Isokinetic In-line Sampling Enables Rapid Characterization of Atomizers and Cyclones for Spray Drying Process Development

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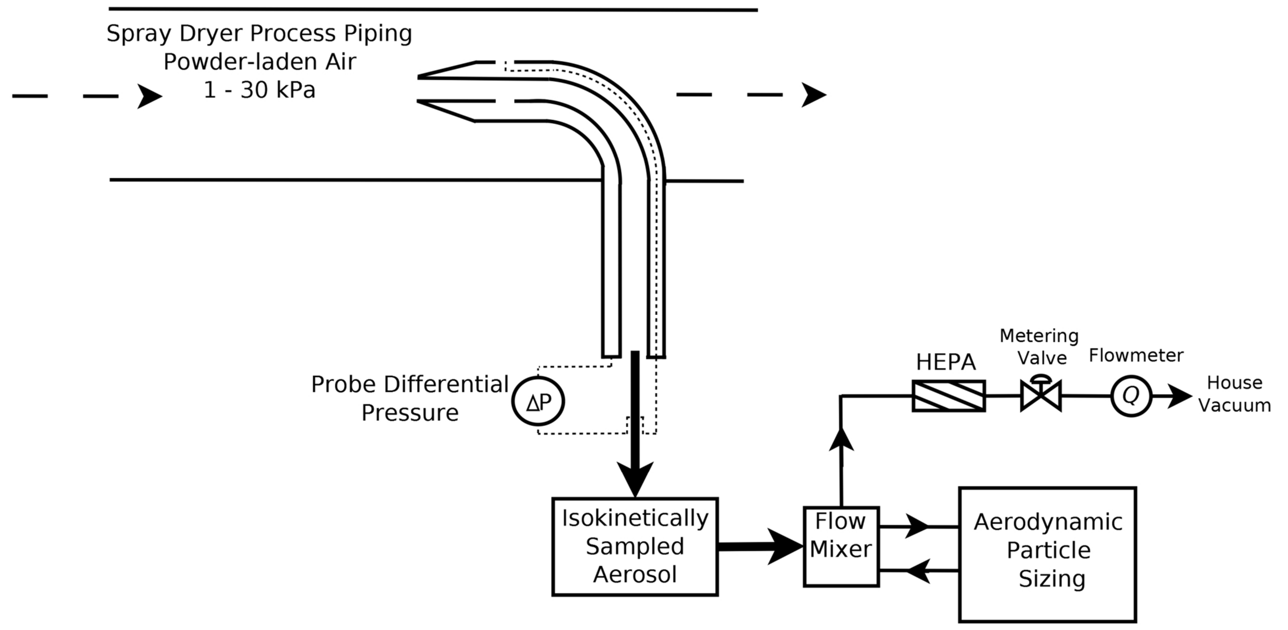
Introduction

- Particle engineering is enabling the next generation of inhalation products
  - Tailoring particle properties to the application maximizes efficiency, repeatability, efficacy of therapy [1-3]
- Spray drying: particle physical properties controllable by modifying formulation and process parameters [4]
  - Requires appropriate models and adequately characterized atomization and collection equipment [5-6]
- An isokinetic sampling system was developed for real time measurement of process aerodynamic particle size distributions, enabling characterization of spray dryer atomizers and cyclones
- The viability of the approach is demonstrated by performance characterization of a twin fluid atomizer and a gas cyclone supplied with the popular Büchi B-290 dryer

Working components of the twin fluid atomizer

Büchi's high-efficiency cyclone design

Materials and Methods



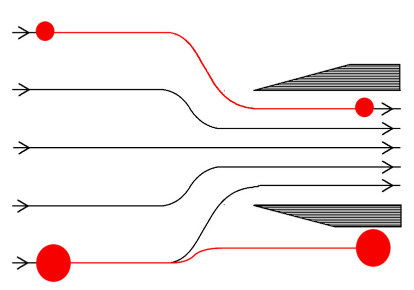
- Atomized droplet diameter distributions for a commercially available twin fluid atomizer were measured indirectly using isokinetic sampling and time of flight aerodynamic particle sizing (TSI 3321 APS Spectrometer)
  - Spray drying disaccharide solutions (aqueous trehalose, sucralose in ethanol) of known concentration resulted in solid spherical particles
  - Atomized droplet diameter distribution is thus related to dry aerosol aPSD:

$$d_{0,50} = \sqrt[3]{\frac{\rho^*}{c_s}}\sqrt[6]{\frac{\rho^*}{\rho_p}}\, d_{a,50} \text{ with } GSD_0 = GSD_a$$

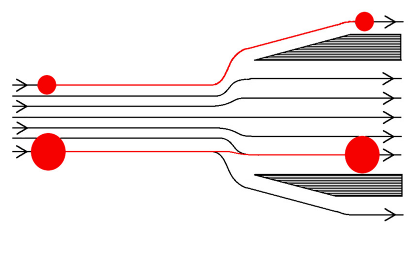
- Separation efficiency curves for a commercially available cyclone were determined at varying gas flow rates by generating a test aerosol then measuring the aPSD upstream and downstream of the cyclone
  - Cyclone fractional efficiency was determined from the count distributions of the feed and overhead fractions:

$$\eta(x_i) = 1 - \frac{f_O(x_i)}{f_F(x_i)}$$

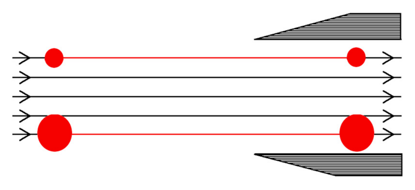
Why Sample Isokinetically?



Super-isokinetic sampling: larger particles are under-sampled, measured aPSD artificially fine



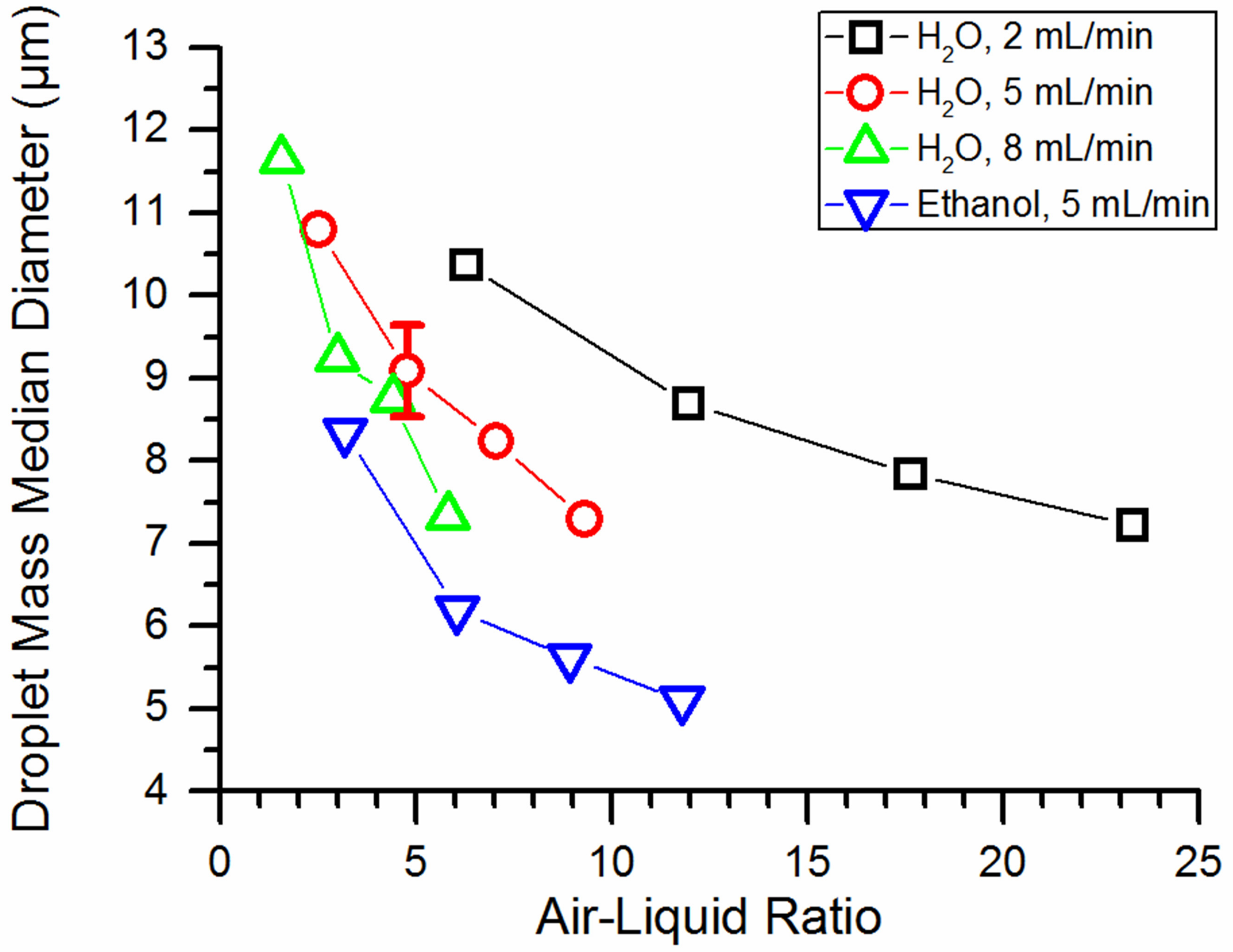
Sub-isokinetic sampling: larger particles are over-sampled, measured aPSD artificially coarse



Isokinetic sampling: sampled aerosol is representative of entire aerosol

Results

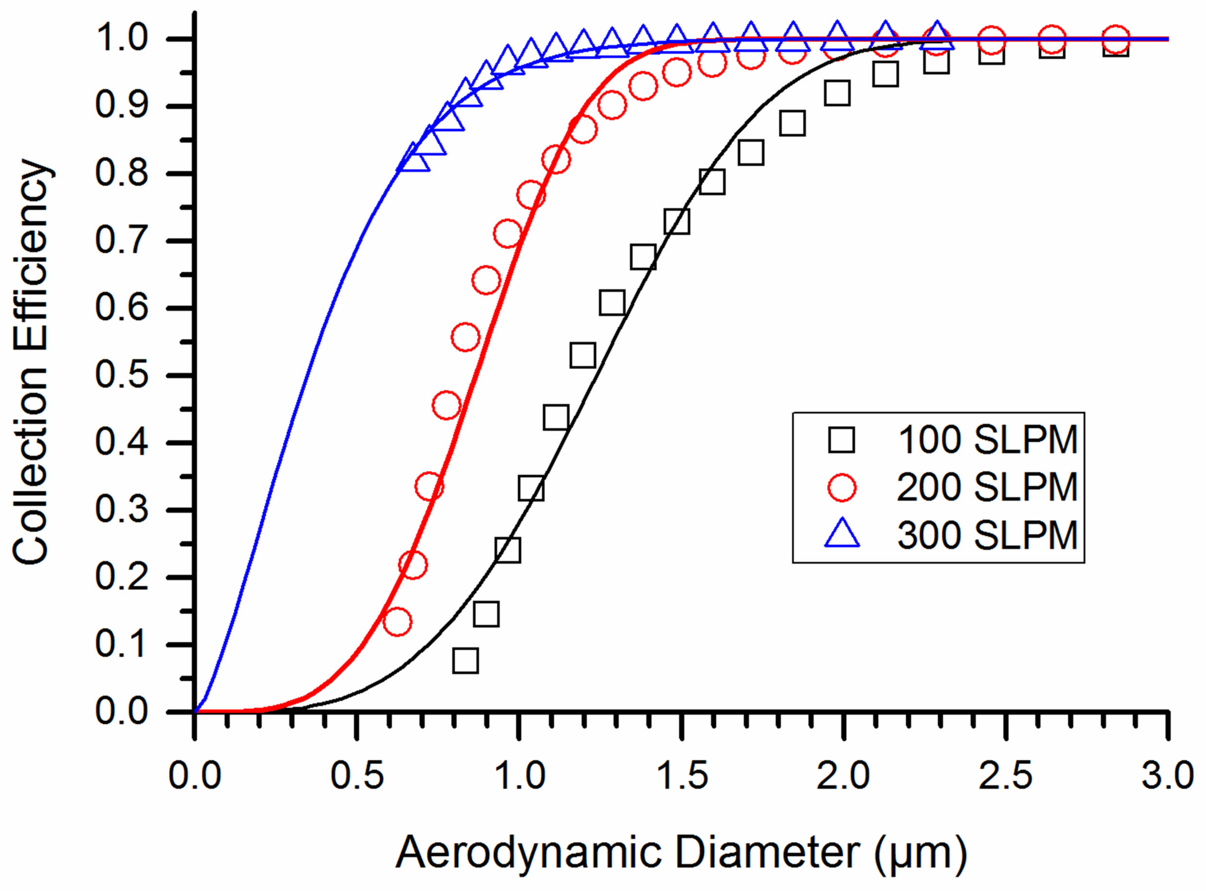
➢ Atomized Droplet Diameter Distributions



Mass median droplet diameter vs. atomization air-liquid ratio for the tested Büchi twin fluid atomizer. An intermediate point was replicated three times to assess measurement variability. The error bar represents one standard deviation.

- Geometric standard deviation 1.4 — 1.7 with overall mean of 1.6; no obvious correlation with spray parameters
- Ethanol spray substantially finer than aqueous spray
- For fixed ALR, increasing the spray rate results in a finer spray
- Droplet size is adjustable by adjusting ALR *via* atomizing gas pressure
- These atomizer characterization data enable prediction of dry particle size for solution spray drying: $d_{p,50} = \sqrt[3]{\frac{c_s}{\rho_p}}\, d_{0,50}$

➢ Cyclone Grade Efficiency Curves



Separation efficiency curves for Büchi's high-efficiency cyclone separator at varying air flow rates. Symbols: measured discrete efficiency data. Closed lines: curve fits to discrete data.

Gas Flow Rate (SLPM)	Cut size x_{50} (μm)	Sharpness parameter m
100	1.24 ± 0.03	3.46 ± 0.30
200	0.84 ± 0.04	3.64 ± 0.72
300	0.35 ± 0.03	1.43 ± 0.14

- Data were fit with nonlinear least squares to estimate 50 % cut size:

$$(x) = 1 - \exp\left[\ln\left(\frac{1}{2}\right)\left(\frac{x}{x_{50}}\right)^m\right]$$

- Typical process flow rate in B290 ~300 L/min; very high efficiency collection of respirable particles is expected

Conclusions

- ➢ Real-time measurement of dried powder APSD in spray drying processes is possible using a novel isokinetic sampling system coupled with a time-of-flight aerodynamic particle sizer
  - ➢ Potential PAT / process monitoring tool
- ➢ The system enables rapid and economical characterization of atomization and collection equipment relative to e.g. PDA
- ➢ These equipment performance data enable predictions of dry particle size distribution using mechanistic modeling techniques
- ➢ Such models reveal critical process parameters, streamline process development, and save time and capital

References

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