Environment-Adaptive Coassembly/Self-Sorting and Stimulus-Responsiveness Transfer Based on Cholesterol Building Blocks

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1. Introduction

Biological species such as phospholipid cell wall and DNA are formed by versatile noncovalent aggregation of multiple components, where small molecules or macromolecules are held together individually or cooperatively, forming biomaterials with diverse functions. Unlike genetically encoded biomolecule organization, abiotic self-assembly of a multiple-component system often shows complex routes, whereby the self-assembly pathway complexity is largely determined by ambient environment, intercomponent interaction, and structural similarity of components.[1–4] Normally, three scenarios can be expected when the self-assembly is triggered in a multicomponent system, i.e., self-sorting, synergistic assembly, and heterojunction.[5] Self-sorting describes selective recognition of mutual counterparts to give orthogonal or parallel aggregation,[6a] which could be further classified as narcissistic and social self-sorting.[6b] Thus, self-sorting is able to endow systems with abundant aggregates, which enables the fabrication of highly ordered materials with sophisticated structure and functionality.[7] Alternatively, when the interaction between different components is relatively strong, they may give rise to mixed supramolecular arrangement either randomly or specifically.[8] The third outcome of multicomponent assembly, often accompanied by heterojunction structural formation, could be assigned as a top–down method, because it needs the pre-assembly of one component as a seed, followed by the self-assembly with another component to give suprastructures.[9]

Designing synergistic self-aggregation or coassembly from multiple components is of vital importance in supramolecular chemistry and materials science.[10] Coassembly allows materials integration at a molecular scale, showing specific advantages over physical blend or hybrid at micro/nanoscale prepared by self-sorting.[11] For instance, liposome and polymersome, which are vesicles self-assembled from lipids and polymeric amphiphiles, are often integrated with targeting ligands, drugs, and bioimaging agents as payloads. Payload

Manipulating the property transfer in nanosystems is a challenging task since it requires switchable molecular packing such as separate aggregation (self-sorting) or synergistic aggregation (coassembly). Herein, a unique manipulation of self-sorting/coassembly aggregation and the observation of switchable stimulus-responsiveness transfer in a two component self-assembly system are reported. Two building blocks bearing the same cholesterol group give versatile topological structures in polar and nonpolar solvents. One building block (cholesterol conjugated cyanostilbene, CCS) consists of cholesterol conjugated with a cyanostilbene unit, and the other one (C_{10}CN) is comprised of cholesterol connected with a naphthalimide group having a flexible long alkyl chain. Their assemblies including gel, crystalline plates, and vesicles are obtained. In gel and crystalline plate phases, the self-sorting behavior dominates, while synergistic coassembly occurs in vesicle phase. Since CCS having the cyanostilbene group can respond to the light irradiation, it undergoes light-induced chiral amplification. C_{10}CN is thermally responsive, whereby its supramolecular chirality is inversed upon heating. In coassembled vesicles, it is interestingly observed that their responsiveness can be transferred by each other, i.e., the C_{10}CN segment is sensitive to the light irradiation, while CCS is thermoresponsive. This unprecedented behavior of the property transfer may shine a light to the precise fabrication of smart materials.
loading will be more effective if the coassembly pathway is adopted. In addition, the coassembly of building blocks appended with electron-rich and electron-poor fused aromatic rings could significantly change the luminescence property and improve electron mobility. The coassembly can occur in any dimensional structures, and sometimes alter pristine morphology and dimension by changing molecular packing parameters. For example, Yan and coworkers observed that the 1D morphology of phenylalanine dipeptide could be finely tuned through the coassembly with dianionic porphyrin, and the generated spheres exhibit excellent photocatalysis and photodynamic properties.

A favorable strategy to construct a coassembly system is to reinforce intercomponent interactions that typically are metal-ligand coordination, hydrogen bonding, halogen bonding, π–π stacking, and van der Waals interactions. Apart from enhancing interactions, another common design protocol is to increase structural similarity of different components. Structural similarity reduces the discrimination and exclusionary possibility during the aggregation process, resulting in the interdigitation arrangement. We recently fabricated coassembled vesicular particles utilizing two aromatic glutamate-based amphiphiles with considerable structural similarity to achieve controllable luminescent color conversion, and the π–π stacking interaction between two components was evidenced as the dominant driving force for the coassembly. In spite of these developments, rational design of coassembly systems still remains a challenge. Tiny variation of functional groups would have profound influence on preferred molecular arrangement in aggregates, where the competition with self-sorting is negligible.

In coassembly arrays, different components are capable of impacting each other, as they are confined in aggregates with a high affinity (distance between building units might be less than 10 Å). These influences can be brought by charge transfer (CT) between electron-poor and rich moieties, energy transfer (ET) between moieties with well-overlapped spectra, and chirality transfer. For instance, researchers utilized building blocks bearing naphthalene diimide and naphthalene moieties to flexibly control the coassembly/self-sorting behavior. Schenning and coworkers demonstrated the control over ET between naphthalene and benzothiadiazole fluorine domains of amphiphilic components in random mixing or self-sorting self-assemblies. It should be noted that the chirality transfer stands for the acquisition of supramolecular handedness for a component without chiral amplification capability from another component with supramolecular chirality. Regardless of these phenomena, transferring properties from one building block to another is still very difficult to realize. It is well known that a considerable number of organic self-assemblies belong to non-equilibrium processes, which endow the self-assembled systems with stimuli-responsiveness. Study of stimulus-responsiveness transfer in multicomponent noncovalently bonded system helps better understand the synergistic effect in living cells, and the responding to external stimuli and transference to adjacent unit are reminiscent of intracellular information conduction. While achieving the transfer of stimuli responsiveness within coassemblies is of great significance to the better understanding of biological information conduction and the fabrication of smart functional materials, it has not been well investigated to the best of our knowledge. Although responsive species have been combined to give multicomponent arrays, the responsiveness is still limited to the intrinsic species without the observation of transference to other component, showing independent behaviors in either self-sorting or coassembled states.

To this end, two new small organic building blocks (Figure 1) with specific structural similarity were rationally designed and synthesized (Figures S1–S6, Supporting Information), namely cholesterol conjugated cyanostilbene (CCS), and cholesterol connected naphthalamide having a flexible long alkyl chain.
(C10CN). Several factors were taken into account in this design. (1) The employment of C10CN with flexible long alkyl chain and π-conjugated naphthalimide group may favor geometrical diversity in response to the solvent environment and temperature. This may help us optimize ambient condition for the coassembly.[32] (2) CCS appended with cyanostilbene could respond to UV light irradiation.[33] (3) C10CN and CCS share the same cholesterol and spacer groups and have different polar head groups, providing possibilities for both coassembly and self-sorting. By systematic studies, it was found that C10CN self-assembles into gels, crystalline flowers, and vesicles in non-polar solvents, nonpolar solvent with a trace amount of water, and aqueous solution, respectively (Figure 1). C10CN and CCS self-sorted in gel and crystalline phases in nonpolar solvents but coassembled in the vesicle phase in water. Further studies revealed that the photosresponsiveness of CCS and the thermostresponsiveness of C10CN could be transferred to each other. Specifically, the light irradiation induces the chiral amplification of the CCS self-assembly, while C10CN is the light-insensitive species with chiral amplification in the C10CN/CCS coassembly. Upon heating, C10CN vesicles undergo the chirality inversion on account of the dehydration, while thermoinsensitive CCS presents thermostresponsion in the C10CN/CCS coassembly.

2. Results and Discussion

2.1. Individual Assemblies

Both of CCS and C10CN exhibit significant adaption toward solvent environment by giving diversified aggregated structures. Solvent exchange protocol enables the well-defined self-assembly of organic building blocks with minimal hydrophilicity, by which means CCS and C10CN with flexible alkyl chains and polar aromatic heads are capable of forming aggregates in aqueous media.[14] To facilitate the self-assembly, CCS and C10CN were predissolved in high water-miscible solvent tetrahydrofuran (THF), which were then injected into water under the sonication. Colloidal stabilities of the assemblies show considerable dependence on the solvent ratio or water volume fraction (fw). CCS dispersion was quite stable without any precipitation (fw from 60 to 90 vol%), yet C10CN dispersion started to precipitate upon the incubation time when fw was lower than 80 vol%, which might be due to the long alkyl chain of C10CN. Then, the morphologies of different dispersions were examined by electron microscopic techniques including scanning electron microscope (SEM) and transmission electron microscope (TEM) shown in Figure 2 and Figures S7 and S8 (Supporting Information). In high fw condition (90 vol%), CCS gave rise to spherical assemblies with diameter about 100 nm (Figure 2a). Magnified TEM images display clear periphery (skin/pool structure), suggesting their hollow nature (Figure 2b), i.e., the vesicle formation.[35] Stepwise decrease of fw influences the size rather than the basic morphology. By decreasing fw from 90 vol% to 60 vol%, the diameter of aggregates elevated from 100 to ~500 nm without varying the vesicular structure. In the SEM studies of CCS, drying process on silicon wafer may result in some broken vesicles as observed (Figure 2d; Figure S7f, Supporting Information). Holes on the surface of these nanoparticles well elucidate the presence of hollow interiors.[36] Similarly, C10CN dispersion with fw = 90 vol% contains vesicles with slight aspect ratio. As compared to CCS, C10CN appended with a long alkyl chain tends to form membranes with larger curvature, and thus may mildly improve 1D growth. When lowering the fw value from 90 to 60 vol%, gradual disappearance of vesicles and the appearance of microscale crystalline plates could be observed (Figure S8e–h, Supporting Information). A possible reason is that less amount of poor solvent water might provide a favorable environment for thermodynamic aggregation to form crystalline structures. Confocal laser scanning microscopy (CLSM) was used to confirm the morphologies in wet state (Figure 2i–l). After being excited by laser (405 nm), both of CCS and C10CN aggregates show greenish yellow emission. Highly dispersed dots were found in vesicle samples. The morphology of crystalline plates under CLSM was also consistent with SEM and TEM observations. In good agreement with electron microscopic studies, lower fw (70 vol%) generates dense and larger aggregates than that of high fw. Solvent ratio-dependent absorption and emission spectra (Figure S9a–d, Supporting Information) reveal that both of CCS and C10CN formed J-type π–π stacking arrays with aggregation-induced emission (AIE)[37] and aggregation caused quenching (ACQ) effects in polar solvent environment, respectively. Concentration-dependent absorption and emission studies show the critical aggregation concentration of 10−5 and 2 × 10−5 M for CCS and C10CN, respectively (Figures S10 and S11, Supporting Information).

Then, the self-assembly behavior was examined in nonpolar solvents such as hexane and decane. The dispersion of CCS in these solvents only resulted in crystalline precipitation. For CCS in nonpolar solvents, molecular aggregation favors 3D growth with large aggregation number, enabling the emergence of bulk crystalline aggregates. Nevertheless, though C10CN shares the cholesterol and spacer groups with CCS, the long alkyl chain significantly facilitates its 1D growth in nonpolar solvents. Both the solvent exchange and direct dispersion methods gave rise to high quality organogels in decane or hexane. Macroscopically, these gels are highly transparent, thermoreversible, thixotropic, and highly stable in sealed vials for at least 3 months. Notably, the critical gelation concentration is as low as 1 × 10−3 M (~0.08% w/v), indicating their high solvent content and supergelation nature.[38]

Good properties of C10CN organogels originate from the nanostructures. We first investigated the nanostructures of organogels by TEM and SEM (Figure 3a–d). Long, flexible, and infinitely aggregated nanofibers constitute the gel networks. Ascribed to intrinsic molecular chirality of the cholesterol unit, some nanofibers present supramolecular chirality, whereby left-handed (M)-twisted fibers could be found. By counting 50 individual nanofibers, the mean diameter of gel fibers was determined as 11 nm. This result means that there was almost no extension on other dimensions during the aggregation, which is reminiscent of supramolecular polymeric gels.[39] We also observed considerably thick bundled fibers in Figure 3c and Figure S12 (Supporting Information).

C10CN organogels showed strong green fluorescent emission under a UV lamp, of which morphology could be probed via CLSM. As shown in Figure 3f,g, fibrous networks are highly entangled, suggesting that the solvent evaporation barely has
an influence on gel morphologies. It should be noted that the bundle effect in hexane might be more active due to the presence of thicker fibers than that in decane. Upon increasing the concentration, C10CN molecule transforms from monomeric state into aggregated state, which is directed by hydrogen bonding between imide and amide groups. Gelation induces the emergence of a small shoulder absorption peak located at 450 nm (Figure 3h) and red-shifted emission from 486 to 507 nm (Figure 3i), indicative of π–π stacking or hydrogen bonding formation by naphthalimide unit. The gradual increase of the decane content in THF–decane mixture could also generate organogels, showing a blue shift in emission spectra (Figure S13, Supporting Information). We then examined the absorption/emission properties of C10CN in solvents with different polarities under the same concentration (Figure S14, Supporting Information), and found that the absorption/emission wavelengths are ultra-sensitive to solvent polarities.

Oscillatory rheology experiments were performed to investigate the viscoelastic properties of gels (Figure 3j,k). In dynamic strain sweep (frequency = 1 rad s⁻¹), gels showed long linear viscoelastic region from 0.01% to 10%. At the condition of γ = 0.1%, both of storage modulus (G’, representing elasticity) and loss modulus (G”, representing viscosity) exhibit an independence to the applied frequency (0.1–100 rad s⁻¹). At the meantime, G’ values are almost 1 order higher than that of G”, and thus the gel system behaves as solid rather than liquid. Mechanical strength of gels is concentration dependent. Complex plateau modulus, which is the weighted average of G’ and G”, has a good linear correlation with concentration (g L⁻¹) on a double logarithmic scale having a slope of 1.86 (Figure 3l). The relationship $G_N \propto C^{1.86}$ was then obtained. This relationship implies that this organogel system is close to the Cates living polymerization model ($G_N \propto C^{2.0}$), demonstrating the existence of supramolecular polymerization-like process during the gelation in nonpolar solvents.[40] Surprisingly, we found that a trace amount of water molecule to the phase behavior, we analyzed the single crystal structure of C10CN. High quality crystals of C10CN were obtained in

Figure 2. Self-assembly of CCS and C10CN in THF–water mixture. a–c) TEM and SEM images of CCS vesicles ($f_w = 90$ vol%, $c = 10^{-4}$ M). d) SEM image of vesicles formed by CCS at a low water volume fraction ($f_w = 60$ vol%, $c = 10^{-4}$ M). e–g) TEM and SEM images of C10CN vesicles ($f_w = 90$ vol%, $c = 10^{-4}$ M). h) SEM image of aggregates formed by C10CN at a low water volume fraction ($f_w = 60$ vol%, $c = 10^{-4}$ M). i–l) CLSM images of CCS aggregates ($f_w = 90$ vol%, $c = 10^{-4}$ M), CCS aggregates ($f_w = 70$ vol%, $c = 10^{-4}$ M), C10CN aggregates ($f_w = 90$ vol%, $c = 10^{-4}$ M), and C10CN aggregates ($f_w = 70$ vol%, $c = 10^{-4}$ M), respectively.
dichloromethane/ethyl alcohol mixed solvent system in the presence of a small amount of water. Single crystal structure and molecular stacking in a unit cell are displayed in **Figure 4a**. No effective $\pi-\pi$ stacking between naphthalimide groups was found in the stacking structure. Solvent molecules including water and ethanol participate in the crystallization via hydrogen bonds. From the highlighted inset in Figure 4a, it could be seen that, two C=O groups from amide and imide units are linked by one water molecule via hydrogen bonding interactions, of which distances are 1.83 and 2.17 Å, respectively. Meanwhile, another imide C=O group was hydrogen-bonded (2.2 Å) to the amide N–H group. Thus, water molecule behaves as the linker of C10CN stacks, which has a high possibility in improving the molecular stacking along 3D (crystalline flowers) rather than 1D (fibers). This speculation was also confirmed by Sureshan and coworkers who employed a cyclohexane-1,3a-diol motif to study the effect of water on the gelation crystallization balance.\[41\] We also utilized Fourier transform infrared spectroscopy to verify hydrogen bonding variations in gels and crystalline flower structures (Figure S16, Supporting Information).

For comparison, we also analyzed the single crystal structure of CCS obtained in dichloromethane (DCM)/hexane (Figure 4b). In the crystal state, no hydrogen bonding can be observed. Although it exhibits a relatively plain aromatic surface with a torsion angle of 177. 94°, the nearest distance between cyanostilbene groups is larger than 5 Å, reflecting the absence of $\pi-\pi$ stacking interaction. However, there is strong van der Waals interaction between cholesterol groups, which stack closely to each other with quite short distance (2–3 Å). Due to the intrinsic molecular chirality of cholesterol, the stacking of C10CN and CCS adopts a slipped manner. Along the c axis, the 1D molecular arrangement exhibits zigzag conformation (Figure 4c), suggesting that the crystal superstructure may be chiral on account of particular molecular stacking, which also supports the helical orientation observed in high resolution TEM (HRTEM) image (Figure S15e, Supporting Information). Additionally, the aggregates including crystals, flower structures, organogels, and vesicles were subjected to film-based powder X-ray diffraction (XRD) characterization to gain more structural information (Figure 4d). Except for the vesicle samples that gave amorphous structures, other samples showed diffraction peaks respectively, implying the existence of long-range ordered molecular arrangements. The powder XRD pattern of CCS-based crystalline precipitates formed in decane was in good agreement with simulated pattern from its single crystal data. For C10CN, peak locations of crystalline precipitates or gels varied significantly as compared to the simulated one, indicating that, under three different self-organization scenarios, C10CN adopts distinct molecular arrangements. For the crystalline precipitates induced by water, similar diffraction peaks located at 5.4°, 8.0°, 10.7°, and 13.2° corresponding to the d-space values of 1.64, 1.1, 0.83, and 0.67 nm possess ratios of...
(1/1);(1/1.49);(1/1.98);(1/2.45), revealing the lamellar molecular stacking of (1/2);(1/3);(1/4);(1/5). The peak at 18.5° with d-spacing of 0.48 nm further verifies the distance found from HRTEM observations. Hump peaks appeared in powder XRD patterns of organogels on account of 1D characteristics, and the first two order peaks corresponding to the d-spacing of 1.93 and 1.60 nm, are close to the ratio of √4:√3, suggesting that self-assembled units may take cubic arrangements. The estimated molecular arrangements in various aggregates were also supported by the small-angle XRD profiles displayed in insets of Figure 4d.

2.2. Coassembly and Self-Sorting Behavior of C10CN and CCS

On account of structural similarity of CCS and C10CN, it is reasonable to deduce that they may form coassembly arrays under certain conditions. In vesicular systems, CCS and C10CN were mixed with different molar ratios from 10:0 to 0:10 and a fixed total concentration (10⁻⁶ m), and the obtained assemblies were characterized by fluorescent emission, circular dichroism (CD), and absorption techniques (Figure S17a–c, Supporting Information). Surprisingly, it was found that the fluorescent emission intensity for the samples with 10–40 mol% was greatly enhanced (Figure S17, Supporting Information) than those of other ratios. The fluorescent intensity of both CCS and C10CN shows increasing tendency upon concentration changes from 10⁻⁶ to 10⁻⁴ m. Thus, the fluorescent enhancement of the mixing systems reveals a possibility of coassembly. In coassembly arrays, C10CN and CCS molecules form an interdigital arrangement where C10CN molecules are isolated, whereby the ACQ effect would be greatly suppressed to give strong emission. In CD studies (Figure 5a), the CCS vesicle system shows a silent Cotton effect at its UV–vis absorption region, but C10CN presents a relatively weak positive Cotton effect around its main absorption peak of 455 nm. Unlike C10CN, the chirality of cholesterol unit in CCS does not transfer to cyanostilbene group, which could be because of its relatively longer spacer (three carbon atoms) than C10CN (two carbon atoms). However, under the appropriate ratios of C10CN (30–50 mol%), strong negative Cotton effects appeared at the absorption region of 360–390 nm, which fall in the absorption region of CCS (Figure S17c, Supporting Information). Furthermore, positive Cotton effect at 450 nm assigned to C10CN was enhanced accordingly. Thus, it could be proposed that there is considerable synergistic effect between the self-assemblies.

The chirality during the self-assembly possesses three levels, namely molecular chirality, chiral amplification (chiral transfer), and macroscopic chirality (or micro/nanoscale chirality that could be recognized by microscope). Clearly, the formation of spherical vesicles rather than helical/twisted objects demonstrates that the supramolecular chirality only reaches chiral amplification level. The realization of chiral amplification in multicomponent self-assembly systems follows two principles, either sergeants–soldiers rule or majority rule, both of which require intimate coassembly between different components. Titration studies by fixing the concentration of one component and increasing the molar ratio of another gradually (Figures 5b; Figures S17d and S18, Supporting Information) were carried...
out to verify the chirality amplification pathways. The maximum emission wavelength blue-shifted from 555 to 530 nm upon the addition of CCS to C10CN vesicle solution. Absorption peaks broadened and shifted upon the addition of the second component on account of the spectrum overlap. After stepwise addition of C10CN into CCS system, adding more than 80 mol% of C10CN could be able to induce Cotton effect enhancement, and 40 mol% of CCS in C10CN system was capable of arousing strong negative Cotton effect. Sergeants–soldiers rule often occurs when adding a relatively small amount (5–20 mol%) of a chiral additive into an achiral analog. The chiral amplification of the coassembly system normally follows the majority-like principle (Figure S18d, Supporting Information). Different from the classic majority rule, the presence of strong cooperative effect within the obtained coassemblies induces effective chiral transfer from cholesterol to cyanostilbene moieties.

Next, we examined the self-assembly behavior of C10CN/CCS mixture in gel and crystalline phases. In the gel state, increasing molar ratio of CCS gradually quenches fluorescent emission of C10CN organogel (Figure S17e, Supporting Information) without varying its maximum absorption, implying the possible occurrence of intermolecular or interaggregate CT. Though the UV absorbance of CCS was enhanced (Figure S17f, Supporting Information), no variation of the CD spectra could be found even the doping fraction of CCS reached 50 mol% (Figure 5c). Therefore, we speculated that the self-sorting dominates in the gel phase.

Synergistic coassembly and self-sorting in vesicle and gel phases were further investigated via morphology studies. Of all mixed samples with differed molar ratios, only spherical vesicles were observed by TEM (Figure 5d–f) and their size distributions are around 100 nm, indicating that the molecular stacking arrays of CCS and C10CN form flexible membranous moieties. In line with CD studies, CCS and C10CN undergo self-sorting during the aggregation in nonpolar solvents, giving individual crystalline plates and fibrous networks (Figure S17g, Supporting Information). In addition to vesicle and gel phases, the self-sorting also occurred in the phase of crystalline precipitates (flower structure) induced by moisture according to the CLSM observation (Figure S19, Supporting Information). Based on the macroscopic chirality (M-type in Figure 3d) and UV/CD spectra of gels, the superhandedness in vesicles would be speculated. At the main UV–vis absorption at 425 nm in the gel phase of C10CN (Figure S17f, Supporting Information), the Cotton effect is negative (Figure 5c). Thus, the positive Cotton effect of C10CN vesicles (Figure 5a) indicates the P-handedness. The chiral amplification in co-assembled vesicle membranes is schematically elucidated in Figure 5g.

Figure 5. Coassembly and self-sorting behavior of CCS and C10CN. a) CD spectra of CCS–C10CN coassembled system with different molar ratios. b) CD spectra of CCS upon the titration of C10CN (concentration of CCS: 10^{-4} M). c) Normalized CD spectra with the addition of CCS in decane gel of CD spectra of C10CN. d–f) TEM images of coassembly systems with the molar ratios of 2:8, 5:5, and 8:2 (CCS:C10CN, total concentration: 10^{-4} M). g) Schematic representation of coassembly induced chiral amplification, where CCS and C10CN were cartooned as yellow and green species, respectively. Samples for vesicles were all prepared in THF–water mixture (f_w = 90%). Note that all emission spectra were excited at a wavelength of 375 nm.
2.3. Transfer of Light-Responsiveness and Thermoresponsiveness in Coassembled Vesicles

From the experiments in the last section, it was found that C10CN and CCS could form intimate coassembly in polar solvent environment. Therefore, it was assumed that the properties of one component might be transferred to another component or to the coassembled vesicles. According to our previous studies,[45,46] cyanostilbene is photoresponsive (254 nm), whereby its conformation would transform from E-(trans) to Z-(cis) isomer, leading to the variation of photophysical and self-assembly behavior. Hereby, we investigated the UV light responsiveness of the build block C10CN in the coassembly using absorption and CD techniques. Coassembled vesicle solutions were deposited in quartz cuvettes sealed by parafilm, which underwent periodic UV light irradiation before characterizations. For pure CCS vesicle system, upon increasing UV irradiation time (from 0 to 10 min), absorption spectra displayed slightly reduced absorbance, demonstrating the occurrence of photoisomerization (Figure 6a).[46] In contrast to the mute Cotton effect before the light irradiation, a weak negative Cotton effect at the absorption area of CCS (around 390 nm) appeared after the irradiation for 2 min, and this CD signal was not enhanced further even under longer irradiation period. Thus, photoisomerization may not effectively enhance the chiral amplification for pure CCS. Next, we introduced C10CN with different molar ratios (at a same total concentration of $10^{-4}$ mol%) to CCS in order to give coassembled vesicles and examined their UV–vis responsiveness (Figure 6b; Figure S20a–c, Supporting Information). For the samples with C10CN ratios of 10 and 20 mol%, there were no active CD signals before the UV light treatment, and active CD signals appeared after the UV light treatment. Significantly, the coassembly with 20 mol% C10CN (Figure 6b) showed strong Cotton effect (up to 100 mdeg from 0). In addition, we observed the CD signal enhancement at the C10CN absorption area (450 nm), meaning that light-responsiveness was transferred to the C10CN moiety. When the molar fraction of C10CN reached 30 mol%, the pristine system possessed relatively strong CD signals, which could be enhanced by UV light irradiation as well. After adding more than 50 mol% C10CN, the coassemblies were insensitive to the UV light irradiation even after long period (Figure S20c, Supporting Information). The anisotropy factor $g$ value at 400 nm was summarized as a function of irradiation time (Figure 6c), which clearly illustrates the UV light-triggered chiral amplification of CCS.

To the best of our knowledge, this is the first coassembly system of which superchirality could be greatly enhanced by photoirradiation, and the light-responsiveness could be effectively transferred to light-insensitive species. Several factors contribute to this particular phenomenon. The synergistic coassembly and the formation of mixed molecular arrangement array are keys to the photoresponsive chirality manipulation, where chiral dopant (C10CN) and photosensitive moiety (CCS) are required. Photoisomerization results in the conformational variation of cyanostilbene as well as the perturbation and destructive influence to the molecular order. It is reminiscent of chiral azobenzene-doped liquid crystal, of which chirality can be controlled by photo irradiation.[47,48] Similarly, the stilbene moiety shares most of the characteristics with that of the azobenzene unit. In contrast to relatively flat conformation of the E-isomer, the Z-isomer of cyanostilbene possesses statically twisted aromatic rings, which can significantly improve the chirality transfer. In addition, bent shaped E-isomer has a greatly reduced dihedral angle of 8.9° as compared to linear shaped Z-isomer of 177.91°,[46] suggesting that free rotation of stilbene...
is restricted after the photoisomerization. Consequently, the Z-isomer owns considerable molecular rigidity and steric hindrance, facilitating the superchirality transfer. Apart from the influence to the chirality amplification, photoisomerization led to morphological variations as well (Figure 6d,e; Figure S20d,e, Supporting Information). Pure CCS vesicles undergo the membrane fusion to form branched nanochannels upon the photoisomerization, the mechanism of which has been elucidated in our last report utilizing another cyanostilbene derivative.\(^{[33]}\) After being mixed by C\(_{10}\)CN (20 and 50 mol%), however, only partially fused/adhered vesicles were obtained. When C\(_{10}\)CN was dominant in the coassembly, vesicle fusion/adhesion totally disappeared, which was replaced by the shape deformation (Figure S20, Supporting Information). At high molar ratio of C\(_{10}\)CN (80 mol%), CCS molecule was isolated as monomeric state in the C\(_{10}\)CN stacking array, which fails in inducing the membrane fusion process. The membrane deformation might be accounted for the perturbation stemmed from conformational variation of cyanostilbene.

Since C\(_{10}\)CN self-assembly is thermally responsive, its thermal properties were investigated spectroscopically via absorption/CD techniques. Nanofiber formation and gelation in nonpolar solvents exhibited supramolecular polymerization behavior as stated above. Thus, a dilute decane solution of C\(_{10}\)CN was subjected to a cooling cycle (cooling rate: 0.5 K min\(^{-1}\)) when the absorption and CD signals were monitored at 2 °C intervals (Figure S21a, Supporting Information). With decreasing temperature, the absorption peak at 417 nm decreased gradually and red-shifted to 428 nm with a shoulder peak at 446 nm, indicating the temperature-responsive aggregation. For CD spectra, it showed silent Cotton effect at relatively high temperatures, while a negative Cotton signal at 427 nm emerged at a temperature of 291 K, indicative of the formation of nanofibers. Further decreasing the temperature enabled red shift of CD peaks from 450 to 485 nm, as a result of electrostatic interaction between stacked chromophores in a shoulder-to-shoulder arrangement. The degree of aggregation \((\alpha_{agg} = (CD_{agg} - CD_{mon})/(CD_{agg}))\) was calculated, which was then plotted against temperature (Figure S21b, Supporting Information). Such a sigmoidal curve, fitted well with Boltzmann equation \((R^2 = 0.99)\), is the characteristic of isodesmic chain growth model.\(^{[49]}\) The isodesmic self-assembly pathway of C\(_{10}\)CN in nonpolar solvents was also supported by absorption-based \(\alpha_{agg}\)-temperature profile (Figure S21c, Supporting Information). Some thermodynamic parameters could then be deduced from this model. For example, the enthalpy release during the chain elongation is \(\Delta H = -969.2\) kJ mol\(^{-1}\) with an equilibrium constant \((K_e = 1.25 \times 10^3)\) at 290 K.

After that, the thermoresponsive properties of CCS and C\(_{10}\)CN assemblies in polar solvents were evaluated. In a well-sealed cuvette, vesicular solution was gradually heated up from room temperature to 80 °C. Though absorption spectra of CCS vesicle system displayed redshift and the increase in absorbance contributed by the partial disorganization at high temperature, no active Cotton effect signals could be observed (Figure 7a), indicative of thermostinsensitivity of CCS in polar solvents. In direct contrast, when being heated, C\(_{10}\)CN vesicle solution was accompanied with helicity inversion (Figure 7b,c). In a relatively dilute state (5 \(\times\) 10\(^{-5}\) m), CD spectra of C\(_{10}\)CN showed a positive Cotton effect peak at 420 nm, corresponding to the absorption of naphthalimide chromophore, which is assigned as P-helicity according to our above analysis. Nevertheless, CD signals converted from positive to negative gradually to generate complete mirror-spectrum, suggesting the inversion of handedness in C\(_{10}\)CN assemblies (M-helicity). Only a minor red shift occurred in its absorption spectra upon heating. In order to gain insight into the chirality inversion, the concentration of C\(_{10}\)CN was elevated to 10\(^{-4}\) m. This concentration

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\caption{Thermoresponsiveness. a–d) CD and UV–vis spectra of CCS (10\(^{-3}\) m), C\(_{10}\)CN (5 \(\times\) 10\(^{-5}\) m), C\(_{10}\)CN (10\(^{-4}\) m), and CCS–C\(_{10}\)CN mixture (total concentration: 10\(^{-4}\) m, molar ratio: 5:5) with 10 °C interval. e) TEM images of C\(_{10}\)CN assemblies at a high temperature (90 °C), where red arrows indicate the emergence of rod-like aggregates. All samples were prepared in THF–water mixture (\(f_w = 90\%\)). f) Effect of heating-induced dehydration on supramolecular helicity inversion: a proposed mechanism.}
\end{figure}
also presented the helicity inversion with a tiny red shift from 440 to 446 nm (Figure 7c). The red shift of CD spectra is due to the red shift of corresponding absorption spectra. As displayed in the bottom image of Figure 8c, the absorbance at 450 nm decreased, while the peak at 490 nm increased accordingly (Figure S22, Supporting Information). The great peak shift (∼40 nm) strongly indicates molecular rearrangement to giving rise to more closely π-stacked arrays, which is induced by heating. Afterward, further characterizations revealed successful transfer of thermoresponsiveness from C10CN to CCS in mixed vesicle membranes (Figure 7d). In coassembled vesicles, the CD signal assigned to C10CN at 428 nm and the CD signal belonging to CCS at 360 nm disappeared stepwise without the observation of inversion. We believed that the hydration/dehydration of vesicular inner core is important to the helicity inversion and helicity silence upon heating.

Based on our moisture-sensitivity studies, C10CN could easily capture a water molecule via hydrogen bonding even in the presence of ultralow moisture content. Thus, in polar aqueous media, C10CN would surely bond with water that occupies at least two hydrogen-bonding sites to result in loosely packed arrangement. In anhydrous nonpolar solvent (gel phase), the mutual impact of strong interamide (imide) hydrogen bonding (Figure S16, Supporting Information) and chiral cholesterol unit generates a preferred orientation of M-helicity. On the other hand, after C10CN coordinates with water, interamide (imide) hydrogen bonding is replaced by H2O–amide/imide hydrogen bonding with a varied orientation, resulting in the occurrence of P-helicity. Under the high temperature condition, water molecule would escape from vesicle membranous inner core, facilitating the reformation of interamide (imide) hydrogen bonding to give the handedness identical to gel phase (M-helicity). Intermamide (imide) hydrogen bonding favors the formation of 1D aggregates, and indeed we observed the emergence of 1D rod-like vesicles/nanoparticles (red arrows in Figure 7e). The dehydration-induced helicity inversion was observed in Figure 7f. In some reported helical inversion systems, the participation of water has a vital importance. For instance, Fenniri et al. elucidated the role of water in chiral inversion by utilizing the chiral guanine and cytosine self-assembly system.[50] They found that water could help establish a hydrogen bonding network and change the conformation of building blocks in the self-assembly geometry. Lee and coworkers[51] revealed the temperature-induced dehydration effect in helical inversion of self-assembled nanotubes, and similar to our study, they believed that the enhanced π–π stacking after the dehydration was the main reason for the helicity inversion. In a coassembled system, temperature-variable absorption spectra only displayed a slight blue shift, indicative of the absence of enhanced π–π stacking. The interdigitation between CCS and C10CN hinders the formation of interamide hydrogen bonding, and thus, upon the dehydration, only mute CD signals were shown in CD spectra.

3. Conclusions

In summary, a two-component supramolecular system based on C10CN and CCS has been constructed, and their individual self-assemblies as well as coassemblies have been systematically studied. The self-assemblies exhibit diverse topological morphologies according to different solvent environments. Self-sorting and coassembly scenarios occur in nonpolar solvents, including the formations of gel and crystalline phases. While in the vesicle phase in aqueous media, C10CN and CCS give mixed self-assembly arrays, where they share stimulus responsiveness. As a result of the unique coassembly, the properties of photoinsensitive C10CN and thermoinsensitive CCS exchange with each other, exhibiting photoresponsiveness and thermosteresponsiveness, respectively. The present work sheds light on how to transfer intrinsic properties between components within coassembled systems.

4. Experimental Section

Experimental details including reagent information, instrument characterization of self-assemblies, and preparation of samples can be found in the Supporting Information.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords

cholesterol, coassembly, nanostructures, property transfer, stimulus responsiveness

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