technical note

Importance of Proper Dry Sample Dispersion Conditions for the Morphologi® G3

Introduction

When characterizing particles in a dry powder using image analysis, it is extremely important to properly disperse the particles. The ideal dispersion will contain no touching particles and the particle density should be the same across the entire sample area. There should also be no gradients in the size distribution across the sample dispersion area, especially if a sub-region will be selected for imaging. To accomplish these goals, it is important to use the proper sample volume and a dispersion method that uniformly disperses particle.

The dispersion method should be gentle enough to ensure no breakage of primary particles. In addition, if the extent of agglomeration is of interest, the method should also be gentle enough to leave the agglomerates intact. On the other hand, if only the primary particle size and shape is of interest, it is ideal to break up agglomerates into undamaged primary particles.

Another concern with dry particle dispersions is toxicity. Most methods of dispersing dry particles can result in a release of particles into the atmosphere, especially if the particle size is small. Therefore, it is desirable to have some way of containing the sample to avoid exposure to the operator.

Malvern Morphologi G3S

The Malvern Morphologi G3S uses an integrated Sample Dispersion Unit (SDU). This unit uses positive pressure to disperse the sample, but the pressure is applied indirectly to the particles. The powder sample is placed in a holder and held by a thin metal foil. Another metal foil is placed in the top of the holder. The air pressure is then used to break the foil and the resulting turbulence disperses the samples onto a glass plate. The particles adopt their most mechanically stable orientation, which generally means that the largest face is oriented toward the camera.

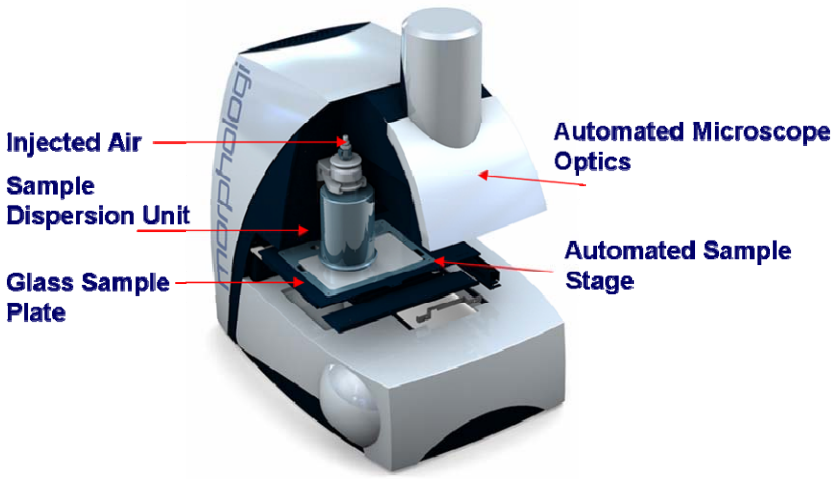

Figure 1: Morphologi G3S with integrated sample dispersion unit (SDU)

The indirect application of pressure in the Morphologi G3S results in a gentle particle dispersion, reducing the likelihood of damaging particles. This can be especially useful for fragile crystalline samples.

Agglomerated samples that need to be separated into their primary particles require a different set of conditions. To this effect, the volume of air inserted in the sample chamber can be increased by an increase of air pressure and injection time. These conditions increase the turbulence and thereby help break aggregates. Another common dispersion method involves driving a powder into a surface, such as a metal ball, to disperse the particles. These collision-based dispersion methods are likely to cause damage to fragile particles. However, a collision method could be advantageous for robust agglomerated particles that are difficult to break up.

As shown in Figure 1, the SDU consists of an enclosed sealed chamber. This is advantageous when handling toxic samples or samples of unknown toxicity. External collision-based methods can increase the exposure risk due to creation of airborne particles. Also, since the SDU is enclosed, the entire sample is dispersed onto the plate, reducing sample waste and minimizing exposure.

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The fact the SDU is integrated into the Morphologi G3S increases the reproducibility of the dispersions. The integration of the dispersion unit allows for inclusion of the dispersion conditions in the standard operating procedure (SOP). This reduces the operator variability. In addition, measuring spoons with known volumes are included with the G3S, further decreasing operator variability.

Comparison of Results

To illustrate the difference between the different dispersion methods, MES (4-Morpholineethansulfonic acid monohydrate) was analyzed using the Morphologi G3S following dispersion with the integrated SDU and a method that disperses by a collision with a metal ball. MES is a good test of the dispersion methods because it is a polydisperse sample that contains many large fragile crystals.

For the SDU, samples were dispersed using two different conditions. A sample volume of 15 mm^3 was dispersed with a pressure of 0.8 bar using 6 µm carrier foils and 4.0 bar using 25 µm carrier foils. For the collision-based method, a similar sample volume was dispersed using a pressure of 1 bar. Overall, the amount of energy applied to the particles increases in the order: SDU (0.8 bar) < SDU (4.0 bar) < collision.

The remaining measurement parameters were identical for both preparation methods. The measurements were performed using 2.5X objective, which covers a nominal particle size range of 13 to 1000 µm.

Plots of the number-weighted circle equivalent (CE) diameter distributions using the three dispersion methods are shown in Figure 2. The CE diameter is defined as the diameter of a circle with the equivalent area as the particle image.

There is a significant difference between the CE diameter distributions for the different dispersions. The sample prepared with the SDU using 0.8 bar appears to be much larger than the other two dispersions and the collision-based method results in the smallest particle size. Since the sample volume, the material and imaging SOP were identical for all three measurements, particle breakage is a likely origin of the particle size differences.

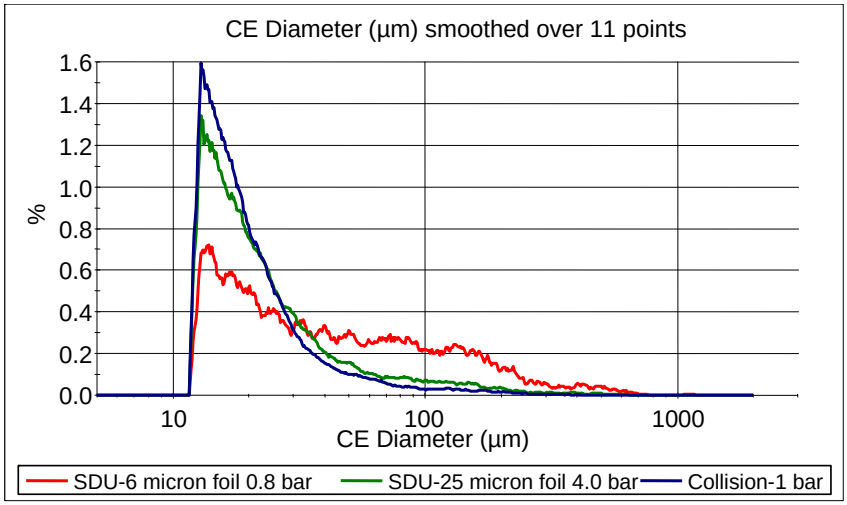

Figure 2: Number-weighted CE diameter distributions for three dispersions of a crystalline sample.

Differences are also seen in the shape distributions. The aspect ratio (width/length) distributions are shown in Figure 3.

Dispersion with the integrated SDU results in more particles with a low aspect ratio. In addition, the 0.8 bar SDU dispersion results in more particles with a low aspect ratio than the 4.0 bar SDU dispersion. These

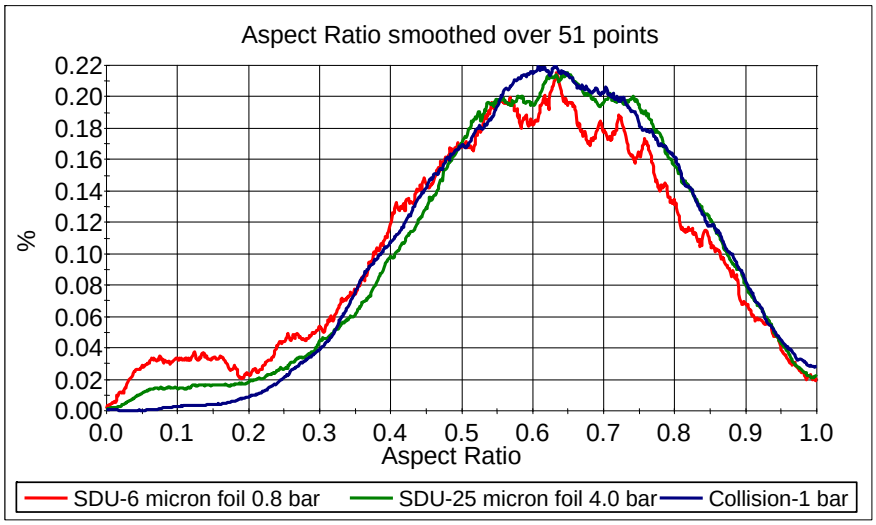

Figure 3: Number-weighted aspect ratio distributions for the three dispersions of a crystalline sample.

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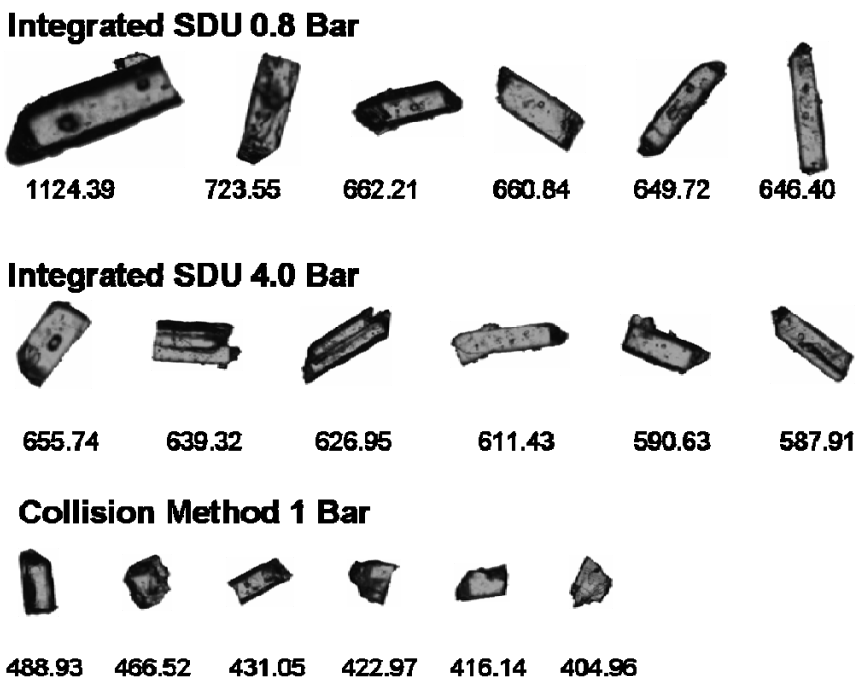

Figure 4: Largest six particle images from all three dispersions. The CE diameters (in µm) are included below each particle image**.**

results are consistent with particle breakage in the more energetic dispersions.

Since the individual particle images are stored, it is possible to examine the particles images to help determine the origin of the differences in results.

Shown in Figure 4 are the largest six particle images from all three dispersions sorted by CE diameter in descending order. The CE diameters (in µm) are included below each particle image. The large particles appear crystalline, suggesting that they may be somewhat fragile, and they do not consist of agglomerates of smaller particles. One interesting feature is that as the energy applied to the particles increases, the number of particles with a CE diameter > 500 microns decreases and the total number of particles increases. This is consistent with particle breakage occurring for the more energetic dispersions.

There is a difference in the large particle shape between the sample preparations. The large particles for the SDU prepared samples are somewhat rod-like and are much longer than they are wide, resulting in low aspect ratio values, especially for the 0.8 bar sample. However, for the collision dispersed sample, the large particles have an aspect ratio much closer to one. This is again consistent with breakage of the large fragile crystalline particles when using the collision-based method.

A comparison of the two SDU prepared samples also indicates that care must be taken even when using the SDU. It is apparent that particle breakage is occurring when using a pressure of 4.0 bar with the SDU, although to a lesser extent than with the collision-based dispersion.

Overall, these results demonstrate the need to properly disperse dry powder samples in order to correctly characterize the particle size and shape. Care must be taken that the sample dispersion does not damage the particles to be sure that the results are representative of the actual particle size and shape.

Conclusion

Sample dispersion is an important factor in properly characterizing the particle size and shape of dry powder samples. A crystalline material was characterized using the Morphologi G3S after dry dispersion using the two pressures with the integrated SDU and an external collision-based method. The dispersion methods resulted in different size and shape distributions. The sample prepared with the collision-based method appeared smaller and more spherical in shape. These results are consistent with particle breakage. Particle breakage also occurred for the higher pressure SDU dispersion, although to a lesser extent. Particle breakage was confirmed as the source of the differences by examination of the images of the largest particles detected in each measurement.

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