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Maximising confidence in chemical ionisation mass spectrometry data

The importance of high quality, accurate and traceable gas reference materials for PTR-MS and SIFT-MS

Chemical ionisation techniques in gas analysis

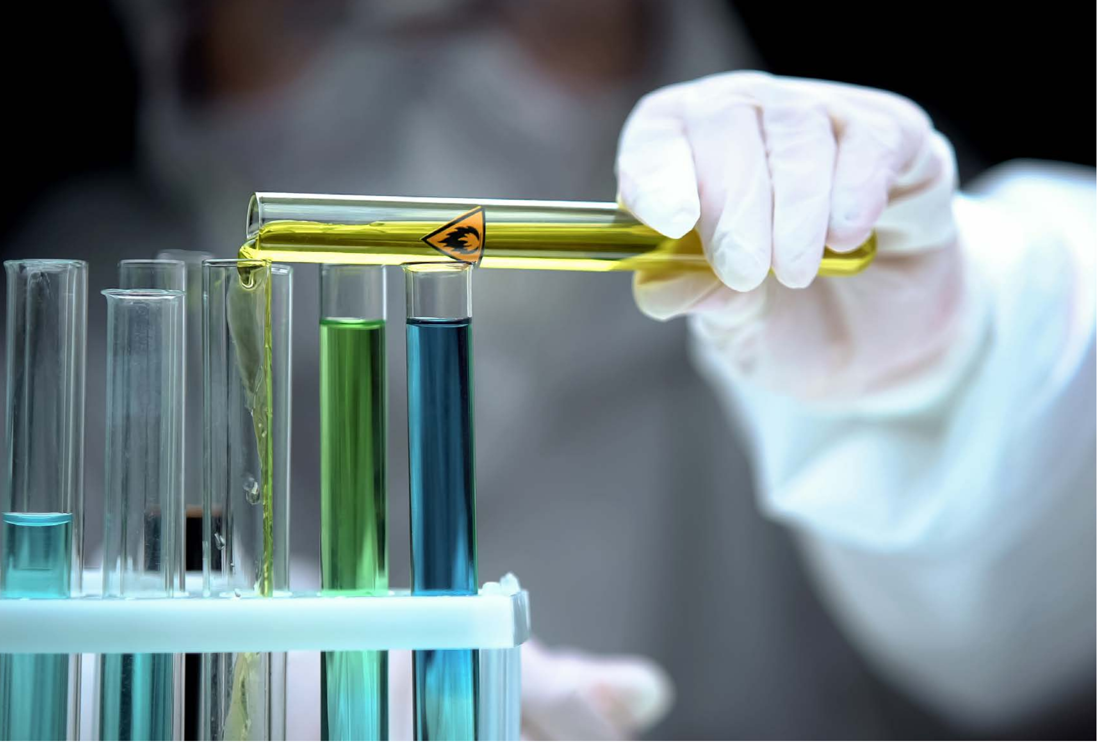
Proton transfer reaction mass spectrometry (PTR-MS) and selected ion flow tube mass spectrometry (SIFT-MS) are portable and field-deployable chemical ionisation technologies that have been around for several decades. They are widely used to quantify a broad range of gases with high time resolution – taking multiple measurements per second – and at low amount fractions (pmol mol^{-1} – the equivalent of a single drop of water in an Olympic-sized swimming pool). These methods can be used with several different reagent ions that ionise the compounds of interest, enabling their detection. One of the major reagent ions used is the hydronium ion (H_3O^+), which ionises all compounds with proton affinities greater than water. This means it avoids interferences from the major components of air – nitrogen, oxygen, argon and carbon dioxide – precluding the need for sample pretreatment.

The PTR-MS and SIFT-MS techniques use H_3O^+ to detect compounds as protonated molecular ions, which are preserved as a result of limited fragmentation due to the minimal excess energy of the proton transfer reaction. This aids compound identification in complex mixtures, without requiring the use of additional methods such as traditional chromatographic separation. The PTR-MS and SIFT-MS methods are especially useful in time-sensitive settings due to their ability to provide real-time measurements and, since their introduction in the mid-1990s, they have found applications in a broad range of industries and research activities. These include in air quality monitoring, environmental research, food and flavour science, safety and security, breath analysis, biological research and the detection of illicit substances.

Key application areas

A key application area for PTR-MS and SIFT-MS is monitoring air quality in cleanrooms in semiconductor manufacturing, a task that has historically relied on checking grab samples every few hours. However, this approach can lead to wasted production for the preceding 1-2 hours before an issue is found. This makes continuous, real-time measurements preferable. Both PTR-MS and SIFT-MS can run continuously, ensuring optimal monitoring in settings like cleanrooms where airborne molecular contaminants can compromise the quality of the resultant semiconductor products.

Measuring the presence, composition and concentration of various gases in both indoor and outdoor applications is equally crucial in a wide range of other industries. Not least of these are instances where gases – along with their oxidative atmospheric products – that are detrimental to human and ecosystem health are emitted from industrial or natural sources. These may include volatile organic compounds (VOCs) that are released from combustion, industrial solvents and even vegetation. Another important application for the two techniques is medical diagnostics, where PTR-MS and SIFT-MS have been used to analyse patient breath samples to investigate metabolic health or the presence of disease.[1] Both platforms are also useful for analysing aromas in food and flavour studies, helping to develop new products and improve existing ones for the best customer experience.[2]



PTR-MS

PTR-MS works by generating H_3O+ ions that ionise compounds in the sample through proton transfer reactions in a flow tube. These ions are then detected and quantified using a mass spectrometer, which identifies compounds based on their mass-to-charge ratio with high time resolution and sensitivity. Gases that have proton affinities larger than water (>691 KJ mol^{-1}) are detectable with PTR-MS. These include most VOCs, with the exception of certain light n-alkanes. As most VOCs have proton affinities less than 900 KJ mol^{-1}, minimal excess energy is imparted following proton transfer. This results in limited fragmentation, also termed soft ionisation, and enables detection of the protonated molecular ion.

This contrasts with traditional electron impact (EI) ionisation, which causes significant fragmentation that complicates the mass spectra if no additional separation steps are applied. Consequently, EI is typically used in conjunction with a chromatographic separation method, such as gas chromatography mass spectrometry (GC-MS). Over the past decade, many PTR-MS instruments have transitioned from quadrupole MS to time-of-flight mass spectrometry (TOF-MS), and have been designed to include advanced ion optics, which dramatically improve sensitivity through higher ion transmission to the detector. The superior mass spectral resolving power of the TOF-MS supports less ambiguous identification and enables an even larger number of compounds to be detected and identified. Modern instruments have even advanced beyond using only H_3O^+ as the reagent ion to expand their ionisation capabilities to other reagent ions, such as the nitrosonium (NO^+) and dioxygenyl (O_2^+) cations.

SIFT-MS

SIFT-MS uses an initial quadrupole mass filter between the source production region and the flow tube to enable the selection of different reagent ions, for example H_3O^+, NO^+ and O_2^+. These ions selectively react with molecules of the compounds of interest in the flow tube, where helium gas assists the flow of ions to the second quadrupole mass filter and detector for analysis. Ions are then separated based on their mass-to-charge ratio, and the system selects one reagent ion at a time, rapidly switching between them in less than a second to provide independent measurements of each analyte. Major strengths of this technique are its compatibility with both positive and negative ion modes, and its ability to work with flammable matrix gases. This is fundamentally different from the PTR-MS technique, where reagent ions move from the source region to the drift tube by diffusion, precluding the use of flammable matrix gases and the rapid selection of reagent ions. This reagent selection step occurs much more slowly with PTR-MS than SIFT-MS, with switches taking over a second each due to the lack of a quadrupole mass filter between the source region and drift tube.

The need for calibration in gas analysis

Consistently collecting accurate data in gas analysis is understandably crucial for long-term measurement records and reliable modelling, and supports confident decision making in critical sectors like healthcare, food safety and environmental protection. However, the quality of results can be significantly impacted by instrument function, with deviations in measurements potentially compromising research outcomes, product safety, and the efficiency and economics of industrial processes. Timely and correct calibration of analytical instruments with recognised reference materials is therefore essential to ensure that measurements are compliant and comparable worldwide.

As a result of the numerous VOCs detectable by PTR-MS, it is impractical to have a calibration gas reference material that covers all observable compounds. Nevertheless, quantification is still possible without the need for specific calibration materials, provided the mass-dependent ion transmission rate is accurately known.[3] However, the transmission of PTR-MS platforms using advanced ion optics diverges from theory at low masses, while poor tuning and ageing of the ion detection system result in deviations at high masses.[4] This means that the mass-dependent ion transmission rate must be determined experimentally by retrieving and constraining the mass-dependent transmission curve of the instrument through calibration with a multicomponent certified reference material (CRM).

In SIFT-MS, the concentrations of the analytes in the flow tube reactor are derived from the ratio of product ion signals to reagent ion signals, using constant rate coefficients for specific conditions. However, instrument-dependent factors, such as reaction time and ion transmission, require regular calibration with automated performance checks. SIFT-MS measurements of analyte concentration therefore primarily rely on the correct assignment of product ions to the analytes, and on the accurate determination of several physical parameters. Quantitative methods for SIFT-MS have advanced in recent years to include a certified gas mixture containing several stable nonpolar gases with known amount fractions of nominally 2 μmol mol^{-1}. These primary reference materials (PRMs) are used during regular, automated performance checks to adjust the parameters involved in quantitation and ensure the device calibration passes the specified criteria. These regular checks with PRMs help to guarantee the long-term stability, repeatability and reproducibility of the SIFT-MS results for more robust analytical performance.[5]

The lack of traceable gas reference materials currently on the market presents significant challenges for researchers, as it hinders the ability to generate comparable results across different studies and instruments, hampering long-term monitoring efforts in various sectors. This highlights the pressing need for accurate, stable and high-quality CRMs and PRMs that can be used to establish international benchmarks for robust and repeatable analytical performance using PTR-MS and SIFT-MS instruments.

The National Physical Laboratory – ensuring confidence in data

The National Physical Laboratory (NPL) is the UK's National Metrology Institute, and provides traceability for gas composition measurements to the international system of units and to recognised international standards. NPL is a global leader in gas metrology, providing high-quality gas reference materials that enable customers to achieve accurate, consistent and comparable measurement data, providing them with confidence in their results. NPL bridges the gap between research and commercial needs, offering unmatched reliability for long-term, reproducible measurements.

Our extensive range of CRMs and PRMs includes a unique 20-component certified gas reference material with a mass range of 32 to 671 (g mol^{-1}) for accurately calibrating the transmission curve of PTR-MS instruments – the only reference material of its kind on the market. We have also developed an eight-component primary gas reference material for validating SIFT-MS instrument performance. NPL's traceable gas reference materials already underpin the accurate measurement of ambient air quality, natural gas, industrial emissions, vehicle and aircraft emissions and occupational exposure markets all over the world.

NPL's 20-component CRM for calibrating the transmission function of PTR-MS instruments includes the following compounds at nominally 1 µmol mol^{-1} within a nitrogen balance gas. The uncertainties for each compound are in the range of 3-10 per cent relative.

benzene	**m-xylene**	**butan-2-one (MEK)**
1,2,4-trichlorobenzene	**dimethyl sulfide (DMS)**	**acetonitrile**
1,2,4-trichlorobenzene	**3-carene**	**3-buten-2-one (MVK)**
1,2,4-trimethylbenzene	**isoprene**	**perfluorotributylamine (PFTBA)**
hexamethylcyclotrisiloxane (D3-siloxane)	**methanol**	**toluene**
octamethylcyclotetrasiloxane (D4-siloxane)	**acetone**	**ethanol**
decamethylcyclopentasiloxane (D5-siloxane)	**acetaldehyde**	

Note: Commonly used names are shown here but the preferred IUPAC names where appropriate are: propan-2-one (acetone), (methylsulfanyl) methane (dimethyl sulfide), 2-methylbuta-1,3-diene (isoprene), but-3-en-2-one (methyl vinyl ketone), butan-2-one (methyl ethyl ketone), 1,3-xylene (m-xylene), 3,7,7-trimethylbicyclo[4.1.0]hept-3-ene (3-carene).

NPL's 8-component PRM for calibrating SIFT-MS instruments includes the following compounds at nominally 2 µmol mol^{-1} within a nitrogen balance gas. The uncertainties for each compound are in the range of 3-5 per cent relative.

1,2,3,4-tetrafluorobenzene	**benzene**	**isobutane**
octafluorotoluene	**p-xylene**	**hexafluorobenzene**
ethane	**toluene**	

Note: Commonly used names are shown here but the preferred IUPAC names where appropriate are: 2-methyl propane (isobutane), 1,2,3,4,5-Pentafluoro-6-(trifluoromethyl)benzene (octafluorotoluene) and 1,4-Xylene (p-xylene).

Custom solutions for bespoke applications

NPL's robust gas reference materials were created in collaboration with the global PTR-MS and SIFT-MS communities to cover the largest mass-to-charge range currently possible and meet the diverse needs of this varied industry. At the same time, our flexible and responsive team also have the capacity, skills and experience to develop tailored reference gas mixtures containing different compounds and amount fractions according to specific research needs.

Get in touch with us for more information on our reference gas portfolio for PTR-MS and SIFT-MS, or to discuss tailor-made solutions for your unique application.

References

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