

# Contactless Conductivity Detection in Ceramic Technology for On-Chip Electrophoresis

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A capacitively coupled contactless conductivity detector produced in Low Temperature Co-fired Ceramic (LTCC) technology for microchip capillary electrophoresis (CE) is reported in this work. Electrodes located outside the measurement channel are used to sense impedance variations caused by conductive ions. The application of LTCC in combination with contactless conductivity detection is very promising because of its high dielectric constant compared to glass or plastics. This enhances the coupling of the excitation signal into the microfluidic channel and thus results in increased detection sensitivities. Successful separations of three inorganic ions confirm the feasibility of LTCC as a material for on-chip CE when used with contactless conductivity detection.

## Introduction

Capacitively coupled contactless conductivity detection is a versatile detection method for bioanalytical applications and has been widely used e.g. for on-chip capillary electrophoresis (CE) devices [1] – [5]. Small dimensions of both the detector and read-out electronics make it an attractive alternative to fluorescence- or optical absorbance-based systems since conductive compounds such as inorganic ions can be sensed without prior chemical modification. The measurement electrodes are located outside the fluidic channel, avoiding direct contact with the buffer solution. Bubble formation impeding the electrophoretic separation process does therefore not occur, increasing the life time of the device.

Low Temperature Co-fired Ceramics (LTCC) as a high-performance material for the fabrication of microfluidic devices is attaining increased attention [6] – [7]. It is based on a mixture of ceramics and a certain proportion of glass which affects physical properties such as material permittivity. In its pre-fired state, LTCC is a flexible tape that can be easily structured using stamping, cutting, embossing or laser micromachining techniques. Once fired, electroosmotic flow properties of LTCC are similar to those of glass, making this material interesting for capillary electrophoresis (CE) chips.

Thick-film pastes made from gold, silver or copper can be used to print conducting paths onto the substrate. This enables the placement of electronic circuit components in surface mount technology directly on the ceramics, minimizing the influence of noise.

LTCC-tapes are available with very high values of material permittivity as compared to plastics or glass. This enhances the measurement signal coupling into the microfluidic channel and leads to higher detection sensitivities.

This paper reports on the fabrication of a CE module with an integrated contactless conductivity detector build up entirely in LTCC technology. Successful CE separations of three inorganic ions were carried out in less than 1 minute.

## Device Description

The CE module is built up by five layers of LTCC tapes (Heratape 707). Each of these layers has a thickness of 138  $\mu\text{m}$  in the unfired state. Microchannels, alignment and via holes as well as liquid inlet and outlet ports were micromachined with a diode pumped NdYAG laser. Figure 1 depicts an exploded view (a) and a cross-sectional photograph (b) of the LTCC-CE module. The separation channel embedded in the device has a width of 100  $\mu\text{m}$  and a total length of 125 mm. For testing purposes a dummy channel is integrated on the same device. It was not used for the experiments.

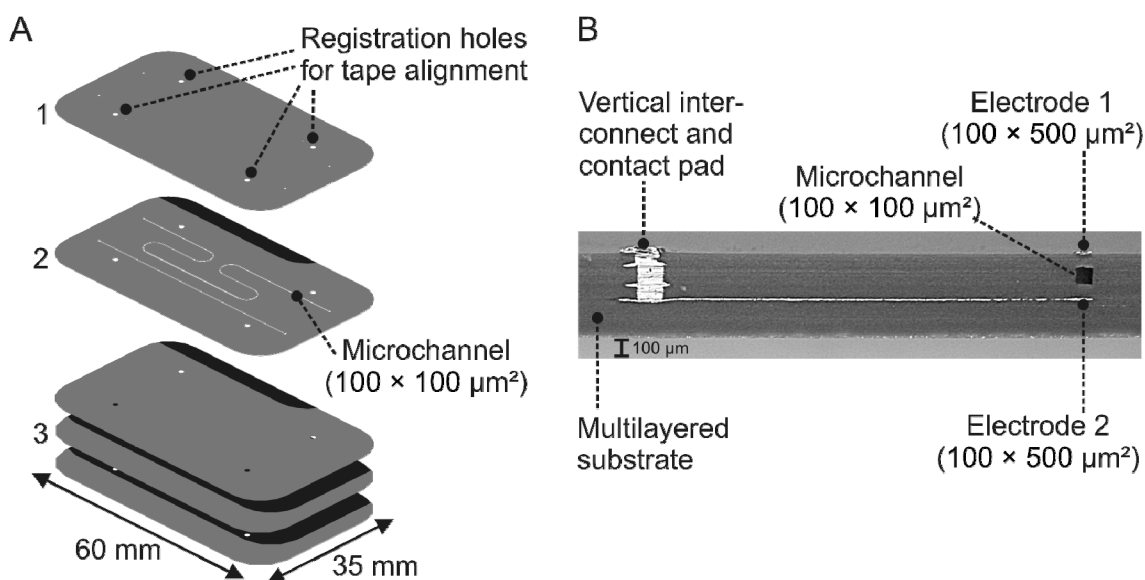


Fig. 1: Exploded view (a) and cross-sectional photograph (b) of the fabricated CE-module. (1) cover layer with electrode contact pads, fluid inlet/outlet ports and registering holes; (2) middle layer comprising separation channels; (3) three bottom layers for mechanical support.

The detection area encompasses two electrodes facing each other, located at opposite sides of the device and separated from the microchannel by a single ceramic layer. Electrodes and conductor metallization were realized by screen printing a silver conductor paste (Heraeus TC 7304A). Via holes filling was conducted by a stencil printing process using the silver paste Heraeus TC 7601. The via provides the vertical electrical connection between the buried bottom electrode and the contact pads on the top layer of the device (Fig. 1 (b)). It was placed in a distance of 3 mm from the channel in order to minimize stray capacitances. The metalized tapes were collated to a stack which was exposed to a lamination process in an isostatic press at a pressure of 100 bar and a temperature of 70  $^{\circ}\text{C}$  for 3 minutes. Firing of the laminated stack was conducted in a conventional belt furnace with a peak temperature of 850  $^{\circ}\text{C}$  and a total cycle time of 90 minutes where the dwell time at peak temperature was 15 minutes. Details and dimensions of the detector are shown in Fig. 1 (b). Inlet and outlet reservoirs are formed by gluing silicon rings on the inlet and outlet ports, which enables fluid-tight filling of the channel using syringes.

## Experimental

### Fluid Handling and Measurement Setup

Sample and buffer solutions were degassed for 5 minutes and filtered through 0.2  $\mu\text{m}$  syringe filters to eliminate gas bubbles and particles. Micro-dispensing needles and syringes were used to fill the sample into the inlet reservoirs. Samples were electrokinetically injected into the microchannel. Between runs the microchannel was rinsed with 10 channel-volumes of run buffer to ensure reproducibility of the experiments. Platinum wires were used as high-voltage electrodes which were positioned in the inlet and outlet ports.

The optimum measurement frequency where the detector shows maximum response depends on the value of the liquid conductivity. In the case of the buffer used in the experiments (10 mmol/l MES/Histidine), maximum sensitivity was found at a frequency of 2.25 MHz. A current-to-voltage converter placed directly on the CE module and connected to a lock-in amplifier (Stanford Research Systems, model SR844) was used to reduce the influence of parasitic stray capacitances on the small changes of the output signal. The data was recorded using a laptop connected to the lock-in amplifier via the IEEE-488 bus.

### Results and Discussion

Successful CE separations of three different inorganic ions are depicted in Fig. 2 (a). The peak heights decrease in the order  $\text{K}^+ > \text{Na}^+ > \text{Li}^+$ . This is related to the different ionic conductivities; however, it is also a result of the applied electrokinetic injection procedure: Ions of higher electrophoretic mobility get loaded into the channel to a greater extent than slower ones.

The linearity of the detector is demonstrated in Fig. 2 (b). From the electropherograms the peak area of the separated samples containing potassium at concentrations from 0.2 to 2 mmol/l was extracted. The correlation coefficient of the linear fit is 99.7 %, which confirms that the measurement signal is a linear function of the liquid conductivity.

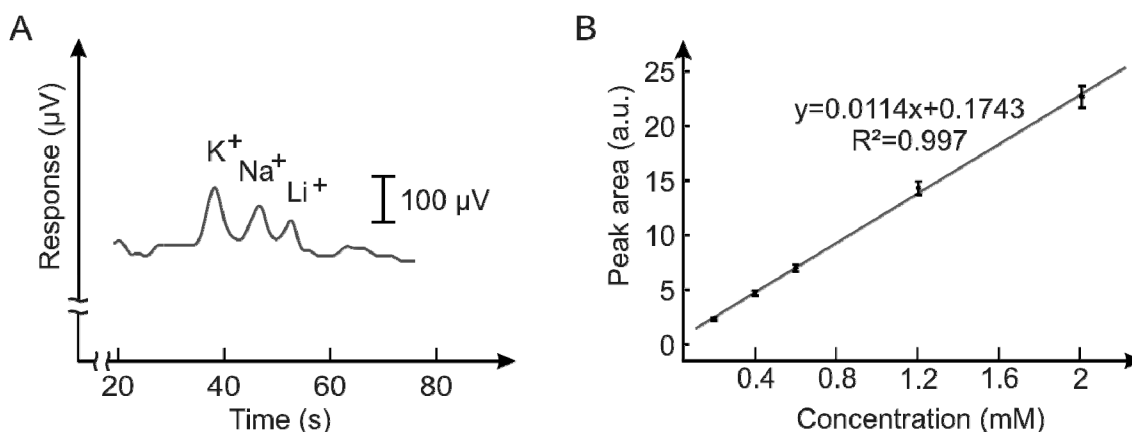


Fig. 2: Electropherograms of a mixture of inorganic cations at concentrations of 200  $\mu\text{mol/l}$  (a) and linear fit of potassium samples at different concentrations (b). Separation parameters: 10 mmol/l MES/Histidine at pH 5.8; separation field strength  $300 \text{ Vcm}^{-1}$ ; injection time 10 s at  $50 \text{ Vcm}^{-1}$ ; effective separation length 11.5 cm.

## Conclusion

In this work the integration of a contactless conductivity detector on a miniaturized CE-module fully assembled in LTCC-technology is demonstrated. The successful separations of inorganic ions are promising for the adoption of LTCC as a novel and versatile low-cost microchip material for miniaturized analytical devices.

The significant advantage of LTCC is its availability with high values of electric permittivity. Currently tapes with dielectric constants of 7 are used. It is planned to use tapes with values up to 200 to further improve detection sensitivity. In future the introduction of a double-T injector for volume-defined sample filling will be investigated to further improve the separation efficiency.

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## References

- [1] F. Laugere, G.W. Lubking, A. Berthold, J. Bastemeijer, M.J. Vellekoop: "Downscaling aspects of a conductivity detector for application in on-chip capillary electrophoresis", *Sensors and Actuators A*, **92**, 2001, pp. 109-114.
- [2] F. Laugere, R.M. Guijt, J. Bastemeijer, G. van der Steen, A. Berthold, E. Baltussen, P. Sarro, G.W.K. van Dedem, M.J. Vellekoop, A. Bossche: "On-Chip Contactless Four-Electrode Conductivity Detection for Capillary Electrophoresis Devices", *Anal. Chem.*, **75**, 2003, pp. 306-312.
- [3] J. Lichtenberg, N.F. de Rooij, E. Verpoorte: "A microchip electrophoresis system with integrated in-plane electrodes for contactless conductivity detection", *Electrophoresis*, **23**, 2002, pp. 3769-3780.
- [4] M. Pumera, J. Wang, F. Opekar, I. Jelinek, J. Feldman, H. Löwe, S. Hardt: "Contactless Conductivity Detector for Microchip Capillary Electrophoresis", *Anal. Chem.*, **74**, 2002, pp. 1968-1971.
- [5] J. Tanyanyiwa, P.C. Hauser: "High-Voltage Capacitively Coupled Contactless Conductivity Detection for Microchip Capillary Electrophoresis", *Anal. Chem.*, **74**, 2002, pp. 6378-6382.
- [6] M. Goldbach, H. Axthelm, M. Keusgen: "LTCC-based microchips for the electrochemical detection of phenolic compounds", *Sensors and Actuators B*, **120**, 2006, pp. 346-351.
- [7] C.S. Henry, M. Zhong, S.M. Lunte, M. Kim, H. Bau, J.J. Santiago: "Ceramic microchips for capillary electrophoresis-electrochemistry", *Anal. Commun.*, **36**, 1999, pp. 305-307.