

Human Breath Acetone Analysis by Mid-IR Laser Spectroscopy: Development and Application

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Abstract: A broadly tunable mid-IR VECSEL based spectrometer is developed and used in a pilot clinical study to investigate the correlation between exhaled acetone concentration and negative energy balance induced by lifestyle interventions. © 2018 The Author(s)

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1. Introduction

It is well known that a large number of volatile compounds appear at the trace level in the human breath, regardless of the individual health condition. A greatly elevated level of the normally occurring species or even the appearance of further compounds in exhaled breath can be an indicator for diseases. This has a tremendous potential for a use in clinical medicine, since it may allow assessing many body functions in a safe, convenient, and reliable way. In this context, breath acetone is gaining an increasing interest as a potential bio-marker of diet efficacy to promote weight loss [1]. For this reason, a method suitable for the monitoring of nutrition on a daily basis would be a considerable asset for both health care professionals and patients.

In this work we address the spectroscopic detection of VOCs using a novel broadly tunable mid-infrared vertical external cavity surface emitting laser (VECSEL) [2]. Its emission bandwidth is centered at 3.38 μm , which overlaps well with the fundamental stretching vibrational band of the C-H bond. Thus, the laser can probe the absorption features of hydrocarbons, aldehydes, alcohols, ketones and many other organic molecules found in human breath. We demonstrate its suitability for the measurement of breath acetone in a proof-of-concept clinical study.

2. Acetone detection in human breath

The breath sample of healthy individuals typically contains < 1 ppm acetone, which increases by about 10-fold in case of diabetic patients or a few times for individuals that are subject to intensive physical exercise or fasting. Due to its low abundance, the absorption of acetone is largely covered by absorptions from other breath constituents, in particular water and methane. Therefore, this challenging task is often addressed by sample preparation involving water removal, which may easily lead to partial loss of acetone. Our aim was to develop a spectroscopic approach relying on the fast and accurate multispectral analyses of a wide spectral region covered by the VECSEL, and accurately quantify the acetone in humid gas samples.

3. Experimental setup

The thermo-electrically stabilized VECSEL is pumped by a 1.55 μm diode with 5 ns long light-pulses at a repetition rate of 100 kHz. The frequency scan is accomplished by an external top mirror, which is movable in the vertical direction by a piezoelectric actuator. A scanning rate of 500 Hz was selected as an optimum between acquisition speed and the number of spectral data points within the scan. The spectral range between 2950 and 2980 cm^{-1} is optimal to cover the absorption features of acetone and isoprene. This new laser source has two limiting factors that had to be addressed prior high precision measurements, namely a pulse to-pulse amplitude variation and an inherent frequency drift. The former was minimized by applying the technique of pulse normalization using a reference optical path with temporal gating [3], while the frequency drift of the laser was actively corrected by a feedback-loop to the piezo voltage.

An astigmatic Herriott multipass cell with an optical path-length of 36 m was used to achieve the necessary sensitivity for acetone measurements. Due to the excellent path-to-volume ratio of the cell, less than 100 ml of breath sample is needed, i.e. less than the tidal volume collected in one single breath.

Synchronous data acquisition, averaging, and multispectral analysis were performed in real time using custom-written software. A multi-channel gas handling system was developed to allow full control on the generated gas

mixtures. This was used not only to verify the accuracy of the fitting procedure, but also to investigate possible spectral interferences and instrumental response to changes in the concentration of the target species [4].

After these validations, the instrument was used in a clinical study to analyze breath samples from volunteers following a strict protocol designed to stimulate adipose tissue lipolysis either by an energy deficient diet or physical activity

4. Results

The laboratory tests indicate a good linearity behavior of the spectrometer within a concentration range that is expected for human breath samples. Despite the strong spectral interference from water and methane, the system was found to reliably and accurately retrieve low acetone concentrations (< 2 ppm) even in the presence of 6% water and 6 ppm methane. A relative precision of 14 ppb or to an absorption noise level of 2.3×10^{-5} has been achieved after an averaging time of 15 minutes. Considering the 36 m optical path this would be equivalent to an absorbance per unit path length noise of $6.4 \times 10^{-9} \text{ cm}^{-1}$.

A total of 234 bag samples, including duplicates, background, and test-runs were analyzed in the frame of a pilot clinical study during which eight healthy male and female volunteers were tested under different conditions: i) after an overnight fast (negative energy balance), ii) after high carbohydrate and low carbohydrate meal ingestion (positive energy balance at high and low insulin), and iii) during exercise in fasting conditions and after meal ingestion. Breath and blood samples were obtained every hour for the measurement of breath acetone concentration and of blood beta-hydroxybutyrate concentrations. Further details will be shown in the presentation.

The preliminary results suggest that breath acetone monitoring may indeed provide useful information in the monitoring of lifestyle interventions.

4. References

- [1] V. Ruzsanyi, P. M. Kalapos, "Breath acetone as a potential marker in clinical practice," *J. Breath Res.*, **11**(2), 024002, (2017).
- [2] M. Fill, A. Khia, M. Rahim, F. Felder, H. Zogg, "PbSe quantum well mid-infrared vertical external cavity surface emitting laser on Si-substrates," *J. Appl. Phys.* **109**, 093101 (2011).
- [3] D. D. Nelson, J. Shorter, J. B. Mc-Manus, M. S. Zahniser, "Sub-part-per-billion detection of nitric oxide in air using a thermoelectrically cooled mid-infrared quantum cascade laser spectrometer," *Appl. Phys. B* **75**, 343-350 (2002).
- [4] B. Tuzson, J. Jágerská, H. Looser, M. Graf, F. Felder, M. Fill, L. Tappy, and L. Emmenegger "Highly selective volatile organic compounds breath analysis using a broadly-tunable Vertical-External-Cavity Surface-Emitting Laser, *Analytical Chemistry*, 89 (12), 6377-6383, (2017).