Stochastic Model of Supercoiling-Dependent Transcription

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Keywords: (DNA, supercoiling, transcription regulation)

DNA is involved in a lot of processes among which replication that is production of two identical replicas of DNA starting from one DNA molecule, and transcription in which a specific piece of DNA is copied into a new molecule: RNA. These processes are achieved by specialised enzymes as DNA polymerase (DNApol) for replication and RNA polymerase (RNApol) for transcription [1].

In order to do their job properly these enzymes need to separate the two complementary strands of DNA molecule and this can lead DNA double helix to a torsional stress that can increase the number of base pairs (bp) per turn of helix (overtwisting) or decrease it (untwisting) and eventually the DNA will tend to coil upon itself forming superhelices (helices of helices) [2]. This phenomenon is commonly known as supercoiling of DNA and it is due to the inherently chiral nature of DNA.

Several observations suggest that DNA supercoiling is intimately related to transcription and that it can regulate gene expression [3]. For example it is well known that RNA polymerase binding is more likely when the DNA molecule is slightly negatively supercoiled in the region of the promoter of the gene involved [2].

In the late 80s Liu and Wang developed the ``twin supercoiled domain" model [4] in order to explain some experimental results. The model is based on the observation that if rotation of the RNA polymerase and its associated transcription machinery is hindered then gene transcription leads to the creation of positive supercoiling ahead of the tracking polymerase and negative supercoiling in its wake (Fig. 1). Within this framework we propose a model [5] that incorporates the dynamics of supercoiling - where polymerases create supercoiling as they unwind the DNA helix - into a stochastic description of gene regulation [6].

We show that when the transcriptionally induced flux of supercoiling J created by RNApol increases, there is a sharp crossover from a regime where torsional stresses relax quickly and gene transcription is random, to one where gene expression is highly correlated and tightly regulated by supercoiling. In the latter regime, the model can displays transcriptional bursts and waves of supercoiling [5,8]. We consider both tandem and divergent or bidirectional genes.

We also show that in the case of a circular DNA molecule with overall positive supercoiling, we find a non-equilibrium phase transition between an absorbing phase, where all genes are switched off due to the supercoiling, and an active phase with a non-zero transcription rate [7].

Besides, within our model we analyse transcriptional bursting dynamics. We find a clear signature of bursty transcription when there is a separation between the timescales of transcription initiation and supercoiling dissipation by topological enzymes. In multigenic DNA domains we observe either bursty transcription, or transcriptional waves [8].

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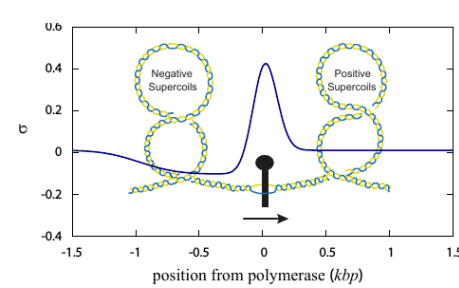
Figure 1. Twin supercoiled domain model and supercoiling density profile during transcription.
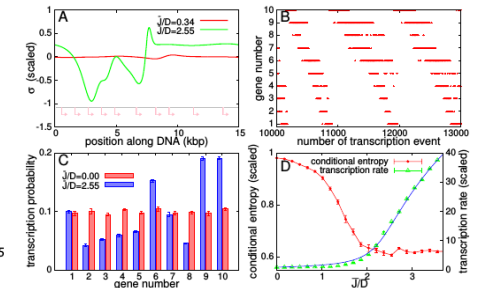

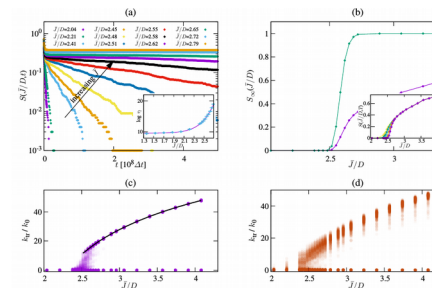Figure 2. Relaxed regime vs supercoiling regulated regime with ranscription waves.

Figure 3. Non-equilibrium phase transition between an absorbing phase and an active phase with non-zero transcription rate.