35th Annual International Conference of the IEEE EMBS
Osaka, Japan, 3 - 7 July, 2013

Glucose Detection in Human Sweat Using an Electronic Nose

Oscar Olarte* §, José Chilo † José Pelegri-Sebastia ‡ Kurt Barbé* and Wendy Van Moer* †
*Dept. ELEC, Vrije Universiteit Brussel, Pleinlaan 2, B-1050 Brussels, Belgium
† University of Gävle, Kungsbcksvgen 47, 801 76 Gävle, Sweden
‡ Dept. Elec. Ing. Universidad Politécnica de Valencia, C. Paranimf 1, 46730-Grao de Gandia, Spain
§ Email: oolarter@vub.ac.be

***Abstract*—In the last years attempts to develop a non-invasive glucose system based on the glucose levels in sweat have been studied. In this paper, 32 metal oxide semiconductor (MOS) sensors operating at different temperatures have been used to develop a multisensor olfactory system that allows to study the glucose levels in sweat. In order to develop repeatable experiments, artificial sweat at different glucose concentrations were developed in the laboratory. The obtained results suggest high viability of the approach. Although, the sensitivity of the sensors system needs to be improved.**

I. Introduction

According with the world health organization there are 347 million people with diabetes around the world, and the projections for 2030 is that diabetes deaths will increase by two thirds. A publication of the Diabetes Control and Complications Trials report [1] shows that the number of glucose monitorings influences the management of diabetes. As a consequence, the number of blood measurements has increased and the patient has to prick several times a day.

Sweat glucose (SG) levels have been previously measured in humans [2] [3]. And in [4] a significant statistic correlation between the SG and blood glucose (BG) levels was found. Based on these findings, it is possible to propose a system based on the glucose concentration in sweat to detect BG levels.

In [5], based on the olfactory system of dogs, data shows a clear correlation between the number of alerts that the dog gave and the number of hypoglycemic states. However, given that the dog training is based on routine, it is not possible to determine if the dog is smelling the glucose level or a routine change. On the other hand, in [6] an attempt based on the acetone in breath, that is a marker for glucose, is used to determine the glucose levels.

In this paper, we propose an electronic odor system to detect glucose in human sweat based on the previous observations that glucose is present in sweat [2] [3], there is a correlation between SG and BG [4] and that glucose has an odor effect [5] [6]. In our attempt, different similes of sweat at different glucose levels are tested employing an electronic system of 32 gas sensors from Figaro Engineering Inc.

In section II and III a description of the human sweat and the experimental setup are presented. In section IV the experimentation is described. Section V presents data preprocessing. Section VI presents the classification results, and finally in section VII the conclusion is presented.

II. Human Sweat

The principal component of sweat is sodium chloride (NaCl). Its mean value is around 350 mg/dL. Different to other sweat components, lactate and urea do not present hypoosmotic concentration with respect to the plasma. Their concentration volumes are around 120 mg/dL and 25 mg/dL respectively. However, the concentration could change depending on the body part where the sweat is collected [2] [7] [8].

Glucose has been reported in significant concentrations of 5 to 20 mg/dL in sweat and it is correlated with blood glucose concentration. [4] [2] [3]. For diabetic patients the SG may exceed 100 mg/dL but most of the research reject these last value [2]. This discussion can be extended since the sweat is principally the product of three different sources: secretion of the eccrine glands, secretion of the aprocrine glands and presumably passive diffusion of water. In this sense, sweat composition varies in relation to the part of the body.

III. Experimental Setup

A. Sensor System

A diagram of the Sensor system is shown in the figure 1. The system is divided in two parts. The electrical part and the chamber section. The electrical part consist of eight electronic boards with four sensors in each of them.

Gas sensors from Figaro Engineering Inc. convert changes in conductivity to an signal which corresponds to the gas concentration [9]. A voltage is applied to the sensor in order to maintain the sensing element at a specific temperature. The ability to have different sensitivity properties is obtained by selecting different sensors and operating temperatures.

The sensors are commercial sensors MOS that are sensitive to various types of gases. Each board includes a voltage regulator controlled by the user interface. The output voltage of each sensor is fed into an amplifier.

The data acquisition, was performed using an analog to digital converter (ADC) from national instrument (NI USB-6218). It has 32 analog inputs, used for data collection from the 32 sensors, and two analog outputs, one used to control the voltage in the regulator and the other to control the electrovalve.

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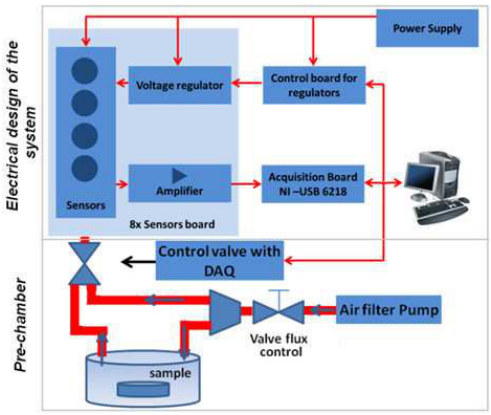

Fig. 1. Electrical design of the system and the sample chamber

The electrovalve controls the flux of air to the sensor system. The air from the pump is split into two streams, one goes through the sample chamber and thereafter to the electrovalve and the other goes directly to the electrovalve. The electrovalve is controlled automatically from an interface. The acquisition experimental process is as follow: clean air passes through the system to clean it during a predetermined time and then passes through the sample chamber during another fixed time. The setup is controlled by a dedicated graphical user interface on a personal computer. A complete description of the whole system can be found in [10].

B. Solutions

In order to do repeatable and controllable experiments, we prepared two base laboratory solutions simulating the sweat content in the thigh and torso. Table I summarizes the composition of these solutions.

TABLE I
COMPOSITIONS OF THE BASE SOLUTIONS

Product	Thigh	Torso
NaCl	351 mg/dL	351 mg/dL
Lactate	123 mg/dL	104 mg/dL
Urea	29 mg/dL	23 mg/dL

The base solutions were done in volumes of 1000 mL. Each base solution was sub-divided and glucose was added until reach glucose concentrations of 0, 40, 70 and 100 mg/dL for the thigh solution and, 0, 10, 15 and 20 mg/dL for the torso solution. The glucose concentrations were chosen in order to cover physiological and non-physiological concentrations.

The solutions were prepared using demineralized water from a Mili-Q system, urea (at 98%), Lactate (at 85%) and glucose (D-glucose at 99%) from Sigma-Aldrich Laboratories. The NaCl (at 99%) comes from VWR-laboratory. The solutions were prepared in a room with controlled temperature and stored in the fridge at around 4 degrees.

IV. Experimentation

Each solution, before doing the experiment, is acclimated during 20 minutes in a room with controlled temperature (24 degrees). Subsequently, the solutions are presented to the sensor system in volumes of 20 mL. It is important to note that the system accepts smaller volumes. It depends in the acquisition time and evaporation rate. For our experiments, the level of evaporation was considered not substantial.

The experimental data acquisition starts by using pure air in order to read the state of the sensors at the environment state. This pre-acquisition is done during 20 sec.

Once the system has read the environment state the electrovalve conducts the air to the sample chamber, where the sweat sample is located (it is done during 160 sec.) Then, the inlet from the chamber is closed and the system read the environment again for 40 sec. more. This process is repeated for 30/50 different realization for each sample.

V. Preprocessing

In this section the data set, the answer sensor selection procedure and the classification signal features are described.

A. Sensor Selection

For each glucose concentration 30/50 repeated measurements were performed for the thigh/torso solutions. Each experiment is composed of 32 signals corresponding to the 32 sensors of the electronic odor system. this means that in total we have 960 and 1600 signals from thigh and torso solutions respectively.

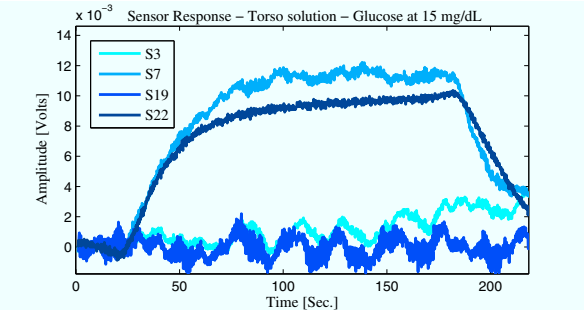

Fig. 2. Sensor Response for sensors 3, 7, 19, 22 from the torso solution at 15 mg/dL

Given that the sensors have different sensitivity properties, controlled by the operating temperature (see section Sensor System), not all sensors respond to the glucose samples. Figure 2 shows, as an example, the answer of four different sensors. Sensors 7 and 22 sense the changes between the pure air and the sweat-glucose sample, while sensors 3 and 19 do not sense any difference, or the noise level is so high that it hides the sensors response.

It is possible to reduce the data set by choosing only the sensors that respond to the presence of glucose. To do that, the measurement uncertainty is estimated in the frequency domain. So, if the standard deviation of a group of measurements is higher than its mean value, the uncertainty is high and that

sensor or group of sensors are discarded. Figure 3 presents an example of the mean and the standard deviation, in the frequency domain, for the measurements of the sensors 3 and 22. In this case, the measurements from sensor 3 are discarded and the measurements from sensor 22 are considered for the identification of the glucose concentration. This procedure is repeated automatically for all data sensors and concentrations.

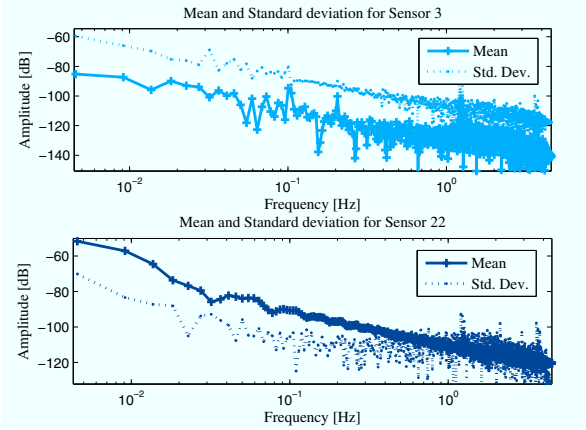

Fig. 3. Mean and standard deviation response in frequency domain for sensor 3 and 22 from the torso solutions at glucose concentration of 15 mg/dL

B. Classification Features

For the analysis process, the multisensor measurements are presented to a classification machine. However, even when a sensor selection procedure is done (as presented in the previous section) each signal is composed of thousands of data. In order to reduce the number of data, a group of features that describe completely the sensor response are chosen.

The features used by our classification system are presented in the Figure 4. They are the transient slope, the saturation slope and late saturation. These properties have been extensively used in neural networks, PCA and olfactory systems applications and are chosen based on their suitability for calculation in hardware and the intuitively-discerned likelihood that they might yield significant discrimination [11] [12] [13].

Employing the classification features some classification algorithms were employed to detect the glucose concentration in the samples. In this paper we restrict the results to the Simple Logistic algorithm using the Waikato Environment for Knowledge Analysis (WEKA) [14] . The system will be evaluated using the confusion matrix. This matrix is a specific table that allows the visualization of the performance of the system. Each column of the matrix represents the instances in a predicted class, while each row represents the instances in an actual class. The name stems from the fact that it makes it easy to see if the system is confusing two or more classes.

Based on the confusion matrix the global accuracy, the precision and the recall of the system are calculated. The global accuracy is the overall correctness of the model. the precision is a measure of the accuracy provided that a specific class has been predicted, and the recall is a measure of the

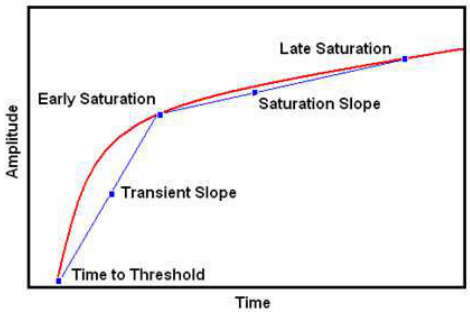

Fig. 4. Classification features

ability of a prediction model to select instances of a certain class from a data set. Finally, in order to complement the performance of the system, the kappa index is calculated. This index compares the accuracy of the system to the accuracy expected from a simple random system [15].

VI. Results

In this section the classification results for each group of data are presented. The classification of the glucose variations presents the capability or sensitivity of the system to detect and classify glucose concentrations, while the classification of the base solutions (sweat solutions at 0 mg/dL of glucose) are related to the specificity of the system.

A. Classification of Glucose Variations

The classification of the glucose variations were done for each group separately. In the thigh sweat group the employed glucose concentrations were 0, 40, 70 and 120 mg/dL while the NaCl, Lactate and Urea concentrations remain constant at the levels presented in the Table I. For the Torso group were employed the glucose concentrations of 0, 10, 15 and 20 mg/dL, while the NaCl, Lactate and Urea concentrations remain constant (see Table I).

1) Thigh Group: In the thigh group (glucose levels of 0, 40, 70 and 100 mg/dL) the minimum glucose variation was 30% (30 mg/dL) of the maximun value (100 mg/dL), and the number of repeated experiments by class was 30. Table II presents the confusion matrix. In this case, correctly classified instances are obtained around 70% with a moderate to substancial kappa index (0.611).

TABLE II
Confusion Matrix

	Predicted Class				
Known Class	0	40	70	100	Precision
0	18	3	6	3	60.0%
40	1	24	1	4	80.0%
70	6	3	20	1	66.7%
100	6	1	0	23	76.7%
Recall	58.1%	77.4%	74.1%	74.2%	

Overall accuracy (OA)= 70.83%
Kappa= 0.611

2) Torso Group: In the torso solution (glucose levels of 0, 10, 15 and 20 mg/dL) the minimum glucose variation was 25% (5 mg/dL.) of the maximun value (20 mg/dL). The number of repeated experiment by class was 50. Tabla III presents the confusion matrix of the classification. For this group of data the correctly classified instances are around 62%. In this case it is important to note the high number of misclassification in the extreme glucose values. 20 experiments belonging to the lower glucose concentration (0 mg/dL) were classified in the higher glucose group (20 mg/dL) and 23 experiments belonging to the high glucose concentration were classified as zero glucose content. On the other hand, adjacent glucose concentration values were better classified presenting zero misclassification.

TABLE III
CONFUSION MATRIX

	Predicted Class				
Known Class	0	10	15	20	Precision
0	29	0	1	20	58%
10	0	37	13	0	74%
15	0	17	33	0	66%
20	23	0	2	25	50%
Recall	55.8%	68.5%	67.3%	55.6%	

Overall accuracy (OA)= 62%
Kappa= 0.493

Even when the classification is lower than in the previous case, the overall accuracy and the kappa index show that the system responds to physiological levels of glucose concentration (the system is sensitive to glucose changes). On the other hand, the misclassification results, could be given because the concentration levels of urea (104 mg/dL) and lactate (23 mg/dl) are higher than the employed glucose concentrations (between 10-20 mg/dL) showing a possible low specificity of the current system configuration (sensor temperature and operational point) to the glucose.

B. Base Solutions Classification

The base solutions represent the mean sweat composition for the torso and thigh. These solutions differ in lactate and urea concentrations (see Table I): 15% for lactate (19 mg/dL) and 20% for urea (6 mg/dL). The number of developed experiments were 30 and 50 for the thigh and torso solutions respectively. The system is able to detect and classify the two solutions with high accuracy. Table IV presents the confusion matrix. The correctly classified instances were superior to 93% supported by a high kappa index of 0.86. This result imply that the sensor system, or the current configuration, responds to the composition of the different sweat solutions.

VII. CONCLUSION

The results show that the electronic odor system is sensitive to changes in glucose concentration even when the changes are in the order of a few mg/dL. The glucose minimum variation was 5 mg/dL. However, the accuracy of the system at that resolution is low.

The high precision of the system classifying the base solutions (0 mg/dL of glucose) shows the effect of the related sweat components in the electronic odor system. This reveals the need to improve the specificity of the system to glucose.

TABLE IV
CONFUSION MATRIX

	Predicted Class		
Known Class	Torso	Thigh	Precision
Torso	50	0	100%
Thigh	5	25	83.3%
Recall	90.9%	100%	

Overall accuracy (OA)= 93.75%
Kappa= 0.862

In the future, the system should be tested at different sensor operation ranges (working temperature and voltage operational point) in order to increase the specificity of the system to the glucose. Furthermore, it is possible to improve the data mining identifying new signal features.

As a conclusion, we can say, that the electronic odor system is a promising strategy to obtain a noninvasive glucose measurement system.

ACKNOWLEDGMENT

Postdoctoral fellowship of the Research Foundation-Flanders (FWO), the Flemish Government (Methusalem Fund METH1), and the Belgian Government (IUAP VII, DYSCO).

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