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Global and ancestral regulation by DNA supercoiling is tuned by promoters'structure

Usual models of transcriptional regulation are centered on transcription factors, which recognize specific sequences in genes'promoters. However, at a more global scale, the physical state of the double helix, embedded in the chromatin fibre, plays a crucial role in genes'expression in vivo. In particular, torsional stress (or DNA supercoiling) is an ubiquitous feature in DNA transactions, which has a strong influence on the initiation step of transcription in bacteria as well as eukaryotes, notably by strongly modulating the energetic cost of opening the double helix for RNA synthesis. DNA supercoiling may thus constitute an ancestral and global transcription factor, as suggested by many recent transcriptomics studies, but for which no quantitative or even qualitative model is available. I will present a thermodynamic model of supercoiling-assisted promoter opening which shows how promoters can be globally and selectively activated by supercoiling variations depending on their structure. Although it might be valid for both bacterial and eukaryotic promoters due to their common structural features, the quantitative analysis is carried more specifically on bacterial promoters, where DNA supercoiling plays a predominant role in the chromatin organization and more data have been accumulated. In vitro and in vivo transcription data are analyzed, which quantitatively confirm the predictions of the models. The universality of the mechanism, which is based on the basal interaction between RNA Polymerase and the promoter elements independently of any additional transcriptional regulator, is then demonstrated by analyzing transcriptomes of several distant bacterial species under conditions of supercoiling variations by antibiotics. We finally reproduce model predictions in vivo on individual promoters in Escherichia coli, by monitoring their expression during time and their response to opposite supercoiling variations. All together, our results demonstrate that DNA supercoiling could act as an important ancestral mode of regulation currently underestimated.

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