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A novel real-time carbon dioxide analyzer for health and environmental applications

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ABSTRACT

To be able to detect carbon dioxide (CO_2) with high accuracy and fast response time is critical for many health and environmental applications. We report on a pocket-sized CO_2 sensor for real-time analysis of end-tidal CO_2, and environmental CO_2. The sensor shows fast and reversible response to CO_2 over a wide concentration range, covering the needs of both environmental and health applications. It is also immune to the presence of various interfering gases in ambient or expired air. Furthermore, the sensor has been used for real-time breath analysis, and the results are in good agreement with those from a commercial CO_2 detector.

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1. Introduction

A capability that can detect carbon dioxide (CO_2) with high accuracy and fast response time is critical for many health and environmental applications [1–15]. For example, measuring CO_2 levels in breath at the end of expiration, known as end-tidal CO_2 ($EtCO_2$), allows for non-invasive evaluation of systemic metabolism, perfusion, ventilation, and cardiac output, which provides doctors and patients with a non-invasive method to diagnose asthma, chronic obstructive pulmonary disease (COPD), and cardiovascular diseases [5,6]. Similarly, monitoring of indoor CO_2 levels allows for the assessment of indoor air quality (IAQ). Higher levels of indoor CO_2 are associated with increased prevalence of certain mucous membrane and sick building syndrome symptoms [15]. Infrared detection technology is currently utilized for measuring CO_2 in breath and air. While useful, this technology experiences strong interference from humidity that is present both in breath and air. Moreover, the infrared approach requires special sample pretreatments in order to reduce the humidity, which further adds to the cost of the device technology and limits its usefulness for applications in clinical settings. In the case of indoor environmental CO_2 sensing, the use of infrared technology is hampered by the interference of environmental humidity making detection of CO_2 levels inaccurate. There is a need, therefore, for developing a compact, low-cost, easy-to-use, and accurate CO_2 sensor for tracking CO_2 in human breath and for monitoring IAQ [16,17].

An alternative to infrared sensing is a detecting method based on colorimetry, which identifies CO_2 based on the change of color of a pH-sensitive indicator [18–23]. Compared to the infrared CO_2 sensors, the colorimetric approach has several potential advantages, including simplicity, miniaturization, low cost, and immunity to humidity changes, thereby making colorimetric sensors an attractive technology. While these sensors may show great promise, their response and recovery time are too slow for breath-by-breath analysis, and their detection limits and reversibility are insufficient to ensure accurate detection of CO_2 in the environment. To solve these problems, many attempts, including pretreatment of the sensing materials have been undertaken to reduce cost and ensure high performance of colorimetric CO_2 sensors. These improvement activities, however, often result in more complex instruments and sensor preparation methods.

In a previous publication, we introduced a portable breath analyzer for the determination of the expired CO_2. The device features a colorimetric sensor that could analyze breath CO_2 concentration accurately, and a fluidic system for efficient delivery of breath sample to the sensing element. A 3D model was created to simulate the sample flow and reaction of CO_2 with the sensing materials and color changes associated with the chemical reactions [24]. Despite the success, the sensor response was slow and semi-reversible, which is not suitable for breath-by-breath CO_2 analysis as needed

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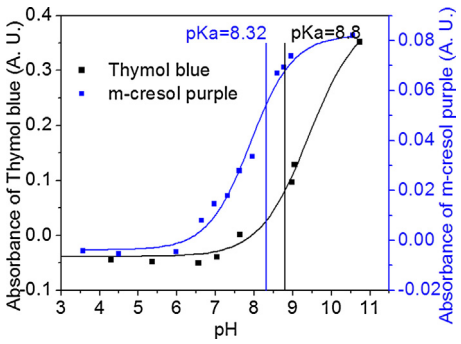

Fig. 1. Titration curves for the HCO_3^-/CO_3^{2-} buffer system modified with thymol blue and *m*-cresol purple. The color changes in the CO_2 sensor were due to the pKa value (for thymol blue: color changes from blue (pH > pKa) to yellow (pH < pKa); for *m*-cresol purple: color changes from purple (pH > pKa) to yellow (pH < pKa)). Compared with thymol blue, *m*-cresol purple changes color more sensitively under neutral to weakly alkaline conditions, which provides a larger dynamic range for the breath CO_2 detection.

for capnography, and moreover, which is insensitive to real-time monitoring of CO_2 in air. In the present work, we report a CO_2 sensor with a response time as fast as ~0.1 s, which enables breath-by-breath analysis (see more details in Sections 2 and 3). Additionally, the sensor has a wide dynamic range (with the CO_2 concentration up to 11.5%), and low detection limit of a few tens of ppm, which are suitable for IAQ monitoring.

2. Experimental

2.1. Reagents and sensor preparation

The colorimetric CO_2 sensor presented in this article was prepared by coating a sensor chip with a solution containing HCO_3^-/CO_3^{2-} buffer and *m*-cresol purple as the sensing element [19,24]. All the reagents used in this work were analytical grade and purchased from Sigma-Aldrich (St. Louis, MO, USA). As described in our previous work, when an ambient air sample or warm breath sample was brought into contact with the sensor chip, the pH of the sensing material decreased, which led to a color change [24]. This color change was detected with an optoelectronic detection system (see details below).

Note that several differences are stayed in the present work with respect to previous work [24]. Regarding the sensor: (a) The sensor substrate uses a fluorinated hydrophobic membrane instead of transparent polyethylene-based plastic; (b) the hydrophobic membrane has microstructures and surface properties that provide faster water desorption and significantly improved sensor time response; and (c) the new indicator, *m*-cresol purple, provides a wider dynamic range of CO_2% concentration due to its lower pKa. Compared with thymol blue [24], *m*-cresol purple changes color more sensitively under weakly alkaline to neutral conditions (pH value: 9.0–6.0), which typically corresponds to the range of normal breath CO_2 levels (1.0-11.5%) [25–27] (Fig. 1).

Regarding the device: (a) For breath applications, the gas flow is designed that both exhalation of breath samples and inhalation of clean air are enabled through the device; the later enables *in situ* sensor regeneration and (b) the device's gas flow component has larger diameter (~20 mm) than the device published in Ref. [24] (few millimeters), which significantly reduces the resistance to breathing, enabling breath-by-breath analysis.

2.2. Device description

The CO_2 sensor chip was inserted into a detection chamber, which included an optoelectronic detection system consisting of a red LED (wavelength = 633 nm, LEDtronics. Inc., CA, USA) as a light source and a photodiode (OSRM GmbH, Germany) as a light detector (Fig. 2a). The response of the sensor was characterized by measuring the change in the intensity of transmitted light caused by the interaction of CO_2 with the sensing element (Fig. 2b). Gas sample, from either the ambient air or a flow containing simulated breath, was directed to the sensor detection chamber with a pump. Real breath test was also conducted by asking a volunteer to breathe into the device via a mouthpiece. The device also contains an electronic circuit, which collects and processes the data from the optoelectronic detection system, and then wirelessly sends the data to a smartphone via a Bluetooth chip.

2.3. Device characterization and validation

Simulated breath samples: To investigate the response of the CO_2 sensor to real breath, a humidified CO_2 gas mixture was employed to simulate the expired air. The simulated expired breath samples were prepared by first mixing 80% N_2 + 20% O_2 air with different amounts of CO_2 (Praxair. Inc.), ranging from 0.03 to 11.5%. The CO_2 mixtures were then pumped through a sealed water system immersed in a thermostatic water bath (Thermo Scientific, USA) at 35 °C to generate 35 °C and 100% relative humidity. The simulated expired gas samples and ambient air were then introduced into the breath analyzer alternately at a flow rate of 6 L/min to simulate expiration and inspiration processes as shown in Fig. 3a.

Simulated environmental samples: For environmental CO_2 analysis, the CO_2 gas mixtures were prepared by mixing ultrahigh purity air with CO_2 to simulate indoor air with CO_2 concentration ranging from 0 to 1350 ppm. The simulated indoor air samples and ultrahigh purity air were then alternately introduced into the CO_2 analyzer at a flow rate of 6 L/min as shown in Fig. 3b.

Sensor signal measurement: The change in light intensity of the CO_2 sensor was used to characterize the color change upon exposure to alternating sampling and purging periods of fixed time. The change in light intensity of the CO_2 sensor is evaluated as sensor signal from the baseline signal. This means that baseline shifts are corrected, which renders relatively small sensor response dispersion error at a given CO_2 concentration (see below for more details). The change in transmitted light of the CO_2 sensor is:

$$\Delta I(t) = I(t) - I(0),$$

where $I(0)$ is the light intensity prior to the exposure of the sensor surface to the gas samples, $I(t)$ is the light intensity at time t during the sampling process. In addition, the performance of this device was further validated using a commercial breath CO_2 analyzer (capnography analyzer from VacuMed, CA) and real breath samples from volunteers (Fig. 3c).

Cross-sensitivity analysis: The interference of other chemicals present in expired air and atmosphere, such as ethanol, acetone, acetonitrile, and NH_3, was investigated by introducing the humidified gas mixtures containing pure N_2 and the interfering gases into the CO_2 analyzer. The response of the CO_2 sensor exposed to the interfering gases was compared with the response of the sensor exposed to 1% CO_2 gas mixture.

3. Results and Discussion

3.1. Sensing mechanism of the CO_2 sensor

The basic sensing principle of the new CO_2 sensor is based on the adsorption and desorption processes of CO_2 in the sensor during the test [24]. Briefly, during the sensing process, as gas samples (either expired breath or environmental air) were introduced into the device, CO_2 was adsorbed by the HCO_3^-/CO_3^{2-} buffer system in