Genomic compaction in virus and prokaryotes

San Luis Potosi State University (UASLP) Mexico
Molecular Biology Course, Faculty of Medicine post-graduate program

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Genomes and compartments

Genome size varies significantly across biological entities.

Viral genomes are compact (10 to 100 kb) and contained within small, efficiently packaged capsids (filamentous or icosahedral).

Bacterial genomes, are larger (10 Mb) and housed in cylindrical cells without a defined nucleus.

Eukaryotic genomes are the largest containing billions of bases organized into chromosomes and contained within a membrane-bound nucleous.

Compartment	Shape	Dimensions	Type of NA	NA Length	Bases
TMV	Filament	0.008 x 0.3 µm	1 x ssRNA	2 µm	6.4 kb
Phage φfd	Filament	0.006 x 0.85 µm	1 x ssDNA	2 µm	6 kb
Adenovirus	Icosahedron	0.07 µm Δ	1 x dsDNA	11 µm	35 kb
Phage T4	Icosahedron	0.065 x 0.10 µm	1 x dsDNA	55 µm	170 kb
Escherichia coli	Cylinder	1.7 x 0.65 µm	1 x dsDNA	1.3 mm	4.2×10^3 kb
Human mitochondria	Oblate spheroid	3 x 0.5 µm	~10 dsDNA	50 µm	16 kb
Human nucleus	Spheroid	6 µm Δ	46 dsDNA	1.8 m	6×10^6 kb

Packaging density

Viruses exhibit the highest nucleic acid densities due to space constraints in capsids.

Prokaryotes and eukaryotes balance DNA compaction with functional accessibility, resulting in moderate densities.

Mitochondrial genomes are highly compacted compared to nuclear DNA due to the organelle's size constraints.

These densities reflect evolutionary adaptations to optimize genome storage and functionality across diverse life forms.

Life Form	Packaging Density (mg/mL)	Description
Viruses	~200–500 mg/mL	Extremely dense; highest among life forms.
Prokaryotes	~10 mg/mL	Moderately dense; compact nucleoid structure.
Mitochondria	~50–100 mg/mL	High density within the small organelle matrix.
Eukaryotic Nucleus	~10–30 mg/mL	Moderately dense; regulated for transcriptional access.

Viral genomes

Viral genomes are highly compact, and range from 2 kb (e.g., Circoviruses) to 2.5 Mb (e.g., Mimiviruses).

DNA viruses can be

- single-stranded (ssDNA) or
- double-stranded (dsDNA).

RNA Viruses can be single-stranded (ssRNA) or double-stranded (dsRNA) and
ssRNA further classified into:

- Positive-sense (+ssRNA)
- Negative-sense (-ssRNA)

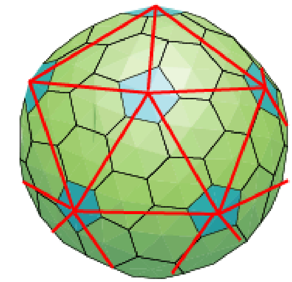
Some viruses have segmented genomes (e.g., Influenza, Hantavirus), while others are continuous (HIV, HPV).

Viral Genome Sizes

	Virus	Genome Type	Genome Size (kb)
1	Bacteriophage MS2	ssRNA (+)	3.6
2	Tobacco Mosaic Virus (TMV)	ssRNA (+)	6.4
3	Influenza A Virus	ssRNA (-)	13.5
4	Hepatitis B Virus (HBV)	dsDNA	3.2
5	Human Immunodeficiency Virus (HIV-1)	ssRNA (+)	9.7
6	SARS-CoV-2	ssRNA (+)	29.9
7	Adenovirus	dsDNA	35.0
8	Phage T4	dsDNA	170.0
9	Herpes Simplex Virus (HSV-1)	dsDNA	152.0
10	Vaccinia Virus	dsDNA	190.0
11	Mimivirus	dsDNA	1250.0

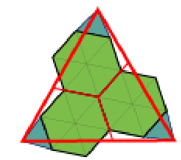
Viral capsids

Viral capsids are protein shells that encase and protect the viral genome, and they exhibit a variety of structural forms optimized for efficiency, stability, and functionality. Below are the major types of viral capsids:

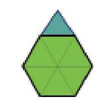

T=7 icosahedral capsid

1. Icosahedral capsid structure:

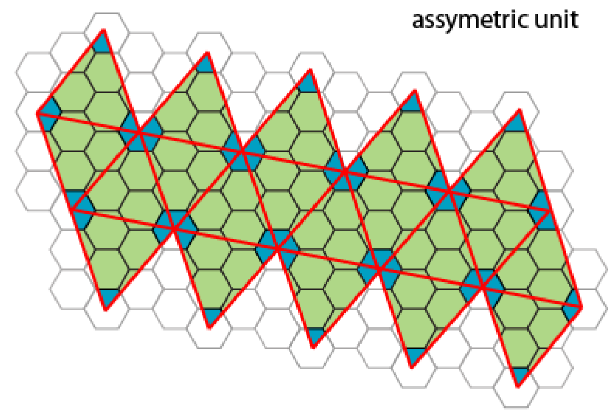
Composed of 20 equilateral triangular faces forming a symmetrical, spherical shape.


Triangular facet

Advantages:
- Highly stable and efficient for packaging nucleic acids.
- Minimal use of protein subunits due to its geometric symmetry.


T=7 icosahedral assymetric unit

Examples:
- Adenovirus
- Poliovirus
- Herpes simplex virus (HSV)



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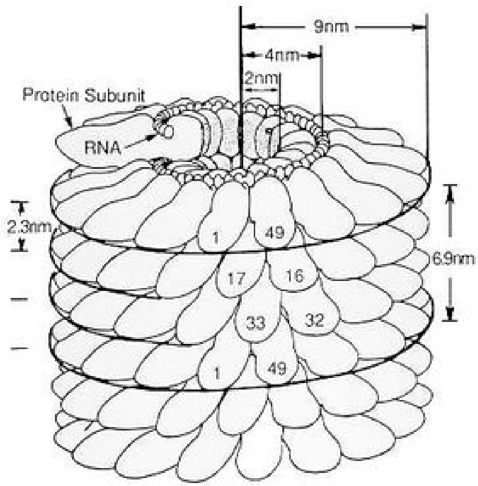
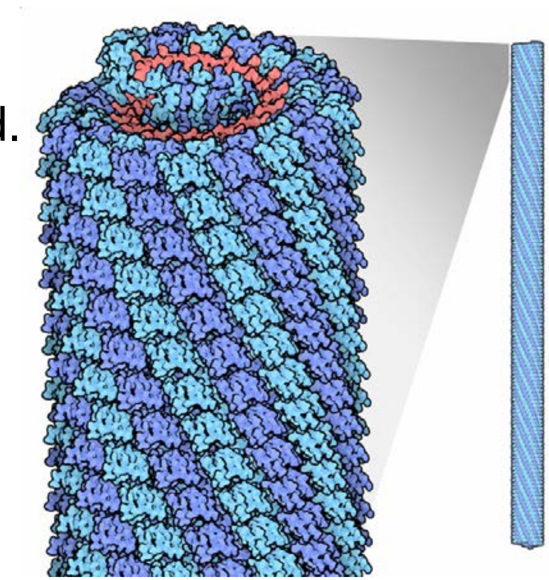


2. Helical capsid structure:

Capsid proteins form a helical arrangement around the nucleic acid, creating a rod-shaped or filamentous structure.

Advantages:

- Flexibility to accommodate varying lengths of nucleic acid.
- Often associated with enveloped viruses.



Examples:

- Tobacco mosaic virus (TMV)
- Rabies virus (RABV)

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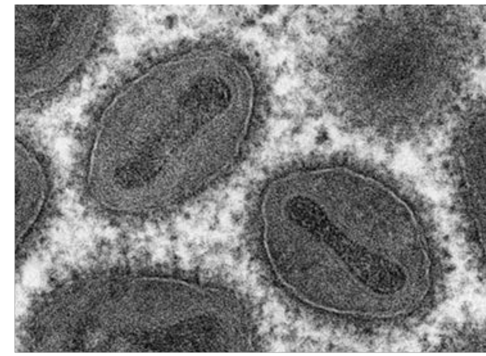


Variola major virus (Orthopoxvirus).

3. Complex capsid structure:

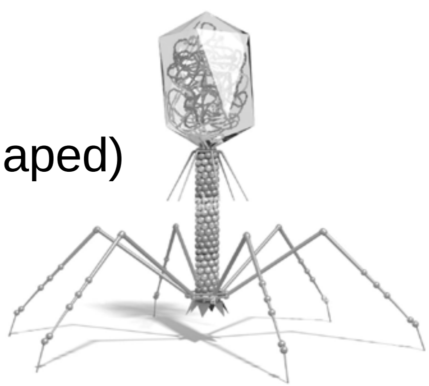
A combination of icosahedral and helical elements, often with additional structures such as tails or fibers.

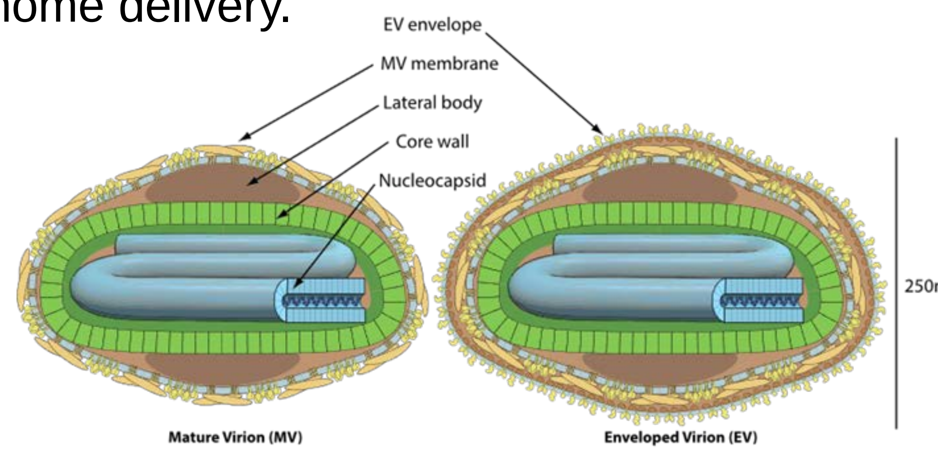
Advantages:

- Specialized for host recognition and genome delivery.

Examples:

- Bacteriophage T4
- Poxvirus (brick-shaped)





Two distinct infectious virus particles exists: the intracellular mature virus (IMV) and the extracellular enveloped virus (EEV).

viralzone.expasy.org

Viral genome condensation

Packaging of DNA/RNA into viral capsid for storage and protection.

Critical for viral replication, transmission, and survival.

Highly efficient and regulated process.

Relies on a combination of electrostatic interactions, specialized packaging proteins, and capsid architecture, reflecting evolutionary adaptations for survival and infectivity.

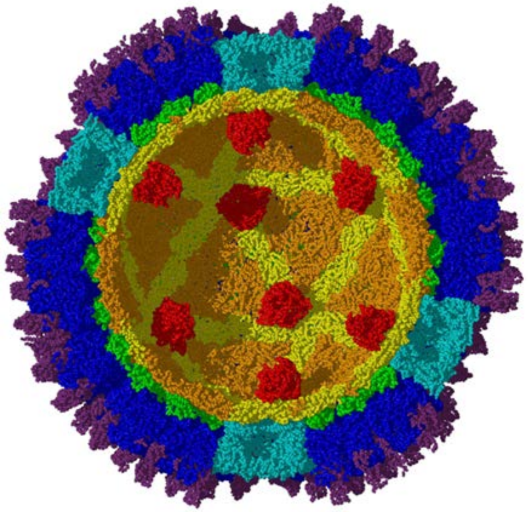
Virus	Genome Type	Capsid Type	Packaging Mechanism	Genome Size
Bacteriophage T4	dsDNA	Icosahedral	ATP-driven molecular motor	~170 kb
Adenovirus	dsDNA	Icosahedral	Protein-mediated condensation	~35 kb
Influenza Virus	-ssRNA	Helical	Nucleocapsid proteins	~13.5 kb
SARS-CoV-2	+ssRNA	Spherical	Nucleocapsid proteins	~30 kb
Ebola Virus	-ssRNA	Filamentous	Nucleocapsid proteins	~19 kb

Viral genome condensation

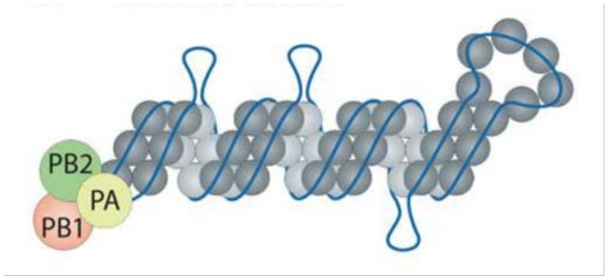
Electrostatic Interactions:
Negatively charged vNA interact with positively charged proteins or ions.

Viral Packaging Proteins:
Specialized proteins bind to the vNA such as Histone-like proteins in bacteriophages or Nucleocapsid proteins in RNA viruses (e.g., TMV).

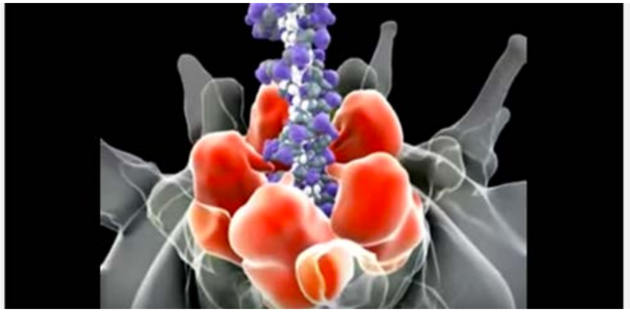
Molecular Motors:
Large viruses, like T4 phage, use ATP-driven molecular motors to force (~60 atmospheres) the genome (170 kb) into the capsid.



Reovirus RdRp λ3 polymerase molecules



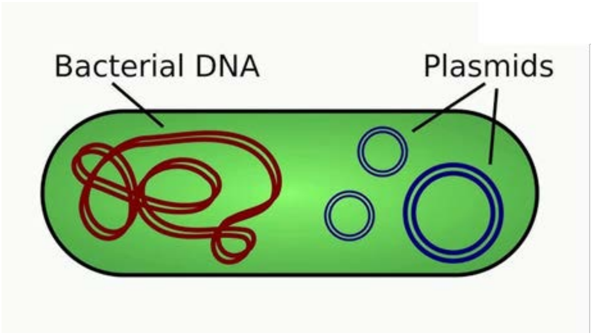
Influenza vRNA nucleoprotein binding



Hutchinson, E. *et al*. (2009). Genome packaging in influenza A virus. The Journal of general virology. 91. 313-28.

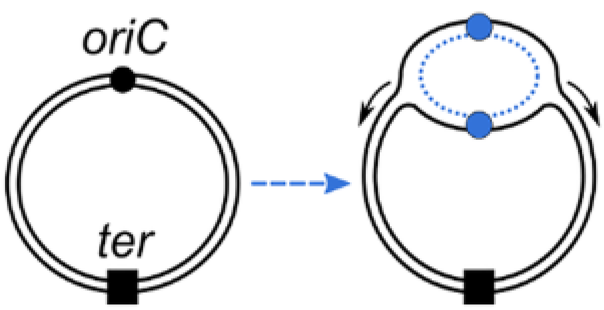
Viral genome condensation

Genophore: The Bacterial Chromosome



Usually circular DNA molecule, although some bacteria and archaea have linear genophores.

Supercoiled and compacted to fit within the cell's nucleoid region (no membrane).



Simpler than a eukaryotic chromosome.

Does not have chromatin or histones (some archaea use histone-like proteins).

Contains essential genes required for the cell's growth, replication, and metabolism (essential genome).

Plasmids are smaller, episomal circular DNA molecules that carry non-essential or accessory genes.

Single replicon having a single origin of replication (OriC).

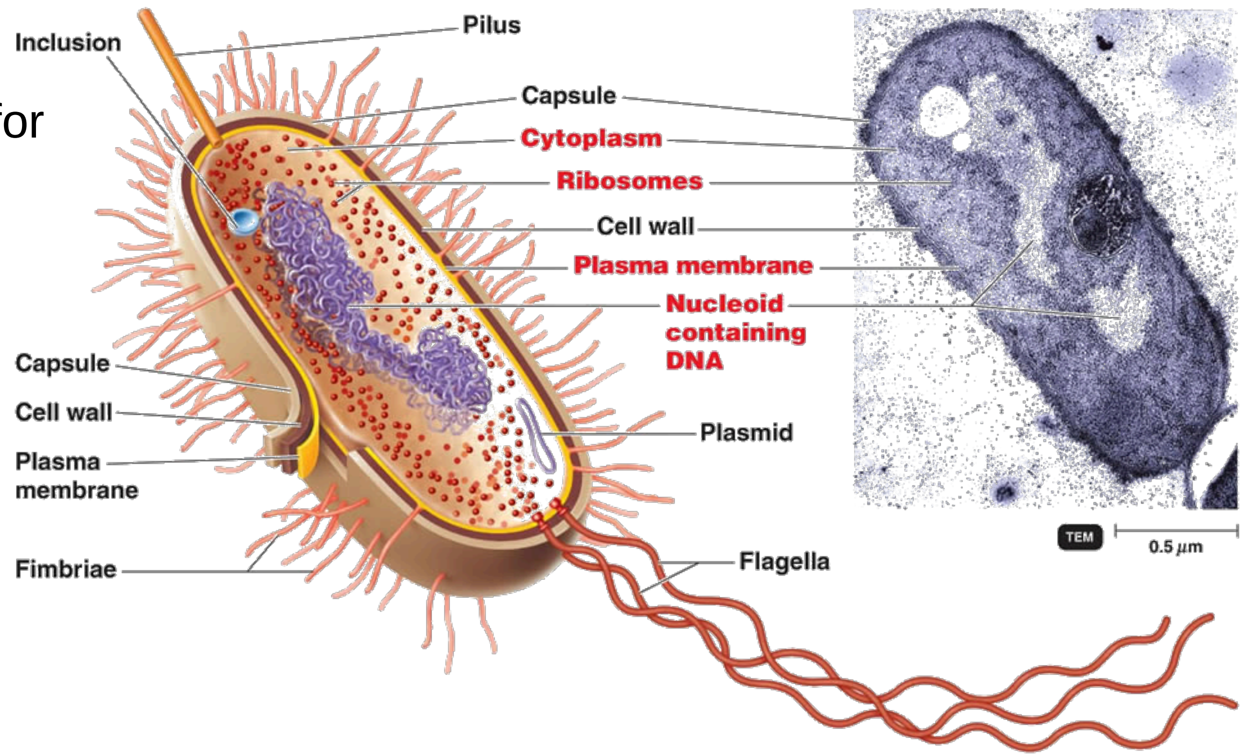
Bacterial Genome Condensation

Bacteria possess a single, circular chromosome that typically measures several million base pairs in length.

Limited space of a bacterial cell (~1–2 µm in diameter).

DNA undergoes extensive compaction through various structural and biochemical mechanisms.

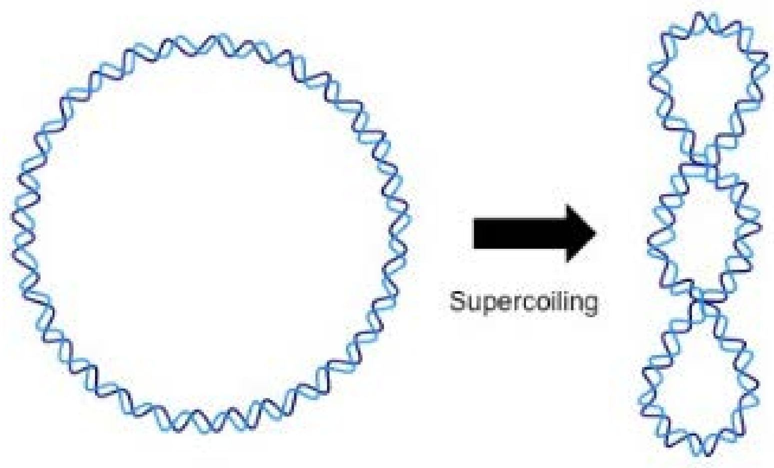
DNA remains accessible for replication, transcription, and repair.



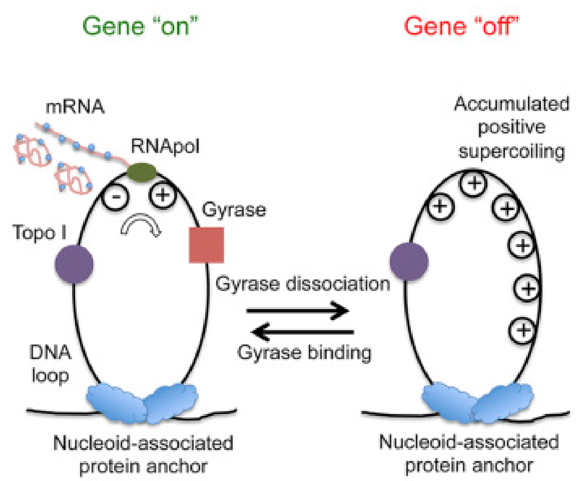
Pearson Education Inc (2010)

Key Mechanisms of Bacterial DNA Compaction

- **Supercoiling**
- Nucleoid-Associated Proteins (NAPs)
- Macromolecular crowding
- DNA looping
- Condensins



- DNA twisted to reduce its size.
- DNA gyrase and topoisomerase induce supercoils.
- Negative supercoiling (loose DNA for transcription)
- Positive supercoiling (tightens DNA for storage).



Pearson Education Inc (2010), Chong S, et al. Mechanism of transcriptional bursting in bacteria Cell. 2014.

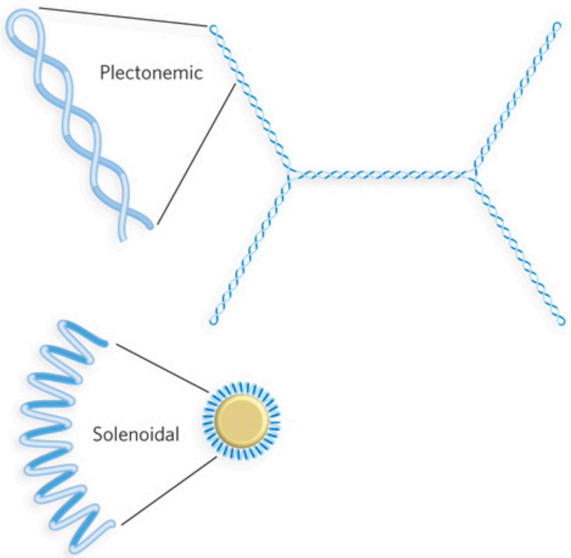
Plectonemic and Solenoid Supercoiling

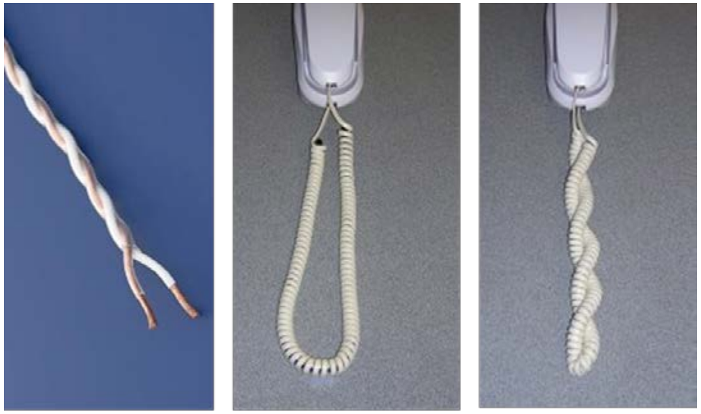
Supercoiled DNA forms three structures:
Plectoneme
Toroid (solenoid)
A combination of both.

Plectonemes are typically more common in nature, and this is the shape most bacterial plasmids will take.

For larger molecules it is common for hybrid structures to form – a loop on a toroid can extend into a plectoneme.

DNA supercoiling is important for DNA packaging within all cells and regulates gene expression.





Plectonemic Solenoid Both

Boles TC, et al. Structure of plectonemically supercoiled DNA. J Mol Biol. 1990 Jun 20;213(4):931-51.

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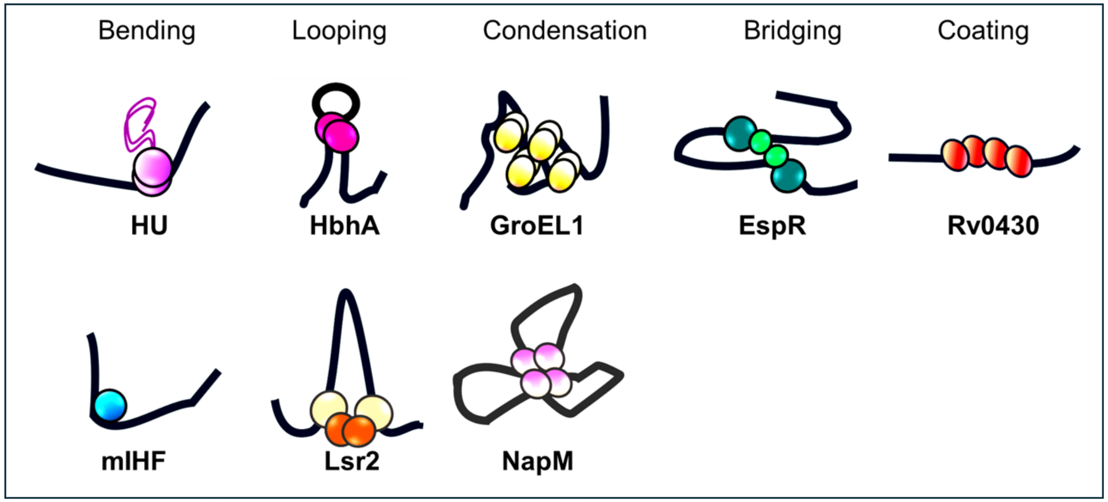

- DNA-binding Proteins promote folding into a compact nucleoid structure.
- HU: Stabilizes bends in DNA.
- IHF (Integration Host Factor): Promotes sharp DNA bending.
- H-NS (Histone-like Nucleoid Structuring protein): Links distant DNA regions.

Pearson Education Inc (2010)

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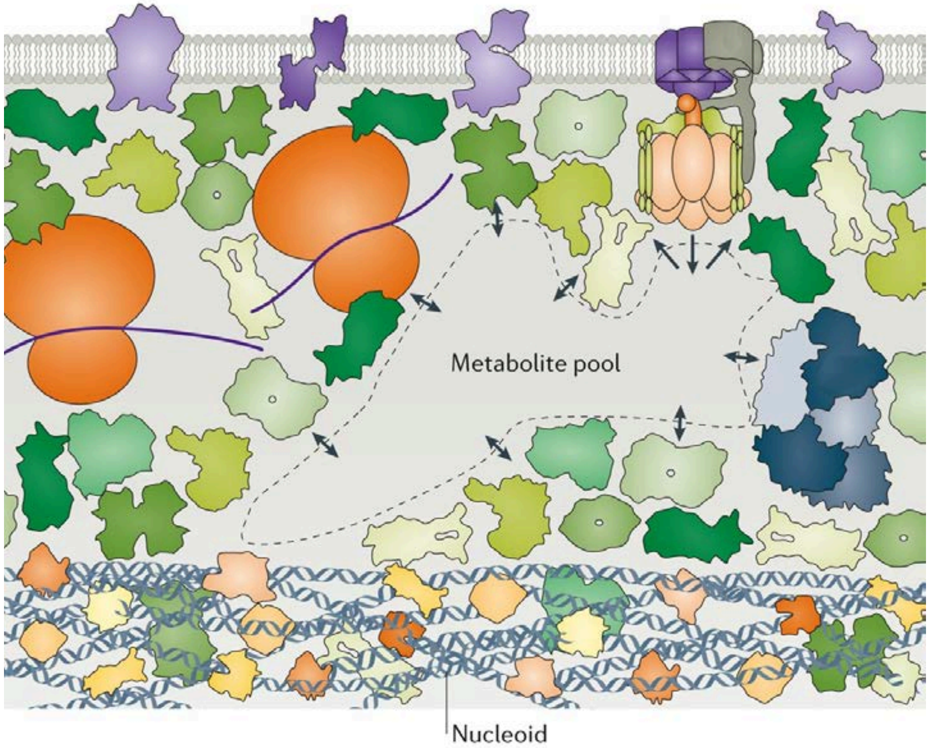

- High concentrations of macromolecules in protoplasm create an environment where DNA is physically compressed.
- This phenomenon alters the behavior of biomolecules, influencing their stability, folding, interactions, and reactions

Nature Reviews Microbiology

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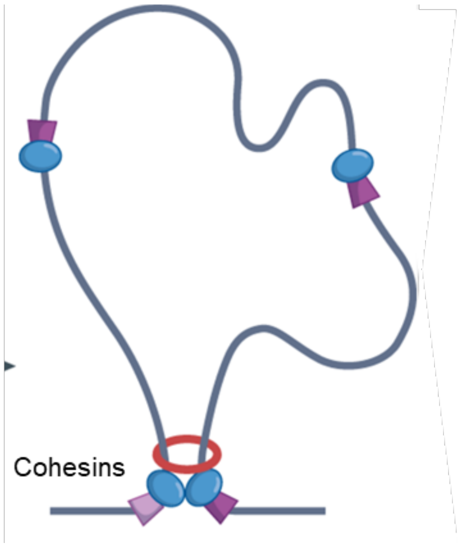
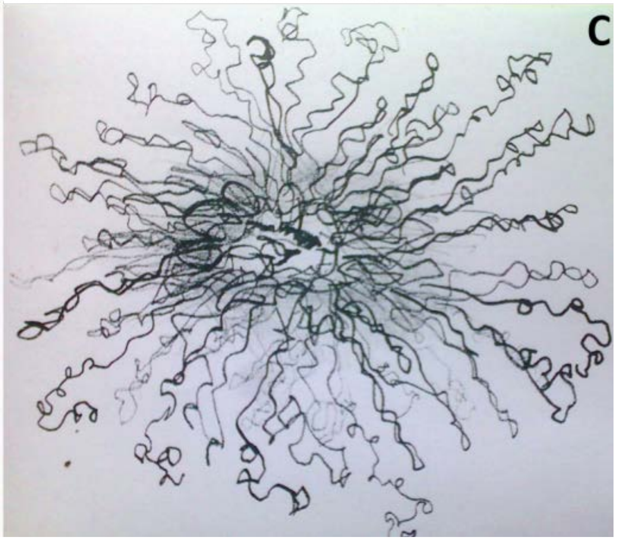


- DNA forms loops anchored by NAPs or transcription machinery.
- Looping allows regions of the genome to be spatially organized for efficient gene expression and replication.



Zhang H, et al. CTCF and R-loops are boundaries of cohesin-mediated DNA loopingMol Cell. 2023 Aug 17;83(16):2856-2871

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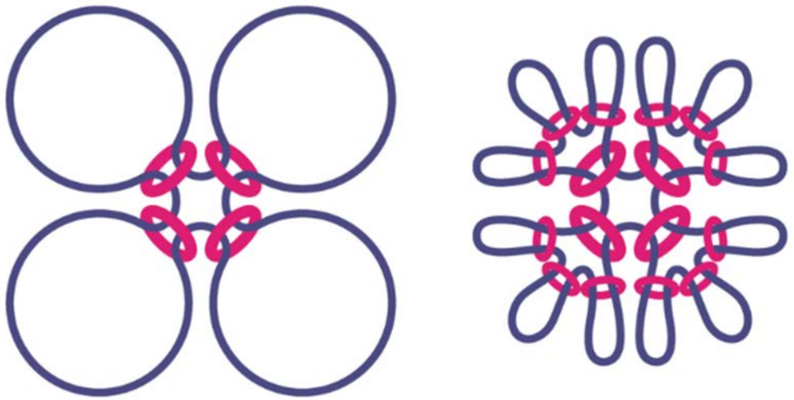
- **Condensins**



- Crucial role in organizing, compacting, and segregating the bacterial genome.
- Belong to the Structural Maintenance of Chromosomes (SMC) family
- Maintain nucleoid architecture, facilitating DNA replication and repair, and ensuring accurate chromosome segregation during cell division.

Zhang H, et al. CTCF and R-loops are boundaries of cohesin-mediated DNA loopingMol Cell. 2023 Aug 17;83(16):2856-2871

Bacterial Polyamines

Small, positively charged molecules that are abundant in bacterial cells and play a crucial role in cellular processes, particularly in DNA stabilization and compaction.

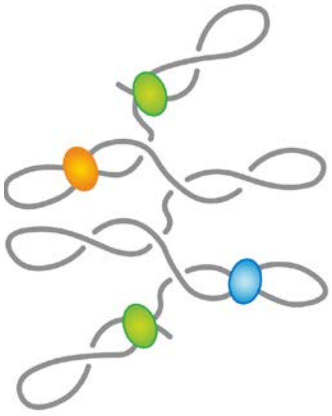
Their positive charge allows polyamines to interact electrostatically with negatively charged DNA, RNA, and acidic proteins.

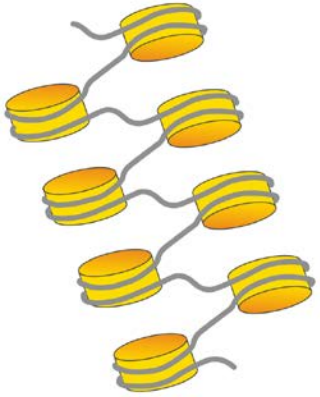
Vital for DNA integrity, cellular structure, and metabolic activity.

The most common bacterial polyamines are:

- Spermidine, isolated by Antonie van Leeuwenhoek from semen
- Putrescine
- Cadaverine

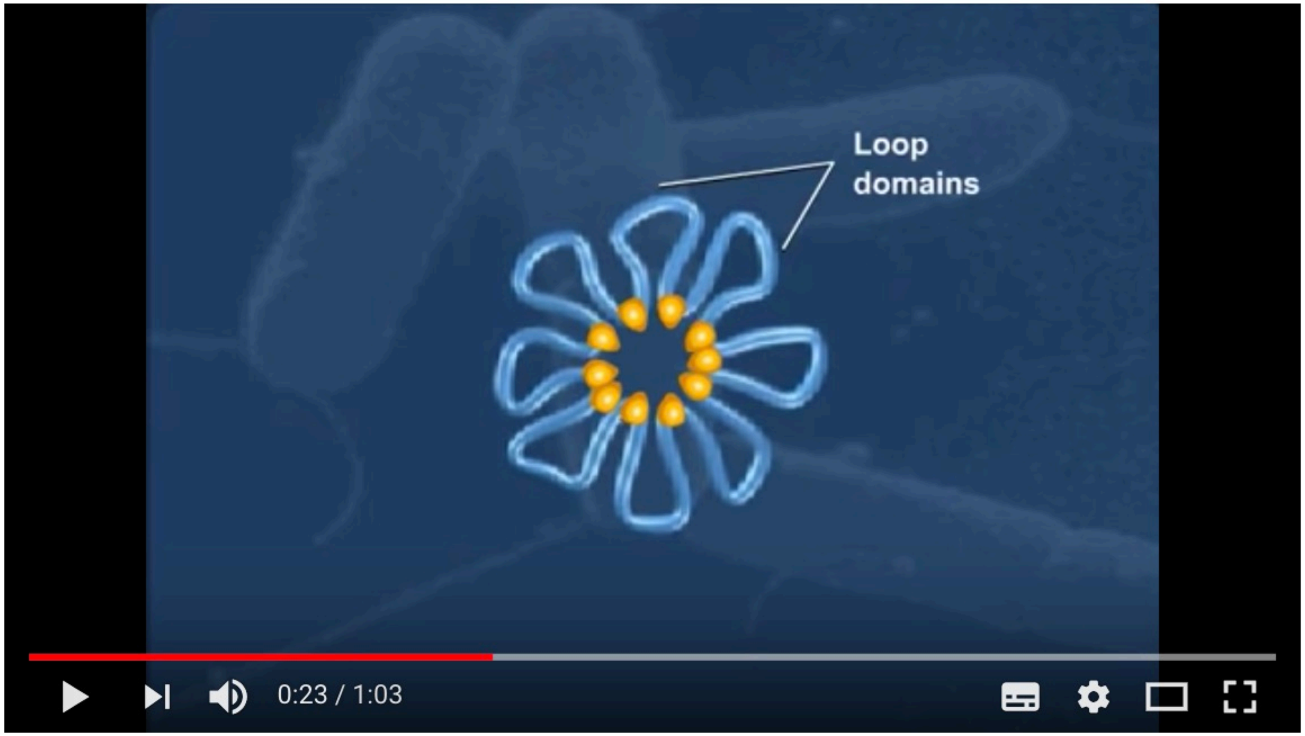
Often associated with decaying organic matter. Contributes to the characteristic odor of decomposition





Subhash C. et al. Architecture of the Escherichia coli nucleoid. PLoS Genet (2019) 15(12)

Bacterial Chromosome Compaction



Cell Structure-Bacterial Chromosome Compaction

https://www.youtube.com/watch?v=30B0wGAID4o

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