Detecting Nanoparticles with Phase-Sensitive Interferometry

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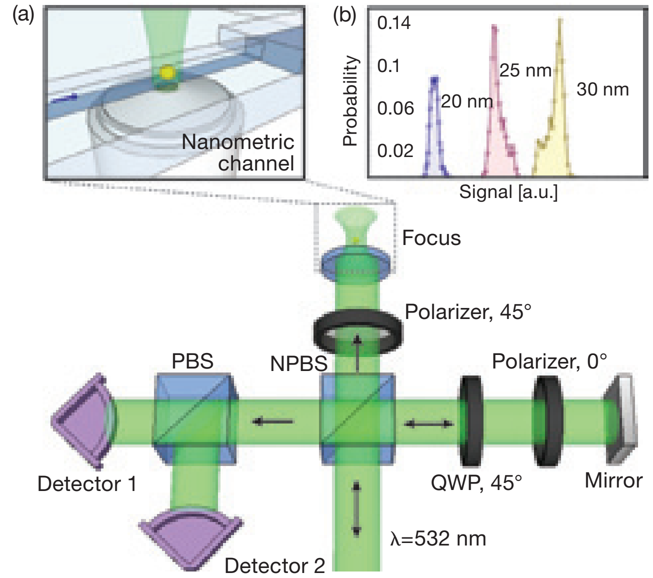
As we learn more about the effect of atmospheric nanoparticles on climate change[1] and human health,[2] careful monitoring of these particles becomes crucial. Nanoparticles appear as pathogens in bioterrorism[3] and as contaminants in manufacturing processes. In medicine, metallic nanoparticles can be used as cancer-fighting agents.[4] An effective measurement system needs to be sensitive to small, single particles. If real-time detection is needed, the scheme should not require labeling the target particles with fluorescent molecules.

Elastic light scattering is convenient for label-free detection. Small particles scatter light only weakly, but phase-sensitive interferometry can greatly increase measurement accuracy. Amplitude and phase decoupling usually relies on heterodyne interferometry, in which a lock-in amplifier demodulates at a beat frequency between the reference and signal beams. Such detection systems tend to be large or electronically complicated due to their reliance on active optical elements, so deployment in the field or clinic is challenging.

We have recently developed an interferometric detection system that decouples amplitude and phase using two orthogonal, simultaneous measurements using passive optical elements. We have shown sensitivity to single 30-nm Au particles.[5] Light is focused on a nanometric channel etched in glass and filled with the particle solution. A particle takes about 1 ms to pass through the focus, scattering light as it goes. The light is collected with a dual-phase interferometer, as shown in (a) of the figure. The optical signal is combined with a circularly polarized reference beam, and a polarizing beamsplitter directs the two orthogonal polarizations on to two detectors. Since the relative phase between reference and signal differs by 90° at the two detectors, amplitude and phase can be decoupled.



Dual-phase apparatus and histograms of particle-detection events. (a) A microscope objective focuses light onto a nanometric channel, and particles flow past. Scattered light is collected by a dual-phase interferometer. (b) Histogram showing results from three different immobilized particles.

The amplitude of the collected signal indicates the size of the particle and contains material information. By collecting signals from many particles, we can construct histograms that represent the population of particles in a sample, as shown in (b) of the figure. In this experiment, three immobilized gold particles of different sizes are moved through the focus on a microscope coverslip. Decoupling amplitude and phase improves measurement precision drastically and effectively separates the peaks. The remaining width is due to electronic noise.

The microscope objective used to focus light on the channels can be replaced with an approximately hemispherical lens called a numerical aperture increasing lens (NAIL) along with a small aspheric lens. Since the NAIL is only a few hundred microns in diameter, it provides even more scalability opportunities. The dual-phase system is useful wherever label-free detection is necessary at a single-particle level. That includes samples with very low concentrations of contaminants, like ultrapure water in semiconductor manufacturing, or in medical studies in which species populations must be characterized. The simplicity and scalable nature of the apparatus makes field deployment feasible for biodefense or atmospheric monitoring. ▲

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