

27 MOLECULAR GENETICS

Activity 1. Identification of the Genetic Material

PROTEIN VS. NUCLEIC ACID

From the early 1900s on, it was generally accepted that the chromosomes contained the hereditary information. However, it was thought that the protein of the chromosome was the information-containing substance and that the DNA was of secondary importance. It was not until 1944 that the role of DNA in heredity was finally established.

In 1928, the British biologist Frederick Griffith performed a series of experiments on mice using two similar strains of bacteria. One strain, called type S, caused pneumonia when injected into test animals. The other strain, called type R, did not. Injection of dead type S bacteria did not cause pneumonia in test animals. However, when Griffith mixed dead type S bacteria with a living culture of type R bacteria and then injected some of the bacteria from the culture into test animals, the mice developed pneumonia. The bacteria found in the mice showed the characteristics of the type S bacteria. The type R bacteria had been transformed into type S bacteria. This process of *transformation* was explained in 1944, when Oswald Avery, Colin MacLeod, and Maclyn McCarthy showed that the DNA from the S bacteria caused the transformation of the R bacteria.

In 1940, Max Delbruck and Salvador Luria started genetic research with viruses. They used a virus that infects bacteria, called a *bacteriophage* (“bacteria eater”). Delbruck and Luria found that 25 minutes after infection a bacterial cell would burst, releasing a large quantity of new viruses. When they opened an infected cell after 12 minutes, they found virus parts and completed virus particles in the cell. They found that the virus particles consisted of a protein coat and an inner core of DNA. The hereditary material of viruses had to be either the protein coat or the DNA inner core.

In 1952, Alfred Hershey and Martha Chase finally resolved the problem of DNA versus protein as the hereditary material. They established two bacteriophage virus cultures. They attached radioactive sulfur to the protein coat of the viruses of one culture and radioactive phosphorus to the DNA core of the viruses of the other culture. Bacteria infected by viruses with the tagged DNA showed a large amount of radioactivity. Those infected by virus particles with the tagged protein displayed almost no radioactivity. The experiment proved that the DNA core entered the cell and carried the genetic instructions that caused the cell to produce more viruses.

The investigations with bacteriophage viruses pointed to DNA as the hereditary material. It also explained the mechanism of viral infection. When a bacteriophage attacks a bacterial cell, the tail of the virus becomes attached to the bacterial cell wall. The DNA core of the virus is then injected into the cell. It takes over the biochemical machinery of the infected cell and causes the production of new virus particles. Eventually, the cell bursts, and new virus particles are released and go on to infect other cells.

Some of the DNA of the infected bacterium may be incorporated into the DNA of the virus. When the new virus particles infect other bacteria, they introduce DNA from the previous bacterial host. The DNA of the first bacterium may then be incorporated into the genetic makeup of the second bacterium. By this process,

called *transduction*, traits of one type of bacteria may be transferred by viruses to other types of bacteria. Since transduction involves a transfer of DNA and has been shown to cause inheritable changes in bacterial cells, it provides further evidence that DNA is the hereditary material.

1. The process in which the DNA from one type of cell causes an inheritable change in a second type of cell is called _____.
2. Viruses that infect bacteria are called _____.
3. Outside a living cell, viruses consist of a coat composed of _____ and a core composed of _____.
4. The portion of the virus that actually enters a cell is the _____.
5. The process by which DNA from one bacterium is transferred to a second bacterium by a virus is called _____.

COMPOSITION AND STRUCTURE OF DNA

Nucleotides

Both DNA and RNA are made up of subunits called *nucleotides*. Each nucleotide contains a nitrogenous base, a 5-carbon sugar, and a phosphate group. There are two types of nitrogenous bases—*purines*, which include adenine and guanine, and *pyrimidines*, which include thymine, cytosine, and uracil. DNA contains the 5-carbon sugar *deoxyribose*, while RNA contains the 5-carbon sugar *ribose*. The nitrogenous bases found in DNA are adenine, cytosine, guanine, and thymine. In RNA, uracil is substituted for thymine. Nucleotides are generally identified by their nitrogenous base. So, in describing the structure of DNA or RNA, adenine-containing nucleotides are shown as A, thymine-containing nucleotides as T, and so on.

1. The subunits that make up nucleic acids are _____.
2. What three components make up a nucleotide?

3. The sugar in RNA is _____, while the sugar in DNA is _____.
4. The nitrogenous base that is found in RNA but not in DNA is _____.
5. The two types of nitrogenous bases found in nucleic acids are _____ and _____.

The Double Helix

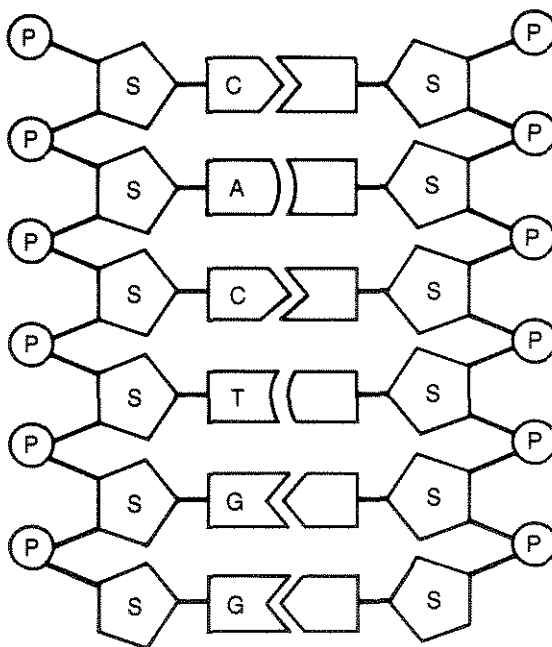
The complicated structure of DNA was worked out in 1953 by James Watson and Francis Crick. According to their model, the DNA molecule is in the form of a *double helix*. That is, it consists of two strands of nucleotides bonded together to form a ladderlike structure, which is then coiled like a spring. In each strand of a DNA molecule, the phosphate group of one nucleotide is bonded to the sugar of the next nucleotide. The two strands are bonded together by hydrogen bonds between pairs of nitrogenous bases. The bonding between the bases is highly specific. Adenine and thymine bond only to each other, and guanine and cytosine bond only to each other.

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Thus, wherever there is a guanine on one strand, there is a cytosine on the other strand. Wherever there is a thymine on one strand, there is an adenine on the other strand, etc. Adenine and thymine are complementary, and guanine and cytosine are complementary. They fit together within the structure of the DNA double helix like pieces of jigsaw puzzle.

1. The DNA molecule has _____ strands.
2. Each strand is a long chain of _____ units.
3. Strands of DNA are held together by hydrogen bonds between the _____.
4. In the bonding between the nitrogenous bases of the DNA strands, adenine bonds only with _____, and cytosine bonds only with _____.
5. The following diagram shows the nucleotide sequence of a segment of a DNA strand. Fill in the complementary nitrogen bases of the second strand.



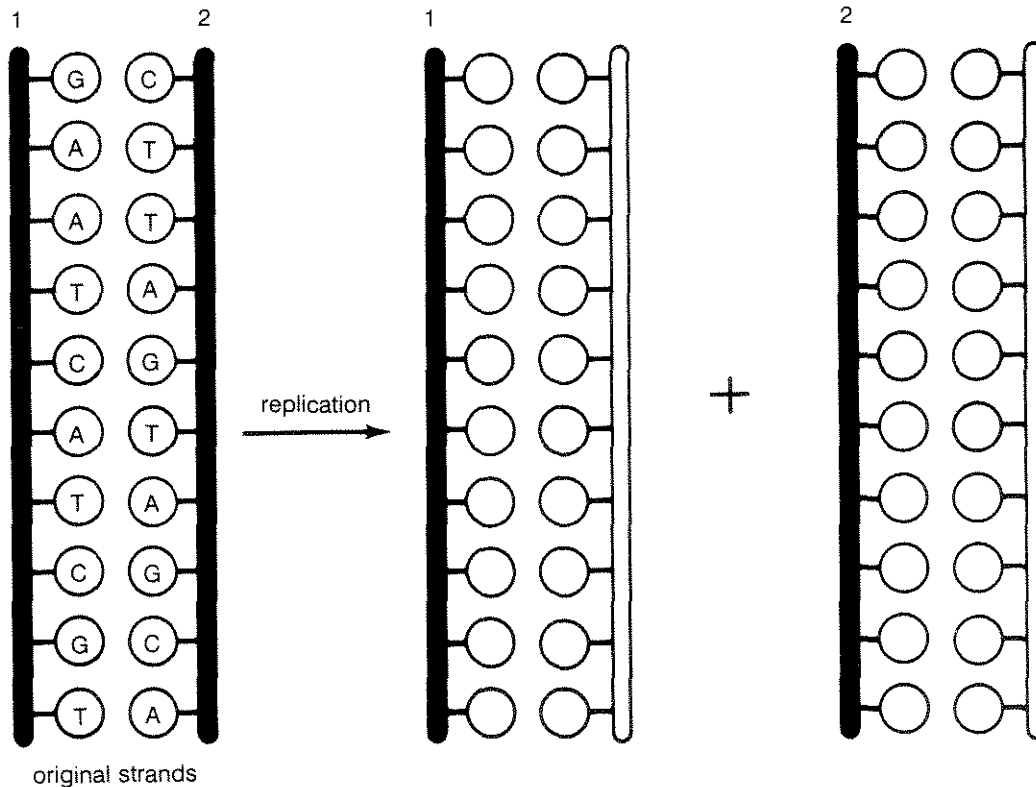
DNA—REPLICATION AND HEREDITARY INFORMATION

When the chromosomes double during interphase, the DNA molecules undergo *replication*—that is, they produce exact duplicates of themselves. Replication begins with a separating of the two DNA strands. Where the strands are separated, the nitrogenous bases are exposed. As the DNA molecule separates along its length, a complex series of enzyme-catalyzed reactions occurs, and complementary nucleotides from the cytoplasm bond to the exposed bases of the original DNA strand and to each other. An A on the original strand will become bonded to a T, a C to a G, etc. Thus, each of the original strands of DNA comes to be bonded to a new complementary strand of DNA. The original strands act as *templates*, or patterns, on which the new strands of DNA form.

The hereditary information in DNA is contained in the sequence of the four different nucleotides along the DNA strands. The process of replication, in which there is an exact duplication of DNA molecules, makes it possible for each cell of an organism to contain the same hereditary information. Expression of this information involves the translation of the information coded in the nucleotide sequence into the synthesis of proteins, a process involving RNA.

1. The process by which new molecules of DNA are formed is called _____
2. In what form is the hereditary information encoded in the DNA molecule?

3. The diagram below shows the nucleotide sequence of a DNA segment. Label the nucleotides in the new strands of DNA formed by replication.



COMPOSITION AND STRUCTURE OF RNA

Like DNA, RNA is composed of nucleotide subunits. Unlike DNA, RNA is single-stranded, and the sugar it contains is ribose instead of deoxyribose. Also, instead of the thymine that is present in DNA, RNA contains the pyrimidine uracil, which is complementary to adenine.

1. How does the structure of RNA differ from that of DNA?

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Activity 2. Genes and Protein Synthesis

THE ONE GENE, ONE ENZYME HYPOTHESIS

The one gene, one enzyme hypothesis explains how DNA controls the biochemical activities of the cell. A gene is a portion of a DNA molecule that defines the expression of a characteristic. It directs the synthesis of a specific enzyme which controls the expression of a specific trait. Enzymes play a central role in biochemical reactions within the cell. They affect the speed of cellular reactions.

In 1945, George Beadle and Edward Tatum, working at Stanford University, published a Nobel prize-winning work involving *Neurospora crassa*, a red bread mold. They discovered that after irradiation of *Neurospora* spores with X rays, some offspring were unable to synthesize an essential growth factor. Instead, the food substance had to be supplied in the nutrient medium.

Exposure to X rays resulted in an alteration of a portion of a DNA molecule, causing a mutation. This in turn altered the arrangement of amino acids in the enzyme controlled by that gene. Since enzymes are specific, the enzyme in its altered state could not react with the substrate to produce the essential growth factor. The biochemical reaction that had been controlled by the enzyme could not go to completion.

1. According to the one gene, one enzyme hypothesis, a single gene controls the production of one _____.
2. The name of the organism used by Beadle and Tatum in their genetics experiments is _____.
3. How were mutations induced in *Neurospora*?

4. According to this experiment, a single mutated gene was unable to produce a necessary _____.
5. What is the name for the modified form of the one gene, one enzyme hypothesis?

PROTEIN SYNTHESIS

In the replication of DNA, existing strands serve as templates for the synthesis of new complementary strands of DNA. Strands of DNA also serve as templates for the synthesis of a type of RNA called *messenger RNA*, or *mRNA*. The mRNA then serves as a template for the assembling of amino acids, which bond together to form polypeptides and proteins. Thus, the sequence of nucleotides in the DNA determines the sequence of nucleotides in the mRNA, which in turn determines the sequence of amino acids in proteins. Two other types of RNA are involved in protein synthesis. These are ribosomal RNA (rRNA) and transfer RNA (tRNA).

1. Messenger RNA serves as a _____ for the assembling of amino acids.

2. What determines the sequence of bases in mRNA?

The Genetic Code

The genetic information is encoded in the sequence of nucleotides in the molecules of DNA. The same information is encoded in the nucleotide sequence of messenger RNA. The code itself consists of specific sequences of three nucleotides. Each such triplet, or *codon*, codes for a particular amino acid. Some amino acids are coded for by more than one triplet. For example, the codes of the amino acid lysine are AAA and AAG.

1. What is a codon?

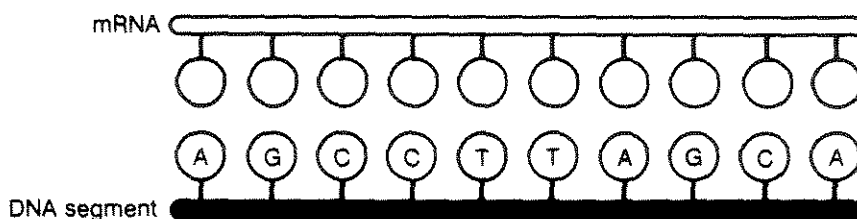
Messenger RNA

Like the replication of DNA, the synthesis of mRNA involves a complex series of enzyme-catalyzed reactions. It begins with the attachment of a particular enzyme to a special site on the DNA molecule. This causes the two strands of DNA to unwind in that area. It is thought that only one of the two strands of DNA serves as a template for RNA synthesis. The RNA nucleotides (ribonucleotides) align along the DNA strand, forming a complementary strand of mRNA. The process by which the hereditary information of the DNA is copied into the mRNA is called *transcription*. The pairing of bases in mRNA synthesis is the same as in DNA replication except that where there is an adenine on the DNA, there is a uracil on the mRNA. Messenger RNA is a short-lived intermediate in protein synthesis. It can be synthesized very rapidly and broken down just as rapidly. From the nucleus where it is synthesized, the mRNA passes into the cytoplasm and becomes attached to ribosomes.

1. The part of a cell in which mRNA synthesis occurs is the _____.

2. Messenger RNA migrates from its site of synthesis and becomes attached to _____.

3. The following diagram shows the sequence of bases in a segment of DNA. Fill in the bases for a complementary segment of mRNA.



Ribosomal and Transfer RNA

Ribosomal RNA, along with some protein, makes up the ribosomes. Transfer RNA, found in the cell cytoplasm, picks up amino acids and carries them to the ribosomes. Both rRNA and tRNA are stable components of the cell. They are not continually synthesized and broken down as is mRNA. Like mRNA, tRNA and rRNA are synthesized by transcription of the DNA template.

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1. The three types of RNA found in the cell are _____ RNA, _____ RNA, and _____ RNA.
2. Ribosomes are made up of _____ and _____.
3. Amino acids are carried to the ribosomes by _____.

ASSEMBLY OF A POLYPEPTIDE

Protein synthesis takes place at the ribosomes. Here, the mRNA from the nucleus acts as a template for the assembly of amino acids. The sequence of bases of the mRNA determines the sequence of amino acids. Each kind of amino acid (there are about twenty) is picked up by a specific transfer RNA and carried to the ribosome. The tRNA has a triplet of exposed nitrogenous bases that are complementary to a triplet of bases (codon) on the mRNA at the ribosome. This triplet of bases on the tRNA is called the *anticodon* because it is complementary to the codon of the mRNA. The tRNA carrying its amino acid becomes temporarily attached to the complementary triplet of the mRNA at the ribosome. In this way, a specific series of amino acids lines up at the ribosome. The order in which the amino acids are arranged is determined by the base sequence (triplets) of the mRNA, and ultimately by the base sequence of the cell DNA.

The amino acids at the ribosome are joined together by dehydration synthesis to form proteins. This is accomplished with energy from ATP and in the presence of specific enzymes. When the protein is complete, it separates from the tRNA, and the tRNA separates from the mRNA.

1. Where does protein synthesis occur in the cell?

2. What determines the sequence of amino acids in a given protein?

3. An _____ is the triplet of bases on tRNA that is complementary to a codon of mRNA.
4. Why does a particular tRNA molecule become temporarily attached only to a specific triplet of mRNA?

5. The type of reaction by which amino acids bond together to form proteins is

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6. Use the following reference list to determine the sequence of amino acids coded for by the following mRNA segment. (Start from the top of the mRNA.)

mRNA	AMINO ACID SEQUENCE
C	1. _____
G	2. _____
U	3. _____
A	4. _____
A	5. _____
U	6. _____
G	7. _____
G	8. _____
A	
G	
G	
U	
A	
G	
A	
A	
U	
U	
C	
A	
A	
G	

Reference List:

AMINO ACID	RNA TRIPLET CODE
valine	GUA, GUG, GUC, GUU
arginine	AGA, AGG, CGA, CGG, CGC, CGU
lysine	AAA, AAG
tryptophan	UGG
glutamic acid	GAG, GAA
phenylalanine	UUU, UUC

7. According to the one gene, one enzyme hypothesis, how does DNA control the biochemical activity of the cell?

Figure 16.1 The one gene—one enzyme hypothesis

