Flying viruses – from biophysical to structural characterization

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Viruses affect basically all organisms on earth. Some are detrimental to human development, whereas those targeting pathogenic bacteria or crop pathogens can be beneficial for us. An integral part of icosahedral viruses is the capsid protein shell protecting the genome. Many copies of the capsid protein often self-assemble into shells of defined size. Low binding affinity of individual subunits allows efficient assembly and gives rise to highly stable particles. These capsids can be studied by native and hydrogen/deuterium exchange mass spectrometry (MS) in terms of stoichiometry, dynamics, assembly pathways and stability. The focus will be on isolate dependent capsid stability and size as well as glycan binding induced dynamics of noroviruses, the main cause of viral gastroenteritis.

Despite the remarkable sensitivity, the structural resolution is limited in native MS. Of special interest to biology is the structural transition upon nucleation of capsid assembly. However, such transient states cannot be purified and are inaccessible for crystallography. Hard X-ray free-electron-lasers (XFELs) offer an opportunity to obtain high resolution structures of single particles. How native MS benefits single particle imaging of transient intermediates at XFELs will be illustrated. Preliminary data and implications for other applications combining native MS and X-rays will be shown, especially how soft X-rays can aid native top-down experiments.