

A Technical Comparison of SIFT-MS and PTR-MS

This document provides a detailed comparison of selected ion flow tube mass spectrometry (SIFT-MS) and proton transfer reaction mass spectrometry (PTR-MS). Both techniques offer real-time analysis for volatile organic compounds (VOCs) in whole air and both claim to use soft chemical ionization.

While SIFT-MS and PTR-MS have similarities, the fundamental difference is that SIFT-MS applies three reagent ions (H_3O^+ , NO^+ and O_2^+) as standard. Application of three reagent ions gives SIFT-MS a significant advantage in the discrimination of isomeric compounds.

Recently a “switchable” reagent ion (SRI-PTR-MS) has become available. However, SRI-PTR-MS lacks the instantaneous reagent ion switching capabilities, stability, usability, specificity, and true soft ionization of SIFT-MS instruments.

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1. An Overview of the technologies

SIFT-MS and PTR-MS are both flow-tube based mass spectrometric techniques that are used to detect and quantify VOCs in whole air in real time. In this section, we briefly review their principles of operation.

a. Principles of SIFT-MS

SIFT-MS uses soft chemical ionization reactions coupled with mass spectrometric detection to rapidly quantify VOCs in real time from whole-gas samples. Three standard chemical ionization agents (or reagent ions) are used (H_3O^+ , NO^+ and O_2^+). These reagent ions are mass selected and react with trace VOCs in very well controlled ion-molecule reactions but *do not* react with the major components of air, allowing SIFT-MS to analyze whole air for trace VOCs to pptv levels.

Soft chemical ionization yields a smaller number of product ions per compound than electron impact mass spectrometry (as used in GC-MS, for example), so gas chromatographic separation is unnecessary. This speeds sample throughput and provides instantaneous quantification of VOCs. Use of multiple reagent ions also greatly reduces interferences, markedly increasing the specificity of SIFT-MS compared with most other whole-gas analysis technologies.

Note that detailed performance data for a SIFT-MS instrument (a Voice200[®]) are provided in the paper Prince, Milligan and McEwan entitled “Application of selected ion flow tube mass spectrometry to real-time atmospheric monitoring” (*Rapid Commun. Mass Spectrom.*, 2010, **24**, 1763–1769).

b. A side-by-side comparison of the techniques

SIFT - MS		Characteristic	SRI - PTR - MS	
REAGENT ION GENERATION	1. Moist air is subjected to a microwave discharge 2. A quadrupole mass filter mass-selects reagent ion 3. Collisions with carrier gas yield reagent ions with very consistent (thermal) energy	Process overview	1. Reagent ion gas supply is selected 2. Gas stream is subjected to electrical discharge in a hollow cathode 3. Without cooling, all ions are injected into sample flow	REAGENT ION GENERATION
	5 – 20 million counts per second	Ion yield	2 – 60 million counts per second	
	Real-time (10 milliseconds)	Ion selection	Off-line (10 seconds)	
	High	Ion purity	High	
	Very consistent, low energy, thermal	Ion energy	Inconsistent, high energy, non-thermal	
	Water; He or H ₂ carrier gas	Consumables required	Water; O ₂	
SAMPLE ANALYSIS	1. Reagent ions collide with reactive compounds to form product ions; these product ions are well known because reagent ions are at thermal energy 2. Product ions and non-reacted reagent ions carried down the flow tube by the carrier gas flow	Process overview	1. Reagent ions collide with reactive compounds to form product ions; these product ions are not well defined because reagent ions have higher energies 2. Product ions and non-reacted reagent ions accelerated down the drift tube by the applied electrical field	SAMPLE ANALYSIS
	Consistent and predictable (all are thermal)	Reaction products	Inconsistent (due to higher, variable ion energies)	
	Low – truly soft chemical ionization (thermal energies by collision with carrier gas)	Fragmentation level	Higher: 1. Elevated initial reagent ion energies; 2. Electric field along drift tube adds more energy	
ION DETECTION (MASS SPECTROMETRY)	1. Ions are sampled into the ion detection region 2. Advanced ion optics is used to enhance transmission of higher mass ions 3. Ions are detected using a quadrupole mass filter and particle multiplier system	Process overview	1. Ions are sampled into the ion detection region 2. Ions are detected using: a. a quadrupole mass filter and particle multiplier system, <u>OR:</u> b. a time-of-flight (TOF) mass spectrometer	ION DETECTION (MASS SPECTROMETRY)
	High (due to use of advanced ion optics technology)	Sensitivity to ions over 120 m/z	Low for quadrupole-based system; better for TOF system	
	Unit mass resolution	Resolution	Unit mass resolution for quad; much better for TOF	
	100 milliseconds	Response time	100 milliseconds	

c. Principles of PTR-MS

In its original form, PTR-MS used just protonated water ions (H_3O^+) as the reagent ion. The “switchable reagent ion” (SRI) source now allows some models of PTR-MS instrument to use the other SIFT-MS reagent ions as well, though the timescale for switching reagent ions is a number of seconds for PTR-MS rather than milliseconds for SIFT-MS. The reagent ions are created in a hollow cathode discharge. They are not mass selected and are injected immediately into a drift tube where reactions occur with VOCs in the gas sample. An electric field gradient is used to carry the ions along a drift tube to the detection region. Depending on the instrument model, detection is either via a quadrupole and particle multiplier tube system, or a time-of-flight mass spectrometer. Identification of the analyte is by means of the resulting product ion mass(es) arising from the reagent ion – analyte reaction.

2. Technical advantages of SIFT-MS over SRI-PTR-MS

This section looks at the technical advantages of SIFT-MS over PTR-MS. Actual SIFT-MS data and screen captures are taken from a Syft Technologies Voice200 instrument. Table 1 outlines the technical key benefits.

Table 1. Key technical benefits of SIFT-MS over PTR-MS.

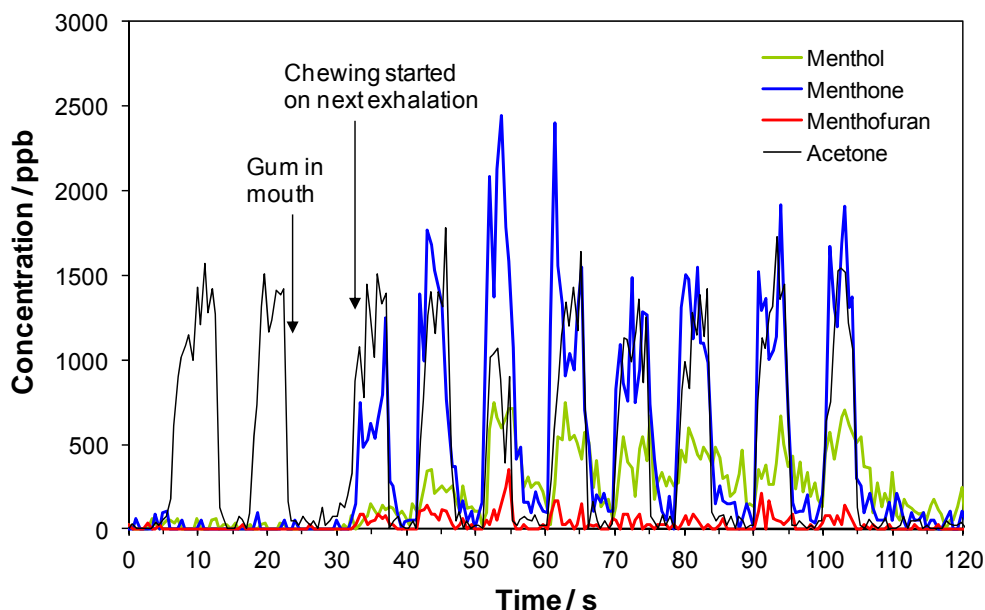
Characteristic	SIFT-MS	SRI-PTR-MS
Reagent ion selection	Real-time switching of reagent ions means all ions can be used in a single analysis of the sample	Switching is offline, requiring multiple scans on one sample, reducing efficiency
Reagent ion energy	Consistent thermal reagent ion energies yield reliable identification and quantitation	Higher (non-thermal) reagent ion energies lead to spectral confusion and poorer quality of quantitation
Detection sensitivity across mass range	Use of an advanced ion optics system gives much improved response to compounds at the higher end of the mass range	Quadrupole instruments struggle to achieve sufficient signal for product ions greater than about 120 m/z

a. Reagent ion selection – real-time switching using SIFT-MS

Switching of reagent ions on a millisecond timescale enables real-time, single-scan resolution of interfering compounds. Only SIFT-MS offers users this capability, with reagent ion changes made in less than 10 milliseconds. This characteristic allows synchronous concentration measurements of one analyte to be made with several reagent ions and/or various compounds to be detected with different reagent ions.

Synchronous measurement is illustrated in Figure 1, where in-mouth analysis has been made while a volunteer is chewing peppermint-flavored chewing gum. In this real-time analysis, menthol was analyzed using the H_3O^+ reagent ion, while menthone, menthofuran and acetone were analyzed using NO^+ . (Acetone is produced by the body through metabolism of lipids, so it acts as a useful marker for breath exhalations.) All data are acquired in a single scan.

Figure 1. Single breath exhalations: in-mouth analysis of flavor compounds arising from peppermint chewing gum and endogenous acetone, using a Syft Voice200 instrument. Menthol was analyzed using H_3O^+ while the three other compounds were analyzed using NO^+ .



A PTR-MS fitted with a switchable reagent ion (SRI) source can utilize the three SIFT-MS reagent ions, but since it lacks a quadrupole mass filter to switch these ions, it must use a very much slower change of source gas and/or ionization conditions in its hollow cathode discharge source. At best, a modified PTR-MS can achieve a change in the order of seconds, by switching from one reagent gas to another. This means that it is impractical to monitor real-time changes with multiple reagent ions.

Table 2 provides a comparison of reagent ion creation and selection in SIFT-MS and SRI-PTR-MS instruments.

Table 2. A comparison of reagent ion generation and selection in SIFT-MS and PTR-MS.

Characteristic	SIFT-MS	SRI-PTR-MS
Water to make H_3O^+	Yes	Yes
Bottled gases to make O_2^+	No	Yes
Time to switch reagent ions	10 ms (uses quadrupole)	10 s (changing of gas supply lines)
Reagent ion purity	High	High

b. Reagent ion energies – implications for analytical results

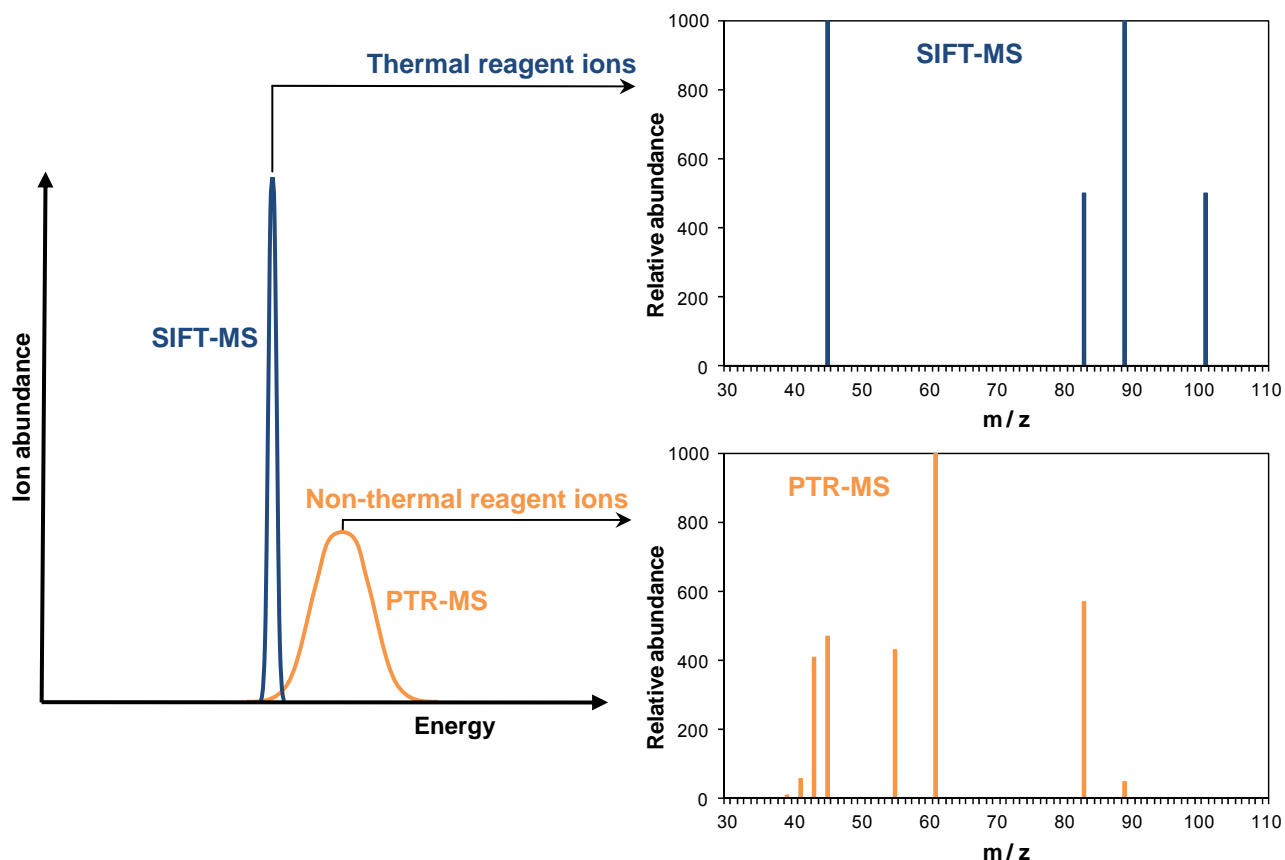
Consistency of reagent ion energy is one of the most critical factors in controlling analyte ionization, which in turn provides very consistent product formation and reliable, stable quantitation. In SIFT-MS, use of a carrier gas enables the chemical ionization process to be controlled much more effectively than in PTR-MS or other variations of chemical ionization mass spectrometry. The carrier gas plays two very important roles in controlling ionization:

- It thermalizes the reagent ions prior to introduction of sample, which means that the energies of the reagent ions are as low and consistent as possible, providing predictable, precise, and ultra-soft chemical ionization. In contrast, reagent ions of elevated and widely distributed energies are injected into the reaction region of the PTR-MS, resulting in reduced stability of the ionization process, with consequent effects on resolving and quantifying compounds.
- It transports the product ions and unreacted reagent ions down the flow tube to the detection region without addition of excess energy that is inherent in PTR-MS, where an electric field is used to accelerate ions down the drift tube to the detection region. Adding additional energy

further complicates mass spectra, reducing specificity and ability to uniquely quantify compounds.

The left-hand side of Figure 2 illustrates the comparative reagent ion energy distributions of PTR-MS and SIFT-MS. These distributions apply to any of the reagent ions used. On the right-hand-side of the figure, an example of non-thermal H_3O^+ reagent ion impact is evident. These spectra were generated from the data cited in Table 3.

Figure 2. Schematic diagram illustrating the different reagent ion energy distributions in SIFT-MS and PTR-MS. The mass spectra on the right-hand side were generated from the H_3O^+ data for the three compounds in Table 3, illustrating the consequences of reagent ion energy on product ion distributions.



Example 1: Product ion distributions with the H_3O^+ reagent ion

Table 3 shows published product ion distributions for H_3O^+ reagent ions in SIFT-MS and PTR-MS instruments. Higher (non-thermal) energies of the PTR-MS H_3O^+ ions are evident from the much higher fragmentation. Further, since H_3O^+ reactions are based on the proton transfer mechanism, compounds with proton affinities close to water (for example, formaldehyde, hydrogen sulfide, and phosphine) are difficult to detect in PTR-MS, due to higher ion energies.

Table 3. Product masses and branching ratios of ions formed from several compounds when ionized using H_3O^+ in SIFT-MS and PTR-MS instruments. Increased fragmentation evident in the PTR-MS data arise from non-thermal reagent ions.

Compound [molar mass; g mol^{-1}]	SIFT-MS product masses in m/z (branching ratio in %)	PTR-MS product masses in m/z (branching ratio in %)
Acetaldehyde [44]	45 (100%) ¹	61 (26%), 45 (47%), 43 (20%), 41 (6%), 39 (1%) ²
Ethyl acetate [88]	89 (100%) ³	89 (5%), 61 (74%), 43 (21%) ²
Hexanal [100]	101 (50%), 83 (50%) ¹	83 (57%), 55 (43%) ²

1. Spanel et al., *Int. J. Mass Spectrom. Ion Processes*, **165/166** (1997), 25-37.

2. Blake et al. *Int. J. Mass. Spectrom. Ion Processes*, **254** (2006), 85-93.

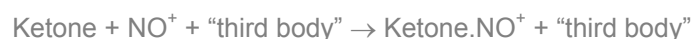
3. Spanel et al., *Int. J. Mass Spectrom. Ion Processes*, **172** (1998), 137-147.

Example 2: Product ion distributions with the NO^+ reagent ion

The non-thermal energies of NO^+ reagent ions in SRI-PTR-MS is evident from published marketing material where it is stated that the dominant mode of reaction of ketones is simple charge transfer:



However, based on the ionization potentials reported in the NIST on-line “webbook” database (<http://webbook.nist.gov/chemistry/>) this should *not* be the case since most small ketones have a higher ionization potential (IP) than NO (see Table 4). The observed SIFT-MS products, which are almost all the result of termolecular association processes:



Here the “third body” represents another atom or molecule that participates in the three-body collision, and though not reacting is critical because it carries away excess energy allowing the Ketone.NO^+ adduct to stabilize. The resulting thermal product ions are shown in Table 4 in the SIFT-MS column. Formation of charge transfer products in SRI-PTR-MS demonstrates the reagent ions are non-thermal and not “soft”.

Table 4. Ionization potentials of several small ketones (see <http://webbook.nist.gov/chemistry/>) and a comment on whether charge transfer products should be observed with thermal NO⁺ reagent ions (ionization potential (IP) = 9.26 eV). The products obtained with thermal NO⁺ ions in SIFT-MS are shown.

Compound (synonyms) [molar mass in g mol ⁻¹]	Ionization Potential (electron volts; eV)	Predicted Charge Transfer Product with Thermal NO ⁺ Ions	Actual Product Ions with Thermal NO ⁺ Reagent Ions (SIFT-MS) ¹
Acetone (propanone) [58]	9.70	No	88 (100%)
Butanone (methyl ethyl ketone; MEK) [72]	9.52	No	102 (100%)
2-Pentanone (methyl propyl ketone) [86]	9.38	No	116 (100%)
3-Pentanone (diethyl ketone) [86]	9.31	No	116 (100%)
2-Hexanone (methyl butyl ketone) [100]	9.35	No	130 (100%)
3-Hexanone (methyl butyl ketone) [100]	9.12 – 9.30 ²	Maybe ²	130 (85%); 100 (15%)

Notes:

1. Reference: Spanel, Ji, Smith, *Int. J. Mass Spectrom. Ion Processes*, **165/166** (1997), 25-37.

2. Two values for the IP are given in the NIST database and the IP of NO⁺ lies between them. The occurrence of some charge transfer product suggests the IP of NO⁺ is similar to that of 3-hexanone.

Quantitation issues

With SIFT-MS, reagent ions are thermalized in the carrier gas stream prior to reaction with analyte in the sample. This allows use of analyte rate co-efficients and products directly from a generic SIFT-MS reaction database that is applicable to thermal ion-molecule reactions. Therefore SIFT-MS provides absolute quantitation of analyte in all these situations – without calibration standards – from the ratio of the product peaks to reagent peaks and the knowledge of the chemical kinetics.

However, because PTR-MS reagent ions are not at thermal energies, the reaction products and rate co-efficients are dependent on the energies of the reagent ions produced for given instrument conditions. This means that there is no generic PTR-MS database of rate co-efficients and branching ratios (as there is for SIFT-MS), because any database applies to a very specific set of drift-tube operating conditions. Consequently, PTR-MS can only undertake absolute quantitation in real time if the products and rate co-efficients have been determined using exactly the same conditions in which the drift tube of the PTR-MS is currently operating. Hence in most situations a series of calibration standards must be run for PTR-MS measurements (in a similar way to GC-MS).

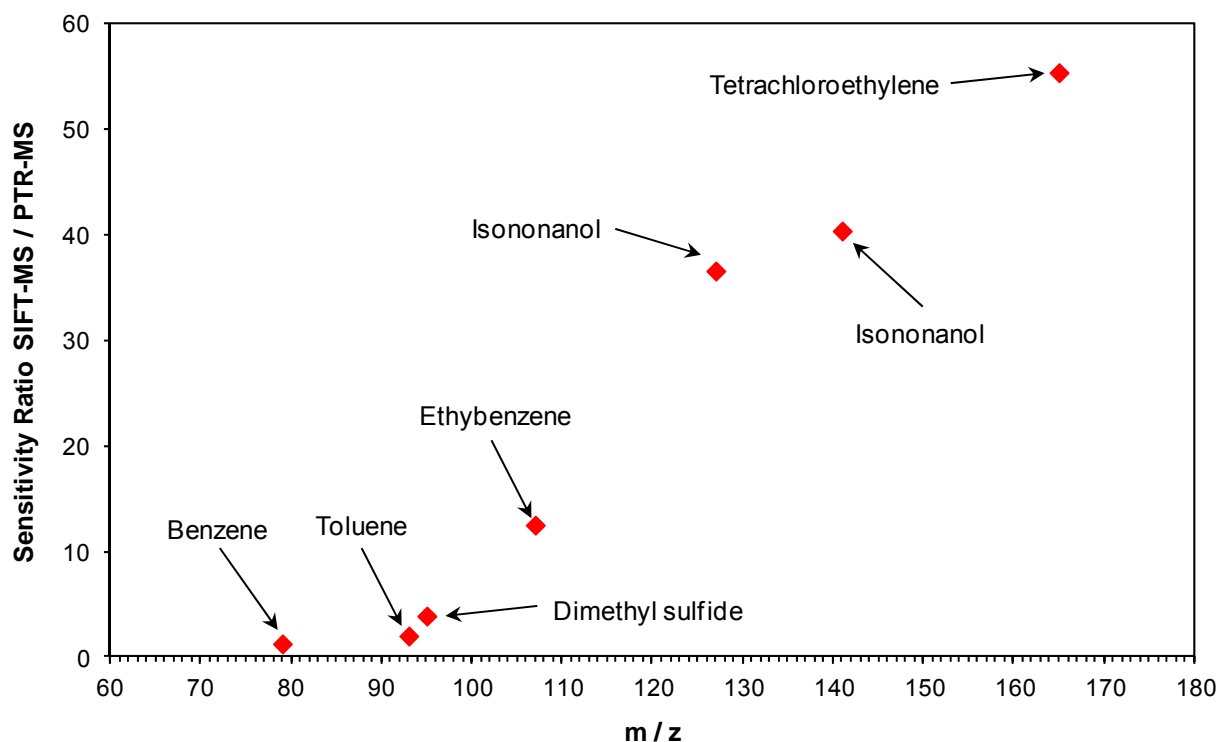
c. Detection mass spectrometers

Product ions and unreacted reagent ions are detected using a mass spectrometer in both SIFT-MS and PTR-MS instruments. Commercial PTR-MS instruments are available with quadrupole or time-of-flight (TOF) mass spectrometers, whereas SIFT-MS instruments only use quadrupoles at the present time. In this section a brief comparison of detection technologies is provided.

“Traditional” quadrupole PTR-MS instruments

Quadrupole detection systems are not all equal. In the Voice200 instrument, Syft introduced ion optics technology that has provided significantly enhanced detection of volatiles with product masses over approximately 100 m/z. The significance of this breakthrough was recently demonstrated in a head-to-head comparison of a Syft Voice200 and a commercial “standard” PTR-MS instrument. The two instruments simultaneously analyzed sample streams delivered from a permeation oven containing permeation tubes (one or several at a time). Although the instruments had similar sensitivities for the H₃O⁺ reagent ion reaction with benzene at m/z = 79 (the Voice200 was 1.27 times higher), Figure 3 shows that SIFT-MS has far superior sensitivity to product ions above about 100 m/z.

Figure 3. The ratio of ion intensity obtained by a Syft Voice200 SIFT-MS instrument to a “standard” PTR-MS, measuring various compounds from the same sample stream with the H_3O^+ reagent ion.



PTR-Time of Flight-MS (PTR-TOF-MS)

In recent years two manufacturers of PTR-MS instruments have offered time-of-flight (TOF) mass analyzers. TOF mass spectrometers can offer improved selectivity and detection of higher mass compounds, however this must be balanced against the main disadvantages of the TOF-based analysis, which are reduced sensitivity, larger size, and significantly higher instrument price than the equivalent quadrupole-based instruments.

Finally, it is important to remember that a TOF-based PTR-MS retains these key disadvantages with respect to SIFT-MS:

- High and variable reagent ion energies, causing increased fragmentation and reduced stability
- Switching of reagent ions is off-line, not real time.

3. Operational advantages of Syft SIFT-MS compared to PTR-MS

In addition to the technical aspects of SIFT-MS and PTR-MS, commercial aspects such as ease of use and serviceability must also be considered. Table 5 provides a summary of these operational considerations.

Table 5. A comparison of operational characteristics of Syft SIFT-MS and PTR-MS commercial instruments.

Characteristic	SIFT-MS (Voice series)	PTR-MS
Ease of use	Suitable for novice and non-technical users through to expert users	Suitable only for expert users
Software	Intuitive, easy-to-use software for both non-technical and expert users	Very basic, scientist-focused software
Configurability	Designed to provide the results a particular level of operator requires	Minimal
Automation	High – including sophisticated self-checks and fully automated validation	Moderate – no performance validation
Internet/network ready	Yes	No
Remote operation	Yes	No
Remote support	Yes	No
Integration	Designed for easy integration into existing operations and workflow	Designed as standalone
Analytical stability	Long term, via SIFT-MS process and automated validation	Short term, due to PTR-MS process (use of drift voltage)

a. Ease of use

Syft provides software solutions for its Voice-series SIFT-MS instruments that make them easy to use and easy to integrate with existing information technology systems.

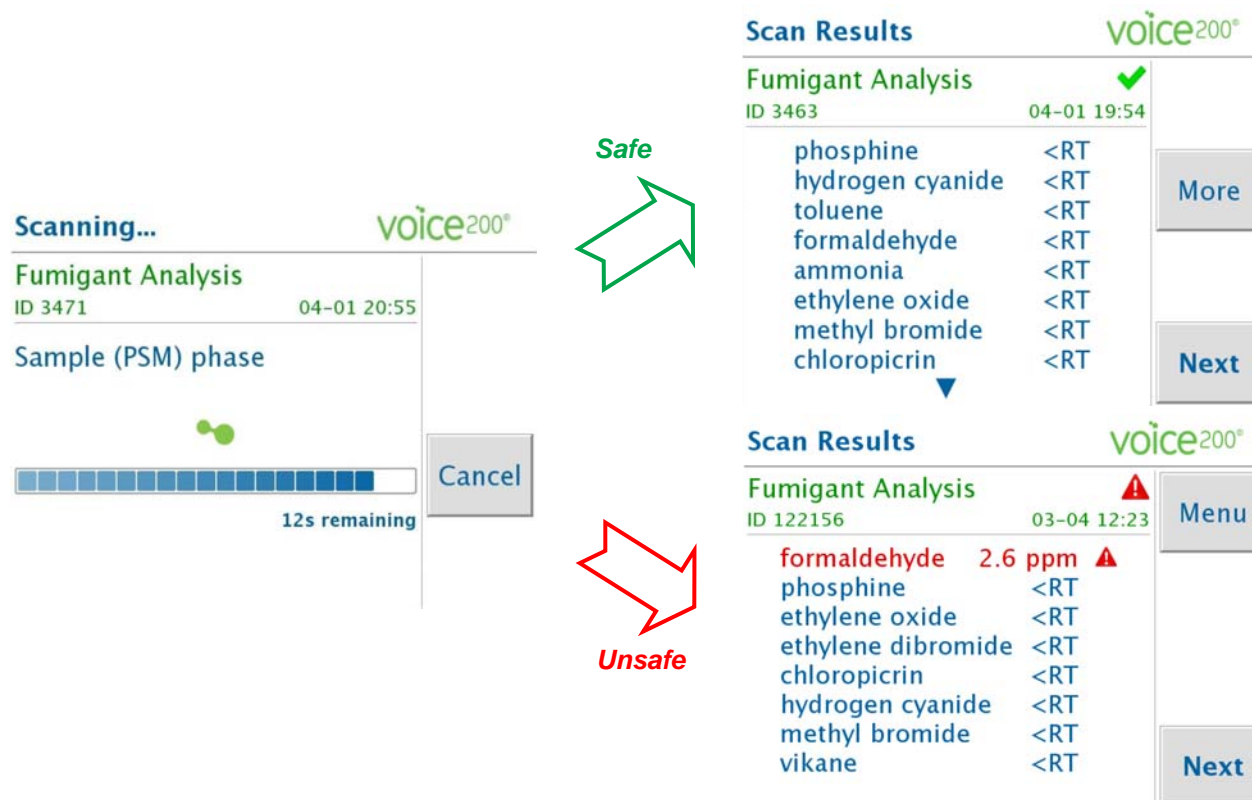
Non-technical and routine users

Although Syft Voice-series instruments are sophisticated devices delivering analysis at the level required by analytical laboratories, they include software that enables even minimally trained users to access the technical advantages. Features designed for such users include:

- Simplified workflows for very easy operation
- Intuitive touchscreen, menu-driven analysis
- Completely customizable target compound lists
- Instantaneous reporting of scan results
- Alarms raised when a specific compound is above a user-defined threshold or if a pattern or trend indicates that a process is outside specification (for example, using multivariate statistics).

Figure 4 illustrates how a laboratory grade analysis has been configured for simple operation for non-technical users of a Voice200 instrument.

Figure 4. Voice-series software is readily configured for use and interpretation by non-technical operators. These screenshots from the Voice200[®] instrument's touchscreen illustrate actual results in a worker safety application.



Technical users and researchers

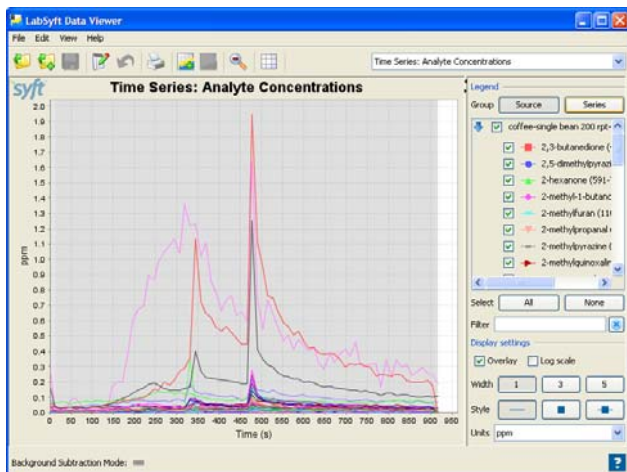
LabSyft is a software package designed for advanced users of Syft Voice-series instruments, such as those in research applications. It allows advanced users to:

- View data as it is generated
- View, manipulate and export data after a scan has finished
- View, search and expand the standard compound library
- Create and edit analytical methods
- Set-up and execute batch scanning.

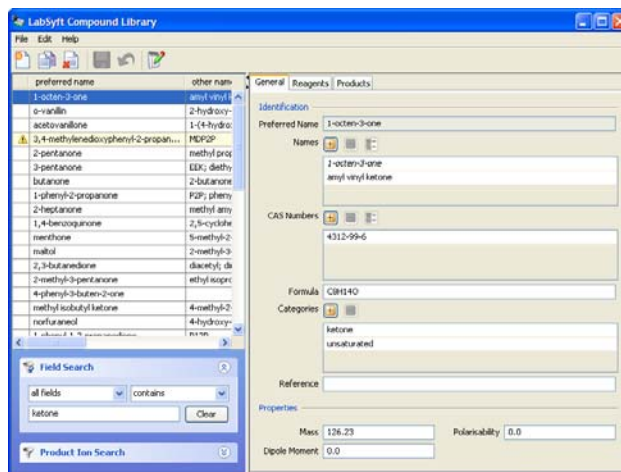
Figure 5 shows screenshots from relevant LabSyft software screens.

Figure 5. Screen shots of various modules in the LabSyft software package for Syft Voice-series SIFT-MS instruments.

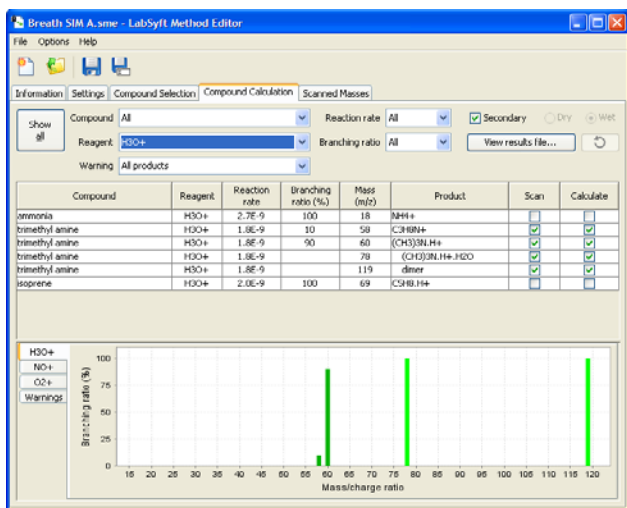
a) Live and data viewer modules



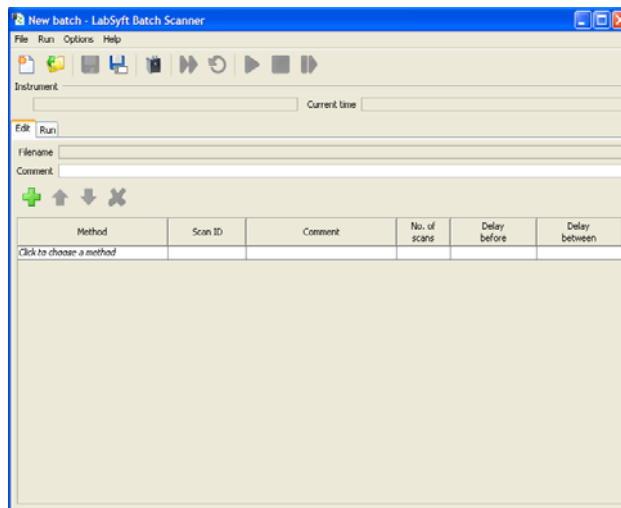
b) Compound library module



c) Method development module



d) Batch scanner module



LabSyft runs on a computer (Windows or Mac) that is connected to the instrument, either directly or across a network. This means files can be created, edited and stored on a remote computer, before being transferred to an instrument. Conversely, data files can be transferred from the instrument to a remote computer for further use.

Network integration and remote access

Syft Voice-series instruments are designed for integration with standard network systems, which provides flexibility on how instruments are operated and supported.

Syft instruments can be accessed via the internet from any appropriately authorized computer anywhere in the world. This access allows data upload and download, full remote operation, and instrument monitoring, error diagnostics and support.

b. Data and stability

Syft's Voice-series instruments intrinsically deliver improved data quality, for the technical reasons discussed in Section 2. In particular, lower reagent ion energies lead to less fragmentation. Consequently, SIFT-MS has significantly lower calibration demands than PTR-MS. Syft instruments also incorporate sophisticated system diagnostics, including an automated daily validation cycle, which tracks instrument performance and maintains system stability.

c. Technical support

Syft and its distributors offer extensive maintenance and support services for Voice-series instruments, accessories and their applications. In particular, the remote access feature of Voice-series instruments allows them to be monitored and supported anywhere that internet access is available.

Examples of technical support and services include:

- **Scheduled Preventative Maintenance:** A regular, six-monthly maintenance visit, by a Syft-approved technician ensures that the Voice-series instrument is properly cared for. All instrument components that require regular maintenance are serviced to their individual manufacturer's recommendations. Recommended schedules for the periodic replacement or overhaul of components are implemented to ensure that all warranty requirements are met. Instrument performance is monitored and verified.
- **Syft-Sure On-Line System Support:** On-line system support ensures that users of Voice-series instruments receive helpful and timely assistance from Syft technical support staff, if they experience any difficulties with the operation of their equipment. A user who needs assistance can log a Support Case via the Support Portal on Syft's website. The case is automatically forwarded to Syft's Support Network and the user is contacted by a Syft technician – within a contractually agreed time of a case being logged. Syft's technician can make a remote data connection to the Voice-series system to diagnose and rectify issues. If on-site intervention or replacement parts are required to resolve an issue, Syft-Sure Contract holders receive high-priority treatment.

4. Summary

Syft Technologies' SIFT-MS instruments provide very clear technical and operational advantages compared to the various commercial forms of PTR-MS. Significant advantages include:

- Rapid switching of reagent ions, allowing multiple reagent ions to be used in a single scan, saving time and sample, and allowing instantaneous results
- True soft ionization with lower energy and less fragmentation, meaning less spectral confusion and more precise compound identification and quantitation
- Enhanced usability, especially:
 - Network compatibility, allowing remote operation, monitoring, fault diagnostics, and support
 - Turnkey applications and a touchscreen interface, allowing users with minimal training to operate the instrument
 - Advanced LabSyft software, allowing research-level users to access the technology's full capabilities
 - Online support and backup, meaning help is never more than a click away.

Before purchasing a PTR-MS, contact Syft or your local distributor for more information on Voice-series analytical solutions.



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