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Field-portable Capillary Electrophoresis Instrument with Conductivity Detection

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Abstract. In this paper a novel capillary electrophoresis chip (CEC) is presented with integrated platinum electrodes and simplified conductivity detector. CEC is fabricated by the method of mechanical modification with probe on organic glass. Capillary electrophoresis chip can rapidly completed ion separation by simulation of concentration distribution and zone-broadening. Detection circuit is simple which can detect pA order current. This system has those advantages such as small volume, low power consumption and linearity, and well suit for field analysis.

1. Introduction
Micro-total analysis systems for biochemical analysis have seen an explosive growth over the past decade based on MEMS (Microelectromechanical System). Particularly attractive are micromachined capillary electrophoresis (CE) chips because of their fast and efficient capabilities [1]. In the development and optimization of CE, there are urgent needs for developing compatible detection modes. Miniaturization of detector is essential. Optical absorption detection and laser-induced fluorescence are, at present, the most widely used detection technique in CE because of their high sensitivity, while their drawbacks need very large and expensive external device, such as the relatively large laser and the photodetector system, which limit miniaturization. Electrochemical method on the chip format, including amperometry, conductometry, and potentiometry could provide a satisfying sensitivity. Furthermore, the electrodes for the detection can be directly integrated onto the chip through photolithographic and mechanical method and thus forms a compact chip system. Electrochemical methods compatible with miniaturization and full on-chip integration is highly desirable and become one of the hottest topics [2].

Amperometric detection is more selective and its application is limited to electro-active species. Applications of this method have mainly been for organic substances of biochemical interest but the detection of heavy metal cations and certain inorganic anions is also possible [3]. Potentiometry has proved to be a useful method for the detection of inorganic ions [4]. The majority of work on potentiometric detection in CE has focused on the use of ion-selective electrodes (ISEs) in the form of ion-selective microelectrodes or coatedwire ion-selective electrodes. The ISEs are difficult to construct and tend to be too fragile to be applicable to routine CE analysis. Compared to the amperometric and potentiometric detections, Conductivity detection is in principle a universal detection method for most modes of CE [5]. Conductivity detection (CD) is based on the change in bulk solution conductivity between two electrodes when an analyte band passes through the electrode gap. Any molecule can be detected if it causes a change in the conductivity between electrodes. The response is proportional to...
the concentration of the analyte ions. Since the signal is obtained from the bulk of the solution and not from the electrode surface and therefore not linked to a specific species. The sensitivity of conductivity techniques is not strongly dependent on the detector (electrode) size. As a result, there is little loss of sensitivity when the electrode size scales down, which should couple well with microelectrode and microchip CE.

Field analysis is becoming more widely used. It usually provides an instant result which allows the cause of any deviating results to be addressed without delay, samples do not have to be stored and preserved, and the methods are generally less expensive than traditional laboratory efforts [6]. Conductivity detection is an attractive candidate for the design of portable instrumentation for ion analysis because of the inherent simplicity of the method and universal detection method for electrophoresis. There have been a few reports involving portable CE/EC instrumentation. Hauser’s group has described the construction of a battery-powered, field-portable CE instrument capable of carrying out amperometric, potentiometric, and conductivity detection [7]. However, this approach, which employed a conventional fused-silica capillary for separation, was not intended for microchip-level application. In this paper we design a field-portable capillary electrophoresis chip with conductivity detection, which gets rid of striction of chemistry workstation. High-voltage power supply is designed for capillary electrophoresis based on piezoelectric ceramic transformer. Detecting circuit is very sample and suit for field analysis.

2. Building of the Microchip with integrated electrode
In this paper a novel capillary electrophoresis chip (CEC) is presented with integrated platinum electrodes and simplified conductivity detector. CEC is fabricated using organic glass. Separate channel is fabricated by the method of mechanical modification with probe, which had applied patent by the MEMS Center of HIT. The structure of probe is shown figure 1 for fabricating capillary chip. This method simplifies the process of techniques avoiding hydrofluoric acid etching glass and silicon. The width and depth of separation channel can be adjusted by changing the height of probe. The plastic microchip, shown in Figure 2, consisted of two sealed organic glass plates with a 60 mm long separation channel (between the run buffer reservoir and the outlet reservoir) and an 20 mm long injection channel (between the sample reservoir and the unused reservoir). The rectangular-shaped electrodes (0.2 mm × 10 mm) were fabricated from two 10μm thick platinum strips. The end side of the electrode was widened to 1 mm to facilitate the electrical connection. These electrodes were fixed to the top of organic glass using a common epoxy and tangency with the end of microchannel. Two electrode is aligned using optical microscope, which can effectively avoid bubble.

Figure 1. CEC with integrated electrode.
(B)buffer reservoir, (S) sample reservoir, (SW) sample waste reservoir, (W) waste reservoir, (E) detection electrode.

Figure 2. Three coordinate measuring machine.

Channel width is 100 μm, channel depth is 28μm. Reservoirs were made by a stainless hole punch for the access of the solutions. With the help of an optical microscope, the patterned electrode was manually aligned to the outlet of the separation channel with a space of 50 mm and an end-columnmode was adopted to minimize the influence of the electrophoretic driven voltage on the
detection. Separate channel is simulated by ANSYS to analysis the phenomenon of electroosmosis, zone-broadening and concentration distribution. Sample is the solution of A\(^+\) which concentration is 0.1mmol/L. From the figure 3, under an applied electric field, the time which A\(^+\) ions migrate from intersectional to detector cell is about 23s. When the sample zone arrives the detector cell, distance of 20\(\mu\)m from the end of microchannel, central concentration is about 0.045mmol/L. According intersectional sample plug comparing with the detector sample plug, zone-broadening is about 300%.

**Figure 3. Simulation of capillary electrophoresis chip with 100\(\mu\)m channel width.**

3. **Basic principle of conductivity detection**

In conductivity detection, the solution resistance \(R\) is calculated from its conductance \(G\), defined as \(G = \frac{1}{R}\) [8]. The value for \(G\) may also be determined from the ratio of the specific conductance \(\kappa\).

\[
G = \frac{\kappa}{A} \frac{L}{L}
\]

Where \(A\) and \(L\) are the cross-section and the length of the hydrophilic strip, respectively. Generally, the conductance \(L_{\text{BGD}}\) of an electrolyte solution containing an ionic species \(E\) mainly depends, besides the concentration \(c\) of the charge carriers and the degree of dissociation \(K\), on the limiting equivalent conductivity \(\lambda\).

\[
L_{\text{BGD}} = \frac{\lambda_{E^+} \cdot C_{E^+} \cdot \alpha_{E^+} + \lambda_{E^-} \cdot C_{E^-} \cdot \alpha_{E^-}}{10^3 K}
\]

The superscript \(C\) indicates the carrier electrolyte. The conductivity of the sample zone \(L_{\text{SMPL}}\) containing an anionic analyte ion \(A^-\) is determined by

\[
L_{\text{SMPL}} = \frac{\lambda_{E^+} \cdot C_{E^+} + \lambda_{E^-} \cdot C_{E^-} + \lambda_{A^-} \cdot C_{A^-}}{10^3 K}
\]

The signal which is finally detected arises from the conductivity difference between sample zone and BGE and is described by

\[
\Delta L = L_{\text{SMPL}} - L_{\text{BGD}} = \frac{C_{A^-} \cdot [\lambda_{E^+} \cdot (1 - K_A) - \lambda_{E^-} \cdot K_A + \lambda_{A^-} - 10^3 K]}{10^3 K}
\]

In this paper an DC voltage is applied to one of the electrodes, a current will be generated through the solution, and measured at the other electrode, which can completed sample detection.

4. **High-voltage power**

Capillary electrophoresis chip generally require external instrumentation for operation. There is on the other hand a high-voltage power supply, which is necessary to provide the driving electric fields for electrophoretic separation [9]. Piezoelectric transformers are widely adopted in high-voltage low-current on-board power systems. They can offer high transform ratio, being, at the same time, generally thinner, lighter and less expensive than magnetic transformers. In this paper piezoelectric transformers is used to generate the high-voltage power supply for microchip-based separation. This system using 24V storage battery generates 12V DC voltage through linear voltage regulation module.
as power supply for system. The TL494 is used for the control circuit of the PWM switching regulator. A PMMN quaternary piezoelectric ceramic transformer is driven by switching oscillator which is composed of pulse width modulation and MOSFET. To maximize energy conversion efficiency, piezoelectric transformers must be matched with the signal frequency input by TL494. A frequency control loop implemented by an error amplifier and a voltage-controlled oscillator (VCO) is commonly adopted. Generally, the voltage which input by piezoelectric transformers is only 3000V, so Power output stage adopts voltage multiplying rectifier to enhance output voltage. The high voltage output stage also provides feedback and monitoring signals which will be processed by the power supply control circuits. All of these components are typically insulated from ground level to prevent arc over. The output voltage by piezoelectric ceramic transformer is rectified and produces an output of 14KV DC for capillary electrophoresis. The ripple of output voltage changes less than 0.2%.

5. Detection circuit

Because the amperometric detection and conductivity detection detect the current signal, a universal circuitry for detector is described in this paper. The design of the detector circuitry is given in Figure 4.

The current-to-voltage converter is the first building block on the side of the detector system, converting the DC current passing through the measurement electrodes into corresponding DC voltage. For precise operation, a fast high-impedance op-amp OPA606 has to be used to limit errors due to leakage currents into the amplifier input. In order to reduce the noise interference the electrode is connected via a short, shielded coaxial cable to receive the electrophoretic current signal. Detector circuitry adopts AD620 (analog device) as key components to amplify the DC voltage signal. The switch allows to select different amplification to electrophoretic current. The AD620 output voltage is developed with respect to the potential on the reference terminal, it can solve many grounding problems by simply tying the REF pin to the appropriate “local ground.” MAX294 is employed to extract the near-DC portion of the signal while removing the radio-frequency part. This stage forms an 8th-order low pass elliptic filter with 33 Hz cut-off frequency. An external capacitor C3 is used to generate a clock using the internal oscillator and determines the cut-off frequency. In this design, selecting 33Hz cut-off frequency is to attenuate 50Hz interference from the environment and improve signal to noise ratio. Through simulation to resistance between the electrodes, this electronic circuitry can detect pA order current. The result of simulation is shown figure 6. In figure 6a electrophoretic current signal is replaced by a sinusoidal signal, 10nA with 1 kHz frequency. Signal B is output signal by AD620 with 2.11V swing. Signal C is low pass filter signal with 1.2μV swing.

The baseline is compensated before analog-to-digital conversion. Data acquisition is accomplished with a HY1232 ADC-12 analog-to-digital converter. The analog-to-digital converter is connected via an RS-232 serial port to a PC. From figure 6, electrophoretic current can be detected using this simple detection circuit. Note that The detection circuit was placed in a shielding box to protect the
electronics from external electric fields. One side of the box was open; this side was placed as close as possible to the sensing electrodes (on the chip), so that the box also acts as a shield for the electrodes.

Figure 5. Signal simulation of detection circuitry.

6. Conclusion
The capillary electrophoresis chip fabricated by the method of mechanical modification has several advantages such as easy fabrication and low cost. The whole system has small volume and low power consumption which can well suit for field analysis. Our next step is on-chip integration and realize veritable lab on chip.

References