

Continuously Tunable Nucleotide/Lanthanide Coordination Nanoparticles for DNA Adsorption and Sensing

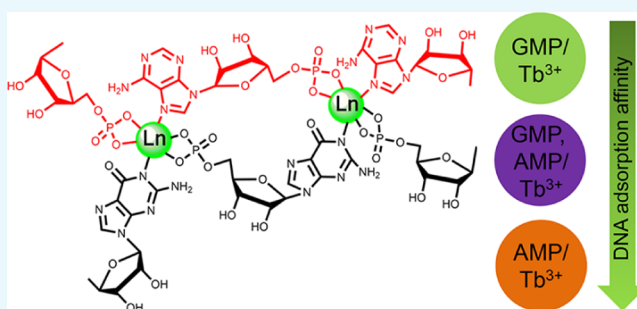
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S Supporting Information

ABSTRACT: Metal–organic coordination polymers (CPs) have attracted great research interest because they are easy to prepare, porous, flexible in composition, and designable in structure. Their applications in biosensor development, drug delivery, and catalysis have been explored. Lanthanides and nucleotides can form interesting CPs, although most previous works have focused on a single type of metal ligand. In this work, we explored mixed nucleotides and studied their DNA adsorption properties using fluorescently labeled oligonucleotides. Adenosine monophosphate (AMP) and guanosine monophosphate (GMP) formed negatively charged CP nanoparticles with most lanthanides, and thus a salt was required to adsorb negatively charged DNA. DNA adsorption was faster and reached a higher capacity with lighter lanthanides. Desorption of pre-adsorbed DNA by inorganic phosphates, urea, proteins, surfactants, and competing DNA was successively carried out. The results suggested the importance of the DNA phosphate backbone, although hydrogen bonding and DNA bases also contributed to adsorption. The AMP CPs adsorbed DNA more strongly than the GMP ones, and using mixtures of AMP and GMP, continuous tuning of DNA adsorption affinity was achieved. Such CPs were also used as a sensor for DNA detection based on the different affinities of single- and double-stranded DNA, and a detection limit of 0.9 nM target DNA was achieved. Instead of tuning DNA adsorption by varying the length and sequence of DNA, the composition of CPs can also be controlled to achieve this goal.



INTRODUCTION

Materials that can adsorb DNA are of great analytical and biomedical importance for applications such as biosensor development,^{1–4} delivery of nucleic acids,^{5,6} and stimuli-responsive materials.^{7–9} To date, many types of inorganic nanomaterials have been tested for this purpose, including metal nanoparticles,^{10–12} carbon-based nanomaterials,^{9,13–16} transition metal dichalcogenides,¹⁷ and metal oxides.¹⁸ They interact with DNA through base chemisorption, π – π stacking, hydrogen bonding, and van der Waals forces, or by binding to the phosphate backbone of DNA.^{19–21} Although DNA adsorption affinity can be tuned by varying the length and sequence of DNA,^{22–25} it is more difficult to tune the interaction by continuously varying the properties of nanomaterials. From materials design standpoint, it is interesting and potentially useful to have materials with continuously tunable affinities for DNA adsorption.

Other intermolecular interactions, such as DNA base pairing interactions and metal coordination, were less explored for DNA adsorption. In this regard, nucleotide-coordinated materials are capable of harnessing such interactions.^{26,27} Coordination polymer (CP) nanoparticles made of metal ions and organic ligands may offer an opportunity to design such

materials. Nucleotides are excellent metal ligands, with both nucleobases and phosphate groups for metal binding. Nishiyabu et al. first reported coordination polymer (CP) nanoparticles formed from various lanthanide (Ln) ions and purine nucleotides.^{28,29} Various applications of such CPs in loading guest molecules and sensing have been explored.^{28–31} Under certain conditions, such materials can also form hydrogels.³² By using other metal ions, such as Zn^{2+} ,³³ Fe^{3+} ,³⁴ Au^{3+} ,^{35–37} and Cu^{2+} ,³⁸ coordination materials forming hydrogels, coating materials, and nanozymes have also been demonstrated.

Lanthanides (Ln) contain 15 elements and they can form CPs with various nucleotides.^{28,39} We have recently performed a systematic titration of lanthanides to nucleotides and found a continuous thermodynamic trend.⁴⁰ We hypothesize that it might be possible to continuously tune the interaction strength between DNA and lanthanide containing CPs by varying the lanthanide and/or nucleotides. In this work, we wanted to achieve two goals: (1) a careful study of DNA adsorption by

Received: June 3, 2018

Accepted: August 7, 2018

Published: August 14, 2018

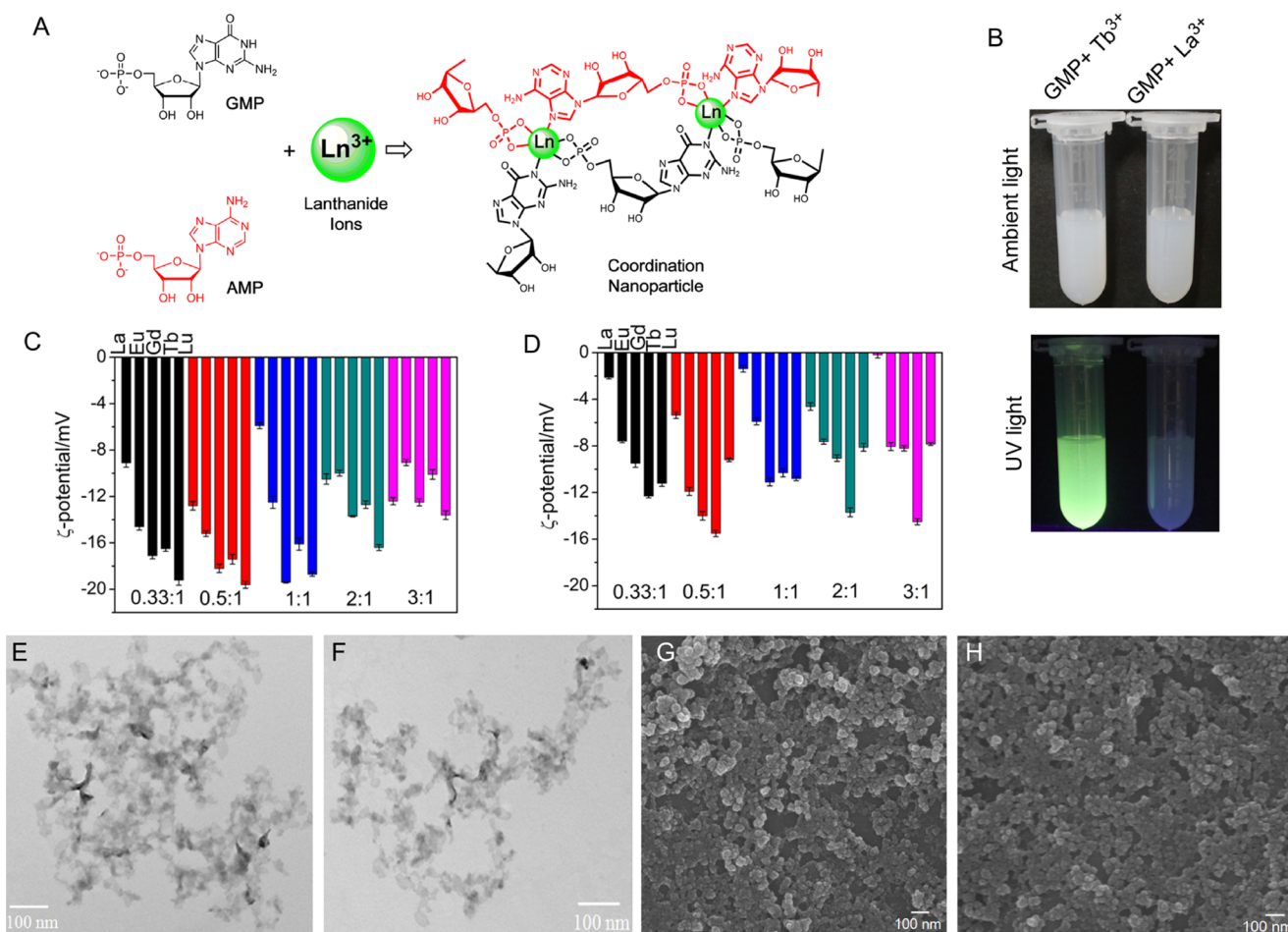


Figure 1. (A) Schematic illustration of CP nanoparticle formation and the structure of the CP of GMP and Ln^{3+} . (B) Photographs of CP nanoparticles formed from GMP/ Tb^{3+} and GMP/ La^{3+} under normal and UV light. ζ -Potential of the CP nanoparticles formed by mixing different Ln^{3+} (La, Eu, Gd, Tb, and Lu) and (C) AMP; or (D) GMP at different ratios (Ln^{3+} /nucleotide = 0.33:1, 0.5:1, 1:1, 2:1, and 3:1). Transmission electron microscopy (TEM) micrographs of the CP nanoparticles formed by mixing Tb^{3+} with (E) AMP, or (F) GMP. Scanning electron microscopy (SEM) micrographs of the CP nanoparticles formed by mixing Tb^{3+} with (G) AMP, or (H) GMP (Tb^{3+} /nucleotide = 1:2). The SEM samples were coated with Pt before imaging.

such CPs in terms of material composition and interaction forces; and (2) tuning DNA adsorption affinity. Finally, preliminary analytical applications of such materials were demonstrated.

RESULTS AND DISCUSSION

Nucleotide-Coordinated Lanthanide Nanoparticles.

Our CPs were prepared by mixing adenosine monophosphate (AMP) or guanosine monophosphate (GMP) with various lanthanides (Ln^{3+}) (Figure 1A). All samples spontaneously formed particles as judged from increased turbidity (Figure 1B), and the Tb^{3+} /GMP sample also showed strong green luminescence, also indicating the coordination reaction.²⁸ Previous work showed that both the nucleobase and the phosphate of these nucleotides are required for forming such CPs,^{28,40,41} and a proposed structure of Ln^{3+} /GMP is also shown in Figure 1A.

To gain a comprehensive understanding of these CPs, we first prepared samples with different ratios between Ln^{3+} (La^{3+} , Eu^{3+} , Gd^{3+} , Tb^{3+} , and Lu^{3+}) and nucleotides (AMP and GMP). We chose these five Ln^{3+} ions to represent the beginning, middle, and end of the series. Because DNA is a polyanion, electrostatic interaction is likely to be important. Therefore, we

measured the ζ -potential of the products (Figure 1C,D). To have a full understanding, we also varied the ratio between Ln^{3+} and the nucleotides. All of them were negatively charged regardless of the ratio, except for La^{3+} /GMP showing a charge close to zero. The negative charges on these materials are attributable to the phosphate group on the nucleotides. The final product was not very much affected by the initial ratio of the reactants, suggesting well-defined and stable complexes were formed. Considering this, a fixed 1:2 ratio of Ln^{3+} /nucleotide was used for preparing the CPs for the subsequent experiments.

The morphology of the Tb^{3+} /AMP and Tb^{3+} /GMP samples was examined by transmission electron microscopy (TEM, Figure 1E,F) and scanning electron microscopy (SEM, Figure 1G,H). They formed nanoparticle aggregates with individual particles being around 40 nm, which was consistent with the literature report.²² These samples were freshly prepared and used, and we have recently noticed that for heavy lanthanides mixed with AMP, their CP nanoparticles would transform into hydrogels after overnight storage.³²

DNA Adsorption by CP Nanoparticles. As Ln^{3+} ions can strongly bind DNA, and nucleotides may also base-pair with DNA, we were interested in studying their DNA adsorption

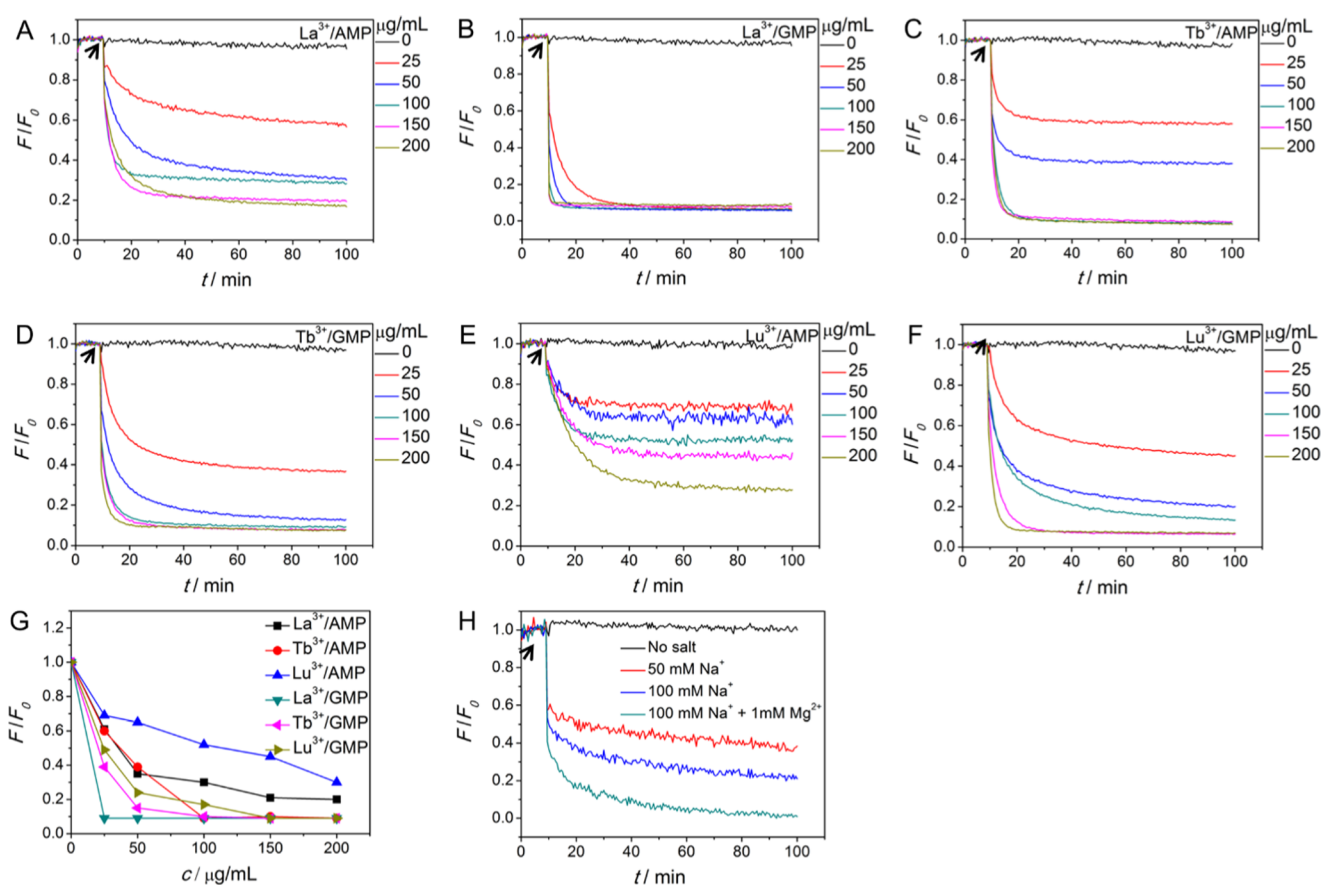


Figure 2. Kinetics of FAM-labeled A₁₅ (20 nM) adsorption indicated by fluorescence quenching after adding various concentrations of (A) La³⁺/AMP, (B) La³⁺/GMP, (C) Tb³⁺/AMP, (D) Tb³⁺/GMP, (E) Lu³⁺/AMP, and (F) Lu³⁺/GMP. The CPs were added at 10 min as indicated by the arrowheads. (G) Relative fluorescence quenching as a function of CP concentration in buffer A (10 mM 2-[4-(2-hydroxyethyl)piperazin-1-yl]ethanesulfonic acid (HEPES), pH 7.6, 100 mM NaCl, and 1 mM MgCl₂). (H) Kinetics of FAM-A₁₅ (20 nM) adsorption by Tb³⁺/GMP (150 $\mu\text{g/mL}$) in the presence of various salt concentrations in 10 mM 2-(*N*-morpholino) ethanesulfonic acid (MES) buffer (pH 6.0).

properties. To achieve a systematic understanding, we varied the sequence of DNA and also the composition of CPs. FAM-A₁₅ DNA (a 15-mer polyadenine with a carboxyfluorescein label) was used as an example to illustrate our experiment. We fixed the concentration of FAM-A₁₅ at 20 nM and monitored its background fluorescence for 10 min. Each CP material was then added at various concentrations (Figure 2A–F). In general, a higher CP concentration induced more fluorescence quenching, which indicated more DNA adsorption. As the emission of FAM did not overlap with the absorption spectra of the CPs (they mainly absorbed in the UV region), the quenching here was attributed to photo-induced electron transfer instead of energy transfer.

With 25 $\mu\text{g/mL}$ of La³⁺/GMP, full DNA desorption was achieved, whereas more Tb³⁺/GMP and even more Lu³⁺/GMP were required to achieve the same quenching efficiency. A similar trend was also observed with the AMP-containing CPs. Therefore, with the same nucleotide, lighter lanthanides were more effective for DNA adsorption. For the same lanthanide, the AMP samples adsorbed the DNA more slowly than the GMP ones. For a quantitative understanding, we plotted the relative fluorescence quenching as a function of CP concentration (Figure 2G). At low CP concentrations, a linear fluorescence quenching was observed. The slopes of these curves represent DNA adsorption capacity. The slope of La³⁺/GMP was ~ 2.2 -fold higher than that of Tb³⁺/GMP and ~ 2.4 -fold higher than that of Lu³⁺/GMP. For AMP, the slope of

La³⁺/AMP was similar to that of Tb³⁺/AMP and ~ 1.9 -fold higher than that of Lu³⁺/AMP. Therefore, the La³⁺-containing CPs had the highest DNA adsorption capacity, whereas the Lu³⁺ ones were the lowest. When AMP and GMP were compared (using the same metal), GMP had a higher adsorption capacity. Therefore, among these combinations, La³⁺/GMP adsorbed the DNA most efficiently. The reason might be its lack of surface charge (Figure 1D).

To confirm the importance of electrostatic repulsion, we then studied the effect of salt concentration using Tb³⁺/GMP (Figure 2H). Without salt, no fluorescence quenching was observed, indicating a lack of DNA adsorption. This can be explained by the long-ranged charge repulsion between the CP and DNA. With 50 mM NaCl, fluorescence quenching occurred. Further addition of 100 mM Na⁺ and 1 mM Mg²⁺ resulted in even faster quenching. Our results indicated that a certain amount of salt was required to overcome the electrostatic repulsion for DNA adsorption.

Stronger DNA Adsorption by AMP CPs. After confirming DNA adsorption, we further explored the mechanism of adsorption by inducing DNA desorption. DNA is made of nucleosides and a phosphate backbone, which are responsible for interacting with various materials. For example, DNA bases stack and hydrogen bond with graphene oxide,¹⁴ and DNA bases coordinate with a gold surface,⁴² whereas the DNA phosphate backbone is mainly responsible for its adsorption on metal oxides.^{19,43}

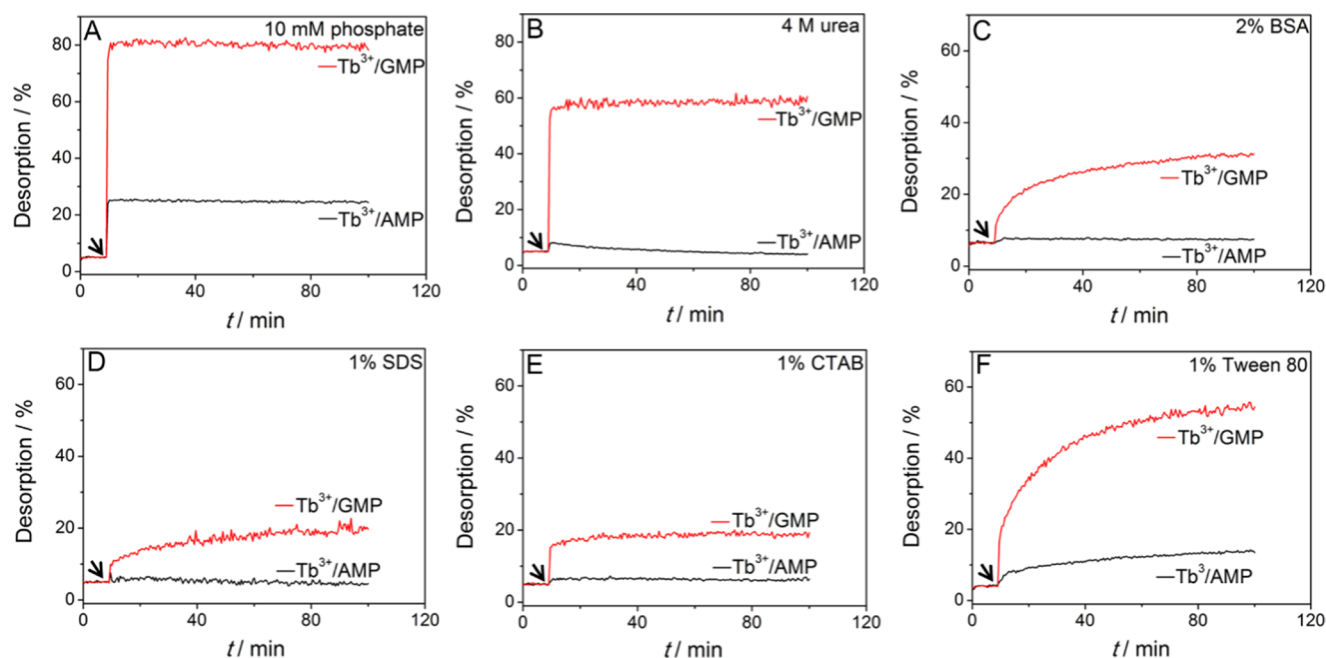


Figure 3. Kinetics of FAM- A_{15} DNA desorption from Tb^{3+} /GMP and Tb^{3+} /AMP CP nanoparticles after adding (A) 10 mM phosphate, (B) 4 M urea, (C) 2% bovine serum albumin (BSA), (D) 1% sodium dodecyl sulfate (SDS), (E) 1% cetyltrimethylammonium bromide (CTAB), and (F) 1% Tween 80 in buffer A. The competing compounds were added at 10 min as indicated by the arrowheads.

We first successively adsorbed a FAM-labeled DNA on Tb^{3+} /AMP and Tb^{3+} /GMP and then washed away the free DNA. To test whether the phosphate backbone of DNA was involved in adsorption, we challenged the samples with 10 mM free inorganic phosphate ions (Figure 3A). An immediate increase in fluorescence was observed in both samples, indicating a quick release of the DNA. The system reached a new equilibrium in a few seconds, after which the signal became stable again. Therefore, the phosphate backbone of DNA was important for its adsorption onto both CPs. This is understandable because the phosphate backbone of DNA can interact with Ln^{3+} .^{27,40} We calculated the percentage of released DNA, and the Tb^{3+} /GMP sample released around 4-fold more DNA than Tb^{3+} /AMP, suggesting that the DNA adsorption affinity on Tb^{3+} /AMP was higher.

Hydrogen bonding plays an important role in DNA adsorption by materials such as graphene oxide.^{14,20} Urea can break hydrogen bonds, and it has been commonly used to probe such interactions. Following this, we exposed our CP nanoparticles with adsorbed DNA to 4 M urea (Figure 3B). Interestingly, over 60% of the DNA was released from Tb^{3+} /GMP, whereas Tb^{3+} /AMP barely released any. Therefore, hydrogen bonding is also an important force for DNA adsorption by Tb^{3+} /GMP. It is unclear whether hydrogen bonding is important for Tb^{3+} /AMP. If not, another type of even stronger interaction must exist, such as Tb^{3+} binding with the DNA phosphate backbone, as indicated by the above phosphate washing experiment.

To further understand DNA adsorption, we then examined DNA displacement by proteins and surfactants, which may also compete with DNA for surface adsorption sites. Bovine serum albumin (BSA) had no effect on Tb^{3+} /AMP, whereas ~30% DNA desorbed from Tb^{3+} /GMP (Figure 3C). Similarly, SDS, a small molecule anionic surfactant, had no effect on Tb^{3+} /AMP, whereas ~20% DNA desorbed from Tb^{3+} /GMP (Figure 3D). For cationic CTAB (Figure 3E) and a higher molecular

weight surfactant, Tween 80 (Figure 3F), Tb^{3+} /AMP also released less DNA. Therefore, under all of these washing conditions, the DNA was adsorbed more tightly on the Tb^{3+} /AMP sample.

DNA-Induced DNA Desorption. After understanding DNA desorption by various denaturing and competing agents, we then studied DNA-induced DNA desorption, which might be useful for DNA detection. We first adsorbed FAM- A_{15} or FAM- T_{15} on Tb^{3+} /AMP or Tb^{3+} /GMP. Then, the four types of nonlabeled 15-mer homo-DNAs were sequentially added to hybridize with or to displace the adsorbed DNA probes as shown in Figure 4A. A few interesting observations were made. First, no DNA desorbed from Tb^{3+} /AMP, regardless of the DNA added (Figure 4B,C). On the other hand, when the probe was adsorbed on Tb^{3+} /GMP, it can be desorbed by other DNA sequences, further confirming the much stronger DNA adsorption affinity of the AMP CPs (Figure 4D,E).

For Tb^{3+} /GMP, adding C_{15} induced the highest adsorption for both probes (Figure 4D,E), whereas T_{15} and A_{15} ranked the next. We have recently observed that poly-C DNA adsorbed on many nanomaterials (e.g., graphene oxide, MoS_2 , and various metal oxides) more tightly than other homo-DNA sequences.^{19,22,44} At the same time, C can base-pair with G, which may also contribute to its stronger affinity on Tb^{3+} /GMP. At this moment, it is unclear which mechanism played a more important role.

In general, FAM- T_{15} was adsorbed more tightly on Tb^{3+} /GMP than FAM- A_{15} , as its signal was much lower. This suggests that in addition to DNA phosphate interactions, DNA bases may also contribute. For example, G/T can form a wobble base pair. At the same time, T_{15} induced more FAM- A_{15} desorption than A_{15} (Figure 4D), and A_{15} induced more FAM- T_{15} desorption than T_{15} (Figure 4E). This suggests that DNA hybridization also played a role in DNA desorption.

The effect of DNA length was then studied using poly-C DNA (Figure 4F,G). C_{15} and C_{30} induced the highest

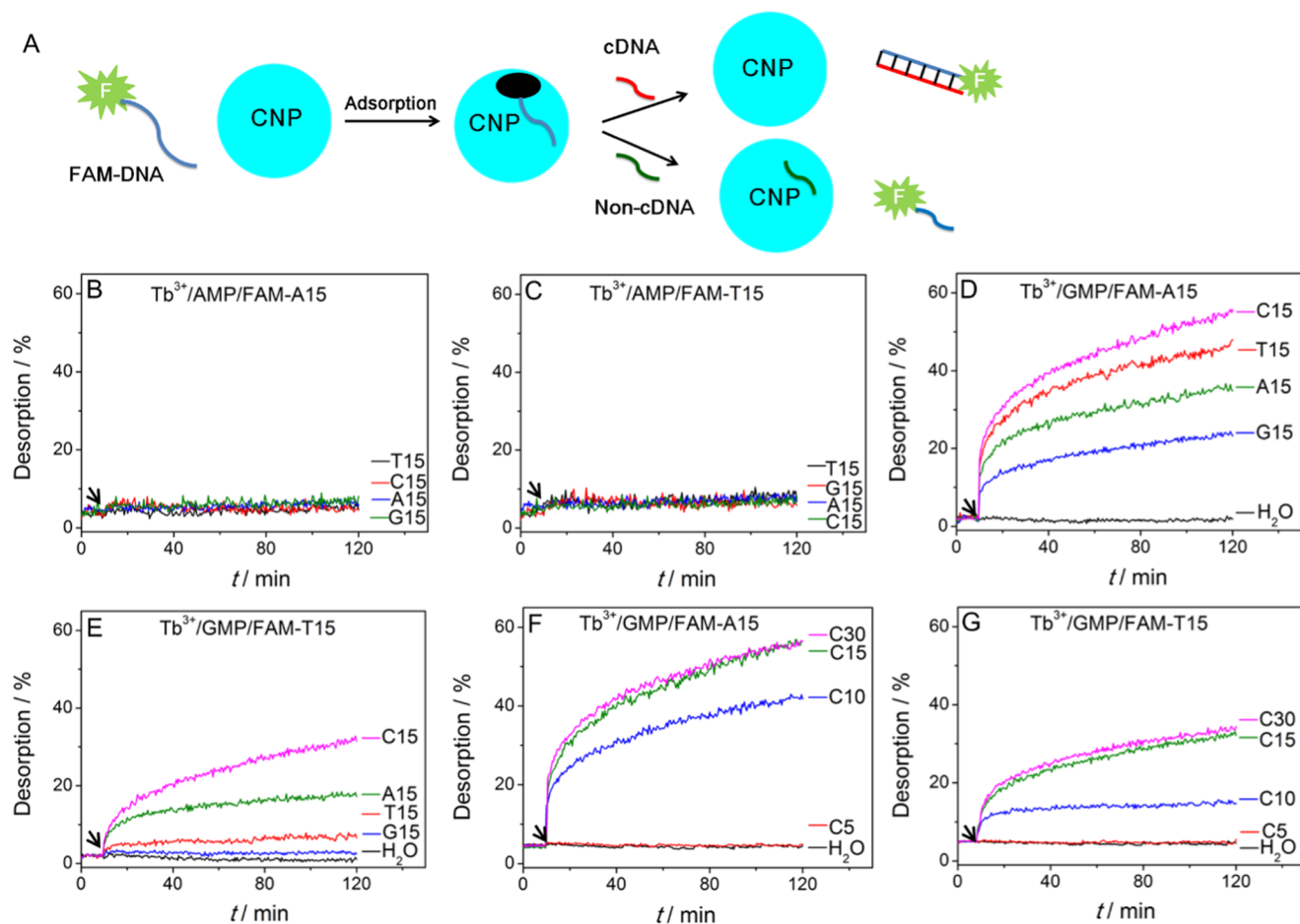


Figure 4. (A) Adsorption of a FAM-labeled DNA resulting in quenched fluorescence, and its subsequent desorption by hybridization to complementary DNA (cDNA) or displacement by a non-cDNA with recovered fluorescence. Kinetics of desorption of FAM-labeled A₁₅ (20 nM) from (B) Tb³⁺/AMP and (D) Tb³⁺/GMP, and FAM-labeled T₁₅ (20 nM) from (C) Tb³⁺/AMP and (E) Tb³⁺/GMP by the four 15-mer nonlabeled homo-DNA (0.4 μ M each) added at 10 min. Kinetics of desorption of (F) FAM-labeled A₁₅ (20 nM) and (G) FAM-labeled T₁₅ (20 nM) from Tb³⁺/GMP by poly-C DNA of different lengths (0.4 μ M each) added at 10 min.

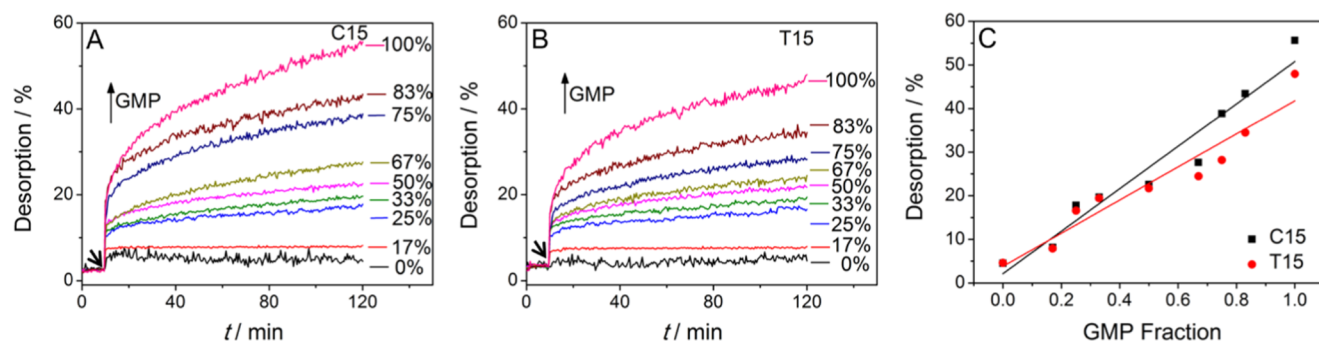


Figure 5. Kinetics of desorption of FAM-labeled A₁₅ (20 nM) from Tb³⁺/(GMP + AMP) by 0.4 μ M (A) C₁₅ and (B) T₁₅ added at 10 min. (C) The percentage of FAM-A₁₅ desorbed from Tb³⁺/(GMP + AMP) at various GMP fractions after adding T₁₅ or C₁₅ for 120 min.

desorption, followed by C₁₀, whereas no desorption was observed with C₅. Note that the amount of DNA desorbed by C₃₀ remained the same as that by C₁₅. Considering that C₃₀ has double the number of nucleotides (at the same DNA molar concentration) compared to C₁₅, it is likely that C₁₅ was already in a favorable configuration for DNA adsorbing on Tb³⁺/GMP, and even longer poly-C DNA could not further improve the affinity.

Fine Tuning Affinity by Mixing AMP/GMP. It seemed that changing from GMP to AMP had a huge influence on the

DNA adsorption affinity of the CPs. We suspected that we might be able to fine-tune the interactions by mixing AMP and GMP at different ratios. To test this idea, we prepared a series of CPs by using GMP/AMP mixtures. We adsorbed FAM-A₁₅ on these CPs, and nonlabeled C₁₅ or T₁₅ was added to desorb the FAM-A₁₅ DNA (Figure 5A,B). In both cases, the more the GMP added, the more the DNA desorbed, and a roughly linear relationship was observed (Figure 5C). This confirmed that we could indeed tune DNA adsorption affinity by using their mixtures.

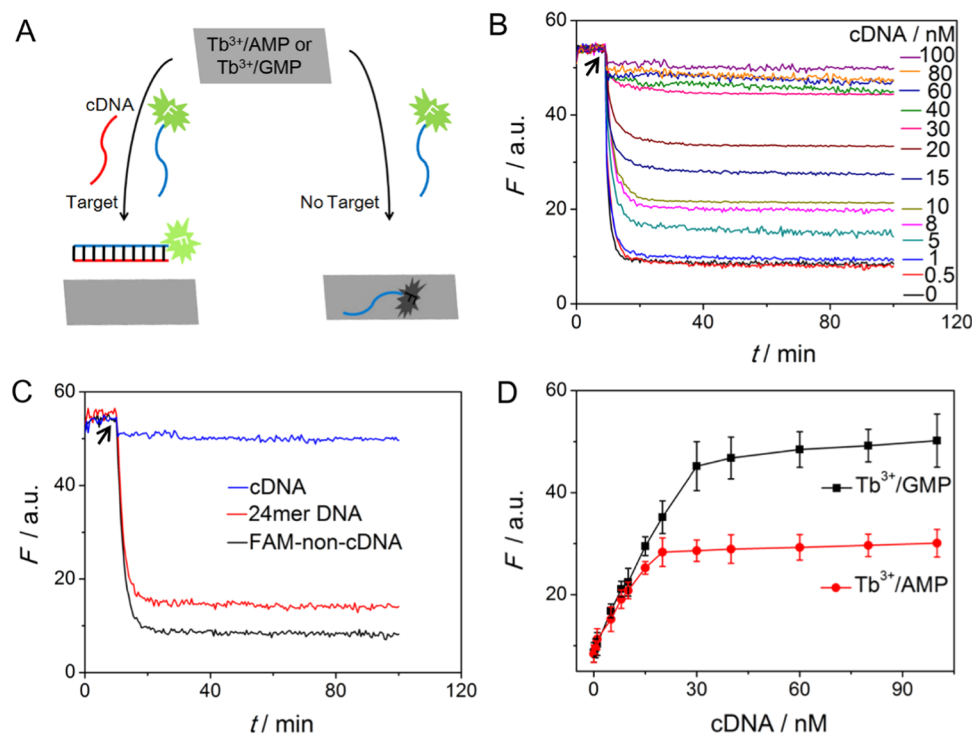


Figure 6. (A) Schematics of DNA sensing based on the difference in single-stranded DNA and double-stranded DNA adsorption of the CPs. (B) Kinetics of FAM-24-mer DNA (20 nM) adsorption by $\text{Tb}^{3+}/\text{GMP}$ (150 $\mu\text{g}/\text{mL}$) in the presence of various concentrations of the target cDNA. (C) Kinetics of the free FAM-24-mer DNA (20 nM) adsorption by 150 $\mu\text{g}/\text{mL}$ $\text{Tb}^{3+}/\text{GMP}$, with a 24-mer nontarget DNA, and with the target cDNA (100 nM), respectively. The arrowheads indicate the time point when $\text{Tb}^{3+}/\text{GMP}$ was added (10 min). (D) The remaining fluorescence of FAM-24-mer (20 nM) adsorption by $\text{Tb}^{3+}/\text{GMP}$ in the presence of various concentrations of the target cDNA.

DNA Sensing. After the aforementioned fundamental studies, we then tested these CP nanoparticles as a sensing platform for DNA detection. As pre-adsorption of probe DNA did not seem to offer sufficient selectivity (e.g., all DNA sequences can induce probe desorption), we used the pre-hybridization strategy as shown in Figure 6A.^{45–47} Here, the probe was a FAM-labeled 24-mer DNA with a random sequence. We first successively hybridized various concentrations of the target complementary DNA (cDNA) with the probe for 10 min, to which $\text{Tb}^{3+}/\text{AMP}$ or $\text{Tb}^{3+}/\text{GMP}$ was added. The kinetics of signaling on $\text{Tb}^{3+}/\text{GMP}$ (Figure 6B) and $\text{Tb}^{3+}/\text{AMP}$ (Figure S1A) were followed. The final fluorescence was higher with a higher concentration of the target DNA, suggesting that adsorption of duplex DNA was less favorable. The kinetics of adsorption was quite fast and the system reached a stable signal in just a few minutes. This cDNA concentration-dependent fluorescence indicates potential sensing applications.

We quantified the relative fluorescence enhancement at 10 min after adding the $\text{Tb}^{3+}/\text{GMP}$ CPs (Figure 6D), and a linear relationship was observed up to 30 nM DNA. We also measured the detection limits of these sensors based on the $3\sigma/\text{slope}$ calculation (σ = background variation in the absence of cDNA) to be 0.9 nM DNA for $\text{Tb}^{3+}/\text{GMP}$. This is comparable to most nanomaterial based DNA sensors.^{13,48–50}

The selectivity was further tested (Figure 6C), where 100 nM nonlabeled 24-mer DNA did not inhibit probe adsorption and the fluorescence still dropped, suggesting that DNA hybridization forming a duplex was required for the inhibited probe adsorption. We also tested the same sensing method with $\text{Tb}^{3+}/\text{AMP}$ (Figure S1B,C). As it has stronger DNA adsorption affinity, the difference between single-stranded and

double-stranded DNA was smaller, and the sensitivity was lower. Finally, we also tested the $\text{Tb}^{3+}/\text{GMP}$ based assay in a lake water sample (Figure S1D), also confirming its selective recognition of the target DNA.

CONCLUSIONS

In summary, we systematically studied DNA adsorption and desorption from various $\text{Ln}^{3+}/\text{nucleotide}$ CP nanoparticles using AMP and GMP as metal ligands. We discovered that DNA was adsorbed more tightly by $\text{Ln}^{3+}/\text{AMP}$. The phosphate backbone binding was very important for DNA adsorption onto these CPs, although DNA bases also contributed to adsorption. Urea, proteins, and surfactants were more effective in displacing DNA from $\text{Tb}^{3+}/\text{GMP}$ than from $\text{Tb}^{3+}/\text{AMP}$. By mixing AMP and GMP at various ratios, we continuously tuned the affinity of DNA adsorption. Using FAM- A_{15} as a pre-adsorbed probe, C_{15} induced more probe desorption than T_{15} from $\text{Tb}^{3+}/\text{GMP}$, suggesting that C_{15} adsorption by $\text{Tb}^{3+}/\text{GMP}$ might be more favorable than its hybridization between T_{15} and A_{15} . $\text{Tb}^{3+}/\text{GMP}$ exhibited higher probe DNA detection sensitivity. Considering the modular nature of such CP materials, it is likely that one could also mix other components including metal ions and different lengths of phosphate (e.g., AMP and ATP) to further fine-tune material properties. These fundamental understandings are valuable for the designing and optimization of materials and devices based on these CP nanoparticles.

MATERIALS AND METHODS

Chemicals. All DNA samples were from Integrated DNA Technologies (IDT, Coralville, IA). The DNA sequences were

A₁₅ (i.e., 5'-AAAAAAAAAAAAAAAA); T₁₅; G₁₅; C₁₅; FAM-A₁₅ (i.e., a carboxyfluorescein label on the 5'-end of A₁₅); FAM-T₁₅; FAM-G₁₅; FAM-C₁₅; FAM-24-mer FAM-ACG-CATCTGTGAAGAGAAGCTGGG; and c-24-mer: CCCAGTTCTCTTCACAGATGCGT. Lanthanum chloride, terbium chloride, lutetium chloride, sodium chloride, magnesium chloride, sodium dodecyl sulfate (SDS), cetyltrimethylammonium bromide (CTAB), bovine serum albumin (BSA), Tween 80, adenosine 5'-monophosphate disodium salt (AMP), and guanosine 5'-monophosphate disodium salt hydrate (GMP) were purchased from Sigma-Aldrich (St Louis, MO). 2-[4-(2-Hydroxyethyl)piperazin-1-yl]ethanesulfonic acid (HEPES) was from Mandel Scientific Inc. (Guelph, ON, Canada). 2-(N-Morpholino) ethanesulfonic acid (MES) monohydrate was from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). Milli-Q water was used for all of the experiments.

Preparation of Nucleotide/Lanthanide CPs. The CPs made of Ln³⁺/AMP and Ln³⁺/GMP were synthesized according to a previously reported method.²⁸ Typically, 1 mL of LnCl₃ aqueous solution (5 mM) was added to 1 mL of AMP or GMP disodium salt solution (10 mM) dissolved in HEPES buffer (100 mM, pH 7.6) under stirring, and white precipitates were formed immediately. After stirring for 2 h at room temperature, the CP products were collected by centrifugation at 14 000 rpm for 10 min followed by washing three times with water and centrifugation. Finally, the CPs were dispersed in 1 mL of water and stored at 4 °C for use. Tb³⁺/(AMP + GMP) CPs with different ratios of AMP/GMP were prepared using the same method.

TEM, SEM, and Dynamic Light Scattering (DLS). TEM was performed on a Philips CM10 microscope. An aqueous droplet containing 100 µg/mL of Tb³⁺/AMP or Tb³⁺/GMP dispersion was placed on a 230 mesh holey carbon copper grid. After 30 s, the excess solution was removed by a piece of filter paper. SEM was performed on a JSM-6330F (acceleration voltage, 15 kV). After drying the CP deposited filter membranes in vacuum, they were coated with Pt using a Hitachi E-1030 ion sputter before imaging. The ζ-potential of the CP nanoparticles was measured by dynamic light scattering (DLS) using a Malvern Zetasizer Nano ZS90 system with a He–Ne laser (633 nm) at 90° collecting optics at 25 °C. In a typical experiment, CPs were dispersed in 10 mM HEPES buffer (pH 7.6).

DNA Adsorption. The kinetics of DNA adsorption were investigated by adding different concentrations of Ln³⁺/AMP or Ln³⁺/GMP with a molar ratio of 2:1 to 100 µL of solution containing 20 nM FAM-labeled DNA in buffer A (10 mM HEPES, pH 7.6, 100 mM NaCl, and 1 mM MgCl₂) at 25 °C. Different salt concentrations were also tested. The fluorescence was measured using a microplate reader (Infinite F200 Pro, Tecan) with 490 nm excitation and 520 nm emission. To test DNA desorption, a 500 µL solution containing Ln³⁺/AMP or Ln³⁺/GMP (2 mg/mL) was respectively incubated with 200 nM FAM-A₁₅ or FAM-T₁₅ in buffer A in the dark at room temperature for 1 h. Then these solutions were washed with buffer A by centrifugation at 15 000 rpm for 10 min and they were finally dispersed in 500 µL of buffer A and stored at 4 °C (called sensor solution).

DNA Desorption. To study DNA desorption, 10 µL aliquots of the above sensor solutions were separately centrifuged, and the supernatant was removed. The pellets were then dispersed in 100 µL of 4 M urea, or 10 mM

phosphate, and the fluorescence intensity was measured. To study DNA desorption induced by proteins and surfactants, each well contained 10 µL of the above sensor solution and 90 µL of buffer A (10 mM HEPES, pH 7.6, 100 mM NaCl, and 1 mM MgCl₂). Then different concentrations of BSA or surfactant (SDS, Tween 80, and CTAB) were added to induce desorption. To displace the adsorbed DNA by DNA, 10 µL of the above DNA sensor solutions was added to each well containing 90 µL of buffer A. Then a final concentration of 0.4 µM nonlabeled DNA homopolymers (A₁₅/T₁₅/C₁₅/G₁₅) was added. To study the effect of DNA length, a final concentration of 0.4 µM C₅, C₁₀, C₁₅, and C₃₀ was added using the same method.

DNA Sensing. In a typical DNA assay, 50 µL of the fluorescent probe FAM-24-mer DNA (20 nM) was hybridized with different concentrations of target c-24-mer DNA in buffer A for 10 min, to which 2 µL of Tb³⁺/AMP or Tb³⁺/GMP (150 µg/mL) dispersion was added. The kinetics of fluorescence change was then measured using the microplate reader.

■ ASSOCIATED CONTENT

● Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.8b01217.

DNA sensing using Tb³⁺/AMP as the probe adsorbing material (PDF)

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Funding

This work was supported by the Natural Sciences and Engineering Research Council of Canada (NSERC), the National Natural Science Foundation of China (No. 21301034), and the National Science of Foundation of Guangdong Province (S2013040014083). Dr L.X. was supported by a China Scholarship Council (CSC 201608440087) to visit the University of Waterloo.

Notes

The authors declare no competing financial interest.

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