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**Technical Note**

# Evaluation of the NanoAerosol Generator by Kanomax FMT Inc. in Aerosolization of Size Standard Nanoparticle and Protein

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## ABSTRACT

A new nebulizer called NanoAerosol Generator (NAG) by Kanomax FMT, Inc. was evaluated experimentally in their performance in aerosolizing sub-100 nm particles and sub-10 nm protein molecules which cannot be aerosolized with conventional compressed-air jet nebulizers due to the interference by a number of residue particles. For the challenge particles, 29 nm-polystyrene latex (PSL) particles and bovine serum albumin (BSA) protein molecules were used as sub-100 nm and sub-10 nm test materials, respectively. For both particles, the aerosolization by the NAG was successful with a clear separation between the peak of the challenge particles and the peak of residual particles in the size distribution spectra. The size distributions of aerosolized 29 nm-PSL particles were compared between the NAG and an electrospray aerosol generator (EAG) with liquid samples of the same particle concentration. The EAG showed clearer separation of the PSL peak from the residual peak; on the other hand, the peak height was taller for the NAG by a factor of 6 than for the EAG, which indicated the generation of airborne particles from a liquid suspension/solution of the same concentration was more efficient for the NAG than for the EAG.

***Keywords:*** Nebulizer; Electrospray; Polystyrene latex; Bovine serum albumin.

## INTRODUCTION

Generation of aerosols by spraying a suspension of solid particles or a solution of non-volatile materials is an essential technique in aerosol and particle studies, and various types of sprayers are used in the laboratory for this purpose (Hinds, 1999; Chen *et al.*, 2011). In our laboratory where aerosol instruments are regularly tested and calibrated, for example, size standard polystyrene latex (PSL) particles are aerosolized by the spray method. Conventional compressed-air jet nebulizers (or atomizers) and electrosprays are most common sprayers. The conventional nebulizer can aerosolize particles in the size range from about 50 nm to a few μm. The electrospray is good at 50-100 nm and even smaller sizes. The difference in the lower size limit between these techniques comes from the difference in the initial size of the droplets formed by the two sprayers. That is, the initial droplet size of the nebulizer is greater than that of the electrospray, which results in larger residual particles. The size of the residual particles from the nebulizer is often as large as 50 nm and overlaps with the particles of 50 nm or smaller. For example, the number weighted size distribution of residue particles when deionized water was sprayed with a conventional nebulizer, TSI model 3076 Constant Output Atomizer, had the mode diameter of 21.5 nm and extended to about 50 nm (Stabile *et al.*, 2013). For this reason, aerosolization of sub-50 nm particles is usually done with the electrospray. However, the electrospray technique may not be applicable for some types of liquids.

Recently, Kanomax FMT Inc. introduced a new nebulizer, i.e., the NanoAerosol Generator (NAG) model 3250. Similar to other nebulizers, the NAG has an impactor after the exit of the nebulizing nozzle to remove large droplets that are formed by spraying. For the NAG, the impactor is located closer to the nozzle, compared with other nebulizers, to reduce the cut-off size of the impaction. The initial mode diameter of the droplets generated by the NAG is 550 nm (Kanomax FMT, Inc., 2017), which is greater than the droplet sizes of not only the electrospray but also other nebulizers, based on the information provided by the manufacturers. For example, the initial droplet size of the TSI model 3480 Electrospray Aerosol Generator (EAG) and that of the TSI model 3076 Constant Output Atomizer (a conventional nebulizer) are 150 nm (TSI Inc., 2012) and 350 nm for water (TSI Inc., 2005), respectively. Nevertheless, the manufacture of the NAG claims that the NAG "produces significantly

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smaller droplets minimizing the influence of non-volatile residue" (Kanomax FMT, Inc., 2017) when compared with other nebulizers. To verify the claim by the manufacturer, we performed experimental evaluations of the performance of the NAG in aerosolizing particles that we often use in our laboratory, namely size standard PSL nanoparticles and proteins, and investigated whether the NAG could aerosolize those sub-50 nm particles without burying them in residual impurity particles.

## EXPERIMENTAL

A schematic of the experimental setup is given in Fig. 1. The setup was simple: An aerosol generator was connected with a tube to an instrument for the measurement of size distribution. The NAG was operated with the sample and nebulizer gas pressures set at 18 psi (0.12 MPa) and 35 psi (0.24 MPa), respectively. The evaporation temperature was set at 60°C. The dilution gas mode was set passive, i.e., the excess air was bled through the vent in the NAG.

The size distribution of the aerosols from the NAG was measured with a scanning mobility particle sizer spectrometer (SMPS) by TSI Inc. (Shoreview, Minnesota, U.S.A.) with a bipolar charge conditioner with Am-241 (3 MBq) in a stainless steel housing by Tsukasa Sokken Co., Ltd. (Tokyo, Japan). The SMPS consisted of a model 3085A Nano DMA, model 3776 Ultrafine Condensation Particle Counter, and model 3082 controller platform, with TSI Aerosol Instrument Manager ver. 10.1 software for measurement control and data acquisition. We did not use the pre-cut impactor. The sheath air and aerosol flow rates of the DMA were set at 15 L $min^{-1}$ and 1.5 L $min^{-1}$, respectively. The CPC was operated in high flow mode. The upscan time was 160 s. The multiple charge and diffusion loss corrections were both turned off in the size distributions presented in this paper, since these corrections were not essential in this study. The SMPS covered the size range between 2.5 nm and 65 nm. The size distribution spectra shown in this paper are the results of averaging of sequential measurements repeated for at least three times. The tubing connection between the NAG outlet and the inlet of the bipolar charge conditioner of the SMPS was made with a conductive silicone tube of the inner diameter of about 6 mm and the length of about 50 cm. There was no diffusion dryer used after the NAG.

To compare directly the performance of the NAG with that of the electrospray, a unit of the electrospray aerosol generator (EAG, TSI model 3480) was placed next to the NAG and the size distribution measurement for the aerosol by the EAG was made with the same SMPS. The tubing connection between the EAG and SMPS was identical in the length (i.e., 50 cm) except that there was a branch for bleeding. The EAG was operated with clean air at the flow rate of 1.5 L $min^{-1}$ without carbon dioxide gas added, and with a capillary of 40 μm in inner diameter. An Am-241 (4 MBq) alpha-ray source was installed in the spray chamber for bipolar charge conditioning.

Two liquid samples were used in the evaluation of the NAG, namely, suspensions of PSL nanoparticles and solutions of bovine serum albumin (BSA) protein. The PSL and BSA used in this study were SC-0030-A by JSR Corp. (Tokyo, Japan) and A9418 by Sigma-Aldrich (Saint Louis, Missouri, U.S.A.), respectively. For the PSL, the raw suspension liquid was diluted with ultrapure water at three concentration levels. BSA was dissolved into ultrapure water at three concentration levels. For the PSL suspension that was aerosolized by the EAG, ammonium acetate was dissolved at the concentration of 2 mM to adjust the electrical conductivity of the liquid. The sample dilution factor was determined by weighing both the liquid to be diluted and the liquid after dilution with an analytical balance of 0.1 mg precision. The relative standard uncertainty of the dilution factor by the above method was estimated to be approximately 10 %. The ultrapure water used for the preparation of the above liquid samples had the nominal resistivity and total organic contents of 18 MΩ cm and 3 ppb, respectively, and was processed with a final filter of the pore size of 0.22 μm.

## RESULTS AND DISCUSSION

The NAG was first evaluated with ultrapure water for the size of residual particles. The size distribution obtained is shown in Fig. 2. Most of the residual particles were

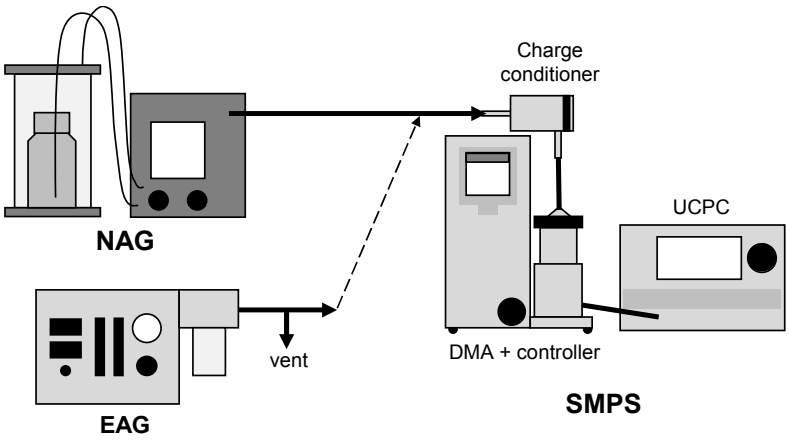


**Fig. 1.** Schematic of the experimental setup.

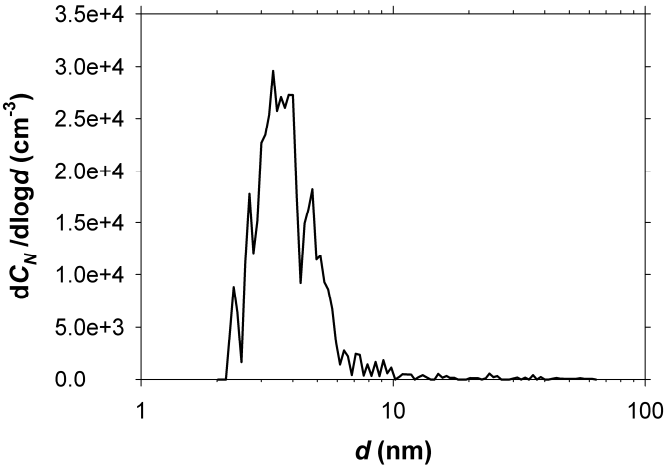


**Fig. 2.** Size distribution of the residual particles formed by nebulization of ultrapure water with the NAG.

smaller than 6 nm, and the mode diameter was 3.5 nm. The size of the residual particles was significantly smaller than that by conventional nebulizers which is usually greater than 20 nm (Stabile *et al.*, 2013).

The second evaluation test was done with the 29 nm PSL. The size distributions are given in Fig. 3. The left plot (Fig. 3(a)) shows the size distributions with the absolute scale in y-axis. Suspensions of three dilution levels, i.e., the dilution factors of $10^3$, $10^4$, and $10^5$, were prepared and used in the evaluation. The height of the PSL peak at about 30 nm decreased as the dilution factor was increased. About the stability of the aerosol generation and the measurement repeatability of the experiment, the total concentration for the PSL peak in the size range between 15 nm and 50 nm varied by 5 % or less in repeated measurements. This good stability and repeatability were maintained throughout this study. The broad peak for residual particles on the left became shorter and shifted to smaller sizes as the dilution factor was increased. The separation between the two peaks was clear at all the three concentration levels, although the bottom of the gap between the two peaks did not go to zero completely. In Fig. 3(b), the size distribution functions were normalized so that the top of the PSL peaks match at unity for the three traces. The PSL peak for the dilution factor of $10^3$ had a slight shoulder around 40 nm on the right, which indicated the formation of PSL doublets. Indeed, the mobility-equivalent diameter of doublet particles of 29-nm spheres was calculated based on Cheng *et al.* (1988) and found to be 35.1 nm and 39.7 nm when the particles are assumed to align parallel and perpendicular to the direction of the particle motion, respectively. These apparent diameters are comparable to the particle size that corresponds to the shoulder. Another possibility for the formation of the shoulder is due to thick coating of the PSL particles with non-volatile residue when the dilution factor was the lowest. From Fig. 3(b), the largest residual particles for the dilution factor of $10^3$ seemed to be about 20 nm. Based on this, we assumed that the maximum volume of the non-volatile residue that coated the 29-nm PSL particles was equal to the volume of 20 nm spherical particles and calculated the diameter of the coated PSL particles. The result was 32 nm, which was too small to explain the formation of the shoulder at about 40 nm. Therefore, we concluded that the shoulder was due to the formation of doublets, and for this PSL with the NAG, the dilution factor should have been greater than $10^3$ to avoid completely the doublet formation. Except the formation of the doublets, the NAG was successful in aerosolizing 29 nm-PSL particles without being significantly interfered by the residual peak in the distribution spectra.

The third evaluation test was performed with BSA. The size distributions obtained for the three concentration levels are shown in Fig. 4. At the highest concentration level of 100 μg mL$^{-1}$ in Fig. 4(a), the monomer peak at 6.4 nm was clearly separated from other peaks. There was no peak for residual particles. This was probably because all droplets formed in the NAG contained at least one BSA molecule and the majority of the particles formed were BSA multimers. While the monomer peak was present, the fraction of the monomers was not large. For the purpose of the formation of airborne BSA monomers, the solution concentration was too high and most of BSA put into the solution was wasted. At the second concentration level of 1 μg mL$^{-1}$ in Fig. 4(b), the monomer peak was the strongest, with some multimers still being present to the right. There was no residual peak. The height of the monomer peak ($4.3 \times 10^6$ cm$^{-3}$ in d$C_N$/dlog$d$), was greater than that of the monomer peak at the concentration of 100 μg mL$^{-1}$ ($2.2 \times 10^6$ cm$^{-3}$). That is, between 1 and 100 μg mL$^{-1}$, more BSA monomers were aerosolized when the BSA concentration was lower. At the third, lowest concentration level of 0.01 μg mL$^{-1}$ in Fig. 4(c), the most dominant peak was that for the monomer. Most of the mulimer peaks seen at the higher concentration levels diminished, and instead the signal from residual particles were visible in the size range between 2 nm and 6 nm in this spectrum. There was no interference of the residual peak signal to the monomer peak. From these observations, the aerosolization of BSA monomers was most successful at the solution concentrations of 0.01 μg mL$^{-1}$ and 1 μg mL$^{-1}$.

An additional measurement was made with the 1 μg mL$^{-1}$ BSA solution to investigate the concentration of the

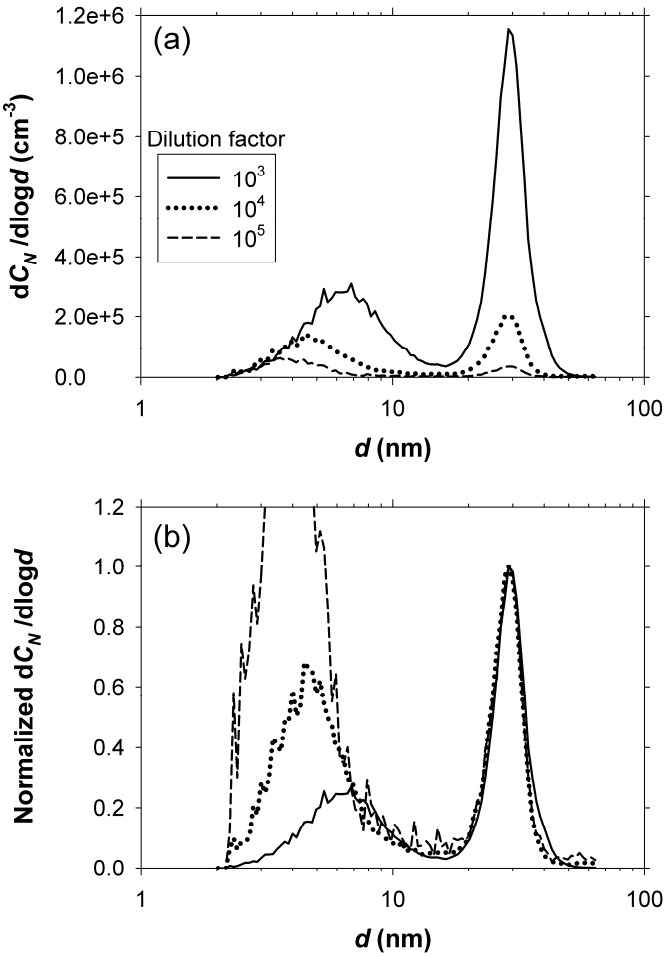


**Fig. 3.** Size distributions of 29 nm-PSL particles by nebulization with the NAG. The three traces in each plot correspond to suspensions prepared at different dilution factors: (a) y-axis in the absolute scale, and (b) y-axis in normalized scale so that the peak heights for the PSL match at unity for the three traces.

monomers after the classification by the DMA. The size classification by the DMA in the SMPS was fixed at 6.4 nm and the concentration after the DMA was recorded with the Ultrafine CPC. The concentration was about $2.5 \times 10^4$ cm$^{-3}$, which would be sufficiently high for many applications, such as instrument testing in sub-10 nm size range.

The fourth evaluation test was performed with the 29 nm-PSL particles again, and the size distributions of the PSL particles aerosolized by the NAG and EAG were compared with each other. For this test, both generators aerosolized PSL suspensions of the same dilution factor of $10^3$, while the suspension for the EAG had additional ammonium acetate of 2 mM as stated earlier. The size distributions taken by the two generators are plotted together in Fig. 5. The gap between the PSL and residual peaks was wider for the EAG. The mode diameter of the residual peak for the EAG was about 4 nm while that for the NAG was about 7 nm, which indicated that the initial droplet size of the NAG was greater than that of the EAG. The mean diameter of the PSL peak calculated for the size range between 25 nm and 33 nm was 29.1 nm for both generators. The above size range was determined so that the shoulder due to doublets in the size distribution of the NAG was not included. The agreement of the mean diameter between the two generators indicated that the residual coating did not affect the particle size when the PSL particles were aerosolized with the NAG. The intensity of the PSL peak was higher for the NAG by about a factor of 6 when compared with the peak height for the EAG. Since the particle concentration in the liquid suspension was about the same (i.e., the raw PSL suspension liquid was diluted by a factor of $10^3$ for both generators), and since the relative uncertainties for the dilution (< 10%) and measurement repeatability (< 5%) were small, the taller PSL peak for the NAG in this side-by-side comparison indicated that the NAG was more efficient in aerosolization of this PSL. It should be noted that, since the droplet size was smaller for the EAG, the particle concentration of the liquid suspension could be increased for the EAG to increase the PSL peak intensity until the magnitude of doublet formation becomes unacceptable, while for the NAG the dilution factor of $10^3$ was already at the limit.

## CONCLUSION

The NAG was evaluated with the PSL nanoparticles and

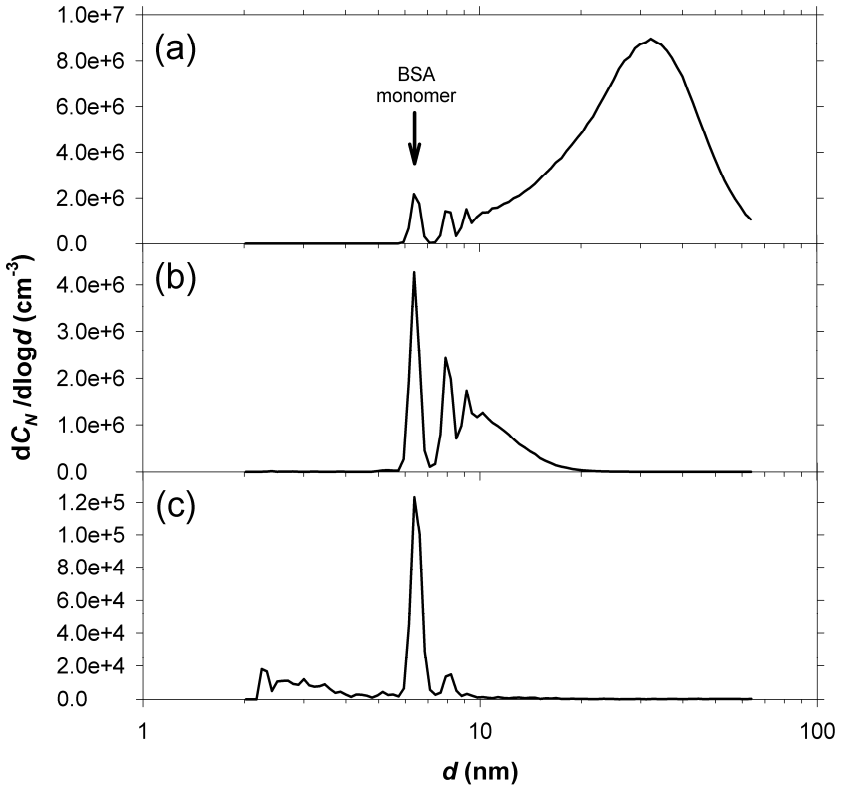


**Fig. 4.** Size distributions of BSA protein molecules nebulized with the NAG at three concentration levels: (a) 100 μg $mL^{-1}$, (b) 1 μg $mL^{-1}$, and (c) 0.01 μg $mL^{-1}$. The down arrow in (a) indicates the position of the monomer peak at about 6.4 nm.

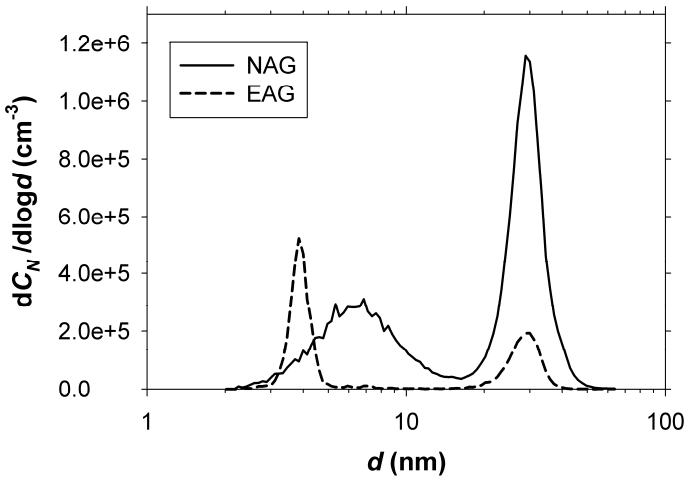


**Fig. 5.** Comparison of the size distributions of 29 nm-PSL particles aerosolized by the NAG and EAG with suspensions of about the same dilution factor of $10^3$.

protein molecules regarding its capability of generating the particles and protein molecules without suffering from the interference with residual particles and multimers in the size distribution. We found the NAG was successfully able to aerosolize the 29 nm-PSL particles and BSA molecules of about 6.4 nm without significant interference. Based on these results, we expect the NAG could be an alternative of the electrospray for aerosolizing particles and molecules of sub-100 nm and even sub-10 nm.

We would like to note that the consumption rate of the sample liquid was much faster for the NAG than for the EAG. In their catalogs, for example, the sample liquid flow rates of the NAG and EAG are 0.5–3.0 mL $min^{-1}$ and 50–100 nL $min^{-1}$ (TSI model 3480 EAG), respectively, and these values are consistent with our experience.

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## DISCLAIMER

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## REFERENCES

Chen, B.T., Fletcher, R.A. and Cheng, Y.S. (2011). Calibration of aerosol instruments. In *Aerosol measurement -- Principles, techniques, and applications, 3rd. Ed.*, John Wiley & Sons, Inc, New York.

Cheng, Y.S., Allen, M.D., Gallegos, D.P., Yeh, H.C. and Peterson, K. (1988). Drag force and slip correction of aggregate aerosols. *Aerosol Sci. Technol.* 8: 199–214.

Hinds, W.C. (1999). *Aerosol technology -- Properties, behavior, and measurement of airborne particles, 2nd Ed.*, John Wiley & Sons, Inc, New York.

Kanomax FMT, Inc. (2017). NanoAerosol Generator Model 3250 catalogue, http://www.kanomaxfmt.com/uploads/5/7/5/4/57542039/nanoaerosol_generator_model_3250_brochure.pdf, Last Access: 10 December 2017.

Stabile, L., Trassierra, C.V., Dell'Agli, G. and Buonanno, G. (2013). Ultrafine particle generation through atomization technique: The influence of the solution. *Aerosol Air Qual. Res.* 13: 1667–1677.

TSI Inc. (2005). Model 3075/3076 Constant Output Atomizer Instruction Manual, Revision J. Shoreview, Minnesota, U.S.A.

TSI Inc. (2012). Electrospray Aerosol Generator Model 3480 catalogue, http://www.tsi.com/uploadedFiles/_Site_Root/Products/Literature/Spec_Sheets/3480.pdf, Last Access: 10 December 2017.

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