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Optimization of Dry Powder Particle Size Analysis

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Abstract:
Development of an advanced dry powder sampling system for laser diffraction particle size analysis was undertaken to improve the availability of this measurement technique for a wide range of materials. Areas for improved performance included automating sample feeding, increasing available dispersion force for highly cohesive powders, broadening the range of sample types that can be measured by the system, and optimizing airflow through the measurement cell to minimize system cleaning. Confirmation testing was performed with a variety of materials including the pharmaceutical excipients magnesium stearate and microcrystalline cellulose to verify these improvements. USP <429>, Light Diffraction Measurement of Particle Size, guidelines were used to test system reproducibility and system accuracy.

Introduction

Laser diffraction has established itself as the leading method of particle size analysis for a wide range of applications. Speed, reproducibility, accuracy, and ease of use make it the most popular method for many reasons.

The technique measures light scattered from the particle surface. The angle of this scattered light depends primarily on the size of the individual particles. The optical system design includes the light source(s), measurement cell, and an array of detectors to measure the intensity of light over the angular range (see Figure 1 below). Further details of the basic technique have been covered in detail in a number of documents. [1, 2]

Figure 1

Historical Development

The earliest laser diffraction particle size analyzers (PSA) had limited measurement range, resolution, and flexibility. Historically the sample would be presented to the measurement zone in a fluid dispersion. This approach has the widest range of applicability for suspensions, emulsions, and dry powder samples that could be analyzed as a dispersion. Dispersion in a fluid also allows the use of alternate fluids that can wet the particle surface, surfactants to aid in dispersion, and mechanical energy such as ultrasonic treatment to disperse agglomerates [1, 3, 4]. With the ongoing development of measurement optics and algorithm, the size range has been extended on current systems such as the HORIBA *Partica* LA-960 that can measure 0.01-5,000 microns.

After the introduction of the laser diffraction technique new applications were encountered where measurement of a powder in the dry state would be preferred for a number of reasons including:

- Water soluble materials requiring toxic or expensive organic solvents for dispersion
- Limiting waste disposal of large quantities of solvent
- The desire to measure some powders in their natural state

Manufacturers of laser diffraction particle size analyzers developed sampling systems for dry powders in response to these requirements. The capabilities of these sampling systems have been highly variable, with performance depending on both the size range and cohesive nature of the sample. It is now estimated that approximately one third of the total market for laser diffraction particle size analyzers is devoted to dry powder analysis [6]. The importance of this market makes it a primary goal for LD PSA manufacturers.

Design Requirements for Dry Powder Feeder

The initial design requirements for the dry powder feeder (DPF) system described in this article included the requirement to handle a variety of sample types including:

- Wide range of particle sizes – ranging from 0.1 to 5,000 µm
- Wide range of sample types and materials
- Powders that may be free-flowing, agglomerated or sticky
- Quantities from a few micrograms to several grams

- Ability to measure either primary particle or agglomerate size
- Variety of particle strength – hard particles to friable crystals

In addition to the performance requirements, the obvious commercial considerations had to be included. Pricing should be in line with the alternative sample dispersion systems offered. The system must be well integrated with the base analyzer, economic to produce, easy to use and automated.

Engineering Design Plan

The DPF system was separated into three primary functional sections for purposes of evaluation of alternative engineering options: sample feeder, disperser/ejector, and cell/exhaust. These three stages essentially transport the sample into the system, disperse the powder using variable air pressure, and measure the scattered light as the material passes through the cell. Although these individual components naturally interact with each other, they can be evaluated as independent functions within the analysis system.

Sample Feeding

The sample feeding function regulates the flow of sample material into the system. The most common feeding mechanism for dry powder feeders is the vibratory feeder. Sample is loaded in a trough and an oscillating electro-magnet shakes the trough to move the particles forward. One of the key requirements for reproducible results is a constant mass flow rate of the powder through the cell during measurement. The sample must be fed into the analyzer at a controlled rate to provide the optimum conditions for the dispersion system and for the light scattering experiment. One key limitation of older systems was difficulty in maintaining consistent sample feed rate during the measurement, resulting in high variability between measurements. Reasons for this include the fact that feed rate is affected by the changing volume of powder on the vibrating tray and size segregation that naturally occurs due to vibration.

This limitation was overcome through automatic control of the vibration rate based on continuous readings of the sample concentration during the measurement. Concentration is measured as a percent of the incident light intensity detected while the sample passes through the cell (transmission, or T %). For example, a 95 T% indicates that the incident light level has been reduced by 5% due to the presence of

the sample in the flow cell. A fast-feedback control loop measures T% continuously and adjusts the vibration rate to keep the concentration in the optimum range for the measurement. The data shown in Figure 2 below shows the improved consistency of T% by feeding the same material with either a fixed speed or automatic control.
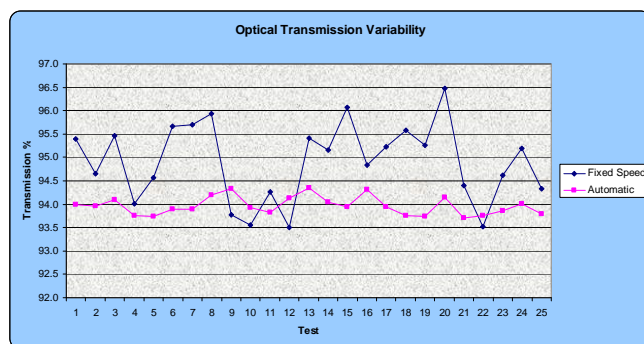

Figure 2

Enhanced automation provides additional benefits including ease of use and the ability to smoothly transfer methods between laboratories. Additional automatic control features including time limits, start and stop on a given T%, and the ability to measure until the tray is empty all facilitate the collection of accurate, reproducible data for a wide range of powder types and sample volumes.

Feeding Aids

Applications experience with hundreds of different powders provided insight into additional developments to improve sample presentation to the system. Design goals of constant flow rate and sample conditioning for pre-dispersion led to unique mechanical devices provided as options for the feeding system.

Improved mass flow rate of the sample was achieved through the use of flow restrictors (or dams) and by adjusting the height of the hopper feeding the powder to the flow trough. Additional flow improvements came by minimizing the flow of agglomerated material (or clumps) into the measurement system. The mechanical energy from vibration of the feeder itself can provide some level of pre-dispersion of clumps, but even with automatic
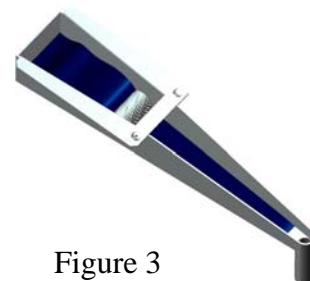

Figure 3

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control of the flow rate it helps to minimize the transfer of agglomerated material into the dispersion nozzle. Feeding agglomerated material into the dispersion nozzle may overload the capabilities of the system and lead to poor dispersion of the sample and erratic results. After evaluating a number of options the use of screens or ball bearings were rejected due to concerns with cross contamination and possible comminution of fragile particles. Instead, a combination of a roller or brush can be placed in the trough (see Figure 3) to break up clumps and disperse loose agglomerates during feeding while not damaging primary particles.

Sample Dispersion

Once a consistent, suitable sample flow rate is achieved the sample must then experience the appropriate level of dispersion required for proper analysis. In most cases, the desire is to reduce agglomerates to the primary particle size without breaking individual particles. The function of the disperser/ejector is to disperse agglomerates and transport the sample stream to measurement zone. The sample disperser must de-agglomerate a wide range of materials but maintain the flexibility to not damage friable materials such as crystalline pharmaceuticals.

There are three mechanisms used to disperse particles in a dry powder feeder as shown in Figure 4 below [from 1].

a) Velocity gradients caused by shear stress:

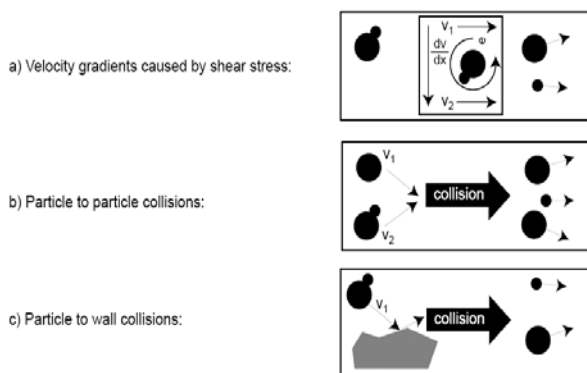b) Particle to particle collisions:

c) Particle to wall collisions:

Figure 4

Dispersion ability in a given design can be improved by simply increasing the air pressure or by designing the sample flow in a tortuous path where the particle stream impacts the wall of the system. Particle to wall collisions can easily cause particle breakage and system wear, so a cell was designed to proved a straight sample flow path with no physical impact of

the particles. Rather than just increasing the turbulence level, a dispersion nozzle was designed that can achieve supersonic speeds through the nozzle. At subsonic speeds, air molecules are "warned" about the incoming obstacle by pressure waves transmitted upstream from the agglomerate with the speed M1. By avoiding the agglomerate, incoming air molecules are producing new pressure waves continuing the process. These waves are the main source of acceleration and dispersion of agglomerates.
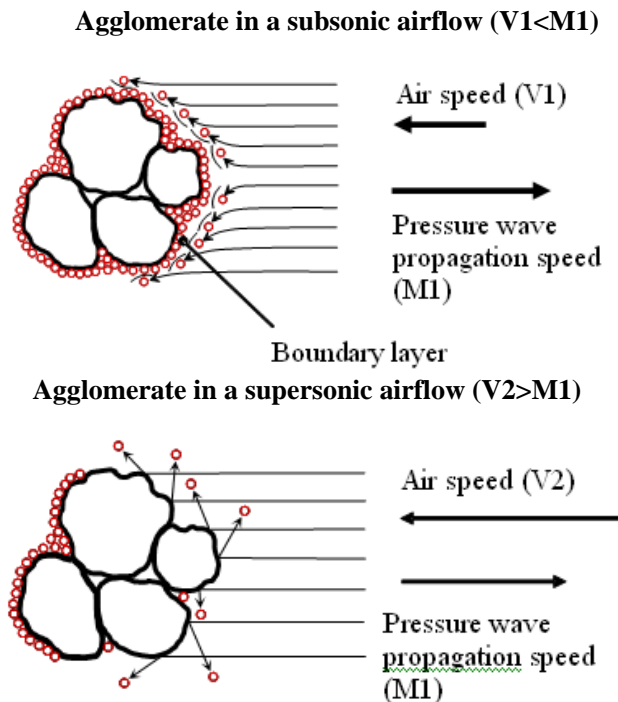
Agglomerate in a subsonic airflow (V1<M1)

Air speed (V1)

Pressure wave propagation speed (M1)

Boundary layer

Agglomerate in a supersonic airflow (V2>M1)

Air speed (V2)

Pressure wave propagation speed (M1)

Figure 5

Due to the high air speed of supersonic flow (>M1), the pressure waves can not propagate upstream. The upstream side of the boundary layer is washed away and the agglomerated particles are directly hit by the incoming air molecules. This effect is potentially far more effective than the subsonic dispersion. Care must be taken in case of fragile materials to avoid damaging the original particles. The ability to reduce air pressure allows for the dispersive force to be adjusted for each unique sample requirements.

The physical design of the flow cell seen in Figure 6 arranges the pressurized air is in a concentric ring around the sample stream. This contains the sample stream, reduces system contamination, eliminates particle-wall collisions, and affects the full sample stream equally. There is little or no contact of the sample particles with the disperser parts. This design

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minimizes nozzle clogging and maximizes the ability to treat fragile particles gently.

In evaluating the design, it became clear that one system nozzle would not be able to properly disperse fine agglomerates and also provide the higher mass flow rates required for larger particle. A smaller nozzle will allow dispersion of very fine agglomerates, but can clog with larger particles. A larger nozzle will allow measurement of coarser particles, but will not have the ultimate dispersive power. Three different nozzles were finally included into the design to accommodate the broadest range of samples possible. While the need to select a different nozzle to optimize conditions for a particular sample might be an extra step, the significantly greater performance this makes possible was decided to be a valuable trade-off. Each nozzle has a broad range of capabilities, so most applications will be able to use a single nozzle for a wide range of sample types or grades.
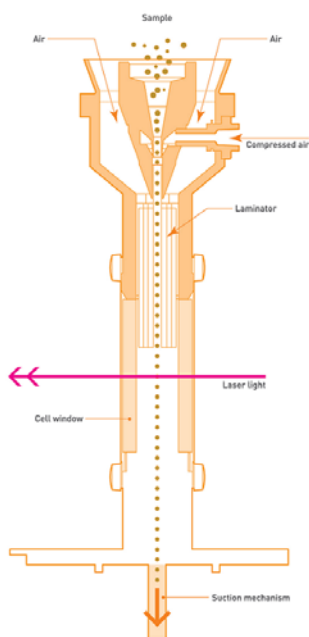

Figure 6

The following example in Figure 7 shows coffee measured dry. This is a difficult sample to feed because of its oily, sticky nature. The large particle size is easy to measure, but the larger diameter nozzle allows for routine measurements without clogging.
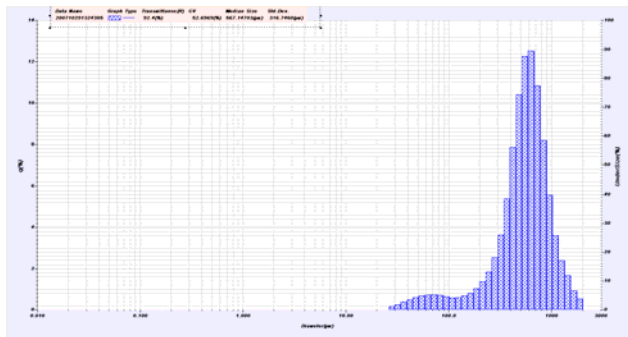

Figure 7

While this nozzle design covers a wide range of materials, the large opening and clearance limits the maximum dispersive power. A smaller diameter nozzle can be exchanged for finer and more cohesive powder, such as the titanium dioxide measurement data shown in Figure 8. Note the ability to measure the tail of the distribution down to 0.1 µm.
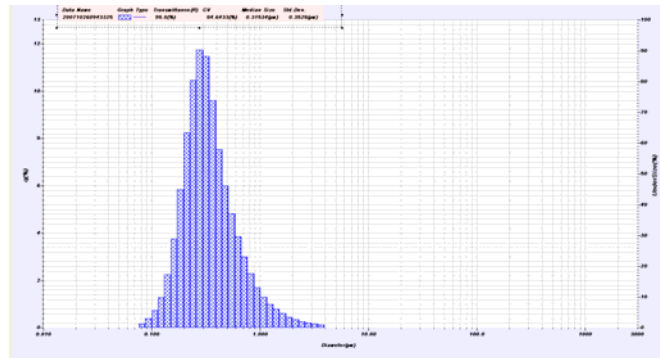

Figure 8

The ability of the system to measure such small particle size materials is a significant advance in capabilities over previously available systems. With a median size of just over 300 nm, this material can be a challenge to disperse even in a wet system. This ability opens up new applications where dry analysis would have been preferred, but dispersion systems were not previously able to properly prepare the sample.

Some powders require no dispersion energy whatsoever in order to measure the size of individual particles. For these applications, an alternate sample cell system was designed with a wide, constant flow path through the cell. A low level of vacuum is applied for sample evacuation and to keep sample flow constant through the measurement cell. This can be beneficial where the user wants to measure the size of a loosely agglomerated material such as powdered milk. The data shown in Figure 9 was collected in this cell to measure steel ball bearings showing the ability of the system to handle very large particles.
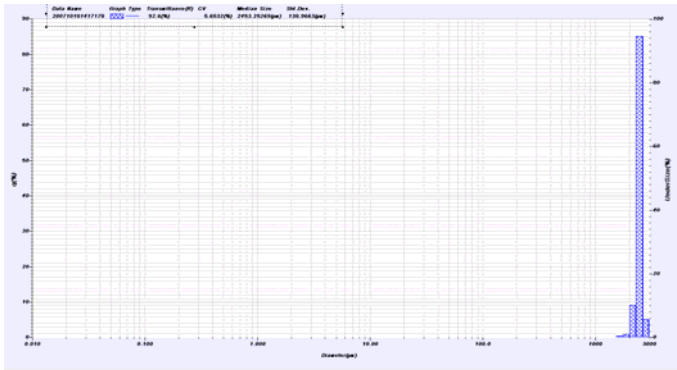
Figure 9

Sample Cell

The sample cell portion of the system transports the dispersed particle stream to the measurement zone and out of the system. This may seem to be an easy task, but a number of variables can have an important effect on total system performance. Early systems had an open measurement chamber with the vacuum simply pulling through the chamber. This is simple and relatively efficient, but relies on a well-balanced vacuum level to match the sample stream being fed in. An open system also allows for velocity biasing, where the larger particles continue to pass through the measurement zone at a high velocity. The smaller, lower-inertia particles slow down in the open system, residing longer in the measurement zone, and being relatively over-reported. In cases where the sample is toxic, an open cell can also have a significant health risk.

The sample cell described in this article uses a closed system for the reasons stated above and took considerable pains to minimize the cell window contamination to reduce maintenance requirements. The sample stream through the cell is surrounded by sheath air fed from the top of the cell through laminators (see Figure 6 above) to maintain parallel, laminar airflow surrounding the sample stream. This limits the turbulence that allows particles to impact the cell windows causing contamination. The continuation of the flow path straight through the bottom of the cell maintains the laminar flow long after the effects of any turbulence would affect measurement.

The balance of airflow through the system is another factor that has a significant effect on total system performance. Setting the vacuum to maximum produces turbulence in the cell, actually reducing airflow and increasing contamination rate. Careful experiments with multiple pressure transducers at different points of the cell found an optimum vacuum-
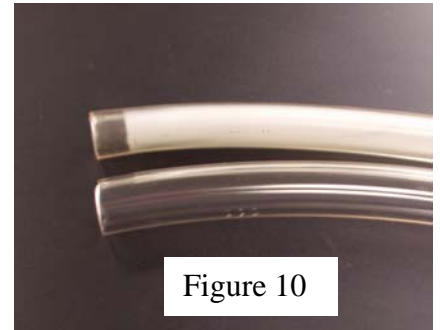
to-pressure matching. The final design includes a vacuum sensor that automatically adjusts vacuum speed to maintain optimum conditions.

Flow Path

The overall flow path was part of the design of the basic instrument. Previous systems had sharp turns in the flow path, which creates turbulence and leads to sample contamination of the system and inhibits the dispersion process. Other systems use a tube to transport the sample after dispersion from the sampling system to the optical chamber.

Figure 10

These tube-feed systems could lead to contamination and may have issues with sample segregation. Figure 10 compares a used feed tube to a clean piece of tubing, showing the amount of material that can be trapped in this type of system and not properly analyzed.

Mounting the dry feeder system on top of the analyzer to allow for a vertical sample flow path has numerous advantages besides eliminating the need for feed tubes. The optical chamber arrangement allows for a vertical flow path of the sample stream, preventing even the largest dense materials from segregating in the system. In addition, the short distance from the dispersion nozzle to the measurement zone reduces any possibility of particles re-agglomerating before measurement. Having the DPF mounted on top of the optical bench also reduces the laboratory footprint, optimizes the use of valuable bench space.

USP <429> Accuracy and Reproducibility Testing

The new USP <429> LIGHT DIFFRACTION MEASUREMENT OF PARTICLE SIZE test provides guidelines for verifying system accuracy and checking sample/method reproducibility. The new DPF system was used in a series of tests as described in USP <429> to confirm suitability for use in the pharmaceutical industry. A series of polydisperse standards were analyzed using the new system to test both accuracy and reproducibility. The USP <429> verification test requires three independent measurements of the standard, calculate the mean and coefficient of variation (COV) for the three

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measurements at the D10, D50, and D90, and then meet the following pass/fail criteria:

Accuracy: The mean values must be within 3% at the D50, and within 5% at the D10 and D90 of the certified values.

Reproducibility: the COV at the D50 must be less than 3%, and less than 5% at the D10 and D90.

Accuracy results for a polydisperse standard are shown below:

PS202 (3-30µm)	D10	D50	D90
Standard Value (µm)	9.14	13.43	20.34
Uncertainty (µm)	0.86	0.86	1.44
ISO standard error	5%	3%	5%
Lower limit (µm)	7.866	12.193	17.955
Measured Result (µm)	9.721	13.916	18.959
Upper Limit (µm)	10.5	14.719	22.869
COV %	0.832	0.231	1.24

Several real-world samples were analyzed as dry powders to test system reproducibility on samples commonly encountered in the pharmaceutical industry. USP <429> guidelines for reproducibility of samples measured following this procedure are shown below:

Reproducibility: Measure at least three times; calculate the mean and COV values at the D10, D50, and D90. The COV at the D50 must be less than 10%, and less than 15% at the D10 and D90. Note: these values can double if the D50 is less than 10 µm.

Both magnesium stearate and microcrystalline cellulose were analyzed as dry powders following the USP <429> procedures and the results are shown in Figures 11 and 12. All results fall comfortably within the USP <429> specifications with COV values ranging from .242 - 1.53%. The USP <429> calculations have been built into the system software to facilitate use in the pharmaceutical industry.
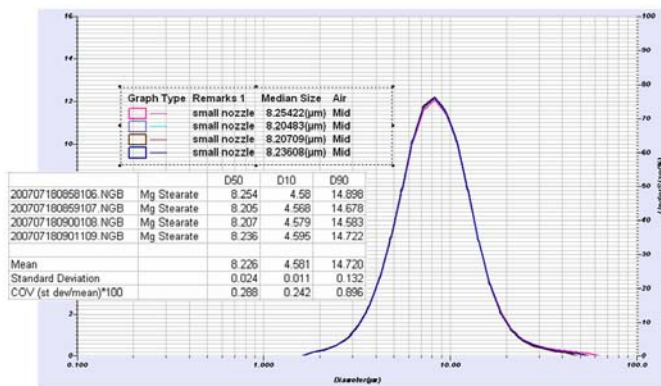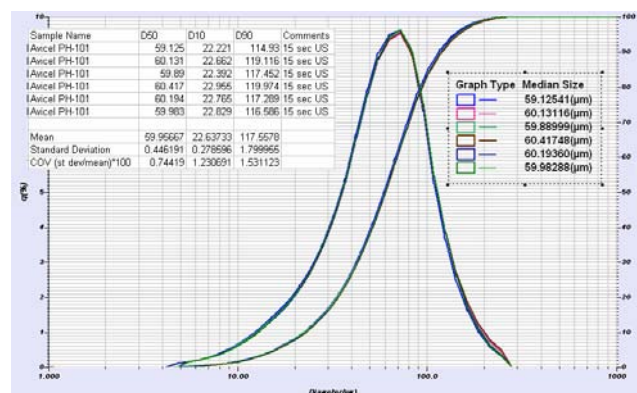

Figure 11

Figure 12

Conclusions

There are many factors to consider when designing modern analytical instruments for the variety of applications they will be used for. Careful attention to the needs of users and industry standards has resulted in a dry powder feeder system that has eliminated many of the impediments to measuring dry powders with laser diffraction particle size analyzers. The final system is capable of meeting USP <429> criteria for system accuracy and reproducibility.

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