1

An Overview of the Cell

All organisms are composed of cells. Some organisms, like an amoeba or a bacterium, consist of a single cell (unicellular organisms). Plants and animals consist of a few hundred to many trillions of cells (multicellular organisms). The structures common to cells and the molecular principles on which cells operate are described in this chapter. The structures and functions of cells are prescribed by genes contained in the DNA molecules of chromosomes. The genetic information in DNA is transcribed into RNA molecules, which in turn are translated into protein molecules. Protein molecules are the principal molecules that prescribe cell structures and functions. Cells duplicate by growing and replicating the DNA in their chromosomes. They distribute the duplicated copies of chromosomes (DNA) to daughter cells, which form by pinching of a cell into two cells.

1.1 Cells

The foundations of cell biology were established in the nineteenth century with two major precepts: all organisms, from the simplest to the most complex, are composed of cells, and all cells arise by the division of preexisting cells. Many millions of kinds of organisms, like bacteria and protozoa, are composed of single cells; hence the term single-celled, or unicellular organisms. Many other species are multicellular, in some cases consisting of a few hundred cells; others are formed of trillions (10^{12}) of cells. For example, an adult human contains more than 10^{14} cells, all derived by a huge number of cell divisions from one initial cell, the fertilized ovum. Cells in the human body are constantly dying and are replaced by more than 25×10^6 cell divisions per second (producing more than 2×10^{12} cells every 24 hours). The many different structural/functional types of cells in a human body are all genetically identical, i.e., contain precisely the same DNA sequences. The differences are created by activating various combinations of genes among the 30,000 or so genes that are common to every cell in the body.

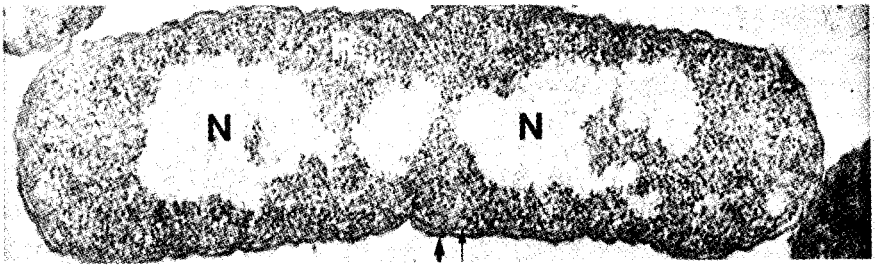
Evolution has given rise to the millions of genetically different organisms that populate the Earth. The number of these contemporary species is not known, but identifications of organisms by analysis of their DNA makes it clear that there are far more species than previously estimated, probably many hundreds of millions. The populations of species is in flux over evolutionary time, with new species arising by genetic (DNA) changes and older species becoming extinct. Our perception of the Earth's organismic population is skewed by the presence of species of multicellular organisms, which strongly tend to dominate our field of view. Vastly more species, occupying a great myriad of microenvironments, make up the unicellular organisms, and evolution is probably a more robust process among these creatures.

In spite of the great genetic diversity that underlies the different species, all organisms, unicellular and multicellular, operate on the basis of the same set of molecular principles. For example, genes in all cells consist of DNA sequences, which when activated are transcribed in RNA molecules. RNA molecules are then translated into protein molecules. Differences among cell species rest on structural/functional differences in proteins prescribed by the different combinations of genes in the different species. As discussed later in this chapter, the number of possible genes, and hence the number of possible different organisms, is enormous.

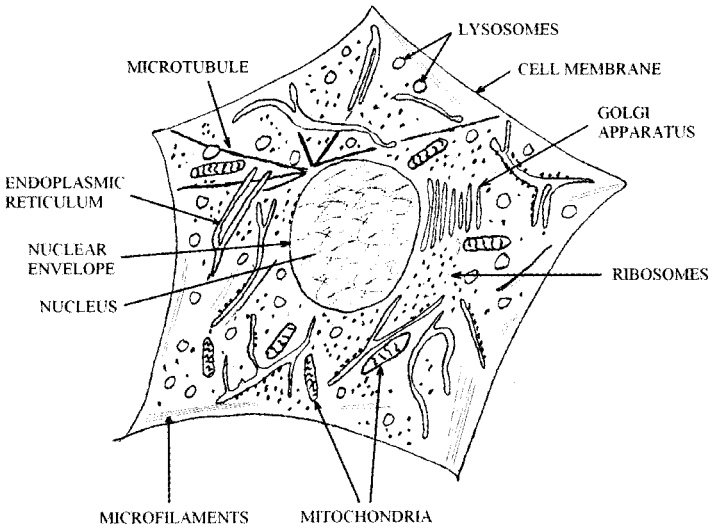
All cells belong to one of two classes: (1) bacteria, which are all unicellular, do not have a membranous envelope around their chromosome(s) to separate them from the rest of the cell, the cytoplasm; (2) eukaryotes (eu=true, karyote=nucleus), which include both unicellular and multicellular organisms, have the chromosomes aggregated into a body surrounded by a membranous envelope built of molecules called lipids – thus this envelope forms a structurally well-defined cell nucleus.

The remainder of this chapter concerns those elements and principles that are common to the structure and function of cells. Note that structures in cells are composed of combinations of proteins, lipids, and nucleic acids. A protein is a macromolecule (a polymer composed of thousands of atoms) consisting typically of several hundreds of small molecules (monomers composed of tens of atoms) called amino acids. There are 20 different amino acids in proteins. There are two kinds of nucleic acids: DNA (deoxyribonucleic acid) and RNA (ribonucleic acid). DNA is built from monomers called nucleotides, which are of four kinds, designated as A, T, G, and C, standing for *adenine, thymine, guanine*, and *cytosine*, respectively. RNA is also built from nucleotides, again of four kinds, A, U, G, and C, where U stands for *uracil*. Note that A, G, and C are found in both, but DNA contains T's and RNA contains U's instead of T's. By interacting, these large molecules form stable, specific aggregates, which then accomplish one or another function.

Figure 1.1a contains a diagram of the generalized structure of a bacterial cell and of a eukaryotic cell. Bacterial cells (Fig. 1.1a) are structurally rather simple, consisting of a cell membrane, ribosomes, a nucleoid or chromatin body containing the chromosome(s), and the cytoplasmic fluid that fills the



(a)



(b)

Fig. 1.1. a A section through a bacterial cell (*E. coli*) observed with an electron microscope. The cell is enclosed by a wall (*thick arrow*). The plasma membrane (*thin arrow*) is just inside the cell wall. The granular appearance is due to ribosomes (*R*). The lighter regions are portions of the nucleoid (*N*) which is separating into two parts. The cell is about to divide, as indicated by the slight indentation of the cell wall in the middle of the cell. Courtesy of N. Nanninga [40]. **b** Diagram of a generalized eukaryotic cell. In addition to the structures shown, all of which are present in almost all eukaryotic cell types, some cell types contain other structures, such as chloroplasts (plant and algal cells), fat vacuoles (fat cells), cilia (protozoans and bronchial lung cells), a flagellum (sperm cells), food vacuoles, and so on.

cell. Some bacterial species possess flagella, which give the cell swimming ability. Bacterial cells are generally no more than a few microns in their longest dimension. Eukaryotic cells (Fig. 1.1b) are structurally more complex and larger — ranging from a few microns to hundreds of microns in their longest dimension. They consist of a cell membrane, a well-defined nucleus containing the chromosomes and delineated by a membranous envelope, ribosomes, cytoplasmic fluid, and a series of membranous structures in the cytoplasm, principally the endoplasmic reticulum, the Golgi apparatus, and lysosomes. They also contain two kinds of fiber: microtubules and microfilaments. In addition, some eukaryotic cells are endowed with other structures such as a tough cell wall (e.g., fungi and plant cells), cilia or flagella for motility, lipid droplets in the cytoplasm, etc. We consider here only those structures common to all eukaryotic cells.

1.2 Major Components of Eukaryotic Cells

The Cell Membrane

A cell is enclosed by a thin membrane composed of lipid and protein molecules. This membrane keeps the cell intact, acting as a barrier that retains ions, molecules, and structures within the cell and excludes substances in their microenvironment. The cell membrane also acts to regulate traffic of certain molecules and ions in and out of the cell. For example, some proteins within the cell membrane work as pumps to bring glucose and other nutrients into a cell and to carry inorganic ions out, generally maintaining the physiological health and balance in the intracellular environment.

The Ribosome

A ribosome is a roughly spherical particle that is too small to see in a light microscope but is clearly visible in the cytoplasm by electron microscopy. A small cell like the bacterium *E. coli* contains more than 20,000 ribosomes. Larger eukaryotic cells may each possess 100,000 or more ribosomes. An individual ribosome consists of about 50 different protein molecules and several RNA molecules (called rRNA molecules). The rRNA molecules provide a scaffold for assembly of the protein molecules arranged in a specific pattern. The entire aggregate, guided by the nucleotide sequences in messenger RNA (mRNA) molecules adhering to the ribosome, assembles amino acids into all the different proteins in a cell, a cytoplasmic process called translation (of mRNA). The many different mRNA molecules are synthesized on DNA templates (genes) in the nucleus (a process called transcription) and then migrate to the cytoplasm to attach to ribosomes.

The Mitochondrion

Mitochondria are membranous organelles present in the cytoplasm of eukaryotic cells. The membranes of mitochondria are composed of lipid molecules and a specific spectrum of protein molecules, which, in concert with proteins dissolved in the fluid phase of the mitochondrion, carry out the terminal part of the breakdown of fuel molecules like glucose to produce adenosine triphosphate (ATP). ATP is the energy molecule used to drive all of the biosynthetic and other activities (e.g., cell motility) of the cell.

The Endoplasmic Reticulum

The endoplasmic reticulum (ER) is an extensive system of membranes in the cytoplasm of eukaryotic cells. The lipid and protein molecules that make up the ER membranes perform various metabolic functions, including the transfer of newly synthesized proteins from ribosomes to the Golgi apparatus (see the next paragraph).

The Golgi Apparatus

The Golgi apparatus consists of a stack of flattened membranous sacs in the cytoplasm of eukaryotic cells. It receives various proteins from the ER, modifies certain of these proteins, e.g., by appending particular sugar molecules to them, and packages the proteins into vesicles for delivery to various other intracellular destinations or for excretion from the cell.

Microtubules and Microfilaments

Microtubules are long tubular structures in the cytoplasm, visible only by electron microscopy, composed of thousands of molecules of a single kind of protein. Microfilaments are long cytoplasmic rodlike filaments, visible only by electron microscopy, composed of thousands of molecules of another kind of protein. Both microtubules and microfilaments often occur in bundles, and both are major elements of the skeletal framework of the eukaryotic cell. They both have roles in cell movement, e.g., the flowing of cytoplasm as occurs in amoeboidlike movement, the movement of chromosomes during cell division, and the contraction that cleaves a cell in two in cell division.

The Lysosomes

The cytoplasm of eukaryotic cells possesses numerous membrane-bound vesicles called lysosomes. Lysosomes contain a variety of digestive enzymes (proteins) that break down large molecules that may have been ingested by a cell. For example, many protozoans (like an amoeba or a ciliate) make a living by

ingesting other microorganisms, both bacteria and eukaryotes, a process called phagocytosis. These ingested food organisms are enveloped in an infolding of the cell membrane to form a vesicle, called a food vacuole. Lysosomes fuse with the food vacuoles, and the lysosomal enzymes break down the proteins, nucleic acids, and lipids of the food organism into smaller molecules, which fuel the metabolism of the cell. Phagocytosis is a major mechanism by which white blood cells ingest and destroy (by means of lysosomal enzymes) bacteria that may have infected a multicellular animal, e.g., a human.

The Cytoplasmic Solution

The structures in the cytoplasm are immersed in a cytoplasmic solution or broth containing a broad spectrum of chemical components, protein molecules, inorganic ions (Ca^{++}, Na^{+}, K^{+}, Cl^{-}, PO_4^{-}, etc.), sugar molecules, amino acids, nucleotides, and many other small organic molecules. These dissolved components support many functions, e.g., amino acids and nucleotides serve as precursor units in the synthesis of proteins and nucleic acids (DNA and RNA), respectively. An important role of the cytoplasmic solution is the coordination and integration of the activities of the structures in the cell, including the nucleus.

These are the major components of eukaryotic cells, although there are numerous other structures and molecular elements that perform specialized functions in a variety of eukaryotic cell types, e.g., cilia, which are hairlike projections in the cell surface that beat in synchronous rhythm to propel a cell through its aqueous environment. Cilia (singular=cilium) are a defining characteristic of a large group of unicellular protozoan species known as ciliates. Ciliates are described in more detail Chap. 2. Much of this book is based on the genetic processes in ciliates.

1.3 Chromosome Structure

Chromosomes are extremely long threadlike structures that contain the DNA molecules of the cell. They form a tangled meshwork in the cell nucleus, making it impossible to discern individual chromosomes even by electron microscopy. However, transiently during cell division chromosomes condense into short thick rods that can be seen even in a light microscope. In this condensed form the chromosomes are distributed to the two daughter cells during cell division, after which they return to their indiscernible, decondensed state. Chromosomes contain the genes in a cell, and in that sense represent the master blueprint for all cell structures and operations. The number of chromosomes, each with its different collection of genes, is characteristic of a cell species. A fruit fly cell has 4 chromosomes, a human cell has 23 different chromosomes, and one species of amoeba has several hundred.

The central element of a chromosome is a single enormously long DNA molecule. Recall that a DNA molecule is a polymer consisting of monomers, called nucleotides. These building blocks are joined together in a long chain (Fig. 1.2a). The nucleotides are of four types, designated A, T, G, and C. Each nucleotide is, in turn, made up of three molecules: a sugar molecule (deoxyribose sugar denoted by S), a phosphate group (P), and a base. The four different nucleotides differ only in their bases, designated A, T, G, and C, giving the nucleotides their names. In a DNA strand the nucleotides are joined in chain fashion through connections between their sugar–phosphate portions (Fig. 1.2b), leaving the bases projecting from the side of the sugar–phosphate backbone.

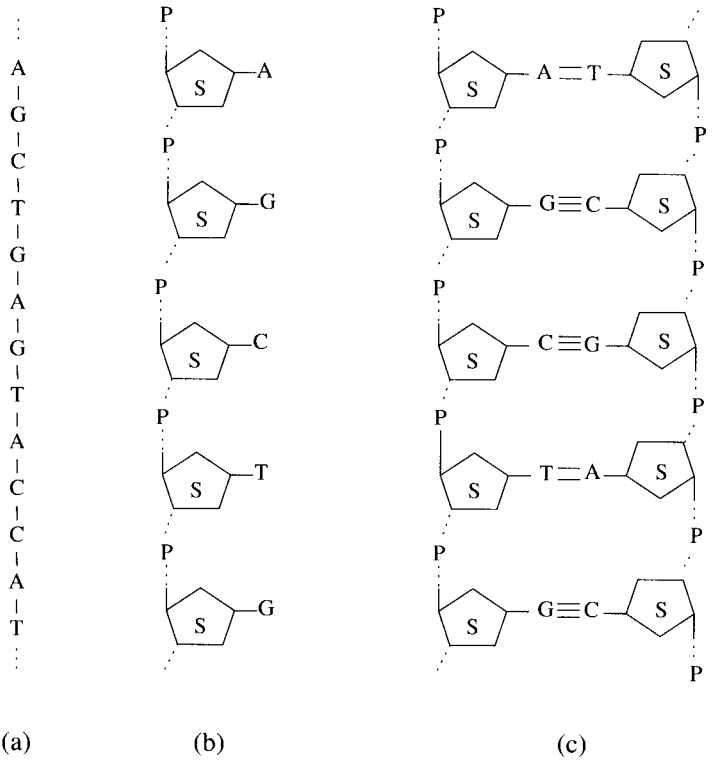


Fig. 1.2. **a** A strand of A, T, G, and C nucleotides in a DNA molecule. **b** A segment of a DNA strand. Nucleotides in DNA are joined to form very long strands by connections between the sugar (S) and phosphate (P) groups in each nucleotide. The bases (A, T, G, and C) in the nucleotides project to the side of the strand. **c** A segment of a DNA double helix. Two nucleotide strands bind to each other by forming base pairs between A and T and between G and C. The two strands are shown here in a simple parallel arrangement. In a double helix the two chains twist around one another in a helical fashion.

The DNA molecule in a chromosome of a bacterium or eukaryotic cell consists, in fact, of two DNA strands wound around each other in helical fashion, forming what is commonly referred to as a DNA double helix or duplex (Fig. 1.2c). The two strands in a duplex interact with each other through binding of the bases in one strand with the bases in the other strand. These interactions of the bases are highly specific, being dictated by the different chemical structures of the four bases. Thus, wherever an A occurs in one strand, it is bound to a T in the other strand; wherever a G occurs in a chain, it is paired with a C in the opposite strand. Each of these A to T (or T to A) and G to C (or C to G) couplings of nucleotides through their bases is called a base pair, and the two DNA strands in a double helix are said to be complementary to one another.

DNA double helices vary in length from chromosome to chromosome; the longest DNA helix among the 23 different chromosomes in a human cell is made up of $\sim 3 \times 10^8$ nucleotides, which is about 10 cm long. Altogether the 23 chromosomes contain more than one meter of DNA; all of this is packed into a spherical nucleus 8 to 10 microns (10^{-6} m) in diameter.

Genes

A gene is a specific sequence of base pairs in a DNA double helix. A gene specifies the sequence of amino acids that is assembled into a chain to make a protein. How this is done is discussed in this section under gene function. The length of a gene depends on the number of amino acids in the particular protein it specifies, and the gene lengths vary over a broad range. On average a gene consists of a segment of 1,000 base pairs in a DNA double helix, and there are many genes in the single DNA molecule in a chromosome. The beginning and end of a gene within a DNA double helix are marked by triplets of nucleotides in one of the two DNA strands; this strand is called the sense strand of the duplex, and the complementary strand is called the antisense strand. The trinucleotide ATG designates the start of every gene, and any one of three different trinucleotides, TGA, TAA, and TAG, specifies the end. These four trinucleotides may be thought of as punctuation marks in a double helix, marking the beginnings and ends of genes in a very long DNA double helix.

Individual genes are separated from one another along DNA by long stretches of nongene DNA base pair sequence that forms spacers between successive genes (Fig. 1.3). Typically, less than 5% of a DNA molecule encodes genes; more than 95% makes up the spacers. Often, spacer DNA is referred to as junk DNA because it has no known function other than separating successive genes in a chromosome by wide distances. If and why such wide separation of genes is in some way important is not known. Nevertheless, a single DNA double helix in a eukaryotic cell may contain many hundreds of genes; the 23 DNA double helices in a human cell contain a total of about 30,000 genes.

Fig. 1.3. The arrangement of genes along a segment of eukaryotic chromosomal DNA. Less than 5% of the DNA molecule encodes genes. Most of the DNA molecule acts as spacers between successive genes.

Diploidy

Most species of eukaryotic cells are diploid that is, each cell contains two copies of every chromosome. For example a human cell has 23 different chromosomes but two copies of each, for a total of 46. One set of 23 was derived from the female parent (an ovum has 23 chromosomes), and one set of 23 from the male parent (a sperm carries 23 chromosomes). Fertilization of an ovum by a sperm creates a cell (the fertilized ovum) with 46 chromosomes, and the vast majority of cells in the body are diploid (the exceptions are ova and sperm cells). Mating can occur between two unicellular organisms that belong to the same species. The process is essentially the same as in multicellular organisms like the human. Mating of unicellular organisms is explained in Chap. 2 about ciliates.

Gene Function

A gene exerts its role in a cell through the protein that it encodes, i.e., proteins are the metabolically active molecules in a cell because of their catalytic and regulatory properties. The DNA sequence in a gene prescribes the sequence of amino acids in the protein that the gene encodes by means of two steps: transcription and translation.

In transcription, the DNA in the gene guides in template fashion the synthesis of an RNA molecule, called a messenger, or mRNA molecule. This is accomplished by transient separation of the two strands in the DNA of the gene. The antisense strand serves as a template to assemble an mRNA molecule using base-pairing rules (Fig. 1.4). Wherever a T occurs in the antisense strand of the gene, an A is added to the mRNA molecule. G is similarly matched by C, and C is matched by G. However, an A in the gene designates a U in the mRNA. In effect, the antisense strand of the gene is complementary to the single-stranded mRNA molecule, except that T is substituted by U in mRNA. The T and U nucleotides are chemically very similar. Thus the sequence of nucleotides in the mRNA is identical to the sense strand of the gene, with the exception that the T's in DNA are substituted with U's in the mRNA. All of this happens very quickly, with many nucleotides per second added to the growing mRNA molecule. These additions are catalyzed by an enzyme (a protein) called RNA polymerase.

Completed mRNA molecules (after several modifications) are then transported to the cytoplasm, where they bind to ribosomes for translation. In

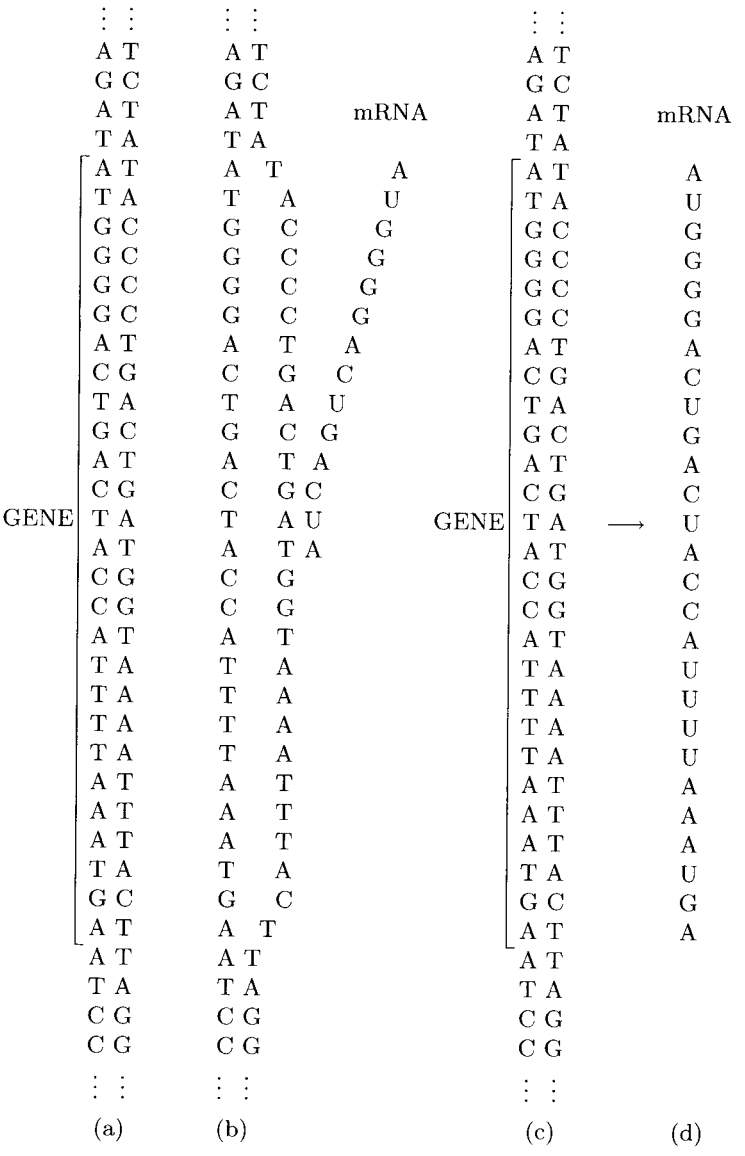


Fig. 1.4. a–d Transcription of a gene into an mRNA molecule: **a** A gene in a DNA duplex. The gene begins with ATG and ends in TGA (stop). **b** The two strands of DNA in the gene have separated, and the antisense strand is serving as a template for assembling an mRNA molecule. The mRNA is only partially formed, separating from its template as it is synthesized. Note that T's in DNA are substituted by U's in mRNA. **c** Transcription has finished and the DNA of the gene has returned to its duplex state. **d** The finished mRNA molecule. Note that the TGA (stop) in the gene is not transcribed into the mRNA molecule.

translating mRNA the ribosome begins with the AUG (equivalent to the ATG at the beginning of the sense strand in the DNA of a gene). The ribosome translates the AUG as the amino acid methionine. Thus, all amino acid chains of proteins begin with methionine. The ribosome moves to the next three nucleotides in the mRNA, interprets them as one of the other 19 amino acids, and joins that amino acid to the methionine. The ribosome translates each successive trinucleotide as a particular amino acid, adding to the growing amino acid chain. Finally, at the end of the mRNA the ribosome encounters UGA, UAA, or UAG and translates this as "stop" and releases the finished amino acid chain (protein). As a ribosome leaves the AUG site and progresses along the mRNA, another ribosome binds to AUG at the beginning of the mRNA; thus, multiple ribosomes are translating the mRNA at any one time, producing multiple identical copies of the particular protein product.

Table 1.1. The genetic code table

First position (5′ end)	**Second position**				**Third position (3′ end)**
	U	C	A	G	
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	Stop	Stop	A
	Leu	Ser	Stop	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

The trinucleotides in the mRNA (or in the sense strand) of the DNA of the gene that prescribe one or another of the 20 amino acids are called codons. Thus, a gene consists of a succession of codons that the cell reads, via mRNA, into a sequence of amino acids. The four bases, A, T, G, and C (or A, U, G, and C in the mRNA), can be combined into 64 different trinucleotide codons. Three of these codons, ATG (AUG in mRNA), TGA (UGA in mRNA), and TAA (UAA in mRNA), are used to define the end of a gene (or the mRNA), and one codon, ATG (AUG in mRNA), defines the amino acid methionine at the beginning of a gene. The remaining 60 triplet codons are unevenly divided among the other 19 amino acids, e.g., the amino acid tryptophan is designated by one codon, isoleucine is designated by three different codons in a gene, and arginine is designated by six different codons; see the genetic code table (Table 1.1), and the table of amino acid names and their three letter abbreviations (Table 1.2). An example of a protein encoded by the sequence of codons of a gene is given in Fig. 1.5.

Table 1.2. The 20 amino acids and their three-letter abbreviations

Name	3-letter abbreviation	Name	3-letter abbreviation
Alanine	Ala	Leucine	Leu
Arginine	Arg	Lysine	Lys
Asparagine	Asn	Methionine	Met
Aspartic acid	Asp	Phenylalanine	Phe
Cysteine	Cys	Proline	Pro
Glutamine	Gln	Serine	Ser
Glutamic acid	Glu	Threonine	Thr
Glycine	Gly	Tryptophan	Trp
Histidine	His	Tyrosine	Tyr
Isoleucine	Ile	Valine	Val

In summary, through gene expression, i.e., the process of transcription and translation, the many hundreds of different proteins needed to form the structures and support the metabolism in a cell are continuously produced.

1.4 Chromosomes and Genes

Cells reproduce by cell division. In order to divide, a cell must first increase in size so that two daughter cells of adequate size can be produced. A major

amino acids	*Met Ala Gly Arg Gly Lys Val Gly Lys Gly Tyr*
sense strand	ATG GCC GGA AGA GGT AAA GTT GGA AAA GGA TAC →
antisense strand	TAC CGG CCT TCT CCA TTT CAA CCT TTT CCT ATG →
amino acids	*Gly Lys Val Gly Ala Lys Arg His Thr Lys Lys*
sense strand	GGA AAG GTT GGT GCC AAG AGA CAC ACC AAG AAG →
antisense strand	CCT TTC CAA CCA CGG TTC TCT GTG TGG TTC TTC →
amino acids	*Ser Leu Lys Glu Thr Ile Met Gly Ile Thr Lys*
sense strand	TCA CTC AAG GAG ACT ATC ATG GGA ATC ACC AAG →
antisense strand	AGT GAG TTC CTC TGA TAG TAC CCT TAG TGG TTC →
amino acids	*Pro Ala Ile Arg Arg Leu Ala Arg Gly Gly Val*
sense strand	CCA GCA ATC AGA AGA CTC GCC AGA GGT GGT GTC →
antisense strand	GGT CGT TAG TCT TCT GAG CGG TCT CCA CCA CAG →
amino acids	*Lys Arg Ile Ser Ser Leu Ile Tyr Glu Glu Thr*
sense strand	AAG AGA ATC TCA TCC CTC ATC TAT GAG GAG ACC →
antisense strand	TTC TCT TAG CGT AGG GAG TAG ATA CTC CTC TGG →
amino acids	*Arg Asp Val Leu Arg Ser Phe Leu Glu Asn Val*
sense strand	AGA AAC GTC CTC AGA TCA TTC CTC GAG AAC GTT →
antisense strand	TCT TTG CAG GAG TCT AGT AAG GAG CTC TTG CAA →
amino acids	*Ile Arg Asp Ser Val Thr Tyr Thr Glu His Ala*
sense strand	ATC AGA GAT TCA GTC ACC TAC ACT GAA CAC GCC →
antisense strand	TAG TCT CTA AGT CAG TGG ATG TGA CTT GTG CGG →
amino acids	*Lys Arg Lys Thr Val Thr Ala Leu Asp Val Val*
sense strand	AAG AGA AAG ACC GTC ACC GCT CTC GAC GTC GTC →
antisense strand	TTC TCT TTC TGG CAG TGG CGA GAG CTG CAG CAG →
amino acids	*Tyr Ala Leu Lys Arg Gln Gly Arg Thr Leu Tyr*
sense strand	TAC GCT CTT AAG AGA CAA GGA AGA ACC CTC TAC →
antisense strand	ATG CGA GAA TTC TCT GTT CCT TCT TGG GAG ATG →
amino acids	*Gly Phe Gly Gly Stop*
sense strand	GGA TTC GGT GGA TGA
antisense strand	CCT AAG CCA CCT ACT

Fig. 1.5. The gene encoding a small protein called histone H4. The sense strand containing the code for the protein is in the *middle*, and the complementary strand is immediately *below* it. The sense strand begins with the three nucleotides ATG, which specifies methionine, and ends with TGA, which means stop, or period. The amino acid chain specified by successive groups of three nucleotides (trinucleotide codons) is shown *above* the DNA double helix.

part of this growth is the synthesis of protein molecules as just described in Sect 1.3. Another essential preparation for cell division is the duplication of the chromosomes so that each daughter cell can receive a full diploid set of chromosomes. In other words, each DNA double helix in every chromosome must first be duplicated if a cell is to divide successfully.

The duplication of DNA molecules is referred to as DNA replication. DNA replication is similar to transcription of DNA in the sense that the DNA serves as a template for making new nucleotide strands, in this case new DNA strands. As in transcription, the two strands in a DNA double helix separate from one another, and the resulting two single strands each serve as a template to guide the polymerization of nucleotides into a complementary strand (Fig. 1.6). The two new complementary strands formed along each of the two template strands remain bound to their template strands, forming in this way two daughter double helices in which one strand in each double helix comes from the original double helix and one strand has been newly synthesized. Of course, the two daughter double helices are identical to each other in nucleotide sequences, and therefore contain precisely the same genes, and are identical to the original parental double helix.

The actual mechanism of DNA replication is a little more complex because the two strands in a double helix have polarities in their sugar–phosphate backbones (Fig. 1.7). In the backbone a phosphate group links the number 3 carbon atom in one sugar (a deoxyribose sugar with five carbon atoms) to the number 5 carbon in the next sugar molecule. One can think of the backbone as sugar molecules linked by phosphate groups through their number 3 and number 5 carbon atoms:

$$C_5\,S\,C_3 - P - C_5\,S\,C_3 - P - C_5\,S\,C_3 - P - C_5\,S\,C_3 - P - \ldots - C_5\,S\,C_3\ .$$

Thus, a DNA strand has a C_5 at one end and a C_3 at the other end; these are called the $5'$ and $3'$ ends (see Fig. 1.7). In a double helix the two DNA strands have opposite polarities, i.e., at the end of a double helix one strand ends in $5'$ and the other in $3'$, as clearly shown in Fig. 1.7. In DNA replication new strands grow continuously by adding nucleotides to a C_3 of a sugar. Adding nucleotides to the $5'$ end is more involved.

Typically, DNA replication in a eukaryotic cell takes several hours. During this time the cell is also growing, increasing all its cytoplasmic components. With the completion of DNA replication and cell growth, the cell undergoes division, producing two genetically identical daughter cells, each of which grows, replicates its DNA, and ultimately divides. Cell division consists of two coordinated events: division of the nucleus, called mitosis, and division of the cytoplasm, called cytokinesis.

Mitosis and Cytokinesis

Mitosis begins with the condensation of all the replicated chromosomes into short, thick rods that, in most species, are clearly visible in the light mi-

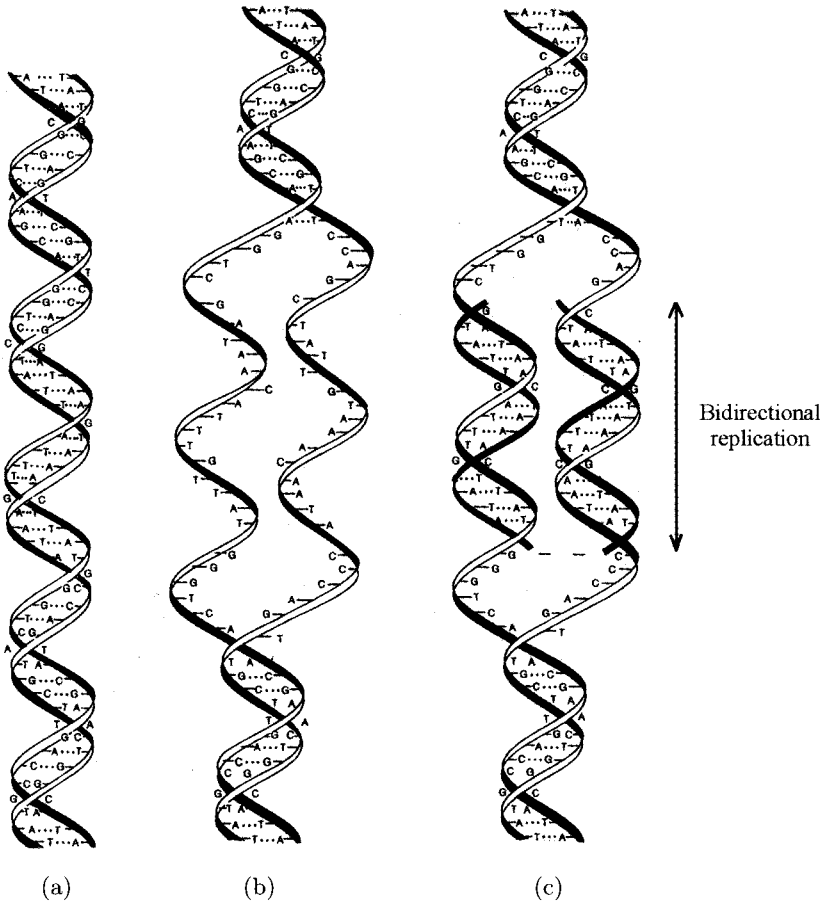


Fig. 1.6. a–c. Replication of the DNA double helix: **a** A segment of a DNA double helix. **b** The DNA double helix has opened into separated strands in a localized region. **c** The separated strands serve as templates for making new complementary strands.

croscope. The replicated state of the chromosomes is clearly evident; each chromosome consists of two identical rods held together side-by-side along their lengths (Fig. 1.8). The condensed replicated chromosomes line up in an equatorial plate of the cell. Next the two rods in each replicated chromosome separate from one another, forming two identical sets of rods, or daughter chromosomes. One set is drawn to one side of the cell, and the other set is drawn to the other side. These daughter chromosome movements are accomplished by a motility mechanism based on microtubules. Simultaneously, a ring of constriction forms in the cell surface at the equatorial plate, formerly occupied by the chromosomes, and contracts, cleaving the cell into two daugh-

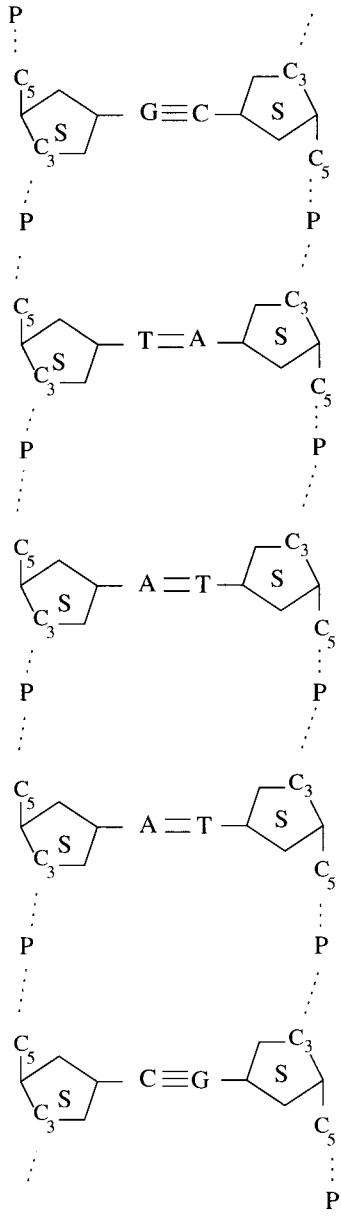


Fig. 1.7. Opposite polarities of the two strands in a DNA duplex. Note that at the *upper end* the left strand ends with P attached to the C_5 of a sugar (S), and the right strand ends with C_3. These are called 5′ and 3′ ends, respectively. At the *lower end* of the duplex the left strand end is 3′ and the right strand end is 5′.

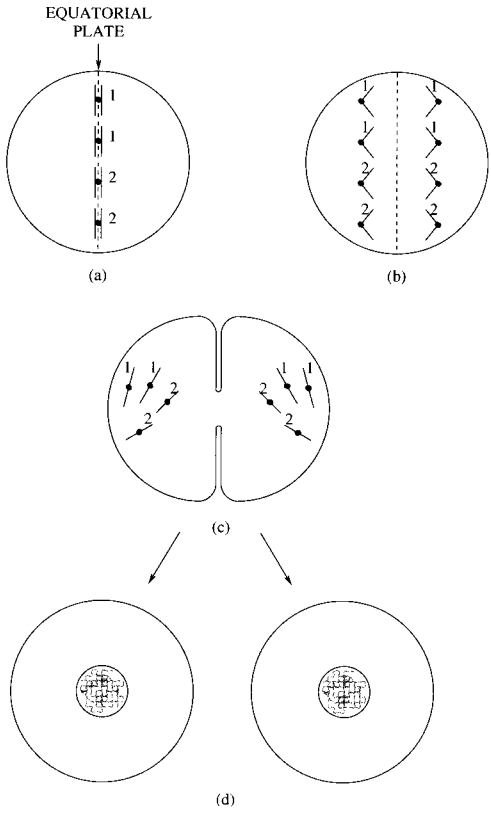


Fig. 1.8. a–d. Mitosis: **a** A diploid set of chromosomes. There are two different chromosomes and two copies of each. Each chromosome has been duplicated (two rods in each, aligned next to one another and held together in the middle). **b** The two rods (daughter chromosomes) in each duplicated chromosome have separated and are being drawn to opposite sides of the equatorial plate. **c** A diploid set of chromosomes is present in each incipient cell, and a cleavage furrow through the equatorial plate is about to complete cytokinesis. **d** The chromosomes in the two daughter cells have decondensed into fine fibrous networks, forming a nucleus in each daughter cell.

ters, each with a set of daughter chromosomes (Fig. 1.8c). This cleavage of the cytoplasm is accomplished by a contractile motility mechanism based on microfilaments. As cytokinesis nears completion, the set of chromosomes in each incipient daughter cell quickly decondenses and forms a nucleus, completing the process of cell division (Fig. 1.8d).

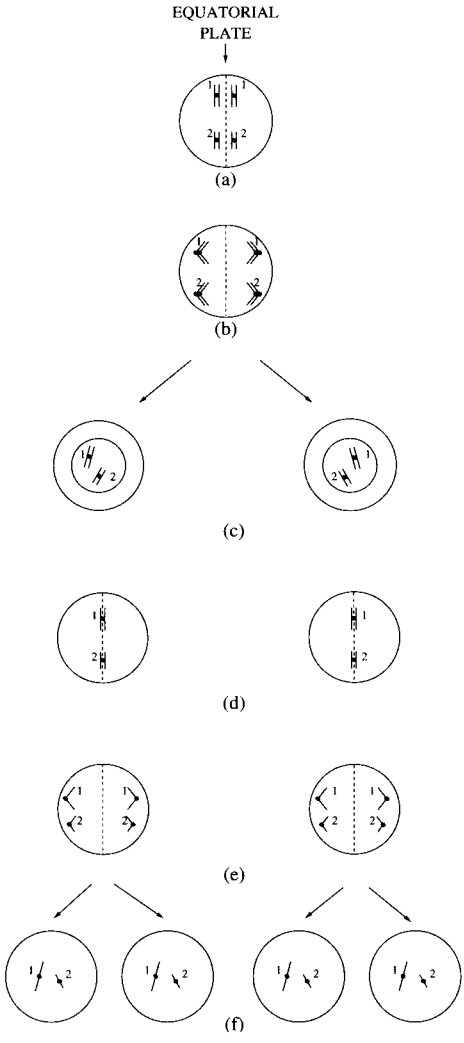


Fig. 1.9. a–f. Meiosis: **a** The two copies of each chromosome in the diploid set of chromosomes have lined up next to each other. There are two different chromosomes in this diploid set. Each chromosome has been duplicated, i.e., consists of two rods. **b** The chromosomes separate. One duplicated copy of each chromosome is drawn to one side of the equatorial plate and the other is drawn to the opposite side. **c** Cytokinesis has created two haploid daughter cells, i.e., each contains one of each of the two different chromosomes, although the chromosomes are in the duplicated state, i.e., two rods in each. **d** The two different duplicated chromosomes in the two haploid cells in (c) line up in an equatorial plate. **e** The two rods in each of the duplicated chromosomes separate and are drawn to opposite sides in each of the two haploid cells. **f** Cytokinesis of the cells in (e) yields four haploid cells with two different unduplicated chromosomes.

Formation of Germ Nuclei — Meiosis

In a multicellular organism like a human, germ nuclei are formed in ova and sperm cells as a prerequisite for cell mating, i.e., fusion of a sperm cell with an ovum. A critical part of the formation of ova and sperm is the reduction from diploidy (two copies of each chromosome) to haploidy (one copy of each chromosome). Thus, when a sperm fuses with an ovum, the two haploid nuclei fuse to form a diploid nucleus and development begins. Reduction from diploidy to haploidy in germ cells (ova and sperm cells) occurs by a modified form of mitosis, called meiosis, in which the two copies of a duplicated chromosome align next to each other in an equatorial plate (Fig. 1.9a) instead of lining up separately, as in mitosis (Fig. 1.8a). The two copies of each chromosome then separate from each other and are drawn to opposite sides of the cell (Fig. 1.9b). Thus, two sets of chromosomes are formed, but unlike in mitosis, every chromosome is still in its double-rod, duplicated form (Fig. 1.9c). Also, each set of duplicated chromosomes now contains one copy of each chromosome (is haploid). The cell completes division, and then each of the two daughter cells immediately divides again, this time in typical mitotic fashion. That is, the haploid set of duplicated chromosomes in each cell lines up in an equatorial plate (Fig. 1.9d), and the two rods in each chromosome separate and migrate to opposite sides of the cell, forming two haploid unduplicated sets of chromosomes (Fig. 1.9e). The two cells divide, producing four haploid daughter cells from one original diploid cell (Fig. 1.9f). Creation of haploid nuclei in preparation for mating in unicellular species is essentially the same. A specific example of this is described for ciliated protozoans in Chap. 2.

Notes on References

A simple description of cell structure and function, cell reproduction, and DNA structure, function, and replication can be found in Prescott [44]. Also, a good description of these topics can be found in Alberts et al. [2].

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