CFEL SCIENCE

SEMINAR

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Pixels and molecules in the clinic: Translation of physics and chemistry into medicine

Illuminating the complexity of biological systems is a daunting task. In particular as the chemical complexity of biological surfaces is highly dynamic and subject to local changes in response to a changing environment. This chemical heterogeneity is a particular important parameter when considering treatment of diseases such as cancer. It is this inconceivably complex heterogeneity that makes tumors so difficult to treat as no single therapy targets all permutations of phenotypes and environment precisely. This implies that to make truly personalized tumor therapy reality a diagnostic method is needed that unravels this spatial and molecular complexity of tumor tissue. The study of molecular signaling processes related to these diseases requires the detection and analysis of the molecules involved as well as the evaluation of their spatial organization. This allows the detailed cellular biotyping under duress and can provide critical insight in the activated pathways related to the progression of disease. Molecular imaging using various laser based techniques in the post-genome era provides insight in metabolomic and proteomic changes during the progression of disease on different scales; from single cells to whole biological systems.

Mass spectrometry based imaging (MSI) has matured to a high throughput tool in biomedical research. MALDI-MSI is routinely used to study protein and peptide distributions on tissue sections for the analysis of molecular signalling processes in various diseases. Studies have demonstrated excellent diagnostic and prognostic value that can be directly translated to the clinic. It is key to employ a multimodal biomolecular imaging approach combined with quantitative analytical proteomics and metabolomics. Innovations in the field target breaking boundaries in resolution, sensitivity and speed. The development of novel approaches such as microscope mode imaging combined with innovative detector technology and cluster based SIMS is one of these development areas. Here we demonstrate how the novel pixelated detectors

The results of the implementation of a pixelated detector array with extremely high charge sensitivity on a MALDI-equipped linear time-of-flight mass spectrometer or stigmatic imaging system are described. This coupling is shown to allow a significant increase in detection efficiency for large macromolecules (i.e., intact antibodies) having m/z values up and above 400,000 and thereby providing a means to make the detection of large macromolecules more accessible in MALDI-mass spectrometry. In addition, the direct imaging capabilities of this detector are shown allow visualisation of mass-dependant spatial distributions in the MALDI ion cloud and the effect the ion optics exerts on the ion cloud. Such capabilities are demonstrated to provide new insights into dynamic chemical phenomena occurring in the ion source, ion optics and allow the visualization of molecular signals of disease.

Host: Jochen Küpper/ CFEL Molecular Physics Seminar