Bioquímica Geral
RFM0004

Nucleotídeos
Ácidos Nucleicos

Departamento de Bioquímica e Imunologia
FMRP-USP

Papel dos nucleotídeos no metabolismo celular

Constituintes dos ácidos nucleicos

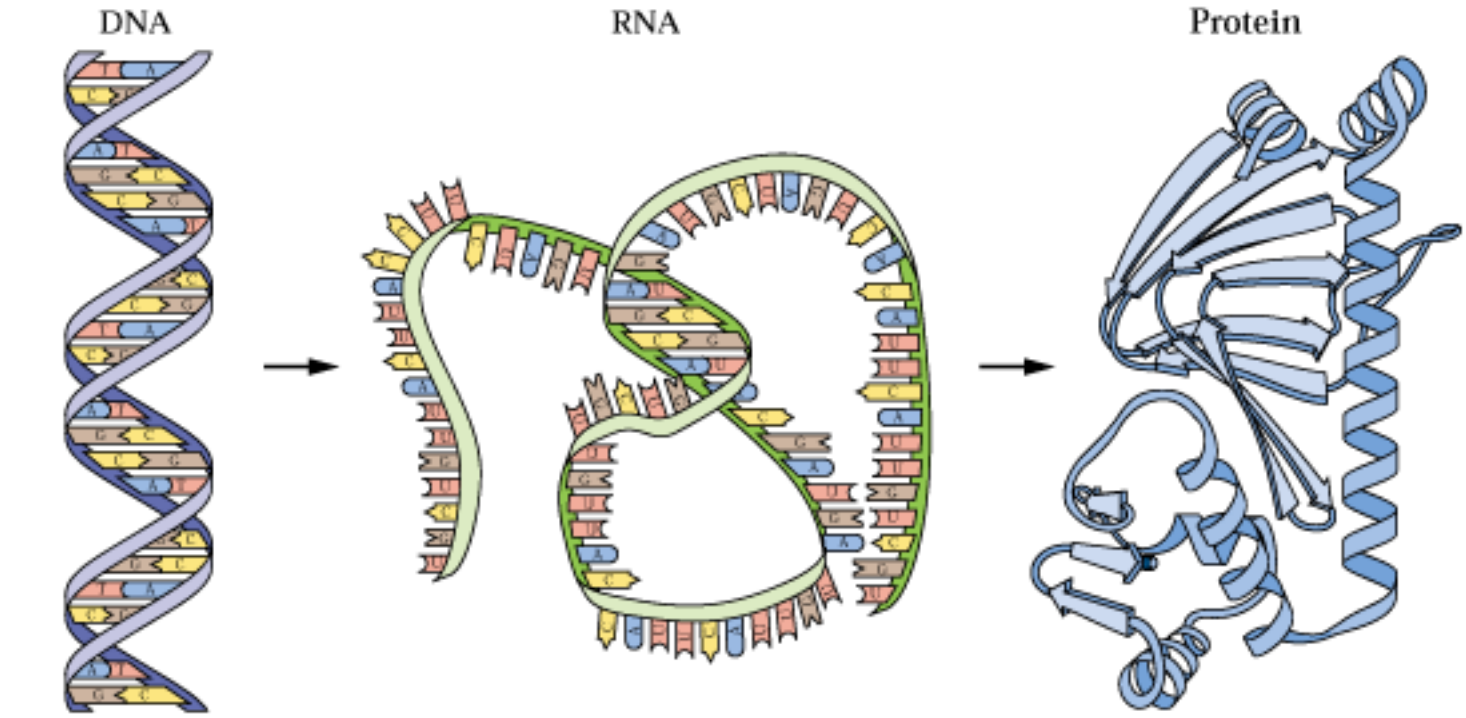
RNA e DNA

Nucleotídeos e Ácidos Nucleicos

- **DNA**: Armazenamento da informacão genética
  - Estabilidade

- **RNA**: várias funções
  - RNA ribossomal (rRNA) - componentes estruturais de ribossomos
  - RNA mensageiro (mRNA) - intermediário
  - RNA transportador (tRNA) - moléculas adaptadoras que traduzem informação do mRNA em amino ácidos
  - snRNA, microRNA, etc

Dogma Central



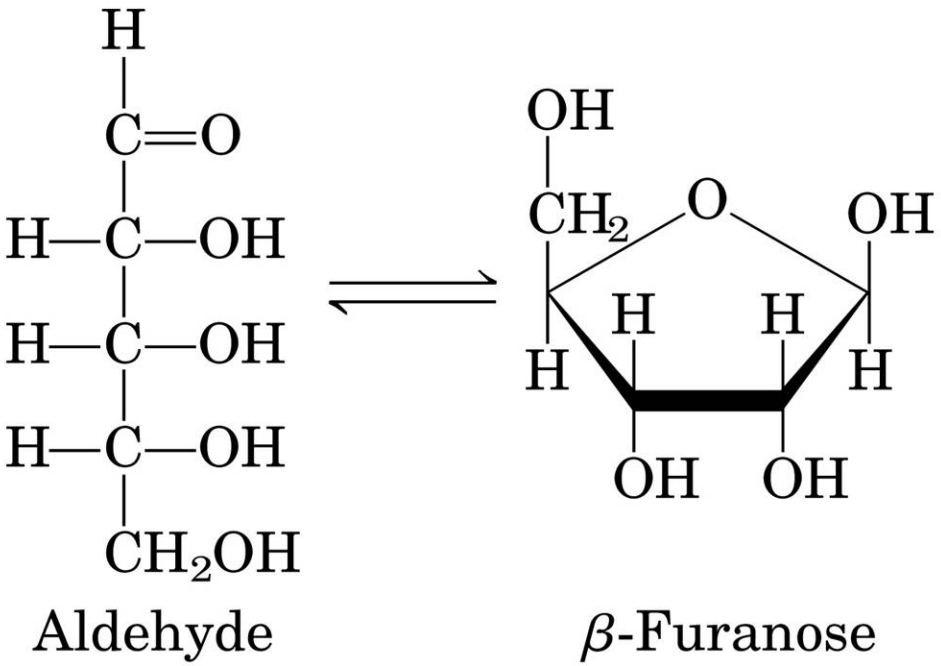
Ácidos Nucleicos

RNA e DNA

Unidades:

- Pentose (5 C)
- Base nitrogenada – pirimidinas
  purinas
- Fosfato - C - 5’

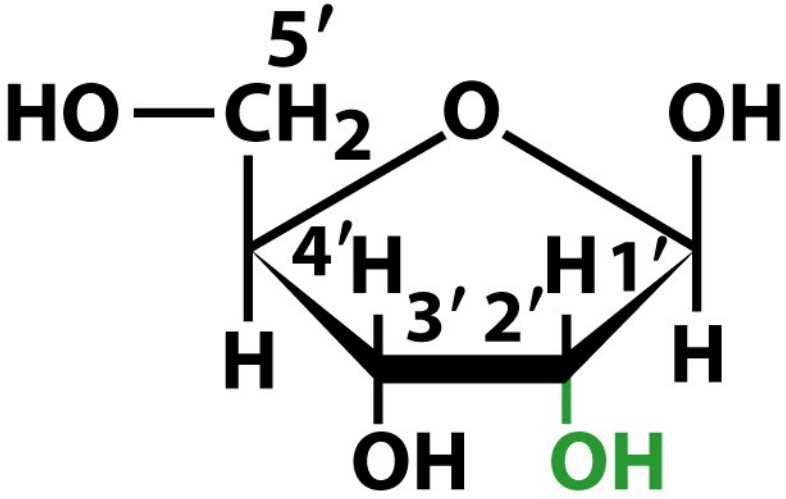
Pentoses



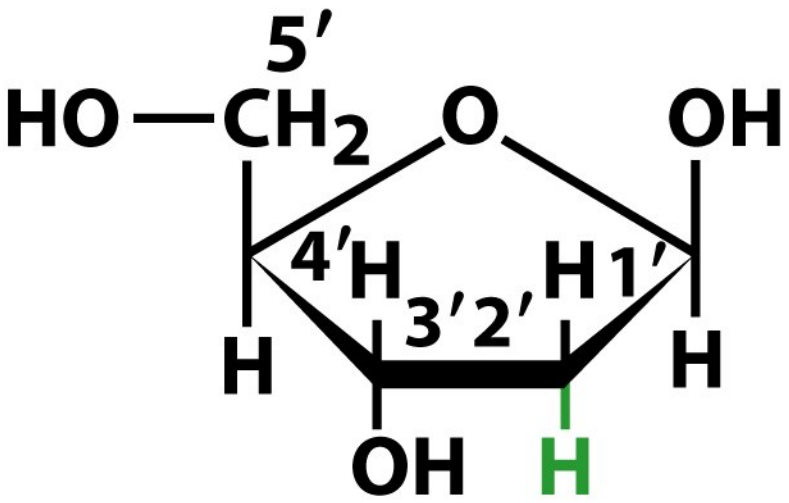
Aldehyde

β-Furanose

Pentoses



Ribose



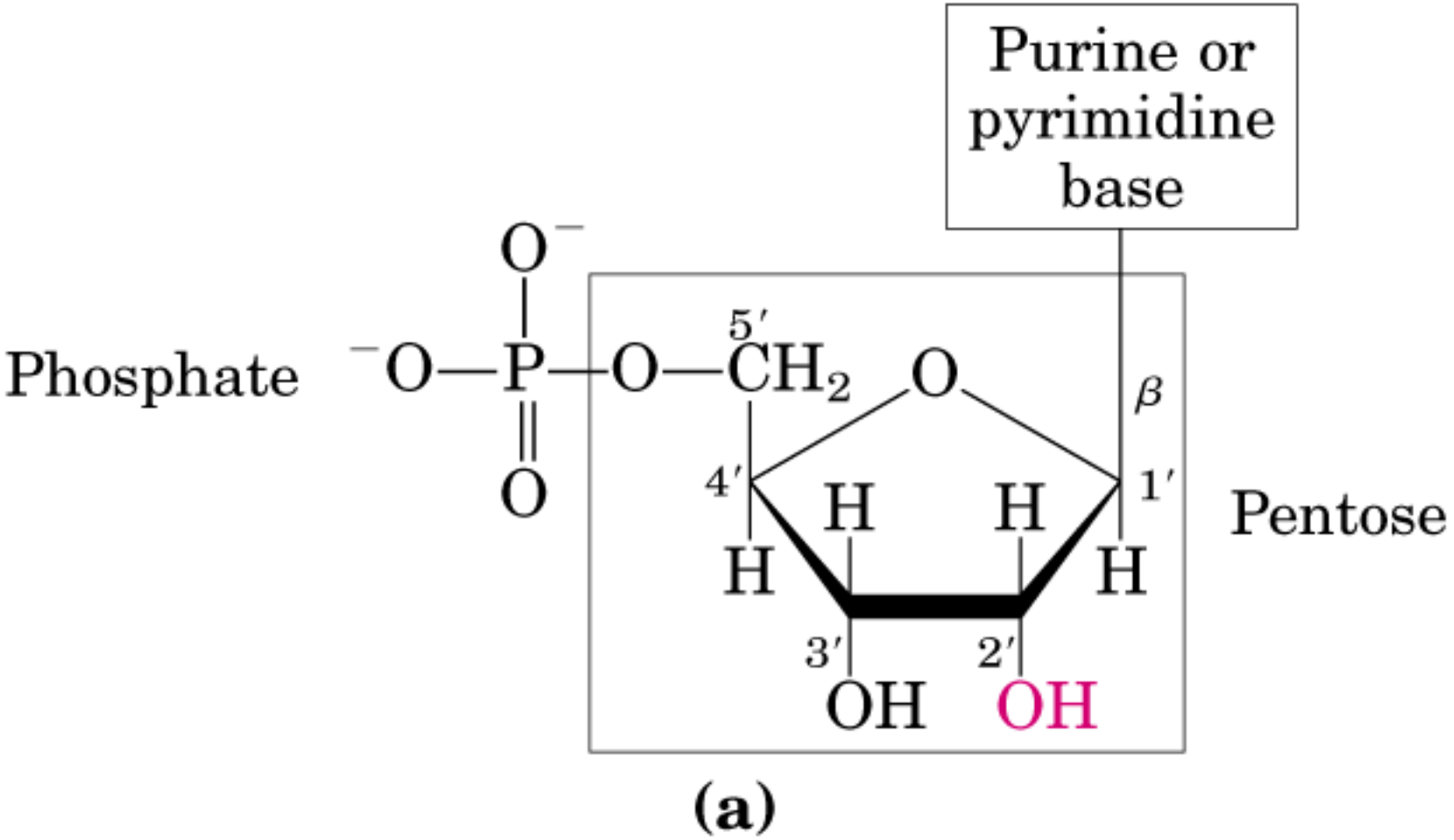
Deoxyribose

Unnumbered figure pg 42 Fundamentals of Biochemistry, 2/e

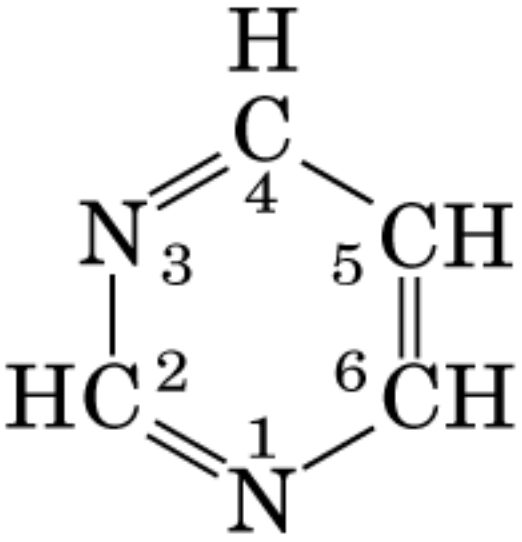
RNA

DNA

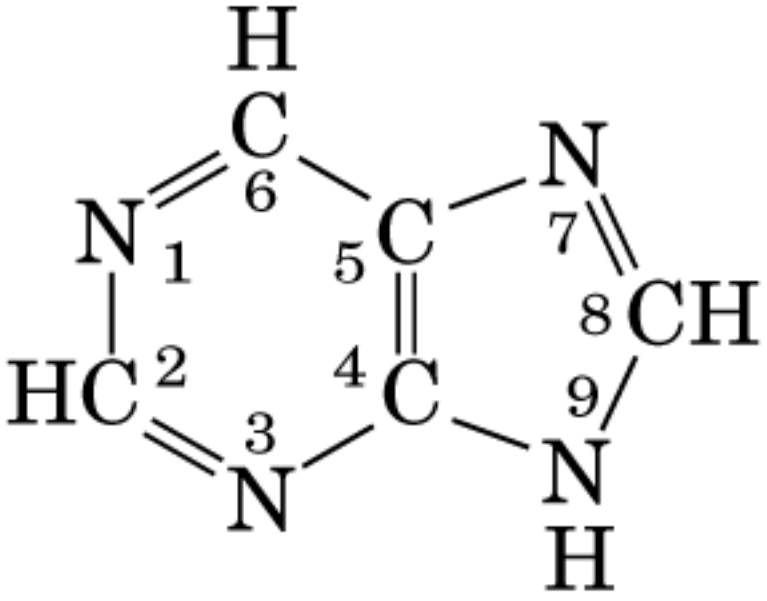
Nucleotídeo



Bases

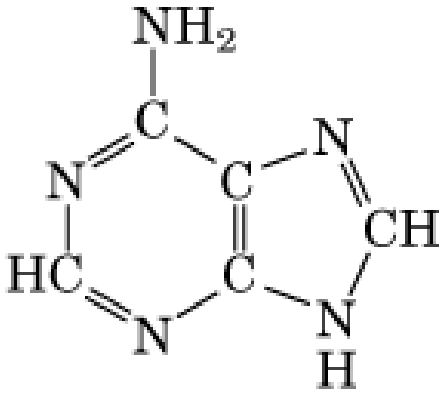


Pyrimidine

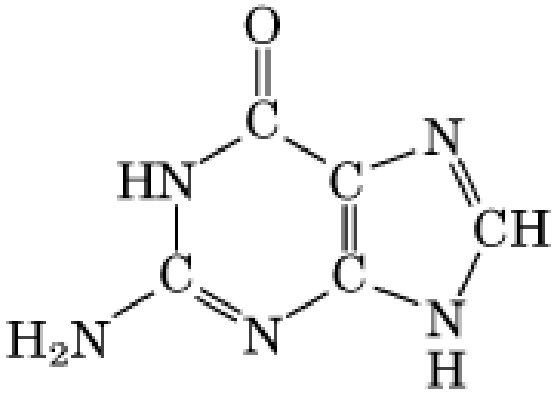


Purine

(b)

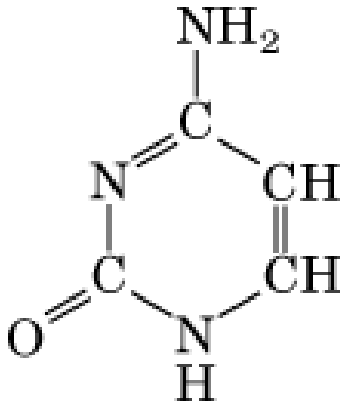


Adenine

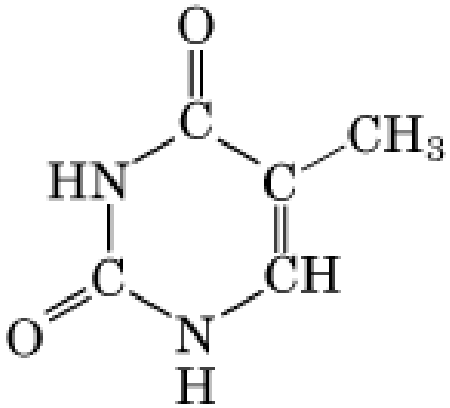


Guanine

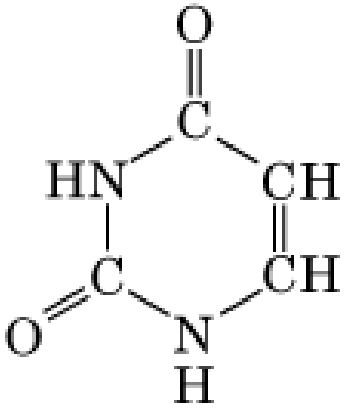
Purines



Cytosine



Thymine
(DNA)



Uracil
(RNA)

Pyrimidines

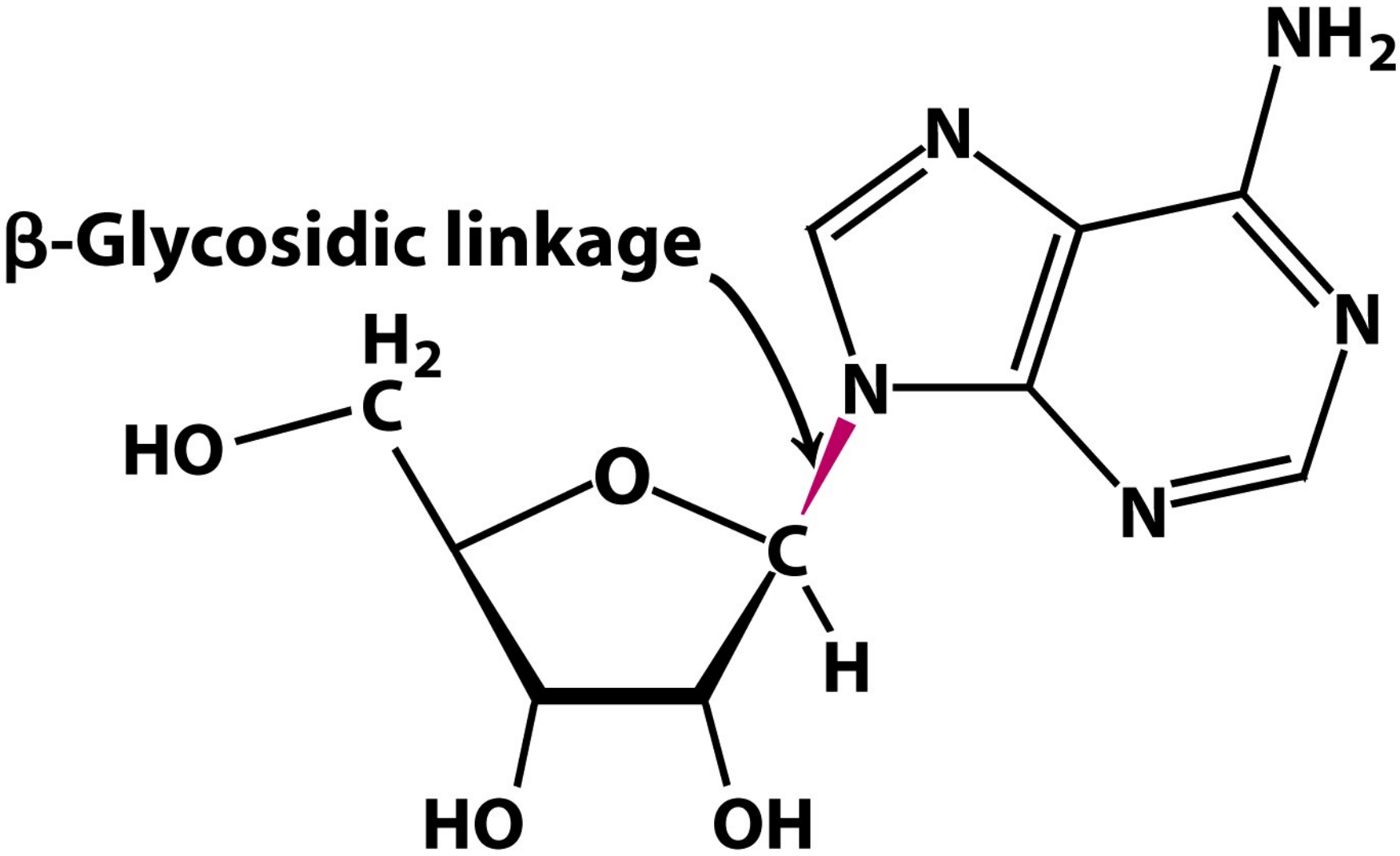


Figure 4-5
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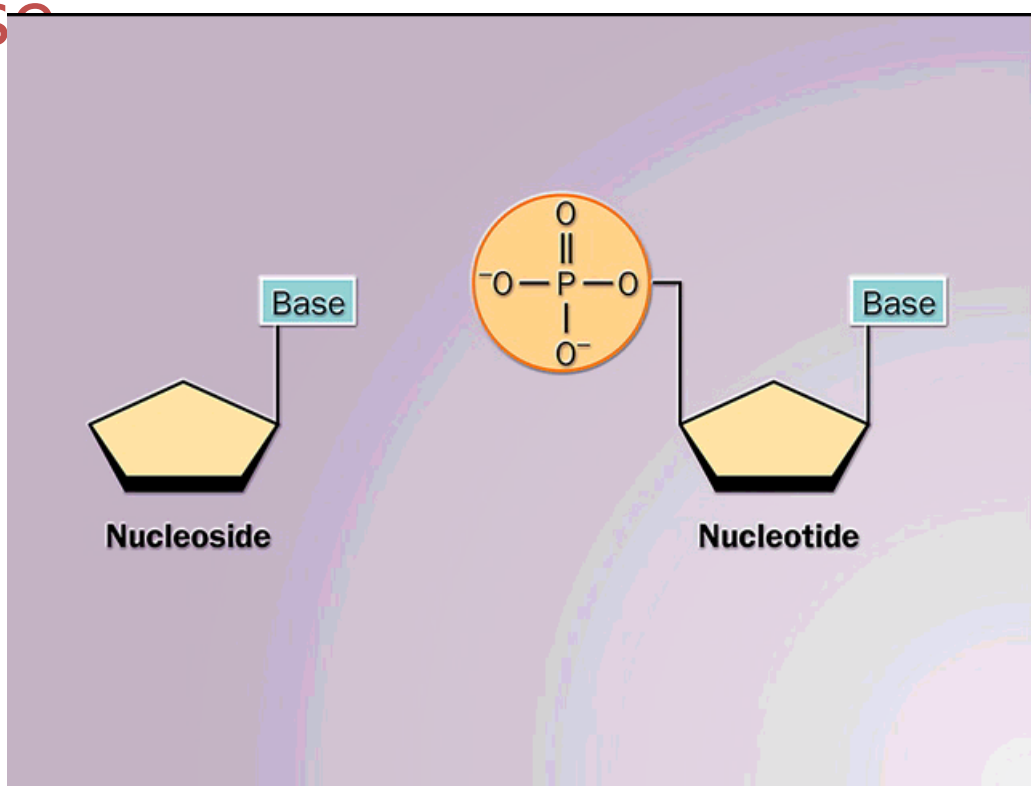
Nucleotídeos

- Base nitrogenada + Pentose + Fosfato
- Nucleosídeo = Base nitrogenada + Pentose



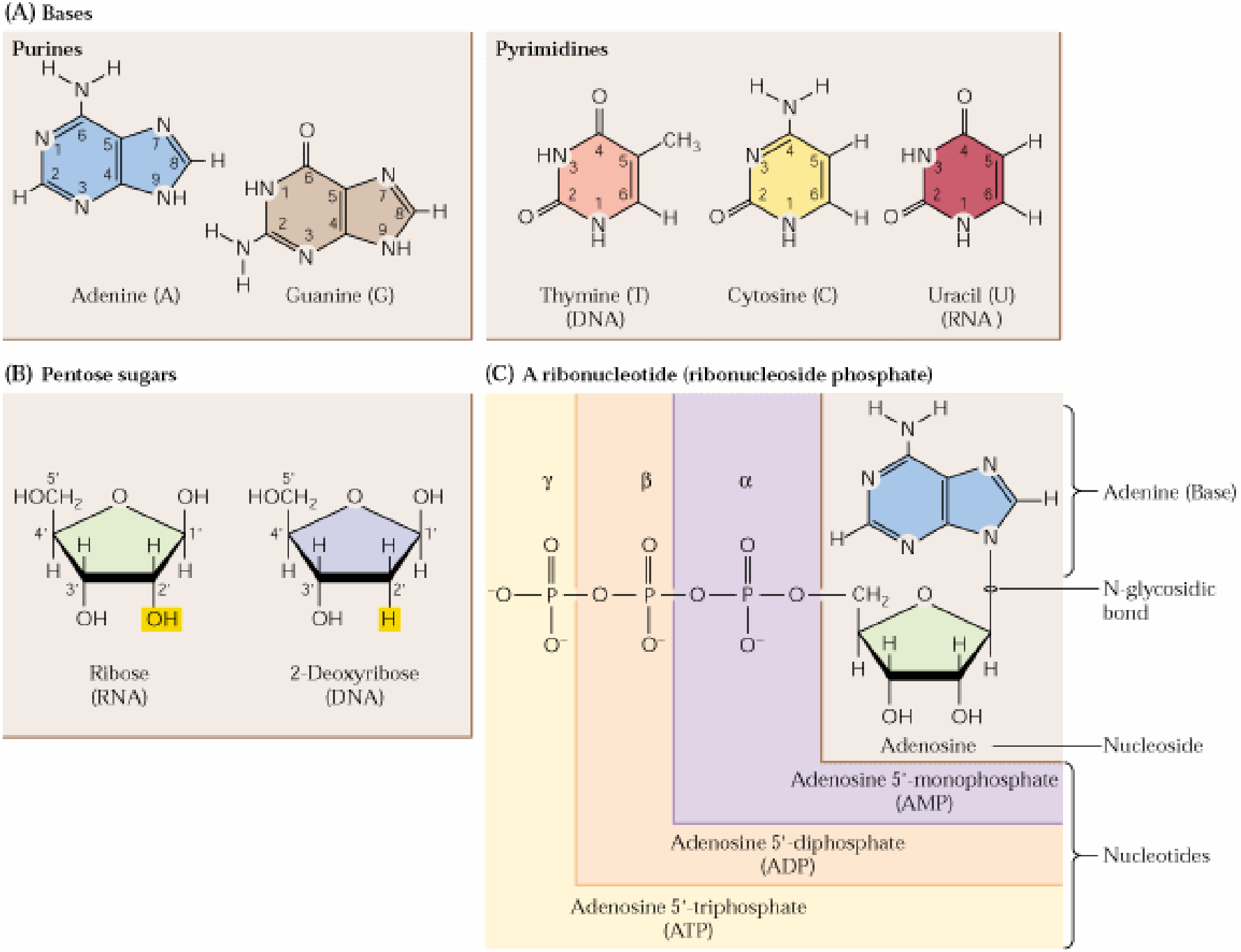
Ácidos Nucleicos

Numeração:

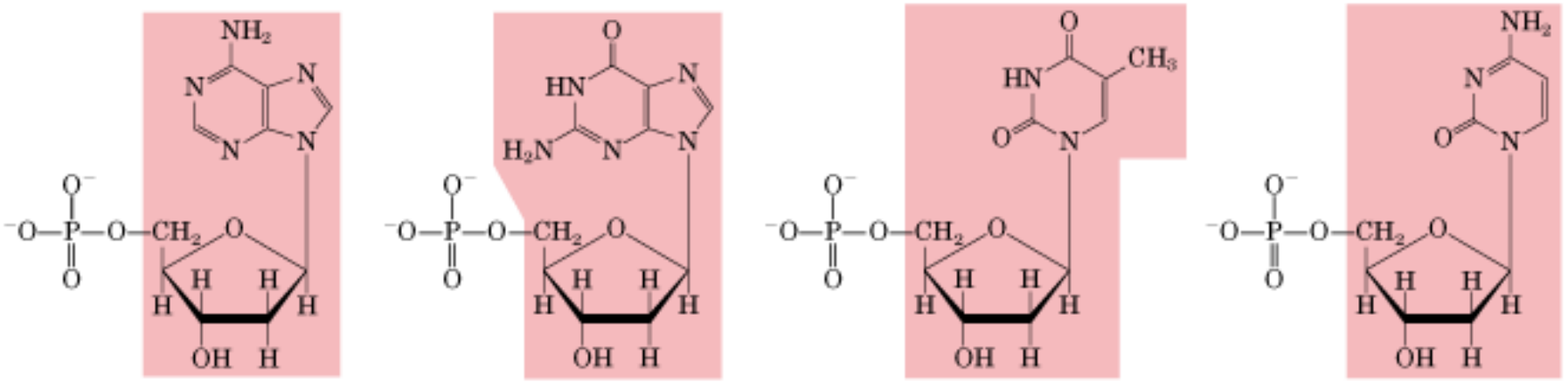
- Pentose = Carbonos – 1’ a 5’
- Base nitrogenada – pirimidinas = 1 a 6
  purinas = 1 a 9
- Ligação pentose – pirimidina – C 1’ N-1
  pentose – purina – C 1’- N-9
- Fosfato 5’: mono-, di-, tri- = fósforo

α β

γ


(A) Bases
Purines
Adenine (A)
Guanine (G)
Pyrimidines
Thymine (T)
(DNA)
Cytosine (C)
Uracil (U)
(RNA)
(B) Pentose sugars
Ribose
(RNA)
2-Deoxyribose
(DNA)
(C) A ribonucleotide (ribonucleoside phosphate)
Adenine (Base)
N-glycosidic bond
Adenosine
Nucleoside
Adenosine 5'-monophosphate (AMP)
Adenosine 5'-diphosphate (ADP)
Adenosine 5'-triphosphate (ATP)
Nucleotides

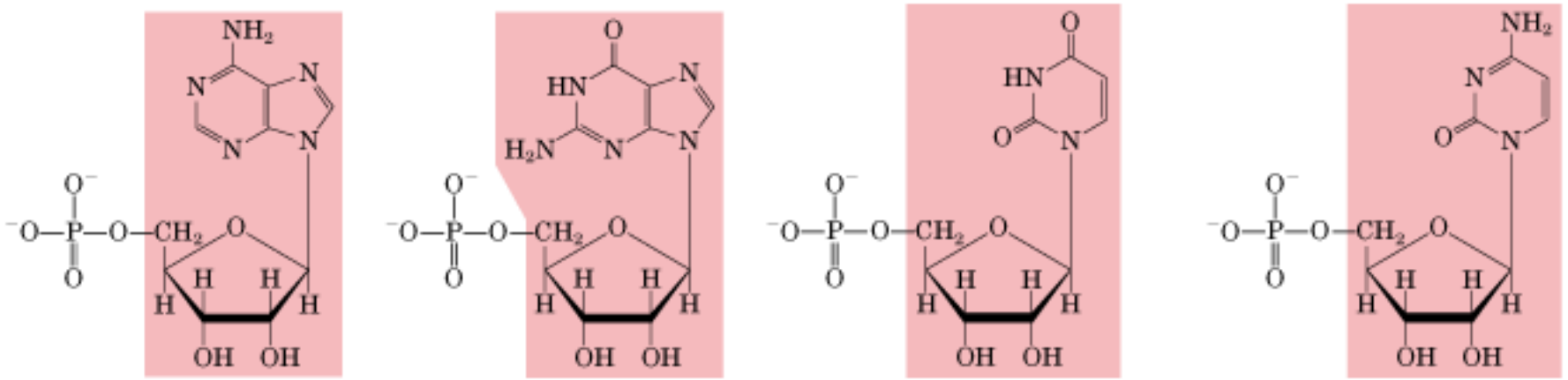
Nucleotídeos , Nucleosídeos



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

(a) Deoxyribonucleotides

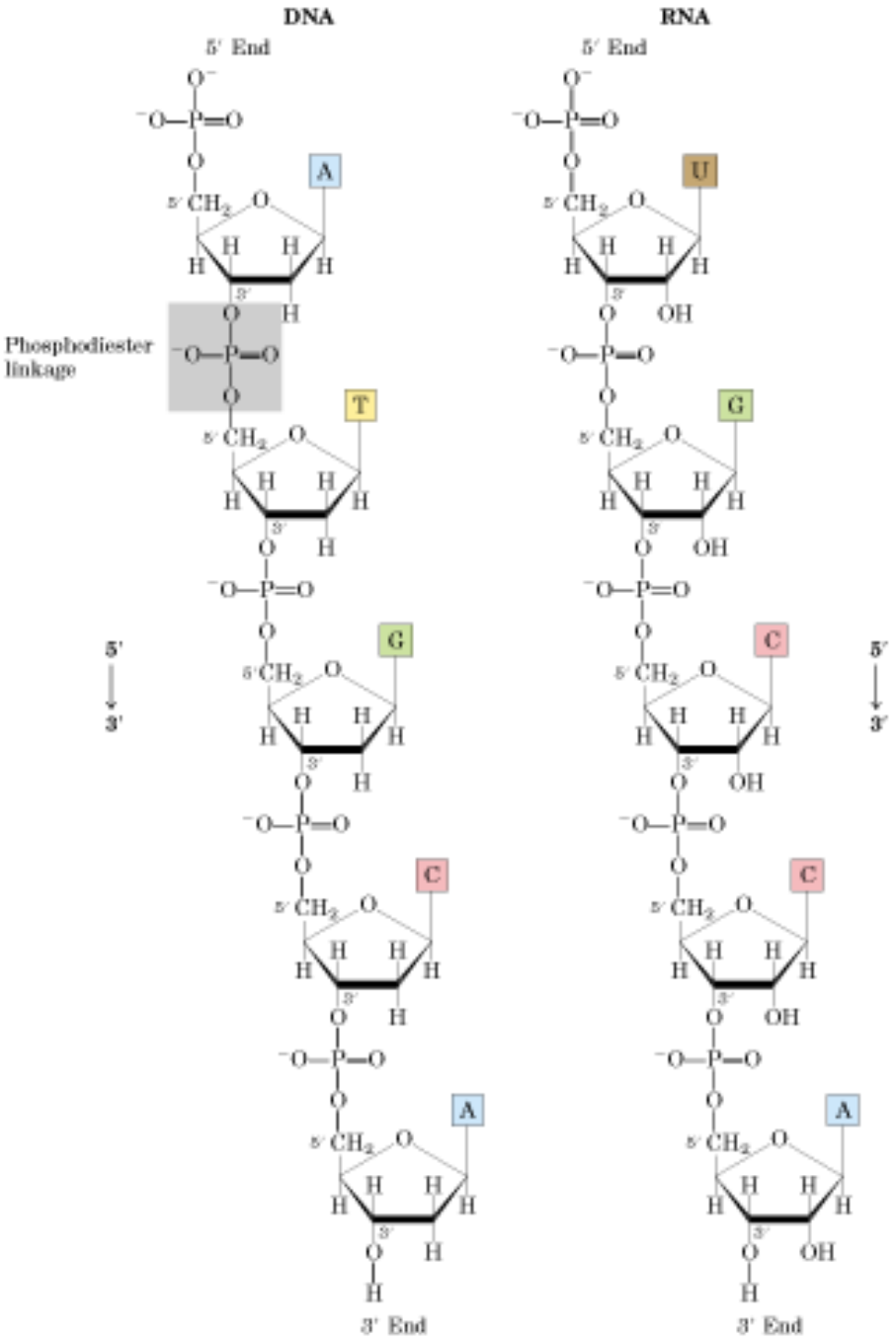
Nucleotídeos , Nucleosídeos



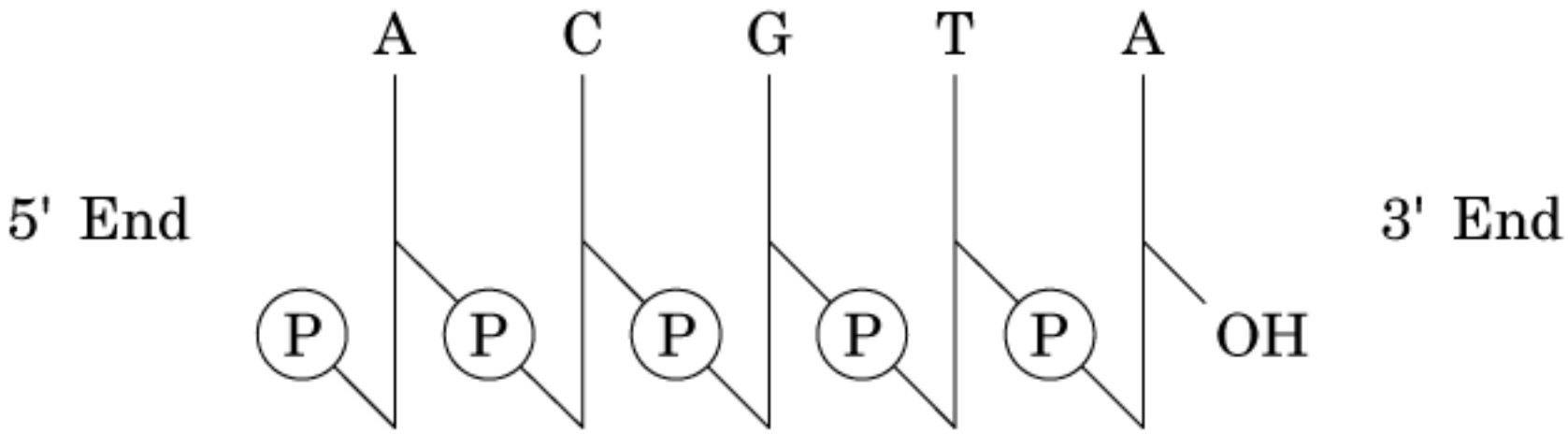
	Adenylate (adenosine 5′-monophosphate)	Guanylate (guanosine 5′-monophosphate)	Uridylate (uridine 5′-monophosphate)	Cytidylate (cytidine 5′-monophosphate)
Nucleotide:				
Symbols:	A, AMP	G, GMP	U, UMP	C, CMP
Nucleoside:	Adenosine	Guanosine	Uridine	Cytidine

(b) Ribonucleotides

Ligação fosfodiéster

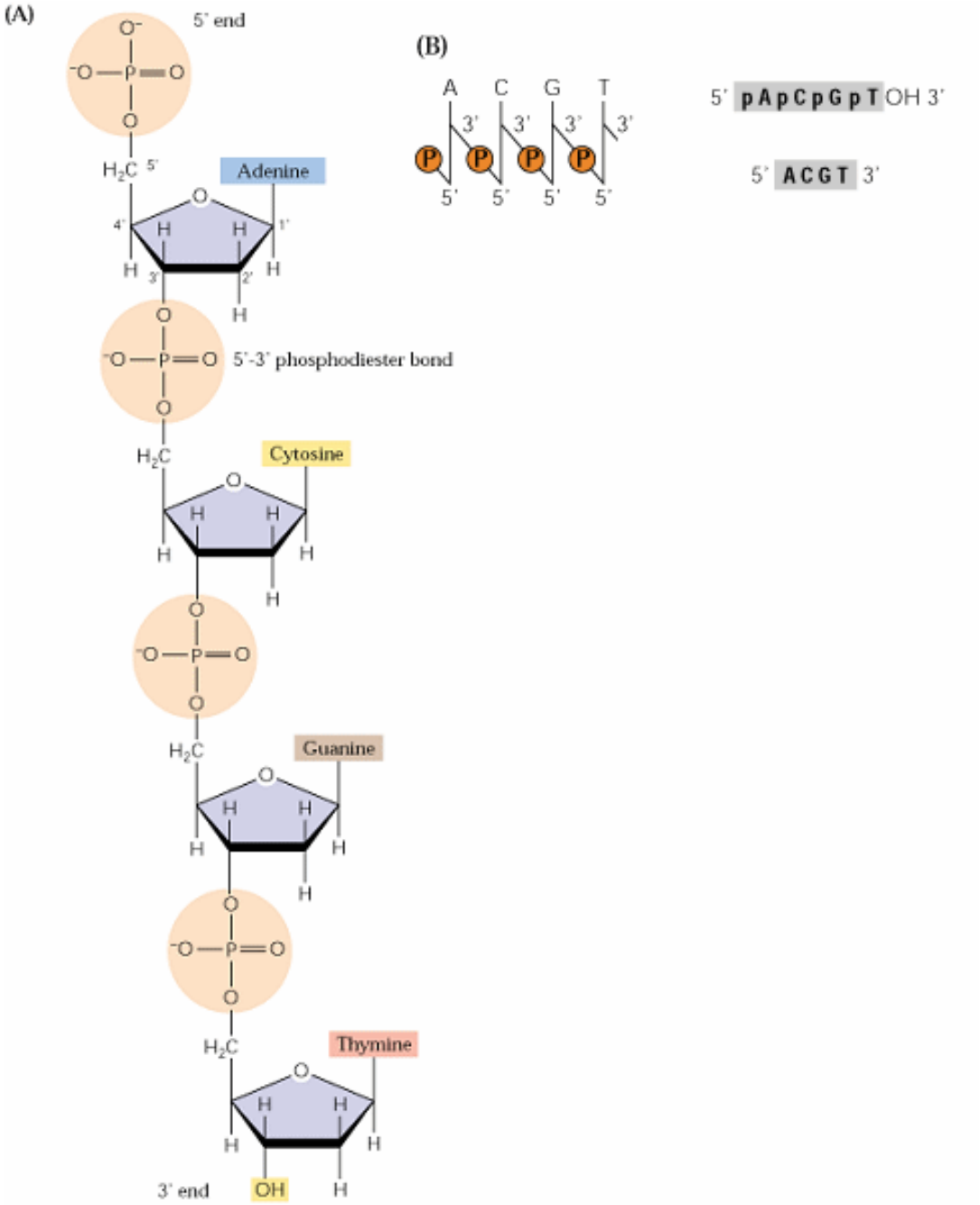


Ligação fosfodiéster

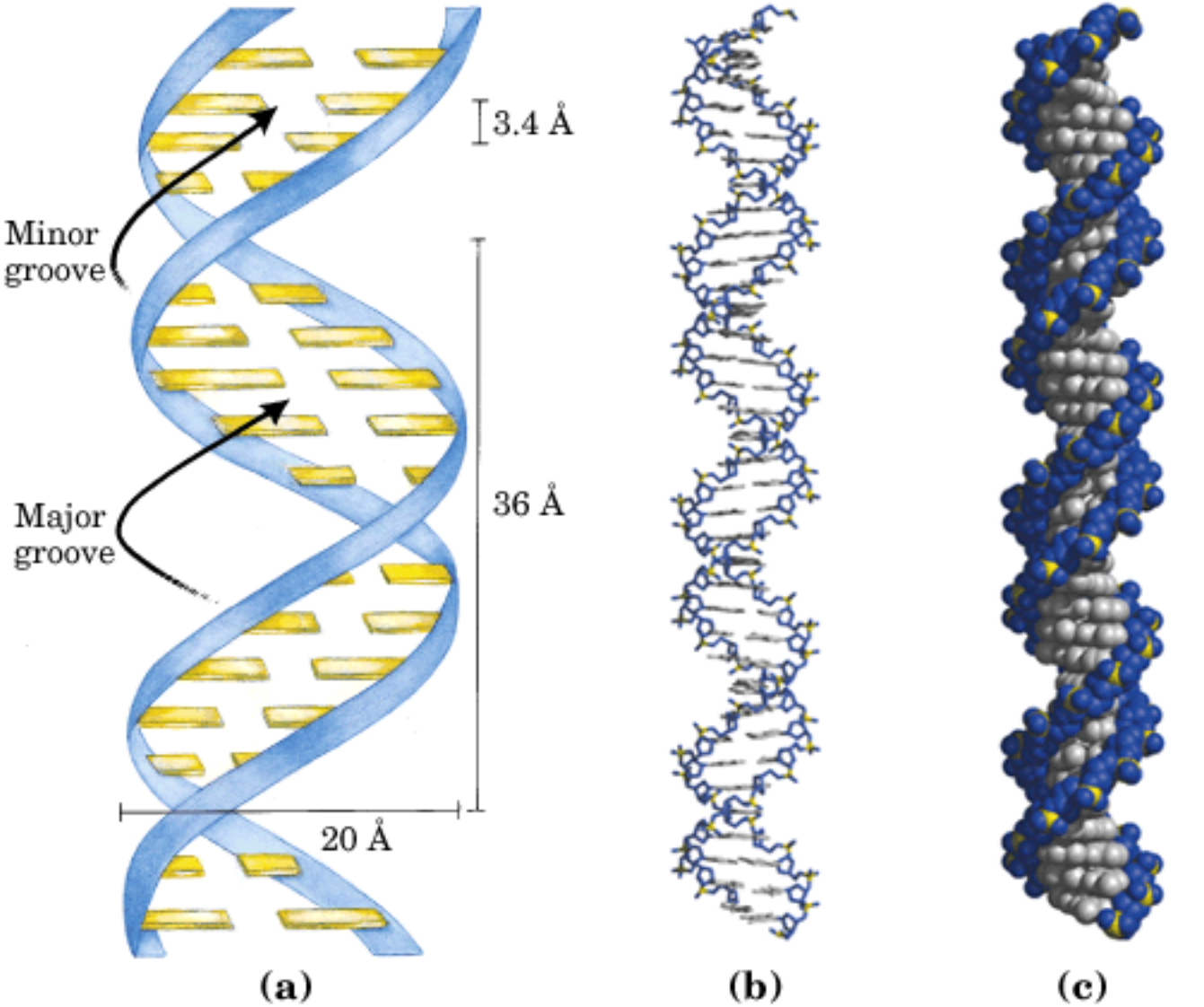


Ligação Fosfodiester

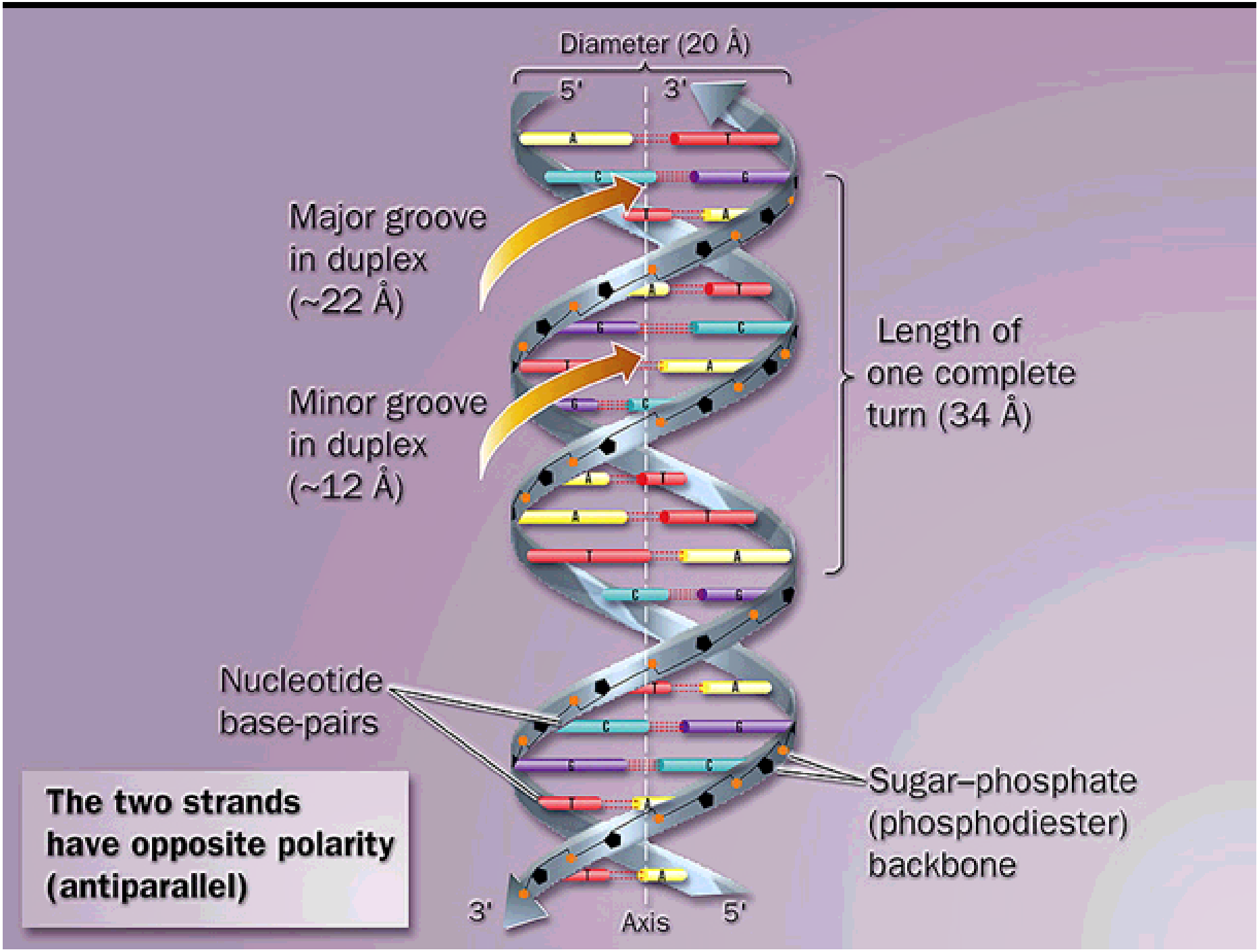
Polaridade
5’ -> 3’



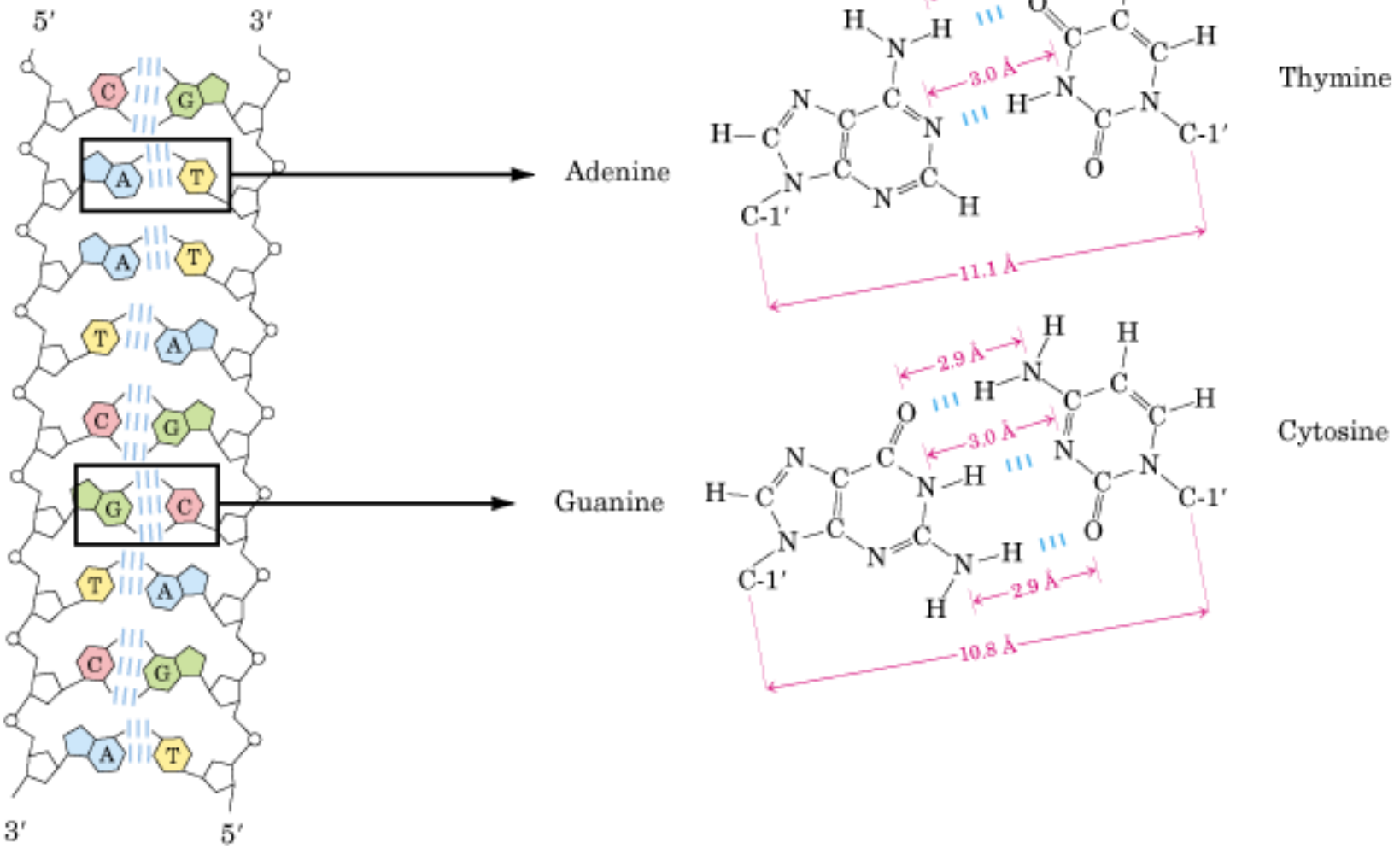
Estrutura do DNA (Watson e Crick 1953)



Dupla hélice


Diameter (20 Å)
5'
3'
Major groove in duplex (~22 Å)
Minor groove in duplex (~12 Å)
Length of one complete turn (34 Å)
Nucleotide base-pairs
Sugar–phosphate (phosphodiester) backbone
The two strands have opposite polarity (antiparallel)
3'
Axis
5'

Pareamento de bases



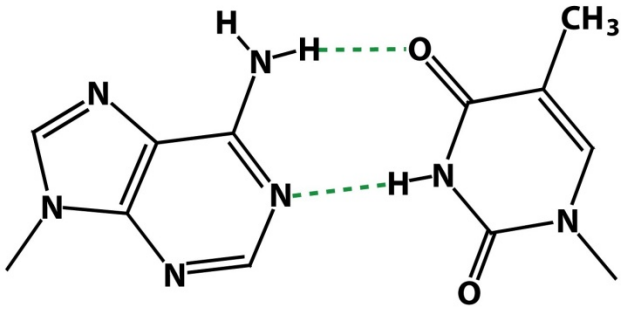


Figure 1-6 part 1
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Pontes de H

Estabilizam dupla hélice

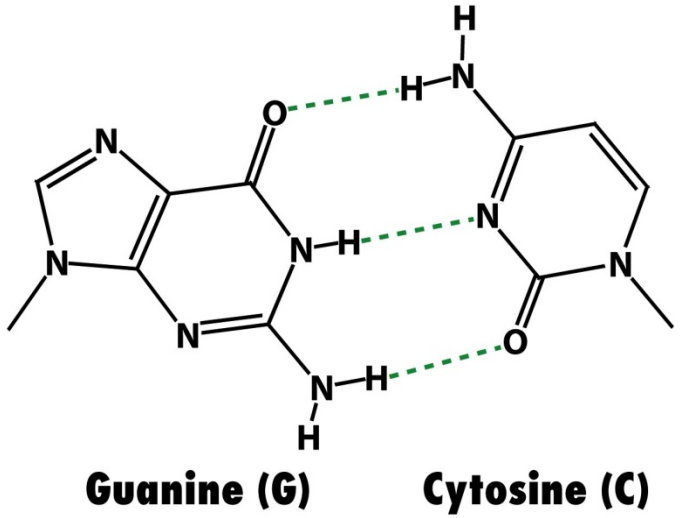

Figure 1-6 part 2
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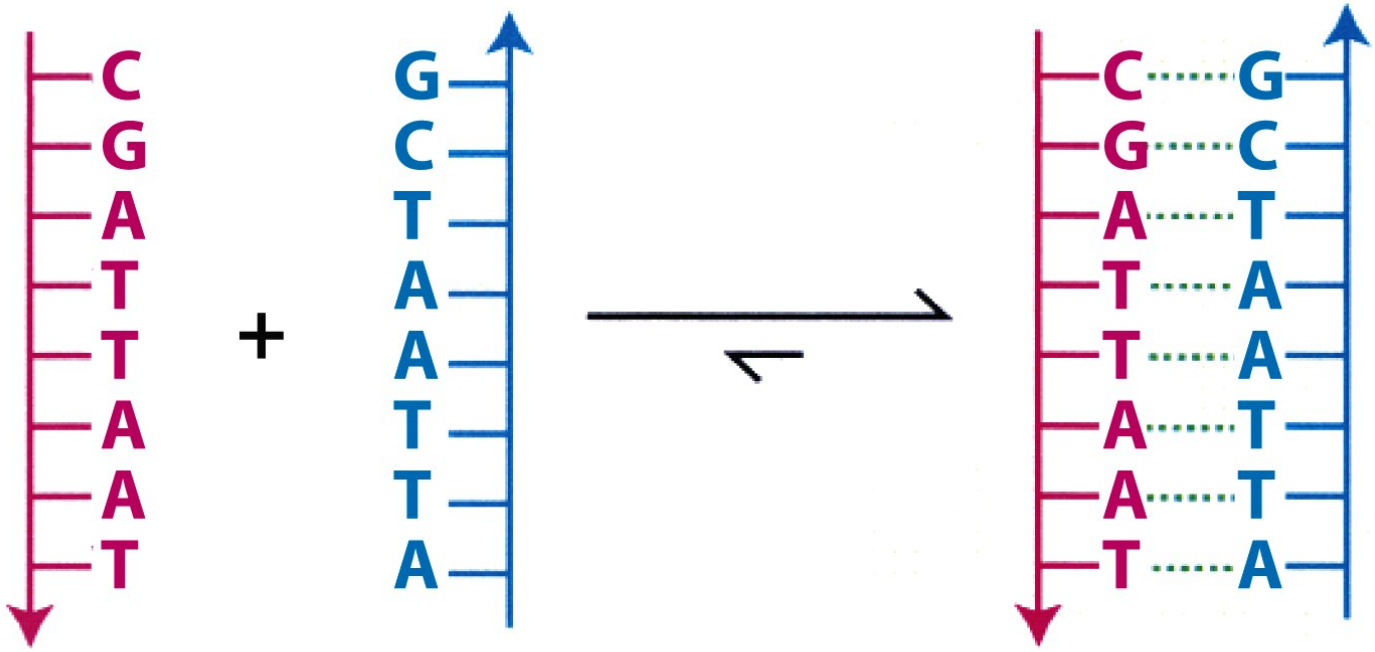

Figure 1-8
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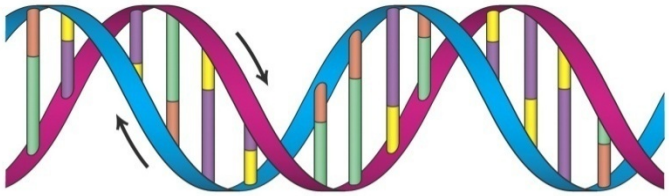

Empilhamento dos pares de bases

Minimiza o contato com moleculas de água

Estabilização da estrutura do DNA

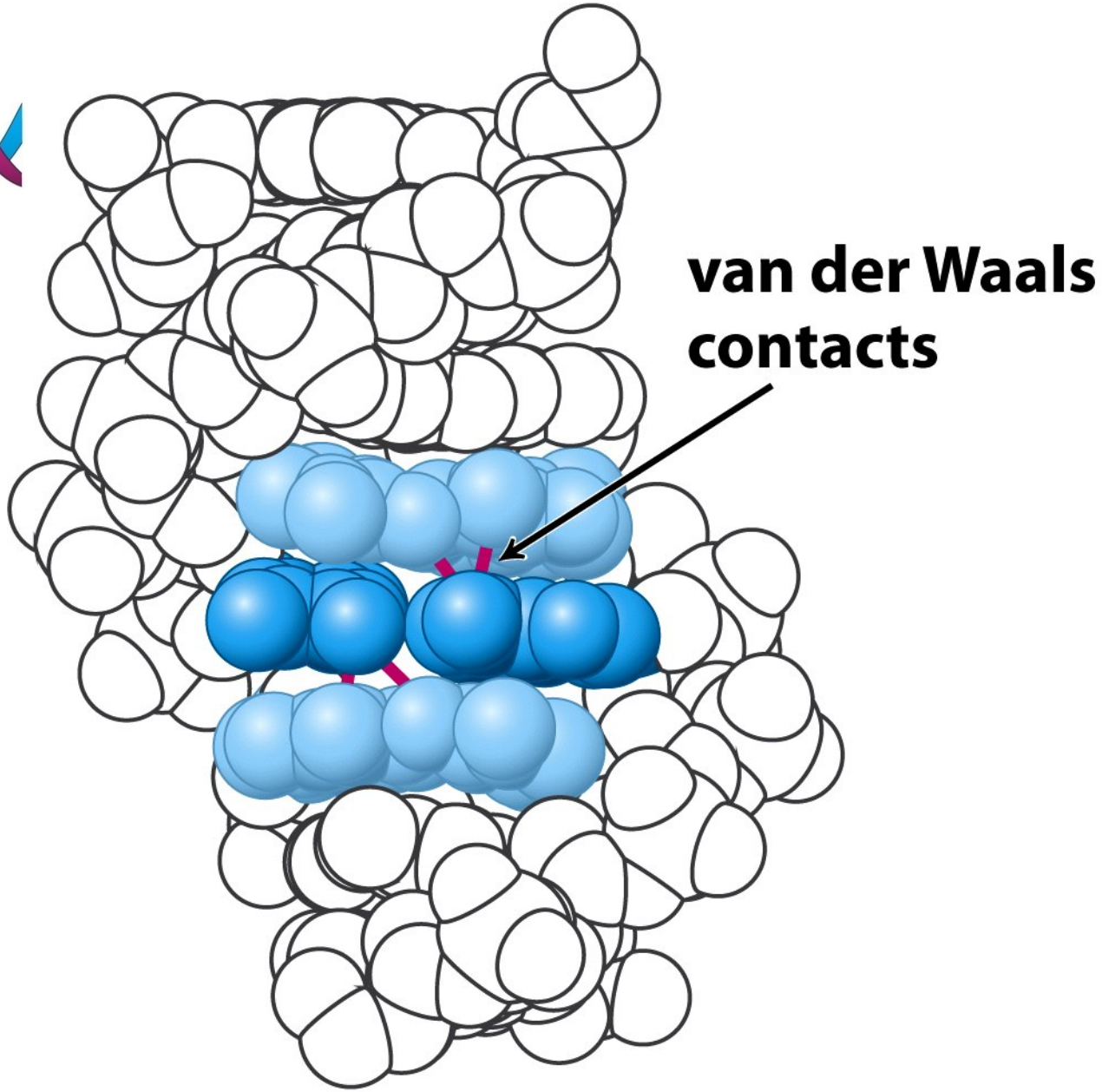

Figure 1-14
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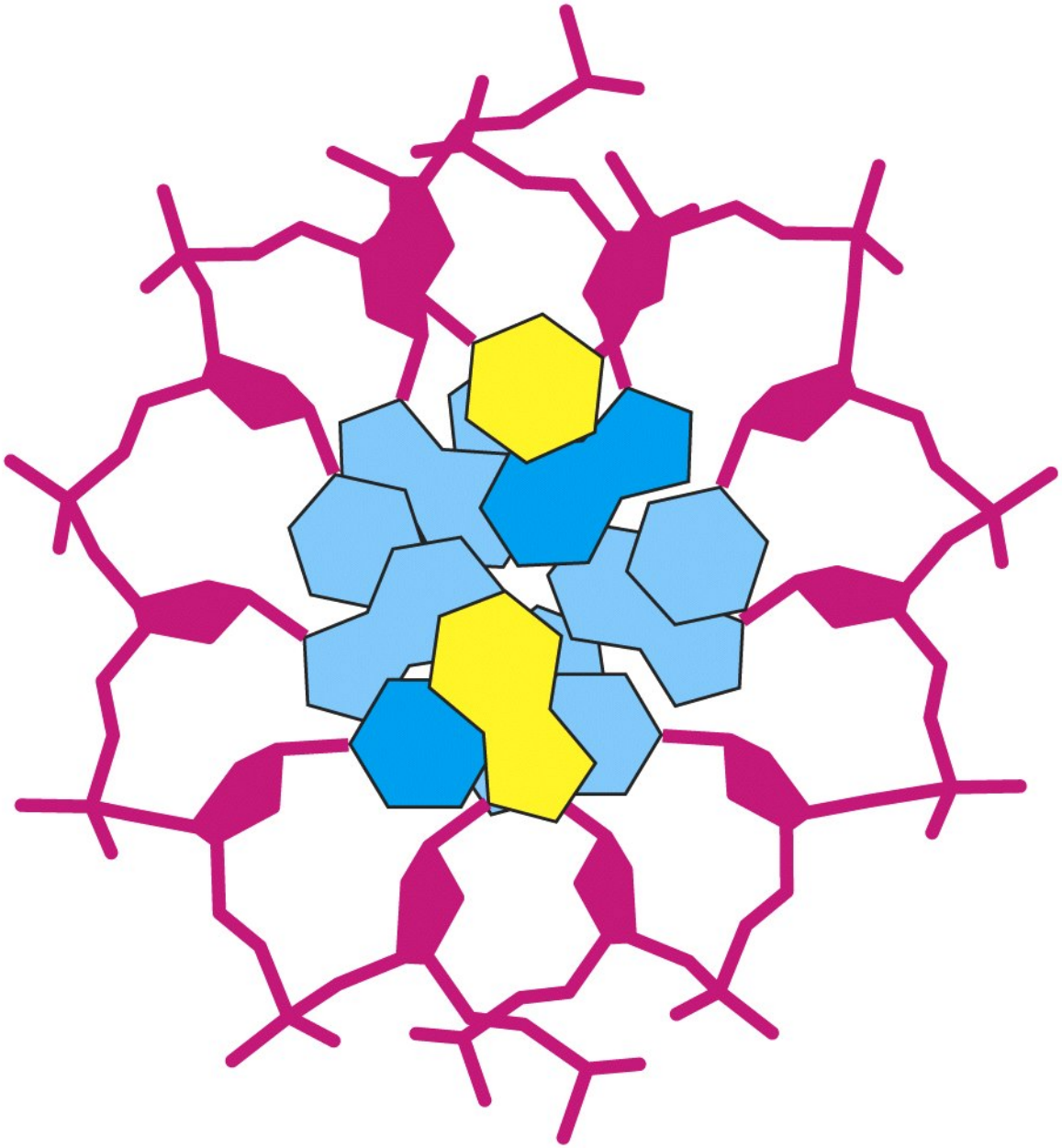

Figure 4-13
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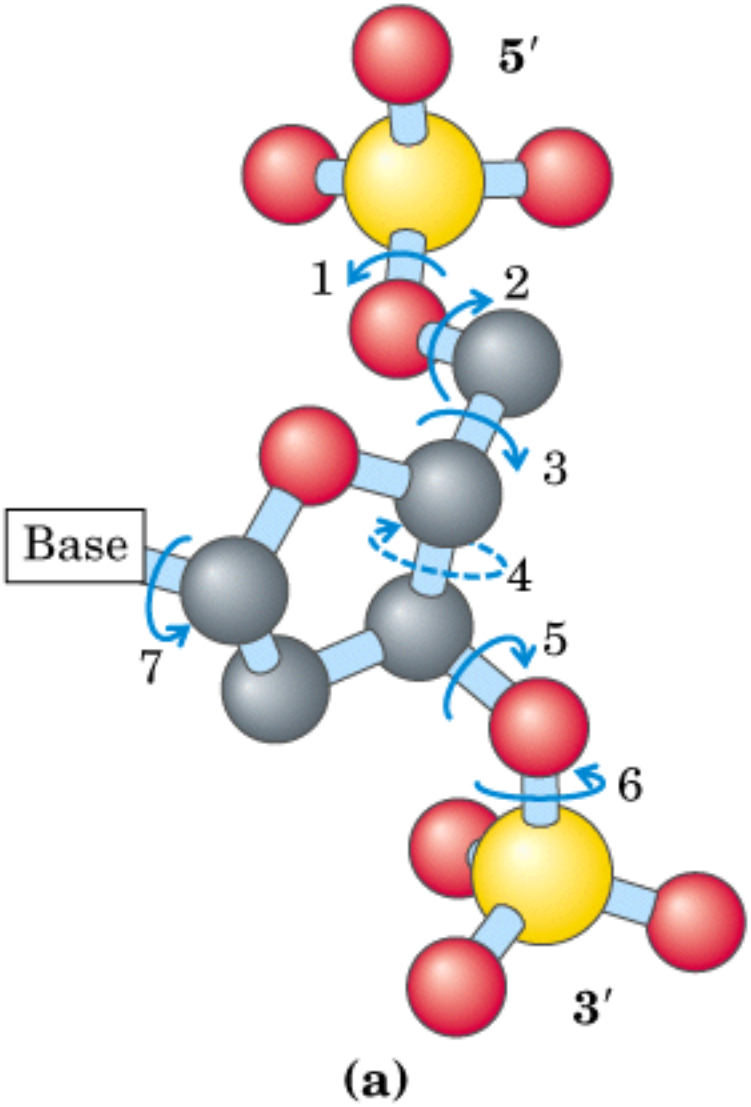
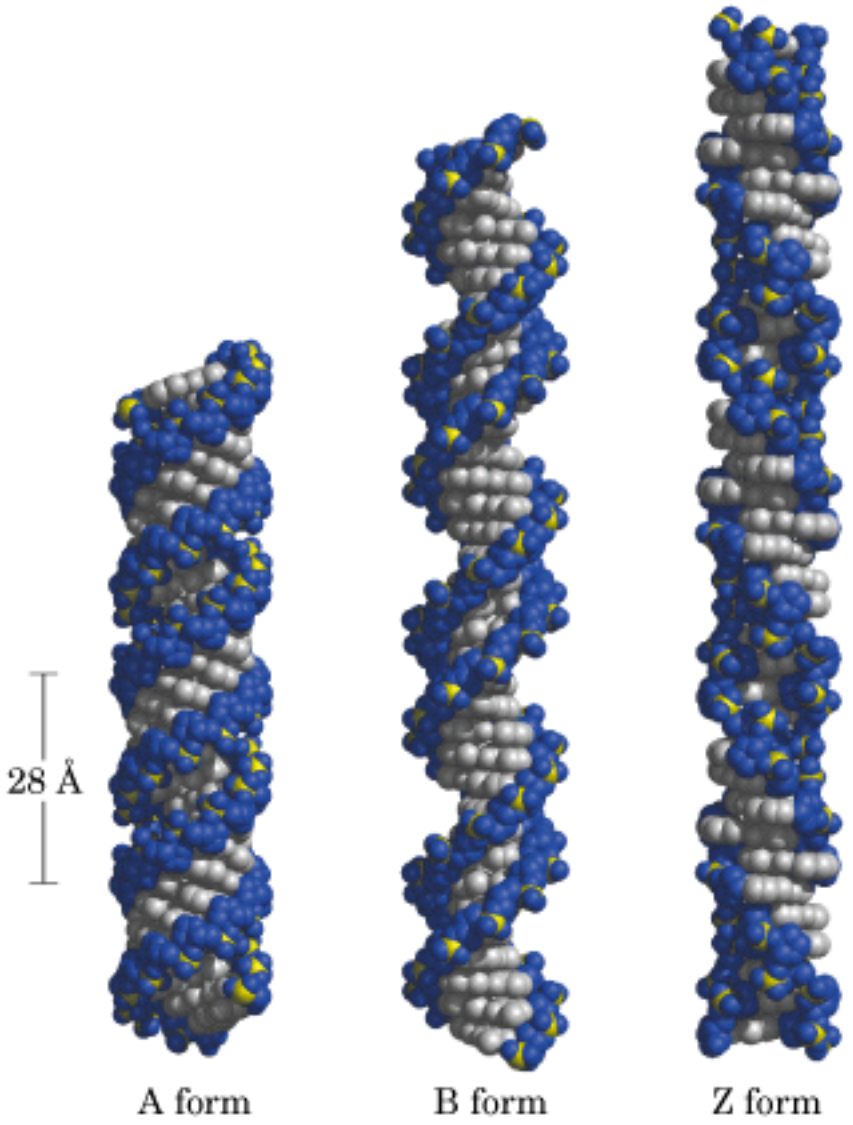
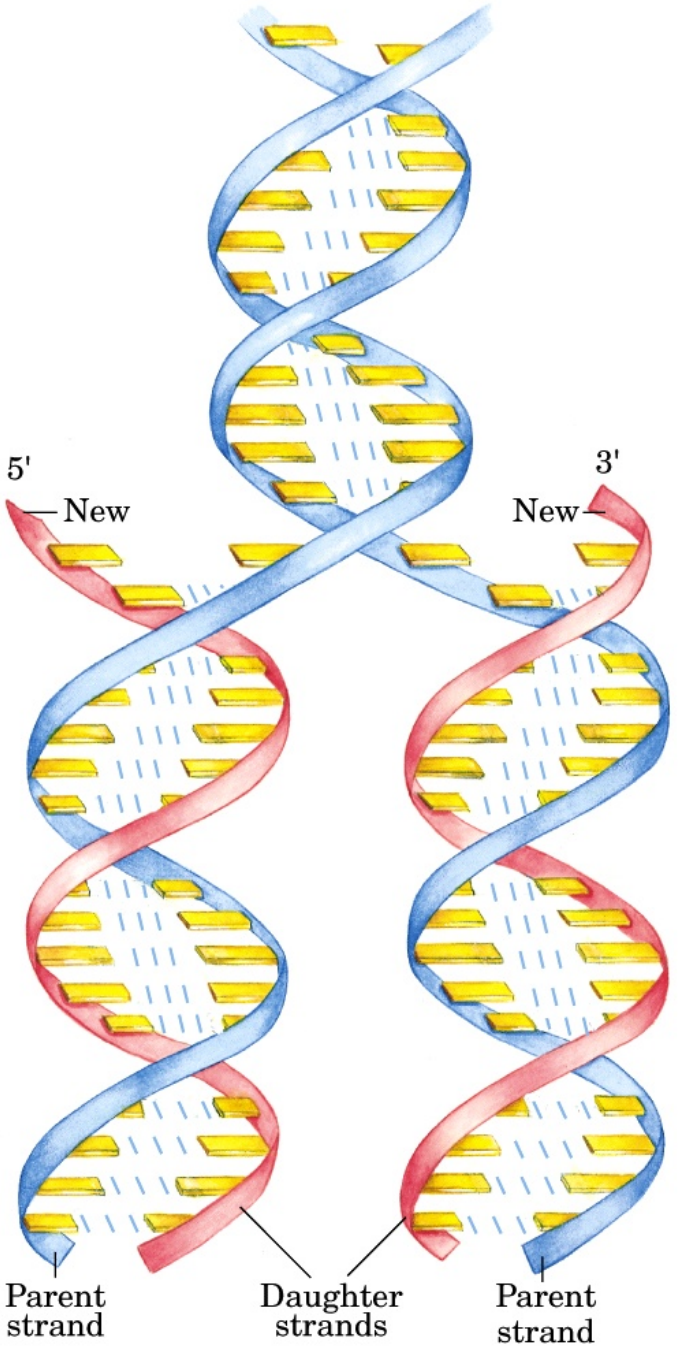
Variações estruturais no DNA





Replicação



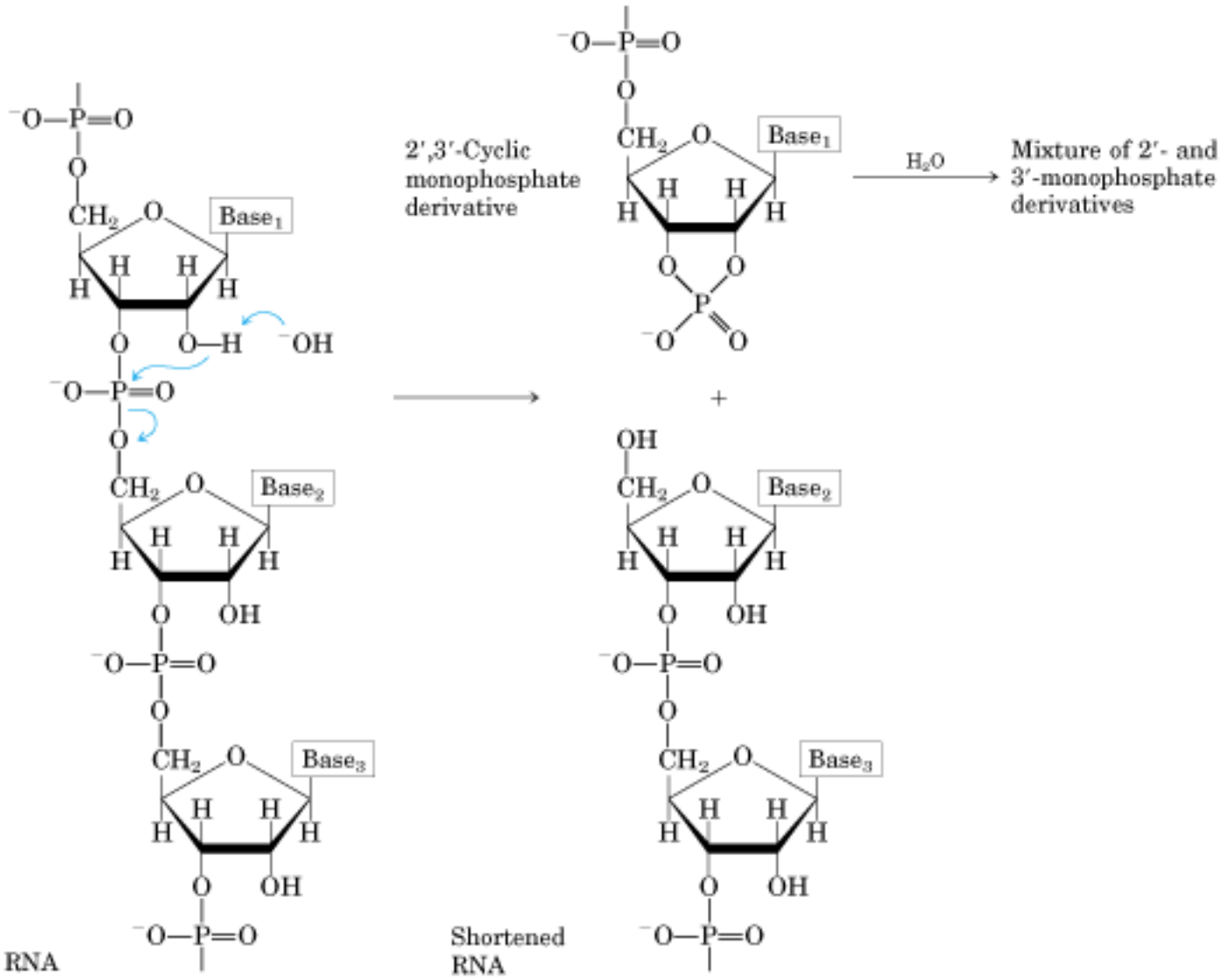
Química de Ácidos Nucleicos

Estabilidade do DNA - depósito genético!

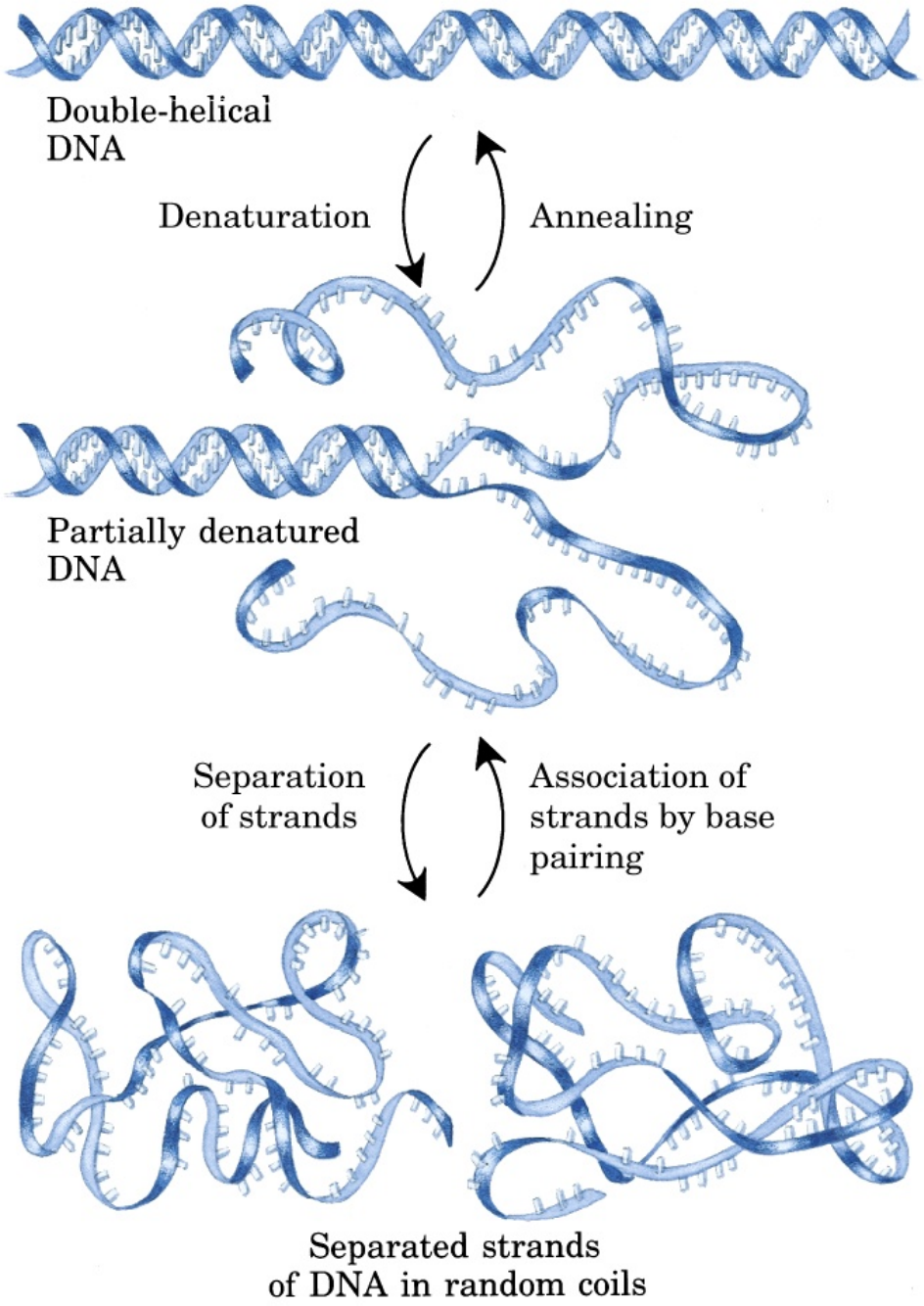
Propriedades

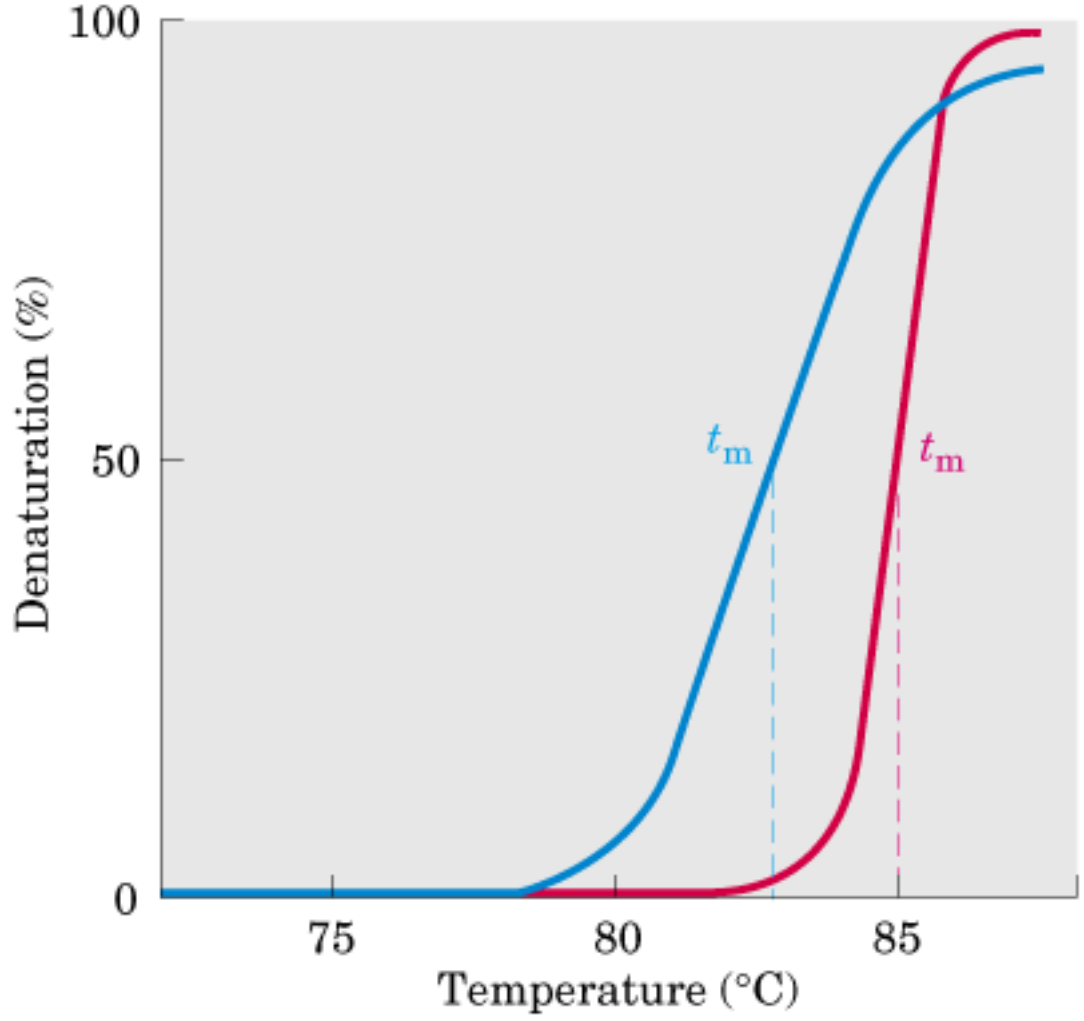
- Desnaturação = separação da dupla fita
  - quebra das pontes de H
  - causado por calor ou pH (e proteínas *in vivo*)
- Renaturação ou anelamento
  - decréscimo da temperatura ou pH
- Alteração na Absorbância (UV) Abs 260 nm
  - hipocromicidade: renaturação
  - hipercromicidade: desnaturação

Hidrólise alcalina do RNA



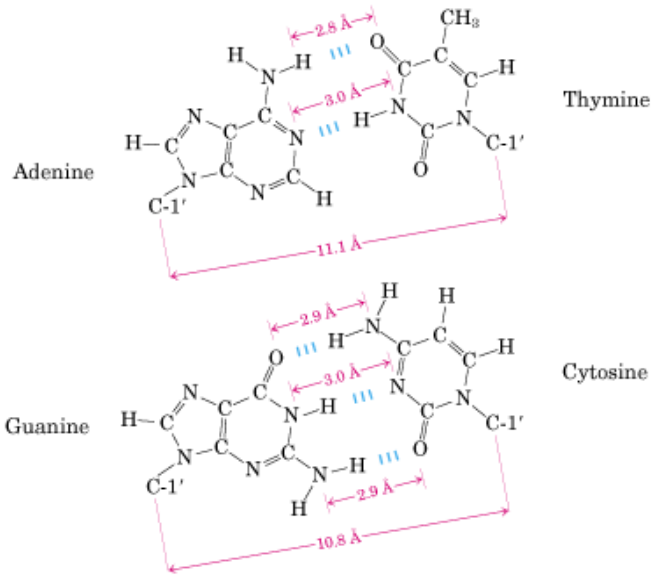
Desnaturação do DNA

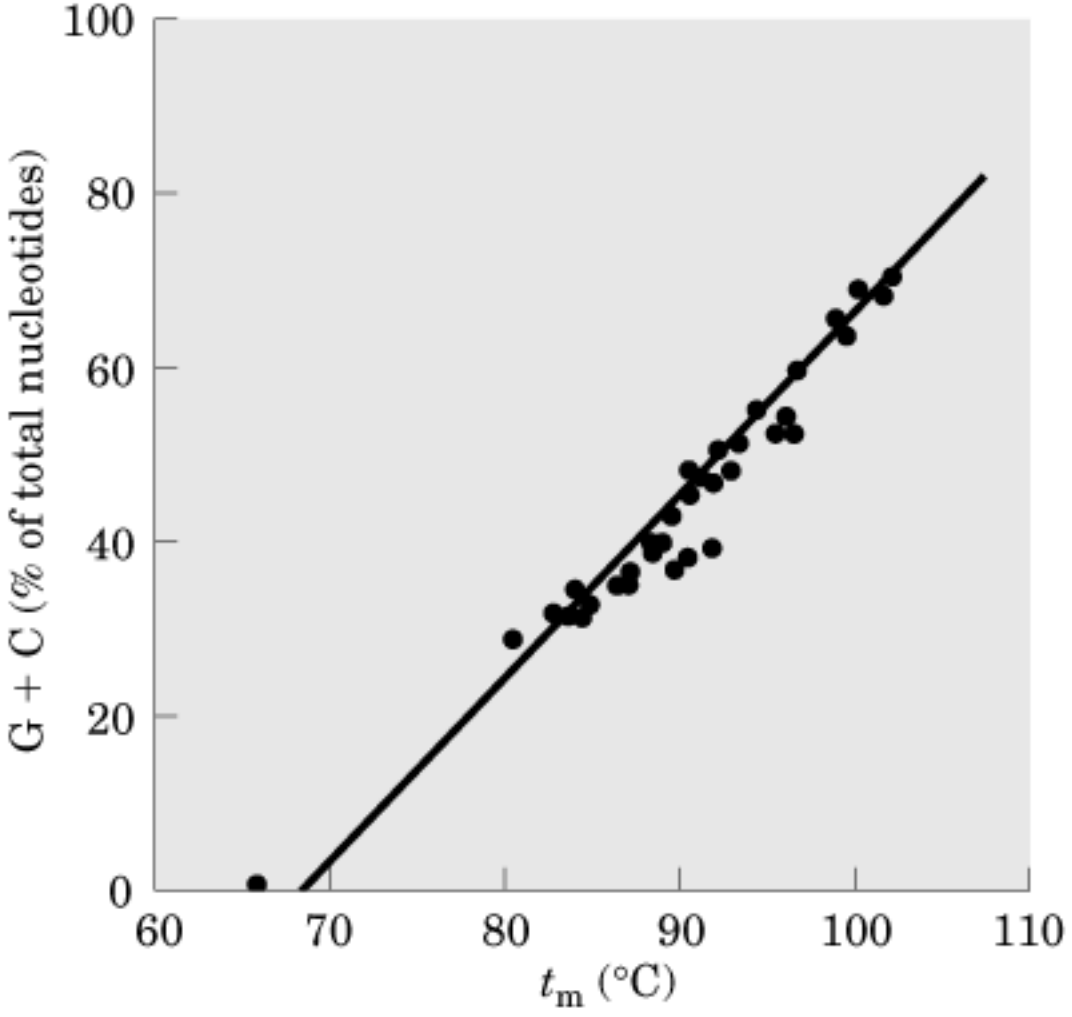




(a)

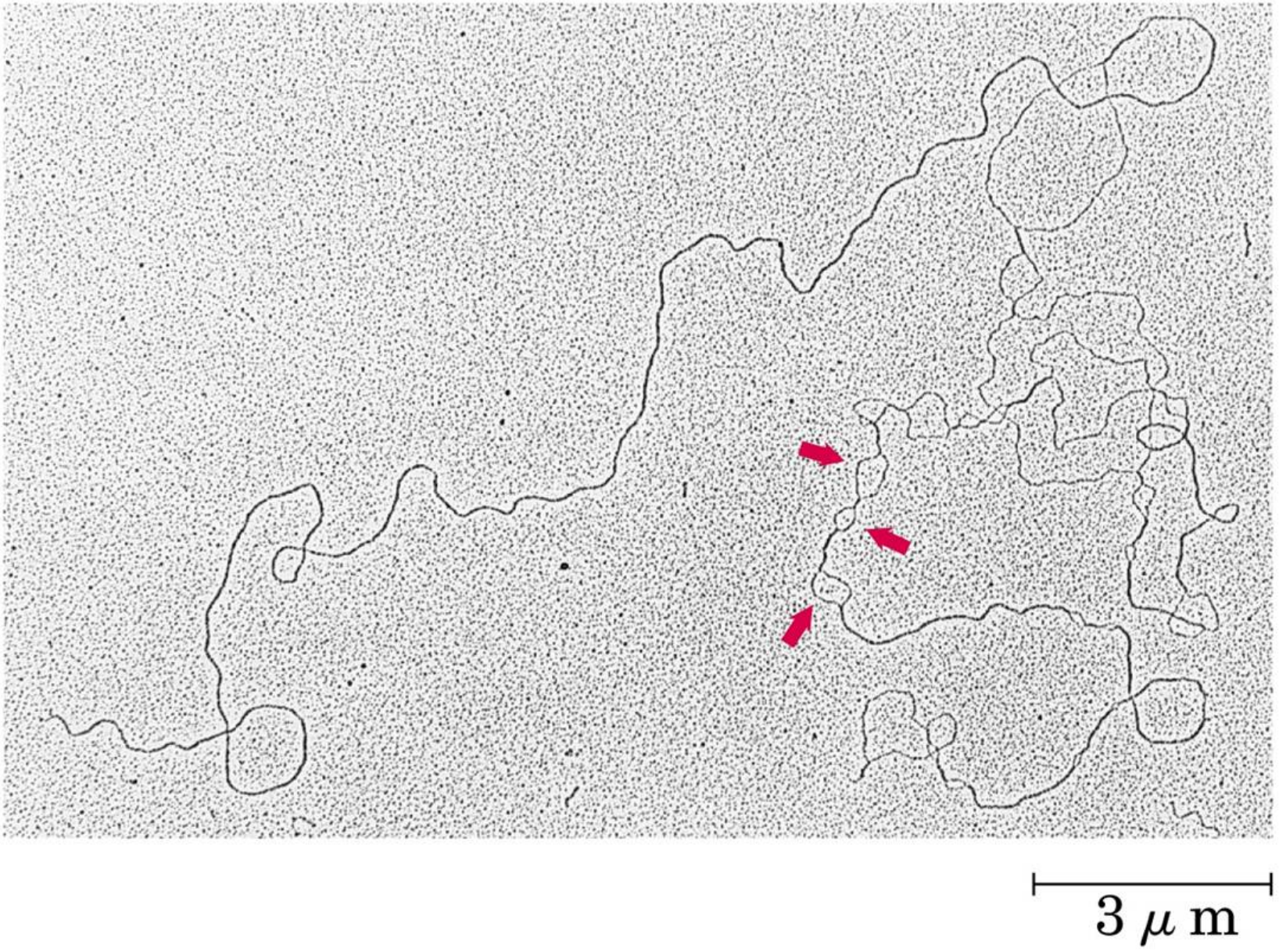
Tm = melting temperature (temperatura de fusão ou dissociação)

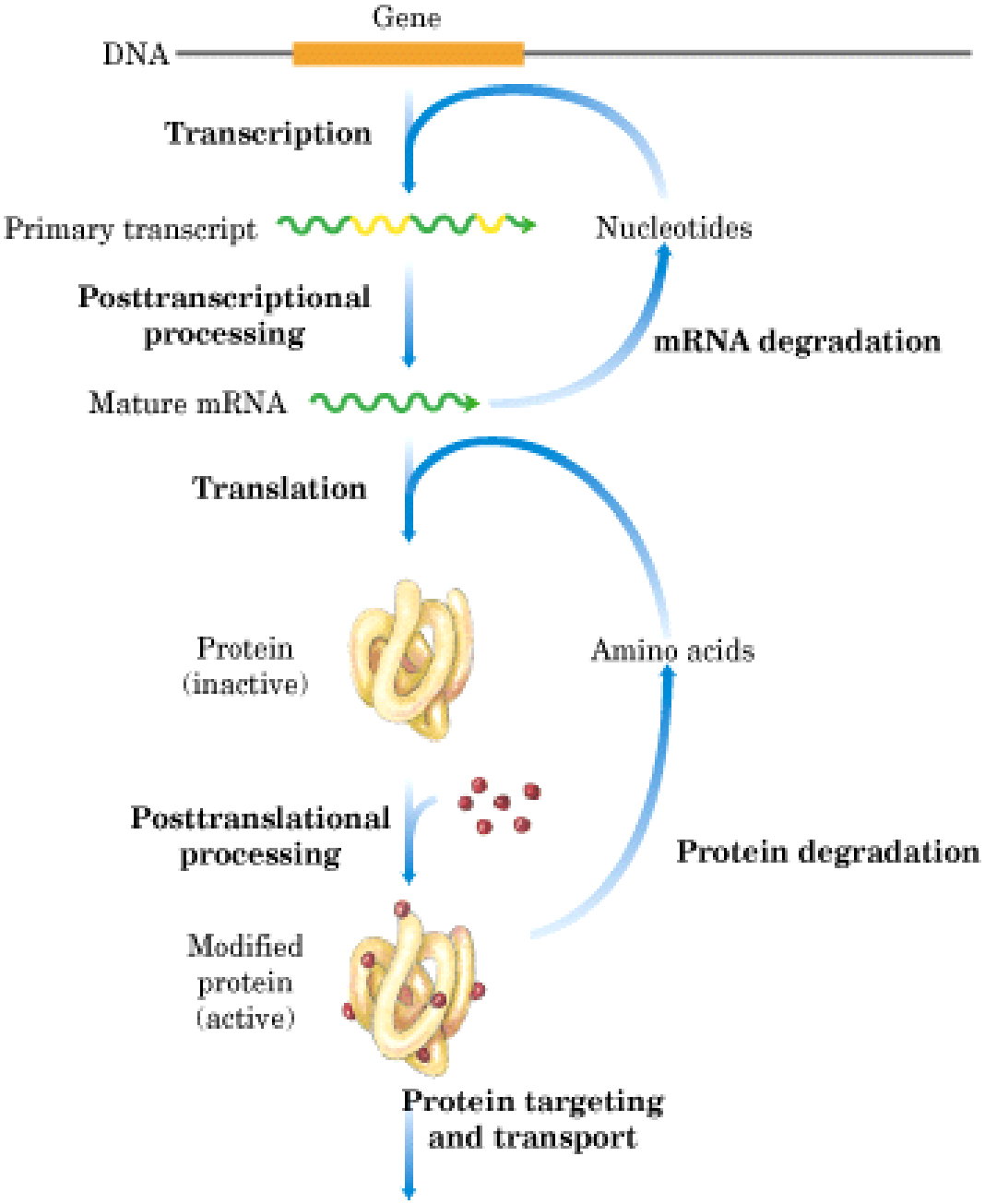

Adenine
Thymine
Guanine
Cytosine
2.8 Å
3.0 Å
11.1 Å
2.9 Å
3.0 Å
2.9 Å
10.8 Å


G + C (% of total nucleotides)
100
80
60
40
20
0
60
70
80
90
100
110
t_m (°C)

(b)

Desnaturação do DNA




Gene
DNA
Transcription
Primary transcript
Nucleotides
Posttranscriptional processing
mRNA degradation
Mature mRNA
Translation
Protein (inactive)
Amino acids
Posttranslational processing
Protein degradation
Modified protein (active)
Protein targeting and transport

Transcrição

5′—GCGGCGACGCGCAGUUAAUCCCACAGCCGCCAGUUCCGCUGGCGGCAU—3′ mRNA

3′—CGCCGCTGCGCGTCAATTAGGGTGTCGGCGGTCAAGGCGACCGCCGTA—5′ Template strand of DNA

5′—GCGGCGACGCGCAGTTAATCCCACAGCCGCCAGTTCCGCTGGCGGCAT—3′ Coding strand of DNA

Figure 4-26
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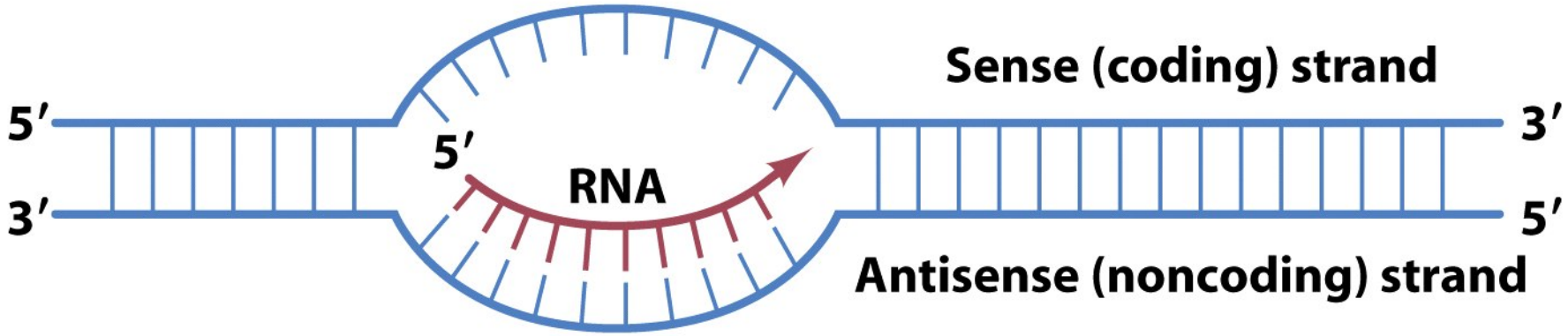

Figure 25-3 Fundamentals of Biochemistry, 2/e

Transcrição: região promotora

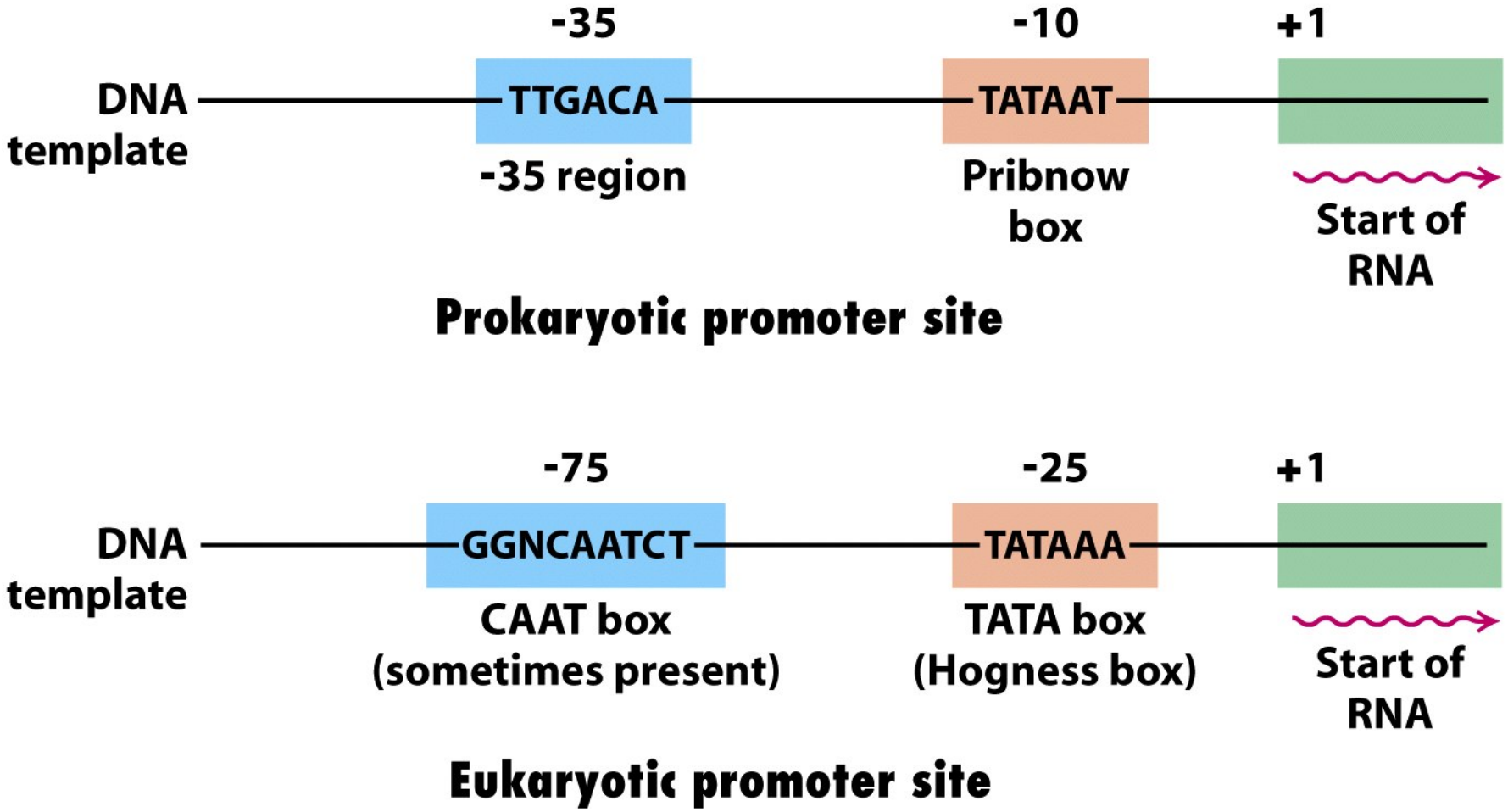

Figure 4-27b
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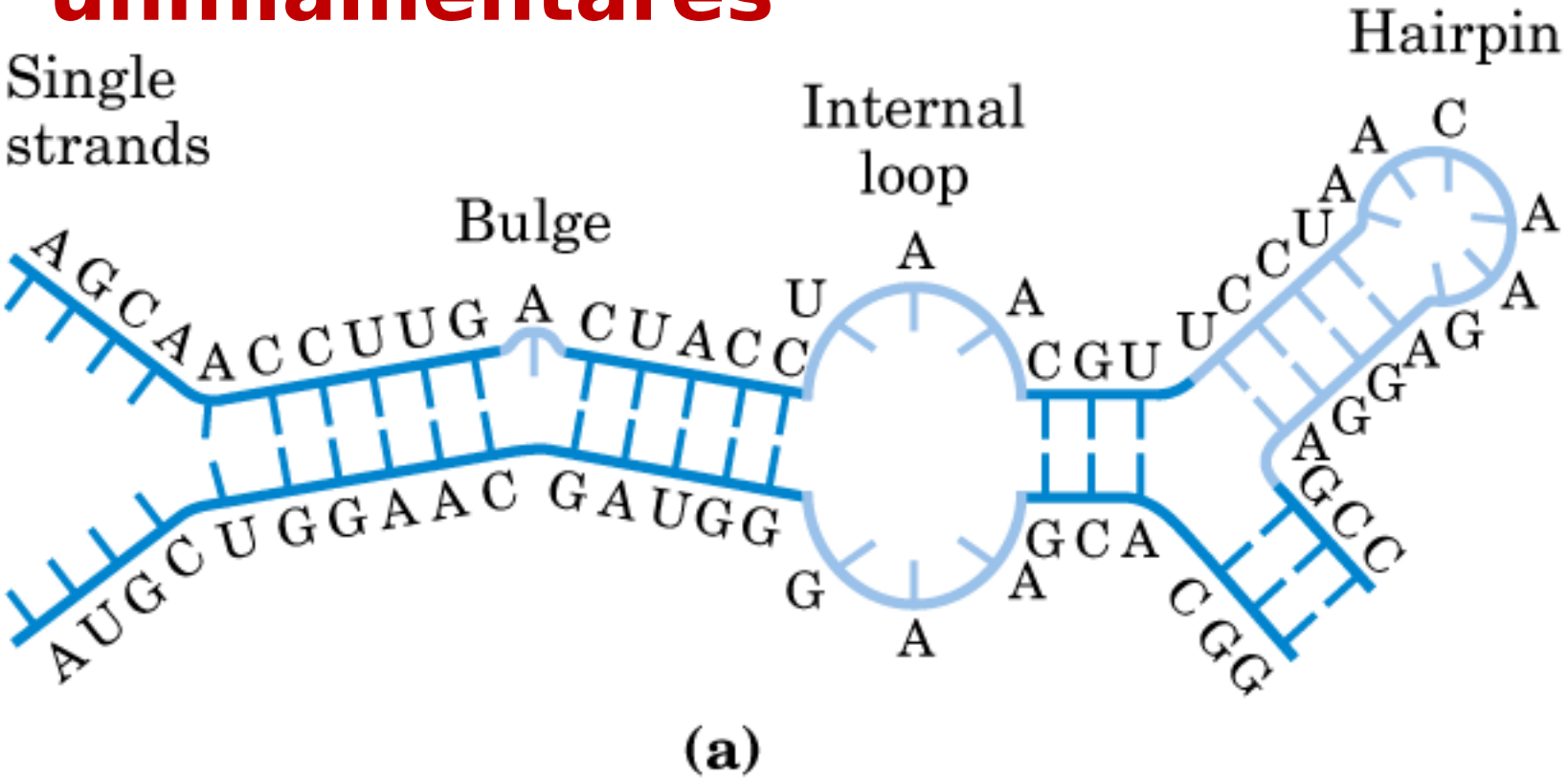
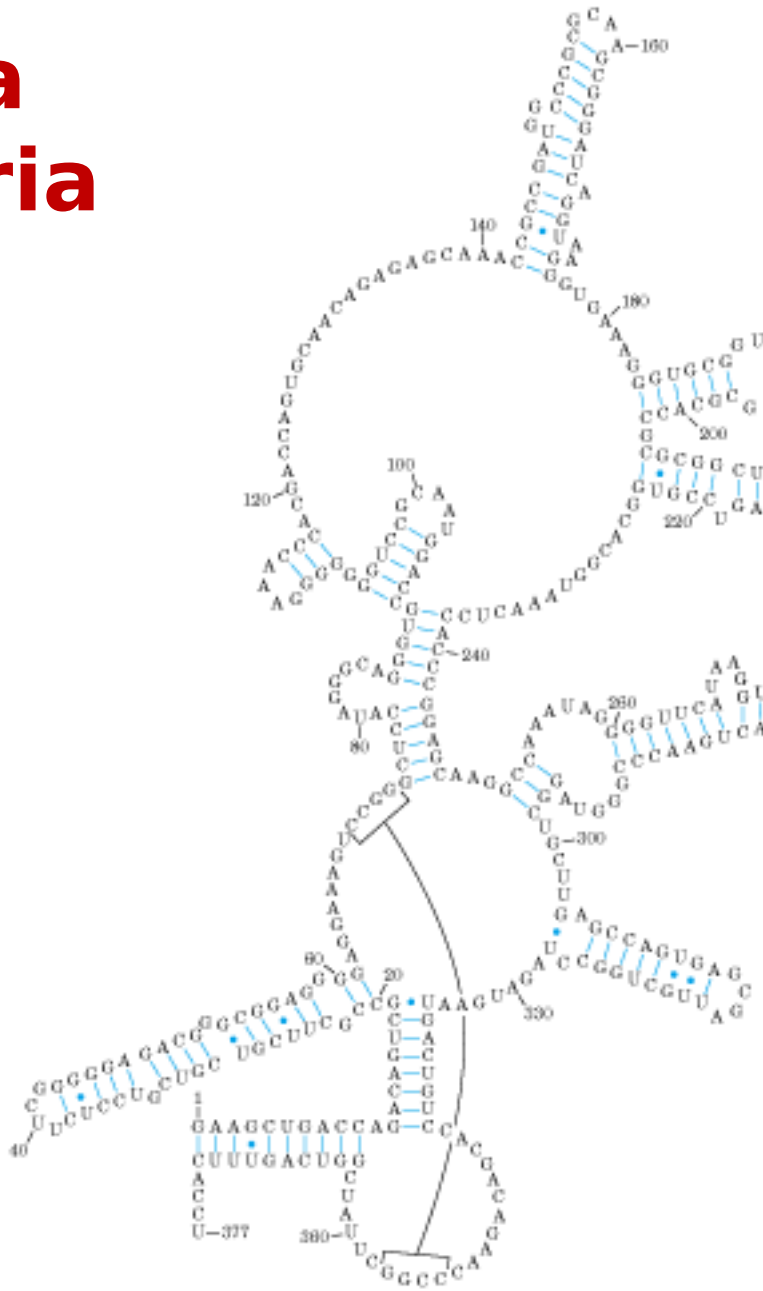
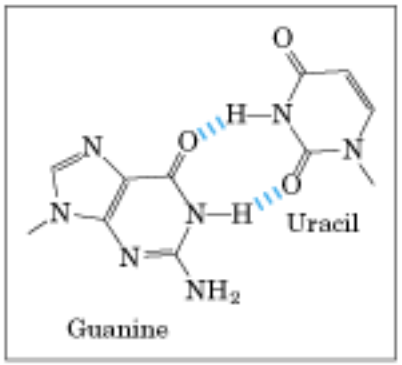
Estrutura: ácidos nucleicos unifilamentares

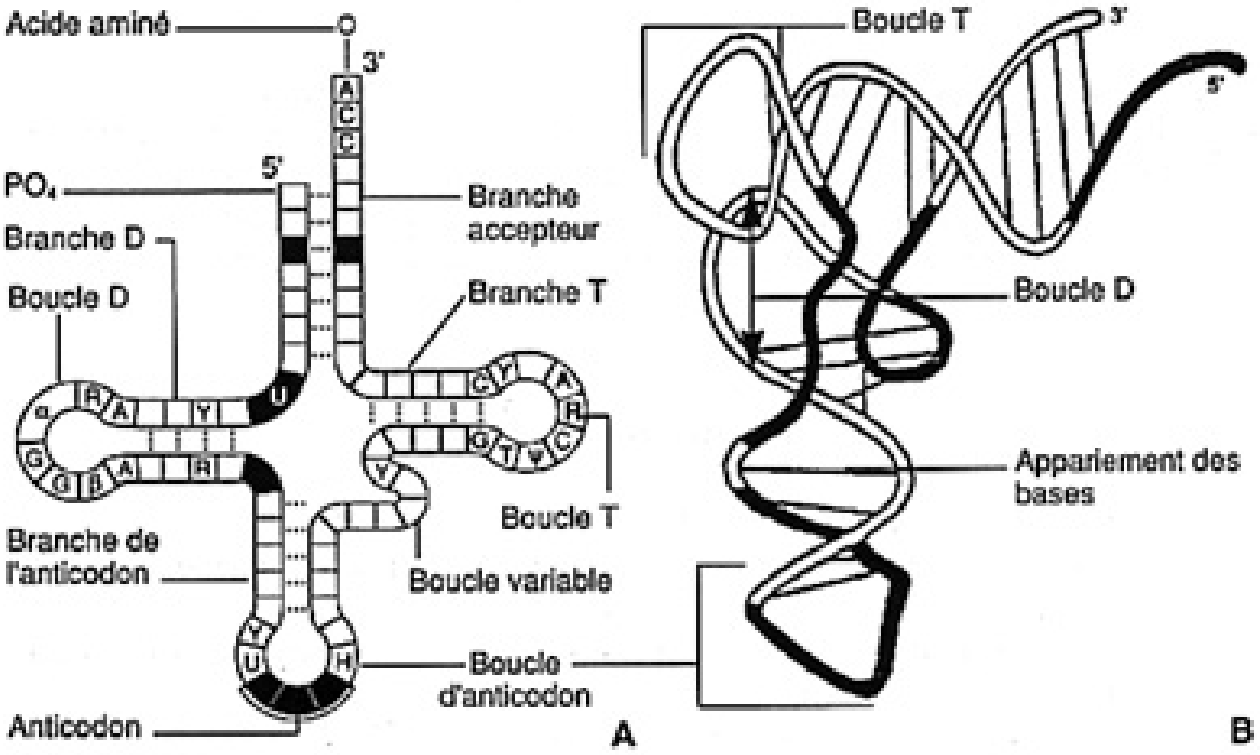


Estrutura secundária RNA

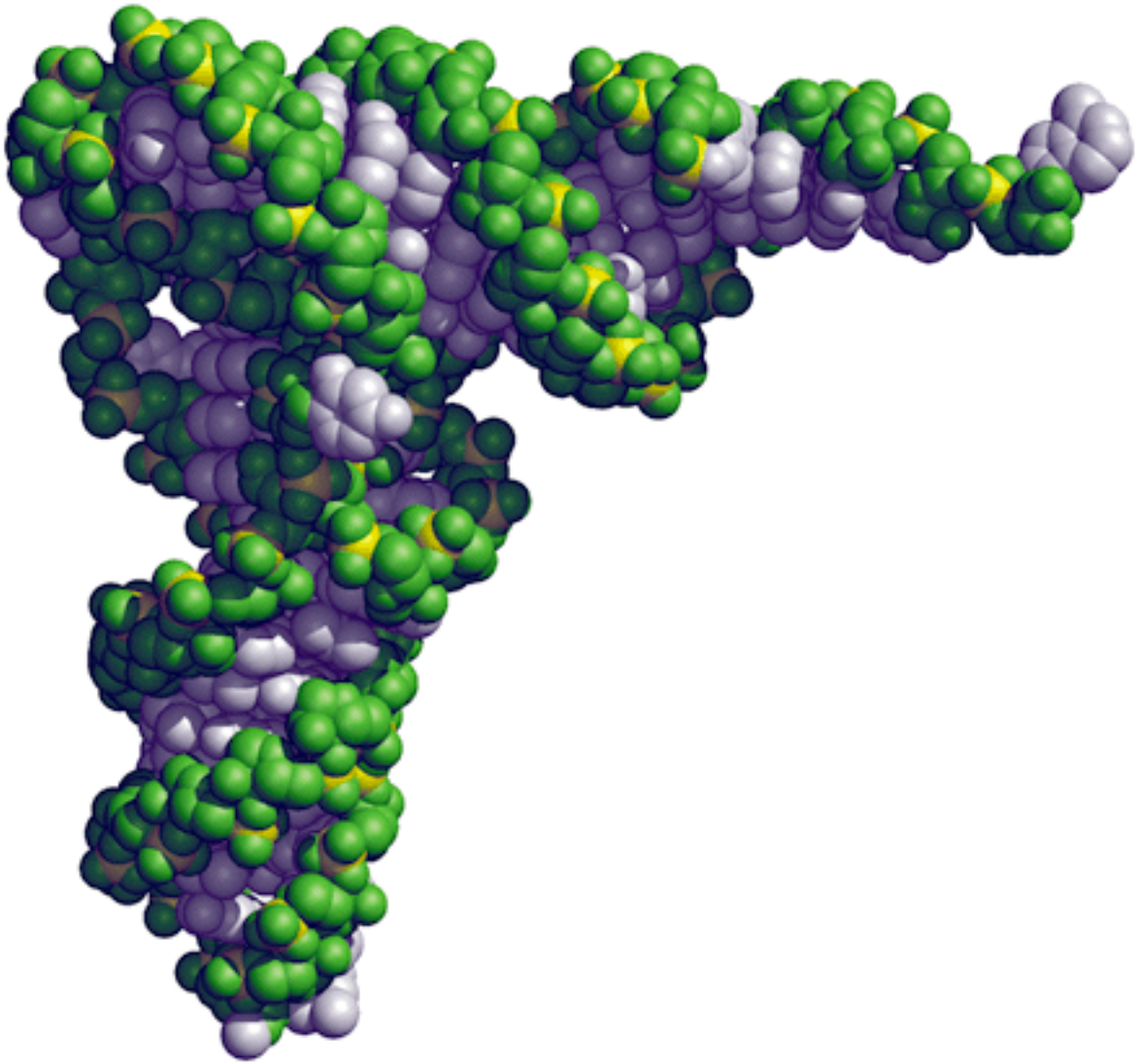




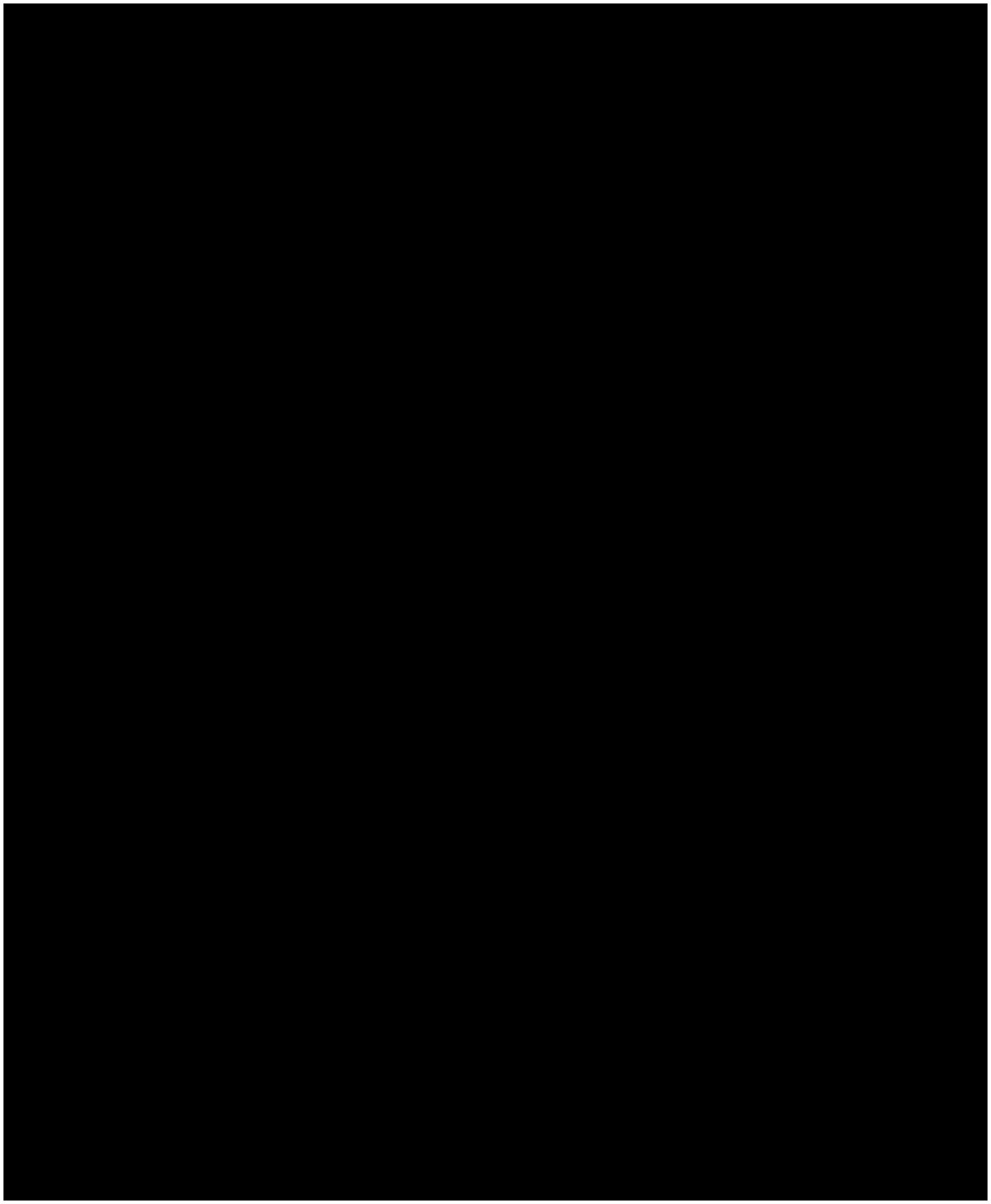
RNA transportador

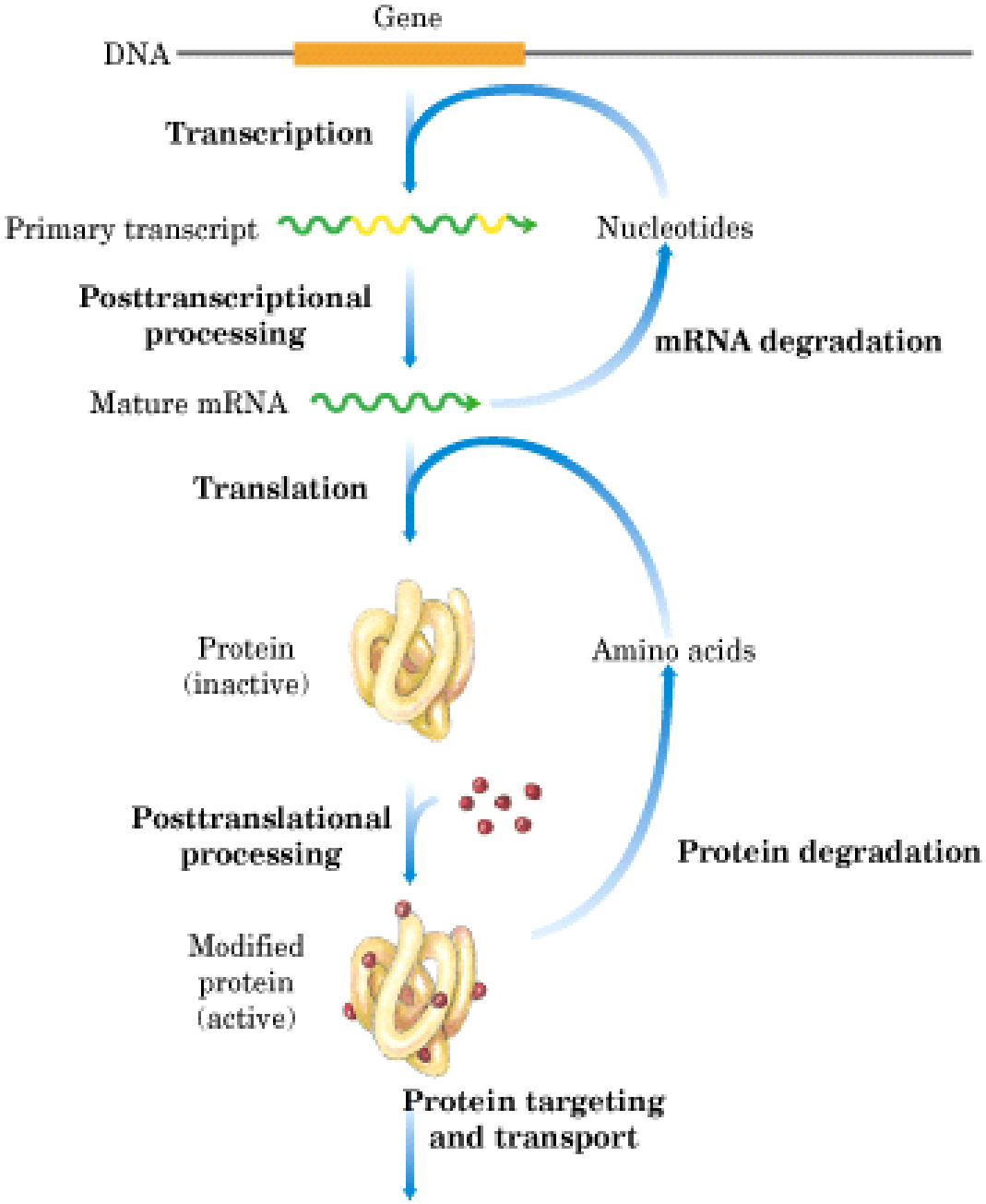


Estrutura 3D: tRNA



Estrutura secundária: RNA ribossomal





RNAs funcionais: tRNA, rRNA, microRNAs..

.

O código genético

First position (5' end)	U	C	A	G	Third position (3' end)
U	UUU Phe UUC Phe UUA Leu UUG Leu	UCU Ser UCC Ser UCA Ser UCG Ser	UAU Tyr UAC Tyr UAA Stop UAG Stop	UGU Cys UGC Cys UGA Stop UGG Trp	U C A G
C	CUU Leu CUC Leu CUA Leu CUG Leu	CCU Pro CCC Pro CCA Pro CCG Pro	CAU His CAC His CAA Gln CAG Gln	CGU Arg CGC Arg CGA Arg CGG Arg	U C A G
A	AUU Ile AUC Ile AUA Ile AUG	ACU Thr ACC Thr ACA Thr ACG Thr	AAU Asn AAC Asn AAA Lys AAG Lys	AGU Ser AGC Ser AGA Arg AGG Arg	U C A G
G	GUU Val GUC Val GUA Val GUG Val	GCU Ala GCC Ala GCA Ala GCG Ala	GAU Asp GAC Asp GAA Glu GAG Glu	GGU Gly GGC Gly GGA Gly GGG Gly	U C A G

Amino acid names:

Ala = alanine
Arg = arginine
Asn = asparagine
Asp = aspartate
Cys = cysteine
Gln = glutamine
Glu = glutamate
Gly = glycine
His = histidine
Ile = Isolevcine
Leu = leucine
Lys = lysine
Met = methionine
Phe = phenylalanine
Pro = proline
Ser = serine
Thr = threonine
Trp = tryptophan
Tyr = Tyrosine
Val = valine

Tradução

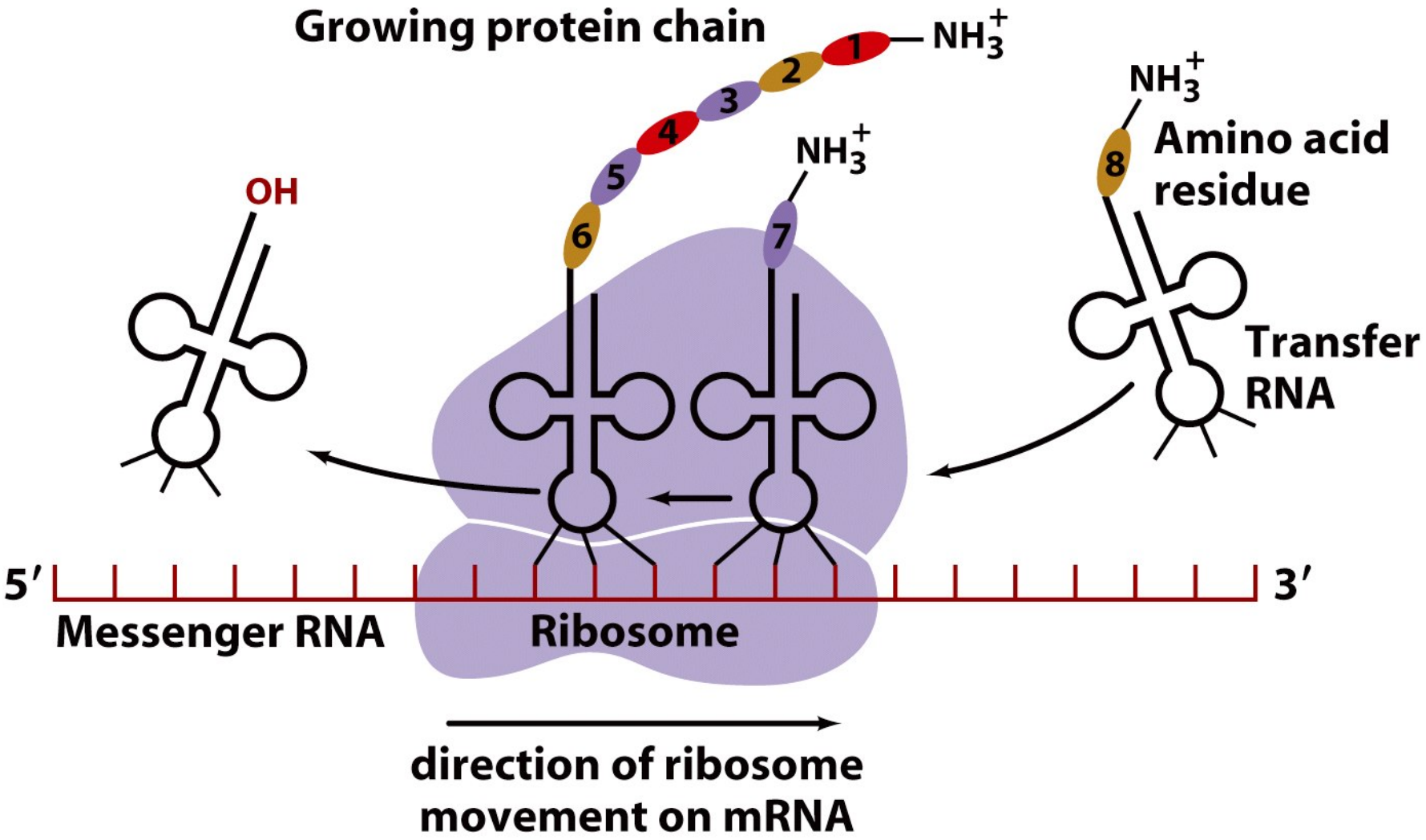
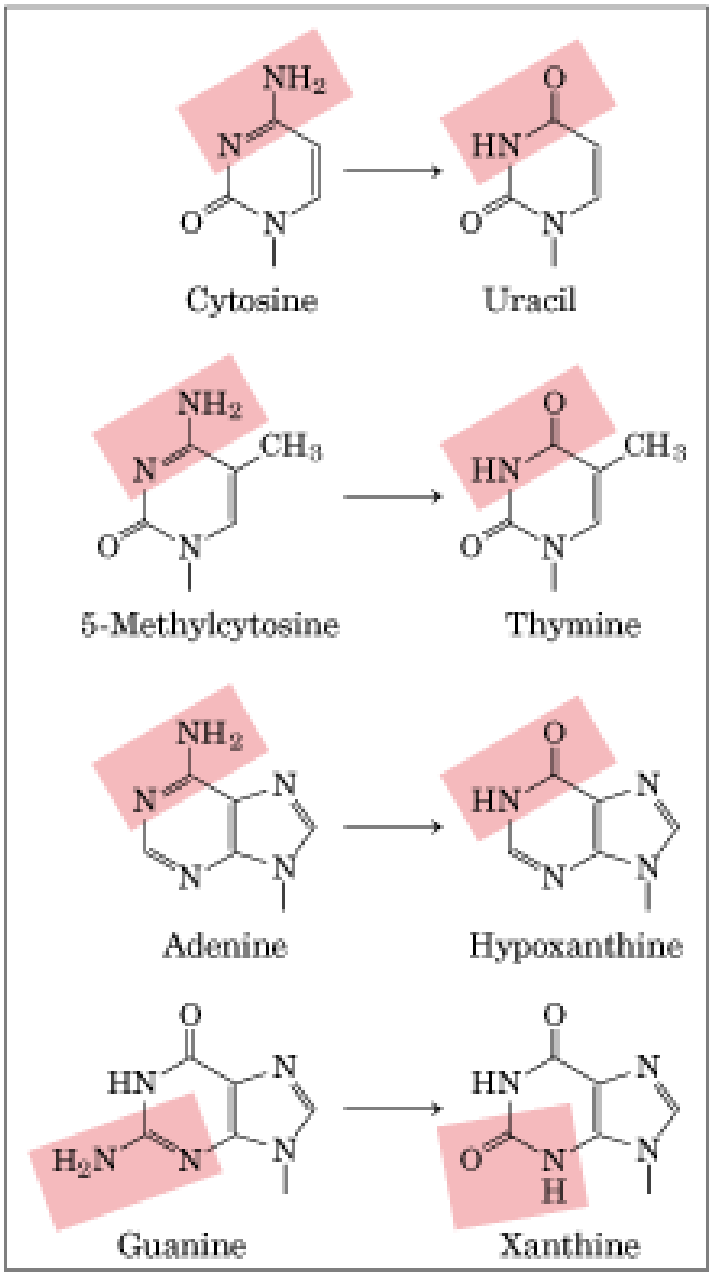


Figure 3-14 Fundamentals of Biochemistry, 2/e



Deamination
(a)

Mutações

Alterações na estrutura do DNA que produzem mudanças permanentes na informação genética

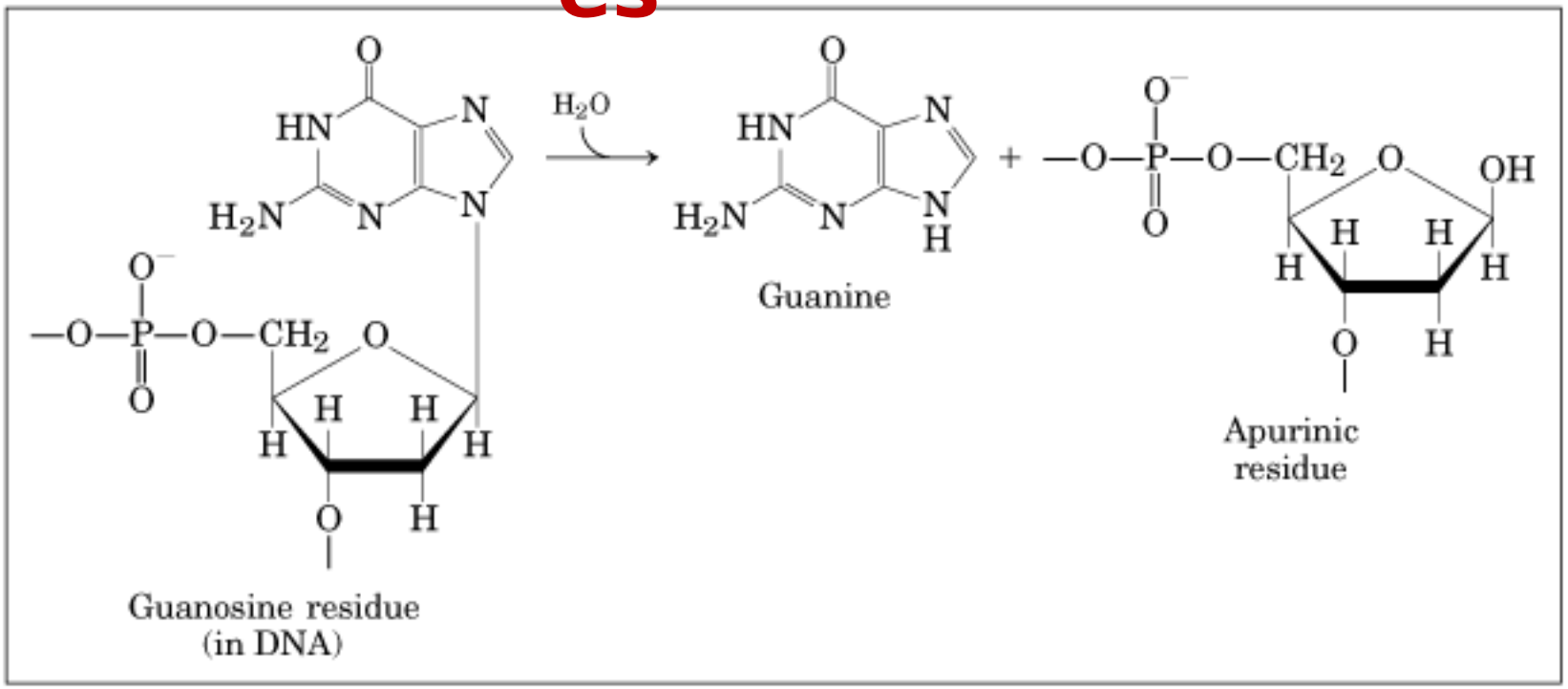
C → U

Em condições normais na célula:

1 em 10^7 residuos em 24h

= 100 eventos por dia

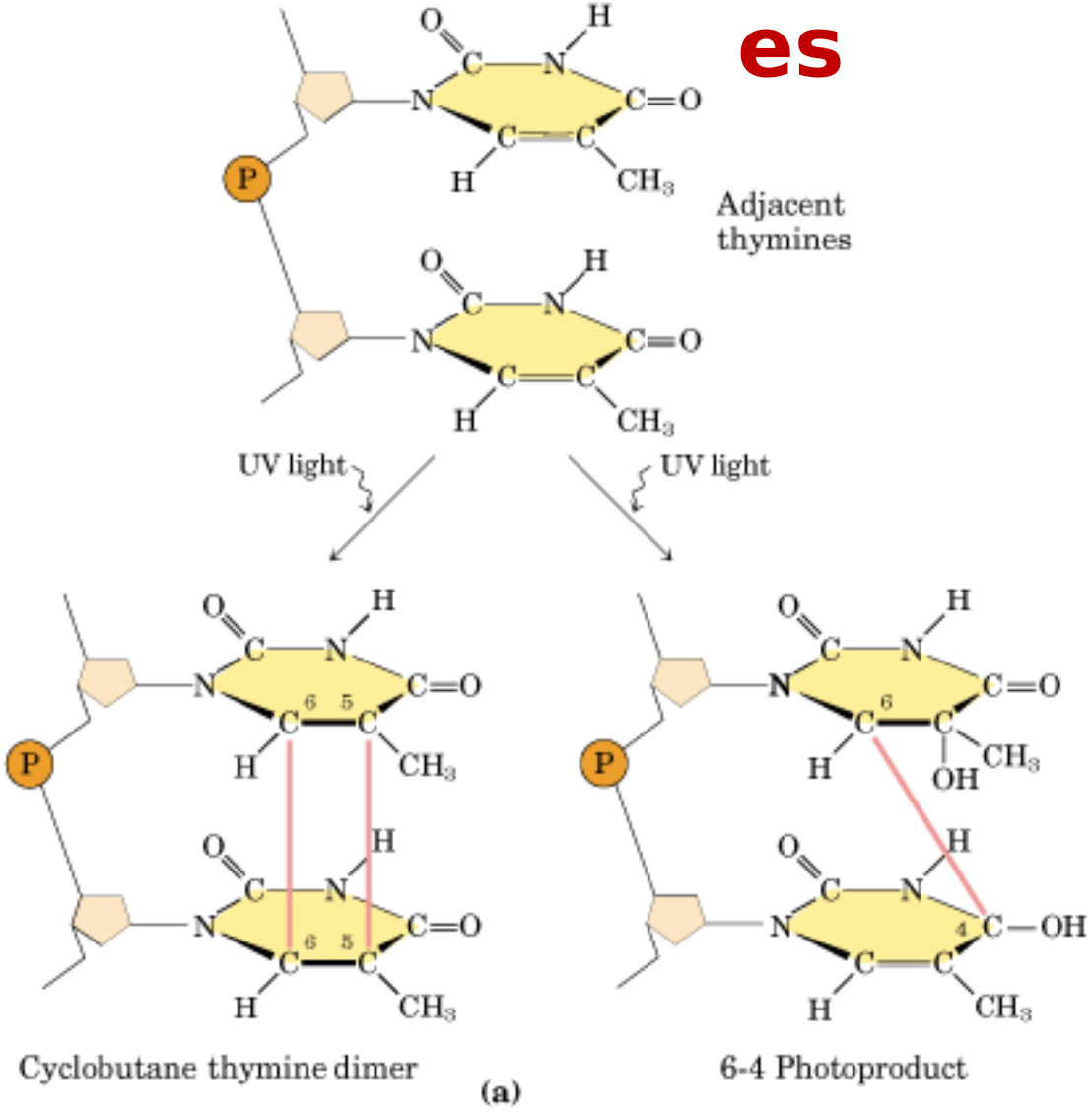
Mutaçõ
es

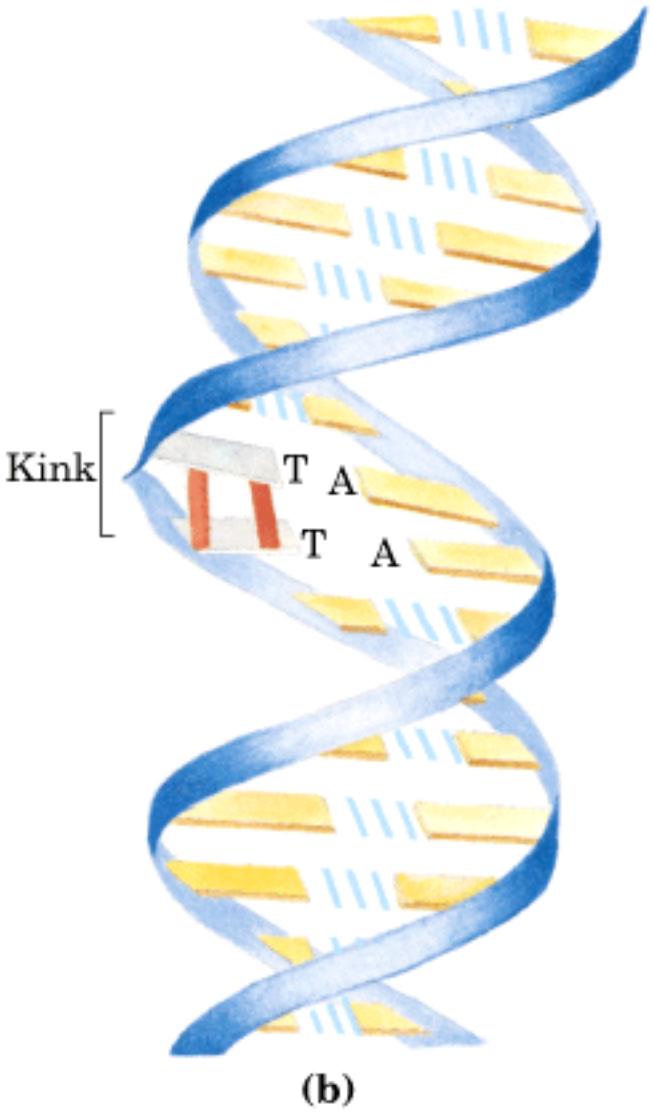


Depurination
(b)

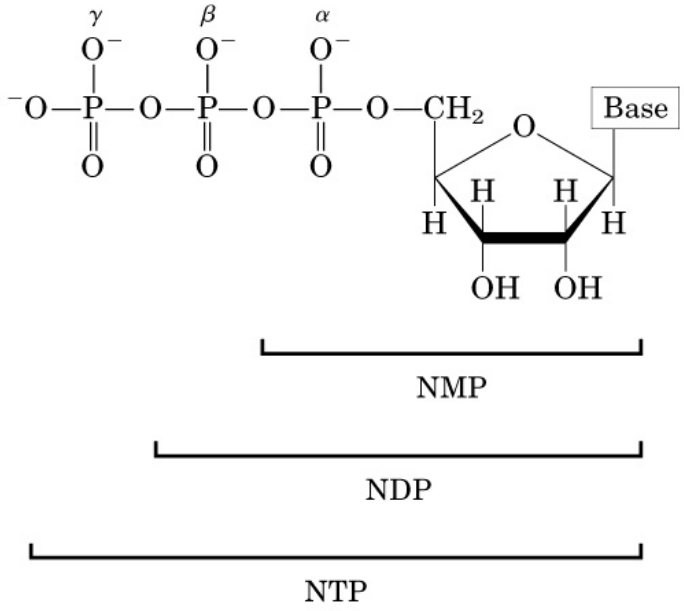
1 em 10^5 purinas em 24h

Mutaçõ es


Adjacent thymines
UV light
UV light
Cyclobutane thymine dimer
6-4 Photoproduct
(a)


Kink
T A
T A
(b)

Outras funções dos nucleotídeos



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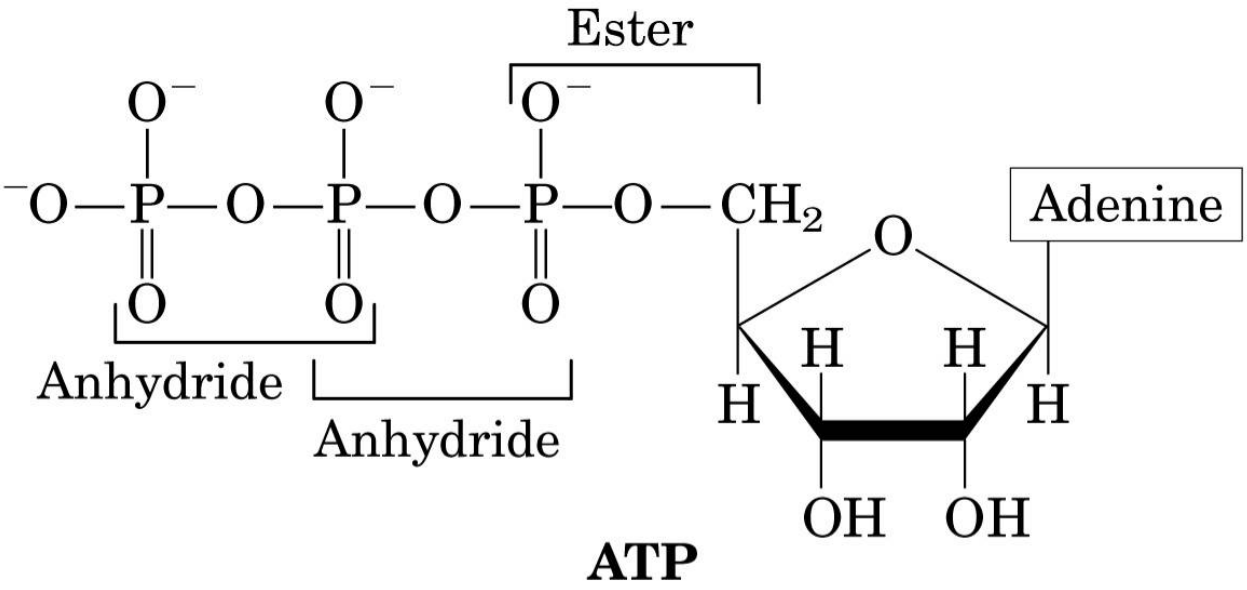
Abbreviations of ribonucleoside 5'-phosphates			
Base	Mono-	Di-	Tri-
Adenine	AMP	ADP	ATP
Guanine	GMP	GDP	GTP
Cytosine	CMP	CDP	CTP
Uracil	UMP	UDP	UTP

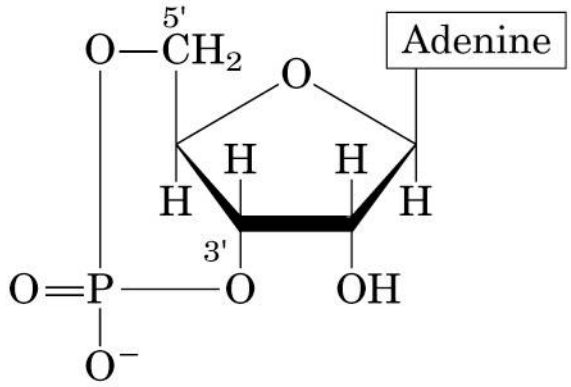
Abbreviations of deoxyribonucleoside 5'-phosphates			
Base	Mono-	Di-	Tri-
Adenine	dAMP	dADP	dATP
Guanine	dGMP	dGDP	dGTP
Cytosine	dCMP	dCDP	dCTP
Thymine	dTMP	dTDP	dTTP

Fonte de energia no metabolismo -> ATP

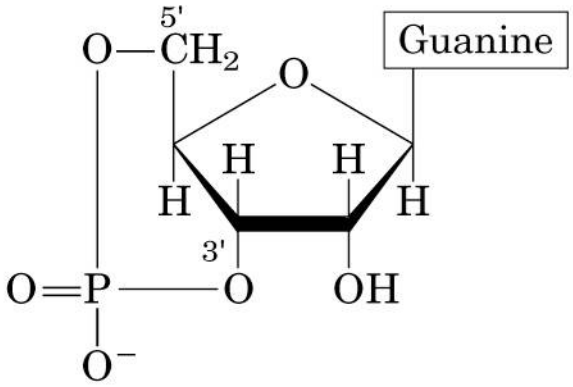
Compostos ricos em energia



Molécula sinal em respostas celulares

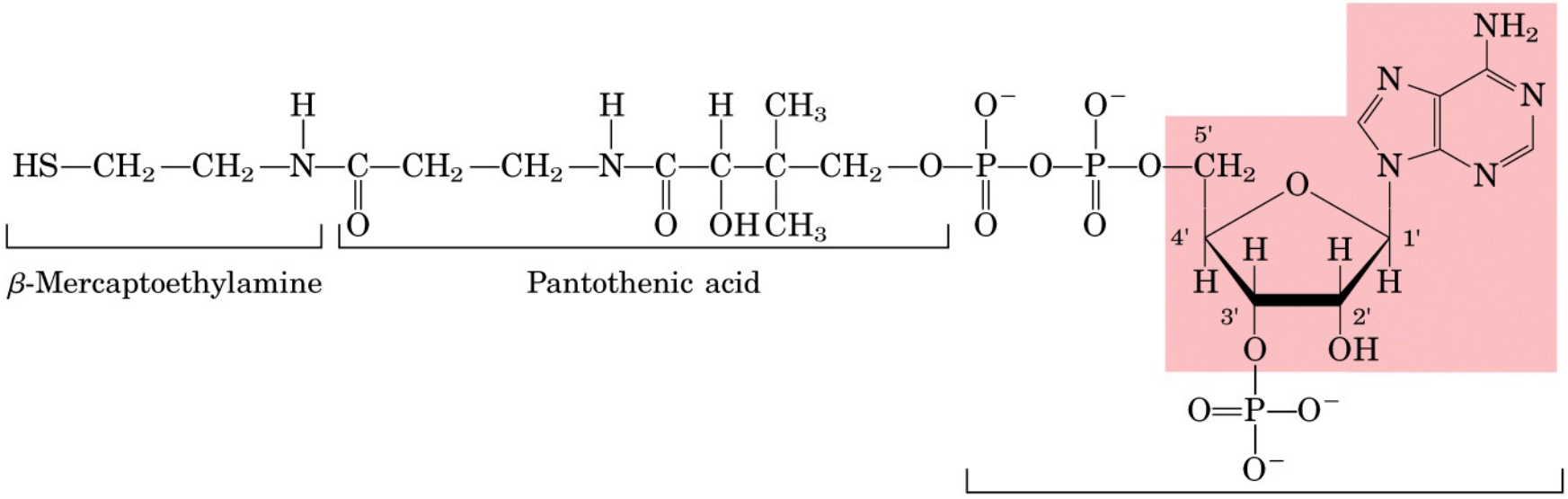


Adenosine 3',5'-cyclic monophosphate
(cyclic AMP; cAMP)



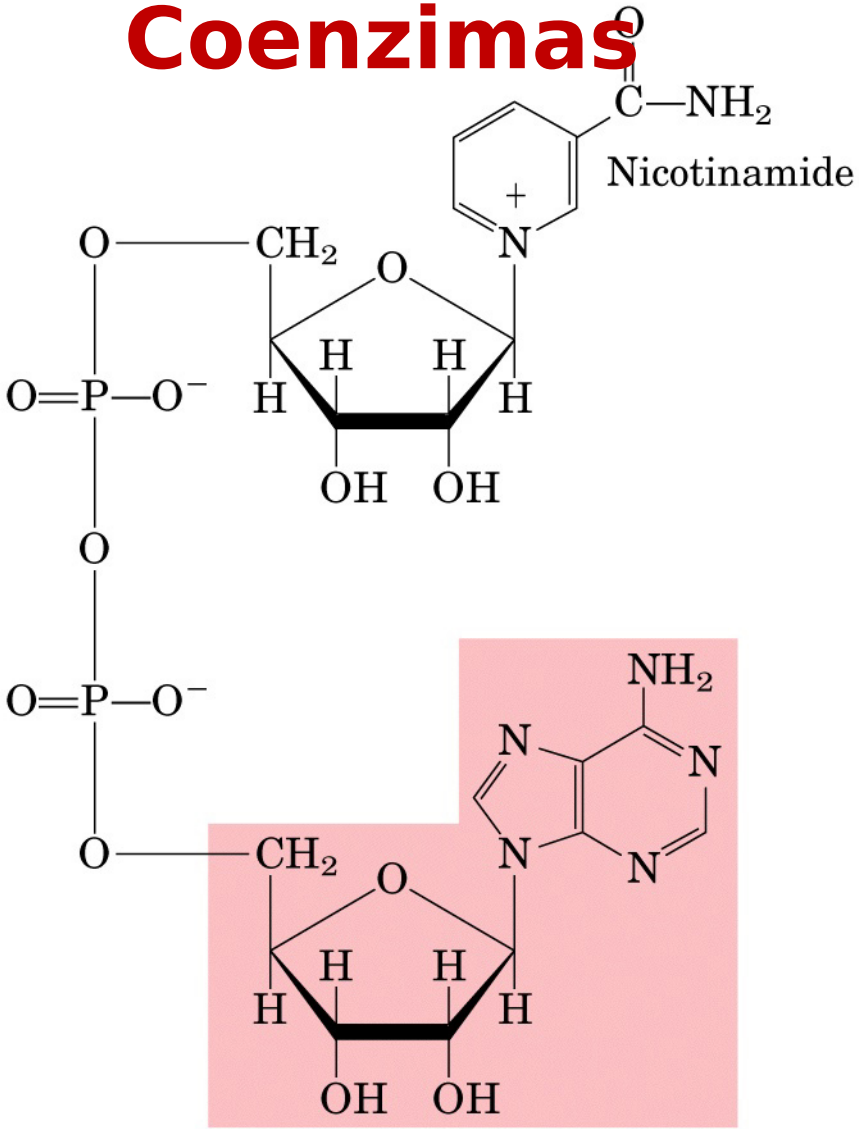
Guanosine 3',5'-cyclic monophosphate
(cyclic GMP; cGMP)

nponente estrutural de enzimas e co-fato



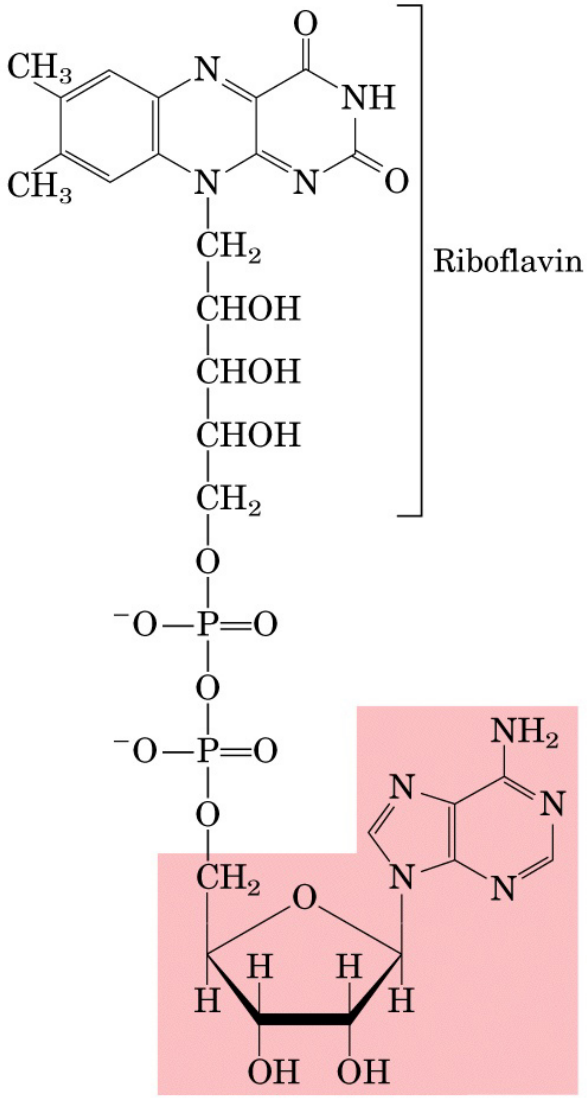
Coenzyme A

Coenzimas



Nicotinamide adenine dinucleotide (NAD^+)

Coenzimas



Flavin adenine dinucleotide (FAD)