Wize Sniffer
A New Portable Device Designed for Selective Olfaction

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Abstract: Digital semeiotics is one of the newest recent challenges for assessing a number of computational descriptors to atherosclerotic cardiovascular diseases that are leading causes of mortality worldwide. These descriptors can be expressed involving (i) morphometric, biometrics and colorimetric of the face; (ii) spectroscopic analysis of skin and iris, of sub-cutaneous substances and the function of subcutaneous tissues, and (iii) compositional analysis of breath and exhaled. In this paper, we describe the design and functionality of the Wize Sniffer (WS), a new portable device for breath analysis limited to an effective number of substances. Within the SEMEOTICON Project by the WS, we intend a hardware/software tool for both the analysis of volatile organic compounds of breath and a platform for data mining and data integration. The WS should be able to provide useful information about the "breathprint", i.e., the analog of fingerprint for the state of health of an individual.

1 INTRODUCTION

Atherosclerotic cardiovascular diseases (ACDs) represent the leading cause of worldwide mortality (World Health Organization. The Global Burden of Disease: 2004 and update 2008; (Lison et al., 2010)). Breath gases are recognized to be excellent indicators of the presence of diseases and clinical conditions. Such gases have been identified as biomarkers using instrumentations such as gas chromatography (GC) or electronic nose (e-nose) (Guo et al., 2007). GC is very accurate but expensive, time consuming and non portable. E-nose has the advantages of low-cost and easy operation, but is not particularly useful for analyzing breath substances. As a consequence, in recent years, the necessity to develop a portable device for breath analysis, easy to use, and feasible for patients living far from medical structures or physicians.

Essentially, a design of a portable device for breath analysis is based on selected chemical sensors that are sensitive to the biomarkers and compunds in breath substances and make use of accurate statistical tools for odor signal preprocessing, classification methods and, in turn, identification of possible diseases if any. In SEMEOTICONS activity, we are developing a device following the above requirement. The device, called Wize Sniffer (WS), captures breath samples, the chemical selective sensors sense the sample and accordingly form a sort of *odorprint* of healthy people or patients with known and specific diseases, in order to evaluate the *well-being* state of a human subject (Miekish et al., 2004). It should be noted that does not exist a general definition of well-being, rather some indices for well-being that can be correlated to cardio-metabolic risk. In addition, such indices are strictly connected to the recognition of behavioural trends and the methods for computing the raw numerical values of such well-being indices must be designed for single individual. However, one critical index of well-being is given by the breath composition. Human breath is largely composed of oxygen, carbon dioxide, water vapour, nitric oxide,

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and numerous volatile organic compounds (VOCs) (Di Francesco et al., 2005); (D'Amico et al., 2007). The type and number of VOCs in the breath changes among different individuals, but there is a common core of breath VOCs which are present in all individuals. The molecules in an individual's breath may be exogenous or endogenous. Exogenous molecules are those that have inhaled or ingested from the environment or other sources such as air or food, thus giving no diagnostic value. Endogenous molecules are produced by metabolic processes and partition from blood via the alveolar pulmonary membrane into the alveolar air. Such endogenous molecules are present in breath relatively to their types, concentrations, volatilities, lipid solubility and rates of diffusion as they circulate in the blood and cross the alveolar membrane. Changes in the concentration of the molecules in VOCs could suggest various diseases or at least changes in the metabolism.

In this paper, for the first time we present the design of a portable device able to operate with a limited number of breath VOCs, normally connected to oxidative stress, thus giving information to physicians on the possible state of wellness of an individual.

2 BREATH ANALYSIS AND WELLNESS STATE

In this section, we describe the correlation between exhaled VOCs and oxidative stress. Oxidative stress is the cause of over 100 diseases, including atherosclerosis or hypertension. In addition, hypertension is a risk factor that can lead to myocardial injury, cardiac failure, aortic aneurysm. The design of a portable device for breath analysis must necessarily work on a limited space of breath VOCs. The most relevant VOCs and their connection to oxidative stress are labelled as follows.

Carbon Monoxide (CO): it is naturally produced by the action of heme oxygenase on the heme for haemoglobin breakdown. This produces carboxyhemoglobin, which is a more stable molecule than oxyhemoglobin. For example, an increase of CO leads haemoglobin to carry less oxygen through the vessels. CO is present in cigarette smoke, and air pollution too. In addition, it is a blood vessel relaxant (vasodilator), and a promoter of neurovascular growth, therefore it could be considered as an indicator of brain tumor growth.

Carbon Dioxide (CO_2): the variation rate of CO_2 can be associated to different metabolic response, for example, CO_2 increases during physical activity or in general with the increment of blood-heat as in a fever. Analogously, there is a decrease in the case of hypothermia. In healthy individuals, partial pressure in arterial blood is very close to the partial pressure in expired gases. 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. Capnography is a technique commonly used for monitoring the concentration of CO_2, or, similarly, its partial pressure using such technique, the max value of a capnogram corresponds to the end of tidal volume of exhaled breath and the steady-state concentrations of each breath. 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, that 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).

Ethanol: the ethanol compound in a breath composition can be classified as endogenous or exogenous. Ethanol endogenous may increase in exhaled gas mixtures because of alcoholic fermentation of an excessive over-load of carbohydrates. Indeed it is originated from microbial fermentation of carbohydrates in the gastro-intestinal tract. Then, it enters in the blood. On the contrary, Ethanol exogenous comes from alcoholic drinks. It is important to note that 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.

Nitrogen Oxide (NO): it is a vasodilator and it modulates inflammatory response (operating in combination with CO and Hydrogen Sulfide).

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. In patients with coronary heart disease, H_2S level in blood is normally reduced, as in the case of hypertension. On the contrary, in haemorrhagic shock, H_2S plasma levels are increased.

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.

Hydrogen and Methane: they are produced by the breakdown of the carbohydrates in the colon by anaerobic bacteria. They can be correlated to overweight problems, and probably to an improper life-style. Nevertheless, their quantity is very low presenting some problems for their detection.

Cigarette smoke: it contains principally Nicotine, CO, NH_3, oxidant substances leading to oxidative stress. After 1 minute smoking, an increase of heart rate can be revealed. Tobacco combustion causes a constriction of blood vessels.

Other factors leading to oxidative stress are cholesterol and fibrinogen. An increase of cholesterol leads to atherosclerotic issues and, similarly, an increase of fibrinogen leads to blood viscosity. In addition, a strong correlation exists between exhaled hydrocarbons and cardiovascular diseases, principally pentane and ethane. In healthy subjects, there is a balance between oxidant molecules (free radicals) and anti-oxidant molecules. When free radicals are balanced, they have a positive effect on the general person wellness and health, because they are involved in many inflammatory processes, thus having a therapeutic potential. On the contrary, when free radicals number exceeds the anti-oxidant ones, this leads to oxidative stress.

3 THE WS DESIGN

The design of the WS platform device operates in three phases: gas collection, sampling and data analysis. During the first phase the subject breaths into a gas sampling box. Our design follows the recent proposal by Guo et al., (2007). The gas is injected into the chamber containing a sensor array. Then, a measurement circuit measures the interaction between the breath and the array sensors. Then signals are filtered and amplified and afterwards sent to computer for further analysis. The WS components are array sensors contained in a customized box, the microcontroller board and the statistical analysis tool.

The array sensors are both commercial and customized with conductive polymers electrospun nanofibers as sensing material. When using a conductive polymer, it is reasonable to have an increased sensor sensitivity and, moreover, the possibility to measure nicotine concentration. Note that a correspondent commercial sensor for nicotine is not available.

Table 1: Specific VOC and corresponding sensitive gas capability of Figaro sensors.

Breath substance	**Baseline levels** (ppm)	**Sensors Sensitivities** (ppm)
CO_2 (in percentage 4%)	40000	30-300
CO	3.5 (14-30 with moke)	50-1000
Ethanol	0.62 153-180	1-10 50-1000
Hydrogen sulfide	0.33	0.1-1
Ammonia	0.42-0.46	1-10 30-300
Hydrogen	9.1	1-10 10-100

The used commercial chemical sensors are provided by the Figaro Engineering Inc. These sensors are very sensitive, robust and resistant to humidity and ageing. In table 1, the sensitivities of such sensors for any VOC to be detected are reported.

Any chemical sensor should have has unique odour-print corresponding to the capacity to sense a single VOC substance. The framework of the WS consists of three modules: signal measurement, signal conditioning and signal acquisition. The array of sensors is contained in the signal measurement module. The measurement circuit is responsible for transforming gas signals into electronic signals. The array sensors are mounted directly or connected with a griddle to a microcontroller board that can operate on the data collected filtering and amplifying them. The microcontroller used in our system is a widely employed open source controller: Arduino 2560 system that can be powered very simply via a USB connection (see Figure 1).

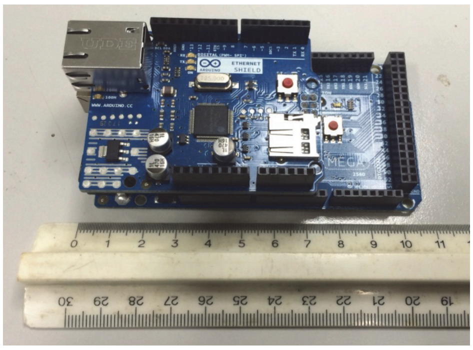

Figure 1: The microcontroller used for the electronic data collection: Arduino Mega 2560 system (based on the AT mega 2560), that can be powered very simply via a USB connection. The VOCs data collected can be loaded on Arduino or sent to computer with the USB connection. The length of the Mega 2560 system is 10 cm.

Figaro Engineering provides the chemical sensors and a general purpose electric scheme to adopt according to the specific use. The ability to sense a selective VOC substance depends on the employed sensing materials. For example, considering the sensor named TGS2600, able to sense CO, Ethanol and iso-butane, the manufacturing procedure is as follows: using thick film techniques, the sensor material is printed on electrodes (noble metal) that have been printed onto an alumina substrate. The main sensing material of the sensor element is tin dioxide (SnO2). One electrode of the sensing material is connected to a pin 2 (see Figure 2) and the other is connected to another pin 3. An RuO2 heater printed onto the reverse side of the substrate and connected to pins 1 and 4 heats the sensing material. Lead wires are Pt-W and connected to sensor pins which are made of Ni-plated Ni-Fe 50%. The sensor base is made of Ni-plated steel. The sensor cap is made of stainless steel and contains 6 pin holes on the top of the sensor. The basic measuring circuit is represented in Figure 2.

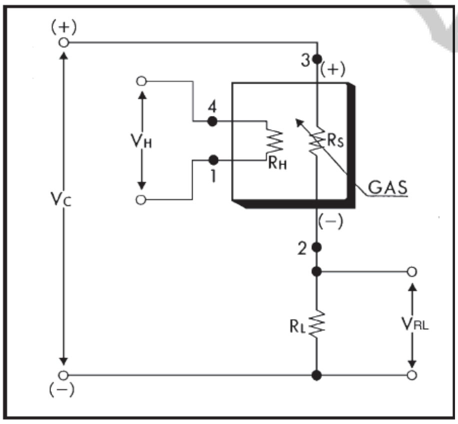

Figure 2: Basic measuring circuit of Figaro chemical sensors.

Circuit voltage (VC) is applied to the electrodes of the sensor element. The behaviour of the sensor element is that of a variable resistance (RS). In order to accord the circuit to the acquiring device it is necessary to use the load resistor (RL). Vc is always required for the circuit power supply, and the polarity shown in Figure 2 must be maintained. The sensor value is measured indirectly as a change in voltage across RL and RS. The signal measurement module measures these voltages and converts them into digital signals. The analog signals are then conditioned by signal filtering and amplifying. The sampling procedure is based on four steps described as follows:

1) before the sampling, the chamber is purged and the sensor returns to a steady state. The baseline value is measured and recorded for data manipulation and normalization;
2) 0~5*s* (injection stage): sampled gas is injected into the chamber at an invariable rate. The particles of sampled gas that are injected and accrue inside the chamber produce a resistance change and cause the amplitude of the signal to rise;
3) 6 ~10*s* (reaction stage): particles in the chamber continue to accumulate on the sensors but the accumulation rate is decreasing. The resistance of the sensor monotonically increases at a decreasing rate, as the amplitude of the signals;
4) 15~90*s* (purge stage): the chamber is purged again. The pump quickly draws out the remaining analyte, thereby shortening the sampling time as well as refreshing the air for the next use.

3.1 Electrospun Nanofibers as Sensing Materials

The sensitivity of commercial sensors, as well as selectivity, can be improved reducing the sensing area. This achievement can be obtained using as sensing material conductive polymers elestrospun nanofibers, (see Figure 3).

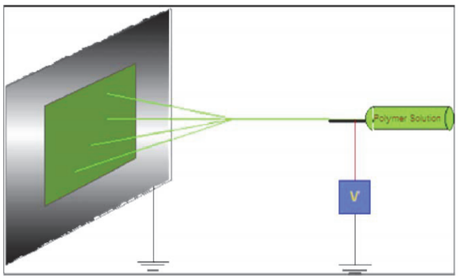

Figure 3: A schematic sketch of electrospinning process.

Electrospinning is a manufacturing process able to produce ultra-fine fibers with diameters ranging from 50-500nm (Ding et al., 2009); (Chen et al., 2011). In the electrospinning process an electric field is generated between a polymer solution and a metal collection screen (collector). The polymer solution is contained in a syringe with a steel capillary tip and a voltage is applied between the tip and the conductive collector. As the electrical potential is increased, the charged polymer solution is attracted to the collector. When the voltage reaches a critical value, the charge overcomes the surface tension of the polymer solution formed on the capillary tip and an electrified jet is produced. As the charged jet flies through the air, it loses the solvent through a quick evaporation and impinges on the collection screen as a thin fiber mat, as shown in Figure 4.

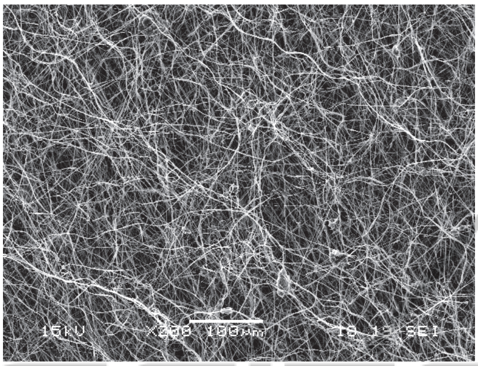

Figure 4: Example of electrospun nanofibers as observed at a Scanning Electron Microscope.

In the development of the WS, we will use electrospun nanofibers as sensing material and conductive polymers, such as polyaniline (PANi), polypirrole (PPY), poly(p-phenylene vinylene) (PPV) and others to be defined yet (Slater et al., 1992); (Slater et al., 1993); (Savage et al., 2001). The advantage of sensors using nanofibers as sensing material would be a general increment of sensitivity and a significant reduction of the response time. Nevertheless, such properties must be evaluated during the measurement stages, and the possible response of such sensors is beyond the scope of the present paper.

3.2 Statistical data processing

Since the operability of WS works on a *reduced space* of breath substances, data analysis requires a particular care because of the various sources of errors. The sensors measure changes in voltage across each sensor and convert the raw signal into a digital value that can be managed by physicians. Our analysis of sensor data requires three steps: signal preprocessing, feature extraction and classification. The aim of signal preprocessing is to compensate drifts and to eliminate irrelevant information so to improve the performance of the subsequent pattern recognition and classification. It is assumed that the dynamic response of any sensors is sampled introducing reasonable time intervals in a particular way for the transient phase. In addition, normalization is used to compensate for sample-to-sample variations caused by analyte concentrations and pressure of oxygen. At this point, we introduce feature extraction from any sample using the standard procedure of principal component analysis (PCA) and, finally, *k*-nearest neighbor voting rule (KNN) will be used as a classifier for the features that extracted by PCA, (Guo et al., 2007).

4 CONCLUSIONS

In this paper, we have presented the basic requirements for the development of the portable device WS, operating on a number of effective VOCs in the breath. Within the SEMEOTICON Project, by the WS we intend a hardware/software tool for both the analysis of VOCs of breath and a platform for data mining and data integration. Similar to a fingerprint, every individual has a "breathprint" that can provide useful information about his or her state of health. Thousands of unique substances in exhaled breath have been identified. These substances include elemental gases, such as hydrogen, nitric oxide (NO), and carbon monoxide, and a vast array of VOCs. The WS design has been conceived to identify target VOCs with selective sensors such as: nitric oxide, alcohols, carbon monoxide and, possibly, other VOC substances based on general requirement by physicians. In turn, the breath gas sensors will be included in a box and interacting with a main processing unit. In its ultimate shape and functionality the WS will be a compact and feasible device to be used in many open environments and the most disparate situations without losing efficiency.

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