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SIMION analysis of a high performance linear accumulation octopole with enhanced ejection capabilities

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Abstract

Here, we present the results of extensive SIMION 7.0 modelling of a new linear octopole ion trap. The octopole was designed to increase the efficiency of an electrospray ion source coupled to a Fourier Transform Ion Cyclotron Resonance (FTICR) mass spectrometer. This improvement was achieved by applying a pulsed axial field to the octopole to eject the ion packet with a time and energy distribution that better match the acceptance criteria of the FTICR cell, thus increasing the trapping efficiency and sensitivity. The axial field was produced by applying a pulsed dc potential to the custom-designed ejection electrodes located between the octopole rods. The time and energy profiles of the ejected ion packets for several electrode shapes were calculated and are discussed in terms of their compatibility with efficient trapping of the ion packet in the FTICR cell. Preliminary experimental results show increased signal using the dc ejection electrodes of approximately 100%.

Keywords: Linear ion trap; Octopole; FTICR; Simulations; Ejection electrodes

1. Introduction

The application of high performance mass spectrometric methods for biomedical analysis has increasing requirements for sensitivity. Often studies involve the analysis of low copy number molecules in a pool of high abundant proteins [1–4]. Chromatographic separation [3,5], capillary isoelectric focussing [6], and capillary electrophoresis [1] have all been used to reduce the complexity of the samples entering the mass spectrometer at any specific time and to concentrate each analyte. Such hyphenated experiments now permit attomole measurements. However, there are still applications where increased sensitivity is desired. High-throughput proteomics applications and specifically the search for biomarkers (up- and down-regulated proteins, post-translation modifications and point-mutations have all been associated with disease) would benefit from increased sensitivity and a higher dynamic range.

Fourier Transform Ion Cyclotron Resonance Mass Spectrometry (FTICR-MS) is an ion trapping technique [7] that distinguishes itself from other types of mass spectrometry: high spectral resolution, for example resolving two peptides that differ in mass by less than the mass of a single electron [8], and high mass accuracy make the FTICR ideally suited for rapid analysis of complex mixtures [1,4,9]. To be compatible with fast separation techniques the ions must be trapped in the FTICR cell preferably without using a trapping gas. The acceptance criteria for the FTICR infinity cell [10] for non gas-assisted trapping with sidekick are: a trapping time window within 0.2–0.4 ms and kinetic energies of ions lower than 2 eV per charge, for ions with m/z lower than 2000 [11].

The sensitivity of an FTICR experiment is influenced by many factors, including efficiency of ion generation, ion-transport and ion detection. Improvements in all aspects continue unabated [12,13]. Collisional cooling of ion beams in 2D-multipoles, operated in an rf-only mode, have improved the performance of FTICR mass spectrometers and are now widely used in all types of mass

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spectrometer [14–17]. Through collisions, the buffer gas reduces the kinetic energy of a particle beam and focuses it on the longitudinal axis of the guiding multipole. This low-energy ion beam can then be focused and transported with high efficiency into the next region of the instrument. It has been shown that if ions are kinetically cooled and accumulated before being pulsed out of the multipole, sensitivity and dynamic range of the experiments are increased [13,16].

However, there is still scope for improving the performance of these linear ion traps. When many ions are present in a linear ion trap, the sensitivity of the measurement can decrease. Space-charge-induced ion discrimination in the multipole can lead to the absence of many expected analyte peaks [18] and multipole storage assisted dissociation (MSAD; space-charge-induced collision-activated dissociation inside the multipole) can lead to fragmentation of the ions of interest [19,20]. Furthermore, the trapping capability of linear ion traps is worse for native bio-macromolecules and their complexes, because their native conformations have smaller collision cross-sections than their de-natured analogues [21]. Though improved trapping has been achieved using increased collision-gas pressure, this causes MSAD to be more problematic [19].

A longer linear multipole ion-trap would alleviate many of the above problems: in a large ion-trap space charge effects occur at larger ion numbers, so the potential for MSAD and ion-discrimination is reduced, and non-covalent complexes have more time to collisionally cool, thus a greater fraction can be trapped. One drawback of a longer trap is that the time distribution of the ejected ions is larger because it takes a longer time for ions located at the beginning of the multipole to move to the end where they can experience the ejection field supplied by the exit lens (during accumulation this lens provides a trapping field). Longer multipoles can lead to lower sensitivity since only a small fraction of the ions accumulated in the multipole are trapped in the FTICR cell. Normally, the multipole length is chosen as a compromise between the ejection time distribution and space-charge considerations.

The time-distribution of the ejected ion packet can be shortened by creating an axial field in the multipole [22]. This would allow the analyst to benefit from the advantages of a longer multipole outlined above. An axial ejection field can be created in several ways without significantly affecting the rf multipole field. Any perturbation of the rf field can reduce the *m*/*z* transmission window. The methods that have been used to date are:

- Segmented multipole rods—by applying a different dc bias to each segment an ejection field can be created with minimal rf-field distortion [23]. In practice, however, because alignment of the segments is key to the design, engineering must be meticulous.
- A set of rings surrounding the multipole—by applying different dc potentials to these rings, an axial field is created with low distortion of the rf field. This design is robust. However, the dc potentials that must be applied to the rings are prohibitively high [24,14].
- Tilted or conical multipole rods—perturbs the rf trapping field making trapping of the incoming ions in the multipole less efficient [24,25].
- Tilted dc wires located inside an octopole [26]—do not affect the rf field significantly, but these wires must be thin making the construction quite fragile and difficult to shape.
- T-shaped electrodes located between quadrupole rods [22]—in this case, four extra electrodes (T-shaped) were placed between the quadrupole electrodes, to which the same dc ejection voltage is applied. By shaping these electrodes, a linear axial field was created through the quadrupole. The setup is simple and the field distortion small.

To increase the efficiency of external accumulation for large ions and to minimize detrimental space-charge-induced artifacts such as MSAD and space-charge induced discrimination, we designed an elongated linear octopole ion trap. To ensure efficient ejection from the octopole, efficient transfer to, and trapping in the ICR cell we added eight T-shaped ejection electrodes, located between the octopole rods, to create an axial field. Extensive simulations were conducted to optimise the time and energy distributions of the ions ejected from the octopole to match the trapping characteristics of the FTICR cell.

2. Description of the simulated accumulation octopoles

The octopole will be used to accumulate ions generated by electrospray ionisation [27], and matrix-assisted laser desorption/ionisation [28]. Consequently, ions covering a wide range of *m*/*z* need to be accumulated, a task best suited to a higher order multipole [29]. The wider *m*/*z* range and higher charge capacity of the octopole compared to that of lower order multipoles (e.g., twice higher than a quadrupole [30]) led to the decision to base our ion trap on an octopole. To increase the multipole order above eight does not yield improvements in performance that would justify the technological complications needed for its realization [31]. To our knowledge this is the first time a linear octopole ion trap equipped with shaped, non-linear, ejection electrodes is considered to enhance the sensitivity of the source of an FTICR-MS.

The octopole is 180 mm long, made of eight circular rods of 6 mm diameter. The field radius of the octopole was chosen such that the ratio $r_{rod}/r_0 = 0.355$. This ratio has been shown to be a good approximation for the ideal octopole field [32]. To maximize the fraction of ions trapped in the linear octopole, the beginning of the octopole was beveled so that octopole fits inside the skimmer of the electrospray ion source. The skimmer and a single electrostatic lens at the end of the octopole