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Integrated Flavor Sensor Using Microbead Array

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***Abstract*—**This research presents the design, fabrication and application of a flavor sensor for an integrated electronic tongue and electronic nose that can allow rapid characterization of multi-component mixtures in a solution. The odor gas and liquid are separated using hydrophobic porous membrane in micro fluidic channel. The sensor uses an array composed of microbeads in micromachined cavities localized on silicon wafer. Sensing occurs via colorimetric and fluorescence changes to receptors and indicator molecules that are attached to termination sites on the polymeric microbeads. As a result, the sensor array system enables simultaneous and near-real-time analyses using small samples and reagent volumes with the capacity to incorporate significant redundancies. One of the key parts of the system is a passive pump driven only by capillary force. The hydrophilic surface of the fluidic structure draws the sample into the sensor array without any moving mechanical parts. Since there is no moving mechanical component in the structure, the size of the fluidic structure can be compact and the fabrication becomes simple when compared to the device including active microfluidic components. These factors should make the proposed system inexpensive to mass-produce, portable and compatible with biomedical applications.

***Keywords*—**Optical Sensor, Semiconductor manufacturing, Smell sensor, Taste sensor.

I. Introduction

A challenging problem in the food and beverage processing industries is how to ensure the quality of products. This is achieved by spending significant time and effort on assessing the flavor of samples. Traditionally, panels of trained experts evaluate quality parameters; however this suffers from a number of drawbacks. For example, sensory panels are time consuming, expensive, discrepancies can occur due to human fatigue or stress and clearly cannot be used for online measurements. Thus the development of alternative methods to organoleptic panels for the objective assessment of food products, in a reliable and cost-effective manner, is highly desirable.

Although e-tongues still stray considerably from natural taste sense, they have shown good correlations with organoleptic scores given by human panelists. Comparing both taste systems, artificial senses are not subjective, do not become tired or infected and can be used in a wider range of samples. Moreover, e-tongues can have better sensitivity than the human tongue and can detect substances undetectable by their natural counterparts. This is because the taste system in humans is not as highly developed. This device can be used for the recognition, classification and quantitative determination of multiple component concentrations [1].

The combination of artificial sensors (for taste and smell) has the potential to reduce the need for flavor panels, since their outcome can be correlated to a human-based sensory experience. The fusion of various measurement techniques was recently proposed to improve the recognition capabilities of the electronic tongue systems [2]. The fusion of data obtained by two electronic tongue systems was presented. However, its liquid sensors and gas sensors were used, respectively. Through this study, we propose a model of integrated sensors, liquid and gas measurement simultaneously on one substrate.

II. Principles

A. Optical Sensor

Sensing is based on the optical changes that occur in receptors and indicator molecules attached to the polymeric microbeads that are typically a few hundred micrometers in diameter. The microbeads are located in a pre-set arrangement of micromachined cavities. The resulting optical signatures form a pattern that can be identified and quantified using Image software on a workstation. Since signal transduction is accomplished by the analysis of the optical (absorbance for colorimetric detection and fluorescence) signals from the microbeads, optical access through the microfluidic structure is required, as illustrated in Fig. 1.

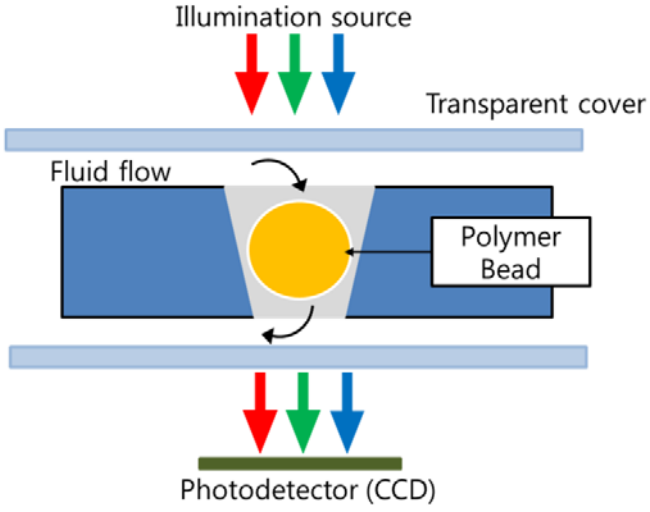

Fig. 1 Optical detection and data analysis systems

An optical illumination source, a white light for

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colorimetric measurement, is positioned above or below the micromachined device, and an illuminating light then passes through the micromachined device to reach the optical detectors, typically CCD [3].

B. Gas/Liquid Separator

A gas/liquid separator working principle is based on capillary forces using a combination of hydrophilic and hydrophobic materials with milli/micro structured channels. The fundamentals for the separation process were established by Thomas Young and Pierre–Simon Laplace. The capillary pressure p_c is defined by the Young–Laplace equation:

$$p_c = 2 \cdot \sigma_{lg} \cdot H \quad (1)$$

whereσ_{lg} represents the surface tension and H the resulting mean curvature between the fluids. For two different sphere radii, r_1 and r_2, which could appear in rectangular or in general in noncircular micro channels, (1) becomes:

$$p_c = \sigma_{lg} \cdot \left(\frac{1}{r_1} + \frac{1}{r_2}\right) \quad (2)$$

In general, the radius of the sphere is expressed by:

$$r_n = \frac{R_n}{\cos\theta} \quad (3)$$

where, R_n represents the corresponding radius of the tube or the distance to the neutral axis of the noncircular channel. The cosine of the contact angle h is given by Young as:

$$\cos\theta = \frac{\sigma_{sg} - \sigma_{sl}}{\sigma_{lg}} \quad (4)$$

where σ_{sg} represents the solid gas interfacial specific energy, also known as free surface energy, r_{sl} the solid liquid interfacial specific energy and σ_{lg} the liquid vapor interfacial specific energy, commonly known as surface tension. To calculate the flow inside a noncircular channel in the same way as in a round tube, it is common to use the hydraulic diameter instead of R_n. With that simplification and the definition of r_n, (2) can be rewritten as:

$$p_c = \frac{4 \cdot \sigma_{lg}}{d_{hyd}} \cdot \cos\theta \quad (5)$$

Equation (5) shows the dependence of the capillary pressure p_c on the geometry, expressed by d_{hyd} and on the properties of the three phases, expressed by r_{lg} and h [4].

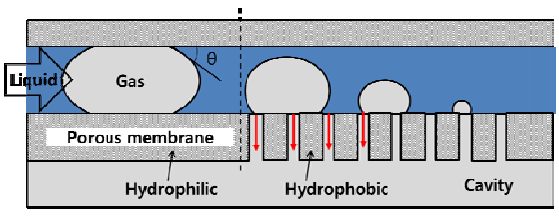

Fig. 2 Schematic of the working principle of the gas/liquid separator

Fig. 2 shows a schematic of the working principle of the orientation independent gas liquid separator. Hydrophobic surfaces causes contact angles in the range of 90◦ to 180◦ and result in negative capillary pressures. In contrary to that, hydrophilic surfaces will result in positive capillary pressures with contact angles in the range of 0◦ up to 90◦. On a hydrophobic layer, the liquid can't pass through the pore due to the negative capillary pressures. And the gas diffuses into the cavity through the pole. It can be separate gas and liquid [5].

III. Design

A. Proposed Model

Fig. 3 shows a cross sectional view and top view of the fluidic structure. The basic structure consists of three layers: the cover glass, the micromachined silicon and the glass substrate. Through the Chanel, prepared solution flow and react with micro bead in cavity. The odor gas and liquid are separated using hydrophobic porous membrane. And react with micro bead individually. The resulting optical signatures form a pattern that can be identified and quantified using Image software. An optical illumination source is positioned above or below the device, and an illuminating light then passes through the micromachined device to reach the optical detectors. It can be detect gas and liquid at a time.

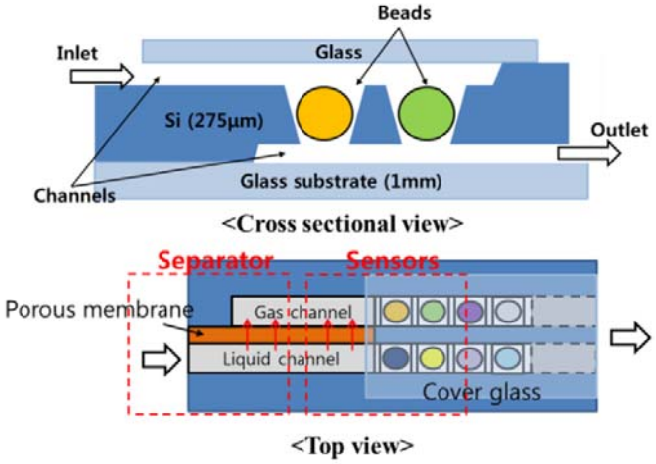

Fig. 3 Crosssectional view and top view of the proposed microfluidic structure

B. Device Fabrication

The silicon is etched twice, firstly, to form the micromachined cavities that support the microbeads and secondly, to form the flow channels. The glass substrate allows optical access and provides mechanical stabilization for the silicon substrate. Fig. 4 shows a schematic diagram of the fabrication procedure. A lightly doped, double side polished 4 in. single crystal (100) silicon wafer was used as the substrate. Anisotropic wet chemical etching has been used to fabricate the micromachined cavities and channels in the single silicon substrate. A silicon nitride (Si_3N_4) layer deposited by LPCVD was used as mask layer for the bulk etch. An array of squares

was patterned on the silicon wafer (Fig. 4 (a)), and the silicon was anisotropically etched to form the cavities (Fig. 4 (b)). Timed-etch stop was used to control the channel depth. During channel etching, the change in the shape of the micromachined cavities was negligible since the typical values for the selectivity of (100) over (111) in planes in KOH etchants is 300–400. The channel depth created by micromachining was about 25 μm (Figs. 4 (c) and (d)).

After all silicon micromachining was completed, a silicon dioxide (SiO_2) layer was deposited using the LPCVD process in order to enhance surface wetting for sample introduction (i.e., to ensure that the chip surfaces are hydrophilic) (Fig. 4 (e)). Separator structure is made of PMMA and covered by a hydrophobic PTFE membrane. A pore size is in the range of 0.2 μm to 1.0 μm. After the silicon substrate fabrication was completed, it was bonded to the glass substrate using anodic bonding (Fig. 4 (f)). After the micromachined silicon substrate was attached tothe glass substrate, each microbead was placed in the etch cavities using a pick-and-place tool to form the sensor array (Fig. 4 (g)). Finally, the cover glass was attached to the rest of the device using a UV curable adhesive (Fig. 4 (h)).

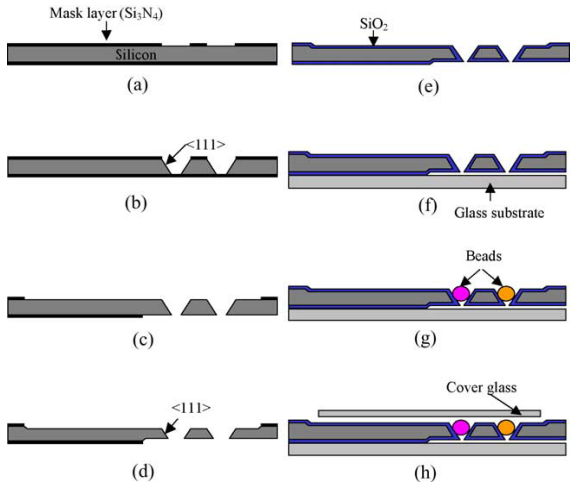

Fig. 4 Schematic diagram of fabrication procedure of the microfluidic device

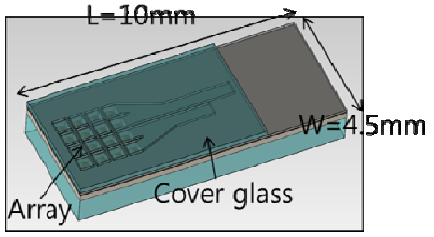

Fig. 5 A three-dimensional scheme of the microfluidic device with the corresponding dimensions

IV. Application

Electronic tongue/nose systems are multisensory devices dedicated to automatic analysis of complicated composition samples and to the recognition of their characteristic properties. Recently, the number of publications covering this topic and its applications has significantly increased.

A. Sensor Fusion: ET/EN Devices

The fusion of various measurement techniques was recently proposed to improve the recognition capabilities of the electronic tongue/nose systems. Recently many researches have been done by the combination of ET/EN in which the analysis of wine performed by the device allowed the determination of the origin of the wine and its properties: tartaric, malic, and lactic acids, alcohol, extract, polyphenols and sugar content, pH, acidity, and density. The analysis of milk led to the estimation of its spoilage and differentiation between pasteurized and UHT samples. Researches in this regard prove that the electronic nose and electronic tongue, used separately, provided only partial information concerning the sample, whereas fusion of them improved classification ability of the system [6]. The combination of various measurement methods provides a better characterization of a sample – the chemical image of the sample becomes more complete because various properties are studied. Moreover, the simulation of two joined senses – taste and smell becomes possible. In some cases, even visual properties of the investigated object can be considered (e.g. the measurement of the reflectance spectra).The fusion of data obtained by gas sensors, electrochemical liquid sensors, and optical system to measure sample colors provided good results in the recognition of wines with regard to their origin and ageing stage. In conclusion, closer simulation of natural sense of taste demands the coupling of even more sensing technologies.

The impression of taste can be expressed as follows:

Taste impression = smell + taste +texture + color + sound + temperature

Therefore, the complete characterization of a sample would demand not only chemical characterization, but physical sensors should also be considered (pressure/tactile sensors, acoustic sensors, temperature sensors).

B. Electrical Nose for Detection of Lung Cancer

Lung cancer is one of the most deadly diseases in the world. If the cancer can be discovered and treated promptly, the survival rate would increase. It has been tried to study and find a non-invasive method to diagnose the disease based on an electronic nose; Electric nose using a virtual SAW sensors array with an imaging recognition algorithm to improve the sensitivity and selectivity has been applied for early detection of lung cancer. One SAW sensor is coated with a PIB polymer and the other uncoated for reference. By using a developed interface of GC, the 11 VOCs in lung cancer patients' breath separated through a capillary column can be absorbed on the polymer and detected by SAW sensors. The electronic nose has some advantages including high sensitivity, low cost and easy operation. The breath from lung cancer patients, chronic bronchitis patients and healthy persons for pathology analysis with this e-nose was studied. The pathophysiology for this diagnosis is still not yet clearly known, and there isn't an accurate clinical technology to diagnose inchoate lung cancer

either, so the patients were tested almost had severe lung cancer [7].

In another study the relation between oral cancer and ion contents was shown. Oral cancer is the sixth most common human cancer, with a high morbidity rate and an overall 5-year survival rate of less than 50%. It is often not diagnosed until it has reached an advanced stage. Therefore, an early diagnostic and stratification strategy is of great importance for oral cancer. In this reference, urine samples of patients with oral squamous cell carcinoma (OSCC, n = 37), oral leukoplakia (OLK, n = 32) and healthy subjects (n = 34) were analyzed by gas chromatography mass spectrometry (GC–MS). Using multivariate statistical analysis, the urinary metabolite profiles of OSCC, OLK and healthy control samples can be clearly discriminated and a panel of differentially expressed metabolites was obtained. Typical total ion current (TIC) chromatograms of urine samples from the OSCC group, OLK group and healthy control group are shown in Fig. 6; obvious differences can be observed among the three urinary chromatograms [8].

In another research the use of volatile production patterns produced by bacterial contaminants in urine samples were examined using electronic nose technology. In two experiments 25 and 45 samples from patients were analyzed for specific bacterial contaminants using agar culture techniques and the major UTI bacterial species identified. These samples were also analyzed by incubation in a volatile generation test tube system for 4-5 h. The volatile production patterns were then analyzed using an electronic nose system with 14 conducting polymer sensors. In the first experiment analysis of the data using a neural network (NN) enabled identification of all but one of the samples correctly when compared to the culture information. In the second experiment it was again possible to use NN systems to examine the volatile production patterns and identify 18 of 19 unknown UTI cases. Only one normal patient sample was mis-identified as an E. coli infected sample. Discriminant function analysis also differentiated between normal urine samples that infected with E. coli and with Staphylococcus spp. This study has shown the potential for early detection of microbial contaminants in urine samples using electronic nose technology for the first time. These findings will have implications for the development of rapid systems for use in clinical practice [9].

Scientists are reporting an advance [10] toward a fast, inexpensive urine test to detect and monitor the effectiveness of treatment for tuberculosis (TB), which is on a rampage in the developing world. Their study appears in the ACS' journal Analytical Chemistry. A team led by Virander Singh Chauhan and Ranjan Kumar Nanda notes that TB strikes an estimated 10 million people and kills 3 million each year, mostly in developing countries. Health care workers diagnose the disease by identifying the TB bacterium in sputum or blood samples. But current tests tend to be time-consuming, sometimes taking days or weeks to give results. The tests also require the use of specially trained personnel or expensive equipment that might not be available in some areas. The scientists describe an advance toward a test that overcomes these drawbacks. They analyzed so-called volatile organic compounds (VOCs) — substances that evaporate easily in the air — present in the urine of TB patients and compared them with VOCs in the urine of healthy patients. The scientists found that infection with TB produces a distinct pattern of certain VOCs in much the same way that distinct fingerprint patterns can identify individuals. Identification of these patterns sets the stage for developing a portable "electronic nose" that can quickly sniff urine samples to detect TB, the scientists suggest.

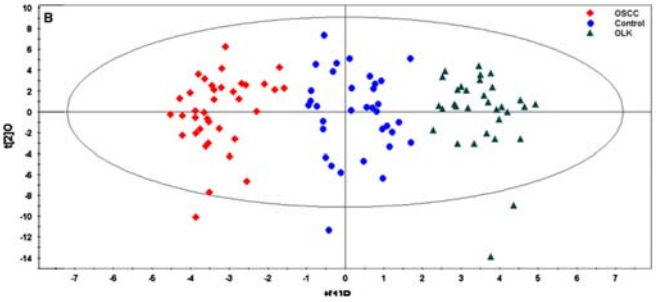

Fig. 6 The scores plot of the spectral data from the OSCC group, OLK group and the healthy control group

While in above researches separate experiments using electronic nose or electronic tongue has been applied for detection of abnormal condition in the body we suggest our design ET/EN in combination for experiments of abnormal condition in the urine. Usually cancers are not detected till it is highly developed in the body. If the cancer can be discovered and treated promptly and at early stages, the survival rate would increase. Our proposed instrument also might be applied for detection of cancers which affect the urine, further research in this regard is necessary for proper conclusion.

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