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Portable Photoacoustic Methane Sensor for Medical Research

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Abstract

Breath analysis can be a useful diagnostic tool, allowing noninvasive, real-time and cost-effective monitoring. A near infrared diode laser based photoacoustic sensor was developed for the measurement of methane concentration in breath. The sensor measures gas samples directly, and different gas handling equipments were prepared for optimal detection of methane emanating from rodents, human breath and respiratory gas mixture. Minimum detectable concentration was 0.25 ppm (3σ) with an integration time of 12 s. Due to its compact design the instrument is portable and robust. A uniquely developed electronic device provides overall system control and measurement automatization. The instrument is installed at a medical research laboratory at University of Szeged.

Key words: breath analysis, diode laser, photoacoustic, methane, medical research

Introduction

Expired human breath contains information on substances in blood because only a slender barrier separates the air in the alveoli of the lung from the blood in capillaries. Numerous studies describing correlations between diseases and the amount of different trace gases in breath have been published [1]. Consequently, there is an increasing interest in developing novel, noninvasive, reliable, low-cost sensors for diagnostics [2].

The aim of the presented work was to construct a methane sensor that can be easily used by non-experts at common clinical practice.
Numerous photoacoustic (PA) spectroscopy based sensors have proved their relevance in life science applications allowing in vivo, noninvasive, real-time measurement of physiologically relevant gases [3]. PA spectroscopy is a subclass of optical absorption spectroscopy and it is based on the phenomenon that absorption of periodically modulated optical radiation followed by non-radiative relaxation gives rise to periodic temperature changes which cause periodic pressure changes (i. e. a sound wave). The amplitude of the generated sound is directly proportional to the concentration of the absorbing gas component.

Experimental

The light source of present system was a fiber-coupled distributed-feedback diode laser (with 15 mW output power from NTT Electronics) emitting around a methane absorption line near 1650 nm [4]. The laser beam was directed through a dual-pass PA cell which contained a cylindrical resonator (length was 3 cm and diameter was 0.43 cm), both were made of stainless steel.

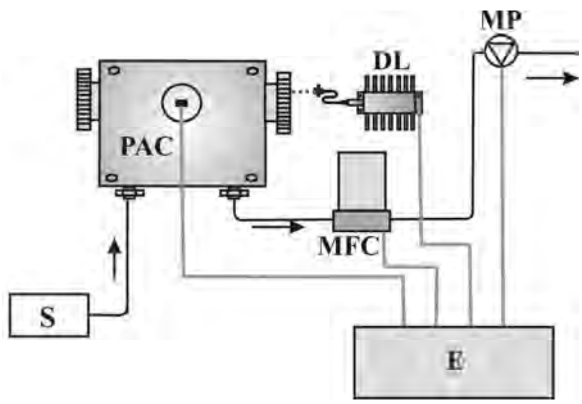

Fig. 1. Schematic view of the instrument. Gas samples (S) are drawn by a membrane pump (MP) into the photoacoustic cell (PAC) where the signal is generated by a diode laser (DL). Gas flow rate can be adjusted with a mass-flow controller (MFC). The electronic unit (E) provides system control and data processing. Arrows indicate direction of the gas flow.

The first longitudinal mode of the resonator was excited by adjusting the modulation frequency of the laser to 5200 Hz. An electret microphone (Knowles, EK-3028) was attached at half length of the resonator because pressure antinode of the first longitudinal mode (PA signal maximum) existed there. The PA cell was temperature-stabilized at 40 °C to deflect inaccuracies deriving from the temperature dependence of the PA signal. Furthermore, high temperature of the cell avoids condensation of water vapor originating from breath. Gas from the sampling chamber is drawn through the PA cell by a membrane pump and the gas flow rate can be controlled by a mass-flow controller. Additionally, an electronic device (Videoton Holding Plc.) provided overall system control and measurement automatization [5]. It consisted of a laser driver and temperature controller, a microphone amplifier, a data processing unit, and several input and output ports. It can be connected to a computer through several communication channels (RS232/RS485, Modbus, or 4-20 mA). The complete PA measuring system was built into a portable, 19″4U instrument box.

The system was calibrated by preparing various gas mixtures (see Fig. 2.). Minimum detectable concentration (3σ) was found to be 0.25 ppm with an integration time of 12 seconds.

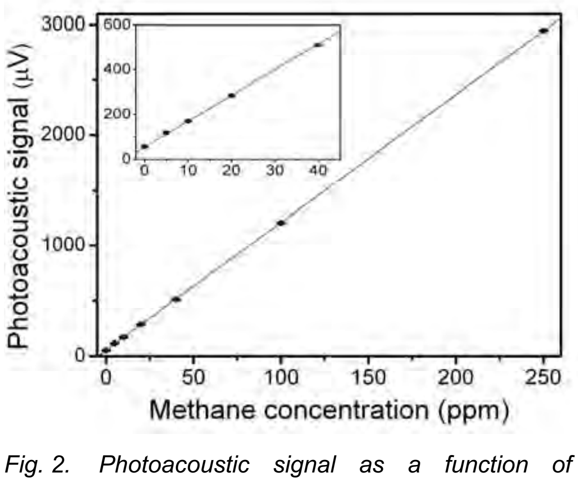

Fig. 2. Photoacoustic signal as a function of methane concentration. Solid line indicates linear regression of data. For clarity the inset shows low methane concentrations.

Cross sensitivity for common components of breath and ambient air were examined, and no measurable instrument response was found for several vol % of carbon dioxide or water vapor. Since the absorbance of CH_4 is several orders of magnitude greater than that of H_2O or CO_2 at 1.65 µm. Absorption spectra of those compounds based on HITRAN data [6] are shown in Fig. 3.

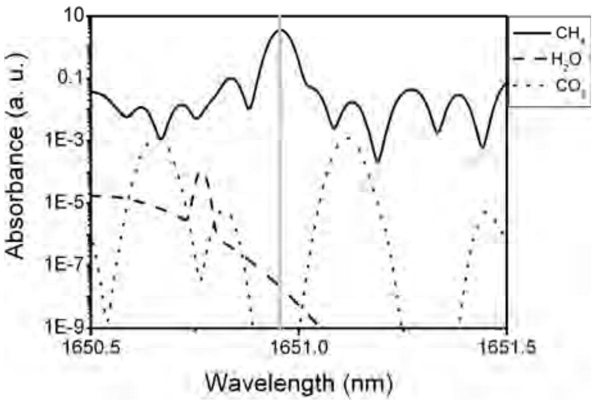

Fig. 3. Absorption spectra of common components of breath based on HITRAN data [6]. CH_4, H_2O and CO_2 are indicated by solid, dashed and dotted lines, respectively. Vertical grey line shows the emission wavelength of the diode laser. Note that the vertical scale is logarithmic.

Gas handling equipments were made of inert materials (including PTFE, glass) to decrease inaccuracies associated with adsorption/desorption processes.

Medical Research – In Vivo Measurements

PA spectroscopy is an excellent method to measure minor concentration changes superimposed on a high background level. Methane production of living organisms may play a role in certain physiologic processes and also may serve as an indicator of different pathologies. In order to investigate this concept measurement of methane emanated from mice and rats, as well as human breath is required.

Methane emissions of a control mouse and a mouse treated with antibiotics are presented in Fig. 4.a,b. Mice were placed into the glass container (volume: 180 cm^3) and the enclosure was not completely gastight in order to replenish sampled gas volume with ambient air. 10 minutes were left for the accumulation of the emitted methane in the container. Gas from the container was subsequently drawn into the PA chamber via a tube made of stainless steel. Measurement periods took 10 minutes. Prior to placing the animals into the container the methane concentration of the air was determined and, as baseline, was used for the calculation of methane emission of the animals. Elimination of intestinal bacteria led to a considerable decrease in methane emission, however, it remained measurable. The results of a set of measurement agreed with theoretical predictions, therefore, several novel studies (with animals and humans) based on the instrument have been started.
For instance, methane biogenesis during sodium azide-induced chemical hypoxia was found in rats with this methane sensor [7].

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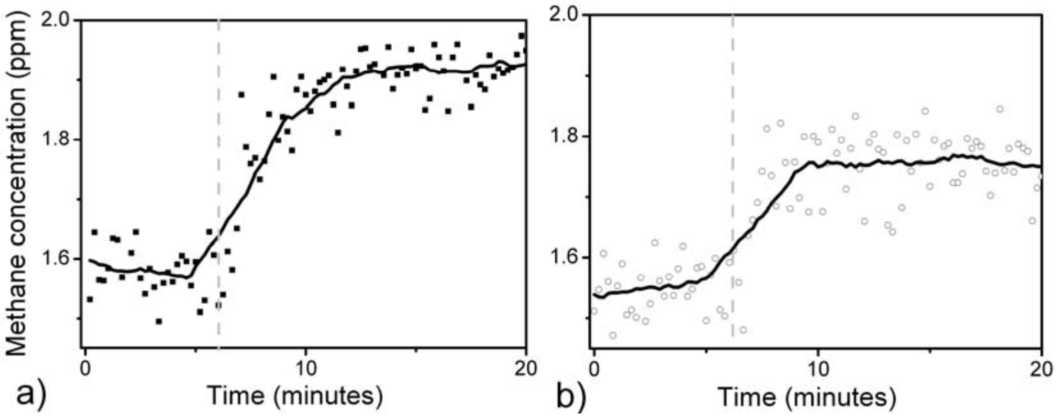

Fig. 4.a,b Methane measurements of two mice (a) a control mouse, (b) a mouse treated with antibiotic. First, methane concentration of room air was measured, vertical dashed lines indicate time when gas flow from the sampling chamber started. Solid grey lines show moving average over 20 points.

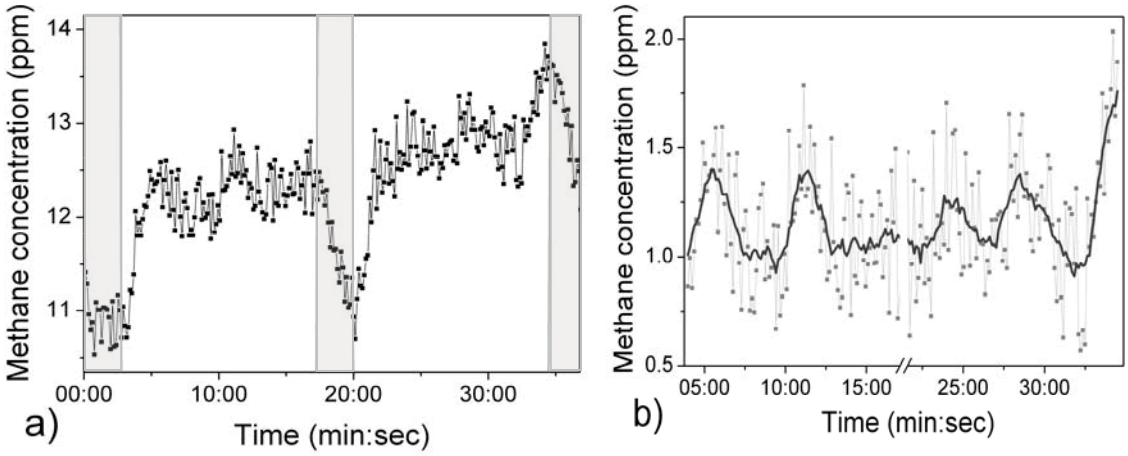

Fig. 5.a,b Methane concentration alterations of expired air during operation. (a) Methane concentration of the expired air; methane originating from the patient is superimposed on the relatively high methane content of the respiratory gas (inhaled air). Grey columns indicate time intervals of background measurements. (b) Methane emanated from the patient, measured data is corrected with background signal. Solid black line shows moving average over 10 points.

Next aim of the development was measuring continuously methane concentration of human breath. Methane concentration alterations of a patient's expired air were determined during an operation. Pressure fluctuations originating from the respirator affects the PA signal as PA signal is proportional to the amount of molecules, which is proportional to the pressure of the gas. Consequently, pressure compensation was essential. It was provided by a membrane pump (with membrane made from PTFE) and by an acoustic filter.

Composition of inhaled air (respiratory gas) had to be taken into consideration because its oxygen concentration was occasionally adjusted and it was found that pure oxygen could contain methane contamination. Nevertheless, variation of the PA signal could originate from the alteration of resonance frequency (because of the speed of sound in the acoustic resonator) in the gas mixture. However, this effect was found to be negligible due to the low difference between the speed of sound in nitrogen and oxygen.

Therefore, background level had to be determined periodically. Consequently, two gas sampling lines were implemented. One measured the inhaled and the other the exhaled air. A three-way magnetic valve switched between them. During the background measurement methane content of the inhaled air (respiratory gas) was determined (Fig. 5. a). The difference between the methane concentration of the exhaled air and the inhaled air (Fig. 5. b) is the methane emission of the patient that can provide valuable information for medical research.

Conclusion

The instrument can be utilized for various sets of measurements by implementing gas sampling units designed for the volume of the available gas samples and safety instructions. The use of diode laser as a light source ensures long lifetime of the sensor and high selectivity, i. e. there is no cross sensitivity to water vapor and carbon-dioxide. The instrument is portable due to its compact design, and requires maintenance yearly.

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