Static and dynamic persistence length in intrinsically-straight DNA

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DNA is often referred to as the molecule of life, due to its central role in all living organisms. DNA stores the information needed by the cell to build the various proteins performing all the tasks needed for its survival and reproduction. This information is stored by forming ordered chains of nucleotides (A, T, C, G) which, for the synthesis of each protein, encode which amino acids are needed and in which order they have to be attached to each other.

At scales above 10 nm, the well-known double helix behaves as a semiflexible polymer (Fig. 1a) with bending rigidity intermediate between rubber and nylon. This is manifested in the thermally-induced bending, which is quantified by a decay in the tangent-vector correlation function with a typical scale equal to roughly 50 nm, known as the persistence length l_p (Fig. 1b-c) [1].

This basic polymer-physics formulation assumes that the minimum-energy configuration for the double helix is a straight rod. However, it is well known that DNA shows a spontaneous curvature depending on sequence [2], which in certain cases can give rise to highly-deformed structures [3]. As a consequence, the tangent-vector correlation function is actually the result of combining the decay induced by the spontaneous curvature and the thermal fluctuations. In the literature, these two contributions are quantified by introducing respectively a static persistence length l_s and a dynamic persistence length l_d [4].

Taking advantage of the periodicity of the double helix, certain sequences have been devised for which the spontaneous curvature is expected to be practically zero. Such sequences are known as intrinsically-straight DNA. Measuring the tangent-vector correlation function of these systems enables experimental access to the dynamic persistence length. However, experimental measurements based on different techniques have provided sensibly-different results [5,6].

In this project, we will tackle this problem by means of accurate coarse-grained simulations [7], in which some of the experimental conditions will be mimicked. The goal is to understand the origin of this discrepancy and to better characterize the contributions to the persistence length, thus providing arguments in favor or against the results reported in the literature.

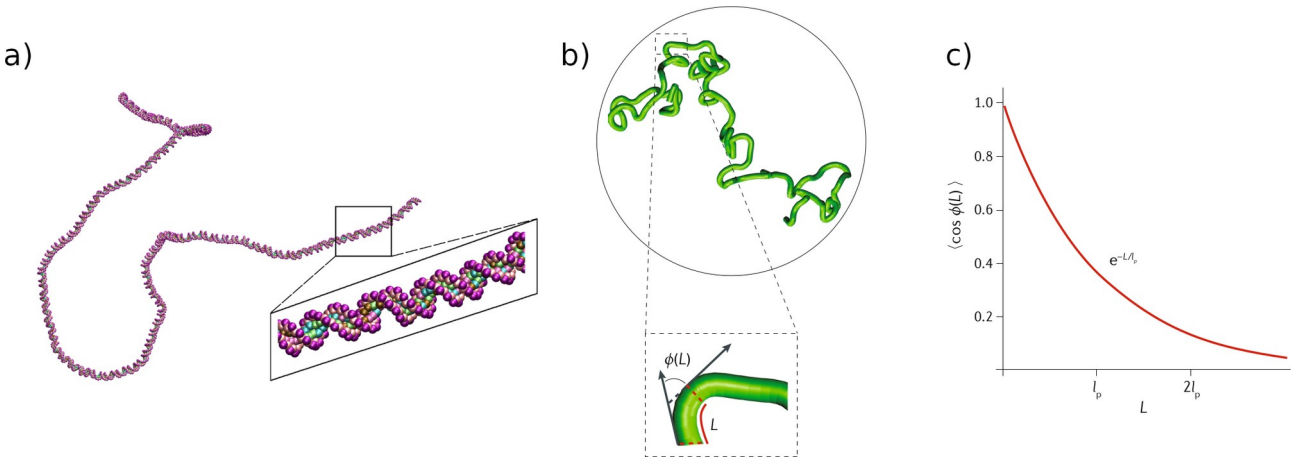

Figure 1: *a) At large scales, the double helix behaves as a semiflexible polymer. b) The bending angle between two points separated by a contour length L is defined as the angle between the tangent vectors at those points. c) The tangent-vector correlation function decays exponentially as a function of the contour length, with a persistence length l_p=50 nm. Panels b) and c) reproduced from [1].*

[1] S. Assenza and R. Mezzenga, “Soft condensed matter physics of foods and macronutrients”, *Nature Reviews Phys.* **1**:551 (2019).

[2] R. Rohs, X. Jin, S. M. West, R. Joshi, B. Honig and R. S. Mann, “Origins of specificity in protein-DNA recognition”, *Annu. Rev. Biochem.* **79**:233-269 (2010)

[3] A. Marín-González, C. L. Pastrana, R. Bocanegra, A. Martín-González, J. G. Vilhena, R. Pérez, B. Ibarra, C. Aicart-Ramos and F. Moreno-Herrero, “Understanding the paradoxical mechanical response of in-phase A-tracts at different force regimes”, *Nucleic Acids Res.* **48**:5024-5036 (2020).

[4] J. S. Mitchell, J. Glowacki, A. E. Grandchamp, R. S. Manning and J. H. Maddocks, “Sequence-dependent persistence lengths of DNA”, *J. Chem. Theory Comput.* **13**:1539−1555 (2017).

[5] J. Bednar, P. Furrer, V. Katritch, A. Stasiak, A.; J. Dubochet and A. Stasiak, “Determination of DNA persistence length by cryo-electron microscopy. Separation of the static and dynamic contributions to the apparent persistence length of DNA”, *J. Mol. Biol.* **254**:579−594 (1995).

[6] M. Vologodskaia and A. Vologodskii, “Contribution of the intrinsic curvature to measured DNA persistence length”, *J. Mol. Biol.* **317**:205−213 (2002).

[7] S. Assenza and R. Pérez, “Accurate sequence-dependent coarse-grained model for conformational and elastic properties of double-stranded DNA”, *J. Chem. Theory Comput.* **18**:3239 (2022).