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Injecting electrospray ions into a Fourier transform electrostatic linear ion trap

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ABSTRACT

A Fourier transform electrostatic linear ion trap (FT-ELIT) is a mass analyzer consisting of a field free region with a reflectron on each side. Ions bounce back and forth and a signal is generated using a centrally located image charge pickup electrode. In this report we describe a technique for injecting packets of ions produced by dim sources such as electrospray ionization (ESI) into an FT-ELIT. The technique involves accumulating and thermalizing ions in a collision cell. The collision cell is equipped with a set of electrodes that enables the creation of an axial electric field that is used to concentrate the accumulated ions near the exit. Further concentration is achieved by reducing the potential on the exit lens of the collision cell prior to ion ejection. We demonstrate that these concentration techniques significantly increase signal intensity. We also use ion optical simulations to show that the signal intensity increases because the concentration increases the spatial charge density of the injected ion cloud not only by compressing the ion cloud in the collision cell, but also by decreasing the time required to eject the ions from the collision cell. We also demonstrate that the concentration techniques do not broaden the kinetic energy distribution of the injected ions; therefore, the concentration does not degrade resolution. Using these injection techniques, we are able to analyze ions produced by ESI ranging from 300 to 2200 m/z in a single injection with high signal-to-noise ratio using FT-ELIT.

1. Introduction

An electrostatic linear ion trap (ELIT) is a relatively new mass analyzer that consists of a field free region with a reflectron on either side [1–4]. An ELIT can be operated as a mass spectrometer in several different ways. In a technique known as charge detection mass spectrometry (CDMS) [5], an individual ion of known energy is captured in an ELIT. The ion ‘bounces’ between the reflectrons and an image charge pickup electrode mounted in the center of the field free region registers a signal during each pass. The frequency of the signals is related to the ion's velocity which can be used along with its energy to calculate its mass-to-charge ratio (m/z). The magnitude of the image charge signal is also proportional to the number of charges (z) on the ion, which can be determined after calibration of the detector. Together, these two measurements allow the determination of mass.

CDMS is most useful for studying large (above 100 kDa) ions. When produced by methods such as electrospray ionization (ESI), such large ions are often quite heterogeneous in terms of both mass and charge, which makes individual species unresolvable with most forms of MS. This problem is circumvented in CDMS which analyzes individual ions. Additionally, larger ions are usually able to carry more charges, making them easier to detect via CDMS. It is for these reasons that many CDMS experiments involving ELITs have been performed on molecules of megadalton size including poly(ethylene oxide)s [6,7], DNAs, [2,8] and protein aggregates [9] including intermediates in virus capsid assembly [10]. Recent improvements to the detection limits of CDMS [11,12] have enabled the analysis of individual protein ions containing as few as nine charges [12].

CDMS is a very promising technique for making mass measurements of large ions for which other MS techniques are unable to resolve individual species. However, CDMS also suffers

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from a few drawbacks. CDMS only works if ions are injected individually. Therefore, measuring enough ions to adequately represent the sample can be time consuming. But perhaps the biggest drawback of CDMS is the fact that image charge detectors have relatively low sensitivity. While some impressive work has demonstrated detection of ions with fewer than ten charges [12], typically tens to around 100 charges are required for detection. This limits the application of CDMS to relatively large ions (above 10 kDa), since most smaller ions are unable to carry enough charge to be detected.

An obvious solution for the problem posed by ions with few charges is to inject many of them together in a packet. While this makes the signal amplitude useless for determining the charge states, such instruments may be capable of determining charge states of low-charge ions by other means, such as measurement of isotope spacing. Early instruments for analyzing low-charge ions using ELITs used pulsed ionization methods [13,14]. Packets of ions from continuous sources were generated by chopping a continuous beam [13,15,16], or by using klystron-like bunching [17]. However, the beam chopping technique works well only for ion sources of relatively high brightness (above 1 nA), as dimmer beams contain very few ions in the approximately 1 μs pulse width suitable for injection into an ELIT.

The heavy isotope analysis community has made great progress on the problem of using ELITs to analyze ions from dim, continuous beams produced by particle accelerators. These groups have developed devices for accumulating and concentrating the continuously produced ions and injecting them into the ELIT in short packets. These groups most often operate the ELIT as a multi-reflection time-of-flight (MR-ToF) instrument that relies upon spaciotemporal focusing of the ion packets at the detector plane. Such instruments typically have very stringent requirements for the injected ion packets. The ion packets are typically formed by first accumulating the incoming, high energy ions in a gas filled stopping cell consisting of a linear, multipole ion trap. The ions are then bunched by transferring them to either a second device such as a short linear multipole ion trap or a three-dimensional ion trap before injecting the ions into the ELIT. Several designs for devices capable of producing suitable ion packets have been reported, including devices based on short [18] or segmented [19,20] linear multipoles as well as a flat trap designed to eject ions orthogonally to the incoming beam [21,22]. A design in which a linear multipole is used to accumulate ESI ions which are then transferred to a short, linear multipole for injection into an ELIT has even been proposed [23]. The electrostatic storage ring community has developed two instruments for analyzing low-charge ions produced by ESI. Electrostatic storage rings have injection requirements similar to ELITs. These instruments use a cylindrical ion trap [24] or a segmented linear multipole [25] as ion accumulation and bunching devices.

Rather than doing CDMS or MR-ToF, we operate our ELIT in a third mode. In our ELIT, signal is acquired using an image charge pickup electrode as in CDMS, but since ions are not injected individually, the magnitude of the image charge signal cannot be used to calculate the number of charges on any specific species. Rather, the Fourier transform (FT) of the time domain signal is used to obtain the ions' frequencies, which are proportional to the inverse square root of m/z [13]. We refer to this mode of operation as FT-ELIT. Like the MR-ToF mode, FT-ELIT requires packets of ions. However, in FT-ELIT no attempt is made to focus the ions at a detector plane, making the spatial extent of the ion packets less important. Spectra can be obtained so long as the ion packet is smaller than the distance corresponding to one trip around the ELIT. Nonetheless, analysis of ions generated by electrospray ionization (ESI), which is a relatively dim ion source, by FT-ELIT requires accumulation and bunching of ions. Rather than using separate devices for accumulation and bunching, we have elected to use a single device to perform both functions. This device consists of a linear quadrupole ion trap (collision cell) equipped with a set of four vane electrodes that allow for the creation of a potential gradient along the axis of the device [26]. Herein, we refer to the vanes as LINAC (for linear acceleration) electrodes. The collision cell allows for effective stopping and accumulation of ions coming in from the ESI source, while the LINAC allows concentration of the accumulated ions near the end of the collision cell closest to the ELIT. Finally, the ion packet is released toward the ELIT for analysis.

In this report we describe our ion accumulation and injection device. We demonstrate the sensitivity enhancement achieved using the LINAC for ion concentration. We also demonstrate an additional means of concentration accomplished by lowering the potential applied to the exit lens of the collision cell. We use ion optical simulations to characterize the effects of the potentials applied to the LINAC electrodes and the exit lens on both the spatial distribution and the energy distribution of the ion packet injected into the ELIT. We demonstrate that the spatial compression and coherent ejection of the ion packet achieved using these ion concentration techniques is responsible for the observed increases in sensitivity, and that this is achieved without broadening the energy distribution of the injected ions.

2. Experimental

2.1. Materials

A 100 μM tetraoctylammonium bromide (TOA) sample was prepared by dissolving the analyte in 49.5% H_2O, 49.5% methanol, 1% acetic acid. Tetraoctylammonium bromide was purchased from Sigma–Aldrich (St. Louis, MO). Methanol and glacial acetic acid were purchased from Malinckrodt (Phillipsburg, NJ). Water was purified with a model D8961 water purifier (Barnstead, Dubuque, IA) prior to use. ESI tuning mix for ion traps was purchased from Agilent (Santa Clara, CA). The mix contains 1.5 μM hexamethoxyphosphazene (HMP), 7.4 μM hexakis(2,2-difluoroethoxy) phosphazene (HEP), 20 μM hexakis(1H, 1H, 3H-tetrafluoropropoxy) phosphazene (HPrP), 20 μM hexakis(1H, 1H, 5H-octafluoropentoxy) phosphazene (HPeP), and 20 μM hexakis(1H, 1H, 7H-dodecafluoroheptoxy) phosphazene (HHP).

2.2. Mass spectrometry

The mass spectrometer has been described previously [27]. In brief, the sample solution is loaded into a pulled glass capillary and placed in front of the sampling orifice. High voltage is applied to a platinum wire in contact with the solution in order to generate an electrospray [28]. Ions are transported to a collision cell equipped with LINAC electrodes where they are accumulated [26]. The rods are driven by a home-built RF power supply operated at 1.09 MHz, 400 V_{p-p}. All four LINAC electrodes are connected to the same DC potential and are made negative (relative to the DC offset of the rods) to attract positive ions towards the exit end of the collision cell. Helium gas is used to raise the pressure inside of the collision cell to ~1–10 mTorr.

For the purposes of this paper, the collision cell rod offset potential is stated relative to earth ground and all other potentials are henceforth relative to the rod offset. During ion accumulation, the rod offset is 0 V and the potentials applied to the LINAC, entrance lens, and exit lens are −250, −20, and 50 V respectively. Ions are then subjected to a potential lift as the rod offset is increased to 1990 V (80 ms ramp) and the aforementioned electrodes are ramped to −1000, 10, and 10 V respectively. It should be noted that in certain experiments the LINAC was ramped