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Contactless conductivity detection for analytical techniques – developments from 2012 to 2014

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Abbreviations:

C^4D – capacitively coupled contactless conductivity detection / detector

DOI – dual opposite end injection

EC – electrochemical cell

EME – electromembrane extraction

FIA – flow injection analysis

MCE – microchip electrophoresis

μ-EME – micro-electromembrane extraction

PDMS – poly(dimethylsiloxane)

PMMA – poly(methylmethacrylate)

SIA – sequential injection analysis

SLM – supported liquid membrane

SPE – solid phase extraction

Abstract

The review covers the progress of capacitively coupled contactless conductivity detection over the two years leading up to mid-2014. During this period many new applications for conventional capillary electrophoresis as well as for microchip separation devices have been reported; prominent areas have been clinical, pharmaceutical, forensic, and food analyses. Further progress has been made in the development of field portable instrumentation based on capillary electrophoresis with contactless conductivity detection. Several reports concern the combination with sample pretreatment techniques, in particular electrodriven extractions. Accounts of arrays of contactless conductivity detectors have appeared which have been created for quite different tasks requiring spatially resolved information. The trend to the use of contactless conductivity measurements for applications other than capillary electrophoresis has continued.

1 Introduction

The development of applications of capacitively coupled contactless conductivity detection (C^4D) has kept its pace during the period covered by this review (approximately from July 2012 to June 2014) with over a hundred new publications. Again, as for the 2 year period covered in the previous review [1], most of these concern conventional capillary zone electrophoresis, and the detector now appears to be well established for this application. A number of reports have once more appeared on C^4D in microchip electrophoresis, with several of these concerning the analysis of relatively complex real samples, but a majority still dealing with design issues.

Several accounts of projects in which C^4D was an enabling technique have appeared. These include field portable instruments, a robotic vehicle for air testing, the *in-situ* study of chromatographic columns, and CE with hydrodynamic pumping. In order to lower the limits of detection, CE-C^4D has also been combined with preconcentration methods, in particular with electrodriven membrane extraction. New applications of C^4D include the monitoring of two-phase flows or the proposal of larger cells for conductivity monitoring in industrial systems. Some more fundamental studies on the impedance characteristics of the detector cell and on its modification have also been carried out.

This review is the last in a series of updates written by the authors [1-4]. The field has also been summarized by other authors, starting with the early reviews by Zemann, one of the protagonists of CE-C^4D, in 2001 and 2003 [5, 6]. This was followed by reviews by Gujit *et al.* in 2004 [7] and Šolínová and Kašička in 2006 [8]. Pumera in 2007 discussed C^4D on microchip devices [9] and Matysik in 2008 discussed C^4D along with amperometric detection [10]. Trojanowicz [11] discussed C^4D in the context of electrochemical detection methods in

flow analysis in 2009. Coltro *et al.* in 2012 summarized the developments of the use of capacitively coupled conductivity detection on microchip devices [12] and Elbashir and Aboul-Enein in 2010 and again in 2012 summarized applications of CE-C^4D [13, 14]. During the period covered by this review (2012-2014), Opekar *et al.* published a summary of some fundamental aspects of C^4D [15] and Matysik and coworkers published an extensive review on the combination of electrochemical methods in general with capillary electrophoresis, including microchip devices [16]. Newcomers to the field who want to gain an understanding of the basics of C^4D may also wish to consult the earlier fundamental publications by do Lago and coworkers [17, 18], Jorgenson and coworkers [19], Opekar *et al.* [15], or publications from our group [20-23].

The review is broken down to different aspects concerning more fundamental developments, applications of CE-C^4D implemented with conventional capillaries and on microchip devices, and new applications other than in capillary electrophoresis. The accompanying tables provide a summary of applications with more detailed information than discussed in the text. Note that some publications may be quoted more than once, if they are relevant in different contexts. We apologize for any oversights.

2 Fundamental aspects

2.1 Improved characterization and cell designs

The basics of the capacitively coupled contactless conductivity cell are fairly well understood, but more details on some aspects are still emerging. It is, however, sometimes difficult to obtain a comprehensive picture, as different authors focus on divergent aspects, use cells with varying characteristics, and use distinct operating conditions. Results reported for different

studies therefore sometimes even appear to be contradictory. It is a bit like the story of the blind men and the elephant.

A schematic drawing of an axial capacitively coupled conductivity cell is shown in Fig. 1 together with a simplified equivalent circuit diagram. Shen and coworkers [24, 25] carried out fundamental studies of this standard cell configuration with an impedance analyzer, and found that the measured wall capacitances are significantly smaller than the values calculated from the formula for a coaxial capacitor. This confirms earlier studies with a different cell in which the capacitances were experimentally determined differently, namely from Bode plots (plots of signal *vs.* frequency) [20]. Shen and coworkers also studied in detail the effect of solution conductivity on wall capacitance and found a clear correlation, *i.e.* the wall capacitance was higher for solutions of higher conductivity [24, 25]. The authors proposed a model for a likely explanation, namely that the field lines between the electrodes are following different paths for materials of different conductivity inside the tubing.

Liu *et al.* [26] discussed a detailed model for a planar contactless detector cell for microchip devices based on the early description by da Silva and do Lago for a tubular cell [27]. This treats the contactless electrodes not as simple capacitors, but as a series of smaller capacitors connected with resistors. Liu *et al.* could show that this more detailed model could better predict their experimental results than the simple model as shown in Fig. 1.

Further publications have appeared on the use of C^4D cells which were operated in series with a large inductor [28, 29] or a piezoelectric quartz crystal [24, 30]. In the latter case the crystals were employed also for their high intrinsic inductance values [30, 31]. The effect of a series inductance is illustrated in Fig. 2, where the modelled frequency response (Bode plot) of a cell

is given according to the simple equivalent circuitry (as shown in Fig. 1) and typical values for wall capacitances and solution resistance for a cell used in CE [20]. In the Bode plot for the cell without inductor the plateau at the high frequency end corresponds to the usual working range where the cell impedance is determined only by the solution resistance and the wall capacitances are negligible. As can be seen, the introduction of the inductor modifies the frequency response so that a maximum is obtained at a lower frequency. However, the maximum signal is still equivalent to that obtained in the plateau region for the cell without inductor as the current is nonetheless limited by the solution resistance. So the series inductor does not give a real gain in sensitivity when it is otherwise possible to work with optimized frequencies. This might not always be the case though. The cell might require operating frequencies which are beyond the bandwidths easily achieved with detector circuitries. The frequency at which the plateau is reached is higher for smaller coupling capacitances and therefore dependent on the cell geometry. It is also dependent on the inner diameter and the conductivity of the solution as lower values of cell resistance will push up the required minimum frequency. Another reason for wanting to move to lower frequencies might be the presence of a significant stray capacitance (direct coupling between the electrodes), which has a more pronounced effect at high frequencies.

2.2 Expanded scope

Several studies have been published which either concern an improvement of CE-C^4D or extend the application of C^4D beyond electrophoresis. Referenced C^4Ds have been reported by two groups. Shen *et al.* described a differential system consisting of two cells with separate pick-up circuitries which were placed at the two ends of the separation capillary [24]. The referenced system reported by Stojkovic *et al.* [32] consisted of a single cell through which the detection end of the capillary was looped back. Both approaches automatically subtract

the background signal and can thus compensate for baseline drifts due to temperature and other reasons.

Mai and Hauser reported a detailed further study on the effects of capillary diameter in the range from 10 to 50 µm and buffer concentration on the detection sensitivity [33]. Note that the use of the standard absorbance detectors is not readily possible with diameters of less than 50 µm. Also investigated was the effect of a concurrent hydrodynamic flow. The study confirmed that narrowest capillaries should be used when employing C^4D as they give best separation efficiency without loss of sensitivity with buffers of optimized concentrations. Hydrodynamic pumping may be employed with capillaries of less than 50 µm diameter for optimization of separation and analysis time without incurring significant band broadening. Stojkovic *et al.* [34] constructed an array of 16 cells which enabled the visualization of the development of the separation of ions along the length of the capillary.

Tůma *et al.* investigated the utility of a multichannel capillary [35]. The fused silica tubing with a standard outer diameter of 360 µm contained 7 channels with round cross-sections of 28 µm diameter. In a comparison with standard capillaries of 25 µm and 75 µm diameter it was found that for the multichannel capillary the sensitivity of a C^4D was approximately proportional to the total cross-sectional area of the channels, which corresponds to the expected behaviour. It can also be expected that the narrower channels lead to higher separation efficiencies. While this was found to be true for the also investigated UV-detection, it could, however, not be confirmed for the C^4D set-up.

Buglione and coworkers [36, 37] investigated the use of non-aqueous solvents in CE-C^4D for the determination of poorly water soluble organic cations (quaternary amines) and anions

(fatty acids) and found that the sensitivity and baseline stability was strongly dependent on the solvent and the electrolytes used, but that for optimized conditions good detection limits below 1 µM could be achieved.

Huang and coworkers [28, 29] produced scaled up versions of the usual dual axial electrode arrangement to tubings with outer diameters of 3.2 mm, 4.9 mm, 7.5 mm and 10 mm and found that these cells were suitable for conductivity measurements of KCl solutions. Thus it appears that the overall behaviour of larger cells is similar to the better studied capillary cells.

Wang et al. [38] described a conductivity sensor based on five axially arranged electrodes, the outer two for applying AC voltage, the 3 inbetween for differential conductivity measurement via the determination of the voltages at the electrodes rather than current as usual. This was used for flow rate measurements in millimeter scale tubings by determination of the velocity of introduced bubbles between the gaps of the inner three electrodes. In a further publication a similar approach for flow rate measurement was used in which the signal was created by introduction of solutions of different conductivity [39].

Wang *et al.* [40, 41] designed an array of 12 contactless electrodes arranged radially on a tubing of 55 mm diameter for the study of inhomogeneous flows. All electrodes can be switched between excitation and pick-up mode and with an appropriate data-acquisition system preliminary results on conductivity distribution inside the tubing could be obtained. Newill *et al.* [42] probably are the first authors to develop a 2D grid of contactless electrodes. 60 electrodes were arranged on a plane and again a switching circuitry allows the selection of the desired electrodes for measuring of the adjacent impedance.

Coltro and coworkers have designed a microfluidic device with three isolated electrodes, one of which was functionalized with biotin [43]. This electrode acted as an impedance sensor for the binding of avidin. The third electrode served as a reference for the solution conductivity and allowed to obtain the net signal via subtraction.

3 Instrumentation

3.1 Portable CE-C^4D-instruments

Portable instrumentation represent an attractive alternative to bench-top analytical systems and the combination of CE with C^4D lends itself very easily for portable applications since the instrumentation is simple and has low power requirements. A new partly automated portable CE-C^4D instrument employing compressed air for automated BGE distribution and hydrodynamic sample injection was reported by Mai *et al.* [44]. A photograph of this instrument can be seen in Fig. 3. The publication included a demonstration that capillary zone electrophoresis may be optimized either for high separation efficiency, low limits of detection, or fast separations, but that not all can be achieved at the same time, and compromises have to be made. In Fig. 4 a baseline separation of 4 ions is shown which was achieved on this instrument in less than 20 seconds. This affirms that fast separations can be carried out in conventional capillaries and that this is not a feature unique to microchip devices. Da Costa *et al.* [45] described an unmanned mobile platform employing CE-C^4D (called lab-on-a-robot) for air sampling and analysis and demonstrated the determination of formic-, acetic- and propionic acid vapours. Applications of portable CE-C^4D systems were further reported for the analysis of warfare degradation products [46], scopolamine in forensic studies [47], determination of inorganic and heavy metal ions in environmental samples [48,

49] and the analysis of post blast residues [50]. Portable CE-C^4D was also used as a scanning device for fraction collection prior to CE-MALDI-MS analyses of peptides [51].

3.2 On-line coupling of CE-C^4D to flow-injection systems

Flow-through techniques, such as flow injection (FIA) and sequential injection analysis (SIA), enable easy and automated operation and their coupling to CE-C^4D has been shown to be beneficial for liquid handling and sample injections in several contributions during the last two years. Mai and Hauser have published a series of manuscripts on coupling a SIA manifold to CE-C^4D and have examined the hyphenated systems for flexible manipulations of sample plugs and BGE solutions before and during CE analyses [33, 44, 52, 53]. Stojkovic *et al.* [53] demonstrated how the application of hydrodynamic pumping during an electrophoretic separation in narrow capillaries could be used to compensate the electroosmotic flow and to optimize the analysis time in the analysis of artificial sweeteners. Mai and Hauser demonstrated different schemes of concurrent anion and cation separations in a single capillary aided by hydrodynamic pumping [52]. For example, by placing the sample into the centre of the separation capillary, simultaneous separations of anions and cations were possible using two C^4Ds at the ends of the capillary. The simultaneous separation of anions and cations was also demonstrated in a flow-through system with two CE capillaries (one for the anion and the other for cation separations) and two C^4Ds by Gaudry *et al.* [54]. Alhusban *et al.* [55] used a similar instrumental set-up, with a single capillary, for on-line lactate monitoring in cell culture media. Automated handling of solutions and samples is also very attractive for separations in short capillaries since manual operations (BGE flushing, sample injection) with short capillaries is rather delicate. Vochyánová *et al*. designed an instrument employing flow-through electrokinetic injection into 10 cm long capillaries (total

length) and demonstrated the rapid analysis of saccharides [56] and human activity stimulants [57] in energy drinks.

3.3 Combination of CE-C^4D with sample pretreatment techniques

Many samples are not suitable for direct injection into a CE-C^4D instrument, either due to low concentrations of target analytes below the detection limit, or a matrix which leads to overload and inadequate separation. As a consequence, sample pretreatment is then required prior to their analysis. In some applications, filtration and considerable dilution of samples might be sufficient to overcome the matrix effects for analyses of major components. On the other hand, in analyses of minor components (especially in clinical applications), such dilutions are not acceptable and other pretreatment techniques, which usually combine removal of matrix components with analyte preconcentration are applied. Standard procedures, such as denaturation, deproteinization, centrifugation and micro-dialysis have been part of the procedures for some of the reports of the last two years reported for the pretreatment of complex and biological samples [58-61].

The recently developed microscale extraction technique of electromembrane extraction (EME) has received particular focus for the pretreatment of complex samples prior to CE-C^4D [62-66]. In EME, ionic analytes are electrophoretically transferred from an aqueous complex sample across a thin layer of a water immiscible organic solvent (in form of a supported or free liquid membrane) into an aqueous acceptor solution. A key characteristic of the extraction technique is its selectivity (*i.e.* elimination of matrix components and transfer of analytes). C^4D is a universal detection technique and in combination with CE enables determination of a broad range of analytes in one run. CE-C^4D has, for the first time, evidenced that EME strictly eliminates proteins, salts and most biochemical compounds and

efficiently transfers small pharmaceutical analytes by simultaneous determination of human serum albumin, inorganic cations, amino acids, creatinine and basic drugs in one single CE run [62]. Further developments of EME, such as application of polymer inclusion membranes in selective transfers of inorganic and organic anions [66, 67] and of organophosphorous herbicides [65] were demonstrated by CE-C^4D. A further down-scaling of EME to a micro format (sub-µL to µL volumes of respective solutions) was demonstrated by CE-C^4D for the recently developed µ-EME across free liquid membranes [63, 64].

Sample pretreatment is normally performed in an off-line fashion and the resulting extract is then manually transferred to the analytical system for injection and analysis. Direct coupling of sample pretreatment to CE-C^4D represents an attractive alternative to the off-line approach, since the manual handling of the sample by the operator is minimized and some tasks or even complete analytical procedures are fully automatized. Santos *et al.* [68] have demonstrated an on-line system coupling an electrochemical cell (EC) to CE-C^4D, which was capable of electrooxidation of otherwise neutral (and therefore for CE not accessible) alcohols, unattended injection, and electrophoretic separation in beverage samples with analytical frequency of 12 analyses per hour. The hyphenated EC-CE-C^4D system was also shown to be suitable for the simultaneous electrooxidation and CE analyses of cationic, anionic and neutral analytes [69]. Kubáň and co-workers have shown that direct coupling of CE-C^4D to thin planar membranes is suitable for direct injection of undiluted biological fluids into separation capillaries. Micro-dialysis membranes [70] and supported liquid membranes [71] were sandwiched between a sample of biological fluid and acceptor solution and CE separation capillary was touching the membrane surface (at the acceptor side) for direct electrokinetic injection of analytes through the membrane. The analytes were transferred by electrokinetic means directly into the capillary whereas matrix components, such as particulate matter,

proteins, lipids and other large molecular compounds were retained by the membranes and did not interfere with subsequent CE measurements. The process is illustrated in Fig. 5, and the determination of formate in blood samples following the direct extraction in Fig. 6.

3.4 C^4D on microchip devices

A number of reports concern the construction of embedded sensing electrodes for microchip devices. While it has previously been demonstrated that it is possible to work with external electrodes [72], embedded electrodes have larger coupling capacitances due to the thinner insulating layers, which can be a benefit because it leads to lower required operating frequencies (see the discussion in section 2.1). Liu and co-workers [73] prepared a PDMS microchip electrophoresis device with embedded electrodes covered with a 0.6 μm thick layer of PDMS acting as the insulating layer. They demonstrated substantially lower limits of detection compared to microchips with the same design but higher insulating layer thicknesses (15 and 50 μm). Coltro *et al.* [43] presented a separation device with electrodes which were isolated with a SiO_2 layer of only 50 nm thickness. Sensing electrodes can be also fabricated by direct injection of molten alloys into microchannels, which are prepared during microchip fabrication, and the technique represents a very economical way for precise electrode fabrication [74, 75]. An alternative is the use of non-metal materials; a conductive polymer (polyaniline, PANI) was shown as a suitable substitute for low-cost fabrication of C^4D as well as of the high voltage electrodes in MCE devices [76].

Different authors reported embedded electrode designs in microchip devices which were not intended for electrophoretic separations. Blaszcyk *et al.* [77] designed a device which employed electrolyte filled channels as contactless electrodes and demonstrated the measurement of conductivity for standard solutions. A new highly stable insulating material

was used for the fabrication of a C^4D sensor, consisting of a 120 nm thick layer of perovskite oxide deposited over Pt electrodes [78]. The sensor was then used for measurements of salt solutions with various conductivities. In microchip devices, planar electrodes are predominantly used, which means that the capacitive coupling in general cannot be as good as for conventional capillaries where tubular electrodes are the norm. Lima *et al.* [79] have thus also implemented concentric electrodes in a microfluidic flow-through device, which encompass the whole channel and have demonstrated a strong improvement in sensitivity compared to conventional planar electrodes [79]. A limit of detection of 344 pM was reported for flowing stream of $LiClO_4$ using the concentric electrodes, which was almost 4 orders of magnitude lower compared to planar electrodes.

Breadmore and coworkers [80] presented an instrument based on a dual channel microchip device with two separation channels and two C^4D cells for the concurrent separation of cations and anions. The microfluidic device was connected to an external manifold consisting of pumps and valves for automated sampling and flushing. Hydrodynamic injection was employed in order to avoid the injection bias which occurs for the otherwise often used electrokinetic injection mode. A photograph of the chip device with attachments is shown in Fig. 7 and electropherograms for the automated repetitive determination of cations and anions are shown in Fig. 8.

A portable, battery powered system was reported by Ansari *et al.* [81], which is very small (14 × 25 × 8 cm) and light (1.2 kg). It operates with detection electrodes which are external to the separation chips. These are therefore much easier and cheaper to manufacture than chip devices with embedded electrodes. In order to ensure high sensitivity, a dual top-bottom electrode configuration was used, which encompasses the separation channel from both sides.

Electrodes are positioned in exchangeable cartridges with various designs (*i.e.* cells with detection gaps from 0.5 to 2 mm), which can be replaced instantly and thereby enable selection of an appropriate detection system optimized either for resolution or for sensitivity. The replaceable C^4D cells were shown suitable for analyses of standard solutions as well as of food and clinical samples and detection limits below 1 μM were achieved.

In-line coupling of solid phase extraction (SPE) to MCE was demonstrated by Zhai *et al.* [82]. In their set-up a short segment (27 mm) of a monolithic SPE column was coupled to a glass/PDMS microchip and all analytical procedures were carried out on the same device. The sample was first injected and pretreated on the SPE column, then washed with methanol into the injection channel and finally separated and detected using C^4D.

A method for fabrication of cheap microchips based on printing the microchannel structure on a thin polyester film using a laser printer and laminating it with a second polyester film, which acts as the microchip cover, was described by Coltro and co-workers [83-85]. C^4D electrodes were fabricated from thin printed circuit boards and were placed on a chip holder underneath the chips. Different processes were used for chip fabrication employing black and white [83, 84] and colour [85] printing of the microchip structures, which showed a surprisingly significant effect of the toner characteristics on separation efficiencies and detection sensitivities.

4 Applications of electrophoresis methods with conventional capillaries

A comprehensive list of CE-C^4D publications in various application fields and of CE-C^4D hyphenations with sample pretreatment and analytical techniques reported in the last two

years is given in Table 1. Additionally, information on recent CE-C^4D applications can also be found in a review article published on general aspects of electrochemical detection methods in CE by Matysik and coworkers in 2012 [16] and in a review article specifically devoted to applications of CE-C^4D by Elbashir and Aboul-Enein also published in 2012 [13].

4.1 Pharmaceutical, clinical and forensic analysis

There is a strong interest in CE-C^4D for the determination of pharmaceutically relevant compounds. The development of new drugs, which possess no chromophores and are therefore not easily detectable by conventional UV-Vis detection, and a general acceptance of CE-C^4D as an economic, rapid and efficient method for the analyses of complex samples resulted into an increased number of CE-C^4D applications in the field.

A range of adulterants, usually synthetic compounds added to natural pharmaceutical formulations, was evidenced in several herbal formulations by recent CE-C^4D studies [86-88]. Various pain-killers [89-92], antibiotics [93, 94], antihypertensives [95], muscle relaxants [96] and enzyme inhibitors [97, 98], were determined in pharmaceutical formulations in order to prove their composition and content of active ingredients. CE-C^4D also enables determination of the active ingredient and its counter-ion, which may often reveal counterfeit medicines, which is a serious problem for medicine markets in poor countries. Vidal *el al.* [98] developed a rapid method for determination of sildenafil, vardenafil and their anionic counter ions (chloride, citrate) using a dual-C^4D electrophoretic system. Determination of diclofenac and its counter-cations was also demonstrated by Cunha *et al.* [92].

CE-C^4D has also often been reported for the determination of ionic analytes in clinical samples, such as in urine, serum, plasma and whole blood. A range of analytes, *e.g.* inorganic

cations, amino acids, human serum albumin and basic drugs were determined in a single run in various complex matrices [62]. Perchlorate was determined after direct electrokinetic injection of several body fluids across supported liquid membranes [71]. A method for collection of a novel biological fluid, exhaled breath condensate, and subsequent analysis of small inorganic ions therein, was demonstrated [99]. Other applications, such as the determination of lactate in cell cultures [55], glycosidic antibiotics in bronchial epithelial lining fluid [59], free/total valproic acid in human plasma [60], and neurotransmitters in periaqueductal gray matter [61], were also reported. The latter application is illustrated in Fig. 9.

Analyses of ionic analytes may also be necessary in forensic/toxicological science and several applications of CE-C^4D were reported in the reviewed period. Scopolamine, a tropane alkaloid, is often used for recreational and predatory purposes. A simple CE-C^4D method for determination of scopolamine and atropine, a related alkaloid, in seeds, drinks and body-lotions was presented by Sáiz *et al.* recently [47]. Methanol poisonings are often reported as a consequence of ethanol adulteration by methanol and subsequent application of the toxic mixture in alcoholic beverages production. In human body, methanol is enzymatically dehydrogenated to formic acid, which is responsible for the serious methanol toxicity. Several reports on CE-C^4D determination of formic acid in body fluids of methanol-intoxicated patients were reported after the recent "Methanol affair" in the Czech Republic [70, 100, 101]. Moreover, CE-C^4D methods can easily be applied to the simultaneous determination of formic acid and other ionic substances, for example, oxalic and glycolic acids, which are the toxicological markers of ethylene glycol poisoning [101].

4.2 Food analysis

Application of CE-C^4D in analyses of food samples is of high relevance, since many analytes are small ions and samples need to be analysed rapidly with minimum sample pretreatment. Determination of short chain aliphatic alcohols (ethanol – 1-pentanol) was reported after electrochemical oxidation of alcoholic and non-alcoholic beers [68]. Fatty acids were determined in margarine and vegetable oil samples using conventional CZE [102] and non-aqueous CE [36]. The separation of the enantiomers of tartaric acid in wine and grapes were carried out by ligand-exchange CE [103]. Eight biogenic amines (*e.g.* spermine, spermidine, putrescine, cadaverine, etc.), which are often reported for their benign biological characteristics, were determined in several liquor samples [104]. A rapid CE-C^4D method for determination of saccharides in energy drinks utilizing short capillaries was described recently by Vochyánová *et al.* [56]. The content of other major components of energy drinks, namely caffeine and taurine, was also examined [57]. Stojkovic *et al.* reported the determination of artificial sweeteners [53].

4.3 Environmental analysis and other applications

The determination of inorganic anions, cations and heavy metals has been reported for environmental samples, namely in lake sediment porewater [48, 49], soil extracts [105] and extracts of aerosol samples (PM2.5) [106]. Nie *et al.* [107] reported the use of CE-C^4D in the analysis of solutions used in corrosion studies [107]. An important reason for choosing CE-C^4D for these applications is its applicability for small sample volumes in the low µL-range. Another consideration was the need to analyse both, cations and anions. This usually requires two runs to be performed, in which the positive and negative ions are determined separately. The simultaneous determination of anions and cations is possible through dual-opposite end injections (DOI) in one run, where cations are injected into one end and anions into the

opposite end of the separation capillary and detection is performed approximately in its centre. Due to its universality this method is greatly facilitated by the use of C^4D. Applications of DOI in CE-C^4D of small inorganic anions and cations in environmental water samples were reported by Kobrin *et al.* [50] and by Naega *et al.* [108].

CE-C^4D analyses of environmental waters were further demonstrated on determination of warfare agent (nitrogen mustard) degradation products [46] and of organophoshorous pesticide glyphosate and its major metabolite aminomethyl phosphonic acid [65]. Volatile organic acids were determined in air after conversion into liquid samples using a tubular porous polypropylene sampling device [45].

Other applications include the determination of three polyphenols in tobacco leafs [109], a set of 14 lanthanides in simulated spent nuclear reactor fuel [110], peroxycarboxylates in commercial peracetic acid [111] and PCR products in genetically modified soybeans [58]. Enzymatic assays of myrosinase were evaluated on the basis of sulphate production and its subsequent CE-C^4D determination [112]. Effective mobilities of non-charged EOF markers were determined in BGE solutions containing sulphated-β-cyclodextrins, which may complex the EOF markers and induce their non-zero effective mobilities [113].

5 Applications of microchip electrophoresis

MCE with C^4D has proved to be useful in the analyses of complex samples. Inorganic cations were determined in rabbit blood serum and urine [81]. Other applications involve determination of ofloxacin and its enantiomers in eye drops [114, 115] and determination of lactate in synovial fluids [116]. A MCE method for determination of partition coefficients of

selected pharmaceuticals, which was based on phase distribution between 1-octanol and water, was also described [117]. Detail on applications of C^4D in MCE reported in the last two years is given in Table 2.

6 Other analytical applications of C^4D

Conductivity measurements in the contactless mode are non-invasive and for this reason have been employed in the examination of narrow-bore chromatographic columns. C^4D was used for the monitoring of the development of a monolithic stationary phase during its *in situ* fabrication [118], the characterization of monolithic capillary columns with integrated gold nano-particles [119], and the characterization of iminodiacetic acid functionalised monolithic columns [120, 121].

In industry applications, important information may be gathered by measurements of flowing streams. In order to obtain measurements at the industrial scale, significantly larger IDs of the tubing are required than can be accommodated with the C^4D cells for CE or LC. Li and co-workers have designed various C^4D measuring cells, which are able to perform conductivity measurements in pipes with IDs up to 7.8 mm. These cells were then shown to be suitable for flow-through measurements via bubble velocity in a two phase (gas-liquid) system [38, 39] and for flow-through measurements of solution conductivities [28, 29].

A microfluidic device with electrochemical cell and C^4D was developed, which combines label-free isothermal amplification of nucleic acids with subsequent real-time monitoring [122]. By using this approach, pure DNA can be determined down to 0.1 pg/mL. Emaminejad *et al.* [123] have demonstrated the use of C^4D on chip for cell counting, and interesting and

potentially very useful application derived from the well-established Coulter counter. When a cell passes between the two electrodes, a drop in conductivity occurs, showing up as a peak when recording the signal *vs.* time, which allows the counting of single cells.

A formerly developed reagent-free SIA system with C^4D was used by Mantim and coworkers for determination of dissolved carbon dioxide in beverages [124]. Newill *et al.* [42] employed their planar 2D grid of contactless electrodes mentioned above for the determination of moisture distribution in the soil of the root area of plants in a special laboratory growth container.

7 Concluding remarks

A solid number of applications of CE-C^4D with conventional capillaries has been reported, which further demonstrates the growing maturity of the method. Frequently commercial detectors are used and C^4D is becoming an accepted part of the toolbox. In comparison to other methods CE-C^4D has the advantage of being universal for all ionic species. It also tends to be more tolerant to the sample matrix and often only a dilution is necessary as pretreatment to avoid an overload. However, for complex samples appropriate clean-up/preconcentration are necessary just as for other analytical methods. In particular, the determination of concentrations below about 1 µM is not possible without preconcentration. For C^4D in microchip devices relatively few real applications have been reported, the majority of publications are still dealing with design issues. This is a somewhat curious situation considering that it is often claimed that microchip methodology is revolutionizing the analytical sciences. One shortcoming of MCE-C^4D might be the limited separation efficiency. The trend to new uses of C^4D outside CE has continued. C^4D dates back about 70 years and

was not new when introduced to CE. However, it is good to see that CE-C^4D has inspired new investigations of the wider merits of C^4D.

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Table 1. Applications of C^4D in conventional CE.

Analytes	BGE composition	C^4D parameters	Mode	Sample type	LODs	Ref.
Food analysis						
Aliphatic alcohols	50 mM Tris, 10 mM HCl, pH 8.6	2 V_{pp}, 600 kHz	EC-CZE	Beer	50 µM	[68]
Amines, biogenic	150 mM 18-crown-6, 500 mM acetic acid	eDAQ, 60 V_{pp}, 550 kHz	CZE	Brandy, liquor	44 – 149 ng/mL	[104]
Artificial sweeteners	150 mM CHES, 400 mM Tris, pH 9.1	380 V_{pp}, 200 kHz	SIA-CZE	Sweetener tablets, soft drinks	3.8 – 6.5 µM	[53]
Caffeine, taurine	40 mM CHES, 15 mM NaOH, 50 mM sodium dodecyl sulfate, pH 9.36	17 V_{pp}, 450 kHz	SIA-MEKC	Energy drinks	24 mg/L	[57]
Fatty acids	100% MeOH + 10 mM deoxycholic acid sodium salt	eDAQ	NACE	Olive and sunflower oil	0.5 µM	[36]
	6 mM methyl-β-CD, 8 mM trimethyl-β-CD in 5 mM Na_2HPO_4/K_2HPO_4, pH 7.4: ACN:MeOH:n-octanol (30:40:25:5)	eDAQ, 100 V_{pp}, 1000 kHz	CZE	Margarines	0.9 – 1.9 µg/mL	[102]
Inorganic cations and anions	12 mM His, 2 mM 18-crown-6, adjusted to pH 4 with acetic acid	20 V_{pp}, 300 kHz	Portable SIA-CZE	Cola, juice, soft drinks	1.5 – 17 µM	[44]
Saccharides	75 mM NaOH	9 V_{pp}, 320 kHz	Syringe pump-CZE	Energy drinks	15 – 35 mg/L	[56]
Scopolamine	10 mM HEPES, Tris, pH 7.6	eDAQ, 100% V_{pp}, 1200 kHz	Portable CZE	Seeds, beverages	2.6 µg/mL	[47]
Tartaric acid enantiomers	7 mM $CuCl_2$, 14 mM trans-4-hydroxy-L-proline, 100 mM ε-aminocaproic acid, adjusted to pH 5 with HCl	Agilent	CZE	Wine, grapes	20 µM	[103]
Pharmaceutical, clinical and other complex sample analysis						
Amikacin, kanamycin	20 mM MES, adjusted to pH 6.6 with His, 0.3 mM CTAB	eDAQ, 100 V_{pp}, 700 kHz	CZE	Pharmaceuticals	0.5 mg/L	[94]
Amikacin, urea	30 mM malic acid, adjusted to pH 4.1 with Arg, 10 mM 18-crown-6	eDAQ, 100 V_{pp}, 1200 kHz	CZE	Bronchial epithelial lining fluid	0.92, 0.14 mg/L	[59]
Anorectics, antidepressants (adulterants)	50 mM phosphate buffer, 50% (v/v) ACN, pH adjusted by 0.1 M H_3PO_4	2 V_{pp}, 600 kHz	CZE	Weight loss products	n.r.	[88]
Caffeine, dipyrone, acetylsalicylic acid	10 mM 3,4-dimethoxycinnamate, 20 mM Tris, pH 8.4	4 V_{pp}, 1.1 MHz	CZE	Pharmaceuticals	5 – 6 µM	[89]
Ciprofloxacin	1.8 mM oxalic acid, 12 mM triethanolamine, pH 8.5	4 V_{pp}, 1.1 MHz	CZE	Pharmaceuticals, milk	5 µM	[93]
Creatinine, choline	5.2 M acetic acid	Agilent, 50 V_{pp}, 1.84 MHz	µEME-CZE	Artificial biological fluids	n.r.	[63]
Diclofenac + counter-cations	10 mM Tris, 10 mM TAPS	n.r.	CZE	Pharmaceuticals	7 – 10 µM	[92]
Diclofenac, codeine	1.8 mM oxalic acid, 10 mM triethanolamine , pH 8.4	4 V_{pp}, 1.1 MHz	CZE	Pharmaceuticals	11, 21 µM	[90]

Diuretics, laxatives (adulterants)	20 mM H_3PO_4, 40 mM NaOH, 30% (v/v) MeOH, pH 9.2	4 V_{pp}, 1.1 MHz	CZE	Food supplements	1.5 – 3.3 mg/kg	[86]
DNA ladder fragments	20 mM Tris, 20 mM CHES, 5% PVP, pH 8.5	380 V_{pp}, 200 kHz	CZE	Bacterial plasmid DNA, soybeans	n.r.	[58]
Formate	20 mM His, 25 mM glutamic acid, pH 4.8	Agilent, 50 V_{pp}, 1.84 MHz	µD-EKI-CZE	Serum, plasma, whole blood	1.5 µM	[70]
	10 mM His, 15 mM glutamic acid, 30 µM CTAB, pH 4.56	20 V_{pp}, 290 kHz	CZE	Serum	2.2 µM	[100]
Glycine, glutamate, GABA	4 M acetic acid, pH 1.9	Agilent	µD-LVSS-CZE	Periaqueductal grey matter	9 – 15 nM	[61]
Hypoglycemics (adulterants)	20 mM sodium acetate, pH 10.0	2 V_{pp}, 600 kHz	CZE	Herbal formulations	2.0 – 5.8 µg/mL	[87]
Inorganic anions	5.2 M acetic acid	Agilent, 50 V_{pp}, 1.84 MHz	µ-EME-CZE	Artificial biological fluids	n.r.	[63]
Inorganic cations	1 M, 3 M or 6 M acetic acid	Agilent, 50 V_{pp}, 1.25 MHz	EME-CZE	Milk, wine, urine, plasma	n.r.	[62]
	5.2 M acetic acid	Agilent, 50 V_{pp}, 1.84 MHz	µ-EME-CZE	Artificial biological fluids	n.r.	[63]
Inorganic cations, inorganic and organic anions	20 mM MES, 20 mM His, 30 µM CTAB, 2 mM 18-crown-6	20 V_{pp}, 290 kHz	CZE DOI	Exhaled breath condensate	0.33 – 0.75 µM	[99]
Lactate	25 mM Tris, 35 mM CHES, 0.02% poly(ethyleneimine), pH 8.65	TraceDec	SIA-CZE	Cell cultures	3 µM	[55]
Lanthanides	LE: 14 mM HIBA or 14 mM HMBA, 10 mM acetic acid, adjusted to pH 4.5 with ammonia TE: 15 mM acetic acid	TraceDec	ITP	Simulated spent MOX fuel	n.r.	[110]
Muscle relaxants	30 mM ammonium acetate, 20 mg/mL HP-β-CD, pH 5.75	TraceDec	CZE	Pharmaceuticals	26 – 28 µM	[96]
Myrosinase kinetics (via SO_4^{2-} analysis)	His/acetic acid, I = 40 mM, pH 4.6	TraceDec	CZE	Enzymatic assays	15 µM (LOQ)	[112]
Na^+, HSA	5.2 M acetic acid	Agilent, 50 V_{pp}, 1.84 MHz	µ-EME-CZE	Urine, serum	n.r.	[64]
Na^+, saccharine, benzoate, ethanol	30 mM Tris, 10 mM HCl, pH 8.6	4 V_{pp}, 1.1 MHz	EC-CZE	Mouthwash antiseptic sample	n.a.	[69]
Oxalate, formate, glycolate	50 mM MES, 50 mM His, pH 6.1	Agilent, 50 V_{pp}, 1.84 MHz	CZE	Serum, saliva, urine, exhaled breath condensate	0.4 – 1.3 µM	[101]
Perchlorate	15 mM nicotinic acid, 1 mM TDAPS, pH 3.3	Agilent, 50 V_{pp}, 1.84 MHz	SLM-EKI-CZE	Milk, wine, urine, serum	0.5 – 5 µg/L	[71]
Performate, peracetate, perpropionate	20 mM Li/CHES, pH 9.8; 20 mM Li/β-alanine, pH 10.2; 20 mM Li/CHES, pH 9.0; 20 mM Li/TAPS, pH 8.5; 20 mM Li/TAPS, pH 8.0; 20	4 V_{pp}, 1.1 MHz	CZE	Commercial peracetic acid	8 – 24 µM	[111]

	mM Li/MOPS, pH 7.5					
Polyphenols	150 mM 2-amino-2-methyl-1-propanol, pH 11.2	20 V_{pp}, 3 – 180 kHz	SPE-CZE	Tobacco leafs	0.08 – 0.15 µg/g (LOQ)	[109]
Promethazine, codeine	1.8 mM oxalic acid, 10 mM triethanolamine, pH 8.4	4 V_{pp}, 1.1 MHz	CZE	Pharmaceuticals	20, 28 mg/L	[91]
Propranolol, hydrochlorothiazide	1.8 mM oxalic acid, 11.3 mM triethanolamine, pH 8.7	4 V_{pp}, 1.1 MHz	CZE	Pharmaceuticals	30, 10 µM	[95]
Sildenafil, vardenafil + their counteranions	0.5 M acetic acid	4 V_{pp}, 1.1 MHz	CZE	Pharmaceuticals	0.75, 0.9 µM	[98]
Terbinafine	10 mM acetic acid, sodium acetate, pH 4.7	4 V_{pp}, 1.1 MHz	CZE	Pharmaceuticals	0.11 mg/L	[125]
Trimethoprim, sulfamethoxazole	Lithium phosphate, pH 7.1	4 V_{pp}, 1.1 MHz	CZE	Pharmaceuticals	1.1, 3.3 µM	[97]
Valproic acid (free and total)	10 mM His, 10 mM MES, 10 µM CTAB, pH 6.5	380 V_{pp}, 200 kHz	CZE	Plasma	80 µg/L	[60]
Environmental analysis						
Amines, aliphatic (nitrogen mustard degradation products)	20 mM MES, adjusted to pH 6.0 with His	eDAQ, 100% V_{pp}, 1200 kHz	Portable CZE	River, well water	5 µM	[46]
Amines, biogenic	150 mM 18-crown-6, 500 mM acetic acid	eDAQ, 60 V_{pp}, 550 kHz	CZE	River, tap, lake water	44 – 149 ng/mL	[104]
Glyphosate, AMPA	12 mM His, 8 mM MOPS, 50 µM CTAB, pH 6.3	eDAQ, 100% V_{pp}, 300 kHz	EME-CZE	River water	43, 64 pg/mL	[65]
Heavy metals	10 mM His, 50 mM acetic acid, 2.5 mM 18-crown-6, pH 4.2, linear polyacrylamide coated capillary	TraceDec	SIA-CZE	Water samples	n.r.	[54]
Inorganic anions	10 mM His, 50 mM acetic acid, 2.5 mM 18-crown-6, pH 4.2, linear polyacrylamide coated capillary	TraceDec	SIA-CZE	Water samples	5 – 61 µg/L	[54]
	20 mM MES, 20 mM His, 20 µM CTAB, pH 6.1	100 kHz	CZE	PM 2.5	5 – 20 µg/L	[106]
	12 mM His, 2 mM 18-crown-6, adjusted to pH 4 with acetic acid	20 V_{pp}, 300 kHz	Portable SIA-CZE	Tap water	0.7 µM	[44]
	11 mM His, 50 mM acetic acid, 1.5 mM 18-crown-6, 0.1 mM citric acid	TraceDec	Portable CZE	Sediment porewater	0.28 – 0.98 µM	[48]
	11 mM His, 50 mM acetic acid, 1.5 mM 18-crown-6, 0.1 mM citric acid	TraceDec	Portable CZE	Sediment porewater	n.r.	[49]
Inorganic anions and cations	10 mM pyromellitic acid, triethanolamine, pH 3.55 10 mM pyromellitic acid, histidine, pH 3.70	eDAQ, 50 V_{pp}, 1000 kHz	CZE DOI	Groundwater	0.009 – 2.51 mg/L	[108]
	20 mM MES, 20 mM His, 20 µM CTAB, 2 mM 18-crown-6	60 V_{pp}, 200 kHz	Portable CZE DOI	Post blast explosive residues	3.7 – 35.7 µM	[50]
Inorganic cations	10 mM His, 50 mM acetic acid, 0.5 mM 18-crown-6, pH 4.1	Agilent	EME-CZE	Water samples	n.r.	[126]
	10 mM His, 50 mM acetic acid, 2.5 mM 18-crown-6, pH 4.2, linear polyacrylamide coated capillary	TraceDec	SIA-CZE	Water samples	16 – 40 µg/L	[54]
	30 mM MES, 30 mM His, 2 mM 18-crown-6, pH 6.1	4 V_{pp}, 1.1 MHz	CZE	Soil samples	7 – 91 µM	[105]
Inorganic cations	11 mM His, 50 mM acetic acid, 1.5	TraceDec	Portabl	Sediment	0.46 –	[48]

and heavy metals	mM 18-crown-6, 0.1 mM citric acid		e CZE	porewater	1.55 µM	
	11 mM His, 50 mM acetic acid, 1.5 mM 18-crown-6, 0.1 mM citric acid	TraceDec	Portable CZE	Sediment porewater	n.r.	[49]
Organic anions	20 mM MES, 20 mM His, 0.2 mM CTAB, pH 6.1	4 V_{pp}, 1.1 MHz	CZE	Air samples	n.r.	[45]
Phosphate	1 mM His, 25 mM acetic acid, pH 3.47	20 V_{pp}, 300 kHz	Portable SIA-CZE	Sewage water	5 µM	[44]
Phosphonic acids, inorganic, organic anions	30 mM MES, 30 mM His, 0.2 mM CTAB, pH 6.1	4 V_{pp}, 1.1 MHz	CZE	Air samples	10 µM	[45]
	Na_2CO_3, $NaHCO_3$, 0.2 mM CTAB, pH 10.2	4 V_{pp}, 1.1 MHz	CZE	Air samples	n.r.	[45]
Industrial applications						
Chloride	10 mM 2,6-pyridinedicarboxylic acid, 0.5 mM CTAH, pH 4	TraceDec	CZE	Industrial waters	10 µg/L	[107]
Heavy metals	10 mM 2,6-pyridinedicarboxylic acid, 0.5 mM CTAH, pH 4	TraceDec	CZE	Industrial waters	100 µg/L	[107]
Standard solutions						
Acid orange 7 + degradation products	20 mM acetic acid	n.r.	CZE	Standard solutions	0.013 – 0.047 µM	[127]
Alkylsulfonates	0.5 M acetic acid	eDAQ	EME-CZE	Standard solutions	n.r.	[67]
Amino acids	2 M acetic acid, 0.1% hydroxyethylcellulose, pH 2.1	DRC^{4}D, 20 V_{pp}, 200 kHz	CZE	Standard solutions	0.1 – 0.4 µM	[24]
Angiotensins I-IV	LE: 10 mM ammonium acetate, pH 4.5; TE: 10 mM acetic acid	Csense One	ITP	Standard solutions	n.r.	[128]
Cl^-, NO_3^-	0.5 M acetic acid	C^{4}D array, 20 V_{pp}	CZE	Standard solutions	n.r.	[34]
Dextran ladder	100 mM formic acid, pH 2.5 or 100 mM acetic acid, pH 2.9	TraceDec	t-ITP-CZE	Standard solutions	10 nM	[129]
Dopamine, adrenaline, noradrenaline	100 mM acetic acid	18 V_{pp}, 320 kHz	CZE	Standard solutions	n.r.	[35]
Glucose, ribose	37.5 mM NaOH, pH 12.5	18 V_{pp}, 320 kHz	CZE	Standard solutions	n.r.	[35]
Inorganic and organic anions	70 mM Tris, 70 mM CHES, 0.2 mM CTAB, pH 8.5	20 V_{pp}, 300 kHz	Portable SIA-CZE	Standard solutions	n.r.	[44]
	MES/His at pH 6.1, 90/90 mM, 60/60 mM, 30/30 mM	20 V_{pp}, 300 kHz	SIA-CZE	Standard solutions	0.4 – 10 µM	[33]
Inorganic and organic anions, inorganic cations, amines and aminoalcohols	90 mM MES, 90 mM His	380 V_{pp}, 200 kHz	SIA-CZE DOI	Standard solutions	n.r.	[52]
Inorganic cations	50 mM acetic acid, 20 mM Tris, pH 4.5	18 V_{pp}, 320 kHz	CZE	Standard solutions	n.r.	[35]
Inorganic cations and heavy metals, inorganic anions	12 mM His, 2 mM 18-crown-6, adjusted to pH 4.0 with acetic acid	380 V_{pp}, 200 kHz	SIA-CZE DOI	Standard solutions	0.3 – 2 µM	[52]
K^+, Na^+	0.5 M acetic acid	C^{4}D array, 20 V_{pp}	CZE	Standard solutions	n.r.	[34]
K^+, Na^+, Li^+	12 mM His, 2 mM 18-crown-6, pH adjusted to 4.0 with acetic acid	RC^{4}D, 200 V_{pp}, 250 kHz	CZE	Standard solutions	1 – 3 µM	[32]

Mobility measurements	20 mM succinic acid, 30 mM LiOH, 60 g/L sulfated-β-CD, pH 5.5	Agilent	CZE	Standard solutions	n.r.	[113]
Monoalkylcarbonates	10 mM $NaHCO_3$, pH 8.3	4 V_{pp}, 1.1 MHz	CZE	Standard solutions	n.r.	[130]
Nicotine, cotinine	45 mM acetic acid, pH 3.0	20 V_{pp}, 20 kHz	CZE	Standard solutions	n.r.	[131]
NO_2^-, NO_3^-, SO_4^{2-}	30 mM MES, 30 mM His	RC^4D, 200 V_{pp}, 250 kHz	CZE	Standard solutions	n.r.	[32]
Peptides	0.75 M acetic acid	60 V_{pp}, 200 kHz	Portable CZE	Standard solutions	2.5 µM	[51]
Perchlorate, inorganic anions	7.5 mM His, 40 mM acetic acid, pH 4.05	380 V_{pp}, 200 kHz	EME-CZE	Standard solutions	2 nM	[66]
Quaternary ammonium ions	MeOH/ACN (90%/10%), 10 mM deoxycholic acid sodium salt	eDAQ	NACE	Standard solutions	0.1 – 0.7 µM	[37]
	0.2 M acetic acid	eDAQ	EME-CZE	Standard solutions	n.r.	[67]

AMPA – aminomethyl phosphonic acid
CTAB – cetyl trimethylammonium bromide
CTAH – cetyl trimethylammonium hydroxide
DRC^4D – differential resonant C^4D
EKI – electrokinetic injection
HIBA – α-hydroxyisobutyric acid
HMBA – 2-hydroxy-2-methylbutyric acid
LVSS – large volume sample stacking
µD – micro-dialysis
MEKC – micellar electrokinetic chromatography
NACE – non-aqueous capillary electrophoresis
RC^4D – referenced C^4D
TDAPS – 3-(*N*,*N*-dimethylmyristylammonio) propanesulfonate
Tween 20 – Polyethylene glycol sorbitan monolaurate
n.r. – not reported

Table 2. Applications of C^4D in microchip electrophoresis.

Analytes	BGE composition	C^4D parameters	Material	Mode	Sample type	LODs	Ref.
Auramine O	5 mM lactic acid, 15% (v/v) MeOH	40 V_{pp}, 60 kHz	Glass/ PDMS	SPE-CZE	Shrimp	2.5 µg/mL	[82]
Cl^-, F^-, HPO_4^{2-}	50 mM acetic acid, 10 mM His, pH 4.2	TraceDec	PMMA	SIA-CZE	Standard solutions	9 – 24 µM	[80]
Glyphosate, AMPA	80 mM CHES/Tris, pH 8.8	4.5 V_{pp}, 320 kHz	Polyester	CZE	Environmental samples	45 – 70 µM	[84]
Inorganic and organic anions	10 mM His, 7 mM glutamic acid, pH 5.53	20 V_{pp}, 300 kHz	PC	CZE	Standard solutions, food samples	12.5 – 45 µM	[81]
Inorganic cations	30 mM MES, 30 mM His, 2 mM 18-crown-6, pH 6.0	20 V_{pp}, 300 kHz	PC	CZE	Standard solutions	1.6 – 12.4 µM	[81]
	6.5 mM maleic acid, 7.5 mM Arg, 1.5 mM 18-crown-6, pH 4.6	20 V_{pp}, 200 kHz	PC	CZE	Urine, serum	n.r.	[81]
K^+, Na^+	20 mM MES, 20 mM His	30 V_{pp}, 120 kHz	PDMS	CZE	Standard solutions	0.07 µM	[73]
K^+, Na^+, Li^+	20 mM MES, 20 mM His, 3% (v/v) EtOH, pH 6.1	10 V_{pp}, 400 kHz	Polyester toner	CZE	Energy drinks, pharmaceuticals	4 – 23 µM	[83]
K^+, Na^+, Li^+	20 mM MES, 20 mM His, pH 6.1	5 or 10 V_{pp}, 400 kHz	Polyester toner	CZE	Standard solutions	n.r.	[85]
K^+, Na^+, Li^+	50 mM acetic acid, 10 mM His, pH 4.2	TraceDec	PMMA	SIA-CZE	Standard solutions	5 – 16 µM	[80]
K^+, Na^+, Li^+	45 mM MES, 55 mM His, pH 5.9	TraceDec	PMMA	CZE	Standard solutions	26 – 73 µM	[76]
K^+, Na^+, Li^+	15 mM MES, 15 mM His	5.5 V_{pp}, 220 kHz	PDMS	CZE	Standard solutions	6.1 – 8.5 µM	[74]
K^+, Na^+, Li^+	20 mM MES, 20 mM His, pH 6.1	6 V_{pp}, 90 kHz	Glass	CZE	Standard solutions	n.r.	[132]
Lactate	10 mM Tris, 1 mM HCl, 0.1 mM CTAB, pH 9.1	90 V_{pp}, 60 kHz	PMMA	CZE	Synovial fluid	6.5 µM	[116]
NH_4^+, Na^+, Li^+	50 mM acetic acid, 10 mM His, pH 4.2	TraceDec	PMMA	CZE	Standard solutions	86 – 326 µM	[75]
Ofloxacin	1 mM MES, 1 mM His, pH 6.5	22 V_{pp}, 60 kHz	PMMA	CZE	Eye drops	21 µg/mL	[115]
Ofloxacin enantiomers	1 mM MES, 1 mM Tris, pH 8.0	22 V_{pp}, 60 kHz	PMMA	CZE	Eye drops	18 – 21 µg/mL	[114]
Partition coefficients – berberine	1 mM acetic acid, 3 mM sodium acetate	60 V_{pp}, 60 kHz	PMMA	CZE	Standard solutions	5.6 µg/mL	[117]
Partition coefficients – lidocaine	1 mM acetic acid, 2 mM sodium acetate, 1% (v/v) EtOH	60 V_{pp}, 60 kHz	PMMA	CZE	Standard solutions	4.0 µg/mL	[117]
Partition coefficients – L-lysine	15 mM boric acid, 5 mM ethanediamine	60 V_{pp}, 60 kHz	PMMA	CZE	Standard solutions	3.1 µg/mL	[117]
Partition coefficients – procaine	1 mM acetic acid, 4 mM sodium acetate	60 V_{pp}, 60 kHz	PMMA	CZE	Standard solutions	2.5 µg/mL	[117]

AMPA – aminomethyl phosphonic acid
CTAB – cetyl trimethylammonium bromide

778 PC – polycarbonate
779 TDAPS – 3-(*N*,*N*-dimethylmyristylammonio) propanesulfonate
780 n.r. – not reported
781

Figure Captions

Fig. 1 Schematic drawing of the standard capillary cell (A) and its simplified equivalent circuit diagram (B). $C_{coupling}$ are the wall capacitances for coupling the excitation voltage into the cell, and the resulting current out to the amplifier. R is the solution resistance. C_{stray} is due to unwanted, parasitic, direct coupling between the electrodes, and can be minimized by including a shield between the two half-cells.

Fig. 2 Predicted cell currents in dependence of the applied frequency for typical values of $C_{coupling}$ (0.1 pF) and R (10 MΩ) for a cell as used for capillary electrophoresis [20] without a series inductor, and series inductors of 1 H and 10 H. The freeware circuit simulator Qucs was employed for the modelling.

Fig. 3 On-site measurement in a sewage treatment plant with the portable CE instrument with automated hydrodynamic injection described in [44].

Fig. 4 Fast separation of 4 anions carried out in a conventional capillary and on a portable CE-C^4D instrument. Reprinted with permission from [44]. Copyright (2013) American Chemical Society.

Fig. 5 Electrokinetic injection across micro-dialysis membrane for direct injection of blood samples reported by Kubáň and Boček [70]. Reproduced with permission from Elsevier.

Fig. 6 Direct analysis of formate in blood samples of a healthy person (a) and a patient intoxicated with methanol (traces b-f) reported in [70]. Reproduced with permission from Elsevier.

Fig. 7 Photograph of the dual channel microchip electrophoresis devices reported by Breadmore and coworkers [80]. Reprinted with permission from [80]. Copyright (2014) American Chemical Society.

Fig. 8 Concurrent electropherograms acquired in the two channels of the device shown in Fig. 7 for automated repetitive injections. Reprinted with permission from [80]. Copyright (2014) American Chemical Society.

Fig. 9 Determination of 1) γ-aminobutyric acid (GABA), 2) glycine, and 3) glutamate in a micro-dialysate of grey brain matter reported by Tůma *et al.* [61]. Reproduced with permission from Elsevier.

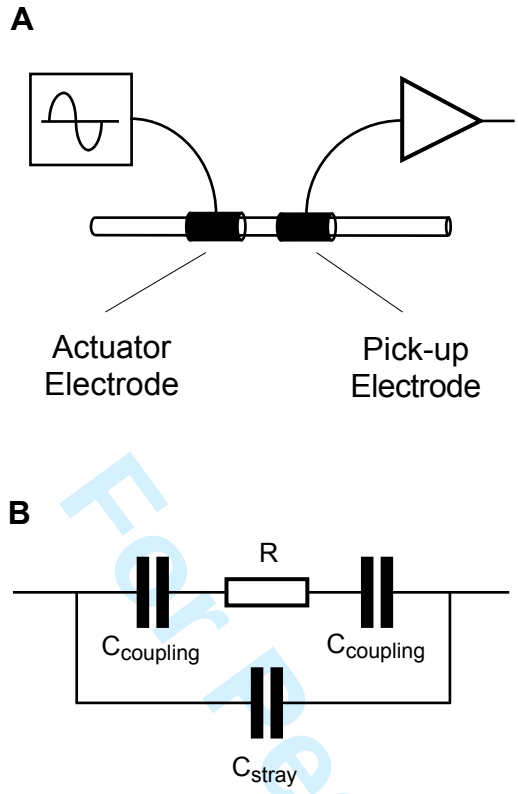

Fig. 1

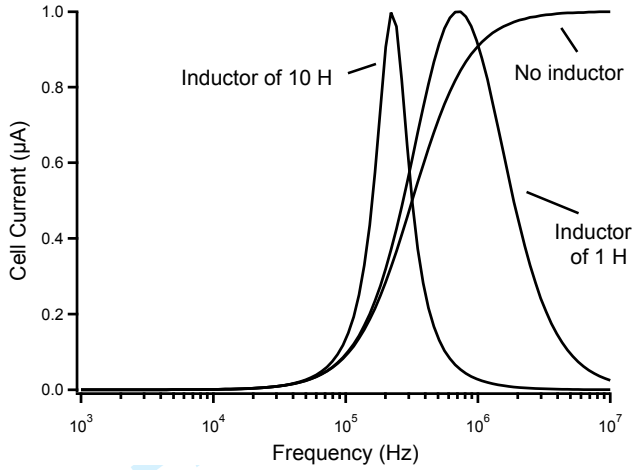

Fig. 2

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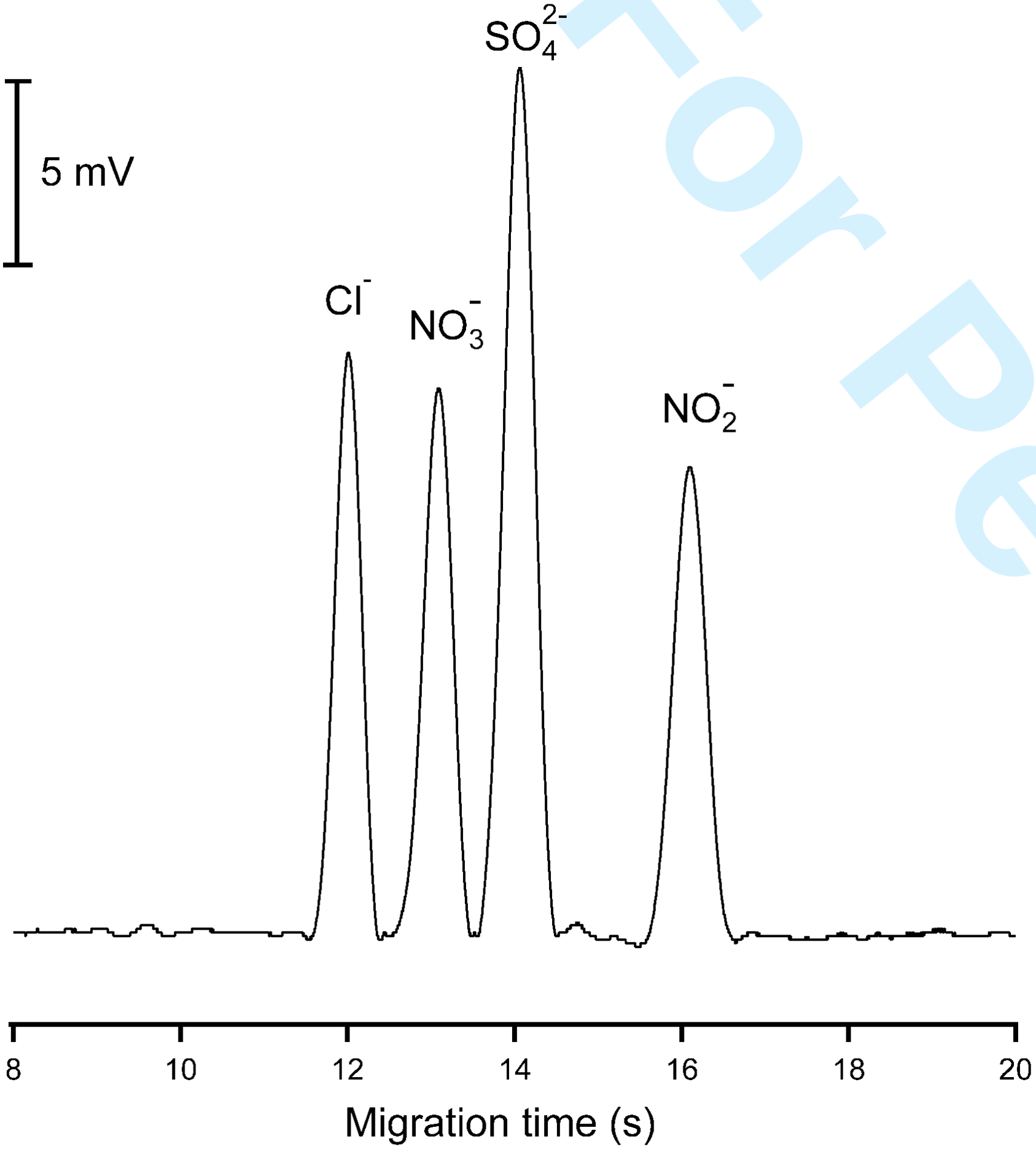
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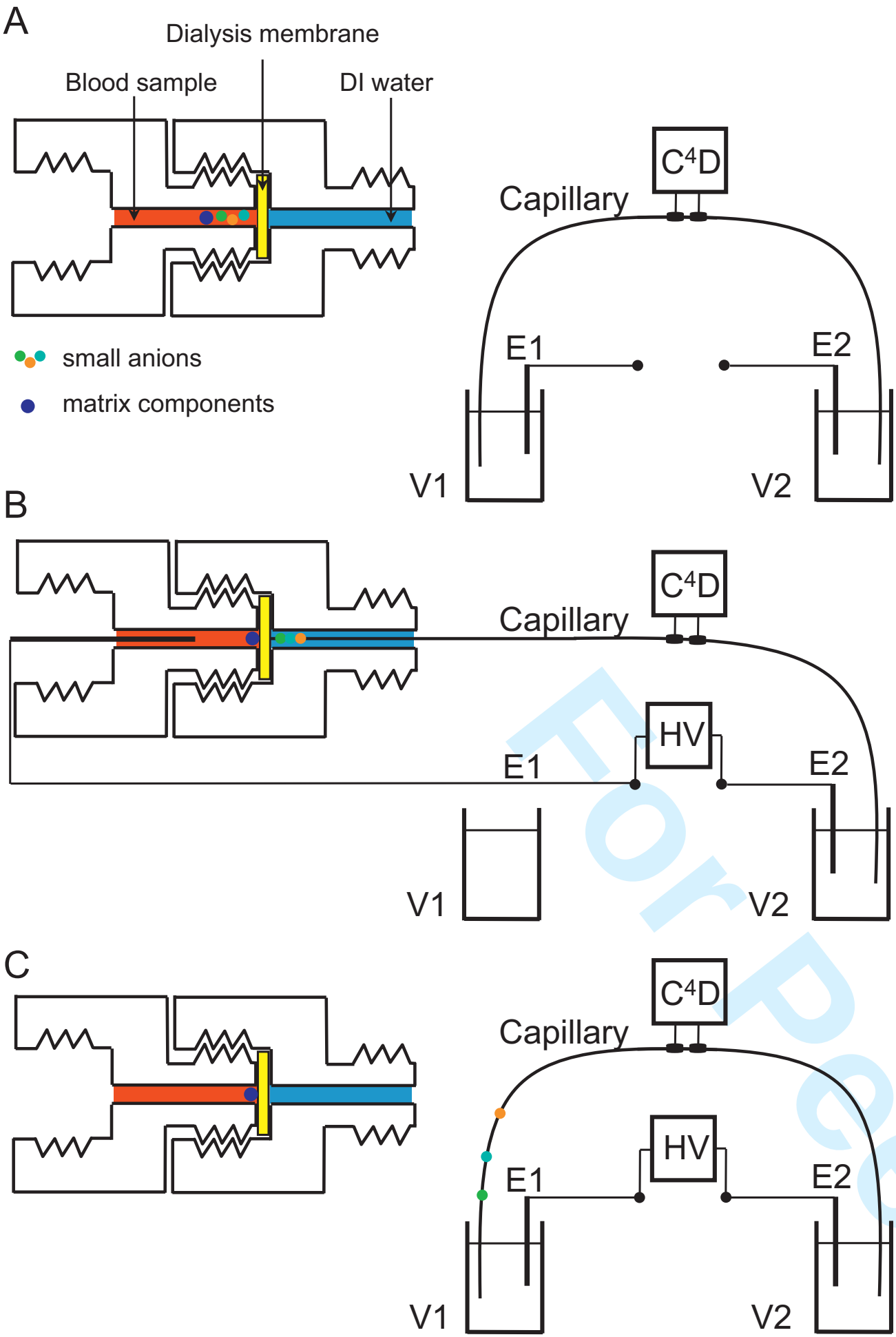
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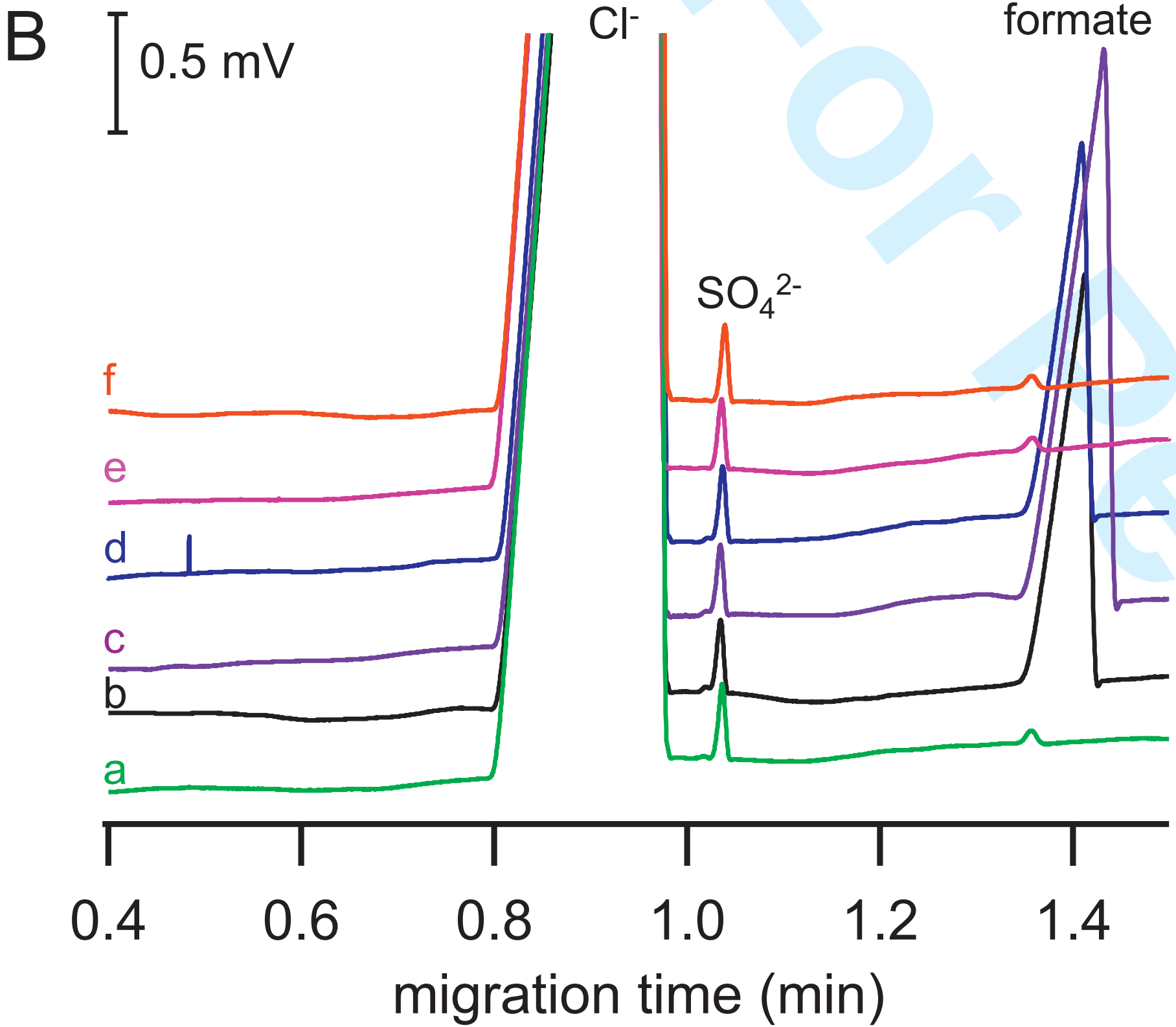
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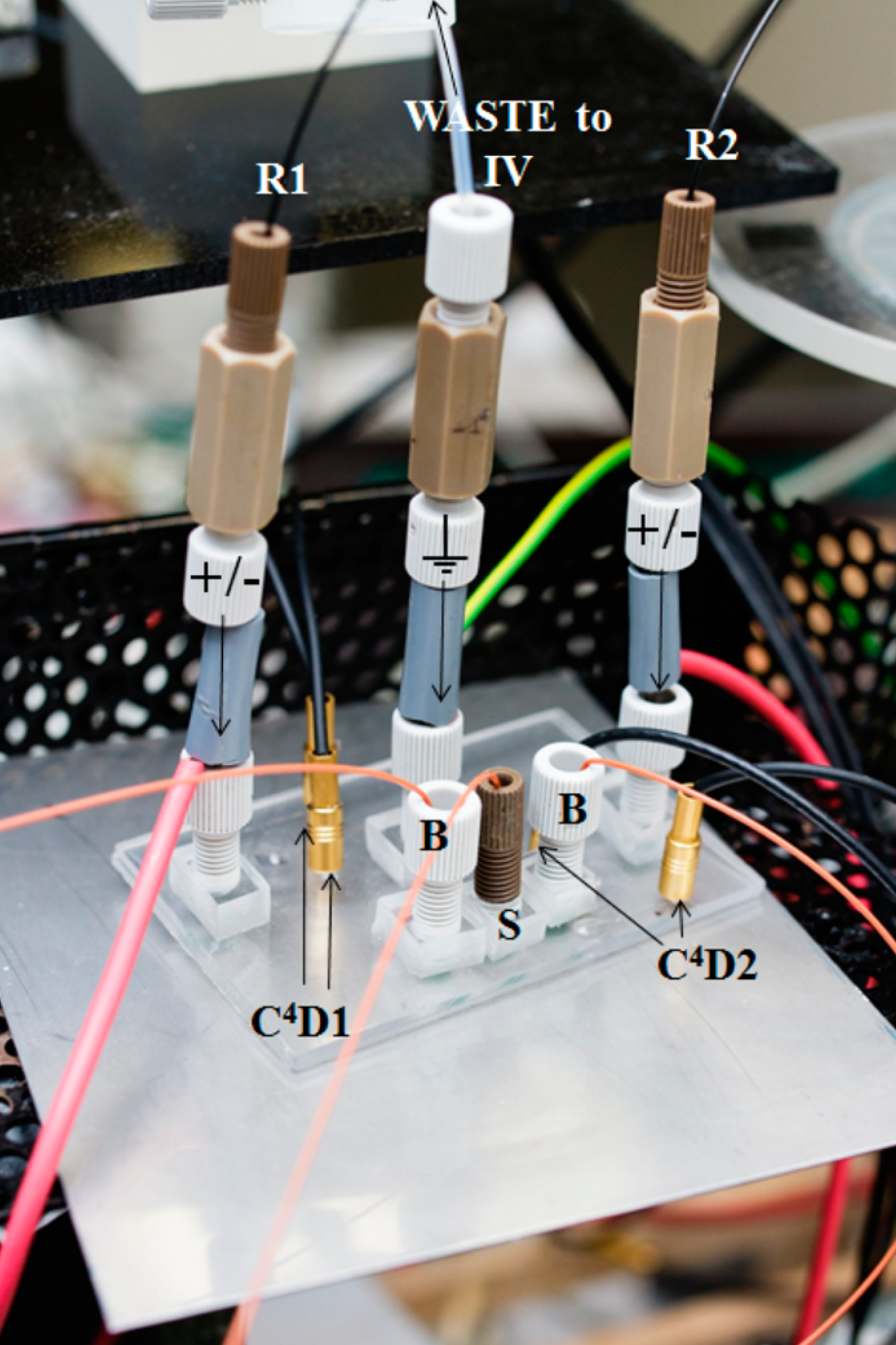
migration time (min)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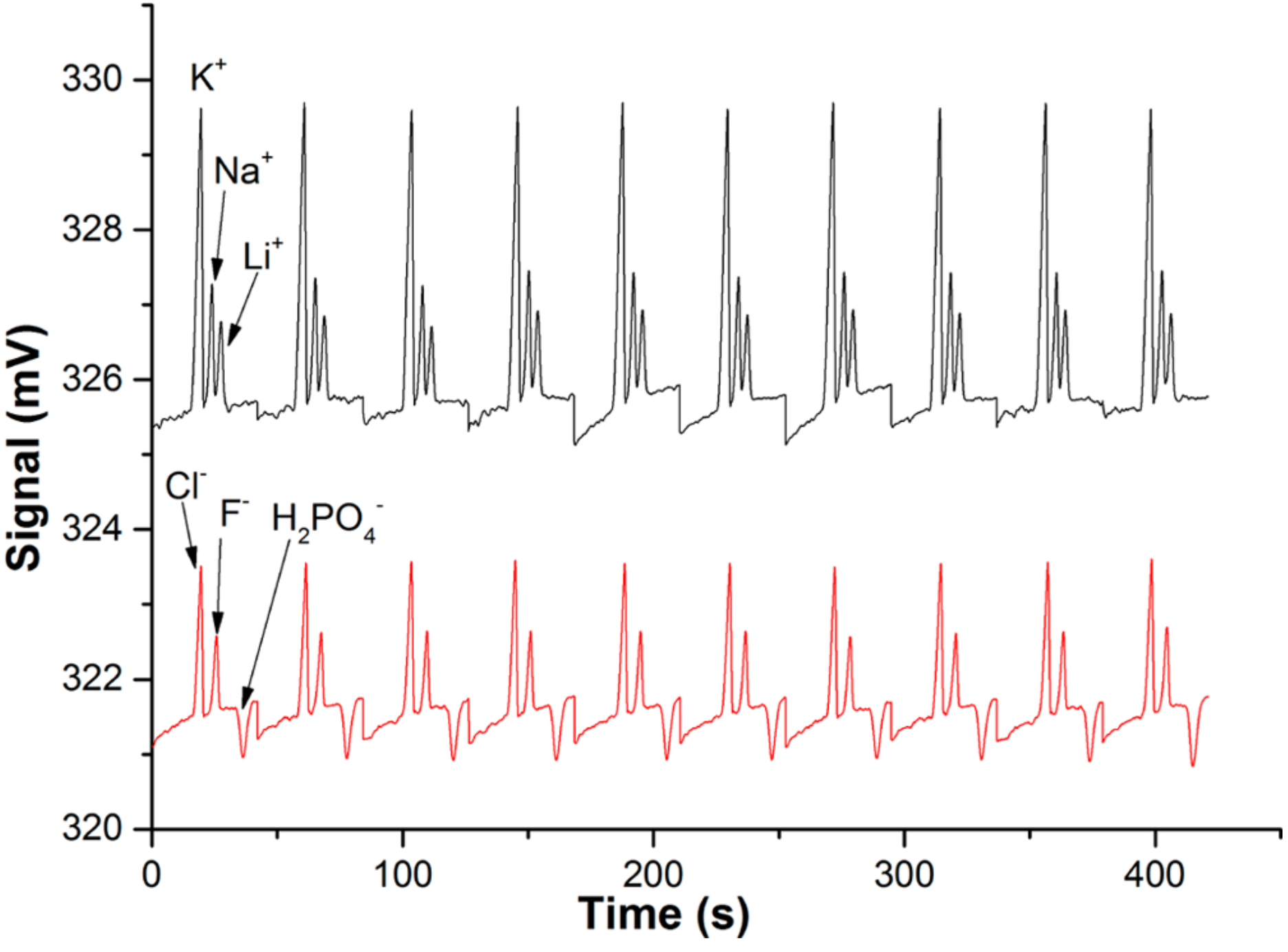
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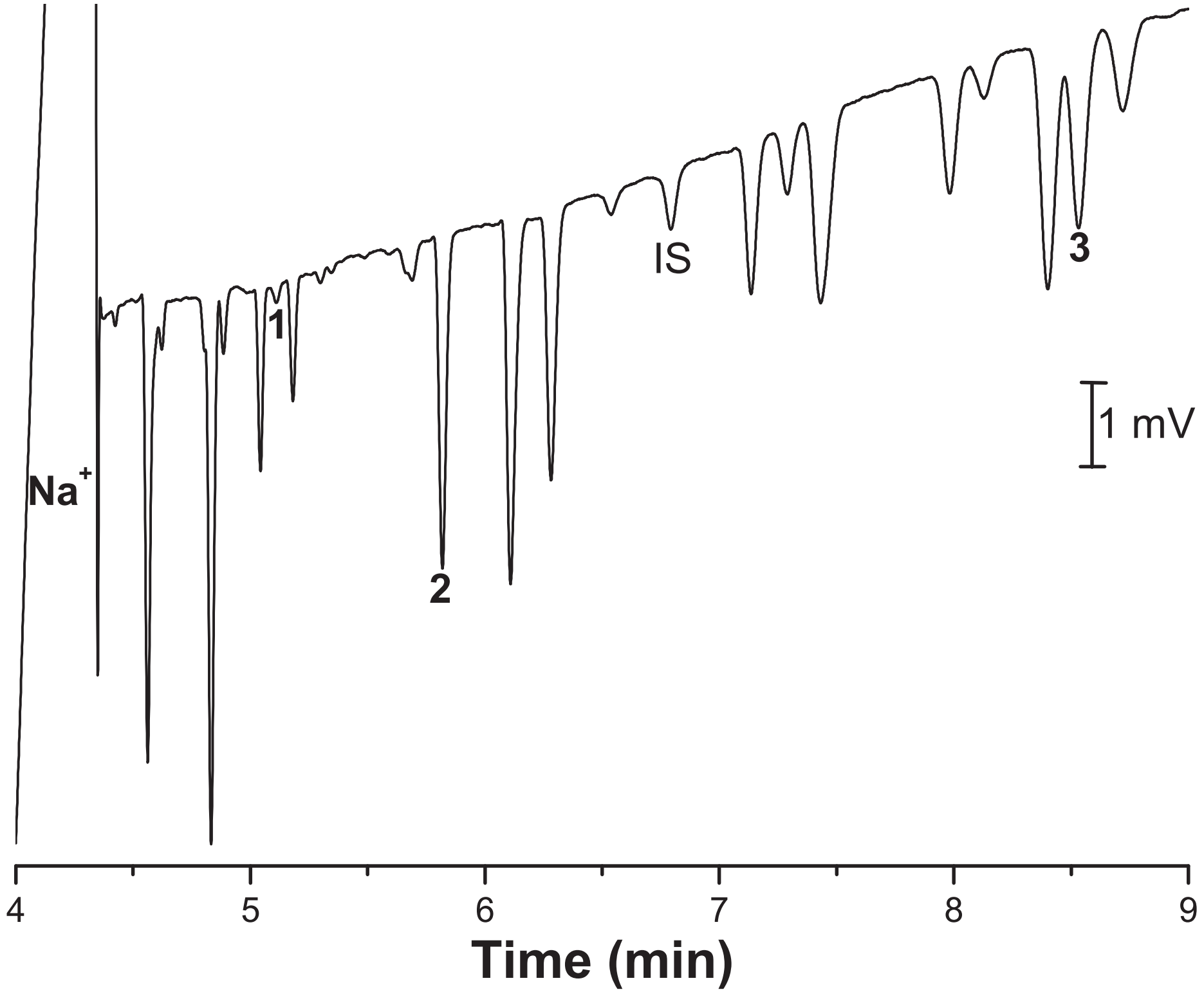
Time (s)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