Department of Physics
Condensed Matter Physics
Clarendon Laboratory, Parks Road, Oxford OX1 3PU

UNIVERSITY OF OXFORD

CONDENSED MATTER SEMINAR

Friday 6 November at 10.00

"Adventures in DNA and RNA replication using single-molecule biophysics"

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Department of Bionanoscience, Delft University, The Netherlands

Genome duplication involves copying DNA (in eukaryotic organisms such as ourselves) or RNA (in many viruses), and how this is carried out by molecular machines that operate at the nanometer-scale is a question of long-standing interest. We are particularly interested in studying the dynamics of these molecular machines, and do so using single-molecule techniques. I will briefly highlight how the field of single-molecule biophysics has been able to advance such techniques over the past few decades, so that the dynamics of diverse sets of motor proteins can now be accurately followed.
I will then describe how a significant improvement of our single-molecule techniques – making them much more high throughput – allows us to investigate enzymatic activity on hundreds of tethered RNA molecules. This allows us to study e.g. the viral RNA-dependent RNA polymerase (RdRp), which is the molecular machine that copies RNA in viruses. Through the errors in copying that it makes, the RdRp is also the primary source of mutations in viral genomes, and as such is a target for broad-spectrum antiviral therapeutics. I will highlight how we can use single-molecule magnetic-tweezers to monitor RdRp elongation dynamics and show how the RdRp can catalyze intramolecular and intermolecular template-switching reactions. The latter underlies viral recombination, a process through which RNAs from different viral species can merge and speed up viral evolution.

I will next describe how single-molecule techniques can now also be used to probe the functioning of molecular machines that are built up from many different components, such as the replisome that carries out accurate DNA replication in eukaryotes. While the overall outline of replisome assembly is understood, little is known about the dynamics of the individual proteins on the DNA and how these contribute to proper complex formation. I will show that using single-molecule optical trapping and confocal microscopy one can illustrate how protein binding, diffusion, sequence recognition, and protein-protein interactions play important roles in the first steps of replisome assembly, and discuss the biological implications thereof.

Host: Prof Achillefs Kapanidis

Zoom ID: https://zoom.us/j/91472444497?pwd=UGUvNkJ6UGV0NEZ4Tm03NmJvMkQydz09