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Characterization of a discontinuous atmospheric pressure interface. Multiple ion introduction pulses for improved performance

Liang Gao [a], Guangtao Li [a], Zongxiu Nie [a], Jason Duncan [a], Zheng Ouyang [b], R. Graham Cooks [a,c,*]

[a] Department of Chemistry, Purdue University, West Lafayette, IN 47907, United States
[b] Weldon School of Biomedical Engineering, Purdue University, West Lafayette, IN 47907, United States
[c] Center for Analytical Instrumentation Development, Purdue University, West Lafayette, IN 47907, United States

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Dedication in celebration and appreciation of the intellectual career of Michael Bowers, with best wishes for continued success.

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ABSTRACT

Discontinuous atmospheric pressure interfaces (DAPI) are used to match the rate of sample introduction to the pumping capacity of miniature mass spectrometers. In this study, the influence of the interface flow conductance and the mass spectrometer pumping speed on ion introduction into a handheld mass spectrometer is investigated. Results show that an intermediate flow conductance (2.6×10^{-3} L/s) gives the best ion introduction efficiency whereas the pumping speed has no influence in the range studied (0.35–7.1 L/s) except that a minimum pumping speed of 0.35 L/s is required. The linear dynamic range decreases with increasing interface open time, a result that corresponds to observations made using standard electrical gating of ion introduction a method that is not available at the high pressures involved in API into miniature systems where ions are transported through pneumatic flow. However, the mechanical opening of the interface with DAPI can be used for automatic gain control (AGC) using an external ion source. Software modifications to allow the use of multiple ion introduction pulses before mass analysis of the trapped ion population improve the detection limits. This method was validated by comparing the results obtained from the same sample using a single ion introduction pulse and multiple ion introduction pulses. In conjunction with this method, a broad-band waveform can be applied to selectively accumulate analyte ions, allowing essentially the entire ion trapping capacity to be devoted to one or more ions of interest.

1. Introduction

The development of miniature ion trap mass spectrometers has been an active research topic, fueled by the promising analytical capabilities resulting from the broad applicability, high sensitivity, high specificity and the convenience of fast in situ analysis with portable instruments [1]. Progress has been made in refining miniature ion trap instruments [2–12], but their applications are still confined to a few areas [13–17]. A key issue is efficient ionization of the sample of interest. Towards this end, various atmospheric pressure ionization (API) sources have been developed to ionize samples in different physical states and from different sample matrices [18–32]. Ions are readily generated by external atmospheric pressure ionization (API) sources but are difficult to transfer into the vacuum manifold efficiently with the limited pumping speed available from miniature mass spectrometers since large quantities of gas are introduced with the ions. As a result, API sources were difficult to use in conjunction with miniature mass spectrometers until the development of the discontinuous atmospheric pressure interface (DAPI) [33].

The DAPI consists of a series of capillaries directly connecting the atmospheric pressure region to the ion trap. Contrary to standard practice in traditional continuous interfaces, ions are introduced into the vacuum manifold discontinuously. Gases carrying ions are pulsed into the ion trap for short periods at flow rates which are too high to be used in the continuous mode. This procedure allows a sufficient number of analyte ions to pass through the DAPI and enter an ion trap fitted with a low pumping speed vacuum system. DAPI has already been demonstrated using the recently developed Mini 11, a 5 kg ion trap miniature mass spectrometer, with only a 3 L/s pumping speed [9]. Samples in the gas phase, liquid phase and solid phase, ionized using API sources including APCI, ESI, and DESI, have been analyzed successfully in the Mini 11 through discontinuous introduction.

Although the DAPI has proven to be an effective ion introduction method, detailed understanding and design consideration have not been reported. It is highly desirable to understand the ion accumulation process inside the ion trap when DAPI is used for ion introduction. Knowledge of the influence of the interface flow

* Corresponding author at: Department of Chemistry, 560 Oval Drive, Purdue University, West Lafayette, IN 47907, United States.
E-mail address: cooks@purdue.edu (R.G. Cooks).

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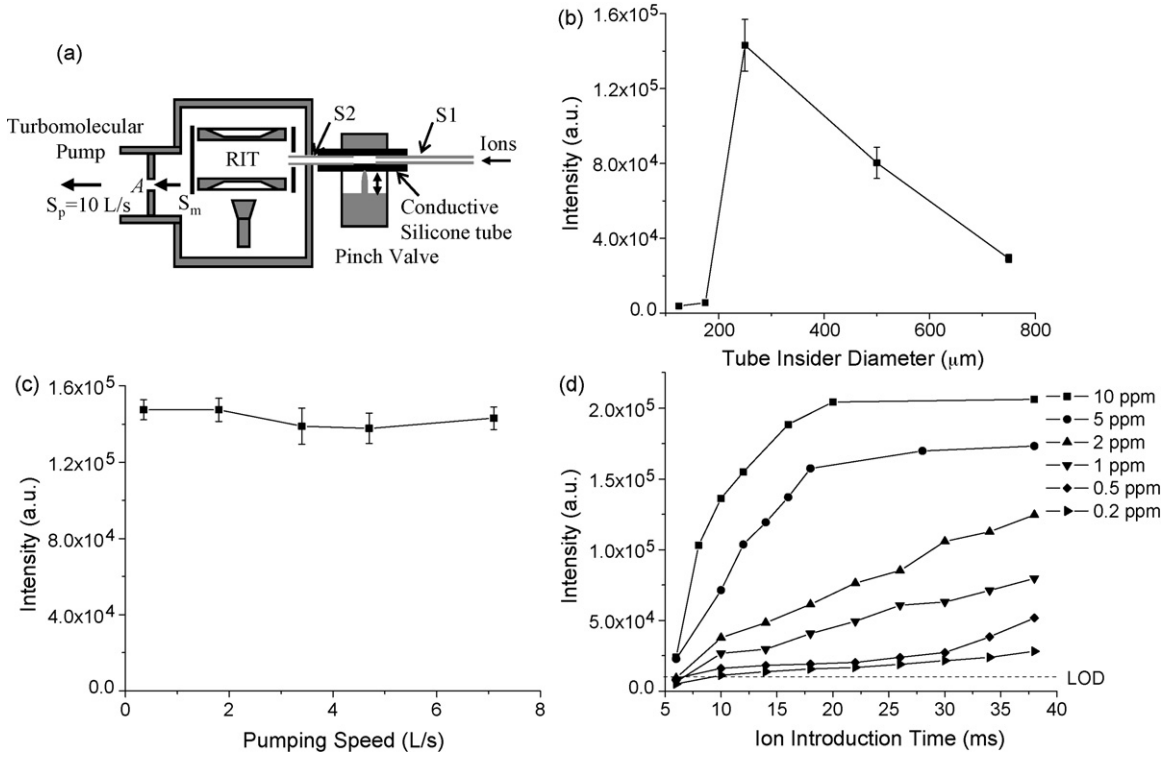

Fig. 1. (a) Instrumentation, including discontinuous interface (DAPI), a rectilinear ion trap (RIT) and electron multiplier. Flange *A* is placed between the turbomolecular pump entrance and the vacuum manifold exit. (b) Ion current at *m*/*z* 443 plotted versus S1 tube inside diameter. (c) Ion current at *m*/*z* 443 plotted versus pumping speed. (d) Ion current plotted versus ion introduction time for Rhodamine B solutions with concentrations of 0.2 ppm, 0.5 ppm, 1 ppm, 2 ppm, 5 ppm and 10 ppm.

conductance and the pumping speed on ion introduction is also important to improve future instrument design. A miniature mass spectrometer was used here to study these aspects of DAPI. Furthermore, a method of multiple ion introduction pulses for DAPI was developed to improve performance.

2. Experiment

A modified Mini 10 mass spectrometer equipped with DAPI was used in these experiments [8,33]. The configuration of the mass analyzer assembly is shown in Fig. 1(a). Ions generated at atmospheric pressure are transferred into the ion trap through the DAPI interface. A standard 5 mm × 4 mm rectilinear ion trap, driven by a 1.3 MHz differential RF signal, is used as the mass analyzer, and an electron multiplier (DeTech 2312, Detector Technology Inc., Palmer, MA) is used to detect ions ejected from the ion trap. The DAPI system consists of two stainless steel capillaries S1 and S2, connected to each other via a conductive silicone tube (i.d. 1.59 mm, o.d. 3.18 mm, length 5 cm). The conductive silicon tube goes through a normally closed pinch valve (390NC24330, ASCO Valve Inc., Florham Park, NJ), which controls the open/closed status of the DAPI. The capillary S1 is the main flow restricting element with an o.d. of 1.59 mm, a length of 10 cm, and an inside diameter as specified herein. The capillary S2, on the vacuum side of the pinch valve, has an i.d. of 1.2 mm, an o.d. of 1.59 mm, and a length of 4 cm. Both stainless steel capillaries, S1 and S2 are electrically grounded at all times.

During operation, a 24 V dc pulse signal lasting for a few milliseconds is applied to the pinch valve at the beginning of each scan cycle to open the DAPI for ion (and gas) introduction; the interface then closes for the remainder of the scan cycle. The manifold pressure rises to $\sim 10^{-1}$ to 10^{-2} Torr after opening of DAPI, then the pumping system slowly restores the vacuum manifold pressure back to $\sim 10^{-3}$ to 10^{-4} Torr for mass analysis in a time period which lasts from hundreds of milliseconds to a few seconds. Next, the multiplier is turned on, and both the RF signal amplitude and resonance ac signal amplitude are scanned to record the mass spectrum. The dc voltages on both ion trap end electrodes are constant at +15 V during the whole scan cycle.

The vacuum system of the instrument consists of a two-stage diaphragm pump (1091-N84.0-8.99, KNF Neuberger Inc., Trenton, NJ), a hybrid turbomolecular pump (TPD011, Pfeiffer Vacuum Inc., Nashua, NH) and a Pirani pressure gauge (MKS 925C, MKS Instruments, Inc., Wilmington, MA). The backing pump with a maximum pumping speed of 5 L/min provides a backing pressure of 3 Torr and the turbomolecular pump provides a pumping speed of 10 L/s. To perform experiments on the effects of pumping speed, a 7.8 mm thick flange *A* with a hole in the center was placed between the turbomolecular pump entrance and the manifold exit, so that the actual pumping speed at the manifold exit could be adjusted by changing the hole size, as calculated using Eq. (1).

$$S_m = \frac{S_P \times C}{S_P + C} \quad (1)$$

In this equation, S_m is the actual pumping speed at the manifold exit, S_p the pumping speed of the turbomolecular pump which is 10 L/s in this instrument, *C* the flow conductance between the manifold and the turbomolecular pump, which can be adjusted by changing the hole size on the flange *A*. The relationship between the flow conductance *C* and the orifice size is discussed in the Supporting Information.

An ESI source with +3 kV ionization voltage and 80 psi sheath gas pressure was used to generate ions in all experiments. All sample solutions were prepared using 1:1 methanol water with 1% acetic acid.

3. Results and discussion

When DAPI is used for ion introduction, gases carrying ions are pulsed into the ion trap while the pinch valve is open. The detection capability and the sensitivity of the instrument are related to the number of ions entering the ion trap during this period, which is mainly determined by the interface flow conductance, and to the amount of gas in which these ions are entrained. Thus, the influence of the interface flow conductance was first studied.

The flow conductance of DAPI is mainly determined by the stainless steel tube S1, so that five 10 cm long tubes with outside diameter of 1.59 mm and inside diameter of 125 μm, 175 μm, 250 μm, 500 μm and 750 μm were used as DAPI S1 tubes (the geometries were selected based on commercial availability). A 10 ppm Rhodamine B solution ionized by ESI was analyzed using each of the tubes in turn. Flange *A* with a 25.4 mm diameter hole, corresponding to 7.1 L/s pumping speed, was used in the experiment. A scan function with 12 ms ion introduction time and 1.2 s cooling time was used for all tubes. The ion current intensity at *m*/*z* 443 in the recorded mass spectra is plotted versus the tube inside diameter in Fig. 1(b). Typical recorded mass spectra are shown in the Supporting Information Fig. S1(a).

The experimental results showed that no signal was detected when the tube inner diameter was 125 μm, and little signal could be detected when the diameter was 175 μm. The maximum signal intensity was obtained when the tube inside diameter was 250 μm; the signal intensity decreased with further increase in the tube inside diameter. It is obvious that more ions can enter the ion trap in the limited ion introduction time when the interface flow conductance is larger. However, the gas flow also becomes greater as the diameter is increased. Hence, in spite of the increase in the total number of analyte ions introduced into the ion trap, it appears that the percentage of these ions that can be trapped decreases. This could be the result of contributions from many factors, including the large volume of gas that must be pumped away. In consequence, the interface flow conductance, when either too large or too small, decreases the instrument detection capability. Very few ions can enter the ion trap when the conductance is too small, whereas a very small fraction can be trapped when the conductance is too large. The tube with 250 μm inside diameter, corresponding to 2.6×10^{-3} L/s flow conductance, gave the best performance, and it was used in the remaining experiments.

In the above experiment, the amount of gas entering the vacuum manifold during the ion introduction period varied with the flow conductance. Therefore, the ion trap pressure during the RF scan was different after the same cooling time and at the same pumping speed. A supplemental experiment was therefore performed to make sure that the small differences in pressure at the time of mass analysis do not affect the detected signal intensity. In the experiment, done using the same interface flow conductance, scan functions with the same ion introduction time and different cooling time were used to analyze the same 10 ppm Rhodamine B solution. The ion current intensity at *m*/*z* 443 was almost the same for all these scan functions. The experimental results confirmed that the detected signal intensity is not influenced by the final pressure as long as it is maintained below 10^{-3} Torr.

Next, the influence of the pumping speed was studied. In order to achieve different pumping speeds, six flanges with center hole diameters of 25.4 mm, 12.7 mm, 9.53 mm, 6.35 mm, 3.18 mm and 1.59 mm were machined and used in the instrument as the flange *A*. The actual pumping speeds corresponding to these dimensions are 7.1 L/s, 4.7 L/s, 3.4 L/s, 1.8 L/s, 0.35 L/s and 0.05 L/s, respectively. A solution of 10 ppm Rhodamine B solution ionized by ESI was analyzed at each pumping speed. A scan function with 12 ms ion introduction time and 1.2 s cooling time was used at all pumping speeds except 0.35 L/s, for which a scan function with 12 ms ion introduction time and 5 s cooling time was used because the pumping speed was too small to restore the original manifold pressure for analysis in the allotted 1.2 s. The instrument could not operate at the pumping speed of 0.05 L/s because the ultimate manifold pressure was too high for mass analysis even with the pinch valve was closed at all times. Mass spectra of Rhodamine B were recorded at each pumping speed (Supporting Information Fig. S1(b)), and the ion current intensity at *m*/*z* 443 plotted versus pumping speed is shown in Fig. 1(c).

The results show that the ion current intensity suffers only minor changes at different pumping speeds. This is reasonable because neither the number of ions introduced through the DAPI nor the number of ions that can be trapped is directly influenced by the pumping speed. The pumping speed mainly determines how fast gas can be pumped away from the manifold so that the manifold pressure can be restored for mass analysis. The greater the pumping speed the shorter the cooling time needed, so that faster analysis can be achieved. The result also demonstrates that the minimum pumping speed required to use the DAPI is no more than 0.35 L/s. This in turn suggests the possibility of using pumps with lower pumping speeds than now used or of using types of pumps other than turbomolecular pumps in miniature mass spectrometers fitted with API sources.

Finally, ion accumulation inside the ion trap was studied. Rhodamine B solutions with concentrations from 0.2 ppm to 10 ppm were prepared. All samples were ionized by ESI and mass spectra were recorded using different ion introduction times ranging from 6 ms to 38 ms. The ion current intensity at *m*/*z* 443 versus the ion introduction time is plotted for each of the samples in Fig. 1(d).

Several phenomena can be noted. First of all, the ion current intensity increases with increasing of ion introduction time for all samples, showing that ions can be trapped and accumulated during the introduction period even though the pressure is high. By means of such ion accumulation, lower limits of detection can be achieved with longer ion introduction times. Secondly, the ion current intensity saturates after a sufficiently long ion introduction time. This can be attributed to the limited ion trapping capacity of the ion trap. Thirdly, samples with higher concentration saturate the ion trap in a shorter introduction time, because larger ion currents are generated during the ionization. The ion current intensity at *m*/*z* 443, when using an ion introduction time of 10 ms, 18 ms and 38 ms, is plotted against the sample concentration in Supporting Information Figs. S2(a), S2(b) and S2(c), respectively. There is a linear range of ion current intensity from 0.2 ppm to 10 ppm with 10 ms ion introduction, from 0.2 ppm to 5 ppm with 18 ms ion introduction, and from 0.2 ppm to 2 ppm with 38 ms ion introduction. The results show that the linear dynamic range decreases with increasing ion introduction time. Ion injection for variable periods is of course a well-developed ion trap operation. However, when DAPI is used for ion introduction, the high and varying manifold pressure makes the operation non-traditional. Necessary changes are required and these involve the physical control of the ion (and accompanying gas) introduction process. The method presented provides a solution such that DAPI is used for ion introduction within the context of changing manifold pressure periodically over a large range.

It also can be seen in Fig. 2 that the saturated analyte ion current intensity for the 10 ppm solution is higher than that of the 5 ppm solution, which is caused by the generation of unwanted ions and the limited total number of ions can be trapped by the ion trap. The ratio of analyte ions to unwanted ions is higher for higher concentration samples. Thus, fewer analyte ions can be trapped when using lower concentration samples.

In order to increase the instrument's detection sensitivity, it is necessary to increase the number of analyte ions that can be trapped. For ion trap mass spectrometers with a traditional continuous interface operating at a pressure at which electrical gating of

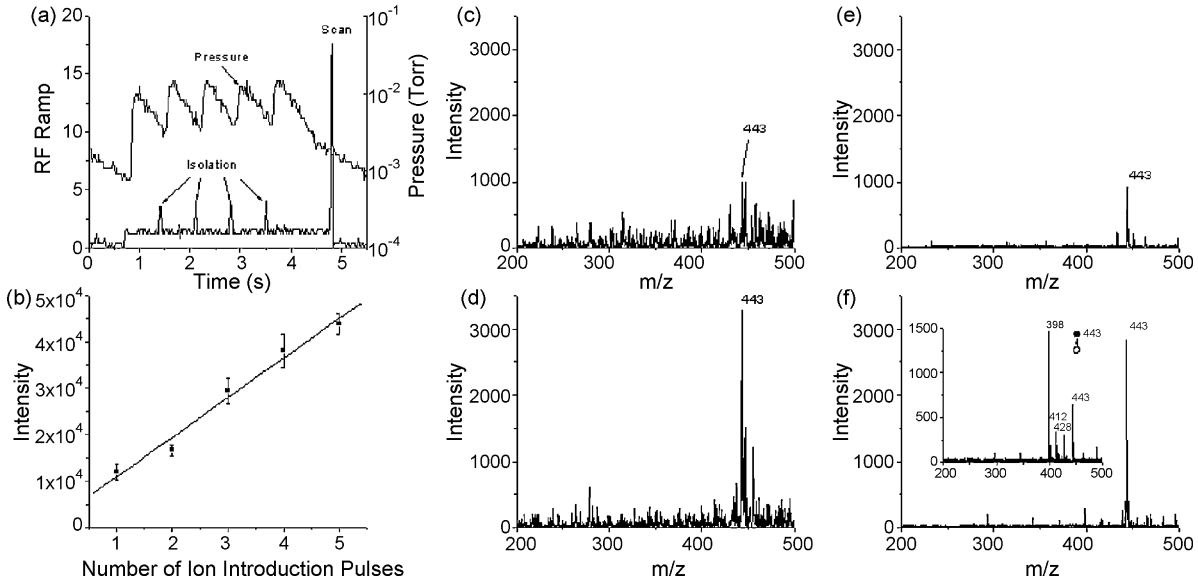

Fig. 2. (a) RF ramp (left axis) and measured pressure (right axis) during five ion introduction periods. (b) Isolated ion current intensity at m/z 443 plotted versus the number of ion introduction periods, each ion introduction period lasts for 30 ms. (c) Mass spectrum of a 0.2 ppm Rhodamine B solution obtained with a single 30 ms ion introduction period scan function. (d) Mass spectrum of a 0.2 ppm Rhodamine B solution obtained after accumulating ions from five 30 ms ion introduction periods. (e) Isolation of m/z 443 and recording of results mass spectrum using single introduction method of Fig. 2(c). (f) Isolation of m/z 443 after the five introduction pulses of Fig. 2(d). The insect shows the product ion mass spectrum of m/z 443 recorded using collision-induced dissociation.

ions can be used, detection limits can be improved by increasing the ion introduction time, so that more analyte ions can be introduced. A method of broad-band ejection during ion injection can also be used to increase the total number of analyte ions trapped by applying broad-band excitation signal during ion introduction [34,35]. Unwanted ions which would normally be trapped are resonantly ejected while analyte ions are still trapped. The analyte is thereby concentrated over the course of the ion injection. Unfortunately, neither method can be used for miniature instruments operating with low capacity vacuum systems. In such cases a DAPI can be used to control ion introduction by also controlling the gas flow in which the ions are transferred into the instrument. The pinch valve can only be opened for a short time span to introduce ions. Otherwise the turbomolecular pump would fail due to the increased gas load. Electrical gating is not possible under the fluid flow conditions encountered. Furthermore, the manifold pressure is too high during the ion introduction period to allow broad-band excitation signal.

An operating method (the scan sequence shown in the Supporting Information Fig. S3) which uses multiple ion introduction periods instead of a single ion introduction period overcomes most of these problems. The pinch valve is opened multiple times for ion (and accompanying gas) introduction in each scan cycle. Each ion introduction period is followed by a cooling period and then an isolation period except for the last ion introduction period, which is only followed by a cooling period without ion isolation. During each cooling period the manifold pressure is restored, and then during each isolation period, a broad-band excitation waveform is applied to eject unwanted ions from the ion trap to make space for the selected analyte ions, so that more analyte ions can be accumulated after multiple times of ion introduction. Mass analysis is performed after the last ion introduction period and cooling period. Information on the analyte ions is obtained with enhanced intensity and with unwanted ions being included in the mass spectrum. The detection capability can be improved by using the multiple ion introduction method for two reasons. One is that ions can be accumulated indefinitely, which is not impossible by using a single ion introduction. The other is that analyte ions of interest can be selectively accumulated in the ion trap by using a broad-band waveform to further increase the total number of analyte ions that can be trapped. It needs to be emphasized that the broad-band waveform selection of the ions of interest can be specific to particular m/z values or m/z ranges.

Scan functions employing one to five 30 ms introduction periods were used to analyze a 0.2 ppm Rhodamine B solution. The variation of vacuum manifold pressure during a five ion introduction pulses scan is shown in Fig. 2(a). Each of the previous four ion introduction periods is followed by a 660 ms cooling period and a 20 ms isolation period, during which a board-band waveform is applied and only ions within the m/z range 440–445 remain in the ion trap. A 1.2 s cooling period is added after the last ion introduction period, and then mass analysis is performed. The manifold pressure increases after each ion introduction period and decreases after each cooling period, at the end of which the isolation can be performed effectively. Isolated ion current intensity at m/z 443 versus the number of ion introduction periods is plotted in Fig. 2(b). It can be seen that the signal intensity increases almost linearly with the number of ion introduction periods, which validates the method and shows that the ion trap is still incompletely filled after five fill periods.

Mass spectra obtained using scan functions which include one 30 ms ion introduction period and five 30 ms ion introduction periods are contrasted in Fig. 2(c) and (d). The isolated spectra of ions at m/z 443 are shown in Fig. 2(e) and (f) respectively. The inset figure in Fig. 2(f) shows the product ion MS/MS spectrum of isolated ions m/z 443. Improved signal intensity can be observed from both Fig. 2(d) and (f). The S/N ratio therefore improves in the same degree as the signal intensity because the noise level does not change when multiple pulses of ions are introduced. The signal intensity and S/N ratio can be further improved with more ion introduction periods if analysis speed requirements allow. (The limitation to 5 times in this experiment was the result of the system constraints.)

4. Conclusion

A DAPI interface was studied with a modified Mini 10 mass spectrometer. The influence of interface conductance and pumping speed on ion introduction performance of the DAPI was examined. The results show that a moderate interface flow conductance gives

the best ion introduction efficiency and that the pumping speed has little influence. The minimum pumping speed required for successful use of the DAPI was found to be no more than 0.35 L/s. Ion accumulation processes in the ion trap were studied also and it was found that the detection limits improve with increasing ion introduction time whereas the linear dynamic range decreases at the same time.

A multiple ion introduction scan method was developed to allow the ion introduction time to be extended indefinitely. By applying a broad-band waveform after each ion introduction period to eject unwanted ions, the total ion trapping capacity can be used to trap analyte ions. Therefore, the instrument performance can be improved significantly in this way compared to a single introduction. Of course, the method is not applicable when requirements for speed of analysis are not met or when the total sample amount is limited or for any other conditions where a long ion accumulation time is not allowed. The improvement in trapping efficiency with use of large interface flow conductance is necessary in these cases, which should be the further focus of the DAPI development.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ijms.2009.01.004.

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