Laboratory Soft X-ray Microscopy for Biomedical Applications

Aurélie Dehlinger[1,2], Dr. Christian Seim[1,2], Valentina Alberini[1,2], Dr. Holger Stiel[2,3], Dr. Antje Ludwig[4,5,6], Sarah Jung[1,2], Daniel Groetzsch[1,2], Vladimir Usatikov[1,2], Dr. Johannes Tuemmler[3], Prof. Dr. Birgit Kanngießer[1,2]
[1]Technische Universität Berlin, Institut für Optik und Atomare Physik, Berlin, Germany, [2]Berlin Laboratory for innovative X-ray technologies (BLiX), Berlin, Germany, [3]Max-Born-Institut (MBI) im Forschungsverbund Berlin e.V., Berlin, Germany, [4]Department of Cardiology, Angiology and Intensive Care Medicine, Deutsches Herzzentrum der Charité, Berlin, Germany, [5]Department of Cardiology, Angiology and Intensive Care Medicine, Charité - Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [6]DZHK (German Centre for Cardiovascular Research), Partner Site Berlin, Berlin, Germany

Background incl. aims:
Soft X-ray microscopy is a powerful tool for three-dimensional investigation of biological material [1]. The water window energy range between the absorption edges of carbon (284 eV) and oxygen (543 eV) provides a strong natural contrast for aqueous samples and offers the possibility for both a high resolution of a few tens of nanometer and a high penetration depth of up to 10 µm. Within the Collaborative Research Center 1340 (CRC) “Matrix in Vision” funded by the German Research Foundation, we use soft X-ray microscopy to investigate the role of the extracellular matrix (ECM) in diseased tissue, as the components and properties of the ECM play a major role in the regulation of cell and tissue function.

Methods:
Alteration of the ECM plays a pivotal role in the progression of inflammatory diseases such as atherosclerosis. Understanding the underlying processes contributing to ECM alterations can aid in early detection during the initial stages of development. The ECM of cryofixed model cells (THP-1 cell line derived from an acute monocytic leukemia patient) has been studied with a laboratory soft X-ray microscope (L-TXM) located at the Berlin Laboratory for innovative X-ray Technologies (BLiX) at TU Berlin. A correlative workflow was developed by integrating a visible light microscope into the L-TXM setup [2], allowing a fast transition between the two modalities, and facilitating sample localization to accelerate 3D cell imaging. Additionally, various upgrades have been performed on the L-TXM setup to enhance stability and increase sample throughput in order to streamline the workflow and address the specific demands of the samples investigated within the CRC.

Results:
The upgraded L-TXM at TU Berlin offers enhanced stability and increased sample throughput for biomedical research within the CRC, resulting in consistent imaging quality over extended acquisition times. Laboratory-based soft X-ray microscopy was able to resolve the THP-1’s glycocalyx – an intricate fragile extracellular structure. Nevertheless, different sample preparations resulted in different thicknesses and lengths of the glycocalyx’s interlocking meshy structure.

Conclusion:
Laboratory soft X-ray microscopy provides unique flexibility and access to high resolution 3D imaging. Recent upgrades of the laboratory setup now enable a more streamlined workflow. The resulting higher sample throughput will help to establish suitable preparation techniques for various cell types for soft X-ray ECM research within the CRC. Combining results from X-ray based analytics with clinical diagnostics adapted for ECM research will help to better understand the role that the extracellular matrix plays in (inflammatory) diseases.

Keywords:

Soft X-ray Microscopy, Extracellular Matrix

Reference:

[1] Kördel, M. et al., (2020). Optica Vol. 7, issue 6, pp. 658-674
[2] Dehlinger, A. et al., (2020). Microscopy and Microanalysis Vol. 26, Issue 6, pp. 1124-1132