Unveiling Chromatin Organization with Single-Molecule Approaches

Chromatin, the ubiquitous complex of DNA and histone proteins, not only compacts our genome but also plays a vital role in regulating access to our genes. Whereas the structure of biomolecules is generally key to understanding their function, the mesoscopic structure of the strings of nucleosomes that form a chromatin fiber is thought to be disordered, conflicting with the high level of control required for accurate transcription regulation. It is well-known, though, that the mechanical properties of DNA depend on sequence, which is (partially) responsible for the positioning of nucleosomes along the DNA. However, a comprehensive experimental study of the implications of DNA sequence on mesoscopic chromatin organization is impeded by the enormous sequence variety found in nature, combined with the observed large temporal and structural fluctuations in these fibers. Our group has established exciting new technologies that make it possible to address this giant challenge. Here, I will share recent results obtained from single-molecule force spectroscopy, single-pair FRET, single-read sequencing, and statistical physics modelling, aiming to understand the structure and dynamics of chromatin fibers and how these depend on DNA sequence.