Linking number can be understood in the terms of two structural components called as writhe (Wr) and twist (Tw).

Writhe can be understood as a measure of the coiling of the helix axis (imagine the writhing in snakes) and twist can be understood as local twisting or spatial relationship of neighboring base pairs.

Whenever there is change in the linking number, some of the strain is compensated by writhe (supercoiling) and some by changes in twist. This can be written as following equation:

Lk = Tw + Wr

Tw and Wr are not always integers and are geometrical properties not topological properties. This is explained by the fact that these properties may be changed by deformation of a closed-circular DNA molecule.

However, changes in the linking number are accompanied by changes in the twist and writhe.

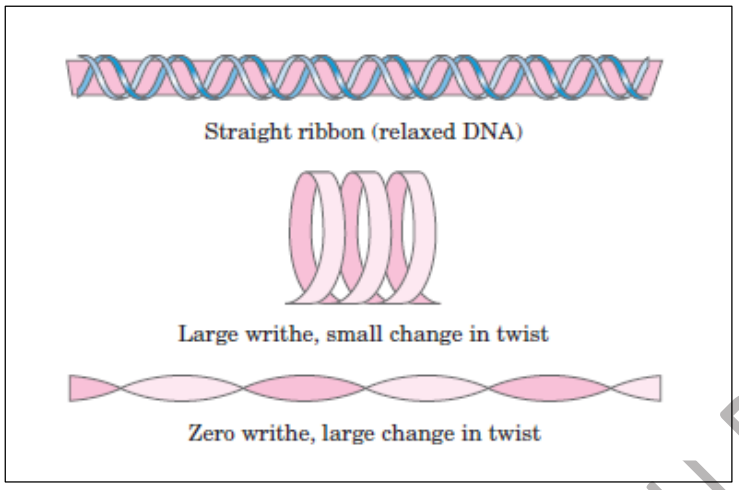

Figure: Ribbon model showing twist and writhe.

From the above discussion, we can understand that for a given closed-circular DNA molecule Lk is invariant. Thus, any change in the twist of DNA shall be accompanied by an equal and opposite change in the writhe and vice-versa. So, we arrive at equation:

ΔLk = ΔTw + ΔWr

In a completely relaxed cccDNA consider the following to understand the interlinking between twist, writhe and linking number.

cccDNA completely relaxed and planar, Wr = 0, so, Lk = Tw.

Assume that above DNA is opened and rotated four times at one end in untwisting sense and then sealed back. At the same time, it is being forced to stay in a plane.

Now, ΔLk = -4 and Wr = 0. Thus, ΔTw = -4.

Now, assume that we do not force the above cccDNA to stay in the plane after untwisting rotations. Now, to accommodate the strain generated by untwisting, there are four right handed superhelical turns.

$Wr = n\sin\gamma$. Here, n = number of superhelical turns and γ is superhelix winding angle and is usually very close to 90^o.

Thus, $Wr = 4 \times \sin 90^o = 4$. Since, ΔTw = 0, ΔLk = ΔWr = -4.

Effect of topology on gene expression:

In general sense, regulation of gene expression can be understood as sum total of all factors that determine whether the gene or group of genes is transcribed and/or translated. In case of topology, DNA supercoiling is an important factor in influencing the gene expression at transcriptional level. The topological issues related to transcription can be divided into two aspects:

1. RNA polymerase binding to the DNA.
2. Binding of transcription factors that influence transcription.

We will discuss the first aspect here for the sake of simplicity.

RNA polymerase binding: Transcription initiation is a complex process and involves various phases that can be regulated by DNA topology changes. Example of these phases are promoter location by RNA pol, formation of initiation complex, synthesis of first phosphodiester bonds and movement of RNA pol from promoter region. An example of change in DNA topology is the distortion caused in DNA upon binding of RNA pol.

The initial RNA pol complex with DNA is known as closed complex and ΔLk associated with its formation is -1.25. This value indicates that wrapping is left handed. At the start of the transcription, closed complex is converted to open complex and ΔLk is now -1.7 and strands around the -10 region in the promoter are completely unwound and separated over a length of 14bp.

It has been proposed that negative writhe associated with the closed complex is converted to untwisting of the promoter in the open complex.

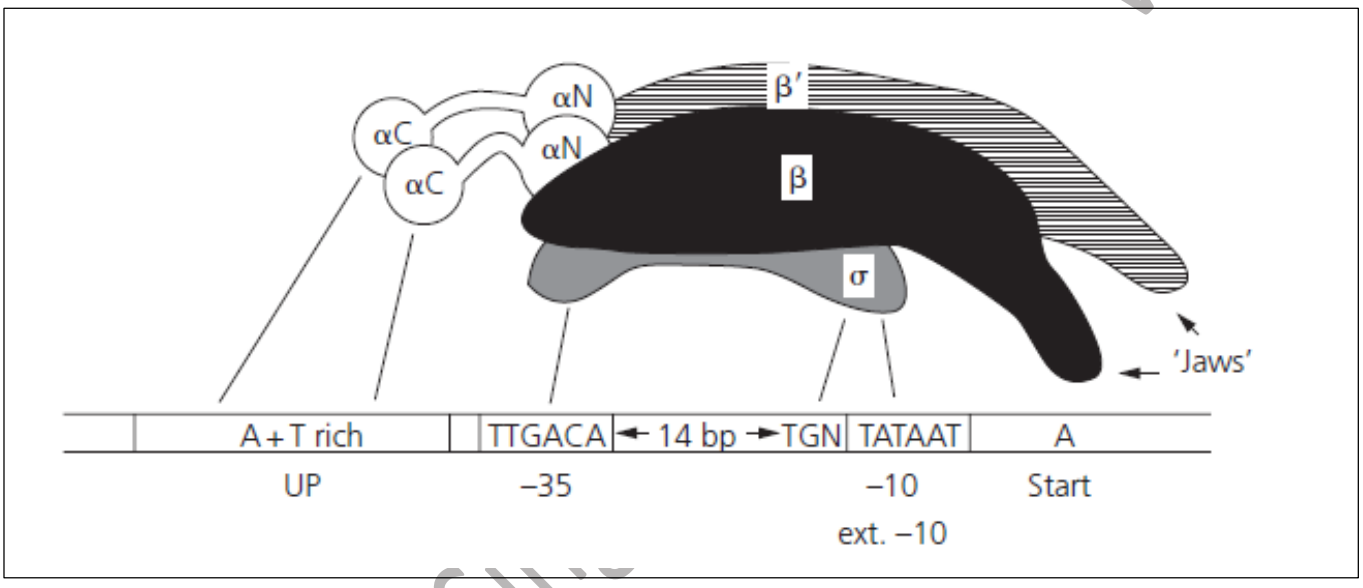

Figure: A schematic representation of *E. coli* RNA pol interacting with a typical promoter showing consensus -10 and -35 sequences. Also shown is the 14bp region that is untwisted on the formation of open complex.

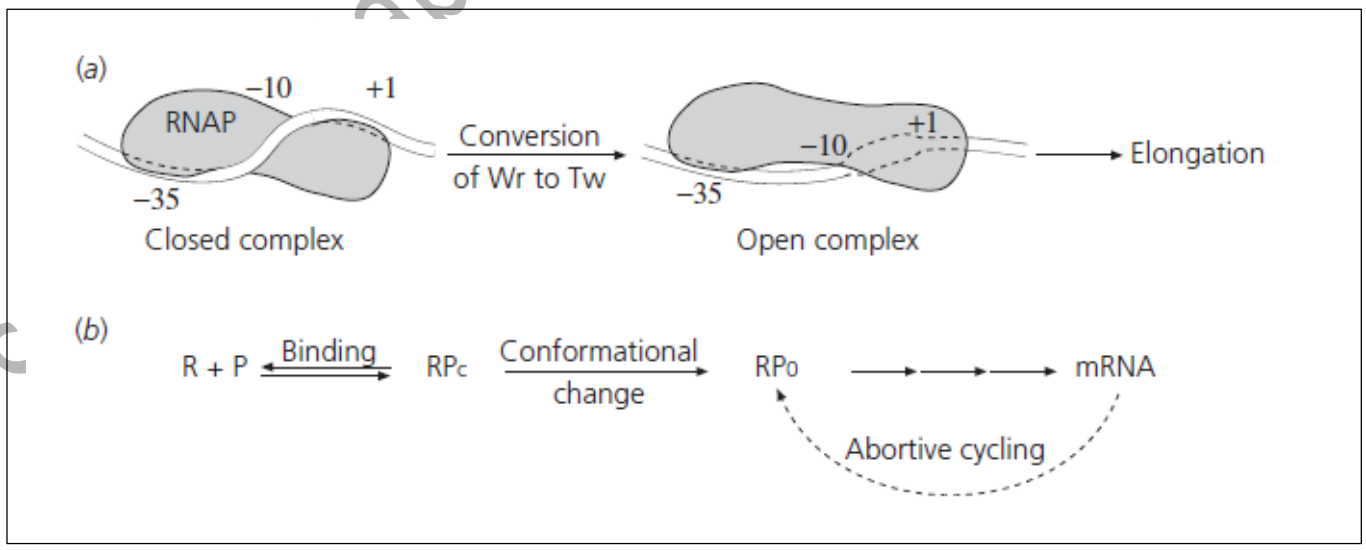

Figure: Transcription initiation at *E. coli* promoters. RPc = closed complex and RPo = open complex.

In general, transcription is promoted by negative supercoiling. However, when we consider one promoter at a time then most of them conform to the general principle but some are unaffected and others are inhibited. An example of these variations can be seen in the response of *E. coli* topoisomerase I and DNA gyrase gene promoters.

Increase negative supercoiling increases the rate of transcription from the topoisomerase I gene (topA) while it reduces initiation from the gyrA and gyrB genes encoding the subunits of DNA gyrase.

Environmental conditions affect the DNA topology which in turn affects gene expression and one such example is seen in case of proU promoter of *Salmonella typhimurium*. Transcription at this promoter increases in response to increased osmotic pressure. The osmotic pressure leads to increased DNA writhing which leads to increased supercoiling. These changes cause local helix destabilization which promotes formation of open complex stimulates transcription at proU promoter.