Development of high sensitivity potentiometric NO$_x$ sensor and its application to breath analysis

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ABSTRACT

Using a combination of similar potentiometric sensors connected in series, a strategy for measuring NO at ppb concentrations has been demonstrated. Sensors numbering from 2 to 20 were fabricated, with each sensor based on YSZ electrolyte with WO$_3$ sensing electrode and Pt-zeolite/Pt as the reference electrode. Use of a catalytic filter allows for the cancellation of interferences due to oxidizable gases, such as CO. The optimum operating temperature of the filter and sensor was determined to be 250 and 425 °C, respectively. For human breath samples, the interference from water was acute enough that only scrubbing through a dry ice/acetone bath led to adequate performance for detection of NO in the 5–80 ppb range with a 20-sensor array. A more practical strategy suitable for clinical analysis was demonstrated by using water saturated air as the background gas. A linear calibration curve in the range suitable for use in clinical analysis is demonstrated.

1. Introduction

Detection of nitric oxide (NO) is an active area of research in fields as diverse as high temperature combustion [1–5] and in clinical analysis [6]. There are many sensing strategies for detection of NO, including optical spectroscopy [7], mass spectrometry [8], chromatography [9], chemiluminescence [10] and electrochemistry [11]. Each method has its advantages and disadvantages, depending on the intended application. Thus, in a clinical setting, chemiluminescence analyzers perform very well, but would not be suited at all for monitoring NO for mobile diesel vehicle exhaust. Also, the extent to which the sensing devices can be miniaturized varies, with solid-state electrochemical sensors enjoying a clear advantage. The focus of this paper is on solid-state electrochemical sensors with selective detection of NO in the ppb range, that can find both physical and biological applications. These types of applications are difficult from the point of view of sensor design. Considerable efforts have been made to fabricate NO$_x$ sensor using different semiconducting oxides (SnO$_2$, ZnO, WO$_3$ and TiO$_2$) thin films and nanostructured materials [12–15]. Nanowires and nanotube field effect transistor (FET) based gas sensors are also attractive for their low level detection [16–18]. Issues of compatibility with the environment, interference effect with other gases

need to be resolved before practical applications can be realized. In the case of turbine emissions, the sensors have to operate at high temperatures, detect at sub-ppm levels and be selective against CO$_2$, CO, hydrocarbons. In the case of breath analysis, sensors have to detect NO concentrations in the 1–100 ppb range, be selective against CO, CO$_2$, hundreds of volatile organic compounds and detect NO in a vapor stream that is almost 100% humidity [19,20].

In this paper, we focus on the breath application, though the data presented indicate that the sensors should also be able to monitor NO in turbine and other high temperature environments. There are several reports in the literature detection of NO in breath, including the use of quantum cascade lasers [21], a combined Kelvin probe and quartz microbalance [22], a WO$_3$ based chemoresistive sensor [23] and chemiluminescence analyzers [24]. We have reported on a potentiometric total NO$_x$ sensor in earlier studies with ppm detection levels and ability to discriminate against CO, hydrocarbons, ammonia, CO$_2$ and humidity [4,25–28]. We have also shown that assembling a 3-sensor array can readily push detection limits of NO to low ppm levels [25]. The present study builds on this concept, and demonstrates that adding identical sensors in series is a viable strategy for reducing detection limits. We demonstrate that using 10 or 20 sensors, NO detection in 1–100 ppb levels is readily accomplished. We then apply these sensors to detect ppb levels NO in human breath, and examine the issues related to sensitivity and selectivity. In addition, there are numerous examples of solid-state potentiometric sensors that can be miniaturized and therefore such designs makes possible the development of inex-

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pensive, portable, light weight, NO sensors. Indeed, colleagues at NASA and elsewhere have taken the first steps to miniaturize complex potentiometric sensors for eventual applications to aerospace and medical applications [29].

2. Experimental

2.1. Materials

The electrochemical sensors were fabricated using yttria stabilized zirconia (YSZ) as solid state electrolyte. Sintered, dense, YSZ (8 mol%) rods of diameter 10 mm and length 12 cm were obtained from Ortech Advanced Ceramics (Sacramento, CA, USA) and cut into ~1.0 mm thick semicircular discs using a LECP VC-50 precision diamond saw (St. Joseph, MI, USA). Pt-wire of ~0.127 mm diameter was obtained from Alfa Aesar (Ward Hill, MA, USA). Pt-ink used for making electrode contact was obtained from Heraeus (West Conshohocken, PA, USA). WO_3 powder used for making sensing electrode was purchased from AlfaAesar Inc. (Ward Hill, MA, USA).

2.2. Catalytic filter preparation

The procedures for the fabrication of platinum loaded zeolite (Pt–Y) used as reference electrode and filter material were described previously [25]. Approximately, 1.0 g of NaY powder (Zeolyst International) was ion-exchanged with 2.5 mM $[Pt(NH_3)_4]Cl_2$ solution. The sample was dehydrated at 300 °C, and then exposed to 5% H_2 450 °C for 6 h.

2.3. Sensor array fabrication

The sensor array was fabricated by adding individual sensors connected in series. The fabrication process of individual sensor unit was described elsewhere [25]. The single sensor was made by attaching two Pt wires on a semicircular YSZ disc using a small amount of commercial Pt ink. To make the sensor array, first the semicircular YSZ discs were attached on an alumina plate with high temperature ceramic glue (Ceramabond, AREMCO product, Part No: 885). The sensor array was dried at room temperature for 4 h and cured at 93 °C, 260 °C and 371 °C separately for 2 h. Sensor arrays with 2, 5, 10, 15 and 20 sensors were fabricated. All YSZ discs were connected in series with Pt wires by using a little amount of Pt-ink. Pt ink was heat treated at 1200 °C for 2 h to secure bonding between the Pt wire and YSZ. WO_3 powder was mixed with α-terpineol to form a paste, which was then painted on one of the top of Pt lead wire and calcined at 950 °C for 2 h to form the sensing electrode. PtY was also mixed with α-terpineol and painted on the top of the other Pt lead wire to form reference electrode and dried at 100 °C.

2.4. Gas sensing measurements

The gas sensing experiments were performed within a quartz tube placed inside a tube furnace (Lindberg Blue, TF55035A). A computer-controlled gas delivery system with calibrated mass flow controllers (MFC) was used to introduce the test gas stream. The test gas mixtures containing different concentration of NO at constant oxygen content of 20 vol% were prepared by diluting NO (500.7 ppb NO in N_2) with O_2 and nitrogen. All gas cylinders were obtained from Praxair (Danbury, USA). The total flow rate was maintained at 500 cm^3/min. A pair of Pt wires was used to connect the sensor to the external leads. The gas mixture from MFCs was introduced into the tube furnace either through or bypassing the PtY filter. The filter is a U-shape quartz tube with 170 mg PtY placed on quartz wool. The accurate measurement of NO concentration in the parts per billion range was independently carried out using a pre-calibrated Sievers 280i nitric oxide analyzer (GE Electronics, Boulder, CO, USA).

The electrochemical potential of the sensor array was recorded by Hewlett–Packard 34970A data acquisition system with 10 MΩ and 10 GΩ internal impedance. The sensor array was tested over the temperature range of 400–600 °C. Fig. 1a shows a schematic of the setup.

2.5. Breath analysis experiment

The breath analysis experiment was performed in three different configurations, as shown in Fig. 1b–d. The critical part was the collection of the breath samples. Exhaled breath sample was collected from volunteers into a Mylar sampling bag, using protocols practiced in the clinical field. The NO concentration in the breath sample was then measured with Sievers instrument. For all volunteers, the amount of NO was less than 10 ppb. In order to establish calibration curves, we needed to get NO at higher concentrations, and this was done by spiking the breath samples in the Mylar bags with bottled NO, and the extra amount introduced was measured with the Sievers unit. The concentration ranges examined were between 5 and 80 ppb NO in breath. The Mylar bags were reused and thoroughly cleaned before each use with flowing nitrogen (99.998% purity) gas. Instead of mass flow controllers, a pump (Hargraves Technology Corporation, Mooresville, NC, USA) was used to maintain a constant flow rate of 500 cm^3/min. In the first series of experiments (Fig. 1b), the breath sample followed the same path through the Pt–Y filter as with the dry bottled gases. In the second series (Fig. 1c), the breath sample was passed through a dry ice/acetone slurry trap to remove the moisture from the collected breath. The inlet of the dry ice trap was connected with a three way valve which allows either breath sample or ambient air. In the third series (Fig. 1d), the breath sample and the ambient air was bubbled through water at room temperature, and no dry ice trap was used.

3. Results

3.1. Assembly of sensor array

The basic unit of the sensor is sintered YSZ with a WO_3 sensing electrode and Pt-zeolite Y (PtY) reference electrode coated on a Pt lead wire [25]. In this study, we have investigated 2, 5, 10, 15 and 20-sensors connected in series. Fig. 2a shows a photograph of a 10-sensor array. Each hemispherical disk is YSZ with WO_3 (yellow) and PtY/Pt (black) electrodes connected in series, and mounted on an alumina plate. The dimension of the 10-sensor array was 1.3 cm × 6.0 cm.

3.2. Sensing response to NO

The sensing response of a 2-sensor and 10-sensor array to dry NO (bottled gas) in the range of 7–125 ppb is shown in Fig. 2b and c (the *y*-axis EMF value is the same for each individual plot in the figure, so the responses can be compared). The sensors were maintained at a temperature of 600 °C in a background gas of 20% O_2/N_2. It is clear that there is a significant increase in EMF for each array with the NO concentration, as well as a higher response with the 10-sensor array as compared to the 2-sensor array (e.g. with 7 ppb NO, the 2-sensor array produced a response of ~0.2 mV as compared to ~2.5 mV for the 10-sensor array). These experiments were then repeated with the 5, 15 and 20 sensor array and the change in EMF is plotted against the NO concentration in Fig. 3a. The slopes increase, as expected on going from 2 to 5 to 10 sensor array, but then drops off unexpectedly for 15- and 20-sensor arrays. The bulk resistances of the arrays were measured at 600 °C and found to be 1, 3.5, 6.3 and 17 MΩ for the 5, 10, 15 and 20-sensor array. We reasoned that the internal impedance of the multimeter (10 MΩ) was not appropriate for the measurements of these high
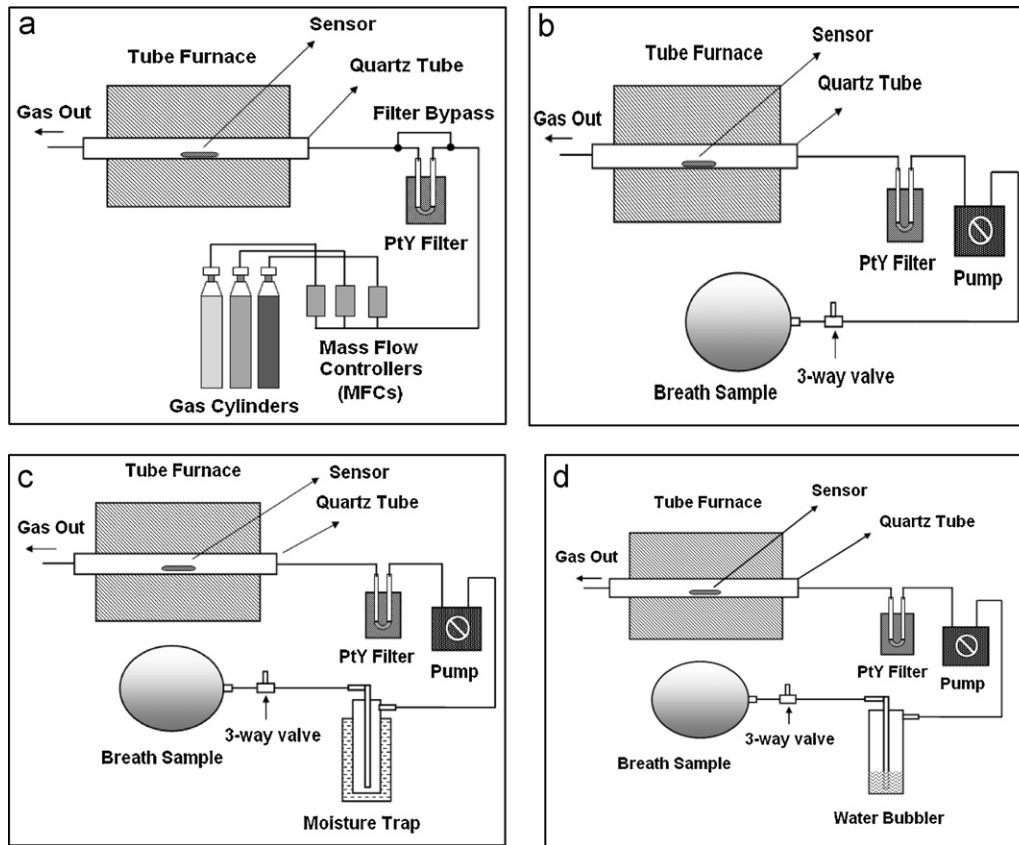
Fig. 1. Schematic diagram of experimental setup with (a) dry NO from certified gas cylinder, (b) breath sample without moisture trap, (c) breath sample using moisture trap of dry ice/acetone and (d) breath sample with water bubbler.
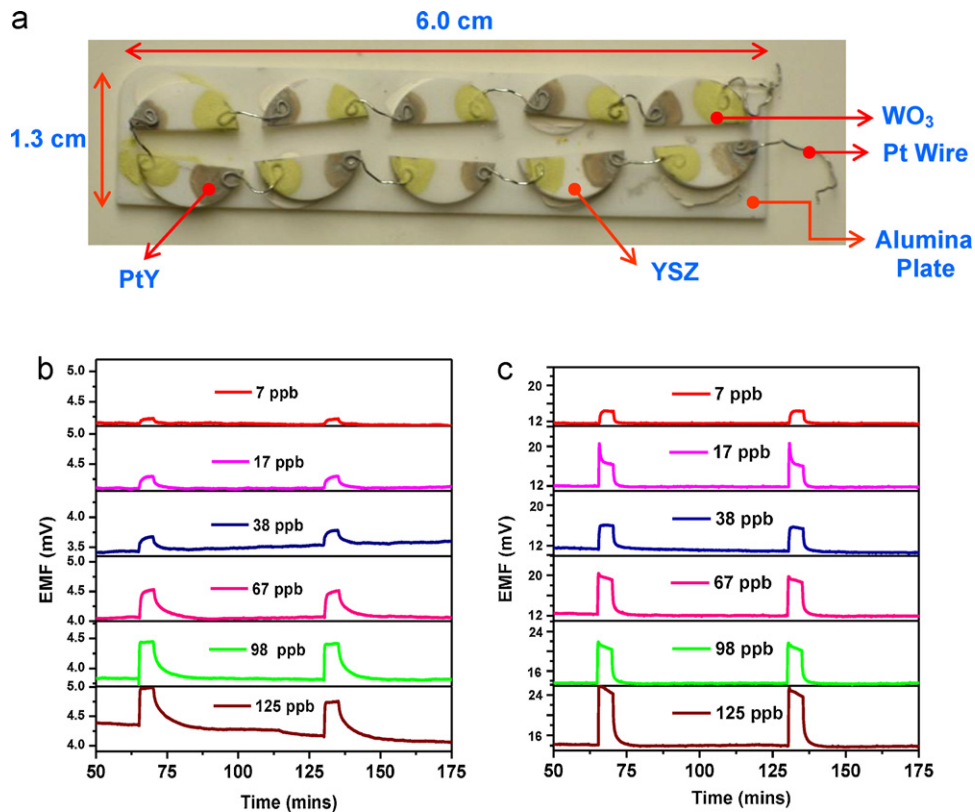

Fig. 2. (a) Photograph of a 10 NO$_x$ sensor array. (b) and (c) Sensor response of a 2- and 10 NO$_x$ sensor array with 7–125 ppb NO without PtY filter. The sensor was tested at 600 °C, 20% O$_2$ and 500 cm^3/min total flow rate.
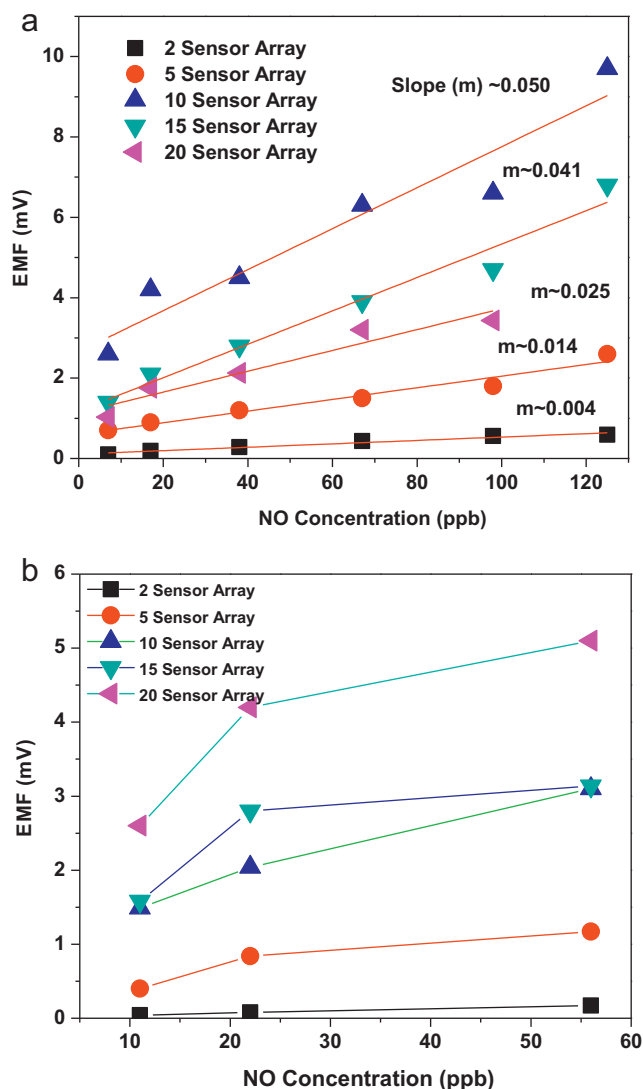
Fig. 3. Change in EMF with NO concentrations for 2, 5, 10, 15 and 20 sensor array (a) with 10 MΩ and (b) 10 GΩ internal resistance on the multimeter. The sensors were tested at 600 °C with 20% O$_2$, total flow rate 500 cm^3/min.

Fig. 4. Response transients to 11–56 ppb NO for a 10 sensor array (a) without and (b) with the NO gas passing through the catalytic PtY filter. The sensor was tested at 425 °C, PtY filter at 250 °C, 20% O$_2$ and a total flow rate 500 cm^3/min. Inset of b: Response transients to 160–320 ppm CO with and without the PtY filter at 200 and 250 °C.

resistance sensors. Thus, the experiments were all repeated with a multimeter with a 10 GΩ internal impedance and these data are shown in Fig. 3b. Over the 10–60 ppb range, the sensors behaved appropriately, with the larger arrays producing stronger signals. Henceforth, all the data shown in this paper is with the 10 GΩ internal impedance multimeter.

3.3. Removal of interfering gases

We investigated the operation of the 10-sensor array at various temperatures (400–600 °C), with the goal of establishing the lowest operational temperature. This was motivated by the fact that a practical embodiment of this device should use the lowest possible temperature in order to minimize the power load. The data at 425 °C was found to be optimum with appropriate response and recovery time of minutes, and the data for the 10-sensor array is shown in Fig. 4a. Adequate EMF changes were observed for NO in the 11–56 ppb range (2–12 mV), though the response/recovery times were slower.

Potentiometric NO$_x$ sensors show strong interference to hydrocarbons and CO [25]. Considering that breath samples have oxidizable gases at much higher concentrations (factor of 1000)
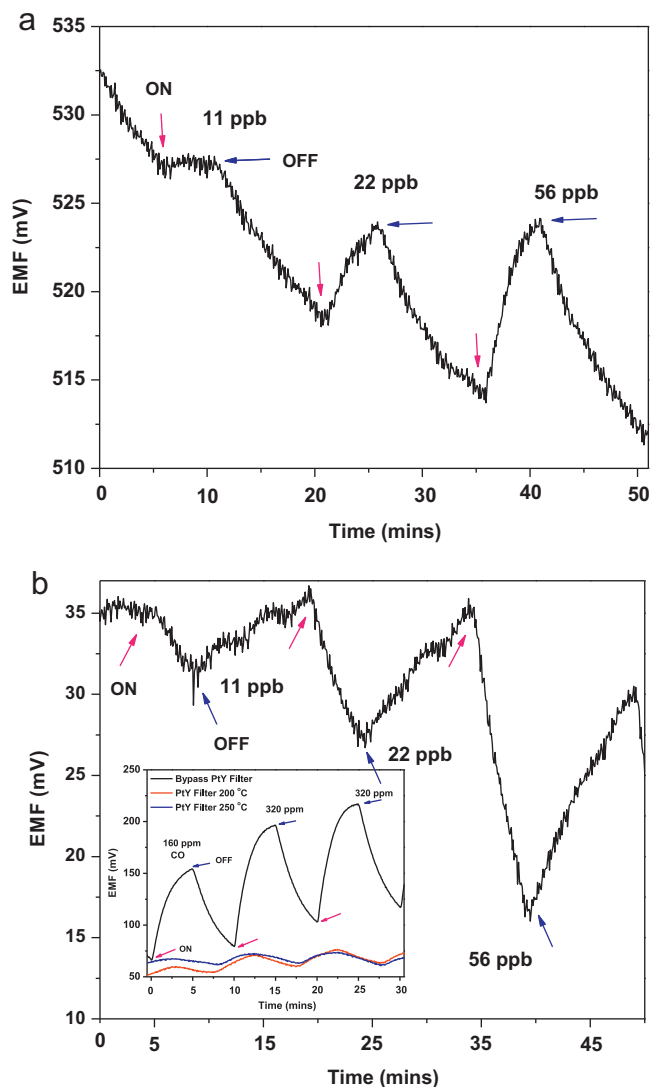
than NO [6], it is essential to have a strategy to remove these gases prior to NO detection. Similar interferences can also be expected in combustion systems. One approach that we have demonstrated previously is the use of a Pt-zeolite catalyst [25–28]. As long as the catalyst is maintained at a temperature different from the sensor, a total NO$_x$ response is observed. The schematic of this apparatus is shown in Fig. 1a. To model the interference, we chose CO. The inset in Fig. 4b shows that 160–320 ppm CO (no NO in the gas stream) produces a very strong response with the 10-sensor array at 425 °C. However, if the CO is passed through a Pt-zeolite Y fitter at 200 or 250 °C, the response to CO is minimized (the wavy baseline is not due to sensor responding to CO, since the rise and crest of the wave does not coincide with gas introduction or shut off).

The response to only NO after it passes through the filter is shown in Fig. 4b, and the signal is in the opposite direction, as compared to comparable NO concentrations that do not pass through the filter (Fig. 4a). The reason for this reversal in signal is that the filter converts the NO to NO$_2$ with almost 98% efficiency at temperatures of 200–250 °C. Signal from NO$_2$ is reversed as compared to NO (NO$_2$ + 2e → O^{2-} + NO) Also, the signal is considerably
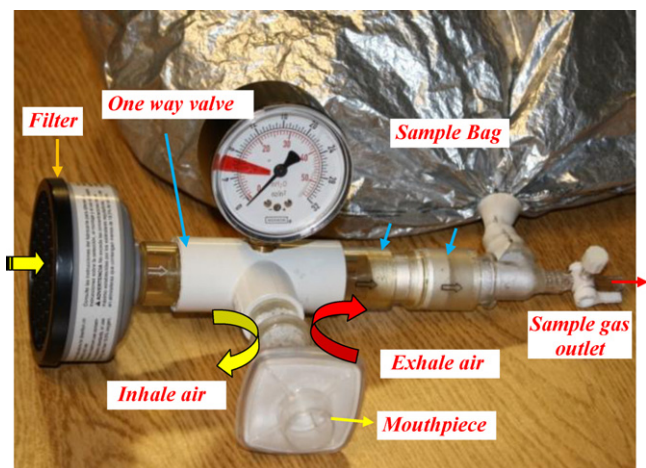
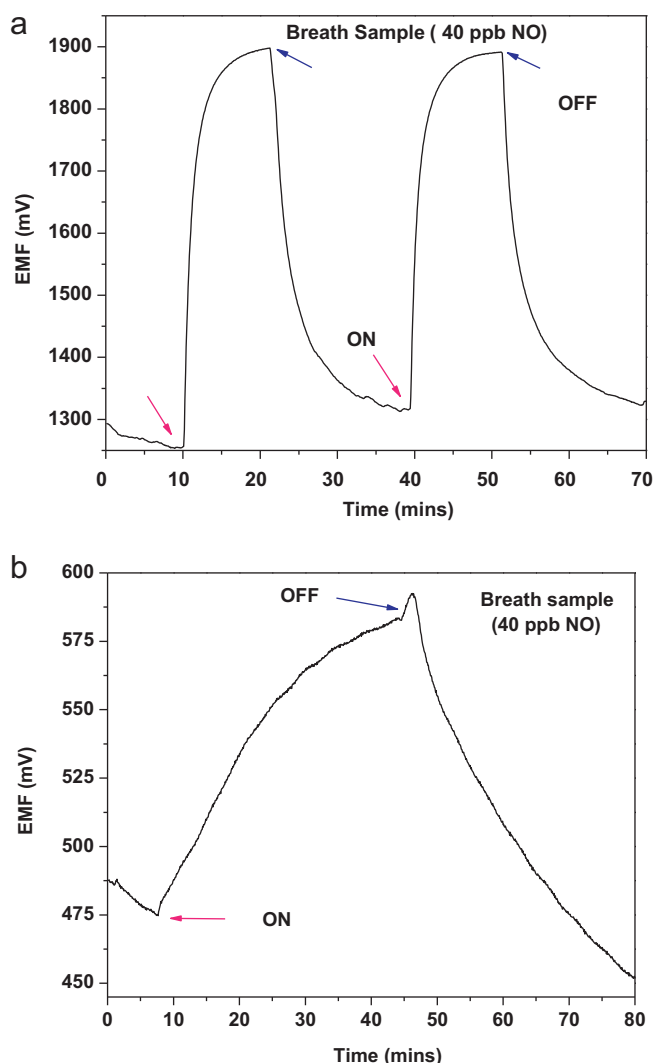Fig. 5. Photograph of breath collection setup equipment.

Fig. 6. Sensor response with breath sample (~40 ppb NO) for a 10-sensor array (a) bypassing PtY filter and (b) with PtY filter at 250 °C. Sample at 425 °C and 500 cm³/min constant flow rate was maintained using a pump.

stronger (5–20 mV for the 11–56 ppb NO passing through the filter) as compared to NO not passing through the filter (Fig. 4a). The stronger signal with the NO_2 arises from the greater driving force for the reduction reaction at higher temperatures, since NO is the more stable product with increasing temperatures [2,25]. All further experiments were carried out with the filter–sensor combination.

3.4. Breath analysis

For breath analysis, the measurement configuration was altered, and shown schematically in Fig. 1b–d. Breath samples from human volunteers were collected in a bag, shown in Fig. 5. The level of NO in the bag was determined with the Sievers chemiluminescence analyzer and for all volunteers was found to be <10 ppb. Thus, to establish the capability of the sensor system it was necessary to get higher concentrations of NO into the bag. This was done by introducing small amounts of bottled NO into the bag containing the human breath (ppb), and the exact level of NO in the bag was measured using the Sievers analyzer.

Fig. 6 shows the data with a 10-sensor at 425 °C for a 40 ppb NO breath sample with the gas either bypassing the Pt–Y filter or through the filter maintained at 250 °C. It is immediately obvious from Fig. 6a that the signal observed (~600 mV) far exceeds what is expected from 40 ppb NO (~10 mV, Fig. 4a). Upon passing this breath sample through the filter, the signal should have reversed (from NO_2, Fig. 4b), but we still observe a NO-like signal of ~100 mV. Passing through the filter does decrease the interference, but does not eliminate them. This filter is primarily good at removing interferences from oxidizable gases, such as CO and hydrocarbons [25–28]. Clearly, there are components in breath that are producing strong interferences and overwhelming the NO signal. Since the breath sample is almost 100% water, our hypothesis was that the interference arises primarily from water. Indeed, bubbling dry NO gas through water gave signals comparable to Fig. 6a (data not shown).

We considered that the most effective way to remove the water interference was to pass the breath through a dry ice/acetone slurry trap maintained at −78 °C, as shown schematically in Fig. 1c. Considering that the boiling point of NO is −158.8 °C, none of the NO is expected to be trapped and the vapor should be completely water free. Fig. 7a shows the response of a 10-sensor array to 5, 20, 30 and 85 ppb NO in breath sample (all on the same y-axis scale). The 10-sensor array does not respond to 5 ppb NO, and barely to 20 ppb NO, but higher concentrations are readily detected. In order to increase the sensitivity to the low ppb NO, breath samples were

analyzed with a 20-sensor array, and results for 8, 15 and 37 ppb are shown in Fig. 7b. Increasing the number of sensors brings the detection limits of the sensor array to levels appropriate for clinical analysis. However, to achieve this low ppb sensitivity, it was essential to remove all of the H_2O from the breath stream. The choice of a dry ice bath, though accomplishing the goal of water removal will be difficult in practice, so alternative strategies were explored.

As is seen in Fig. 6, there is a large change in signal upon exposing the sensor array to water, and this signal is stable as long as water is in the gas stream. So, a strategy was to use humid air as the background gas. The experiment involved saturating both the background air and the breath sample by bubbling through water, prior to exposure to the sensor (Fig. 1d). These data for a 20-sensor array are shown in Fig. 8a, for 8, 17, 46 and 82 ppb NO. Clearly, this is a workable strategy and does not need removal of the water, but just ensuring the background gas and the breath stream are both water saturated. Fig. 8b shows the calibration curve for the 20-sensor array over the range relevant for clinical analysis. The signals from the dry sample were higher (Fig. 7b) as compared to the water saturated gases, but the slopes of the calibration curves were found to be similar.
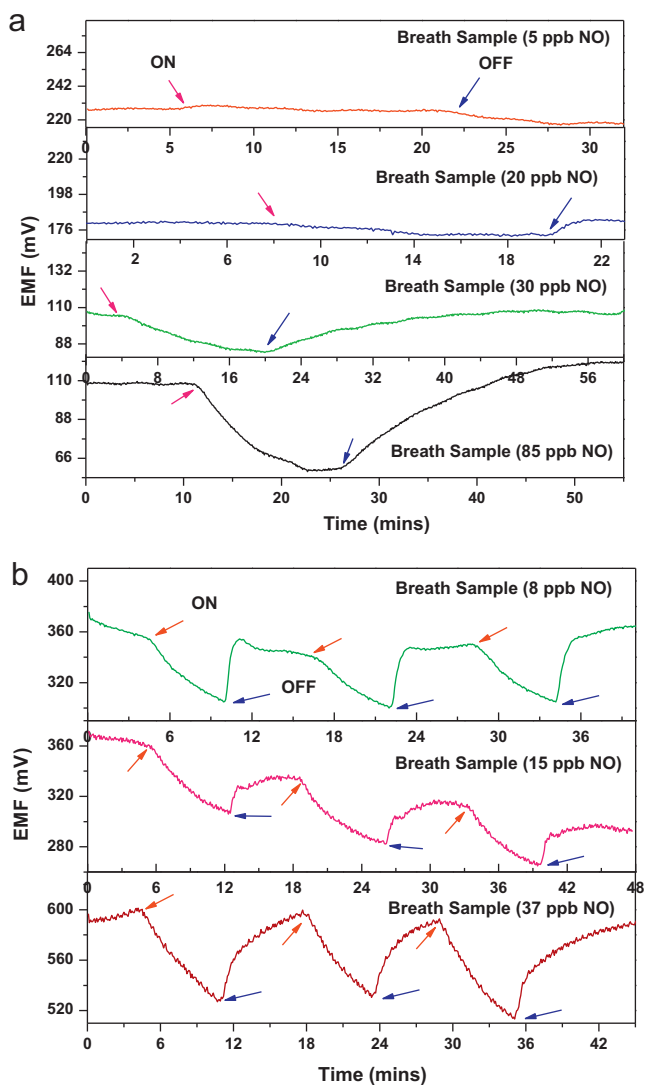
Fig. 7. Response transients with breath samples for (a) 10 and (b) 20 sensor array. The samples were tested at 425 °C, PtY filter at 250 °C and using moisture (dry ice) trap.

Fig. 8. (a) Response transients to 8–82 ppb breath sample for a 20 sensor array. The signals were measured by passing breath samples as well as reference air through water. (b) Variation of EMF with different NO concentrations in breath. Sample was at 425 °C and PtY filter at 250 °C.

4. Discussion

The particular sensor unit used in the arrays in this paper has been studied extensively [25–28]. The choice of WO$_3$ as sensing electrode and PtY/Pt as the reference electrode is based on their chemical reactivity for NO$_x$ equilibration, with WO$_3$ being poor and PtY/Pt very efficient [25–28]. Other studies have also examined the advantages of WO$_3$ as a sensing electrode for potentiometric sensors [5].

All of the data with the sensor arrays (Figs. 2, 7 and 8) demonstrates the concept of increasing sensitivity by combining potentiometric sensors in series. This concept has been reported earlier with potentiometric oxygen sensors [30]. However, with increase in the number of sensors, the resistance of the device also increases, and the measurement needs to be carried out with appropriate high impedance instruments.

For measuring relatively dry NO in the ppb range, 10-sensor array was adequate (Fig. 4). Interferences such as CO, hydrocarbons can be removed with a catalytic filter, as long as the filter temperature is maintained at a different value as compared to the sensor. Our optimum data was obtained with the catalytic filter at 250 °C and sensor at 425 °C. Such devices can be used for measuring low
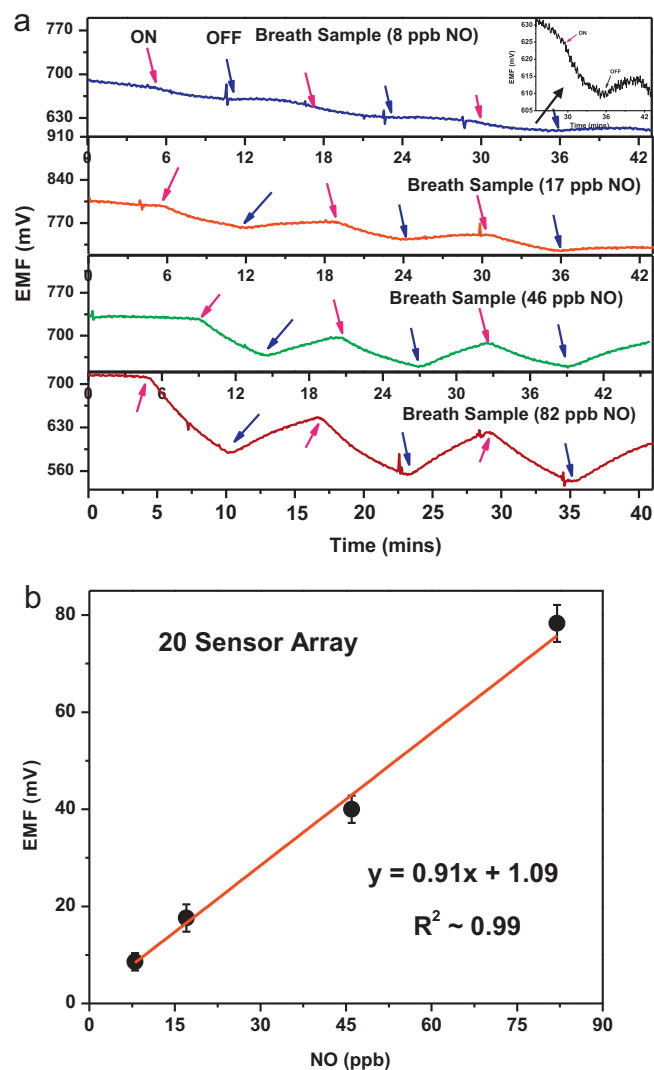
levels of NO in combustion environments, as generated in turbine engines.

However, measuring NO in breath samples was more difficult, primarily due to the high water content. We have presented two strategies for negating the effect of water. The first one was by freezing the water out by passing the breath through a dry ice bath. Combining the bath with the catalytic filter, we were able to get reasonable signals for NO in breath at concentrations relevant for clinical analysis (1–100 ppb), but it required the use of a 20-sensor array. The second more practical strategy of minimizing the water effect was to use water saturated air as the background gas. Both these water neutralization strategies resulted in calibration curves for NO with similar slopes, and provide confidence in the measurement techniques. However, the absolutely dry gases did provide stronger signal by a factor of ~1.5 over the water saturated samples.

Calibration curves with analyte gas usually show a logarithmic relationships to gas concentration for mixed potential sensors, whereas the calibration curve in Fig. 8b shows a linear dependence (R^2 = 99%). Previous studies with CO in air with potentiometric sensors have also shown a linear dependence at low concentrations and explained with the help of mass transport considerations [31]. An added advantage of measuring the low concentrations is there-

fore the linearity of the calibration curve, making clinical analysis more convenient.

Acknowledgement

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Biographies

Suvra Prakash Mondal received his masters degree in physics in 2003 from the Vidyasagar University, West Bengal, India. He completed his doctorate work from the Department of Physics and Meteorology at Indian Institute of Technology, Kharagpur, India in 2009. He is currently working as a post doctoral fellow in the Department of Chemistry at The Ohio State University. His present research interest is the development of high sensitive NO$_x$ gas sensor for human breath analysis.

Prabir K. Dutta received his PhD degree in chemistry from the Princeton University. After four years of industrial research at Exxon Research and Engineering Company, he joined The Ohio State University, where currently he is a professor of chemistry. His research interests are in the area of microporous materials, including their synthesis, structural analysis and as hosts for chemical and photochemical reactions.

G.W. Hunter is the lead for Intelligent System Hardware and the technical lead for the Chemical Species Gas Sensors Team in the Sensors and Electronics Branch at NASA Glenn Research Center. He has been involved with the design, fabrication, and testing of sensors for over 20 years. This work has included the use of micro and nano technology, the integration of sensor technology into smart systems, and the demonstration and application of sensor technology for a range of applications.

B.J. Ward is a senior engineer-sensor development for Makel Engineering, Inc. His work is focused on the research and development of chemical detection systems including miniaturized chemical microsensors for applications including trace gas detection, emissions monitoring, fire detection, and fluid monitoring as well as advanced microplasma-based spectrometry systems. He holds BS, MS, and PhD degrees in chemical engineering from the Case Western Reserve University.

D. Laskowski has significant experience in asthma, pulmonary hypertension and physiology research. In addition, he has spent significant time building equipment to measure physiological phenomena. His specialty is pulmonary physiology. He has over 50 papers and has built analytical equipment for many large institutions. He also has patents pending on two recent inventions.

R.A. Dweik, is the director of the Pulmonary Vascular Program at Cleveland Clinic. He is board certified in internal medicine, pulmonary disease, and critical care medicine. His clinical interests are in pulmonary hypertension and asthma. His research interests are in exhaled breath analysis and the role of nitric oxide in cardiopulmonary physiology and disease especially pulmonary hypertension and asthma.