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The Plasmonic Ruler Goes 3D!

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Noble metal nanoparticles have distinct optical properties arising from localized surface plasmon resonance (LSPR). It is well-established that a LSPR spectrum depends strongly on the size and shape of the nanoparticles as well as on the distance between the nanoparticles.[1] The precise measurement of the interparticle distance-dependent LSPR spectrum has been the fundamental principle of many analytical methods in biology. These types of bioassays can be done with a large ensemble of particles either in homogenous solutions (i.e. colorimetric assays[2]) or on substrates.[3] Alternatively, the assay can be carried out through individual particles (i.e. single-particle-based LSPR). The single-particle-based LSPR technique has the advantages of high detection sensitivity, a good S/N ratio, low sample consumption, and multiplexing potential.[4]

Under a dark-field microscope, individual metal nanoparticles can easily be observed as they scatter light intensely and do not blink or photobleach.[5] When two nanoparticles are in close proximity, their plasmon resonances couple with each other and generate a light-scattering spectrum depending strongly on the interparticle distance. This effect has been used to create one-dimensional plasmon rulers, that is, two nanoparticles linked with (bio)chemical linkers. Under high-resolution dark-field imaging spectroscopy, distinct spectral shifts triggered by biomolecular binding events and/or biological processes can be measured based on their modulation of the linkers and in turn the distances of two individual plasmonic particles. This one-dimensional plasmonic ruler has been successfully used to detect DNA conformational change,[6] DNA bending[7] and RNA cleavage.[8]

Recently, writing in *Science*, Na Liu, Mario Hentschel, Thomas Weiss, A. Paul Alivisatos, and Harald Giessen have reported a more powerful plasmonic ruler, a 3D plasmonic ruler, where multiple plasmonic nanoparticles are put in a spatial arrangement. This 3D plasmonic ruler in combination with high-resolution plasmon spectroscopy and plasmon-induced transparency as well as high-order resonances offers a blueprint for optically determining the structural dynamics of single 3D entities.[9]

The emergence of this pioneering work is a result of the advances in nanofabrication techniques, theoretical simulation, and high-resolution spectroscopy techniques. Using high-precision electron-beam-based top-down fabrication techniques and layer-by-layer stacking nanotechnologies, the researchers fabricated a 3D plasmonic structure containing five gold nanorods (Figure 1). In their design, a nanorod is stacked between two pairs of parallel nanorods. The two pairs of parallel rods

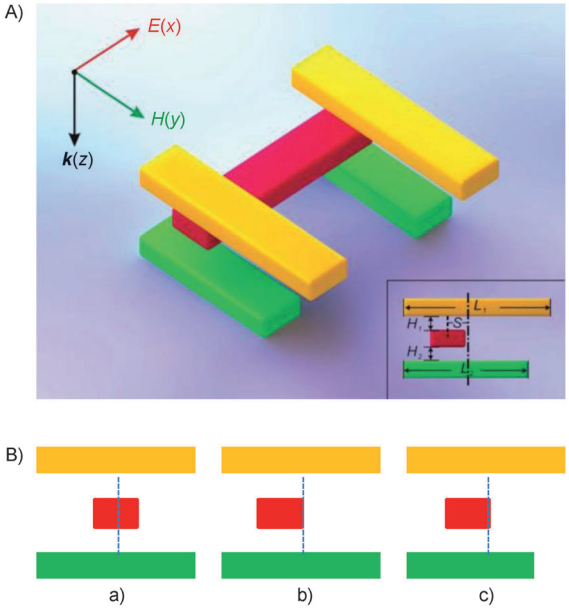

Figure 1. A) 3D plasmonic ruler. B) A series of samples with different symmetry. Reproduced with permission from the American Association for the Advancement of Science.[9]

are precisely controlled to have either equal or different lengths. The vertical distance of the middle nanorod to the top and bottom parallel rods and its distance to the symmetry axis of the bottom rod pair are also controlled precisely. The optical measurement of the system showed a strong coupling between the single nanorod and the two nanorod pairs that leads to generation of two sharp quadrupolar resonances in the broad dipolar resonance profile. This double plasmon-induced transparency enables high-resolution plasmon spectroscopy as evidenced by readily observable changes in the optical spectrum associated with any conformational change of the 3D plasmonic structure. This forms the basis for this 3D structure to be used to measure spatial conformation of complex macromolecular processes and biological processes, as well as their dynamic evolution.

To verify the plasmonic mode of the 3D structures of different configurations, the optical properties were measured by a Fourier-transform infrared spectrometer with electric field polarization parallel to the middle rod. The research team found

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that with a symmetry configuration (Figure 1 B-a) there is only a single broad resonance visible from the excitation of the dipolar plasmons in the single nanorod. When the symmetry is reduced, that is, when a displacement is introduced to the middle rod (Figure 1 B-b), and furthermore length difference of the two parallel pairs is introduced (Figure 1 B-c), excitation of the quadrupolar modes occurs, giving rise to two and three transmittance peaks, respectively. The use of this 3D structure for measuring spatial or structures changes relies on the high sensitivity of the quadrupolar resonance, that is, the sharp spectral features. The team has further confirmed that minute conformational changes in the 3D structure can give rise to an appreciable variation in the optical spectra, by experimenting and simulating the resonance with lateral displacement and vertical displacement of the middle rod. They conclude that several tens of nanometers displacement (both lateral and vertical) can give rise to significant spectral shifts.

The world's first 3D plasmonic ruler with nanometer-scale sensitivity to conformational changes can be a powerful tool for studying many soft-matter systems. Among many candidate analyte systems, studying nucleic acids related dynamic processes could be largely benefited from this 3D plasmonic ruler. For example, in transcription-factor–DNA binding events, dynamic details in terms of protein occupancy dependent DNA bending and protein dimerization upon DNA binding, and so forth, could be detected upon selective attachment of DNA or proteins to different nanorods. In addition, this 3D ruler could also be useful for identifying chromatin proteins that can bind and loop DNA fragments for high-order architectures. Spatial determination of genome frameworks is of great importance in determining nuclear functions such as transcription activation, insulation, or enhancer blocking, a central research topic in chromatin biology. Currently there are only limited experimental tools available to test genome organization.[10] In general, it is expected that real-time monitoring of the spectral changes will provide a direct measurement of biomolecules in the process of binding, reorganization, and organization. Rich information will be generated compared to conventional methods [e.g. gel mobility shift assays[11] and scanning force microscopy (SFM)[12]] that provide only a snapshot and an average approximation of what is occurring.

Despite the enormous potential of the 3D plasmonic ruler, a number of challenges need to be resolved before this 3D nanoruler can be in place for tailoring complex dynamic processes. One major challenge is to achieve selective attachment of the DNA or protein to specific nanorods in the 3D structure. Whether conventional electrochemically addressable functionalization of individual rods will offer a solution is a subject of further discussion. In addition, further improving the spatial resolution to several nanometer or subnanometer scale would be a great challenge. Success in that will further widen the application of the 3D ruler.

Keywords: gold · nanostructures · plasmonic ruler · plasmon spectroscopy · surface plasmon resonance

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