Electronic Supplementary Material (ESI) for Analytical Methods.
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Supplementary Information

Integrated Microfluidic Aptasensor for Mass Spectrometric Detection of Vasopressin in Human Plasma Ultrafiltrate

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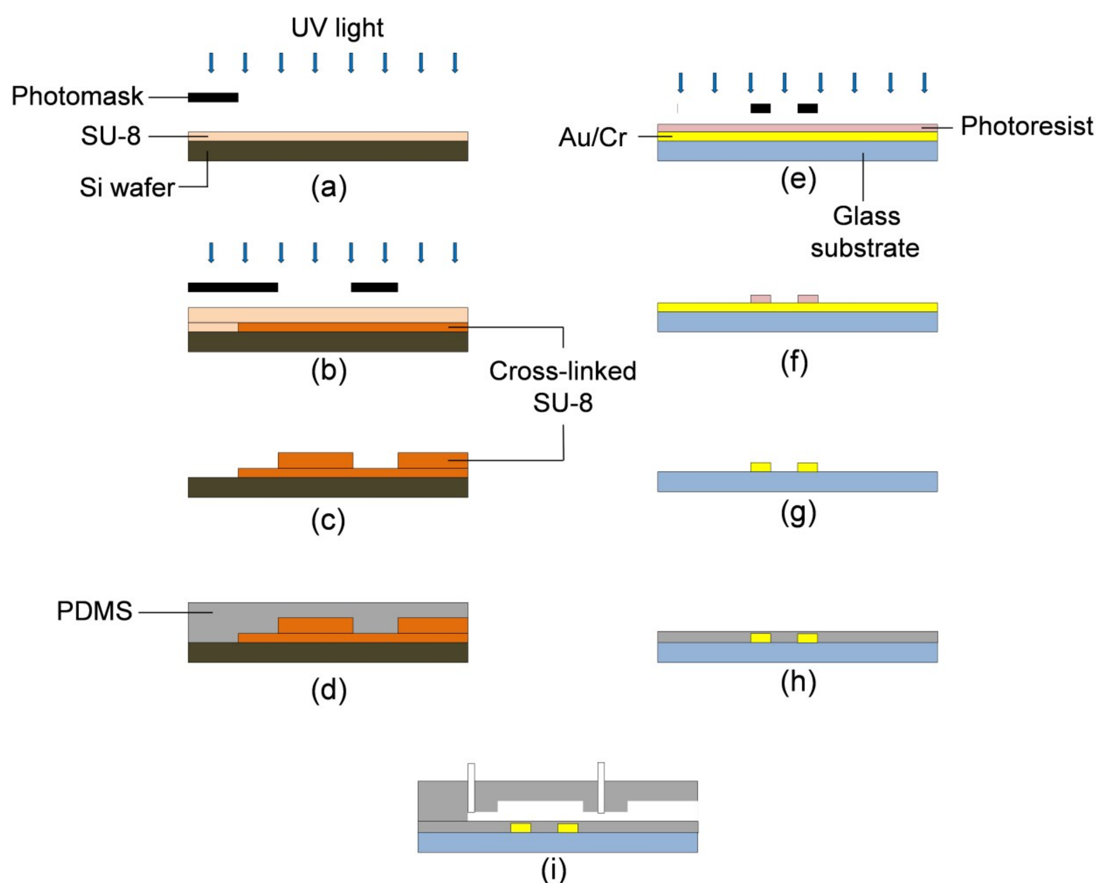

Fig. S1 Fabrication processes for the integrated microdevice. (a-c) Fabrication of SU-8 mold. (d) PDMS layer casting using the SU-8 mold. (e-h) Micro-patterning of metallic bilayer (Au/Cr) on a glass substrate using photolithography for a resistive microheater and temperature sensor. (i) Packaging of the microdevice by PDMS bonding.

The integrated microdevice was fabricated by bonding a polydimethylsiloxane (PDMS) layer onto a glass substrate incorporating a patterned microheater and temperature sensor. To fabricate a SU-8 mold, two layers of SU-8 were spin-coated onto a cleaned silicon wafer followed by UV exposure and baking steps. PDMS pre-polymer (Sylgard 184, Dow Corning) was then poured onto the mold and baked for 1 hr at 80 °C (Figure S1a-d). The microstructured PDMS layer was then peeled off from the mold. In the meantime, chrome (Cr) and gold (Au) layers were consecutively deposited on a cleaned glass substrate

by thermal evaporation. Following photolithographic patterning of the metal layers, the substrate was passivated with a thin PDMS layer using spin coating (Figure S1e-h). The PDMS layer was then bonded to the substrate following oxygen plasma surface treatment (Figure S1i).

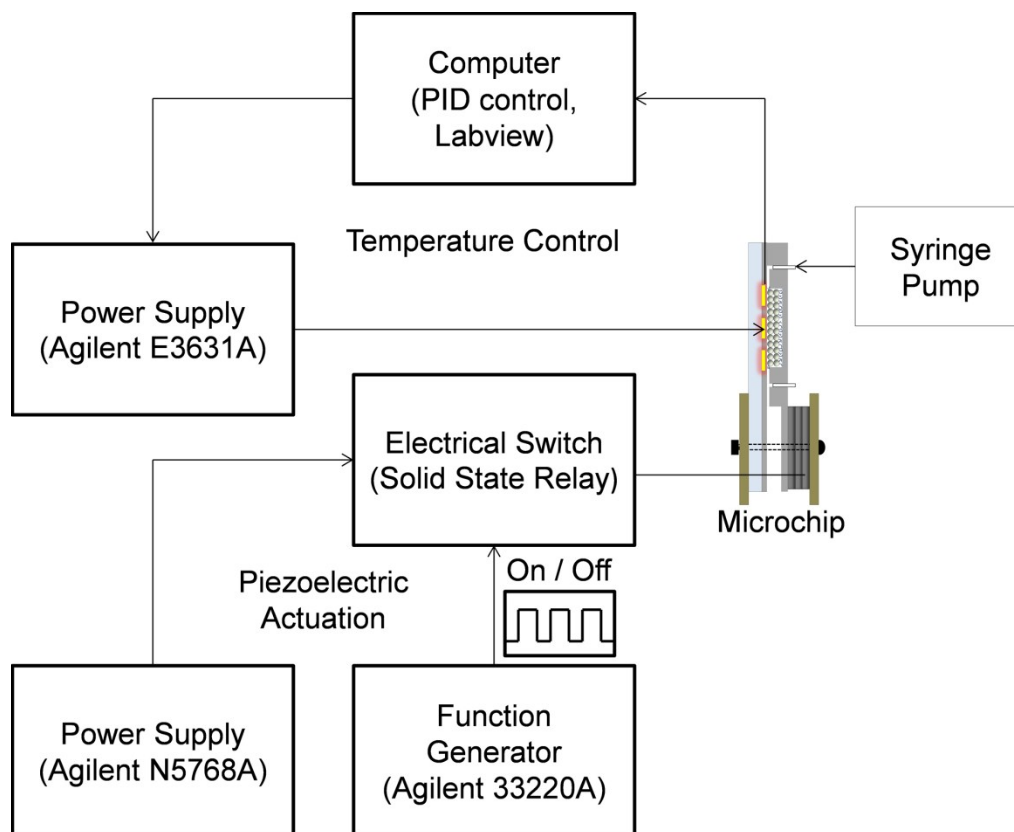

Fig. S2 A schematic of the experimental setup. The microdevice is operated by closed-loop temperature control and PZT actuation.

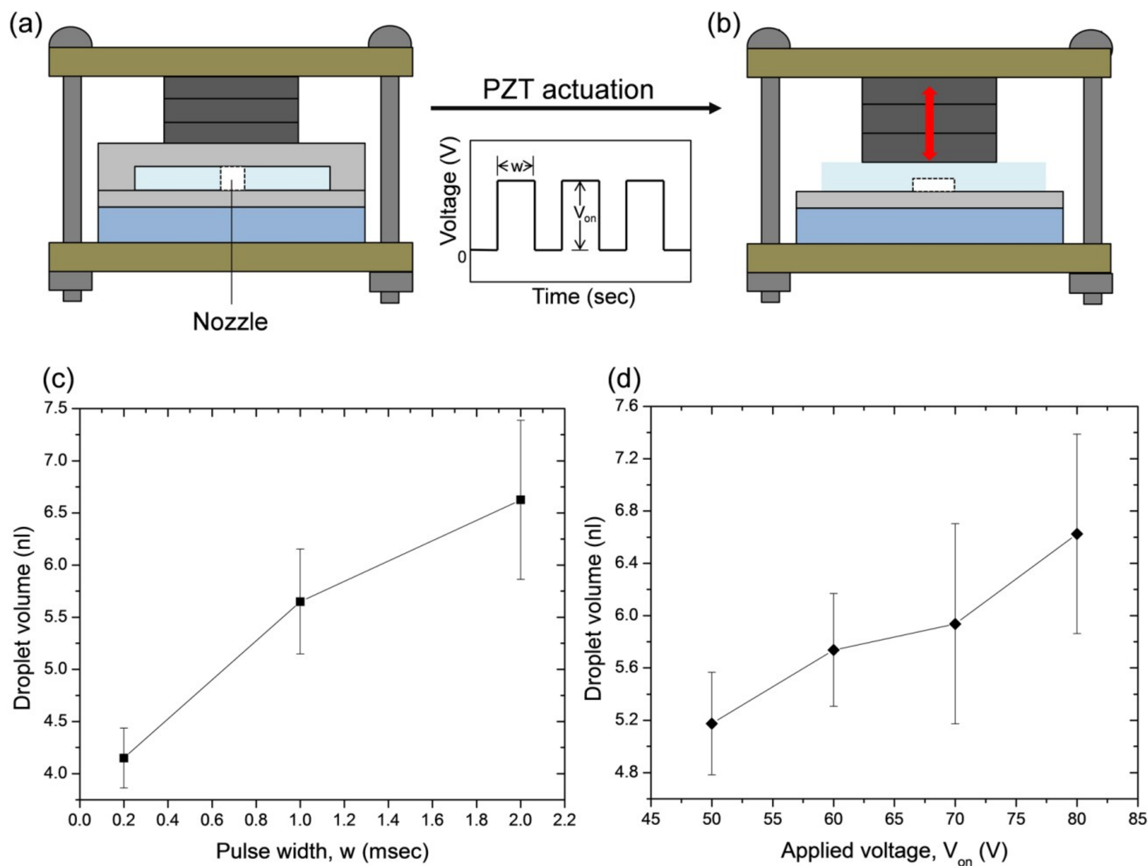

Fig. S3 Principle of PZT spotting: (a) A PZT stack actuator is placed on top of the spotting chamber, and plastic holders hold the actuator with the chip. (b) A PZT actuation is intermittently triggered by applying DC voltages (50-80 V) inducing a linear displacement ($\Delta t \sim 6$ μm at 80 V) of the PZT stack actuator, thus resulting in the deformation of the top PDMS layer (2 mm thick). Due to the spontaneous pressure increase in the chamber, a droplet with a volume of 4 to 7.5 nl is ejected through a square-shaped nozzle (150 μm×150 μm). Characterization of the PZT nanoliter-droplet ejector showing the dependence of the dispensed droplet volume on (c) pulse width, w and (d) voltage applied, V_{on}. It was noted that the volume dispensed proportionally increased with parameters, w (c) and V_{on} (d), which are related to the duration of driving stroke and physical displacement of the actuator respectively. In all experiments, measurements were performed in triplicates, from which averages and standard deviations were computed.

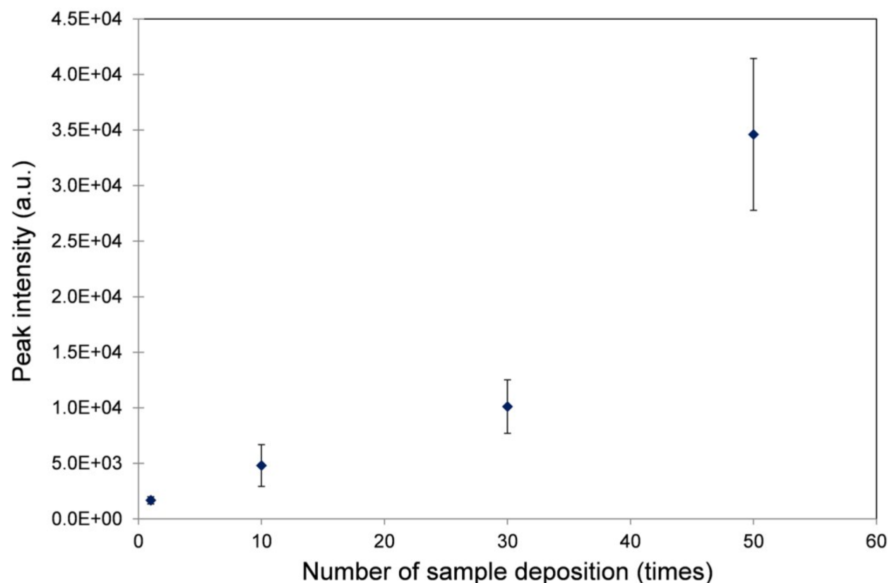

Fig. S4 Determination of an optimal number of sample deposition for MALDI-TOF mass spectrometric detection of AVP: The intensities of mass spectral peak for AVP were measured with varying numbers of sample deposition. A time interval of 30 sec was given between depositions to allow a sample droplet to be dried completely, thereby avoiding undesired droplet accumulation that increases a dried MALDI spot size. Experimental results showed that MALDI responses proportionally increased with the number of sample deposition in the range of 1 to 50 times, indicating that analyte molecules were accumulated on the spot by repeated depositions. It was also observed that the thin matrix layer was frequently dissolved with sample depositions more than 50 times, precluding the MALDI-TOF mass spectrometric analysis.

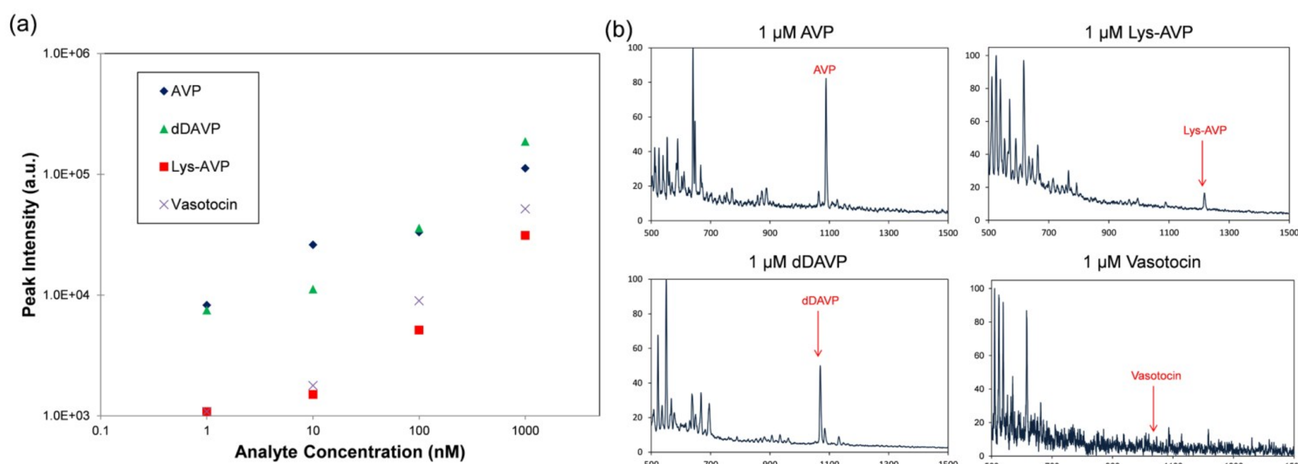

Fig. S5 Internal standard selection: Various polypeptides (vasotocin/ dDAVP/ Lys-AVP) were first selected as internal standard candidates based on the similarity of chemical structure and molecular weight with AVP. (a) To find the best internal standard of AVP producing the most similar MALDI response with AVP, these polypeptides at 100 nM were tested. Experimental results showed that dDAVP (green triangle) yielded more similar MALDI responses with AVP compared to the other two analytes, Lys-AVP (red square) and vasotocin (blue cross). (b) In addition, their binding characteristics toward the AVP-specific aptamer on beads were tested at 1 µM by chip processing followed by MALDI mass spectrometry. Only dDAVP showed a peak with a comparable intensity to AVP, while peaks representing Lys-AVP and vasotocin were not observed in MALDI spectra, concluding that dDAVP molecules were specifically captured by our aptamer. Based on both results, dDAVP was chosen as the internal standard for relative quantification of AVP in this work.