

Particle Size Analysis Using Differential Centrifugal Sedimentation

Introduction

Differential Centrifugal Sedimentation (DCS) is based on a well-known scientific principle, Stokes' law, and is capable of accurately measuring particle sizes between 2nm and ~75µm with an accuracy of 2%

Theory

An established method of determining the size of an unknown particle involves measuring the rate at which it settles in a liquid of known density and viscosity. Stokes' law is commonly [1] expressed as:

$$V = \frac{(\rho_P - \rho_F)}{180\eta} R^2 g \quad (1)$$

Where, V is the particle velocity (ms⁻¹), ρ_P is the particle density (gcm⁻³), ρ_F is the fluid density (gcm⁻³), η is the fluid viscosity (Pas),

R is the particle diameter (m) and g is the gravitational acceleration (ms⁻²).

Relying on gravity to produce a settling effect takes a long time and renders the sedimentation method unsuitable for nano-sized particles. However, if a large centrifugal force is applied to the system, the experimental time is minimised and, more importantly, the lower size limit at which particles can be measured is greatly reduced. Using speeds of up to 24000 rpm particles as small as a few nanometres can be accurately sized.

Instrumentation and Operation

The CPS Disc Centrifuge is comprised of a motor driven disc, a monochromatic light source and appropriate detector. A cross-sectional schematic of the instrument is displayed in Figure 1.

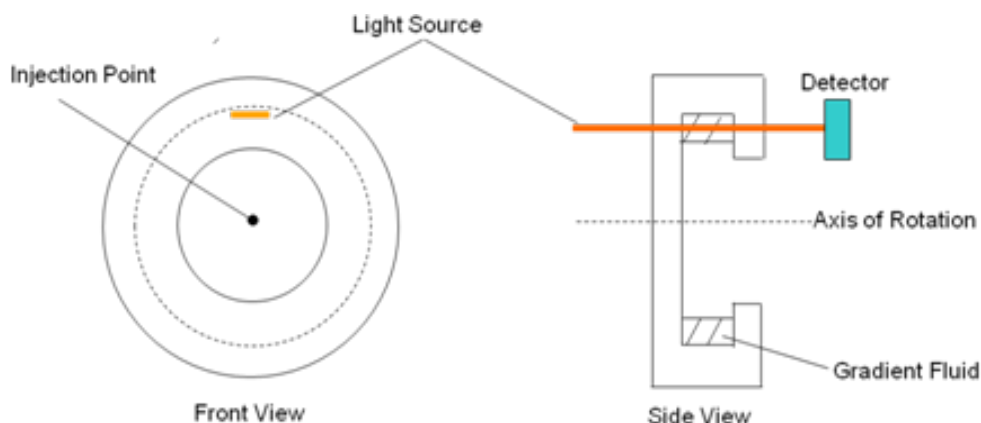


Figure 1: Cross-sectional schematic of a typical disc design.

As shown, the disc is hollow, and once running at the desired speed [selected using a knowledge of the approximate particle size and density] and is filled with a liquid containing a density gradient. To create a density gradient, nine consecutive injections

are made into the disc, each of a lower fluid density than the preceding one. The minimum density of the gradient should be slightly higher than the density of the liquid in which the sample is dispersed, and the maximum density should be no greater than

the particles to be measured [2]. Samples are prepared for analysis by diluting in a fluid which is miscible with the fluid used to build the gradient. Both aqueous and non-aqueous systems can be measured.

To calibrate the time axis with particle size, a standard sample of known size and density is injected into the system [2]. After agitating the sample to ensure it is well dispersed, 100µl of sample is injected into the disc and measurement started.

When the sample is injected, it strikes the rear inside face of the disc and forms a thin film, which spreads as it accelerates toward the surface of the fluid. When the sample dispersion reaches the fluid surface, it quickly spreads over the surface, because it is of lower density. Once a sample is on the fluid surface, sedimentation of individual particles begins [2]. The particles move towards the outer edges of the disc at different rates depending on their size. A detection beam of monochromatic light with a wavelength of 405nm is passed through the disc at a fixed distance from the injection point. When the path of the light is interfered with due to particles passing through it, their time-of flight is used, in conjunction with Equation 1, to calculate the particle size distribution.

Figure 2 shows typical DCS data. When two different samples are measured, spectra clearly display differences in particle size distributions. There is also some evidence of polydispersity in each sample demonstrating the high resolution capability of the technique.

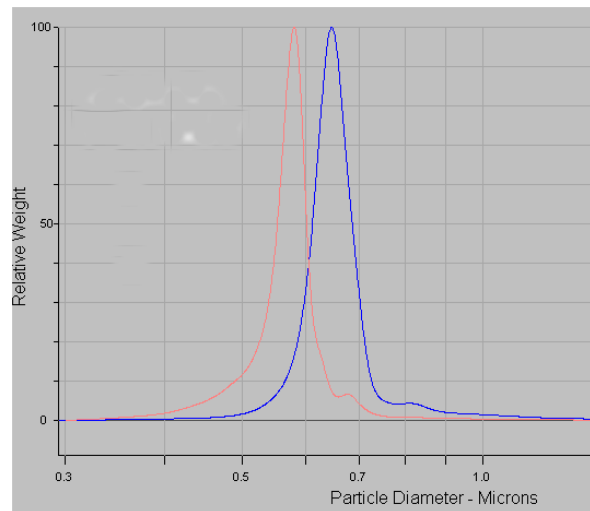


Figure 2: Example data showing the difference in spectra acquired from two samples with different size distributions.

Applications

Because of the achievable resolution, sensitivity and reproducibility, the range of samples appropriate for analysis is wide, and includes:

- Powdered (water soluble) drugs
- Virus particles
- Protein molecule clusters and virus-like particles (to below 20 nm)
- Polymer latexes (aqueous) with any particle density
- Emulsions of oils and waxes
- Ground and precipitated calcium carbonate
- Inorganic pigments and fillers
- Ground sucrose, starch and flour

Conclusions

Disc centrifugation is a fast, reliable and high resolution technique for the measurement of particle size distributions of fine particulates.

References

1. G. G. Stokes: 'Mathematical and physical papers', Vol. I-V; 1880-1905, Cambridge, Cambridge University Press.
2. H. Vegad: 'Old' technique reborn for nanoparticle size analysis with unparalleled resolution, Powder Metallurgy, 2007, VOL 50