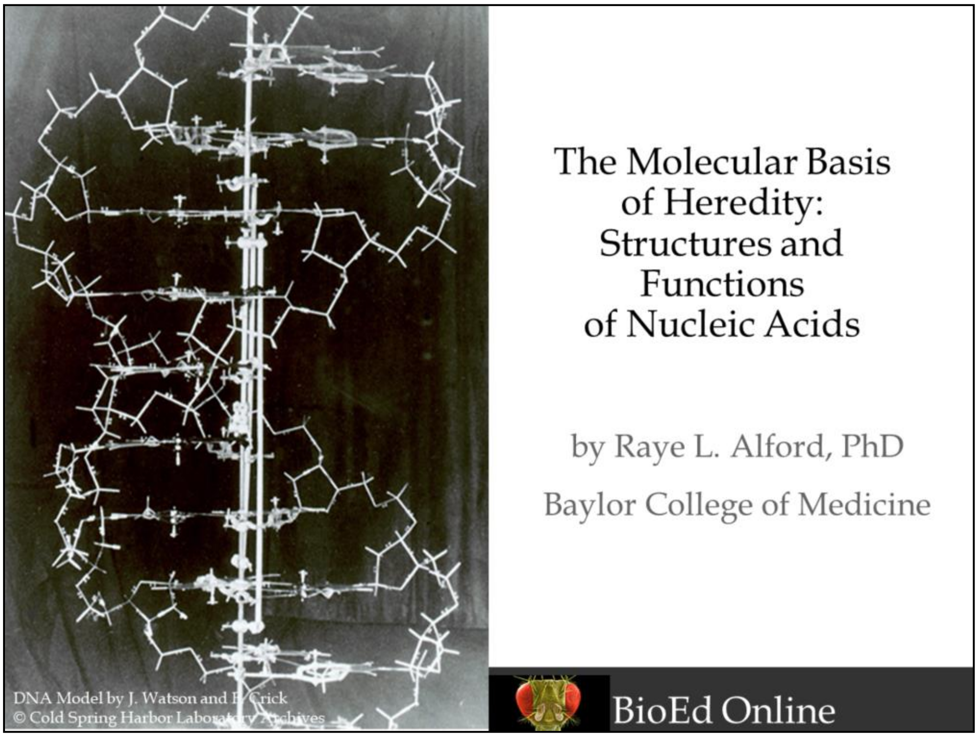

Structures and Functions of Nucleic Acids

In this slide set, we will explore the structures and functions of nucleic acids, including DNA and RNA, and their roles within cells.

Illustration:

The image on this slide is a photograph of the model of the DNA molecule built by Drs. James Watson and Francis Crick in 1953. Drs. Watson and Crick used this model to depict their proposed structure for the DNA double helix. The hypothesized structure was derived from X-ray diffraction data produced by Drs. Maurice Wilkins and Rosalind Franklin. The model was constructed from metal scraps obtained from a machine shop.

Drs. Watson and Crick published their proposed DNA structure in the journal, *Nature*, on April 2, 1953 (Volume 171, page 737). For their work, Drs. Watson, Crick and Wilkins were awarded the Nobel Prize in Physiology or Medicine in 1962. Dr. Franklin died before 1962. Since Nobel Prizes are awarded only to living individuals, she could not be honored.

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The Chemical Heritage Foundation. (2002.) Chemical Achievers: James Watson, Francis Crick, Maurice Wilkins, and Rosalind Franklin. The Chemical Heritage Foundation. Retrieved 2-28-2005 from http://www.chemheritage.org/EducationalServices/chemach/ppb/cwwf.html

Image Reference:

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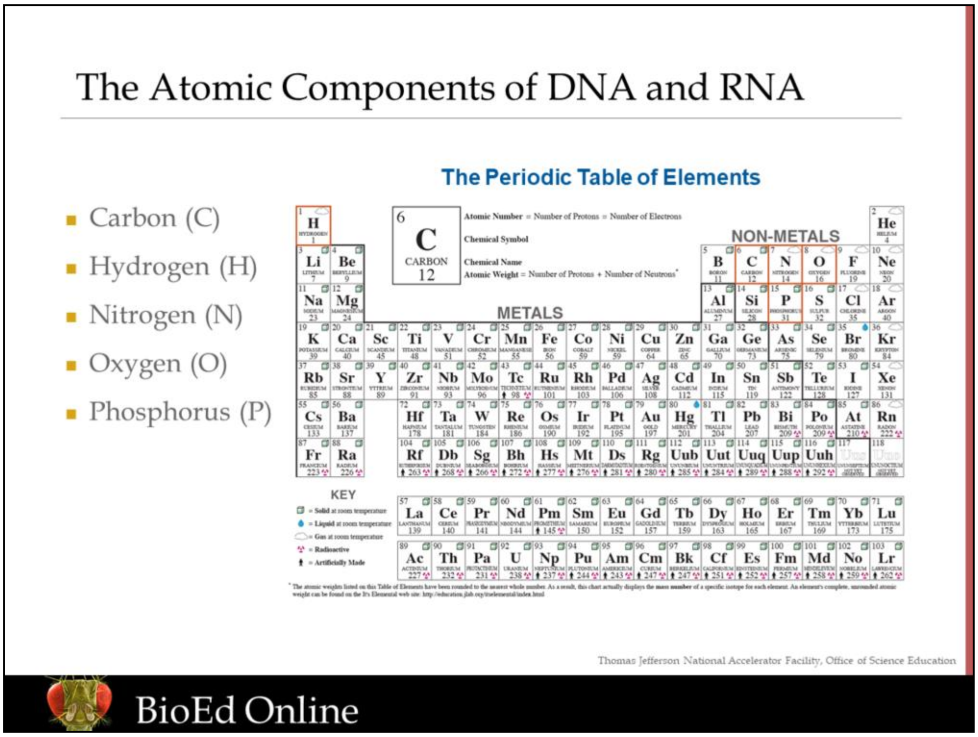

The Atomic Components of DNA and RNA

The acronym DNA stands for **d**eoxyribo**n**ucleic **a**cid. The acronym RNA stands for **r**ibo**n**ucleic **a**cid. DNA and RNA are large biological molecules (also known as macromolecules) that encode the genetic information of all known living things. They encode, in biochemical terms, the language of life.

The elements found in DNA and RNA include carbon, hydrogen, nitrogen, oxygen, and phosphorus.

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Berg, J.M., Tymoczko, J.l., and Stryer, L. (2002). *Biochemistry (5th ed.)*. W.H. Freeman and Co.

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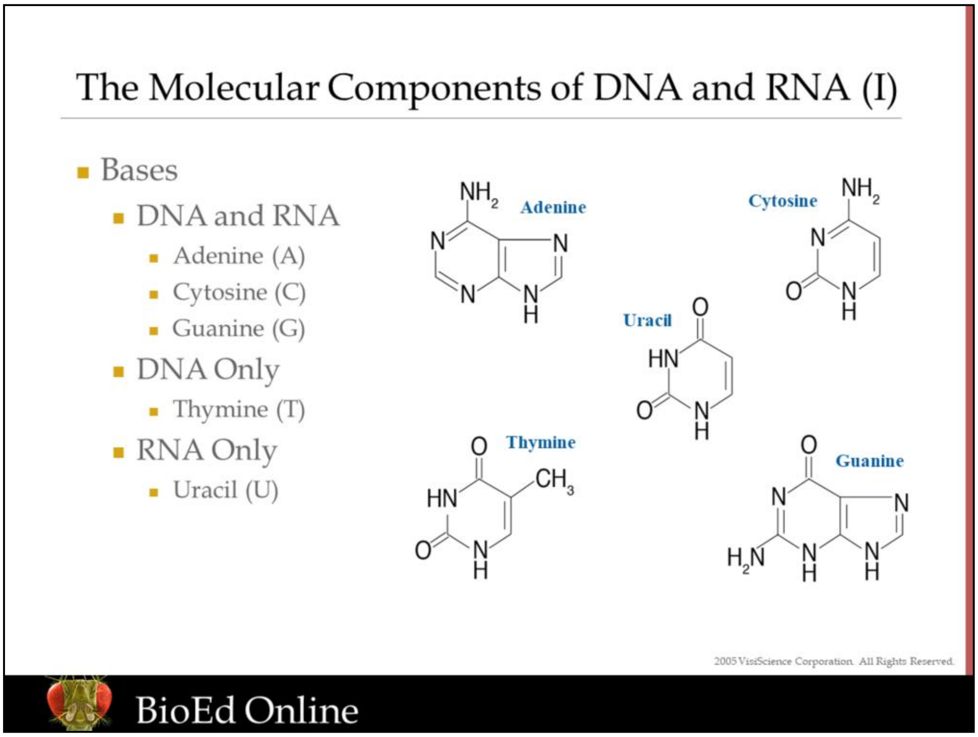

The Molecular Components of DNA and RNA (I)

The atoms that make up DNA and RNA are organized into two primary molecular components: bases and pentose sugars with attached phosphate groups. The bases are the key informational components of DNA and RNA, the letters of the DNA and RNA alphabet. The bases of DNA include adenine (A), cytosine (C), guanine (G), and thymine (T). Each base consists of a nitrogen-containing component called an amine. The side groups attached to the amines differ among the bases. Although RNA also uses A, C, and G, RNA does not use T. Instead, RNA substitutes the base uracil (U) for T.

References:

Berg, J.M., Tymoczko, J.l., and Stryer, L. (2002). *Biochemistry (5th ed.)*. W.H. Freeman and Co.

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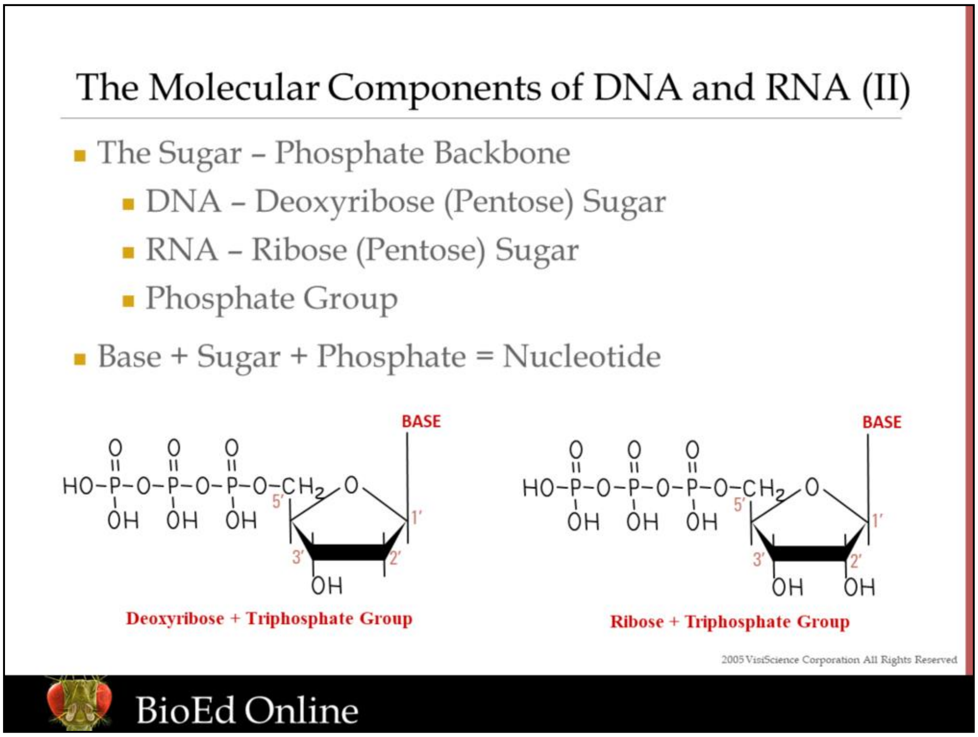

The Molecular Components of DNA and RNA (II)

The bases of DNA and RNA are attached, as shown in the drawings, to the 1′ (one prime) carbon of a pentose (five carbon) sugar. This pentose sugar is part of the sugar-phosphate backbone of the DNA and RNA macromolecule.

Also attached to the pentose sugar is a triphosphate group. The triphosphate group is attached to the 5′ (five prime) carbon of the pentose sugar. Together, the triphosphate group, the pentose sugar and the base make a molecule called a nucleotide.

Nucleotides frequently are used as units of measure to describe the length of a DNA or RNA molecule. For example, a segment of DNA or RNA often is said to a specified number of nucleotides long. In addition, nucleotides can be a measure of distance. In this case, the nucleotide unit describes the number of intervening nucleotides between one position in a DNA or RNA molecule and another. For example, one might say the mutation in gene A that causes disease B is 25 nucleotides away from the first nucleotide of the gene.

A deoxynucleotide bearing an adenine base is called a 2′-deoxyadenosine-5′-triphosphate, or dATP. A deoxynucleotide bearing a cytosine base is called a 2′-deoxycytidine-5′-triphosphate, or dCTP. A deoxynucleotide bearing a guanine base is called a 2′-deoxyguanosine-5′-triphosphate, or dGTP. A deoxynucleotide bearing a thymine base is called a 2′-deoxythymidine-5′-triphospate, or dTTP.

A ribonucleotide bearing an adenine base is called an adenosine 5′-triphosphate, or ATP. A ribonucleotide bearing a cytosine base is called a cytidine 5′-triphosphate, or CTP. A ribonucleotide bearing a guanine base is called a guanosine 5′-triphosphate, or GTP. A ribonucleotide bearing a uracil base is called a uridine 5′-triphosphate, or UTP.

Note in the drawing on the left that there is only one hydroxyl group (-OH) attached to the pentose sugar, at the 3′ carbon position. This makes this pentose sugar a deoxyribose sugar. The deoxyribose sugar is the sugar that makes up DNA.

Note in the drawing on the right that there are two hydroxyl (-OH) groups attached to the pentose sugar, at the 2′ and 3′ carbon positions. This makes the pentose sugar a ribose sugar. The ribose sugar is the sugar that makes up RNA.

References:

Berg, J.M., Tymoczko, J.l., and Stryer, L. (2002). *Biochemistry (5th ed.)*. W.H. Freeman and Co.

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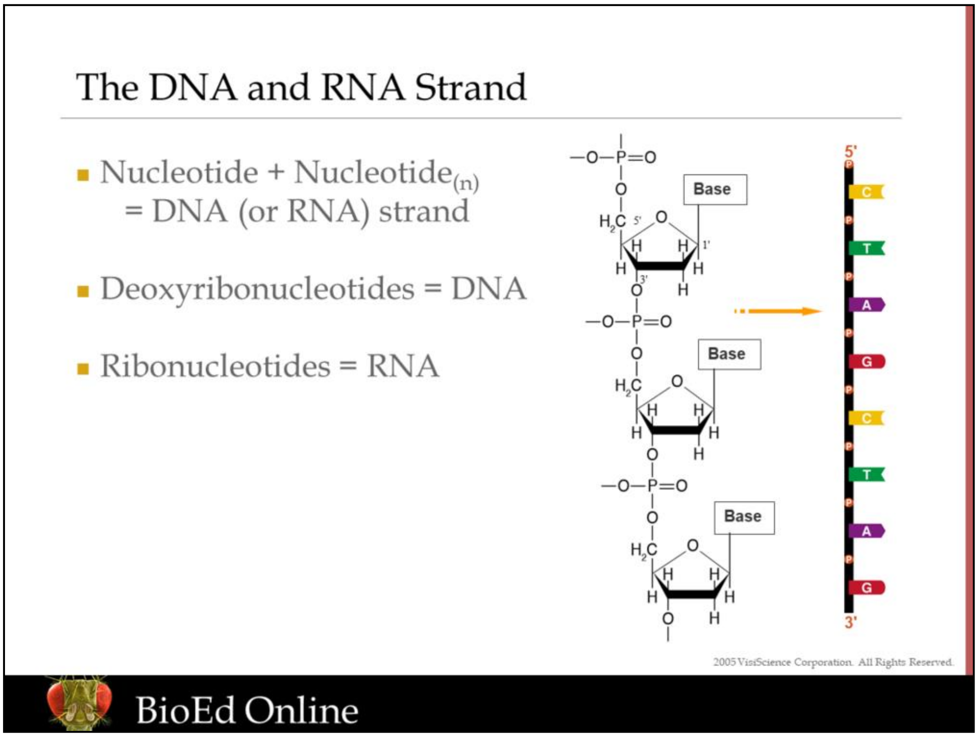

The DNA and RNA Strand

DNA and RNA nucleotides join, through a single phosphate, to form a string of DNA or RNA nucleotides, or a strand of DNA or RNA. When deoxyribose sugar nucleotides join, they make a DNA strand, as shown in the drawing on the left. When ribose sugar nucleotides join, they make an RNA strand.

When nucleotides join together to form a strand of DNA or RNA, the terminal two phosphates of the phosphate group are cleaved off and the remaining phosphate of one nucleotide is joined to the 3′ carbon of the last nucleotide of the existing strand. The 5′ to 3′ orientation of the nucleotides in the diagrams indicate the relative positions of the 5′ and 3′ carbons of the pentose sugars. Nucleotides are always linked 3′ carbon to 5′ carbon, through a phosphate group.

DNA strands are synthesized by an enzyme called DNA polymerase. RNA strands are synthesized by enzymes called RNA polymerases.

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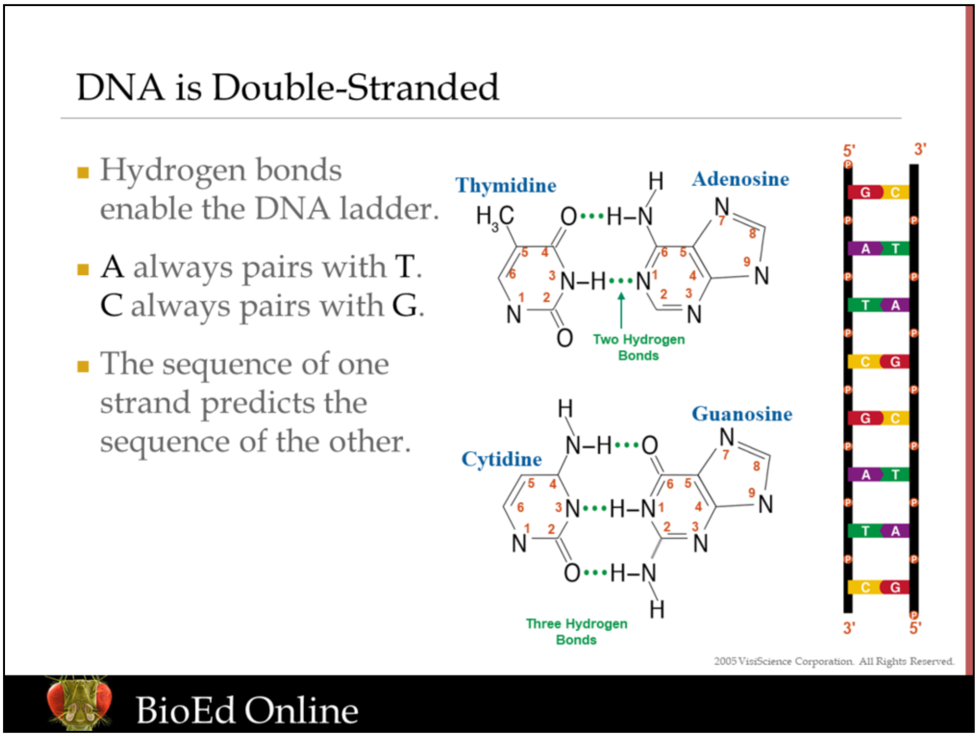

DNA is Double-Stranded

One of the most significant findings of Watson, Crick, Wilkins, and Franklin was that at the physiological pH and temperature of living cells, DNA usually is found as a double-stranded molecule. When DNA forms a double-stranded molecule, the strands are joined together through hydrogen bonds that form between the bases. In the double-stranded DNA molecule, an A base always pairs with a T base and a C base always pairs with a G base. Once joined, the bases are referred to as base pairs.

As shown, A-T base pairs form through two hydrogen bonds and C-G base pairs form through three hydrogen bonds. Because of the specificity of the hydrogen bonding, A always pairs with, or is complemented by, T, and C always pairs with, or is complemented by, G, and the two strands of a double-stranded DNA molecule are said to be complementary. The complementarity of base pairing means that knowing the nucleotide sequence of one strand of a double-stranded DNA molecule allows one to predict the nucleotide sequence of the other strand.

The length of a double-stranded DNA molecule often is described by the number of base pairs in the helix. For example, a double-stranded DNA molecule containing 27 pairs of A-T and C-G from one end to the other would be said to be 27 base pairs long. Base pairs also can be used as a unit of genetic distance. For example, two genes can be said to be a specified number of base pairs apart in a segment of DNA.

DNA and RNA strands are oriented according to the ribose sugars within them. The 5′ end of a strand of DNA (or RNA) is the end toward which the 5′ carbon of the pentose sugar lies. The strands of double-stranded DNA run antiparallel, or in opposite directions. That is, as shown in the illustration on the right, the 5′ end of one strand of DNA forms hydrogen bonds with the nucleotides at the 3′ end of its complementary strand.

RNA molecules within cells typically are single-stranded at physiologic temperature and pH. However, they frequently fold upon themselves to form secondary structures wherein a single RNA molecule forms intramolecular base pairs. As with many other biological molecules, the shape created by folding affects how the molecule functions inside cells. Although one RNA molecule may associate with another in some circumstances, RNA does not typically form long intermolecular double-stranded structures like DNA does.

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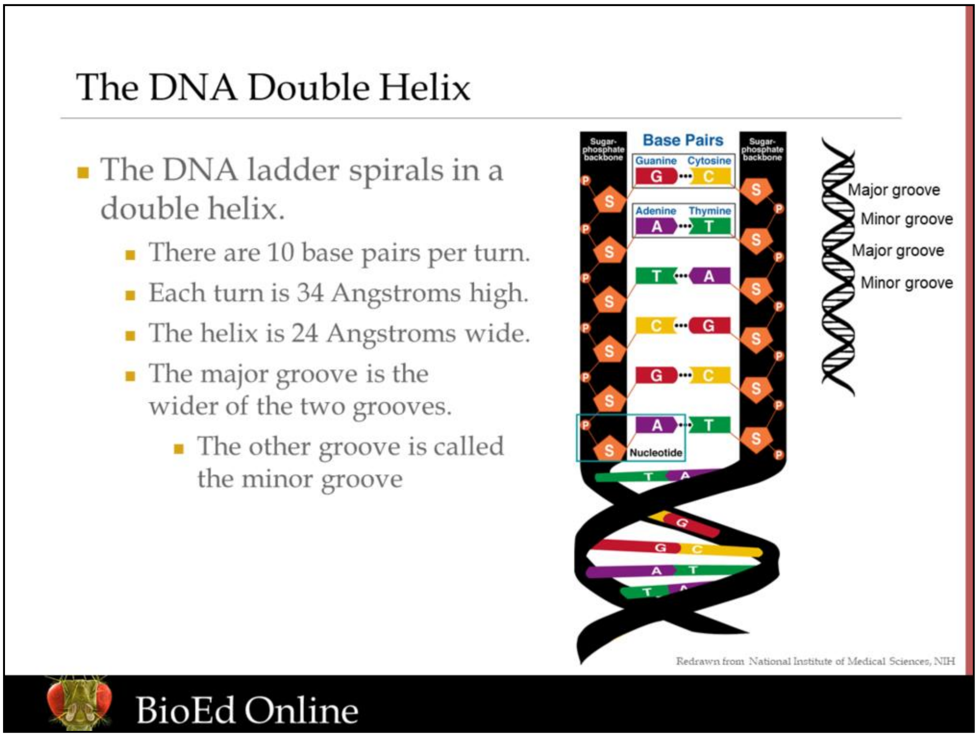

The DNA Double Helix

Double-stranded DNA is not a straight ladder-like molecule. Rather it turns in a helix, like a spiral staircase. The DNA helix is called a double helix because it is made of two complementary strands of DNA. The paired bases lie in the center of the spiral, forming the steps of the DNA spiral staircase. The sugar phosphate backbones form the railings of the DNA spiral staircase.

The hydrogen bonds between the base pairs that hold the two sides of the helix together can be broken easily. The DNA double helix can be forced to separate into its component strands by increasing the temperature or the pH of the solution in which it is suspended. If the temperature and/or pH is lowered back to physiologic levels, the complementary DNA strands will find one another in solution and re-hybridize into a double helix, in which A again pairs with T, and C pairs with G for the entire length of the strands. This physical property of DNA complementarity is the basis not only for the replication and transcription of DNA, but also for most molecular genetic testing technologies through which the sequence of DNA is investigated to diagnose genetic disease and determine paternity or personal identity. Replication is the process by which a DNA molecule reproduces itself. Transcription is the process through which DNA serves as the template for the synthesis of RNA.

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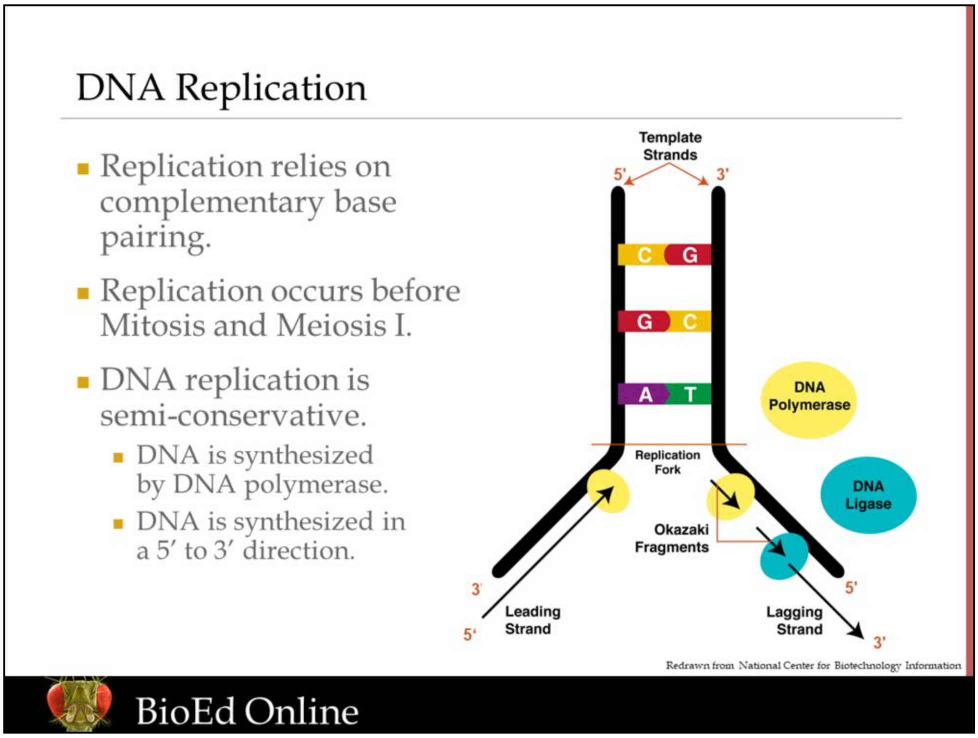

DNA Replication

Prior to mitosis (the process by which non-reproductive or somatic cells divide) and meiosis (the process by which germ cell precursors divide to form sperm, egg, or other reproductive cells), each DNA double helix within a cell is duplicated. This process, called DNA replication, begins at precise locations encoded within DNA molecules. These sites are called origins of replication.

Enzymes called helicases facilitate unwinding of the DNA double helix. Once unwound, the DNA strands are replicated. DNA polymerase enzymes copy each strand of the DNA, relying on the complementarity of DNA base pairing to replicate each strand faithfully. Because of the precise process by which each strand of DNA is used as the template to produce another strand, DNA replication is said to be semi-conservative. That is, each new DNA double helix is made up of one old strand and one new strand of DNA.

On the leading strand, DNA is replicated in long 5′ to 3′ segments. However, on the lagging strand, DNA synthesis must proceed 5′ to 3′ in short fragments called Okazaki fragments. Okazaki fragments, believed to be ~1,000 to 2,000 bases in length, are joined together by enzymes called ligases to complete replication of the lagging strand.

DNA polymerase has a built-in proofreading capability. Because of this, DNA replication is a remarkably reliable process. In humans, the error rate is believed to be less than one base pair per billion.

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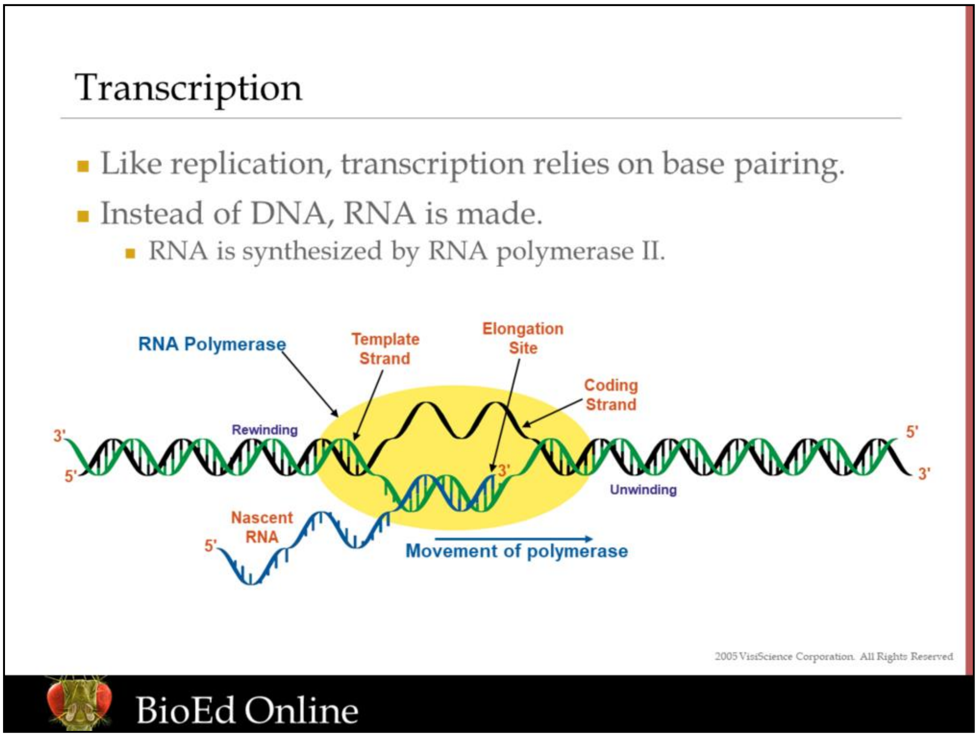

Transcription

Genes—the instructions for making the RNA and proteins needed to build and maintain cells and organisms—are embedded within the nucleotide sequence of the DNA double helix. DNA serves as the repository of these biologic instructions which consist of a specific series of nucleotides that are handed down from cell to cell and parent to offspring.

In order to implement the instructions encoded within the genes, DNA uses RNA as a messenger. RNA is formed through a process called transcription. During transcription, an enzyme called RNA polymerase II utilizes the precise base pairing between DNA and RNA nucleotides to synthesize an RNA molecule that is a complementary copy of one of the DNA strands. However, instead of incorporating deoxynucleotides into the nascent strand like the DNA polymerase does during replication, an RNA polymerase incorporates ribonucleotides into the growing nucleotide strand. The RNA molecule is synthesized in a 5′ to 3′ direction.

Genes have distinct starting and stopping points that are encoded within the DNA molecule. These signals specify where transcription of a particular gene should start and where it should stop. The coding strand of the DNA molecule is the strand that bears the same sequence as the RNA that will be made (with the substitution of uracil for thymine). As such, RNA polymerase "reads" the non-coding strand of the DNA molecule, so that when it synthesizes the complementary molecule, the sequence matches that of the coding strand of the DNA. The coding strand is so-called because it is the sequence that specifies the amino acid composition of the protein to be made.

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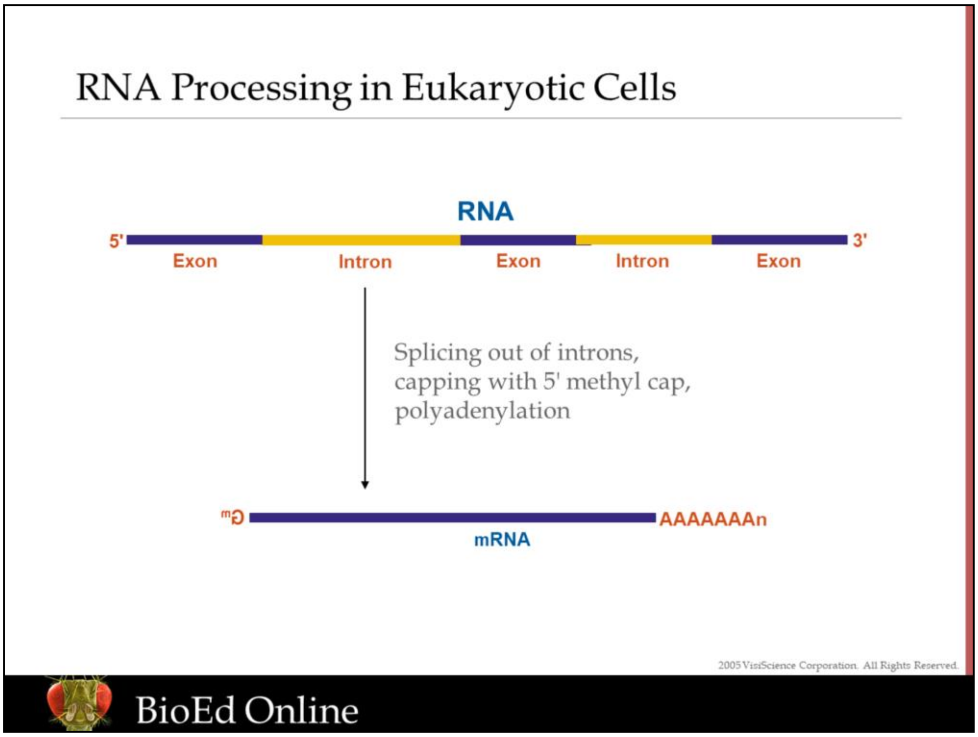

RNA Processing in Eukaryotic Cells

The RNA molecules made within eukaryotic cells must be processed before they can be used as messengers of the DNA code. Eukaryotic genes contain introns that must be removed. Introns are non-coding segments of DNA, of variable size, that separate the coding segments, or exons, of the genes of eukaryotic organisms. During RNA processing, the introns are removed from RNA molecules in a complex process called splicing. In addition, a methyl group called a 5′ cap is attached to the 5′ end of the RNA, and a polyA tail is added to the 3′ end of the RNA in a process called polyadenylation. The resulting processed RNA is called a messenger RNA (mRNA). Processed mRNAs migrate from the nucleus (the site of their transcription and modification) to the cytoplasm for translation by ribosomes.

Prokaryotic genes typically do not contain introns, although there are some exceptions. As such, there is usually no splicing of RNA molecules in prokaryotic cells. Prokaryotic RNAs also are not capped or polyadenylated as are eukaryotic RNAs. Further, in prokaryotic cells, there is no nucleus to separate the processes of transcription and translation, so transcription and translation often occur simultaneously, with RNA molecules being translated into proteins as they are being transcribed from the prokaryotic DNA. A newly discovered branch of the tree of life is the domain Archaea. Members of the domain Archaea are prokaryotes, as are bacteria. However, some genes of members of the domain Archaea have introns and share other structural and functional similarities with eukaryotes (organisms with a cell nucleus surrounded by a membrane).

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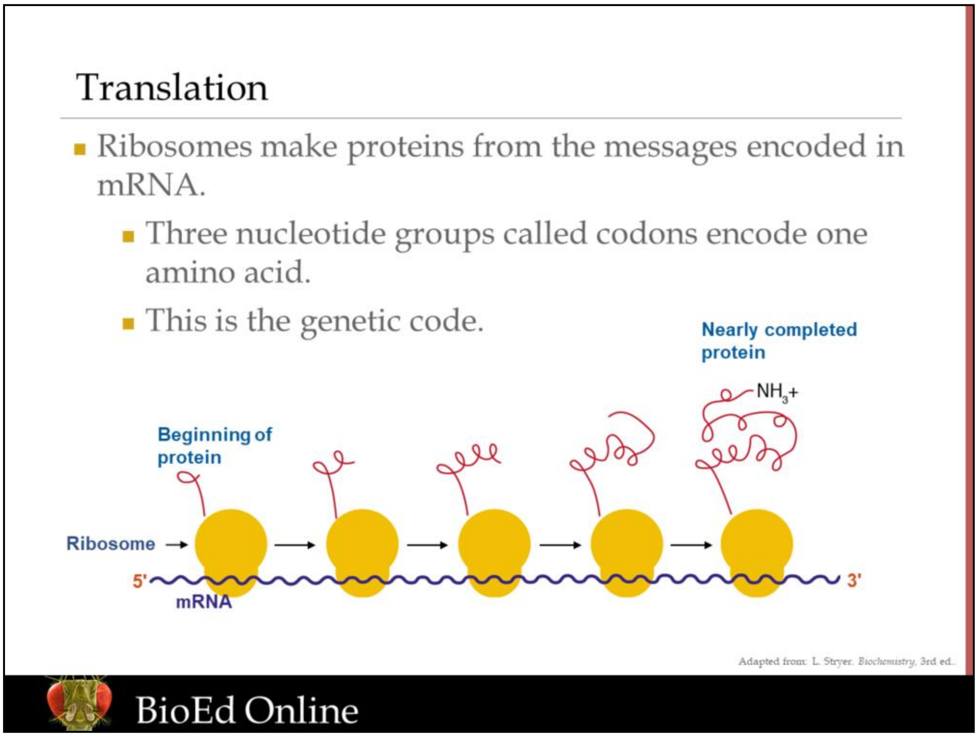

Translation

After processing, messenger RNA (mRNA) is transported from the nucleus of eukaryotic cells to the cytoplasm, where it comes into contact with ribosomes, the protein-making machinery of the cell. Ribosomes progress down the mRNA strand, in a 5′ to 3′ direction, creating a protein as they go. Ribosomes are complex structures made of protein and RNA, and can be found floating freely within the cytoplasm of eukaryotic cells or attached to the rough endoplasmic reticulum (RER).

Transfer RNA (tRNA) is the mediator for translation. tRNAs of eukaryotes are transcribed by an enzyme called RNA polymerase III. Like mRNAs, tRNAs undergo processing, but the processing of tRNAs is somewhat different from that of mRNA. tRNAs are cleaved from precursor RNAs and modified by the addition of nucleotides to their 3′ ends, and by methylation and other enzymatic modifications of certain ribonucleotides. The tRNA precursors of eukaryotes also contain an intron that must be removed by splicing.

tRNAs include an anti-codon loop, which contains a three-nucleotide long segment of RNA that binds to a complementary three-nucleotide long segment in an mRNA called a codon. tRNAs also have an attached amino acid. When a tRNA anti-codon associates, under the guidance of the ribosome, with its complementary mRNA codon, the amino acid attached to the tRNA is transferred from the tRNA to the growing protein molecule. As the ribosome moves down the mRNA molecule, additional tRNA molecules come in, bind to the codons embedded within the nucleotide sequence of the mRNA, and add amino acids to the growing protein, as specified by the nucleotide sequence of the mRNA and the gene from which it was transcribed.

Another class of RNAs, called ribosomal RNAs, are components of ribosomes. The ribosomal RNAs, rRNAs, of eukaryotes are transcribed by an enzyme called RNA polymerase I and also are processed before assembly into ribosomes.

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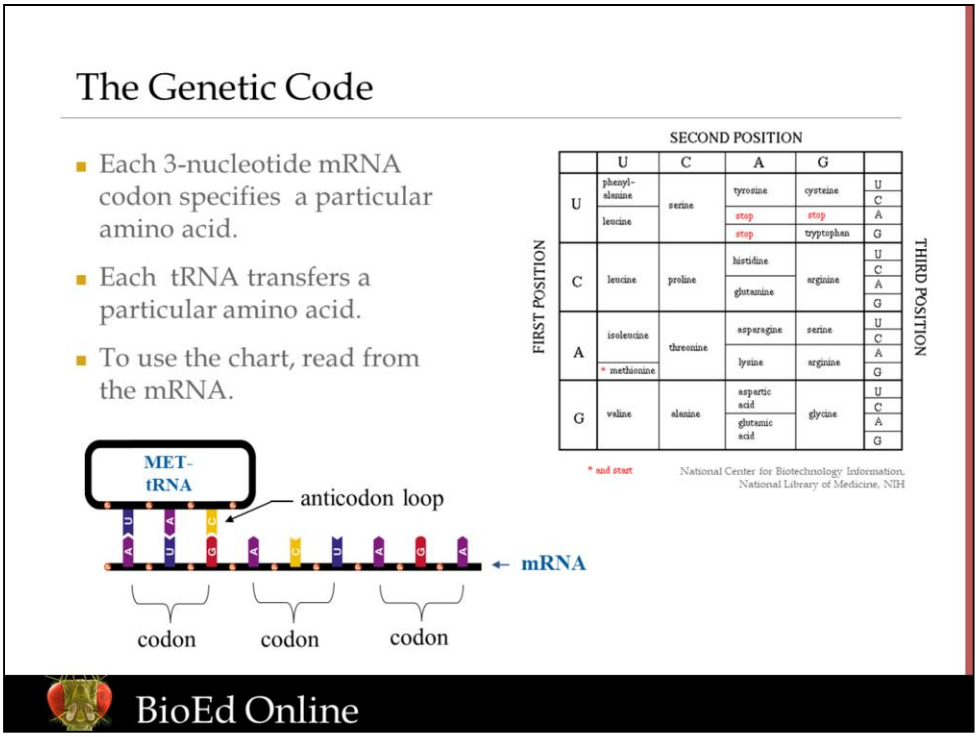

The Genetic Code

In mRNA, each three-nucleotide codon specifies a particular amino acid. As such, an mRNA has at least three times as many nucleotides as the protein it encodes has amino acids. mRNAs also often contain non-translated 5′ and 3′ sequences that typically serve regulatory or other purposes.

Note in the diagram on the left how the anti-codon loop of the tRNA molecule is complementary to the three-nucleotide codon sequence in the mRNA. This tRNA carries a methionine, MET, amino acid (typically the start, or initial, amino acid of a nascent eukaryotic protein). The complementarity of codon and anti-codon insures proper amino acid incorporation into growing protein molecules.

The table demonstrates the genetic code. The 20 different amino acids are shown in the center of the table, while the nucleotides of the various codons are shown around the outside edges, with the first position of the triplet codon on the left side, the second position across the top, and the third position down the right side of the table.

As shown, there are 64 possible codons but only 20 amino acids. This makes the genetic code redundant; that is, some amino acids are coded for by more than one codon. Note in the table how the codons UCU, UCC, UCA, UCG, AGU, and AGC all code for the amino acid serine. The redundancy of the genetic code means that not every change, or mutation, of the nucleotide sequence within a gene will result in a change in the encoded protein.

At the end of each mRNA is a final codon, called a stop codon. This codon tells the ribosome that construction of the protein is complete. The ribosome then falls off the mRNA strand and the newly completed protein is released for further processing and migration to its final intra- or extra-cellular destination.

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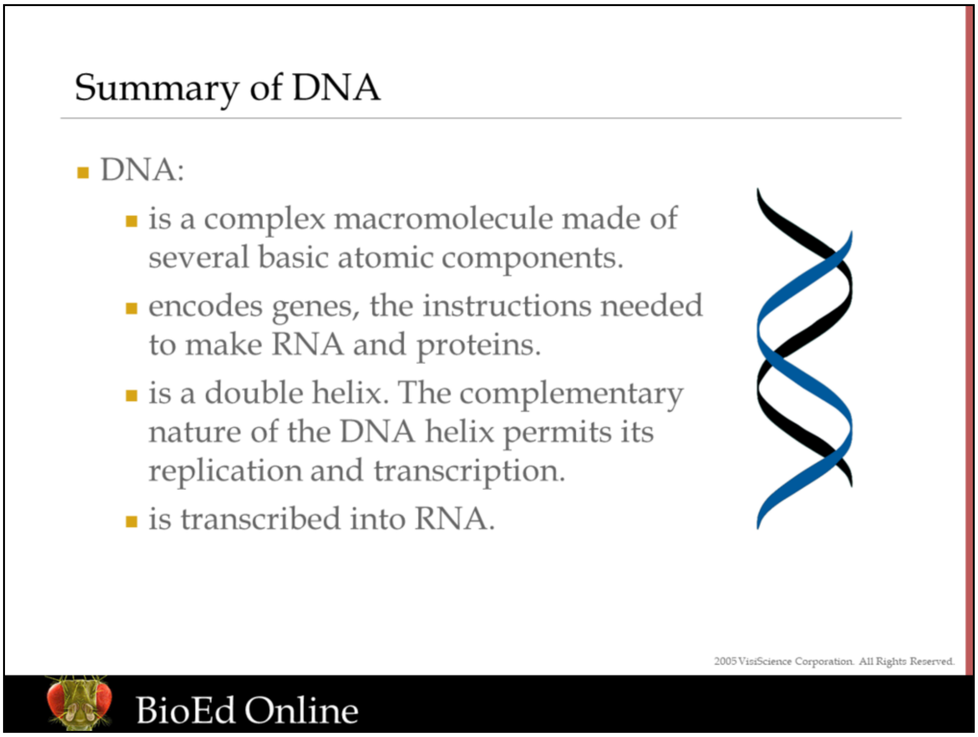

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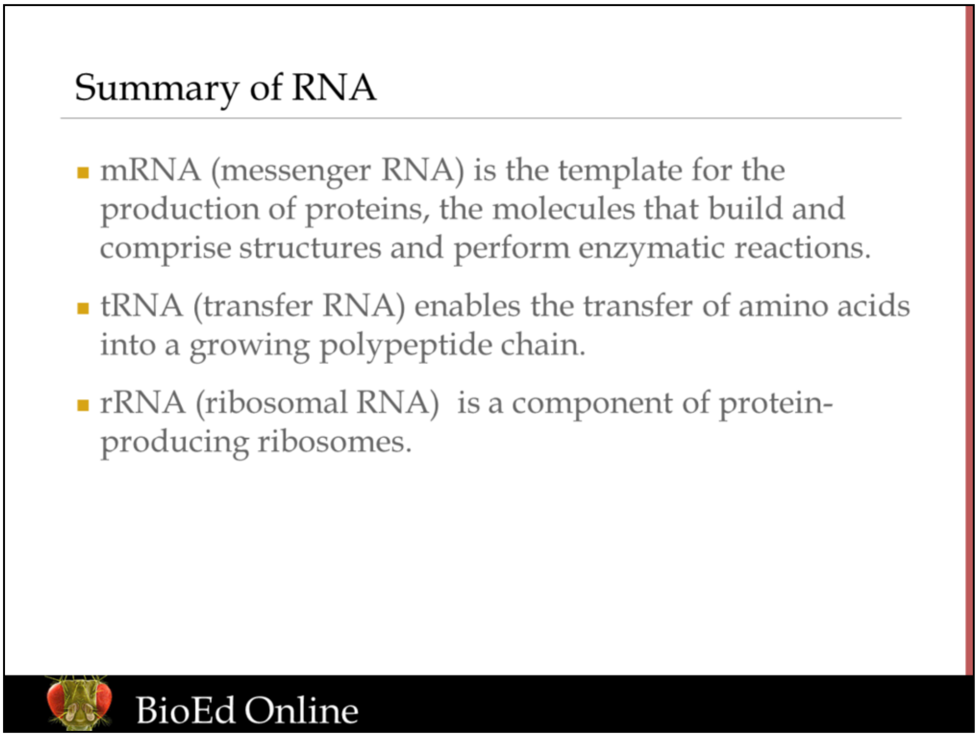

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