

LASER IN BIOPHOTONICS

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LASER PHOTOACOUSTIC SPECTROSCOPY METHOD
FOR MEASUREMENTS OF TRACE GAS CONCENTRATION
FROM HUMAN BREATH

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Abstract. Laser Photoacoustic Spectroscopy (LPAS), a very powerful technique for measuring trace gas concentration at sub ppb level, can be used to detect compounds from the normal human breath. LPAS setup used consists of a home-built CO₂ laser, a photoacoustic cell, a vacuum/gas handling system, and a detection unit. We present the transfer modality of ethylene collected in aluminized bags to the PA cell by using a fast transfer and a gas flow controller. We monitored the evolution in time of the concentration level for ethylene detected from a healthy human. To reduce the amount of CO₂ which is ~ 5 % of the breath, a KOH scrubber needs to be implemented. We have investigated the presence of the KOH scrubber using two recipients with different volumes, where its presence is compulsive and a bigger volume has to be considered.

Key words: laser photoacoustic spectroscopy, CO₂ laser, gas concentration detection.

1. INTRODUCTION

There have been isolated more than 400 volatile organic compounds in normal human breath which are present in very low concentrations (in part-per-million: ppm (1 ppm = 10⁻⁶ atm) or part-per-billion: ppb (1 ppb = 10⁻⁹ atm)). Their presences could be linked to kidney or liver malfunction, asthma, diabetes, cancer, ulcers and other disorders. Laser Photoacoustic Spectroscopy method (LPAS) is a very powerful investigation technique which is capable of measuring trace gas concentration at sub ppb level [1].

Measurement of human biomarkers in exhaled breath using LPAS method technique capable of measuring trace gas concentration at sub ppb level, promise to revolutionize the manner in which diagnostics are carried out today and may soon lead to rapid diagnostics, improved results, decreased cost, and expanded life span. For example, the detection of ammonia level from human breath can serve for determining the time necessary for optimal degree of dialysis for a patient with end-stage renal disease at every session.

LPAS method can also be used for detection of a wide variety of industrial gases, including benzene, hydrogen cyanide, acetylene, carbon monoxide and carbon dioxide, and poisonous gases (hydrogen cyanide), explosives (TNT, PETN) or harmful drugs (heroin, morphine, narcotine). Many agriculturally interesting gases (ethylene, methane, water vapor concentration, carbon dioxide, ammonia, ozone) can be measured in situ and in real time with CO₂ and CO laser based photoacoustic spectrometers [2-4].

LPAS experimental setup used in the present work consists of a home-built CO₂ laser, a photoacoustic (PA) cell, a vacuum/gas handling system, and a detection unit. We present the transfer modality of ethylene as a gas sample which is collected in aluminized bags to the PA cell using two approaches, by a direct and fast transfer and by gas flow controller. We monitorized the evolution in time of the concentration level for ethylene at a known concentration and the level of ethylene detected from a healthy human.

Due to the fact that carbon dioxide makes up ~ 5 % of the breath and the CO₂ laser lines are slightly absorbed by this gas, it is necessary to introduce the KOH scrubber to remove most of the carbon dioxide from the exhaled air. We have investigated the presence of the KOH scrubber using two recipients with different volumes, and found out that its presence is compulsive and a bigger volume has to be used in order to reduce the amount of the certain gases which interfere with the trace gas to be measured.

1.1 LASER PHOTOACOUSTIC SPECTROSCOPY (LPAS) SETUP

The experimental system of the photoacoustic detection system is presented in Fig. 1 [5, 6]. As a radiation source is used a home-built, line-tunable and frequency-stabilized CO₂ laser, its emission spectrum overlaps with the absorption fingerprint of ethylene and ammonia. The laser emits continuous wave radiation with an output power of 2-7 W and is tunable between 9.2 and 10.8 μm on 57 different vibrational-rotational lines. The CO₂ laser is especially useful for detecting ethylene and ammonia, because, in the first case, one of its laser lines, 10P(14) transition near 10.53 μm, overlaps with the ethylene's strongest spectral features and, in the second case, 9R(30) transition near 9.22 μm, is nearly coincident with the strong sR(5,K) multiplet of ammonia.

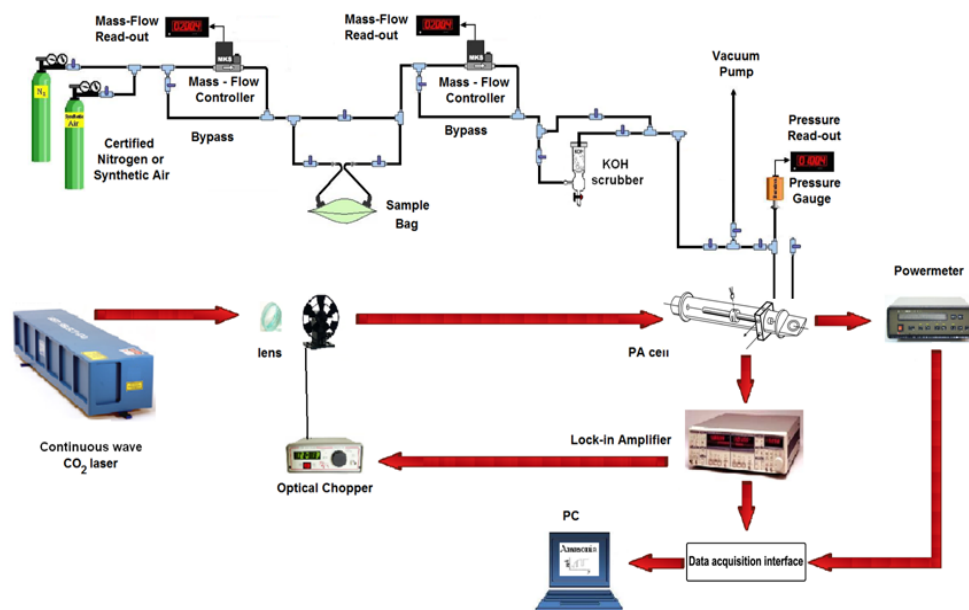


Fig. 1 – General scheme of the photoacoustic detection system with a CO₂ laser.

The laser beam is amplitude modulated by an optical chopper, focused by a ZnSe lens and introduced in the PA cell. The laser power used to excite the sample gas inside the PA cell is measured by a two channel powermeter.

The acoustic waves produced in the PA cell are detected with four miniature microphones connected in series. The PA signal, proportional to the trace gas concentration is applied to a lock-in amplifier which detects and measures very small single frequency AC signals. The output signals of the lock-in amplifier and of the powermeter are then converted into digital signals by a 12-bit high speed A/D board and processed by a computer. A software program for graphic and instrumentation permits to obtain and process the experimental results. The absolute trace gas concentrations are processed by the computer and the results are displayed on the screen.

The gas handling system is an important part of the experimental set-up for the gas level concentration measurements (upper part of the general scheme of the photoacoustic detection system from Fig. 1), ensuring gas purity in the PA cell. The handling system can perform several functions without being necessary any disconnections, can be used to introduce the sample gas in the PA cell at a controlled flow rate, to pump out the cell, and to monitor the total and partial pressures of gas mixtures. In order to transport the gas to the PA cell, the transport lines were realized of Teflon to minimize adsorption and contamination. Connections to the inlet and outlet valves of the PA cell were made via flexible Teflon tubing so as to minimize the coupling of mechanical vibrations to the PA

cell. The gas handling system consists of two gas flow controllers MKS 1179A (0–1000 sccm) [sccm – standard cubic centimeters per minute, 1 sccm at 0°C = 7.436×10^{-7} mol/s] and MKS 2259CC (0–200 sccm) which are connected to a digital four-channel instrument MKS 247C, an aluminium-coated plastic bag filled with sample gas.

The sample bags are aluminized bags from Quintron Inc., provided with valves which seal them after filling. Fig. 2 shows the samples bags before filling and after when is connected to the LPAS system.



Fig. 2 – a) Chemically inert aluminized bags with mouthpieces in the right hand side and b) aluminium-coated plastic bag filled with the sample gas and connected to the PA system.

The minimum detectable concentration which can be detected with the LPAS system is calculated with the following equation:

$$c_{\min} = \frac{V_N}{\alpha P_L C S_M}, \quad (1)$$

where $V = V_N$ is the voltage of the photoacoustic signal for a signal to noise ratio equal with 1 (SNR = 1), α [$\text{cm}^{-1} \cdot \text{atm}^{-1}$] is the absorption coefficient for a given laser line, P_L [W] is the unmodulated peak value of the power laser, C [$\text{Pa} \cdot \text{cm}/\text{W}$] is cell constant, and S_M [mV/Pa] is the total responsivity of the four microphones ($S_M = 80$ mV/Pa). The cell constant C was calculated for a mixture of calibrated 1 ppm of C_2H_4 in N_2 at a total pressure of 1 013 mbarr, on 10P(14) line of the CO_2 laser, where $\alpha = 30.4 \text{ cm}^{-1} \cdot \text{atm}^{-1}$ and was obtained $C = 3\,500 \text{ Pa} \cdot \text{cm}/\text{W}$.

An important parameter of the PA cell is the responsivity R [$\text{V} \cdot \text{cm}/\text{W}$] which is defined as the amplitude of the electric signal provided by the microphones on the unity absorbed power of the molecules on the unity length:

$$R = C \cdot S_M. \quad (2)$$

For the above data, the cell responsivity was calculated $R = 280 \text{ V} \cdot \text{cm}/\text{W}$.

1.2 NONINVASIVE GAS DETECTION

The transfer modality to the PA cell of the gas sample which is collected in aluminized bags was realised using two approaches: i) by a direct and fast transfer and ii) by gas flow controller to deliver stable and known flows of the gas to the PA cell. We monitored the evolution in time of the concentration level for ethylene as a gas sample at a known concentration and the level of ethylene detected from a healthy human.

i) direct and fast transfer ensure a response time of seconds for monitoring of the trace gas concentration in the sample gas.

ii) gas flow controller is realised with the gas flow controller MKS 1179A at 300 sccm rate. This procedure was implemented in order to minimize any tendency for the vapor to stick to the cell walls and the effects of internal outgassing of contaminants which would otherwise lead to increasing background signals during an experimental run. Connections to the inlet and outlet valves of the PA cell were realised using flexible Teflon tubing in order to minimize the coupling of mechanical vibrations to the PA cell. The pressure of the gases introduced to the PA cell was determined by use of three Baratron pressure gauges (MKS Instruments, Inc.): 622A (0-1 000 mbarr), and 122A (0-100 mbarr), with a PDR-C-2C two channel digital instrument.

The transfer of the sample gas from the sample bag to the PA cell was realized at a controlled flow rate at 300 sccm, and the total and partial pressures of the gas were monitored. The samples bags were filled at atmospheric pressure with ethylene at a known concentration (10 ppm) and transferred to the PA cell using the above described two procedures. The average final pressure inside the PA cell was measured for the ethylene transfer ~ 915 mbarr, whereas for the breath samples from healthy humans the average final pressure was ~ 750 mbarr.

The responsivity of the PA cell depends on the pressure of the gas inside the cell. Taking into account the fact that the sample bags filled from the healthy humans and from the patients with different disorders differ from one case to another, there is necessary to know the pressure's dependency of the PA cell responsivity. Representation of this dependence is presented in Fig. 3, where for above measured average pressures $R \sim 236$ cmV/W and ~ 191 cmV/W respectively.

Experimental measurements realised for healthy humans show that the concentration levels of the ethylene detected with the controlled transfer modality is smaller compared with the direct and fast transfer due to the proper absorption of certain gases (carbon dioxide and water vapors) which interfere with the trace gas to be measured with the KOH scrubber. The level of ethylene concentration measured from the breath of a healthy human was ~ 11 – 30 ppb for the controlled transfer modality, whereas for the fast transfer ~ 460 – 800 ppb.

There are three types of breath traps used in order to reduce the amount of residual gases from the gas to be measured: chemical, cryogenic, and adsorptive. Chemical trapping usually uses traditional “wet chemistry”, breath is bubbled through a reagent solution that captures a specific compound, such as ethanol or acetone. The method is simple and direct, the disadvantages are poor sensitivity and the physical effort required of the donor. In cryogenic trapping, the biomarkers are captured by freezing, the breath travels through a tube immersed in such cooling fluids as liquid nitrogen, which is at -196 degrees Celsius. Unfortunately, a cold trap also freezes the water and carbon dioxide in the breath and may rapidly become plugged by ice. Adsorptive trapping has become the most convenient and most widely used method today. It captures biomarkers by binding them to agents such as activated carbon and absorptive resins. Recent advances in microprocessor controlled thermal desorbers, which automatically “bake off” and concentrate trapped compounds, have made the technique even more convenient [7].

Using the controlled transfer modality two different KOH scrubber recipients were investigated (KOH Trap 1 with a volume of about 13 cm^3 and KOH Trap 2 $\sim 88\text{ cm}^3$). The trace gas concentration of ethylene from the breath of a healthy human without KOH scrubber and with the use of KOH Trap 1 and 2 are illustrated in Fig. 4.

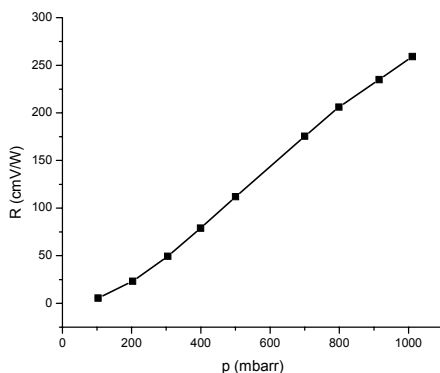


Fig. 3 – Responsivity of the PA cell *versus* pressure of the gas sample inside the cell.

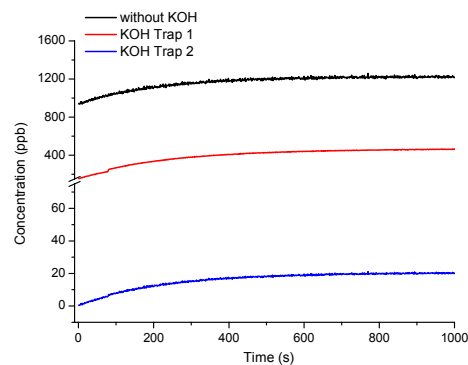


Fig. 4 – The trace gas concentration of ethylene from the breath of a healthy human without KOH scrubber and with KOH Trap 1 and KOH Trap 2.

These experimental results show that the presence in the LPAS system of the KOH scrubber is compulsive and a bigger volume of the KOH trap is useful to be used in order to reduce the amount of the certain gases which interfere with the trace gas to be measured, where the concentration of the detected sample decreased by a factor of ~ 60 .

2. CONCLUSIONS

In the present work, the transfer modality of ethylene as a gas sample to the PA cell using two approaches, a direct and fast transfer and a gas flow controller were investigated. We monitored the evolution in time of the concentration level for ethylene at a known concentration and the level of ethylene detected from a healthy human. The procedure of gas flow controller was implemented in order to minimize any tendency for the vapor to stick to the cell walls and the effects of internal outgassing of contaminants which would otherwise lead to increasing background signals during an experimental run.

Experimental measurements realised for healthy humans show that the concentration levels of the ethylene detected with the controlled transfer modality is smaller and recommended to be used compared with the direct and fast transfer.

We have investigated the presence of the KOH scrubber using two recipients with different volumes, and found out that its presence is compulsive and a bigger volume has to be used in order to reduce the amount of the certain gases which interfere with the trace gas to be measured.

Measuring human biomarkers in exhaled breath is expected to revolutionize diagnosis and management of many diseases and may lead to rapid, improved and lower-cost diagnosis.

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