Spectral Scattering Imaging for Single Particle Detection and Size Discrimination

Abdulkadir Yurt[1*], George G. Daaboul[2], Xirui Zhang[2], Bennett B Goldberg[4] and M. Selim Unlu[2, 3]

[1] *Material Science and Engineering, Boston University, Boston, MA 02215, USA*

[2] *Biomedical Engineering, Boston University, Boston, MA 02215, USA*

[3] *Electrical and Computer Engineering, Boston University, Boston, MA 02215, USA*

[4] *Physics Department, Boston University, Boston, MA 02215, USA*

Abstract—We investigate an optical imaging technique which is capable of detecting and size discriminating single nanoparticles which are below the diffraction limited resolution. Our technique employs wide-field detection and processing of interferometric signal due to the elastically scattered light and reference light at different visible wavelengths. The simulation and experimental results prove the technique to be promising for fast, high throughput and label-free bio-sensing application for nanoparticles in the range of 50nm-150nm in diameter.

Nanoparticle detection has gained considerable attention in biomedical research [1], material characterization [2], national security [3] and in other fields. Recently various optical techniques have been suggested for label-free single particle detection and size determination [4, 5]. Although these optical techniques offer sensitive detection many challenging issues are yet to be overcome such as low throughput, cost-effectiveness and reliability etc.

In this work we introduce a robust optical imaging method which is capable of detecting and size discriminating of nanoparticles that are very small comparing the wavelength of incident light. The technique is based on spectral measurement of interference of the elastically scattered light from nanoparticles and reflected reference light. The proposed optical setup comprises of a telescopic imaging system with a high NA achromatic objective and CCD in addition to several led sources at different peak wavelengths in Kohler illumination configuration.

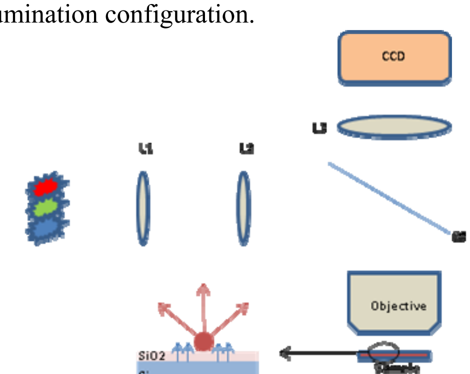

Figure 1: The Optical Setup. L: Lens, BS: Beam splitter. Brown arrows show scattered and blue arrows shows only normally reflected light from slab.

We first study the problem theoretically. A modified Mie Theory [6] is initially employed to calculate the scattered far-field and the result is compared with Rayleigh Theory (RT). It is seen that the error for size determination is less than 5% for particles less than λ/5 and it decreases for smaller particles. Therefore the RT is favored due to its simplicity and low computation cost. According to RT the polarizability of a spherical particle is:

$$\alpha = 4\pi\varepsilon_m r^3 \frac{\varepsilon_p-\varepsilon_m}{\varepsilon_p+2\varepsilon_m} \quad (1)$$

Where r is the particle radius, ε_p is the particle permittivity and ε_m is the medium permittivity. In the conventional dark field microscopy the detected signal which scales with $|\alpha|^2$ is quite small to be measured for particles below hundred nanometers whereas the interferometric signal scales with $|\alpha|$ thus decreasing detection floor and increasing dynamic range. Assuming an ideal Kohler Illumination scheme we deduce the intensity which each single nanoparticle sense is spatially coherent due to the quasi-homogenous field properties [7]. We apply Angular Spectrum Representation (ASR) [8] to calculate the detected fields with spectral background signal on the CCD due to particles on the focal plane of the objective.

In order to study the optical technique we model a low index material whose index is close to biological materials. We choose polystyrene (PS) spherical beads with diameters of 70nm, 100nm and 150nm as our test sample. The beads are sparsely dispersed on a wafer of which has a 500nm thick silica layer on top.

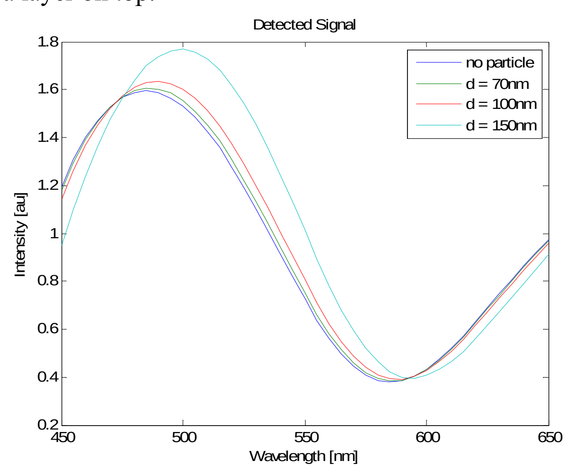

Figure 2: Simulated spectral response with different size of PS beads and bare substrate. (d: diameter)

As expected from RT the detected signal decreases for longer wavelengths. For experimental verification we choose three led colors at peak wavelengths: 470nm, 525nm and 625nm. We successfully detect and size-sort each of several thousands of particles within seconds. The simulation and experimental results also match quite well. The experimental SNR suggests that even smaller particles down to 50nm are within our detection range.

In summary, we report a high throughput, fast, cost-effective imaging technique for single particle detection and size discrimination. We expect the technique to be a promising tool for label-free sensing of small bioparticles such as virions and proteins in future.

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