

Enhancing analytical confidence and detection limits for IC and LC by coupling them to single quadrupole MS

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ABSTRACT

Purpose: To demonstrate the advantages of single quadrupole mass spectrometry (MS) to Ion Chromatography (IC) and liquid chromatography (LC) applications and to discuss the design features of the new Thermo Scientific™ ISQ™ EC single quadrupole mass spectrometer.

Methods: An IC system using anion-exchange chromatography separations was coupled with a single quadrupole MS with a heated electrospray (HESI) ion source to determine ionic compounds. An HPLC system using reverse-phase separations with MS was used to determine non-ionic compounds.

Results: For a range of applications, the employment of single quadrupole MS significantly improves method detection limits and resolves chromatographically co-eluting components in the orthogonal MS dimension, thus aiding in improved automatic peak integration, more accurate quantitation, and avoiding false positives and false negatives.

INTRODUCTION

Traditional IC and HPLC applications have relied on the bulk physical property monitoring detectors: e.g., conductivity (for IC) and UV-Vis or PDA (for HPLC). With ever-increasing regulatory pressure and general tendencies in analytical chemistry to aim for better detection limits and have a higher degree of confidence in analyte identification and quantitation (i.e., reduce false positives and their contribution to quantitation), there is an emerging trend to couple (hyphenate) IC and HPLC with mass-selective detectors. This tendency is antagonized primarily and only by (a) the traditionally high cost of MS (higher than stand-alone bulk property detectors) and (b) the real and perceived difficulty of MS adoption and operation, especially with ESI and HESI ion sources. We present a newly developed single quadrupole mass spectrometer (MS) specifically designed to overcome those two limiting factors and destined for routine applications, including environmental, food and beverage, and medicinal chemistry. The new MS incorporates technological innovations in the hardware and software realms to help resolve the MS adoption problems. The presented MS hardware design features allow easy coupling and switching between both ion chromatography and liquid chromatography.

MATERIALS AND METHODS

Sample Preparation

For IC applications, juice and wastewater samples were diluted 100-fold or 1000-fold prior to injection. The animal feed samples were extracted with deionized water, centrifuged at 18000 × g for 10 min, filtered (0.45 µm), and diluted 100-fold with deionized water prior to injection.

Test Methods

Ion Chromatography

Several ion chromatography applications are shown. The anion analytes were separated by anion-exchange chromatography using Thermo Scientific™ Dionex™ IonPac™ columns optimized for the separation of the analyte class. The electrolytic suppressor provided desalting of the eluent (mobile phase) providing a low baseline for the conductivity detector and low chemical noise for the single quadrupole MS. The analysis was facilitated by using the high-pressure-capable Thermo Scientific™ Dionex™ Integri™ HPIC™ system or the Thermo Scientific™ Dionex™ ICS-5000+ HPIC™ system. The chromatographic conditions are shown in the figures.

HPLC

Thermo Scientific™ Vanquish™ HPLC, with UV-Vis and PDA stand-alone detectors, was employed.

Mass Spectrometry

Thermo Scientific™ ISQ™ EC single quadrupole mass spectrometer in Full Scan (FS) and Selected Ion Monitoring (SIM) modes was used.

Data Analysis

A single software, Thermo Scientific™ Chromeleon™ chromatography data system (CDS) software version 7.2 was designed to provide both instrument control, data acquisition, and easy MS data analysis for the IC or LC coupled to the ISQ EC mass spectrometer.

RESULTS

The newly designed ISQ EC single quadrupole mass spectrometer has several areas of design innovation targeting ease of adoption, intuitive, experiment-based, self-paced learning, and user experience that would be easily mastered by both novices and experts. On the hardware side, the ISQ EC MS design features a double off-axis ion path (Figure 1) and fixed and pre-optimized orthogonal (90-degree) modular HESI II ion source (Figure 2), both contributing to and resulting in the exceptional signal stability both over time (Figure 3) and when analyzing heavy matrix. ISQ EC MS was specifically designed with enhanced low-m/z performance, featuring lower-end mass axis starting at m/z 10, which makes it especially suited for IC-MS (Figure 4).

Figure 1. New ISQ EC mass spectrometer instrument schematic.

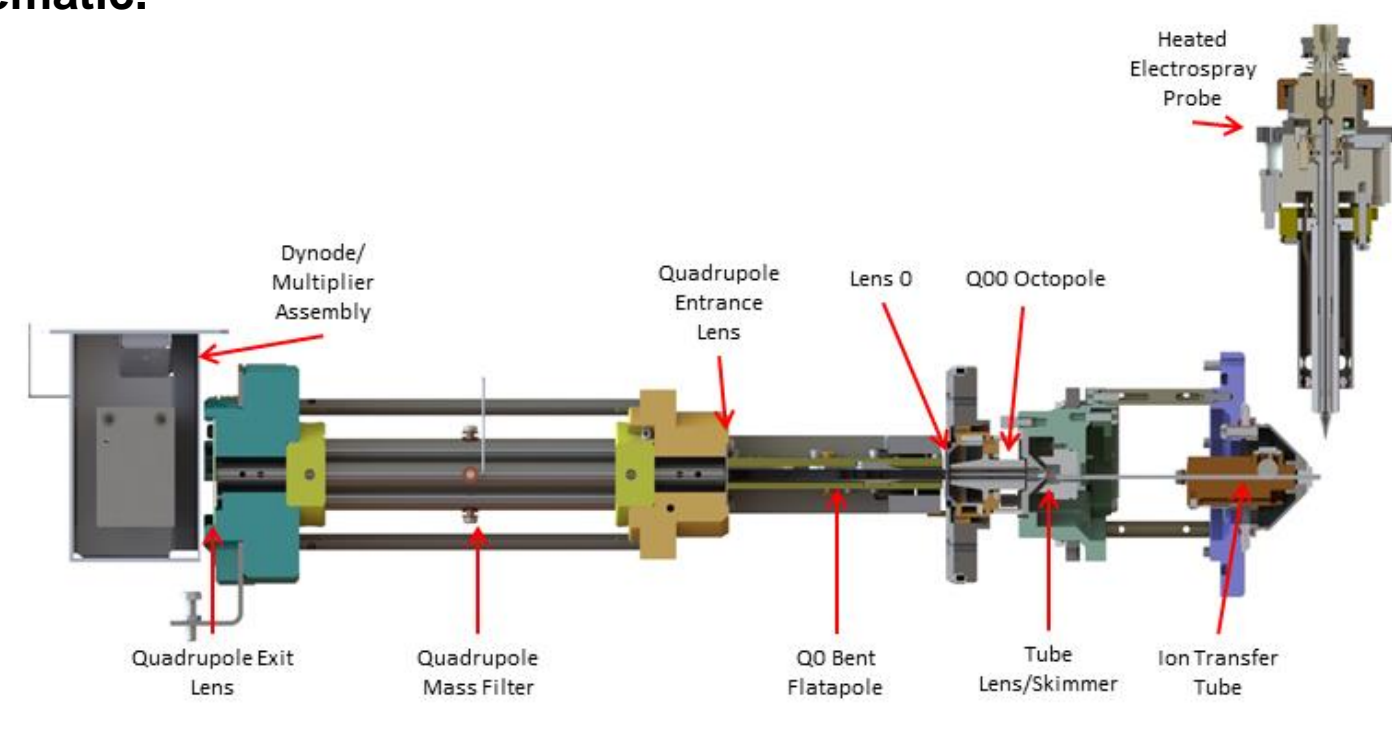


Figure 3. ISQ EC MS long-term signal stability.

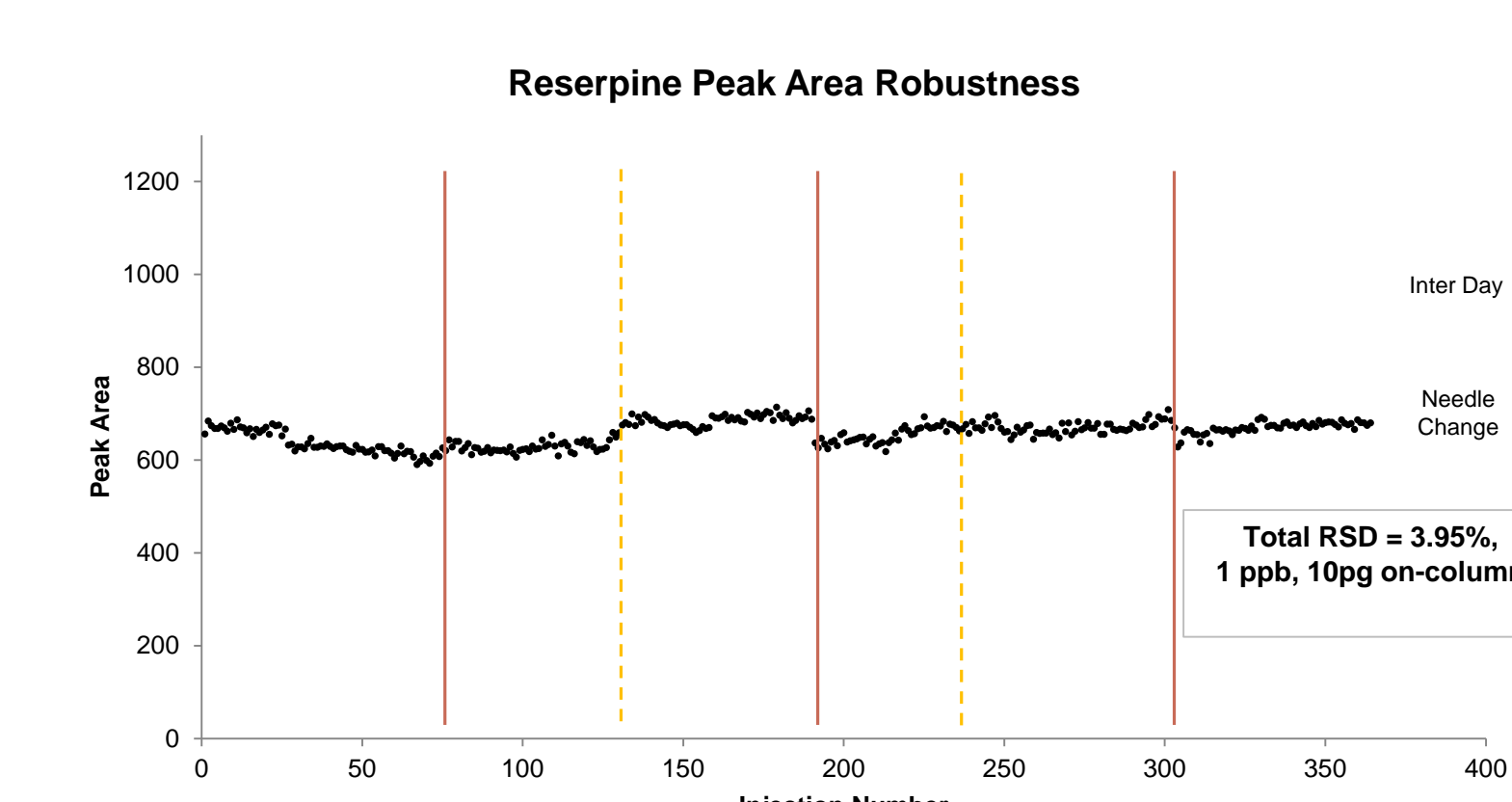


Figure 5. IC-MS (IC mass detector) instrument control panel.

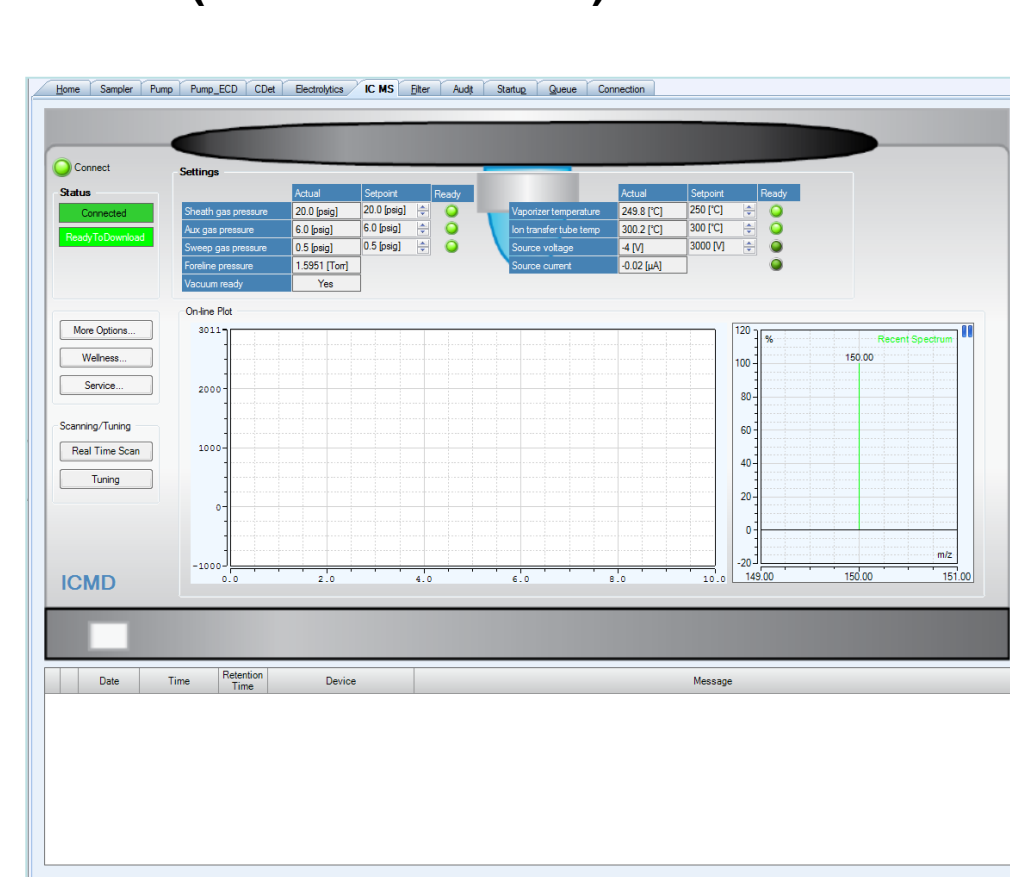


Figure 7. Instrument method wizard using Easy and Basic Modes to develop a starting MS method.

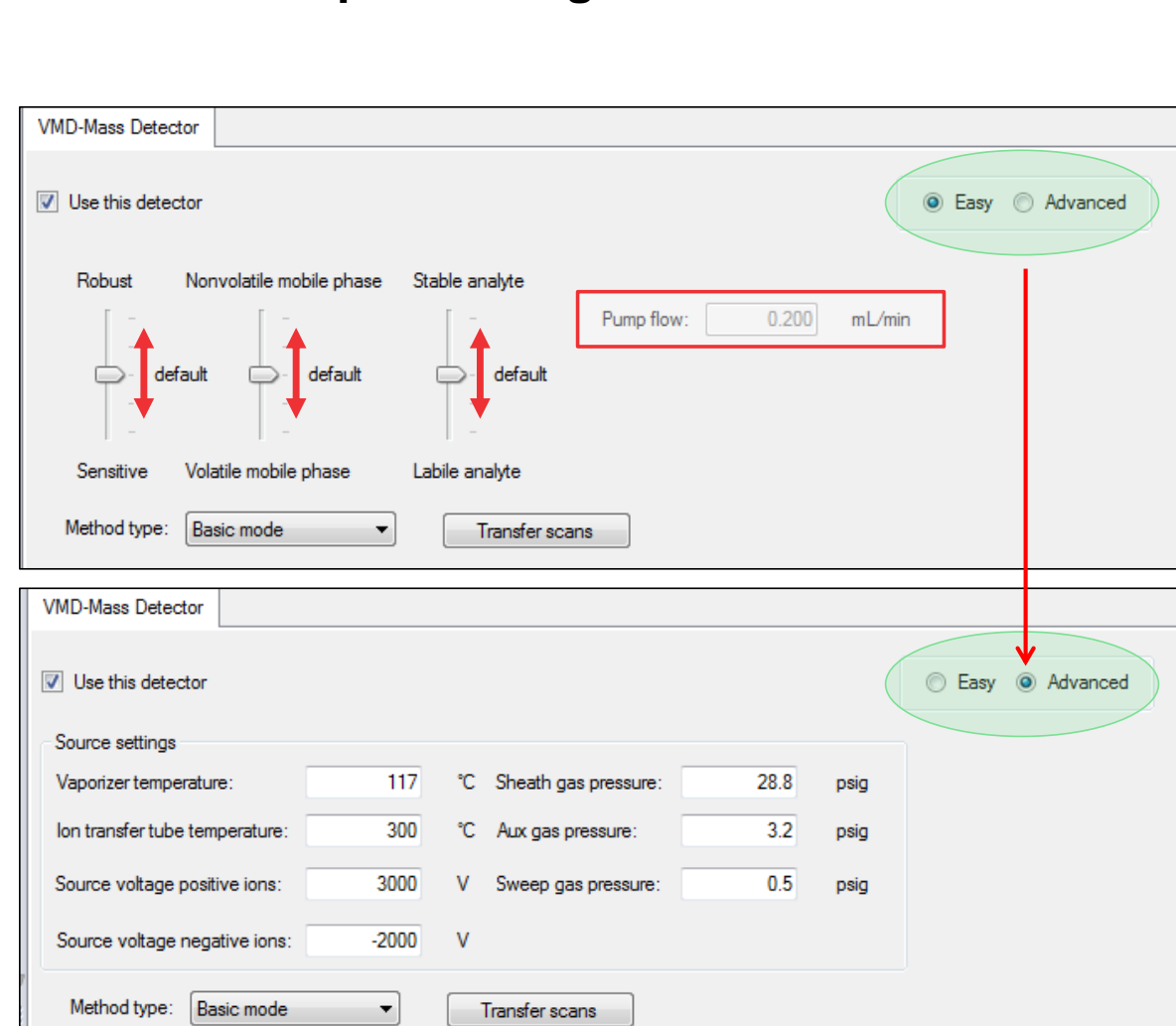


Figure 2. ISQ EC MS fixed orthogonal HESI design.

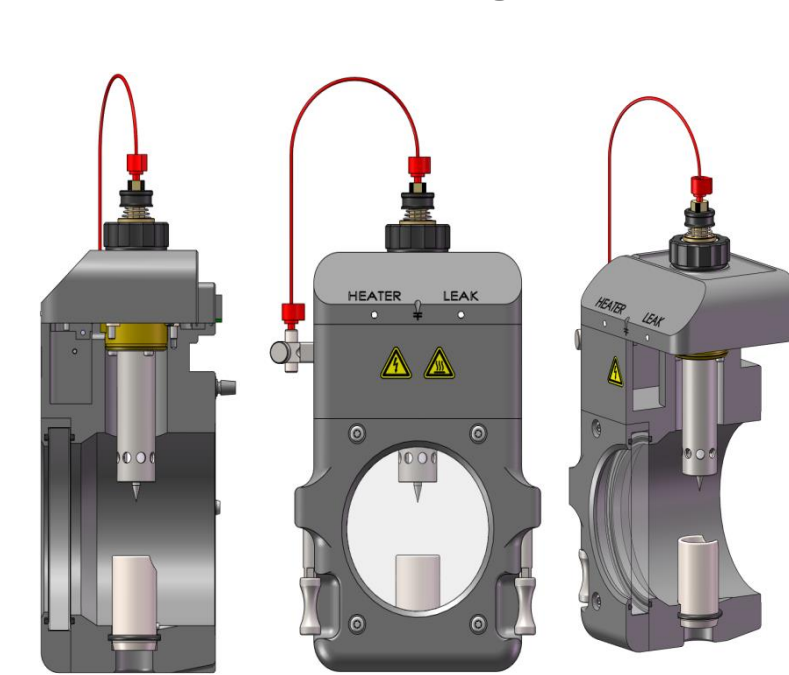


Figure 4. ISQ EC MS low m/z performance.

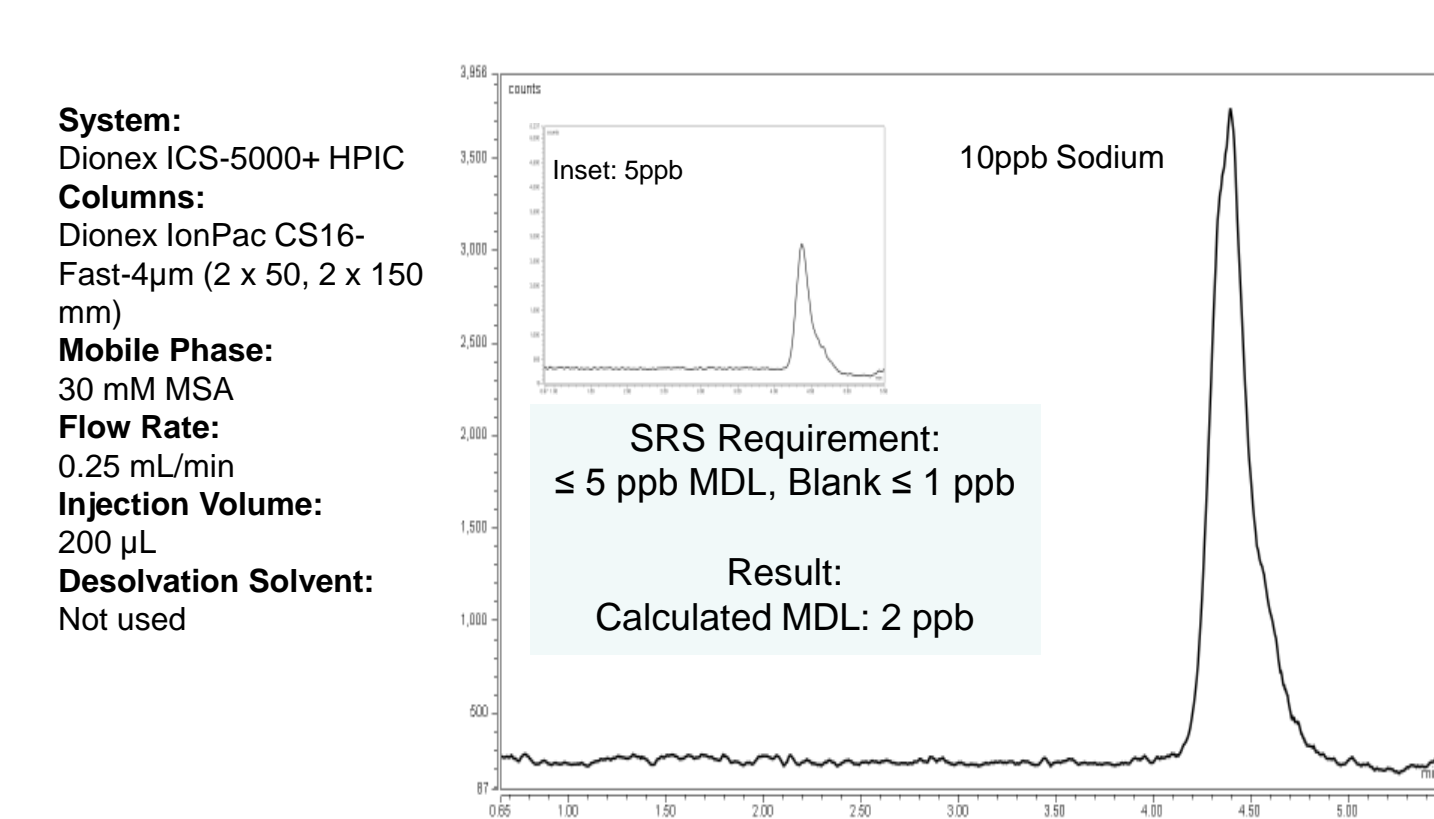


Figure 6. Panel listing MS filters that can be automatically extracted through Intelligent Run Control (IRC).

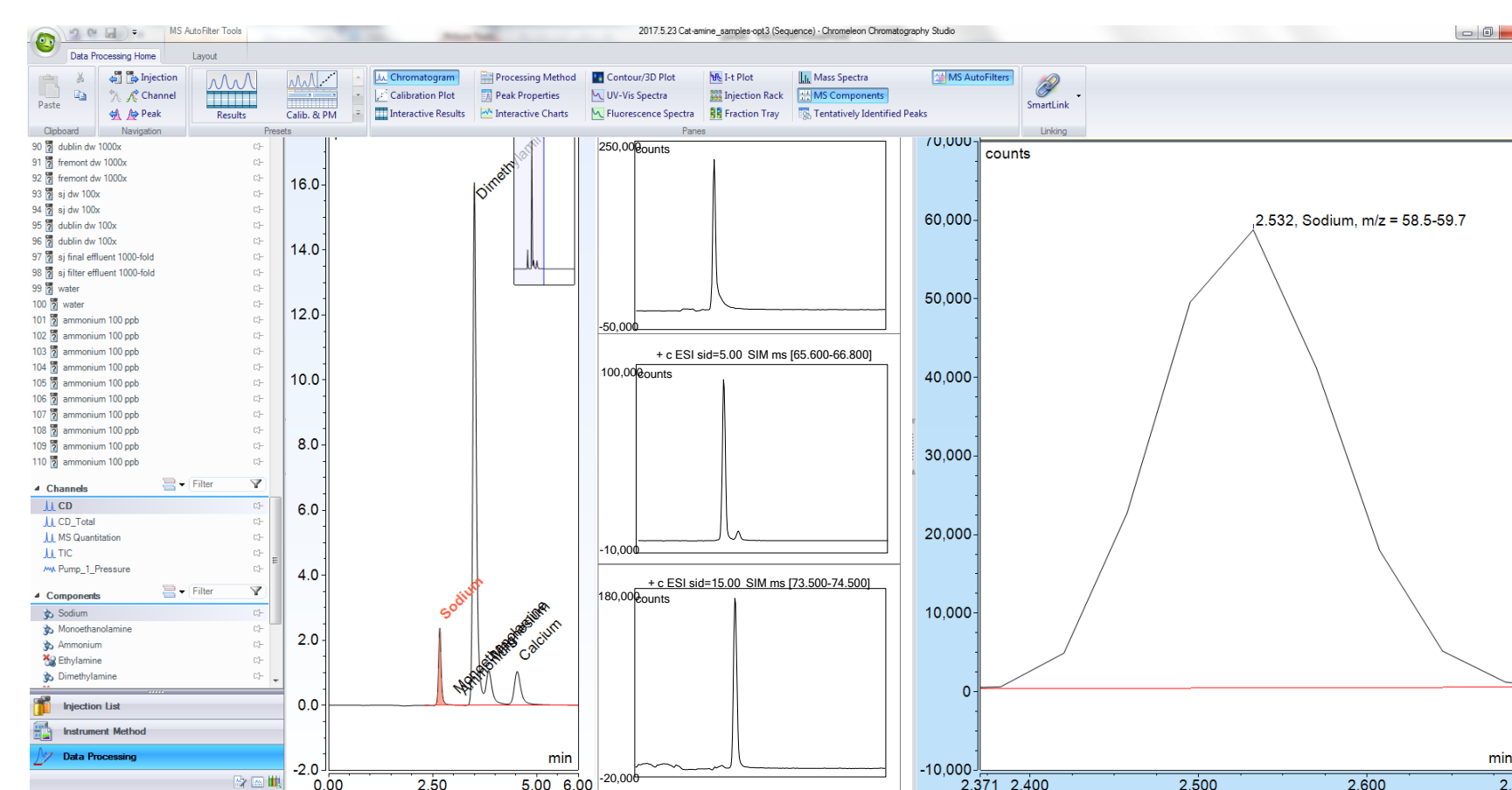
Filter Name	Retention Time (min)	Abundance	Mass (m/z)
Succinate	4.77	34718	117
Malate	4.79	42018	133

Figure 8. Transfer from Easy and Basic to Scan and Advanced modes for more detailed optimization.

Parameter	Value
Flow Rate	0.25 mL/min
Injection Volume	200 µL
Resolution	10000
Scan Rate	10000

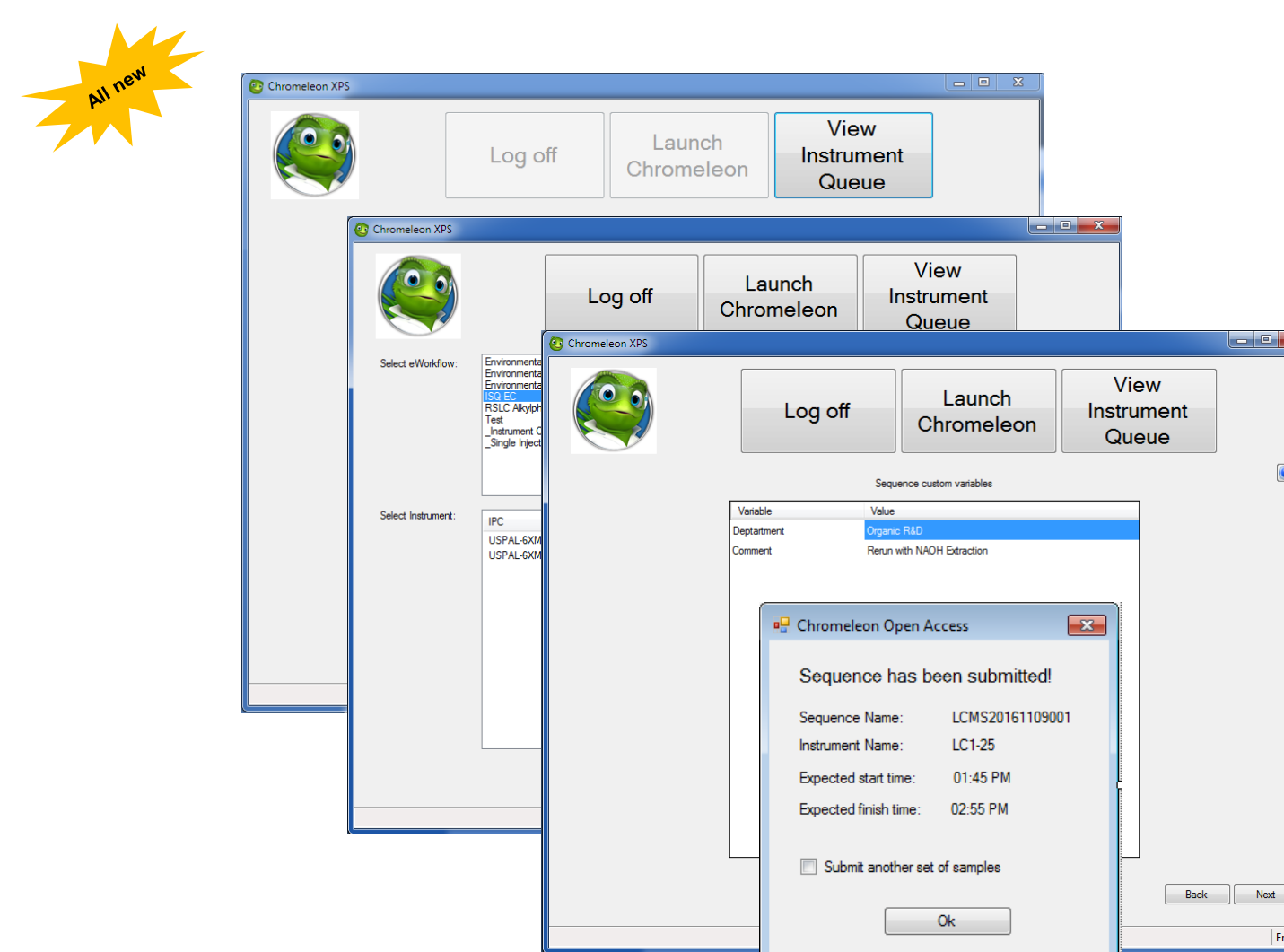
On the software side, the ISQ EC MS is the first mass spectrometer with the Chromeleon CDS software native, completely integrated instrument control driver (Figure 5), which allows it to take advantage of many unique and powerful features of the Chromeleon CDS software that are well-known to chromatographers. For example, the Intelligent Run Control (IRC) feature of the Chromeleon CDS software allows automatic extraction of all MS (e.g., SIM) channels right after the acquisition completion (Figure 6). To further make the adoption of the ISQ EC MS by chromatographers as easy as possible, there is an Easy mode in the mass spectrometer method development and instrument control area, providing an intuitive way for every chemist to set up an initial IC-MS or LC-MS method, with the knowledge of the physical properties of the sample and mobile phase (Figure 7) as the first encounter and initial approach to a hyphenated technique. Later on, as the expertise of the IC-MS or LC-MS user grows, the switch to an Advanced mode (Figure 8) can be done for a finer control of the method conditions. The full power of the Chromeleon CDS software, including, for example, the SmartLink feature (Figure 10) is available to process the MS data.

Figure 10. Processing method using the MS Quant template showing CD channel, MS Filters, and the MS Component individually or together with Smart Link.



For non-analytical chemists who want to take advantages of the power of mass spectrometry (e.g., synthetic organic or medicinal chemists confirming the molecular mass of a newly synthesized compound), Chromeleon XPS (Figure 9) allows streamlining the sample-to-results eWorkflows with minimal interaction and knowledge of the analytical technique.

Figure 9. Chromeleon XPS Walk-Up Software.



1. Log on
2. Chose method
3. Chose Instrument
4. Edit custom information (i.e. target mass)
5. Edit sample name(s)
6. Put sample in assigned sampler position
7. Run
8. Receive Data and Report to your email

To put the new ISQ EC to real-world tests, a plethora of applications was performed in both IC-MS and LC-MS hyphenation combinations. Several of these applications are reported here. The analysis of the organic acids (OAs) in the animal feed matrix (Figure 11) illustrates the orthogonal (i.e. supplemental to the retention time vs. analog signal of a bulk property detector two-dimensional chromatographic plot alone) dimension of mass spectrometry, separating two chromatographically co-eluting compounds, indistinguishable by the traditional conductivity detector.

Figure 11. Organic acids in animal feed.

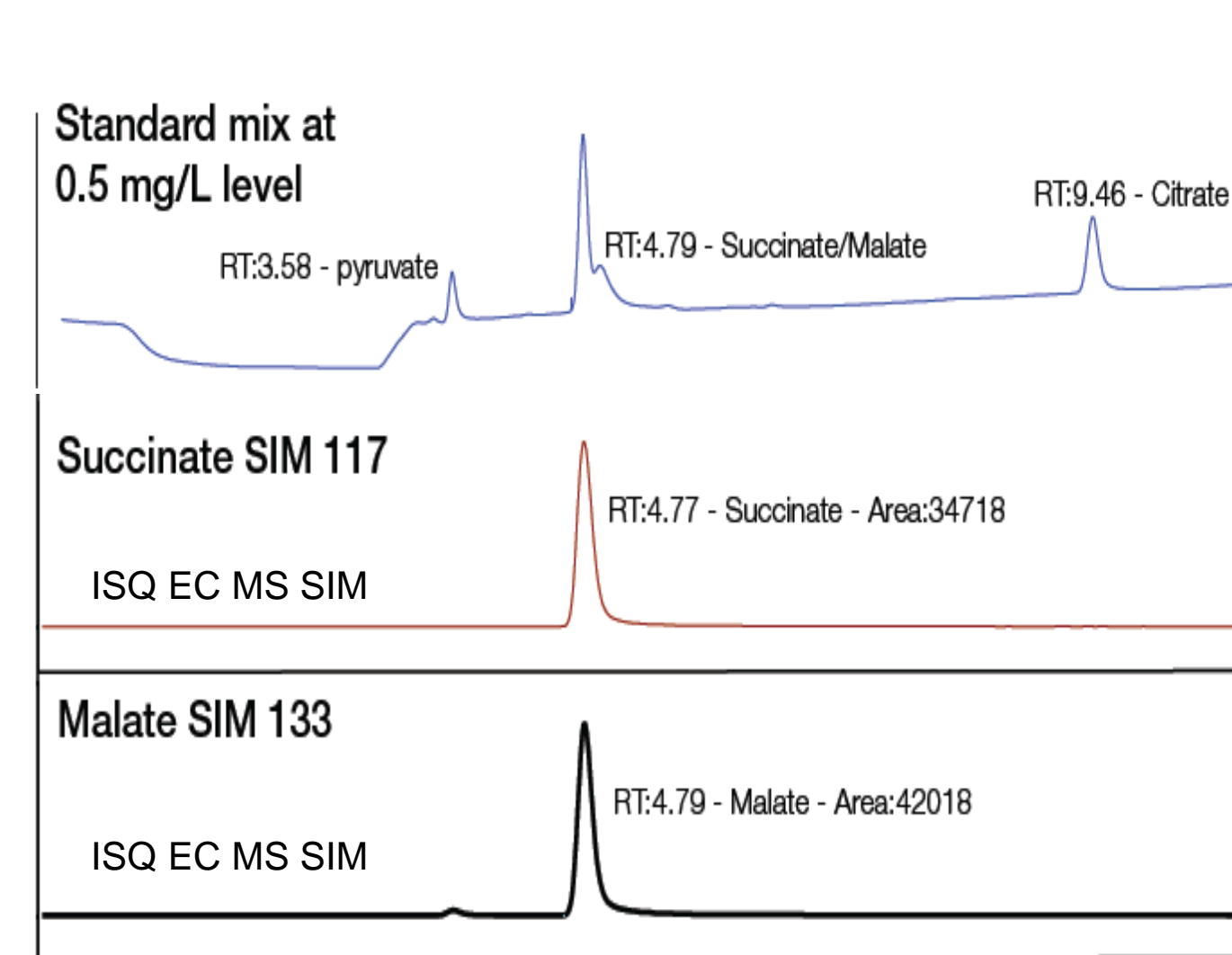
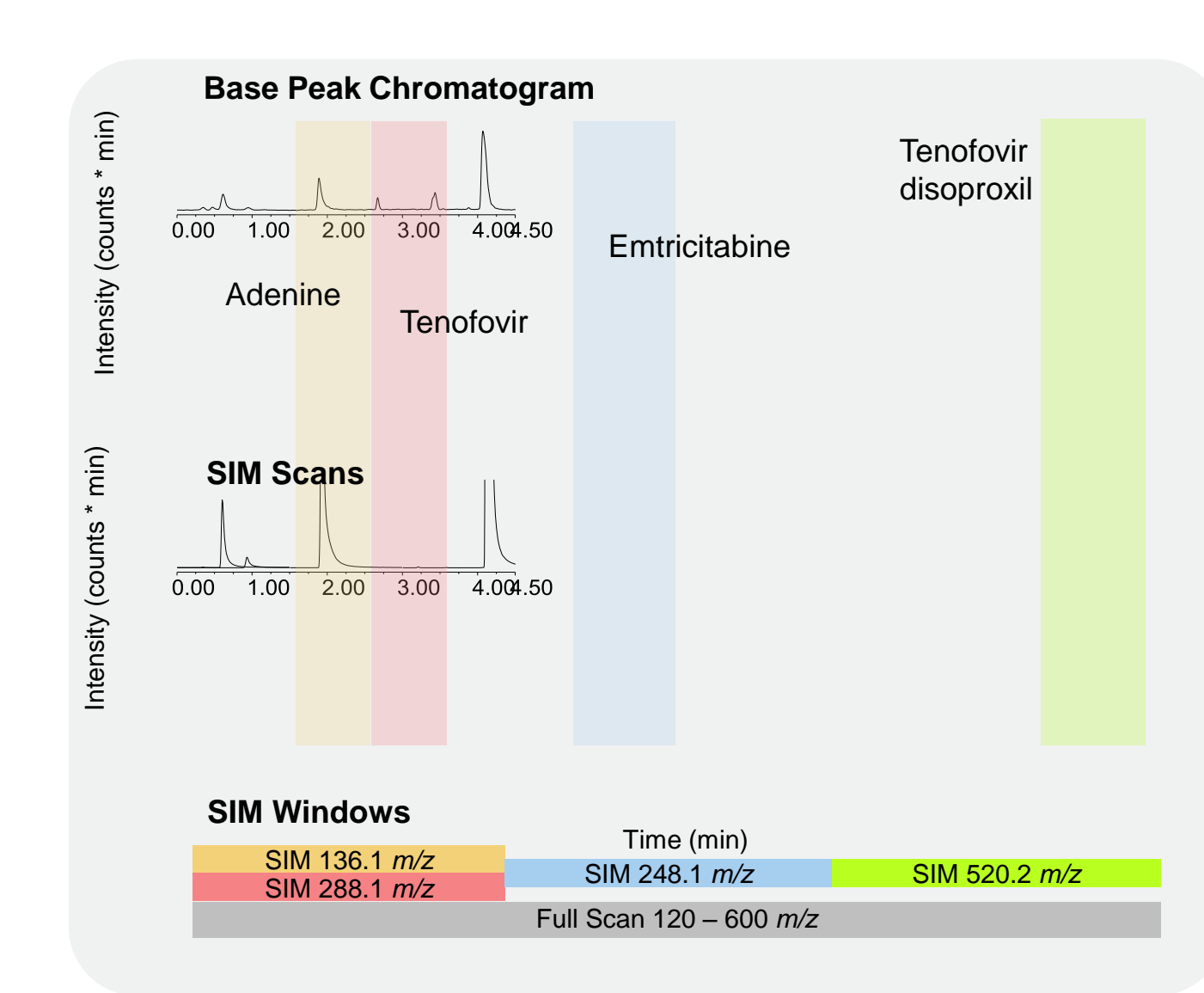


Figure 12. HIV combined drug impurity profiling by LC-MS.



The ISQ EC MS is capable of performing both SIM and Full Scan in one injection, as exemplified in the medicinal chemistry LC-MS example on Figure 12, as well as handling the challenging food and beverage matrices in the analysis of cations and low-mass amines in spoiled juices (Figures 13 and 14).

Figure 13. Cranberry juice, refrigerated for two years.

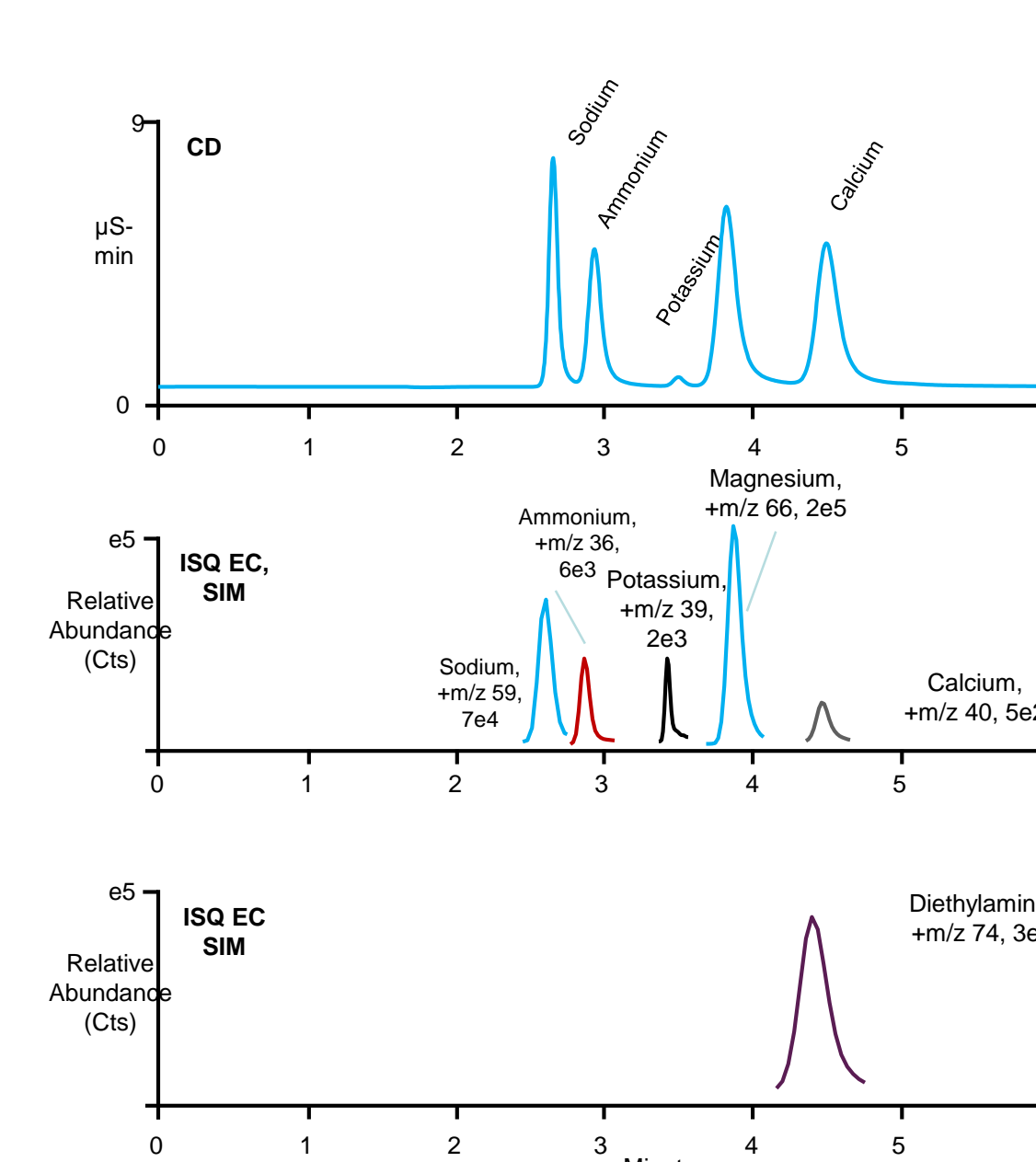
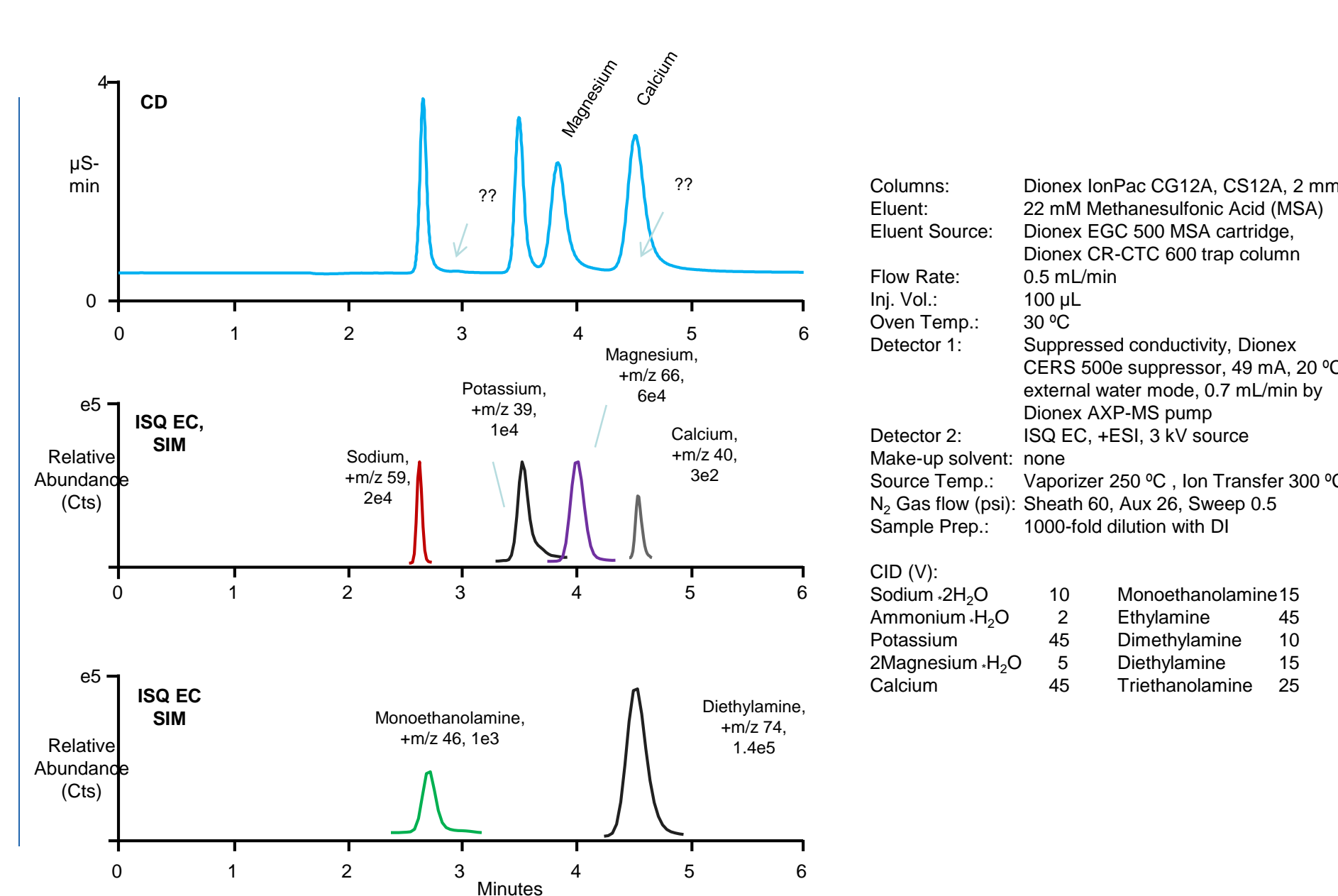


Figure 14. Hidden amines in moldy grape juice.



CONCLUSIONS

The newly designed ISQ EC single quadrupole mass spectrometer has been demonstrated to have excellent performance in several applications in both IC-MS and LC-MS hyphenation, with unparalleled low-mass performance in IC-MS, detecting bare, unsolvated cations and amines as well as organic acids in the anionic form. The experiment-based, novice-oriented method editor interface allows an immediate and successful MS method creation with the knowledge of the sample and solvent (eluent) physical parameters, which has never been possible before. The Chromeleon XPS walk-up optional software further expands the accessibility and makes the adoption of the hyphenated IC-MS and LC-MS available to the masses of synthetic and non-analytical chemists interested in securing more actionable knowledge about their samples with minimum efforts.

TRADEMARKS/LICENSING

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