Development of Quantum-Cascade Laser Based Biosensor Technology

by Thomas Harman

ABSTRACT—Researchers are developing new types of sensitive, selective, real-time gas sensors based on continuous wave and pulsed quantum cascade lasers for various chemical sensing applications, such as medical diagnostics, environmental monitoring, and industrial process control. Tunable laser absorption spectroscopy in the mid-infrared spectral region is a sensitive analytical technique for trace gas quantification. During the past year a nitric oxide (*NO*) gas sensor was developed based on a novel thermoelectrically cooled, continuous wave, distributed feedback quantum cascade lasers operating at 5.45 mm (1835 cm^{-1}) and 5.22 mm (1916 cm^{-1}), and off-axis integrated cavity output spectroscopy (OA-ICOS) combined with a wavelength modulation technique. Its purpose is to determine *NO* concentrations at the sub-ppbv levels that are essential for such applications. The sensor employs a 50 cm long high-finesse optical cavity that provides an effective pathlength of ~ 700 m. Research efforts achieved a noise equivalent (SNR = 1) minimum detection limit of 0.4 ppbv with a 1 second observation time.

THE DEVELOPMENT OF COMPACT OPTICAL SENSORS FOR NITRIC oxide detection is of interest for a number of applications, such as environmental monitoring,[1] atmospheric chemistry,[2] industrial process control,[3] combustion studies,[4] and medical diagnostics.[5,6] *NO* is involved in many vital physiological processes in the human body. For example, an elevated level of NO in exhaled breath is correlated with airway inflammation in asthmatic patients. Knowledge of *NO* concentrations in the exhaled breath of these patients may allow health care providers to adjust therapeutic drug dosages.[7,8] For medical diagnostics purposes, it is essential to time-resolve the *NO* concentration as a function of a breath cycle phase, because the corresponding air samples originate in the different parts of the respiratory tract. This application requires a sensor response time of £1 second and a *NO* minimum detection sensitivity of < 1 ppbv. Such high sensitivity, rapid response measurements are possible with laser absorption spectroscopy in the fundamental absorption band of *NO*.

Distributed feedback quantum cascade lasers (DFB QCLs) operating in a pulsed or continuous wave (CW) mode are promising spectroscopic sources because of their narrow linewidths, single mode operation, tunability, output power, reliability, and compactness. Until recently, CW operation of QCLs was possible only at cryogenic temperatures, and room temperature (RT) operation was realized only with pulsed operation at a low duty cycle, but recent developments in QCL technology now permit CW operation at room temperature or temperatures which can be obtained by thermoelectric cooling.[9,10]

Goals of the project

In this research, we utilize a novel and now commercially available TEC, CW, DFB quantum cascade laser fabricated by our collaborating team from the University of Neuchatel, Switzerland.[9] The DFB CW QCL characteristics, such as a narrow laser spectral width (£3 MHz,[11] necessary for efficient laser to cavity coupling and high average power, make CW TEC QC lasers more suitable than pulsed QCLs for ICOS-based sensor platforms for real world applications. These systems avoid the size and complications of liquid nitrogen cooling required by earlier QC lasers. The basic sensor platform is an OA-ICOS configuration with a 50 cm long optical cavity. A wavelength modulation technique (harmonic detection) was implemented in order to reach sub-ppbv levels of NO detection sensitivity.

Results

Exhaled nitric oxide (*NO*) is an important biomarker in asthma and other respiratory disorders. We studied the optical performance of a *NO*/CO_2 QCL-based sensor employing integrated cavity output spectroscopy capable of real-time *NO* and CO_2 measurements in a single breath cycle. Furthermore, the off axis ICOS sensor performance was compared to a chemiluminescent *NO* analyzer and a non-dispersive infrared (NDIR) CO_2 absorption capnograph. Differences between the gas analyzers were assessed by the Bland-Altman method to estimate the expected variability between the gas sensors. The OA-ICOS sensor measurements were in good agreement with the data acquired with the two commercial gas analyzers. The sensor had a noise-equivalent sensitivity (1Û) for *NO* of 0.4 ppbv with a 1-s averaging time. Potential improvements to the ICOS sensor include incorporating higher reflectivity mirrors and utilizing the stronger *NO* absorption line at 1900 cm^{-1}. This work demonstrates the performance characteristics and merits of mid-infrared spectroscopy for exhaled breath analysis.

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SYSTEMS—M.S. student Anjana Garud, with her B.S. degree from Manipal Academy, India, studies systems engineering at UHCL.

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