# Design of a Breath Analysis Device for Self-monitoring and Remote Health-care

D. Germanese[1], M. D'Acunto,[1,2] and O. Salvetti[1]
[1]*CNR-ISTI, Institute of Information Science and Technology, National Research Council, via Moruzzi 1, Pisa, Italy*
[2]*CNR-ISM, Institute of Structure of Matter, National Research Council, via Fosso del Cavaliere 100, Roma, Italy*

Keywords: Self-monitoring, Breath Analysis, Home-care, Gas Sensors, Portable Device, Signal Processing.

Abstract: Technique as new as promising, breath analysis enables the monitoring of biochemical processes in human body in a non-invasive way. This is why it is drawing, more and more, the attention of scientific community: many studies have been addressed in order to find a correlation between breath volatile organic compounds (VOCs) and several diseases. Despite its potential, breath analysis is still far from being used in clinical practice. These are some of the principal reasons: (i)high costs for the standard analytical instrumentation; (ii)need of specialized personnel for the interpretation of the results; (iii)lack of standardized procedures to collect breath samples. Our aim is to develop a device, which we call Wize Sniffer (WS), based on commercial gas sensors, which is: (i)able to analyse breath gases in real time; (ii)portable; (iii)low-cost; (iv)easy-to-use also for non-specialized personnel. Another aim is to foster homecare, that means promote the purchase and the use, also in home environment, of such device. The Wize Sniffer is composed of three modules: signal measurement, signal conditioning and signal processing. To satisfy the goal of developing a device by using low-cost technology, its core is composed of an array of commercial, low cost, semiconductor-based gas sensors, and a widely employed open source controller: an Arduino board. To promote the use of such device also in home environment, and foster its daily use, it is programmed in order to send breath test results also to a remote pc: the pc of user's physician, for example. In addition, the design of the Wize Sniffer is based on a modular configuration, thus enabling to change the type of the gas sensors according to the breath molecules to be detected. In this case, we focus our attention to the prevention of cardio-metabolic risk, for which the healthcare systems are registering an exponential growth of social costs, by monitoring those dangerous habits for cardio-metabolic risk itself.

## 1 INTRODUCTION

Nowadays, the gold standard methods for gas analysis are techniques such as Gas Chromatography (GC), or Proton Transfer Reaction- Mass Spectrometry (PTR-MS), and they can be used to analyze also breath gases with high accuracy and sensitivity (D. Guo et al., 2010). On the other hand, these methods are very expensive; moreover, the analysis, very time consuming, can be performed only by specialized personnel.

More recent approaches exploit e-noses to analyze the breath. E-noses, based on gas sensors, may lose in sensitivity and accuracy with respect GC/PTR-MS, but they are able to detect in real time some specific molecules. The most commonly used sensors for e-noses are solid state gas sensors. Their working principle is based on a reversible interaction of the gas with the surface of a solid state material, which results in a physical effect, depending on the sensing material, used to achieve the detection of gases in solid state gas sensors. For example, optical processes employ infra-red absorption of gases, whilst chemical processes allow detecting the gas by means of a selective chemical reaction with a reagent. The detection of this reaction can be performed by measuring the conductivity change of gas-sensing material, or the change of capacitance, work function, mass, optical characteristics or reaction energy released by the gas/solid interaction.

E-noses are designed for broader applications (environmental, industrial ones), rather than for medical field. Nowadays, the e-noses that are used for breath analysis exploit very expensive approach to detect breath compounds, and they are suitable for one (or, at most, two) molecule only; we can mention Bedfont's PiCO+Smokerlyzer (able to



Germanese, D., D'Acunto, M. and Salvetti, O.
Design of a Breath Analysis Device for Self-monitoring and Remote Health-care.
In *Doctoral Consortium (DCBIOSTEC 2016)*, pages 9-14

detect the exhaled Carbon Monoxide) and NOBreath (able to detect the exhaled Nitric Oxide), (www.bedfont.com/shop/smokerlyzer, www.bedfont.com/shop/nobreath), Toshiba's research prototype Breathalyzer (able to detect the exhaled Acetone) (www.toshiba.co.jp/about/press/2014_03/pr1801.htm).

In this work we present the first prototype of the Wize Sniffer (WS), a portable device based on chemical semiconductor-based gas sensor array which represents a low-cost effort to analyze exhaled breath in real time. In particular, the WS is able to monitor in real time a specific number of breath molecules related to noxious habits for cardio-metabolic risk and oxidative stress. Not only: an Arduino board is programmed to read sensors' output and send breath analysis results to a remote personal computer, which might be the one's own, or the physician's one. In addition, the modular configuration of the WS enables to change the gas sensors to detect other types of breath molecules thus personalizing the device. The use of a low-cost technology, the compactness of the device and the possibility to send the results also to a remote personal computer, allow for a user's daily screening, also in home environment.

## 2 BREATH COMPOUNDS DETECTED BY THE WIZE SNIFFER AND CLINICAL IMPLICATIONS

Breath is composed of oxygen, carbon dioxide, water vapor, nitric oxide, and a large number of volatile organic compounds (VOCs) which origin can be endogenous (that means, they originate from metabolic processes that occurs in human body and participate to alveolar exchanges) or exogenous (that means, they derive from food, or beverages, or dermal adsorption) (W. Miekisch et al., 2004).

As a consequence, we can affirm that each breath contains fundamental information about the internal state of a person. Indeed, more than 35 of the VOCs present in our breath have been assessed as *biomarkers* for particular diseases or metabolic disorders: for example, increased level of ammonia in breath may be related to renal diseases (D. Guo et al., 2010); ethane and pentane derive from lipid per-oxygenation in case of oxidative stress (M. Phillips et al., 2003; F. Pabst et al., 2007).

We focus our attention on a set of breath molecules, some of which related to those noxious habits for cardio-metabolic risk, such as smoking and alcohol intake. The molecules detected by the Wize Sniffer are listed here:

- **Carbon monoxide (CO):** it is naturally produced by the action of heme oxygenase on the heme for haemoglobin breakdown. This produces carboxyhemoglobin, which is more stable than oxyhemoglobin. Indeed, an increase of CO leads haemoglobin to carry less oxygen through the vessels. CO is present in cigarette smoke, very dangerous for cardio-metabolic risk. Its baseline value in a healthy subject is round about 3.5ppm (up to 14-30ppm in smokers);
- **Hydrogen ($H_2$):** it derives from the breakdown of the carbohydrates in the intestine and in the oral cavity by anaerobic bacteria. Its baseline value is round about 9.1ppm;
- **Ammonia ($NH_3$):** an increase of $NH_3$ in blood may be caused by cigarette smoke, renal failure, cardiac failure, changes in cardio-circulatory system. Its baseline value is round about 0.42ppm;
- **Ethanol ($C_2H_6O$):** exhaled ethanol can be classified as endogenous or exogenous. Exogenous Ethanol comes from alcoholic drink. It is recognized that ethanol breakdown leads to an accumulation of free radicals into the cells, a clear example of oxidative stress. Ethanol may cause arrhythmias and depresses the contractility of cardiac muscle. Its baseline value is round about 0.62ppm;
- **Carbon dioxide ($CO_2$) and Oxygen ($O_2$):** Their variations show how much $O_2$ is retained in the body, and how much $CO_2$ is produced as a by-product of cellular metabolism. In most forms of lung diseases and some of congenital heart disease (cyanotic lesions-bluish-grey discoloration of the skin, lack of $O_2$ in the body), a decrease of $CO_2$ exhaled rate is commonly observed. It must be noted that the breathing rate influences the level of $CO_2$ in the blood: slow breathing rates cause Respiratory Acidosis (i.e., increase of blood $CO_2$ partial pressure, which may stimulate hypertension or heart rate acceleration). On the contrary, too rapid breathing rate leads to hyperventilation, which may provoke Respiratory Alkalosis (i.e., decrease of blood $CO_2$ partial pressure, no longer fits its role of vasodilator, leading to possible arrhythmia or heart trouble). Their

baseline values are round about 40000ppm for $CO_2$ and 13-15% for $O_2$;

- **Hydrogen Sulfide ($H_2S$):** it is a vascular relaxant agent, and has a therapeutic effect in various cardiovascular diseases (myocardial injury, hypertension). In general, $H_2S$ could have therapeutic effect against oxidative stress due to its capability to neutralize the action of free radicals. Its baseline value is round about 0.33ppm.

# 3 WIZE SNIFFER'S HARDWARE AND SOFTWARE ARCHITECTURE

A block scheme of WS is shown in Figure 1. Basing on this scheme, we can describe the framework of WS as composed of three modules: signal measurement, signal conditioning and signal acquisition.

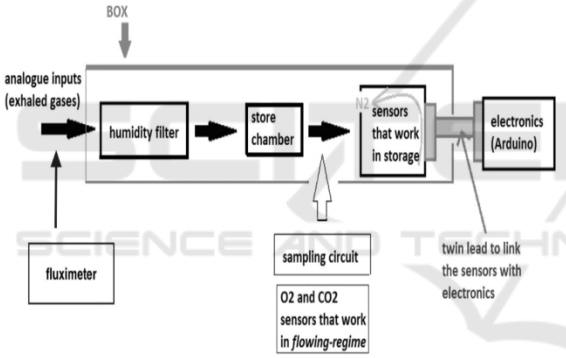


Figure 1: Schematic sketch of the WS's architecture. The core is an acquiring device which includes a gas sampling box (of 600ml according to the tidal volume (D. Shier et al., 2007) and made up of ABS and Delrin) where six gas sensors are placed, and a micro-controller board. Since the sensors' output is affected by the water vapour present in exhaled gases, a HME filter is placed at the beginning of a corrugated tube reducing the humidity from initial 90% to 60-70%. In addition, the humidity percentage is monitored within the sampling box, as well as the temperature. Other two gas sensors having shorter response time work in flowing-regime by means of a sampling pump, which works at 120 ml/s. A flow-meter monitors the exhaled breath volume. A flushing pump purges the chamber and recovery the sensors' steady state between two consecutive measures.

The measurement circuit (store chamber + gas sensor array) detects the breath molecules and transforms gas signals into electronic signals, which are processed by the microcontroller board. The microcontroller used in our system is a low cost, widely employed open source controller: Arduino Mega 2560 with Ethernet module. Table 1 summarizes all the VOCs detected by the WS, and the gas sensors used. Most of the gas sensors are manufactured by Figaro Engineering, and they are not expensive at all. They are based on a metal-oxide semiconductor sensing element, that is, a variation of sensing element's internal resistance occurs when it detect gas particles.

Table 1: VOCs to be detected and gas sensors used.

| Breath molecule | Sensor and its sensitivity (ppm) |
|---|---|
| Carbon monoxide | TGS2442 (50-1000ppm), TGS2620 (50-5000ppm) |
| Ethanol | TGS2602 (1-10ppm) and TGS2620 (50-5000ppm) |
| Carbon dioxide | TGS4161, 0-40000 |
| Oxygen | MOX20, 0-16% |
| Hydrogen sulfide | TGS2602, 1-10 |
| Ammonia | TGS2444 (10-100ppm) and TGS2602 (1-10ppm) |
| Hydrogen | TGS821 (10-5000ppm), TGS2602 (1-10ppm) and TGS2620 (50-5000ppm) |

As briefly described in Section 4, in order to receive breath test results from the WS even on a remote Personal Computer (for example, the physician's one), a client-server architecture is implemented. It means, the Arduino Mega2560 processes sensors' raw data, executes a daemon on port 23, waits a command line from the PC and provides the data. A measure is considered valid if the user's exhaled volume equals at least 600ml (store chamber's volume, see Figure 1). How the WS microcontroller board analyzes row data is described in the next section. In figure 2 the final configuration of the Wize Sniffer is shown.

Figure 2: Final configuration of the first prototype of the Wize Sniffer.

# 4 WS FUNCTIONALITY TESTS AND DATA PROCESSING

If, on one hand, developing a device by using low-cost technology means facilitating its purchase and use, on the other hand, especially in this case, this may represent a challenge. A challenge in terms of data processing, because, on one side, semiconductor-based gas sensors are, of course, very low cost, very easy to be integrated and very sensitive; on the other side, they are not selective and they are affected by cross-sensitivity (in Table 1 we can note that the sensors TGS2602 and TGS2620 detect more than one molecule). Their non-selectivity and their cross-sensitivity have implications on data analysis, making it very complicated, especially if a quantitative analysis of the detected molecules should be done. Moreover, the behaviour of such type of gas sensors is not linear.

For our purposes, we aim to make a quantitative analysis of the detected molecules. It means we aim to calculate the concentration (in ppm) of the detected breath molecules. Such approach requires:

- an accurate reconstruction of the sensors' sensitivity curves under our measurement conditions (32°C+/-10% and 70%RH+/-10%, it means, conditions that are very close to the breath physiological ones);
- a model to describe how each input (it means, each molecule) influences the output (it means, the variation in sensors' internal resistance). The simplest model may be represented by a linear regression;
- an accurate evaluation of sensors' cross sensitivity;
- an accurate evaluation on how temperature and humidity affect sensors' outputs;
- a model to calculate the concentration of each molecule.

Meanwhile, since this approach is taking considerable time, we are exploiting a more traditional approach for data analysis based on features extraction (by means of Principal Component Analysis) and classification (by means of K-Nearest Neighbour algorithm). In any case, a signal pre-processing is needed to compensate drifts and sample-to-sample variations. This more traditional approach has been implemented first using a synthetic database of 114 subjects containing individuals of different age (in the range 30-60 years old), habits (moderate/heavy smokers, non-smokers, teetotal, moderate/heavy drinkers), lifestyles (sedentary/ sporty, etc.), and body type. This database was implemented as if all the gas sensors worked correctly, in ideal conditions. Plotting the results of the analysis of the synthetic database by the PCA (Figure 3), several clusters, highlighted by means of an algorithm based on KNN (Figure 4) can be identified.

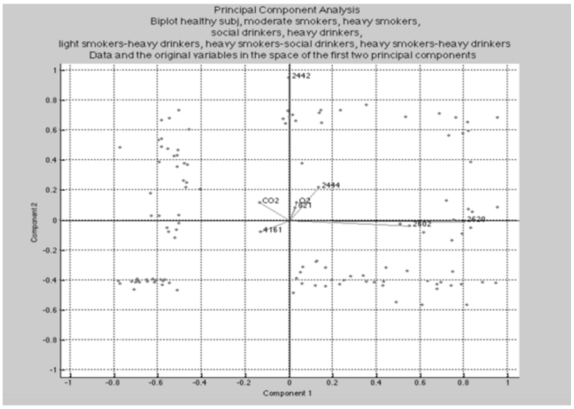


Figure 3: Biplot of the synthetic database in the first two principal components. Several clusters can be distinguished.

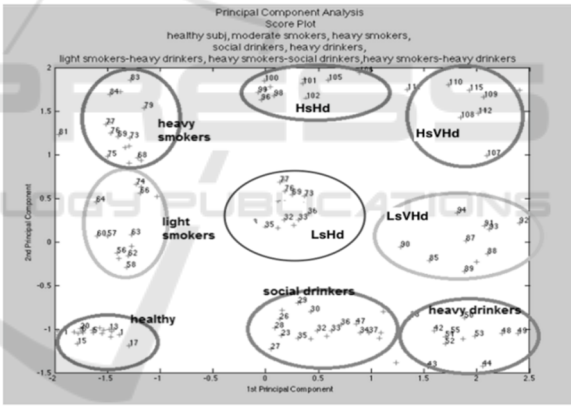


Figure 4: Score plot of the synthetic database analysed by Principal Component Analysis; LsHd = Light Smokers, heavy drinkers; LsVHd = Light Smokers, very heavy drinkers; HsHd= Heavy Smokers, heavy drinkers; HsVHd = Heavy Smokers, very heavy drinkers. For "Healthy class" we intend subjects with low cardio-metabolic risk.

Then, a measuring protocol has been draft in order to test the Wize Sniffer on a population of 26 healthy individuals, with different age (range 30-60 years old), habits, lifestyles, body type. Why just healthy? Because in this case we are focusing on cardio-metabolic risk, not on a disease. By detecting molecules related to those noxious habits for cardio-metabolic risk, the Wize Sniffer should not make a diagnosis, but should only help the user to monitor his/her well-being and lifestyle. Indeed, as shown in

Figure 4, the classifier classifies the subjects according to their habits. For a single-subject monitoring, further statistical analysis over long time periods should be carried out to evaluate if the subject increases/decreases his/her cardio-metabolic risk basing on a change of class.

For the measuring protocol, the methodological issues about breath sampling procedure have been taken into account (W. Miekisch et al., 2008). In practice are used three methods of sampling: "alveolar (end-tidal) sampling", if only systemic volatile biomarkers are to be assessed, "mixed expiratory air sampling" (which corresponds to a whole breath sample), "time-controlled sampling" (which corresponds to a part of exhaled air sampled after the start of expiration; this method shows large variations of samples compositions because of wide variations of individual breathing manoeuvers). For our purposes, mixed expiratory air sampling method was chosen, since our interest was focused on both endogenous and exogenous biomarkers. In addition, since the composition of single breaths may vary considerably from each other, because of different modes and depth of breathing, in order to average breath-by-breath fluctuations in composition due to the irreproducible lung emptying and flow variations (F. Di Francesco et al., 2008), we preferred a sampling of multiple (three) quite breaths.

The KNN classifier was able to correctly classify 20/26 subjects, as shown in Table 2. While an alcohol consumption up to 1-2 Alcohol unit/ day is often considered not dangerous (in healthy subjects), smoking is considered very noxious in any case.
We can note that the classifier seems to be not able to recognize smoker subjects. Actually this may be due to Carbon Monoxide sensor which has a minimum LOD of 50ppm (very high), thus resulting not able to detect Carbon Monoxide even in heavy smoker subjects. Indeed, we are testing the performances of another Carbon Monoxide semiconductor-based gas sensor, MQ-7, which should be more sensitive and it has a lower LOD (round about 20ppm, but we are evaluating its response also to lower concentration, for example 2-5ppm). In addition, its cost is lower than the one of CO Figaro gas sensor.

Table 2: Outcome of the KNN classifier used for classify WS data. In the I column, the subject's ID; in the II column subject's habits are reported; in the III column the outcome of the KNN classifier; in the IV column the right/wrong classification is commented.

AU= Alcohol unit; CIG.= cigarette; D= day; W= week

| Subj ID | Habits | Classification | Comment |
|---|---|---|---|
| 215 | 1 AU/D | No risk | ok |
| 218 | 1 AU/twice a W | No risk | ok |
| 211 | 12-13 CIG / D; 1 AU / 4-5 times a W | No risk | heavy smoker |
| 201 | 1 AU /once a W | No risk | ok |
| 207 | 1 AU/1-2times a W | No risk | ok |
| 213 | teetotal, non smoker | No risk | ok |
| 208 | 1 AU / 3 times a W | No risk | ok |
| 221 | teetotal, non smoker | Heavy Drinker | No risk |
| 220 | 1 AU /2 times a W | Heavy Drinker | No risk |
| 214 | 1 AU < once a W | No risk | ok |
| 206 | 1 AU/5-6times a W | No risk | ok |
| 205 | 1 AU 3 times a W | No risk | ok |
| 223 | 2 CIG /D; 1 AU / twice a W | No risk | ok |
| 212 | 1 AU / D | No risk | ok |
| 216 | 1 AU / once a W | No risk | ok |
| 217 | teetotal, non smoker | No risk | ok |
| 203 | 1 AU < once a W | No risk | ok |
| 209 | 1 AU < once a W | No risk | ok |
| 202 | 1 AU/5-6times a W | No risk | ok |
| 210 | 1-2 AU / D | No risk | ok |
| 225 | 4 CIG /D; 1 AU < once a W | No risk | Light smoker |
| 224 | 1 AU < twice a W | No risk | ok |
| 204 | 1-2 CIG /D; 1 AU < 2 times a W | Heavy Drinker | Light smoker |
| 219 | 1 AU/2 times a W | No risk | ok |
| 226 | 1 AU /once a W | No risk | ok |
| 222 | 10-15 CIG / D; 1 AU / once a W | No risk | heavy smoker |

# 5 CONCLUSIONS

Here we described the first prototype of a low-cost, portable device for the *self*-monitoring of those noxious habits for cardio-metabolic risk by detecting in the breath molecules principally related to smoking habit and alcohol intake. Anyway, its modular configuration and its ease of use allow changing the type of gas sensors according to the breath molecule to be detected, and the disorder to be monitored. The low cost and compactness of the device allow for a daily screening that, even if without a real diagnostic meaning, could represent a pre-monitoring, useful for an optimal selection of more sophisticated and standard medical analysis.

Further studies will be addressed in order to improve the performances of the WS, and to investigate the criticalities of such type of device and of breath analysis in general. In particular:

- the metabolic pathway of the breath molecules to be detected will be studied in depth;

- breath sampling methods will be further investigated. A standardized procedure for breath sampling may be very useful, since the composition of each breath is largely influenced by many factors, such as lung volume (Jones J.G., 1967), posture (Anthonisen N.R. et al., 1970), flow rate (Jones J.G. and Clarke S.W., 1969), ambient air (F. Di Francesco et al., 2008);
- as described in Subsection 5.3, a model to calculate the concentration of the detected molecules, based on the non-linear behaviour of semiconductor gas sensors, will be implemented; then, the quantitative analysis performed by the Wize Sniffer may be compared to the one performed by the gold standard (Mass Spectrometry, for example);
- the number of functionality tests will be increased, and more experimental results will be provided;
- the possibility to develop ad-hoc gas sensors based on semiconductor polymers as sensing element will be investigated (Ding B. et al., 2009).

## ACKNOWLEDGEMENTS

This work was funded in the framework of the Collaborative European Project SEMEOTICONS (SEMEiotic Oriented Technology for Individuals CardiOmetabolic risk self-assessmeNt and Self-monitoring), grant N. 611516.

Massimo Magrini, Paolo Paradisi, Marco Righi, and COSMED s.r.l. are warmly acknowledged for useful support.

## REFERENCES

Anthonisen N. R., Robertson P. C. and Ross W. R., 1970. Gravity-dependent sequential emptying of lung regions. In *J. Appl. Physiol., 589-95*.

Di Francesco F., Fuoco R., Trivella M., Ceccarini A., 2005. Breath Analysis: trends in techniques and clinical applications. In *Microchemical Journal, vol.79, no 1-2, pp.405-410*.

Di Francesco F., Loccioni C., Fioravanti M., Russo A., Pioggia G., Ferro M., Roehrer I., Tabucchi S., Onor M., 2008. Implementation of Fowler's method for end-tidal air sampling. In *Journal of Breath Research*.

Ding B., Wang M., Yu J., Sun G., 2009. Gas sensors based on electrospun nanofibers. In *Sensors 2009.*

Guo D., Zhang D., Li N., Zhang L., Yang J., 2010. A novel breath analysis system based on electronic olfaction. In *IEEE Transaction on Biomedical Engineering*.

Jones J.G.., 1967. The effect of pre-inspiratory lung volumes on the result of the single breath $O_2$ test. In *Respiratory Physiology, 375-85*.

Jones J.G., Clarke S.W., 1969. Effect of expiratory flow rate on regional lung emptying. In *Clin. Sci. 343-56*.

Miekisch W., Kischkel S., Sawacki A., Lieban T., Mieth M., Schubert J.K., 2008. Impact of sampling procedures on the result of breath analysis. In *Journal of Breath Research*.

Miekisch W., Schubert J.K., Noeldge-Schomburg G.F.E., 2004. Diagnostic potential of breath analysis- focus on volatile organic compounds. In *Clinica Chimica Acta, 347, pp.25-39*.

Pabst F., Miekisch W., Fuchs P., Kischkel S., Schubert J.K., 2005. Monitoring of oxidative and metabolic stress during cardiac surgery by means of breath biomarkers: an observational study. In *Journal of Cardiothoracic Surgery, 2:37*.

Phillips M., Cataneo R. N., Greenberg J., Grodman R., Salasar M., 2003. Breath Markers in oxidative stress in patients with unstable angina. In *Heart Disease, vol.5*.

Risby T.H. and Solga S.F., 2006. Current status of clinical breath analysis. In *Applied Physics B 85, pp.421-426.*

Shier D., Butler J., Lewis R., 2007. Hole's Human Anatomy & Physiology . *11th Ed., McGraw-Hill*.