DNA and Protein Synthesis - “Life is a Three Letter Word!” - CHAPTER NOTES

RNA: RIBONUCLEIC ACID: how DNA communicates its message.

- RNA is the genetic material of some viruses and is necessary in all organisms for protein synthesis to occur. RNA could have been the “original” nucleic acid when life first arose on Earth some 3.8 billion years ago.
- Like DNA, all RNA molecules have a similar chemical organization, consisting of nucleotides.
- Like DNA, each RNA nucleotide is also composed of three subunits:
  1. a 5-carbon sugar called RIBOSE.
  2. a PHOSPHATE group that is attached to one end of the sugar molecule.
  3. one of several different nitrogenous BASES linked to the opposite end of the ribose.
- There is one base that is different from DNA -- the base URACIL is used instead of thymine (G, A, C) are otherwise the same as for DNA).
- RNA is SINGLE-STRANDED, unlike DNA which is double stranded. RNA, therefore, is not a double helix.

- RNA is produced from DNA by a process called TRANSCRIPTION. The steps of transcription are as follows:
  1. A specific section of DNA unwinds, exposing a set of bases.
  2. Along one strand of DNA (called the "sense" strand), complementary RNA bases are brought in. In RNA, Uracil binds to the Adenine on DNA. As in DNA, cytosine binds to guanine. The other strand of the DNA molecule (the "missense" strand), isn't read in eukaryotic cells.
  3. Adjacent RNA nucleotides form sugar-phosphate bonds.
  4. The RNA strand is released from DNA (RNA is a single-stranded nucleic acid).
  5. The DNA molecule rewinds, and returns to its normal double helix form.
  6. Once produced, the mRNA strand is often processed (certain sections called introns are cut out, a "Poly-A" tail is added to the 3' end, and a "cap" is added to the 5' end).
- RNA can then leave the nucleus and go into the cytoplasm.
- The enzyme involved in transcription is known as RNA polymerase.
- This process occurs in the nucleus (and, in particular, dark coloured spots in the nucleus called nucleoli (singular = nucleolus)).

Gene Expression Levels

- histone
- chromatin
- DNA
- primary mRNA
- posttranscriptional control
- mature mRNA
- nuclear envelope
- nuclear pore
- translational control
- polypeptide chain
- posttranslational control
- functional protein
- plasma membrane

This mRNA transcript is ready to move into the cytoplasm.

Transcription is going on here—the nucleotides of mRNA are joined by the enzyme RNA polymerase in an orderly manner to a strand of DNA.

One portion of DNA—a particular gene or genes—is transcribed at one time.
There are 3 types of RNA, each with different functions.

**rRNA, tRNA, and mRNA – The agents of Protein Synthesis**

- RNA that is involved in protein synthesis belongs to one of three distinct types: ribosomal RNA (rRNA), transfer RNA (tRNA), and messenger RNA (mRNA).

  - **RIBOSOMAL RNA** (rRNA) - becomes a structural part of ribosomes and serves as a genetic link between mRNA and tRNA. Ribosomal RNA is associated with protein, forming bodies called ribosomes. Ribosomes are the sites of protein synthesis.
  - Ribosomal RNA varies in size and is the most plentiful RNA. It constitutes 85% to 90% of total cellular RNA.
  - **TRANSFER RNA** (tRNA) - is used to deliver amino acids from the cytoplasm to the ribosome. There is a different tRNA for each amino acid. The function of each type of tRNA is to bring its specific amino acid to a ribosome.
    - The tRNA molecules consist of about 80 nucleotides and are structured in a cloverleaf pattern. They constitute about 5% of the cell's total RNA.
  - **MESSENGER RNA** (mRNA) - carries the genetic code contained in the sequence of bases in the cell's DNA from the nucleus to the ribosome.
    - mRNA: acts as a "go-between" for DNA in the nucleus and the ribosomes in the cytoplasm.
    - mRNA constitutes 5% to 10% of the cell's RNA.

---

**The Central Dogma of Molecular Biology**

- this is sometimes summed up as "one gene, one protein"
- mRNA, once produced, leaves the nucleus through pores in the nuclear envelope, and enters the cytoplasm. This is where **TRANSLATION** occurs.
- Translation is the process that changes the RNA message into the actual protein. It occurs at the surface of the RIBOSOME.
- The order of the bases in DNA, and then subsequently mRNA, determines the
**amino acid sequence** of the protein being made.

- Each amino acid **is coded for by 3 bases** (this is known as a **TRIPLET CODE**)
- There are **20 different amino acids**, but only **4 different bases** in DNA/RNA.
- Each three-letter unit of mRNA is called a **CODON**.
- There are **4³** (= 64) codons possible --> therefore there are **easily enough codons to code for all the necessary amino acids**.
- In fact, the **same amino acid** is often specified by more than one codon. However (and this is very important), the reverse is **never** true: that is, any one codon only specifies **ONE amino acid** -- there is no vagueness in the code (e.g. CCU will **always** produce proline).
- The code also contains **“punctuation.”** It tells when to **start** reading the gene for a particular protein and when to **stop**.
- Each codon corresponds to an **amino acid**, or a "start" or "stop" synthesis signal. And **here it is**, the most important chart in all of Biology: the **GENETIC CODE**!

<table>
<thead>
<tr>
<th>AAU</th>
<th>AAC</th>
<th>AAG</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASPARAGINE</td>
<td>LYSINE</td>
<td>ASPARAGINE</td>
</tr>
<tr>
<td>CAU</td>
<td>CAC</td>
<td>CAA</td>
</tr>
<tr>
<td>HISTIDINE</td>
<td>GLUTAMINE</td>
<td>GLUTAMINE</td>
</tr>
<tr>
<td>GAC</td>
<td>GAA</td>
<td>GAG</td>
</tr>
<tr>
<td>ASPARTIC ACID</td>
<td>GLUTAMIC ACID</td>
<td>GLUTAMIC ACID</td>
</tr>
<tr>
<td>UAU</td>
<td>UAC</td>
<td>UAG</td>
</tr>
<tr>
<td>TYROSINE</td>
<td>STOP</td>
<td>STOP</td>
</tr>
</tbody>
</table>

- The genetic code is **universal**: the same codons stand for the same amino acids in all living things (well, **almost** all living things). This "Biochemical Unity" suggests that all living things have a **common evolutionary ancestor**.

The steps in **TRANSLATION**: can be divided into **3 subprocesses**:

1. **INITIATION**: the mRNA, with its **START CODON** (AUG) attaches to the "R" site of the ribosome.
   - The **AUG codon always initiates translation** and codes for the amino acid **methionine**.
   - **tRNA** binds to the **start codon** of mRNA. The tRNA has a **binding site of 3 bases** called an **ANTICODON** that is **complementary** to the mRNA codon. Therefore, the codon of mRNA of AUG is "read" by a tRNA that has a **UAC anticodon**. The tRNA that has this anticodon carries, at its tail, the amino acid **methionine**.
   - **This methionyl-tRNA** is in the **P site** of the ribosome. The **A site** next to it is available to the tRNA bearing the next...
amino acid.

- There is a specific tRNA for each mRNA codon that codes for an amino acid.

2. **ELONGATION:** more amino acids are added and connected together to form a polypeptide, as specified by the mRNA sequence.
   - an incoming amino-acyl-tRNA (lets call this AA₂-tRNA₂) recognizes the codon in the A site and binds there.
   - a peptide bond is formed between the new amino acid and the growing polypeptide chain.
   - the amino acid is removed from tRNA₁ (bond breaks between aa₁ and tRNA₁)
   - the tRNA₁ that was in the P site is released, and the tRNA in the A site is translocated to the P site.
   - the ribosome moves over one codon along the mRNA (to the right in our diagram, or more specifically in the 5’ ----> 3’ direction.)
   - This movement shifts the tRNA₂ (which is attached to the growing amino acid chain) to the P site.
   - tRNA₃ with aa₃ can now move into A site and bind with the next codon on mRNA.
   - THIS PROCESS REPEATS, and the CHAIN ELONGATES as long as there are new codons to read on the mRNA.

3. **TERMINATION:** The process above repeats until a special codon, called a STOP CODON, is reached.
   - There are 3 Stop codons: **UAA, UAG, UGA**.
   - the stop codons do not code for amino acids but instead act as signals to stop translation.
   - a protein called release factor binds directly to the stop codon in the A site. The release factor causes a water molecule to be added to the end of the polypeptide chain, and the chain then separates from the last tRNA.
   - the protein is now complete. The mRNA is now usually broken down, and the ribosome splits into its large and small subunits.
   - the new protein is sent for final processing into the endoplasmic reticulum and golgi apparatus.

**Please Label these Parts**

- Often, many ribosomes will simultaneously transcribe the same mRNA. In this way, many copies of the same protein can be made quickly. These clusters of ribosomes are called polysomes.

**GENETIC MUTATIONS**

- During the molecular maneuvering that occurs with DNA replication, if nucleotides are lost, rearranged, or paired in error, the resulting change in instruction of the genetic code could lead to a protein that does not function properly when the DNA's code is translated.
- A **MUTATION** is a change in an organism resulting from a chemical change in the structure of a gene.
- Although mutations have occurred throughout history, it wasn't until 1927 that Herman Muller, an American geneticist, developed the first experiments to study how and why they occurred. Genetic mutations can be
caused by both internal and external factors. Any factor that can cause a mutation is called a MUTAGEN
(e.g. Dioxins, benzene, UV light, asbestos, DDT, cigarette smoke, x-rays etc. etc.)
• Change will first be reflected in the RNA copy, then in the enzyme or other protein that the RNA codes for, and finally in the appearance of new traits in the living organism.
• There are two main categories of mutations: GENE MUTATIONS (affect only one gene), and CHROMOSOMAL MUTATIONS (affect many genes) because they affect entire chromosomes or parts of chromosomes).
• A mutation occurs because of the alteration in one or more base pairs of the DNA molecule, garbling the existing genetic code. Sometimes the pattern of normal base pairing is altered, causing the substitution of one base pair for another. Sometimes the pairing capacity of a specific base is changed, producing abnormal base pairing. Sometimes an extra base is added, sometimes a base is deleted. Mutations where bases are added or deleted are called frameshift mutations.
• It takes only a single different pair of bases to produce a different or imperfect organism.
• Consider an analogy of a “mutation” to a sentence in English.

EXAMPLE OF THE EFFECT OF A MUTATION:

ORIGINAL MESSAGE: THE BIG DOG BIT TED AND RAN OFF

DELETION/FRAME SHIFT: THE BID OGB ITT EDA NDR ANO FF

• Try it for yourself: Here is a section of DNA before a mutation.

| DNA | T | A | C | G | G | G | C | T | C | T | A | G | C | G | A | G | A | T | A | T | T |
| mRNA | A | U | G | C | C | C | G | A | G | A | U | C | G | C | U | C | U | A | A | A | A |
| a.a. | Methionine | Proline | Glut. acid | Isoleucine | Alanine | Leucine | Stop |

• Here the same section is after one extra base (a G in the third codon) has been added to the original sequence.

| DNA | T | A | C | G | G | G | G | C | T | C | T | A | G | C | G | A | G | A | T | A | T | T |
| mRNA | A | U | G | C | C | C | G | A | G | A | U | C | G | C | U | C | U | A | A | A | A |
| a.a. | Methionine | Proline | Arginine | Valine | Arginine | Serine | Isoleucine |

• Here the same section is after two bases have been switched from the original sequence.

| DNA | T | A | C | C | G | G | C | T | C | T | A | G | C | G | G | G | A | T | A | T | T |
| mRNA | A | U | G | G | C | C | G | A | G | A | U | C | G | C | C | U | A | U | A | A |
| a.a. | Methionine | Alanine | Glut. Acid | Isoleucine | Alanine | Leucine | Stop |

• Notice the different effects that different “point” mutations can have!
• If there is a change in the DNA that causes a change in the significant part of the mRNA codon(s), a different amino acid will be translated, and a different protein will be made. Usually random changes are HARMFUL (frequently mutations are lethal). About one time in million, the change might actually improve the protein (this is called a BENEFICIAL MUTATION). Beneficial mutations, while infrequent, drive the evolution of species!
• Occasionally, a mutations will be “neutral” – that is it will have no effect on the protein produced (as in the case of the second mutation in the second example above), or it will change an amino acid on a non-vital part of the protein.
• Gene mutations can cause GENETIC DISORDERS. For example, with the disease of SICKLE CELL ANEMIA, the normal round-shaped red blood cells are intermingled with some having a sickle shape. The sickle cells block the veins and arteries. As fewer and fewer normal red blood cells are able to pass through the congested blood vessels, the tissue and cells become starved for oxygen and other nutrients. This disease occurs when one amino acids present in the hemoglobin (the molecule of red blood cells responsible for oxygen and carbon dioxide transport) is misplaced because of an error in the messenger RNA which was made by a piece of DNA with one of its base pairs out of arrangement.

So, there are two main types of mutations:

Sickle-cell Disease — Hemoglobin Chain

Hb\textsuperscript{A} valine histidine leucine threonine proline glutamate glutamate

1 2 3 4 5 6 7

Hb\textsuperscript{B} valine histidine leucine threonine proline valine glutamate

Sickle-cell Disease — Glutamate vs. Valine

\[ \text{CH}_2 - \text{CH}_2 - \text{C}^\text{\textsuperscript{\text{-O}}} - \]

Glutamate (polar R group)

\[ \text{H}_2 \ 	ext{CH}_3 \ 	ext{CH}_3 \ 	ext{CH}_3 \]

Valine (nonpolar R group)
1. **GENE Mutations**: affect only a single gene. May be caused by a change (e.g. substitution, deletions, additions) in a single nucleotide. The effect on the individual depends on the gene’s role. The sickle-cell anemia is a good example of a genetic disorder caused by a gene mutation.

2. **CHROMOSOMAL Mutations**: occur after chromosomes are broken (e.g. due to exposure to radiation, addictive drugs, pesticides) and reform abnormally. Pieces of chromosomes can be lost, added, or whole chromosomes can be lost or added.