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Smart Microfluidic and Analytical Devices Based on Electrochemical Principles

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Abstract

Electrochemical techniques are attractive to realize compact devices with integrated components. Devices directed to clinical and biological applications have been developed. Efficient transport of solutions can be realized by capillary action and electrowetting. The valve including a gold electrode can be opened at a mixed potential when a solution in a controlling flow channel passes through a zinc part connected to the gold electrode. An autonomous bidirectional bubble-based pump can also be realized by changing the mixed potential. Furthermore, the mixed potential can be used to improve sensitivity of coulometric detection.

1. Introduction

Miniaturization of analytical devices or laboratory instruments has advanced remarkably over the last two decades in a trend of the micro total analysis system (μTAS) or Lab-on-a-Chip researches. We have developed analytical devices for clinical and biological applications particularly based on electrochemical principles. Although a major application of electrochemistry has been bio/chemical sensing, the range of applications covers other auxiliary functions such as the control of microfluidic transport and pH regulation. With these components integrated on a chip, smart user-friendly devices will be realized. Recent progress of the electrochemical devices and their applications to biochemical analyses will be presented.

2. Integrated Electrochemical Sensors

Major components of electrochemical devices are electrodes. For voltammetric, amperometric, and coulometric sensing, a three-electrode system is used. On the other hand, a pair of electrodes consisting of an ion-selective electrode and a reference electrode is used for potentiometric sensing of ions. Advantages of electrochemical devices are as follows [1]:

(1) Easy miniaturization by thin-film or thick-film microfabrication techniques
(2) Batch-fabrication
(3) Easy integration of same or different components including sensors, microfluidic components, and circuits for signal processing.

The sensing electrodes can also be made sensitive to biomolecules by immobilizing enzymes, antibodies, or DNAs on the surface of the electrode. Some of our representative examples include a protein chip [2], a device for the diagnosis of bovine subclinical mastitis [3], and a device to investigate the effect of signal molecules on ammonia removal of active sludge [4].

Other than these, a pH regulator has been fabricated using a nonstandard three-electrode system with a pH-sensitive reference electrode [5]. The device will be effective to maintain the pH of a solution in a small compartment or a flow channel. Although often neglected, a key component in these devices is the reference electrode. We have developed a thin-film Ag/AgCl structure covered with a protecting layer with AgCl layer grown from pinholes [6]. The structure improved the durability of the electrode significantly. Successful operation of our devices relies on the unique structure.

2. Autonomous Microfluidic Devices

Electrowetting-Based Valves

For efficient transport of solutions in microfabricated flow channels and control of the movement of solutions, capillary action and electrowetting are useful [7]. We have used flow channel structures consisting of a hydrophilic glass and hydrophobic poly(dimethylsiloxane) (PDMS). Wettability of gold surface can be changed by applying a potential with respect to an appropriate electrode. The contact angle change can be 60 degrees. The change can be enhanced by using micro- or nano-structures [8]. A simple valve can be created by forming a gold electrode in a constricted region of the flow channel. Transport of a solution to the valve is based on capillary action. The valve is opened by applying a potential to the gold electrode. The valve can be placed at branches in a flow channel network. Solutions can be injected into selected flow channels when necessary. The mechanism has already been used in some miniaturized analytical devices including a protein chip with a function of solution exchange [9] and a device to monitor ammonia metabolism of hepatocytes [10].

By using the valve electrode in a three-electrode system with a pH-sensitive reference electrode, a pH responsive valve can also be fabricated [11]. The valve can also be sensitive to glucose and urea. A pH filter that passes solutions of a limited pH range can be realized by using two valve electrodes.

Autonomous Switching of Electrowetting-Based Valves

By using a composite electrode consisting of gold and zinc and the mixed potential generated there, the electrowetting-based valve can be opened autonomously following the movement of solution in another flow channel [12]. Along with a flow channel with the valve, a controlling flow channel with a zinc electrode connected to the gold valve electrode is formed. The flow channels are connected with a liquid junction. When a solution is introduced into the main flow channel, the solution stops at the valve. However, when the second solution is introduced into the controlling flow channel and the solution wets the zinc electrode there, the valve opens at a mixed potential and the solution in the flow channel passes through the valve region. With this mechanism, a microfluidic timing circuit and logic circuits such as AND and OR gates can also be fabricated [13]. Solutions in reservoirs of some flow channels can start to flow sequentially or simultaneously accompanying the opening of the valves. The timing can be more elongated and/or more precise by using an array of flow channels for control [14].

Autonomous Bubble-Based Pump

The mixed potential used for switching of the valves can also be used to control the operation of a bubble-based bidirectional micropump. For this purpose, we have used production and shrinkage of hydrogen bubbles on a platinum black electrode. Although shrinkage of the bubbles is difficult with a simple planar electrode, the application of platinum black solved this problem [14]. A flow channel was formed to accommodate the pump and two other flow channels were formed to change the mixed potential to the negative and positive directions. The flow channels were connected with each other with a liquid junction. A composite electrode that connects solutions in the three flow channels was formed exposing platinum black, zinc, and silver in the corresponding flow channels, respectively. When solutions are introduced into the controlling flow channels and wet the metal parts sequentially, bubbles are produced or shrunk in the pump and the solution in the flow channel moves. Two pumps were operated sequentially by injecting necessary solutions one by one using the integrated microfluidic timing circuits [13].

As a novel style of microfluidics, plug-based microlfluidics is attracting attention. A plug refers to a fragment of a solution confined in a flow channel. We have fabricated a device for efficient handling of plugs separated by air [15]. By using a simple T-junction, procedures required in biochemical analyses, including measurement of solution volumes and sorting and merging of plugs, can be realized. Although the movement of the plugs currently reles on pressure driving, the bubble-based micropumps mentioned above may be integrated for programmed processing of solutions.

3. Sensitive Electrochemical Detection

For the determination of analytes in liquid plugs of the nL or pL order, coulometry is advantageous. In conventional coulometric analysis of components in a liquid plug, background charge increases monotonically as time elapses, whereas the charge originating from Faradaic current tends to saturate as the analyte depletes [16]. Therefore, by measuring the charge at a later time, sensitivity is improved. However, reduction of the lower detection limit needs more consideration. To solve this problem, the mixed potential can be used again. By converting a target analyte to silver deposited on an electrode in another flow channel and measuring the amount of silver by coulometry, sensitivity can be improved significantly and the lower detection limit can be reduced to 30 nM (3σ) for hydrogen peroxide, which is lower than that achieved using the same electrode by the conventional coulometry by one order of magnitude.

Depending on the sample solution. electroactive interferents may pose a problem. The influence can be eliminated by shifting the mixed potential to the negative side. To this end, copper was used instead of silver. In a research directed to the application of the diagnosis of bovine subclinical mastitis, detection sensitivity was improved by more than one order of magnitude for detection of superoxide secreted from neutrophils compared with the device mentioned earlier [17]. The detection was not affected by hydrogen peroxide in the solution produced from supeoxide.

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