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Wireless Electronic Smell System for the Detection of Diseases Through the Exhaled Breath

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This article presents the design and development of a wireless electronic smell system called "SOE-I", with the purpose of detecting and monitoring diseases (for example: Respiratory) by means of exhaled breath. For this purpose, a group of patients with respiratory problems (i.e. COPD) and a group of control patients (i.e., healthy or smokers) were evaluated with the sensory system. This system was performed through a high-speed wireless module where the main function is to obtain the data from a remote site, and which was coupled to a sensory system composed of 8 Metal Oxide Gas Sensors (MOS), where the breath sample was conditioned. Once the data was acquired, the data processing software was developed to carry out the characteristic analysis of the disease, where a clear discrimination of the samples of COPD with respect to healthy samples was obtained, achieving a 92% of variance through Principal Component Analysis (PCA) method and a Linear discriminant analysis (LDA) technique to classify the data set. With this equipment, an early diagnosis of a non-transmissible or transmissible disease could be made, preventing other people (i.e, medical personnel) from being infected.

1. Introduction

During the last decades several institutions have carried out a study about the volatile organic compounds (VOC) generated by the body due to causative diseases (Broza et al., 2014), which can be detected and measured by means of blood, body fluids and exhaled breath, these studies have managed to conclude that exhaled breath can identify more than 2000 VOC considered normal but depending on the increased or decreased concentration may indicate a disease condition (Phillips et al., 2013). Techniques for the detection of these compounds have also been developed, such as the multisensory perception systems (E-nose), which have also been projected as an early and safe diagnostic method because they are non-invasive (Martinez et al., 2013). With the development of these techniques, great progress has been made mainly with diseases such as lung cancer, diabetes (Yu et al., 2005), COPD (Chronic Obstructive Pulmonary Disease) (Duran et al. al., 2012), among others, these studies have made it possible to determine that in various diseases a VOC pattern can be found by which the presence of a disease can be identified (Peng et al, 2010). The progress of this diagnostic technique allowed the development of electronic noses for various medical, environmental and food applications (Alam et al.,2013), many of these marketable devices have been developed to be used in general in different areas (Santos et al.,2012), so they are not developed specifically for the analysis of breath.

2. Materials and Methods

2.1 Sensor Array

The implementation of multisensory perception technologies for the diagnosis and detection of diseases through the breath, involves the study and analysis of volatile compounds in the bronchi or alveolar air (last portion of the breath), assuming the relationship that exists between the VOCs and a disease (characteristic pattern), the array of sensors in the device must be sensitive to those mixtures of volatile compounds. Figure 1 shows the matrix of gas sensors used in the measuring device, which were selected according to the volatile compounds of the breath. Therefore, for the development of portable measuring equipment, 8 commercial MOS sensors were implemented, where the characteristics of each of these sensors are described in Table 1.

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Figure 1: (a) SOE-I sensor array

Table 1: Specification of the sensor array

#	Sensor-MOS	Application	Sensitivity (ppm)
1	SP-3	Alcohol, toluene	50-300
2	MQ 3	Alcohol, ethanol, smoke	100-300
3	TGS 822	Organic solvents, carbon monoxide	50-5000
4	MQ 138	Benzene, toluene, alcohol, acetone, propane, formaldehyde, hydrogen	10-1000
5	MQ 137	Ammonia, ethanol	5-200
6	TGS 813	methane, propane, butane	500-10000
7	TGS 800	Carbon monoxide, methane, isobutane, hydrogen, ethanol	1-100
8	MQ 135	Ammonia, sulfur and benzene	10-1000
9	DTH22	Temperature y Humidity	

2.2 System Structure

The sampling device designed for the SOE-I system (Figure 2a) consists of four modules: the sensor chamber, the purge system, the control circuits and the display interface, the wireless data acquisition card and the Host computer. (application for data processing); each of the sub-systems has the following specific function: Data conditioning and acquisition, purging and data processing, to obtain more representative information (characteristic pattern) for the corresponding analysis (detection and monitoring). Figure 2b illustrate the flow chart of the SOE-I system.

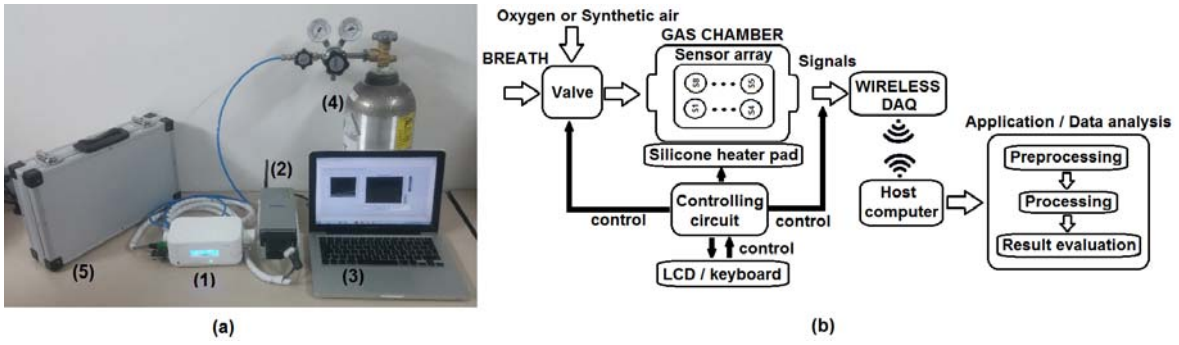

Figure 2: (a) SOE-I system: (1) Sampling device, (2) Wireless data acquisition device, (3) Host computer / Application, (4) Gas for purging, (5) portable suitcase; (b) System flow diagram

Figure 3 (a) illustrates the measurement chamber with the following elements inside: Gas sensor array, Temperature and humidity sensor, which was built in aluminium with a capacity of 30 mL, this volume allows a higher concentration of the sample, reaching a rapid response from the sensors. A silicone heater (Silicone Heater Pad) was attached to the interior of the chamber, as shown in Figure 3b., With the aim of controlling the humidity resulting from the exhaled breath, avoiding the condensation of VOC's inside the chamber, therefore its interior was heated to 65 ºC, reducing the relative humidity inside it. It was also possible to correct the drifts of the sensors due to the compensation of temperature and humidity.

Figure 3: (a) multisensory chamber, (b) top view SOE-I device

The purge stage basically has two objectives: cleaning (purging) the chamber after the entry of a sample and avoiding the memory effect of the MOS sensors; with the above, the same conditions are established within the chamber to optimize the repeatability of the device. Figure 4 shows the direction in which the flow of synthetic air and breath travel through the chamber.

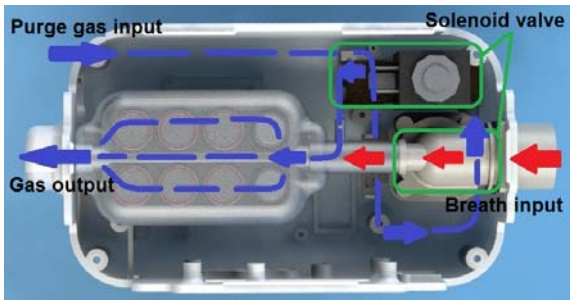

Figure 4: Purge system: direction of gas flow

For the control and monitoring of the SOE-I modules, a control and visualization circuit were implemented, which regulates the temperature inside the chamber, controls the purge system and also contains a set of visual indicators (i.e. LCD, status LED), sound (Buzzer) and remote activation for data acquisition. The actions of activation and verification of the state of the device can be activated by means of the keyboard and the LCD screen of the device.

2.3 Wireless data acquisition (WDAQ)

The data acquisition was carried out by means of the wireless module cDAQ 9191 and the NI 9207 analog module of National Instruments, with a 24-bit ADC and sampling rate of 500 Samples / second. The WDAQ has two modes of wireless connection: Infrastructure and Ad-Hoc, for the first mode the connection with the Host computer and the second mode, a WIFI network is generated limited to the range of the signal (20 meters maximum) with possibility of expansion.

2.4 Sampling procedure

The tests were performed with volunteer patients diagnosed with COPD, chronic smokers (with and without diagnosis of COPD) and healthy people (Table 2), where each of them signed an informed consent. Each patient was fasting in each test performed in order to avoid contamination of the sample with external agents.

Table 2: Number of samples in each class.

Class	Number	Age
Healthy	20	15 - 55
COPD	40	40 -70
Smoking	8	45 -60

The sampling stage was carried out with the preparation of the device, initially locating the filter and the nozzle, where then the heaters and the sensors were activated. Consecutively, the purge stage and the wireless connection to the computer are activated and after 8 minutes the temperature of the device and the

base lines of the sensors are stabilized. After this time the device starts the acquisition and the patient places the mouth in the mouthpiece to begin the exhalation; the sound indicator of the device generates a signal activating the acquisition of data. The exhalation should be continuous until the patient feels that his lungs are empty. Once the measurement is completed, the purge process begins. Figure 5 presents the response of the sensor array to a sample of exhaled breath of a volunteer with COPD and a sample of a healthy volunteer, where the difference between the breath samples can be evidenced, mainly this difference that presents in the response of the sensors MQ-138, MQ137, MQ135, SP-31 and MQ-03, where the response of the sensors to a sample of COPD is of greater magnitude in comparison with the sample of a healthy volunteer and in the TGS sensors -813, TGS-822 and TGS-813 the magnitude is simulated; Basically, this indicates that there is an "imbalance" in the chemistry of the body in the presence of a disease such as COPD. All samples were acquired in random way since the test was made when each patient was appearing.

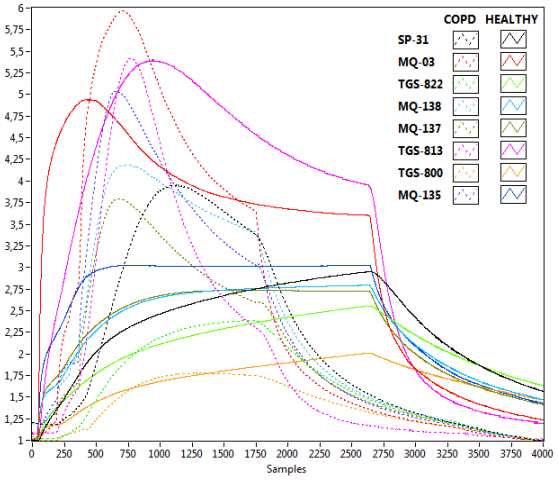

Figure 5: Response of the sensor array to a breath sample (COPD – Healthy)

3. Data Analysis

The preprocessing of data was done by means of characteristic extraction methods, normalization and pattern recognition. Initially the static parameter of the original data set (matrix of 4000x544 data, where the columns is the response of the sensors for each breath sample captured and the rows are the digital samples obtained from the A/D converter) was extracted in order to obtain the maximum information $X_{ij} = Y_{ij} - Y_i$ where, the signal Y_i or "baseline" is the steady state response of the sensors in the presence of gas purge (oxygen or synthetic air), Y_{ij} is the response of sensor i in the presence of odor j and X_{ij} is the resulting matrix; then they were normalized by scaling and centring techniques $X'_{ij} = \left(X_{ij} - \bar{X}_j\right)/S_j$, where $\bar{X}_j$ is the mean and S_j is the standard deviation. The processing was carried out with the PCA method (discriminatory method), which projects the high dimension data in a subspace of low dimension through the variance that highlights the most important information of the data set and that is described in the first two PC's. , additionally as an alternative method, LDA was implemented, with the objective of corroborating the results obtained when being projected in a two-dimensional plane. As a last step to confirm that there is really a discrimination (separation) between the analysed samples, support vector machine (SVM) was implemented in order to obtain the classification of the set of related samples (clusters), for this analysis a matrix was generated in order randomized data obtained with the PCA or LDA methods, to then be divided into two groups (50% combined training and 50% combined validation).

4. Analysis and Discussion

To evaluate the performance of the SOE-I system, breath samples were obtained from patients with COPD (previously confirmed their diagnosis through the clinical history) to be compared with patients influenced by other factors such as: Smoking and controls or healthy people. For the acquisition of these breath samples the procedure described above was followed. The analysis of the samples in Table 2 was carried out with the following configuration that allowed obtaining the best results: manipulation of the baseline, extraction of static parameters and auto scaling. In Figure 5 the resulting clusters of each group of samples are projected applying PCA as a discriminatory method and SVM for classification, Figures 5a-b show the discrimination resulting from the samples of COPD (red label) and chronic smoking (green label), compared to healthy samples (blue label), in which a variance of 86.4% and 97.35% respectively and a 100% classification were

obtained in both cases; in Figure 5c the discrimination of the three groups of samples was obtained a variance of 92% and its classification was carried out in two stages, in the first stage, the chronic smoking samples and healthy samples were linked and compared with the COPD samples, where 53% classification was obtained; in the second stage, the samples of COPD and smoking were linked and compared with healthy samples, where 97% classification was obtained.

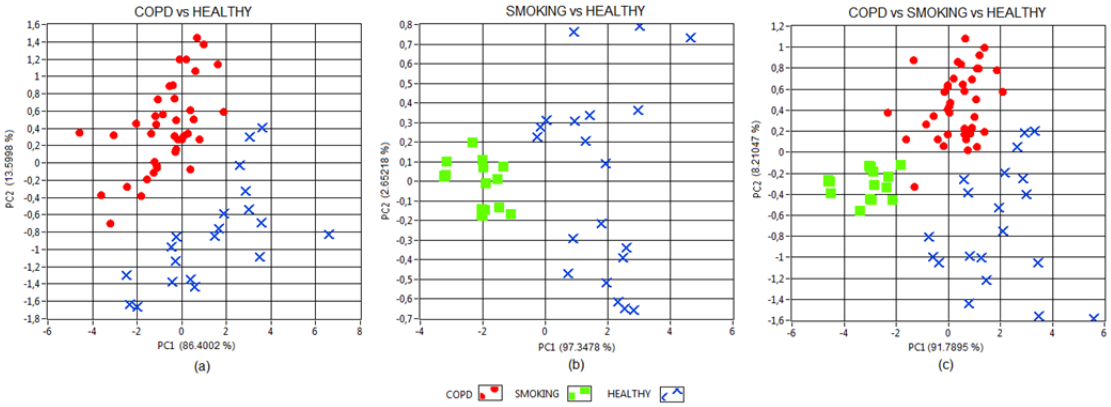

Figure 5: PCA Graph: (a) COPD vs Healthy, (b) Smoking vs Healthy, (c) COPD vs Smoking vs Healthy

As can be seen in each of the projections, the system managed to obtain a clear discrimination of the three categories, in addition to representing the correlation between the samples of COPD and smoking which was verified with the clinical history of volunteers with chronic smoking. On the other hand, analysing the loads obtained from the PCA analysis (Figure 6), it can be determined that all the sensors reached a high degree of relevant information, where only the S2 sensor did not have great relevance in terms of the contribution of information, in addition it can be deduced that sensors S3, S6 and S7 had similar responses, which would reduce the size of the resulting data by omitting the information of two of these sensors.

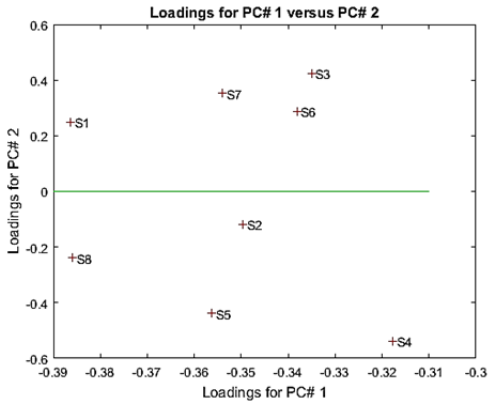

Figure 6: Loadings from PCA (sensor array)

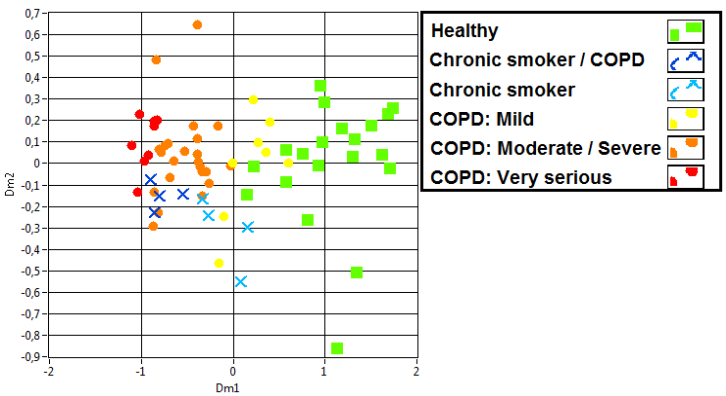

Figure 7: levels of severity of COPD and correlation of chronic smoking

In an additional analysis where each breath sample of COPD was related to the clinical history (severity level) of each volunteer and making a change in the configuration of extraction of static parameters for $X_{ij} = \log((|Y_{ij} - Y_i|)/Y_{ij})$ and changing the discriminative method for LDA, which obtained a clearer projection, it was possible to obtain a projection of levels as shown in Figure 7, where the COPD samples are projected progressively according to their level of severity. Likewise, a more evident correlation of the chronic smoking samples was obtained as a condition that can lead to the suffering of COPD.

5. Conclusions

As can be observed in the COPD patient tests and chronic smoking, the SOE-I system managed to capture the most representative VOCs and identify the characteristic pattern of each group of exhaled breath samples, as a result the resulting projections proved the discriminative capacities of the patient. system, in the same way the projection of levels allows a certain degree an early diagnosis of a disease, therefore proving the premise on which this type of studies is based, where due to a disease the body chemistry is affected as It can be observed in the response of the sensors to a sample of breath of COPD compared to a sample of a healthy person, it was also proved how the habit of chronic smoking manages to affect health in such a way that it can derive first of all in the suffering of COPD.
A next stage to be developed for the validation of the SOE-I system will be the inclusion of analytical methods such as spectrometry in order to obtain the most representative biomarkers of a transmissible or non-transmissible disease, which will allow a more efficient training of the system to achieve an accurate diagnosis, which will outline the wireless system to be implemented in health centres and hospitals, where it promises to be a support tool for medical diagnosis.

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