Dry-Mass Sensing for Microfluidics

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Introduction

Traditional quantification methods for microfluidics typically require either extrinsic reporters – such as fluorescent labels – or have low sensitivity and may depend on the specific chemical environment as well as unknown material parameters (e.g., extinction coefficient, dielectric constant). Therefore, measurement outcomes can be difficult to interpret. Determining the dry mass of the analyte, however, is a direct measure of a physically well-defined quantity.

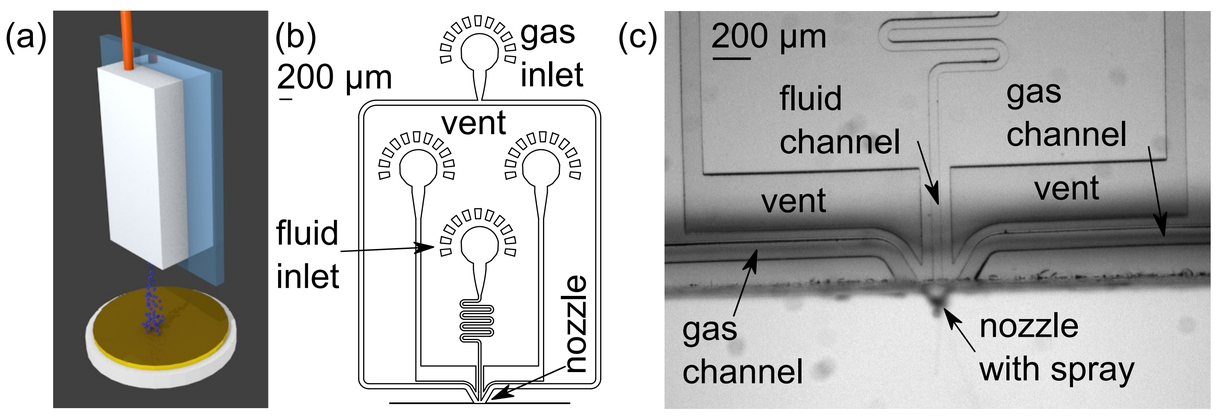

Fig 1: (a) Schematic representation of the approach for measuring dry mass from a microfluidic device. (b) Drawing of the spray nozzle. (c) Photograph of a spray being generated from a microfluidic channel.

The approach in a nutshell [1,2]:
- Spray-dry [3,4] the contents of a microfluidic channel onto the vibrating surface of an electromechanical sensor (quartz crystal microbalance; QCM)
- Decouple the spray to allow the solvents to dry (shutter)
- Determine the frequency shift of the resonator to quantify the deposited mass

Proof of Concept

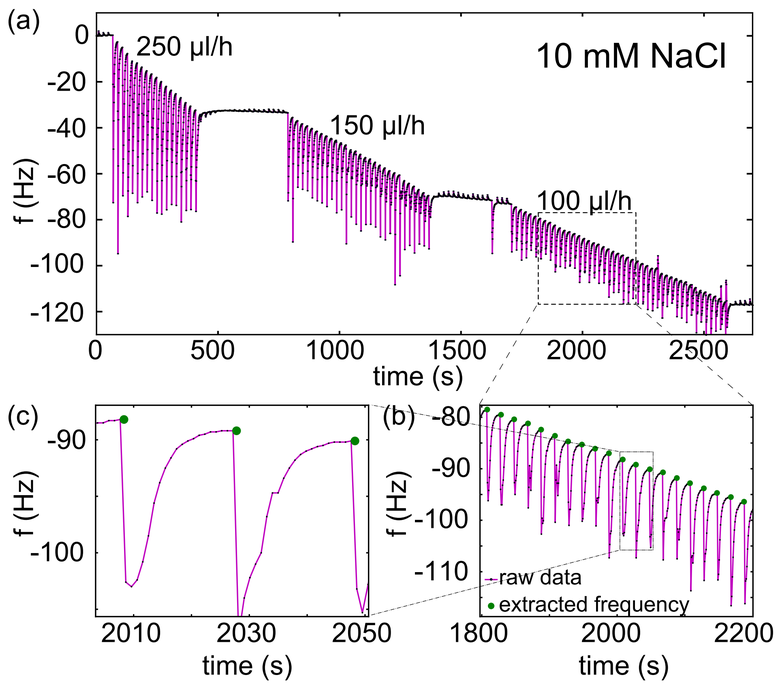

Fig 2: (a) Measured frequency shift as a function of time for different applied flow rates. A shutter controls the analyte deposition for 0.5 s, followed by drying and equilibration during 19.5 s.
(b) and (c) Magnified views on individual spray bursts. Upon opening the shutter the resonance frequency decreases sharply and stabilises at a slighlty lower value (given by the deposited mass) after evaporation of the solvent.

References

[1] T. Müller, D. A. White, T. P. J. Knowles, Appl Phys Lett **105**, 214101 (2014).
[2] T. Müller, D. A. White, T. P. J. Knowles, GB Patent Application No. PCT/GB2014/053383 (2014).
[3] J. Thiele *et al.*, Lab Chip **11**, 2362 (2011).
[4] E. Amstad, C. Holtze, D. A. Weitz, PCT Int Appl No. 61/733,604 (2012).
[5] P. J. Cumpson and M. P. Sheah, Meas Sci Technol **1**, 544 (1990).

Characterisation and Results

1 mg/ml Lysozyme
100 ul/h
0.5 s shutter
19.5 s drying

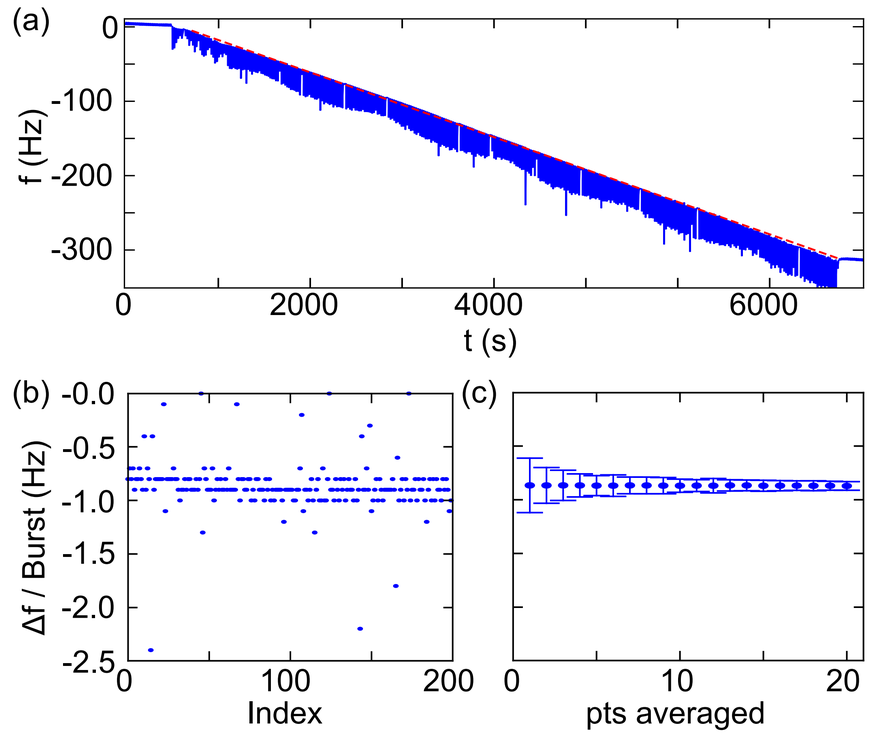

Fig 3: (a) Measured frequency shift as a function of time. (b) Frequency shift of the central 200 bursts in (a). (c) Average frequency shift and corresponding standard deviation when averaging over consecutive bursts.

- Stable operation during hours
- Linear decrease of the resonance frequency with deposited mass
- Measure deposition rates of ug/h
- Averaging over 5 spray bursts leads to an accuracy of +/- 0.09 Hz

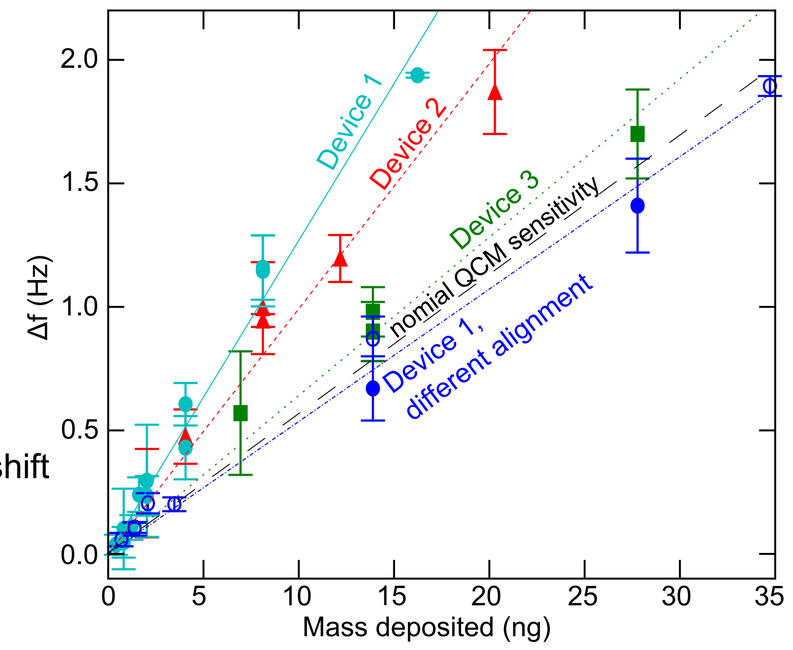

Fig 4: Average frequency shift per single spray burst in a series of 5, averaged over tens to hundreds of bursts.

- Nanogram detection sensitivity for salt and protein
- Orientation of spray with respect to QCM influences the response function
- Sensitivity can be calculated [5], but also simply calibrated

Conclusion and Outlook

- Dry analyte mass is determined by spray-drying the contents of a microchannel onto a QCM
- Accurate, quantitative label-free detection method with nanogram sensitivity
- Can be integrated with microfluidic preprocessing methods such as electrophoretic separation to form lab-on-two-chips applications
- Intrinsic calibration-method available

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