In-Situ Sizing of Powders and Crystals Using Phase Doppler Measurement Technique[†]

Amir A. Naqwi & Chris W. Fandrey
TSI Inc.*

Rebanta Bandyopadhyay and
David J.W. Grant

Dept. of Pharmaceutics, Univ. of Minnesota**

Abstract

Phase Doppler technique is a non-intrusive optical device for in-situ measurement of single particles. In the case of an irregular particle, it provides a deterministic measure of particle velocity and statistical information about the particle size in the form of a phase shift signal. By collecting sufficient signals, velocity-resolved particle size distributions can be reconstructed. This is demonstrated by comparing phase Doppler measurements of irregular particles with an aerodynamic particle sizer. Preliminary measurements in a crystallizer are also presented. The present device is shown to work with near back-scatter collection of scattered light; hence, leads to a robust setup that can be used under the conditions of limited optical access.

1. Introduction

In many industrial particulate flows, the particles under investigation have irregular and complex structures. It is desirable to use these real particles in field tests as well as laboratory studies that may be aimed at understanding the corresponding particulate process. Optical techniques provide a convenient means for in-situ measurement of such particles. However, the light scattering characteristics of the irregular particles deviate significantly from those of homogeneous spherical particles, that are frequently used as models for estimating the particle response.

In fact, an irregular particle of a given size can generate many different values of a certain light scattering property. The corresponding ambiguity in the measurements is dealt with in many different ways in the previous works. Some of the previous approaches are reviewed by Naqwi and Fandrey [1].

In an earlier experimental work, Bottlinger and Umhauer [2] took into consideration the entire histogram of scattered intensities generated by a single irregular particle. These probability functions were used to relate the size distribution of a polydisperse suspension to the corresponding measured intensity distribution, using a matrix formulation.

The present technique is similar to the above approach; however, instead of intensity, phase shift between sinusoidal signals of a phase Doppler system is measured. As shown by Naqwi [3], the measured phase distribution can be expressed as an integral involving the unknown size distribution and a kernel function, referred to as monosize phase distribution (MPD) function. The MPD function represents the phase distribution corresponding to a single particle size.

The phase Doppler technique is superior to the intensity based instrumentation, as phase shift is less susceptible to electronic noise than intensity. Also phase is not affected significantly by variations in the laser power due to presence of particles in the path of the laser beam. Furthermore, phase Doppler provides a deterministic measure of the particle velocity in addition to a stochastic measure of its size, so that velocity resolved phase distributions can be measured.

For the sake of completeness, the principle of the phase Doppler technique is briefly reviewed in the following section. The stochastic model for the response of irregular particles is given in Sec. 3. An experimental setup for measurement of MPD is described in the subsequent section, which also presents the measured MPDs and their moments for different type of irregular particles. In Sec. 5, measurements in a bench-top crystallizer are presented. The final section summarizes the progress so far and highlights the future plan of work.

* St. Paul, MN 55164, U.S.A.

**Minneapolis, MN 55455, U.S.A.

[†] Received March, 1998

2. Principle of Phase Doppler Technique

The phase Doppler system for sizing and velocimetry of particles is shown in **Fig. 1**. The output beam of an Argon-Ion laser is transmitted to the beam conditioning optics which is connected to the transmitting probe that focuses pairs of monochromatic beams, such that they cross at the focal point, where interference fringes are produced. As a particle crosses these fringes, it scatters light, which oscillates in time with a frequency that is proportional to the velocity component normal to the fringes. Laser beam pairs of different color are used to measure different components of velocity.

The oscillatory signals collected by the two receivers have the same frequency but are shifted in phase, which is used to measure the particle size. The signal conditioning electronics employ photomultipliers to convert the optical signals into electrical signals.

The output of the electronics is routed to a signal processor, which determines the frequency of the individual signals and phase shift between the phase Doppler signals. The modern processors are capable of transferring the measured data at a high speed to a computer where a software package reduces the results and displays them in real-time.

Fig. 1 Layout of a phase Doppler system

3. Stochastic Model for Response of Irregular Particles

A stochastic model is described by Naqwi [3] for the response of irregular particles. This model assumed that a single 'size' can always be associated with a particle. In the previous work, this size was the

particle volume as measured by a Coulter counter. The aerodynamic size, as measured by an Aerodynamic Particle Sizer, is used in the present work to represent the particle size.

Various irregular particles of the same size respond differently to a phase Doppler system as their features differ from each other at random and they cross the measuring volume with random orientations. In a hypothetical experiment, many particles with the same size D are measured by a phase Doppler system, or the same particle is made to cross the measuring volume many times with random orientations. The resulting phase distribution function $q(D, \Phi)$ represents the broadening of the phase Φ for a given size D . Function q will be referred to as *monosize phase distribution* (MPD) function. It is very narrow for small particles and becomes broader with increasing particle size. Using an appropriate optical configuration, MPD may be confined to a 360° range of phase shift, so as to avoid the ambiguity associated with the periodic nature of phase.

Using the concept of MPD, the probability density function $P(\Phi)$ for the phase shift signals generated by a polydisperse suspension, may be expressed as

$$P(\Phi) = \int_{D=D_{\min}}^{D_{\max}} q(D, \Phi) p(D) dD, \quad (1)$$

where $p(D)$ is the particle size distribution.

In Eq. (1), the functions p and q are assumed to satisfy the normalization condition, i.e. when they are integrated over the entire range of D and Φ respectively, the net result is 1. As a consequence, P also satisfies the normalization condition.

After calibrating a system, i.e. specifying the function q , Eq. (1) represents the relationship between the measured phase distribution $P(\Phi)$ and the unknown size distribution $p(D)$. The latter can be deduced if Eq. (1) is discretized as below:

$$\vec{P} = [Q] \vec{p} \Delta D, \quad (2)$$

where $\vec{P}$ and $\vec{p}$ are vectors with n elements of $P(\Phi)$ and $p(D)$ respectively; i.e. both the phase distribution and the size distribution are divided into n bins each. The n columns of matrix $[Q]$ – hereafter referred to as MPD matrix or calibration matrix – represent MPDs for n discrete particle sizes.

In order to solve Eq. (2), inverse of the above matrix is needed, so that

$$\vec{p} = \frac{[Q]^{-1} \vec{P}}{\Delta D}. \quad (3)$$

However, the above solution is numerically unstable.

As shown by Naqwi and Fandrey [1], inversion can be obtained by imposing linear constraints on the least squares solution to the above problem.

4. Measurement of Monosize Phase Distribution Function

The experimental setup for the measurements of MPD function is shown in **Figs. 1-3**. The laser beams passed through a window in the Aerodynamic Particle Sizer (APS) nozzle assembly (**Figs. 2 and 3**), where they were focused at the exit of a nozzle.

Fig. 2 Calibration setup

Fig. 3 APS nozzle assembly

These beams generated interference fringes with a spacing of 6.27 μm .

The nozzle assembly itself was connected to the APS which controlled the flow through the nozzle. The purpose of the APS and nozzle assembly was to accelerate particles so that a relationship between their velocity and aerodynamic size could be determined. The assembly was also connected to a particle generation instrument such as a small-scale powder disperser (TSI model 3433) or a fluidized bed aerosol generator (TSI model 3400).

The experimental procedure consisted of calibrating the relationship between velocity and aerodynamic size using spherical PSL particles of known size and then gathering and analyzing data with two samples of crystalline Alumina (Al_2O_3) powder of mean sizes 2.44 μm and 4.98 μm . Also measurements were taken with Arizona road dust, corn starch and quartz powder.

Immediately following the calibration of the system the two samples of Alumina particles were aerosolized using a Fluidized Bed Aerosol Generator. For each sample, a large set of data was collected. Only the data points with valid measurements for both velocity and phase were used in the analysis. Each data set was broken up into velocity bins which were then changed into an aerodynamic size using the APS calibration data.

The phase distributions and their moments are computed for bins with over 500 data points in them. Bins with less than 500 points were considered to be statistically unreliable and were not used for purposes of analysis. Typical phase distributions are shown in **Fig. 4**. These correspond to alumina and corn starch particles. Microscopic images of these particles are also included in **Fig. 4**.

As expected, MPDs broaden with increasing particle size. For similar aerodynamic sizes, the MPD of corn starch is broader than that of alumina. These data may be indicative of a general trend; i.e. MPDs of particles with external irregularities would tend to be sharp-peaked like a Laplace distribution and those of smooth particles with internal inhomogeneities would be Gaussian-like.

The data in **Fig. 4** have clearly shown that the size information can be obtained with phase shift measurements near backscatter. They also show that the mean values of MPD functions are nearly zero. Also, MPDs are symmetric; i.e. the odd moments of phase distribution are zero. The particle size information is contained in the even moments.

Fig. 4 Measured MPDs for Alumina and corn starch

Figure 5 show the relationship between the aerodynamic particle size and the first three even moments of the alumina, corn starch and test dust particles. The following parameters are plotted:

$$\left(\frac{1}{N} \sum_{i=1}^N \Phi_i^n \right)^{1/n} = \left(\int_{-180^\circ}^{+180^\circ} \Phi^n q(D, \Phi) d\Phi \right)^{1/n}, \quad (4)$$

where $n = 2, 4 \text{ \& } 6$.

The parameter Φ_i represents the individual phase shift signals for a given particle size, so its moment can be expressed as an integral of the corresponding MPD function.

Good linear fits with the line passing through the origin are obtained between the above parameter and the aerodynamic particle size D for all the samples considered. The slopes of the lines are comparable for alumina and test dust as these particles have similar morphology. Phase distributions are broader for corn starch particles. Mathematically, the linear fits of Fig. 5 can be expressed as

$$\int_{-180^\circ}^{+180^\circ} \Phi^n q(D, \Phi) d\Phi = f_n D^n, \quad (5)$$

where f_n is the proportionality constant for the n th moment.

The correlation in Eq. (5) applies to monosize particles. An equivalent of this correlation for a polydisperse suspension can be obtained by integrating Eq. (5) over the entire particle size range; i.e.,

$$\int_{D_{\min}}^{D_{\max}} \int_{-180^\circ}^{+180^\circ} \Phi^n q(D, \Phi) d\Phi p(D) dD = f_n \int_{D_{\min}}^{D_{\max}} D^n p(D) dD. \quad (6)$$

Rearranging the order of integration on the left-hand side of Eq. (6) and invoking Eq. (1),

$$\int_{-180^\circ}^{+180^\circ} \Phi^n P(\Phi) d\Phi = f_n \int_{D_{\min}}^{D_{\max}} D^n p(D) dD. \quad (7)$$

Alternatively,

$$\frac{1}{N} \sum_{j=1}^N \Phi_j^n = f_n \frac{1}{M} \sum_{k=1}^M D_k^n, \quad (8)$$

where Φ_j is one of the N phase shift signals generated by a polydisperse suspension, and D_k is the size of one of the M particles in that suspension. The above

Fig. 5 Higher moments of phase distribution

equation shows that the n th moment of the measured phase distribution is proportional to the n th moment of the particle size distribution. In other words, the correlations shown in Fig. 5 imply that if the second, fourth and sixth moments of phase distribution are measured on a polydisperse suspension, then the mean, square-mean and cube-mean of D^2 can be determined. These moments of D^2 can be reduced to mean, standard deviation and skewness of D^2 distribution. If it is known that D^2 (or D) has a mono-modal distribution, then the first three moment would allow to reconstruct the distribution fairly well, without resorting to an elaborate inversion scheme, as discussed by Naqwi and Fandrey [1].

5. Measurements in a Crystallizer

Measurements were conducted in a model batch crystallizer with controlled-cooling as shown in Fig. 6. The design and use of such a crystallizer has been described by Brown et al. [4]. The rate of cooling and hence the degree of supersaturation can be controlled using external circulation of a coolant by means of a bath circulator that can be programmed to

Fig. 6 Schematic diagram of the batch crystallizer

cool at any pre-planned linear rate. The crystallizer consists of a 6-liter cylindrical, jacketed glass vessel with a motor-driven agitator that ensures small and uniform crystals and reduced run-time.

The optical system used for the measurements was similar to the one illustrated in Fig. 1. The fringe spacing in the measuring volume was $46.3 \mu\text{m}$ and there were about 10 fringes in the measuring volume. Measurements could be taken as much as 10 mm inside the crystallization vessel as, under the conditions of complete crystallization, the crystal concentration became so high that the laser beams did not penetrate farther.

Typical signals are shown in Fig. 7. Each plot in this figure contains two curves – depicted by the solid line and the dotted line – representing the bursts collected by the two receivers of the phase Doppler system. About 80% of signal pairs had comparable amplitudes as shown in the top plot of Fig. 7. Also the phase shift was nearly constant along the burst. This result is in disagreement with the results of similar tests done by Onofri [5].

In the experimental setup of Onofri, the fringe spacing was about $12 \mu\text{m}$ and the irregular metallic particles were $400\text{--}500 \mu\text{m}$ in size, i.e. about 40 times larger than the fringe spacing. On the other hand, the ratio of particle size to fringe spacing was confined to

Fig. 7 Microscopic views of burst pairs with probability of occurrence of 80%, 15% and 5% respectively

about 4 in the present experiments. This difference between the two experimental settings explains the discrepancy in the phase behavior. Earlier work by Naqwi [3] has shown that a meaningful relationship between phase response and particle size is obtained only if the largest particle size does not exceed 4 times the fringe spacing. Direct examination of the signals suggests that constancy of phase shift within a burst is a pre-condition for the statistical behavior of the phase shift to be sensitive to particle size.

In-situ measurements in a crystallizer were conducted with a solution of lysine monohydrochloride in

Fig. 8 Evolution of phase distribution and mean size during solution cooling.

a mixture of methanol and water. Elongated rod-like crystals and rounded crystals were produced with a 1:1 and a 3:2 weight-by-weight ratio of water to methanol respectively. The histograms of signal phase shift, measured at different temperatures are shown in **Fig. 8**. The phase histogram broadens with the decreasing temperature, i.e. with the growth of the crystals. Standard deviation of the phase shift is converted to mean particle size using an estimated conversion factor. The final crystal size is comparable to the SEM micrograph shown in **Fig. 9**.

According to **Fig. 8**, mean particle size appears to be invariant over a wide range of initial temperatures (from 35°C to 15°C). The measured standard deviation over this range was about 10°. The actual standard deviation may have increased from a very small value to about 10°, i.e. the measurement resolution appears to be limited to 10°.

Figure 10 shows the correlation between the velocity and the standard deviation of phase shift for rounded particles. These curves represent size-velocity correlations and indicate that the fastest upward motion (>0.6 m/s) is clearly exhibited by smaller crystals.

Fig. 9 SEM micrograph of the rounded crystals

Fig. 10 Size-velocity correlations for the rounded crystals

For intermediate temperatures, large values of standard deviation occur only over a narrow range of velocity; i.e. crystals appear to grow within streams that flow fairly uniformly and streams wander around, so they do not remain in the phase Doppler measuring volume all the time.

6. Conclusions

This work has clearly demonstrated that the phase Doppler technique can be used for in-situ measurement of crystal size and velocity, while collecting data in backscatter. Experimental studies show a linear relationship between the standard deviation of the phase shift and the aerodynamic particle size. Also the fourth and sixth roots of the fourth and sixth moments of the phase distribution respectively are related linearly to the aerodynamics particle size.

These relationships hold for irregular particles of diverse structures and morphology.

The above relationships allow a convenient means to convert the measured phase distribution into a size distribution. However, the present hardware limits the dynamic range of particle size to about 5:1. The variance of the phase shift is determined not only by the optical signals but also by the random time delay in the photomultipliers that are used to convert the optical signals into electronic signals.

Although the random delay variations are small, i.e. limited to ± 2 ns, they cause large phase errors as the in-coming optical signals have a 40 MHz carrier frequency that is needed to determine the direction of motion of the crystals. The period of the optical signals is about 25 ns, so the standard deviation of random delay variations is about 10° . Hence, the instrument is not sensitive to small crystals whose standard deviation for the phase shift is smaller than 10° . Also there is an upper limit of about 50° for the standard deviation of the largest measurable particle. At the upper limit, the entire phase shift range of 360° is filled and phase signals begin to wrap around for larger particles.

Given the above upper and lower limits on the standard deviation of the phase shift, the measurable particle size range is limited to 5:1.

The above limitation can be overcome by reducing the carrier frequency. The electronic delay problem can be completely eliminated by using a frequency of 1 MHz, instead of 40 MHz. In the present hardware, one of the two laser beams is shifted by 40 MHz using an acousto-optic modulator (AOM). Although AOM cannot be operated at a much lower frequency, two such devices can be used to shift both the beams by say 40 and 39 MHz, so the effective shift between the beams would be 1 MHz. The above option will be evaluated in the future work. It is expected that a 50:1 dynamic range of particle size can be covered with appropriate hardware.

Acknowledgment

The authors are grateful to the National Institute of General Medical Sciences of USA for the financial support of this work. Program Director: Dr. Peter Preusch.

References

- 1) Naqwi A. and Fandrey C.: Phase Doppler measurements of irregular particles and their inversion to velocity-resolved size distributions, *Powder Handling & Processing* 9 (1997) 45–51
- 2) Bottlinger M. and Umhauer H.: Single particle light scattering size analysis: quantification and elimination of the effect of particle shape and structure, *Part. Part. Syst. Charact.* 6 (1989) 100–109
- 3) Naqwi A.: Sizing of irregular particles using a phase Doppler system, *Part. Part. Syst. Charact.* 13 (1996) 343–349
- 4) Brown R., York P. and MacLaine J. Q.: The role of crystallization conditions in the control of final product character, *Pharm. Res.* 7 (1990) S-107
- 5) Onofri, F.: Prise en compte de la dimension finie des faisceaux d'éclairage en granulométrie optique: Anémométrie Phase Doppler – Diagnostics des Milieux Diphasiques, Doctoral Thesis, Faculty of Science, University of Rouen (1995).

Author's short biography

Amir A. Naqwi

Dr. Naqwi received his Ph. D. in Mechanical Engineering from Stanford University in 1987 and has worked for several years at the University of Erlangen, Germany. He is author of numerous publications and patents pertaining to laser instrumentation, especially instrumentation for diagnostics of particulate flows. He is currently the Advanced Products Manager in Laser Diagnostics Division of TSI Incorporated and serves on several scientific committees, including the Advisory Board of the journal *Particle and Particle System Characterization*.

Chris W. Fandrey

Chris Fandrey is a graduate of the University of Minnesota in Mechanical Engineering and has worked in the Particle Technology Laboratory there for over three years. He has been employed at TSI Incorporated, initially as an engineering intern, and now as a Research Engineer. He is the author of several publications on the phase Doppler technique for sizing irregular particles and glass fibers.

Rebanta Bandyopadhyay

Rebanta Bandyopadhyay is Research Investigator in the Advanced Candidates Liquids Area at the Bristol-Myers Squibb Pharmaceutical Research Institute in New Brunswick, NJ. He obtained B. Pharm. (first class, honors) in 1991 from Jadavpur University, Calcutta, India, and M. S. in Pharmaceutical Sciences from the University of Mississippi in 1993. In 1998, he graduated from the University of Minnesota with a Ph. D. in Pharmaceutics under the supervision of Professor David J. W. Grant. The focus of his research was the influence of crystal properties on the tableting performance of lysine derivatives. The influences of the crystallization conditions on the hydration state and the morphology of the recrystallized phase were also studied. Rebanta Bandyopadhyay received the Best Poster Award at the Midwest Meeting of the American Association of Pharmaceutical Scientists, held at Chicago in May, 1997, for his work on the influence of thermodynamic activity of water on the hydration state and the crystal habit of L-lysine monohydrochloride. During his graduate studies, Rebanta Bandyopadhyay held a research assistantship at the University of Minnesota and received a Honors Fellowship from the University of Mississippi. He also received the Emami Award from the Indian Pharmaceutical Association for his performance in the undergraduate program. Memberships include AAPS, Rho Chi, Phi Kappa Phi, and Sigma Xi.

Author's short biography

David J.W. Grant

David Grant is Professor of Pharmaceutics, College of Pharmacy, University of Minnesota, Minneapolis. He is a graduate of Oxford University, UK: B.A. in Chemistry in 1960; D.Phil. in Physical Chemistry in 1963; M.A. (Keble College, 1963); and D.Sc. for recognized published research on the physical chemistry of pharmaceutical systems (October 1990). He has held academic appointments at the University College of Sierra Leone (then affiliated to the University of Durham, UK), at the University of Nottingham, UK, and at the University of Toronto, Canada. In 1988, he was appointed to the William and Mildred Peters Chair in Pharmaceutics, University of Minnesota. Since January 1994 David Grant has served as Associate Editor of the Journal of Pharmaceutical Sciences. He is also a member of the Editorial Advisory Board of the journals "Pharmaceutical Development and Technology" and "Kona Powder and Particle". In April 1998 he was elected to the Board of Directors of Hosokawa Micron International, Inc. David Grant has worked on bacterial drug resistance and metabolism and, since 1972, on the physical chemistry of pharmaceuticals in which he is co-author of an undergraduate text. In 1978 and 1980 he worked on the intermolecular interactions of drugs in solution at the University of Kansas in the laboratory of the late Dr. Takeru Higachi, with whom he is the co-author of a book on the solubility behavior of organic compounds. Since 1978 David Grant has been studying the crystal engineering of drugs and the properties of the solid state, particularly the thermodynamics, solvation, polymorphism, crystallization, compaction, solubility, and dissolution of drugs. His recent work has focused on doping, hydration, hydrogen bonding, and chirality in the solid state. He is the author or co-author of over 120 scientific articles and reviews and serves as a consultant for numerous companies that manufacture fine chemicals and pharmaceuticals. David Grant is a Fellow of AAPS and the Royal Society of Chemistry (Chartered Chemist, UK). Memberships also include AAAS, AACP, ACA, ACS, AIChE, APhA and Rho Chi.