Self-Assembly

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Confining Molecules within Aqueous Coordination Nanoparticles by Adaptive Molecular Self-Assembly**

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Molecular inclusion phenomena have been widely studied because of their applications in many disciplines, as exemplified by catalysis,[1] separation,[2] sensors,[3] pharmaceutics,[4] and electronics.[5] In line with the lock-and-key metaphor,[6] molecular recognition of guest molecules has been studied on the basis of preformed host compounds.[7,8] In contrast, the surprising ability of the immune system to produce antibodies in response to antigens inspired chemists to develop guest-induced assembly of receptors from multiple fragments.[9,10] In spite of the potential advantage of this molding approach, there remain limitations in the design of molecular fragments that constitute libraries, in the intermolecular interactions to connect them, and in the type and size of template molecules.

A simpler approach is to employ adaptive self-assembly of subunits that are capable of forming molecular networks by flexibly following the shape of guest molecules. One of the adaptive molecular assemblies ubiquitous in nature is hydration shells, whereby amorphous hydrogen-bonding networks of water are formed around dissolved molecules by flexibly covering their surfaces. By replacing these hydrogen-bonded water shells with molecular networks, adaptive supramolecular shells could be obtained. We recently reported that coordination nanoparticles (CNPs) were spontaneously formed in water from a wide variety of nucleotides and lanthanide ions.[11] Nucleotides are key molecules of life that play central roles in metabolism and show rich structural diversity. They are composed of nucleobases, ribose or 2′-deoxyribose linkers, and phosphate groups, whose structures are regarded as bidentate ligands. Lanthanide ions meanwhile exhibit large coordination numbers and high coordination flexibility. The combination of these components is suitable for making amorphous coordination networks that are self-assembled to accommodate the size and shape of guest materials. Interestingly, a variety of water-soluble functional materials such as fluorescent dyes, inorganic nanocrystals, and biopolymers are readily co-assembled in these coordination networks, revealing the feature of adaptive self-assembly.[11b]

Despite these interesting phenomena, however, very little is known about the basic properties of coordination networks, including their effect on the properties of confined guest molecules. As the networks are formed from nucleotides and lanthanide ions in aqueous media, it is expected to influence the degree of hydration, thermal mobility, and conformational freedom of water-soluble guest molecules. Herein, we describe unique interfacial properties of polymeric coordination shells self-assembled from nucleotides and lanthanide ions. These chiral coordination networks were found to exert conformational restraints on guest molecules and display surprising barrier properties against molecular oxygen (Figure 1).

The encapsulation of guest molecules in nucleotide–lanthanide nanoparticles was performed by mixing aqueous lanthanide chlorides and aqueous solutions containing nucleotides and dye molecules. Typically, aqueous gadolinium(III) chloride ($GdCl_3$) was added to an aqueous mixture of adenosine 5′-monophosphate (AMP) disodium salt and

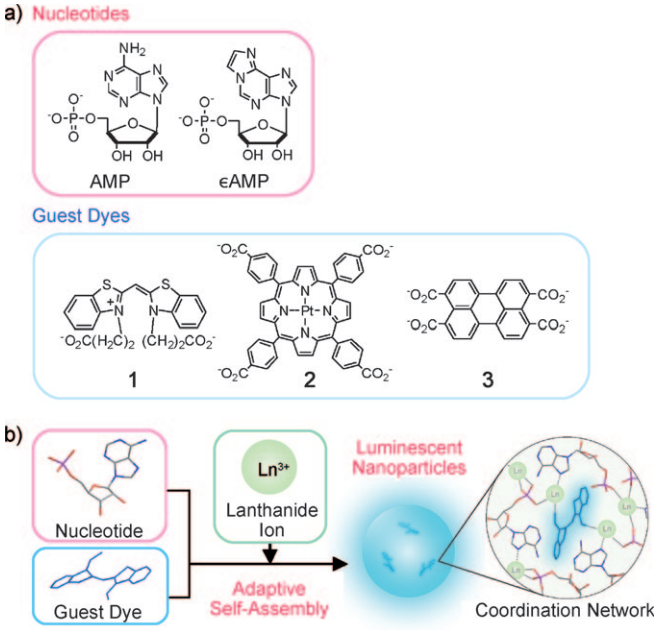

Figure 1. a) Molecular structures of nucleotides (AMP, εAMP) and guest dyes (**1**–**3**) employed in this study. b) A schematic illustration of the adaptive inclusion of guest dye molecules by growing nanoparticles of nucleotides and lanthanide ions in water.

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cyanine dye **1** with stirring. Nanoparticles with average diameter of 30 nm were formed, as observed by scanning and transmission electron microscopy (SEM and TEM, Figure 2). Powder X-ray diffraction analysis and IR spectroscopy showed that these nanoparticles consist of amorphous coordination networks, in which both phosphate and nucleobase units interact with Gd^{3+} ions.[11b] Anionic dyes **1**–**3** were effectively incorporated into AMP/Gd^{3+} CNPs through coordination of carboxylate groups to Gd^{3+} ions (Figure S1 in the Supporting Information).[11b] The UV/Vis absorption spectrum of an aqueous dispersion of **1** incorporated in AMP/Gd^{3+} CNPs (**1**@AMP/Gd^{3+} CNPs) revealed an absorption band at 432 nm (Figure 3a, top), which is slightly red-shifted relative to that observed for **1** in pure water ($\lambda_{max} = 425$ nm; Figure S3 in the Supporting Information). As absorption bands ascribed to aggregated dye molecules[12] are not observable, the small red-shift observed reflects incorporation of **1** in the hydrophobic interior of AMP/Gd^{3+} CNPs. Figure 3b shows the fluorescence spectra of **1** in water (dashed line in blue) and of **1**@AMP/Gd^{3+} CNPs (red), together with pictures of the aqueous dispersions. In pure water, cyanine dye **1** shows very weak fluorescence under UV light (Figure 3b, fluorescence quantum yield $\Phi_F < 1\%$), because of prevailing nonradiative thermal deactivation of the singlet excited state promoted by free conformational rotation around the central methyne moiety.[13] Very interestingly, intense blue emission was observed when **1** was incorporated in AMP/Gd^{3+} CNPs ($\Phi_F \approx 49\%$, Figure 3b). The significant increase in fluorescence intensity indicates that the conformational rotation of cyanine dye **1** in AMP/Gd^{3+} CNPs is highly restricted by the surrounding coordination networks.[14] This view is supported by the increased fluorescence intensity of **1** in viscous environments, such as ethylene glycol (Figures S5–S7 and Table S1 in the Supporting Information).

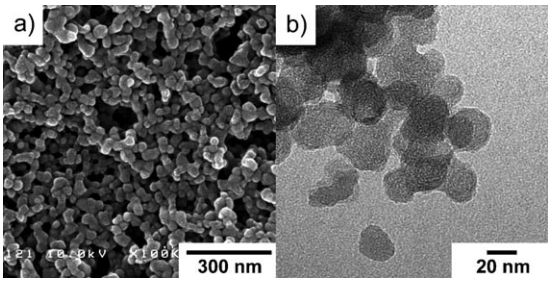

Figure 2. a) SEM and b) TEM images of cyanine dye **1**@AMP/Gd^{3+} CNPs. Spherical CNPs with an average diameter of 30 nm were obtained by mixing aqueous solutions of $GdCl_3$, AMP, and **1**.

The confinement of **1** in the coordination networks of AMP/Gd^{3+} CNPs was further supported by circular dichroism (CD) spectroscopy. Although dye **1** is an achiral molecule, a CD signal with a negative Cotton effect was observed at 433 nm in aqueous AMP/Gd^{3+} (Figure 3a, bottom). The observed circular dichroism is apparently induced by the chiral coordination networks, since no CD signal was observed for the aqueous mixture of **1** and AMP without Gd^{3+} ion (Figure S8 in the Supporting Information). These observations indicate that dye **1** is fixed in the chiral

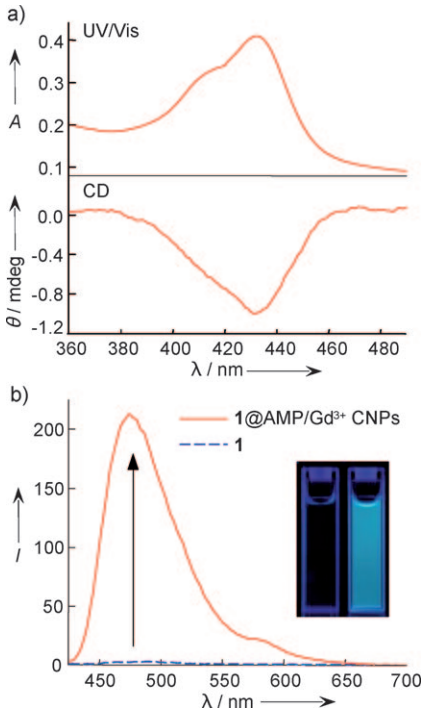

Figure 3. a) UV/Vis absorption and CD spectra of **1**@AMP/Gd^{3+} CNPs in water. $[\mathbf{1}] = 5.0\times10^{-6}$ mol L^{-1}; $[AMP] = [GdCl_3] = 5.0\times10^{-4}$ mol L^{-1}. b) Fluorescence spectra of aqueous dispersion of **1**@AMP/Gd^{3+} CNPs and **1** in water. $[\mathbf{1}] = 5.0\times10^{-6}$ mol L^{-1}, excitation wavelength: 410 nm. Inset: photographs of aqueous **1** (left) and aqueous suspension of **1**@AMP/Gd^{3+} CNPs (right) under UV light (365 nm).

coordination network with restricted conformational freedom, and the chirality of a ribose unit is amplified via the self-assembly. It is notable that Gd^{3+} ions play multiple roles. Firstly, they provide amorphous but rigid coordination networks with AMP. Secondly, they serve as points to tie up anionic guest molecules inside the chiral coordination network.[11b]

The restricted conformational mobility of confined guest molecules should reflect the presence of rigid and dense coordination networks in CNPs. It is expected that such molecular networks show barrier properties. To evaluate the barrier performance, the permeation of oxygen through coordination networks was investigated, because of the current strong demands for supramolecular oxygen barriers.[15] Platinum porphyrin (PtP) **2** was selected as a guest molecule, since it shows high phosphorescence quantum yields even at room temperature. The high quantum yields result from effective intersystem crossing, which is enhanced by spin–orbit coupling of the heavy metal center.[16] In contrast, the triplet-state population is readily deactivated in the presence of molecular oxygen, a property which makes PtP compounds highly sensitive oxygen sensors.[17]

In aerated water, **2** showed very weak phosphorescence with low quantum yield ($\Phi_F < 1\%$), as expected (Figure 4a, dashed line). In contrast, **2**@AMP/Gd^{3+} CNPs showed significantly increased phosphorescence intensity with a quantum yield as high as 5% (Figure 4a, solid line). To our surprise, **2**@AMP/Gd^{3+} CNPs maintained their phosphorescence intensity at more than 80% even in oxygen-saturated

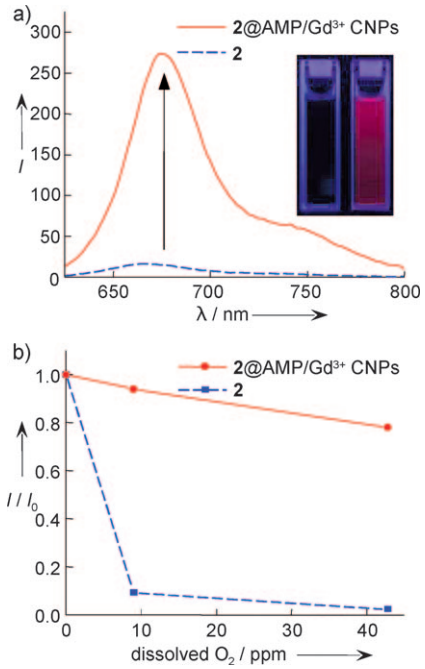

Figure 4. a) Emission spectra of **2**@AMP/Gd^{3+} CNPs and **2** in aerated water. Inset: photographs of aqueous **2** (left) and aqueous suspension of **2**@AMP/Gd^{3+} CNPs (right) under UV light (365 nm). b) Relative phosphorescence intensities of **2**@AMP/Gd^{3+} CNPs and **2** with increasing oxygen concentrations in water. Conditions: **2**@AMP/Gd^{3+} CNPs: [**2**] = 5.0×10^{-6} mol L^{-1}; [AMP] = [$GdCl_3$] = 5.0×10^{-4} mol L^{-1}; **2**: [**2**] = 5.0×10^{-6} mol L^{-1}; excitation wavelength: 516 nm for **2**@AMP/Gd^{3+} CNPs and 506 nm for **2**.

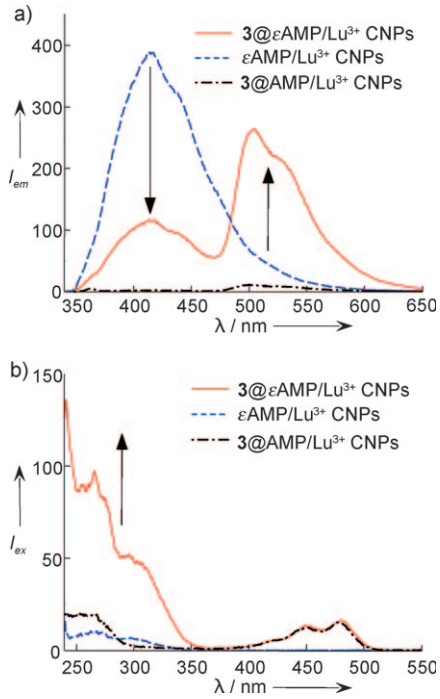

Figure 5. a) Fluorescence and b) excitation spectra of **3**@εAMP/Lu^{3+} CNPs, εAMP/Lu^{3+} CNPs, and **3**@AMP/Lu^{3+} CNPs in water. Conditions: **3**@εAMP/Lu^{3+} CNPs: [εAMP] = [Lu^{3+}] = 2.5×10^{-5} mol L^{-1}; [**3**] = 1.25×10^{-7} mol L^{-1}; εAMP/Lu^{3+} CNPs: [εAMP] = [Lu^{3+}] = 2.5×10^{-5} mol L^{-1}; **3**@AMP/Lu^{3+} CNPs: [AMP] = [Lu^{3+}] = 2.5×10^{-5} mol L^{-1}; [**3**] = 1.25×10^{-7} mol L^{-1} in 1.0×10^{-3} mol L^{-1} HEPES buffer at pH 7.4; excitation wavelength for fluorescence spectra: 320 nm; excitation spectra were monitored at an emission wavelength of 600 nm.

aqueous solution (Figure 4b, solid line). This is in contrast to **2** in water, which showed significant quenching of phosphorescence with increasing oxygen concentration (Figure 4b, dashed line). These results show that collision of oxygen with **2** is inhibited in aqueous **2**@AMP/Gd^{3+}, indicating that the dense coordination network shells provide an effective barrier against molecular oxygen (Figures S9–S13 in the Supporting Information). The observed oxygen barrier properties require that the Pt porphyrin complex is fully covered by the coordination network, as **2** underwent strong triplet quenching when it was adsorbed on the outer surface of preformed AMP/Gd^{3+} CNPs (Figure S14 in the Supporting Information).

The ability to confine molecules inside coordination nanoparticles and thus preclude oxygen quenching is a feature suitable for developing light-harvesting functions (Figure 5). To study the fluorescence resonance energy transfer from the host shell to the encapsulated guest molecules, we employed 1,N^6-ethenoadenosine 5′-monophosphate[18] (εAMP) and perylene dye **3** as donor and acceptor, respectively. In water, εAMP gives a fluorescence peak centered at 415 nm, which is close to the absorption maximum of perylene dye **3** (λ_{abs} = 458 nm, Figure S15 in the Supporting Information). The spectral overlap between these components satisfactorily meets the conditions for Förster-type resonance energy transfer (FRET) to occur.[19]

The perylene dye **3** was confined in εAMP/Lu^{3+} CNPs by mixing aqueous solutions of lutetium(III) chloride ($LuCl_3$) and εAMP in the presence of **3**. As reference samples, the host εAMP/Lu^{3+} CNPs, which do not contain **3**, and **3**-doped AMP/Lu^{3+} CNPs in which εAMP was replaced by AMP were prepared (Figures S16–19 in the Supporting Information). The host εAMP/Lu^{3+} CNPs without **3** gave fluorescence at 420 nm (Figure 5a, dashed line). In contrast, upon photoexcitation of ethenoadenine chromophore in the aqueous suspension of **3**@εAMP/Lu^{3+} CNPs (λ_{ex} at 320 nm), an intense fluorescence peak of **3** appeared at 504 nm (Figure 5a, solid line). The fluorescence intensity of εAMP in **3**@εAMP/Lu^{3+} CNPs was significantly quenched relative to that of the host CNPs (εAMP/Lu^{3+} CNPs). The fluorescence of guest perylene dye **3** observed in aqueous **3**@εAMP/Lu^{3+} CNPs is apparently sensitized by εAMP molecules assembled in CNPs, since its intensity (solid line) is significantly higher than that observed for **3**@AMP/Lu^{3+} CNPs (Figure 5a, dashed-dotted line). In addition, the excitation spectrum of aqueous **3**@εAMP/Lu^{3+} CNPs monitored at 600 nm showed considerable intensity in the absorption band of εAMP around 300 nm (Figure 5b, solid line), relative to that observed for εAMP/Lu^{3+} CNPs (dashed line). By taking into account that **3** is introduced in CNPs at a low molar ratio of 0.5 mol% (relative to εAMP and Lu^{3+} ions), the high guest fluorescence intensity of **3** in aqueous **3**@εAMP/Lu^{3+} CNPs indicates the contribution of efficient energy migration among εAMP molecules self-assembled in the coordination network. It is noteworthy that efficient energy transfer is

observed despite the amorphous coordination structure of the CNPs. This result could be attributed to a small concentration of intrinsic energy trap sites. The stacking of ethenoadenine chromophores, for example, is prevented by the presence of bulky ribose units. In addition, both donor and acceptor components are densely assembled in CNPs and shielded from dynamic quenching by molecular oxygen. These features would suppress the deactivation of singlet excited states and lead to the observed efficient energy transfer property.

In conclusion, coordination nanonetworks of nucleotides and lanthanide ions in CNPs show chiral microenvironments in which guest molecules are densely confined with restricted conformational mobility. The confined environment remarkably enhanced the luminescence intensity of the functional dyes, induced circular dichroism, and showed barrier properties against dissolved molecular oxygen. Thus, the adaptive inclusion by coordination networks provides opportunity to disclose latent functionality of guest molecules in water. These features would have an impact on the research of CNPs.[20] Although further study is required to develop adaptive self-assemblies with molecularly controlled thickness and enhanced water solubility,[21] the wide availability of natural and synthetic ligands, guest molecules, and metal species in the present approach may allow application of adaptive inclusion phenomena in many disciplines.

Experimental Section

Platinum porphyrin dye **2** and perylene dye **3** were synthesized according to reported procedures.[18b,22] All other chemicals and materials were purchased and used as received. Water was purified with a Direct-Q system (Millipore Co.). Preparation and purification of nanoparticles were conducted as reported previously.[11b] Dye-doped nucleotide/lanthanide CNPs were prepared by mixing aqueous lanthanide chloride and aqueous nucleotide containing guest dye. Typically, to an aqueous solution (2.0 mL) of $GdCl_3$ ($[GdCl_3] = 1.0 \times 10^{-3}$ mol L^{-1}) was added an aqueous solution (2.0 mL) of AMP containing dye **1** ($[AMP] = 1.0 \times 10^{-3}$ mol L^{-1}, $[\mathbf{1}] = 1.0 \times 10^{-5}$ mol L^{-1}, 2 mL) at room temperature. Nanoparticles were obtained in aqueous suspensions, which were used for spectroscopic experiments after ultrasonication. Further experimental details are described in the Supporting Information.

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