Review Article

Inexpensive and versatile measurement tools using purpose-made capillary electrophoresis devices coupled with contactless conductivity detection: A view from the case study in Vietnam

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ABSTRACT

In this study, the development of purpose-made capillary electrophoresis (CE) devices with capacitively coupled contactless conductivity detection (C^{4}D) as a simple and inexpensive measurement tool and its applications for water monitoring, food control and pharmaceutical analyses in Vietnam are reviewed. The combination of CE and C^{4}D, both relying on the control of the movements of ions in an electrical field, can be realizable even with a modest financial budget and limited experimental skills and expertise. Different CE-C^{4}D configurations designed and developed for various applications were highlighted. Some perspectives for a wider recognition of its potential in Vietnam and for rendering this technique as an analytical tool for the population are discussed.

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1. Introduction

Capillary electrophoresis (CE), with its advantageous properties of covering a wide range of accessible analytes, high separation efficiency, short analysis time, low power requirements, limited consumption of chemicals, ease of installation, operation and maintenance, is a particularly interesting candidate for analytical instrumentation. It is inherently much simpler than chromatography for ion separations, as it is achieved by the application of a high voltage and does not require a stationary phase. The separation efficiency is inherently very good, and high plate numbers according to the Van Deemter theory are obtained even with a simple apparatus. The employment of a high voltage as a driving force allows elimination of the use of expensive, complicated and sometimes irreplaceable high-pressure components as in high

pressure liquid chromatography (HPLC). However, the sensitivity of the popularly used optical detection in CE of at least 100 times worse than that of the standard UV absorbance detection in HPLC (mainly due to a limited optical path length across the capillary of 50 μm i.d. in general), has rendered it less attractive than the pressure-driven counterpart. In addition, a too small detection volume in CE leads to difficulties in manipulation with any on-column or post-column detection techniques.

The marriage between CE and contactless conductivity detection, whose creation of the detection signal is based on the same property as the CE separation, on the other hand, has offered many advantages over its standard coupling with UV detection. The ions are simply manipulated with voltages applied through electrodes. In principle, any charged species which can be separated in electrophoresis can also be detected with a conductivity detector. This feature is important, as UV absorption is not suitable for most inorganic ions nor is sensitive detection possible for organic ions lacking a strong chromophore. The contactless property allows a measurement without any contact between the electrodes and the solution inside the capillary. The launch of its new configuration in 1998 [1,2], termed capacitively coupled contactless conductivity
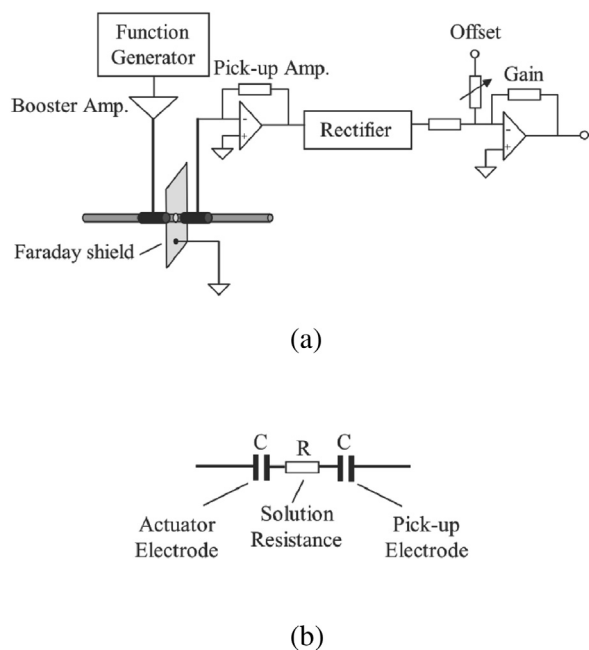
Fig. 1. Schematic drawing of C^{4}D in an axial arrangement. (a) Schematic drawing of the electronic circuitry; (b) Simplified circuitry.

detection (C^{4}D) and based on tubular electrodes arranged side by side along the axis of the capillary has led to a full adaptation of this approach for narrow separation channels in CE. With C^{4}D, the difference between the conductivities of the analytes from that of the background electrolyte (BGE) can be measured without having the electrodes in contact with the sample. Commercial detectors have been available for some time [3,4], but the in-house construction is possible with limited mechanical and electronic facilities [5–7]. In fact, due to the relative simplicity of CE, it is also feasible to build entire instruments relatively easily, which is not possible these days for most methods. Three additional positive features of CE-C^{4}D that make it even more suitable for versatile and screening analytical purposes are portability for mobile deployment [8–11], customer-oriented CE configuration for adaptation to different financial and expertise situations [12,13], multi-channel setup for concurrent determination of various analytes having different characteristics [14–16]. The employment of CE-C^{4}D to solve various analytical challenges, notably in environmental monitoring, food control, pharmaceutical and clinical analysis, has been reviewed for several times [17–25]. Both instrument and application aspects of CE-C^{4}D were addressed exhaustively in these reviews. Instrumental optimization was also proposed therein for performance improvement,
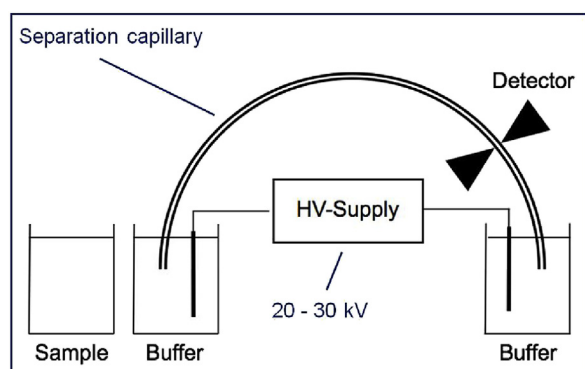

Fig. 2. Arrangement of a basic CE setup.

for example the employment of high excitation voltage to boost the sensitivity of C^{4}D, or the removal of some electronic components to minimize power consumption so that the whole system can be operated for several hours with the battery-powered mode. Fundamentals of CE-C^{4}D can also be found in these reviews.

Herein we highlight the development of in-house-made CE-C^{4}D devices towards the purpose of analytical instrumentation for non-expert users. This paper can be considered as the view of the authors towards the potential and applicability of CE-C^{4}D as inexpensive and versatile measurement tools based on the works carried out in Vietnam over 5 years. These works include i) instrument design and development (implemented together with the group of Prof. Peter Hauser − University of Basel, Switzerland), ii) instrument deployment in Vietnam and subsequent instrumental optimizations for adaptation to the operating conditions in Vietnam and iii) methodology developments using the developed instruments. The applications of in-house made CE-C^{4}D instruments notably for water monitoring, food control and pharmaceutical analysis with the case study in Vietnam are highlighted. The potential of compact CE-C^{4}D as an analytical tool for the people is also discussed.

2. Instrumentation development

2.1. Capacitively coupled contactless conductivity detection

The basic arrangement of an axial C^{4}D, which was first introduced independently by Zemann et al. [1] and by da Silva and do
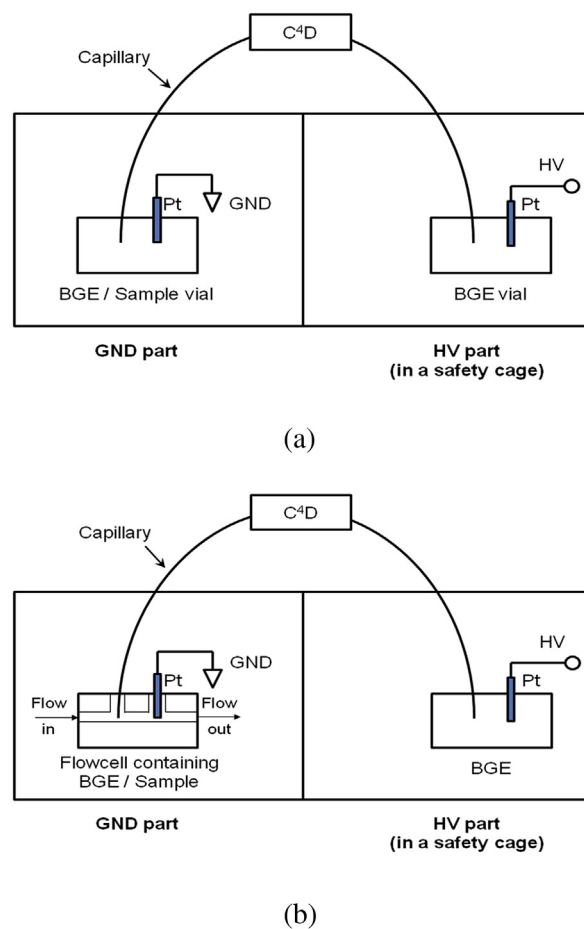

Fig. 3. Schematic drawings of a CE arrangement with a) manual injection mode; b) automated injection mode with extension with a fluidic module. HV: high voltage; GND: ground; BGE: background electrolyte; Pt: Platinum electrode.

Table 1
A tentative list of components needed for construction of a CE system.

Component	Functionality	Supplier(s)[a]	Remark
High voltage generation module	To provide a high electrical field required for electrophoretic separation	Spellman, EMCO, eDAQ, LabSmith	Spellman products are the most frequently used ones
2-gate or 3-gate valves	For stopping or diverting the fluidic flow	NResearch, Lee company, Fluigent, Elvesys, Takasago	A special electronic board is required for NResearch products to prevent overheating during operation.
Stepper motor-driven syringe	For precise delivering/manipulation of fluidic flows	Tecan, Labsmith	Required for CE extended with SIA operation
Capillaries	The separation channel in CE	Polymicro Technologies, UpChurch	Bare fused silica capillaries are most frequently used. PEEK capillaries or coated silica capillaries with inert surfaces can be used as well but are more expensive
Electrodes	To provide high voltage and ground electrodes needed to create a high electrical field along the capillary	Advent	Platinum electrodes are preferably used. But inert steel electrodes can also be a more economic alternative.
Pumps	To aspire and deliver the sample plug	KNF, Takasago	The peristaltic pumps from Takasago provide a more smooth and slow flow.

[a] Only the suppliers whose products were tested by the authors were listed in this table.
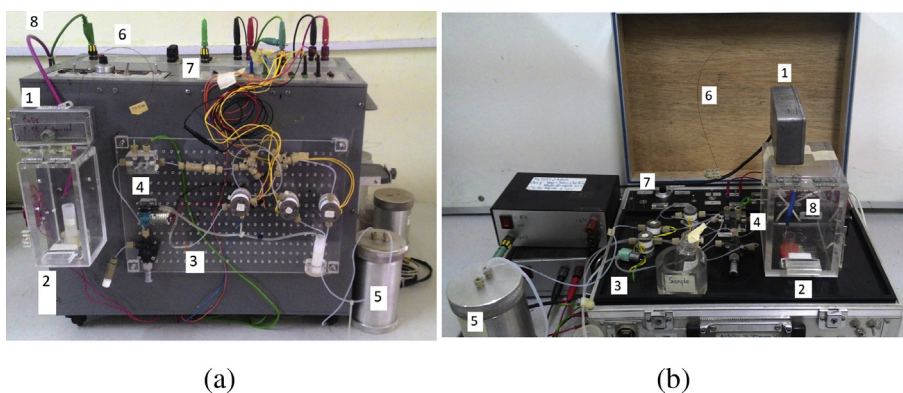

(a)   (b)

Fig. 4. Different in-house made portable single-channel CE instruments deployed in Vietnam. a) Semi-automated CE; b) Fully automated CE. 1) C[4]D; 2) Safety cage; 3) Grounded manifold, including valves, pumps, flowcell interface and flow splitter; 4) Flowcell interface accommodating the ground electrode and one end of the capillary; 5) Gas-pressurized container for delivery of the background electrolyte; 6) Fused silica capillary; 7) Electronic board and 220VAC-to-12VDC inverter and 8) High voltage cable.

Lago [2] in 1998, and is still widely used nowadays, is illustrated in Fig. 1. Two electrodes of a few millimeter lengths, namely actuator and pickup electrodes, made from conductive silver varnish or short metallic tubes, which are separated by a gap of typically 1 mm, are placed side by side around the capillary. Cells can be readily made for capillaries of the standard 365 μm outer diameter.

The two external electrodes form two capacitors (C) with the solution inside the capillary. The equivalent circuitry of a conventional contactless conductivity cell, as shown in Fig. 1b, can be represented by an arrangement of two double layer capacitances C connected to the solution resistance R. An AC excitation voltage with a high frequency of several hundred kHz is applied at the actuator electrode. The current (I) passing through such a circuitry is dependent on the applied alternative voltage (V) and frequency (f) as expressed by the following equation:

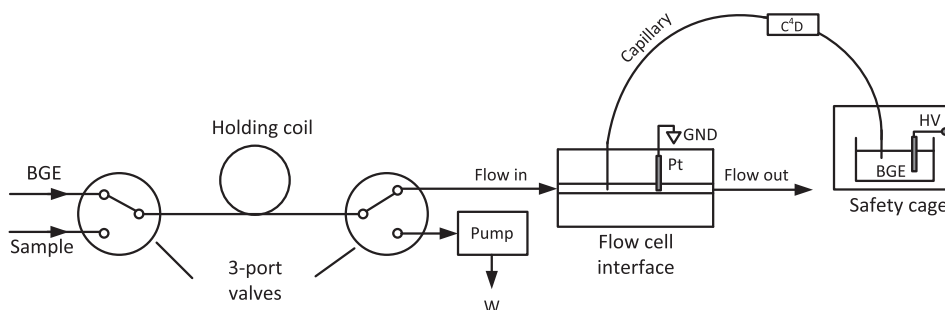$$I = \frac{V}{\sqrt{R^2 + \left(\frac{1}{2\pi f C}\right)^2}}$$

Fig. 5. Diagram of the fluidic connections of the in-house-made gas-based single-channel CE instrument. Pt: platinum electrode; BGE: background electrolyte; W: waste. The flowcell interface is grounded, while the voltage is applied from the detector end.
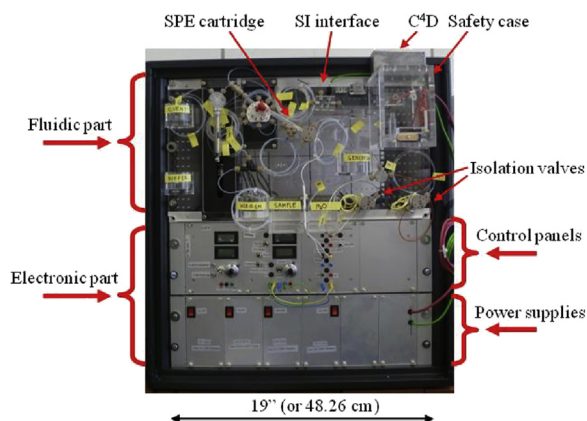
Fig. 6. The automated SIA-CE-C^{4}D system for unattended monitoring operation.

The AC current signal, which is picked up at the second electrode, first has to be transformed into a voltage with a feedback resistor and then rectified to obtain a recordable DC signal that varies with conductivity changes. Typically, the background signal should be suppressed electronically ("offset" or "zeroed") before amplifying the measured signal to obtain the best resolution of the analogue-to-digital converter. For more details on fundamental aspects of C^{4}D consult the papers by Hauser and Kubáň [23,25—27]. The design of C^{4}D was then downscaled into an all-in-one-cell configuration where the excitation and signal pickup modules were integrated into one single cell [6,28]. High excitation voltages of up to 200 V created with an integrated micro-transformer were subsequently used in this miniaturized C^{4}D version in order to significantly improve the signal to noise ratios [7,11]. With unprecedented simplicity in terms of geometry and electronic circuitry, the construction of a C^{4}D cell is relatively easy and therefore can be done in-house. Together with the introduction of commercially available C^{4}D units, this contributes to the extreme popularity of C^{4}D as a robust detection technique for CE. All recent applications in Vietnam carried out with CE-C^{4}D have been implemented with this high-voltage miniaturized version of C^{4}D.

2.2. Capillary electrophoresis instrumentation

Capillary electrophoresis is a separation technique based on the movement of charged species in a microchannel under a high

electrical field. Illustration of a basic CE setup is shown in Fig. 2. This setup was used for the first purpose-made portable CE instrument that was deployed in Vietnam [29]. The core components of the system include i) a high voltage generator module, ii) a high voltage electrode and a ground (GND) one, iii) a capillary and iv) the vials containing either the samples or background electrolytes (BGEs). As no high-pressure components are required, a CE system can be assembled relatively easily in a lab without the need for special infrastructure. This feature renders CE especially suitable for Vietnam in particular and developing countries in general where limited funding and little expertise are available. Depending on the requirements of portability and/or automation, different fluidic components, *i.e.* valves, pumps, flow-cell interfaces *etc.* can be integrated into the basic CE setup. A schematic drawing of a CE arrangement extended with a fluidic module is illustrated in Fig. 3. Except for manual CE where sample injection and capillary flushing can be realised at the high voltage side, fluidic manipulation in other more advanced CE systems is normally carried out at the ground end in order to dissociate the low-voltage powered components (e.g. valves, pumps etc.) from the high voltage used to create the electrical field for electrophoresis. As the construction of a CE system is relatively easy, different configurations *i.e.* portable or bench-top setups with manual, semi-automated or automated manipulation, single or multiple operation channel(s) can be made without recourse to a complex and costly electronic workshop. A list of components that are needed for construction of a CE system is shown in Table 1. Note that the list is given in order to offer the readers an overview of a purpose-made CE arrangement. It therefore should be considered tentative and subjective rather than comprehensive. The employment of some components in the list is optional and can be upgraded/replaced depending on the desired functionality of the system.

2.2.1. Portable CE

The use of portable instrumentation for field analysis is of interest due to rapid availability of results, elimination of complications with sample storage and transport, and better cost effectiveness than conventional bench-top analytical systems. CE-C^{4}D, with the aforementioned advantages, is a particularly interesting candidate for portable analytical instrumentation. The first portable CE instrument coupled with C^{4}D was reported by Hauser et al., in 2007 [29]. In this version, all operations including sample injection, capillary flushing, vial changing and high voltage triggering were done manually by an operator. Mai et al. then gave an account of upgrading this manual operation into semi-automated
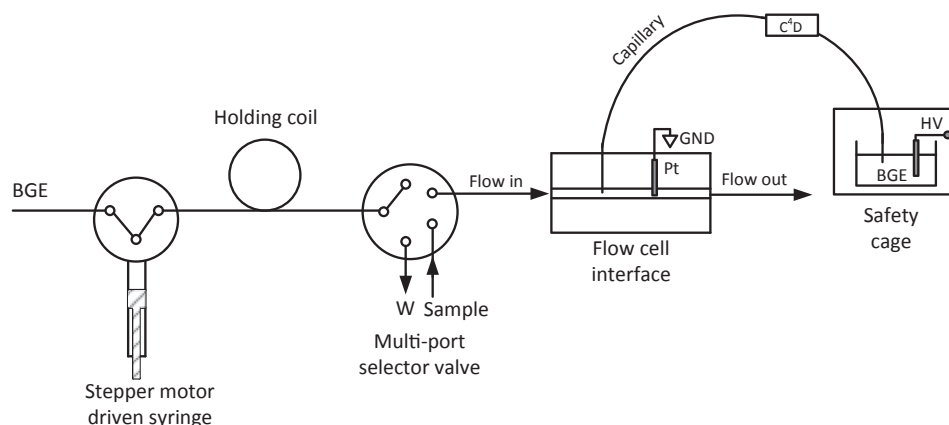

Fig. 7. Diagram of the fluidic connections of the in-house-made SIA-CE instrument. Pt: platinum electrode; BGE: background electrolyte; W: waste. The flowcell interface is grounded, while the voltage is applied from the detector end.
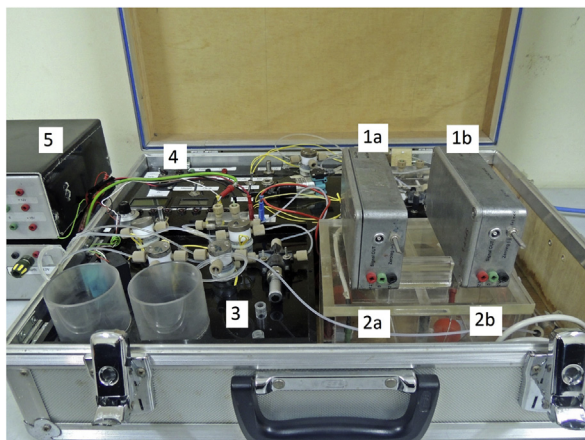
Fig. 8. The in-house-made portable dual-channel CE system using two individual BGEs. 1a and 1b) C^4Ds; 2a and 2b) High voltage chambers that contain high voltage cables and electrodes; 3) Grounded manifold, including valves, pumps, flowcell interfaces and flow splitters; 4) Electronic board; 5) Power supply.

[11,13] and fully automated versions with the computer control [10,15,30–32]. Photos of two portable CE systems that are in use in Vietnam are illustrated in Fig. 4. Though the arrangements are different, these portable single-channel CE instruments share the same components including a safety cage, a grounded manifold, a flowcell interface accommodating the ground electrode and one end of the capillary, a gas-pressurized container for delivery of the BGE, an electronic board and a 220VAC-to-12VDC inverter. The operation principle of these gas-based instruments is illustrated with the schematic drawing in Fig. 5. Gas pressurization and miniature stop valves were employed for fluidic manipulation instead of motor driven syringe pumps and rotary valves in order to reduce the construction cost and minimize the system sizes and power consumption. The BGE is propulsed through the system by pressurizing a reservoir containing the BGE with compressed air. The pressure can be regulated with a regulating valve and monitored with a small gauge. For the fully automated format, the sample is loaded into a sample loop by using a small pump to aspirate the sample through a thin tube and subsequently moved to the flowcell interface that accommodates one end of the capillary and the ground electrode. A fraction of the sample is pushed into the capillary for hydrodynamic injection by applying a back-pressure for a determined period of time. For the semi-automated version, sample injection is done manually from the high-voltage end via the siphoning effect. In both automated and semi-automated configurations, flushing of the flowcell interface and the manifold ahead of the interface, as well as of the capillary is implemented by opening or blocking the outlet of the interface during the propulsion of the BGE from the pressurized container. The Plexiglas cage contains the high voltage electrode and cable, and must be isolated from the other electronic and fluidic parts of the instrument. A microswitch is equipped on the Plexiglas cage to interrupt the high voltage upon opening. In the battery-powered mode, these portable instruments can operate for more than 7 h before recharging is required. Alternatively, main power can be utilized when available using a 220VAC to 12VDC inverter.

2.2.2. Automated bench-top CE-C^4D extended with sequential injection analysis

Commercial CE-instruments designed for the laboratory are not well suited for on-site deployment and coupling to external sample handling manifolds. It is, on the other hand, relatively easy to construct a CE-separation unit as part of an extended sequential

injection analysis (SIA) manifold. Such a coupling is considered the marriage between the powerful separation mechanisms of electrophoresis with the automation concepts of the sequential injection technique. This SIA-CE combination can enjoy both the noteworthy advanced aspects of CE and SIA, i.e. high separation efficiency, low sample and electrolyte consumption, experimental simplicity, programmable and precise handling of small liquid volumes, and cost-effectiveness. The combination of SIA − CE − C^4D developed by our groups (see Fig. 6) was exploited for unattended monitoring [33], automated preconcentration prior to separation [34] and pressure-assisted applications [35–37]. Using a stepper-motor syringe pump with a rotary valve controlled by a purpose-made graphical computer interface, the system can implement the whole analytical protocol, including sample aspiration and injection, capillary flushing, high voltage triggering and data recording, in an automated manner. It can function for several days without manual intervention of an operator, rendering it potential for remote monitoring applications. The system can also be used for routine analysis during the methodology development step. A schematic drawing of the SIA-CE-C^4D system is depicted in Fig. 7. The heart of the SI manifold consists of a bi-direction motor-driven syringe pump and a multi-port rotary valve with a holding coil between the two units. The BGE is first filled into the syringe before it is pushed through the holding coil and the multi-port valve into the flowcell interface for flushing the capillary or the interface. Aspiration of a plug of the sample solution into the holding coil and passing this volume to the capillary inlet are carried out via pulling and pushing the syringe to deliver back and forth the sample plug through a selected gate of the multi-port rotary valve. Sample injection into the capillary is carried out hydrodynamically by pressurization of the interface while pushing the sample plug past the capillary inlet. As the sample volume to be injected into the capillary is in the nL range, only a tiny part of the dispensed sample plug is needed. Electrophoretic separation is carried out by applying the high voltage from the detection end, with the second electrode in the flowcell interface being grounded. With the use of a computer-controlled syringe pump and multi-port valve, precise manipulation of the BGE/sample is made possible with excellent operation predictability and reproducibility. Renewal of BGE at the high voltage end of the capillary can be done either manually by emptying and refilling the BGE vial, or automatically using another flowcell interface. In the latter case, efficient flushing of the liquid volume at the high voltage electrode is done through either the capillary itself or an auxiliary tubing. Excess liquid from the outlet of the flowcell interface at the high voltage end was collected within the safety cage. Automated flushing of the interfaces at the grounded and high voltage ends allows the instrument to implement the whole analytical protocol without manual intervention of an operator.

2.2.3. Multi-channel CE-C^4D

The development of methods which allow the simultaneous separation of anionic and cationic species in CE is of high interest as otherwise for samples in which analytes of both charges must be determined two separate runs are required. Grace to the possibility of precise and rapid adjustment of the detection point merely by moving the detector cell along the capillary, the incorporation of C^4D to CE has indeed repeatedly been used for concurrent determination of cations and anions [14,16]. Thanks to the simplicity and fully electronic principle of CE, concurrent separations of both cations and anions in a single run employing more than one capillary at the same time is not much of a complication.

Multi-channel CE instruments, where separations of cationic and anionic species were simultaneously realized on independent capillaries, using different high voltage power supply modules and different miniaturized C^4D detectors were developed for the bench-
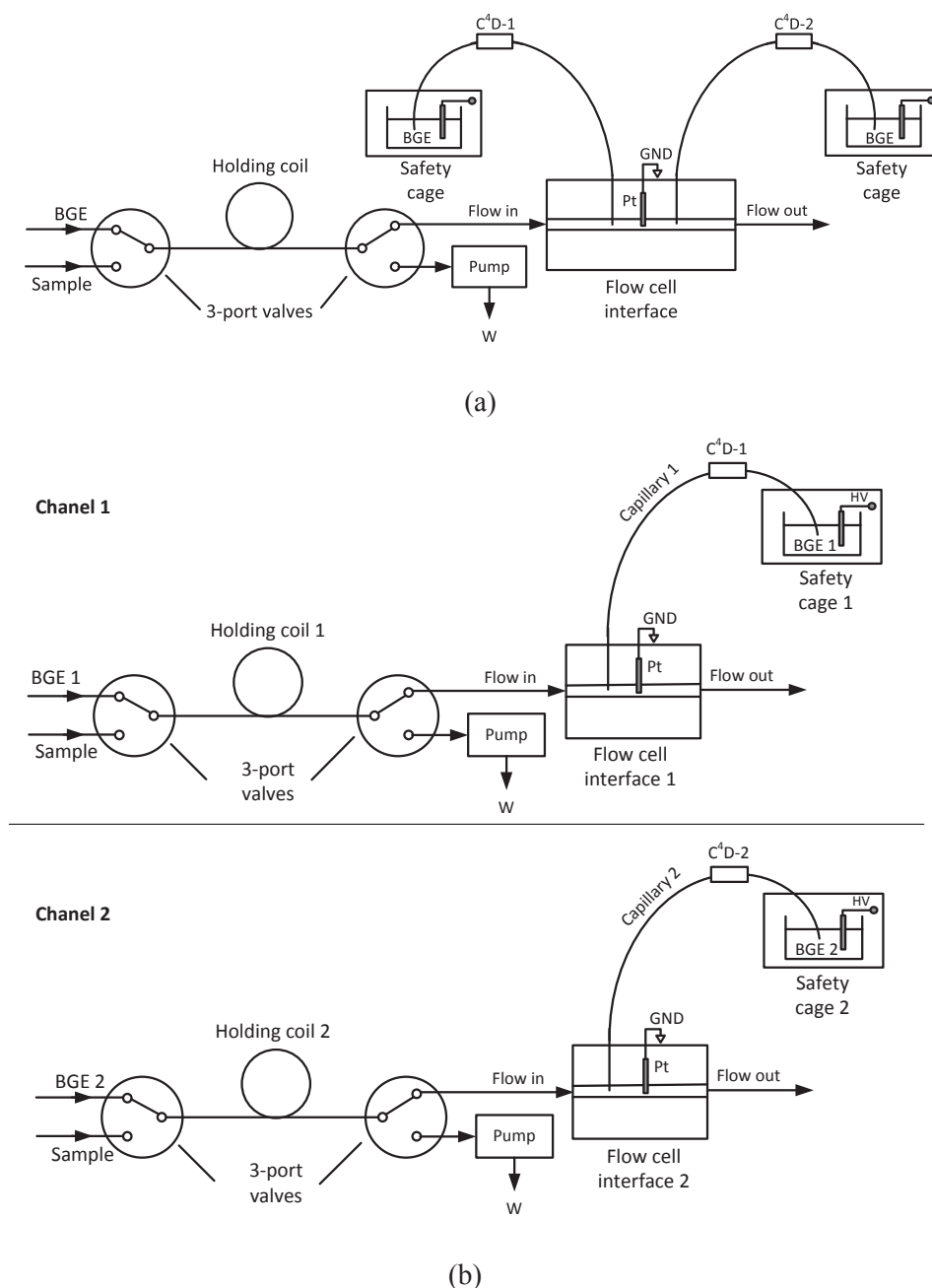
(a)

(b)

Fig. 9. Diagram of the fluidic connections of the in-house-made gas-based dual-channel CE instrument. a) Dual-channel CE using one common BGE; b) Dual-channel CE using two individual BGEs. Pt: platinum electrode; BGE: background electrolyte; W: waste.

top configuration [7] and portable format [15,32]. Depending on applications, operation with either a single BGE [7,32] or with individual BGEs [15,38] can be selected. A photo of a portable dual-channel CE using two individual BGEs is illustrated in Fig. 8. A schematic drawing describing different versions of the multi-channel CE format is shown in Fig. 9. The fluid handling system is based on pneumatic pumping (i.e. pressurization of a reservoir of containing BGE with compressed air) and two-/three-port valves to direct the flow. The main operations of sample aspiration and injection, capillary flushing, flowcell interface rinsing and high voltage application were adopted from those of the aforementioned gas-based single-channel CE system. In the dual-channel configuration that employs only 1 single BGE, both capillaries share a common electrical ground electrode for the application of the electrophoresis

voltage, which is also located in the flowcell interface (see Fig. 9a). The separation voltages are applied at the detection ends of the two capillaries. For safety reason, the vials with the high voltage electrodes are enclosed in isolation cages fitted with microswitches to interrupt the power on opening. Two detectors were used to visualise the electromigration of the target species in two capillaries. When electrophoretic separations of two different classes of analytes are required, a dual-channel CE setup using individual BGEs is needed (see Fig. 9b). This setup allows independent optimizations of separation conditions for positively and negatively charged species. Each channel of this setup functions independently as an automated gas-based compact CE system (see the description in the previous section). Compared to dual-channel CE setups that share one common buffer for both separation channels, this instrument using two

Table 2
Applications developed in Vietnam using purpose-made CE-C^{4}D instruments.

Analytes[a]	Matrix	Instrument used	Remark
Environmental applications			
Major inorganic cations (K$^+$, NH$_4^+$, Na$^+$, Ca^{2+}, Mg^{2+}) and anions (Cl$^-$, SO$_4^{2-}$, NO$_3^-$, NO$_2^-$, phosphate)	Surface water, groundwater and waste water	Manual or automated, single our multi-channel CE	Sample treatment is required for groundwater samples
Nitrogen-species (NH$_4^+$, NO$_3^-$, NO$_2^-$)	Groundwater contaminated with ammonium	Dual-channel bench-top CE	Monitoring the biological removal of NH$_4^+$
Inorganic arsenate and arsenite	Groundwater	Manual single-channel CE	Sample treatment is required for groundwater samples
Pharmaceutical pollutants (ibuprofen, diclofenac, bezafibrate, ketoprofen and mefenamic acid)	Surface water and wastewater from hospital and municipal discharges	Dual-channel portable CE	Sample preconcentration by solid phase extraction (SPE) is required prior to CE-C^{4}D operation
Rare-earth elements	Ore and anti-corrosion samples	Manual single-channel CE	The sample treatment process was adopted from that for ICP-MS operation.
Food control applications			
Artificial sweeteners	Beverages, fish sauce	Semi-automated single-channel CE, automated portable triple-channel CE	Dilution without further sample treatment prior to CE-C^{4}D operation
Preservatives and additives (organic acids)	Beverages	Semi-automated single-channel CE, automated portable triple-channel CE	Dilution without further sample treatment prior to CE-C^{4}D operation
Beta-agonists	Pig feed and pork meat	Semi-automated single-channel CE	Sample preconcentration is required.
Drug screening applications			
Amphetamine-type stimulants (3,4-methylenedioxy methamphetamine (MDMA), methamphetamine (MA), 3,4-methylenedioxy amphetamine (MDA) and 3,4-methylenedioxy-N-ethylamphetamine (MDEA))	Illegal tablets and urine samples from suspected users seized by the police at recreational clubs	Semi-automated single-channel CE	Only dilution without further sample treatment is required for tablet samples, whereas sample preconcentration by SPE is required for urine samples prior to CE-C^{4}D operation.
Sabultamol	Pharmaceutical syrup	Semi-automated single-channel CE	Only dilution without further sample treatment is required for tablet samples.
Pharmaceutical compounds	Urine samples	Dual-channel portable CE	Sample preconcentration by solid phase extraction (SPE) is required prior to CE-C^{4}D operation

[a] Many other (unpublished) analytes have been determined with CE-C^{4}D, and are listed in the application notes in our website (www.CE-Vietnam.com).

individual running buffers allows concurrent determination of analytes belonging to different categories in a single run. Basing on this instrumental principle, a setup with more than 2 separation channels is also made possible.

3. Applications

A summary of the applications developed in Vietnam using the purpose-made CE-C^{4}D instruments is shown in Table 2. The first environmental application of this technique in Vietnam was demonstrated by Nguyen et al. [39] for separation of inorganic arsenate species (As(V)) in groundwater. This was followed by the work on sensitive determination of inorganic trivalent arsenic (As (III)) using online electrokinetic preconcentration [12]. The CE-C^{4}D determination of major inorganic anions (Cl$^-$, SO$_4^{2-}$, NO$_3^-$, NO$_2^-$ and phosphate) and cations (K$^+$, Na$^+$, Ca^{2+}, Mg^{2+}, Na$^+$ and NH$_4^+$), considered as the primary indicators of water environment quality were as well communicated in this work [12]. Pham et al. reported the monitoring of the biological removal of ammonium from contaminated groundwater using one dual-channel CE-C^{4}D instrument [7]. The employment of CE-C^{4}D instruments has recently been expanded to the screening of various pharmaceutical pollutants in different water matrices in Hanoi [38] and simultaneous determination of rare earth elements in ore and anti-corrosion coating samples in Vietnam [40].

Purpose-made CE-C^{4}D instruments have been used as a simple and efficient tool for food quality control and drug screening in Vietnam. The triple-channel CE system was used for analyses of artificial sweeteners and preservatives in drinks and fish source [15]. Beta-agonists in pig-feed samples were determined using the semi-automated CE-C^{4}D instrument [11]. Salbutamol in

pharmaceutical syrups was also determined using the same system [11]. In a related application, the purpose-made CE-C^{4}D instrument was used for screening determination of different amphetamine-type stimulants in illegal drugs and urine samples [13]. More application notes for food control and pharmaceutical analyses have been developed and can be found elsewhere [41].

4. Perspectives: lab-on-a-chip electrophoresis instrumentation and applications

The combination of contactless conductivity detection with the electrophoretic separation of ions leads to a selective and highly versatile technique, which is still fairly simple as both separation and detection are achieved largely by electronic means. When combining the two techniques, the contactless approach to conductivity measurements is a significant improvement as it leads to an intrinsic electrical separation of the detector signal from the separation voltage and allows a significant simplification in the construction of the cell as well as the entire instrument. The electronic features of these techniques also allow downscaling of the (purpose-made) CE-C^{4}D configurations into a lab-on-a-chip format, i.e. microchip electrophoresis (MCE), with the aim of further reducing the construction cost and instrumental dimensions, thus rendering this approach more suitable for mobile deployment and widespread use. A basic MCE setup, as shown in Fig. 10, includes a high voltage generation module, a microchip with microchannels for sample introduction and electrophoretic separation, electrodes, a detection module and a fluidic platform if hydrodynamic injection and automated fluidic manipulation are implemented. The most frequently practiced injection technique in MCE is electrokinetic injection where an electrical field is employed as the driving force to
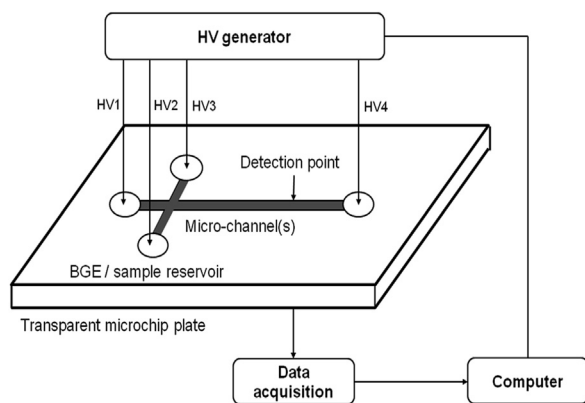
Fig. 10. Arrangement of a basic MCE setup. HV: high voltage cables and electrodes.

guide the sample flow into the separation channel. Hydrodynamic injection (HD) for introduction of the sample plug on the other hand is less often employed due to i) complication with precise pressurization for fluidic manipulation in microchip channels and reservoirs and ii) requirement of purpose-made instrumentation. Though efforts to implemented HD in MCE have been communicated [42], much room is still available for development and exploitation of this technique. From the view of the authors, some certain knowledge about instrument conception, electronics and programming as well as relevant infrastructure are needed for this purpose as commercial devices that allow both automated fluidic manipulation and MCE at the same time are not readily available. As MCE and CE both rely on the same principle, *i.e.* the application of a high electrical field over a microchannel, the development of MCE can profit from purpose-made CE instrumentation where different components (see Table 1) can be reused with little modification. A transition phase where only parts of a CE system are miniaturized whereas the capillary is still used instead of a microchip microchannel [43] can facilitate the process of down-scaling CE into MCE. Applications for MCE have been developed and communicated, for example for food quality control [44,45], pharmaceutical and biomedical analysis [46,47] and environmental analysis [48]. These would facilitate the MCE methodology development for specific applications in Vietnam where environmental pollution, food contamination and counterfeit drugs have become a serious problem for the population whereas inexpensive and portable/transportable devices for these analyses are always in need.

5. Conclusions

To the opinion of the authors based on the case study on CE-C^{4}D employment in Vietnam, (purpose-made) compact CE and MCE instrumentation can be seen as an affordable solution for the thirst of inexpensive and simple analytical devices for quality controls of the (aqueous) environment, food and pharmaceutical products in developing countries. Where expense is an issue, typically in the scientific community and industry in Vietnam, the 'marriage' between CE/MCE and C^{4}D can provide a low-cost solution for versatile measurements. With the purpose of bringing CE/MCE — C^{4}D as a cost-effective and simple analytical tool for the population, extension of the number of CE/MCE — C^{4}D applications is envisaged.

Acknowledgements

References

[1] A.J. Zemann, E. Schnell, D. Volgger, G.K. Bonn, Contactless conductivity detection for capillary electrophoresis, Anal. Chem. 70 (1998) 563—567.

[2] J.A.F. da Silva, C.L. do Lago, An oscillometric detector for capillary electrophoresis, Anal. Chem. 70 (1998) 4339—4343.

[3] Istech, www.istech.at, www.istech.at.

[4] eDAQ, www.edaq.com, www.edaq.com.

[5] J. Tanyanyiwa, B. Galliker, M.A. Schwarz, P.C. Hauser, Improved capacitively coupled conductivity detector for capillary electrophoresis, Analyst 127 (2002) 214—218.

[6] M. Stojkovic, B. Schlensky, P.C. Hauser, Referenced capacitively coupled conductivity detector for capillary electrophoresis, Electroanalysis 25 (2013) 2645—2650.

[7] T.T.T. Pham, T.D. Mai, T.D. Nguyen, J. Sáiz, H.V. Pham, P.C. Hauser, Automated dual capillary electrophoresis system with hydrodynamic injection for the concurrent determination of cations and anions and application to the monitoring of biological ammonium removal from contaminated ground water, Anal. Chim. Acta 841 (2014) 77—83.

[8] M. Greguš, F. Foret, P. Kuban, Portable capillary electrophoresis instrument with contactless conductivity detection for on-site analysis of small volumes of biological fluids, J. Chromatogr. A 1427 (2016) 177—185.

[9] A.P. Lewis, A. Cranny, N.R. Harris, N.G. Green, J.A. Wharton, R.J.K. Wood, K.R. Stokes, Review on the development of truly portable and in-situ capillary electrophoresis systems, Meas. Sci. Technol. 24 (2013).

[10] T.D. Mai, T.T.T. Pham, J. Sáiz, P.C. Hauser, Portable capillary electrophoresis instrument with automated injector and contactless conductivity detection, Anal. Chem. 85 (2013) 2333—2339.

[11] T.A.H. Nguyen, T.N.M. Pham, T.T. Doan, T.T. Ta, J. Sáiz, T.Q.H. Nguyen, P.C. Hauser, T.D. Mai, Simple semi-automated portable capillary electrophoresis instrument with contactless conductivity detection for the determination of beta-agonists in pharmaceutical and pig-feed samples, J. Chromatogr. A 1360 (2014) 305—311.

[12] H.A. Duong, M.D. Le, K.D.M. Nguyen, Peter C. Hauser, H.V. Pham, T.D. Mai, In-house-made capillary electrophoresis instruments coupled with contactless conductivity detection as a simple and inexpensive solution for water analysis: a case study in Vietnam, Environ. Sci. Process Impacts 17 (2015) 1941—1951.

[13] T.A.H. Nguyen, T.N.M. Pham, T.T. Ta, X.T. Nguyen, T.L. Nguyen, T.H.H. Le, I.J. Koenka, J. Saiz, P.C. Hauser, T.D. Mai, Screening determination of four amphetamine-type drugs in street-grade illegal tablets and urine samples by portable capillary electrophoresis with contactless conductivity detection, Sci. Justice 55 (2015) 481—486.

[14] I.J. Koenka, T.D. Mai, P.C. Hauser, J. Saiz, Simultaneous separation of cations and anions in capillary electrophoresis - recent applications, Anal. Methods 8 (2016) 1452—1456.

[15] T.D. Mai, M.D. Le, J. Saiz, H.A. Duong, I.J. Koenka, H.V. Pham, P.C. Hauser, Triple-channel portable capillary electrophoresis instrument with individual background electrolytes for the concurrent separations of anionic and cationic species, Anal. Chim. Acta 911 (2016) 121—128.

[16] J. Sáiz, I.J. Koenka, T.D. Mai, P.C. Hauser, C. García-Ruiz, Simultaneous separation of cations and anions in capillary electrophoresis, TRAC-Trend Anal. Chem. 62 (2014) 162—172.

[17] A.A. Elbashir, H.Y. Aboul-Enein, Recent applications and developments of capacitively coupled contactless conductivity detection (CE-C4D) in capillary electrophoresis, Biomed. Chromatogr. (2014), http://dx.doi.org/10.1002/bmc.3230.

[18] P. Kuban, P.C. Hauser, Contactless conductivity detection for analytical techniques-developments from 2012 to 2014, Electrophoresis 36 (2014) 195—211.

[19] P. Kubáň, P.C. Hauser, Contactless conductivity detection for analytical techniques: developments from 2010 to 2012, Electrophoresis 34 (2013) 55—69.

[20] A.A. Elbashir, H.Y. Aboul-Enein, Recent advances in applications of capillary electrophoresis with capacitively coupled contactless conductivity detection (CE-C4D): an update, Biomed. Chrom. 26 (2012) 990—1000.

[21] A.A. Elbashir, H.Y. Aboul-Enein, Applications of capillary electrophoresis with capacitively coupled contactless conductivity detection (CE-C(4)D) in pharmaceutical and biological analysis, Biomed. Chrom. 24 (2010) 1038—1044.

[22] P. Kubáň, P.C. Hauser, Ten years of axial capacitively coupled contactless conductivity detection for CZE - a review, Electrophoresis 30 (2009) 176—188.

[23] P. Kubáň, P.C. Hauser, A review of the recent achievements in capacitively coupled contactless conductivity detection, Anal. Chim. Acta 607 (2008) 15—29.

[24] V. Šonlínová, V. Kašička, Recent applications of conductivity detection in capillary and chip electrophoresis, J. Sep. Sci. 29 (2006) 1743—1762.

[25] P. Kubáň, P.C. Hauser, Contactless conductivity detection in capillary electrophoresis: a review, Electroanalysis 16 (2004) 2009—2021.

[26] P. Kubáň, P.C. Hauser, Fundamental aspects of contactless conductivity detection for capillary electrophoresis. Part I: frequency behavior and cell geometry, Electrophoresis 25 (2004) 3387—3397.

[27] P. Kubáň, P.C. Hauser, Fundamental aspects of contactless conductivity detection for capillary electrophoresis. Part II: signal-to-noise ratio and stray capacitance, Electrophoresis 25 (2004) 3398—3405.

[28] M. Stojkovic, I.J. Koenka, W. Thormann, P.C. Hauser, Contactless conductivity detector array for capillary electrophoresis, Electrophoresis 35 (2014) 482—486.

[29] P. Kubáň, H.T.A. Nguyen, M. Macka, P.R. Haddad, P.C. Hauser, New fully portable instrument for the versatile determination of cations and anions by capillary electrophoresis with contactless conductivity detection, Electroanalysis 19 (2007) 2059—2065.

[30] J. Sáiz, T.D. Mai, P.C. Hauser, C. García-Ruiz, Determination of nitrogen mustard degradation products in water samples using a portable capillary electrophoresis instrument, Electrophoresis 34 (2013) 2078—2084.

[31] J. Sáiz, T.D. Mai, L. María López, C. Bartolomé, P.C. Hauser, C. García-Ruiz, Rapid determination of scopolamine in evidence of recreational and predatory use, Sci. Justice 53 (2013) 409—414.

[32] J. Sáiz, M.T. Duc, I.J. Koenka, C. Martin-Alberca, P.C. Hauser, C. Garcia-Ruiz, Concurrent determination of anions and cations in consumer fireworks with a portable dual-capillary electrophoresis system, J. Chromatogr. A 1372 (2014) 245—252.

[33] T.D. Mai, S. Schmid, B. Müller, P.C. Hauser, Capillary electrophoresis with contactless conductivity detection coupled to a sequential injection analysis manifold for extended automated monitoring applications, Anal. Chim. Acta 665 (2010) 1—6.

[34] T.D. Mai, B. Bomastyk, H.A. Duong, H.V. Pham, P.C. Hauser, Automated capillary electrophoresis with on-line preconcentration by solid phase extraction using a sequential injection manifold and contactless conductivity detection, Anal. Chim. Acta 727 (2012) 1—7.

[35] T.D. Mai, P.C. Hauser, Pressure-assisted capillary electrophoresis for cation separations using a sequential injection analysis manifold and contactless conductivity detection, Talanta 84 (2011) 1228—1233.

[36] T.D. Mai, P.C. Hauser, Anion separations with pressure-assisted capillary electrophoresis using a sequential injection analysis manifold and contactless conductivity detection, Electrophoresis 32 (2011) 3000—3007.

[37] T.D. Mai, P.C. Hauser, Simultaneous separations of cations and anions by capillary electrophoresis with contactless conductivity detection employing a sequential injection analysis manifold for flexible manipulation of sample plugs, J. Chromatogr. A 1267 (2012) 266—272.

[38] M.D. Le, H.A. Duong, M.H. Nguyen, J. Saiz, H.V. Pham, T.D. Mai, Screening determination of pharmaceutical pollutants in different water matrices using dual-channel capillary electrophoresis coupled with contactless conductivity detection, Talanta 160 (2016) 512—520.

[39] H.T.A. Nguyen, P. Kubáň, V.H. Pham, P.C. Hauser, Study of the determination of inorganic arsenic species by CE with capacitively coupled contactless conductivity detection, Electrophoresis 28 (2007) 3500—3506.

[40] T.A.H. Nguyen, V.R. Nguyen, D.D. Le, T.T.B. Nguyen, V.H. Cao, T.K.D. Nguyen, J. Saiz, P.C. Hauser, T.D. Mai, Simultaneous determination of rare earth elements in ore and anti-corrosion coating samples using a portable capillary electrophoresis instrument with contactless conductivity detection, J. Chromatogr. A 1457 (2016) 151—158.

[41] CE-Vietnam, www.CE-Vietnam.com, www.CE-Vietnam.com.

[42] R.M. Saito, W.K.T. Coltro, D.P. de Jesus, Instrumentation design for hydrodynamic sample injection in microchip electrophoresis: a review, Electrophoresis 33 (2012) 2614—2623.

[43] I.J. Koenka, J. Saiz, P. Rempel, P.C. Hauser, Microfluidic breadboard approach to capillary electrophoresis, Anal. Chem. 88 (2016) 3761—3767.

[44] A. Martin, D. Vilela, A. Escarpa, Food analysis on microchip electrophoresis: an updated review, Electrophoresis 33 (2012) 2212—2227.

[45] L. Ferey, N. Delaunay, Food analysis on electrophoretic microchips, Sep. Purif. Rev. 45 (2016) 193—226.

[46] N. Nuchtavorn, W. Suntornsuk, S.M. Lunte, L. Suntornsuk, Recent applications of microchip electrophoresis to biomedical analysis, J. Pharm. Biomed. Anal. 113 (2015) 72—96.

[47] J.S. Creamer, N.J. Oborny, S.M. Lunte, Recent advances in the analysis of therapeutic proteins by capillary and microchip electrophoresis, Anal. Methods 6 (2014) 5427—5449.

[48] J.C. Jokerst, J.M. Emory, C.S. Henry, Advances in microfluidics for environmental analysis, Analyst 137 (2012) 24—34.