Inorganic Nanostructures with Strong Chiroptical Activity

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Chirality is one of the most remarkable geometrical properties with a variety of manifestations in the material world. The discovery of chirality in inorganic nanostructures spurred the rapid growth of fundamental and applied studies involving chiral nanoscale particles in chemistry, biology, medicine, and physics. While many factors make chiral inorganic nanostructures significant to researchers from many backgrounds, the unique characteristic that drives research in this area is their ability to exhibit high chiroptical activity. In this review, we specifically address its origin in juxtaposition with chiral organic nanostructures. Chiroptical activity depends on multiple factors, including the degree of asymmetry and the size of the object, compared with light wavelength. Nonetheless, it is the high polarizability that distinguishes chiral inorganic matter from what is known from organic chemistry and biology. More importantly, strong light-matter interaction between chiral nanostructures and circularly polarized photons has direct implications for the long-standing fundamental questions about the origin of homochirality on earth and new possibilities for chiral catalysis. Increased insight into chiroptical activity also deepens the existing knowledge about the nanoscale matter and expands its technological applications.

Keywords: chirality, optical activity, circular dichroism, light-matter interactions, nanoparticles

Introduction

Chiral objects are not superimposable with their mirror images, which is equivalent to the presence of chiral center, axis, or plane. These mirror-symmetric forms of chemical compounds, or enantiomers, have identical physical properties except how they rotate the plane of linearly polarized (LP) light; one rotates it to a specific angle, and the other rotates to the opposite direction of an equal angle, a phenomenon known as optical activity. One enantiomer is designated as dextrorotatory (σ), rotating LP light in a right-handed or clockwise manner, and the other as levorotatory (τ), rotating LP light in a left-handed or counterclockwise fashion. The absolute configuration of the molecules in three-dimensional (3D) space is designated as R or S, based on Cahn–Ingold–Prelog priority rules. An imbalance of the quantity of right and left enantiomers in a mixture is traditionally known as enantiomeric excess (ee) and is determined by the equation: 

\[ ee = \frac{(R - S)}{(R + S)} \]

where R and S are the concentrations of right- and left-handed molecules in a substance, respectively.

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Chiral compounds could be investigated using many conventional spectroscopic techniques, including electronic circular dichroism (ECD or CD), vibrational CD (VCD), diffuse reflectance CD (DRCD), fluorescence-detected CD (FDCD), Raman optical activity (ROA), and single-particle circular differential scattering (CDS). In recent review papers, Sang et al. discussed different circularly polarized luminescent nanomaterials, which could be studied using circularly polarized luminescence spectroscopy; Langer et al. considered enantioselective discrimination of chiral molecules via surface-enhanced Raman scattering (SERS) technique. However, the primary method for studying optical activity is CD, which is based on different absorption of left and right circularly polarized light (CPL) by chiral compounds. For quantitative analysis of the optical activity of liquid solutions and dispersions the dissymmetry factor (1 - factor) is used, which is defined as \( g = \frac{\Delta \varepsilon}{\varepsilon} = \frac{\varepsilon_L - \varepsilon_R}{\varepsilon_L + \varepsilon_R} \), where \( \Delta \varepsilon \) is molar CD, \( \varepsilon \) is molar extinction, and \( \varepsilon_L \) and \( \varepsilon_R \) are the molar extinction coefficients for left- and right-handed CPL, respectively. As could be seen from this equation, the dissymmetry factor excludes the effects of the sample concentration and cell path length on the optical activity of a sample.

Uncovering chirality in nanoparticles (NPs) was a new phenomenon that accelerated the developmental pace of the field of chirality and opened up new horizons in nanoscience. As a result of multiple studies, the reasons for the appearance of optical activity in nanostructures emerged. To date, it has become apparent that even a single-chiral NP is a complex system whose optical activity is caused by several factors simultaneously. In practice, it is quite challenging to determine the contribution of each particular factor because all of them are intertwined.

Currently, the field of chiral nanomaterials is experiencing active growth due to the following scientific and practical reasons: (1) Although chiral NPs could possess similar geometry as chiral organic compounds, their physics of light-matter interactions differs considerably. The advantages of NPs over organic compounds include the ability to control their properties during synthesis, as well as the possibility to achieve significantly higher dissymmetry factors, and in some cases, the \( g \)-factors of nanoscale materials exceed the typical \( g \)-factors of chiral molecules by a factor as high as \( 10^3 \). (2) Chiral NPs reveal some similarities such as size, charge, shape, and functional groups, with biomolecules, which suggest that NPs could function as biomolecule mimics, making it possible to develop new chirality-convergent technologies. (3) In-depth knowledge of the phenomenon of chirality at the nanoscale level brings us closer to the answers to long-standing fundamental questions like the origin of homochirality on Earth. (4) The practicality of nanoscale chirality is unquestionable since chiral nanostructures offer new technological solutions in many

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Figure 1 | (a) Structural formulas of chiral organic molecules involved in the nanoparticles chiroptical activity. (b) Optimized geometry of graphene sheet in GQDs model. L-GQD and D-GQD refer to those edges stabilized with L- and D-cysteine (Cys), respectively. Adapted with permission from Ref. 19. Copyright 2016 American Chemical Society. (c) Comparative images of the structures of serum albumin and water-soluble CdTe quantum dots.
fields, including biosensing, chiral catalysis, enantioselective separation, information technologies including quantum computing, and biomedical imaging.

Thus, chiral nanomaterials are of interest not only from a fundamental point of view but also for a wide range of potential applications. Both of these aspects have been widely considered earlier by several scientific groups, as outlined in this review.

### Interaction of Circularly Polarized Light with Chiral Organic Molecules and Nanoparticles

Chiral organic compounds and chiral nanomaterials might be similar in size, geometry, charge, and shape (Figure 1) and have relatively similar intensity of their chiroptical activity. For example, the $g$-factor of chiral graphene quantum dots (GQDs), presented in Figure 1b, is $\sim 1 \times 10^{-4}$, which is comparable to that of many chiral organic compounds ($10^{-4}$ to $10^{-5}$). For example, the $g$-factor of chlorin e6 (Ce6) monomers is $\sim 3 \times 10^{-4}$. However, in some cases, chiral nanostructures are characterized with $g$-factors that are two to three orders of magnitude higher, compared with that of their organic counterparts. To understand the reason for the observed difference, it is necessary to consider how the substances absorb CPL.

The magnitude of a CD amplitude is usually estimated using molar CD $\Delta \varepsilon$ and/or $g$-factor, in quantum mechanical theory of CD for this purpose, a rotatory strength $R$ is used, which is calculated in accordance with the Rozenfeld equation as the imaginary part of the scalar product of the electric and the magnetic transition moments between the ground state 0 and an excited state a in Eq 1 as follows:

$$R_{0a} = \text{Im}\{\langle \Psi_0 | \hat{\mu} | \Psi_a \rangle \cdot \langle \Psi_0 | \hat{m} | \Psi_a \rangle \} = \text{Im}\{\mu_{0a} \cdot m_{a0}\}$$ (1)

where $\Psi_0$ and $\Psi_a$ are the wave functions for the ground state 0 and excited state a, $\hat{\mu}$ and $\hat{m}$ are the corresponding electric and magnetic moment operators, and $\mu_{0a}$ and $m_{a0}$ are the electric and magnetic transition dipole moments, respectively.

There is a direct relationship between the electric dipole $\mu$ and the electric field $E$ with the proportionality factor $\alpha$, which is called polarizability, and reflects how easily the charge distribution could be distorted. This correlation is described in Eq 2:

$$\mu = \alpha E$$ (2)

As presented in Table 1, the polarizability of NPs is much higher than that of organic compounds. Therefore, it is expected that the interaction of incident photons with the nanoscale materials should exceed those of similarly sized organic objects.

### Table 1 | Polarizabilities of Various Organic Molecules and Inorganic NPs

<table>
<thead>
<tr>
<th>Specific Object</th>
<th>Polarizability [Å$^3$]</th>
<th>Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organic molecules</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbonyl sulfide</td>
<td>2.4</td>
<td>27</td>
</tr>
<tr>
<td>Water</td>
<td>1.19</td>
<td>28</td>
</tr>
<tr>
<td>Ammonia</td>
<td>2.31</td>
<td>28</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>2.49</td>
<td>28</td>
</tr>
<tr>
<td>Acetaldehyde</td>
<td>4.6</td>
<td>28</td>
</tr>
<tr>
<td>Sulfuric acid</td>
<td>6.2</td>
<td>28</td>
</tr>
<tr>
<td>Acetone</td>
<td>6.4</td>
<td>28</td>
</tr>
<tr>
<td>Phenol</td>
<td>11.19</td>
<td>29</td>
</tr>
<tr>
<td>Butadiene</td>
<td>8.34</td>
<td>29</td>
</tr>
<tr>
<td>Hexatriene</td>
<td>14.14</td>
<td>29</td>
</tr>
<tr>
<td>Octatetraene</td>
<td>22.81</td>
<td>29</td>
</tr>
<tr>
<td>Decapentene</td>
<td>33.79</td>
<td>29</td>
</tr>
<tr>
<td>Dodecahexene</td>
<td>48.00</td>
<td>29</td>
</tr>
<tr>
<td>Tetradecaheptene</td>
<td>66.03</td>
<td>29</td>
</tr>
<tr>
<td>Hexadecacontene</td>
<td>88.72</td>
<td>29</td>
</tr>
<tr>
<td>Octadecanone</td>
<td>116.58</td>
<td>29</td>
</tr>
<tr>
<td>Benzene</td>
<td>10.09</td>
<td>29</td>
</tr>
<tr>
<td>Naphthalene</td>
<td>17.80</td>
<td>29</td>
</tr>
<tr>
<td>Anthracene</td>
<td>27.49</td>
<td>29</td>
</tr>
<tr>
<td>Tetracene</td>
<td>39.43</td>
<td>29</td>
</tr>
<tr>
<td>Li$_2$ (990 K)</td>
<td>34±3</td>
<td>30</td>
</tr>
<tr>
<td>Na$_2$ (736 K)</td>
<td>30±3</td>
<td>30</td>
</tr>
<tr>
<td>K$_2$ (569 K)</td>
<td>61±5</td>
<td>30</td>
</tr>
<tr>
<td>Rb$_2$ (534 K)</td>
<td>68±7</td>
<td>30</td>
</tr>
<tr>
<td>Cs$_2$ (515 K)</td>
<td>91±7</td>
<td>30</td>
</tr>
<tr>
<td>Semiconductor NPs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CdSe NPs, radius from 1.4 to 2.4 nm</td>
<td>$\sim 10^4$</td>
<td>31</td>
</tr>
<tr>
<td>PbSe NPs, radius from 1.2 to 3.3 nm</td>
<td>$\sim 10^{-10}^5$</td>
<td>32</td>
</tr>
<tr>
<td>InAs NPs, a radius of 2.0 nm</td>
<td>$\sim 10^4$</td>
<td>33</td>
</tr>
<tr>
<td>CdSe NPs, average radii of 22, 24, 26, 29, and 37.5 Å</td>
<td>$\sim 10^4$</td>
<td>34</td>
</tr>
<tr>
<td>CdSe/ZnS, 37.5 Å CdSe NPs</td>
<td>$\sim 10^4$</td>
<td>35</td>
</tr>
<tr>
<td>CdSe/ZnSe epitaxial NPs</td>
<td>$\sim 10^5$</td>
<td>36</td>
</tr>
<tr>
<td>Fe$_3$O$_4$, a hydrodynamic diameter of 15 nm</td>
<td>$\sim 10^5$</td>
<td>36</td>
</tr>
<tr>
<td>Ag, a radius of 20 nm</td>
<td>$\sim 10^6$</td>
<td>37</td>
</tr>
</tbody>
</table>

Like many other properties of nanomaterials, the polarizability could also be tuned by varying the parameters of NPs, as well as ambient conditions (e.g., temperature). Figure 2 illustrates how the polarizabilities of various semiconductor NPs depend on their size and composition. As indicated, the polarizability of NPs tends to
increase as their sizes increase. For instance, Wang et al. revealed that the polarizability of cadmium selenide (CdSe) NPs with radii ranging from 1.4 to 2.3 nm was approximately proportional to the fourth power of the NP radius (Figure 2a). Meanwhile, this dependence had linear characteristic for CdSe NPs with radii ranging from 2.1 to 3.8 nm (Figure 2d). Accordingly, from these results and Eq 1, it could be concluded that with size increase, the CD strength of chiral NPs would increase. However, that is not necessarily so. As shown from Eqs. 1 and 2, polarizability is one of the multipliers that could affect rotatory strength. Thus, if the other parameters decreased with increasing NP size, it is be expected that the optical activity would not increase, and many research results are indicative of this viewpoint.

Optical Activity of Individual Nanoparticles and Their Assemblies

It has been demonstrated that both individual NPs and their assemblies could enhance optical activity. In most cases, chiral nanostructures are synthesized using chiral molecules (amino acids, proteins, peptides, and DNA), CPL, and various self-assembly methods. The simplicity of their creation allows for significantly expanded applications of chiral nanomaterials in multiple emerging technologies.

Individual nanoparticles

Optical activity of inorganic NPs was first demonstrated in 1998 by Schaaff et al. in gold (Au) NPs, which was followed by the finding of chirality in semiconductor NPs by Gun’ko et al. In both cases, chiroptical activity of NPs was established using CD spectroscopy. The first studies on chiral NP assemblies of were reported by Chen et al., Chen et al., and Mastroianni et al. In addition to CD spectroscopy, the chirality of NP assemblies was also revealed using transmission electron microscopy (TEM).

Initial studies, aimed at a better understanding of the origin of chiroptical activity in nanostructures were centered on individual metal NPs and nanoclusters. It was suggested by Schaaff and Whetten that this phenomenon could be associated with either the: (1) intrinsically chiral structure of the metal-cluster core; (2) chiral

Figure 2 | Polarizabilities of various semiconductor NPs as a function of their radius (r): (a) CdSe NPs. The data were obtained from Ref. 31. (b) CdSe and PbSe NPs. Adapted with permission from Ref. 32. Copyright 2007 American Chemical Society. (c) Indium arsenide (InAs) NPs. Adapted with permission from Ref. 33. Copyright 2010 American Chemical Society. (d) CdSe (black squares) and CdSe/ZnS NPs (red circle). The data were obtained from Ref. 34.
spatial pattern formed by adsorbed molecules on the intrinsically achiral metal-cluster core; or (3) influence of the chiral centers of adsorbed molecules on the electronic structure of the metal core electrons while both the core and the adsorption pattern of the capping molecules are achiral. Garzón et al.61,62 performed theoretical studies on the structural properties of Au clusters, which demonstrated that the lowest-energy (most stable) isomers of bare (Au28 and Au55) and thiol-passivated [Au28(SCH3)36 and Au38(SCH3)24] clusters corresponded to chiral nanostructures. These studies provided theoretical support for the existence of chirality in metal clusters.

Since not all chiral molecules could induce chirality in NPs, the chiral environment also needed to be considered in this process. For instance, Mulligan et al.63 used surface second-harmonic generation measurements to demonstrate that the ability of an adsorbate to induce chirality onto the electronic structure of a metal surface was associated with its adsorption character, which could be perturbed only if at least three noncollinear and nonequivalent chiral adsorbate groups were close to the metal surface (“chiral footprint”). This effect was revealed as a result of a comparative study of optically active second-harmonic generation measurements of a Cu(111) metal surface with the chiral molecules, 2-butanol64 and 1-(1-naphthyl)ethylamine,65 adsorbed onto it. The authors observed that the surface electronic structure of Cu(111) was not strongly perturbed by the adsorption of monolayers of 2-butanol, while 1-(1-naphthyl)ethylamine reversibly induced chirality onto the electronic structure of the metal surface. This phenomenon was associated with the fact that three different chemical groups of 1-(1-naphthyl) ethylamine were in close proximity to the metal surface, as distinct from 2-butanol, which did not have a “chiral footprint,” as it adopted a geometry where only a hydroxyl group was close to the surface. This result also showed that, along with CD spectroscopy and other methods for studying chiral compounds, surface second-harmonic generation appeared to be enantiomer sensitive, and that the possibility that optical activity in metal NPs might also occur as a result of dipolar interactions between chiral adsorbates and nonchiral metal NPs, and that the orientation of an electric dipole of a molecule toward the vector connecting the centers of NP and the molecule strongly influences the resultant CD bands. This description of the phenomenon matched the experimental data obtained by Siock et al.,66 as part of the study of optical properties of peptide-functionalized 10 nm Au NPs. It was found that the experimental observation of the appearance of a CD signal at 520 nm, which corresponded with the Au NP’s surface plasmon resonance frequency, was in accordance with the calculated CD spectra obtained within the dipolar approximation.

Rapid progress in the synthesis of metal NPs allowed controllable fabricated NPs with spherical shapes, cubes, rods, octahedrons, platelets, helices, and spirals, as well as complex structures of core/shell type.70–76

Levi-Belenkova et al.74 studied optical properties of Ag nanocubes with chiral polyproline II-based helical peptides (NH2−CPPPPPPPPPP−OH (C−P8) and NH2−PPPPPPPPPP−OH (P8−C), adsorbed on their surface. These peptides had the same CD spectra and differ only in the location of the Cys unit: in C−P8, it was at the N-terminus and, in P8−C, it was at the C-terminus, which allowed the authors to realize inverted adsorption orientation of peptides on the NP surface. Analysis of optical properties of the resultant hybrids revealed that the signal of the induced plasmonic CD strongly depended on the peptide’s orientation toward the surface of the nanocubes. Hence, the two chiral molecules with the same helicity, induced opposite CD by adsorbing onto the surface with reversed ends of the helix (Figure 3a), thereby, leading to a suggestion that this phenomenon could be associated with multipolar effects at plasmon resonances, involving the hot spots created at the cube apexes and edges.

Lu et al.73 reported that DNA-functionalized Au/Ag core/shell nanocubes displayed new CD bands in the

The VCD spectra revealed the two-point attachment of N-isobutyryl-Cys by thiol and carboxyl groups, and the authors suggested that the observed optical activity in metal-based transitions was associated with bidentate binding of chiral adsorbate, which, in turn, led to a chiral “footprint” on the particle surface.

Further, it was demonstrated that not only small molecules but also large biomolecules, such as DNA and peptides, could induce chirality in individual NPs.54–58

Shemer et al.64 first reported the high optical activity of a surface plasmon excitation band of silver (Ag) NPs grown on a poly(dG)−poly(dC) double-stranded DNA scaffold, which was supposed to have arisen from the chiral nature of the metal core templated by DNA.

Along with the mechanisms responsible for the appearance of chiroptical properties in individual metal NPs proposed by Schaff et al.,50,51,52,53 Govorov et al.59 considered the possibility that optical activity in metal NPs might also occur as a result of dipolar interactions between chiral adsorbates and nonchiral metal NPs, and that the orientation of an electric dipole of a molecule toward the vector connecting the centers of NP and the molecule strongly influences the resultant CD bands. This description of the phenomenon matched the experimental data obtained by Siocik et al.,66 as part of the study of optical properties of peptide-functionalized 10 nm Au NPs. It was found that the experimental observation of the appearance of a CD signal at 520 nm, which corresponded with the Au NP’s surface plasmon resonance frequency, was in accordance with the calculated CD spectra obtained within the dipolar approximation.
near-visible region, while the “naked” nanocubes did not show any CD signal. Compared with a CD signal of free DNA (∼240–280 nm), plasmon-induced CD signals of hybrid nanostructures were characterized by a giant CD amplification of up to two orders of magnitude per molecule. The authors associated this effect with the exciton–plasmon interactions between DNA and nanocubes, and indicated the crucial role of DNA orientation on the surface of the nanocubes in this process. They also stressed the importance of Ag nanocube geometry for the CD enhancement, which was revealed due to the experimental and theoretical comparison of the NPs with those of other shapes and materials.

Hou et al.76 also examined the importance of plasmonic NP shape in the inducement of plasmonic CD as part of an investigation of Au/Ag core/shell NPs with Cys molecules preincubated on the core/shell interface, and observed that these Cys molecules induced intense plasmonic CD signals for Au nanorods passivated with Ag, resulting from the strong electric field around Cys, confirmed by Raman spectra. Nonetheless, decreasing the aspect ratio of Au nanorods was accompanied by the reduction of CD signal intensity (Figure 3b), and the spherical core/shell NPs did not demonstrate any apparent plasmonic CD signals.

Intense CD signals in the visible range were also observed from the Au core–DNA–Ag shell NPs.77 As shown in Figure 3c, g-factors of these individual NPs were dependent on the thickness of the Ag shell. The authors inferred that the interactions between the DNA and the plasmons led to the appearance of the plasmonic CD, which was amplified further through the electromagnetic coupling and plasmonic oscillation between the Au core and the Ag shell.

Recently, Yan et al.78 reported the synthesis and optical properties of starfruit-like Au NPs (Figure 4a). These nanostructures were prepared through Au overgrowth on Au nanorods, preincubated with Cys molecules, which controlled the Au growth mode and the formation of hot spots within the shell. The authors suggested that strong plasmonic CD observed from the resulted nanostructures might have been caused by entrapped Cys molecules within the hot spots, which enhanced the signal via local field effect. It was also revealed that increasing the Cys concentration significantly enhanced the CD response. Lee et al.79 designed individual 3D chiral
Au nanostructures of helicoid shape with g-factor ≈ 0.2. Optical activity, handedness, and chiral plasmonic resonance of these nanostructures were controlled by the utilization of amino acids and peptides, which influenced the growth rate of certain crystal facets. The authors reported that the formation of intrinsically chiral high-Miller-index surfaces, due to the presence of “kink” sites in the nanoparticles during growth, was essential for the creation of these chiral nanostructures. In turn, the enantioselective interactions between the surface of NPs and the amino acids and peptides led to asymmetric evolution of the NPs and the formation of helicoid morphologies that consisted of highly twisted chiral elements. In furtherance of this work, the authors recently studied the influence of different components (e.g., Cys, hexadecyltrimethylammonium bromide (CTAB), L-ascorbic acid) on the chiral development of the NPs and, on this basis, synthesized chiral plasmonic nanoparticles of the rhombic dodecahedral shape with intense optical activity.80

Saito and Tatsuma81 fabricated chiral plasmonic nanostructures using CPL as the sole source for generating chirality. They applied twisted electric field distributions around the achiral Au nanocuboids under CPL irradiation. This resulted in a bottom-up fabrication of chiral plasmonic nanostructures via site-selective deposition of PbO2 based on plasmon-induced charge separation, which occurred when a plasmonic NP was in contact with a semiconductor such as TiO2 (Figure 4b).

Another important class of chiral NPs is the semiconductor colloidal quantum dots. Gao et al.82 recently summarized state-of-the-art progress of their synthesis, fundamental understanding of their properties, and their potential applications. The optical activity of semiconductor nanomaterials was first demonstrated by Gun’ko et al.42 in 2007 in the absorption region of CdS NPs stabilized with chiral penicillamine molecules during aqueous syntheses of NPs. Since the photoluminescence of the CdS NPs was the result of the nature of the defects/trapped states rather than an excitation one, the authors assumed that the observed optical activity was, most likely, caused by the chiral penicillamine-induced distortion of the NP surface atoms. DFT calculations...
revealed that penicillamine strongly distorted the surface Cd atoms of the CdS NPs and transmitted an enantio-meric structure to the surface layers, associated electronic states, while the NP core remained undistorted and achiral. Also, Zhou et al. observed the profound effect of chiral Cys ligands on the growth kinetics and the optical properties of CdTe NPs synthesized in aqueous solution. A combination of detailed experimental analysis with theoretical calculations allowed the authors to conclude that the atomic origin of chiral sites in the NPs studied, in which the atoms were arranged as tetrahedrons, was topologically similar to that of organic compounds, and therefore, chirality could occur when all four atomic positions were nonequivalent. This effect was also reported for CdSe NPs and CdS nanotetrapods.

It was later demonstrated, using the example of CdSe NPs, that optically active semiconductor NPs could be prepared from NPs obtained by a high-temperature organometallic synthesis with the postsynthetic replacement of achiral hydrophobic NP ligands with water-soluble chiral ligands [e.g., Cys, penicillamine, glutathione (GSH), and others]. The authors established the phenomenon responsible for the appearance of optical activity in these NPs by replacing the chiral Cys ligands with achiral 1-dodecanethiol (DDT). DDT-capped optical activity in these NPs by replacing the chiral Cys ligands with achiral hydrophobic NP ligands with water-soluble chiral ligands [e.g., Cys, penicillamine, glutathione (GSH), and others]. The authors established the phenomenon responsible for the appearance of optical activity in these NPs by replacing the chiral Cys ligands with achiral 1-dodecanethiol (DDT). DDT-capped CdSe NPs were soluble in toluene and displayed identical absorption spectra as the Cys-capped CdSe NPs; however, they did not show CD signal. Thus, the authors concluded that two possible mechanisms determined the optical activity of the NP: (1) CdSe chiral surface induced by bound Cys, and (2) coupling between the electric fields of Cys and CdSe. Concurrently, several other research groups demonstrated the conservation of optical activity in CdTe and CdS/ZnS NPs after replacing the chiral ligands with achiral ones, which was explained by the chiral memory effect for CdTe NPs and the intrinsic chirality of CdSe/ZnS nanocrystals caused by the presence of naturally occurring chiral defects.

During the last decade, many efforts have been made to study optical activity in semiconductor NPs depending on a number of factors, including NP size, chemical composition, shape, shell thickness, crystal structure, as well as type and concentration of surface stabilizers. Balaz et al. studied the optical activity of Cys-capped CdSe NPs of different diameters (2.9–5.2 nm) and proposed a model in which the optical activity of the NP could result from the hybridization of the ligand highest occupied molecular orbital (HOMO) with the NP valence band states. This hypothesis was supported by a detailed analysis of induced CD spectra of CdSe, CdS, and core/shell CdSe/CdS (quasi-type II), CdS/CdSe (inverted type I), and Cu$_2$S/CdSe (type II) NPs. Nevertheless, Ben-Moshe et al. explained that experiments performed on core/shell NPs could not differentiate between a surface structural distortion mechanism and an electronic hybridization mechanism, since both of these effects are expected to decay when the chiral ligands surface separates from the hole. Thus, as in the case of chiral metal nanoclusters, optical activity in semiconductor NPs could be caused by several mechanisms.

The area of chiral nanomaterials goes far beyond metallic and semiconductor NPs, and includes chiral magnetic, polymeric, ceramic, carbon, mercury sulfide, molybdenum disulfide, silica, and graphene NPs. Regardless of the type of NP, it is difficult to overestimate the role of chiral molecules in the origin of optical activity in NPs. However, the opposite is true when it is considered that the effect of NPs on the optical activity of molecules has not been widely investigated. In the meantime, Maoz et al. observed the amplification of chiroptical activity of riboflavin by surface plasmons of the Au islands (Figure 5a) and associated it with near-field interactions, which were molecule–plasmon, dipole–dipole, or multipolar coupling. Recently, it was established experimentally that the g-factor of the chiral tetrahydropyronium molecule Ce6 increased threefold when it was bonded to CdSe/ZnS NPs (Figure 5b). It was explained that this effect resulted from the hybridization of NP hole levels with the molecular orbitals of Ce6. Also, both penicillamine molecules adsorbed on the surface of CdS NPs and GSH molecules adsorbed on the surface of CdTe NPs (Figure 5c) exhibited flipped CD signals, compared with those of free molecules. Moreover, Govorov et al. demonstrated by DFT simulations that even an achiral planar molecule could become optically active as a result of electrostatic interaction with an achiral quantum dot. As displayed in Figure 5d, the induced CD signal decreases rapidly with increased molecule–NP distance. These changes in the optical activity of molecules in the presence of NPs could be used for sensing of chiral molecules. On the other hand, a change in the optical activity of a molecule might provoke modifications in its spatial configuration and functional properties, thereby, causing changes in stereospecific interactions of a molecule with chemical and biological objects, which could be beneficial for other applications of chiral hybrid nanostructures, such as targeted drug delivery.

**Nanoparticles assemblies**

Self-assembly is a phenomenon in which individual components arrange themselves into ordered structures of complex geometries and superlattices. Building blocks that are capable of self-organization include a wide diversity of objects such as liquid crystals, peptides, micelles, lipid vesicles, DNA, RNA, and NPs. Therefore, it is not surprising that the self-organization process contribute tremendously to the development of physics, chemistry, and biology. Two driving forces exist in all systems — van der Waals and electrostatic forces.

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interactions—but in some cases, coordination, covalent bonding, and hydrogen bonding, as well as hydrophobic interactions, could also take place.

Studies on the self-assembly of NPs constitute a significant area of nanoscience that channels the development of new functional materials with unique properties. Also, they highlight the unification of properties of inorganic and biological matter at nanoscale level, that has direct representation in chirality of inorganic NPs.

Figure 5 | (a) Top: Scheme of the experiment, bare Au islands (lateral dimensions: 75 nm x 64 nm, average height ~20 nm) are covered with a 19 nm thick poly(methyl methacrylate) (PMMA) film, which includes embedded riboflavin molecules. Middle and Bottom: absorption and CD spectra, respectively, of bare Au islands, Au + PMMA, Au, and riboflavin embedded in PMMA and riboflavin/PMMA deposited on bare glass. Also shown is the absorption spectrum of Au islands after the PMMA and riboflavin were removed by acetone dipping. Adapted with permission from Ref. 117. Copyright 2013 American Chemical Society. (b) Absorption (dash-dot) and CD (solid lines) spectra of free Ce6 (black lines), CdSe/ZnS NPs (red line), and CdSe/ZnS-Ce6 complexes (blue lines) in dimethyl sulphoxide (DMSO). Reproduced with permission from Ref. 22. Copyright 2016 SPIE. (c) CD spectra of L- and D-glutathione (GSH) (left) and the L- and D-GSH-NPs (right). Adapted with permission from Ref. 119. Copyright 2011 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim. (d) Model of a complex composed of CdTe NP (NP diameter = 4 nm) and molecule separated with distance R (left) and calculated CD signals for this model (right). Adapted with permission from Ref. 69. Copyright 2010 American Chemical Society.
Along with the chiroptical activity from individual NPs, their assemblies at different scale (nano, meso, and micro) with chiral configurations displayed unusually high CD amplitudes in IR and near-IR parts of the spectrum (Figure 4). Following the initial finding with Au NPs, multiple studies appeared, describing strong polarization rotation for nanoscale assemblies of Au nanorods. Passaseo et al. reviewed various micro and nanostructures of helical shape regarding their optical properties as a function of the material type (metals and dielectrics) and spatial arrangement.

Chen et al. reported chiral assemblies of Au NPs, which were self-organized through the polymerase chain reaction (PCR). The assembly process was determined by the density of the primer on the surface of Au NPs and the number of PCR cycles, generating a mixture of dimers, trimers, tetramers, and others, with gradually increasing complexity. CD bands of the resulted NP assemblies corresponded to those of plasmon oscillations of the multi-NP systems of Au colloids. The authors concluded that the intense optical activity of the superstructures originated from the chiral 3D arrangement of NPs in space.

Another attractive approach for forming chiral NP assemblies is the use of single-stranded DNA; since each strand has a unique sequence, it is possible to place specifically a different type of NP at each tip. Mastroianni et al. confirmed this concept through the use of four different sizes of Au NPs (5, 10, 15, and 20 nm), which were arranged into discrete pyramidal nanostructures using double-stranded DNA (dsDNA) as a scaffold to control the placement of the nanocrystals. Yan et al. engineered DNA-driven, self-assembled chiral pyramids from four different metal and/or semiconductor NPs with yields of ~80%. The resultant R- and S-enantiomers of chiral pyramids displayed strong chiroptical activity in the visible spectral range (g-factors ~ 1.9 x 10^-4). The authors also emphasized that all NPs contributed to the chiroptical activity of the pyramids. Therefore, the positions of CD signals could be varied in a wide range of UV and visible wavelengths (350–550 nm) by choosing a particular type of NP as building blocks. Later, Shen et al. showed that 3D chiral tetrahedrons with intense CD could be formed using DNA origami, even when identical Au NPs were employed.

Recently, Mokashi-Punekar et al. discussed comprehensively advances in the studies of NP superstructures of helical shape in which discrete NPs were arranged in 3D assemblies about the screw axis. For instance, Cheng et al. introduced an efficient way to design 3D nanostructures of helical shape with strong and controllable chiroptical properties by using inorganic silica nanohelices with tunable handedness and sizes as chiral templates and individual Au NPs as plasmonic active units. As shown in Figure 6a, the resultant assemblies were characterized by pronounced arrangement of Au NPs, following the helical silica template and with intense chiroptical activity (g-factor of ~ 1 x 10^-4). Moreover, it was revealed that the size with diameter varying from 4 to 10 nm, and the organization of the Au NPs on the surface of the helical silica template influenced the optical activity of the whole complex structure. Further, Yan et al. recently reported the assembly of semiconductor Cys-stabilized CdTe NPs into helices with an enantiomeric excess of ~ 100%. Figure 6b shows the TEM images and CD spectra of the resulted assemblies. Analysis of optical properties of the helices revealed that they had strong chiroptical activity across a broad range of wavelengths from 300 to 1300 nm with g-factors approaching 0.06. The position of the CD peaks could be tuned between 800 and 1200 nm by varying the pitch from 390 to 940 nm, changing the water–methanol ratios and altering the concentration of Cd. The authors obtained high chiroptical activity, structural uniformity, enantiomer selectivity, and assembly yield of ~ 80% because of careful optimization of reaction conditions and chemistry of the NP surfaces. Hao et al. developed chiral superstructures of helical shape, which were based on chiral FeS quantum dots assembled with chiral hydrogels and have strong CD and circularly polarized luminescence signals in the visible region, and observed that CD signals of the assemblies could be tuned with irradiation by CPL, which was shown to change the helical pitch length. They concluded that the structural and optical properties of the assembled helices could be optimized by varying chemical means, such as solvent, pH, and ligand density, as well as using CPL.

The formation of chiral pyramids and helices from NPs are not the only methods for producing chiral NP assemblies. Han et al. investigated optical properties of assemblies of Au nanorods with different patterns: they obtained end-to-end and side-by-side aggregations by varying the concentration of the cetyltrimethylammonium bromide (CTAB) surfactants in nanorod solutions, while the concentration of the added Cys remained constant. They found that side-by-side assemblies demonstrated a more intensive plasmonic CD signal, compared with the end-to-end ones. The authors concluded that observed conformation of modulated plasmonic CD enhancement was associated with the change in the electromagnetic interactions between nanorods in the assemblies and could be amplified further through the careful choice of the aspect ratio of the nanorods. Shimomori and Mochizuki designed side-by-side Au nanorod assemblies driven by an interaction between CTAB-stabilized Au nanorods with human serum albumin (HSA). These nanostructures possessed intense chiroptical activity, leading to a suggestion that the solvent composition could manipulate the handedness of the assemblies. In other recent work, Cheng et al. used the reversible addition–fragmentation chain-transfer (RAFT) polymerization to synthesize poly(methacrylate hydroxyethyl-3-indole propionate) (PIPEMA) and...
poly(2-hydroxyethyl methacrylate) (PHEMA), which were used as surface ligands for Au nanorods to induce side-by-side Au nanorod assemblies with strong CD (Figure 6c). They also found that the molecular weight of the polymers could manipulate the CD signal of the assemblies.

Lu et al. investigated a single v-shaped Au nanorod dimer using dark-field scattering techniques in CD.

Figure 6 | (a) TEM images (top) and CD spectra (bottom) of helical superstructures made using Au NPs with various sizes. Reproduced with permission from Ref. 134. Copyright 2017 American Chemical Society. (b) SEM images (top), CD and g-factor spectra (bottom) of helices assembled from CdTe NPs stabilized with L, D, racemic-Cys. For the SEM images obtained in the case of racemic-Cys, red and blue dots are used to mark the left-handed and right-handed helices, respectively. Adapted with permission from Ref. 135. Copyright 2019 American Chemical Society. (c) Top: TEM image of the Au nanorods assemblies induced by PIPEMA192 (pH 13.4). Bottom: CD spectra of the Au nanorods assemblies induced by PIPEMA with different molecular weights. Adapted with permission from Ref. 139. Copyright 2019 American Chemical Society. (d) CDS-active Au nanorod dimer–BSA complexes with chiral (left) and achiral (right) configurations. Top: High-angle annular dark-field scanning transmission electron microscopy (HAADF-STEM) images and the corresponding geometric models extracted from the tomographic reconstructions. Bottom: Experimental single-particle CDS spectra of the chiral dimer (left) and the achiral dimer (right). Adapted with permission from Ref. 141. Copyright 2019 The Authors, some rights reserved, exclusive licensee American Association for the Advancement of Science. No claim to original U.S. Government Works.
measurements. The authors observed that the CDS from the obliquely excited nanorod dimer resulted in a specific bisignate peak–dip spectral shape at hybridized energies of the dimer. This phenomenon was associated with extrinsic chirality, dependent on the geometry configurations of the chiral arrangement. They also found that the differential scattering intensity could be tuned by varying the in-plane orientation angle of the dimeric structure, the incident angle, and the structure angle between the long axes of the two nanorods in the dimer. The conclusion made from this study was that there were strong interactions between the CPL and the dimer since the extrinsically chiral system had a g-factor of ∼0.4. In a more recent work, the origin of the optical activity in Ag nanorod assemblies templated by bovine serum albumin (BSA) was revealed by Zhang et al. They performed a single-particle approach for the comprehensive investigation of single nanorods, parallel aggregates, twisted aggregates, and complex asymmetric assemblies (Figure 6d). These investigators combined single-particle CDS spectroscopy, based on the differences in scattering intensity of left and right CPL by an object, with correlated tomographic reconstruction and electromagnetic simulations. Their results showed that only aggregated nanorod–BSA complexes were CD active. Cryo-electron microscopy and Raman spectroscopy demonstrated that BSA not only induced the formation of chiral assemblies but also created hot spots for strong coupling between chiral proteins and surface plasmons, which led to the presumption that both effects could work synergistically through the creation of superchiral near fields.

As discussed earlier, typical chiral assemblies of NPs have helical, tetrahedral, or twisted geometries; thus, it is expected that simple pairs of spherical NPs should not exhibit any optical activity. However, it has been reported that unexpected chirality and CD bands appeared in the visible spectral region for Ag–Au NP dimers assembled through antibody–antigen bridges, and this phenomenon was attributable to the nonideal spherical shape of the NPs, which could be described as prolate ellipsoids with an aspect ratio of ∼1.1–1.2. These dimers acquired scissor-like conformation with long axes of the NPs forming a dihedral angle of about 9°, which resulted in chirality of the NP pair. The consistency of its sign was due to the specific conformation of the bridging biomacromolecules, which broke the enantiomeric equivalence of the NP pairs. The authors demonstrated that the strong polarization rotation of the concentrations of these aggregations allowed their use in biological analysis.

**Chirality as Biomimetic Property of Nanostructures**

Various researchers have drawn inspirations from nature to design engineered systems since the first tools were made in the stone age by early humans. Developments in nanoscale engineering, even more so, facilitated the advances in biomimetics. At first sight, NPs appeared to have nothing in common with biomolecules, but as it was discussed earlier, they reveal distinct similarities to biomolecules with nanoscale dimensions (Figure 1).

Today, it could be stated that the fundamental concepts regarding NPs functionalities as biomolecule mimics, proposed almost 10 years ago, have more than been achieved. For instance, similar to HSA, CdTe NPs could prevent aggregation of amyloid-β peptides into fibrils efficiently, to restrain this key pathological feature of many neurodegenerative disorders. Also, ZnO NPs, in the form of pyramids, plates, and spheres, could inhibit the activity of the carbohydrates glycosidic bond hydrolysing enzyme, β-galactosidase, in a biomimetic manner.

Considering that the majority of biomolecules are chiral, it is logical to assume that the NPs that imitate them might also exhibit chirality. Thus, chiral Cys-coated CdTe NPs were utilized as biomimetic endonucleases for DNA scission. Under illumination with either left- or right-handed CPL, provided by a 405 nm laser, the DNA was selectively cut by the NPs between the T and A bases of the restriction site GAT′ATC (‘ indicates the cut site). This means that the chirality of the NPs limited them to interact only at that specific site, and therefore, highlighted their biomimetic identity. It should be noted that this artificial DNA endonuclease reaction was performed successfully both with in vitro living cells and with in vivo animal models.

Another essential phenomenon that allows constructed structures to mimic biological motifs is supramolecular self-assembly. Lin et al. recently demonstrated that the assembly of nucleobase–peptide conjugates into nanohelices is a promising strategy to design sophisticated and structurally diverse nucleobase–derived nanobiomaterials. The authors reported the preparation of helical fibrils developed through chiral self-assembly of nucleobase–peptide conjugates, where achiral nucleobases, similar to polymerized nucleic acids, are arranged helically on the surface of fibrils. In this approach, the supramolecular chirality of the nucleobase–peptide conjugates could be adaptively imparted to metallic NPs, covering them to generate structures with plasmonic chirality that exhibit improved colloidal stability significantly.

In other recent work, Lv et al. developed biomimetic chiral photonic crystals displaying a g-factor of ∼1.6 through the Langmuir–Schaefer assembly of colloidal inorganic NiMoO4·xH2O nanowires. The optical properties of such nanostructures could be manipulated by interlayer arrangement. Interestingly, these crystals could mimic the intricate helical structure and circularly polarized color reflection in beetles.
Origin of Homochirality on Earth

The biomimetic properties of NPs and their chirality might, perhaps, also lead to unexpected conceptual bridge to some of the old questions that humans pose since the discovery of chirality by Pasteur, namely, what is the origin of homochirality on Earth? At a first glance, it might seem that there is a gulf between the chiral NPs and an answer to this question and others. Nevertheless, the photonics of chiral inorganic nanostructures could bring new insights in this direction. Consider the following example: flat ribbons of lengths 1–4 μm were made of several layers of individual cadmium sulfide/cadmium telluride (CdS/CdTe) NPs, fabricated from slow oxidation of Te layers of individual cadmium sulfales of the dust grains in interstellar clouds. Also, it was racemic compounds asymmetrically in the organic manva explosions could be one CPL source that intron radiation from the neutron star remnants of supernova explosions could be one CPL source that intron radiation from the neutron star remnants of supernova explosions could be employed in the detection of amyloidogenesis of human islet amyloid polypeptide. This is the peptide whose aggregation is associated with type 2 diabetes. Kumar et al. observed that Au nanorods adsorbed onto helical protein fibrils via noncovalent interactions, but showed no apparent interactions with monomeric proteins. The amyloid structure resulted in a helical nanorod arrangement, which, in turn, led to an intense optical activity at the surface plasmon resonance wavelengths, leading to the suggestion that this phenomenon could be employed in the detection of amyloids in Parkinson’s and prion diseases.

Chiral plasmonic NPs and ensembles based on them are being actively studied for use as various sensors and biosensors. Zhao et al., using chiroplasmonic assemblies of gold NPs, designed the first chirality-based probe for the sensitive detection of serum alpha-fetoprotein, an oncofetal glycoprotein, which served as the most effective marker of hepatocellular cancer. Olesiak-Banska et al. demonstrated experimentally that the two-photon CD Au25([Captopril]18) nanoclusters were two orders of magnitude higher than their one-photon CD counterparts, which made it possible to use these materials as chirality-sensitive contrast probes in nonlinear microscopy.

Faridi et al. demonstrated that mesoscopic chiral silica nanoribbons could be used against the amyloidogenesis of human islet amyloid polypeptide. This is the peptide whose aggregation is associated with type 2 diabetes. Kumar et al. observed that Au nanorods adsorbed onto helical protein fibrils via noncovalent interactions, but showed no apparent interactions with monomeric proteins. The amyloid structure resulted in a helical nanorod arrangement, which, in turn, led to an intense optical activity at the surface plasmon resonance wavelengths, leading to the suggestion that this phenomenon could be employed in the detection of amyloids in Parkinson’s and prion diseases.

Since magnetic NPs could be controlled by an external magnetic field, these NPs find their application in the stereospecific recognition of chiral compounds, and also, for their enantioseparation. Thus, chiral magnetic Fe2O4 NPs, which exhibit high enantioselectivity via a combination with mussel-inspired polydopamine (PDA) chemistry, involving surface-initiated atom transfer radical polymerization, were developed for effective enantioseparation of L- and D-tryptophan enantiomers.

Chiral nanostructures could play the role of chiral catalysts in asymmetric catalysis, which is one of the most promising applications of chiral nanomaterials to date. Yasukawa et al. presented a comprehensive overview of the progress in asymmetric C–C bond formations, catalyzed by chiral ligand-modified metal NPs, and emphasized on the new approaches for the development of more efficient catalyst systems. Besides, Savitha et al.

Practicality of Nanoscale Chirality

Besides some of the long-standing fundamental questions, chirality-related research in nanoscience is rapidly expanding, due to the numerous potential applications and technological solutions offered by chiral NPs and their assemblies in sensing, enantioselective recognition, chiral catalysis, chiral separation, advanced optical devices, and information technologies. Also, they could be applied in biomedicine as drug delivery vehicles, imaging, biosensing, and as therapeutic agents. Ma et al. and Gogoi et al. recently presented comprehensive reviews on advanced chirality-based biosensors and state-of-the-art approaches of enantiomeric recognition and separation, respectively, demonstrating the great progress made in this field. For instance, there are sensing nanoplasmons that allow assaying chiral recognition between enantiomers with the naked eye.

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discussed the potential of various bimetallic chiral nanoparticles (e.g., Rh/Cu, Fe/Cu, Fe/Pd, Pt/Fe, Pd/Au, Rh/Au) for use as catalysts in asymmetric synthesis. Recently, Slocik et al.\textsuperscript{168} investigated catalytic activities of Au NPs templated with left-handed (\textit{\textalpha}-flga3) peptide (dykdddkpyssgampmpf) or right-handed (\textit{\textbeta}-FlgA3) peptide (DYKDDDDKPYSSGAPPMPF) by monitoring the Au surface-mediated reduction of 4-nitrophenol to 4-aminophenol via measurements of the decrease in absorbance of the product at 400 nm in the presence of chiral peptide templated NPs. They found that the \textit{\textbeta}-flga3 and \textit{\textbeta}-FlgA3 templated Au NPs yielded rate constants of 0.033 and 0.017 s\textsuperscript{-1}, respectively, and associated the faster rate of \textit{\textbeta}-flga3 with a higher-ordered arrangement of surface Au atoms and/or higher substrate accessibility to the Au surface. Nonetheless, citrate-capped Au NP colloids, without the peptide coating, exhibited a much slower rate (0.009 s\textsuperscript{-1}), demonstrating the importance of a combination of peptide with chiral Au NPs to achieve maximum catalytic activity. Accordingly, the authors emphasized the value of carrying out further studies, using \textit{\textbeta}-peptides to achieve enhanced catalytic rates of the NPs.

Studies of chiral nanoparticles for asymmetric catalysis go far beyond just metal NPs. For instance, Jiang et al.\textsuperscript{169} presented a review of self-assembled chiral nanostructures as chiral catalysts, considering the catalytic properties of nanocages, nanotubes, nanorods, micelles, and vesicles. Also, Hao et al.\textsuperscript{170} observed that penicillamine-stabilized Cu\textsubscript{2+} NPs (g-factor \approx 0.01) could demonstrate photocatalytic activity on BSA cleavage. Figure 7a is a display of sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) of the irradiated mixture of BSA and L-penicillamine-stabilized NPs. The selective cleavage of BSA was revealed by the appearance of new product bands, one with a lower molecular weight of 61 kDa. Analyzing the decrease in the intensity of electrophoretic bands, the authors observed that L-penicillamine-stabilized Cu\textsubscript{2+},S NPs demonstrated the highest catalytic performance under left-handed CPL (79%), while LP light and right-handed CPL allowed catalytic activity of only 53% and 20%, respectively. The authors explained this phenomenon to be due to the fact that the left-handed CPL activated a larger number of L-penicillamine-stabilized NPs than other light conditions, which increased the number of hot electrons by adsorbing the related rotation of polarized light. No cleavage was observed without light, NPs, or by using other ligands (Cys, cystine, GSH, thioglycollic acid, cysteamine, 3-mercaptopropionic acid) but penicillamine. The authors revealed that hydroxyl radicals, which according to electron paramagnetic resonance (EPR) spectroscopy data, increased in quantity during left-handed CPL irradiation (Figure 7a), were those reactive species that induced the cleavage of proteins.

Li et al.\textsuperscript{171} showed that supraparticles (SPs) replicating the structure of subcellular nanoscale assemblies constructed from chiral ZnS NPs serve as biomimetic enantioselective photocatalysts that convert L- or D-tyrosine (Tyr) into dityrosine (diTyr). Figure 7b (left) demonstrates that ZnS NPs carrying L-penicillamine preferentially catalyzed L-Tyr, while SPs made from D-penicillamine preferentially catalyzed D-Tyr. Figure 7b (right) shows that L-ZnS-Au SPs preferentially catalyzed the photo-oxidation of L-Tyr over D-Tyr. These chiral SPs displayed enantioselectivity of 20–30%, which is about 5–10 times higher than previously studied biomimetic photocatalysts for oxidative phenol coupling.\textsuperscript{172-175} Furthermore, they were able to carry out the catalytic conversion in water rather than in organic solvents, which is attractive from the perspective of environmental friendliness and product cost.

Zhang et al.\textsuperscript{176} reported enantioselective peroxidase-like activity of conjugates based on D- and L-Cys MoS\textsubscript{2} NP and Cu\textsuperscript{2+} ions toward D- and L-tyrosinol enantiomers. The oxidation product of tyrosinol was detected by analyzing the change in absorbance at 210 nm. As seen in Figure 7c, both the D- and L-Cys-MoS\textsubscript{2} NPs/Cu\textsuperscript{2+} led to chiral selective oxidation of D- and L-tyrosinol enantiomers, while unmodified MoS\textsubscript{2} NPs plus Cu\textsuperscript{2+} or Cu\textsuperscript{2+} alone did not induce oxidation of tyrosinol. Thus, the results showed that D-Cys-MoS\textsubscript{2} NPs/Cu\textsuperscript{2+} exhibited much higher catalytic activity than L-Cys-MoS\textsubscript{2} NPs/Cu\textsuperscript{2+} in the catalysis of the oxidation of D-tyrosinol, and vice versa. Therefore, the analysis of the recent advances of chiral nanomaterials demonstrates their feasibility to act as enantioselective catalysts.

It was also discovered that chiral NPs enantioselectively interact with living cells. Zhang et al.\textsuperscript{177} showed that Au NPs, stabilized with d-glutathione (d-GSH), were more toxic to human gastric cancer (MGC-803) and human gastric epithelial (GES-1) cells lines than the NPs stabilized with the \textit{\textalpha}-form (\textit{\textalpha}-GSH). The authors found that NPs with both types of chirality caused an increase in the regulation of genes involved in cell rescue and stress response. However, only NPs carrying d-GSH induced an increase in the regulation of transcripts involved in response to metabolism and biosynthesis. CdTe NPs, stabilized with \textit{\textalpha}- or d-GSH, also displayed differences in cytotoxicity with respect to human liver cancer (HepG2) cells, whereas d-GSH-NPs was less cytotoxic than \textit{\textalpha}-GSH-NPs.\textsuperscript{178} The authors found that the ability of NPs to induce cell death correlated with their capability to induce autophagy, which, in turn, depended on chirality. However, the intracellular accumulation of both \textit{\textalpha}- and d-GSH-NPs was essentially the same. Wang et al.\textsuperscript{179} conducted a systematic study of the adsorption behaviors of BSA onto the chiral surfaces of Au NPs. The adsorption of BSA onto both \textit{\textalpha}- and d-surfaces of Au NPs showed discernible differences regarding the thermodynamics, adsorption orientation, exposed charges, and affinity. Accordingly, the authors

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Figure 7 | (a) Left: SDS-PAGE diagram showing the light dependence on the cleavage of BSA by L-penicillamine-stabilized NPs with exposure to different kinds of light for 12 h (1 - molecular marker; 2 - BSA; 3 - BSA + right-handed CPL; 4 - BSA + LP light; 5 - BSA + left-handed CPL). Right: Detection of hydroxyl radical by EPR spectroscopy. Adapted with permission from Ref. 170. Copyright 2019 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim. (b) Left: The dependence of photoluminescence intensity of diTyr at 414 nm on the time of photocatalytic reaction with ZnS SPs of different handedness of the catalyst and the substrate. Right: The dependence of photoluminescence intensity at 306 nm on photocatalytic reaction time with L-ZnS–Au SPs for different Tyr enantiomers. Adapted with permission from Ref. 171. Copyright 2019 Springer Nature. (c) The time-dependent absorbance changes of D-tyrosinol (left) and L-tyrosinol (right) in the presence of L-Cys–MoS2 NPs/Cu2+, D-Cys–MoS2 NPs/Cu2+, MoS2 NPs/Cu2+, and Cu2+ system with H2O2 at 210 nm. Adapted with permission from Ref. 176. Copyright 2018 American Chemical Society.
proposed the salt-bridge interaction as a significant driving force of the protein-nanochiral interface interaction. The spatial distribution features of the functional groups of chiral molecules on the nanosurface played a crucial role in the formation and location of the salt bridges, which determined the BSA adsorption orientation and binding strength to chiral surfaces. Sequentially, BSA corona coated on nanochiral surfaces affected their uptake by cells. Thus, the enantioselective biological activity of chiral NPs is a complex phenomenon, which could be associated with many factors, including different accumulations of NPs in cells, various cytotoxicity mechanisms (generation of reactive oxygen species [ROS], apoptosis, or autophagy), as well as specific interactions with proteins.

### Conclusion

In this review, the origin and implications of strong light-matter interactions in chiral inorganic nanostructures are elaborated. Much higher dynamic polarizability of the inorganic materials, compared with organic and biological nanostructures of similar size and geometry led to multiple increase in the order of chiroptical activity. This effect manifested commonly in exceptionally large intensity in the CD of media containing chiral inorganic nanostructures. Furthermore, collective behavior of chiral inorganic nanostructures resulted in chirality transfer to chiral assemblies at larger scales. Meanwhile, they retained all the attributes of chiroptical activity of chiral inorganic NPs and provided means of tuning the spectral window of chiral optics to the desirable wavelengths. These findings provided a plausible pathway to the origin of homochirality on Earth with the CPL emission of the early stars, and the chirality of the inorganic nanoscale materials comprising interstellar particles. Novel practical implementations of chiral inorganic materials included polarization optics and chiral catalysis. The latter was found to be enhanced substantially in the presence of NPs with high polarizability, while retaining environmental robustness. Assemblies of chiral nanostructures with high porosity could serve as versatile chiral catalysts due to a combination of the chiral environment in the nanochannels of the NPs and their strong light-matter interactions.

### Conflict of Interest

There is no conflict of interest to report.

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### References


