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Detection of colorectal cancer biomarkers in the presence of interfering gases☆

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ABSTRACT

Medical studies have shown that tumor growth is accompanied by protein changes that may lead to the peroxidation of the cell membrane, with consequent emission of volatile organic compounds (VOCs). VOCs can be detected through breath or intestinal gases and are biomarkers for colorectal cancer (CRC). The analysis of VOCs represents a non-invasive and potentially inexpensive pre-screening technique. An array of chemoresistive gas sensors, based on screen-printed Metal OXide (MOX) semiconducting films, has been selected to identify gaseous compounds of oncological interest, i.e. benzene, 1-iodo-nonane and decanal, from the main interferers that can be found in the intestine. MOX sensors are able to detect concentrations down to about 10th ppb, as experimentally proven in previous works, so they can identify very slight differences in concentration among gas mixtures. In this work it has been proven that the array used is able to identify tumor markers singularly and in combination with other gases both in wet and dry conditions. Moreover, the sensors chosen can discriminate target VOCs from interferers even at low concentrations.

1. Introduction

Nano-materials can offer promising non-invasive methods to detect and prevent cancer [1]. It is known that VOCs emissions, produced by the peroxidation of the cell membrane or by cellular metabolism, are linked to tumor presence and growth and they can be detected directly from the headspace of cancer cells or through exhaled breath [2,3]. Indeed, changes in the blood chemistry lead to measurable modifications in the breath composition due to exchanges inside the lungs, e.g. in the range of 20–100 ppb for several VOCs [4], as well as in feces from normal digestion [5]. Aim of this work is to study the detection of VOCs indicators of CRC, identifying the most selective sensors for these compounds, in order to analyze intestinal gases in which these biomarkers should convey. The most relevant VOCs which may indicate CRC presence are benzene compounds, 1-iodo-nonane ($C_9H_{19}I$) and decanal ($C_{10}H_{20}O$) [4–6]. The main gases that can interfere in this context are H_2, CH_4, H_2S, SO_2, N_2, NO_2 and NO, these being the main components of the intestinal gas mixture.

2. Material and methods

2.1. Sensors properties

We tested several MOX for this dedicated experiment, and the selected sensing materials, the most promising ones, as confirmed by the reported data, are listed in Table 1. Sensors are prepared via screen-printing technique, after the deposition of the MOX paste on alumina substrate. They are provided with a heater made of platinum on the backside, while the contacts are made of gold. The screen-printing procedure is reported in *Printed films: Materials science and applications in sensors, electronics and photonics* [11].

A typical screen consists of a network of finely twisted steel wires (of 100 μm), stretched over a frame of aluminum. Sensors have been electrically characterized in a laboratory setup using gas

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Table 1
Composition of the metal–oxide sensors chosen for the array.

Name	Film composition	Firing temperature (°C)
ST20 650	SnO_2, TiO_2 (20%)	650
ST25 650	SnO_2, TiO_2 (25%)	650
ST25 + Au1%	SnO_2, TiO_2 (25%), Au (1%)	650
ST30 650	SnO_2, TiO_2 (30%)	650
ZnO 650	ZnO	650
ZnO 850	ZnO	850
TiTaV	TiO_2, Ta_2O_5, vanadium oxide	650
STN	SnO_2, TiO_2, Nb_2TiO_7	650

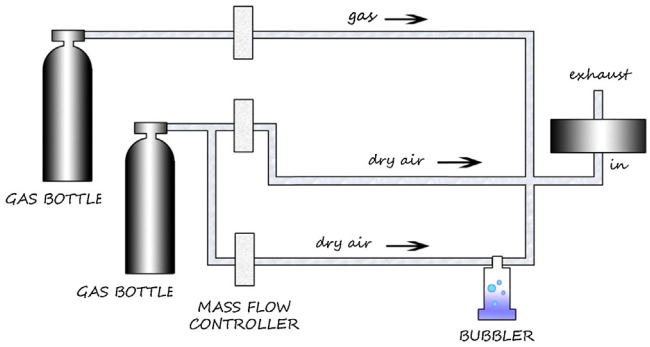

Fig. 1. Scheme of the experimental setup for gases from bottles. The bottles are connected to mass flow controllers. The first line conveys the target gas (e.g. C_6H_6 or interferers), the second line conveys dry air, the third one is employed once the measure is taken in wet conditions. Air and gases arrive at the sensors chamber.

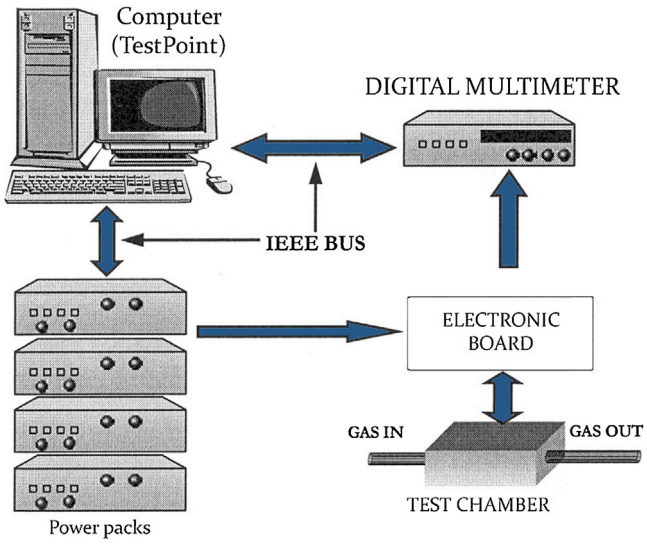

Fig. 2. Laboratory setup.

bottles as origin for gas targets and interferences. The system is sketched in Fig. 1, while the setup for the acquisition of the signal is shown in Fig. 2.

We selected ZnO (with two different thermal treatments, 650 and 850 °C), four solid solutions of SnO_2 and TiO_2, a solution of TiO_2, Ta_2O_5 and vanadium oxide and a solution of SnO_2, TiO_2 and Nb_2TiO_7 (all these material were treated thermally at 650 °C). The annealing temperatures synthesis and structural, morphological and thermal characterizations of these nanostructured materials are reported in literature [7–9]. The increase of the firing temperature is directly related to the increase of the radius of the nano-spheres composing the sensing material. After testing MOX sensors, in previous works [10,11], with firing temperatures ranging between 650 and 950 °C, we have chosen the firing

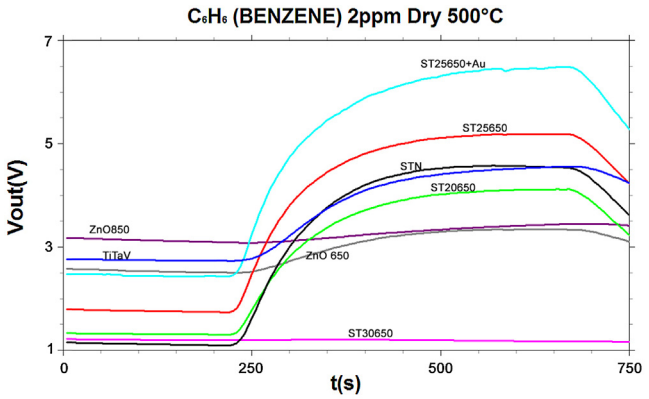

Fig. 3. Example of sensors response to C_6H_6 before normalization. On the *y*-axes there is the output voltage (V_{out}).

temperatures 650 °C (for tin/titanium-oxide-based sensors) and 850 °C (for the zinc-oxide-based sensor) as the ones at which they give the highest response. The most common formulation for screen-printable paste is listed in Tab.11.9 of the book *Printed films: Materials science and applications in sensors, electronics and photonics* [13]. As reported on pag. 298 of the book, specific paste compositions are highly proprietary. The thickness of the sensing layers is about 30 μm (thick film sensors) and they were obtained by screen-print pastes synthetized from these powders (by adding a proper amount of organic vehicles) onto miniaturized alumina substrates equipped with pre-deposited electrodes and the heater [12]. The gas sensing measurements were performed by means of the flow-through technique [13–15].

Responses from sensors are given by the dimensionless formula:

$$R = \frac{V_{\text{plateau}}}{V_{\text{baseline}}}, \tag{1}$$

which removes all the dependence of the sensors response on the geometry. Fig. 3 shows an example of sensors response to C_6H_6 before normalization. The material characterization was carried out by using scanning electron microscopy (SEM). A SEM image of the film is shown in Fig. 4 to appreciate the morphology.

2.2. Experimental setup

The sensors were located into a gas flow chamber, inside which an artificial atmosphere were injected and controlled by pc-driven mass-flow controllers. The gases were from certified bottles and

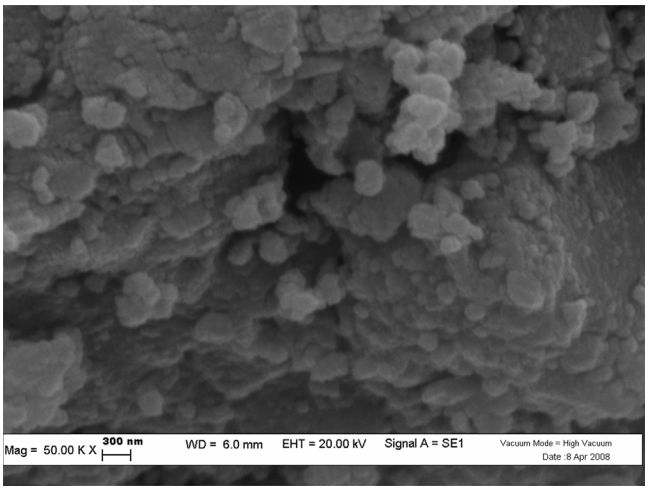

Fig. 4. SEM image of the sensor ST30 (tin and titanium oxide) fired at 650 °C.