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DNA topology and supercoling

Lec:4 For the third stage

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DNA TOPOLOGY

Dictionary explains topology as "The study of geometrical properties and spatial relations unaffected by the continuous change of shape or size of figures"

The topology of DNA, explains how the two complementary single strands are intertwined.

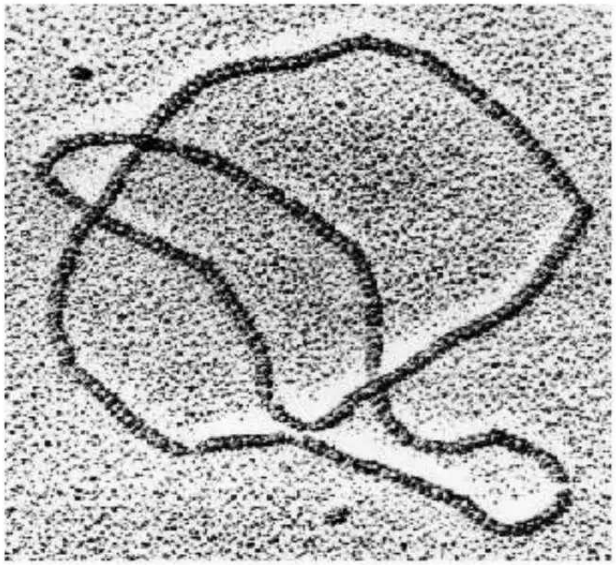
DNA topology encompasses supercoiling, knots, and catenanes.

CHARACTERISTICS

- The topology of closed circular DNA is characterized by the linking number (Lk), which is the number of links between two complementary single strands.
- Linking number is demonstrated by
  - Twist (Tw) - number of times the two strands are twisted around each other
  - Writhe (Wr) - the geometric coiling of the double helix

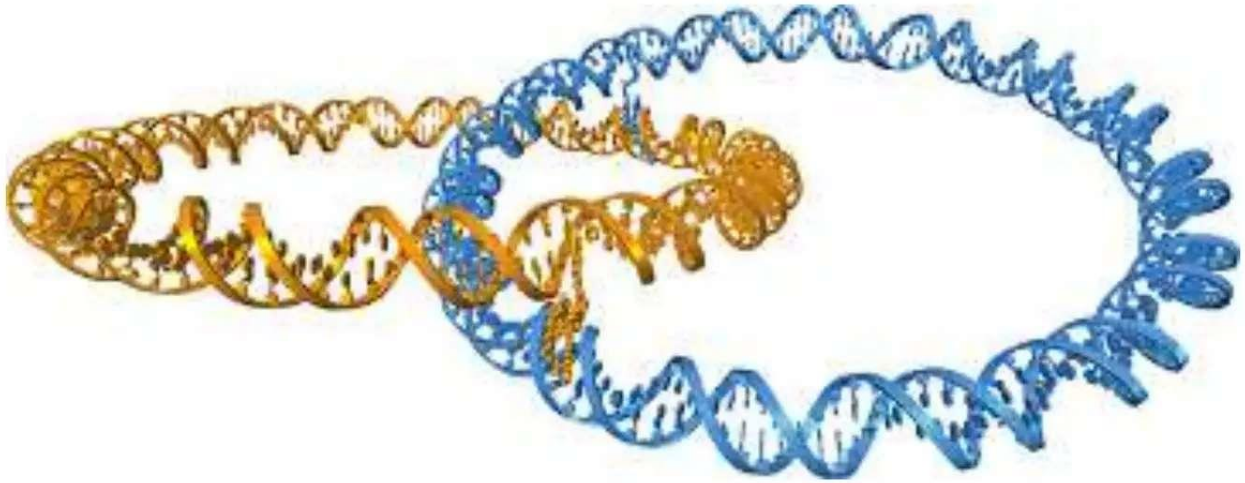
KNOTS

- Entanglement of flexible curves leads to knots



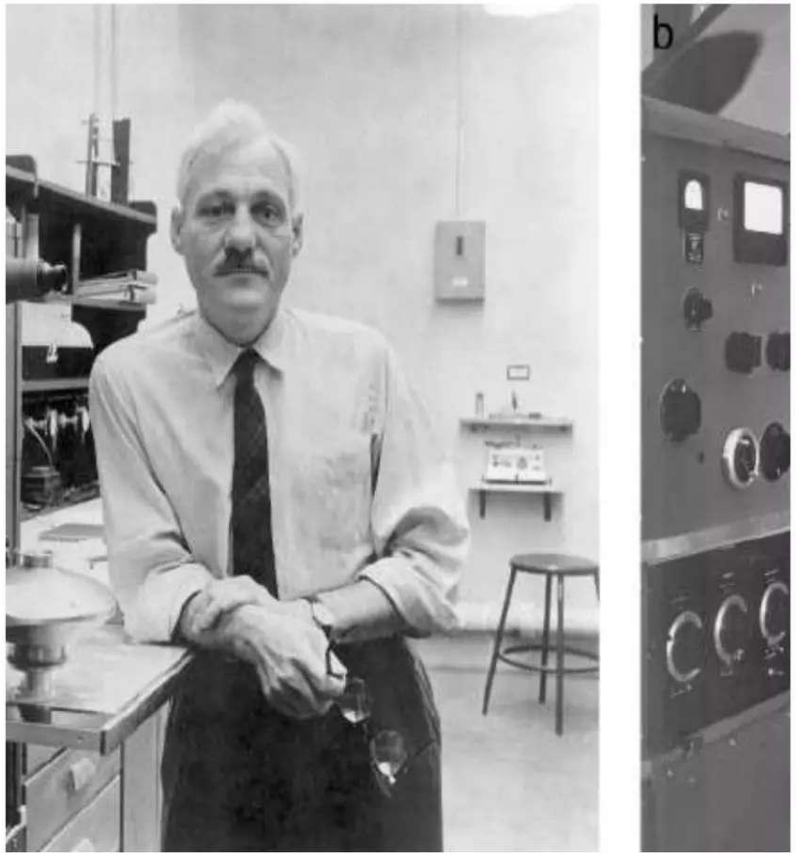
CATENANES

- Topologically linked circular DNA molecules are called Catenanes.
- Usually, they appear at the end of replication of circular DNA.



SUPERCOILING

- Super coiling refers to the additional twisting of a DNA strand
- Advantage of supercoiling
  - Reduce the space required for DNA packaging, allowing for more efficient storage of DNA
- First observed by Jerome Vinograd at the California Institute of Technology in 1963.

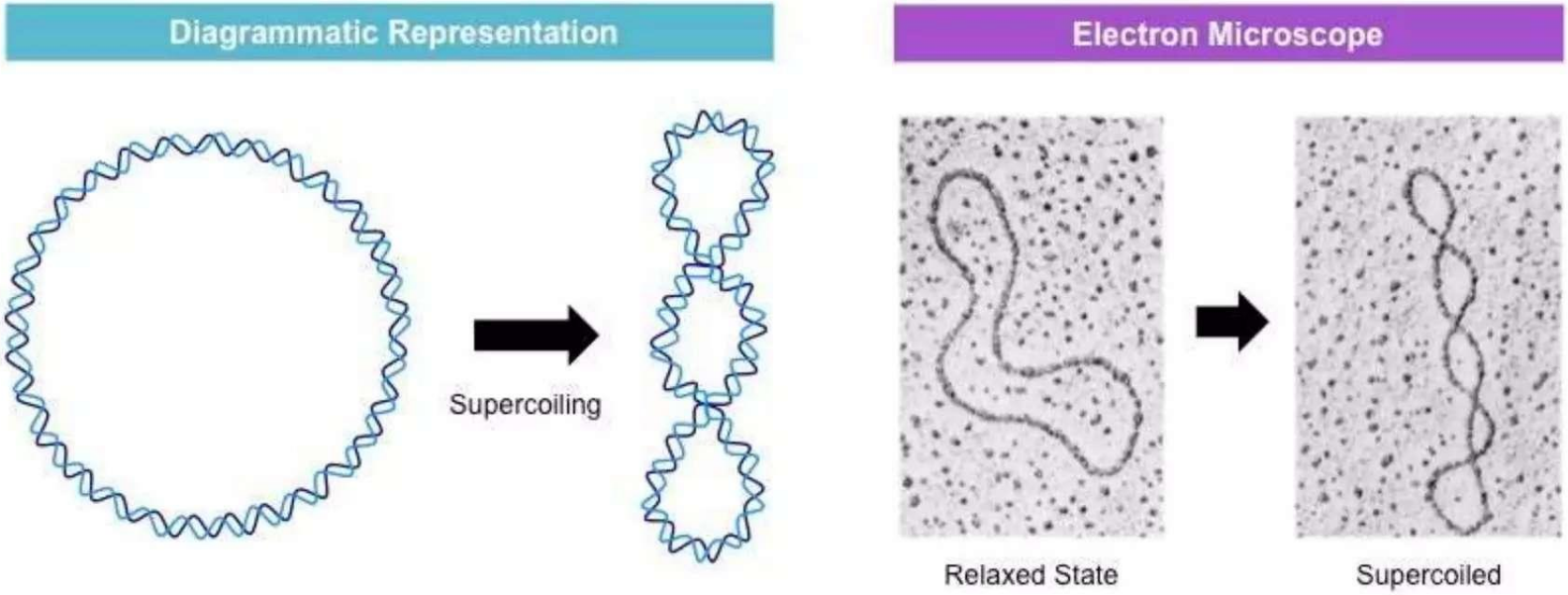


Vinograd: (February 9, 1913 – July 7, 1976), American biochemist

OBSERVATION

- Jerome Vinograd and his colleagues observed two closed, circular DNA molecules of identical molecular mass exhibit very different rates of sedimentation during centrifugation.
- Further analysis indicated that the DNA molecule sedimenting more rapidly had a more compact shape because the molecule was twisted upon itself and occupies a smaller volume and moves more rapidly

SUPER COILING



When *same type of molecule in a supercoiled state and relaxed state is* subjected to gel electrophoresis, the highly compact, supercoiled form moves rapidly. The same when subjected to ultra-centrifugation, supercoiled DNA settles at the bottom more faster.

Overwound DNA

- Positive supercoiling
- Positive supercoiling of DNA occurs when it is twisted even tighter until the helix begins to distort and "knot.“
- Rarely DNA forms positive supercoiling eg: positive supercoils in front of the transcription site

Underwound DNA

- Negative supercoiling
- Involves twisting *against* helical conformation which preferentially underwinds and "straightens" at low twisting stress, and knots the DNA into negative supercoils at high twisting stress.
- Most DNA is negatively supercoiled. Eg: Circular DNAs like mitochondrial, viral, Bacterial and eukaryotic chromosome.

ENZYMES IN DNA TOPOLOGY

- **Topoisomerases** – enzymes that change the topology of the DNA.
- The first DNA topoisomerase was discovered by James Wang in 1971
- Cells contain a variety of topoisomerases
- Broadly classified as
    - Type I topoisomerases
    - Type II topoisomerases

Chinese-born American biochemist and biologist

Topoisomerases

Type I topoisomerases

- It create a transient break in one strand of DNA
- Convert supercoiled DNA to relaxed form.
- Plays significant role during DNA replication and transcription

Type II topoisomerases

- Transient break in both strands
- It can supercoil and relax DNA, tie a DNA molecule into knots or untie; *cause a population of* independent DNA circles to become interlinked (*catenated)* or vice versa.
- Human topoisomerase II is a target for drugs (e.g., etoposide and doxorubicin) to prevent resealing of DNA in rapidly dividing cells and are therefore used in the treatment of cancer

Questions:

Q: What does DNA topology describe?
A: DNA topology describes how the two complementary strands of DNA are intertwined, including features like supercoiling, knots, and catenanes.

Q: What is supercoiling and what is its advantage?
A: Supercoiling is the additional twisting of a DNA strand, and its advantage is that it reduces the space required for DNA packaging, making DNA storage more efficient.

Q: **What is the main difference between Type I and Type II topoisomerases?**
A: Type I cuts one DNA strand; Type II cuts both strands.

Q: What is the difference between positive and negative supercoiling?
A: Positive supercoiling occurs when DNA is overwound, while negative supercoiling occurs when DNA is underwound.

Mcq

Q: Which statement correctly describes Type II topoisomerases?

A) They cut only one strand of DNA
B) They relax DNA without using ATP
C) They cut both strands of DNA and can supercoil or relax DNA
D) They only function during transcription

Positive supercoiling of DNA occurs when:

A) DNA is relaxed
B) DNA is underwound
C) DNA is overwound and twisted tighter
D) DNA is broken into fragments

Q: Most DNA is found in which supercoiled form?

A) Positive supercoiling
B) Negative supercoiling
C) Relaxed form
D) Linear unwound form

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