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Multianalyte Sensor Array using Capillary-Based Sample Introduction Fluidic Structure: Toward the Development of an "Electronic Tongue"

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Abstract

A micromachined fluidic structure for the introduction of liquid samples into a chip-based sensor array composed of individually addressable polymeric microbeads has been developed. The structure consists of a separately attached cover glass, a single silicon chip having micromachined channels and microbead storage cavities, and a glass carrier. In our sensor array, transduction occurs via colorimetric and fluorescence changes to receptors and indicator molecules that are covalently attached to termination sites on the polymeric microbeads. Data streams are acquired for each of the individual microbeads using a CCD. One of the key parts of the structure is a passive fluid introduction system driven only by capillary force. The velocity of penetration of a horizontal capillary for the device having a rectangular cross section has been derived, and it is quite similar to the Washburn Equation calculated for a pipe with a circular cross section having uniform radius. The test results show that this system is useful in a μ-TAS and biomedical applications.

Key Words : Chemical sensor array, Microbeads, Microfluidic, Capillary, μ-TAS

1. Introduction

The development of smart sensors with chemical and biological responses has become increasingly important for medical, environmental, military, and industrial processing applications. The development of receptors, detection principles, and device fabrication techniques is all important factors in the success of chemical and biological detection systems. Technical and economic factors both affect the development of the microfluidic devices involved in these types of detection systems. The motivations and advantages include reduced initial sample volume, the minimal usage of expensive reagents, increased functionality and parallelism in sample analysis resulting in faster analysis time, compact size, and low-cost.

Combinatorial arrays of chemical sensors have been synthesized to address a wide variety of analyses, thereby enabling the investigation of a large number of possible molecule interactions in parallel[1]. For many important applications, such as medical processing, a solution-phase analysis is desired without requiring the decomposition of the analytes[2].

In this paper a micromachined fluidic structure for a chip-based sensor array that allows the rapid characterization of multi-component mixtures in a solution is described. The micromachined structure consists of micromachined storage cavities combined with a covering glass layer that confines the microbeads and fluidic channels. One of the key parts of the system is a passive pump driven only by capillary force. The wetting surface of the fluidic structure draws the sample into the sensor array without any moving mechanical parts resulting in compact size and easy fabrication of the device when compared to the active microfluidic components.

2. The Hybrid Micromachined Platform

Sensing is based on colorimetric and fluorescence changes that occur in receptors and indicator molecules that are attached to termination sites on the polymeric microbeads that are typically a few hundred μm in diameter. The microbeads are located in a pre-set arrangement of micromachined cavities localized on silicon wafer. Spectral data (composed of R-G-B light intensities) are extracted from each of the individual

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beads using a CCD. The resulting patterns are used for analyte indentification and quantification using Image Pro Plus 4.0 software from Media Cybernetics on a workstation[3]. 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, so that false signals can be recognized in contrast to real signals[2-5].

Since signal transduction is accomplished by the analysis of the optical (e.g., absorption) properties of the microbeads, an optical illumination source (e.g., a white light for colorimetric measurement[2,3]) is positioned above or below the micromachined device, and an illuminating light then passes through the micromachined device to reach the optical detectors, typically a CCD as illustrated in Fig. 1(a).

Microbeads have been widely used since they are convenient solid phase supports for receptors, have good optical properties, and can be easily and inexpensively acquired. Bead material choice is based on the method of derivatization and also its compatibility with aqueous solution[3,4,6]. Typical materials for the microbeads are polystyrene-polyethylene glycol, agarose, and glass.

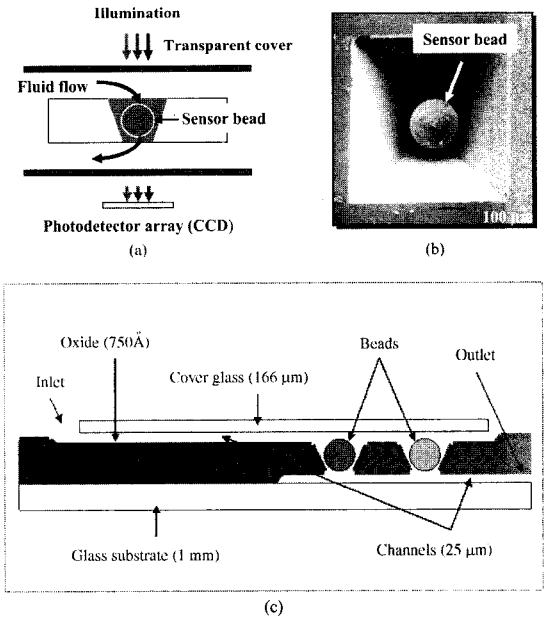

Fig. 1. (a) Schematic illustration of micromachined storage cavities used to confine sensitized micro-beads, (b) Scanning electron micrograph of the micromachined cavity and a polymer bead, and (c) Cross sectional view of the microfluidic structure.

However, some of the beads actually change size (e.g., swell or shrink) when the chemical environment changes. For a polystyrene-polyethylene glycol bead, typically microbeads with a diameter of about 150 μm in a dry state change their size to that of about 230 μm in a wet state. The swelling makes it easy for the microbeads to break into loss from its addressable location. Hence, we have chosen to use a confining structure (micromachined cavities and cover glass) to keep the beads in proper location while providing an undisturbed optical path through the microbeads and allowing for fluid flow through the micromachined cavities which serves as reaction and analysis chambers. Fig. 1(b) shows scanning electron micrograph of the micromachined cavity and a polymer sensor bead.

3. Fluidic Device Fabrication

Fig. 1(c) shows a cross-sectional view of the new fluidic structure, consisting of three layers: the cover glass, the micromachined silicon, and the glass substrate. The fabrication process has been selected to protect receptors and indicator molecules that may be sensitive to the normal processes used in chip fabrication. The silicon is micromachined twice using bulk anisotropic etching, firstly, to form the micromachined cavities that support the microbeads and secondly, to form the capillary flow channels. 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 etchant is 300 – 400[1]. After all silicon micromachining is completed, a silicon dioxide layer was deposited to enhance surface wetting during later sample introduction. The silicon chip is then bonded to the BOROFLOAT™ glass substrate using anodic bonding. After the micromachined silicon substrate is attached to the glass substrate, each microbead is placed in the etch cavities to form the sensor array. Finally, the cover glass is attached to the rest of the device using a UV curable adhesive.

4. Results and Discussion

A number of previous devices have used surface tension to transport liquids without the need of any moving mechanical parts; such forces are considered to be dominant in the micro domain[7,8]. In our device, a horizontal

capillary has been utilized to introduce the sample fluid; for such a system, one quantity of interest is the velocity of the fluid front v (i.e., the velocity of the leading liquid-air interface as the sample is first drawn into the system). In order to study the impact of inlet channel dimension on this velocity, one can start with fluidic resistance defined as the ratio of pressure drop over flow rate, analogous to electrical resistance. The fluidic resistance, R, for rectangular channels with width ($w = 8 \times 10^3$ m) much larger than depth ($h = 25 \times 10^6$ m) in the laminar flow regime is approximately[1],

$$R = \frac{\Delta P}{Q} = \frac{12\mu x}{wh^3} \quad (1)$$

where P is the pressure difference, Q is the volume flow rate, μ is viscosity of the sample fluid, and x is the penetration distance of the leading liquid-air interface from the inlet port to channel. The velocity of penetration was derived and given as

$$u = \frac{\gamma h}{6\mu x}\cos\theta \quad (2)$$

where γ is the contact angle and θ is the surface tension. Eq. (2) is quite similar to the Washburn equation calculated for a pipe with a circular cross section having uniform radius[9]. For water and a contact angle of 0 (characteristic of the highly hydrophilic oxide surface), Eq. (2) predicts a velocity at 14.75 mm into the channel of 20.6 mm/s, that compares well with the observed velocity at this point of 20 mm/s.

As the fluid approaches an array of micromachined cavities, one general trend was observed for many dif-

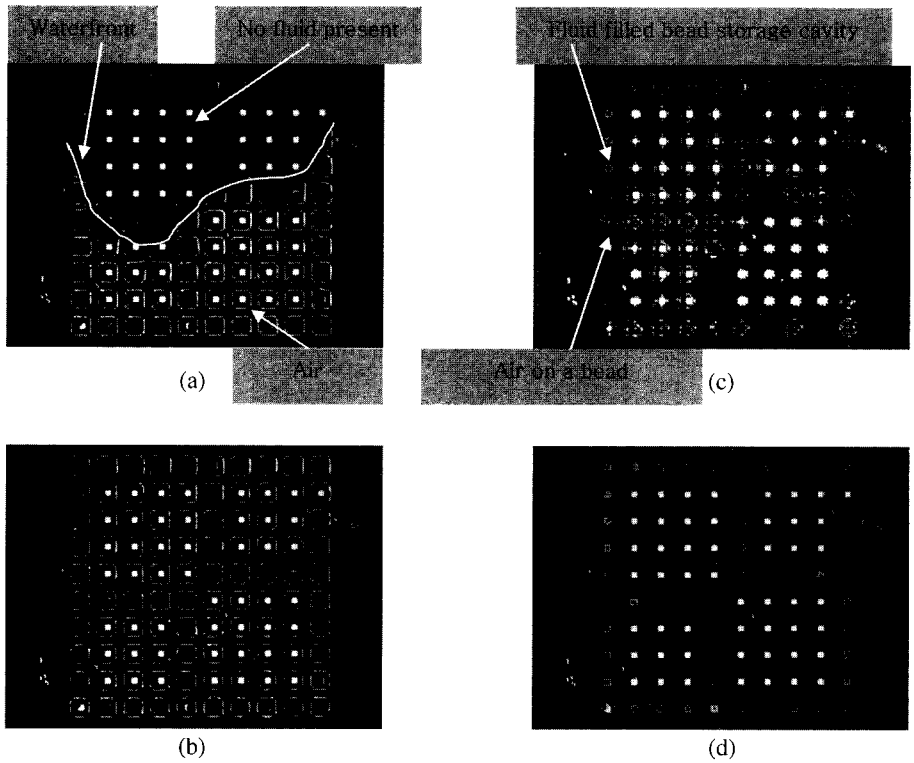

Fig. 2. Photomicrographs of a water sample as it flows through the chip.
(a) Waterfront approaches the cavities and the water passes around and between the cavities, with air clearly seen in the cavities themselves.
(b) The water has passed completely around and between all the cavities, but at this point all the cavities are still filled by air.
(c) The water flows into the cavities and the order in which the air in the cavities disappear varies from chip to chip, and does not seem to be strongly correlated with physical location in the array.
(d) All the cavities have been filled with the water and air has totally disappeared.

ferent devices: the water always flows completely around the array and into the spaces between the individual cavities before the fluid begins to flow into the cavities themselves. This may be caused by the loss of driving source above the micromachined cavities that is surface tension. Hence, the fluid flows easily around the array and into the spaces between the cavities, which is similar to the electrical current that prefers to flow in a way that is less resistive. This is illustrated by Fig. 2, showing how a water sample flows through the system. Typically the water front nears the array and reaches the micromachined bead storage cavities approximately 3 seconds after water was first placed at the inlet of the chip. Fig. 2(a) shows the system at $t = 3.6$ seconds, as the water passes around and between the cavities, with air clearly seen in the cavities themselves. Fig. 2(b) shows the system at $t = 4$ seconds, showing that the water has passed completely around and between all the cavities, but at this point all the cavities are still filled by air. Fig. 2(c) shows the system at $t = 4.5$ seconds as flow begins into the cavities. The flows of the air in the cavities are slightly different from each cavity and from chip to chip. This is probably due to slightly different surface effects across the micromachined array randomly generated during the chip fabrication. Finally at $t = 10$ seconds (Fig. 2(d)) all the cavities have been filled with water, and air has totally disappeared.

Fig. 3 shows a typical graph of red, green and blue transmitted light intensities for an alizarin complexone bead as the pH 1 HCl solution moves through the chip. The intensities were initially constant and then changed slightly for a short time as the fluid flowed across the

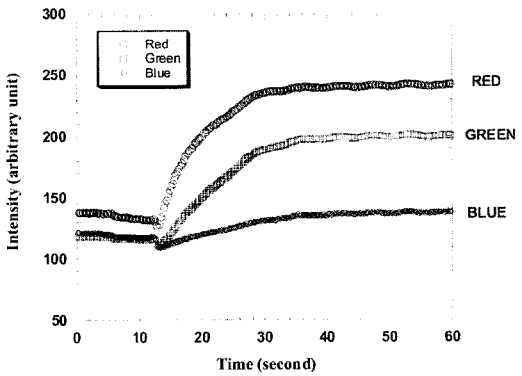

Fig. 3. Change in transmitted light intensity for an alizarin bead as a pH 1 HCl test solution is pulled through the chip by capillary force.

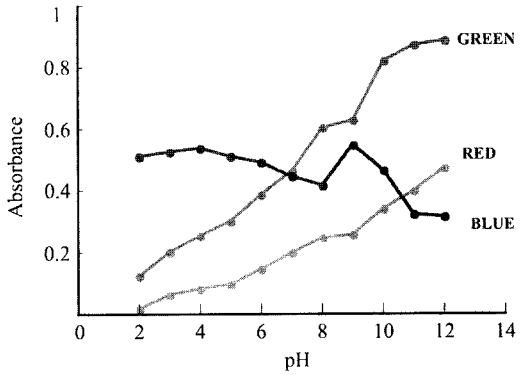

Fig. 4. Absorbance values of the alizarin complexone beads that is exposed to 10 different solution with pH values from 2 to 12.

cover glass over the beads. At some point in time, the R-G-B transmitted light intensity begins to change, and finally results in an overall color change in the beads from purple (before sample introduction) to orange (after complete response to the pH 1 solution). Using basic sensing scheme, Fig. 4 shows absorbance values of the alizarin complexone beads as the pH is varied over the range of 2 – 12[3, 10]. The actual chemical sensing is well described by Goodey *et al.*[3].

5. Conclusion

The development and initial characterization of a micromachined fluidic structure for the introduction of liquid samples into a chip-based sensor composed of an array of polymeric microbeads has been presented. One of the key parts of this system is a passive pump driven only by the capillary force, making the device simple and compact. The velocity of penetration of a horizontal capillary for the device having a rectangular cross section has been successfully derived. The microstructure was compatible with the basic sensing scheme for chemical detection requiring optical access through the microfluidic device. The system with simple fabrication procedure and the compact size of the microstructure could be beneficial for a μ-TAS.

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