Supplemental Information for:

Mass, Mobility and MS^n Measurements of Single Ions Using Charge Detection Mass Spectrometry

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Additional Experimental Details

Samples. Polyethylene glycol (PEG) with a nominal molecular weight of 8 MDa was obtained from Sigma Aldrich (St Louis, MO, USA) and was used without further purification. PEG solutions were prepared at a concentration of 60 nM in a 1:1 water-methanol solution.

Mass Spectrometry. Experiments were performed using the single particle analyzer of mass and mobility (SPAMM), a home-built charge detection mass spectrometer, a schematic of which is shown in Figure 1. Ions are formed by nanoelectrospray ionization using borosilicate capillaries that have tips pulled to an inner diameter of approximately 1 μm. A platinum wire is inserted into the capillary so as to contact the sample solution. A potential of +1-2 kV with respect to ground is applied to the capillary to initiate ion formation by electrospray. The resulting ions are transferred to vacuum using a Z-spray source (Waters, Milford, MA) modified to contain an extraction cone with a smaller 0.5 mm hole to improve differential pumping between the source and first vacuum stage. Typical voltages inside the source are +350 V for the exterior sample cone and +210 V for the interior extraction cone, with a pressure of 1 Torr between the cones. The source is heated to 80 °C for all samples.

After the extraction cone, ions are guided through the next vacuum stage at a pressure of 3×10^{-4} Torr by a pair of RF-only quadrupole ion guides (Ardara Technologies, Ardara, PA). The ion guides operate at a frequency of 1.89 MHz with a peak-to-peak potential of 1500 V and a DC offset potential of +204 V and +170 V for the first and second ion guides, respectively. The quadrupole ion guides are separated by a gate valve. The potential offset in the first ion guide defines the nominal energy of the ions. After the ion guides, ions pass through a lens with a potential of +180 V and into an electrostatic turning quadrupole (Ardara Technologies, Ardara, PA) in a third differentially pumped vacuum chamber at a pressure of 6×10^{-7} Torr. The turning

quadrupole is used as an energy filter that works by bending ions within a selected energy range 90° into the detection chamber. The energy range selected for transmission into the trap depends on the potentials applied to the outside walls of the quadrupole and each pole, with each diagonally opposed pair of poles at the same potential. The walls, outer and inner poles were set to +140 V, +220 V and +120 V, respectively, which selects a distribution of ion energies centered at 209 eV/charge with a standard deviation of 3.2 eV/charge.

The energy selected ions are accelerated though a 1.0 mm conductance limit at a potential of -250 V into a final vacuum chamber with a pressure of 5×10^{-9} Torr where they are trapped and detected. The detection system consists of one stainless steel tube in between two conical trapping electrodes based on the design of Schmidt et al.[55] The tube has an inner diameter (ID) of 7.1 mm and is 28.2 mm long. This tube is held in place by insulators inside grounded shielding. The total distance separating the two trapping electrode is 37.7 mm. The detector tube is connected to a CoolFET charge sensitive preamplifier (Amptek, Bedford, MA) containing an A250 preamplifier and JFET cooled to -50 °C by a Peltier cooler. The preamp is housed in a shielded box inside the vacuum chamber, and the signal is passed to a shaping amplifier consisting of a differentiator, integrator and two voltage amplifiers (Amptek A275) and a signal filter outside the vacuum chamber. Data are recorded at a rate of 5 MHz on a computer with an analog to digital converter card (ATS9350, AlazarTech, Pointe-Claire, Canada) and stored for analysis offline. For trapping times longer than 2 s, the sampling rate is decreased to 2 MHz so that the entire trajectory can be recorded in one transient. The detector response measured using a test capacitor is 21 μV/charge.

Ions with approximately 200 eV/charge are trapped inside the detector when both cone electrodes are at 330 V. The electrode in the back of the trap is set to 330 V for the entire

trapping even, and the front electrode is changed between an initial ground potential and 330 V with a MOSFET switch to allow ions into and out of the trap. After detecting a charge pulse greater than a set amplitude, the switch is triggered and the front potential is raised and maintained for a predetermined maximum trapping time during which data is acquired. After the measurement, the front voltage is lowered for 5.0 ms to allow ions to leave and enter the trap. The fraction of events for which successful ion trapping occurs is approximately 40%.

An ion entering a detector tube induces an image charge of opposite sign on the tube. Inverting and shaping the square wave signal from that tube produces a pattern consisting of a leading positive peak and trailing negative peak for a positive ion. The amplitude of each peak is proportional to the charge of the ion, and the spacing between the peaks is proportional to the velocity of the ion.[54] The minimum charge on an ion for this signal pattern to be detected above the noise is approximately 225 charges. Data is analyzed with a program designed to find peaks of a consistent size and spacing that is described in detail elsewhere.[54]

Simulations

Determining Energy per Charge of Individual Ions. The ion energy was determined from the turning time ratio using data from simulations of ions traveling along the central axis of the trap. The relationship between the ion kinetic energy and turning time ratio was fit with a cubic polynomial and the ion energy for a given turning time ratio is determined from that polynomial fit.

The turning time ratio for a given energy depends on both the distance an ion enters the trap of the central axis and the angle at which the ion enters the trap. The uncertainty in the ion energy obtained from the turning time ratio was obtained by simulating ions that enter the trap

off center and by simulating ions that enter the trap at various angles. At 1.0 mm off center, the uncertainty in the ion energy is ~0.5% and this is an upper limit because the radius of the trap entrance is only 0.75 mm. Similarly, ions can enter the trap at a maximum angle of 1.5° but these ions are not trapped. To determine the average turning time ratios for ions entering at an angle off the trap axis, 8 MDa and 1000 charge ions with 193-253 eV/charge and an initial trajectory 0.5° and 1° off axis were simulated with a maximum time of 10 ms during which time they made ~250 passes through the trap (Figure S-1). The range of ion energies that can be trapped for ions entering the trap off center is narrower than for those that enter the trap on axis. For ions entering the trap 1° off center with energy in the middle of the trapping range, the turning time ratios are close to those for ions with 2 eV less energy traveling on the trap axis resulting in an energy uncertainty of ~1%. However, ions near the high and low end of the trapping range do not have stable trajectories for the full 10 ms. Ions with 193-194 and 246-253 eV/charge are not trapped, even though ions with this energy per charge are trapped when they start on the axis of the trap. Thus, the distance off center from which the energy uncertainty is determined depends on the ion energy. The maximum turning time ratio for ions entering 1° off the trap axis is 2.21 for 245 eV/charge ions. However, ions with larger turning time ratios are observed in experiments. These ions must have entered the trap without such a large off-axis angle so the uncertainty in determining the ion energy is obtained for a lower off-center angle.

For ions entering the trap 0.5° off axis, average turning time ratios are similar to ions with up to 1 eV less energy traveling on the trap axis, resulting in an uncertainty of ~0.5%. The trapping range for these ions extends from 194-251 eV/charge. The maximum turning time ratio is 2.34 at 251 eV/charge, which is still less than the maximum turning time ratio of 2.45 at 253 eV/charge for ions entering on the trap axis. The energy uncertainty associated with ions

entering off the trap axis correspondingly decreases for ions with high turning time ratios. To account for this effect of high energy ions not remaining trapped if they enter off the trap axis, the overall energy uncertainty for all energies was estimated at ~1%.

Ion Mobility of Precursor. To obtain the velocity of the precursor ion after losing mass in the absence of collisions, an ion with the initial mass and kinetic energy of the precursor that loses a constant mass in each time step was simulated. The simulated mass loss was 0.00274 Da in each 0.01 μs time step corresponding to the mass of the precursor at 1.9 s, which is when the precursor ion stopped losing mass in the experiment. The velocity was then calculated from the time between the ion crossing through the plane on each side of the tube in its last pass through the tube.

Calculation of Normalized Velocity Loss. The velocity of the precursor ion and sixth fragment ion decreases as a result of collisional dampening. The rate at which this occurs was normalized for the different ion lifetimes by dividing the percent velocity loss of both ions by their respective lifetimes. The ions have different oscillation frequencies and thus different distances traveled in a given time. To correct for this distance effect, the rates of velocity loss are normalized by dividing by their respective frequencies. The lifetime of the original precursor is 2.11 s and its average frequency is 30.56 kHz. The loss of velocity due to collisional dampening is 4.7%, and the normalized velocity decrease is 0.072% per thousand cycles. The lifetime of the final fragment is 1.52 s and its average frequency is 21.94 kHz. The velocity loss from collisional dampening is 1.7%, and the resulting normalized velocity decrease is 0.050% per thousand cycles.

Figures

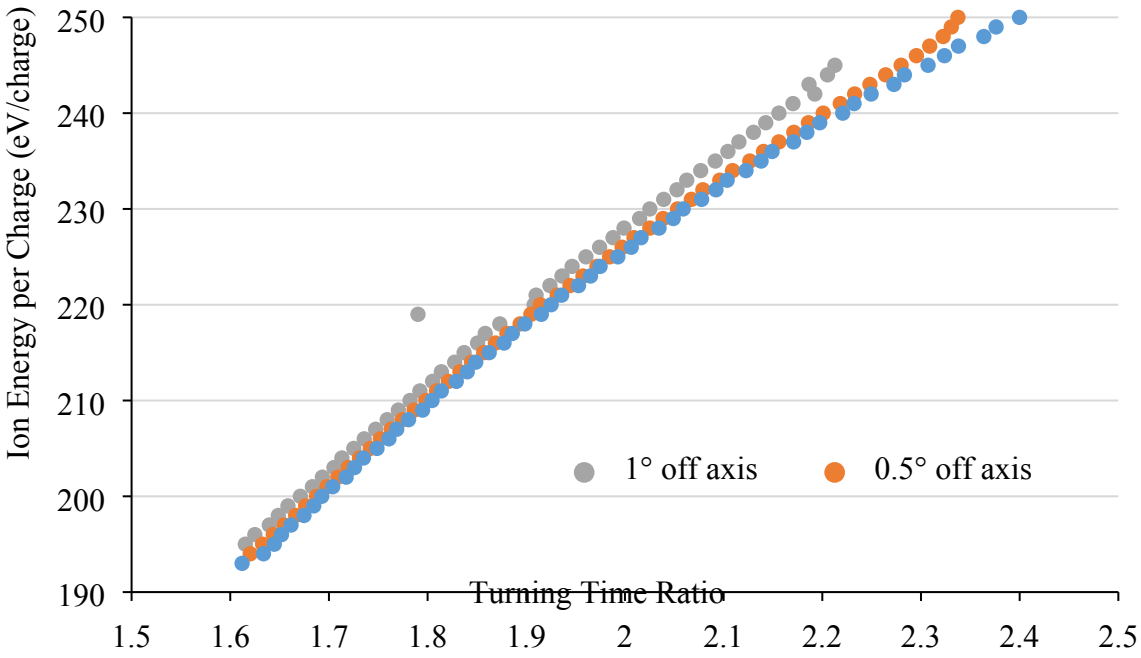

Figure S-1: Ion energy per charge as a function of turning time ratio for ions starting on the center of the trap traveling parallel to the trap axis and at 0.5° and 1° off axis.