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Isoprene sensor/breathalyzer for monitoring sleep disorders

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Abstract:
This work describes an isoprene sensor/breathalyzer concept for the detection of sleep disorders. Breath isoprene is proposed here as a biomarker signaling wakefulness according to reports in the medical literature. Hexagonal tungsten trioxide was used as the sensing element and it was able to detect and discriminate among various isoprene concentrations in the range of 300 ppb to 1 ppm and above-the range of interest for the targeted application. The fast response, high sensitivity, and non-invasive, non-intrusive nature of the isoprene detector suggests that it can potentially be used as a diagnostic tool for sleep apnea.

Key words: isoprene sensor, breathalyzer, sleep disorders, sleep apnea

Introduction
The increase in isoprene concentration under normal conditions depends on sleep and isoprene is believed to play a role in sleep regulation and to also be involved in sleep upholding [1-3]. Studies involving human subjects where their breath samples were collected in 1L Teflon bags, through the use of gas chromatography and mass spectroscopy have confirmed that healthy humans (15 to 60 years old) who stay awake have an isoprene level of 14.6 +_ 6.4 nmol/L (i.e 8.2-21 nmol/L) [1]. The molar mass of isoprene is 68.12g/mol so the normal isoprene concentration in wakefulness corresponds to: 509ppb - 1.43 ppm in adults. When fallen asleep, their isoprene levels were raised to 3ppm or more. Furthermore, “in the absence of sleep during the night, the concentration of isoprene in the breath did not increase” [1]. Since isoprene gas has a high volatility and a boiling point at 34°C it’s concentration may rapidly change in the exhaled breath for a transition from sleep to wakefulness. Furthermore, in adults, isoprene levels do not depend on age, gender, diet or fasting-just on sleep under normal conditions [1]. Isoprene may increase with exercise, during myocardial infarction, and increased cardiac output, that is under stressful conditions [2]. Therefore, monitoring the isoprene levels in exhaled breath under normal conditions may provide for a non-invasive method to detect, monitor, and control sleep disorders, such as sleep apnea.

The work described here involves the development of an isoprene sensor for the detection of sleep disorders. Whereas our group has developed several other isoprene detectors (e.g. as part of a flu monitoring breathalyzer system, among others) [4-5], the sensing range in this technology is set from a few hundred ppb and to a few ppm of isoprene. The resistive sensor technology described here can be directly integrated into the breathalyzer platform that we have demonstrated in our earlier research [4-5].

Experimental methods
Hexagonal Tungsten Trioxide Powders that were prepared by hydrothermal processing were used to prepare sensors. The substrates used were 15mmX15mm alumina plates with interdigitated gold electrodes acquired from the electronics design center at CWRU (product design 102). Sensing tests were carried out using our gas flow bench using dry or breathing air as the background gas. Testing temperature was 350°C and the sensor calibration step was completed prior to the gas sensing. XRD diffraction analysis was carried out at CEMAS as well as SEM analysis using the Phenom ProX available in our lab.

Results and Discussion
The as-received powders were found to aggregate in clusters ranging in size from a few to 100microns (see figure 1). The crystal structure of the material is the hexagonal phase of the tungsten trioxide. The XRD spectrum shown in Figure 2 matches with the JCPDS file

01-085-2460 (reference Oi et al, J. Solid State Chem. 96, 13, (1992). This is a metastable polymorph of the tungsten trioxide system. It does not follow the ReO_3 arrangement of the stable polymorphs but rather it represents an open structure with hexagonal and triangular prism channels formed by the arrangement of WO6 octahedra.

Fig. 1. Back-scattered electron micrograph of the powder material used as sensing element

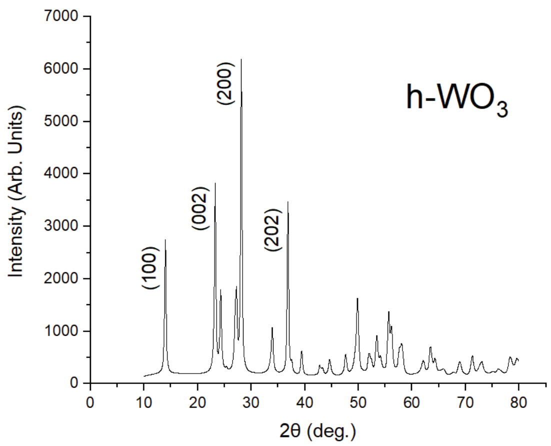

Fig. 2. XRD pattern corresponding to the hexagonal polymoirph of tungsten trioxidesopace group P63/mcm (193).

In the open channel structure of the hexagonal phase every three adjacent octahedron units connect with each other by sharing corner oxygen atoms in the same layer. Such connection extends along the a, b, c axes in a hexagonal lattice to form a network. The hexagonal prism channels along the c-axis allow for small molecules to travel through it.

Sensing data: The responses of the material to isoprene concentration between 300ppb and 1ppm are reported in Figure 3. There is an order

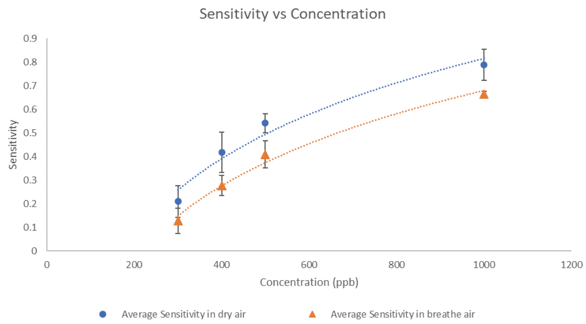

Fig.3 Sensor Sensitivity to Isoprene Gas

of magnitude increase in the sensitivity of the sensor between the lowest and the highest isoprene concentration value. This suggests that it is feasible to detect changes in the exhaled breath for individuals that in a state of sleep and those suffering from wakefulness with this sensor.

Tab. 1: Sensing data

Isoprene Concentration (ppb)	**300**	**1000**	**Distribution coefficient (R^2)**
Average Sensitivity in dry air	0.2	0.8	0.9661
Average Sensitivity in breathing grade air	0.1	0.7	0.9881

Also, testing in breathing air as background gas increased the sensor's sensitivity.

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