Nano-capillary electrophoresis for environmental analysis

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Abstract Many analytical techniques have been used to monitor environmental pollutants. But most techniques are not capable to detect pollutants at nanogram levels. Hence, under such conditions, absence of pollutants is often assumed, whereas pollutants are in fact present at low but undetectable concentrations. Detection at low levels may be done by nano-capillary electrophoresis, also named microchip electrophoresis. Here, we review the analysis of pollutants by nano-capillary electrophoresis. We present instrumentations, applications, optimizations and separation mechanisms. We discuss the analysis of metal ions, pesticides, polycyclic aromatic hydrocarbons, explosives, viruses, bacteria and other contaminants. Detectors include ultraviolet–visible, fluorescent, conductivity, atomic absorption spectroscopy, refractive index, atomic fluorescence spectrometry, atomic emission spectroscopy, inductively coupled plasma, inductively coupled plasma–mass spectrometry, mass spectrometry, time-of-flight mass spectrometry and nuclear magnetic resonance. Detection limits ranged from nanogram to picogram levels.

Keywords Environmental pollutants analyses · Nano-capillary electrophoresis · Separation mechanism · Metal ions · Pesticides · Polycyclic aromatic hydrocarbons · Explosives · Viruses · Bacteria · Future perspectives

Introduction

Electrophoresis is referred as migration of ions or charged species under the influence of an electric field. In the beginning, electrophoresis was carried out in solution (Arne 1937) and on gel, bed, slab, rod, etc. supports. Later on these were replaced by capillaries leading to the development of capillary electrophoresis. During the course of advancements, capillaries have also been replaced by microchips. The technique is called as microchip electrophoresis name. Moreover, in 2009, Ali et al. (2009) defined this modality of electrophoresis as nano-capillary electrophoresis in their book published by Wiley, USA. It was due to the facts that mostly all the aspects in nano-capillary electrophoresis are being controlled at nano- or low levels of quantization. The definition of nano-capillary electrophoresis is a modality of electrophoresis involving samples in nano liter, mobile phase flow in nano milliliter per minutes with detection at nanogram per milliliter.

The other synonyms for this are microchip capillary electrophoresis and microchip electrophoresis. During the course of time, some publications appeared in the literature on nano-capillary electrophoresis and related topics (Nogami et al. 2007; Sanghavi et al. 2013a, b, 2014, 2015; Yan and Wang 2007; Yola et al. 2014a, b, c). Figure 1 indicates publications from 2005 to 2014. A perusal of these publications indicates growing interest and demand of nano-capillary electrophoresis. It is due to high

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Fig. 1 Number of publications on nano-capillary electrophoresis (2005–2014; source SciFinder)

versatility, speed, sensitivity and inexpensive running cost. Nowadays, it is considered as an innovative technique in separation science. During the last few years, this technique is being used for qualitative and quantitative analyses for various molecules in different matrices at nano- or low detection levels. Moreover, it is a suitable technique for the analyses of the environmental samples, especially of low amounts and poor concentrations the pollutants.

These features have attracted the environmental researchers for the analyses of the environmental pollutants. In view of these facts, it is gaining importance day by day in water, agriculture and horticulture sciences. The environment is getting contaminated by over growth population and industries. Some contaminants are present at trace level. We assume their absence in our body. But during the course of time, these enter into our body and accumulate, resulting in the various serious side effects, diseases and problems. Therefore, it is an urgent need to have the knowledge of trace pollutants in our environment, especially in water, air and food stuffs. This problem is being tackled by nano-capillary electrophoresis. During the last few years, some reviews appeared in the literature on nano-capillary electrophoresis (Brocke et al. 2001; Büttgenbach et al. 2006; Doherty et al. 2003; Evenhuis et al. 2004; Hisamoto et al. 2006; Huikko et al. 2003; Jin et al. 2000; Lazar et al. 2003; Nischang and Tallarek 2007; Pumera 2006a, 2008; Regnier et al. 1999; Sung et al. 2005; Xu and Baba 2004; Zamfir 2007), but there is no review dedicated to the environmental analyses.

In view of these facts, the attempts have been made to describe the state of the art of nano-capillary electrophoresis for the environmental analyses. The topics include instrumentation, applications, optimization, separation mechanism, challenges and future prospectives.

Nano-capillary electrophoresis

Like conventional capillary electrophoresis, nano-capillary electrophoresis also has similar configuration. Difference is only in the miniaturization of all the components. Nano-capillary electrophoresis instrumentation is discussed briefly in the following subsections.

Separation chip

Increasing demand of analyses at nano- and pico-levels compelled scientists to develop microchip-based nano-capillary electrophoresis. It has many advantages such as high speed, reduced sample volume and high separation efficiency (Fredrickson and Fan 2004; Manz et al. 1992a, b; Zamfir 2007; Zhang and Yin 2006). The integration of all the components of nano-capillary electrophoresis onto a chip comprises microchannel network for sample pre- and post-handlings, chemical reactions, separation and detection. Manz et al. (1992b) reported planar chips technology for miniaturization and integration in nano-capillary electrophoresis. Generally, nano-capillary electrophoresis cross-channel chips are made of silica or glass or other materials such as poly(dimethylsiloxane), with $50 \times 20 \mu\text{m}$ cross-sectional dimension of channel and 5 cm as separation channel length. Glass is considered as the best material due to its favorable electrical insulation and thermal conductivity. Besides, it is also useful for electrokinetic pumping using electroosmotic flow instead of mechanical pumping. Quartz is the best glass for this purpose due to its good transparency in ultraviolet region.

A graphic representation of nano-capillary electrophoresis with sample injection, background electrolyte and separation is shown in Fig. 2. The detail information

Fig. 2 A schematic representation of nano-capillary electrophoresis

on the different components of nano-capillary electrophoresis is out of the scope of this article. However, the interested readers should consult a book on this topic (Ali et al. 2009). Pamme (2007) wrote a review article on continuous flow separations in microfluid devices. The author described methods of continuous injection, real-time monitoring as well as continuous collection. Furthermore, author also reported that in continuous flow separation the sample components are deflected from the main direction of flow. These are either by force field (electric, magnetic, acoustic, optical, etc.) or by intelligent positioning of obstacles, in combination with laminar flow profiles.

The microchips are prepared by various methods such as photolithography, wet chemical procedures and dry etching. Normal background electrolyte of conventional capillary electrophoresis may be used in nano-capillary electrophoresis effectively. There is no special background electrolyte required in nano-capillary electrophoresis. However, the solvents and reagents should be of high-performance liquid chromatography and analytical grades. Normally, phosphate buffers of different pHs and ionic strength are used in nano-capillary electrophoresis. However, other buffers such as acetate, borate and ammonium citrate have also been used. The different organic modifiers such as acetonitrile and methanol may be used to improve separation. Additionally, normal surfactants of conventional capillary electrophoresis may be used in nano-capillary electrophoresis.

Kenyon et al. (2011) reviewed the advances in nano-capillary electrophoresis of January 2008 to July 2010 period. The authors discussed the developments in sample preparation, sample conditioning and separations of different molecules. Similarly, Zhao et al. (2013) presented a review on the advances of chip making and detection technologies. The authors discussed in detail the manufacturing processes and detection methods. Guihen and O'Connor (2010) reviewed the applications of nano-capillary electrophoresis. The authors highlighted the future

needs of nano-capillary electrophoresis. Besides, the pros and cons of detection in nano-capillary electrophoresis were also discussed. Recently, Castro and Manz (2015) reviewed the status of nano-capillary electrophoresis with special emphasis on the advances in technology and applications.

Ryvolová et al. (2010) reviewed the importance and applications of portable nano-capillary electrophoresis for the analyses of anions. The review focused on the state of the art of portable nano-capillary electrophoresis including miniaturization of functional parts, sample introduction, separation, detection and future developments. In all these reviews, it was observed that the authors attempted to discuss the impact of nano-capillary electrophoresis on scientific community and future prospects. Furthermore, it was realized that electrochemical detection may be suitable for portable nano-capillary electrophoresis. Additionally, it was also observed that future of portable nano-capillary electrophoresis seems to be quite interesting due to online applications.

Sample injection

Sample injection in nano-capillary electrophoresis is very important aspect for the reproducible results along with low mass detection limits (in absolute units). Of course, samples injection in nano-capillary electrophoresis is a challenging job due to small volume requirement (Futterer et al. 2004). The controlled injection of small amount of the samples is the prerequisite for the successful analyses in nano-capillary electrophoresis. The main sample injection modes in nano-capillary electrophoresis are electrokinetic (Alarie et al. 2001), sequential (Fang et al. 1999), pressure pinched (Bai et al. 2002), hydrodynamically (Solignac and Gijs 2003), hydrostatic pressure (Gai et al. 2004), push/pull (Wu et al. 2004) and bias-free pneumatic (Cho et al. 2005). The interested readers should consult some reviews on the sample loading techniques (Fang 2004; He et al. 2006; Karlinsey 2012). However, some important reviews are briefed herein. Kong and Shin (2004) described multifunctional sample injection methods based on injection voltages. The various voltages were applied for damping solutions. Saito et al. (2012) presented a review on sample injection with special emphasis on the basic principles, instrumentation designs and performance. The authors discussed pros and cons of the electrokinetic and hydrodynamic sample injection methods.

Buettgenbach and Wilke (2005) wrote an article on continuous sample flow sample injection method. As per the authors, the device presented good functional integration for miniaturized analyses. Ito et al. (2005) reported a simple sample loading method in nano-capillary electrophoresis. Sample loading was carried out on microchip-

fabricated poly(dimethylsiloxane). The discontinuous electrophoretic mobility at sample polymer interface may be considered as an advantage.

Besides, sample compaction effect was also moderate in ordinary size dependent. Cho et al. (2005) described pneumatic sample injection in nano-capillary electrophoresis. It was observed that the technique was capable to inject 10.0 nL sample without sampling bias. The authors used red ink, fluorescein and dichlorofluorescein as test compounds. Zhang et al. (2006) reported an injection method by exploiting flows generated by negative pressure, electrokinetic and hydrostatic forces. The task was achieved using a single syringe pump and power supply at constant voltage. During loading, a partial vacuum in the headspace of a sealed sample waste reservoir was generated. The precisions of the migration times were of 3.3 and 1.5 % for rhodamine 123 and fluorescein sodium, respectively.

Detection

Detection in nano-capillary electrophoresis is also a crucial feature to achieve nano analyses task. The most commonly used detectors are ultraviolet–visible, fluorescent, conductivity, atomic absorption spectroscopy, refractive index, atomic fluorescence spectrometry, atomic emission spectroscopy, inductively coupled plasma, inductively coupled plasma–mass spectrometry, mass spectrometry, time-of-flight mass spectrometry and nuclear magnetic resonance. In spite of the uses of these sensitive detectors, the detection sensitivity at nano level is still a difficult task. To handle this issue, various advancements have been made in detectors from time to time. One of the innovations is suitable and exact hyphenation of the detectors with nano-capillary electrophoresis. It was observed that hyphenation resulted in the increased sensitivities of many detectors.

The volume of detector cell in ultraviolet–visible detector is found to increase the sensitivity. Currently, mass spectrometer chip-based detectors can be coupled with nano-capillary electrophoresis, leading to quite good sensitivities. Some reviews (Brivio et al. 2005; Chen et al. 2006; Garcia and Henry 2007; Kitagawa and Otsuka 2011; Lazar et al. 2006; Stachowiak et al. 2004; Xu and Baba 2004; Zamfir 2007) are appeared in the literature on detection in nano-capillary electrophoresis. These describe various advancements, hyphenations and working capacities. In this series, Wu et al. (2004) described the advances in electrochemical detectors. The authors discussed operation modes and working electrodes, eliminating the separation currents and applications. Interestingly, future of these detectors was predicted well by the authors.

Brivio et al. (2005) reported supramolecular nano flow electrospray ionization on chip, providing good sensitivity.

Chen et al. (2006) reviewed electrochemical detection for monitoring the environmental pollutants. The emphasis was laid down on the fabrication of nano-capillary electrophoresis, sample pre-treatments, electrochemical detection and electron capture detector-nano-capillary electrophoresis hyphenation. The authors predicted electron capture detector-nano-capillary electrophoresis as an ideal instrument for the environmental analyses. Really, statements given by these authors are encouraging to scientific community and hopefully beneficial too.

Zamfir (2007) reviewed sheathless interfaces of nano-capillary electrophoresis with electrospray ionization mass. The authors discussed several aspects of sheathless interfaces. Similarly, Kitagawa and Otsuka (2011) reviewed the advances in nano-capillary electrophoresis instrument with special emphasis on mass detection. Among many interfaces, electrospray ionization and laser desorption ionization were discussed in detail due to their ease of coupling with miniaturization system. Garcia and Henry 2007 discussed motivation of nano-capillary electrophoresis and electron capture detector hyphenation. The authors presented modification strategies in the instrument development and electrode configurations.

During writing of this article, it was observed that the mass detectors have been used frequently in nano-capillary electrophoresis because of their low mass detection limits (in absolute units). Furthermore, ease of hyphenation made these detectors of choices. However, other detectors have also been coupled with nano-capillary electrophoresis. Furthermore, it was realized that hyphenation technique is not fully developed. It needs more attention of the researchers in the future. Briefly, choice of the detector depends on the types of the analytes to be studied. It is important to mention here that mass- and element-based detectors are useful for the environmental analyses.

Alves Brito-Neto et al. (2005) described capacitively coupled contactless conductivity detection in nano-capillary electrophoresis. The authors presented the theoretical and practical complexity in the detection. The authors carried out modeling studies and suggested that sensitivity depends on the electrolyte co-ion and counterion, cell geometry and its positioning and operating frequency. This paper is important to design experimental setup. Chen et al. (2007) described detection of potassium ion with 10 $\mu\text{mol L}^{-1}$ detection limit using contactless conductivity detection. The advantages lie in the fact that nano-capillary electrophoresis was independent to detection electrodes. Furthermore, it was easy to replace chip and other operations with detection in the different positions of the channel available. Zhai et al. (2014) described a simple glass/PDMS microfluidic chip for on-line sample pretreatment and contactless conductivity detection. The authors performed sample extraction, injection, separation and

detection automatically in sequence. The detection limit reported was $2.5 \mu\text{g mL}^{-1}$ using contactless conductivity detection.

Mahabadi et al. (2010) optimized capacitively coupled contactless conductivity detector for NH_4^+ , K^+ , Ca^{2+} , Na^+ , Mg^{2+} , Li^+ , Br^- , Cl^- , NO_2^- , NO_3^- , SO_4^{2-} and F^- ions. The detection limits ranged from 1.5 to $0.3 \mu\text{M}$. The detection limit and number of ions analyzed indicated quite a good detection. There are many papers on contactless conductivity detection in nano-capillary electrophoresis. These are beyond the scope of this article. The interested readers should consult a review on this topic (Pumera 2007).

Applications of nano-capillary electrophoresis in the environmental analyses

The analyses of the environmental pollutants are carried out by two steps. These are sample preparation and separation, respectively. These are discussed in the following subsections. Jokerst et al. (2012) presented a review on microfluidics for the environmental analyses. The authors discussed sample preparations, detections, microchip integrations, applications and future directions. It was observed that review describes both nano chromatography and nano electrophoresis while the present review is dedicated to nano-capillary electrophoresis only.

Sample preparation

The environmental samples contain many compounds and impurities. Besides, low concentrations of the analytes are out of the detection limits of the conventional instruments. Sometimes, the environmental samples are also in low amount such as at explosion sites. Therefore, sample preparation is an integration part in the analyses of various pollutants before nano-capillary electrophoresis. Of course, the classical way of sample preparation may be applied in nano-capillary electrophoresis, but these are time-consuming and costly. Contrarily, the hyphenation strategies with nano-capillary electrophoresis provide fast and automated analyses within short time and few efforts. Moreover, online coupling of sample preparation techniques with nano-capillary electrophoresis is capable to deal with samples having extremely low concentrations. It is due to low chances of concentration loss of the analytes in online sample preparation techniques.

Furthermore, online sample preparation methods reduce the chances of laboratory chemicals contamination. In view of these facts, some researchers attempted to couple the sample preparation devices with nano-capillary electrophoresis (Long et al. 2007; Ramsey and Collins 2005). It has been

observed that online hyphenations of sample preparation techniques are useful for the analyses of samples having low volume and concentrations of the pollutants. These techniques are highly selective in nature and provide least interference in the analyses due to various impurities present in unknown matrices. Some reviews also appeared in the literature addressing this issue.

Ali et al. (2008) described the applications of hyphenated techniques. The state of the art of hyphenation of various techniques viz. solid-phase extraction, microsolid-phase extraction, dialysis and chromatographic modalities is discussed. Van Midwoud and Verpoorte (2008) reported the sample pre-concentration techniques in microfluidic devices. The authors discussed miniaturization of well-known techniques such as conventional capillary electrophoresis and high-performance liquid chromatography. Sueyoshi et al. (2008a) reported various online sample preparation techniques with special emphasis on partial filling technique. The researchers named it as transient trapping. Yamamoto et al. (2008) discussed field-amplified stacking, micellar sweeping, isotachopheresis, perm-selectivity and solid-phase extraction as pre-concentration techniques for nano-capillary electrophoresis. Furthermore, the authors presented research on highly effective pre-concentration of anionic samples using sulfonate-type polyacrylamide gel fabricated in situ photopolymn.

Sueyoshi et al. (2008b) described the advances of online sample pre-concentration-based dynamic and static methods. The dynamic techniques comprised field-amplified stacking, isotachopheresis, sweeping and focusing. The authors provided applications and sensitivity enhancements of these pre-concentration techniques. Chun-Chee et al. (2011) described microchip-based pre-concentration techniques and their working mechanisms. The authors also discussed the strategies for improvement of the detection limits. Giordano et al. (2012) presented online sample pre-concentration as a necessary step in chip-based separation techniques. The authors emphasized to develop more advanced hyphenation techniques to improve the detection limits and removal capacities. These researchers tried to acquaint readers with some options for concentrations enhancements.

Kitagawa et al. (2012) discussed developments and applications of online sample pre-concentration techniques to improve detections. The authors emphasized on the sample pre-concentrations due to the changes in the migration velocities of the analytes in two or three discontinuous solutions systems. These workers described online sample pre-concentration methods for nano-capillary electrophoresis, i.e., field strength or chemically modified changes in the migration velocities. The techniques, comprising exploiting field strength-induced changes in velocity, were field-amplified sample stacking, isotachopheresis and transient

isotachopheresis. On the other hand, the techniques involving chemically induced changes were sweeping, transient trapping and dynamic pH junction. Giordano et al. (2012) discussed various sample preparation techniques with emphasis on fundamental principles. Both electrophoretic and non-electrophoretic modes of pre-concentration are discussed.

Gong et al. (2006) developed a sample pre-concentration unit by introducing sample buffer plug. It was observed that the detection sensitivity was improved by 94, 108 and 160 times for fluorescein-5-isothiocyanate, fluorescein disodium and 5-carboxyfluorescein, respectively. Sueyoshi et al. (2008c) presented an online sample pre-concentration technique, which was called as transient trapping. It had improved the efficiencies of nano-capillary electrophoresis. The authors presented theoretical model of a trap-and-release mechanism enabling a short micellar zone. It was partially injected into separation channel for effective concentration and separation field. Nano-capillary electrophoresis with tr-trapping was used on fabricated 5-way-cross microchip using sodium dodecyl sulfate and rhodamine dyes. The separation of dye was achieved within 3.0 s only. It was observed that tr-trapping technique resulted in rapid and high resolution with short analyses time.

A layout and dimensions of solid-phase extraction-nano-capillary electrophoresis is shown in Fig. 3 (2007) indicating coupling of solid-phase extraction with nano-capillary electrophoresis. Coupling was found suitable for the analyses of several analytes including dyes. From the above discussion, it was observed that sampling should be carried out to avoid any change in the chemical compositions of the analytes. The concentrations of the species depend on the strategy adopted in the sample preparations. Of course, online sample preparation methods are good

choices for nano-capillary electrophoresis. Much work has been carried out on online nano sample preparation techniques. However, there are still some issues to be addressed, which include economy, eco-friendly and applicability in the real-life samples.

Separation and identification of the pollutants

There are many pollutants present in our environment. These are of organic, inorganic and biological origins. Generally, these pollutants are present in the environment at trace levels (Ali and Aboul-Enein 2004, 2006). Therefore, nano-capillary electrophoresis is the best technique for the analyses of these contaminants. Moreover, nano-capillary electrophoresis is suitable for the analyses of ions and other charged species (Wakida 2001). Some publications appear in the literature in this area. Method development is very important issue in nano-capillary electrophoresis for the analyses of the pollutants. It begins with the selection of suitable sample preparation, background electrolyte, applied voltage, detector, sample injection, etc.

First of all, suitable sample preparation method is developed and optimized. The structures of the pollutants to be monitored are explored with selection of detection mode. In case of ultraviolet-sensitive pollutants, the $\lambda_{\max}$ values are characteristic features and need to be determined. The selection of background electrolyte is carried out by keeping in mind the wavelength cut of the buffers. Generally, 10 kilovolts is starting potential followed by its optimization as per the requirements. The analyses of the different environmental pollutants by nano-capillary electrophoresis are discussed in the following subsections.

Fig. 3 A schematic representation of the integrated solid-phase extraction-nano-capillary electrophoresis with **a** photograph of the multilayer device, **b, c** micrograph and schematic diagram of the packed microsolid-phase extraction column between two shallow weirs (Long et al. 2007)

Metal ions

Some heavy metals are notorious water contaminants with high toxicities and carcinogenicities (Stoeppler 1992; Duffus 2002). Moreover, most of these exist at trace level and out of the scope of the detection of the conventional instruments. Therefore, nano-capillary electrophoresis is the best technique for determination of such low concentration metal ions. Some research papers are available on metal ion analyses by this modality of capillary electrophoresis.

Vogt et al. (2005) reported detection of sodium, potassium and lithium by a chip concept, in terms of stability and reproducibility of separation and detection. The relative standard deviations obtained were lower than 1 and 3 % for migration times and peak heights. Kutter et al. (1998) reported magnesium and calcium by nano-capillary electrophoresis after sample stacking and on-chip complexation with 8-hydroxyquinoline-5-sulfonic acid. Feng et al. (2004) described a portable nano-capillary electrophoresis system with potential gradient detection for the analyses of alkali metals sodium, potassium and lithium. The separation conditions were buffer (10 mM Tris, 5 mM acetic acid, pH 4.5), sample loading at 2 kilovolts for 10 s and applied voltage 2 kilovolts. As per the authors, design of the system had many advantages such as simplicity, miniaturization and wide applicability.

Hui et al. (2006) reported separation and identification of barium and magnesium ions by nano-capillary electrophoresis within 30 s. The experimental conditions were 1.5 kV applied potential, sodium acetate background electrolyte and inductively coupled plasma ionization detection. The separation was good as shown in Fig. 4. The authors also described instrumentation as an interface of nano-capillary electrophoresis—inductively coupled plasma on poly(dimethylsiloxane) chip. A stainless steel tube was placed orthogonal onto the exit of nano-

capillary electrophoresis separation channel for cross-flow nebulization with a supplementary flow of buffer solution at channel exit. The nebulization and transport efficiency of nano-capillary electrophoresis—inductively coupled plasma interface were approximately 10 %. Rohlíček and Deyl (2002) reported the standard operations such as washing, preconditioning, separation and inner surface modification of chip channel. A chip of maximum dimension (30 × 60 mm) was used for the analyses of cations. It was also observed that other dimensions of chips required only a minimum adjustment of equipment viz. setting of chip sliding rails and adequate arrangement of the exchangeable heads.

The applications of equipment were demonstrated for the analyses of sodium, potassium and lithium cations. The experimental conditions were electrokinetic injection at 200 V for 5 s, 20 mM morpholinoethanesulfonic acid-20 mM His (pH 5.5) background electrolyte and applied voltage 600 V.

Henares et al. (2007) reported a novel drop-and-sip technique of fluid handling for the analyses of divalent cations [Ca(II), Zn(II) and Mg(II)] by nano-capillary electrophoresis. Nano-capillary electrophoresis was integrated with plural different reagent-release chips, acting as various biochemical sensors. Yuan et al. (2012) described a nano-capillary electrophoresis method for the determination of Hg(II). Background electrolyte used was 0.25 % bromophenol blue with 40 % Ficoll 400. Instrument was operated at 150 V. Liu et al. (2012) developed a nano-capillary electrophoresis method for the analyses of Mn(II), Cd(II), Co(II) and Cu(II) using 2-morpholinoethanesulfonic acid and histidine as background electrolyte constituents. The optimization was achieved by varying background electrolyte concentrations and conductivity detection conditions. The best separation of metal ions achieved was at 20 volts within 100 s with 0.7–5.4 μM as concentration detection limits. It was observed from these findings that the method is fast, inexpensive and capable to detect metal ions at low concentrations.

Some elements ions exist in different oxidation states having different toxicities. For example, As(III) is 60 times toxic than As(V). Therefore, speciation is an important area to determine the exact toxicities of elements. Besides, the changes in oxidation states of elements also have crucial affects on the degree of bioavailabilities and toxicities (1922). Therefore, some papers describe speciation of elements using nano-capillary electrophoresis.

Li et al. (2005a) carried out speciation of arsenic using online nano-capillary electrophoresis hyphenation with hydride generation atomic fluorescence spectrometry. The task was achieved within 54 s. Microchannel used was 90 mm long. The working conditions were 2500 V as applied potential with a mixture of 25 mM H_3BO_3 and 0.4 mM cetyl trimethyl ammonium bromide (pH 8.9) as

Fig. 4 Electropherograms of barium and magnesium ions by nano-capillary electrophoresis (Hui et al. 2006). ICP inductively coupled plasma

background electrolyte. As per the authors, precision (relative standard deviation, $n = 5$) ranged from 1.9 to 1.4 % for migration time, 2.1 to 2.7 % for peak area and 1.8 to 2.3 % for peak height for two arsenic species (Fig. 5), showing good speciation within 55 s. Similarly, Matusiewicz and Ślachciński (2012) used hydride generation nano-capillary electrophoresis for arsenic speciation. A baseline separation of As(III) and As(V) was obtained within 70 s using borate buffer and cetyl trimethyl ammonium bromide (pH 9.5) as background electrolyte on 26-mm-long channel. The applied voltage was 2.8 kilovolt. The relative standard deviations of peak height, based on six determinations of 50 ng mL⁻¹ standard of As(III) and As(V), were 5 and 7 %, respectively. The detection mass limits (in absolute units) were 3.9 and 5.4 ng mL⁻¹ for As(III) and As(V), respectively.

Li et al. (2005b) used a hybrid technique for fast speciation of Hg(I) and MeHg(II) by directly interfaced nano-capillary electrophoresis with atomic fluorescence spectrometry. Both the species were separated as their cysteine complexes within 64 s. The precisions (relative standard deviation, relative standard deviation, $n = 5$) of peak area, migration time and peak height for 2.0 mg L⁻¹ Hg(II) and 4.0 mg L⁻¹ MeHg(I) (as Hg) were ranged from 2.1 to 2.9 %, 0.7 to 0.9 % and 1.5 to 1.8 %, respectively.

Pesticides

Pesticides are toxic, carcinogenic and tissue degradative in nature. Generally, pesticides damage liver and nervous systems. Besides, some pesticides are also enzyme disturbing leading to different types of diseases. The different permissible limits of pesticides are prescribed by different agencies. But their occurrence in water, even at trace level, may be hazardous to human beings. Therefore, nano-capillary electrophoresis is a suitable technique to monitor pesticides at trace level.

Fig. 5 Electropherogram of arsenite and arsenate species by nano-capillary electrophoresis (Li et al. 2005b)

Wang et al. (2001) used nano-capillary electrophoresis with amperometric detector for the analyses of organophosphorus pesticides (paraoxon, methyl parathion, fenitrothion and ethyl parathion). The separation time was 140 s. The experimental conditions were 20 mM morpholinoethane sulfonic acid (pH 5.0) containing 7.5 mM sodium dodecyl sulfate, separation voltage 2000 V, injection voltage 1500 V, injection time 3 s and detection potential -0.5 V (vs Ag/AgCl). Furthermore, the same group (2002) used nano-capillary electrophoresis for separating organophosphonate nerve agents (sarin and soman) and degradation products (alkyl methylphosphonic acids) with contactless conductivity detection. The authors used their method to monitor these agents in river water sample within 50 s. Shin et al. (2006) described a miniaturized fluorescence detection chip in nano-capillary electrophoresis for the analyses of atrazine. The photodiode fluorescence filter was fixed in poly(dimethylsiloxane) microfluidic chip. It was kept just below the microfluidic channel. A mixture of 570 nM fluorescence-labeled atrazine and 700 nM anti-atrazine antibody was injected, which was separated in 25-mm-long microfluidic channel.

Islam et al. (2012, 2015) reported a simple and rapid nano-capillary electrophoresis amperometric detection method for the analyses of simazine, atrazine and ametryn in soils and groundwater samples. The capillary was filled with 1.5 % agarose for good separation. The experimental conditions were 100 voltage, 200 mM KCl in methanol as background electrolyte and pulsed amperometric detection. The electropherograms of simazine, atrazine and ametryn were appeared at 58, 66 and 74 s, respectively. In another attempt, the same group (2015) determined triazine herbicides (simazine, atrazine and ametryn) in agriculture soils using nano-capillary electrophoresis. The experimental conditions were 200 mM KCl as background electrolyte, applied voltage 100 V and amperometric detection. The electropherogram of simazine, atrazine and ametryn appeared at 59, 67 and 71 s, respectively. It was realized from the findings of these papers that the developed methods are rapid, inexpensive and reproducible.

These may be used to determine these herbicides in other environmental samples. It was observed from the results of these two publications that the separation of herbicides was quite good. Furthermore, these methods may be applied to monitor the reported herbicides in other environmental samples such as water, sediment and air.

Polycyclic aromatic hydrocarbons

Polycyclic aromatic hydrocarbons are widely dispersed organic environmental pollutants including water, air and food stuffs. Some polycyclic aromatic hydrocarbons are genotoxic, mutagens and carcinogens (European commission 2002; International Agency for Research on Cancer

1983, 1987; Rojas et al. 2004). Polyaromatic hydrocarbons enter into the human body via air, water and food, leading to various health problems. Generally, these pollutants are found in the environment at low concentrations. Therefore, nano-capillary electrophoresis is the best technique to monitor their exact concentrations.

Recently, Ferey and Delaunay (2015) presented a review on the priority pollutants polyaromatic hydrocarbons using nano-capillary electrophoresis. The authors discussed the different approaches for the analyses of these pollutants by nano-capillary electrophoresis. Amanda et al. (2009) described the analyses of nine polycyclic aromatic hydrocarbons using portable nano-capillary electrophoresis. The experimental conditions were 10 mM sulfobutylether- β -cyclodextrin, 40 mM methyl- β -cyclodextrin, 5 mM carbonate (pH 10.0) as background electrolyte. Seven and two polycyclic aromatic hydrocarbons were separated in extraterrestrial and terrestrial matters, respectively. The developed method was used to determine these polycyclic aromatic hydrocarbons in Lake Erie, chimney sample from the Guaymas Basin and Yungay Hills region of the Atacama Desert. It was observed that analyzed polycyclic aromatic hydrocarbons were 9,10-diphenylanthracene, anthracene, anthanthrene, fluoranthene, perylene and benzo[ghi]fluoranthene. Furthermore, a critical evaluation of this method confirmed its applicability in real-life samples.

Benhabib et al. (2010) reported multichannel mars organic analyzer, a portable nano-capillary electrophoresis for analysis of polycyclic aromatic hydrocarbons. Nano-capillary electrophoresis comprised a four-layer microchip of eight analysis systems integrated with a microfluidic network for autonomous fluidic processing. The developed method was used to monitor benzo[a]pyrene and perylene polyaromatic hydrocarbons in Lake Erie. It was concluded from this paper that the developed method had improved detections with fully integrated autonomous operations. Furthermore, this work may be used in future for the successful analysis of polycyclic aromatic hydrocarbons in the environment.

Explosives

In the last few years, the terrorist activities have increased greatly globally. The terrorists are using new technology-based explosives containing various chemicals. Additionally, the military operations are also contaminating our environment using explosives. Generally, the explosives concentrations are low in the atmosphere after blast. The analyses of aerosols for explosives are gaining impetus nowadays. Therefore, an analytical method of low injection amount and detection is required. This facility is provided by nano-capillary electrophoresis. Therefore, this modality

of electrophoresis has great status in forensic science. In view of these facts, some researchers attempted to develop nano-capillary electrophoresis methods for the separation and identification of various explosives in the environment.

Pumera (2006b) presented a review article on the analyses of explosives using nano-capillary electrophoresis. The most important explosives described in this article are (i) compounds containing unstable peroxide group (triacetone triperoxide), (ii) nitrated organic compounds [2,4,6-trinitrotoluene, hexahydro-1,3,5-trinitro-1,3,5-triazine, methyl-2,4,6-trinitrophenylnitramine (tetryl), nitroglycerin and (iii) inorganic nitrate, chlorate, or perchlorate salts (NH_4NO_3 , KNO_3 or NH_4ClO_4). Of course, nitrated organic explosives are being used for centuries. Nowadays, 1,3,5-trinitroperhydro-1,3,5-triazine and octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine are very popular and powerful explosives. These are being used globally in various activities.

Wang et al. (2002a) reported separation and identification of pre- and post-blasts cations and anions using nano-capillary electrophoresis within 60 s. Low electromotive force of poly-(methyl methacrylate) chip material facilitated the rapid switching between analyses of cations and anions using the same microchannel and run buffer. It has also provided fast measurement of seven explosive-related cations and anions. Furthermore, the same workers (2002a, b, c) discussed the future advancement of nano-capillary electrophoresis for the detection of triacetone triperoxide. The advantages of ultraviolet degradation of triacetone triperoxide to hydrogen peroxide and microfluidic amperometry method had been highlighted for fast separation and detection of organic peroxides. Furthermore, Wang et al. (2002b) reported dual electrochemical microchip detection system having two orthogonal detection modes viz. conductivity and amperometry. These modes facilitated the measurements of inorganic and nitroaromatic explosive components on single-channel microchip. Total assay of explosive mixture took 2 min time.

Bromberg and Mathies (2003) reported an homogeneous immunoassay for detection of 2,4,6-trinitrotoluene and its analogues. The assay was based on fast separation of an equilibrated mixture of an anti-2,4,6-trinitrotoluene antibody, fluorescein-labeled 2,4,6-trinitrotoluene and unlabeled 2,4,6-trinitrotoluene or its analogue. Limit of mass detection (in absolute units) was 1.0 ng mL^{-1} . Furthermore, Bromberg et al. (2004) described high-throughput homogeneous immunoassay for detection of 2,4,6-trinitrotoluene using nano-capillary electrophoresis. Limit of mass detection (in absolute units) achieved was 1.0 ng mL^{-1} .

Ding et al. (2008) described analyses of chemical warfare agent and their degradation products using poly(dimethylsiloxane) microchip electrophoresis with contactless conductivity detection. The detected molecules were five alkyl methylphosphonic acids, isopropyl methylphosphonic acid,

pinacolyl methylphosphonic acid, *O*-ethyl-*N,N*-dimethyl phosphoramidate, ethyl methylphosphonic acid and methylphosphonic acid. Under optimized conditions, analysis was completed within 2.0 min time. The detection limit ranged from 1.3 to 4.5 mg L⁻¹. The reported method was applied to natural water resources such as lake and tap waters.

Viruses and bacteria

Nano-capillary electrophoresis may be an ideal technique to monitor viruses and bacteria in the environment due to its miniaturization nature. Monitoring of viruses and bacteria by nano-capillary electrophoresis is of great concern in water-borne disease (Ebersole and McCormick 1993). Therefore, use of nano-capillary electrophoresis in routine monitoring of viruses and bacteria seems to be remarkably striking (Vrouwe et al. 2007; Weiss et al. 2007; Zhuang et al. 2007). These pathogens are monitored due to their dissimilar movements without the need for time-consuming sample preparation (1993).

Huang et al. (2006) used integrated microfluidic chip of poly(dimethylsiloxane) and soda-lime glass for monitoring bacteria *Streptococcus pneumoniae* and ribonucleic acid of dengue-2 virus. The authors claimed their method applicable in the fields of molecular biology, genetic analysis, infectious disease detection, etc. Zhou et al. (2004) reported monitoring of syndrome corona virus by nano-capillary electrophoresis. The assembly consisted of laser-induced fluorescence microfluidic chip analyzer, glass microchip [for both polymerase chain reaction and capillary electrophoresis], chip thermal cycler [(based on dual Peltier thermoelectric elements, a reverse transcription-polymerase chain reaction), syndrome corona virus diagnostic kit and deoxyribonucleic acid electrophoretic sizing kit. As per the authors, assembly allowed efficient deoxyribonucleic acid amplification of syndrome corona virus followed by electrophoretic sizing and detection on the same chip.

Tsai and Su (2006) developed a microreverse transcription-polymerase chain reaction chip for quantitative monitoring of tumor viruses. The authors integrated test sample reservoirs, a reverse transcription-polymerase chain reaction meanders and nano-capillary electrophoresis on a monolithic chip. Kolivoska et al. (2007) monitored human rhinovirus serotype 2 on a commercially available nano-capillary electrophoresis. The authors labeled proteinaceous capsid of human rhinovirus serotype 2 with cystine 5 for the detection via red laser (λ_{max} 630 nm). The resolution of sample was improved on adaptation of the separation conditions, mainly by adjusting sodium dodecyl sulfate concentration of background electrolyte. The same workers (2007) described monitoring of viral capsids and human rhinovirus serotype 2 and subviral particles using

nano-capillary electrophoresis with fluorescence detector. Lagally et al. (2004) described monitoring of various bacterial strains within a 10 min.

Law et al. (2007) presented fast microchip electrophoretic method for monitoring rapid identification of purified enteropathogenic *Escherichia coli* bacteria. The separation was achieved on poly(dimethylsiloxane) chip using laser-induced fluorescence detection within 2.0 min time. The method was optimized using applied voltage, concentration of buffer and buffer modifier, injection voltage and duration of injection. Furthermore, Law et al. (2009) described the monitoring of enteropathogenic *Escherichia coli* bacteria. As per the authors, sample preparation was important in this study. The separation was achieved on poly(dimethylsiloxane) chip using laser-induced fluorescence detection.

Miscellaneous pollutants

Besides the above-discussed pollutants, some other environmental contaminants have also been analyzed by nano-capillary electrophoresis. Wang et al. (2005) used nano-capillary electrophoresis for the analyses of phenolic and other related compounds. The authors optimized separation by sample flow rate, applied voltages and background electrolytes. It was observed that peak intensity was independent of flow rate. Le Saux et al. (2006) studied the binding constants of 2-naphthalenesulfonate and some phenols (phenol, 4-chlorophenol and 4-nitrophenol) with β -cyclodextrin using nano-capillary electrophoresis. The authors discussed issue of competitor choice in relation to its appropriateness for proper monitoring of interaction. Fleger et al. (2004) presented a method for analysis of sulfanilazochromotrop dye. The authors also described a coupling between multimode polymer wave guides and microfluidic channels on a poly(methyl methacrylate)—nano-capillary electrophoresis with optical detection. It was observed that peak was sharp.

Edel et al. (2004) described separation of fluorescent dyes on a thin-film polymer light emitting diodes as integrated excitation source in nano-capillary electrophoresis. Nikcevic et al. (2007) evaluated molded poly-(methyl methacrylate) chips as potential candidates for electrophoresis. The performance of single-lane plastic microchip electrophoresis separation was evaluated using a mixture of two fluorescein and fluorescein isothiocyanate dyes. The reproducibility of average migration time ratios of fluorescein and fluorescein isothiocyanate on different chips is shown in Fig. 6. Ujiie et al. (2000) used quartz chips for separation of rhodamine B and sulforhodamine at 14.4 and 66.6 cm separator lengths. Buffer used was 20 mM phosphate at 2 kilovolts applied voltage. The separation was achieved within 70 s. Nuchtavorn et al.

Fig. 6 Representation of reproducibility of average migration times ratio of fluorescein and fluorescein isothiocyanate for different chips (Nikcevic et al. 2007)

(2013) used nano-capillary electrophoresis for separation of methylene blue, Nile blue, toluidine blue and brilliant cresyl blue using 26–90 mM NH_4OAc , 26–70 mM NaOAc , 26–70 mM LiCl and 15–40 mM $\text{Ca}(\text{NO}_3)_2$ and 870 mM acetic acid in dimethyl sulphonamide as background electrolyte. The optimization was achieved using methanol and acetonitrile. Sampling was done by electrokinetically at 1400 V for 50 s. The separating voltage was 1500 V at 25 °C. An excellent separation was observed within 50 s running time. Furthermore, it was observed that method may be used for monitoring these dyes in any environmental sample.

Feng et al. (2004) used portable nano-capillary electrophoresis for the analyses of alkaloids such as strychnine and brucine. The separation was achieved using 40 mM ammonium acetate buffer, 0.1 % acetic acid and 50 % methanol as background electrolyte, sample loading at 2 kilovolts for 30 s and applied voltage of 2 kilovolts. It was observed that both alkaloids separated within 4 min. Gertsch et al. (2010) described online analysis of perchlorate in drinking water using portable nano-capillary electrophoresis. The surfactants used were sulfobetaine, i.e., *N*-hexadecyl-*N,N*-dimethyl-3-ammonio-1-propane sulfonate and *N*-tetradecyl-*N,N*-dimethyl-3-ammonio-1-propane sulfonate. The authors optimized method by varying various parameters. It was observed that variation in the concentrations of surfactants resulted in the best separation. The detection used was conductometry with mass detection limits (in absolute units) of 3.4 and 5.2 ppb in standard and real-water samples, respectively. It was observed from this work that the method is fast and selective and requires minimum amount of sample.

Masar et al. (2012) reported the determination of chloride, sulfate and nitrate in drinking water by nano-capillary electrophoresis. The authors used isotachophoretic pre-concentration technique for sample preparation. An aspartate background electrolyte (pH 4.2) containing *bis*-,

tris-propane and *N*-dodecyl-*N,N*-dimethyl-3-ammonio-1-propanesulfonate was used. The limits of mass detection (in absolute units) were 40–120 ng mL^{-1} . The developed method was reproducible leading to a precise quantitation of the analytes. It was observed that the reported ions were separated baseline within 7.5 min. Lu et al. (2004) determined cyanide in vapor and liquid phases by nano-capillary electrophoresis within 40 s. The detection was carried out by laser-induced fluorescence for monitoring fluorescent isoindole derivative formed by the reaction of cyanide with 2,3-naphthalene dicarboxaldehyde and taurine. Some other applications of nano-capillary electrophoresis in the environmental analyses are given in Table 1.

Optimization

As usual optimization is the backbone of any analytical method. The same is true in case of nano-capillary electrophoresis. Optimization provides fast separation, low amount of injection, low limit of detection and minimum amount of energy and manpower consumption. Therefore, it is the most important aspect in nano-capillary electrophoresis methods. The most crucial parameters to be optimized in nano-capillary electrophoresis include types of buffers, concentration of buffers and pHs of buffers. Besides, applied voltage and amount of injection are also important for optimization. Sometimes, size of chip and capillary chip length and diameters may be exploited to achieve the best separation of the analytes. Generally, a moderate voltage is maintained in nano-capillary electrophoresis for good separation. For the best separation, background electrolyte conductivity must be higher than samples that can be achieved using buffers as background electrolyte. Besides, the main function of buffers is to maintain pH of background electrolyte, responsible for maximum separations.

Most commonly used buffers in nano-capillary electrophoresis include phosphate, acetate, borate and ammonium citrate. These are used with different concentrations and pHs. The electrolyte identity and concentration should be chosen cautiously for the best possible analyses. The selection of the background electrolytes depends on their conductivities and types of the pollutants to be analyzed. The relative conductivities of different electrolytes can be estimated from their conductivities (defined as the concentration of sodium chloride, which has the same electrical conductance as the substance under study).

Generally, low ultraviolet absorbing compounds are used for preparing buffers in case of ultraviolet detection. During write up of this article, it was observed that most of the applications of nano-capillary electrophoresis are with mass spectrometric detection. Therefore, volatile components are required for high sensitivity and long lives of these detectors.

Table 1 Applications of nano capillary electrophoresis for analyses of the environmental pollutants

S. no.	Environmental pollutants	Matrices	Microchips	Experimental conditions	Detectors and mass detection limits (in absolute units)	References
1.	Calcium and magnesium	Lab. synthesized sample	Glass	20 mM MES–20 mmol Histidine	LIF, 20–40 nM	Rohlicek and Deyl (2002)
2.	Chromium(III), cobalt and copper	Lab. synthesized sample	PDMS	1 % H ₂ O ₂ and 5 mM TDPO in pure acetonitrile	Chemiluminescence, 493 nM	Liu (2003)
3.	Cobalt and copper	Lab. synthesized sample	Fused silica	1 × 10 ^{−3} M luminol & 2 × 10 ^{−2} phosphate buffer (pH 4.50)	Chemiluminescence, 12.5 nM	Huang et al. (2001)
	Copper metal ion	Envtl. water	Glass	20 mM pH 6.0 Tris, 3.10 × 10 ^{−5} M, RBPpOH, 10 % acetonitrile, injection voltage: 400 V; Sample loading time: 40 s; separation voltage: 900 V	LIF	Meng et al. (2010)
3.	Arsenic	Drinking and mineral water	Glass	6.3 × 10 ^{−5} M ammonium molybdate, 5.0 × 10 ^{−6} M ammonium vanadate, 0.01 M sulfuric acid and 1.0 × 10 ^{−4} M CTAB	89 nM	Som-Aum et al. (2008)
4.	Cr(VI)	Surface water	Glass	Buffer containing 1,5-diphenylcarbazine	LED, 50 ppb	Alves-Segundo et al. (2001)
5.	Sodium, potassium, calcium, magnesium, ammonium, fluoride, chloride, nitrate and sulfate	Bottled drinking water	PMMA	MES-His buffer at 10 and 30 mM	Contactless conductivity, 2.9–22 µg/L	Mahabadi et al. (2010)
6.	Sodium, potassium, ammonium, chloride, nitrate, monomethylammonium and perchlorate	Air explosives	PMMA	MES/Histidine (20 mM, pH 6.1)	Contactless conductivity, 50–80 µM	Wang et al. (2003)
7.	Sodium, potassium, ammonium, chloride, nitrate, monomethylammonium and perchlorate	Air explosives	PMMA	20 mM MES-20 mM His (pH 6.1)	Contactless conductivity	Wang et al. (2004)
8.	Sodium, ammonium and monomethylammonium	Lab. synthesized sample	PMMA	20 mM MES/Histidine (pH 6.1)	Contactless conductivity	Muck et al. (2004)
9.	Sodium, potassium, lithium, fluoride, chloride & dihydrogen phosphate	Lab. synthesized sample	PMMA	50 mM acetic acid/10 mM Histidine at pH 4.2	Contactless conductivity, 1.5 to 24 µM	Gaudry et al. (2014)
10.	Sulfate, nitrate, chloride and oxalate	Air	PDMS	17 mM picolinic acid, a sulfate-binding electrolyte cation (19 mM), a zwitterionic surfactant with affinity toward weakly solvated anions (19 mM <i>N</i> -tetradecyl, <i>N,N</i> -dimethyl-3-ammonio-1-propanesulfonate)	Contact conductivity, 19 nM	Noblitt et al. (2009)
11.	Chloride, nitrate, perchlorate, chlorate & hexafluorophosphate oxalate, acetylenedicarboxylate, malonate, succinate, glutarate, adipate, and pimelate.	Lab. synthesized sample	PDMS	10 mM nicotinic acid/0.05 wt % Triton X-100 (pH 3.6), 150 V & 1.40-s injection	Conductivity, 71–500 nM	Noblitt and Henry (2008)
12.	Tetrabutylammonium iodide	Lab. synthesized sample	Glass	–	Ion-trap MS	Ramsey and Ramsey (1997)
13.	Fluorescent dye	Lab. synthesized sample	PDMS	Ester dimethyl sulfoxide buffer	Fluorescence	Jiang et al. (2010)
14.	Fluorescein, rhodamine B and rhodamine 6G	Lab. synthesized sample	Glass	10 mM Hepes (adjusted with 2 M NaOH to pH 7), 0.1 % Tween 20, and 0.1 % HPMC	Fluorescence	Kohlheyer et al. (2008)
15.	Rhodamine dyes	Lab. synthesized sample	Glass	Sodium borate buffer (pH 9.2)	TOF-MS	Lazar et al. (2000)
16.	Butyl rhodamine B	Lab. synthesized sample	Glass	Bis(2-carboxyphenoxy)-3,5,6-trichlorophenyl oxalate and H ₂ O ₂ in different ratio	Chemiluminescence, 10 ^{−9} M	Shen et al. (2006)

Table 1 continued

S. no.	Environmental pollutants	Matrices	Microchips	Experimental conditions	Detectors and mass detection limits (in absolute units)	References
17.	Rhodamine B and fluorescein	Lab. synthesized sample	Glass	20 mM MES/histidine solution at pH 6.35	Fluorescence	Zalewski et al. (2008)
18.	Naphthalene, phenanthrene and pyrene	Lab. synthesized sample	Glass	Glass, 5 mM NaCl, 50 % (v/v) acetonitrile	UV	Constantin et al. (2001)
19.	Anthracene, pyrene, 1,2-benzofluorene and benzo[a]pyrene	Lab. synthesized sample	Quartz	Quartz, Gradient, 10 mM Tris (pH 8.2) with 52 % (v/v) acetonitrile for 10 s and 56 % (v/v) ACN until the end of the analysis	LIF, 1–8.1 nM	Broyles et al. (2003)
20.	Naphthalene, acenaphthylene, acenaphthene, fluorene, phenanthrene, anthracene, fluoranthene, pyrene, benzo[a]anthracene, chrysene, benz[b]fluoranthene, benzo[k]fluoranthene, benzo[a]pyrene, dibenz[a,h]anthracene, benzo[g,h,i] perylene, indeno[1,2,3-cd]pyrene	Lab. synthesized sample	Monolith	Glass, 20 mM Tris (pH 8.5), 80 % (v/v) ACN	LIF	Fintschenko et al. (2001)
21.	Naphthalene, acenaphthylene, fluorene, anthracene, fluoranthene, pyrene, benzo(a)-anthracene, chrysene 7benzo(a)pyrene	Lab. synthesized sample	Glass	5 mM phosphate buffer (pH 6.8)	Fluorescence	Augustin et al. (2007)
22.	2,4,6-Trinitrotoluene	Lab. synthesized sample	Glass	10 mM phosphate, pH 7.6	Fluorescent, 1.0 ng/mL	Bromberg and Mathies (2003)
23.	2,4,6-Trinitrotoluene	Lab. synthesized sample	PDMS	Triacetate buffer containing ethanol, glycerol, and Tween 20	Fluorescent, 1.0 ng/mL	Bromberg and Mathies (2004)
24.	Explosive compounds (TNB, DNB, NB, TNT, tetryl, 2,4-DNT, 2,6-DNT, 2-, 3-, and 4-NT, 2-Am-4,6-DNT & 4-Am-2,6-DNT)	Soil	Glass	50 mM borate, pH 8.5, 50 mM SDS, 5 μ M Cy7, applied voltage 1–4 kV.	Epifluorescence, 1 mg mL ⁻¹	Wallenborg and Bailey (2000)
25.	Endocrine disruptor phenolic compounds (bisphenol, nonylphenol, phenyl phenol & octylphenol)	Air explosives		10.0 mM H ₃ PO ₄ 110.0 mM SDS 1 1.0 M urea (low-pH BGE, pH 2.1)	Amperometric detection, 7.1 and 11.1 fM	Wang et al. (2002a, b, c)
26.	Dissolved organic carbon (BOD, COD & TOC)	Surface water	Polymethylm ethacrylate	CHES (0.1 M) and Tris (0.1 M), pH 9.0	Laser-induced fluorescence	Shen et al. (2010)
27.	Phenolic endocrine disruptors	Drinking and surface water	Glass	70.0 mM phosphate buffer solution (pH 8.5) and 10.0 mM H ₃ PO ₄ 110.0 mM SDS 1 1.0 M urea (low-pH BGE, pH 2.1)	Electrochemical, 7.1–11.1 fM	Noh et al. (2010)
28.	Haloacetic acids (dichloroacetic acid, haloacetic acid & monochloroacetic acid)	Recreational water	PDMS	Acetate & borate buffers of different concs. & pHs, separation potential 11,200 V	Contactless conductivity, 38–500 ppb	Ding and Rogers (2010)
29.	<i>E. coli</i>	Recreational water	PMMA	Phosphate buffer of different concs. & pHs	6–10 cfu/mL	Dharmasiri et al. (2010)
30.	Aldehydes	Air	Glass	25 mM SDS (pH 9.2) & added with 20 % ACN & 10 % 1-propanol, separation voltage 2500 V	Electrochemical, 7.2–9.2 mM	Dossi et al. (2009)
31.	<i>E. coli</i>	Lab. synthesized sample	PDMS	0.1 M acetate buffer (pH 4.5)	0.2 cfu/mL	Beyor et al. (2009)
32.	Endocrine disruptors	Water in Styrofoam containers	PDMS	30 mM 2-(N-morpholino) ethanesulfonic acid (MES)	Amperometric, 59 nM	Ha et al. (2009)

ACN Acetonitrile, BGE background electrolyte, BOD biological oxygen demand, CTAB cetyl trimethyl ammonium bromide, CHES 2-(cyclohexylamino)ethanesulfonic acid, COD chemical oxygen demand, Cy7 cyanine 7, ECD electron capture detector, ED electrochemical detection, DNB *p*-dinitrotoluene, DNT 2,4-dinitrotoluene, HPMC hydroxypropyl methylcellulose-50, LED light-emitting diode, LDI laser desorption ionization, LIF Light-induced fluorescence, MS Mass detector, MCE Microchip electrophoresis, MES 2-(N-morpholino) ethanesulfonic acid, NB nitrobenzene, NCE nano-capillary electrophoresis, NESI, nano flow electrospray ionization, PDMS poly(dimethylsiloxane), PGD potential gradient detection, PMMA poly(methyl methacrylate), PSA prostate-specific antigen, RDX hexahydro-1,3,5-trinitro-1,3,5-triazine, SDS sodium dodecyl sulfate, TDPO bis[2-(3,6,9-trioxadecanoyloxycarbonyl)-4-nitrophenyl] oxalate, TOC total organic carbon, TOF-MS time-of-flight mass detector, TNB 1,3,5-trinitrobenzene, TNT trinitrotoluene, μ -TAS micrototal analysis system, UV ultraviolet

This limitation restricts the choice of electrolytes. The required pH also determines the type of buffers. Generally, phosphate and citrate buffers are used for low pH values. Basic buffers such as borate and tris-, *N*-cyclohexyl-3-aminopropanesulfonic acid are used as the suitable background electrolytes for high pH values. Due to the above-cited facts, every researcher optimized separations in nano-capillary electrophoresis, but out of them some have described optimization strategies in their papers. During the write up of this article, we found some optimization procedures, which are described in the following paragraphs briefly.

Wang et al. (2002c) described nano-capillary electrophoresis optimization of paraoxon, methyl parathion, fenitrothion and ethyl parathion. The optimized parameters were morpholinoethane sulfonic acid buffer as background electrolyte, a 72-mm-long separation channel and an applied voltage. The effects of voltage, buffer concentration and pH and sodium dodecyl sulfate concentrations were studied. The best separations occurred at 155–2500 voltage, morpholinoethane sulfonic acid buffer (20 mM, pH 5.0) with 10 mM sodium dodecyl sulfate concentration. The authors applied this method for detection of the reported analytes in the river water samples. The implications of on-site environmental monitoring and fast security screening/warning were highlighted.

Nuchtavorn et al. (2013) presented optimization strategies for the best separation of methylene blue, Nile blue, toluidine blue and brilliant cresyl blue using different organic solvents as organic modifiers. The authors used 60 % methanol, 60 % acetonitrile and 100 % dimethyl sulphonamide. The results are shown in Fig. 7. It is clear from this figure that the best separation was with 100 % dimethyl sulphonamide. These authors also used different background electrolytes, i.e., ammonium acetate, sodium acetate, lithium chloride and calcium nitrate. It was observed that the best separation was with 80 mM ammonium acetate. Similarly, Masar et al. (2012) used four

Fig. 7 Effect of different organic modifiers on the separation of basic blue dyes, MB methylene blue, TB toluidine blue, NB Nile blue and BC brilliant cresyl blue (Nuchtavorn et al. 2013)

different background electrolytes for an excellent separation of chloride, sulfate and nitrate ions in drinking water. It was observed that the best separation was using background electrolyte having background anion (18 mM aspartate), counterion (5.94 mM bis-tris propane), additive [0.1 % methylhydroxyethylcellulose] and complexing agent (50 mM α -cyclodextrin) at pH 4.19.

Mechanism of separation

As usual small cations have high charge/densities (q_i/r_i) ratio and, hence, large ionic mobilities. The principally striking electrophoretic property should be responsible for rapid separations with high efficiency. It is rare unless the special precautions are taken care. The different charges on various species may be advantageous for their separations in nano-capillary electrophoresis due to charge-controlled migration. In nano-capillary electrophoresis, sample injection, separation in capillary and detection are integrated on single chip with anode and cathode electrodes at the inlet (sample loading) and detector sides, respectively. Hence, the molecules with positive charges move from anode to cathode and detected by a suitable detector.

The movements of species from anode to cathode are controlled by the electrophoretic and electroosmotic mobilities. Therefore, migration of charged molecules is restricted by the sum of electrophoretic and electroosmotic mobilities. The electrophoretic mobilities of the species depend on their charges and the sizes. Contrarily, there is no relation among the charges, sizes and electroosmotic mobility. The species with different charge/radii ratios move at different electrophoretic velocities under the influence of applied voltage. Greater charge/radius ratio is responsible for larger mobility. It leads to low migration time. Consequently, species with high charge is eluted first followed by smaller charge species. The electroosmotic mobilities for all the species remain almost same but help their migration toward cathode.

In this way, charged molecules eluted with various migration times due to the collective effects of the different electrophoretic and electroosmotic mobilities. Additionally, the interactions of the species with capillary wall via dispersion interactions, steric effects, van der Waals forces, etc. also play important roles for the diverse mobilities of the species.

Future challenges and prospectives

Of course, nano-capillary electrophoresis is an emerging modality of capillary electrophoresis. It is gaining good reputation in the separation science. Some authors (Chin et al. 2007; Castro and Manz; 2015; Manz 2008; Mijatovic et al. 2005; Pennathur et al. 2008) reviewed the future

challenges and prospectives of nano-capillary electrophoresis. During write up of this article, it was observed that nano-capillary electrophoresis is not fully developed. It needs more advancement for the analyses of all the environmental pollutants. It has certain drawbacks such as difficult to analyze neutral pollutants.

Moreover, it is tedious to analyze neutral pollutants in the complex fluids. Besides, coupling with detectors, washing and injection procedures and working stability are still not fully developed. Imprecise injection, limited separation efficiency, early stage of commercialization and low sensitivity of absorption detection may be considered as other drawbacks. But it is believed that future developments will solve this limitation. The sample injection alignment, chip interface and detection need more advancement to tackle the limitations of nano-capillary electrophoresis. The perfect surface modification of chip channel may be helpful for acceptable electromotive force for the analyses of neutral pollutants. Furthermore, total integration of microcapillaries, valves, flow and pressure sensors may be good developments.

Besides, hyphenations of sampling techniques and detectors are straight away required. In spite of all these challenges, the separation and identification of the environmental pollutants by nano-capillary electrophoresis are gaining importance continuously due to pressing demand at trace levels. Moreover, nano-capillary electrophoresis is extremely inexpensive modality of electrophoresis. Hence, raising cost of chemicals and economic pressure are also compelling scientists to use nano-capillary electrophoresis. All these facts dictate bright future of nano-capillary electrophoresis. Interestingly, nano-capillary electrophoresis has a great and thrilling future for the analyses of various molecules on celestial bodies such as Mars, Europa, Titan, Enceladus and Moon. It is due to its portability, high sensitivity, high integration, automatization, broad range of applications and low amount of power and chemical requirements.

Conclusion

Of course, notable developments have occurred in nano-capillary electrophoresis with some applications in the different disciplines of science and technology. The analyses of several pollutants can be carried out in small samples or matrices with extremely low concentrations. But till date nano-capillary electrophoresis has been used for the analyses of few pollutants only. Therefore, it is urged that nano-capillary electrophoresis methods should be developed for the analyses of all types of the pollutants. The capability to monitor virus and bacteria is a unique feature of nano-capillary electrophoresis, especially for water-borne diseases. Really, monitoring of the pathogens

by nano-capillary electrophoresis is of great concern for the welfare of our society. In fact, nano-capillary electrophoresis is still not fully developed and under its development stage. Many mysteries of the environmental science may be explored after complete development of nano-capillary electrophoresis instrument.

Definitely, nano-capillary electrophoresis will be a commanding and practical technique for nano analyses of the various pollutants in the near future. Briefly, nano-capillary electrophoresis is a big accomplishment in separation science with bright future. Let us hope for the best future of nano-capillary electrophoresis.

Compliance with ethical standards

Conflict of interest There is no conflict of interest.

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