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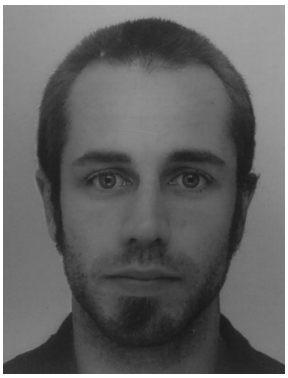
Use of structural mass spectrometry for the study of soluble and membrane complexes.



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Structural Mass Spectrometry (MS) encompasses an extending range of methods aiming at collecting as much structural information as possible on a biomolecule or its related complexes. Often reduced to the analysis of the primary structure of proteins, MS has evolved over the past 20 years to provide information on the secondary, tertiary and even quaternary structure of proteins[1]. Furthermore, the systems investigated with these methods became more and more complex, as many developments have progressively overcome the main challenges of their size, heterogeneity and/or solubility. Their huge potential and complementarity to other classical biophysical methods have driven an increasing number of users to develop these techniques and more crucially, manufacturers to provide dedicated instruments and solutions/kits that are now commercially available, as we will see in this talk.
After a brief description of the main structural MS methods, I will focus on the use of native MS and ion mobility (IM). Native MS utilizes the ability of electrospray ionization to project large protein complexes into the gas-phase, while preserving the non-covalent interactions involved in maintaining structure and binding to substrates. Ion mobility, a gas-phase electrophoretic technique, can be used in tandem with MS measurements to provide an additional dimension of separation based on the orientationally averaged collision cross section (CCS) of the analytes. These techniques offer the opportunity to study challenging protein assemblies, which are often heterogeneous and dynamic in nature, at increased levels of resolution and sensitivity provided by MS. Membrane proteins are one such family of challenging proteins, whose solubility limitations often frustrates efforts by conventional techniques. In this talk, we will see how these methods can be applied to detergent solubilized membrane proteins[2,3] and biotherapeutics such as antibody-drug conjugates[4].

References:

1 **Marcoux J** and Robinson CV **(2013)** "Twenty years of gas phase structural biology" **Structure** 21(9) : 1541-1550.
2 **Marcoux J**, Wang S, Politis A, Reading E, Ma J, Biggins P, Zhou M, Tao H, Zhang Q, Chang G, Morgner N, Robinson CV **(2013)** "Mass spectrometry reveals synergistic binding of nucleotides, lipids and drugs to a multidrug resistance efflux pump" **Proceeding of the National Academy of Sciences** 110(24) : 9704-9709.
3 **Marcoux J**, Politis A, Marshall D, Rinehart D, Wallace MI, Tamm LK, Robinson CV **(2014)** "A new model for full length OmpA: native mass spectrometry reveals partial dimerization via C-ter domain" **Structure** 22(6) : 781-790.
4 **Marcoux J**, Wagner-Rousset E, Campion T, Colas O, Corvaïa N, Van Dorsselaer A, Beck A, Sanglier-Cianférani S **(2015)** "Use of native mass spectometry and ion mobility for the measurement of drug-antibody ratios of Trastuzumab emtansine, a lysine-linked antibody drug conjugate" **Protein Science** ***In Press.***

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