ELECTRONIC SUPPLEMENTARY INFORMATION (E.S.I.)

Compact 3D-Printed Interface for Coupling Open Digital Microchips with Venturi Easy Ambient Sonic-Spray Ionization Mass Spectrometry

Jie-Bi Hu,[a] Ting-Ru Chen,[a] Chia-Hsien Chang,[b] Ji-Yen Cheng,[c]

Yu-Chie Chen,[a,d] Pawel L. Urban*[a,d]

[a] *Department of Applied Chemistry, National Chiao Tung University;*

Hsinchu 300, Taiwan

[b] *ASUSTeK Computer Inc.*

Taipei, 11259, Taiwan

[c] *Research Center for Applied Sciences, Academia Sinica*

Taipei 11529, Taiwan

[d] *Institute of Molecular Science, National Chiao Tung University;*

Hsinchu 300, Taiwan

* Corresponding author; fax +886-3-5723764.

Additional experimental details

Fabrication of open digital microfluidic chips

The ITO glass sheets were diced to obtain pieces of specific size: 50 × 40 mm. They were cleaned with the following solvents: pure water, ethanol, acetone, isopropanol. The substrate was subjected to washing in every solvent in the presence of ultrasounds (600 W, DC600H; Delta, Taipei, Taiwan) for 5 min. Subsequently, the substrate was placed in an oven at 130 °C for 30 min to remove residual water. After cooling down, the substrate was coated with a 2:1 (v/v) mixture of the Aldrich negative photoresist and the thinner solution. Typically, a ~ 0.7 mL aliquot of the coating solution was applied to every piece of ITO glass prior to spin-coating at 200 rpm for 10 s, followed by coating at 500 rpm for 20 s. After coating, the microchips were "soft-baked" on a hot plate at 85 °C for 20 min. The coating and the subsequent treatment were conducted inside a laminar air flow chamber, in the dark. After cooling down, the microchips were exposed with a custom-made plastic soft film photomask (JiLaiWeiChuang, Taoyuan, Taiwan) to ultraviolet (UV) light (~ 25 mW cm^{-2}, AG350-4N; M&R Nano Technology, Taoyuan, Taiwan) for 10 s. Afterwards, the microchips were put in the development bath for 45 s, and subsequently rinsed with isopropanol. They were dried in the stream of nitrogen gas. The dry chips were baked again on the hot plate at 120 °C for 15 min, and then slowly cooled down. Etching was conducted by immersing the microchips in ~ 19% hydrochloric acid at 80 °C for ~ 90 s. Next, the microchips were rinsed with pure water, washed in acetone, followed by peeling off the residual photoresist. The microchips were then dried under the stream of nitrogen gas. Then, they were cleaned again with the following solvents: pure water, ethanol, acetone, and isopropanol. They were submerged in every washing liquid, and placed in an ultrasonic bath for 5 min. Then, the microchips were put into oven (130 °C) for 30 min to remove residual water. At this point, the electric contacts on the longer edges of the microchips were protected with adhesive tape. A ~ 0.7 mL aliquot of the negative photoresist SU-8 2002 was subsequently dispensed onto the microchips, and spin-coating was conducted at 500 rpm for 10 s, followed by spin-coating at 3000 rpm for 30 s. After this step, the microchips were "soft-baked" on the hot plate at 95 °C for 2 min. Afterwards, they were exposed to UV light (~ 25 mW cm^{-2}) for 6 s. Post-exposure baking was conducted at 95 °C for 2.5 min. Subsequently, the microchips were cooled down. In order to solidify the SU-8 layer, "hard bake" at 120 °C was conducted for 2 min. The microchips were cooled down again. Eventually, to render the surface of the microchips sufficiently hydrophobic, a ~ 0.5 mL aliquot of dilute Cytop was coated onto the upper surface of every microchip by spin-coating at 1500 rpm for 30 s. Finally, Cytop was annealed with SU-8 by heating the microchips on a hot plate at 180 °C for 1 hour. The microchips were cooled down to room temperature, and stored in a proper way, to prevent deposition of dust, in the dark. Please note that the coating with Cytop increased the contact angle of a 10-μL water droplet from 68° to 102°.

Design and assembly of the interface

The interface was printed in 9 parts, which were subsequently joined with screws or glue. It includes the frame for stable mounting at the mass spectrometer, a platform for the open digital microfluidic chip, a holder for the Peltier element (hot side up covered with ~ 3-mm thick aluminium plate; TEC1-03103, 3.5 V, 3.3 A; Centenary Materials, Shanghai, China) and a fan (MC30100V1-0000-A99; Sunonwealth Electric Machine Industry, Kaohsiung, Taiwan), a holder for the Venturi pump, a holder for a modified PCI-type connector interfaced to the chip, a plate for alignment of sample delivery and ion source capillary, a roof incorporating fan and filter to provide laminar flow of clean air, sash with observation window, holders for two peristaltic μ-pumps (RP-Q1.2N-P20A-DC3V, flow rate ~ 0.32 mL min^{-1}; Takasago Electric, Nagoya, Japan), and reagent vials (**Fig. 1B**).

Additional table

Table S1. Operation steps of the 3D-printed EWOD-based DMF system coupled with mass spectrometer.

No.	Step	Time / s
1	Analysis started by the user (touch-screen panel or remote control)	2
2	Dispensing reagents from reservoirs	3
3	Individual droplets move to the mixing zone	0.6
4	Merging droplets and mixing (optional)	2.8
5	Incubation	0-240
6	Final droplet moves to the outlet of microchip (inlet of the Venturi pump sampling capillary)	0.7
7	Detection by V-EASI-MS	10-20

Additional figures

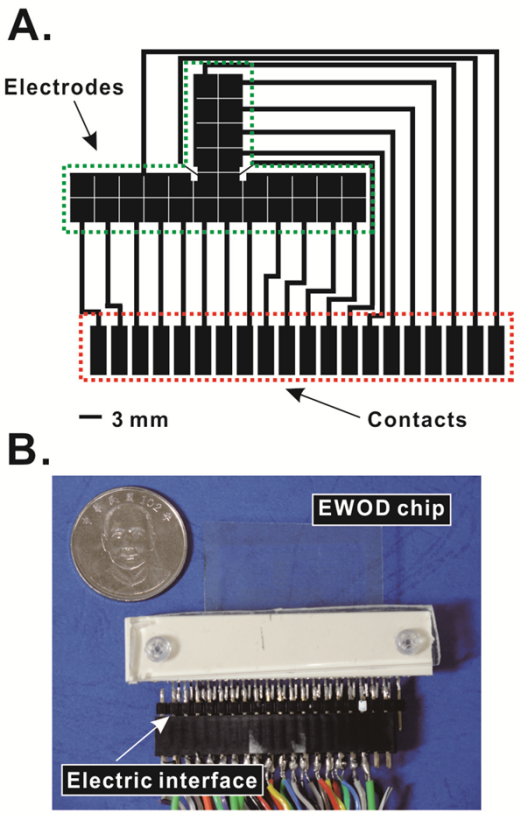

Figure S1. The digital microfluidic microchip fabricated in this study using ITO-coated glass as substrate. (A) Electrode layout. (B) Photograph of the final microchip fitted with a modified electric contact socket.

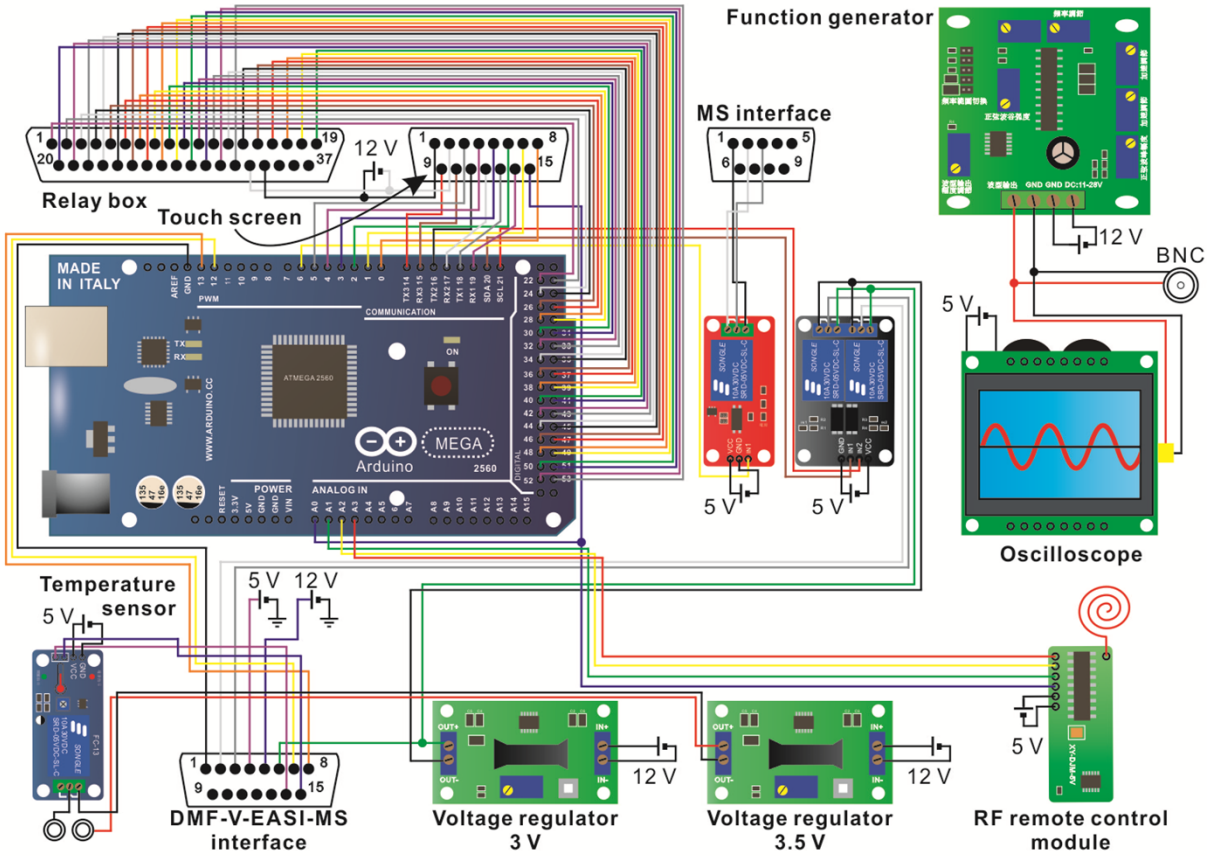

Figure S2. A simplified scheme of the electronic control device coupled with the DMF-V-EASI-MS interface.

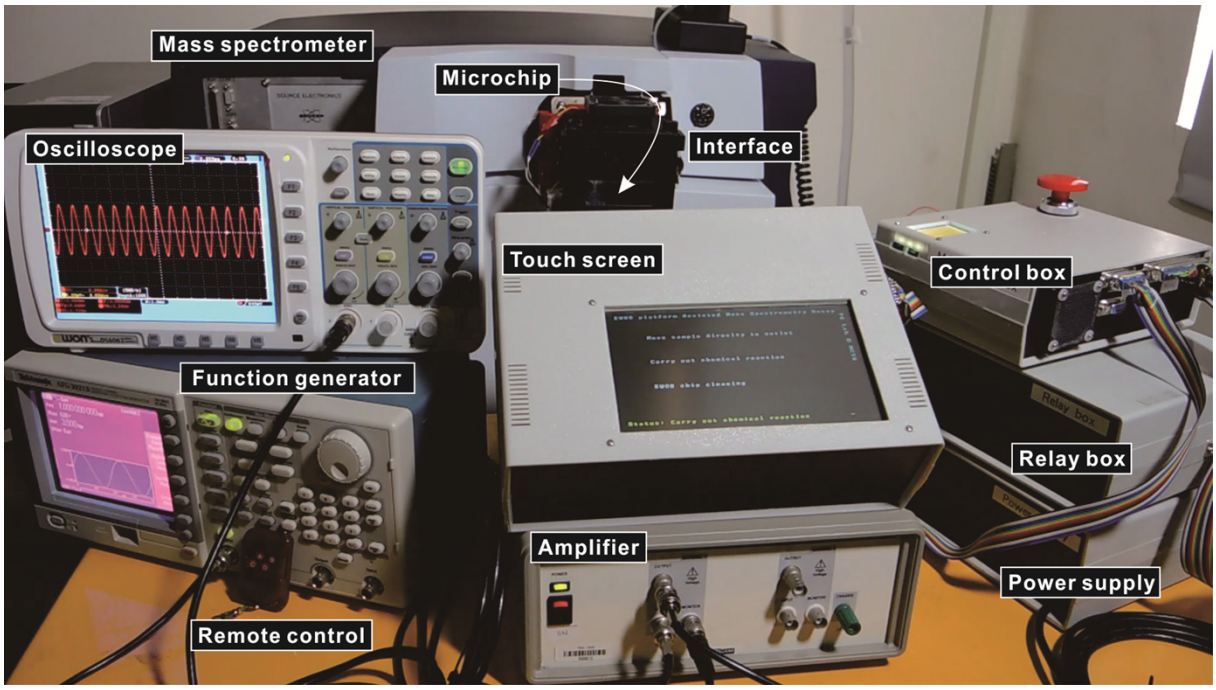

Figure S3. Photograph of the 3D-printed EWOD-based DMF system and auxiliary equipment, coupled with the ion-trap mass spectrometer.