QUANTITATIVE VOLUME DETERMINATION OF DISPENSED NANOLITER DROPLETS ON THE FLY

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ABSTRACT

In this paper we present a sensor for non-contact monitoring of dispensed micro-droplets on the fly. In extension to our previous work [1], the sensor now allows for a direct, quantitative volume determination of single liquid droplets in the volume range from 20 to 100 nl. The improved electronic transducer enables to measure the droplet volume with an accuracy of ΔV ± 3 nl. The sensor signal provides a variety of information about the monitored droplet like for examples droplet velocity. This paper considers in particular the influence of the droplet velocity on the volume measurement. It turned out that the velocity effect can be fully compensated, if the signals are interpreted correctly.

KEYWORDS

Capacitive sensor; non-contact detection; nanoliter dispensing; process control

INTRODUCTION

The selective application of well defined aliquots of liquid in the pico- to nanoliter range has gained in interest in many different applications in the past years. The highly precise dosage of small amounts of chemical reagents in the field of pharma research and combinatorial chemistry as well as accurate proportioned quantities of lubricants or cooling agents for certain industrial processes are required. Often contactless dispensing systems are applied to deliver sample liquids as single free flying droplets with precise defined volumes at a high spatial resolution. It is obvious that dispensing systems in the pico to nanoliter range require proper process control systems to evaluate the stability and reproducibility of the dispensing process and the applied liquid quantity. Various methods to monitor a dispensing process and to evaluate droplet volume have been reported, e.g. highly precise gravimetric balances or stroboscopic imaging systems. Drawbacks of these commercially available systems are their high cost and mostly huge installation size. Further, the loss or contamination of sample liquid has to be considered, if the control system requires contact to the dispensed liquid.

The presented capacitive droplet sensor is designed to overcome the common drawbacks by its small size, integration with the dispenser and the focus on a direct, contamination-free and accurate measurement.

MEASUREMENT PRINCIPLE

The considered capacitive measurement method presented earlier in more detail [1] works like sketched in figure 1. A liquid droplet with a dielectric constant $\varepsilon_r \neq 1$, introduced in between the electrodes of an open plate capacitor leads to an increase of its average capacity. Theoretically, the change of the capacity depends on the size of the present droplet and the dielectric constant of the dispensed media only, like described by equation (1) [2]:

$$\Delta C = 4 \cdot \pi \cdot \varepsilon_0 \cdot \frac{r_{droplet}^{\;3}}{s \cdot^2} \cdot \frac{\varepsilon_r - 1}{\varepsilon_r + 2} \tag{1}$$

where ΔC is the average change of the measurement capacitor's capacity induced by a droplet, ε_0 the permittivity of the vacuum, s the distance of the capacitor electrodes, $r_{droplet}$ the droplets radius and ε_r the dielectric constant of the droplet's liquid. This equation holds for exactly spherical shaped droplets measured at stationary conditions with an open plane parallel capacitor.

However, in reality a dispensed droplet passes through the capacitor with a specific velocity and fluctuations in the droplets shape. Even long jets can occur, depending on the ejection characteristics of the specific liquid. Further, the presented measurement capacitor consists of two half shell electrodes, thus equation (1) can only be considered as a first approximation.

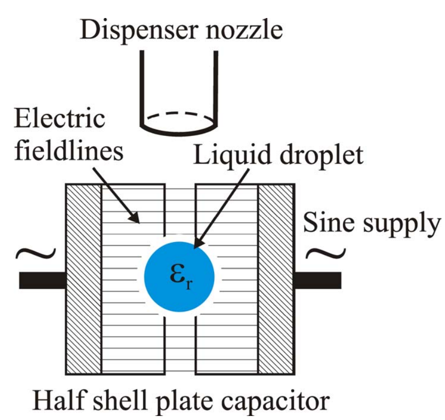


Figure 1: Principle sketch of the capacitive measurement concept; a droplet passes through the electric field of the half shell plate capacitor

SENSOR PROPERTIES

Fabrication

The experimentally studied sensor is completely manufactured in standard PCB (printed circuit board) technology. Therefore, an easy integration of the sensor capacitor and a very cost effective realisation of the whole sensor unit are realised. The measurement capacitor is fabricated by a symmetrically sliced standard through connection (via) with an inner diameter of 1.2 mm. Thus, two half shell electrodes are created, which enable a droplet to pass through, see figure 2. A considerable advantage for the use of half shell electrodes is the specific shape of the electric field, which increases the significance of the capacitive measurement [3].

Principle and conditions

The electrical transformation of the changes in capacitance to significant, interpretable voltage signals is based on a shift in the gain responds of a sine supplied active high pass filter, see figure 3. A sine voltage amplitude of V_{PP}= 20 V at a frequency of f_{Sens}= 160 kHz enables the generation of significant changes in the voltage amplitude at the input stage of the first operational amplifier (OPA). The extracted signals have to be further conditioned by two successive amplification steps, an adapted rectification and an active low-pass smoothing according to Butterworth. Finally, the generated analogue signals are digitised by an A/D board with a sample delay Δt= 8 µs and stored on a computer for further processing. A fundamental detail to enable accurate capacitive measurement of small changes in capacity is a so called “guard ring”, which protects the measurement chain form the influence of occurring bulk- and surface leakage currents. Due to the inverting input stage of the first operational amplifier (OPA), see figure 3, the guard can simply be connected to the circuits ground potential [4].

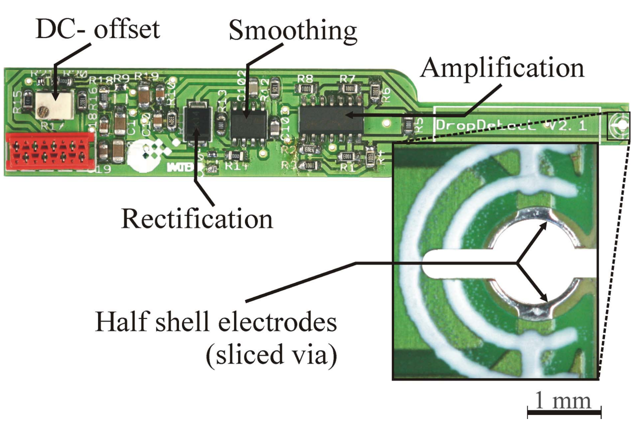


Figure 2: Sensor PCB prototype V2.1 adapted to the PipeJet™ dispenser [5]; sensor capacitor fabricated by a sliced standard through connection (enlarged aspect)

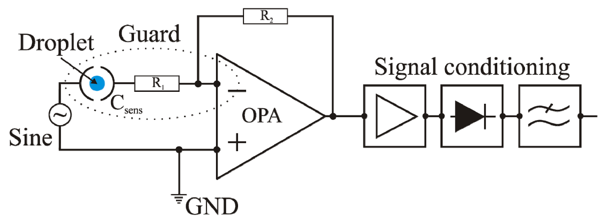


Figure3: Block diagram of the measurement chain with detailed signal generating unit

EXPERIMENTS

Setup

The measurement setup to perform the presented experiments consisted of a PipeJet™ R2 dispenser from BioFluidix, combined with an adapted sensor holder and the sensor PCB prototype shown in figure 2. The PipeJet™ dispenser is a piezo-electric driven dispenser, which generates free-flying droplets in the nanoliter range. The volume and velocity of the droplets can be adjusted by varying the extension length and extension velocity of the piezo-electric actuator [5].

The volumes of the droplets were determined by a high precision gravimetric balance (Sartorius SC2), which was installed below the sensor. Thus each dispensed droplet is monitored by the sensor before it impinges on the balance. A stroboscopic camera completes the setup, which enables to image the droplet’s shape, fluctuations and velocity with respect to the dispensing parameters.

Results

For characterisation of the sensor single droplets of pure water were dispensed through the sensor capacitor for a variety of different volumes and velocities. The described measurement setup enabled to determine the volume and velocity of each single droplet independently from the generated sensor signal.

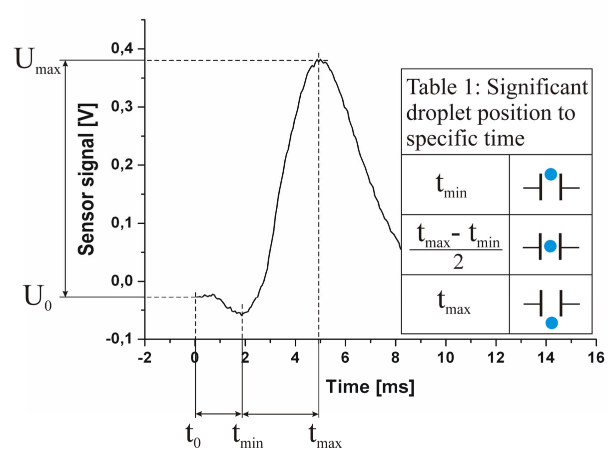


Figure 4: Typical analogue sensor signal for pure water droplets. Table 1 shows particular droplet position with respect to the sensor capacitor at dedicated points in time.

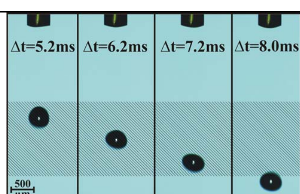
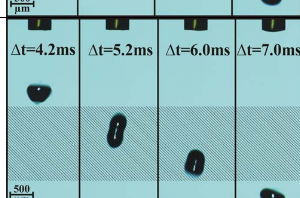
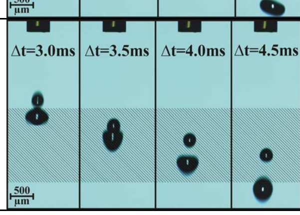
A typical sensor signal, generated by a pure water droplet is shown in figure 4. Table 1 depicts the time specific line-sections of the signal, correlated to particular droplet positions. Time t_{min} to t_{max} is the time of flight of a droplet through the sensor capacitor. From this an estimate for the droplets head-velocity can be deduced according to equation (2):

$$v_{droplet} = \frac{s}{t_{\max} - t_{\min}} \tag{2}$$

where s is the height of the sensor capacitor (s= 1.6 mm). The change in the signal amplitude U_0 to U_{max} is caused by the change in capacity induced by the passing droplet. The falling slope of the signal beyond t_{max} is caused by the decay of the electronic read out circuit after the droplet has passed the capacitor. The signal correlation to the droplet positions were determined by experimental evaluation while comparing stroboscopic images at certain points in time to the generated signals.

An example for the droplet's flight through the sensor is given in table 2. It shows different droplet sequences, recorded by stroboscopic imaging at different droplet velocities. The left column compares the droplet's velocity estimated from the images (u_{DStro}) with the velocity calculated by eq. (2) (u_{DSig}). The corresponding piezo extension velocity defining the droplet ejection characteristics and velocity is also displayed. The images in the right column show that droplets start splitting at increasing velocity, which affects the capacitive measurement enormously.

Table 2: Stroboscopic images of droplets at different velocity (u_{DStro}, gained from the images; u_{DSig} is estimated by equation (2); u_{piezo} is the dispensers piezo extension velocity). The image sequences are correlated to the corresponding velocity data.

Piezo extension velocity: u_{piezo}= 100 µm/ms Droplet head-velocity: u_{DStro} = 0.5 ±0.06 m/s u_{DSig} = 0.47 ±0.04 m/s	
Piezo extension velocity: u_{piezo}= 150 µm/ms Droplet head-velocity: u_{DStro} = 0.78 ±0.08 m/s u_{DSig} = 0.76 ±0.06 m/s	
Piezo extension velocity: u_{piezo}= 175 µm/ms Droplet head-velocity: u_{DStro} = 1.02 ±0.09 m/s u_{DSig} = 1.05 ±0.08 m/s	

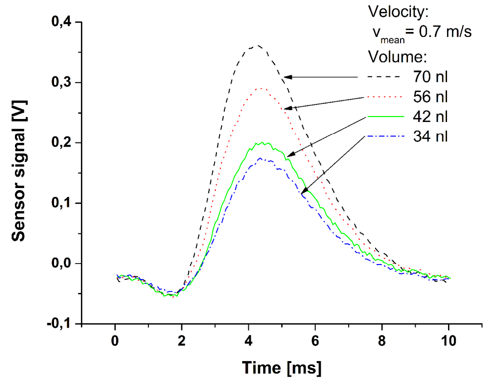


Figure 5: Typical sensor signals for pure water droplets of one velocity but different volumes

Thus, droplets at velocities faster than 1.0 m/s, resulting in satellite generation, weren't considered for the presented results.

Experimental studies have shown that there is a very good linear correlation from signal peak value (U_{max}) to the droplet volume. Figure 5 shows as example four sensor signals generated by droplets of the same velocity but different volumes. The correlation of the peak signal value to the droplet volume is clearly visible and allows for a volume determination at constant velocities.

Nevertheless, droplet velocity does affect the signal shape significantly, which can be seen in figure 6. It depicts five sensor signals, generated by pure water droplets of nearly the same volume at different velocities (velocity range $u_{droplet}$= 0.5 – 1.0 m/s). Obviously the velocity influence leads to different maximum signal peak values for droplets of equal volumes, thus a direct volume determination from the peak signal is not possible in this case. This effect on the sensor signal was analysed experimentally for a wide range of volumes and velocities ($u_{droplet}$= 0.5 – 1.0 m/s, $V_{droplet}$ = 20 – 100 nl). It turned out that the decrease of U_{max} correlates also very well with the corresponding velocity increase at constant volumes. Linear regressions are shown in figure 7.

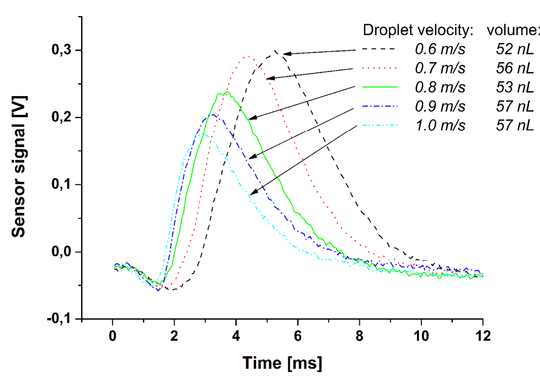


Figure 6: Sensor signals for pure water droplets of equal volumes at different droplet velocities. The velocities were estimated from each single signal by equation (2).

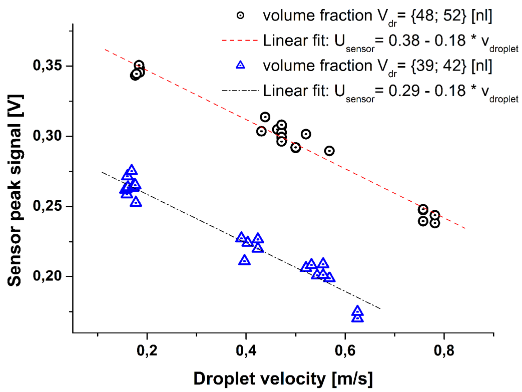


Figure 7: Correlation of droplet velocity to the sensor peak signal for two droplet volume ranges

The different depiction symbols indicate for droplets of two volume fractions (circle: $V_{droplet}$ = {48; 52} [nl]; triangle: $V_{droplet}$= {39; 42} [nl]).

The parallel shift between the liner regressions (slope= 0.18 Vs/m for both) suggest that for a given volume range the change of U_{max} is linear with same slope for different volume ranges. Therefore a volume factor can be defined which relates the peak signal voltage to a specific droplet velocity, like follows:

$$F_{volume} = U_{\max} + 0.18 \cdot u_{droplet} \tag{3}$$

The factor 0.18 characterizes the linear correlation from signal peak value to droplet velocity at constant volumes. It has been found in the experiments that this factor is fairly constant for all considered volume ranges.

The resulting correlation of volume-factor according to equation (3) to the measured droplet volume is shown in figure 8. There, 200 measurements of droplets with volumes in the range of 22 – 87 nl and velocities from 0.17 to 0.96 m/s are depicted. The obviously high linear correlation of the volume factor allows for direct volume and velocity determination based on the sensor signal alone.

Therefore, first the droplet velocity has to be calculated according to equation (2). Then equation (3) is set equal to the linear regression, gained from figure 8, to determine the droplet volume as follows:

$$V_{droplet} = \frac{\left(U_{\max} + 0.18 \cdot u_{droplet}\right) - 0.05}{0.006} \tag{4}$$

Thus, equation (4) serves to determine the droplet volume from information, which is completely provided by the sensor’s analogue output signal. It can be seen as calibration function for the presented sensor with respect to the droplet velocity effect to the analogue signals. By this approach a measurement accuracy of < ±3 nl can be achieved.

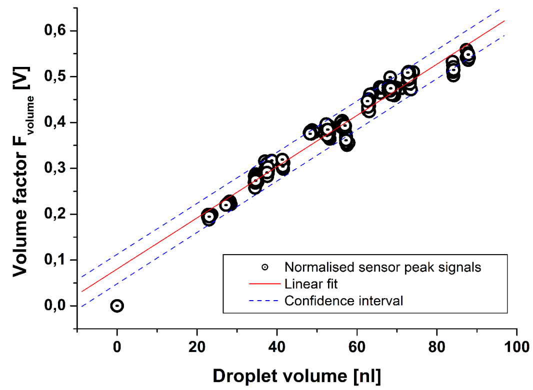


Figure 8: Correlation of the droplet volume to the volume factor [n= 200]. The dashed lines indicate for a confidence interval of 90%. (Correlation coefficient r_{xy}= 0.98)

CONCLUSION

We have presented for the first time a contactless capacitive sensor, which allows for the quantitative volume determination of single nanoliter droplets at unknown velocities. The proposed volume factor enables to compensate the velocity effect on the sensor signal and to result in volume measurements accuracies of < ±3 nl for droplets in the range of 20 to 100nl. The small and easy adaptable sensor is applicable to a variety of contactless dispensing systems and extends the field of process control technology for industrial- and research dispensing applications.

ACKNOWLEDGEMENTS

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