**Internship project**

# Protein droplets on a DNA wire

## Optical tweezers to decipher biocondensate formation

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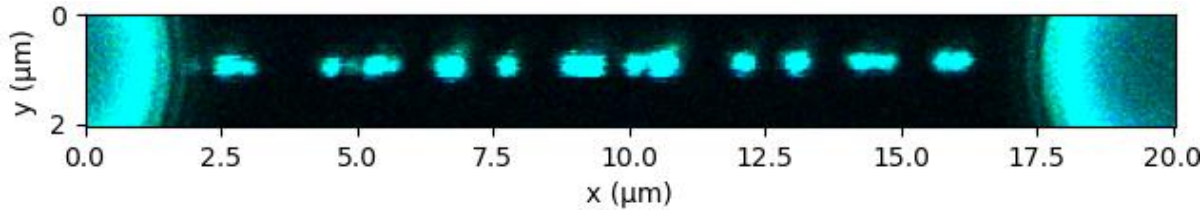


**Figure 1 : DciA droplets on dsDNA**. Confocal scan of DciA proteins (blue dots) bound on a DNA tether (not visible) attached to two microbeads (blue disks at left and right).

Inside our cells, compartments also known as organelles enable to separate and regulate biomolecular processes : e.g. DNA replication in the nucleus or ATP production inside the mitochondria. Beyond these objects delimited by lipid bilayers it has been shown more recently that membrane-less structures known as biomolecular condensates can also segregate specific molecules. Such assemblies are formed by a demixing process called liquid-liquid phase separation (LLPS), in which molecular partners spontaneously enrich in a condensed phase usually forming droplets.

It was shown notably by fluorescence microscopy that biocondensates play a preponderant role in molecular processing, such as DNA transcription and repair, RNA splicing or chromatin condensation. These structures may be of different compositions (one or more molecular type) and exhibit different physical properties (solid, liquid, visco-elastic). In medical research, condensopathies have been associated with various pathologies from neurodegenerative diseases to cancer.

In many cases, the mechanism by which biocondensates are formed remains to be deciphered mainly because of their size and temporal dynamics. Here at the Physics Laboratory of ENS de Lyon / CNRS, we propose a single molecule approach using cutting-edge technology to manipulate DNA molecules together with a protein involved in DNA maintenance, DciA,. This protein from *Deinococcus radiodurans*, has been shown to form LLPS with DNA molecules and is postulated to be able to recruit other repair factors [1].

Using optical tweezers coupled with confocal microscopy and a microfluidic control [2], we will characterize the formation, the structure and the dynamics of these assemblies. Based on the ability of our system to exert and measure forces at the same time as they are visualized in fluorescence microscopy, our aim will be to understand the key molecular processes involved.

References :

[1] Marsin S, Jeannin S, Baconnais S, Walbott H, Pehau-Arnaudet G, Noiray M, Aumont-Nicaise M, Stender EGP, Cargemel C, Le Bars R, Le Cam E, Quevillon-Cheruel S. DciA, the Bacterial Replicative Helicase Loader, Promotes LLPS in the Presence of ssDNA. J Mol Biol. 2025 Jan 15;437(2):168873. doi: 10.1016/j.jmb.2024.168873.
[2] B. Molcrette, L. Chazot-Franguiadakis, F. Liénard, Z. Balassy, C. Freton, C. Grangeasse, & F. Montel, Experimental study of a nanoscale translocation ratchet, Proc. Natl. Acad. Sci. U.S.A. 119 (30) e2202527119,