A Device for Self-monitoring Breath Analysis

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***Abstract*—Let's think about the numerous diagnostic screening methods. How many of them are invasive? How many of them present side effects? How many of them are expensive? We can affirm that the majority of the regular prophylactic checkups are sufficiently invasive, expensive and, sometimes, painful to discourage the subjects from participating in preemptive diagnostic procedures. As a consequence, in recent years, the need for the development of low cost, non invasive, rapid tools for the monitoring of metabolic processes has been increased. Breath analysis, performed by means of gas sensor array, may be an example of this kind of tools. In this paper, we will present the development of a portable, low cost, easy to use device for breath analysis, based on commercial semiconductor-based gas sensor array. We will describe its design, both from a hardware and software point of view. In addition, by describing the functionality tests of the device and the experimental results, we will highlight the pros and cons that come from the use of such type of low cost adopted technology to analyze breath molecules.**

Keywords–Breath analysis; Semiconductor gas sensors; Data analysis; Low cost technology; E-noses.

I. INTRODUCTION

Many of us frequently avoid classical diagnostic procedures (gastroscopy, colonscopy, X-rays, blood samples, magnetic resonance (RM), etc.) because of their costs, or because often they are invasive, and sometimes painful, too. As a consequence, the need for simpler, cheaper, less invasive methods of screening is becoming more and more considerable.

Many studies have been addressed to investigate the metabolic pathways of breath molecules in order to exploit breath analysis to monitor the metabolic processes that occur in human body in a non invasive way [1][2][3]. For instance, according to [4], kidney diseases may be investigated by analyzing the concentration of ammonia in exhaled breath; ethane and pentane may derive from lipid per-oxygenation in case of oxidative stress ([5]); acetone has been investigated as a biomarker for diabetes, as it seems to be correlated with blood glucose level ([6]).

Such studies were conducted by using chemical analysis technologies and methodologies: selected ion flow tube mass spectrometry, for instance, or proton transfer reaction mass spectrometry, or gas chromatography- mass spectrometry. All these techniques are the gold standard for gas analysis, being very sensitive and accurate. On the other hand, they are very expensive and time consuming; moreover, the results can be analyzed only by specialized personnel.

As a consequence, in recent years, the idea of exploiting gas sensor array to analyze breath molecules [7] has been arisen. E-noses, quicker than a gas chromatograph, are able to follow the trend in time of breath molecules. In many studies, they have been employed to monitor volatile biomarkers related to cancer [8], or microbial infection [9], or asthma [10]. Toshiba's recent research prototype "Breathalyzer" [11] is able to monitor breath acetone. Bedfont [12] Smokerlyzer detects high concentrations of carbon monoxide present in smoker's breath.

Nonetheless, the technology used by the majority of such e-noses is expensive [13] or requires complex circuitry [14][15]. Moreover, often the existing e-noses used for monitoring breath biomarkers are not purposely designed for clinical field. In this paper, we present the development of a device, so called Wize Sniffer (WS) [16], able to monitor in real time a set of breath biomarkers. In particular, the aim of our work was to develop a device which was:

- able to analyse breath gases in real time;
- portable;
- based on low-cost technology, to foster its purchase and use;
- easy-to-use also for non-specialized personnel, to promote its use also in home environment.

In particular, 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, HARDWARE AND SOFTWARE

The idea of the Wize Sniffer was born in the framework of European SEMEOTICONS (SEMEiotic Oriented Technology for Individual's CardiOmetabolic risk self-assessmeNt and Self-monitoring) Project. SEMEOTICONS aims at developing a multi-sensory platform, with the appearance of a mirror, the so called "Wize Mirror", which is able to detect, in human face, all those "signs" related to cardio-metabolic risk. The Wize Sniffer will be integrated in the Wize Mirror, detecting all those molecules present in human exhaled breath related to the noxious habits for cardio-metabolic risk (smoking, alcohol intake, metabolic disorders).

Nonetheless, the modular configuration of the Wize Sniffer allows for changing the gas sensors according to the molecules to be detected, and, in addition, for using the Wize

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Sniffer also as a stand-alone device.

A. Molecules detected by the the WS

In this section we describe briefly the breath molecules detected by the Wize Sniffer and how they are related to those noxious habits for cardio-metabolic risk: metabolic disorders, alcohol intake, smoking.

- **Carbon Monoxide (CO)**: it is present in cigarette smoke, very dangerous for cardio-metabolic risk. 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 show how much O2 is retained in the body, and how much CO_2 is produced as a by-product of cellular metabolism. 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); Too rapid breathing rate (hyperventilation) may provoke Respiratory Alkalosis (i.e., decrease of CO_2 concentration in blood, it 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** (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;
- **Ethanol** (C_2H_6O): Ethanol derives 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;
- **Hydrogen Sulfide** (H_2S): it is a vascular relaxant agent, and has a therapeutic effect in various cardio-vascular diseases (myocardial injury, hypertension). Its baseline value is round about 0.33ppm.

B. Hardware and Software

In Figure 1, the Wize Sniffer first prototype's structure is shown. The acquiring system is based on a gas sampling box (of 600ml according to the tidal volume [17] and made up of (ABS) and Delrin) where six gas sensors are placed, and a micro-controller board. Other two gas sensors work in flowing-regime by means of a sampling pump. A heat and moisture exchanger (HME) filter is placed at the beginning of a corrugated tube to absorb the water vapor present in the breath. A flow-meter monitors the exhaled breath volume. A flushing pump purges the chamber to recovery the sensors' steady state between two consecutive measures.

As outlined before, our first aim was to develop a device based on low cost technology. Indeed, we used a widely employed opensource micro controller board to read, collect and analyze gas sensors' data: an Arduino Mega2560 with Ethernet module.

Regarding the gas sensor array, optical, carbon nano fiber (CNF), quartz crystal microbalance (QCM), metal oxide semiconductors (MOS), conducting polymers (CP), and surface acoustic wave (SAW), are the most common gas sensor types employed in e-noses [7]. Although very sensitive and able to detect concentrations lower than 10ppb, optical gas sensors are expensive and often they cannot be miniaturized. Also CNF-based gas sensors are expensive, especially for their fabrication and manufacturing, too. SAW and QCM-based gas sensors have very high sensitivity but they need complex circuitry and, in the case of QCM-based gas sensors, they have a poor signal-to-noise ratio.

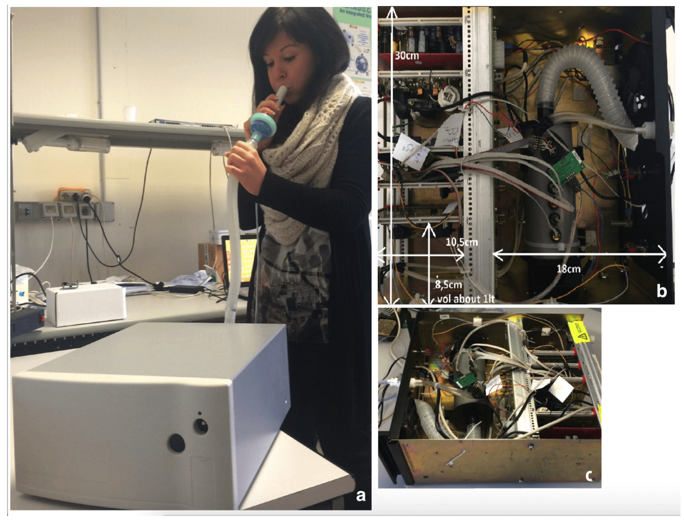

Figure 1. a) Wize Sniffer first prototype's hardware. b) and c) show its internal configuration.

Then, our choice was to employ MOS-based gas sensors. They have long life, strong sensitivity, rapid recovery; in addition, they are low cost and easy to be integrated in the circuitry. Unfortunately, humidity strongly affects their behavior, as well as cross-sensitivity [18]. To reduce the water vapor present in exhaled breath from 90% up to 60% a HME filter is used. In addition, humidity (as well as temperature) is monitored within the gases store chamber (by means of a Sensirion SHT11). Cross-sensitivity makes these sensors be non-selective. This may be a problem for data processing (see Section III). In Table I, all the used gas sensors are listed, as well as the detected breath molecules.

TABLE I. SENSORS INTEGRATED IN THE WIZE SNIFFER'S ACQUIRING SYSTEM

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

In a second step of our work, we will try to develop CP-based gas sensors. Such type of sensors present the same MOS-based gas sensors' pros and cons, but they are highly adaptable

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and they can be configured in several ad-hoc solutions. In particular, we will try to exploit Polyaniline sensitivity to detect Nitric Oxide, a well-known marker for endothelial function [19].

As outlined in the previous sections, we aimed to develop a device which could be used not only in medical centers, but also in home environment. Indeed, a client-server architecture is implemented in order to send breath test results also to a remote Personal Computer: the user, after running a test, can forward the results to the family doctor, for instance (see Figure 2).

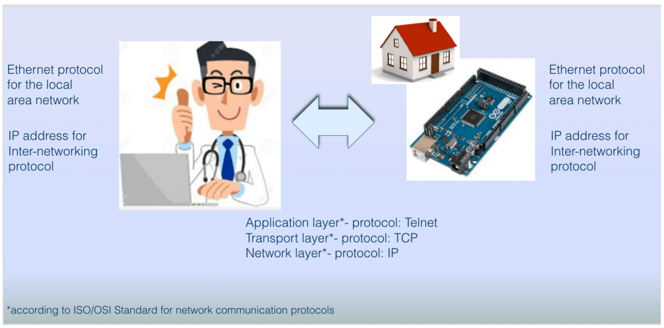

Figure 2. Client- server architecture including Wize Sniffer

It means that Arduino Mega2560 is programmed to process sensors' raw data and to execute a daemon on port 23. It waits a command line from the remote 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). The next section describes how the WS microcontroller board analyzes row data.

III. Experimental Tests and Data Analysis

As described in Section II-B, semiconductor-based gas sensors are, on one side, very low cost, very easy to be integrated in the circuitry and very sensitive; on the other side, they are not selective, because of cross-sensitivity, and their behavior is strongly dependent on humidity.

Starting from raw data (see Figure 3), our aim is to calculate, as accurately as possible, the concentrations of the molecules present in exhaled breath and to be detected by the Wize Sniffer. It is understandable how the cross-sensitivity makes this aim a challenge, since there is not a single sensor for each breath compound. Moreover, we deal with something extremely variable: breath gases. Exhaled breath composition is strongly influenced by factors such as heart rate, breath flow rate [20], posture [21], ambient air [22], lung volume [23], breath sampling [24]. Consequently, breath composition may exhibit not only a strong inter-variability (among different subjects), but also a marked intra-variability (relative to the same subject). As a consequence, we have to face, on one hand, with an uncertainty of measure which derives from all those factors that affect the gas sensors' behavior; on the other hand, we have un uncertainty due to all the physiological conditions that may influence the breath composition. This is summarized in Figure 4. Note that, in our case, also factors such as BMI, sex, age, subject's lifestyle may influence the breath composition: for example, alcohol disposal in men is different than the one in women, and, in addition, it depends on body mass index (BMI), as well.

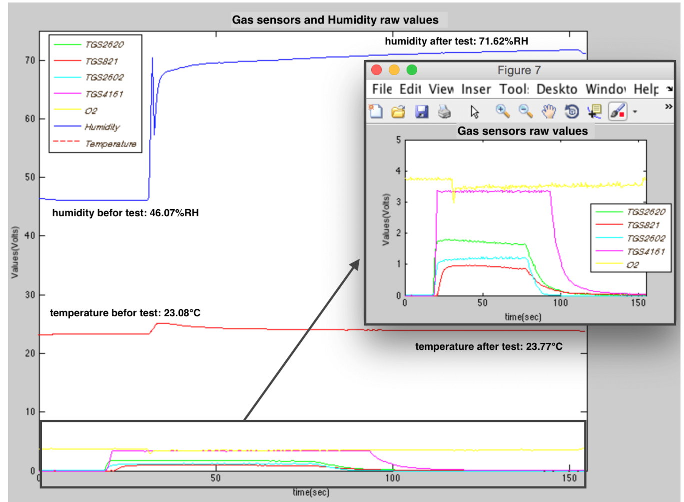

Figure 3. Raw breath curves. Also temperature and humidity trends are plotted.

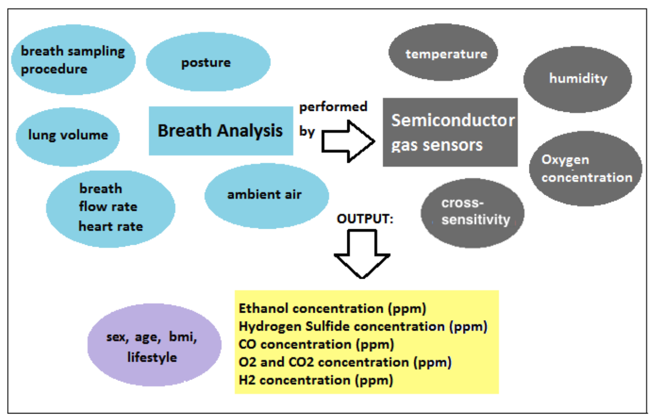

Figure 4. Breath analysis performed by semiconductor-based gas sensors. In the circles, all the influencing factors, both for breath analysis and gas sensors' behavior.

For these purposes, these are the experimental steps we are following:

- to investigate the behavior of semiconductor-based gas sensors in our measurement conditions: 30C+/-7% and 70%RH+/-5%, that are the ones that occur in the store chamber when a breath analysis is performed (see Figure 3);
- to investigate how the cross sensitivity affects their output, that means, how the several molecules influence each other in the chemical interaction with the sensors' sensing element;
- all this knowledge about gas sensors has to be exploited and applied to perform breath analysis and calculate molecules' concentrations.

A. Gas Sensors' Behavior Data Analysis

The aim of this phase of the work is to understand gas sensors' behavior under our measurement conditions: 30C+/-

7% and 70%RH+/-5%. In particular, we want to study not only their response to a well-known gas concentration, but also their behavior when humidity increases, due to the exhaled breath. In addition, in this phase, also the cross sensitivity has to be addressed.

In Figure 5, the MQ7 (CO sensor) output is plotted as a function of the humidity. The relationship between the humidity and MQ7 output can be fitted with a power model.

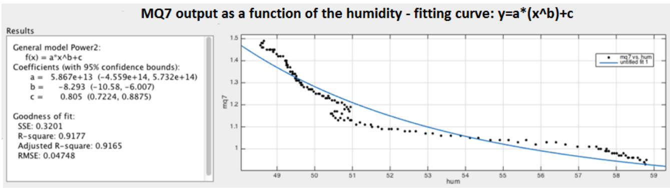

Figure 5. The relationship between MQ7 sensor and humidity is plotted. A power model is used for fitting curve.

It can be easily noted how the humidity strongly affects such type of gas sensors; as a consequence, 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), an increase in sensor's output. Keeping the humidity constant, sensor's output will depend on the gas concentration (CO concentration, in this case) only (as shown in Figure 6).

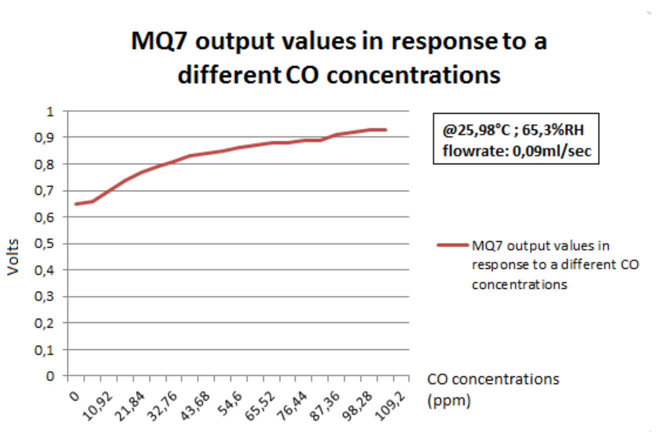

Figure 6. MQ7 sensor output as a function of different carbon monoxide concentrations. Measurement conditions: 25.98C, 65.3%RH

Unfortunately, when a breath analysis is performed, breath flow-rate may be kept low and constant, but the humidity inevitably rises in value. Figure 7 shows the relationship (modeled by a power law) between MQ7 sensor's output and different CO concentrations.

The cross sensitivity is investigated by keeping the humidity constant, of course, and by injecting in the test chamber, where the gas sensor under investigation is placed, well-known mixed gases concentrations (the experimental set-up is shown in Figure 9). In this way, how the different compounds add together and influence gas sensors' output can be understood. In Figure 8, the contributions of well-known carbon monoxide and hydrogen gaseous mixes on TGS2620 sensor's output are shown. TGS2620, as reported in Table I, is sensitive to ethanol, carbon monoxide and hydrogen. When, for instance, the sensor is exposed to a gaseous mix of 100ppm of carbon monoxide and 20ppm of hydrogen, its output (at about 28C, 61%RH) will be 1,01V. By investigating such behavior of semiconductor gas sensors, the "weight" of each compound on the output can be addressed. A simple model able to describe this phenomenon can be based on a linear regression.

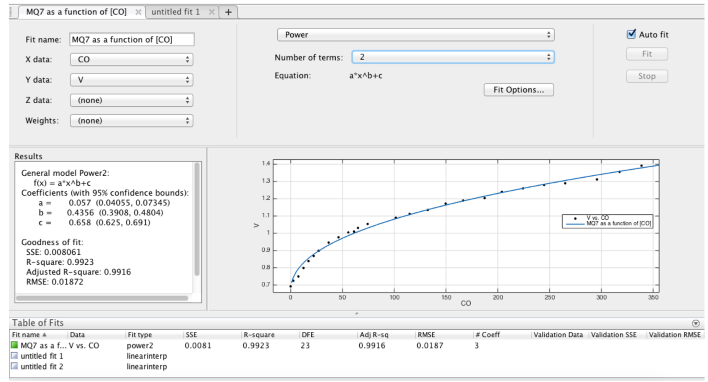

Figure 7. The relationship between MQ7 sensor's output and well-known CO concentrations is plotted. A power model is used for fitting curve. Measurement conditions: 25.98C, 65.3%RH

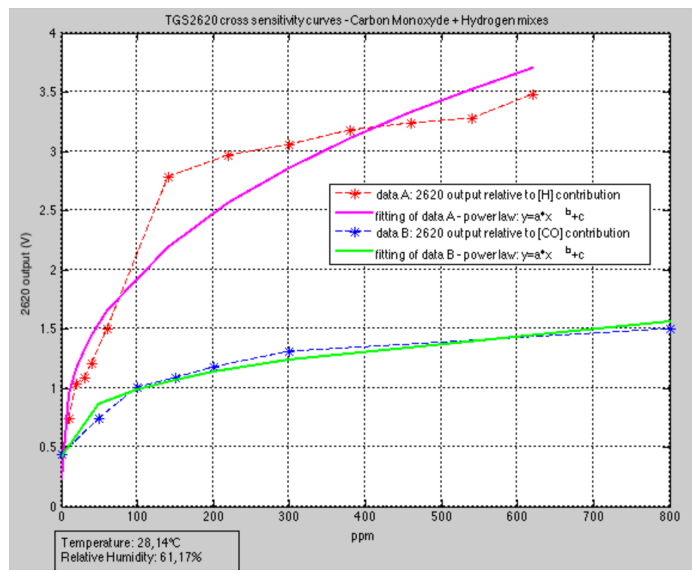

Figure 8. The contributions of well-known carbon monoxide and hydrogen gaseous mixes on TGS2620 sensor's output. It can be noted that such sensor is much sensitive to hydrogen than to carbon monoxide, especially at lower concentrations.

Finally, as already reported in Figure 4, the knowledge about sensors' behavior must be applied to breath analysis field: breath analysis, performed by semiconductor-based gas sensors, will have to take into account also the model which describe such type of gas sensors' behavior.

B. Breath Test Analysis

Our aim is 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

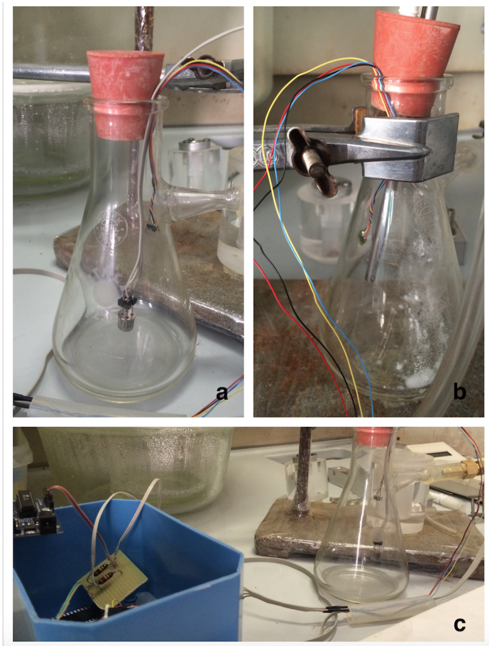

Figure 9. a) Experimental setup for gas sensors tests. b)The humidity is kept constant by means of a saturated solution of NaCl placed on the bottom of the vial. c) The data stream from sensors is read by an Arduino board.

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 (see Figure 4) that can influence breath composition.

We are developing such model by using a statistical approach. Meanwhile, we are also exploiting another approach for data analysis, more classical, based on Principal Component Analysis and K-nearest neighbor (KNN) classification algorithm. In Figure IV, we can see how this approach works.

For this purpose, a measurement protocol was draft and it involved a population of 26 healthy individuals, with different age (range 30-60 years old), habits, lifestyles, body type. We choose healthy individuals because, in this case, we are detecting those breath molecules related to cardio- metabolic risk. As a consequence, the Wize Sniffer does not make a diagnosis, but it only should help the user to monitor his/her well-being and lifestyle. For the measuring protocol, the methodological issues about breath sampling procedure had been taken into account [24], since (as shown in Figure 4) the breath sampling may strongly influence the breath composition. Actually, there is not a standardized procedure to sample the breath. The most common methods of sampling are three: "alveolar sampling" (it is used 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, but this method shows large variations of samples compositions). For our purposes, mixed expiratory air sampling method was chosen, since our interest was focused on both endogenous and exogenous biomarkers. The individuals 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 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.

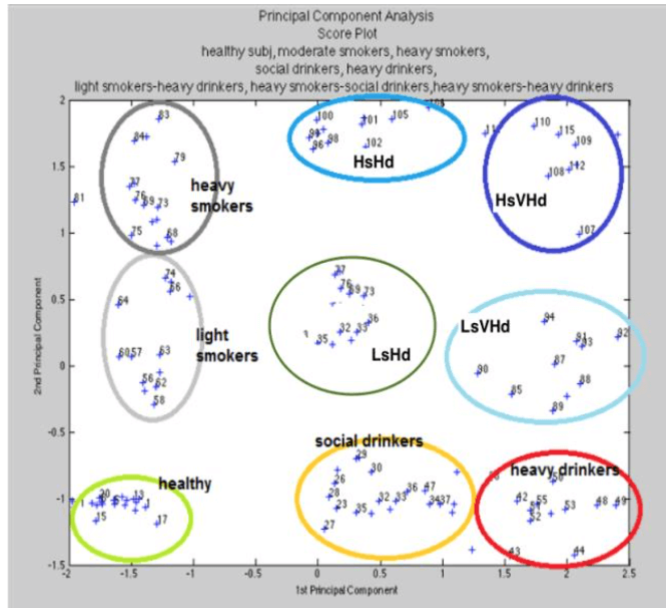

Figure 10. Score plot of the data analysed by Principal Component Analysis.

The raw data can be divided into 9 clusters according to subjects' habits: "Healthy" (that means subjects with low cardio-metabolic risk), "Light Smoker", "Social Drinker", "LsHd" (that means Light Smokers, heavy drinkers), "LsVHd" (that means Light Smokers, very heavy drinkers), "HsHd" (that means Heavy Smokers, heavy drinkers), "HsVHd" (that means Heavy Smokers, very heavy drinkers). The KNN classifier is able to correctly classify in 85,96% of cases.

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.

IV. Conclusion

In this paper, we described the development of a portable, easy-to-use device for breath analysis based on low-cost technology. In particular, the device makes use of an array of low-cost, semiconductor-based gas sensor array.

Such type of gas sensors are, of course, very robust, sensitive and easy to be integrated in the circuitry. That allows for having a modular configuration for the acquiring system and then for changing the gas sensors according to the molecules to be detected. On the other hand, semiconductor-based gas sensors require a very robust data post-processing in order to take into account all the influencing factors. In the case of breath analysis, the humidity plays an important role in that sense, as well as the cross sensitivity.

In addition, standardized procedures for breath sampling should be defined.

Thus, we retain that a big effort in this direction should be devoted. Having something low-cost, portable, easy to use, affordable to maintain, and so exploiting the great potential of

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breath analysis, may allow for a non-invasive daily monitoring that, even if without a real current diagnostic meaning, could represent a pre-screening in any case.

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