Methods of Particle Size Determination – A Review

Introduction

The analysis of particles and characterisation of their size and shape is of great importance in a number of industries including food, construction, biopharma and pharmaceutical. The size of the granules that are used in the manufacture of capsules, tablets and effervescent tablets will have an effect on the disintegration rate, dissolution rate and the absorbance rate. There exists a number of methods of determining particle size of which the most common include sieve analysis, laser diffraction, dynamic light scattering and direct imaging techniques. Frequently, the results of these methods do not correlate well with each other when examining the same samples. This can be attributed to the differences in the fundamental measurement principles used by each method to determine particle sizes.

The fundamental operating principles of the methods of direct imaging sieve analysis, laser diffraction and dynamic light scattering are presented here in an effort to gain an understanding of the difference of results as measured by each method. The operating principles are discussed in terms of fundamental principles, correlation with particle properties, instrument configuration and the limitations of each method.

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Eyecon$_2$™

The Eyecon$_2$ particle characteriser is a direct imaging particle size analyser that measures size and shape information of particles in the size range of 50 - 5500µm in real-time. The Eyecon$_2$ is a non-destructive, non-product contact analytical instrument which can be used as a bench-top laboratory instrument and in-line as a process analytical technology. The method of direct imaging which is utilised by the Eyecon$_2$ allows images of samples to be captured which convey surface morphology and reports shape information. The Eyecon$_2$ is suitable for measurement of wet and dry powders and bulk solids. The Eyecon$_2$ allows the tracking of particle size growth and decrease in process as it continuously captures and processes data in real-time.

Figure 2: The Eyecon$_2$ particle characteriser setup at-line

Figure 1: The Eyecon$_2$ particle characteriser setup In-line on a GPCG30 Fluid bed

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Principle

The Eyecon$_2$ calculates particle size distributions based on the measurement of individual particles within a sample image. By utilising intense pulses of light from an array of front facing LEDs, particles which are moving up to 10 m/s can be captured by the camera sensor without the presence of motion artefacts. The LEDs pulse at high intensity every 0.65 seconds illuminating the sample to be measured. The front facing direct illumination affords the ability to distinguish overlapping particles. The camera sensor is synchronised with the pulsing of the LEDs to capture the sample material while it is illuminated. These captured images are then processed by the software EyePASS™ where the particle detection algorithm identifies and measures individual particles within the captured image.

Measurement data which is recorded and calculated by the Eyecon$_2$ include the D_{10}, D_{25}, D_{50}, D_{75}, D_{90} as numeric and volumetric size with Mean and Median values all trended in real time with live histogram and S-curve results.

Determination of the D-values is achieved by first fitting individual particles with an ellipse in order to determine the minimum and maximum diameter of the particle, d_{min} and d_{max}.

The magnitude of the 3rd dimension is predicted by the average of d_{min} and d_{max} to get d_{avrg}.

The 3D volume of the ellipse which surrounds any particle is calculated using the equation:

$$Volume = \frac{\pi}{6} \times D_{min} \times D_{max} \times D_{avrg}$$

The D-values computed by notionally arranging all particles measured in order of ascending volume. The total volume is computed first. An iterative algorithm then adds the volumes starting with the smallest and working up to the largest. The $D_{10,}$ D_{25}, D_{50} etc. are the particles which corresponded to reaching 10%, 25% and 50% of the cumulative volume respectively. All recorded data is analysed in real-time to determine the overall process D-values based on the data captured throughout the whole recording session. The process is explained in further detail in the Innopharma Technology paper titled "*Eyecon$_2$ – Explanation of D-Value Determination Method*".

Correlation with particle properties

Particles that are identified by the software EyePASS are fitted with an ellipse that is constructed based on an applied edge detection algorithm. Applying an ellipse to a particle for the determination of the volume based on the maximum and minimum diameter and average of the min and max will result in a tighter, typically smaller volume fit than the cubed diameter of an equivalent circle fit to the same particle. This allows the Eyecon$_2$ to more accurately calculate particle volume which will affect the subsequently calculated D-Values.

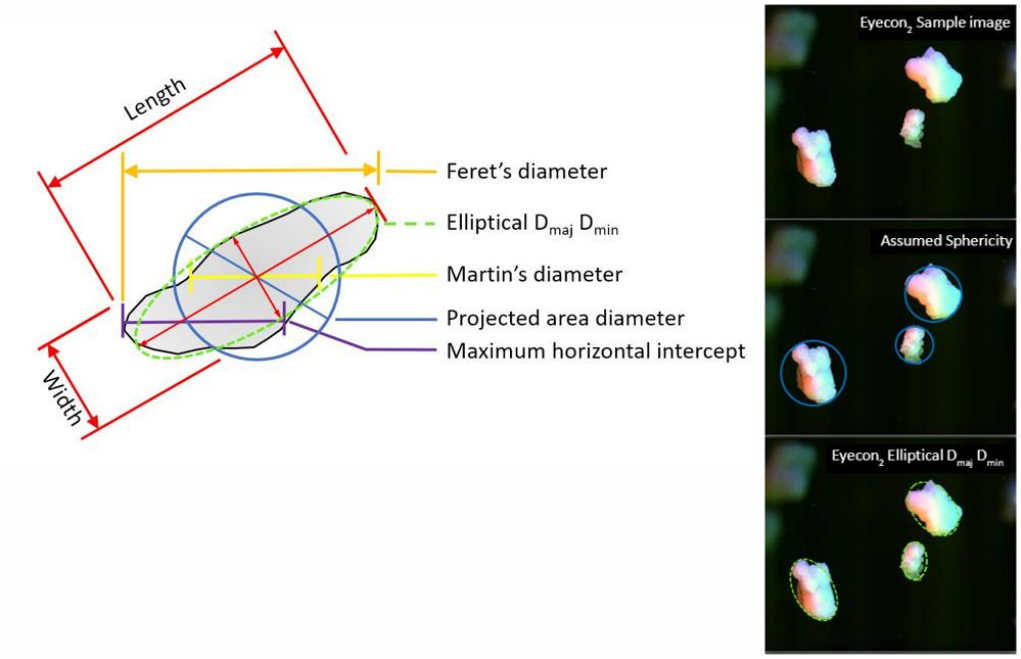

Figure 3: A Representation of the ellipsoid that is fitted to particles using the Eyecon$_2$ software EyePASS compare to other methods of particle size detection.

The eccentricity or shape of each particle is calculated and is presented as an average eccentricity for the full recording session as well as the relative standard deviation of the eccentricity. Eccentricity can aid in blend uniformity and homogeneity analysis. Eccentricity is explained further in the Innopharma Technology paper titled "*Eyecon$_2$/EyePASS Shape Measurement Method*".

A key advantage of front facing direct illumination compared to other direct imaging methods that use a backlight is the ability to distinguish overlapping particles. Backlight imaging can silhouette multiple particles which are overlapping on the same axial plane as the light source which results in the erroneous identification of a larger particle than is presented. The Eyecon$_2$ can correctly identify overlapping particles, the particle at the forefront of the grouped particles will be analysed.

Particles whose boundaries are obscured will not be included for particle sizing. This will reduce oversizing or under-sizing of particle size measurement as a result of overlapping particles.

Limitations

The Eyecon$_2$, like all other particle size measurement systems has areas in which it is not suitable to obtain highly accurate measurement results. Below are listed some of the areas in which the Eyecon$_2$ is restricted from obtaining accurate and repeatable particle size measurements.

- Limits of detection of particles from 50 - 5500µm in size.
- Difficulty in obtaining accurate measurement results of dark particles without algorithm optimisation by user. This is a trial and error process and can take some time to optimise.
- The Eyecon$_2$ relies on direct illumination of sample for particle identification within the algorithm and therefore transparent materials such as glass and some polymers cannot be accurately measured.
- Highly reflective particles are difficult to measure due to reflections.
- The focal length of the system is limited which means samples must be adequately close in order to appear in focus and measurable by the system.
- The depth of field is small which means that material with a very wide sample range distribution will be difficult to measure at the extremes of the distribution curve.

Sieve Analysis

Sieve analysis is a method of determining the particle size distribution of a material. The process separates fine particles from more course particles by passing the material through a number of sieves of different mesh sizes, essentially fractioning particles within certain sieve bin sizes. This mass fraction of particles is measured and weighed so a cumulative distribution can be constructed. Sieve analysis is the most traditional and widely known method used to characterise particle size distributions. There are 2 types of sieve analysis that can be carried out; wet sieving and dry sieving. Wet sieving is suitable for particle sizes from 20µm up to 3mm while dry sieving is suitable for particles from 30µm up to 125mm.

Principle

The material to be analysed is vibrated through a series of sequentially decreasing sieves using a single, or combination of horizontal, vertical or rotational motion. Particles under motion will eventually orientate to present their 2 smallest dimensions to the sieve mesh opening and pass to the next sieve of smaller nominal opening. Upon completion of the sieving process the weight of the sieves are measured and compared to the weight of the sieves before addition of the sample. This gives the mass of material on each sieve. Through addition of the mass fraction on each sieve, from the smallest to the largest sieve size, a cumulative mass distribution of material is obtained. By using sieves with different mesh sizes it is possible to construct a cumulative particle size distribution for the test material.

Correlation with Particle Properties

Determining specific particle sizes with sieve analysis is not possible due to the fact that particles are not measured but are instead said to lay within a size range that is determined by the mesh size of the sieve on which the material is located and the next sequentially larger sieve mesh size, this is sometimes referred to as a bin. For a sieve tower the arrangement of the mesh sizes is rarely linearly increasing as this would require an impractically large sieve tower.

When the weight of all material on each sieve is recorded then it is possible to construct a mass distribution based on the mesh size of each sieve and the mass of material recorded on each sieve which results in a cumulative mass distribution as in Figure 5

Figure 4: Sieves of different mesh sizes and diameters.

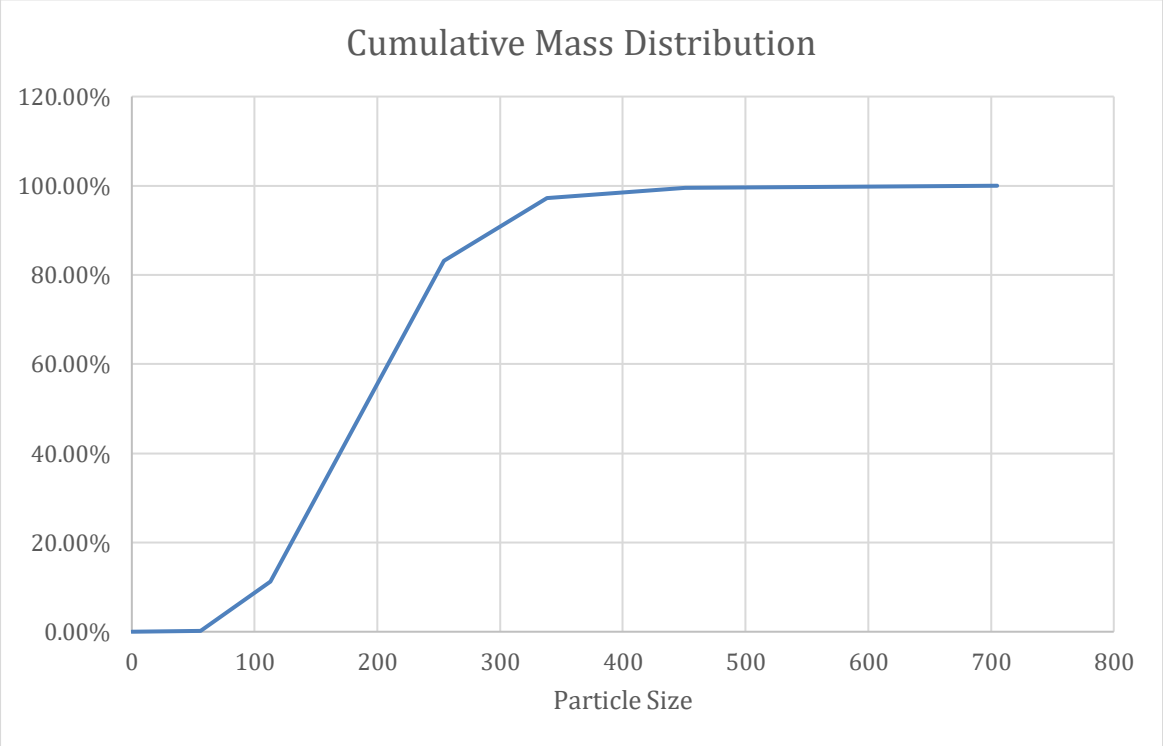

Figure 5: Cumulative mass distribution that is typical of the S-Curve profile obtained from sieve analysis. D-Values are interpolated from this graph.

From this graph the required D-Values can be interpolated as data is only provided at discreet particle sizes which are dependent on sieve mesh sizes selected by the user. While interpolating for a specific D-Value will yield a fast calculation of the required measurement the curve against which the interpolated value is found may not represent how the particle size range is distributed within a specific sieve range. Sieve analysis presumes a linearly distributed particle size range between two discreet sieve sizes in order to fit the cumulative mass S-curve.

Limitations

Sieve analysis while simplistic in its principle and operation is not without its limitations of measurement, of which a number of these are examined. Frequently sieve analysis is used as the standard against which other methods of particle size analysis are measured.

- For elongated and flat particles, a sieve analysis will not yield reliable mass-based results.
- Sieve analysis does not account for particle shape effects of different particles. The 2 minor dimensions of a 3-dimensional particle dictate whether a particle passes through a mesh opening. The major dimension does not affect the particle size calculation or the particle size distribution.
- Sieve analysis may not have the ability to provide high resolution for a sample with a narrow distribution owing to the limited range of mesh sizes available.
- No further particle shape information is available from sieve analysis without additional examination of the particles using other measurement methods.
- Sieve analysis does not have the ability to analyse single particles.
- Sieve analysis has longer measurement times and a lower measurement speed than that of laser diffraction or direct imaging.
- Sieves are prone to blinding. This is the obstruction of the sieve openings by the material that is being analysed. It occurs as a result of particles of the same or similar diameter to the sieve openings becoming lodged within the apertures of the sieve. This reduces the available openings for other particles to pass through and can result in particles that are smaller than the sieve apertures being trapped on that sieve. This will greatly affect the mass distribution and thus accuracy of the PSD.
- Sieve analysis is an offline method of particle size distribution and is lacking in any real-time ability for the monitoring of processes.
- No particle images can be obtained using sieve analysis.

Laser Diffraction

Laser diffraction is a method of calculating the particle size distribution (PSD) of a sample material by analysing the scatter pattern of light from said sample. As light interacts with particles it forms a scatter pattern which is detected and measured by an array of sensors. As the angle and intensity of the scatter pattern is a function of the particle size[1] it is possible to mathematically infer particle size information from the scattered light of an observed sample. Particle size information for a given sample is presented as a volume fraction distribution based on the diameter of the sphere of equivalent volume of the observed particle.

Principle

The fundamental principle governing the determination of particle size by laser diffraction is the interaction of light with a particle, when light comes in contact with a particle, that incident light is altered in some way which is usually characteristic of the particle. Some of the interactions which can take place include reflection, refraction, absorption and diffraction as presented in Figure 6.

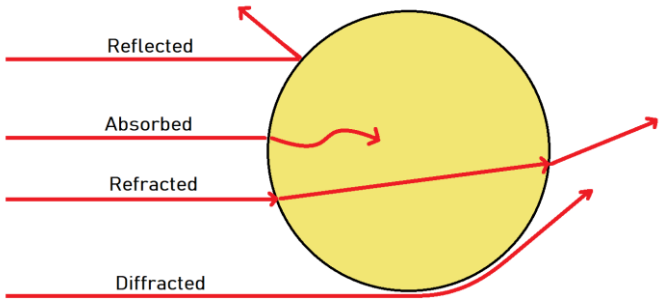

Figure 6: Modes of interaction of incident light with particles and surfaces.

As is evident from the methods name, laser diffraction is a method which determines particle size by measurement of the amount of diffraction which occurs from the interaction of a laser with a particle. For light which is said to have undergone diffraction, it has been scattered from the particle surface resulting in a distribution of scattered light.

The degree of scattering is dependent on both the incident wavelength, although typically a HeNe laser operating at 632.8 nm is used, and more importantly the particle size. Smaller particles result in a larger scattered light distribution. The particle size and hence the particle size distributions can therefore be ascertained by measuring the angular variation in scattered light from a laser beam incident on a sample as measured by an array of detectors.

A number of predictive models exist and are utilised to describe the relationship between particle size and light scattering. These models vary in their approach and so each have

[1] Stojanovic Z., Markovic S. Determination of Particle Size Distribution by Laser Diffraction TECHNICS – NEW MATERIALS 21 (2012)

applicable particle sizes over which they can accurately predict. The choice of which model is used is therefore influenced by the particle size range of interest but also the degree of complexity of each model.

Laser diffraction uses one or a combination of three models of predictive measurement - Fraunhofer approximation model, Rayleigh scattering model and Mie scattering model. Rayleigh and Mie scattering theories are independent theories which describe two differing situations; Rayleigh scattering occurs when the particle is smaller in size than the wavelength of the incident light while Mie scattering occurs when the particle is much larger than the wavelength of the incident light. The Fraunhofer approximation is a related and simplified approximation to Mie theory and as such is applicable only to particles in and above the micrometre range.

The Fraunhofer approximation model describes the expected intensity distribution of scattered light when particles are over 10 times the wavelength of the incident light, the scattering angle of the light is relatively small (<30°) and the detector is located in the far field. This makes it well suited to measuring larger particles and can reduce the complexity of the measurement process by eliminating the requirement for prior knowledge of the refractive index of the sample material and surrounding medium. However, in the region of 1 – 100 µm and below, its accuracy drastically reduces. The use of the more complex Rayleigh and Mie models are therefore required.

The Rayleigh model is used to predict the size of particles that are much smaller than the wavelength of light being used for the investigation. Rayleigh scattering assumes the incident light is elastically scattered by the sample particles i.e. the incident light loses no energy to the scattering particle. It predicts an angular distribution of scattered light with an intensity as described by the Rayleigh equation:

$$I = I_0 \left(\frac{1 + cos^2 \theta}{2R^2} \right) \left(\frac{2\pi}{\lambda} \right)^4 \left(\frac{n^2 - 1}{n^2 + 2} \right)^2 \left(\frac{d}{2} \right)^6$$

Where I_0 is the initial intensity of light, R is the distance between the particle and observer, n is the refractive index of the particle, d is the diameter of the particle and θ is the scattering angle. The intensity of radiation scattered using this model is equal in the forward and backward directions.

When the particle size is greater than 10% of the wavelength of the incident light the accuracy of the Rayleigh equation breaks down rendering it necessary to use the Mie theory of scattering for prediction of particle size.

Mie scattering theory is a special solution to Maxwell's equations of electromagnetism which again describes elastic scattering of light by a sphere-shaped particle. It predicts an angular

distribution of scattered light with an intensity as described by the following equation where a stronger forward scattering is found than with Rayleigh scattering:

$$I = E\left\{k^2 D^4 [JI]^2 \theta + [K_1\theta]^1 + [K_3\theta]^3 + [K_5\theta]^5 + \frac{k^4 d^6 (m-1)^2 \theta^6}{8\pi}\right\}$$

Where E is the flux of incident light, k and K are constants, JI is the Bessel function of the first order, θ is the scatter angle, d is the diameter of the particle and m is the complex refractive index.

The three models differ in the particle size ranges over which they are accurate and applicable while each successively adds a degree of complexity. The use of both the Rayleigh and Mie models require some prior knowledge of the sample particles and their surrounding medium such as the refractive indices of the sample in order to obtain meaningful particle size.

Table 1 summarizes the particle size ranges over which the differing models are applicable in order of increasing model complexity.

Table 1: Predictive model applicable particle size ranges

Particle Size Range Approximation (µm)	Wavelength (nm)
6.33 – 3000*	Fraunhofer Approximation Model
0.01 – 0.063	Rayleigh Model
0.064 – 6.33	Mie Theory Model
**provided that the scatter angle of diffracted light is relatively small (θ < 30°).*	

Correlation with Particle Properties

As briefly mentioned previously, the angular variation and intensity of scattered light from a particle interaction is directly related to the particle size larger particles scatter light through lower angles and with greater intensity as small particles as presented in Figure 7.

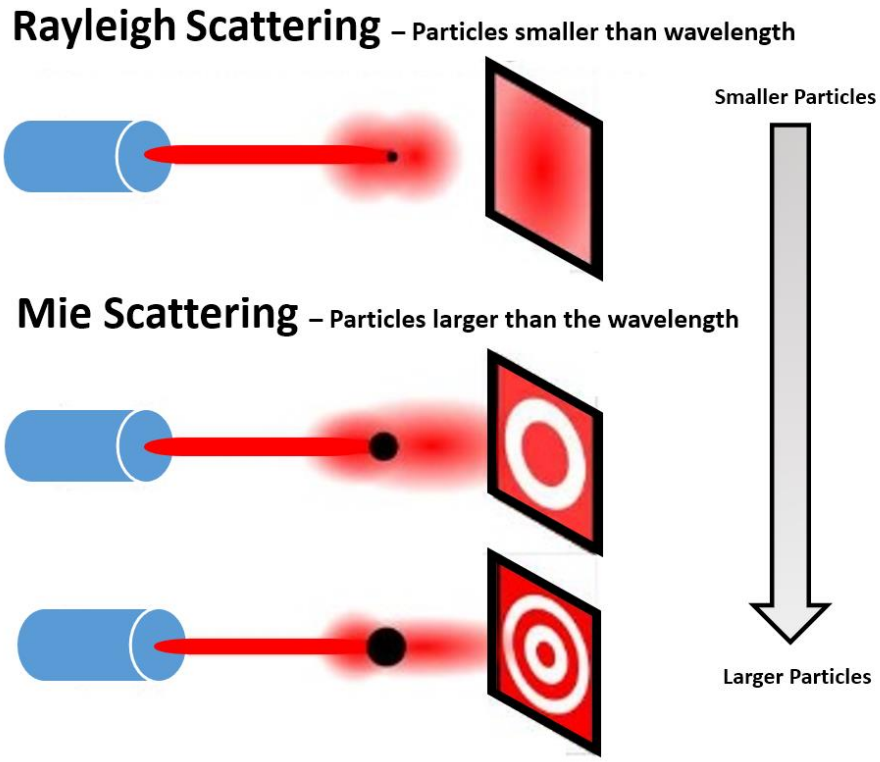

Figure 7: Scatter angle for particles

Depending on the particle size and hence, the applicable predictive model applied, slightly differing angular distributions occur. Rayleigh scattering results in an isotropic scattering distribution with equal probability of forward scatter as back scatter. However, Mie scattering demonstrates a preference for forward scattering with an anisotropic distribution resulting in *lobe* like features as presented in Figure 8.

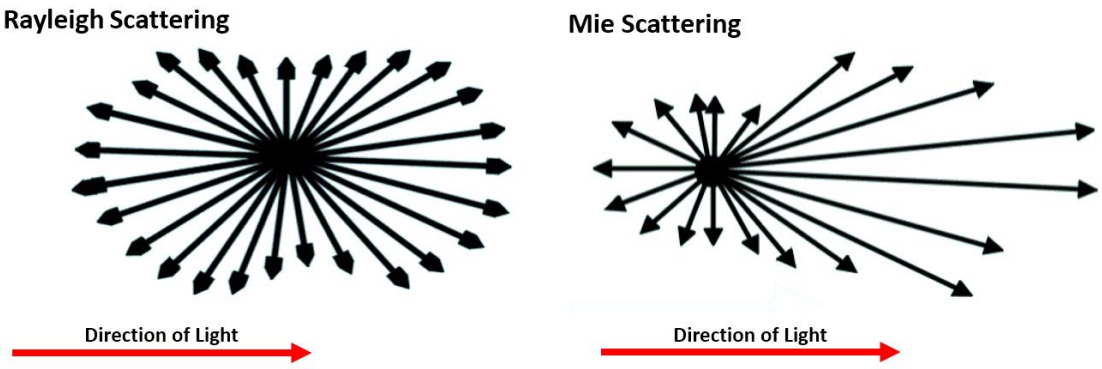

Figure 8: Scatter direction from Rayleigh and Mie scattering.

Both of these distributions show a strong dependence on the diameter of the particle from which the light was scattered as is evident from the Rayleigh and Mie equations presented in the previous section. Therefore, by measuring the intensity of scattered light, the appropriate equation can be solved for the particle diameter and hence a PSD drawn.

However, both the Rayleigh and Mie equations contain a number of other dependencies such as refractive index and empirical constants. This leads to the requirement of a significant amount of prior knowledge of the measurement environment. While the refractive index is readily measurable, the empirical constants are not so. Typically, manufacturers will calibrate the instrument with known particles, solving the equations in advance creating solution matrices relating scattered light intensity to the most probable particle size.

Instrumentation Configuration

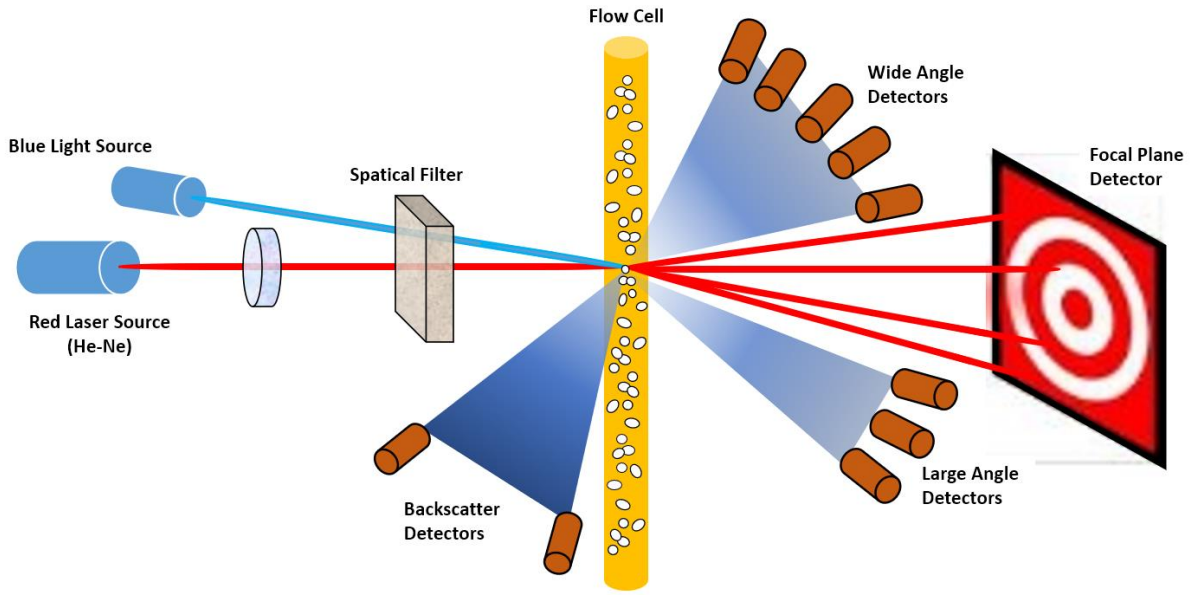

Figure 9: A typical laser diffraction instrumentation configuration.

A typical laser diffraction instrument will comprise of light source, optical lens, flow cell, low angle and high angle detector arrays.

A dual light source system is used to allow for the detection of particles up to 3000µm in diameter and down to 0.01µm in diameter. As the scattering pattern is a function of the ratio of particle diameter to laser wavelength it is necessary to provide two light sources in order to ensure equal sensitivity at both extremes of the limits of detection. The red laser light source is used for larger particles while the blue LED light source is used for the detection of smaller particles.

The array of detectors, back scatter detectors and focal plane detector are all responsible for recording the scatter angle of the radiation after contact with the sample. The scatter angle is related to the particle size and allows for particle size information to be calculated using the Mie theory. Large particles tend to result in small scatter angles, where as small particles can result in large scatter angles and reflection of radiation.

The flow cell which is not visible in Figure 9 but is represented by the flow of sample particles allows for the ideal presentation of the sample for laser diffraction analysis. Sample material is usually brought into the system under vacuum and is presented for the laser and LED light sources by way of the flow cell.

Limitations

As with any scientific method, there a number of restrictions, caveats and difficulties surrounding the use of said method. Presented now are a selection of some of these limitations of using laser diffraction.

Firstly, there are a number of steps that must be taken prior to analysis in order to allow an accurate and reliable measurement to be obtained using laser diffraction as a method of PSD analysis. The optical properties of the sample to be analysed as well as the surrounding medium must be known before the optical model can be established. For new or composite materials this can be a problem resulting in the establishment of the optical model along the process.

However, knowing the refractive index may not permit the use of laser diffraction as only under specific values of refractive indices for both the sample and medium can the models return accurate predictions of particle size. Therefore, it is often a trial and error process that is used to determine the appropriate refractive indices necessary for accurate measurement.
Finally, particle size analysis by laser diffraction is based on two assumptions. The first being that the particles in question are perfect spheres and the second is that the material is homogeneous and therefore has a uniform refractive index. The assumption that all particles are spherical has an effect on the accuracy of the measurement of particles as the eccentricity of the sample changes. In constructing the volume distribution of the sample, the individual particle volume is calculated by assuming a perfect sphere however, it has been shown that the size of a non-spherical particle is larger than the equivalent sphere of the same volume as calculated by laser diffraction (Jonasz, 1991). As such laser diffraction underestimates the volume of high eccentricity particles.
In summary, laser diffraction as a method of particle size distribution analysis is subject to the following limitations:

- The selection of incorrect refractive indices for establishing the optical model can result in erroneous measurements.
- The assumption that all particles are perfect spheres can reduce the accuracy of the measurement as samples with high eccentricity will reduce the accuracy of the results.
- The analysis of non-homogeneous samples can result in incorrect measurements due to the changing refractive index values.
- Measurement times can range from 2 – 10 minutes.
- Testing must be carried out offline which limits the use of laser diffraction as a method of in process control.

Dynamic Light Scattering

Dynamic Light Scattering (DLS), sometimes referred to as Quasi-Elastic Light Scattering (QELS) and Photon Correlation Spectroscopy (PCS), is an optical method of determining particle size properties within a disperse sample by observing the change in scattered light intensity as a function of time.

For a stationary solution, Brownian motion (random motion of colloidal particles due to physical interactions/collisions with the molecules in a solution) results in a constantly changing particle position and so for an incident source of light, a changing scattered light intensity. The rate of change of the light intensity is related to the particle size distribution in that small particles fluctuate more often producing a more rapid change in scattered intensity. The change in scattered light intensity can therefore provide information on the diffusion conditions within the sample for which the relation to particle size is understood.

Principle

The fundamental process which governs DLS is that of interference: when two waves interact, they can combine in such a manner that the resultant wave is either an amplified or diminished superposition of the initially interacting waves as is presented in Figure 10. When the scattered waves interference is constructive, the DLS detector records high light intensity; and equally when waves interference is destructive, the detector records low light intensity.

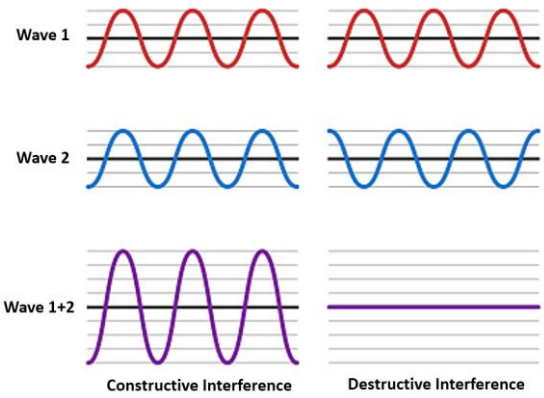

Figure 10: Constructive and Destructive Interference

Therefore, given the large incident intensity associated with DLS set ups, many photons can interfere both constructively and destructively due to the many possible scattering angles. If this process was to be imaged, a speckle pattern such as that of Figure 11 would be observed, where various areas of bright and dark *spots* are present representing the constructive (bright spots) and destructive (dark spots) regions.

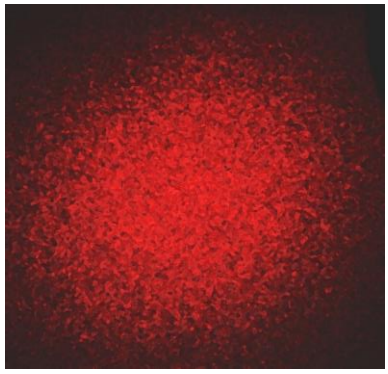

Figure 11: Laser Diffraction Speckle Pattern

As the particles in the sample to be measured relocate due to Brownian motion, so do the position, number of, and intensities of spots in the speckle. Consequently, the resultant total intensity as measured will also fluctuate somewhat similarly to Figure 12 – smaller particles are displaced more rapidly than larger particles and therefore, so too does the scattered light intensity.

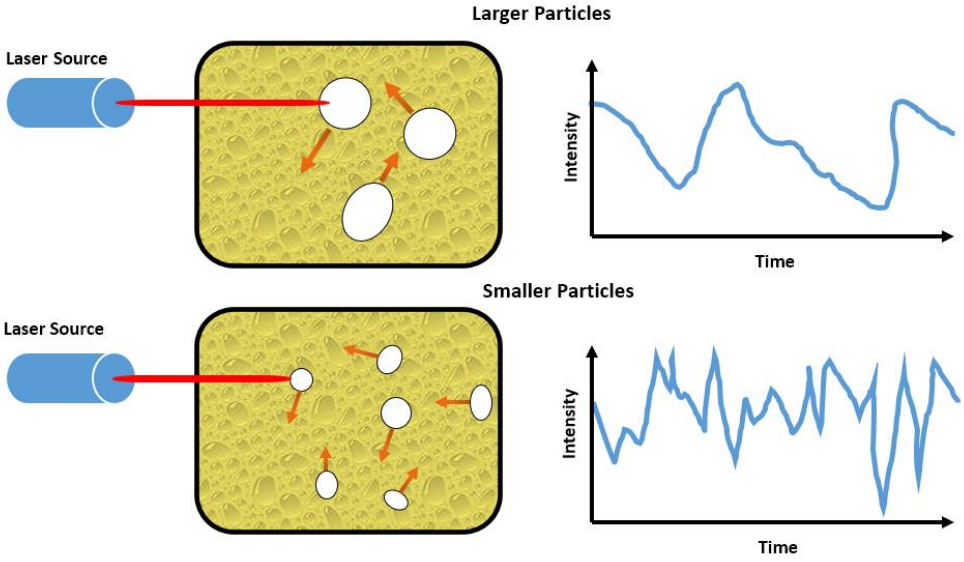

Figure 12: Intensity Fluctuations

Correlation with particle properties

The initial step to extracting the particle information is to monitor the change in the scattered intensity with time at high temporal resolution, on the order of nano to millisecond, and determine the correlation of the changing signal to itself at a time t_0 – the so called *Autocorrelation Function, G(τ)*:

$$G(\tau) = \langle I(t) \cdot I(t + \tau) \rangle$$

Where $I(t)$ is the light intensity at a time t and $I(t + \tau)$ is the light intensity at a time t plus a delay time τ.

At some point after t_0 (or a time t plus a delay time τ), the correlation will cease to exist indicating a complete change in the particle distribution within the sample as can be seen from the correlograms of Figure 13.

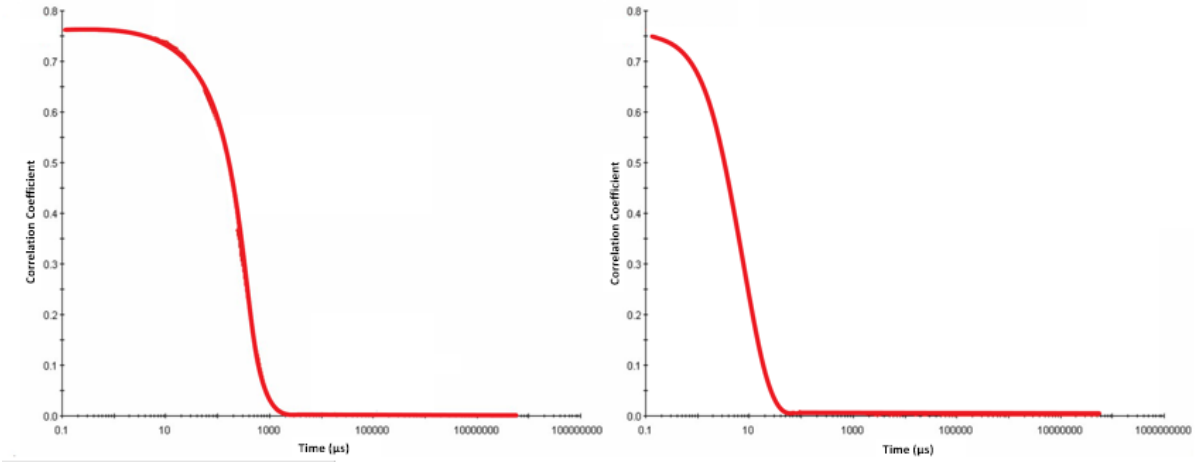

Figure 13: DLS Correlogram

The shape and duration of the correlograms give an indication of the particle information in a number of ways; for a monodisperse sample, smaller particles will result in the correlogram decaying to 0 sooner (Figure 13 right panel versus left), the time at which the curve begins to significantly decay indicates the size of the particles, and the steeper the decay, the more monodisperse the sample.

As mentioned, it is the diffusion kinetics which drive the fluctuations in the intensity and hence the correlogram. The line width (Γ , FWHM) of the correlogram can be related to the *Diffusion Coefficient* (D_T) as:

$$\Gamma = D_T q^2$$

Where

$$q = \frac{4\pi n}{\lambda} sin\frac{\theta}{2}$$

Where n is the refractive index of the sample, λ is the incident wavelength and θ is the scatter angle.

The diffusion coefficient as defined by the Einstein – Stokes law for diffusion in solutions relates the diffusion kinetics of a solution to the mean particle hydrodynamic diameter ($\overline{D_h}$) as

$$\overline{D_h} = \frac{k_B T}{6\pi\eta D_T}$$

Where k_B is the Boltzmann constant, T is the absolute temperature and η is the viscosity.

Therefore, by determining the correlogram line width, the mean particle radius of the sample can be determined by the Einstein – Stokes relation.

Following on from the above, the diffusion coefficient can be related to the correlogram via the autocorrelation function redefined as:

$$G(\tau) = A[1 + B\exp(-2D_T q^2 \tau)]$$

The autocorrelation function may therefore be extracted by fitting the correlogram with a single exponential for a monodisperse sample in a process commonly known as *Cumulants Analysis* defined under ISO13321 Part 8. Alternatively, for polydisperse samples, multiple exponentials may be fit.

From this, a particle size distribution can be drawn and as it is formed by monitoring of relative degrees of light scattering, it is known as the *Intensity Size Distribution*. From this distribution, a number of other parameters are defined, namely the z-average and polydispersity index.
The z-average is the preferred DLS method of quoting the mean particle size. It is defined as the harmonic mean particle size as calculated from the intensity size distribution. The polydispersity index is an indicator of the distribution width.

Determination of Mass and Volume

Some applications require knowledge regarding the number, mass or volume distribution within a sample. In order to determine the number or volume distribution using DLS, the MIE theory of light scattering is applied. A description of which is available in the literature. Unfortunately, there is no direct method of determining the mass distribution as the density of particles needs to be known. Further methods must be utilised to determine the mass distribution.

Instrumentation Configuration

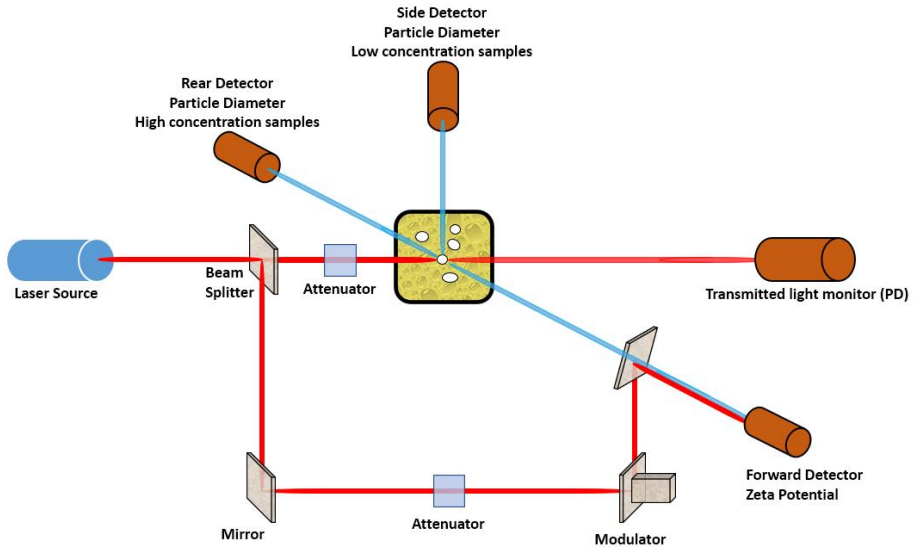

Figure 14: DLS Instrumentation Configuration

Typically, the instrumental set up for DLS is comprised of four components: light source, optics, detector system and digital correlator, as seen in Figure 14.

The light source to perform DLS is typically a continuous wave laser operating in the visible wavelength range. Table 2 adapted from (Tscharnuter, 2000) highlights some typical lasers used. The use of visible wavelengths is fundamentally set by the physics of scattering where for Rayleigh scattering, the probability of scattering is inversely proportional to the fourth power of the wavelength (λ^{-4}) while the scatter intensity is proportional to the 6th power of the particle diameter (d^{-6}).

Table 2: Common Laser types and wavelengths used in DLS (Tscharnuter, 2000)

Type	Wavelength (nm)
HeNe	632.8
Laser Diodes	635 – 780
Ar^+ (Air & Water Cooled)	488 – 514.5
DPSS (Frequency Doubled)	532

The detectors are typically Photomultiplier Tubes (PMTs) though Avalanche Photodiodes (APDs) have also been used. The digital correlator allows a measurement of the correlation function by successively measuring light intensities while keeping track of previous measurement resulting in a determination of the autocorrelation function.

Limitations

The following limitations are applicable to dynamic light scattering:

- The sample must be in solution.
- It is an offline method.
- Low resolution with closely spaced size populations with a difference of size of less than a factor of three, DLS will not precisely characterise a polydisperse sample.
- Multiple light scattering when one particle is scattered by another before reaching the detector it hinders accurate calculation of particle size.
- It is typically employed for particle sizes in the range 0.002 – 2µm.
- Very sensitive to temperature, solvent viscosity, and refractive index.
- Sensitive to contamination e.g. from dust.

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