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Automated on-chip droplet dispensing with volume control by electro-wetting actuation and capacitance metering

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Abstract

In this work, a method is presented for controlling on-chip droplet dispensing by electro-wetting actuation in conjunction with capacitance feedback. The method exploits the built-in capacitance of an electro-wetting device to meter the droplet volume and control the dispensing process. A self-contained system is built to provide continuous-flow loading, capacitance measurement, and electro-wetting chip control. Automated droplet generation at rates up to 120 droplets/min is demonstrated for droplets of 0.1 M KCl aqueous solution dispensed onto 1 mm pitch buried electrodes and a 500 μm channel gap. The reproducibility of the droplet volumes is tested against dispensing parameters including production rate, fluid viscosity, channel aspect ratio, dispensing needle position and dispensing volume. The overall reproducibility is ±5% for production rates varying from 8 to 45 droplets/min and ±6% for fluidic viscosity ranging from 1 to 58 Cst, which implies the application of the method to wide ranges of solutions and pressures. Feedback metering compares well with droplet dispensing without capacitance feedback, which gives a reproducibility of ±13% for on-chip dispensing from a reservoir and ±12% for constant pressure-assisted dispensing.

Keywords: Microfluidics; Volume control; Droplet dispensing; Electro-wetting

1. Introduction

In micro total analysis systems (μTAS), liquid handling with high precision is of paramount importance, since the accuracy of assays is largely determined by the fluid volume control of the reagent dosing. Precision, often referred to as reproducibility, is measured by the standard deviation of a set of volumes divided by the mean. In drug discovery applications, this figure of merit must be below ±10% and preferably ±5% for some applications [1]. Microdialysis applications, which monitor human glucose, lactate, and glutamate/pyruvate require that the precision in dosing of preset liquid volumes be controlled within ±2%.

In continuous-flow systems, volume control is achieved by incorporating feedback in liquid handling either though a flow sensor [2–4] or using Chronoflow [5] such that flow rates can be regulated against varying pressure differences. Another option is by direct liquid metering based on an electrochemical principle [6,7]. For microfluidic systems, where liquids are manipulated as droplets, Handique et al. [8] described an approach to droplet metering by introducing a hydrophobic patch in a microcapillary channel. By stopping the wetting of the solution at the boundary of a hydrophobic patch, the precise position of the air/liquid interface was achieved. Then by pneumatic actuation with an external or on-chip pressure chamber, individual droplets were split off and propelled to the next section of the device. An alternative method was proposed by Nisisako [9] by which pico/nanoliter-sized droplets were generated through permeating a dispersed phase (sample) into a continuous flow (oil) at a T-junction of a microchannel.

The drawbacks of current droplet dispensing techniques include the difficulty in fabrication and integration with existing droplet manipulation methods, such as pneumatic handling [10], dielectrophoresis [11], thermocapillary [12], electrostatic [13], electrochemical [7] and electro-wetting [14], and the precision as well as flexibility in liquid volume control.

Droplet creation by electro-wetting actuation was demonstrated by Fair and co-workers [15,16] and Cho et al. [17]. It was shown that droplets could be created from on-chip reservoirs by forming a liquid protrusion from the liquid in the reservoir followed by subsequent droplet pinch off with proper control of an electrode actuation sequence. Another

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option was to use an off-chip pressure source through which liquid could protrude and retract along a series of electrodes. A droplet could then be formed on a selected electrode that remained activated while the liquid was retracted [15,18].

A few issues arise when droplets are formed with simple electro-wetting actuation without pressure assistance. One is that a high actuation electric field is required to conform the liquid front to the electrode dimensions when the liquid protrusion is formed. In addition, the dependence of the electrode control sequence on liquid properties and surface conditions makes it a difficult task to automate the dispensing process. Furthermore, on-chip reservoir dimensions set the upper limit on the total number of droplets that can be produced. Finally, it is impossible to generate droplets at high production rates due to the physical limitation of the dispensing process. The same controllability issues arise when droplets are dispensed with pressure assistance. Variations in liquid properties and system dimensions make it difficult to determine the magnitude of the required pressure to adjust the corresponding flow rate of liquid feeding. Most essentially, both methods suffer from degeneration of channel surfaces and insulating layers at high electrode voltages, which largely determine the reproducibility of droplet volumes, especially when large numbers of droplets are desired.

Static capacitance was used by Verheijena and Prins [19] in measuring the contact angle and wetting velocity in an electro-wetting configuration. For a droplet sandwiched in the channel of the electro-wetting chip in [14], the droplet volume can be approximated by the contact area multiplied by the gap between two parallel plates used to confine the droplet. With the contact area measured by static capacitance, droplets of high precision in volume can be dispensed with feedback control in an electro-wetting chip. In this work, a device that uses capacitance feedback to meter droplet volume for dispensing has been developed [20]. High reproducibility, controllability as well as reasonable droplet production rates have been achieved for dispensing droplets of aqueous solutions of different viscosities in the microliter/nanoliter scale. The system can be used for sample loading and reagent dosing as well as real-time control of droplet volumes during on-chip liquid handling. The overall schematic of the system is discussed in Section 3. The principle of droplet volume control with capacitance metering is described and analyzed in the section on design and analysis. The droplet dispensing process is demonstrated and discussed in the section on results and discussion. In the same section, the issues of on-chip droplet volume calibration are taken into account.

2. Design and analysis

2.1. The capacitance of a droplet

A cross-section of an electro-wetting actuator is shown in Fig. 1. When a discrete droplet aligns with the bottom electrode, a capacitor is formed between the bottom surface of the droplet and the buried control electrode [15]. Contact to the capacitor is made through the liquid droplet and the top ground electrode. The equivalent capacitance between the control electrode and the droplet is a function of the droplet volume, which only depends upon the area that the droplet covers. This area is independent of the liquid's properties and surface chemistry. Alignment of a droplet with the buried control electrode is easily realized by activating the control electrode that produces a hydrophilic surface region and restrains the spreading of the droplet.

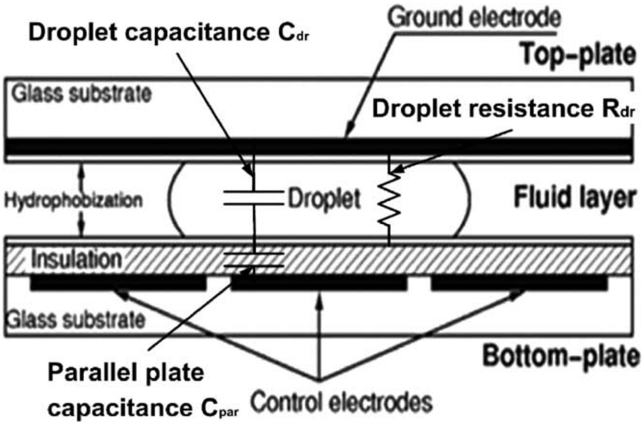

Fig. 1. Side view of an electro-wetting chip with intrinsic parallel plate capacitance illustrated. When a conducting discrete droplet aligns with the buried electrode, a capacitor is formed between the bottom surface of the droplet and the buried control electrode. Contact to the capacitor is made through the liquid droplet, the top ground electrode and control electrode.

For current fabricated devices with square electrodes of 1 mm pitch and 400 μm channel gap, the insulator covering the control electrode is 800 nm of Parylene C and a 60 nm Teflon AF1600 layer. Assuming a droplet is perfectly aligned with the buried control electrode, the measured capacitance is expected to change with droplet volume as in Fig. 2.

It can be seen in Fig. 2 that once the droplet fully overlaps the area above the control electrode, the slope of the capacitance versus volume curve decreases as does the accuracy of capacitive volume metering for a given capacitance measurement resolution. For instance, if the resolution of the capacitance measurement is 1 pF, then the accuracy of the volume metering degrades rapidly when the fluid volume exceeds 314 nl. For droplet volumes below 314 nl, the resolution for volume metering in Fig. 2 is 12 nl. Then the accuracy, defined as the percentage of the actual volume variation from the expected volume, would be 3.8%. The acceptable range of operation, when maximum error is within 10%, is for droplet volumes less than 450 nl. The analysis points out that there are some limitations in using unit size square electrodes to sense and meter droplets with diameters larger than the dimensions of the control electrode.

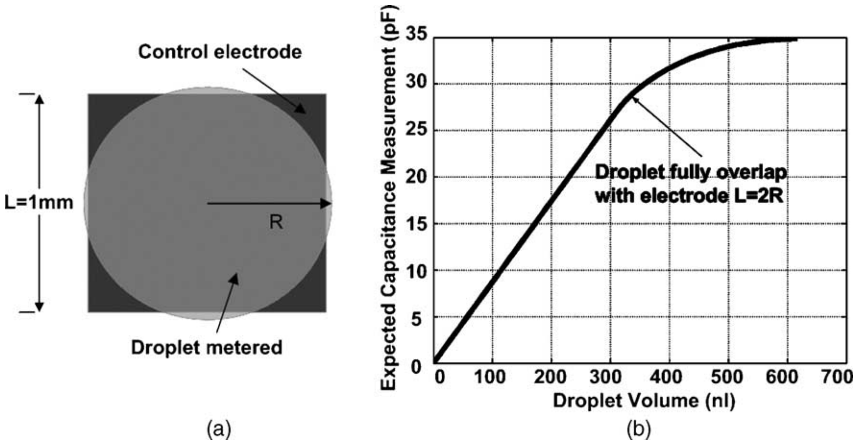

Fig. 2. (a) Top view of a droplet aligned with the control electrode buried underneath the insulating layer. (b) Expected capacitance magnitude vs. droplet volume when a 1 mm pitch size square electrode is used to position a droplet in a 400 μm channel gap. After the droplet is fully overlapped with the electrode, the linearity of the measurement will decrease significantly.

Sources of inaccuracy come from the varying capacitance and resistance of the droplet itself, since the capacitance measurement has to be made through these components, as shown in Fig. 1. The dielectric constant of pure water is as high as 78.4. An ionic solution, however, has a dielectric constant 80 times smaller. Thus, whereas the capacitance of a droplet of pure water 1 mm in diameter and 300 μm in height is on the order of 2 pF, the capacitance of a similar droplet of ionic solution would be only about 25 fF. The resistivity of high purity water is usually 0.1–20 MΩ cm. The resistivities of KCl solutions of 0.01, 0.1 and 1 M concentrations are around 700, 80 and 9 Ω cm, respectively [21]. This analysis shows that if a high concentration of ionic compound is contained in the droplet, the capacitance and resistance across the droplet are negligible. However, when the droplet is scaled down in size, the resistance across the droplet increases. Thus, variations in size and ionic content may mean that the droplet capacitance and resistance cannot be neglected.

Another contribution to the inaccuracy of droplet volume metering is misalignment between the droplet and the control electrode, although misalignment can be reduced by activating the control electrode with high voltage and/or using special electrode shapes. When an oil medium is used in the system of Fig. 1, an added contribution to capacitance inaccuracy is the time-dependent change in capacitance of a droplet residing on an energized electrode for a long period of time. This phenomenon is due to the time-dependent decrease in the thickness of the oil interface between the droplet and the transport surface.

The last, but non-trivial, contribution to capacitance inaccuracy is the conformation of a droplet to the electrode shape. Since the level of conformation is a function of fluidic interfacial tension, aspect ratio (pitch/gap), and actuation voltage, varying contact areas may result when these parameters change.

3. Experimental

3.1. Continuous-flow loading and coupling

Fig. 3 is a schematic of the overall system for droplet dispensing. An electric motor driven pump provided the pressure source for loading liquid samples. A pressure regulator from Cole-Parmer was employed to adjust the pressure range from 0 to 60 psig. A solenoid three-way valve controlled by a computer was used to provide continuous-flow cut-off. The valve was shown in the experiment to be removable at flow rates smaller than 5 μl/min. The continuous liquid feeding channel was coupled to the electro-wetting chip through a 300 μm outer diameter micro-capillary needle, which was sandwiched between the plates and positioned at a right angle to the linear array of electrodes.

3.2. Actuation control and capacitance measurement

A voltage switch for droplet actuation and capacitance measurement were built out of a custom made board and DIO card (NI PCI 6534). Software programmed with Labview 6.0 was written to control the dispensing process. The capacitance was measured with a simple oscillation method, and multiple sensing points within the microchip were provided. The schematic of the capacitance measuring circuit is shown in Fig. 4.

Since the accuracy of the measurement was influenced by the variation of the droplet resistance, the deviation of the oscillation frequency from the desired frequency was estimated through HSPICE simulation by varying the magnitude of the series-connected resistor R_{dr}, assuming a fully overlapped droplet with $C_{\mathrm{par}} = 30$ pF. The simulation indicates that around 5 kHz variations in oscillation frequency occur as the KCl solution varied from 0.01 to 1 M concentration, which suggests that to meter constant volume

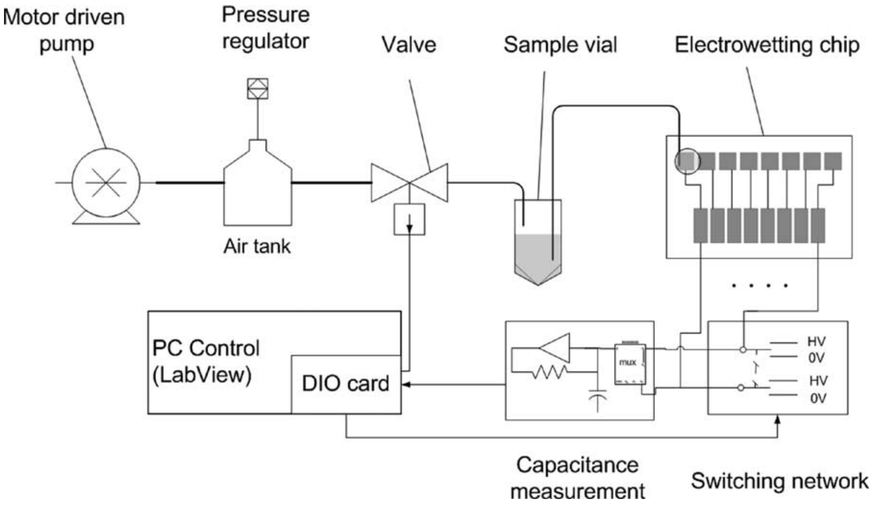

Fig. 3. Schematic of droplet dispensing system setup. Droplets are introduced on the chip from a pressure controlled continuous-flow source of liquid. An electronic system monitors the capacitance between the droplet and a reference electrode. When the desired volume (capacitance) is achieved, a feedback loop shuts off the liquid source.

droplets of variable concentration, a 5 kHz difference in the droplet cut-off frequency is required. In practice, for different solutions, a calibration was necessary to relate the measured frequency with real metered droplet volume.

3.3. Droplet dispensing with capacitance feedback

The operating procedure for the experimental apparatus in Fig. 3 was as follows: liquid was first deposited above an activated electrode with the off chip pressure source. The amount of liquid accumulated was metered by dynamic measurement of the capacitance between the electrolyte liquid and underlying activated electrode. The incremental change of the capacitance reflected the increasing foot-print area of the deposition. The dispensing volume was determined by the cut-off capacitance magnitude of the measured electrode. When the required volume was obtained, the droplet was produced by actuating the liquid and splitting it away from the inlet by electro-wetting actuation.

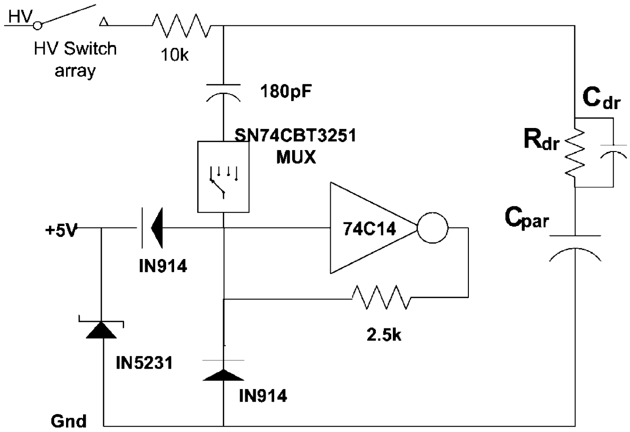

Fig. 4. Ring oscillator circuit used to measure the capacitance between control electrode and ground electrode. The presence of a droplet modulates the frequency of the ring oscillator. Over 50 kHz frequency variation can be sensed with the presence of a complete overlapping droplet on a 1 mm pitch size electrode, which is sampled by a data acquisition card (NI6534) with a sampling rate of 2 MHz. The multiplexer allows multiple detection points in a microchip detected with one oscillator circuit.

There are several advantages in this method over previously demonstrated approaches [16–18]. First, it is possible to achieve high precision in droplet volume for varying fluidic properties, channel geometry (electrode dimensions, gap), actuation voltage and droplet production rate, since the dispensing process is less sensitive to these parameters. Secondly, the dispensing volume is adjustable over a certain range given specific sensing electrode dimensions. Thirdly, the method reduces the complexity in adjusting the pressure source for liquid feeding and retracting, making it possible to dispense droplets with high production rates in an automated fashion. Fourth, the dispensing process tends to be influenced less by defects on surfaces and insulator layers as opposed to the methods in [16–18]. Finally, capacitance metering provides an interface between continuous-flow systems and discrete droplet based systems by automatically responding to the changing flow rates of a continuous-flow system.

3.4. Droplet size measurement

Droplet formation was observed using a microscope and captured by a high-speed video camera with full frame size (width 720 pixels, height 380 pixels) at 30 frame/s. Droplet size was measured by counting the pixels. The measurement setup is shown in Fig. 5.

4. Results and discussion

Initially, regular unit size electrodes were used for droplet metering. Droplet dispensing is demonstrated in Fig. 6,

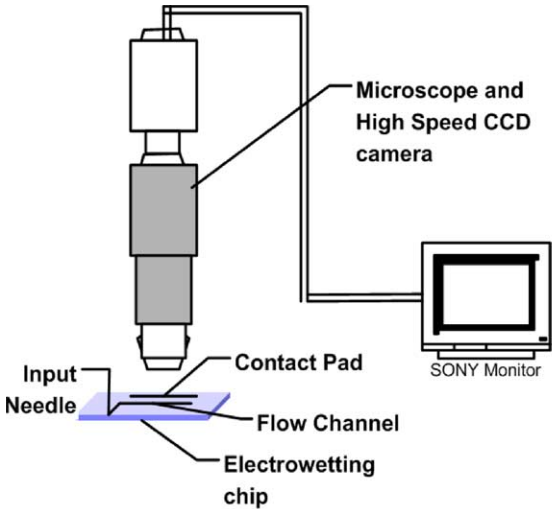

Fig. 5. Measurement setup for visually capturing the droplet dispensing process and monitoring the actual droplet size. The setup consists of a microscope and high-speed CCD camera to capture the image and a position system to align the electro-wetting chip.

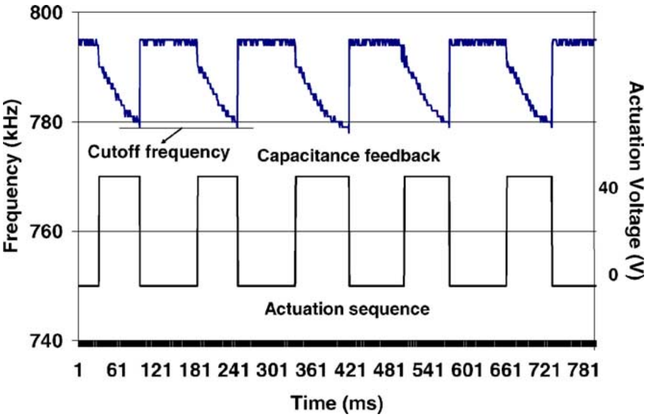

Fig. 7. Capacitance feedback representing the droplet formation and dispensing process with the corresponding actuation sequence on the sensing and metering electrode.

which shows time-lapse pictures of a droplet being formed from a source of 0.1 M KCl solution. The process is automated by simply setting the value of cut-off capacitance.

The dynamic capacitance measurement associated with droplet generation is shown in Fig. 7. Frequency is the direct readout of the oscillation circuit and is used to represent the capacitance measurement. The larger the frequency, the smaller the capacitance measured. The decrease of frequency corresponds to the accumulation of droplet volume on the dispensing electrode, and the rapid increase in frequency corresponds to the splitting of the droplet from the inlet. The time when droplets should be propelled away from the inlet is set by the cut-off frequency. Note that a few uncertainties in capacitance measurement may contribute to the precision of droplet metering. One is the fluctuation of frequency possibly due to the electronic noise injected by the power supply. The magnitude of the frequency fluctuation corresponds to around a 2% error in volume metering for a 1 mm electrode pitch configuration. The error should increase for smaller pitch size.

To evaluate the performance of the dispensing system, the effects of needle position, channel aspect ratio, dispensing volume, production rate and viscosity on reproducibility were investigated. In the study, the sample droplets were generated sequentially with full automation.

4.1. Effect of production rate on reproducibility

Tables 1 and 2 show the effect of production rate on volume reproducibility for droplets dispensed on 1 mm pitch electrodes and a 500 μm channel gap, estimated based on 42 sample droplets generated for each production rate. Different droplet production rates were realized by adjusting the flow rate with the pressure regulator. These data suggest that a small flow rate does have a small, but favorable effect on controlling volume reproducibility. At higher production rates up to 120 droplets/min, reproducibility is similar to that at 60 droplets/min. Fig. 8 shows the distribution of droplet volumes at production

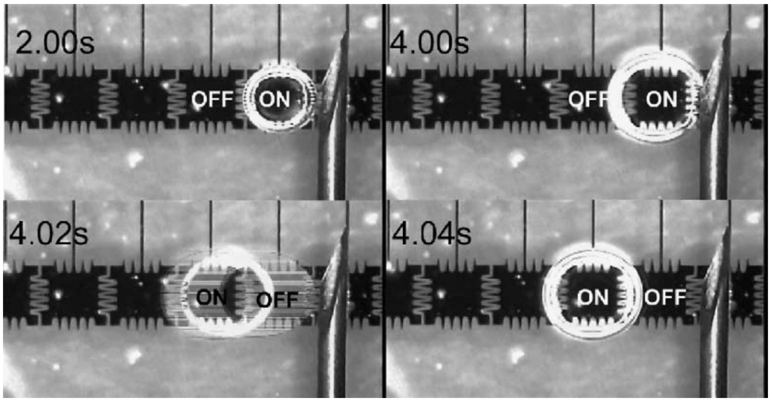

Fig. 6. Time elapse pictures of one droplet formation and generation of 0.1 M KCl solution in 1 Cst silicon oil from 300 μm diameter needle on chip of 1 mm pitch size and 400 μm gap. The electrical activation sequence of the electrodes is indicated.

Table 1
Effect of production rate on volume reproducibility for droplets dispensed on 1 mm pitch electrodes and a 500 μm channel gap, estimated based on 42 sample droplets for each production rate

Production rate (no./min)	Reproducibility (%)
8	±1.2
45	±4.4
60	±5.2

Different production rates are achieved by varying the flow rate of continuous-flow loading with adjusted pressure.

Table 2
Effect of viscosity on volume reproducibility, estimated based on 42 sample droplets for each viscosity, for droplets dispensed at a production rate of 8 droplets/min on 1 mm pitch electrode and 500 μm channel gap

Viscosity (Cst)	Reproducibility (%)
1	±1.2
15	±3.4
58	±3.5

The solutions with different viscosity are obtained by adding varying amounts of sucrose to the 0.1 M KCl solution.

rates of 8 and 45 droplets/min, respectively. The overall reproducibility is ±5% for production rates varying from 8 to 45 min^{-1} evaluated on 84 sample droplets with 42 droplets randomly chosen from each group.

An important conclusion from the statistics is that due to capacitance feedback, the pressure differences caused by the variation of external pressure magnitude can be regulated automatically to give a uniform droplet volume.

4.2. Effect of viscosity on reproducibility

By adding sucrose to the KCl solution of the droplets, it is possible to vary the viscosity between 1 and 58 Cst. Table 3 shows that the viscosity of the dispensed solution slightly influences the reproducibility of the dispensing process. The overall reproducibility is ±6% for viscosity varying from 1 to 58 Cst, evaluated on 84 sample droplets with 42 sample droplets randomly chosen from each group. According to the Hagen–Poiseuille law, $F = \pi \Delta P r^4 / 8 \mu l$. Flow rate ($F$) is proportional to pressure difference (ΔP) between the ends of a pipe and inversely proportional to the coefficient of viscosity μ, where l is the length of the pipe and r is the radius of the pipe. Hence, with the same production rate and a 58-fold difference in viscosity, there is a 58-fold variation in pressure difference in the injector needle. It proves the capability of capacitance feedback to generate droplets of uniform volume by automatically regulating over a large range of pressure caused by fluidic property variations.

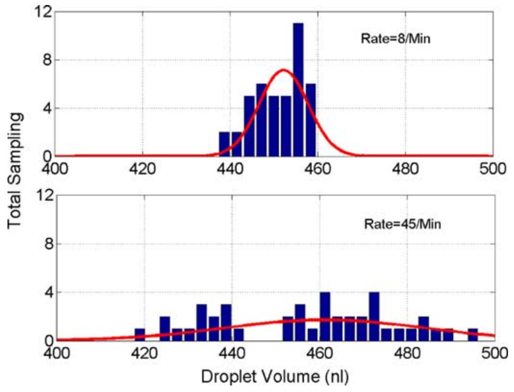

Fig. 8. Distribution of volumes of 0.1 M KCl solution droplets formulated on chip of 1 mm pitch electrode and 500 μm gap at production rates of 8 and 45 droplets/min, respectively.

Table 3
Effect of dispensing volume on reproducibility evaluated on 42 sample droplets from each group

	Average dispense volume (nl)		
	63	477	1900
Pitch size (mm)	0.35	1	1.5
gap (μm)	300	500	600
Production rate (no./min)	60	45	20
Reproducibility (%)	±9	±4.4	±6.1

Different dispensing volumes are achieved by generating droplets on electrodes with varying pitch size and gap.

4.3. Effect of needle position and channel aspect ratio on reproducibility

Two types of needles were tested, one 300 μm in diameter, another 500 μm in diameter. Measurements on droplet volume reproducibility show that there is no significant difference for the two sized needles as long as similar flow rates were maintained. Instead, the hydrophobic property of the needle outlet and the position of the needle with respect to the sensing electrode are relevant to the reproducibility of the dispensing process. As indicated in Fig. 6, the needle is positioned at the side of the sensing electrode and at a right angle to the electrode array. This position has an effect on the repeatability of the droplet formation process. If the needle is positioned too far apart from the sensing electrode, unrestrained spreading of the liquid from the inlet may occur. On the other hand, the overlap of the control electrode with the needle will undermine the alignment between the liquid drop and the control electrode, resulting in inaccurate droplet metering. The angle of the needle relative to the electrode array is also relevant. The right angle is favorable to successful splitting of the droplet from the needle outlet, partly due to the fact that it lessens the “stickiness” of the liquid to the needle surface. The shape of the needle outlet is believed to facilitate the droplet creation process as well. It is observed that as opposed to a common capillary tube with flat outlet, it is much easier to propel a droplet away from the outlet when the capillary needle is used. Similarly, when the needle is more hydrophobic, there is little delay when splitting a droplet from the needle’s outlet through electro-wetting actuation. This delay is believed to be one of the major causes of volume variation.

It was observed that when the channel aspect ratio (pitch size/gap) is increased to around 7, it becomes difficult to split droplets away from the needle outlet through electro-wetting, and variation of splitting time results in large variations of droplet volume. On the other hand, if the aspect ratio approaches unity, the electro-wetting effect could not position the droplet well with the sensing electrode, and the droplet had a tendency to float away or misalign with the sensing electrode, causing failure or inaccuracy in droplet dispensing. For the special channel dimension (1 mm pitch) the authors investigated, it was preferred to keep the aspect ratio around 2.5.

4.4. Effect of dispensing volume on reproducibility

Table 3 shows the dispensing reproducibility for varying droplet volumes dispensed on 0.35, 1 and 1.5 mm pitch size electrodes with a 300 μm diameter needle. For each volume, 42 sample droplets were measured. The reproducibility starts to degenerate at volumes around 60 nl. This is partly due to the fact that at smaller pitch size and large aspect ratio (pitch/gap), the droplet touches a very small area of the sensing electrode, leading to the degradation of the capacitance measurement resolution and the misalignment between the droplet and control electrode. In addition, small volumes are more sensitive to the variation of flow rate. The statistics show the limitation in using a capillary needle as a fluidic coupler, since the needle diameter could not scale with channel gap. A better option is to couple continuous flow through a hole in the top plate while making a capillary channel with a spacer layer as was done in [17].

4.5. Effect of continuous-flow loading on reproducibility

Two modes of continuous-flow loading were tested. One operated in the mode shown in Fig. 1 in which a solenoid valve was used to cut-off the continuous flow when droplet volumes reached the expected value. The use of a valve provides a negative pressure that facilitates the splitting of the droplet from the inlet. However, it is quite possible that a valve would not be present in the continuous-flow system coupled to the chip. So another mode of operation was tested in which a pump was directly coupled to the chip by a micro-capillary needle. The pump used was a CMA 107 microdialysis pump that gives continuous sample loading with flow rates adjustable up to 5 μl/min. A sequence of 50 sample droplets was produced using the pump. During the process, the flow rate of the pump was manually modified within the 2 μl/min range. The data show that the droplet dispensing system can produce uniform droplet sizes in the absence of the valve. In addition, the dispensing mechanism automatically regulates the changing flow rate by maintaining the size of the droplet generated. This suggests the potential of coupling a wide variety of continuous systems to droplet based electro-wetting chips by capacitance metering. Based on 50 sample droplets, the reproducibility of droplet generation using the microdialysis pump was ±4.4%. Droplets that fall outside of the first standard deviation range can be discarded by routing them to a waste reservoir on chip. In this way, one can select an acceptable reproducibility dynamically, keeping and using only those droplets of acceptable volume.

4.6. Comparison with other droplet dispensing approaches

Droplet dispensing without capacitive feedback from on-chip reservoirs or with pressure assistance was demonstrated in [16,17]. The dispensing was accomplished by first extending a liquid column from an on-chip reservoir by activating a series of electrodes. The electrodes other than the one where the droplet is to be formed are then deactivated. The electrode in the reservoir was activated to retract the liquid and pinch-off a droplet. The droplet volume was defined by the electrode dimension and channel gap. The procedure is illustrated in Fig. 9. As the process is quite sensitive to the operation conditions including aspect ratio, droplet/oil interfacial tension, liquid volume in the reservoir, number of pinch-off electrodes, actuation voltage, and surface defects, it is very difficult to predict and to automate the control sequence. Manual adjustment of the operating parameters, such as the number of pinch-off electrodes, actuation frequency and actuation voltage, are required for each specific solution and channel configuration. In addition, dynamic adjustment may be required from one droplet to the other throughout the dispensing process. For instance, it is observed that for droplets of 0.1 M KCl solution with 0.01% Triton-X dispensed from a 4 mm diameter on-chip reservoir onto 750 μm electrodes and 100 μm gaps, depending on the initial curvature and liquid volume in the reservoir, two or three intermediate electrodes are required to achieve pinch-off. The volume of sample droplets, however, is affected by the number of pinch-off electrodes,

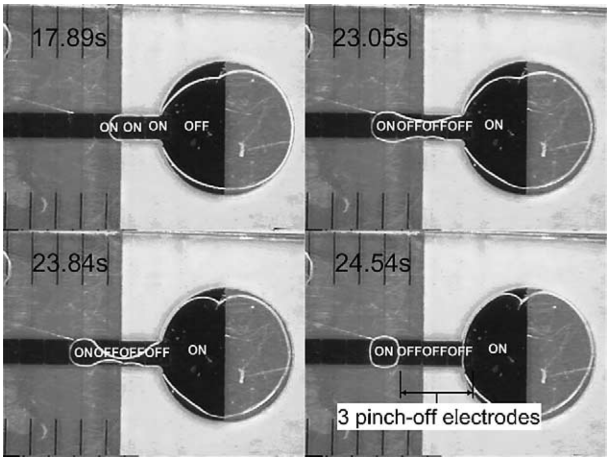

Fig. 9. Droplet of 0.1 M KCl solution with 0.01% Triton-X dispensed from on-chip reservoir of 4 mm diameter into the channel of 750 μm pitch electrode and 100 μm gap at 55 V actuation voltage.

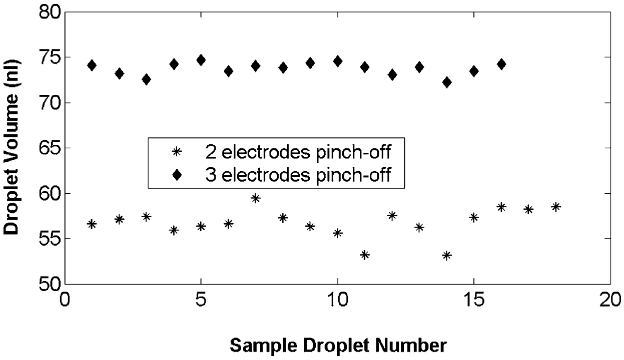

Fig. 10. Varying volume of sample droplets of 0.1 M KCl solution with 0.01% Triton-X dispensed from an on-chip reservoir.

as shown in Fig. 10. The reproducibility is ±3 and ±1%, respectively, for two and three pinch-off electrode configurations, respectively, evaluated based on 16 sample droplets from each group. The overall reproducibility is around ±13%. These results suggest that the change of operating parameters will affect the droplet volume significantly.

Droplet dispensing from an off-chip pressure source was demonstrated in [15]. The time elapse pictures of single-droplet creation are illustrated in Fig. 11. The process is similar to that of on-chip dispensing, except that the liquid feeding and retracting is provided by an external pressure source instead of solely by electro-wetting actuation. Likewise, the droplet volume is determined by the electrode dimensions and channel gap. The operating conditions include liquid properties, channel geometry, external pressure magnitude, actuation voltage and operating frequency for liquid feeding and retracting. It was observed that in one cycle, a relative stable droplet volume could be achieved. However, the variation of the external pressure caused a considerable variation of droplet volume. Even under conditions of constant pressure and operating frequency, the reproducibility was ±12%, based on 79 sample droplets of 0.1 M KCl solution generated with 1.2 mm pitch electrodes in a 500 μm gap channel. The statistics show the advantage of using capacitance feedback in droplet dispensing in terms of reproducibility. When controllability is important, a precise and programmable pump is usually needed to realize practical off-chip dispensing when no feedback is available.

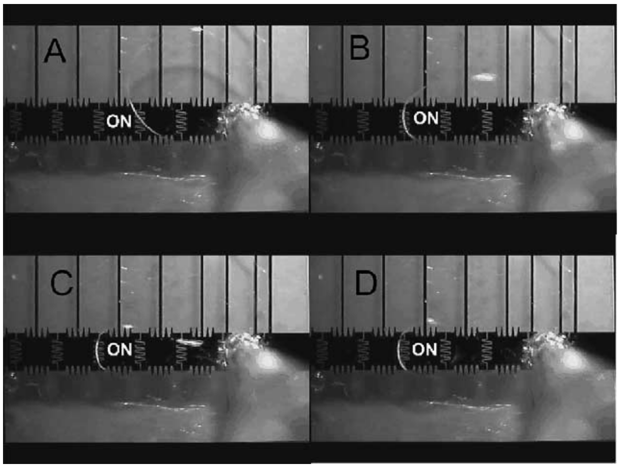

Fig. 11. Droplet of 0.1 M KCl solution dispensed from off-chip pressure source into the channel of 1.2 mm pitch electrode and 500 μm gap.

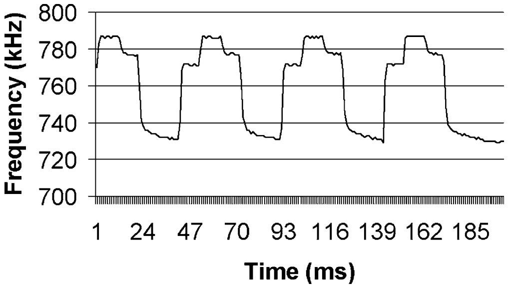

Fig. 12. Frequency response of a ring oscillator circuit when moving a droplet across a 1.5 mm pitch sensing electrode periodically.

4.7. Droplet volume on-chip calibration

An additional application of droplet metering with capacitance feedback is droplet volume on-chip calibration. Volume calibration could be realized by a static measurement in which a droplet is transported to a sensing electrode with the maximum capacitance measured to determine the droplet volume. Another option is through dynamic capacitance measurements in which the measured droplet is actuated across the sensing electrode repeatedly. For a certain solution, a preferred actuation frequency for droplet transport can be determined. At such a frequency, an average maximum capacitance can serve as the reference value to determine the droplet's volume. Fig. 12 shows capacitance monitoring results when repeatedly moving a droplet cross a sensing electrode of 1.5 mm pitch size. The lowest frequencies indicate the alignment between the droplet and sensing electrode, while the highest frequencies indicate the non-overlapping between the two. The stepwise increase of the frequencies implies that the droplet still partly overlaps with the sensing electrode when it is moved one step over to the adjacent electrode. The average value of the lowest frequency can serve as the reference to evaluate the droplet volume.

5. Conclusions

A capacitance feedback method has been demonstrated for controlled volume generation of droplets with electro-wetting actuation. In this method, the droplet volume is metered by measuring the intrinsic capacitance value between electrolyte droplet and a buried control electrode. By regulating the pressure differences caused by fluidic properties, channel geometry, and external pressure values, the dispensing mechanism allows good control of droplet volume and fast, automated droplet creation. The reproducibility of droplet volume is ±5% for production rates ranging from 8 to 45 droplets/min for droplets of 0.1 M KCl solution dispensed on 1 mm pitch electrodes and a 500 μm channel gap. For the same configuration, the reproducibility is ±6% for droplets with a 58-fold difference in fluidic viscosity generated at 8 droplets/min production rate. The method can also be scaled to meter small droplet volumes down to the 100 nl range. The reproducibility of droplet volumes compares well with on-chip droplet production without capacitance feedback, which gave an overall reproducibility ±13%.

Improved capacitance measurement resolution and continuous-flow loading could further increase the reproducibility of droplet volume. Besides, to couple a continuous-flow system to an electro-wetting chip with micro-capillary needle coupling, there are some limitations since the needle size cannot scale proportionally with the electrode size. A better fluidic coupler is desired if scalability is the concern. Another possibility is to combine droplet dispensing methods such as [17,18] with droplet volume on-chip calibration using capacitance metering.

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