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Design, fabrication and test of a microfluidic nebulizer chip for desorption electrospray ionization mass spectrometry

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Abstract

This paper presents design, microfabrication, and test of a microfluidic nebulizer chip for desorption electrospray ionization mass spectrometry (DESI-MS) in proteomic analysis. The microfluidic chip is fabricated using cyclic olefin copolymer (COC) substrates. The fluidic channels are thermally embossed onto a base substrate using a nickel master and then a top substrate is thermally bonded to seal the channels. Carbon ink embossed into the top COC substrate is used to establish electrical connection between the external power supply and the liquid in the channel. The microfluidic chip to external capillary connection is fabricated using Nanoport™ interconnection system. Preliminary leakage test was performed to demonstrate the interconnection system is leak-free and pressure test was performed to evaluate the burst pressure. Finally, the nebulizer chip was used to perform DESI-MS for analyzing peptides (BSA and bradykinin) and reserpine on the nanoporous alumina surface. DESI-MS performance of the microfluidic nebulizer chip is compared with that obtained using a conventional DESI nebulizer.

1. Introduction

Desorption electrospray ionization (DESI) is a method that allows direct sampling of an analyte deposited on a surface under ambient conditions [1]. Recently, DESI-MS has been used for proteomic analysis and it has been shown that DESI, electrospray ionization (ESI) and laser desorption ionization (LDI) observe complementary set of peptides [2,3]. The performance of DESI method is mainly dependent on the sample surface and the ion source. Previously, we have reported use of a nanoporous alumina surface which performed better as compared to the other commonly used surfaces in DESI-MS [4]. To date, development of nebulizer chips for DESI-MS has received no attention from the miniaturization community. Due to the recent advancements in the microfabrication technology, miniaturized/microfluidic ion sources are increasingly coupled with mass spectrometer.

Recently, microfluidic nebulizer chips have been fabricated for atmospheric pressure chemical ionization (APCI) and atmospheric pressure photo ionization (APPI) and capillary electrophoresis-mass spectrometry. A silicon-glass microfluidic nebulizer chip has been reported by Franssila et al. [5]. The liquid sample is nebulized and vaporized in the channel

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and the vaporized sample exiting the nozzle is ionized by an external corona needle. An all-glass microfluidic nebulizer chip for mass spectrometry is reported by Saarela et al. [6]. Combined with versatile operation modes including APCI and APPI, the chip can be used with less polar and even non-polar samples.

A microfabricated nebulizer as an integral part of a capillary electrophoresis-mass spectrometry chip was reported by Zhang et al. [7]. The combination of the pneumatic nebulizer with the separation channel represents integration of two independent systems (CE and electrospray interface) on a single chip. A microfluidic nebulizer chip with one liquid and two gas ports was used to demonstrate use of a microfabricated reusable multi-inlet PDMS fluidic connector [8]. Because the connector chip was fabricated independently of the microfluidic chip it significantly improves the assembly yield of the fluidic system as the microfluidic chip is not subjected to gluing or other assembly operations. A nebulizer microchip was reported [9] that can be used for APCI-MS. The ionization was achieved using an external corona discharge needle positioned some distance from the microchip heated nebulizer. A microfabricated nebulizer with a built-in heater for APPI-MS is presented [10]. The use of the microfabricated nebulizer chip for analysis of different analytes is demonstrated and the results compared with those obtained from conventional APPI sources. A microfabricated nebulizer chip that combines APPI-MS with gas-chromatography (GC) or capillary LC was presented [11]. The analytical performance of GC- and capLC-microchip APPI-MS was evaluated with some polycyclic aromatic hydrocarbons, amphetamines, and steroids.

In this work, we present design, microfabrication, and test of a microfluidic chip for DESI-MS. First, the microfluidic device is described including the nebulizer chip and the Nanoport™ interconnection system (Upchurch Scientific, Oak Harbor, WA). Then, the device fabrication procedure is thoroughly discussed. Furthermore, the results of the device characterization are presented and discussed. Then, DESI-MS performance of the microfluidic chip and a comparison of performance between the microfluidic chip and the conventional nebulizer is presented and discussed. Finally, conclusions of this work are presented.

2. Description of the microfluidic device

2.1 Nebulizer chip

A schematic of the microfluidic nebulizer chip is depicted in Fig. 1. The chip is fabricated on COC (Zeonor - COC, 1020R, Zeon Chemicals L.P., Louisville, KY) substrates. The chip has an embossed liquid channel to carry the sample liquid and two gas channels to carry nebulizer gas for stable and efficient ionization, and to help transport the desorbed ions from the sample surface to the MS inlet. The liquid and gas channels are embossed onto the base substrate with two gas channels located symmetrically on both sides of the liquid channel. This arrangement is essential in order to achieve symmetrical gas flow around the solvent spray. An asymmetric gas flow leads to destabilization of the spray plume and hence results in inefficient ionization. Carbon ink is used to make electrical connection from the external voltage source to the sample liquid in the channel. Carbon ink conductor is thermally embossed into the back of the top substrate and then the two substrates are thermally bonded.

The chip design includes two fluidic inlets- one for the liquid sample and the other for the nebulizer gas. Mechanical milling was used to fabricate the fluidic inlets. To avoid interference, the spacing between the liquid and gas inlets was determined based on the size of the fluidic connectors. The overall size of the chip is 50×20mm. The embossed gas channels have 100 × 50µm cross-sections throughout and the liquid channel has 100×50µm cross-section close to the inlet which is reduced to 50×50µm towards the channel orifice. The external liquid and gas capillaries are connected to the liquid and gas channels through the Nanoport fluidic interconnection system.

2.2 Nanoport interconnection system

A schematic representation of the Nanoport interconnection system is depicted in Fig. 2. The gasket fits into the recess on the bottom of the coned port. The bottom of the coned port is bonded to the chip using epoxy adhesive and, the bonding is then thermally cured. Next, a 360 μ m OD fused silica capillary is inserted through the coned nut and the nut is tightened into the coned port. The compression force generated between the coned nut and the capillary due to tightening of the nut forms the fluidic seal.

3. Device fabrication procedure

A schematic of the process flow used for fabrication of the microfluidic nebulizer chip is depicted in Fig. 3.

3.1 Fabrication of the nickel master

A nickel wafer Ni 200, 1.6 mm thick, (McMaster, Atlanta, GA) is used to prepare the master. The wafer is lapped with Aluminum Oxide as the abrasive in Vehicle 101 (Lapmaster, IL). The lapped nickel wafer was cleaned in an ultrasonic cleaning bath, successively using acetone, methanol and DI water, each for approximately 30 min. The substrate is then spun coated with Omnicoat (Microchemical Corp., Newton, MA) at 3000 rpm for 40 sec. The Omnicoat layer serves as an adhesive (release) layer for the photoresist. The wafer is placed inside an oven at 180 °C for 2min to facilitate bonding of the Omni coat onto the wafer. The wafer is then spun coated with SU-8-50 (Microchem Corp., MA) to achieve a film thickness of 50 μ m. The wafer is then baked 65 °C for 3 min, then at 95 °C for 15 min. The SU-8 is patterned by exposing 350nm UV-light through a photomask for 15 sec. Then, the wafer is baked at 65 °C for 2 min, then 95 °C for 9 min. Then, SU-8 is developed in 2-(1-methoxy) propyl acetate 97% for 5 min with intermittent stirring. The Omni coat layer is then released by developing ultrasonically in 101 Developer (Micro Chemical Corp.) for 1 min, followed by DI water rinse for 2 min, then developing in MFTM 319 (Rohm Haas) for 30 sec followed by DI water rinse for 2 min.

The bottom surface of the Ni wafer is connected with a conductive wire (copper coated with nickel) and then sealed using an insulating tape to avoid deposition of nickel. The wafer is dipped into electroplating solution with the channel side of the wafer facing a nickel electrode (anode). An image of the electroplating system is shown in Fig. 4. A nickel electrode is connected to the +ve polarity of the power supply forming the anode, and the wafer is connected to the -ve polarity forming the cathode. The electroplating system is connected to a PC and is controlled using LABVIEW. The conditions used for the electroplating process is depicted in Table-1. An image of the Ni-master is shown in Fig. 5.

3.2 Hot embossing

The nickel master is used to emboss the liquid and the gas channels into the bottom COC substrate. The temperature and pressure used during the embossing process are 145 °C, and 100 psi, for approximately 5min.

3.3 Carbon ink conductor

A solution is prepared by mixing Zeonor with methylcyclohexane, with the concentration of Zeonor 10% by volume. The carbon ink is prepared by homogeneously mixing spherical carbon powder with the prepared solution. The concentration of the carbon in the solution is 90% by weight. The carbon ink is first printed onto a glass plate, dried and then embossed into a COC substrate using hot press at 113°C for 5min.

3.4 Thermal bonding

The two substrates, one with the embossed channels and the other with the embossed carbon ink are bonded together using a Tetrahedron Associates (SanDiego, CA) MTP-8 press. The bonding occurs through a five-step process with each step having specified temperature, pressure and time as presented in Table-2.

3.5 Device-to-external capillary connection

A schematic representation of the fabrication procedure for the Nanoport interconnection system is depicted in Fig. 6. The connector holes (for liquid and gas) are micro-milled using 360 μ m OD end mill. An optimum spindle rotational speed of 2000 rpm and feed rate of 200 mm/min was used. The Nanoport system is assembled by inserting the gasket into the groove on the bottom of the coned port and mounting the ring-shaped adhesive onto the bottom of the coned port. The coned port is attached and clamped to the device with the coned port opening aligned with the milled hole on the device. The assembly is placed in a 120 °C oven for 60 min to cure the adhesive bond. The assembly is removed from the oven and allowed to cool naturally to room temperature, and the clamp is removed. The externally capillary is inserted into a coned nut which is then screwed into the coned port. A fluidic seal is formed due to the compression force between the frusto-conical part of the coned nut and the capillary due to tightening of the coned nut. An image of the nebulizer chip utilizing Nanoport interconnection system is shown in Fig. 7.

4. Device characterization

4.1 SEM images

The edge of the bonded-chip is trimmed using microtome, and the edge-view of the device is observed using a Scanning Electron Microscope (SEM Instrument-Hitachi, TM-1000). The openings of the channels are ensured to be free from debris prior to taking the SEM images using a microscope. The SEM system is connected to a PC and controlled using software-Hitachi TM-1000. The magnification and focus are adjusted and then the SEM images are analyzed using software - Quart PCI-image management system.

The SEM images of the edge view of the embossed liquid-gas channels (open) and the bonded nebulizer chip are depicted in Fig. 8(a) and (b), respectively. The close-up SEM images of the embossed (open) liquid and gas channels are shown in Fig. 8(c) and (d), respectively. The close-up SEM images of the bonded liquid and gas channels in the device are shown in Fig. 8 (e) and (f), respectively. The bonded liquid channel has width of 62 μ m at the top, 51 μ m at the bottom and a depth of 48 μ m. Similarly, the bonded gas channel has a width of 115 μ m at the top, 98 μ m at the bottom and a depth of 45 μ m.

4.2 Preliminary leakage test

Preliminary leakage test was performed to make sure that the chip and the NanoportTM interconnection system is leak-free. The external capillaries were connected to a syringe pump and air was blown through the system at moderate pressure while submerging the device in water. No leakage was observed at the interconnection region and the bubbles flowed out exclusively at the nebulizer liquid (gas) orifice as shown in Fig. 9. This test indicated that there was no leakage in the chip or in the interconnection system.

4.3 Pressure test

A HPLC system (Hewlett Packard, Series 1100) was used for conducting pressure test to evaluate the burst pressure of the NanoportTM interconnection system. The edges of the device were kept sealed. The external capillaries connected to the liquid/gas channels of the

microfluidic nebulizer chip through the Nanoport™ interconnection system were connected to the outlet capillary of the HPLC pump. The liquid was pumped into the device channels at an initial flow rate of 0.5 $\mu\text{L}/\text{min}$. The fluid pressure in the channel and the connecting capillaries increased with time until the interconnection systems failed. Followed by this, a sudden drop in pressure with time was observed. The pressure versus time characteristics for the Nanoport™ interconnection system is presented in Fig. 10. The burst pressure was measured to be 7.2 bar.

5. DESI-MS performance of the nebulizer chip

DESI-MS performance of the microfluidic nebulizer chip was evaluated by analyzing reserpine, bradykinin and BSA tryptic digests on the nanoporous alumina surface [4]. The DESI-MS performance of the nebulizer chip was compared with that of a conventional DESI nebulizer [4] under the same operating and geometric conditions.

5.1 Instrumentation

The instrumentation used in the DESI-MS includes the microfluidic nebulizer chip, an in-house designed DESI ion source, and the nanoporous alumina surface. A detailed description of the DESI ion source and the nanoporous alumina surface is presented in [4].

5.2 Sample preparation

The procedure reported in [4] was used to prepare the BSA tryptic digests, reserpine and bradykinin samples and the spray solvent.

5.3 Experimental setup and procedure

The experimental setup for the DESI-MS tests using the nebulizer chip utilizing the Nanoport interconnection system is depicted in Fig. 11. The liquid sample (volume 1.0 μL) was deposited on the nanoporous alumina surface and dried. Then, the porous alumina surface was placed onto the movable surface of the DESI ion source. The nebulizer chip was mounted onto the ion source-platform of the DESI system. The orifice of the nebulizer chip was inclined to the horizontal and pointed toward the sample. The spray solvent (ionizing agent) was infused into the liquid channel using a syringe pump with a capacity of several micro-liters. The sample in the liquid channel was connected to the external power source through the carbon ink conductor.

The sheath gas (He) was carried through the gas-channels. This was required to assist in the ionization process and stabilize the spray. The electrospray generated from the orifice of the nebulizer chip was directed toward the sample, thus ionizing the sample. These sample ions were carried into the MS assisted by the nebulizing gas and detected. A ThermoFinnigan LCQ mass spectrometer (LCQ Tune Plus software) was used for ion detection, which was connected to a PC for data collection and analysis. The operating and geometric conditions used in the experiments are as follows- flow rate 100 nL/min, inclination angle 60°, MS orifice-sample distance 3mm, sample-MS capillary distance 2mm.

5.4 Results and discussion

Optimum operating conditions and geometric parameters identified for the microfluidic nebulizer chip and the conventional nebulizer are presented in Table-3. The DESI-MS mass spectrum of reserpine is presented in Fig. 12. The peak at m/z 609 is from the protonated molecular ion of reserpine. The DESI-MS mass spectrum of bradykinin is presented in Fig. 13. The peak at m/z 904.5 indicates presence of bradykinin. The DESI-MS mass spectrum of BSA tryptic digest is presented in Fig. 14. Several peaks in the spectrum match with the m/z

peaks available in the protein sequence database for tryptic fragments of BSA, indicating presence of BSA tryptic digest, as presented in Table-4.

The maximum signal intensity obtained using the microfluidic nebulizer chip was compared with that obtained using the conventional DESI nebulizer [4] for each of the biosamples, both working under their optimum operating and geometric conditions. From the results presented in Table-5, it is observed that higher ion intensity was obtained using the microfluidic nebulizer chip as compared to the conventional DESI nebulizer. This may be due to more efficient ionization occurring in the case of the microfluidic nebulizer chip.

The limits of detection (LODs) of various samples obtained using the nebulizer chip and the conventional nebulizer are presented in Table-6. Significantly lower limit of detection was observed in the case of the nebulizer chip. This may be because, use of microfluidic nebulizer chip leads to efficient ionization (ion desorption) and it was possible to collect sample ions from a much smaller sample spot.

In addition to providing higher ion intensity and lower limits of detection (LODs), the microfluidic nebulizer chip offers several other advantages. The microfluidic nebulizer chip also can operate at extremely low flow rates (i.e. as low as 50 nL/min) and therefore provides the benefit of low sample consumption. A more stable signal was obtained using the nebulizer chip because of its ability to operate at lower flow rates. The conventional nebulizer which operates at a much higher flow rate (1500 nL/min), ablates/consumes the analyte faster than the nebulizer chip for the same amount of deposited analyte. The nebulizer chip has both the liquid and gas channels on the same chip while the conventional DESI nebulizer has several components (Tee, ferrules, capillaries) that require time consuming and cumbersome assembly procedure. This makes the nebulizer chip more convenient to use and consistent in behavior as compared to the conventional nebulizer. The dimensions of the features of the microfabricated nebulizer can be varied to any size, whereas the conventional nebulizer is limited to available tubing size. Additionally, the nebulizer chip is compatible with microfabrication and thus batch production. The microfluidic nebulizer chip could be a cost effective alternative to the conventional DESI nebulizer for DESI-MS experiments in proteomic analysis.

6. Conclusions

In this chapter, design, microfabrication, and test of a microfluidic device for DESI-MS in proteomic analysis was presented. First, a detailed description of the microfluidic device including the nebulizer chip and the interconnection systems was provided. Then, the device fabrication procedure including the fabrication of the nickel master, embossing, thermal bonding and fabrication of the interconnection systems were described. The device was characterized based on SEM images of the channel cross-section, a preliminary leakage test, followed by a HPLC test. The fabricated channel size was measured to be approximately same as designed. A preliminary leakage test was performed on the nebulizer chip utilizing Nanoport interconnection system. The air bubbles were observed to exit exclusively at the nebulizer orifice indicating a leak-free interconnection. Then, HPLC test was performed to evaluate the burst pressure of the interconnection system. Finally, the DESI-MS performance of the microfluidic nebulizer chip and the conventional nebulizer were compared. The results show that the microfluidic nebulizer chip has several advantages over the conventional DESI emitter including higher sensitivity, lower limits of detection (LODs), low sample consumption, signal stability, lower cost and compatibility with microfabrication.

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References

1. Takats Z, Wiseman JM, Golagan B, Cooks RG. *Science* 2004;306:471–473. [PubMed: 15486296]
2. Nayak R, Knapp DR. *Anal Chem* 2007;79:4950. [PubMed: 17547367]
3. Nayak R, Sen AK, Knapp DR, Liu J. *Anal Chem* 2008;80(22):8840–8844. [PubMed: 18937429]
4. Sen AK, Nayak R, Darabi J, Knapp DR. *Biomed Microdevices* 2008;10(4):531–538. [PubMed: 18204903]
5. Franssila S, Marttila S, Kolari K, Ostman P, Kotiaho T, Kostiaainen R, Lehtiniemi R, Fager CM, Manninen J. *J Micromech Sys* 2006;15(5):1251–1259.
6. Saarela V, Haapala M, Kostiaainen R, Kotiaho T, Franssila S. *Lab A Chip* 2007;7:644–646.
7. Zhang B, Liu H, Karger BL, Foret F. *Anal Chem* 1999;71(15):3258–3264. [PubMed: 10450166]
8. Saarela V, Franssila S, Tuomikoski S, Marttila S, Östman P, Sikanen T, Kotiaho T, Kostiaainen R. *Sens and Act B* 2005;114(1):552–557.
9. Östman P, Marttila SJ, Kotiaho T, Franssila S, Kostiaainen R. *Anal Chem* 2004;76(22):6659–6664. [PubMed: 15538790]
10. Kauppila TJ, Östman P, Marttila S, Ketola RA, Kotiaho T, Franssila S, Kostiaainen R. *Anal Chem* 2004;76(22):6797–6801. [PubMed: 15538806]
11. Haapala M, Luosujärvi L, Saarela V, Kotiaho T, Ketola RA, Franssila S, Kostiaainen R. *Anal Chem* 2007;79:4994–4999. [PubMed: 17530739]

Biographies

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Prof. Knapp has over 37 years experience in biomolecular mass spectrometry and approximately 18 years experience in peptide and protein analysis. He is the author of a standard reference in analytical chemistry, Handbook of Analytical Derivatization Reactions (Wiley-Interscience). His laboratory achieved the first complete mass spectrometric mapping of an integral membrane protein (rhodopsin). His current research interests include microfluidic devices for proteomic analysis, methodology development for increasing depth of proteomic analysis, and cerebrospinal fluid proteomics. He is particularly interested in technology development for proteomic analysis.

Fig. 1.
Schematic of the microfluidic nebulizer chip

Fig. 2.
Cross-sectional view of the connector socket and mating 360 μ m OD tubing

Fig. 3.
Process flow for fabrication of the nebulizer chip

Fig. 4.
Photograph of the electroplating system

Fig. 5.
An image of the nickel master

Fig. 6.
Fabrication of the Nanoport connection system

Fig. 7.
Nebulizer with Nanoport connection system

Fig. 8. SEM image of (a) Embossed liquid-gas channels (b) Bonded liquid-gas channels (c) Open liquid channel (d) Open gas channel (e) Bonded liquid channel (f) Bonded gas channel

Fig. 9.
Preliminary leakage test for the Nanoport interconnection system

Fig. 10. Pressure versus time characteristics for the Nanoport™ interconnection system in the chip

Fig. 11.
DESI-MS test using the microfluidic nebulizer chip with Nanoport interconnection system

Fig. 12.
DESI-MS mass spectrum of reserpine

Fig. 13.
DESI-MS mass spectrum of bradykinin

Fig. 14.
DESI-MS mass spectrum of BSA tryptic digests

Table 1

Electroplating conditions

Step	Pulse on (ms)	Pulse off (ms)	Output voltage (V)	Current density (mA/cm ²)	Duration (min)
1	200	160	2.0	2	1
2	200	160	2.0	4	5
3	200	160	2.0	10	240
4	200	160	2.0	4	5

Table 2

Thermal bonding conditions

Step	Temp (deg)	Force (lb)	Time (min)
1	225	25	10
2	235	220	2.5
3	240	15	5
4	215	15	5
5	105	120	3

Table 3

Optimized operating conditions

	Nebulizer Chip	Conventional Nebulizer
Flow rate ($\mu\text{l}/\text{min}$)	0.5	5
Inclination Angle ($^{\circ}$)	60	60
Tip-Surface distance (mm)	2	4
Spray Voltage (kV)	1.5	4
Capillary voltage (V)	-25	-25
Collection Angle ($^{\circ}$)	20	20

Table 4

BSA tryptic digests fragments

Theoretical mass	DESI-MS using Nebulizer Chip
432.26	432.5
649.33	649.4
689.37	689.1
789.47	789.5
820.47	820.5
847.50	847.5
898.48	898.5
922.49	922.4
1001.59	1001.8
1024.46	1024.8
1143.55	1143.8
1163.63	1163.7
1283.71	1283.5
1305.72	1305.8
1308.77	1308.8
1419.69	1419.7
1479.80	1479.8
1567.74	1567.7
1639.94	1639.9
1811.01	1811.0

Table 5

Comparison of ion intensities obtained using the nebulizer chip and the conventional nebulizer

	Nebulizer Chip	Conventional
Reserpine	2.35E+07	1.18E+06
Bradykinin	7.81E+07	6.23E+06
BSA tryptic digests	4.62E+08	2.57E+07

Table 6

Comparison of limits of detection (LODs)

Analyte	Nebulizer chip	Conventional
Reserpine (ng/ μ l)	0.5	5
Bradykinin (ng/ μ l)	0.75	10
BSA Digests (ng/ μ l)	1.25	25