PEPTIDE FRAGMENTATION:
SEQUENCE AND SIZE EFFECTS ON PEPTIDE FRAGMENTATION

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Fragmentation of peptides is widely used in proteomics to gain sequence information on native or post-translationnaly modified peptides. Further information is related to protein database in order to achieve identification of either a protein or of the nature and position of post-translational modifications (PTMs). Up to now, most of these studies have only relied on the measurement of fragment masses and the intensities of the fragments are often left aside.

In this lecture, after a brief introduction on the currently accepted mechanism for thermal-like activation methods (CID, IRMPD, BIRD, …) and on the various models devised for electron transfer based activation methods (ECD, ETD), we will focus on the elements available in the literature showing key parameters identified for both type of activation methods. For thermal type activations, the mobile proton model[1,2] serves as a good basis in the interpretation of fragmentation pathways. Recent literature has shown that the cyclisation pathways play a major role in defining fragment abundances, but also in the formation of a number of minor fragments which, although minor, can account for a large fraction of the fragment ions. In this vein, we will introduce how the analysis of database fragmentation data proved an important source for understanding fragmentation behavior.

In a third part, we will focus on the analysis of electron induced fragmentation, and mostly ECD fragmentation which have been a major focus of our group in the past years. In ECD fragmentation, focus has been usually put on the formation of *c* and *z*-type fragments. Our work focused on the more global picture, taking also into account other fragment types. Based on both the analysis of a large fragment database[3,4] and detailed analysis of specific synthetic peptides, it can be shown : 1) that fragments other than *c* and *z* ions are major contributors in some ECD fragmentation spectra ; 2) that the relation between these pathways is strongly dependent on the peptide size and on the nature of amino-acids present in the sequence ; 3) that preferred positions for backbone cleavage can be identified for all fragment type and 4) that this position differs for each fragment-type. Based on these results, a model in which three independent pathways are in competition for the ECD fragmentation of peptides is proposed.

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