MATH:7450 (22M:305) Topics in Topology: Scientific and Engineering Applications of Algebraic Topology

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http://www.math.uiowa.edu/~idarcy/AppliedTopology.html
Biologically relevant topological structures of DNA. Depicted are schematics of the three topological forms of DNA that topoisomerases maintain and modulate.

CATCG

G

TAGCG

G

CAGCG

G

TAGCG

G

nick

nick

CATCG

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TAGCG

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CAGCG

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TAGCG

G
DNA substrate = starting conformation of DNA before protein action

Usualy unkotted, and supercoiled

Meiotic double-strand breaks in yeast artificial chromosomes containing human DNA

Grzegorz Ira, Ekaterina Svetlova, Jan Filipski

http://www.personal.psu.edu/rch8/workmg/Struc_Nucleic_Acids_Chpt2.htm
Structure of the nucleosome.

Barbi M et al. Interface Focus 2012;2:546-554
One of the many possible models of chromatin fibre, in a more condensed (a) and a less condensed (b) configuration.
FIGURE 12  Typical conformations of nicked circular DNA 3500 base pairs in length. The illustration was obtained by computer simulation of the equilibrium conformational set (Klenin et al., 1989). The values of $W_r$ for each simulated conformation are shown.
supercoiled DNA

\[ [\text{Na}^+] = 0.2 \text{ M} \]

\[ [\text{Na}^+] = 0.01 \text{ M} \]

\( W_r = -18.3 \)

\( W_r = -18.8 \)

\( W_r = -10.7 \)

\( W_r = -10.4 \)

FIGURE 16 Typical simulated conformations of supercoiled DNA in solution containing 0.2 M NaCl (left) and 0.01 M NaCl (right). The conformations of the model chains correspond to DNA 3.5 kb in length and \( = -0.06 \).
Topoisomerase II performing a crossing change on DNA:

Proposed mechanisms for type I topoisomerases.

Dekker N H et al. PNAS 2002;99:12126-12131
Topoisomerase are involved in

• Replication
• Transcription
• Unknotting, unlinking, supercoiling.
• Targets of many anti-cancer drugs.
Type II topoisomeraseases are proteins which cut one segment of DNA allowing a second DNA segment to pass through before resealing the break.
Supercoiled DNA-directed Knotting by T4 Topoisomerase*

(Received for publication, April 25, 1991)

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Simplification of DNA Topology Below Equilibrium Values by Type II Topoisomerasers

Valentin V. Rybenkov, Christian Ullsperger, Alexander V. Vologodskii, Nicholas R. Cozzarelli*

Type II DNA topoisomerasers catalyze the interconversion of DNA topoisomers by transporting one DNA segment through another. The steady-state fraction of knotted or catenated DNA molecules produced by prokaryotic topoisomerasers was found to be as much as 80 times lower than that of the enzymes. These enzymes also yield a tighter distribution of DNA topology below equilibrium. Thus, topoisomerasers do not merely juxtapose DNA segments but control a global property of the DNA. It is tempting to speculate that type II topoisomerasers use the energy of the reaction to preferentially remove the topological links that pose a hindrance to transcription.
What products would you predict if topoisomerase acted exactly once on the following 5 crossing knot?
Lynn Zechiedrich and Jennifer Mann, unpublished result.
All possible topoisomerase-mediated reaction pathways from the unknot to 5.1 involving rational knots with less than 14 crossings.

Darcy I K et al. Nucl. Acids Res. 2008;36:3515-3521
How can topoisomerase acting locally determine best action for global result, unknottning the DNA??
Model of type II topoisomerase action.
DNA disentangling by type-2 topoisomerase.

Buck GR, Zechiedrich EL.
The hooked juxtaposition hypothesis.

(a) 

(b) 

The juxtaposition-centric computational approach.

Recombination:

Direct Repeats

Inverted Repeats