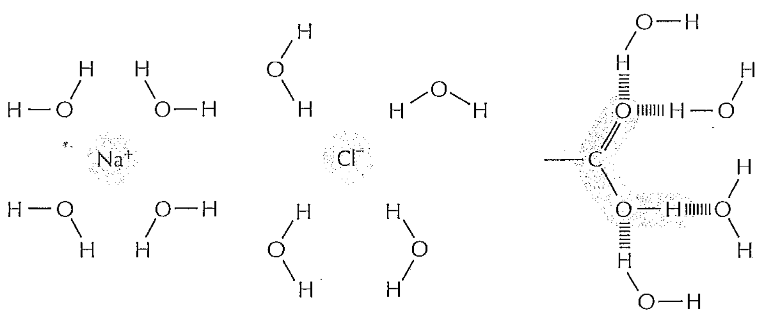
Molecules of water join together transiently in a hydrogen-bonded lattice. Even at 37°C, 15% of the water molecules are joined to four others in a short-lived assembly known as a "flickering cluster."



The cohesive nature of water is responsible for many of its unusual properties, such as high surface tension, specific heat, and heat of vaporization.

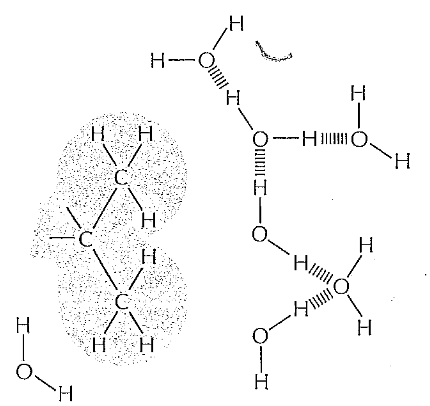
HYDROPHILIC AND HYDROPHOBIC MOLECULES

Because of the polar nature of water molecules, they will cluster around ions and other polar molecules.



Molecules that can thereby be accommodated in water's hydrogen-bonded structures are hydrophilic and relatively water-soluble.

Nonpolar molecules interrupt the H-bonded structure of water without forming favorable interactions with water molecules. They are therefore hydrophobic and quite insoluble in water.



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