A novel micropump droplet generator for aerosol drug delivery: Design simulations

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One challenge of generating a liquid aerosol is finding an efficient way to break up bulk amounts of the compound into micron-sized droplets. Traditional methods of aerosol generation focus on the principle of creating the liquid droplets by blowing air at high speed over or through a liquid. In this study, a novel micropump droplet generator (MDG) is proposed based on a microfluidics device to produce monodisperse droplets on demand (DoD). The micropump design was employed to both pump the fluid into the air and to encourage droplet breakup and aerosol formation. Computational simulation modeling of the new MDG was developed and validated with comparisons to experimental data for current generators. The device was found to produce an aerosol similar to a vibrating orifice DoD device. Most importantly, the input power required by the newly proposed device (MDG) was several orders of magnitude below existing DoD generators for a similar droplet output. Based on the simulation results obtained in comparison with current DoD generators, the MDG device performed effectively at higher frequencies, smaller nozzle diameters, and regardless of the liquid viscosity of the solution. © 2010 American Institute of Physics. [doi:[10.1063/1.3517231](https://doi.org/10.1063/1.3517231)]

I. INTRODUCTION

Droplet formation in a gaseous atmosphere is of importance in many engineering and scientific applications, such as medical nebulizers,^{1–4} inkjet printing, DNA microarray systems, and spray cooling. For respiratory drug delivery, nebulizers are ideal for the delivery of high doses of medication to the airways and have major applications today in the treatment of asthma and chronic obstructive pulmonary disease.^{5,6} However, a drawback of conventional nebulizers is the highly polydisperse nature of the aerosol and the low deposition efficiency of the drug in the lungs. On average, only 10% of the dose released from the nebulizer will reach the site of action in the respiratory tract.^{7,3} Droplet generators with less polydispersity that can generate an aerosol during the inhalation portion of the breathing cycle can theoretically improve drug delivery to the lungs. Some advanced nebulizers have been developed and demonstrate significant potential for the implementation of smart, portable inhalation therapy platforms.^{8–10,3} With these devices, approximately 60%–70% of droplets can be deposited in the lungs.^{11–13,4} Nevertheless, there remain considerable challenges that need to be addressed before such personalized delivery systems can be realized.⁸ Furthermore, upper airway deposition and aerosol loss may still be too large even with these next generation devices for the delivery of some envisioned inhaled medications with narrow therapeutic windows that require precise dosing to the lungs.

A number of liquid droplet ejectors have been proposed, developed, and manufactured. These devices include pressure atomizers,¹⁴ rotary atomizers,¹⁵ air-assist atomizers,¹⁶ and airblast atomizers,¹⁷ all of which have been investigated extensively. In addition to using an air stream to

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atomize or break up the liquid, several methods with other principles for liquid aerosol generation have been developed, including vapor condensation,^{18,19} ultrasound,^{20,21} and surface acoustic waves.¹⁰ With the development of MEMS and the demand for high quality inkjet printing, droplet on demand (DoD) generators using micronozzle technology have been proposed and manufactured. In these devices, single droplets or a series of droplets can be produced. Unlike the conventional liquid droplet devices, which atomize the bulk fluid as a spray aerosol, the DoD ejector avoids the undesirable satellite droplets around the primary droplet, which produces a highly monodisperse and controllable aerosol. Due to the inherent simplicity and efficiency, ink-jet print heads with DoD ejectors have become a major share of the printer market²² and are responsible for considerable interest in the study of droplet formation. In the field of respiratory drug delivery, vibrating mesh nebulizers have recently been introduced²³ and characterized.²⁴

Many different techniques have been used to investigate DoD generators and most of these investigations have focused on the features of various device structures and droplets properties.²⁵ Doring *et al.*²⁶ and Shield *et al.*²⁷ experimentally investigated the temporal evolution of the entire process and several key stages of DoD drop formation were captured. Meinhart and Zhang²⁸ utilized a PIV system to measure the velocity flow field and visualized the liquid jet and drop formation from a SEAJet print-head.²⁹ Tseng *et al.*³⁰ used a LED, a microscope, and a charge-coupled device (CCD) camera to record the images of droplets and analyze the droplet characteristics of many different types of inkjet nozzles. Dong *et al.*³¹ applied flash photography to obtain sequential images as a process for visualizing the DoD droplet formation. Kwon³² developed a measurement technique for the jetting speed and drop diameter using CCD camera images with varied trigger times. Numerical simulations of DoD dynamics have been carried out for years based on one-dimensional models^{33,34} by solving momentum and wave transport equations. The simulation results provided understanding for drop formation but failed to predict the temporal evolution of the drop velocity and shape through inadequate models of interfacial physics. Numerical algorithms that can capture interfacial physics have been developed and include front-tracking,³⁵ boundary integral,³⁶ capturing,³⁷ level set,³⁸ and volume-of-fluid (VOF)³⁹ methods. A Galerkin-finite element approach with dimensionless parameters of the fluid field and two-phase interface has been applied extensively.^{40–44} All of these approaches have inherent strengths and weaknesses. Among them, the VOF method has been proven effective and successful for its robustness and is extensively applied in the investigation of ink-jet DoD printing.^{45–47,22}

The DoD generators mentioned above for ink-jet printing mostly produce the liquid droplets by high speed nozzles or supply the fluid with an aspiration mode, where the fluid is not refilled continuously during operation. The droplets for medical applications such as aerosol formation or microinjection require a continuous supply of droplets for accurate dosing. Koombua *et al.*⁴⁸ proposed a micropump with three nozzles/diffusers fabricated with polydimethylsiloxane, which can convey a liquid continuously. The micropump is valveless and produces no backflow that typically impedes the performance of these devices. Both liquid and particle transport through this micropump have been investigated by Koombua *et al.*⁴⁸ and Su and Pidaparti.⁴⁹ In this study, we propose the novel concept of droplet generation through this micropump and refer to it as the “micropump droplet generator” (MDG).

The proposed micropump droplet generator has not previously been explored. It is expected that the wall motion of the micropump will help to move the fluid out of the device without requiring an upstream pressure head and will facilitate jet instability and droplet breakup. The feasibility of this concept needs to be investigated prior to device fabrication and experimental testing. Therefore, the main objective of this study is to apply a numerical technique that combines computational fluid dynamics (CFD) simulations and two-phase flow modeling to investigate the feasibility of generating droplets with the valveless micropump used as a MDG. For comprehensive evaluation, we will not only investigate whether this device can generate liquid droplets but also explore characteristics of this device and compare it with a standard vibrating orifice droplet generator.

II. THEORETICAL MODELS AND SOLUTION METHODS

Droplet ejection from the micropump to a gas phase is typical problem in two-phase flow and can be solved using CFD simulations by tracking the volume fraction of each of the fluids throughout the computational domain. Two computational domains were considered for this system. One is the micropump domain, which is filled by a single-phase liquid. The other is the spray domain, where the liquid phase coexists with the gas phase. The details of the computational methods used in this study are briefly described below.

A. CFD analysis

The Navier–Stokes equations govern the flow in both the micropump domain and the spray domain. The flow in both domains is assumed to be laminar, isothermal, and incompressible. The transient laminar flow model combined with a moving mesh approach was employed in order to simulate the flow field in the micropump with moving boundaries actuated by a theoretical piezoelectric material.

For mass conservation, the continuity equation can be expressed as

$$\frac{D(\alpha_i \rho_i)}{Dt} + \nabla \cdot (\alpha_i \rho_i \vec{V}) = 0, \quad (1)$$

where α_i is the volume fraction of the i th phase, which obeys the constraint $\sum_{i=1}^n \alpha_i = 1$. For the system considered in this study, the local density is dependent on the volume fraction in each cell, which is given as

$$\rho = \alpha_1 \rho_1 + \alpha_2 \rho_2. \quad (2)$$

The momentum equation for flow can be expressed as

$$\frac{D(\rho \vec{V})}{Dt} + \nabla \cdot (\rho \vec{V} \vec{V}) = -\nabla P + \nabla \cdot (\mu(\nabla \vec{V} + \nabla \vec{V}^T)) + \vec{F} + \rho \vec{g}, \quad (3)$$

where $\vec{V}$ is the velocity vector, P is the pressure, ρ is the fluid density, and μ is the fluid dynamic viscosity. At the interface, the body force F stems from the interfacial surface tension term. To address numerical issues at the interface of the gas and liquid, the continuum surface force model proposed by Brackbill *et al.*⁵⁰ is applied. With this model, the surface tension forces acting on the interface are transformed to volume forces in regions near the interface as

$$F = \sigma \kappa \nabla \alpha, \quad (4)$$

where σ is the liquid surface tension coefficient and κ is the interfacial curvature. By summing the tensile forces acting on an interfacial fluid element with a computational expression for the vector curvature, the net surface is given as a sum of forces normal and tangential to the interface. This model is ideally suited for a Eulerian interface and has been validated for both the static and dynamic interfaces on which the surface tension acts.

To obtain the time-dependent flow field, the governing equations are solved numerically. The simulations were carried out by a general purpose CFD solver FLUENT 12 (ANSYS/FLUENT, Inc.) with the finite volume method and the transient solution was implemented by the implicit marching technique. At every time step, the moving mesh approach updated the pump wall location to drive the flow with a new discretized computational domain and the governing equations [Eqs. (1)–(4)] were solved. A convergence criterion of 10^{-5} for residuals of the mass and momentum equations was used for controlling the number of iterations. A second-order accurate scheme was selected for spatial discretization to reduce the iteration error. The SIMPLE algorithm was used for solving the pressure-velocity coupling. This procedure was repeated at every time step until a converged solution for the instantaneous flow field was obtained.

FIG. 1. Diagram of a nozzle-plate vibrating orifice system (Ref. 22).

B. Wall motion

A user-defined function written in C programming language was implemented to control the movement of the pump walls. While the fluid-wall membrane interaction can affect the movement of the membrane, this effect is neglected in this study. The motions of actuation are governed by the following expression to create periodic volume expansions and contractions of the micropump chambers:

$$s(x,t) = A \sin \frac{\pi x}{L} \sin 2\pi f t, \quad (5)$$

where $s(x,t)$ is the displacement of the membrane and f is the vibrating frequency. The sequence of membrane motions was described in the fluid transport study by Su and Pidaparti.⁴⁹

III. MODEL VALIDATION

In order to validate the numerical approach described above, simulations were performed on a typical ink-printing vibrating orifice DoD generator, which was proposed by Lai *et al.*²² This ink-jet DoD generator has a nozzle plate combined with a flat-plate piezoelectric material, as shown in Fig. 1. The entrance diameter of the nozzle is 111.5 μm and the exit diameter is 34 μm . The thickness of the flat-plate piezoelectric material is 46 μm . Both the experiments and CFD predictions were performed by Lai *et al.*,²² where a vibration signal was applied to the piezoelectric material and altered its dimensions periodically with an amplitude of 0.275 μm and a frequency of 61.7 kHz, with water as the working fluid. A pressure difference of 0 Pa was set as the boundary condition at the inlet and the outlet. No-slip boundary conditions were applied at an interface between the flat-plate and the working fluid. At the initial time, a hemispherical liquid drop was placed on the flat-plate which moves up and down corresponding to the vibration of the realistic nozzle plate, thus causing a pressure difference between the liquid and the ambient atmosphere so as to expel the aerosol. Both the hemispherical water drop on the flat-plate and the air around the hemispherical water drop and near the orifice are static prior to the simulated vibration.

Figure 2 illustrates the numerical grid for simulation of the ink-jet DoD generator proposed by Lai *et al.*²² A hexahedral mesh was built in GAMBIT, and 16 830, 23 780, and 38 900 control volumes were applied to perform a grid independence study. The numerical results indicate that the solution with a mesh density of 38 900 hexahedral cells produces a grid independent result. A snapshot of liquid droplets at 174.5 μs after activation predicted by the current numerical approach is shown in Fig. 3(c). For comparison, the visualized microimage of the liquid shape at 174.5 μs by Lai *et al.*²² and their numerical predictions are presented in Figs. 3(a) and 3(b), respectively. Figure 3 indicates that both (current and previous) numerical results show the liquid is ejected continuously, which is consistent with the experiment. Furthermore, the experimental test has five droplets in the field of view while the present validation shows the same quantity of

FIG. 2. Numerical grid for validation.

droplets [Fig. 3(c)]. On the other hand, the experimental snapshot [Fig. 3(a)] shows one elongated droplet nearest the orifice with two spherical droplets further downstream. Continuing from that, the next two spherical droplets have a greater separation distance. The predictions of the current numerical approach [Fig. 3(c)] show many of these experimental attributes. Specifically, the current numerical approach predicts similar droplet shape, similar droplet location, and the same quantity of droplets compared with the experimental data. Quantitatively, the droplet volume and average velocity from the current numerical simulations are 22.4 pl/s and 4.15 m/s, respectively. These values agree well with the measured volume and average velocity reported as 22.8 pl/s and 4.3 m/s,²² respectively. The error between measured and predicted average velocities is thus 3.48% and the error of droplet volume is 1.8%. These comparisons indicate that the predicted results involving both quantitative and qualitative aspects agree satisfactorily with experimental result and the current numerical simulation is sufficiently accurate to reliably evaluate the proposed liquid droplet generator.

FIG. 3. Droplets by (a) experimental measurement (Ref. 22), (b) numerical simulation (Ref. 22), and (c) the current numerical approach.

IV. RESULTS AND DISCUSSION

Different from currently available DoD generators as considered above, a valveless micropump is proposed to generate liquid droplets. The proposed MDG is illustrated in Fig. 4. This micropump was previously presented by Koombua *et al.*⁴⁸ to pump fluid continuously and has a combination of diffuser-nozzle elements. The unique operating characteristics of the proposed micropump result from a specific sequence of membrane motions (Fig. 4), which in practice is achieved by a piezoelectric actuator and can be accurately controlled by an externally supplied voltage. The same micropump in this study is applied to eject the fluid to the surrounding air with a rectangular cross-sectional height (h) of $16\text{ }\mu\text{m}$, width of $40\text{ }\mu\text{m}$ at the inlet, and width of $20\text{ }\mu\text{m}$ at the outlet. It is anticipated that the oscillatory motion of the membrane walls will create an additional instability in the fluid and produce breakup at lower Reynolds numbers than required for typical fluid-in-air jets.

A. Feasibility of droplet ejection

Using the methods discussed in Sec. II, the CFD analysis was carried out for the micropump with a 1 MHz actuation frequency. The working fluid of the micropump was assumed to be water with a density of 998.2 kg/m^3 and viscosity of $0.001\text{ }003\text{ kg/m s}$. A zero pressure difference was set as the boundary condition between the inlet and the outlet. No-slip boundary conditions were applied at the interface between the micropump walls and the working fluid. At the initial activation time, the liquid filled in the whole micropump chamber, and the orifice was facing the air environment. Both the liquid in the micropump chamber and the air near the orifice were static prior to the actuation of the unit.

Figure 5 shows the numerical grid for the proposed micropump droplet generator, which was generated by GAMBIT (ANSYS, Inc.) software. Three levels of grid density were considered. Grids

FIG. 4. Liquid droplet generation by the valveless micropump.

of coarse (8188 cells), medium (12 100 cells), and fine density (17 240 cells) were constructed to establish grid convergence of the results. Based on an analysis of the velocity field and flow rate of the MDG, a negligible difference was observed between the medium and fine density grids. Therefore, the fine density grid was used to report the final solution results.

Figure 6 illustrates streamlines and droplets near the exit orifice of the MDG with a 1 MHz actuation frequency. A “cat-eye” vortex was formed near the exit of the micropump and this aerodynamic characteristic deforms the fluid exiting the micropump. As the fluid moves forward, the aerodynamic force, the surface tension, and the internal force in the fluid act together to form regular spherical droplets after the initial ejection from the MDG. The formed droplets have the same size as the exit diameter of the micropump nozzle ($20\text{ }\mu\text{m}$) and the droplet velocity is around 20 m/s. These physical conditions are favorable for droplets to resist the aerodynamic disturbances from the surrounding air ($We = \rho U^2 D / \sigma < 1$) and prevent the droplets from breaking up. Figure 6 indicates that the flow field far from the MDG is free of the aerodynamic disturbances found at the nozzle and the formed droplets travel in a stable aerodynamic environment.

Figure 7 shows the temporal evolution of liquid droplets ejected by the micropump at an actuation frequency of 1 MHz at different instances in time. It is observed in the figure that the proposed micropump droplet generator can discharge monodisperse droplets continuously after an initial startup period. The first droplet, which was generated into a still environment, has a larger size and is slightly irregular. Following this lead droplet, the subsequent droplets are highly

FIG. 5. Numerical grid for the valveless micropump.

uniform with a diameter equal to the exit size of the MDG. The three parallel lines in Fig. 7 indicate that the droplet velocity is similar among the droplets. However, some differences in the gaps between the droplets are observed as the droplets draft behind one another and are slowed due to hydrodynamic drag.

FIG. 6. Flow field around the droplets near the exit of the micropump.

B. Advantages of the present MDG

Advantages of DoD techniques over continuous segmented flow techniques have been suggested by many previous investigations on ink-jet generators,⁵¹ such as added flexibility and elimination of undesired properties. In this study, an advantage of the current MDG over other DoD generators is illustrated in Fig. 8. This figure shows the droplets produced by the ink-printing DoD generator from Lai *et al.*²² and by the current MDG. For comparison, the nozzle dimension of the previous ink-jet DoD generator is the same as the current MDG and the actuation frequency is also the same. It is observed that the spatial gap between the neighbor droplets ejected by the previous DoD generator is smaller than that with the current MDG. Furthermore, velocities produced by the MDG are higher. These larger gaps and higher velocities can likely reduce droplet interaction effects in the stream and pose lower risk for coagulation. Higher droplet velocity will increase delivery speed, which may be advantageous in many applications. In addition, the current MDG supplies liquid in a continuous flow manner as droplets are ejected by the generator. This is advantageous compared with the previous ink-jet DoD generator, in which the liquid is supplied by aspiration and requires refilling (Fig. 1).

Figure 8 illustrates that the droplet size in both droplet generation systems is the same, which is determined by the exit orifice size. Furthermore, the number of droplets generated is the same, which is dependent on the actuation frequency. As a result of identical droplet size and number,

FIG. 7. Temporal evolution of liquid droplets ejected by the MDG at an actuation frequency of 1 MHz.

FIG. 8. Comparison between a previous DoD generator and the present MDG design.

FIG. 9. Theoretical model for calculating the energy consumption.

the two generators produce equivalent flow rates for a given exit diameter and actuation frequency. However, the downstream droplet velocities are observed to be different between the two systems, which is associated with the higher momentum of the MDG system.

In order to illustrate the high efficiency of the MDG, Fig. 9 provides a theoretical model to calculate the energy consumption for both the previous and current systems. From the fundamental mechanics of incompressible flow, the complete stress tensor acting on the interface of the actuator can be expressed using the constitutive equation for a Newtonian fluid⁵² as

$$\tau_{ij} = -p\delta_{ij} + 2\mu S_{ij}, \quad (6)$$

where p is the fluid pressure, μ is the fluid viscosity, and S_{ij} is the strain rate tensor of the fluid. This constitutive equation includes the force components, such as the pressure and shear stress due to the viscosity,⁵² which are responsible for the energy consumption to drive the fluid. Therefore, the work done by the walls can be expressed as

$$\delta W = \int_A s_i \tau_{ij} dA_j, \quad (7)$$

where s_i is the wall displacement of the actuation unit, A is the interfacial area of the actuator with the fluid, and dA_j is the surface area vector of the local control volume element. From Eq. (7), the power required by the actuator unit in one vibrating cycle can be expressed as

$$P = 1/T \oint_{T,A} \delta W = 1/T \oint_{T,A} s_i \tau_{ij} dA_j, \quad (8)$$

where T is the vibrating time period.

Based on the above fundamental mechanics, a user-module was developed in FLUENT to calculate the power consumption for both systems and the results are presented in Fig. 10. It is observed that the power input for the DoD injector is much higher than that for the MDG. In fact, the MDG generates the same flow rate of liquid and droplet size, but requires over two orders of magnitude less power than the other state-of-the-art DoD generator. These differences in power consumption are determined by the different dynamic characteristics in these two systems. In the previous DoD injector, the power input to the system must overcome the aerodynamic resistance from the surrounding air, while the power input to the current micropump only drives the fluid in the pump body. The aerodynamic force for the former is much higher than the driving force in the latter since larger operating units are required by the previous DoD system [Fig. 9(b)]. Further-

FIG. 10. Power input for previous DoD system and the present MDG design.

more, the vibrating walls of the current MDG system may help to create instability in the liquid jet. In addition, the current micropump droplet generator does not need any pressure head. The power input is only required for driving the vibration of the walls.

C. Effect of actuation frequency

Figure 11 shows the instantaneous liquid droplets ejected by the micropump with different actuation frequencies. It can be observed that with the increase in actuation frequency, the droplets move faster. This observation agrees with the fundamental fact that the fluid receives more kinetic energy with the faster vibration of the membrane. In addition, the higher frequency of the vibrating cycle ejects the droplets in a shorter time and more droplets can be observed at the same time interval. It can also be seen that the actuation frequency does not affect the droplets size, and the size of droplets is mainly determined by the diameter of the nozzle.

Figure 12 presents the effect of the actuation frequency of the MDG on the average velocity of droplets and average volume flow rate. In this figure, it is observed that both the droplet velocity and volume flow rate are approximately proportional to the frequency of the micropump. It is found that the droplet velocity is approximately proportional to the frequency of the micropump. In contrast, the droplet size is not affected by the frequency. The amount of droplets ejected by the micropump is determined by the frequency of actuation and thus the volume flow rate is also directly proportional to the frequency.

D. Effect of orifice diameter

To analyze the effect of the nozzle diameter on droplet generation, simulations were performed in the micropump with 1 MHz frequency with exit diameters ranging from 25 to 5 μm . Figure 13 illustrates the instantaneous liquid droplets ejected by the micropump with different

FIG. 11. Instantaneous liquid droplets ejected by the micropump at $50\ \mu\text{s}$ for different actuation frequencies.

FIG. 12. Effect of actuation frequency of micropump on the droplet velocity and volume flow.

FIG. 13. Instantaneous liquid droplets ejected by the micropump with different nozzle diameters.

nozzle diameters during the initial formation phase and at $32\mu\text{s}$. It can be observed that the droplet diameter varies with the nozzle diameter. Figure 13 also shows that the droplets ejected by the smaller nozzle move faster than the droplets ejected by the larger nozzle diameter. The droplet sizes shown with diameters of $10\mu\text{m}$ and above are likely best suited for nasal drug delivery. For

FIG. 14. Effect of nozzle diameter of micropump on the droplet velocity and volume flow.

drug delivery to the lower respiratory airways, the size of drug droplets is required to be in a narrow range of 1–5 μm .¹² In order to investigate the feasibility to produce droplets within such a narrow range with MDG, a simulation with a 5 μm nozzle diameter was performed and the snapshot of the droplets at the initial phase and at 32 μs is shown in Fig. 13. It is observed that the MDG can produce monodisperse droplets of a 5 μm diameter.

Figure 14 presents the effect of nozzle diameter on the droplet velocity and volumetric flow. As indicated above, the droplet velocity decreases with the increase of the nozzle diameter and the variation is not linear. Since the amount of droplets ejected out of the MDG is determined by the actuation frequency, the average volume flow rate increases with the nozzle diameter and droplet size. It is noted that the droplet velocity range is consistent with current soft mist medical inhalers, such as the Respimat, as reported by Longest and Hindle.⁵³

E. Effect of liquid viscosity

The effect of increases in liquid viscosity on the spray quality in pressure-swirl nozzles has been observed by Lefebvre and Wang,¹⁶ in which the droplet size decreases with increases of the liquid viscosity. In order to investigate the effect of liquid viscosity on the characteristics of the present MDG, three liquid viscosities (0.8017×10^{-6} , 1.005×10^{-6} , and 2.505×10^{-6} m^2/s , which represent a range of potential drug in carrier solutions) were considered and the actuation frequency of the MDG was maintained as 1 MHz. Figure 15 shows a snapshot of droplets ejected by the micropump through the 20 μm orifice at 30 μs with different viscosities. It is observed that the liquid viscosity has no effect on the size of formed droplets. As the viscosity will modify the flow of the liquid by friction in the liquid and at the boundary, the fluid is ejected out of the micropump domain with higher velocity for the lower viscosity cases and the droplets travel faster. Different from the adverse effect in pressure-swirl nozzles observed by Lefebvre and Wang,¹⁶ the current micropump eliminates the adverse particle-size dependent effect of liquid viscosity. That is, the droplet size and the droplet volumetric flow rate are not influenced by the liquid viscosity.

FIG. 15. Instantaneous liquid droplets ejected by the micropump at $30 \mu\text{s}$ (1 MHz actuation frequency) with different viscosities of the liquid.

V. CONCLUSIONS

This study investigated the production of liquid droplet by a valveless micropump consisting of three nozzle/diffuser elements. CFD simulations combined with VOF two-phase flow modeling was performed. The results obtained illustrate the feasibility of the MDG and the relationships between actuation frequency, fluid flow, and droplet properties. The main findings in this study are summarized as follows:

- (1) It is feasible to generate liquid droplets by a valveless micropump (MDG). The droplets initially have elaborate shapes and quickly become spherical.
- (2) The droplets generated by the MDG are highly monodisperse and the size is only affected by the outlet nozzle diameter.
- (3) The droplet velocity and volume flow rate are approximately proportional to the actuation frequency of the MDG.
- (4) The droplet velocity decreases with an increase of the nozzle diameter, and the overall average volumetric flow rate increases with the nozzle diameter.
- (5) The liquid viscosity has a small influence on the droplet velocity but no effect on the volumetric flow rate and size of the droplets.
- (6) Compared with an existing state-of-the-art DoD generator, the current MDG supplies fluid through a continuous operation mode. Higher droplet velocities can be obtained for the same actuation frequency. Spatial gaps are larger between droplets, which will reduce coagulation.
- (7) The previously reported adverse effect of liquid viscosity on droplet size is eliminated with the MDG.
- (8) Perhaps most significantly, simulations showed that the proposed design reduces power input by two orders of magnitude compared with a state-of-the-art DoD vibrating orifice device for an equivalent droplet size and flow rate.

Based on these findings, the MDG may provide useful advantages in the field of aerosol drug delivery. This is a broad field that includes drug delivery to the nasal airways, pulmonary region (tracheobronchial and alveolar airways), and dermal liquid injection. Targeting drug delivery to the nasal airways typically requires producing droplets of $10 \mu\text{m}$ or greater.⁵⁴ This size is required

to ensure deposition in the nasal airways without aerosol penetration to the lungs. The combination of monodisperse droplets greater than $10\text{ }\mu\text{m}$ and the observed velocities produced by the MDG may be ideal for targeting drug delivery to specific parts of the nasal airways, such as the olfactory region, which is a desired site of deposition for medicines to treat neurological disorders.⁵⁵ Considering pulmonary drug delivery, sizes in the range of $1\text{--}5\text{ }\mu\text{m}$ are typically required to bypass the extrathoracic airways and deposit in the lungs. Typically, high velocity droplets are detrimental to the delivery of pulmonary medicines because of increased impaction in the mouth-throat region. For the $5\text{ }\mu\text{m}$ droplets produced by the MDG, the observed initial velocity was 35 m/s . This initial velocity is consistent with other current “soft mist” spray inhalers, such as at the RespimatTM,⁵³ and one order of magnitude below the spray velocities issuing from the nozzle of frequently used metered dose inhalers.⁵⁶ It is expected that the initial droplet velocity of 35 m/s and size of $5\text{ }\mu\text{m}$ will result in relatively low spray momentum and not increase mouth-throat deposition by impaction.⁵⁶ For both nasal and pulmonary targeted medicines, multiplexing of the MDG will be necessary to provide sufficient quantities of medicine to be delivered in a reasonable amount of time. Considering dermal injections, the droplet sizes and velocities observed in these results are likely not sufficient to penetrate the skin as a liquid aerosol. However, smaller droplets and higher velocities may be achieved by further reducing the outlet diameter.

In conclusion, this initial proof-of-concept numerical study has shown that the proposed MDG was capable of producing a range of aerosol sizes, was controlled by vibrating frequency, and operated on significantly less input power than current DoD designs. Furthermore, viscosity was found to not adversely affect droplet generation. Future studies are now required to develop a physical prototype of the MDG, prove the advantages of the MDG that were observed numerically, develop multiplexed systems, and apply the MDG to aerosol drug delivery testing.

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