SEMINAR: UNIVERSITY OF TSUKUBA: INSTITUTE OF BASIC MEDICAL SCIENCES

演題: Ion Mobility-Mass Spectrometry for Protein Complexes

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会場：医学系学イノベーション棟８階講堂
Institute of Basic Medical Sciences: Health and Medical Science Innovation Laboratory, Auditorium, 8th Floor）

要旨：Ion Mobility-Mass Spectrometry for Protein Complexes

Recently native approaches in mass spectrometry combined with ion mobility have been applied to characterize the conformations of proteins and other biomolecules, as well as the composition, topology and subunit arrangement of large protein complexes. But what does a measured collision cross section really tell us about the conformational space of a protein or the subunit arrangement of a complex? How critical is the absence of bulk solvent in the gas phase, and how much do the measured size and the flexibility depend on the internal energy ('temperature') of the ions?

We are using nano-ESI coupled with T-wave IM-MS (Waters Synapt G1 and G2) to assess the structure and conformational space of a couple of well understood proteins and complexes, and correlate the data with results from other biophysical methods such as size-exclusion chromatography, surface plasmon resonance and small-angle x-ray and neutron scattering. In direct comparison, closely related protein sequences (e.g. mutations, truncations or post-translational modifications) show subtle changes which are frequently reflected in the position and width of the drift time profile (i.e. “size” and “flexibility”). The global, structural effects of ligand binding can also become apparent using IM-MS in screening approaches.

In addition, we can for example determine the threshold of unfolding or the 50% unfolding point as an indirect measure of the gas-phase stability of native biomolecular structures. Taken together these data highlight the importance of controlling the internal energy of ions carefully in the experiment, and raise some critical points regarding the measurement of absolute (rather than relative) sizes by IM-MS. They also demonstrate the level of information we can extract from careful, systematic measurements of collision cross sections of ions of biochemical and pharmaceutical interest.

REFERENCES

Department of Biochemistry Oxford: http://www.bioch.ox.ac.uk/aspsite/index.asp?pageid=654

Department of Chemistry Antwerp: http://www.ua.ac.be/main.aspx?c=frank.sobott

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