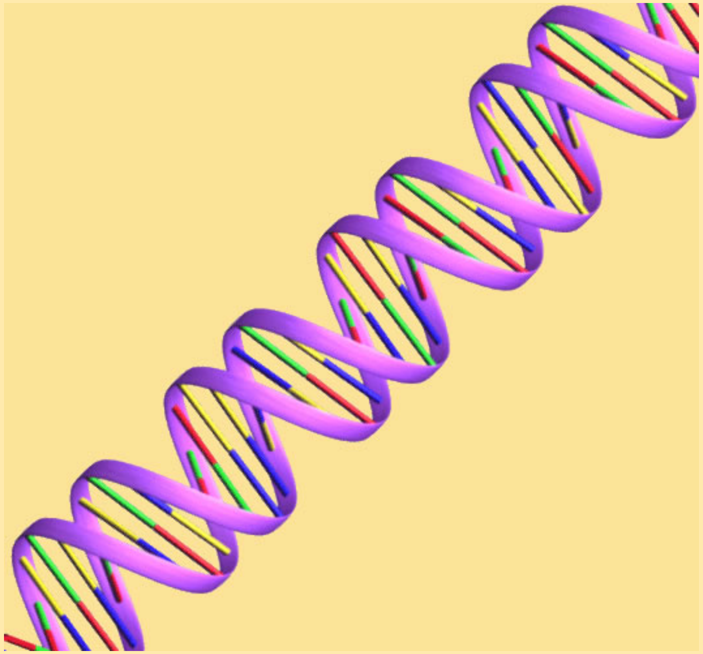
OVERVIEW OF DNA



Southwest Center for Microsystems Education

Overview of DNA Learning Module

Unit Overview

This unit provides an overview of DNA (Deoxyribonucleic acid), its role as genetic material, its molecular components and structure, and DNA replication.

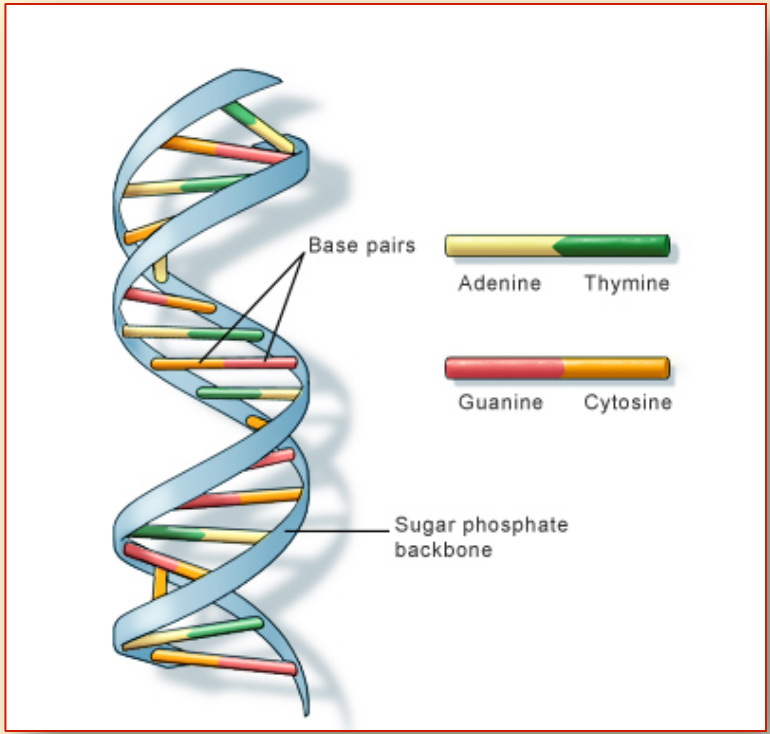
This information is necessary to better understand the role of microelectromechanical systems (MEMS) in DNA analysis, disease diagnostics, and gene therapy.

Objectives

- Evaluate the role of DNA as genetic material
- Describe the molecular components of DNA
- Describe the structure and replication of DNA

Introduction

- Deoxyribonucleic acid (DNA) is a long polymeric molecule found in most cells that functions as the carrier of genetic information.
- The information carried in the linear sequence of base pairs in DNA defines an organism. *(see graphic)*



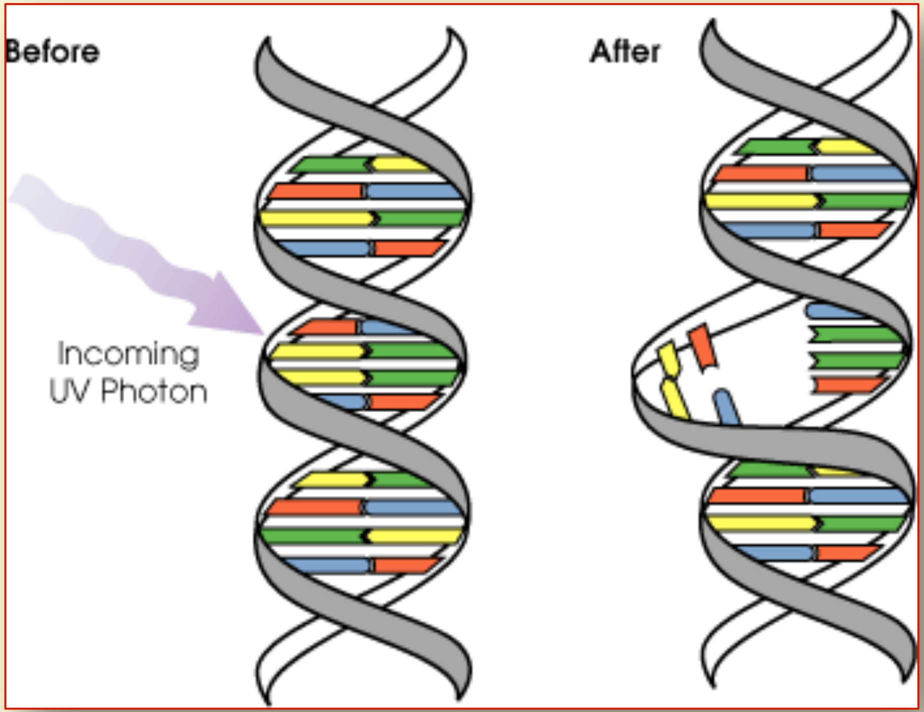
Base Pairs Structure of DNA [Image source: U.S. National Library of Medicine]

Introduction

Changes in the linear sequence (mutations or polymorphisms) explain differences between individuals and diagnose diseases such as cancer.

Causes of mutations:

- mistakes in DNA replication during cell division
- radiation
- chemical exposure
- ultraviolet (UV) light



Mutation formation: *Ultraviolet (UV) photons harm the DNA molecules of living organisms in different ways. In one common damage event, adjacent bases bond with each other, instead of across the "ladder." This makes a bulge, and the distorted DNA molecule does not function properly. (Illustration by David Herring)[Image courtesy of Earth Observatory, NASA]*

DNA Analysis and Microtechnology

The application of microtechnology has helped in the analysis of the DNA molecule.

- Polymerase chain reaction (PCR)
- Sanger dideoxy method of DNA sequencing
- DNA probes in DNA microarrays
- Single nucleotide polymorphisms (SNPs) in forensics

Fields that can benefit from the DNA and microtechnology partnership:

- Energy sources and environmental screening
- Agriculture and livestock breeding
- Risk assessment.

Applications of DNA in Biomedical

Applications of DNA in the medical field:

- Improve diagnosis of a disease
- Execute rational drug design
- Create custom drugs
- Utilizing DNA in gene therapy
- Improve monitoring and disease therapy

The Human Genome Project

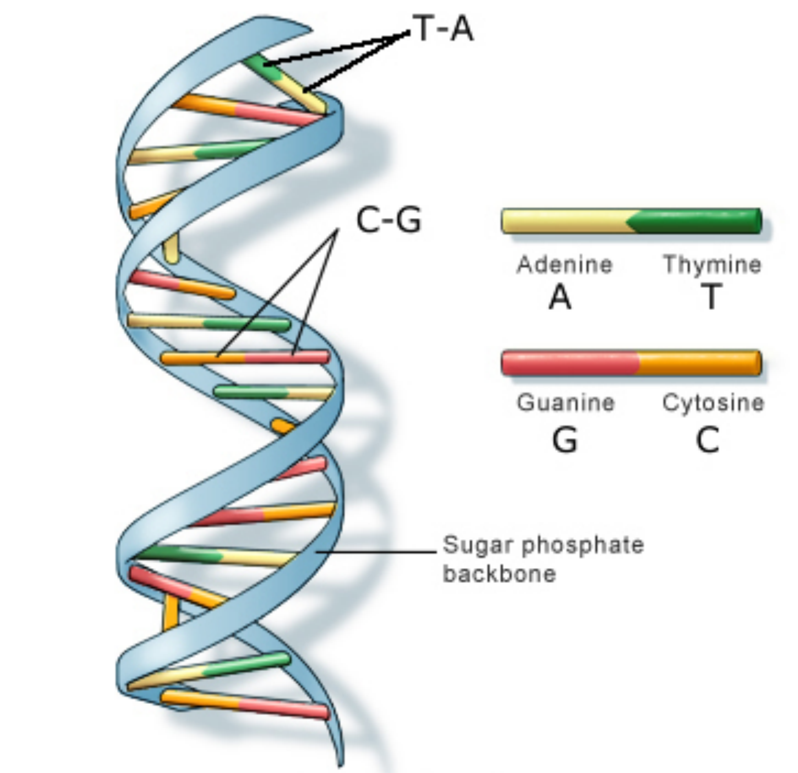
In 2003, the Human Genome Project completed sequencing the entire human genome. The project sequenced the 3 billion base pairs that make up the human genome and identified all of the sequences of DNA that encoded genes.

The project information and technologies were transferred to the private sector. One transfer application involves diagnosing and predicting disease and disease susceptibility. This has led and will lead to many diagnostic aids.

Data from The Human Genome Project

Another outcome of the project was the finding that the human genome encodes approximately 20-25,000 genes.

The sequence data from this finding was able to be stored in databases because the information stored DNA is digital and two-dimensional. The rungs are base pairs of A-T, T-A, G-C, C-G. *(see graphic)*



Source: US National Library of Medicine

DNA Exploration

During the 1920's, scientists had resolved that chromosomes were composed of both DNA and protein.

It remained to be resolved which of these molecules (DNA or protein) constituted the genetic material of the cell.

Further Exploration of DNA

In 1928, scientists discovered that a "chemical" from one type of bacteria was capable of transforming another bacterium from a non-virulent to virulent type.

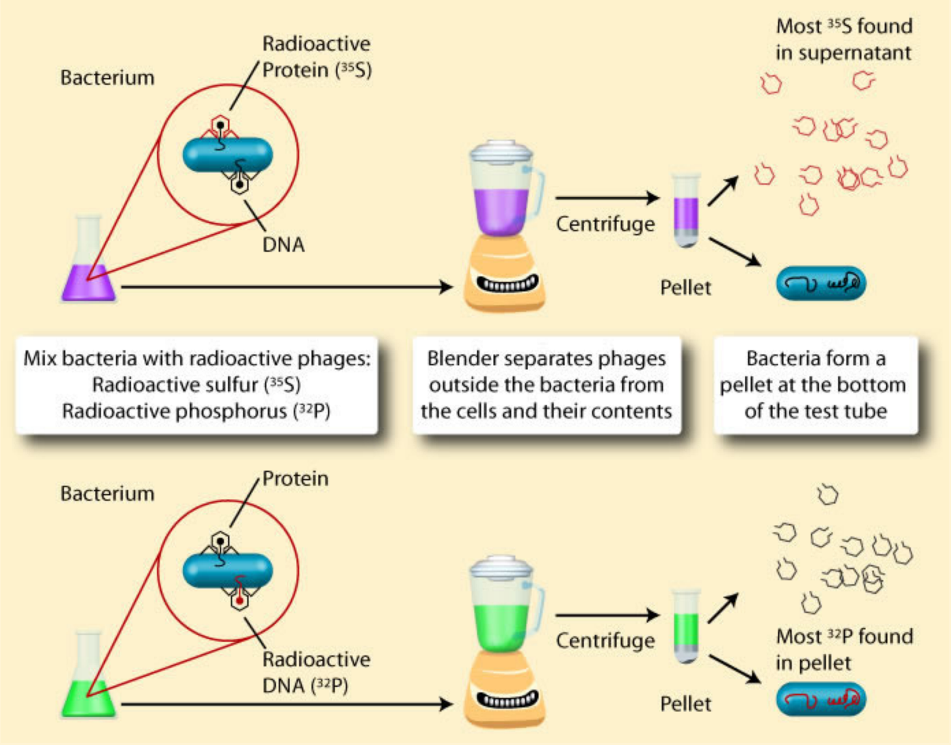
In 1952, Hershey and Chase's experiments demonstrated that the chemical was DNA.

Martha Chase and Alfred Hershey (1963) [Photo by: Karl Maramorosch. Printed with permission.]

Hershey-Chase Blender Experiments

Hershey and Chase used ^{32}P- or ^{35}S-labeled T2 bacteriophage in separate experiments to infect bacteria and follow the radioactive material through a productive infectious cycle.

Their findings ruled out protein as the genetic material and supported the role of DNA as the carrier of genetic information.



Hershey-Chase Blender Experiments

Chargaff’s Rule

Early studies demonstrated that DNA was chemically composed of a repeating structure of the sugar deoxyribose linked to phosphate and four nitrogenous bases (adenine, thymine, cytosine and guanosine).

In 1950, Chargaff examined the nitrogenous base content and determined that the content of adenine equaled the content of thymine, and the content of guanosine equaled the content of cytosine.

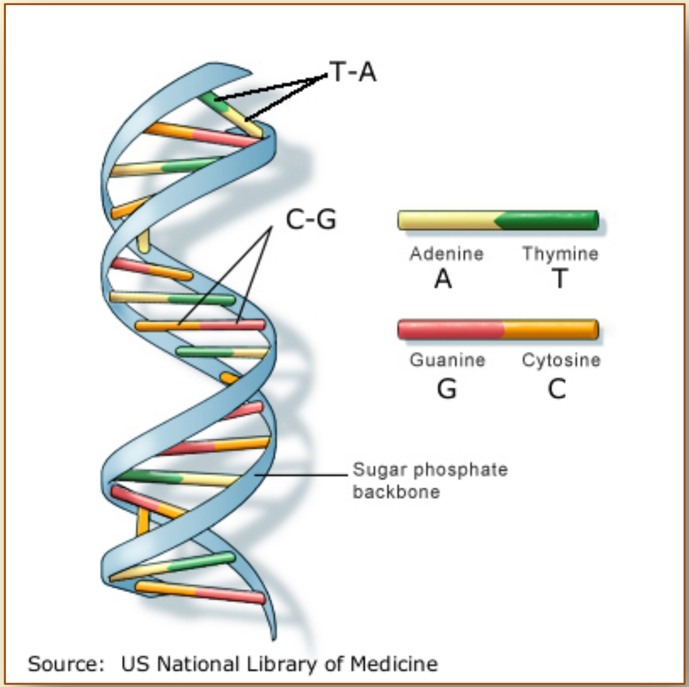
This relationship became known as **Chargaff's Rule**.

DNA Features

In 1953, the structure of DNA was described using the chemical description of the molecule in conjunction with the X-ray crystallography data from Rosalind Franklin and Maurice Wilkins.

Four key features were noted:

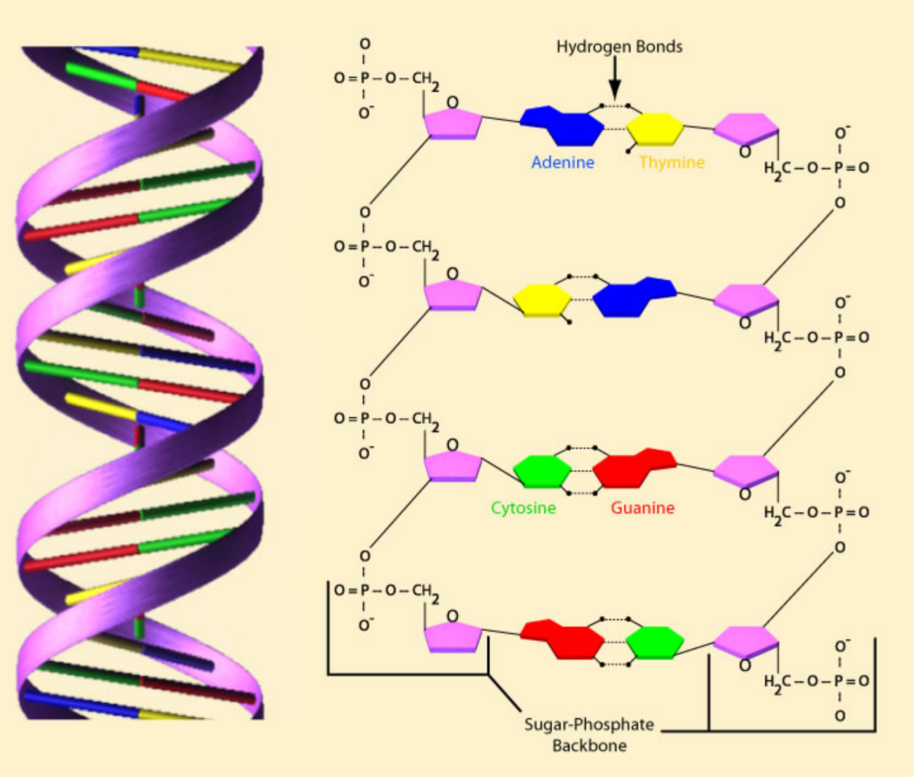
1) DNA structure is a double-stranded (ds) helix
2) The molecule exhibits a uniform diameter
3) The molecule is right-handed
4) The two strands are anti-parallel and demonstrate complementary base-pairing (fulfilling Chargaff's Rule).



Double-strand DNA showing Base Pairing

Base Pairing of DNA

The base pairing provides a model for the precise replication of the DNA molecule. The genetic information in the molecule is stored in the linear sequence of the base pairs.

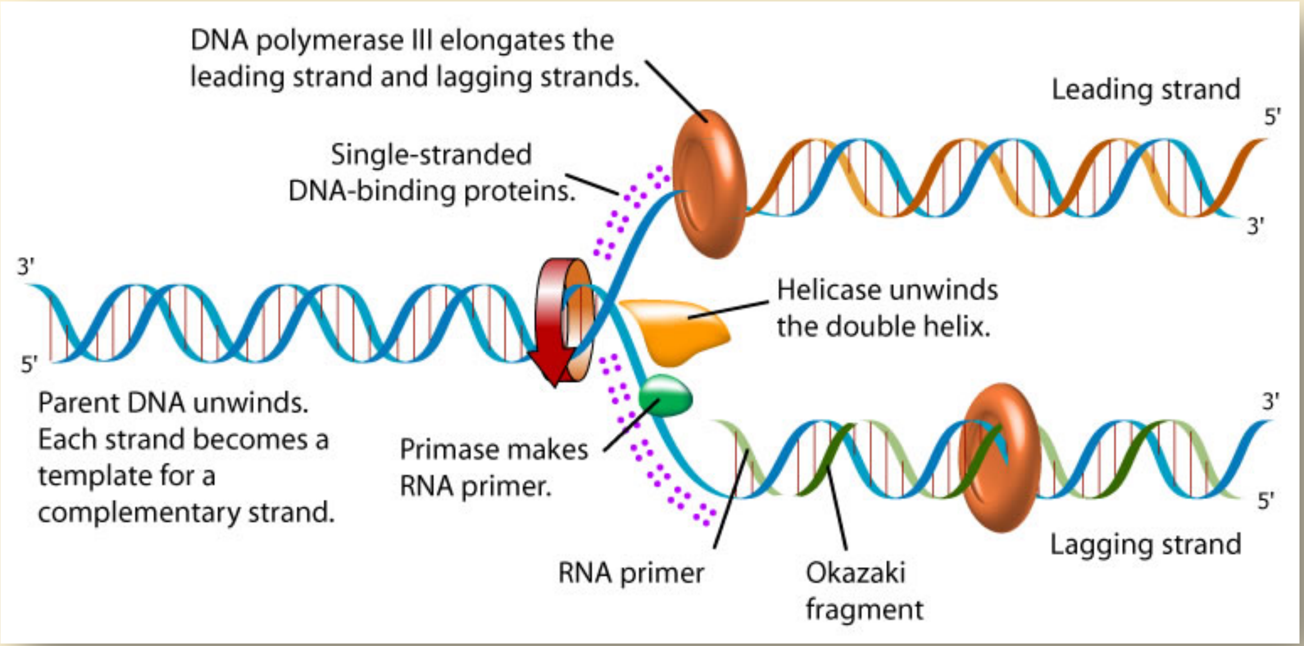


Double-strand DNA showing Base Pairing

DNA Replication

- In 1957, Messelson and Stahl demonstrated that a double helix DNA molecule separated into two single strands can be replicated with each strand serving as a template on which its complementary strand is assembled.
- DNA replication is a challenging process insuring the correct copying of the genetic information from the original DNA molecule to its replications.
- DNA replication involves numerous enzymes and proteins.

DNA Replication – Two Basic Steps

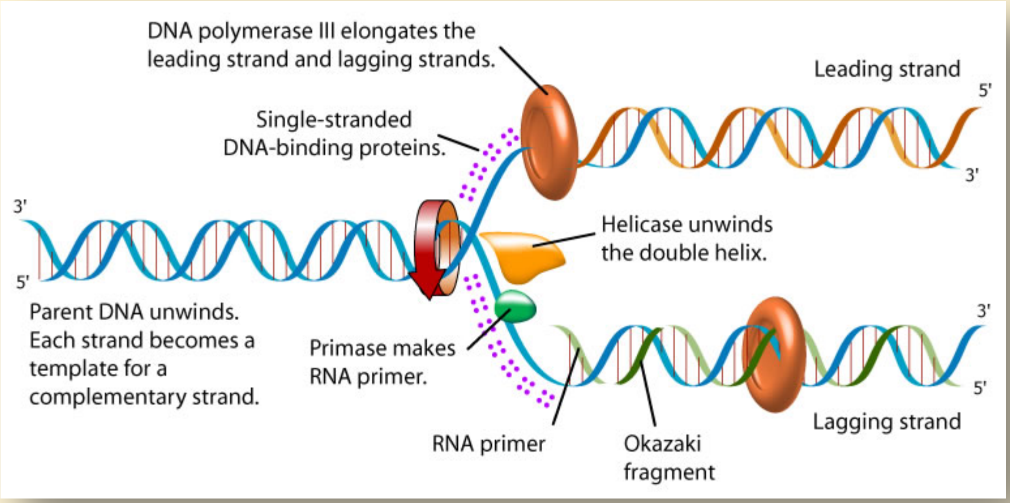


- The DNA helix is unwound at the site of replication
- New nucleotides are linked by covalent bonding to each growing new strand only at the 3' end which contains a free hydroxyl group.

DNA Replication

Replication begins at an origin of replication (ori).

- ❖ The hydrogen bonds that bind the base pairs are broken allowing the double helix to split or divide.
- ❖ A molecule of a DNA polymerase binds to one strand of the DNA and moves along the strand using it as a template for assembling a leading strand of nucleotides and reforming a double helix.

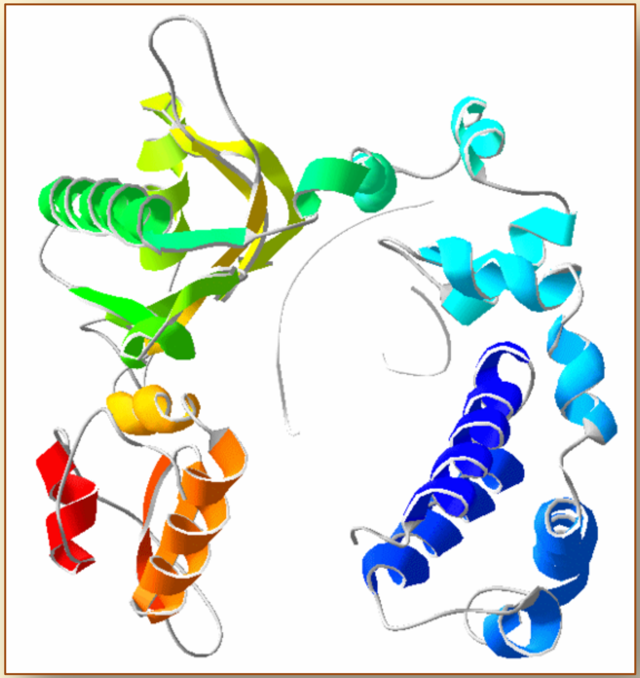


- ❖ A molecule of a second type of DNA polymerase binds to the other template strand as the double helix opens. This molecule must synthesize discontinuous segments of polynucleotides (called <u>Okazaki</u> fragments).
- ❖ Another enzyme, stitches these together into the <u>lagging strand</u>.

Replication Primer

DNA replication requires a primer. The primer is a short stretch of Ribonucleic acid (RNA) synthesized by the enzyme, primase. In later replication steps, the RNA primer is removed and filled in with DNA.

Cells contain several DNA polymerases. One is involved in chromosome replication, and others are involved in primer removal and DNA repair.



DNA Polymerase
[Image courtesy of Magnus Manske: English Wikipedia Project]

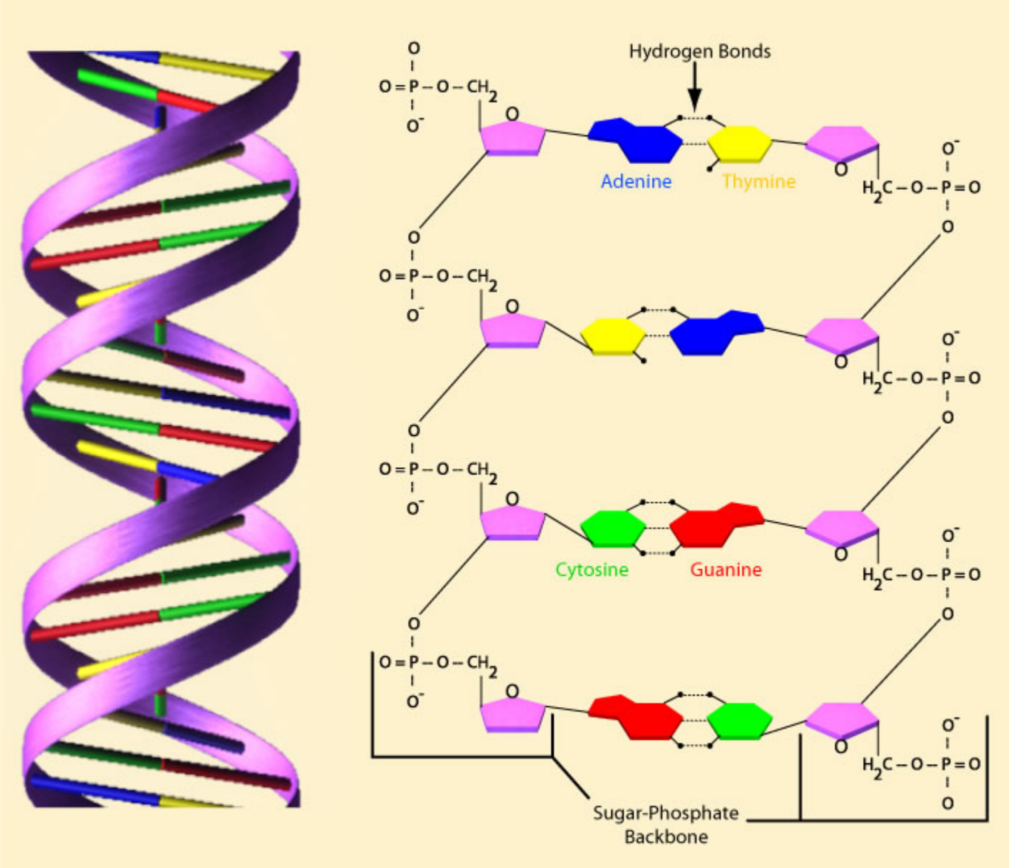
Review

Reference the figure *Double Strand DNA showing Base Pairing.*

Based on this figure, what is the charge on a molecule of DNA? Explain your answer.

The rungs of the ladder are composed of the paired nitrogenous bases. *What interactions hold the bases together?*

What implications does this have for unzipping the two strands of DNA?



Double Strand DNA showing Base Pairing

Summary

DNA is the genetic material with the genetic information stored in the linear array of nitrogenous bases.

The DNA molecule is composed of the sugar deoxyribose, phosphate groups, and the nitrogenous bases.

Summary

The molecular structure is a double-stranded helix with the sugar and phosphate groups forming the ladder and the nitrogenous bases forming the steps of the ladder.

DNA replication is a complex process that requires many enzymes and proteins, and follows a semi-conservative model for replication.

Disclaimer

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