DNA dynamics, flow, and gelation by binding ligands and architectural proteins

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 a series of polyamines and two bacterial nucleoid associated proteins (NAP), that is H-NS and Hfq. They differ in their modes of operation, but the key factors are charge and specific ligand interaction. The effects of all of these agents on the dynamics of the genome will be evaluated using a combination of passive and active micro-rheology assays. Besides the properties of the flow, as observed by micro-rheology, molecular transport will also directly be monitored by microscopic video tracking of fluorescence labelled DNA and protein.

The combination of the experimental methodologies and a systematic exploration of the various modes of cross-linking will provide fundamental understanding of the dynamics of the genome. This is obviously of great importance in biology, but there are also implications in biotechnology such as in (epi)genetic profiling. The candidate should have a background in biological chemistry, biophysics and/or soft condensed matter physics. A one year contract will initially be offered, with the possibility of extension for a total duration of 30 months. The project is a collaboration between the groups of van der Maarel (NUS), Arluison (Saclay), and Berret (Paris Diderot). The postdoc will be based in Singapore, but some of the experiments will be done in Paris (funding for short term visits is available).

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