Approaches and applications of Fourier transform-ICR mass spectrometry to proteome analysis with high resolution and high selectivity

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The development of efficient "soft ionisation" methods in the last years has provided the basis for the molecular characterisation of biopolymers by mass spectrometry. In contrast to previous limitations in the molecular weight range amenable, electrospray ionisation (ESI-MS) and matrix assisted laser desorption ionisation (MALDI-MS) have provided access to biopolymers > 100 kDa. The recent development of Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometry enabled a breakthrough for the *high resolution* mass spectrometric structure analysis of biopolymers using both ESI and MALDI ionisation [1]. Present studies in our laboratory in bioanalytical applications of FT-ICR mass spectrometry [2] focus on (i) the analysis of complex peptide mixtures in proteome studies and in combinatorial mixtures; and (ii) the identification of antigenic determinant structures of mono- and polyclonal antibodies using the mass spectrometric epitope mapping method developed in our laboratory [3,4]. In combination with 2D gel electrophoresis the *high* (sub-ppm) *mass determination accuracy and isotopic fine structure* by FT-ICR-MS provide particular advantages for the identification of proteins with medium and low abundance; for such applications microchip-ESI-approaches have been recently adapted to FT-ICR-MS.

Major goals of new application areas of FT-ICR-MS are (i) the structure analysis of cell surface proteins and their interaction molecules; (ii) epitope elucidation of antigen target proteins in autoimmune diseases; and (iii) high resolution sequence determinations and characterisation of structure modeifications of target proteins in proteome analysis. These applications are integrated in several research projects and interdisciplinary collaborations at the Departments of Chemistry and Biology of the University of Konstanz (*i.a.,* DFG-project "*high resolution biopolymer structure analysis"*; DFG-priority programme *"Cellular mechanisms of Alzheimers`disease"*; EU-project *"New microfluidic-mass spectrometry technologies for high performance proteomics"*; "*Competence centre for proteome analysis"* at the University of Konstanz), and the initiation of a European Research Training Centre for High Performance Mass Spectrometry. Recent applications of FT-ICR-MS to neuro-proteomics, interactions of target proteins for Alzheimer`s disease (amyloid precursor proteins & presenilins), and analysis of target antigens for auto-immune diseases will be discussed. In these studies a new approach ("affinity proteomics") has been developed with which FT-ICR-MS is also providing unprecedented identification *selectivity* for proteins from complex biological mixtures. [5]

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