Accepted Manuscript

Title: Skin Alcohol perspiration Measurements Using MOX Sensors

Authors: B. Lawson, K. Aguir, T. Fiorido, V. Martini-Laithier, R. Bouchakour, Ch. Reynard-Carette, M. Bendahan

PII: S0925-4005(18)31717-9
DOI: <https://doi.org/10.1016/j.snb.2018.09.082>
Reference: SNB 25388

To appear in: *Sensors and Actuators B*

Received date: 23-3-2018
Revised date: 14-9-2018
Accepted date: 20-9-2018

Please cite this article as: Lawson B, Aguir K, Fiorido T, Martini-Laithier V, Bouchakour R, Reynard-Carette C, Bendahan M, Skin Alcohol perspiration Measurements Using MOX Sensors, *Sensors and amp; Actuators: B. Chemical* (2018), <https://doi.org/10.1016/j.snb.2018.09.082>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Skin Alcohol perspiration Measurements Using MOX Sensors

B. Lawson, K. Aguir, T. Fiorido, V. Martini-Laithier, R. Bouchakour, Ch. Reynard-Carette and

M. Bendahan

Aix Marseille Univ, Université de Toulon, CNRS, IM2NP, Marseille, France

Corresponding author: Khalifa.aguir@univ-amu.fr

Abstract

The aim of this study is to develop the first system based on chemical MOX sensors for monitoring ethanol on the skin after consumption. Thus, non-invasive measurements to monitor alcohol concentration and their correlation with blood and breathe Alcohol become possible. Transdermal alcohol emissions by perspiration have been investigated during clinical trials to demonstrate the relevance of this method. First, three commercial MOX sensors were used after calibration in respect of the thermodynamic conditions of the skin surface. Then, six volunteers have been selected for clinical trials with two cohorts of BAC target: 0.5 g/l and 0.8 g/l, and the three different sensors have been integrated in a wristband. We observed that the skin emits ethanol concentrations and we found a consistent correspondence between the kinetics of blood, breath and perspiration. MOX sensors can reliably estimate whether a drinker consumed a low or significant amount of alcohol. After validating this method, we developed our sensors based on tin dioxide thin sensitive layers with thickness of 50nm. Sensitive properties of the films to ethanol were studied in the conditions of the skin surface.

The sensor shows a higher response to ethanol ($r = 7.8$ for 50 ppm) with relative humidity of 50% and a lower consumption (55 mW) than commercial sensors (MICS 5524: 65 mW).

ACCEPTED MANUSCRIPT

Keywords: metal Oxide sensor, gas sensor, ethanol detection, perspiration, transdermal alcohol.

1. Introduction

Alcohol is one of the most important factors of avoidable death across the world, and represents a high socio economic cost due to the alcohol related incidents and health concerns (Alcoholism, alcoholic cirrhosis, cancer of upper aero digestive tracts, etc...), which continue to increase [1-3]. Currently, the most commonly used alcohol detection methods are the analysis of biological fluids such as blood, breath, or urine [4-6]. However, these detection techniques have a limit of efficiency by not allowing continuous monitoring or passive detection of the alcohol concentration in a non-invasive way. There is a growing need to monitor indirectly the blood alcohol level of people who have jobs at risks, or for abstention from alcohol for medical or legal reasons [7, 8].

Breathalyzers are widely used to determine BAC (Blood Alcohol Concentration) indirectly, thanks to breath sample collection. Henry's law allow to estimate BAC with a factor of 2100 comparing to BrAC (Breath Alcohol Concentration), but its results can be alter by humidity, temperature, and individuals traits or by environmental factor [9]. One of the research areas currently being investigated, is the detection of trace of alcohol on biological fluids existing around the skin [10-13].

The interstitial fluid located just below the skin (around 500 μm of the stratum corneum) have an ionic composition similar to blood, and has been recently studied for alcohol monitoring. The device is composed of an assembly of pyramidal structures with micro-needles incorporating Pt and Ag wires, each with a micro cavity opening and integrating alcohol

oxidase enzyme for the detection of ethanol in the interstitial fluid. However this device is invasive even if it is very low scale [10, 14-15].

Skin is considered as the largest organ in the body with around 1.5 m² surface area in adults and the water loss (insensible perspiration) of the human skin shows a wide variations between 3 and 25 $\mu\text{g H}_2\text{O cm}^{-2}\text{min}^{-1}$ on the forearm [15]. Thus, since several decades the increasing of noninvasive means for human lives safety, created great interest in research field of volatile organic compounds (VOCs) detection in human body for wearable sensor applications. The literature reported up to 400 VOCs emitted by human skin including ethanol. Indeed, alcohol consumption generates the increase of ethanol concentration emitted by skin [16]. After ethanol ingestion, it is metabolized principally by the liver and a little part is removed in pure state by exhaled air or breath and also through the skin in proportion of 1 % of consumed alcohol reported by Nyman and Palmlov [17-18].

Recent works used iontophoresis and electrochemical biosensing methods for determining the BAC by monitoring ethanol concentration in sweat (sensible perspiration) induced by pilocarpine via iontophoresis and amperometric detection of ethanol [12]. The biosensor is composed by alcohol-oxidase enzyme and the Prussian blue electrode transducer. We notice the correlation between the BAC and the values measured by the biosensor, however the device is combined with a bulky non-wearable iontophoretic system, and required calibrating the devices [8]. Besides other electrochemical biosensors based on iontophoresis and amperometric detection of ethanol on a wearable temporary-tattoo platform have been developed to detect alcohol on sweat [8, 12].

Skin emitted also insensible perspiration which enable to detect trace of alcohol and correlate with Blood Alcohol Concentration. Indeed, water is lost from the skin in two ways: constant, not visible, unnoticeable sweat in vapor phase from epithelial surface (insensible perspiration)

and sweat in liquid phase secreted by sweat glands [17-18]. Thus, insensible perspiration has been studied in literature and allowed the development of both wearable devices (SCRAM and WristAS) for measuring traces of alcohol on the skin [18-21]. The SCRAM is the ankle bracelet currently used in USA by judicial system for monitoring alcohol consumption by measuring ethanol in insensible perspiration. These devices are composed by electrochemical sensors, are wearable and provide a reliable transdermal alcohol concentration. However they are bulky and need regularly recalibration [17, 19].

In this document we will discuss a first wearable metal oxide gas sensors which enable noninvasive alcohol monitoring on the skin. Our work consisted in the development of Metal Oxide (MOX) sensor capable to detect ethanol in insensible perspiration. The metal oxide gas sensors are interesting because of their small size, low power consumption, continuous and noninvasive measurements, good sensitivity and short response time and can be integrated in embedded and autonomous device [23-25].

In the first stage, we monitored continuously transdermal alcohol concentration (TAC) with commercial MOX microsensors and we correlated these data with blood (BAC) and breath (BrAC) alcohol concentration, during clinical tests. With the aim to perform the clinical trials, we selected 3 commercial MOX microsensors with good sensitivity to ethanol and we integrated them in electronic bracelet.

After demonstrating that the ethanol is emitted through the skin in an amount sufficient to be detected by the MOX sensors, we developed the first MOX multisensors for ethanol monitoring through the skin, more sensitive and with the possibility of selective detection. The sensitive material of SnO_2 thin film were deposited by RF reactive magnetron sputtering on new transducers developed at the IM2NP Laboratory. MOX Sensor properties will be investigated under ethanol exposure with interfering as humidity.

2. Experiment

2.1. Experimental Setup

An innovative and automated sensor calibration system was designed and built thanks to the APPRISE (Personal Assistant of Health Prevention) project from Aix-Marseille University (Foundation A*MIDEX) in order to test and study the sensor performances under ethanol exposures. The experimental setup (Figure 1) was divided into three parts:

- Generation and control bench of ethanol, acetone and humidity vapors. Ethanol vapor is generated by permeation system with different stages of dilutions via several automated mass flow controllers (Figure 1a). Ethanol concentrations have been studied between 1 ppm and 100 ppm with relative humidity of 50 %
- An environmental chamber with temperature control and an integrated test cell made in our laboratory to characterize and calibrate the sensors in the presence of various ethanol concentrations (Figure 1b)
- A control and data acquisition systems (Figure 1c).

The gas flow rate is fixed at 250 sccm. Ethanol vapor is carried in the test chamber placed in the environmental chamber at 33 °C which corresponds to the average temperature of the skin surface. The sensor resistances are measured directly by three Keithley 2450 sourcemeters with a constant current biased sensor.

Figure 1. Experimental setup for ethanol microsensors characterization and calibration: Vapor generation (a), Test chamber (b) and Data acquisition system (c).

2.2. Sensors calibration in Laboratory test bench

We selected three commercial VOCs sensors according to two criteria: ethanol sensitivity and power consumption: MICS 5524 (SGX Sensors), TGS 8100 (Figaro Sensors) and CCS 801 (Cambridge Sensors) see table 1.

Table1: Electrical parameters of MOX gas sensors used during clinical trials

	unit	TGS 8100	MICS 5524	CCS 801
Current Polarization	μA	20	1.7	1.4
Power consumption	mW	15	65	36
Heater voltage	V	1.8	2.2	1.4
Response 50 ppm (RH: 50%)		2.56	3.83	2.04

The sensors were exposed to different ethanol concentrations during 30 s from 1 ppm to 100 ppm with 50 % relative humidity at a flow rate of 250 sccm. The MICS 5524 sensor showed the best sensitivity (Figure 2) under ethanol vapor despite high relative humidity rate (RH 50 %). Therefore, we present only the results of the sensor MICS 5524 during the clinical trials.

Figure 2. Comparison of commercial sensor responses under different ethanol concentrations

At a concentrations of 80 and 100 ppm, we observe two response levels, probably due to the sensors saturation, hence the non-repeatability of the measurements.

2.3.Clinical trials

2.3.1.Subjects and criteria

All protocols were approved by the Ethics Committee and the National Agency for Safety of Medicines and health Products (ANSM) and conducted according to Good Clinical Practices and all subjects gave written informed consent before starting the trials. A total of six Caucasian healthy adult alcohol drinkers (Alcohol consumption between 3 to 14 standard glasses/week) composed of three men and three women were recruited and financially compensated for their participation. Participants were recruited according to several inclusion criteria. These characteristics included for example the age (between 22 and 28), a current or past psychiatric disorder history, substance dependence history (no smoker or <5 cig/day), a body mass index between 19 to 28 kg/m². Demographic characteristics are given in table 2.

2.3.2.Trial description

Trial lasted one day for each participant. Subjects were asked to fast after midnight on the day of trial and it was confirmed via self-report on the morning of trial. Subjects' urine and breath samples were collected to perform drug, alcohol and pregnancy tests immediately upon arrival at the pharmacology center of the Timone hospital at 7:00 am. Then the subjects took a breakfast low in lipid and fitted 2 wristbands, the first integrated MOX gas sensors and the other wristband included humidity and temperature sensors. The wristbands were placed on the subjects wrist so the sensors were almost directly facing the skin (about 2 mm). Volunteers began alcohol administration 30 min after putting the wristbands on, allowing them to create a base line of MOX sensors. Alcohol consumption lasted for 10 to 15 min before we began the breath and blood sample collection to determine the Breath Alcohol Consumption (BrAC) and

the Blood Alcohol Consumption (BAC), while MOX sensor measured alcohol emitted through the skin by insensible perspiration (TAC). A meal was provided four hours after alcohol administration. The test ended ten hours after alcohol consumption and the subjects BAC controlled at 0.0 g/l for at least 3h minimum. Then the wristbands were removed. The Subjects confirmed they were in total sobriety before leaving.

2.3.3. Alcohol administration protocol

The alcohol was given orally, which is the most described protocol found in literature and which corresponds to the usual practice of alcohol ingestion. During the trial two different targets of BAC will be studied: BAC of 0.5 g/l and 0.8 g/l, in compliance with the limits laid down by French legislation. The main alcohol beverages consumed by each subject consisted of a strong alcohol at 40 % (Vodka) mixed with a fruit juice. The amount of alcohol consumed by each subject was calculated using the Widmark formula which is widely used but not absolute and therefore may have some variability [20]. The final volume of beverage was between 300 to 400 ml, depending on the subjects' corpulence.

Table 2: Subject demographic characteristics and parameters of alcohol consumption

Subject	1	2	3	4	5	6
sex	Female	Male	Female	Male	Female	Male
Age (years)	25.5	24.5	26.0	25.0	23	24.5
Weight (Kg)	54	70	47	75	58	77
Target (BAC)	0.5	0.5	0.5	0.5	0.8	0.8
Alcohol consumed (ml)	47.0	54.0	73.0	79.0	83.5	129.0

2.3.4. Sample and Data collection

Blood samples were collected to determine and monitor the alcohol pharmacokinetics depending on the amount ingested. The Blood samples were taken at precise time: T15' (15 minutes after the end of consumption), T30', T45', T60', T1h30, T2h, T2h30, T3h, T4h, T6h, T8h, T10h. The total amount of blood was 84ml. The determination of BAC in the plasma was performed by gas chromatography (GC) coupled to an Agilent 6850 Flame Ionization Detector (FID). The chromatographic column is a Macherey-Nagel capillary column OPTIMA WAX 30m-0.25mm-0.25 μ m.

The Breath Alcohol concentration were measured at: T15'(15 minutes after the end of consumption), 30', 45', 60', 1h30, 2h, 2h30, 3h, 4h, 6h, 8h, 10h using Alcotest® 7410 Plus from Dräger.

Transdermal alcohol concentration were performed thanks to wristband which integrated a circuit of MOX gas sensors (TGS 8100, MICS 5524, CCS801) on a PCB included in little cavity with a size of 0.5 cm³. The cavity is opened on the top of the wrist skin surface. The mobile test bench (Figure 3) and this specific wristband (Figure 4) have been especially designed for clinical trials. MOX gas sensors were polarized with a constant current (I) and the conductance variation were measured by three Keithley 2450 sourcemeters continuously all the time of clinical trial for each subjects.

Figure 3. Mobile test bench for clinical trials

Figure 4. Bracelet with the three MOX sensors

2.4. SnO₂ sensors for transdermal ethanol monitoring

2.4.1. Sensitive material SnO₂

We selected tin dioxide based sensitive layer relying on the results reported in the literature. Tin dioxide is n-type semiconductor oxide with a wide-band-gap (3.6 eV), and a wide range of applications for various types of oxidizing or reducing gas/vapor detection. It is one of the most sensitive layer used [25-31]. Our SnO₂ sensitive thin layers were deposited by RF reactive magnetron sputtering technique on transducers patented by the CNRS-AMU-IM2NP laboratory. These transducers are designed to have three sensors and two heaters in the same membrane.

In this study we will present only the response of the central sensor. A thickness of 50nm of the sensitive layer was measured by Dektak-6 profilometer. In fact, the thickness of the sensitive layers plays a major role in improving the sensitivity of the sensors. The choice of a thickness of 50 nm follows from previous studies and literature [32]. During the deposition process a residual gas pressure and the Ar/O₂ mixture were fixed respectively at 22 μbar and 40 %/60 %. Finally an annealing under dry air at 500 °C for 12 hours was done in order to improve the film oxidation, the nano-crystallization, and the stability of the sensitive layer.

Figure 5 shows the XRD patterns of SnO₂ thin film. The diffraction peaks show tetragonal rutile structure of SnO₂ (JCPDS N°72-1147).

Figure 5. XRD patterns of SnO₂ deposited by RF reactive magnetron sputtering

3. Results and discussions

3.1. Clinical results trials

3.1.1. Blood Alcohol Concentration

After collecting and analyzing blood samples from each subjects, we observed that only the subjects n°6 (Male) and n°1 (Female) actually achieved the expected blood alcohol levels, see figure 6.

Figure 6. Blood Alcohol Concentration Peaks by GC-FID analysis according to clinical trial subjects

We focused the results on the subjects N ° 1 and N ° 6, because it is for these subjects that the measurement protocol was the most successful and which reached the blood alcohol concentration expected for (respectively 0.5 g / l and 0.8 g / l), following ingestion of the alcohol dose.

3.1.2. Comparison of BAC, BrAC, TAC

The sensor conductance variations have been carried out continuously during the clinical trials. Figures 7 and 8 illustrate the evolution of Blood, Breath and Transdermal Alcohol Concentrations as function of time respectively for Subjects N°1 (peak BAC: 0.5 g/l) and N°6 (peak BAC: 0.8 g/L). Transdermal Alcohol Concentration is based on MICS sensor conductance value. The first measurements were not very satisfactory as the sensors already detected the ethanol in the ambient air coming from the glass before consumption. Also, we had to improve the measurement protocol by isolating the sensor from the environment of the room by improving the tightness of the bracelet to be sure only the ethanol obtained by perspiration will be detected.

After drinking alcohol, blood tests and breath analyses showed a rapid rise in blood alcohol levels to a maximum of about 30 min for subject N°1 and 45 min for subject N°6.

Figure 7. Comparison of BAC, BrAC, and TAC for subject N°1

Regarding subject N°1, after the ingestion of the alcohol, it took 2h30 to stop traces of alcohol in the breath and 3h to no longer have any traces of alcohol in the blood and have

a peak delay of about 25 minutes. Beside, on the skin the sensor conductance don't thoroughly return to base line even 10 hours after alcohol ingestion. This kinetics is comparable with other MOX sensors and for other subjects. This can be explained by a very slow evacuation rate of alcohol through the skin [18-19].

Figure 8. Comparison of BAC, BrAC, and TAC for subject N°6

Regarding subject N°6, it takes about 6h to stop traces of alcohol in the blood and in the breath. In the same way we will note an increase in the conductance of the MOX sensors, followed by a slow decrease in both cases. This variation can therefore be correlated with the concentration of alcohol in the blood. These results show that the quantity of ethanol evaporated from the skin is sufficient quantity to be detected by MOX sensors by perspiration and the blood alcohol level (BAC) can be estimated after sensors calibration. We can also observed that the TAC alcohol curve (G) is right shifted from the BrAC and BAC alcohol curves, with a peak delay of about 80 minutes and took longer to reach zero. This behavior of the sensor responses is certainly due to the metabolism of the human body at the skin level. The same kinetic behavior was observed in alcohol elimination by urine [22].

After demonstrating that the alcohol emitted by the skin after consumption can be detected by the MOX sensors and can be correlated with the blood alcohol Concentration, we will develop our MOX sensors based on SnO₂ sensitive layer, that will be more sensitive to ethanol, with a more stable baseline and with lower power consumption than the current sensors.

3.2. SnO₂ Gas sensor results

3.2.1. Working temperature

Gas sensors were characterized using the ethanol test bench previously described in section “experimental setup 2.1”. Figure 9 illustrates the sensor dependence to the temperature using different concentrations (10 and 50 ppm) of ethanol with relative humidity of 0% and a gas flow rate of 250 sccm. The responses increase with temperature up to 280°C and seems to be decreasing after this temperature. It is well known that the response has a maximum for a given temperature. Indeed the increase of the sensitivity can be attributed to the fact that the thermal energy supplied is high enough to overcome the activation energy barrier to enable the redox reaction and a significant increase in electron concentration induced from the sensing reaction. Here we had chosen to operate at 280 °C which represents our optimal temperature. Therefore we set the operating temperature at 280 °C, the power required to reach this temperature is 55 mW.

Figure 9. SnO₂ Sensor response versus temperature for ethanol concentrations with RH of 0%

3.2.2. SnO₂ sensors sensitive properties to ethanol

The sensors were exposed to different concentration of ethanol. Ethanol concentrations have been studied between 1 ppm and 100 ppm with relative humidity of 50 % during 30 s. The gas flow rate is fixed at 250 sccm with a temperature of 33 °C. The sensors were polarized at 1 V and the power consumption was fixed at 55 mW for the three sensors, which corresponds to the optimum working temperature around 280 °C. Figure 10 shows the SnO₂ typical sensor response to ethanol. It can be seen that the sensor shows a high sensitivity, a baseline stability and fast response and recovery. These results can be attributed to the transducer used and to the sensitive layer properties.

Figure 10. Sensor response for ethanol concentrations, from 1 ppm to 100 ppm

In fact, in metal oxide ethanol sensors as SnO₂ sensors, the interaction between ethanol molecules and lattice oxygen O₀^x can be described by the reaction (in Kröger-Vink) as below [33]:

In the same way, the interaction between ethanol molecules and adsorbed species as O₂⁻ and O₂²⁻ can be described as:

As a result, the conductivity of the sensor will increase with the ethanol concentration due to the electrons produced by these reactions, as SnO₂ is an n-type semiconductor.

Otherwise our SnO₂ sensor response was compared to commercial sensors, used during the selection of commercial MOX sensors (TGS 8100, MICS 5524, CCS 803, CCS 801, TGS 2620, TGS 2602) for clinical trials, see figure 11.

Figure 11. Comparison of sensors response to ethanol

All sensors were tested at their optimum power of ethanol detection (TGS 8100: 15 mW, MICS 5524: 65 mW, CCS 803: 36 mW, CCS 801: 36 mW, TGS 2620: 210 mW, TGS 2602: 280mW and

our SnO₂ sensors: 55mW) under two different concentrations of ethanol: 10 ppm and 50 ppm with a relative humidity of 50%. It's easy to see that our sensor is more sensitive than the commercial sensors tested and therefore will have a better detection of the transdermal alcohol on the surface of the skin.

However the SnO₂ sensors can be more or less sensitive to ethanol and interference gases. The reactivity between gases and the sensitive layer is a key part of the selectivity.

4. Conclusion and perspectives

This study reports real possibilities to detect ethanol vapor through perspiration across the skin using MOX sensors. The results confirm that the two concentrations of ethanol absorbed by the volunteers (0.5 g/l and 0.8 g/l) can be discriminated. So, we have seen that it is possible to monitor non-invasively the blood alcohol levels. The responses were slightly shifted in time due to the body metabolism processes. The delay between BAC peak and TrAC peak has varied between 25 and 80 min. To improve MOX sensor sensitivity, we developed metal oxide sensor based on SnO₂ sensitive nanostructured material. The sensors characterization have demonstrated a high response to ethanol and a fast response and recovery times compared to commercial sensors. These sensors should allow a better detection of alcohol on the skin surface. Additional studies will improve the selectivity of the sensors by the use of all three sensors of our chip.

Acknowledgment: We wish to thank AMU-AMIDEX for their financial support. We also thanks the "Centre de Pharmacologie Clinique et d'Evaluations Thérapeutiques (CPCET)" of La Timone

Hospital for their staff involvement and Alain COMBES for his technical support throughout this work.

References

1. J.I. Castillo-Manzano, M. Castro-Nuno, X. Fageda, L. Lopez-Valpuesta, An assessment of the effects of alcohol consumption and prevention policies on traffic fatality rates in the enlarged EU. Time for zero alcohol tolerance, *Transportation Research Part F: Traffic Psychology and Behavior* 50 (2017) pp. 38-49.
2. S. Rahman, E.A. Engleman, R.L. Bell, Chapter Six – Recent advances in nicotinic receptor signaling alcohol abuse and alcoholism, *Progress in Molecular Biology and Translational Science* 137 (2016) pp. 183-201.
3. A. Rundio, Understanding Alcoholism, *Nursing Clinics of North America* 48 (2013) pp. 385-390.
4. P.D. Thungon, A. Kakoti, L. Ngashangva, P. Goswami, Advances in developing rapid, reliable and portable detection systems for alcohol, *Biosensors and Bioelectronics* 97 (2017) pp. 83-99.
5. J.C. Verster, M. Mackus, A.J. Van de Loo, J. Garsesen, Andrew Scholey, The breathtaking truth about breath alcohol readings of zero, *Addictive Behaviors* 70 (2017) pp. 23-26.
6. A.P. Drummond-Lage, R. Gomes de Freitas, G. Cruz, L. Perillo, M.A. Paiva, A.J. Wainstein, Correlation between blood alcohol concentration (BAC), breath alcohol concentration (BrAC) and psychomotor evaluation in a clinical monitored study of alcohol intake in Brazil, *Alcohol* 66 (2018) pp. 15-20.

7. M. Chan, D. Esteve, J.Y. Fourniols, C. Escriba, E. Campo, Smart wearable systems: current status and future challenges, *Artificial Intelligence in Medicine* 56 (2012) pp. 137- 156.
8. J. Kim, I. Jeerapan, S. Imani, T.N. Cho, A. Bandodkar, S.Cinti, P.P. Mercier, J. Wang, Noninvasive alcohol monitoring using a wearable tattoo-Based iontophoretic-biosensing system, *ACS sensors* 8 (2016) pp. 1011-1019.
9. W. Adrian, The measurement of breath alcohol concentration and the inherent physiology of the lung, *Alcohol, Drugs and Traffic Safety* 2 (1981) pp. 622-636.
10. M. Venugopal, K.E. Feuvrel, S. Bambot, M. Faupel, A. Panangadan, A. Talukder, R. Pidva, Clinical evaluation of a novel interstitial fluid sensor system for remote continuous alcohol monitoring, *IEEE sensors Journal* 8 (2008) pp. 71-80.
11. A.M. Vinu Mohana, J.R. Windmillerb, R.K. Mishraa, J. Wanga, Continuous minimally-invasive alcohol monitoring using microneedle sensor arrays, *Biosensors and Bioelectronics* 91 (2017) pp. 574-579.
12. M. Gamella, S. Campuzano, J. Manso, G. Ganzalez de Riveria, F. Lopez-Colino, A.J. Reveijo, J. M. Pingarron, A novel non-invasive electrochemical biosensing device for in situ determination of the alcohol content in blood by monitoring, *Analytica Chimica Acta* 806 (2014) pp. 1-7.
13. R. Swift, Direct measurement of alcohol and metabolites, *Society of the Study of Addiction* 98 (2003) pp. 73-80.
14. M. Sawdon, E. Kirkman, Capillary dynamics and the interstitial fluid-lymphatic system, *Anaesthesia and Intensive Care medicine* 18 (2017) pp. 309-315.
15. F. A. J. Thiele and K. G. Van Senden, Relationship between skin temperature and the insensible perspiration of the human skin, *The Journal of Investigative Dermatology*, 47 – 4 (1966) pp. 307-312.

16. P. Mochalski, J. King, K. Unterkofler, H. Hinterhuber, A. Amann, Emission rates of selected volatile organic compounds from skin of healthy volunteers, *Journal of Chromatography B* 959 (2014) pp. 62-70.
17. P.R. Marques and A.S. McKnight, Evaluating Transdermal Alcohol Measuring Devices, Report of Pacific Institute for Research and Evaluation (2007) Grant No.DTNH22-02-D-95121.
18. J.C. Anderson and M.P. Hlastala, The kinetics of transdermal ethanol exchange, *Appl Physiol.*100 (2006) pp. 649-655.
19. J.S. Hawtorne and M.H. Wojcik, Transdermal alcohol measurement: a review of the literature, *Can. Soc. Forensic Sci.*39 (2006) pp. 65-71.
20. E.M.P. Widmark, Principles and Applications of Medico Legal Alcohol Determination, Davis Biomedical Publications (1981).
21. K.M. Dubowski, Absorption, distribution and elimination of alcohol: Highway safety aspects, *Journal of Studies on Alcohol and Drugs* 10 (1985).
22. R.D. Batt, K.E. Crow, Adsorption, distribution and elimination of alcohol, *Human Metabolism of Alcohol* 1 (1989).
23. X. Liu, S. Cheng, H. Liu, S. Hu, D. Zhang, H. Ning, A survey on gas sensing technology, *Sensors* 12 (2012) pp. 9635-9665.
24. H.J. Kim, J.H. Lee, Highly sensitive and selective gas sensors using p-type oxide semiconductors: overview, *Sensors and Actuators B* 192 (2014) pp. 607-627.
25. S.H. Yan, S.Y. Ma, W.Q. Li, X.L. Xu, L. Cheng, H.S. Song, X.Y. Liang, Synthesis of SnO₂-ZnO heterostructured nanofibers for enhanced ethanol gas-sensing performance, *Sensors and Actuators B* 221 (2015) pp. 88-95.
26. J. Zhan, S. Wang, Y. Wang, M. Xu, H. Xia, S. Zhang, Facile synthesis of highly ethanol-sensitive SnO₂ nanoparticles, *Sensors and Actuators B* 139 (2009) pp. 369-374.

27. L.K. Bagal, J.Y. Patil, M.V. Vaishampayan, I.S. Mulla, S.S. Suryavanshi, Effect of Pd and Ce on the enhancement of ethanol vapor response of SnO₂ thick films, *Sensors and Actuators B* 207 (2015) pp. 383-390.
28. S. Wang W. Yu, C. Cheng, T. Zhang, M. Ge, Y. Sun, N. Dai, Fabrication of mesoporous SnO₂ nanocubes with superior ethanol gas sensing property, *Materials Research Bulletin* 89 (2017) pp. 267-272.
29. Q. Wang, X. Kou, C. Liu, L. Zhao, T. Lin, F. Liu, X. Yang, J. Lin, G. Lu, Hydrothermal synthesis of hierarchical CoO/SnO₂ nanostructures for ethanol gas sensor, *Journal of Colloid and Interface Science* 513 (2018) pp. 760-766.
30. Highly sensitive and low detection limit of ethanol gas sensors based on hollow ZnO/SnO₂ spheres composite material, *Sensors and Actuators B* 245 (2017) pp. 551-559.
31. P.Ivanov, E. Llobet, X. Vilanova, J. Brezmes, J. Hubalek, X. Correig, development of high sensitivity ethanol gas sensors based on Pt-doped SnO₂ surfaces, *Sensors and Actuators B* 99 (2004) pp. 201–206.
32. K. Aguir & al, Role of the active layer thickness on the sensitivity of WO₃ gas sensors, *Int. J. Nanotechnol.*, 471(2012) pp. 3–7.
33. Y. Liu, E. Koep, M. Liu, A Highly Sensitive and Fast-Responding SnO₂ Sensor Fabricated by Combustion Chemical Vapor Deposition, *Chem. Mater.* 17(2005) pp. 3997-4000.

Author Biographies

Bruno Lawson is a PhD student since 2015 at the microensors team of IM2NP of Aix Marseille University and CNRS, France. He started his research on chemical microensors for gas and vapor detection of transdermal alcohol on the skin after consumption. He got a Master degree in microelectronic detection systems at Aix Marseille University after doing internship on study of gas sensors for air quality control in the same team from March to July 2015. He was graduated in license of applied Physics and electronics in 2012 from the Catholic University of Togo. Currently, his research activity is focused on chemical sensor with highly sensitive and selective for ethanol toward medical diagnosis.

Khalifa Aguir is a Professor at Aix Marseille University, France. He was awarded his Doctorat d'Etat ès Sciences degree from Paul Sabatier University, Toulouse 1987. He was during the 16 years the head of Microensors Group at the Institute of Materials Microelectronic Nanosciences of Provence (IM2NP-CNRS) at Aix-Marseille University, Marseille. His principal research interests are directed towards metal – oxide thin films gas microensors, selectivity, signal treatments and multivariable analysis, modeling, flexible current sensors. He is the author of over 200 publications and international conferences. Referee of several scientific journals, he has conducted numerous expertise and he is a member of scientific committees of international conferences.

Tomas Fiorido is a Research Engineer at Aix-Marseille University, France. He received his PhD from Paul Cezanne University (France) in 2009. The research performed within the framework of this thesis concerned the realization and the characterization of new gas, light and temperature sensors based on polymer material layered over flexible supports. Currently, his research activities are focused on the realization organic or inorganic thin films for sensors,

on the engineering of gas microsensors, smoke detector and on the miniature calorimeter for nuclear.

Virginie Laithier is a lecturer at Aix-Marseille University, France. She received her PhD in 2012 at the Aix Marseille University. Since 2008, she has been with the Sensors Group at the Institute of Materials, Microelectronics and Nanoscience of Provence (IM2NP). The research performed within the framework of her thesis concerned thermal simulations and microfluidic gas sensor fabrication and characterization. Her current work involves gas sensors micro-technologies.

Rachid Bouchakour is a Professor at Aix Marseille University, France. He was awarded his PHD in Physics (1988) and Habilitation à Diriger les Recherches (1995) from Paris 6 University. He was Director of the Institute of Materials Microelectronic Nanosciences of Provence (IM2NP-CNRS) at Aix-Marseille University, Marseille, from 2006 to 2015, Research Director of Polytech 'Marseille, from 2007 to 2012 and many other directions on the teaching side. He has conducted numerous expertise in various French organizations ANR, ANRT, MSTP and AERES. His principal research interests are directed towards microelectronics, physics of semiconductor devices, modeling and simulation, reliability of silicon technologies, nonvolatile innovative memories. He is the author of over 190 publications, international conferences, patents, books and he is a member of scientific committees of IEEE international conferences.

Christelle Reynard Carette is Assistant professor at Aix-Marseille University, France. She is currently the Co-head of the Microsensors Team at the Institute of Materials Microelectronic Nanosciences of Provence. She received her PhD in 2001 and HDR in 2011 at the Aix Marseille University. Her activity field is dedicated to instrumentation, measurement, metrology,

thermal transfers, nuclear fission and calorimetry in MTR (material testing reactor). Referee of several scientific journals, she is a Co-chair of Animma international conference.

Marc Bendahan is a Professor at Aix-Marseille University, France. He is currently the head of the Microsensors Team at the Institute of Materials Microelectronic Nanosciences of Provence and Lecturer at the Institute of Technology. He was awarded his PhD degree from AMU in 1996 with a thesis on shape memory alloys thin films for micro-actuator applications. He is specialized in thin films preparation and characterization for applications in microsystems. His principal research interest is now directed towards the conception, realization and electrical characterization of microsensors: gas microsensors based on inorganic metal-oxides and organic materials, flexible temperature and pressure sensors.