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Bio-Transducers for Biomedical Applications

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1. Introduction

In recent years, health equipments and transducers used by individuals at home have become popular for the health care of patients suffering chronic disease to control the health condition. For example, the hypertension patients may estimate their health condition by measuring the blood pressure every day at home.

Health care without a doctor and medical instruments poses many problems. In the present medical facility, the biological information of the patients is collected by complex medical equipment which assists the doctor doing the medical treatment. Among various types of medical tests, blood analysis is an important approach for obtaining health bio/chemical information about the patient's health.

The biological information released from the human body is a complex form of chemical and physical data. The importance of bio/chemical information widely known in the medical field. In these connections, more numerous biological information should be collected to promote the health and medical care with convenient approach.

On the other hand, many kinds of volatile organic compounds (VOC) in the gas-phase, which defined as the specified malodorous substances by the American Conference of Governmental Industrial Hygienists (ACGIH) and the Environment Agency Government of Japan, have been reported to induce chronic disease such as sick-house syndrome. Novel transducers with high gas-selectivity are required for convenient measurement at home and ubiquitous environmental assessment.

We have constructed several kinds of wearable sensors for transcutaneous oxygen monitoring, tear conductivity measurement, glucose analysis. In addition, novel gas sensors (bio-sniffer) with high gas-selectivity have been also developed using biochemical recognition materials (i.e. enzyme) for the analysis of the expiratory gas and the environmental assessment.

2. Wearable oxygen sensor

Transcutaneous oxygen sensor has been in use for monitoring arterial oxygen pressure in premature infants to prevent Retinopathy of Prematurity at NICU [1,2]. Current sensors with a rigid cylindrical cell are fixed to the infant skin with adhesive plaster, resulting in common skin rashes and general discomfort for the infants. A newly oxygen sensor with flexibility and wearability such as clinical wet-pack has been required for transcutaneous monitoring in comfort.

We have constructed and evaluated a wearable oxygen sensor designed for direct contact with body surfaces and applied for transcutaneous oxygen monitoring.

The wearable oxygen sensor (thickness: 84 μm) was constructed using both gas permeable membrane and non-permeable membrane coated with Pt- (2000 Å) and Ag/AgCl (3000 Å) electrodes by microfabrication techniques, respectively; these membranes offers chemical stability, tear resistance and flexibility as shown figure 1. The electrolyte solution of 0.1 mol/l KCl was pouched into the two membranes by epoxy-adhesive and heat-sealing system [3].

Fig. 1 Photograph of the wearable oxygen sensor.

Behavior of the wearable oxygen sensor was evaluated with the performance of the dissolved oxygen (DO) measurement and calibrated using test solution of distilled water or sodium sulfite solution.

As the results of applying sodium sulfite solution to decreasing DO concentration, the current output of the wearable oxygen sensor decreased rapidly following addition of sodium sulfite solution. The current output of the sensor device was linearly related to the concentration of the dissolved oxygen over a range of 0.0–8.0 mg/l, with a correlation coefficient of 0.999 deduced by regression analysis, as shown by the equation.

$$\text{sensor output } (\mu A) = 0.24 + 5.11\ [\text{DO (mg./l)}]$$

The tip of the wearable oxygen sensor was placed directly onto the forearm skin surface with a commercial available skin warmer and thermistor, and fixed by an adhesive bandage. The outputs of the wearable oxygen sensor and the thermistor were monitored continuously for an inhalation of various concentration of oxygen (21 % to 60 % to 21 %). A transcutaneous oxygen pressure (tcPO2) was calculated from the output current of the wearable sensor.

Figure 2 shows the typical response for transcutaneous oxygen pressure and the skin temperature. As the figure indicates, tcPO2 value was rapidly increased by the inhalation of 60 % oxygen air, and decreased by 21 % oxygen air.

The skin surface was controlled at 39 °C as indicated in the figure.

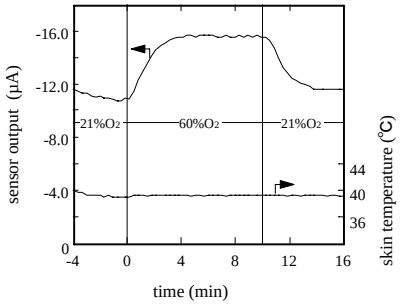

Fig. 2 Typical output of transcutaneous oxygen monitoring by the wearable sensor.

3. Bio-sniffer (biochemical gas sensor) for ethanol

The detection and quantification of gaseous substances, such as odors, toxic and combustible gases, with high sensitivity and selectivity are required in many different areas. In addition, some substances in the gas phase can be related to human health and behavior. For example, chemical malodors can affect human mental and physical condition [4]. Expiratory gas analysis would provide a non-invasive, convenient and safe method of diagnosing and monitoring disease states. One of the major applications of the breath analysis is in the quantification and detection of ethanol in expiratory gas after alcohol consumption. In this work, we have constructed a bio-sniffer using the enzyme catalytic reaction for measurement of gaseous substances.

Figure 3 illustrates the structure of the bio-sniffer for measurement of ethanol vapor. The sensor consisted of an enzyme electrode, a homemade reaction cell with two compartments for liquid and gas phases, and a porous diaphragm membrane between these compartments. The enzyme electrode was constructed using a commercially available Clark-type dissolved oxygen electrode with an enzyme membrane.

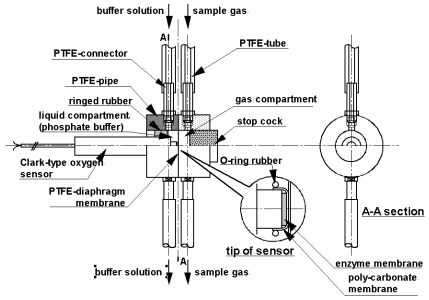

Fig. 3 Structure of bio-sniffer for ethanol.

Alcohol oxidase (EC 1.1.3.13) was used for constructing the enzyme electrode. Gaseous substances in the gas compartment could diffuse through into the liquid compartment of the reaction cell through the PTFE diaphragm membrane.

The sensor current decreased rapidly following application of ethanol, followed by a steady state current which gradually increased to the initial output following standard air application. The decrease in output current relates to the concentration of ethanol in the gas phase, since ethanol that diffuses through the enzyme membrane is oxidized by AOD using oxygen as electron acceptor, causing a decrease in the concentration of dissolved oxygen.

The steady output was related to the concentration of ethanol in the gas phase over the range 1.57 to 41.5 ppm (correlation coefficient of 0.992, covering the ethanol selective detection limit (6.1 ppm) in human [5]), deduced from exponential regression analysis of the log-log plot by a method of least squares according to the following equations:

$$\text{output (\%)} = 3.00 \, [\, \text{gaseous ethanol (ppm)} \,]^{0.943}$$

The selectivity of both the bio-sniffer device and the commercially available semi-conductor gas sensor for several gases and blends of gases is shown in Figure 4. The semi-conductor gas sensor responded to all of the applied gases, confirming the extremely poor selectivity of such devices as generally known. The bio-sniffer using an immobilized AOD electrode, however, gave negligible responses to all the chemicals other than ethanol.

The bio-sniffer thus possessed much greater selectivity and accuracy than the semi-conductor gas sensor. The bio-sniffer for ethanol has a simple construction, high selectivity and low detection limit, covering the concentration range encountered in breath after alcohol consumption and the sensing range of smell in humans.

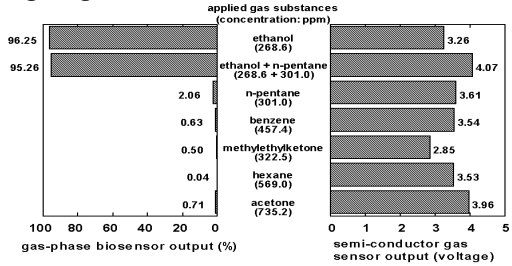

Fig. 4 Gas selectivity of the bio-sniffer and semi-conductor gas sensor using various kinds of applied gas substances.

Acknowledgements

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