Characterization of Nanoparticle Dispersions by Size and Scattering Intensity Simultaneously

D. Griffiths*, P. Hole**, J. Smith** and B. Carr**

*NanoSight USA, 3027 Madeira Ave., Costa Mesa, CA 92626, USA duncan.griffiths@nanosight.com
**NanoSight Ltd., Amesbury, Wiltshire, SP4 7RT, UK Patrick.hole@nanosight.co.uk

ABSTRACT

A novel multi-parameter characterization system for nanoparticles is described. This system builds on the Nanoparticle Tracking and Analysis (NTA) technique for the simultaneous visualization and individual sizing of nanoparticles based on their Brownian motion. NTA employs a novel particle illumination method, allowing direct observation of particles in suspension. The technique described is extended to allow not just the characterization of size, but also light scattering intensity on an individual *particle-by-particle* basis. This multi-parameter measurement capability allows sub-populations of nanoparticles of varying characteristics to be resolved in a complex mixture. Changes in one or more of such properties can be followed in real time and *in situ*.

Keywords: Colloids, nanoparticle, characterization, sizing, DLS.

1 INTRODUCTION

The analysis of nanoparticle properties is an increasingly important requirement in a wide range of applications areas (e.g. nanoparticle toxicity, pigments, ceramics, nanoparticle drug delivery design, healthcare, etc.) and is usually carried out by either electron microscopy or dynamic light scattering (DLS). Both techniques suffer from disadvantages; the former requiring significant cost and sample preparation, the latter frequently generating only a population average size, which itself can be heavily weighted towards larger particles within the population.

A new method of microscopically visualizing individual nanoparticles in a suspension, called Nanoparticle Tracking and Analysis (NTA), allows their Brownian motion to be analyzed and from which the particle size distribution profile (and changes therein in time) can be obtained on a particle-by-particle basis [1-3]. The technique offers significant advantages over traditional light scattering techniques (such as DLS- and SLS-based systems) for the characterization of polydispersed populations of nano-scale particles. Independent of particle density or refractive index, NTA dynamically tracks individual particles within the range of 10 - 1,000nm and provides size distributions along with a real-time view of the nanoparticles being measured.

This technique provides critical information to many fields of research including metal and ceramic colloids, inks and pigments, oil samples, silicates, viruses, proteins and other bio-colloidal systems where samples are typically polydisperse and also where an absolute concentration measurement which is of use, as the technique also has the ability to measure particles down to a concentration of 10^6 particles per ml.

2 MEASUREMENT METHODOLOGY

A small (250µl) sample of liquid containing particles at a concentration in the range 10^6-10^{10} particles/ml is introduced into the scattering cell through which a finely focused laser beam (approx. 40mW at λ=635nm) is passed. Particles within the path of the beam are observed via a microscope-based system (NanoSight LM10) or dedicated non-microscope optical instrument (NanoSight LM20) onto which is fitted a CCD camera.

The motion of the particles in the field of view (approx. 100 x100 µm) is recorded (at 30 frames per second) and the subsequent video analyzed. Each and every particle visible in the image is individually but simultaneously tracked from frame to frame and the average mean square displacement determined by the analytical program. From this can be obtained the particle's diffusion coefficient. Results are displayed as a sphere-equivalent, hydrodynamic diameter particle distribution profile. The only information required to be input is the temperature of the liquid under analysis and the viscosity (at that temperature) of the solvent in which the nanoparticles are suspended. Otherwise the technique is one of the few analytical techniques which is absolute and therefore requires no calibration.

Results can be obtained in typically 30-60 seconds and displayed in a variety of familiar formats (diameter, surface area or volume on either linear or log scale). The instrument can be programmed to carry out repeat measurements of dynamically changing samples to analyze dissolution, aggregation and particle-particle interactions. Notably, because the instrument visualizes particles on an individual basis, particle concentration is recoverable. Once analyzed, the sample is simply withdrawn from the unit for re-use, if required.

The minimum particle size detectable depends on the particle refractive index but for highly efficient scatterers, such as colloidal silver, 10nm particles can be detected and

analyzed. For weakly scattering (e.g. biological) particles, the minimum detectable size may only be >50nm. The upper size limit to this technique is defined by the point at which a particle becomes so large (>1000nm) that Brownian motion becomes too limited to be able to track accurately. This will vary with particle type and solvent viscosity but in normal (e.g. aqueous) applications is approximately 800-1000nm. See www.nanosight.com for details.

3 SIZE DETERMINATION BY NANOPARTICLE TRACKING ANALYSIS

Brownian motion in a Newtonian fluid is governed by the Stokes-Einstein equation. Whilst the motion clearly occurs in three dimensions, NTA observes motion only in two dimensions. It is possible to determine the diffusion coefficient from measuring the mean squared displacement of a particle in the two observed dimensions;

$$\overline{(x,y)}^2 = \frac{4TK_B t}{3\pi\eta d}$$

where the first term is the mean squared displacement, T, is temperature, K_B is Boltzmann's constant, t is the time period (here given by 1/*framerate*), η is viscosity and d is the hydrodynamic diameter.

By tracking the centers of the particles the mean squared displacement for each and every particle is calculated. This process is depicted below in figure 1. By recording a video of particles (fig 1a), tracking them (fig 1b) and compiling the resulting sizes a particle size distribution is established (fig 1c).

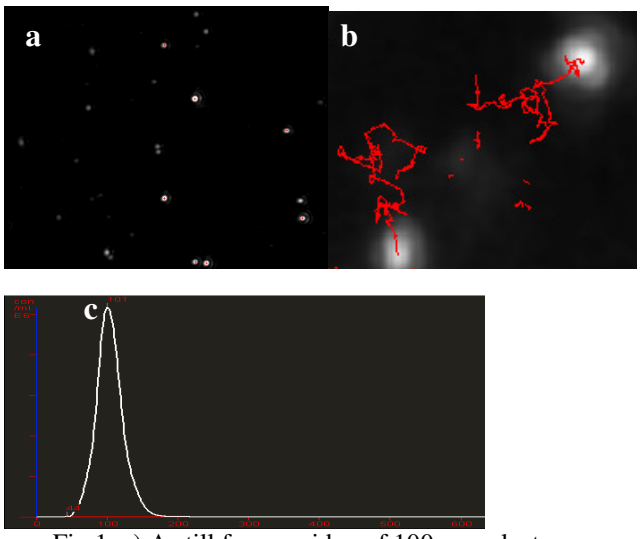

Fig 1. a) A still from a video of 100nm polystyrene calibration particles, b) showing only some (for clarity) of the Brownian motion trajectories analysed and c) subsequent particle size distribution.

The technique works well for a wide range of particle sizes as is shown in figure 2 showing repeat measurements on calibration nanoparticles comparing quoted values (as given for NIST-traceable Duke Scientific, polystyrene latex particles) to the particle sizes as measured by the NTA technique.

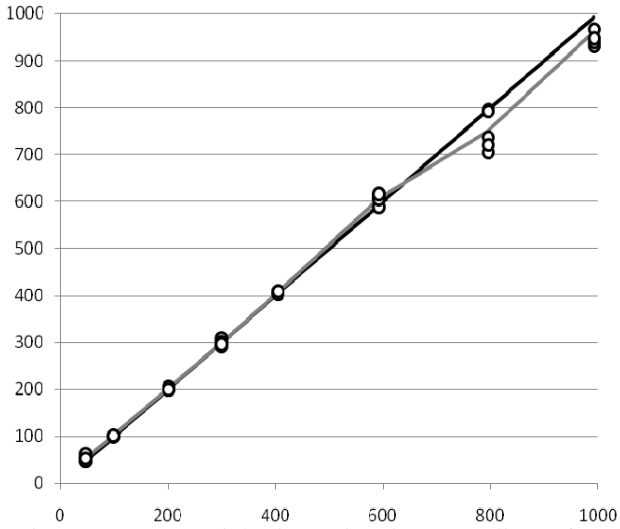

Figure 2. NTA particle size estimation (grey line) of polystyrene calibration spheres when compared to quoted values (dark line) based on average of 4 analyses performed for 60 seconds with each sample.

All particle types can be measured and in any solvent type, providing that the particles scatter sufficient light to be visible (i.e. are not too small or indexed matched).

4 INTENSITY DISTRIBUTION ANALYSIS

In addition to measuring the particle size for each and every particle, it is possible to extract further information about the particles. The intensity of the light scattered is strongly dependent on the particle size. Therefore simultaneously measuring the intensity of light scattered along with the particle size can further be used to gain more information about the particles. This can either infer information about the size distribution at higher resolution than previously possible or give an indication of the different particle materials used.

The results shown in Fig 3 were obtained from an analysis of a mixture of 200 and 300nm latex beads (overlaid with the normal particle size distribution plot, 3b) and shows that the two populations can be well resolved from each other. Furthermore, because the technique analyses particles on an individual basis and can collect information on their relative brightness as well as their size (measured dynamically) these two data can be combined to give an intensity v size plot (Fig 3c). This capability shares many features in common with conventional flow cytometry but is unique in this deeply sub-micron size range. [4]

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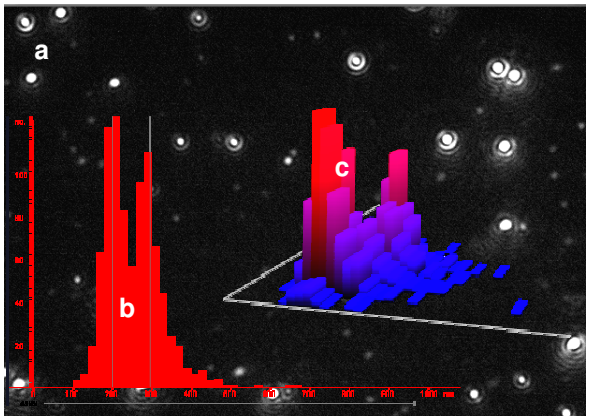

Fig. 3 A mixture of 200nm and 300nm particles; a) still image, overlaid with b) analysis plot and c) 3D number v. relative intensity v. diameter plot.

Figures 4 and 5 compare and contrast a heterogeneous mix (gold nanoparticles of 50nm and polystyrene latex of 100nm) to a homogenous mix of different sized particles (polystyrene nanoparticles of 100nm and 200nm). Note how the intensity distributions demonstrate that the 50nm (gold) particles scatter at higher intensity than the 100nm (polystyrene latex particles). This example uniquely demonstrates for the first time the ability of the technique to differentiate species not just on their hydrodynamic size but also by their scattering ability.

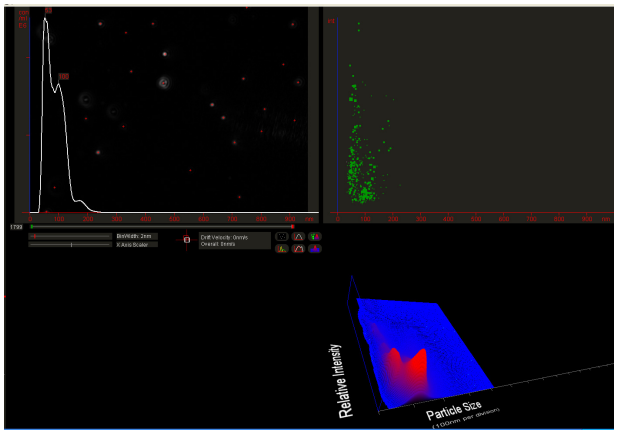

Figure 4: Particle size distribution, intensity scatter plot, and intensity map for a 50nm gold, 100nm polystyrene mix.

5 CONCLUSION

The technique is robust and low cost representing an attractive alternative or complement to higher cost and more complex methods of nanoparticle analysis such as lights scattering or electron microscopy that are currently employed. The technique uniquely allows the user a simple and direct qualitative view of the sample under analysis (perhaps to validate data obtained from other techniques such as PCS) and from which an independent quantitative estimation of sample size, size distribution and concentration can be immediately obtained. [5-7].

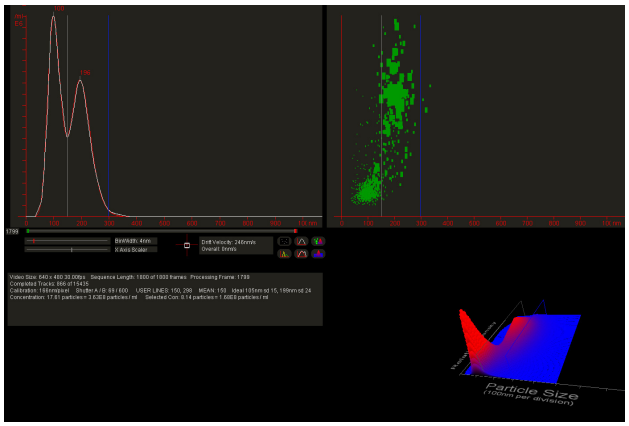

Figure 5: Particle size distribution, intensity scatter plot, and intensity map for a 100 and 200nm polystyrene mix.

REFERENCES

[1] CARR, R (2005), NanoParticle Detection and Analysis, 27th International Fine Particles Research Institute (IFPRI) Meeting, June 25-29th, 2006, SANTA BARBARA, USA

[2] CARR, R., DIAPER, T. and BARRETT, E. (2005) NanoParticle Tracking Analysis – The Halo system. Abs Proc 9th Particulate Systems Analysis Conference 2005, September, Stratford-upon-Avon, UK

[3] WARREN, J and CARR, R (2006) 'A Novel Method for Characterisation of Nanoparticle Dispersions', Nanoparticelle: sintesi e caratterizzazione, Politecnico di Torino, Italy 8 March 2006

[4] van der SCHOOT, A (2007) "Sizing of nanoparticles by visualising and simultaneously tracking the Brownian motion of nanoparticles separately within a suspension" ChinaNANO2007 –Abs. International Conference on Nanoscience & Technology, June 4, 2007, Beijing, China.

[5] GHONAIM, H., LI, S., SOLTAN, M.K., POURZAND, C. and BLAGBROUGH, I. S. (2007) "Chain Length Modulation in Symmetrical Lipopolyamines and the effect on Nanoparticle Formulations for Gene Delivery", British Pharmaceutical Conference, Manchester, 10th Sept, 2007

[6] SAVEYN, H., De BAETS, B., HOLE, P., SMITH J. and VAN DER MEEREN, P. (2008) Accurate particle size distribution determination by Nanoparticle Tracking Analysis based on 2-D Brownian dynamics simulation in Abs PSA2008, Stratford on Avon, September, 2008

[7] MONTES-BURGOS, I., SALVATI, A., LYNCH, I. and DAWSON K. (2007) "Characterization techniques for nanoparticle dispersion" at European Science Foundation (ESF) Research Conference on Probing Interactions between Nanoparticles/Biomaterials and Biological Systems, Sant Feliu de Guixols, Spain, 3 November 2007