Supplementary Material (ESI) for Chemical Communications

Electronic Supplementary Information

Strong polyelectrolyte quantum dot surface for stable bioconjugation and layer-by-layer assembly applications

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Synthesis of surface ligands that containing different functional group:

a) Lipoic Acid NHS-Ester.

Lipoic Acid NHS-Ester was prepared by following the procedure described in the literature.[S1] 2.42 mmol of (±)-α-Lipoic acid (0.50 g) and 2.91 mmol of N-hydroxysuccinimide (0.335 g) were dissolved in 15 ml of tetrahydrofuran (THF) at 4 ℃. 2.91 mmol of dicyclohexylcarbodiimide (0.60 g) dissolved in 2 ml THF was added slowly. The solution was warmed to room temperature while stirring for 5h. The side product was filtered. The solvent was removed by evaporator and obtained solid crude product. The solid crude product was dissolved in ethylacetate(EA), and the remaining side products were removed by filtration. The product was further purified by recrystallization using EA/Hexane (1:1 v/v). Yield: 85.9 %. ^{1}H NMR : (300 MHz, $CDCl_3$): δ (ppm) 3.58 (m, 1H), 3.13 (m, 2H), 2.84 (s, 4H), 2.63 (t, J=7.3 Hz, 2H), 2.46 (m, 1H), 1.92 (m, 1H), 1.84-1.48 (m, 6H).

b) Sodium 2-(5-(1,2-dithiolan-3-yl)pentanamido)ethanesulfonate

Sodium 2-(5-(1,2-dithiolan-3-yl)pentanamido)ethanesulfonate was prepared by following the procedure described in the literature with modifications.[S2] 3.0 mmol of Lipoic acid NHS-ester was dissolved in 18 ml of dioxane. 4.5 mmol of Taurine was dissolved in 18 ml of 0.25 N Sodium carbonate buffer solution.

The pH of the Taurine solution was adjusted to 7.6 using sodium hydroxide solution (NaOH(aq)). The lipoic acid NHS-ester dioxane solution and the Taurine solution were slowly mixed together at -5 ℃, while stirred for 24 h at room temperature. Precipitated side products were removed by filtration. The solvent was evaporated using rotary evaporator. The crude product was mixed with small amount of NaOH aq. solution and extracted into isopropanol/chloroform/EA mixed solvent layer. The crude product solution was dried with sodium sulfate and the solvent was evaporated. The crude product was redissolved in water. Side products were removed by filtration. The crude product solution was freeze dried to yield the solid product. ^{1}H NMR : (300 MHz, $CDCl_3$): δ (ppm) 3.63 (m, 1H), 3.50 (t, J=6.7 Hz, 2H), 3.13 (m, 2H), 3.01 (t, J=6.8 Hz, 2H), 2.41 (m, 1H), 2.19 (t, J=7.3 Hz, 2H), 1.91 (m, 1H), 1.74-1.30 (m, 6H); m/z (FAB) 311.94 (M^- $C_{10}H_{18}NO_4S_3$ requires 312.04).

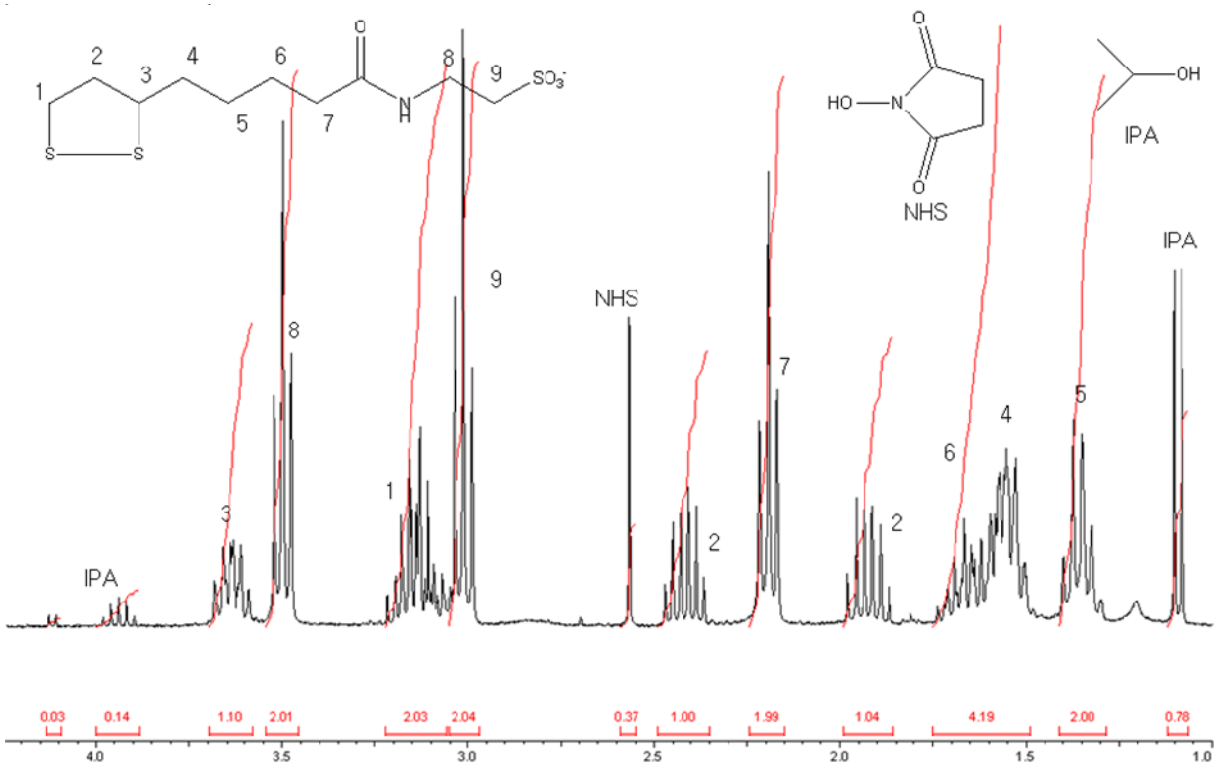


Figure S1 ^{1}H NMR data of Sodium 2-(5-(1,2-dithiolan-3-yl)pentanamido)ethanesulfonate

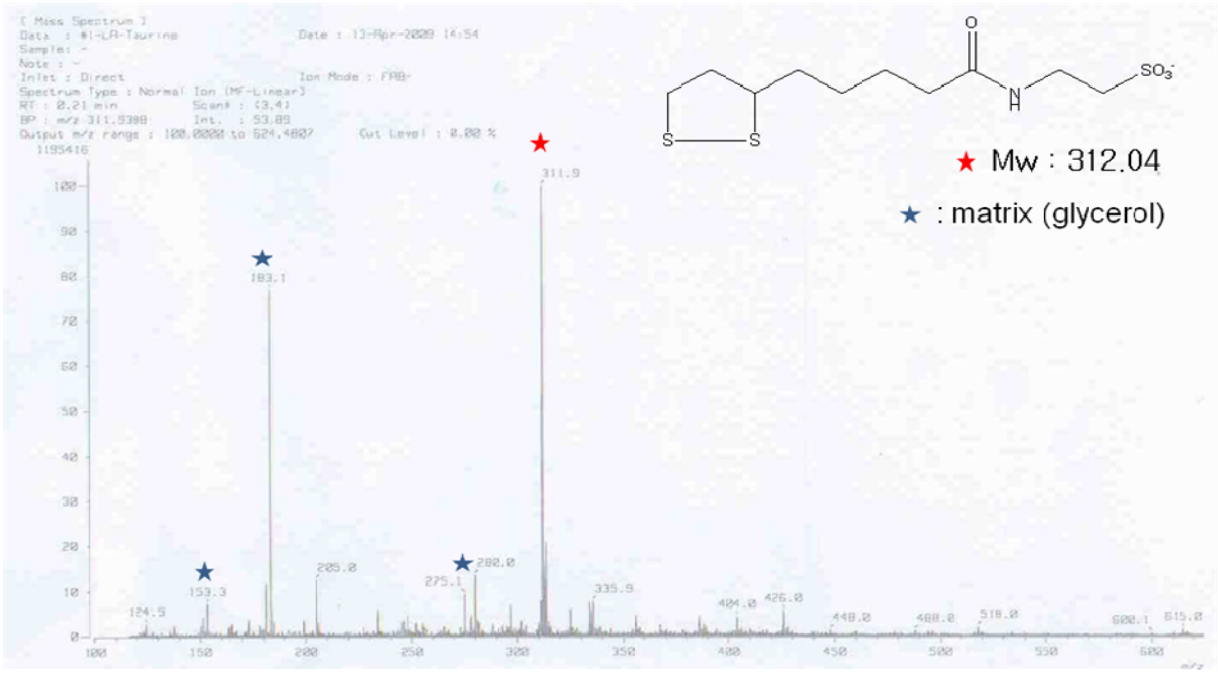


Figure S2 Mass spectra of Sodium 2-(5-(1,2-dithiolan-3-yl)pentanamido)ethanesulfonate

c) N-(2-trimethylammonioethyl)1,2-dithiolane-3-pentanamide chloride

N-(2-trimethylammonioethyl)1,2-dithiolane-3-pentanamide chloride was prepared by following the procedure described in the literature with modifications.[S3] 3.0 mmol lipoic acid NHS-ester was dissolved in 18 ml dioxane. 4.5 mmol (2-aminoethyl)trimethyammonium chloride was dissolved in 18 ml 0.25 N sodium carbonate buffer solution, and the pH was adjusted to 7.6 by adding NaOH aq solution. The lipoic acid NHS-ester dioxane solution and the (2-aminoethyl)trimethyammonium chloride solution were slowly mixed together at -5□ and stirred for 24 h at room temperature. The side products were removed by vacuum filtration. The solvent was evaporated using rotary evaporator. The crude product was dissolved in the least volume of NaOH(aq) and extracted into IPA/Cloroform/EA layer. It was dried with sodium sulfate and the solvent was evaporated. The crude product was redissolved in water. The undissolved side products were removed by filtration. The crude product solution was freeze dried to yield the product. ^{1}H NMR : (300 MHz, $CDCl_3$): δ (ppm) 3.70-3.57 (m, 3H), 3.42 (t, J=6.7 Hz, 2H), 3.91-3.07 (m, 11H), 2.41 (m, 1H), 2.22 (t, J=7.3 Hz, 2H), 1.91 (m, 1H), 1.72-1.29 (m, 6H); m/z (FAB) 290.99 (M^+ $C_{13}H_{27}N_2OS_2$ requires 291.16).

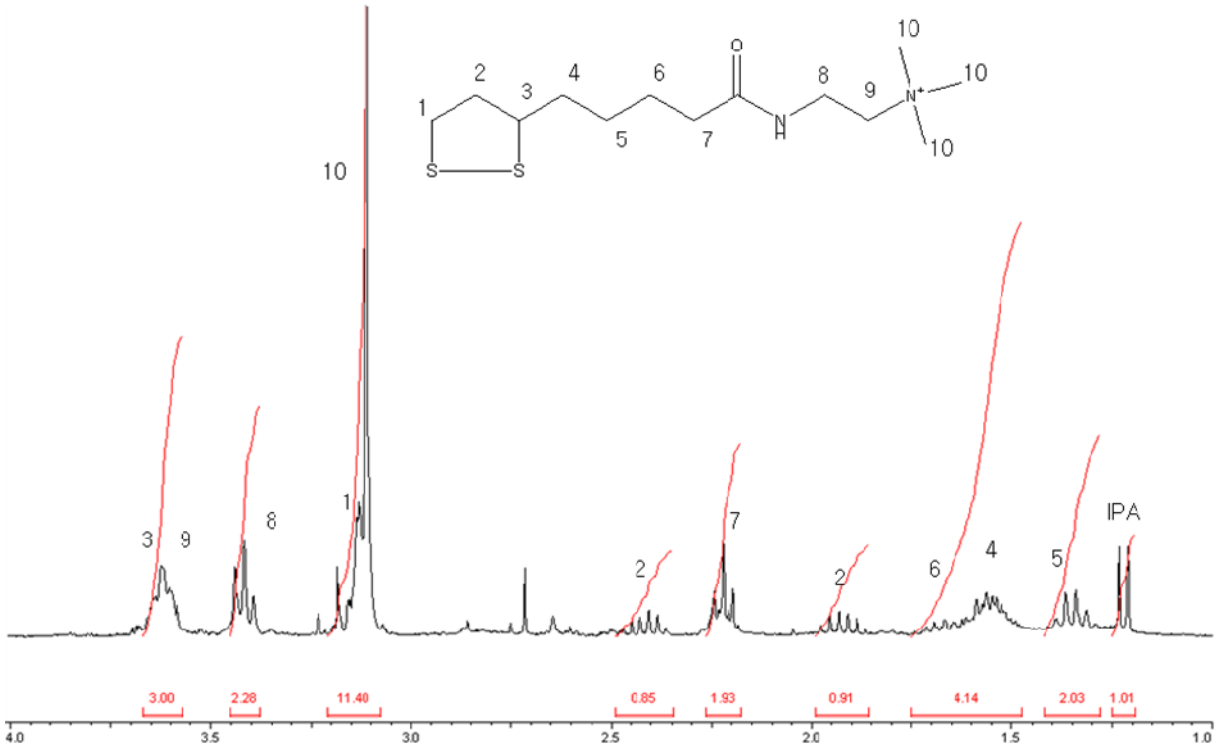


Figure S3 ^{1}H NMR data of N-(2-trimethylammonioethyl)1,2-dithiolane-3-pentanamide chloride

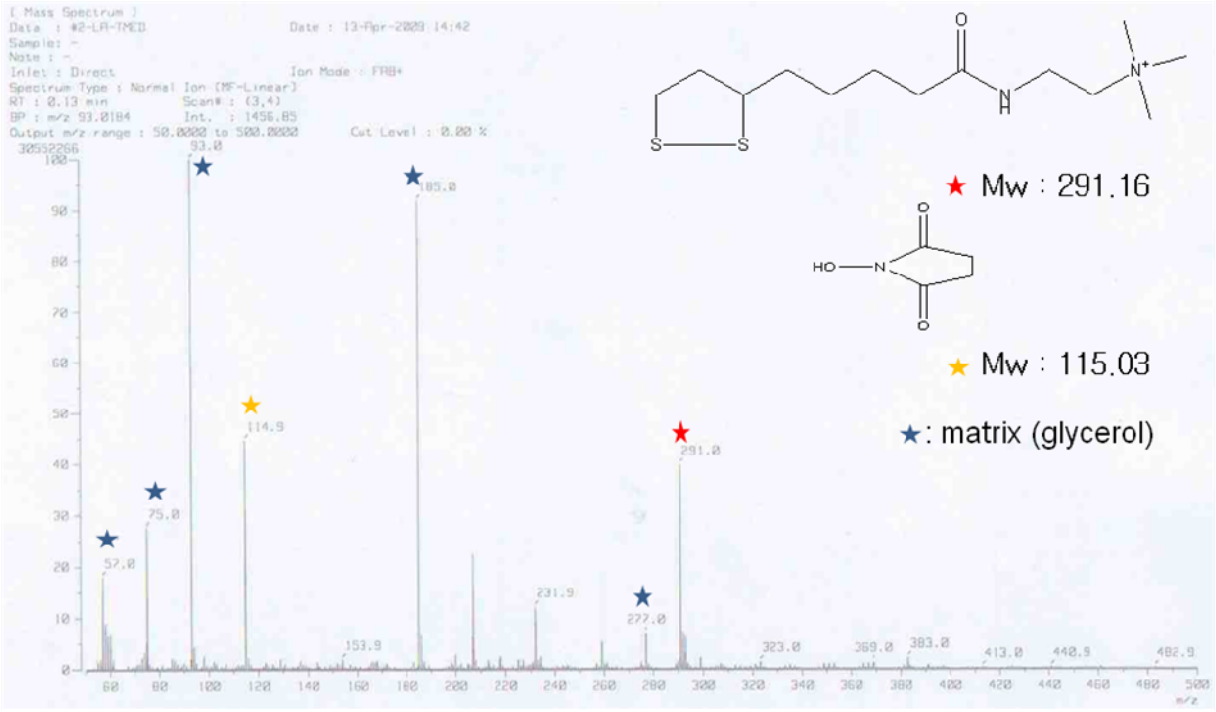


Figure S4 Mass spectra of N-(2-trimethylammonioethyl)1,2-dithiolane-3-pentanamide chloride

d) N-(2-aminoethyl)-5-(1,2-dithiolan-3-yl)pentanamide

20 mmol of (±)-α-Lipoic acid and 26 mmol of 1,1'-carbonyldiimidazole (CDI) were dissolved in 30 ml anhydrous chloroform and stirred under N_2 flow for 20 minutes at room temperature. The solution was added dropwise to 100 mmol ethylenediamine in an ice bath and stirred for 2 hours under N_2 gas flow. The crude product was filtered and washed three times by 10% NaCl aqueous solution and by 10 mM NaOH aqueous solution. It was dried with magnesium sulfate and the solvent was removed using rotary evaporator to obtain yellow liquid product (4.0 g). Reaction yield was 80.5%.

e) N-(2-(dimethylamino)ethyl)-5-(1,2-dithiolan-3-yl)pentanamide

20 mmol of (±)-α-Lipoic acid and 26 mmol of 1,1'-carbonyldiimidazole (CDI) were dissolved in 30 ml anhydrous chloroform and stirred under N_2 flow for 20 minutes at room temperature. The solution was added dropwise to 100 mmol N,N-dimethylethane-1,2-diamine in an ice bath and stirred for 2 hours under N_2 gas flow. The crude product was filtered and washed three times by 10% NaCl aqueous solution and

by 80 mL of 10 mM NaOH aqueous solution. It was dried with magnesium sulfate and the solvent was removed using rotary evaporator to obtain yellow liquid product.

Synthesis of Quantum dots

Materials

Oleic acid, tech. (90%), trioctylphosphine, tech. (90%, TOP), 1-octadecene, tech. (90%, ODE), oleylamine, tech. (70%), diethylzinc, bis(trimethylsilyl)sulfide (95%), and (±)-α-Lipoic acid were purchased from Aldrich. Cadmium acetate dehydrates (99.999%), and selenium shots (99.99%) were purchased from Alfa Aesar and Strem, respectively.

Synthesis of CdSe/CdS/ZnS Core/Shell/Shell Quantum dots [S4,S5]

Synthesis of bare CdSe quantum dots: For cadmium precursor, cadmium acetate 1.2 mmol was dissolved in 6.0 mmol of oleic acid at 100 °C under vacuum. After the solution had cooled to room temperature, the cadmium precursor was mixed with selenium precursor. The selenium precursor was previously prepared by dissolving 6.0 mmol of selenium shots in 6 ml of TOP in glove box. 40 ml of ODE and 6 mmol of oleylamine were loaded into a 50 ml 3-neck flask, and heated to 300 °C under nitrogen gas flow. At this temperature, the mixture of cadmium and selenium precursors was quickly injected into the reaction flask and the temperature was maintained at 280 °C. The reaction mixture was kept stirred until desired size of CdSe nanocrystals was obtained. Upon completion, the mixture was cooled to room temperature, and diluted by hexanes. For purification, the product mixture was precipitated by excess methanol, collected by centrifugation, and redispersed to small amount of hexanes.

CdS/ZnS shell deposition: For cadmium precursor, cadmium acetate 0.3 mmol was dissolved in 1.5 mmol of oleic acid at 100 °C under vacuum. When the solution had cooled to room temperature, the cadmium precursor was mixed with sulfide precursor. The sulfide precursor was previously prepared by dissolving 45 μL of bis(trimethylsilyl)sulfide in 3 mL of TOP in glove box. For precursor of zinc and sulfide, 130 μL of diethylzinc and 240 μL of bis(trimethylsilyl)sulfide were dissolved to 5 mL of TOP. 45 mL of ODE was loaded to the 50 ml 4-neck flask. Under nitrogen gas flow, 9.0×10^{-4} mmol of CdSe bare nanocrystals were placed to the reaction flask. When the temperature of the reaction flask reached 120 °C, the mixture of Cd and S precursors was slowly added using a syringe pump. After 30 minutes for the CdS shell growth, the temperature was raised up to 140 °C followed by dropwise addition of the mixture of Zn

and S precursors. The temperature was maintained for 30 minutes for the ZnS shell growth. The final product of CdSe/CdS/ZnS (Core/Shell/Shell) QD was purified by a similar method described above.

Surface Modification of CdSe/CdS/ZnS Core/Shell/Shell Quantum dots

Surface Modification with sulfonate surface ligand or quaternary ammonium surface ligand

CdSe/CdS/ZnS (Core/Shell/Shell) QDs were ligand exchanged by sulfonate surface ligands or quaternary ammonium surface ligands. Excess amount (typically million times excess of the moles of QD) of the surface ligands (oxidized form) were dissolved in PBS. 2 equimolar sodium borohydride was added to the solution and vigorously stirred for 30 minutes under N_2 gas flow at room temperature. The QD chloroform solution was mixed to the PBS solution and further stirred for 4 hours at room temperature. When QDs in chloroform were introduced to the disulfide-ligands in PBS, no active sodium borohydride were thought to present in the solution considering the reactivity and decay properties of the reductant. As the ligand exchange proceeds, the QDs were transferred from the organic chloroform layer to the PBS aqueous layer. To remove excess free surface ligands, the QD solution was dialyzed twice using Amicon 50 kDa M_W cutoff centrifugal filter.

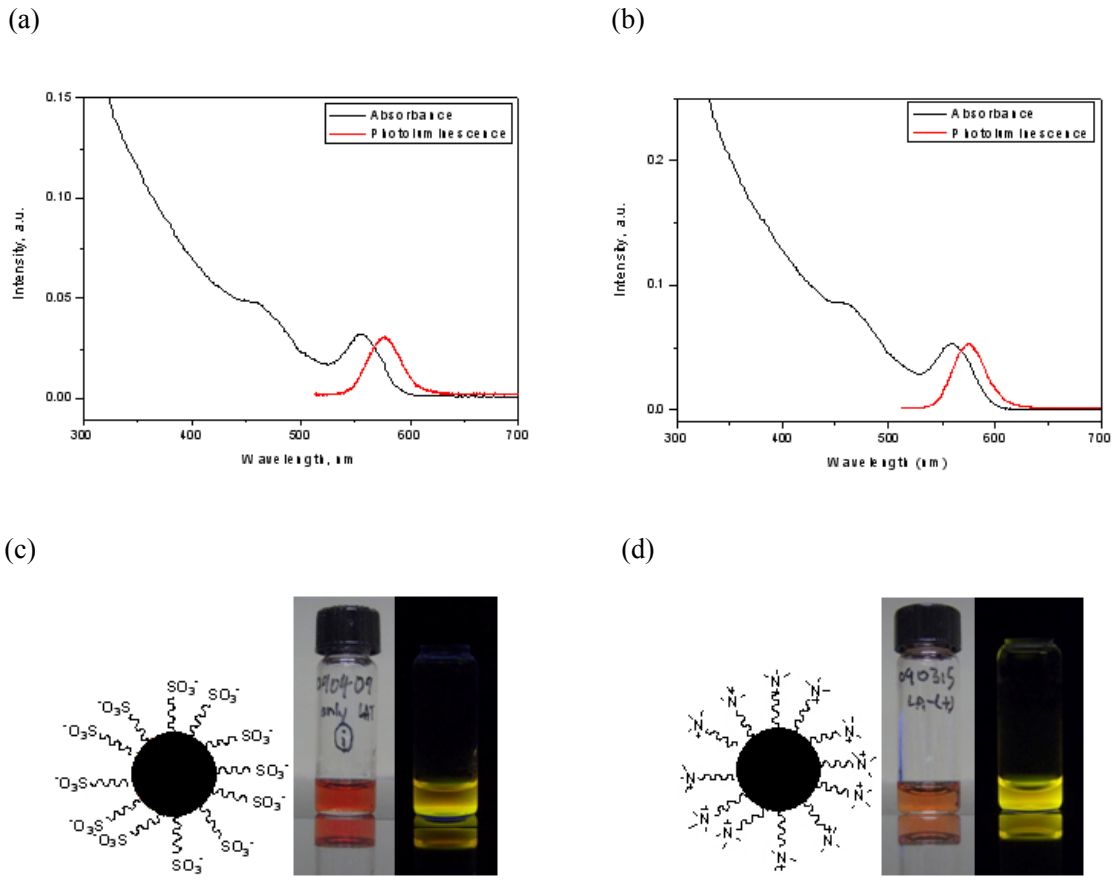


Figure S5 Absorption spectra (black lines) and photoluminescence spectra (red lines) of quantum dots modified by sulfonate surface ligands (a) and quaternary ammonium surface ligands (b). Illustration (left) and photo images under room light (middle) and under UV lamp illumination (right) of aqueous quantum dots solution that were surface modified by sulfonate surface ligands (c) and quaternary ammonium surface ligands (d).

(a) (b)

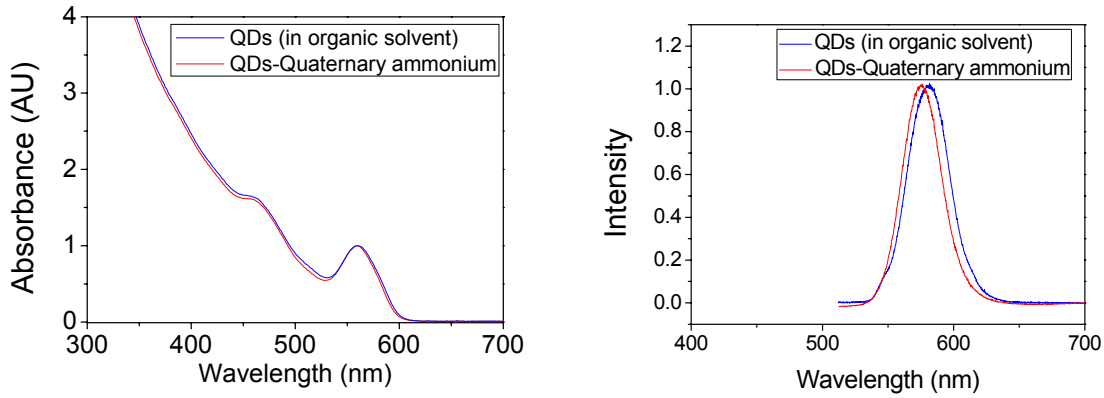


Figure S6 Absorption spectra (a) and photoluminescence spectra (b) of quantum dots modified by quaternary ammonium surface ligands before the ligand exchange in chloroform solution (blue lines) and after the ligand exchange in PBS solution (red lines).

Gel electrophoresis of QDs-sulfonate and QDs-quaternary ammonium

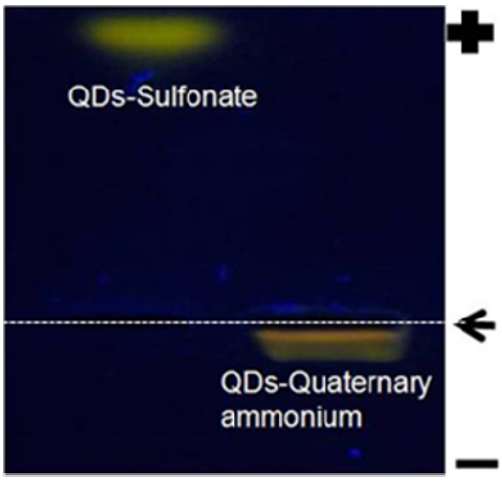
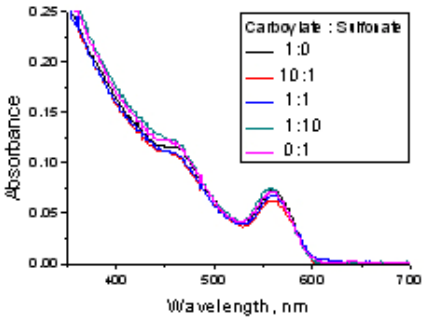


Figure S7 Gel electrophoresis of quantum dots that were surface modified by sulfonate surface ligand (left) and quaternary ammonium surface ligand (right) (1% agarose gel, pH 6.0 MES buffer). Positive and negative signs: direction to electrodes; arrow and the broken white line indicating the positions of the starting wells.

Surface Modification with a mixture of the carboxylate surface ligand and the sulfonate surface ligand

CdSe/CdS/ZnS (Core/Shell/Shell) QDs were ligand exchanged by a mixture of the carboxylate surface ligands and the sulfonate surface ligands. The amount of surface ligand was used typically more than ten thousand times excess of the number of QDs. The surface ligands (oxidized form) were dissolved in PBS buffer solution. 2 equimolar sodium borohydride was added to the solution and vigorously stirred for at least 30 minutes under N_2 gas flow at room temperature. The QD solution (in chloroform) was added to the ligand solution and further stirred for at least 4 hours at room temperature. The QDs were transferred from the organic layer to PBS buffer layer. To remove excess free surface ligands, the QD solution was dialyzed twice using Amicon 50 kDa M_W cutoff centrifugal filter.

(a)



(b)

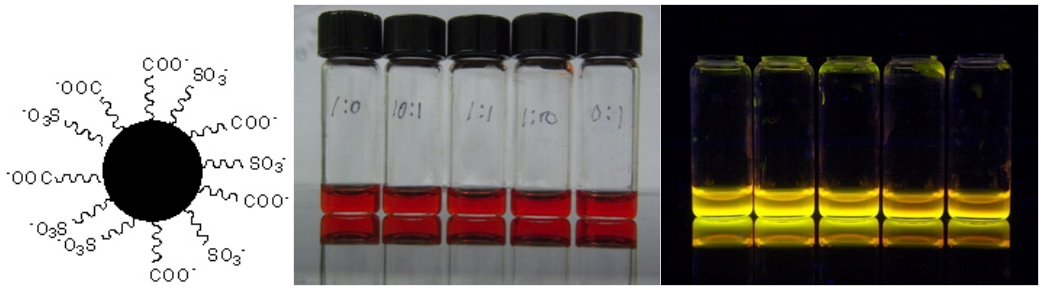


Figure S8 Absorption spectra (a), illustration (left) and photo images under room light (middle) and under UV lamp illumination (right) (b) of quantum dots modified by mixtures of the carboxylate surface ligand and the sulfonate surface ligand with the ratio of 1:0, 10:1, 1:1, 1:10, and 0:1 in PBS buffer solution.

Surface Modification with a mixture of the primary amine surface ligand and the tertiary amine surface ligand

CdSe/CdS/ZnS (Core/Shell/Shell) QDs were ligand exchanged with a mixture of the primary amine surface ligands and the tertiary amine surface ligands. The amount of surface ligands was used typically more than ten thousand times excess of the number of QDs. The surface ligands (oxidized form) were dissolved in PBS buffer solution. 2 equimolar sodium borohydride was added to the solution and vigorously stirred for at least 30 minutes under N_2 gas flow at room temperature. The QD solution (in chloroform) was added to the ligand solution and further stirred for at least 4 hours at room temperature. The QDs were transferred from the organic layer to PBS buffer layer. To remove excess free surface ligands, the QD solution was dialyzed twice using Amicon 50 kDa M_W cutoff centrifugal filter.

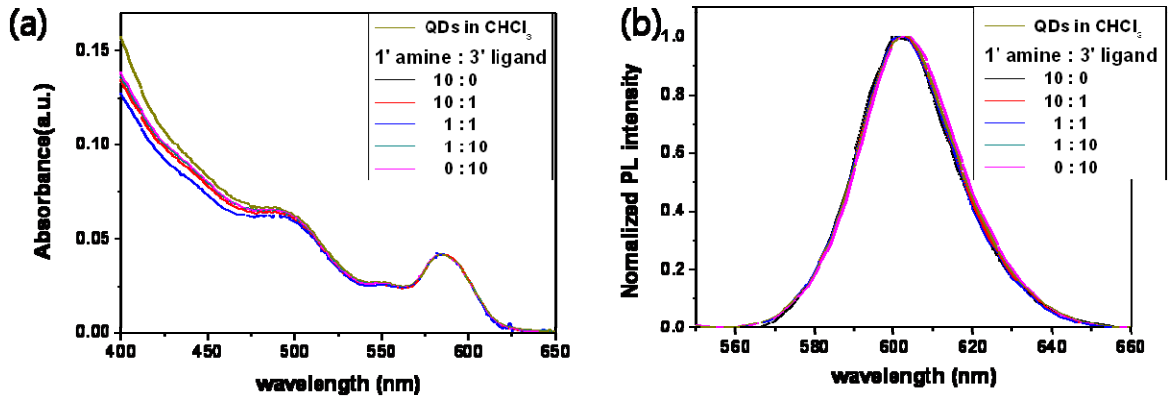


Figure S9 Absorption (a) and photoluminescence spectra (b) of quantum dots modified by mixtures of the primary amine surface ligands and the tertiary amine surface ligands with the ratio of 10:0, 10:1, 1:1, 1:10, and 0:10 in PBS buffer solution.

Preparation of the quantum dot layer-by-layer assemblies

Negative charged QD solution was prepared by dissolving sulfonated decorated QDs in PBS buffer solution. Positive charged QD solution was prepared by dissolving quaternary ammonium salt decorated QDs in PBS buffer solution. A slide glass was cleaned for 4 h with sonication in piranha solution (H_2SO_4:H_2O_2 =7:3). The glass was dipped into 2 % Poly(diallyldimethylammonium chloride) (PDDA) solution in 0.5 M NaCl for 20 min and washed with D.I. for 2 min. The substrate was dipped into the negatively charged QD solution for 20 min and washed with D.I. for 2 min. The substrate was dipped into the positively charged QD solution for 20 min and washed with D.I. for 2 min. The cycle of dipping into the negative charged QD solution, washing and dipping into the positive charged QD solution was repeated up to the desired number of cycles.

Estimation of QD volume fraction

The CdSe core size of CdSe/CdS/ZnS(Core/Shell/Shell) QD (i.e., bare CdSe quantum dot before the shell deposition) was 4.9 nm in diameter. CdS shell layer was ignored since it is thought to be very thin. ZnS shell thickness was determined as 0.8 nm by TEM measurements, as the QDs were approximately spherical with the average diameter of 6.5 nm. For the inorganic QD core and shell, $n_{CdSe,\ bulk} = 2.47$ and $n_{ZnS,\ bulk} = 2.27$ were used for the refractive indices. Organic layer (mostly originated from the surface ligands) of 1 nm thickness was assumed to uniformly surround the QD with the refractive index of 1.4. The volume fraction of QD was determined using following equation;

$$n_{LbL} = n_{air} * f_{air} + n_{CdSe/ZnS} * f_{CdSe/ZnS} + n_{org.} * f_{org.}$$

, where f_{air} , $f_{CdSe/ZnS}$ and f_{org} denote respectively the volume fraction of air, QDs and organics to the total volume of the LbL-assembled film. The QD volume fraction was estimated to be $f_{CdSe/ZnS} \approx 21\%$.

Supporting References:

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