Quantum Cascade Laser-Based Sensor Platform for Ammonia Detection in Exhaled Human Breath

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Abstract: An ammonia sensor for clinical breath analysis based on a CW mid-infrared quantum cascade laser and quartz-enhanced photoacoustic spectroscopy with a detection sensitivity of 20 ppbv (1σ) with a 0.3 s time resolution is reported.

OCIS codes: (280.3420) Laser sensors; (300.6340) Spectroscopy, infrared; (140.5960) Semiconductor lasers; (170.4580) Optical diagnostics for medicine

Monitoring of trace amounts of ammonia (NH_3) at levels of parts in 10^9 by volume (ppbv) is important for applications in medicine and the life sciences. Breath analysis is a well established, non-invasive tool for the clinical diagnosis and therapeutic monitoring of a number of health pathologies. Exhaled human breath contains as many as 400 molecules, some of which are potential biomarkers for a variety of human illnesses and diseases. Abnormal levels of these biomarkers in breath signal adverse medical conditions.

The detection of ammonia in exhaled breath is of particular interest as it has been linked to renal and liver diseases [1-3], peptic ulcers, and helicobacter pylori infection [4]. Typically, ammonia is present at levels of a few hundreds ppbv in alveolar breath of healthy humans. Elevated ammonia levels (≥1 ppmv) in breath are an indication of a cellular dysfunction. Hence, the target detection sensitivity of an ammonia breath gas analyzer is at the ppbv level. Moreover, for breath tests it is essential to develop an ammonia sensor with a fast response time of ≤ 1 second in order to allow the monitoring of the exhaled breath waveform. Laser-based spectroscopy in the mid-infrared spectral region is an effective analytical approach for real time breath analysis and the quantification of breath metabolites (see [5] and Refs. within).

In this work we report on the development of a breath ammonia analyzer based on quartz-enhanced photoacoustic spectroscopy (QEPAS). QEPAS [6,7] is a technique that allows quantification of trace species in small gas samples (down to ~1 mm^3). This capability can be particularly useful in real time breath measurements as the small volume (~5 mm typical dimensions) permits fast gas exchange inside the QEPAS gas cell.

Ammonia has strong fundamental absorption lines in the mid-IR spectral region centered at 1000 cm^{-1} (10 µm), which are ~200 times more intense than those in the near-infrared region. In this work an epi-side down thermoelectrically cooled (TEC) mid-IR CW distributed feedback (DFB) quantum cascade laser (Maxion Technologies, Inc., model # DQ9-M532P) was used. The laser is installed in a housing equipped with a thermoelectric Peltier cooler capable of precise temperature control and provides a maximum power of ~30 mW at 5°C. The laser power, voltage-current (V-I) and spectral characteristics are presented in Fig. 1. The optical frequency tuning range with the injection current is ~4.5 cm^{-1}. Several ammonia absorption lines centered at 1046.4 cm^{-1} can be accessed by this quantum cascade laser (QCL). These lines have no interference with water vapor, which is abundant in exhaled human breath (~5%). However the QCL tuning range covers several CO_2 lines, which can be used for internal calibration during the breath cycle. HITRAN-based simulated absorption spectra of NH_3 and CO_2 at relevant concentrations are depicted in Fig. 2.

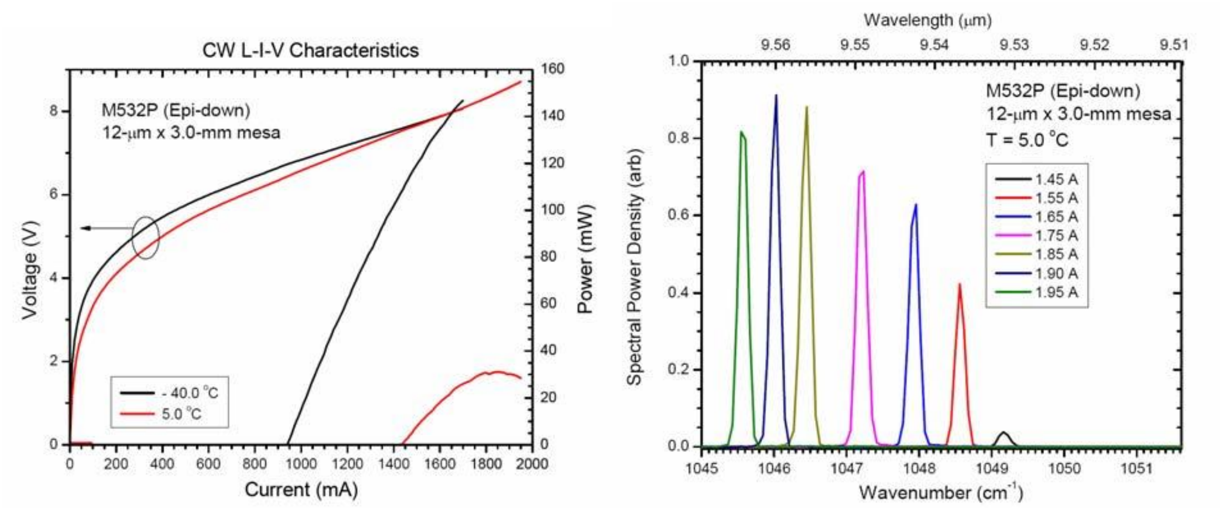

Fig. 1. Power, V-I and spectral characteristics of the CW DFB QCL (Maxion Technologies, Inc., Model # DQ9-M532P)

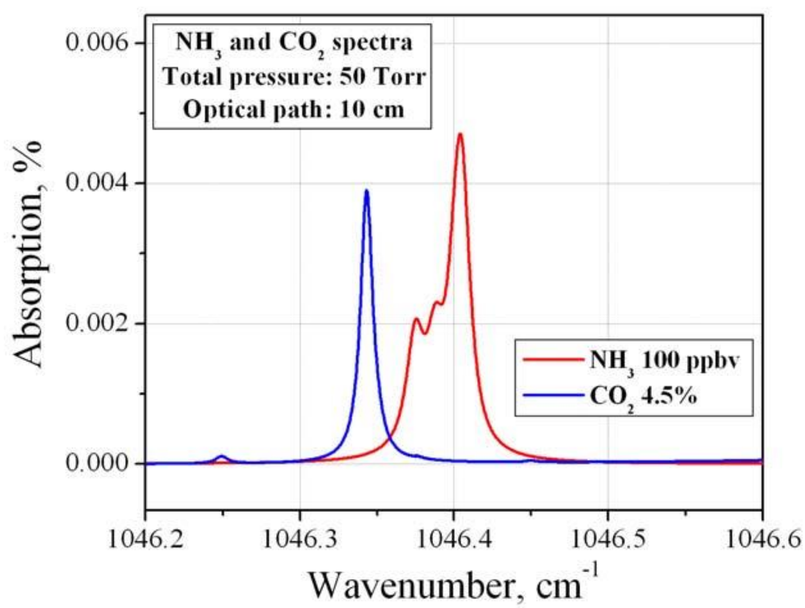

Fig. 2. HITRAN-based simulation of absorption spectra for NH_3 (100 ppbv) and CO_2 (4.5%) within the QCL tuning range. N_2 is used as the diluting gas.

A schematic of the apparatus used in this study is shown in Fig. 3. Briefly, light from the QCL is directed into a QEPAS cell. The laser output is tunable from 1045.0 cm^{-1} to 1049.5 cm^{-1} by varying the injection current. A reference cell with a 100 ppmv NH_3 in UHP N_2 is used to lock the laser radiation frequency to the target ammonia absorption line. A gas standard generator (Kin-Tek, Model # 491M) based on a permeation tube technology provides calibration mixture with NH_3 concentrations ranging from 10 to 5000 ppbv in a diluting gas (such as N_2 or air).

The current ammonia sensor performance and attainable sensitivity are presented in Fig. 4. The lock-in amplifier time constant is set to 0.1 s, which corresponds to a data acquisition time for a single point measurement of ~ 0.3 s (filter slope is 12 dB/oct). In this case a minimum detection limit of 20 ppbv (1σ) is routinely achieved. The actual time resolution of the gas sensor is presently limited by the ammonia adsorption to the walls of the gas system. This issue will be addressed by elevating the sensor temperature above 40°C.

A systematic study of the performance and merits of a QEPAS and QCL-based sensor configured for exhaled ammonia concentration measurements as well as real time breath measurements will be reported.

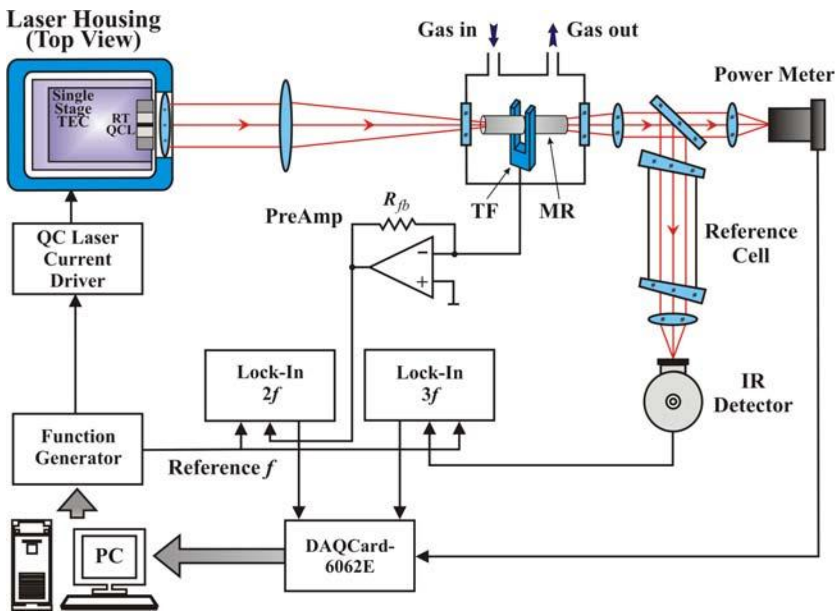

Fig. 3. QEPAS-based ammonia sensor architecture.

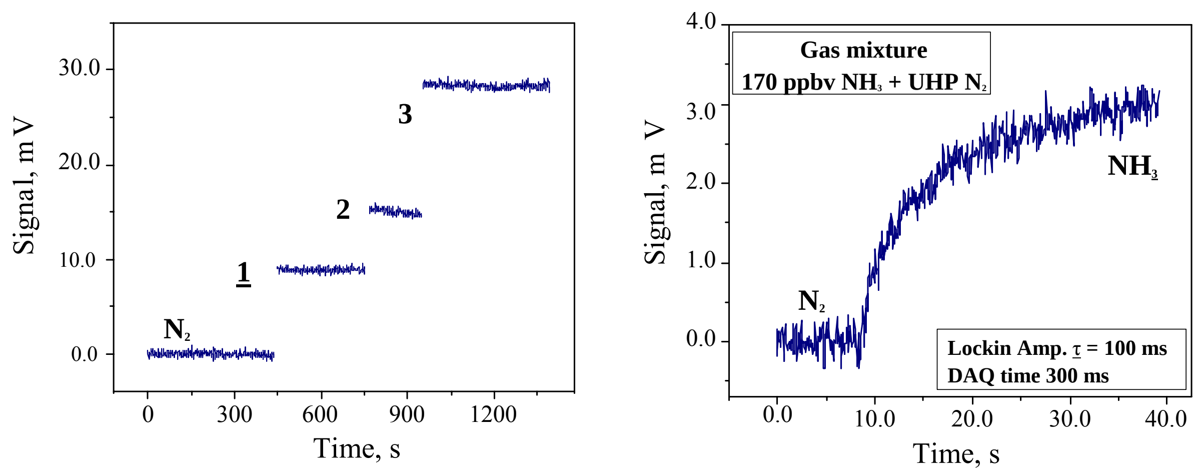

Fig. 4. Sensor performance. Left plot: step concentration measurements were made using a gas standard generator (**1** – 300 ppbv, **2** – 500 ppbv, **3** – 1000 ppbv). Right plot: temporal sensor response to the concentration change.

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