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NMR analysis of organic ligands on quantum-dots

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Abstract Quantum dot (QD) is an emerging novel nanomaterial that has wide applicability and superior functionality with relatively low cost. Nuclear magnetic resonance (NMR) spectroscopy has been contributed to elucidate various features of QDs and to improve their overall performance. In particular, NMR spectroscopy becomes an essential analytical tool to monitor and analyze organic ligands on the QD surface. In the present mini-review, application of NMR spectroscopy as a superb methodology to appreciate organic ligands is discussed. In addition, it was recently noted that ligands exert rather greater influence on diverse features of QDs than our initial anticipation, for which contribution of NMR spectroscopy is briefly reviewed.

Keywords quantum dots, quantum dot ligands, nanocrystal ligands, NMR spectroscopy

Introduction

Quantum dots (QDs) are nano-sized crystalline semiconductors that have various advantages such as superior performance, easy fabrication, wide compatibility, and relatively low cost.[1] QDs have been extensively studied in the fields of material science, energy, biology, and clinical applications.[1–3] Although there are several distinctive architectural types, QDs are typically composed of inorganic core particles and organic ligand molecules surrounding cores.[1] Inorganic nano-crystals constitute the QD cores, which play major roles manifesting desired functional properties as a semiconducting material. On the other hand, organic ligand molecules passivate the surface atoms of QD cores (Figure 1).[4] The interaction between inorganic core and organic ligands is a critical factor to determine the growth pattern of inorganic nano-crystal; modulation of this interaction is an important strategy to differentiate nano-crystal shape and resultant functionality of QDs.[5] At complete QD particles, the ligand interaction with a core is also important to improve their processability, solubility, performance, and stability. QD ligands passivate the surface-exposed inorganic atoms of cores, thus constituting the functional and protective interface against solvents or specific media (Figure 1).[4,6] In addition, QD ligands can be exchanged with other

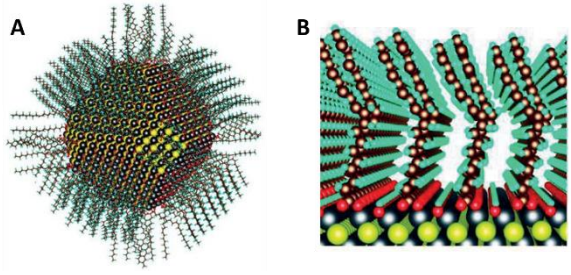

Figure 1. Structure of ligands on PbS QDs. (A) The simulated atomic structure of 5-nm diameter PbS QD with oleic acid as passivating ligands. (B) Detailed view showing interaction between oleic acid (upper layer; C: small black, H: teal, O: red) and the surface (bottom layer; Pb: black, S: yellow) of PbS nanocrystals. Adapted with permission from Boles *et al.*[4]

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organic/inorganic ligands by employing simple ligand-exchange procedures. Ligand exchange is frequently used for diverse purposes, such as solubility modulation to non-polar/polar solvents, reactivity change to certain chemical moieties, and control of electron-conducting properties.[4] In particular, for biological and medical application of QDs, ligand exchange procedures constitute essential steps to reduce toxicity of QDs and to enhance its necessary functionality.[3,7]

Evident importance of ligands, therefore, has facilitated development of various analytical tools to characterize ligands on QDs, among which nuclear magnetic resonance (NMR) spectroscopy has made significant contribution to advance our understandings to QD ligands.[8] The difficulty to investigate ligands on QD originates from their chemical complexity and heterogeneity; these are inevitable challenges that are caused by harsh and complicated synthesis procedures as well as non-uniform and less-controlled ligand exchange protocols. NMR spectroscopy has several advantages to resolve complexity of QD ligands, *e.g.* superb analytical power to characterize organic molecules and compatibility to various forms of samples.[9]

The present mini-review focuses on discussing essential approaches of NMR spectroscopy to investigate QD ligands. Although solid-state NMR has also contributed much to understand many facets of QDs, most studies for QD ligands employed solution-state NMR spectroscopy due to its unique superiority to investigate organic molecules, discussion of which is presented here.

Ligand characterization with ^{1}H NMR

To identify QD-bound ligands and confirm their chemical integrity is an essential step for evaluating stability, functionality, and overall performance of QDs, for which NMR spectroscopy is one of the most useful tools. Several NMR technologies have been developed to reveal various aspects of QD-bound ligands.[8] First of all, collection of ^{1}H NMR spectra is a simple yet insightful way to identify organic

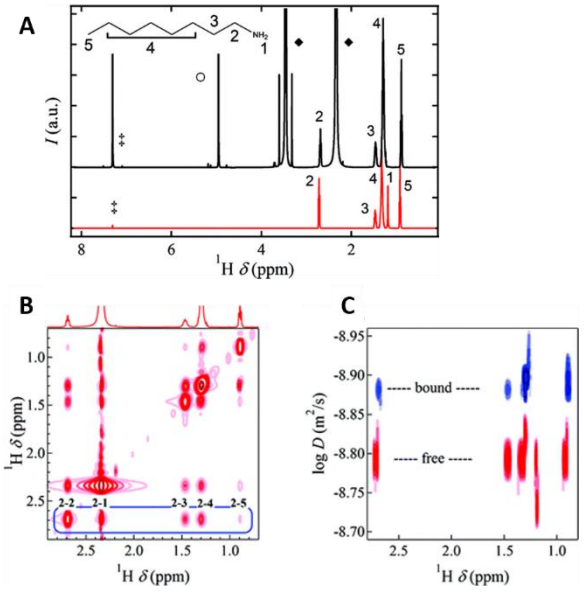

Figure 2. QD-bound ligand can be studied with ^{1}H NMR. (A) 1D ^{1}H NMR spectra of QD-bound octylamine (the upper black spectrum) and of its free form (the lower red spectrum) are shown. The structure of octylamine is shown in the upper left side of the panel. Signals assigned to the certain nuclei at the octylamine structure are marked with their designated numbers. Signals originating from $CDCl_3$ and methanol are marked with ‡ and ◆, respectively. (B) Typical 2D NOESY spectrum of QD-bound octylamine. (C) 2D DOSY spectrum of QD-bound (blue) and free (red) octylamine. Adapted with permission from Hassinen *et al.*[10] Copyright (2010) American Chemical Society.

molecules in QD samples, speculate their chemical states, and estimate their relative quantities (Figure 2A).[1,10] Notably, despite noticeable limits for accurate quantification, ^{1}H NMR has been routinely used to measure the quantity of ligands and calculate how much of the QD core surface is covered by organic molecules; this ‘coverage’ is a rough yet quick indicator to predict stability and overall quality of QDs. Notably, as QD particles usually have a size of a few nanometers, ^{1}H NMR signals of QD-bound ligands often broaden out, particularly for nuclei constrained close to the core, which greatly hampers accurate quantification of ligands. Moreover, QD ligands are frequently complex mixtures of organic/inorganic molecules, further underscoring caveats of using 1H NMR signals for rigorous ligand quantification.

On the other hand, NMR spectroscopy provides

simple means to distinguish bound vs. free ligands in QD samples.[8,10,11] Because QD bound-ligands behave like much larger molecules than free ligands, NMR signals, even from the same chemical moieties, can be differentiated based on two spectral features. Firstly, nuclear Overhauser effect (NOE) signals exhibit distinguishable patterns; free ligands give relatively weak positive NOE peaks, while QD-bound ligands show strong negative NOE peaks (Figure 2B).[12] In addition, diffusion ordered spectroscopy (DOSY), in which NMR signals are to be separated with the diffusion rates of corresponding molecules, provides direct evidence whether a set of NMR signals are indeed originated from QD-bound molecules or not (Figure 2C).[12] Moreover, NMR analysis using a DOSY technique is advantageous to estimate hydrodynamic radius of QD particles, providing unique information to appreciate diffusive behaviors of QDs in their solution state.[12]

Analysis of ligand exchange processes

As discussed above, ligand exchange is a critical procedure for improving stability and expanding compatibility and functionality of QDs.[4] Typical ligand exchange procedures involve incubation of QDs in the solution containing an excess amount of desired ligand molecules, and NMR spectroscopy has an advantage to directly monitor ligand exchange and to appreciate dynamic features in the exchange processes.[12–14] Knauf *et al.* used ^{1}H NMR spectroscopy to monitor ligand exchange processes and evaluate which functional moiety is efficient for replacing oleic acid from CdSe nanocrystals (Figure 3).[14] Oleic acid is the ligand that is most frequently employed for many types of QDs. In order to make ligand exchange more visible with ^{1}H NMR spectroscopy, they employed ligands that contain a terminal alkene group (Figure 3A), thus giving characteristic signals in the ^{1}H NMR spectrum (Figure 3B). Subsequently, by following ^{1}H NMR spectra, they were able to follow ligand exchange from oleic acid to target ligands and to estimate exchange efficiency. Particularly, they found that oleic acid can be exchanged bi-directionally with ligands having the terminal group of carboxylic acid. In contrast, they observed unidirectional exchange from oleic acid to ligands with phosphonic acid or thiol at their ends (Figure 3A).

Characterization of ligand-ligand interactions

NMR spectroscopy has been used to characterize interactions not only between ligands and cores but also among ligand molecules.[11,12,15] Compared to other analytical techniques, NMR spectroscopy exhibits

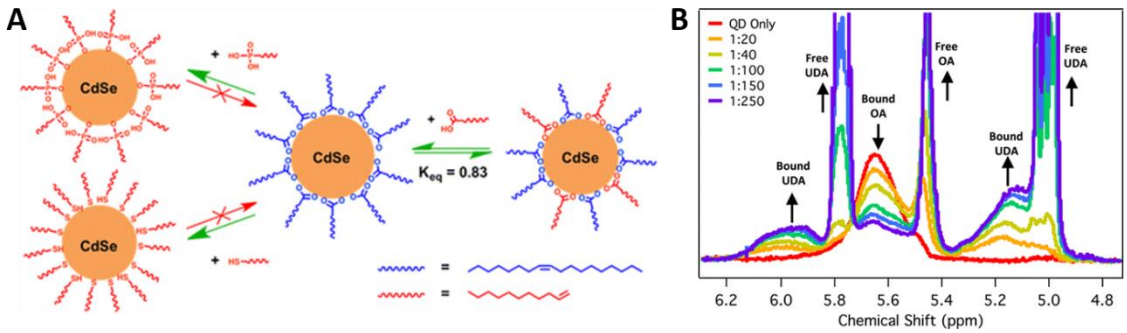

Figure 3. Ligand exchange can be directly monitored with NMR spectroscopy. (A) NMR spectroscopic data proved that oleic acid (blue) on CdSe QDs can be exchanged bidirectionally with the ligand having a carboxylic acid group at its end, while, upon being replaced by the ligand having phosphonic acid or thiol group at its end, oleic acid cannot replace it back. (B) The ^{1}H NMR spectra of a series of samples having different ratios of ligands are taken to estimate bound vs. free ligand population and follow ligand exchange processes. The relative ratios of undec-10-enoic acid (UDA) to the amount of QD are shown on the upper left side. The original ligands of QD was oleic acid (OA). Adapted with permission from Knauf *et al.*[14] Copyright (2016) American Chemical Society.

superiority to observe dynamic and transient ligand-ligand interactions and to evaluate their effects on QDs. Moreels *et al.* observed ligand association and dissociation by changing ligand concentration in the QD sample, and calculated relative ratios of QD-bound vs. free ligands with ^{1}H NMR spectra.[11] From this, they were able to extract association/dissociation curves of ligands against QDs and calculate energetic contributions for ligand-core and ligand-ligand interactions. On the other hand, Liu *et al.* used NMR spectroscopy to investigate the effect of ligand-ligand interaction for the distribution of ligands on the QD surface.[15] To this end, Liu *et al.* employed ligands that have differential packing propensities. They mixed these ligands in various combinations, let them absorbed onto QDs, and measured the chemical shift perturbation of each ligand molecules over various ratios of ligand mixtures. In addition, they collected NOESY spectra to monitor direct contacts between ligands. From these observations, they concluded that ligand distribution on QD surface indeed depends on the packing propensities of ligands; uniform and non-uniform ligand distribution could be observed according to the packing preference of ligands. In other words, this indicates that ligand distribution on QD surface can be rather heterogeneous depending on their structural and chemical properties.[6,15]

Conclusions

QDs are one of the most promising nano-materials that have many superior features as a novel semi-conducting material. In order to maximize their applicability and functionality, various architectural designs and synthesis procedures are developed.[1] Because most of the desired properties of QDs originate from their core parts, many efforts have been accumulated to appreciate how nanocrystalline cores are made and to investigate how they could be further optimized.[1] In contrast, our understanding to the organic ligand parts of QDs are still poor. This is particularly due to their chemical complexity, complicated dynamics, and heterogeneous nature.[4] Luckily for us, NMR spectroscopy has various advantages to study heterogeneous and dynamic systems, and has indeed contributed much to elucidate various intriguing features and to improve stability and performance of QDs. NMR spectroscopy is the field whose technical development is still actively on-going. Therefore, it is expected that NMR spectroscopy will greatly advance our understanding to QD ligands and help to expand functionalities of QDs.

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