Novel automated multi-principle volume calibration system for non-contact micro and nano liter liquid handling devices

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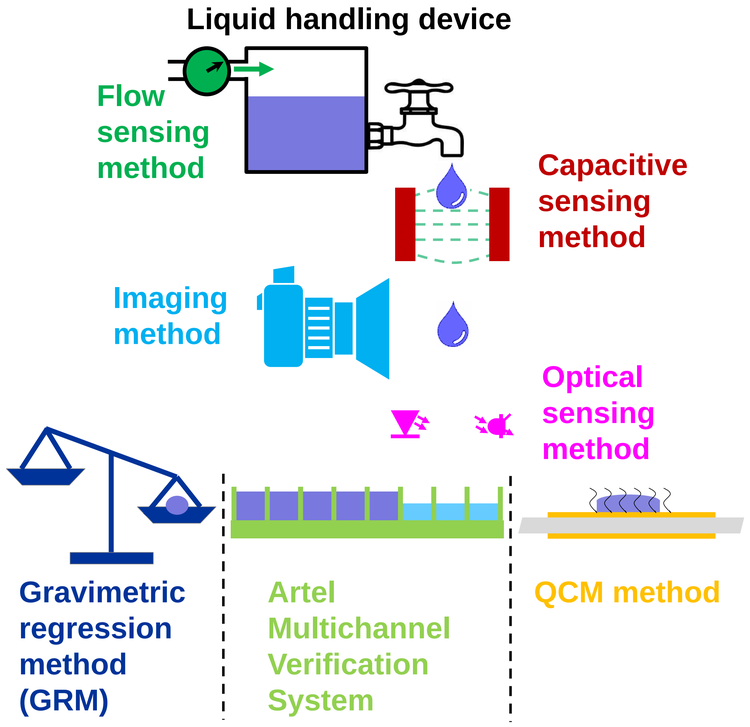
Overview

- **Multi-principle volume measurement system**
- **4 online + 1 (from 3) offline methods measuring the same liquid aliquot (from pl to sub-µl)**
- **Full automated with software #Drop (dispensing, sampling, processing, environment monitoring)**
- **Best tool to calibrate liquid-handling devices and standardize liquid volume measurements**

Working principle

A flow sensor is attached to the opening of the reservoir of a liquid handling device and detects the air-reflow during droplet ejection. The released droplet travels sequentially through the electric field of a capacitive sensor, a 3mm gap allowing for stroboscopic imaging and an optical sensor. At last, the droplet can be characterized by Artel-MVS, or by an ultra-microbalance, or by a hydrogel coated QCM sensor.



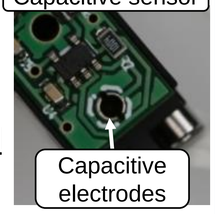
Concepts of the multi-principle liquid volume measurement

Measurement methods

Flow sensing method

- Air reflow → time integration → volume
- Calibrated with high precise pulsation-free neMESYS syringe pump system (cetoni)
- Evaluated working range: 20 nl -100 nl

Capacitive sensing method

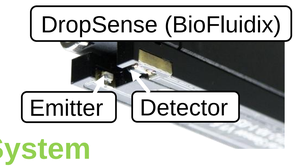


- C change when droplet flying through → liquid volume
- Evaluated working range: 20 nl -100 nl

Imaging method

- Stroboscopic photographing of droplet in flight
- Processing with auto-thresholding algorithm
- Calibrated with NIST-traceable 1951 USAF
- Evaluated working range 200 pl – 100 nl

Optical sensing method

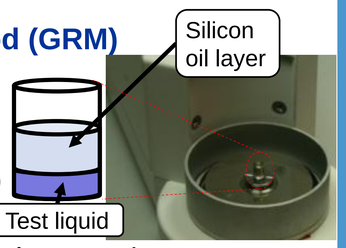


- Equal to one pixel camera
- High demand on alignment

Artel Multichannel Verification System

- Filling MTP with automated x-y linear stage
- Commercialized traceable dual-dye absorbance measurement system (Artel)

Gravimetric regression method (GRM)



- Extension of ISO 4787
- Easy traceability to SI
- Expanded uncertainty ($k = 2$) ≈ 2.6nl – 13nl @ 5 nl – 1 µl
- Against evaporation: numerical regressive compensation and silicon oil layer

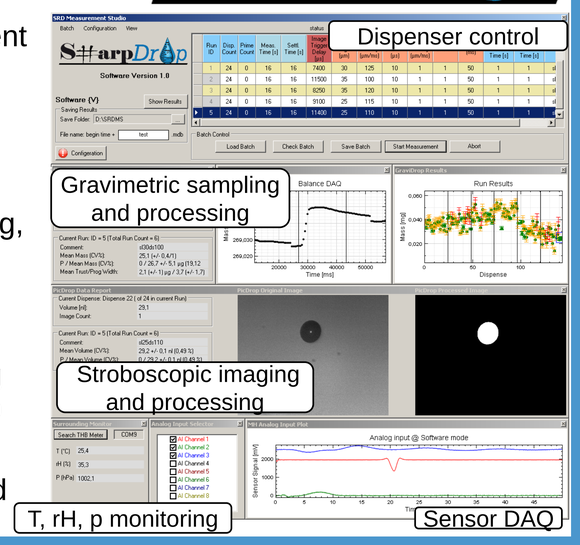
QCM method

- Resonance freq. change → droplet mass
- Liquid → semi solid phase through surface attached hydrogel coating
- Evaluated working range 200 pl – 15 nl

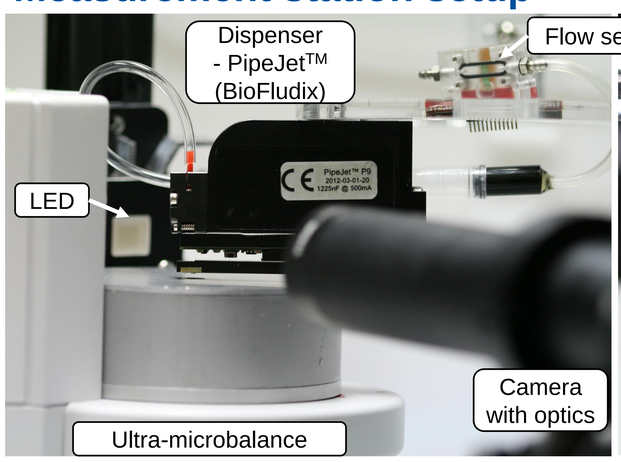
Full automation

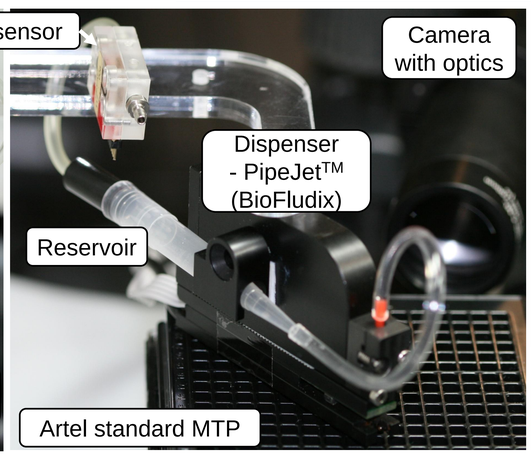
SharpDrop

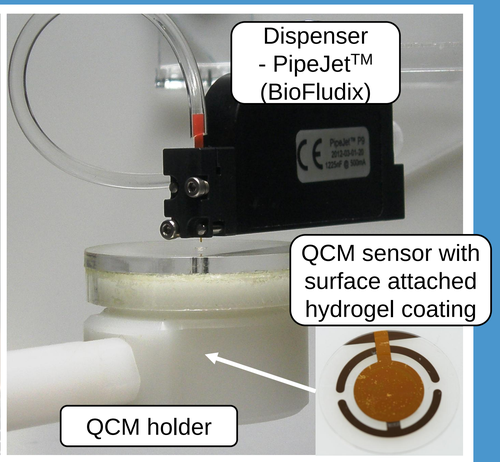
- Support six measurement methods
- Automated sampling, processing, data banking, dispenser controlling
- Monitor surrounding condition @ each exp.
- Modularized



Measurement station setup



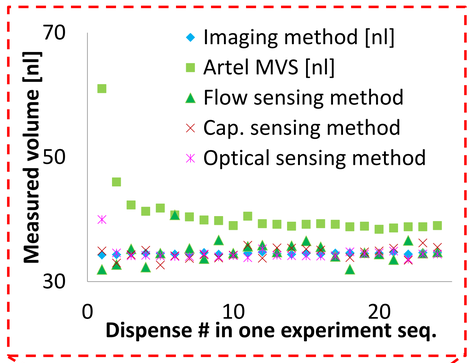


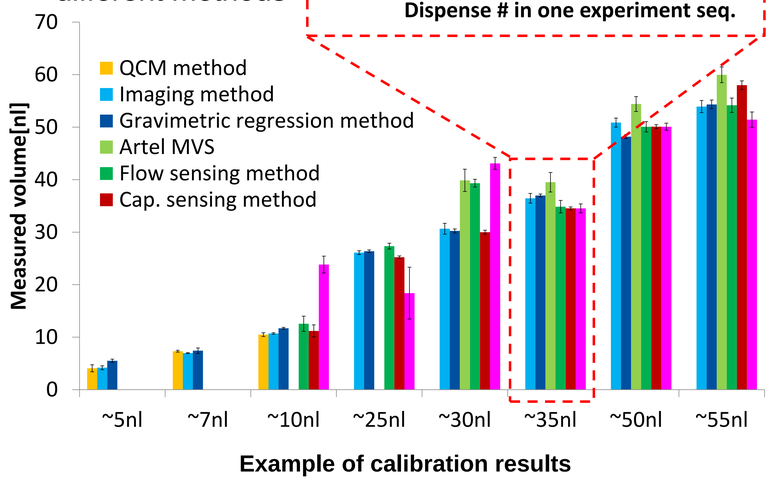


Results and conclusions

The presented liquid calibration system demonstrates a significant improvement beyond state-of-the-art in terms of multi-principle combination and full automation. This powerful system could support to establish a universal low volume liquid calibration standard for µHTS.

- Compare performance of sensors and methods on each single aliquot / droplet
- Benchmark of 7 different methods





Example of calibration results

Acknowledgments

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