Partitioning surface ligands on nanocrystals for maximal solubility

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A typical colloidal nanoparticle can be viewed as a nanocrystal-ligands complex with an inorganic single-crystalline core, the nanocrystal, bonded with a monolayer of organic ligands. The surface chemistry of nanocrystal-ligands complexes is crucial to their bulk properties. However, deciphering the molecular pictures of the nonperiodic and dynamic organic-inorganic interlayer is a grand technical challenge, and this hampers the quantitative perception of their macroscopic phenomena. Here we show that the atomic arrangement on nanocrystal surface and ligand-ligand interactions can be precisely quantified through comprehensive solid-state nuclear magnetic resonance (SSNMR) methodologies. The analyses reveal that the mixed ligands of n-alkanoates on a CdSe nanocrystal segregate in areal partitions and the unique arrangement unlocks their rotational freedom. The mathematical model based on the NMR-derived ligand partition and dynamics successfully predicts the unusual solubility of nanocrystal-ligands complexes with mixed ligands, which is several orders of magnitude higher than that of nanocrystal-ligands complexes with pure ligands.
M任何天然和人工的材料都是层间相互作用的节点，它们通过共价键作用于结构面具有不同的特征和无限制的多样性。例如，表面配体是纳米晶体-配体复合物的一个重要组成部分，并且显著地影响其性质，如光学性能、稳定性和生物相容性。此外，溶液可加工性对于器件制造至关重要。

对于纳米晶体-配体复合物来说，它们的分子内核的尺寸及其分布对于多种参数，如发光效率、电子和光学特性和溶液可加工性，都是决定性的。因此，控制和预测这些纳米晶体-配体复合物的性质变得至关重要。在最近的研究中，概念化的新熵配体被引入，它们可以显著提高纳米晶体-配体复合物的溶解度，并且可以用光学和电子光学技术来打印电子和光电元件。重要的是，熵配体的可用性及其在合成和处理中的作用，为纳米晶体-配体复合物提供了新的途径，可以显著提高它们的溶解度。通过混合不同类型和长度的碳氢链配体，可以显著提高纳米晶体-配体复合物的溶解度，并且可以完全分散在0.8 mL的氯仿中，而单配体纳米晶体-配体复合物很难溶解。

在纳米晶体-配体复合物中，不同类型的配体和长短不一的碳氢链配体具有简单、通用和易于处理的性质，可用于纳米晶体-配体复合物的合成和处理。在解决溶解度问题时，熵配体的作用是至关重要的。熵配体的概念可以定义为一种适用于多种无机配体的通用策略。例如，通过将单种类型的n-烷基酸配体与不同链长的邻近配体混合，可以显著提高纳米晶体-配体复合物的溶解度。

为了说明表面配体的混合作用，我们使用了固体NMR序列，称为中心-带只检测交换（CODEX）29，在其中，13C-13C横向弛豫超快，可以通过13C-13C偶合网络来观察配体的表面分布。具体来说，我们通过编码序列来观察纳米晶体-配体复合物中纯配体的溶解度，以及带有不同比例的熵配体的纳米晶体-配体复合物的溶解度。通过这种方法，我们可以观察到纳米晶体-配体复合物中不同配体的表面分布。
methodology for probing nanoscale atomic distribution. Compared to other methods, the spin-labeling is chemically non-disruptive and the sensitive dipolar interaction is much more amendable for quantitative modeling.

Figure 2a shows the CODEX decay of the nanocrystal-ligands complexes with pure myristate ligands, which provides the basis for our analysis. The double exponential feature can be described by a non-uniform distribution of small bundles consisting of ~4–6 ligands considering the structural heterogeneity of nanoparticles. The revealed ligand bundles corroborates the earlier report which described the islands of myristates, which provides the basis for our analysis. The double exponential feature can be described by a non-uniform distribution of small bundles consisting of ~4–6 ligands considering the structural heterogeneity of nanoparticles (See Supplementary methods, Supplementary Fig. 4). As we can see, each of the patterns are highly distinctive by their width and shape, e.g., the positions of their edges and horns. In general, the more flexible the sites are, the narrower the patterns would be. Deuterium $^2$H NMR quadrupolar pattern is a versatile probe to identify different modes of segmental reorientation of organic molecules. Figure 3a shows the respective $^2$H patterns (under 2 kHz MAS) of an individual CD$_2$ site which undergoes different dynamic modes probable for surface ligands, namely static, trans-gauche$^+$-gauche$^-$ (tgg) rotation, and cone diffusion (described in Supplementary methods, Supplementary Fig. 4).

To model our mixed-ligand systems, we invoked two general ligand partition schemes with fundamentally distinct features, namely ligands distributed in random (Random, Fig. 2c) and areal segregation of either myristates or hexanoates (Areal, Fig. 2d). Matching of experimental CODEX curves for different hexanoate fractions clearly identified the areal partition of surface ligands. Therefore, our NMR investigation successfully realized a geometric classification of surface morphology of nanocrystal-ligands complexes with mixed ligands.

Revealing the dynamic picture of surface ligands. Though the partition of ligands may have profound implications on the ligand–ligand interactions, it is still a steady (or average) picture and the sites are, the narrower the patterns would be. Deuterium $^2$H NMR quadrupolar pattern is a versatile probe to identify different modes of segmental reorientation of organic molecules. Figure 3a shows the respective $^2$H patterns (under 2 kHz MAS) of an individual CD$_2$ site which undergoes different dynamic modes probable for surface ligands, namely static, trans-gauche$^+$-gauche$^-$ (tgg) rotation, and cone diffusion (described in Supplementary methods, Supplementary Fig. 4). As we can see, each of the patterns are highly distinctive by their width and shape, e.g., the positions of their edges and horns. In general, the more flexible the sites are, the narrower the patterns would be.

We carried out $^2$H NMR measurements under variable temperatures on nanocrystal-ligands complexes with fully deuterated myristates and protonated hexanoates. Figure 3b shows two sets of representative $^2$H patterns obtained at 245 and 300 K (other temperatures in Supplementary Fig. 3a). Evidently,
the differences in chain flexibility between different types of nanocrystal-ligands complexes are more pronounced at the lower temperature.

We deconvoluted each of the patterns in Supplementary Fig. 4 into the three dynamic modes described above with relative populations corresponding to the number of methylene units. Accordingly, we obtained the histograms of flexibility along the myristate ligand at different temperatures, based on the deconvolutions of $^2$H patterns. The blue, green and gray bars represent static deuterium, tgg rotation and cone diffusion, respectively.

As a step further, we pursued site-specific quantification of ligand dynamics with the DIPSHIFT method, a two-dimensional NMR sequence resolving the $^1$H–$^{13}$C heteronuclear dipolar coupling of each carbon resonance. The averaging effect of $^1$H–$^{13}$C coupling is a quantitative reference for the segmental

![Fig. 3 $^2$H NMR line shapes and chain flexibility.](image)

**Fig. 3** $^2$H NMR line shapes and chain flexibility. **a** The three distinct dynamic modes of methylene units and the corresponding $^2$H NMR patterns under 2 kHz magic-angle spinning. These dynamic modes could present in a hydrocarbon chain at different temperatures or at different positions, e.g., the middle segment or the free end. **b** $^2$H NMR patterns for nanocrystal-ligands complexes with pure ligands ($f_{He} = 0$) and nanocrystal-ligands complexes with mixed ligands ($f_{He} = 0.68$) with fully deuterated myristates at 245 and 300 K. **c** The histograms of methylene flexibility along the myristate ligand at variable temperatures, based on the deconvolutions of $^2$H patterns. The blue, green and gray bars represent static deuterium, tgg rotation and cone diffusion, respectively.
motion of surface ligands. The DIPSHIFT sequence takes advantage of favorable $^{13}$C spectral resolution and does not require isotope enrichment. Figure 4a shows the theoretical DIPSHIFT curves for different $^{1}$H–$^{13}$C coupling strengths in the fast motion regime. The observed coupling strength, i.e., the residual dipolar coupling, can be converted into the opening angles of cone diffusion model (Supplementary Fig. 5c). A shallower dip corresponds to a weaker coupling, and therefore a larger opening angle.$^{38}$

Figure 4b presents the $^{13}$C spectra of ligands of nanocrystal-ligands complexes with either pure myristate or mixed ligands, where resolvable signals are assigned to the segments of

| Hexanoate fraction | 0   | 0.05 | 0.68 |
|-------------------|-----|------|------|
| Hexanoate fraction | 0   | 0.05 | 0.68 |
| Dissolution enthalpy $\Delta^{m}H_{NC}$ (kJ mol$^{-1}$) | 308 | 304 | 265 |
| Dissolution entropy $\Delta^{m}S_{NC}$ (J mol$^{-1}$K$^{-1}$) | 874 | 892 | 916 |
| Melting point, $T_m = \Delta^{m}H_{NC}/\Delta^{m}S_{NC}$ (K) | 354 | 343 | 291 |
| Total interaction energy $E_{tot}$ (kJ mol$^{-1}$) | 305 | 304 | 278 |
| Ligand-ligand interaction energy $E_{ligand}$ (kJ mol$^{-1}$) | 303 | 302 | 274 |
| Inter-particle interaction energy $E_{core}$ (kJ mol$^{-1}$) | 1.5 | 1.5 | 3.9 |

Table 1 The thermodynamic parameters of nanocrystal-ligands complexes obtained via light scattering (top panel) and via NMR-based calculations (bottom panel)
n-alkanoates (inset, Fig. 4b). From head to tail along the hydrocarbon chain, the depth of the dip decreases gradually, confirming an increasing flexibility towards the end of methyl group (Fig. 4c). After theoretical conversion of the measured 1H-13C coupling, the opening angles of each myristate segment were obtained for different ligand fractions. Figure 4d shows that the opening angles of myristates on nanocrystal-ligands complexes with mixed ligands ($f_{He} = 0.68$) were found to be much wider than those on nanocrystal-ligands complexes with pure ligands ($f_{He} = 0$), confirming substantially weakened ligand–ligand interaction and significantly enhanced chain dynamics.

Predicting the solubility based on ligand–ligand interactions. Our earlier work based on macroscopic measurements revealed that the dissolution of nanocrystal-ligands complexes is equivalent to a two-step process. In the first step, the solid is melted, which is accompanied by dramatic changes in the enthalpy and intramolecular entropy. In the second step, the melted solid and solvent, two liquids, are mixed, which involves mostly the ideal entropy change of mixing. As long as the inorganic core is relatively small (<5 nm) and the hydrocarbon chain is reasonably long, the enthalpy of dissolution ($\Delta^m H_{NC}$) of the entire process is dominated by the destruction of ligand–ligand interactions. At the same time, a large amount of intramolecular conformational entropy ($\Delta^m S_{NC}$) would be released (Table 1).

Based on the molecular pictures revealed by our NMR studies, we would like to show that the macroscopic solubility of nanocrystal-ligands complexes can be predicted directly from their molecular partition and dynamics. We first predicted the interaction energy ($E_{ligand}$) using the dispersion energy model for hydrocarbon chains. Such calculations were grounded on the fact that the free volume of each methylene unit (Fig. 5a) can be quantified by the opening angle determined by DIPSHIFT experiments. In addition, the calculation considered the interparticle interaction of nanocrystal cores ($E_{core}$) although it makes up a relatively small contribution to the total interaction energy ($E_{tot}$). The results (described in Supplementary methods, Supplementary Fig. 6) showed that the total interaction energy is largely equivalent to dissolution enthalpy (Table 1). Our calculation ultimately predicted the solubility values for a range of nanocrystal-ligands complexes with mixed ligands at the room temperature, which agree well with the measured values (Fig. 5b).

Our work reached a revealing conclusion that the exceptional solubility of nanocrystal-ligands complexes with entropic ligands is quantitatively dictated by the dynamic behavior of ligands along with their partition on the surface of a nanocrystal. The molecular picture established in this work serves as a theoretical blueprint for the flourish of entropic ligands in the field of colloidal nanocrystals. Moreover, our NMR methodology will be applicable to diverse disordered and dynamic nanostructures and could provide crucial guidance for the dedicated regulation of their surface properties.

**Methods**

**Synthesis of CdSe-ligands complexes.** The synthesis of CdSe nanocrystals was performed by injecting a 1.0 mL Se-octadecene suspension (0.2 mol L$^{-1}$) into a hot (250 °C) mixture of CdO, myristic acid and 1-octadecene in a 50 mL three-neck flask. Needle-tip aliquots were taken for UV–vis and photoluminescence measurements to monitor the reaction until the desired size has been reached. The reaction mixture of the CdSe-ligands complexes was further purified according to the procedures described in Supplementary methods, and infrared measurement verified that remaining ODE and free acids had been fully removed.

**Preparation of nanocrystal-ligands complexes with mixed ligands.** Ten milligram purified complexes with pure myristate ligands were dissolved in 0.5 mL chloroform in a 4 mL vial and kept at 50 °C as a clear solution. Hexanoic acid with molar ratios ranging from 0.1 to 2 relative to bonded myristate ligands was added into solution for 2 h. The resulting nanocrystal-ligands complexes with mixed ligands were purified, and the solids have been vacuumed for 12 h to remove residual solvents.

**Measurement of ligand fractions.** The fraction of hexanoate on nanocrystal-ligands complexes with mixed ligands (Supplementary Table 1) was determined by gas chromatography. The measurements were carried out on samples digested by saturated hydrochloric acid. The molar ratio of hexanoic acid to myristic acid in the digested solution is assumed to be the same as the ratio of those two ligands on nanocrystal surface.

**Surface density of ligands.** The hydrogen and carbon mass fractions of nanocrystal-ligands complexes were determined by elemental analysis of purified samples. The surface density of nanocrystal-ligands complexes with pure ligands was determined to be ~135 ligands per crystal according to the formula provided in the Supplementary methods. The ligand densities for nanocrystal-ligands complexes with mixed ligands are about the same as their pure-ligand precursors as shown in Supplementary Table 1.

**Solubility measurement.** The solubility at room temperature was determined by the UV–vis absorbance of saturated solutions of CdSe complexes. The solubility of complexes at various temperatures was measured by the scattering method, in which a known concentration of dissolved complexes in chloroform was slowly cooled down from a relatively high temperature. The scattering intensity of 750 nm...
laser shows a sudden jump when the concentration reaches the solubility at the specific temperature.

**NMR experiments.** $^{13}$C CODEX experiments were carried out on a Bruker Avance III HD 600 MHz spectrometer using a 1.3 mm triple channel magic-angle spinning (MAS) probe. The spinning speed was 8 kHz and $^{13}$C chemical shift was referenced to the adamantane signal at 38.5 ppm on the tetramethylsilane (TMS) scale. The $^{13}$C experiments were performed on a Bruker Avance III HD 600 MHz spectrometer using the solid echo pulse sequence under 2 kHz MAS or under static conditions. The $^{3}$H-$^{11}$C-H DIPSHIFT experiments were carried out on a Bruker Avance III HD 400 MHz spectrometer using a 3.2 mm triple channel MAS probe with a spinning speed of 4431 Hz (calculated from the $^1$H homonuclear decoupling strength). Typical radio frequency fields strengths were 62.5 kHz for $^{13}$C, 100 kHz for $^{2}$H and 100–115 kHz for $^{11}$C. The magic angle and field homogeneity of the spectrometers were optimized with KBr and adamantane, respectively. The temperature of NMR experiments was controlled by the Bruker BCU II unit.

**Modelling of ligand partition and interactions.** The detailed analysis of CODEX and DIPSHIFT experiments and the methods for numerical modelling are described in the Supplementary methods.

**Data availability**

The data that support the findings of this study are available from the corresponding authors upon reasonable request.

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