Expressão gênica

Do DNA à proteína

Bibliografia sugerida: Lehninger – Princípios de Bioquímica

Cap. 8 – Nucleotides and nucleic acids

8.1 – Some basics

- Nucleotides and Nucleic Acids Have Characteristic Bases and Pentoses
- Phosphodiester Bonds Link Successive Nucleotides in Nucleic Acids
- The Properties of Nucleotide Bases Affect the Three-Dimensional Structure of Nucleic Acids

8.2 – Nucleic acid structure

- DNA Stores Genetic Information
- DNA Molecules Have Distinctive Base Compositions
- DNA Is a Double Helix
- Messenger RNAs Code for Polypeptide Chains
- Many RNAs Have More Complex Three-Dimensional Structures

8.3 – Nucleic acid chemistry

- DNA and RNA Can Be Denatured
- Nucleic Acids from Different Species Can Form Hybrids

O dogma central da biologia

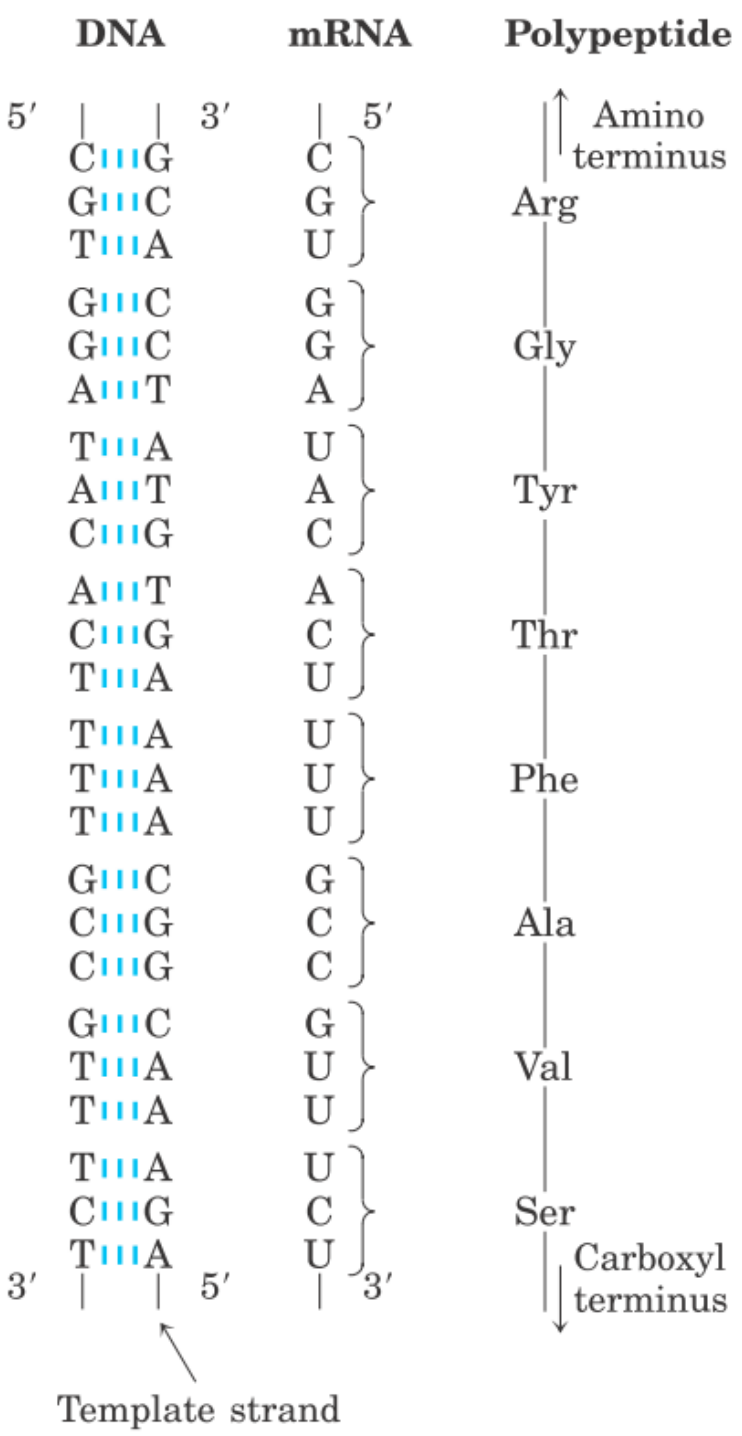
DNA

↓ **Transcrição**

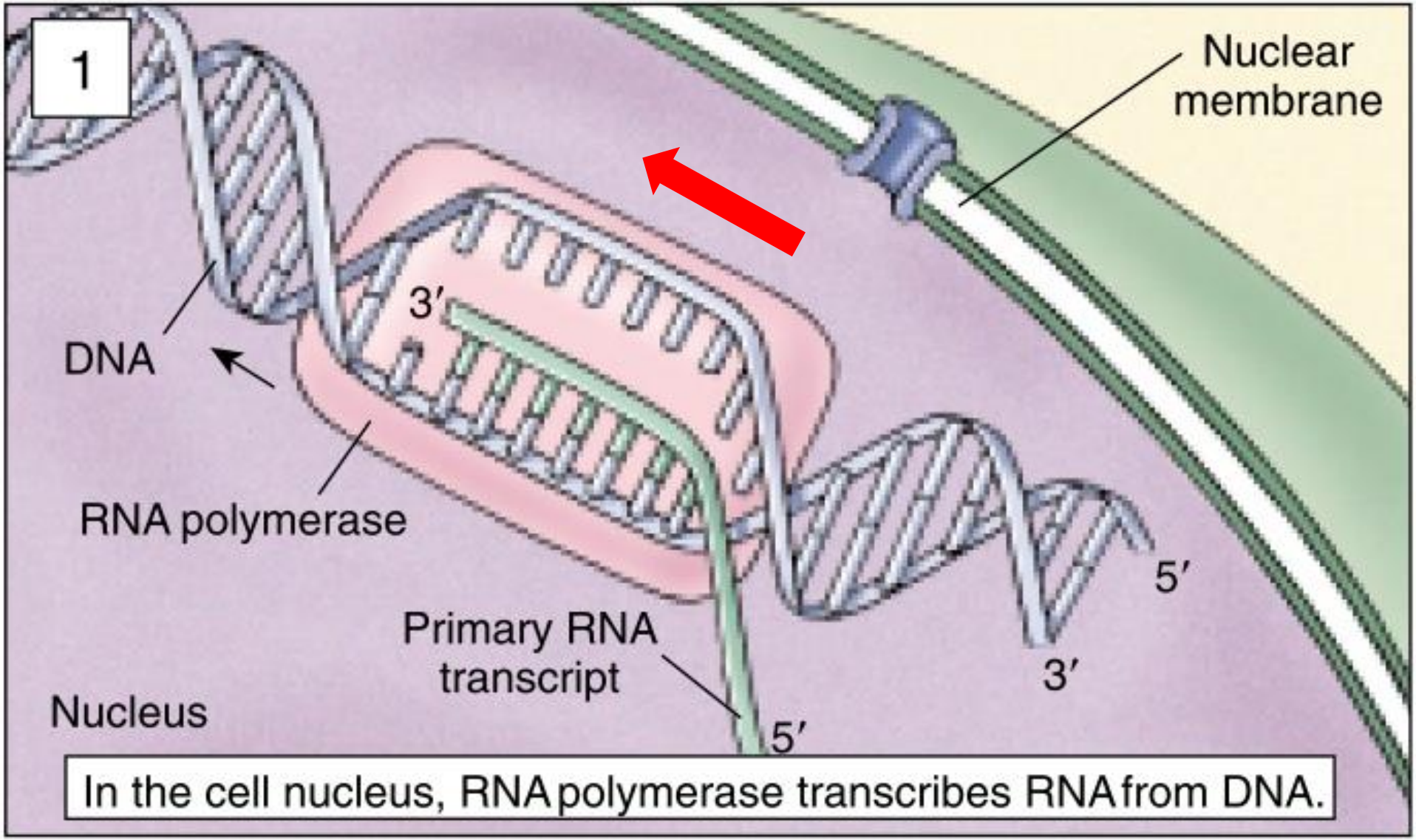
mRNA

↓ **Tradução**

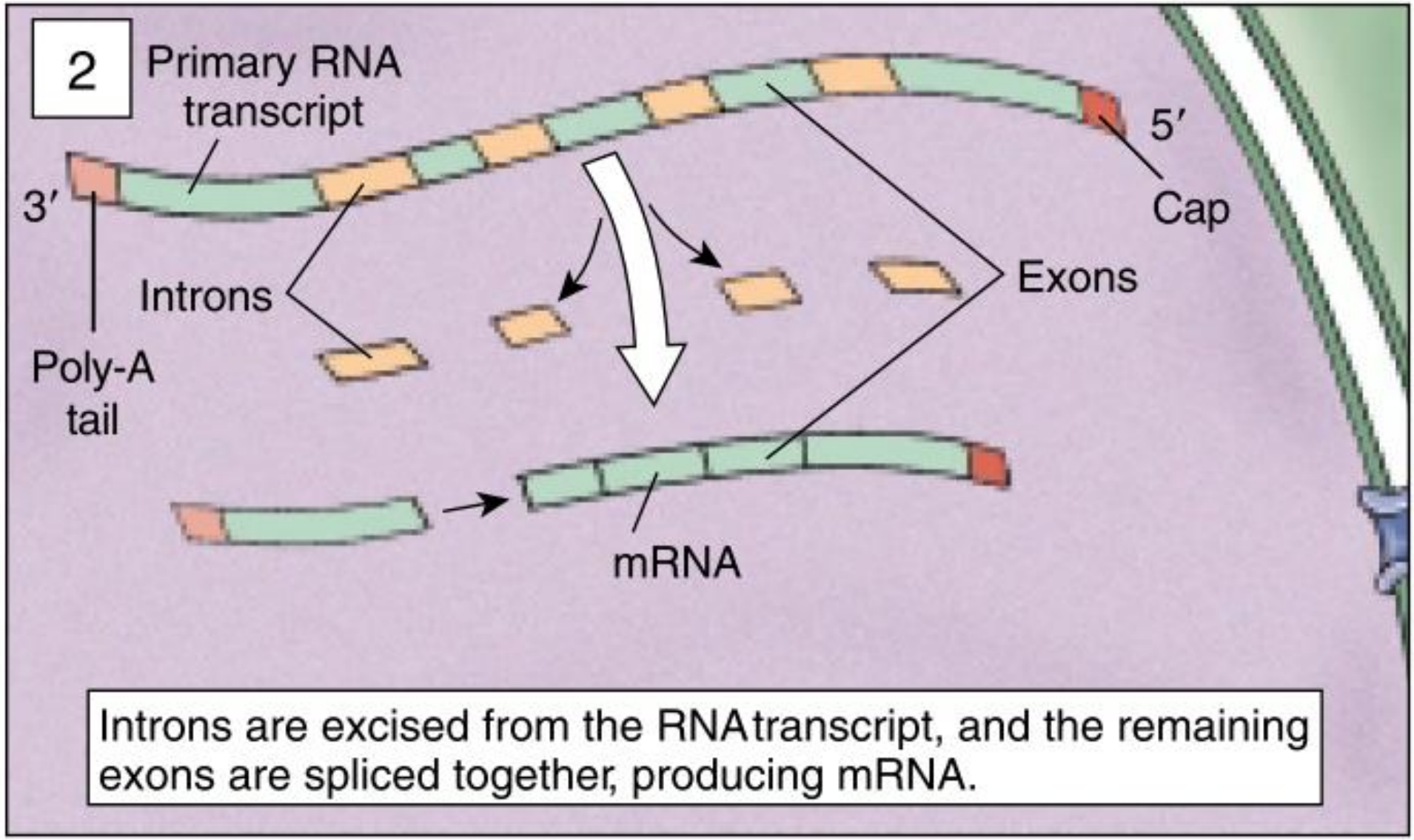
Proteína



Transcrição

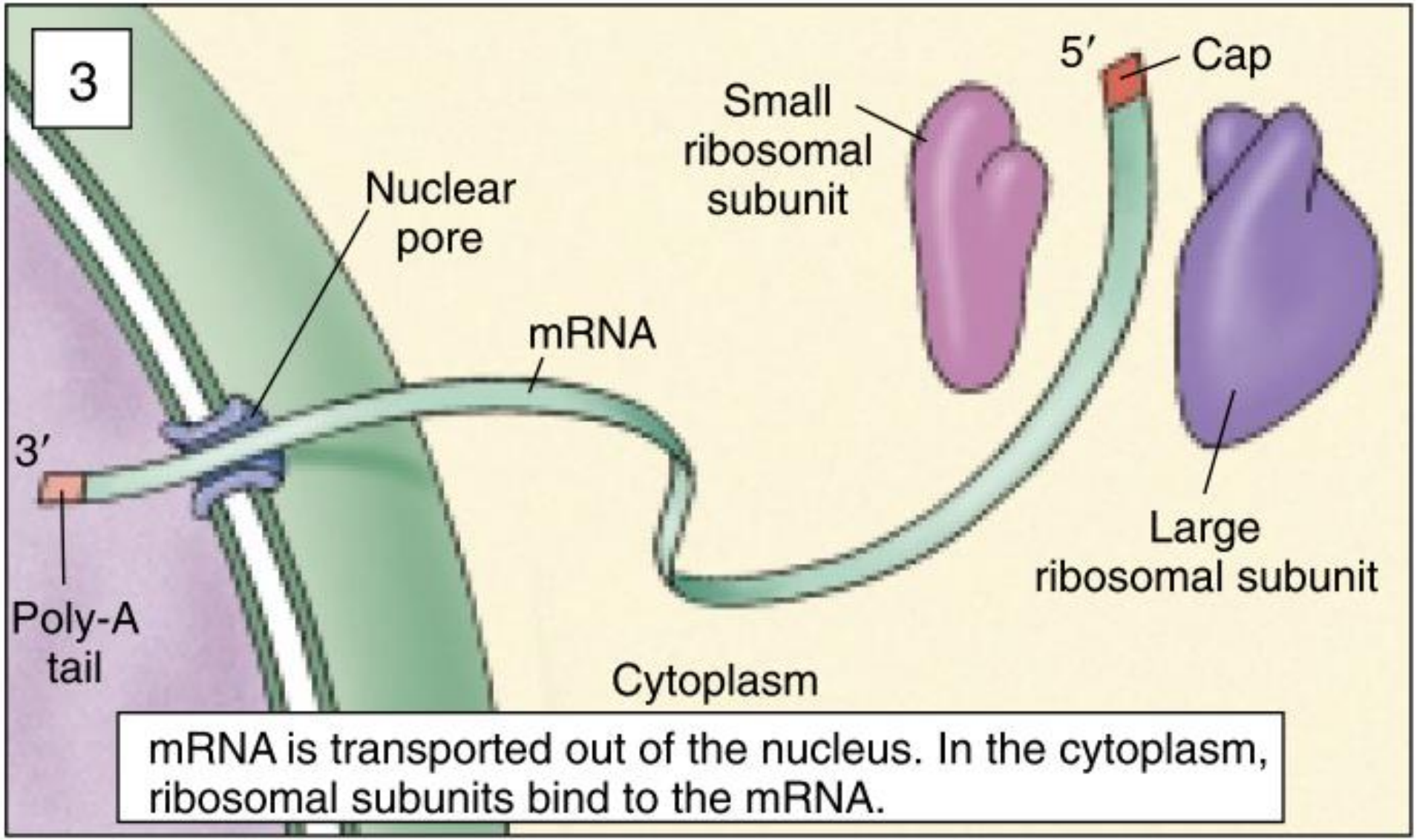


Splicing

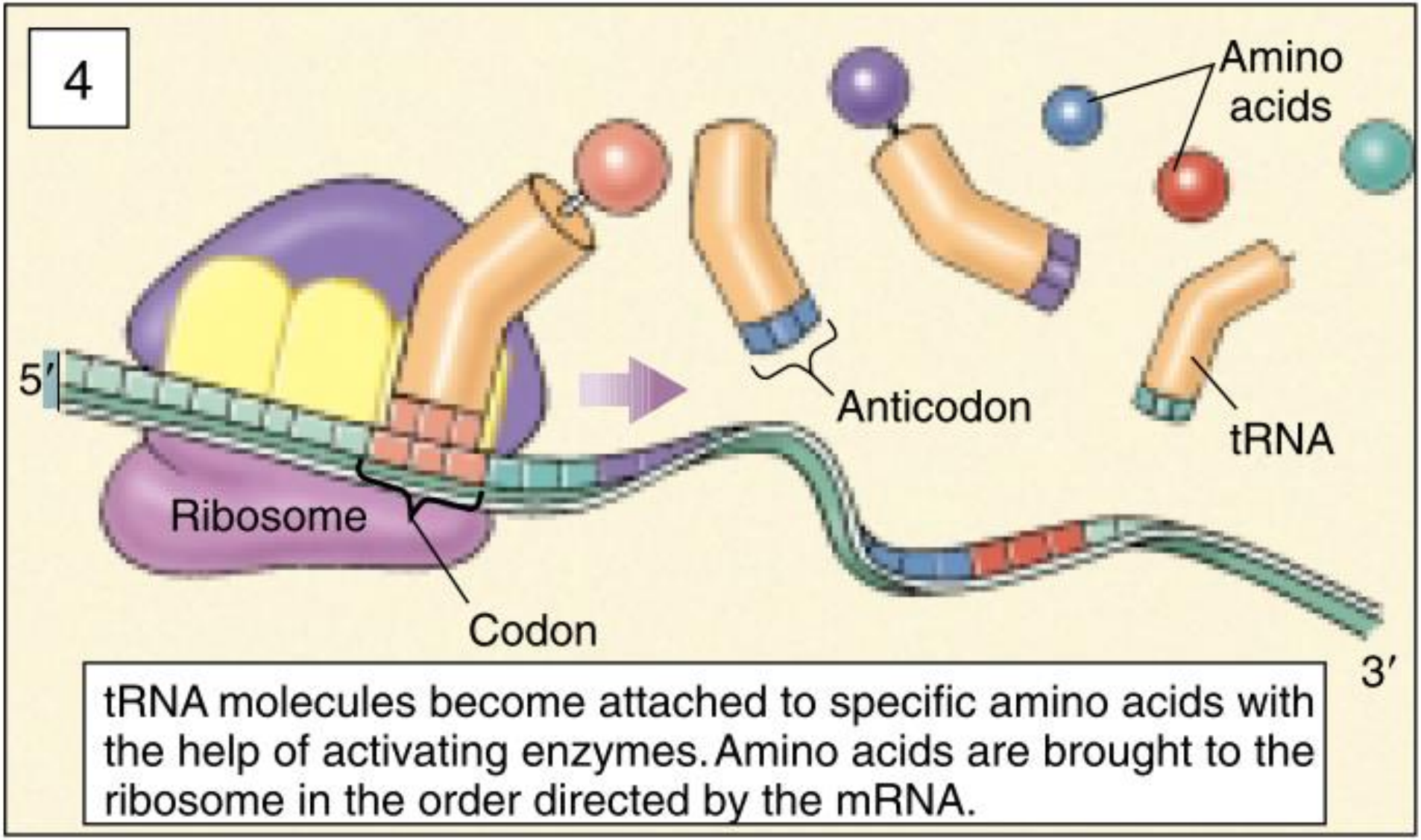


Introns are excised from the RNA transcript, and the remaining exons are spliced together, producing mRNA.

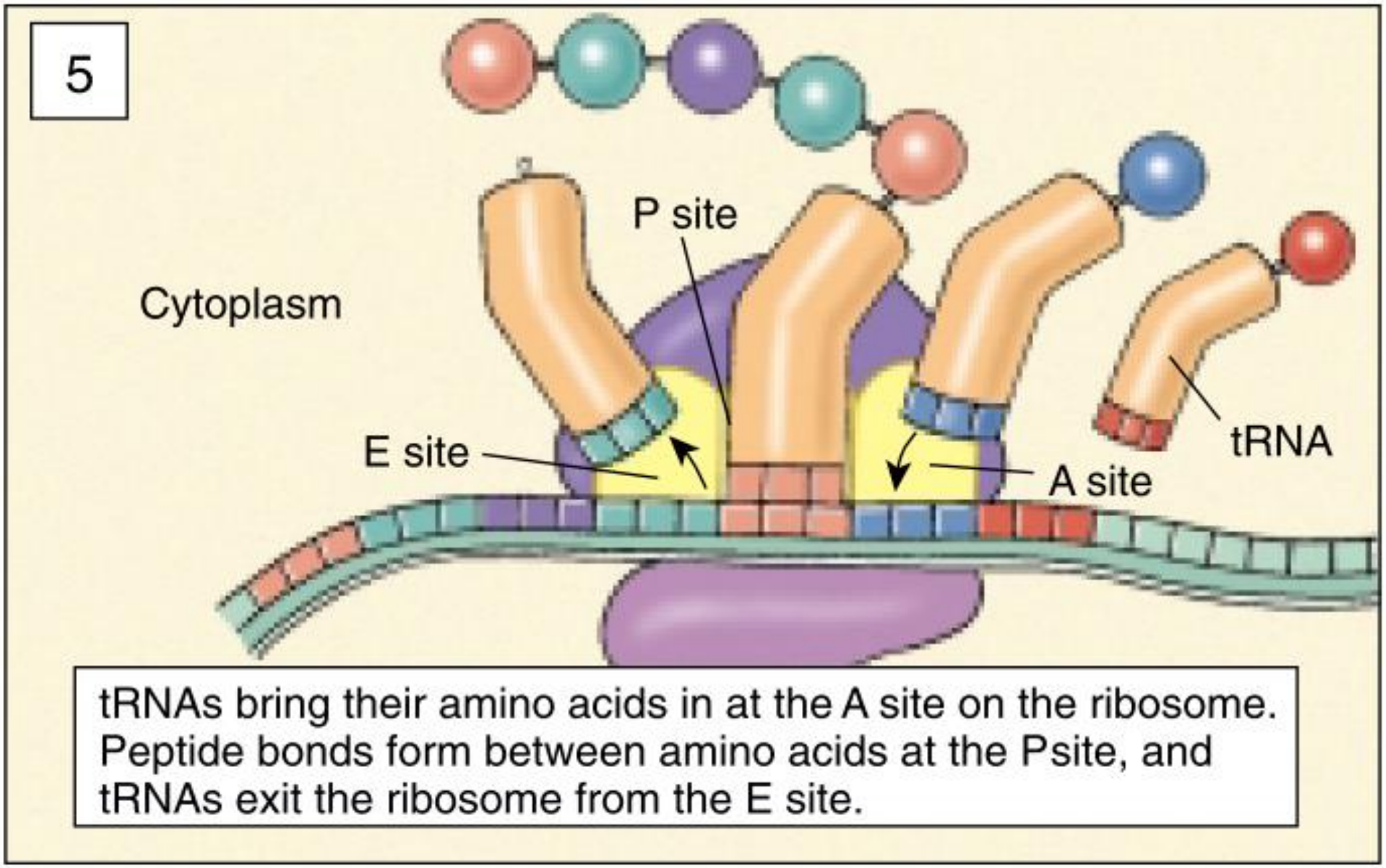
Tradução


3
5′
Cap
Small ribosomal subunit
Nuclear pore
mRNA
3′
Poly-A tail
Large ribosomal subunit
Cytoplasm
mRNA is transported out of the nucleus. In the cytoplasm, ribosomal subunits bind to the mRNA.

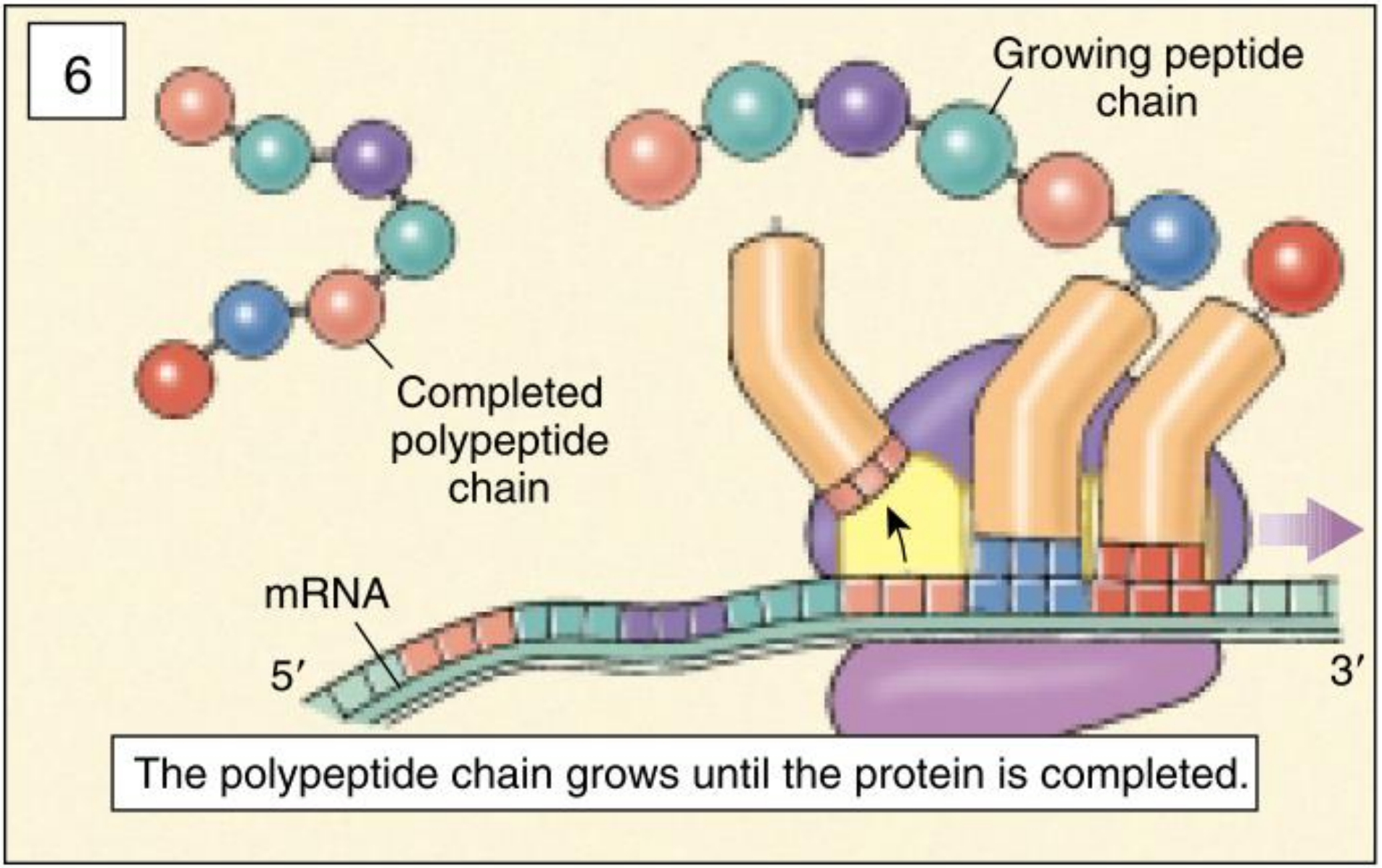
Tradução


4
Amino acids
5′
Anticodon
tRNA
Ribosome
Codon
3′
tRNA molecules become attached to specific amino acids with the help of activating enzymes. Amino acids are brought to the ribosome in the order directed by the mRNA.

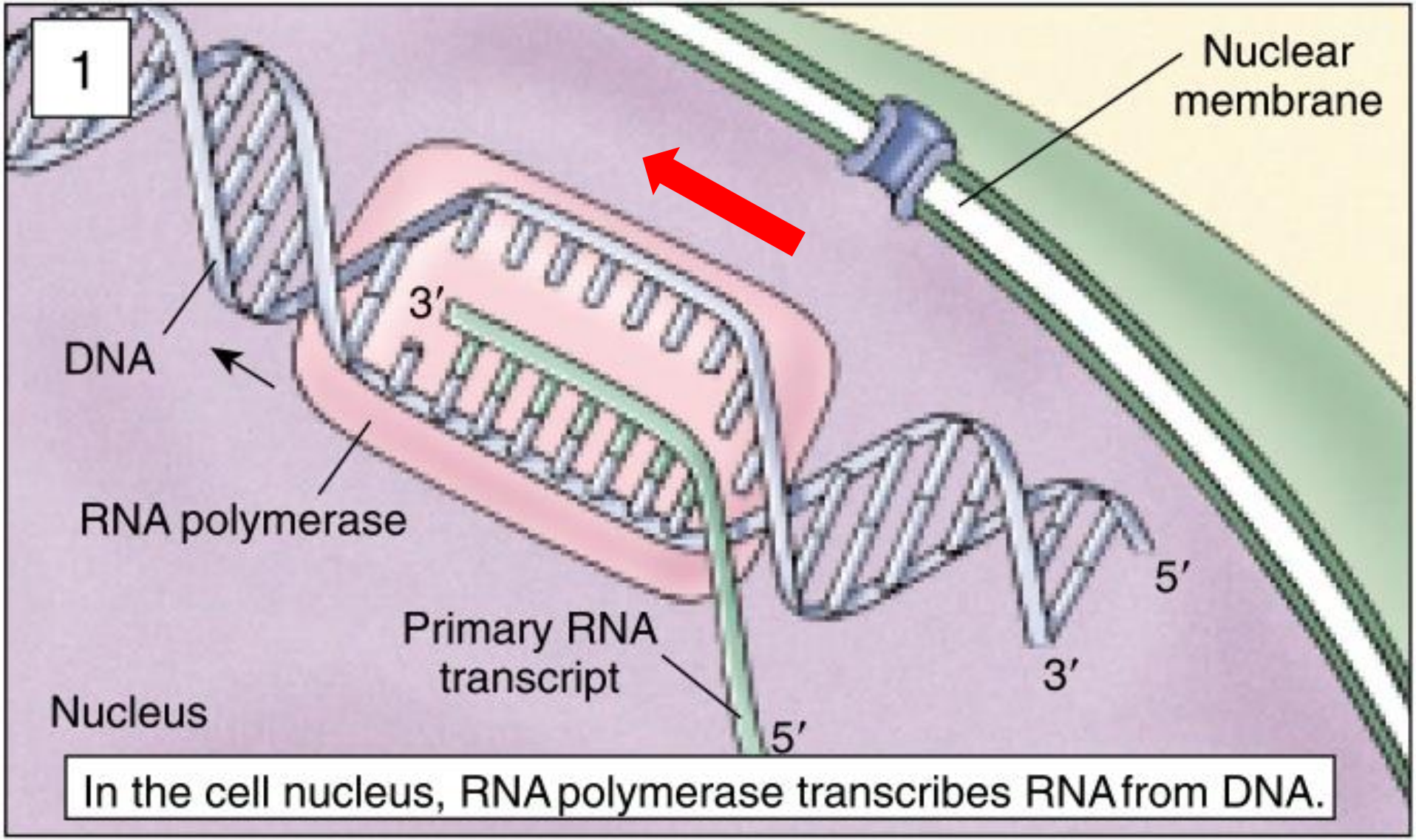
Tradução

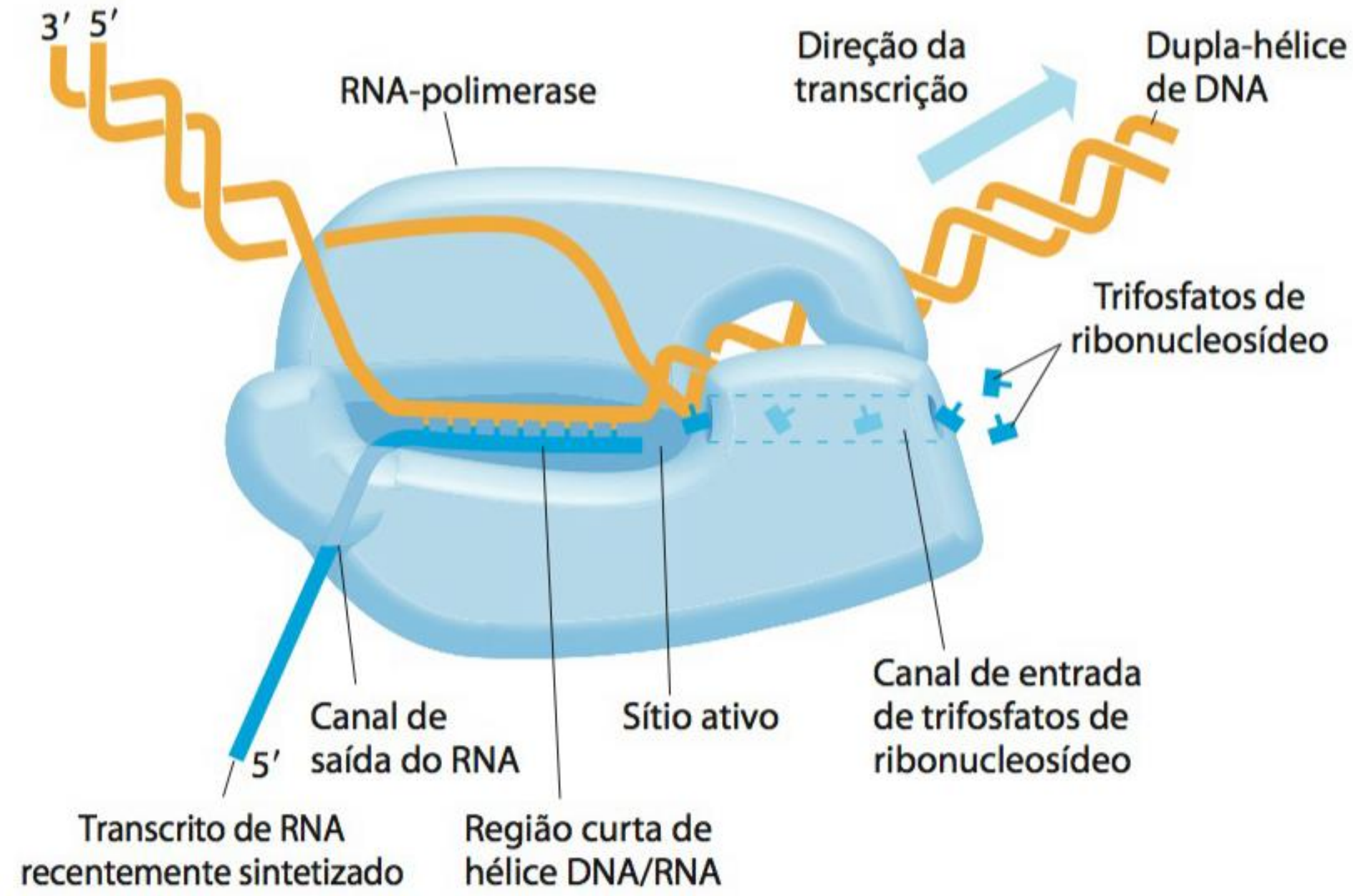

5
P site
Cytoplasm
E site
A site
tRNA
tRNAs bring their amino acids in at the A site on the ribosome. Peptide bonds form between amino acids at the Psite, and tRNAs exit the ribosome from the E site.

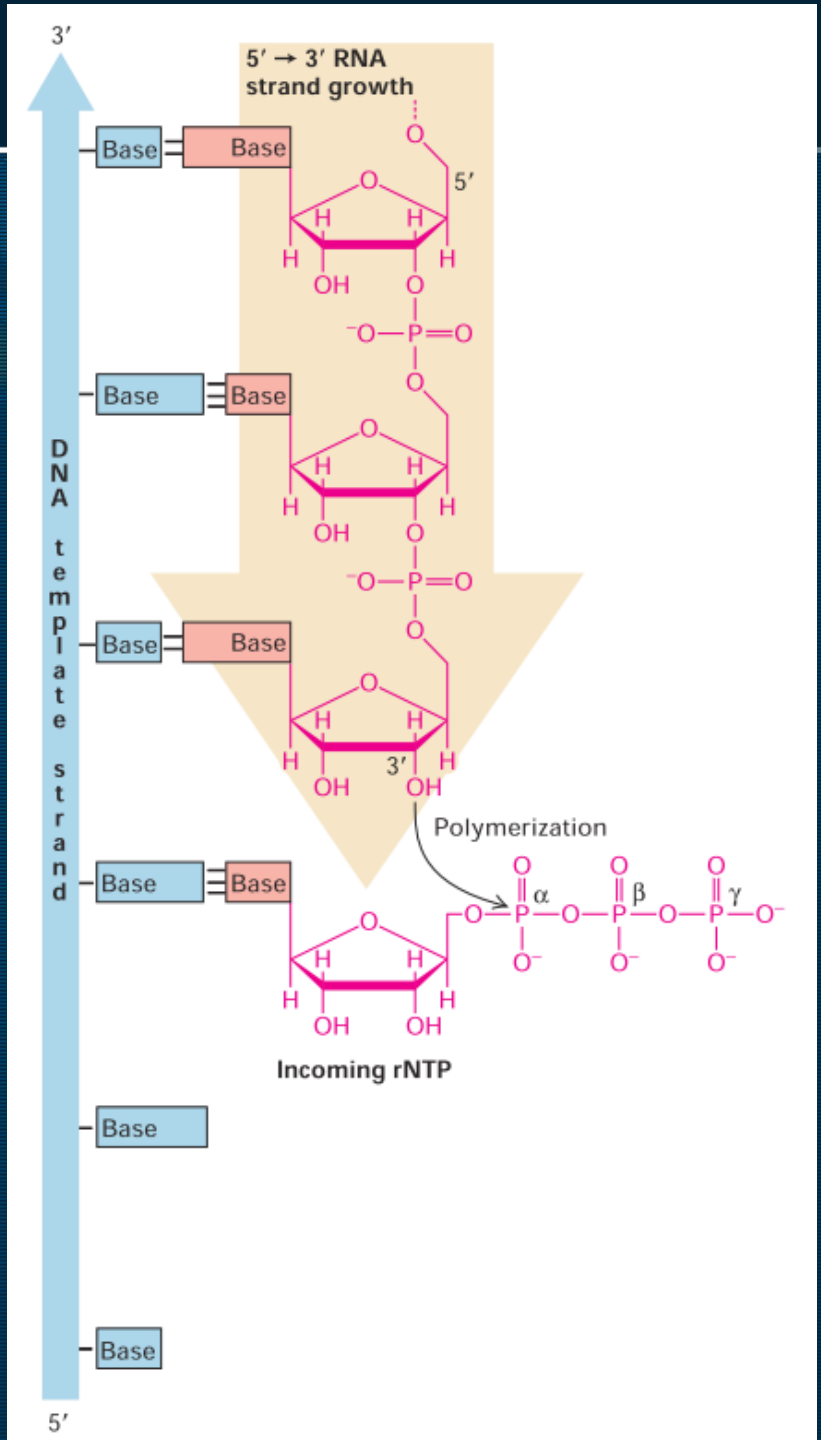
Tradução

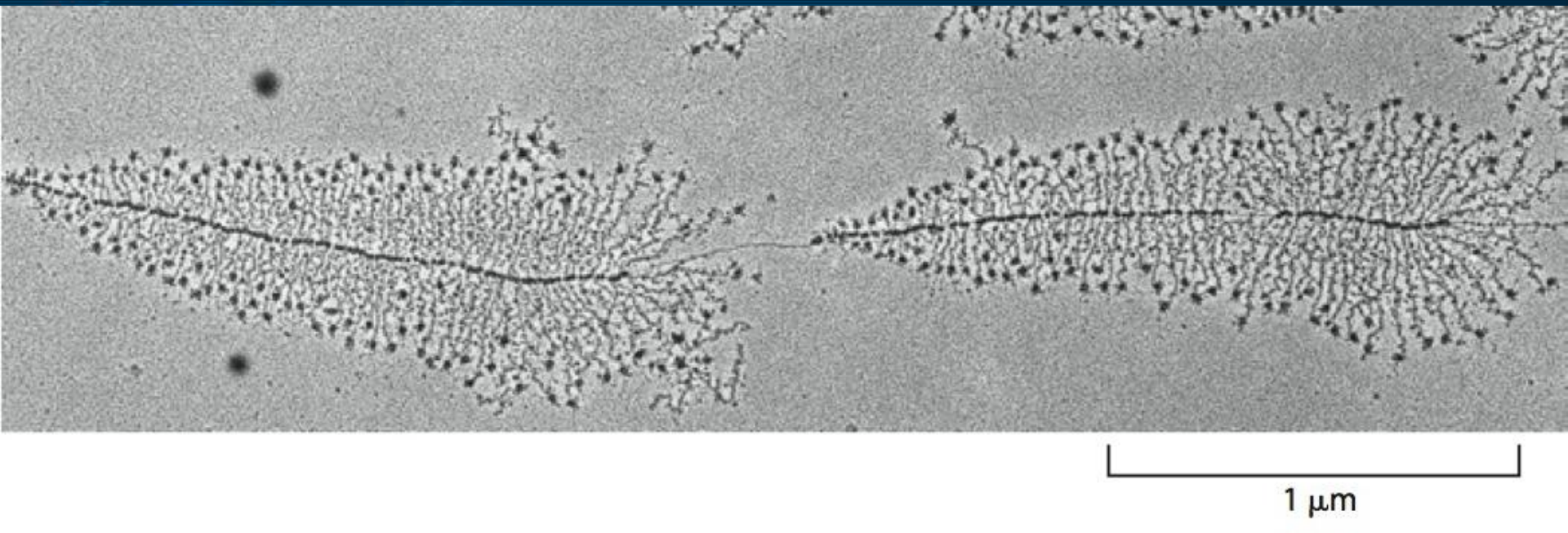

6
Growing peptide chain
Completed polypeptide chain
mRNA
5′
3′
The polypeptide chain grows until the protein is completed.

Transcrição

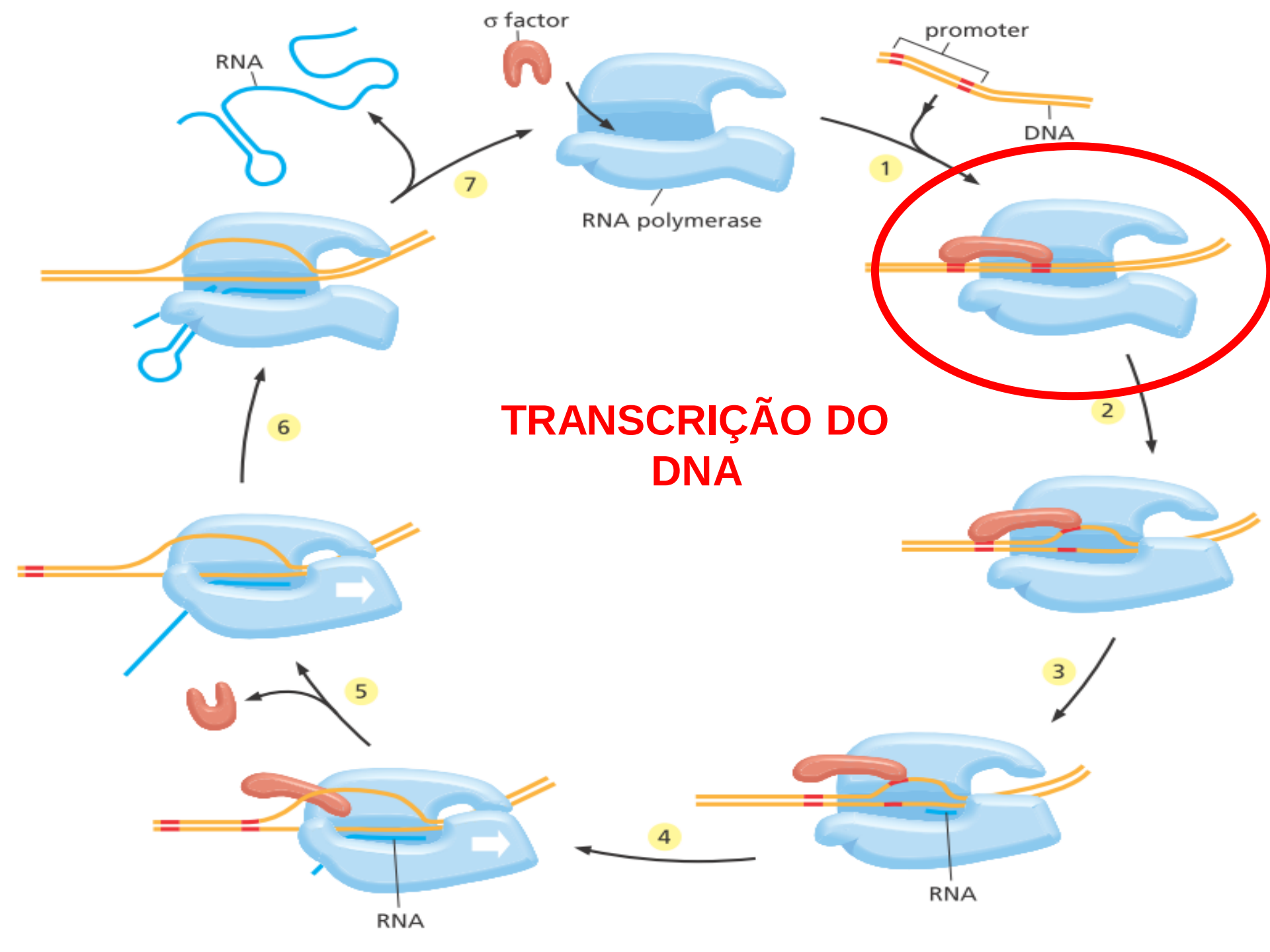



3′ 5′
RNA-polimerase
Direção da transcrição
Dupla-hélice de DNA
Trifosfatos de ribonucleosídeo
Canal de saída do RNA
Sítio ativo
Canal de entrada de trifosfatos de ribonucleosídeo
5′
Transcrito de RNA recentemente sintetizado
Região curta de hélice DNA/RNA


3′
5′ → 3′ RNA strand growth
DNA template strand
Base
5′
3′
OH
Polymerization
α
β
γ
Incoming rNTP
5′

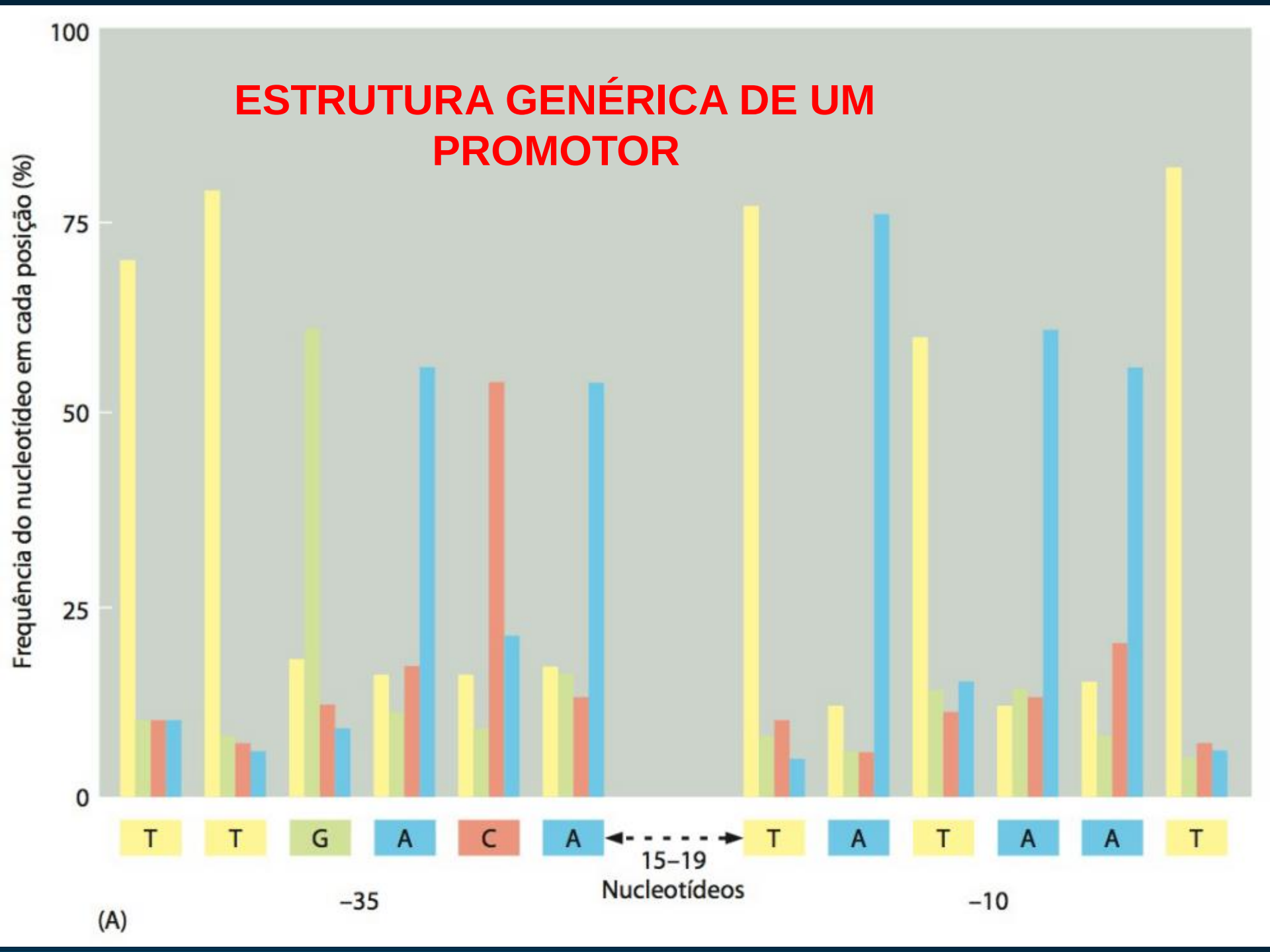


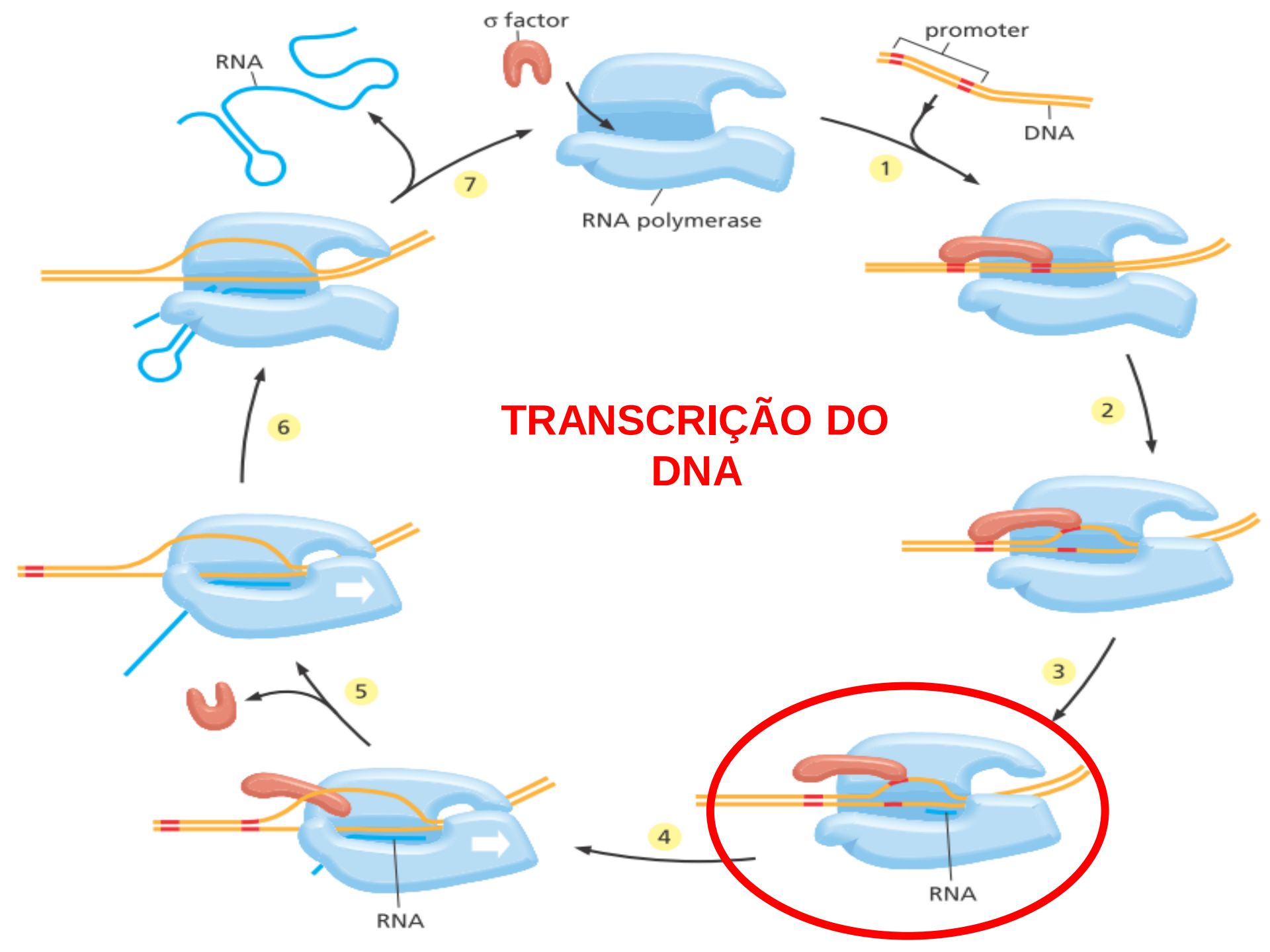
Transcrição de dois genes vista ao microscópio. Múltiplas RNA polimerases transcrevendo simultaneamente dois genes ribossomais.



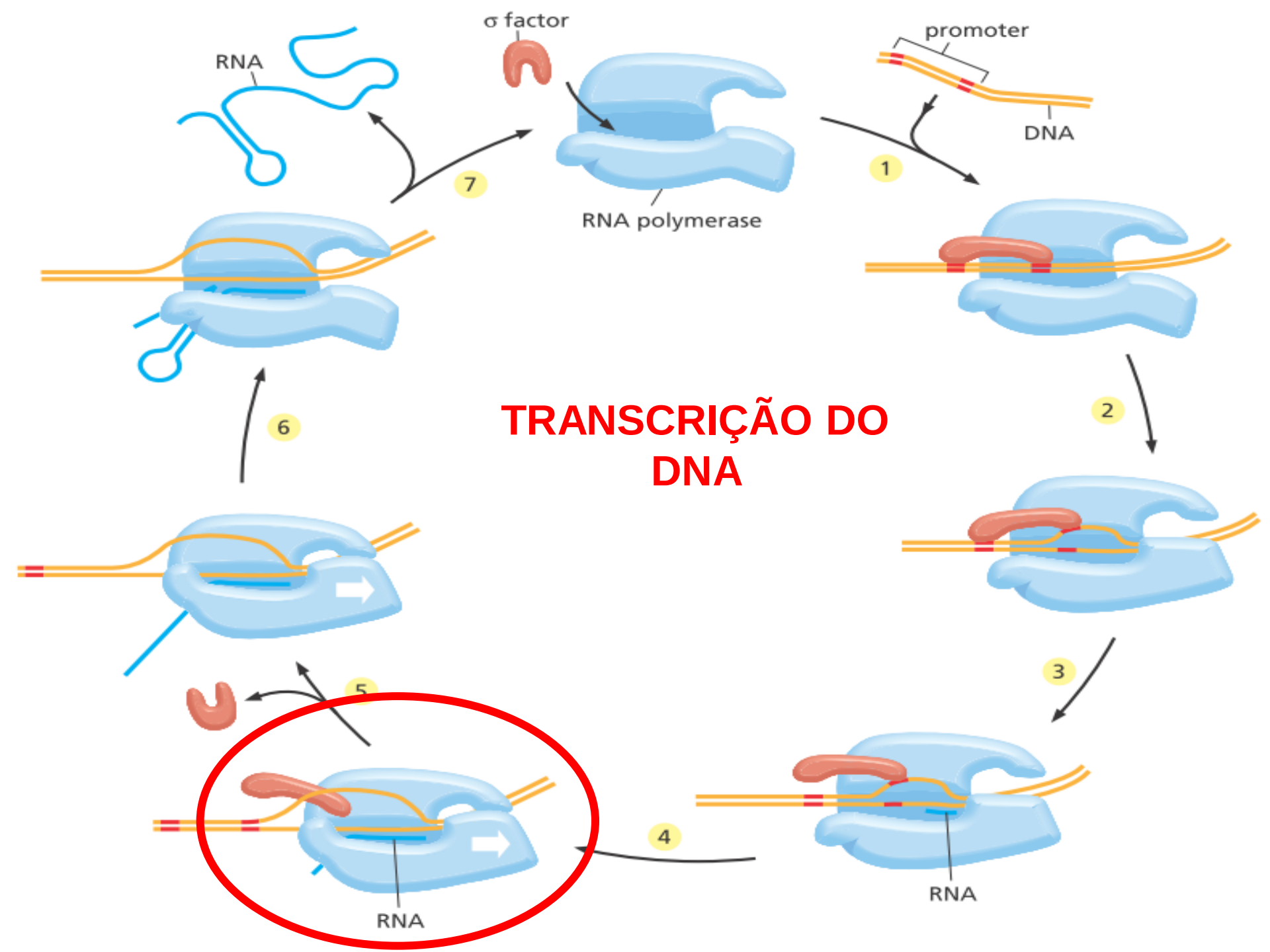
TRANSCRIÇÃO DO DNA

ESTRUTURA GENÉRICA DE UM PROMOTOR

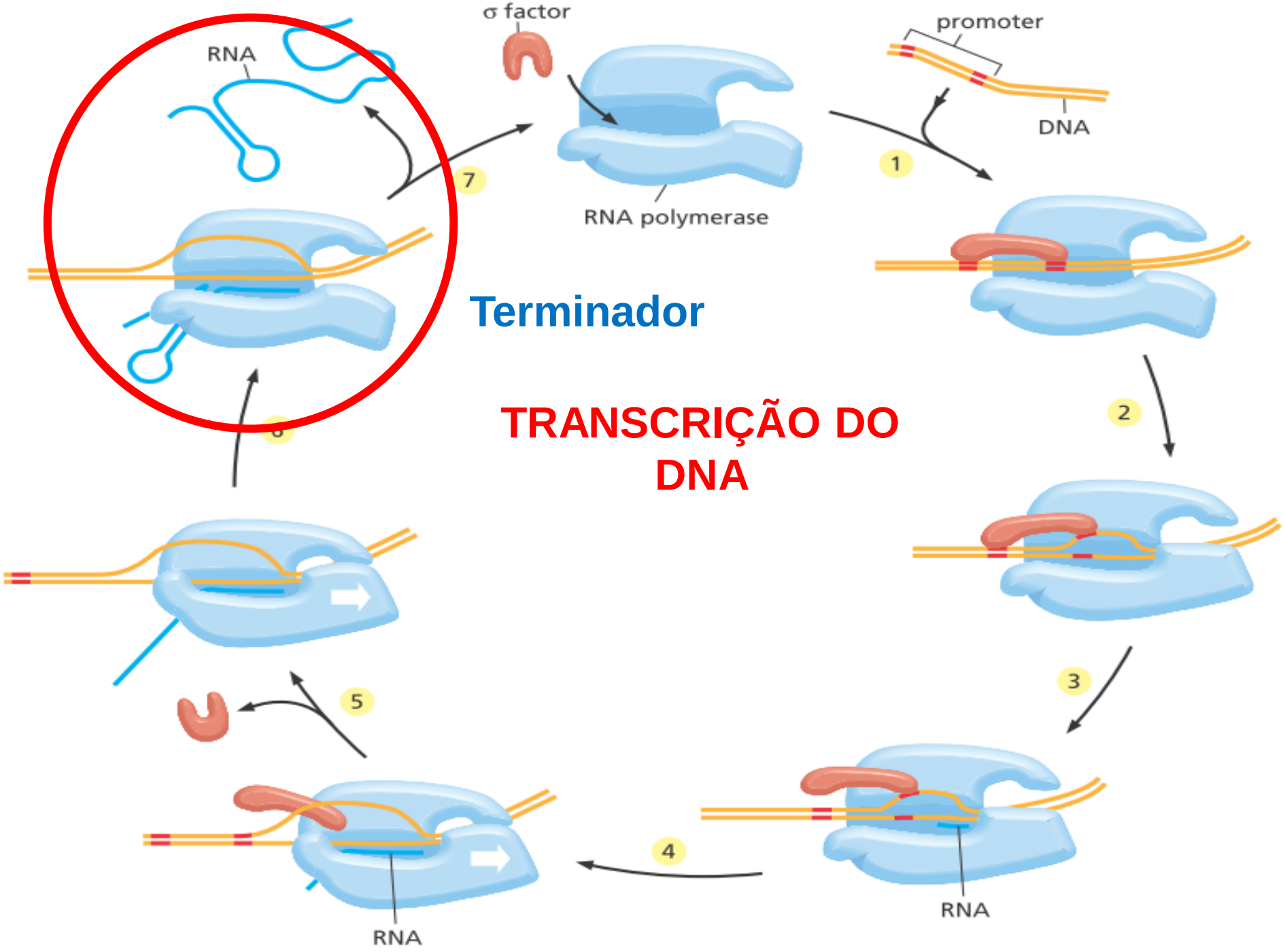




TRANSCRIÇÃO DO DNA

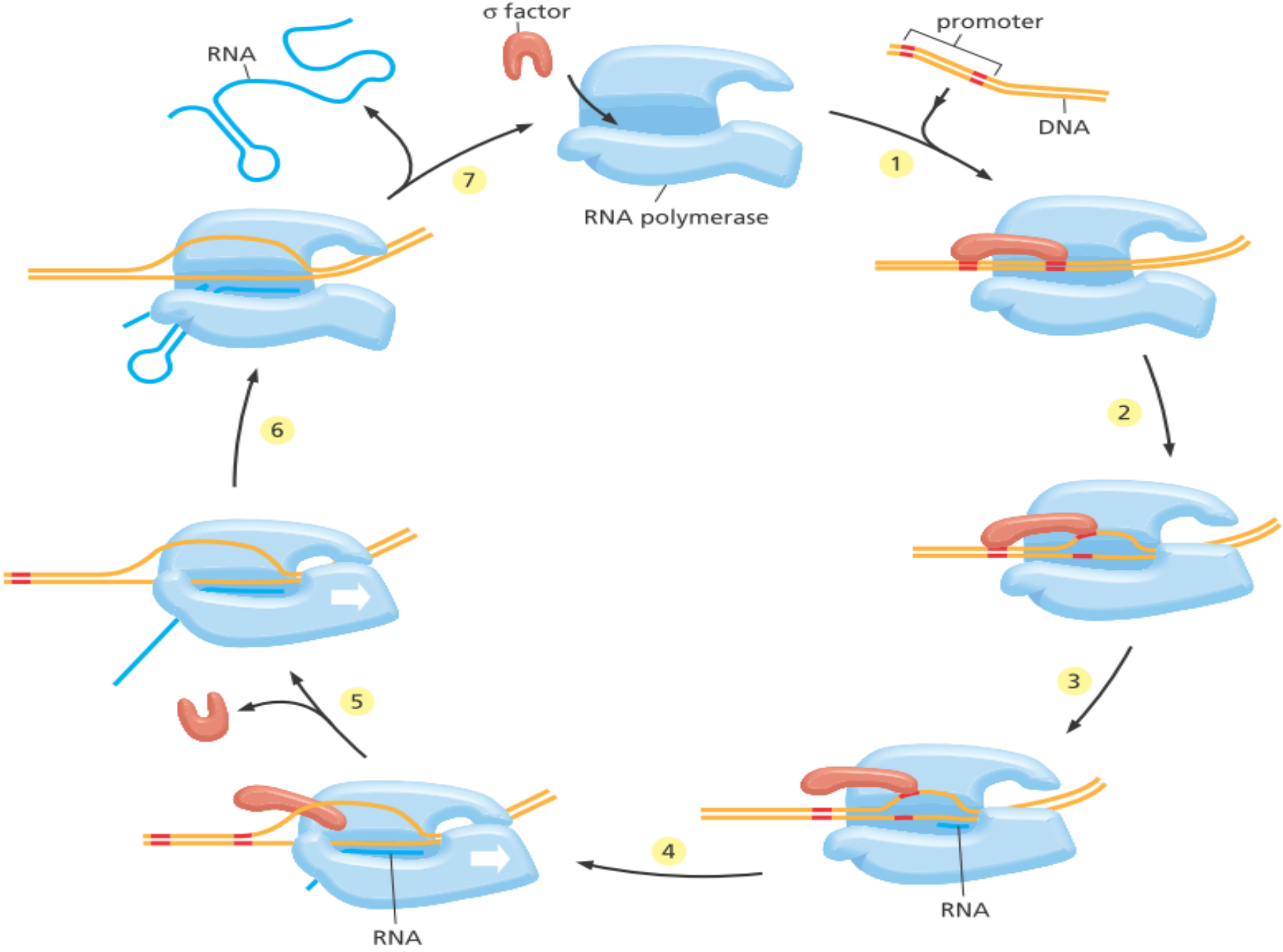


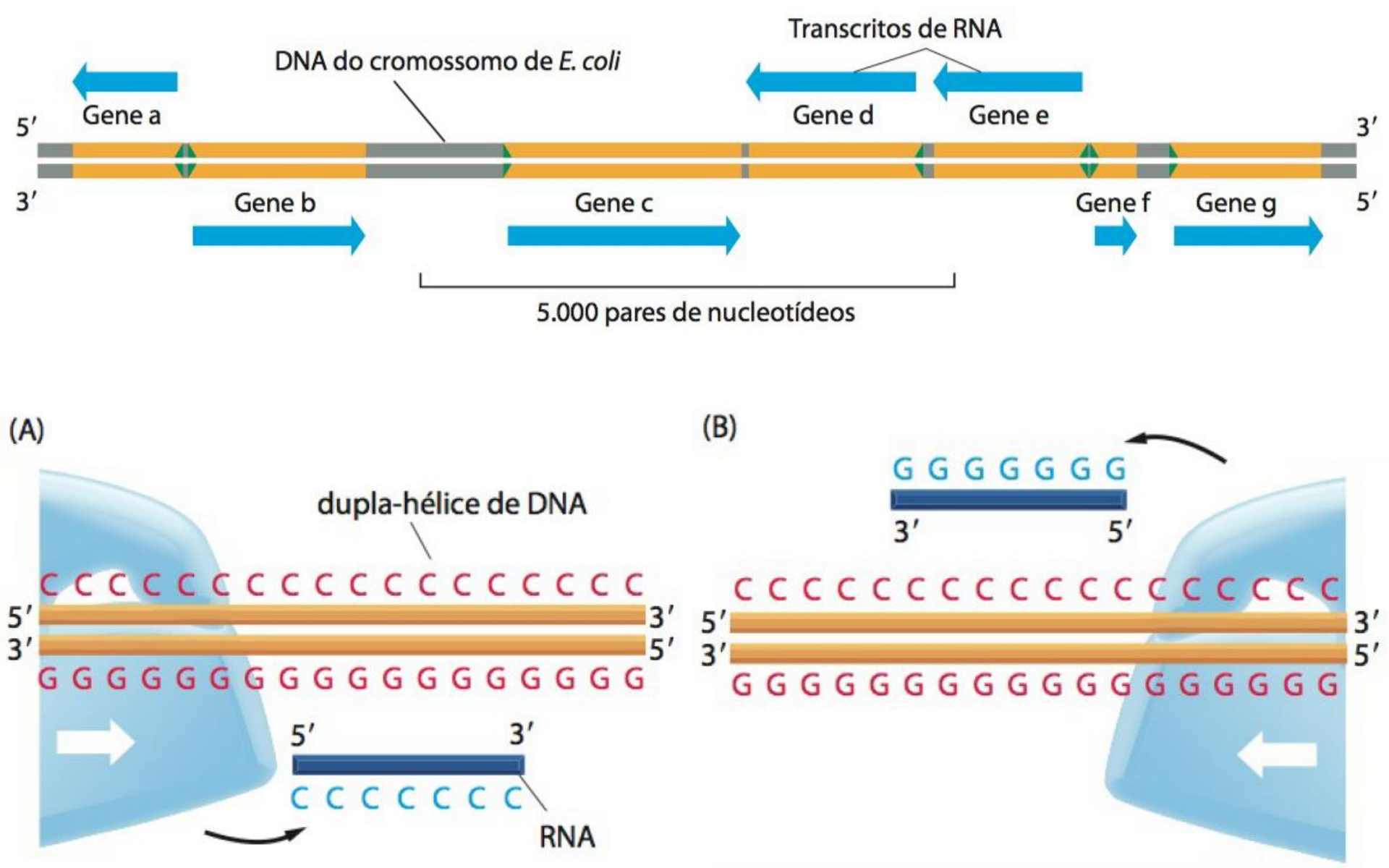
TRANSCRIÇÃO DO DNA



Terminador

TRANSCRIÇÃO DO DNA

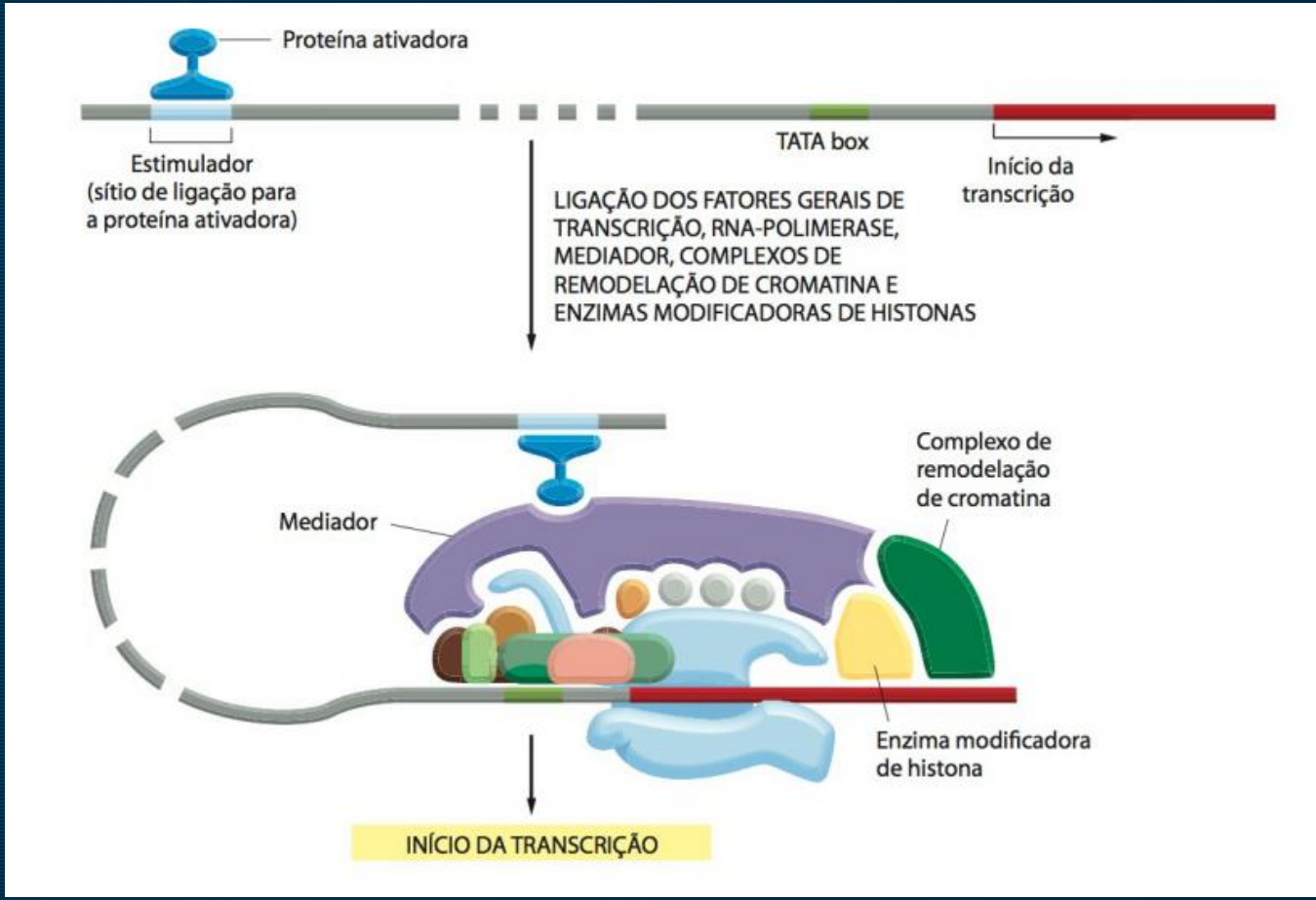

σ factor
promoter
RNA
DNA
RNA polymerase
1
2
3
4
5
6
7
RNA
RNA

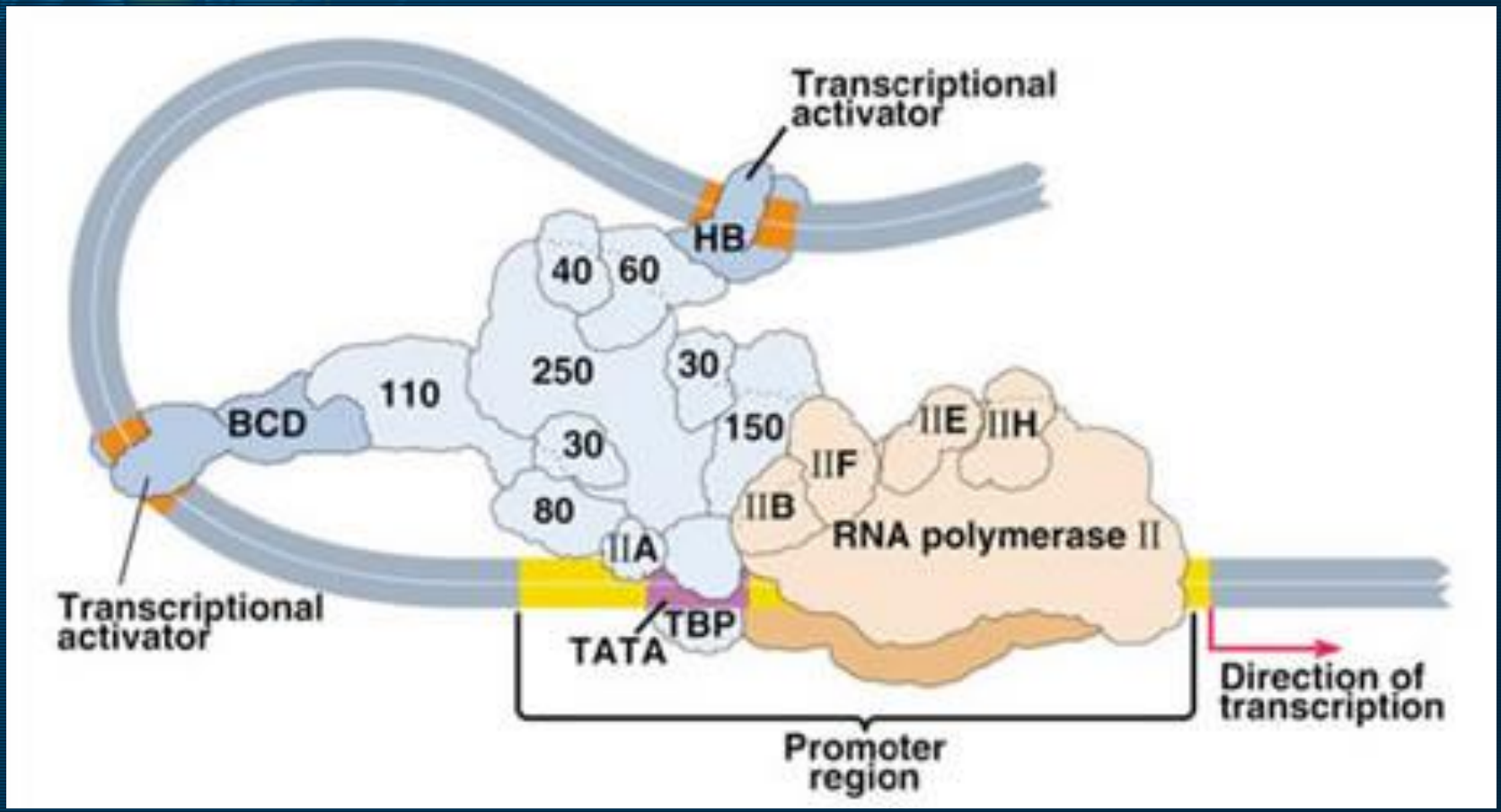


Uma RNA-polimerase que se move da esquerda para a direita sintetiza o RNA utilizando a fita de baixo como molde.

Uma RNA-polimerase que se move da direita para a esquerda sintetiza o RNA utilizando a fita de cima como molde.

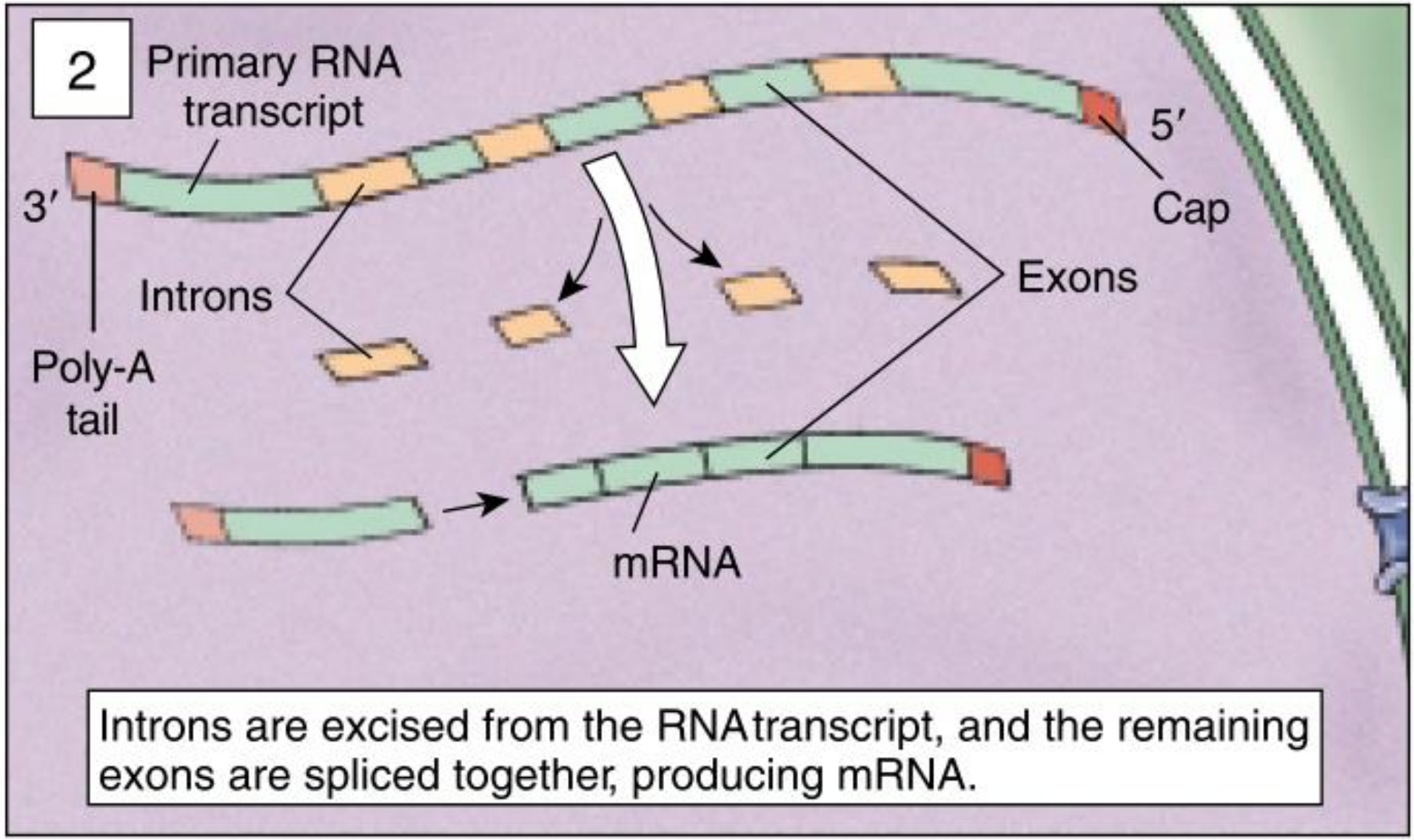
A RNA polimerase eucariótica necessita de diversos fatores gerais de transcrição (TFII – fatores de transcrição para polimerase II)



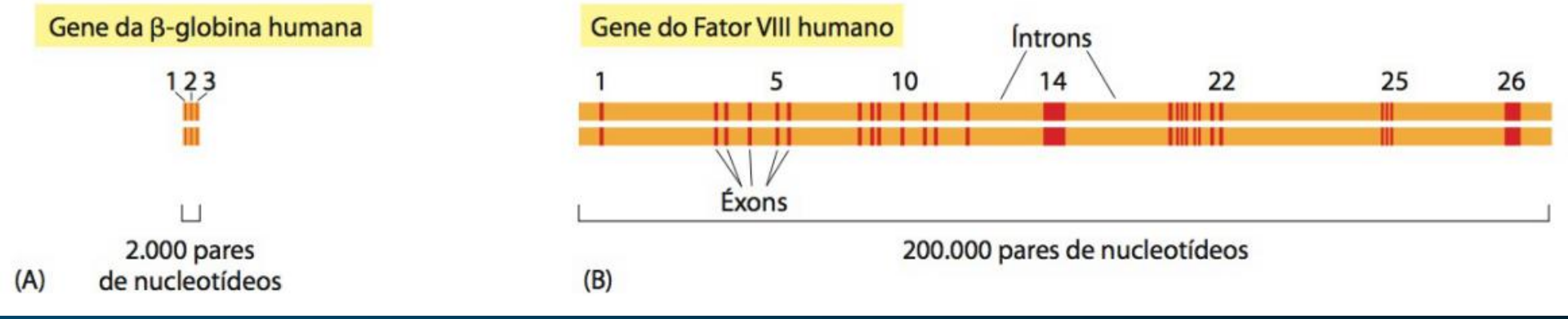

Transcriptional activator
HB
40
60
250
30
110
BCD
150
30
IIE
IIH
IIF
IIB
80
RNA polymerase II
IIA
Transcriptional activator
TBP
TATA
Direction of transcription
Promoter region

Video transcrição em eucariotos

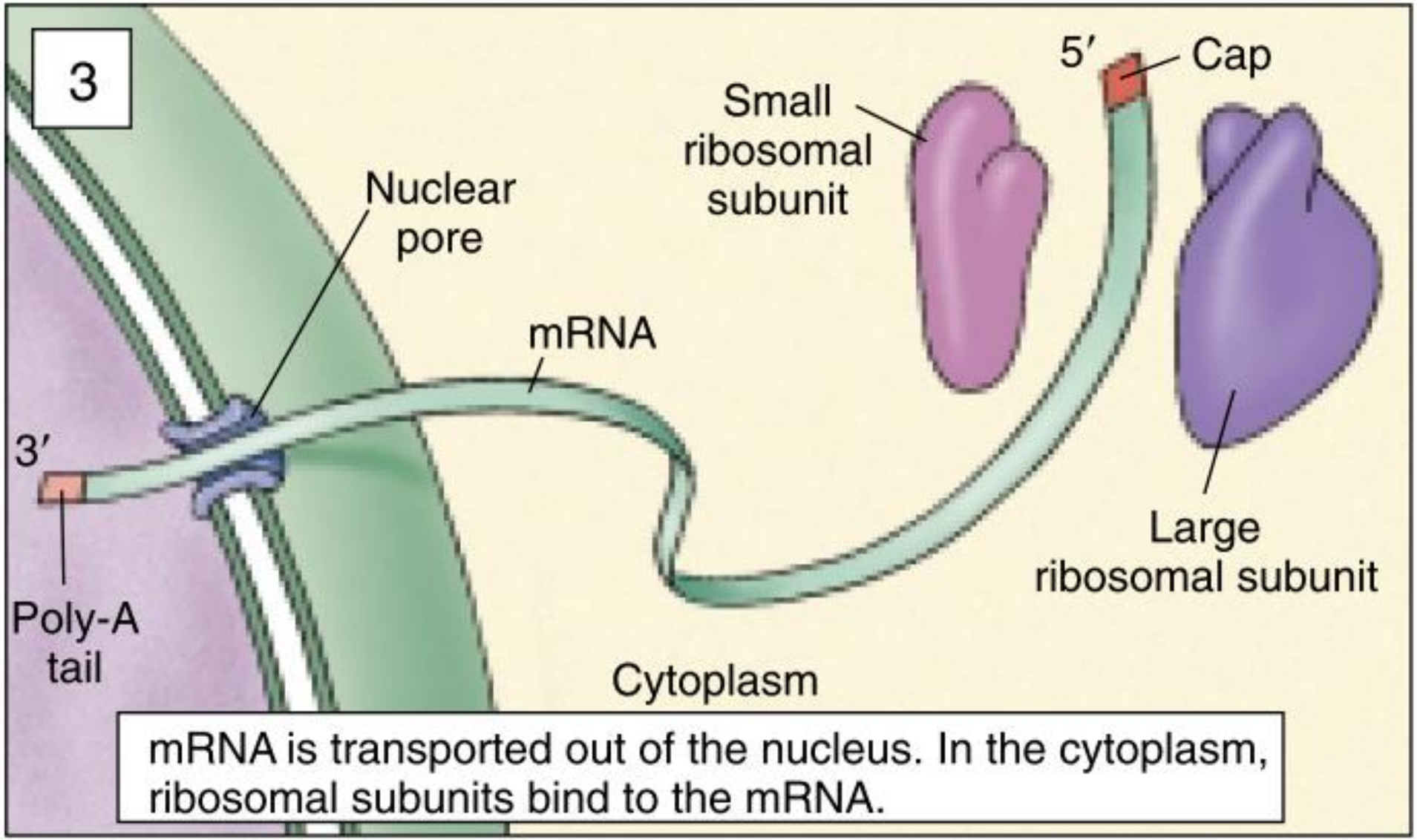
Splicing



Introns are excised from the RNA transcript, and the remaining exons are spliced together, producing mRNA.

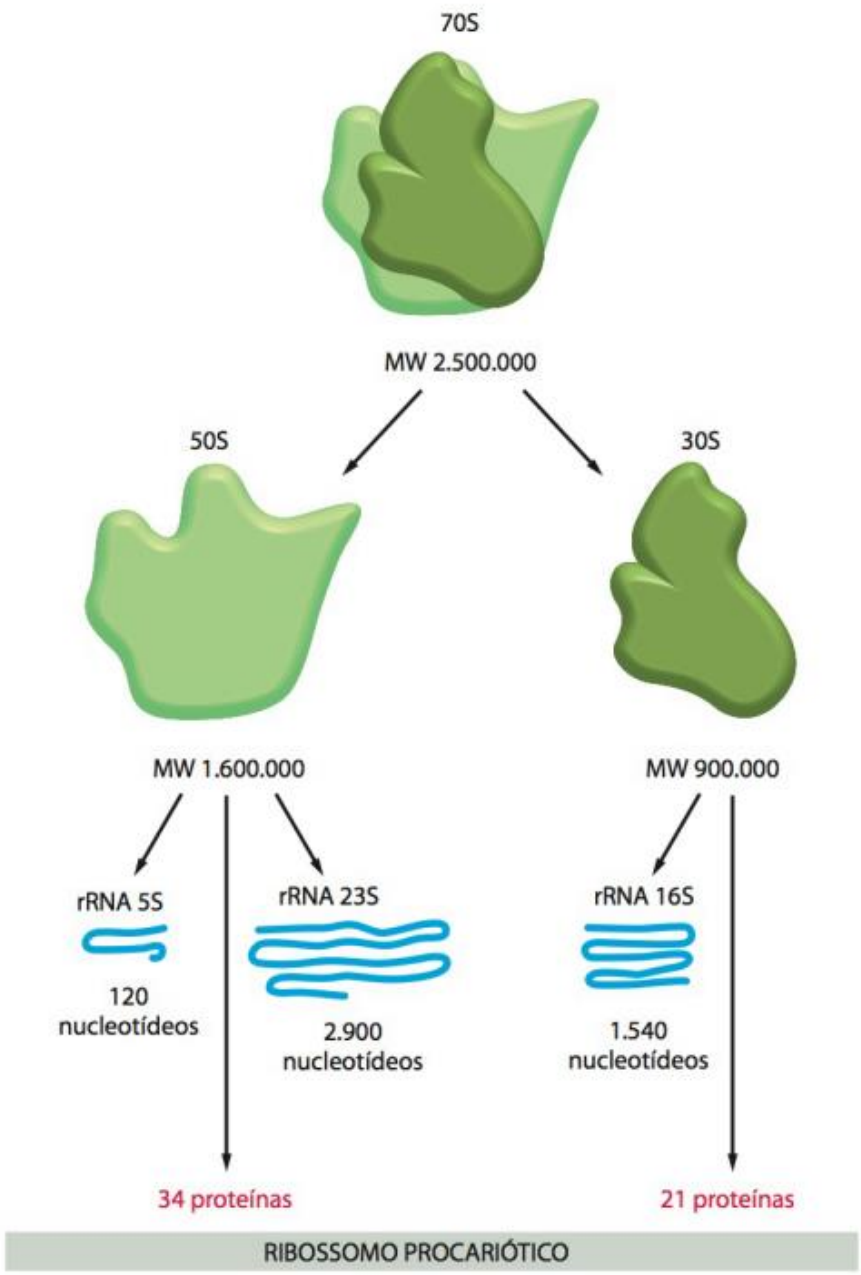

Gene da β-globina humana
1 2 3
2.000 pares
de nucleotídeos
(A)
Gene do Fator VIII humano
Íntrons
1
5
10
14
22
25
26
Éxons
200.000 pares de nucleotídeos
(B)

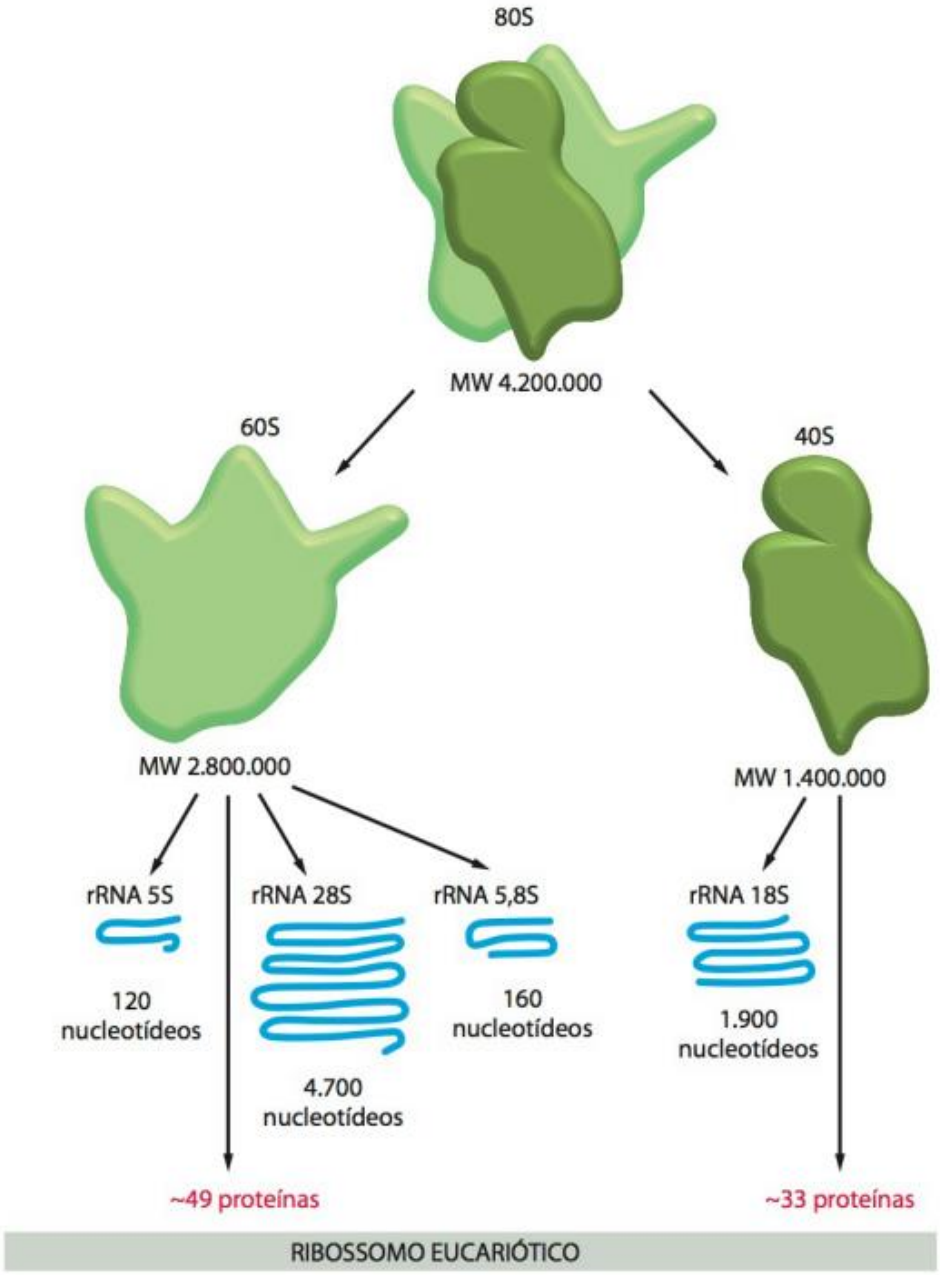
Migração do RNA do núcleo para o citoplasma

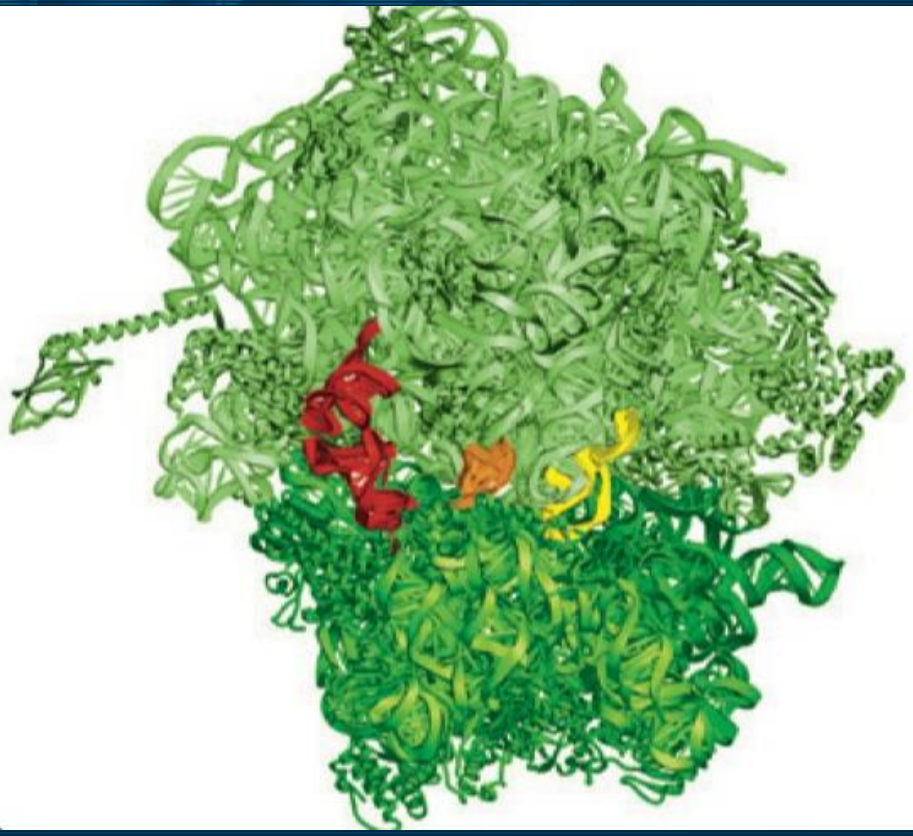


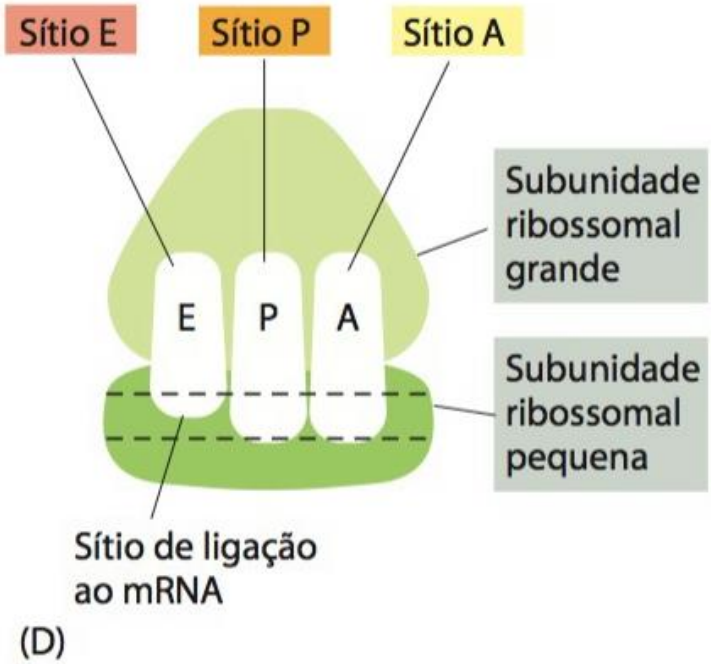
Os ribossomos asseguram a exatidão da ligação do tRNA correspondente e a manutenção do quadro de leitura correto durante toda a síntese da proteína.

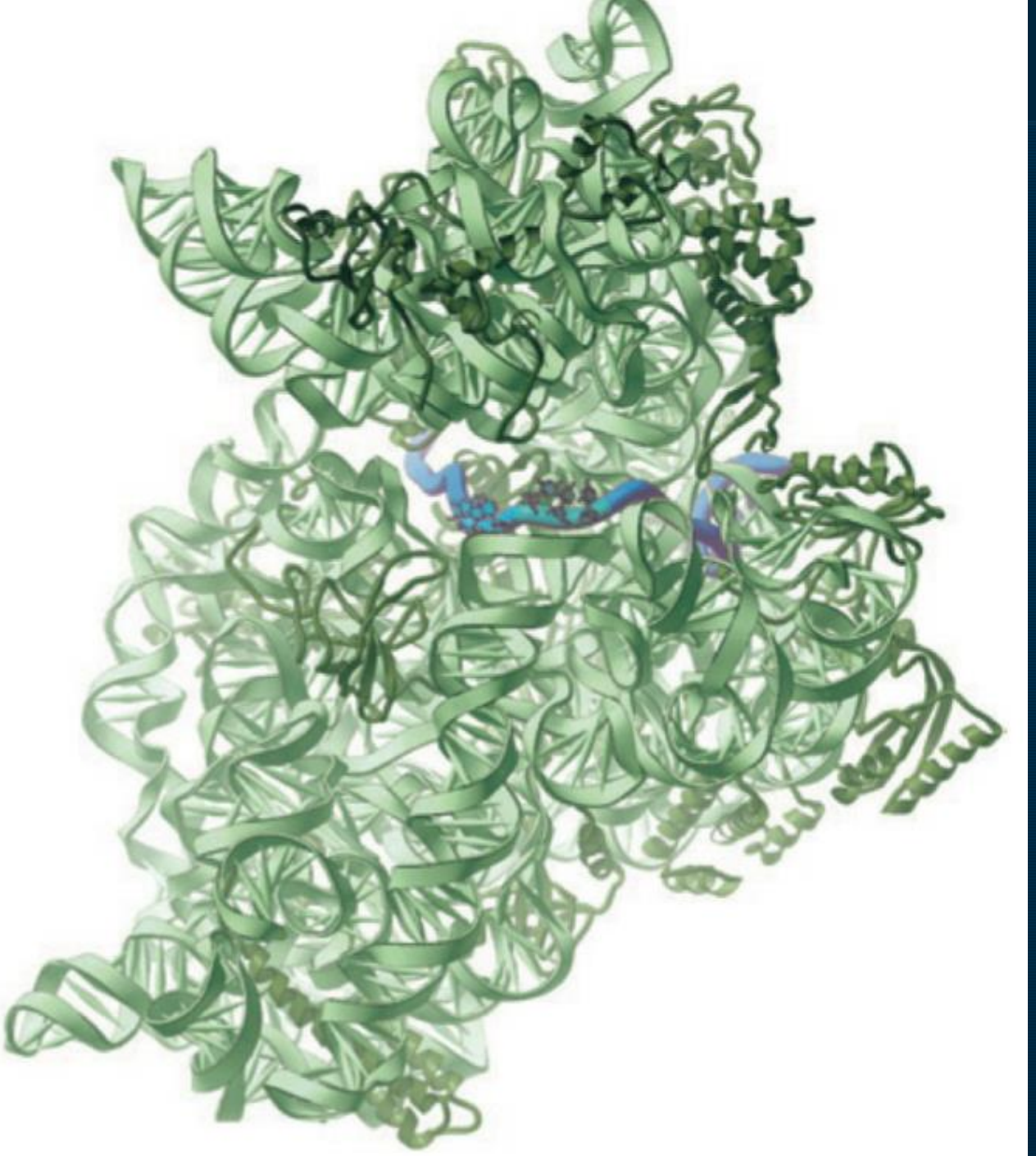
Constituem uma maquinaria complexa, formada por mais de 50 proteínas diferentes e pelos RNA ribossomais (rRNA).


70S
MW 2.500.000
50S
30S
MW 1.600.000
MW 900.000
rRNA 5S
120
nucleotídeos
rRNA 23S
2.900
nucleotídeos
rRNA 16S
1.540
nucleotídeos
34 proteínas
21 proteínas
RIBOSSOMO PROCARIÓTICO

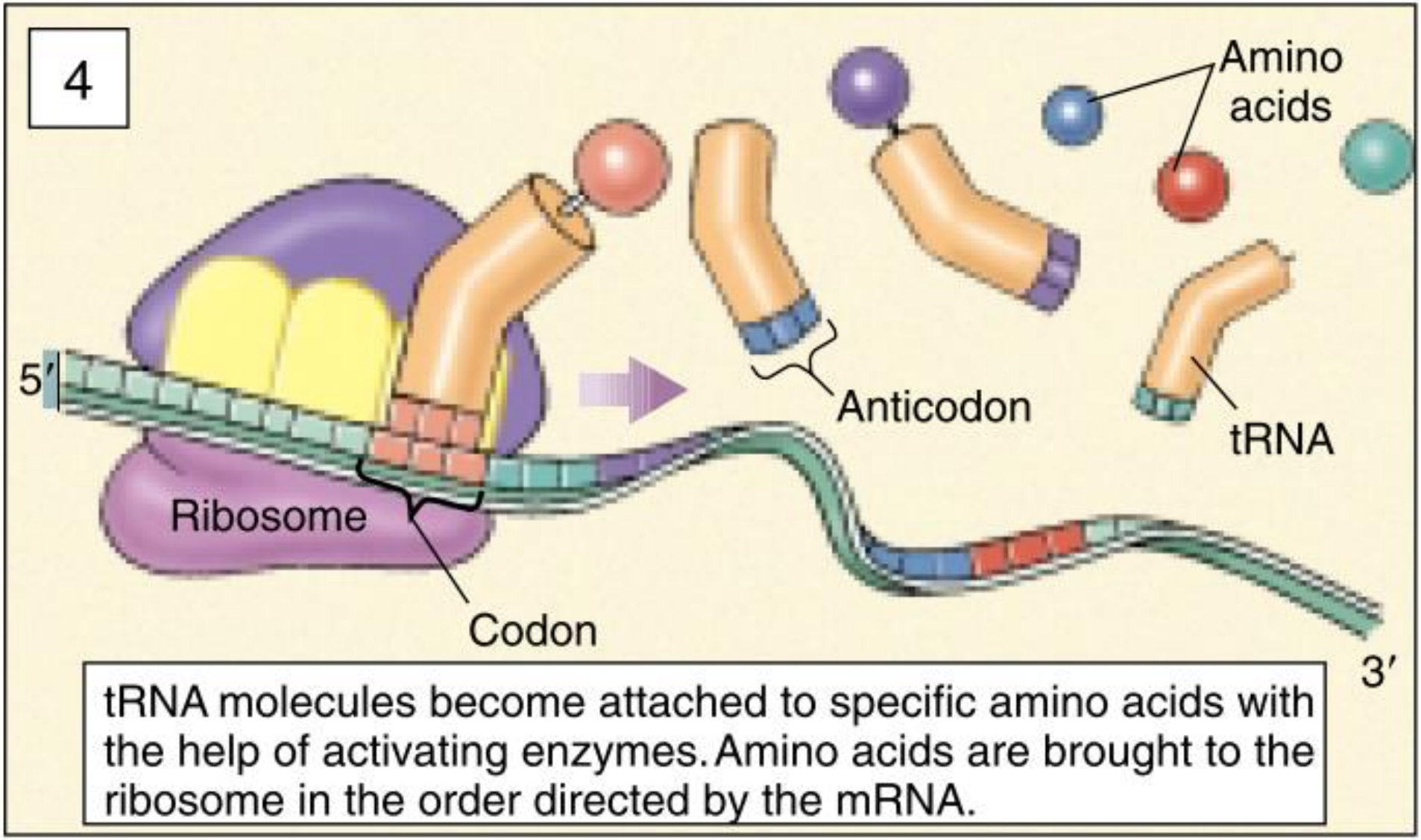

80S
MW 4.200.000
60S
40S
MW 2.800.000
MW 1.400.000
rRNA 5S
120
nucleotídeos
rRNA 28S
4.700
nucleotídeos
rRNA 5,8S
160
nucleotídeos
rRNA 18S
1.900
nucleotídeos
~49 proteínas
~33 proteínas
RIBOSSOMO EUCARIÓTICO



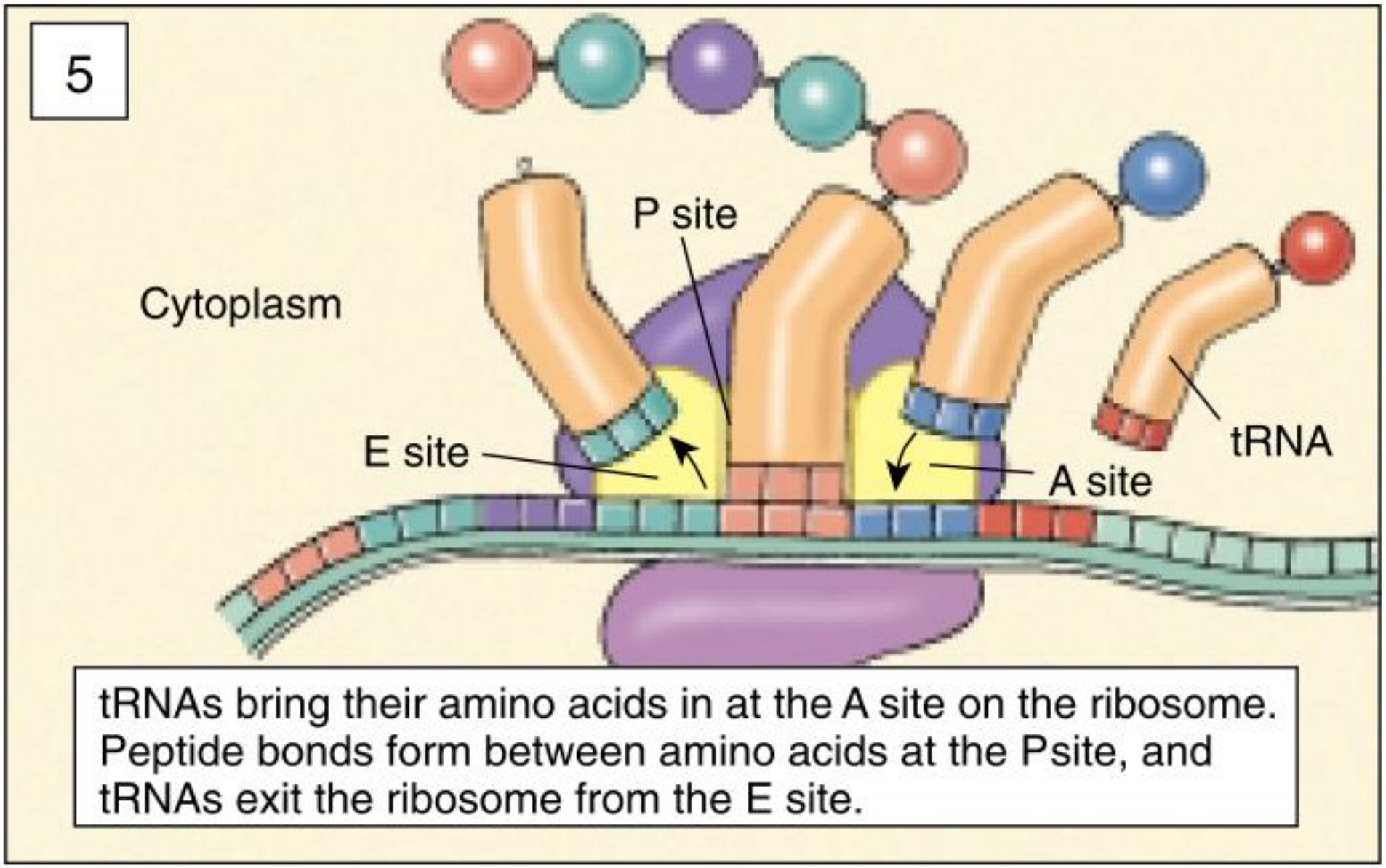

Sítio E
Sítio P
Sítio A
Subunidade ribossomal grande
E
P
A
Subunidade ribossomal pequena
Sítio de ligação ao mRNA
(D)



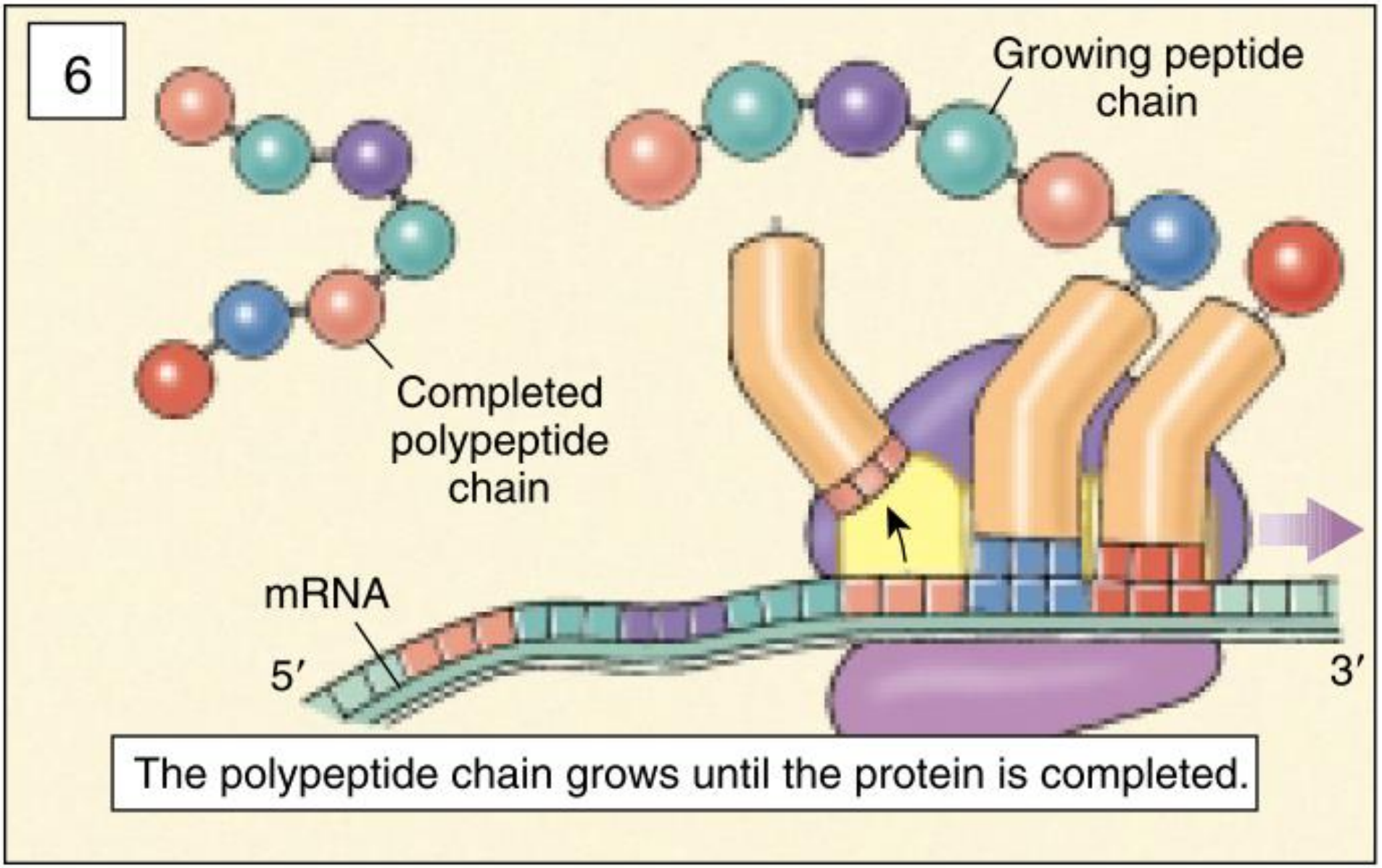
Tradução


4
Amino acids
5′
Anticodon
tRNA
Ribosome
Codon
3′
tRNA molecules become attached to specific amino acids with the help of activating enzymes. Amino acids are brought to the ribosome in the order directed by the mRNA.

Tradução

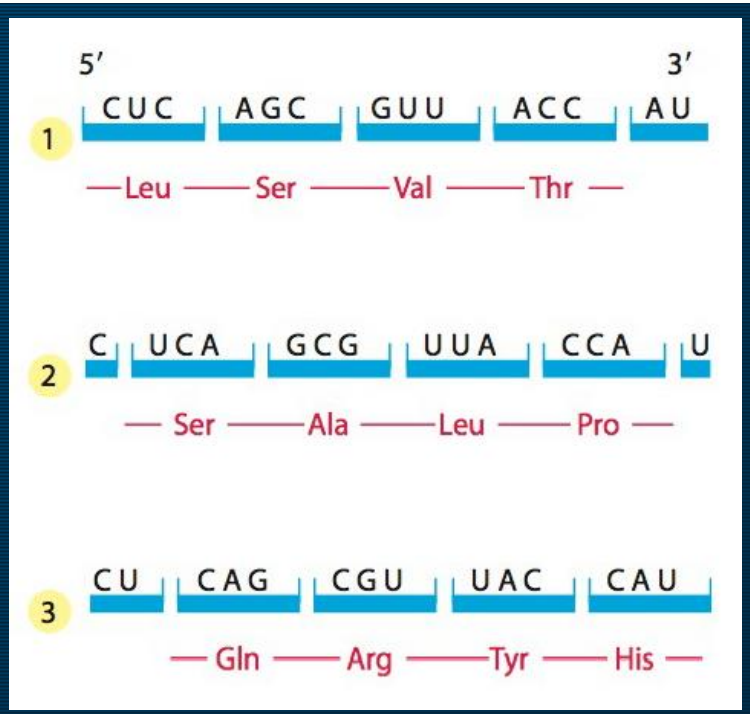

5
P site
Cytoplasm
E site
A site
tRNA
tRNAs bring their amino acids in at the A site on the ribosome. Peptide bonds form between amino acids at the Psite, and tRNAs exit the ribosome from the E site.

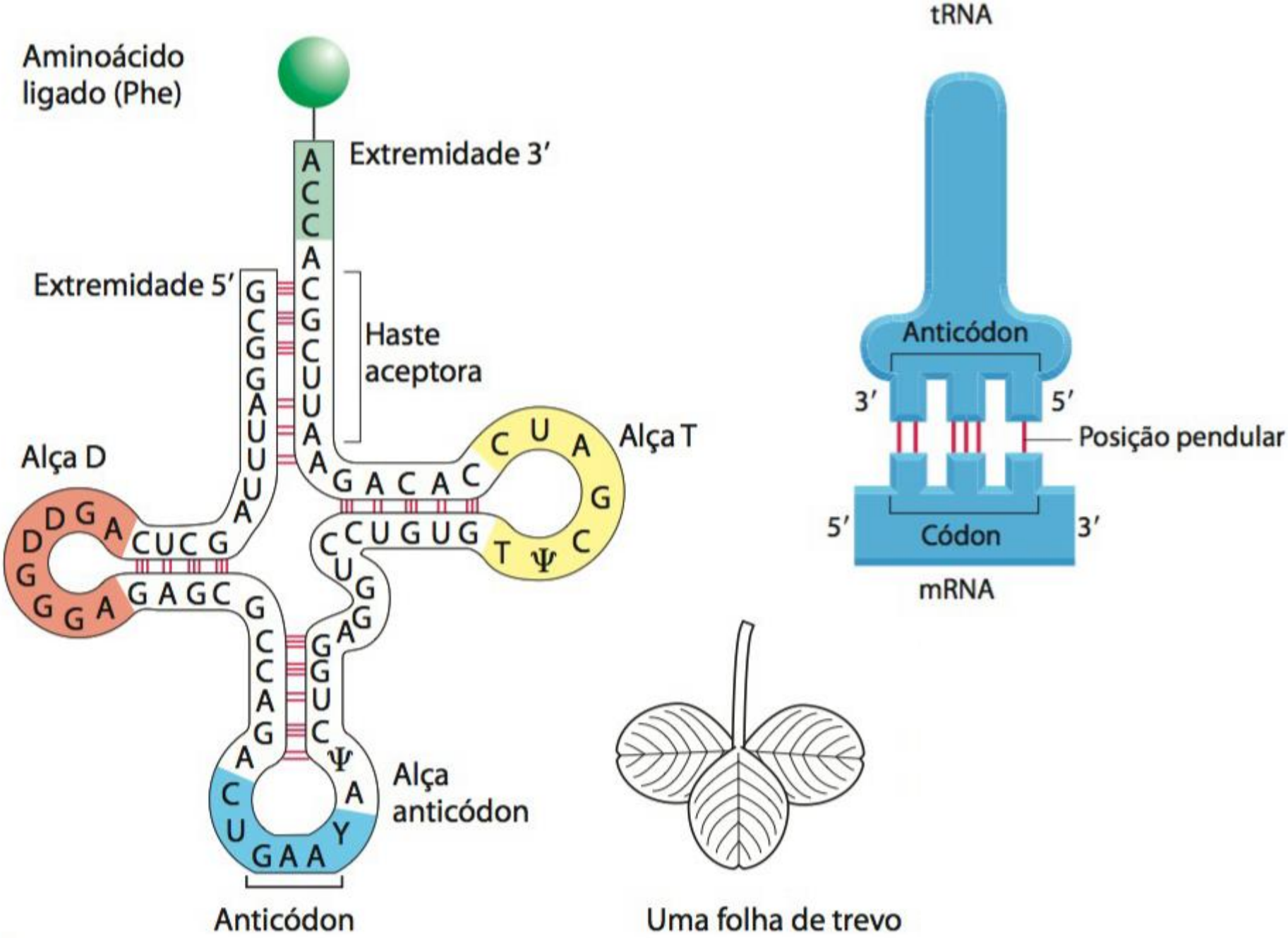
Tradução

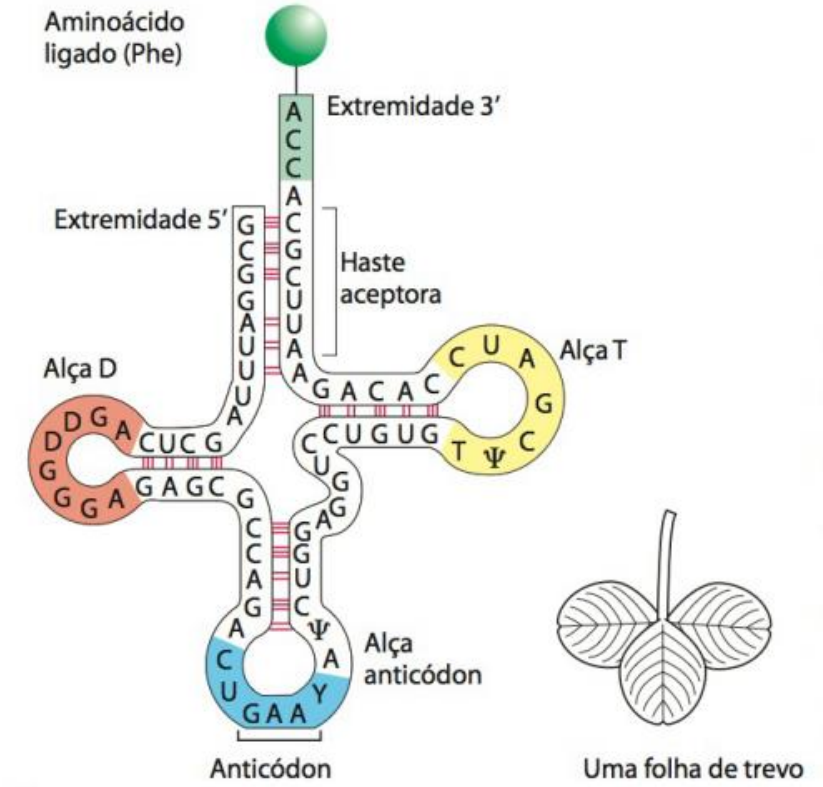

6
Growing peptide chain
Completed polypeptide chain
mRNA
5′
3′
The polypeptide chain grows until the protein is completed.

O código genético

GCA GCC GCG GCU	AGA AGG CGA CGC CGG CGU	GAC GAU	AAC AAU	UGC UGU	GAA GAG	CAA CAG	GGA GGC GGG GGU	CAC CAU	AUA AUC AUU	UUA UUG CUA CUC CUG CUU	AAA AAG	AUG	UUC UUU	CCA CCC CCG CCU	AGC AGU UCA UCC UCG UCU	ACA ACC ACG ACU	UGG	UAC UAU	GUA GUC GUG GUU	UAA UAG UGA
Ala	Arg	Asp	Asn	Cys	Glu	Gln	Gly	His	Ile	Leu	Lys	Met	Phe	Pro	Ser	Thr	Trp	Tyr	Val	Término
A	R	D	N	C	E	Q	G	H	I	L	K	M	F	P	S	T	W	Y	V	

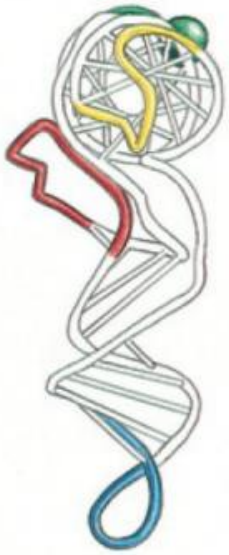



Aminoácido ligado (Phe)
Extremidade 3′
Extremidade 5′
Haste aceptora
Alça D
Alça T
Alça anticódon
Anticódon
tRNA
Anticódon
3′
5′
Posição pendular
5′
Códon
3′
mRNA
Uma folha de trevo

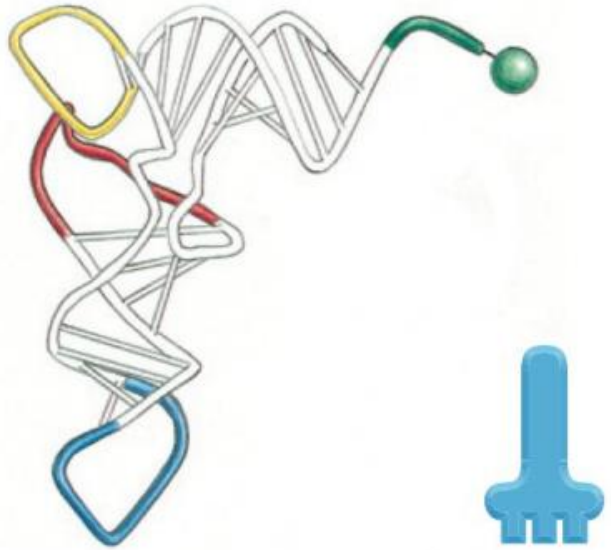


(A)

Uma folha de trevo



(B)



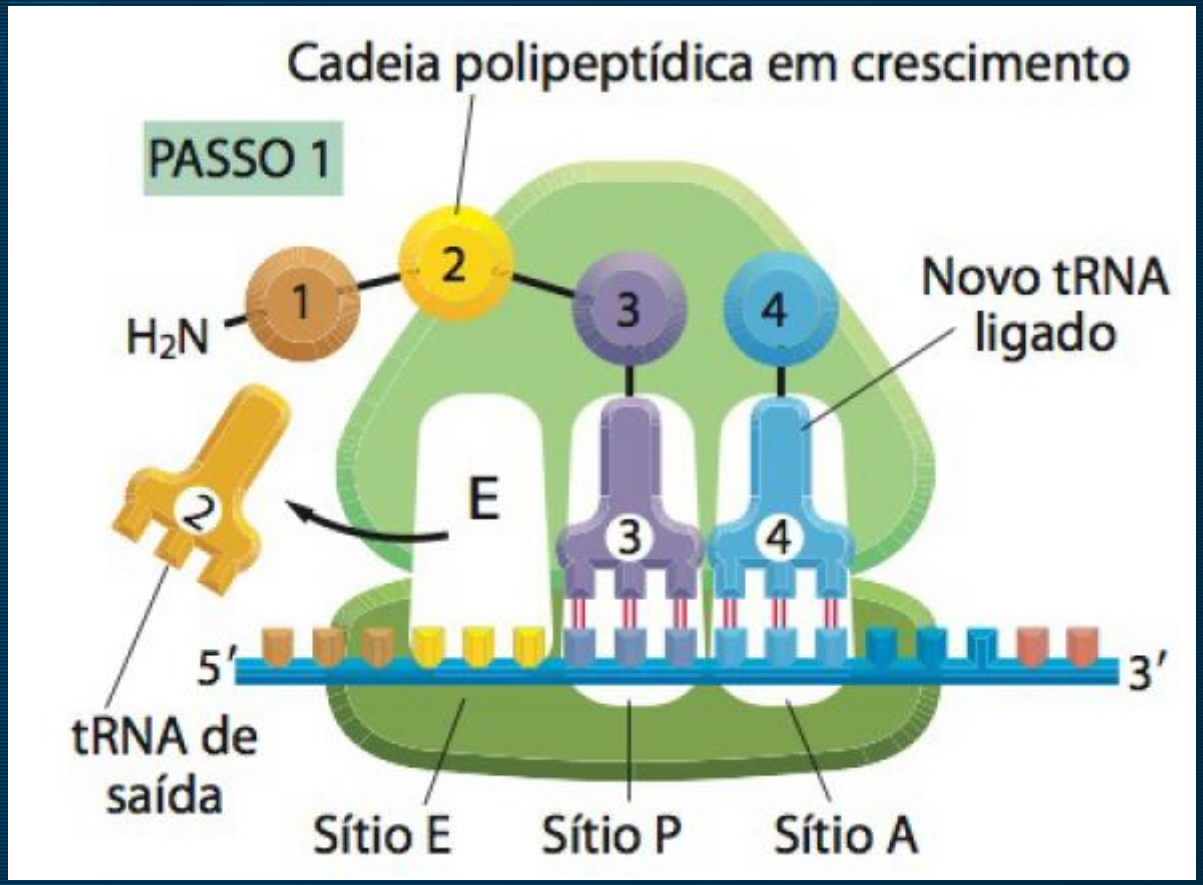
(C)

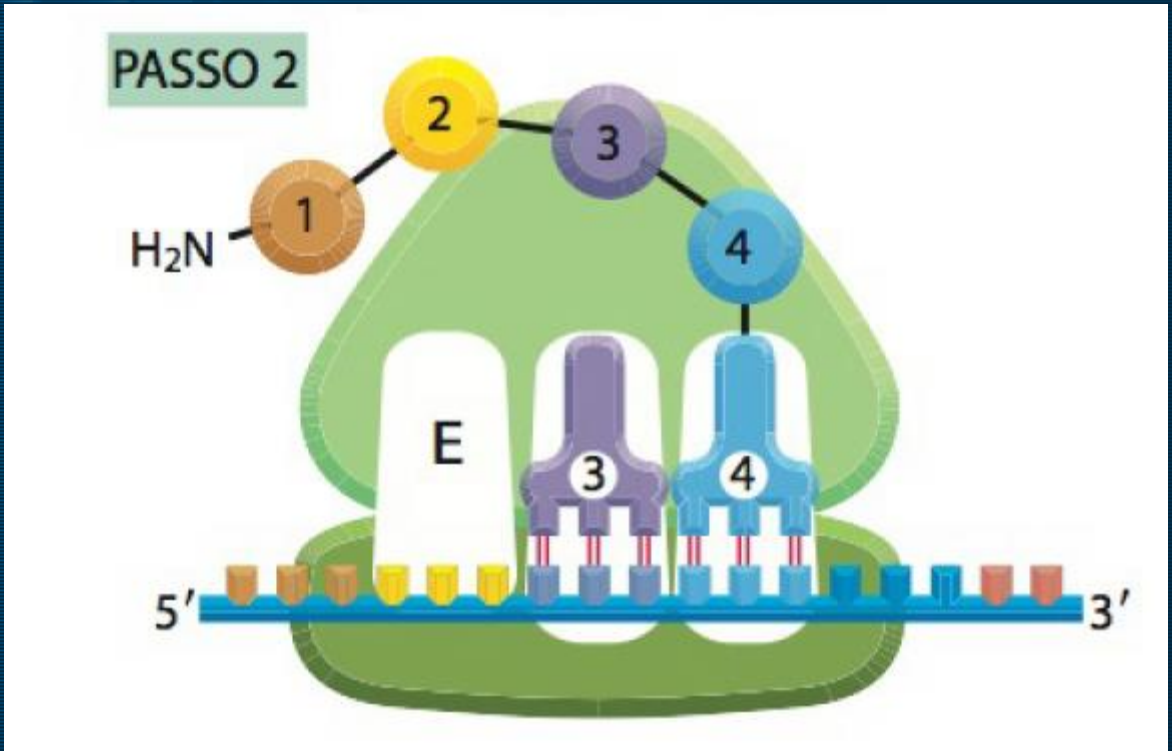
(E)

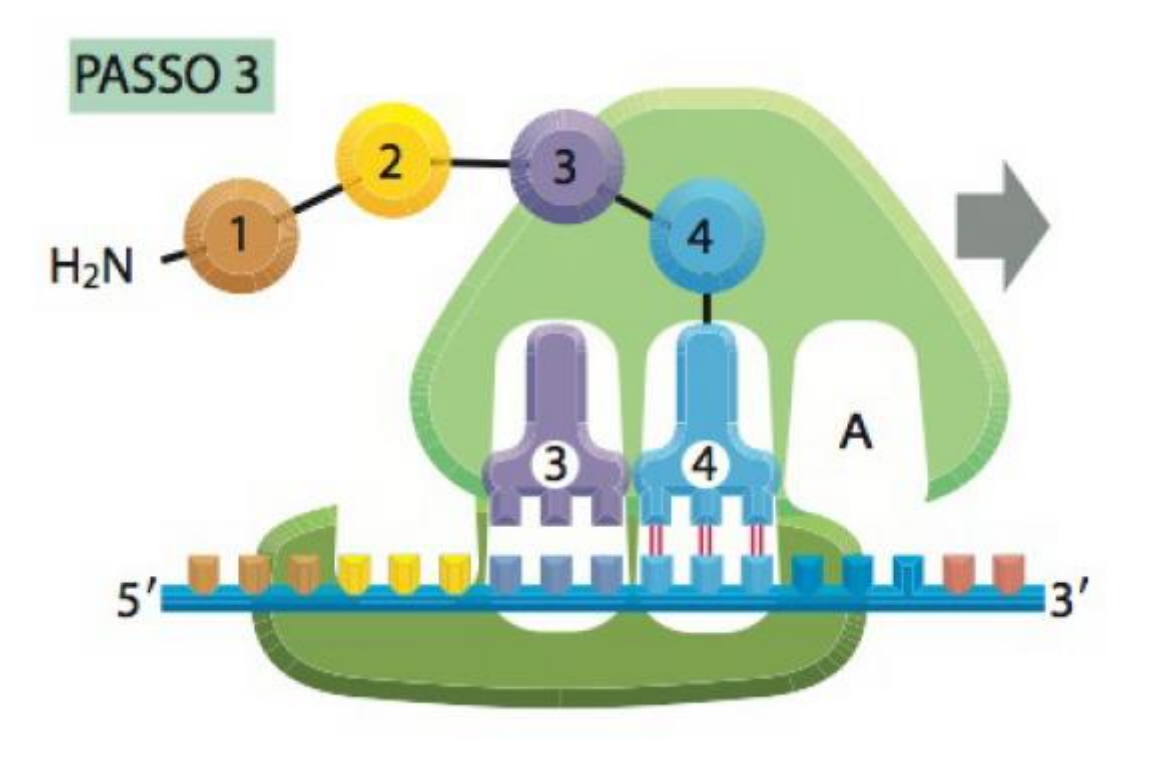
5′ GCGGAUUUAGCUCAGDDGGGAGAGCGCCAGACUGAAYAΨCUGGAGGUCCUGUGTΨCGAUCCACAGAAUUCGCACCA 3′

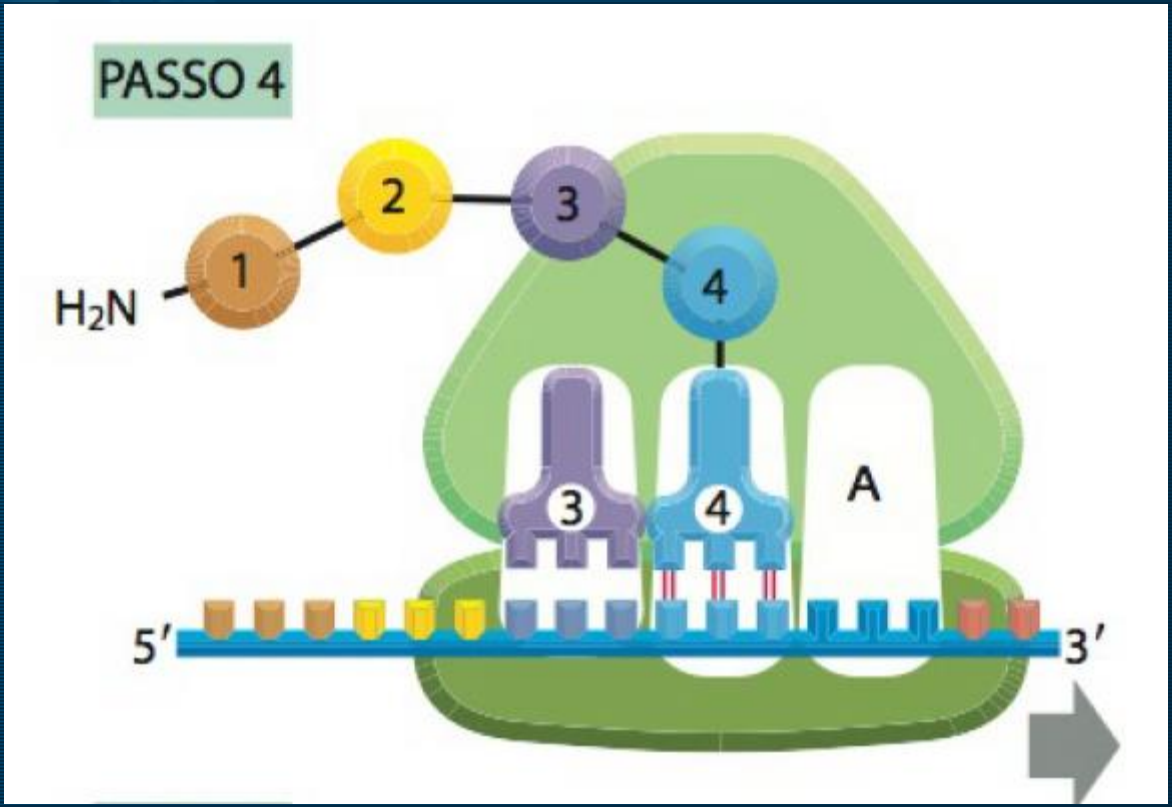
(D)

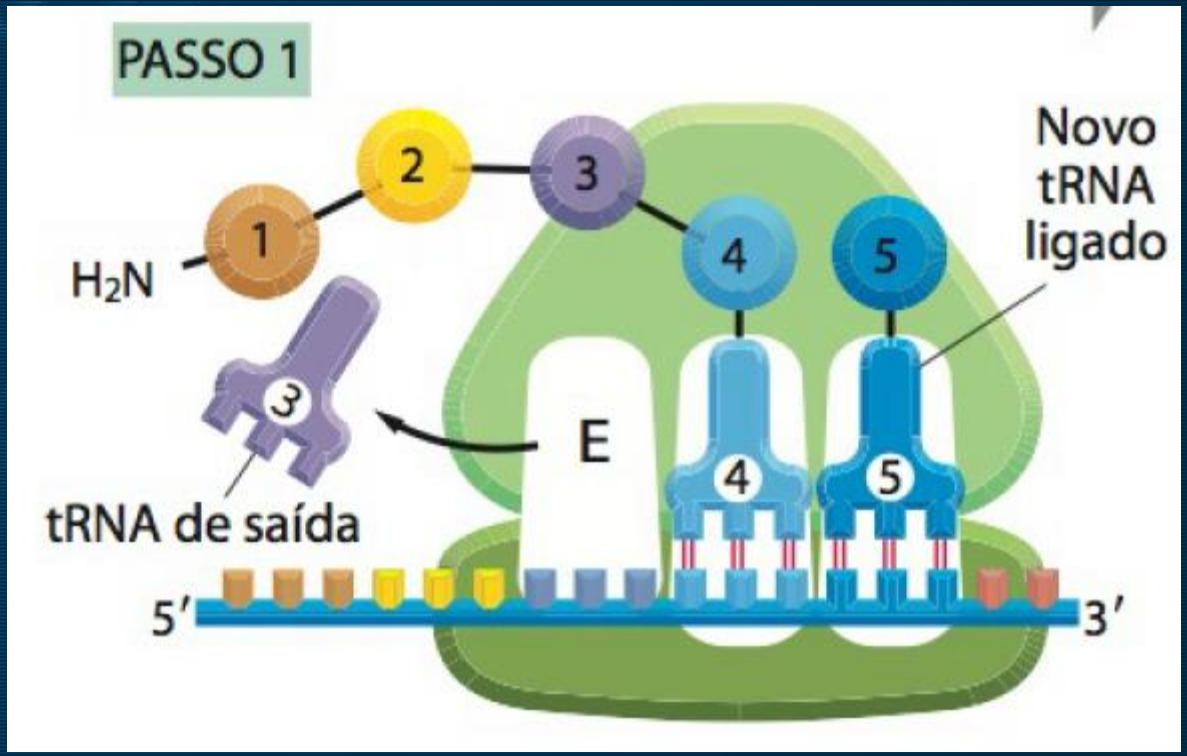
anticódon


Cadeia polipeptídica em crescimento
PASSO 1
1
2
3
4
H2N
Novo tRNA ligado
2
E
3
4
5′
3′
tRNA de saída
Sítio E
Sítio P
Sítio A


PASSO 2
2
3
1
H_2N
4
E
3
4
5′
3′


PASSO 3
2
3
1
4
H_2N
3
4
A
5′
3′


PASSO 4
2
3
1
4
H_2N
3
4
A
5′
3′


PASSO 1
Novo
tRNA
ligado
2
3
1
4
5
H2N
3
E
4
5
tRNA de saída
5′
3′

O ribossomo catalisa a ligação peptídica

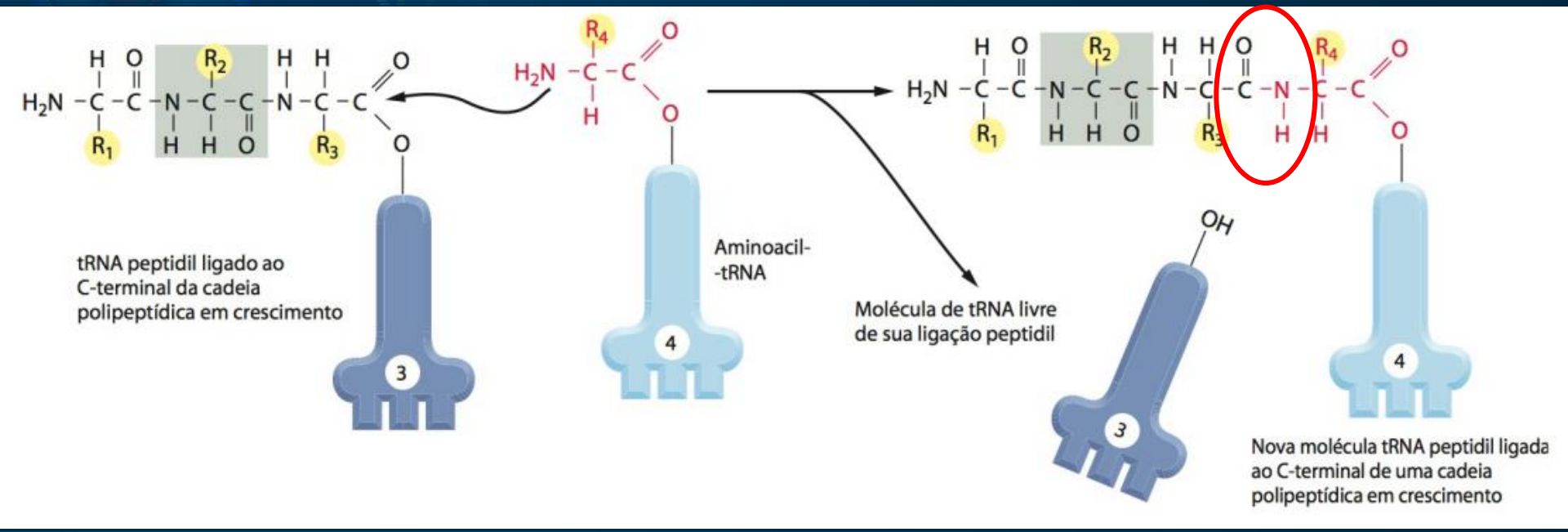
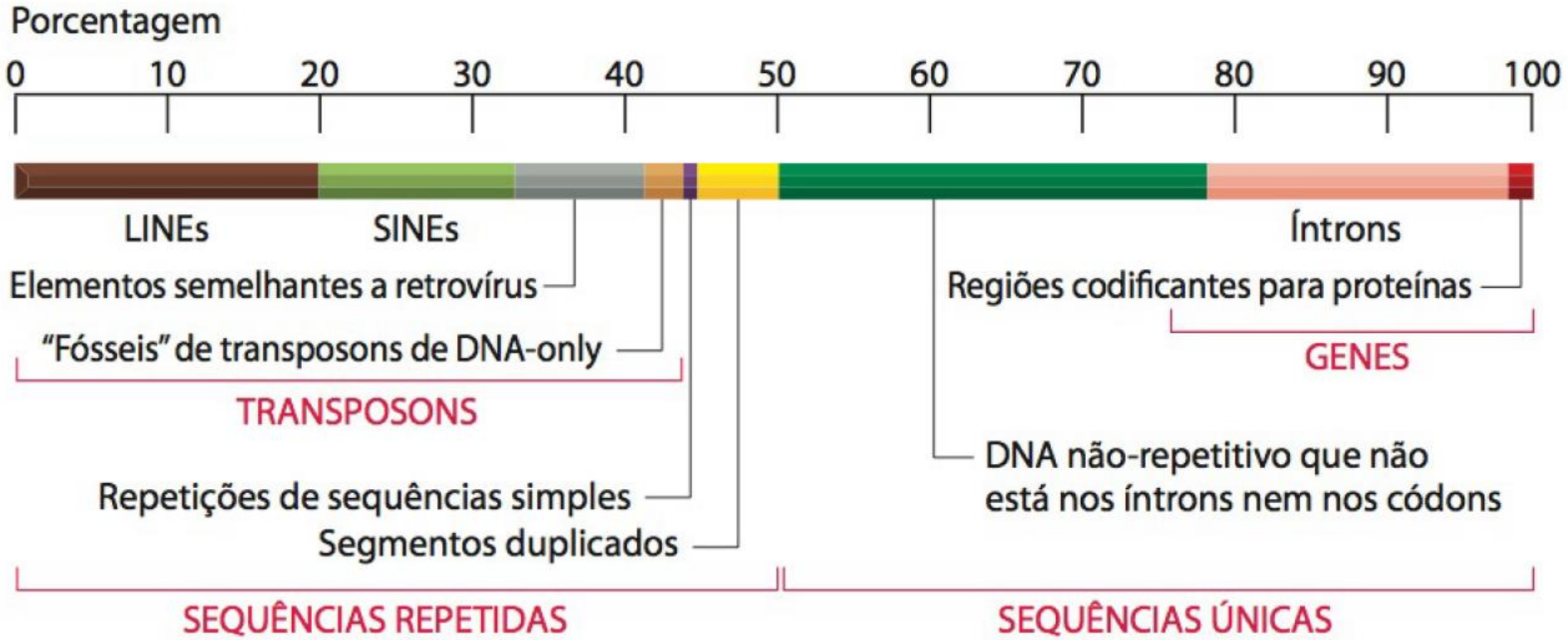


Tabela 4-1 Algumas estatísticas vitais do genoma humano

	Genoma humano
Comprimento do DNA	$3{,}2 \times 10^9$ pares de nucleotídeos*
Número de genes	Aproximadamente 25 mil
Maior gene	$2{,}4 \times 10^6$ pares de nucleotídeos
Tamanho médio dos genes	27 mil pares de nucleotídeos
Menor número de éxons por gene	1
Maior número de éxons por gene	178
Número médio de éxons por gene	10,4
Tamanho do maior éxon	17.106 pares de nucleotídeos
Tamanho médio dos éxons	145 pares de nucleotídeos
Número de pseudogenes**	Mais de 20 mil
Porcentagem de sequências de DNA nos éxons (sequências codificantes de proteínas)	1,5%
Porcentagem de DNA em outras sequências altamente conservadas***	3,5%
Porcentagem de DNA nos elementos repetitivos com várias cópias	Aproximadamente 50%


Porcentagem
0
10
20
30
40
50
60
70
80
90
100
LINEs
SINEs
Elementos semelhantes a retrovírus
"Fósseis" de transposons de DNA-only
TRANSPOSONS
Repetições de sequências simples
Segmentos duplicados
SEQUÊNCIAS REPETIDAS
Íntrons
Regiões codificantes para proteínas
GENES
DNA não-repetitivo que não está nos íntrons nem nos códons
SEQUÊNCIAS ÚNICAS