Synthesis of Metal Oxide Nanomaterials for Early Lung Disease Detection

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Abstract. Metal oxide nanomaterials from bulk zinc oxide and tin oxide powders were synthesized via Horizontal Vapor Phase Crystal Growth deposition technique. Synthesized nanomaterials were deposited in a silica quartz tube where it acts as sensing element of the gas sensor. Volatile organic compounds (VOCs) were utilized as identifier for lung disease which served as analytes to interact with the gas sensor. The sensitivity test was measured using its response time and voltage difference. An immediate voltage response time with an average of 3 seconds was observed upon exposure of the analyte to the sensor. Selectivity test was analyzed through radar plots of tin oxide and zinc oxide which depicted that each metal oxides have distinct sensing capabilities in terms of sensed VOC gases.

1. Introduction

One of the most important challenges in medicine, life science, ecology and food industry is creating of rapid, ultrasensitive, and economical methods for the detection of biochemical entities, different protein, DNA, and different pathogens, including viruses, bacteria, environment gases, etc. Unique possibility for the creation such as bio-nanosensors with commendable selectivity and good sensitivity gives nano-sensors based on single nanomaterial. There are different types of sensors. Nano-optic, nano-plasmonic and nanophotonic sensors can provide record sensitivity down to detection of a single virus [1,2,3] or a molecule [4-6]. Nano-optic, nano-plasmonic and nanophotonic sensors can provide record sensitivity down to detection of a single virus [1,2,3] or a molecule [4,5,6] . These bio-nanosensors operate on whispering gallery micro-nano-resonators [1], microcavities [2], nano-optofluidics [3], optomechanics [4], nanoplasmonics [5,6], nanophotonics [7] principles. The other type of nanotechnological label-free bio-sensors with good selectivity and sensitivity are based on single nano-object, like nanoparticle, nanotubes, nanowires, graphene layer, etc. Such bio-nanosensors represent individual nanodevices, produced from single nanoparticle, nanotube, nanowire, graphene layer, etc. It can reach femto and even atto-molar sensitivity and can recognize a single virus or a large molecule [8-10]. Development of bio-nanosensor technology has been fast emerging. Now mechanical bottom up nanomanipulation and nano-assembling based on shape memory alloy nanogripper [11,12] is going to provide such technology. With this assembly, the sensing capability of the sensors will be at its
optimum condition. This sensors can be used to detect lung disease markers. In the Philippines, the existing detection methods (direct sputum microscopy and GeneXpert) for lung disease are rarely available, expensive, and complicated to use as early detection tool. It requires experts, good infrastructure and good quality sputum sample [13,14]. Therefore, a need of simpler and faster way in diagnosing lung disease is the primary goal of this study. It will provide medical personnel a solution to address the complexity of the said detection methods into a less complicated and rapid way of diagnosing patients. The non-contact mechanism of the device avoids the risk of infection to the personnel. The device is intended to be portable and cheap, thus is beneficial to both patients and medical institutions. The said tool would help improve the services provided by such institutions. In this study, metal oxide nanomaterials such as SnO₂ and ZnO are used in the fabrication of a VOC gas sensor. The produced nanowires for the gas sensor in the Philippines will undergo mechanical bottom up nanomanipulation and nano-assembling based on shape memory alloy nanogripper [11,12] by their Russian collaborators.

2. Methodology
The fused quartz tube (silica) with dimensions of around 8.5 mm inner diameter, 11.5 mm outer diameter, and 12 inches in length was used as the container of the metal oxide powders (zinc oxide and tin oxide). One of its end was sealed using a high temperature blow torch fuelled by a mixture of LPG and oxygen. It was then cleaned using a Branson ultrasonicator at 40 kHz frequency for 30 minutes to remove the contaminants then air-dried to remove the excess water inside the tube. Fifty (50) milligrams of metal oxide powder (zinc oxide and tin oxide) of 99% purity and <5-micron grain size obtained from Merck was weighed and placed into a clean closed-end quartz tubes. The said quartz tube was then evacuated using a Thermionics High Vacuum System decreasing the pressure to about 10⁻⁶ Torr. The quartz tubes was then fully sealed by using the high-temperature blow torch to a length of ~15 cm. The Horizontal Vapor Phase Crystal Growth (HVPG) Technique was used in the fabrication of the metal oxide nanomaterials patented by Santos, Quiroga, and Salvador (2011) and has produced a number of studies concerning synthesis of nanomaterial.

The sealed quartz tubes were baked in a Thermolyne horizontal tube furnace. The furnace was programmed at a ramp time of 40 minutes, at a growth temperature of 1200 °C, and at 8 hours growth time where it followed the horizontal vapor phase crystal growth. To characterize the nanomaterials that were grown on the inner walls of the quartz tube, it was sectioned into three zones with 5-cm length each. Each zone was further divided into 2 sections (A and B) as shown in Fig. 1. To identify the temperature gradient that is necessary for the growth of the nanomaterials, the tubes were inserted halfway through the furnace and monitored by a type-K thermocouple. The tube was positioned such that Zone 1, where the bulk powder is located, was inside the furnace; the middle of zone 2 was located at the brim of the furnace; and zone 3 which was the opposite end was completely outside the furnace (Fig. 1). After the set time for crystal growth, the set up was cooled to room temperature.

All characterizations were done by the Integrated Micro-Electronics, Inc. (IMI) Group. The deposits on quartz tube fragments were characterized using Scanning Electron Microscope (SEM) and Energy Dispersive X-ray (EDX). The section with the highest density of nanowires and rods were picked as gas sensing substrate. The collected substrate’s edges were gold sputtered which serves as the ohmic contact (Fig 2). AWG #30 wire was fused at the four ends of the gold electrodes. Once dried, the substrate was soldered into a circuit board. In the circuit, an input voltage of 9V and 10 kΩ variable resistor was utilized to calibrate the sensitivity of the sensor. The sensor was connected in parallel with a DC voltmeter and LED. The voltmeter used was a Passport Interfaced PascoScientific Voltage Sensor and DataStudio which was used for data-acquisition in measuring the voltage response of the sensor. The change in the resistance of the material resulting to a change in voltage measurement was recorded via PascoScientific Voltage sensor.
The design of the prototype device was coordinated with the Lung Center of the Philippines as preparation for commercial use in the future. Seven prepared analytes (VOCs) were allowed to individually interact in each set-up with the sensing layer through the injection port of the chamber. Gas sensing was done in an ambient temperature for several trials. Heater and alcohol vapor were used in purging the sensor. Sensitivity of the metal oxide sensors was measured through response time and voltage difference. Selectivity capability of each gas sensing material were analyzed by plotting the data in a radar plot, using Principal Component Analysis (PCA).

3. Results and Discussion
The two metal oxide nanomaterials were subjected to morphological and elemental composition characterization. Three different areas were collected from the identified zones of synthesized zinc oxide and tin oxide samples. All areas showed a nanowire structures due to the elongated wire-like geometry of the nanomaterials. The average thickness of the nanowires were measured: Area 1 (914.8 nm), Area 2 (161.8 nm), and Area 3 (648.6 nm). Based on EDX profiling, all areas exhibit zinc, as the highest atomic wt % in its composition, indicative of zinc oxide powder as precursor. Oxygen is also present in its composition indicative of the use of metal oxide as precursor and silicon on Area 2 which is attributed to the silica tube substrates. Due to the strong penetration of the electrons used in EDX, presence of carbon is attributed to the carbon tape used as place holder of the sample. As for tin oxide, the average thickness of nanowires were measured: Area 1 (558.8 nm), Area 2 (738.4 nm), and Area 3 (335.2 nm). All areas exhibited tin as the highest atomic wt % in its composition indicative of tin oxide powder as precursor and strontium depicted on Area 3 may be attributed as dust gathered while preparing the sample before testing. Oxygen was also present in its composition indicative of the use
of metal oxide as precursor. The strong penetration of the electrons used in EDX sampling may cause the carbon on its composition attributed to the carbon tape beneath the sample. This only shows that HVPG technique is an effective method to synthesize nanowire structures.

![Figure 3](image3.png)

**Figure 3.** Morphology of zinc oxide nanomaterials in three different areas.

![Figure 4](image4.png)

**Figure 4.** Morphology of tin oxide nanomaterials in three different areas.

The data gathered during gas sensing was presented in the table below. Selectivity and sensitivity capability of each gas sensing material were identified by plotting the data in a radar plot, using Principal Component Analysis (PCA), and observing the response time of each gas sensing voltage measurements. Other metal oxide was added during selectivity test to further identify the capability of the sensor to select analyte of interest.
Table 1. Voltage Reading Data (V)

| Chemical        | Baseline | Zinc oxide | Tin oxide | Other Metal Oxide |
|-----------------|----------|------------|-----------|------------------|
| Nonanal         | 6.2      | 6.353      | 6.21      | 6.25             |
| Octanol         | 6.2      | 6.23       | 6.42      | 5.62             |
| Hexanal 3       | 6.2      | 6.32       | 6.23      | 6.33             |
| Valeraldehyde   | 6.2      | 6.22       | 6.38      | 6.40             |
| Acetaldehyde    | 6.2      | 6.40       | 6.34      | 6.22             |

A 6.2-V baseline was set. Average values were used in radar plotting and PCA analysis. It is evident that each metal oxide showed a different response spectrum to gases. An immediate voltage response an average of 3 seconds was observed upon exposure of the analyte to the sensor. The average values of each analyte for each metal oxides were used and plotted in a radar plot to see how the analytes react to each metal oxide. Radar plots of tin oxide showed that analytes octanal (6.42 V), valeraldehyde (6.38 V), and acetaldehyde (6.34 V) have a very active response to the sensor. On the other hand, since the baseline is set to be 6.2 V, nonanal (6.21 V) and hexanal (6.23 V), have a very subtle responses with tin oxide. While for zinc oxide, the radar plot indicated that analytes acetaldehyde (6.40 V) and nonanal (6.353 V) have a very active response to the sensor. It should be noted that hexanal (6.32 V) also has a response with tin oxide. Subsequently, octanal (6.23 V) and valeraldehyde (6.22 V) have little response to zinc oxide. It is evident that each metal oxide exhibit a unique radar plot profile representing its selectivity property for each gases.

A statistical procedure is needed in order to make distinctions more apparent. In the case of gas sensing, principal component analysis was needed for distinguishability and to strengthen the sensitivity analysis of the radar plots above. The PCA was plotted using xlstat in excel spreadsheet. Active observations were the voltage measurement readings while the active variables were the two
metal oxides. This graph shows that tin oxide and zinc oxide responses to the gases are statistically distinguishable.

![Biplot (axes F1 and F2: 82.93 %)](image_url)

**Figure 7.** Principal Component Analysis plot.

### 4. Conclusions
Horizontal Vapor Phase Growth technique transforms bulk structures to nanowires on zinc oxide and tin oxide. The smallest diameter measurement in nanowires was on Area 2 of zinc oxide which is 146 nm, while the largest was on Area 1 of tin oxide which is 1040 nm. The enhanced growth of nanowires and high surface-to-volume ratio of synthesized nanomaterials increases the sensitivity of the device due to higher interaction between the analytes and the sensing element. Gas sensors can be considered sensitive in terms of response time and voltage difference measurements results and its responses to the gases are statistically distinguishable. This only signified that tin oxide and zinc oxide are compatible as an array of sensors in terms of its selectivity property. Therefore, metal oxide gas sensors were successfully synthesized which detected the prepared VOCs. All nanowires that were produced will be subjected for nanomanipulation by the Russian collaborator in order to enhance its properties.

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