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 airflow 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.

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

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

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