



Contribution ID: 126

Type: **Contributed poster**

## **Hitting proteins with a sledgehammer – combining native mass spectrometry with an XFEL**

*Monday, 25 June 2018 18:45 (15 minutes)*

Native mass spectrometry (MS) enables the ionization and transfer of intact non-covalent protein complexes into the gas phase. As such, it is a perfect tool to study proteins and their assemblies in a mass and conformation specific manner. This enables MS to probe structural transitions which proteins and their complexes undergo, e.g. during a viral lifecycle. Such transient states are of high importance for structural biology, but most often cannot be purified and are inaccessible for crystallography.

Despite its remarkable sensitivity and selectivity, the structural resolution in native MS alone is limited. The amount of structural information could be vastly increased by its combination with powerful hard X ray free electron lasers (XFELs) such as the already established LCLS in Stanford or the European XFEL, the world's most intense light source so far, which has just become operational in Hamburg. These instruments promise an opportunity to obtain high resolution structures of single particles. Reciprocally, native MS could solve some of the issues with delivering sample into the beam and could also add another dimension of possibilities by manipulating and selecting charged molecules in the gas phase prior to their imaging.

This contribution will highlight the benefits of native MS for single particle imaging of transient protein intermediates at XFELs. It will also describe our plans and ongoing work to bring native MS to European XFEL single particle beamline as well as present our initial feasibility studies on achievable ion fluxes.

### **Acknowledgement:**

This work has been funded by the German Federal Ministry of Education and Research (BMBF Verbundprojekt 05K2016). The Heinrich-Pette-Institut, Leibniz Institute for Experimental Virology is supported by the Free and Hanseatic City of Hamburg and the German Federal Ministry of Health.

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**Session Classification:** Poster session