DNA Topology Notes
Jason Kahn

Best source: Bates and Maxwell, “DNA Topology”

Helical nature of DNA has profound implications: DNA being long, stiff, and helical means that there is potential for long-range communication between sites but also long-range interference between processes. DNA transcription, replication, and recombination all are affected by:

DNA Topology

DNA topology is one of the hardest concepts in molecular biology. It is fundamental to all DNA transactions, though often ignored. We can get away with this only because the cell has devoted a huge amount of machinery to solving topological problems. Does a Lexus driver know all the adjustments the hundreds of on board computers make?

Topology is the study of properties of materials that depend on connectivity among parts rather than on their particular shapes: they are invariant to shape changes. Examples include the four-color map theorem (seven colors for a donut), or the fact that a coffee cup with one handle and a donut are topologically the same, geometrically and gastronomically different. Taking a bite out of a donut makes it topologically the same as a sphere. Think of a piece of Teflon-coated Silly Putty in the shape of either cup or donut. Our model for DNA is the rubber hose. When the two strands are ligated to form a closed (topological) circle, then we can define topological invariants and geometric variables.

Definition of Linking Number: The number of times one strand crosses the other. Always an integer, invariant to shape changes. Can only be changed by breaking and rejoining at least one strand. The same molecule can be converted into different forms with different linking numbers: “topoisomers.”

Illustrate calculation of linking number from two intertwined strands.

$Lk° = $ Lk of relaxed DNA = N bp/hr bp/turn. Note that this need not be an integer, which becomes very important for the properties of small DNA. The nearest integer is Lk_m
$\sigma = (Lk - Lk°)/Lk°$ = superhelical density

It is energetically expensive to supercoil DNA, with the free energy being proportional to the square of superhelical density (for large DNA). As we will see, supercoiling must show up as either substantial bending or else overtwisting/melting. This means that energy can be stored in supercoiling.

Turns out that linking (crossing over of one strand on the other) can be partitioned into Twist and Writhe (Tw and Wr), and that

$$Lk = Tw + Wr$$

Tw and Wr are geometric, not necessarily integers (in fact, only integers for DNA constrained to have its helix axis in a plane), and they can interconvert.

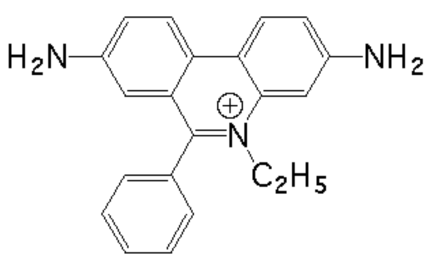
Twist is the local intertwining of the backbones, the familiar helical structure.

Tw° = N (bp)/hr (bp/turn) relaxed twist
Wr° = 0

Writher is the non-planarity of the helix axis itself. It can be calculated from a double integral over all the inter-contour vectors. It's more intuitive to think of counting nodes, and the writhe is then the average of counting nodes from all possible viewpoints. A "tight node" will be visible from almost all angles.

Draw interconversion of plectoneme, solenoid, bubble, untwisted form. Energy stored in DNA can drive the formation of an transcription bubble. Also, note that in the plectoneme the DNA helix axes approach each other closely, leading to dramatic enhancement in the probability of forming DNA loops, that would otherwise be limited by the high enthalpy of bending.

Note that the negatively supercoiled plectoneme is a right-handed superhelix, solenoid is left-handed. Plectoneme is the form adopted by free DNA, toroid is the form of supercoiling seen in nucleosomes. Leads to remarkable compaction.
Intercalating drugs like ethidium bromide also can interconvert among superhelical forms, and this is seen/used practically in agarose gel electrophoresis of plasmids and also in making negatively supercoiled DNA.



ethidium

Concept of restrained and unrestrained supercoiling. Restrained is held in place by proteins, i.e. it is thermodynamically stable, paid for by protein-DNA binding energy. Unrestrained is not thermodynamically stable. It is induced by motor proteins like polymerases or by DNA gyrase, which burns energy to induce supercoiling.

Anything this important will be highly regulated…topoisomerase enzymes are essential to life. For example, in cell division, Lk must go from N/10.5 (about 500000 for E. coli) to zero between parental DNA strands. We will discuss Type I and Type II topoisomerases