TOPIC 5

Molecular Genetics

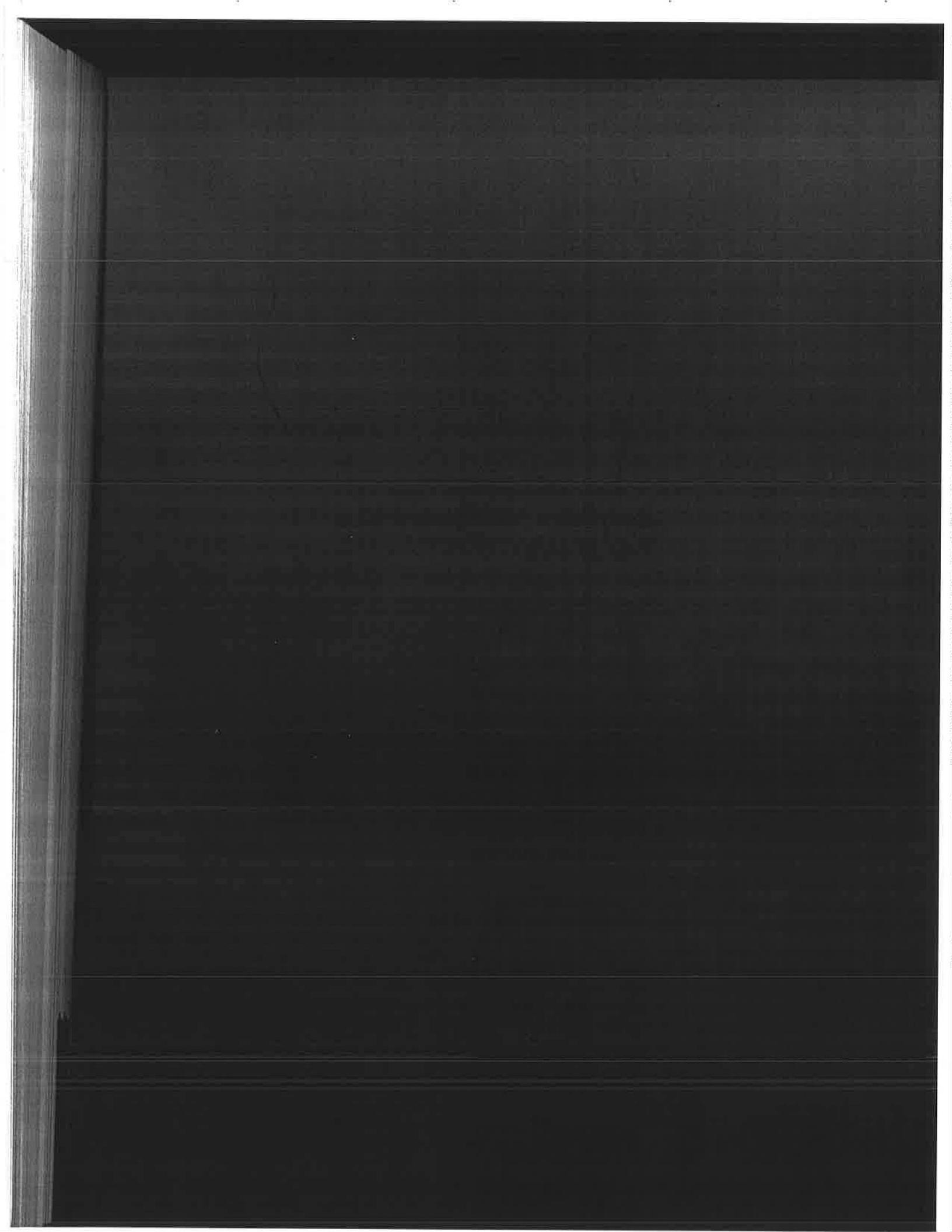
Chapter 16: The Molecular Basis of Inheritance

YOU MUST KNOW

- The structure of DNA.
- The knowledge about DNA gained from the work of Watson, Crick, Wilkins, and Franklin; Avery, MacLeod, and McCarty; and Hershey and Chase.
- The major steps of replication.
- The difference between replication, transcription, and translation.
- The general differences between the bacterial chromosomes and eukaryotic chromosomes.
- How DNA packaging can affect gene expression.

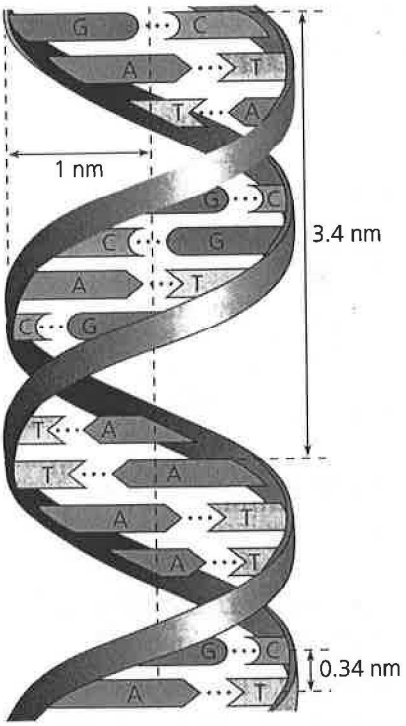
Concept 16.1 DNA is the genetic material

- Once chromosomes were known to carry genes, the next question became which of the two organic compounds that make chromosomes, DNA or protein, was the genetic material?
  - In 1952 **Alfred Hershey and Martha Chase** answered this question utilizing *bacteriophages*—viruses that infect bacteria. Bacteriophages were excellent organisms for this study, in part because they are made of only two organic compounds, DNA and protein. Hershey and Chase used a radioactive isotope of phosphorus to tag the DNA in one culture of bacteriophages and radioactive sulfur to tag the protein in a second culture. Their results clearly showed that only the DNA entered bacteria infected by the virus; the radioactive protein never entered the cell. This research convinced scientists that DNA must be the genetic material.
- The next big question centered on the structure of DNA. Would the structure of DNA give any clues as to how it functioned as the genetic material?
  - **James Watson and Francis Crick** were the first to solve the puzzle of the structure of DNA. Critical to their success was the work of Rosalind Franklin and Maurice Wilkins, both working in the field of X-ray crystallography.

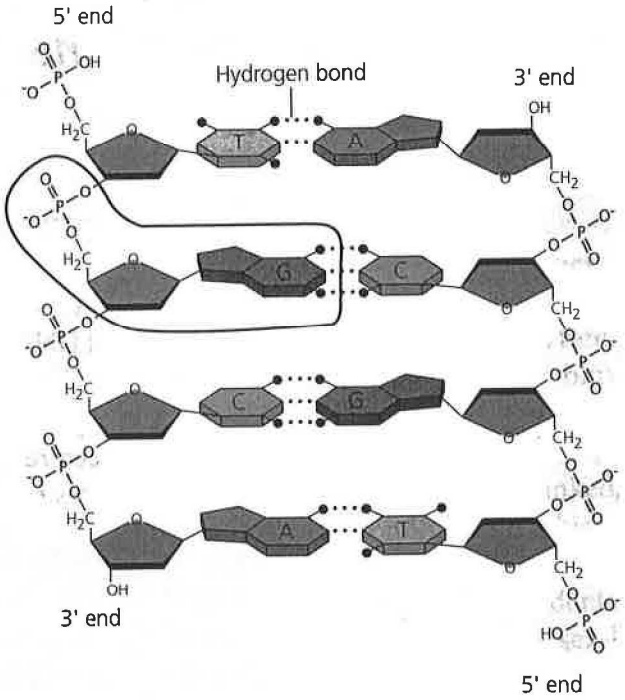


- **X-ray crystallography** is a process used to visualize molecules three-dimensionally. X-rays are diffracted as they pass through the molecule, and they bounce back to produce patterns that can be interpreted through mathematical equations. Through this technique, a rough blueprint of the molecule was formed.

- Watson and Crick's model determined four major features of DNA. Find each major point by following Figure 5.1 as the model is explained.



Key Features of DNA Structure



Partial Chemical Structure

Figure 5.1 Structure of DNA

- DNA is a **double helix**, which can be described as a twisted ladder with rigid rungs. The side, or backbone, is made up of sugar-phosphate components, whereas the rungs are made up of pairs of nitrogenous bases.
- Notice that a single nucleotide is circled in Figure 5.1. It is composed of a sugar (deoxyribose) attached to a phosphate and a nitrogen base.
- The nitrogenous bases of DNA are adenine (A), thymine (T), guanine (G), and cytosine (C). In DNA, adenine pairs only with thymine, and guanine pairs only with cytosine.
- Notice that the chain on the right side of the model runs in one direction, while the left side of the chain runs in the opposite, upside-down direction. The strands are termed **antiparallel**. The left side runs 5′ to 3′ while the opposite strand runs 3′ to 5′. (Recall that the carbons are numbered, and you will see that the number 5 carbon and number 3 carbon and the resultant nucleotides are flipped relative to each other.) Nucleic acid strands are always antiparallel, whether they are DNA/DNA or DNA/RNA or RNA/RNA interactions.

Concept 16.2 Many proteins work together in DNA replication and repair

> ***TIP FROM THE READERS***
> You are responsible only for these enzymes of replication: DNA polymerase, ligase, helicase, and topoisomerase. For transcription, know the role of RNA polymerase.

- **Replication** is the making of DNA from an existing DNA strand. DNA replication is *semiconservative.* This means that at the end of replication, each of the daughter molecules has one old strand, derived from the parent strand of DNA, and one strand that is newly synthesized. Study Figure 5.2 to see the pattern of semiconservative replication.

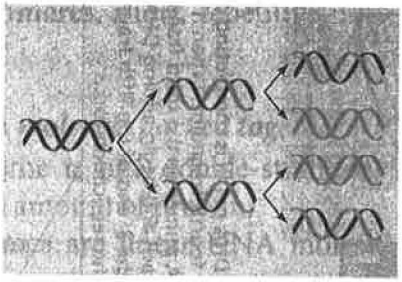


Figure 5.2 Semiconservative replication

> ***TIP FROM THE READERS***
> Know the difference between *replication* (DNA to DNA), *transcription* (DNA to RNA), and *translation* (RNA to protein). In essay questions that use these terms, often 25% of the students confuse the processes!

- The replication of DNA includes six major points:

1. The replication of DNA begins at sites called the *origins of replication.*
2. Initiation proteins bind to the origin of replication and separate the two strands, forming a *replication bubble.* DNA replication then proceeds in both directions along the DNA strand until the molecule is copied.
3. A group of enzymes called **DNA polymerases** catalyzes the elongation of new DNA at the replication fork.
4. DNA polymerase adds nucleotides to the growing chain one by one, working in a 5′ to 3′ direction, matching adenine with thymine and guanine with cytosine.
5. Recall that the strands of DNA are antiparallel. This means that DNA replication occurs continuously along the 5′ to 3′ strand, which is called the **leading strand**. The strand that runs 3′ to 5′ is copied in series of segments and termed the **lagging strand**. Read steps 1–3 in Figure 5.3 to visualize this process.
6. The lagging strand is synthesized in separate pieces called **Okazaki fragments**, which are then sealed together by **DNA ligase** (step 4, Figure 5.3), forming a continuous DNA strand.

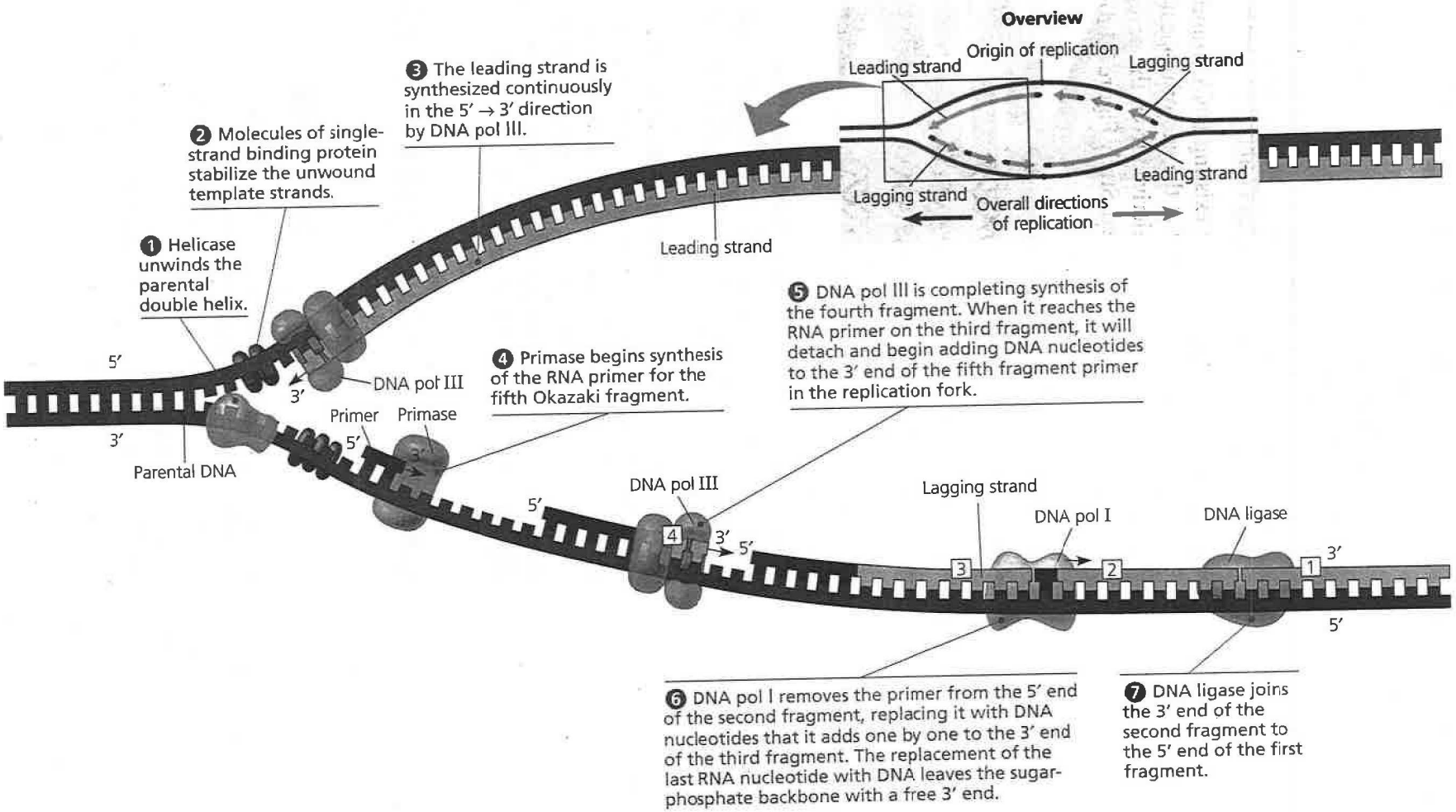


Figure 5.3 DNA replication

- There are several different factors contributing to the accuracy of DNA replication:
  - The specificity of base pairing (A = T, G = C)
  - **Mismatch repair**, in which special repair enzymes fix incorrectly paired nucleotides
  - **Nucleotide excision repair**, in which incorrectly placed nucleotides are excised or removed by enzymes termed **nucleases**, and the gap left over is filled in with the correct nucleotides
- The fact that DNA polymerase can add nucleotides only to the 3′ end of a molecule means that it would have no way to complete the 5′ end of the DNA molecule at the end of the chromosome. Every time the chromosome is replicated for mitosis, a small portion of the tip of the chromosome is removed. To avoid losing the terminal genes, the linear ends of eukaryotic chromosomes are "capped" with **telomeres**, short, repetitive nucleotide sequences that do not contain genes.

Concept 16.3 A chromosome consists of a DNA molecule packed together with proteins

- A bacterial chromosome is one double-stranded, circular DNA molecule associated with a small amount of protein.
- Eukaryotic chromosomes are linear DNA molecules associated with large amounts of protein.
- In eukaryotic cells, DNA and proteins are packed together as **chromatin**. Eukaryotic DNA shows four levels of packaging. Visualize each level of packaging by studying Figure 5.4 (see next page) as you read the information provided there.
- As DNA becomes more highly packaged, it becomes less accessible to transcription enzymes. This reduces gene expression. In interphase cells, most chromatin is in the highly extended form **(euchromatin)** and is available for transcription, but some remains more condensed **(heterochromatin)**. Heterochromatin is largely inaccessible to transcription enzymes and, thus, generally is not transcribed. Barr bodies are heterochromatin.

Chapter 17: From Gene to Protein

YOU MUST KNOW

- The key terms *gene expression*, *transcription*, and *translation*.
- The major events of transcription.
- How eukaryotic cells modify RNA after transcription.
- The steps to translation.
- How mutations can change the amino acid sequence of a protein.

1. The **lytic cycle** ends in the death of the host cell by rupturing it (lysis). In this cycle, a bacteriophage injects its DNA into a host cell and takes over the host cell's machinery to synthesize new copies of the viral DNA as well as protein coats. These self-assemble, and the bacterial cell is lysed, releasing multiple copies of the virus.
2. In the **lysogenic cycle** the bacteriophage's DNA becomes incorporated into the host cell's DNA and is replicated along with the host cell's genome. The viral DNA is known as a **prophage**. Under certain conditions the prophage will enter the lytic cycle, described on the previous page.

- **Retroviruses** are RNA viruses that use the enzyme **reverse transcriptase** t transcribe DNA from an RNA template. The new DNA then permanently inte grates into a chromosome in the nucleus of an animal cell. The host transcribe the viral DNA into RNA that may be used to synthesize viral proteins or ma be released from the host cell to infect more cells. *Example*: HIV is a retrovirus

Concept 19.3 Viruses, viroids, and prions are formidable pathogens in animals and plants

- **Viroids** are circular RNA molecules several hundred nucleotides in length tha infect plants. They cause errors in regulatory systems that control plant growth
- **Prions** are misfolded, infectious proteins that cause the misfolding of norma proteins they contact in various animal species. *Examples* of diseases caused b prions include mad cow disease and, in humans, Creutzfeldt-Jakob disease.

Chapter 20: Biotechnology

WHAT'S IMPORTANT TO KNOW?

The Curriculum Framework expects that you are familiar with a technique of modern biotechnology, as well as an example of a product of genetic engineering. Your teacher may not cover all of the possibilities described in this chapter.

YOU MUST KNOW

- The terminology of biotechnology.
- The steps in gene cloning with special attention to the biotechnology tools that make cloning possible.
- The key ideas that make PCR possible.
- How gel electrophoresis can be used to separate DNA fragments or protein molecules.

Concept 20.1 DNA cloning yields multiple copies of a gene or other DNA segment

- The key to unlocking the concepts of biotechnology is to understand the term Know the following commonly used terms:
  - **Genetic engineering** is the process of manipulating genes and genomes.
  - **Biotechnology** is the process of manipulating organisms or their components for the purpose of making useful products.

- **Recombinant DNA** is DNA that has been artificially made, using DNA from different sources—and often different species. An example is the introduction of a human gene into an *E. coli* bacterium.
- **Gene cloning** is the process by which scientists can produce multiple copies of specific segments of DNA that they can then work with in the lab.
- **Restriction enzymes** are used to cut strands of DNA at specific locations (called **restriction sites**). They are derived from bacteria.
- When a DNA molecule is cut by restriction enzymes, the result will always be a set of **restriction fragments**, which will have at least one single-stranded end, called a **sticky end**. Sticky ends can form hydrogen bonds with complementary single-stranded pieces of DNA. These unions can be sealed with the enzyme **DNA ligase**.

■ Follow the steps that may occur to clone a gene in Figure 5.14.

1. *Identify and isolate the gene of interest and a **cloning vector**.* The vector will carry the DNA sequence to be cloned and is often a bacterial plasmid, as shown in Figure 5.14.

In this example, a human gene is inserted into a plasmid from *E. coli*. The plasmid contains the amp^R gene, which makes *E. coli* cells resistant to the antibiotic ampicillin.

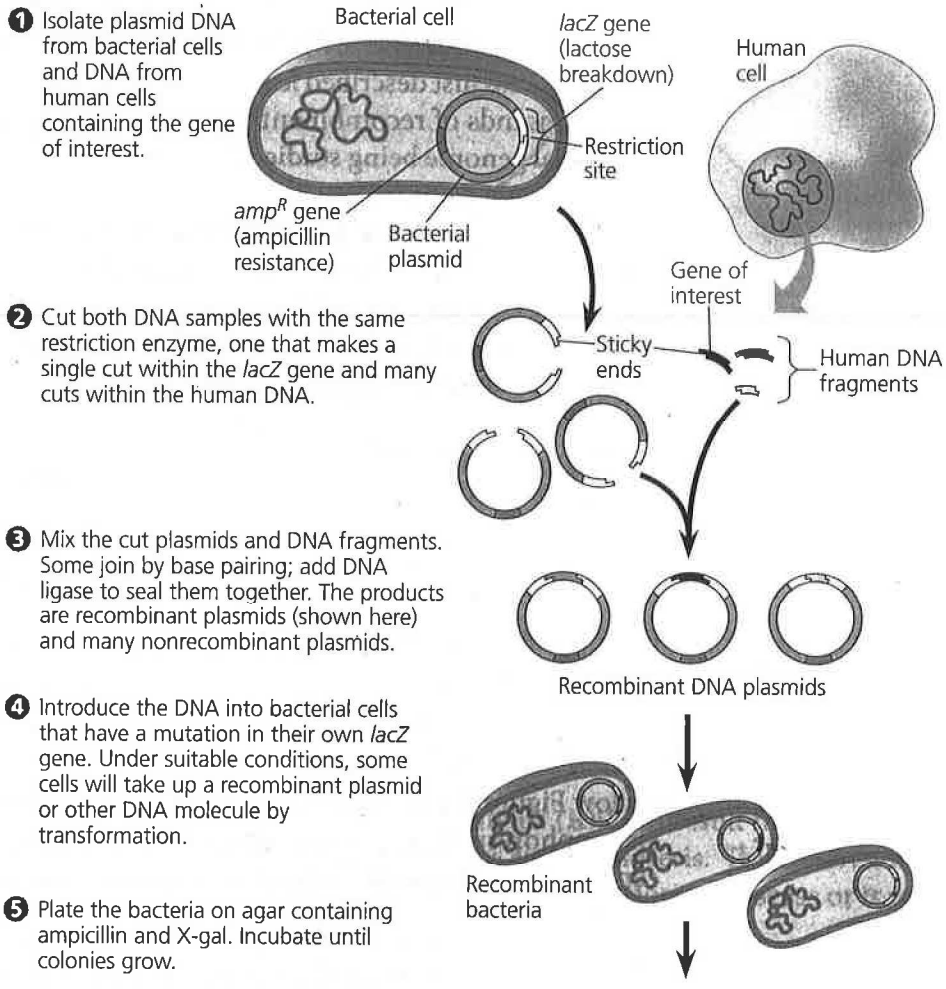


Figure 5.14 Cloning a human gene in a bacterial plasmid

2. *Cut both the gene of interest and the vector with the same restriction enzyme.* This gives the plasmid and the human gene matching sticky ends.
3. *Join the two pieces of DNA.* Form recombinant plasmids by mixing the plasmids with the DNA fragments. The human DNA fragments can be sealed into the plasmid using DNA ligase.
4. *Get the vector carrying the gene of interest into a host cell.* The plasmids are taken up by the bacterium by *transformation.* The process of transformation is a key part of Investigation 8.
5. *Select for cells that have been transformed.* The bacterial cells carrying the clones must be identified or selected. This can be done by linking the gene of interest to an antibiotic resistance gene or a *reporter gene* such as green fluorescent protein. In AP Investigation 8, we use an ampicillin-resistant plasmid. Any bacterial cells that do not pick up the plasmid by transformation will be killed when grown on agar with the antibiotic ampicillin.

- The next problem is finding the gene of interest among the many colonies present after transformation. A process known as **nucleic acid hybridization** can be used to find the gene. If we know at least part of the nucleotide sequence of the gene of interest, we can synthesize a probe complementary to it. For example, if the known sequence is G-G-C-T-A-A, then we would synthesize the complementary probe C-C-G-A-T-T. If we make the probe radioactive or fluorescent, the probe will be easy to track, taking us to the proper gene of interest.
- The process just described leads to a genomic library. A **genomic library** is a set of thousands of recombinant plasmid clones, each of which has a piece of the original genome being studied. A **cDNA library** is made up of complementary DNA made from mRNA transcribed by reverse transcriptase. This technique rids the gene of introns but may not contain every gene in the organism.
- **PCR** (polymerase chain reaction) is a method used to amplify a particular piece of DNA without the use of cells. PCR is used to amplify DNA when the source is impure or scanty (as it would be at a crime scene). Figure 5.15 shows the basic steps of the PCR procedure.

Concept 20.2 DNA technology allows us to study the sequence, expression, and function of a gene

- **Gel electrophoresis** is a lab technique used to separate macromolecules, primarily DNA and proteins. The principles of this separation of DNA include:

1. An *electric current* is applied to the field. DNA is negatively charged and migrates to the positive electrode.
2. *Agarose gel* is used as a matrix to separate molecules by size. The gel allows smaller molecules to move more easily than larger fragments of DNA.
3. The DNA must be stained or tagged for visualization.

Follow Figure 5.16 (on page 140) as the specific steps are shown. Because gel electrophoresis of DNA is a required AP Lab, pay special attention to the concepts explained in the figure.

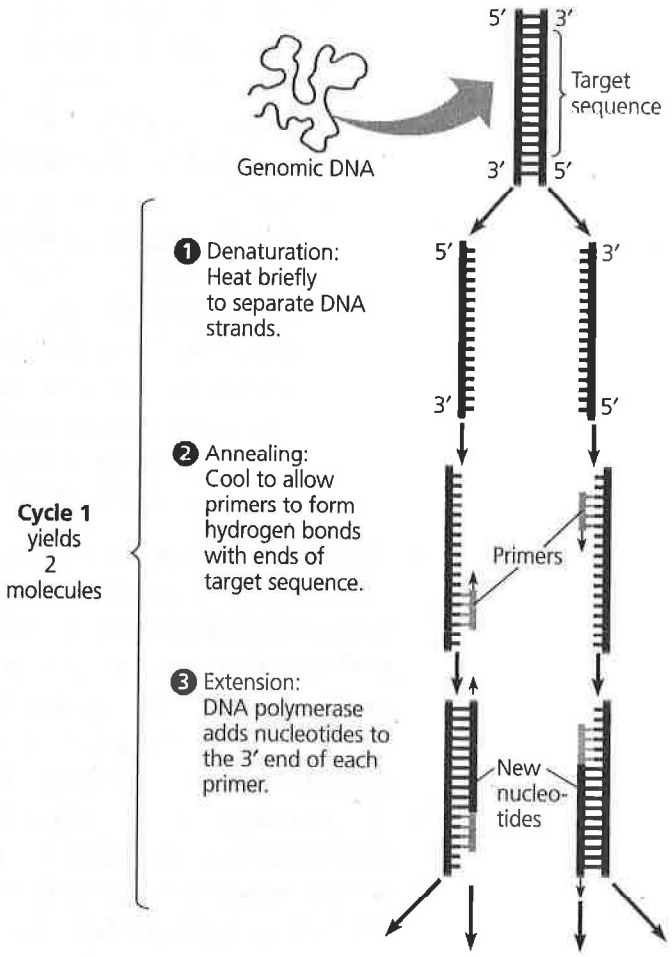


Figure 5.15 Polymerase chain reaction (PCR)

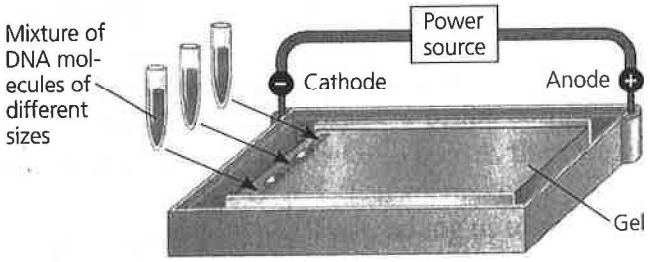
- Genome-wide studies of gene expression are made possible by the use of **DNA microarray assays**. DNA microarray chips work as follows:
    1. Small amounts of single-stranded DNA fragments representing different genes are fixed to a glass slide in a tight grid, termed a *DNA chip*.
    2. mRNA molecules from the cells being tested are isolated and converted to cDNA by reverse transcriptase, then tagged with a fluorescent dye.
    3. The cDNA bonds to the ssDNA on the chip, indicating which genes are "on" in the cell (actively producing mRNA). This enables researchers, for example, to see differences in gene expression between breast cancer tumors and noncancerous breast tissue.
- **Restriction fragment length polymorphisms (RFLPs)** result from small differences in DNA and can be detected by electrophoresis. The difference in banding patterns after electrophoresis allows for diagnosis of disease or is used to answer paternity and identity questions.

Gel Electrophoresis

APPLICATION Gel electrophoresis is used for separating nucleic acids or proteins that differ in size, electrical charge, or other physical properties. DNA molecules are separated by gel electrophoresis in restriction fragment analysis of both cloned genes (see Figure 20.10) and genomic DNA (see Figure 20.11).

TECHNIQUE Gel electrophoresis separates macromolecules on the basis of their rate of movement through a polymeric gel in an electric field: The distance a DNA molecule travels is inversely proportional to its length. A mixture of DNA molecules, usually fragments produced by restriction enzyme digestion (cutting) or PCR amplification, is separated into bands. Each band contains thousands of molecules of the same length.

1. Each sample, a mixture of DNA molecules, is placed in a separate well near one end of a thin slab of gel. The gel is set into a small plastic support and immersed in an aqueous solution in a tray with electrodes at each end.



2. When the current is turned on, the negatively charged DNA molecules move toward the positive electrode, with shorter molecules moving faster than longer ones. Bands are shown here in blue, but on an actual gel, the bands would not be visible at this time.

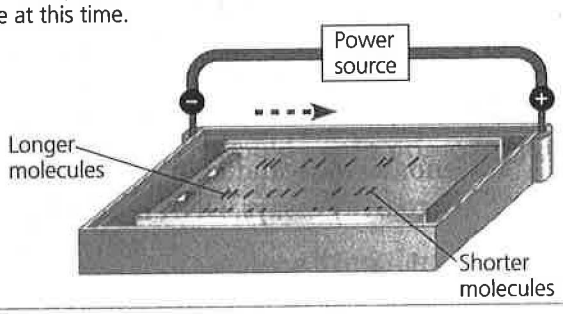


Figure 5.16 Gel electrophoresis

Concept 20.3 Cloning organisms may lead to production of stem cells for research and other applications

- In animal cloning the nucleus of an egg is removed and replaced with the diploid nucleus of a body cell, a process termed *nuclear transplantation*. The ability of a body cell to successfully form a clone decreases with embryonic development and cell differentiation.
- The major goal of most animal cloning is reproduction, but not for humans. In humans, the major goal is the production of **stem cells**. A stem cell can both reproduce itself indefinitely and, under the proper conditions, produce other specialized cells. Stem cells have enormous potential for medical applications.

- **Embryonic stem cells** are *pluripotent*, which means capable of differentiating into many different cell types. The ultimate aim is to use them for the repair of damaged or diseased organs, such as insulin-producing pancreatic cells for people with diabetes or certain kinds of brain cells for people with Parkinson's disease.

Concept 20.4 The practical applications of DNA technology affect our lives in many ways

There are many different uses for DNA technology, some of which are as follows:

- **Diagnosis of disease:** A number of diseases can be detected by RFLP analysis (e.g., cystic fibrosis, sickle-cell disease) or through amplification of blood samples to test for viruses (e.g., HIV).
- **Gene therapy:** The alteration of an afflicted individual's genes. Gene therapy holds great potential for treating disorders traceable to a single defective gene, such as cystic fibrosis.
- **The production of pharmaceuticals:** Gene splicing and cloning can be used to produce large amounts of particular proteins in the lab (e.g., human insulin and growth hormone).
- **Forensic applications:** DNA samples taken from the blood, skin cells, or hair of alleged criminal suspects can be compared to DNA collected from the crime scene. *Genetic profiles* can be compared and used to identify persons at that crime scene.
- **Environmental cleanup:** Scientists engineer metabolic capabilities into microorganisms, which are then used to treat environmental problems, such as removing heavy metals from toxic mining sites.
- **Agricultural applications:** Certain genes that produce desirable traits have been inserted into crop plants to increase their productivity or efficiency. An organism that has acquired by artificial means one or more genes from another species or variety is termed a **genetically modified (GM) organism**. Currently, a debate is in progress over the safety of GM organisms.

Chapter 21: Genomes and Their Evolution

YOU MUST KNOW

- How prokaryotic genomes compare to eukaryotic genomes.
- The activity and role of transposable elements and retrotransposons.
- How evo-devo relates to our understanding of the evolution of genomes.
- The role of homeotic genes and homeoboxes.

Concept 21.2 Scientists use bioinformatics to analyze genomes and their functions

- **Bioinformatics** is the use of computers, software, and mathematical models to process and integrate the incredible volume of data from these sequencing projects. In addition to DNA sequences, protein interactions are analyzed in an approach called *proteomics*.

- *Systems biology* aims to model the behavior of entire biological systems, and is enhanced by bioinformatics. This has many applications, including medical ones—for example, in the understanding and treatment of cancers.

Concept 21.3 Genomes vary in size, number of genes, and gene density

- More than 1,200 genomes have now been sequenced. In general, bacteria and archaea have fewer genes than eukaryotes, and the number of genes in eukaryotic genomes is less than was expected. For example, the human genome has only about 20,000 genes.
- How could so many proteins be made with so few genes? The answer lies in extensive *alternative gene splicing* of RNA transcripts. Recall that this process results in more than one functional protein from a single gene.

Concept 21.4 Multicellular eukaryotes have much noncoding DNA and many multigene families

- Only a tiny part of the human genome—1.5%—codes for proteins or is transcribed into rRNAs or tRNAs. Much of the rest is **repetitive DNA**, sequences that are present in multiple copies in the genome.
- **Transposable elements** make up much of the repetitive DNA. These are stretches of DNA that can move from one location to another in the genome with the aid of an enzyme, *transposase*. There are two types:
  - **Transposons** move by means of a DNA intermediate.
  - **Retrotransposons** move by means of a RNA intermediate, and leave a copy at the original site. The process involves *reverse transcriptase*, an enzyme seen before in retroviruses.
- Transposons can interrupt normal gene function if inserted in the middle of a functional gene, or alter gene expression if inserted into a regulatory element. While these effects may be harmful or lethal, over many generations some may have small beneficial effects. The resulting genetic diversity provides raw material for natural selection.
- **Multigene families** are collections of two or more identical or very similar genes. A classic example is the *human α-globin and β-globin* gene families. Here, the genes for different human globins are on different chromosomes.

Concept 21.5 Duplication, rearrangement, and mutation of DNA contribute to genome evolution

- How might genes with novel functions evolve? Duplication events can lead to the evolution of genes with related functions, such as those of the α-globin and β-globin gene families. Mutations and transpositions can occur, and nonfunctional *pseudogenes* may be found in the clusters. Ultimately, new genes with new functions may occur.

Concept 21.6 Comparing genome sequences provides clues to evolution and development

- **Evo-devo** is a field of biology that compares developmental processes to understand how they may have evolved and how changes can modify existing organismal features or lead to new ones.

- **Homeotic** genes are master regulatory genes that control placement and spatial organization of body parts by controlling the developmental fate of groups of cells.
- A **homeobox** is a widely conserved 180-nucleotide sequence found within homeotic genes. When we say that a sequence is *widely conserved*, this means that it is found in many groups (e.g., fungi, animals, and plants) with very few differences. This hints at the relatedness and common evolution of all life-forms.

Level 1: Knowledge/Comprehension Questions

1. Which of the following is NOT a potential control mechanism for regulation of gene expression in eukaryotic organisms?
   (A) the degradation of RNA
   (B) the transport of mRNA from the nucleus
   (C) the lactose operon
   (D) transcription
   (E) gene amplification

2. Which of the following exists as DNA surrounded by a protein coat?
   (A) retrovirus
   (B) virus
   (C) eukaryotic cell
   (D) prokaryotic cell
   (E) ampicillin

3. A goat can produce milk containing the same polymers present in the silk produced by spiders when particular genes from a spider are inserted into the goat's genome. Which of the following reasons describes why this is possible?
   (A) Goats and spiders share a common ancestor and, thus, produce similar protein excretions.
   (B) The opposite is true, too—when genes from a goat are inserted into a spider's genome, the spider produces goats' milk instead of silk.
   (C) The proteins in goats' milk and spiders' silk have the same amino acid sequence.
   (D) The processes of transcription and translation in the cells of spiders and goats are fundamentally similar.
   (E) The processes of transcription and translation in the cells of spiders and goats produce exactly the same proteins anyway.

4. Restriction enzymes are generally used in the laboratory for which of the following reasons?
   (A) restricting the replication of DNA
   (B) restricting the transcription of DNA
   (C) restricting the translation of mRNA
   (D) cutting DNA molecules at specific locations
   (E) cutting DNA into manageable sizes for manipulation

Directions: The group of questions below consists of five lettered choices followed by a list of numbered phrases or sentences. For each numbered phrase or sentence, select the one choice that is most closely related to it. Each choice may be used once, more than once, or not at all.

Questions 5–9

(A) Transcription
(B) Translation
(C) Transposon
(D) DNA methylation
(E) Histone acetylation

5. A mobile segment of DNA that travels from one location on a chromosome to another, one element of genetic change

6. The addition of groups to certain bases of DNA after DNA synthesis; this is thought to be an important control mechanism for gene expression

7. The synthesis of polypeptides from the genetic information coded in mRNA

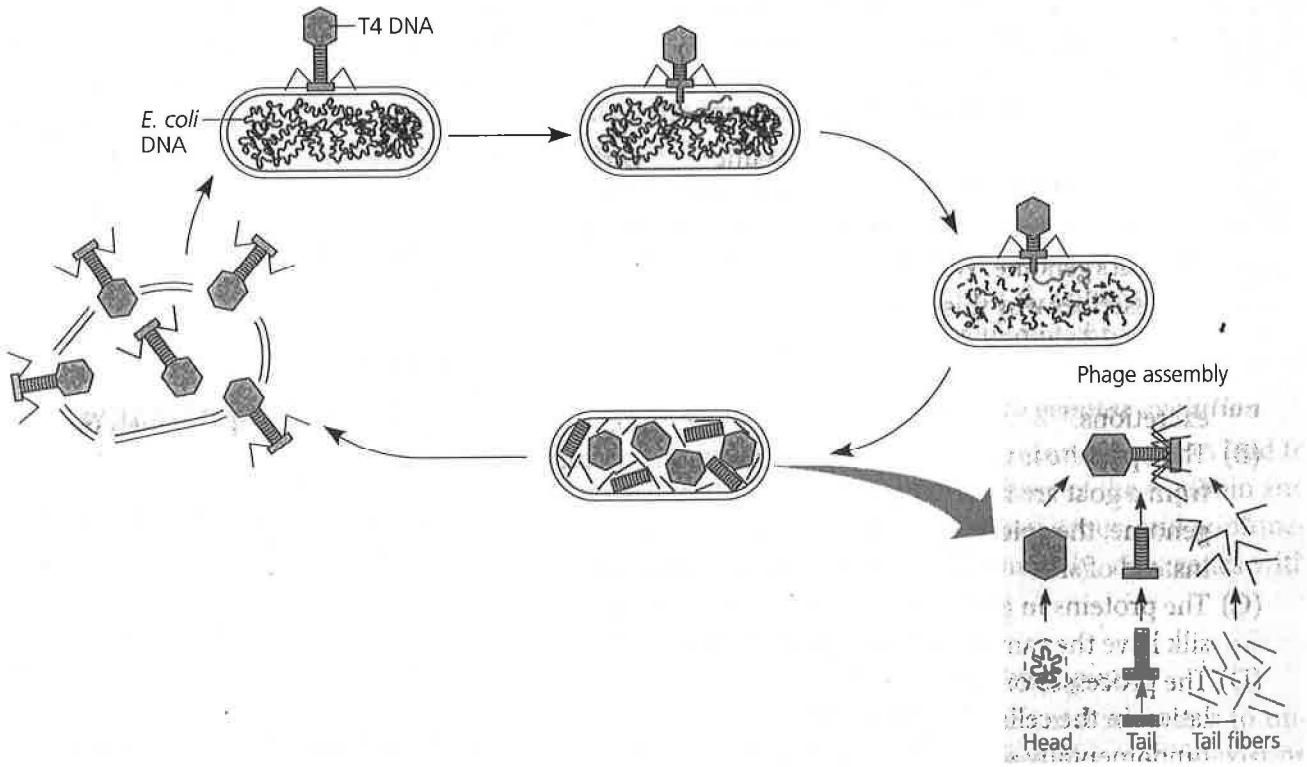
8. The synthesis of RNA from a DNA template

9. The attachment of groups to particular amino acids of specific proteins; this is thought to be an important control mechanism for gene expression

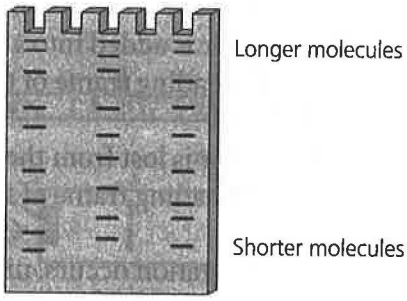
10. The figure below shows which of the following processes?
    (A) the lytic cycle of a phage
    (B) the lysogenic cycle of a phage
    (C) transposition
    (D) retrovirus infection
    (E) mutualism

11. The actions of which of the following enzymes are responsible for ensuring that chromosomes do not decrease in length with every round of replication?
    (A) telomerase
    (B) DNA ligase
    (C) DNA polymerase
    (D) helicase
    (E) primase

12. PCR (polymerase chain reaction) allows target segments of DNA to be produced quickly because it enables lab technicians to do which of the following?
    (A) Isolate gene-source DNA.
    (B) Insert DNA into an appropriate vector.
    (C) Introduce the cloning vector into a host cell.
    (D) Amplify DNA samples.
    (E) Identify clones carrying the gene of interest.



Questions 13–14 refer to an experiment that was performed to separate DNA fragments from three samples radioactively labeled with ^{32}P. The fragments were then separated using gel electrophoresis. The visualized bands are depicted below:



Completed gel

13. When the electric field was applied, the fragments of DNA in each of the three samples migrated to different locations along the gel because
    (A) the fragments differed in their levels of radioactivity.
    (B) the fragments differed in their charges—some were positively charged, whereas others were negatively charged.
    (C) the fragments differed in size.
    (D) the fragments differed in polarity.
    (E) the fragments differed in solubility.

14. How many sites on DNA were cut by the particular restriction enzyme used in Sample 1 (the leftmost sample)?
    (A) 5
    (B) 6
    (C) 7
    (D) 8
    (E) 9

15. A bacterium is infected with an experimentally constructed bacteriophage composed of the T2 phage protein coat and T4 phage DNA. The new phages produced would have
    (A) T2 protein and T4 DNA.
    (B) T2 protein and T2 DNA.
    (C) a mixture of the DNA and proteins of both phages.
    (D) T4 protein and T4 DNA.
    (E) T4 protein and T2 DNA.

16. RNA viruses require their own supply of certain enzymes because
    (A) host cells rapidly destroy the viruses.
    (B) host cells lack enzymes that can replicate the viral genome.
    (C) these enzymes translate viral mRNA into proteins.
    (D) these enzymes penetrate host cell membranes.
    (E) these enzymes cannot be made in host cells.

17. In genetic engineering, DNA ligase is used for which of the following purposes?
    (A) to act as a probe for locating cloned genes
    (B) to create breaks in DNA in order to allow foreign DNA fragments to be inserted
    (C) to seal up nicks created in newly created recombinant DNA
    (D) to ensure that "sticky ends" of like DNA fragments do not re-anneal
    (E) in Southern blotting

Directions: The group of questions below consists of five lettered choices followed by a list of numbered phrases or sentences. For each numbered phrase or sentence, select the one choice that is most closely related to it. Each choice may be used once, more than once, or not at all.

Questions 18–22

(A) tRNA
(B) mRNA
(C) Poly-A tail
(D) RNA polymerase
(E) rRNA

18. An example of a post-transcriptional modification

19. Binds to the promoter on DNA to initiate transcription

20. Along with proteins, comprises ribosomes

21. Binds to free amino acids in the cytoplasm

22. Travels out of the nucleus and into the cytoplasm where it serves as a template in translation

23. The expression of eukaryotic genes can be controlled at all the following stages of protein synthesis EXCEPT
    (A) initiation of transcription.
    (B) RNA processing.
    (C) DNA unpacking.
    (D) degradation of protein.
    (E) acetylation of DNA.

24. After eukaryotic transcription takes place, mRNA undergoes several modifications before leaving the nucleus to take part in translation. One of these is the cutting out of nonessential sections of mRNA and the subsequent splicing together of stretches of mRNA necessary for the final functional molecule. Which of the following mRNA sections are spliced together into the finished mRNA molecule?
    (A) introns
    (B) exons
    (C) genes
    (D) coding sequences
    (E) ribozymes

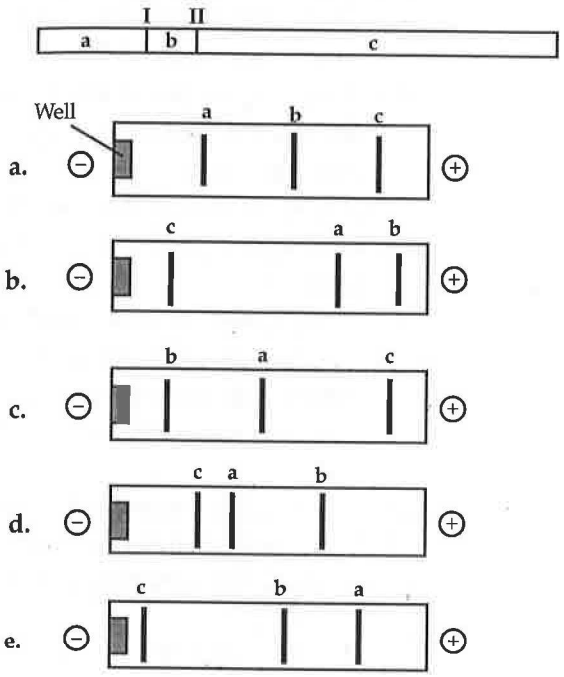
25. In the process of eukaryotic translation, the term *wobble* refers to
    (A) the tendency of the two ribosome subunits to come closer to one another and to separate at different points in translation.
    (B) the tendency of the amino acid loosely attached to the tRNA to move back and forth before finally attaching to the polypeptide chain.
    (C) the fact that the genetic code is redundant.
    (D) the fact that the anticodon and codon bind very loosely.
    (E) the fact that the third nucleotide of a tRNA can form hydrogen bonds with more than one kind of base in the third position of a codon.

26. Which of the following is an example of a missense mutation?
    (A) A nucleotide and its partner are replaced with an "incorrect" pair of nucleotides, which destroys the function of the final protein.
    (B) A nucleotide pair is added into a gene, destroying the reading frame of the genetic message.
    (C) A nucleotide pair is lost from the gene, destroying the reading frame of the genetic message.
    (D) A frameshift mutation occurs, ultimately causing the production of nonfunctional proteins.
    (E) A nucleotide pair substitution occurs, which causes the codon to code for an amino acid that may not be the "correct" one, although translation continues.

27. In analyzing the number of different bases in a DNA sample, which result would be consistent with the base-pairing rules?
    (A) A = G
    (B) A + G = C + T
    (C) A + T = G + T
    (D) A = C
    (E) G = T

28. At the end of DNA replication, each of the daughter molecules has one old strand, derived from the parent strand of DNA, and one strand that is newly synthesized. This explains why DNA replication is described as
    (A) conservative.
    (B) largely conservative.
    (C) nonconservative.
    (D) semiconservative.
    (E) unconservative.

29. The segment of DNA shown below has restriction sites I and II, which create restriction fragments a, b, and c. Which of the following gels produced by electrophoresis would represent the separation and identity of these fragments?



30. Which of the following is a difficulty in getting prokaryotic cells to express eukaryotic genes?
(A) The signals that control gene expression are different and prokaryotic promoter regions must be added to the vector.
(B) The genetic code differs because prokaryotes substitute the base uracil for thymine.
(C) Prokaryotic cells cannot transcribe introns because their genes do not have them.
(D) The ribosomes of prokaryotes are not large enough to handle long eukaryotic genes.
(E) The RNA splicing enzymes of bacteria work differently from those of eukaryotes.

31. One of the characteristics of retrotransposons is that
(A) they code for an enzyme that synthesizes DNA using an RNA template.
(B) they are found only in animal cells.
(C) they generally move by a cut-and-paste mechanism.
(D) they contribute a significant portion of the genetic variability seen within a population of gametes.
(E) their amplification is dependent on a retrovirus.

32. You have affixed the chromosomes from a cell onto a microscope slide. Which of the following would NOT make a good radioactively labeled probe to help map a particular gene to one of those chromosomes? (Assume DNA of chromosomes and probes is single-stranded.)
(A) cDNA made from the mRNA transcribed from the gene
(B) a portion of the amino acid sequence of that protein
(C) mRNA transcribed from the gene
(D) a piece of the restriction fragment on which the gene is located
(E) a sequence of nucleotide bases determined from the genetic code needed to produce a known sequence of amino acids found in the protein product of the gene

33. The human genome appears to have only one-third more genes than the simple nematode, *C. elegans*. Which of the following best explains how the more complex humans can have relatively few genes?
(A) The unusually long introns in human genes are involved in regulation of gene expression.
(B) More than one polypeptide can be produced from a gene by alternative splicing.
(C) Human genes code for many more types of domains.
(D) The human genome has a high proportion of noncoding DNA.
(E) The large number of SNPs (single nucleotide polymorphisms) in the human genome provides for a great deal of genetic variability.

34. Multigene families are
    (A) groups of enhancers that control transcription.
    (B) usually clustered at the telomeres.
    (C) equivalent to the operons of prokaryotes.
    (D) sets of genes that are coordinately controlled.
    (E) sets of identical or similar genes that have evolved by gene duplication.

35. Homeotic genes
    (A) encode transcription factors that control the expression of genes responsible for specific anatomical structures.
    (B) are found only in *Drosophila* and other arthropods.
    (C) are the only genes that contain the homeobox domain.
    (D) encode proteins that form anatomical structures in the fly.
    (E) are responsible for patterning during plant development.

Level 2: Application/Analysis/Synthesis Questions

After reading the paragraphs, answer the question(s) that follow.

Exposure to the HIV virus doesn't necessarily mean that a person will develop AIDS. Some people have genetic resistance to infection by HIV. Dr. Stephen O'Brien from the U.S. National Cancer Institute has recently identified a mutant form of a gene, called CCR5, which can protect against HIV infection. The mutation probably originated in Europe among survivors of the bubonic plague. The mutated gene prevents the plague bacteria from attaching to cell membranes and, therefore, from entering and infecting body cells.

Although the HIV virus is very different from the bacterium that causes the plague, both diseases affect the exact same cells and use the same method of infection. The presence of the mutated gene in descendants of plague survivors helps prevent them from contracting AIDS. Pharmaceutical companies are using this information as the basis for a new approach to AIDS prevention. This would be very important in areas of the world where the mutation is scarce or absent, such as Africa.

1. The most likely method by which the mutated CCR5 gene prevents AIDS is by
    (A) covering the cell membrane.
    (B) rupturing the nuclear membrane.
    (C) attacking and destroying the HIV virus particles.
    (D) coding for a protective protein in the cell membrane.

2. Which of the following shows the steps of a viral infection in the proper order?
    (A) Virus locates host cell → enters nucleus → alters host cell DNA → destroys cell membrane.
    (B) Virus locates host cell → alters host cell DNA → host cell produces copies of virus → copies enter host cell nucleus → nucleus leaves cell.
    (C) Virus locates host cell → penetrates cell membrane → enters nucleus → alters host cell DNA → host cell produces copies of virus.
    (D) Virus locates host cell → forms hydrogen bonds → changes DNA to RNA → host cell produces copies of virus.

3. Conjugation, transformation, and transduction are all ways that bacteria
    (A) reduce their DNA content.
    (B) increase the amount of RNA in the cytoplasm.
    (C) increase their genetic diversity.
    (D) alter their oxygen requirements.

After reading the paragraph, answer the question(s) that follow.

Four decades after the end of the Vietnam War, the remains of an Air Force pilot were discovered and returned to the United States. A search of Air Force records identified three families to which the remains might possibly belong. Each family

had a surviving twin of a missing service member. The following STR profiles were obtained from the remains of the pilot and the surviving twins from the three families.

	Air Force Pilot	Family 1	Family 2	Family 3
1		—		
2	—	—		—
3	—			—
4		—		
5	—	—	—	—
6			—	
7	—	—	—	—
8			—	
9		—		
10	—			—
11			—	
12		—		
13	—		—	—

4. In order to match the pilot's remains to the correct family using DNA profiling,
   (A) the majority of the STR bands must match.
   (B) each of the 13 STR bands must match.
   (C) the bands for site 13 must match.
   (D) bands 5 and 7 must match.

5. Based on analysis of the STR sites shown, does the missing pilot belong to any of these three families?
   (A) No, none of the families match.
   (B) Yes, family 1 matches.
   (C) Yes, family 2 matches.
   (D) Yes, family 3 matches.

6. Which of the following mutations would be most likely to have a harmful effect on an organism?
   (A) a deletion of three nucleotides near the middle of a gene
   (B) a single nucleotide deletion in the middle of an intron
   (C) a single nucleotide deletion near the end of the coding sequence
   (D) a single nucleotide insertion downstream of, and close to, the start of the coding sequence

7. Which of the following is NOT true of RNA processing?
   (A) Exons are cut out before mRNA leaves the nucleus.
   (B) Nucleotides may be added at both ends of the RNA.
   (C) Ribozymes may function in RNA splicing.
   (D) RNA splicing can be catalyzed by spliceosomes.

8. What is the basis for the difference in how the leading and lagging strands of DNA molecules are synthesized?
   (A) The origins of replication occur only at the 5′ end.
   (B) Helicases and single-strand binding proteins work at the 5′ end.
   (C) DNA polymerase can join new nucleotides only to the 3′ end of a growing strand.
   (D) DNA ligase works only in the 3′ → 5′ direction.

Free-Response Question

1. *Genes are located on chromosomes and are the basic unit of heredity that is passed on from parent to child, through generations.*

   (a) **Explain** how a chromosomal mutation could occur and why mutations are detrimental to the organism in which they take place.

   (b) **Explain** why it is more common for human males to be color-blind or have hemophilia than females.

   (c) Proper gene dosages are critical to normal development and function. How do we maintain proper gene dosages related to the X chromosome, given that females have two copies of the chromosome and males only one?