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Quantitative insights into topoisomerase activity during gene transcription

While the feedback between transcription and DNA supercoiling is well understood theoretically and *in vitro*, it remains to be quantified *in vivo*. In this talk, I will present our work where we fill this gap by realizing, on a plasmid in *Escherichia coli*, the conceptual "twin transcriptional-loop model"[1] that is the basis of theoretical and *in vitro* studies. In particular, we measured how gene expression varies with promoters and distances to the topological barriers. We find that gene expression depends on the distance to the upstream barrier but not to the downstream barrier, with a promoter-dependent intensity. I will then present a first-principle biophysical model of DNA transcription that is able to quantitatively rationalize these findings. This model integrates binding, initiation and elongation of RNA polymerases parametrized with available *in vitro* measurements, as well as the action of topoisomerases for which parameters are constrained by our experimental results. By comparing it with the data, it supports that TopoI and gyrase must both act specifically, respectively upstream and downstream the gene, and predicts TopoI to be less active than gyrase. It also highlights antagonistic effects of TopoI, which both facilitates elongation and tends to repress initiation [2].

[1] Liu, L.F., Wang, J.C., 1987. Supercoiling of the DNA template during transcription. PNAS. 84, 7024–7027.

[2] Boulas, I., Rimsky, S., Espeli, O., Junier, I., Rivoire, O., 2022. Assessing in vivo the impact of gene context on transcription through DNA supercoiling. bioRxiv.

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