Snapshots of actively transcribing influenza polymerase

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The flu is caused by the highly infectious, rapidly evolving and potentially dangerous influenza virus. The genetic material of the influenza virus is single-stranded RNA. During an influenza infection, the viral RNA-dependent RNA polymerase uses the genomic RNA as a template firstly to synthesise viral messenger RNA, which is then translated into viral protein by the cellular protein synthesis machinery, and secondly, in a distinct process, to generate genome copies. The genome copies together with the newly synthesized viral proteins are then packaged into progeny virions that can go on to infect other cells and organisms. Our goal is to understand at atomic resolution the unique mechanisms whereby influenza polymerase performs transcription and replication of the viral genome. This is not only of fundamental interest but will also help understand avian to human interspecies transmission of the virus and promote development of new anti-influenza drugs targeting the polymerase.

To achieve this goal we have used a combination of the complementary methods of X-ray crystallography and single particle cryo-electron microscopy (cryoEM), most often performed at the ESRF, to determine structures of the polymerase in various functional states. In particular, recent advances in cryoEM have permitted a series of snapshots of transcribing polymerase to be obtained that, for this system, are superior in resolution to that previously obtained by X-ray crystallography. These structures constitute a molecular movie of the polymerase machine in action. In addition, structures will be presented showing the mode of action of the newly approved anti-influenza drug Xoflusa (baloxavir marboxil) that directly inhibits transcription by the polymerase and possible ways how the virus can become resistant to the drug.

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Nanostructure analysis in real space: PDF studies of nanoparticle chemistry

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Nanomaterials have come to play a huge role in modern materials chemistry: By nanosizing the functional materials used for a range of applications, e.g. batteries and catalysis, many properties can be improved. This development has challenged our understanding of structure/property relations, as the conventional techniques for material characterization break down for structures on the nanoscale. However, total scattering combined with Pair Distribution Function analysis allows us to look further into nanostructure and establish this relation for many advanced functional materials,[1] opening a whole new level of insight for material chemists.

Here, I will present recent work illustrating how we use total scattering to characterize nanomaterial structure and show how Pair Distribution Function analysis can be used to elucidate the atomic arrangements in even the tiniest of nanoparticles and nanoclusters, with special focus on metal and metal oxide nanoparticles.[2,3] Using PDF, we observe that new structural motifs, unstable in the bulk form, become dominant in nanoscale materials. In gold clusters, for example, we use PDF analysis to determine the atomic arrangement in 2 nm particles, where *fcc* structures are no longer stable.[2] In oxide materials, we see that defects know from bulk materials completely dominate the atomic structure on the nanoscale, and changes the atomic arrangement significantly, highly affecting their properties.[3] We also apply total scattering techniques to gain a new understanding of the reactions and processes taking place during crystallization of materials. In situ PDF methods allow following structural changes throughout a synthesis, all the way from an ionic cluster in solution, over amorphous intermediates and to the final crystalline material, making it possible to gain new insight into nucleation mechanisms.[5] I will furthermore show how total scattering combined with computed tomography can open for a range of new *in situ* studies, as nanostructure can now be positionally resolved.

References

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LEAPS Sets Sails

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The European Synchrotrons and Free Electron Lasers have a long history of fruitful collaborations in a healthy competitive environment. Now they are joining forces to master the challenges of the next decades by adding their capabilities in smart specializations, and developing together the European strategy for photon science.

LEAPS, the League of European Accelerator-based Photon Sources, includes sixteen institutions as founding members, hosting national and international facilities, and representing a total community of 35000 researchers. SESAME has joined as first Associated Member.

Scientific and technical developments for next generation sources, innovation programs, technological transfer for industrial capacitation, better services to users, opening to the world, training and education, are the main stream of the collaboration.

LEAPS is developed in cooperation with the European Commission, calling to a new paradigm of co-funding participation of national funding agencies to such kind of programs. A first Pilot Project, LEAPS-INNOV, will be presented in the forthcoming H2020 call, while organizing the future programs to be developed in Horizon Europe.

Coherent X-rays: high-resolution imaging for all

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The use of coherent X-rays for imaging has been steadily increasing for the past 25 years, from phase contrast imaging to coherent diffraction and ptychography experiments, resulting in two and three-dimensional material inspection with a spatial resolution down to about 10 nanometers. This progress will soon be enhanced by the Extremely Brilliant Source upgrade, leading to an improved spatial and temporal resolution. However for a long time coherent diffraction techniques were mostly used by a limited community as much focused on the methodology than on the materials.

I will present the various techniques which can be used for standard small-angle imaging, yielding the sample's electronic density, with applications from brain imaging to fuel cells, as well as those in the Bragg geometry, giving access to strain information, e.g. for semi-conductor nano-structures or catalysts. Most importantly I will show how algorithms and data processing have improved during the last few years, providing a more robust data analysis which can be performed with limited supervision or hand-tuning. Additionally, efforts on a more efficient use of modern computing resources allows much faster two or three-dimensional reconstructions, both during and after the experimental time. These advances, along with the improved photon flux, should pave the way for the application of high-resolution coherent imaging techniques with a larger community.