Lecture 24 (11/13/24)

Nucleic Acids

A. Nucleotides
   1. parts
   2. nomenclature
   3. numbering
   4. properties

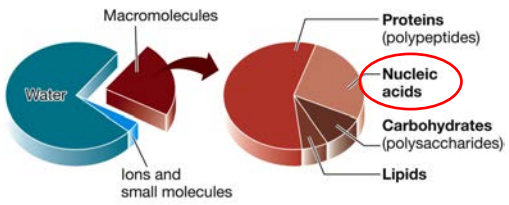
B. Nucleic Acids
   1. Polymer: **the phosphodiester bond**
   2. H-bonds
   3. Roles
      a. Nucleotides
      b. Nucleic acids

C. The 4 S's
   1. Size
      a. genomes
      b. RNAs
   2. Solubility
   3.Shape
   4.Stability

TODAY
- Reading: Ch8; 294-296, 263-269
  Ch24; 885-890
- Homework #23

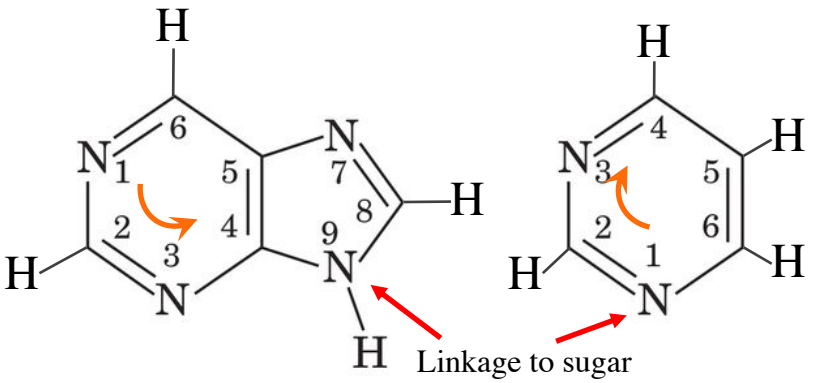
NEXT
- Reading: Ch8; 269-274
  Ch24; 891-894
- Homework #24

Nucleotides & Nucleic Acids



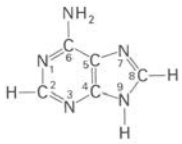
Definition of Nucleotides

The Nitrogenous Bases of Nucleotides are Derivatives of Purine & Pyrimidine

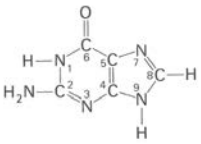


Chemical Structures of Nucleotide Bases

Purines

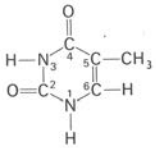


Adenine (A)

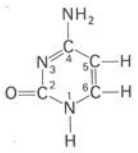


Guanine (G)

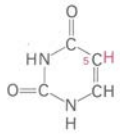
Pyrimidines



Thymine (T)

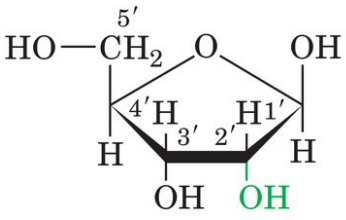


Cytosine (C)

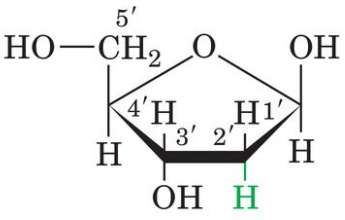


Uracil (U)

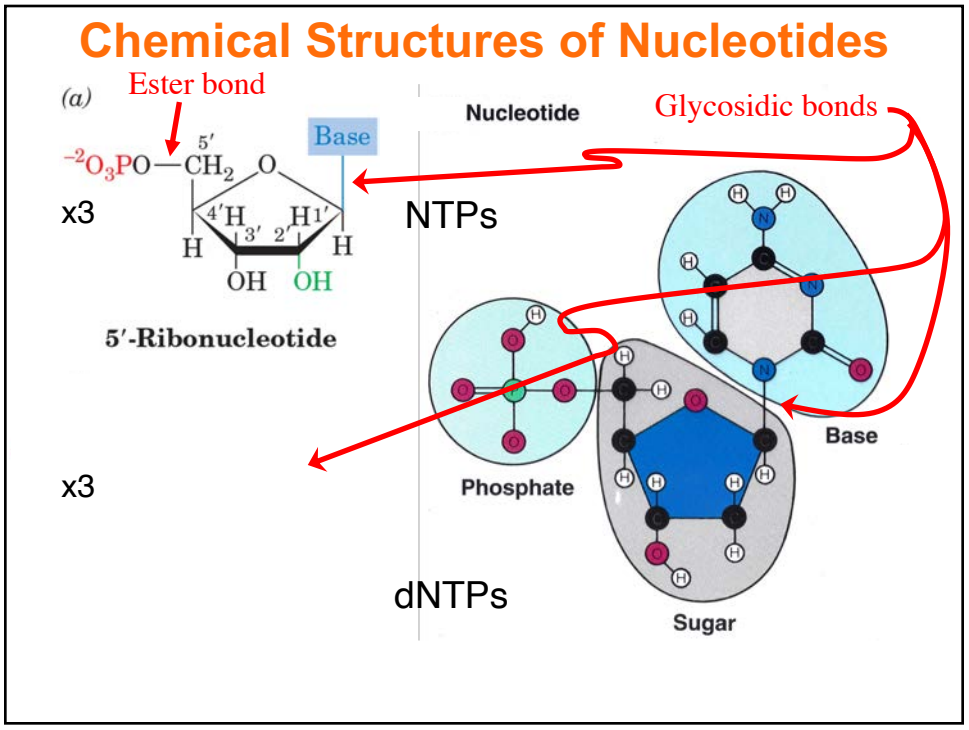
Sugars of Nucleotides are Either Ribose & Deoxyribose

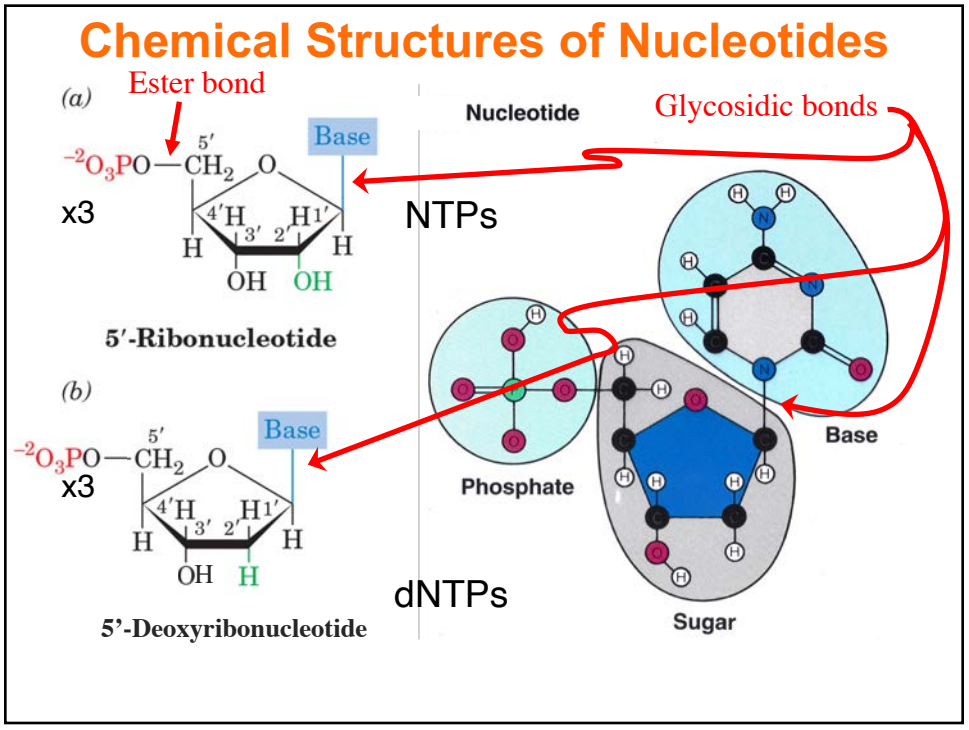


Ribose



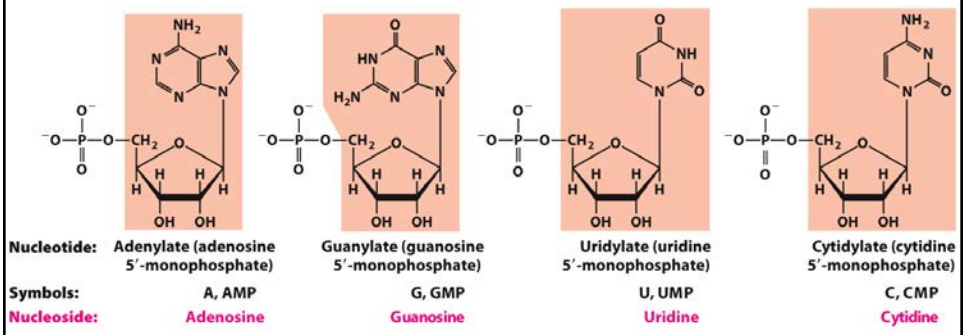
Deoxyribose


Chemical Structures of Nucleotides
(a)
Ester bond
Base
x3
5′-Ribonucleotide
x3
Nucleotide
Glycosidic bonds
NTPs
Base
Phosphate
Sugar
dNTPs


Chemical Structures of Nucleotides
(a)
Ester bond
Base
x3
5′-Ribonucleotide
(b)
Base
x3
5’-Deoxyribonucleotide
Nucleotide
Glycosidic bonds
NTPs
Base
Phosphate
Sugar
dNTPs

Nomenclature: Ribonucleotides

You need to know structures, names, numbering, and symbols (both one-letter (A) and three-letter (AMP) codes).



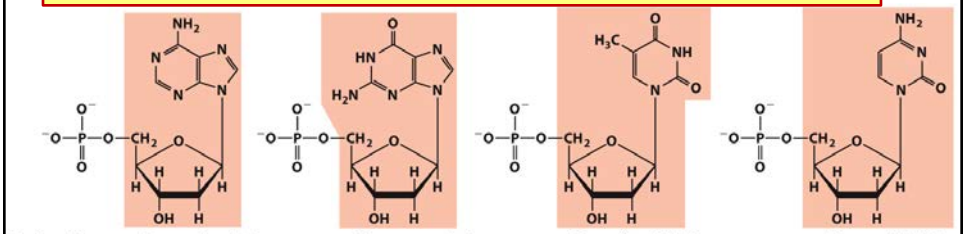
Nucleotide:	Adenylate (adenosine 5′-monophosphate)	Guanylate (guanosine 5′-monophosphate)	Uridylate (uridine 5′-monophosphate)	Cytidylate (cytidine 5′-monophosphate)
Symbols:	A, AMP	G, GMP	U, UMP	C, CMP
Nucleoside:	Adenosine	Guanosine	Uridine	Cytidine

Ribonucleotides

Ribonucleosides

Nomenclature: Deoxyribonucleotides

You need to know structures, names, numbering, and symbols (both two-letter (dA) and four-letter (dAMP) codes).



Nucleotide:	Deoxyadenylate (deoxyadenosine 5′-monophosphate)	Deoxyguanylate (deoxyguanosine 5′-monophosphate)	Deoxythymidylate (deoxythymidine 5′-monophosphate)	Deoxycytidylate (deoxycytidine 5′-monophosphate)
Symbols:	A, dA, dAMP	G, dG, dGMP	T, dT, dTMP	C, dC, dCMP
Nucleoside:	Deoxyadenosine	Deoxyguanosine	Deoxythymidine	Deoxycytidine

Deoxyribonucleotides

Deoxyribonucleosides

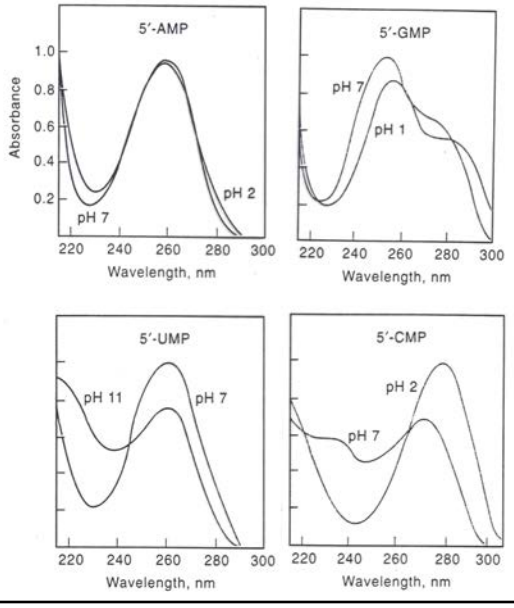
Nucleotides:
Nomenclature

Nucleotide and nucleic acid nomenclature

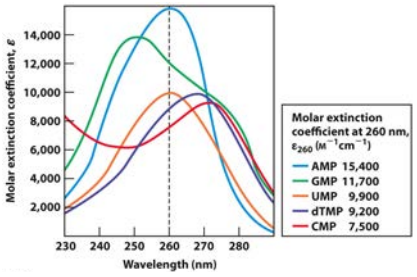
Base	Nucleoside*	Nucleotide*	Nucleic acid
-ine	-osine	-ylate	
Purines			
Adenine	Adenosine Deoxyadenosine	Adenylate Deoxyadenylate	RNA DNA
Guanine	Guanosine Deoxyguanosine	Guanylate Deoxyguanylate	RNA DNA
Pyrimidines	-idine	-idylate	
Cytosine	Cytidine Deoxycytidine	Cytidylate Deoxycytidylate	RNA DNA
Thymine	Thymidine or deoxythymidine	Thymidylate or deoxythymidylate	DNA
Uracil	Uridine	Uridylate	RNA

Nucleoside and *nucleotide* are generic terms that include both ribo- and deoxyribo- forms. Note that here ribonucleosides and ribonucleotides are designated simply as nucleosides and nucleotides (e.g., riboadenosine as adenosine) and deoxyribonucleosides and deoxyribonucleotides as deoxynucleosides and deoxynucleotides (e.g., deoxyriboadenosine as deoxyadenosine). Both forms of naming are acceptable, but the shortened names are more commonly used.

Nucleic Acid Bases, Nucleosides, and Nucleotides



Nucleotide	Extinction Coefficient at pH 7.0 ($M^{-1}cm^{-1}$) x10^3	λ_{max} (nm)
AMP	15.4	260
GMP	11.7	248
CMP	7.5	280
dTMP	9.2	270
UMP	9.9	260

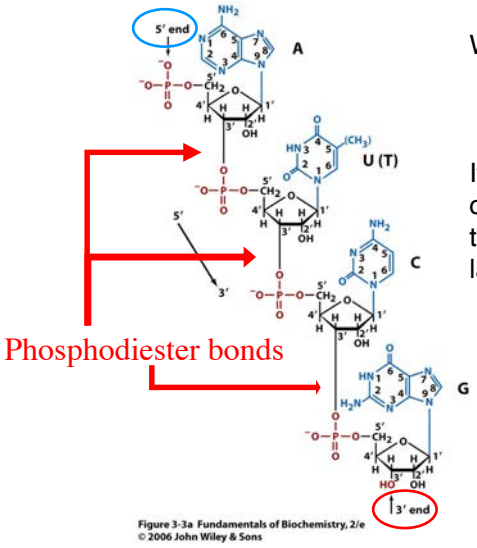


Definition of Nucleic Acids

Nucleic acid – polymer of nucleotides

The Phosphodiester Bond

Nucleic acid – polymer of nucleotides – directionality 5'→3'



When you write a sequence:

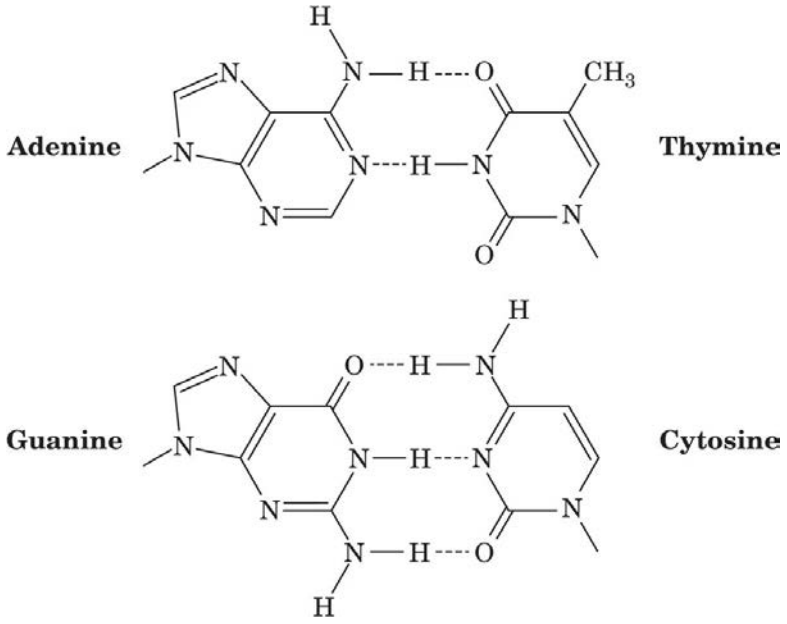
ATCG

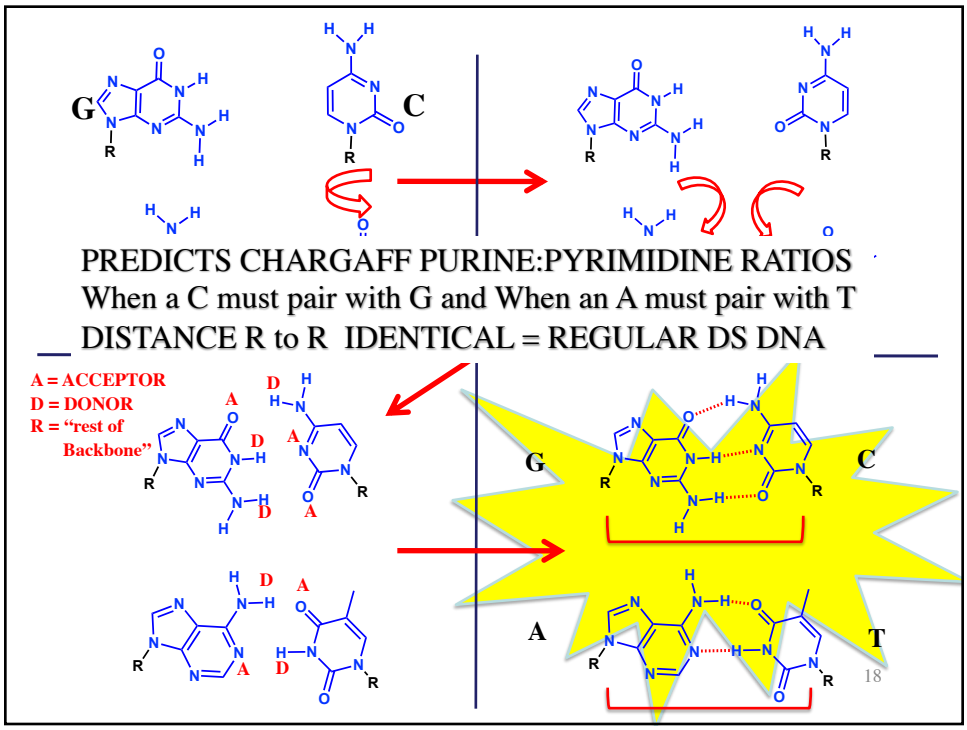
It is assumed that the 5'-end is on the left and the 3'-end is on the right, unless otherwise labeled.

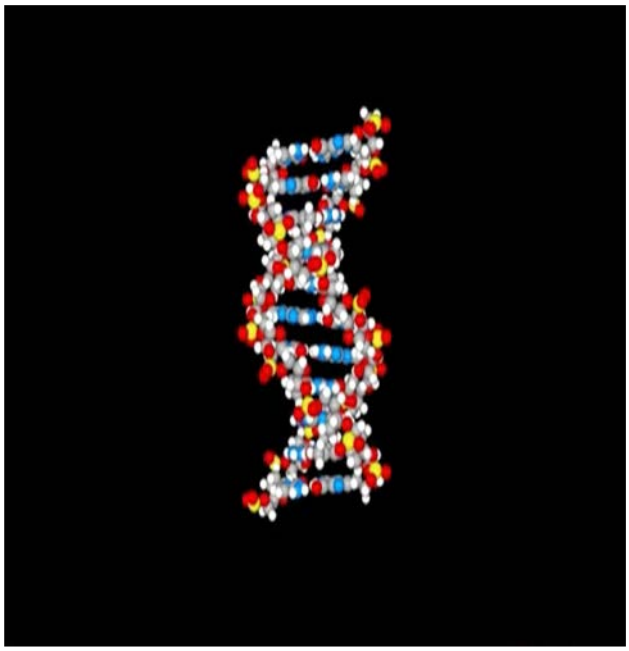
5'-ATCG-3'

3'-GCTA-5' same molecule

Complementary Base Pairing in DNA




G
C
PREDICTS CHARGAFF PURINE:PYRIMIDINE RATIOS
When a C must pair with G and When an A must pair with T
DISTANCE R to R IDENTICAL = REGULAR DS DNA
A = ACCEPTOR
D = DONOR
R = "rest of Backbone"
G
C
A
T
18



Watson-Crick Base Pairs

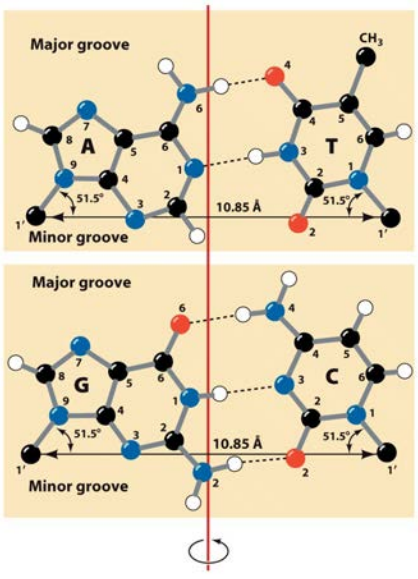
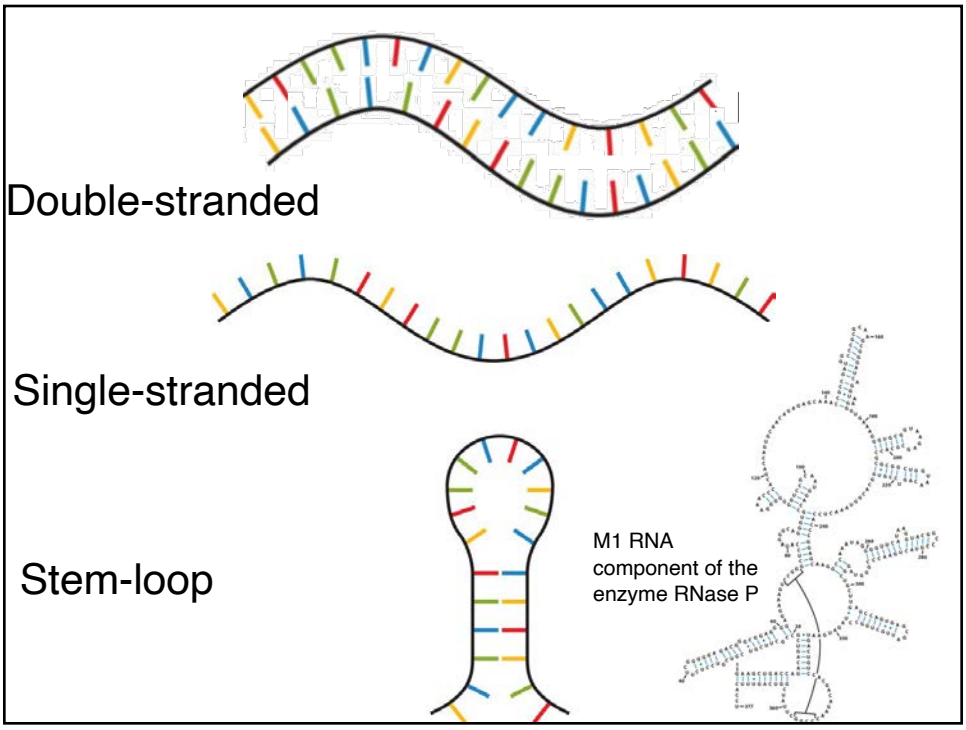


Figure 24-1



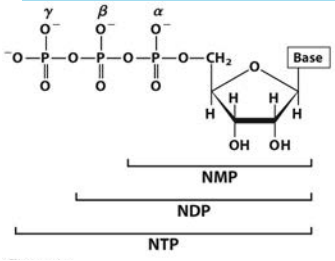
Roles of Nucleotides

The most well known is ATP:

Important roles of other nucleotides:

- Energy rich (high energies of hydrolysis, but kinetically stable)
  besides ATP, includes: GTP, CTP, UTP
- Carrier molecule (key intermediates in metabolism)
  UDP-sugars, CDP-lipids, NADH, FAD
- Secondary messengers (cAMP, cGMP)
- Other cofactors for enzymes

Other Functions of Nucleotides: Energy Source



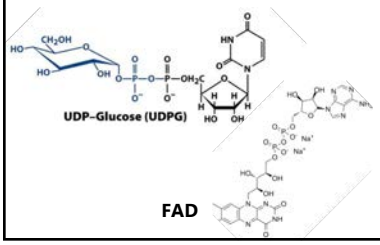
Abbreviations of ribonucleoside 5′-phosphates			
Base	Mono-	Di-	Tri-
Adenine	AMP	ADP	ATP
Guanine	GMP	GDP	GTP
Cytosine	CMP	CDP	CTP
Uracil	UMP	UDP	UTP

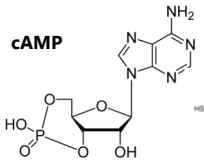
Abbreviations of deoxyribonucleoside 5′-phosphates			
Base	Mono-	Di-	Tri-
Adenine	dAMP	dADP	dATP
Guanine	dGMP	dGDP	dGTP
Cytosine	dCMP	dCDP	dCTP
Thymine	dTMP	dTDP	dTTP

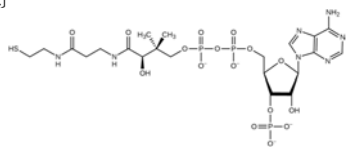
Carrier molecules

Secondary messengers

Other cofactors for enzymes







Roles of Nucleic Acids

- Information storage
- Information retrieval
- Information translation
- Information processing
- Information preservation

Key experiments by Griffiths, Avery, and Hershey & Chase

The 4 S's

Size

Solubility

Shape

Stability

The 4 S's

Size

Solubility

Shape

Stability

Nucleic Acids: Size

Genome Sizes

TABLE 28-2. SIZES OF SOME DNA MOLECULES

Organism	Number of base pairs (kb)[a]	Contour length (μm)
Viruses		
Polyoma, SV40	5.1	1.7
λ Bacteriophage	48.6	17
T2, T4, T6 bacteriophage	166	55
Fowlpox	280	193
Bacteria		
Mycoplasma hominis	760	260
Eschericia coli	4,700	1,600
Eukaryotes		
Yeast (in 17 haploid chromosomes)	13,500	4,600
Drosophila (in 4 haploid chromosomes)	165,000	56,000
Human (in 23 haploid chromosomes)	2,900,000	990,000
Lungfish (in 19 haploid chromosomes)	102,000,000	34,700,000

[a] kb = kilobase pair = 1000 base pairs (bp).

Source: Kornberg, A. and Baker, T.A., *DNA Replication* (2nd ed.), *p.* 20, Freeman (1992).

TABLE 3-3 Some Sequenced Genomes

Organism	Genome Size (kb)	Number of Chromosomes
Mycoplasma genitalium (human parasite)	580	1
Rickettsia prowazekii (putative relative of mitochondria)	1,112	1
Haemophilus influenza (human pathogen)	1,830	1
Escherichia coli (human symbiont)	4,639	1
Saccharomyces cerevisiae (baker's yeast)	12,070	16
Plasmodium falciparum (protozoan that causes malaria)	23,000	14
Caenorhabditis elegans (nematode)	97,000	6
Arabidopsis thaliana (dicotyledonous plant)	119,200	5
Drosophila melanogaster (fruit fly)	180,000	4
Oryza sativa (rice)	389,000	12
Danio rerio (zebra fish)	1,700,000	25
Gallus gallus (chicken)	1,200,000	40
Mus musculus (mouse)	2,500,000	20
Homo sapiens	3,038,000	23

Nucleic Acids: Size

Genome Sizes
(from DNA sequence)

TABLE 24-2 DNA, Gene, and Chromosome Content in Some Genomes

	Total DNA (bp)	Number of chromosomes[a]	Approximate number of genes
Escherichia coli K12 (bacterium)	4,641,652	1	4,494[b]
Saccharomyces cerevisiae (yeast)	12,157,105	16[c]	6,340[b]
Caenorhabditis elegans (nematode)	90,269,800	12[d]	23,000
Arabidopsis thaliana (plant)	119,186,200	10	33,000
Drosophila melanogaster (fruit fly)	120,367,260	18	20,000
Oryza sativa (rice)	480,000,000	24	57,000
Mus musculus (mouse)	2,634,266,500	40	27,000
Homo sapiens (human)	3,070,128,600	46	20,000

Note: This information is constantly being refined. For the most current information, consult the websites for the individual genome projects.
[a]The diploid chromosomes number is given for all eukaryotes except yeast.
[b]Includes known RNA-coding genes.
[c]Haploid chromosomes number. Wild yeast strains generally have eight (octoploid) or more sets of these chromosomes.
[d]Number for females, with two X chromosomes. Males have an X but no Y, thus 11 chromosomes in all.

Nucleic Acids: Size

RNA Sizes

Table 5-1
RNA molecules in *E. coli*

Type	*Relative amount (%)*	*Sedimentation coefficient (S)*	*Mass (kd)*	*Number of nucleotides*
Ribosomal RNA (rRNA)	80	23	1.2×10^3	3700
		16	0.55×10^3	1700
		5	3.6×10^1	120
Transfer RNA (tRNA)	15	4	2.5×10^1	75
Messenger RNA (mRNA)	5		Heterogeneous	

The 4 S's

Size

Solubility

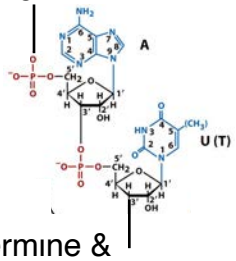
Shape

Stability

Nucleic Acids: Solubility

The polymer is a poly-anion

The pK_a of the phosphodiester is ~2.0



Consequences:

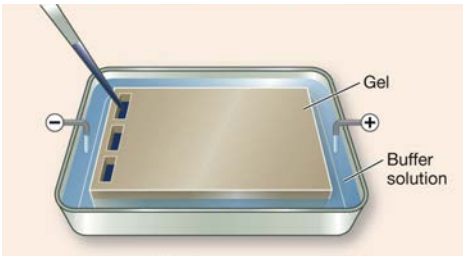
1) A counter ion:

required for solubility and stability.
usually Na^+, K^+, and/or Mg^{+2}
in cell, also use of polyamines; spermine & spermidine.

2) Easily separated by electrophoresis:

Every nucleotide has one (1) negative charge.
so charge/mass ratio is constant.
so can separate by size (similar in concept to SDS-PAGE).

Nucleic Acids: Solubility



Nucleic acids can be separated by **gel electrophoresis**.

Polymers can be placed in a well in a semisolid gel and an electric field is applied across the gel.

Negatively charged Nucleic acids move towards positive end.

For polymers of the same shape, smaller polymers travel faster than larger polymers.

For polymers of the same size, more compact topolgies travel faster than less compact ones.

The 4 S's

Size

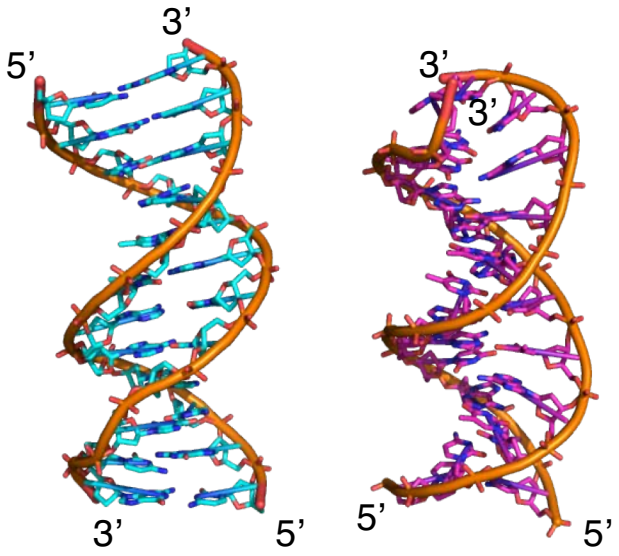
Solubility

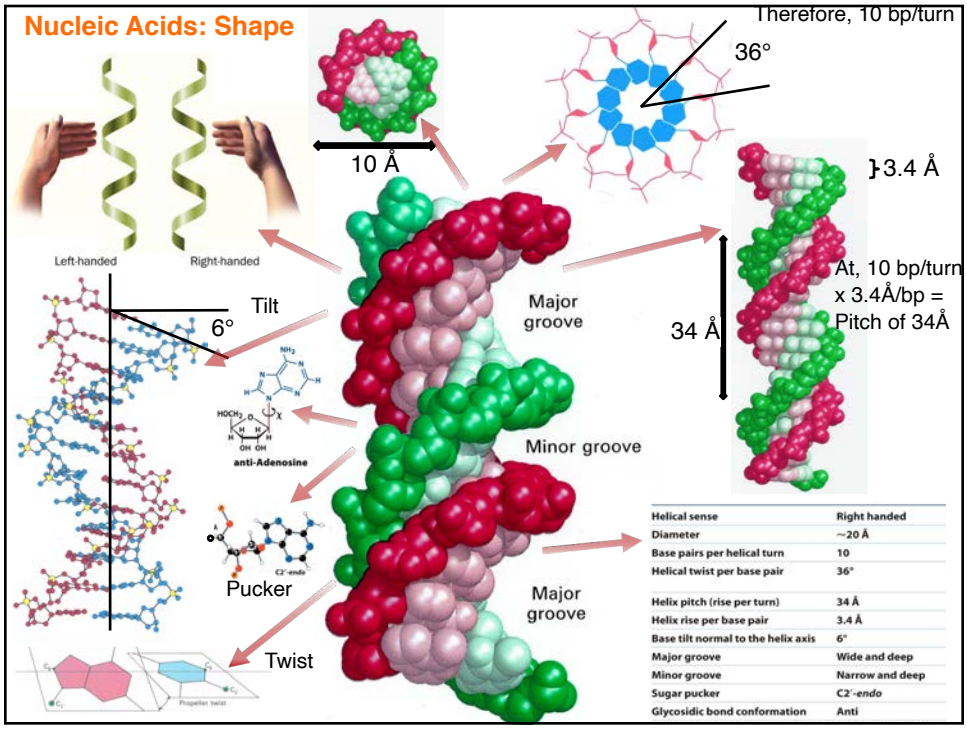
Shape

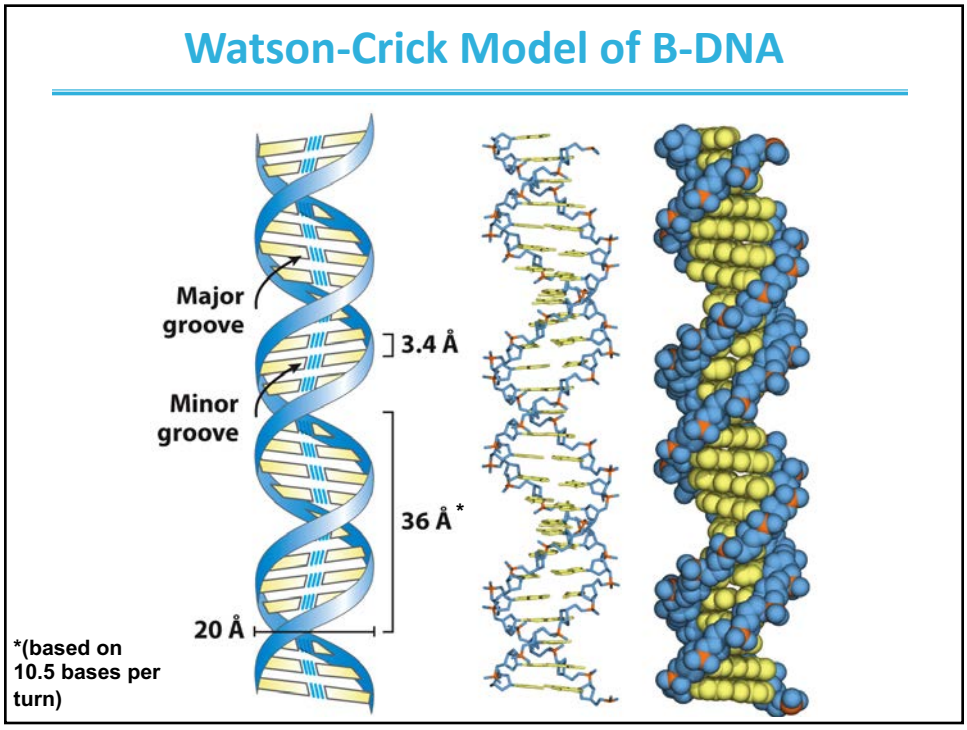
Stability

Nucleic Acids: Shape

ANTIPARALLEL dsDNA **PARALLEL dsDNA**

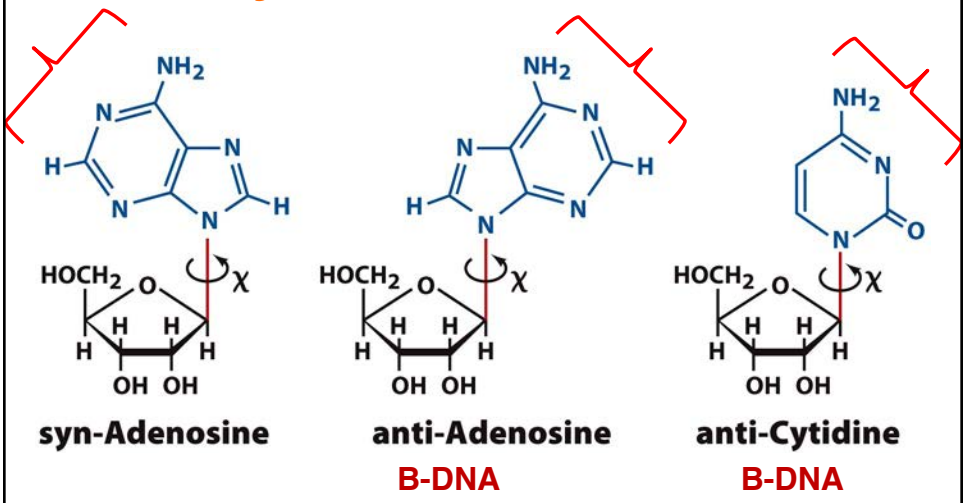



Nucleic Acids: Shape
Therefore, 10 bp/turn
36°
10 Å
3.4 Å
Left-handed
Right-handed
Tilt
6°
Major groove
34 Å
At, 10 bp/turn x 3.4Å/bp = Pitch of 34Å
anti-Adenosine
Minor groove
Pucker
Major groove
Twist
Helical sense Right handed
Diameter ~20 Å
Base pairs per helical turn 10
Helical twist per base pair 36°
Helix pitch (rise per turn) 34 Å
Helix rise per base pair 3.4 Å
Base tilt normal to the helix axis 6°
Major groove Wide and deep
Minor groove Narrow and deep
Sugar pucker C2′-endo
Glycosidic bond conformation Anti


Watson-Crick Model of B-DNA
Major groove
3.4 Å
Minor groove
36 Å*
20 Å
*(based on 10.5 bases per turn)

Nucleic Acids: Shape

Sterically Allowed Base Orientations



Notice the bp interface