A novel ultrasonic method for characterizing suspensions of nanoparticles

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Introduction

We describe a new Ultrasonic Pulsed Doppler Technique (USPD) that measures the ultrasonic power backscattered from suspended particles and has demonstrated the potential to provide rapid automated measurement of nanoparticle concentration. It may also be capable of measuring particle size distribution and particle compressibility.

The key features of the USPD system are:

- Single small probe transducer, 4 mm diameter
- Small sample volumes, about 1 ml or less
- Data acquisition requires 10 – 30 min.
- Stirring:
  - Required for negatively buoyant species
  - Not required for neutrally buoyant species (most nanoparticles)
- Optically opaque samples can be measured.
- Through-wall non-contact operation possible.

To date, backscattered ultrasonic power has been measured for a variety of materials:

- BSA
- Dendrimers (4 nm)
- TiO_2 colloids (4 nm)
- Polymer beads (as small as 40 nm)
- Carbon nanotubes
- Perfluorocarbon emulsions
- Beta cells
- Murine embryonic stem cell aggregates (spheroids)
- Rat and human Islets of Langerhans

Acoustic Backscatter

Bursts of ultrasonic energy in a narrow frequency band are both launched into the suspension by, and the backscatter detected by, a transducer in the chamber wall (or outside of an acoustically transparent wall). In the long wavelength limit, $\lambda >> a$ where λ is the acoustic wavelength and a is the particle radius, a particle can be modeled as a fluid sphere. The backscattered pressure wave $p_s(r)$ from a particle a distance r to the transducer, due to an incident plane wave $p_i(r)$, follows:

$$\Phi = \frac{rp_s(r)}{p_i(r)} = \frac{1}{3}k_0^2 a^3 \left[\frac{\kappa_1 - \kappa_0}{\kappa_0} - \frac{3(\rho_1 - \rho_0)}{2\rho_1 + \rho_0} \right]$$

compressibility density

where

$k_0 = \omega/c = 2\pi/\lambda = 2\pi f/c$, where c is the sound speed in the medium
κ_1 and κ_o are the compressibilties of the particles and the medium
ρ_1 and ρ_0 are the densities of the particles and the medium
Φ is called the angular distribution factor (related to the scattering cross section by $\sigma = |\Phi|^2 / \pi a^2$).

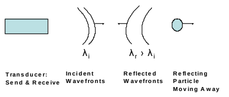
The terms in the brackets represent the compressibility and density contrasts between the particle and the fluid medium. If there is no contrast, the wave could not distinguish the particle from the medium and there would be no backscatter. This scattering strength is proportional to the square of frequency and the cube of particle radius.

Doppler Shift

In the USPD system the particles are measured while in motion. This motion can be due to:

stirring: necessary for negatively buoyant particles

acoustic streaming: movement away from the transducer due to nonlinear effects of large acoustic fields and large field gradients; similar to electromagnetic radiation pressure

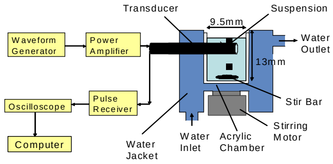


Doppler-shifted backscattered energy from a moving particle

The backscattered energy is detected at frequencies that differ from the original because of the Doppler effect associated with the motion of the particles. Placing the backscattered signals at frequencies differing from the interrogating frequency greatly simplifies their measurement. The incident and backscattered signals can be separated by Fourier analysis despite their huge dynamic range difference.

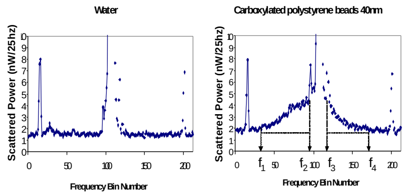
USPD System Overview

In the current USPD system, a 1.2 ml sample is placed in a temperature controlled acrylic test chamber that can be stirred to suspend the particles. The transducer, seated horizontally and usually flush with the wall (shown below in another position used for self calibration), injects a series of tone bursts at 16 MHz into the sample. This ultrasonic energy is focused by a lens into a small volume 1.6 mm into the fluid. The ultrasonic field and its gradients generate acoustic streaming away from the transducer in this focal volume. The incident and Doppler-shifted back-scattered energy from the particles returned to the transducer are conditioned and sent to a LeCroy 6030 digital oscilloscope for processing.



USPD system arrangement and test chamber

The signal from the transducer is converted to a power spectrum displaying backscattered power *P* in 25-Hz wide bins *vs.* frequency f by an FFT. Power outside the main peak at 16 MHz (the interrogating signal) is that which is backscattered from the particles and is proportional to their concentration.



Average spectra: Water (no signal) and 40 nm carboxylated polystyrene beads (Polysciences Inc.)

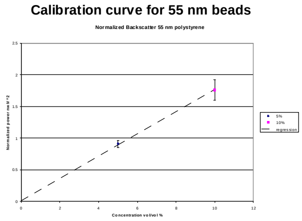
The total signal is the sum of powers over frequencies above and below the main peak representing power backscattered from particles moving towards and away from the transducer:

Backscattered Power = B $= \Delta f \sum_{f_1}^{f_2} P(f_i) + \Delta f \sum_{f_2}^{f_4} P(f_i)$

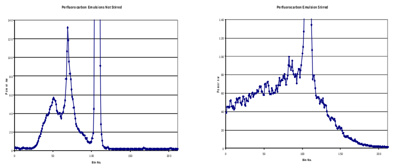
This backscattered power (typically ten to hundreds of nanowatts) is proportional to the total volume of particles in the sample. This power is proportional to the concentration C and the square of the angular distribution factor. The proportion-ality constant A is a function of incident signal power, system noise, fluid flow properties, etc. The power vs. concentration curve (the calibration curve) is then:

$$B = A\,\Phi^2\,C$$

Calibration curve for 55 nm beads

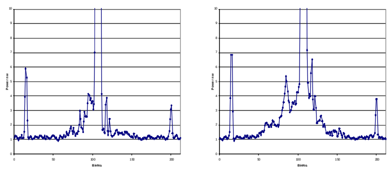


180 nm (nom.) Perfluorocarbon Emulsion 2.5% vol/vol Size Measurement



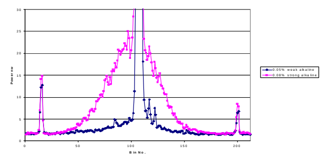
Strong backscatter is observed. Multiple peaks in non-stirred average spectrum (left) suggests two particle sizes. This was confirmed by Nanotrac® (Microtrac Inc.) measurements.

4 nm Dendrimers 5% wt/wt



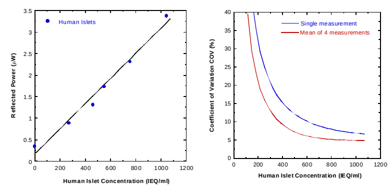
Preliminary spectra for 4 nm STARBURST® PAMAM Dendrimers; Ethylenediamine CORE, Tris SURFACE by Dendritic Nanotechnologies, Inc. show relatively strong backscatter both without (left) and with stirring (right).

Carbon Nanotubes



Backscatter increases strongly with alkalinity for stirred carbon nanotubes. This effect is much stronger than can be explained by the concentration difference.

Precision: Human Islets Example



Backscattered power is linear with concentration of human islets. The standard deviation for measurements with human islet regression calibration is less than 10% for concentrations as low as approximately 600/ml for a single measurement and as low as about 400/ml for four replicate measurements of 250 spectra (32 minutes)

CONCLUSIONS

The USPD system has detected backscatter from a wide range of particles as small as 4 nm, using a single transducer. Special test volumes are not required.

Concentration measurements have been made with biological samples and beads down to 40 nm diameter. Similar measurements with sub 10-nm particles appear possible.

Preliminary measurements with perfluorocarbon emulsions suggest that the system may be able to measure particle size distribution.

Measurement of particle compressibility may be possible, potentially opening a window on the physical properties of nanoparticles.