Breath acetone monitoring by portable Si:WO_3 gas sensors

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ABSTRACT

Breath analysis has the potential for early stage detection and monitoring of illnesses to drastically reduce the corresponding medical costs. Here, a portable acetone sensor consisting of flame-deposited and in-situ annealed, Si-doped epsilon-WO_3 nanostructured films was developed. The chamber volume was miniaturized, reaction- and diffusion-limited gas flow rates were identified and sensing temperatures were optimized resulting in low limits of detection and short responses at realistic relative humidities. The acetone content in the breath of test persons was monitored continuously (even in the presence of isoprene) and was in good agreement with state-of-the-art proton transfer reaction - mass spectrometry (PTR-MS). Such chemo-resistive sensors can accurately track acetone concentration and become an alternative to more elaborate breath analysis techniques.

Keywords: breath analysis, nanoparticles, gas sensor, acetone, PTR-MS

1 INTRODUCTION

Noninvasive detection of diseases by breath analysis is a fast, economically viable and simple alternative to blood analysis and endoscopy [1]. It is based on the fact that several hundred volatile organic compounds (VOC) appear in the human breath with concentrations ranging from ppt to ppm. A particular focus centers on real-time analysis of exhaled breath, even with breath-to-breath resolution. More specifically, the detection of acetone in the human breath is promising for non-invasive diagnosis and painless monitoring of diabetes type-1 (no finger pricking). The acetone concentration in the breath varies from 300 to 900 ppb in healthy people [2] and to more than 1800 ppb for diabetics [3]. Nevertheless, acetone concentrations in the breath are not simply related to glucose levels in the blood and additional research will be necessary to make it a viable marker compound for clinical routine.

The requirements for application of exhaled breath analysis in clinical routine are still challenging. Moreover, the development of small hand-held devices able to provide reliable and continuous real-time measurement of important breath markers such as acetone is desirable. Several methods have indeed demonstrated a remarkable potential for breath acetone measurement. Gas chromatography with flame ionization detection (FID), PTR-MS, and selected ion flow tube mass spectrometry (SIFT-MS), for example, have shown high selectivity, sufficient sensitivity and low limit of detection for several VOC. They are, however, quite costly and have rather limited portability. In this regard, chemo-resistive gas sensors based on semiconductor nanoparticles are very attractive for breath analysis [4] offering low fabrication costs, high sensitivity, sufficiently low limit of detection and strong miniaturization potential.

Here, portable chemo-resistive gas sensor devices have been developed and applied to real breath acetone detection. The devices consist of highly performing 10 mol% Si-doped WO_3 nanoparticle films that have been directly-deposited and in-situ annealed onto interdigitated platinum electrodes located at back-heated alumina substrates [5]. The sensitivity and selectivity of these portable devices to acetone was optimized by their operating parameters (e.g. sensor temperature and inlet gas flow rate). The breath acetone concentration of several healthy subjects was measured using these devices and compared to the corresponding measurements by PTR-MS. The influence of the physical conditions of the subjects (e.g. rest or sports activity) and variation in the concentration of other endogenous VOC (e.g. isoprene) on the sensor response was monitored exploring the potential of these sensors for real breath analysis.

2 EXPERIMENTAL

A flame spray pyrolysis (FSP) reactor was used for synthesis and direct deposition of 10 mol% Si-doped WO_3 nanoparticle films onto Al_2O_3 substrates featuring a set of Pt electrodes. The alumina substrate had interdigitated Pt lines and a Pt resistance temperature detector (RTD) on one side and a Pt heater on the other side [5].

The WO_3 crystal size and phase composition were characterized by X-ray diffraction (XRD). Prior to sensing tests, the sensors were kept in an oven at 500 °C for 5 hours at ambient pressure to stabilize the nanoparticle size and avoid further sintering during sensor measurements. The simulated breath was prepared by mixing synthetic air (Pan Gas, 99.999%) and humid air with acetone/ethanol (10 ppm in synthetic air, Pan Gas 5.0) to obtain the desired concentration, as described in more detail elsewhere [6]. The sensors were placed inside a T-shaped tube chamber and placed onto a Macor holder connected to a voltmeter to

measure the film resistance and to a power source to heat the sensors. The operating temperature (T_O) was varied between 250 and 390 °C and measured with the embedded Pt RTD on the substrate. The sensor response (S) is:

$$S = R_{air}/R_{analyte} - 1 \quad (1)$$

where Rair is the film resistance in air at a given relative humidity (RH) and Ranalyte is that resistance at a given concentration of acetone or ethanol at that RH. The cross-sensitivity to humidity (CS) is:

$$CS = abs\,[(S_{dry} - S_{RH})/\,S_{dry}]\cdot 100 \quad (2)$$

where Sdry and SRH are the sensor responses at dry air and a given RH.

Real breath measurements were performed with the aid of a respiratory flow controlled mask that allowed sampling of specific breath segments into the Si:WO_3 sensors device and a high-sensitivity PTR-MS (Ionicon Analytik GmbH, Innsbruck) [7]. Gas sampling was accomplished by a heated Teflon tube using an insulated heating wire (TNI Medical, Freiburg, Germany). A constant flow rate of 70 mL/min was kept during all breath measurements while the temperature of the Si:WO_3 sensor was set at 350 °C. Measurements during physical activity are carried out on a computer-controlled, semi-supine medical ergometer operating at constant levels of power independently of the pedal speed. A supporting bed stabilizes the torso of the volunteer thereby reducing movement artifacts appearing in the acquired physiological signals. Different persons (subjects) in good health between 25 and 35 years old were tested. The acetone and isoprene signals were the counts per second measured at m/z=59 (mass-to-charge ratio) and m/z=69, respectively.

3 RESULTS AND DISCUSSION

The WO_3 nanoparticles were optimally doped with 10 mol% Si. The nanoparticles collected downstream of the sensor substrate consisted of pure ε-WO_3 with crystal size of about 10 nm [5]. This nanoparticle film composition was selected for its optimal thermal stability, selectivity and sensitivity even in humid conditions [6]. Figure 1 shows the sensor response ratio between acetone and ethanol (selectivity) for dry air, 40 and 90% RH at 350 °C. The acetone selectivity over ethanol, in fact, initially increases and then rather levels off at these three conditions. While the absolute sensor response to acetone decreased with increasing RH, the selectivity against ethanol increased even further. More in detail, at ambient relative humidity (40% RH), the sensor response to acetone was 7 - 16 times higher than that of ethanol. At realistic human breath conditions (90% RH), the sensor response to ethanol was 14 - 28 times higher than that to ethanol. The increase in selectivity at a higher RH may be due to the occupation of ethanol reaction sites on the WO_3 surface by H_2O related species [6].

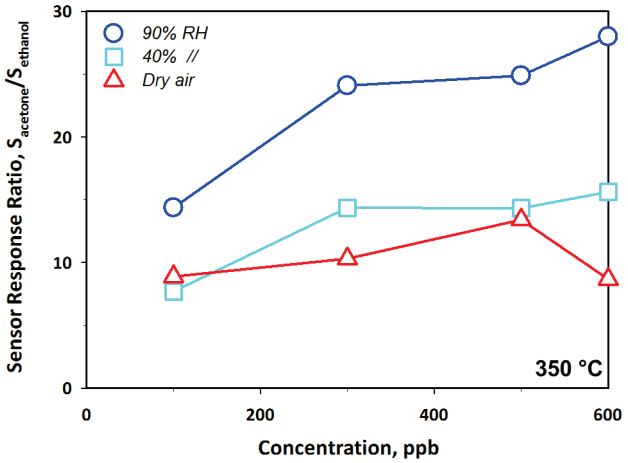

Figure 1: The sensor response ratio (selectivity) between acetone and ethanol increases with increasing RH from 100 to 600 ppb each.

Using this device, the breath acetone concentration of test persons at rest or during physical activity was measured and was in agreement to that by highly accurate PTR-MS [8]. The concentration of acetone in the tidal part of the respiratory cycle of a healthy test person at rest was measured by the present Si:WO_3 sensor (black) and PTR-MS for acetone (grey line). At the start of breath sampling, the sensor resistance decreased rapidly and recovered to the initial value after stopping the breath flow. The calibrated sensor response corresponded to about 900 ppb acetone concentration on the average. This was in good agreement (~95%) with the acetone concentration reading of the PTR-MS, 880 ppb (grey line). Furthermore, the sensor response was robust against variations of the exhaled breath flow rate facilitating application of these sensors to breath analysis. The influence of physical activity (breath pace) and breath isoprene concentration on the sensor response were investigated in detail for the end tidal exhalation volume during continuous breathing.

4 CONCLUSIONS

Portable acetone sensors made by flame spray pyrolysis, direct deposition and in-situ annealing of 10 mol% Si-doped WO_3 nanoparticles were developed and tested for breath analysis. The sensors were highly selective and sensitive to acetone, regardless of background RH. Acetone concentrations as low as 20 ppb were measured with good signal to noise ratios. These sensors were applied to breath acetone monitoring of healthy subjects and compared directly to high-sensitivity PTR-MS measurements of the same breath samples. The present Si-doped WO_3 sensors were highly selective to acetone both at rest and during physical activity showing reliable acetone measurement, independent of respiratory pace.

5 ACKNOWLEDGMENTS

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