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Non-specific DNA-protein interaction: how proteins can diffuse along DNA

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The structure of DNA binding proteins (DNA-BPs) enables a strong interaction with their specific target site on DNA through direct interactions with DNA base pairs. However, recent single molecule experiment reported that proteins can diffuse on DNA. Interactions between proteins and non-specific DNA should therefore play a crucial role during the target search.

Nucleotides being negatively charged, the positive surface of DNA-BPs is expected to collapse onto DNA. This is indeed what is observed by means of Monte Carlo simulations for an oversimplified model of the system where the DNA is represented by a cylinder and the protein by a sphere. However, the most characteristic aspect of DNA-BPs is their shape complementarity with DNA [1]. We showed that, if the concave shape of DNA-BPs is taken into account, a counter-intuitive repulsion between the two oppositely charged macromolecules exists at a nanometer range [2,3], which pushes the protein in a free energy minimum at a distance from DNA. As a consequence, a favorable path exists along which proteins can slide without interacting with the DNA bases. When a protein encounters its target, the osmotic barrier is completely counter-balanced by the local H-bond interaction, thus enabling the sequence recognition.

The implications of such a behavior on the protein 1D diffusion along DNA recently observed both in vitro and in vivo [4,5] will be the goal of future investigations.

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Orateur: Mme BARBI, Maria