When Mass Spectrometry Meets Nanoparticles. Weighing, Manipulating and Fragmenting Single Nanoparticles in the Gas Phase

T. Doussineau, P. Dugourd, R. Antoine

Institut Lumière Matière, UMR5306 Université Lyon 1-CNRS, Université de Lyon 69622 Villeurbanne cedex, France

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A new mass spectrometer based on charge detection has been developed. It enables the determination of mass distribution of various macromolecules and nanoparticles. By using an ion trap coupled to a CO$_2$ laser, photoinduced dissociation of such macroions can be studied at the single ion level giving uniquely access to intrinsic features such as fragmentation patterns and unimolecular dissociation activation energy.

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1. INTRODUCTION

Mass is a critical feature of compounds related to their quantity of matter, their inertia, as well as their energies. To measure mass one can use a scale or a balance, both of which rely on Earth’s gravity. The balances we use today in our laboratories can even detect masses down to 10$^{-7}$ g but this measurement method becomes inadequate below this limit. Although this low mass can be measured by mass spectrometers that use electric or magnetic field to separate ionized compounds according to their mass-to-charge ($m/z$) ratio. However conventional mass spectrometry (MS) has limitations for weighing macroions with masses higher than one megadalton (1 MDa or 10$^{18}$ g) [1]. Above this limit, mass-to-charge ($m/z$) spectra become unsolvable due to the fact that high mass ions may carry an unresolvable distribution of charges. Moreover large ions may not all have exactly the same mass due to sample heterogeneity (i.e. polydispersity), residual absorbsates such as water molecules and counter ions.

One solution to overcome these limitations is to measure both the mass-to-charge ratio ($m/z$) and the charge ($z$) for each ion. This single ion mass spectrometry enables one to construct a histogram of mass yielding the true mass distribution. A convenient way to measure the charge of individual ions is to use image charge detection. A multi-charged ion in the proximity of a conductive surface impresses on it an equal and opposite image charge. This approach was pioneered by Shelton in 1960 for characterizing multiply charged microparticles [2]. Based on this concept of image current detection, mass-spectrometry (CD-MS) coupled to electrospray ionization (ESI) was introduced by Benner and coworkers in 1995 for weighing macroions with masses higher than one megadalton. The passage of a multicharged ion through the detection tube induces on it a voltage proportional to the charge of the ion and inversely proportional to the capacity of the system. The duration of this induced signal is equal to the time-of-flight (ToF) of the ion through the detector. By measuring simultaneously velocity and charge of individual ions, and together with measuring the acceleration voltage, one can compute the mass of the ion. This allows one to extend the limit of conventional mass spectrometry towards high mass compounds, as demonstrated for large DNA strands [4, 5], viruses [6, 7], liquid droplets [8] and macropolymers [9, 10].

While a single stage MS experiment determines the mass of an analyte, tandem MS (MS/MS) can provide information on its structure. Typical MS/MS experiments involve mass selection of the ion of interest in the first MS stage, excitation of the ion followed by its dissociation and mass analysis of the resulting fragment ions in the second MS stage. MS/MS has been used to elucidate the structure of a variety of small to medium-sized molecular ions. Due to the difficulty of detecting large size ions, MS/MS on compounds of megadalton (MDa) molecular weight is almost an unexplored field yet. We recently implemented tandem mass spectrometry for experiments on single electrosprayed ions from compounds of megadalton molecular weight, using two charge detection devices (CDDs) [11] This paper briefly describes the mass spectrometry developments for mass and structural determination of nanoparticles.

2. WEIGHING, MANIPULATING AND FRAGMENTING SINGLE NANOPARTICLES IN THE GAS PHASE

2.1 Instrumentation

We developed a custom-built tandem charge detection mass spectrometer (CD-MS/MS) composed by an electrospray ionization source (ESI) coupled to two CDDs. The ESI source generates highly charged macroions which are guided by an ionic train to the mass spectrometer (Figure 1). Ions are guided by an ionic train to the vacuum stage chamber (∼10$^{-6}$ mbar) which contains two identical CDDs used as a tandem mass spectrometer. Each CDD consists of a conductive tube collinear to the ion beam and connected to a field-effect transistor (JFET). The picked up signal given by the passage of a single ion through the detection tube is amplified by a low-noise charge-sensitive preamplifier and then shaped and differentiated by a home-built amplifier.
The signal is recorded with a waveform digitizer card. The data are transferred to a desk-top computer where they are analyzed with a custom-written user program. Calibration in charge was performed using a test capacitor that allowed a known amount of charge to be pulsed onto the pick-up tube.

The first CDD is used in a single-pass mode and allows ions to be selected and measured in the second CDD. In the single-pass mode, the picked up signal from each single ion composing the sample generated in the electrospray source is measured. Electrical noise limits the charge measurements in CD-MS. A root mean square (rms) noise of ± 250 e is usually obtained, and a precision in charge measurement of about ~15%. In addition to the reduction of noise in the charge measurement circuit, an approach that improves the limit of the charge measurement is to re-measure the charge on individual ions by using an array of charge detection devices or electrostatic ion trap. However, the moderate precision in charge measurement is largely compensated by the high count rate that can be achieved (1000 ions/s). From the analysis of each waveform one can thus rapidly determine, knowing the acceleration voltage, the mass of each single ion that has travelled through the tube.

The second CDD is used as a gated electrostatic ion trap, as proposed by Benner [12]. The conductive tube surrounded by two ion mirrors (inset Figure 1) and preceded by an ion gate. Ions are selected both in m/z and z by synchronisation of the first CDD and the ion gate. A selected ion can be trapped between the 2 ion mirrors if correct voltages are applied on the electrodes of the ion mirror. During the trapping time a continuous wave CO₂ laser can be used in a synchronized manner to irradiate the trapped ion through a ZnSe window for ~50 ms.

2.2 Molecular weight determination of nanoparticles

In the single-pass mode each single ion composing the sample generated in the electrospray source can be detected and measured. On this basis mass distributions of synthetic NIST standard polystyrene particles (100 nm diameter) were accurately determined. Obtained averaged molar masses can be con verted in diameter of spherical particles and are in good agreement with those given by the supplier. The versatility of the electrospray source to “make fly elephants” [13] allowed us to study a large panel of nano-objs such as gold and silica nanoparticles. As an example, Figure 2b shows mass distributions obtained for a colloidal suspension of gold nanoparticles. An important aspect of charge detection MS is that charge of NPs can be measured simultaneously with their mass. This allowed to us to explore the charging capacity of NPs in the gas phase and the correlation between the charge of particles in solution and in the gas phase.

2.3 Trapping and infrared multi-photon dissociation of single megaladon ions

A single macroion selected in mass and charge can be trapped in the second CDD during several tens of milliseconds, which corresponds to several hundreds of oscillations. This generates an electric wavelet on the detector. The first benefit is that we can re-measure charge and time-of-flight as many times as the ion oscillates in the trap improving the z and m/z precision of CD-MS measurements. Fig. 3a shows the experimental raw time domain signal for a trapped ion created by a single highly charged electrospray ion of PEO (mass of 20 MDa and 1550 charges) travelling back and forth through the ion trap. The Fourier transform of this signal (inset in Fig. 3a) shows a peak at 13.8 kHz indicating the fundamental oscillation frequency, which corresponds to an m/z of 12900 Da/e. The first
3. CONCLUSION

CD-MS and CD-MS/MS working in the single-pass and multi-pass modes, respectively, provide unique data on compounds of molar mass ranging from megadalton to gigadalton. In particular the determination of molar mass distribution of various nano-objects has been demonstrated and this key characterization may be extended to the so-called ‘nanoworld’. The implementation of an electrostatic ion trap significantly improves the precision of mass measurements and allows one to study kinetics of dissociation of large macroions. In particular, IRMPD was found to be a promising tool for studying unimolecular dissociation of large macroions at the single ion level.

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