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COMMUNICATION

A gold nanoparticle-based SERS reporter that rolls on DNA origami template

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Abstract: Plasmonic nanostructures with distinct spatial configuration and geometry are of considerable significance because of their desired optical response. These optical responses have close relationship with the inter-particle parameters in plasmonic nanostructures. However, the precise control of the consecutive variation of these parameters remains a formidable challenge. Here, we demonstrate a gold nanoparticle (AuNP) -based plasmonic nano-reporter, in which a AuNP performs as a walker to stepwise roll directionally and progressively on DNA origami. Using another AuNP as a stator, the rolling of the AuNP reporter could generate the inter-particle distance variation, which would be monitored by surface-enhanced Raman scattering (SERS). Our method opens up a door to develop an optical reporter that monitoring inter-particle variations in plasmonic nanostructures.

Plasmonic nanostructures with distinct spatial configuration and geometry are of considerable significance since they are the key platforms for displaying the desired optical response and electromagnetic properties.[1] Because high stability and unique optical properties, gold nanoparticles (AuNPs) are the most studied metal nanoparticles for plasmonics.[2] The plasmonic properties of AuNP-based nanostructures are born with the plasmon oscillation. Among the typical factors to influence the plasmon oscillation such as geometric configuration between AuNPs, the inter-particle distance is of significant importance.[3] Hence, creation of well-ordered AuNP-based plasmonic nanostructures with precise inter-particle distance demands a big heap of control over the assembly of materials at the nanoscale.

Structural DNA nanotechnology exhibits great potential towards this goal.[4] Due to the well-established functionalization of AuNPs by thiol DNA (SH-DNA), DNA nanostructures has been employed as linkers or templates for the self-assembly of AuNP-based plasmonic nanostructures.[5] DNA origami nanostructures with precise addressability and custom designed shapes give rise to self-assemble discrete AuNP-based nanostructures.[6] Previous studies show that SH-DNA modified AuNPs are anchored onto the templates by hybridization of SH-DNA with capture part of staples in the DNA origami. Therefore, the distance and orientation between AuNPs are inherited by the relative sites of staples in the DNA origami templates.[7] Because most DNA origami templates are static DNA nanostructures, the plasmonic properties such as surface plasmonic resonance (SPR) and surface enhanced raman scattering (SERS) of these AuNP-based have been assured.[8]

In fact, a formidable challenge remains in precise control of the consecutive variation of inter-particle parameters in AuNP-based plasmonic nanostructures. Due to their controllable and precise motion in nanoscale, dynamic DNA devices may provide the possibility to solve the problem. In between, DNA walking devices behave a consecutive movement either triggered by DNA strands displacement or enzyme cleavage. An elegant example by Liu et al. demonstrated that DNA walking devices could drive the gold nanorods walking on DNA origami template, each step of which was in situ monitored by circular dichroism.[9] Herein, we demonstrate a AuNP-based dynamic plasmonic nano-system. Using one AuNP as a stator, the other AuNP performs as a walker to stepwise roll directionally and progressively on DNA origami. Motivated by strands displacement of DNA strands, the successive rolling of AuNP walker triggers a series of consecutive variation of inter-particle distance. This variation may lead to immediate spectral response changes that

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can be reported optically. Hence, the dynamic plasmonically coupled system is monitored by the successive alteration of SERS signals.

The rectangle DNA origami (100 * 70nm) was synthetized by folding a long single-stranded DNA (M13mp18) scaffold with a series of staple strands and specific capture strands (Figure S1). The stator is immobilized at one corner of DNA origami with the capture strands, whereas the roller with its track are specifically paved to impose directional rolling. Along the track, six anchor sites A–F are utilized to establish five rolling stations, which are evenly separated by 6 nm. Five binding sites B–F with identical footholds are extended from the origami. Each standpoint contains two parts: a binding segment (nine nucleotides, green) for hybridization with a roll strand of the roller as well as a toehold fragment (eight nucleotides, coloured), which is differently sequenced at different binding sites for achieving programmable reactions. At each station, the anchor site accommodates the size of roller to ensure their stable binding. Two AuNPs are selected as roller (yellow) and stator (red). They are fully covered with two kinds of SH-DNA strands, which contain segments for hybridization.

Figure 1 Schematic of the rolling system. Two AuNPs are assembled parallel to each other on a rectangle DNA origami template. The yellow AuNP represents the 'roller' while the red AuNP represents the 'stator'. The rolling track consists of six anchor sites (A–F) extended from the origami surface to define five rolling stations. The distance between the neighbouring stations is 6 nm, which also corresponds to the step size. On addition of removal strand C'' and blocking strand A', two toehold-mediated strand-displacement reactions occur simultaneously, the roller implements one step forward. By five steps forward, the roller arrives at the station.

After the anchor sites C-F are deactivated by respective protecting strands (indigo, blue, purple, black), the AuNP-rollers located at the start site A and B by hybridization with the protuding part of the staples. To drive the AuNP-rollers rolling forward, blocking and removal strands are specifically designed. As illustrated in Figure 1, the blocking strand A' hybridize fully with the protuding part of the staples to dissociate one foot of the AuNP-roller. Simutanously, the removal C'', which is fully complementary to the protecting strands, drives the AuNP-roller to stand on the anchor sites of B and C. Either dissociation from the former anchor site or association to the new sites are initiated via strand-displacement reaction. What needs to be emphasized is that blocking strands would eliminate the roller to go backwards. It is crucial to underline that during the process of dissociation from A and attaching to C, one set of the roller's feet stay bound to site B, in case of the roller off the track. When successive removal and blocking strands are added to the system, roller AuNP executes stepwise movements by programmable attaching (detaching) its feet on (from) the track through base pairing (de-hybridization) with the anchor sites (coded A–F in Figure. 1).

Figure 2 Schematic illustration and AFM images of rolling device. (a) The start station and distance statistic histogram, (b) the middle station and distance statistic histogram, (c) the final station and distance statistic histogram.

Schematic and AFM images in Figure 2 demonstrates the rolling device based on the track of the rectangular origami (Figure S2). When the stator AuNP and roller AuNP were binding to the capture location and anchor site A, B on the origami, they were at start station. The vertical distance of central point between two AuNPs was zero at this state (Figure 2a). On the rectangular origami templates, AuNP-dimers were clearly parallel and discrete in uniform. We counted 100 dimers to get an overall statistics and found most of them had the ideal distance consistent with the theoretical arithmetic. This geometrical alteration benefited from the well-designed sequence with acceptable secondary structure, structural integrity and excellent rigidity of the

rectangle origami template. Moreover, the low level of incorrect products indicates minimal crosstalk between different kinds of DNA molecules present in the reaction medium. The stepwise rolling was fueled by toehold-mediated strand-displacement reactions along with introduced removal and blocking strands. When the roller AuNP rolled onto the anchor site C and D, the average distance of the midpoint between two AuNPs was 12 nm measured by AFM, which validated the successful rolling on the rectangular DNA origami platform (Figure 2b). The rolling machine continued to function by import removal strands E', F' and blocking strands C', D' to reach the final station. AFM images and statistical data in Figure 3c could reflect the tactics. Distance further expanded to 26 nm and the rolling yield of AuNP-dimers was 37% after 4 rolling procedures.

In order to further verify the versatility of the strategy and reflect the change of SERS signal, we untilized two 15 nm AuNPs as the stator and roller. They were anchored to the origami templates as the same approach (Figure 3a and S3). Because the 15 nm AuNPs have larger size, the step was enlarged to 16 nm. After the removal and blocking strands were added, the rollers were drived onto the anchor site C and D (Figure 3b) and the anchor site E and F (Figure 3c). All circumstances can be characterized by AFM discretely and intuitively. These results showed that the DNA origami and strand displacement reaction are effective for the placement and movement of AuNPs.

Figure 3 Schematic illustration and AFM images of 15 nm AuNPs rolling on the track of the rectangular DNA origami.

Rational reconfigurable organization of metallic building blocks with active media can be tailored to exhibit novel plasmonic properties. Among them, SERS of metallic materials has attracted a lot of attention in optical properties study, as proposed theoretically and verified by experiment. Previous studies showed that AuNP assemblies in proper distance would generate stronger electric intensity than individual AuNP. The distances between AuNP rolling system is broaden enlarge from 13 to 53 nm as the rolling process (Figure S4). Hence, the rolling AuNP would act like a SERS reporter which may generate and vanish the coupling of plasmons between AuNPs. We employed 4-Mercaptobenzoic acid (4-MBA) served as a Raman-active molecule which could covalently attached the AuNP-dimers by the strong interaction of Au-S bond. The frequency of 1580 cm^{-1} and 1075 cm^{-1} in the SERS spectra were clearly attributed to 4-MBA. Compared to individual AuNPs samples (black curve), the AuNP-dimers at start station (red curve), middle station (blue curve) and final station (purple curve) obtained different intensity of enhanced signals under SERS detection with the accumulative total of ten times (Figure 4). Taken the peak at 1075 cm^{-1} for example, the SERS signal intensity reduced from 1418.2 $\pm$ 91.9 to 479.4 $\pm$ 46.1 a.u. with the rolling movement in the nanostructures (Figure S5). This can be explained by the elimination of hot spots which generated by the small gaps between closely spaced AuNPs.

Figure 4 Typical SERS spectra of 4-MBA attached to AuNP-dimers in start, middle and final station based on DNA origami.

In summary, we demonstrated a AuNP-based plasmonic nano-reporter, in which the AuNP performs as a walker to stepwise roll directionally and progressively on DNA origami. Using another AuNP as a stator, the rolling of the reporter could generate the inter-particle distance variation, which would be monitored by SERS. The concept of precise controlling the nanoscale movement of AuNP enabled by DNA nanotechnology will prod profound significance in multiple disciplines. First, the nano building blocks can stride different distance authorizing the detection of distance dependent interaction attainable. Second, the rollers can stride along multidirectional routes and perform different landscapes on 2D or 3D templates. Third, the new generation of artificial synthetic machine works not only as a dynamic element to carry out mechanical movement but also as an optical reporter, which can be envisioned in situ to reflect the shape changes at nanoscale. This noninvasive, stable and all-optical approach stimulates the emitter with fully coordinated motion at the nanoscale accuracy and leverages distance-dependent interaction between single emitters and plasmonic nanoparticles into spacious scope. Our reporter concept also expands an exciting prospect of generating functional large-scale nanodevices that coordinate biochemical, electrical and optical landscapes for active transport and information processing.

Experimental Section

All short oligo-DNA strands were purchased from Sangon (PAGE purification). SH-DNA was purchased from Takara (high-performance liquid chromatography purification). 5 nm and 15 nm AuNPs were obtained by BBI. All of chemicals were supplied by Sigma. M13mp18 ss-DNA was purchased from New England Biolabs.

5 μL and 1 μL 100 nM SH-DNA was respectively added to 100 μL 5 nm and 15 nm AuNP solution in 0.5×TBE buffer (89 mM Tris, 89 mM boric acid, 2 mM EDTA, pH 8.0). The mixtures were incubated at room temperature for four hours. 10 μL of 3 M NaCl was added slowly into the reaction solution for 4 times in 2 hours with the final concentration of NaCl reached 300 mM. Then the solutions were allowed to sit at 25 °C overnight. The DNA functionalized 5 nm AuNPs were purified by repeated centrifugation for four times (12000 rpm, 30min) and 15 nm AuNPs by repeated centrifugation for four times (9000 rpm, 30min). Each time, the supernatant was carefully removed and then the AuNPs were resuspended in a 0.5×TBE buffer to get rid of excess SH-DNA. The concentration of AuNPs was measured using UV-Vis spectroscopy.

DNA origami template was obtained in a one-pot construction, in which 2.5 nM of M13mp18 DNA was mixed with 25 nM of staple and capture strands in a 1 × TAE/Mg^{2+} (40 mM Tris-HCl, 20 mM Boric acid, 2 mM EDTA and 12.5 mM magnesium acetate, pH 8.0) buffer. They were annealed from 95 °C to 20 °C which was slowly decreasing the temperature at a rate of 1 °C min^{-1}. We added 10 times excess of the protecting strands c, d, e and f into the origami mixture and incubated at room temperature for 0.5 h to seal off the anchor sites C, D, E and F. To remove the extra strands, the prepared DNA origami was filtered by the 100 kDa (MWCO) centrifuge filters for four times.

The stator-AuNP and roller-AuNP were mixed with the origami template at a molar ratio of 3:3:1. The assembly was performed by annealing the samples from 45 °C to 30 °C four times and then cooling to 4 °C. A drop of 5 μL mixture was deposited onto freshly cleaved mica for 5 minutes. Then, the sample was washed by water and blow-dried. It was then mounted on a J scanner of AFM and imaged in tapping mode.

Small amount with high concentrations of the blocking chain A' and removal chain C' were added to the above mixture at 37 °C for 4h to drive the AuNP rolling. Along with other blocking and removal strands adding into the solution, the AuNP rolled 4 steps to the final location. The solutions at middle station and final station was performed by AFM, too.

The samples at start, middle and final states were incubated on a 5mM 4-MBA (99% ethanolic) solution for 2 h followed by a thorough rinse on pure ethanol. The SERS spectra were recorded by a confocal Raman microscope (In Via, Renishaw, England) equipped with a 633 nm He-Ne laser. A 100× objective, resolution grating of 1800 grooves, and a slit of 100 μM were used on all measurements. The spectra ranged from 1000 to 1850 cm^{-1}. For all measurements, the experimental parameters are as follows: excitation wavelength 633 nm, objective 20×, laser power 0.08 mW, acquisition time 10 s.

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Layout 1:

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