

In this revised version of their preprint, the authors have done an excellent job of introducing their model and the biology related to DNA supercoiling more effectively. Altogether, this work provides an insightful theoretical analysis of the potential impact of the coupling between DNA supercoiling and transcription on the evolution of genome organization and on the role of DNA supercoiling in regulatory networks. For these reasons, I strongly recommend the publication of this manuscript.

In the following, I provide additional comments that the authors could consider for the final version of their manuscript.

- I believe there is still room to improve the evolutionary take-home message: i) by mentioning in the title the term "adaptation" or "evolution", and ii) by rephrasing, for example, in the abstract the sentence "We present a model of gene transcription and DNA supercoiling..." to something like "We present a model of genome evolution driven by transcription-supercoiling coupling...". This is particularly important given that the work is (nicely) introduced by stating "Here, we address a different question that has never been subject to detailed analysis: how the transcription-supercoiling coupling may drive genome evolution." (Lines 141-143) and concluded with "To the best of our knowledge, this work is the first to propose a model to investigate the role of the coupling between gene transcription and DNA supercoiling in the evolution of the structure of bacterial genomes." (Lines 596-598)
- In response to their response to my point A.2: I do not think that anyone can argue for a specific value for d_{max} that is more relevant than another one, as we do not have a good understanding of the situation in vivo. In particular, strong heterogeneities along the genome are expected. Instead, I believe the authors' statement that "values of d_{max} under 4 kb actually prevent the evolution of inhibition of A genes in environment B (data not shown)" deserves to be mentioned in the manuscript as i) it helps to understand the authors' choice of $d_{max}=5$ kb and ii) this is an interesting prediction of the model.
- In response to their response to my point A.3: I agree with the authors' response that $\Delta \sigma = 0$ is not compatible with two environments. However, I wonder whether the high sensitivity of the system to the introduction of $\Delta \sigma \neq 0$ does not obscure the existence of two solutions at $\Delta \sigma = 0$. This could be easily tested.