Ácidos Nucleicos

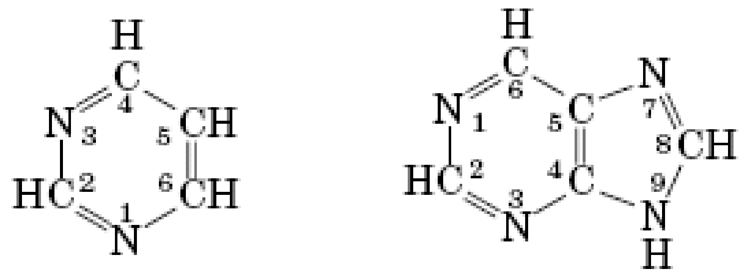
Box 1

Time line of the discovery of the structure of DNA

1869 Fritz Miescher discovers that the nuclei of pus cells contain an acidic substance to which he gave the name 'nuclein'. Later he finds that nuclein is composed of a protein and a compound to which the name nucleic acid, and subsequently DNA, will be given.

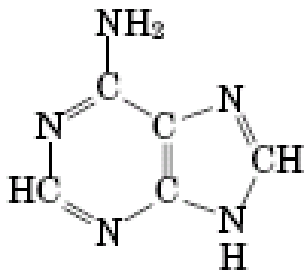
1919 Phoebus Aaron Levene proposes the 'tetranucleotide' structure of DNA, whereby the four bases of DNA were arranged one after another in a set of four.

Bases

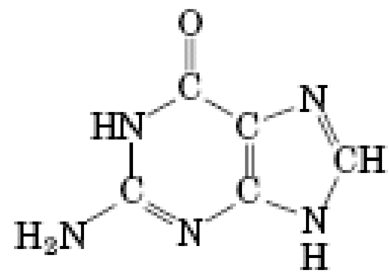


Pyrimidine Purine

(b)

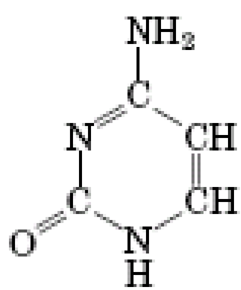


Adenine

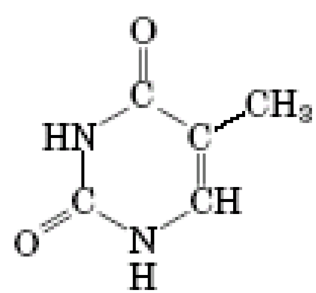


Guanine

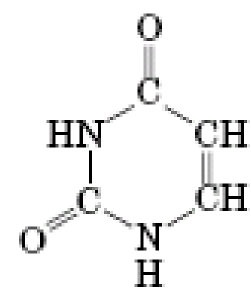
Purines



Cytosine

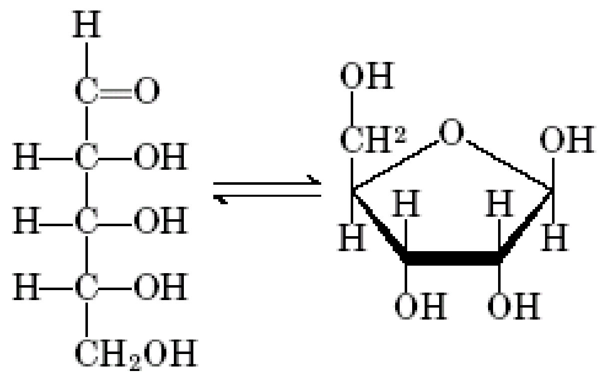


Thymine
(DNA)



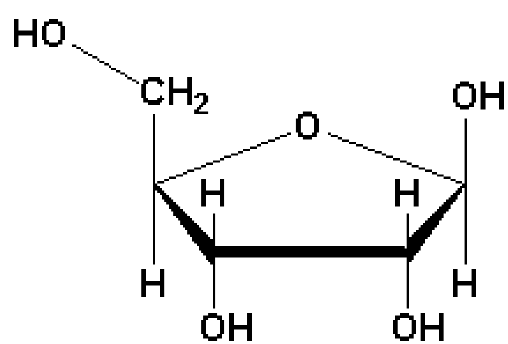
Uracil
(RNA)

Pyrimidines

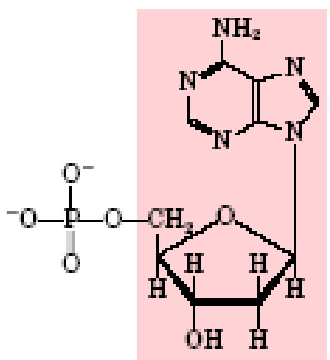
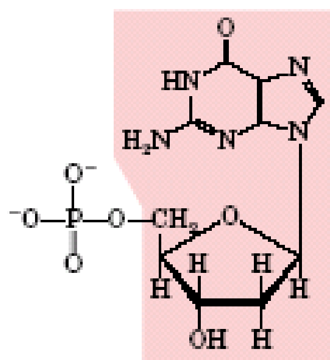
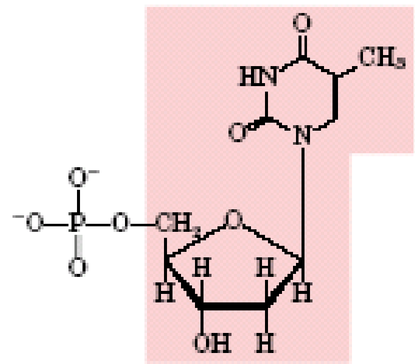
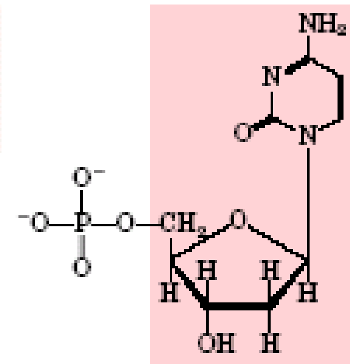


Aldehyde $\quad$ β-Furanose

(a)

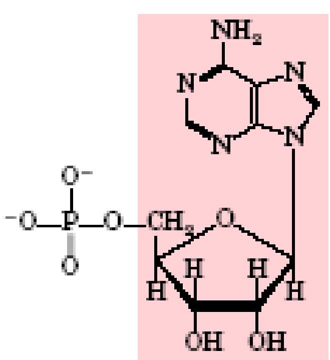
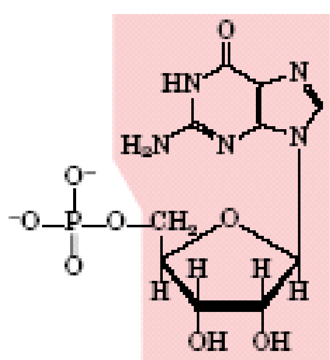
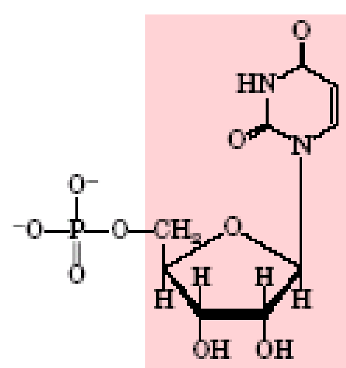
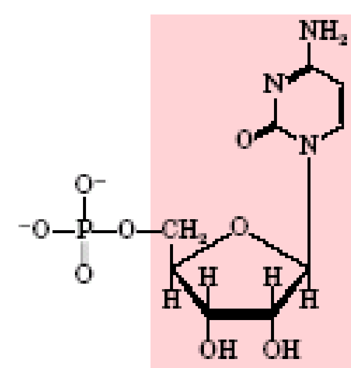


D-Ribose

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

(a) Deoxyribonucleotides

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

table 10–1

Nucleotide and Nucleic Acid Nomenclature

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

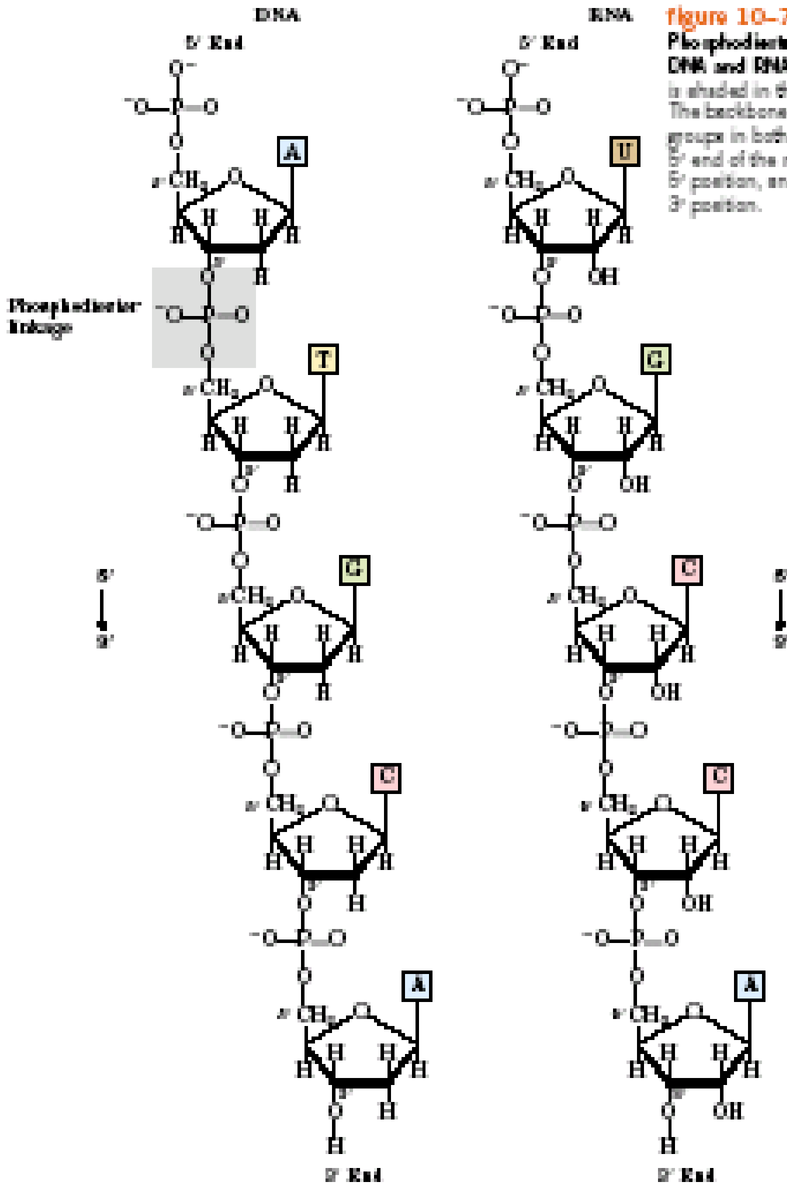
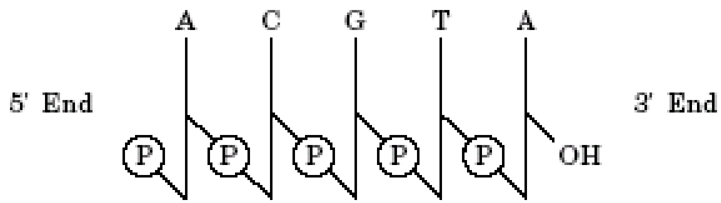


figure 10–7

Phosphodiester linkages in the covalent backbone of DNA and RNA. The phosphodiester bonds (one of which is shaded in the DNA) link successive nucleotide units. The backbone of alternating pentose and phosphate groups in both types of nucleic acid is highly polar. The 5′ end of the macromolecule lacks a nucleotide at the 5′ position, and the 3′ end lacks a nucleotide at the 3′ position.

Estructura primaria



pACGTA.

1928 Frederick Griffith finds that a substance in heat-killed bacteria can cause heritable changes in the live bacteria alongside them. He calls the phenomenon 'transformation'.

1938 Rudolf Signer, Torbjorn Caspersson and Einer Hammarsten find molecular weights for DNA between 500,000 and 1,000,000 daltons. Levene's tetranucleotide must be a polytetranucleotide.

1944 Oswald Avery, Colin MacLeod and Maclyn McCarty establish the chemical identity of Griffith's transforming principle as DNA, and they suggest that it may function as the genetic material.

1949 Erwin Chargaff reports that DNA base composition varies from one species to another, yet the ratio between the quantities of the two purine bases, adenine and thymine, and that between the quantities of the two pyrimidine bases, guanine and cytosine, remains about the same, namely one to one.

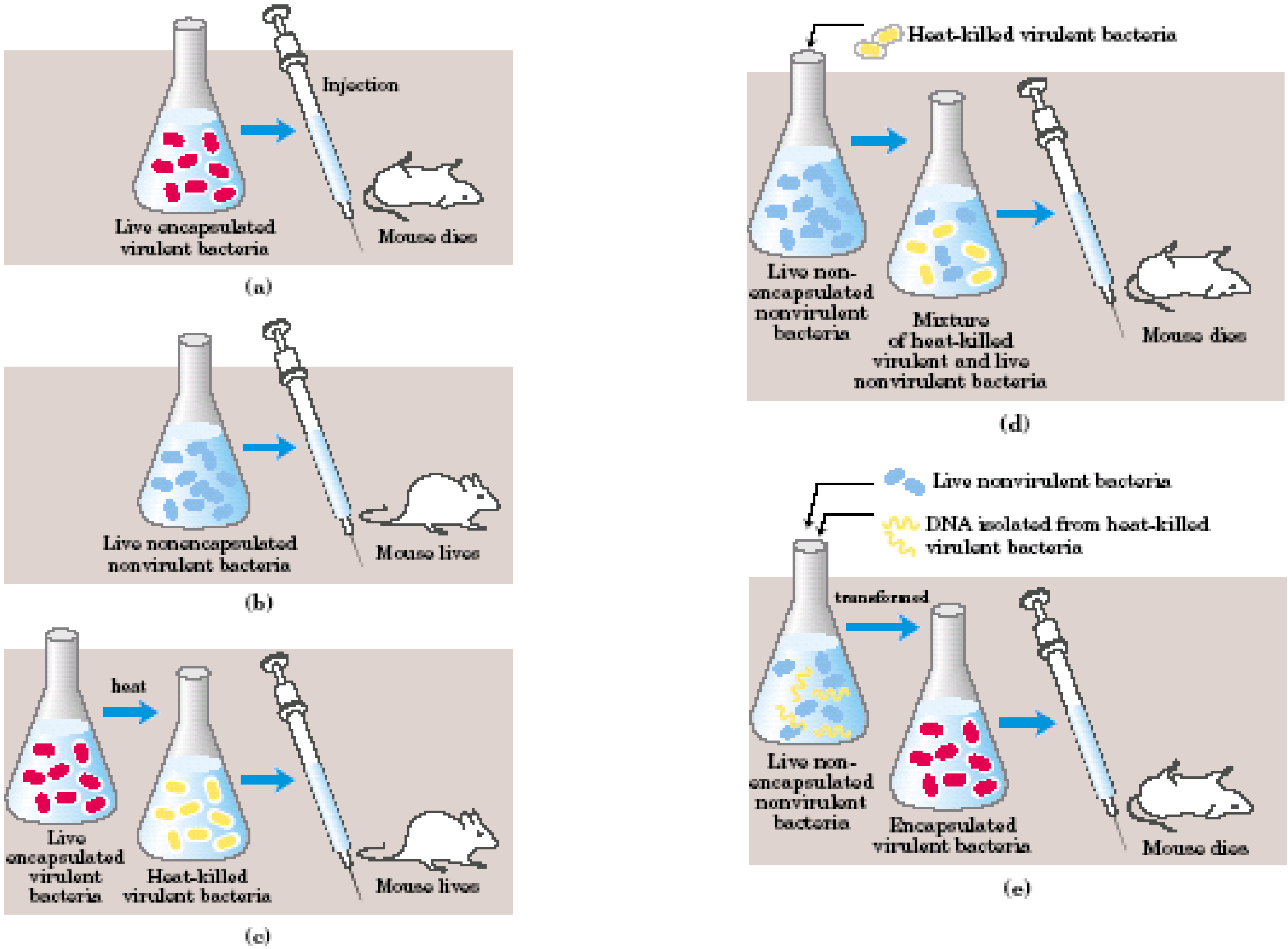
$A + G = T + C.$

1949 Roger and Colette Vendrely, together with André Boivin find half as much DNA in the nuclei of sex cells as they find in the body cells, thus paralleling the reduction in the number of chromosomes, making DNA look like the genetic material.

1951 Rosalind Franklin distinguishes two forms of DNA, the paracrystalline B form and the crystalline A form.

1952 Al Hershey and Martha Chase find that DNA but scarcely any protein from an infecting bacterial virus enters the bacterial cell and can be recovered from the progeny virus particles.

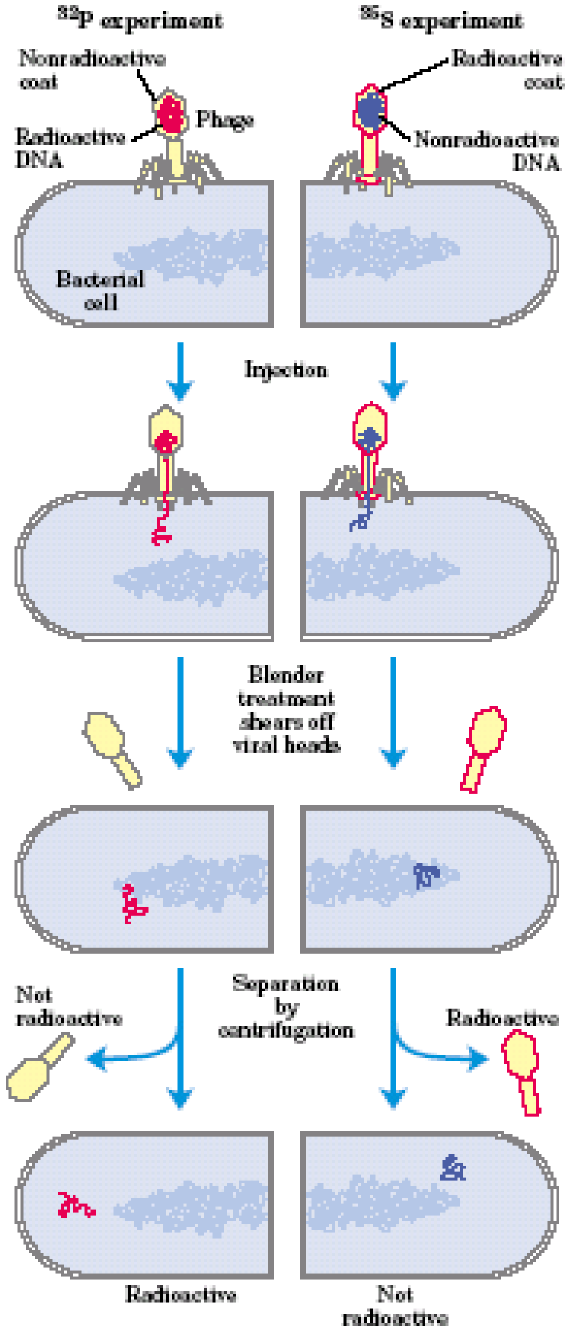
The Avery-MacLeod-McCarty experiment.



Griffith exp.

Sustancia “transformante”

La sustancia “transformante” de Griffith era el DNA



The Hershey-Chase experiment.

Experimentos de Chargaff

Source	Mol % of Bases					Ratios	
	Adenine (A)	Guanine (G)	Cytosine[a] (C)	Thymine (T)	(G + C)	A/T	G/C
Bacteriophage ϕX174	24.0	23.3	21.5	31.2	44.8	0.77[b]	1.08[b]
Bacteriophage T7	26.0	23.8	23.6	26.6	47.4	0.98	1.01
Escherichia coli B	23.8	26.8	26.3	23.1	53.2	1.03	1.02
Neurospora	23.0	27.1	26.6	23.3	53.8	0.99	1.02
Corn (maize)	26.8	22.8	23.2	27.2	46.1	0.99	0.98
Tetrahymena	35.4	14.5	14.7	35.4	29.2	1.00	0.99
Octopus	33.2	17.6	17.6	31.6	35.2	1.05	1.00
Drosophila	30.7	19.6	20.2	29.5	39.8	1.03	0.97
Starfish	29.8	20.7	20.7	28.8	41.3	1.03	1.00
Salmon	28.0	22.0	21.8	27.8	44.1	1.01	1.01
Frog	26.3	23.5	23.8	26.8	47.4	1.00	0.99
Chicken	28.0	22.0	21.6	28.4	43.7	0.99	1.02
Rat	28.6	21.4	21.6	28.4	42.9	1.01	1.00
Calf	27.3	22.5	22.5	27.7	45.0	0.99	1.00
Human	29.3	20.7	20.0	30.0	40.7	0.98	1.04

Source: Data taken from H. E. Sober (ed.), *Handbook of Biochemistry,* 2nd ed. (Chemical Rubber Publishing Co., 1970). Values for higher organisms vary slightly from one tissue to another, probably as a result of experimental error.

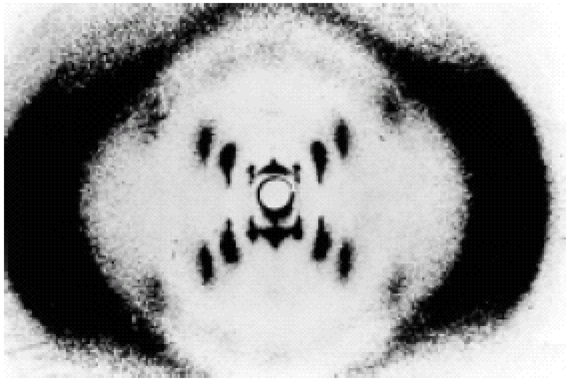
[a] Amount includes, for some organisms, a few percent of a modified base, 5-methylcytosine.

[b] This bacteriophage has a single-strand DNA, which need not follow Chargaff's rule.

Estructura secundaria

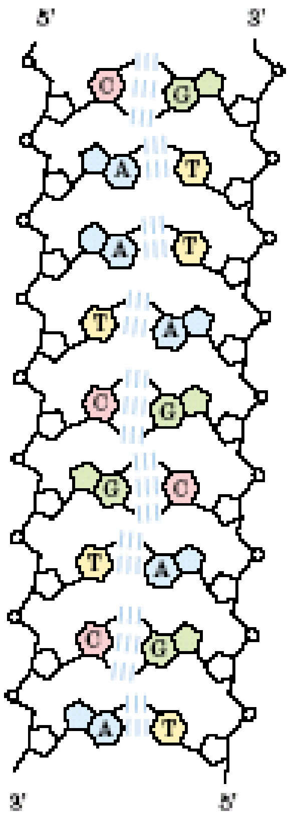
Rosalind Franklin
1920–1958

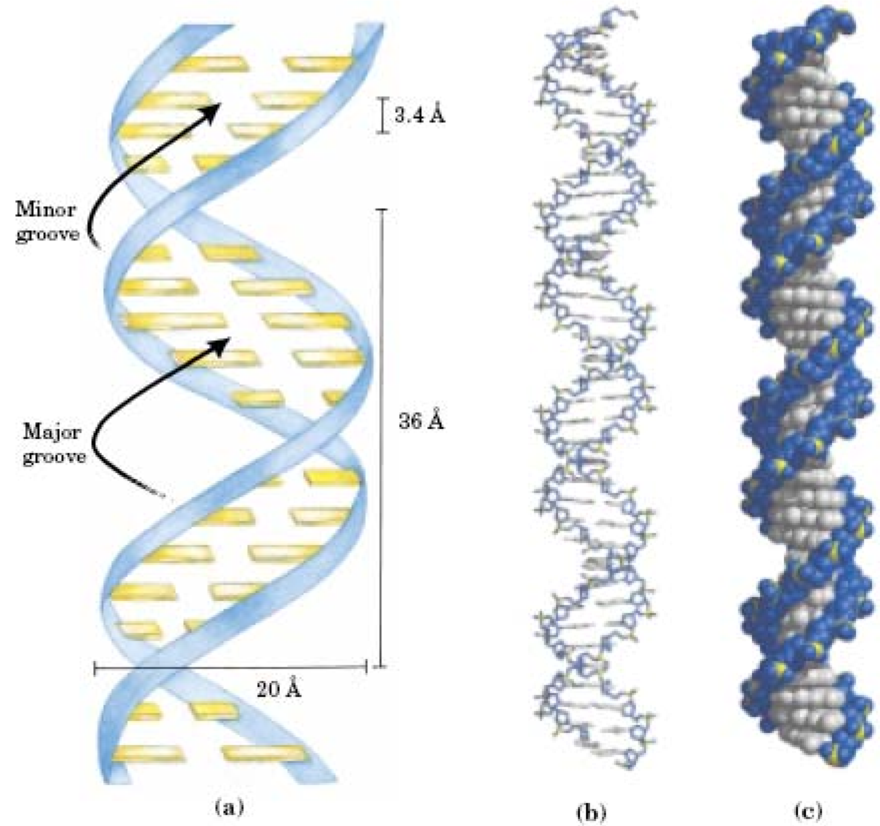
Maurice Wilkins



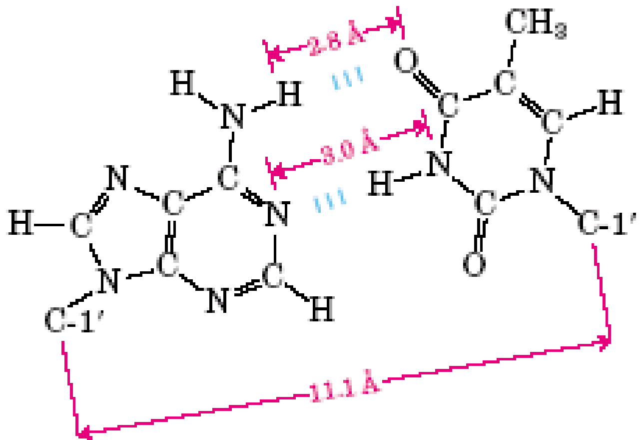
James Watson

Francis Crick



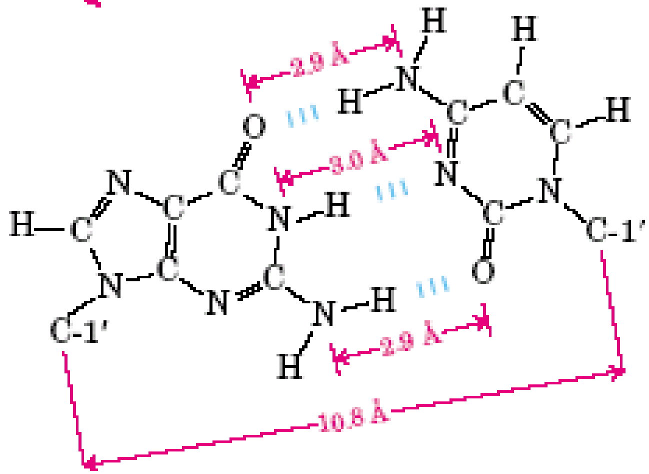


Adenine

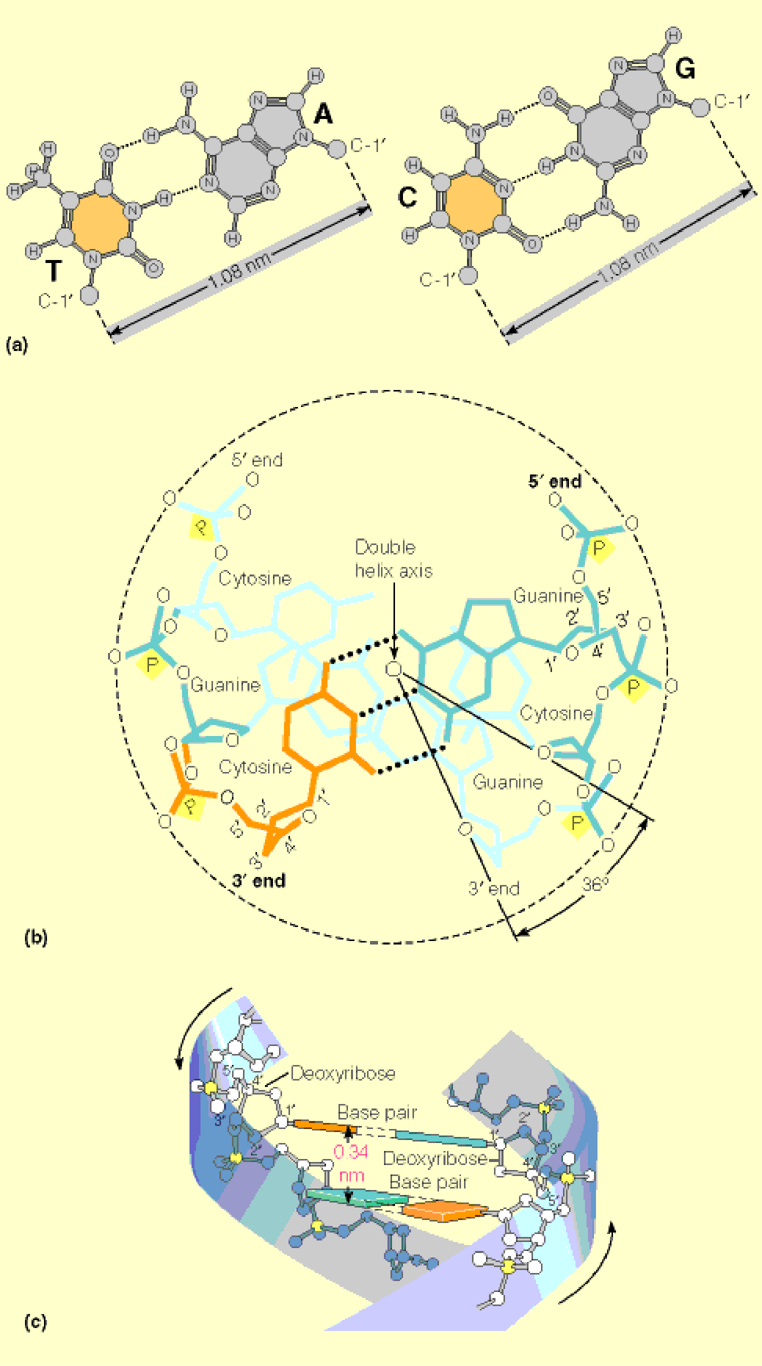


Thymine

Guanine

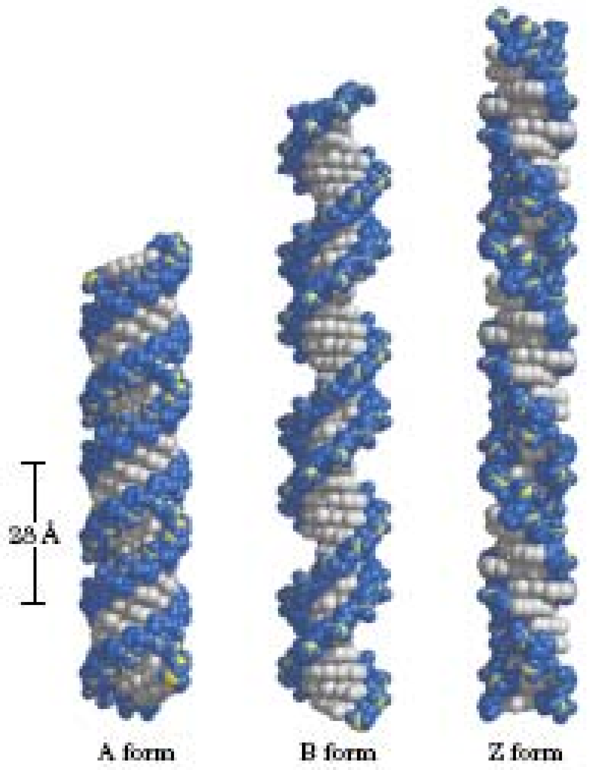


Cytosine

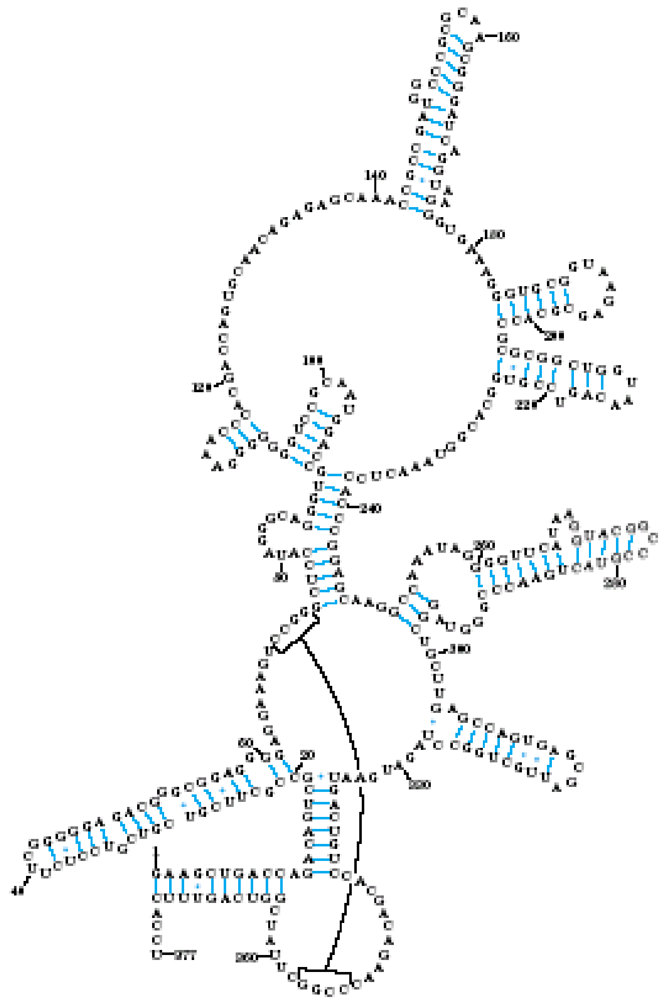


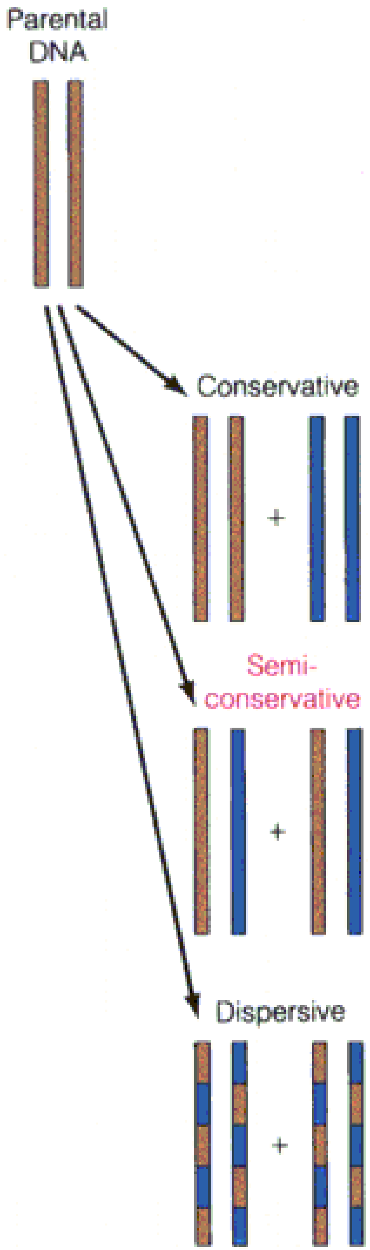
A
T
G
C
C-1′
1.08 nm
(a)
5′ end
5′ end
Double
helix axis
Cytosine
Guanine
Guanine
Cytosine
Cytosine
Guanine
3′ end
3′ end
36°
(b)
Deoxyribose
Base pair
0.34
nm
Deoxyribose
Base pair
(c)

1952 Rosalind Franklin and Raymond Gosling produce a magnificent X-ray diffraction pattern of the B form of DNA.
1953 James Watson and Francis Crick, Rosalind Franklin and Raymond Gosling, Maurice Wilkins, W. E. Seeds, Alec Stokes and Herbert Wilson, and Bertil Jacobson all publish on the structure of DNA[2–8].
1954 George Gamow suggests a DNA code for the synthesis of proteins.
1955 Seymour Benzer analyses the fine structure of the genetic material of a bacterial virus at a level close to the distances that separate the individual bases along the DNA chain.
1957 Francis Crick proposes 'the sequence hypothesis' and 'the central dogma'.
1958 Matthew Meselson and Franklin Stahl demonstrate the semi-conservative replication of DNA.
1959 Arthur Kornberg and colleagues isolate the enzyme DNA polymerase.
1961 Marshall Nirenberg and Johann Heinrich Matthaei show that a sequence of nucleotide can encode a particular amino acid, laying the foundations for deciphering the genetic code.
1962 The Nobel prize in medicine is awarded to James Watson, Francis Crick and Maurice Wilkins.



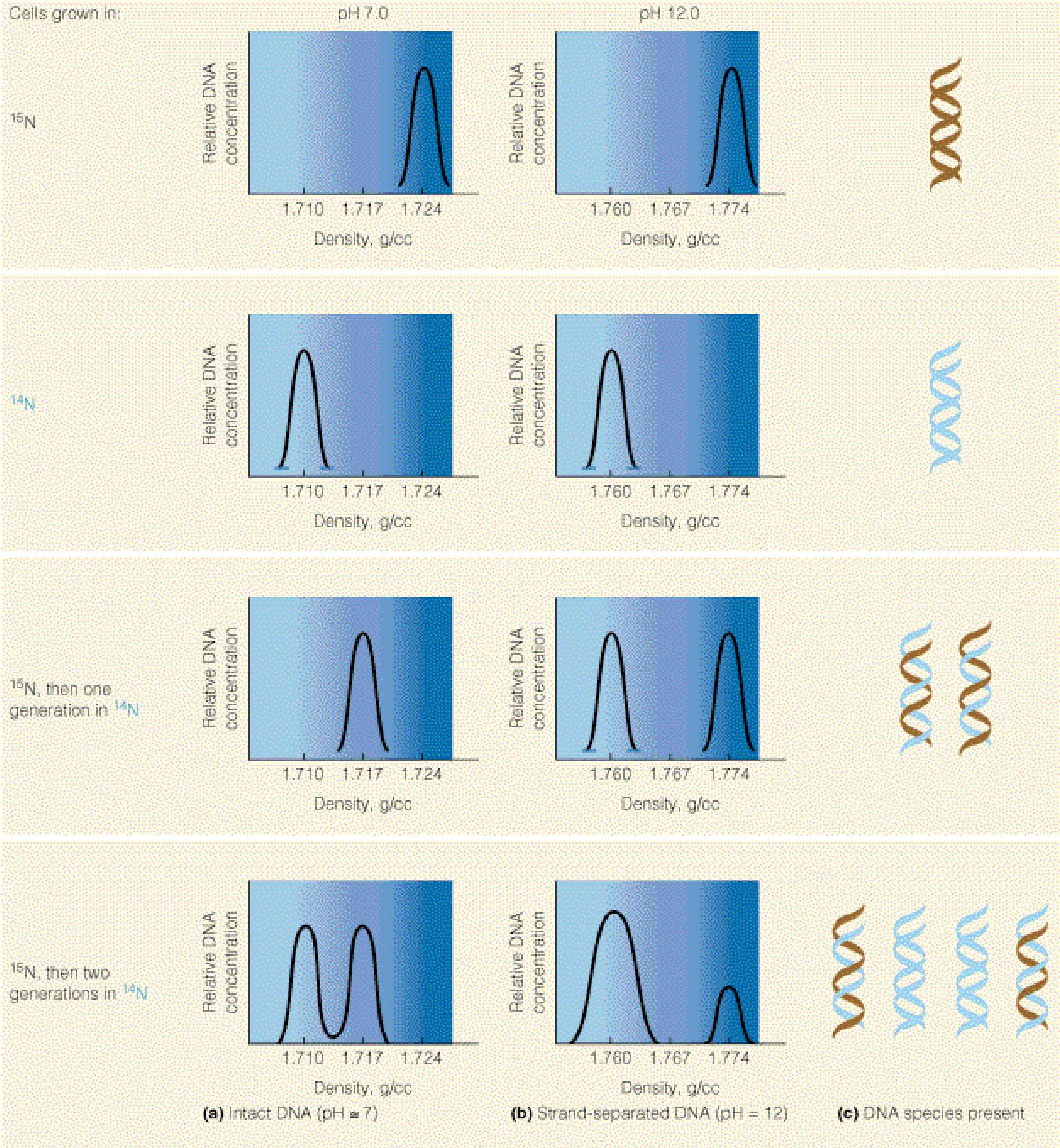
	A form	B form	Z form
Helical sense	Right handed	Right handed	Left handed
Diameter	~26 Å	~20 Å	~18 Å
Base pairs per helical turn	11	10.5	12
Helix rise per base pair	2.6 Å	3.4 Å	3.7 Å
Base tilt normal to the helix axis	20°	6°	7°
Sugar pucker conformation	C-3′ endo	C-2′ endo	C-2′ endo for pyrimidines; C-3′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



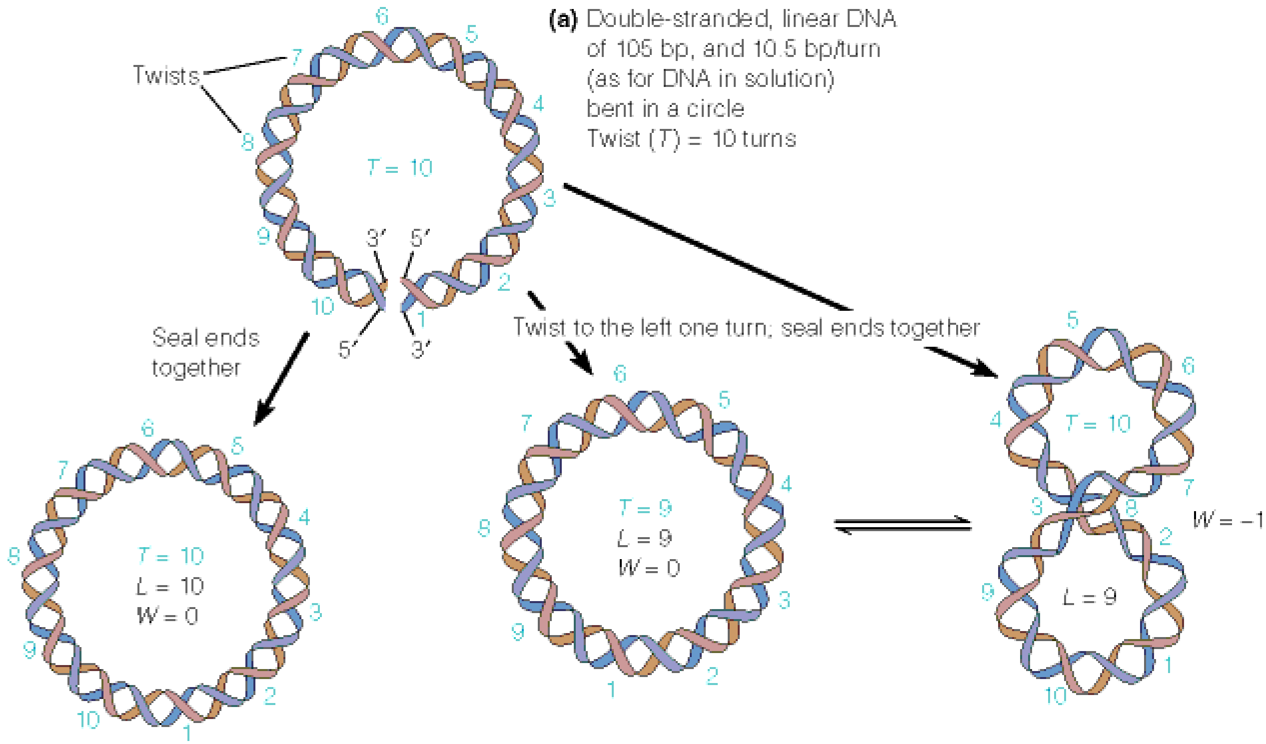


Replicación

Experimento de



Estructura terciaria



(a) Double-stranded, linear DNA of 105 bp, and 10.5 bp/turn (as for DNA in solution) bent in a circle
Twist (*T*) = 10 turns

(b) Unstrained circle: Double-stranded circular DNA
Linking number (*L*) = 10
Twist (*T*) = 10 turns
bp/turn = 10.5
Writhe (*W*) = 0

(c) Strained circle: Double-stranded circular DNA
Linking number (*L*) = 9
Twist (*T*) = 9 turns
bp/turn = 11.67
Writhe (*W*) = 0

(d) Supercoil: Double-stranded DNA
Linking number (*L*) = 9
Twist (*T*) = 10 turns
bp/turn = 10.5
Writhe (*W*) = −1

Propiedades fisicoquímicas

Estabilidad del enlace

El enlace fosfodiester es inestable a pH muy ácidos y temperatura ambiente.

A pH alcalinos el DNA es estable hasta pH 11 pero el RNA se hidroliza a pH superiores a 7.5

A pH mayores que 11 tengo completa desnaturalizacion (inicialmente se rompen los puentes de hidrógeno y a pH mayores se hidrolizan los enlaces).

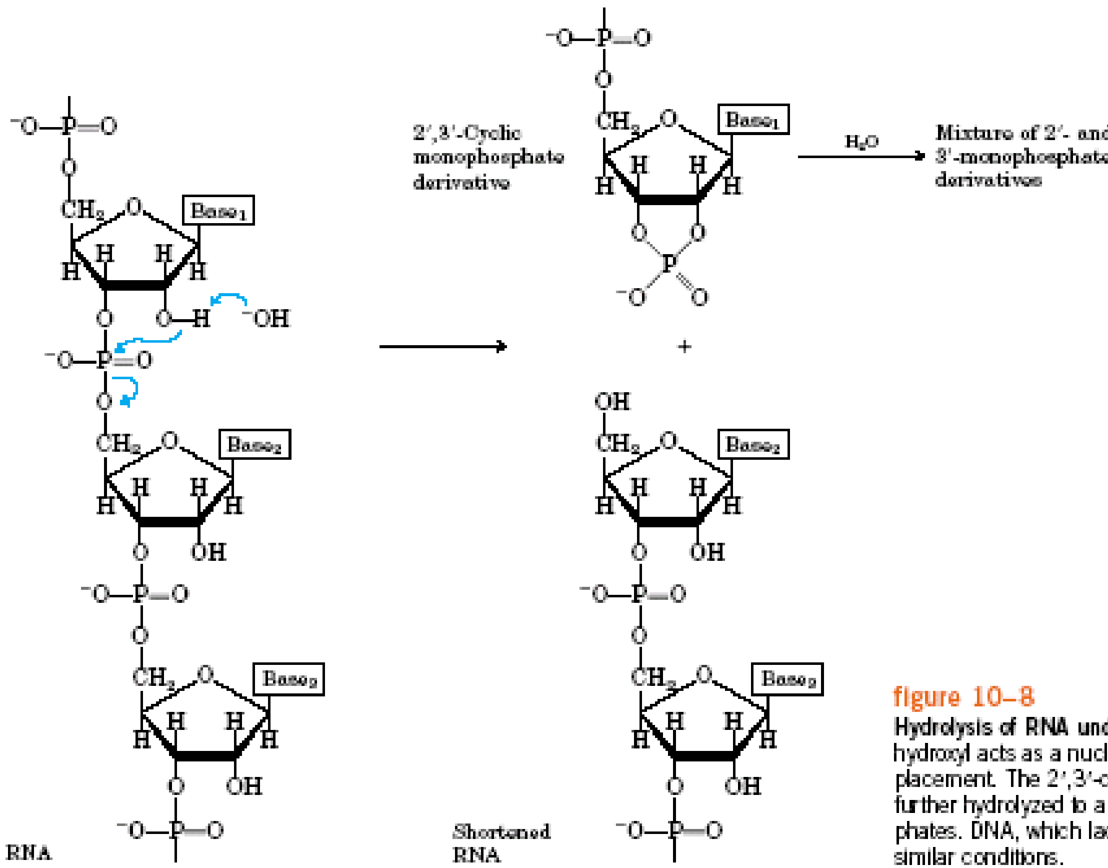
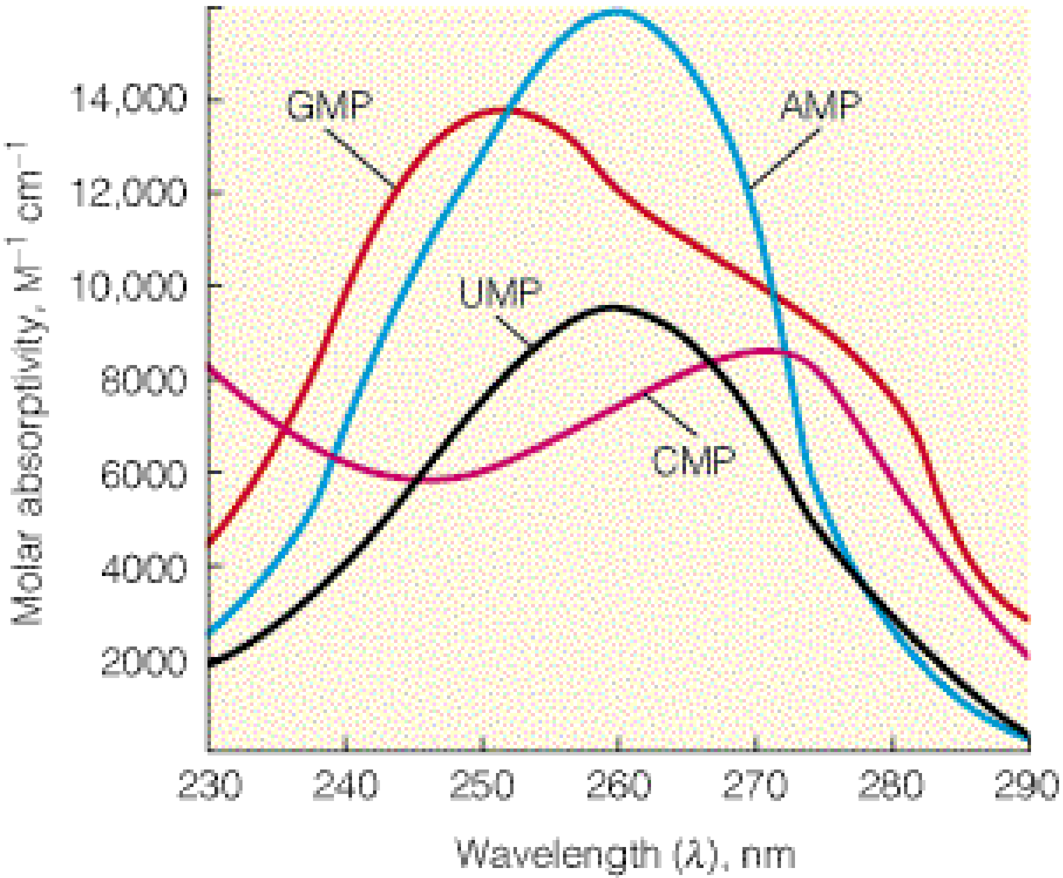


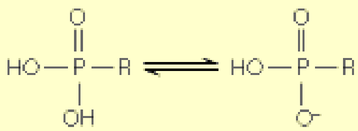
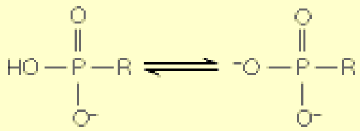
figure 10–8

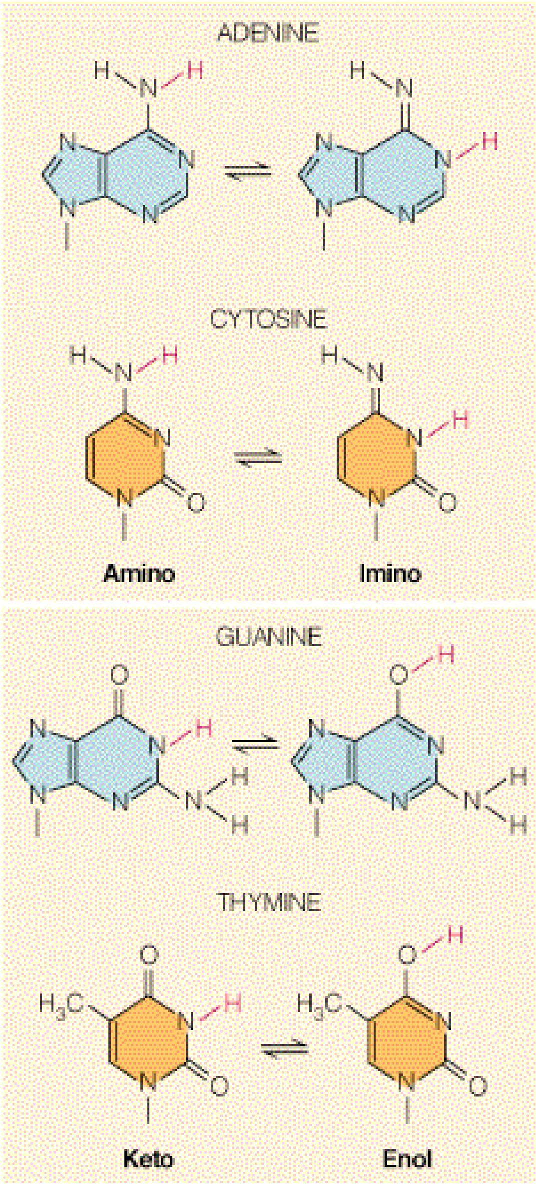
Hydrolysis of RNA under alkaline conditions. The 2′ hydroxyl acts as a nucleophile in an intramolecular displacement. The 2′,3′-cyclic monophosphate derivative is further hydrolyzed to a mixture of 2′- and 3′-monophosphates. DNA, which lacks 2′ hydroxyls, is stable under similar conditions.

Propiedades espestroscópicas



Propiedades acido-base

	Phosphate		Base	
	Primary Ionization  pK_{a1} + H^+	Secondary Ionization  pK_{a2} + H^+	pK_a	Reaction (as Loss of Proton from)
5′ AMP	0.9	6.1	3.8	N-1
5′ GMP	0.7	6.1	2.4	N-7
			9.4	N-1
5′ UMP	1.0	6.4	9.5	N-3
5′ CMP	0.8	6.3	4.5	N-3



Tautomerismo

Temperatura de fusión