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## Nanoliter droplet characterization using vibrating crystal sensor with surface-attached polymer hydrogel coating

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### Abstract

This paper presents a novel method for nanoliter droplet characterization using a polymer coated sensor of a low-cost quartz crystal microbalance (QCM). The gold electrode of the crystal sensor was coated by a surface-attached polymer hydrogel film of about 2 $\mu$ m thickness using simple spin casting and photocrosslinking procedure [1,2]. The resonance frequency of the coated crystal sensor was continuously recorded at the sample rate of 2 Hz over 90 seconds before and after loading a micro droplet of filtered double-distilled water. Good repeatability (max. CV = 3.8%) and good linearity ( $r_{(x,y)} = 0.995$ ) of the maximum resonance frequency shift have been observed during 144 dispenses for 6 different droplet volumes in the range from 3 nl to 13 nl. A calibration line for the measured domain of the maximum frequency shift in relation to droplet mass was established according to the gravimetric calibration of the used dispenser with an ultra-microbalance.

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### 1. Introduction

In 1959 QCM was firstly introduced by Sauerbrey as a new method for mass measurement [3]. In contrast to the commercial analytical ultra-microbalance which can only detect 0.1  $\mu$ g, QCM is able to detect mass down to 0.1 pg [4]. Therefore, QCM has always been regarded to have high potential to

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extend the conventional gravimetric volume calibration standards from microliter- into nanoliter- or even picoliter range. In previous studies it has been proposed to employ the vibrating crystal sensor to measure the mass of deposited droplets. For instance, Han Zhuang reported in 2007 their model for loading spreading liquid droplet of about 2  $\mu\text{l}$  on a QCM sensor and got good consistency with silicon oil experiment [5]. Woosuck Shin reported in 2008 an experiment of monitoring inkjets droplets using QCM and showed the possibility to predict dispensing volume in the nanoliter range [6]. However, none of these works has shown any convincing repeatability study due to unpredictable and non-ideal spreading of dispensed droplet on the sensor surface in open air condition. According to the mega-gravity field theory described by Vasile Mecea [4], the sensitivity as well as the repeatability of QCM response may increase dramatically if the loaded liquid exhibits like a solid film in contact with the sensor. With this idea we fabricated a 2  $\mu\text{m}$  thick surface-attached hydrogel film (PDMAAm-MaBP) on the gold surface of the AT-Cut QCM crystal sensor. The surfaced-attached hydrogel film assures a good cohesion of the loaded liquid with the vibrating crystal and helped QCM to be sensitive to the mass of whole droplet instead only sensitive to the liquid molecules contact on surface as in the case of blank sensor. The sensing amplitude gains consequently significant improvement by a factor 12.3 in local experimental condition. The performance of the coated sensor has been evaluated by a large amount of experiments. For the first time a comprehensive repeatability study of QCM application in liquid weighing is presented. With help of a calibration line to droplet mass, which was established with an ultra-microbalance, the QCM with coated sensor can be used for further droplet characterization. This novel, simple and feasible approach might support the final breakthrough of a new gravimetric standardization for the nanoliter and picoliter liquid-handling-calibration.

## 2. Surface-attached hydrogel coating on gold surface of QCM sensor



Fig. 1: Sensor of QCM100, coated with about 2 $\mu\text{m}$  thick surface-attached and cross-linked polymer hydrogel

The polymer hydrogel coated on the QCM sensor (Fig. 1) was produced by a simple photocrosslinking of films of statistical copolymers comprising methacryloyloxybenzophenone (MaBP) and polydimethylacrylamide (PDMAAm) with UV light (wavelength = 350nm). Covalent attachment of the hydrogel film to the gold surface of the QCM sensor is achieved by means of a benzophenone-based monolayer [1,2]. The coating covers the gold electrode of the front surface and according to the measurement with ellipsometer nanofilm\_ep3sw from Accurion GmbH the thickness in the center is  $2104.2 \pm 0.6$  nm.

## 3. Evaluation and results

To evaluate the coated sensor a high performance dispenser PipeJet P9 [7] (BioFluidix GmbH, Germany) is applied to generate the required nanoliter droplets. The nozzle of the dispenser is positioned about 5 mm above the center of the coated gold electrode (Fig. 2(a)), which is mounted in a QCM holder

(QCM100, Stanford Research System Inc.). The frequency of QCM100 was measured by a frequency counter HP-5316B and automatically logged by custom made software at a sampling rate of 2Hz. The used double distilled water was filtered carefully with an Acrodisc® syringe filter with GHP membrane to avoid nonvolatile residue. A droplet, which impinged on the sensor surface, entails a characteristic decrease of the resonance frequency like shown in Fig. 2b. Because of evaporation the resonance frequency returns back after reaching a decreasing peak. After about 90 seconds the dispensed droplet is evaporated and the resonance frequency returns to its initial value. The next dispense measurement can start automatically. The repeatability of the maximal frequency shift, represented by the coefficient of variation (CV), is always below 3.8% for each droplet mass between 3 nl and 13 nl (Fig. 2(b)).

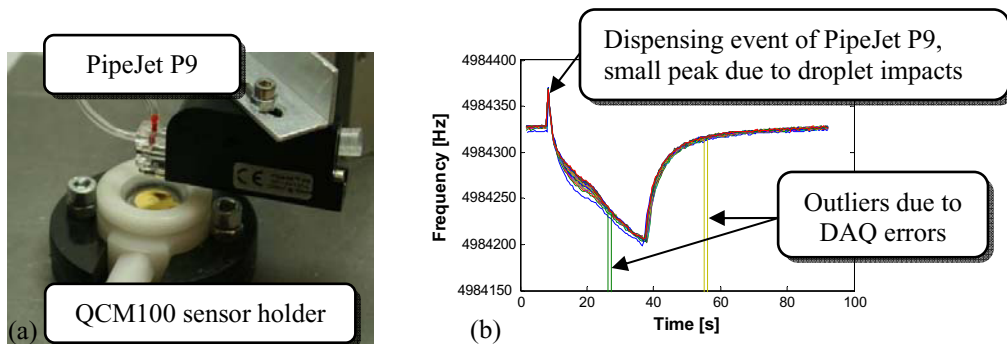


Fig. 2: (a) Experiment setup to evaluate the coated QCM sensor. (b) Typical frequency shift of loading nanoliter droplets (shown results of 24 dispense measurements with loading 13 nl droplets). The average maximal frequency shifts with the standard deviation by loading droplets with different masses are plotted in Fig.4.

Immediately after 24 individual dispenses at one volume the QCM was replaced by an ultra-microbalance XP2U/M from Mettler Toledo Inc. to calibrate the droplet weight (Fig. 3) [8]. In order to reduce the evaporation the small weighing capsule (ID x H 6mm x 8mm, elemental Microanalysis) is prefilled by about 50  $\mu$ l double distilled water and 100  $\mu$ l silicon oil layer (DOW CORNING® 200).

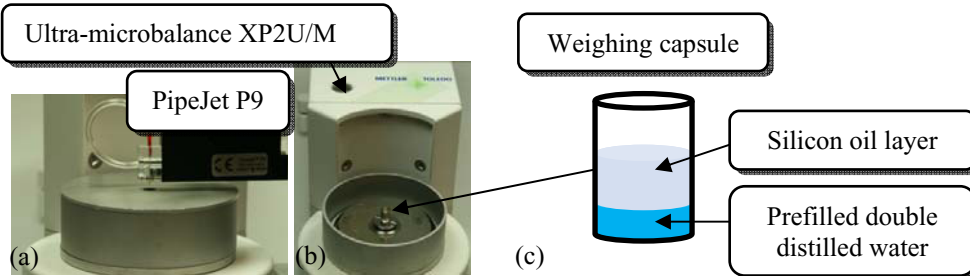


Fig. 3: (a) Droplet calibration setup with ultra -microbalance XP2U/M. (b) Weighing capsule placed in the center of ultra-microbalance. (c) The weighing capsule is prefilled with double distilled water (about 50  $\mu$ l) and silicon oil layer (about 100  $\mu$ l).

The processes described above have been repeated totally 288 times (144 dispenses to crystal sensor and 144 dispenses to ultra-microbalance) at 6 different droplet masses in the range from 3 nl to 13 nl. The summarized results are shown in fig. 4. It was found that the maximal frequency shift of QCM correlates in a linear manner with the mass of the dispensed droplets in the considered domain ( $r_{(x,y)} = 0.995$ ). The sensitivity reaches 5.2 Hz/ $\mu$ g. The offset of about 54.6 Hz is caused by the surface-attached coating. The

linear trend line of the maximal frequency shift to droplet mass is considered as calibration line for the measured domain and could be used for further droplets characterization.

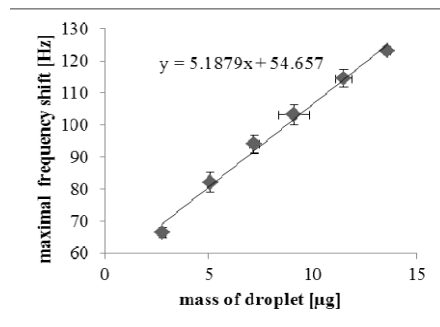


Fig. 4: Maximal frequency shift by 6 calibrated droplet masses (3  $\mu\text{g}$  to 13  $\mu\text{g}$  of distilled water equal to about 3 nl to 13 nl). Error bar in x direction: standard deviation of dispenser calibration with ultra-microbalance (24 measurements). Error bar in y direction: standard deviation of the maximal resonance frequency shift by loading one nanoliter droplet (24 measurements).

#### 4. Conclusion and outlook

A novel approach for nanoliter droplets calibration with a polymer hydrogel coated crystal sensor is presented in this paper. Good repeatability and linearity as well as a calibration line to ultra-microbalance prove the feasibility of the presented calibration method in the nanoliter range. This approach constitutes a significant progress beyond the state-of-the-art in terms of comprehensive repeatability study and therefore might open new application filed of QCM for nano and pico liquid-handling-calibration.

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