

Virtual Electronic Nose for Simultaneous Detection of Hydrogen and Methane in Breath on the Diagnosis of Gastrointestinal Diseases

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Abstract:

Breath test is a prevalent detection method for gastrointestinal function, which is widely used on the diagnosis of carbohydrate malabsorption, small intestinal bacterial overgrowth (SIBO) and other gastrointestinal diseases. This study proposed a non-invasive method utilizing a virtual electronic nose to simultaneously detect hydrogen and methane concentration in breath which were corrected by the carbon dioxide to eliminate the effect on the alveolar gas. The detection range of the virtual electronic nose system was 1-200 ppm, and the resolution was 1 ppm, and the precision was less than 10%, and the single detection time was significantly shortened to 90s, as well as the size reduced to (40cm×30cm×15cm). Forty-seven cases of healthy people and patients were collected, and the types of concentration curve were judged accurately, and the SIBO diagnostic model was established. This method has the advantages of high specificity, non-invasive and simplicity of operation, so that can be used for the detection of increasing volume of clinical and domestic patients.

Key words: virtual electronic nose, breath test, hydrogen and methane detection, diagnosis model, gastrointestinal diseases

Introduction

Small intestinal bacterial overgrowth (SIBO) is a condition in which the small bowel is colonized by excessive numbers of aerobic and anaerobic microbes that are normally found in the large intestine. The gold standard for clinical diagnosis of SIBO is small intestinal fluid culture, while the sampling is invasive and the sample location is limited and easy to be contaminated. The work presented here designed a virtual electronic nose to simultaneously detect H₂ and CH₄ concentration in breath which were corrected by the CO₂. The SIBO diagnostic model was established and validated by forty-seven cases of healthy people and SIBO patients.

Method and experiment

H₂, CO₂ and volatile fatty acids (VFA) are produced by the bacterial fermentation (BF) of the carbohydrates. CH₄ is majorly produced by hydrogenation of CO₂ by methanogenic bacteria (MB) in the gut. The generation of these gases transfer through the intestinal wall into the venous circulation to the lungs, from where they can be quantitatively measured in exhaled air.

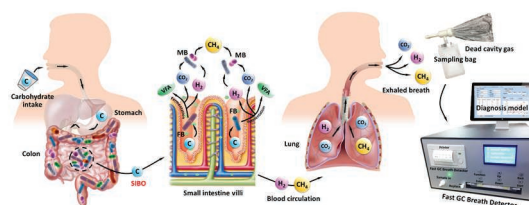


Fig. 1. Hydrogen and methane breath test and system pattern diagram.

The schematic diagram of virtual electronic nose is shown in Fig. 2A. The gas chamber and sensors were continuously cleaned by filtered room air when the system was in standby state (blue line). The sample gas was pumped into the sample loop automatically (green line) and the carrier gas put the sample into the chamber after the three-way valves switched paths (purple line). CO₂ was detected by an infrared sensor and H₂ and CH₄ are separated by the chromatographic column, and then reacted with a metal oxide semiconductor (MOS) sensor. Within 90 seconds, the instrument displays corrected H₂, CH₄, and CO₂ concentrations on the display. Fig. 2B shows the material object of the virtual electronic nose.

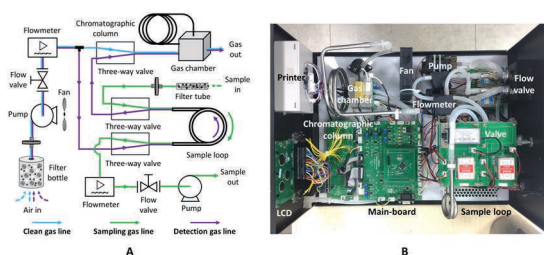


Fig. 2. Virtual electronic nose design: A-schematic diagram, B-material object.

The gas chamber, as shown in Fig.3A, was made of metal material for good thermal inertia whose temperature was controlled accurately. There is a cylindrical tank inside the gas chamber as reaction area just covering the sensitive material of the MOS sensor. The gas flows vertically to the MOS sensor surface from top of the reaction area through the gas inlet, and exhaust through the gas outlet which is connected with the side wall to ensure that the MOS sensor could output the response quickly and recover the baseline shortly.

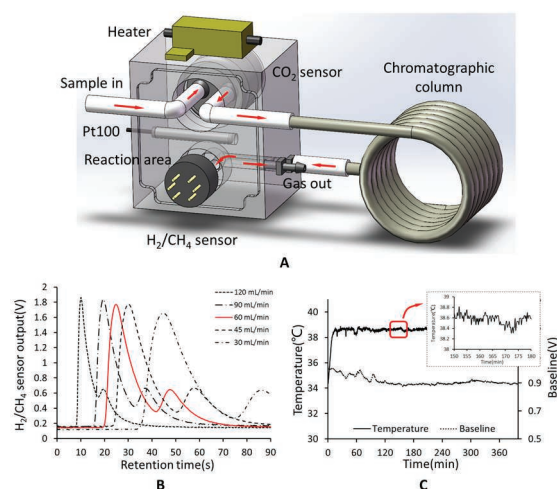


Fig. 3. Gas chamber design: A-schematic diagram, B-impact by different flow rates, C-temperature control and baseline drift.

Results and discussion

Fig.3B shows the impact on output response of the MOS sensor by different flow rates. Considering the accuracy and detection cycle, the instrument is allowed to enter the calibration and detection state when the flow rate of carrier gas is in the range of 60 ± 3 mL/min. Fig.3C shows the temperature control of the gas chamber and baseline drift of MOS sensor. The temperature of gas chamber is 38 ± 0.5 degrees Celsius after warming up for two hours, and the baseline of sensor output reaches a stable state basically.

The detection range of CO₂ concentration is 0.1-10 %, and the detection range of H₂ and CH₄ is 1-200 ppm. The sensors were calibrated by the

standard gas concentration gradient with 3 times (see Fig.4A, 4B). The correlation between the characteristic value and the concentration gradient was analyzed, and the calibration formula was obtained (see Fig.4C, 4D). The peak positions of H₂, CH₄ and CO₂ have good repeatability and the correlation coefficients (R^2) of fitting curves are all greater than 0.99. The detection resolution of CO₂ is 0.1 %, and the detection resolution of H₂ and CH₄ is 1 ppm.

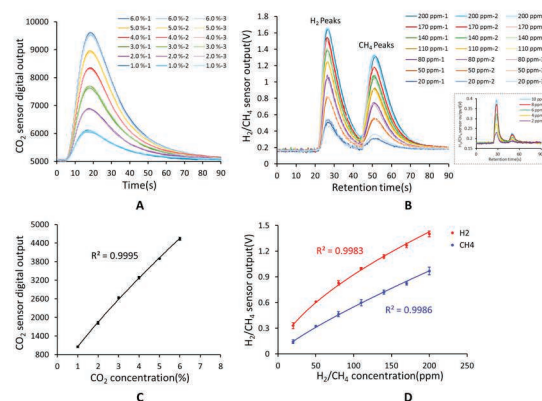


Fig. 4. Sensors calibration: A-CO₂ concentration gradient responses, B-H₂/CH₄ concentration gradient responses, C-CO₂ fitting curve, D- H₂/CH₄ fitting curve.

The SIBO positive diagnostic criteria and model were established in combination with the North American [1] and the Rome consensus [2]. Parts of cases analysis with typical positive and negative unimodal and bimodal curves are shown in Fig.5. The peak time may refer to the fermentation position of lactulose in the intestine. In positive unimodal model, early flat high peak expresses bacterial overgrowth may happen in the ileum, while in positive bimodal model, the SIBO may occur in the jejunum.

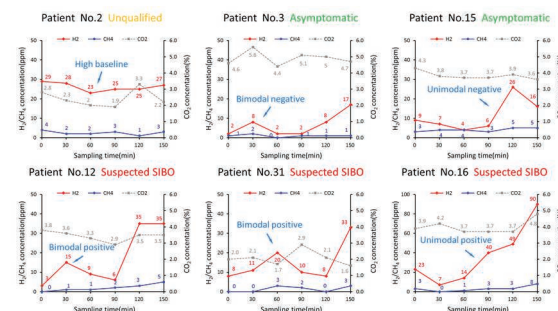


Fig. 5. SIBO diagnosis model and samples analysis.

References

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