Johns Hopkins Engineering

Molecular Biology

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Module 2 / Lecture 2

Nucleic acids

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Nucleic acids

Transcription and Translation

$$\text{DNA} \xrightarrow{\textit{transcription}} \text{RNA} \xrightarrow{\textit{translation}} \text{PROTEIN}$$

Nucleic Acids

Nucleic acids are macromolecules paramount importance to the cell because of their role in the storage, transmission, and expression of genetic information.

Nucleic acids are linear polymers of nucleotides, strung together in a genetically determined order that is critical to their role as informational macromolecules.

The two major types of nucleic acids are DNA (**deoxyribonucleic acid**) and RNA (**ribonucleic acid**). DNA and RNA differ in terms of their chemistry and their role in the cell.

RNA contains the five-carbon sugar ribose in each of its nucleotides, whereas DNA contains the closely related sugar deoxyribose.

DNA serves primarily as the **repository** of genetic information, whereas RNA molecules play several different roles in the expression of that information that is, during protein synthesis.

Nucleic Acids

Messenger RNA (mRNA) contains the information that dictates amino acid sequence during polypeptide synthesis.

Transfer RNA (tRNA) brings the correct amino acid to the next site in a growing polypeptide chain.

Ribosomal RNA (rRNA) the third major type of RNA, is an important constituent of the ribosomes that serve as the site of protein synthesis.

The Monomers Are Nucleotides

Nucleic acids are informational macromolecules that contain non-identical monomeric units in a specified sequence.

The monomeric units of nucleic acids are called **nucleotides**.

Nucleotides exhibit less variety than amino acids; DNA and RNA each contain only four different kinds

Each nucleotide consists of a fivecarbon sugar, a phosphate group, and a nitrogen-containing aromatic base. The sugar is either D-ribose (for IRNA) or D-deoxyribose (for DNA).

The phosphate is joined by a phosophoester bond to the 5' carbon of the sugar, and the base is attached at the 1' carbon. The base maybe either a purine or a pyrimidine.

DNA contains the purines: adenine (A) and guanine (G) and the pyrimidines: cytosine (C) and thymine (T).

RNA also has adenine, guanine, and cytosine but contains the pyrimidine uracil (U) in place of thymine.

Like the 20 amino acids present in proteins, these 5 aromatic bases are among the 30 most common small molecules in cells.

Polymers: DNA and RNA

The bases in DNA are the

purines - **adenine** (A) and **guanine** (G)

and the **pyrimidines - thymine** (T) and **cytosine** (C).

In RNA, thymine is replaced by the pyrimidine **uracil** (U).

ATP is the energy-rich compound used to drive a variety of reactions in the cell, including the activation of monomers for polymer formation.

Nucleotides actually play two roles in cells:

1. They are the **monomeric units of nucleic acids**
2. And, they **serve as intermediates in various energy transferring reactions**.

Polymers: DNA and RNA

Nucleic acids are linear polymers formed by linking each nucleotide to the next through a phosphate group.

Specifically, the phosphate group already attached by a phosphoester bond to the 5' carbon of one nucleotide becomes linked by a second phosphoester bond to the 3' carbon of the next nucleotide.

In essence, this is a **condensation** reaction, with the -H and -OH groups coming from the sugar and the phosphate groups, respectively.

The resulting linkage is called a 3', 5' phosphodiester bond.

The polynucleotide formed by this process has an intrinsic directionality, with a 5' hydroxyl group at one end and a 3' hydroxyl group at the other end.

By convention, nucleotide sequences are always written from the 5' end to the 3' end of the polynucleotide.

Polymers: DNA and RNA

Nucleic acid synthesis requires both energy and information, just as protein synthesis does.

Information is required for nucleic acid synthesis because successive incoming nucleotides must be added in a specific, genetically determined sequence.

For this purpose, a pre-existing molecule is used as a template to specify nucleotide order.

For both DNA and RNA synthesis, the template is usually DNA.

The essence of template-directed nucleic acid synthesis is that each incoming nucleotide is selected because it’s base can be recognized by (will interact with) the base of the nucleotide already present at that position in the template.

Polymers: DNA and RNA

This recognition process depends on an important chemical feature of the purine and pyrimidine bases.

These bases have carbonyl groups and nitrogen atoms capable of hydrogen bond formation under appropriate conditions.

Complementary relationships between purines and pyrimidines allow them to form two hydrogen bonds with T (or U) and C to form three hydrogen bonds with C.

This pairing of A with T (or U) and C with C is a fundamental property of nucleic acids.

Genetically, this base pairing provides a mechanism for nucleic acids to recognize one another.

A DNA Molecule Is a Double-Stranded Helix

One of the most significant biological advances of the twentieth century came in 1953 in a two-page article in *Nature.*

Francis Crick and James Watson postulated a **double-stranded helical structure for DNA the now famous double helix** that not only accounted for the known physical and chemical properties of DNA but also suggested a mechanism for replication of the structure.

The double helix consists of two complementary chains of DNA twisted together around a common axis to form a right-handed helical structure that resembles a circular staircase.

A DNA Molecule Is a Double-Stranded Helix

The two chains are oriented in opposite directions along the helix, one in the 5’-3' direction and the other in the 3’-* 5' direction.

The backbone of each chain consists of sugar molecules alternating with phosphate groups.

The phosphate groups are charged and the sugar molecules contain polar hydroxyl groups, so it is not surprising that the sugar phosphate backbones of the two strands are on the outside of the DNA helix, where their interaction can be maximized.

The pyrimidine and purine bases, on the other hand, are aromatic compounds with less affinity for water.

They are oriented inward, forming the base pairs that hold the two chains together.

A DNA Molecule Is a Double-Stranded Helix

To form a stable double helix, the two component strands must be not only *antiparallel* (running in opposite directions) but also ***complementary.***

Each base in one strand can form specific hydrogen bonds with the base in the other strand directly across from it. From the pairing possibilities, this means that each A must be paired with a T, and each G with a C.

In both cases, one member of the pair is a pyrimidine (T or C) and the other is a purine (A or G). The distance between the two sugar-phosphate backbones in the double helix is just sufficient to accommodate one of each kind of base.

A DNA Molecule Is a Double-Stranded Helix

We envision the sugar-phosphate backbones of the two strands as the sides of a circular staircase, then each step or rung of the stairway corresponds to a pair of bases held in place by **hydrogen bonding**.

The **right-handed** Watson-Crick helix is actually an idealized version of what is called *B-DNA.*

B-DNA is the main form of DNA in cells, but two other forms may also exist, perhaps in short segments interspersed within molecules that consist mainly of *B-DNA*.

A-DNA has a right-handed helical configuration that is shorter and thicker than *B-DNA*.

Z-DNA, on the other hand, is a left-handed double helix that derives its name from the zigzag pattern of its longer, thinner sugar phosphate backbone.

RNA Structure

RNA structure also depends in part on base pairing, but this pairing is usually between complementary regions within the same strand and is much less extensive than the inter-strand pairing of the DNA duplex.

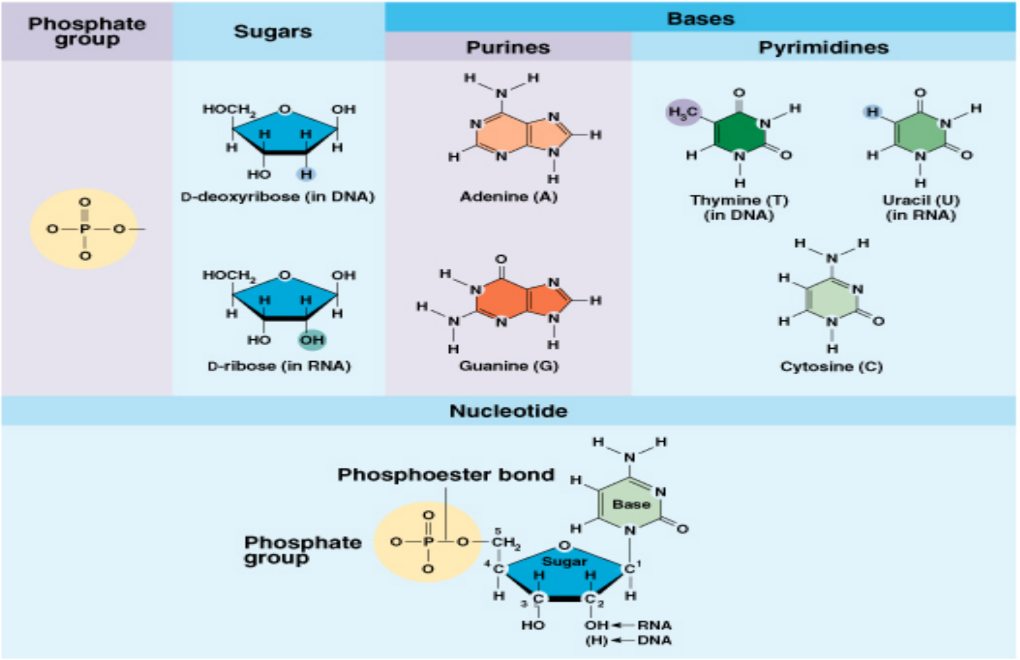
Of the various RNA species, secondary and tertiary structures are well understood only for *tRNA* molecules.

The Bases, Nucleosides, and Nucleotides of RNA and DNA

Table 3-4 The Bases, Nucleosides, and Nucleotides of RNA and DNA

	RNA		DNA	
Bases	*Nucleoside*	*Nucleotide*	*Deoxynucleoside*	*Deoxynucleotide*
Purines				
Adenine (A)	Adenosine	Adenosine monophosphate (AMP)	Deoxyadenosine	Deoxyadenosine monophosphate (dAMP)
Guanine (G)	Guanosine	Guanosine monophosphate (GMP)	Deoxyguanosine	Deoxyguanosine monophosphate (dGMP)
Pyrimidines				
Cytosine (C)	Cytidine	Cytidine monophosphate (CMP)	Deoxycytidine	Deoxycytidine monophosphate (dCMP)
Uracil (U)	Uridine	Uridine monophosphate (UMP)	—	—
Thymine (T)	—	—	Thymidine	Thymidine monophosphate (dTMP)

The Structure of a Nucleotide



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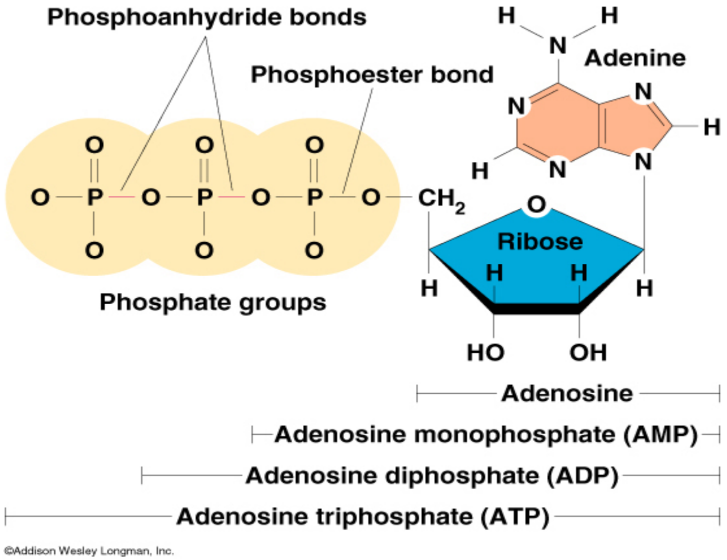
In RNA, a nucleotide consists of the five-carbon sugar D-ribose with an aromatic nitrogen-containing base attached to the 1 prime carbon and a phosphate group linked to the 5prime carbon by a phosphoester bond.

Carbon atoms in the sugar of a nucleotide are numbered from 1prime to 5 prime to distinguish them from those in the base, which are numbered without the prime.

In DNA, the hydroxyl group on the 2prime carbon is replaced by a hydrogen atom, so the sugar is D-deoxyribose.

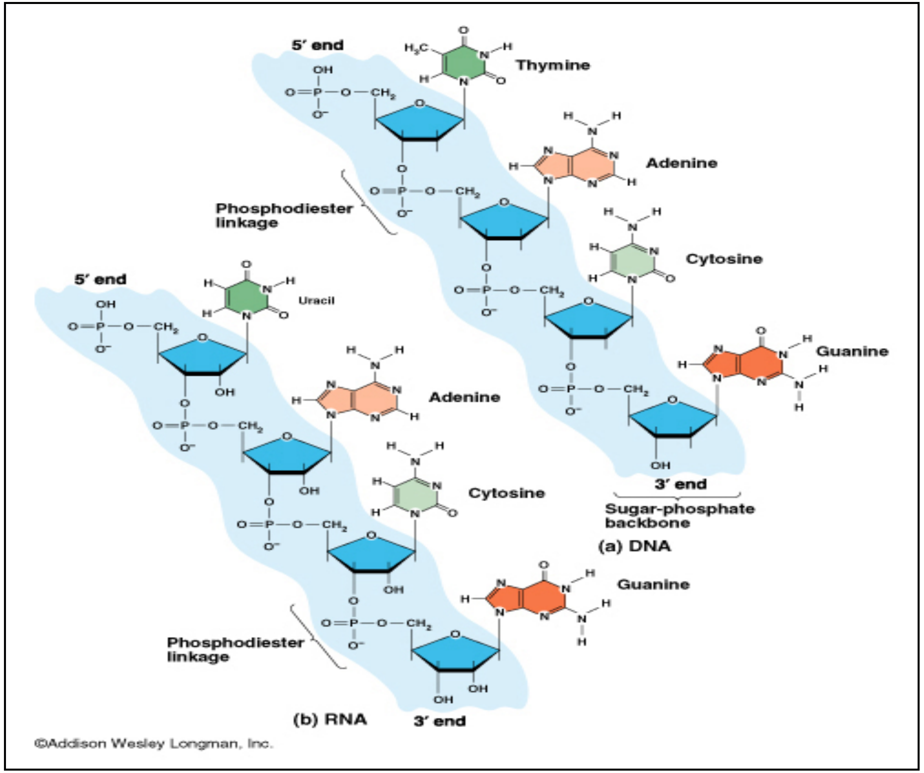
The bases in DNA are the purines adenine (A) and guanine (G) and the pyrimidines thymine (T) and cytosine (C). In RNA, thymine is replaced by the pyrimidine uracil (U).

The Phosphorylated Forms of Adenosine



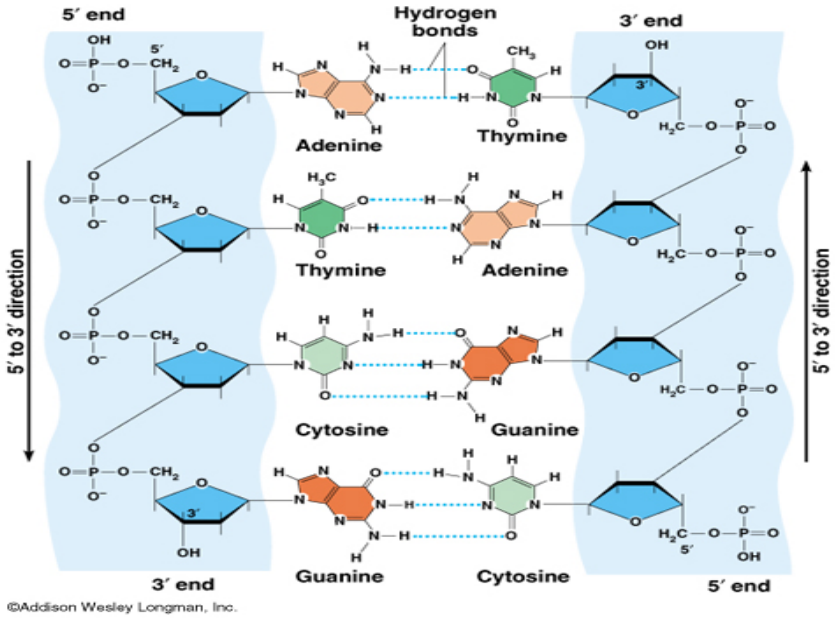
- Adenosine occurs as the free nucleoside, the monophosphate (AMP), the diphosphate (ADP), and the triphosphate (ATP).
- The bond that links the first phosphate to the ribose of adenosine is a low-energy phosphoester bond, whereas the bonds that link the second and third phosphate groups to the molecule are higher-energy phosphoanhydride bonds.
- (Recall that the terms "low-energy" and "higher-energy" refer not to the bonds themselves, which always require energy to break them, but to the amount of free, or useful, energy that is liberated upon the hydrolysis of the bond.
- As we will see in Chapter 13, the hydrolysis of a phosphoanhydride typically liberates 2-3 times as much free energy as does the hydrolysis of a phosphoester bond.)

The Structure of Nucleic Acids



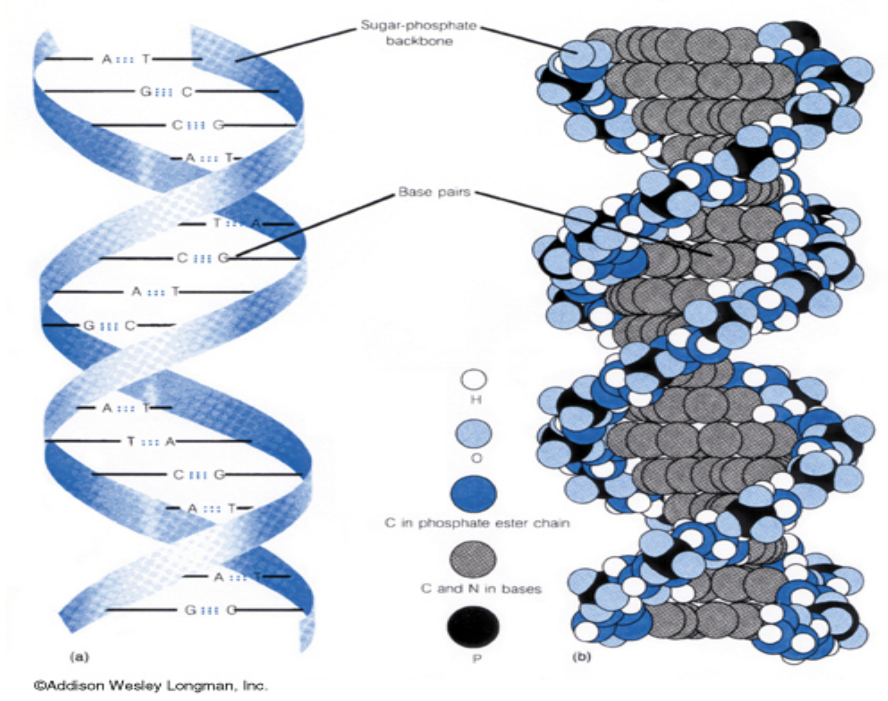
- Nucleic acids consist of linear chains of nucleotides, each containing a sugar, a phosphate, and a base. The sugar is (a) deoxyribose in DNA and (b) ribose in RNA.
- Successive nucleotides in the chain are joined together by 3 prime, 5 prime phosphodiester bonds.
- The resulting polynucleotide has an intrinsic directionality, with a 5 prime end and a 3 prime end.
- The backbone of the chain (blue) is an alternating sugar-phosphate sequence, from which the bases jut out.

Hydrogen Bonding in Nucleic Acid Structure



The hydrogen bonds (blue dots) between adenine and thymine and between cytosine and guanine account for the AT and CG base pairing of DNA. Notice that the AT pair is held together by two hydrogen bonds, whereas the CG pair has three hydrogen bonds. If one or both strands were RNA instead, the pairing partner for adenine would be uracil (U).

The Structure of Double-Stranded DNA



a) A schematic representation of the double-helical structure of DNA. The continuously turning strips represent the sugar-phosphate backbones of the molecule, while the horizontal bars represent paired bases of the two strands.

(b) A space-filling model of the DNA double helix, with color-coded H, O, C, N, and P atoms.

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