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Can we predict DNA biological activity from the study of its local fluctuations ?

Michel Peyrard[1], Santiago Cuesta-Lopez[1,3], Titus S. van Erp[1,2] and Johannes-Geert Hagmann[1]

[1] *Ecole Normale Supérieure de Lyon, France*
[2] *Catholic University of Leuven, Belgium*
[3] *University of Zaragoza, Spain*

DNA dynamics is essential for its biological function. The genetic code could not be read without a local unwinding of the double helix, and large openings, the so-called "DNA bubbles", are supposed to allow the formation of some specific DNA structures, such as the T-loop that stabilizes the end of the chromosomes.

Mesoscopic DNA models give a fairly accurate description of the thermal denaturation of DNA, i.e. the separation of the two strands by heating, and they predict the existence of localized fluctuations which are reminiscent of the "breathing" of the double helix observed by biologists.

Thus it is tempting to try to use these models for the prediction of the biological activity of DNA. It has been speculated that the formation of bubbles of several base-pairs length, due to thermal fluctuations, might reveal biologically active sites. A comparison between molecular dynamics simulations of the PBD DNA model and experiments suggest that it could be the case, but this observation is not unambiguous as large bubbles appear only seldom so that the statistical significance of the results can be questioned. We introduce a new method, that is orders-of-magnitude faster than molecular dynamics to analyze these bubbles [1] and show that presently the PDB model is not able to detect biologically active sites.

This does not exclude a correlation between DNA fluctuations and biological activity, but it could imply that the model is not yet able to properly relate the local opening and the base-pair sequence. In order to improve it, a comparison with experiments measuring the local fluctuations of DNA as a function of its sequence is necessary. We discuss such experiments and introduce some improvements of the model to bring it closer to the goal of predicting biological activity of DNA from physical studies of a highly simplified model.

[1] Titus S. van Erp, Santiago Cuesta-Lopez, Johannes-Geert Hagmann, Michel Peyrard, *Can one predict DNA Transcription Start Sites by studying bubbles?* Phys. Rev. Lett. **95**, 218104 (2005)