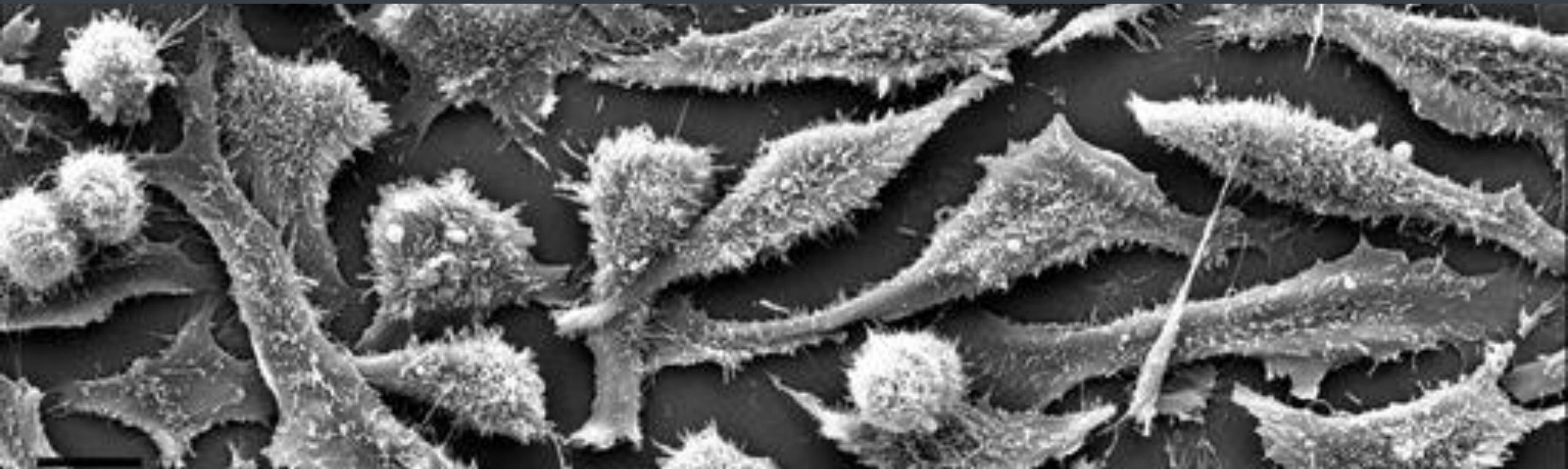
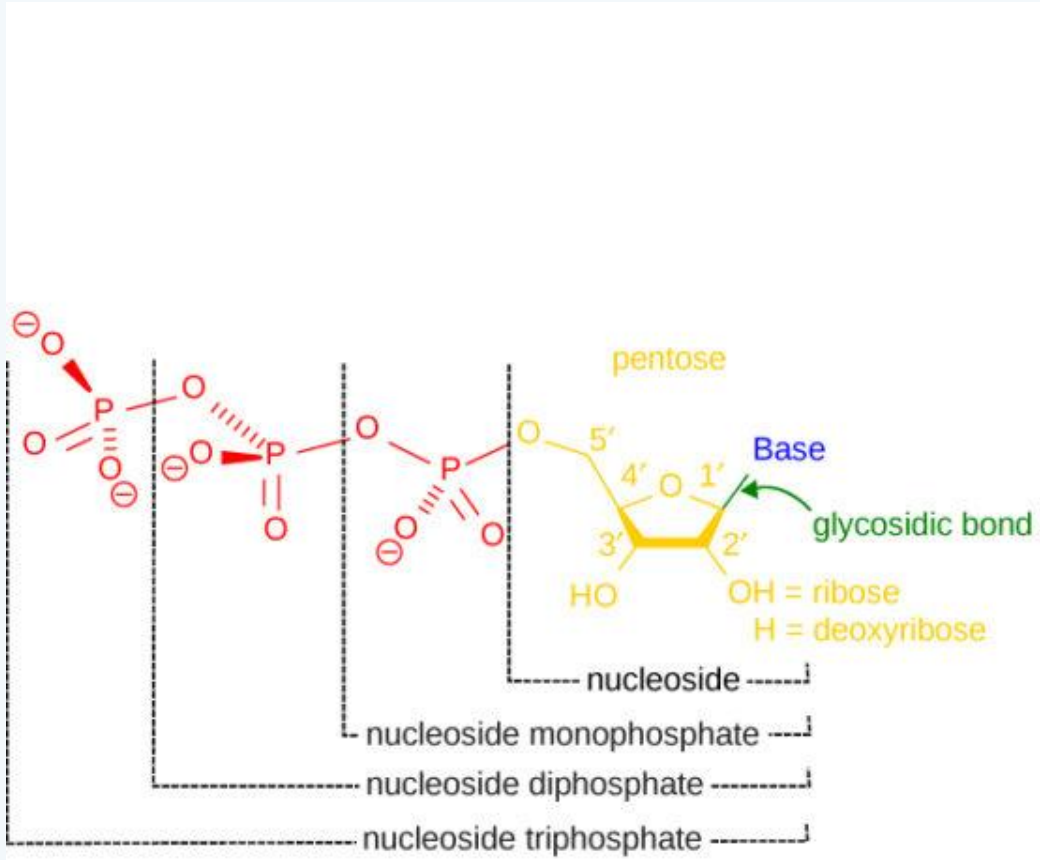
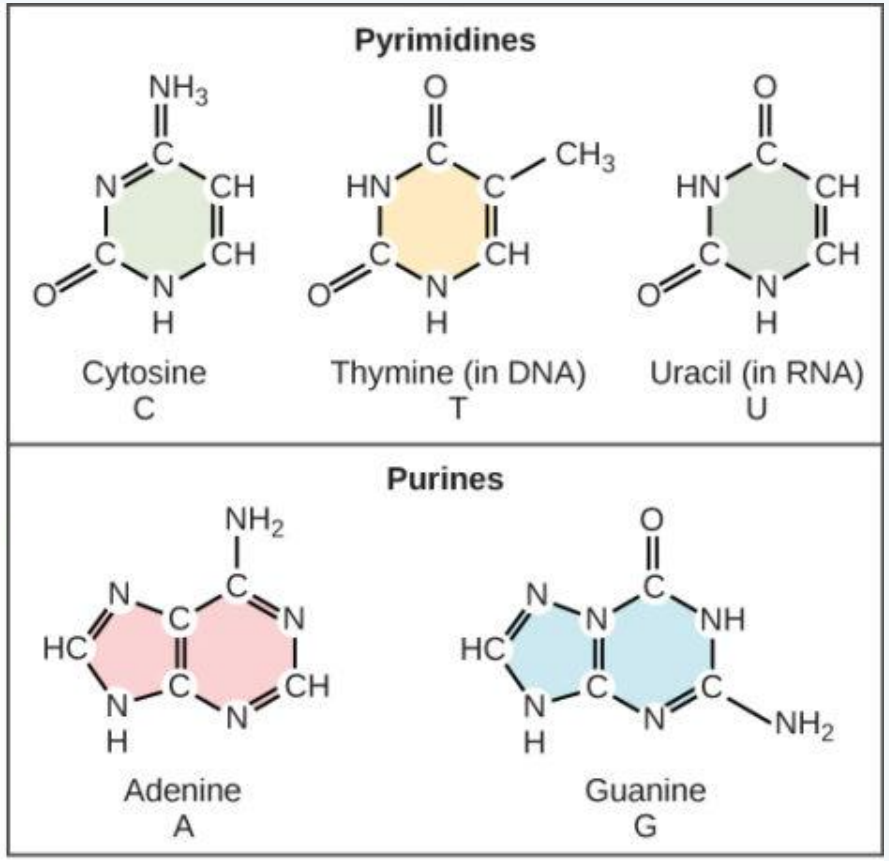
DNA Structure and Replication

Biology for Majors



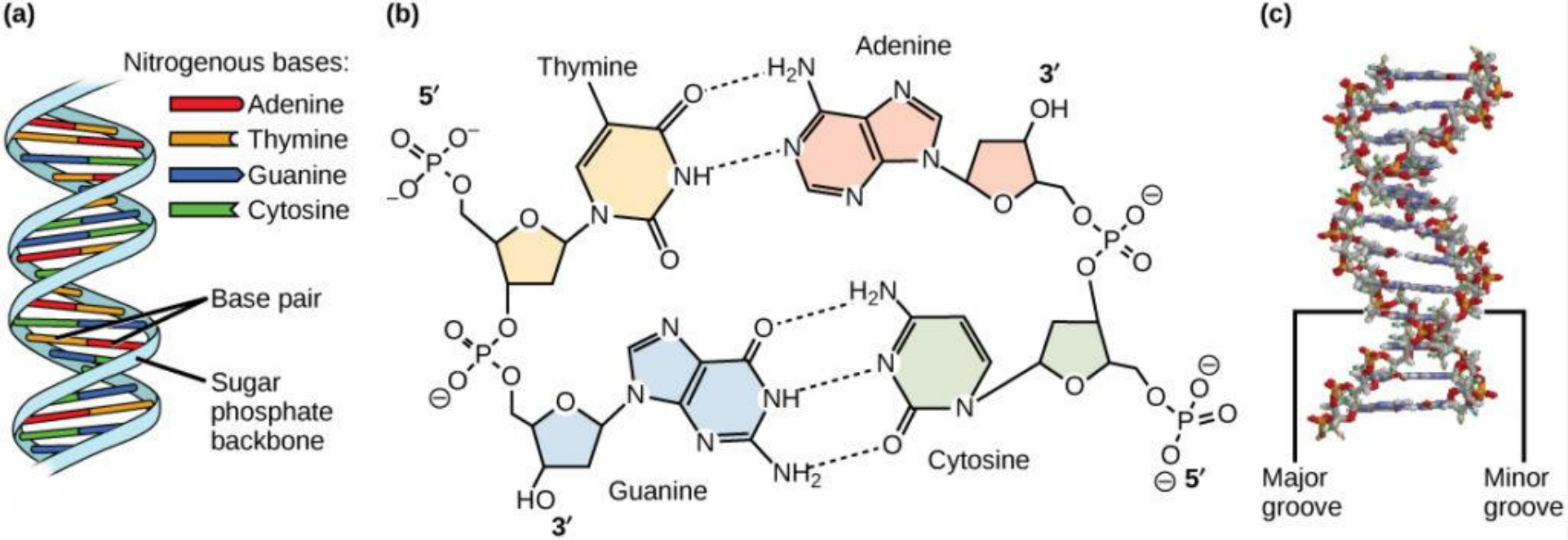
Structure of DNA





The building blocks of DNA are nucleotides. Each nucleotide is made up of a sugar, a phosphate group, and a nitrogenous base. The sugar is deoxyribose in DNA and ribose in RNA.

Double Helix, Phosphodiester Bonds, and Major and Minor Grooves



DNA has (a) a double helix structure and (b) phosphodiester bonds. The (c) major and minor grooves are binding sites for DNA binding proteins during processes such as transcription (the copying of RNA from DNA) and replication.

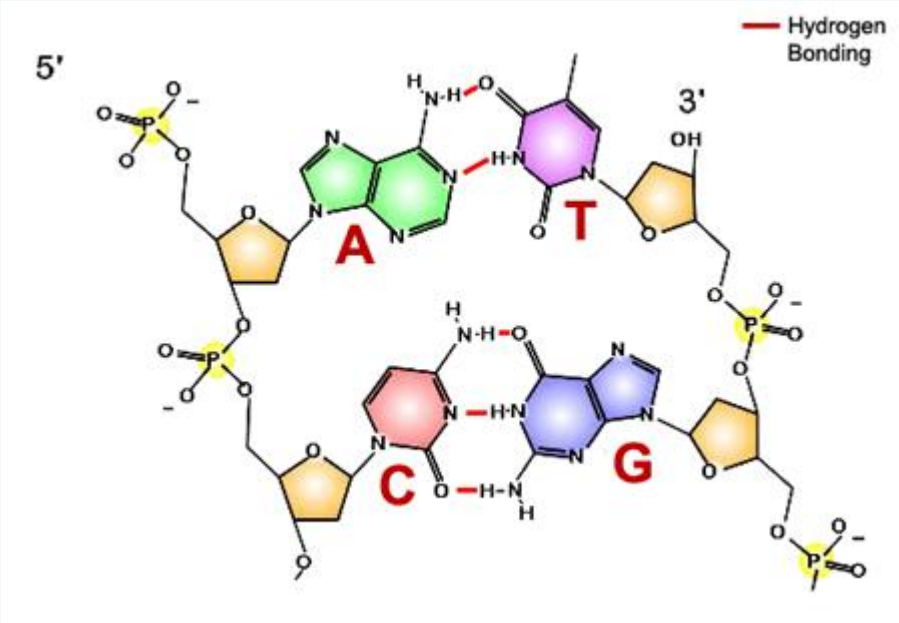
Storing Information in DNA

In order for DNA to function effectively at storing information, two key processes are required:

1. Information stored in the DNA molecule must be copied, with minimal errors, every time a cell divides. This ensures that both daughter cells inherit the complete set of genetic information from the parent cell.
2. The information stored in the DNA molecule must be translated, or expressed. In order for the stored information to be useful, cells must be able to access the instructions for making specific proteins, so the correct proteins are made in the right place at the right time.

Genetic Information

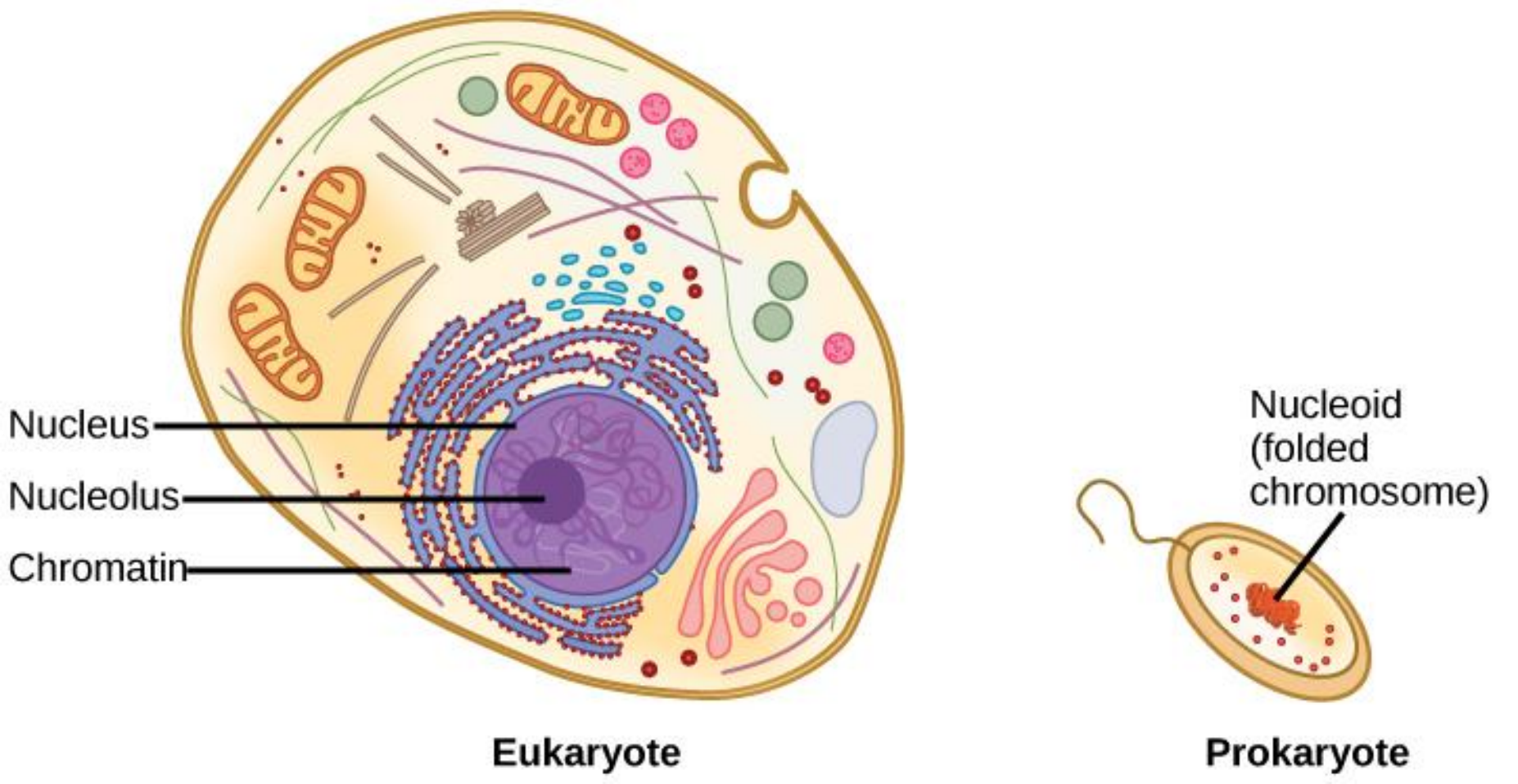
The sequence of the four bases provides all the instructions needed to build any living organism. Complementary bases form hydrogen bonds with each other within the double helix. The bigger bases (purines) pair with the smaller ones (pyrimidines). This keeps the width of the double helix constant. More specifically, A pairs with T and C pairs with G.



DNA to RNA

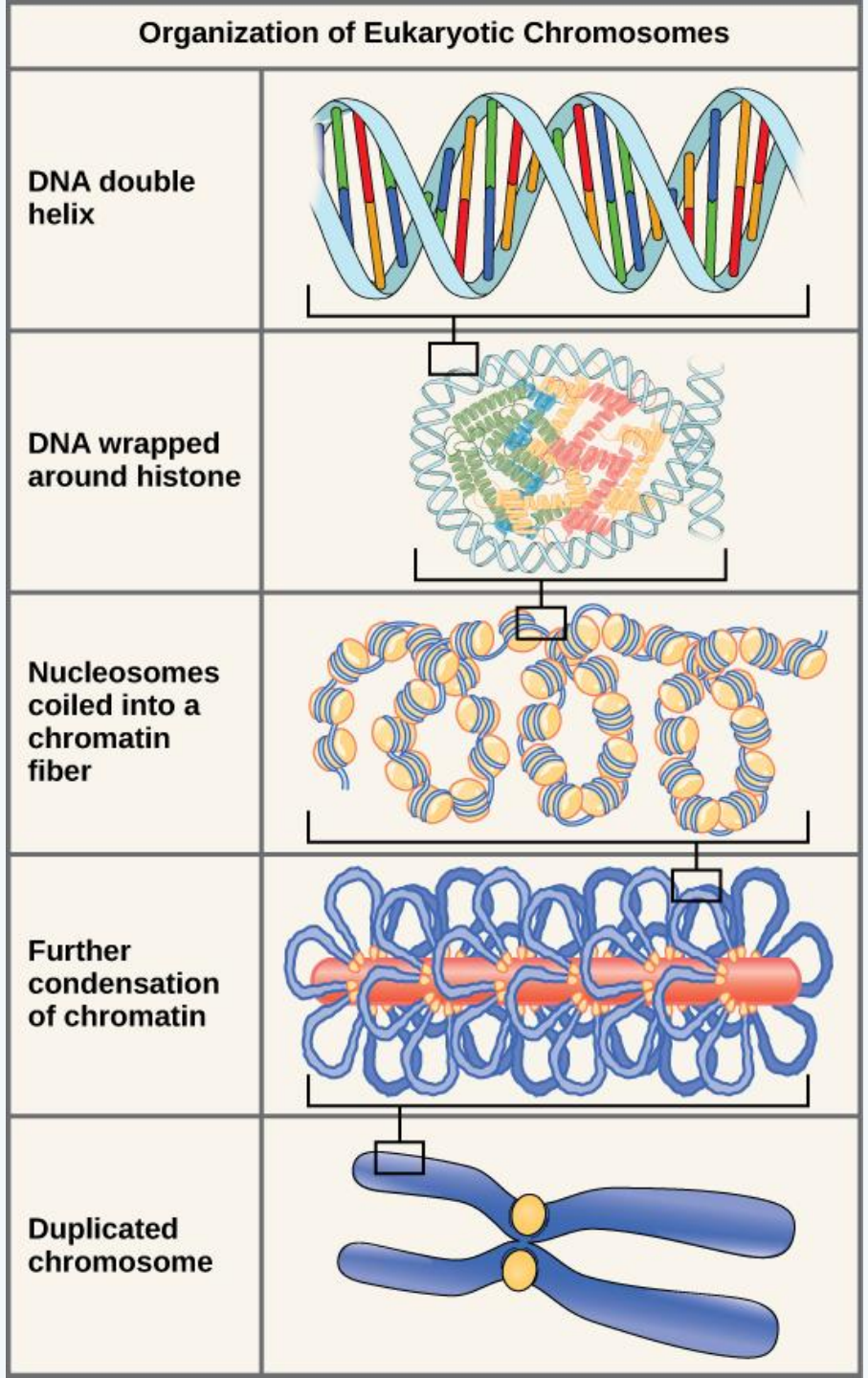
Genetic information is organized into genes: each gene contains information for making a functional product. The genetic information is first copied to another nucleic acid polymer, RNA (ribonucleic acid), preserving the order of the nucleotide bases. Genes that contain instructions for making proteins are converted to messenger RNA (mRNA). Some specialized genes contain instructions for making functional RNA molecules that don't make proteins but are required for protein synthesis, transfer RNA (tRNA), and ribosomal RNA (rRNA).

Chromosomes in Prokaryotes and Eukaryotes



Organization of Eukaryotic Chromosomes

These figures illustrate the compaction of the eukaryotic chromosome.



History of DNA

DNA was first isolated from white blood cells by Friedrich Miescher, who called it nuclein because it was isolated from nuclei.

Frederick Griffith's experiments with strains of *Streptococcus pneumoniae* provided the first hint that DNA may be the transforming principle.

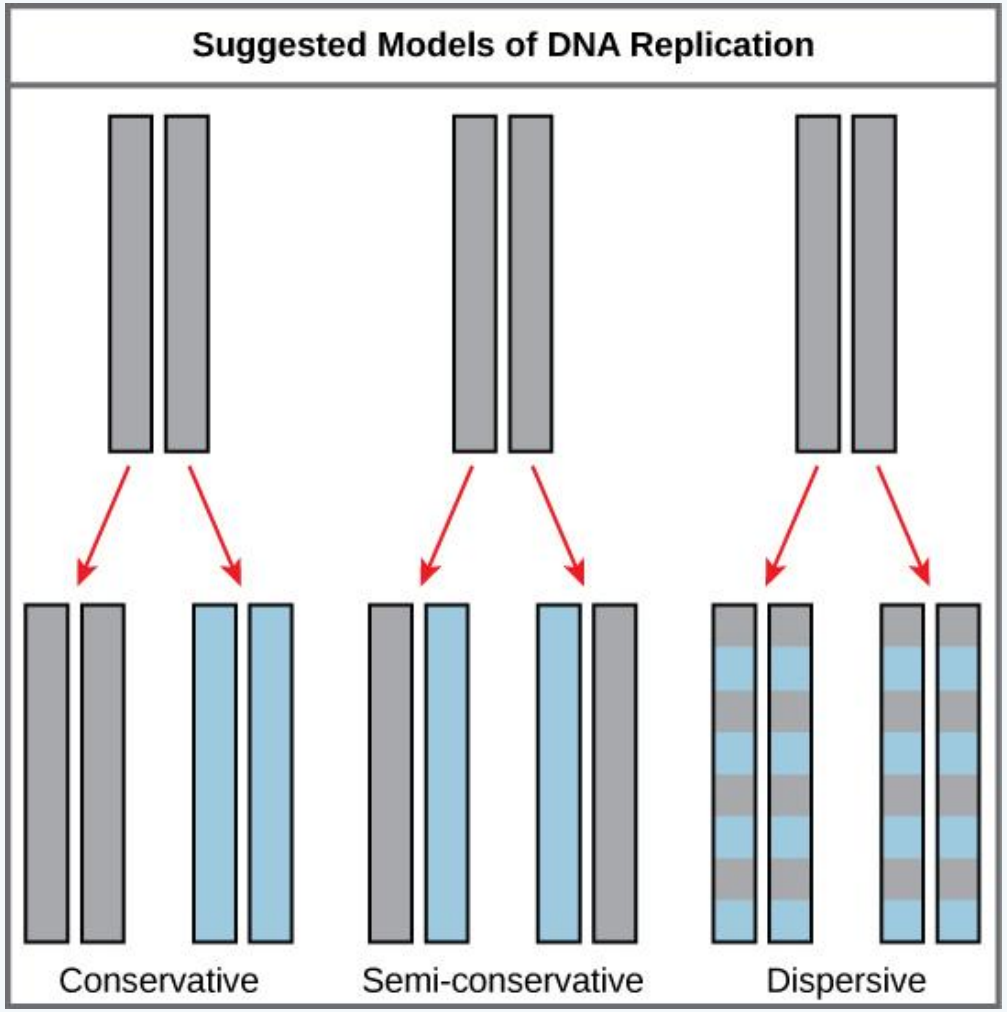
Avery, MacLeod, and McCarty proved that DNA is required for the transformation of bacteria.

Later experiments by Hershey and Chase using bacteriophage T2 proved that DNA is the genetic material.

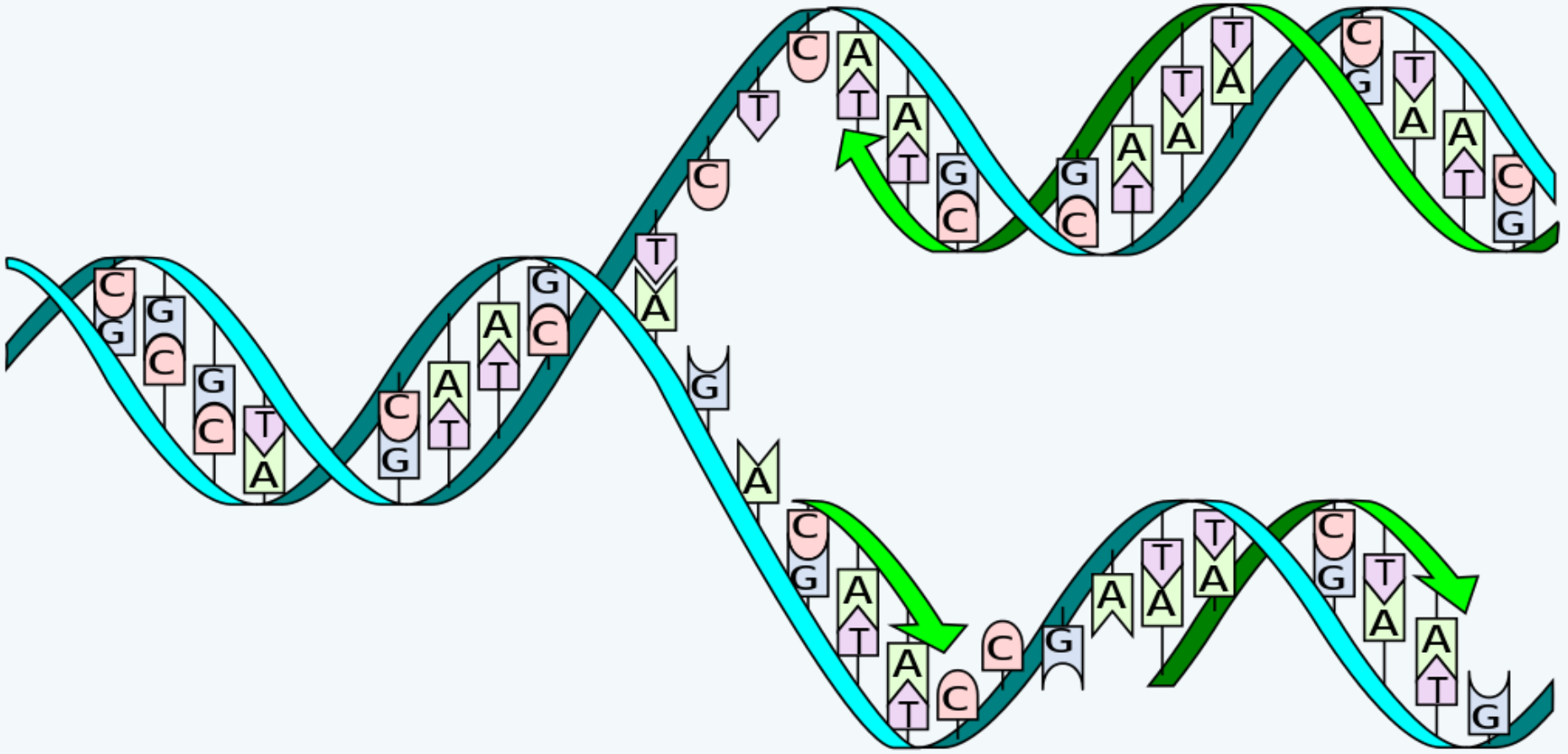
Chargaff found that the ratio of A = T and C = G, and that the percentage content of A, T, G, and C is different for different species.

DNA Replication

The model for DNA replication suggests that the two strands of the double helix separate during replication, and each strand serves as a template from which the new complementary strand is copied. Each of the two parental DNA strands acts as template for new DNA to be synthesized; after replication, each double-stranded DNA includes one parental or "old" strand and one "new" strand as in the semi-conservative model at right.



The Double Helix Separates

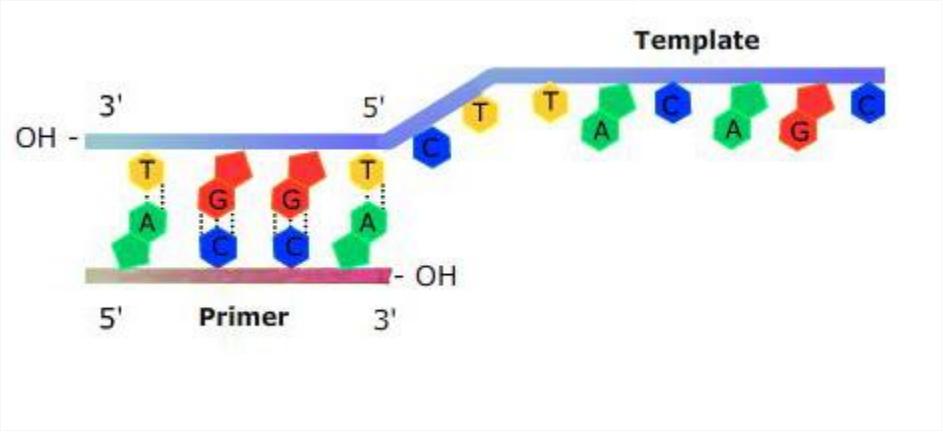


Major Enzymes

Replication in eukaryotes starts at multiple origins of replication. A primer is required to initiate synthesis, which is then extended by DNA polymerase as it adds nucleotides one by one to the growing chain. The leading strand is synthesized continuously, whereas the lagging strand is synthesized in short stretches called Okazaki fragments. The RNA primers are replaced with DNA nucleotides; the DNA remains one continuous strand by linking the DNA fragments with DNA ligase.

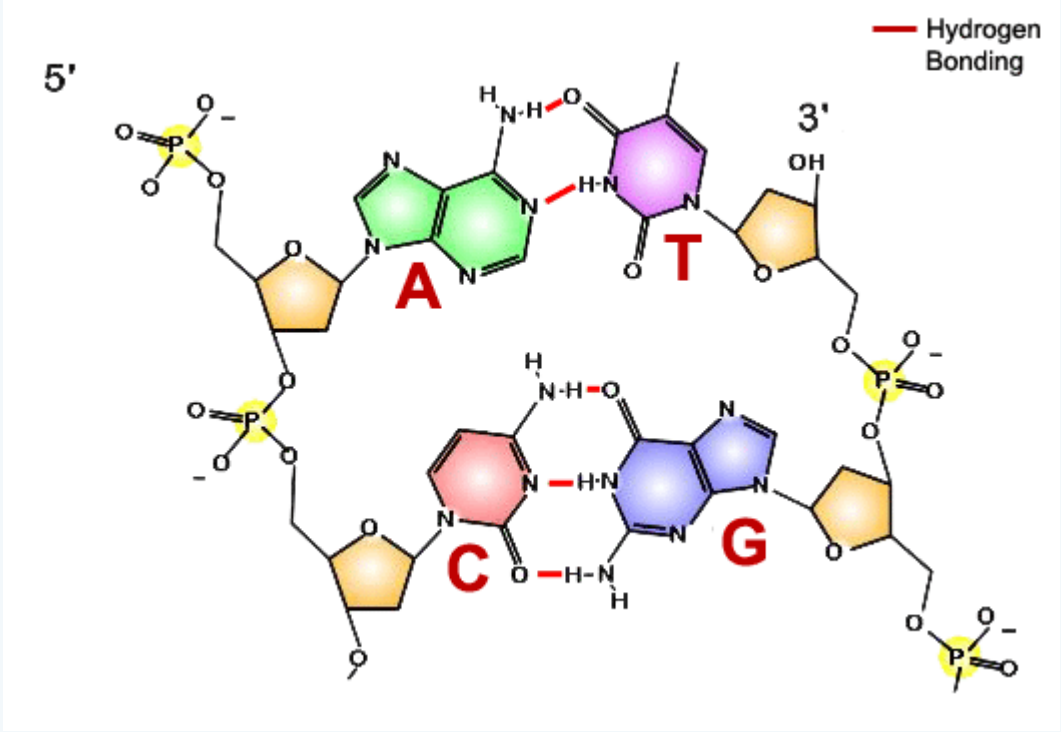
DNA Polymerase and Primer Sequences

DNA polymerase needs an "anchor" to start adding nucleotides: a short sequence of DNA or RNA that is complementary to the template strand will work to provide a free 3′ end. This sequence is called a primer.

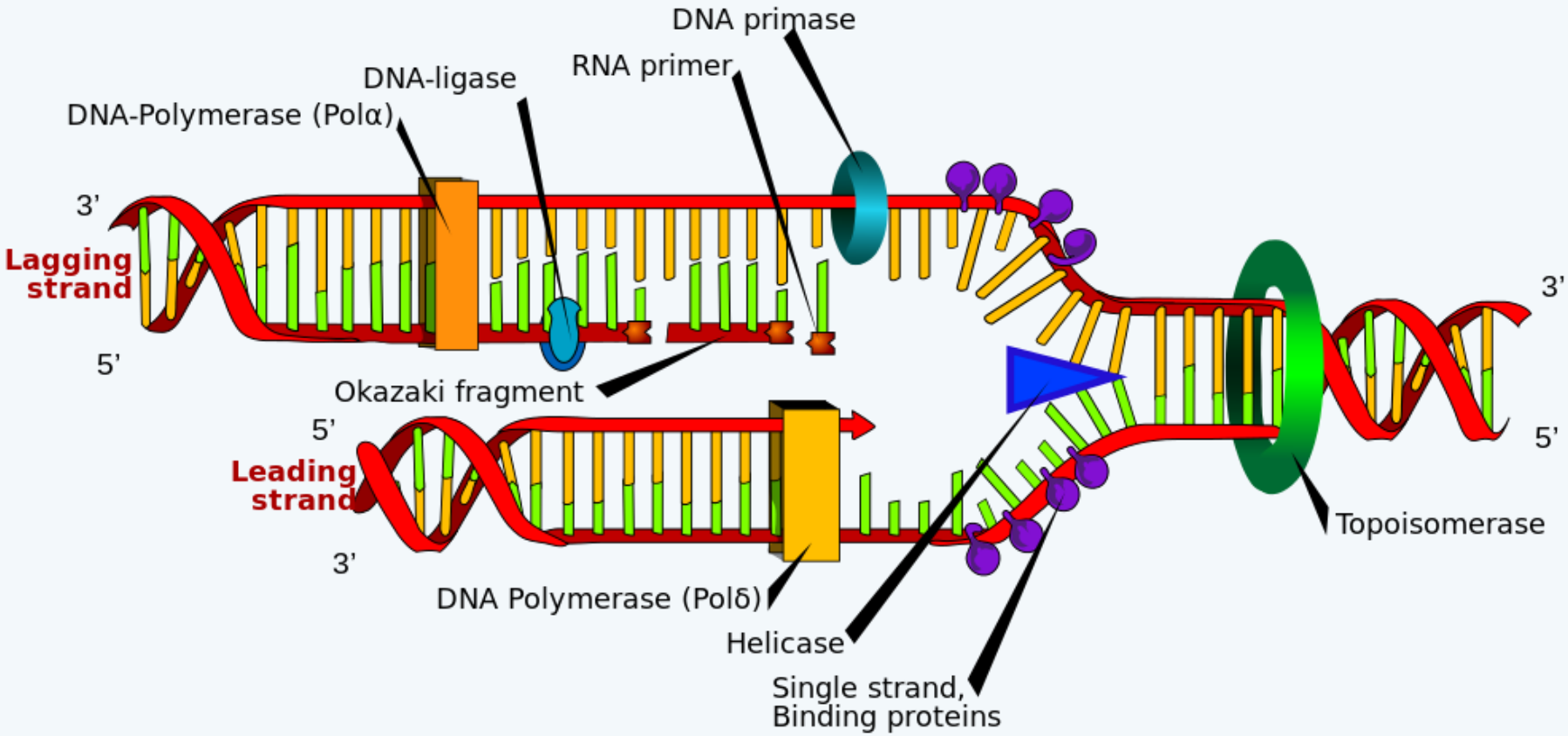


DNA Polymerase and Base Pairs

How does DNA polymerase know in what order to add nucleotides? Specific base pairing in DNA is the key to copying the DNA: if you know the sequence of one strand, you can use base pairing rules to build the other strand.



Enzymes at Work



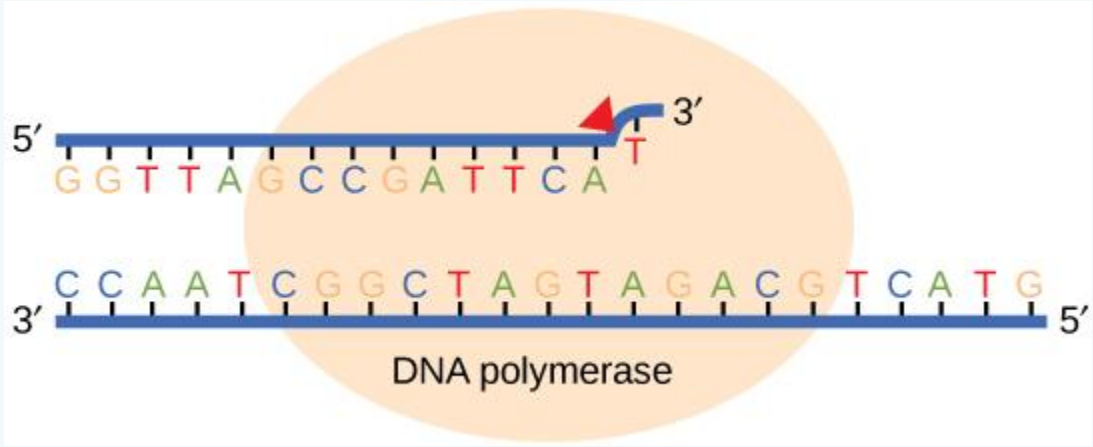
Important Enzymes in DNA Replication

Enzyme	Function
Topoisomerase	Relaxes the super-coiled DNA
DNA helicase	Unwinds the double helix at the replication fork
Primase	Provides the starting point for DNA polymerase to begin synthesis of the new strand
DNA polymerase	Synthesizes the new DNA strand; also proofreads and corrects some errors
DNA ligase	Re-joins the two DNA strands into a double helix and joins Okazaki fragments of the lagging strand

Practice Question

What does DNA Polymerase do?

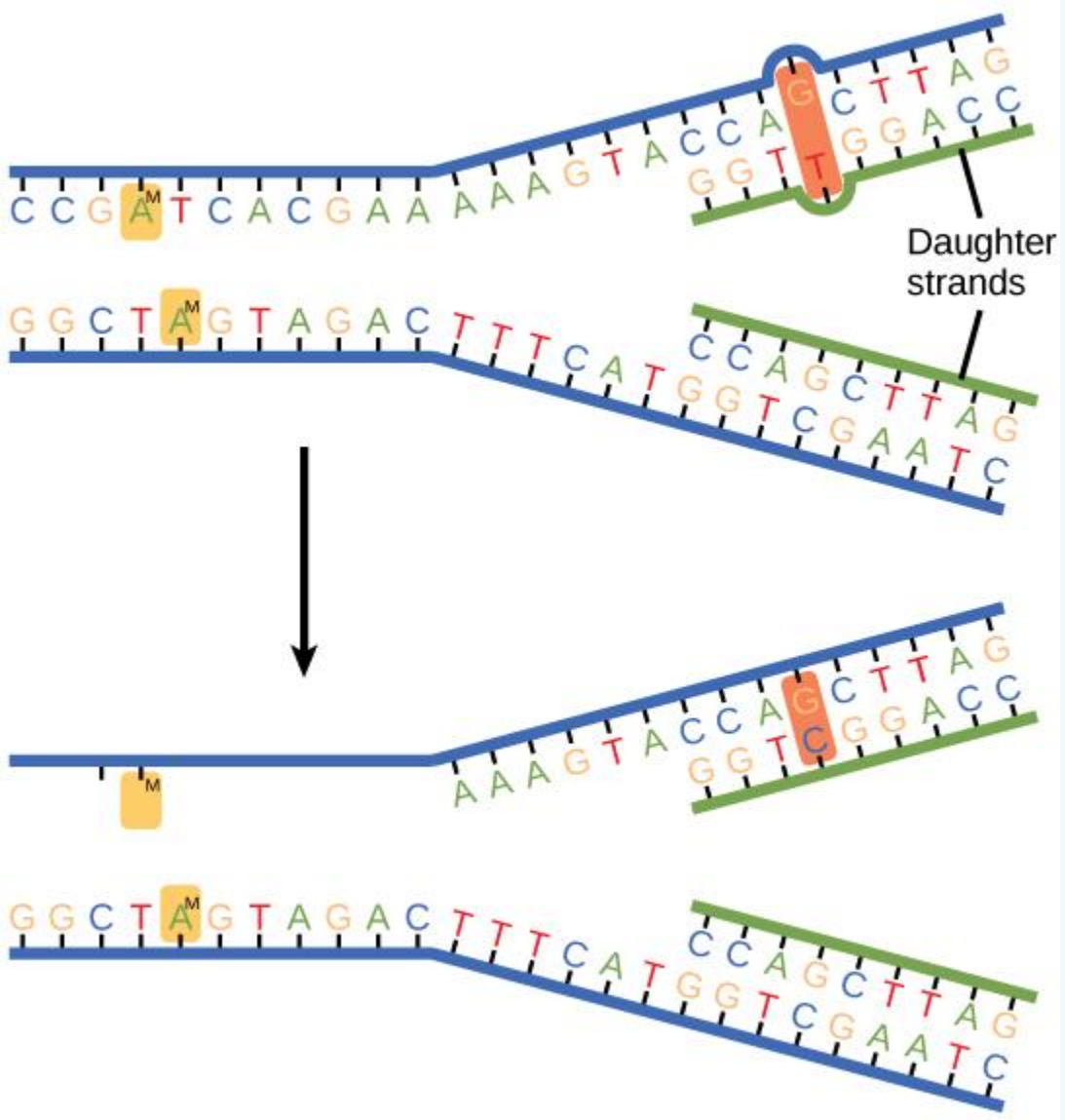
Proofreading



Proofreading by DNA polymerase corrects errors during replication. If an incorrect base has been added, the enzyme makes a cut at the phosphodiester bond and releases the wrong nucleotide and replaces it with the correct one.

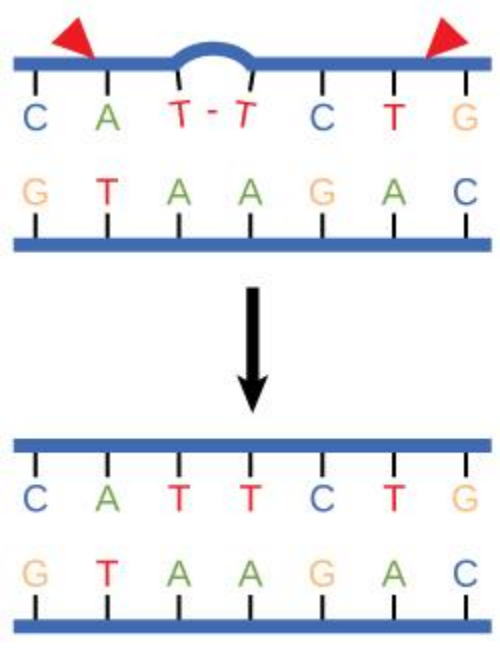
Mismatch Repair

Sometimes the incorrectly added base is detected after replication. The mismatch repair proteins detect this base and remove it from the newly synthesized strand by nuclease action. The gap is now filled with the correctly paired base.



Nucleotide Excision

Nucleotide excision repairs thymine dimers. When exposed to UV, thymines and other pyramidines lying adjacent to each other can form thymine dimers. In normal cells, they are excised and replaced.



Telomeres

The ends of the chromosomes pose a problem during DNA replication as polymerase is unable to extend them without a primer.

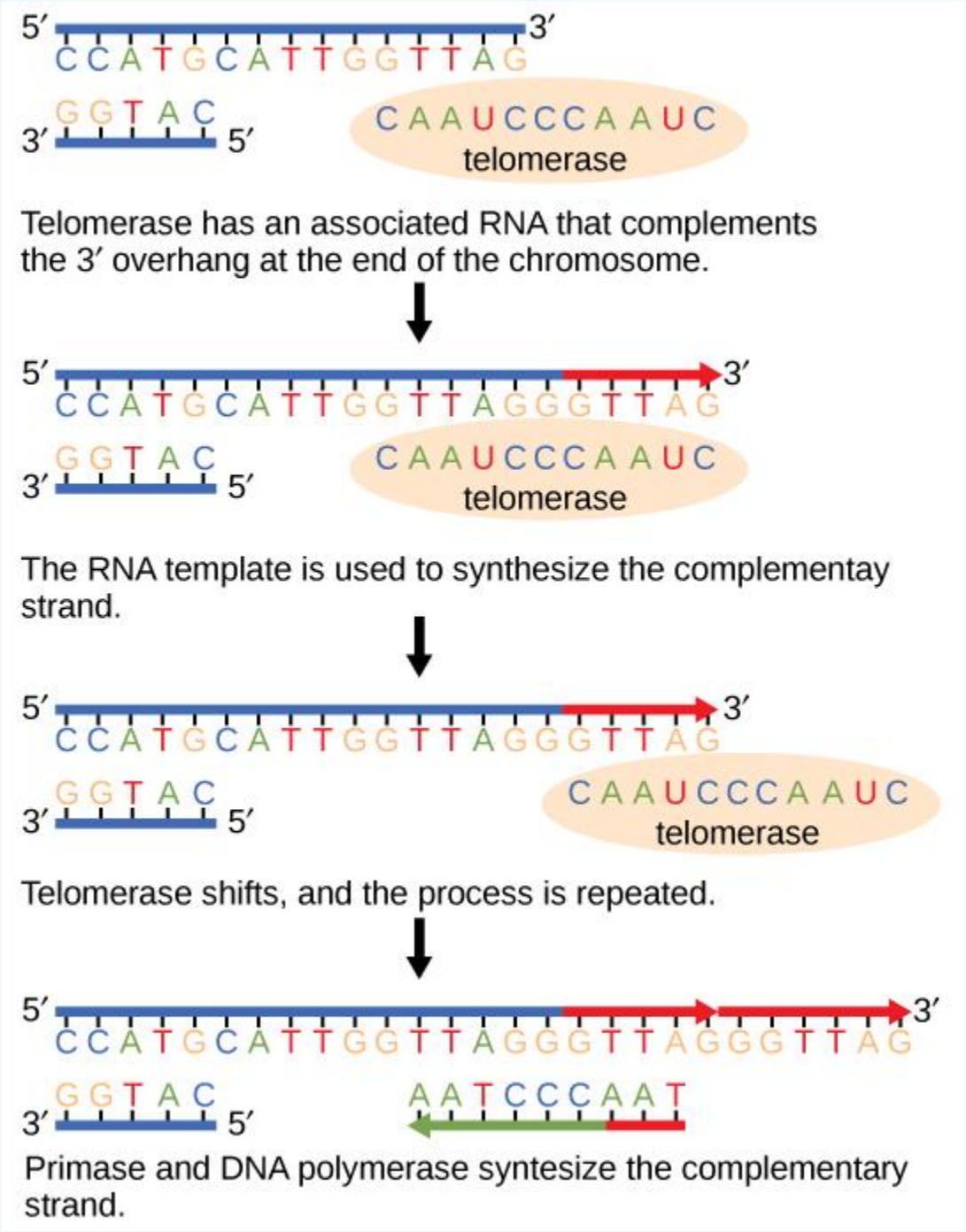
Telomerase, an enzyme with a built-in RNA template, extends the ends by copying the RNA template and extending one end of the chromosome.

DNA polymerase can then extend the DNA using the primer.

In this way, the ends of the chromosomes are protected. This is important as evidence indicates telomere length may play a role in regulating cell division and the process of aging.

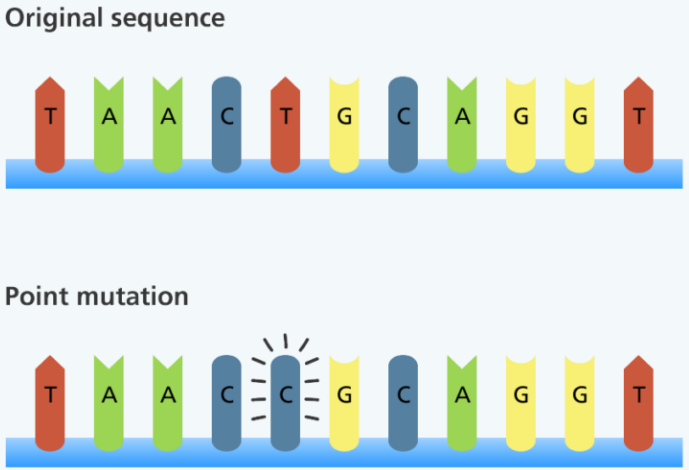
Telomerase

The ends of linear chromosomes are maintained by the action of the telomerase enzyme.



DNA Mutations

A **mutation** is a change that occurs in our DNA sequence, either due to mistakes when the DNA is copied or as the result of environmental factors such as UV light and cigarette smoke. Often cells can recognize any potentially mutation-causing damage and repair it before it becomes a fixed mutation. Mutations contribute to genetic variation within species. Mutations can also be inherited, particularly if they have a positive effect. However, mutation can also disrupt normal gene activity and cause diseases, like cancer.



Major Types of Mutations

DNA polymerase can make mistakes while adding nucleotides. Most mistakes are corrected, but if they are not, they may result in a mutation defined as a permanent change in the DNA sequence.

Mutations can be of many types, such as substitution, deletion, insertion, and translocation.

Mutations in repair genes may lead to serious consequences such as cancer.

Mutations can be induced or may occur spontaneously.

Gene mutations can be classified in two major ways:

- **Hereditary mutations** are inherited from a parent and are present throughout a person's life in virtually every cell in the body. When an egg and a sperm cell unite, the resulting fertilized egg cell receives DNA from both parents. If this DNA has a mutation, the child that grows from the fertilized egg will have the mutation in each of his or her cells.
- **Acquired (or somatic) mutations** occur at some time during a person's life and are present only in certain cells, not in every cell in the body. These changes can be caused by environmental factors or can occur if a mistake is made as DNA copies itself during cell division. Acquired mutations in somatic cells (cells other than sperm and egg cells) cannot be passed on to the next generation.

Mosaicism

Somatic mutations that happen in a single cell early in embryonic development can lead to a situation called **mosaicism**.

These genetic changes are not present in a parent's egg or sperm cells, or in the fertilized egg, but happen a bit later when the embryo includes several cells.

As all the cells divide during growth and development, cells that arise from the cell with the altered gene will have the mutation, while other cells will not.

Depending on the mutation and how many cells are affected, mosaicism may or may not cause health problems.

Polymorphism

Genetic alterations that occur in more than 1 percent of the population are called **polymorphisms**.

They are common enough to be considered a normal variation in the DNA.

Polymorphisms are responsible for many of the normal differences between people such as eye color, hair color, and blood type.

Although many polymorphisms have no negative effects on a person's health, some of these variations may influence the risk of developing certain disorders.

Quick Review

- How does DNA store genetic information?
- What is the role of complementary base pairing in the precise replication process of DNA?
- What is the impact of DNA mutations?