HIGHLY SENSITIVE ROOM TEMPERATURE SENSOR BASED ON NANOSTRUCTURED

K₂W₇O₂₂ FOR DIAGNOSIS DIABETES

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ABSTRACT

Diabetes is one of the most rapidly-growing chronic diseases in the world. Acetone, a volatile organic compound in exhaled breath, shows a correlation with blood glucose and has proven to be a biomarker for type-1 diabetes. Measuring the level of acetone in exhaled breath can provide a non-invasive, low risk of infection, low cost, and convenient way to monitor the health condition of diabetics. There has been continuous demand for the improvement of this non-invasive, sensitive sensor system to provide a fast and real-time electronic readout of blood glucose levels. A novel nanostructured K₂W₇O₂₂ (potassium tungsten oxide) has been recently used to test acetone with concentration from 0 parts-per-million (ppm) to 50 ppm at room temperature. This thesis work involves in designing K₂W₇O₂₂ sensor with an improved sensitivity and detection limit .For future work, a device has proposed to detect low concentration of acetone for practical use purpose.

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DEDICATION

I want to dedicate my work to my friends and family.

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1. INTRODUCTION

1.1. Diabetes, a Fatal Disease

Diabetes, the seventh leading cause of death in the United States, is a precursor to a heterogeneous group of disorders and is indicated by high blood glucose levels [1,2]. Based 2017 statistics, about 30.3 million people in the U.S. have diabetes, or about 9.4% of the U.S. population [3]. There are many ways to diagnose type 1 diabetes [4], such as the A1C test (a blood test that indicates blood glucose levels) [5], Fasting Plasma Glucose test (FPG), or Oral Glucose Tolerance Test (OGTT) [6]. However, these diagnosing methods are inconvenient, costly, and painful. Also, if we can have a device which can be a tool to screen or diagnose diabetes at a very early stage, it can particularly prevent the population with prediabetes to develop full-scale diabetes.

1.2. Significance of Breath Acetone Detection

Human breath contains a number of volatile organic compounds (VOCs). These compounds contain a lot of useful information related to a human's health condition and diseases. Therefore, breath VOCs can be used as biomarkers to provide essential information for disease diagnosis and monitoring. For example, acetone (CH₃COCH₃) can be used to evaluate diabetes [7,8], toluene (C₆H₅CH₃) is the biomarker to evaluate lung cancer [7]. The advantages of using VOCs as diagnostic tools include being harmless to the body, convenient to carry, low cost, and non-invasive. If a VOC can be used as a biomarker for diabetes mellitus and becomes a method to diagnose disease at an early stage with a convenient, much cheaper, and non-invasive way, most patients could be benefit from this technique and get their diseases controlled in time .Acetone gas is one of many such VOCs and is present in the sub-ppm range. Breath acetone shows a correlation with the blood glucose levels in human body [9].

1.3. Origin of Breath Acetone

In Liver, there are production of three ketone bodies: Acetone (C_3H_6O), Acetoacetate ($C_4H_6O_3$) and 3- β - hydroxybutyrate (3BH). Acetone is produced from these sources in the body: one is from the decar- boxylation of acetoacetate and the other is from dehydrogenation of isopropanol [10]. The following reaction shows that acetone con- version process through acetoacetate:

$CH_3COCH_2COO+H \rightarrow CH_3COCH_2COOH \rightarrow CH_3COCH_3+CO_2$

During fasting period acetoacetate is observed approximately 37% and in diabetic patients it is about 52% [11, 12]. Acetone enters to lungs and it passes through exhaled breath, it also eliminated through urine from lungs [13]. Generally, in exhaled breath, the acetone concentration is usually in the range of 0.3–0.9 ppm (parts per million) for a healthy person and above 1.8 ppm for a diabetic patient [14].



Figure 1. Zone of Diabetes in corresponding with exhaled breath acetone concentration.

1.4. Traditional Method of Glucose Monitoring

Generally people use blood sample or urine sample to monitor glucose level. Though urine sample indicates a marker for glucose monitoring, it becomes less reliable while is high blood glucose [15]. Also, people use dipsticks to take blood samples which is not more than a semiquantitative test [16]. Above all, those methods are inconvenient, and costly.

1.5. Acetone Monitoring Methods

There are many ways to detect acetone from exhaled breath, such as: Gas Chromatography-Mass Spectrometry (GC-MS) [17,18]; Selected Ion Flow Tube Mass Spectrometry (SIFT-MS) [19]; Proton Transfer Reaction-mass Spectrometry (PTR-MS) [20]; High Performance Liquid Chromatography (HPLC) [21]; Ion Mobility Spectrometry (IMS) [22,23]; Laser Spectroscopic techniques, including Tunable Diode Laser Absorption Spectroscopy (TDLAS) [24], and Cavity Ringdown Spectroscopy (CRDS) [25]. All these methods requires a bag to collect the breath and send it to laboratory for analysis. These techniques are complicated in operation, expensive, timeconsuming complicated sample preparations and unavailable in small clinic or home settings [26].

1.6. Problem Statement

The thesis work reports a non-invasive sensor based on nanostructured material K₂W₇O₂₂ (KWO) to detect acetone from breath for the purpose of diabetes monitoring. Researchers have developed various metal –oxide sensor to detect acetone in non-invasive way with different materials such as Pt-InN [27], Polypyrrole (PPy)-WO₃ [28], Ni/InGaN/GaN [29], and Pd/TiO₂/Si [30]. Unfortunately, none of those materials have shown any promising results to use the sensor for detecting low concentration of acetone. KWO based acetone sensor show good selectivity towards acetone with better sensitivity and stability. In this work, the fabrication, testing results, circuit design for the sensor has described. Further, the future work for developing a promising device has pointed out in the end.

2. SENSING MECHANISM OF KWO BASED ACETONE SENSOR

Figure 2 shows the sensing interaction between the acetone molecule and the sensor. Nanostructured KWO was measured to be a p-type semiconductor via a Hall Effect [31] measurement (Ecopia HMS-3000). Also, it showed good room-temperature ferroelectric properties [32]. All these unique properties of KWO can make it effectively attract high polar acetone molecules and result in an increase of the resistance [32, 33,34]. Under exposure of acetone gas towards the sensor, acetone gas transfer electrons to KWO consequently, electrons and holes recombines each other resulting in increase in resistance. This incident reveals that KWO is a p-type semiconductor [35] and acts as a chemiresistive sensor [36].



Figure 2. Electrostatic attraction between acetone molecules and the KWO based acetone sensor.

A basic chemiresistor consists of a sensing material that bridges the gap between two electrodes [36].Theoretically, and chemiresistive-based sensors can detect even tiny amounts of change of charges, e.g., electrons or holes analytes [37,38]. This can be reflected via a small change of resistance of sensing material, e.g., KWO, when it is exposed to a very low concentration of acetone. Generally, due to the limitations of the detecting circuit, device structure, etc., it is not easy to observe such a small change of resistance while the acetone concentration is too low. Considering the practical application of the acetone sensor in diabetes, it is necessary to sensitively

detect a concentration of acetone less than 0.9 ppm. Therefore, later we designed circuit integrated with KWO based acetone sensor to detect low concentration of acetone.

The morphology of the KWO film was studied with scanning electron microscopy (SEM) (Figure 3) and the film shows a highly porous structure made of a three-dimensional mesh of randomly orientated and interconnected nanorods.



Figure 3. SEM image of the interconnected 3D mesh structure of a KWO thin film.

3. SENSOR FABRICATION AND SYNTHESIS PROCEDURE

We used six inch glass wafer as substrate for sensor fabrication. At first, we made soft bake of wafer. Then photoresist [39] layer had made on the top side of the wafer. After that, the mask had aligned with the wafer using Aligner and then complete the section of Photolithography [40]. Photolithography is a technique that is used to define the shape of the micro structures on a wafer. Further, the sputtering had done with gold target of 1000Å on the wafer. Then the lift off process had done on acetone solvent to remove unnecessary gold portion from the wafer on. Figure 4 shows the six inch wafer after lift-off. Finally, the wafer was diced using dicing machine to get the separate sputtered glass slide.



Figure 4. Six inch gold sputtered wafer after lift-off.

Figure 5 shows synthesis of KWO material using hydrothermal method to process the sensor slide.



Figure 5. Hydrothermal method for synthesis KWO material.

4. EXPERIMENT SYSTEM

Figure 6 shows the sketch of the whole testing system. Acetone gas, supplied from the tank, was at the concentration of 50 ppm. The concentration of acetone can be diluted via mixing 50 ppm acetone with air.



Figure 6. Block diagram of the testing system.

The acetone and the air are supplied from two different channel which is controlled by two valve. A specific time duration is setup for the valve (ex. 60sec, 120sec). The function of the valve is opposite to each other that is when acetone channel valve is on, air valve is off or vice versa. The concentration of acetone has changed by mixing air. The quantity of acetone and air is controlled by flow meter. In the sensor chamber, the sensor is setup. Alligator clips are used to connect the with electrometer [41] .Then the electrometer is connected to the computer with NI USB [42]. We use LabVIEW [43] to collect data from the computer.

5. CHARACTERISTICS RESULTS OF ACETONE SENSOR

Sensitivity is the most important parameters for evaluating the sensing performance of sensors [44]. Sensitivity is defined as the variation in current ratio for specific gas concentration. If Igas and Iair are the current values of the sensor, then the sensitivity, S [27] is:

Sensitivity (S) = $(I_{gas} - I_{air})/I_{air}$

5.1. Operation of KWO at Room Temperature

The good feature of KWO is that it can operate at room temperature, as shown in Figure 7, which means we can make a low-power consumption device sensing acetone molecule and consequently causing the resistance change at room temperature. The reason of room-temperature operation is that KWO shows good room temperature ferroelectric property and therefore there has excellent charge transfer between KWO and acetone molecule.



Figure 7. Response curve of KWO sensor at 50 ppm concentration of acetone.

The basic advantages of operating a sensor at room temperature include: it doesn't need external power supply therefore the net cost for the device is reduced. A list of materials [27- 30, 45-46, 47, 48-54] summarized in Table 1 which are used in chemical sensors have to operate at elevated temperature in order to sensitively detect acetone.

Operating Temperature (°C)	References	
90	[28]	
200	[27]	
25	[34,35, 47]	
100	[30]	
100	[29]	
300	[48]	
300	[49]	
300	[49]	
500	[50]	
300	[51]	
400	[52]	
210	[53]	
400	[54]	
	Operating Temperature (°C) 90 200 25 100 300 300 300 300 200 210	

Table 1. List of materials that is sensitive to acetone at different operating temperature.

5.2. KWO Growing Temperature

We had grown KWO material on four different temperature (160°C, 180°C, 210°C and 225°C) by hydrothermal method to study the morphology effect on sensing performance. We have conducted sensing on 50 ppm acetone using different KWO growing at different hydrothermal temperature. Figure 8 indicates the sensitivity is highest using KWO growing at 225°C.



Figure 8. Sensitivity of the sensor at different growing temperature.

Beside the morphology effect, Figure 9 shows the Raman spectroscopy of the samples of 160° C and 225° C. It is noticed that the ε -phase is more dominated while KWO has been grown at higher temperature .Considering ε -phase is the main reason to introduce ferroelectric property in KWO, it can explain why KWO@225°C has better and stronger sensing response to acetone.



Figure 9. Raman Spectra of acetone sensor at growing temperature 160°C and 225°C.

5.3. Humidity Cross Interference Effect on KWO Based Acetone Sensor

Humidity is one of important factors to cause problems for sensors made by semiconducting materials. While, human breath contains very high concentration of water vapor (relative humidity (RH) in breath up to ~100%) [55], and always varies in individuals, such as diet, and metabolism. Therefore, a breath sensor should be stable, reliable, and less sensitive to humidity with maintaining high sensitivity. For this purpose, we studied the water vapor effect on KWO to detect acetone at room temperature. We found, as shown in Figure 10, that KWO nanorods have much less response to water vapor even if RH is high, 80%. Also, the sensitivity of KWO to water vapor doesn't change a lot while RH is from 10% to 80%, showing good resistance to RH. These all mean that the performance of KWO nanorods is not affected by relative humidity.



Figure 10. Sensitivity change of acetone sensor at different % of RH.

As we know earlier that, KWO is a p-type semiconductor with good charge transfer capability and strong room-temperature ferroelectricity. These result in a strong interaction between the sensing material, KWO, and high dipole moment molecules-acetone. Water molecules, as we know, are typical electrophiles. While, in a p-type semiconductor, holes are the majority carriers. This could be the reason that H₂O molecules cannot easily be attached onto KWO. On the other hand, although H₂O molecules are polar, comparing to acetone molecules, its dipole moment (μ =1.855D) is lower than the dipole moment of acetone (μ =2.88D). As a ferroelectric material, KWO favors to interact with molecules with a higher dipole moment, acetone. All these factors result in a low sensitivity to water vapor on KWO nanorods but high sensitivity to acetone. This makes the nanostructured KWO a very competitive material for use as a breath analyzer for detecting exhaled acetone [46].

5.4. Sensitivity of KWO Based Acetone Sensor

In human breath, the concentration of acetone as showing before (Figure 1) is very low. It requires a high sensitive device to accurately detect acetone. Figure 11 shows the sensitivity in terms of voltage that was found for the acetone concentration from 0 to 6.25 ppm. From the curve, we see that the sensitivity shows a linear relationship between the detected signal to the acetone from 0 to 6.25 ppm. Also, Figure 11 reveals an improvement of the sensitivity of the sensor when detecting acetone. The sensitivity is still about 50.75% even when the concentration of acetone was only about 0.1 ppm (much less than threshold 0.7 ppm). The details about the circuit has explained on ref [47].



Figure 11. Sensitivity readings due to change in concentration of acetone for 0–6.25 ppm.

5.5. Stability of Acetone Sensor

Stability is also an important parameter for the sensor to provide consistent reading over the time. We have tested the stability sensor for the duration of 15 days. We had found that within 15 days the response is almost stable.



Figure 12. Stability of the sensor for 15 days.

5.6. Selectivity of Acetone Sensor

In our exhaled breath there are different amount of volatile organic compound. On ref. [56-57], it is mentioned that there are less than 1 ppm of acetone, methanol and ethanol in breath. As those compounds are small in amount. We want to investigate our sensors performances towards those three gases. We took 2.86 ppm for each gases and tested them for using four different sensor slides with different surface treatments in order to improve selectivity. Figure 13 indicates the selectivity result of the sensor for acetone, methanol and ethanol gases. We notice that KWO with treated by L121 (a polymer surfactant) shows the best selectivity to acetone although all these four materials have good selective response to acetone.



Figure 13. Selectivity of KWO grown with K equal to 1.8 and 2.0, as well as treated with and without surfactant

5.7. Comparison with Acetone Sensitive Different Structure Material

Table 2 exhibits the sensing performances based above materials for application in acetone detection. From ref. [58], Compare with other four materials, KWO based acetone sensor have lowest detection limit, highest sensitivity with operating in room temperature.

Materials	Device Structure	τ (s)	OT* (°C)	S (%)	Detection Limit
					(ppm)
PPy-WO ₃ (20%)	Hybrid Nanocomposite	NA	90	3.34×10 ⁻⁴	0.37
Pt-InN	Ultra-thin FET	NA	200	5.07	0.4
$K_2W_7O_{22}$	Chemiresistor	12.5	25	50.75	0.1
Pd/TiO ₂ /p-Si	MIS	~ 15	100	16	10
Ni/InGaN/GaN	Heterostructure	~7.6	100	1.021	100

Table 2. Data analysis of five different materials to detect acetone.

*OT: Operating Temperature; NA: Not Available; t: response time; S: sensitivity

6. CURRENT ISSUE AND POTENTIAL SOLUTIONS

6.1. Color Change Problem and Possible Solution

While the excellent ferroelectric property of KWO provides sensitive response to acetone, it also can easily cause ferroelectric-electrochromic effect [59-60]. We found the color is changed to blue when a voltage is applied on KWO thin film. While this color change happens, the sensing performance is degraded. The sensor doesn't respond to acetone when it is deep blue color. A small external heat is a possible solution to resists this color change and helps the sensor to respond to acetone gas continuously for long time. To set an optimum temperature to heat the sensor, I heat the sensor from room temperature to 70.32°C and found that the sensor is sensitive while heating it 30°C -36°C and after a certain increment of temperature above that reduce the response. It's because the property of semiconductor material is that the resistivity of the material decreases with the increase of the temperature [61-66]. Figure 14 shows the sensing response to 50 ppm acetone at different temperatures.



Figure 14. Sensor response to 50ppm acetone at different temperatures.

Figure 15 shows about the small amount of heat (36.65°C) towards the sensor can help to prevent the color change. Here we applied 1 volt towards the sensor directly to check the color reason for 5 hours. No obvious color change can be observed.

Initial 1V

Figure 15. Heating of acetone sensor at 36.65°C for 1 Volt with 5 hours on each set.

From figure 15 we can conclude that, there is no significant color change while the film is heated at 36.65°C. We also reduce the temperature to 36.65°C to see the response of the sensor.

Figure 16 shows that 36.65°C also helpful to prevent the color change. So it means we can prevent the color change using small external heat for the sensor.

Sensitivity: 122.9%

a) With Micro heater $(36.65^{\circ}C)$

Sensitivity: 12.5%



b) Without Micro heater

Figure 16. Response of KWO sensor towards acetone a) with micro heater 36.65°C. b) without micro heater.

From figure 16 it is pretty much clear that a small heat up resists the color change of KWO based acetone sensor.

6.2. Device Optimization and Circuit design

At the beginning, the sensor testing has done onto the large system. Later we try to optimize our system and make it smaller handhold device. To detect the signal, we made a cost-efficient circuit with components such as resistors, potentiometers, op-amp (model name: LM741 CNNS) [67], and 9 V battery. The printed circuit board (PCB) was designed by OSHPARK (a PCB fabrication company, Portland, OR, USA) [68]. As shown in Figure 17, we used 10 M Ω and 50 M Ω resistors connected with a single pole double through (SPDT) switch [69] for compatible adjustment with the sensor resistance while testing different ranges of acetone concentration. A 10 $M\Omega$ resistor was used to calibrate the sensing response for lower concentrations of acetone from 0 to 6.25 ppm and a 50 M Ω resistor was chosen to calibrate the sensing response for a broad range of acetone from 0-50 ppm. The other branch of the Wheatstone bridge was introduced with a potentiometer to make zero correction of the circuit. Also, we introduced buffer amplifiers [70] in the circuit to avoid the impedance problem and to get unity gain. Because the signal from sensor detection is weak, we used a differential amplifier to amplify the signal. The voltages were taken from the two branches of the Wheatstone bridge. The amplification ratio was set up in accordance with the range of acetone detection. For instance, to detect a low concentration of acetone (0-6.25)ppm, we needed to amplify the signal 10-fold. Figure 18a shows our PCB circuit board and Figure 18b shows the schematic diagram of the circuit. We used two 9 V batteries to make +9 V and -9V potential differences. The amplification of the signal was set in between the range of -9 V to +9V and the output was clipped beyond that range. The output from the circuit was measured on an electrometer.



Figure 17. Schematic diagram of Wheatstone bridge.



Figure 18. (a) PCB layout of the gas detection circuit; (b) Schematic diagram of the amplified circuit.

For further improvement of the device, I consider the some more feature onto the improved device. I used Arduino Nano [71] to control the sensor, reset the value. In the OLED display, the value of ΔR ($R_{acetone} - R_{air}$) has showed. Figure 18 shows the schematic block diagram of the sensor device. For fixed resistance, I have chosen 10M Ω and the sensor resistance increases depending on the concentration of acetone. Then the output of the voltage divider goes to the buffer amplifier [72]. Buffer amplifier keep the voltage constant with unity gain. Then the output has taken to the low pass filter. A low-pass filter (LPF) is a filter that passes signals with a frequency lower than a

selected cutoff frequency and attenuates signals with frequencies higher than the cutoff frequency [73].I select 10Hz signal to pass from the buffer amplifier to the Arduino. More frequency signal has cut off.



Figure 19. Block diagram of the improved sensor device.

With Arduino programming I convert the voltage change towards corresponding resistance change and finally the resistance has shown on to the display. Figure 20 shows the exterior look of improved sensing devices.



Figure 20. Improved sensing devices

7. FUTURE WORK

The designed device has considered the initial resistance (R_{air}) of the sensor corresponding for a particular point of RH. Our more investigation have found that the initial resistance changes with the change of RH. Particularly, it goes down with the increase of RH. So to get the better sensitivity, we need to consider this incident. To solve this problem, we can use Raspberry Pi [74] for continuous monitoring the initial resistance and record the value. After that, getting resistance while exposure to acetone gas, we can just subtract the initial resistance from it to get most accurate ΔR . Also we need to integrate microheater, fan, and RH sensor to the device.

In our breath there are there is 90-100% RH as we discussed earlier. RH is a big impedance for the sensor to detect acetone. So I think if we can use anhydrous [75] (ex. CaSO₄), to reduce the RH, the sensing response will be more accurate. At the same time we need consider whether acetone is absorbed by the anhydrous or not.

8. CONCLUSION

KWO based acetone sensor has developed by our group to detect acetone for the purpose of diagnose diabetes in the early stage. In this thesis, we reported the fabrication of the sensor, characteristic of the sensor, the developed device integrated with the sensor and their response and the future development of the sensor. If the sensor can sense acetone properly from real breath sample, it will be a prominent low cost, non-invasive, portable, convenient device for the diabetic patient.

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