A Closed-loop, Non-linear, Miniaturised Capillary Electrophoresis System Enabled by Zeta-potential Modification of Electroosmotic Flow

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Problem Outline

Miniaturised capillary electrophoresis (CE) systems tend to have short channel lengths which makes it difficult to achieve good separation of complex mixtures of ions. In CE, ionic species migrate along a capillary (or channel) at a migration velocity which is dependant on their electrophoretic mobility and the electroosmotic flow (EOF).

$$\textbf{Migration Velocity} = (\text{Electrophoretic Mobility} + \text{EOF Mobility}) \times \textbf{E-field}$$

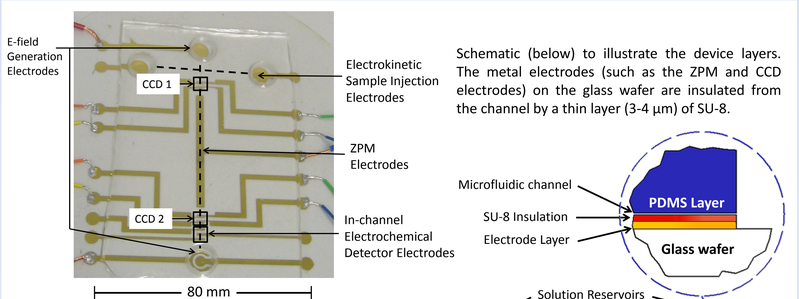
Ion	Mobility (m^2/Vs)[1]
Al^{3+}	6.2725 x 10^{-8}
Cr^{3+}	6.8996 x 10^{-8}
Cu^{2+}	5.5188 x 10^{-8}
Fe^{2+}	5.5575 x 10^{-8}
Fe^{3+}	7.0029 x 10^{-8}
Mn^{2+}	5.5034 x 10^{-8}
Ni^{2+}	5.1092 x 10^{-8}

[1] Values calculated with data taken from: Petr Vanýsek, *"Ionic Conductivity and Diffusion at Infinite Dilution"* – **CRC: Handbook of Chemistry and Physics (88th Edition)**, 2007-2008

An application area we are interested in is the identification of corrosion by-products. As shown in the table on the left, the mobilities of key metal ions are very similar making their separation in a conventional laboratory CE system difficult, and challenging in a miniaturised system. To address this issue we have developed a novel separation technique where we cycle the ions up and down the channel by periodically changing the direction of the EOF, thus realising a greater effective channel length for separation. Control of the EOF is achieved by the modification of the channel wall zeta-potential by placing an electrode close to the channel wall - the zeta-potential modification (ZPM) electrode.

Microfluidic Device

The device was fabricated in our state-of-the-art cleanroom facility using photolithographic techniques. Gold electrodes are patterned on a glass wafer; the microfluidic channels is formed in a layer of PDMS which is reversibly sealed to a layer of SU-8 that selectively insulates some of the underlying electrodes. A closed-loop system is enabled by the inclusion of contactless conductivity detectors (CCDs) at both ends of the channel which indicate when the ZPM voltage controlling the EOF needs to be switched.



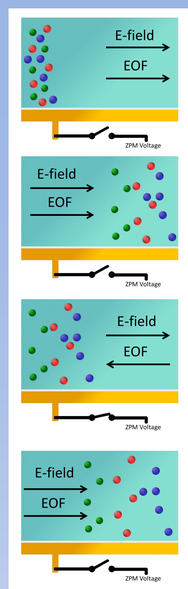
Photograph of microfluidic device (above); the channel is highlighted with the dashed line. The channel width, depth and length are 200 µm, 35 µm and 80 mm respectively.

Schematic (below) to illustrate the device layers. The metal electrodes (such as the ZPM and CCD electrodes) on the glass wafer are insulated from the channel by a thin layer (3-4 µm) of SU-8.

Theory of Operation

The figure on the right shows the normal mode of operation in which a sample is injected at the start of the channel and subjected to an E-field. After some time, the ions in the sample reach the end of the channel and have become slightly separated. At this point a potential is applied to the ZPM electrode to reverse the EOF. This will move all the ions in the sample back to the start of the channel; separation continues during this process. Once the ions reach the start of the channel, the potential applied to ZPM electrode is switched off and the sample migrates along the channel once again, still separating. This process is repeated until the desired separation is achieved.

CCDs located at each end of the channel inform when the sample arrives at the channel ends, enabling a microprocessor based system to decide when to switch the ZPM voltage. This creates a novel robust closed-loop control system which is insensitive to sample migration time.



Step 1: Start
Sample of mixed ions injected into channel.

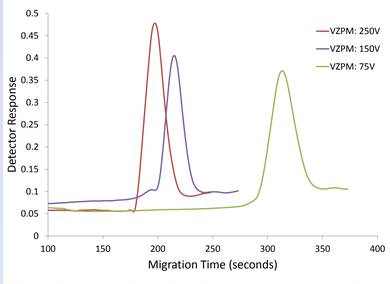
Step 2: Sample Approaches End of Channel
Sample starts to separate but many ions overlap.

Step 3: Voltage Applied to ZPM Electrode
EOF reversed sending ions back to start of channel whilst maintaining their separation.

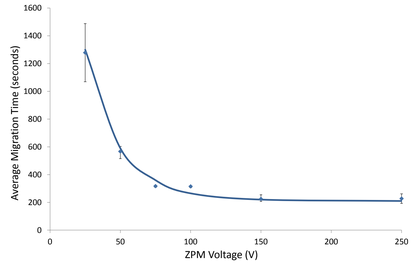
Step 4: Sample Approaches End of Channel Again
Separation of sample is improved compared to that at the end of step 2.
If further separation is required then the process from step 3 can be repeated.

Extension to Technique
Greater separation resolution can be obtained by taking this technique to the extreme, where the zeta-potential is modified such that the EOF is equal and opposite to the electrophoretic velocity of the slowest species of interest. Under this condition maximum separation resolution with respect to the slowest species is obtained. However, this requires very precise control of the EOF. A robust solution would be to use a method which modifies the EOF to give a long sample transit time as it travels along the channel.

Experimental Results



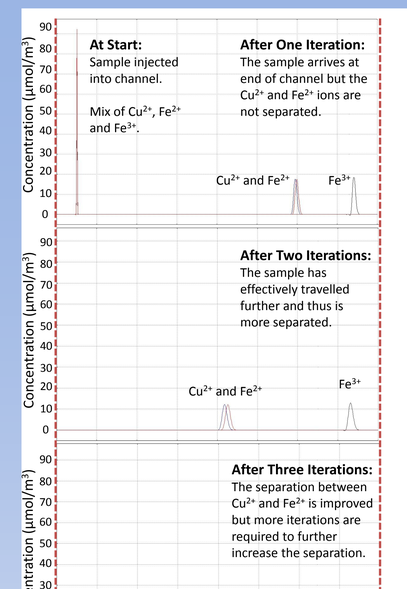
The effect on migration time caused by varying the ZPM voltage is illustrated in the graph above where a fluorescein dye was used as a sample with a phosphate buffer (pH 7.2). A separation voltage of 300 V was applied over the 80 mm long channel. With negative ZPM voltages (not shown) we were able to visually confirm reversal of the EOF.



The figure above shows the effect of varying the ZPM voltage on the migration time of a fluorescein dye over a voltage range from 25 V to 250 V. At lower voltages it takes longer for the sample to get to the end of the channel, therefore the EOF can be significantly reduced. At high voltages it can be seen that the EOF is increased, up to a limiting level.

COMSOL Simulation Results

To illustrate the benefit of bi-directional transit along the channel length, a model was developed using COMSOL Multiphysics (v. 4.1). The results presented from this simulation, shown in the figure on the right, assume zero EOF during sample transit toward the end of the channel. At the start a sample mixture of three ions is injected, assuming a Gaussian distribution. After the first iteration the Fe^{3+} ions are separated from the Cu^{2+} and Fe^{2+} ions. This separation improves on each further iteration. After the third iteration, the Cu^{2+} and Fe^{2+} peaks start to become noticeably separated. These simulation results indicate that further iterations will lead to a greater separation of Cu^{2+} ions from Fe^{2+} ions.



Simulation results from COMSOL showing the separation of three metal ions increasing for every repeated transit along the channel length.

Conclusions and Future Work

This work has discussed a novel miniaturised CE system for ion separation using EOF modification to effectively increase the channel length. The concept of modification of EOF by control of zeta-potential has been experimentally verified, and the microfluidic device has been fabricated. The use of contactless conductivity detectors at either end of the channel along with associated microprocessor circuitry creates a closed-loop control system. The use of a closed-loop control system means that it:

- has application in a variety of different scenarios;
- is not restricted by the range of mobilities within a sample;
- requires minimal sample preparation;
- is insensitive to environmental variations;
- does not require calibration;
- has the potential to be an important component in autonomous field measurement systems.

Future work will involve refining the device in order to progress towards a fully integrated system.

Project Dissemination

Results from the project have been presented at 3 national conferences, 5 international conferences and published in 12 peer reviewed proceedings and journals. For more information visit the project website: http://www.mdfshm.ecs.soton.ac.uk

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