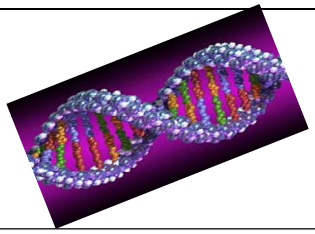
Molecular Genetics

Chapter 17



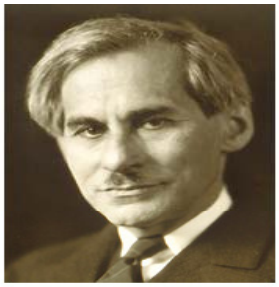
Biology 3201

Section 17.1
Isolating the Material of Heredity

- Fridrich Miescher, was the first person to isolate **nucleic acid**
  - He called it **nuclein**
- Nearly 100 yrs later, scientists connected nucleic acids and Mendel's "factors of inheritance"

Components of Nucleic Acids

- Upon closer inspection, Miescher's nuclein was found to be made up of strand-like complexes of nucleic acids and proteins.
- In the early 1900's, **Phoebus levene** made several discoveries about nucleic acids
  - There is, not one, but two types, each differing by a sugar



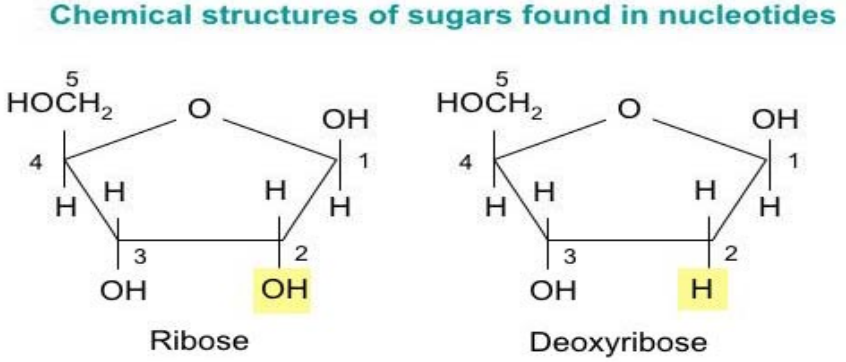
Phoebus Aaron Theodor Levene

Two Types of Nucleic Acid

1. **Ribonucleic Acid**
   - Contained a 5-carbon sugar called **ribose**
   - Also called RNA
2. **Deoxyribonucleic Acid**
   - Contained a different 5-carbon sugar called **deoxyribose**
   - Also called DNA

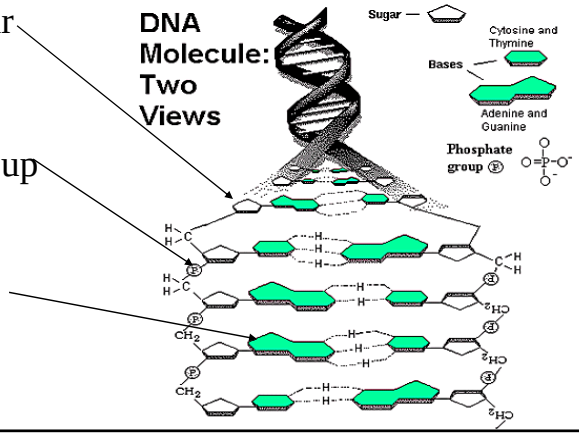
- Levene determined that these nucleic acids were composed of long chains of individual units called **Nucleotides**

Ribose vs. Deoxyribose



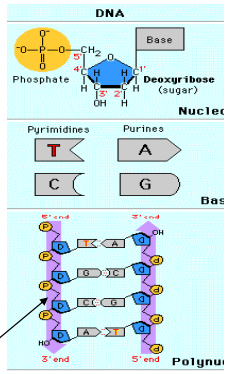
Three Parts of a Nucleotide

1. A 5-carbon sugar
2. A phosphate group
3. A nitrogen base



The Nitrogen Bases

- **DNA Bases**
  - Thymine (T)
  - Cytosine (C)
  - Guanine (G)
  - Adenine (A)
- **RNA Bases**
  - Uracil (U)
    - Replaces thymine
  - Cytosine
  - Guanine

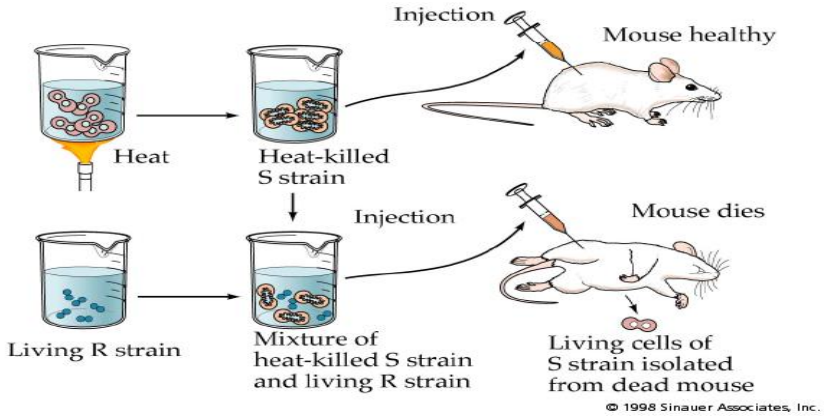


Sugar – phosphate bonds allow long nucleic acid chains to be formed

Evidence for the Role of DNA in Heredity

- In 1928, Fred Griffith studied the bacteria responsible for the pneumonia epidemic in London, Eng.
- His Experiment
  - He used dead Streptococcal bacteria as a control
  - He found that dead pathogenic (disease causing bacteria) had passed on their pathogenic properties to non-pathogenic bacteria.
  - He called this the **Transforming principal**,

Griffith's Experiment Explained…



Avery, MacLeod and McCarty

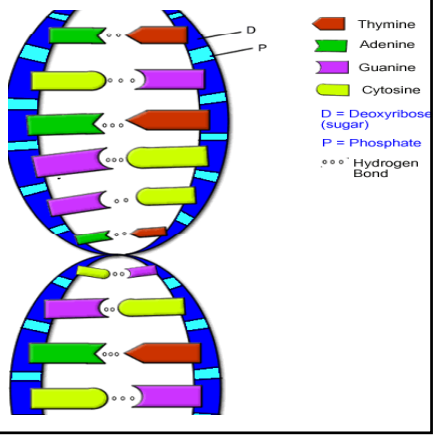
- 1944 - Took up the challenge to figure out the transformation principal after Griffith's death
- Their results on pathogenic bacteria:
  - When treated with a protein-destroying enzyme transformation still took place
  - When treated with DNA-destroying enzyme transformation did NOT occur
  - When treated with RNA-destroying enzyme transformation took place
- The conclusion: DNA caused the transformation!!

Erwin Chargaff

- Late 1940's – Studied DNA and made the following discoveries
  - The 4 nucleotides in DNA are NOT present in equal amounts, as once thought
  - Nucleotide composition varies from species to species
    - Composition within a species, however, is constant

More of Chargaff's Work

- In **any** sample of DNA the following is true:
  - Amount of Cytosine = Amount of Guanine
  - Amount of Thymine = Amount of Adenine
- This constant is called "Chargaff's Rule"



Hershey and Chase

- 1952 – Did an experiment using T4 bacteriophage viruses and radioactive labeling techniques
- They performed two "Blender" experiments
  1. Viruses with radioactively labeled DNA and a normal protein coat
  2. Viruses without radioactive DNA, but had a radioactive protein coat

The Blender Experiments (pg. 571)

Radioactive DNA/ Normal coat

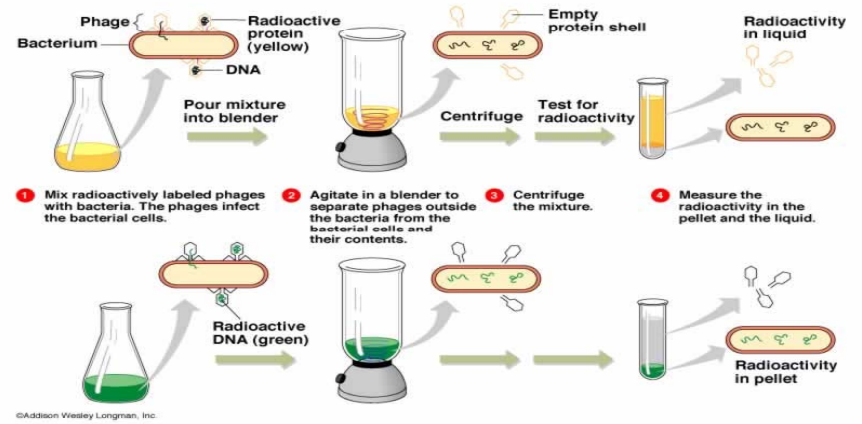
- Viruses mixed with E. coli bacteria allowing the DNA to be injected
- Virus coats and bacteria separated by blender and centrifuge
- Results: Bacterial cells found to be radioactive, indicating DNA entered the bacterial cells

Normal DNA/ Radioactive coat

- Viruses mixed with E. coli bacteria allowing DNA to be injected
- Virus coats and bacteria separated by blender and centrifuge
- Results: Bacterial cells were not radioactive, indicated that the protein coat did not enter the cells.

Conclusion: The genetic information transferred from virus to bacteria was only possible as a result of the DNA being injected into the bacterial cells.

The Blender Experiment Explained…



Suggested Section Review

- Read pages 566 – 572 in the textbook

- Questions page 572
  - 1, 2, 3, 4, 5,
  - Be able to label the diagram in question 6
  - Explain the work of the scientists in question 8

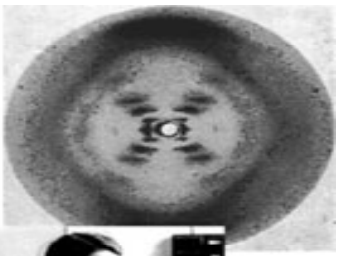
  You do not need to hand in these questions, but they are good review for the exam

Section 17.2
The Structure of Nucleic Acids

- By the late 1940's scientists knew that DNA was made up of:
  - A sugar
  - Phosphate group
  - Nitrogenous base
- What they did not know was how the DNA strand was arranged

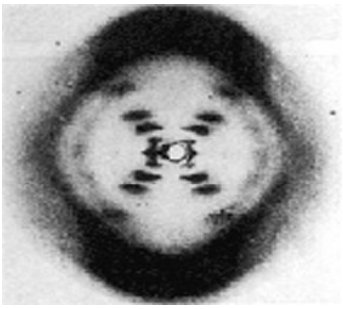
Rosalind Franklin & Maurice Wilkins

- Used X-Rays to photograph the DNA molecule
- They concluded that:
  - DNA had a helical structure
  - Nitrogenous bases were located on the inside of the molecule
  - Sugars and phosphates were on the outside of the molecule



More on Franklin

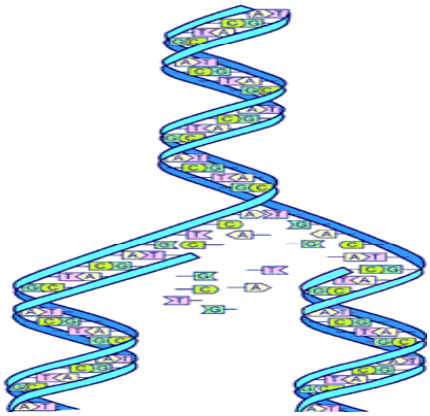
- Shaded areas of the X-ray image indicated helical structure
- She identified 2 discernable patterns recurring at 0.34 nm and 3.4 nm
- DNA in water
  - Hydrophobic base - inside
  - Hydrophilic sugary backbone – outside
- She died of cancer in 1958, believed to have been from exposure to the x-rays in her research



James Watson & Francis Crick

- Produced a structural model of the DNA double helix
  - **DNA double helix model**
  - **The model used today**
- Published a paper shortly before Franklin died and received a Nobel prize
- It is believed that they were at visiting Franklin's lab and saw her work. This indirectly tipped them off on the helical shape that she originally concluded.

The Double Helix

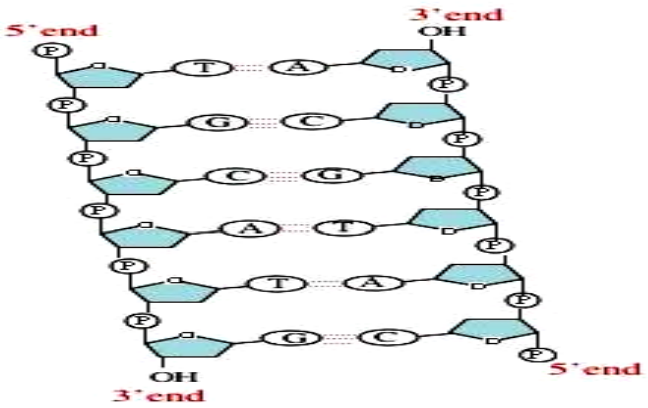


- DNA is made up of two long strands of nucleotides in the shape of a double helix
- In its unwound state, the DNA molecule resembles a ladder (aka Ladder structure)
- Four bases fall in two categories:
  - **Purines** – guanine and adenine
  pyrimidines – cytosine & thymine
- Watson and Crick concluded that a purine always joins with a pyrimidine

Complementary Base Pairing

- Pairing of nitrogenous bases in the centre of the DNA molecule is called **complimentary base pairing**. Pairing can occur in the following ways:
  - Adenine – Thymine → by 2 Hydrogen bonds
  - Thymine – Adenine → by 2 Hydrogen bonds
  - Cytosine – Guanine → by 3 Hydrogen bonds
  - Guanine - Cytosine → by 3 Hydrogen bonds

Anti-parallelism

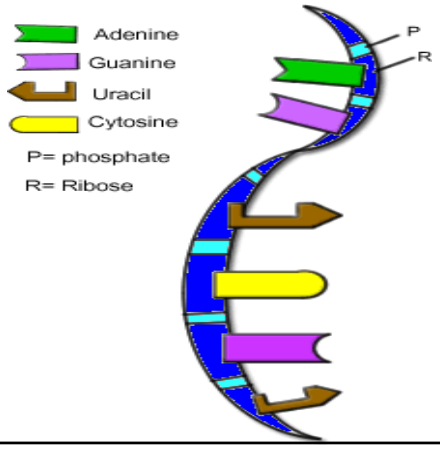


DNA video clip

- DNA STRUCTURE

RNA

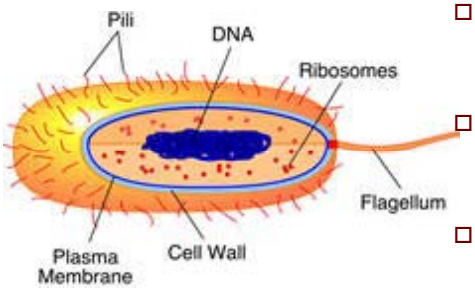
- Three differnces from DNA
  1. Sugar is a ribose, while DNA has a deoxyribose
  2. RNA has uracil instead of thymine as in DNA
  3. RNA is only a single strand



Organization of Genetic Material

- Scientists examine cells to determine how DNA is organized within a cell
- There are two main types of cells:
  - Prokaryotes (bacteria)
  - Eukaryotes (everything else)
- Structure of the DNA varies in each type of cell

Prokaryotes



- Most have a single, double-stranded DNA molecule
- Since there is no nucleus, the DNA floats freely within the cell
- Proteins cause the DNA to coil tightly forming a **nucleoid region**
- May have small circular pieces of DNA called **plasmids**

Eukaryotes

- All cells have double-stranded DNA
- DNA is arranged into **chromosomes** within the nucleus
- Each chromosome contains a double stranded DNA molecule and a protein called a **histone**
- A typical chromosome contains:
  - 60% Protein
  - 35% DNA
  - 5% RNA
- Chromosomes are joined together to form a long, fibrous material called **Chromatin**

Genes and the Genome

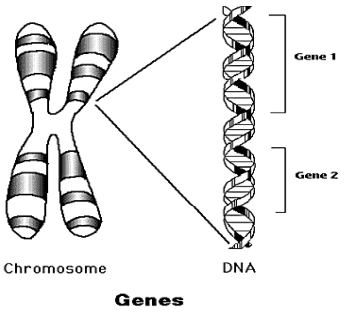
- Studies have shown that there are patterns in how heredity information is organized at the molecular level that are shared by different organisms. They are:
  - How individual genes are organized
  - How the individual's genome is organized

Genes

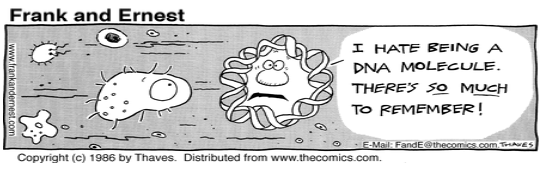
- A gene is a subunit of DNA
- Chromosomes in a cell carry genes
- Different species have their own unique arrangement of genes
  - Though many genes are common between species

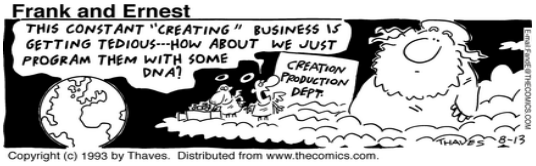
What IS a Gene?

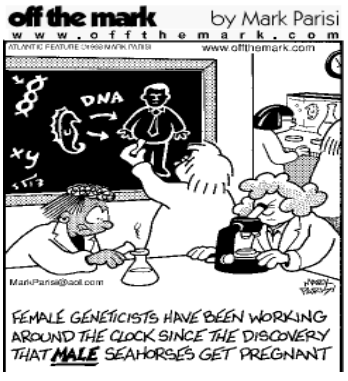
- Portion of inherited information that defines on particular trait of an organism's physical characteristics
- Are responsible for coding for proteins and some non-protein products



DNA Humour ☺







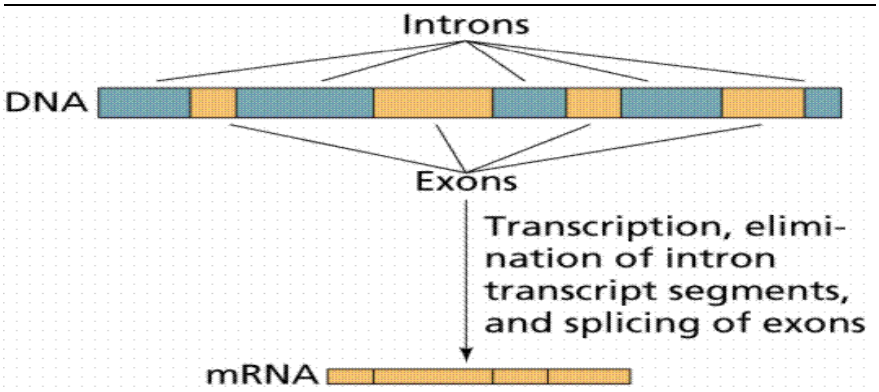
Arrangement of the Genome

- Each chromosome has its own unique arrangement of genes
  - Gene density varies among chromosomes
    - Ex. Ch. # 4 has about 200 genes, while Ch. # 14 has about 1450 genes
- Different organisms have different numbers of genes
  - An amoeba has about 7000 genes while humans have about 35,000 genes

Eukaryote Genes

- Each genes if made up of two different regions
  - Exons → Coding or **ex**pressed regions of a gene
  - Introns → Non-coding nucleotide sequences
    - Can make up over 50% of the length of a gene
- More complex organisms tend to have more introns, while simple organisms like bacteria or yeasts have none or few introns

Introns and Exons



Suggested Section Review

- Read Pages 573 – 581 in textbook
- Review DNA extraction Lab
  - We will do this before the week is over
- Questions on Page 581
  - 1, 2, 3, 4, 5, 9, 10, 11, 14
- Due Date: TBA

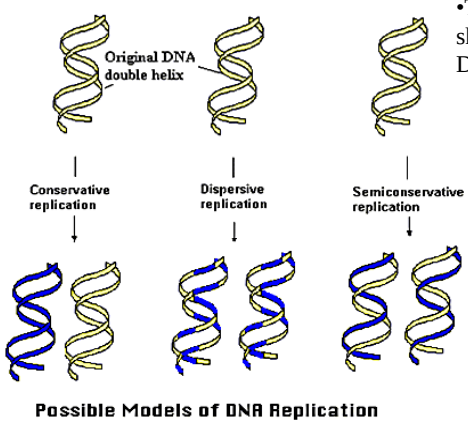
Section 17.3
DNA Replication

- Humans have about 1 trillion cells
- Each of these cells is genetically identical to the zygote from which they formed
- For this to happen:
  1. The genome must be copied quickly
  2. The genome must be copied accurately

The Replication Process

- DNA replication is a process from which two molecules of DNA are made from one
- Called a semi-conservative model
  - Meaning each of the two new DNA molecules contains one original (parent) strand and one new strand

Possible Modes of Replication



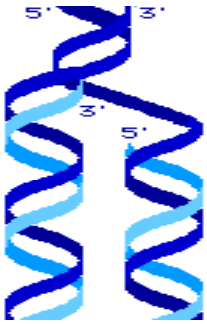
Possible Models of DNA Replication

•The two original strands of DNA are shown in yellow (light); newly synthesized DNA is blue (dark)

- **Conservative replication** would leave intact the original DNA molecule and generate a completely new molecule.
- **Dispersive replication** would produce two DNA molecules with sections of both old and new DNA interspersed along each strand.
- **Semiconservative replication** would produce molecules with both old and new DNA, but each molecule would be composed of one old strand and one new one

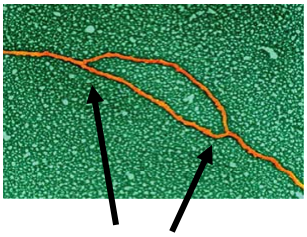
Three Stages of the Replication Process

1. Initiation
2. Elongation
3. Termination



1. Initiation

- The DNA double helix begins to unwind itself
- DNA is a tightly bound stable structure for most of a cell's life
- DNA unwinds at special points along the strand called **replication forks**
- Enzymes called **helicases** are responsible for unraveling short segments of DNA



Replication forks

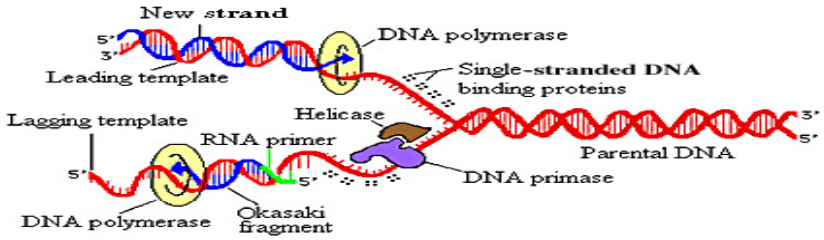
2. Elongation

- Assembly of two new DNA strands begins
- An enzyme called **DNA polymerase** helps to attach new nucleotides to the DNA strand
- Newly replicated DNA can be found in short segments called **Okazaki fragments** ranging from 1 to 2 thousand nucleotides in length

Still Elongating

- Replication occurs in the 5’ to 3’ direction of one DNA strand while it occurs in the 3’ to 5’ direction on the other strand. The enzyme **DNA primase** begins this process
- **Leading strand** - The strand replicating in the 5’ to 3’ direction
- **Laggin strand** – The strand replicating in the 3’ to 5’ direction
- Okazaki fragments are joined together by an enzyme called **DNA ligase**

Replication Processes



Collaboration of Proteins at the Replication Fork

Replication Animation

3. Termination

- The stage when the new DNA molecules reform into helices or double helices
  - Daughter DNA strands rewind forming their stable helical structure
- Each new daughter DNA molecule is slightly shorter than its parent
  - Chromosomes lose about 100 base pairs with each replication

Telomeres & Chromosome Shrinkage

- In eukaryotic cells special regions called **telomeres** which have the base sequence TTATGGG are attached to the ends of each chromosome
- These sequences have no role in the development and thus the chromosome can lose them with each replication and not lose any important genetic information

Like the hard ends on your shoelaces, telomeres are the protective bits of DNA at the ends of your chromosomes.

- One theory: chromosome shrinkage is related to symptoms of aging

Err is to human… and DNA replication

- Though we would like to believe that DNA replication is an orderly step by step process, this is usually not the case. Just as we make mistakes, so can the replication process
  - Wrong bases may be inserted into the new DNA
  - Nucleotide bases may be damaged (ie. By radiation)
- When this happens, mutations or other serious problems can occur in the DNA molecule

Proofreading and Correction

- To prevent errors from occurring, the enzyme DNA polymerase is able to check to see whether bases are actually bonding together by hydrogen bonding
  - No H-bonding means there is a base mismatch
  - The incorrect base is replace with the correct one
- DNA replication involves dozens different enzymes and other proteins working together as a **replication machine** to get the job done correctly and virtually error-free

DNA Repair Animation

Suggested Section Review

- Read Pages 582 – 588
  - You MUST know the enzymes involved and their functions
    - Page 587 – Table 17.1
- You must be able to explain the replication process and draw basic diagrams on a test
- Questions on page 588
  - 1, 2, 3, 4, 9,

Section 17.4
Protein Synthesis & Gene Expression

- DNA stores information in the form of a code that we call the **genetic code**
- Genetic code is based on the order of the base pairs that make up the DNA molecule
- The sequence of nucleotide determines the sequence of amino acids within a protein

Genetic Code

- Transfer of genetic information from DNA to protein is called **genetic expression** which occurs in two stages:
  1. **Transcription**
     - Information is copied from DNA onto an RNA molecule (inside the nucleus of the cell)
  2. **Translation**
     - RNA moves from the nucleus to the cytoplasm where it helps to make a polypeptide (protein)

Codons Based on RNA Nucleotides

First base in codon	Second base in codon: U	C	A	G	Third base in codon
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	STOP	STOP	A
	Leu	Ser	STOP	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

The Genetic Code

- Using combinations of three nucleotides, the DNA molecule creates code words that represent the 20 amino acids (Pg. 590 table 17.2)
- Each set of three bases is called a **codon**
  - Some amino acids (AA) are coded for by more than one codon, while others, only by one
  - Each set of 3 amino acids is called a **reading frame**
- Codons are represented by the RNA base sequences

How Reading Frames Work

NORMAL CODE

DNA Sequence

TAC GCC GAC TTA G

RNA Sequence

AUG CGG CUG AAU

Amino acid sequence

met – arg – leu - asn

ALTERED CODE

Deletion in DNA

TAC GCC GCT TAG

New RNA sequence

AUG CGG CGA AUC

New AA sequence

met – arg – arg - iso

How does this work?

- DNA sequence: T-A-C-A-G-T-A-T-C

Find the complimentary RNA sequence

- RNA sequence: A-U-G-U-C-A-U-A-G

Match each codon with the amino acid to get the sequence

- AA sequence: Met – Ser – Stop

(methionine / start – serine – stop)

3 Characteristics of the Code

1. Redundancy
   - More than one codon can code for the same amino acid – lots of repetition
2. Continuous
   - Code reads as a series of 3-letter codons without spaces, punctuation or overlap
3. Universal
   - Code is virtually the same in all organisms making is possible to transfer information

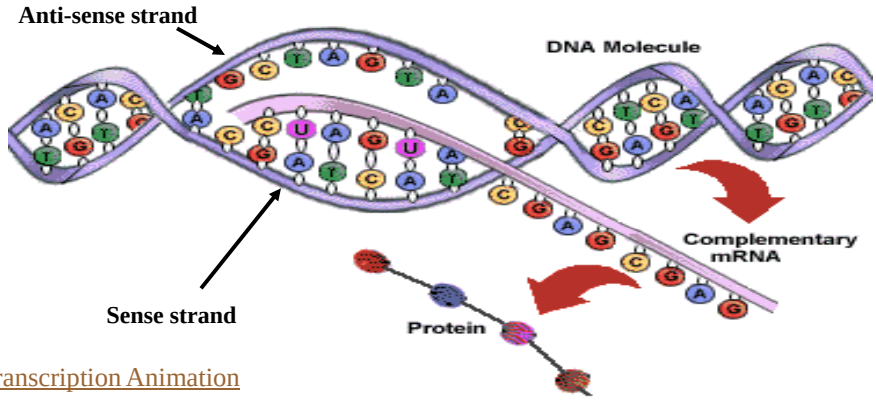
Transcription I

- Process by which a small portion of the DNA is copied onto a special type of RNA called messenger RNA or mRNA
- mRNA carries information from the nucleus of a cell to the cytoplasm to become a protein
- RNA polymerase is the catalyst for the production of the RNA molecule

Transcription II

- DNA has two strands
  - Sense strand and Anti-sense strand
- ONLY the sense strand is transcribed into RNA
- RNA polymerase opens up the DNA double helix allowing the mRNA to be formed from exposed nucleotide bases
- Transcription continues along the DNA until a stop codon is reached. The RNA and polymerase separate and a special nucleotide sequence is added to the 3' and 5' ends

Transcription Illustrated

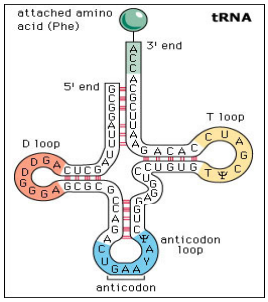


Transcription Animation

Translation I

- The reading of mRNA by a ribosome so that proteins can be formed in the cytoplasm

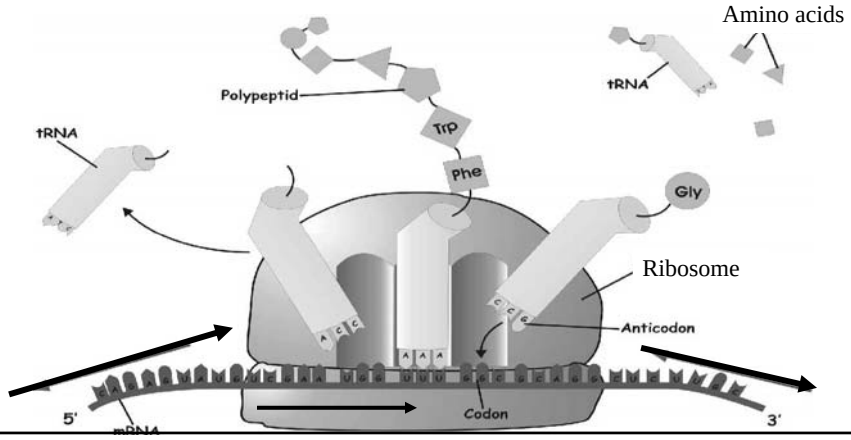
1. mRNA comes in contact with a ribosome
2. **Transfer RNA (tRNA)** joins to the mRNA. One end of the tRNA carries an amino acid which will be used to make a protein. The opposite end has a 3-base nucleotide sequence called an **anti-codon** that joins with a sequence of mRNA codons



Translation II - Animation

- After the first tRNA binds to the mRNA a second will join next to it, adding its amino acid to the chain. When the third tRNA binds the first tRNA molecule is "bumped" out of the ribosome. With each new tRNA a new amino acid is added to the polypeptide chain.
- The cycle of amino acids linking together is repeated until a "stop" codon (UAA, UAG or UGA) is reached. Once this tRNA is read, the amino acid is released from the ribosome and the protein is formed

Translation Illustrated

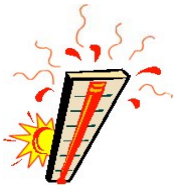


Regulating Gene Expression

- Every living cell has the ability to respond to it environment by changing the kinds and amounts of polypeptide (proteins) it produces
  - By controlling this process, the cell can regulate gene expression
- There are a number of factors that control the rate of transcription and translation

Factors Effecting Gene Expression

- Changes in temperature or light



- Presence or absence of nutrients in the environment
- Presence of hormones in the body
  - Development of an organism is governed by this regulation of gene expression

Mutations

- The genome of an organism is not stable
  - The overall structure of DNA is constantly changing
- Changes that take place within genes provide, what we call, **genetic variation** Permanent changes in the DNA are called mutations
  - Some mutations are inheritable, while others are not
- **Germ cell mutations** – Mutation in DNA of the gametes (germ cells). Can be passed on
- **Somatic cell mutation** – Mutations in the body cells. Cannot be passed on to offspring (ie. Cancer)

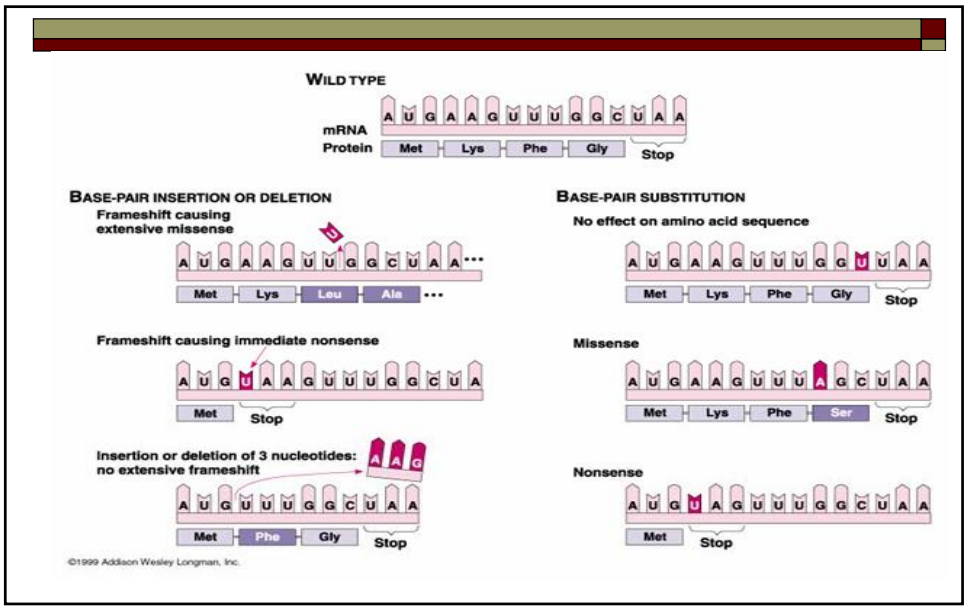
Genetic variations make all humans and races different from one another

Types of Mutations

- **Point mutations** – small changes in the nucleotide sequence of genes. Maybe be one nucleotide replacing another, deletion or insertion
- **Silent mutations** – Has no negative effect on the cells in which they occur. May be in exons or simply in "unused" DNA
- **Mis-sense mutations** – Cause slight alteration of a protein. May be beneficial or harmful depending on the protein(s) affected
- **Nonsense mutations** – Make a gene unable to code for a functional protein. Usually caused by changes to the start/ stop codons

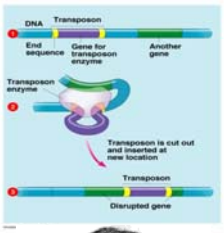
Nucleotide Insertions/ Deletions

- One or two nucleotides in a sequence of codons can produce a **frameshift mutation**
  - This is when a nucleotide insertion or deletion causes and entire frame of a gene to be altered
  - See page 597 – fig. 17.33 for an example



Chromosomal Mutations

- Involve the rearrangement of genetic material which affects genes
- May involve:
  - Exchange of portions of chromosomes between sister chromatids or chromosomes
  - Loss of chromosome pieces
  - Duplication of chromosome segments



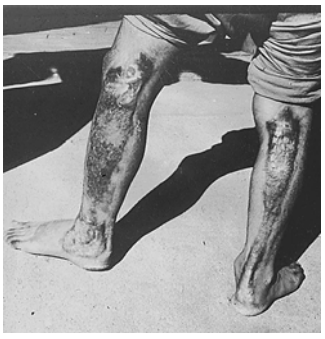
- Barbara McClintock found jumping genes called **transposons** that are short strands of DNA capable of moving from one location to another. (pg 597-598)

Causes of Mutations

- **Spontaneous mutations** – caused by molecular interactions that occur naturally inside a cell. The rate of these mutations varies among different organisms
- Environmental factors can increase the rate of mutations. These are called **induced mutations**
- **Mutagen** – Any substance or event that increases the rate of mutation in an organism
  1. **Chemical**
  2. **Physical**

Physical Mutations

- Agents which can forcibly break a nucleotide sequence causing random changes in one or both strands of DNA
  - X-Rays
  - Gamma rays
  - Ultraviolet (UV) radiation



Effects of radiation

Chemical Mutations

- A molecule that can enter a cell's nucleus and cause mutations by reacting with the DNA
- Chemical mutagens insert themselves into the DNA molecule and this cause a mutation
  - Chemicals in the air
  - Chemicals in cigarettes / smoke
  - Heavy metals

One of the most common mutagens around

Mutations: General Information

- Each organisms genes undergoes 1000's of mutations during a lifetime
- Most mutations are repaired by the cell's own enzymes
- Some mutations cannot be repaired, and these build up over the lifetime of the cell leading to cellular damage
- Cancer is an example of a disorder caused by accumulated mutations – cells begin to divide uncontrollably
- Any mutagen which can cause cancer is called a **carcinogen**

Suggested Section Review

- Read Pages 589 – 600
  - Be able to draw basic diagrams showing transcription & translation
  - Know the types of mutations and examples
  - Be able to transcribe DNA/RNA/Amino Acid sequence
- Questions page
  - 1, 2, 3, 4, 5,

Chapter Overview Assignment

- Questions Page 601 – 602
  - **1 – 9, 11, 13, 15, 16, 17, 18, 20, 21**
    Due Tuesday April 3, 2007
- Test scheduled for:
  - **THURSDAY APRIL 5, 2007**

All Animations will be available on the Bio 3201 website for download