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EDITORIAL

Proton Transfer Reaction-Mass Spectrometry Applications in Medical Research

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Gathering information about a subject's physiological and pathophysiological condition from the 'smell' of breath is an idea that dates back to antiquity. This intriguing concept of non-invasive diagnosis has been revitalized by 'exhaled breath analysis' in recent decades. A main driving force was the development of sensitive and versatile gas-chromatographic and mass-spectrometric instruments for trace gas analysis. Ironically, only non-smelling constituents of breath, such as O_2, CO_2, H_2, and NO have so far been included in routine clinical breath analysis. The 'smell' of human breath, on the other hand, arises through a combination of volatile organic compounds (VOCs) of which several hundred have been identified to date. Most of these volatiles are systemic and are released in the gas-exchange between blood and air in the alveoli. The concentration of these compounds in the alveolar breath is related to the respective concentrations in blood. Measuring VOCs in exhaled breath allows for screening of disease markers, studying the uptake and effect of medication (pharmacokinetics), or monitoring physiological processes.

There is a range of requirements for instruments for the analysis of a complex matrix, such as human breath. Mass-spectrometric techniques are particularly well suited for this task since they offer the possibility of detecting a large variety of interesting compounds. A further requirement is the ability to measure accurately in the concentration range of breath VOCs, i.e. between parts-per-trillion (pptv) and parts-per-million (ppmv) range.

In the mid 1990's proton transfer reaction-mass spectrometry (PTR-MS) was developed as a powerful and promising tool for the analysis of VOCs in gaseous media. Soon thereafter these instruments became commercially available to a still growing user community and have now become standard equipment in many fields including environmental research, food and flavour science, as well as life sciences. Their high sensitivity for VOCs with detection limits down to sub-pptv levels without pre-concentration and their highly linear signal response over seven orders of magnitude make PTR-MS instruments valuable tools for exhaled breath analysis. The 'soft' chemical ionization process in PTR-MS largely avoids fragmentation, providing interpretable spectra without pre-separation. This is especially important for complex gas mixtures such as breath. Even more interesting, PTR-MS instruments analyse a gas sample in real-time and do not require any sample pre-treatment. This offers the possibility for online breath analysis with breath-to-breath resolution. This special issue on PTR-MS applications in medical research contains articles exploring different medical applications of PTR-MS. These applications include screening studies, where the breath composition of a large number of patients is investigated to, e.g., determine influences of demographic data on breath concentrations (Schwarz *et al* 2009 *J. Breath Res.* **3** 027003). In online monitoring studies the breath of one subject is continuously measured, e.g., to study rapid changes in breath volatiles under physical exercise (King *et al* 2009 *J. Breath Res.* **3** 027006). Other papers address more elementary breath research and discuss the interpretation of exhaled breath

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composition in the presence of fragmenting and overlapping compounds (Schwarz *et al* 2009 *J. Breath Res.* **3** 027002), examine the different causes of variability in the measurement of breath samples (Thekedar *et al* 2009 *J. Breath Res.* **3** 027007), and compare blood and breath concentrations directly (O'Hara *et al* 2009 *J. Breath Res.* **3** 027005). Potential sources for breath markers are also explored, by analysing the head-space emissions from microbial culture samples (O'Hara and Mayhew 2009 *J. Breath Res.* **3** 027001). Finally, a recent technological advancement in PTR-MS technology promises several advantages especially for breath gas analysis, which is demonstrated by on-line breath sampling with a PTR-time-of-flight (PTR-TOF) instrument (Herbig *et al* 2009 *J. Breath Res.* **3** 027004).