MICROFABRICATION OF LOW THERMAL MASS HEATED NEBULIZER CHIPS FOR MASS SPECTROMETRY

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Abstract — A low thermal mass Si-glass heated nebulizer chip for mass spectrometry is presented. The chips are used to mix a liquid sample (ca. 10 μL/min) and with a nebulizer gas (N₂ at ca. 100 mL/min) and vaporize the mixture. They are suited to work with multiple atmospheric pressure ionization methods. Miniaturization of heated nebulizer chips increases sensitivity, performance and flexibility for mass spectrometry.

The microsystem includes a sample channel with an in-plane converging exit nozzle and a resistive copper heater, located on the channel roof, enabling operation temperatures above 450 °C. Excessive Si is etched away for reduction of heat losses due to conduction, and improvement of the heater efficiency. The chip is designed to ensure low temperatures at the side of fluidic inlet, allowing an easy connection of nebulizer gas with a polymeric sealant.

The jets are characterized by scanning with a miniature thermocouple perpendicularly to the stream direction. Jet temperatures and shape can be evaluated with the acquired cross-sectional 2-dimensional temperature maps. Jets are found to stream without spreading, creating small spot sizes depending on nozzle dimensions.

Keywords: Microfluidics, mass spectrometry, silicon microprocessing, thermal MEMS

I - Introduction

In order to combine mass spectrometry with microfluidic devices, the sample flow rates have to be compatible with the ionization techniques, which range from nanoliters/min to microliters/min. Heated nebulizer chips have been implemented with atmospheric pressure chemical ionization (APCI), atmospheric pressure photoionization (APPI), atmospheric pressure thermospray ionization (APTSI), electrospray ionization (ESI), and desorption atmospheric pressure photoionization (DAPPI) [1]. Heated nebulizer chips have also been combined with liquid chromatography [2], a common separation step, to achieve higher analytical performance.

In this work, the design, fabrication and characterization of a low thermal mass heated nebulizer chip is presented. The chip has reduced thermal mass because all silicon outside active areas is etched away by DRIE. This enables smaller heating powers and faster temperature ramp rates. The chip is made by bonding a silicon wafer anodically to a glass wafer. The silicon part includes a sample channel, inlets for both sample and nebulizer gas, an in-plane exit nozzle and a resistive heater wire on the channel roof made of copper. The nozzle size has also been scaled down. Thermal scanning has been used to show that the scaled down hot gas jet retains its pencil-like, very confined shape.

II - Experimental Details

A. Chip design

The chip fabrication requires three photomasks: one for the heater wire design on the top side, one for the sample channel design on the bottom side and one for the nebulizer gas inlets on the top side. Total length of the channel is 35 mm. Towards the exit nozzle all excessive silicon is etched away leaving a 20 mm long channel with 150 μm thin sidewalls. The meandering heater wire is located on the channel roof as shown in Fig. 1. The idea of this design is to maximize the heat flow to the channel, while simultaneously keeping the temperature rise as small as possible on the inlet side, in order to allow easy connection of the nebulizer gas. Therefore the heater is separated 2 mm from where the silicon is etched away, and the connection pads are designed as heat sinks.

B. Heated nebulizer chip fabrication

The heated nebulizer chip consists of a 100 mm diameter <100> silicon wafer, bonded to a borosilicate glass (Pyrex) bottom wafer. The top wafer features an etched channel with a copper heater on its roof. The 500 μm thick Pyrex wafer is not processed at all; it is joined to the 380 μm thick silicon wafer by anodic bonding to seal the channels only. Main process steps are shown in Fig. 2. First, 300 nm of silicon dioxide and then 300 nm of silicon nitride are deposited by plasma enhanced chemical vapor deposition (PECVD). Both layers are grown at 400°C to achieve dense films with low thermal
stresses [3-5]. Silicon dioxide is used as an insulation layer, silicon nitride as a diffusion barrier for copper oxidation. Next, 17 nm of chromium, 300 nm of copper and again 17 nm of chromium are sputtered onto silicon nitride. Chromium is used adhesion promotion of copper. The metal films are patterned using standard photolithography (AZ5214E photoresist) and wet etching. Chromium is etched in 37% hydrochloric acid at room temperature (etch rate ca. 0.5 nm s\(^{-1}\)). Copper is etched in 1 : 1 : 2 HCl-H\(_2\)O\(_2\)-H\(_2\)O at room temperature (etch rate ca. 50 nm s\(^{-1}\)). After resist removal (I) 300 nm of silicon nitride is deposited onto the heater side by PECVD at 400°C. Then a 50 nm alumina (Al\(_2\)O\(_3\)) hard mask is deposited on both sides of the wafer simultaneously (II). Alumina is grown by atomic layer deposition (ALD) at 220°C: first precursor, trimethylaluminum (TMA), is introduced and given time to be absorbed until a continuous monolayer covers all surfaces. Then excessive precursor is purged away and the next gaseous precursor water is introduced. Both precursors react, forming a monolayer of alumina [6]. The reaction happens between two monolayers and is thereby self-limiting. The reaction chamber is purged after the reaction is finished and the procedure starts anew. Alumina is patterned with standard lithography and wet etching in buffered hydrofluoric acid (BHF) at room temperature (1 : 1, etch rate ca. 1 nm s\(^{-1}\)). Underlying nitride and oxide layers are dry etched by reactive ion etching (RIE). After mask removal 250 µm deep channels are etched from the bottom side into the silicon by pulsed deep reactive ion etching (DRIE, Bosch process) (III). Before etching from the top side, the channel mask has to be removed in BHF, in order to free the bonding surface from alumina. Therefore the heater side is protected with a photoresist coating. After removal of the protective coating, silicon is etched from the top side by Bosch DRIE. The wafers are bonded by anodic bonding at 400°C with an applied voltage of 600 V (IV). Finally the chips are separated with a dicing saw.

B. Jet characterization

Jet shapes were characterized by temperature scanning measurements (Figure 3) were done with a miniature thermocouple (TC) with a ‘V’ shaped 5 mm long tip made of 25 µm thick wire (KFT-25-200-100, Anbe SMT Co, Japan). Tip size mainly determines resolution and response time of the temperature measurements [7]. The thermocouple was mounted to a motorized xyz-table (F-206 Hexapod, PI, Germany). The nebulizer chip was connected to nitrogen (flow rate 100 mL/min) and a power source and positioned in a manner that the produced nitrogen jet streams along x-direction of the xyz-table. The thermocouple scans three 3x3 mm\(^2\) yz-planes at 1 mm, 5 mm and 10 mm distance to the exit nozzle creating cross-sectional temperature maps of the heated nitrogen jet. Temperature is measured using 0.1 mm step size.

C. Mass spectrometer experiment

The new low thermal mass heated nebulizer chip is applied to an atmospheric pressure photoionization mass spectrometer to verify chip performance. A SCIEX API 3000 mass spectrometer was used. Nitrogen was used as the nebulizer gas with a flow rate of 100 mL min\(^{-1}\). Toluene dopant (3.5 µL min\(^{-1}\)), needed for the ionization process, was mixed to the nebulizer gas. The sample contained 1 µM of paracetamol, benzo[a]pyrene, testosterone and verapamil in a 50/50 methanol/water solution. Sample flow rate was 10 µL min\(^{-1}\) and heater power 3 W.

III - Results and Discussion

A. Chip fabrication

DRIE allows etching of deep channels with highly vertical sidewalls, without restrictions due to crystal orientations. Sidewall angles of 87° were achieved, leading to an undercut of up to 13 µm for the 250 µm deep channels. DRIE also permits nozzle design for jet shape improvement. SEM pictures of a 200 µm and a 300 µm nozzle are shown in Fig. 4 and Fig. 5.

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**Figure 2: Main steps of the fabrication process of low thermal mass heated nebulizer chips.**

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**Figure 3: Jet characterization setup.**
The frontal surfaces in Fig. 4 and 5 are both mechanically cut with a dicing saw.

Copper was introduced as a heater material instead of platinum [1,2] to reduce costs and process complexity (aqua regia etch step is difficult). However, the use of copper bears some problems: copper diffuses into silicon and silicon dioxide [8]. A diffusion barrier is required in order to protect the silicon dioxide isolation layer. Silicon nitride, deposited at 400°C, successfully prevented device failure due to copper diffusion up to at least 500°C.

Another issue when utilizing copper is its lower resistivity in comparison to platinum, thus heater dimensions have to be redesigned. The 72 mm long and 300 nm thick meandering heater wires had resistances of roughly 45 Ω and enabled operation temperatures above 450°C.

The silicon channel wall material with the heater on top improved heater efficiency, due to better heat conduction in comparison to a heater located on the glass side [1]. At 3 W heating power jet temperatures of 350°C at 1 mm distance were achieved, whereas an all-glass chip with platinum heater reached only 290°C at the same distance.

**B. Jet characterization**

Cross-sectional temperature maps of the jets produced by the new nebulizer chips are shown in Fig. 6. Maximum gas jet temperatures are 350°C at 1 mm, 275°C at 5 mm and 215°C at 10 mm distance to the exit nozzle for both chips. The spot sizes depend on the nozzle dimensions: the 300 µm nozzle produces a 0.32 mm² spot, whereas the 200 µm nozzle produces a 0.20 mm² spot. The spot was defined as area with temperatures higher than 85% of the respective maximum temperature.

**C. Mass spectrometry**

Functionality of the presented chip tested with APPI-MS measurements. The new chip showed comparable analytical performance to earlier devices. The acquired spectrum or paracetamol, benzo[a]pyrene, testosterone and verapamil are shown in Fig. 7.
IV - Conclusions

The new design which eliminates glass processing, and replaces it with double sided silicon processing, is advantageous because the cumbersome masking required for deep glass etching can be avoided. It necessitated redesign of a chip holder, as now both electrical and fluidic connections are from the same side.

Copper heater performs as expected, but its long term reliability at elevated temperatures remains to be studied. The reliability of thin silicon walls needs also to be assessed. Similar reduced thermal mass device [10] has maximum operating temperature of 130°C only.

The reduced thermal mass results in higher operating temperatures. The temperature of the gas jet is ca. 30°C hotter for the same heating power.

References