Analysis of Breath-related Volatile Organic Compounds with Laser Absorption Spectroscopy

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Analysis of volatile organic compounds (VOCs) in breath has the potential for non-invasive and inexpensive medical diagnostics. This requires, however, highly sensitive and selective analytical techniques. Laser-absorption spectroscopy (LAS) is a promising candidate for future point-of-care diagnostics and health status monitoring. This method is already established for selective quantification of inorganic molecules in the mid-infrared (mid-IR) spectral range, providing a fast and accurate response, and having the potential for compact, easy-to-use and cost-effective instrumentation.

We expanded the application of LAS for the detection of VOCs by using a novel extended-tuning quantum-cascade (QC-XT) laser [1], coupled to a 76-m-optical-path multipass cell (MPC), and that covers the spectral range between 1063–1102 cm^{-1}[2]. By means of a gas calibration unit (HovaCAL) single and multi-compound gas standards of breath-relevant VOCs at ppm (or ppb) level with variable water content were generated. Several VOCs, containing up to four carbon atoms (C4), reveal significant fine structure in their ro-vibrational spectrum. Such distinct narrow features were also observed for larger rigid or symmetrical molecules (~C6).

Currently, we are adopting the spectrometer for in-situ breath analysis by designing an inlet system that minimises gas-exchange times and VOC adsorption, prevents water condensation, and allows for constant gas pressure in the MPC. Spiking of the breath samples either with a deuterated internal standard or with the analyte of interest was used for method validation. Excellent precision (typically ~1 ppb for 25 s averaging time) and high accuracy was achieved with a time resolution of 360 ms. Typical relative expanded uncertainty (k=2) of <2% has been found in the spiking experiments. The outstanding selectivity and accuracy of the method are a result of the broad measuring spectral range, high spectral resolution, and the unique spectral fingerprints of the investigated VOCs.

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[1] Yves Bidaux, Alfredo Bismuto, Camille Tardy, Romain Terazzi, Tobias Gresch, Stéphane Blaser, Antoine Muller, Jerome Faist, *Applied Physics Letters*, **2015**, *107*, 221108.
[2] Raphael Brechbühler, Miloš Selaković, Philipp Scheidegger, Herbert Looser, André Kupferschmid, Stéphane Blaser, Jérémy Butet, Lukas Emmenegger, Béla Tuzson, *Analitical Chemistry*, **2023**, *95*, 5, 2857–2864
[3] https://www.exhalomics.ch/ (Accessed: 11.02.2023)