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A New Conjoined RF Ion Guide for Enhanced Ion Transmission

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Abstract

We describe a novel conjoined ion guide that operates at intermediate pressure between API sources and

the analyzer of a tandem quadrupole.

Benefits

Increases in sensitivity and ion transmission greater than 25 x were observed compared with standard ion guides

Introduction

The use of RF-only ion guides in mass spectrometers is widespread. They are of particular utility in intermediate pressure regions between atmospheric pressure ionization sources and the higher vacuum analyzer chambers. Progress on the efficiency of ion acceptance and transport in such devices at ever-increasing operating pressures has been significant over the past 15 to 20 years with designs utilizing more traditional multi-pole ion guides through to various stacked ring electrode designs that operate well in the tens of mbar regime[1,2]. Here, we discuss the design and performance of a novel conjoined stacked ring ion guide that provides highly effective off-axis ion transportation through the intermediate pressure region of a tandem quadrupole mass spectrometer, while minimizing contamination of ion optical elements.

Experimental

Instrumentation

The instrument used in these studies was a prototype Xevo TQ-S tandem quadrupole instrument, shown schematically in Figure 1. In essence, this instrument has an additional stage of differential pumping between the API source and the analyzer chamber, which is located in a novel off-axis RF ion guide device, shown in Figure 2. This new conjoined ion guide consists of two stacked ring electrode arrangements, which have parallel ion optical axes but that are radially offset by about 11 mm, as shown in Figure 3.

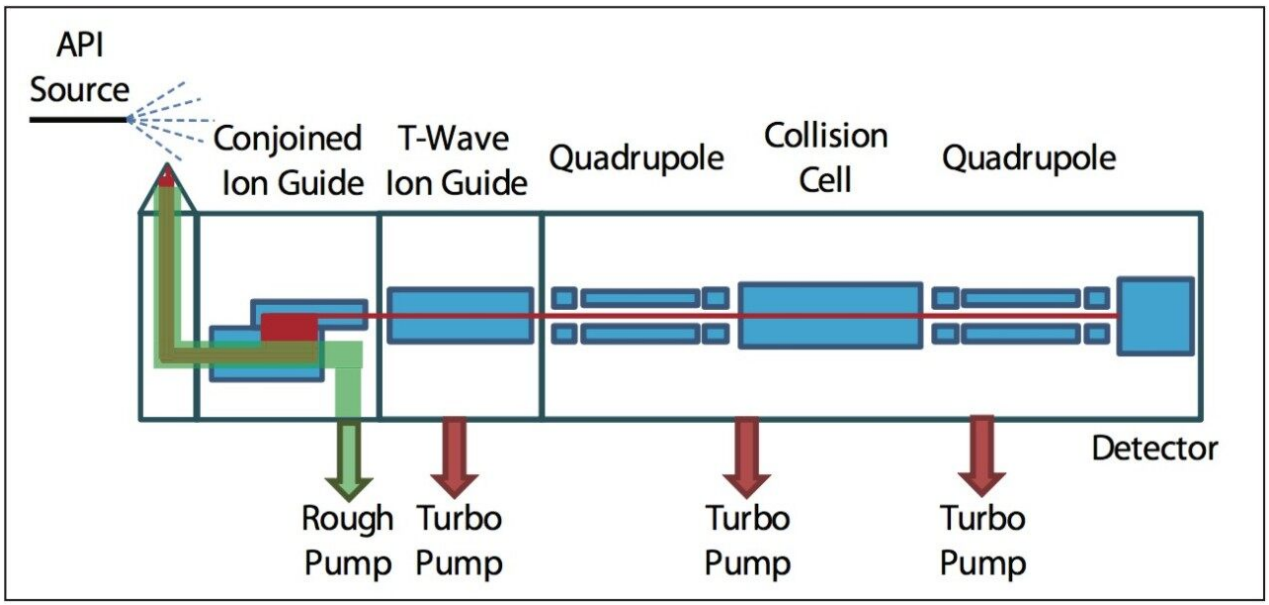

Figure 1. A schematic diagram of the Xevo TQ-S tandem quadrupole mass spectrometer.

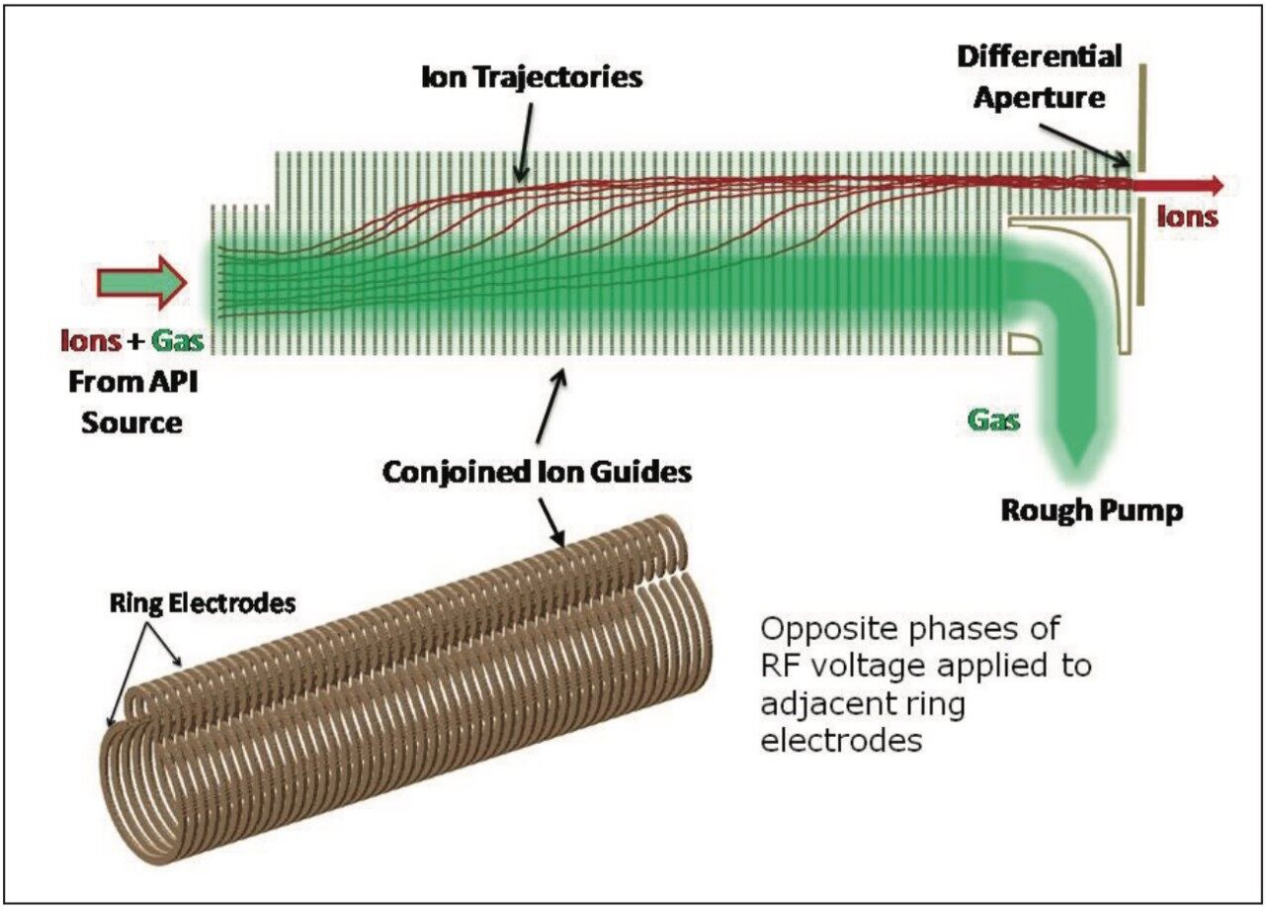

Figure 2. Diagrams of the conjoined stacked ring ion guides.

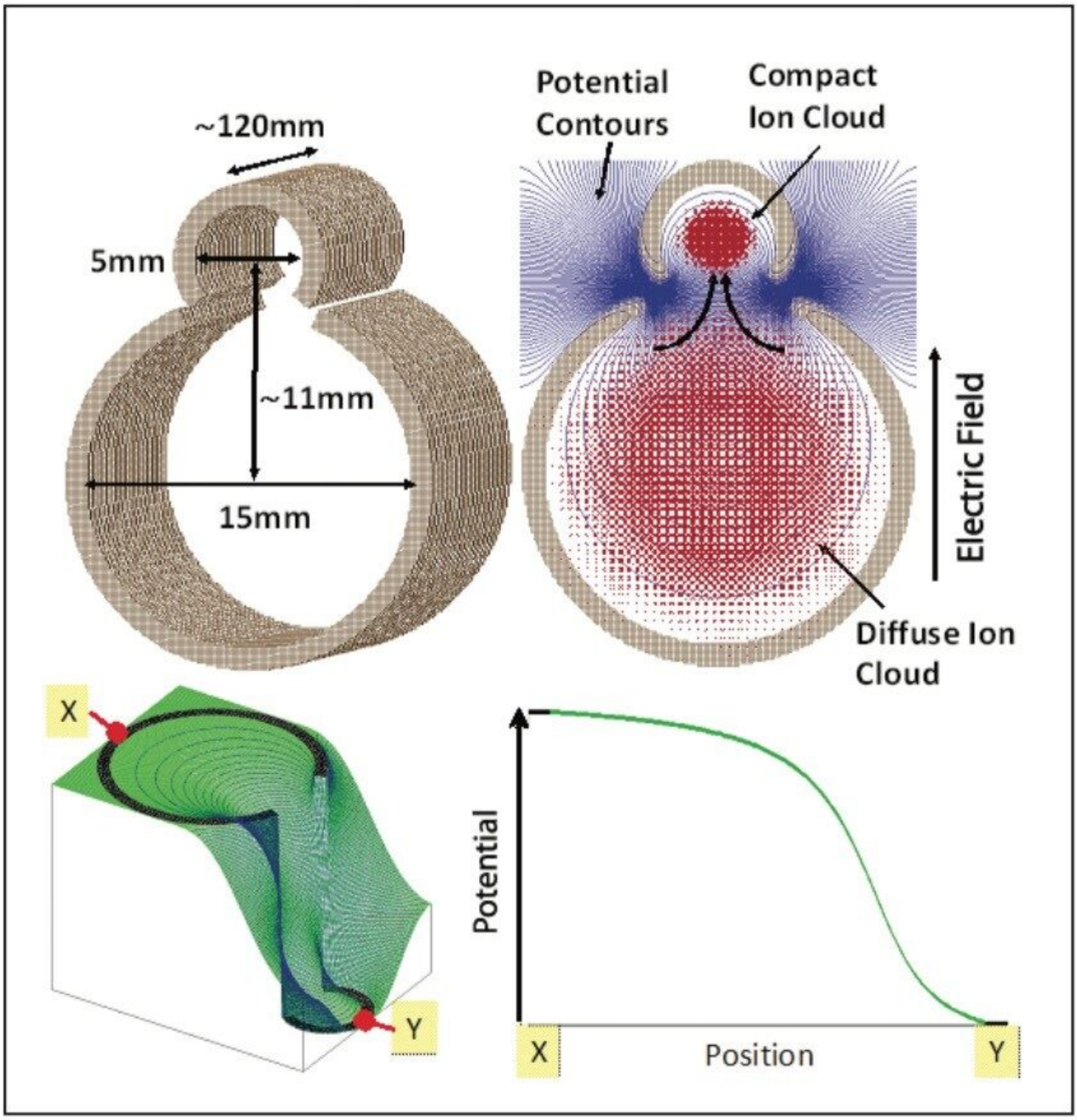

Figure 3. Diagrams of the conjoined ion guide device showing approximate dimensions and the ion transfer and focusing nature of the applied DC offset between the large and small diameter sections.

Along the radial dimension between the ion guides, the ring electrodes are slotted providing a path for ion movement. The first, larger diameter (15 mm) section of the guide is aligned with the ion ingress from the source region. A DC potential difference between this region and the second, smaller diameter (5 mm) ion guide extracts and focuses the ions from the main gas stream into the second guide. The ion optical axis of the second ion guide is aligned with the ion optical axes of the subsequent ion guide and quadrupoles. A

significant benefit of this off-axis design is that gas and other entrained neutrals streaming in from the source are essentially prevented from entering, and contaminating, subsequent stages of the mass spectrometer.

Simulations

Initial studies were carried out using the SIMION (v8) ion optics package to identify suitable geometries for the conjoined ion guide device and to prove the principle of operation. Collisions between the ions and neutrals were accounted for in SIMION using the provided hard sphere collision program. Figure 4 shows the results of simulations for the conjoined guide geometry, shown in Figure 2, where the trajectories of nine *m/z* 500 ions are displayed. In Figure 4(a), no DC offset was applied between the conjoined guides. In Figure 4(b) a 25 V offset was employed, and demonstrates that the ions were effectively transferred and focused from one region to the other.

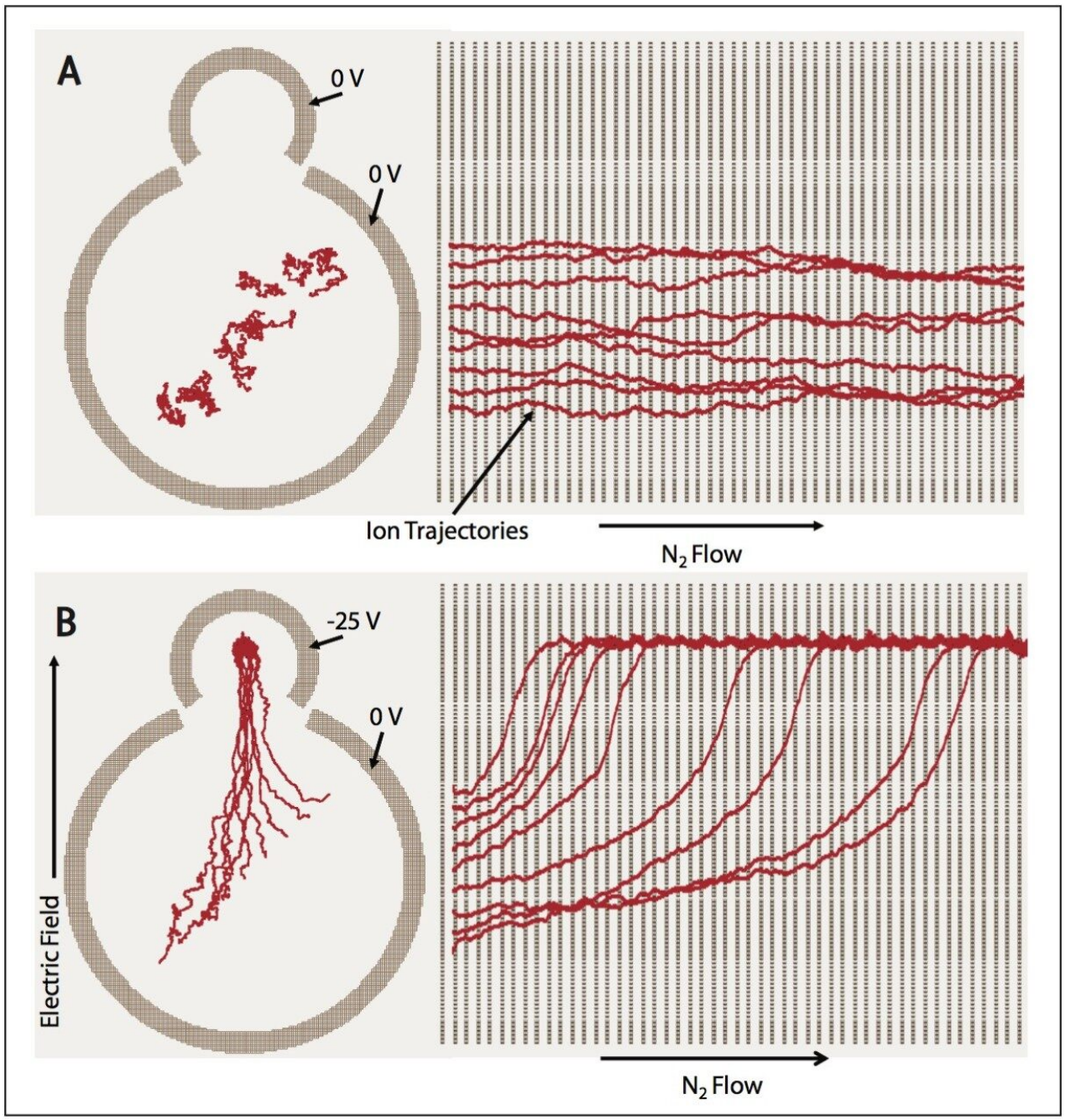

Figure 4. SIMION simulation of ion transit through the conjoined ion guide device: (a) with no potential difference between the sections (b) with 25 V between the sections. N_2 : 1 mbar and 500 m/s, ion collision cross section: 100Å^2, RF : 1 MHz and 200 V pk-pk.

Results and Discussion

Various geometries of conjoined ion guides were assessed primarily focused on the radial separation of the two guides and the length of the overlap region. Figure 5 shows the preliminary data obtained using a modular instrument with a common tandem quadrupole analyzer assembly, and the ability to swap between a standard single source ion guide arrangement and the dual ion guide arrangement with the additional stage of pumping for the conjoined ion guide. Gains in transmission approaching 25 x were realized with this geometry.

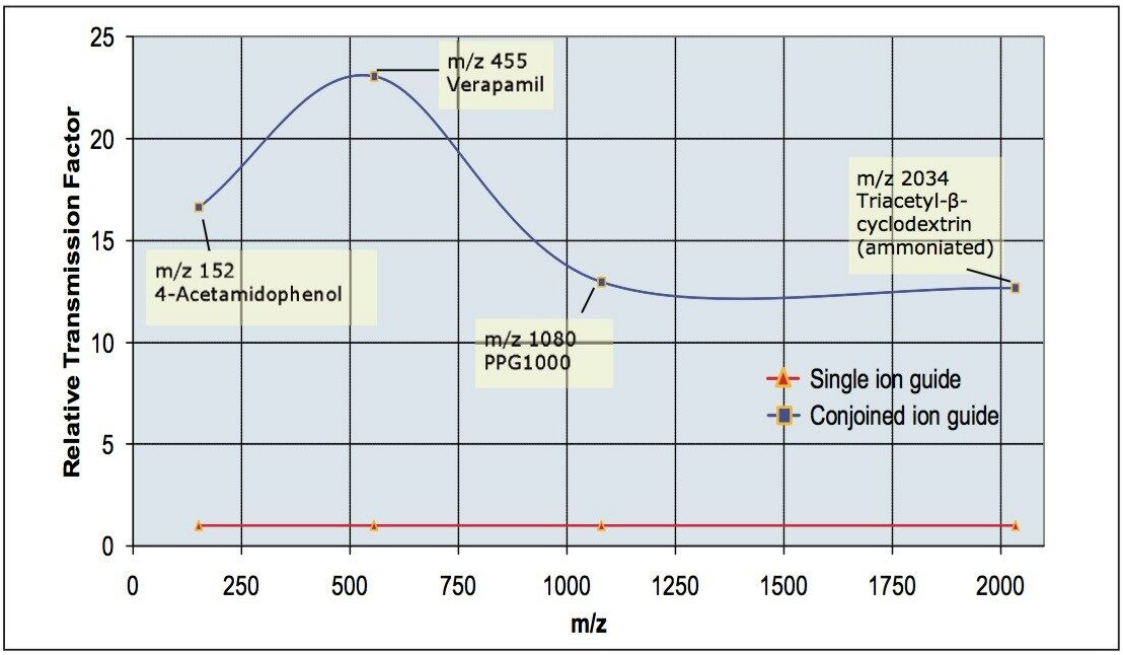

Figure 5. Transmission increases using the conjoined ion guide on the modular instrument compared to the single ion guide. Samples infused at 5 µL/min into the ESI source.

Transmission Characteristics

With an overall instrumental constraint for the length of the conjoined guide to be ~120 mm, and from the modular instrument investigations, a guide with dimensions shown in Figure 3 was found to give broadly optimal performance. The 15 mm diameter section contains 62 plates, the 5 mm diameter section, 78 plates with an overlap of 56 plates, arranged as shown in the top diagram of Figure 2.

A prototype Xevo TQ-S System was then constructed incorporating the new conjoined ion guide. The second source ion guide is a standard 100 mm long T-Wave^3 device, shown in Figure 1. The conjoined ion guide chamber was rough pumped to a few mbar using an oil-free scroll pump. Figure 6 shows the optimized signals obtained on the new prototype as a function of sampling cone aperture size, leading to the choice of 0.8 mm as standard. Figure 7 shows the transmission properties as a function of the RF amplitude and DC offset applied to the conjoined guide. For fast switching experiments, it was found that

operating the conjoined guides with a T-Wave was beneficial in maintaining sensitivity while reducing inter-channel cross talk.

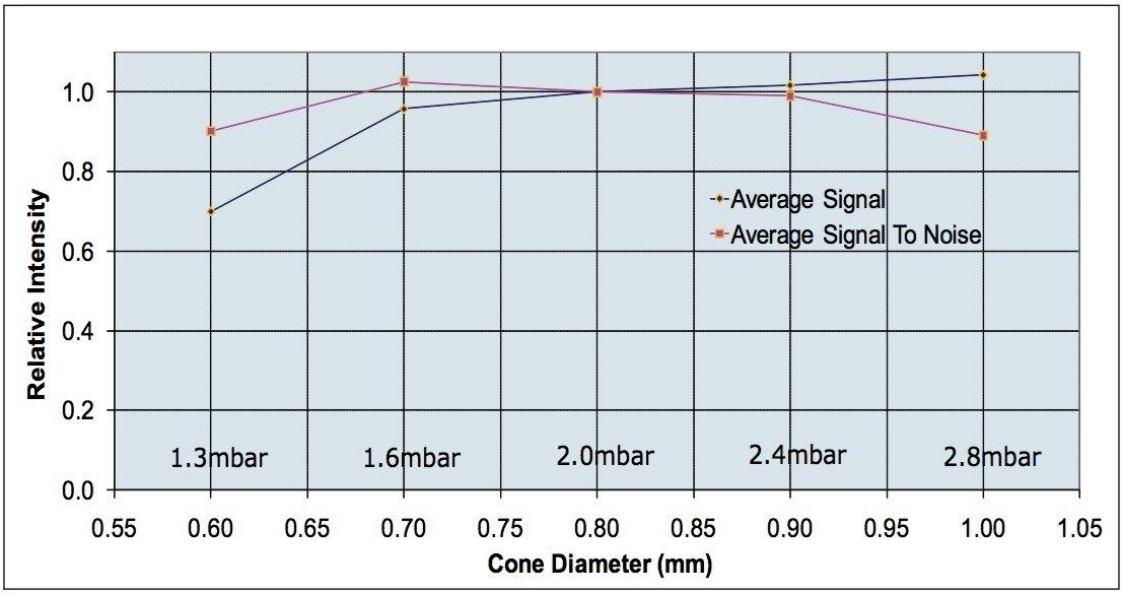

Figure 6. Transmission and s/n characteristics as a function of sample cone diameter for the sum of the signals at m/z 152, 455, 1080, and 2034. Also shown are the pressures measured in the chamber housing the conjoined guide.

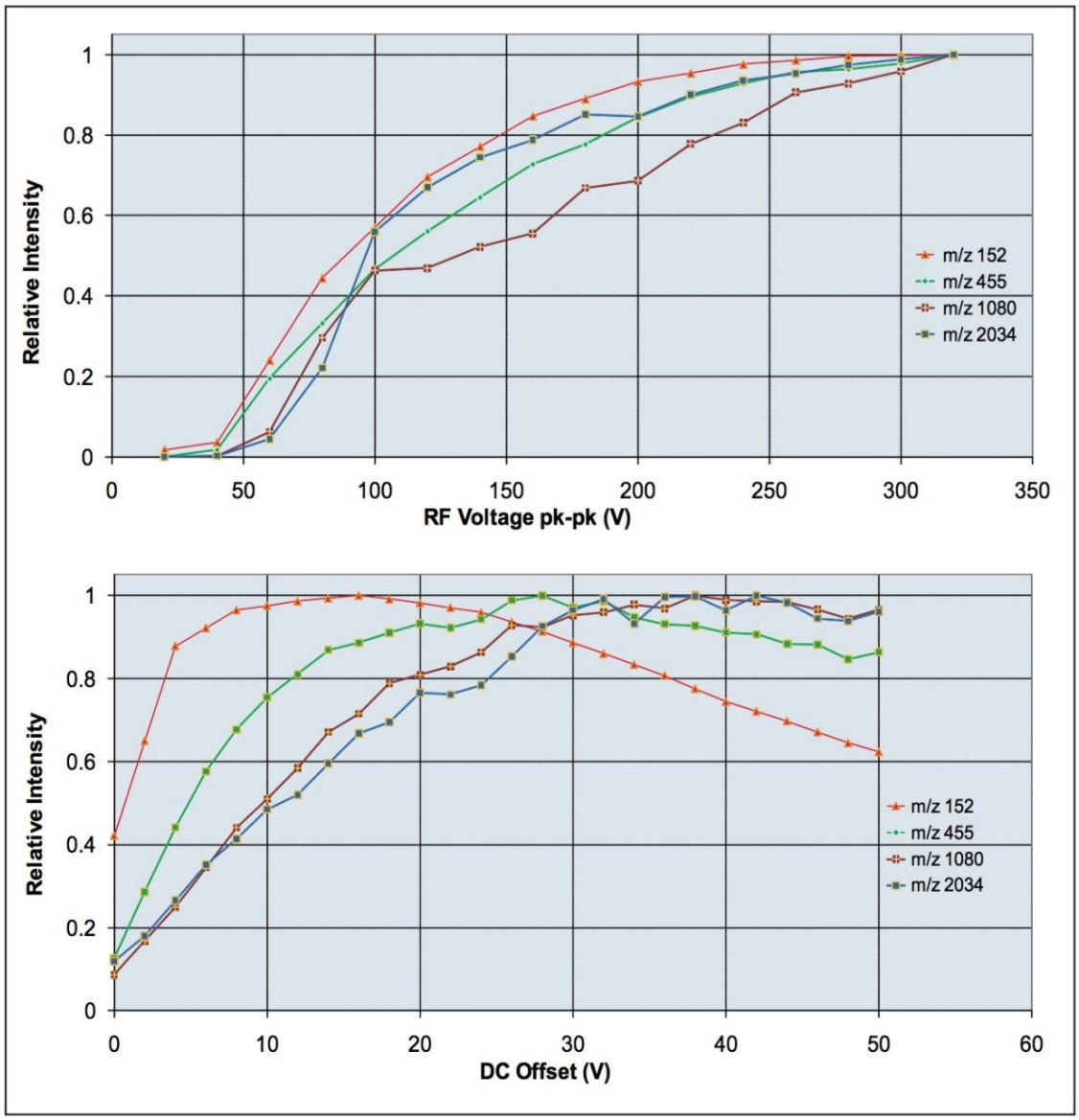

Figure 7. Transmission properties of the conjoined ion guide as a function of RF amplitude (at 1 MHz) and DC offset, with the 0.8 mm cone.

System performance

To evaluate the overall instrumental performance of the prototype Xevo TQ-S System housing the conjoined ion guide, several tests were performed and the results compared with a standard Xevo TQ instrument with the single source ion guide. Figure 8 shows the results of a UPLC/MRM acquisition on reserpine where signal and signalto- noise increases of 25 x and 5 x respectively were observed with the new conjoined guide system. Table 1 is a list of the performance gains using the conjoined guide system for a range of compound analyses by UPLC/MRM. Figure 9 shows preliminary data indicating the good robustness of the conjoined guide system with < 5% RSD variation in peak area from 1000 injections of

verapamil-spiked plasma protein precipitate.

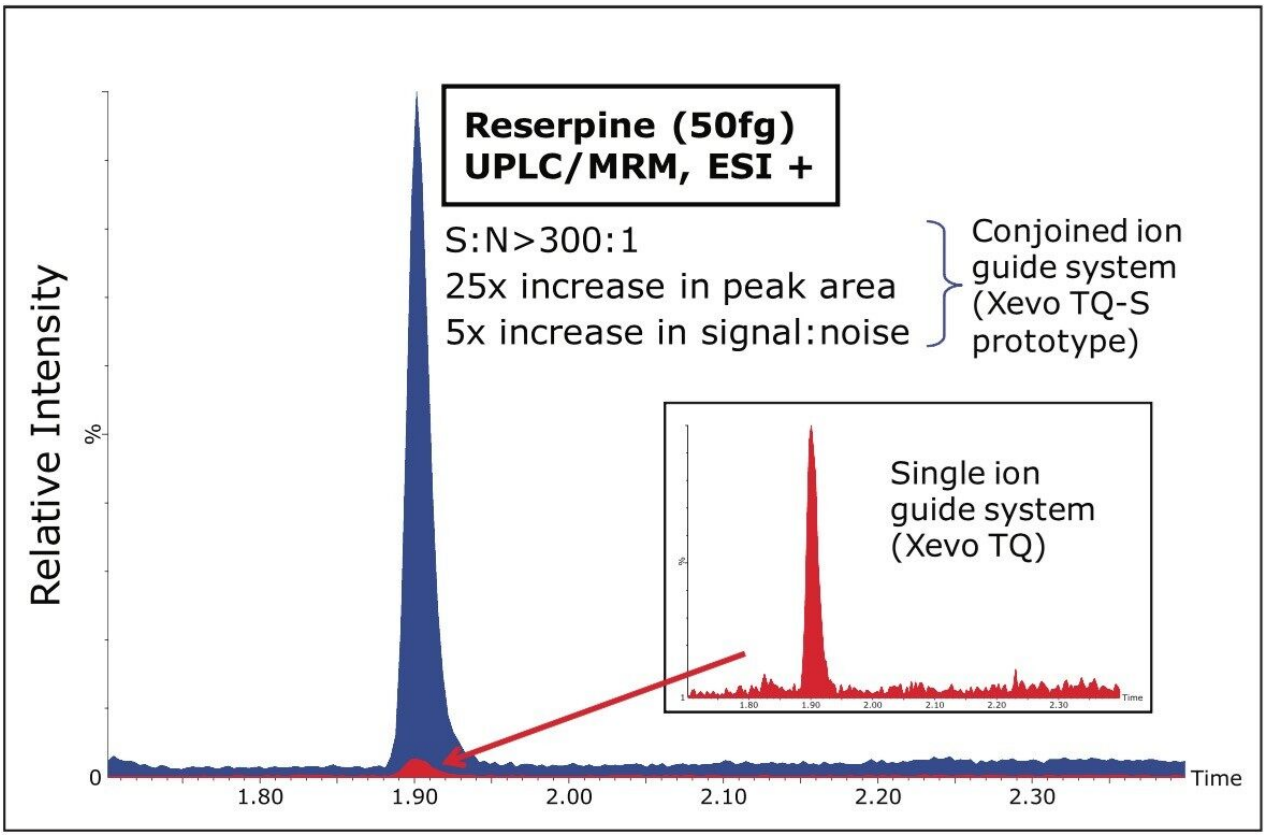

Figure 8. Reserpine, 50 fg on-column. 800 µL/min gradient elution on a 50 x 2.1 mm BEH C_{18} Column.

Compound Name	Ionisation Mode	Relative Peak Area	Relative S:N
Fenuron	ESI+	30	7
Metamitron	ESI+	32	15
Acephate	ESI+	27	7
Chlortoluron	ESI+	27	8
Aldicarb	ESI+	27	6
Demeton S Methyl	ESI+	26	9
Phoxim	ESI+	64	19
Kresoxim Methyl	ESI+	64	4
Azinphos Methyl	ESI+	42	6
Azoxystrobin	ESI+	45	4
Dimethoate	ESI+	23	10
Acetamiprid	ESI+	30	28
Fluticasone	ESI+	30	3
Formoterol	ESI+	39	4
Nefadazone	ESI+	28	3
Desmopressin	ESI+	129	25
Salmeterol	ESI+	41	8
Alprazolam	ESI+	21	13
Reserpine	ESI+	25	5
Ibuprofen	ESI-	13	16
Prostaglandin E2	ESI-	30	37

Table 1. UPLC/MRM acquisition results for various compounds highlighting the factor of increase in performance of the Xevo TQ-S with the conjoined ion guide over the Xevo TQ single ion guide system.

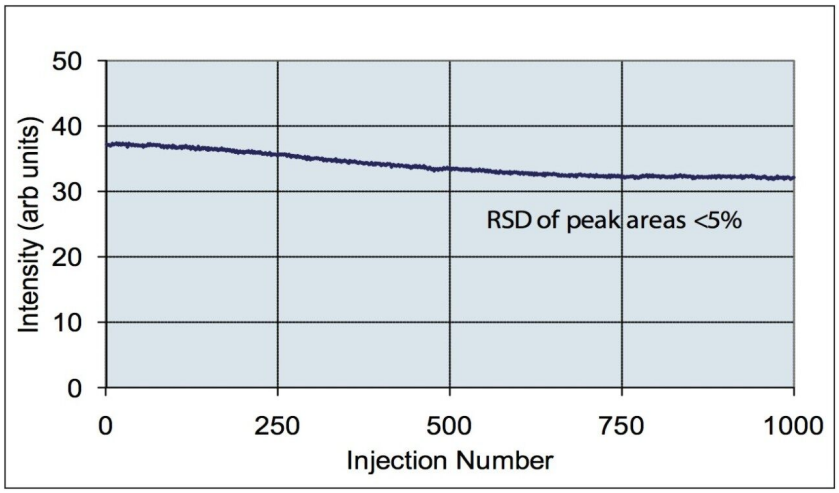

Figure 9. Replicate injections of verapamil, 10 pg/µL spiked into supernatant from 2:1 ACN:plasma protein precipitation. Preliminary data indicating system robustness. 600 µL/min gradient elution on a 50 x 2.1 mm BEH C_{18} Column.

Figure 10 illustrates the extreme levels of performance of the conjoined guide system. Here a robustly cleaned UPLC System facilitated quantitation of verapamil at the 0.1 fg (220 zeptomoles or around 150,000 molecules) on column level.

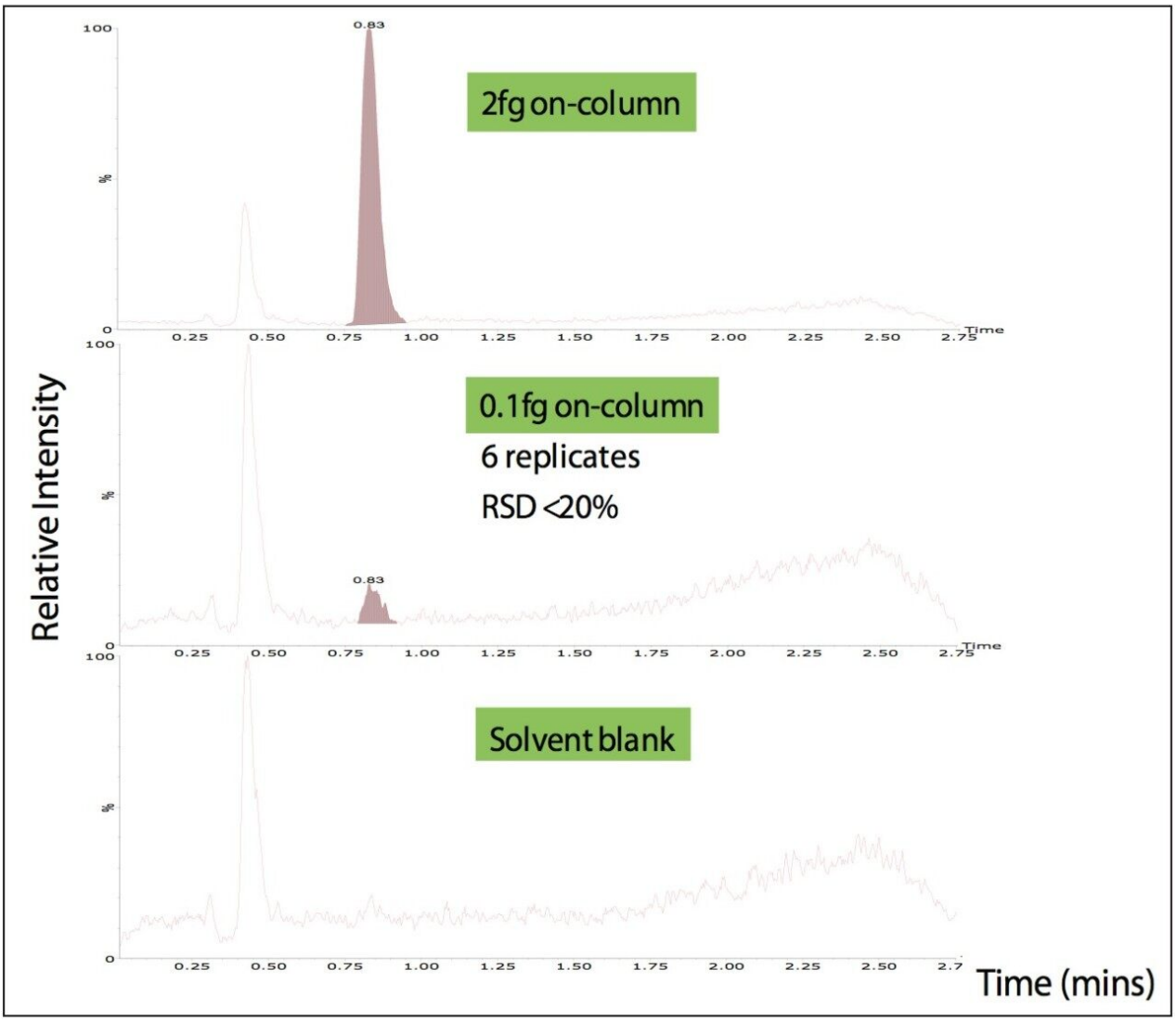

Figure 10. UPLC/MRM acquisitions of verapamil. 400 µL/min gradient elution on a 50 x 2.1 mm BEH C_{18} Column.

Conclusion

- A novel conjoined ion guide operating at the intermediate pressure between the API source and the analyzer of a tandem quadrupole has been described.
- Transmission increases generally > 25 x have been observed and s/n increases generally > 5 x.
- The off-axis design provides robust performance.
- Ultimate limits of detection in the hundreds of zeptomoles on-column are achievable with a well-

conditioned UPLC.

References

1. BA Thomson, *Can J Chem*. 76: 499, 1998.
2. RT Kelly, AV Tolmachev, JS Page, K Tang, RD Smith, *Mass Spec. Rev*. 29: 294, 2010.
3. The travelling wave device described here is similar to that described by Kirchner in U.S. Patent no. 5,206,506 (1993).

Acknowledgement

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