Application note 2017.03

Particle size analysis of non-spherical particles

Determining the size of non-spherical particles presents a challenge to the analytical chemist. Such particles cannot be fully characterized by a single dimension even though many sizing techniques reduce the size of these particles to the diameter of an equivalent sphere. An equivalent sphere is a sphere that is equivalent in the property which is being measured, such as light scattering or sedimentation. Such techniques give valuable data which can be used to control products and processes, but they neglect shape information which could be influential in determining the behaviour of the product.

Shape is also a complicating factor for many techniques because it influences the size measurement in a way which cannot be readily interpreted by the analyst. Non-spherical particles are best accommodated using a sizing technique which measures a specific dimension of the particle or using image analysis which can deliver a large number of particle size and shape parameters.

The best approach

Although light scattering methods are regarded as determining the diameter of a sphere of equal volume, we should remember that light scattering takes place at refractive index boundaries, i.e. at the edges of particles, and the pattern of light scattering depends not only on the size, but also the shape of the particle. It is therefore an over-simplification to assume that laser diffraction measurements are strictly volume based. In the case of a spherical object this is true, but our real life encounters with particles indicate that the majority are non-spherical and light scattering methods can therefore be in error. We have other tools at our disposal such as laser obscuration time (LOT)[1] and image analysis. LOT determines a specific chord length across a particle without assuming particle shape. Image analysis is a powerful tool to characterize both particle size and shape.

Whatever technique we use, our aim is to use particle characterization data as a predictive tool for product or process performance. Image analysis gives us a range of parameters to help us gain this understanding. However, it is also convenient to derive particle diameters from image analysis data and two typical diameters are shown in Figure 1. Now let's consider how we can characterize the

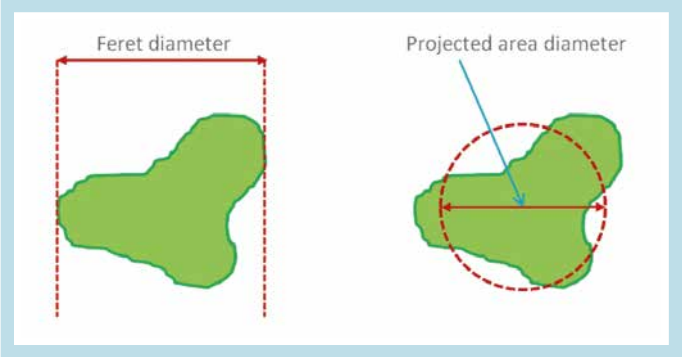

Figure 1. Image analysis can yield a number of particle diameters. The Feret diameter is a shape related diameter whereas the projected area diameter is not specifically related to particle shape.

size of a highly acicular particle such as the fibres represented in Figure 2. The cut lengths of fibres shown in Figure 2 are similar in shape to many of the particles delivered by crystallization processes in a number of industries. When particles of this type are analyzed by laser diffraction as a liquid suspension, a broad size distribution is observed as shown in Figure 3.

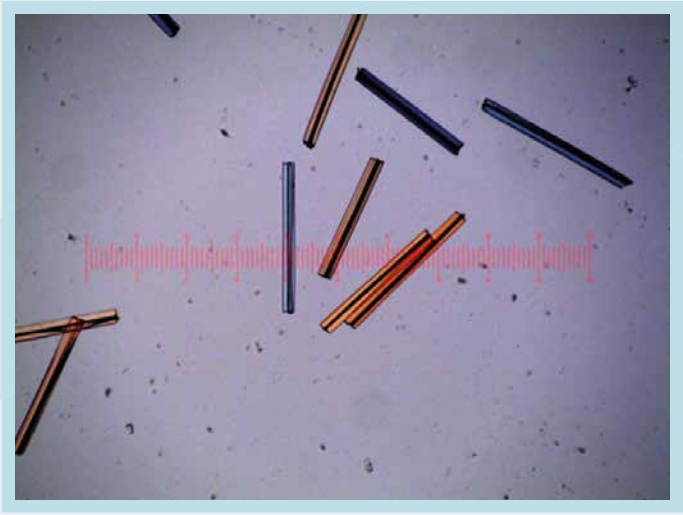

Figure 2. Light microscopy photomicrograph of rayon fibres, 500 x 44 µm (fibres were kindly supplied by Minifibres Inc, Florida, US).

The distribution includes modes corresponding to the minor and major chords, i.e. the length and breadth of the particles. However, the laser diffraction data do not provide specific particle dimensions which would be of most value in characterizing these types of particles.

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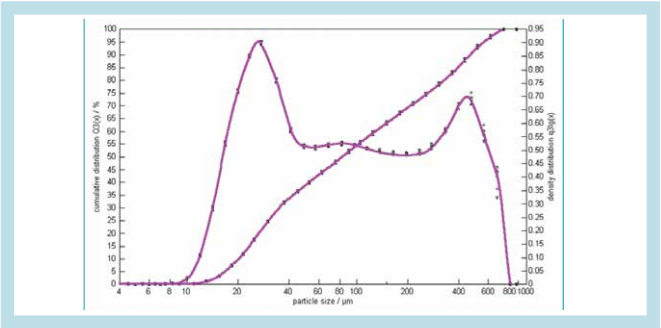

Figure 3. Laser diffraction data for 500µm fibres in liquid suspension.

More specific particle size distributions can be obtained from a shape-specific sizing technique such as laser obscuration time or image analysis. In the case of laser obscuration time, valid transitions are only obtained across the width of the particle and a volume histogram and cumulative distribution for the width of the particles is shown in Figure 4. The median value for this distribution is 44 µm, which is consistent with the manufacturer's specification.

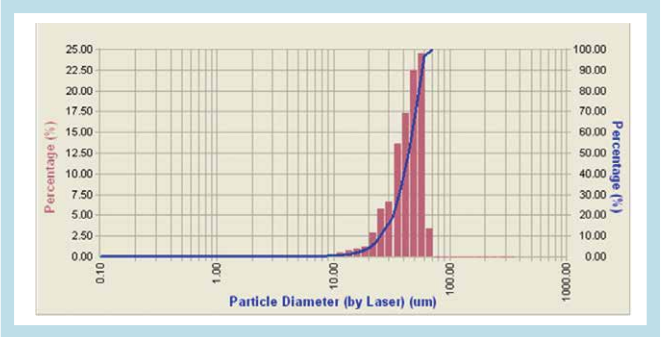

Figure 4. LOT data for ca. 500 µm (l) x 44 µm (diameter) rayon fibres. The LOT technique determines the width of the fibres.

The length of the fibres can be readily obtained from image analysis of the fibre dispersion and Figure 5 shows the number histogram and cumulative undersize distributions for the maximum Feret diameter. The mode of the distribution was determined as 465 µm and the median was 484 µm.

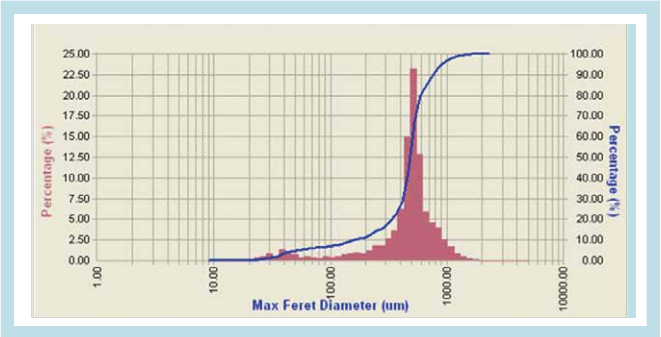

Figure 5. Frequency histogram and cumulative undersize distributions for ca. 500 µm rayon fibres using the maximum Feret diameter.

Equally challenging particles are curled fibres such as those seen in the excipient HPMC. These are not so well characterized using the Feret diameters as the fibres are not linear, so two additional parameters can be determined, the specific fibre length and width as shown in Figure 6. These parameters can be of significant value in quantifying batch to batch differences.

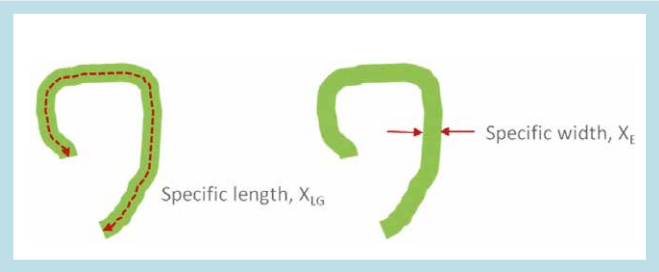

Figure 6. Specific length and width can be readily determined using image analysis. Refer to ISO standard: ISO 9276-6: 2008 (E).

The derived parameter, elongation (ratio of the specific width to the specific length) is shown in Figure 7 to differentiate three batches of HPMC.

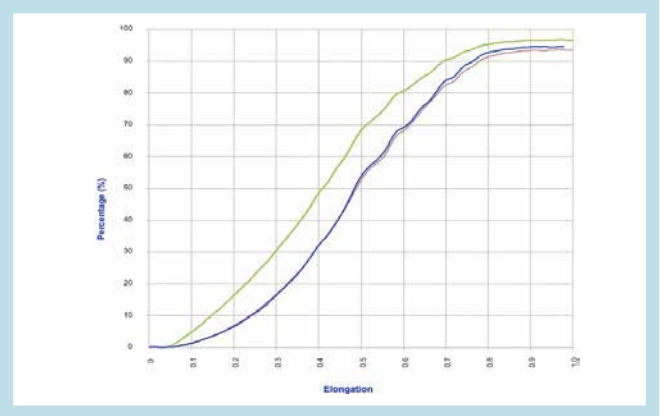

Figure 7. Cumulative number distribution for elongation obtained from image analysis for three batches of HPMC.

Summary

Particle size analysis of non-spherical objects requires methodology which correctly evaluates the impact of particle shape on the size measurement. This can be achieved using sizing techniques such as LOT. Another approach is to use image analysis which gives access to a wide range of meaningful size and shape data.

References

1. AmbiValue Application Note, 2017.01 Particle size analysis related to dissolution and crystallization studies.