Zooming in on dynamic proteins: how the dynamic structure of proteins dictate their function

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The biological function of many macromolecules such as proteins and nucleic acids are tightly coupled to their (dynamic) conformation. Misfolded or unfolded proteins are known to be either (partially) inactive or to even display toxic functionality. Studying how macromolecules fold correctly, undergo conformational changes and assemble into biomolecular condensates is crucial to understand biological mechanisms underlying diseases. Single-molecule force spectroscopy provides a unique capability to isolate individual biomolecules and observe conformational transitions and unfolding processes as they happen in real-time.

Here, I present a platform that correlatively combines high-resolution optical tweezers, fluorescence imaging, and microfluidics: the C-Trap. This set-up allows to directly observe the dynamics and mechanics involved in protein conformation changes, and the influence of small molecules on protein conformation and function. Moreover, the C-Trap enables the assembly of biomolecular condensates (protein droplets) on and with individual DNA/RNA molecules, in order to manipulate and measure the material properties of such assemblies.

I will discuss the latest scientific breakthroughs enabled by the C-Trap in the field of protein dynamics and protein aggregation/condensation, and will highlight how dynamic single molecule analysis was critical for the scientific conclusions and the impact of the findings.