FUNDAMENTALS OF BIOCHEMISTRY

Topic: Nucleotides And Nucleic Acids

BY

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"A segment of a **DNA** molecule that contains the information required for the synthesis of a functional biological product, whether protein or RNA, is referred to as a gene."

References
1. Lehninger PRINCIPLES OF BIOCHEMISTRY Fourth Edition: David L. Nelson and Michael M. Cox
2. BIOCHEMISTRY; DONALD VOET and JUDITH G. VOET

- **Nucleotides** have three characteristic components: (1) a nitrogenous (nitrogen-containing) base, (2) a pentose, and (3) a phosphate.
- **Nucleoside** have two characteristic components: (1) a nitrogenous base, (2) a pentose.
- **The nitrogenous bases** are derivatives of two parent compounds, pyrimidine and purine.
- The bases and pentoses of the common nucleotides are heterocyclic compounds.
- Nucleotides are phosphate esters of a five-carbon sugar in which a nitrogenous base is covalently linked to C1 of the sugar residue.

References
1. Lehninger PRINCIPLES OF BIOCHEMISTRY Fourth Edition: David L. Nelson and Michael M. Cox
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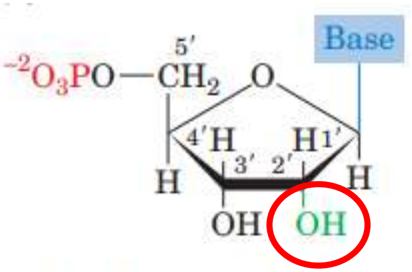
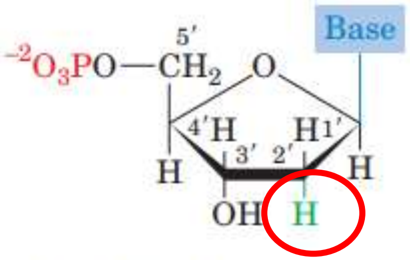
- In ribonucleotides, the monomeric units of RNA, the pentose is D-ribose, whereas in deoxyribonucleotides

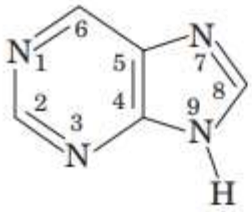


Ribonucleotides



Deoxyribonucleotides

- Major purine components of nucleic acids are adenine and guanine residues.
- Major pyrimidine residues are those of cytosine, uracil, and thymine.



Purine

Pyrimidine

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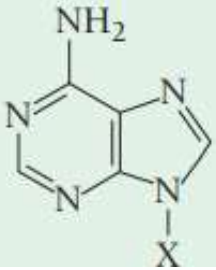
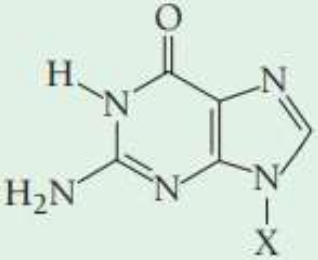
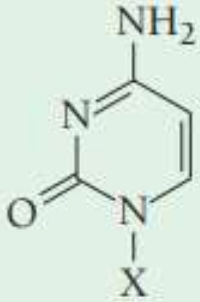


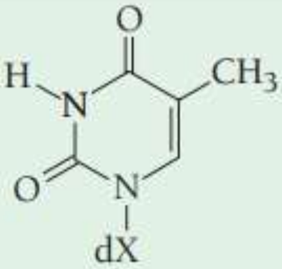
Adenine
Ade
A



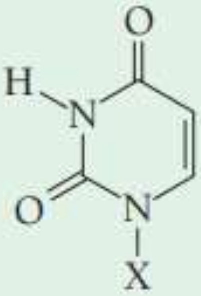
Guanine
Gua
G



Cytosine
Cyt
C



Thymine
Thy
T



Uracil
Ura
U

References

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- The chemical structures of the nucleic acids were elucidated by the early 1950s largely through the efforts of Phoebus Levene, followed by the work of Alexander Todd.
- Nucleic acids are, with few exceptions, linear polymers of nucleotides whose phosphate groups bridge the 3’ and 5’ positions of successive sugar residues.
- The phosphates of these polynucleotides, the phosphodiester groups, are acidic, so that, at physiological pH’s, nucleic acids are polyanions.
- Polynucleotides have directionality, that is, each has a 3’ end (the end whose C3’ atom is not linked to a neighboring nucleotide) and a 5’ end (the end whose C5’ atom is not linked to a neighboring nucleotide)

References
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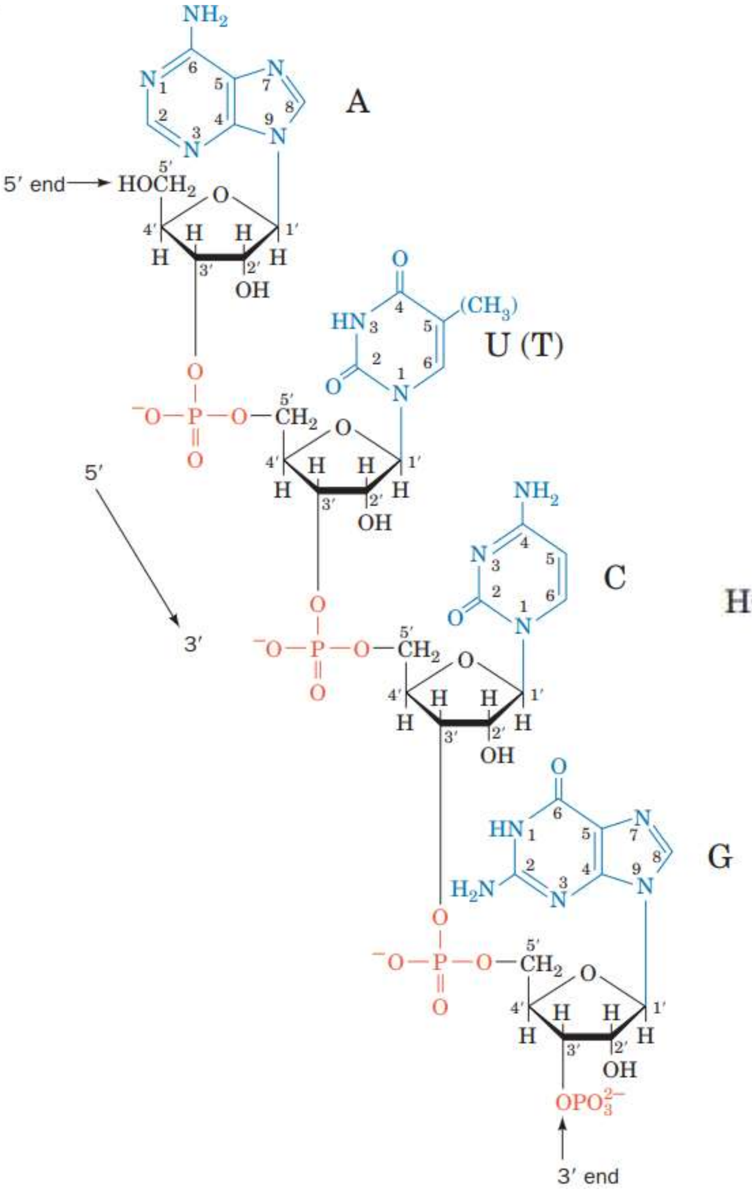

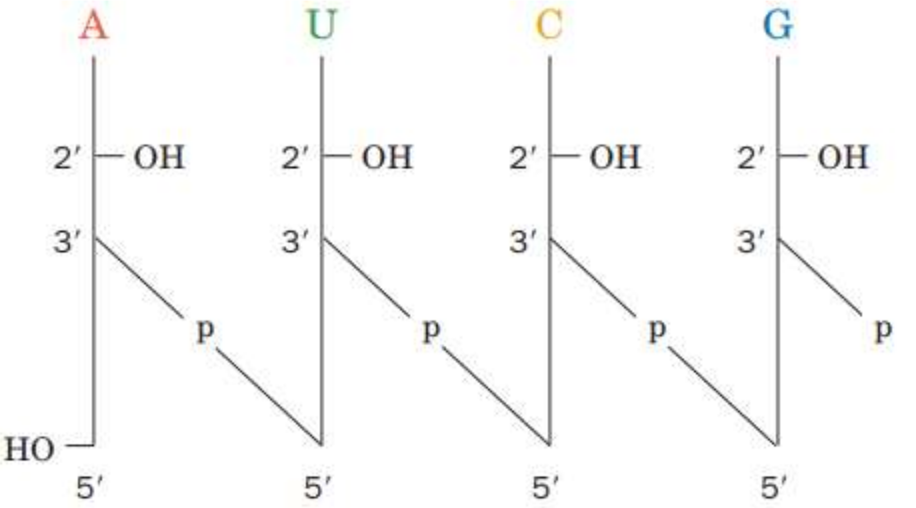

Chemical structure of a nucleic acid. (a) The tetranucleotide adenyl-3’,5’-uridyl-3’,5’-cytidyl 3’,5’-guanylyl-3’-phosphate. The sugar atom numbers are primed to distinguish them from the atomic positions of the bases. By convention, a polynucleotide sequence is written with its 5’ end at the left and its 3’ end to the right.

Thus, reading left to right, the phosphodiester bond links neighboring ribose residues in the 5’ & 3’ direction.

The above sequence may be abbreviated ApUpCpGp or just AUCGp.

References
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Chargaff's Rules

- DNA's Base Composition Is Governed by Chargaff's Rules DNA has equal numbers of adenine and thymine residues (A & T) and equal numbers of guanine and cytosine residues (G & C).
- These relationships, were discovered in the late 1940s by Erwin Chargaff, who first devised reliable quantitative methods for the separation and analysis of DNA hydrolysates.
- DNA's base composition varies widely from 25% to 75% G + C among different organisms.
- In mammals G + C ranges from 39% to 46%.
- RNA, which usually occurs as single-stranded molecules, has no apparent constraints on its base composition.

References
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Chargaff's Rules

1. The base composition of DNA generally varies from one species to another.

2. DNA specimens isolated from different tissues of the same species have the same base composition.

3. The base composition of DNA in a given species does not change with an organism's age, nutritional state, or changing environment.

4. In all cellular DNAs, regardless of the species, the number of adenosine residues is equal to the number of thymidine residues (that is, A = T), and the number of guanosine residues is equal to the number of cytidine residues (G = C). From these relationships it follows that the sum of the purine residues equals the sum of the pyrimidine residues; that is, A + G = T + C.

References
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The Watson–Crick Structure of DNA

- In 1953 James Watson and Francis Crick postulated a three-dimensional model of DNA structure
- It consists of two helical DNA chains wound around the same axis to form a right-handed double helix
- The hydrophilic backbones of alternating deoxyribose and phosphate groups are on the outside of the double helix, facing the surrounding water.
- The furanose ring of each deoxyribose is in the C-2’ endo conformation
- The purine and pyrimidine bases of both strands are stacked inside the double helix, with their hydrophobic and nearly planar ring structures very close together and perpendicular to the long axis.
- The offset pairing of the two strands creates a **major groove** and **minor groove** on the surface of the duplex
- Each nucleotide base of one strand is paired in the same plane with a base of the other strand
- Watson and Crick found that the hydrogen bonded base pairs, G with C and A with T, are those that fit best within the structure, providing a rationale for Chargaff’s rule that in any DNA, G = C and A = T

References
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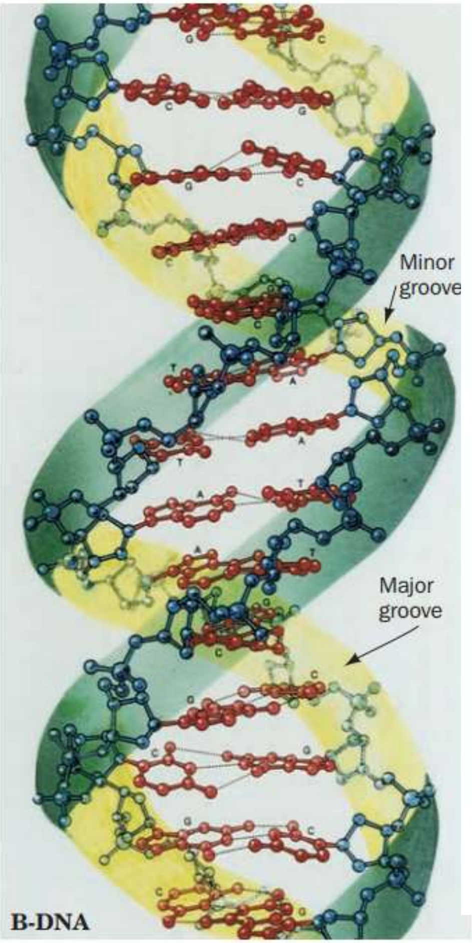
The Watson–Crick Structure of DNA



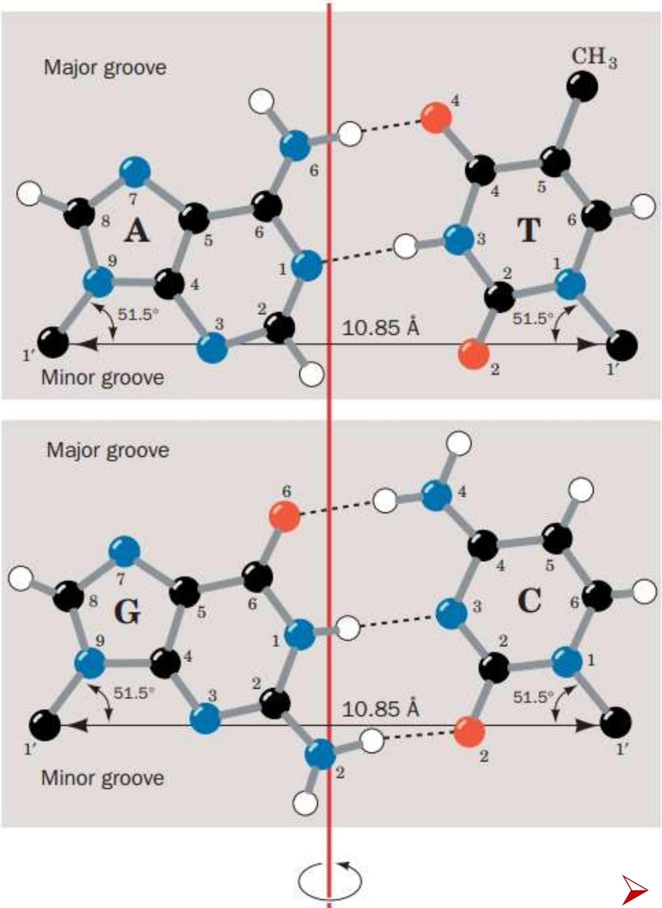


Fig: Watson–Crick base pairs

Fig: Three-dimensional structure of B-DNA

- Three hydrogen bonds can form between G and C, symbolized G ≡ C, but only two can form between A and T, symbolized A=T.
- This is one reason for the finding that separation of paired DNA strands is more difficult the higher the ratio of GC to AT base pairs.

➢ **The DNA double helix, or duplex, is held together by two forces, hydrogen bonding between complementary base pairs and base-stacking**

References
1. Lehninger PRINCIPLES OF BIOCHEMISTRY Fourth Edition: David L. Nelson and Michael M. Cox
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The Watson–Crick Structure of DNA: B-DNA

- B-DNA is regarded as the native (biologically functional) form of DNA because, for example, its X-ray pattern resembles that of the DNA in intact sperm head

1. It consists of two polynucleotide strands that wind about a common axis with a right-handed twist to form an 20-Å-diameter double helix.
2. The two strands are **antiparallel** (run in opposite directions) and wrap around each other such that they cannot be separated without unwinding the helix.
   The bases occupy the core of the helix and the sugar–phosphate chains are coiled about its periphery, thereby minimizing the repulsions between charged phosphate groups.
3. The planes of the bases are nearly perpendicular to the helix axis. Each base is hydrogen bonded to a base on the opposite strand to form a planar base pair.
4. Hydrogen bonding interactions, also known as complementary base pairing, result in the specific association of the two chains of the double helix.
5. The “ideal” B-DNA helix has 10 base pairs (bp) per turn (a helical twist of 36° per bp) and, since the aromatic bases have van der Waals thicknesses of 3.4 Å and are partially stacked on each other the helix has a pitch (rise per turn) of 34 Å.

References
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DNA Can Occur in Different Three-Dimensional Forms

DNA is a flexible molecule because of the rotation around bonds in the sugar–phosphate (phosphodeoxyribose) backbone, and bending, stretching, and melting of the strands due to thermal fluctuation .

DNA structural variations generally do not affect the key properties of DNA defined by Watson and Crick: strand complementarity, antiparallel strands, and the requirement for AT and GC base pairs.

Structural variation in DNA reflects three things: the different possible conformations of the deoxyribose, rotation about the contiguous bonds that make up the phosphodeoxyribose backbone, and free rotation about the C-1’–*N*-glycosyl bond Because of steric constraints, purines in purine nucleotides are restricted to two stable conformations with respect to deoxyribose, called syn and anti .

Pyrimidines are generally restricted to the anti conformation because of steric interference between the sugar and the carbonyl oxygen at C-2 of the pyrimidine.

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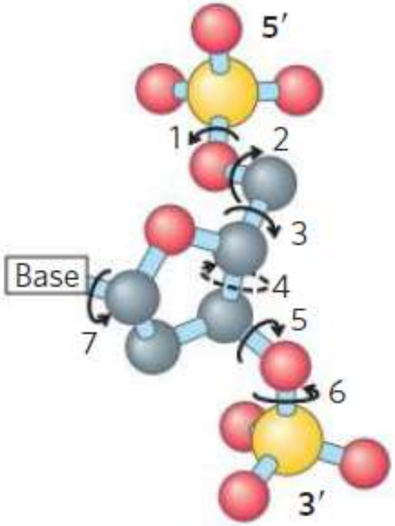
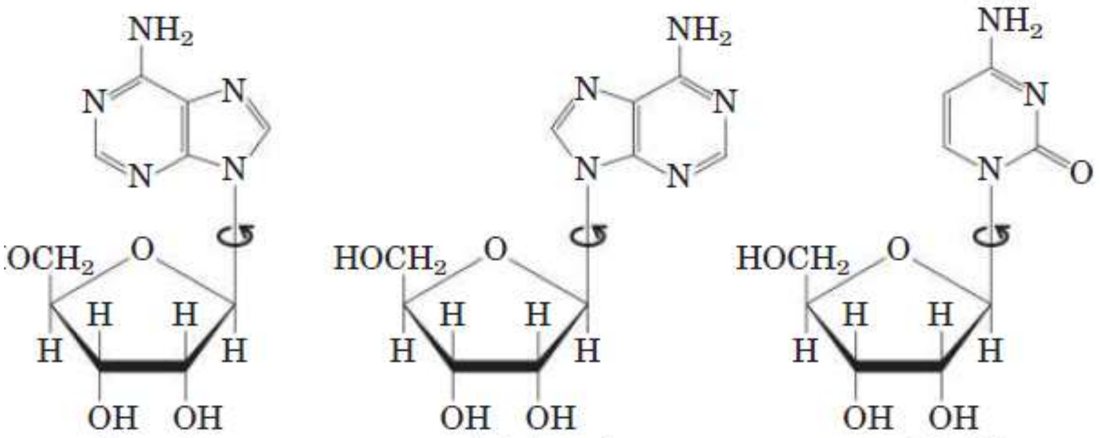


(a)



syn-Adenosine *anti*-Adenosine *anti*-Cytidine

(b)

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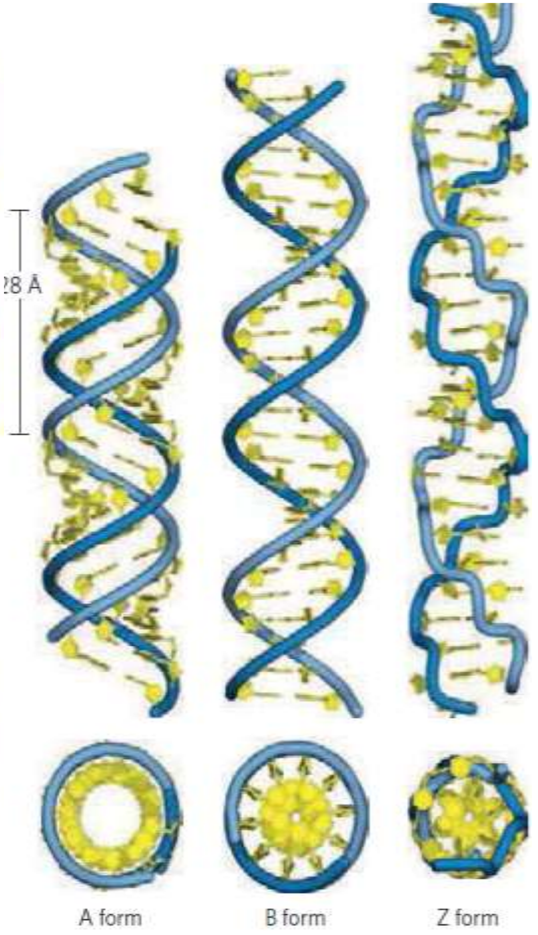

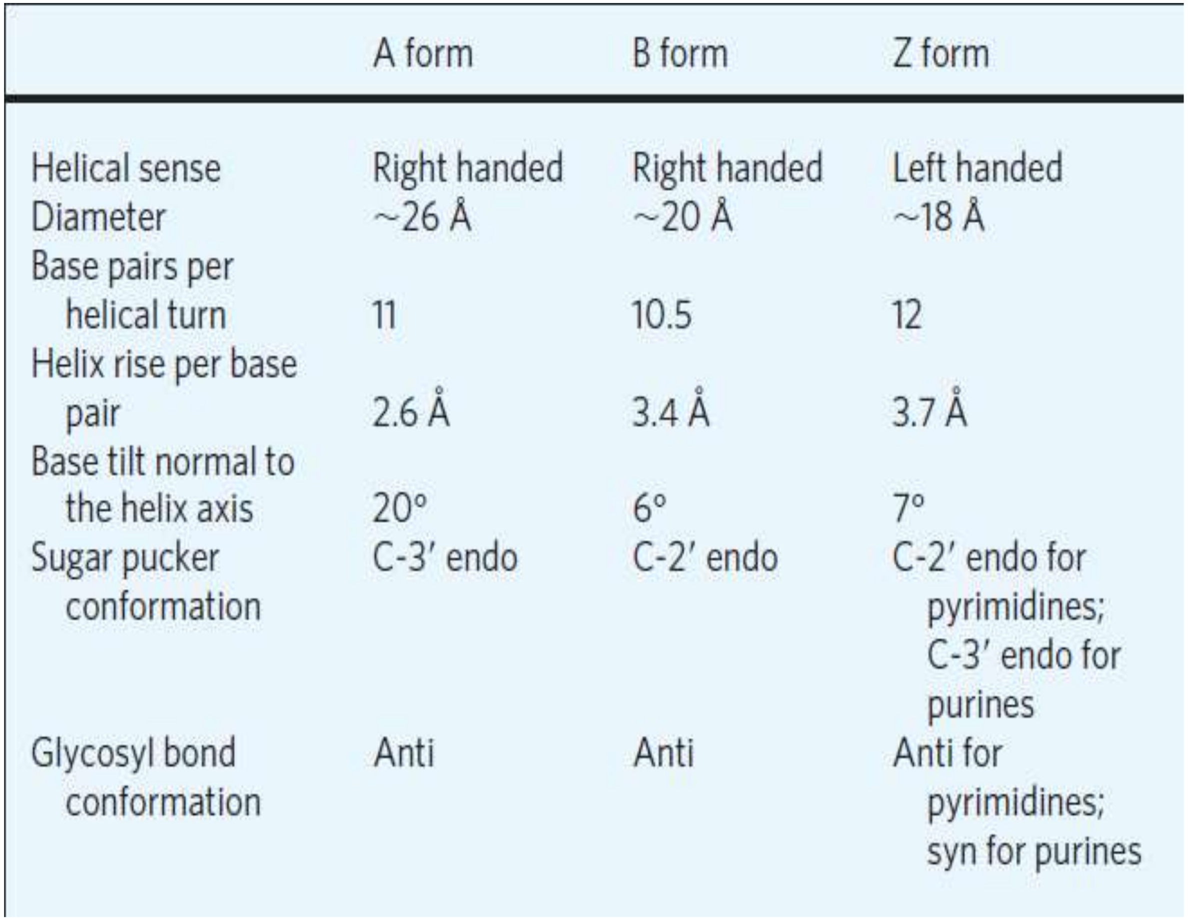

	A form	B form	Z form
Helical sense	Right handed	Right handed	Left handed
Diameter	~26 Å	~20 Å	~18 Å
Base pairs per helical turn	11	10.5	12
Helix rise per base pair	2.6 Å	3.4 Å	3.7 Å
Base tilt normal to the helix axis	20°	6°	7°
Sugar pucker conformation	C-3′ endo	C-2′ endo	C-2′ endo for pyrimidines; C-3′ endo for purines
Glycosyl bond conformation	Anti	Anti	Anti for pyrimidines; syn for purines

Fig: Comparison of A, B, and Z forms of DNA.

Riboses and bases are shown in yellow

Phosphodiester backbone is represented as blue rope.

References
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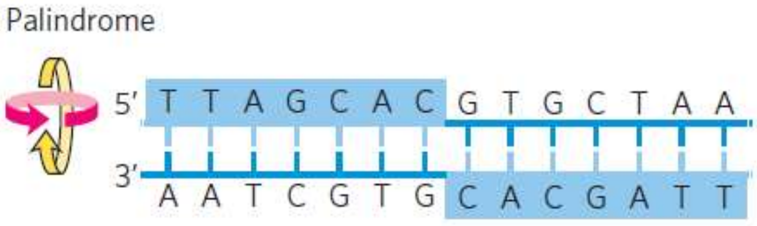
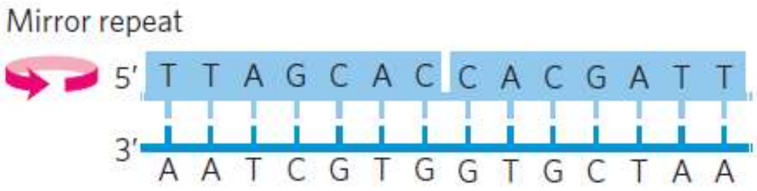
Unusual Structures of DNA Sequences

Palindromes are sequences of double-stranded nucleic acids with twofold symmetry. In order to superimpose one repeat (shaded sequence) on the other, it must be rotated 180 ^{0} about the horizontal axis then 180 ^{0} about the vertical axis, as shown by the arrows.

A mirror repeat, on the other hand, has a symmetric sequence within each strand. Superimposing one repeat on the other requires only a single 180 ^{0} rotation about the vertical axis.



Palindromes



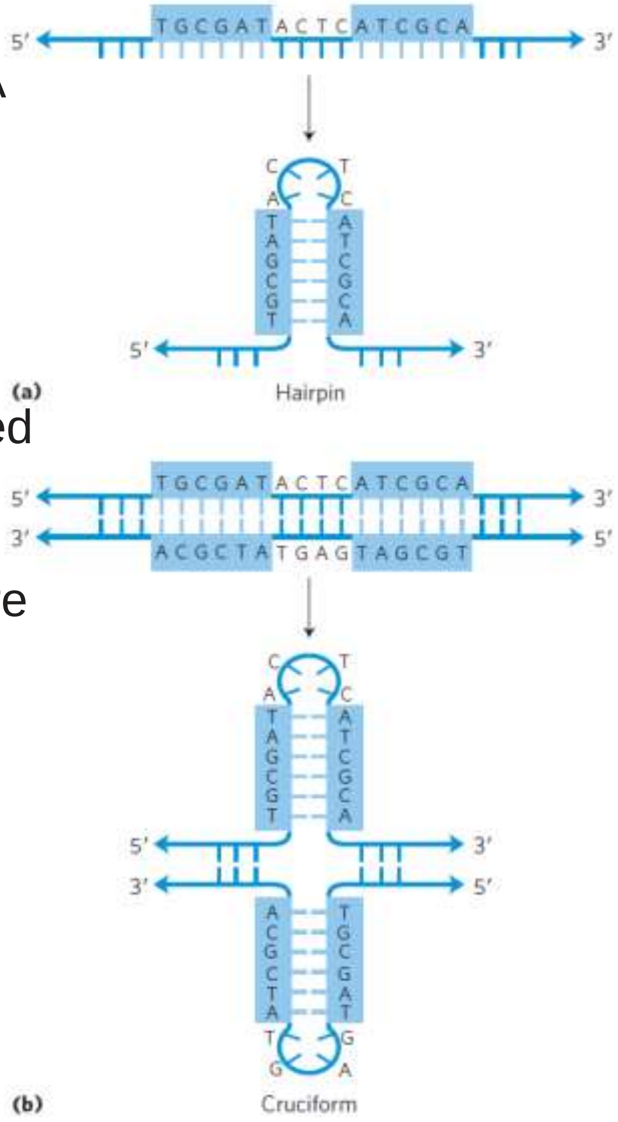
$C\equiv G\cdot C^{+}$

Unusual Structures of DNA Sequences

Hairpins and cruciforms. Palindromic DNA (or RNA) sequences can form alternative structures with intrastrand base pairing.

(a) When only a single DNA (or RNA) strand is involved, the structure is called a hairpin.

(b) When both strands of a duplex DNA are involved, it is called a cruciform. Blue shading highlights asymmetric sequences that can pair with the complementary sequence either in the same strand or in the complementary strand.



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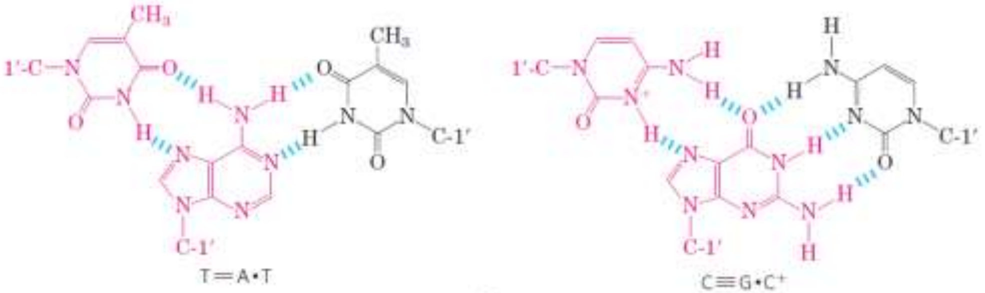
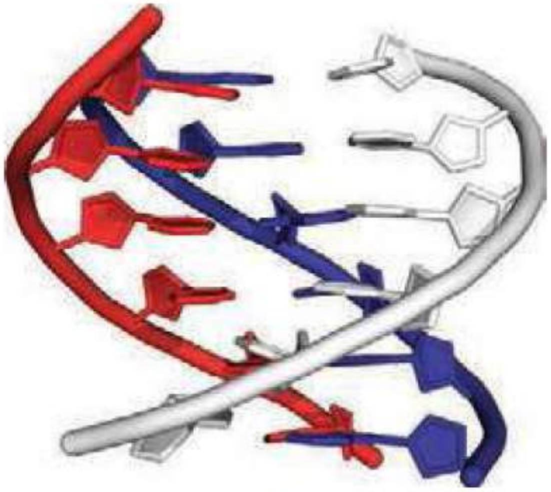
Hoogsteen triplex DNAs

Several unusual DNA structures involve three or even four DNA strands. Nucleotides participating in a Watson-Crick base pair can form additional hydrogen bonds, particularly with functional groups arrayed in the major groove. For example, a cytidine residue (if protonated) can pair with the guanosine residue of a GC nucleotide pair ; a thymidine can pair with the adenosine of an A T pair.

the non-Watson-Crick pairing is called **Hoogsteen pairing**, after Karst Hoogsteen, who in 1963 first recognized the potential for these unusual pairings.

Hoogsteen pairing allows the formation of **triplex DNAs**. The triplexes are most stable at low pH because the CG.C triplet requires a protonated cytosine.





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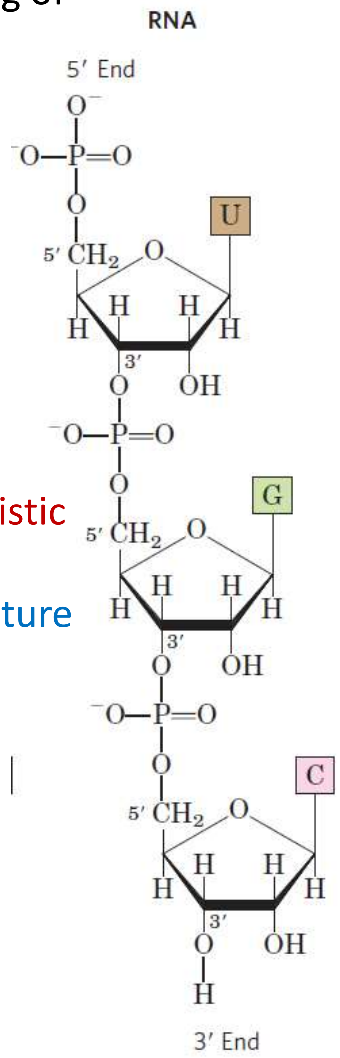
RIBONUCLEIC ACID

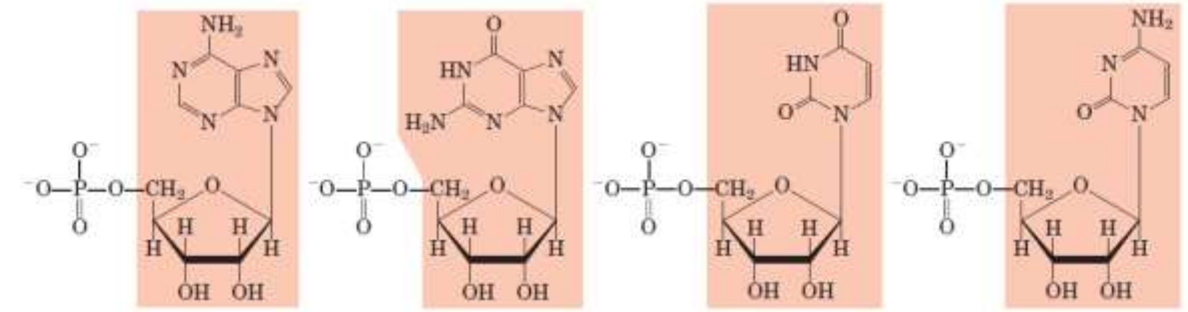
Ribonucleic acid (RNA), like DNA, is a long, unbranched macromolecule consisting of nucleotides joined by 3’ to 5’ phosphodiester bonds.

The number of ribonucleotides in RNA ranges from 75 to many thousands.

Differences with DNA

- The sugar moiety in RNA, to which the phosphate and the nitrogen bases are attached, is *ribose* rather than 2’- deoxyribose of DNA.
- Ribose contains a 2’-hydroxyl group not present in deoxyribose.
- RNA contains the pyrimidine *uracil* (U) in place of thymine which is characteristic of DNA molecule.
- The native RNA is *single-stranded* rather than a double-stranded helical structure characteristic of DNA.





Nucleotide:	Adenylate (adenosine 5′-monophosphate)	Guanylate (guanosine 5′-monophosphate)	Uridylate (uridine 5′-monophosphate)	Cytidylate (cytidine 5′-monophosphate)
Symbols:	A, AMP	G, GMP	U, UMP	C, CMP
Nucleoside:	Adenosine	Guanosine	Uridine	Cytidine

(b) Ribonucleotides

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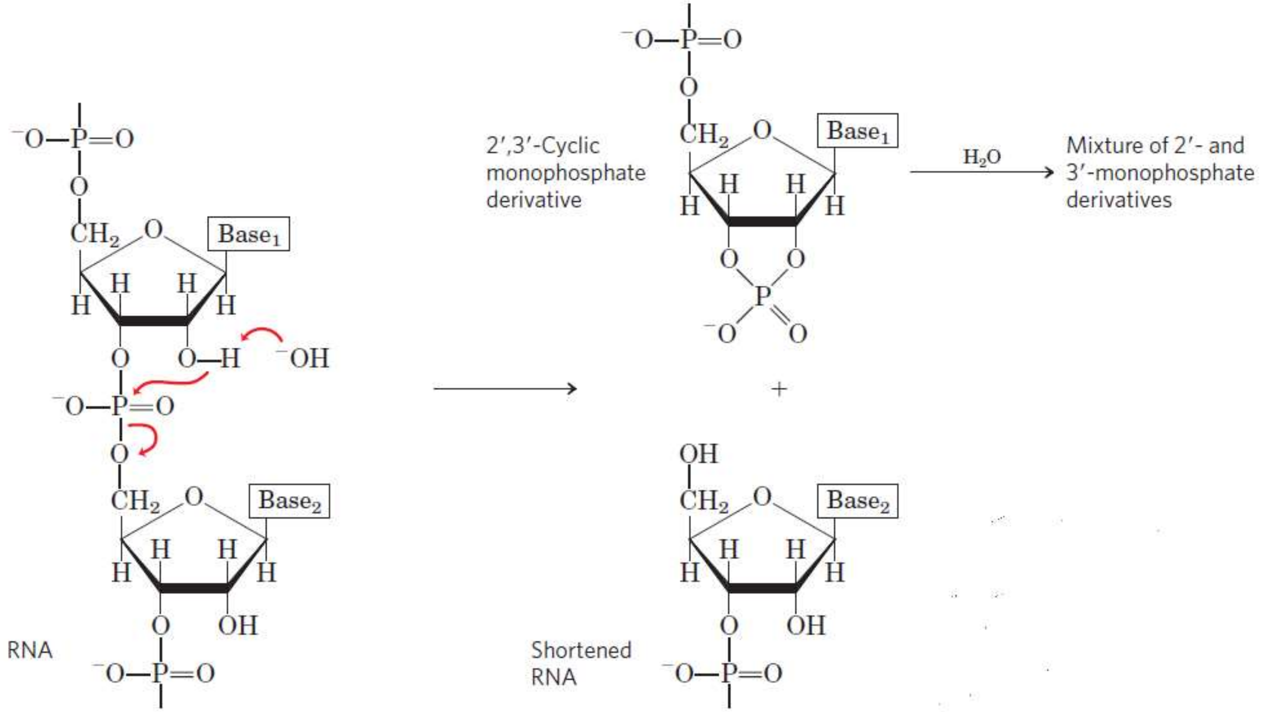
- RNA can be hydrolyzed by weak alkali to 2′, 3′- cyclic diesters of the mononucleotides *via* an intermediate compound called 2′, 3′, 5′-triester.



- Hydrolysis of RNA under alkaline conditions
- The 2’ hydroxyl acts as a nucleophile in an intramolecular displacement.
- The 2’,3’-cyclic monophosphate derivative is further hydrolyzed to a mixture of 2’- and 3’ monophosphates.
- *RNA is alkali-labile whereas DNA is alkali-stable*.
- DNA, which lacks 2’ hydroxyls, is stable under similar conditions.

References
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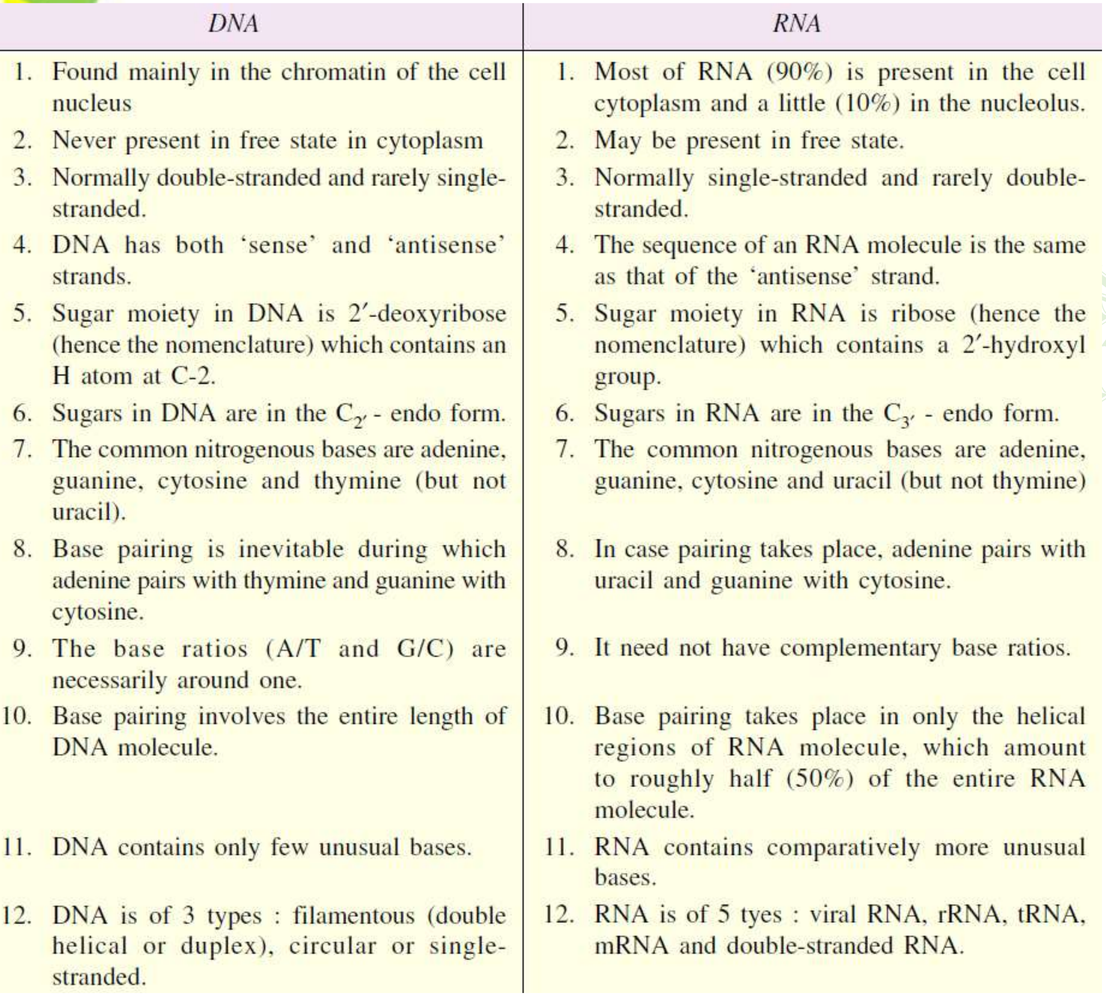
- Since the RNA molecule is single-stranded and complementary to only one of the two strands of a gene, *it need not have complementary base ratios*. In other words, its adenine content does not necessarily equal its uracil content, nor does its guanine content necessarily equal its cytosine content



DNA	*RNA*
1. Found mainly in the chromatin of the cell nucleus	1. Most of RNA (90%) is present in the cell cytoplasm and a little (10%) in the nucleolus.
2. Never present in free state in cytoplasm	2. May be present in free state.
3. Normally double-stranded and rarely single-stranded.	3. Normally single-stranded and rarely double-stranded.
4. DNA has both 'sense' and 'antisense' strands.	4. The sequence of an RNA molecule is the same as that of the 'antisense' strand.
5. Sugar moiety in DNA is 2′-deoxyribose (hence the nomenclature) which contains an H atom at C-2.	5. Sugar moiety in RNA is ribose (hence the nomenclature) which contains a 2′-hydroxyl group.
6. Sugars in DNA are in the $C_{2'}$ - endo form.	6. Sugars in RNA are in the $C_{3'}$ - endo form.
7. The common nitrogenous bases are adenine, guanine, cytosine and thymine (but not uracil).	7. The common nitrogenous bases are adenine, guanine, cytosine and uracil (but not thymine)
8. Base pairing is inevitable during which adenine pairs with thymine and guanine with cytosine.	8. In case pairing takes place, adenine pairs with uracil and guanine with cytosine.
9. The base ratios (A/T and G/C) are necessarily around one.	9. It need not have complementary base ratios.
10. Base pairing involves the entire length of DNA molecule.	10. Base pairing takes place in only the helical regions of RNA molecule, which amount to roughly half (50%) of the entire RNA molecule.
11. DNA contains only few unusual bases.	11. RNA contains comparatively more unusual bases.
12. DNA is of 3 types : filamentous (double helical or duplex), circular or single-stranded.	12. RNA is of 5 tyes : viral RNA, rRNA, tRNA, mRNA and double-stranded RNA.

References
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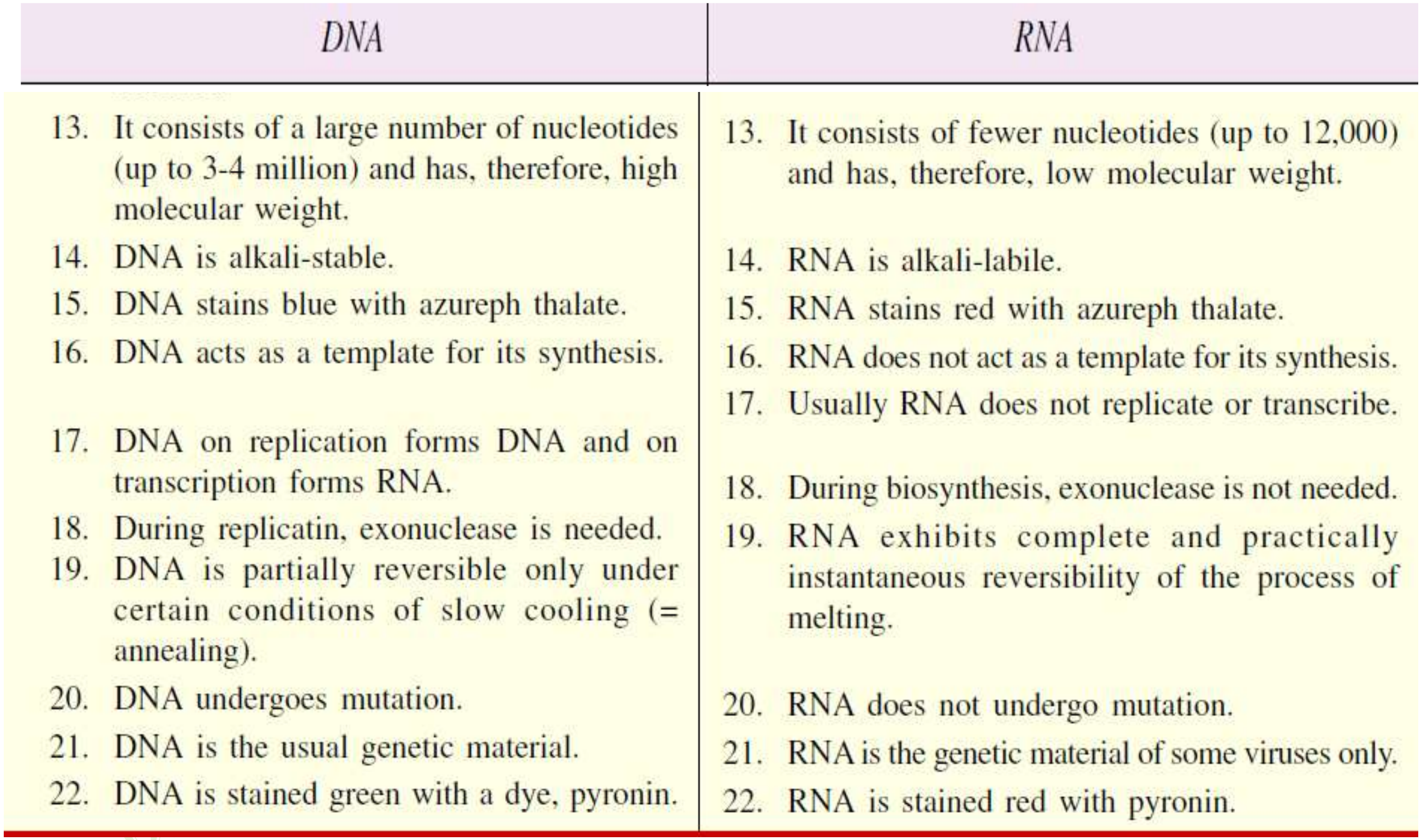

DNA	*RNA*
13. It consists of a large number of nucleotides (up to 3-4 million) and has, therefore, high molecular weight.	13. It consists of fewer nucleotides (up to 12,000) and has, therefore, low molecular weight.
14. DNA is alkali-stable.	14. RNA is alkali-labile.
15. DNA stains blue with azureph thalate.	15. RNA stains red with azureph thalate.
16. DNA acts as a template for its synthesis.	16. RNA does not act as a template for its synthesis.
17. DNA on replication forms DNA and on transcription forms RNA.	17. Usually RNA does not replicate or transcribe.
18. During replicatin, exonuclease is needed.	18. During biosynthesis, exonuclease is not needed.
19. DNA is partially reversible only under certain conditions of slow cooling (= annealing).	19. RNA exhibits complete and practically instantaneous reversibility of the process of melting.
20. DNA undergoes mutation.	20. RNA does not undergo mutation.
21. DNA is the usual genetic material.	21. RNA is the genetic material of some viruses only.
22. DNA is stained green with a dye, pyronin.	22. RNA is stained red with pyronin.

References
1. **Lehninger PRINCIPLES OF BIOCHEMISTRY Fourth Edition: David L. Nelson and Michael M. Cox**
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All nucleotide bases absorb UV light, and nucleic acids are characterized by a strong absorption at wavelengths near 260 nm *Increase in absorption of ultraviolet light* (= *Hyperchromic effect*). As a result of resonance, all of the bases in nucleic acids absorb ultraviolet light. And all nucleic acids are characterized by a maximum absorption of UV light at wavelengths near 260 nm. When the native DNA (which has base pairs stacked similar to a stack of coins) is denatured, there occurs a marked increase in optical absorbancy of UV light by pyrimidine and purine bases, an effect called **hyperchromicity** or **hyperchromism** whch is due to unstacking of the base pairs. This change reflects a decrease in hydrogen-bonding. Hyperchromicity is observed not only with DNA but with other nucleic acids and with many synthetic polynucleotides which also possess a hydrogen-bonded structure.

References
1. **Lehninger PRINCIPLES OF BIOCHEMISTRY Fourth Edition: David L. Nelson and Michael M. Cox**
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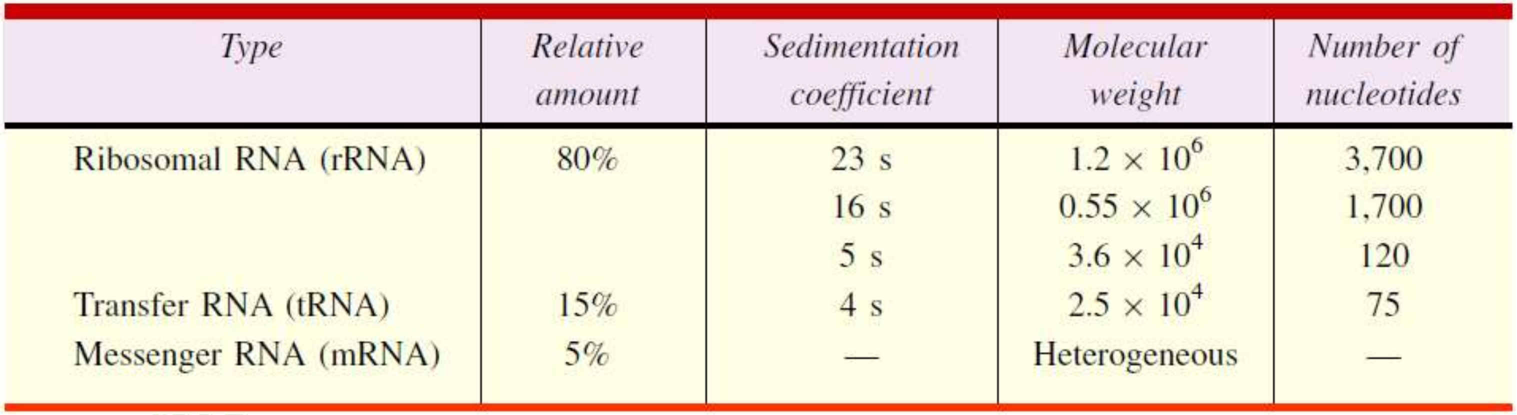
Types of RNA

In all procaryotic and eucaryotic organisms, 3 general types of RNAs are found : *ribosomal*, *transfer* and *messenger RNAs*. Each of these polymeric forms serves as extremely important informational links between DNA, the master carrier of information and proteins.

The 3 types of RNA molecules differ from each other by size, function and general stability.

RNA molecules in Escherichia coli

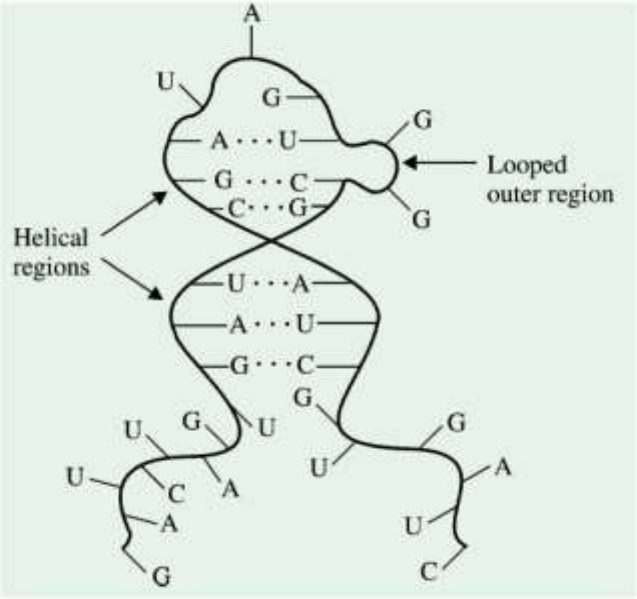


Type	*Relative amount*	*Sedimentation coefficient*	*Molecular weight*	*Number of nucleotides*
Ribosomal RNA (rRNA)	80%	23 s	1.2×10^6	3,700
		16 s	0.55×10^6	1,700
		5 s	3.6×10^4	120
Transfer RNA (tRNA)	15%	4 s	2.5×10^4	75
Messenger RNA (mRNA)	5%	—	Heterogeneous	—

References
1. Lehninger PRINCIPLES OF BIOCHEMISTRY Fourth Edition: David L. Nelson and Michael M. Cox
2. BIOCHEMISTRY; DONALD VOET and JUDITH G. VOET

Ribosomal RNA (rRNA) or Insoluble RNA

- *It is the most stable form of RNA* and is found in ribosomes.
- In the bacterium, *Escherichia coli*, there are 3 kinds of
- RNA called 23 s, 16 s, and 5 s RNA because of sedimentation behaviour.
- One molecule of each of these 3 types of rRNA is present in each ribosome.
- *Ribosomal RNA is most abundant of all types of RNAs* and makes up about 80% of the total RNA of a cell.
- Ribosomal RNA represents about 40-60% of the total weight of ribosomes.
- rRNA are necessary for ribosomal assembl and seem to provide a specific sequence t which the messenger RNA moelcule can bind in order to be translated.



Ribosomes	*rRNA*
Procaryotic ribosomes 30 s	16 s,
50 s	23 s, 5 s
Eucaryotic ribosomes	
40 s	18 s
60 s	5 s, 28 s

References
1. **Lehninger PRINCIPLES OF BIOCHEMISTRY Fourth Edition: David L. Nelson and Michael M. Cox**
2. **BIOCHEMISTRY; DONALD VOET and JUDITH G. VOET**

Transfer RNA (tRNA) or Soluble RNA (sRNA)

Transfer RNA is the smallest polymeric form of RNA.

the tRNA is about 15% of the total RNA of the cell.

The tRNA remains dissolved in solution after centrifuging a broken cell suspension at 100,000 X gravity for several hours

The tRNA molecules serve a number of functions, the most important of which is to act as specific carriers of activated amino acids to specific sites on the protein- synthesizing templates.

The function of tRNA is to bind the specific amino acids

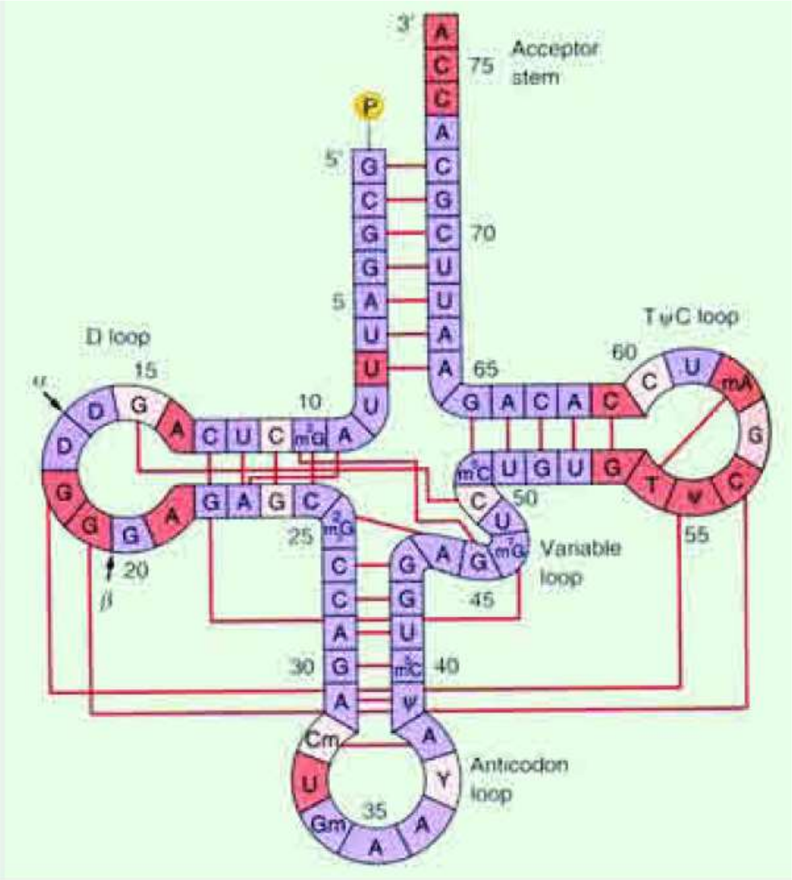
In a bacterial cell, there are more than 70 tRNAs and in eukaryotic cells, this number is even greater, because there are tRNAs specific

Holley first suggested the '*cloverleaf*' model which is based on a secondary structure which would contain a maximum of intramolecular hydrogen bonding.

The alanyl-tRNA of yeast consists of an unbranched chain of 77 ribonucleotides including 8A, 11U, 25G, 23C and 10 unusual nucleosides which are inosine, ribothymidine, dihydrouridine, pseudouridine and methylated derivatives of inosine and guanosine.

References
1. **Lehninger PRINCIPLES OF BIOCHEMISTRY Fourth Edition: David L. Nelson and Michael M. Cox**
2. **BIOCHEMISTRY; DONALD VOET and JUDITH G. VOET**

- The 5′ terminus is phosphorylated whereas the 3′ terminus has a free hydroxyl group.
- the *5′-phosphate is shown at the left hand and the 3′-hydroxyl on the right side.*
- The attachment site for the amino acid alanine is 3′-hydroxyl group of the adenosine residue at 3′ terminus of the molecule.



References
1. **Lehninger PRINCIPLES OF BIOCHEMISTRY Fourth Edition: David L. Nelson and Michael M. Cox**
2. **BIOCHEMISTRY; DONALD VOET and JUDITH G. VOET**

Common Structural Features Cloverleaf Model Of tRNA

1. All tRNA molecules have a common design and consist of 3 folds giving it a shape of the cloverleaf with four arms ; the longer tRNAs have a short fifth or extra arm. The actual 3-dimensional structure of a tRNA looks more like a twisted L than a cloverleaf .

2. All tRNA molecules are unbranched chains containing from 73 to 93 ribonucleotide residues, corresponding to molecular weights between 24,000 and 31,000 (Mitochondria contain distinct RNAs that are somewhat smaller). For example, tRNAAla contains 77 nucleotides, tRNATyr contains 78 nucleotides, tRNASer contains 85 nucleotides.

3. They contain from 7 to 15 unusual modified bases. Many of these unusual bases are methylated or dimethylated derivatives of A, U, G and C. These include nucleotides of pseudouridine, various methylated adenines and guanines, methylated pyrimidines such as thymine and 5-methylcytosine and others. Not all these are present in any one source of tRNA but *pseudouridine* (ϕ*U*) *is the most abundant and universally distributed*. 4. The 5′ end of tRNAs is phosphorylated. The 5′ terminal residue is usually guanylate (pG).

5. The base sequence at the 3′ end of all tRNAs is CCA. All amino acids bind to this terminal adenosine *via* the 3′-OH group of its ribose.

6. About 50% of the nucleotides in tRNAs are base-paired to form double helices.

7. The conventional numbering of nucleotides begins at the 5´ end and proceeds toward the 3´ end.

References

1. **Lehninger PRINCIPLES OF BIOCHEMISTRY Fourth Edition: David L. Nelson and Michael M. Cox**
2. **BIOCHEMISTRY; DONALD VOET and JUDITH G. VOET**

Tertiary structure of a tRNA molecule.

The specified amino acid is attached at the CCA 3′ terminus. The amino acid (or amino acceptor) arm and TΨC) arm form a continuous double helix, and the anticodon (AC) arm and the DHU (D) arm form the other partially continuous double helix. These 2 helical columns meet to form a twisted L-shaped molecule.

is probably closer to reality than the postulated cloverleaf structure.

The important features observed by them are :

1. The molecule is L-shaped.
2. There are 2 segments of the double helix. Each of these helices contains about 10 base pairs which correspond to one turn of the helix. These helical segments are perpendicular to each other, thus forming an L.
3. The CCA terminus containing the attachment site for the amino acid is at one end of the L. The other end of the L is occupied by the anticodon loop. The DHU and TϕC loops form the corner of the L.
4. The CCA terminus and the adjacent helical region do not interact strongly with the rest of the molecule. This part of the molecule may change conformation during amino acid activation and also during protein synthesis on the ribosome.

References
1. **Lehninger PRINCIPLES OF BIOCHEMISTRY Fourth Edition: David L. Nelson and Michael M. Cox**
2. **BIOCHEMISTRY; DONALD VOET and JUDITH G. VOET**

Tertiary structure of a tRNA molecule.

Messenger RNA (mRNA) or Template RNA

The abundance of RNA in the cytoplasm and its role in protein synthesis suggested that the genetic information of nuclear DNA is transmitted to an RNA which functions at the sites of protein synthesis.

In 1961, the two Nobel laureates, Francois Jacob and Jacques Monod postulated that control of protein formation, at least in certain microorganisms, is determined by the rate of synthesis of templates. This requires that the templates do not accumulate in contrast of the constant presence of DNA, rRNA and tRNA. They, therefore, suggested the transient existence of an RNA, which they called “the messenger” RNA (mRNA).

References
1. Lehninger PRINCIPLES OF BIOCHEMISTRY Fourth Edition: David L. Nelson and Michael M. Cox
2. BIOCHEMISTRY; DONALD VOET and JUDITH G. VOET

- Later, they proposed that “the messenger” should have the following properties :
- 1. The messenger should be a polynucleotide.
- 2. The base composition of the messenger should reflect the base composition of the DNA that specifies it.
- 3. The mRNA should be very heterogeneous in size because genes or groups of genes vary in length. They also correctly assumed that 3 nucleotides code for one amino acid and that the molecular weight of an mRNA should be at least a half million.
- 4. The messenger should be, for a short period, associated with ribosomes.
- 5. The messenger should be synthesized and degraded very rapidly.
- *Messenger RNA is most heterogeneous in size and stability among all the types of RNAs.*
- It is synthesized on the surface of DNA template.
- It has base sequence complementary to DNA and carries genetic information or ‘message’ (hence its nomenclature) for the assembly of amino acids from DNA to ribosomes, the site of protein synthesis.
- It is synthesized by *DNA-dependent RNA polymerase*.
- If mRNA carries the codes for the synthesis of simple protein molecule, it is called ***monocistronic*** *type* and if it codes for more than one kind of protein, it is known as ***polycistronic*** *type* as in *Escherichia coli*.

References
1. **Lehninger PRINCIPLES OF BIOCHEMISTRY Fourth Edition: David L. Nelson and Michael M. Cox**
2. **BIOCHEMISTRY; DONALD VOET and JUDITH G. VOET**