Simultaneous, Real-time, Mutli-parameter Analysis of Nanoparticles in Liquids

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A new nanoparticle sizing and characterization technique is described allowing nanoparticles in a suspension to be individually but simultaneously detected and analysed in real time using a laser-based microscope system. The technique uniquely allows the user a simple and direct qualitative view of the sample under analysis and from which an independent quantitative estimation of sample size, size distribution and concentration can be immediately obtained.

Nanoparticles of all types and in any solvent can be detected, sized and counted through video-based tracking of their Brownian motion when illuminated by a specially configured laser beam. Examples of analyses of a wide range of sample types will be shown including nano-emulsions from pharmaceutical and clinical applications and metal oxides and nano-ceramics from the chemical, pigments and coatings industries.

Novel advances in the technique will be described which allow each particle to be simultaneously analysed not just in terms of its size but also light scattering power (mass/refractive index) and fluorescence from which 3D plots of size v. light scatter or fluorescence can be produced.

Introduction

In a wide range of industry sectors it is increasingly important to obtain accurate estimates of size, size distribution and concentration of nanoscale particles. However, existing techniques for obtaining such information (e.g. electron microscopy, light scattering) are time consuming, complex and the results difficult to interpret, particularly in samples which are heterogeneous in composition or which contain a range of particle sizes, e.g. are polydisperse.

A newly developed method for the direct and real-time visualisation and analysis of nanoparticles in liquids has become available and is called Nanoparticle Tracking Analysis (NTA)[1]. Using a laser-illuminated microscopical technique, Brownian motion of nanoparticles is videoed and analysed in real-time by a CCD camera, each particle being simultaneously but separately visualised and tracked by a dedicated particle tracking image analysis programme. Because each and every particle is visualised and analysed separately, the resulting estimate of particle size and particle size distribution does not suffer from the limitation of being an intensity weighted, z-average distribution which is the norm in conventional ensemble methods of particle sizing in this size regime, e.g. the well established method of Dynamic Light Scattering (DLS) or Photon Correlation Spectroscopy (PCS).

Size vs. Intensity

The benefit of being able to simultaneously measure two independent parameters such as particle scattering intensity and particle diameter (from dynamic behaviour) is valuable in resolving mixtures of different particle types (e.g. distinguishing between inorganic and polymer particles of the same diameter). Similarly, small differences in particle size within a population can be resolved with far higher accuracy than would be achieved by other ensemble light scattering techniques.
Fig 1 shows a mixture of 50nm gold particles and 100nm polystyrene. It can be seen that the 50nm gold nanoparticles scatter light more effectively than the 100nm latex despite the fact

they are smaller. This is uniquely characterised by a negative slope on the 3-d graph.

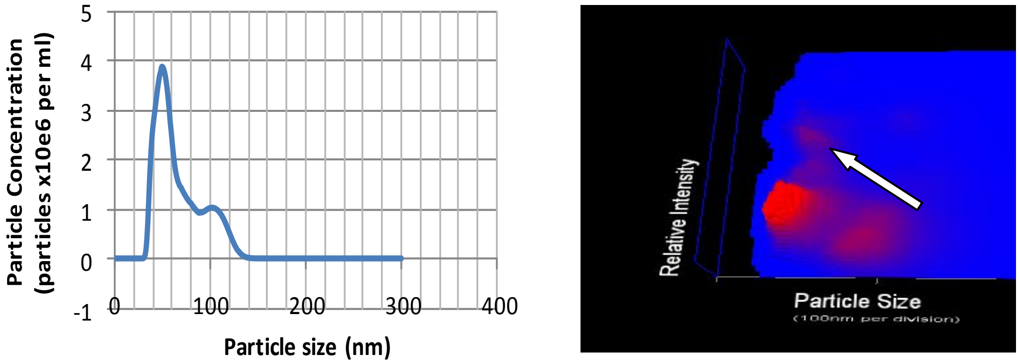

Fig 1. a) A particle size distribution of 50nm Au nanoparticles and 100nm polystyrene. b) a 3D plot of size v. intensity v. concentration of the same sample.

Size vs. Fluorescence

A recent development allows fluorescence measurement of specific particle types to be characterised (sized, counted, etc.) in complex mixtures through, for instance, the use of fluorescently labelled antibodies and other probes.
In Fig 2, a mixture of fluorescently labelled 50nm beads mixed with non-fluorescent 200nm beads can be measured under light scattering mode, in which a) both populations are analysed or b) using fluorescent filters, only the fluorescent population are seen.

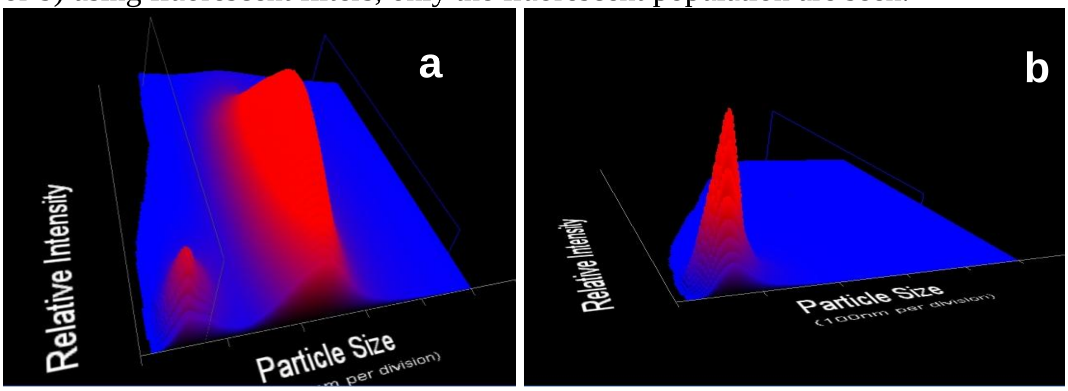

Fig 2. a) Measurement of size and number by light scattering was made using the standard red laser. b) Using a second laser emitting at a shorter wavelength only light emitted from the fluorescent beads was measured.

Conclusion

NTA is a direct and fast technique by which nanoparticles in their natural solvated state in a liquid can be rapidly detected, sized and counted. While limited to particles of 10-20nm and above and to concentration ranges between $10^7 – 10^9$ particles per ml, the ability to simultaneously visualise and analyse nanoparticles on an individual basis allows for much improved resolution of polydisperse and/or heterogeneous sample types. The technique can be used to complement existing techniques for the sizing of nanoparticles (e.g. DLS, PCS) allowing data obtained from these methods to be validated by direct microscopical observation of the sample.

References

1 Carr, R., Hole, P.,Malloy, A., Nelson, P., Wright, M. and Smith, J. (2009), Applications of nanoparticle tracking analysis in nanoparticle research – a mini-review, European Journal of Parenteral & Pharmaceutical Sciences 2009; 14(2): 45-50

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