

Nanomolar Sensitivity Chirality Transfer from Designed Helical Repeat Proteins to Achiral CdS Nanorods

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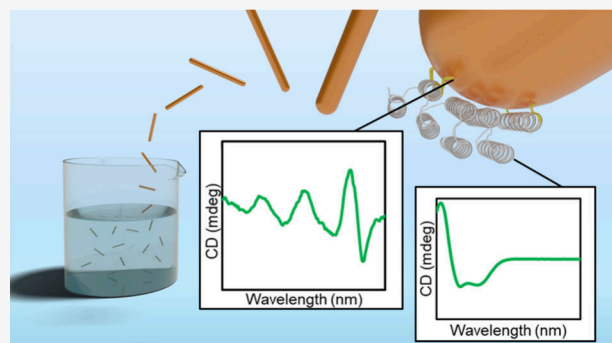
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ABSTRACT: Bridging chirality across length scales with inorganic–organic hybrid materials is a rapidly expanding area of research. Here, we establish asymmetry at CdS nanorod (NR) interfaces using a designed helical repeat protein bearing four cysteine residues (DHR-4Cys). Hydrophobic NRs are transferred into water with glycine, and then glycine is displaced by DHR-4Cys, leveraging the thiophilicity of cadmium. Circular dichroism (CD) in the visible, coincident with CdS electronic transitions, reveals a chiral DHR-4Cys:CdS interface. The dissymmetry factor [g -factor = 4.5×10^{-4} (short NRs) and 5.0×10^{-4} (long NRs)] is weakly dependent on the NR length, and CD persists at nanomolar protein loadings. Additionally, control experiments demonstrate that DHR-4Cys:CdS NR chirality is dictated by the local coordination of Cys with no significant contribution from the chiral secondary structure of the protein (g -factors of short and long Cys:CdS NRs are 4.8×10^{-4} and 4.0×10^{-4} , respectively). Together with far-UV CD and transmission electron microscopy, which provide evidence of preserved protein structure, these results provide the first demonstration that a structurally defined protein can induce chirality in CdS nanocrystals while maintaining protein structure at biologically relevant concentrations.

KEYWORDS: CdS, nanorod, chirality, designed protein, g -factor, circular dichroism



Chiral inorganic nanocrystals (NCs) are an emerging class of materials with potential applications in imaging, sensing, enantioselective catalysis, and spintronics.^{1–5} Historically, Au NCs have been the most-studied material in this class, in which chiral molecules have been shown to induce asymmetry across several length scales. At the smallest scale, molecular asymmetry of the Au NC lattice can arise during the nucleation and growth stage using chiral ligands as stabilizers, resulting in g -factors as high as 10^{-1} .^{6–8} At the length scale of the Au NC interface, asymmetry can emerge in achiral Au NCs via chiral molecule interactions on the NC surface.^{9,10} Finally, macroscale architectures or assemblies can generate Au NCs in chiral configurations.^{11–15}

While chiral Au NCs have been historically the most well-studied, chiral semiconducting NCs of CdE (E = S, Se, Te) have seen exceptional progress in the last 20 years. The first example of chirality in CdE NCs was reported in 2007 by Malony et al., who used penicillamine as a ligand to synthesize aqueous CdS NCs.¹⁶ While this report is fundamental to building our understanding of chiral NCs, ultimately controlling the morphology and optical properties of NCs in polar solvents has remained an outstanding challenge. Expanding on this observation of interfacial asymmetry, in 2013 Balaz and co-workers demonstrated that achiral,

hydrophobic CdSe NCs could be made chiral via aqueous ligand exchange with cysteine (Cys), yielding g -factors of 10^{-4} .^{17,18} While the mechanism of interfacial chirality remains unclear, it has since been shown that this ligand exchange method can produce g -factors of up to 10^{-3} for CdE nanorods (NRs).¹⁹ At the largest length scale, Kotov and co-workers have demonstrated micron-length helical assemblies of chiral CdTe NCs with g -factors of 10^{-2} using interfacial Cys.^{20–22} Robinson and co-workers have also demonstrated CdS cluster-based chiral helices with millimeter-sized domains and g -factors up to 1.3.²³

There are many examples of using chiral small molecules to create asymmetry in CdE across these length scales; however, there are far fewer studies that have incorporated proteins. Proteins offer chiral architectures comprised of chiral amino acid building blocks. Recently, Spangler and co-workers used designed proteins to template the growth of chiral CdS NCs;

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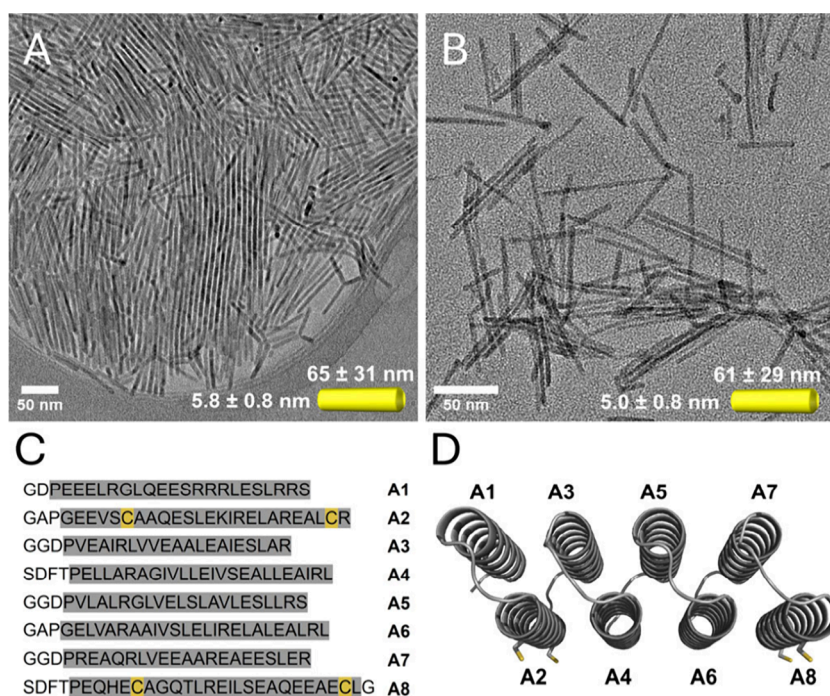


Figure 1. (A) TEM and sizing of longer hydrophobic CdS NRs with an average width of 5.8 ± 0.8 nm and length of 65 ± 31 nm, drop cast from toluene. (B) TEM and sizing of longer glycine:CdS NRs after ligand exchange with an average width of 5.0 ± 0.8 nm and a length of 61 ± 29 nm, drop cast from water. (C) DHR protein sequence containing eight α -helices (gray) and four Cys residues (yellow), two in the A2 and two in the A8 helical segments. (D) Structure of DHR-4Cys with Cys residues in the A2 and A8 α -helices. The four cysteine residues are displayed, while the remaining residues are hidden for clarity.

however, a g -factor was not reported.^{24,25} In 2024, we reported the first example of inducing chirality in CdS quantum dots (QDs) using polypeptides with g -factors approaching 10^{-4} .²⁶ Chiral assemblies of CdE NCs with biomolecules (proteins, polypeptides, or DNA) are scarce.¹⁴ This lack of examples highlights the difficulties of incorporating biomolecules that are highly sensitive to their environments (pH, temperature, ionic strength, etc.) and CdE NCs with charged surfaces that require passivation for colloidal stability.

Additionally, in the biomolecule:CdE examples, the systems are limited by accessible biomolecule concentration (10 – 450 μ M),^{14,24–26} likely due to synthetic and solubility limitations. In contrast, to the best of our knowledge, when performing biphasic aqueous ligand exchanges to achieve interfacial asymmetry in CdE NCs, the lowest concentration of Cys used is 1 mM²⁷ (typically 10 – 100 mM).^{17–19,28–32} The large discrepancy in concentration and the high pH conditions used in these ligand exchanges are not feasible for incorporating biomolecules. While there are established methods for the direct covalent attachment of NCs to biomolecules, these methods use small molecules on the NC surface to bind to targeted amino acids, with no reported chirality. An ideal system would exploit the protein's intrinsic chirality by enabling direct interfacial interactions between its amino acid side chains and the NC. To design such a direct bioinorganic interface, achiral and water-soluble NCs are ideal.

To minimize biomolecule concentrations for observable chiroptical response, here we incorporated CdS NRs, as NRs have been shown to exhibit an order-of-magnitude increase in g -factors or compared to QDs.³² Additionally, while we previously reported induced chirality in CdS QDs with polypeptides, the polypeptides used were intrinsically disordered with low complexity,³³ which made them ideal for

simple surface chelation of CdS. To our knowledge, no prior report has demonstrated that proteins with well-defined tertiary structure can transfer chirality to CdS NCs. Previous reports have been limited to small molecules, disordered polypeptides, or biomolecule templated growth, none of which address whether a folded protein can impose asymmetry at an inorganic interface. In this study, we aim to introduce complexity and order into biomolecules and determine whether establishing a protein:CdS interface induces asymmetry, and whether it does so while maintaining the protein structure. To do this, a designed helical repeat (DHR) protein containing eight α -helices and four Cys residues (DHR-4Cys) was prepared. This protein contains amino acids with additional chelating side chains, including aspartic acid (Asp), glutamic acid (Glu), histidine (His), and lysine (Lys), in addition to the four Cys residues. Moreover, all four Cys residues are located on one side of the protein's plate-like structure, which we hypothesized would be ideal for binding to the CdS surface with minimal interparticle aggregation. Such a CdS:DHR complex could be considered as a monomer in the deterministic construction of chiral structures across larger length scales, given the precedent for the assembly of such designed proteins into macromolecular chiral motifs like helices.^{34,35}

We employed a robust aqueous ligand exchange method to directly establish a protein:CdS interface using NRs. To understand the role of CdS NR length on induced chirality, we synthesized two different NR lengths. Next, we used CD absorbance spectroscopy to probe interactions between CdS and DHR-4Cys by monitoring the NR electronic transitions. Additionally, we examined the protein structure on the CdS surface using far-UV CD absorbance spectroscopy and transmission electron microscopy (TEM), and measured the

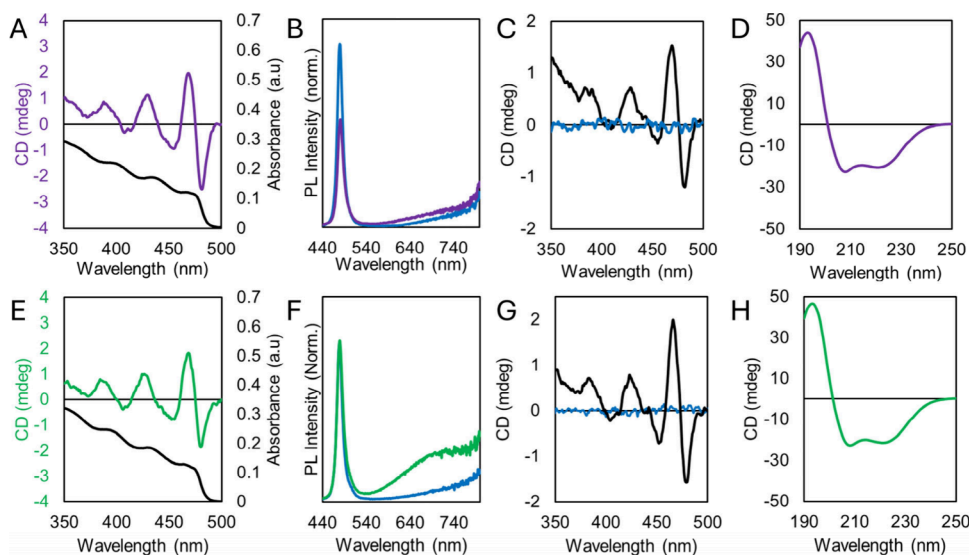


Figure 2. Spectroscopic data of long CdS NRs incubated with DHR-4Cys: (A) CD and absorbance spectra of 75 nM long CdS NRs (5.0 ± 0.8 nm by 61 ± 29 nm) incubated with $13.5 \mu\text{M}$ DHR-4Cys in Tris at pH 8.6. (B) Normalized PL spectra of long Cd NRs (5.0 ± 0.8 nm by 61 ± 29 nm) before (blue) and after (purple) incubation with $13.5 \mu\text{M}$ DHR-4Cys in Tris buffer at pH 8.6 (412 nm excitation wavelength). PL spectra were normalized by absorbance at 412 nm. (C) CD spectra of 75 nM long CdS NRs incubated with $54 \mu\text{M}$ Cys (black) and $81 \mu\text{M}$ Asp, $540 \mu\text{M}$ Glu, $13.5 \mu\text{M}$ Lys, and $13.5 \mu\text{M}$ His (blue) in Tris buffer at pH 8.6. (D) UV CD spectrum of long DHR-4Cys:CdS NRs after dialysis against nanopure water. [DHR-4Cys:CdS NR]: 2 nM. Spectroscopic data of short CdS NRs incubated with DHR-4Cys: (E) CD and absorbance spectra of 75 nM short CdS NRs (4.9 ± 0.6 nm by 18 ± 5 nm) incubated with $13.5 \mu\text{M}$ DHR-4Cys in Tris at pH 8.6. (F) Normalized PL spectra of short Cd NRs (4.9 ± 0.6 nm by 18 ± 5 nm) before (blue) and after (green) incubation with $13.5 \mu\text{M}$ DHR-4Cys in Tris buffer at pH 8.6 (412 nm excitation wavelength). PL spectra were normalized by absorbance at 412 nm. (G) CD spectra of 75 nM short CdS NRs incubated with $54 \mu\text{M}$ Cys (black) and $81 \mu\text{M}$ Asp, $540 \mu\text{M}$ Glu, $13.5 \mu\text{M}$ Lys, and $13.5 \mu\text{M}$ His (blue) in Tris buffer at pH 8.6. (H) UV CD spectrum of long DHR-4Cys:CdS NRs after dialysis against nanopure water. [DHR-4Cys:CdS NR]: 2 nM.

thermal stability of DHR-4Cys on the surface of CdS NRs with variable-temperature CD absorbance. Finally, we tested the sensitivity of our exchange method using nanomolar concentrations of DHR-4Cys (~ 2 equiv per NR). For the first time, we report induced chirality in CdS NRs using a highly ordered DHR protein, with detection using CD down to the nanomolar concentration regime.

While the mechanism of ligand-induced chirality in CdE NCs is not fully understood, prior studies have proposed that coordination of chiral ligands to CdE can transfer chirality through physical distortion of the lattice or via electronic coupling between the molecular orbitals of the ligands and excitons of the NCs.^{31,36} As previously mentioned, chiral CdSe NRs have been reported as more chiroptically active than chiral CdSe QDs.³² This is proposed to be caused by a crossover of the highest occupied molecular orbitals (HOMO) from Se $4p_x$ and $4p_y$ frontier orbitals in NCs to Se $4p_z$ orbitals in NRs with aspect ratios greater than ~ 1.2 .^{37,38} This crossover results in an increase in linear polarization within CdSe NRs, which is hypothesized to couple strongly to molecular orbitals of chiral molecules on their surface.³² Motivated by this, we tested whether increasing the available surface area for DHR-4Cys to bind to CdS NRs would impact the induced optical properties. To do this, two different length CdS NRs were synthesized with the same width dimensions in hydrophobic conditions, adapting a literature procedure³⁹ (see Methods). The resulting hydrophobic NRs were dispersible in nonpolar solvents and analyzed via TEM and powder X-ray diffraction (PXRD). TEM sizing analysis reveals that the longer NRs have dimensions of 5.8 ± 0.8 nm by 61 ± 29 nm (Figure 1A), and the dimensions for the shorter NRs are 6.0 ± 0.7 nm by 22 ± 6

nm (Figure S1), while PXRD confirms their wurtzite structures (Figure S2A,B).

Recognizing the lack of examples of chirality transfer between proteins and CdE in the literature, we propose that establishing chirality at the NC interface through localized binding of amino acids within an ordered protein structure is an important step in bridging length scales of chirality from the protein:CdE NC interface to protein-directed chiral assemblies of NCs. Inspired by the thiophilicity of cadmium demonstrated in Cys-containing zinc-finger domains,^{40–42} we have previously leveraged the thermodynamic favorability of thiolate–Cd interactions by first exchanging hydrophobic NCs with achiral and water-soluble glycine. Following solubilization of the NCs, glycine is readily displaced by Cys-containing polypeptides as indicated by induced CD absorbance corresponding to the electronic excitations of the NCs.²⁶ For context, there are few literature examples of inducing interfacial chirality in achiral Au NCs with biomolecules.^{43,44}

Due to the basic pH and high ligand concentrations required for exchanging hydrophobic CdE NCs into aqueous media,^{17,18,27,29,31,32,45,46} we have developed a robust ligand exchange that solubilizes CdS NCs with glycine, which preserves the achiral structure of the CdS NCs.²⁶ Adapting this procedure, we found that the CdS NRs are readily exchanged into water (see Methods). After aqueous exchange, the longer NRs have dimensions of 5.0 ± 0.8 nm by 61 ± 29 nm (Figure 1B), and the shorter NRs become 4.9 ± 0.6 nm by 18 ± 5 nm (Figure S3). While both the width dimensions decrease by approximately 1 nm, the length dimensions remain unchanged after the glycine ligand exchange. Once exchanged, the achiral glycine:CdS NRs are indefinitely stable in solutions containing 1.78 M glycine in 1 M tetramethylammonium

hydroxide (TMAOH) at pH 10.3. While we have found this glycine exchange to be robust for CdS NRs and QDs, isolating these NCs for NMR and IR surface-chemistry studies has remained an outstanding challenge due to the high ionic strength required to keep the glycine-capped NCs colloiddally stable.

Glycine, the only achiral amino acid, contains carboxylate and amine binding groups to passivate the surface cadmium of the NRs. Ligand exchange with glycine temporarily chelates surface cadmium to render NRs water-soluble, after which glycine is displaced by cysteine in DHR-4Cys via thermodynamically favorable thiol coordination.⁴⁷ DHR-4Cys contains eight α -helices and four Cys residues with other carboxylate side chain amino acids in their vicinity (Figure 1C). By design, DHR-4Cys has four Cys residues spaced approximately 3 nm apart on the same face of a roughly 4×4 nm plate-like protein structure (Figure 1D).

A challenge in displacing glycine from CdS NRs with a structured protein is the high equivalents of glycine (10^6 /NR) required to solubilize the CdS NRs. To obtain reasonable optical densities, we used a working concentration of 75 nM CdS with ~ 100 mM glycine. Additionally, the use of PBS buffer in these systems caused precipitation of the NRs, presumably due to the high salt concentrations. To preserve the DHR-4Cys structure and colloidal stability of the glycine:CdS NRs, solutions were buffered with tris-(hydroxymethyl)aminomethane (Tris) at pH 8.6 before the addition of DHR-4Cys (see Methods), where the achiral NRs maintain their optical properties (Figures S4 and S5). Once the achiral CdS NRs are incubated with DHR-4Cys, CD absorbance is observed corresponding to the electronic transitions of the long and short CdS NRs (Figure 2A,E), demonstrating CdS surface asymmetry upon the introduction of the protein without changes in the NR absorbance spectra (Figure S6). The similarities in the CD spectra between the long and short NRs (Figure S7A) can be rationalized by the similarities in their respective absorbance spectra (Figure S7B), signifying 2D NR confinement as a dominant contributor to induced chirality in these systems.

Accompanying the appearance of CD absorbance, changes in the photoluminescence (PL) spectrum are also observed (Figure 2B,F). Comparison of the glycine:CdS NRs [Figure 2B(blue),F(blue)] and DHR-4Cys:CdS NRs [Figure 2B-B(purple),F(green)] shows a decrease in intensity at the band edge feature (481 nm) and increased trap state emission (600–800 nm) in the normalized PL spectra, consistent with thiol coordination of CdS NCs.^{48,49} Circularly polarized luminescence measurements were attempted; however irreversible PL instability under the required excitation conditions prevented reliable quantification of luminescence. Using CD absorbance and PL spectroscopies, we conclude that the protein is successfully bound to the CdS NRs, demonstrating the first example of asymmetry in CdS arising from protein conjugation at its interface.

The appearance of CD absorbance corresponding to the CdS NR electronic transitions and quenching of the band edge PL feature in the presence of DHR-4Cys suggests that the thiophilicity of surface cadmium is a strong enough thermodynamic driving force to bind DHR-4Cys on the surface of the NRs even in the presence of 100 mM glycine. To confirm the Cys residues were responsible for the induced chirality, CdS NRs were incubated with Cys (54 μ M), resulting in CD absorbance that matches the DHR-4Cys:CdS NR

systems [Figure 2C(black),G(black)]. To determine the influence of amino acids in the protein containing carboxylate and imidazole side chains, CdS NRs were incubated with a mixture of aspartic acid (Asp, 81 μ M), glutamic acid (Glu, 540 μ M), lysine (Lys, 13.5 μ M), and histidine (His, 13.5 μ M), and no visible CD response was observed [Figure 2C(blue),G-(blue),G(blue)]. Similarly, no visible CD response was observed with micromolar concentrations of Asp, Glu, Lys, or His alone (Figure S8). These results highlight the high affinity for Cys on the surface of the glycine:CdS NRs and are consistent with the irreversible binding of thiols on CdSe QDs reported by Dempsey et al.⁴⁷ From this report and the results reported here, we propose at μ M concentrations, ligand competition could only arise from thiol binding groups in the protein. To confirm DHR-4Cys maintains its structure once bound to the NRs, DHR-4Cys:CdS NRs were dialyzed against nanopure water to remove unbound DHR-4Cys and monitored via deep UV CD spectroscopy (Figure 2D,H), which matched the line shape of unbound DHR-4Cys (Figure S9), confirming the preservation of the proteins' α -helicity on the NR surface. Additionally, after dialysis and dilution, the DHR-4Cys:CdS NRs maintain their chiroptical response corresponding to the electronic transitions of the CdS NRs (Figures S10 and S11).

For normalized chirality, *g*-factors of DHR-4Cys:CdS NRs, Cys:CdS NRs, Cys:CdS QDs, and polypeptide:CdS QDs were compared (Table S1). We found comparable *g*-factors for short DHR-4Cys:CdS NRs (4.5×10^{-4} at 468 nm) and long DHR-4Cys:CdS (5.0×10^{-4} at 469 nm) (Figure S12), indicating that increased surface area along the length facets did not significantly impact optical activity. These results are consistent with previous reports on Cys:CdSe NRs by Tang and co-workers, who observed that NRs with aspect ratios ≥ 3 did not exhibit significant differences in induced chirality when ligand exchanged with Cys,³² which supports our findings with CdS NRs with varying aspect ratios (short ~ 4 and long ~ 12 aspect ratios, respectively). This previous report and our work suggest that the chiroptical activity of NRs with an aspect ratio of 3 or more is primarily dictated by the 2D confinement dimension.

To understand the impact of the secondary structure of DHR-4Cys on induced chirality, we compared the *g*-factors obtained when incubating the short and long CdS NRs with 13.5 μ M DHR-4Cys and 54 μ M free Cys (Figure S13). Comparing *g*-factors of short DHR-4Cys:CdS NRs (4.5×10^{-4} at 468 nm) with short Cys:CdS NRs (4.8×10^{-4} at 466 nm) (Figure S13A), and long DHR-4Cys:CdS NRs (5.0×10^{-4} at 469 nm) with long Cys:CdS NRs (4.0×10^{-4} at 469 nm) (Figure S13B) shows no significant differences in *g*-factor. The close match in both magnitude and line shape between the DHR-4Cys:CdS and Cys:CdS CD responses indicates that chiral induction arises predominantly from local thiolate–Cd interactions, with no detectable additional contribution from the higher-order protein structure under these conditions. Examination of the short and long Cys:CdS NRs vs the Cys:CdS QDs (1.2×10^{-4}) shows a 3-fold increase in *g*-factor consistent with higher *g*-factors of NRs vs QDs.³² Comparison of our previous polypeptide:QD system [valine (V)–proline (P)–glycine (G)–V–G]₅₄-Cys:CdS QDs (0.7×10^{-4}) to the CdS NRs shows over a 6-fold increase in *g*-factor of the DHR-4Cys:CdS NRs compared to the polypeptide:QDs.²⁶ This observation reinforces the mechanism of chirality transfer arising from an electronic origin governed by the covalency of the thiolate–Cd interaction at the interface. Due to the large

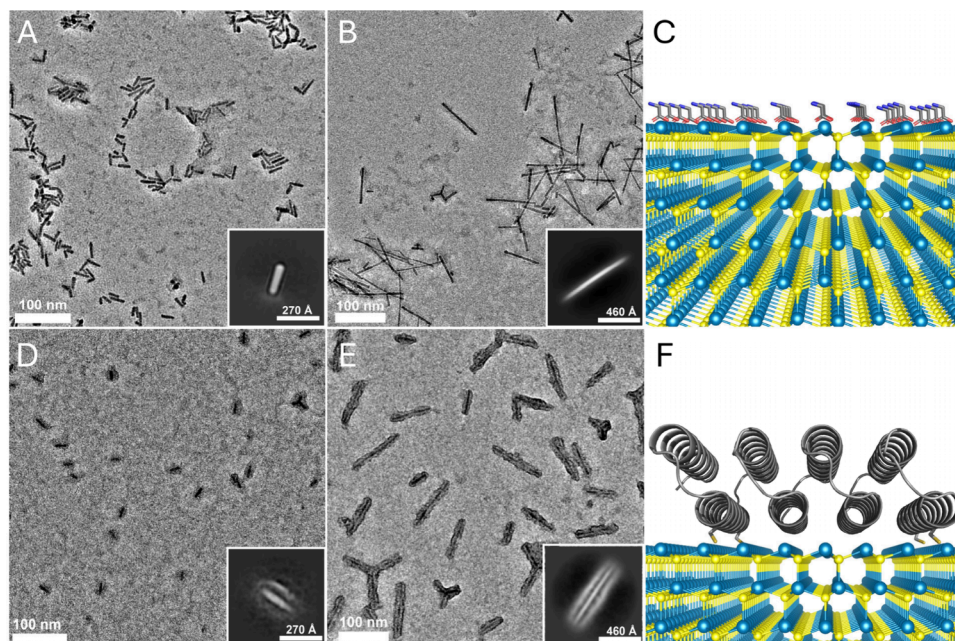


Figure 3. (A) Negative stain TEM of short glycine:CdS NRs and 2D class averaging of glycine ligand shell (inset). (B) Negative stain TEM of long glycine:CdS NRs and 2D class averaging of glycine ligand shell (inset). (C) Idealized CdS NR surface interaction with glycine carboxylate group at pH 8.6: cadmium (teal), sulfur (yellow), carbon (gray), and nitrogen (blue). (D) Negative stain TEM of short DHR-4Cys:CdS NRs and 2D class averaging of protein ligand shell around NRs (inset). (E) Negative stain TEM of long DHR-4Cys:CdS NRs and 2D class averaging of protein ligand shell around NRs (inset). (F) Idealized surface interaction of DHR-4Cys on CdS directed through Cys residues in A2 and A8 α -helices.

amount of coordinating amino acids at the interface of the protein, we would expect significantly greater surface cadmium distortions in the DHR-4Cys CdS NRs compared to the Cys:CdS NRs, and for the chirality transfer to be amplified if a structure-based mechanism were operative.

To visualize the CdS NRs with glycine on their surface compared to DHR-4Cys, negative-stained TEM and 2D class averaging reveal significant differences in ligand shell density between protein-bound and glycine-bound NRs (Figure 3). The negative-stained TEM and class averaging of the short glycine:CdS NRs (Figure 3A) and long glycine:CdS NRs (Figure 3B) reveal NRs with no observable ligand density. This is expected due to the size of glycine ($\text{\AA}$ -scale) compared to the size of the CdS NRs (nm-scale) (Figure 3C). Through negative-stained TEM and 2D class averaging, a protein shell thickness of 2–3 nm is found on the surface of short DHR-4Cys:CdS (Figure 3D) and long DHR-4Cys:CdS NRs (Figure 3E). These results confirm that the protein is bound to the NR surface DHR-4Cys, and the protein still maintains its helical structure (Figure 3F). Comparison of the unbound and bound protein TEM also shows much less interparticle aggregation in the protein-bound system, which suggests an increase in NR colloidal stability with the DHR protein on its surface.

To test the stability of the plate-like structure of the DHR-4Cys on the NR surface, we monitored its α -helical structure using variable-temperature CD (Figure 4A,B). Moderate changes were observed in the CD spectra of the α -helical structures in the DHR-4Cys:CdS NRs (Figures 4A and S14). When monitoring the collapse of the α -helical structures of the DHR-4Cys:CdS NRs vs the DHR-4Cys, we see no significant differences in stability of the protein on the surface of the NR vs unbound (Figure 4B). Additionally, moderate changes in the CD signal intensity of the NRs are observed across the same temperature range (Figure S15). These results demonstrate that CdS NRs can be directly bound to highly

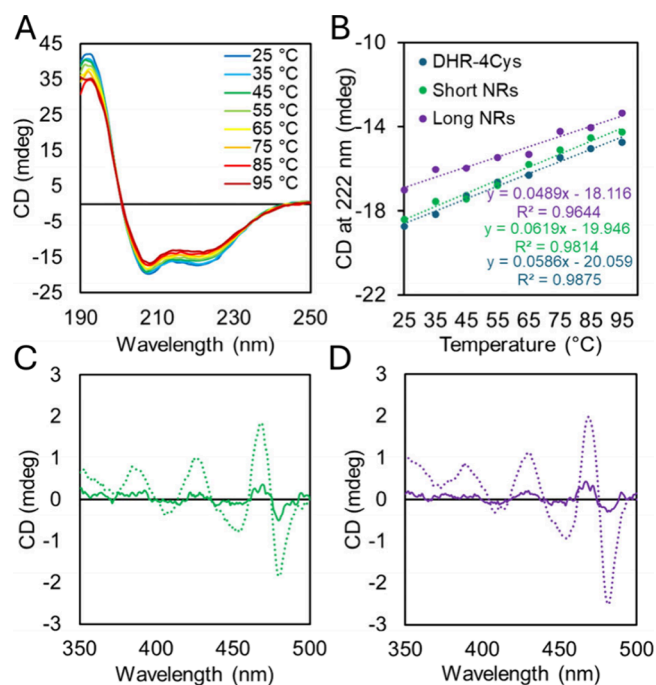


Figure 4. (A) Variable-temperature CD spectra of long DHR-4Cys:CdS NRs (2 nM) in the UV. (B) Plot of CD absorbance of DHR-4Cys (~ 59 nM) unbound (blue), short DHR-4Cys:CdS NR (3 nM) (green), and long DHR-4Cys:CdS NRs (2 nM) (purple). CD absorbance values were monitored at 222 nm. (C) CD absorbance overlay of 75 nM short CdS NRs with 170 nM (solid green) and 13.5 μM DHR-4Cys (dashed green) in Tris buffer of pH 8.6. (D) CD absorbance overlay of 75 nM long CdS NRs with 170 nM (solid purple) and 13.5 μM DHR-4Cys (dashed purple) in Tris buffer of pH 8.6.

ordered proteins without degradation of their structures, making them viable candidates for NCs in chiral hybrid inorganic–organic materials in which chirality spans the NC–protein interface and facilitates the hierarchical assembly of the NCs within a protein scaffold.

We hypothesized that minimal equivalents of protein to NC will be ideal for bridging chirality from protein:NC interfaces to protein:NC assemblies to maximize through-space charge transport of NCs, as Kotov and co-workers have previously described.⁵⁰ To highlight the sensitivity of the achiral interface of glycine:CdS NRs toward chiral DHR-4Cys, CD absorbance spectra of 75 nM of short CdS NRs incubated with 170 nM DHR-4-Cys (Figure 4C, solid green) and 13.5 μ M DHR-4Cys (Figure 4C, dashed green trace) show a weak optical response consistent with the CD line shape found in the higher protein concentration samples. Additionally, CD absorbance of 75 nM long CdS NRs with 170 nM DHR-4-Cys (Figure 4D, solid purple) and 13.5 μ M DHR-4Cys (Figure 4D, solid purple) shows optical response of the NCs at nM concentration of protein. To demonstrate the impact morphology has on chiroptical response in these systems, we incubated the same concentration of CdS QDs and DHR-4Cys and observed no optical CD absorbance arising from the QD electronic transitions (see Methods and Figure S16). These results emphasize the advantage of using CdS NRs to bridge chirality from the surface to protein assembly length scales in inorganic–organic hybrid materials, as the CdS NR surface is sensitive enough to detect just nM concentrations of protein.

NC chirality has been demonstrated to arise across molecular, interfacial, and macromolecular length scales. While there have been several successful efforts across these length scales using small molecules, there have been limited examples of using proteins to induce asymmetry in NCs. For the first time, we have demonstrated that chirality can be induced in CdS NRs using a protein with an ordered structure. We demonstrate that this phenomenon arises from CdS NR surface asymmetry introduced by chelating Cys residues in the protein with no significant chirality contribution from the α -helical backbone. We were able to show that the α -helical and plate-like tertiary structure of the protein is preserved when a protein is bound to a CdS NR surface. Additionally, we report the g -factors of 4.5×10^{-4} for 4.9 ± 0.6 nm by 18 ± 5 nm NRs and 5.0×10^{-4} 5.0 ± 0.8 nm by 61 ± 29 nm DHR-4Cys:CdS NRs, demonstrating that NR length does not significantly impact g -factor. Excitingly, we have also demonstrated that the surface of the glycine:CdS NRs is sensitive enough to detect just nM concentrations of DHR-4Cys while no CD response is observed in spherical CdS NCs for μ M concentrations of DHR-4Cys. Moving forward, we believe these results can inform the design of chiral biomolecule:NC interfaces and serve as a starting point for deterministic construction of protein:NC assemblies with chirality across length scales.

■ ASSOCIATED CONTENT

SI Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.nanolett.5c06115>.

Complete experimental methods, supplemental electron microscopy, PXRD, optical spectroscopy, and CD data and analysis (PDF)

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Notes

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