Important Points on DNA topology

1. Topology applies strictly to covalently closed circular DNA molecules. Within the cell, even linear DNA molecules (linear chromosomes, for example) are constrained by anchoring proteins to form closed domains. The rules of topology are applicable within these closed domains.

2. When you apply the thumb rule to define the sign of a DNA node, make sure that you ***really*** cross the thumb over the index finger. Place the thumb over the index finger such that they make an angle of ~90 degrees.

   A node that matches the thumb-index finger crossing of the right hand has a + sign. A node that matches the thumb-index finger configuration of the left hand has a – sign.

3. In the context of a normal DNA node, the thumb represents the segment of the strand on the top; the index finger represents the strand at the bottom.

4. In the context of supercoiled DNA, the thumb represents the double helical segment at the top; the index finger represents the DNA segment at the bottom. Or, you may think of this node as one formed by the crossing of the DNA axis over itself.

5. For right handed DNA, a crossing between the two strands has a positive sign and a magnitude of ½. For every complete turn of DNA, there are two such crossings. Hence, according to our convention, one complete turn of DNA contributes a linkage unit Lk = ½ + ½ = 1.

   For left handed DNA, the Lk contribution by one turn of DNA is (-1/2) + (-1/2) = -1.

6. Remember the Linkage relationship: Lk = Tw + Wr

   Lk is integral; Wr and Tw may be integral or fractional.

7. Twist is description of the way one DNA strand winds around the axis or the second DNA strand. The local twist represents the angular displacement of the strand when one moves a very short distance from point A to point B along the DNA axis. When the DNA axis is planar, the twist measures the number of turns a strand winds around the axis. Twist is an integer in this case.

8. Writhe measures the crossings of the DNA axis over itself, and denotes the non-planarity of the axis. When the axis is entirely planar, there are no crossings of the axis, and writhe becomes equal to zero. This represents the relaxed state of DNA, where Lk becomes equal to the twist.

9. A supercoiled node is created by the crossing of the DNA axis, or the crossing between two segments of the duplex DNA. At this node there are four strand crossings: One W/C; one C/W; one W/W; one C/C (W = Watson strand; C = Crick strand). Contrast this with a normal DNA node, where there is one crossing between strands (either W/c or C/W). At the supercoiled node, the linkage contribution is made by the W/C and C/W crossings; the C/C and W/W crossings do not contribute to linkage. Hence the magnitude of a supercoiled node = twice the magnitude of the strand crossing in DNA = ½ + ½ = 1. The sign of the node depends on whether the supercoiling is

positive or negative. In negative supercoiling, by our thumb rule convention, the node sign is negative (-). In positive supercoiling the sign is positive (+).

10. Negatively supercoiled DNA is underwound; positively supercoiled NDA is overwound. Both are under torsional stress. They are in higher energy states than relaxed DNA. When a strand is nicked it will rotate around the axis to remove the torsional stress and return to the relaxed state. The direction of rotation in the two cases is opposite. For the same degree of supercoiling, both positive and negative supercoils release the same amount of energy upon relaxation.

11. Superoiling can be plectonemic or solenoidal. Supercoiling of plasmids in bacterial cells is plectonemic, the supercoiling of chromosomes around histone cores in eukaryotes is solenoidal. When the torsional stress of supercoiling is left on its own, it is accommodated primarily by twisting deformation of the axis (plectonemic supercoiling). When it is supported by a protein core, it is accommodated primarily by a bending (writhing) deformation. This relates to the fact that writhe and twist are interchangeable, one can be readily partitioned into the other (remember the demonstration in class).

12. A plectonemic supercoil node and a solenoidal supercoil node have the same magnitude, 1. For negative supercoils, the sign is negative (-); for positive supercoils, the sign is positive (+).

13. The handedness switches when a plectonemic super coil is converted into a solenoidal one. A negative supercoil is right handed in the plectonemic form; it is left handed in the solenoidal form. A positive supercoil is left handed in the plectonemic form; it is right handed in the solenoidal form.

14. Toposiomerases change linking number in DNA. Type I enzymes change linking number in units of one. This is because they cut single strands, and reseal after single strand passage. Type II enzymes change linking numbers in units of two. This is because they cut double strands and reseal them after passage of a double stranded DNA segment.

15. Remember the different ways in which negative supercoiling helps physiological processes in the living cell:

    (A) It helps compaction of DNA and packaging of genomes into the small volumes of prokaryotic cells or eukaryotic nuclei.

    (B) The dynamic slithering (reputation) and branching in supercoiled DNA can facilitate distant DNA sites to come into proximity.

    (C) Negative supercoiling can promote processes that require strand separation (replication, transcription) by helping local DNA unwinding.

    (D) Negative supercoiling can help bending of DNA and assist the binding of proteins that bend DNA. An example is formation of nucleosomes, the basic unit of chromatin in eukaryotic nuclei (solenoidal supercoiling).

(E) The energy of supercoiling can be utilized to assemble protein-DNA complexes with a defined DNA path within them. The precise topologies of these complexes are critical for the chemical steps of the reactions that they catalyze. (Wait for discussions of site-specific recombination; DNA transposition).

(F) It follows from (E) that supercoiling can serve as a topological filter that selects for defined orientations between two DNA sites (head-to-head or head-to-tail) that result in their productive interaction.

Summary

Please also go the ‘Summary’ where several of the points above are assembled in a series of slides.

Getting the topological concepts of DNA straight will help you immensely in following the logic of nearly all DNA transactions in the living cell in a clear and rational way.