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A polysilicon nanoelectrospray–mass spectrometry source based on a microfluidic capillary slot

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Abstract

A novel micromachining process for the fabrication of miniaturised polysilicon-based nanoelectrospray ionisation–mass spectrometry (nanoESI–MS) sources is developed in this paper. The nanoESI source topology is composed of two highly planar triangular free-standing cantilevers which form a microfluidic capillary slot having a width (w) and a height (h). A combination of low pressure chemical vapour deposition (LPCVD), pattern-transfer, reactive ion etching (RIE) and sacrificial layer etching is used to fabricate the nanoESI sources which project horizontally beyond the edge of a silicon substrate by a length of 800 μm. NanoESI sources having two different capillary slot dimensions are tested: $w \times h = 1.8\,\mu m \times 2\,\mu m$ and $2.5\,\mu m \times 5\,\mu m$. The sources have been tested on an ion trap mass spectrometer (MS) using a standard peptide sample (Glu-Fibrinopeptide B) at a concentration of 1 μM. The resultant mass spectra show that the microfabricated capillary slot-based nanoESI sources presented here demonstrate state-of-the-art performances in terms of electrospray ionisation voltage (0.7 kV) and test solution aqueous concentration (90% H_2O).

Keywords: Nanoelectrospray ionisation; Silicon microtechnology; Microfluidics; Lab-on-a-chip; Micro-TAS; Mass spectrometry; Proteomics

1. Introduction

In the context of life sciences, shrinking a whole laboratory, or even part of one, onto a single microfluidic circuit is currently both a major scientific and technological challenge. In order to achieve this goal, it has become clear that the application of microtechnology is the key to realising the so-called 'Laboratory-on-a-chip' (LOC) or 'Micro Total Analysis System' (μTAS) [1–4]. We focus here on an integrated nanoelectrospray ionisation (nanoESI) source for LOC dedicated to macromolecule (peptides, proteins, etc.) identification by nanoelectrospray ionisation–mass spectrometry (nanoESI–MS). An integrated electrospray ionisation source is required in order to couple the LOC to a mass spectrometer (MS). The source is essentially a world-to-chip microfluidic device, the basic function of which is bringing a test liquid, which contains the unidentified macromolecules, to a sharp point. Application of a high voltage (HV) to the liquid then forms a Taylor cone resulting in an electrospray of ionised macromolecules contained in droplets which are accelerated towards the input of the MS for analysis. The main advantages in terms of fabrication of micromachined ESI sources [5–17] over their fused silica and borosilicate capillary tube-based counterparts [18] are several-fold: (i) batch produced, (ii) device-to-device reproducibility, (iii) lower cost, and (iv) compatibility with LOC. The advantages in terms of performance are: (i) enhanced analysis conditions, (ii) improved sensibility, (iii) test-to-test reproducibility, and (iv) compatibility with the use of robotics. We have previously validated the concept of such sources based on a capillary slot [19]. However, in the quest for improved performances through miniaturisation, we turn here to silicon-based microtechnology. We make use of polycrystalline silicon

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(polysilicon) which has been used for the fabrication of Micro Electro-Mechanical systems (MEMS) devices [20–22] and is now starting to be used by the microfluidics community [23].

In this paper, we present the fabrication and testing of an integrated nanoESI source based on silicon-based micromachining techniques for coupling an LOC to a mass spectrometer. The nanoESI sources are based on highly planar low-stress triangular polysilicon cantilevers which project horizontally from a silicon wafer and form a microfluidic capillary slot having a nib-like topology.

2. Design

2.1. Source topology

The originality of the source is the open topology which relies on a capillary slot rather than a capillary tube. Fig. 1 shows the topology of the nanoESI–MS sources fabricated for this study. The sources are comprised of the following elements: a 350 μm thick support wafer (Si) measuring 8000 μm × 6200 μm, and a polysilicon layer in which the following features are defined: a reservoir measuring 4500 μm × 3200 μm, a capillary slot having a total length (l) of 2400 μm, a width (w) and a height (h) formed by two polysilicon cantilevers which project horizontally beyond the edge of the silicon support wafer. A horizontal projection enables simple coupling of the chip to the input of the mass spectrometer. The reservoir is intended to contain the sample test liquid whilst capillary slot leads the test liquid along the slotted cantilever by capillary action from the reservoir to source tip. The source is then placed at the inlet of the mass spectrometer for testing. The high voltage required for electrospraying is applied to the n-type doped silicon wafer, thus enabling a low resistance path to the liquid in the reservoir. The triangular-shaped cantilevers which form the point-like feature necessary for nanoESI are fabricated from non-doped polysilicon and have a length up to 800 μm and a thickness of 2–5 μm, i.e. a maximum cantilever aspect ratio of 400, the point angle is 53°. This can be contrasted to our previous work [19] using SU-8 which has a lower value of Young's modulus and greater stresses [24] than polysilicon. The slotted polysilicon-based cantilevers for this study form a capillary slot having dimensions of $w \times h = 1.8\ \mu m \times 2\ \mu m$ and 2.5 μm × 5 μm, i.e. a capillary slot aspect ratio (h/w) of 1.1 and 2.5. These values were chosen to give a capillary slot surface area (wh) of the order of capillary tube-based nanoESI sources [18].

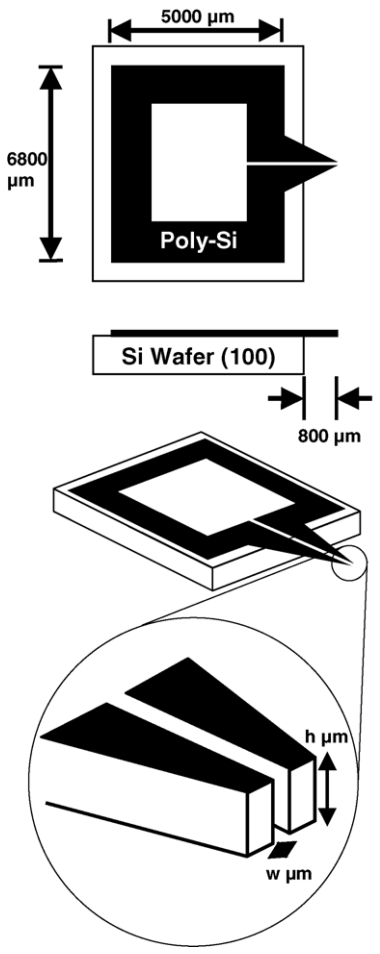

Fig. 1. Topology of the polysilicon-based nanoESI–MS sources based on a microfluidic capillary slot showing the slot dimensions, width (w) and height (h).

2.2. Materials

In an effort to miniaturise the capillary slot dimensions and approach the dimensions attainable using capillary tube based nanoESI sources, i.e. diameter = 1–5 μm, silicon-based microtechnology has been used. The topology of the interface presented here requires long rigid triangular cantilevers which form a well-defined microfluidic capillary slot over the whole length of the source which is intended to bring a liquid to a point. If we consider the mechanical requirements of the cantilever, deflection of such a structure is determined by: (i) the total length, (ii) the width, (iii) the thickness, (iv) the Young's modulus, and (v) the bending moment due to internal stresses. The requirement here of a long, point-like structure implies that polysilicon [25–27] is an excellent choice as the Young's modulus of as-grown polysilicon has been measured to be between 120 GPa and 200 GPa [28–30]. However, the mechanical properties of as-grown polysilicon depend strongly on the deposition and post-deposition conditions [28]. Minimal internal stresses are possible if optimisation of the growth and post-growth conditions are obtained [25,29,31–34]. A residual stress (compressive) of 2 μm thick as-grown LPCVD polysilicon deposited on a thermal silicon dioxide has been measured to be of the order of 200 MPa [31]. However, stresses can be reduced to near zero following a post-growth anneal [31].

3. Fabrication

Fig. 2 describes the silicon-based micromachining process which has been developed for the fabrication of the polysilicon-based cantilever nanoESI sources. This process consists of the following steps: (i) pre-defined cleaving lines and sacrificial etch release layer deposition, (ii) low-stress polysilicon deposition, pattern-transfer and reactive ion etching (RIE), and finally, (iii) sacrificial etching, supercritical drying and dicing.

3.1. Mask design

A set of three photomasks was designed using the software *Wavemaker*© (BML, London, UK) in order to fabricate the nanoESI sources. The photomasks were produced using an EBP G5000+ nanomasker (Leica, VA, USA) which contained a total of 25 ESI emitters incorporated into the mask design in a 5×5 array.

3.2. Pre-defined cleaving lines and sacrificial etch release layer

A 3 in. diameter n-type doped silicon wafer having a (1 0 0) orientation was employed for the fabrication of the cantilever structures. Firstly, a SiO_2 thermal oxide (200 nm) layer is grown by dry oxidation in a furnace. This oxide serves two purposes: firstly, as a masking layer during the tetramethylammonium hydroxide (TMAH) wet-etch [35,36] of the silicon in order to form the cleaving lines in the silicon wafer and secondly, as the sacrificial layer for the release of the slotted cantilevers from the silicon wafer surface. This layer is thus initially patterned using photolithography in order to form the SiO_2 mask for wet etching the cleaving lines. The thermal SiO_2 layer is protected using a positive photoresist (AZ4562) having a thickness of approximately 6 μm and subsequently wet etched using a buffered oxide etch solution (BOE) 7:1 solution (NH_4F:HF); the etch rate was 80 nm min^{-1}. Following removal of the AZ4562, a TMAH solution at 80 °C is used to locally etch the silicon in order to form cleaving lines in the silicon wafer. These cleaving lines are to later serve during the dicing step in order to leave the cantilevers free-standing and projecting horizontally over the edge of the silicon wafer following an etch release step. Having observed that this oxide was undamaged following the TMAH wet etch, this same oxide is then subsequently patterned in order to form the mesa features which act as the sacrificial etch release layers underneath the polysilicon cantilevers.

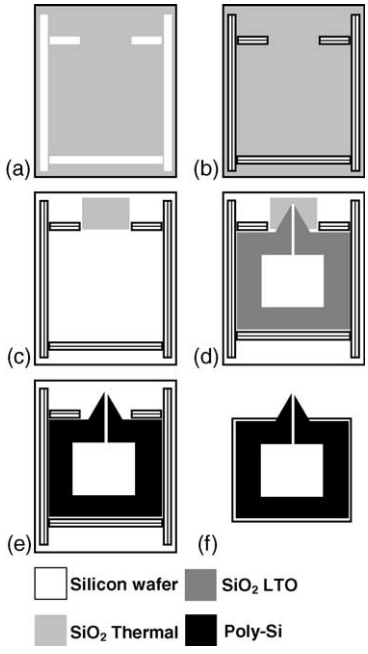

Fig. 2. Silicon-based micromachining process sequence for the fabrication of the polysilicon-based nanoESI–MS sources: (a) deposition and patterning of thermal SiO_2, (b) formation of cleaving lines in the silicon wafer, (c) patterning of the sacrificial etch release layer, (d) pattern-transfer and RIE of the polysilicon, (e) sacrificial etch, and (f) device dicing.

3.3. Polysilicon deposition and pattern-transfer

A layer of non-doped polycrystalline silicon (2–5 μm) is deposited onto the wafer using low-pressure chemical vapour deposition (LPCVD) by the thermal decomposition of silane (SiH_4) at a temperature of 585 °C, a pressure of 200 mTorr and a flow rate of 80 sccm. Under these conditions, the deposition rate of the polysilicon was observed to be approximately 4.7 nm min^{-1}. In order to minimise the internal stresses in this layer, a high temperature anneal at a temperature of 1050 °C for a duration of 60 min is performed. This duration was kept constant irrespective of the thickness of the polysilicon.

A low temperature silicon dioxide (LTO) layer is then deposited on the polysilicon which serves as the pattern-transfer layer. The required thickness of this layer is dependent on the polysilicon thickness to be etched using RIE. As the polysilicon layers here ranged from 2 μm to 5 μm, the LTO silicon dioxide masking layer was determined to be 400 nm and 1 μm. The LTO SiO_2 pattern-transfer layers were also deposited using LPCVD techniques (SiH_4: 70 sccm/O_2: 150 sccm/N_2: 25 sccm), at a temperature of 420 °C and a pressure of 150 mTorr. The deposition rate of the LTO SiO_2 was observed to be 21 nm min^{-1}. An LTO SiO_2 layer was chosen as opposed to a thermal oxide in order to avoid oxidising the polysilicon. As the LTO layer is used as mask during the pattern-transfer stage, in order to define the slotted cantilevers in the polysilicon, it has to be patterned using a positive photoresist layer (S1818) and RIE (CF_4/CHF_3). The thickness of the S1818 photoresist mask depends on the thickness of LTO SiO_2 to be etched. We measured the etch rate of the LTO and S1818 to be approximately 26 nm min^{-1} and 35 nm min^{-1}, respectively, during a (CF_4: 40 sccm/CHF_3: 40 sccm, power = 125 W, pressure = 50 mTorr) based RIE. Hence, in order to obtain a sub-2 μm line-width resolution for the capillary slots, the S1818 masking layer was varied from 1.2 μm to 1.9 μm in order to successfully perform

the pattern-transfer. Following the S1818 removal using an oxygen plasma, the slotted cantilever structures are then defined in the polysilicon using a chlorine-based (Cl_2/He) RIE (MDC-Trion, AZ, USA). The parameters for this etch were as follows: Cl_2, 4 sccm; He, 8 sccm; power = 200 W; pressure = 100 mTorr. The etch rate of the polysilicon was observed to be of the order of 110 nm min^{-1}. Scanning electron micrography (SEM) of the resultant structures revealed that the etched walls were highly vertical in all cases. Indeed, chlorine-based RIEs are known to produce the relatively high aspect ratio features required for the formation of such microfluidic slots which are needed here to produce the required capillary action. Finally, it can be noted that the etch rate of the LTO under these Cl_2/He plasma conditions used here was observed to be of the order of 11 nm min^{-1}.

3.4. Etch release and dicing

The triangular cantilevers are released from the silicon wafer surface by wet etching the sacrificial etch release layer of thermal oxide present underneath the polysilicon cantilevers. A solution of HF:H_2O 50% was used to perform this as the wet etch selectivity between the SiO_2 and the polysilicon is very high for concentrated HF solutions [37]. However, sacrificial oxide etch-rates in the literature vary enormously [37]. We observed that a wet etch duration of 3 h was sufficient to remove the thermal SiO_2 (200 nm) under the triangular cantilevers (maximum under etch area of SiO_2 = 0.6 mm^2). SEM observations and surface profiler roughness measurements revealed that the polysilicon was not affected by this etch. In addition to this, the HF wet-etch solution simultaneously removes the LTO pattern-transfer layer.

A problem which is often encountered whilst fabricating such structures is sticking during the drying phase following sacrificial layer removal. This can be solved by sublimation-based drying technique based on a methanol/water mixture. The problem of sticking is especially acute if large beam aspect ratios are required, as is the case here. In order to solve this problem, we have employed two methods: (i) a super-critical drying technique using the sublimation of CO_2 in order to avoid drying from the liquid to the gas phase, and (ii) wafer cleaving under a liquid, either H_2O or isopropanol (IPA), by placing a drop of liquid on the cantilever prior to cleaving.

Firstly, a super-critical drying process using a CPD 1100 (SC Fluids, NH, USA) was then employed which uses the sublimation of CO_2. Following this stage, the individual microfluidic devices containing the cantilevers were cleaved by making use of the pre-defined cleavage lines. Using this process, we recuperated 13 intact microfluidic devices from a total of 25 fabricated on the wafer for the first batch, i.e. an initial yield of approximately 50%. It should be noted at this point that in following runs, a more simple 'cleaving-under-liquid' method was successfully employed to dice the individual devices by placing a drop of either water or IPA on each cantilever prior to cleaving. Fig. 3 shows a global image

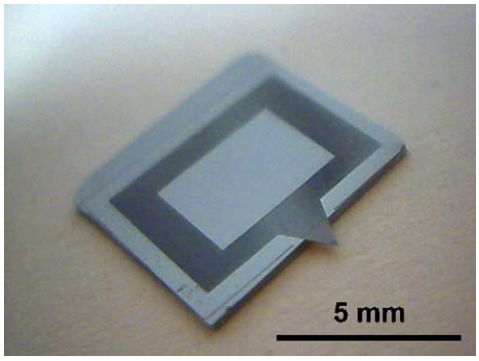

Fig. 3. Photograph of a polysilicon-based nanoESI–MS source following dicing.

of a completed nanoESI source. The polysilicon cantilevers are clearly seen to project horizontally over the edge of the silicon support wafer. It is observed that the dicing does not always follow the pre-defined cleaving lines over the complete length of the device; this is due to the slight misalignment between the pre-defined cleaving lines and the natural cleavage planes of the silicon wafer incurred during the initial photomask alignment stage. Fig. 4 shows optical microscopy images of typical slotted cantilevers obtained from this process which demonstrate that the length of the cantilever can be easily varied from (a) 800 μm and (b) 100 μm depending on the position of the pre-defined cleaving lines. Fig. 5 shows an SEM image which revealed the longest cantilever structures produced by this process (800 μm) to be highly in-plane resulting from minimisation of the internal stresses of the

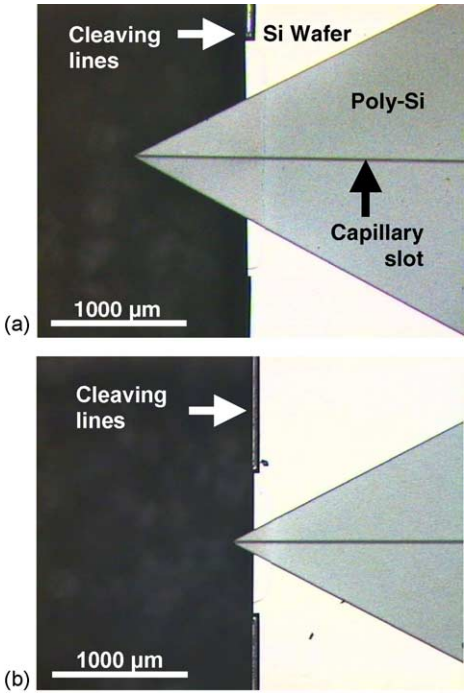

Fig. 4. Optical images of polysilicon-based nanoESI–MS sources demonstrating that the cleaving lines can be used to control the cantilever length: (a) cantilever length = 800 μm, (b) cantilever length = 100 μm.

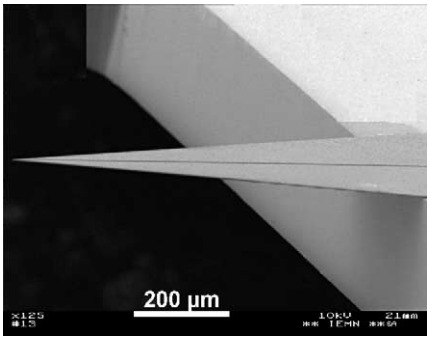

Fig. 5. SEM image of a polysilicon-based nanoESI–MS source. Cantilever length = 800 μm.

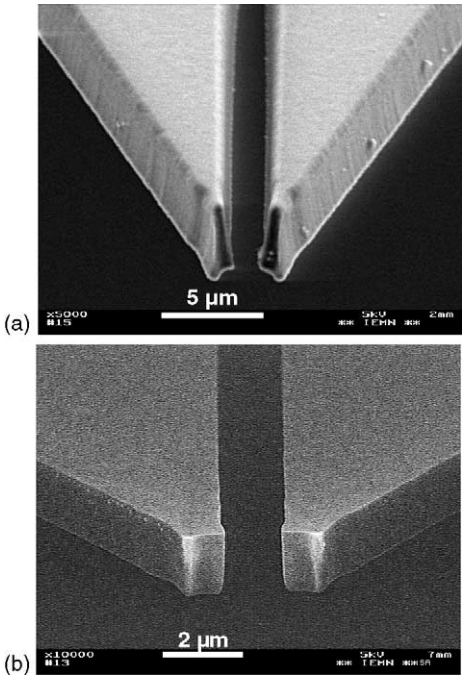

Fig. 6. Close-up SEM of polysilicon-based nanoESI–MS sources; cantilever length = 800 μm: (a) slot width (w) = 2.5 μm, slot height (h) = 5 μm, and (b) w = 1.8 μm, h = 2 μm.

polysilicon via the employment of the high-temperature post-deposition annealing step of the polysilicon. Fig. 6 shows SEM images of the tip of typical slotted cantilever structures produced by the process: (a) $w \times h = 2.5\,\mu m \times 5\,\mu m$, and (b) $w \times h = 1.8\,\mu m \times 2\,\mu m$. It should be noted at this point that the high uniformity of the polysilicon growth is reflected in the fact that the capillary slot dimensions are preserved over the whole length of the free-standing section.

4. Results

4.1. Microfluidic tests

We performed microfluidic tests in order to assess the filling of the capillary slots by a test liquid. As the slot

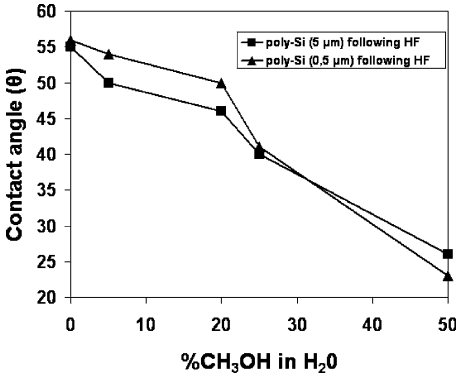

Fig. 7. Static contact angle of different concentration water/methanol/formic acid solutions on LPCVD polysilicon.

dimensions are well below the capillary constant (κ) = $\gamma/\rho g$ = 2.7 mm, the spontaneous imbibition of the test liquid into the capillary slot is determined uniquely by the slot dimensions w and h and the static contact angle (θ_c) on the slot walls at the liquid–vapour interface. Fig. 7 shows the measured static contact angles (θ_c) of typical buffer solutions on polysilicon surfaces. We chose a buffer solution and concentrations which are routinely used in MS testing. Liquid test solutions were prepared by mixing de-ionised water, methanol (CH_3OH) and formic acid (CH_2O_2). We varied the H_2O:CH_3OH ratio from 100:0 to 50:50 whilst the percentage of formic acid was held constant at 0.1%. The static contact angles were measured by automatic deposition of fixed droplet volumes (0.5 μl) onto the polysilicon surface using a DigiDrop contact angle meter (GBX, Lyon, France). In order to assess the effect of layer thickness on the surface quality, measurements were made on as-deposited polysilicon material having a thickness of 0.5 μm and 5 μm following a sample cleaning procedure of HF:H_2O (50:50) for 1 min. The contact angles presented in Fig. 7 were seen to vary from approximately 55° to 25° as the water concentration was reduced from 100% to 50%. The sample thickness is seen to have only a small effect on the static contact angle (<5°). Spontaneous imbibition of the liquid into the capillary slot occurred for: (i) a capillary slot having an aspect ratio of 2, i.e. capillary slot dimensions of 2.5 μm × 5 μm using a 90:10 aqueous concentration (θ_c = 50°), and (ii) for a capillary slot having an aspect ratio of 1.11 (1.8 μm × 2 μm) using a lower aqueous concentration of 50:50 (θ_c = 25°). It should be noted that these tests revealed an advantage of polysilicon-based sources over our previous SU-8-based sources [19] in that polysilicon is more hydrophilic than SU-8 using these test liquids; hence, imbibition occurs at a lower source aspect ratio (h/w) for a given water/methanol concentration. These observations were used in order to determine the tests' solution concentrations to be used for the mass spectrometry tests. A summary of the microfluidic tests is shown in Table 1. A more detailed analysis of the spontaneous imbibition of a liquid into a microfluidic capillary slot and

Table 1
A summary of the microfluidic tests

H_2O:CH_3OH + (HCOOH 0.1%) on polysilicon	Static contact angle (θ_c (°))	$w \times h = 1.8\,\mu m$ $\times 2\,\mu m$; $h/w = 1.1$	$w \times h = 2.5\,\mu m$ $\times 5\,\mu m$; $h/w = 2$
50:50	25	Imbibition	Imbibition
90:10	50	–	Imbibition

thus the consequences for the design of such sources will be discussed by the authors elsewhere [38].

4.2. Mass spectrometry

The mass spectrometry tests were carried out using an ion trap mass spectrometer (LCQ Deca XP+, Thermo Finnigan, San Jose, CA). The source was placed on a standard tip holder and presented to the MS inlet as described elsewhere [19]. The tip holder includes an *xyz* micropositioning stage as well as a metallic zone which allows for direct application of the ionisation voltage to the rear-side of the silicon wafer. Thus, due to the semi-conducting properties of the silicon, the ionisation voltage can be applied to the test liquid without the need of a wire inserted into the reservoir [19]. The liquid test sample was manually loaded into the reservoir of the source using a micropipette although a robot could be used. Once deposited into the reservoir, the liquid sample enters the capillary slot by capillary action and reaches the tip of the source. Upon application of the HV, a Taylor cone forms at the end of the capillary slot and electrospraying occurs. The total ion current (TIC) was recorded during for all experiments and the mass spectra were plotted using *Excalibur* software (Thermo Finnigan, San Jose, CA) as an average over this acquisition time.

MS tests were carried out using a standard peptide sample (Glu-Fibrinopeptide B) purchased from Sigma (l'Isle Abeau, France) using a solution concentration of 1 μM. These test solutions were prepared from an initial concentrated solution of water:methanol (H_2O:CH_3OH), 0.1% HCOOH; the H_2O:CH_3OH ratio being varied from 50:50 to 95:5. The MS tests were carried out using samples at a peptide concentration of 1 μM. In addition, the aqueous/organic ratio was varied in order to assess and optimise the source performance. It was observed that as the aqueous concentration was varied from 50% to 95%, whilst keeping the Glu-Fibrinopeptide B concentration at 1 μM, all tips were seen to perform well: electrospraying occurred upon application of an initial ionisation voltage of 1.2 kV resulting in a stable total ion current and an intense mass spectrum. Fig. 8 shows a typical TIC obtained during the MS measurements which demonstrates that the electrospraying was very stable using these polysilicon-based nanoESI sources. The capillary slot dimensions here were 2.5 μm × 5 μm, the H_2O:CH_3OH = 90:10 and the ionisation voltage was 0.9 kV.

Fig. 9 represents the MS resulting mass spectra obtained using sources with two different capillary slot dimensions: (a) 2.5 μm × 5 μm, and (b) 1.8 μm × 2 μm. It can be

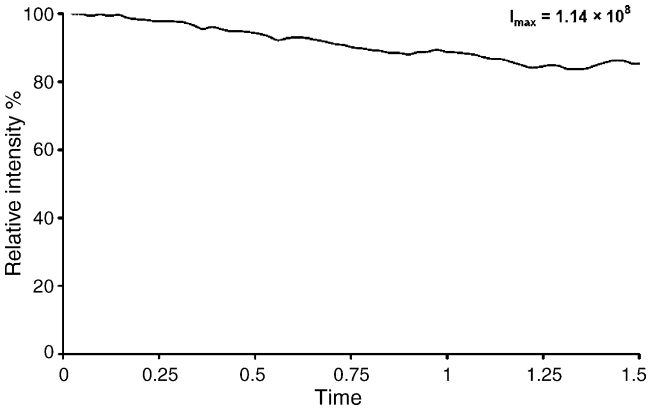

Fig. 8. Total ion current (TIC) signal over a 1.5 min period using a polysilicon-based ESI source having capillary slot dimensions of 2.5 μm × 5 μm. The peptide sample is Glu-Fibrinopeptide B solution prepared with a 90:10 H_2O:CH_3OH, 0.1% HCOOH solution (concentration = 1 μM); the ionisation voltage is 0.9 kV.

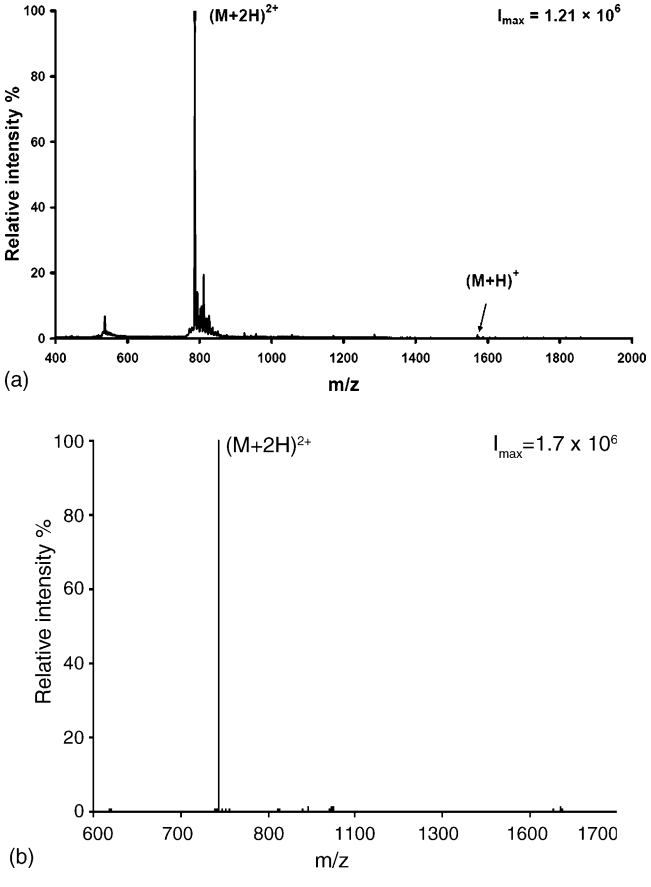

Fig. 9. Mass spectrum obtained using a polysilicon-based nanoESI source having capillary slot dimensions of (a) 2.5 μm × 5 μm (peptide sample = Glu-Fibrinopeptide B, H_2O:CH_3OH = 90:10, 0.1% HCOOH, concentration = 1 μM), ionisation voltage is 1 kV; and (b) 1.8 μm × 2 μm (peptide sample = Glu-Fibrinopeptide B, H_2O:CH_3OH = 75:25, 0.1% HCOOH, concentration = 1 μM), ionisation voltage is 0.7 kV.

observed that both spectra present an intense single peak corresponding to the doubly charged species $(M + 2H)^{2+}$ of the Glu-Fibrinopeptide B. This intense peak occurs at an m/z ratio of 786.5. The presence of the single intense peak can be attributed to the smaller slot dimensions of the sources presented here in comparison to previous work as we have previously observed that a strong presence of the singly charged peak $(M + H)^{+}$ is related to larger slot dimensions [19]. However, a very small $(M + H)^{+}$ peak can be identified in the mass spectrum obtained using the polysilicon source having slot dimensions of 2.5 μm × 5 μm; see Fig. 9(a).

There are two important results to be highlighted from this study: firstly, the ionisation voltage value could be decreased to 0.7 kV without any marked degradation of the analysis quality and signal-to-noise ratio using the source having capillary slot dimensions of 1.8 μm × 2 μm and secondly, the aqueous concentration could be increased to 90% without any marked degradation on the analysis quality or signal-to-noise ratio using the source having capillary slot dimensions of 2.5 μm × 5 μm ($h/w = 2$). This can be compared to previous observations using SU-8-based nanoESI sources where the maximum measurable water:methanol concentration was 50:50 using a source having an aspect ratio of 4.4 [19]. Indeed, the aspect ratio follows a cosine relationship as a function of static contact angle [38]. Hence, the smaller the static contact angle, the smaller the capillary slot aspect ratio required for imbibition. The source having capillary slot dimensions of 1.8 μm × 2 μm was seen to produce an intense mass spectrum at a reduced value of ionisation voltage (0.7 kV). This ionisation voltage is state-of-the-art in the context of both capillary tube-based and micromachined ESI sources. This low value of onset ionisation voltage can be explained by the fact that the onset ionisation voltage value for electrospraying reduces with the tip radius. This has been observed for fused silica and borosilicate capillary tube-based nanoESI sources [18]. It is interesting to note that a mass spectrum was observed for the 1.8 μm × 2 μm source (h/w = 1.1) using a test solution having an aqueous:methanol proportion of 75:25. In this case the cosine relationship [38] implies that imbibition should not occur for a slot having an aspect ratio of less than 1.3. However, it is possible that the contact angle of the liquid on the slot walls is not equal to the contact angle which is measured on an as-grown polysilicon surface following an HF clean. This could be explained by either the presence of a native oxide or by the RIE derived slot wall surface having a different surface energy to that of the as-grown polysilicon surface. However, due to the lower aspect ratio (h/w) of the 1.8 μm × 2 μm source, the capillary effect was not present to enable analysis of a test solution having an aqueous:methanol proportion of 90:10. In contrast, since spontaneous imbibition was observed using the 2.5 μm × 5 μm source, analysis of a highly aqueous solution was possible using this source. An increased aqueous content is an advantage as the use of organic solvents often leads to the destruction of molecular complexes and hinders such interaction studies. Thus, a lower ionisation voltage and high aqueous content provide analysis of biological samples under soft conditions so as to preserve the biological analytes. This allows for the preservation of molecular interactions and thus the study of proteins and complexes in their native conditions.

5. Conclusions

We have fabricated and tested an integrated nanoESI–MS electrospray emitter tip based on the idea of a capillary slot. This source topology contains two free-standing, highly parallel, triangular cantilevers which form a microfluidic capillary slot which is filled with a test liquid spontaneously by capillary action. The cantilevers are formed from low-stress polycrystalline silicon (polysilicon) material deposited by LPCVD techniques and fabricated by pattern-transfer and chlorine-based RIE methods. Following a sacrificial etch release, the polysilicon cantilevers are observed to be highly planar and project horizontally over the edge of a silicon wafer by a length of 800 μm, resulting in a maximum aspect ratio of 400. The source design incorporates microfluidic capillary slots having dimensions ($w \times h$) of 1.8 μm × 2 μm and 2.5 μm × 5 μm. For all sources, these dimensions are preserved along the full length of the source. We have demonstrated that both (i) the capillary slot dimensions of the source and (ii) the aqueous content of the test liquid determine the spontaneous imbibition of the liquid into the capillary slot. In addition, we observe that the slot dimensions determine the ionisation voltage which needs to be applied in order to observe an intense mass spectrum having a high signal-to-noise ratio. The mass spectrometry analysis produced state-of-the-art performances in terms of ionisation voltage (0.7 kV). In addition, we demonstrate nanoESI sources which are able to work with high aqueous concentration samples (H_2O:CH_3OH = 90:10) which allows MS analysis in native conditions.

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References

[1] H. Anderson, A. Van den Berg, Microfluidic devices for cellomics: a review, Sens. Actuators B 92 (2003) 315–325.

[2] D. Reyes, D. Iossifidis, P. Auroux, A. Manz, Micro Total Analysis Systems. 1. Introduction, theory and technology, Anal. Chem. 74 (2002) 2623–2636.
[3] D. Figery, D. Pinto, Proteomics on a chip: promising developments, Electrophoresis 22 (2001) 208–216.
[4] J. Voldman, M. Gray, M.A. Schmidt, Microfabrication in biology and medicine, Annu. Rev. Biomed. Eng. 1 (1999) 401–425.
[5] M.S. Wilm, M. Mann, Analytical properties of the nanoelectrospray ion source, Anal. Chem. 68 (1996) 1–8.
[6] G.A. Valaskovic, F.W. McLafferty, Long-lived metallized tips for nanoliter electrospray mass spectrometry, J. Am. Soc. Mass Spectrom. 7 (1996) 1270–1272.
[7] Q. Xue, F. Foret, Y.M. Dunayevskiy, P.M. Zavracky, N.E. McGruer, B.L. Karger, Mulitchannel microchip electrospray mass spectrometry, Anal. Chem. 69 (1997) 426–430.
[8] R.S. Ramsey, J.M. Ramsey, Generating electrospray from microchip devices using electroosmotic pumping, Anal. Chem. 69 (1997) 1174–1178.
[9] B. Zhang, H. Liu, B.L. Karger, F. Foret, Microfabricated devices for capillary electrophoresis–electrospray mass spectrometry, Anal. Chem. 71 (1999) 3258–3264.
[10] C. Yuan, J. Shiea, Sequential electrospray analysis using sharp tip channels fabricated on a plastic chip, Anal. Chem. 73 (2001) 1080–1083.
[11] J. Kameoka, R. Orth, B. Ilic, D. Czaplewski, T. Wachs, H.G. Craighead, An electrospray ionisation source for integration with microfluidics, Anal. Chem. 74 (2002) 5897–5901.
[12] G.A. Schultz, T.N. Corso, S.J. Prosser, S. Zhang, A fully integrated monolithic microchip electrospray device for mass spectrometry, Anal. Chem. 72 (2000) 4058–4063.
[13] P. Griss, J. Melin, J. Sjodahl, J. Roeraade, G. Stemme, Development of micromachined hollow tips for protein analysis based on nanoelectrospray ionisation mass spectrometry, J. Micromech. Microeng. 12 (2002) 682–687.
[14] A. Desai, Y.-C. Tai, M.T. Davis, T.D. Lee, Electrospray nozzle for mass spectrometry, in: Proceedings of the International Conference on Solid-State Sensors and Actuators Transducers, 1997.
[15] L. Lin, P. Pisano, Silicon processed micro-needles, IEEE J. Micromech. Syst. 8 (1999) 78–84.
[16] J.S. Kim, D.R. Knapp, Microfabricated PDMS multichannel emitter for electrospray ionisation mass spectrometry, J. Am. Soc. Mass Spectrom. 12 (2001) 463–469.
[17] V. Gobry, J. Oostrum, M. Martinelli, T.C. Rohner, F. Reymond, J.S. Rossier, H.H. Girault, Microfabricated polymer injector for direct mass spectrometry, Proteomics 2 (2002).
[18] M.S. Wilm, M. Mann, Electrospray and Taylor-cone theory, Dole's beam of macromolecules at last? Int. J. Mass Spectrom. Ion Processes 136 (1994) 167–180.
[19] S. Arscott, S. Le Gac, C. Druon, P. Tabourier, C. Rolando, A micronib nanoelectrospray source for mass spectrometry, Sens. Actuators B 98 (2004) 140–147.
[20] J.M. Bustillo, R.T. Howe, R.T. Muller, Surface micromachining for microelectromechanical systems, Proc. IEEE 86 (8) (1998) 1552–1574.
[21] R.T. Howe, R.S. Muller, Polycrystalline silicon micromechanical beams, J. Electrochem. Soc. 130 (6) (1983) 1420–1423.
[22] R.T. Howe, R.S. Muller, Stress in polycrystalline and amorphous silicon thin films, J. Appl. Phys. 54 (8) (1983) 4674–4675.
[23] J.W. Berenschot, N.R. Tas, T.S.J. Lammerink, M. Elwenspoek, A. van den Berg, Advanced sacrificial poly-Si technology for fluidic systems, J. Micromech. Microeng. 12 (2002) 621–624.
[24] H. Lorenz, M. Despont, M. Fahrni, N. LaBianca, P. Vettiger, P. Renaud, SU-8: a low-cost negative resist for MEMS, J. Micromech. Microeng. 7 (1997) 121–124.
[25] H. Guckel, T. Randazzo, D.W. Burns, A simple technique for the determination of mechanical strain in thin films with applications to polysilicon, J. Appl. Phys. 57 (5) (1985) 1671–1675.
[26] S. Lucas, K. Kis-Sion, J. Pinel, O. Bonnaud, Polysilicon cantilever beam using surface micromachining technology for applications in microswitches, J. Micromech. Microeng. 7 (1997) 159–161.
[27] T.P. Burg, S.R. Manalis, Suspended microchannel resonators for biomolecular detection, Appl. Phys. Lett. 83 (13) (2003) 2698–2700.
[28] W.N. Sharpe Jr., B. Yuan, R. Vaidyanathan, R.L. Edwards, Measurement of Young's modulus, Poissons's ratio and tensile strength of polysilicon, in: Proceedings of the 10th IEEE International Workshop on Microelectricalmechanical Systems, Nagoya, Japan, 1997, pp. 424–429.
[29] D. Maier-Schneider, J. Maibach, E. Obermeier, D. Schneider, Variations in Young's modulus and intrinsic stress of LPCVD-polysilicon due to high-temperature annealing, J. Micromech. Microeng. 5 (1995) 121–124.
[30] W.N. Sharpe Jr., S.B. Brown, G.C. Johnson, W. Knauss, Round-robin tests of modulus and strength of polysilicon, in: Microelectromechanical Structures for Materials Research, San Francisco, CA, 1998, pp. 57–65.
[31] L. Chen, J. Miao, L. Guo, R. Lin, Control of stress in highly doped polysilicon multi-layer diaphragm structures, Surf. Coat. Technol. 141 (1) (2001) 96–102.
[32] X. Zhang, T.-Y. Zhang, M. Wong, Y. Zohar, Rapid thermal annealing of polysilicon thin films, J. Microelectromech. Syst. 7 (4) (1998) 356–364.
[33] J. Yang, H. Kahn, A.-Q. He, S.M. Phillips, A.H. Heuer, A new technique for producing large-area as-deposited zero-stress LPCVD polysilicon films: the multipoly process, IEEE J. Microelectromech. Syst. 9 (4) (2000) 485–494.
[34] H. Guckel, J.J. Sniegowski, T.R. Cristenson, S. Mohney, T.F. Kelly, Fabrication of micromechanical devices from polysilicon films with smooth surfaces, Sens. Actuators 20 (1989) 117–122.
[35] U. Schnakenberg, W. Benecke, P. Lange, TMAH etchants for silicon micromachining, in: Tech. Digest 6th Int. Conf. Solid State Sens. Actuators (Transducers), San Francisco, 1991, pp. 815–818.
[36] O. Tabata, R. Asahi, H. Funabashi, S. Sugiyama, Anisotropic etching of Si in TMAH, Sens. Actuators A 43 (1992) 51–57.
[37] J. Buhler, F.-P. Steiner, H. Baltes, Silicon dioxide sacrificial layer etching in surface micromachining, J. Micromech. Microeng. 7 (1997) R1–R13.
[38] M. Brinkmann, S. Arscott, S. Le Gac, C. Druon, P. Tabourier, C. Rolando, Microfluidic design principles of capillary slot-based electrospray sources, Appl. Phys. Lett., accepted for publication.

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