Flow-Focusing Monodisperse Aerosol Generator for Calibration of Spray Diagnostics Instruments

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ABSTRACT

A new instrument for generating monodisperse droplets is introduced and tested with a phase Doppler interferometer. The present device is an advancement of the technology underlying Vibrating Orifice Aerosol Generator (VOAG), which has been a key tool for generating monodisperse droplets and aerosols since 1970s (Berglund & Liu 1973). In a VOAG instrument, a liquid jet is formed by forcing the liquid out of an orifice, while ultrasonic perturbation is used to break up the jet into uniform droplets. Drop diameter is typically twice the orifice diameter. This approach has been highly successful for generating relatively large drops (e.g. greater than 50 micron), but it is difficult to implement for generating fine droplets (such as droplets smaller than 25 micron), as smaller orifices are easily clogged or otherwise damaged due to the high liquid pressure needed to maintain the liquid flow. This problem is solved in the present device, referred to as Flow-focusing Monodisperse Aerosol Generator (FMAG), which does not require fine orifices for generating fine liquid jets (Duan et al. 2015). Instead, FMAG utilizes flow-focusing to reduce the diameter of a relatively large liquid jet to the desired size. Liquid is released from a nozzle with a fairly large internal diameter (100 micron in the present realization). It is subsequently attenuated using flow-focusing. Using this approach, a final jet diameter of 5 microns is easily realized. FMAG was used to measure the transfer function of a Phase Doppler Interferometer (PDI) for standard configurations using off-axis angles of 30 and 60 degrees. FMAG-generated aerosols were also used to calibrate a non-standard PDI configuration utilizing an off-axis angle of 15 degrees representing an experimental setup with limited optical access. Also, FMAG is shown to be valuable for generating monodisperse aerosol of solutions of fragile molecules (such as enzymes) without damaging their chemical structure.

1. Introduction

Flow-focusing Monodisperse Aerosol Generator (FMAG) is a newly developed instrument for generation of standard droplets and particles that can be used for calibration of optical particle sizing instruments. Principle of FMAG is elaborated in Fig. 1. An earlier device, Vibrating Orifice Aerosol Generator (VOAG), utilizes controlled breakup of a liquid jet to generate monodisperse droplets (Berglund & Liu, 1973). As shown in Fig. 1, liquid jet is formed by forcing the liquid out of an orifice, while acoustic waves are sent along the jet to cause excitations with a wavelength...
that lies in the range of jet’s natural instability. As a result, the jet breaks up into uniform droplets. Drop diameter is typically twice the orifice diameter. This approach has been highly successful for generating relatively large drops, but it is difficult to implement for generating fine droplets, as smaller orifices are easily clogged or otherwise damaged due to the high liquid pressure needed to maintain the liquid flow.

As illustrated in Fig. 1, FMAG does not require fine orifices for generating fine liquid jets (Duan et al. 2015). Instead, FMAG utilizes flow-focusing to reduce the diameter of a relatively large liquid jet to the desired size. Liquid is released from a nozzle with a fairly large internal diameter (100 micron in the present device). It is subsequently attenuated using flow-focusing air (‘FF Air’ in Fig. 1). Using this approach, a final jet diameter as small as 5 microns is realized.

The attenuated jet in FMAG is broken into uniform droplets using ultrasonic perturbation in a manner similar to VOAG. Use of FF Air has two main advantages: (1) FMAG generates fine droplets without using narrow orifices that are prone to damage and clogging, (2) Unlike VOAG, FMAG does not require replacing orifices to cover a wide droplet size range; only flow rate of FF Air needs to be changed to generate a wide range of droplet diameters. Current version of FMAG is shown to cover a monodisperse droplet diameter range of 10 to 150 microns using a single nozzle.
2. Instrument Description

A complete FMAG system is shown schematically in Fig. 2. The spray head contains a piezoelectric crystal and inlet ports for the liquid and FF Air. The electrical and fluid lines leading to the head are flexible, enabling mounting on a bench to release droplets in any direction. The ultrasonic frequency controller, syringe pump and FF Air pressure controller are placed in a box with a display of operating conditions that the user can adjust.

![Fig. 2 FMAG System](image)

FMAG includes additional hardware for drying the droplets of solutions to generate monodisperse solid particles as small as 0.5 micron. Additional components are shown in light gray in Fig. 2. They include a drying column that receives dilution air through the Dilution Air Flow Controller. In order to prevent electrostatic aerosol losses, the particles are neutralized using a bipolar corona source (Romay et al. 1994).

Operation of FMAG can be explained adequately using three physical principles:

1. In order to be broken reliably into monodisperse droplets, a liquid jet needs to have an appropriate balance of inertia and surface tension force. High surface tension prevents
formation of the jet and if the jet is formed, it may be intermittent if the surface tension is too high. On the other hand, high inertia makes the jet unstable and prevents effective use of ultrasonic excitation to break it into monodisperse droplets. In other words, FMAG operates well within a narrow range of Weber numbers, which leads to a three-half power-law relationship between the liquid volume flow rate (Q) and the liquid jet diameter. Recognizing that the liquid drop diameters resulting from the breakup of the liquid jet scale with the jet diameter in accordance with the Rayleigh instability criterion, $Q \propto D^{3/2}$, where $D$ is the droplet diameter. Gray regions in Figs. 3 and 4 represent this relationship and identify the region where liquid jet is stable enough to be broken into monodisperse droplets using ultrasonic excitation. Figs. 3 is based on the surface tension and density of water and Fig. 4 is representative of a typical organic solvent (e.g. methanol or isopropyl alcohol).

2. Inside the spray head, the liquid jet is exposed to FF Air pressure ($\Delta p$), which vanishes as it leaves the spray head. Hence, mechanical work is constantly being done on the jet at a rate of $Q \Delta p$. This work is mostly converted into the kinetic energy of the attenuated jet. At a given $\Delta p$, this energy balance leads to a quadratic relationship between the liquid flow rate and the jet diameter (and hence the drop diameter), i.e. $Q \propto D^2$. As shown in Figs. 3 and 4, solid lines pertaining to constant $\Delta p$ values have slightly larger slope than the stable jet region on a log-log plane. For a stable-jet operation, $\Delta p$ needs to be reduced as the desired drop diameter is increased.

3. Under the condition of monodisperse droplet generation, one drop is released in each cycle of ultrasonic excitation, i.e. $\pi D^3/6 = Q/f$, where $f$ represents the ultrasonic frequency. For a given frequency, there is a cubic relationship between the liquid flow rate and the droplet diameter, i.e. $Q \propto D^3$. Lines of constant ultrasonic frequency (dotted lines) are included in Figs. 3 and 4 and show how frequency needs to be reduced as the droplet diameter is increased.
Fig. 3 FMAG operating condition selection guide for water and aqueous solutions
Fig. 4 FMAG operating condition selection guide for common organic solvents and solutions

Charts like Figs. 3 and 4 can be used to select the operating conditions (liquid flow rate, FF Air pressure, and ultrasonic frequency) for reliably generating monodisperse droplets of a given liquid. Under the conditions of monodisperse droplet generation, FMAG does not need calibration. Droplet diameter based on \( \frac{\pi D^3}{6} = \frac{Q}{f} \) relation is generally accurate to 0.1%, as both \( Q \) and \( f \) are known with high accuracy. These charts are not applicable to the extreme cases of high viscosity (which is neglected in the Rayleigh instability criterion) or high FF Air pressure, which may lead to choked flow at the exit of the spray head.

3. Phase Doppler Measurement of FMAG-Generated Droplets

FMAG is valuable for calibrating and/or validating the operation of laser particle sizing instruments, such as phase Doppler interferometer (PDI), which is also known as particle dynamics analyzer (PDA) and phase Doppler particle analyzer (PDPA); see Bachalo et al. (1984) and Buchhave et al. (1984). Fig. 5 shows results of our recent measurement of phase shift versus
droplet diameter for a PDI system (Artium Technologies, Inc.) using monodisperse water droplets (10 – 63 µm in diameter) generated by a single nozzle of FMAG. To cover the same size range, VOAG requires changing orifices several times. Also, the smallest droplet diameter from a commercially available VOAG is specified to be 21 microns, as smallest available orifice is 10 micron in diameter. On the other hand, the current FMAG hardware is capable of attenuating liquid jets to about 5 microns, resulting in monodisperse droplets of 10 micron in diameter. Geometric standard deviation of the droplets in Fig. 5 was ≤1.01 for diameters greater than 40 µm, and <1.035 for all the droplet diameters.

![Fig. 5](image)

**Fig. 5** Measured phase versus drop diameter relations for a PDI system at different off-axis angles

Besides the standard off-axis angles of 30 and 60 degrees, Fig. 5 includes results from a non-standard phase Doppler configuration, i.e. 15 degree off-axis angle. This configuration is generally not recommended but may be considered as a compromise if the experimental setup has limited optical access and does not allow larger off-axis angles. FMAG measurements at 15 degree off-axis angle show that this non-standard setup is acceptable for a droplet size range of 10-55 microns. This is verified by the Mie scattering simulations of Fig. 6 for a similar phase Doppler system. The code used for Mie scattering calculations is described by Naqwi & Durst (1991). As shown in Fig. 6, large errors and uncertainties in the measurement at 15 degree off-axis angle are expected only if the particle size is smaller than 10 micron.
For droplet diameters of 10 micron, PDI-measured size distribution was broader at 15 degree off-axis angle, as shown in Fig. 7. This may have been caused by the fluctuations in the phase-diameter relationship as predicted by the simulations of Fig. 6. Besides determining the feasibility of non-standard phase Doppler geometries, FMAG may also be used to validate and calibrate phase Doppler measurements for non-standard particle compositions, e.g. spherical particles with optical inhomogeneity or birefringent and/or light attenuating behavior.
Fig. 7 Size histograms of 10 micron droplets measured with PDI
4. Generation of Monodisperse Enzyme Droplets using FMAG

Besides being a calibration and validation means for optical particle sizing instruments, FMAG is valuable as a means for ‘gently’ spraying materials with fragile chemical structures. Large biological molecules, as well as cells and microorganisms often need to be sprayed in order to study their behavior in aerosol form or to formulate them as powders. Conventional spraying processes involving strong mechanical shear or impact can damage the fragile structure of the biological material. Flow focusing, leading to liquid breakup, is shown to cause minimal damage to E-Coli bacteria (Thomas et al. 2008). FMAG is valuable for laboratory studies in which microorganisms need to be aerosolized, e.g. rodent inhalation studies involving airborne pathogens.

Another area of interest is pre-formulation studies of spray drying processes for enzymes and probiotics in food and pharmaceutical industries. For a pre-formulation study, Schutyser et al. (2012) considered droplet generation using a device based on ink-jet principle (or VOAG principle), which typically results in 200 µm drops that could be dried by allowing them to freefall in a 30 m tall column. FMAG enables a much more compact setup for such pre-formulation studies. One of the enzymes of interest for such studies is lipase Schutyser et al. (2012), used extensively in food industry. Preliminary results of lipase activity after spraying with FMAG to generate 15 µm drops are given in Fig. 8.

For this study, lipase enzyme (Sigma Cat# L3126) was dissolved in water at 5 mg/ml concentration (100-500 units/mg). The liquid was filtered with 0.45 µm filter and injected into FMAG at 2 ml/hr flow rate. Aerosols were collected for 10 minutes. For FMAG, two settings were used: one with ultrasonic frequency transducer turned on and the other with the transducer turned off. Lipase solution was also aerosolized using a conventional nebulizer Aeroneb™ and collected for analysis. All 3 samples were analyzed using lipase enzyme activity kit (Sigma Cat# MAK046). The lipase activity was measured in units of enzyme generating 1.0 µmoles of glycerol from triglycerides per minute. Figure 8 shows enzyme activity for 3 tests performed. The enzyme activity of FMAG-sprayed liquid was unchanged with frequency transducer turned off. The ultrasonic perturbation lowered the enzyme activity by about 10%, whereas vibrating mesh nebulizer caused a 30% drop in the enzyme activity.
4. Conclusions

References
