Real time ammonia detection in exhaled human breath using a distributed feedback quantum cascade laser based sensor

Rafal Lewicki*1, Anatoliy A. Kosterev1, David M. Thomazy1, Terence H. Risby2, Steven Solga3, Timothy B. Schwartz3, and Frank K. Tittel1
1Department of Electrical and Computer Engineering, Rice University, Houston, Texas 77005
2Bloomberg School of Public Health, The Johns Hopkins University, Baltimore, MD 21205
3St. Luke’s Hospital, Bethlehem, PA 18015

ABSTRACT

A continuous wave, thermoelectrically cooled, distributed feedback quantum cascade laser (DFB-QCL) based sensor platform for the quantitative detection of ammonia (NH₃) concentrations present in exhaled human breath is reported. The NH₃ concentration measurements are performed with 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. An air-cooled DFB-QCL was designed to target the interference-free NH₃ absorption line located at 967.35 cm⁻¹ (λ=10.34 μm). The laser is operated at 17.5 °C, emitting ~ 24 mW of optical power at the selected wavelength. A 1σ minimum detectable concentration of ammonia for the line-locked NH₃ sensor is ~ 6 ppb with 1 sec time resolution. The NH₃ sensor, packaged in a 12"x14"x10" housing, is currently installed at a 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.

Keywords: Quartz enhanced photoacoustic spectroscopy, wavelength modulation, distributed feedback quantum cascade laser, trace gas ammonia detection.

1. INTRODUCTION

Exhaled breath is a mixture of more than a thousand molecules, some of which are present at parts per billion (ppb) or even parts per trillion (ppt) concentration levels [1]. These molecules provide a unique breath profile of the health condition and have endogenous and exogenous origins. 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 by other routes (e.g. dermal absorption) [2]. The concentrations of some of the exhaled molecules can be used as biomarkers for the identification and monitoring of human diseases or wellness states [3]. Therefore, a breath test is becoming increasingly important as a non-invasive procedure for clinical diagnostics [4]. The potential of the breath in medicine was first recognized in ancient times by Hippocrates, considered to be the father of medicine, who suggested that a specific breath odor might reflect a certain disease. The earliest recorded studies of the human breath, related to the role of oxygen in combustion and respiration, were performed more than 200 years ago by Lavoisier and Laplace [4-5].

Currently, the standard analytical chemistry instrumentation for the exhaled human breath analysis is based on gas chromatography and its various detection methods such as flame ionization detection [6-7], mass spectrometry [8], ion mobility spectrometry [9], or selected ion flow tube mass spectrometry [10]. In recent years, several laser based breath analyzers, capable of sensitive and real time detection of molecular species in breath samples, were demonstrated with different laser spectroscopic techniques [11-13]. Promising results from previous studies have confirmed that optical sensors have a considerable potential for monitoring of exhaled breath [14]. In this paper, a novel quantum cascade laser based optical breath sensor for ammonia detection will be described. By monitoring ammonia

* Rafal.Lewicki@rice.edu; phone 1 713 348-2614; fax 1 713 348-5686; www.ece.rice.edu/lasersci/
4. REAL TIME HUMAN BREATH DATA

An NH₃ sensor system for the real time monitoring of ammonia concentration levels in exhaled breath was designed to collect breath samples multiple times with ~3 min intervals between each sample. These intervals are needed to remove the remaining ammonia out of the system. An example of the breath ammonia profile was demonstrated in Fig. 7a, where the authentic ammonia concentration level, representing both a normal and an abnormal physiological body processes, is at ~450 ppb (at the plateau point). The first part of the breath profile shown in Fig 7a, associated with highest detected NH₃ concentration of ~650 ppb, reflects the ammonia concentration in the oral cavity. This concentration is mostly related to oral bacterial processes of ingested food and beverages (cite). For each NH₃ breath measurement, the NH₃ profile is displayed in the real time on the laptop and on the Loccioni breath analyzer screen and then saved and stored on a laptop and the Loccioni memory stick for later data processing.

![NH₃ breath sample](image)

Fig. 7a) An example of the breath ammonia profile, taken at the Bethlehem, PA clinical testing site; b) CO₂ concentration [%], airway pressure [mbar] and NH₃ concentration [ppb] profiles of the same single breath exhalation.

Single breath exhalation profiles for CO₂ concentration [%], airway pressure [mbar] and NH₃ concentration [ppb] are depicted in Fig. 7b. It is clearly visible that no significant delay between airway pressure and breath ammonia profile is observed, which confirms that the NH₃ sensor has an extremely fast response, as desired. In addition, after the breath sampling process is completed, fast ammonia decay from the system is also observed.

5. SUMMARY

Monitoring of ammonia concentration in exhaled breath using laser spectroscopy techniques provides a fast, non-invasive diagnostic method for human subjects with liver and kidney disorders. The achieved minimum detectable concentration of NH₃ (1σ) with DFB-QCL based QEPAS sensor was 6 ppbv with a 1 sec time resolution. This sensitivity is sufficient for detecting exhaled breath ammonia concentrations, which are estimated to be between 0 and 1 ppm in healthy humans. The fast sensor response time was obtained by shortening the length of the breath sampler tube and by keeping the metal components of the sensor at 38°C to minimize ammonia adsorption effects. By using a commercial breath sampler (Loccioni, Italy) with a built-in capnograph device, the CO₂ concentration measurements are performed independently. In addition, the breath sampler helps to standardize the breath collection process by monitoring and maintaining the pressure of exhaled breath within a certain acceptable range. Laser spectroscopy with a mid-infrared, room temperature, continuous wave, high performance DFB QCL is a promising analytical approach for real time breath analysis and the quantification of breath metabolites. Moreover the QEPAS sensor technology is 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.
References

MBE growth and characterization of dilute nitrides for mid-infrared optoelectronic devices

M. de la Mare¹, A. Krier¹*, Q. Zhuang¹ & P.J. Carrington

¹Physics Department, Lancaster University, Lancaster, LA1 4YB, UK

A. Patane²

²School of Physics and Astronomy, University of Nottingham, Nottingham NG7 2RD, UK

ABSTRACT

We report the molecular beam epitaxial growth of narrow gap dilute nitride InAsN alloys onto GaAs substrates using a nitrogen plasma source. The photoluminescence (PL) of InAsN alloys with N-content in the range 0 to 1% which exhibit emission in the mid-infrared spectral range is described. The sample containing 1% N reveals evidence of recombination from extended and localized states within the degenerate conduction band of InAsN. A comparison of GaAs and InAs based material shows little change in PL linewidth such that the change in substrate does not cause significant reduction in quality of the epilayers. The band gap dependence on N content in our material is consistent with predictions from the band anti-crossing model. We also report the growth of InAsSbN/InAs multi-quantum wells which exhibit bright PL up to a temperature of 250 K without any post growth annealing. Consideration of the power dependent PL behaviour is consistent with Type I band alignment arising from strong lowering of the conduction band edge due to N-induced band anti-crossing effects.

Keywords: Molecular beam epitaxy, Dilute nitrides, Photoluminescence, Mid-Infrared, Quantum Wells

INTRODUCTION

Dilute nitride alloys containing a small amount of nitrogen are of particular interest due to the large band gap reduction¹,², giving rise to interesting physical phenomena³ and holding great potential for the development of innovative device applications⁴,⁵. The addition of small amounts of nitrogen (<1%) into narrow band gap materials such as GaAs and InAs is attracting increased attention because it can facilitate emission in the technologically important mid-infrared (2-5 µm) spectral range⁶. The incorporation of N can increase the electron effective mass and equalise the density of states, thus reducing Auger recombination and inter-valence band absorption processes⁷ which currently limit the quantum efficiency of mid infrared light sources. Previously many investigations have been directed towards the (In)GaAsN/GaAs material system with low nitrogen content for its ability to operate between 1.1-1.5 µm as required for optical fibre communications⁸,⁹. The unique band gap behaviour of this system opens many new possibilities for device applications especially the 1.3µm VCSEL¹⁰-¹² which is a low cost light source required for optical area networks⁸. So far the best performance of InGaAsN based edge emitting lasers was achieved using molecular beam epitaxy with a radio frequency plasma cell as the nitrogen source. These materials showed significantly improved performance with comparable efficiencies to that of InGaAsP laser diodes with a high characteristic temperature of around 215 K¹³,¹⁴. Materials operating at 2.38 µm have been demonstrated using InAsN/GaAs quantum wells however, mid-infrared lasers utilizing dilute nitrides operating > 3µm have not yet been realised due to the difficulty in growing device quality epitaxial material. Recently photoluminescence (PL) emission from bulk InAsN has been reported¹⁵ and associated with strong carrier localisation effects arising from disorder¹⁶. More recently, following further optimisation of the growth parameters, InAsN with bright PL has been obtained for nitrogen contents up to 2.5% and with emission up to 4.5 µm¹⁷,¹⁸.

* a.krier@lancaster.ac.uk