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A Simple Strategy for Prompt Visual Sensing by Gold Nanoparticles: General Applications of Interparticle Hydrogen Bonds**

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Visual sensing based on gold nanoparticles (GNPs) is important and attractive because the intense red color arising from surface plasmon (SP) absorption[1] allows the outcome of analytical measurements to be read with the naked eye. The typical mechanism for such colorimetric sensing involves a color change from red to blue through the analyte-triggered aggregation of GNPs.[2–5] Herein, we report an opposite transformation in which the GNPs are initially aggregated and promptly become dispersive in response to an analyte. To achieve the goal of rapid sensing, the interparticle attraction for the initial aggregation should be easily weakened by the analyte–GNP interactions. Scheme 1 illustrates the proposed concept. The GNPs are bifunctionalized by ([15]crown-5)$CH_2O(CH_2)_4SH$ (denoted 15c5-C_4-SH) and thioctic acid (TA), which are responsible for recognition and GNP aggregation, respectively. Pb^{II}, a common environmental contaminant that is detrimental to human health, is selected as the target ion for this model system because its association constants with 15c5 and acetic acid are 3630[6] and 500,[7] respectively, which are considerably higher than those of most metal ions. The affinity of Pb^{II} toward the functionalities imposes positive electrostatics on the GNPs and leads to a very fast aggregation-to-dispersion transformation. Herein, we show that this methodology offers a rapid, highly selective, and sensitive Pb^{II} sensor.

Chemical reduction of $HAuCl_4$ by sodium citrate was employed to synthesize water-soluble and spherical gold sols.[8] The GNPs were then bifunctionalized by a two-step method[9] in which the physisorbed anions are first displaced by TA, which is subsequently exchanged by crown ether thiols.[9,10] This approach typically yields GNPs with a diameter of (18 ± 3) nm and ligated by nominally 14500 thiol legs, one third of which are crown ether thiols.[10] The solvent system for immediate sensing of Pb^{II} ions was prepared by mixing an aqueous solution of the GNPs with methanol. An aliquot (1.80 mL) of the GNPs in the solvent

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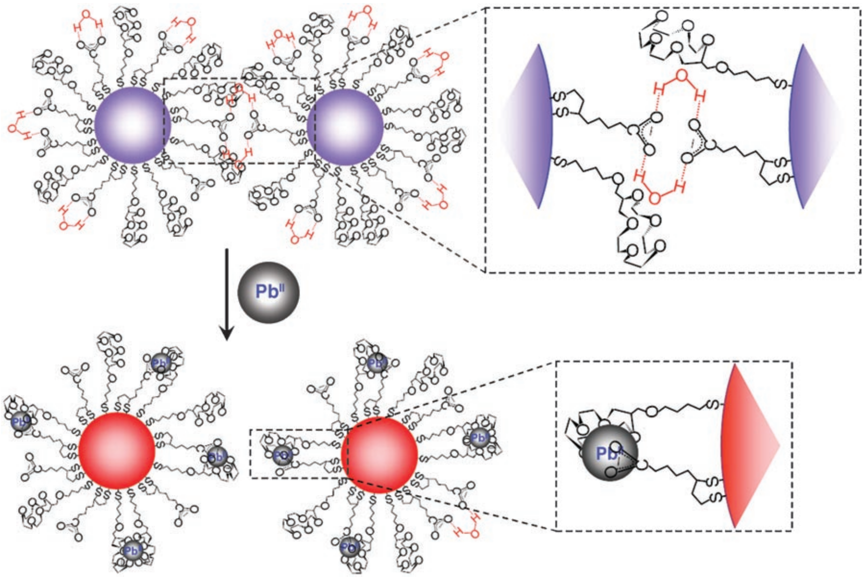

Scheme 1. Proposed methodology for the recognition of metal cations by GNPs in methanol/water. The GNPs initially aggregate as a result of hydrogen bonds between carboxylic acid residues. The crown ether moiety selectively hosts metal ions whose positive charge produces electrostatic repulsion and results in dispersive GNPs.

mixture was subjected to a trial assay. Figure 1 shows that, one second after exposure to Pb^{II}, the solution transformed from blue to red, which is opposite to most sensing events of GNPs. The Supporting Information includes a video clip that demonstrates the promptness of the distinct color change.

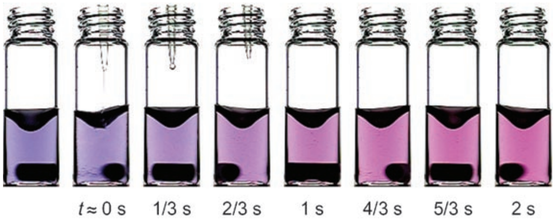

Figure 1. Photographs in chronological order that show the rapidity of Pb^{II} sensing. The snapshot on the far left was taken prior to the introduction of an aliquot (0.10 mL) of Pb^{II} (2.50 nmol) by micropipette. The approximate time for each frame is noted under the photographs. The concentration of the 15c5-C$_4$/TA-GNPs in the vial is 0.22 mg mL^{-1}. The solvent system is methanol/water (90%, v/v; 1.80 mL) buffered to pH 8.00 by 10 mM sodium Tris·HCl. Tris = tris(hydroxymethyl)aminomethane.

The change in color signifies that the presence of Pb^{II} triggers the events associated with a blue-shift of the SP absorption, indicative of the transformation of GNPs from aggregation to dispersion.[11–14] This scenario is supported by the shift of the SP band from 700 to 525 nm (Figure 2a), and confirmed by the size distribution of the GNPs whose average hydrodynamic diameter is reduced from (700 ± 70) to (47 ± 17) nm (Figure 2b). To show the selectivity and sensitivity of the bifunctionalized GNPs toward Pb^{II} ions, the extinction ratios at 530 and 660 nm are plotted against the concentrations of a variaty of metal ions in Figure 3. The extinction coefficients at the two wavelengths indicate the relative amounts of dispersive and aggregated GNPs.[11,12] The extinction ratio climbs sharply for Pb^{II} within a narrow range between 0.25 and 2.50 μM, whereas they are unaffected by other metals at a 100-fold or higher concentration level. The narrow concentration range may offer a pass-or-fail diagnostic test by visual determination. The results demonstrate the selectivity of this sensing scheme toward Pb^{II} ions.

The effect of the amount of water in the methanol/water solutions of the GNPs was examined. The GNPs appear slightly purplish when the water content is more than 20% and become dispersive at 30% (see the Supporting Information). For solutions of GNPs containing less than 20% water, ten recipes with water contents

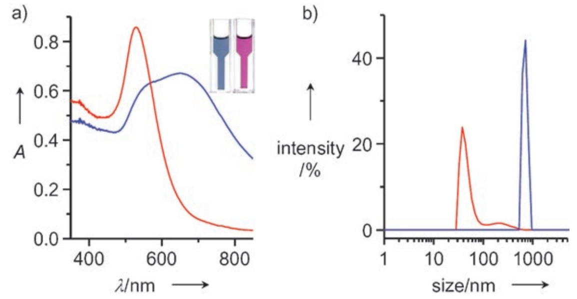

Figure 2. a) UV/Vis spectra and b) size distribution of the 15c5-C$_4$/TA-GNPs before (blue traces) and after (red traces) addition of Pb^{II} (2.50 nmol). All experimental conditions, including the volume and the concentrations of Pb^{II} and GNPs, are identical to those in Figure 1.

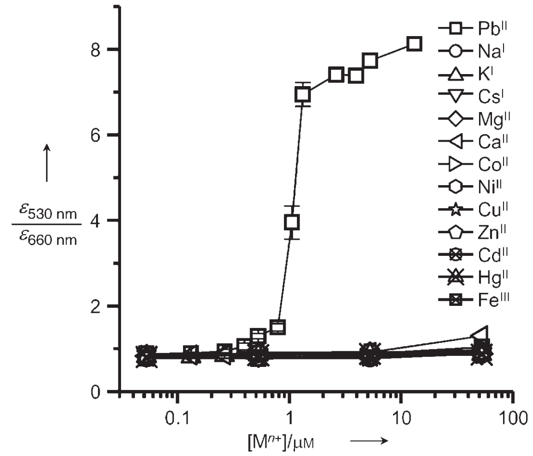

Figure 3. Selectivity and sensitivity of 15c5-C$_4$/TA-GNPs toward Pb^{II} ions. UV/Vis spectra for extinction ratios (530 over 660 nm) were obtained about 3 min after the GNPs (1.80 mL) were exposed to the metal cations. The *x* axis represents the concentration of the metal cations in the solution (1.90 mL).

ranging from 2% to 18% were studied to optimize the sensing performance. However, to the naked eye they exhibit almost identical color and the responsive range of Pb^{II} concentrations, although a plot of extinction ratio ($\varepsilon_{530\,nm}/\varepsilon_{660\,nm}$) against concentration differentiates their sensitivity by UV/Vis spectrometry. A water content of 10% is employed in this study because with this quantity (that is, 1.0 mL aqueous GNPs mixed with 9.0 mL methanol) it is easy to prepare the assay with accuracy and thus minimize the experimental deviation.

To clarify the effect of the crown ether and carboxylic moieties on the sensing mechanism, control experiments using GNPs with tailored surface functionality were carried out. To limit the presence of carboxylic acid at the GNP/solution interface, a crown ether thiol with a long spacer (([15]crown-5)$CH_2O(CH_2)_{12}SH$) was synthesized and used to modify the GNPs such that the carboxylic moieties were buried within the organic shell. In 90% methanol, this 15c5-C_{12}/TA-GNP solution appears red, which demonstrates that hydrogen bonding between interparticle carboxylic moieties is responsible for the initial aggregation of 15c5-C_4/TA-GNPs. The role of the carboxylic moieties in Pb^{II} sensing was further investigated by using TA-GNPs that contained no crown ether thiol. The color of these GNPs is blue, and shows no discernible difference from that of 15c5-C_4/TA-GNPs. However, the TA-GNP solution does not respond to Pb^{II} ions even at a concentration 20-fold higher than that of Figure 1. Therefore, the sensing activity of the 15c5 moiety, rather than the carboxylic moieties alone, is indispensable to the signaling of an aggregation-to-dispersion transformation.

It is well-documented that aggregation of carboxylic acid-terminated GNPs takes place in organic solvents as a result of the formation of interparticle hydrogen bonds.[15–18] How does this attractive force become repulsive and why is this transition selective for Pb^{II} over other common metal ions? The key factors are electrostatic interactions between the GNPs and the relative size of the crown ether cavity to the diameter of the metal ion. The electrical potential at the hydrodynamic shear plane around a particle, namely the zeta potential, has been applied to predict the stability of nanosuspensions.[19,20]

For example, the criterion for nanoparticles being stable exclusively by electrostatic repulsion is a zeta potential larger than +30 mV or more negative than −30 mV.[19,20] In the 90% methanol solvent, the zeta potential of 15c5-C_4/TA-GNPs increases with the amount of metal ion (Figure 4), which suggests some level of affinity of the ions toward either the carboxylic acid or crown ether moiety. Among the metal ions, only Pb^{II} can rapidly lift the zeta potential value higher than +30 mV, an apparent driving force that impairs the interparticle hydrogen bonding and triggers dispersive GNPs. Although other ions might also be caged in the crown ether cavity, the electrostatic repulsion appears insufficient to break the hydrogen bonds between the GNPs. Alternatively, GNPs may develop aggregates on account of a 2:1 15c5-to-cation sandwich complex when the crown ether cavity (1.70–2.20 Å)[21] is too small to accommodate the metal cations, for example, K^{I} (2.76 Å).[22] In either pathway the blue color of the GNP solution remains unchanged.

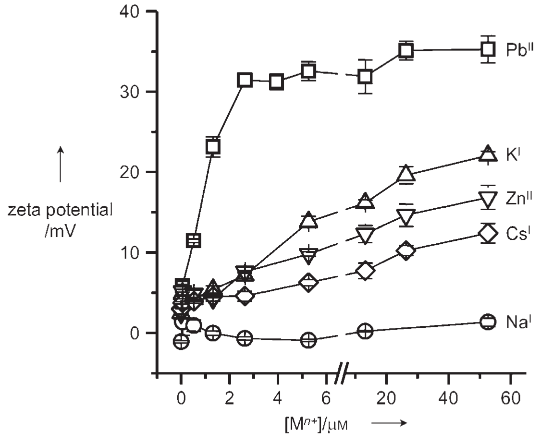

Figure 4. Zeta potential of 15c5-C_4/TA-GNPs in response to metal ions. The measurements were performed 3 min after the metal ions were added to the 90% methanol solvent system.

The diameter of Pb^{II} is 2.38 Å,[23] only slightly larger than that of the 15c5 cavity (1.70–2.20 Å),[21] and the structures of 1:1[7,24] and 2:1[7,25] 15c5–Pb^{II} complexes have both been found in the literature. To further elaborate the sensing mechanism, zeta potential measurements were carried out for the aforementioned 15c5-C_{12}/TA-GNPs. After exposure to Pb^{II} (2.50 nmol) in 90% methanol, the zeta potential of the GNPs jumps from less than 10 mV and instantly reaches a plateau of +30 mV, indicative of the formation of a 15c5–Pb^{II} complex. The color is red throughout the concentration examined (0.0–1.0 mM), and thus the possibility of interparticle sandwich complexation is ruled out. On the contrary, 2:1 sandwich complexation takes place in aqueous medium, where the same 15c5-C_{12}/TA-GNPs (3.0 mL, 0.40 $mg\,mL^{-1}$) are also sensitive to Pb^{II} (2.50 nmol) and the solution turns from red to blue.

The intriguing solvent-dependent response is consistent with how the solvent polarity may shape the microstructures of the highly flexible ethylene glycol moiety. The polar water molecules attract and exteriorize oxygen atoms of the crown ether, and thus expedite a 2:1 sandwich complexation of 15c5-functionalized nanoparticles to metal ions.[10,22,26] In methanol, the hydrophobic ethylene units become the exterior of the crown ether cavity.[27] The Pb^{II} ion is hosted by one crown ether or sandwiched by neighboring crown ether moieties at the same 15c5-C_{12}/TA-GNP. Therefore, the value of the zeta potential increases and the GNPs do not aggregate.

In addition to the above 15c5–Pb^{II} complexation schemes, there is an alternative for 15c5-C_4/TA-GNPs. Note that the crown ether thiol has a short methylene spacer. The relative chain length of crown ether thiol and TA configures a cooperative sensing scheme (the enlarged frame of Scheme 1), in which the electrostatic attraction of Pb^{II} and carboxylate is facilitated by the chelation of a proximal crown ether moiety. The Pb^{II} takes over the hydrogen-bonding sites, and therefore the driving force for the initial aggregation is weakened and is displaced by electrostatic repulsion, which leads to dispersive GNPs.

In summary, we have demonstrated a novel and simple signaling scheme that promptly activates the color transformation of GNPs by breaking the interparticle hydrogen bonds. By taking advantage of the favorable diameter ratio of Pb^{II} to the crown ether cavity of the 15c5 moiety, the bifunctionalized GNPs are shown to be highly selective to Pb^{II} ions. The high extinction coefficient of GNPs allows the determination of Pb^{II} down to 1 μM using the naked eye. This methodology can be generalized for other analytes of interest by using moieties such as assorted macrocycles, cyclodextrins, and many host functionalities.

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