

PORTABLE EXHALED BREATH ANALYZER EMPLOYING FLUCTUATION-ENHANCED GAS SENSING METHOD IN RESISTIVE GAS SENSORS

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Abstract

This paper presents a portable exhaled breath analyser, developed to detect selected diseases. The set-up employs resistive gas sensors: commercial MEMS sensors and prototype gas sensors made of WO_3 gas sensing layers doped with various metal ingredients. The set-up can modulate the gas sensors by applying UV light to induce physical changes of the gas sensing layers. The sensors are placed in a tiny gas chamber of a volume of about 22 ml. Breath samples can be either injected or blown into the gas chamber when an additional pump is used to select the last breath phase. DC resistance and resistance fluctuations of selected sensors using separate channels are recorded by an external data acquisition board. Low-noise amplifiers with a selected gain were used together with a necessary bias circuit. The set-up monitors other atmospheric parameters interacting with the responses of resistive gas sensors (humidity, temperature, atmospheric pressure). The recorded data may be further analysed to determine optimal detection methods.

Keywords: resistance gas sensor, fluctuation enhanced sensing, flicker noise, gas detection, breath sample collection.

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1. Introduction

Breath analysis is one of the most promising non-invasive medical diagnostic methods which may be implemented in a portable and low-cost device. There has been found about 3000 different *volatile organic compounds* (VOCs) in the exhaled breath [1]. Unfortunately, no characteristic VOC has been identified for the considered diseases. Usually, there is a set of VOCs of various concentrations which are characteristic for a disease of interest and may be utilized for medical diagnosis. The VOCs are present in the exhaled breath at highest concentration at its final stage when intensively emitted by pulmonary alveoli. Their presence is due to metabolic reactions, characteristic for various illnesses. Concentrations of the VOCs may span across several orders of magnitude, usually from a few ppt (10^{-12}) up to a few ppm (10^{-6}), recognizable even by the human smell sense. So small concentrations are difficult to be detected by cheap gas sensors. A few various types of gas sensors have been developed and may be used to this aim. A review of the-state-of-the-art of available gas sensors' technologies is available elsewhere [2–4].

Resistive gas sensors are very promising sensors for medical diagnosis due to their low cost, fast response, reliability and easy measurement of their DC resistances altered by the ambient atmosphere. The main drawbacks are their limited selectivity and sensibility, and drift of parameters in time. These limitations are the main driving force for their further enhancement. New nanotechnology materials help to develop more selective resistive gas sensors [2]. New gas sensing layers use nanostructures (e.g. nanoparticles, carbon nanotubes, silicon nanowires) which are more sensitive due to an increased gas sensing area. A very promising technology is based on using metal nanoparticles functionalized with organic ligands. These structures are more sensitive to selected VOCs and may operate at the room temperature. The organic ligands attract selected VOCs by ensuring more selectively their adsorption. This mechanism is very attractive and assures better selectivity at the cost of more plausible and stable immobilization of the organic receptor by blocking its functionality. Additionally, the large variety of gas sensing layers of different materials have still limited applications for some of VOCs of interest in detection of selected illnesses. All these problems mean that we have to propose other measurement methods to enhance gas detection and attenuate adverse effects of crossing gasses or varying humidity in practical applications. Thus, we propose to use a *fluctuation-enhanced gas sensing* (FES) method which improves gas detection by applying low-frequency resistance fluctuations as an additional source of information about the ambient atmosphere. This method was effectively used in different applications [5]. It improved sensitivity of gas detection methods even hundreds times when compared with DC resistance measurements only and when applied to mono-sized nanoparticle materials, securing a greater gas sensing area [6].

The mentioned methods require collection of exhaled breath samples and their further analysis. A few independent methods of this process have been proposed by using inert bags to preserve the exhaled breath (e.g. Tedlar bag, Mylar bag [7]) or an adsorbent in the glass tube (e.g. Tenax tube using porous polymer Anasorb®727 as an adsorbent), or by blowing directly into the gas chamber being part of the breath analyser set-up [8]. These methods require different costs but some of them may preserve the samples for a few months by placing them in a refrigerator for biological samples for further analysis with different methods.

We know that other methods, except for the mentioned FES method, exist to improve selectivity and sensitivity of gas sensors. Temperature modulation or UV light irradiation for the gas sensing layers exhibiting the photocatalytic effect (e.g. TiO_2 , WO_3) are very popular due to simplicity of their practical applications and resulting improvement in gas sensing [9–12]. These methods are very attractive thanks to reducing drift effects on the characteristics of resistive gas sensors because of applying modulation and recording differences in the gas sensor response. These methods may increase sensitivity and selectivity up to the level acceptable for the exhaled breath analysis.

In our prototype breath analysing unit a set of eight gas sensors was applied to form an array of gas sensors of different sensitivity for the VOCs of interest, like ethanol, formaldehyde, nitric dioxide, etc. The collected data may be analysed by using detection methods requiring intense calculations, performed by an attached personal computer. The designed unit can analyse the exhaled breath samples released from the adsorbent. Its further development may provide the real-time analysis of the exhaled breath. Details of the gas sensing unit are presented in Section 2. Data recording and processing are presented in Section 3, including some examples of experimental data. The proposed set-up was designed and manufactured to obtain a low-cost device which could be used by the medical staff. The following steps of its further evolution are also discussed. This device was designed as part of the EU project TROPSENSE, focused on detection of tropical diseases, but its concept may be also utilized for other diseases [13].

2. Measurement set-up

In the first step of the exhaled breath analyser operation the breath samples are collected. This may be done either off-line or on-line. The EU project supporting financially the prepared analyser required collection of the exhaled breath samples in different hospitals and in different countries due to a limited number of patients and their availability in different periods. Therefore, the developed unit should be able to analyse the samples collected off-line and stored in a refrigerator for biological samples before their analysis. Fig. 1 presents a block diagram of the exhaled breath collection procedure. A patient blows into the sterilized plastic tube with a valve to preserve the last stage of the exhaled breath. Next the preserved sample is shifted slowly through the adsorbent in the glass tube. This procedure is repeated five times to increase concentrations of the exhaled VOCs in the adsorbent. The adsorbent consists of two layers separated by a cotton layer to check whether the flow of the collected breath was done in a proper way. The prepared sample can be preserved even for a few months when kept in a refrigerator for biological samples, or shipped at a temperature of a few Celsius even to remote places for further analysis. Application of the adsorbent removes humidity from the exhaled breath.

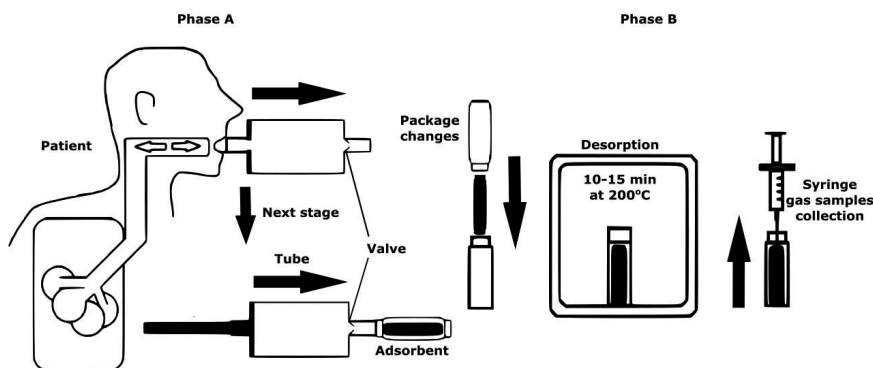


Fig. 1. A block diagram of preparing an exhaled breath sample.

Before the analysis the adsorbent with the adsorbed VOCs was placed into a sterile glass vial and heated up to 200°C for 15 min in an oven to be released. This procedure secures about 20 ml of the exhaled VOCs in the vial above the adsorbent. That amount has to be introduced into the prepared metal gas chamber (Fig. 2). We use a syringe and a rubber membrane to shift the sample between the glass vial and the gas chamber containing the sensors. The gas chamber has to be cleaned before measurement by blowing a synthetic air. This procedure makes measurements independent of variations of unavoidable contaminants or humidity in the laboratory air. An additional syringe is used to secure an under-pressure, necessary to obtain a place for the breath sample injected from the second syringe (the left one in Fig. 2). The applied valves can be enriched by a tiny air pump (controlled by a pressure sensor) which can be used to collect on-line the last part of the exhaled breath, as in similar applications [14], to give immediately the diagnosis results. We will apply this solution in the updated version of our set-up.

The manufactured analyser contains eight different gas sensors placed inside the gas chamber. We have designed the chamber to use various gas sensors: commercial sensors (e.g. TGS8100, MiCS-6814 – including three different sensors) made in the MEMS technology and optimised to detect a wide range of VOCs, or prototype gas sensors made of a thin layer of TiO₂ or WO₃ doped



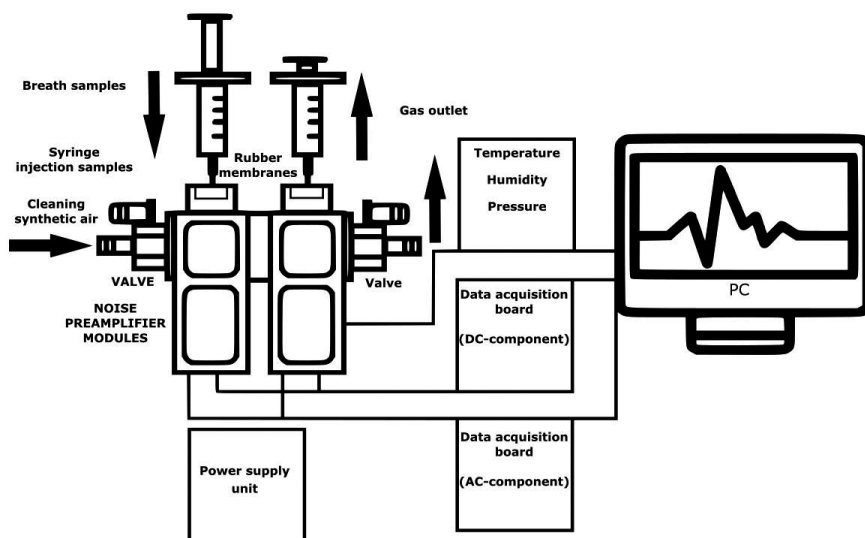


Fig. 2. A block diagram of the designed measurement set-up for exhaled breath analysis.

by metal particles (*e.g.* Au, Ag, Pt or Fe) and placed on a ceramic and heated layer. The detection limit of commercial sensors depends on the type of VOCs and is about a few ppm or even slightly lower. The detailed values for selected VOCs are given by the producers [17–19]. We suppose that the proposed FES method may decrease these threshold values below a single ppm. These prototype layers exhibit the photocatalytic effect and therefore additional UV LEDs may be used for their irradiation. Some of these sensors may be prepared by very simple methods, like painting a mixture of nanoparticles and graphene flakes [11]. Additionally, their sensing properties may be easily modified by temperature modulation or UV light irradiation [15, 16]. The applied commercial gas sensors are placed in a plastic encasement and therefore cannot be modulated by UV light [17, 18]. Additionally, some recently developed sensors are integrated with an electronic circuit to obtain a digital interface (*e.g.* SGP30 [19]). Such sensors can be also employed in the developed set-up but without the capability of applying the FES method. These sensors are very tiny, consume little energy for heating and are optimised to detect some of VOCs which may be present in the exhaled breaths of ill patients.

Figure 3 presents photos of the manufactured analyser. The main part of the unit is the metallic gas chamber with a volume of about 22 ml. The gas chamber was made of polished aluminium parts. The sensors are placed in the gas chamber using screw-in tips. The designed electronic units with the sensors are mounted directly to the tips by a seal to secure tightness. The electronic circuits are designed to mount various types of sensors and comprise the following parts (Fig. 4): a sensor bias unit using a low-noise operational amplifier MAX4478 and a switcher selecting the bias current value up to a few mA, a DC voltage channel with a buffer based on an operational amplifier MAX4478, an AC voltage channel with a high-pass filter and a low-noise voltage amplifier with amplification of a few hundreds V/V. The circuit is shielded using a copper plate to avoid external interferences. This part adjusts the AC and DC components to be measured by the data acquisition board with a 24-bit A/D converter and controlled by a separate computer using LabWindows/CVI software. The external part of the set-up can be integrated with the prepared electronic unit by adding a microcontroller and selecting a de-

tection algorithm, as proposed elsewhere [20]. We are able to sample the DC and AC channels with a frequency of up to tens kHz which is sufficient to identify $1/f$ (flicker) noise dominating in this frequency range. The flicker noise intensity depends on the ambient atmosphere of the resistive gas sensor and can be used to improve gas detection. Only the low-frequency resistance fluctuations depend on the ambient atmosphere and therefore we have to scale the recorded voltage fluctuations observed across the gas sensor to make it independent of the bias circuit. The detailed procedure of the necessary scaling for various bias circuits can be found elsewhere [21].

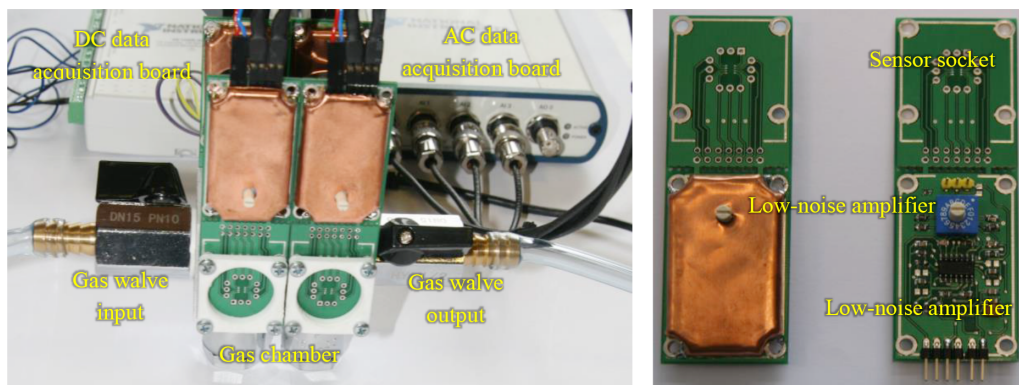


Fig. 3. Photos of the designed and manufactured exhaled breath analyser using the FES method and modulation by UV light irradiation: the set-up with board (left) and the designed electronic circuit shielded by a copper plate with the visible electronic the data acquisition switcher to set a bias current value of the gas sensor (right).

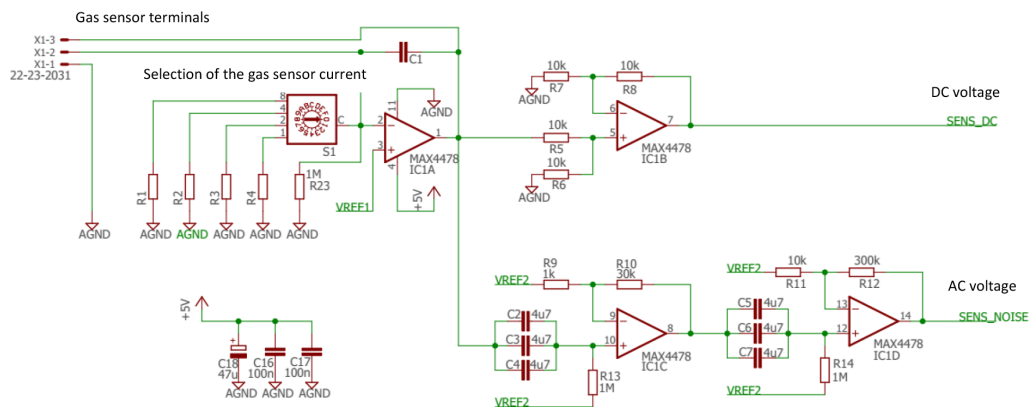


Fig. 4. The electronic circuit of the designed set-up to record voltage across the gas sensor placed in the feedback loop of the low-noise operational amplifier MAX4478; the set-up filters out DC and AC voltage components into two separate channels.

3. Data recording and processing

Various detection algorithms may be applied to determine the presence of the VOCs of interest in the exhaled breath [5, 22–25]. The proposed algorithms are selected due to their relatively

good detection results but their effectiveness and eventual optimization requires more in-depth analysis, especially when cross-gasses reduce the detection accuracy. The algorithms utilize the estimated power spectral densities of resistance noise as the input vectors.

A composition of the VOCs of interest depends on the illness influencing metabolic reactions in a patient's body and therefore we employ selected algorithms, but we are not able to determine which one is the best. This fact is the reason why the A/D converters and the control software are separated from the rest of the set-up because we can easily modify the measurement conditions to adjust to the voltage range of the applied A/D converters and to apply various detection algorithms. This part requires more flexibility, but after fixing the AC signal amplification and the detection algorithm we may implement it in a more compact way.

We have mentioned that the proposed set-up can use the prototype WO_3 gas sensing layers at modulated UV light. These gas sensing layers are very promising for breath analysis, as presented elsewhere [26]. In that case, the input data of the detection algorithm comprises a set of a few vectors of power spectral densities. We can expect a serious improvement in the detection rate when these gas sensing layers are applied. A similar improvement may be expected by applying dopants or temperature modulation to other popular gas sensing materials [27, 28], or by applying other gas sensors and the FES method [29].

Examples of experimental data for DC resistance and noise induced by changes of the ambient atmosphere are presented in Fig. 5 and Fig. 6, respectively. We have measured commercial gas sensors made in the MEMS technology: TGS 8100 and MiCS-6814. The MiCS-6814 sensor consists of three different sensors optimised for the selected VOCs: NO_x , CO and NH_3 . It is visible that all sensors are sensitive to the applied ethanol diluted in a synthetic air (Fig. 5). A relative change of the DC resistance reached a factor of ten times when the ethanol concentration increased to 50 ppm. At the same time the power spectral density of voltage fluctuations observed at the output of the set-up changed by about 20 dB from the level observed at the ambient atmosphere of synthetic air. The observed low-frequency noise is $1/f$ noise of an intensity dependent on the ambient atmosphere. The noise was recorded for about 20 s to obtain the number of sam-

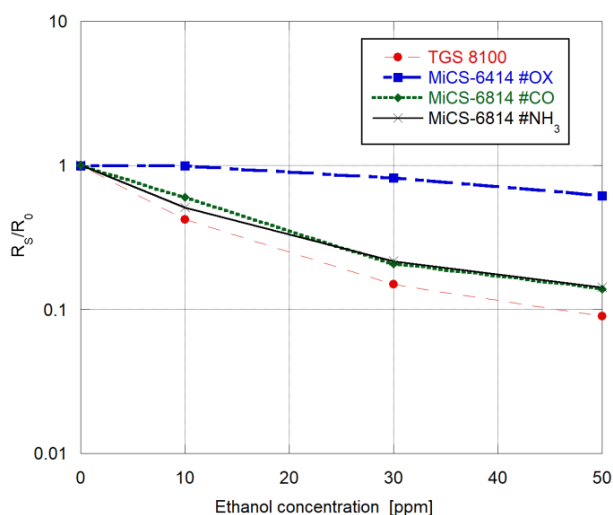


Fig. 5. Results of DC resistance R_S measurements of the TGS 8100 and MiCS-6814 sensors at the ambient atmosphere of ethanol diluted in a synthetic air; R_0 – sensor DC resistance at the ambient atmosphere of synthetic air, commercial TGS 8100 and MiCS-6814 sensors (three sensors in the same housing) were used.

ples necessary to estimate the power spectral density at a reasonable random error of estimation, limited to about 10%.

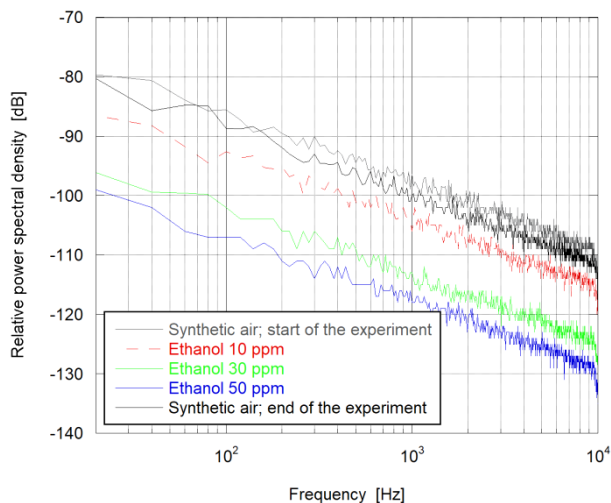


Fig. 6. Relative changes of voltage power spectral densities estimated from the recorded noise by using the prepared measurement set-up.

The experiments show that the noise level returns to its original value. We have observed that the noise level changes were more intense at low gas concentrations. It should help to identify the VOCs of interest but requires application of various detection algorithms to determine the most interesting one. We can claim that no changes in the slope of the measured flicker noise should reduce complexity of detection algorithm. Moreover, we may resign from estimation of the power spectral density by using the FFT algorithm and complicated calculations, and reduce our estimation to estimating the variance of noise in selected sub-bands, as proposed earlier [30, 31]. It means that the simplified detection algorithm and adding A/D converters controlled by microcontrollers to the developed measurement set-up would decrease its size, energy consumption and costs.

The responses of the applied gas sensors are quite different. We observe relatively intense changes of DC resistances and faster responses for commercial sensors when compared with the prototype sensors. The sensors based on WO_3 layers respond at smaller pace due to a greater volume, but may be easily more selective due to the application of different dopants. When the exhaled breath is introduced into the gas chamber we observe an intense change of DC resistances and their fluctuations. This is mainly due to a change of humidity, but further experiments using the breath samples collected by Tenax tubes will be performed soon.

The set-up monitors atmospheric parameters (temperature, pressure and humidity) by using the digital environment BME 280 sensor. The collected data may be used either to confirm stability of the applied environmental conditions or to compensate the data by considering shifts of DC characteristics at different humidity values. This compensation should require additional calibrating measurements because we identify gas mixtures and the effects of gas crossing complicate such compensation when compared with the data observed for calibrating gases. The working temperatures were selected for the applied gas sensors by using a DC voltage suggested by the producers of commercial gas sensors or by measuring temperatures of the ceramic base covered by the WO_3 gas sensing layer.



4. Conclusions

The reported study presents a low-cost measurement set-up determining the composition of the exhaled breath by employing selected resistive gas sensors. Additionally, we enclose a description how the exhaled breath samples are collected and used, and possible further development of the set-up by applying a controlled tiny electrical pump.

We present the detailed construction of the developed portable unit which uses a fluctuation-enhanced gas sensing method. The method requires application of low-noise amplifiers and DC resistance measurements. Some of the applied gas sensors can be modulated by UV light and therefore an additional circuit controlling the UV LED diodes was also designed. The set-up may be used for eight resistive gas sensors at the same time. Four sensors can be measured by recording their DC resistances and resistance fluctuations in parallel but the set-up may be enriched to perform these measurements in eight channels in parallel. The collected data may be used by various algorithms to detect the VOCs of interest and enable the illness detection.

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