LGN0114 – Biologia Celular

Estrutura e Função dos Ácidos Nucleicos

No. 4356 April 25, 1953 NATURE 737

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[1] Young, F. B., Gerrard, H., and Jevons, W., *Phil. Mag.*, **40**, 149 (1920).
[2] Longuet-Higgins, M. S., *Mon. Not. Roy. Astro. Soc., Geophys. Supp.*, **5**, 285 (1949).
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MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

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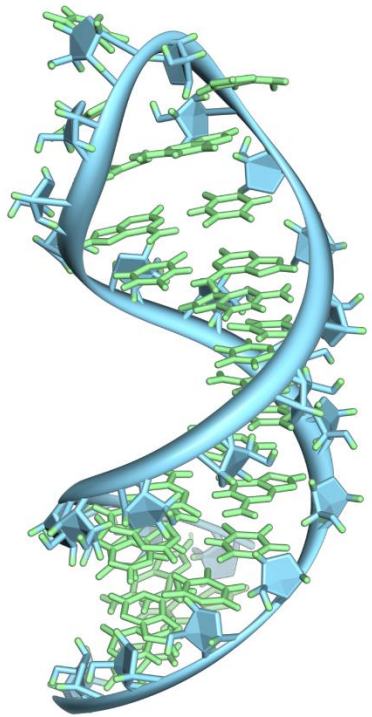
This figure is purely diagrammatic. The two ribbons symbolize the two phosphate–sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

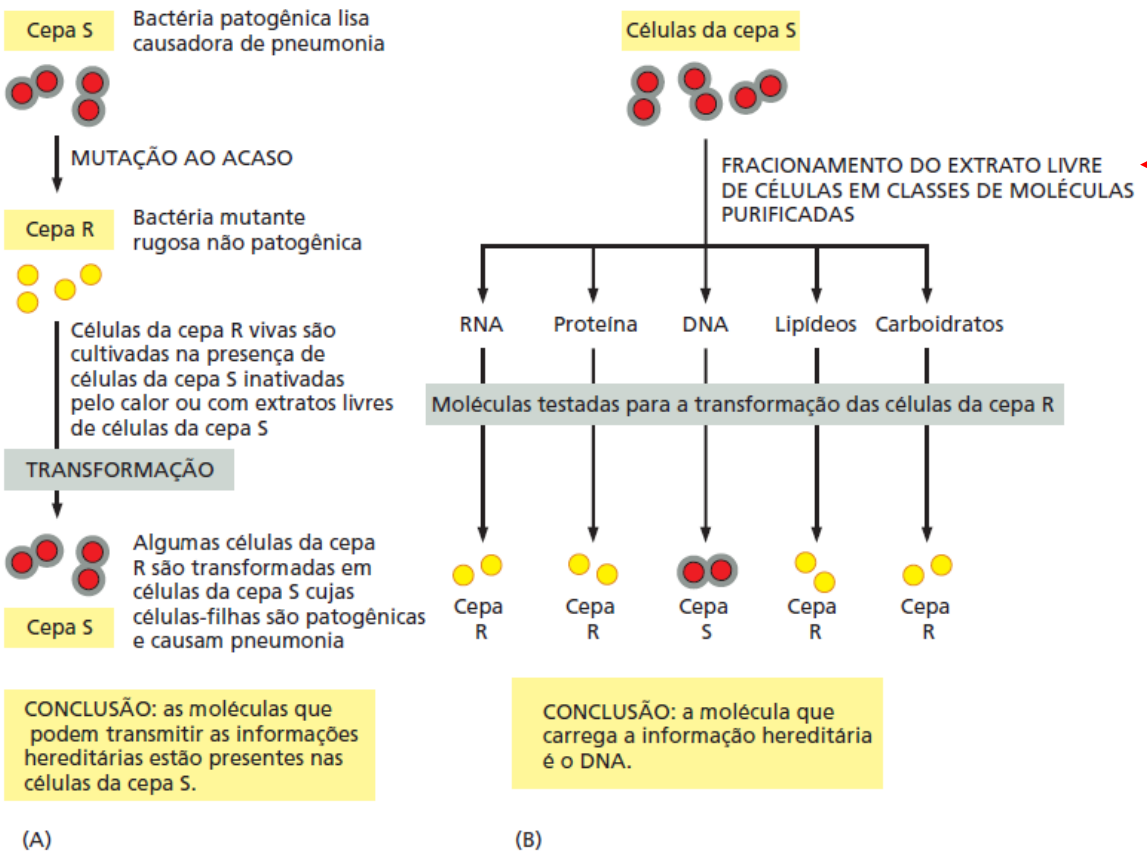
Aula 4

Antonio Figueira
figueira@cena.usp.br



DNA como material genético

Fred Griffith 1929



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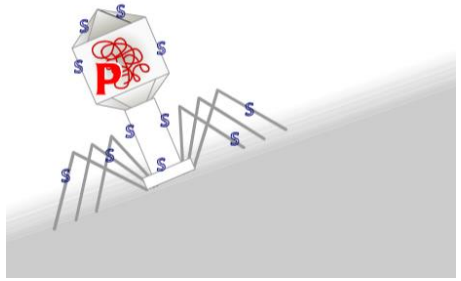
Oswald Avery
Colin McLeod
Maclyn McCarty
1944

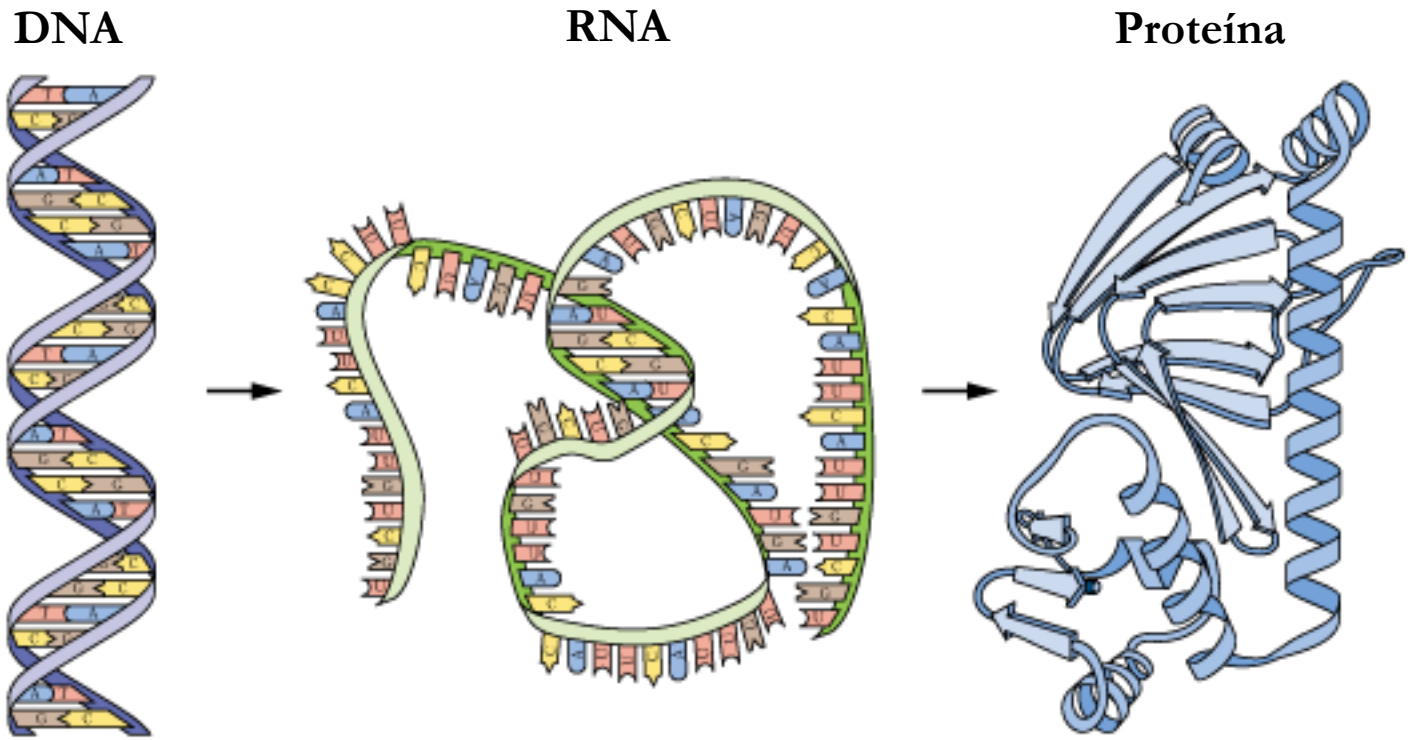


Alfred Hershey 1952

http://www.dnaftb.org/17/animation.html

DOGMA CENTRAL DA BIOLOGIA

A informação genética, armazenada nos cromossomos, é transferida às células filhas através da **replicação do DNA**, sendo expressa através da **transcrição em mRNA** e **traduzida** subsequentemente em cadeias polipeptídicas (**proteínas**)



Fluxo da Informação Genética

REPLICAÇÃO

5’ ATG GAG TTA TTG AAC TCT TAC AAT 3’

3’ TAC GTC AAT AAC TTG AGA ATC TTA 5’

DNA

3’ TAC CTC AAT AAC TTG AGA ATC TTA 5’

5’ AUG GAG UUA UUG AAC UCU UAG AAU 3’

TRANSCRIÇÃO RNA mensageiro = mRNA

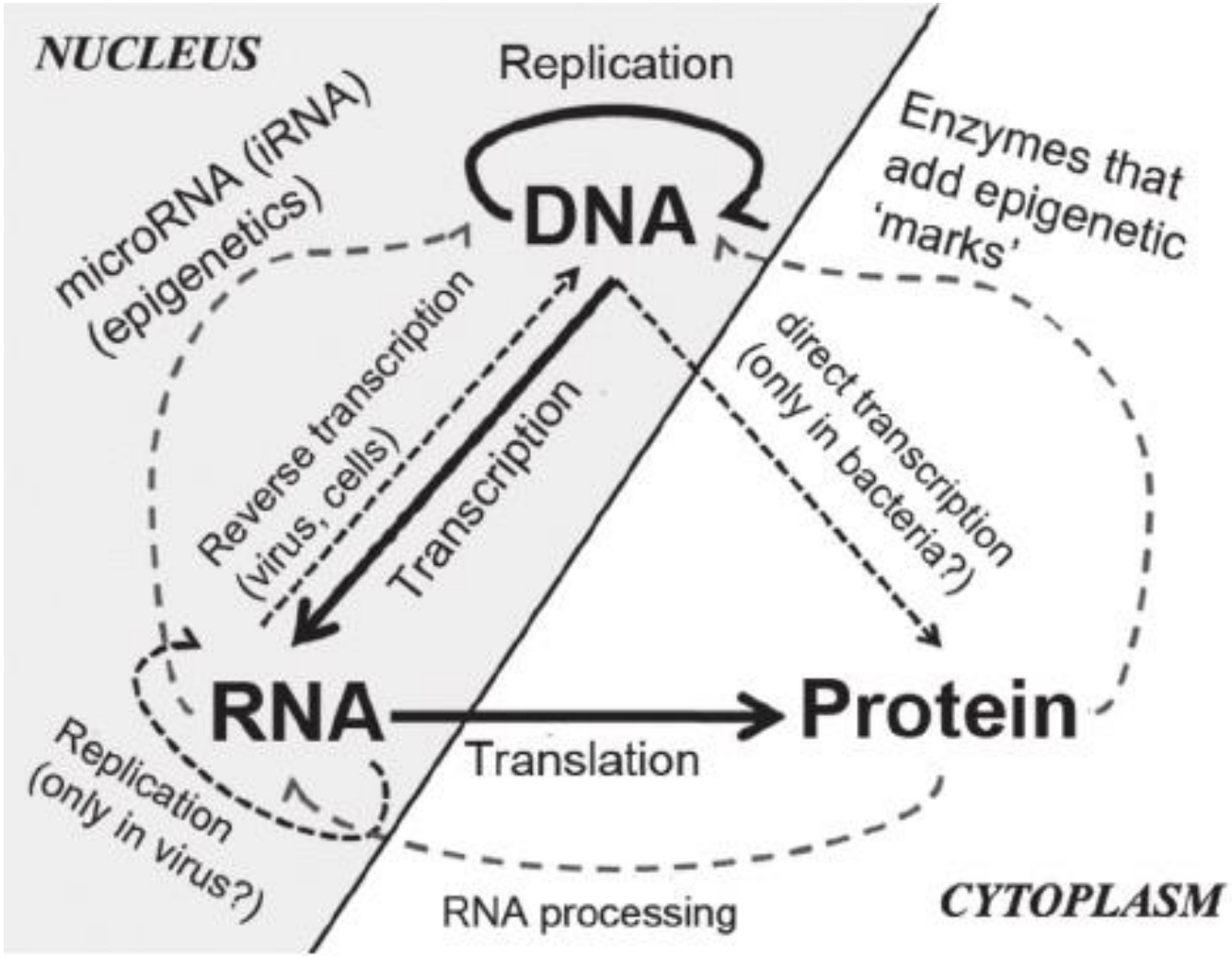
RNA

TRADUÇÃO

PROTEÍNA

AUG	GAG	UUA	UUG	AAC	UCU	UAG	AAU
M	E	L	L	N	S	Y	N

Fluxo da Informação Genética



Dogma que não é Dogma!

Função do Material Genético

1. Função genotípica: replicação

2. Função fenotípica: expressão gênica

3. Função evolutiva: variabilidade
(mutações, transferência horizontal de genes...)

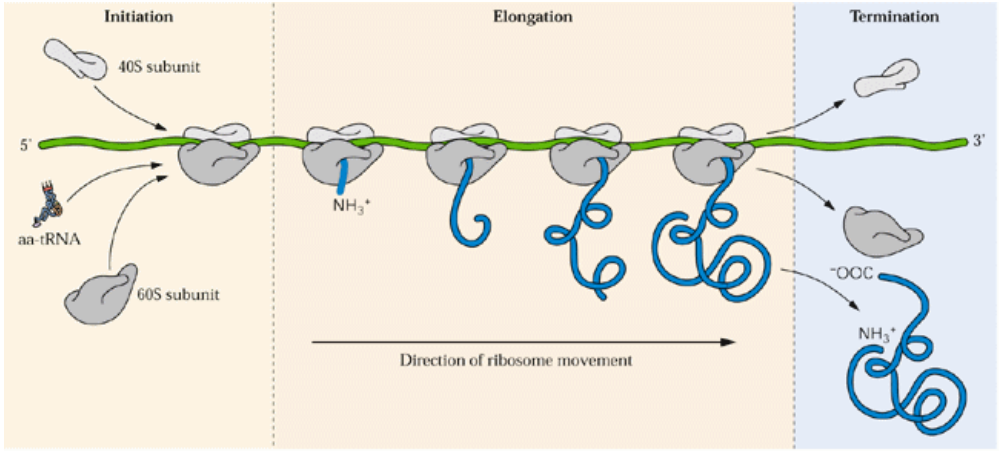
Ácidos Nucleicos

- **DNA**: Armazenamento da informação genética
  - **Estabilidade**
- **RNA**: síntese de macromoléculas - várias funções
  - **RNA ribossomal (rRNA)** - componentes estruturais de ribossomos
  - **RNA mensageiro (mRNA)** - contém a informação genética para a sequência de aminoácidos das proteínas
  - **RNA transferência (tRNA)** - identifica e transporta os aminoácidos até o ribossomo
  - snRNA, snoRNA, microRNA, ncRNA

snRNA = *small nuclear RNA* - spliceossomos

snoRNA = *small nucleolar RNA* – montagem ribossomo

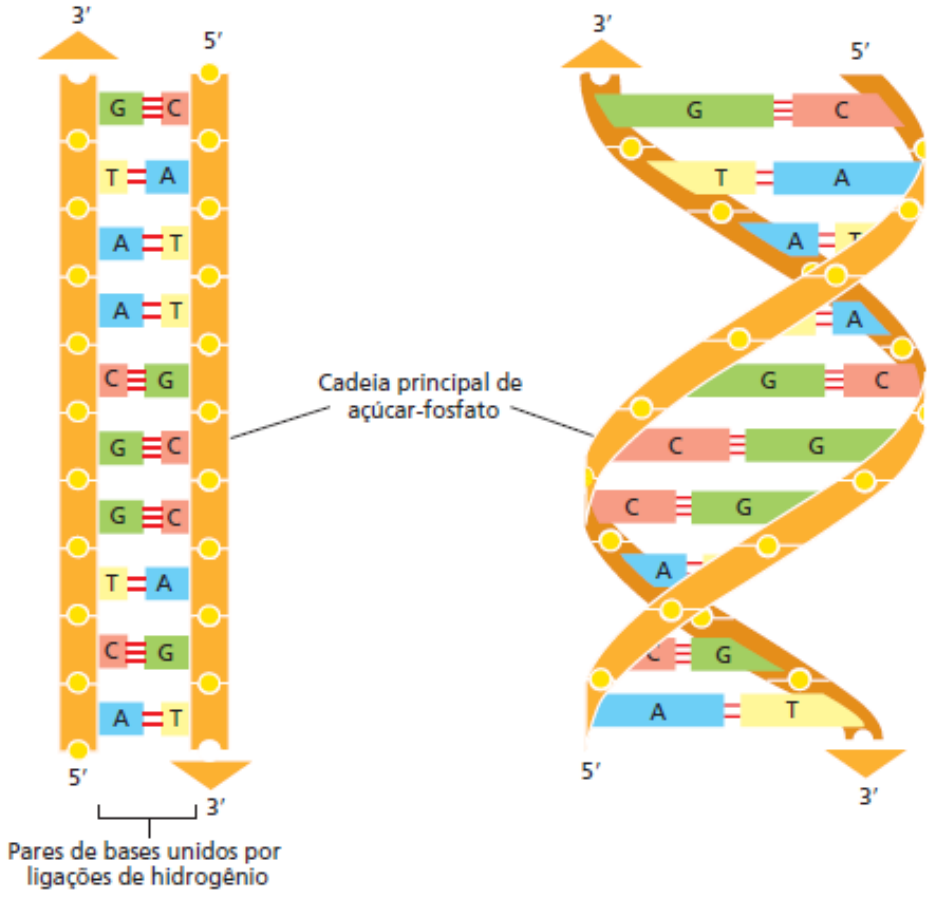
ncRNA = *non-coding RNA* – RNA regulatórios



DNA

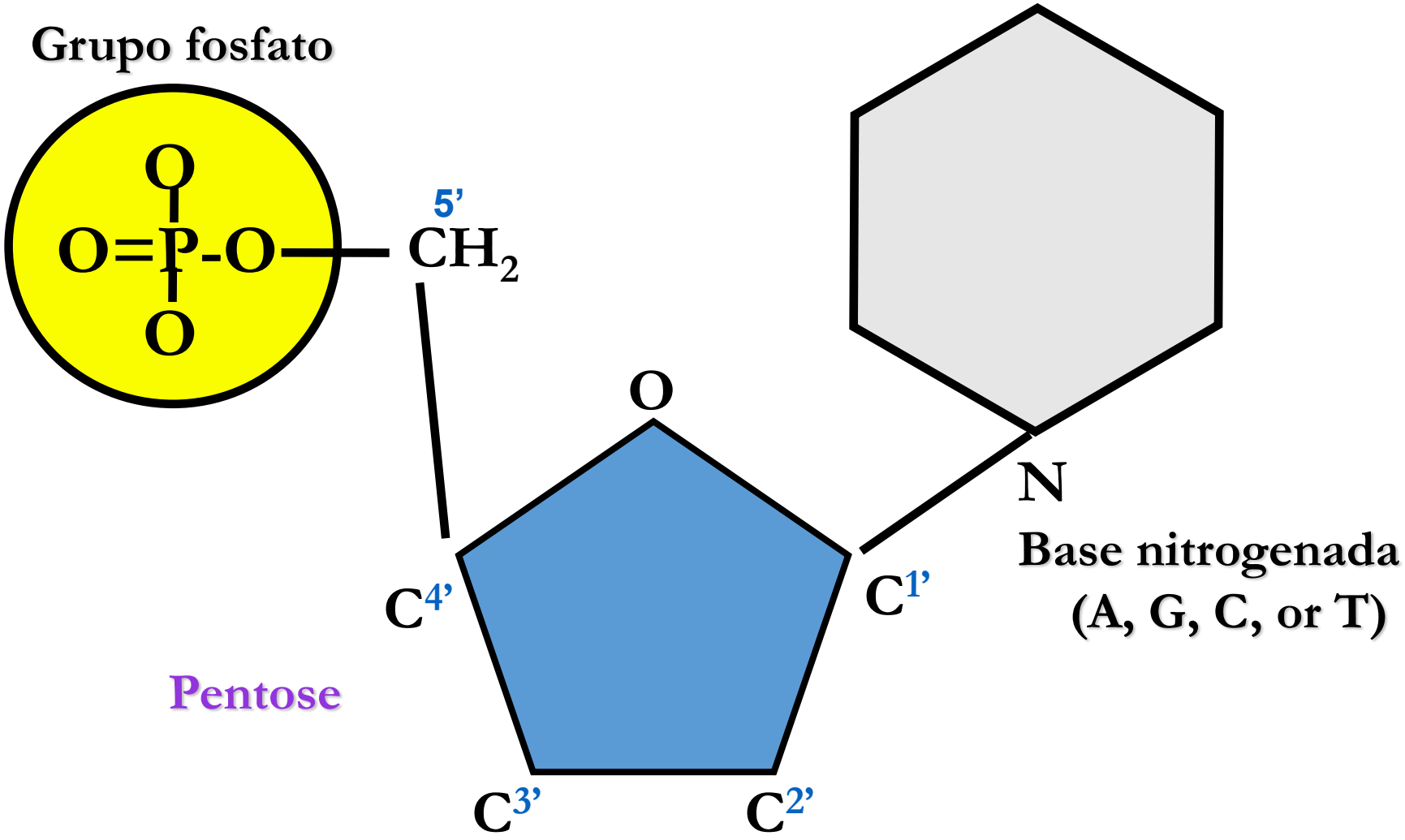
Fita dupla de DNA

Dupla-hélice de DNA



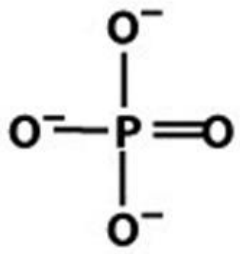
ÁCIDOS NUCLEICOS

São polímeros de nucleotídeos



Componentes dos Nucleotídeos

(1)
Um grupamento fosfato:

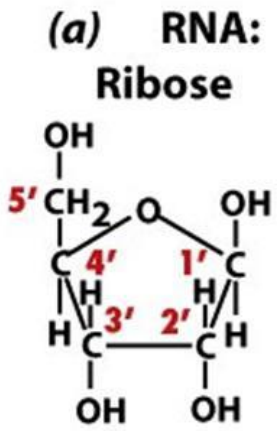


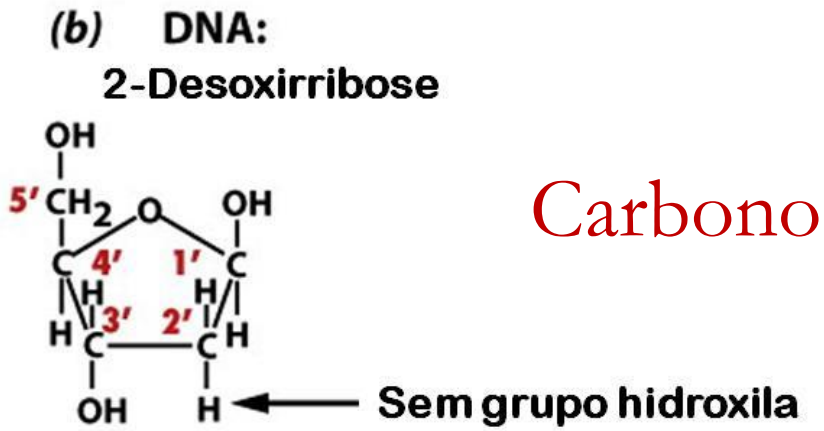
Carbono 5’

Nucleotídeo sem fosfato é nucleosídeo!!!

(2)

pentoses (açúcares de 5 carbonos)

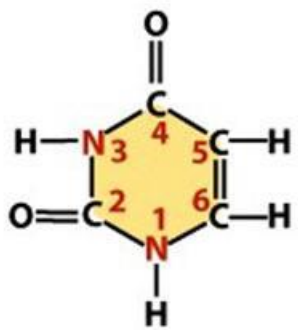




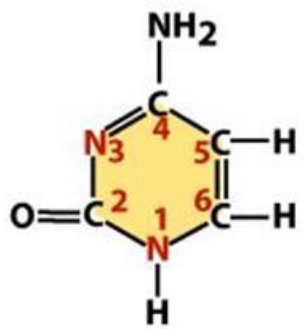
Carbono 2’

(3)
Uma base cíclica contendo Nitrogênio

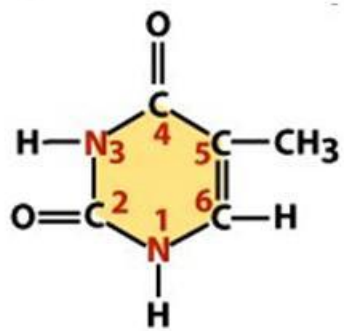
(a) **RNA** *(b)* **DNA e RNA** *(c)* **DNA**



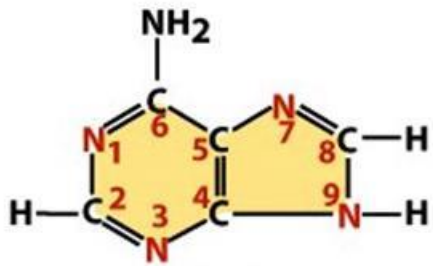
Uracila



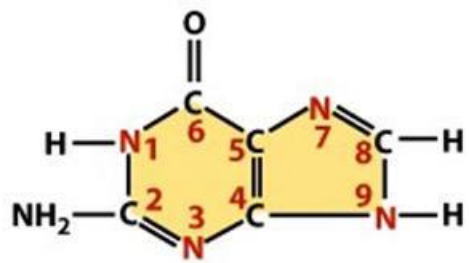
Citosina



Timina



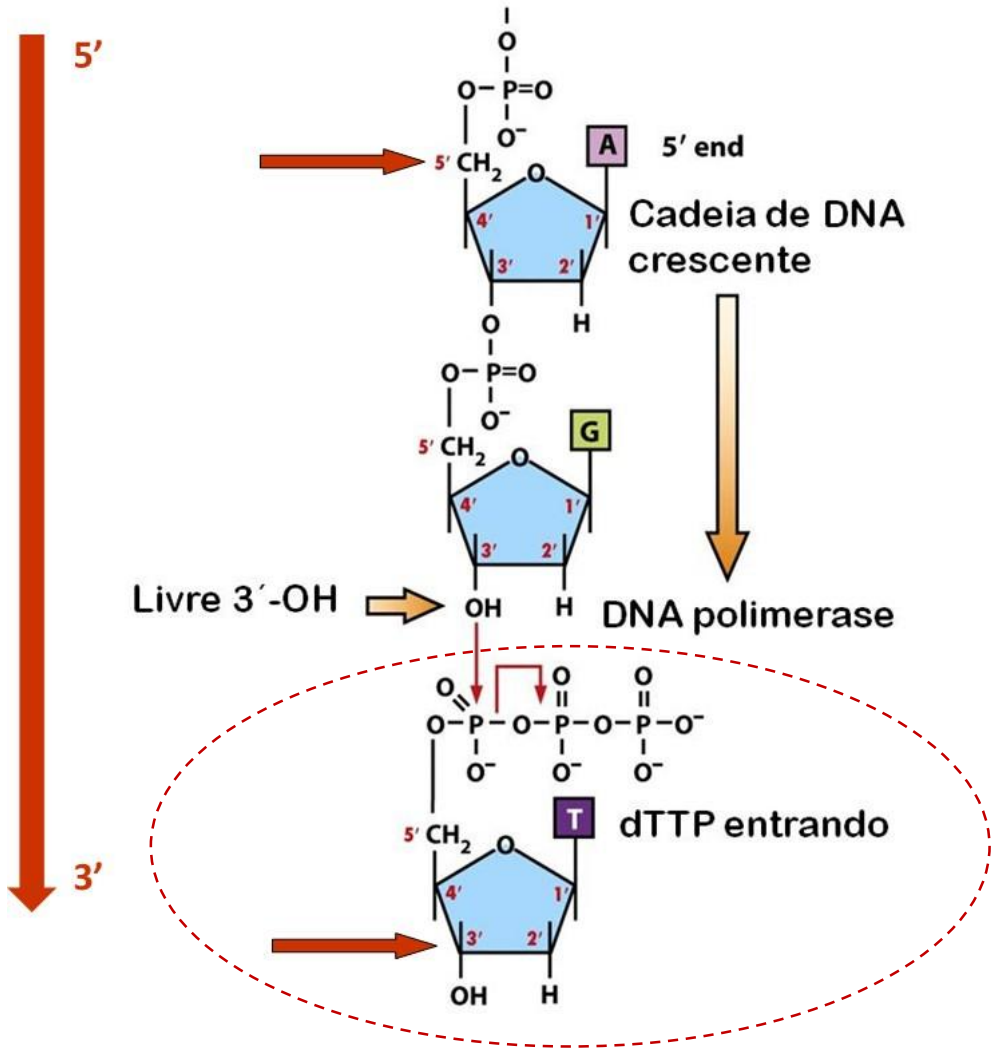
Adenina



Guanina

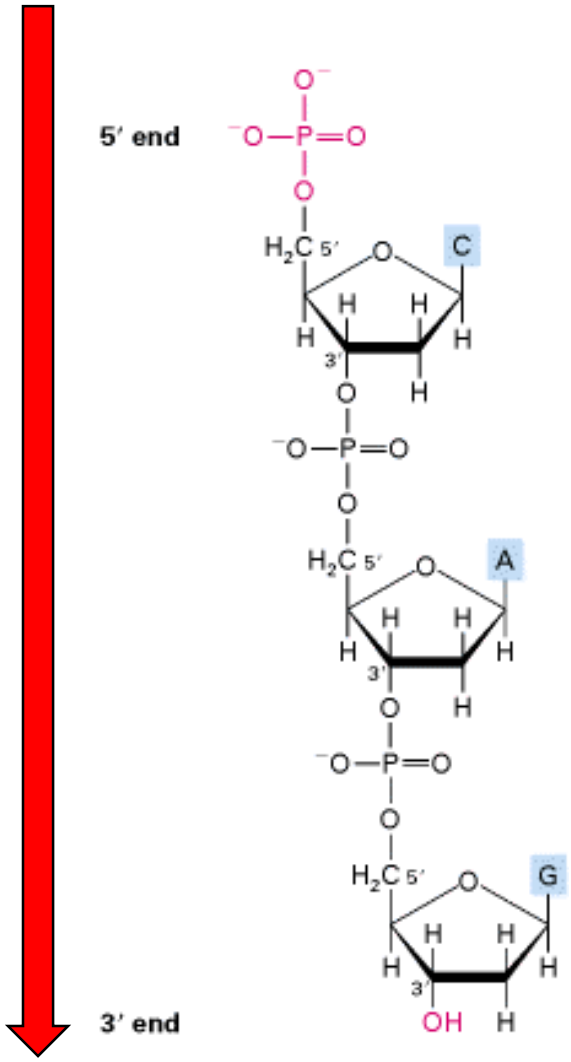
Purinas: A, G
Pirimidinas: U, T, C

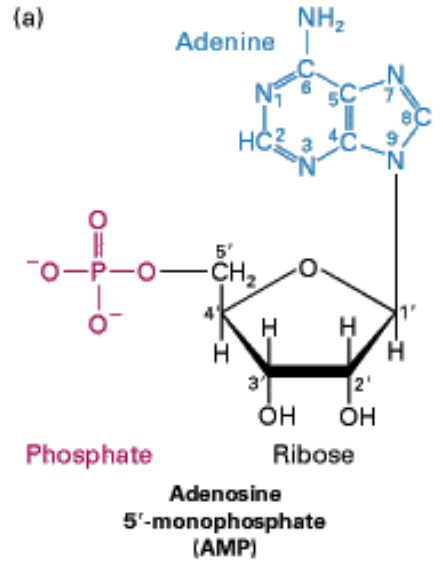
Ácidos Nucleicos são formados por ligações fosfodiester

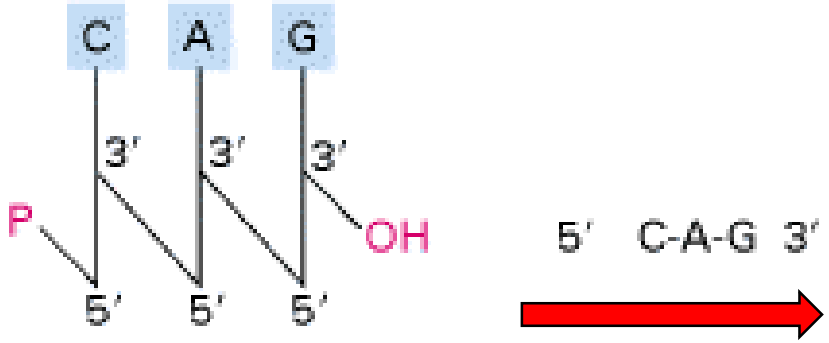


Nucleotídeo livre está na forma de trifosfato

Ligações fosfodiéster - polarização 5’ – 3’



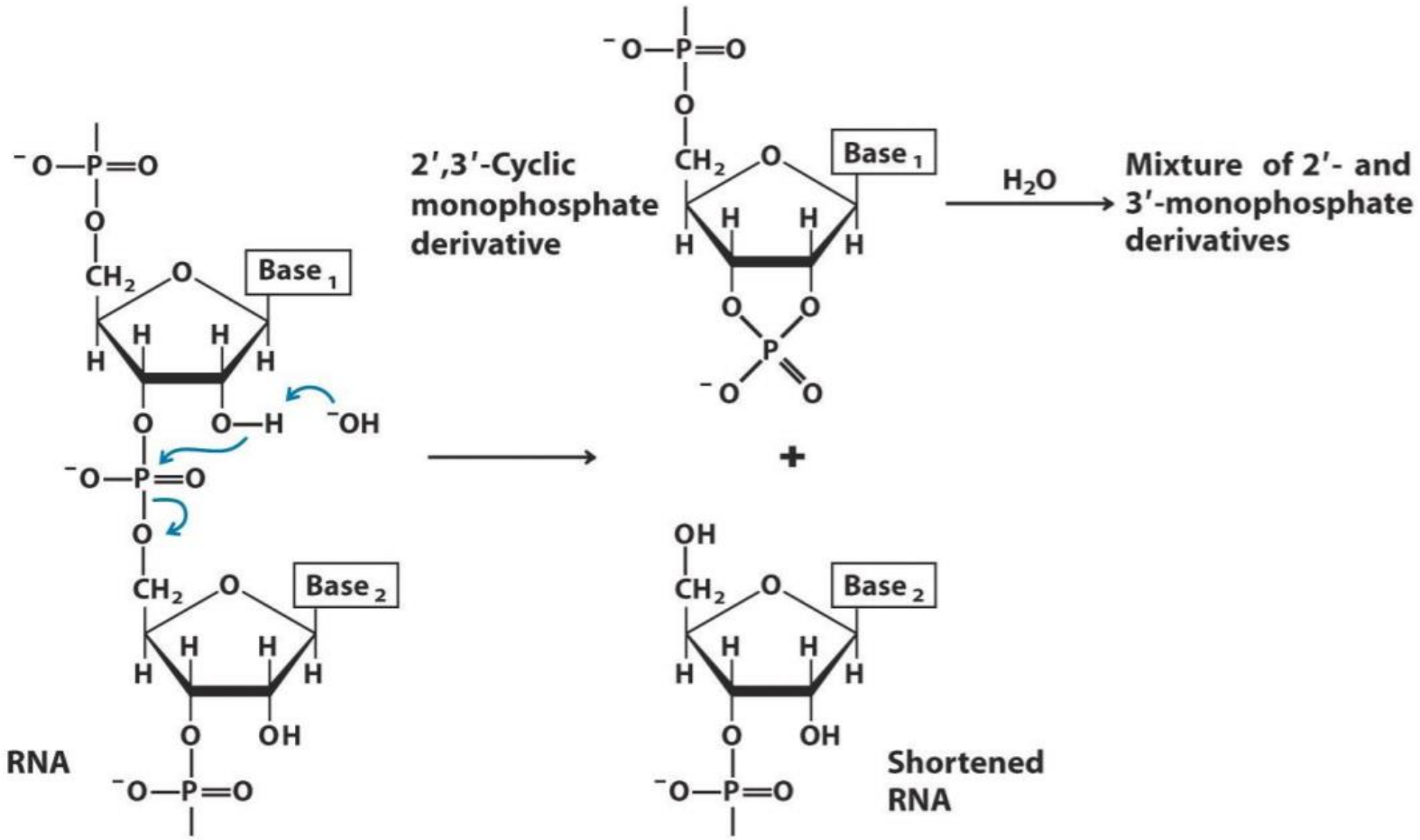




- entre o carbono 3’ do nucleotídeo de “cima” e o carbono 5’ do nucleotídeo de “baixo”

Porque o RNA é mais lábil?

Efeito de pH alcalino



Porque o Timina (DNA) x Uracil (RNA)?

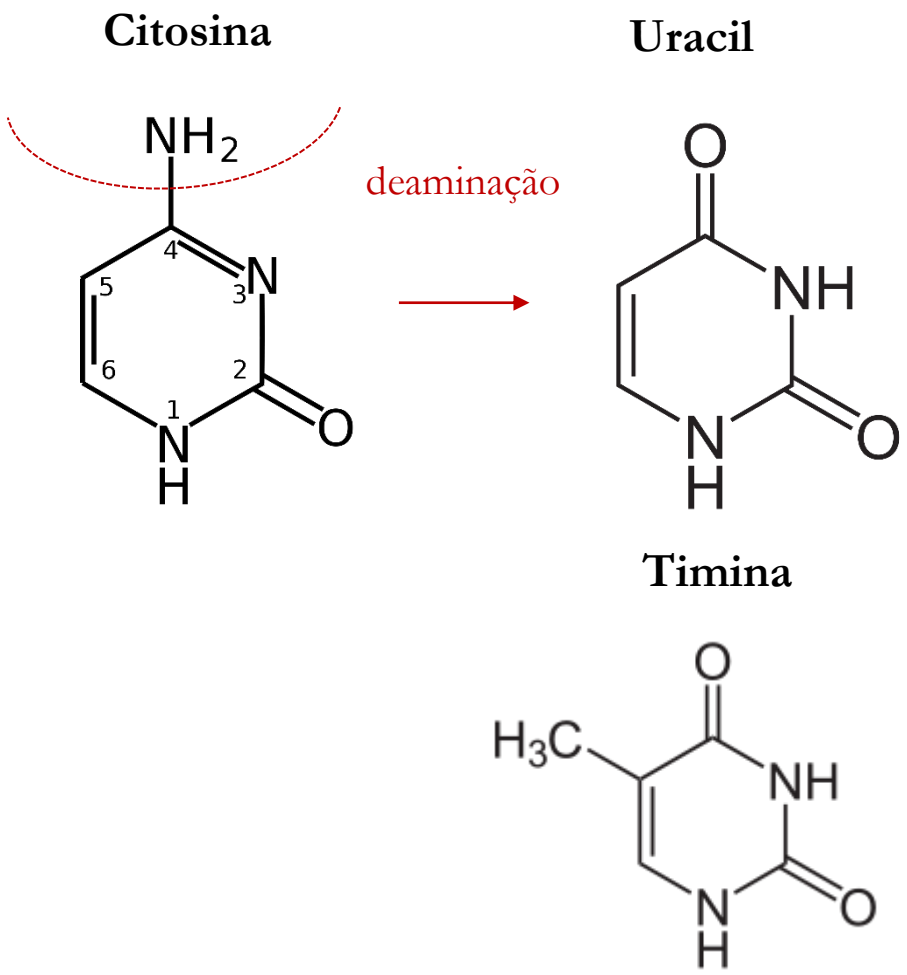
Deaminação de Citosina a Uracil

Ocorre naturalmente

Afeta o significado da sequência

Perda de amina em C -> U

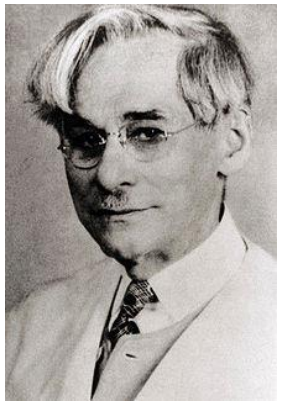
Reconhecido em DNA



<u>Pareamento em D</u>NA

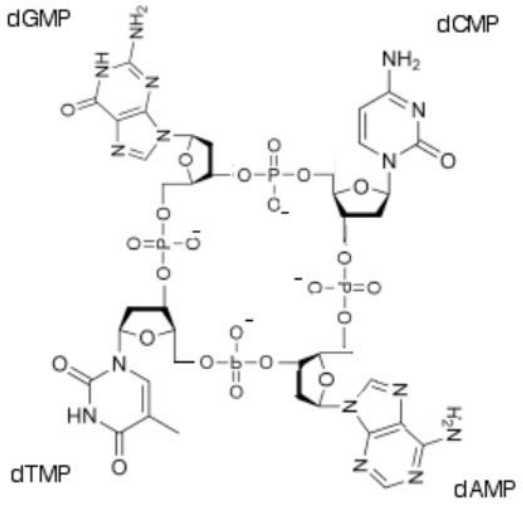
C – G passaria a ser U-G

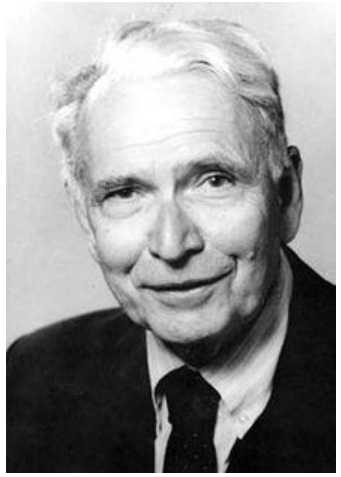
Na replicação incorreria em erro



Phoebus Levene

Hipótese dos Tetranucleotídeos





Erwin Chargaff

Regra de Chargaff

DNA SOURCE	ADENINE	THYMINE	GUANINE	CYTOSINE
Calf Thymus	1.7	1.6	1.2	1.0
Beef Spleen	1.6	1.5	1.3	1.0
Yeast	1.8	1.9	1.0	1.0
Tubercle Bacillus	1.1	1.0	2.6	2.4

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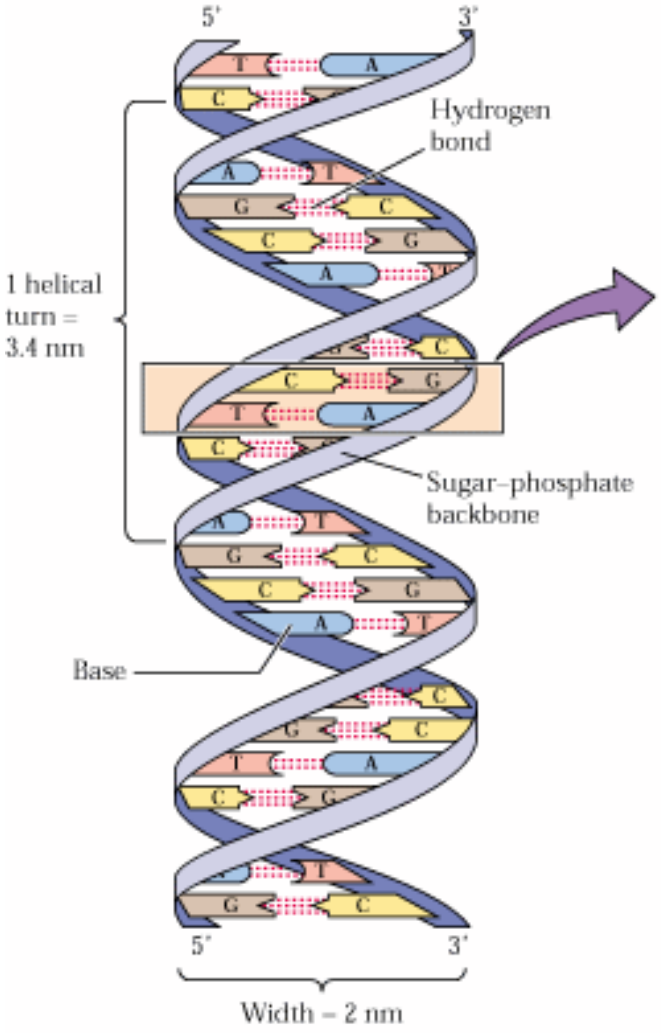
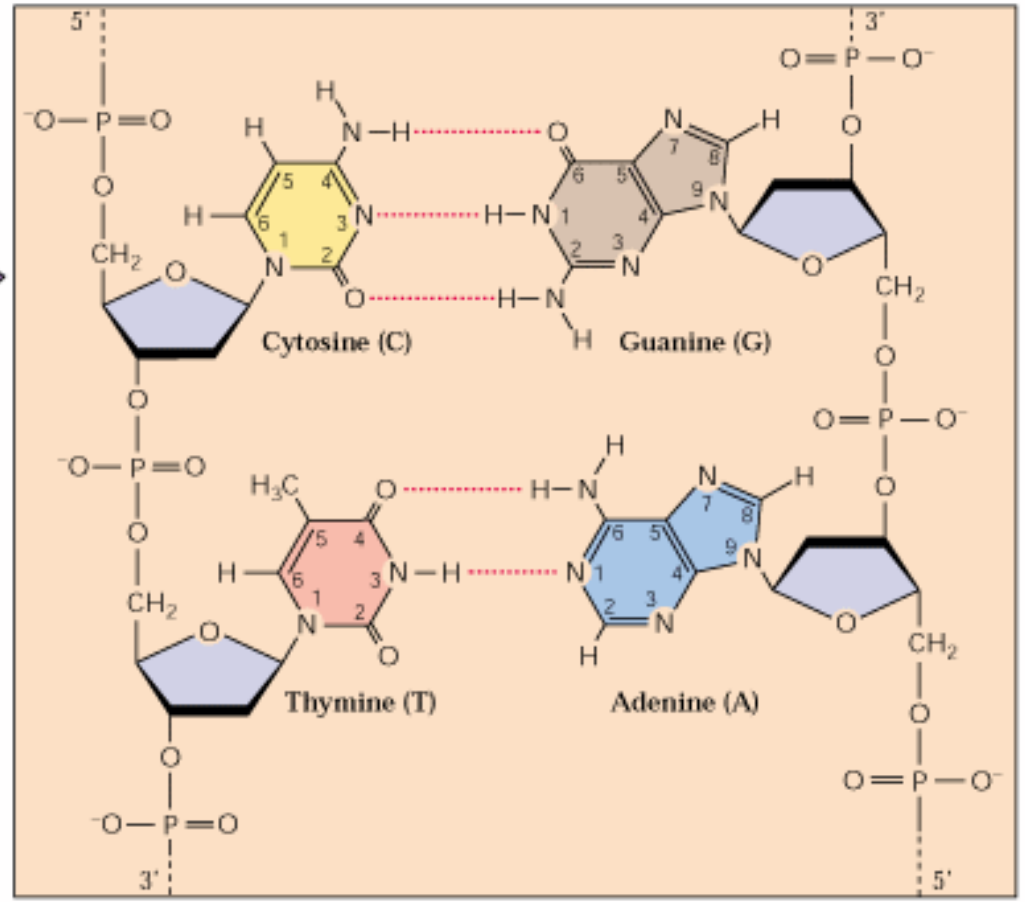
http://www.dnaftb.org/19/animation.html

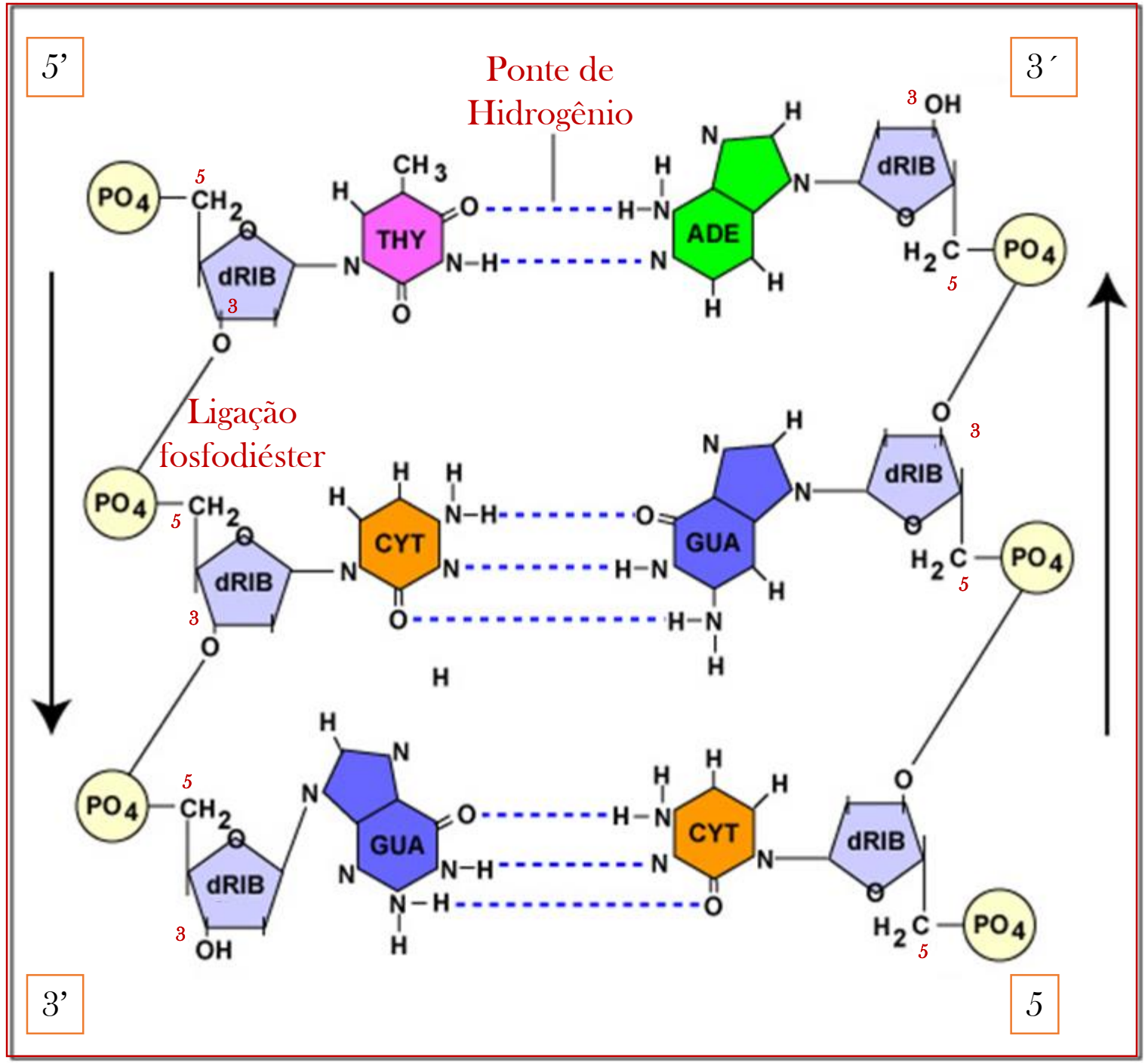
DNA - Ácido Desoxirribonucleico



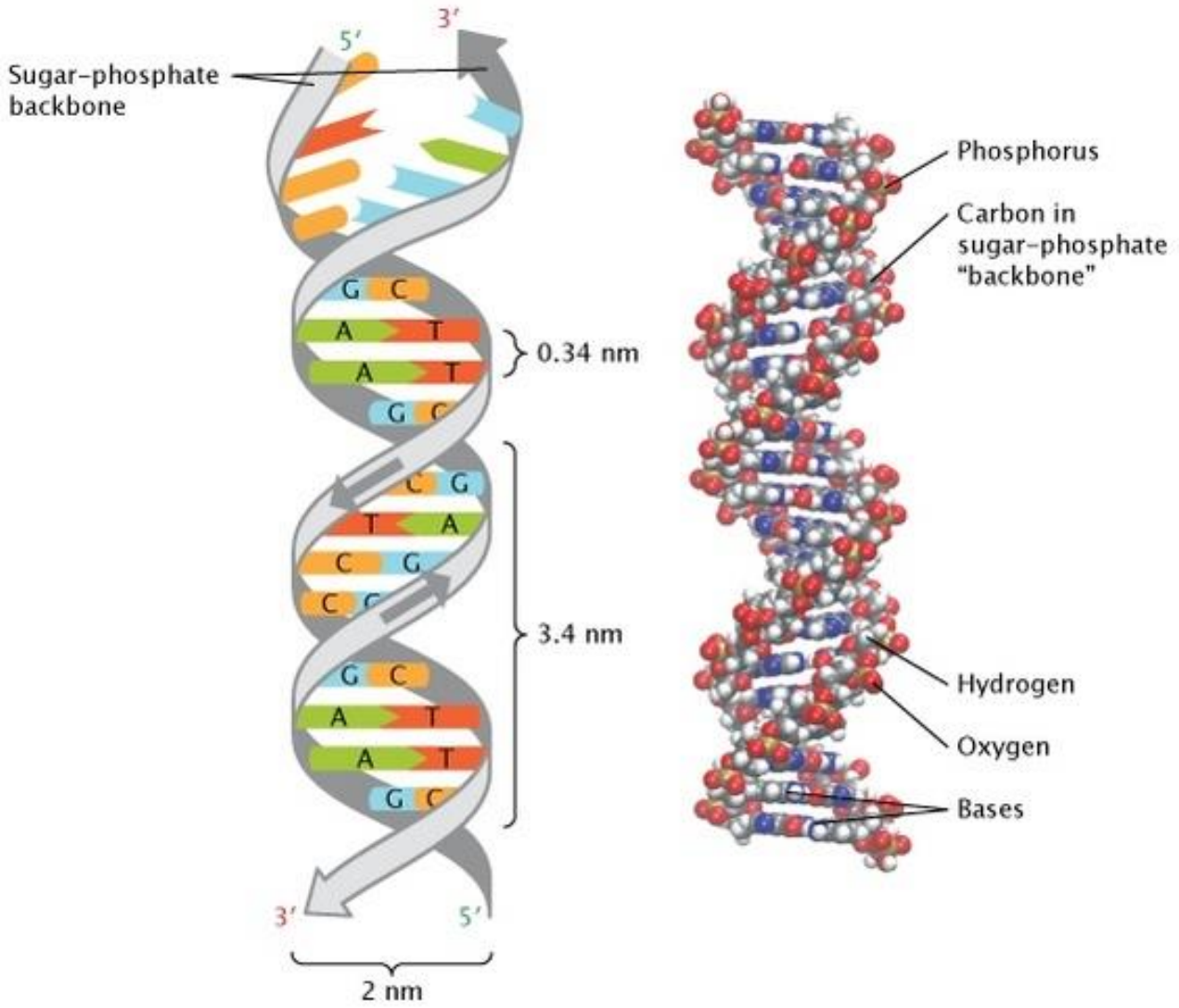


DNA – Fita Dupla!

- Duas cadeias independentes
- Dupla hélice, sentido direito
- Hélices antiparalelas
- Complementariedade das bases
    - Eixo externo hidrofílico - deoxiribose + fosfato
    - Bases hidrofóbicas (planas) no interior
    - Bases ligadas por pontes de H


5’
3´
Ponte de
Hidrogênio
Ligação
fosfodiéster
3’
5
PO4
CH2
dRIB
THY
ADE
CYT
GUA
OH
CH3
H
N
O

DNA – Fita Dupla!



Características da Dupla Hélice

- Contém duas fitas de polinucleotídeos ("corrimão") **antiparalelas**
- O esqueleto de cada fita é formado por desoxirribose e fosfato
- O grupo fosfato ligado ao carbono 5' de uma desoxirribose se liga covalentemente ao terminal hidroxila do carbono 3' da próxima unidade
- As purinas e pirimidinas estão voltadas para dentro da hélice
- Cada base forma **pontes de H** com uma base oposta a ela, formando um par de bases
- **3,4 Å** separam os planos ("degraus"), onde bases adjacentes estão localizadas
- A dupla hélice faz uma volta completa com 10 nucleotídeos (**34 Å**)
- Existem em média 25 pontes de H dentro de cada volta completa da hélice, promovendo uma **estabilidade de ligação tão forte** como uma ligação covalente
- O diâmetro da hélice é cerca de 20 Å

Principais Tipos de RNA

RNAs ocorrem no núcleo e citoplasma

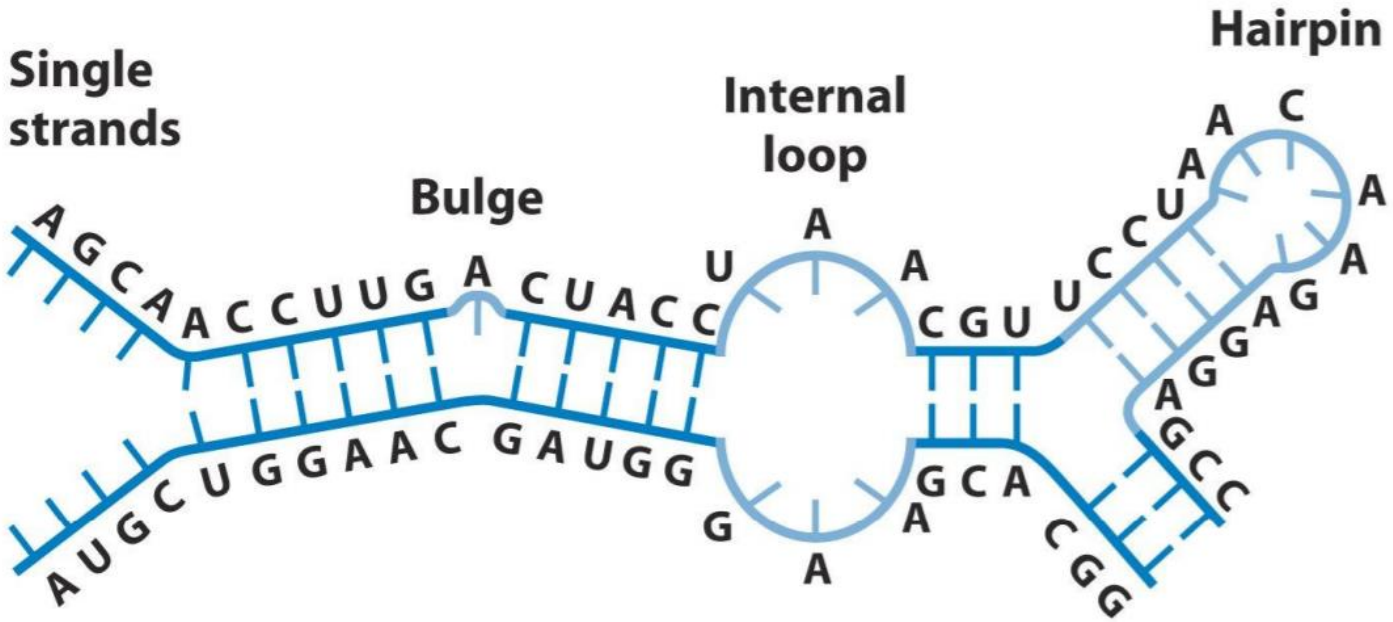
RNA mensageiro (mRNA): contém a informação genética para a sequência de aminoácidos das proteínas

RNA transferência (tRNA): identifica e transporta os aminoácidos até o ribossomo

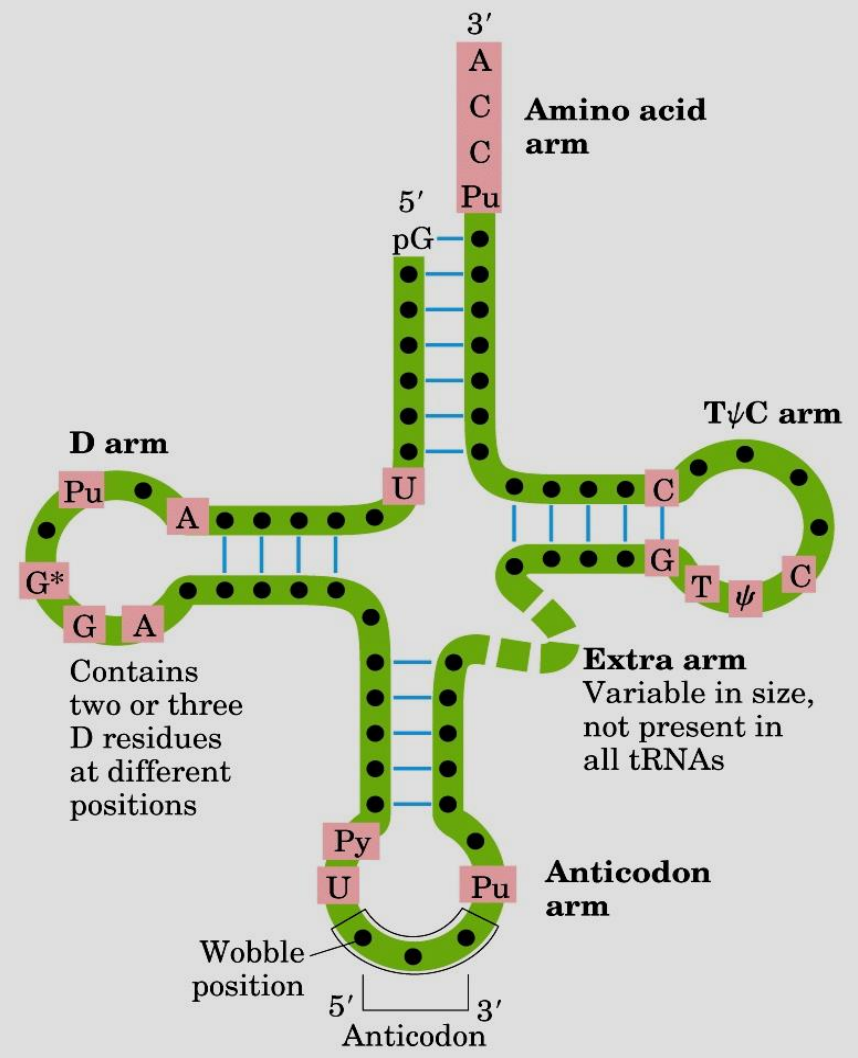
RNA ribossômico (rRNA): constituinte dos ribossomos

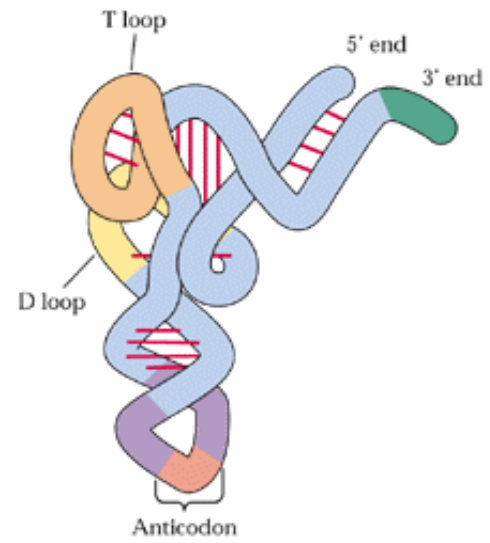
Estrutura de RNA

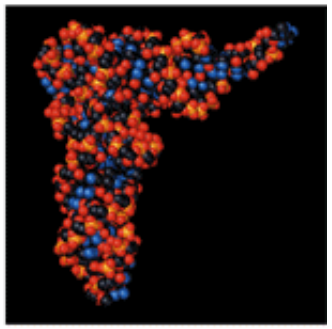
- RNA não possuem estrutura regular como DNA
- As estruturas de RNA são complexas e únicas
- Pareamento de bases similar a DNA forma estruturas

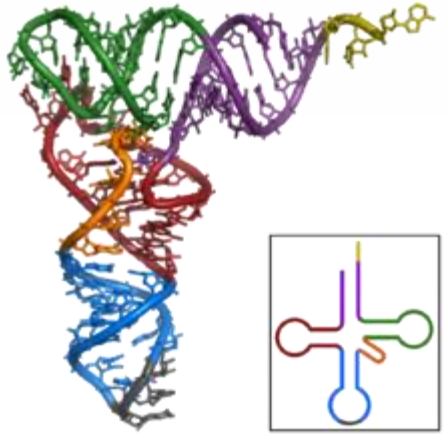


RNA transportador - tRNA

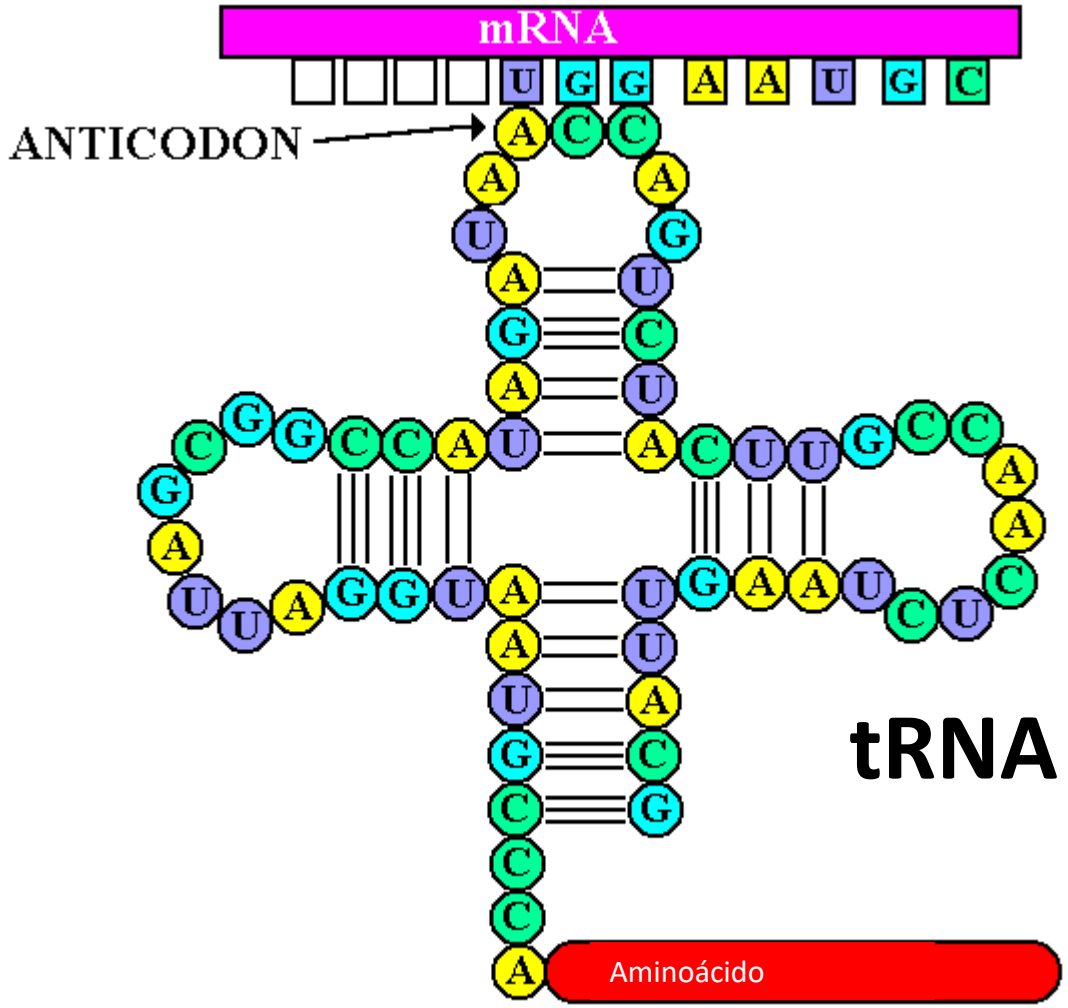






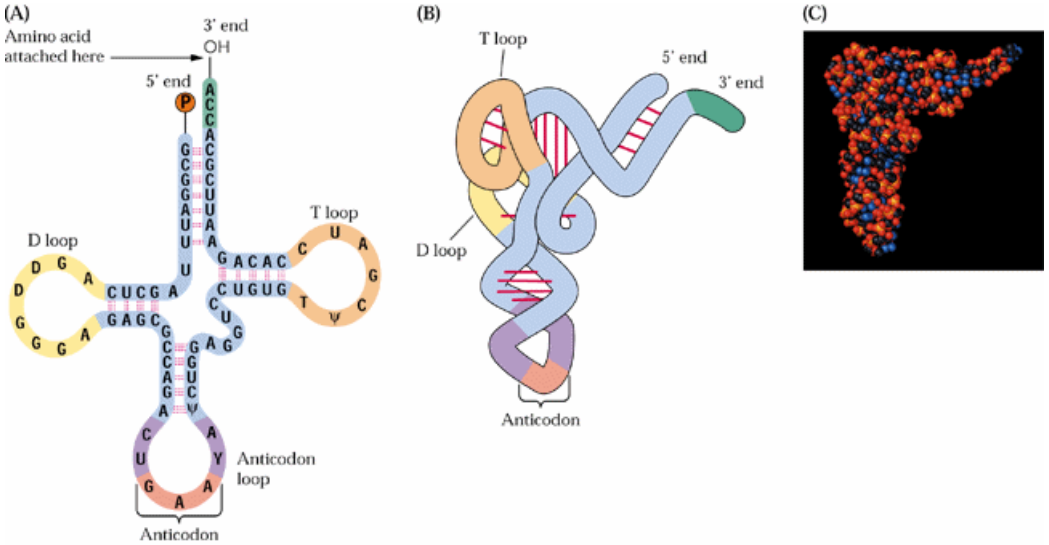


Reconhece códons em mRNA - anticódon

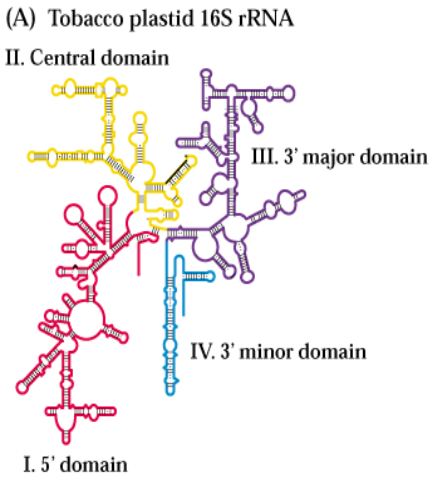


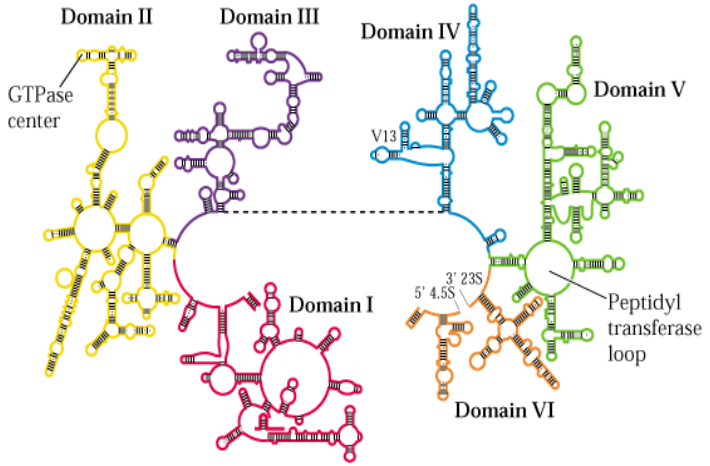
tRNA

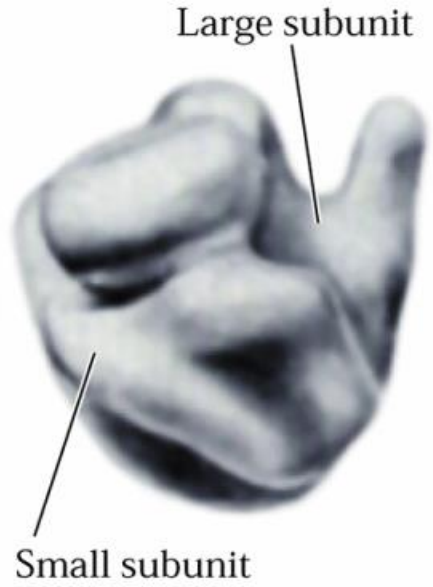
tRNA →


(A)
Amino acid attached here
3' end
OH
5' end
P
D loop
T loop
Anticodon loop
Anticodon
(B)
T loop
5' end
3' end
D loop
Anticodon
(C)

rRNA

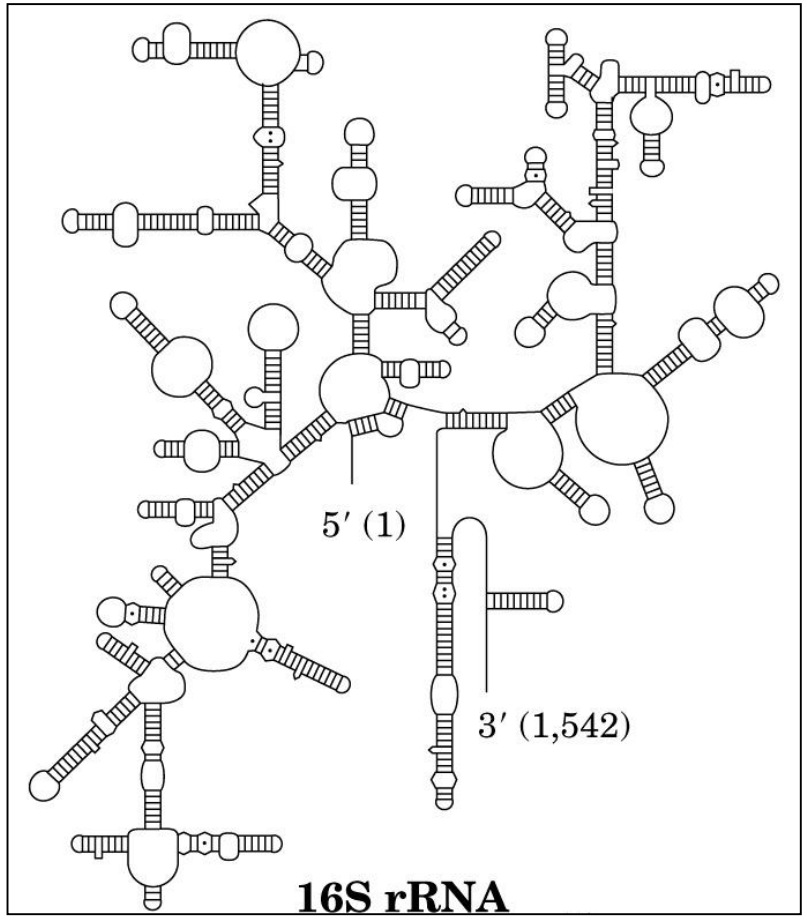

(A) Tobacco plastid 16S rRNA
II. Central domain
III. 3' major domain
IV. 3' minor domain
I. 5' domain


(B) Tobacco plastid 23S and 4.5S rRNAs
Domain II
Domain III
Domain IV
Domain V
GTPase center
V13
Domain I
3' 23S
5' 4.5S
Peptidyl transferase loop
Domain VI


Large subunit
Small subunit

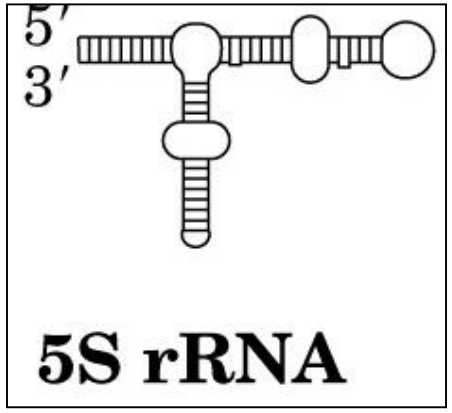
RNA ribossômico - rRNA

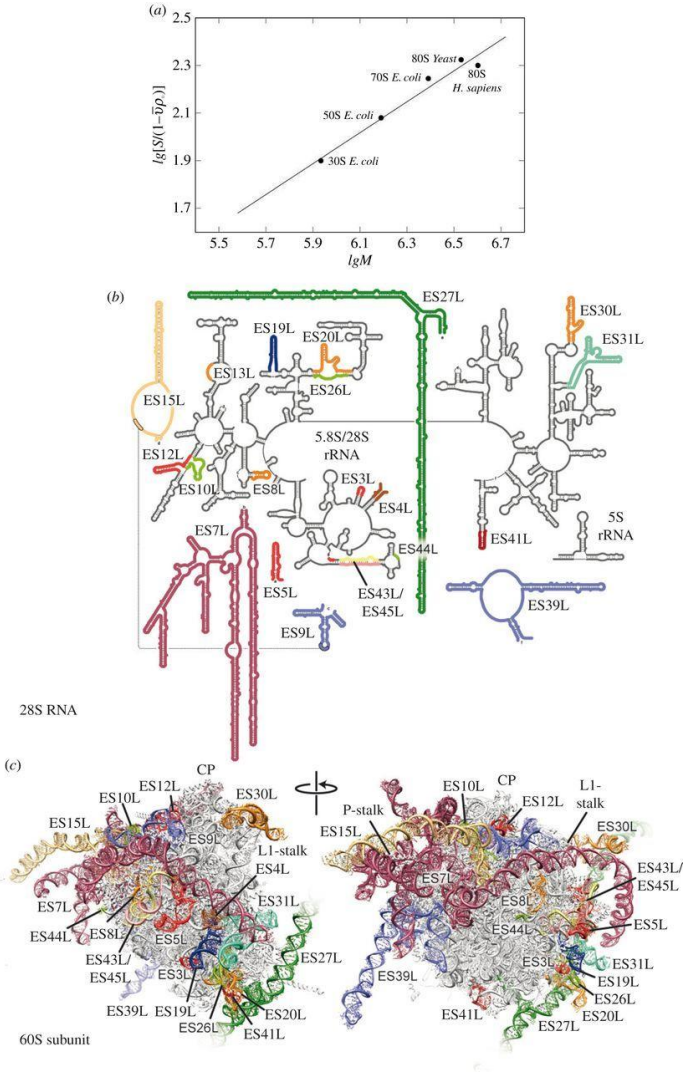
Possuem estrutura tridimensional específica visando promover a estabilidade e atividade catalítico nos ribossomos



Exemplos de rRNAs:

- Estrutura secundária com grampos e alças

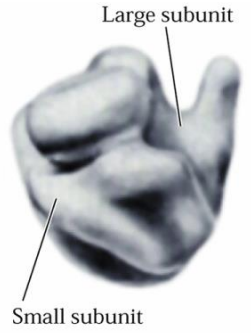




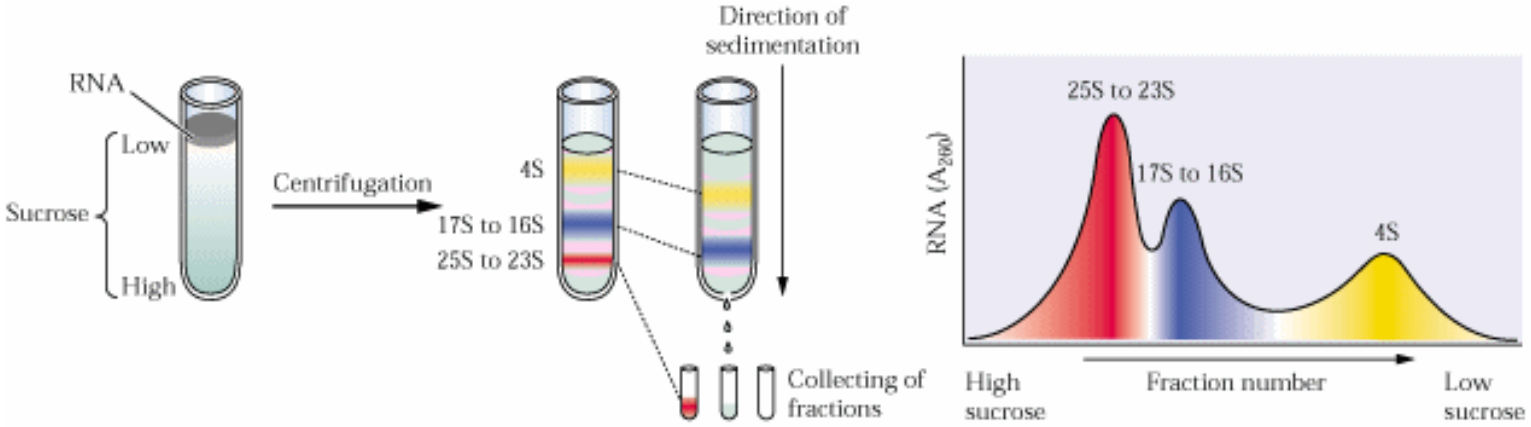
Yusupova & Yusupov 2017

Ácidos Nucleicos - RNA

RNA ribossomal - rRNA

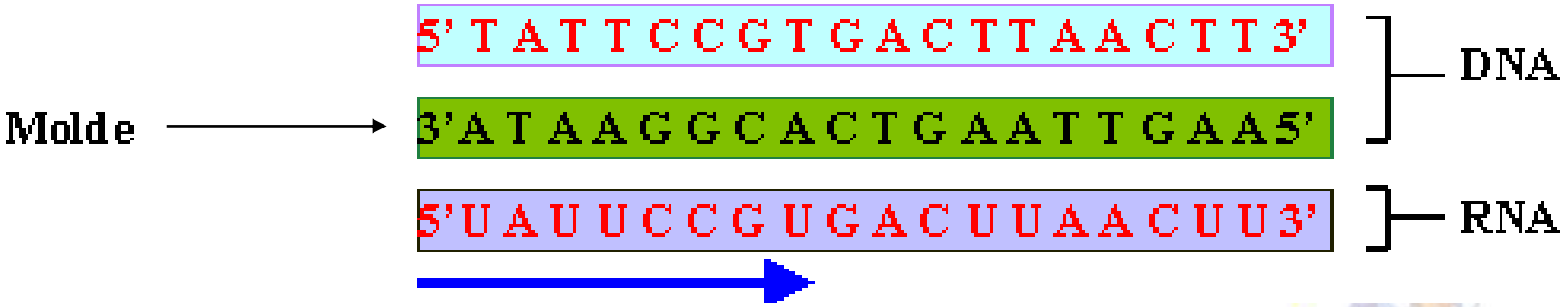


- mais abundante na célula (>80%)
- síntese nuclear
- combinado com proteínas - ribossomo
- procarioto 70S - (23S + 5S) (16S)
- eucarioto 80S - (28S+5.8S+5S) (18S)

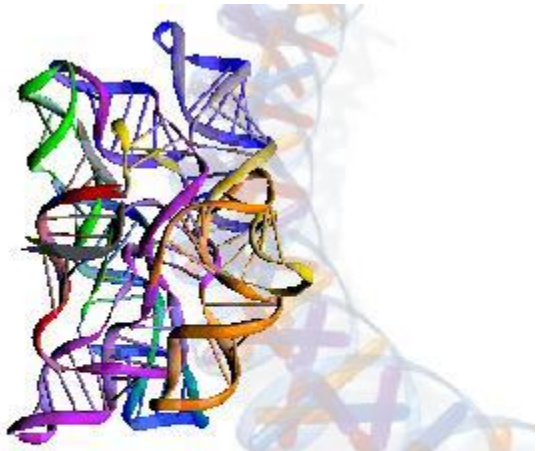


RNA mensageiro - mRNA

1 trinca de bases nitrogenadas = 1 códon



Primeira Base (5')	Segunda Base: U	Segunda Base: C	Segunda Base: A	Segunda Base: G	Terceira Base (3')
U	UUU, UUC – Fenil-alanina	UCU, UCC, UCA, UCG – Serina	UAU, UAC – Tirosina	UGU, UGC – Cysteine	U
	UUA, UUG – Leucina		UAA, UAG – Stop codon	UGA – Stop codon; UGG – Tryptophan	C
C	CUU, CUC, CUA, CUG – Leucina	CCU, CCC, CCA, CCG – Prolina	CAU, CAC – Histidina	CGU, CGC, CGA, CGG – Arginina	A
			CAA, CAG – Glutamina		G
A	AUU, AUC, AUA – Isoleucina	ACU, ACC, ACA, ACG – Treonina	AAU, AAC – Asparagina	AGU, AGC – Serina	U
	AUG – Metionina start codon		AAA, AAG – Lisina	AGA, AGG – Arginina	C
G	GUU, GUC, GUA, GUG – Valina	GCU, GCC, GCA, GCG – Alanina	GAU, GAC – Ácido Aspártico; GAA, GAG – Ácido Glutâmico	GGU, GGC, GGA, GGG – Glicina	A
					G

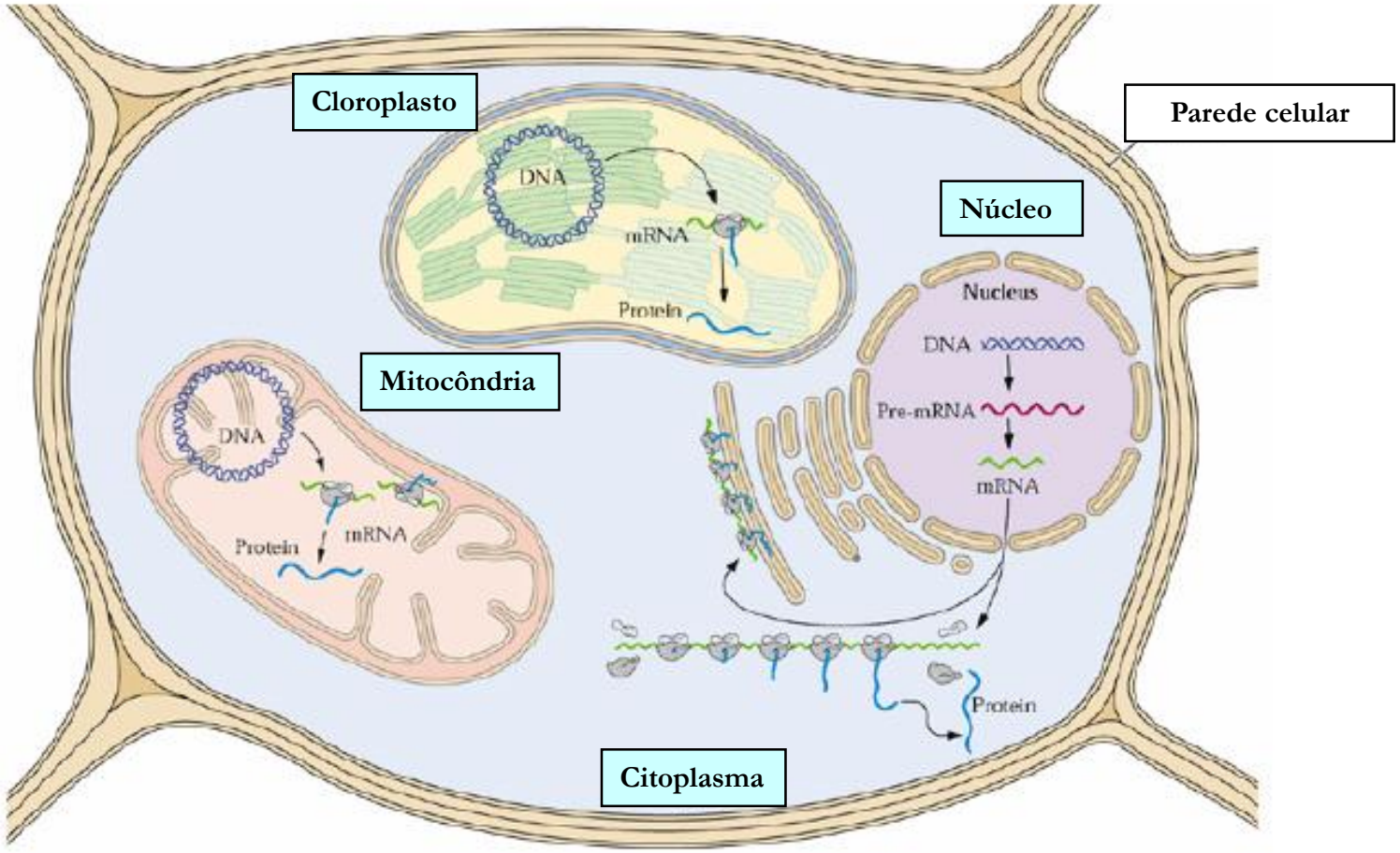


Estrutura secundária de um RNA mensageiro

Código Genético Universal

Amino acid	3-Letter code	1-Letter code	Codons
Alanine	Ala	A	GCC, GCU, GCG, GCA
Arginine	Arg	R	CGC, CGG, CGU, CGA, AGA, AGG
Asparagine	Asn	N	AAU, AAC
Aspartic acid	Asp	D	GAU, GAC
Cysteine	Cys	C	UGU, UGC
Glutamic acid	Glu	E	GAA, GAG
Glutamine	Gln	Q	CAA, CAG
Glycine	Gly	G	GGU, GGC, GGA, GGG
Histidine	His	H	CAU, CAC
Isoleucine	Ile	I	AUU, AUC, AUA
Leucine	Leu	L	UUA, UUG, CUA, CUG, CUU, CUC
Lysine	Lys	K	AAA, AAG
Methionine	Met	M	AUG *start codon* -iniciador
Phenylalanine	Phe	F	UUC, UUU
Proline	Pro	P	CCU, CCC, CCA, CCG
Serine	Ser	S	UCU, UCC, UCA, UCG, AGU, AGC
Threonine	Thr	T	ACU, ACC, ACA, ACG
Tyrosine	Tyr	Y	UAU, UAC
Tryptophan	Trp	W	UGG
Valine	Val	V	GUU, GUC, GUA, GUG
"Stop"	—	—	UAA, UAG, UGA *stop codon* -terminador

Três genomas em plantas: cromossomial, plastidial e mitocondrial



Estudo Dirigido

1. Diferenças fundamentais entre DNA e RNA;
2. Estrutura e função do DNA;
3. Principais características da dupla hélice do DNA;
4. Principais tipos e funções dos RNAs.

Capítulo 2 – Componentes químicos das Células

Capítulo 5 – DNA e Cromossomos

Alberts, B.; Bray, D.; Hopkin, K.; Johnson, A.; Lewis, J.; Raff, M.; Roberts, K.; Walter, P. 2011. ***Fundamentos da Biologia Celular***. 3ª Edição brasileira. Artmed, Porto Alegre