DNA: STRUCTURE AND REPLICATION

- DNA
  - was known to be a chemical in cells by the end of the nineteenth century,
  - has the capacity to store genetic information, and
  - can be copied and passed from generation to generation.
- The discovery of DNA as the hereditary material ushered in the new field of **molecular biology**, the study of heredity at the molecular level.

DNA and RNA Structure

- DNA and RNA are nucleic acids.
  - They consist of chemical units called **nucleotides**.
  - A nucleotide polymer is a **polynucleotide**.
  - Nucleotides are joined by covalent bonds between the sugar of one nucleotide and the phosphate of the next, forming a **sugar-phosphate backbone**.

Watson and Crick's Discovery of the Double Helix

- James Watson and Francis Crick determined that DNA is a **double helix**.
- Watson and Crick used X-ray crystallography data to reveal the basic shape of DNA.
- Rosalind Franklin produced the X-ray image of DNA.
- The model of DNA is like a rope ladder twisted into a spiral.
  - The ropes at the sides represent the sugar-phosphate backbones.
  - Each wooden rung represents a pair of bases connected by hydrogen bonds.
- DNA bases pair in a complementary fashion:
  - adenine (A) pairs with thymine (T) and
  - cytosine (C) pairs with guanine (G).

DNA Replication

- When a cell reproduces, a complete copy of the DNA must pass from one generation to the next.
- Watson and Crick's model for DNA suggested that DNA replicates by a template mechanism.
- DNA can be damaged by X-rays and ultraviolet light.
- **DNA polymerases**
  - are enzymes,
  - make the covalent bonds between the nucleotides of a new DNA strand, and
  - are involved in repairing damaged DNA.
- DNA replication ensures that all the body cells in multicellular organisms carry the same genetic information.
- DNA replication in eukaryotes
  - begins at specific sites on a double helix (called origins of replication) and
  - proceeds in both directions.

THE FLOW OF GENETIC INFORMATION FROM DNA TO RNA TO PROTEIN

- DNA provides instructions to
  - a cell and
  - an organism as a whole.

How an Organism's Genotype Determines Its Phenotype

- An organism's *genotype* is its genetic makeup, the sequence of nucleotide bases in DNA.
- The *phenotype* is the organism's physical traits, which arise from the actions of a wide variety of proteins.
- DNA specifies the synthesis of proteins in two stages:
    - **transcription**, the transfer of genetic information from DNA into an RNA molecule and
    - **translation**, the transfer of information from RNA into a protein.
- The major breakthrough in demonstrating the relationship between genes and enzymes came in the 1940s from the work of American geneticists George Beadle and Edward Tatum with the bread mold *Neurospora crassa*.
- Beadle and Tatum
    - studied strains of mold that were unable to grow on the usual growth medium,
    - determined that these strains lacked an enzyme in a metabolic pathway that synthesized arginine,
    - showed that each mutant was defective in a single gene, and
    - hypothesized that the function of an individual gene is to dictate the production of a specific enzyme.

- The one gene–one enzyme hypothesis has since been modified.
- The function of a gene is to dictate the production of a polypeptide.
- A protein may consist of two or more different polypeptides.

From Nucleotides to Amino Acids: An Overview

- Genetic information in DNA is
    - transcribed into RNA, then
    - translated into polypeptides,
    - which then fold into proteins.
- What is the language of nucleic acids?
    - In DNA, it is the linear sequence of nucleotide bases.
    - A typical gene consists of thousands of nucleotides in a specific sequence.
- When a segment of DNA is transcribed, the result is an RNA molecule.
- RNA is then translated into a sequence of amino acids in a polypeptide.
- Experiments have verified that the flow of information from gene to protein is based on a triplet code.
- A **codon** is a triplet of bases, which codes for one amino acid.

The Genetic Code

- The **genetic code** is the set of rules that convert a nucleotide sequence in RNA to an amino acid sequence.
- Of the 64 triplets,
    - 61 code for amino acids and
    - 3 are stop codons, instructing the ribosomes to end the polypeptide.

- Because diverse organisms share a common genetic code, it is possible to program one species to produce a protein from another species by transplanting DNA.

Transcription: From DNA to RNA

- Transcription
  - makes RNA from a DNA template,
  - uses a process that resembles the synthesis of a DNA strand during DNA replication, and
  - substitutes uracil (U) for thymine (T).
- RNA nucleotides are linked by the transcription enzyme **RNA polymerase**.

Initiation of Transcription

- The “start transcribing” signal is a nucleotide sequence called a **promoter**, which is
  - located in the DNA at the beginning of the gene and
  - a specific place where RNA polymerase attaches.
- The first phase of transcription is initiation, in which
  - RNA polymerase attaches to the promoter and
  - RNA synthesis begins.

RNA Elongation

- During the second phase of transcription, called elongation,
  - the RNA grows longer and
  - the RNA strand peels away from its DNA template.

Termination of Transcription

- During the third phase of transcription, called termination,
  - RNA polymerase reaches a special sequence of bases in the DNA template called a **terminator**, signaling the end of the gene,
  - polymerase detaches from the RNA and the gene, and
  - the DNA strands rejoin.

The Processing of Eukaryotic RNA

- In the cells of prokaryotes, RNA transcribed from a gene immediately functions as **messenger RNA (mRNA)**, the molecule that is translated into protein.
- The eukaryotic cell
  - localizes transcription in the nucleus and
  - modifies, or processes, the RNA transcripts in the nucleus before they move to the cytoplasm for translation by ribosomes.

- RNA processing includes
  - adding a **cap** and **tail** consisting of extra nucleotides at the ends of the RNA transcript,
  - removing **introns** (noncoding regions of the RNA), and
  - RNA splicing, joining **exons** (the parts of the gene that are expressed) together to form **messenger RNA** (mRNA).

- RNA splicing is believed to play a significant role in humans
  - in allowing our approximately 21,000 genes to produce many thousands more polypeptides and
  - by varying the exons that are included in the final mRNA.

Translation: The Players

- Translation is the conversion from the nucleic acid language to the protein language.

Messenger RNA (mRNA)

- Translation requires
  - mRNA,
  - ATP,
  - enzymes,
  - ribosomes, and
  - transfer RNA (tRNA).

Transfer RNA (tRNA)

- **Transfer RNA (tRNA)**
  - acts as a molecular interpreter,
  - carries amino acids, and
  - matches amino acids with codons in mRNA using **anticodons**, a special triplet of bases that is complementary to a codon triplet on mRNA.

Ribosomes

- Ribosomes are organelles that
  - coordinate the functions of mRNA and tRNA and
  - are made of two subunits.
- Each subunit is made up of
  - proteins and
  - a considerable amount of another kind of RNA, **ribosomal RNA (rRNA)**.

Ribosomes

- A fully assembled ribosome holds tRNA and mRNA for use in translation.

Translation: The Process

- Translation is divided into three phases:
  - initiation,
  - elongation, and
  - termination.

Initiation

- Initiation brings together
  - mRNA,
  - the first amino acid with its attached tRNA, and
  - two subunits of the ribosome.
- The mRNA molecule has a cap and tail that help the mRNA bind to the ribosome.

- Initiation occurs in two steps.
  - An mRNA molecule binds to a small ribosomal subunit, then a special initiator tRNA binds to the **start codon**, where translation is to begin on the mRNA.
  - A large ribosomal subunit binds to the small one, creating a functional ribosome.

Elongation

- Elongation occurs in three steps.
  - **Step 1: Codon recognition.** The anticodon of an incoming tRNA pairs with the mRNA codon at the A site of the ribosome.

  - **Step 2: Peptide bond formation.**
    - The polypeptide leaves the tRNA in the P site and attaches to the amino acid on the tRNA in the A site.

    - The ribosome catalyzes the bond formation between the two amino acids.

  - **Step 3: Translocation.**
    - The P site tRNA leaves the ribosome.
    - The tRNA carrying the polypeptide moves from the A to the P site.

Termination

- Elongation continues until
  - a **stop codon** reaches the ribosome's A site,
  - the completed polypeptide is freed, and
  - the ribosome splits back into its subunits.

Review: DNA→ RNA→ Protein

- In a cell, genetic information flows from
  - DNA to RNA in the nucleus and
  - RNA to protein in the cytoplasm.

- As it is made, a polypeptide
  - coils and folds and
  - assumes a three-dimensional shape, its tertiary structure.
- Transcription and translation are how genes control the structures and activities of cells.

Mutations

- A **mutation** is any change in the nucleotide sequence of DNA.
- Mutations can change the amino acids in a protein.
- Mutations can involve
  - large regions of a chromosome or
  - just a single nucleotide pair, as occurs in sickle-cell disease.

- Mutations within a gene can be divided into two general categories:
  - nucleotide substitutions (the replacement of one base by another) and
  - nucleotide deletions or insertions (the loss or addition of a nucleotide).
- Insertions and deletions can
  - change the reading frame of the genetic message and
  - lead to disastrous effects.

Mutagens

- Mutations may result from
  - errors in DNA replication or recombination or
  - physical or chemical agents called **mutagens**.
- Mutations
  - are often harmful but
  - are useful in nature and the laboratory as a source of genetic diversity, which makes evolution by natural selection possible.

VIRUSES AND OTHER NONCELLULAR INFECTIOUS AGENTS

- Viruses share some, but not all, characteristics of living organisms. Viruses

- possess genetic material in the form of nucleic acids wrapped in a protein coat,
- are not cellular, and
- cannot reproduce on their own.

Bacteriophages

- **Bacteriophages**, or **phages,** are viruses that attack bacteria.
- Phages consist of a molecule of DNA, enclosed within an elaborate structure made of proteins.
- Phages have two reproductive cycles.
    - In the lytic cycle,
        - many copies of the phage are produced within the bacterial cell, and
        - then the bacterium lyses (breaks open).

    - In the lysogenic cycle,
        - the phage DNA inserts into the bacterial chromosome and
        - the bacterium reproduces normally, copying the phage at each cell division.

Plant Viruses

- Viruses that infect plants can
    - stunt growth and
    - diminish plant yields.
- Most known plant viruses have RNA rather than DNA as their genetic material.
- Many of them, like the tobacco mosaic virus, are rod-shaped with a spiral arrangement of proteins surrounding the nucleic acid.
- Viral plant diseases
    - have no cure and
    - are best prevented by producing plants that resist viral infection.

Animal Viruses

- Viruses that infect animals cells
    - are a common cause of disease and
    - may have RNA or DNA genomes.
- Many animal viruses have an outer envelope made of phospholipid membrane, with projecting spikes of protein.
- The reproductive cycle of an enveloped RNA virus can be broken into seven steps.

HIV, the AIDS Virus

- The devastating disease AIDS (acquired immunodeficiency syndrome) is caused by HIV (human immunodeficiency virus), an RNA virus with some special twists.
- HIV is a **retrovirus**, an RNA virus that reproduces by means of a DNA molecule.
- Retroviruses use the enzyme **reverse transcriptase** to catalyze reverse transcription, the process of synthesizing DNA on an RNA template.
- The behavior of HIV nucleic acid in an infected cell can be broken into six steps.
- HIV infects and eventually kills several kinds of white blood cells that are important in the body's immune system.
- While there is no cure for AIDS, its progression can be slowed by two categories of medicine that interfere with the reproduction of the virus.

Viroids and Prions

- Two classes of pathogens are smaller than viruses.
    1. *Viroids* are small, circular RNA molecules that infect plants.
    2. ***Prions*** are misfolded proteins that somehow convert normal proteins to the misfolded prion version, leading to disease.
- Prions are responsible for neurodegenerative diseases including
    - mad cow disease,
    - scrapie in sheep and goats,
    - chronic wasting disease in deer and elk, and
    - Creutzfeldt-Jakob disease in humans.