Research projects 2018-2019 – Master Internships

Effects of binding ligands and Architectural proteins on dynamics, flow, and gelation of DNA

Supervisor: *Indicate the references of the person who will directly supervise the student's project..*

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Host Laboratory: *Indicate the references of the laboratory where the student will work for the project.*

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Collaboration:

Dr. Véronique Arluison: CEA Saclay, France
Frank Wien : Synchrotron Soleil, France

Describe the team that the student will join for the project.

The intern will join a group of 5 researchers, composed of 3 postdocs (Evdokia Oikonomou, Victor Baldim, Milad Radiom), one intern (Larissa Ferreira) and one permanent position (J.-F. Berret, DR CNRS). Our research group develops novel functional structures, devices and systems with stimuli-responsive features at the nano and microscales. Our objectives also deal with applications in medicine, biology and in the environment. It includes the development of tools for imaging and therapy in vivo, microfluidics and microrheology as well as the study of living system-machine interfaces.

Project description

In organisms, the genetic material is often, if not always in a crowded and congested state. Folding of DNA is facilitated by a myriad of biophysical processes, which is only partially understood. Here, we focus on an exemplary selection of key players responsible for folding of the genome in viruses and bacteria, that is a series of polyamines and nucleoid associated proteins (NAPs). These ligands bind on DNA, modify the secondary structure and mechanical properties of the double helix, and mediate bridging interactions between different segments of the same or different DNA molecules. In particular, DNA folding and compaction are thought to be related to protein and/or ligand mediated bridging interactions. Cross-linking by bridging interactions is expected to affect DNA dynamics and the properties of its flow. Gelation might also occur if (semi)-permanent bridges are formed.

The project encompasses a systematic investigation of the effect of cross-linking bridging interactions on the dynamics and concomitant rheological properties of DNA.
The specific aims are:

- Do condensing ligands and proteins affect genome dynamics?
- Is this related to bridging interactions between different DNA molecules or segments thereof?
- Does this result in gelation of the genome with implications for the machinery of life?

In order to achieve these objectives, a selection of biologically relevant compaction agents need to be investigated. These agents are the two bacterial nucleoid associated proteins, H-NS and Hfq. The proteins H-NS and Hfq in the bacteria differ in their modes of operation, but the key factors are charge and specific ligand interaction. The NAP effects on the dynamics of the genome will be evaluated using a combination of passive and active micro-rheology assays.

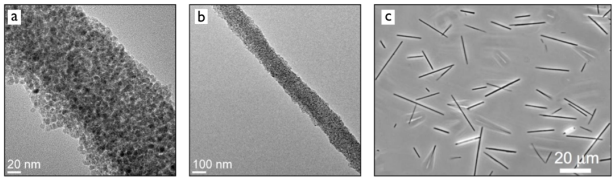

Figure 1: a and b) Transmission electron microscopy of magnetic wires made from 10 nm iron oxide nanoparticles. c) Phase-contrast image of wires observed by optical microscopy.

For *active* microrheology measurements, magnetic wires with diameter 500 nm and length 5 µm to 50 µm will be synthesized (Figure 1). The wires are then submitted to an external rotating magnetic field. The technique is known as Magnetic Rotational Spectroscopy (MRS).

The shear viscosity η can be determined from the wire motion recorded by video-microscopy as a function of the time. The advantage of MRS is its broad frequency range, from 10^{-4} and 10^{2} rad s^{-1}. Crowded media, such as crosslinked DNA dispersions can be characterized by long relaxation times (> minutes) that can only be accessed with low frequency testing. From the structure and mechanical response of the NAP/DNA dispersions, fundamental information on the ligand binding properties, secondary structures of the double helix will be obtained.

The present project will be carried out in close collaboration with Véronique Arluison from the CEA Saclay and with Frank Wien from le Synchrotron Soleil.

Related references

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2. Frka-Petesic, B., K. Erglis, J.-F. Berret, A. Cebers, V. Dupuis, J. Fresnais, O. Sandre, R. Perzynski, J. Magn. Magn. Mater. **2011**, 323, 1309.
3. Chevry, L., N. K. Sampathkumar, A. Cebers, J. F. Berret, Phys. Rev. E **2013**, 88.
4. Berret, J.F., Nature Communications **7**, 10134 (2016), DOI: 10.1038/ncomms10134
5. Malabirade, A., K. Jiang, K. Kubiak, A. Diaz-Mendoza, F. Liu, J. A. van Kan, J.-F. Berret, V. Arluison, and J. R. C. van der Maarel, Nucleic Acids Research **2017**