

## BCH-201:Nucleotides and Nucleic acids

Nucleotides and Nucleic acids are compounds containing Nitrogen bases (aromatic cyclic structures possessing nitrogen atoms) as part of their structure. **Nucleic acids** are linear, unbranched polymers of nucleotides.

Nucleotides consist of three parts:

1. A five-carbon sugar (hence a **pentose**). Two kinds are found:

- **Deoxyribose**, which has a hydrogen atom attached to its #2 carbon atom (designated 2'), and
- **Ribose**, which has a hydroxyl group there.

Deoxyribose-containing nucleotides, the **deoxyribonucleotides**, are the monomers of deoxyribonucleic acids (**DNA**).

Ribose-containing nucleotides, the **ribonucleotides**, are the monomers of ribonucleic acids (**RNA**).

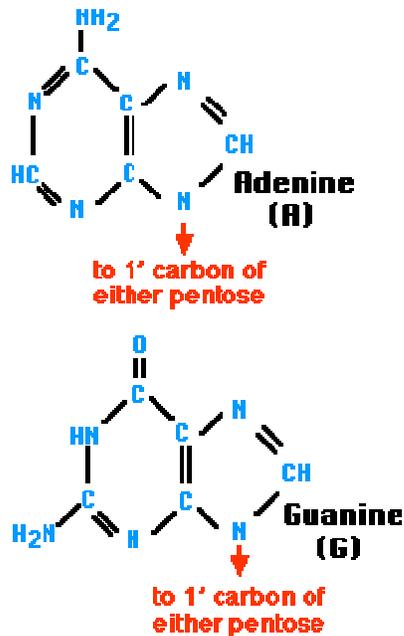
2. A nitrogen-containing ring structure called a **base**. The base is attached to the 1' carbon atom of the pentose. In **DNA**, four different bases are found:

1. two **purines**, called **adenine (A)** and **guanine (G)**
2. two **pyrimidines**, called **thymine (T)** and **cytosine (C)**

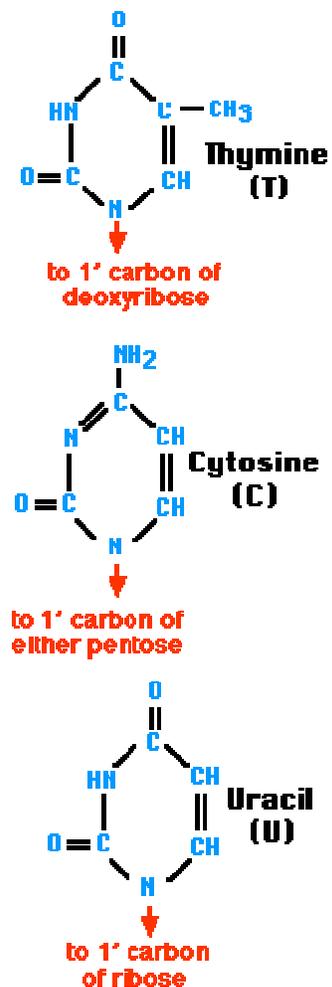
**RNA** contains:

1. The same purines, **adenine (A)** and **guanine (G)**.
2. RNA also uses the pyrimidine **cytosine (C)**, but instead of thymine, it uses the pyrimidine **uracil (U)**.

## The Purines



## The Pyrimidines



The combination of a base and a pentose is called a **nucleoside**.

The pentose sugar of the nucleotides is joined to the bases by  **$\beta$ -N-glycosidic bonds**. The  $\beta$ -N-glycosidic linkage is between  $N^9-C^1$  for purine bases and  $N^1-C^1$  for pyrimidine bases.

- One (as shown in the first figure), two, or three **phosphate** groups. These are attached to the 5' carbon atom of the pentose. The product in each case is called a **nucleotide**.

Both DNA and RNA are assembled from **nucleoside triphosphates**.

For **DNA**, these are **dATP, dGTP, dCTP, and dTTP**.

For **RNA**, these are **ATP, GTP, CTP, and UTP**.

In both cases, as each nucleotide is attached, the second and third phosphates are removed.

The nucleosides and their mono-, di-, and triphosphates					
	Base	Nucleoside	Nucleotides		
<b>DNA</b>	Adenine (A)	Deoxyadenosine	dAMP	dADP	dATP
	Guanine (G)	Deoxyguanosine	dGMP	dGDP	dGTP
	Cytosine (C)	Deoxycytidine	dCMP	dCDP	dCTP
	Thymine (T)	Deoxythymidine	dTMP	dTDP	dTTP
<b>RNA</b>	Adenine (A)	Adenosine	AMP	ADP	ATP
	Guanine (G)	Guanosine	GMP	GDP	GTP
	Cytosine (C)	Cytidine	CMP	CDP	CTP
	Uracil (U)	Uridine	UMP	UDP	UTP

### **Function of Nucleotides:**

- Participate in the majority of biochemical reactions
- ATP - - energy currency (also ADP, AMP)
- UDP-glucose - - glycogen biosynthesis
- CoA, NAD<sup>+</sup>, NADP<sup>+</sup>, FAD are derivatives of nucleotides
- cAMP - - regulation of cellular processes (signaling)
- Nucleoside triphosphates (NTP) - - RNA
- Deoxynucleoside triphosphates (dNTP) - - DNA

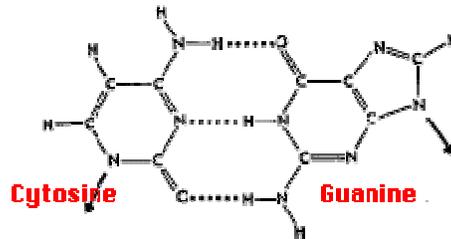
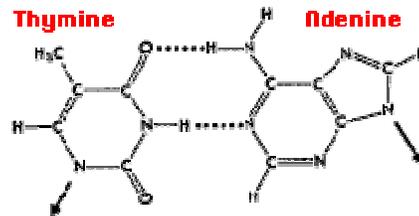
## NUCLEIC ACIDS.

**Nucleic acids are defined as biopolymers that are involved in the preservation/storage and transmission of genetic information from one generation to another.** The nucleotides that make up the nucleic acids are linked by phosphodiester bonds between 3' and 5' positions of the sugars. The linkage is called a **3'-5' phosphodiester bond**.

### Base Pairing

The rules of base pairing (or nucleotide pairing) are:

- **A** with **T**: the purine adenine (A) always pairs with the pyrimidine thymine (T)
- **C** with **G**: the pyrimidine **cytosine** (C) always pairs with the purine **guanine** (G)



This is consistent with there not being enough space (20 Å) for two purines to fit within the helix and too much space for two pyrimidines to get close enough to each other to form hydrogen bonds between them.

But why not A with C and G with T?

The answer: only with A & T and with C & G are there opportunities to establish **hydrogen bonds** (shown here as dotted lines) between them (two between A & T; three between C & G). These relationships are often called the rules of **Watson-Crick** base pairing, named after the two scientists who discovered their structural basis.

The rules of base pairing tell us that if we can "read" the sequence of nucleotides on one strand of DNA, we can immediately deduce the complementary sequence on the other strand.

The rules of base pairing explain the phenomenon that whatever the amount of adenine (A) in the DNA of an organism, the amount of thymine (T) is the same (called Chargaff's rule). Similarly, whatever the amount of guanine (G), the amount of cytosine (C) is the same.

## **RIBONUCLEIC ACID (RNA)**

Several types of RNA are synthesized in the nucleus of eukaryotic cells. Of particular interest are:

- **messenger RNA (mRNA)**. This will later be **translated** into a polypeptide.
- **ribosomal RNA (rRNA)**. This will be used in the building of **ribosomes**: machinery for synthesizing proteins by translating mRNA.
- **transfer RNA (tRNA)**. RNA molecules that carry amino acids to the growing polypeptide.
- **small nuclear RNA (snRNA)**. DNA transcription of the genes for mRNA, rRNA, and tRNA produces large precursor molecules ("**primary transcripts**") that must be processed within the nucleus to produce the functional molecules for export to the cytosol. Some of these processing steps are mediated by snRNAs.
- **small nucleolar RNA (snoRNA)**. These RNAs within the nucleolus have several functions (**described below**).
- **microRNA (miRNA)**. These are tiny (~22 nucleotides) RNA molecules that regulate the expression of messenger RNA (mRNA) molecules. [**Discussion**]
- **XIST RNA**. This inactivates one of the two X chromosomes in female vertebrates. [**Discussion**]

### **Messenger RNA (mRNA)**

Messenger RNA comes in a wide range of sizes reflecting the size of the polypeptide it encodes. Most cells produce small amounts of thousands of different mRNA molecules, each to be translated into a peptide needed by the cell.

Many mRNAs are common to most cells, encoding "housekeeping" proteins needed by all cells (e.g., the enzymes of glycolysis). Other mRNAs are specific for only certain types of cells. These encode proteins needed for the function of that particular cell (e.g., the mRNA for hemoglobin in the precursors of red blood cells).

### **Ribosomal RNA (rRNA)**

There are 4 kinds. In eukaryotes, these are

- **18S rRNA.** One of these molecules, along with some 30 different protein molecules, is used to make the **small subunit** of the ribosome.
- **28S, 5.8S, and 5S rRNA.** One each of these molecules, along with some 45 different proteins, are used to make the **large subunit** of the ribosome.

The S number given each type of rRNA reflects the rate at which the molecules sediment in the ultracentrifuge. The larger the number, the larger the molecule (but not proportionally).

The 28S, 18S, and 5.8S molecules are produced by the processing of a single primary transcript from a cluster of identical copies of a single gene. The 5S molecules are produced from a different cluster of identical genes.

### **Transfer RNA (tRNA)**

There are some 32 different kinds of tRNA in a typical eukaryotic cell.

- Each is the product of a separate gene.
- They are small (~4S), containing 73-93 nucleotides.
- Many of the bases in the chain pair with each other forming sections of double helix.
- The unpaired regions form 3 loops.
- Each kind of tRNA carries (at its 3' end) one of the 20 **amino acids** (thus most amino acids have more than one tRNA responsible for them).
- At one loop, 3 unpaired bases form an **anticodon**.

- Base pairing between the anticodon and the complementary codon on a mRNA molecule brings the correct amino acid into the growing polypeptide chain.

### **Small Nuclear RNA (snRNA)**

Approximately a dozen different genes for snRNAs, each present in multiple copies, have been identified. The snRNAs have various roles in the processing of the other classes of RNA. For example, several snRNAs are part of the spliceosomes that participate in converting pre-mRNA into mRNA by excising the introns and splicing the exons.

### **Small Nucleolar RNA (snoRNA)**

As the name suggests, these small (60–300 nucleotides) RNAs are found in the nucleolus where they are responsible for several functions:

- Some participate in making ribosomes by helping to cut up the large RNA precursor of the 28S, 18S, and 5.8S molecules.
- Others chemically modify many of the nucleotides in rRNA, tRNA, and snRNA molecules, e.g., by adding methyl groups to ribose.
- Some have been implicated in the alternative splicing of pre-mRNA to different forms of mature mRNA.
- One snoRNA serves as the template for the synthesis of telomeres.

In vertebrates, the snoRNAs are made from **introns** removed during RNA processing.

### **Noncoding RNA**

Only messenger RNA encodes polypeptides. All the other classes of RNA, including types not mentioned here, are thus called noncoding RNA. Much remains to be learned about the function(s) of some of them. But, taken together, noncoding RNAs probably account for two-thirds of the transcription going on in the nucleus.

## **HYDROLYSIS OF NUCLEIC ACIDS.**

Hydrolysis of Nucleic acids by selective methods can be achieved chemically or enzymatically.

### **Chemical method of hydrolysis:**

#### **ACID HYDROLYSIS:**

RNA is relatively resistant to the effects of dilute acid, but gentle treatment of DNA with 1Mm HCl leads to hydrolysis of purine glycosidic bonds and the loss of purine bases from the DNA without affecting the pyrimidine deoxyribose bonds or the phosphodiester bonds of the backbone. At other chemical conditions, selective removal of pyrimidine bases occurs. In most cases, both Nucleic acids can be hydrolysed to their constituent bases by the treatment with 72% perchloric acid ( $\text{HClO}_4$ ) for 1 hour. The resulting nucleic acid derivative which is devoid of purine bases is called **APURINIC ACID**; while that devoid of pyrimidine bases is called **APYRIMIDINIC ACID**.

#### **ALKALI HYDROLYSIS:**

DNA is not susceptible to alkaline hydrolysis. On the other hand, RNA is alkali labile and is readily hydrolyzed by dilute sodium hydroxide.

### **Enzymatic hydrolysis of Nucleic acids:**

Enzymes that hydrolyse nucleic acids are called **NUCLEASES**.

Some nucleases can hydrolyse linkages between 2 adjacent nucleotides at internal positions in the DNA or RNA strand and proceed stepwise from that end. Such nucleases are called **ENDONUCLEASES**. Another class of nucleases can hydrolyse only the terminal nucleotide linkage, some at the 5' and others at the 3' end; these are called **EXONUCLEASES**.

**DNases (deoxyribonucleases) acts only on DNA**

**RNases(ribonucleases) are specific for RNA.**

