Chapter 10

From DNA to Proteins Transcription and RNA Processing

A. Life requires two basic functions
    1. Living organisms must be able to store and faithfully transmit genetic information during reproduction
    2. They must have the ability to catalyze chemical transformations to fire the reactions that drive life processes
B. RNA can serve as a biological catalyst. It can excise 400 nucleotides from its RNA in the absence of any protein
    1. **Ribozymes:** catalytic RNA molecules can cut out parts of their own sequences, connect some RNA molecules together, replicate others, and even catalyze the formation of peptide bonds between amino acids
        a. This led to the discovery that RNA was the original genetic material
    2. RNA molecules serves as both carriers of genetic information and as catalyzes that drove the chemical reactions needed to sustain and perpetuate life
    3. Also RNA may have acquired the ability to synthesize protein-based enzymes, which are more efficient catalysts
        a. Enzymes took over more of the catalytic functions leading too…
            i. RNA to become regulated to the role of information storage and transfer
            ii. DNA with its chemical stability an faithfully replication, eventually replaced RNA as the primary carrier of genetic information

10.1 RNA, Consisting of a Single Strand of Ribonucleotides, Participates in a Variety of Cellular Function

A. The Structure of RNA
    1. RNA, like DNA is a polymer consisting of nucleotides joined together by phosphodiester bonds
    2. Difference between the structures
        a. RNA nucleotides have ribose sugars (unlike DNA dioxyribose sugars)
        b. RNA has a free hydroxyl group on the 2'-carbon atom of the ribose sugar (DNA deoxyribose sugar lacks this free hydroxyl group)
        c. Because of the free hydroxyl group RNA degrades rapidly under alkaline conditions (DNA is more stable)
        d. RNA contains uracil instead of thymine in DNA
        e. RNA is usually single stranded consisting of one polynucleotide chain (DNA double stranded consisting of two polynucleotide strands joined by hydrogen bonding between complementary bases)
    3. Although RNA is single stranded, short complementary regions within a nucleotide strand can pair and form secondary structures
B. Classes of RNA
    1. **Ribosomal RNA(rRNA):** along with ribosomal protein subunits make up the ribosome, the site of protein assembly
    2. **Messenger RNA(mRNA):** carries the coding instructions for polypeptide chains from DNA to the ribosome
        a. After attaching to a ribosome, an mRNA molecule specifies the sequence of amino acids in a polypeptide chain and provides a template for joining amino acids
    3. **Pre-messenger RNAs(pre-mRNAs):** precursor molecules are the immediate products of transcription in eukaryotic cells

a. They are modified extensively before becoming mRNA and exiting the nucleus for translation into protein
b. Bacterial cells do not possess pre-mRNA in bacteria transcription takes place concurrently with translation

4. **Transfer RNA(tRNA):** serves as the link between the coding sequences of nucleotides in the mRNA and amino acid sequence of nucleotides in the mRNA and the amino acid sequence of a polypeptide chain
    a. Each tRNA attaches to an amino acid and helps incorporate it into a polypeptide chain
5. **Small nulear RNAs(snRNAs):** combine with small protein subunits to form **small nuclear ribonucleoproteins(snRNPs):** participate in the processing of RNA, converting pre-mRNA into mRNA
6. **Small nucleolar RNA(snoRNAs):** take part in the processing of rRNA
7. **microRNAs(miRNAs)** and **small interfering RNAs(siRNAs):** are found in eukaryotic cells and carry out RNA interference (RNAi) a process in which these small RNA molecules help trigger the degradation of mRNA or inhibit their translation into protein.

10.2 Transcription Is the Synthesis of an RNA Molecule from a DNA Template

A. All cellular RNAs are synthesized from DNA templates through the process of transcription
    1. In many ways similar to replication the big difference is the length of the template
    2. In replication ALL nucleotides in the DNA template are copied. In transcription only small parts of the DNA molecule-usually a single gene-are transcribed into DNA
        a. Because not all the gene products are needed at the same time or in the same cell
    3. Much of the DNA does not encode a functional product, and transcription of such sequences would be pointless
    4. Transcription is highly selective: individual genes are transcribed only as their products are needed
B. Transcription requires three major components
    1. A DNA template
    2. The raw materials(substrates) needed to build a new RNA molecule
    3. The transcription apparatus, consisting of the proteins necessary to catalyze the synthesis of RNA
C. The Template for Transcription
    1. The transcribed strand
        a. The template for RNA synthesis is a single strand of the DNA double helix
        b. **Template strand:** the one nucleotide strand of DNA used for transcription
        c. **Nontemplate strand:** is not ordinarily transcribed
            i. Although only one strand is transcribed, different genes may be transcribed from different strands
    2. During transcription, an RNA molecule that is complementary and antiparallel to the DNA template strand is synthesized
    3. **Transcription unit:** is a stretch of DNA that encodes an RNA molecule and the sequences necessary for its transcription containing three critical regions
        a. **Promoter:** a DNA sequence that the transcription apparatus recognizes and binds
            i. It indicates which of the two DNA strands is to be read as the template and the direction of transcription
            ii. It also determines the transcription start site, the first nucleotide that will be transcribed into RNA
            iii. In most transcription units the promoter is located next to the transcription start site but it is not, itself, transcribed

b. **RNA-coding-region:** a sequence of DNA nucleotides that is copied into an RNA molecule
c. **Terminator:** a sequence of nucleotides that signals where transcription is to end
    i. Transcription stops only after the terminator has been copied into RNA

4. The terms upstream and downstream to refer to the direction of transcription and the location of nucleotide sequences surrounding the RNA-coding sequence
    a. Downstream as transcription takes place: it binds to the promoter and moves toward the terminator
    b. The sequence on the nontemplate strand is written with the 5' end on the left and the 3' end on the right
    c. Nucleotides downstream at the start site are assigned positive numbers, and nucleotides upstream at the start site are assigned negative numbers

D. The Substrate for Transcription
    1. RNA is synthesized from **ribonucleoside triphosphates**
        a. Nucleotides are added one at a time to the 3'-OH group of the growing RNA molecule therefor transcription is 5'→3' the same as DNA synthesis
        b. Two phosphate groups are cleaved from the incoming ribonucleoside triphosphate; the remaining phosphate group participates in a phosphodiester bond that connects the nucleotide to the growing RNA molecule
        c. Reaction (PP_i is pyrophosphate)
        $RNA_n + Rntp \rightarrow RNA_{n+1}\ PP_i$
        d. RNA synthesis is complementary and antiparallel, but does not require a primer

E. The Transcription Apparatus
    1. **RNA polymerase:** carries out all the required steps of transcription
        a. The action of RNA polymerase is enhanced by a number of accessory proteins that join and leave the polymerase at different stages of the process
            i. Each accessory protein is responsible for providing or regulating a special function
    2. Bacterial RNA polymerase
        a. **Core enzyme:** the heart of most bacterial RNA polymerases which contain five subunits. It catalyzes the elongation of the RNA molecule by the addition of RNA nucleotides
            i. **Sigma factor:** controls the binding of RNA polymerase to the promoter. Without it RNA polymerase will initiate transcription at a random point along the DNA
            ii. **Holoenzyme:** when sigma has associated with the core enzyme, RNA polymerase binds stably only to the promoter region and initiates transcription at the proper start site
                a. Sigma is only required for promoter binding and initiation; when a few RNA nucleotides have been joined together, sigma detaches from the core enzyme
                b. each sigma initiates the binding of RNA polymerase to a particular set of promoters
    3. Eukaryotic RNA polymerases
        a. **RNA polymerase I:** transcribes Rna
        b. **RNA polymerase II:** transcribes pre-mRNAs, snoRNAs, miRNAs, and snRNAs
        c. **RNA polymerase III:** transcribes small RNA molecules- specifically tRNAs, small rRNA, miRNAs, and snRNAs
        d. **RNA polymerase IV:** functions in the nucleus and transcribes siRNAs that play a role in DNA methylation and chromatin structure