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Hitting proteins with a sledgehammer - structural characterization with X-rays

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Native ion mobility mass spectrometry (MS) is a perfect tool to study protein complexes in a mass and conformation specific manner. Despite remarkable sensitivity and selectivity the structural resolution is limited in native MS. On the other hand, it allows monitoring structural transitions, which proteins and protein complexes undergo, e.g. during the viral lifecycle. However, such transient states cannot be purified and are inaccessible for crystallography.

The European XFEL, the world's most intense hard X-ray free-electron laser (XFEL), has just become operational and offers an opportunity to obtain high resolution structures of single particles. The benefits of native MS for single particle imaging of transient intermediates at European XFEL and initial feasibility studies on achievable ion flux will be presented. Furthermore, we have tested native MS in conjunction with the soft XFEL FLASH and PETRA P04 soft X-ray synchrotron radiation. Our recent results show potential for soft X-rays protein complex fragmentation and dissociation for structural proteomics. The available intensity could alleviate proposed upper size limits for UV photo dissociation of protein complexes.

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