A novel Ion Processor Device for High-Throughput Analysis in a High-Resolution Mass Analyzer


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Introduction

Ion accumulation devices are routinely used to chase ion packets prior to pulsed extraction into an analyzer. A prominent example is the C-Trap coupled to a Thermo Scientific™ Orbitrap™ analyzer. Compared to conventional orthogonal extractors found in QToF instruments, these benefit from vastly higher duty cycle but require a compromise between buffer gas pressure to capture and thermally ions and minimized fragmentation and scatter during extraction.

A novel ion accumulation and extraction device formed of two pressure regions for parallel accumulation/fragmentation and extraction is introduced. It has a unified, phase-locked RF pseudopotential channel for seamless transfer of pre-cooled analytic ions to overcome common limitations of ion transfer energy, cooling time, device size and buffer gas pressure. Axial accumulation and movement are performed via DC electrodes, allowing fast movement/processing of reduced pressures.

Figure 1 shows a schematic of the ion processor. In a), the general scheme including ion movement inside the ion processor is presented. The ion processor is divided into two regions, a High Pressure Region and a Low Pressure Region. The High Pressure Region is optimized to accumulate/fragment ions while the Low Pressure Region is preparing ions for injection into the Thermo Scientific™ Orbitrap™ Analyzer. Both regions are operated in parallel, i.e. accumulation is done in parallel to preparation/arrangement into the Orbitrap analyzer. In b), crucial components of the ion processor are highlighted. At the entrance of the ion processor, a steel aperture acts as an entrance lens. DC potentials are changed as a function of time in order to transfer ions between the regions and to extract ions into the analyzer.

Experimental

An example instrument was constructed based on a Thermo Scientific™ Orbitrap Exploro™ platform mass spectrometer coupled to the novel Thermo Scientific™ Orbitrap™ Astral™ analyzer. A detailed description of the ion processor is highlighted in Figure 2. The instrument is geared for high quality full-MS scans in the Orbitrap at low mass and parallel high-speed handling of up to many MS/MS acquisitions in the Astral analyzer.

The key performance characteristics of the processor were measured with electrophoretically injected ions of Thermo Scientific™ Penta™ Flexible™ calibration solution and intact proteins. Ions could be isolated with quadrupole mass filter before sending them to the ion processor.

Figure 2. Experimental instrument incorporating Orbitrap analyzer and ion processor combined with Astral analyzer.

Results

Flexible spectrum: Figure 3 shows a typical 10,000 ion FlexiMass full-MS spectrum, acquired at a high repetition-rate (single acquisition).

Figure 3. 10,000 ion FlexiMass full-MS spectrum.

Fragmentation: Ion fragmentation is performed by applying a DC offset potential to the high-pressure region of the ion processor. Ions are accelerated into the high-pressure region where they undergo high-energy collisions and consequently dissociate. After dissociation, ions accumulate in the low-pressure region of the ion processor. This accumulation is initiated by changing the DC potential of the first region. After transfer, ions are trapped by DC gradients in the low-pressure region. After successful trapping, ions are elevated to 400 before the extraction sequence starts. The high-pressure region is immediately switched back into ion accumulation/fragmentation mode as the last ion packet can arrive. In Figure 5, fragmentation spectra for MRM/m/z 524 and Ultraplex m/z 1532 are presented. For comparison, an Ultraflex MS/MS acquired in the Orbitrap analyzer is shown in c).

Figure 4. Comparison of number of ions for MRM/m/z 524 (left axis) and total number of ions (right axis) as function of injection time. Isolation range of 190-2000 and RF amplitude of 1475 Vpp.

Figure 5. a) MS/MS spectrum of MRMA524 for 100ions recorded at 200Hz. b) Comparison of Ultraplex m/z 1532 MS/MS spectrum between Astral analyzer and c) Orbitrap analyzer.

Ion Capacity: Trapping capacity and linear response with injection time is crucial for many analytical applications. This was proved by scanning ion accumulation time under varying conditions like for example varying isolation windows. Intervals of individual ion species and overall ion current have been evaluated. A typical example can be found in Figure 6.

Figure 6. Comparison of number of ions for MRM/m/z 524 (left axis) and total number of ions (right axis) as function of injection time. Isolation range of 190-2000 and RF amplitude of 1475 Vpp.

Intact Proteins: The ion processor is also suitable for handling intact proteins. Figure 7 shows 100s averaged profile spectra of isolated myoglobin (17040Da) over both a wide mass range and zoomed into a single charge envelope. The device still allows the acquisition of individual spectra at 200Hz, in order to get good quality spectra however, at least 100 averaging is required. Unwanted fragmentation and scatter during extraction is well controlled.

Figure 7. Myoglobin full-MS profile spectrum and zoom in m/z 17040 envelope.