Sequence dependence of mechanical properties of DNA studied via molecular simulations

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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 nucleic acids (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.

From a molecular perspective, nucleic acids are organized in two strands forming a double helix. For the molecular machines to use the information encoded in DNA, they first need to physically access it. In the last few years, it has been shown that the double helix displays many local deformations, which promote or inhibit access from such machines, due to both the geometrical arrangement of the distorted double helix and the elastic response to external mechanical stress. These deformations and elasticity are directly determined by the specific sequence of nucleic acids. Hence, it is believed that the cell actively exploits these features to control the rate at which each DNA sequence is translated into proteins [1,2].

Due to the existence of this mechanism, the DNA community is actively engaged in understanding how sequence affects elastic and conformational properties of DNA [3]. In the present project, we will study this problem via molecular simulations exploring scales from the atomistic level (Angstroms) up to chains made of hundreds of nucleic acids (hundreds of nanometers). We will assess the properties of special sequences known from the literature (such as A-tracts, i.e. sequences rich in A content [4,5]) as well as possibly identify novel sequences with peculiar properties to propose for experimental testing. The master student will become acquainted with molecular simulations tools such as AMBER or LAMMPS, as well as applying elastic models in the context of statistical mechanics.

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