A MALDI-Mobility/OTOF for Complex Peptide Mixture Analysis

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The combination of mobility spectrometry with TOF mass spectrometry is a long known concept [1]. Its use in combination with modern ionization methods has been done for ESI [2,3,4]. In this work we combine mobility/TOF with MALDI [5].

Ions are produced at high pressure with a nitrogen LASER. They drift along the axis of a mobility cell in a homogenous field. At the exit of the drift cell they enter a low-pressure region where they are focussed into a parallel beam and extracted into an orthogonal extracting time-of-flight analyzer (OTOF).

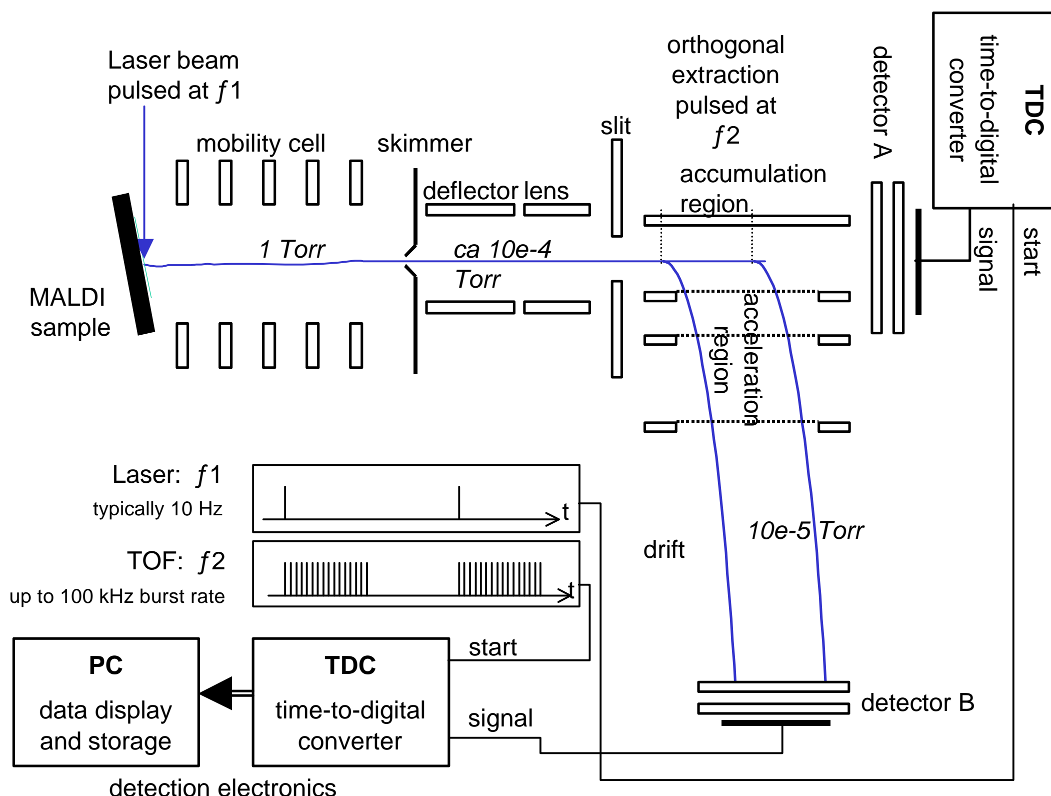

Figure 1: Overview of the MALDI-Mobility/OTOF

This results in a 2-dimensional separation (mobility and mass), similar to LC/MS or GC/MS. The mobility separation significantly reduces mass spectral congestion of complex mixtures in proteomics. The pulsed characteristic of MALDI matches very well the intrinsic timing requirements of a mobility/TOF. In addition, saturation of acquisition electronics is reduced as the ions from each LASER shot get distributed into many mass spectra. This puts back single-ion-counting electronics (TDC) into the field of MALDI-TOFMS. Mobility drift times are now in the range of 1 ms and will be in the range of 10 ms when going to higher drift chamber pressures. Using a compact orthogonal extracting TOF allows the use of extraction frequencies of up to 50 kHz. Consequently, each mobility spectrum is mass-scanned 50 to 500 times.

Figure 2 shows a mobility spectrum of a trypsin digest of cytochrome C with four different mass spectra taken from different regions of the mobility spectrum. For comparison the spectra of the same sample acquired with conventional high vacuum MALDI is shown. MALDI at high pressure characteristically differs from high vacuum MALDI [5].

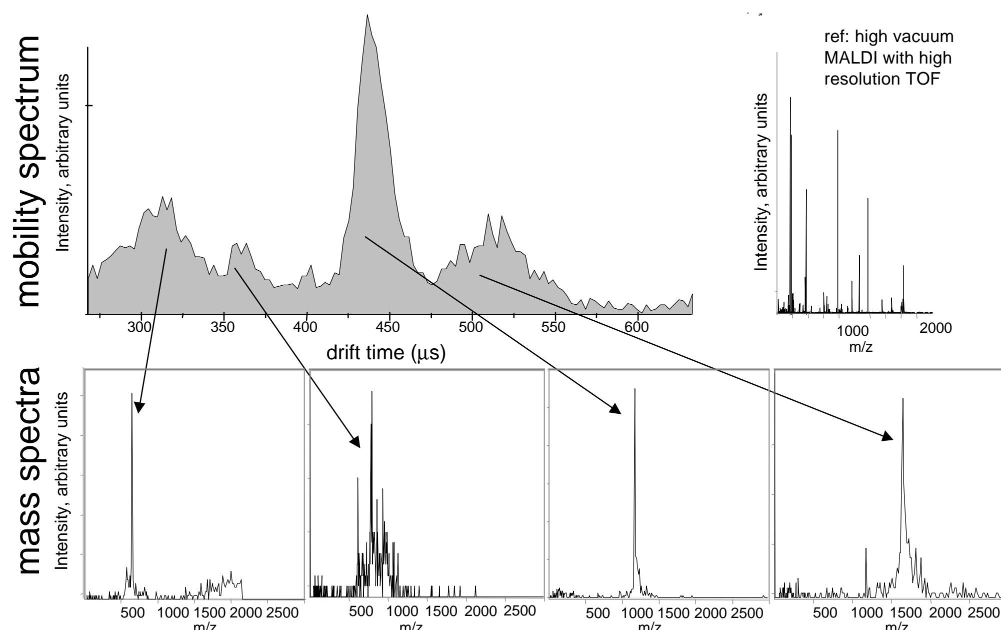

Figure 2: Peptide mixture from a trypsin digest of cytochrome C

Parent ion selection and fragmentation can be done in the skimmer region. Due to the separation of the ionization process from the mass analyzer the mass resolution is now no longer limited by the sample preparation or the ionization process and the same resolution can be achieved for all fragment ions. In the current setup only a low resolution TOF analyzer is implemented. The mobility resolution is up to 25 and will be increased at higher pressure to separate more complex mixtures. The sensitivity is in the picomole range in spite of transmission losses. Figure 3 shows 3D data from our present instrument.

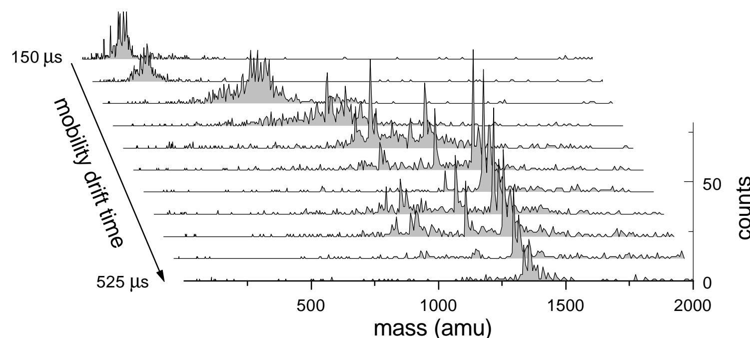

Figure 3: Mobility/TOF data for vitamin B12

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