Exciton Energy Transfer-Based Fluorescent Sensing through Aptamer-Programmed Self-Assembly of Quantum Dots

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ABSTRACT: A novel exciton energy transfer-based ultrasensitive fluorescent sensing strategy for the detection of biological small molecules and protein has been established through split aptamer-programmed self-assembly of quantum dots (QDs). The signal is produced from exciton energy transfer of the self-assembled QDs. The recognition is accomplished using an aptamer sensor scaffold designed with two split fragment sequences, which specifically bind to the model analytes. The extent of particle assembly, induced by the analyte-triggered self-assembly of QDs, leads to an exciton energy transfer effect between interparticles, giving a readily detectable fluorescent quenching and red shift of the emission peak, which enables us to quantitate the target in dual signal modes. The application of the technique is well demonstrated using two representative split aptamer-based model systems for the detection of adenosine and thrombin. The sensitivity of this exciton energy transfer-based fluorescent sensing is much better than that of plasmonic coupling-based colorimetric methods. Limit of detections (LODs) down to 12 nM and 15 pM can be achieved for adenosine and thrombin, respectively. The sensing strategy is proposed as a general platform for robust and specific aptamer−target analysis which could be further developed to monitor a wide range of target analytes. The concept and methodology developed in this work shows a good promise in the study of molecular binding events in the biological and medical applications.

Molecule-mediated self-assembly of nanoparticles is of great scientific interest because architecturally defined collective properties from multiple nanoparticles could lead to applications such as photonic antennas, plasmonic nanodevices, and optical sensing. Different nanoscale components such as gold nanoparticles, graphene oxides, carbon nanotubes, quantum dots (QDs), etc. have been self-assembled and exploited for the development of various exquisite sensing systems. On the basis of their distance-dependent plasmonic coupling interaction, gold nanoparticles have been developed as a general platform for robust colorimetric detection methodology. As for semiconductor QDs, with their unique photophysical properties of continuous absorption spectra, narrow and tunable emission, and high photostability, QDs have shown potential for use in biological imaging and chemical analysis. In particular, their fluorescence properties are also interparticle-spacing dependent, and this facilitates a simple and distinguishable signal readout for optical sensing. Recently, several approaches to the self-assembly of QDs to explore their collective optical properties for fluorescent sensing have been reported. Nie et al. have proposed a label-free fluorescent detection of protein kinase activity through electrostatic interaction induced QDs aggregation. Zhou and co-workers reported glucose mediated self-assembly of phenylboronic acid modified QDs for cellular quantification. Our group also has developed a fluorescence turn-on nanoprobe based on F− ion triggered reversible assembly of QDs. However, the signal transduction mechanism of the assembled QDs for sensing has not been well elucidated, and most of the reports lack specific biological information-containing ligand molecules to efficiently guide the self-assembly of QDs. It is desirable for utilization of biological recognition of small molecules, protein, and nucleic acids, to program the assembly processes in the fields of bioanalysis, biomedical diagnostics, etc.

Aptamers are single-stranded RNA or DNA oligonucleotides with unique intramolecular conformations that hold distinct binding properties to various targets, including small molecules, proteins, and even entire organisms. Various aptamer-based sensing methods have been developed, and the biggest advantages of the aptamer sensor are that oligonucleotides can be chemically synthesized at very low cost and they show good stability during long-term storage. Recently, by utilizing their high specific molecular recognition ability, several studies have been performed with QD-based fluorescence readout. While molecularly mediated self-assembly of QDs...
might provide a novel basis for fluorescent sensing, we are unaware of any studies which have examined the self-assembled QDs from the perspective of combination with aptamer acceptors. Mediation of the assembly of QDs by an aptamer target may yield a facile means of fabricating a QD assay with collective optical properties in response to concentration changes of the analytes.

As proof-of-concept, we report aptamer-programmed self-assembly of QDs for sensitive fluorescent sensing. Two well-characterized adenosine and thrombin-specific aptamers are chosen as models. Generally, molecule-mediated assembly of nanoparticles usually requires polyvalent molecular recognition interactions so that a sandwich-format structure could be established. In our design, the aptamer was split into two flexible single strand deoxyribo-nucleic acid (ssDNA) fragments, which are attached to different populations of QDs. The target, working as a molecular linker, reassembles the two pieces of ssDNA into the intact aptamer tertiary structure and then programs the self-assembly of fluorescent QDs. The detection strategy of our proposed approach is illustrated in Figure 1. An anti-adenosine aptamer sequence has 27-nt (5′-ACC TGG GGG AGT ATT GCG GAG GAA GGT-3′).

The aptamer is split as two different fragments, ABA1 (ABA is adenosine binding aptamer) and ABA2. They could not form stable intermolecular duplexes in the absence of adenosine. After addition of adenosine, the two pieces reassemble into intact tertiary structure and the adenosine aptamer fragments mediated sandwich complex can form. As a consequence, a significant fluorescence quenching and band-shift occur due to the exciton energy transfer between the aggregated QDs, which enable us to quantitate adenosine in dual signal modes. The combination of the specific molecular recognition of aptamers with the diverse, strong signal transduction capacity of the assembled QDs renders this approach a selective and sensitive response. More important, this approach allows diverse aptamers, functionalized on the surface of QDs, to satisfy the particular requirements of the sensing applications.

### EXPERIMENTAL SECTION

**Materials and Instruments.** Cadmium perchlorate hexahydrates (Cd(ClO₄)₂·6H₂O, 99%) were purchased from Acros Organics. Thioglycolic acid (98%), 1-ethyl-3-[3-dimethylamino propyl] carbodiimide hydrochloride (EDC), and N-hydroxysuccinimide (NHS) were purchased from Sigma-Aldrich. Telluride powders were purchased from Sinopharm. Human α-thrombin (from human plasma, lyophilized powder, ≥2000 NIH units·mg⁻¹ protein), adenosine, cytidine, guanosine, and uridine (99%) were all purchased from Sigma-Aldrich. Unless otherwise noted, all reagent-grade chemicals were used as received. The water used in all experiments was of Millipore Milli-Q grade.

All the oligonucleotide sequences used in this study were synthesized and purified through high performance liquid chromatography (HPLC) by Sangon Biotechnology Inc. For adenosine, the split aptamer sequence information was list as follows, 5′-NH₂-C₆-TTT TTT TAC CTG GGG GAG TAT-3′, denoted as adenosine binding aptamer 1 (ABA1); 5′-NH₂-C₆-TTT TTT GCG GAG GAA GGT-3′, denoted as adenosine binding aptamer 2 (ABA2). The dilution buffer solution was 40 mM borate buffer, pH = 7.8. The reaction buffer solution was 40 mM borate buffer with 137 mM NaCl and 2.7 mM KCl, pH = 7.8. For thrombin, the split aptamer sequence information was list as follows, 5′-NH₂-C₆-TTT TTT CTT TGG TGT TTG-3′, denoted as thrombin binding aptamer 1 (TBA1); 5′-TGG TTG TTT TTT T-C₆-NH₂-3′, denoted as thrombin binding aptamer 2 (TBA2).

Fluorescence spectra were recorded on a Hitachi F7000 fluorescence spectrophotometer, and the measurements were performed with excitation wavelength at 370 nm. Time-resolved fluorescence measurements were conducted on...
Fluorolog-Tau-3 spectrophuorometer (Jobin Yvon) with a NanoLED pulsed diode excitation at 461 nm. Absorption spectra were recorded on a UV–vis 1601 Shimadzu spectrophotometer. Dynamic light scatter (DLS) experiments were carried out in a Malvern Nano-ZS system equipped with a He–Ne laser working at 633 nm to examine the hydrodynamic diameter (number-weighted mean diameter). Transmission electron microscopy (TEM) was performed on a JEO-L1230 microscope. The samples for TEM were obtained by drying sample droplets from water dispersion onto a Cu grid coated with a lacy carbon film, which was then allowed to dry prior to imaging. Agarose gel electrophoresis was used to prove whether aptamer-modified QDs were successfully prepared. 1× TAE (Tris-acetate-ethylene diamine tetra acetic acid (EDTA)) buffer (dilution of 5× TAE buffer: 4 mM Tris, 2 mM acetic acid, 0.2 mM EDTA, pH 8.0) was used as the electrophoresis buffer. The concentration of agarose gel was 1%. Bromophenol blue was used as an indicator in the electrophoresis. Aagarose gel electrophoresis was carried out at 5.0 V cm⁻¹ constant voltages for 1.0 h by using a DYY-III43A electrophoresis apparatus (Beijing Liuyi Inc.).

Preparation of Aptamer Fragment-Modified QDs. Thioglycolic acid-capped CdTe QDs were prepared via a method described in the literature with minor modifications.28 The mole concentration of QDs was determined as a procedure reported by Peng et al.29 Split aptamer ABA1 and fluorescent QDs were bridged with EDC-NHS coupling agents. Thioglycolic acid-capped QDs in dilution buffer were incubated with EDC and NHS (QDs/EDC/NHS = 1:100:150 in molar ratio) for 15 min. Then, a batch of ABA1 solution was added (QDs/ABA1 = 1:25 in molar ratio) and incubated for 120 min. The redundant DNA was removed by ultracentrifugation. The ABA1 aptamer sequence labeled QDs (ABA1-QDs) were diluted with borate buffer and stored at 4 °C. Modifications of ABA2, TBA1, and TBA2 with QDs were performed with similar procedures, and the corresponding labeled QDs were denoted as ABA2-QDs, TBA1-QDs, and TBA2-QDs, respectively.

Fluorescent Detection of Aptamer Targets. For adenosine detection, identical ABA1-QDs and ABA2-QDs were mixed in reaction borate buffer, and then, different concentrations of adenosines were gradually added. After incubation for 60 min at room temperature, fluorescent spectra of the mixture were recorded. For identifying the target-specificity of this sensing system, the assay for adenosine analogue solutions of uridine, cytidine, and guanosine were performed. The fluorescence quenching efficiency can be calculated from the following equation: \( I = \left( \frac{F_0 - F}{F_0} \right) \), where \( F_0 \) and \( F \) are the fluorescence intensity of QDs in the absence and presence of target. The band-shifts were obtained from the emission peak change before and after analyses addition.

All assay conditions for fluorescent detection of thrombin were the same as those used for the detection of adenosine, except that the adenosine aptamer was replaced by antithrombin aptamer (TBA1 and TBA2; QDs: DNA = 1:5 in molar ratio; the optimal concentration of TBA1-QDs and TBA2-QDs was 125 nM, respectively). Subsequently, for identifying the target-specificity of this sensing system, bovine serum albumins (BSA), human serum albumins (HSA), and myoglobin (Mb) were assayed in the same way as thrombin.

RESULTS AND DISCUSSION

Aptamer-Programmed Self-Assembly of QDs. Hydrophilic thioglycolic acid-capped CdTe QDs were prepared for fluorescent labeling of aptamer sequences. The reason that thioglycolic acid-capped QDs were chosen is that thioglycolic acid is being intensively studied as chelating ligands for fluorescent QDs, and the terminal carboxylic group can be conjugated with nearly all protein or peptide molecules as well as a host of other macromolecules.28 The bulk room-temperature linear absorption and fluorescent spectra of the CdTe QDs are shown in Figure S1(A), Supporting Information. The peak of the first exciton absorption transition is centered at 585 nm, and the peak of the fluorescence is Stokes-shifted from the absorption by approximately 24 nm to a center value of 609 nm. In addition, the HRTEM image of QDs is shown in Figure S1(B), Supporting Information, and their diameter was estimated to be 4.1 ± 0.5 nm by Gaussian fitting.

The 27-nt anti-adenosine aptamer was chosen as a representative for biological functionalization of QDs. This aptamer shows high affinity to adenosine with a dissociation constant (\( K_d \)) of 6 ± 3 μM.30 The aptamer contains two highly conserved guanine-rich regions, two invariant adenine residues, and two regions of predominant Watson–Crick covariation. The integer aptamer was designed into two pieces of sequences used as sensing probes, and they appeared as random-like single strands in the absence of the target (Figure S2, Supporting Information).31,32 Generally, the main concern about the split aptamer is that the splitting makes minimal disturbance on their target recognition. In this design, no significant perturbation of the ligand-binding abilities was found.33–35 Each one was equipped with an additional amino residue in the terminus for further bioconjugation. A 6-mer polyT (polyT6) between the amino groups and 5 Grp of ABA2, TBA1, and TBA2 with QDs were successfully covalently linked to QDs. We expected that split aptamers were bridged with a general EDC-NHS coupling system. Aagarose gel electrophoresis was used to prove whether aptamer-modified QDs were successfully prepared. Under the electric field at 100 V constant voltages for 1.0 h, the thioglycolic acid-capped QDs presented in the electrophoresis lane (a) moved to the positive electrode, but the ABA1-QDs complex (lane b) and ABA2-QDs complex (lane c) moved more quickly (Figure S3, Supporting Information). The faster mobility of the aptamer fragment-QDs complex compared with bare QDs was ascribed to a higher negative potential after the aptamer fragment grafted on their surface. The results clearly demonstrated that split aptamers were successfully covalently linked to QDs. We expected that the aptamer fragment anchored on the surface of QDs would be able to form stable sandwich-format complexes with adenosine. The sandwich detection model is described in Figure 1. The adenosine aptamer was designed into two flexible ssDNA pieces, ABA1 and ABA2, which were then attached on the surface of different QDs, respectively. The target molecule adenosine can glue ABA1 and ABA2 together; subsequently, the nanoparticles come closer to each other to form aggregates, which led to a significant fluorescence quenching and band red-shift due to the exciton energy transfer of the assembled QDs.

We first challenged this sensor with a detection of 10 μM adenosine. The introduction of adenosine triggered the assembly of the ABA1-QDs and ABA2-QDs. The adenosine-
induced assembly of the QDs was well reproducible from batch to batch. DLS was used to validate the adenosine-mediated self-assembly on the basis of the hydrodynamic diameter \(D_h\). Figure 2A shows a set of size data for the assembly of QDs in the presence of adenosine. Upon the addition of adenosine to the solution containing ABA1-QDs and ABA2-QDs, the average \(D_h\) value increased from 7.7 \(\pm\) 2.3 to 513.4 \(\pm\) 94.9 nm, providing a strong indication of the conversion of single nanoparticle assembly into aggregates. Furthermore, transmission electron microscope (TEM) images were taken to examine the morphology of the adenosine-mediated assembly of QDs. The TEM images are representative of the characteristic particle sizes and shapes on the entire TEM grid for all the samples. The introduction of adenosine led to an increase in the particle size of the QDs assemblies (Figure 2B). The morphology of the assemblies revealed many small QDs closely packed and thus suggested the target triggered self-assembly of the nanoparticles.

The adenosine-induced close packing of the QDs significantly affected the luminescence properties of the resultant assemblies. Figure 3A shows the photoluminescence spectra of QDs before and after adenosine addition. The emission spectra of the QDs assemblies showed a reduction in their fluorescence intensity and a 5.5 nm red shift from 609.0 to 614.5 nm. This band shift corresponded to an energy difference of 18.2 meV between the free QDs in solution and the QDs assemblies. Two different mechanisms existed to explain the fluorescence quenching of QDs upon self-assembly: electronic coupling and exciton energy transfer.\(^{12,36,37}\) The former suggested that strong electronic coupling between neighboring QDs can cause hybridization of the band edge orbital, which leads to fluorescence quenching, accompanied by a red-shift in both absorption and fluorescence spectra. In the latter mechanism, though, exciton energy of higher bandgap QDs is migrated to smaller bandgap QDs, which can cause fluorescence quenching, accompanied by only red-shift of emission peak. To validate the fluorescence quenching mechanism, their absorbance spectra were obtained. As illustrated in Figure 3B, compared to that of the free QDs in solution, the absorbance spectrum for the QDs assemblies showed no obvious change, which indicated possible exciton energy transfer between closely packed QDs. Further evidence for the exciton energy transfer among QDs was also obtained from emission lifetime measurements by monitoring the emission intensity as a function of time as shown in Figure 3C. The exciton lifetime of the aptamer-functionalized QDs in solution was determined to be 18.7 \(\pm\) 0.4 ns, and those for the QDs assemblies were found to be 16.4 \(\pm\) 0.5 ns (Figure S4, Supporting Information). The difference in the lifetimes of the free and aggregate nanoparticles is mainly from the emission intensity for the initial 20 ns. The approximately 2.3 ns reduction in the lifetime of the QDs excitation can be rationalized as arising from the exciton energy transfer from small to large QDs. This was consistent with that reported in our previous work for cysteamine-capped QDs, where pH induced aggregation of QDs, which was accompanied by a fluorescence quenching and bandshift.\(^{15}\) Therefore, adenosine induced fluorescence self-quenching as well as a red-shift in emission peak mainly originated from exciton energy transfer in the assembled QDs. In detail, because spectral broadening arises from the size distribution of individual QDs in the QDs ensemble, an exciton energy transfer tends to occur from the smaller to larger QDs, which leads to a fluorescence red shift. On the other hand, partially nonluminescent QDs exist in the QDs ensemble, probably because of certain surface defects, so that an exciton energy transfer will result in a nonradiative exciton recombination and fluorescence self-quenching.\(^{26-38}\) Thus, the exciton energy transfer interaction of the assembled QDs provides feasibility of the adenosine sensing based on the aptamer-programmed assembly of QDs.

A series of control experiments was furthermore carried out to prove that this sensor could recognize adenosine accurately and sensitively; i.e., such fluorescence attenuation and bandshift...
were specific to the binding of adenosine with the engineered aptamer. First, when only one of the aptamer fragment modified QDs, ABA1-QDs or ABA2-QDs, was tested for adenosine sensing, no obvious fluorescent change was observed at the same concentration of adenosine (10 μM) (Figure 4A).

Both of the ABA1-QDs and ABA2-QDs resulted in the complementary sequence aptamer. First, when only one of the aptamer fragment were specific structural formation was essential for the adenosine binding. The result also suggested that the split aptamer fragments maintained a high binding capability to their targets. In addition, adenosine analogs guanine, cytosine, and uridine were employed to identify the target-specificity of this detection system under the same experimental conditions. As shown in Figure 4B, none of the adenosine analogs could elicit a response relative to that of adenosine, which implied that the sensor had excellent selectivity toward adenosine. Such a high selectivity was imparted definitely by the specific recognition of split aptamer toward adenosine.

**Kinetics of the Self-Assembly.** The self-assembly of biofunctional QDs was dominated by two processes: the recognition of aptamer fragments with target and the collisions between interparticles. The self-assembly process greatly relied on the recognition of aptamer fragments with target, and thus, aptamer DNA coverage on the surface of QDs was a key factor for this fluorescent sensing. The relation of fluorescence quenching with adenosine for various mole ratios of split-aptamer to QDs was recorded (Figure S5, Supporting Information). It was found that the self-assembled fluorescent QDs probe had the most sensitive response at split-aptamer concentration of 25 times to QDs (nDNA/nQDs = 25, in molar ratio). Under this condition, the actual number of aptamer strands grafted on each QD was calculated according to the adsorption change of aptamer before and after bioconjugation, and it was estimated that on the average about 11 aptamers were anchored on each QD. In addition, the self-assembly process also greatly relies on the probability of the collisions between particles. Thus, this is a concentration-dependent process. A high concentration of QDs is in favor of their self-assembly and consequently highly efficient fluorescence self-quenching. The influence of the QD amounts on the extent of adenosine-induced fluorescent quenching was examined (Figure S6, Supporting Information). When 50 nM QDs were used, the quenching efficiency reached a maximum. A higher concentration of QDs decreased fluorescence quenching efficiency instead, and it was probable that a mass of QDs rendered a high fluorescent background and a poorly sensitive response for detection.

To provide a better understanding of this system, a kinetic assay of the self-assembly process was performed. Usually, a self-assembly process is monitored by dynamic light scattering or a transmission electron microscope. We, for the first time, monitored the kinetics of the self-assembly of QDs using fluorescence quenching efficiency. The fluorescence was recorded at a time span of 4 min. As shown in Figure 5, the kinetics of aptamer mediated QDs aggregation exhibits a sigmoidal behavior, with three distinct phases. The initial rate of aggregate formation is slow, and the second phase is characterized by rapid, self-assembled aggregation. The final phase is the reduction of aggregation rate with an asymptotic approach to the equilibrium aggregate fraction. Similar sigmoidal kinetics was observed in many intermolecular interaction-based self-assembly processes. This was consistent with that reported in a previous work for antigen-mediated QDs aggregation. It was suggested that this was a nucleation limited aggregation process. From the kinetics data, it was also determined that the reaction progressed to a substantial extent in 20 min and was almost completely finished in 36 min. An understanding of self-assembly kinetics in this system may lead to improvements in sensitivity and specificity of this novel detection technique.

**Fluorescent Sensing of Adenosine.** The exciton energy transfer-based fluorescence responses enable us to quantitate the adenosine. The fluorescence emission spectra of biofunctional QDs solution spiked with various concentrations of adenosine were shown in Figure 6A. Fluorescence intensity was very sensitive to the change of adenosine concentration. With increasing amount of adenosine, it clearly showed a gradual intensity decrease as well as a red shift of emission wavelength. The change of fluorescent spectra resulted from the adenosine triggered aggregation of QDs. A linear relationship (R² = 0.99) between the fluorescent quenching and the adenosine concentration was obtained over the range of 12−200 nM (Figure S7, Supporting Information). The limit of detection at 12 nM (3σ) can be obtained. This sensitivity is comparable to or better than that of the reported detection method for adenosine listed in Table S1, Supporting Information.
Particularly, the proposed fluorescence-based tool was ca. 4 orders of magnitude lower than that of plasmonic coupling-based colorimetric methods, as reported previously. This exciton energy transfer of QDs is an intrinsically long-range resonance energy transfer process, which is a close $R^{-6}$-dependent relationship. We believe the high sensitive response of the assay was also ascribed to the high exponent distance-dependent relationship. Meanwhile, on the basis of the fluorescence attenuation, the binding affinity of QDs-aptamer to adenosine was determined (Figure S8, Supporting Information). QDs-aptamer shows a higher binding affinity ($K_d = 0.11$ μM) than that of aptamer ($K_d = 6$ μM) by 55-fold. Thus, the combination of the specific molecular recognition of aptamers with the diverse, strong signal transduction capacity of assembled QDs also offers this method a high sensitivity. In addition, it was interesting that the adenosine-induced red shift of the fluorescent emission as a function of adenosine concentration followed the same trend with that of the adenosine-induced fluorescent quenching (Figure 6B). Thus, this also allowed us to quantitate the adenosine in different signal modes. The emission color change provides the possibility for direct nake eye-based discrimination, and this was consistent with that reported by Nie et al. Fluorescent Sensing of Thrombin. The versatility of the proposed sensing strategy was further addressed using another model system based on the recognition of a short aptamer from thrombin. Thrombin has a 15-nt binding aptamer, 5′-GGTTGGTGTGGTTGG-3′. The aptamer binds to the fibrinogen-binding site of thrombin by folding G-quadruplex structure, with a dissociation constant ($K_d$) of $\sim 100$ nM. As illustrated in Figure 7A, the aptamer was split into two sequences as reported previously. The terminal amino group and a 6-mer polyT were modified at the 5′ end of the one split fragment sequence and another at the 3′ end. This was different with the design of split aptamer against adenosine, which is because the split thrombin binding aptamers bind with the target in a consistent orientation. Although the attachment of the biological molecules on QDs with control over final valence and orientation is quite hard to ascertain, it is inferred that this design herein is convenient to make the aptamer far from the surface of QDs to maintain the conformation of aptamer for recognition of thrombin. Both of the split aptamers were immobilized on a different batch of QDs in a buffered pH 7.4 loading solution. The particle suspensions were repeatedly centrifuged to remove unbound aptamer, and the buffer was then replaced with Tris-HCl buffer (pH 7.4, 140 mM NaCl, 1 mM MgCl₂). As thrombin was gradually added, the aggregation of QDs occurred, which was accompanied by a gradual fluorescence quenching and bandshift (Figure 7B). It was observed that the extent of fluorescence quenching and bandshift were smaller than those of adenosine. In this assay, concentration of thrombin down to 15 pM was achieved (Figure S9, Supporting Information). The sensitivity of this proposed method is about 1 order of magnitude higher than that of the previously reported colorimetric detection of...
thrombin. Importantly, the assay was quite selective, and no such fluorescence self-quenching phenomenon was observed when thrombin was replaced by other proteins, like human serum albumin (HSA), bovine serum albumin (BSA), and myoglobin (Mb) (Figure 7C). Thus, this strategy for biomolecular sensing, based on the controlled self-assembly of fluorescent QDs functionalized with smartly designed aptamer receptors, is envisioned as a robust and general platform that can be further developed to monitor a wide variety of target analytes.

## CONCLUSION

In summary, a fluorescent QDs nanoprobe through aptamer-programmed self-assembly was developed for the sensitive and selective detection of small biological molecules and protein. The method was based on the QDs aggregation-triggered fluorescence quenching and bandshift due to exciton energy transfer effects. In this sensing platform, the assembled QDs act as signal transducer while aptamer acts as recognition element, which render this method with high sensitivity and selectivity. Meanwhile, the aptamer molecule modified on the surface of QDs allows diverse aptamer function to satisfy the particular requirements of sensing applications. Therefore, this stimulus-responsive self-assembly of QDs technology may be expanded for the design of other aptamer sensors and show a great promise for application in the fields of clinical diagnosis and the construction of optoelectronic biosensing.

## ASSOCIATED CONTENT

* Supporting Information

Synthesis of fluorescent quantum dots, absorption and fluorescent spectra, TEM imaging, gel electrophoresis, the optimization experiments, and LOD calculation. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes
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