

Quantum-cascade-laser-based optoacoustic detection for breath sensor applications

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Abstract— Continuous wave, thermoelectrically cooled, quantum cascade laser based sensor platform for the quantitative detection of exhaled human breath is reported. The sensor is based on a 2f wavelength modulation quartz enhanced photoacoustic spectroscopy (QEPAS) technique, which is very well suited for real time breath analysis, due to the fast gas exchange inside a compact QEPAS gas cell. The quantum cascade laser has been designed to target the interference-free NO absorption line at 1900.075 cm^{-1} . A 1σ minimum detectable concentration of ~ 8 parts per billion in volume with 1 sec time resolution was obtained. Preliminary breath test demonstrated extremely fast response and fast signal decay.

Keywords - Quartz enhanced photoacoustic spectroscopy, wavelength modulation, Breath sensor, trace gas detection

I. INTRODUCTION

To date, researchers have identified over 500 different compounds contained in human breath, some of which are present at parts per billion (ppb) or even parts per trillion (ppt) concentration levels [1]. These molecules have both endogenous and exogenous origins and provide information about physiological processes occurring in the body as well as environment related ingestion or absorption of contaminants [2]. The sources of endogenous molecules are normal and abnormal physiological processes, whereas the sources of exogenous molecules are: inspiratory air, ingested food and beverages, or any exogenous molecule that has entered the body [2]. While the presence and concentration of many of these molecules are poorly understood, many “biomarker” molecules have been correlated to specific diseases and metabolic processes. Such correlations can result in noninvasive methods of health screening for a wide variety of medical conditions.

Therefore, a breath test is becoming increasingly important as a non-invasive procedure for clinical diagnostics [3]. Development of trace gas sensor technologies is a key factor in the advancement of breath analysis. Small, affordable, easy-to-use, sensitive and accurate techniques are needed for detection of breath compounds. Ideally, exhaled molecules can be quantified in real-time using a hand-held device [2].

Several methods of trace molecular detection have been applied to the problem of breath analysis, including optical detection [4,5], mass spectrometry [6,7], and electronic “noses” [8]. Analytical instrumentation involving mass spectrometry with or without prior separation by gas chromatography is the most commonly used method to quantify exhaled molecules. Currently, atmospheric pressure ionization mass spectrometry (API-MS) and selected ion flow tube mass spectrometry (SIFT-MS) are the most frequently used methods for direct breath analysis [2]. In recent years, the development of new mid infrared laser sources has given a new impulse to infrared laser-based trace gas sensors. In particular, single mode quantum cascade lasers (QCLs) have become very attractive for mid-infrared gas sensing techniques thanks to single-frequency operation, narrow linewidth, high powers at mid-IR wavelengths (3 to 24 μm), room temperature and continuous wave (CW) operation [9,10]. They overcome some of the major drawbacks of other traditional mid-IR laser sources, i.e. lack of continuous wavelength tunability and large size and weight of gas lasers (e.g. CO and CO₂), large size and cooling requirement of lead salt diode lasers, complexity and low power of nonlinear optical sources.

New infrared semiconductor laser based trace gas sensor technology offers the feasibility of compact (hand held), reliable, non-aliasing, user friendly, autonomous and low-cost devices without sacrificing high detection ranges from ppmv, to sub-ppbv levels depending on the specific biomarker gas species and the detection method employed [11,12]. Quartz enhanced photoacoustic spectroscopy (QEPAS) is particularly suited for applications where continuous monitoring of targeted exhaled gases with sensitivity, selectivity and fast response are required, such as in critical care and operating room settings, thanks to the fast gas exchange inside the compact QEPAS gas cell, which acts as an absorption detection module. QEPAS does not require consumable products or an operator. Single-molecule exhaled breath QEPAS sensors are already demonstrated. For example, an exhaled ammonia sensor is currently installed at the medical breath research center in Bethlehem, PA and tested as an instrument for non-invasive verification of liver and kidney disorders based on human breath samples [13].

II. QEPAS

A. Technique

QEPAS sensor technology is based on a novel approach to photoacoustic detection which employs a quartz tuning fork (QTF) as a resonant acoustic transducer [14]. A QEPAS sensor detects a weak acoustic wave that is generated when optical radiation interacts with a trace gas. The pressure wave excites a resonant vibration of the QTF which is then converted into an electric signal due to the piezoelectric effect. Subsequently, the electric signal, which is proportional to the concentration of the gas, is measured by a transimpedance amplifier. QEPAS sensors have been used with various laser sources including near-infrared (NIR) and mid-infrared (MIR) semiconductor lasers (both distributed feedback and external cavity), optical parametric oscillators (OPO), and fiber amplifiers, and was applied to the detection of different chemical species including molecules with unresolved vibrational absorption bands. Merits of QEPAS compared to conventional photoacoustic spectroscopy (PAS) include better QEPAS sensor immunity to environmental acoustic noise, a simple spectrophone design. These advantages make the QEPAS technology competitive with and in many cases preferred to other trace gas sensing methods. A commonly used QEPAS-based spectrophone consists of a QTF and a so-called microresonator (mR). The mR is formed by one or two thin tubes, and a QTF is positioned between or beside the tubes to probe the acoustic vibration excited in the gas contained inside the tubes. The use of a mR increases the QEPAS sensitivity 10 times or more and isolates the QTF from accidental acoustic resonances in the

sensor enclosure, which can otherwise distort the QEPAS signal. QEPAS based trace gas sensors are capable of ultra-sensitive trace gas detection and is suitable for real time breath measurements, due to the fast gas exchange inside a compact QEPAS gas cell, which acts as an absorption detection module (ADM). The total volume of a typical QEPAS ADM is $\sim 3.8 \text{ cm}^3$. It can be made even smaller in an alternative cell design, because, the volume of the analyzed gas sample is limited by the dimensions of the QTF and the acoustic microresonator tubes to $\sim 3 \text{ mm}^3$.

B. Sensor architecture

In this work a CW water-cooled EC-QCL (Daylight Solutions model 21052-MHF) operating at $\lambda=5.26 \text{ }\mu\text{m}$ was employed as the spectroscopic light source. The optical power of the source was $\sim 80 \text{ mW}$. Precise and continuous control of the laser wavelength can be performed by using two different methods. The optical frequency can be scanned over $\sim 1 \text{ cm}^{-1}$ by applying a modulated voltage of up to 70 V peak-to-peak at 1 Hz to a piezoelectric translator attached to the diffraction grating element of the EC-QCL. For higher modulation frequency, an internal bias-tee allows external modulation of the QCL current to obtain up to 0.1 cm^{-1} peak to peak optical frequency modulation at up to 2 MHz.

The QEPAS-based gas sensor architecture is depicted in Fig 1. To enhance the QEPAS signal, and hence increase the trace gas detection sensitivity the quartz tuning fork (QTF) used in this work was coupled with an acoustic organ pipe type mR. Metal tubes with a length of 4.0 mm each and inner

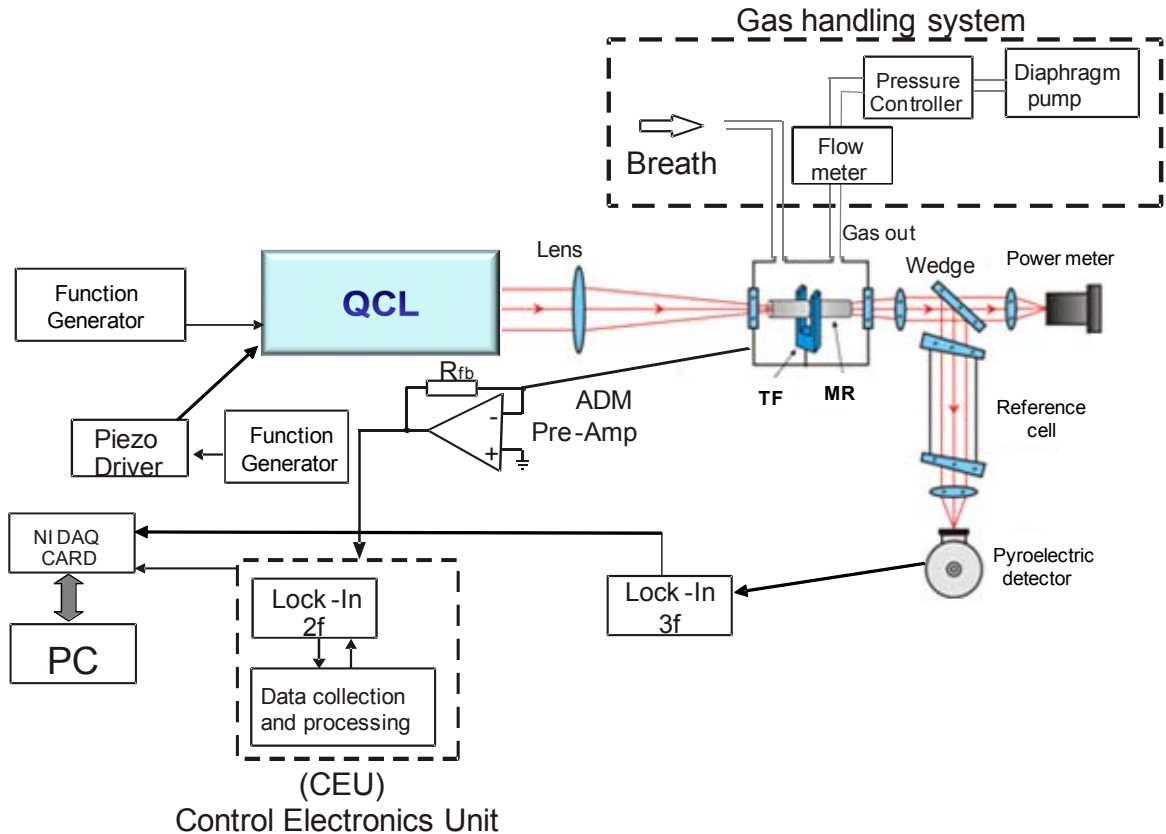


Figure 1. Schematic of EC-QCL-based QEPAS breath sensor. TF—tuning fork; MR—micro-resonator

diameter of 0.84 mm were mounted on both sides of the QTF. The gap between the flange of each tube and the QTF surface was $\sim 30 \mu\text{m}$. The Q factor of the QTF is 6450 at 210 Torr and decreases to 2740 at atmospheric pressure, with resonant frequencies of 32760.4 Hz and 32751.8 Hz, respectively. The QEPAS spectrophone (SPh) consisting of the QTF and the mR is mounted inside a vacuum-tight cell with ZnSe windows. The pressure and flow rate of the sample gas through the SPh are controlled and maintained at the optimum level using a pressure controller (MKS Instruments Type 640) and a flow meter (MKS Instruments Type 179A). The QCL beam is focused by using a 12.5 mm diameter ZnSe lens with a 25 mm focal length and passes through the SPh tubes. The laser beam exiting the SPh passes through an optical gas cell (length 10 cm) filled with a 2% NO in N_2 and subsequently is incident on a pyroelectric detector. Wavelength locking function was performed using the 3 f component of the detector output as the reference in a feedback algorithm.

Wavelength modulation (WM) technique is implemented by applying a sinusoidal dither to the diode laser current at half of the QTF resonance frequency and detecting the QTF response at 2f by means of a lock-in amplifier. The piezoelectric signal generated by the QTF is detected by a custom designed transimpedance amplifier (feedback resistor $R_{fb}=10 \text{ M}\Omega$). Subsequently the signal is demodulated by a lock-in amplifier and digitalized by a NI data acquisition card, which is connected to a personal computer. After a human subject breathes into a mouth piece or certified gas mixture is injected, the collected sample enters the optical sensor. Inside the sensor the gas passes through the SPh, the pressure controller followed by a mass-flow meter and is then released into the atmosphere by means of a compact oil free diaphragm pump. The flow rate through the NO sensor was fixed by a needle valve to 75 ml/min and the pressure value was set and controlled at 210 Torr.

III. RESULTS

According to the HITRAN database the fundamental absorption band of NO is located in the spectral region from 1780 to 1950 cm^{-1} . We perform preliminary studies [15] to choose the best absorption line in terms of intensity and presence of possible interference such as water and CO_2 . We selected the strong and quasi interference-free absorption doublet R(6.5) at 1900.075 cm^{-1} , which is unresolved at our pressure-temperature conditions. Since high concentrations of H_2O vapor are expected in many practical applications, including the analysis of exhaled breath samples and combustion products, we use humidified gas sample to calibrate the sensor. A certified 10 ppmv NO in N_2 mixture was used to obtain known concentrations of the investigated gas in the 0.1 – 10 ppmv range. We use a Nafion material based humidifier (PermaPure) to add water vapour to the gas mixture. The 1 σ minimum detectable concentration of NO for a calibrated mixture of 10ppm NO in humidified N_2 is achieved at $\sim 8 \text{ ppb}$ (see black plot in Fig. 2). However, for the line scanning method, additional noise related to the current frequency tuning process can be introduced into the system.

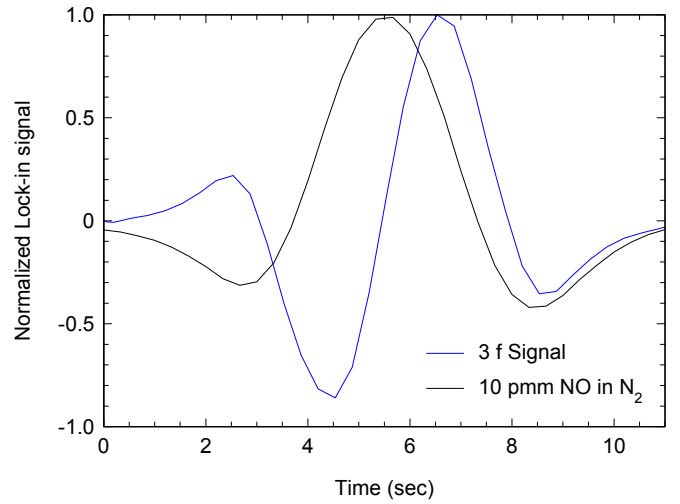


Figure 2. 2f QEPAS signal (black) and reference channel 3f signal (blue) when QCL is tuned across the 1900.075 cm^{-1} line

In addition each scan lasts several seconds, which is too long for breath test applications where a fast system response is required. For a background free sensor system, where no significant baseline drift is observed, a more convenient method is to acquire data only at one selected laser frequency corresponding to the peak of the investigated NO absorption line. Therefore, a line-locking scheme was implemented to always keep the laser frequency at a fixed position. A 3f pyroelectric detector signal with a zero crossing point exactly at the maximum of the 2f WM QEPAS signal was used as a reference for the line-locking technique. A 3f signal was also demonstrated in Fig. 2 as a blue plot. An example of continuous measurements after locking a laser frequency to the NO absorption line is demonstrated in Fig. 3.

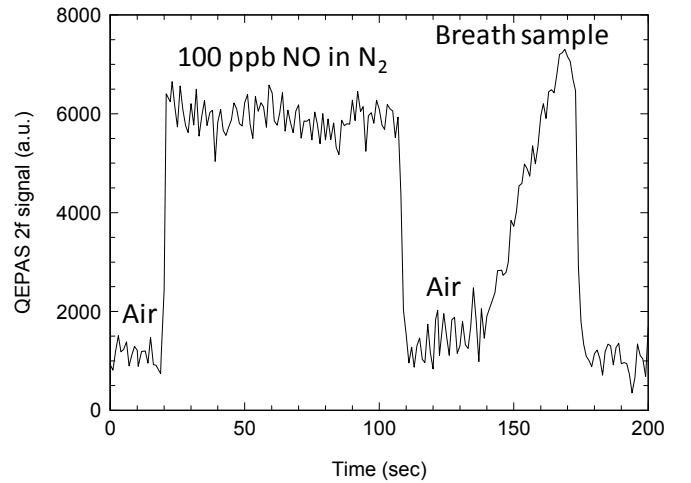


Figure 3. 2f QEPAS signal when laser was locked to the 1900.075 cm^{-1} line.

In this experiment the analyzed gas medium was alternately switched between laboratory air samples a certified 100ppb NO in humidified N_2 as the diluting gas and a breath sample. The data points for all measurements demonstrated in Fig. 3 were acquired with a 1 sec time resolution.

It is clearly visible that no significant delay between airway pressure and breath NO profile is observed, which confirms that the NO sensor has an extremely fast response, as desired. The signal in presence of laboratory air sample rapidly drop to background level, demonstrating the absence of interfering effects from other gas species, such as water vapor, CO₂, CO etc.. In addition, after the breath sampling process is completed, fast signal decay from the system is also observed. Finally, Allan variance analysis indicates long term stability of the NO sensor.

IV. CONCLUSIONS

Monitoring of nitric oxide concentration in exhaled breath using laser spectroscopy techniques provides a fast, noninvasive diagnostic method for human subjects. The achieved minimum detectable concentration of NO (1σ) with an external cavity QCL based QEPAS sensor was 8 ppbv with a 1 sec time resolution. This sensitivity is sufficient for detecting exhaled breath nitric oxide concentrations, which are estimated to be between 0 and 100 ppb in healthy humans. The QEPAS sensor technology has been demonstrated to be a robust technology for the development of sensitive, compact sensor systems that might be used in a doctor's office for non-invasive verification of a human subject's medical condition.

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