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Miniaturized Detectors for a Chemical Analysis System

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ABSTRACT

Recently, several studies about miniaturized chemical analysis systems fabricated with micromachining methods were reported. These systems have some advantages, such as fast response, small amount of sample, and low consumption of reagents, as compared with the conventional system. With such a small system, design of the detector units is very important to monitor analytical performance. This paper introduces some examples of micromachined detectors for miniaturized chemical analysis systems.

Index Entries: Miniaturized detector; micromachining; ISFET; flow cell; chemiluminescence.

INTRODUCTION

Micromachining is one of the most remarkable technologies nowadays. This technology originated in Stanford University and University of California Berkeley in the 1970s. It was started by making mechanical structures, devices, and sensors using a silicon process. The pressure sensors (*1*) and accelerometers (*2*) made by the micromachining method have already been used. On the other hand, the integrated chemical analysis system for liquid was proposed in 1984. Ruzicka et al. made an integrated flow injection analysis (FIA) system and applied it to enzymatic

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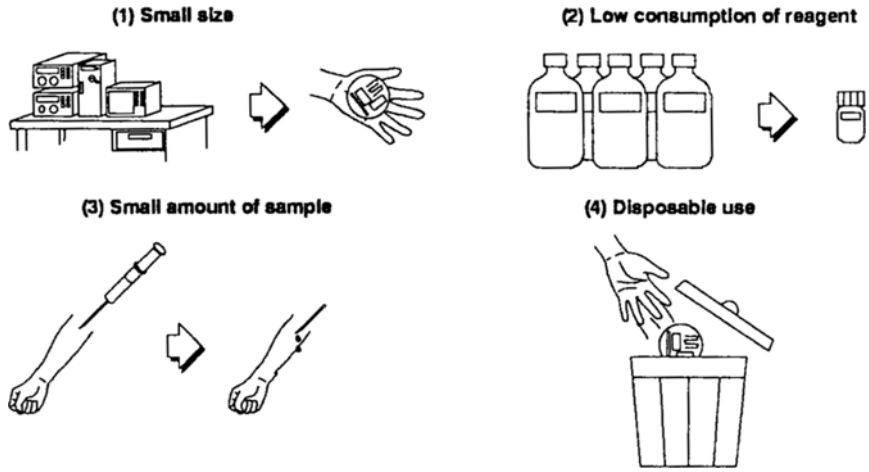

Fig. 1. Advantages of the miniaturized chemical analysis systems.

analysis (3). Furthermore, some studies to make miniaturized chemical analysis systems were already reported (4,5). These analysis systems have some advantages, such as fast response, small amount of sample, and low consumption of reagents, as compared with the conventional system (Fig. 1). This paper introduces some examples of miniaturized detectors for chemical analysis system.

MINIATURIZED DETECTORS

Small Volume Optical Detector

Manz et al. made an optical detector that has very small internal volume (Fig. 2) (6). The detector consists of two pieces of silicon. The upper chip provides the inlet and outlet holes of the light. The lower chip includes the liquid flow channel fabricated by anisotropic etching. In this device, the reflection on the inner wall of the liquid flow channel can be utilized to obtain a longer optical flow path. Because the anisotropically etched surface of the silicon is flat, the diffused reflection seems to be small. In their device, the liquid flow channel length is 1 mm, but the optical path length will become >1 mm. In addition, the cell volume was only 15 nL. In Manz' group, a helium-neon laser and a photodiode were used as a light source and a photo detector, respectively.

ISFET Flow Cell

De Rooji et al. fabricated a multi channel ISFET flow cell for the detector of the FIA system (7). ISFET is suitable for integration to a micromachined structure because ISFET is fabricated using the same process. They inte-

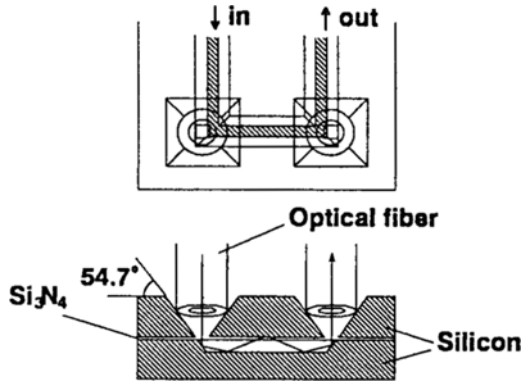

Fig. 2. Structure of the small volume optical detector.

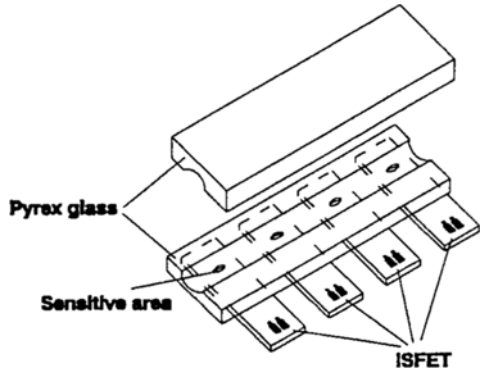

Fig. 3. Structure of the multi-ISFETs detector.

grated four ISFETs, which were used as a pH, potassium, and calcium sensor, and a reference, respectively. These devices were anodically bonded on a small volume flow cell made from Pyrex. The internal volume of the detector was about 12 μL (Fig. 3). They also constructed the liquid analysis system by the combination of this ISFET detector and a micromachined pump.

Micro Electrochemical Flow Cell

We fabricated the micro electrochemical flow cell using silicon micromachining techniques (*8*). Fig. 4 shows the structure of the device. The size of the device is 10×20 mm. A V-shaped groove was fabricated on the silicon chip by etching, sized 100 μm wide, 70 υm deep, and 5 mm long. The inlet and outlet of the liquid were also made by etching. On the Pyrex, gold electrodes were formed by evaporation and photolithography. The cell volume was about 20 nL except for the inlet and outlet hole.

This device was used as an electrochemical detector for liquid chromatography of catecholamines. Fig. 5 shows the chromatogram of the

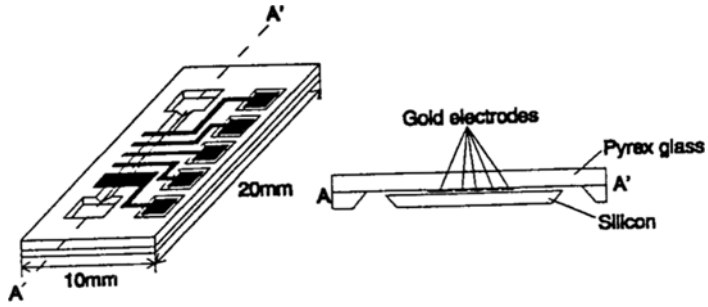

Fig. 4. Structure of the microelectrochemical flow cell.

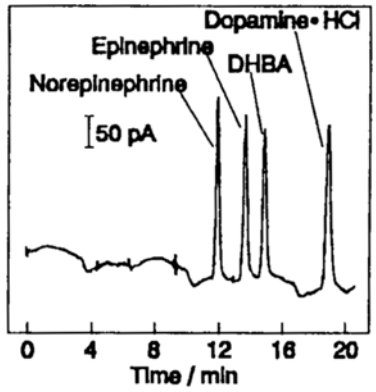

Fig. 5. Chromatogram of catecholamines using microelectrochemical flow cell.

standard solution the catecholamines. Almost the same result occurs except the current intensity as the conventional electrochemical detector was obtained.

High-Sensitive Electrochemical Detector Using Redox Cycling Reaction

The studies to increase the sensitivity of the miniaturized electrochemical detector were carried out by Matsue et al. (*9*). They utilized the redox cycling reaction using an interdigitated microarray electrode. The potential of the one electrode was set at the oxidized potential and another one was at reduced potential using a dual-channel potentiostat. Then, the electrochemically reversible species was oxidized and reduced cyclically. Finally, one molecule was detected many times in the detector. Therefore, the oxidation or reduction current seemed to increase. In addition, this array electrode brought another benefit; suppression of the undesired influence of interfering species. When the interfering species is electrochemically irreversible, for example, ascorbic acid or uric acid, the effect of these substances can be decreased using this detector. Fig. 6 shows the chromatograms of a standard sample of the catecholamines, which also contained L-ascorbic acid and uric acid. Working electrode 1 was set at 0.8

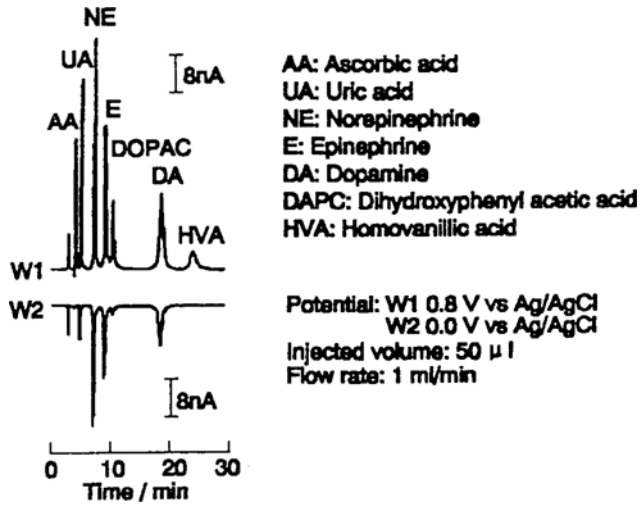

Fig. 6. Chromatogram of catecholamines using redox cycling detector.

V and working electrode 2 at 0.0 V. The chromatogram observed at working electrode 1 shows the peaks for all species. However, the chromatogram observed at working electrode 2 gives selectively the peaks for catecholamines. Since ascorbic acid and uric acid are irreversibly oxidized at electrode 1, the products are hardly reduced at electrode 2. On the other had, catecholamines are electrochemically reversible, so the peaks for catecholamines can be amplified by the redox cycling.

Multichannel Electrochemical Detector

A multichannel electrochemical detector was also developed by Matsue's group (*10*). The 16 lines of the working electrode are fabricated by photolithography, whose size was 0.1 mm wide with 0.05 mm spacing between lines. When each electrode is set at a different potential, 16 channels of electrochemical measurement can be carried out simultaneously. Additionally, each electrode potential is swept stepwise by the function generator. Larger number channels of electrochemical measurement can be also carried out. This electrochemical detector gives information concerning redox potential of the substances in addition to redox current. Therefore, the identification of the substances by voltammogram becomes possible.

Fig. 7 shows the result of applying to the detector of HPLC. The sample contains ascorbic acid, epinephrine, uric acid, and dopamine. A potential resolution was 10 mV, and identification of the species was possible from the potential at which the current started to increase. In this scanning potential method, the current was sampled at least 20 ms after each potential step to eliminate the influence of the charging current. Thus, it takes 0.27 s to scan one time through 80 channels. This value is no problem with the conventional HPLC system.

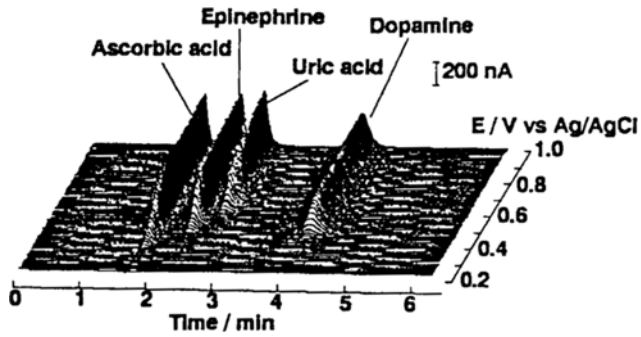

Fig. 7. Chromatogram of catecholamines using multichannel electrochemical detector.

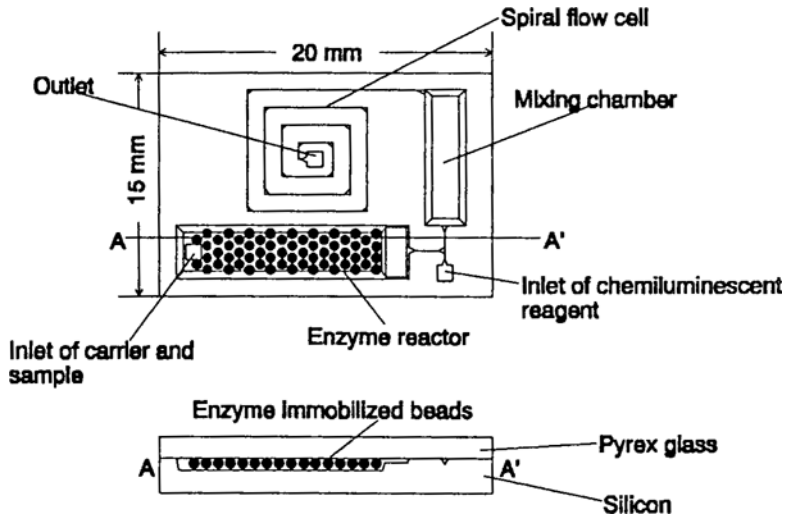

Fig. 8. Structure of the chemiluminescence detector.

Chemiluminescence Detector

We also fabricated a micromachined chemiluminescence detector (*11*). The chemiluminescent detection method has higher sensitivity than spectroscopic or electrochemical methods. Chemiluminescence with luminol is especially suitable for enzyme-based FIA because it has high sensitivity and high selectivity to hydrogen peroxide. Furthermore, the chemiluminescent detector does not require a light source, so it is convenient for miniaturization of the system.

Fig. 8 shows the structure of the chemiluminescence detector. On the silicon substrate, an enzyme reactor, a mixing chamber, and a spiral flow cell were made by etching. The whole size of the detector was 15×20 mm, and the total internal volume was about 15 μL. Enzyme immobilized glass

beads, diameter 100 μm, were packed into the column and a photodiode was placed onto the spiral flow cell. This detector was applied to determination of glucose and lactate contained in human serum.

CONCLUSION

As described previously, many studies of the miniaturized chemical analysis system carried out previously. Among them, some studies concerned with the total system were already reported. To construct the total analysis system by micromachining, there are two concepts for integration. One is that all of the units are integrated on one substrate. This is an ideal system to increase the analytical performance. However, if many mechancal moving devices are involved, the fabrication procedure becomes too complicated. Therefore, a capillary electrophoresis system that has no or little mechanical parts is suitable.

Another concept is the hybrid system, which consists of several units that are connected to each other. In the FIA system, which includes the piezoelectric pump or valve, the hybrid concept is more suitable than total integration. Each unit is replaceable when some unit becomes in bad condition. In this system, it is more important to keep the analytical performance higher than to connect between the units. In the studies reported until now, almost all systems used small diameter tubes glued on the device. This method is not considered practical, because the many connecting points cause a decrease in analytical performance. Therefore, development of an excellent connection method is as important as improvement of sensitivity in the miniaturized chemical analysis system.

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