

Biomedical
Science

Molecular
Genetics



BMS23010C | Fall 2026-2027

Molecular Genetics & Processes

Molecular Structure of Chromosomes



Free Session

A+ is more than just a platform





Chromosomes & Genomes

RECAP

Types of chromatin

Forms of DNA

Structure of DNA

Chromosomes are the structures within living cells that contain the genetic material.

Genome refers to the **entire complement of genetic material** in an organism or species.

In bacteria

The genome is typically a **single circular chromosome**.

In eukaryotes

Genetic material sits in **different cellular compartments**.

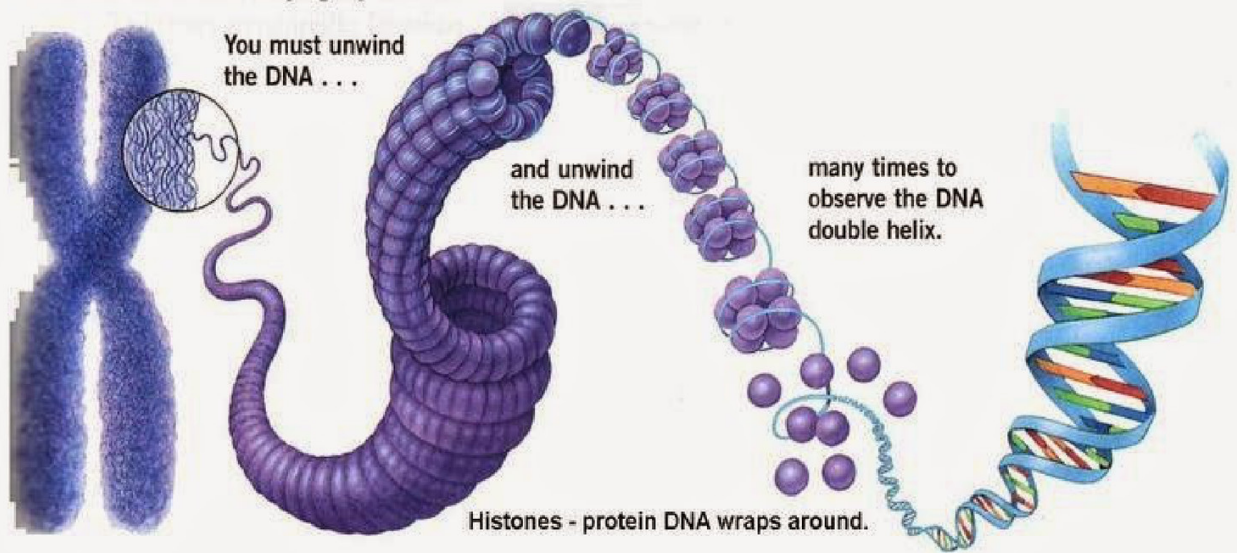
THE HUMAN NUCLEAR GENOME

22 autosomes, the **X chromosome**, and — in males — the **Y chromosome**.

Eukaryotes also have a mitochondrial genome, and plants have a chloroplast genome.

FIGURE 7.7 Chromosome Structure

Chromosome contain very tightly wound DNA





What Chromosomal Sequences Must Do

The primary function of the genetic material is to **store the information** needed to produce the characteristics of an organism.

FOUR PROCESSES THEY MUST FACILITATE

- 1 Synthesis of **RNA and cellular proteins**. — **which is ...?**
- 2 **Replication** of chromosomes. — **what do we call this process?**
- 3 Proper **segregation** of chromosomes. — **which phase?**
- 4 **Compaction** of chromosomes so that they fit within living cells. — **meaning?**



Sets of Chromosomes

One or more sets

Eukaryotic species carry **one or more sets** of chromosomes in the cell nucleus.

Linear chromosomes

Each set is composed of several different **linear chromosomes**.

Humans: 2 × 23

Two sets of 23 chromosomes each — a total of **46**.

One long molecule each

Typically **tens of millions to hundreds of millions** of base pairs long.



Key Features of Eukaryotic Chromosomes

Usually linear

Eukaryotic chromosomes are **usually linear**.

They occur in sets

Many species are **diploid** — somatic cells contain **2 sets** of chromosomes.

Enormous length

A typical chromosome is **tens of millions to hundreds of millions** of base pairs in length.

Genes interspersed

A typical chromosome contains between **a few hundred and several thousand** different genes.

Many origins of replication

Interspersed about every **100,000 base pairs**.

One centromere

Forms a recognition site for the **kinetochore proteins**.

Telomeres at both ends

Specialized sequences located at **both ends** of the linear chromosome.

Repetitive sequences

Common near **centromeric and telomeric** regions, but may also be interspersed throughout.



Fun Fact — Two Metres in Six Microns

2 metres of DNA



packed into


a 6 μm nucleus

- Stretch out all the DNA in a single human cell and it would be about **2 metres (6 feet)** long.
- Yet it is tightly packed into chromosomes that fit inside the nucleus — an area only about **6 micrometers** across.
- The packing is possible thanks to proteins called **histones**, which help the DNA coil and fold into a highly organized, compact structure.



Genome, Chromosome, Chromatin or Gene?

Feature	Genome	Chromosome	Chromatin	Gene
Scope	Entire genetic content of an organism	Individual DNA molecules within the genome	DNA-protein complex forming chromosomes	Specific DNA sequences within chromosomes
Components	All genes and non-coding DNA	DNA + proteins (histones)	DNA + proteins (histones)	Segments of DNA that encode functional products
Function	Overall blueprint for the organism	Carry and organize genetic information	Regulate access to DNA for transcription, replication	Encode instructions for proteins/RNAs
Example	Human genome	Human chromosome 1	Euchromatin and heterochromatin within chromosomes	The CFTR gene responsible for cystic fibrosis



Eukaryotic vs. Bacterial Chromosomes

What differs between the sequences of eukaryotic and bacterial chromosomes?

Centromeres & telomeres

Eukaryotic chromosomes have them. **Bacterial chromosomes do not.**

Repetitive sequences

Eukaryotic chromosomes typically have **many more** of them.



Three Regions Beyond the Genes

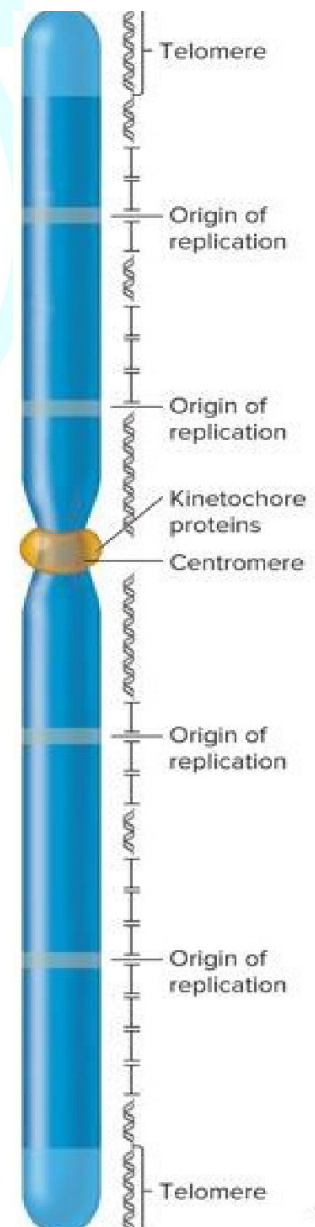
Besides genes, chromosomes contain three regions required for **replication and segregation**:

Origins of replication

Centromeres

Telomeres

- **Origins of replication** are chromosomal sites necessary to initiate DNA replication.
- Bacterial chromosomes contain **only one** origin.
- Eukaryotic chromosomes contain **many**.





Telomeres

Repetitive DNA sequences at the **ends of linear chromosomes** in eukaryotic cells.

Function

- Protect chromosome ends from **degradation**.
- Prevent the loss of important genetic information during **DNA replication**.

Characteristics

- Repetitive nucleotide sequences — e.g. **TTAGGG** in humans.
- Associated with specific proteins that form a **protective cap**.

Telomerase

An enzyme that **extends telomeres**, counteracting the shortening that happens during DNA replication.

RELEVANCE IN AGING AND DISEASE

Telomere shortening is linked to **aging** and diseases like **cancer**.



Centromeres

Regions on chromosomes where **kinetochores** form — essential for **spindle fiber attachment** during cell division.

Function

- Ensure **proper segregation** of chromosomes during mitosis and meiosis.
- Serve as the site of **kinetochore assembly**.

Characteristics

- Typically near the **center** of the chromosome — but the location can vary.
- Made of specific repetitive DNA, such as **alpha satellite DNA** in humans.

Role in cell division

Spindle fibers attach to **kinetochores** at the centromere, pulling sister...

AND IF THERE IS NO CENTROMERE?

The primary concern with centromere loss is **chromosomal instability** — leading to **aneuploidy and cancer**.



How Long is a Eukaryotic Gene?

A typical eukaryotic gene runs **several thousand to tens of thousands of base pairs.**

Less complex eukaryotes

In yeast, genes are relatively small — often **several hundred to a few thousand** base pairs long.

More complex eukaryotes

In mammals, protein-encoding genes tend to be **much longer**, because of **introns** — noncoding intervening sequences.



Exons & Introns

RNA molecule



splicing removes introns



exons remain

- An **exon** is a region of an RNA molecule that remains after splicing has removed the introns.
- In mRNA, the **coding sequence of a polypeptide** is contained within the exons.
- Introns run **100 bp to 10,000 bp** — and large introns can greatly increase the lengths of eukaryotic genes.

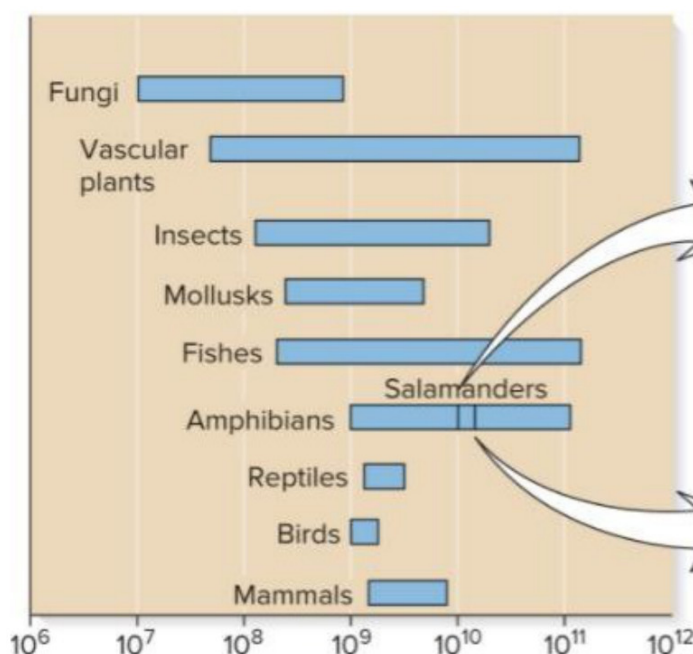


Sizes of Eukaryotic Genomes

Eukaryotic species vary dramatically in genome size — and that variation is **not related to the complexity of the species.**

A TALE OF TWO SALAMANDERS

Plethodon richmondi and *Plethodon larselli* are closely related, yet differ considerably in genome size — the genome of *P. larselli* is **over twice as large**.



(a) Genome sizes (nucleotide base pairs per haploid genome)



(b) *Plethodon richmondi*



(c) *Plethodon larselli*

- Large size is due to the accumulation of many copies of **repetitive DNA sequences**.
- In some species these amounts have reached **enormous levels**.
- Repetitive sequences **do not encode proteins**, and their function remains a matter of controversy and great interest.



Unique Sequences in the Human Genome

Eukaryotic genomes contain sequences that are **unique**, **moderately repetitive**, or **highly repetitive**.

The vast majority of proteins in eukaryotic cells are encoded by genes present in **one or a few copies**. In humans, unique sequences make up roughly **41% of the entire genome**.

2%

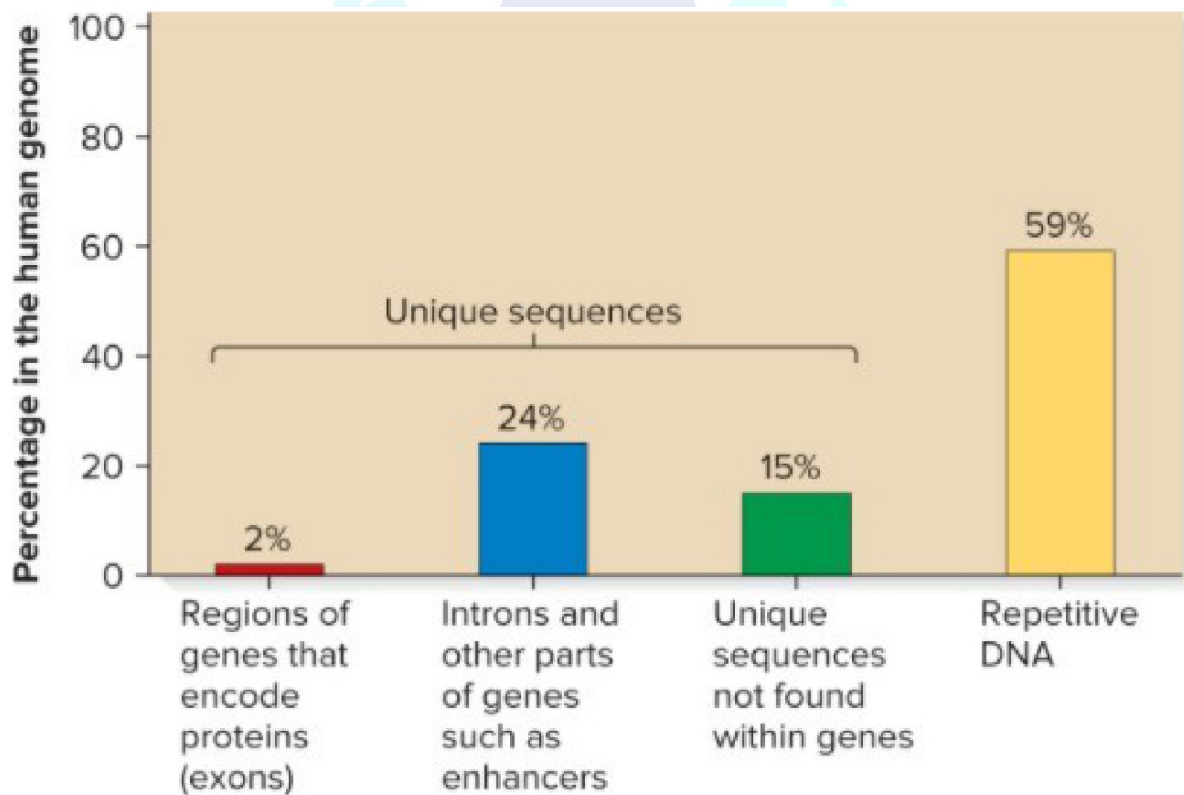
Protein-encoding regions of genes.

24%

Introns.

15%

Unique regions not found within genes.



Classes of DNA sequences



Moderately Repetitive Sequences

- Found **a few hundred to several thousand times** in a genome.
- In a few cases they are multiple copies of the same gene — the genes encoding **ribosomal RNA (rRNA)** are found in many copies.
- They may play a role in the **regulation of gene transcription and translation.**
- Some play no functional role and are derived from **transposable elements (TEs)** — short segments of DNA able to move within a genome.



Highly Repetitive Sequences

- Found **tens of thousands, even millions** of times throughout a genome.
- Each copy is relatively short — from **a few nucleotides to several hundred** in length.
- The widely studied **Alu family**, found in humans and other primates, is approximately **300 bp long.**

	MODERATELY REPETITIVE	HIGHLY REPETITIVE
Copies per genome	A few hundred to several thousand	Tens of thousands to millions
Length of each copy	—	A few nucleotides to several hundred
Example	Genes encoding rRNA	Alu family, ~300 bp
Possible role	Regulation of transcription and translation	—



Interspersed & Tandem Repeats

- Repetitive sequences like the **Alu family** are **interspersed** throughout the genome.
- Some moderately and highly repetitive sequences are clustered together in a **tandem array** — also known as a tandem repeat.
- In *Drosophila*, **19%** of the chromosomal DNA consists of highly repetitive sequences found in tandem arrays.
- Two related sequences, **AATAT** and **AATATAT**, are repeated.

AATATAATATAATATAATATAATATAATAT
TTATATTATATTATATTATATTATATTATA



Transposition

Sizeable portions of many species' genomes are composed of repetitive sequences — in many cases due to **transposition**: a process in which a **short segment of DNA is inserted into a new location** in the genome.

The DNA segments that transpose themselves are **transposable elements (TEs)** — sometimes called **"jumping genes"** because they are inherently mobile.



Simple Transposition — Cut and Paste

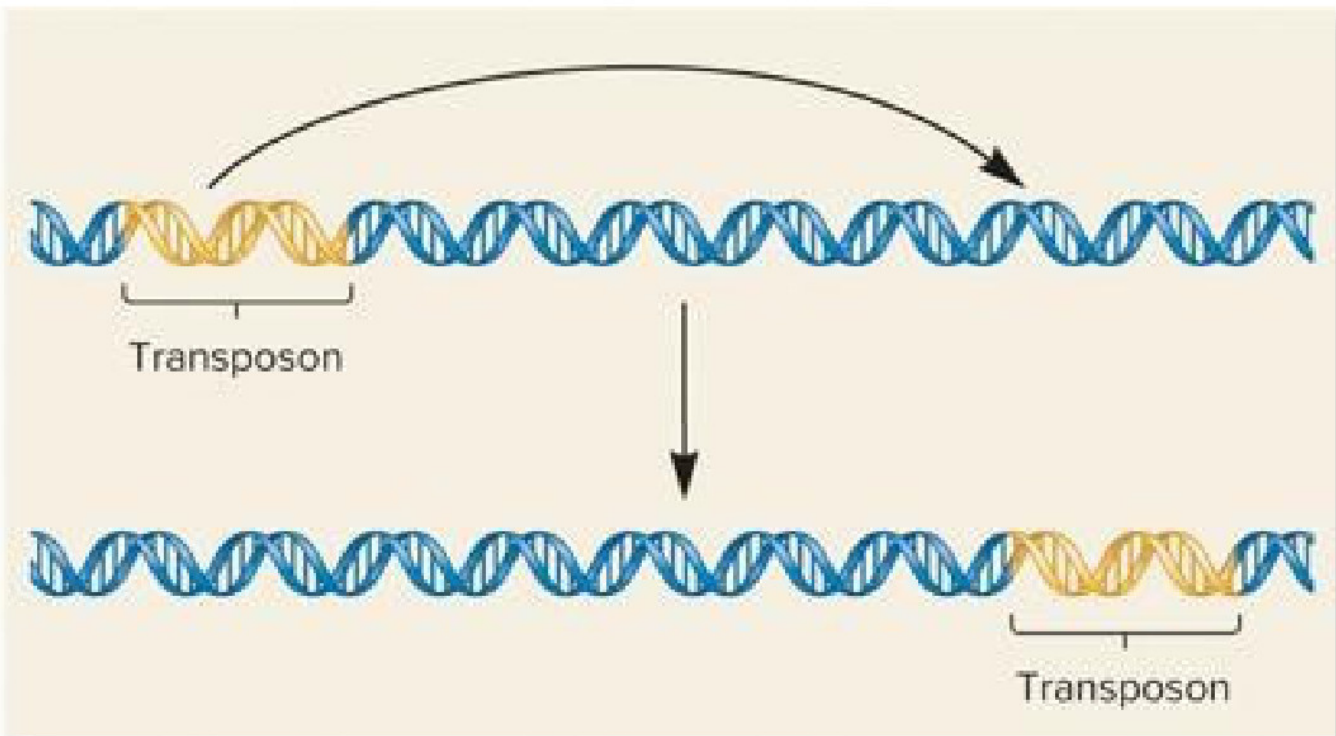
FIRST IDENTIFIED

Transposable elements were first identified by **Barbara McClintock** in the early **1950s**, during her classic studies with corn plants.

In **simple transposition**, the TE is removed from its original site...

...and transferred to a **new target site**.

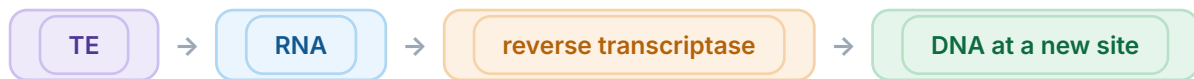
Called a **cut-and-paste mechanism** — the element is cut out of its original site and pasted into a new one.



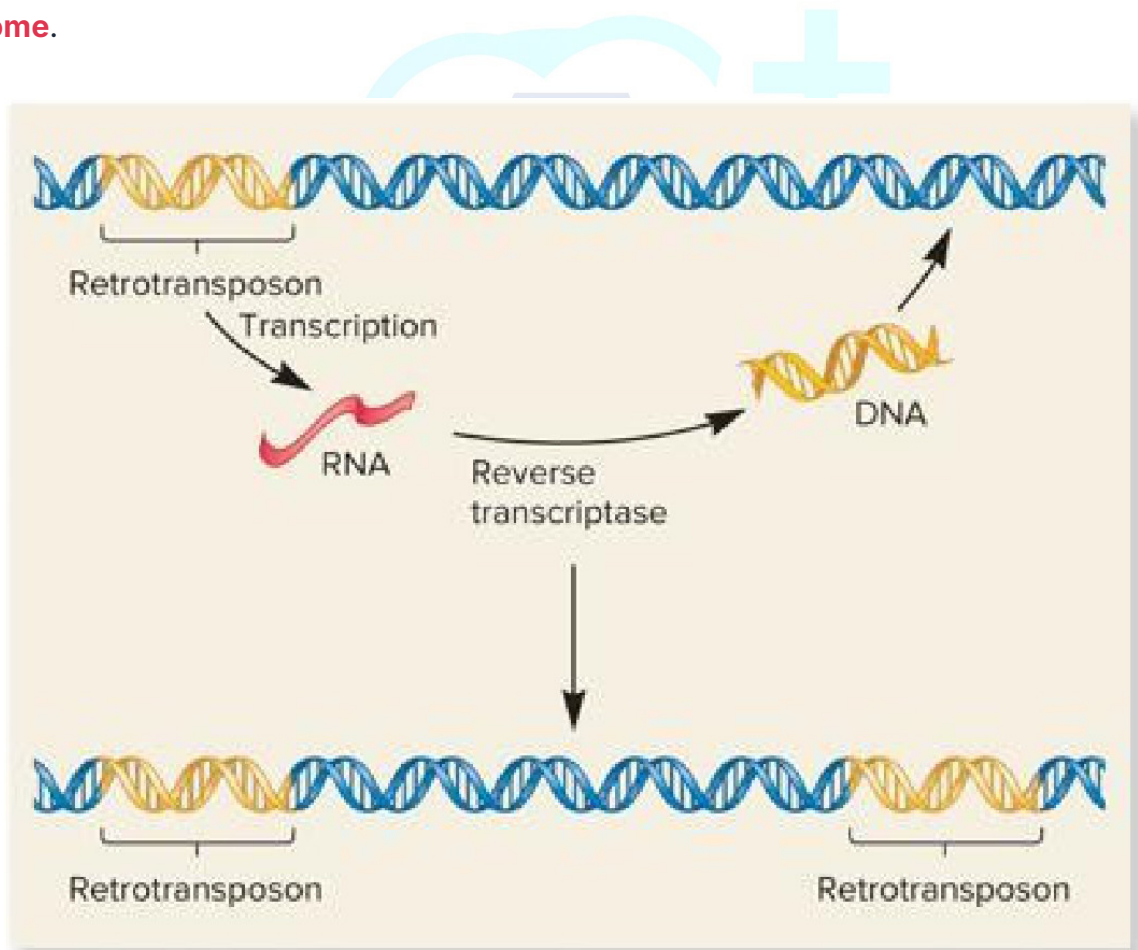
(a) Simple transposition



Retrotransposition — Copy via RNA



- TEs that move this way are known as **retrotransposons**, or retroelements.
- They move via an **RNA intermediate**. This form of transposition, termed **retrotransposition**, is found **only in eukaryotic species**, where it is very common.
- The element is transcribed into RNA; the enzyme **reverse transcriptase** then uses that RNA as a template to synthesize a DNA molecule, which is integrated into a **new region of the genome**.





Structure of Eukaryotic Chromosomes

Inside the nucleus

A distinguishing feature of eukaryotic cells: their chromosomes sit within a cellular compartment known as the **nucleus**.

One long molecule

The DNA in a typical eukaryotic chromosome is **single, linear, double-stranded**, and may run **hundreds of millions** of base pairs.

DNA + protein

The DNA–protein complex found within eukaryotic chromosomes is termed **chromatin**.



The Repeating Unit of Chromatin

What is the repeating structural unit of chromatin?

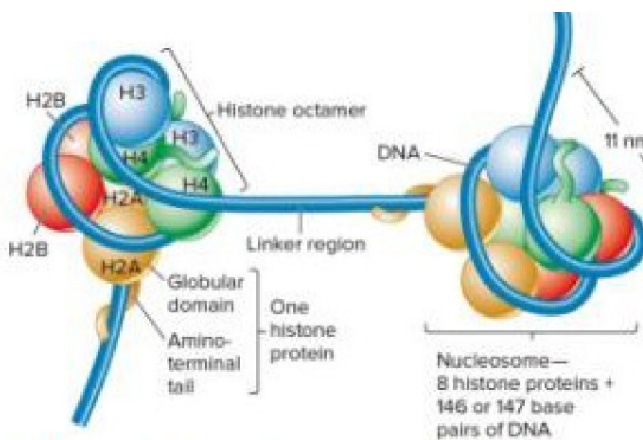
The nucleosome

A **double-stranded segment of DNA** wrapped around an **octamer of histone proteins**, or histones.

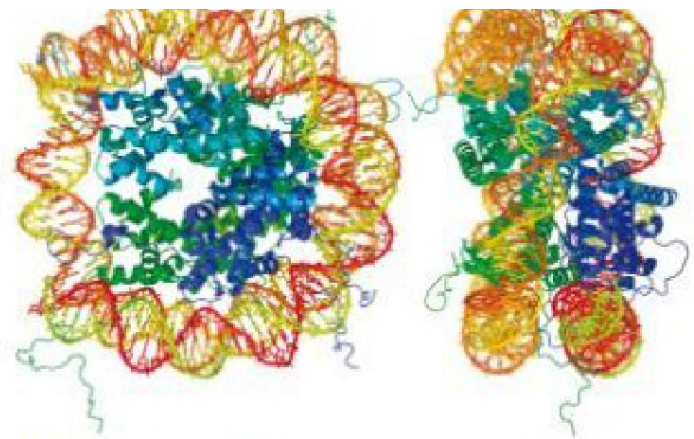


Nucleosome Structure

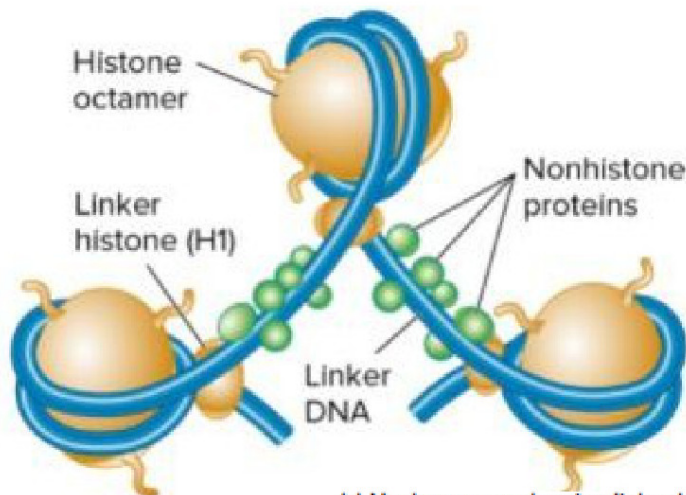
- a A nucleosome consists of **146 or 147 bp of DNA** wrapped around an **octamer of core histone proteins**.
- b A model for the structure of a nucleosome as determined by **X-ray crystallography**. The drawing shows **two views** of a nucleosome.
- c The **linker region** of DNA connects adjacent nucleosomes. The **linker histone H1** and the nonhistone proteins also bind to this linker region.



(a) Nucleosomes showing core histone proteins



(b) Molecular model for nucleosome structure



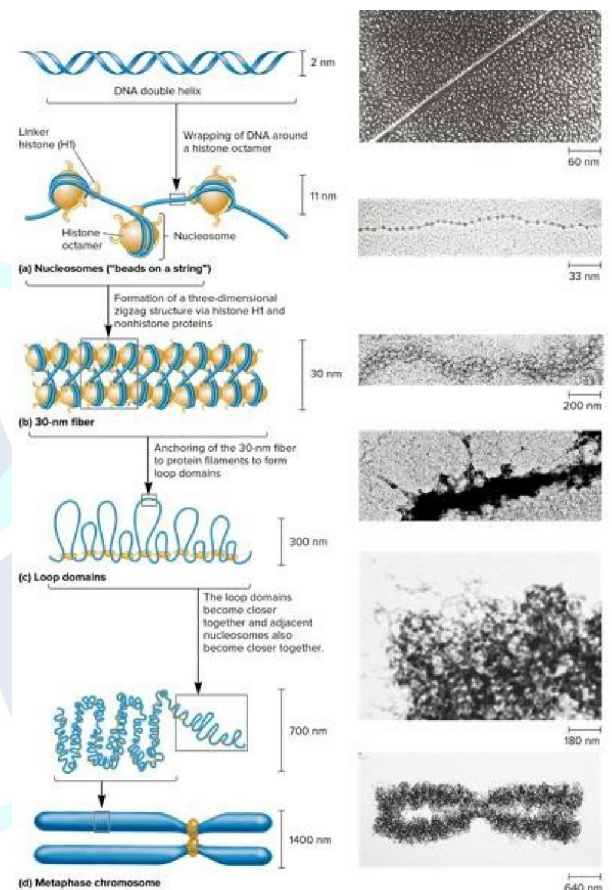
(c) Nucleosomes showing linker histones and nonhistone



Metaphase Chromosomes Are Highly Compacted

When eukaryotic cells prepare to divide, the chromosomes become **very condensed, or compacted**.

- 1 Wrapping of DNA around **histone octamers** to form the **nucleosome**.
- 2 Formation of a **30-nm fiber**, in which nucleosomes form a **zigzag structure** via binding of histone H1 and nonhistone proteins to the DNA.
- 3 The 30-nm fiber then forms **loop domains** — the predominant form of chromatin in nondividing cells (**euchromatin**).
- 4 These condense even further, typically forming the characteristic **X-shaped structure** at metaphase.



This additional level of compaction greatly shortens the overall length of a chromosome and produces a diameter of approximately **700 nm**.



Check Yourself

Q1 Which of the following are moderately repetitive sequences?

1. Genes that encode rRNA

2. Most protein-encoding genes

3. Both a and b

4. None of the above

Q2 Which types of transposable elements rely on an RNA intermediate for transposition?

1. Insertion elements

2. Simple transposons

3. Retrotransposons

4. All of the above

Q3 The function of transposase is...

1. to recognize inverted repeats

2. to remove a TE from its original site

3. to insert a TE into a new site

4. all of the above

Q4 What are the components of a single nucleosome?

1. About 146 bp of DNA and four core histone proteins

2. About 146 bp of DNA and eight core histone proteins

3. About 200 bp of DNA and four core histone proteins

4. About 200 bp of DNA and eight core histone proteins



DNA Extraction — From a Practical Point of View

- Explain the purpose of each DNA extraction step (lysis → protein/lipid removal → DNA).
- Match common **reagents** to their function.
- Perform a complete extraction with either **columns** or **magnetic beads**.
- Assess DNA **yield and purity**, and troubleshoot common problems.



Concept Map

1

Lysis

detergent + EDTA +
protease

2

Separate

DNA from proteins/lipids —
chaotrope/organic

3

Bind

silica or beads

4

Wash

ethanol

5

Elute

low-salt, Tris



Equipment & Consumables

☐ Microcentrifuge ($\geq 12,000 \times g$) or magnetic rack for beads

☐ Heat block (37–56 °C) or water bath

☐ Vortex (avoid for HMW DNA) and pipettes — wide-bore tips when needed

☐ Spin columns or magnetic beads; collection tubes

☐ Qubit fluorometer (preferred) or NanoDrop; 1.5/2.0 mL low-bind tubes

☐ Optional: fume hood if using phenol/chloroform, PPE



Protocol A: Spin Column — Steps 1–3

Step 1 • Sample lysis

- **What:** add lysis buffer (chaotropic salts) + proteinase K to the sample. Mix; incubate — e.g. 56 °C for 10–30 min.
- **Why:** chaotropic salts denature proteins; proteinase K digests proteins and nucleases, freeing the DNA.
- **Note:** include RNase A if you want DNA only.

Step 2 • Binding

- **What:** add ethanol (or isopropanol) per kit ratio; transfer to the spin column; centrifuge.
- **Why:** ethanol helps DNA bind to the **silica membrane** under high-salt conditions.
- **Note:** discard the flow-through carefully — the DNA is on the membrane.

Step 3 • Washing

- **What:** add Wash Buffer 1; spin and discard the flow-through.
- **Why:** removes **proteins, salts, and residual inhibitors**.



Protocol A: Spin Column — Steps 4–5

Step 4 • Dry spin

- **What:** spin the empty column for 1–2 min.
- **Why:** evaporates residual ethanol, which can **inhibit enzymes**.
- **Note:** critical for good downstream performance.

Step 5 • Elution

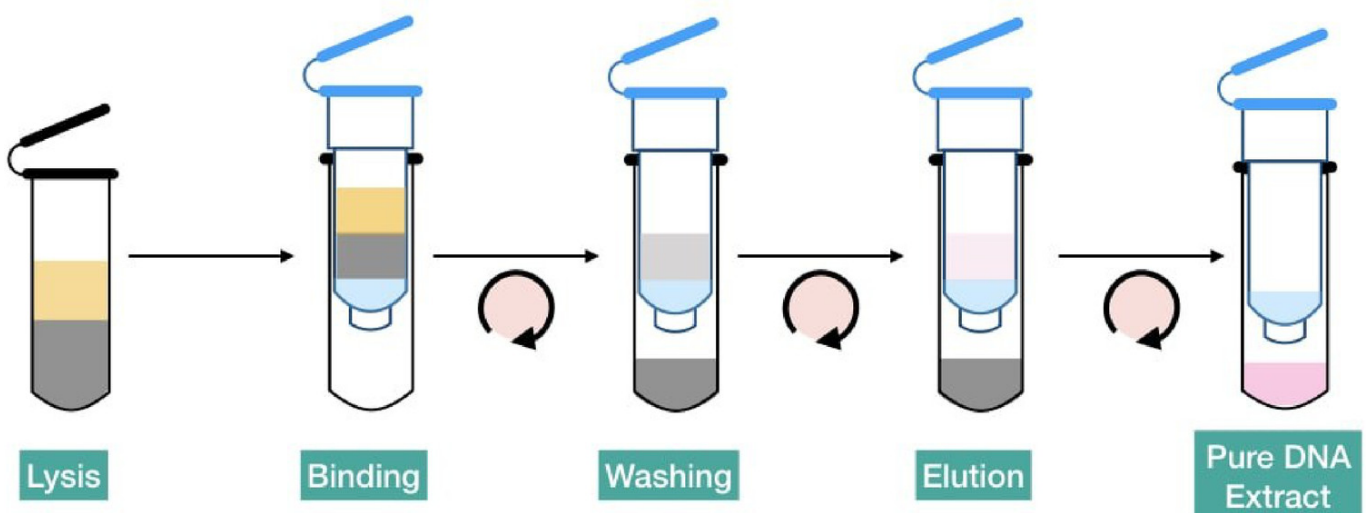
- **What:** place the column in a clean tube; add pre-warmed elution buffer (or nuclease-free water); incubate 1–5 min; spin.
- **Why:** the **low-salt buffer** disrupts DNA–silica interactions, releasing the DNA.



Spin-Column Summary



Spin-Column DNA extraction





Protocol B: Magnetic Beads

STEP 1

Lysis — as in Protocol A.

Step 2 · Bind

- **What:** add beads + binding buffer (PEG/salt); mix until the DNA binds the beads.
- **Why:** PEG and salt promote DNA **adsorption onto the bead surface**.

Step 3 · Separate

- **What:** place the tube on the magnetic rack; wait until the solution clears; remove the supernatant.
- **Why:** the magnet immobilizes the beads so contaminants can be removed.
- **Notes:** do not disturb the pellet; change tips between steps.

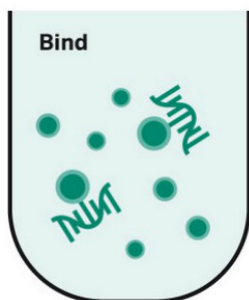
Step 4 · Wash

- **What:** wash beads with **70% ethanol** (1–2×) while on the magnet; remove the wash.
- **Why:** removes salts, proteins, and inhibitors.
- **Notes:** briefly air-dry — avoid over-drying, since cracking reduces elution.

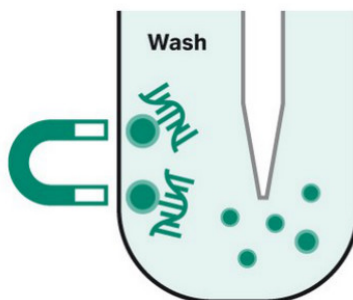
Step 5 · Elute

- **What:** off the magnet; add elution buffer/water; mix; incubate; back on the magnet and transfer the eluate.
- **Why:** **low-salt conditions** release the DNA from the beads.
- **Notes:** warm elution (37–55 °C) can increase yield.

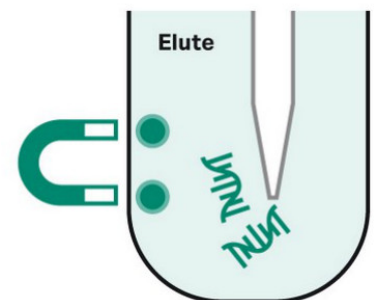
Magnetic particles are added to sample and bind to target molecule



Magnetic particles are captured and remainder of sample is washed away



Target molecule is released from magnetic particles for further analysis





To Summarise...

SITES

3

Regions beyond the genes

- Origins of replication — one in bacteria, many in eukaryotes
- Centromeres — kinetochore assembly and segregation
- Telomeres — protect the ends of linear chromosomes

GENOME

41%

Unique sequences in humans

- Exons 2% · introns 24% · unique non-genic 15%
- Moderately repetitive: a few hundred to several thousand copies
- Highly repetitive: tens of thousands to millions of copies

SIZE



Genome size vs. complexity

- Genome size is not related to species complexity
- *P. larselli*'s genome is over twice that of *P. richmondi*
- Large genomes accumulate copies of repetitive DNA

MOBILE

2

Transposition pathways

- Simple transposition — cut and paste
- Retrotransposition — via an RNA intermediate
- TEs first identified by Barbara McClintock in the early 1950s

PACKING

700

Nanometres at metaphase

- Nucleosome: 146–147 bp around a histone octamer
- 30-nm fiber → loop domains → X-shaped metaphase chromosome
- 2 m of DNA fits inside a 6 μ m nucleus

EXTRACTION

5

Steps in DNA extraction

- Lysis → separate → bind → wash → elute
- Spin column: DNA binds silica under high salt
- Magnetic beads: PEG and salt drive adsorption

THE THROUGH-LINE

Chromosomal sequences exist to serve four processes — synthesis, replication, segregation, and compaction.