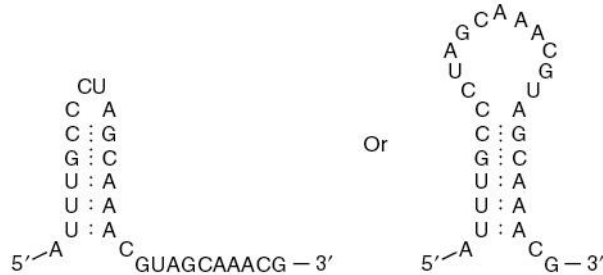


S1. A hypothetical sequence at the beginning of an mRNA molecule is

5'–AUUUGCCCUAGCAAACGUAGCAAACG...rest of the coding sequence

Using two out of the three underlined sequences, draw two possible models for potential stem-loop structures at the 5' end of this mRNA.

Answer:



S2. Describe the previous experimental evidence that led Watson and Crick to the discovery of the DNA double helix.

Answer:

1. The chemical structure of single nucleotides was understood by the 1950s.
2. Watson and Crick assumed that DNA is composed of nucleotides that are linked together in a linear fashion. They also assumed that the chemical linkage between two nucleotides is always the same.
3. Franklin's diffraction patterns suggested several structural features. First, it was consistent with a helical structure. Second, the diameter of the helical structure was too wide to be only a single-stranded helix. Finally, the line spacing on the diffraction pattern indicated that the helix contains about 10 base pairs per complete turn.
4. In the chemical analysis of the DNA from different species, the work of Chargaff indicated that the amount of adenine equaled the amount of thymine and that the amount of cytosine equaled the amount of guanine.
5. In the early 1950s, Linus Pauling proposed that regions of proteins can fold into a secondary structure known as a helix. To discover this, Pauling built large models by linking together simple ball-and-stick units. In this way, it becomes possible to determine if atoms fit together properly in a complicated three-dimensional structure. A similar approach was used by Watson and Crick to solve the structure of the DNA double helix.

S3. Within living cells, a myriad of different proteins play important functional roles by binding to DNA and RNA. As described throughout your textbook, the dynamic interactions between nucleic acids and proteins lie at the heart of molecular genetics. Some proteins bind to DNA (or RNA) but not in a sequence-specific manner. For example, histones are proteins that are important in the formation of chromosome structure. In this case, the positively charged histone proteins actually bind to the negatively charged phosphate groups in DNA. In addition, several other proteins interact with DNA but do not require a specific nucleotide sequence to carry out their function. For example, DNA polymerase, which catalyzes the synthesis of new DNA strands, does not bind to DNA in a sequence-dependent manner. By comparison, many other proteins do interact with nucleic acids in a sequence-dependent fashion. This means that a specific sequence of bases can provide a structure that will be recognized by a particular protein. Throughout the textbook, the functions of many of these proteins will be described. Some examples include transcription factors that affect the rate of transcription, proteins that bind to centromeres, and proteins that bind to origins of replication. With regard to the three-dimensional structure of DNA, where would you expect DNA-binding proteins to bind if they recognize a specific base sequence? What about DNA-binding proteins that do not recognize a base sequence?

Answer: DNA-binding proteins that recognize a base sequence must bind into the major or minor groove of the DNA. This is where the bases would be accessible to a DNA-binding protein. Most DNA-binding proteins, which recognize a base sequence, actually fit into the major groove. By comparison, other DNA-binding proteins, such as histones, which do not recognize a base sequence, bind to the DNA backbone.

S4. The formation of a double-stranded structure must obey the rule that adenine hydrogen bonds to thymine (or uracil) and cytosine hydrogen bonds to guanine. Based on your previous understanding of genetics (from this course or general biology courses), discuss reasons why complementarity is an important feature of DNA and RNA structure and function.

Answer: One way that complementarity underlies function is that it provides the basis for the synthesis of new strands of DNA and RNA. During replication, the synthesis of the new DNA strands occurs in such a way that adenine hydrogen bonds to thymine and cytosine hydrogen bonds to guanine. In other words, it is the molecular feature of a complementary double-stranded structure that makes it possible to make exact copies of DNA. Likewise, the ability to transcribe DNA into RNA is based on complementarity. During transcription, one strand of DNA is used as a template to make a complementary strand of RNA.

In addition to the synthesis of new strands of DNA and RNA, complementarity is important in other ways. As mentioned in chapter 9, the folding of RNA into a particular secondary structure is driven by the hydrogen bonding of complementary regions. This event is necessary to produce functionally active tRNA molecules. Likewise, stem-loop structures also occur in other types of RNA. For example, the rapid formation of stem-loop structures is known to occur as RNA is being transcribed and to affect the termination of transcription.

A third way that complementarity can be functionally important is that it can promote the interaction of two separate RNA molecules. During translation, codons in mRNA bind to the anticodons in tRNA (see chapter 13). This binding is due to complementarity. For example, if a codon is 5'-AGG-3', the anticodon is 3'-UCC-5'. This type of specific interaction between codons and anticodons is an important step that enables the nucleotide sequence in mRNA to code for an amino acid sequence within a protein. In addition, many other examples of RNA-RNA interactions are known and will be described throughout this textbook.

S5. An important feature of triplex DNA formation is that it is sequence specific. The synthetic third strand incorporates itself into a triple helix so that a thymine in the synthetic DNA will bind near an AT pair in the biological DNA and a cytosine in the synthetic DNA will bind near a GC pair. From a practical point of view, this opens the possibility of synthesizing a short strand of DNA that will form a triple helix at a particular target site. For example, if the sequence of a particular gene is known, it may be possible to make a synthetic piece of DNA that will form a triple helix somewhere within that gene according to the T to AT, and C to GC rule. Triplex DNA formation is known to inhibit gene transcription. In other words, when the synthetic DNA binds within the DNA of a gene, the formation of triplex DNA prevents that gene from being transcribed into RNA. Discuss how this observation might be used to combat diseases.

Answer: Triplex DNA formation opens the exciting possibility of designing synthetic pieces of DNA to inhibit the expression of particular genes. Theoretically, such a tool could be used to combat viral diseases or to inhibit the growth of cancer cells. To combat a viral disease, a synthetic DNA could be made that specifically binds to an essential viral gene and thereby prevents viral proliferation. To inhibit cancer, a synthetic DNA could be made to bind to an oncogene. (Note: As described in chapter 22, an oncogene is a gene that promotes cancerous growth.) Inhibition of an oncogene could prevent cancer. At this point, a primary obstacle in applying this approach is devising a method of getting the synthetic DNA into living cells.