Available online at www.sciencedirect.com
SCIENCE DIRECT®
Talanta 64 (2004) 1018–1023
Talanta
www.elsevier.com/locate/talanta

Miniaturized capillary electrophoresis system with a carbon nanotube microelectrode for rapid separation and detection of thiols

Gang Chen [a,*], Luyan Zhang [a], Joseph Wang [b]

[a] *Department of Chemistry, Fudan University, 138 Yi-xue-yuan Road, Shanghai 200032, PR China*
[b] *Department of Chemistry and Biochemistry, New Mexico State University, Las Cruces, NM 88003, USA*

Received 30 January 2004; received in revised form 23 April 2004; accepted 27 April 2004
Available online 9 June 2004

Abstract

Multi-walled carbon nanotube (CNT) was mixed with epoxy to fabricate microdisc electrode used as a detector for a specially designed miniaturized capillary electrophoresis (CE)–amperometric detection system for the separation and detection of several bioactive thiols. The end-channel CNT amperometric detector offers favourable signal-to-noise characteristics at a relatively low potential (0.8 V) for detecting thiol compounds. Factors influencing the separation and detection processes were examined and optimized. Four thiols (homocysteine, cysteine, glutathione, and *N*-acetylcysteine) have been separated within 130 s at a separation voltage of 2000 V using a 20 mM phosphate running buffer (pH 7.8). Highly linear response is obtained for homocysteine, cysteine, glutathione, and *N*-acetylcysteine over the range of 5–50 μM with detection limits of 0.75, 0.8, 2.9, and 3.3 μM, respectively. Good stability and reproducibility (R.S.D. < 5%) are obtained reflecting the minimal adsorption of thiols at the CNT electrode surface. The new microchip protocol should find a wide range of bioanalytical applications involving assays of thiol compounds.

Keywords: Miniaturization; Capillary electrophoresis; Amperometric detection; Carbon nanotube; Homocysteine; Cysteine; Glutathione; *N*-Acetylcysteine

1. Introduction

Aminothiols are of physiological importance as biological agents and metabolites. The levels of these compounds in biological matrices such as plasma and urine are valuable biomarkers in a number of clinical situations. Increased levels of homocysteine and cysteine are associated with risk of cardiovascular diseases [1]. The ratio of glutathione to glutathione disulfide indicates the redox status of cells [2]. In addition, *N*-acetylcysteine is an important mucolytic agent used to reduce the viscosity of pulmonary secretions in respiratory diseases [3]. Liquid chromatography (LC) is the most widely used method for the determination of thiols in biological fluids [4–6] and pharmaceutical formulations [3]. Another important instrument strategy for the determination of thiols is capillary electrophoresis (CE) coupled with laser-induced fluorescence [7,8] or electrochemical [9,10] detector. A substantial challenge to the development of electrochemical methods for thiol detection was that the direct oxidation of thiols at solid electrodes is slow and usually large overpotentials are required [10]. This problem is alleviated by indirect detection on mercury amalgam electrodes [9] and a coenzyme pyrroloquinoline quinone modified carbon electrode [10] at detection potential of 0.1 and 0.3 V (versus Ag/AgCl electrode), respectively. Recently, it has been reported that the carbon nanotube (CNT) modified electrode exhibited efficient electrocatalytic activity to the oxidation of cysteine and glutathione when it was used as an amperometric detector of LC [11]. Zhao et al. have demonstrated the electrocatalytic oxidation of cysteine at CNT by cyclic voltammetry and reported the kinetics parameters of the process [12]. Since Iijima reported the existence of CNT in 1991 [13], it has been of great interest to scientists for many applications due to its attractive electronic, chemical, and mechanical properties [14]. The unique properties of CNT make them extremely attractive for electrochemical detection (ED) [15]. Recent investigations demonstrated that CNT shows strong electrocatalytic activity and minimization of surface fouling when it was employed to improve the electrochemical response of some important

* Corresponding author. Tel.: +86 21 6466 1130; fax: +86 21 6564 1740.
E-mail address: gangchen@fudan.edu.cn (G. Chen).

0039-9140/$ – see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.talanta.2004.04.022

bioactive substances [16–19]. A variety of carbon nanotube electrodes have been fabricated for sensing different redox compounds including CNT modified screen-printed carbon electrode [20], CNT powder microelectrode [21], CNT/Teflon composite electrodes [22], CNT screen-printed electrode [23], etc. To our best knowledge, there are no early reports on CNT-based detectors for conventional CE systems. The ability of CNT to promote the electron-transfer reaction of some important compounds and resistance to surface fouling suggest it a promising material to fabricate electrochemical detector for micromachined CE systems.

During the past decade, microfluidic analytical systems have undergone an explosive growth. Much attention has been paid to CE microchips owing to their advantages of high performance, design flexibility, reagent economy, high throughput, miniaturization, and automation [24,25]. These microchip analysis systems hold considerable promise for biomedical and pharmaceutical analysis, clinical diagnostics, environmental monitoring, and forensic investigations. They can dramatically change the scale and speed at which chemical analysis is performed. Electrochemical detection offers great promise for CE microchips, with features that include high sensitivity, inherent miniaturization of both the detector and control instrumentation, low cost, low-power demands, and high compatibility with micromachining technologies [26,27]. The performance of CE–ED microchips is strongly influenced by the working electrode material. The working electrode should provide favorable signal-to-background characteristics as well as a reproducible response. A range of materials including platinum, gold, and various forms of carbon have thus been found useful for chip-based electrochemical detection [26,27].

In this work, CNT–epoxy composite has been pressed into fused silica capillary to fabricate microdisc electrode. It was employed as the end-column amperometric detector of a miniaturized CE system for the detection and separation of four bioactive thiols. The new CNT-based CE detector offers favorable signal-to-background characteristics, good resistance to surface fouling, strong electrocatalytic activity, and sharp peaks for thiols. The fabrication details and performance of the new miniaturized CE–ED protocol for monitoring thiol compounds are discussed and demonstrated in the following sections.

2. Experimental

2.1. Reagent and solutions

DL-Homocysteine, L-cysteine, reduced glutathione, and *N*-acetyl-L-cysteine were all obtained from Sigma (St. Louis, MO, USA). Other chemicals were analytical grade. Stock solutions (10 mM) of all thiols were made in doubly distilled water (Medical Center of Fudan University, Shanghai, China). Samples were made by diluting stock solutions with appropriate amount of running buffer prior to use. The graphite powder and the multi-walled carbon nanotube (MWCNT, 2–15 nm diameter, 1–10 μm length), with a ~95% purity, were both supplied by Aldrich (Wilwaukee, WI, USA).

2.2. Apparatus

Details of the high-integrated miniaturized CE–ED system were similar to a previous system [28]. A ±30 kV high-voltage dc power supply (Shanghai Institute of Nuclear Research, China) provided a voltage between the ends of the capillary. The inlet of the capillary was held at a positive potential with the outlet of capillary in detection cell effectively grounded. The separations proceeded in an 8.5 cm length fused silica capillary fixed on a glass plate. In order to prevent the operator from shocking by the high voltage and assure the safety of the CE system, the entire CE system was enclosed in a Plexiglas box with a safety switch wired to terminate the high-voltage output whenever the box was opened. An YS73-4A-3-KVA alternate constant-voltage power supply (Shanghai Keyi Instrumental Factory, Shanghai, China) was employed to suppress the voltage fluctuation of the power line.

2.3. Fabrication of the miniaturized CE system

The laboratory-built miniaturized CE–ED system shown in Fig. 1 was constructed using a 25 mm × 75 mm × 1 mm microscope glass slide (g) as a base plate. An 8.5 cm length of 25 μm i.d., 360 μm o.d. fused silica capillary (Polymicro Technologies, Phoenix, AZ, USA) was used as the separation channel. It was inserted into three 1.5 cm length stainless steel tubes ((c), (f), and (i); 0.40 mm i.d., 0.67 mm o.d.) made of hypodermic stainless steel needles. Subsequently, the tubes and an Ag/AgCl wire (d) were glued onto the glass slides (g) by quick epoxy as shown in Fig. 1. After the epoxy was sealed, the capillary was removed. And then, a small ring made of the inner part of the cap of a 1.5 ml polypropylene microcentrifuge tube was glued onto the glass slide with the Ag/AgCl wire and one end of the two stainless steel tubes ((c) and (f)) accommodated inside the cell to serve as the detection cell (e). The metal tubes (c), (f), and (i) served as grounding electrode, auxiliary electrode, and high-voltage electrode, respectively. They also allowed accurate alignment of detection electrode (b) and capillary (h) coaxially in the detection cell. All of the metal tubes were connected to copper wires (a) by conductive silver epoxy (Chemtronics, Kennesaw, GA, USA). The end of the capillary in the detection cell is the outlet. Sample solution was introduced into the capillary from the inlet of the capillary electrokinetically. The metal tube (Fig. 1A (i)), around the inlet of capillary, served as a contact to the high-voltage power supply. The metal tube (i) and inlet of capillary were both immersed into a 0.7 ml microcentrifuge polypropylene tube (Fig. 1A (j)) containing the sample or run-buffer solution (for the sampling and separation steps, respectively).

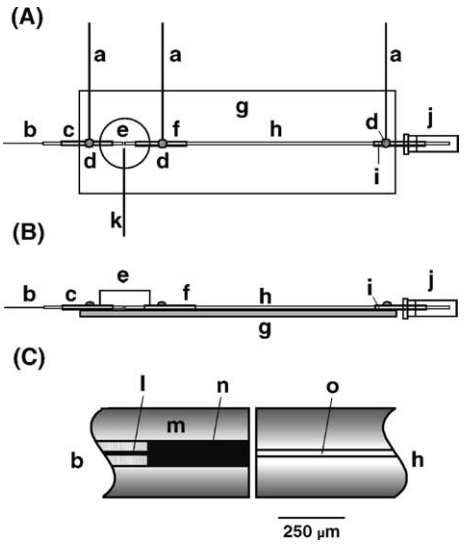

Fig. 1. (A) Top and (B) side views of the schematic diagrams of the high-integrated miniaturized capillary electrophoresis system coupled with amperometric detection. Also shown (C) the interface between microdisc electrode (b) and separation capillary (h). (a) Copper wire; (b) microdisc detection electrode; (c) grounding tube electrode; (d) conductive epoxy; (e) detection cell; (f) auxiliary tube electrode; (g) microscopic glass plate; (h) 25 μm i.d. fused silica capillary; (i) high-voltage tube electrode; (j) plastic vial for running buffer or sample solution; (k) Ag/AgCl wire reference electrode; (l) 50 μm diameter copper wire; (m) 100 μm i.d. fuse silica capillary; (n) carbon nanotube–epoxy or graphite–epoxy composite microdisc electrode; and (o) separation channel.

The channel inlet was held at a positive potential while the outlet was maintained at a ground potential. The solution in the vial was retained by the surface tension although the orientation of vial mouth is horizontal.

2.4. Electrode fabrication

A piece of copper wire (Fig. 1C (l); 6 cm long, 50 μm diameter) was inserted into a 3.0 cm long fused silica capillary (Fig. 1C (m); 100 μm i.d.×360 μm o.d., Polymicro Technologies, Phoenix, AZ, USA) and a 1.5 mm opening was left in the capillary for the subsequent filling of the CNT–epoxy or graphite–epoxy composite. The other end of the capillary was sealed together with copper wire by quick epoxy. Epoxy resin and hardener (Zhejian Cixi Tiandong Adhesive Co. Ltd., Ningbo, China) was mixed thoroughly at a volume ratio of 2:1. The MWCNT powder and epoxy resin/hardener were hand-mixed in a ratio of 1:1 (w/w). The CNT–epoxy composite was subsequently packed into capillary by pressing the opening end of capillary (to a depth of ∼1.5 mm) into a sample of the composite. The CNT–epoxy composite should touch the copper wire inside the capillary tightly for conductive contact (as shown in Fig. 1C). The composite was then allowed to cure at 60 °C for 3 h. The graphite–epoxy composite electrode used for comparison was prepared in the same procedures.

2.5. End-column amperometric detection

Before use, the microdisc electrode was successively polished with emery paper and alumina powder, sonicated in doubly distilled water, and finally the surface of microdisc electrode (Fig. 1A (b)) was positioned carefully opposite the outlet of the capillary through the guiding metal tube (Fig. 1A (c)). The distance between the electrode surface and the capillary outlet was adjusted to ∼25 μm by comparison with the bore (25 μm) in the capillary while being viewed under a microscope (Fig. 1C). The ends of metal tubes (c), (f), and (i) outside the detection cell (e) and small vial (j) were sealed by silicone grease not only to immobilize the detection electrode (Fig. 1A (b)) and separation capillary (Fig. 1A (h)), but also to prevent solutions from leaking. Electrochemical Analyzer 832 A (Shanghai Chen-Hua Instruments Co., Shanghai, China) was used to provide a constant potential to the working electrode and measure the output current in combination with the three-electrode electrochemical cell consisting of the laboratory-made microdisc working electrode (b), the auxiliary electrode (f), and the Ag/AgCl wire reference electrode (k) using the "amperometric *i–t* curve" mode. The electropherograms were recorded with a time resolution of 0.1 s (without any software filtration) while applying the detection potential. Sample injections were performed after stabilization of the baseline. All experiments were performed at room temperature.

2.6. Electrophoretic procedure

The capillary were treated before use by rinsing with 0.1 M NaOH and deionized water for 10 min each. The running buffer is 20 mM phosphate buffer (pH 7.8). The detection cell (Fig. 1A (e)) was filled with buffer solution. The sample solution was introduced into the separation channel by applying a voltage of 2000 V between the sample vial (Fig. 1A (j)) and the grounded detection cell (Fig. 1A (e)) for 2 s. Subsequently, the inlet of capillary and high-voltage electrode were immersed into the running buffer vial (Fig. 1A (j)) and the separation voltage was applied between the high voltage and grounding electrodes (Fig. 1A (c and i)) for separation running.

3. Results and discussion

The miniaturized CE set-up used was specially designed to accommodate the CNT–epoxy composite microdisc electrode for sensing several bioactive thiols. It is just composes of a self-alignment detection cell system, a sample solution or running buffer vial, and a piece of fused silica capillary. The new miniaturized CE design facilitates the analysis of multiple discrete samples through a simplified electrokinetic introduction of highly reproducible sample zones (Fig. 1A). Such horizontal introduction is carried out directly in the separation channel by alternate placement of the capillary

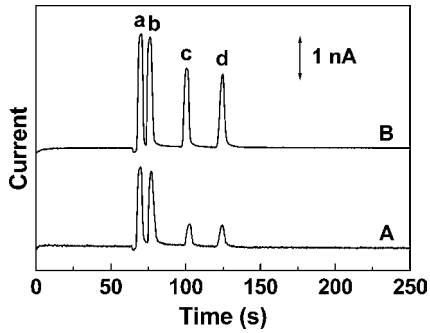

Fig. 2. Electropherograms for mixtures containing (a) 50 μM homocysteine; (b) 50 μM cysteine; (c) 100 μM glutathione; and (d) 100 μM *N*-acetylcysteine at the (A) graphite–epoxy and (B) carbon nanotube–epoxy composite microdisc electrodes. Operation conditions: separation and injection voltage, +2000 V; injection time, 2 s; running buffer, 20 mM phosphate buffer (pH 7.8); detector potential, +0.85 V (versus Ag/AgCl wire).

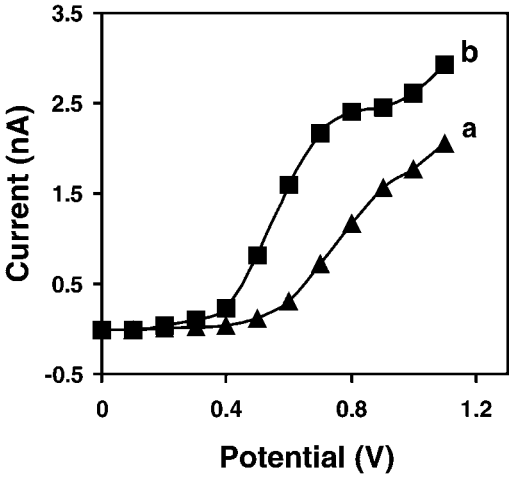

Fig. 3. Hydrodynamic voltammograms for 50 μM cysteine at (a) graphite–epoxy and (b) carbon nanotube–epoxy composite microdisc electrodes. Other conditions, as in Fig. 2.

inlet in vials containing sample or buffer solutions. This sample introduction results in the insertion of highly reproducible sample plugs and allows rapid replacement of different samples with no apparent carry-over. In the present system, two stainless steel tubes were sealed in the detection cell by epoxy with 360 μm o.d. fused silica capillary inserted inside so that they can guide the outlet of capillary to the surface of the disc electrode coaxially as shown in Fig. 1C, allowing easy and fast replacements of capillary and microdisc electrode made of capillary. It is characterized by its advantages of simple design and fabrication, high integration, reduced alignment time, and low cost. In addition, good electrode–capillary alignment can be easily achieved in a wall-jet configuration because the outer diameters of separation capillary and the capillary-based detection electrode are the same and the inner diameter of capillary to the diameter of the disc working electrode is at a ratio of 1:4. In this experiment, the distance was about 25 μm in considering the peak current, peak broadening, and background noise. As working, reference, auxiliary, grounding, and high-voltage electrode are all accommodated on a small plate, the integration of the miniaturized CE system is very high.

In the present work, the CNT–epoxy composite microdisc electrode was coupled with the specially designed CE system as an end-column amperometric detector. The attractive performance of the CNT microchip detector is indicated from detection of four bioactive thiols offering enhanced sensitivity, lower noise levels, and well-resolved peaks. The favourable signal-to-background characteristics of the CNT detector are coupled with a greatly improved resistance to surface fouling. Shown in Fig. 2 are the typical electropherograms for (a) homocysteine, (b) cysteine, (c) glutathione, and (d) *N*-acetylcysteine recorded with (A) graphite and (B) CNT composite electrode detectors. The four thiols can be separated with well-defined and resolved peaks with CNT–epoxy composite electrode used as working electrode within 130 s. It can be also observed that the current response of the four thiols at the CNT composite electrodes is much higher than that at graphite composite electrode under the same operation conditions. This may be attributed to the faster electron-transfer rate on the surface of CNT electrode. The higher sensitivity of the CNT detector is in good agreement with the hydrodynamic voltammograms (HDVs, as will be illustrated below) and leads to low detection limits. Such performance indicates that MWCNT is a promising material for fabricating detection electrode for CE microchip.

Fig. 3 depicts the typical hydrodynamic voltammograms for the oxidation of 50 μM cysteine on the (a) graphite–epoxy and (b) CNT–epoxy composite microelectrodes. The curves were recorded point-wise over the 0.0 to +1.1 V range by changing the applied potential by 0.1 V. The current response of the CNT composite electrode is higher than that of graphite composite electrode at the same potential although geometric areas of both electrodes are the same. When the applied potential exceeds +0.60 V for (a) and +0.40 V for (b), the peak current of both electrodes raises rapidly. However, the current response increases much slowly upon increasing potential above +0.90 V for (a) and +0.80 V for (b), respectively. The applied potential of the CNT working electrode was, therefore, maintained at +0.80 V (versus Ag/AgCl wire), under which condition the background current was not too high and the signal-to-noise ratio was the highest. The half-wave potentials at the (a) graphite and (b) CNT composite microdisc electrode are +0.73 and +0.54 V for cysteine. The electrocatalytic activity toward the investigated analyte is pronounced as the half-wave potentials on CNT electrode have decreased by approximately 200 mV in comparison with that on graphite electrode. The HDV of Fig. 2 indicates that the CNT electrodes allow amperometric detection with higher sensitivity and at significantly lower operating potentials. Because the background current is low at lower potentials, the stability of the electrode can be enhanced so that the

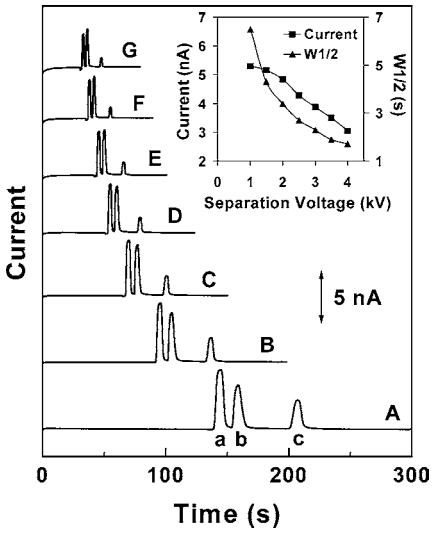

Fig. 4. Influence of the separation voltage on the response of the carbon nanotube–epoxy composite microdetector for a mixture containing 100 μM homocysteine (a); 100 μM cysteine (b); and 100 μM glutathione (c). Also shown (in the inset) are the resulting plots of the peak current and half peak width ($W_{1/2}$) of homocysteine upon the separation voltage. Separation voltage: (A) 1000 V; (B) 1500 V; (C) 2000 V; (D) 2500 V; (E) 3000 V; (F) 3500 V; and (G) 4000 V. Working potential: 0.8 V (versus Ag/AgCl wire). Other conditions, as in Fig. 2.

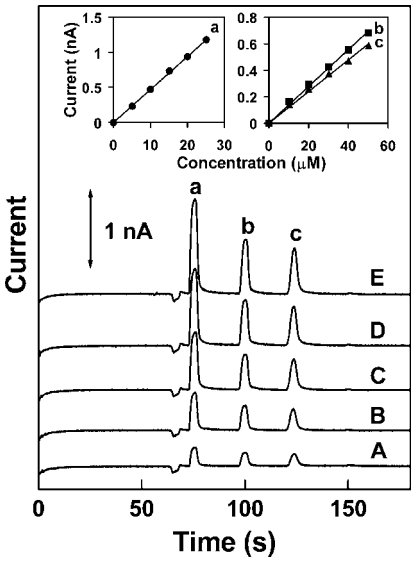

Fig. 5. Electropherograms for mixtures containing increasing levels of (a) cysteine; (b) glutathione; and (c) *N*-acetylcysteine in increments of 5 μM (for (a)) and 10 μM (for (b) and (c)) on carbon nanotube–epoxy composite microdisc electrodes. Also shown (in the insets) are the resulting calibration plots. Working potential, 0.8 V (versus Ag/AgCl wire). Other conditions, as in Fig. 2.

reproducibility is improved. The ability of carbon nanotube to promote electron-transfer reactions on the electrode has been attributed to their special electronic structure and high electrical conductivity [18].

Fig. 4 shows the influence of the separation voltage upon the separation and detection of 100 μm (a) homocysteine, (b) cysteine, and (c) glutathione. As expected, increasing the separation voltage from 1000 to 4000 V (A–G) dramatically decreases the migration time for all three thiol compounds from 33.0 to 145.5 s (homocysteine), from 36.6 to 159.7 s (cysteine), and from 47.8 to 208.0 s (glutathione). Also shown (in the inset) is the effect of the separation voltage upon the peak current and half peak width ($W_{1/2}$) of homocysteine. The current response of the homocysteine decreases in a nearly linear fashion with the increase of separation voltage indicating that the actual working potential shifted negatively upon raising the separation voltage. The peak width (at half-height) of (a) homocysteine, (b) cysteine, and (c) glutathione decreases from 6.4, 6.5, and 6.8 s to 1.6, 1.7, and 1.7 s, respectively. Note also that despite of the high detection potential, flat baselines and low noise levels are maintained even at high separation voltages. Such behavior indicates an effective isolation from the high separation voltage. Moreover, higher separation voltages may result in higher Joule heat that directly affects the separation efficiency of this method. However, too lower separation voltages will increase the analysis time considerably which in turn cause peak broadening. Based on experiments, 2000 V was chosen as the optimum voltage to accomplish a good compromise.

The CNT–epoxy composite electrode detector offers a well-defined concentration dependence. Electropherograms for mixtures containing increasing levels of (a) cysteine, (b) glutathione, and (c) *N*-acetylcysteine in increments of 5 μM (for (a)) and 10 μM (for (b) and (c)) on a CNT–epoxy composite microdisc electrode are shown in Fig. 5 (A−E). Defined peaks proportional to the concentration of the three thiols are observed. The resulting calibration plots (shown as inset) are highly linear with sensitivities of 47.4, 13.9, and 12.0 nA mM^{-1} for (a) cysteine, (b) glutathione, and (c) *N*-acetylcysteine, respectively (correlation coefficients: 0.999, 0.997, and 0.998). Detection limits of 0.8 μM cysteine, 2.9 μM glutathione, and 3.3 μM *N*-acetylcysteine were estimated from the response for a mixture containing (a) 2.5 μM cysteine, (b) 5 μM glutathione, and (c) 5 μM *N*-acetylcysteine (based on *S*/*N* of 3; not shown), indicating the favorable signal-to-noise characteristics of the CNT composite electrode. The linearity of homocysteine is similar to that of cysteine with sensitivity of 50.5 nA mM^{-1}. The corresponding detection limit was evaluated to be 0.75 μM.

Good precision is another attractive feature of the new CNT detector/separation microchip protocol. The precision was examined from a series of eight repetitive injections of a sample mixture containing 50 μM cysteine, 100 μM glutathione, and 100 μM *N*-acetylcysteine. Reproducible signals were obtained with R.S.D. of 2.1% (cysteine), 3.2% (glutathione), and 2.8% (*N*-acetylcysteine) for the peak currents. Such good precision reflects the reduced surface fouling of the CNT electrode.

In conclusion, we have demonstrated the utility and the advantages of CNT–epoxy composite amperometric

detectors coupled to the compatible high-integrated CE microsystem for the detection and separation of thiols. The advantages of the present set-up are its simple design and construction, low cost, high degree of integration, portability, high performance, and speed. The attractive properties of CNT composite microelectrode including their favourable signal-to-background characteristics, negligible adsorption, and electrocatalytic properties to bioactive thiols make the CNT microelectrode a very promising material for detection in CE systems and other micromachined flow analyzers. The new microchip protocol offers great promise for a wide range of bioanalytical applications involving assays of thiol compounds.

Acknowledgements

Financially support from the Natural Science Foundation of China (NSFC, Grant No. 20075008) is gratefully acknowledged.

References

[1] S. Yardim-Akaydin, Y. Ozkan, E. Ozkan, M. Torun, B. Simsek, Clin. Chim. Acta 338 (2003) 99.
[2] A. Meiste, M.E. Anderson, Annu. Rev. Biochem. 52 (1983) 711.
[3] B. Toussaint, C. Pitti, B. Streel, A. Ceccato, P. Hubert, J. Crommen, J. Chromatogr. A 896 (2000) 191.
[4] A.E. Katrusiak, P.G. Paterson, H. Kamencic, A. Shoker, A.W. Lyon, J. Chromatogr. B 758 (2001) 207.
[5] J. Krijt, M. Vackova, V. Kozich, Clin. Chem. 47 (2001) 1821.
[6] K. Amarnath, V. Amarnath, K. Amarnath, H.L. Valentine, W.M. Valentine, Talanta 60 (2003) 1229.
[7] P. Lochman, T. Adam, D. Friedecky, E. Hlidkova, Z. Skopkova, Electrophoresis 24 (2003) 1200.
[8] E. Causse, P. Malatray, R. Calaf, P. Charpiot, M. Candito, C. Bayle, P. Valdiguie, R. Salvayre, F. Couderc, Electrophoresis 21 (2000) 2074.
[9] S.A. Pasas, N.A. Lacher, M.I. Davies, S.M. Lunte, Electrophoresis 23 (2002) 759.
[10] T. Inoue, J.R. Kirchhoff, Anal. Chem. 74 (2002) 1349.
[11] X.N. Cao, L. Lin, Y.Z. Xian, W. Zhang, Y.F. Xie, L.T. Jin, Electroanalysis 15 (2003) 892.
[12] Y.D. Zhao, W.D. Zhang, H. Chen, Q.M. Luo, Sens. Actuators B: Chem. 92 (2003) 279.
[13] S. Iijima, Nature (London) 354 (1991) 56.
[14] R.H. Baughman, A. Zakhidov, W.A. de Heer, Science 297 (2002) 787.
[15] Q. Zhao, Z.H. Gan, Q.K. Zhuang, Electroanalysis 14 (2002) 1609.
[16] Z.H. Wang, J. Liu, Q.L. Liang, Y.M. Wang, G. Luo, Analyst 127 (2002) 653.
[17] G. Zhao, S.Q. Zang, K.Z. Liu, S. Lin, J. Liang, X.Y. Guo, Z.J. Zhang, Anal. Lett. 35 (2002) 2233.
[18] J. Wang, M. Musameh, Analyst 128 (2003) 1382.
[19] M. Musameh, J. Wang, A. Merkoci, Y.H. Lin, Electrochem. Commun. 4 (2002) 743.
[20] J. Wang, G. Chen, M.P. Chatrathi, M. Musameh, Anal. Chem. 76 (2004) 298.
[21] Y.D. Zhao, W.D. Zhang, H. Chen, Q.M. Luo, Talanta 58 (2002) 529.
[22] J. Wang, M. Musameh, Anal. Chem. 75 (2003) 2075.
[23] J. Wang, M. Musameh, Analyst 129 (2004) 1.
[24] E. Verpoorte, Electrophoesis 23 (2002) 677.
[25] D.R. Reyes, D. Iossifidis, P.A. Auroux, A. Manz, Anal. Chem. 74 (2002) 2623.
[26] J. Wang, Talanta 56 (2002) 223.
[27] W.R. Vandaveer, S.A. Pasas, R.S. Martin, S.M. Lunte, Electrophoresis 23 (2002) 3667.
[28] G. Chen, X.H. Han, L.Y. Zhang, J.N. Ye, J. Chromatogr. A 954 (2002) 267.