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Detection of colorectal cancer biomarkers in the presence of interfering gases

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Abstract

Nanotechnology has considerable promise for the detection of cancer. Medical studies show 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 semiconducting films, has been selected to discriminate gases of oncological interest, as benzene, 1-iodo-nonane or decanal, from the main interferers in the gut.

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Keywords: VOC; colorectal cancer; interferers; chemoresistive; sensor; benzene; 1-iodo-nonane; decanal.

1. Introduction

The combination of nanotechnology with the need of medicine to find a non-invasive method to detect and prevent cancer is a rapidly evolving field. It is known that VOCs emissions are linked to tumor growth and they can be detected directly from the headspace of cancer cells or through exhaled breath [1]. In fact changes into the blood chemistry lead to measurable modifications in the breath by exchanges through the lung, e.g. in the range of 20÷100 ppb for several VOCs [2]. Aim of this work is to study 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 are benzene compounds, 1-iodo-nonane ($C_9H_{19}I$) and decanal ($C_{10}H_{20}O$) [2,3], that interfere with H_2, CH_4, H_2S, SO_2, N_2, NO_2 and NO, composing the intestinal gas mixture.

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2. Experimental results

The chosen materials are ZnO (with two different thermal treatments), 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. Pastes obtained from these powders are used to screen-print sensing layers onto miniaturized alumina substrates [4]. The response at various temperatures was observed both in dry (RH~0%) and in wet conditions (18%<RH<60%). Choosing the most favorable temperatures of each sensor for benzene detection, the intestinal standard gas mixture was approximately reproduced into the sensors chamber. CO_2 is not considered because it is well known that it is hardly detected by chemoresistive sensors [4]. Fig. 1 shows the responses of the sensors array to benzene (5ppm) in dry conditions inside a mixture of CH_4 (10ppm), H_2 (60ppm) and synthetic dry air (80% N_2 and 20% O_2), while in Fig. 2 a similar situation is reproduced in wet conditions (RH: 38%). What emerges analyzing these data is that hydrogen is the most influent interferer, always resulting in very high response. However, the sensor TiTaV (titanium, tantalum, vanadium oxides) is not sensitive to it and shows a great selectivity to small quantities of C_6H_6 even in the presence of hydrogen. This piece of evidence confirms the noticeable capability of TiTaV to detect benzene singularly [5] or with respect to secondary interferers (Fig. 3,4).

Tests with 1-iodo-nonane were made in dry conditions using an empty gas bubbler to evaporate it, because it was originally in liquid form. The weight of reagent was measured with a precision balance. We use this value to calculate the number of moles and to obtain an average value of the concentration. To identify the best detecting temperature for each type of sensing material, we tested the response at several working temperatures (350, 400, 450, 500, 550, 600°C), as shown in Fig. 5. The sensor ZnO 850 (zinc oxide, fired at 850°C) and STN (tin, tantalum, niobium oxides) are the ones that give the best responses to this compound, confirming results for tin oxide-based sensors of our previous work [5], taken in wet conditions. Therefore humidity does not change the trend of the responses to 1-iodo-nonane but only reduce their value.

Also tests with decanal were made in dry ambient with the same procedure used for 1-iodo-nonane and with the same sensors array. Responses are summarized graphically in Fig. 6. The sensors ST20 650 (tin, titanium oxides at 20% fired at 650°C), STN and ST25 650 (tin, titanium oxides at 25% fired at 650°C) are the best responding ones to decanal. This evidence highlights the property of tin oxide-based films to have a high response to this VOC, instead TiTaV does not show much affinity to it.

We made also a test with 1-iodo-nonane ($2.57 \cdot 10^{-4}$ mol) and decanal ($7.46 \cdot 10^{-4}$ mol) in combination, in wet conditions, to see if the interference of the two VOCs alters the sensors responses observed in the previous measurements. The working temperature chosen is the same for all sensors (450°C). Results are shown in Fig. 7. The response of tin oxide-based sensors remains high, while the ZnO 850, the most sensitive material for 1-iodo-nonane, shows a low response.

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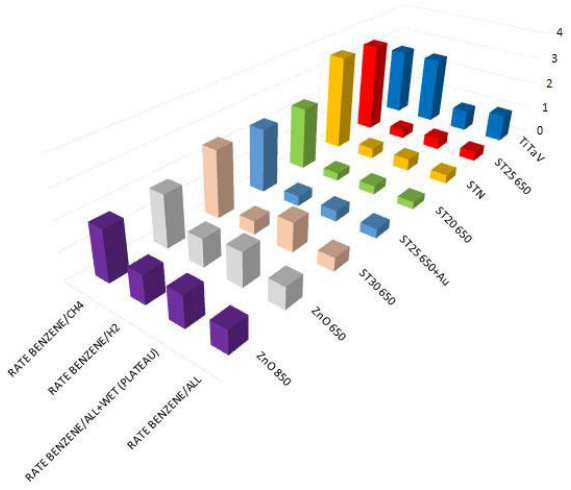

Fig.1: analysis of the total and partial response rates (ratio between responses) of the sensors array to C_6H_6 (5ppm) in a mixture of CH_4 (10ppm), H_2 (60ppm) and dry air (N_2: 80%, O_2: 20%). Humidity is used as an interferer.

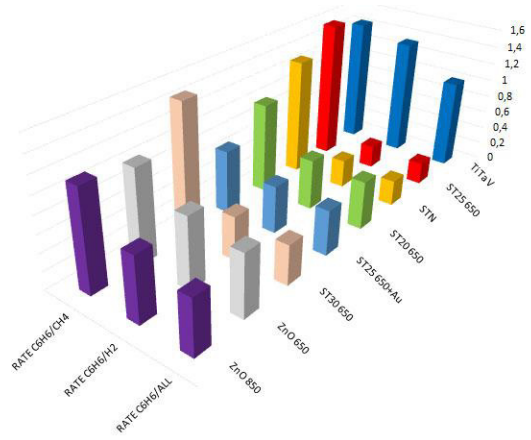

Fig.2: analysis of the total and partial response rates (ratio between responses) of the sensors array to C_6H_6 (2ppm) in a mixture of CH_4 (10ppm), H_2 (60ppm) and wet air (N_2: 80%, O_2: 20%, RH: 38%).

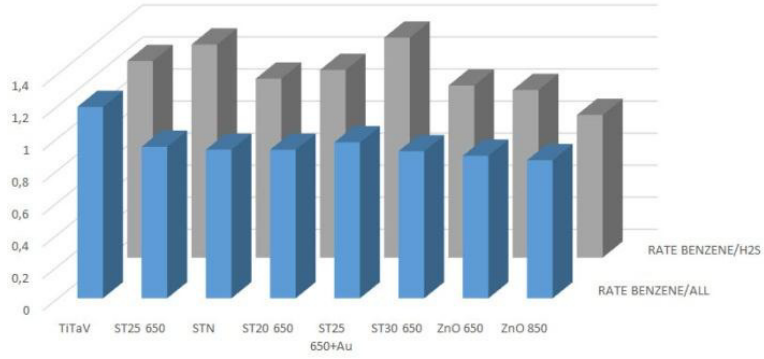

Fig.3: sensor responses to C_6H_6 (2ppm) inside a mixture of wet air (RH~20%) and two minor intestinal interfering gases NO_2 (2ppm) and H_2S (20ppm). Temperature chosen are the ones at which the sensor responses to NO_2 become negligible. Benzene is well detected into this partial interfering ambient.

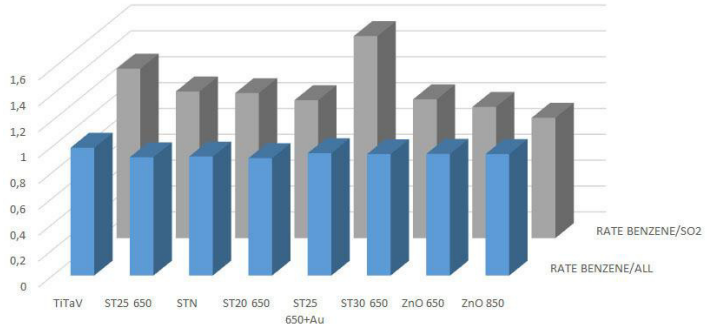

Fig.4: sensor responses to C_6H_6 (2ppm) inside a mixture of wet air (RH~34%) and two minor intestinal interfering gases NO (2ppm) and SO_2 (2ppm). Temperature chosen are the ones at which the sensor responses to NO become negligible. Benzene is well detected into this partial interfering ambient.

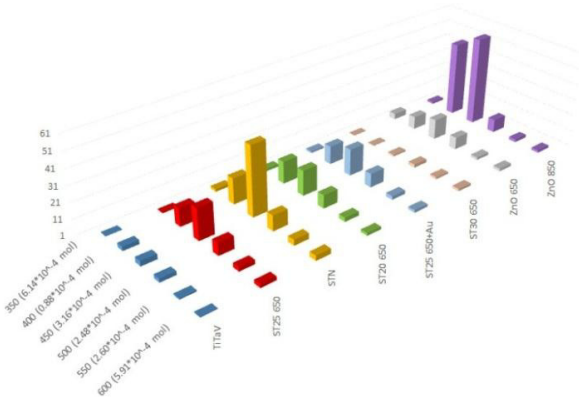

Fig.5: sensor responses to $C_9H_{19}I$ in dry conditions. Temperatures ranges between 350 and 600°C with steps of 50°C. Under parenthesis is shown the quantity of reagent (moles) taken for each measure.

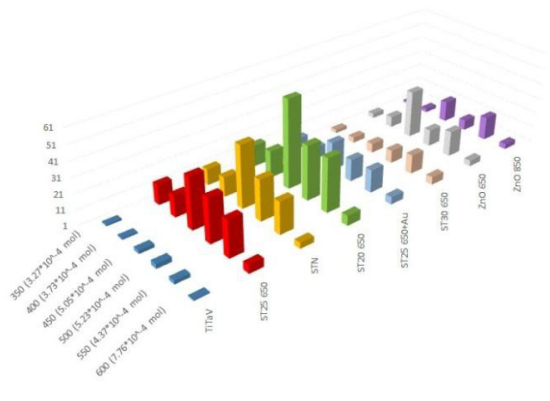

Fig.6: sensor responses to $C_{10}H_{20}O$ in dry conditions. Temperatures ranges between 350 and 600°C with steps of 50°C. Under parenthesis is shown the quantity of reagent (moles) taken for each measure.

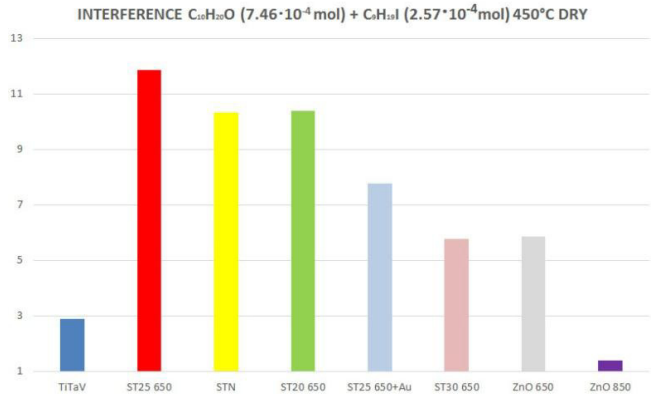

Fig.7: sensor responses to $C_9H_{19}I$ and $C_{10}H_{20}O$ in combination, in wet conditions. Working temperature of all sensors is fixed at 450°C. Under parenthesis is shown the quantity of reagent (moles) taken for each measure.