Chapter 13: DNA, RNA, and Proteins

Lecture Notes
13.1 THE STRUCTURE OF DNA
EQ: HOW DOES THE STRUCTURE OF DNA RELATE TO ITS FUNCTION?
• Known since the late 1800s:
  1. Heritable information is carried in discrete units called **genes**
  2. Genes are parts of structures called **chromosomes**
  3. Chromosomes are made of deoxyribonucleic acid (**DNA**) and **protein**
• **KEY CONCEPT:** DNA was identified as the genetic material through a series of experiments.

• Transformed bacteria revealed the link between genes and DNA

• F. Griffith worked with two strains of *Streptococcus pneumoniae* bacteria
  – S strain caused pneumonia when injected into mice, killing them
  – R strain did not cause pneumonia when injected
### Griffith Transformation Experiment

**Mouse injected w/bacteria**  

- **(a)** Living R strain  
  - Mouse remains healthy.

- **(b)** Living S strain  
  - Mouse contracts pneumonia, dies.

- **(c)** Heat-killed S strain  
  - Mouse remains healthy.

- **(d)** Living R strain, heat-killed S strain  
  - Mouse contracts pneumonia, dies.

### Results

- R strain does **not** cause pneumonia
- S strain **does** cause pneumonia
- Heat-killed S strain does **not** cause pneumonia
- Substance from heat-killed S strain **can** transform harmless R strain into deadly S strain

### Conclusions
Genes Are Made of DNA

- Deductions from Griffith’s experiment (1920s)
  - Living safe bacteria (R strain) were changed by something in the dead (but normally disease-causing) S strain
  - The living R strain bacteria were transformed by genetic material released by the S strain

- Later findings by Avery, MacLeod, and McCarty (1940s)
  - The transforming molecule from the S strain was DNA
Avery’s Experiments

- Avery identified DNA as the transforming principle.
- Avery isolated and purified Griffith’s transforming principle.
- Avery performed three tests on the transforming principle.
  - Qualitative tests showed DNA was present.
  - Chemical tests showed the chemical makeup matched that of DNA.
  - Enzyme tests showed only DNA-degrading enzymes stopped transformation.
Hershey and Chase

- Hershey and Chase confirm that DNA is the genetic material.
- Hershey and Chase studied viruses that infect bacteria, or bacteriophages.
  - They tagged viral DNA with radioactive phosphorus.
  - They tagged viral proteins with radioactive sulfur.
- Tagged DNA was found inside the bacteria; tagged proteins were not.
Structure/Shape of DNA

• **KEY CONCEPT:** DNA structure is the same in all organisms.

• DNA = Deoxyribonucleic Acid
  – A Nucleic Acid is a polymer built from monomers

• DNA is made of chains of small subunits called **nucleotides**

• Each nucleotide has three components:
  1. Phosphate group
  2. Deoxyribose sugar
  3. One of four **nitrogenous bases**
     – Thymine (T)
     – Cytosine (C)
     – Adenine (A)
     – Guanine (G)

Nucleotides pair according to the number of $H^+$ bonds of the nitrogenous bases.
The nitrogen containing bases are the only difference in the four nucleotides.

<table>
<thead>
<tr>
<th>PYRIMIDINES = SINGLE RING</th>
<th>PURINES = DOUBLE RING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Name of Base</strong></td>
<td><strong>Structural Formula</strong></td>
</tr>
<tr>
<td>thymine</td>
<td><img src="image" alt="Thymine" /></td>
</tr>
<tr>
<td>cytosine</td>
<td><img src="image" alt="Cytosine" /></td>
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</tbody>
</table>
• DNA has a Double Helix shape
  – 2 strands connected to each other
    • Strands actually run in opposite directions ↑↓
  – Resembles a “twisted ladder”
  – Strands have an order in which they are connected
  – Chargaff’s base pairing rules:
    • Amount of A = T and C = G
    • Adenine – Thymine (A-T)
    • Guanine – Cytosine (G-C)
Watson and Crick

- **Discovered by Franklin, Wilkins, Watson, & Crick**
  - Watson & Crick get most credit for determining the three-dimensional structure of DNA by building models.
  - They realized that DNA is a double helix that is made up of a sugar-phosphate backbone on the outside with bases on the inside.
• Watson and Crick’s discovery would not have been done without Franklin’s photo!
• Watson and Crick’s discovery built on the work of Rosalind Franklin and Erwin Chargaff.
  – Franklin’s x-ray images suggested that DNA was a double helix of even width.

The diffraction pattern determined the helical nature of the double helix strands (antiparallel). The outside linings of DNA have a phosphate backbone, and codes for inheritance are inside the helix.
DNA Structure

• Nucleotides always pair in the same way. Complementary base pairs hold the two DNA strands together.

• The base-pairing rules show how nucleotides always pair up in DNA.
  – A pairs with T
  – C pairs with G

• Because a pyrimidine (single ring) pairs with a purine (double ring), the helix has a uniform width.
• The backbone is connected by covalent bonds.
• The bases are connected by hydrogen bonds.
• How can a molecule with only 4 simple parts be the carrier of genetic information?
• The key lies in the sequence, not number, of subunits.
• Within a DNA strand, the four types of bases can be arranged in any linear order, and this sequence is what encodes genetic information.

• The sequence of only four nucleotides can produce many different combinations.
  – A 10 nucleotide sequence can code for greater than 1 million different combinations.
13.2 REPLICATION OF DNA
EQ: WHAT IS THE PURPOSE OF DNA REPLICATION? WHY IS IT IMPORTANT?
DNA Replication

• **KEY CONCEPT:** DNA replication copies the genetic information of a cell.

• All cells come from pre-existing cells

• Cells reproduce by dividing in half
  – Mitosis

• Each of two daughter cells gets an exact copy of parent cell’s genetic information
• Duplication of the parent cell DNA is called replication
  – Occurs during the S (synthesis) phase of Interphase
  • This occurs before mitosis begins
  • Ensures new cell is exactly like the old cell
DNA Replication

- DNA serves only as a template.
- Enzymes and other proteins do the actual work of replication.
- **Step 1:** Enzymes unzip the double helix at a starting point.
  - On some strands this may happen in multiple spots to speed up the process.
  - Free-floating nucleotides form hydrogen bonds with the template strand.
• **Step 2:** DNA Polymerase (enzyme) inserts and attaches new nucleotides onto the existing “parent” strand.
• This forms the double helix.
• Polymerase enzymes form covalent bonds between nucleotides in the new strand.
  – “extra” nucleotides are found in the nucleus of a cell
Step 3: Two new molecules of DNA are formed, each with an original strand and a newly formed strand.
- Newly made strands coil back up and are ready for use.
DNA is unzipping

New nucleotides have been added

Free Nucleotides

New double helix with 1 old & 1 new strand
• Replication is fast and accurate.
• DNA replication starts at many points in eukaryotic chromosomes.

There are many origins of replication in eukaryotic chromosomes.

• DNA polymerases can find and correct errors.
13.3 RNA AND GENE EXPRESSION
EQ: WHAT IS THE PURPOSE OF TRANSCRIPTION?
How does DNA relate to genotypes & phenotypes?

- Genotype is the genetic “make-up”
  - Genotype is the sequence of DNA molecules on a strand of DNA
- Phenotypes are the specific, expressed traits
  - Phenotypes are provided by different proteins and the functions of those proteins.
- So what is the connection?
  - Genes are composed of sequences of DNA
    - Genotype!
  - These genes are “codes” for certain proteins
  - The “matching” protein made is the expression of the trait (phenotype)
From DNA to RNA to Proteins

- A few Items to know:
  - DNA is found in genes and genes are found in chromosomes
  - All of those are found inside the nucleus of the cell ONLY!

- DNA is turned to proteins through a process called **Protein Synthesis**
  - This involves actions that occur in the cell’s nucleus and cytoplasm
  - This involves the DNA, RNA, and ribosomes
  - This process involves many steps and is constantly occurring within the cells of all living things!
Transcription

- **KEY CONCEPT:** Transcription converts a gene into a single-stranded RNA molecule.
- RNA carries DNA’s instructions.
- The central dogma states that information flows in one direction from DNA to RNA to proteins.
- The central dogma includes three processes.
  - Replication
  - Transcription
  - Translation
- RNA is a link between DNA and proteins.
RNA – Ribonucleic Acid

- Like DNA it is a nucleic acid
- Nucleotides are slightly different from DNA
- RNA differs from DNA in three major ways.
  1. RNA has a ribose sugar.
  2. RNA has uracil instead of thymine.
  3. RNA is a single-stranded structure (only one sided (not 2)).

- The 4 Nitrogenous Bases for RNA
  - Adenine (A)
  - Guanine (G)
  - Cytosine (C)
  - Uracil (U) (no Thymine)
    (Uracil is a substitute)

Base pairs of RNA are
- A-U
- G-C
RNA Vocabulary

- **RNA** - contains the sugar ribose, the base uracil replaces thymine, and usually is single stranded.

Three major types of RNA found in living cells:
- **Messenger RNA (mRNA)** - molecules are long strands of RNA nucleotides that are formed complementary to one strand of DNA. They travel from the nucleus to the ribosome to direct the synthesis of a specific protein.
- **Ribosomal RNA (rRNA)** - is the type of RNA that associates with proteins to form ribosomes in the cytoplasm.
- **Transfer RNA (tRNA)** - are smaller segments of RNA nucleotides that transport amino acids to the ribosome.
Comparison of RNA & DNA

**DNA**
- Deoxyribose Sugar
- Thymine
- 2 strands
- Double Helix
- Found inside nucleus

**RNA**
- Ribose Sugar
- Uracil
- Single Strand
- In or out of nucleus

**Nitrogenous Bases:**
- Adenine
- Cytosine
- Guanine
Protein Synthesis – Step 1

• **Transcription** – DNA’s nucleotide sequence is converted to RNA
  – sequence is “copied” on messenger RNA (mRNA)
  – Occurs inside the nucleus
  – Resembles DNA replication
  – DNA strands separate at a specific spot
  – RNA bases are paired with DNA sequence
    • RNA polymerase links the RNA to the DNA
Transcription

- RNA polymerase and other proteins form a transcription complex.
- The transcription complex recognizes the start of a gene and unwinds a segment of it.
Transcription cont...

- Nucleotides pair with one strand of the DNA
- RNA polymerase bonds the nucleotides together.
- The DNA helix winds again as the gene is transcribed.
The RNA strand detaches from the DNA once the gene is transcribed.
During transcription, RNA nucleotides base-pair one by one with DNA nucleotides on one of the DNA strands (called the template strand). RNA polymerase links the RNA nucleotides together.
Transcription makes three types of RNA.

- Messenger RNA (mRNA) carries the message that will be translated to form a protein.
- Ribosomal RNA (rRNA) forms part of ribosomes where proteins are made.
- Transfer RNA (tRNA) brings amino acids from the cytoplasm to a ribosome.
• The transcription process is similar to replication.

• Transcription and replication both involve complex enzymes and complementary base pairing.

• The two processes have different end results.
  – Replication copies all the DNA; transcription copies a gene.
  – Replication makes one copy; transcription can make many copies.
Translation

- **KEY CONCEPT**: Translation converts an mRNA message into a polypeptide, or protein.
- Amino acids are coded by mRNA base sequences.
- Translation converts mRNA messages into polypeptides.
- A codon is a sequence of three nucleotides that codes for an amino acid.
Amino Acids:

- Subunits of protein are called **amino acids**
- Only 20 amino acids (a.a.) in all life
- Amino acids link together make different proteins.
Three bases code for 1 amino acid
The genetic code matches each codon to its amino acid or function.

- three stop codons
- one start codon, codes for methionine
Translation cont...

- A change in the order in which codons are read changes the resulting protein.

- Regardless of the organism, codons code for the same amino acid.
Translation cont...

- Amino acids are linked to become a protein.
- An anticodon is a set of three nucleotides that is complementary to an mRNA codon.
- An anticodon is carried by a tRNA.
• Ribosomes consist of two subunits.
  – The large subunit has three binding sites for tRNA.
  – The small subunit binds to mRNA.
For translation to begin, tRNA binds to a start codon and signals the ribosome to assemble.

A complementary tRNA molecule binds to the exposed codon, bringing its amino acid close to the first amino acid.
The ribosome helps form a polypeptide bond between the amino acids.

The ribosome pulls the mRNA strand the length of one codon.
Translation cont...

- The now empty tRNA molecule exits the ribosome
- A complementary tRNA molecule binds to the next exposed codon.
- Once the stop codon is reached, the ribosome releases the protein and disassembles.
Summing up Translation

- The mRNA is broken into codons
  - Groupings of three mRNA sequences (AUG, CGA)
- Transfer RNA (tRNA) matches with the mRNA
  - This occurs in the ribosome (in cytoplasm)
- Amino Acids are added to each tRNA anticodon
  - Anticodons “match” up with a mRNA codon
- AA are added until a polypeptide is formed
  - Typically several hundred amino acids long
  - Multiple polypeptides form a protein

AUCGGCUUAGAC  \(\rightarrow\) mRNA
AUC GGC UUA GAC  \(\rightarrow\) codon
Chapter 14: Genes in Action
CHAPTER 14.1 MUTATION AND GENETIC CHANGE
When things go wrong...

- Are mutations heritable?
- Are mutations beneficial/harmful/both?
- Are mutations the cause of evolution?
- What are mutations?
• Find the base pairs that are incorrect in this strand of DNA.

GGATATTACCGTTGAAAGCAT
CCGATGATGCCCAACTGGCGCA
• Find the base pairs that are incorrect in this strand of DNA.

GGATAT TACCCTTGAAGACAT
CCGATGATGGCCAAACTGGCGCA
↑↑↑↑↑↑↑↑
Genetic MUTATION

- A change in the nucleotide sequence of a gene
Mutations

- **KEY CONCEPT:** Mutations are changes in DNA that may or may not affect phenotype.
- Some mutations affect a single gene, while others affect an entire chromosome.
- A mutation is a change in an organism’s DNA.
- Many kinds of mutations can occur, especially during replication.
- A **point mutation** substitutes one nucleotide for another.
POINT MUTATION/SUBSTITUTION

THE BIG FAT CAT ATE THE WET RAT
THE BIZ FAT CAT ATE THE WET RAT
Sickle Cell

Single nucleotide substitution

Ex: in sickle cell disease, valine is substituted for glutamate (GUA for GAA)

Normal Hemoglobin

Sickle Hemoglobin

Note: The Sickle hemoglobin image is drawn at 50% of the size of the Normal hemoglobin

http://carnegiescience.edu/first_light_case/horn/lessons/images/hemoglobins.GIF
DELETION

- THE BIG FAT CAT ATE THE WET RAT
- THB IGF ATC ATA TET HEW ETR AT

Ex: cystic fibrosis
Cystic Fibrosis (CF) is caused by a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. The most common cause is a deletion of 3 base pairs in the CFTR gene for phenylalanine. This leads to the production of a dysfunctional CFTR protein, which affects the transport of chloride ions across cell membranes. In unaffected individuals, mucus is hydrated by water molecules entering by osmosis, but in people with cystic fibrosis, sticky mucus traps bacteria and cannot be cleared by tiny hairs of the lung lining.
<table>
<thead>
<tr>
<th>Nucleotide</th>
<th>ATC ATC TTT GGT GTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amino Acid</td>
<td>Ile  Ile  Phe  Gly  Val</td>
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</table>
- THE BIG FAT CAT ATE THE WET RAT
- THE BIG ZFA TCA TAT ETH EWE TRA

Ex: Crohn’s disease
FRAMESHIFT MUTATIONS

• Insertion or deletion changes the reading frame:

THE BIG FAT CAT ATE THE WET RAT
THE BIG ZFA TCA TAT ETH EWE TRA T

• Now you’re making a completely different amino acid sequence!
- A **frameshift mutation** inserts or deletes a nucleotide in the DNA sequence.
DUPLICATION

THE BIG FAT CAT ATE THE WET RAT
THE BIG FAT FAT CAT ATE THE WET RAT
EXPANDING MUTATION

(TANDEM REPEATS) ex: fragile X syndrome

THE BIG FAT CAT ATE THE WET RAT
THE BIG FAT CAT CAT CAT ATE THE WET RAT
THE BIG FAT CAT CAT CAT CAT CAT ATE THE WET RAT
Which mutations can be passed to offspring?

- Somatic or sex-cell mutations?
- Why?
Chromosomal Mutations

- Chromosomal mutations affect many genes.
- Chromosomal mutations may occur during crossing over
  - Gene duplication results from unequal crossing over.
Chromosomal Mutations cont...

- Translocation results from the exchange of DNA segments between nonhomologous chromosomes.
Chromosomal and Gene mutations

- Mutations may or may not affect phenotype.
- Chromosomal mutations tend to have a big effect.
- Some gene mutations change phenotype.
  - A mutation may cause a premature stop codon.
  - A mutation may change protein shape or the active site.
  - A mutation may change gene regulation.

Cystic fibrosis
Mutations and their effects

• Some gene mutations do not affect phenotype.
  – A mutation may be silent.
  – A mutation may occur in a non-coding region.
  – A mutation may not affect protein folding or the active site.
• Mutations in body cells do not affect offspring.
• Mutations in sex cells can be harmful or beneficial to offspring.
• Natural selection often removes mutant alleles from a population when they are less adaptive.
Causes of Mutations

- Mutation’s can be caused by several factors.
- Replication errors can cause mutations.
- Mutagens, such as UV ray and chemicals, can cause mutations.
- Some cancer drugs use mutagenic properties to kill cancer cells.
14.2 REGULATING GENE EXPRESSION &
14.3 GENOME INTERACTIONS
Gene Expression and Regulation

- **KEY CONCEPT:** Gene expression is carefully regulated in both prokaryotic and eukaryotic cells.
- Prokaryotic cells turn genes on and off by controlling transcription.
- A promotor is a DNA segment that allows a gene to be transcribed.
- An operator is a part of DNA that turns a gene “on” or ”off.”
- An operon includes a promoter, an operator, and one or more structural genes that code for all the proteins needed to do a job.
  - Operons are most common in prokaryotes.
  - The *lac* operon was one of the first examples of gene regulation to be discovered.
  - The *lac* operon has three genes that code for enzymes that break down lactose.
The **lac** operon acts like a switch.
- The **lac** operon is “off” when lactose is not present.
- The **lac** operon is “on” when lactose is present.
Eukaryote gene expression

- Eukaryotes regulate gene expression at many points.
- Different sets of genes are expressed in different types of cells.
- Gene expression regulates cell function through the synthesis of proteins.
  - Genes encode proteins and proteins dictate cell function.
  - Therefore, the thousands of genes expressed in a particular cell determine what that cell can do.
Hox genes

- **Homeobox genes:** Transcription factors that determine whether a segment of an embryo will form head, thorax or abdomen.

[Image of Hox gene expression in embryos]
Introns and Exons

- RNA processing is also an important part of gene regulation in eukaryotes.
- mRNA processing includes three major steps
  - Introns are removed and exons are spliced together.
  - A cap is added.
  - A tail is added.
• Example of what the mRNA looks like before it’s sent to a ribosome…
  – Adds protective 5’ cap and poly-A tail to 3’ end of mRNA before it leaves nucleus.