# Nanomaterial Characterisation Challenges

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## ABSTRACT

There has been a large amount of research and investment into the toxicological effects of nanomaterials on the environment. One of the more recent developments in this area is the European Commission definition from 2011 of the term "nanomaterial" . This definition indicates a "Nanomaterial means a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for more than 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1nm – 100nm…", is driving a requirement for higher resolution measurement techniques.

Within this context and background we review some of the latest development activity using light scattering techniques and separations devices aimed at addressing the requirements for number based (quantitative) measurement on Nanomaterials.

***Keywords***: nanotechnology, nanomaterials, dynamic light scattering, resonant mass measurement, nanoparticle tracking analysis.

## 1 INTRODUCTION

Conservative estimates of worldwide 2010 nanomaterial production volumes would be ~ 270K tons with a market value of ~ $6bn [1]. The production volume in 2016 is conservately estimated to reach ~ 350K driven by demand from applications in electronics, energy, medicine, chemicals, coatings and catalysts. The increasing amount of nanomaterials available in the market creates great opportunities, however it also has the potential for some risk caused by the toxicological effect of these materials when released into the environment [2].

Nanotoxicology is emerging as an important subdiscipline of nanotechnology. Nanotoxicology refers to the study of the interactions of nanostructures with biological systems with an emphasis on elucidating the relationship between the physical and chemical properties (e.g., size, shape, surface chemistry, composition, and aggregation) of nanostructures with induction of toxic biological responses [3].

## 2 EU DEFINITION

The European commission published a recommended common definition for Nanomaterials in 2011 (2011/696/EU) in which it defined a "nanomaterial as follows [4]:

1) "Nanomaterial" means a natural, incidental or manufactured material containing particles in an unbound state or as an aggregate or as an agglomerate and where for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1nm to 100nm.
2) In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50% may be replaced by a threshold between 1 and 50%.

By derogation from point 1, fullerenes, graphene flakes and single wall carbon nanotubes with one or more external dimensions below 1nm should be considered as nanomaterials.

### 2.1 Instrumentation work to date

The Joint Research Council (JRC) issued a report in 2012 which looked at a wide variety of instruments and their ability to meet the requirements of the EU definition and in particular the abilty to offer a number based size distribution in the range 1nm to 100nm [5].

They concluded that there are a variety of scientific technical challenges related to the measurement of materials in the implementation of the recommended nanomaterial definition. Particular challenges are the requirement of measuring the constituent particles inside aggregates, regardless of the strength with which the individual particles are bound, the difficulty to convert the experimentally measured signals to accurate number size distributions for polydisperse materials, and to detect and count particles at the lower size range of the definition (smaller than 10nm). In summary the report concluded that "none of the currently available methods can determine for all kinds of potential nanomaterials whether they fulfill the definition or not." It was indicated that a range of measurement methods are required to investigate wther nanomaterials fulfil the regulatory definition.

# 3 NUMBER BASED DISTRIBUTIONS

## 3.1 High resolution techniques

Resolution describes the ability of a measuring device to distinguish meaningfully between closely adjacent values of size. We typically describe the (estimated) broadening of a monodisperse peak by a technique as a measure for its resolution.

It is expressed as a coefficient of variation ($v_{techn}$ ,%). Thus, a higher value means a lower resolution. The value given can be related to the definition of resolution as used in chromatography. For example, R = 1.5 corresponds with a relative size difference of $6v_{techn}$ and gives about 2% valley height in between two symmetrical Gaussian peaks of equal height. Alternatively, the term ``peak capacity'' is sometimes used. It relates to $1/v_{techn}$.

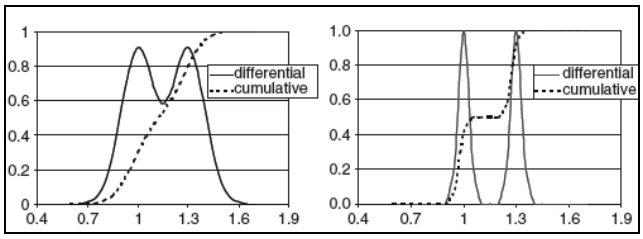


Fig.1 Illustration of resolution for two normal distributions with modes 1 and 1.3; differential and cumulative curves.

It will be clear that resolution is also related to the width of the size classes applied in Particle Size Distribution (PSD) determination: at least three classes are involved if there are two peaks with one valley in between. If the amounts in the classes are in some way correlated, then more classes may be required. An illustration of resolution is given for a 50/50 mixture in Fig. 1. This figure also shows that differential/density curves give an easier identification of the presence of two peaks than cumulative curves.

The resolution of the different measurement techniques is limited by different factors:
• Degree of Brownian motion or particle convection during sedimentation.
• Spread of sieve apertures in a sieving medium.
• Homogeneity of electrical field in ESZ aperture.
• Number of pixels per particle in image processing.
• Difference in signals from particles of different size.
• Width of chosen or given size classes.
• Degree of smoothing applied in calculation of PSD from detector signals.

For most industrial products, high resolution is not very important, as their size distribution is usually wide. Still, adequate resolution is required for sufficient sensitivity with respect to the amount of material in specified size classes.

For very narrow PSD's, for example standard reference materials, resolution is highly relevant. First, higher resolution allows easier discrimination between particles of different size. Secondly, it allows unbiased determination of the width of the PSD. And, finally, it enables quantitative determination of small agglomerates.

## 3.2 Dynamic Light Scattering

The variation with time of the scattered laser light intensity at some defined angle by a collective of particles, dispersed in air or in a transparent liquid, is measured. The rate of change of this intensity is related to the diffusion coefficient of the particles, which in turn is related to particle size by the Stokes-Einstein equation. Several mathematical methods are used for conversion of the intensity-time relationship to a PSD. The fact that this conversion is ill-conditioned and has a poor signal-to-noise ratio limits the amount of PSD information that can be obtained. Thus, usually the simple "cumulants" method is favored for data analysis; it leads only to a mean size and a value for PSD width. Other methods claim to lead to a PSD, but often results are not stable. There are two versions for measurement. The conventional technique operates usually at an angle of 90°, or another specified angle, at very low concentration. New techniques, such as fiber-optics quasi-elastic light scattering (FOQELS) and diffusive wave spectroscopy, use back-scattered light and may operate at higher concentration. Then, particle-particle interactions often influence the particle movement and, thus, the sizing result.

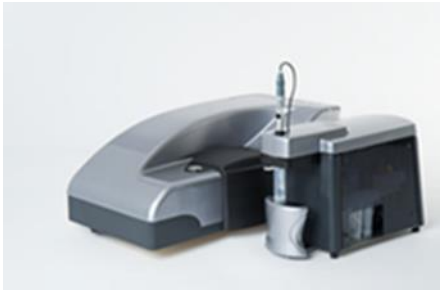

Fig.2 Zetasizer (DLS) product with titrator

## 3.3 Field Flow Fractionation

Asymmetrical flow FFF is frequently used in the high-resolution separation of nanoparticles and proteins. Laminar flow of the eluent through a thin separation channel results in a parabolic flow velocity. For asymmetrical flow FFF, the field is generated by pumping eluent through a permeable lower plate, which is covered by an ultrafiltration membrane.
This applied field-flow (cross-flow) is perpendicular to the channel flow, driving injected particles toward the membrane (accumulation wall). In a typical separation scheme, particles are constantly driven toward the

accumulation wall by the cross-flow while thermal motion of the particles (i.e., Brownian motion) counteracts the field. As elution proceeds, smaller particles assume a higher mean steady-state distance from the wall and thus elute at a faster rate. In contrast, larger particles (with lower diffusion coefficients) occupy regions closer to the accumulation wall and show greater retention. The eluting particles may be conveniently detected by DLS, which is a powerful means to assess the size of the individual eluting particles.

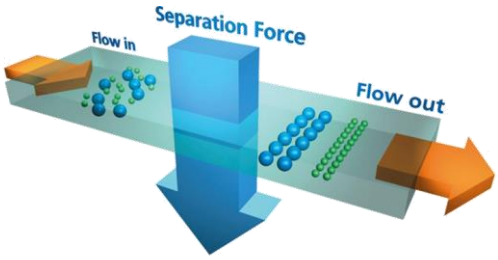


Fig.3 FFF Schematic

## 3.4 Nanoparticle Tracking Analysis

NTA (Nanoparticle Tracking Analysis) products derive the hydrodynamic size and under some circumstances other parameters (concentration, zeta potential and speciation) of particles in the size range from 10-2000 nanometres. This instrument uses a microscope to observe the light scattered by individual particles suspended in an optical cell and illuminated with a laser and then tracking their diffusion under Brownian motion.

The light scattered by the particles is captured using a scientific digital camera and the motion of each particle is tracked from frame to frame. This rate of particle movement (diffusion coefficient) is related to a sphere with equivalent hydrodynamic radius as calculated through the Stokes-Einstein equation. This is exactly the same approach which is used to calculate size from the diffusion coefficient measured by Dynamic Light Scattering (DLS). However, as NTA calculates particle size on a particle-by particle basis it can offer advantages over DLS, for instance in terms of size resolution and the ability to provide absolute concentrations. Also, since video clips form the basis of the analysis, accurate characterisation of real-time events such as aggregation and dissolution is possible. One other major advantage of NTA technology over DLS is the ability to discriminate between different populations even when the size is equivalent. This may simply be achieved by monitoring the intensity of light scattered by the different populations or through the use of fluorescent labelling of the different entities combined with different wavelength lasers and optical filters.

Fig.4 NS300 – NTA type unit

## 3.5 Resonant Mass Measurement

RMM (Resonant Mass Measurement) is a technique which measures the mass buoyancy of particles to provide information on the size of nanoparticles. At the heart of the instrument is a MEMS (Micro Electronic Mechanical System) sensor within which there is an embedded microfluidic channel. A suspension containing particles of interest is pumped through the microfluidic channel. One by one, particles are introduced to the cantilever structure within the sensor, causing the cantilever's resonant frequency to alter by an amount directly proportional to the particle's buoyant mass in its suspending fluid.

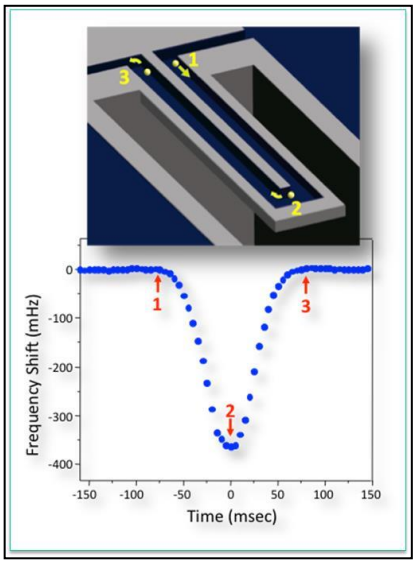


Fig.5 Archimedes MEMS schematic

Fig. 5 shows a schematic of the MEMS sensor at the heart of the Archimedes system indicating the flow of a particle through the channel. As the particle flows through the channel (1 to 3), the oscillating frequncy of the MEMS sensor changes which is directly related to the mass of the particle which can be converted to a size by knowing the density of the particles under study. The technique can distinguish between nanoparticles which are denser than the fluid in the cantilver and cuase the frequency to shift down

and potential air bubbles which are lighter than the fluid and cause the frequency of the cantilver to shift up.

Fig.6 Archimedes system

The system can come with different MEMS sensors which have different size channels embedded in them which allows the system to cater for different particle size ranges. The system has been shown to be both accurate, measuring to within 1% accuracy on NIST traceable standards and also offer high resolution with an ability

## 4 CONCLUSION

As indicated in the introduction it is difficult to obtain a number based size distribution for nanomaterials as defined by the EU definition. However a combination of techniques can start to address the requirements in the area. DLS can offer an indication as to whether a material might be a nanomaterial or not and in particular if it sits in the size range 1nm to 100nm. However DLS is what be described as an essemble technique and has limited resolution in defining different size bands.

To achieve higher resolution DLS would need to be combined with a separation technique which could be FFF or there is the potential to use alternative higher resolution techniques which measure on a particle by particle basis such as NTA or RMM. The EU definition is up for renewal at the end of 2014, however is unlikely that the number based requirement will be altered as this is seen as important within the context of toxicology studies. The requirements and drivers in the area of toxicology will invariablly drive future instrumentation development and this will include improvements in the number based capability of systems.

| Technique | Size range | Resolution | Speed of analysis | Particle number quantification? |
|---|---|---|---|---|
| DLS | 1 nm to 1 µm | Moderate | Very fast | Calculated from intensity |
| DLS + Separation (e.g. FFF or SEC) | 1 nm to 1 µm | Very good | Slow | Calculated from intensity with improved resolution. Concentration detector option |
| Nanoparticle tracking analysis (NTA) | 30 nm to 1 µm | Good | Fast | Semi quantitative |
| Resonant mass measurement (RMM) | 50 nm to 1 µm or 300 nm to 5 µm | Good | Slow | Quantitative |

Fig.7 Comparison of high resolution techniques

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