# **DNA TOPOLOGY**



DNA (shown at the left) is a right handed helix.

**B**. The 'rise' of the helix' is the same as that of a normal carpenter's wood screw (shown at center). When you turn the screw driver in the clockwise direction (right handed sense), the screw is driven forward into a wooden board.

**C**. The projection of the double helix in the plane of the paper (shown at the right) denotes the crossings between the Watson strand (thick line) and the Crick strand (thin line). At each crossing (also called a 'node'), the continuous line is in the front (towards you); the discontinuous (broken) line is behind (away) from you.

For the purpose of the topological convention we use, we will ignore the opposite chemical polarity of the two DNA strands (one running in the 5' to 3' direction and the other in the 3' to 5' direction as one traverses along the DNA axis).

# The thumb rule:

For right handed DNA, Each crossing of the Watson-Crick strands can be represented by the two arrows at the left (remember that we chose to ignore the polarity of the DNA strands).

For left handed DNA, the crossing is represented by the two arrows at the right.



Now let us use the thumb as the top (continuous) arrow (or DNA strand) and the index finger as the bottom (broken) arrow (or DNA strand). So cross the thumb over the index figure (*and I mean really cross, by placing your thumb above the index finger*).

You see that the crossing at the left fits the thumb-index finger configuration of the right hand. In our convention we assign this crossing a '+' sign. As we discussed in class, the linkage contributed by this crossing (formed by the two strands or 'curves' in space) is +1/2.

The crossing at the right fits the thumb-index finger configuration of the left hand. We assign this crossing a negative sign. Or the linkage contributed by it is -1/2.

There are two crossings for every turn of DNA. Thus, in right handed and left handed DNAs, one turn of DNA contributes a linkage of 1. The sign in the former case is '+'; and in the latter case, it is '-'.

# Relaxed covalently closed circular DNA

A circular DNA molecule is relaxed if its axis, shown by the dashed line in the figure below, lies entirely in on plane, say the plane of the paper. The thick and thin continuous lines represent the two DNA strands.



Fig. 1

#### Supercoiled DNA

If we break a strand in a relaxed DNA circle, change the number of turns by adding or removing them, and close the strand again, the DNA will no longer be relaxed. It will be under torsional stress, and will absorb this stress by the double helix coiling over itself. Or in other words, the DNA axis crosses itself or is no longer planar. The DNA is said to be writhed or supercoiled. An under-wound DNA molecule (fewer turns than the relaxed state) is said to be negatively supercoiled. An over-wound DNA molecule is said to be positively supercoiled.

#### Linking number, writhe and twist: the linkage equation

The linking number Lk for a covalently closed circular DNA molecule is the number of times one strand crosses the other. For a relaxed molecule the Lk can be referred to as Lk0. Lk is a topological property of DNA.

Lk can be expressed as the algebraic sum of two geometric properties, twist (Tw) and writhe (Wr). Twist refers to the manner in which one strand winds around the second. Writhe refers to the non-planarity of the DNA axis.

### Lk = Tw + Wr

For relaxed DNA, Wr = 0; or Lk = Tw. That is, twist is equal to the number of turns between the Watson and Crick strands.

However, In supercoiled DNA, Lk is not equal to Tw, since Wr is no longer non-zero. Imagine that you break the strand in a relaxed molecule, and reseal it after taking out 'n' turns (see Fig. 2). The DNA is now under-wound or negatively supercoiled. As a result, the tendency of the axis is to be non-planar.

Let us now imagine that by some means, we counteract this force, and keep the axis planar. Hence we impose zero writhe in the molecule as shown at the left in Fig. 2. This is one extreme way of accommodating the torsional stress. In the other extreme, we let the stress to be counteracted entirely by coiling (non-planarity) of the axis, that is, entirely by writhe. In reality, supercoiled DNA consists of all possible dynamic conformations ranging from the one shown at the left (no writhe) to that shown at the right (no change in twist). Or, supercoiling, which is a change in Lk, can be partitioned into Tw and Wr in a myriad ways.Let us illustrate supercoiling with a simple example as follows. Imagine a relaxed DNA circle with a 1000 bp. We assume that there are 10 bp per every turn of DNA. Or this molecule contains a 100 turns, or its Lk0 = 100. Lk = Tw + Wr; In our relaxed molecule, Wr = 0.

Lk0 = 100 = Tw + 0

Let us remove 20 turns from this molecule by breaking a strand and resealing it. Now there are only 80 turns in this molecule, or Lk = 80.

$$Lk = 80 = Tw + Wr.$$

If we force the axis to be planar, thus keeping Wr = 0,

80 = Tw + 0

The twist is now 80, and therefore the pitch of the helix changes, it is no longer 10 bp per turn, rather 1000/80 or 12.5 bp per turn. This is the case illustrated in Fig. 2 at the left.



Now, let us keep the twist the same (100 turns; 10 bp per turn), and partition the negative supercoiling entirely into writhe.

Lk = 80 = 100 + WrWr = 80 - 100 = -20

Or the axis coils over itself 20 times. This is negative supercoiling. By our thumb rule convention, the signs of these negative supercoil nodes are minus (see Fig. 3 below).

f you do the above exercise by adding 20 turns, you get positive supercoiling, and the signs of the supercoil nodes will be positive (Fig. 3).



# **Plectonemic supercoiling**

Note that the superhelices in Fig. 3 are plectonemic, that is, one double helical segment winds around another (just like the Watson strand winds around the Crick strand in the normal DNA helix). The negative superhelix has a right handed configuration. The positive superhelix has a left-handed configuration.

DNA supercoiling in bacterial plasmids and chromosomes are of the plectonemic variety. Read further for another type of supercoiling.

**Warning**: Please don't confuse the handedness of a helix with the right hand or left hand thumb rule we used to assign node signs. The handedness of a helix simply tells you whether it follows the threading of a carpenter's screw (right handed) or is the other way round (left handed). Sorry, we have only two hands; not four! So keep the conventions straight!



### Solenoidal supercoiling

Supercoiling can also be of the solenoidal type (Fig. 4; right). In eukaryotes, negatively supercoiled DNA is wrapped around the histone core. Topologically, solenoidal supercoiling and plectonemic supercoiling are equivalent. That is, negative supercoils have a minus sign in both cases, and positive supercoils have a plus sign. However, the handedness of the supercoil wrap (or helix) is opposite in the two types. Plectonemic negative supercoiling gives a right handed helix with minus nodes; solenoidal negative supercoiling gives a left handed helix, also with minus nodes. Plectonemic positive supercoiling gives a left handed helix with plus nodes; and solenoidal positive supercoiling gives a right handed helix with plus nodes as well.

### Final Reminder!!

1. Normal double stranded DNA is a double helix; it is plectonemic; the Watson strand coils around the Crick strand and vice versa.

2. The DNA superhelix is also a double helix; it may be plectonemic (prokaryotes) or solenoidal (eukaryotes); Here rather than two strands, two double helical segments coil around each other; hence the name superhelix (a super double helix formed from two normal double helices).

3. The thumb rule is used to assign only node signs; + for Watson-Crick crossings in right handed DNA; + for positive supercoil nodes; - for negative super coil nodes. It does not say anything about the handedness of supercoils.

4. To assign handedness for plectonemic or solenoidal supercoils, use the right handed carpenter's screw as the reference.