


Internship proposal 2011-2012

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*Dynamics of nano-target search in the context of Homologous Recombination*

**Scientific project:**

**CONTEXT:** How a nano-searcher finds its nano-target is a general problem in statistical physics. It becomes vital when the searcher is a damaged DNA fragment trying to find its counterpart on the intact homologous chromosome. If the two copies can be paired, that intact homologous sequence can be used as a template to reconstitute the damaged DNA sequence, enabling the cell to survive without genetic mutations. This process, called *Homologous Recombination*, is essential for the maintenance of genome integrity and is promoted by the protein *Rad51* in mammals.

*Homologous Recombination* involves complex protein-DNA interactions, applying forces and torques upon the DNA molecule, which deeply modify the DNA structure. *Rad51* proteins wrap around the damaged DNA, unwinding it by 15° per base pair and stretching it by 50% as compared to normal B DNA. It is believed that this deformation is instrumental in sequence recognition and in the strand exchange, which is ultimately necessary to rebuild two functional DNA.

**PROBLEMS AND MOTIVATION:** The *Homologous Recombination* is among the most complex enzymatic reactions. Several partners are involved: at least the intact and the damaged DNA molecule, the *Rad51* protein and a given amount of energy (*ATP hydrolysis*). In addition the DNA molecules are long helices with specific sequences, they are entangled during the homology search and *Rad51* acts cooperatively to catalyse the reaction. How this reaction can be fast and reliable remains unknown.

**OBJECTIVE:** In this complex context, we want to understand at which step of the *Homologous Recombination* the energy released by the ATP is transformed in mechanical work and if this energy is stored in the DNA/*Rad51* complex or it is dissipated to ensures the irreversibility of the process.

We use a new generation of magnetic tweezers to manipulate a single DNA molecule. Thus, we will determine the forces and the torques applied by *Rad51* to the DNA during the *Homologous Recombination*. The DNA elongation ( $dl$ ) and torsion ( $d\theta$ ) are measured under a given torque ( $\Gamma$ ) and a controlled stretching force ( $F$ ). This simultaneous measurement will allow us to determine the work ( $dW = F \cdot dl + \Gamma \cdot d\theta$ ) developed by the *Rad51* protein at each step of the recombination process.

**Techniques in use:** Single Molecule magnetic tweezers

**Applicant skills:** The applicant should be a physicist with a good background in statistical thermodynamics. Experience in biochemistry is welcome.

**Granted internship:** yes ( 417 €/month)

**C'nano IdF laboratory :** yes

**Possibility for a thesis:** yes (type of grant : not allocated yet)