Ultrasonic Pulsed Doppler (USPD): A Backscatter Technique for Characterization of Particles and Nanoparticles

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Introduction

Principles of operation

- Ultrasonic backscatter
- Focused transducer
- Very small sample volume (<< 1 mm^3)
- Particle motion by
  - stirring or
  - process flow or
  - induced by interrogating signal
- Doppler-shifted backscattered signals
  - avoids clutter
  - provides large dynamic range

Advantages

- High concentration and/or opaque samples
- Single small probe transducer:
  - Can be incorporated into existing equipment
- Through-wall non-contact operation possible
- Special sample volumes not required
- U.S. Patent No. 7,543,480; two others pending

Measurements

- Concentration
- Particle Size
- Particle Compressibility
- Flow velocity
- …

Particles studied:

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

Rayleigh Acoustic Backscatter

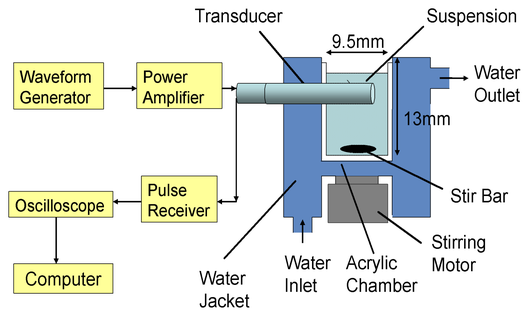
$$\Phi = \frac{r p_s(r)}{p_i(r)} = \frac{1}{3} k_0^2 a^3 \left[\frac{\kappa_1 - \kappa_0}{\kappa_0} - \frac{3(\rho_1 - \rho_0)}{2\rho_1 + \rho_0} \right]$$

compressibility contrasts — density contrasts

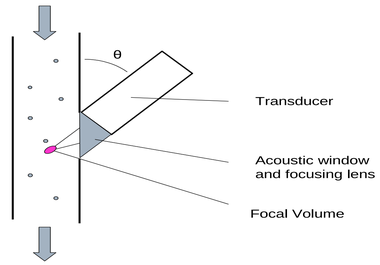
a is particle radius a << λ
$k_0 = \omega/c = 2\pi/\lambda = 2\pi f/c$, c is the sound speed in the medium
κ_1 and κ_o are the compressibilties of the particles and the medium
ρ_1 and ρ_0 are the densities of the particles and the medium
Φ is the angular distribution factor (related to the scattering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

USPD System Overview

Laboratory test chamber

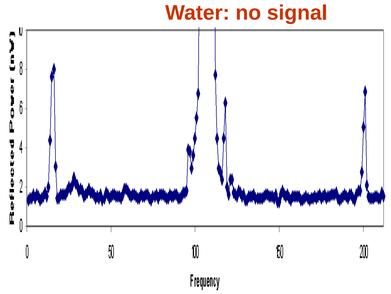


In-line particle monitoring

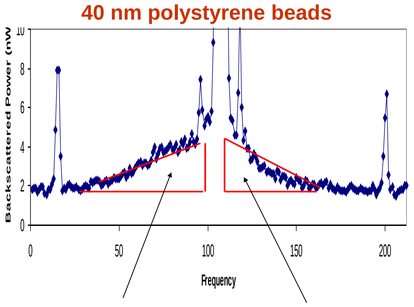


Concentration Measurements with Backscattered Power Spectra from Stirred Suspension. Large main peak is 16 Mhz interrogating tone burst.

Water: no signal



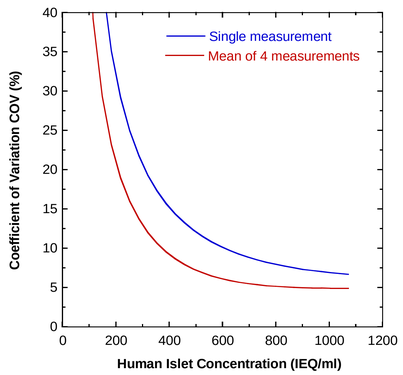
40 nm polystyrene beads

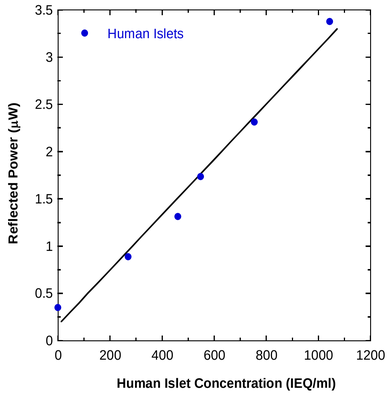


Backscattered Power = B $= \Delta f \sum_{f_1}^{f_2} P(f_i) + \Delta f \sum_{f_2}^{f_4} P(f_i)$

Concentration = C x B / Φ^2

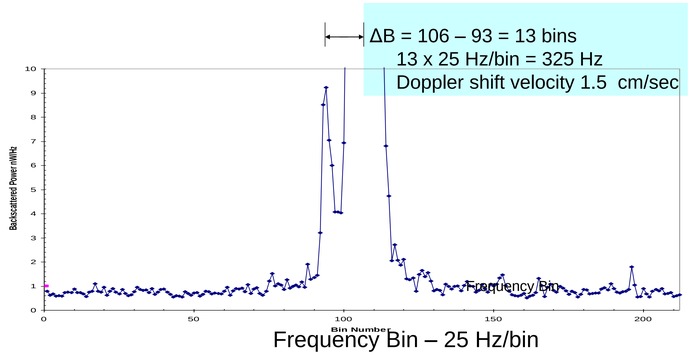
Precision: Human Islets Example





Particle Size Measurement

Interrogating ultrasound accelerates particles away from transducer by streaming or related phenomenon. Spectral peaks show Doppler shift representing velocity from which particle size can be inferred. Center frequency 16 Mhz.

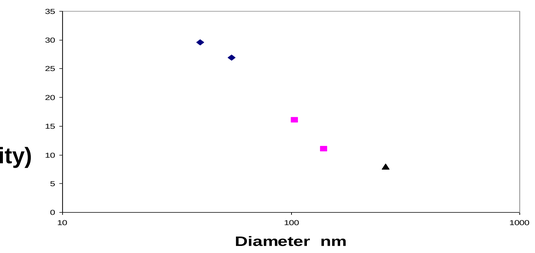


Frequency Bin – 25 Hz/bin

Size Measurements, Five Particles
Calibration of peak position vs. size

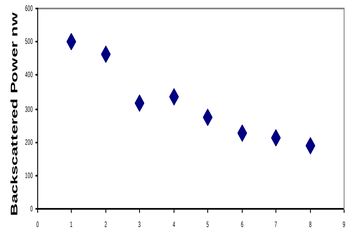
ΔB = **Bins from 106**

(frequency shift &velocity)

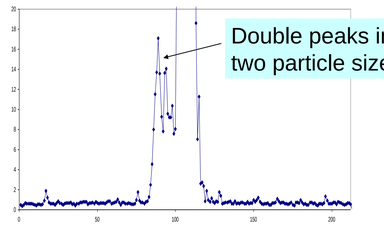


Particle Frangibility: Particles appear to break in two as backscatter decreases and two Doppler peaks appear.

Backscatter drops by factor of two



Sizing spectrum after exposure to ultrasound indicating two particle sizes



Double peaks imply two particle sizes.

Protein (BSA) Expansion with drop in pH
Backscatter increases with molecular size.