Original scientific paper

Informacije MIDEM
Journal of Microelectronics,
Electronic Components and Materials
Vol. 44, No. 2 (2014), 126 – 136

Micropreconcentrators In Silicon-Glass Technology for the Detection of Diabetes Biomarkers

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Abstract: In the present study concentration factors (CF) obtained for diabetes biomarkers such as acetone, propane, ethanol and ethylbenzene in a micropreconcentrator structure are presented. The concentration factor is defined as the ratio of gas preconcentration after and before preconcentration process. It was calculated from GC measurements as the ratio of peak area before and after desorption. The micropreconcentrator was manufactured using silicon-glass technology. The structure is 1.68 mm thick and has lateral dimensions 2 cm by 2 cm. It contains a 12 cm-long channel etched in an Si wafer. The micropreconcentrator is based on thermal desorption, and therefore the Pt heater was positioned at the bottom of the structure. The paper presents the technology behind the micropreconcentrator, and the thermal and preconcentration measurements of the manufactured structures. The Carboxen-1018 adsorbent material used in the experiments has also been studied. It is recommended by Sigma-Aldrich as a promising material for measuring concentrations of volatile organic compounds present in human breath. The lowest concentration factor value is around 30 for a mixture of diabetes biomarkers and the highest around 2800 for a single biomarker, i.e. acetone. The gas mixture has been prepared from certified gases using mass flow controllers (MFC) and a GC/MS setup.

Keywords: Breath analysis, gas detectors, silicon-glass technology, micropreconcentrators

Mikro predkoncentratorji tehnologije silicij-steklo za določevanje biomarkerjev diabetesa

Izvleček: Raziskava predstavlja koncentracijske faktorje (CF) biomarkerjev diabetesa, kot so aceton, propan, etanol in etilbenzen, v mikro predkoncentratorski strukturi. Faktor koncentracije je določen kot razmerje predkoncentracije plina pred in po predkoncentracijskim procesom. Računan je iz GC meritev vršnih površin pred in po desorpciji. Mikro predkoncentrator je razvit v tehnologiji silicij-steklo. Struktura je 1velika 2 x 2 cm^2 in 1.68 mm debela. Vsebuje 12 cm, v silicijevo rezino jedkan, kanal. Ker mikro predkoncentrator deluje na osnovi termične desorpcije, je Pt grelec nameščen na dno strukture. Članek predstavlja tehnologijo mikro predkoncentratorja ter termične in predkoncentratorske meritve izdelanih struktur. V raziskavah je bil, kot absorpcijski material, uporabljen Carboxen-1018, ki ga podjetje Sigma-Aldrich promovira za meritev hlapnih organskih deležev v izdihanem zraku. faktor koncentracije za mešanico biomarkerjev diabetesa je 30, najvišji faktor koncentracije za posamezen biomarker pa 2800. Plinska mešanica je bila pripravljena iz certificiranih plinov s pomočjo kontrolerjev masnega pretoka in GC/MS merilnega mesta.

Ključne besede: analiza dihanja, detektorji plina, tehnologija silicij-steklo, mikro predkoncentratorji

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1 Introduction

According to data provided by the World Health Organization (WHO), 347 million people worldwide have diabetes. WHO projects that diabetes will be the seventh leading cause of death in 2030 [1]. Current management of diabetes is mainly based on repeated testing of blood glucose. Other key metabolic variables such as insulin and lipids are less frequently controlled [2]. Blood glucose measurement is an invasive method, with a risk of serious consequences for the patient in case of infection. Frequent blood testing is especially necessary for patients receiving insulin treatment. The global recommendation is for patients to monitor their blood glucose concentration at least 3 times daily [3]. However, this is expensive, impractical and can be painful. New approaches for diabetes monitoring have been under consideration for many years. One alternative non-invasive method is breath analysis [4 -

8]. The human breath contains almost 3500 different volatile organic compounds (VOCs) [9]. Some of them are biomarkers, since their presence in breath indicates disease. The total number of diseases that can be detected by breath analysis is still unknown. However, results of breath analysis are presented in many papers, including research on lung cancer [10 - 13], chronic obstructive pulmonary disease [14], metabolic disorders [15], oxidative stress [16], asthma [17], helicobacter pylori infection [18], diabetes [19, 20] and others. An average breath sample contains around 200 VOCs [9]. The concentrations of biomarkers in human breath are typically in the range of several ppt (parts per trillion) to several hundred ppb (parts per billion). Due to this, the portable devices for breath analysis have to detect biomarkers in such concentration range. Commercially-available gas sensors are under development for measuring samples at several tens parts per million (ppm). Furthermore, they have a lower selectivity for compositions of a few VOCs in a gas sample. A cheap and very effective method of decreasing the limit of detection and improving selectivity is the utilization of gas preconcentrators. Conventional preconcentrators are usually glass or stainless steel tubes filled with an adsorbent material. Similar solutions are also used in breath analysis [21, 22]. However, these structures have large lateral dimensions and they consume too much power to be used in portable devices.

The paper describes micropreconcentrator structures as a solution that overcomes these limitations. The micropreconcentrator designed by the author uses silicon micromachining technology and silicon as a base material. The channel is embedded inside the structure. The channel width of the micropreconcentrator is 300 and 350 μm. The Pt heater was positioned at the bottom of the structure and covered by a dielectric layer with the exception of the pads. In order to seal the channel from the top, glass anodic bonding is used. The main advantage of this is that it provides full control over the process of filling the spiral-shaped channel with adsorbent grains. Micropreconcentrators are well known in silicon-glass technology [23-28]. Bassam *et al* presented a MEMS-based multi-inlet/outlet preconcentrator coated with polymer adsorbents using inkjet printing [29]. The concentrator factor (CF) was in the 15 - 32 range for a single inlet/outlet port and around 1000 for multi-port design for pure nonane. Camara *et al* presented a micro gas preconcentrator with improved performance for pollution monitoring and detection of explosives. The authors used Tenax-TA as the adsorbent material, and they obtained a CF of around 23 (at exposure time of 45 min) for nitrobenzene (initial concentration of 1 ppm) [30]. Later, the same group presented a micro gas preconcentrator in porous silicon for benzene preconcentration [31]. The "practical" concentration factor was around 55 for pure benzene, and it was largely dependent on the preconcentrator's external parameters such as the detection system (at 5 min adsorption time and 250 ppb initial concentration). Ivanov *et al* presented a silicon micropreconcentrator for detecting benzene [32]. The obtained concentration factors were between 5.28 and 40.25 for different flows and exposure times to benzene.

A literature review highlighted the efforts to develop miniaturized preconcentrators for assessing lower detection levels for a single gas, mainly for benzene. There are very few papers presenting full investigation results on preconcentration levels of diabetes biomarkers. This paper presents the obtained concentration factor for a single gas (acetone, propane, ethanol or ethylbenzene), as well as for a mixture of diabetes biomarkers.

1.1 Diabetes biomarkers in exhaled breath

Previously, the author has focused on acetone [33], since patients with diabetes tend to have higher acetone levels in their breath than healthy people. Exhaled acetone levels are usually around 300-900 ppb for healthy subjects and over 3000 ppb for patients with diabetes [34]. Analysis of acetone in breath has been used as a supplementary diagnostic tool for diabetes. However, analysis of the exhaled acetone is insufficient to control glucose levels in diabetes. Galasetti *et al* reported results of their studies into plasma glucose [35]. Eight patients with type 1 diabetes (T1DM) and 17 healthy control patients were investigated. Two groups of four gases (cluster A: acetone, methyl nitrate, ethanol, ethylbenzene; cluster B: 2-pentyl nitrate, propane, methanol, acetone) were used as covariance to their models. The exhaled ethanol levels were between 9.6 and 45.0 ppb, acetone 280 - 364 ppb, methyl nitrate 5 - 216 ppb, and ethylbenzene 46 - 434 ppt. This 4-gas model works as a method of breath-based glucose detection with a mean correlation coefficient of 0.91 (R = 0.70 - 0.98) compared to standard glucose measurements [35].

Blood ethanol measurements are very common. "Haziness" (blurred vision) is defined when blood ethanol falls in the 0.5-1.0 g/l range, which corresponds to 130-260 ppm in breath. In higher doses ("inebriation"), the effects of alcohol on the brain contribute to the loss of balance and coordination, loss of the ability to judge distance and height as well as dizziness. For "slight inebriation" (1.0-1.5 g/l) and "inebriation" (1.5-2.5 g/l), breath equivalents are 260-390 ppm and 390-650 ppm, respectively [36].

The presence of propane in breath is not fully explained. M. Barker *et al* measured exhaled VOCs and

ambient air from patients who suffer from cystic fibrosis and controls. Results show that the exhaled propane concentration is the same for both groups (1.95 ppb), when background propane concentration was approx. 1.38 ppb [37]. Rudnicka *et al* investigated patients with lung cancer. The exhaled propane was between 3.45 ppb and 5.96 ppb for healthy subjects and 3.19 ppb - 9.74 ppb for patients with lung cancer [12].

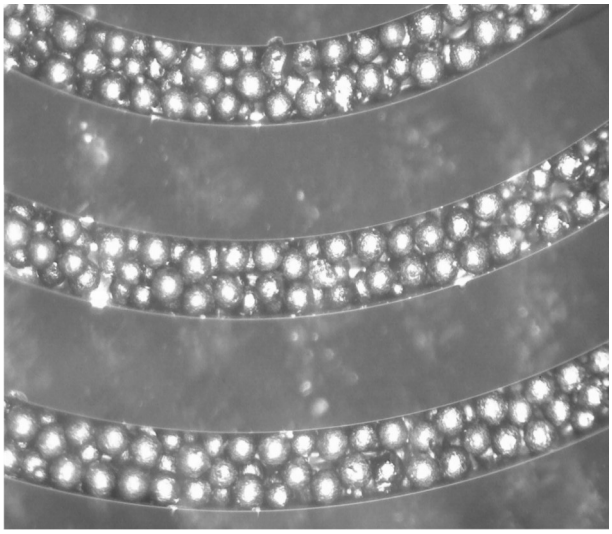
In [38], the authors report that 80% of ethylbenzene and xylenes are metabolized by hepatic enzymes in the human body. In this case, the exhaled ethylbenzene concentrations are lower than in inhaled air. On the other hand, some metabolic changes can modify the inhaled/exhaled ratio [2]. In [39], the authors measured exhaled ethylbenzene in the 46 ppt - 434 ppt range and methyl nitrate in the 5 ppt - 216 ppt range for hyperglycaemia. Achieving such low concentrations of VOCs is one of the most difficult stages of the preconcentration measurements.

2 Experimental

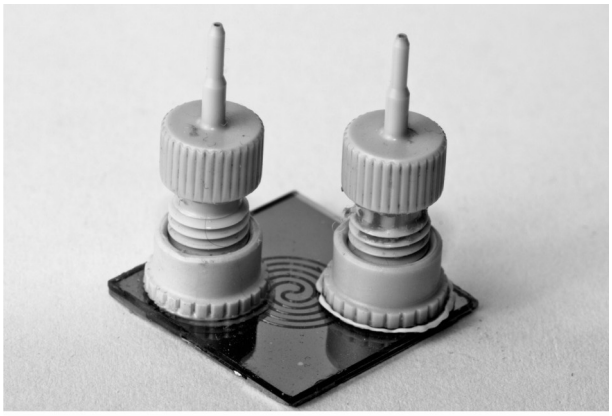
2.1 Basic limitations in micropreconcentrator fabrication

The microchannel shape and surface roughness are critical parameters for micropreconcentrators filled with adsorbent material. Due to this fact the fabrication process of micropreconcentrators was based on deep reactive ion etching (DRIE) of silicon substrate and the anodic bonding process. The microchannels were etched using the Bosch process, with an SiO_2 layer used as a masking material for the process. The manufacturing details was reported in [33]. The micropreconcentrators were fabricated with two microchannel dimensions: 300 µm x 300 µm x 120 mm, and 350 µm x 350 µm x 120 mm. The microchannel volumes are 1.08 μm^3 and 1.47 μm^3, respectively. The approximate adsorbent weight in the micropreconcentrator is 2.59 µg ± 0.8 µg. The channel width and depth were selected to prevent clogging of the adsorbent material inside the channel (Fig.1a.) However, some defects appeared during the fabrication process. For this reason, a few structures had a channel that could not be filled. Before filling the micropreconcentrator with the adsorbent material, the channel was examined using an optical microscope.

In recently reported structures, the gas inlet/outlet ports were placed on the edge of the structures. In the proposed solution, the gas ports are made with a glass cover. The author has investigated gas ports with a differently sized diameter. A filled micropreconcentrator with a NanoPort (NanoPort N-131, IDEX, Health & Science LCC, WA, USA) is presented in Fig.1b.



a) Optical image of the channel filled with Carboxen-1018

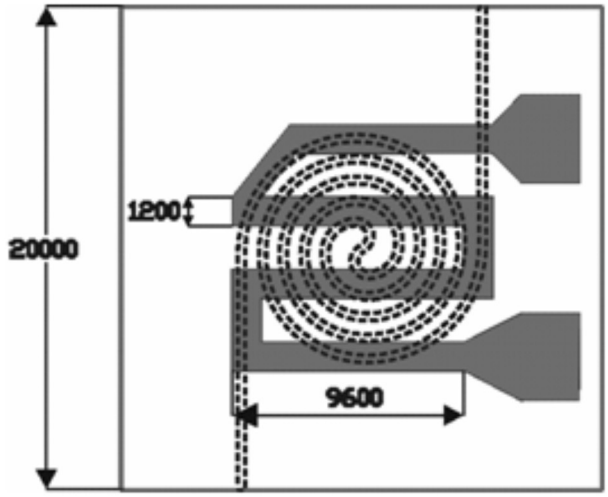


b) micropreconcentrator with assembled NanoPorts

Figure 1: The micropreconcentrator filled with Carboxen-1018 and gas inlet/outlet ports.

2.2 Thermal and Electrical Measurements

As already mentioned, the micropreconcentrator is based on thermal desorption. Desorption temperature is dependent on the type of adsorbent material. The main goal is to achieve this temperature as fast as possible and then to stabilize it during the desorption process. Moreover, temperature distribution inside the channel needs to be uniform. The microheater was deposited to cover the entire working area of the microchannel (Fig.2). The nominal resistance was 40Ω ± 2Ω. The desorption temperature was set to 220°C; this was achieved after approx. 35 s (with a 10 W power supply) when gas was flowing through the microchannel (25 ml/min). For the purpose of controlling the micropreconcentrator temperature a Temperature Resistance Coefficient (TCR) of the Pt heater paste was measured. The value of TCR is 2026 ppm/°C.



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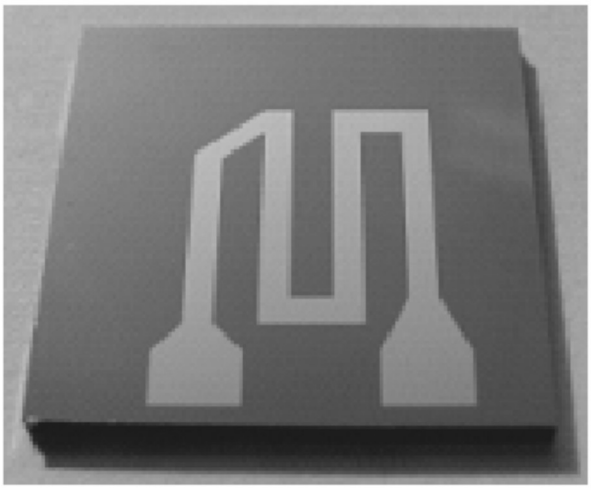


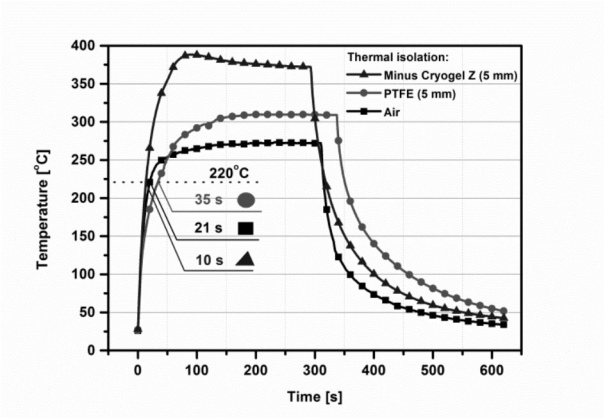
(b)

Figure 2: a) heater topology with dimensions, b) the micropreconcentrator - view of the heater side.

The desorption can be improved if the micropreconcentrator is placed in isolation. Using the Minus Cryogel Z material (Aerogels Poland Nanotechnology) with a very low thermal conductivity (0.0014 W/mK), the desorption temperature is achieved after approx. 10 s with a 7 W power supply (Fig.3a). To reduce power consumption the lateral dimensions have to be reduced. New micropreconcentrator concept is still under investigation. The power consumption vs. temperature was presented on Fig. 3b.

2.3 Preconcentration Process

Before taking the measurements, the micropreconcentrators are conditioned under specific parameters. The author used a typical time - temperature profile for adsorbent made with CMS (Carbon Molecular Sieve). To start with, the temperature was around 100°C for at least 30 minutes. Then, it was increased to 200°C and



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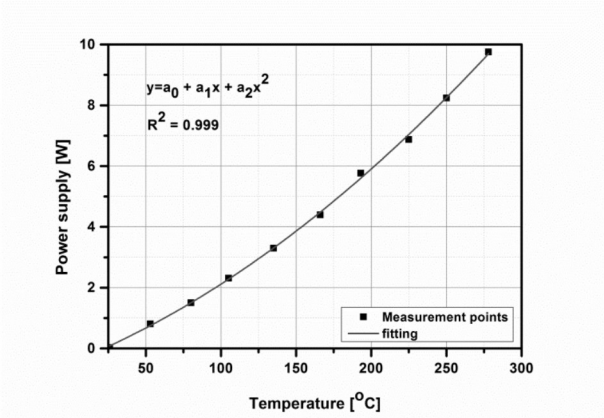


(b)

Figure 3: a) temperature changes over time for different thermal isolation, b) power supply vs. temperature for micropreconcentrator with Minus Cryogel Z isolation

300°C for 1h, respectively. At the end, the temperature was set to 350°C for around 30 minutes. The author used nitrogen (6N) as the carrier gas. The author previously investigated adsorbent materials from the Carbon Adsorbent Sampler Kit (Sigma-Aldrich, St. Louis, MO 63178, USA) which contains eight different adsorbents. On the basis of the obtained results and data provided by the company, Carboxen-1018 was selected as a promising material for breath analysis. During the experiment, the author used four gases with certified concentrations: acetone (80 ppm and 800 ppb), ethanol (500 ppm), propane (1000 ppm), and ethylbenzene (100 ppb). A schematic view of the measurement system is presented in Fig 4. The measurement system was built using a Drechsler gas washing bottle and a 6-port electrically-actuated microvalve. Five gas lines were connected to the bottle. Mass flow controllers (MKS Instruments, MA, USA) were used to control the flow rate, while synthetic air was used to obtain lower concentrations of the investigated biomarkers. The gas mixture flow rate was set to 25 ml/min (same as the car-

rier gas). The maximum obtained value was around 28 ml/min. This was due to several factors, such as the microchannel being completely filled with adsorbent material (Fig.1a), and the hole diameter in the glass cover being too small (100 μm).

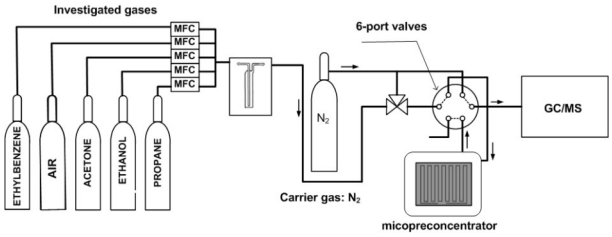


Figure 4: Gas preconcentration measurement system

Micropreconcentrator efficiency is measured using concentrator factors. The concentration factor is determined by (1):

$$CF = \frac{V_{sample}}{V_{desorbed}} = \frac{V_{sample}}{W_h \cdot u} \quad (1)$$

where: V_{sample} - sampled volume, $V_{desorbed}$ - desorbed volume, W_h - width of injection band (min), u - desorption flow rate (ml/min) [40]. According to Poiseuille's equation flow rate in preconcentrator could be determined by:

$$u = \frac{dV}{dt} = v\pi r^4 = \frac{\pi r^4 \Delta P}{8\eta L} \quad (2)$$

where: u - volumetric flow rate, V - volume (m³), t - time (s) , v is mean fluid/gas velocity along the length of the tube (m/s), r is the internal radius of the tube (m), ΔP is the pressure difference between the two ends (Pa), η is the dynamic fluid/gas viscosity (Pa·s), L is the total length of the tube in the x direction (m). The Poiseuille's law corresponds to Ohm's law for electrical circuits, where volumetric flow rate is analogous to the current and pressure drop is analogous to the voltage. In this case resistance is:

$$R = \frac{8\eta L}{\pi r^4} \quad (3)$$

Equation (3) describes resistance in the tube, where resistance is inversely proportional to the fourth power of the radius. Referring to equations (1), (2) and (3) we can pre-calculate concentration factor in designed preconcentrator structures. Unfortunately theoretical calculations usually are different than experimental results. The difference is correlated with compressible nature of some gases and with non-laminar flow through the preconcentrator channel. Theoretical calculations should be performed before the experiment in order to predict what could be expected.

The experiments have four stages: pre-purge, adsorption, purge, and desorption; each takes a specific length of time. The pre-purge stage was performed for at least 10 minutes under carrier gas to clean gas line connections and stabilize the pressure in the reference analyzing setup (GC/MS). The author used an SRI-310 GC with an AB-Plot Q capillary column and a MS Hiden HPR-20 system with high sensitivity (5 ppb for mass up to 510 amu).

The adsorption time was adjusted during the measurements to calculate the CF vs. adsorption time. After adsorption, the second purge step was set to 1 minute and desorption for at least 3 minutes. After 3 minutes, the investigated gases were fully desorbed (Fig. 5.)

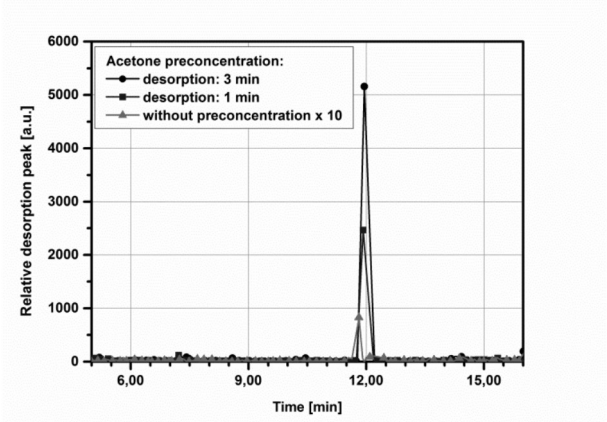


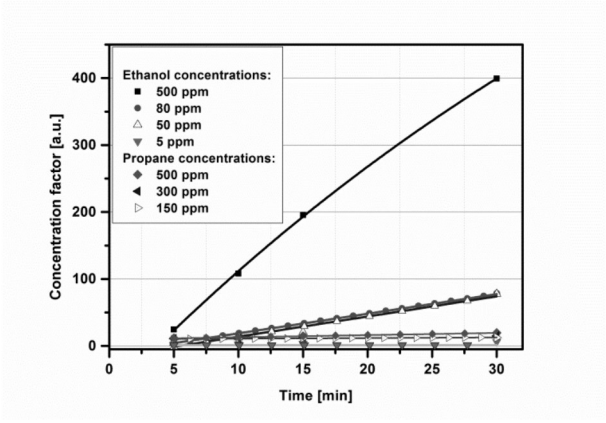
Figure 5: Desorption peak for different desorption time at constant flow rate set to 25 ml/min

The concentration factor was obtained for gas mixtures with various VOCs concentrations. Taking into account all the literature reports, the author measured the concentration factor for a single biomarkers, as well as for a mixture of diabetes biomarkers. Before conducting clinical studied, it is necessary to perform a number of basic investigations in the laboratory. It is essential to achieve repeatable measurement results for a wide range of concentrations.

3 Results

To start with, the author measured concentration factors for different concentrations of ethanol and propane separately. The results are presented in Fig. 6a. The maximum value of CF (400) was obtained for an initial concentration of ethanol of 500 ppm and 30 min adsorption time. The CF for 500 ppm, 50 ppm and 5 ppm of ethanol was 400, 77.8 and 6.5, respectively. The maximum CF for propane was 19.5 at an initial concentration of 500 ppm and 30 min adsorption time. Carboxen-1018 is useful for adsorption/desorption of

small analytes, such as C_2 - C_3 hydrocarbons. However, it is less well suited to propane (C_3H_8) and ethylbenzene (C_8H_{10}), even at initial concentrations in the ppm range. In the next measurements, concentration factors were obtained for a mixture of acetone (80 ppm) with ethanol and propane at different concentrations. The results are presented in Fig.6b. The highest CF value was obtained when acetone was mixed with 500 ppm ethanol, reaching approx. 2325 for 30 min adsorption time. The CF for acetone with propane at 500 ppm was approx. 215 at the same conditions.



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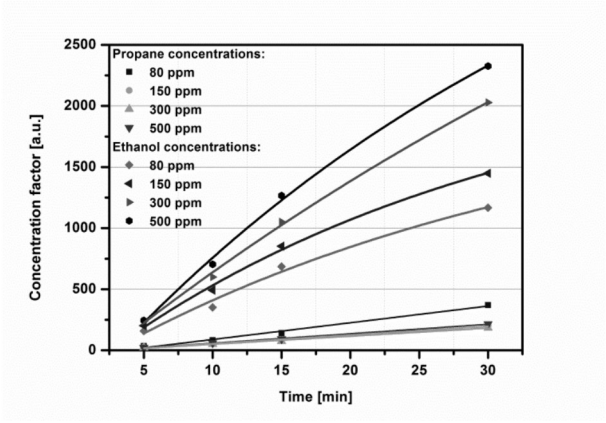
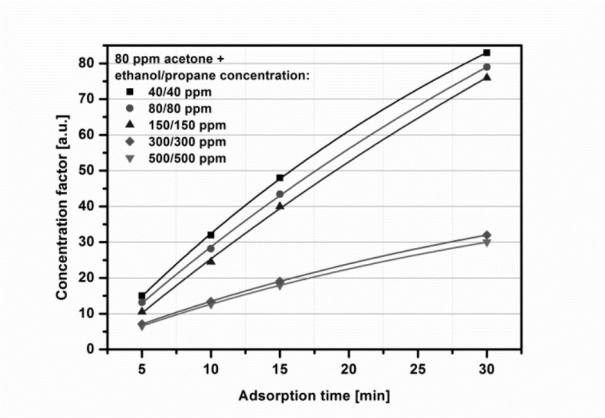


(b)

Figure 6: Concentration factor vs. adsorption time for the channel filled with Carboxen-1018 and different concentrations of: a) propane and ethanol, b) propane and acetone, ethanol and acetone

The next step in the laboratory experiments was measuring CF for a range of mixtures of acetone, ethanol and propane. The acetone concentration was set to 80 ppm and 800 ppb, and the ethanol/propane concentration was varied during the experiments. Concentration factors for such mixtures of gases vs. adsorption time are presented in Fig.7a. and Fig.7b, respectively.



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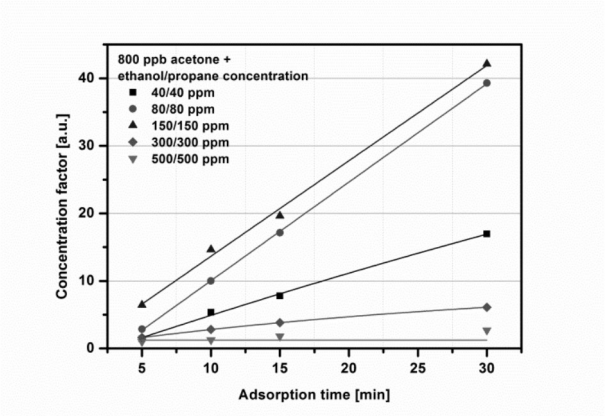


(b)

Figure7: Concentration factor vs. adsorption time for the channel filled with Carboxen-1018 and: a) 80 ppm acetone, b) 800 ppb acetone with different ethanol/propane concentrations,

The CF_{MAX} for different combinations of acetone and other diabetes biomarkers (at 5 and 30 min adsorption time) are presented in table 1.

Table 1: Maximum Concentration Factors obtained for various compositions of diabetes biomarkers

Diabetes biomarker name	Initial concentration of VOCs	Adsorption time [min]	CFMAX
Propane	500 ppm	5	11.70
		30	19.50
Acetone	800 ppb	5	3.77
		30	19.53
	80 ppm	5	360.00
		30	2831.00
Ethanol	500 ppm	5	24.60
		30	400.00
Ethylbenzene	100 ppb	5	1.00
		30	1.00

Ethanol + Acetone	500ppm + 80 ppm	5	244.45
		30	2324.38
	500 ppm + 800 ppb	5	1.30
		30	2.00
Propane + Acetone	80 ppm + 80 ppm	5	35.55
		30	376.63
	80 ppm + 800 ppb	5	20.00
		30	66.00
Ethanol + Propane + Acetone	40 ppm + 40 ppm + 80 ppm	5	15.00
		30	83.02
	150 ppm + 150 ppm + 800 ppb	5	6.42
		30	42.14
Ethylbenzene + Ethanol	100 ppb + 500 ppm	5	1.70
		30	1.95
Ethylbenzene + Propane	100 ppb + 500 ppm	5	1
		30	1.08
Ethylbenzene + Acetone	100 ppb + 80 ppm	5	18.30
		30	53.5
	100 ppb + 800 ppb	5	1
		30	1.12
Ethylbenzene + Acetone + Ethanol	100 ppb + 80 ppm + 5 ppm	5	12.25
		30	30.53
	100 ppb + 800 ppb + 5 ppm	5	1
		30	1.05
Ethylbenzene + Acetone + Ethanol + Propane	100 ppb + 80 ppm + 10 ppm	5	7.30
		30	25.12
	100 ppb + 800 ppb + 10 ppm	5	1.05
		30	2.00
Ethylbenzene + Acetone + Ethanol + Propane	100 ppb + 80 ppm + 5 ppm + 5 ppm	5	11.32
		30	30.00
	100 ppb + 800 ppb + 5 ppm + 5 ppm	5	1.50
		30	1.75

The final composition of gases consists of ethylbenzene, acetone, ethanol and propane. The ethanol concentration was changed, and acetone, ethylbenzene and propane concentrations were set to values that had previously been calibrated and certificated. The concentration factor results for this experiment are presented in Fig.8.

As it is shown in Fig.8. there is a linear correlation between concentration factor for the acetone and ethanol concentration in the composition of acetone (80 ppm), ethylbenzene (100 ppb), propane (5 ppm) and ethanol (5 - 500 ppm). The highest concentration factor for acetone is obtained for lower ethanol concentration. The measurements results confirmed, that there is evidently a significant lower adsorption capacity of

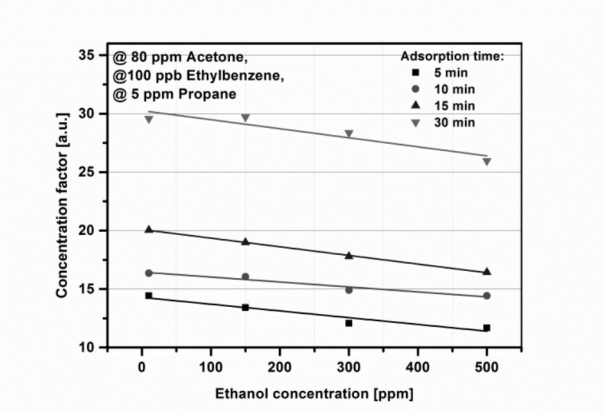


Figure 8: Concentration factor vs. ethanol concentration for the channel filled with Carboxen-1018 and 80 ppm acetone, 5 ppm propane and 100 ppb ethylbenzene.

the acetone in the present of interfering gases such as: propane and ethylbenzene. Due to fact, that Carboxen-1018 possess a large percentage of narrow (60-70 nm) micropores, is useful for the adsorption/desorption of small analytes, such as: C_2-C_3 hydrocarbons. The obtained concentration factor for acetone (30 min adsorption) was in the range 25-30 for different ethanol concentrations. To compare, the concentration factor was approx. 2831, 2324, 376, 53 for pure acetone, acetone with ethanol, acetone with propane and acetone with ethylbenzene, respectively (Table 1).

4 Prospectives

In the experiments, the GC/MS analysis setup was used only as the reference analyzer. In table 1 the concentration factors for different diabetes biomarkers concentration and adsorption time were presented. The micropreconcentrator with CFs >10 is suitable to use it with metal oxide (MOX) sensor array. A gas sensor array will be used in the final application. The author is currently developing arrays based on MOX sensors with a higher sensitivity and selectivity for diabetes biomarkers [41, 42]. MOX sensors are commonly used in many industrial and medical applications, including breath analysis [43]. However, the market still lacks sensors for the detection of diabetes biomarkers. Promising results were obtained by M. Righettoni *et al.* They proposed an acetone detector based on Si-doped WO_3 nanoparticles made in the gas phase. The acetone sensor responded to the 3 ppm acetone concentration [44]. Due to this, the preconcentration remains a useful method of detecting exhaled acetone and other diabetes biomarkers. The concentration factors can be improved further by choosing preconcentration of two or three steps. Each step should to be dedicated

to concentrating different VOCs. Before commercialization the breakthrough time has to be determined. It can be done using the Wheeler-Jonas equation (4). It is the most widely used to estimate the breakthrough time of organic compounds on activated carbon:

$$t_b = \frac{W_e W_B}{C_0 Q} - \frac{\rho_B W_e}{k_v C_0} \ln\left(\frac{C_0 - C_x}{C_x}\right) \quad (4)$$

where: t_b is breakthrough time (min), W_e the equilibrium adsorption capacity (g/g), W_B is the bed mass (g), C_0 is the challenged concentration (g/l), C_x is the fraction of C_0 where breakthrough is measured (g/l), k_v is kinetic rate coefficient (1/min), ρ_B - density (g/cm^3), Q - gas flow rate (ml/min).

To apply this equation the two parameters, W_e and k_v, must be determined. Only W_e can be determined independently using some analytics method, i.e. gas chromatography or mass spectrometry. The k_v must be determined empirically. However, the W_e in most cases is determined from a series of breakthrough experiments [45]. Even a slight deviation between the calculated equilibrium adsorption capacity and the effective adsorption capacity required for (4) may cause a significant error into the estimated breakthrough time. The effect of such error is discussed in [46]. Due to this limitation the t_b is somewhat difficult to predict. First, k_v cannot be measured directly experimentally. It has to be calculated either from the breakthrough time or from breakthrough curves. Second, there are different concept regarding how it should be calculated from (4). Some concepts are summarized in a review in paper [47]. So far, the three models for predicting adsorption rate coefficient have been developed. A model proposed by Jonas [48], an alternative model suggested by Wood [49]. Third model has been proposed by Lodewyckx and Vasant [50]. The major limitation of cited models is that they are not based on a systematic investigation of the parameters that might influence on adsorption rate coefficient, such as: velocity, inlet concentration, adsorbent material properties (carbon properties) and volatile organic compounds properties.

In this work the author presents the results of systematic investigation on concentration factor obtained in micropreconcentrator filled with Carboxen-1018 and for various concentration of the diabetes biomarkers. Such experiments are necessary for better understanding the fundamental behavior of adsorbent material under selected VOCs exposure. In the presented results, the following fitting equation was used (5):

$$y = A_1 - A_2 \cdot \exp(-kt) \quad (5)$$

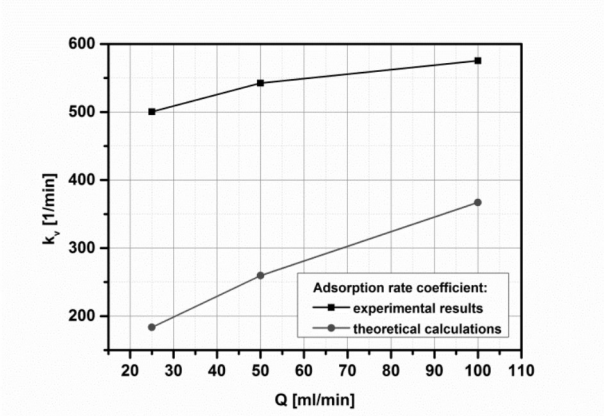
where: A_1, A_2, k - constant, t - adsorption time.

The experimental coefficient can be easily calculated from the fitting equation (5). Referring to equations (4) and (5) as well as data provided by the company we can pre-calculate adsorption rate coefficient in designed preconcentrator structures (6):

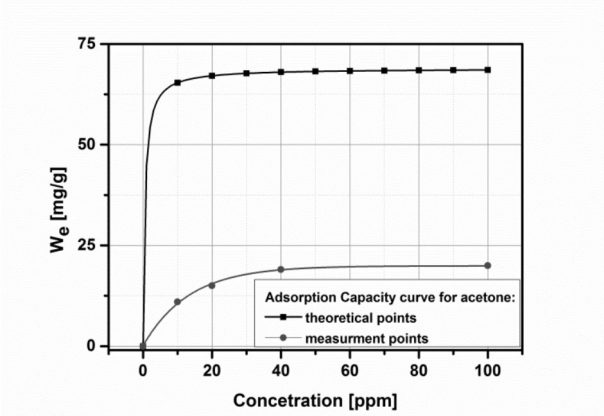
$$k_v = -\frac{\rho_B \cdot Q \cdot \ln(A_2)}{W_B} \quad (6)$$

where: W_B is the bed mass (g), ρ_B - density (g/cm^3), Q - gas flow rate (ml/min).

Fig.9a. shows the adsorption rate coefficient obtained from model proposed by Jonas [48] and from experimental results. Due to the fact that, k_v is a function of



(a)



(b)

Figure 9: a) Adsorption rate coefficient vs. gas flow rate calculated based on experimental results for micropreconcentrator filled with Carboxen-1018 and upon exposure to acetone as well as theoretical calculations from Jonas model, b) equilibrium adsorption capacity vs. concentration for acetone obtained from experimental results for micropreconcentrator filled with Carboxen-1018 and from theoretical calculations.

superficial velocity, microchannel geometry and particle shape/size, there are limits of the applicability of the estimated parameters. Thus, the k_v obtained from experimental results and mathematical calculations are not of the same order of magnitude. It is generally necessary to determine k_v and W_e empirically. The equilibrium adsorption capacity obtained from experimental results and theoretical calculations for acetone for micropreconcentrator filled with Carboxen-1018 are presented in Fig.9b. As it can be seen, for concentrations higher than 100 ppm the W_e for micropreconcentrator filled with Carboxen-1018 achieved a constant value.

The resulting data can then be used directly to estimate the breakthrough time as well as adsorbent mass, which would be required to efficiently preconcentrate acetone. However, the main aim is to estimated the breakthrough time for all of the examined vapors as well as to compare with those measured with humid air, which is still under investigations. The investigation results would be used to manufacture the micropreconcentrators with suitable geometrical dimensions. In other words, such results help to determine the microchannel geometry which provide suitable concentration factor for acetone and it can be used to preconcentrate acetone in breath.

5 Conclusions

Based on results reported by scientists, it can be assumed that a typical concentration of diabetes biomarkers in breath is a few hundred ppb. To analyze such concentrations using portable devices, it is necessary to use preconcentration methods. Exhaled breath contains many VOCs, although some would have been inhaled from ambient air. It needs to be analyzed before the experiment. In this paper the results obtained for the micropreconcentrator using silicon-glass technology filled with Carboxen-1018 are presented. The obtained concentration factor was approx. 2831 for 30 min adsorption time. Blanco *et al* [51] present the preconcentrator for benzene vapours. The obtained concentration factor was less than 400 for different adsorbent materials and different flow rates at 30 min adsorption time. Dow and Lang [52] present a micromachined preconcentrator for ethylene monitoring system. The obtained concentration factor was in the range of 40 - 120 for different adsorption time and desorption flow rate. Tian *et al* [53] present a novel micropreconcentrator employing a laminar flow patterned heater for micro gas chromatography. The obtained concentration factor was approx. 118 for acetone after 30 min adsorption time. However, the concentration factor obtained for xylene was approx. 2015. The CF is highly dependent on adsorption time, gas flow and desorption temperature. The obtained CFs are sufficiently high to use fabricated devices in diabetes biomarker analysis. The micropreconcentrator with concentration factors higher than 10 can be used as a part of portable microsystem. The obtained CFs for a single diabetes biomarkers as well as for a mixture of diabetes biomarkers are quite good in comparison with other results presented in the Introduction part. A microsystem with three-step preconcentration and gas sensor array is currently under investigation. High humidity of breath also needs to be taken into account, as does the humidity of ambient air.

6 Acknowledgments

This work was supported by the NCN Preludium Grant UMO-2013/09/N/ST7/01232

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Arrived: 20. 12. 2013
Accepted: 18. 03. 2014