PipeJet: A Simple Disposable Dispenser for the Nano- and Microliter Range

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This paper reports on a simple, disposable non-contact dispenser for the nano- and microliter range. In contrast to other known dispensers manufactured by silicon micromachining[1–4] the new device simply consists of an elastic polymer tube with a circular cross section. Actuation is done by a piezostack driven piston, squeezing the tube at a defined position near the open end by a significant fraction of the cross section. In contrast to drop-on-demand devices based on an acoustic actuation principle,[5] the squeezing of the tube leads to a significant mechanical displacement of the liquid. Our experiments tested a large number of media in the viscosity range from 1 to 27 mPas. Some of our experiments tested up to approximately 2,000 mPas. Frequency characteristics showed an independent dosage volume for water up to a frequency of 15 Hz for tubes with an inner diameter of approximately 200 μm. Standard deviation within 1,000 shots resulted in an excellent CV (standard deviation/dosage volume) of less than 2% of the dosage volume. Using tubes with an inner diameter of approximately 1,000 μm and a print frequency of 340 Hz, a flow rate of less than or equal to 143 μL/s could be reached. Beyond the possibility to dispense pure liquids, emulsion paints with particles that have a diameter of approximately 40 μm have also been printed successfully. (JALA 2004;9:300–6)

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INTRODUCTION

Handling liquid volumes from several microliters down to a few nanoliters with high reliability and high accuracy within a single platform is very important in drug development, modern diagnostics, chemistry, and especially for the reduction of the assay volumes particularly in high-throughput screening (HTS) applications. Compared to the conventional pipetting systems, where the precision of the dosage volumes below 1 μL is limited by capillary and adhesive forces, dosage systems with free-flying liquid jets or drops have an important advantage that allows them to avoid these surface interactions. Because of the variety of different fluids used in chemical and biochemical laboratories with very different properties it is essential that the dispenser provides a dosage volume nearly independent of fluid properties like viscosity, surface tension, or density. It is thus not necessary to calibrate the system after every liquid used. For medical devices it is also recommended that all contaminated parts be disposable and, therefore, have a low cost and be easy to handle. Further there is an increasing demand for dispensers which can dose fluids containing particles or beads. Applications, such as color printing with emulsion paint or medical applications containing beads, for diagnostics require devices particularly insensitive to clogging.

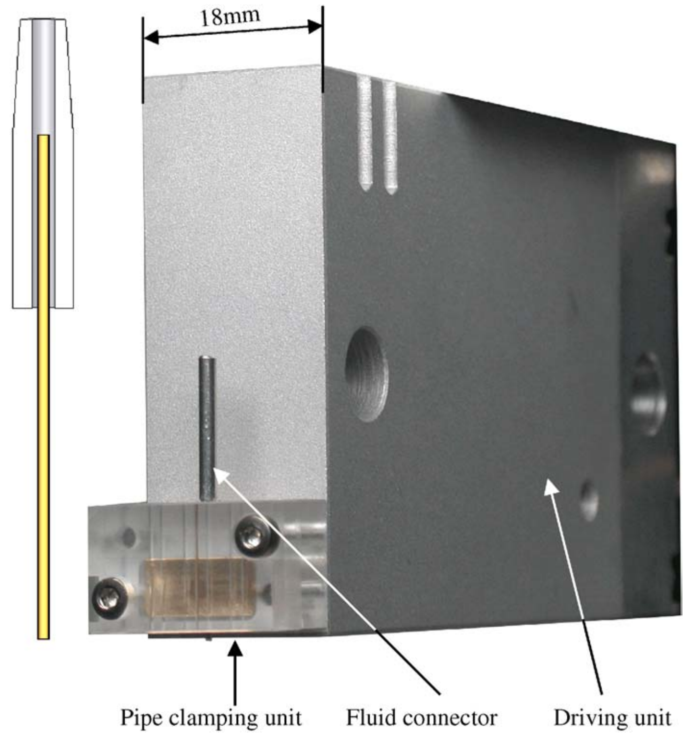

Figure 1. The PipeJet dispenser prototype and CAD drawing of the disposable tube.

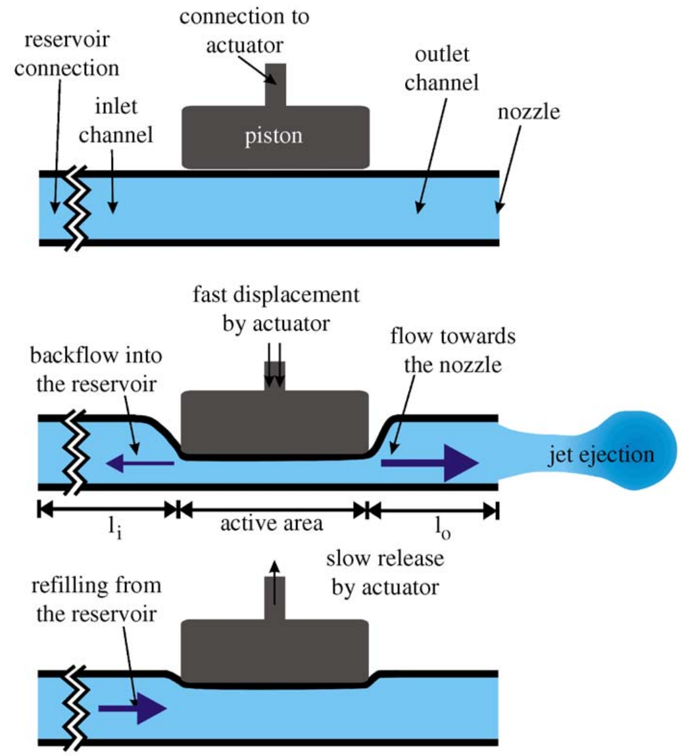

Figure 2. Working principle of the PipeJet dispenser.

System description

The key element of the dispensing technique termed "Pipe-Jet"-technology is a commercially available polymer tube clamped between two jaws like depicted in Fig. 1. The back end of the tube is connected to a reservoir and serves as a supply channel. The front end sticks out of the mount and forms the nozzle for liquid ejection. By a fast displacement of a piston connected to a piezostack actuator, the tube is squeezed on an active area of approximately 5 mm in length displacing the liquid toward both ends of the tube (Fig. 2). Due to the low fluidic resistance between the actuation area and the nozzle, most of the displaced volume is ejected as a free liquid jet as shown in Fig. 3. The amount of delivered fluid can be defined, on one hand, by the size and position of the piston, the ratio of the fluidic resistances pointing toward the orifice and the reservoir, and by the diameter of the tube used. On the other hand, the volume can be regulated by varying the piston stroke within a given setup. A chamfered active area of the actuator toward the nozzle outlet also leads to a flow in this preferred direction and therefore a higher dosage volume. The dosage process is finished by a slow release of the piston leading to the reset of the tube deformation. During this process the tube is refilled by capillary forces allowing the system to be ready for the next dosage event.

Results

The working principle sketched in Fig. 2 has been proven by stroboscopic and gravimetric measurements using the prototype displayed in Fig. 1. For the experiments we used a tube with an inner diameter of 200 μm and a wall thickness of 25 μm. At a piezostack displacement of 40 μm and a displacement velocity of 90 μm/ms droplets of approximately 22.5 nL have been obtained. Stroboscopic and long-term gravimetric measurements are summarized in Figs. 3 and 4. Obviously the droplet ejection is very stable, no tail or satellite droplets can be observed. Recording a stroboscopic photo sequence will result in a fluent video. This video shows that every ejected droplet is very similar in shape and velocity. The CV (standard deviation/dosage volume) of the dosage volume at 1.6% is excellent (cf. Fig. 4); there is no noticeable change in the dosage volume on changes of the hydrostatic pressure acting from the reservoir within a given range depending on the diameter of the tube used. Typically, this ranges from a level of 1 mm below the nozzle to 50 mm above it. As confirmed in a long term experiment the performance stays stable over at least 10,000,000 cycles.

One reason for the good performance of the PipeJet dispenser is that there is almost no material surrounding the nozzle as in other dispensers,[1,2] except in the thickness of the tube. Thus liquid is securely kept within the tube and no wetting of the nozzle surroundings can occur, which could lead to pending droplets or spreading of liquid on the nozzle plate. Further, the tube has a nearly perfect circular shape with no edges leading to an optimum flow field.

The polymer and adhesive used are highly resistant against bases (tested up to pH 13.5) and acids (tested up to pH 2) as well as against solvents typically used in HTS (tested

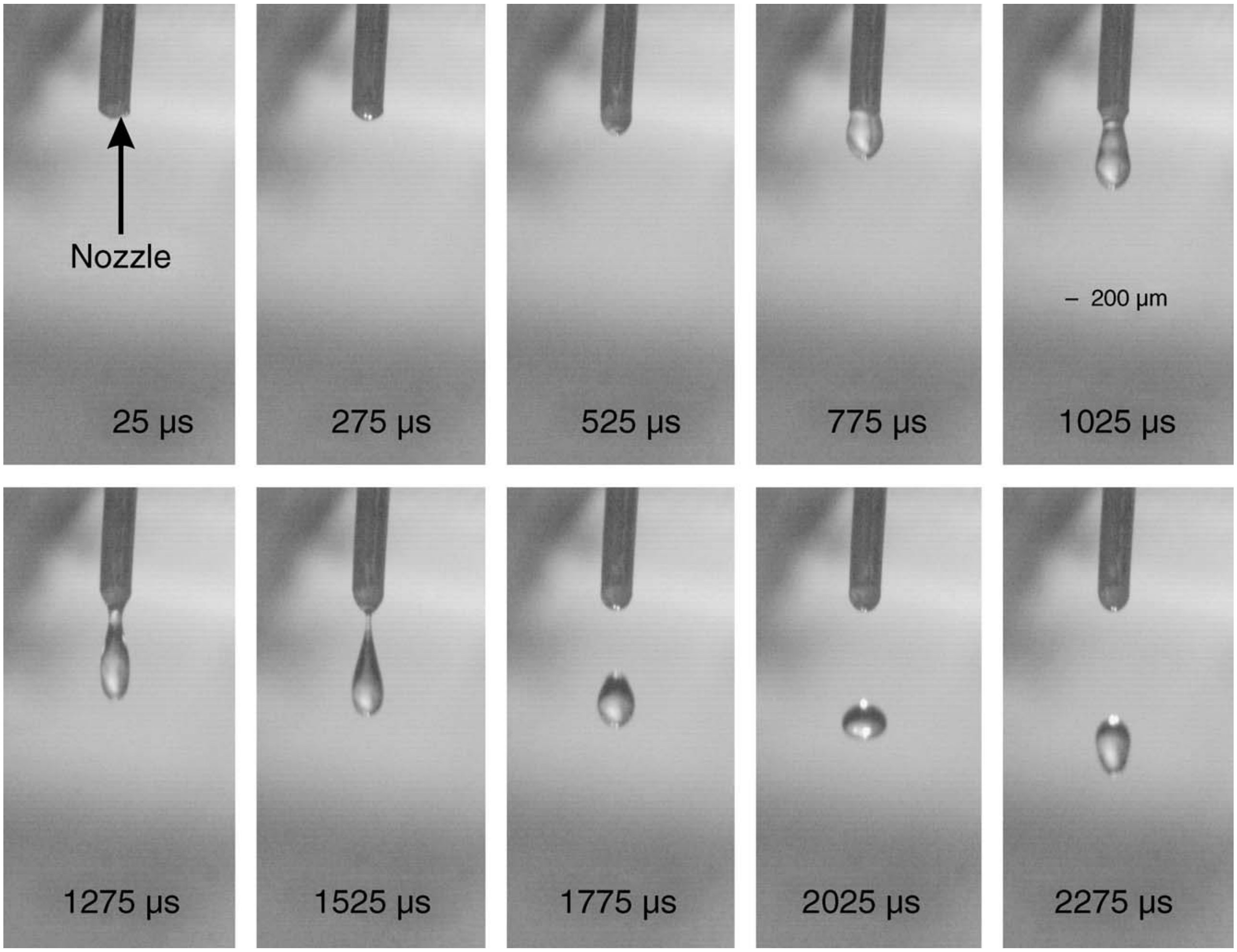

Figure 3. Stroboscopic pictures of an ejection process.

with pure DMSO, acetonitrile, Freon, methanol, ethanol, and acetone). They are also stable at elevated temperatures (tested up to 120°C) and are not cytotoxic. Different media in the viscosity range from 1 to 27 mPas have been dispensed successfully as can be seen in Fig. 5. With 200 µm tubes, we achieved dosage volumes nearly independent of viscosity up to 20 mPas similar to Ref. 1. The dispenser even worked with methanol and ethanol, which are usually difficult to handle due to their low surface tension. The frequency characteristics show a frequency independent dosage volume up to frequencies of 15 Hz (Fig. 6) with a very long tube with a diameter of 200 µm. At higher frequencies, the significant flow resistance of the tube limits the capillary refill, leading to a smaller volume of the single droplet and a constant flow rate. The minimal refilling time, and thus, the maximum frequency can be estimated by assuming that the volume (V) that has just been shot out of the tube needs to be refilled only by capillary forces (p_{cap}). As they have to work against the fluidic resistance of the tube (R_{fl}), a net flow (q) is generated. The following equation assumes that the volume that needs to be refilled is very small compared to the volume inside the tube, so that the capillary pressure and the capillary resistance can be considered constant:

$$V = q \cdot t = \frac{p_{cap}}{R_{fl}} \cdot t \tag{1}$$

Rewriting the fluidic resistance of a circular tube as a function of the viscosity and tube diameter like given in Ref. 6 leads to

$$t = \frac{R_{fl} \cdot V}{p_{cap}} = \frac{\eta \cdot l \cdot V}{\pi r^3 \cdot \sigma \cdot \cos\Theta} \propto \frac{l}{r^3} \tag{2}$$

where η defines the fluids viscosity, σ its surface tension, and Θ the contact angle between the tube material and the fluid. The remaining parameters (r = radius of the tube, l = length of the tube) can be varied to optimize the dosage frequency.

For water ($\cos\Theta = 0.21$) this gives a theoretical maximum dosage frequency of 20 Hz for the above-mentioned tubes which agrees quite well with the performed measurements. For shorter tubes with a diameter of 200 µm and a dosage volume of 25 nL, 78 Hz could theoretically be obtained.

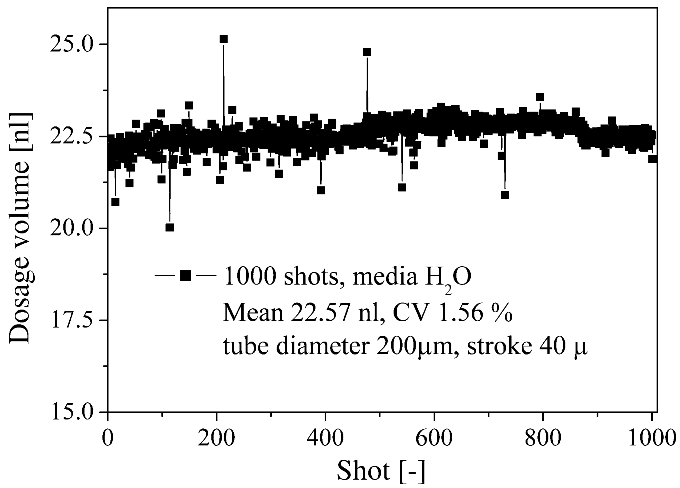

Figure 4. Long-term measurement of the dosage volume at a frequency of 0.1 Hz.

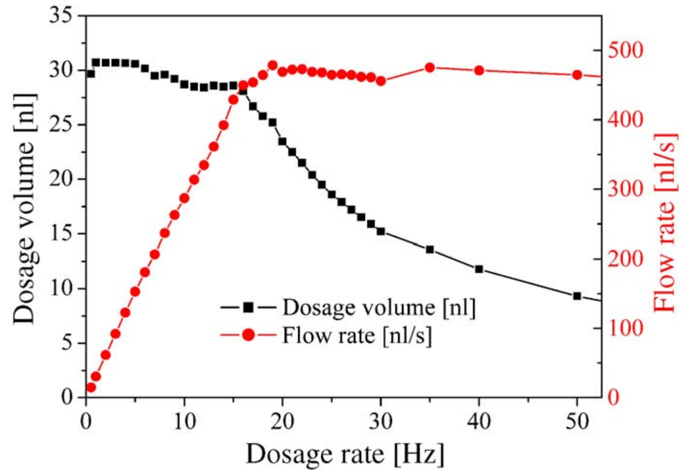

Figure 6. Frequency dependency of the dosage volume of H_2O at a piezo stroke of 40 µm. At frequencies above 20 Hz, the capillary refill limits the flow rate and leads to smaller single droplets.

Larger tubes having an inner diameter of 500 µm (which leads to a larger droplet volume of 50 nL per shot at the maximum attainable piezostroke of 40 µm) provide a maximum frequency of 613 Hz theoretically. Such high-dosage rates were experimentally obtained using a 500-µm tube and a dosage volume per shot of about 53 nL. With this setup flow rates less than or equal to 15.7 µL/s have been reached for operating frequencies up to 290 Hz. For a tube of 1,000-µm diameter, the maximum obtainable flow rate was found to be 143 µL/s at a droplet volume of 420 nL with a frequency of 340 Hz. The limiting factor here however was not the refilling time, but the frequency limit of the driving electronics. For the standard liquids used in biochemistry (viscosity range up to 10 mPas), it is suggested to use a slower dosage frequency like 50 Hz leading to a constant flow rate for all fluids with no need for recalibration. For totally unknown fluids, the calibration can be performed optically: The droplets become smaller when the cut-off frequency is passed. The tube material allows for the capillary refill of polar and non-polar liquids (is hydrophilic and lipophilic), so water and oils can be dispensed without modification. For a better refill of aqueous fluids, the surface can easily be treated to further increase its wettability.

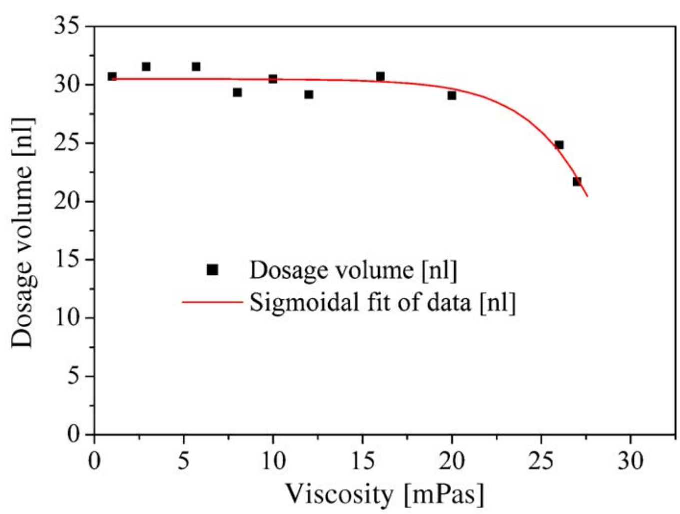

Figure 5. Dosage volume depending on the viscosity at a frequency of 0.1 Hz with 50-µm stroke and different glycerol/water dilutions getting the different viscosities.

With more powerful actuation electronics and actuators, and therefore a higher and faster stroke, it was even possible to dispense a motor oil with a dynamic viscosity of about 72 mPas as well as an emulsion paint with a particle size of approximately 40 µm and a dynamic viscosity of approximately 200 mPas at a frequency of 1 Hz. Surprisingly, and fortunately, no clogging was observed when using a 200-µm tube. In further experiments using 500-µm tubes, the dynamic viscosity range could further be expanded to approximately 2,000 mPas using undiluted dispersion paint.

The above-mentioned electronics for actuating the piezostack provide a maximum charging current of 8 A, with a minimum time step size of 1 µs, and a very short relaxation time of only 400 ns. With this performance the piezostack can be operated at a maximum cycle frequency of about 340 Hz, a maximum stroke of 160 µm, and a velocity of 500 µm/ms.

The ejected droplet volume can be defined by varying different parameters such as the diameter of the tube, the piston stroke, the dimension and the shape of the active area, and finally the fraction of inlet-channel length to nozzle-channel length. Increasing the piston stroke, the active area, or the fraction of inlet- and nozzle-channel length l_i/l_o leads to an increase of the ejected volume. In Fig. 7 the dependency of the dosage volume on the piston stroke is displayed. Obviously there is a linear correlation between the dosage volume and the piezostack stroke. The comparison with simulation results which are also illustrated in Fig. 7 leads to a good agreement in the stroke characteristics.

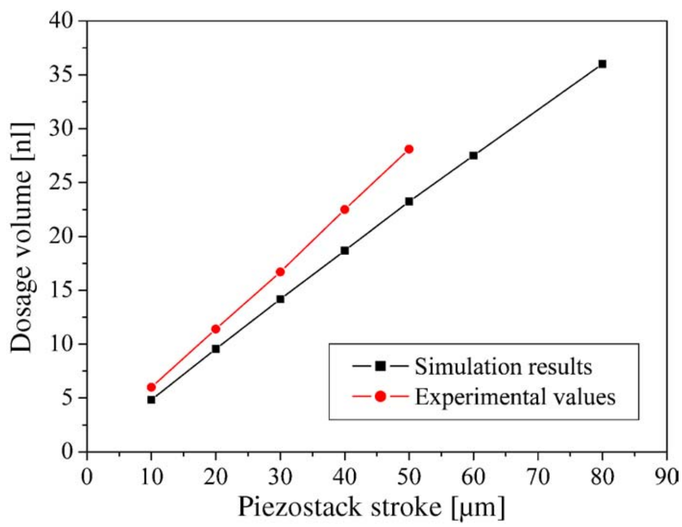

Figure 7. Measured and simulated dosage volume for H_2O depending on the piezostack stroke at a frequency of 0.1 Hz. ($l_i/l_o = 8$ for the simulations).

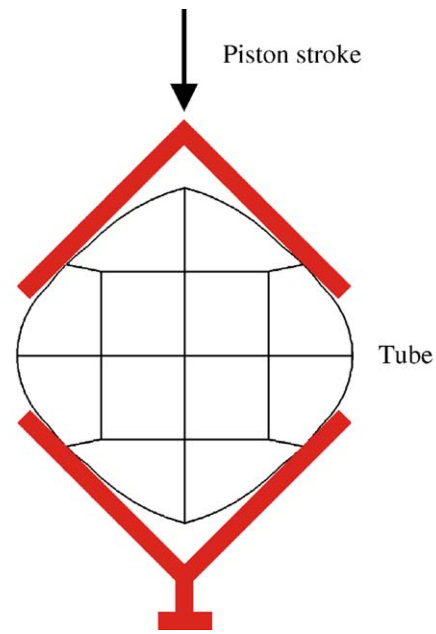

Figure 8. Boundary condition for the simulations and resulting squeezing of the tube.

Simulations

Computational fluid dynamics (CFD) simulations of the dispensing process have been performed using the commercial available simulation package ACE+ of CFDRC.[7] The movement of the stroke was implemented as a boundary condition in a three-dimensional model of one-fourth the tube utilizing all symmetries as displayed in Fig. 8. Due to the large deformation of the tube it was not possible to simulate all materials of the dispenser and the resulting fluid-structure interaction (FSI)[8] with the existing simulation tool. Instead, only the fluidic part of the tube was simulated using the piston deflection as a moving boundary condition. This way it has been proven that the dosage volume depends linearly on the actuator stroke resulting in a variability of dosage volume from 4.8 to 36 nL (cf. Fig. 7) for 200-µm tubes. Simulations worked well up to a stroke of 80 µm which corresponds to 40% of the tube diameter. A larger displacement was not possible because of convergence problems of the simulation algorithm.

In order to find the optimum tubing dimensions, we simulated different ratios of inlet length l_i to outlet length l_o (Fig. 9). We found that the dosage volume can be varied from 13 nL ($l_i/l_o = 1$) to 19 nL ($l_i/l_o = 8$) at a stroke of 40 µm. Comparing the simulated volume of 19 nL ($l_i/l_o = 8$) with the gravimetric measured droplet volume of 22.5 nL with the same piezostroke leads to a deviation of 15%. This disagreement is speculated to be caused by the fact that the fraction of inlet and outlet channel in the real experimental setup was considerably higher (cf. Fig. 9). For the used experimental setup, the l_i/l_o fraction was estimated to be approximately 100.

To also have a qualitative comparison of experimental droplet shapes and simulation, additional simulations were performed using the volume of fluid (VOF) method[9] and keeping track of free surface boundaries as they occur in droplet dispensing applications. In this case it was necessary to substitute the moving boundary condition at the walls of the tube with an equivalent pressure boundary condition at the orifice, obtained from a previous simulation without the VOF algorithm. This was necessary to avoid convergence problems caused by the large tube deformation and the VOF module. First the pressure inside the tube at the moving grid boundary condition (cf. Fig. 8) was recorded with the orifice defined as the outlet. This pressure characteristic was subsequently used as a boundary condition for the new

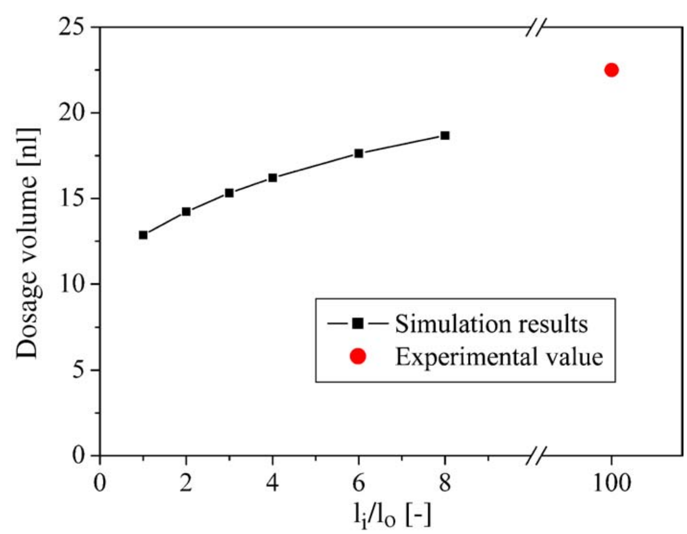

Figure 9. Simulated dosage volume of H_2O depending on l_i/l_o, where l_i and l_o are the length of the inlet and outlet channels, respectively, compared to the experimental value (40-µm stroke).

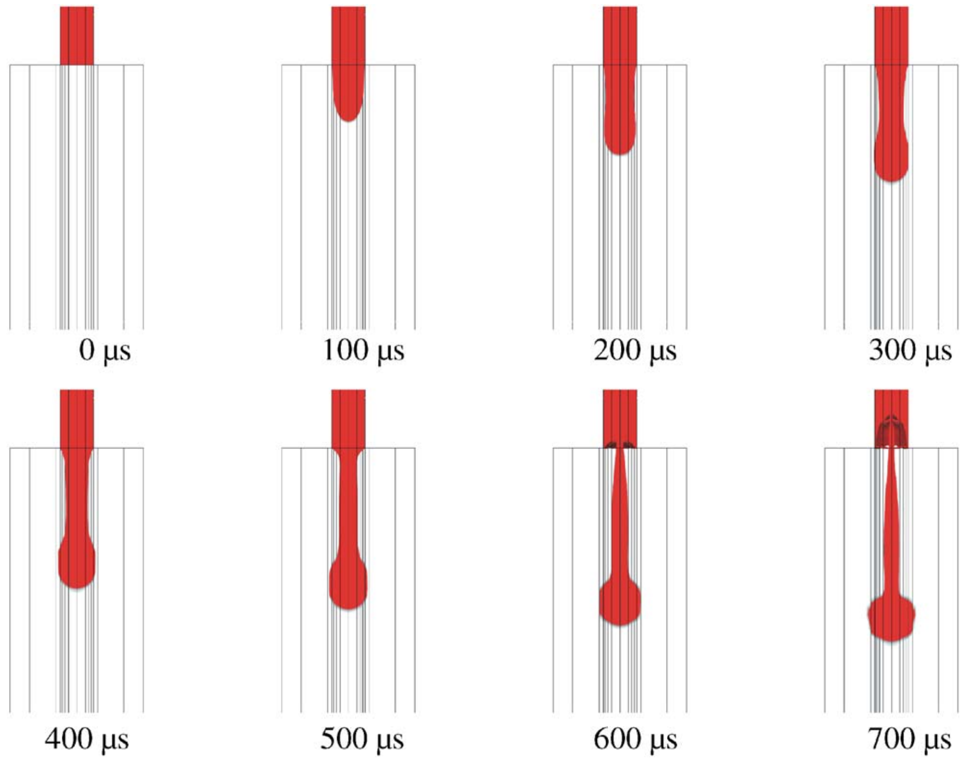

Figure 10. Simulation results of a droplet ejection of H_2O using the volume of fluid (VOF) method ($l_i/l_o = 8$, 40-µm stroke).

simulation without accounting for the tube deformation. Compared to the stroboscopic pictures (cf. Fig. 3), the shape of the ejected droplet depicted in Fig. 10 shows very good agreement. Unfortunately, there are some discrepancies in the time behavior. The simulation indicates a faster droplet ejection compared to the experiments. The reason for this might be the applied approximation which neglects the tube deformation and the FSI. Further investigations are required to clarify this point and to improve the CFD model.

Conclusions and outlook

We presented a new nano- to microliter dispenser based on a low-cost polymer tube. Compared to other micromachined dispensers the PipeJet is based on low-cost parts and materials and is simple to fabricate. A wide dynamic viscosity range from 1 to 2,000 mPas has been printed successfully so far with the presented prototype. One essential advantage of the method is that the dosage volume is nearly independent of the viscosity up to 20 mPas. The standard deviation of typically less than 2% within 1,000 shots is excellent. The presented device also provides the possibility to dispense emulsions containing particles or beads up to 1/5 of the tube diameter without clogging.

Possible applications for the PipeJet are all areas where the handling of liquids is necessary like medical or biological laboratory applications, oil, adhesive, or liquid metal dosing. Moreover all kinds of particle or bead dispensing like magnetic beads for life-science applications or emulsion paint can be achieved. Apart from its extraordinary performance in the nanoliter range the ultimate advantage of the technology is the low-cost fluidic part formed by the tube. This makes the device especially suited for disposable applications.

Future work will be related to integrating the presented prototype into liquid handling workstations and to explore the possibility to aspirate liquid via the tube. Thus in combination with a stepper motor driven syringe, the PipeJet might turn out as an interesting nano-pipetting option.

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