

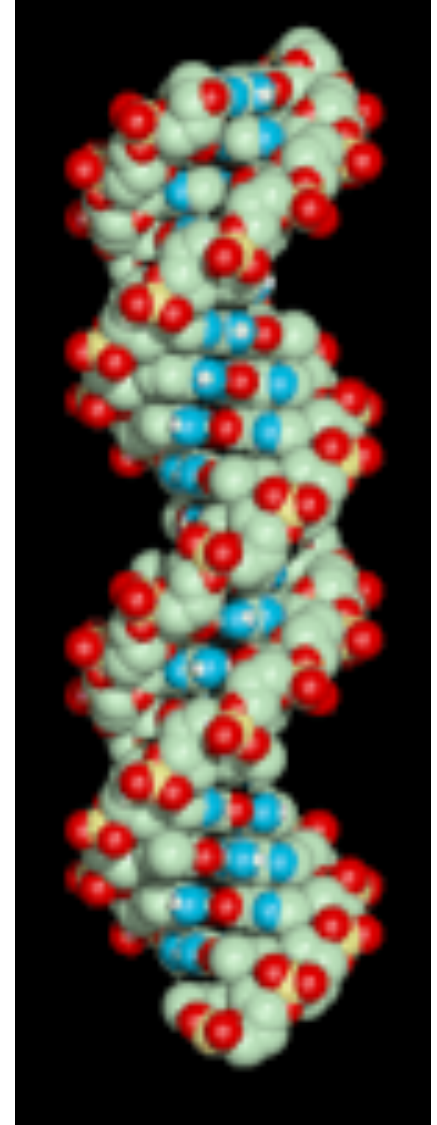


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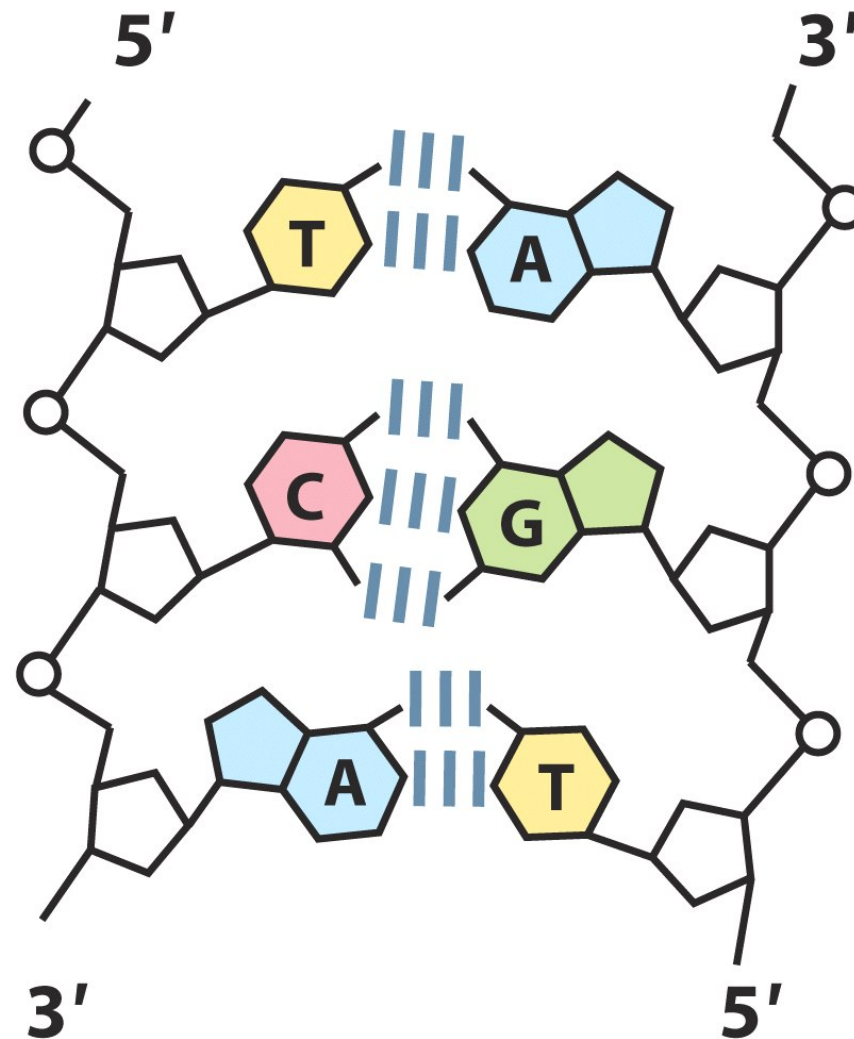
# QBQ0317 - 2020

## Aula 2

# Estrutura de Ácidos Nucleicos



# Estrutura de Ácidos Nucleicos

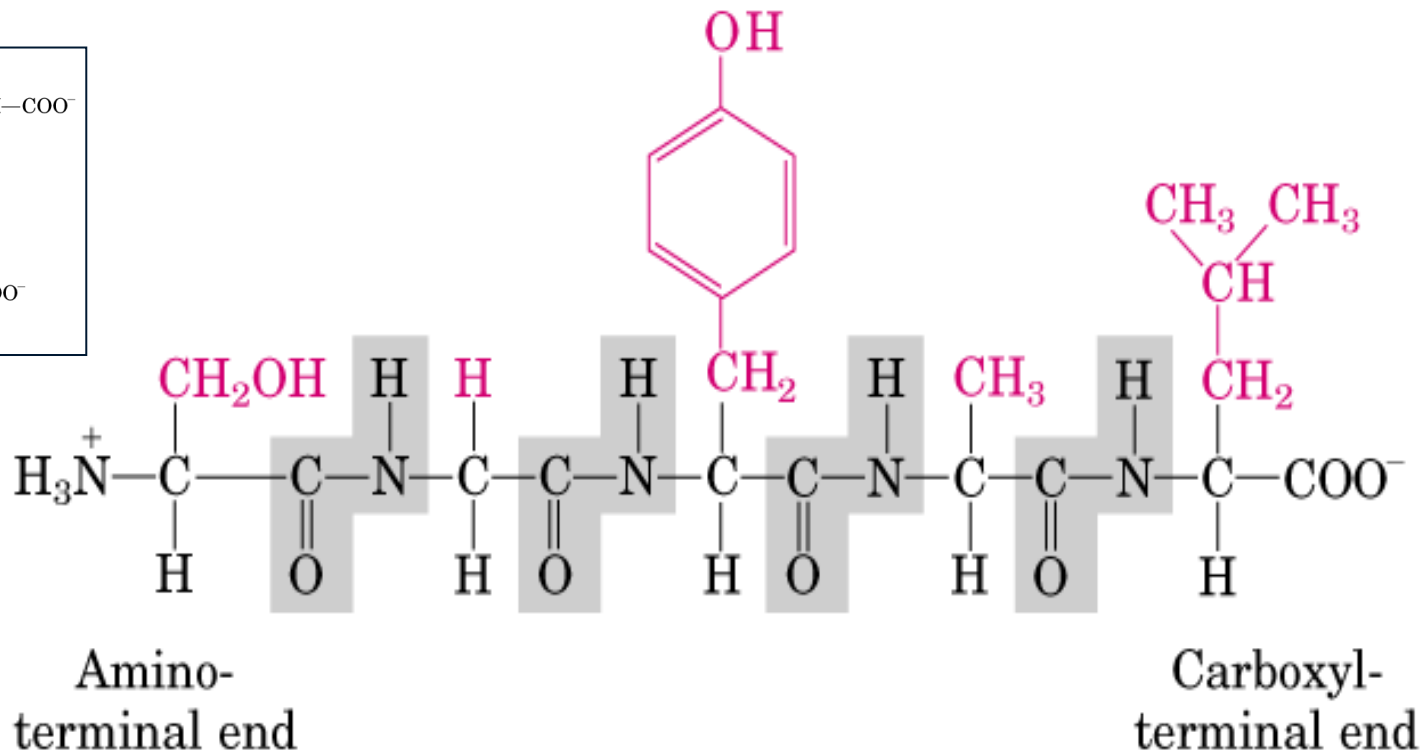
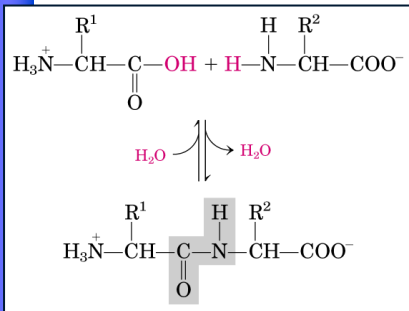


# Proteínas x DNA

- Os dois são macromoléculas formadas pela ligação covalente de monômeros/subunidades
- As subunidades de cada macromolécula têm uma parte da estrutura comum e uma parte variável
- Subunidades de DNA e proteína têm estrutura química distinta
- As ligações que unem os monômeros têm natureza distinta

# Revisão: estrutura de proteínas

- Cadeias formadas da condensação de aminoácidos por ligações peptídicas (amida)



Proteínas têm composição e número de aminoácidos específicos,

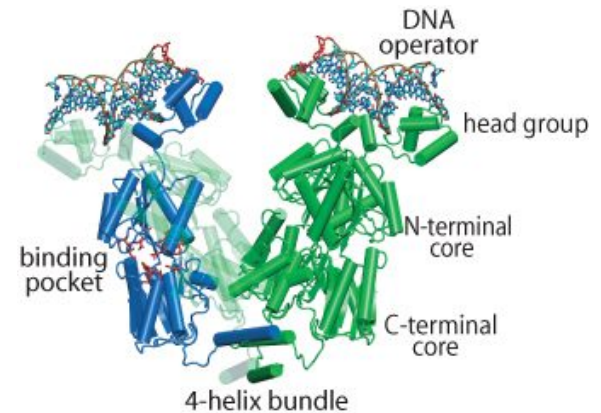
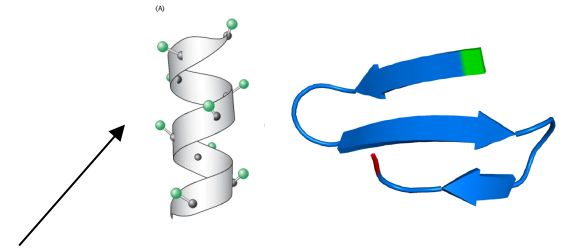
→ Estrutura primária (ordem dos aa)

que determinam sua forma

→ Estruturas secundária, terciária e quaternária

e função

→ determinada pela estrutura e pelas propriedades das cadeias laterais dos aa



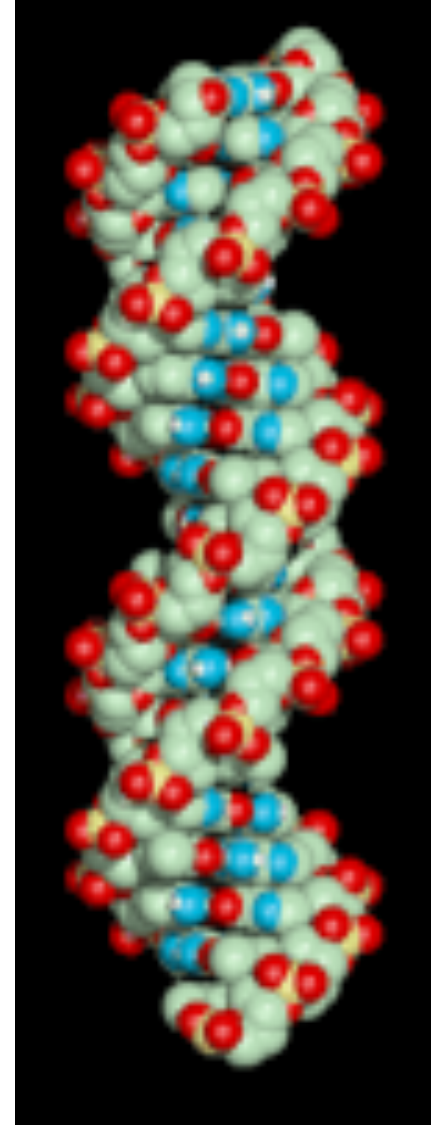


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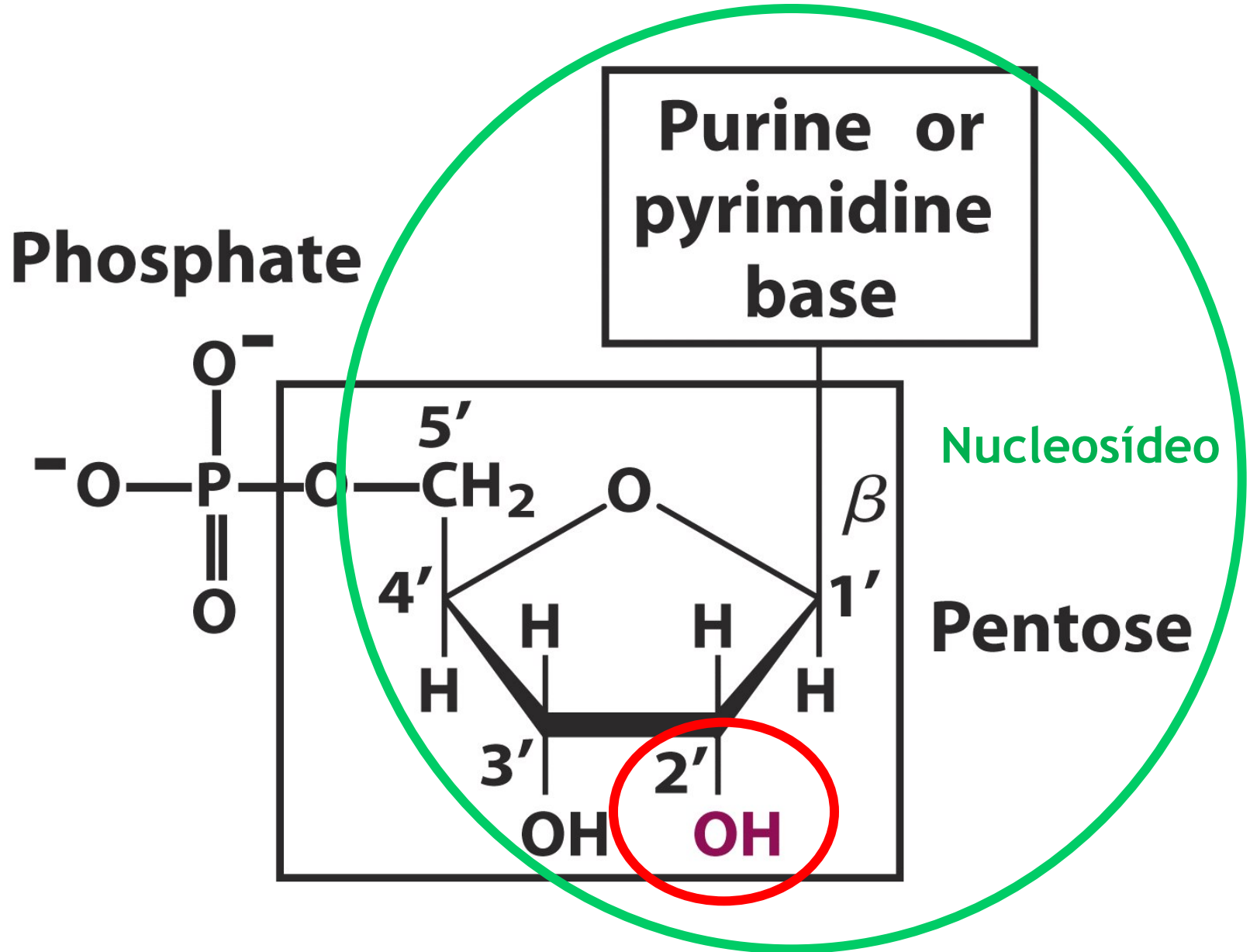
## Aula 2

# Estrutura de Ácidos Nucleicos

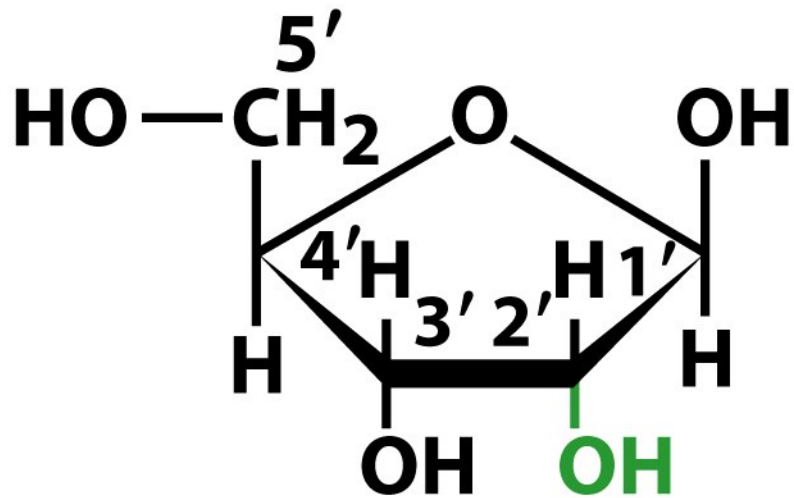


**Ácidos nucleicos são  
formados por  
nucleotídeos**

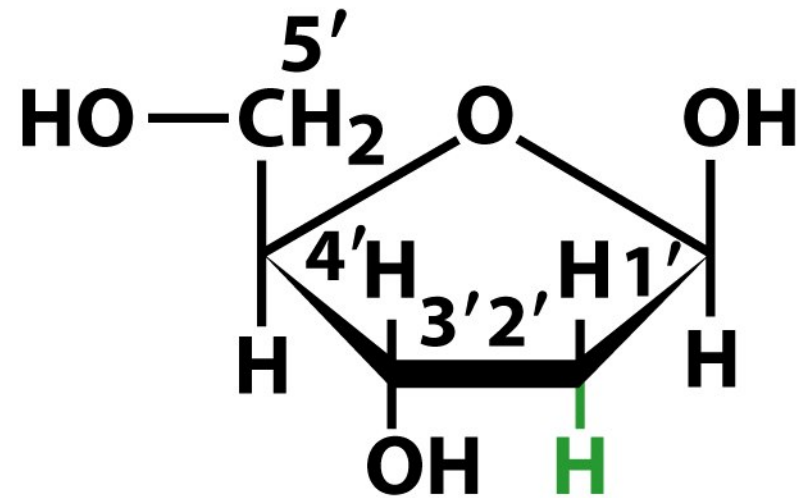
# Componentes dos Nucleotídeos





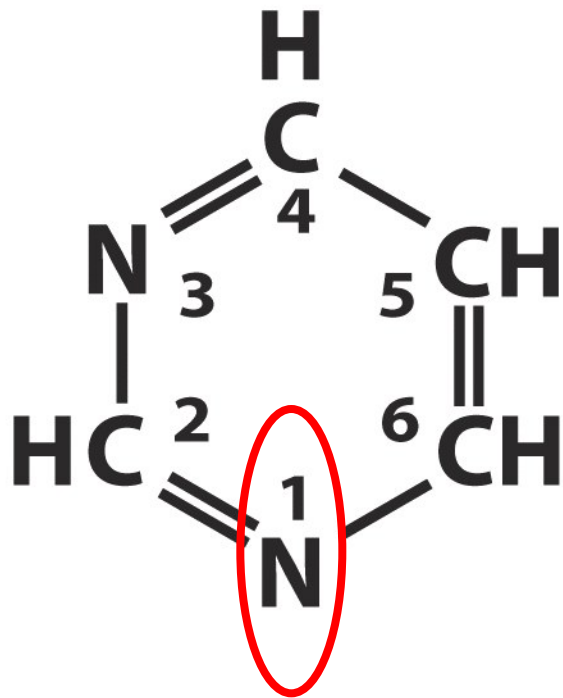


**Ribose**

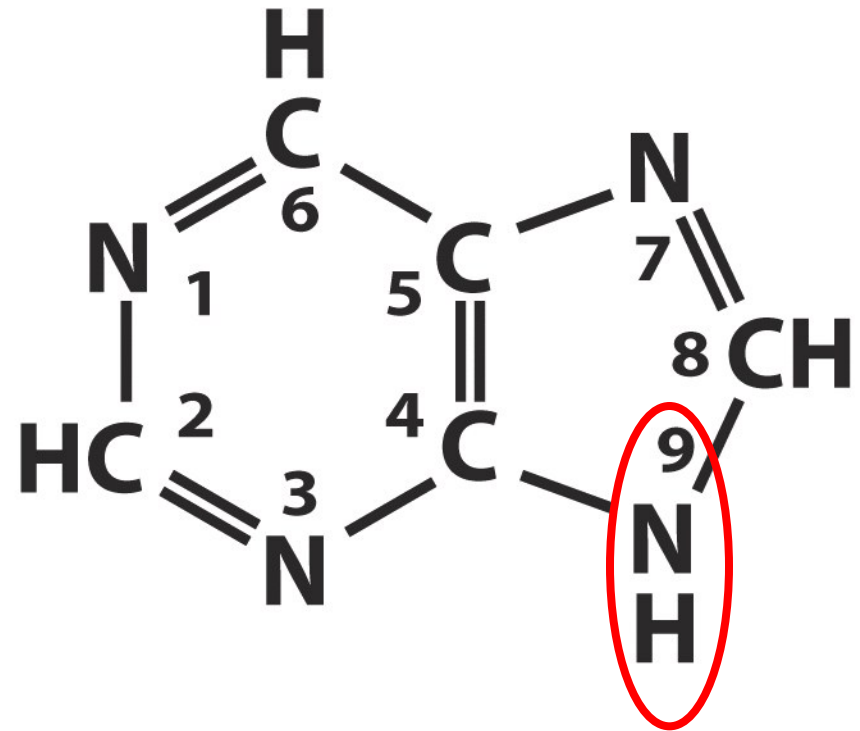


**Deoxyribose**

# Bases nitrogenadas

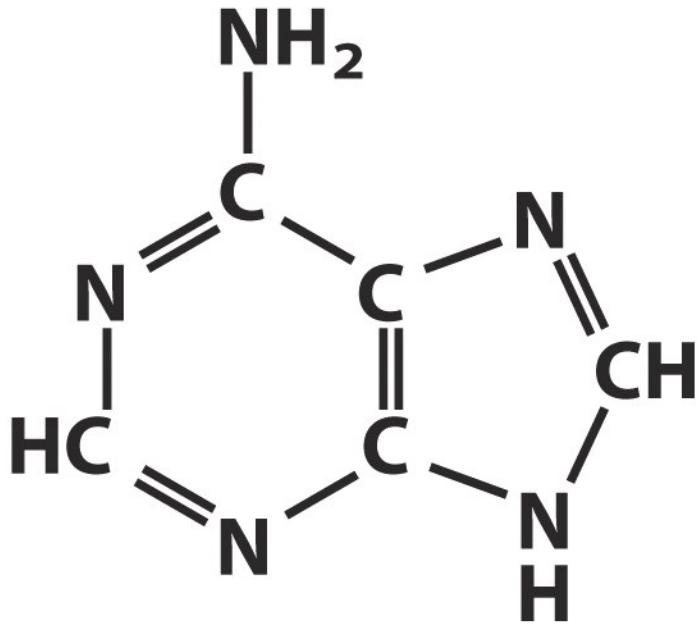


**Pyrimidine**

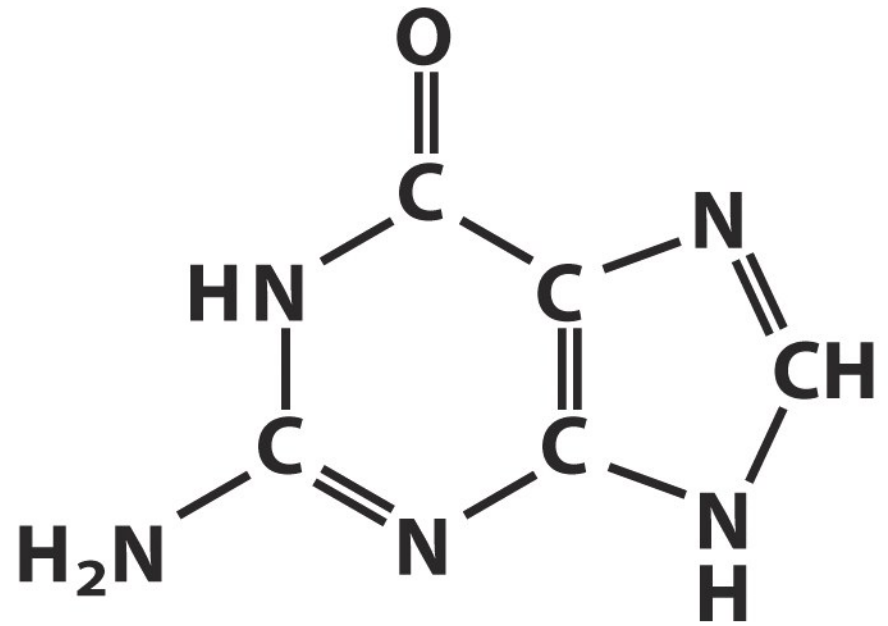


**Purine**

Ligação com posição 1' da pentose

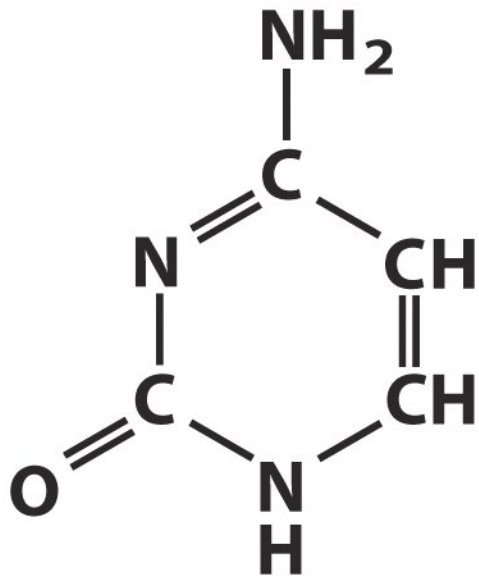


**Adenine**

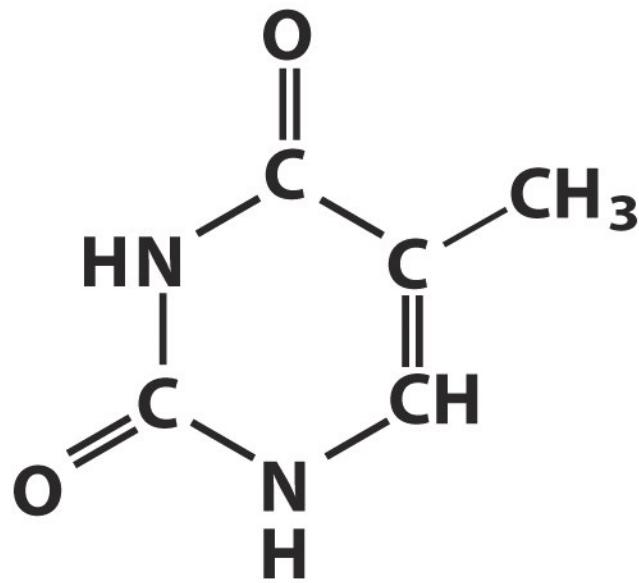


**Guanine**

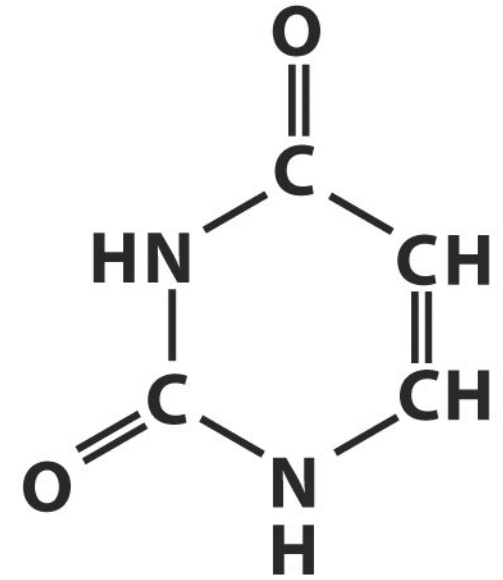
**Purines**



**Cytosine**

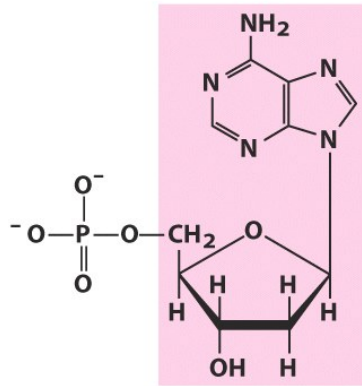


**Thymine  
(DNA)**



**Uracil  
(RNA)**

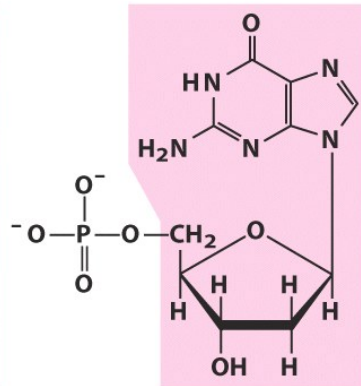
**Pyrimidines**



**Nucleotide:** Deoxyadenylate  
(deoxyadenosine  
5'-monophosphate)

**Symbols:** A, dA, dAMP

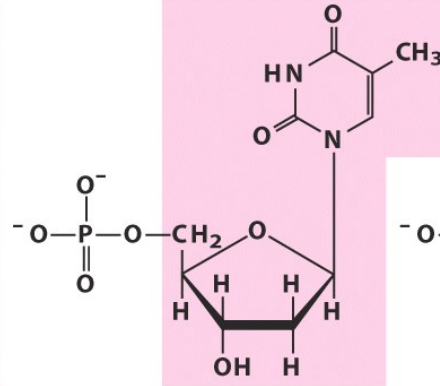
**Nucleoside:** Deoxyadenosine



**Nucleotide:** Deoxyguanylate  
(deoxyguanosine  
5'-monophosphate)

**Symbols:** G, dG, dGMP

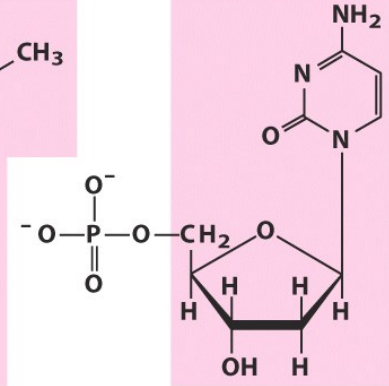
**Nucleoside:** Deoxyguanosine



**Nucleotide:** Deoxythymidylate  
(deoxythymidine  
5'-monophosphate)

**Symbols:** T, dT, dTMP

**Nucleoside:** Deoxythymidine

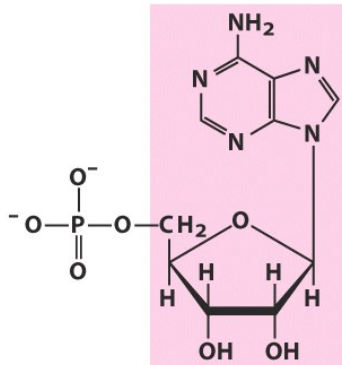


**Nucleotide:** Deoxycytidylate  
(deoxycytidine  
5'-monophosphate)

**Symbols:** C, dC, dCMP

**Nucleoside:** Deoxycytidine

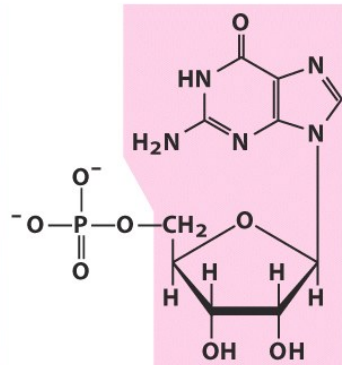
**(a) Deoxyribonucleotides**



**Nucleotide:** Adenylate (adenosine  
5'-monophosphate)

**Symbols:** A, AMP

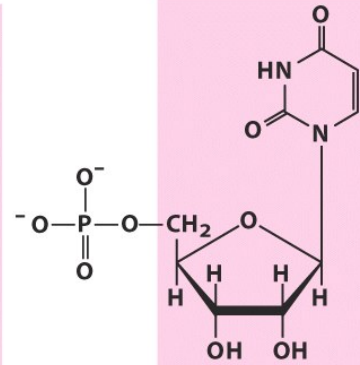
**Nucleoside:** Adenosine



**Nucleotide:** Guanylate (guanosine  
5'-monophosphate)

**Symbols:** G, GMP

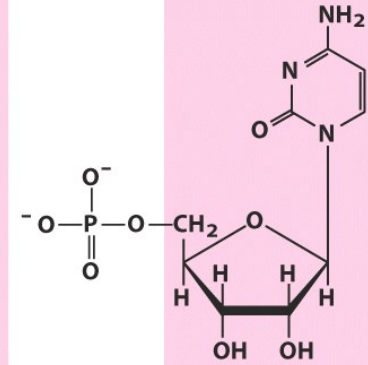
**Nucleoside:** Guanosine



**Nucleotide:** Uridylate (uridine  
5'-monophosphate)

**Symbols:** U, UMP

**Nucleoside:** Uridine



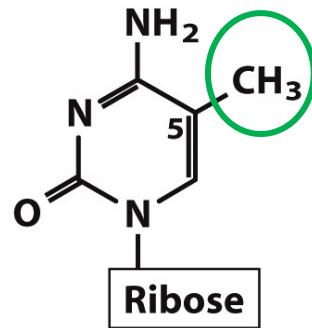
**Nucleotide:** Cytidylate (cytidine  
5'-monophosphate)

**Symbols:** C, CMP

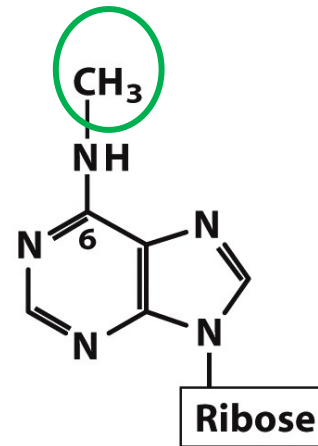
**Nucleoside:** Cytidine

**(b) Ribonucleotides**

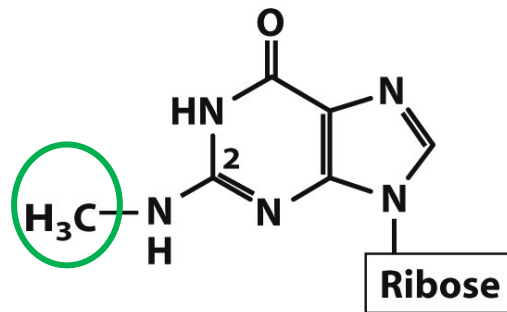
# Bases no DNA podem sofrer modificações químicas fisiológicas



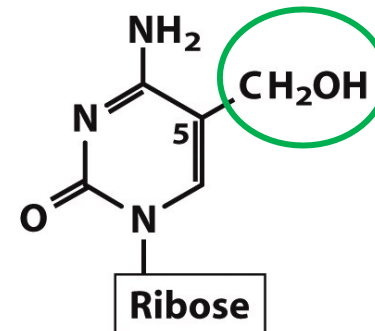
5-Methylcytidine



N<sup>6</sup>-Methyladenosine



N<sup>2</sup>-Methylguanosine



5-Hydroxymethylcytidine

Figure 8-5a  
Lehninger Principles of Biochemistry, Fifth Edition  
© 2008 W. H. Freeman and Company

Epigenética



# Estrutura do DNA

# Descoberta da estrutura do DNA

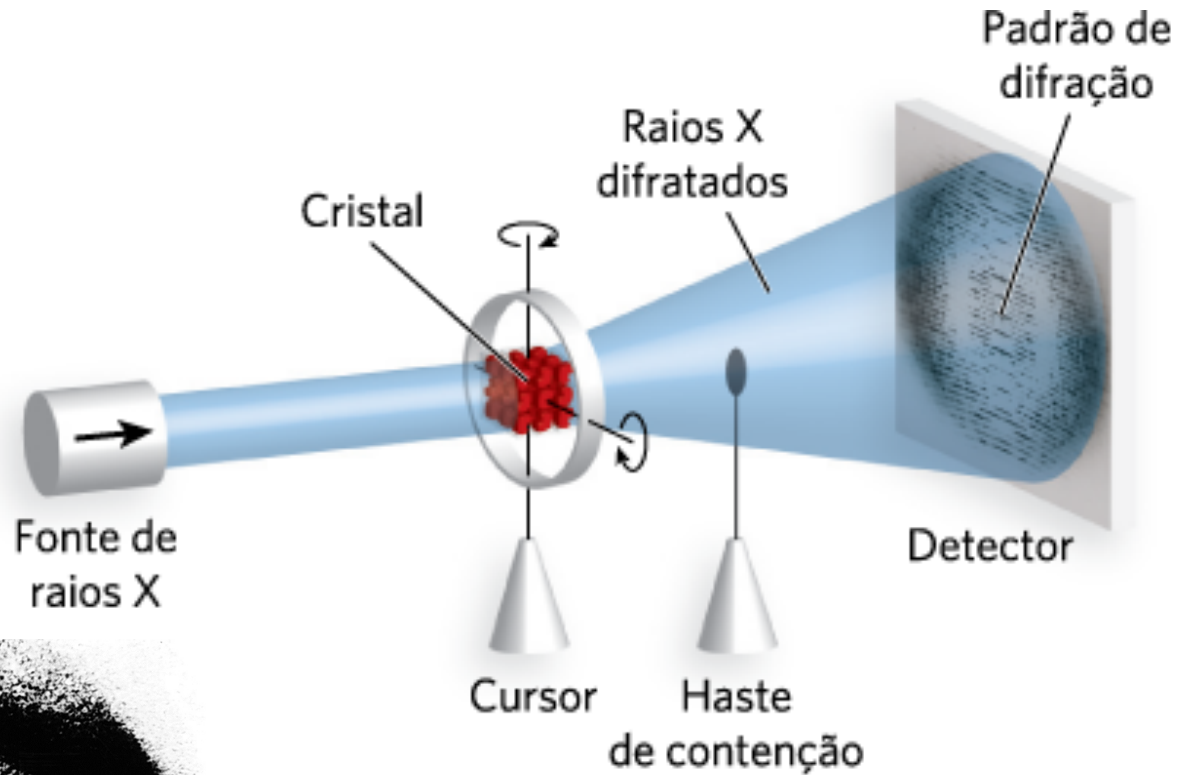
- Dados biofísicos
  - Padrões de difração de raio X



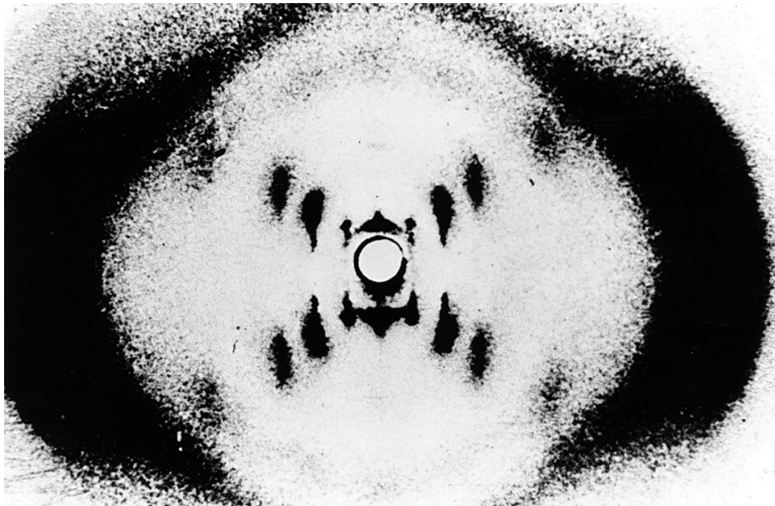
# Difração de Raio X do DNA



(a)



Rosalind Franklin



Rosalind Franklin and Maurice Wilkins, ~1950

# Descoberta da estrutura do DNA

- Dados biofísicos
  - Padrões de difração de raio X
- Razão entre as bases - regras de Chargaff

# Regras de Chargaff

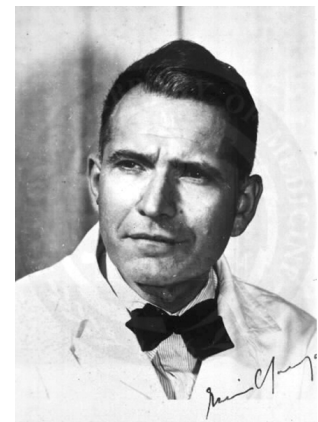
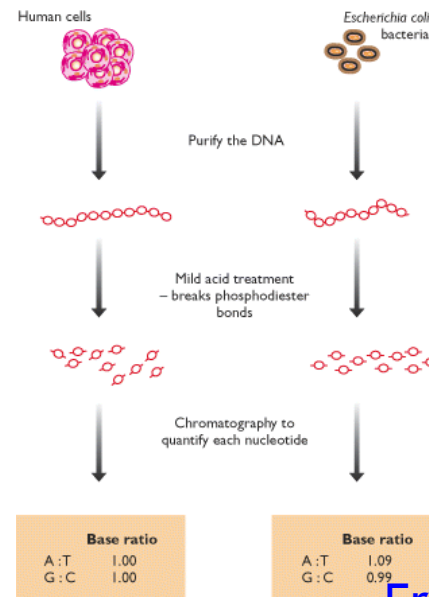
- Composição de bases do DNA (%)
  - varia de uma espécie a outra
  - invariável entre indivíduos da mesma espécie
  - não muda com idade, nutrição ou ambiente

- Em *todos* os DNAs:

➤  $A = T$

➤  $G = C$

➤  $A + G = T + C$



Erwin Chargaff, 1940's

# Descoberta da estrutura do DNA

- Dados biofísicos
  - Padrões de difração de raio X
- Razão entre as bases - regras de Chargaff
- Modelos estruturais

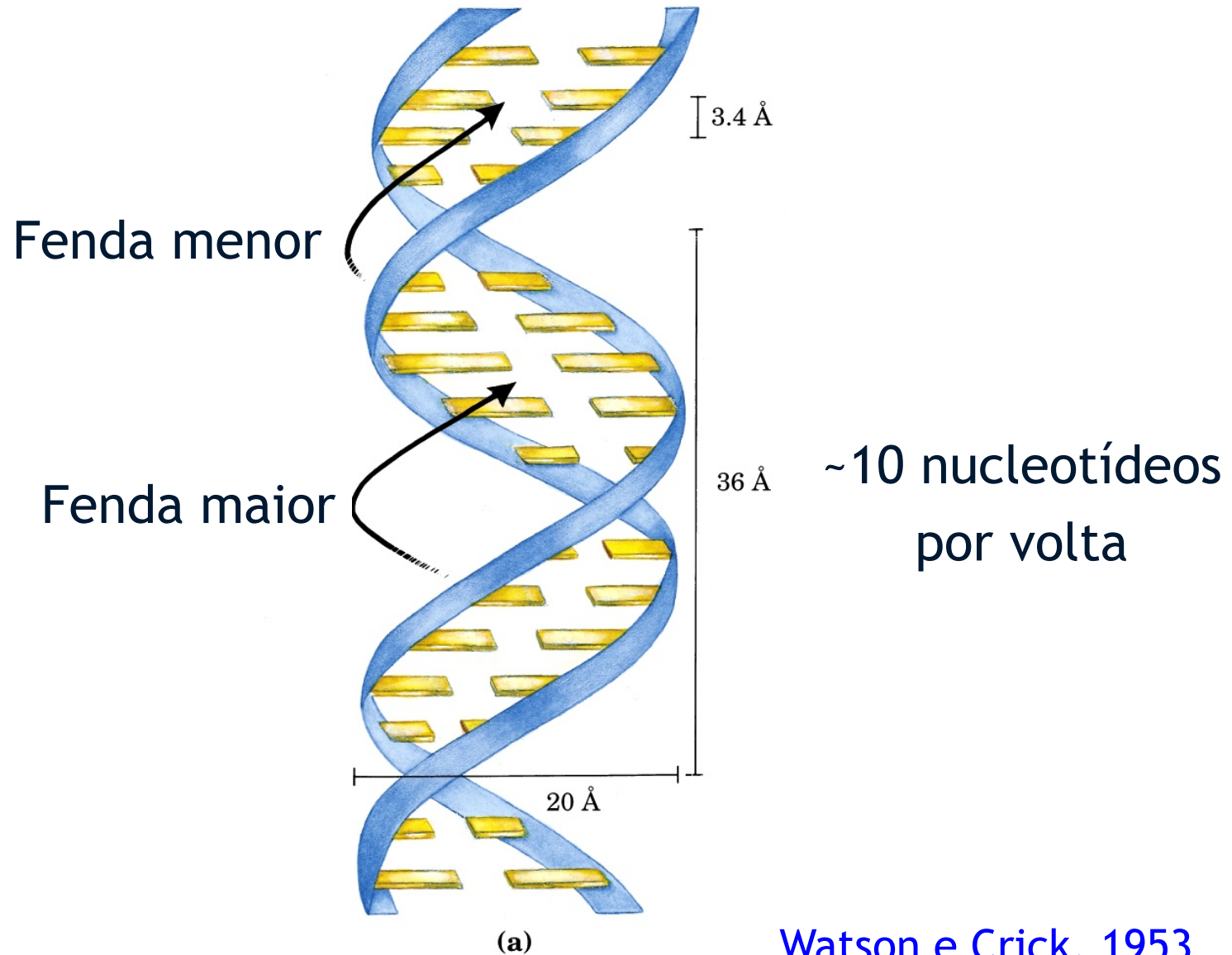


1953

James  
Watson

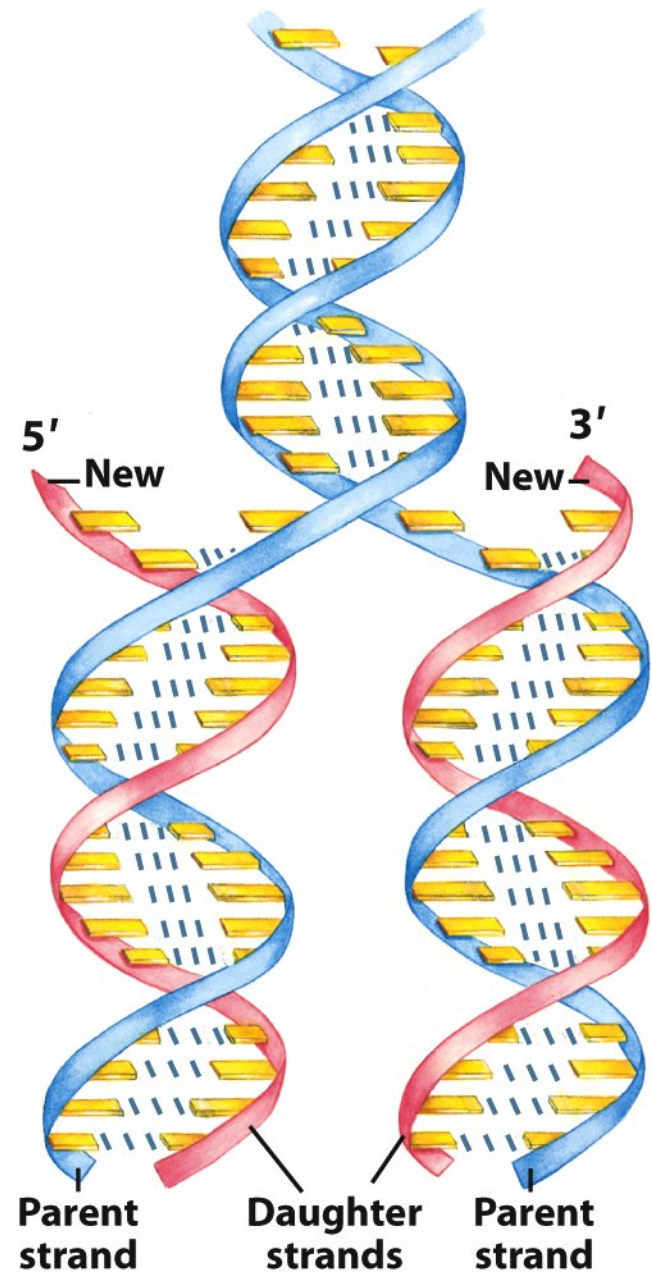
Francis  
Crick

# Modelo de Dupla Hélice



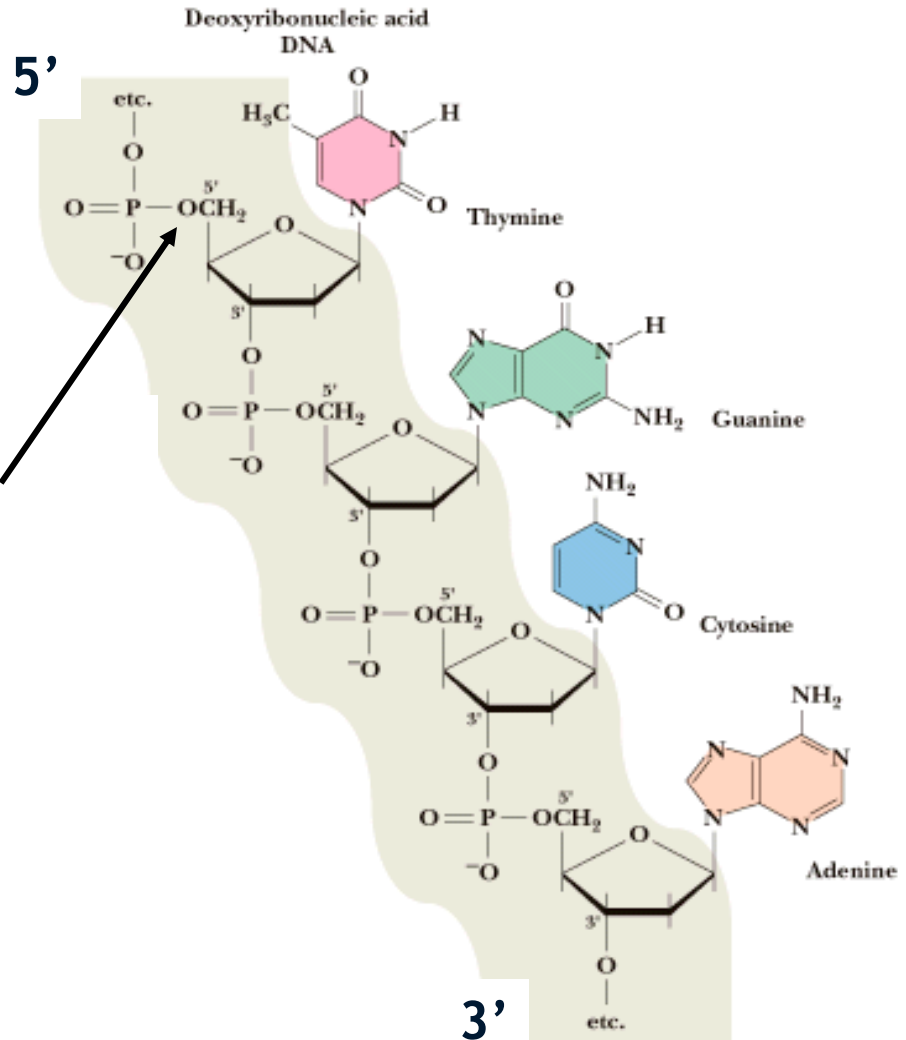
Watson e Crick, 1953

# Função do DNA: Estoque e transferência da informação genética

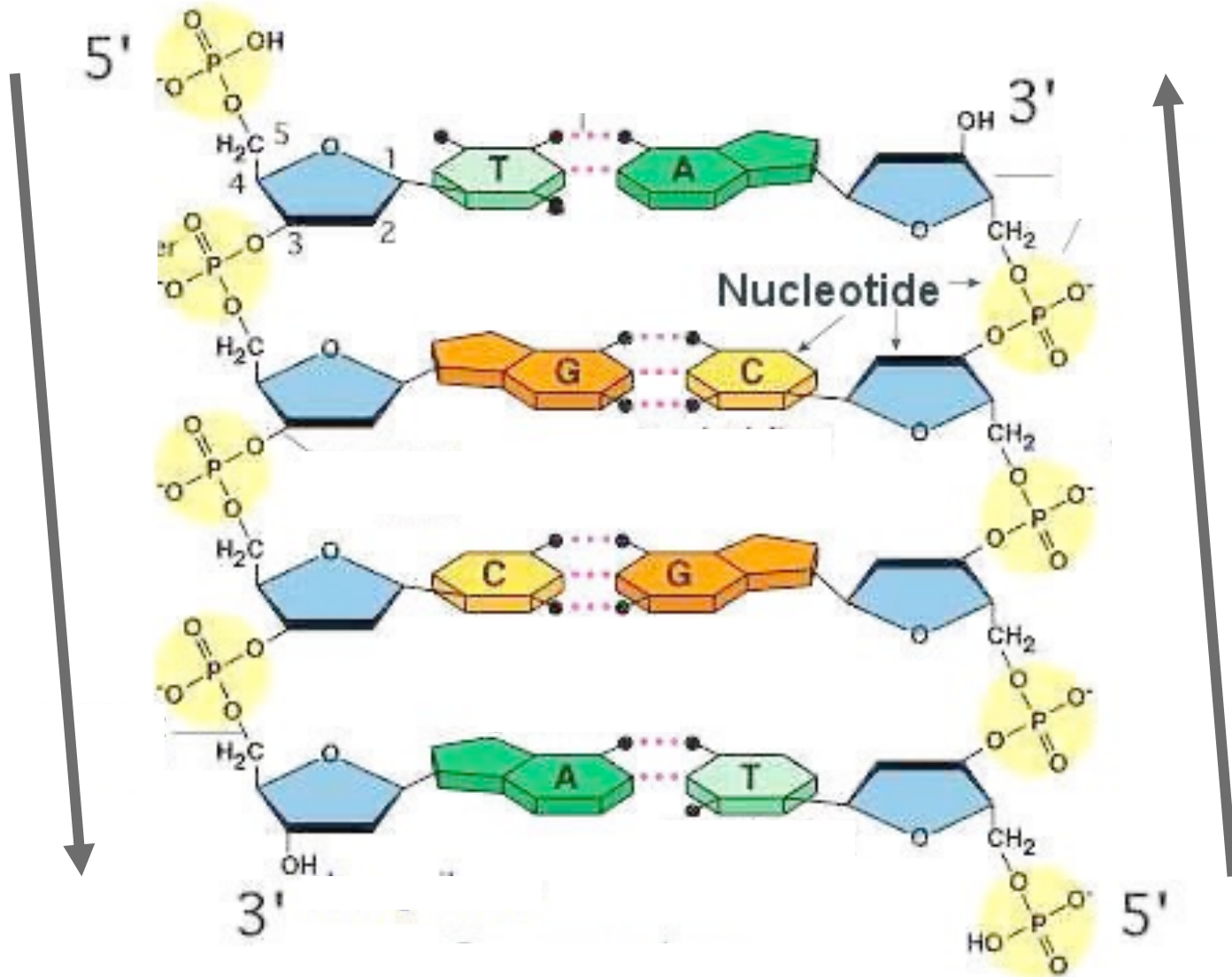


# Esqueleto da fita de DNA

Ligações fosfodiéster  
(covalentes)



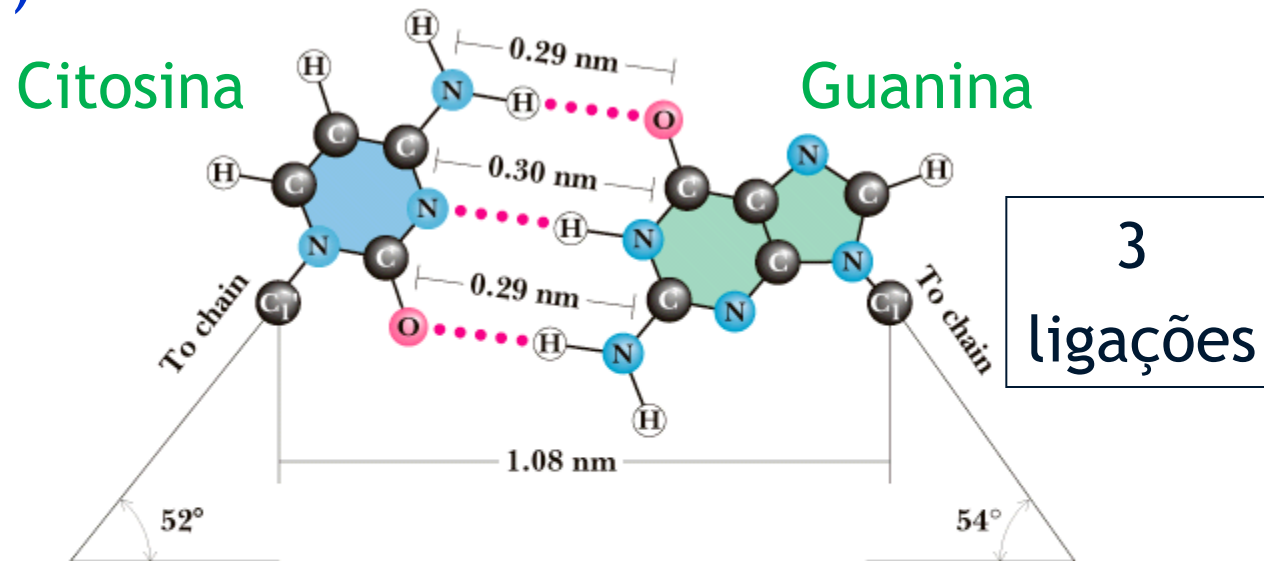
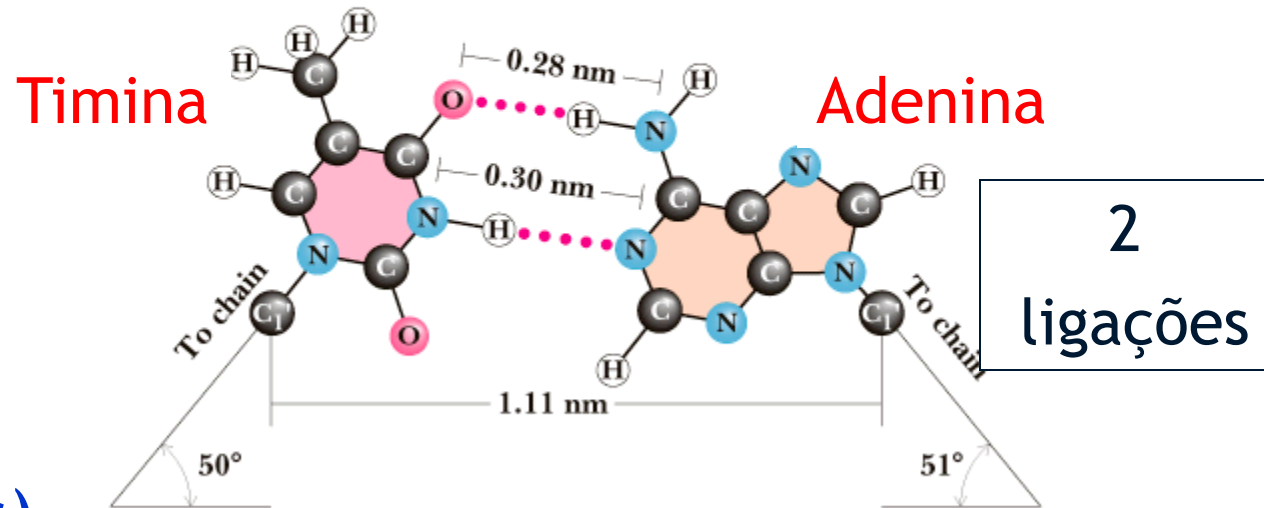
# Fitas são antiparalelas





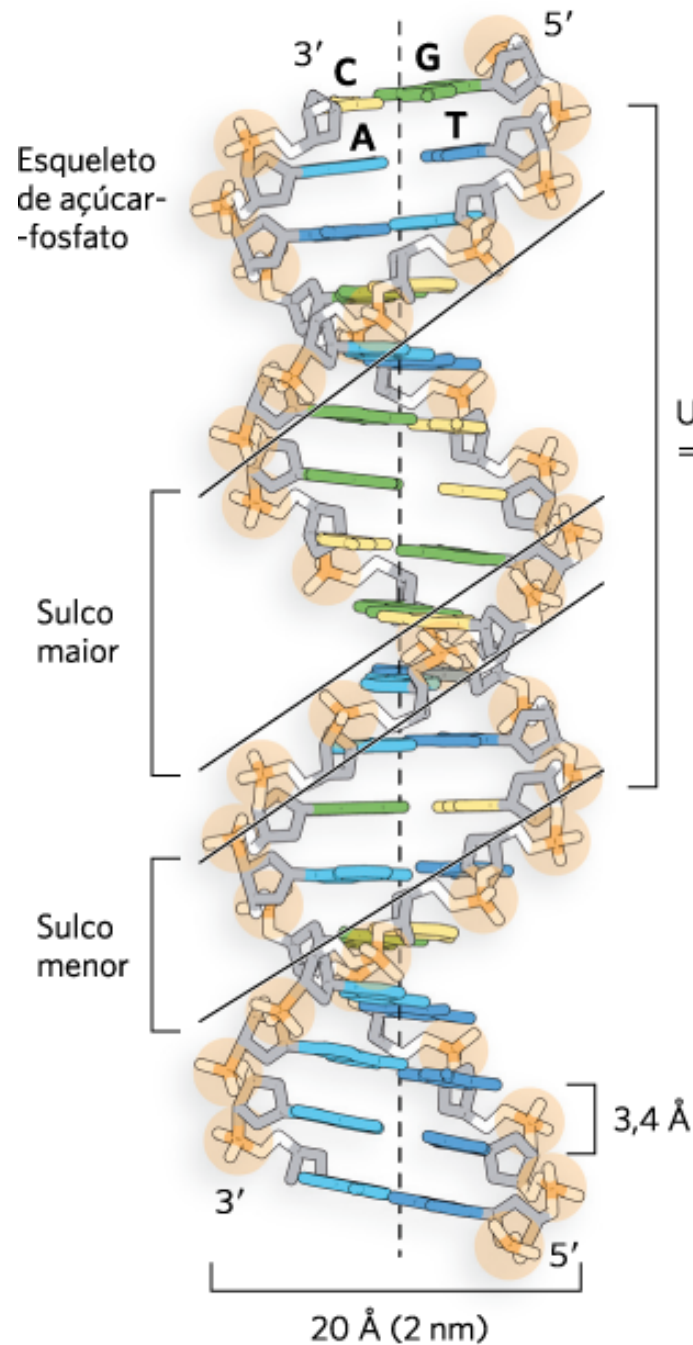
# Pareamento entre as bases

Ligações de Hidrogênio (não-covalentes)

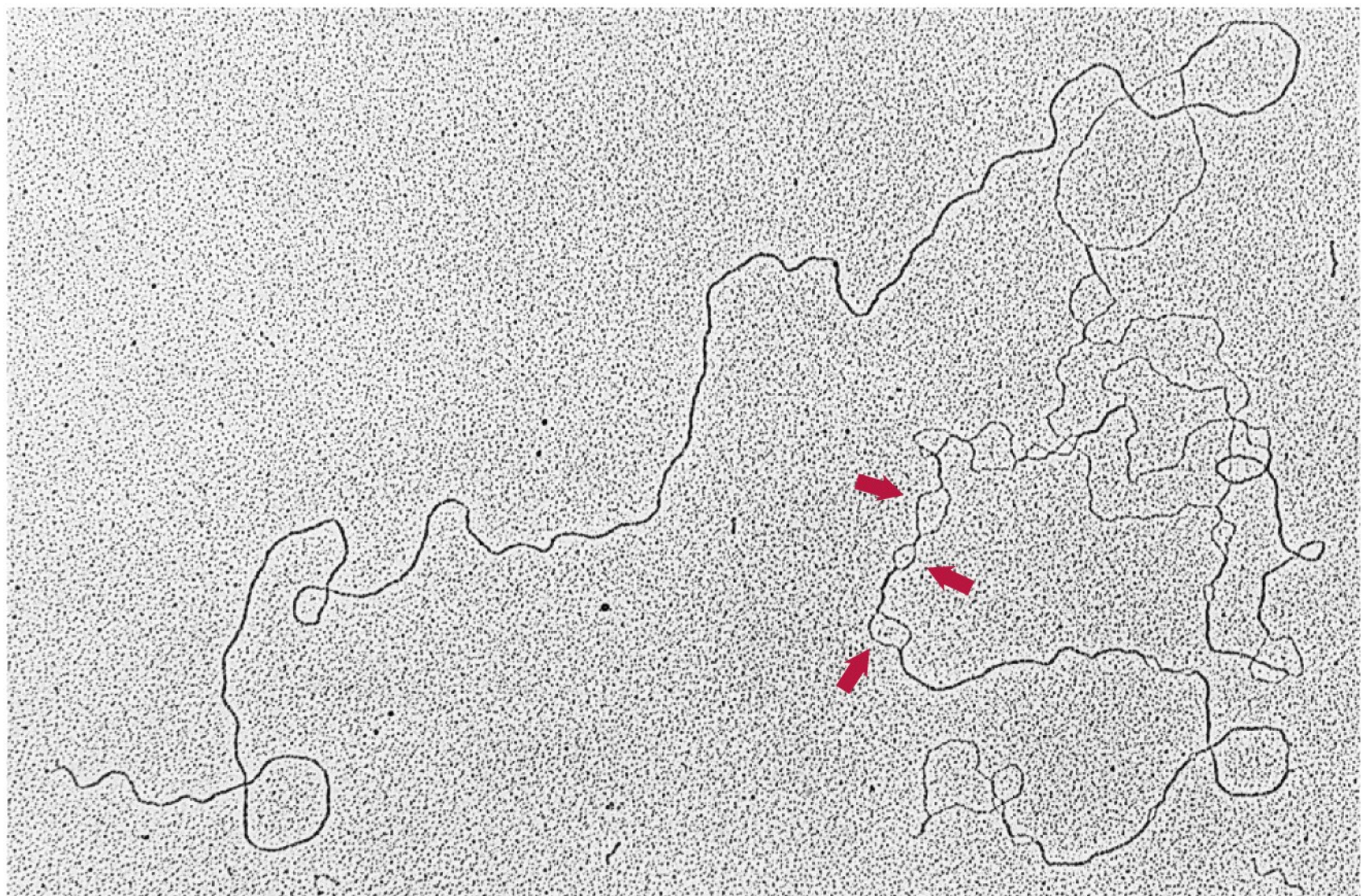




# Dupla hélice de DNA: Watson-Crick, 1953

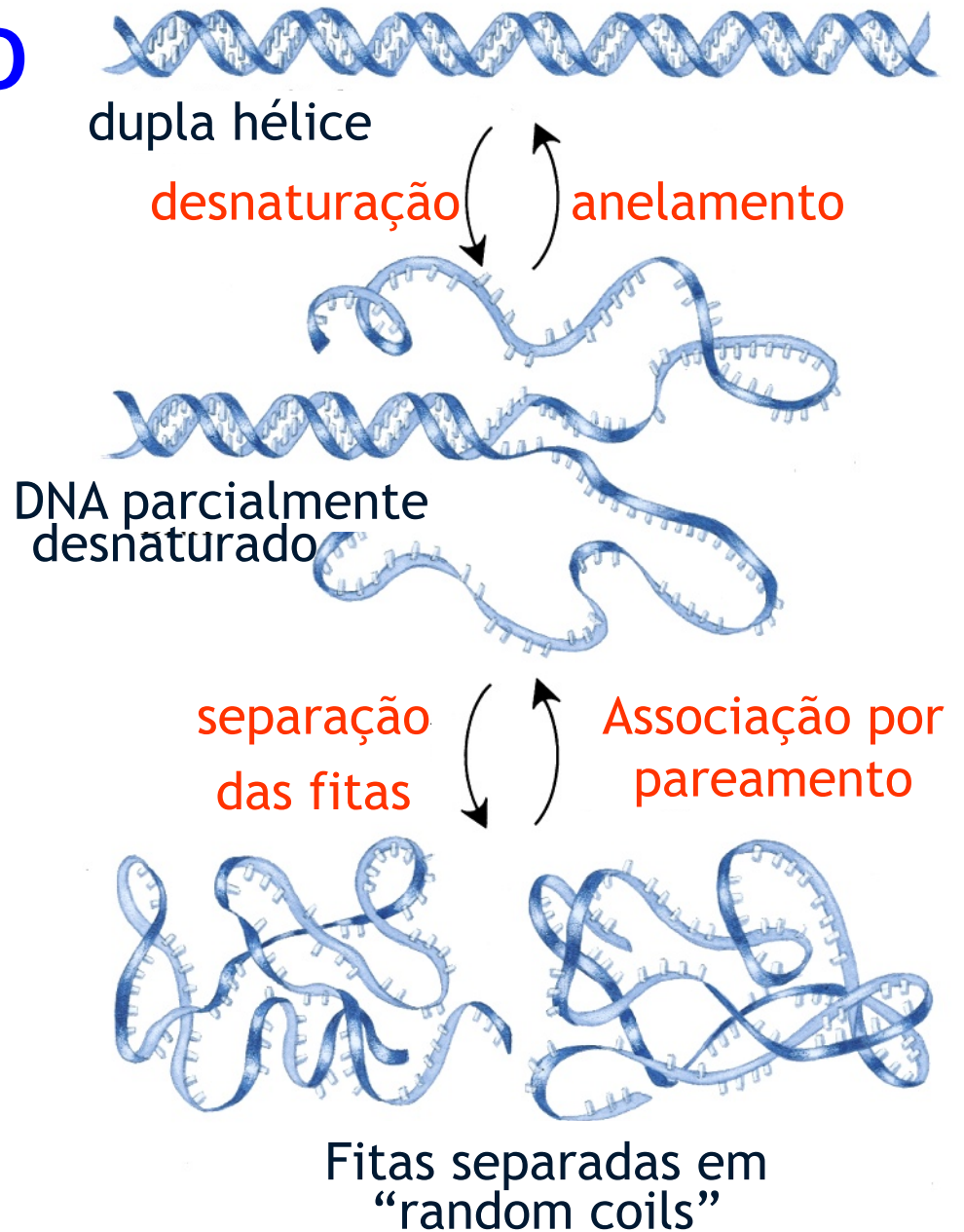


- duas cadeias antiparalelas enroladas em torno de um eixo
- esqueleto de fosfato para fora/ pares de bases para dentro da hélice dupla
- bases perpendiculares ao eixo da hélice, separadas por 3,4 angstroms
- diâmetro da hélice = 20 angstroms



3  $\mu\text{m}$

# Desnaturação do DNA = Abertura das fitas



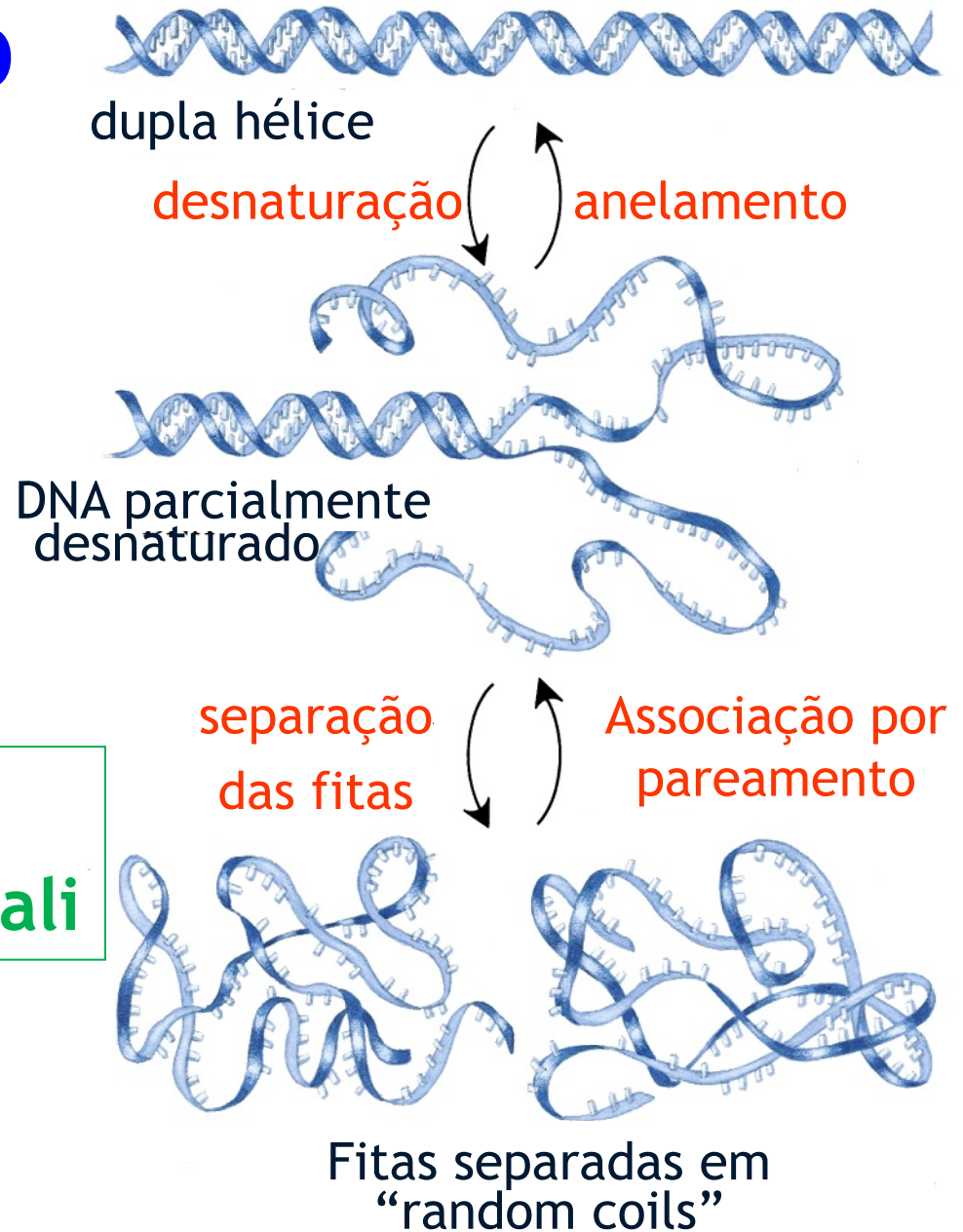
# Desnaturação do DNA

=

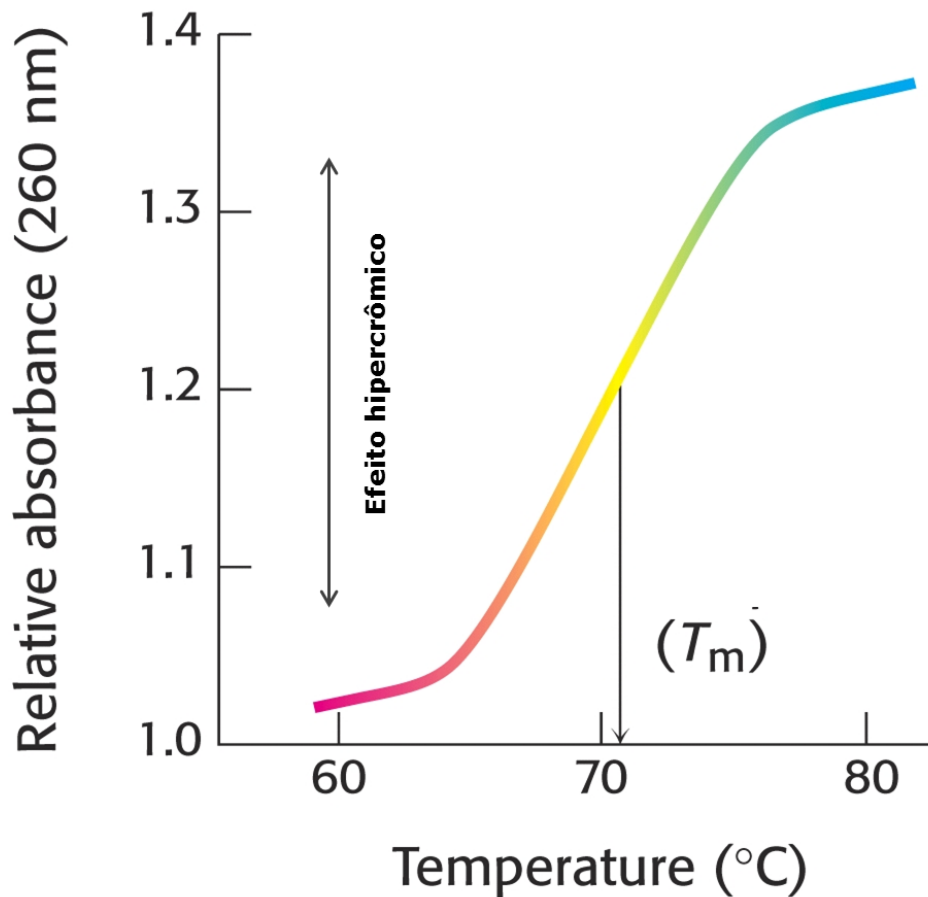
# Abertura das fitas

Calor

Tratamento com álcali



# Desnaturação do DNA

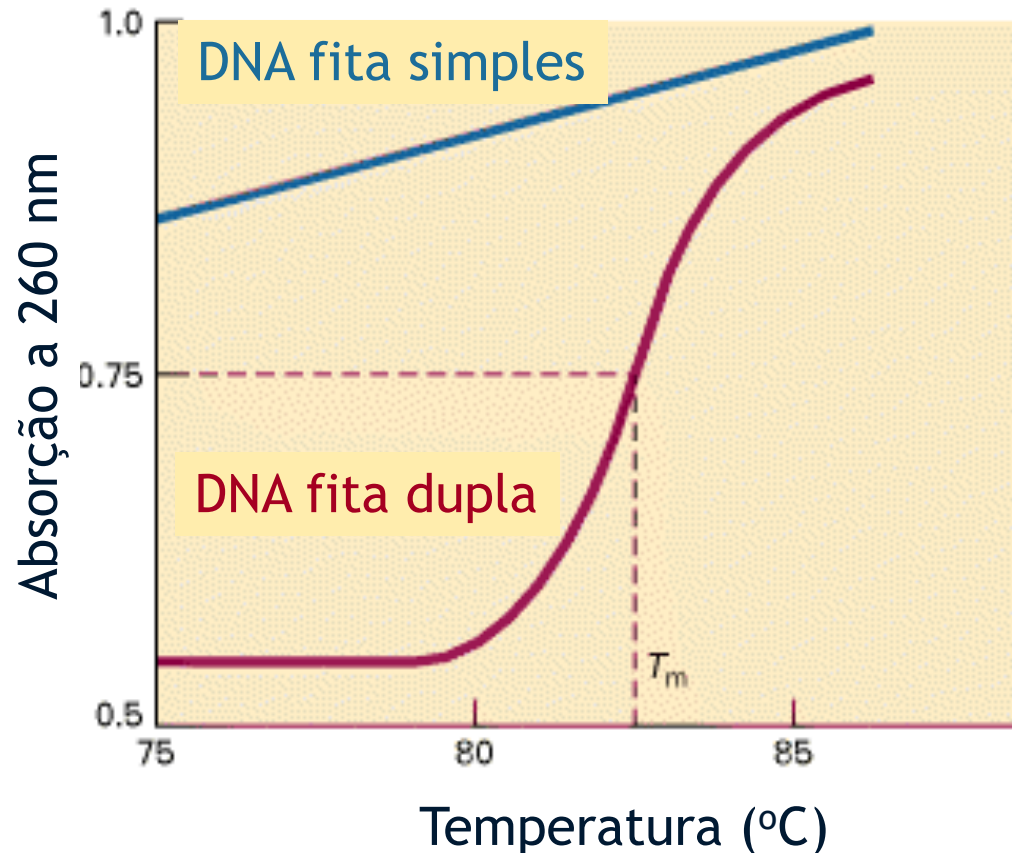


Rompimento das ligações de H entre as bases

$T_m$  = Temperatura de fusão (50% do DNA está desnaturado)

Efeito hiper-crômico (aumento da absorvância pela maior exposição dos anéis das bases)

# Desnaturação do DNA

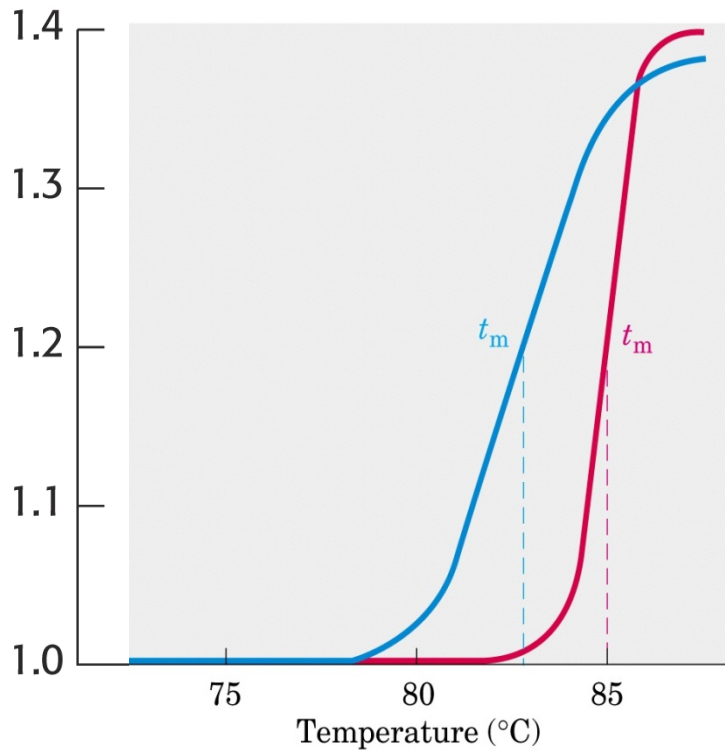


$T_m$ : temperatura em que 50% das fitas estão dissociadas

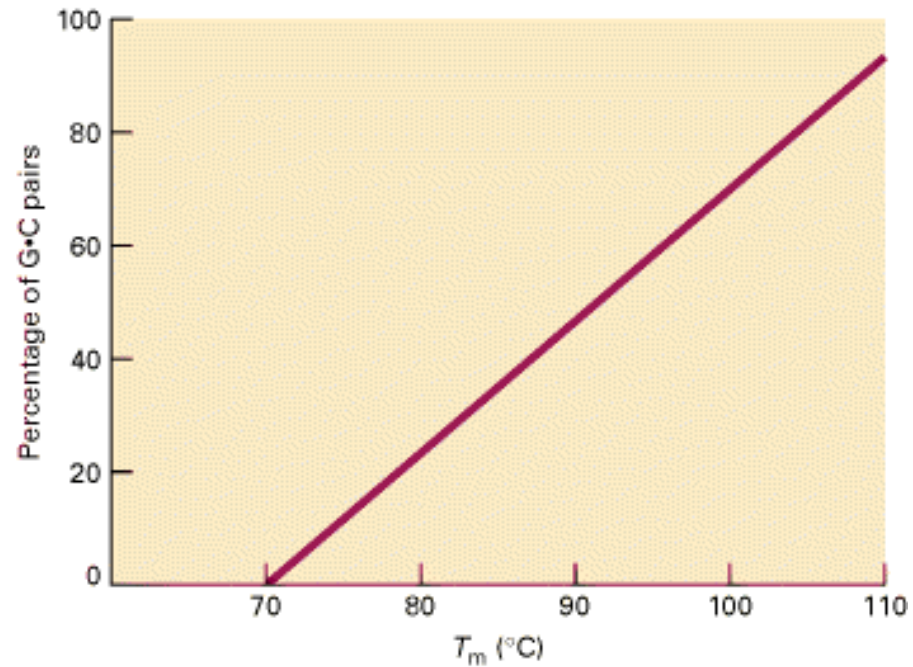


# $T_m$ varia com %G+C

Relative absorbance (260 nm)



(b)



NEWS • 21 FEBRUARY 2019

# Four new DNA letters double life's alphabet

*Synthetic DNA seems to behave like the natural variety, suggesting that a broader swathe of chemicals could support life than the four that evolved on Earth.*

Matthew Warren

<https://www.nature.com/articles/d41586-019-00650-8>

- O que são as letras do DNA?
- Que características elas devem ter para que o DNA mantenha sua estabilidade estrutural?
- Seria possível transcrever esse DNA em RNA?
- E sintetizar uma proteína com a informação contida nele?



# Estrutura do RNA

DNA

RNA

Ligação  
fosfodiester

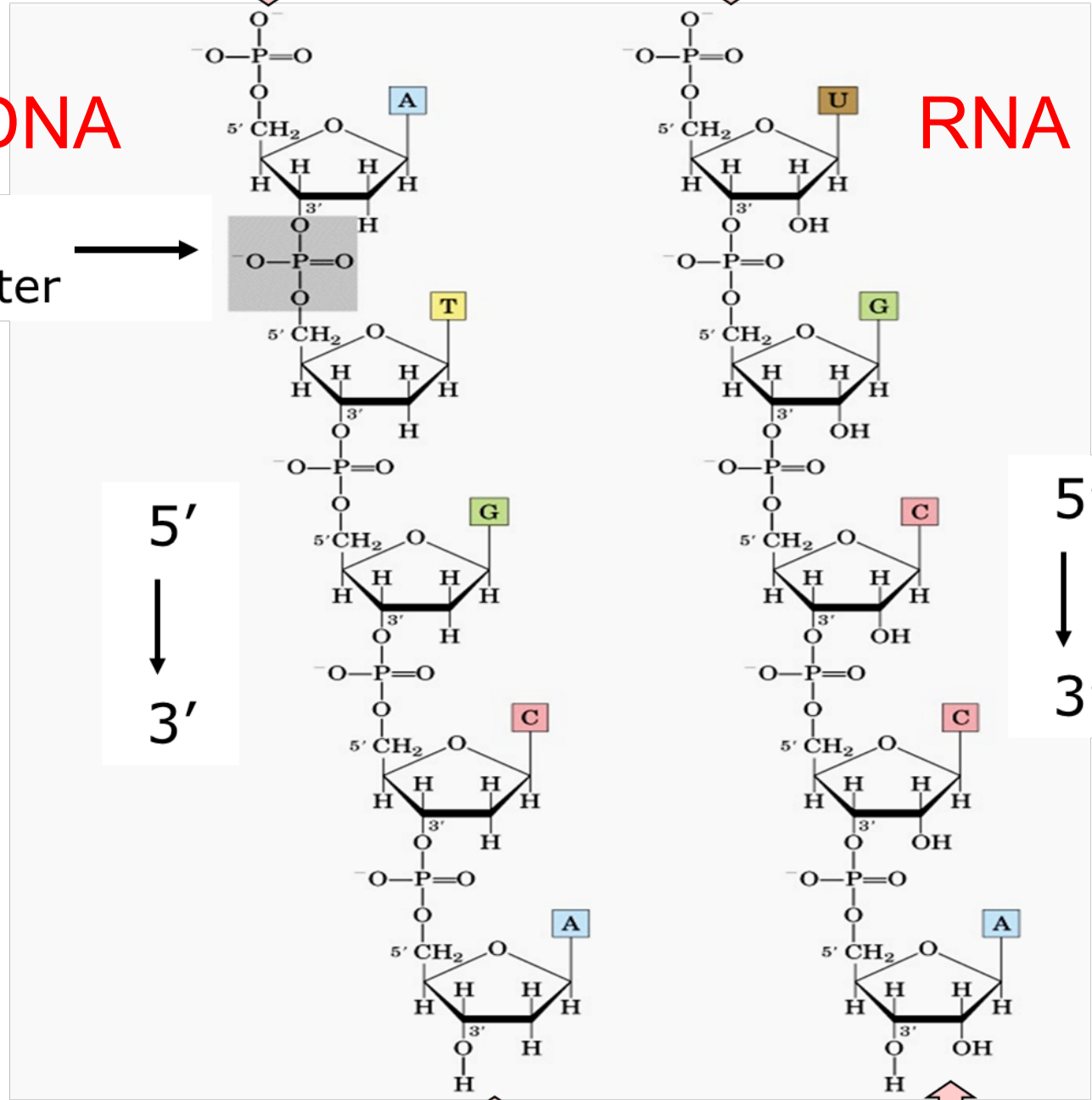


Extremidade 5'

Extremidade 3'

5'  
↓  
3'

5'  
↓  
3'



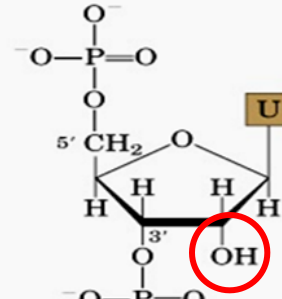
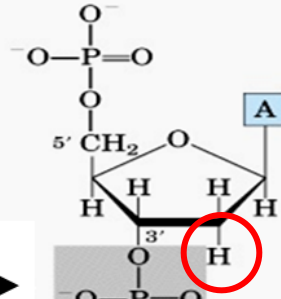
DNA

RNA

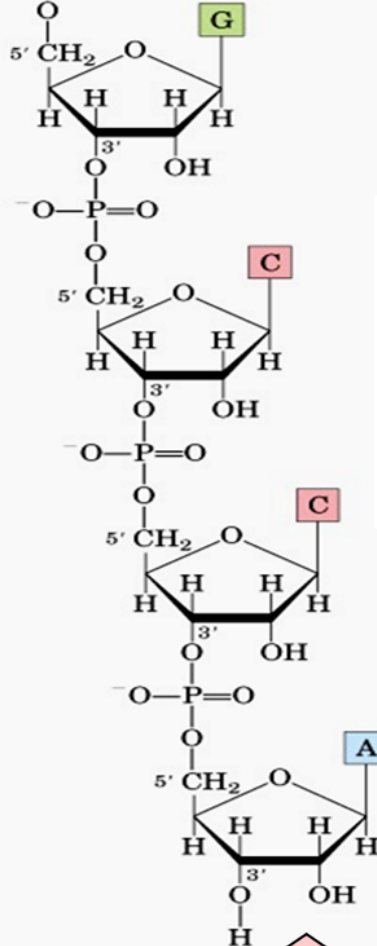
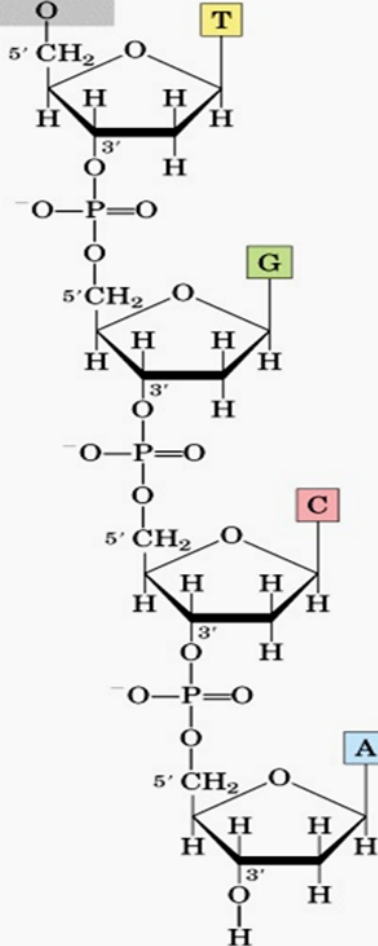
Ligação  
fosfodiester



Extremidade 5'



5'  
↓  
3'



5'  
↓  
3'

Extremidade 3'

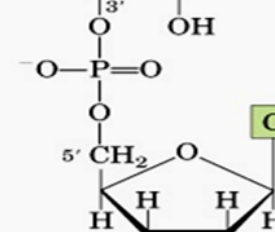
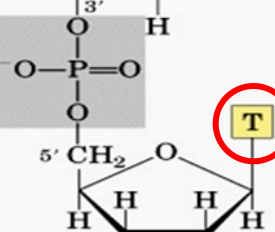
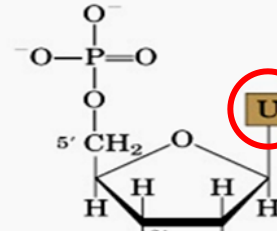
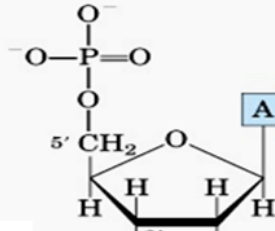
DNA

RNA

Ligação  
fosfodiester



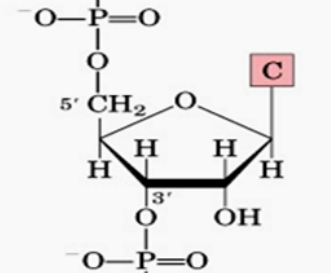
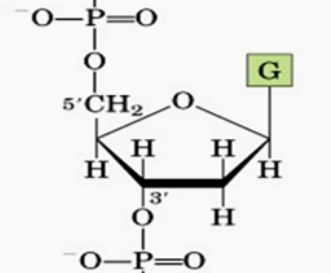
Extremidade 5'



5'



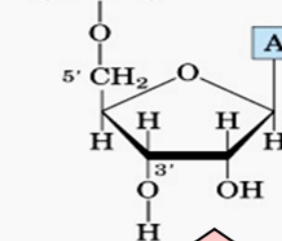
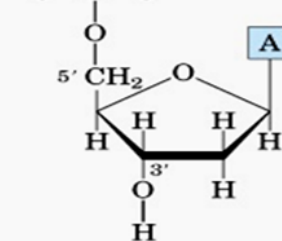
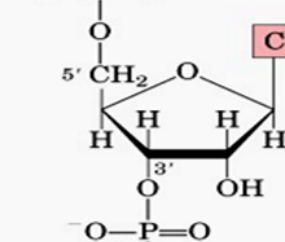
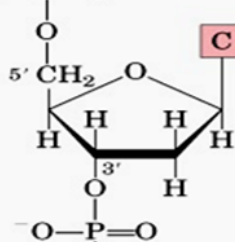
3'



5'



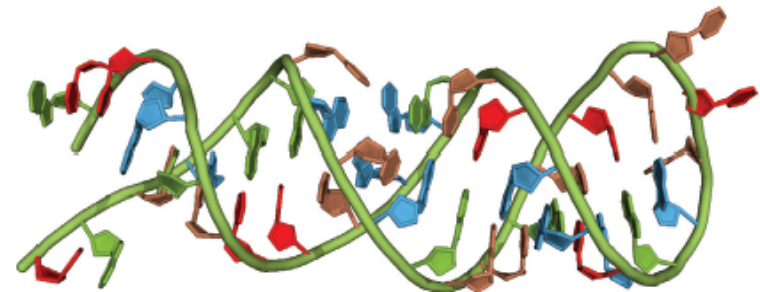
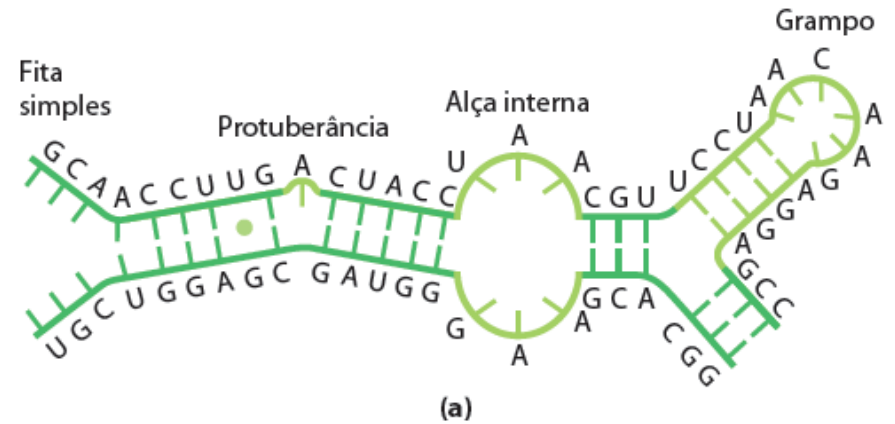
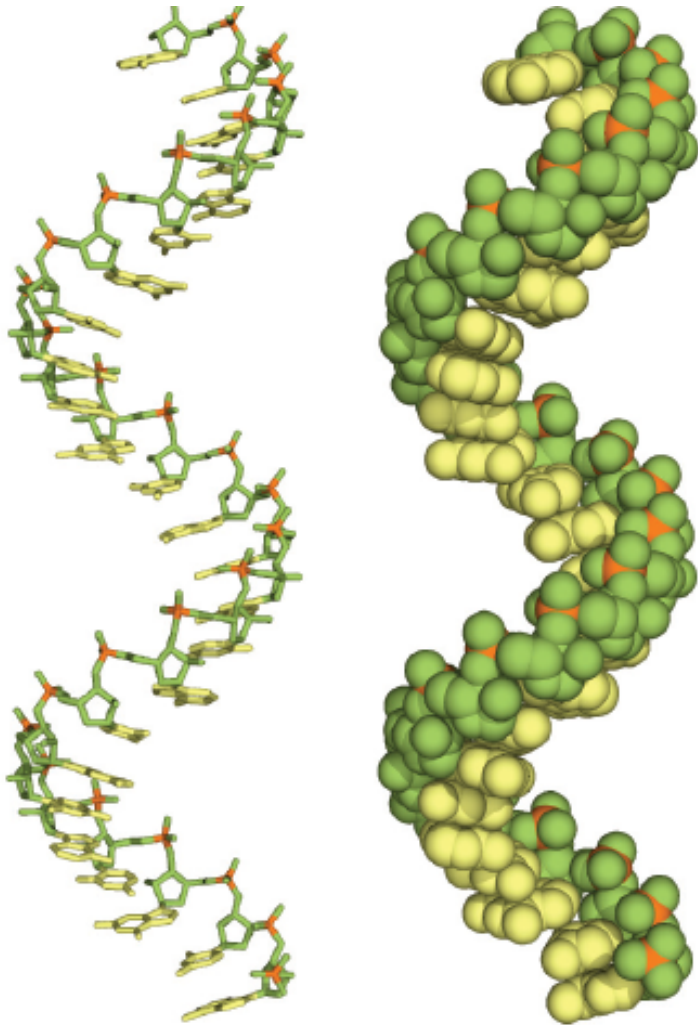
3'



Extremidade 3'



# Estrutura de RNA



Dupla-hélice em forma de grampo

(b)

Fita simples pode se dobrar e parear entre si

# Classes de RNAs

- RNAs codificadores de proteínas:
  - mRNA (RNA mensageiro)
- RNAs não codificadores:
  - tRNA (RNA transportador)
  - rRNA (RNA ribossomal)
  - outros ncRNAs

**QUADRO 5.2** Moléculas de RNA em *E. coli*

Tipo	Quantidade Relativa (%)	Coefficiente de Sedimentação (S)	Massa (kd)	Número de Nucleotídeos
RNA ribossômico (rRNA)	80	23	$1,2 \times 10^3$	3.700
		16	$0,55 \times 10^3$	1.700
RNA transportador (tRNA)	15	5	$3,6 \times 10^1$	120
		4	$2,5 \times 10^1$	75
RNA mensageiro (mRNA)	5		Heterogêneo	



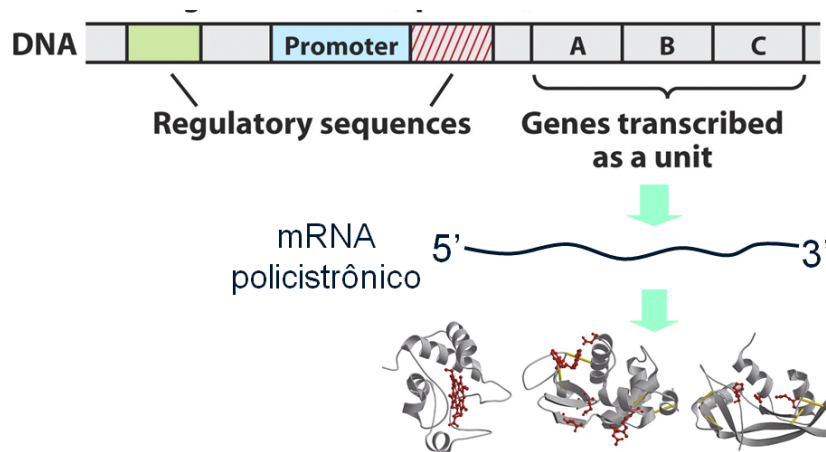
# Classes de RNAs não codificadores de proteínas (ncRNA)

- tRNA: transporta os aminoácidos ativados até os ribossomos
  - rRNA: principal componente dos ribossomos
  - snoRNA\* (RNA nucleolar pequeno): maturação de ribossomos e tRNAs
  - snRNA\* (RNA nuclear pequeno): processamento do mRNA
  - gRNA (RNA guia): sistema CRISPR (imunidade de bactérias)
  - sRNA (*small* RNA): modula tradução e estabilidade de mRNAs
  - miRNA\* (micro RNA)
  - siRNA\* (RNA de interferência)
  - outros....
- } silenciamento gênico

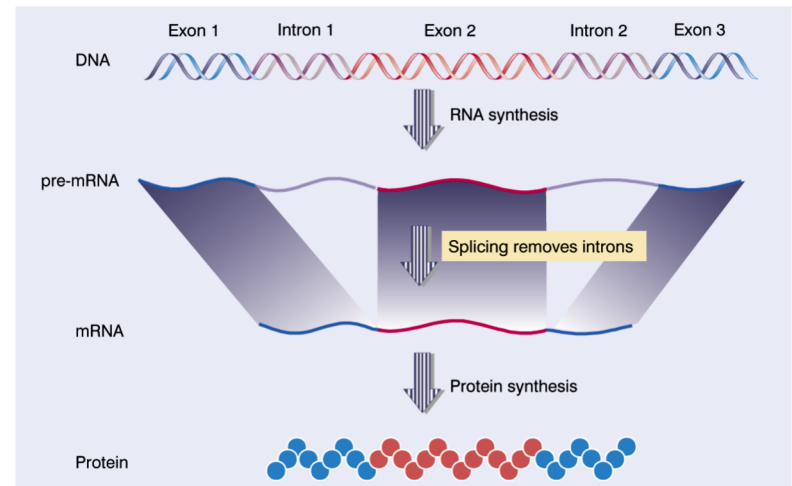
\* apenas em eucariotos

# RNA mensageiro (mRNA)

- Informação para a síntese de proteínas
- Um ou mais genes em bactérias

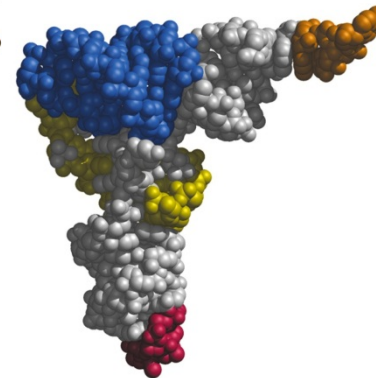
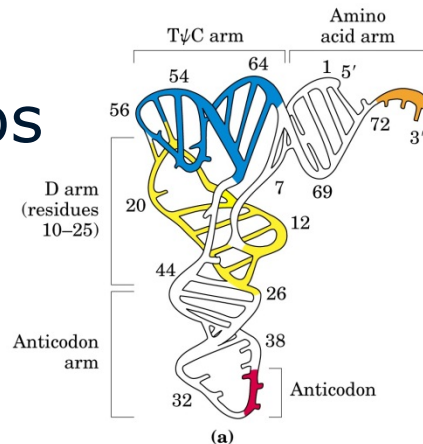
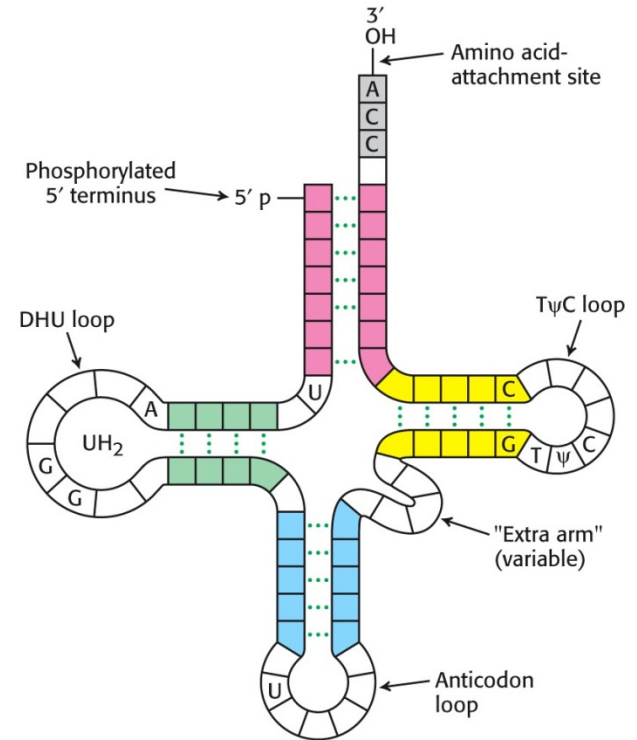


- Processamento no núcleo (eucariotos)

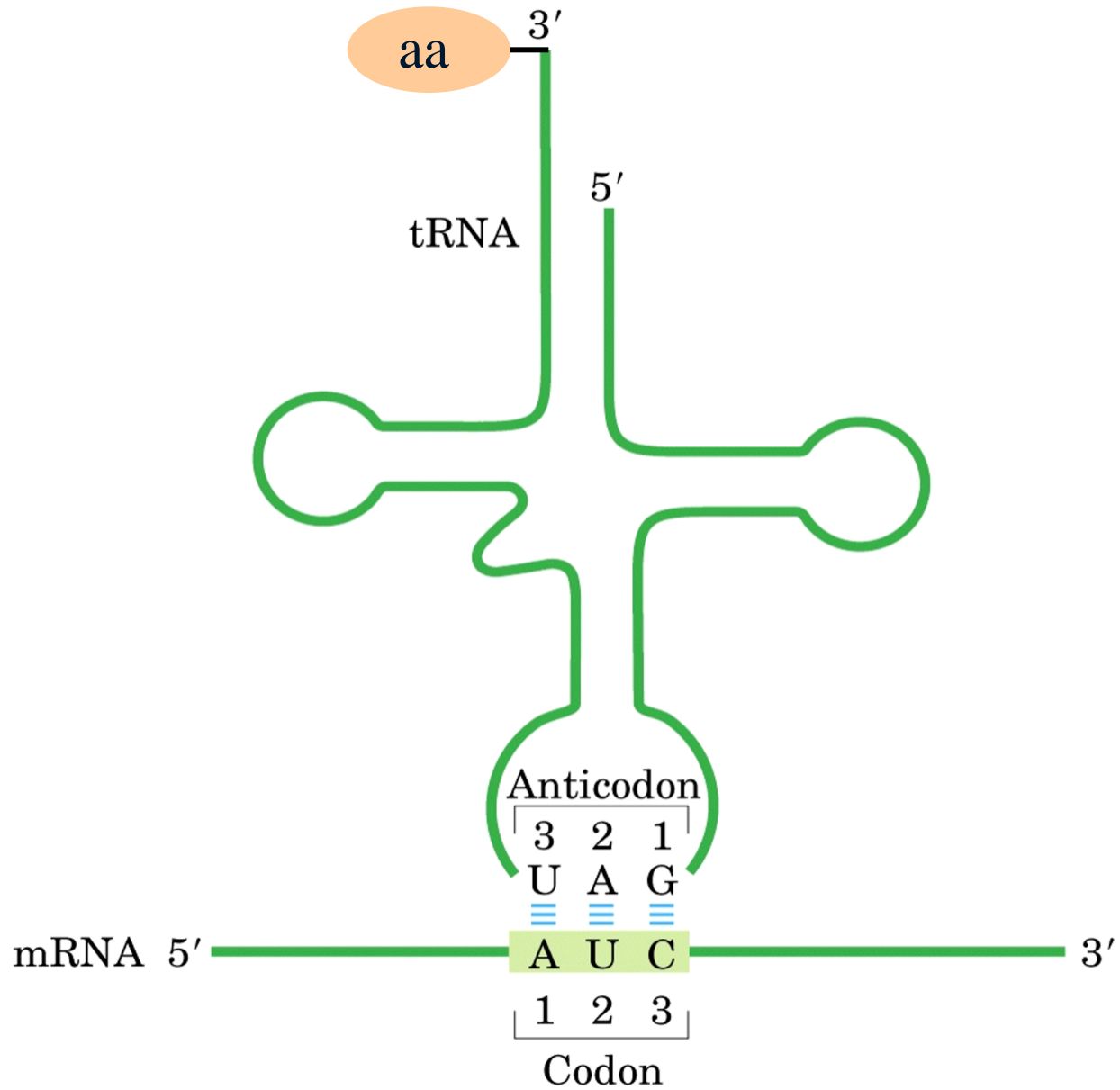


# RNA transportador (tRNA)

- Estrutura secundária com grampos e alças formando um trevo
- Bases modificadas depois da transcrição
- ~ 70-100 nucleotídeos

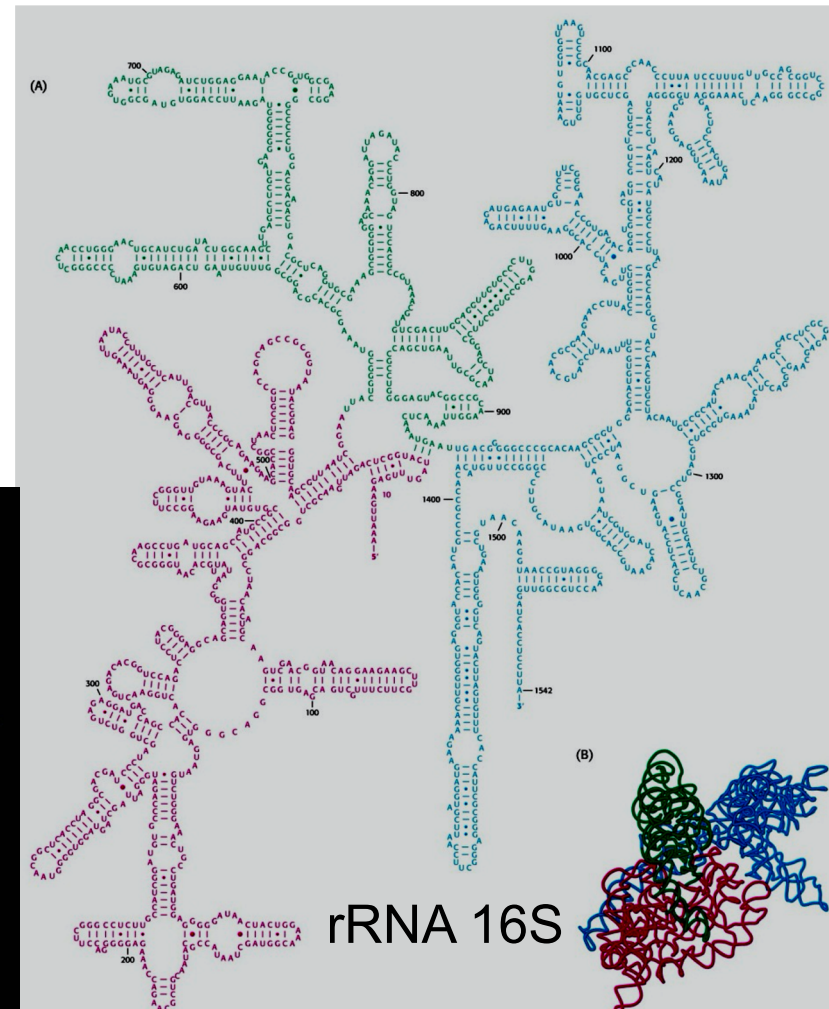
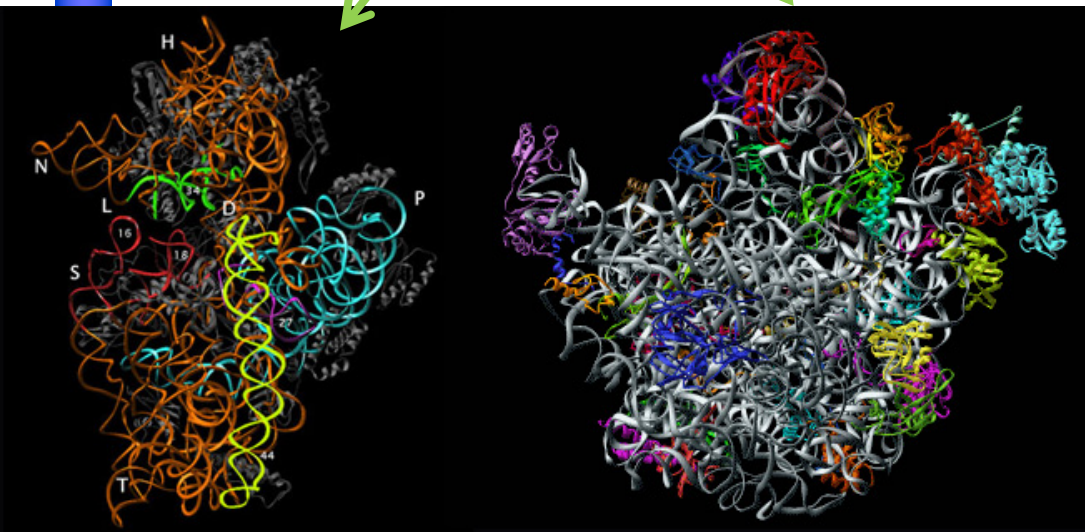
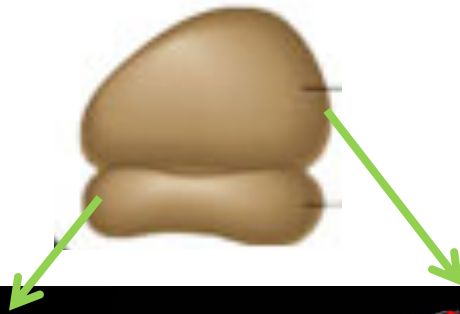


# Pareamento tRNA-mRNA



# RNA ribossomal (rRNA)

- 90% do RNA total do RNA da célula
- Associado a proteínas ribossomais

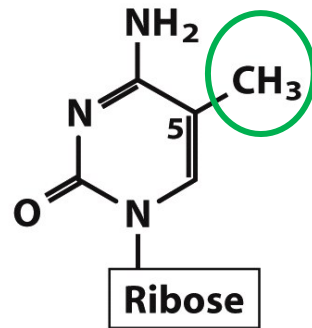


# RNA

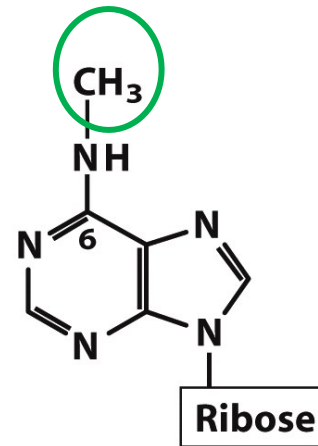
- Fita simples pode formar estruturas muito mais complexas do que a dupla hélice do DNA
- Estruturas dependem da sequência e do pareamento entre bases na mesma fita
- Funções diferentes para estruturas diferentes!

# Slides adicionais

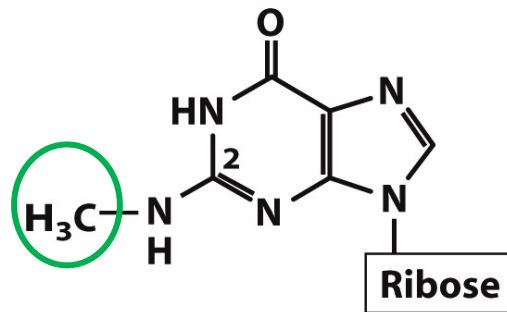
# Bases no DNA podem sofrer modificações químicas fisiológicas



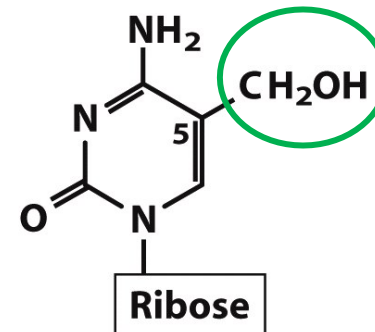
5-Methylcytidine



N<sup>6</sup>-Methyladenosine



N<sup>2</sup>-Methylguanosine



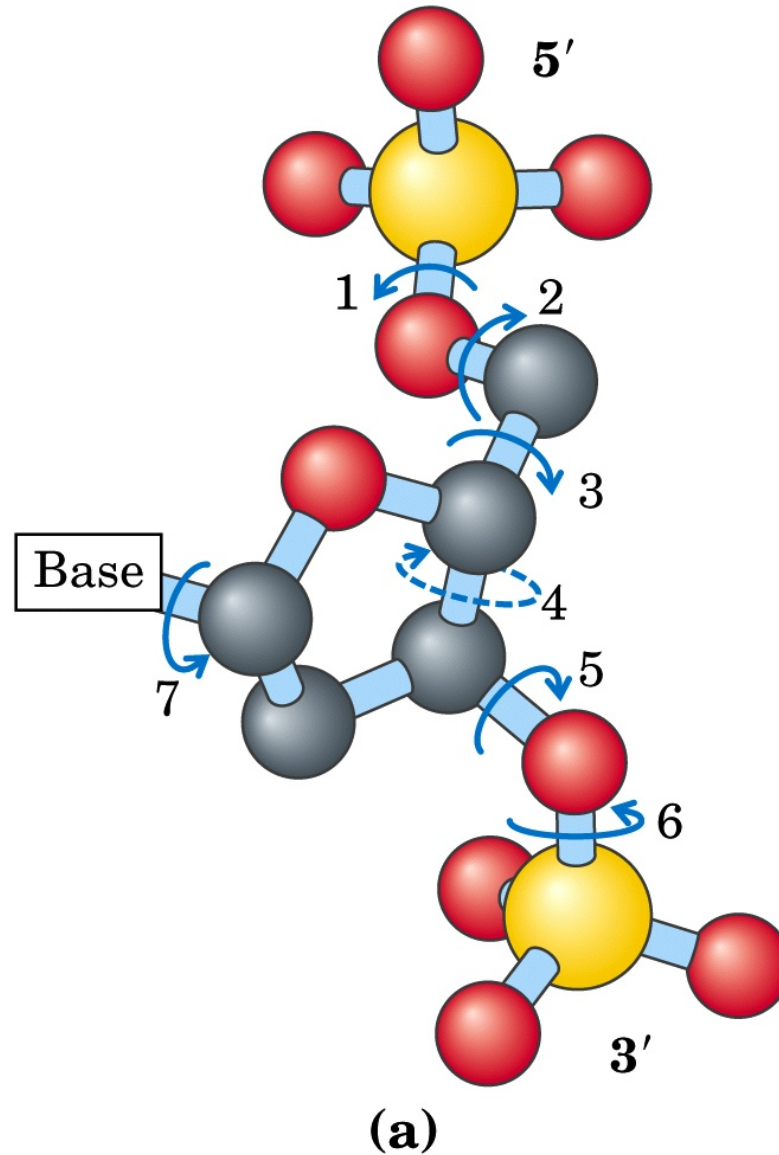
5-Hydroxymethylcytidine

Figure 8-5a  
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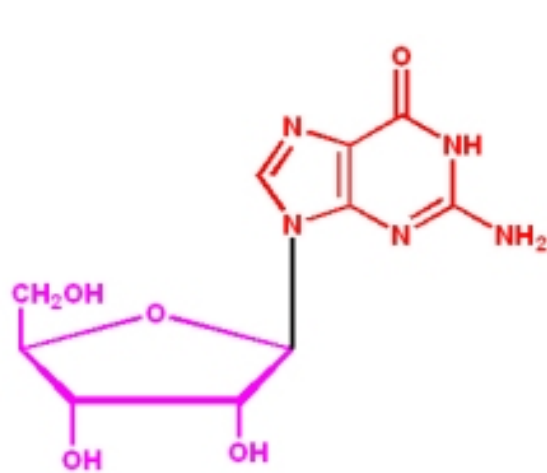
# Epigenética



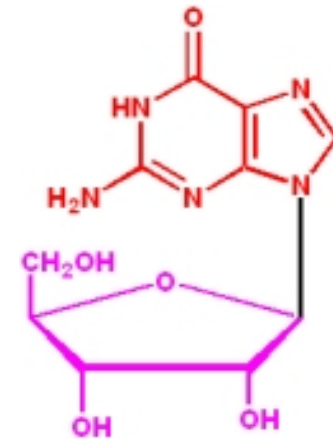
# Flexibilidade das ligações no DNA



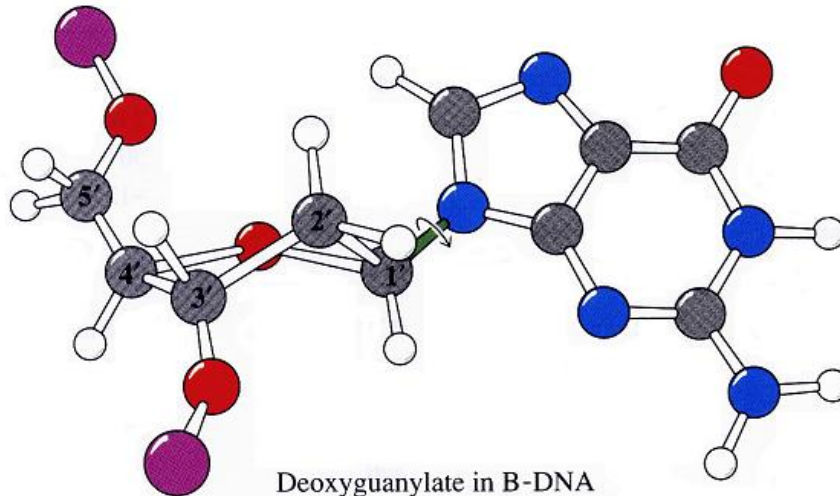
# Flexibilidade das ligações no DNA



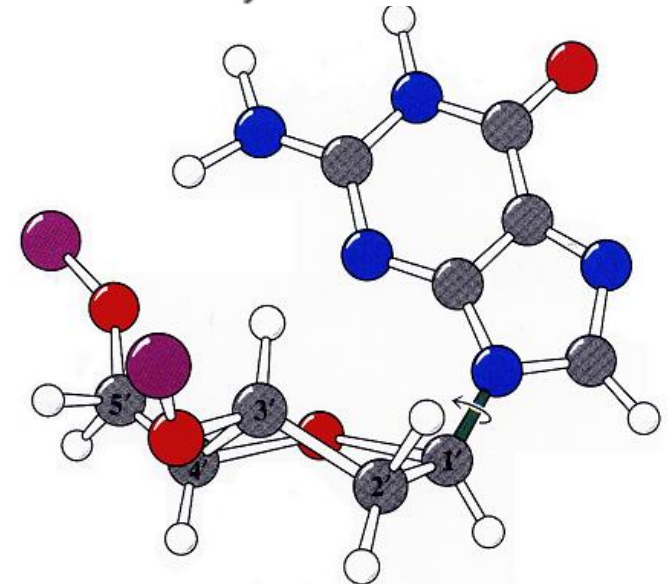
*anti* Guanosine



*syn* Guanosine



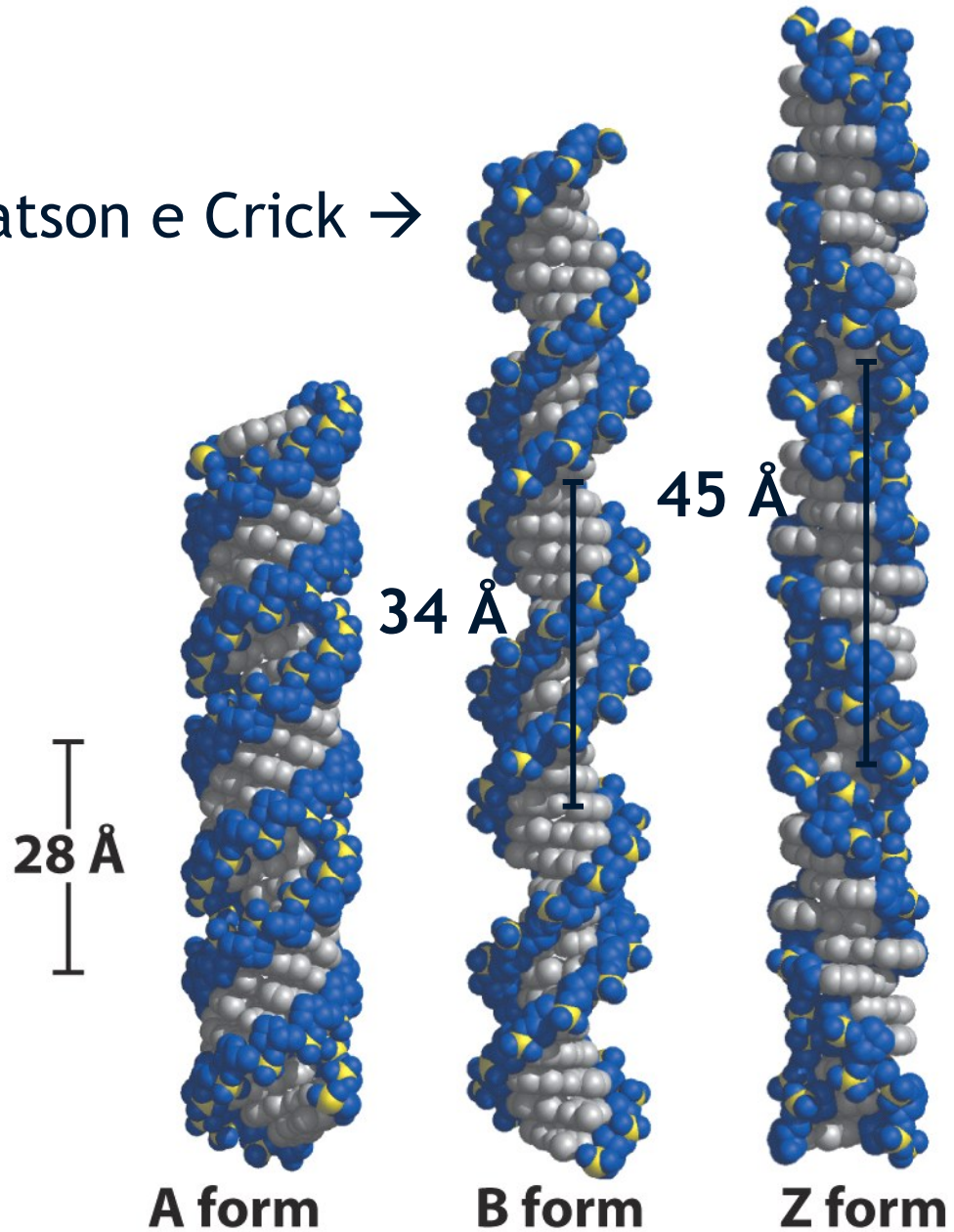
Deoxyguanylate in B-DNA  
*anti* conformation



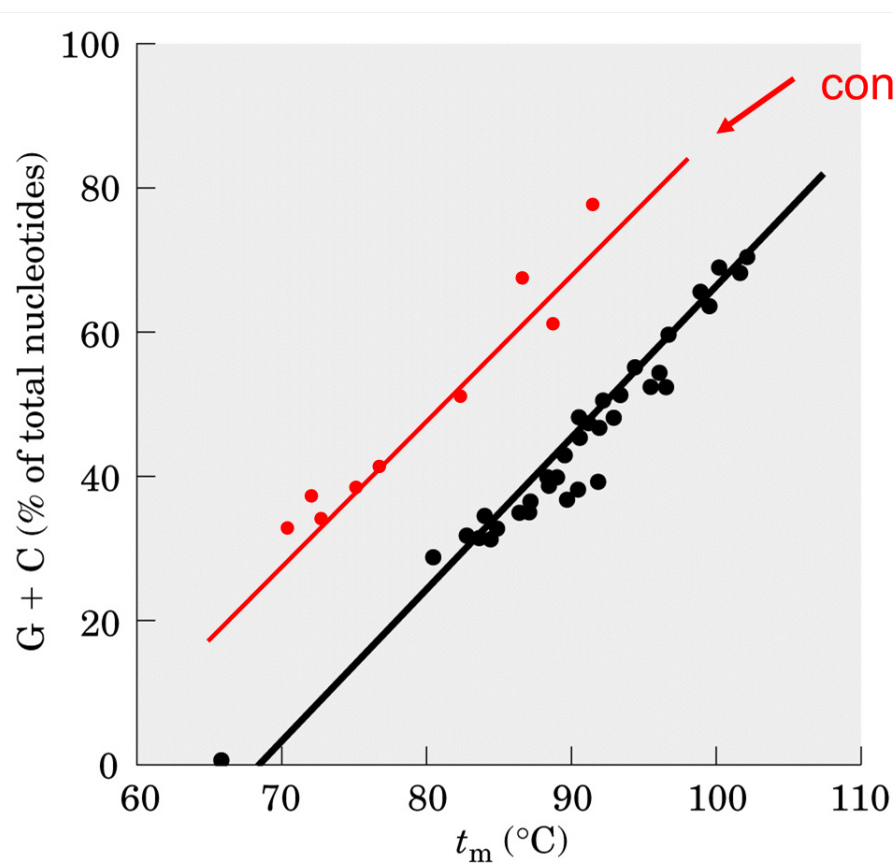
Deoxyguanylate in Z-DNA  
*syn* conformation

# Formas do DNA

Forma B - Watson e Crick →



# T<sub>m</sub> varia com a concentração de sal

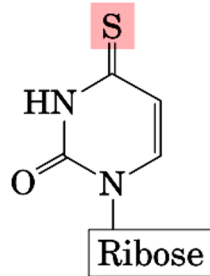


Baixa  
concentração  
de sal

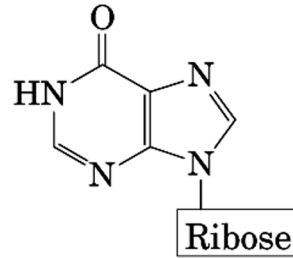
↓sal → repulsão eletrostática  
das fitas do DNA carregado  
negativamente favorece a  
separação (diminui a  $T_m$ )

↑sal → A dupla fita é mais  
estável (aumenta a  $T_m$ )

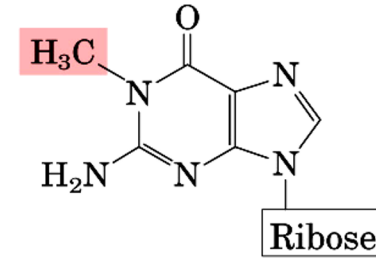
# Bases modificadas no tRNA



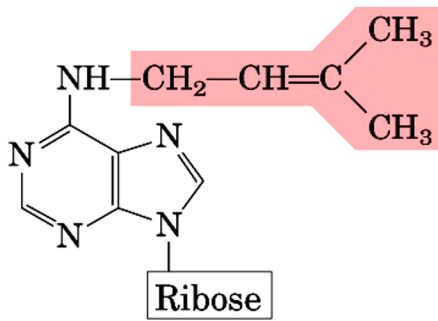
4-Thiouridine ( $S^4U$ )



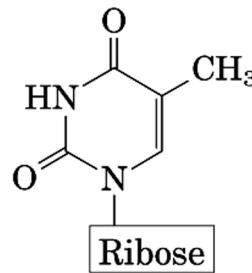
Inosine (I)



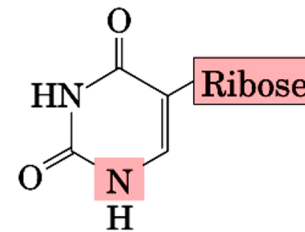
1-Methylguanosine ( $m^1G$ )



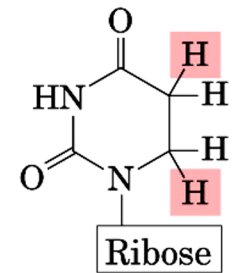
$N^6$ -Isopentenyladenosine ( $i^6A$ )



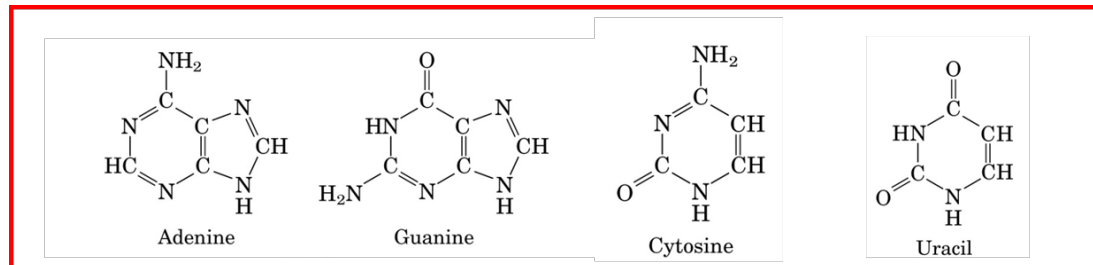
Ribothymidine (T)



Pseudouridine ( $\psi$ )



Dihydrouridine (D)



# Slides extras

## ESTRUTURA DE PROTEÍNAS

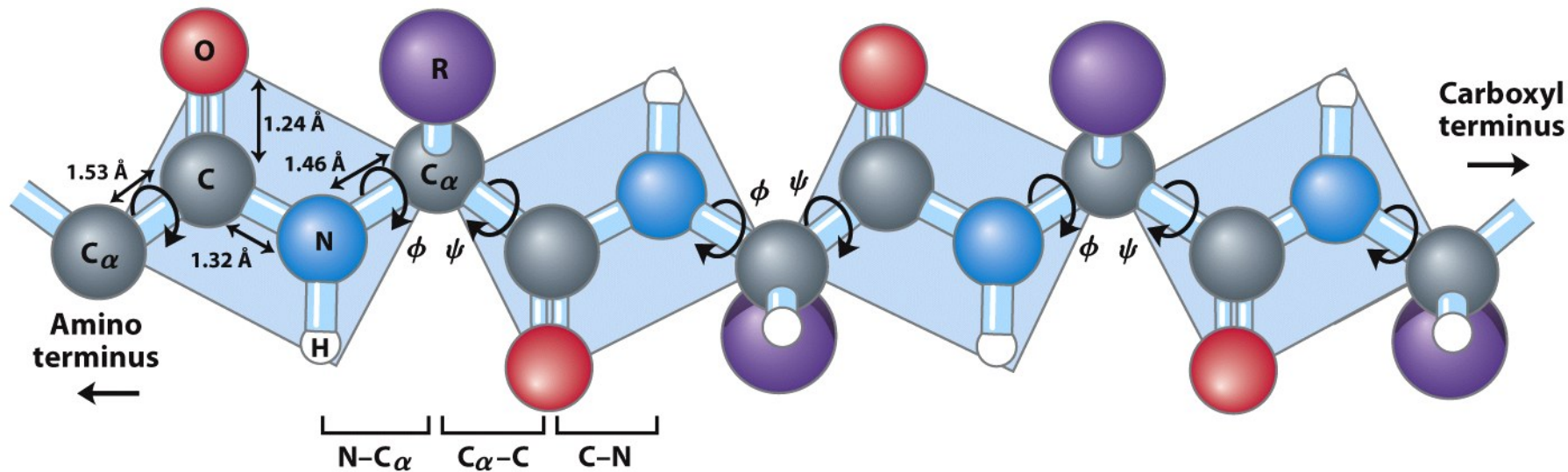


Figure 4-2b

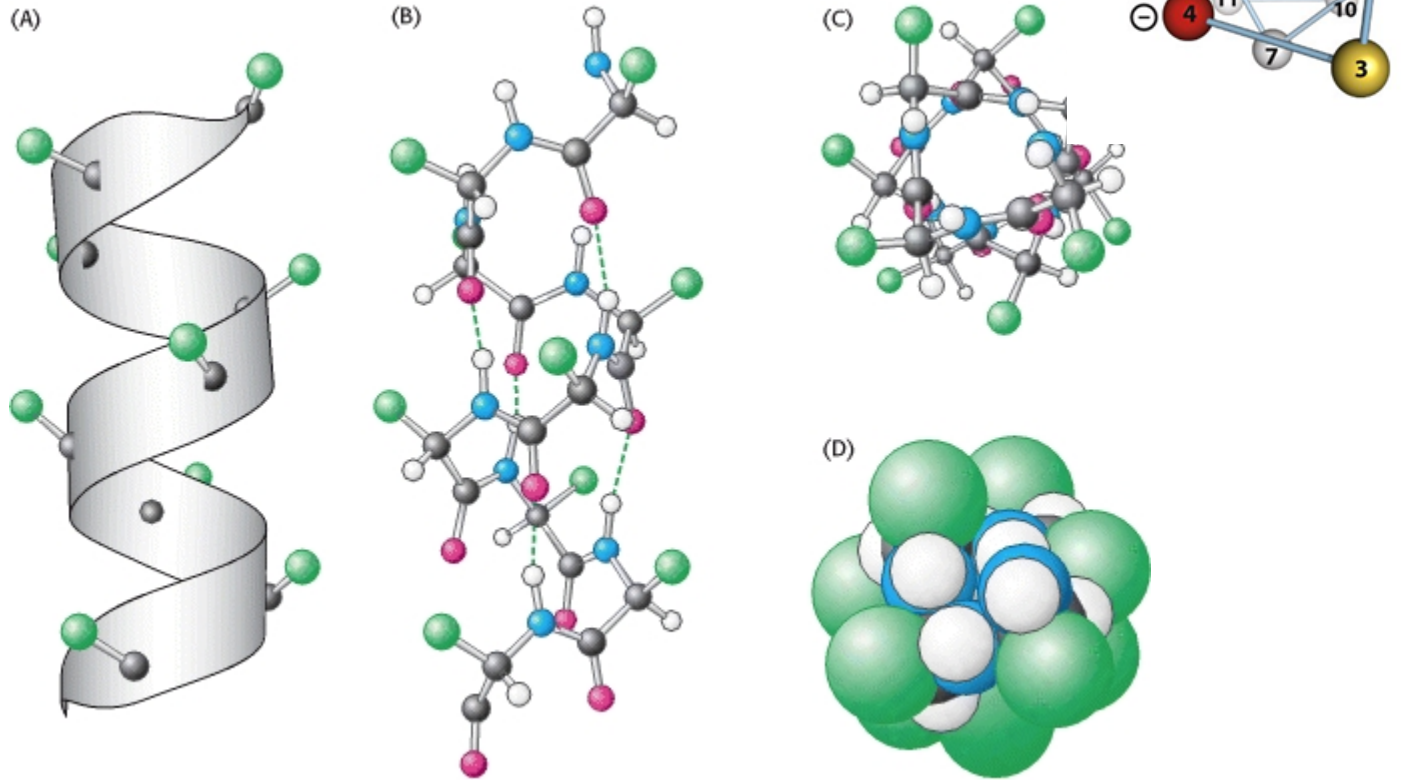
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# Estruturas secundárias regulares de proteínas globulares

- Estabilizadas por ligações de hidrogênio entre grupos NH e C=O do esqueleto da cadeia
- Ângulos  $\phi$  e  $\psi$  praticamente idênticos ao longo da cadeia
- $\alpha$  hélice, folha  $\beta$  [e  $\beta$ -turn (volta  $\beta$ )]

# $\alpha$ hélice



Esqueleto mais compacto

$0^\circ < \psi < -70^\circ$  ( $C\alpha$  - carbonila)

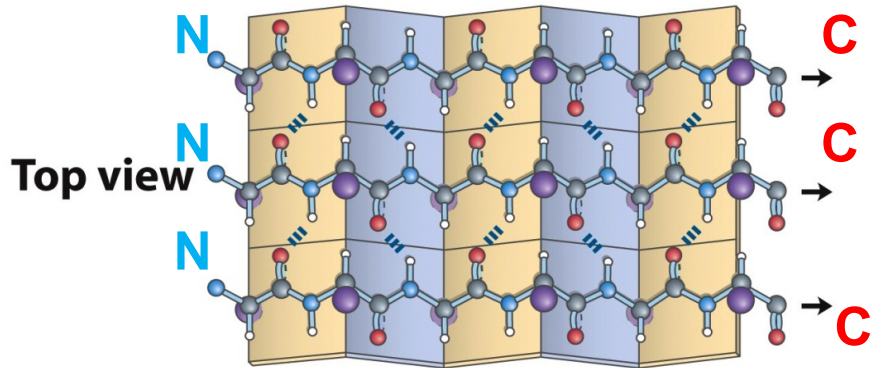
- 3,6 resíduos de aa por volta

- Ligações de H paralelas ao eixo, entre 1 aa e o 4º aa seguinte
- Cadeias laterais voltadas para fora

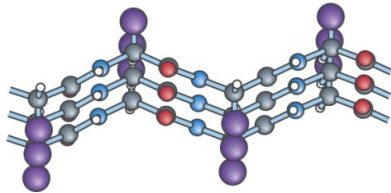


# Folhas $\beta$

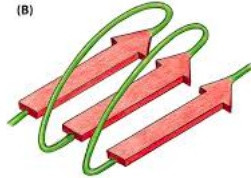
## Parallel



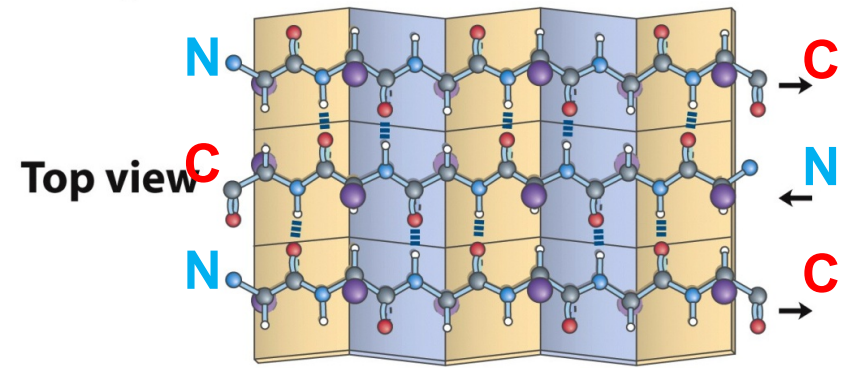
## Side view



(B)



## Antiparallel



## Side view

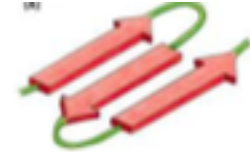
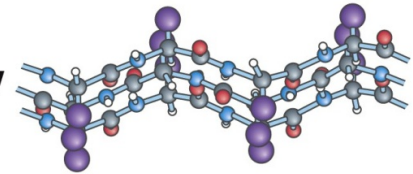
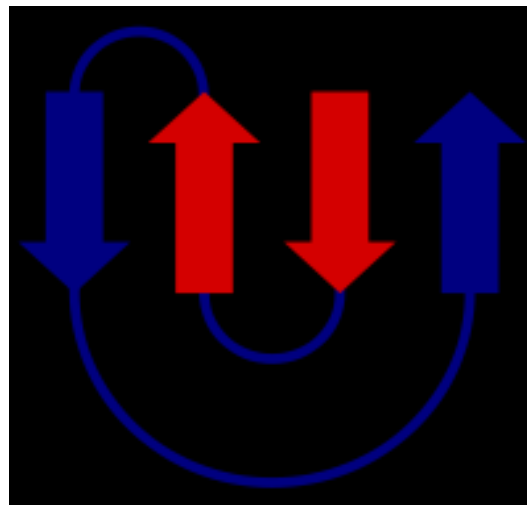
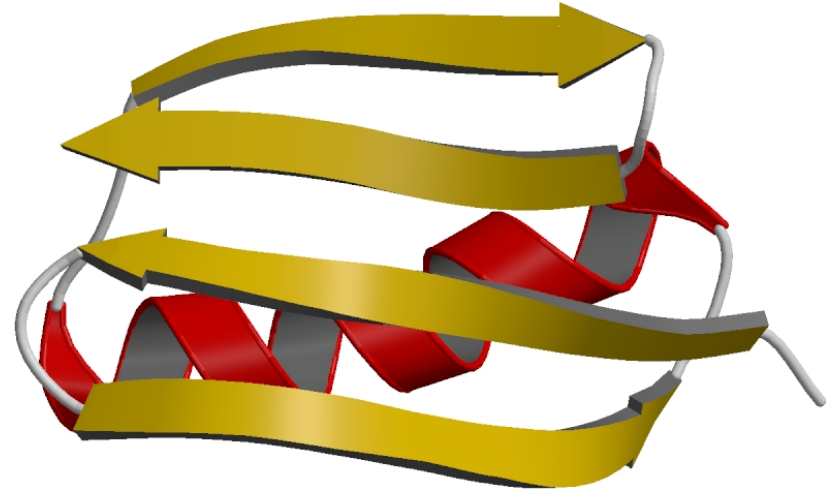
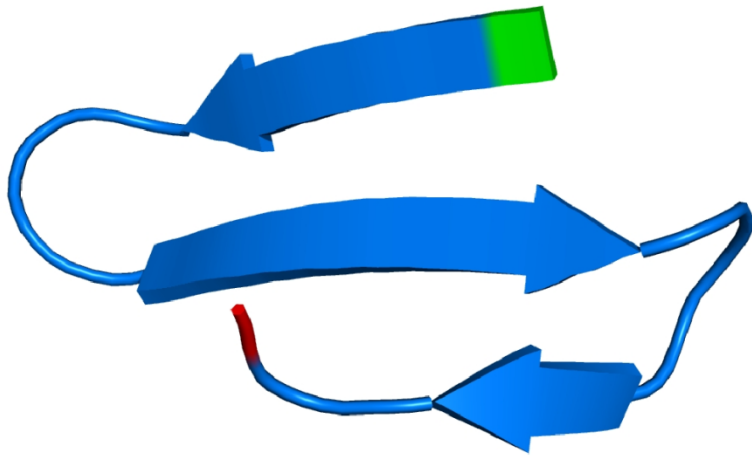


Figure 4-6b  
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Figure 4-6a  
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- Esqueleto mais distendido que as alfa-hélices ( $90^\circ < \psi < 180^\circ$ )
- Pontes de H entre aa mais distantes
- Cadeias laterais em planos alternados
- Paralelas ou antiparalelas

# Folhas $\beta$



- A direção da seta indica a direção N-para C-terminal

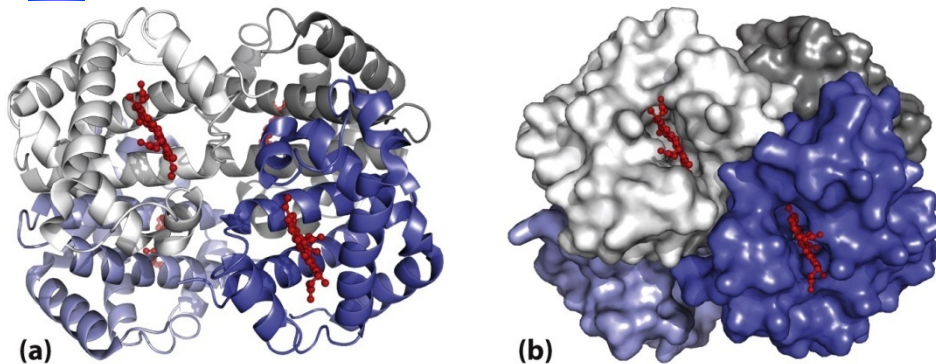
- Proteínas globulares

# Estrutura Terciária

- Arranjo espacial total da cadeia polipeptídica
- Cadeias laterais (radicais) dos aa participam de interações;
  - hidrofóbicas
  - pontes salinas (ligações iônicas)
  - pontes de hidrogênio
  - pontes dissulfeto
- Globulares ou fibrosas

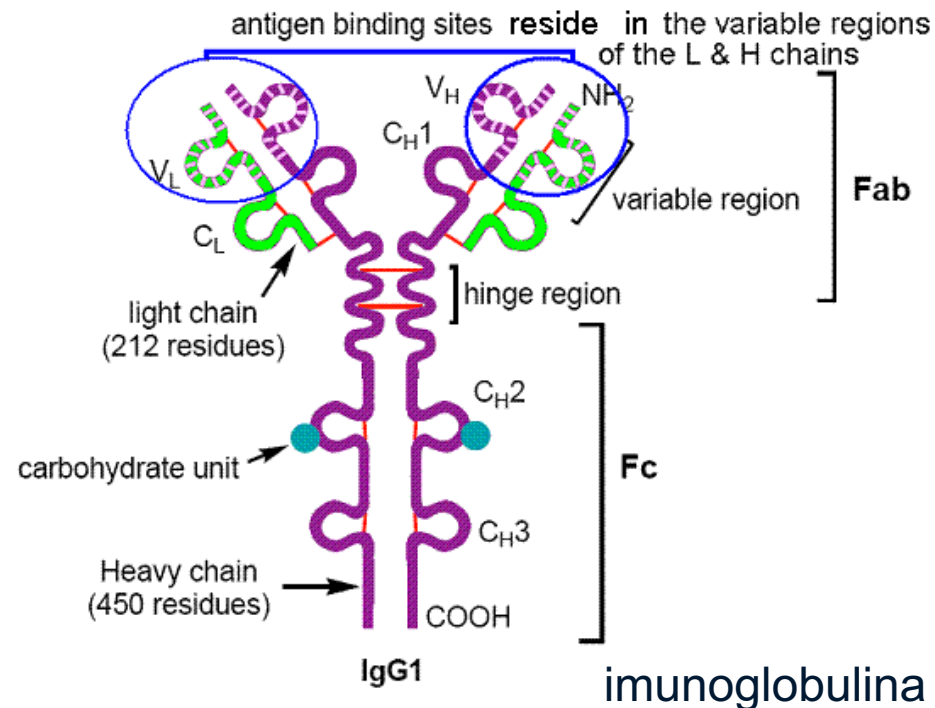
# Estrutura Quaternária

- Associação de cadeias polipeptídicas (subunidades)
- Estabilizada pelas mesmas forças que a estrutura terciária



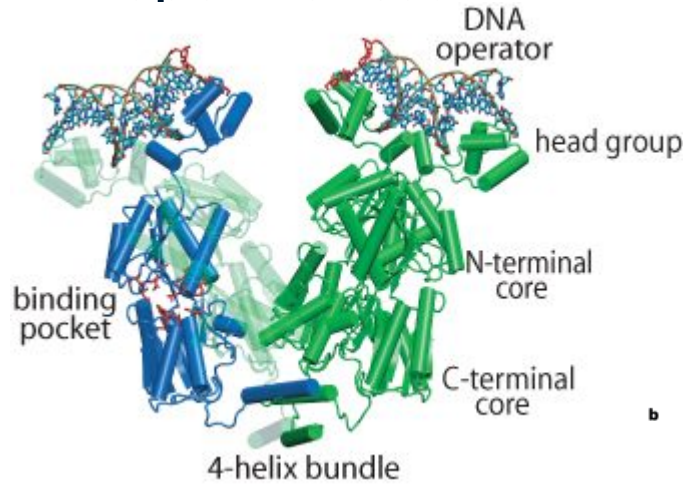
hemoglobina

Figure 4-22  
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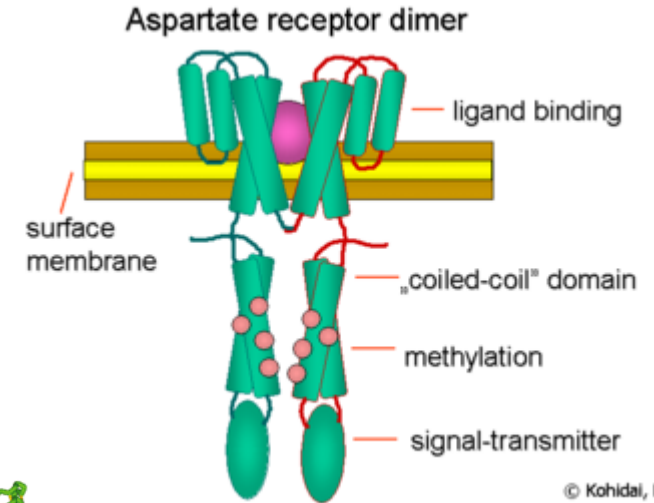


# Domínios proteicos

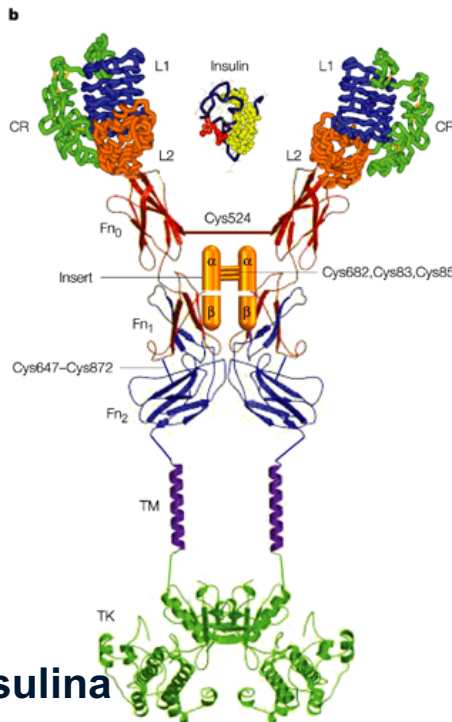
Regiões de uma proteína com estrutura e função “independentes”



**Repressor Lac**



© Kohidal, L



**Receptor de insulina**