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Nanostructure-initiator mass spectrometry

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The ability of mass spectrometry to generate intact biomolecular ions efficiently in the gas phase has led to its widespread application in metabolomics, proteomics, biological imaging, biomarker discovery and clinical assays (namely neonatal screens). Matrix-assisted laser desorption/ionisation (MALDI) and electrospray ionisation have been at the forefront of these developments. However, matrix application complicates the use of MALDI for cellular, tissue, biofluid and microarray analysis and can limit the spatial resolution because of the matrix crystal size (typically more than 10 mm), sensitivity and detection of small compounds (less than 500 Da). Secondary-ion mass spectrometry has extremely high lateral resolution (100 nm) and has found biological applications although the energetic desorption/ionization is a limitation owing to molecular fragmentation. Here, we introduce nanostructure-initiator mass spectrometry (NIMS), a tool for spatially defined mass analysis. NIMS uses 'initiator' molecules trapped in nanostructured surfaces or 'clathrates' to release and ionize intact molecules adsorbed on the surface. This surface responds to both ion and laser irradiation. The lateral resolution (ion-NIMS about 150 nm), sensitivity, matrix-free and reduced fragmentation of NIMS allows direct characterization of peptide microarrays, direct mass analysis of single cells, tissue imaging, and direct characterization of blood and urine.

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Microchip ionization mass spectrometry in drug analysis

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Miniaturization of analytical instruments utilizing microfabrication technology has been one of the hottest research topics in analytical chemistry over the past decade. Driving force to this is an increasing demand for low-cost instruments capable of rapidly analyzing very small amounts of samples with a high level of automation. A concept termed both "Miniaturized total analysis systems (μ-TAS)" and "Lab-on-a-chip" aims to develop integrated micro-analytical systems to perform complete analysis cycles (e.g. sample pre-treatment, chemical reactions, analytical separation, detection and data handling steps) on a single micro-device.

In the most micro-fluidic applications so far, on-chip detection has relied on optical detection, and for sensitivity reasons, fluorescence (FL) detection has been the most commonly utilized. Among the detection techniques alternative to optical detection, mass spectrometry (MS) has gained rapidly enhanced interest in chip-based analysis, and during the last few years great amount of reports have been published in the field. At present, the main focus is in integrating ionization methods to micro separation systems with MS.

Miniaturization of atmospheric pressure ionization techniques has gained rapidly enhanced interest in chip-based analysis. Electrospray ionization (ESI) is currently the method of choice to connect a microchip with mass spectrometry (MS). The flow rates used with microfluidic devices (nl-μl/min scale) are ideal for optimal sensitivity in ESI-MS. Different materials, such as silicon, glass, polymers have been used in fabrication of microchips. Recently, SU-8 polymer has been shown to be highly suitable material for microfluidic separations and electrospray ionization.

Even though ESI is an excellent method for polar and ionic compounds, its sensitivity for neutral and non-polar compounds may be poor. Atmospheric pressure chemical ionization (APCI) and especially atmospheric pressure photoionization (APPI) offer alternative ionization techniques that are capable to ionize with high efficiency non-polar compounds. Recently, we presented microchip APCI and APPI, which allow flow rates down to 50 nl/min making it directly compatible with microseparation systems. The chips provide excellent sensitivity, robust analysis, good reproducibility and cost efficient manufacturing. The feasibility of the APCI and APPI microchips in coupling of micro liquid chromatography and gas chromatography to mass spectrometry is presented.

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Proteomic microchips

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The basic goal of a proteomic microchip is to achieve efficient and sensitive high throughput protein analyses, carrying automatically out several measurements in parallel. A protein chip would either detect a single protein or a large set of proteins for diagnostic purposes, basic proteome or functional analyses. Such analyses would include, e.g. interactomics, general protein expression studies or detecting structural alterations or secondary modifications. Visualization of the results may occur by simple immunoreactions, general or specific labeling or mass spectrometry. The complexity of human proteome exceeds by far that of the genome and it is estimated that we express around 500,000–1,000,000 different proteins or variations thereof. It seems obvious that we are unable to create antibodies to all these proteins in the near future, thus excluding the possibility to use immunoarray technology for to detect complex protein expression alterations. Neither are we able to detect most of the low abundant proteins by any general or specific protein staining method. Finally, also the limitations both in sensitivity and specificity in current mass spectrometers highlight the difficulties we are facing in proteome analysis of today.

While microchip sized protein arrays with a limited number of antibodies are currently available from several manufacturers, we do only have a few other chips to choose