Versatile Platform Employing Desorption Electrospray Ionization Mass Spectrometry for High-Throughput Analysis

ARTICLE *in* ANALYTICAL CHEMISTRY · JULY 2008

Impact Factor: 5.64 · DOI: 10.1021/ac800803x · Source: PubMed

6 AUTHORS, INCLUDING:

Xiaoxiao Ma
Purdue University
16 PUBLICATIONS **341** CITATIONS
SEE PROFILE

Xinrong Zhang
Tsinghua University
188 PUBLICATIONS **6,908** CITATIONS
SEE PROFILE

Anal. Chem. **2008,** *80,* 6131–6136

Versatile Platform Employing Desorption Electrospray Ionization Mass Spectrometry for High-Throughput Analysis

Xiaoxiao Ma, Mengxia Zhao, Ziqing Lin, Sichun Zhang,* Chengdui Yang, and Xinrong Zhang*

Department of Chemistry, Key Laboratory for Atomic and Molecular Nanosciences of Education Ministry, Tsinghua University, 100084, Beijing, P. R. China

A simple and easy-to-build high-throughput analysis system was constructed. The system consisted of three major components: (1) a multichannel device with 16 parallel capillaries, (2) a desorption electrospray ionization (DESI) source, and (3) a linear ion trap mass spectrometer. When analyses were performed, the multichannel device was moved horizontally on a translation stage controlled by a step motor. Our design expands the functions of DESI, in which the liquid sample in capillary was driven out by the nebulizing gas, ionized, and then transferred to a mass spectrometer. To assess the high-throughput performance of the system, 5 mg/L 1,3-diethyl-1,3-diphenylurea (DDU) solution and 10 mg/L angiotensin I solution were alternatively loaded into the reservoirs and capillaries in the multichannel device. Results indicated that analyses of the all the samples in 16 capillaries were completed within 1.6 min, which means a throughput of 600 samples/h. Reactive DESI experiment was also successfully performed with this system to show the feasibility of online derivatization. The relative standard deviations for a single capillary and five identical capillaries were 7.6 (n = 16) and 12.3%, respectively. Linear relative abundance response was achieved for DDU (r=0.9971).

High-throughput analysis plays a key role in the acceleration of combinatorial chemistry,[1–3] drug discovery,[4–7] and environmental monitoring,[8] which presents great challenges to analytical chemistry. As a powerful instrument for structural elucidation and quantitative analysis, mass spectrometry (MS) plays an important role in high-throughput analysis and is increasingly becoming the method of choice.[9–11] Current high-throughput analytical approaches coupled with the mass spectrometer include combination of multidimensional chromatography[12,13] or 96 (384, 768, and 1536) microtiter plate[14,15] with MS. In addition, microfluidic devices used for MS analysis have also gained wide interests because the small dimensions of these devices significantly reduce sample amounts and increase separation efficiency.[16,17] Moreover, for high-throughput analysis, parallel channels can be easily fabricated in the microfluidic devices to allow for simultaneous separation and detection.[18–21]

Generally, MS is an instrument that analyzes one sample at a time. Therefore, the current high-throughput analysis system aims

Table 1. Experimental Parameters for DESI

incident angle	60°
flow rate of the solvent	5 μL/min
outlet pressure of the nebulizing gas	1 atm
dc voltage applied to the syringe tip	4000 V
capillary temperature	250[a]
capillary voltage	35 V
MS inlet to sample distance	5 mm
spray tip to surface distance	2 mm

[a] For reactive DESI experiment, a capillary temperature of 150 °C was selected.

* To whom correspondence should be addressed. Tel: +86-10-6278-7678. Fax: +86-10-6277-0327. E-mail: xrzhang@chem.tsinghua.edu.cn; sczhang@mail.tsinghua.edu.cn.

(1) Fujimoto, K.; Takahashi, H.; Ito, S.; Inoue, S.; Watanabe, M. *Appl. Surf. Sci.* **2006**, *252*, 2446–2449.
(2) Potyrailo, R. A.; Ezbiansky, K.; Chisholm, B. J.; Morris, W. G.; Cawse, J. N.; Hassib, L.; Medford, G.; Reitz, H. *J. Comb. Chem.* **2005**, *7*, 190–196.
(3) Tang, L.; Fitch, W. L.; Smith, P.; Tumelty, D.; Cao, K.; Ferla, S. W. *Comb. Chem. High Throughput Screen* **2001**, *4*, 287–293.
(4) Korfmacher, W. A. *Drug Discovery Today* **2005**, *10*, 1357–1367.
(5) Wu, S. H.; Yang, L.; Gao, Y. A.; Liu, X. Y.; Liu, F. Y. *J. Chromatogr., A* **2008**, *1180*, 99–107.
(6) Roddy, T. P.; Horvath, C. R.; Stout, S. J.; Kenney, K. L.; Ho, P. I.; Zhang, J. H.; Vickers, C.; Kaushik, V.; Hubbard, B.; Wang, Y. K. *Anal. Chem.* **2007**, *79*, 8207–8213.
(7) Gao, L.; Cheng, X.; Zhang, J.; Burns, D. J. *Rapid Commun. Mass Spectrom.* **2007**, *21*, 3497–3504.
(8) Wenner, B. R.; Douglass, P. M.; Shrestha, S.; Sharma, B. V.; Lai, S. Y.; Madou, M. J.; Daunert, S. *Adv. Fluoresc. Sensing Technol. V* **2001**, *2*, 59–70.
(9) Zhang, L. H.; Dang, F. Q.; Baba, Y. *J. Pharm. Biomed. Anal.* **2003**, *30*, 1645–1654.
(10) Aebersold, R.; Goodlett, D. R. *Chem. Rev.* **2001**, *101*, 269–295.
(11) Domon, B.; Aebersold, R. *Science* **2006**, *312*, 212–217.
(12) Pan, S.; Zhu, D.; Quinn, J. F.; Peskind, E. R.; Montjne, T. J.; Lin, B. Y.; Goodlett, D. R.; Taylor, G.; Eng, J.; Zhang, J. *Proteomics* **2007**, *7*, 469–473.
(13) Saravanabhavan, G.; Helferty, A.; Hodson, P. V.; Brown, R. S. *J. Chromatogr., A* **2007**, *1156*, 124–133.
(14) Yao, M.; Zhu, M. S.; Sinz, M. W.; Zhang, H. J.; Humphreys, W. G.; Rodrigues, A. D.; Dai, R. *J. Pharm. Biomed. Anal.* **2007**, *44*, 211–223.
(15) Zhang, B. L.; Foret, F.; Karger, B. L. *Anal. Chem.* **2001**, *73*, 2675–2681.
(16) Finkelstein, J. M. *Nature* **2006**, *442*, 254–254.
(17) Janasek, D.; Franzke, J.; Manz, A. *Nature* **2006**, *442*, 374–380.
(18) Liu, C. N.; Toriello, N. M.; Mathies, R. A. *Anal. Chem.* **2006**, *78*, 5474–5479.
(19) Shadpour, H.; Hupert, M. L.; Patterson, D.; Liu, C. G.; Galloway, M.; Stryjewski, W.; Goettert, J.; Soper, S. A. *Anal. Chem.* **2007**, *79*, 870–878.
(20) Toriello, N. M.; Liu, C. N.; Mathies, R. A. *Anal. Chem.* **2006**, *78*, 7997–8003.
(21) Bula, W. P.; Verboom, W.; Reinhoudt, D. N.; Gardeniers, H. *Lab Chip* **2007**, *7*, 1717–1722.

10.1021/ac800803x CCC: $40.75
Published on Web 06/28/2008

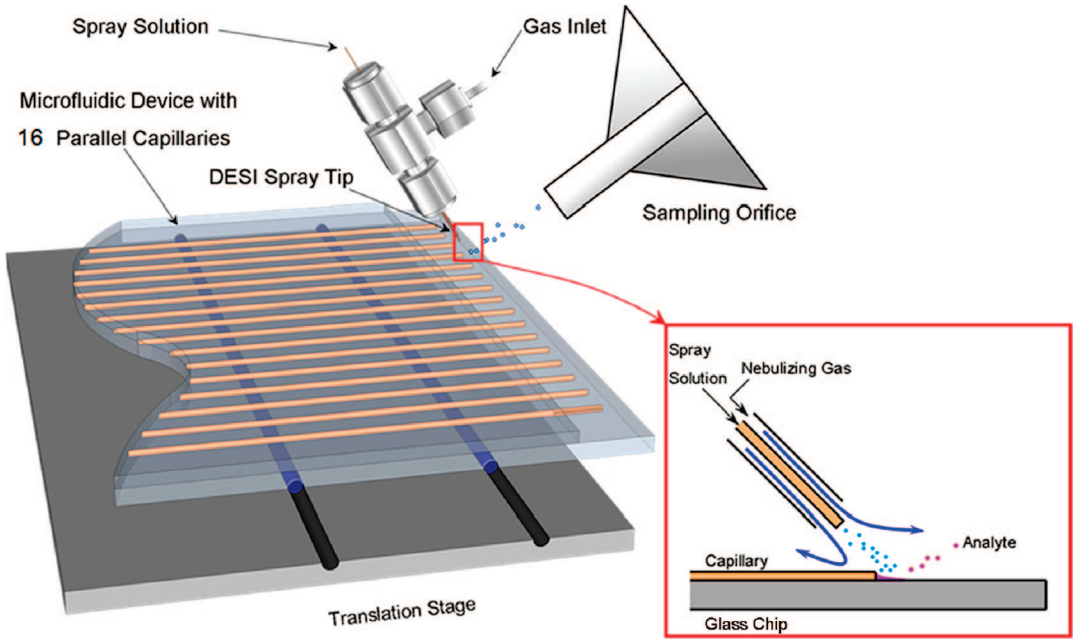

Figure 1. Overall design of coupling a multichannel device with the MS, using DESI as an interface, for high-throughput analysis. The multichannel device consisted of 2 glass chips with 16 embedded parallel capillaries (not to scale). Details are provided in the expanded side view of the device.

at improving sample introduction throughput and accelerating or multiplexing the separation process.[22–24] As a novel "soft" ionization technology, electrospray ionization (ESI) has been widely used in mass spectrometry, which can be easily coupled with various liquid chromatographies. Hitherto, there have already been various approaches to combine ESI-MS with single- and multiple-channel devices for high-throughput analysis,[15,25–28] such as single-channel CE/ESI-MS,[15] multichannel ESI-MS,[25] and multiplexed electrospray interface.[29] In these approaches, Zhang et al.[15] established a high-throughput microfabricated single-channel CE/ESI-MS system that could perform sampling from a microwell plate automatically with a subatmospheric ESI chamber. Liu et al.[25] developed a multichannel device with an array of electrospray tips inserted into channels, using a stationary HV source to connect to the electrode in a certain ESI tip for generating electrospray.

Desorption electrospray ionization (DESI) has been well established as a fast, simple, and robust ionization method under ambient conditions.[30–32] In this method, samples are unnecessary to be introduced into vacuum or an inaccessible region very close to the vacuum system, but are directly ionized under ambient conditions and carried into the MS by the nebulizing gas.[30,31] Charged droplets formed in an electrospray are directed toward a surface where their impact causes desorption of samples from the surface in the form of gas-phase ions.[30] Until now, DESI has been widely used for direct analysis of various samples such as explosives,[33] metabolites,[34,35] drugs,[34,36] and biological molecules[31,37] on various surfaces. It has also been used for direct desorption/ionization of samples from living organisms,[31,37] biological tissues,[38,39] tablets,[40,41] and thin-layer chromatography.[42,43] Based on its characteristic of ambient surface desorption/ionization, DESI has potential to be employed in high-throughput analysis by coupling with multichannel devices.

In this work, we proposed a method utilizing a DESI source to interface a multichannel device with a mass spectrometer, which could be potentially used for high-throughput analysis. To test

(22) Frycak, P.; Schug, K. A. *Anal. Chem.* **2008**, *80*, 1385–1393.
(23) Wilson, J.; Vachet, R. W. *Anal. Chem.* **2004**, *76*, 7346–7353.
(24) Yang, L. Y.; Mann, T. D.; Little, D.; Wu, N.; Clement, R. P.; Rudewicz, P. J. *Anal. Chem.* **2001**, *73*, 1740–1747.
(25) Liu, H. H.; Felten, C.; Xue, Q. F.; Zhang, B. L.; Jedrzejewski, P.; Karger, B. L.; Foret, F. *Anal. Chem.* **2000**, *72*, 3303–3310.
(26) Feng, B. B.; McQueney, M. S.; Mezzasaima, T. M.; Slemmon, J. R. *Anal. Chem.* **2001**, *73*, 5691–5697.
(27) Felten, C.; Foret, F.; Minarik, M.; Goetzinger, W.; Karger, B. L. *Anal. Chem.* **2001**, *73*, 1449–1454.
(28) Briem, S.; Pettersson, B.; Skoglund, E. *Anal. Chem.* **2005**, *77*, 1905–1910.
(29) de Biasi, V.; Haskins, N.; Organ, A.; Bateman, R.; Giles, K.; Jarvis, S. *Rapid Commun. Mass Spectrom.* **1999**, *13*, 1165–1168.
(30) Cooks, R. G.; Ouyang, Z.; Takats, Z.; Wiseman, J. M. *Science* **2006**, *311*, 1566–1570.
(31) Takats, Z.; Wiseman, J. M.; Gologan, B.; Cooks, R. G. *Science* **2004**, *306*, 471–473.
(32) Takats, Z.; Wiseman, J. M.; Cooks, R. G. *J. Mass Spectrom.* **2005**, *40*, 1261–1275.
(33) Justes, D. R.; Talaty, N.; Cotte-Rodriguez, I.; Cooks, R. G. *Chem. Commun.* **2007**, 2142–2144.
(34) Kauppila, T. J.; Talaty, N.; Kuuranne, T.; Kotiaho, T.; Kostiainen, R.; Cooks, R. G. *Analyst* **2007**, *132*, 868–875.
(35) Kauppila, T. J.; Wiseman, J. M.; Ketola, R. A.; Kotiaho, T.; Cooks, R. G.; Kostiainen, R. *Rapid Commun. Mass Spectrom.* **2006**, *20*, 387–392.
(36) Weston, D. J.; Bateman, R.; Wilson, I. D.; Wood, T. R.; Creaser, C. S. *Anal. Chem.* **2005**, *77*, 7572–7580.
(37) Wiseman, J. M.; Ifa, D. R.; Cooks, R. G.; Venter, A. *Nat. Protoc.* **2008**, *3*, 517–524.
(38) Wiseman, J. M.; Ifa, D. R.; Song, Q. Y.; Cooks, R. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 7188–7192.
(39) Wiseman, J. M.; Puolitaival, S. M.; Takats, Z.; Cooks, R. G.; Caprioli, R. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 7094–7097.
(40) Hu, Q. Z.; Talaty, N.; Noll, R. J.; Cooks, R. G. *Rapid Commun. Mass Spectrom.* **2006**, *20*, 3403–3408.
(41) Chen, H. W.; Talaty, N. N.; Takats, Z.; Cooks, R. G. *Anal. Chem.* **2005**, *77*, 6915–6927.
(42) Kauppila, T. J.; Talaty, N.; Salo, P. K.; Kotiah, T.; Kostiainen, R.; Cooks, R. G. *Rapid Commun. Mass Spectrom.* **2006**, *20*, 2143–2150.
(43) Van Berkel, G. J.; Ford, M. J.; Deibel, M. A. *Anal. Chem.* **2005**, *77*, 1207–1215.

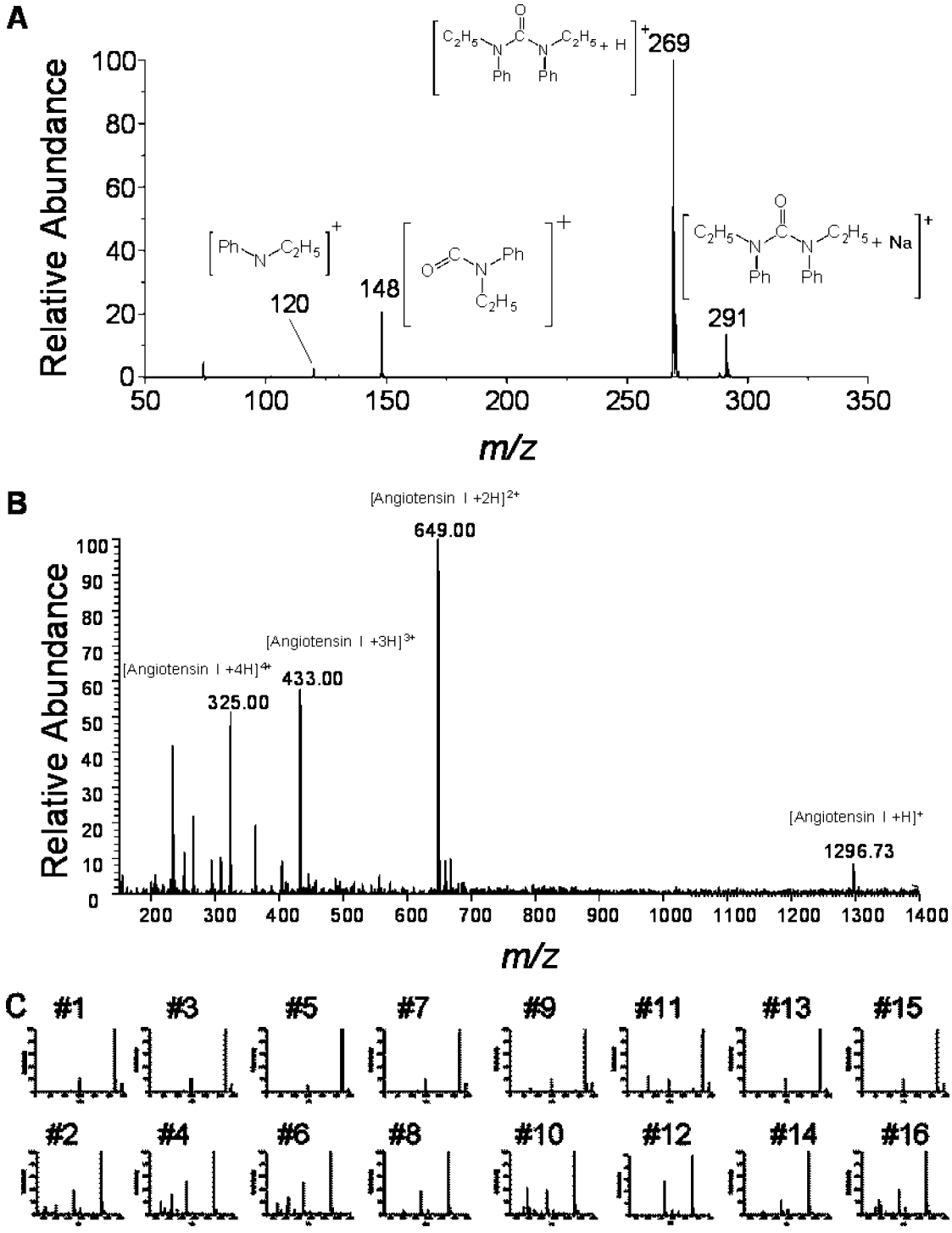

Figure 2. Five milligram per liter standard DDU solution and 10 mg/L angiotensin I human acetate alternatively loaded into sequential rows of the multichannel device. All 16 samples were analyzed using conditions as in Figure 1A and B, typical mass spectra of 5 mg/L DDU and 10 mg/L angiotensin I human acetate, respectively; (C), mass spectra of the samples in 16 capillaries on the multichannel device. Capillaries 1, 3, 5, 7, 9, 11, 13, and 15 were filled with 5 mg/L DDU solution, Capillaries 2, 4, 6, 8, 10, 12, 14, and 16 were filled with 10 mg/L angiotensin I solution.

the applicability of this method, a multichannel device with 16 capillaries was fabricated. When the outlet of a certain capillary was aimed at by the DESI tip, the high-speed nebulizing gas generated a pressure drop around it, and liquid in this capillary was driven out, ionized, and then transferred into the mass spectrometer. At the same time, liquids in other capillaries did not flow out and could not be analyzed by DESI-MS. In this way, automatic start and stop of liquid flows might be achieved without any specific interface during sequential sample analyses. We demonstrated the high-throughput performance of the system by sampling each channel for 5 s under optimized conditions. Analyses of all 16 samples were completed within 1.6 min, which means a throughput of 600 samples/h. Postcolumn online derivatization was also successfully achieved, which provides a convenient approach for the detection of analytes with low ionization efficiency.

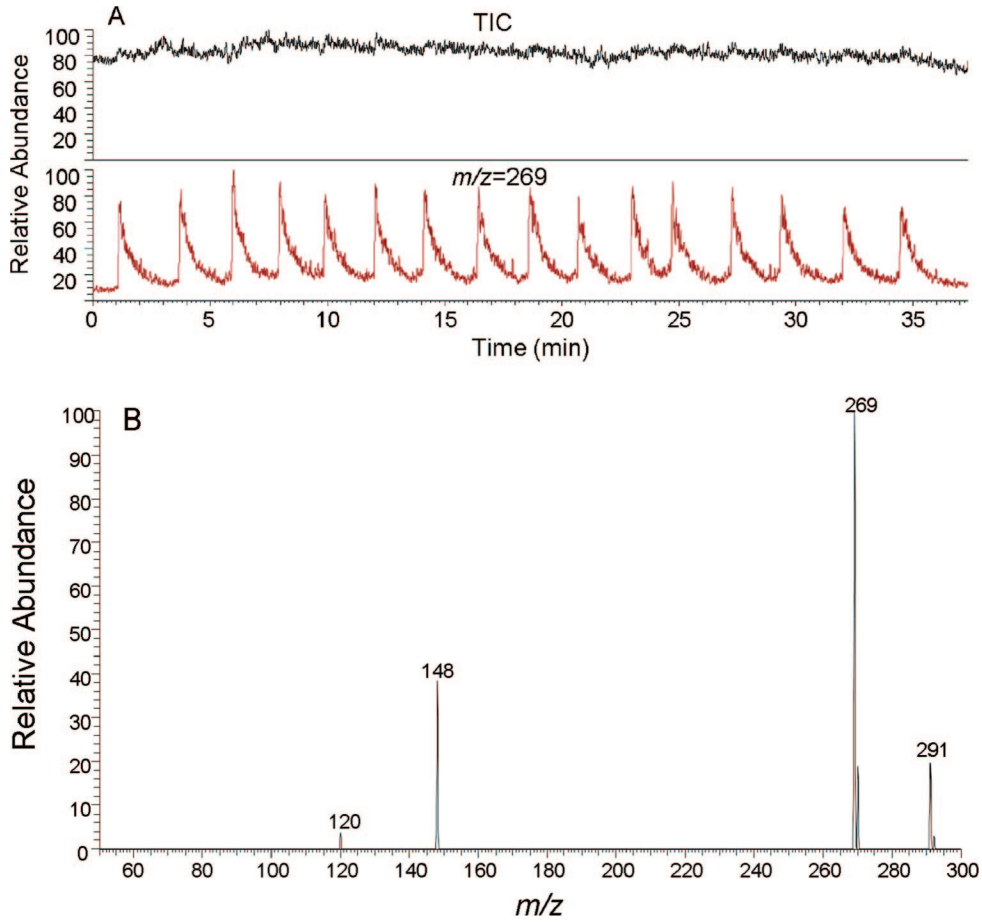

Figure 3. (A), Total ion current (TIC) and extracted ion current (*m*/*z* 269) of 16 sequential injections of 10 mg/L DDU to show the reproducibility of a single capillary coupled with the DESI-MS system. (B), Mass spectrum of DDU with the background subtracted. Carrier, water; sample volume, 50 nL. DESI-mass spectrum was smoothed with an 11-point boxcar filter.

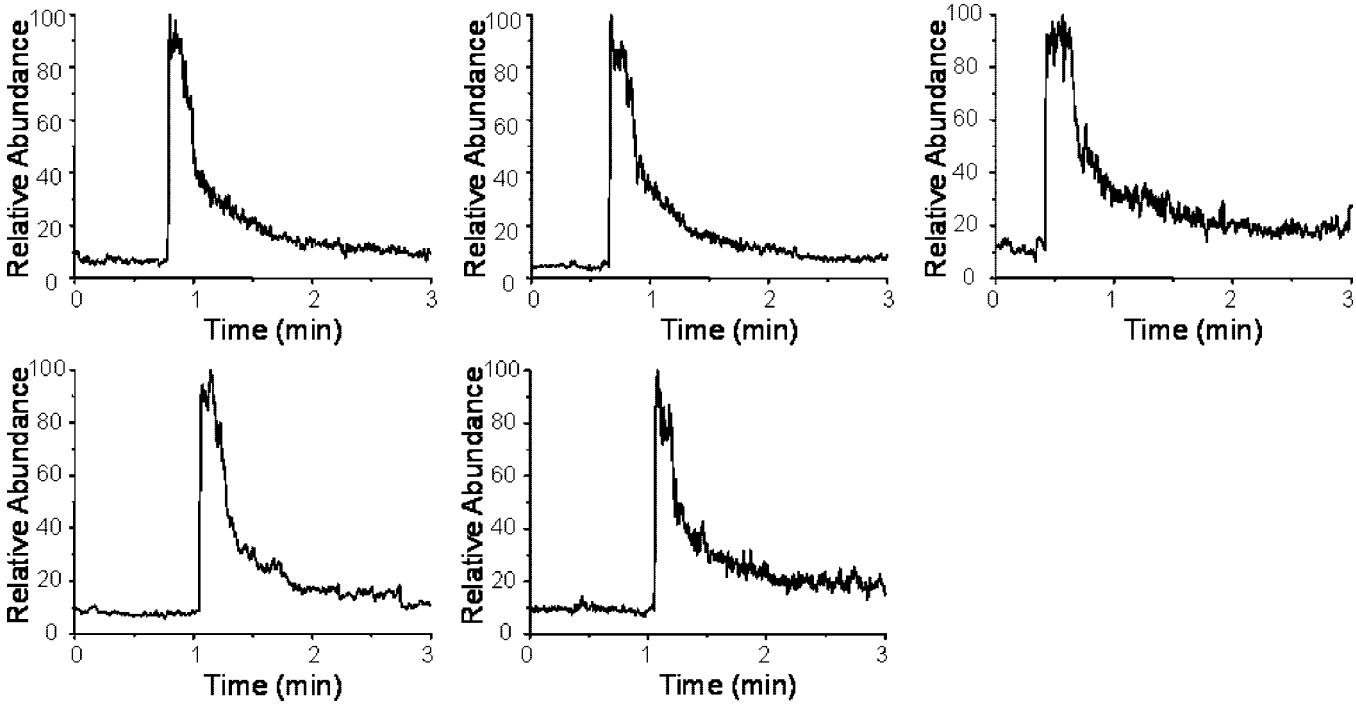

Figure 4. Extracted ion current (*m*/*z* = 269) of a single injection of 20 mg/L DDU solution to show the reproducibility among 5 different capillaries. Carrier, water; sample volume, 50 nL. DESI-mass spectra were smoothed with a 7-point boxcar filter.

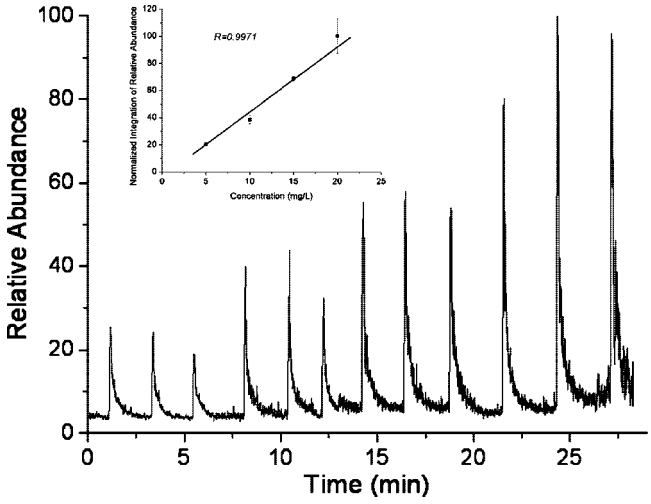

Figure 5. Typical recordings of sequential injections of 5, 10, 15, and 20 mg/L DDU solutions to show the linear relationship between the sample concentration and the extracted ion current ($m/z = 269$). (Inset was the linear regression curve showing the relative coefficient to be $r = 0.9971$.) Carrier, water; sample volume, 50 nL. DESI-mass spectrum was smoothed with a 7-point boxcar filter.

EXPERIMENTAL SECTION

Samples and Reagents. All chemicals used were of analytical-reagent grade unless otherwise specified. Water was deionized and further purified with a Milli-Q water purification system (Millipore, Milford, MA) and was used throughout all the experiments. 1,3-Diethyl-1,3-diphenylurea (DDU) and angiotensin I human acetate (Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu) were purchased from Sigma-Aldrich and dissolved in methanol and water, forming stock solutions of 50 and 100 mg/L, respectively. The stock solutions were diluted to appropriate concentrations when being used. D-Fructose and benzeneboronic acid were purchased from Alfa Aesar. All capillaries were purchased from Hebei Yongnianruifeng Chromatographic Instruments Co, Ltd. (Hebei, China).

DESI Ion Source. A home-built DESI source consisting of a gas sprayer and a manual X−Y stage was used to adjust the position and spray angle of the DESI spray tip. The spray emitter was composed of a longer inner capillary (100-μm i.d., 150-μm o.d.) and a concentric outer capillary (250-μm i.d.). The inner capillary protruded ~1 mm out from the end of the outer capillary. This distance may be manually adjusted to change their position with respect to each other by manipulation of adjustment screws. Nitrogen gas went through the circular space between the inner and outer capillaries and sprayed the solution of 50% (v/v) methanol in water in the inner capillary. The spray solution was delivered into the T union via a 250-μL syringe (Hamilton) and was biased to 4000 V via an external high-voltage (HV) power supply. The power was in electrical contact with the syringe tip, which was connected to a side port of the T union. Nitrogen gas was connected to another port of the T union to nebulize the spray solution. A solvent flow rate of 5 μL/min was used in all experiments, except otherwise specified.

Experimental Parameters of DESI-MS. Experiments were performed on a Finnigan LTQ linear ion trap mass spectrometer (Thermo Fisher Scientific, Inc., San Jose, CA) tuned for ion detection under optimized conditions. DESI and reactive DESI experiments were performed in positive and negative ion modes, respectively. For simplification, all DESI-MS experiments were performed at atmospheric pressure and room temperature.

To investigate the feasibility of the platform, a variety of compounds were tested, including amino acids, peptides, exhilarants, and other compounds (see Supporting Information). Because of its simple fragments and high sensitivity, 5 mg/L DDU was selected as a representative compound for the optimization of experimental parameters and subsequent investigations of the reproducibility and relationship between the relative abundance responses and different concentrations of analyte. For each sample, recorded spectra for the blank substrate were used for background subtraction. All spectra recorded were background subtracted, unless otherwise specified. The experimental parameters used throughout the experiments are listed in Table 1.

Fabrication of the Multichannel Device. The multichannel device consisted of 2 glass chips and 16 parallel capillaries built between the chips, with each capillary connected to a separate reservoir (Figure 1). The capillaries had an i.d. of 75 μm and an o.d. of 200 μm. Two glass chips (78 mm × 90 mm × 2 mm, L × W × H) were utilized for device fabrication. One was used as the upper glass chip by cutting off 7 mm from the edge using a glass cutter, and the other was used as the bottom glass chip. The 16 capillaries were then sequentially situated on the bottom glass chip, with a spacing of 5 mm to avoid cross-contamination during analyses. All capillaries were glued between the two glass chips. As illustrated in Figure 1, the multichannel device was mounted on a computer-controlled translation stage (Shenzhen Senyuming Technical Development Corp., Guangdong, China) and was driven by a step motor.

Procedures. High-throughput analysis was performed by filling the reservoirs and channels in the multichannel device with two different samples alternatively (capillaries 1, 3, 5, 7, 9, 11, 13, and 15 were filled with 5 mg/L DDU solution and the rest filled with 10 mg/L angiotensin I solution). By linearly moving the multichannel device, samples were sequentially analyzed by DESI-MS. Then, a reactive DESI experiment was carried out based on a previous report:[44] 300 mg/L benzeneboronic acid adjusted to pH 9.22 was used as the spray solution, and 10 mg/L D-fructose was used as the sample. To evaluate the robustness of the system, we investigated the reproducibility of a single capillary in the microchip, using 10 mg/L DDU as a sample. 50 nL of sample was injected into the main stream at regular intervals by a flow injection approach, with a total DDU amount of 500 pg in each injection. The reproducibility of five different capillaries was also investigated in the same approach. Then, to show the potential of the system for quantitative analysis, a concentration series of 5, 10, 15, and 20 mg/L DDU was sequentially loaded into a capillary, and each was repeated three times.

Safety Considerations. *When experiments were performed, high dc voltage was applied to the tip of the syringe. Actions for insulation of both the operator and the MS with the high-voltage source should be taken to avoid dangers.*

RESULTS AND DISCUSSION

High-Throughput Analysis. As illustrated in Figure 1, we designed a high-throughput analysis platform based on DESI-MS.

(44) Chen, H.; Cotte-Rodriguez, I.; Cooks, R. G. *Chem. Commun.* **2006**, 597–599.

Utilizing this system, high-throughput analysis was easily achieved without any special designed interface. Furthermore, online postcolumn derivatization could be successfully performed by adding reagent in the spray solution intended to allow particular molecular/ion reactions,[44–46] and thus improve ionization efficiency, which expands the applicability of this high-throughput analytical platform.

To demonstrate the high-throughput performance of the system, reservoirs in the microchip were filled with 5 mg/L DDU and 10 mg/L angiotensin I alternatively. The microchip was then mounted on the 3-D translation stage. In this way, each sample was analyzed for 5 s by DESI. When the analysis of a certain sample was completed, the next channel was moved to DESI. The time needed to change the capillary was 1 s. Therefore, 6 s in total was required to complete the analysis of a single sample, and all 16 samples were analyzed within 1.6 min.

Panels A and B in Figure 2 show the typical spectra of DDU and angiotensin I. The protonated molecules of $[DDU + H]^+$ give an abundant signal at m/z 269, with the signal at m/z 291 corresponding to sodiated molecules of $[DDU + Na]^+$. The other two signals at m/z 120 and 148 are fragments generated by cleavage of the C−N bond. For angiotensin I, signals at m/z 1297, 649, 433, and 325 are peptide molecules with one, two, three, and four protons, respectively. The signal of $[\text{angiotensin I} + 2H]^{2+}$ at m/z 649 is the most abundant. No sample cross-contamination was observed, since different samples were in different channels and there was an enough spacing of 5 mm between two neighboring channels. Figure 2C shows the 16 spectra corresponding to all 16 samples in the capillaries, demonstrating the validity of utilizing the system to perform high-throughput analysis. Further improvement might be expected by microfabrication of the whole device in a single piece: casting channels with identical size in microfluidic chips to substitute capillaries used in the current design. It is worth noting that the sampling time might be further reduced, as demonstrated in previous literature for scanning parameter optimization.[47]

Reactive DESI Experiment. As an effective method for directly sampling condensed-phrase samples in ambient environment, another feature of DESI is the use of a spray solution intended to allow particular molecular/ion reactions[44–46] to improve ionization efficiency. In this experiment, a reaction based on reactive DESI was conducted to investigate the potential of using postcolumn online derivatization for compounds with low ionization efficiency. Taking the reactive DESI of D-fructose[44] as an example, 350 mg/L aqueous solution of benzeneboronic acid (pH 9−10) was used as the spray solution, and the reactant ions in the charged droplets spraying onto the capillary outlet reacted with 10 mg/L D-fructose. All mass spectra were obtained in the negative ion mode. Results of postcolumn online derivatization are shown in Figure S-1 (see Supporting Information). Besides this kind of reactions, other standard solution-phase reactions[48] can also be realized under ambient conditions.

Analytical Performance. The reproducibility was investigated by analyzing sequentially injected 10 mg/L DDU plugs in a capillary. As shown in Figure 3, a reproducibility of RSD of 7.6% was achieved for 16 sequential injections based on the integration of the 16 peaks of the extracted ion mass spectrum. Successively, the reproducibility among five different capillaries was investigated. In this way, a single injection into five different capillaries was performed. Figure 4 showed five extracted ion mass spectra of one injection of 20 mg/L DDU solution into five identical capillaries, with the capillary-to-capillary RSD to be 12.3%, which indicated that a good reproducibility may be achieved by careful positioning of capillary outlets. The potential of the system for quantitative analysis was also illustrated by a linear relationship between the relative intensity and the concentration of standard DDU solution (Figure 5). A regression equation of $\text{NPAI} = 4.78c - 3.65$ ($R = 0.9971$) was obtained, in which NPAI represents normalized peak area integration and c corresponds to the concentration of DDU, and the LOD for the DDU solutions was 1.0 mg/L (signal/noise = 10:1).

CONCLUSIONS

This work presents a multichannel device coupled with DESI-MS for high-throughput analysis. The high-throughput performance of our system has been demonstrated by fulfilling analyses of all 16 samples within 1.6 min. The applicability of the system for sample characterization and quantification was demonstrated by the reproducibilities and linear relationship. Our design possesses the following virtues: (1) because the high voltage is applied to DESI spray emitter, electrode needed to generate electrospray in each capillary is unnecessary; (2) DESI could not only ionize the analytes in capillaries but also drive them out; therefore, no additional interface is needed between the microchip and the mass spectrometer; (3) for analytes with low ionization efficiency, online postcolumn derivatization can be achieved by adding appropriate reagents in the spray solution. In addition, the system has ideal potentials to be used on various high-throughput platforms, such as multichannel devices used to perform on-chip separation and derivatization prior to DESI-MS analysis, thereby expanding applications of the system in various complicated contexts.

ACKNOWLEDGMENT

This work was supported by National Natural Science Foundation of China (20535020 and 20635002). We gratefully acknowledged valuable suggestions about DESI technique from Dr. Zheng Ouyang in Purdue University, West Lafayette.

SUPPORTING INFORMATION AVAILABLE

The results of postcolumn online derivatization and mass spectra of amino acids, exhilarants, and other compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

(45) Cotte-Rodriguez, I.; Chen, H.; Cooks, R. G. *Chem. Commun.* **2006**, 953–955.
(46) Takats, Z.; Cotte-Rodriguez, I.; Talaty, N.; Chen, H. W.; Cooks, R. G. *Chem. Commun.* **2005**, 1950–1952.
(47) Pasilis, S. P.; Kertesz, V.; Van Berkel, G. J. *Anal. Chem.* **2007**, *79*, 5956–5962.
(48) Sparrapan, R.; Eberlin, L. S.; Haddad, R.; Cooks, R. G.; Eberlin, M. N.; Augusti, R. *J. Mass Spectrom.* **2006**, *41*, 1242–1246.

Received for review April 21, 2008. Accepted May 29, 2008.

AC800803X