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Biography

Hui Yang received B.S. and M.S degrees in Mechanical and Electrical Engineering from Xiamen University, China in 2006 and 2009, respectively, and Ph.D. degree in Microsystems and Microelectronics from Ecole Polytechnique Fédérale de Lausanne (EPFL), Switzerland in 2014. Between 2014 and 2015, she was a post-doctoral scientist in Laboratory of Microsystems in EPFL. She joined IMEC at Leuven, Belgium, in 2015. She is now working in the Department of Life Science and Imaging. Her research interests focus on optofluidics and in-vitro diagnostics.

Fast Detection of Single Nanoparticles in a Microfluidic Channel and Super-Resolution Imaging of Sub-Wavelength Nanostructures with Dielectric Microlenses

Conventional optical microscopes are limited by the so-called diffraction limit and can resolve features of around half of the wavelength of illumination λ. Besides, as the light collection capability of a standard microscope objective is limited by its numerical aperture (NA), only relatively large objects can be detected because the scattered light intensity decreases with decreasing size. While a microsphere is known to act as a focusing microlens, when it has a refractive index contrast relative to the fluid medium less than 2:1 and a diameter between several to tens of λ, a highly-focused propagating beam from the shadow-side surface of the microsphere is generated due to constructive interference of the light field. This beam is termed as "photonic nanojet" and has a sub-λ full width at half-maximum (FWHM) transverse dimension and typically is several λ in length. Due to the properties of the photonic nanojet, microspheres can be used to detect nanoparticles and generate images of the objects with super-resolution.

The first part of this presentation introduces the fast detection of gold and fluorescent nanoparticles, down to 20 nm in size, during their motion in water-based medium in a microfluidic device by using a conventional bright-field or fluorescence microscope. A very interesting predicted property of a photonic nanojet is that the presence of a particle, much smaller than λ and positioned within the nanojet, significantly enhances backscattering of the light through the microsphere [1]. In this work, an array of dielectric microspheres is firstly positioned at the bottom of a microfluidic channel. The microspheres based on melamine resin are electrostatically self-assembled in a microwell array template on a glass substrate. These microspheres with high refractive index (n = 1.68) act as microlenses, focusing the illumination light originating from the microscope objective into photonic nanojets, which expose the fluid medium within the microfluidic channel (see Figure 1). When a nanoparticle in the medium is randomly transported through a nanojet, its back-scattered light (for a bare gold nanoparticle) or its fluorescent emission is strongly enhanced and instantaneously detected by video microscopy. The working principle of this technique and the test results on gold and fluorescent nanoparticles are shown in Figure 2, respectively. The experimental intensity is found to be proportional to the area occupied by the nanoparticle in the nanojet and can be used for size-dependent detection of the nano-objects in the medium. The further potential of this technique is also demonstrated by detecting immunocomplexes conjugated to the gold nanoparticles (see Figure 3). In future, this technique, which dynamically exploits the unique properties of a photonic nanojet, could evolve in a general tool to detect objects of environmental or biological importance, such as even smaller nanoparticles, viruses, other biological agents, or single molecules.

Alternatively, the use of dielectric microspheres on top of the objects can achieve near-field focusing and magnification, which in turn results in the capability to resolve features beyond the diffraction limit. Once the microspheres are placed on top of the sample object, they collect the underlying sample’s near-field nanofeatures and subsequently transform the near-field evanescent waves into far-field propagating waves, creating a magnified image in the far-field, which is collected by a conventional optical microscope. Our previous work demonstrated the potential of the technique by resolving the structure of fluorescently stained centrioles, mitochondria, chromosomes, and the mitochondrial encoded protein expression in a mouse liver cell line [2]. This work indicated that the development of the photonic nanojet is essential to the super-resolution imaging capability of a microsphere, however, the exact link remained unclear. In our recent study, the role of the photonic nanojet for super-resolution imaging is discussed in a quantitative way [3]. A numerical study of the light propagation through microspheres of different size using the finite element method (FEM) is performed. This allows characterizing the photonic nanojet at the rear-surface of a microsphere and relating the microsphere’s theoretical magnification factor to the light focusing capability of the photonic nanojet (see Figure 4). Furthermore, a systematic experimental study is performed, using microspheres with different sizes to image linear test nanostructures. The experimental magnification factor and the point spread function that is analytically determined from the images allow evaluating the resolution of the optical system, which is shown to directly correlate with the calculated properties of a microsphere’s photonic nanojet. In conclusion, due to these physical insights, dielectric microspheres will be increasingly used in the future, providing a straightforward and robust tool to be integrated with a conventional microscope for super-resolution optical microscopy. Recent study shows that this technique can be used for scanning microscopy, this will be briefly introduced in the talk.

Due to the demonstrated performance and future potential of using dielectric microspheres integrated with microfluidics for optical detection and imaging, this talk will be of high importance to the interdisciplinary research community formed by the attendees of Optofluidics2017.

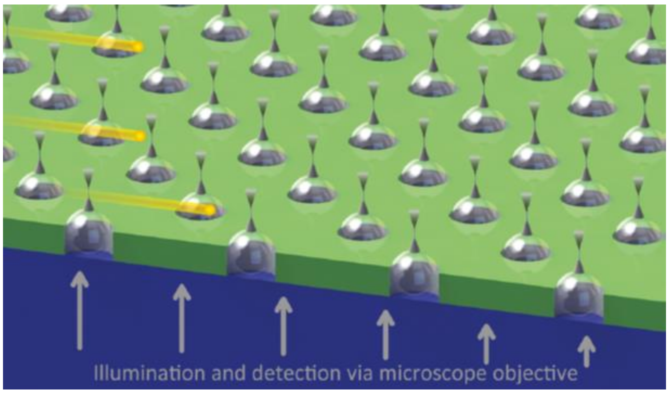

Figure 1. Schematic illustration of the optical detection of nanoparticles. Dielectric microspheres are patterned in a microwell template on a glass substrate and an optical microscope with low-NA objective is placed beneath the thus formed microlens array. Illumination light from the objective is focused by each microlens into a photonic nanojet. When a nanoparticle, randomly dispersed in a water-based medium, is transported through a nanojet, its backscattered light is instantaneously detected via the microscope objective.

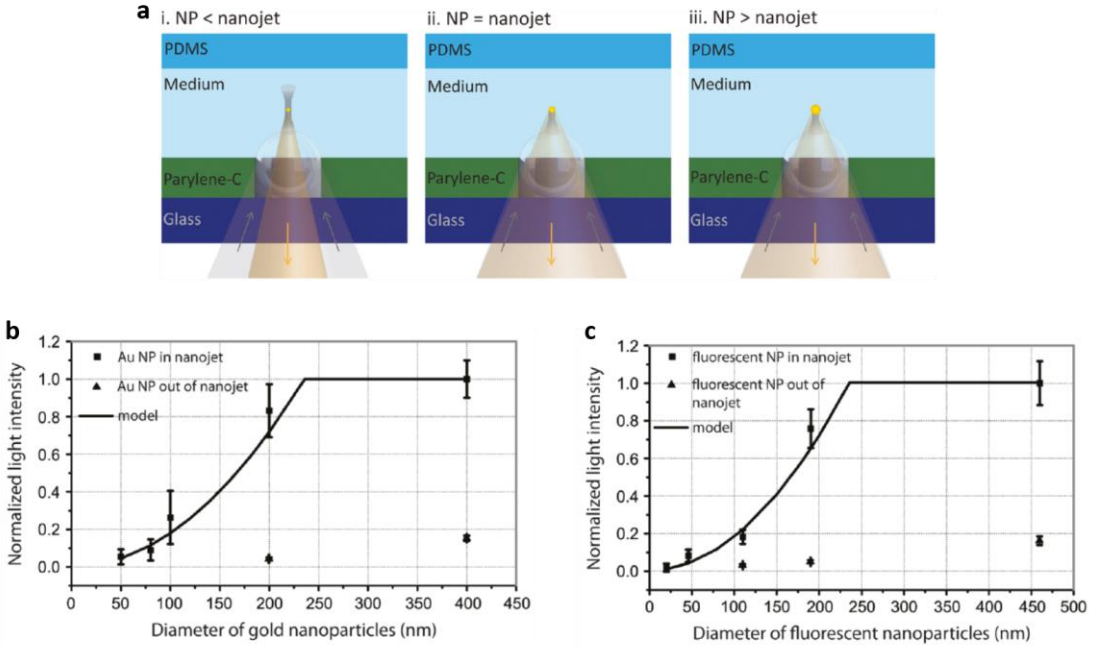

Figure 2. (a) Detection principle of the scattered/emitted light from a nanoparticle transported in a PDMS microfluidic structure. (i) The nanoparticle is smaller than the transverse dimension of the photonic nanojet and part of the illumination light is backscattered; (ii) the nanoparticle has the same size of the photonic nanojet, and all the light focused by the microsphere is backscattered; (iii) the nanoparticle is bigger than the nanojet and the backscattered light is not further enhanced. (b,c) Normalized backscattered light intensity of Au nanoparticles and fluorescent nanoparticles, respectively, positioned within and outside of a nanojet, as a function of the nanoparticle size. The full curve corresponds to a geometrical model, points represent the average from 20 measurements, error bars the variance.

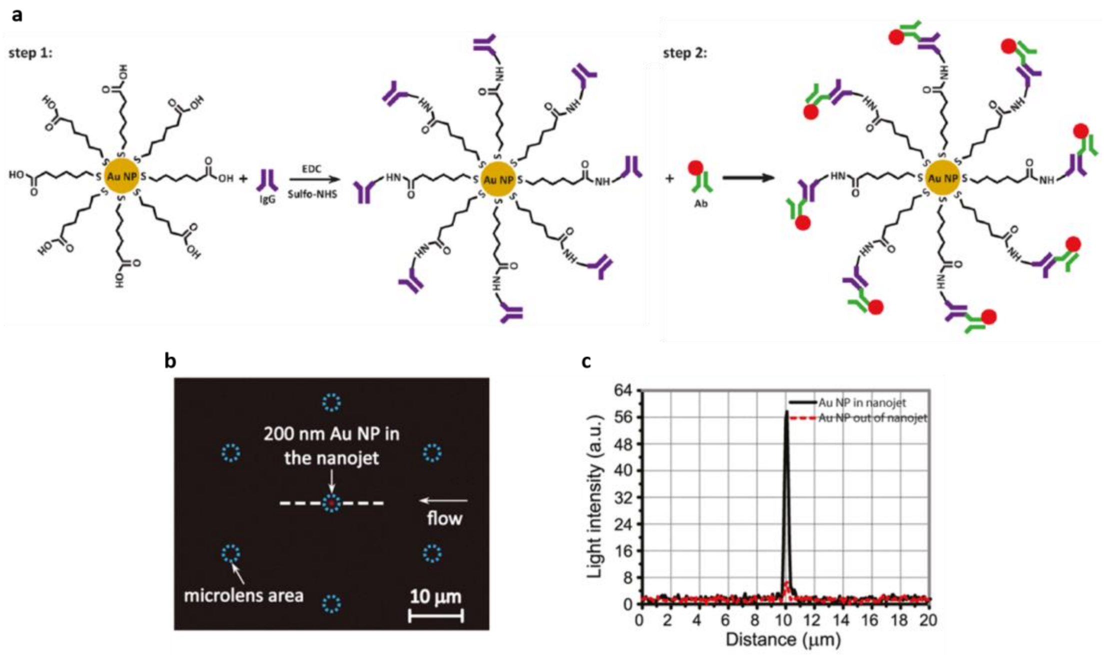

Figure 3. Detection of mouse IgG on functionalized Au nanoparticles using AlexaFluor647-labeled anti-mouse IgG detection antibodies, all spiked in PBS. (a) Schematic two-step conjugation protocol. (b,c) Microscopic image (b) and intensity profile (c) along the dashed lines in (b) for fluorescently labeled Au nanoparticles of 200 nm. These particles are also detectable when they are outside a nanojet, and the latter intensity profile is also plotted in (c) for comparison.

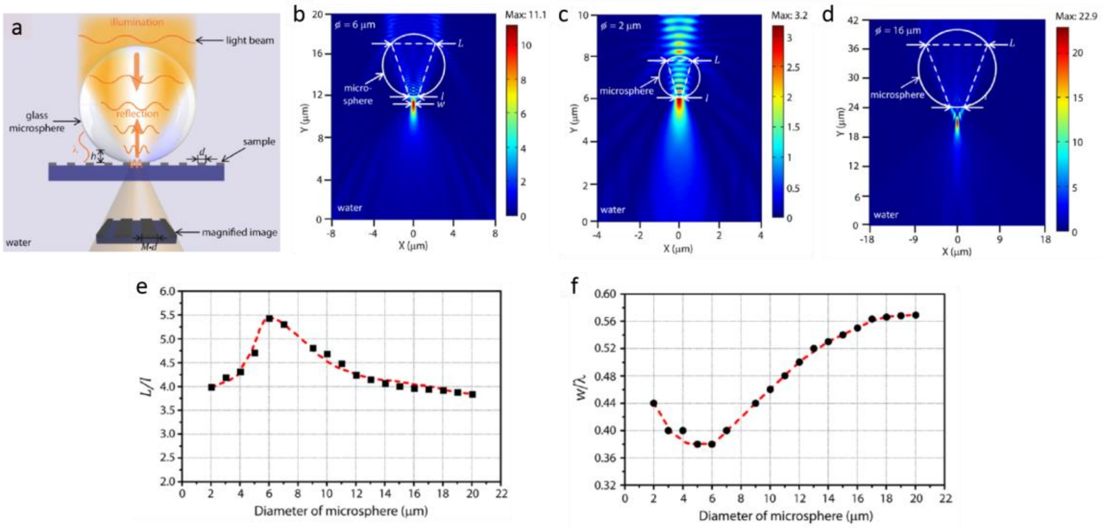

Figure 4. (a) When a microsphere is positioned on a grating structure with line width *d* and illuminated from the front, the light reflected by the grating allows detecting a virtual image with magnification factor *M*, when the distance *h* between the microsphere and the grating is small enough (of order of the illumination wavelength λ). (b,c,d) FEM simulation of the light propagation through a 6, 2 and 16 μm Ø barium titanate microsphere immersed in water, respectively. The linear region where substantial refracted light enters the microsphere at its front surface is referred to as *L*, while the width of the exiting beam at the rear surface is denoted as *l*; the waist of the

nanojet is referred to as *w*. (e) FEM simulation results of the light focusing capability of a microsphere, expressed by the ratio *L/l*, as a function of the microsphere diameter. The dots are obtained from the simulation, while the red dotted line is a guide to the eye. (f) FEM simulation results of the normalized waist of the photonic nanojet *w/λ*, as a function of the microsphere diameter. The dots are obtained from the simulation, while the red dotted line is a guide to the eye.

References

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