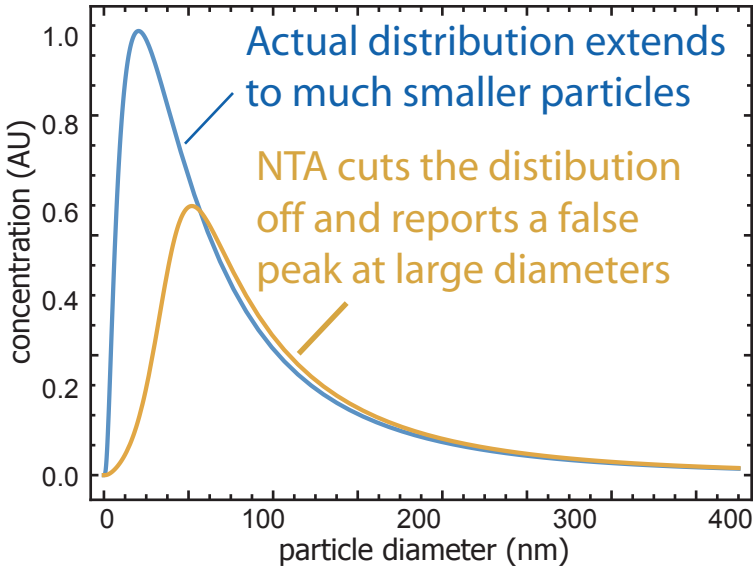
Spectradyne®
Particle Analysis

Where's my peak?

Nanoparticle tracking analysis vs. resistive pulse sensing

Nanoparticle tracking analysis (NTA) is a tool used for the measurement of nanoparticles suspended in solution. It works by illuminating a sample with a laser, and monitoring the image generated by the scattered light from the particles. As the particles move, due to Brownian motion, the motion can be monitored in time, and this motion can be analyzed to extract the number and diameter of the particles in the suspension. NTA however suffers from two distinct drawbacks: First, NTA relies on strong contrast between the index of refraction of the particles and that of the solution. Second, NTA has significant difficulties measurring broad, polydisperse solutions.

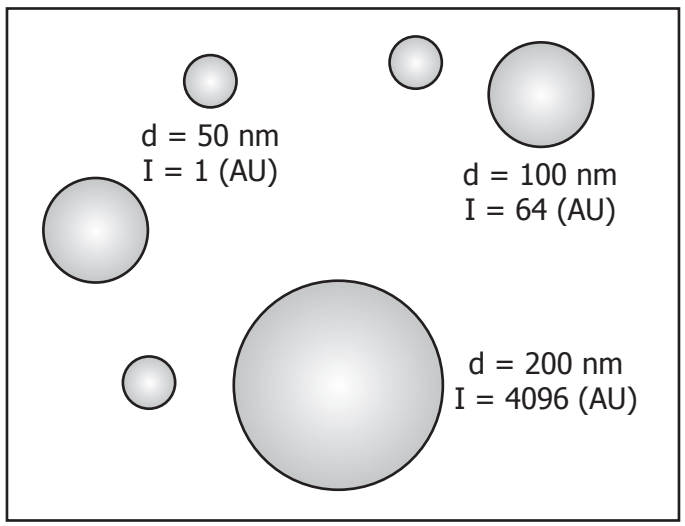


A common problem associated with NTA is that, when challenged with a polydisperse mixture of particles, it reports a peak in the distribution of particles when in fact no such peak is actually present. The reason for this is due to how NTA works. For particles smaller than a few hundred nanometers, **Rayleigh scattering** determines the intensity of the scattered light used to monitor the moving nanoparticles. This intensity scales inversely with the illuminating wavelength to the fourth power, but more importantly, it scales with the particle diameter to the **sixth power**. This can be seen in the formula for the scattering cross-section:

$$\sigma = \frac{2\pi^5}{3}\frac{d^6}{\lambda^4}\left(\frac{n^2-1}{n^2+1}\right)^2$$

Here **n** is the particle's index of refraction; note that if n is close to 1, as with biological particles, the cross section can become very small. The scattered light intensity does not directly provide the diametric measurement; that is instead extracted from the particles' Brownian motion, which allows extraction of the particles' hydodynamic radii.

As a result of the diameter to the sixth power dependence, the light intensity scattered from larger particles is much higher than that from smaller particles. NTA can then miss the much dimmer small particles, and thus mis-report the relative abundance of small compared to large particles.This is illustrated schematically in the left figure below, which shows the relative scattering intensity for three different particle diameters.



This effect has been reported in the published literature (see Ref. 1), and the figure above, adapted from Ref. 1, shows how this can affect the measured particle distribution, where the blue curve shows the true particle distribution, and the orange curve shows what NTA might report, assuming that NTA over-reports larger particles in proportion to their scattering cross-section. This creates a false peak in the distribution, due to the increase of intensity with diameter, until the falling concentration of particles at larger diameters overwhelms this effect.

Resistive pulse sensing (RPS), as employed in Spectradyne's unique microfluidics-based nCS1™, by contrast detects and measures each individual particle by electronic means, avoiding the size and index contrast challenges of NTA-style measurements. Every particle has equal weight in the statistical distribution, and RPS therefore reports the true distribution of particles. At Spectradyne, **every particle counts**™.

1. E. Van Der Pol et al., "Optical and non-optical methods for detection and characterization of microparticles and exosomes," J. Thromb. and Haem, 8: 2596–2607 (2010)

  email: info@spectradynellc.com