Twisted Genetics: DNA and Knots

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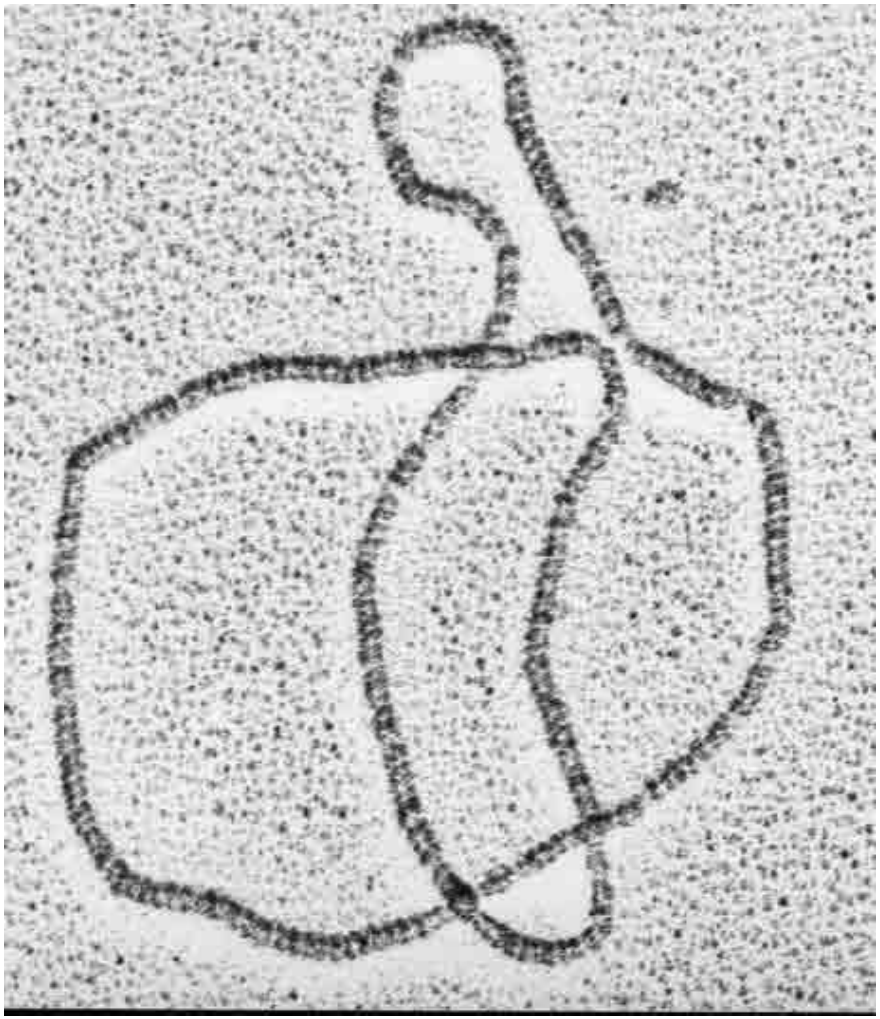
Intersession 2017
Hitchhiker's Guide to Algebraic Topology

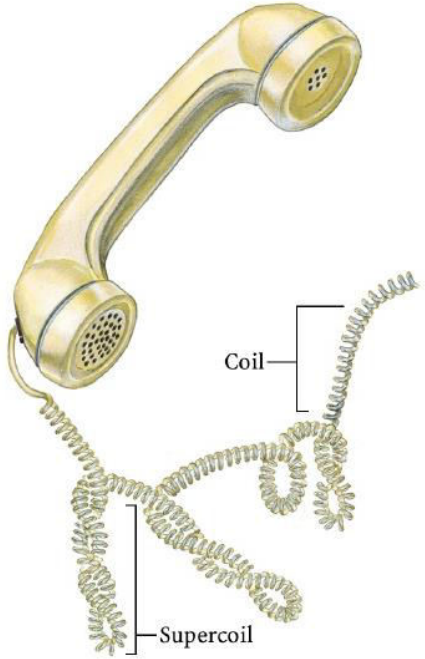
Not Just Circles

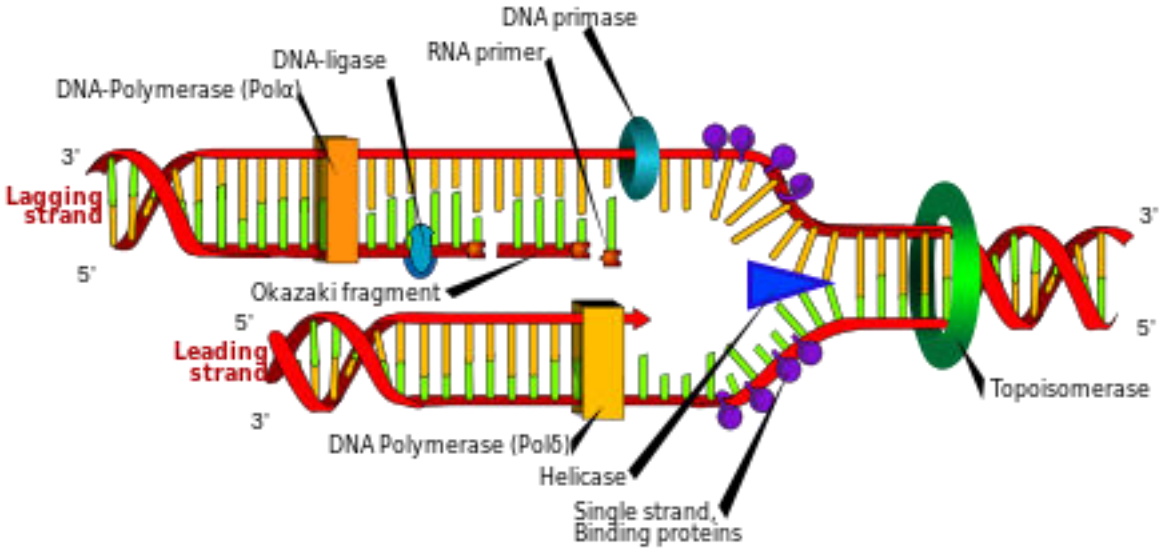


- Need to create compact structures like chromosomes
- Happens because the DNA is most stable as a low tension state
- Result of super coiling of DNA

Super Coiling

- Natural Occurrence during DNA replication





- Can actually inhibit further DNA replication

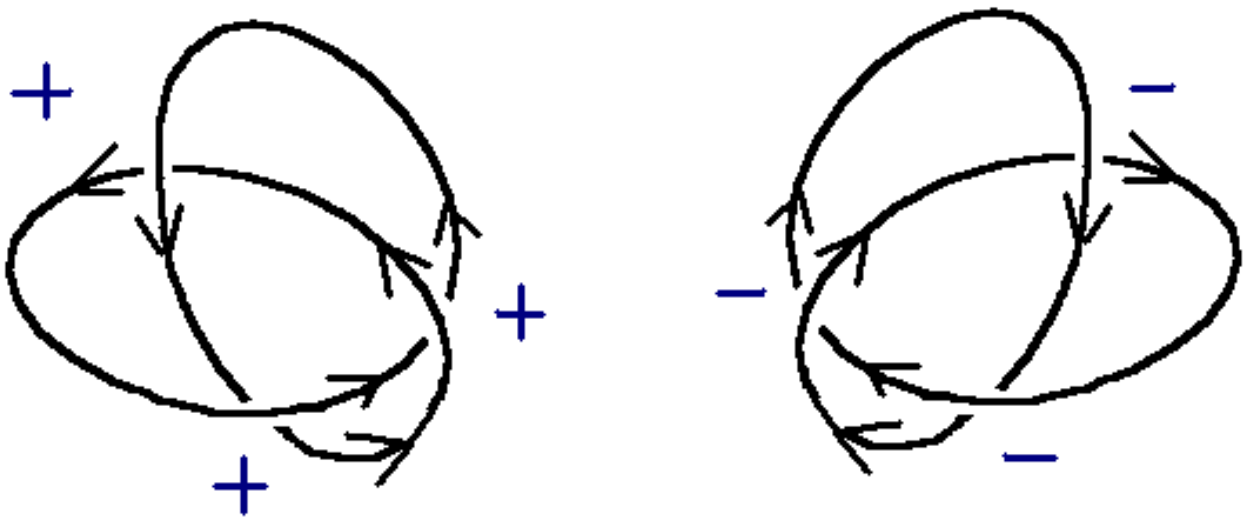
Importance of DNA Knots

- DNA needs to move between knotted and unknotted form for DNA replication and transcription
- Affects DNA expression, thus affecting cell characteristics
- Cells can uses it as an additional level of epigenetic control

Basic Classifications Used

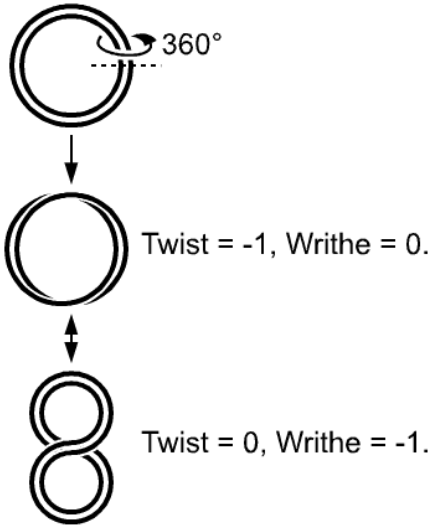
- Double points is just a fancy name for crossings
- Writhe= sum of orientation at each double point (+1 for clockwise, -1 for counter-clockwise)
- Twist=how many times the DNA spirals
- Linking Number= Twist + Writhe
  - The linking number always stays the same not matter how the DNA is changed unless something is cleaved

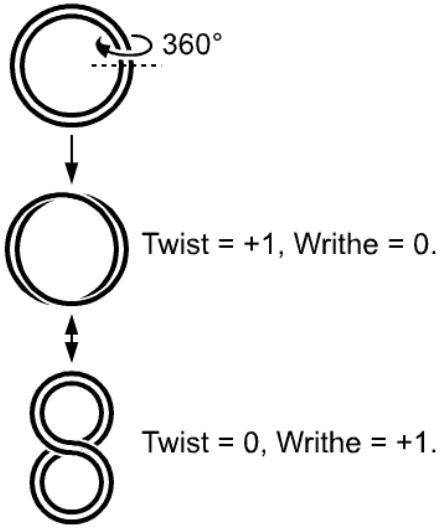
Example of DNA Knot Classification

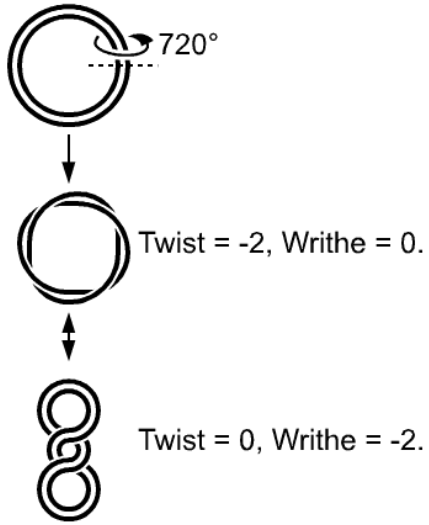


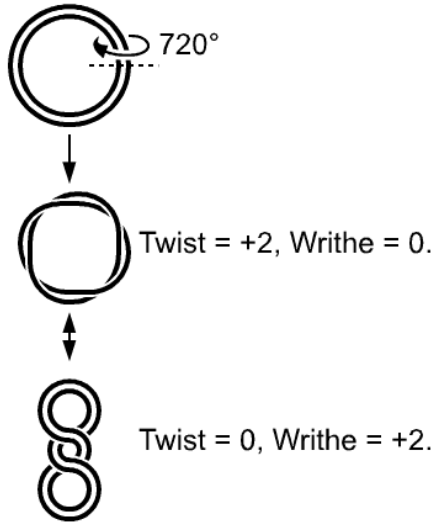
A trefoil in its two form with writhe numbers of +3 and -3 respectively

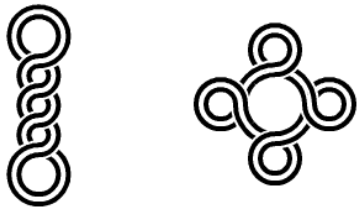
Example of DNA Knot Classification



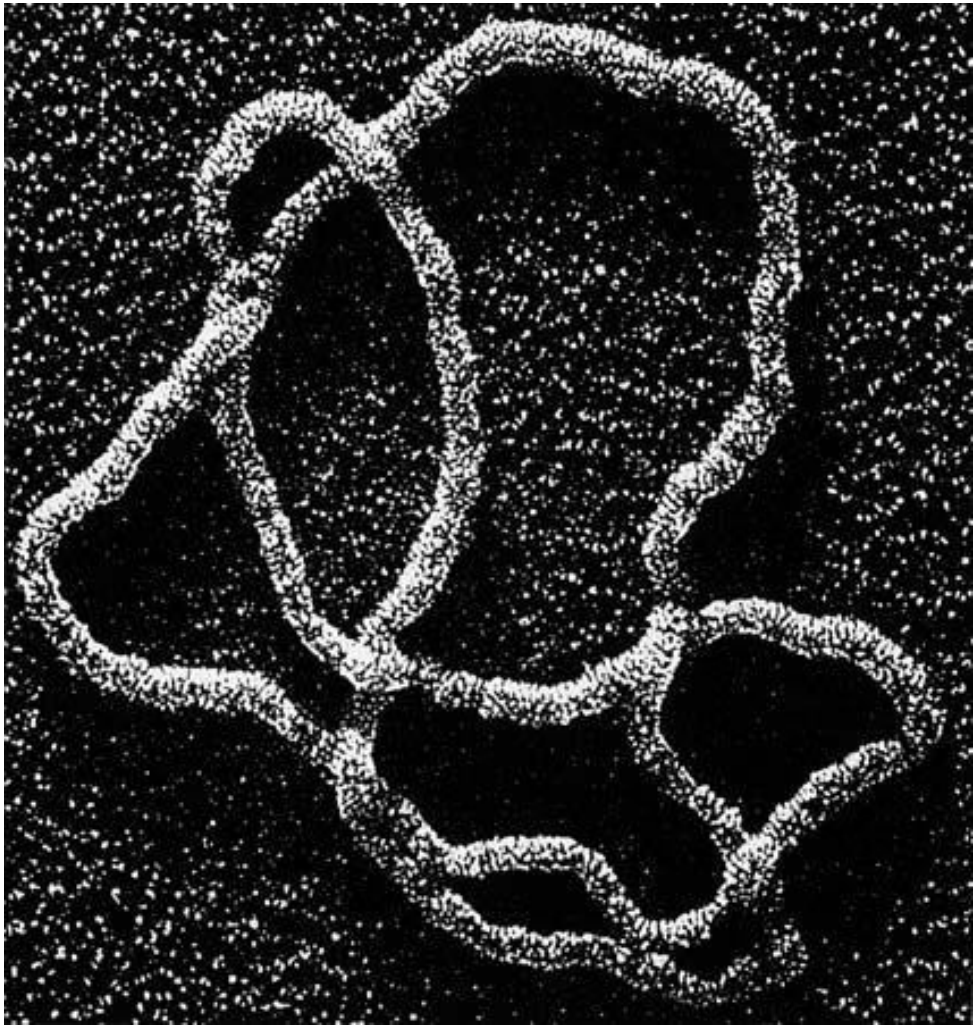






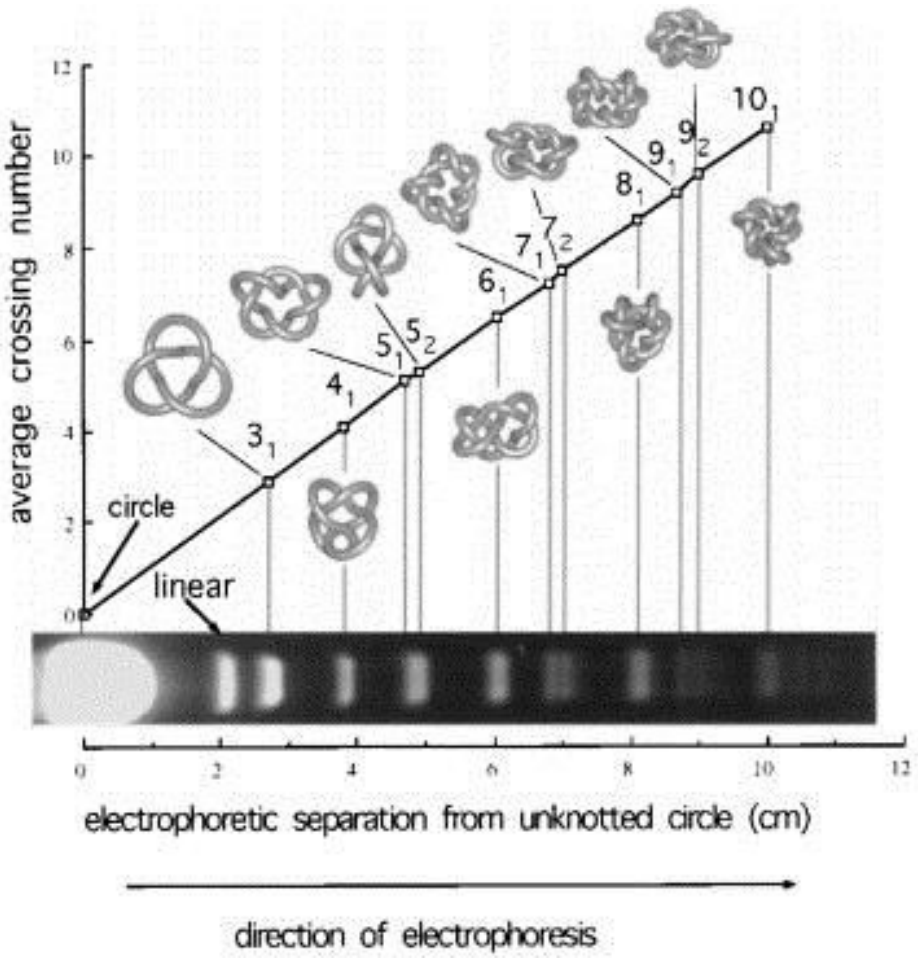


Electron Microscopes



- Uses protein coating to see surface
- Requires very high resolution to know exactly what is happening at each crossing

Using Gel Electrophoresis



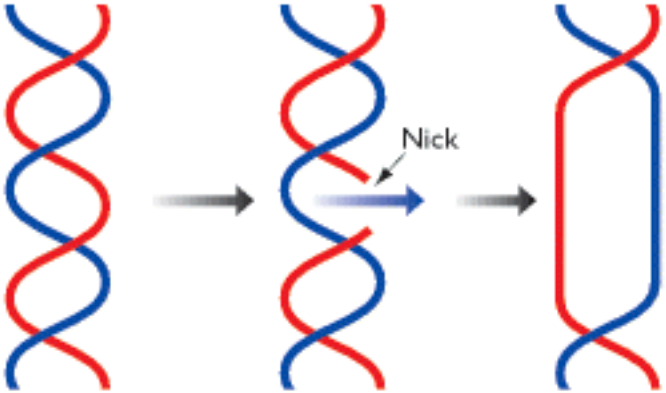
- Relates the Crossing Number of a DNA knot to gel electrophoresis
- Almost an exact linear relationship
- Allows researches to more easily determine a knot without using a scanning electron microscope

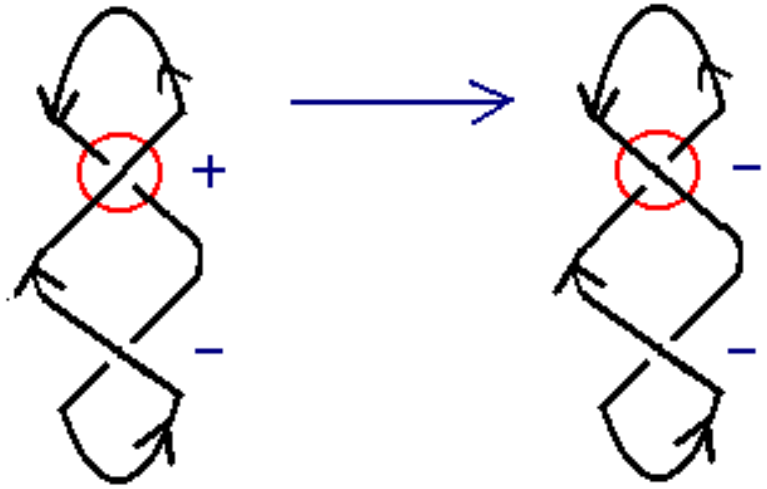
The Enzymes

Topoisomerases

Type I

Type II

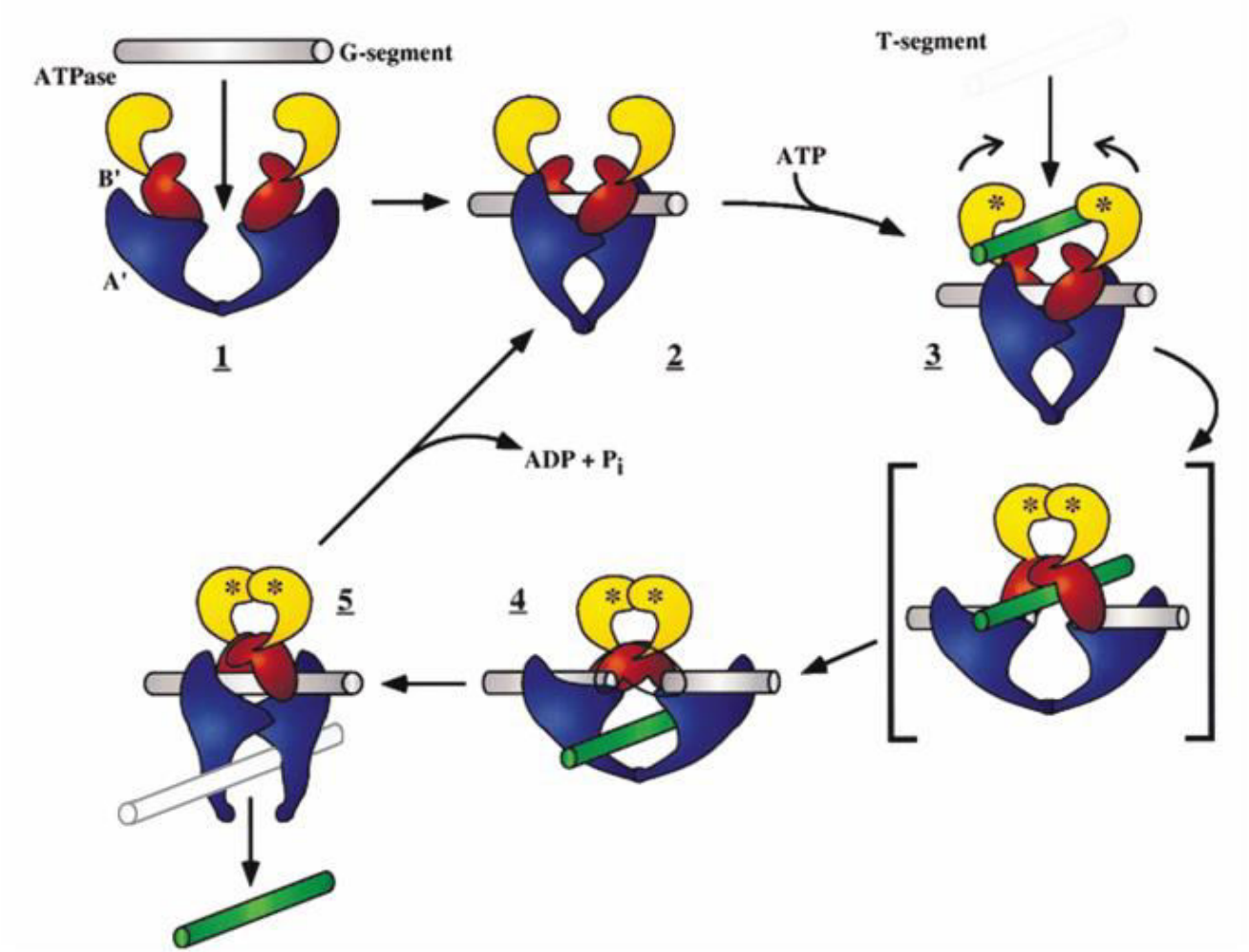




Relieves Twists and Stress

Unknots a knot

Type II Topoisomerase Mechanism

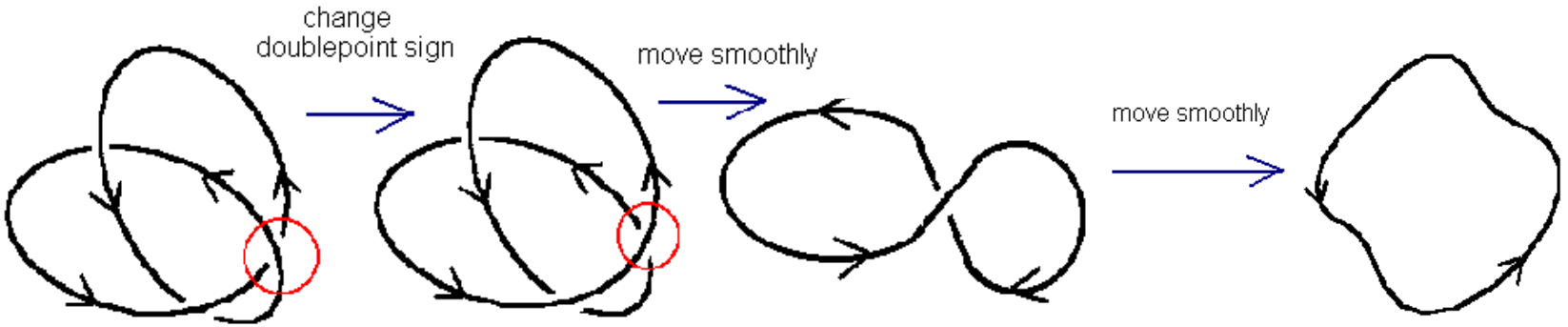


Topoisomerase Inhibitors as Cancer Treatment

- Prevents the ligation step of topoisomerase
  - Doesn't allow the DNA to reform a double helix
- Introduces double and single strand breaks in the DNA
- Cell discovers breaks during replication and then commits cell suicide (apoptosis)

The Unknotting Number

- How many action of the type II topoisomerase are needed to get the unknot



- Determines the reaction rate of unpacking the DNA

Questions?