A pH-triggered Reversible Aggregation of Gold Nanorods Modified with Denatured Bovine Serum Albumin

Changqing Zhu,* Xin Wang, Yunsheng Xia, Peng Wang, and Yan Li
Anhui Key Laboratory of Chemo-Biosensing, College of Chemistry and Materials Science, Anhui Normal University, Wuhu 241000, P. R. China

(Received May 29, 2008; CL-080543; E-mail: zhucq@mail.ahnu.edu.cn)

Water-soluble gold nanorods have been endowed with satisfying chemical stability and functionality through successfully surface modifying with chemically reduced bovine serum albumin. A pH-induced and highly reversible aggregation has been performed with obvious absorption wavelength shifts, allowing monitoring pH in the wide range of 4.2 to 9.4.

Gold nanoparticles (GNPs) are promising building blocks for assembly into nanostructured functional materials because of their size- and shape-dependent optical and electrical properties.[1] Compared with similarly sized spherical gold nanoparticles, rod-shaped gold nanoparticles (known as gold nanorods: GNRs) can provide additional benefits for biochemical sensor applications. In addition to a transverse surface plasmon band (TSPB) at about 520 nm, GNRs possess another characteristic absorption band at a longer wavelength assignable to the longitudinal surface plasmon band (LSPB). The latter not only could be tuned by adjusting the aspect ratios from the visible to the NIR region but also is extremely sensitive to changes in the dielectric properties of the surroundings of the GNRs.[2]

It is well known that the cetyltrimethylammonium bromide (CTAB) layer,[3] essential for fabrication and stabilization of GNRs, is toxic to every biosystem.[4] Thus, the following surface modification to remove CTAB becomes a key technique to realize practical applications of GNRs in biochemistry. Up to now, silica,[5] poly(ethylene glycol) (PEG),[6] and egg phosphatidylcholine (PC)[7–10] have been used as alternative stabilizing agents. Also, it was noted that DNA, a macrobiomolecule, has recently been used to modify GNRs, which demonstrated specific organization of GNRs into anisotropic 3D aggregates through DNA hybridization.[11] Herein we present another strategy to produce biocompatible GNRs by conjugating denatured bovine serum albumin (dBSA) to the surface of GNRs. The resulting GNRs display high chemical stability. Meanwhile, a pH-induced and highly reversible aggregation with obvious spectral change has been performed, providing an ideal pH-sensing scheme in the wide pH range of 4.2 to 9.4.

The GNRs were obtained using a seed-mediated growth method described by Nikoobakht and El-Sayed with a little modification,[12] followed by centrifugation purification. The dBSA was prepared by chemically treating BSA (Sigma) with $NaBH_4$, based on a previous literature report.[13] Then, a measured amount of dBSA solution was added into the purified GNRs with stirring to obtain dBSA-modified GNRs (see Supporting Information[14]).

The raw GNRs are stable in the original, high-CTAB content solution but become unstable and lose characteristic absorption when CTAB is removed from the solution. On the contrary, the dBSA-modified GNRs remain well-suspended for a month even after removing CTAB (Figure S1). MicroRaman spectra reveal that the CTAB bilayer has been displaced by dBSA (Figure S2), which should account for the satisfying chemical stability of the resulting GNRs.

The absorption spectra of the dBSA-modified GNRs in the range pH from 4.2 to 9.4 are showed in Figure 1. At initial pH 4.2, two characteristic absorption bands, TSPB and LSPB, appear at 522 and 637 nm, respectively. Obvious spectral change occurs to the latter when the pH of the system is changed to 9.4. With addition of different amounts of NaOH solution, the absorption peak at 637 nm gradually decreases in intensity and broadens in profile, accompanied with a peak blue-shifted to much shorter wavelength (607 nm) in a short time, indicating the formation of huge GNR aggregation.[15] Interestingly, when the pH changes from 9.4 back to 4.2 with addition of different amount of HCl solution, the peak at 607 nm increases and red-shifts almost to its original position. The spectral reversible recovery reflects that the dBSA-modified GNRs are not only extremely sensitive to the environmental changes but also stable enough to endure a certain amounts of acids and bases.

The corresponding transmission electron microscopy (TEM) images in the above-mensioned pH range are shown in Figure 2, which illustrates a pH-induced aggregation/dispersion of dBSA-modified GNRs. At pH 4.2, the dBSA-modified GNRs with average aspect ratio of 2.5 are well-dispersed (Figure 2a). At pH 9.4, the GNRs undergo an aggregation (Figure 2b). With a decrease of the pH back to 4.2, the GNRs become well dispersed again (Figure 2c). No doubt, the aggregation behavior of dBSA-modified GNRs should be responsible for the reversible absorption change observed. From Figure 2b it can also be seen that the anisotropic assembly of the dBSA-modified GNRs, i.e., the single structural change in the lateral (side-to-side) orientation, was not present, which disagrees with those inferred by us from the blue shift of the LSPB. This may be ascribed to the relative equilibrium of the driving force for the anisotropic assembly in the surroundings of the GNRs, owing

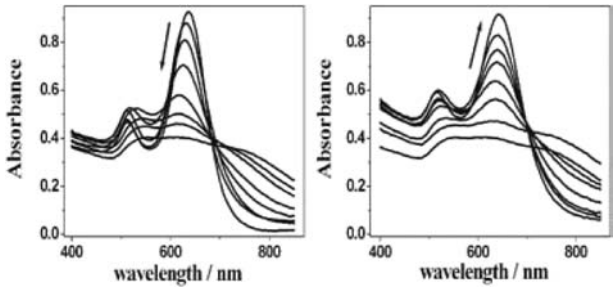

Figure 1. UV–vis spectra of dBSA-modified GNRs solution when the pH is changed from 4.2 to 9.4 (left) and back to 4.2 (right).

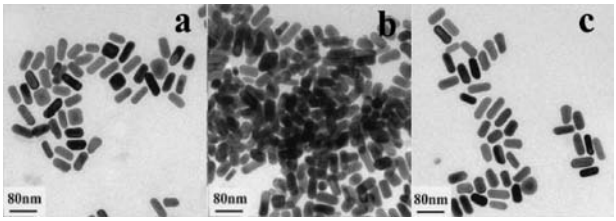

Figure 2. TEM images of dBSA-modified GNRs observed when the pH is changed from 4.2 (a) to 9.4 (b), and back to to 4.2 (c).

to the too small aspect ratio of the GNRs prepared, similar to the case of spherical gold nanoparticles.

From the zeta potential measurements at different pH values (Figure S3), a scheme of pH-triggered GNRs aggregation could be inferred, which should be controlled by electrostatic and hydrophobic interaction. At pH 4.2, the initial zeta potential of the GNR solution measured is 47.6 mV, which means that the electrostatic repulsion between GNRs is strong enough to make them in general isolated. While the pH of the solution increases to 9.4, the potential decreases to 19.0 mV, indicating that the electrostatic repulsion was weakened. Thus, the hydrophobic interaction[16] between GNRs predominated, which triggered the GNR aggregation. When pH reverses to 4.2, the zeta potential increases to 49.2 mV, the GNRs become well suspended again for the same electrostatic repulsion of GNR surface.

The reversibility of pH-dependent aggregation/dispersion of the dBSA-modified GNRs was checked by monitoring the maximum wavelength of the LSPB with cycling the pH of the solution between 4.2 and 9.4. Figure S4 gives the wavelength variation of the first four cycles recorded at the start and end. At the start of each cycle (pH 4.2), the LSPB presents a maximum around 637 nm, which blue-shifts to about 607 nm at the end of each cycle (pH 9.4). The reasonable reversibility kept up to four cycles, after which the spectral recovery became difficult because of the increased ionic intensity of the system after too much acid and base were introduced. The fact also shows that the aggregation process involves in electrostatic interaction.

As shown in Figure S5, there is a good linear correlation between the maximum wavelength of the LSPB and pH, allowing monitoring pH in the wide range of 4.2 to 9.4. Also the corresponding reversible color change (Figure S6) facilitates the pH observation with the naked eye.

In conclusion, we successfully modified the GNRs with dBSA and endowed the GNRs with an improved stability and functionality. In virtue of the electrostatic and hydrophobic interaction of the protein, the resulting GNRs underwent a pH-induced reversible aggregation process. And obvious spectral changes allow pH-sensing in the wide range of 4.2 to 9.4 at long-wavelength region (>600 nm). To our best knowledge, it is the first time to use protein to modify GNRs and realize pH-triggered reversible aggregation of GNRs. Using the present strategy, we believe, the anisotropic assembly is expected for GNRs, by controlling experimental condition and employing the GNRs of bigger aspect ratio. The further work is under way.

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14 Supporting Information is also available electronically on the CSJ-Journal web site, http://www.csj.jp/journals/chem-lett/index.html.

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