A Low Cost Technology-based Device for Breath Analysis and Self-monitoring

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***Abstract*—Here, we describe the development of a portable device, based on low cost technology, able to collect and analyze in real time the composition of the breath. Despite its great potential, breath analysis is not widely used in clinical practice: high costs for standard analytical instrumentation (i.e., gas chromatograph-mass spectrometer), the need for specialized personnel able to read the results and the lack of standardized protocols to collect breath samples, set limits to its exploitation. The presented device, named *Wize Sniffer*, is based on commercial gas sensors and a widely employed open-source controller; in addition, it is very easy to use also for non-specialized personnel. The *Wize Sniffer* is composed of three modules: signal measurement, signal conditioning and signal processing. The idea was born in the framework of the European SEMEiotic Oriented Technology for Individual's CardiOmetabolic risk self-assessmeNt and Self-monitoring (SEMEOTICONS) Project, in order to monitor individual's lifestyle by detecting in the breath those molecules related to the noxious habits for cardio-metabolic risk. Nonetheless, the modular configuration of the *Wize Sniffer* makes it usable also for other applications by changing the type of the gas sensors according to the molecules to be detected.**

Keywords–Bio-signals; Breath analysis; Signal processing; E-noses; Semiconductor gas sensors.

I. INTRODUCTION

Breath analysis is a technique as new as promising. On one hand, it enables the monitoring of biochemical processes: the volatile organic compounds (VOCs) from the metabolic processes are generated within the body, travel via the blood, participate to the alveolar exchanges and appear in exhaled breath; on the other hand, breath is easily and non-invasively accessible [1], [2], [3]. Many studies aim for assessing the clinical potential of breath analysis: exhaled pentane and ethane were investigated as lipid per-oxygenation product in case of oxidative stress [4]; breath ammonia can be a useful biomarkers both for the evaluation of clinical treatments in case of renal diseases [5], [6] and for monitoring the level of severity in case of liver diseases [7]. Nonetheless, despite its great potential, the use of breath analysis in clinical diagnostic is limited because of the high costs of the specific, high accurate instrumentation (i.e., gas chromatograph, mass spectrometer) and the need of expert personnel to perform the analysis, which also are very time consuming [5].

Recently, e-noses are gaining the attention of the scientific community. Formerly designed for broader applications (environmental gases monitoring, for instance), in recent years the idea of exploiting e-noses also for clinical applications has been arisen [8]. E-noses allow for performing breath analysis in a very short time, being quicker than a gas chromatograph. Since they are able to follow the trend in time of breath molecules, in many studies they have been employed in different fields of medicine: in oncology, for instance, to monitor volatile biomarkers related to cancer [9], in infectiology [10], in respiratory medicine to evaluate asthma [11]. Nevertheless, the majority of such e-noses exploit very expensive technology [12], [13] or requires complex circuitry [14], [15]. By developing the *Wize Sniffer* (WS), presented in this paper, we aimed to overcome this limitations:

- it is a portable device for the monitoring of a number of breath molecules in real time;
- it is entirely based on low cost technology: the employed gas sensors are commercial, semiconductor-based and easily embeddable in the circuitry; breath signals are analyzed by a widely employed open source controller: Arduino Mega2560;
- the WS is very easy to use, also for non-specialized personnel. However, it is programmed in order to send breath analysis results also to a remote care center.

The WS was conceived in the framework of SEMEOTICONS European Project [16]. It aimed to develop the *Wize Mirror*, a multi-sensory platform having the appearance of a mirror, able to assess individual's well-being state by detecting in the human face all those signs related to cardio-metabolic risk [17]. The WS was designed to be integrated in *Wize Mirror*'s hardware platform in order to detect in human breath the molecules related to those noxious habits for cardio-metabolic risk: alcohol intake, wrong diet,

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smoke. Not only: we aimed to develop a device, which could be also used in a stand-alone configuration and for broader applications, thanks to its modular configuration [18], [19].
In the paper, Section II lists the molecules detected by the WS and describes the device's general architecture; Section III explains the WS functionality tests and the experimental results, later discussed in Section IV.

II. The Wize Sniffer, how it works

A. Breath compounds detected by the WS

The WS is composed of an array of semiconductor-based gas sensors able to detect those breath VOCs considered as indices of noxious habits for cardio-metabolic risk:

- **Carbon monoxide** (CO): it is the major compound of cigarette smoke and it is very dangerous, even in minimal part. Its baseline value for a non-smoker subject is round about 3.5ppm, and it reaches 14-30ppm in smokers;
- **Oxygen and carbon dioxide** (O_2 and CO_2): their variations can be considered as a measure of the metabolism, that means, how much O_2 is retained in the body, and how much CO_2 is produced as a by-product of cellular metabolism. Their baseline values are respectively 40000ppm and 13-15%;
- **Hydrogen** (H_2): it is related to the carbohydrates breakdown in the intestine and in the oral cavity by anaerobic bacteria. Its baseline value is round about 9.1ppm, but it may vary from an individual to another, especially in case of lactose intolerance;
- **Ethanol** (C_2H_6O): it derives from alcoholic drinks. Ethanol breakdown leads to an accumulation of free radicals into the cells, causing oxidative stress. Its baseline value is round about 0.62ppm;
- **Hydrogen sulfide** (H_2S): it is a vascular relax agent; for instance, it has a therapeutic effect in hypertension. Its baseline value is round about 0.33ppm.

B. Wize Sniffer, hardware and software

In Figure 1, WS' hardware is shown. The user blows once into a disposable mouthpiece, placed at the beginning of a corrugated tube. A flowmeter allows for assessing the exhaled gases volume. A heat and moisture exchanger (HME) filter absorbs the water vapor present in exhaled breath, reducing the humidity which affects gas sensors' behavior. The gases reach the sampling box (whose capacity is 600ml according to the tidal volume [20]), which can be considered as the signal measurement module. Indeed, within the sampling box, made up of ABS and Delrin, six semiconductor-based gas sensors are placed. Other two gas sensors work in *flowing regime* by means of a sampling pump, which inject the gases from the sampling box at a fixed rate (120ml/sec). Within the gas sampling box also a sensor for temperature and humidity (Sensirion SHT11) is placed. Sensors' output are pre-processed by a signal conditioning module. A series of voltage buffer amplifiers is used to transfer sensors' signal from the measurement module to the micro-controller board: an Arduino Mega2560 with Ethernet module (which is low cost, widely employed and has an open source integrated development environment). At the end of a breath test, a flushing pump "purges" the sampling box to recovery the sensors' steady state.

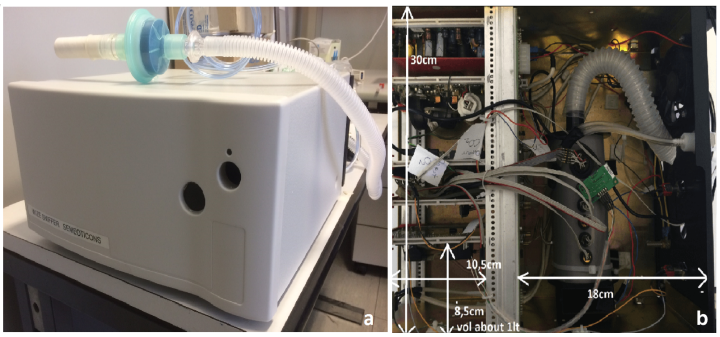

Figure 1. Wize Sniffer's hardware. a) external configuration; b) internal configuration.

In Table I, all the gas sensors are listed. Our choice was to employ MOS-based gas sensors, manufactured by Figaro Engineering, because of their long life, strong sensitivity, rapid recovery; in addition, they are low cost (20-30Euro on average) and easy to be integrated in the circuitry. As mentioned before, humidity strongly affects their behavior, as well as cross-sensitivity [21], which makes these sensors be non-selective.

TABLE I. MOS-based gas sensors integrated in the Wize Sniffer's measurement module.

Detected molecule	*Sensor*	*Best detection range*
Carbon monoxide	TGS2442	50-1000ppm
	MQ7	20-200ppm
	TGS2620	50-5000ppm
Ethanol	TGS2602	1-10ppm
	TGS2620	50-5000ppm
Carbon dioxide	TGS4161	0-40000ppm
Oxygen	MOX20	0-16%
Hydrogen sulfide	TGS2602	1-10ppm
Hydrogen	TGS821	10-5000ppm
	TGS2602	1-10ppm
	TGS2620	50-5000ppm
	MQ7	20-200ppm
Ammonia	TGS2444	1-100ppm
	TGS2602	1-50ppm

The aim of developing a device which could be used also in a stand-alone configuration, and which could be useful for user self-monitoring and self-surveillance, also in home environment, is evident about software implementation. We implemented a client-server architecture (Figure 2) in order to send breath data also to a remote personal computer. It means that, after performing a test and processing the results, the device, thanks to an internet connection and a communication protocol, can send the results to the family doctor, for instance. For this purpose, Arduino is programmed to process sensors' raw data and to execute a daemon on port 23. By implementing a Telnet server, it waits a command line from the remote personal computer and provides the data.
Finally, in Figure 3, WS' operation modes are shown. In the smaller picture, the WS is working as a *Wize Mirror*'s tool. In the other picture, the WS is working as a stand-alone device.

III. Wize Sniffer functionality tests and data analysis

Breath analysis performed by low-cost technology based gas sensors is a great challenge. If, on one hand, semiconductor-based gas sensors are low cost, robust and very

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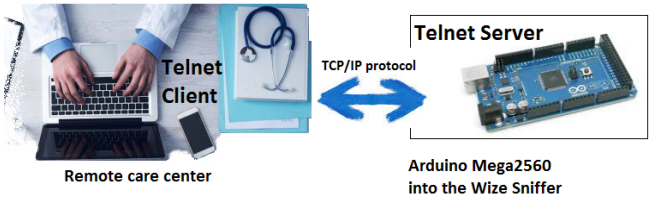

Figure 2. Wize Sniffer's client-server architecture including Arduino Mega2560 with Ethernet module

Figure 3. The two Wize Sniffer's configurations.

simple to integrate in the circuitry, on the other hand, their behavior is strongly affected by humidity and cross-sensitivity. It means that there is not a single sensor for each compound, but each sensor may be sensitive to many VOCs. As a consequence, the estimation of the breath molecules' concentration is an arduous challenge. Nevertheless, we tried to do a step toward this direction: we investigated gas sensors' sensitivity in our measurement conditions (30C+/-7%, 70%RH+/-5%, that are the ones that occur in the sampling box during a breath test). Not only, we also investigated how the several breath molecules influence each other in the chemical interaction with the sensors' sensing element.

Moreover, breath gases are something extremely variable: breath composition may vary according to heart rate, breath flow rate [22], posture [23], ambient air [24], lung volume [25], breath sampling mode [26]. Exhaled breath is affected by a strong inter-variability (among different subjects), and also by a marked intra-variability (relative to the same subject). As summarized in Figure 4, we have to face first with an uncertainty of measure relative to those factors that affect the gas sensors' behavior; then, we have also un uncertainty due to all the physiological conditions that influence breath composition. For instance, in our case, also factors such as BMI [27], sex, age may influence ethanol's concentration in breath.

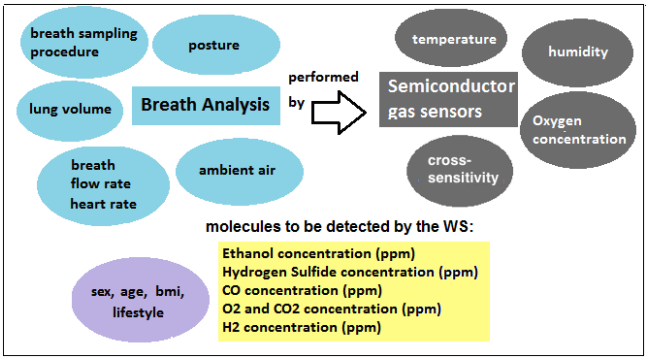

Figure 4. All the influencing factor (in the circles) related to breath analysis performed by semiconductor-based gas sensors.

A. Sensitivity tests on gas sensors with well-known gases concentrations

These experimental tests aimed to reproduce our measurement conditions when a breath analysis is performed: in particular, the temperature in the gas sampling box increases up to 30C+/-7% and the humidity reaches 70%RH+/-5%. We investigated sensors' response to a well-known gases concentrations, as well as their cross sensitivity.

Figure 5 shows how the humidity strongly affects such type of gas sensors (in this case, MQ7 sensor, sensitive to CO). The relationship between humidity and sensors' output generally can be modeled by means of a power law:

$$V_{out} = f(hum) = a * (hum^b) + c \quad (1)$$

where a and c are constant. Understanding such a behavior is useful to calculate humidity sensors' drift and then compensate it. We considered the entire range of humidity variation (for instance, 50%-55%RH in the case of MQ7, as shown in Figure 5) and then we calculated the slope of the curves. Based on the slope, drift coefficients were assessed as the decrease in sensors' output (Volt) per unit decrease in humidity (eq. 2):

$$S_d = \Delta V / \Delta hum \quad (2)$$

Also the gas flow rate indirectly influences gas sensors' behavior: a high flow-rate leads to a decrease in humidity, which causes (as shown in Figure 5), a decrease in sensor's output. By keeping the humidity constant, sensor's output will depend on the gas concentration only. Indeed, by means of the experimental set-up that is shown in Figure 6, we kept the humidity at 70%RH+/-5% by means of a saturated solution of NaCl placed on the bottom of the vial; then, we injected in the vial well-known gases concentrations. In Figure 7, we can see TGS2620 output when well-known concentrations of carbon monoxide, ethanol and hydrogen were separately injected into the vial. Also in this case, the relationship between sensor's output and gases contraction can be modeled by means of an equation similar to eq.1.

In order to assess TGS2620 cross sensitivity, well-known mixed concentrations of the three gases were injected into the vial at the same time. In this way, how the different VOCs add together and influence gas sensors' output can be understood. In Figure 8, the results are shown. Each gas

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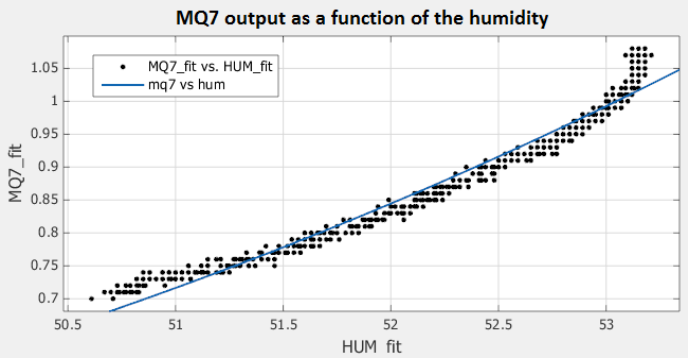

Figure 5. The relationship between MQ7 sensor and humidity is plotted. A power model is used for fitting curve.

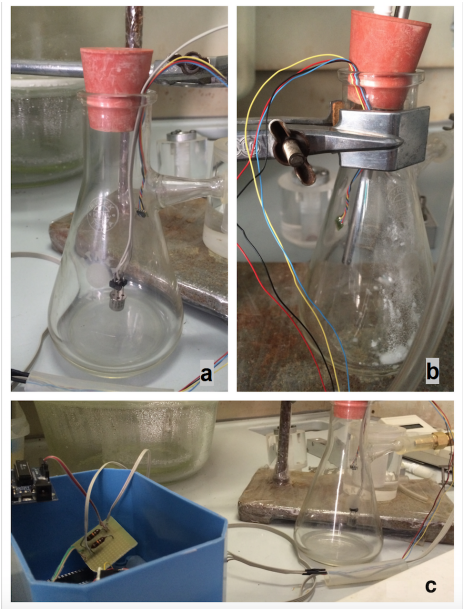

Figure 6. a) and b) Experimental setup. c) The data stream from sensors is read by an Arduino Mega2560 board via serial port.

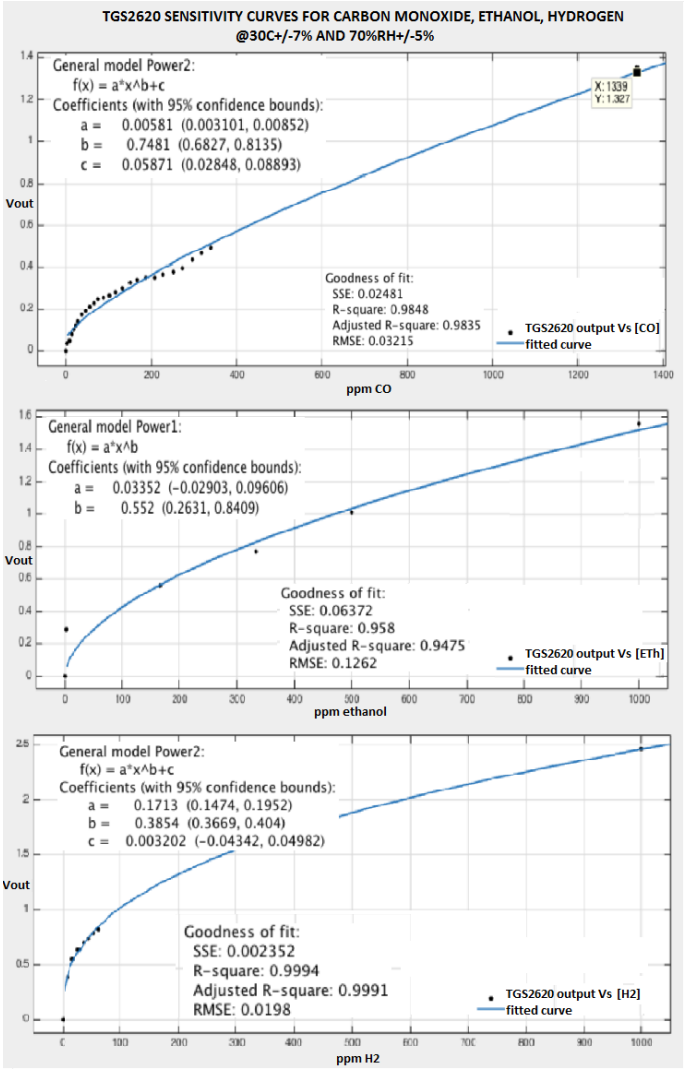

Figure 7. The curves show the relationship between TGS2620 output and well-known concentrations of CO, (first plot), C_2H_6O (second plot) and H_2 (third plot).

contribution can be modeled by a power law (see eq. 1). By investigating such behavior of semiconductor gas sensors, the "weight" of each compound on the output can be addressed. A simple model to describe this phenomenon can be based on a linear regression.

B. WS functionality test: the clinical validation

The WS underwent a clinical validation in three research centers: CNR in Pisa and Milan, CRNH (Centre de Recherche en Nutrition Humaine) in Lyon. The validation campaign involved 77 volunteers overall. The population was composed of individuals with different habits and lifestyle, as shown in Figure 9. People had to answer some questionnaires about their lifestyle, among which Audit test and Fagerstrom test, which respectively assess the alcohol and smoke dependence. 35% of them was no-risk subjects (that means, subject which never smoke, and with no-or-very low risk drinking); 6% of them was light smokers (low nicotine dependence); 19% of them was heavy smokers (high nicotine dependence); 17% of them was social drinker (low risk drinking); there were not people with high or increasing risk drinking (heavy drinkers); 23% of them was a combination of the previous classes.

A measuring protocol was draft, which took into account the methodological issues about breath sampling procedure [26] that, as shown in Figure 4, may strongly influence the breath composition. Actually, there is no standardized procedures to sample the breath. The most common methods of sampling are three: "alveolar sampling" (that is used if only the VOCs participating to the alveolar exchanges are to be assessed), "mixed expiratory air sampling" (which corresponds to a whole breath sample), "time-controlled sampling" (which corresponds to the exhaled air sampled after the start of expiration). For our purposes, mixed expiratory air sampling method was chosen, since our interest was focused on both endogenous and exogenous biomarkers. The subjects took a deep breath in, held the breath for 10sec., and then exhaled once into the corrugated tube trying to keep the expiratory flow constant and to completely empty their

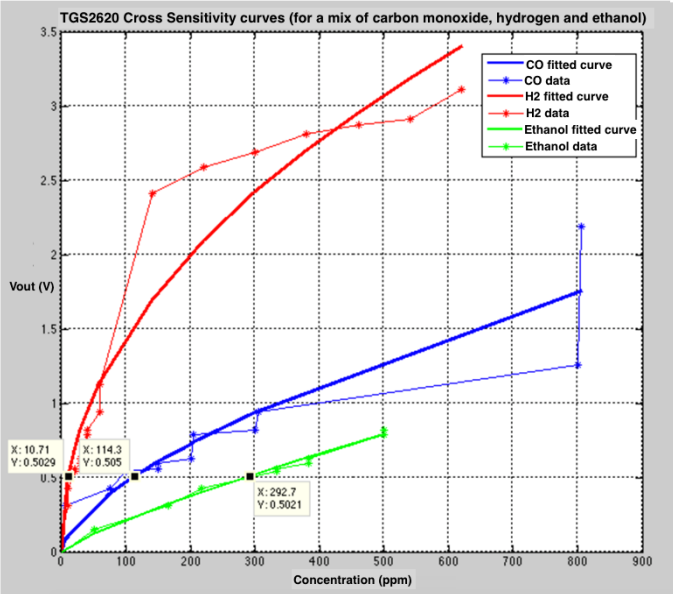

Figure 8. The curves show the relationship between TGS2620 output and well-known concentrations of CO, (blu plot), C_2H_6O (green plot) and H_2 (red plot).

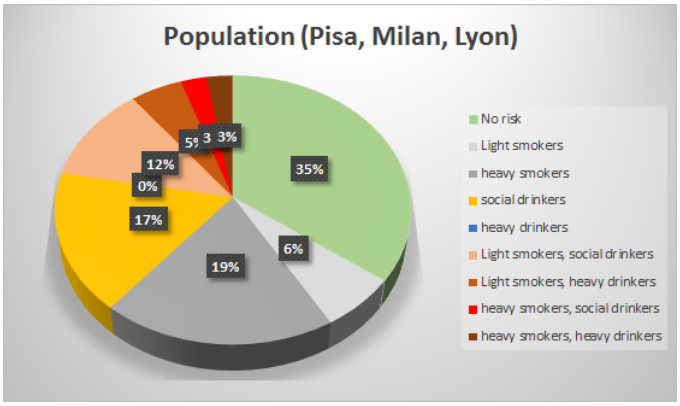

Figure 9. The population involved in SEMEOTICONS clinical validation.

lungs. The study was approved by the Ethical Committee of the Azienda Ospedaliera Universitaria Pisana, protocol n.213/2014 approved on September 25th, 2014; all patients provided a signed informed consent before enrollment.

The aim was to assess if the WS was able to monitor and evaluate the individuals' noxious habits for cardio-metabolic risk (smoke and alcohol intake in particular). In Subsection III-A we have confirmed, by means of experimental tests, the cross-selectivity of the sensors, which make their responses ambiguous. As a consequence, because of the difficulty of making an accurate quantitative analysis of VOCs' concentrations, we exploited another approach for data analysis, more classical, based on multivariate methods of pattern recognition. Pattern recognition, by exploiting the cross-correlation, extracts informations contained in sensors' outputs ensemble.

Sensors' raw data first were zero-centered and normalized, thus putting in evidence the qualitative aspects of the data. Then, Principal Component Analysis (PCA) was performed, in order to provide a representation of the data in a space of dimensions lower than the original sensors space. In particular, the first two components were extracted, exploiting 89% of variance. By the PCA we also removed the noise of the sensors. In Figure 10 and 11 the biplots of PCA scores are shown. In the 3D-plot, in particular, several cluster can be identified. Furthermore, in 2D-plot, we can see that the two first principal components seem to arrange according to the two first noxious habits for cardio-metabolic risk: Component 1 seems to be representative of smoking (MQ7 vector is aligned with it), as well as Component 2 seems to be representative of alcohol intake and wrong diet (TGS2602, TGS2620, TGS821 vectors are aligned with it).

After assessing the presence of clusters, the data were

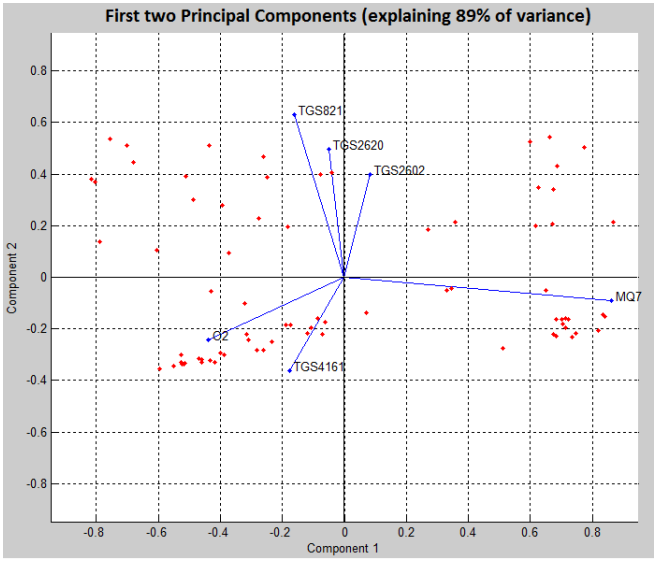

Figure 10. First two Principal Components.

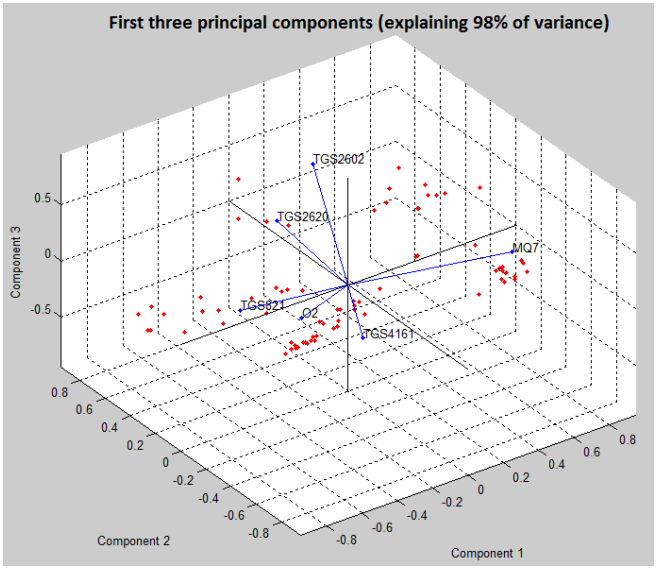

Figure 11. First three Principal Components.

processed with a K-nearest neighbor (KNN) classification

algorithm, previously trained with the data coming from another acquisition campaign. The aim was to classify the subjects according to their habits: "Healthy" (that means, no cardio-metabolic risk), "Light Smoker", "Heavy Smoker", "Social Drinker", "Heavy Drinker", "LsSd" (Light smokers, Social drinker), "LsHd" (tLight smokers, Heavy drinkers), "HsSd" (Heavy smokers, Social drinker), "HsHd" (Heavy smokers, Heavy drinker). The Audit and Fagerstrom questionnaires were our ground truth. It is important to highlight that 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. The KNN classifier was able to correctly classify in 89,61% of cases. Errors are due to TGS2602 and TGS2620 cross-sensitivity for hydrogen. In fact, for instance, three "no-risk" subjects were classified as "social drinker" because of high hydrogen contribution which caused a rise in these sensors voltage output.

IV. Conclusion

In this paper, we described the development of a portable, very easy-to-use, low cost technology-based device for real-time breath analysis. The Wize Sniffer is based on an array of low cost, semiconductor-based gas sensors. Such type of gas sensors are, of course, very sensitive and easy to be integrated in the circuitry. On the other hand, they require a very robust data post-processing because of the difficulty of discriminating the molecules' contribution due to sensors' cross sensitivity. Pattern recognition algorithms turn out the best way to overcome such problem. Nevertheless, our aim will be to develop a model in order to calculate, as accurately as possible, the concentration of breath molecules to be detected by the WS, in order to compare such concentrations with the reference ones (see Subsection II-A). This model should be based on the data regarding the gas sensors' behavior (see Subsection III-A), but it also has to take into account other parameters (Figure 4) that can influence breath composition.
In addition, the fact that the WS is able to detect a large number of VOCs, allows for using such device in broader applications: for instance, TGS2444, selective to ammonia, could be exploited to monitor patients with acute liver diseases. In addition, its modular configuration allows for changing the type of the sensors according to the molecules to be detected. Therefore, we retain that a big effort should be devoted in order to foster breath analysis in clinical practice. Not only, having a portable device for real-time breath analysis, easy to use, affordable to maintain, may allow for a daily self-monitoring also in home environment.

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