Biomedical Science

Molecular Genetics

BMS 23110A | Fall 2026-2027

Protein Structure and Function

DNA Transcription

جميع الأوراق والمحتويات التابعة للمنصة محمية بموجب حقوق الملكية الفكرية.
يُمنع منعاً باتاً نسخ، أو نشر، أو مشاركة أي محتوى أو مستندات تخص المنصة بأي شكل دون إذن مسبق. ويُعد أي تجاوز أو مخالفة لهذا القرار خرقاً قانونياً يعرض مرتكبه للمساءلة والملاحقة القانونية الفورية

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HOW DOES THE INFORMATION FLOW IN THE CELL?

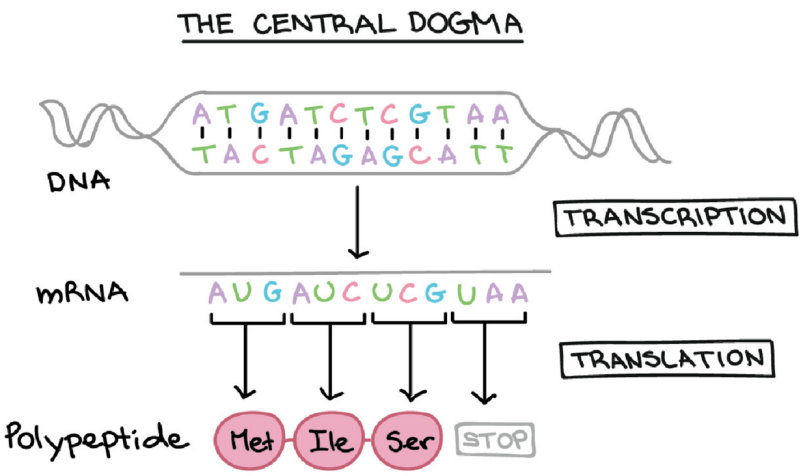
Central Dogma & Transcription

01

DNA · RNA · Protein · Transcription · Translation

THE CENTRAL DOGMA

DNA → RNA → Protein



DNA → mRNA (transcription) → polypeptide (translation)

What Is Transcription?

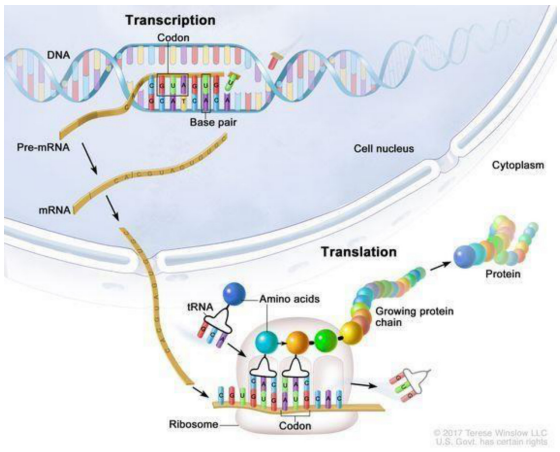
DEFINITION

Transcription

The process where information stored in DNA is **copied into RNA,** thereby making it available for either **protein synthesis** or other cellular functions.

Protein synthesis

Other cellular functions



Transcription in the nucleus; translation at the ribosome

Main Components of Transcription

The gene
to be transcribed

The mRNA
resulting from transcription

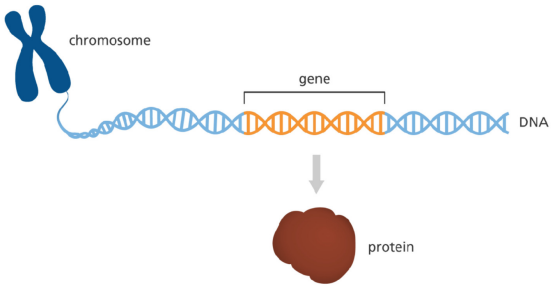
The machinery
enzymes involved in transcription

What Is the Gene?

Gene
A **sequence of DNA** that can be transcribed.

OTHER DEFINITIONS

- Others define the gene as the **unit of hereditary**.
- Others define it as the sequence of DNA that provides the **information to produce a protein.**

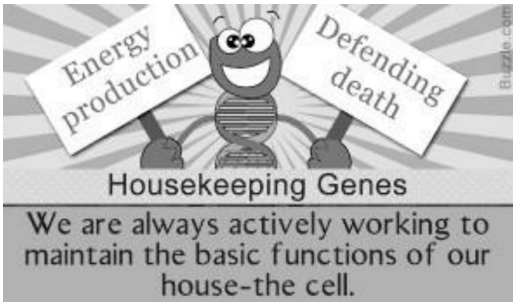


Chromosome → DNA → gene → protein

When Is a Gene Called a Housekeeping Gene?

Housekeeping gene

When it encodes proteins or RNA molecules that are **essential for the normal activities** of all living cells.



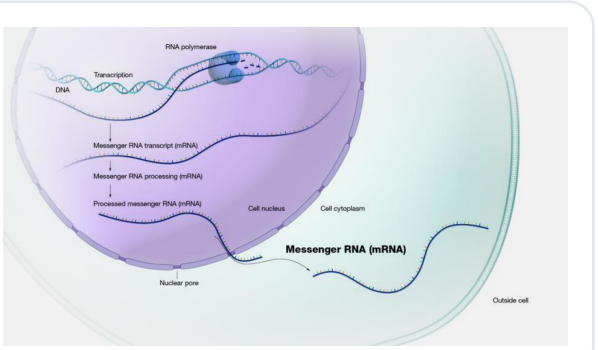
01 THE BASICS

What Is mRNA?

Complementary copy
One type of RNA that is transcribed **complementary to a segment** of one of the strands of DNA.

Small and unstable
It represents a **small percentage** of the total cellular RNA, but it is an **unstable form** that degrades directly after translation.

More stable in eukaryotes
However, mRNA in **eukaryotes** is **more stable** than mRNA in prokaryotes.



Eukaryotic Cell vs Prokaryotic Cell

Eukaryote
A cell that has a **true nucleus** (a nucleus surrounded by a membrane).

vs

Prokaryote
No nucleus.

WHERE EACH STEP HAPPENS

	Eukaryotes	Prokaryotes
Transcription	Inside the nucleus (DNA → mRNA)	In the cytoplasm
Translation	In the cytoplasm (mRNA → protein)	In the cytoplasm

How Does This Affect Transcription?

Eukaryotes
nucleus → cytoplasm

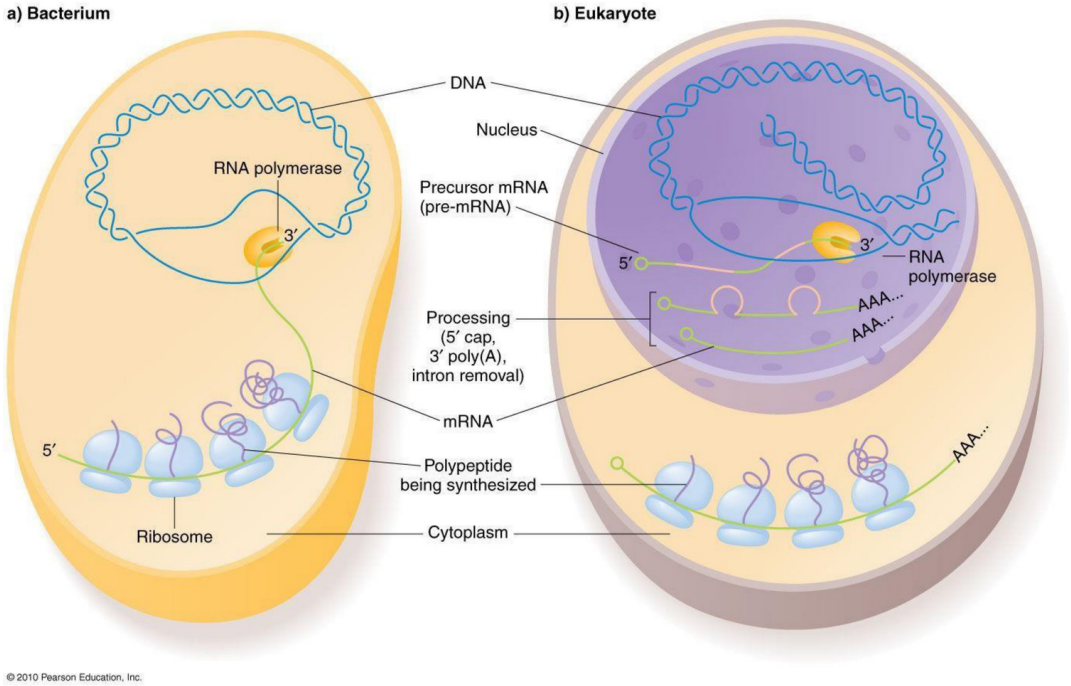
The DNA is inside the nucleus, and transcription (DNA→mRNA) happens **inside the nucleus**; then the mRNA should leave to the cytoplasm, where translation (mRNA→protein) takes place.

That's why the mRNA undergoes some **post-transcription modifications** to protect it during this journey.

Prokaryotes
cytoplasm only

Both transcription and translation occur **in the cytoplasm.**

The mRNA doesn't go through post-transcriptional modifications and is **less stable** than mRNA in eukaryotes.



(a) Bacterium · (b) Eukaryote

02 RNA POLYMERASE

WHAT ARE THE ENZYMES INVOLVED IN TRANSCRIPTION?

RNA Polymerase

02

DNA-directed RNA synthesis | Transcription complex | Core enzyme | Sigma σ | Holoenzyme

DEFINITION

RNA polymerase

The enzyme that catalyzes the **DNA-directed RNA synthesis** (making of RNA from DNA), or transcription.

Part of a complex

RNA polymerase works as a part of the **transcription complex.**

Eukaryotes vs prokaryotes

The function and characters of RNA polymerases in eukaryotes are **similar** to prokaryotes, but they are **more complex.** So we start with prokaryote RNA polymerase and transcription in prokaryotes.

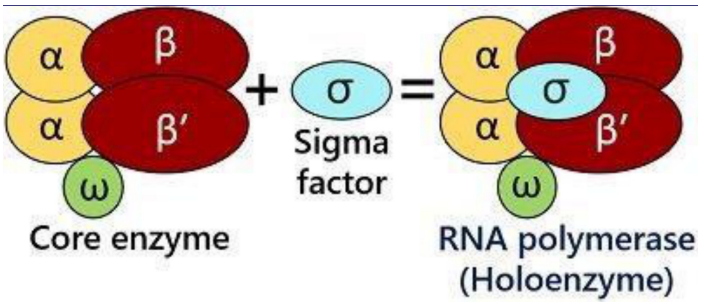
RNA Polymerase from *E. coli*

Core RNA polymerase is isolated from *E. coli* cells as a **multimeric protein** (formed from multiple units) with **four** different types of subunits:

- alpha α × 2 copies
- beta β
- beta prime β′
- omega ω

THE FIFTH UNIT — SIGMA Σ

Not part of the core enzyme. When sigma σ binds to the core enzyme, the enzyme becomes a **holoenzyme.**



Core enzyme + sigma factor = RNA polymerase (holoenzyme)

02 RNA POLYMERASE

What Is the Function of Each Unit?

TABLE **Subunits of *E. coli* RNA polymerase**

Subunit	No. of molecules	Function
alpha α	2	The **scaffold** (base) for assembly (collection) of the other subunits.
beta β	1	Forms the **active site** of the enzyme (active site = where the enzyme activity happens).
beta prime β′	1	Makes the active site with the previous unit, and this unit is **where the DNA strand binds.**
omega ω	1	Not well understood.
sigma σ	1 (forms the holoenzyme)	Comes and joins the core to form the holoenzyme **only at the initiation** of transcription.

Steps of Transcription

Initiation
Assembly of the transcription complex at the promotor

→

Elongation
More nucleotides added to the growing RNA

→

Termination
End of transcription at termination sequences

STEP 1 OF TRANSCRIPTION

Initiation & Promotors

03

Transcription complex | Promotor | Operon | lac operon

How it starts

Initiation starts by the **assembly of a transcription complex** in the initiation site.

Where does this happen?

In the **promotors**: the regions of DNA where the transcription initiates.

How Many Promotors Are There in the DNA?

Eukaryotes

Each gene has **its own promotor.**

vs

Prokaryotes

More than one gene can have the **same promotor.**

The transcription of these genes starts at the same time and they are transcribed together — usually because these genes produce proteins that act together for the same function.

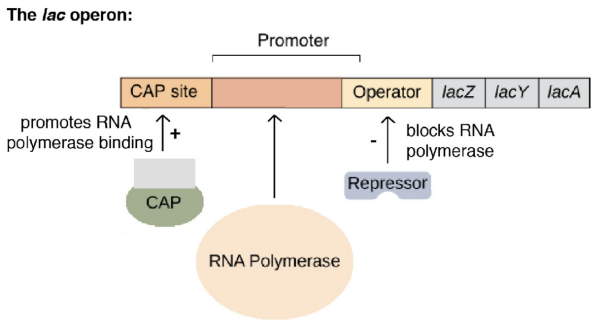
DEFINITION · ONLY IN PROKARYOTES

Operon

When more than one gene have one promotor and are transcribed together, this unit is called an **operon.** This is only found in prokaryotes.

EXAMPLE — THE LAC OPERON

The enzymes needed to **metabolize lactose** in *E. coli* are found beside each other and act under **one promotor effect.** This is called the **lac operon**.

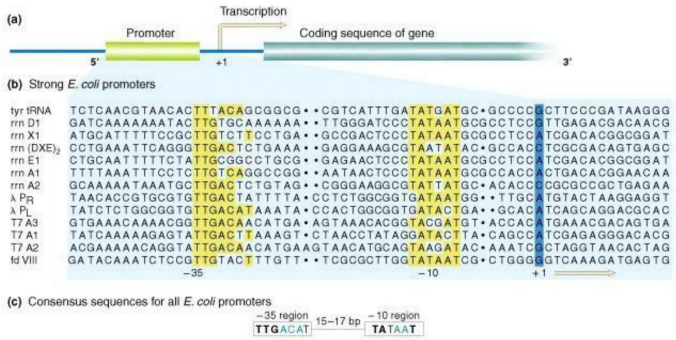


The lac operon: CAP site, promoter, operator, lacZ, lacY, lacA

Characteristics of Promotors

Consensus sequences

Analysis of the promotor sequence revealed **similarities in the DNA sequences** in these regions. The patterns of similarities between promotors are called **consensus sequences.**



Strong E. coli promoters and their consensus sequences

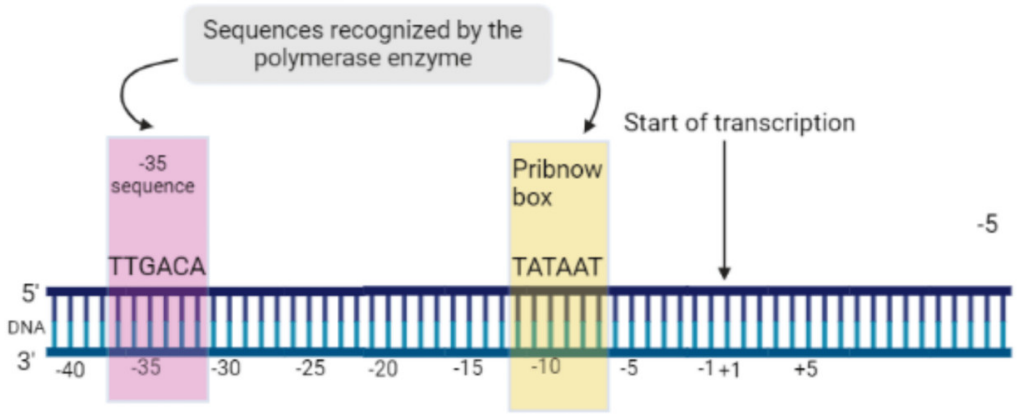
CONSENSUS SEQUENCES IN THE *E. COLI* PROMOTOR

"−10 region" — Pribnow box

A common sequence **10 bases before** the initiation site, with the sequence **[5′-TATAAT-3′].**

"−35 region"

Another consensus sequence, around **35 bases before** the start site.



Sequences recognized by the polymerase enzyme: the −35 sequence and the Pribnow box, upstream of the start of transcription

IN EUKARYOTES

There are similar sequences in the promotors, and the **"TATA box"** is one example of these.

03 INITIATION

Promotor Strength

RECOGNITION

These sequences are recognized easily by the **sigma σ unit** of the RNA polymerase in *E. coli*.

Strong promotors

Found in genes that need to be transcribed at a **high rate** : the sequences of the −10 and −35 regions are **very similar** to the consensus sequences.

vs

Weak promotors

Have **lower similarities** in these regions; found in genes that are **transcribed less frequently.**

Initiation — Step by Step

INITIATION IS A SLOW PROCESS

The RNA polymerase **holoenzyme searches** for the promotor and binds to it.

↓

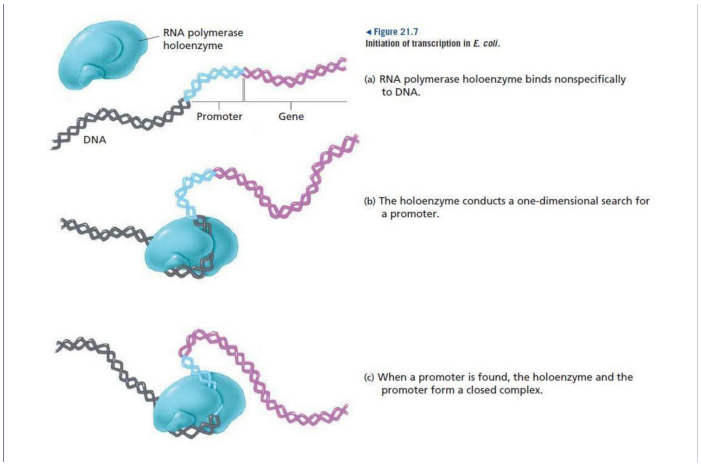
Unwinding of the DNA double helix starts (separating the two strands).

↓

A **transcription bubble** forms.

↓

One of the strands, the **template strand,** is located at the polymerization site of the enzyme.



Initiation in E. coli: the holoenzyme binds DNA, searches for a promoter, then forms a closed complex

03 INITIATION

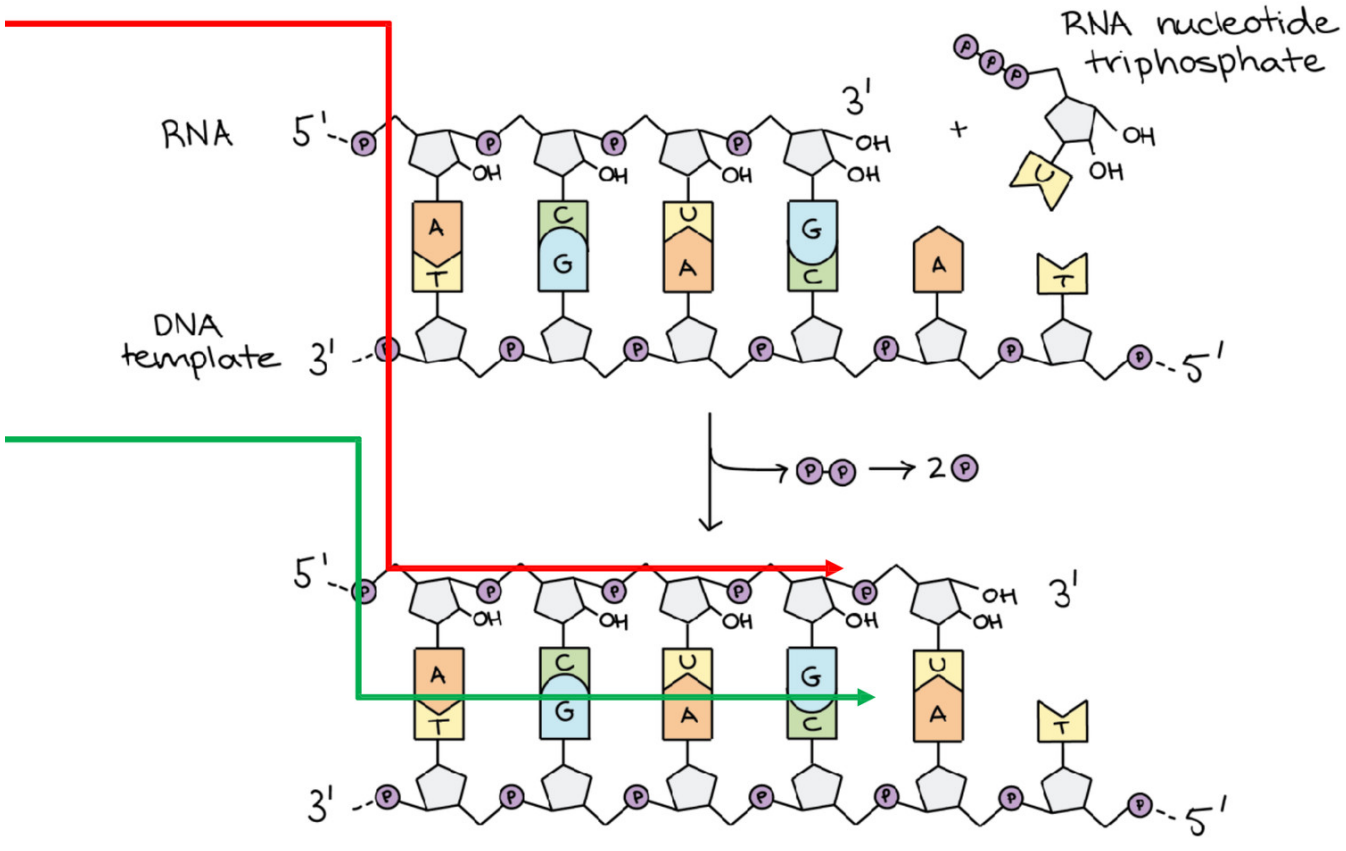
The First Phosphodiester Linkage

Ribonucleoside triphosphates

UTP, GTP, CTP or ATP arrive into the **active site** and form **hydrogen bonds** with the nucleotides of the template strand.

The linkage

A **phosphodiester linkage** forms between two of these ribonucleoside triphosphates.



RNA nucleotide triphosphates joining the growing RNA on the DNA template

04 ELONGATION

STEP 2 OF TRANSCRIPTION

Elongation

04

Polymerization | RNA–DNA helix | ~10 nucleotides | Promoter clearance | NusA

DEFINITION

Elongation

A **polymerization reaction** in which more nucleotides are added to the growing RNA in the newly forming RNA–DNA helix.

RNA about 10 nucleotides long

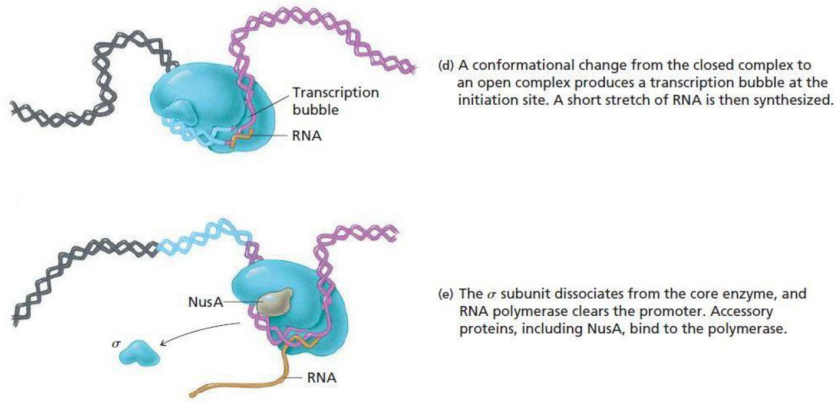
The RNA polymerase holoenzyme undergoes a **transition** from the initiation to the elongation mode.

Promoter clearance

The transcription complex moves away from the promoter along the DNA template. This step is called promoter clearance.

Helper proteins

Some proteins are needed to help the RNA polymerase from the initiation to the elongation form. **NusA** is one of these proteins.



(d) The closed complex becomes an open complex with a transcription bubble · (e) The σ subunit dissociates; accessory proteins, including NusA, bind to the polymerase

05 TERMINATION

STEP 3 OF TRANSCRIPTION — END OF TRANSCRIPTION

Termination

05

Termination sequences | Rho-dependent | Rho-independent | Pause sites | Hairpin

Transcription complexes **assemble at promoters** and, in bacteria, they **disassemble at the end of genes** at specific sequences called **termination sequences.**

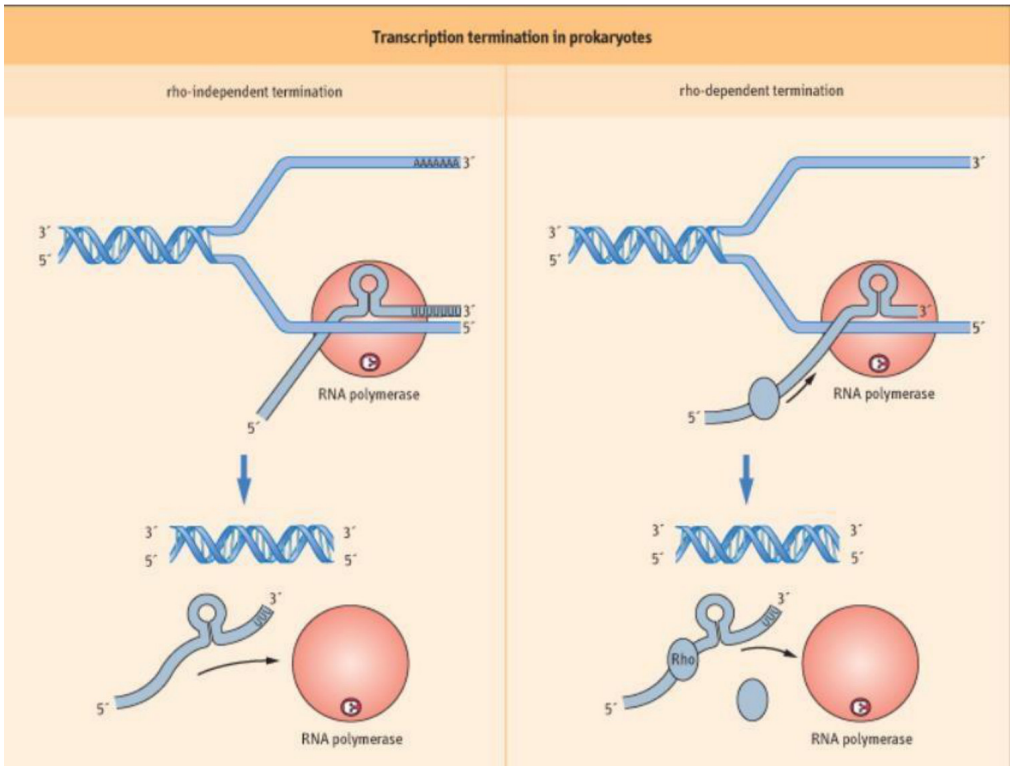
IN PROKARYOTES, THERE ARE TWO TYPES OF TERMINATION SEQUENCES

Rho-dependent termination

Sequences that need the help of a protein called **"rho"** to help in the transcription termination.

Rho-independent termination

Sequences that cause **instability in the elongation complex,** so they simply stop the process without the need of a protein.



Transcription termination in prokaryotes

05 TERMINATION

Pause Sites

Before termination

The growing RNA strand reaches **pause sites.**

WHY DOES THE ELONGATION COMPLEX PAUSE HERE?

These are regions **rich in G/C**: it is difficult to break the hydrogen bonds between these bases, so the elongation complex **slows down or even stops** at these regions.

G/C
3 hydrogen bonds bind G/C

A/T
2 hydrogen bonds bind A/T

What Is a Palindrome?

Pausing usually happens in regions that are **palindromic.**

DEFINITION

Palindrome

Can be read **from right to left and from left to right** similarly.

13677631
palindromic number

kayak
palindromic word

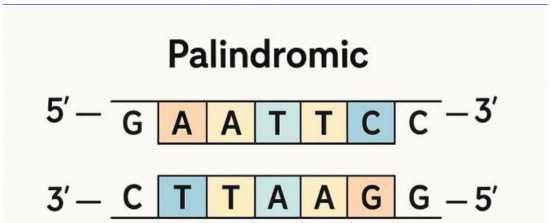
Hannah
palindromic word

05 TERMINATION

Palindromic DNA Sequences

The **5′ to 3′ sequence on one strand** must be the same as the 5′ to 3′ sequence on the other strand's **reverse complement.**

- Top strand (5′ to 3′): **GAATTC**
- Bottom strand (complement + reverse): **GAATTC**
- Palindromic — a **mirror image** in the 5′ to 3′ direction on both strands.



Effect of a Palindromic DNA Sequence on Transcription

Pausing is **exaggerated** at sites where the DNA sequence is palindromic.

↓

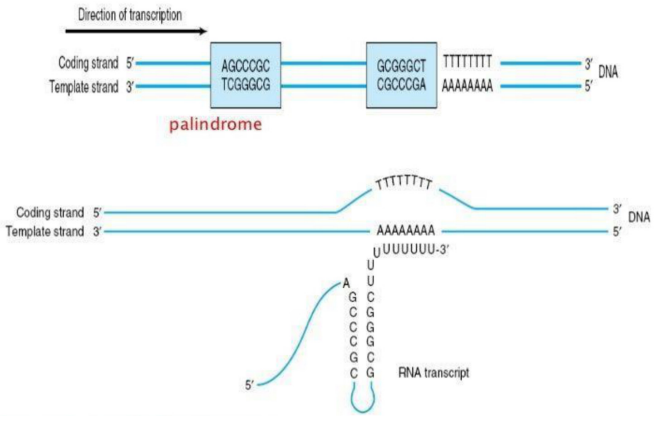
When the DNA is transcribed, the newly synthesized mRNA can form a **hairpin** at these sites.

↓

Formation of an RNA hairpin may **destabilize the RNA–DNA hybrid** in the elongation complex.

↓

This partial disruption of the transcription bubble probably causes the transcription complex to **cease elongation.**



A palindrome in the DNA and the RNA transcript

THE CHAIN OF EVENTS

Palindromic site → **RNA hairpin** → **RNA–DNA hybrid destabilized** → **Elongation ceases**

06 EUKARYOTES

SIMILAR TO PROKARYOTES, BUT MORE COMPLEX AND HIGHLY REGULATED

Transcription in Eukaryotes

06

Chromatin | 3 RNA polymerases | Transcription factors | Gene organization | Post-transcriptional modifications

Transcription in eukaryotes is generally similar to that in prokaryotes, but **more complex and highly regulated.** There are **five main differences** between eukaryotes and prokaryotes in transcription.

TABLE **Eukaryotic vs prokaryotic transcription**

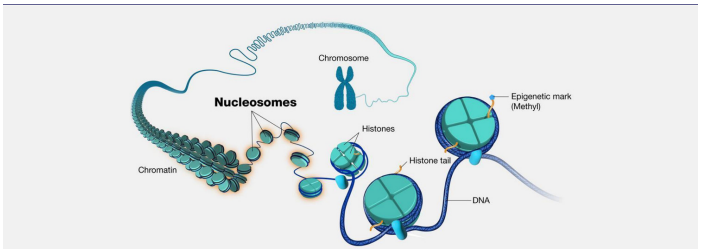
Difference	Eukaryotes	Prokaryotes
1 · Chromatin structure	DNA is packaged into chromatin, making it **less accessible** — an additional level of transcriptional control.	Absent
2 · RNA polymerases	**Three** main RNA polymerases (I, II and III).	A **single** RNA polymerase
3 · Transcription factors	Initiation requires **multiple general transcription factors** to recruit RNA polymerase to the promoter.	A **sigma factor** guides RNA polymerase to the promoter
4 · Gene organization	Each gene has **its own promoter** and is typically transcribed individually.	Genes often organized into **operons** and transcribed together as a single mRNA
5 · Post-transcriptional modifications	mRNA transcripts **undergo** post-transcriptional modifications.	Absent

1 · Chromatin Structure

Packaged DNA

In eukaryotes, DNA is packaged into **chromatin** (DNA wrapped around **histone proteins** to make nucleosomes), making it less accessible.

This adds an additional level of transcriptional control that is **absent in prokaryotes**.



Chromatin, histones and nucleosomes

2 · RNA Polymerases

Eukaryotes have **three main RNA polymerases:**

RNA polymerase I	RNA polymerase II	RNA polymerase III
Transcribes genes that encode **ribosomal RNA (rRNA).**	Transcribes genes encoding for **proteins to produce mRNA,** besides some genes encoding small non-coding RNA (snRNA).	Transcribes genes encoding **transfer RNA (tRNA)** and other small RNAs.

REMEMBER

Prokaryotes have a **single RNA polymerase.**

5 · Post-transcriptional Modifications

Remember: transcription in eukaryotes happens **inside the nucleus.**

→ The new mRNA transcript must go out to the **cytoplasm** to carry the message to **ribosomes**, where proteins are synthesized.

→ Accordingly, eukaryotic mRNA transcripts undergo **post-transcriptional modifications** — absent in prokaryotes.

07 REGULATION

TURNING TRANSCRIPTION ON OR OFF

Regulation of Transcription

07

Housekeeping genes | Regulated genes | Activators | Repressors | Cis & trans

WHAT DO WE MEAN BY REGULATION?

Regulation

The mechanisms used to **turn a biological process on or off** according to the cell/organism needs.

REGULATION IN TRANSCRIPTION

Housekeeping genes

CONSTITUTIVELY EXPRESSED

Like those involved in basic cellular functions such as **metabolism, structure, or ribosome production**.

Constitutively expressed because **every cell needs them all the time** to survive and function.

vs

Regulated genes

TURNED ON OR OFF

Their transcription is turned on or off depending on the **cell type, developmental stage, or environmental signals.**

How Regulated Genes Are Controlled

Regulatory proteins

The initiation of transcription of regulated genes is controlled by **regulatory proteins** that bind to specific DNA sequences.

Two directions

Transcriptional regulation can be **positive** or **negative.**

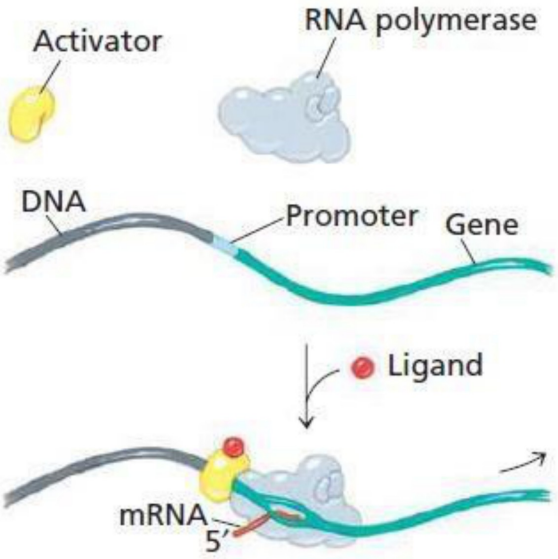
Positive Regulation — Activators

Silent or slow
Some genes are not transcribed, or transcription happens **very slowly**, until a protein called an **activator** is present.

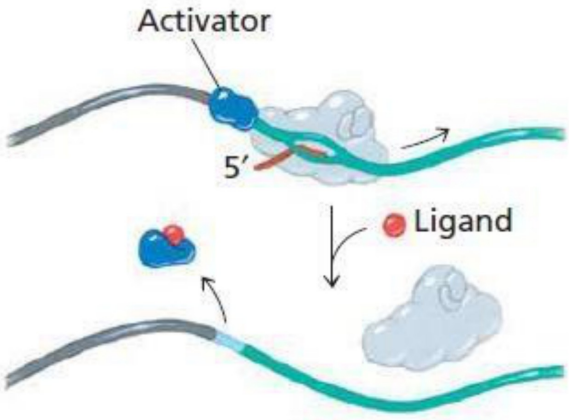
Positively regulated
In this case the gene is **positively regulated.**

How activators work

- The activator binds to the DNA to activate transcription **only after a ligand binds** to it.
- In some cases, the activator bound to DNA is **removed by another ligand** binding to it.



(a) An activator with bound ligand stimulates transcription.



(b) An activator stimulates transcription. In the presence of ligand, the activator is inhibited.

Negative Regulation — Repressors

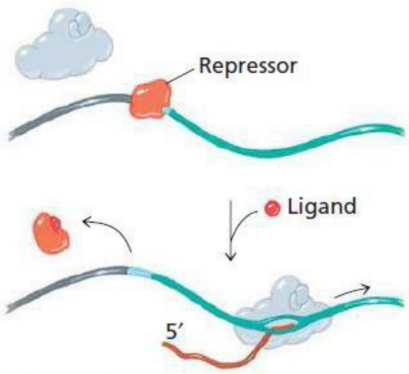
Transcription is prevented by a regulatory protein called a **repressor.** This happens when the gene needs to be **negatively regulated**.

- The repressor is **always present**, and transcription doesn't happen until the repressor is removed.
- The repressor is removed — leaving the space for the transcription complex to work — only after a **specific ligand** is attached to it.

DEFINITION

Inducer

The ligand that is able to **remove the repressor,** inducing transcription.



(c) A repressor prevents transcription. Binding of ligand (inducer) to the repressor inactivates the repressor and allows transcription.

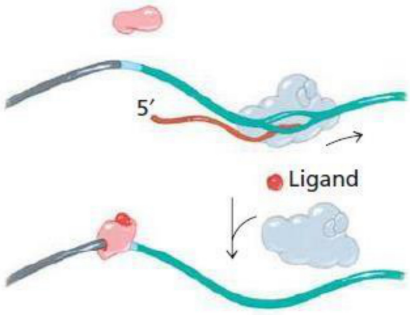
Co-repressors

When the repressor needs help

In some cases, the repressor needs the help of a **ligand** to be able to bind to the DNA.

CO-REPRESSOR

This ligand is called a **co-repressor,** because it helped the repressor in binding and repressing the transcription.



(d) In the absence of ligand, the repressor does not bind to DNA. Repression occurs only when ligand (corepressor) is present.

Trans-acting Regulators

Why "trans"?

All the previously described regulators are **trans-acting regulators** because they regulate DNA transcription but they are **out of the DNA**.

Trans refers to something acting from the opposite side.

TRANS-ACTING REGULATORS INCLUDE

- Transcription factors
- Activators
- Repressors
- Co-repressors
- Other proteins or RNAs

...that are able to affect the transcription **positively or negatively**.

Cis-acting Regulators

ARE THERE CIS-ACTING REGULATORS? YES

A cis-regulator refers to the presence of a **specific DNA sequence** that regulates the transcription of a gene **on the same DNA**.

↑ Enhancers — cis +

DNA sequences able to **increase the activity of RNA polymerase II** in transcribing a gene — a "cis" positive regulatory effect.

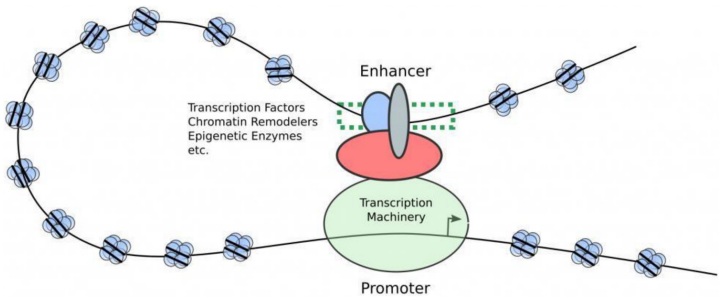
- Located **upstream** (before the 5′ end) or **downstream** (after the 3′ end) of the initiation site.
- Can be close or far from the promotor.

↓ Silencers — cis –

Another cis-acting regulator: DNA sequences able to **reduce the activity of transcription** of a gene (silence it).

DNA LOOPING

Even if these cis-acting regulators are far, the **looping of DNA** can bring them closer to the promotor of a gene so they can exert their effect. **Specific proteins** can bind to enhancers and silencers to bring them closer to their affected genes.



DNA looping brings an enhancer close to the promoter and the transcription machinery

RECAP

To Summarise...

The basics

Dogma	DNA → RNA → protein
Transcription	information in DNA copied into RNA
Components	the gene · the mRNA · the machinery (enzymes)
mRNA	unstable; more stable in eukaryotes

Cell type & transcription

Eukaryotes	nucleus → cytoplasm; mRNA modified for protection
Prokaryotes	all in the cytoplasm; no modifications

RNA polymerase (*E. coli*)

Core	α×2 (scaffold), β + β′ (active site), ω
Holoenzyme	core + sigma σ, only at initiation

Initiation

Promotors	own promotor in eukaryotes; operons in prokaryotes (lac operon)
Consensus	−10 Pribnow box TATAAT · −35 region · TATA box
Strength	strong = close to consensus, high rate
Steps	search → unwind → bubble → template strand

Elongation

Reaction	nucleotides added in the RNA–DNA helix
~10 nt	switch to elongation mode; promoter clearance
Helper	NusA

Termination

Types	rho-dependent · rho-independent
Pause sites	G/C-rich (3 H-bonds) and palindromic
Hairpin	destabilizes RNA–DNA hybrid → elongation ceases

Eukaryotic differences

Five	chromatin · 3 RNA pols · general TFs · one gene/promoter · post-transcriptional modifications
Pol I / II / III	rRNA / mRNA + snRNA / tRNA + small RNAs

Regulation

Positive	activator + ligand switches transcription on
Negative	repressor removed by inducer; co-repressor helps binding
Trans / cis	proteins off the DNA vs enhancers & silencers on it