From a single DNA molecule to genome repair

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It is generally accepted that the process of aging is, at least in part, a consequence of progressive degradation of the organism's genome. DNA damage can be of a physical or chemical nature; examples of such lesions include those which appear as a result of exposure to UV radiation or to the mutagenic compounds present in tobacco smoke (such as formaldehyde). At the same time, DNA damage also occurs during the course of normal genome replication preceding cell division; lesions characteristic of this process are base insertions, deletions or mismatches resulting from imperfect DNA replication. Protein systems responsible for genome repair are essential to cell survival. Their dysfunction is most often associated with severe diseases such as cancer.

Our work focuses more specifically on repair of physically and chemically damaged DNA characterized by "bulky" lesions in which the natural structure of the DNA double helix is strongly distorted. DNA repair is a complex multi-step process which requires specialized enzymes. From an experimental standpoint such multi-step reactions are particularly difficult to study in bulk as it is almost impossible to maintain synchronization of a population of molecules throughout such a process. Nevertheless, so-called "single-molecule" techniques allow one to follow in vitro and in real-time the behavior of an individual DNA molecule bearing a specific DNA lesion.

In vitro "single-molecule" nanomanipulation techniques, such as magnetic tweezers, allow us to monitor and control in real-time the mechanical and conformational properties of a single DNA molecule. It becomes then possible to detect the action of a protein on DNA. Using a DNA bearing a specific DNA lesion, we can monitor in real-time reparation processes with a single-molecule, single lesion resolution.