Adaptive Supramolecular Nanomaterials Based on Strong Noncovalent Interactions

Boris Rybtchinski*

Department of Organic Chemistry, Weizmann Institute of Science, Rehovot 76100, Israel

ABSTRACT Noncovalent systems are adaptive and allow facile processing and recycling. Can they be at the same time robust? How can one rationally design such systems? Can they compete with high-performance covalent materials? The recent literature reveals that noncovalent systems can be robust yet adaptive, self-healing, and recyclable, featuring complex nanoscale structures and unique functions. We review such systems, focusing on the rational design of strong noncovalent interactions, kinetically controlled pathway-dependent processes, complexity, and function. The overview of the recent examples points at the emergent field of noncovalent nanomaterials that can represent a versatile, multifunctional, and environmentally friendly alternative to conventional covalent systems.

KEYWORDS: noncovalent bond · adaptivity · recycling · nanostructure · recyclable material · adaptive materials · nanomaterials · self-assembly · supramolecular polymer · supramolecular gel · hydrogel · hydrophobic interactions · pathway-dependent self-assembly · noncovalent synthesis · hydrogen bond · supramolecular multivalency · stimuli-responsive materials · supramolecular reaction · ionic self-assembly · complexity · noncovalent network · host–guest interactions · kinetic control · self-assembly mechanism · nonequilibrium self-assembly · nanoparticles · nanoparticle assembly

Almost all functional materials produced today are held together by strong, irreversible bonds. These bonds make such materials robust but, under normal conditions, they lack the ability to change, making them difficult to process and recycle. In contrast, noncovalent bonds are reversible and sensitive to environment, entailing adaptivity and stimuli-responsiveness that can be employed to achieve facile fabrication and recycling, self-healing, and multifunctionality. Furthermore, noncovalent synthesis based on molecular self-assembly enables facile construction of complex arrays, unfeasible by means of covalent chemistry.[1−7] However, most noncovalent interactions are weak and perceived as inadequate for creating materials that can represent a viable alternative to covalent systems. Indeed, a single noncovalent bond is weak, but what if many noncovalent bonds are working in concert? Interestingly, some very robust polymeric materials owe a significant fraction of their strength to multiple noncovalent interactions, such as multiple π-stacking and hydrogen bonds in Kevlar (poly(1,4-phenylene terephthalamide).[8] Another example relates to water-based systems: self-assembly in aqueous medium based on a combination of multiple noncovalent interactions is responsible for robustness, complexity, and adaptivity of biological systems.[9] Multiple (multivalent) noncovalent interactions were employed to construct a variety of functional materials,[10−12] which in a few cases exhibit *robustness similar to covalent arrays*.

Noncovalent synthetic methodology is only starting to emerge.[13] Rational design of noncovalent nanoscale arrays is challenging as it implies controlled manipulation of multiple noncovalent bonds, involving complex bonding modes, unlike the "one bond at a time" pattern of covalent synthesis. Strong noncovalent interactions introduce further challenges. The generally practiced noncovalent self-assembly methodology employs a paradigm of rapidly equilibrating systems where the assemblies are thermodynamic products. In the regime of strong noncovalent interactions more complex patterns involving (multiple) *stable kinetic products* may operate. A related challenge concerns adaptivity. If noncovalent interactions are too strong, the system may lack adaptivity and reversibility. It would resemble the covalent systems in strength, but may lose the advantageous qualities of self-healing and recyclability. In this respect, the strength of noncovalent bonding and/or external stimuli must be optimized to result in adaptive properties. Advantageously, unlike their covalent counterparts, most noncovalent bonds are sensitive to environment, and thus, even the strongest hydrophobic bonds can be broken when water is replaced with a suitable solvent, while strong ionic bonds can be

* Address correspondence to boris.rybtchinski@weizmann.ac.il.

Received for review July 7, 2011 and accepted August 26, 2011.

10.1021/nn2025397

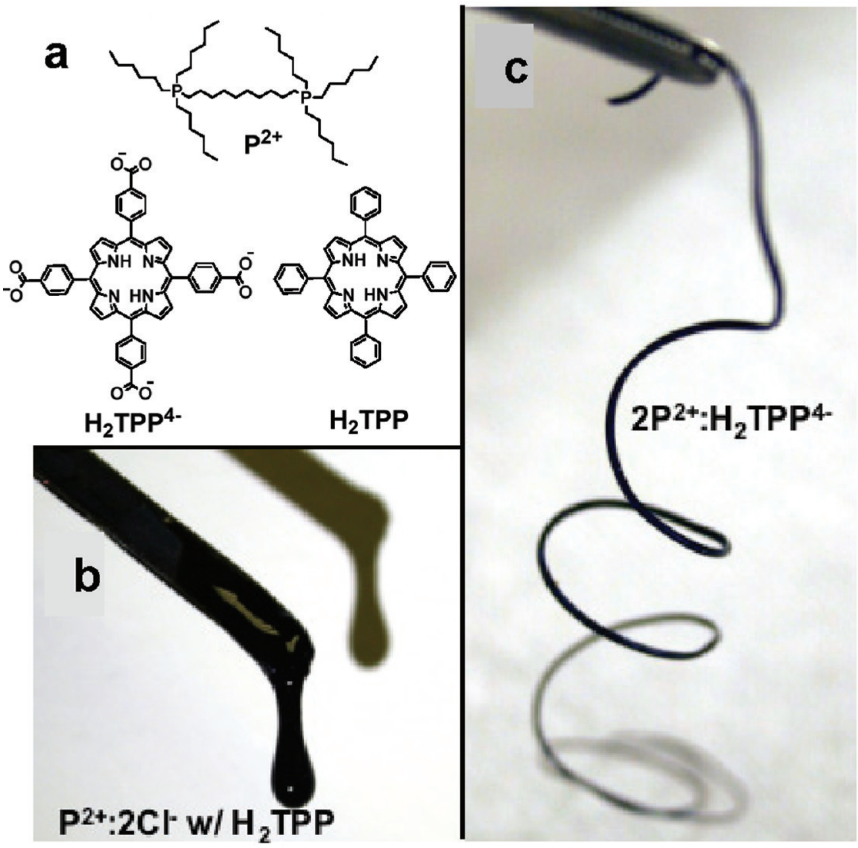

Figure 1. (a) Chemical structures of the phosphonium dication and porphyrins. (b) Photograph of a control system based on P^{2+}:2Cl^-/H_2TPP, indicating low viscosity (~1000 Pa s; $G' \approx 2500$ Pa, $G'' \approx 1500$ Pa), resulting in liquidlike properties. (c) Photograph of the shape-persistent fiber pulled from the ionic network 2P^{2+}:H_2TPP^{4-}. Adapted from ref 34. Copyright 2008 American Chemical Society.

weakened (screened) using a polar solvent or an electrolyte. An additional point of challenge is related to complexity of systems based on multiple bonding modes, for example, involving a combination of ionic, hydrophobic, and hydrogen bonds in a single array. While enabling a high degree of complexity and order, such systems are difficult to design because of complicated synergy of different bonding motifs.

If we succeed in achieving strong noncovalent bonding and can rationally design the assemblies, what materials are to be targeted? In which applications can noncovalent systems assembled from simple building blocks rival their covalent counterparts? The answer to these questions will depend on the developments in the field, but success in fabrication of supramolecular polymers[14,15] and dendrimers,[16] noncovalent nanoprintboards,[17] stable noncovalent containers (macroscopic sacs),[18] robust self-healing gels,[19] and recyclable nanoscale filtration membranes[20] points at several promising directions.

This review focuses on research dealing with key challenges in the design and synthesis of robust noncovalent nanoarrays and their utility as adaptive materials: (1) achieving strong noncovalent bonding; (2) rational design of systems based on strong noncovalent interactions; (3) efficient synthetic (self-assembly) methodologies targeting robustness, adaptivity, and complexity that preferably employ small molecules as primary building blocks; (4) reversibility and stimuli responsiveness relevant to adaptivity and recycling.

VOCABULARY: adaptive material —an array that can respond to external stimuli by change in structure and function. Noncovalent systems lead to adaptivity due to the sensitivity of noncovalent bonds to their environment and multiple stimuli • **multivalent noncovalent interactions** —a mode in which interacting entities are connected through multiple noncovalent bonds leading to stronger bonding • **pathway-dependent self-assembly** —a kinetically controlled assembly process where different supramolecular arrays are constructed from a single building block as a function of the self-assembly path. Advantageous since it is an economical way to achive diversity.

ACHIEVING ROBUSTNESS WITHOUT LOSING ADAPTIVITY

The approaches to strong noncovalent interactions are discussed according to the type of the interaction and addressing the adaptivity of the systems. We note that the qualities of robustness and adaptivity can be achieved employing coordination chemistry[12,21−26] and dynamic covalent chemistry,[12,27,28] which are beyond the scope of this review. We also note that robustness can be achieved by covalent capture of noncovalently preorganized systems.[29,30]

Ionic Bonds. Bonds between oppositely charged moieties are among the strongest noncovalent interactions, and significant research effort has been devoted to employ Coulombic forces in self-assembly of nanoscale systems.[31−33]

The ionic bonds have been recently utilized to create assemblies based on a combination of doubly charged ionic liquids (dications) that upon mixing with various polyanions produce networks with high viscosity.[34] When a dication bearing two covalently linked tetraalkyl phosphonium moieties is combined with a porphyrin tetracarboxylate, the resultant system exhibits remarkable viscosity of 10^6 Pa·s at ambient conditions (Figure 1). In fact, this material has solidlike properties, indicated by its relative values of the storage and loss moduli (~10^7 and 10^6 Pa, respectively), and can be pulled into fibers from hot melts and molded into shape-persistent structures (Figure 1c). The system is created by neat ionic compounds, and is sensitive to the presence of polar solvents. Consequently, the decrease in viscosity of several orders of magnitude occurs with the addition of small amounts of water, as observed in diphosphonium/polyacrylate ionic networks.[35] The design of ionic networks employs the interaction of multiply charged species, similar to that utilized in a variety of assemblies based on charge compensation (see below). The ionic networks appear to be generally accessible *via* a design involving ionic liquids bearing several charged groups and a complementary oppositely charged polyion.[36] The internal structure of the ionic liquids is yet to be addressed.

In general, electrostatic interactions depend on solvent polarity. For example, in water, an average binding energy between a pair of oppositely charged ions is estimated to be as low as ~5 kJ/mol.[37] Thus, screening the charges by a solvent should be taken into account if the ionic systems are to be assembled in solution, which is the most convenient fabrication methodology. In polar solvents, and especially in water, only multiple ionic bonds in small molecular systems,[38−42] polymers,[43−45] or in combination with other types of bonds[31,32] result in sufficiently robust systems. The term ionic self-assembly (ISA)[31] has been introduced for systems that exhibit multiple and cooperative binding modes in order to distinguish them from plain electrostatic interactions. Thus, interactions of oppositely charged polyelectrolytes involve multiple ion bonds, leading to strong bonding. Secondary interactions such as π-stacking and hydrophobic bonding play a significant role in ISA, resulting in higher degree of order and structural hierarchy.[31,32,46] Importantly, the addition of large amounts of salts results in weakening of the ionic bonds since Coulombic forces are screened by salt ions, enabling disassembly to render strongly bonded systems adaptive.[31] Electrostatic assemblies can be also sensitive to solvent polarity and changes in pH. Importantly, the ionic bonding motif is general and a variety of charged molecules are readily accessible, providing a vast self-assembly tool-box. Excellent reviews of the field are available.[32,45,46] We review here a number of systems that involve strong bonding and can be prepared with a high degree of structural control at the nanoscale, suggesting strategies toward rational design of robust noncovalent materials.

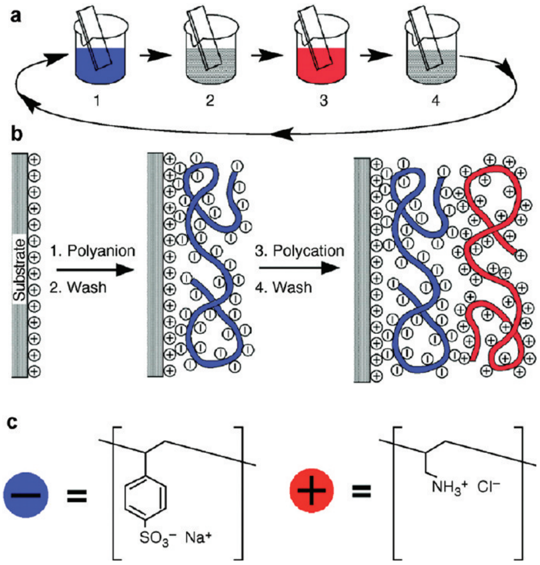

Figure 2. Film deposition using slides and beakers. (a) Steps 1 and 3 represent the adsorption of a polyanion and polycation, respectively, and steps 2 and 4 are washing steps, leading to the simplest film architecture, $(A/B)_n$. More complex film architectures require only additional absorption/washing steps and a different deposition sequence. (b) The first two adsorption steps, depicting film deposition starting with a positively charged substrate. Counterions are omitted for clarity. (c) Chemical structures of two typical polyions, the sodium salt of poly(styrene sulfonate) and poly(allylamine hydrochloride). Adapted with permission from ref 43. Copyright 1997 American Association for the Advancement of Science.

Layer-by-layer (LBL) self-assembly of oppositely charged polymeric electrolytes (polycations and polyanions) attached to a substrate represents the most mature and widely employed methodology for the creation of robust systems based on ionic self-assembly (Figure 2).[43,47,48] In most cases, stable solid-state materials are targeted, hence their reversible disassembly was not addressed in the majority of the systems under study. Yet, in general, the polyion LBL assemblies exhibit adaptivity: they can be annealed *via* simple immersion in salt solution as a result of electrolyte-induced screening of ionic bonds.[43]

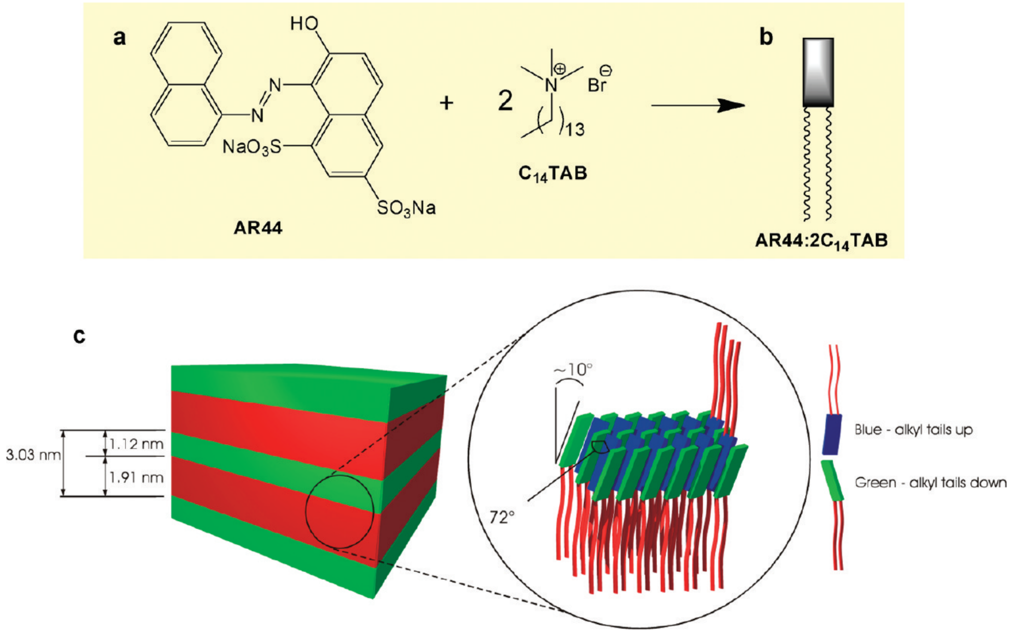

Figure 3. (a,b) Formation of a primary building block (b) based on ionic bonding. (c) Model for structure of AR44:$2C_{14}TAB$-based array: the green layers correspond to the dye phase, and the red ones to the alkyl phase. The structure was elucidated using X-ray diffraction methods. Adapted from ref 55. Copyright 2002 American Chemical Society.

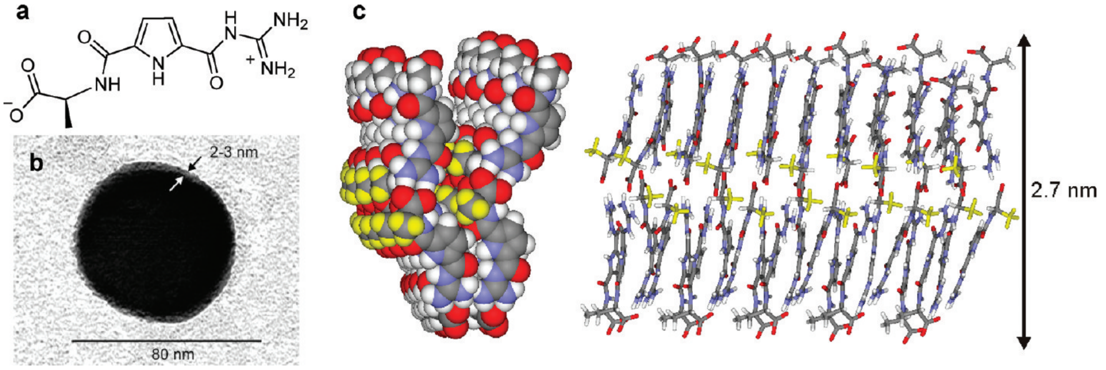

Figure 4. (a) Chemical structure of the zwitterion. (b) TEM image of a vesicle. (c) Model for the bilayer comprising the vesicle membrane. Adapted with permission from ref 32. Copyright 2010 Royal Society of Chemistry. Adapted from ref 62. Copyright 2008 American Chemical Society.

Advantageously, in LBL self-assembly, various materials can be incorporated in multilayer films, whose structure is easily controlled by the deposition sequence.[43,47−50] Electrostatic and other types of LBL assembly have been utilized to create robust composite materials with unique mechanical and optoelectronic properties.[50−54]

Overall, LBL-based systems are robust and can be rationally designed since their structure is controlled by the deposition sequence. However, once created, they cannot be *reversibly* disassembled, as their multilayer structure would not spontaneously reassemble in one step. Nevertheless, noncovalent LBL systems can be stimuli-responsive and self-healing.[54]

When the oppositely charged ISA moieties are assembled in solution without using a solid support, direct control of structure is more challenging than in substrate-based LBL. However, in systems where π-stacking and hydrophobic forces cooperate with ionic bonding a remarkable degree of nanoscale order can be obtained.[31,32,46] Charged aromatic dyes represent an especially advantageous class of molecules for ISA, as they are readily available, prone to π-stacking, and photoactive. Thus, self-assembly of negatively charged azo-dyes with cationic surfactants resulted in highly organized arrays where a balance of electrostatic, hydrophobic, and π-stacking interactions is responsible for the creation of diverse complex architectures.[31] A representative system assembled from tetradecyltrimethylammonium bromide ($C_{14}TAB$) and Crystal Scarlet (AR44) azo-dye reveals nanoscale order with phase separation into lamella, featuring the crystalline two-dimensional layers formed by stacked dyes (the distance between them is 3.6 Å, typical of π-stacking), and

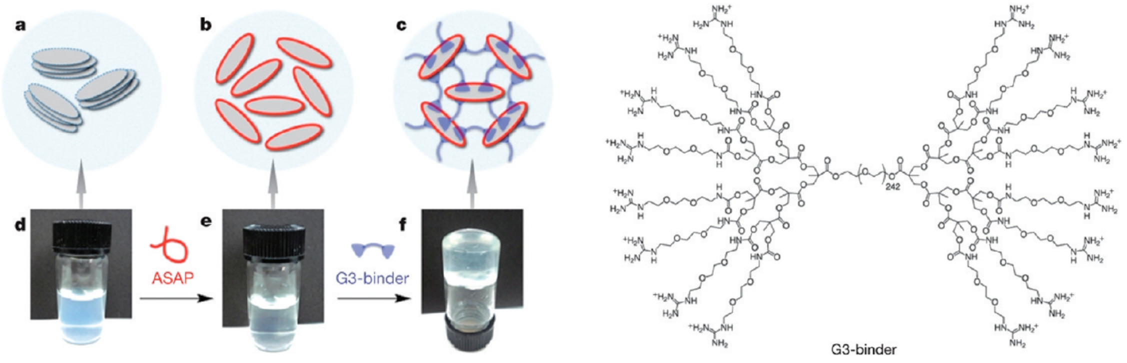

Figure 5. Hydrogelation process: (a) Clay nanosheets (CNSs), entangled with one another, are (b) dispersed homogeneously by interaction of their positively charged edge parts with anionic sodium polyacrylate (ASAP). (c) Upon addition of a dendritic binder G3, exfoliated CNSs (whose surface is negatively charged) are cross-linked to develop a 3D network. (d−f) Photographs showing the evolution of the systems upon addition of the components. Adapted with permission from ref 19. Copyright 2010 Nature.

ammonium alkyl moieties bound to the dyes, alternating into the two alkyl layers adjacent to the dye layer (Figure 3).[55] As the dye scaffolds are highly ordered and parallel to each other, such systems are birefringent.[56] Although mechanical properties of these assemblies were not studied, multiple noncovalent interactions together with the systems' crystallinity imply significant robustness. π-Stacking/hydrophobic interactions between the anisotropic dye molecules represent a critical aspect in the formation of ordered 1 nm-thick crystalline planes that are composed of tightly packed rigid dye scaffolds in a herringbone arrangement. Attesting to thermal stability of the system, a solid−solid transition at 140 °C occurs with preservation of the outer crystal shape of the dye layer.[55] The assemblies are solid-state arrays that precipitate upon mixing oppositely charged components to the point of full charge compensation, but can be redissolved using high concentration of salts.

Ionic bonds in combination of π-stacking/hydrophobic interaction of aromatic dyes were also employed to create well-defined responsive nanostructures[57] and supramolecular polymers in aqueous media.[58] Nanotubes and other nanostructures based on the interaction of oppositely charged porphyrins have been reported,[59] and ionic bonding has been utilized for self-assembly of carbon nanotube and fullerene derivatives.[51]

In an "all-in-one" design strategy, H-bonding, ionic, and π-stacking motifs were combined in a single self-complementary zwitterionic building block, comprising amino acid and guanidinium moieties (Figure 4).[60,61] This simple molecule has been shown to form self-assembling vesicles with diameters ranging from 25 to 50 nm that feature bilayer membranes. The latter are constructed from linear dimers stacking in an antiparallel fashion to promote further interaction of oppositely charged groups and additional π-stacking between the aromatic moieties.[62] The vesicles showed pH-dependent reversible disassembly, valuable for the development of stimuli-responsive nanocontainers.[63] The zwitterion-based systems demonstrate that multiple interactions of various types combined in a single molecule act in concert to result in well-defined assemblies. Thus, simple zwitterion molecules, giving rise to a high degree of organization, introduce self-complementarity as an efficient design strategy.

Multivalent electrostatic interactions between organic and inorganic moieties can be especially advantageous. In a recently reported example, a dendritic macromolecule with multiple positively charged termini strongly binds clay nanosheets (having negatively charged surface) to form a self-assembled 3D hydrogel network, which can be molded into shape-persistent, free-standing objects because of its great mechanical strength (Figure 5).[19] Yet, it is remarkably adaptive: following damage, the system self-heals rapidly and completely. The related organic/clay LBL systems have been reported to possess unique mechanical robustness;[52] however, their adaptivity has not been studied.

Recent reviews on nanostructures created by electrostatic self-assembly of multiply charged inorganic nanoscale objects such as polyoxometallates (POMs),[33,64,65] and metal or semiconductor nanoparticles[66−70] are available. Although significant progress has been made in understanding the factors controlling their self-assembly and adaptivity, mechanical properties of such systems have not been addressed.

Overall, ionic self-assembly is advantageous due to its generality, strong bonding, and structural control (especially in LBL assemblies). The noncovalent materials based on a combination of ionic and π-stacking/hydrophobic interactions demonstrate nanoscale order, robustness, and multiple stimuli-responsiveness that are very promising for materials applications. Hybrid systems take advantage of rigidity (inorganic moiety), flexibility (organic moiety), and multivalency: for example, multiply charged inorganic moieties such as clay nanosheets greatly enhance robustness of noncovalent systems.[19,52,71]

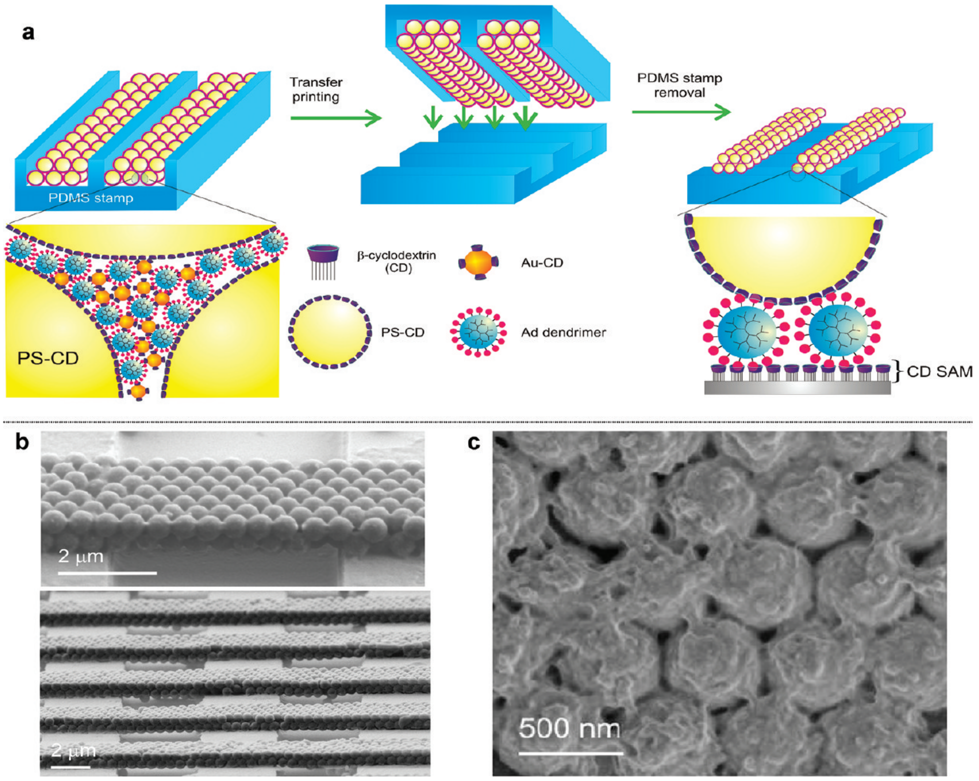

Figure 6. (a) Preparation of the hybrid particle bridges held together by a "supramolecular glue" (Ad dendrimer/Au-CD) on a topographically patterned CD SAM. (b) SEM images of the freestanding hybrid particle structures. (c) SEM images after 30 LBL assembly cycles of Ad dendrimer/Au-CD glue holding together the PS-CD nanoparticle crystals. Adapted with permission from ref 82. Copyright 2009 Wiley. Adapted with permission from ref 83. Copyright 2009 Wiley-VCH.

Multivalent Host–Guest Interactions. Multivalent interactions are pivotal for creating robust noncovalent systems,[11,72–74] and examples of multivalent electrostatic interactions are described in the previous section. Here we focus on noncovalent systems that employ other types of interactions (host–guest) and involve interfaces (created by solid surfaces, dendrimers, and nanoparticles) covered with noncovalent binders (ligands). Such interfaces can be viewed as multivalent noncovalent entities, resulting in strong binding if the geometries of the binding moieties are optimized to promote a maximal number of noncovalent interactions.[72,75] One of the most developed systems involves interfaces functionalized with β-cyclodextrin (CD), a host ligand having a hydrophobic cavity that can bind organic guest molecules (*e.g.*, adamantane (Ad) and ferrocene (Fc)) in aqueous media, forming complexes through hydrophobic interactions.[11,17,76] While the binding constant of a single CD–Ad interaction is $\sim 1 \times 10^5$ M^{-1}, multiple CD–guest interactions are several orders of magnitude stronger (see later).

Multivalent interactions between β-cyclodextrin self-assembled monolayers (CD SAMs) and molecules modified with multiple hydrophobic guest moieties have been studied. The binding of adamantyl-terminated dendrimers, with 8, 16, and 32 adamantyl end groups to CD SAMs results in thermodynamically stable assemblies, showing no appreciable desorption in pure water.[77] Although the desorption rate for the generation-4 dendrimer, which has four interactions with the CD SAM, is extremely slow, it can be accelerated in the presence of high concentrations of CD, enabling adaptivity of the system.[77] In another approach, redox chemistry has been used to achieve adaptivity, bringing about reversible desorption of strongly bound Fc-based dendrimers from CD SAMs.[78] Furthermore, various nanoparticles have been strongly yet reversibly bound to surfaces using dendrimers as "supramolecular glue",[79,80] including the possibility to construct LBL-type systems.[81–83] The robustness of these systems enabled fabrication of electronic devices that allow control over rectification in supramolecular tunneling junctions.[84]

Addressing the fundamental question of how strongly multivalent interactions enhance binding constants, it was found that the divalent interaction at the CD SAMs resulted in a binding constant of 10^{10} M^{-1}, 3 orders of magnitude higher than that for the corresponding divalent interaction in solution (10^7 M^{-1}).[85] This large effect is due to a difference in effective concentration, and was rationalized using a probing volume concept. Thus, the probing volume for the uncomplexed guest at the surface is less than half of that in solution, where only a single cavity is available in a larger probing volume, resulting in much stronger

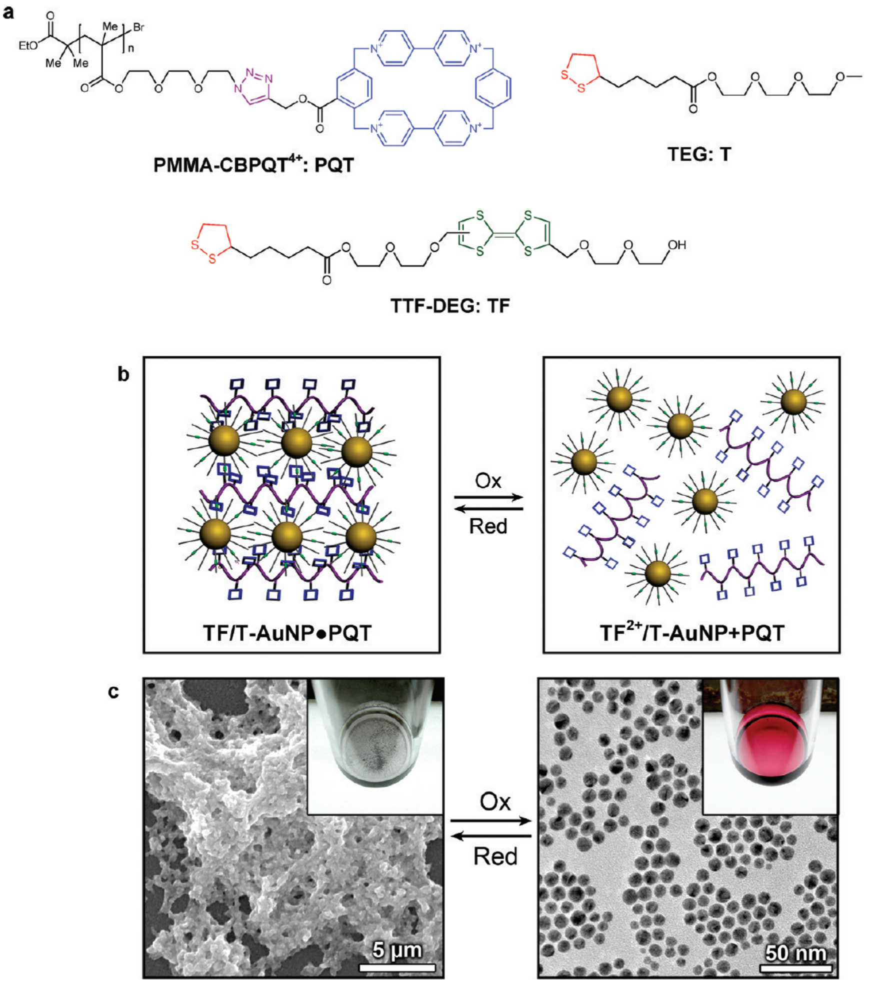

Figure 7. (a) Chemical structures of noncovalent binders. (b) Reversible binding of AuNPs that can be controlled *via* redox chemistry. (c) Left: SEM image of TF/T-AuNP·PQT; Right: TEM image of TF^{2+}/T-AuNP+PQT. Insets: photographs of the corresponding samples. Adapted with permission from ref 100. Copyright 2009 Nature.

binding to the surface than to the solution-phase array.[85]

Multivalent interactions are sufficiently robust to create free-standing nanoparticle composites. Free-standing polystyrene (PS) nanoparticle bridges held together by host−guest interactions between gold nanoparticles covered with CDs and dendrimers bearing adamantane moieties were obtained by transfer printing onto topographically patterned substrates (Figure 6).[82,83] Remarkably, AFM bending test measurements showed that these noncovalent systems exhibited a bending modulus of 1.2 ± 0.4 GPa, *similar to that of polystyrene*, attesting to remarkable robustness stemming from multivalent noncovalent interactions.[83]

Importantly, molecular interactions at biological membranes usually involve multivalent interactions, which are stronger and more selective than monovalent ones.[74] Similarly to the described above multivalent interactions at solid surfaces, such interactions at self-assembled vesicular membranes take advantage of high local concentration of the interacting species. Thus, cyclodextrine or cucurbituril-based vesicle membranes strongly bind multivalent guest molecules.[86−91] Adaptivity is achieved *via* varying concentration of the competing ligands that attenuate multivalent binding strength. In a related approach, fluid supported lipid bilayers incorporating multiple noncovalent binders provide an excellent platform for obtaining accurate thermodynamic information on multivalent protein−ligand interactions: these are normally characterized by strong binding (up to nanomolar equilibrium dissociation constants).[92] Multivalent host−guest interactions employing cucurbit[8]uril that hosts two complementary pendants (viologen and naphthoxy groups) attached to polymer chains have been used to create robust stimuli responsive hydrogels.[93]

Analogously to the systems described above, nanoparticle assemblies can benefit from the strong multiple noncovalent interactions between capping ligands (sometimes also employing external multivalent binding moieties).[67−70,94−99] Owing to their multivalent nature and extended binding areas, such interactions can be strong enough to result in *kinetically*

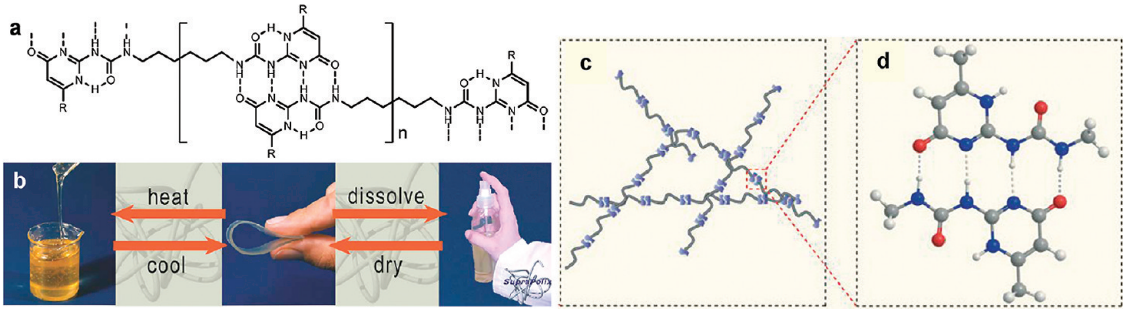

Figure 8. (a) Chemical structure of a polymer based on 2-ureido-4[1*H*]-pyrimidinone (UP). (b) Adaptive properties of the bulk polymers based on UPs. (c) Schematic of a polymer structure. (d) Molecular model of a self-complementary UP_2 binding unit. Adapted with permission from refs 2, 15, and 110. Copyright 2001 American Chemical Society, 2008 Nature, and 2004 Elsevier, respectively.

trapped nanoparticles assemblies, requiring additional energy input in order to equilibrate them.[94]

An example of adaptive nanoparticle assemblies is presented in Figure 7. Here, gold nanoparticles (AuNP) functionalzed with a variety of noncovalent binders (a TTF-based example is shown in Figure 7) were reacted with a polymer bearing complementary noncovalent guest pendants, bis-paraquat cyclophanes (PMMA-$CBPQT^{4+}$, Figure 7a).[100] The ligands on the AuNPs interacted with the paraquat rings *via* $\pi-\pi$ stacking, [C$-$H$\cdots$O] or [C$-$H$\cdots\pi$] interactions, resulting in the formation of pseudorotaxanes and leading to multivalently bound polymer/NP aggregates, whose sizes and solubilities can be tuned by the molar ratio between the cyclophane and the NP capping ligands. The aggregates are stimuli-responsive and can be reversibly disassembled using simple redox chemistry (Figure 7b,c).

Summarizing, supramolecular multivalency is a powerful tool for creating strongly bonded assemblies. In particular, interfaces (solid surfaces, nanoparticles, vesicles, *etc*.) covered with multiple noncovalent binders lead to strong interactions. Adaptive behavior (disassembly) can be induced using competitive ligands, redox chemistry, and other stimuli. Structural control in these systems is facilitated by the presence of an interface that restricts and directs the self-assembly process. The general character of multiple noncovalent bonding at interfaces and the hybrid nature of the systems enable a broad palette of design approaches and possible functionalities, advantageous for creating adaptive nanomaterials.

Hydrogen Bonds. A significant research effort has been devoted to developing strong H-bonding moieties (based on multiple H-bonds) leading to well-defined nanoscale assemblies.[101,102] Larger scale fibrous arrays, supramolecular polymers, assembled *via* hydrogen bonds,[2,26,103−105] exhibit sufficient strength and unique adaptivity, constituting an important class of stimuli-responsive materials. Supramolecular dendrimers,[16] capsules,[106] other nanoscale systems,[102,107,108] and LBL polymer assemblies[109] have been also fabricated employing multiple hydrogen bonding.

One of the most versatile binding motifs, self-complementary 2-ureido-4[1*H*]-pyrimidinone (UP, Figure 8), features strong quadruple H-bonding, dimerizing in toluene with an association constant of $K_{\mathrm{dim}} = 6 \times 10^8\ \mathrm{M}^{-1}$.[14,110] Application of such H-bonding units as associating end-groups in di- or multifunctional molecules has resulted in the formation of supramolecular polymers with high degrees of polymerization.[2,14,15,110] These polymers have unique temperature responsiveness due to the heat-induced breaking of hydrogen bonding leading to depolymerization, which can be reversed upon cooling (Figure 8).

Multiple hydrogen bonds have been employed to create a supramolecular rubber, in which polymer chains are cross-linked through H-bonds.[111] Unlike conventional rubbers, these systems, when broken or cut, can be repaired by bringing together fractured surfaces that self-heal at room temperature, recovering extensibility. These materials can be easily processed and recycled.

An interesting example of photofunctional adaptive nanomaterial involves hydrogen bonding between polystyrene-block-poly(4-vinylpyridinium methanesulphonate, P4VP(MSA)) and 3-*n*-pentadecylphenol (PDP), which forms highly ordered arrays with a long lamellar period.[112] The system is green at room temperature due to a photonic bandgap created by its periodic structure (dielectric reflector). On heating, hydrogen bonds are broken, leading to a sharp and reversible transition to uncolored material due to a collapse of the periodic lamellar structure responsible for the dielectric reflectivity bandgap. Such adaptive behavior is potentially useful for creating functional coatings, sensors, and photonic thermoresponsive materials. The P4VP(MSA)/PDP system has been also used to create stimuli-responsive nanoparticle assemblies.[113]

Aromatic Stacking. π-Stacking between large aromatic surfaces leads to strong bonding. A well-known manifestation of strong π-stacking is the fact that large polycyclic aromatic hydrocarbons (PAHs) have very low solubility in organic solvents, with the larger PAHs being practically insoluble. Computational studies

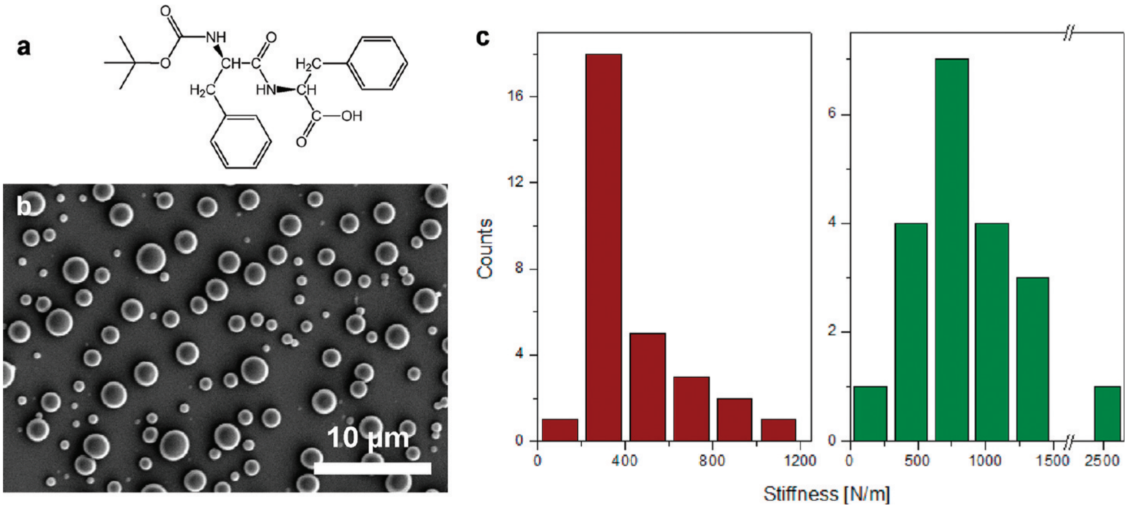

Figure 9. (a) Chemical structure of Boc-Phe-Phe-OH. (b) SEM image of the nanospheres. (c) Their stiffness distribution: (left) stiffness of the spheres with diameters of approximately 200 nm; (right) stiffness of the spheres with diameters of approximately 1 μm. Adapted with permission from ref 132. Copyright 2010 Wiley-VCH.

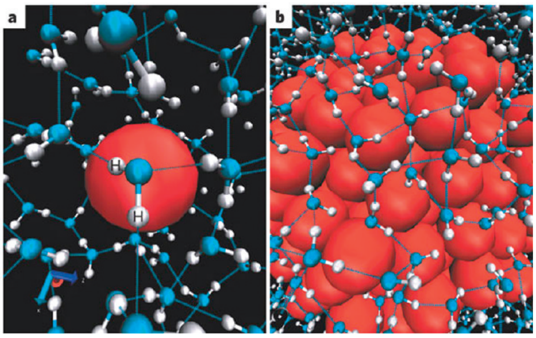

Figure 10. The space-filling size of the hydrophobic (red) particle in panel a is similar to that of a methane molecule. The hydrophobic cluster in panel b contains 135 methane-like particles that are hexagonally close-packed to form a roughly spherical unit of radius larger than 1 nm. For the single cavity pictured in panel a, each water molecule can readily participate in four hydrogen bonds. The water molecules in panel b are not typical of the bulk and cannot go around the hydrophobic region, having typically three or fewer hydrogen bonds. Adapted with permission from ref 141. Copyright 2005 Nature.

revealed π-stacking energy of 16–18 kcal/mol in the case of tetracene.[114] Strong π-stacking is mostly due to dispersion interactions,[114–117] but electrostatic interactions have also been suggested to play a role in determining the structure of π-stacked systems.[116,118,119] Excellent reviews devoted to supramolecular π-stacked systems are available.[117,120–126] The recent developments in the field include synthesis and nanoscale self-assembly of well-defined graphene-like aromatic systems, which involve very strong π-stacking interactions.[127–130] These systems have advantageous electronic properties and have been utilized for device applications.[128,131]

One of the most mechanically robust noncovalent systems reported to date is based on an aromatic peptide, owing its mechanical strength to a three-dimensional aromatic stacking network.[132,133] In the most interesting example, mechanical properties of nanospheres formed by the self-assembly of the Boc-Phe-Phe-OH peptide (Boc = *tert*-butoxycarbonyl, Phe = phenylalanine) were studied using AFM indentation-type experiments (Figure 9).[132] The spheres demonstrated remarkable metallic-like point stiffness of up to 885 N/m and a Young's modulus of up to 275 GPa, making Boc-Phe-Phe-OH nanostructures the stiffest organic system reported to date with a stiffness that is comparable to that of steel (*ca.* 200 GPa) and carbon fibers (*ca.* 300 GPa).[132]

π-Stacking plays an important role in complex liquid crystalline structures resulting from dendron and rod–coil copolymer-based self-assembly.[7,134,135] π-Stacked systems have been also employed in nanoarrays mimicking solar energy conversion functions,[136,137] and self-healing systems based on π-stacking interactions have been reported.[138]

Related to the possibility of rationally designing stacked arrays, face-to-face aromatic interactions lead to molecular stacks, whose growth is defined by stacking geometry, often leading to well-defined one-dimensional molecular motifs.[122,124,136] The molecular stacks can further interact resulting in more complex structures, having morphologies that are difficult to control, as in the case of 3D stacked networks responsible for exceptional mechanical robustness of Boc-Phe-Phe-OH nanospheres.

Hydrophobic Interactions. Liquid water comprises a dynamic three-dimensional network of hydrogen bonds (∼5 kcal/mol each), which, if disrupted by hydrophobic surfaces (Figure 10), will force them to aggregate in order to decrease the energetically unfavorable water/hydrophobic interface.[9,139–141] Such hydrophobic interactions are ubiquitous in biological

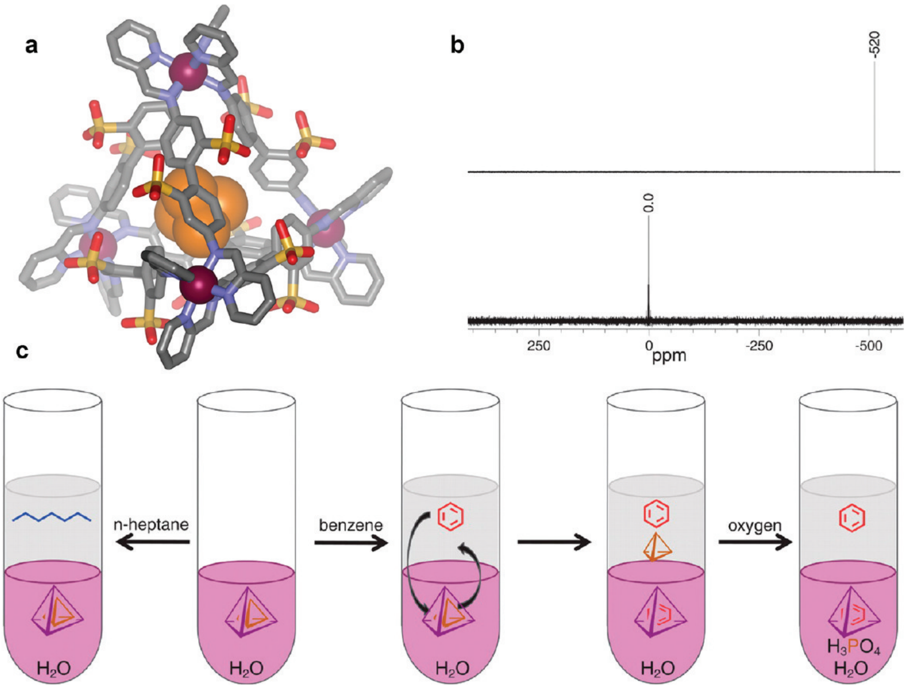

Figure 11. (a) Crystal structure of the cage with entrapped P_4. (b) ^{31}P NMR spectrum showing (top) entrapped P_4 peak and (bottom) H_3PO_4 peak following replacement of P_4 with benzene and oxidation. (c) Extraction of P_4 from the cage by *n*-heptane is not possible, whereas replacing P_4 with a suitable guest (benzene) results in the facile removal of P_4 into the organic solvent and oxidation in the presence of oxygen. Adapted with permission from ref 154. Copyright 2009 American Association for the Advancement of Science.

systems, and responsible for protein folding and aggregation, membrane formation, and other processes.[9] Thus, water, due to its 3D network of hydrogen bonds, can be viewed as the cohesive energy-rich "matrix" that aspires to minimize hydrophobic surface area in contact with it, inducing aggregation. If a rigid hydrophobic surface reaches several nm^2, the hydrophobic interactions may, in principle, reach a very significant strength. For example, if rigid, flat hydrophobic surfaces reach more than 5 nm^2 in size, the "unfavorability" of their exposure to water is more than 30 kcal/mol, as estimated using oil–water interfacial tension energy (70 cal/$Å^2$), a good approximation for hydrophobic surfaces larger than 1 nm^2.[141]

Self-assembly driven by relatively strong hydrophobic interactions in aqueous solutions has been reported for amphiphilc block copolymers,[142−145] aromatic rod-shaped molecules,[146] and host–guest complexes.[147] For example, robust nanotubes self-assembled from coronene amphiphiles in water and water/THF mixtures are held together by hydrophobic and $\pi-\pi$ interactions.[148,149] Hydrophobic interactions also play a key role in the self-assembly of various peptide amphiphiles,[150] and contribute significantly to the stability of LBL assemblies.[151] We note that the comprehensive theory of hydrophobic interactions is yet to be developed.[9] The complexity of the interactions between water and large solutes precludes exact estimation of interaction energies that depend not only on overall hydrophobic surface area but also on the

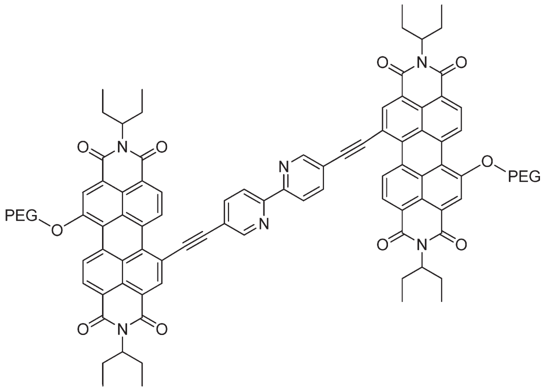

Figure 12. Chemical structure of PP2b. PEG = polyethylene glycol.

shape[152] and chemical nature of the solute. The intricate dynamic behavior of a hydrogen-bonded network of water[153] also contributes to the complexity of aqueous self-assembly. We discuss here several recent examples of noncovalent systems where hydrophobic interactions bring about strong binding, leading to robust arrays, some of which are applicable as nanomaterials.

Hydrophobic interactions have been recently shown to induce a dramatic change in chemical properties. Thus, pyrophoric white phosphorus (P_4) is rendered air-stable within the hydrophobic cavities of self-assembled container (cage) molecules, formed in water from organic ligands and iron(II) ions (Figure 11).[154] This is due to strong host–guest interactions between

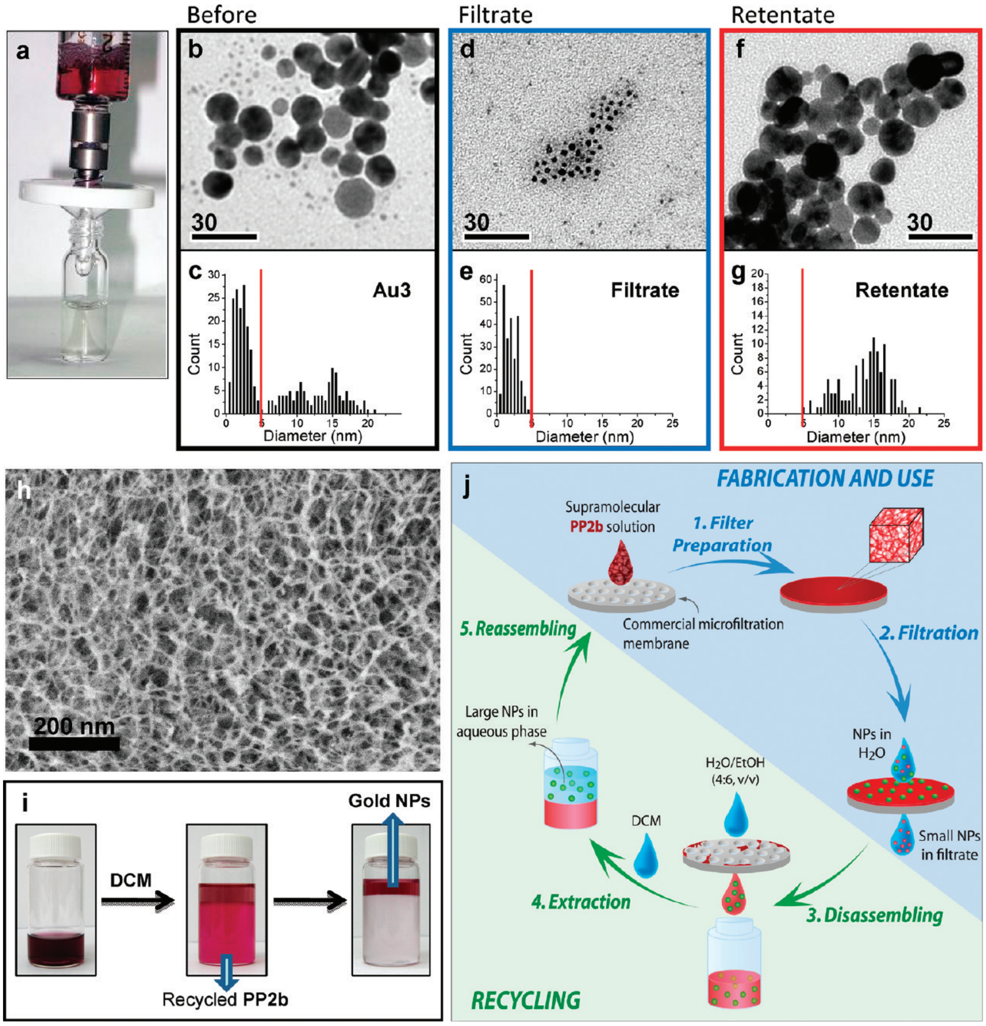

Figure 13. Filtration of gold nanoparticles (AuNPs covered with mercaptopropionate, Au3). (a) Photograph of the filtration experiment: red-colored AuNP solution is passed through the membrane deposited on a syringe filter. The filtrate is almost colorless due to the retention of larger AuNP. (b) Representative TEM images of Au3 before filtration and (c) the corresponding particle size histogram. (d) TEM image of the filtrate and (e) the corresponding histogram. (f) TEM image of the retentate and (g) the corresponding histogram; red lines in the histograms indicate the cutoff of the filter. (h) Cryo-SEM image of the deposited membrane, showing uniform nanoporous structure. (i) Photographs showing the retrieval of PP2b (*via* extraction with dichloromethane, DCM) and AuNPs (remains in aqueous layer) from the water/ethanol mixture. (j) Scheme of fabrication, use, and recycling of the supramolecular membrane. Adapted with permission from ref 20. Copyright 2011 Nature.

the hydrophobic P_4 and the cavity (matching in size and shape), preventing release of P_4 into solution. At the same time the cavity is too small to accommodate both P_4 and O_2 or oxidized species, averting phosphorus oxidation. The phosphorus can be released in controlled fashion, without disrupting the cage, by adding the competing guest (*e.g.*, benzene).[154] The strong interactions and reusable nature of the system may lead to new materials for storage and release of sensitive molecules.

Hydrophobic cavities created by the interior of coordination compounds have been employed to encapsulate hydrophobic moieties of fitting sizes, and to induce unique reactivity modes.[155−157] Organic cavitands assembled *via* hydrophobic interactions have been also reported.[158,159]

Nanostructured solid-like three-dimensional (3D) systems such as gels, having uniform morphology over the entire bulk of the material and based on strong noncovalent forces, appear to be most advantageous in terms of robustness, adaptivity, and extended nanoscale order. To achieve solid-like viscoelastic behavior in supramolecular systems, 3D network based on entangled linear aggregates (fibers) must form, spanning the bulk of the system, and eventually resulting in gelation.[160] Supramolecular gels have promising applications in a large variety of fields, including medicine, stimuli-responsive materials, and solar energy conversion.[160−168] Supramolecular hydrogels are composed of water and a small amount (usually 0.1 to 10 wt %) of gelator molecules, and some hydrogels can exist for long periods of time without drying.[165,166,169]

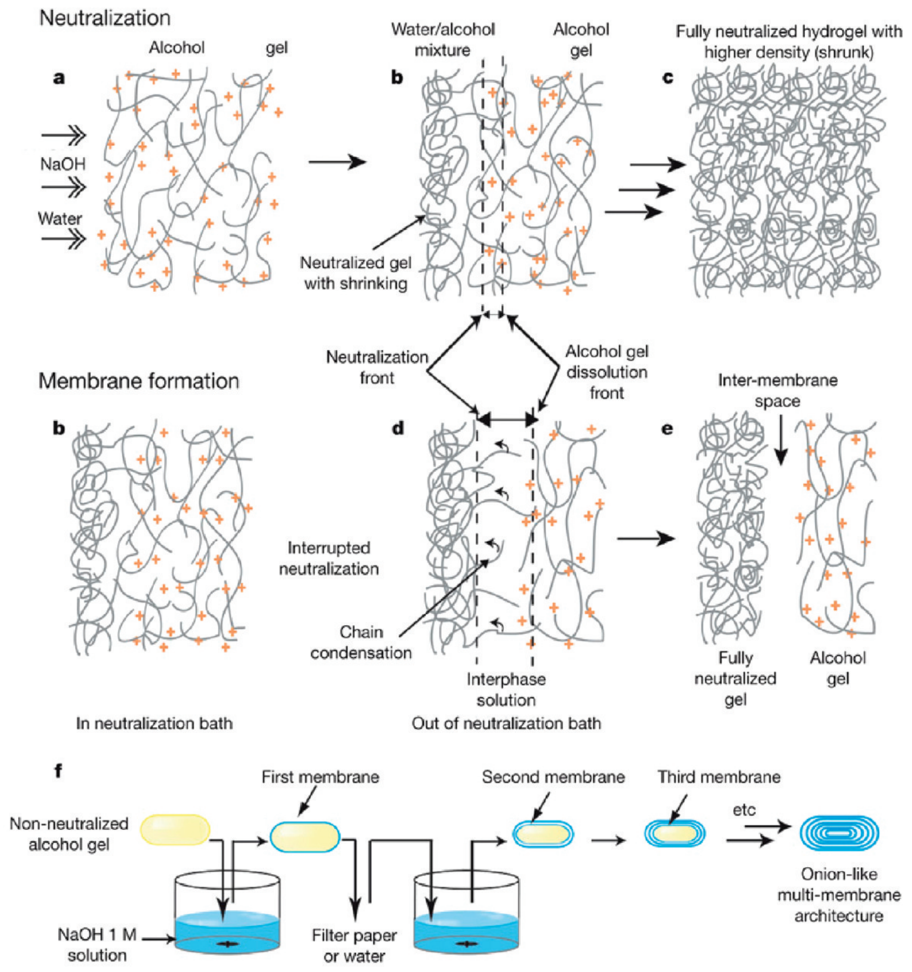

Figure 14. (a) Non-neutralized alcohol gel introduced into the neutralization bath. (b) Chain condensation and shrinkage of the alcohol gel due to the disappearance of ionic repulsions during the neutralization step. (c) Fully neutralized shrunk hydrogel after a complete neutralization. (d) Formation of the interphase solution and collapse of the polymer chains during the interruption of the neutralization step. (e) Intermembrane space formation after complete condensation of the residual polymer chains in the interphase solution. At the end of the process, the multimembrane system is thoroughly washed. (f) Overview of the multistep neutralization process. Adapted with permission from ref 174. Copyright 2008 Nature.

These systems can be also easily disassembled (*e.g.*, using organic solvents) and reassembled in water, enabling fast and facile *recycling*. The mechanistic insight into hydrogel self-assembly is limited, and many hydrogels were discovered serendipitously.[166] The rational design of gels, for example, *via* a crystal-engineering approach, in which the single-crystal structure of a molecule and its interaction modes are correlated with gelling aptitudes,[170] is only starting to emerge. We review here several recent examples of robust water-based noncovalent (gel) networks that demonstrate self-healing, recyclability, and nanoscale order, representing an entry into adaptive functional nanomaterials competitive with their covalent counterparts in robustness and performance.

We have shown that the supramolecular 3D networks in a fluid aqueous solution and in a hydrogel form assembled from perylene diimide amphiphile (**PP2b**, Figure 12) possess exceptional robustness and show multiple stimuli-responsiveness.[171] Reversible charging allows for switching between gel and fluid solution states, resulting in switching on and off the material's birefringence. Temperature-triggered shrinkage of the gel leads to the (reversible) expulsion of the aqueous solvent. The material deposited on the commercial filters from water solutions (which contain self-assembled 3D networks) creates a supramolecular membrane with a uniform nanoporous structure (Figure 13h) that is sufficiently robust to be used for ultrafiltration (Figure 13).[20] The membrane thickness was readily adjusted by changing the amount of supramolecular solution that was used for preparation. A thin (~12 μm) membrane was used for filtering various gold nanoparticles and consistently showed a 5-nm cutoff size. The membrane's permeance (pressure normalized flux) is comparable to commercially available membranes with similar rejection properties.[172] A thicker (~45 μm) membrane was used for chromatographic separation of 2.5−4.0 nm CdTe quantum dots. Remarkably, due to its supramolecular

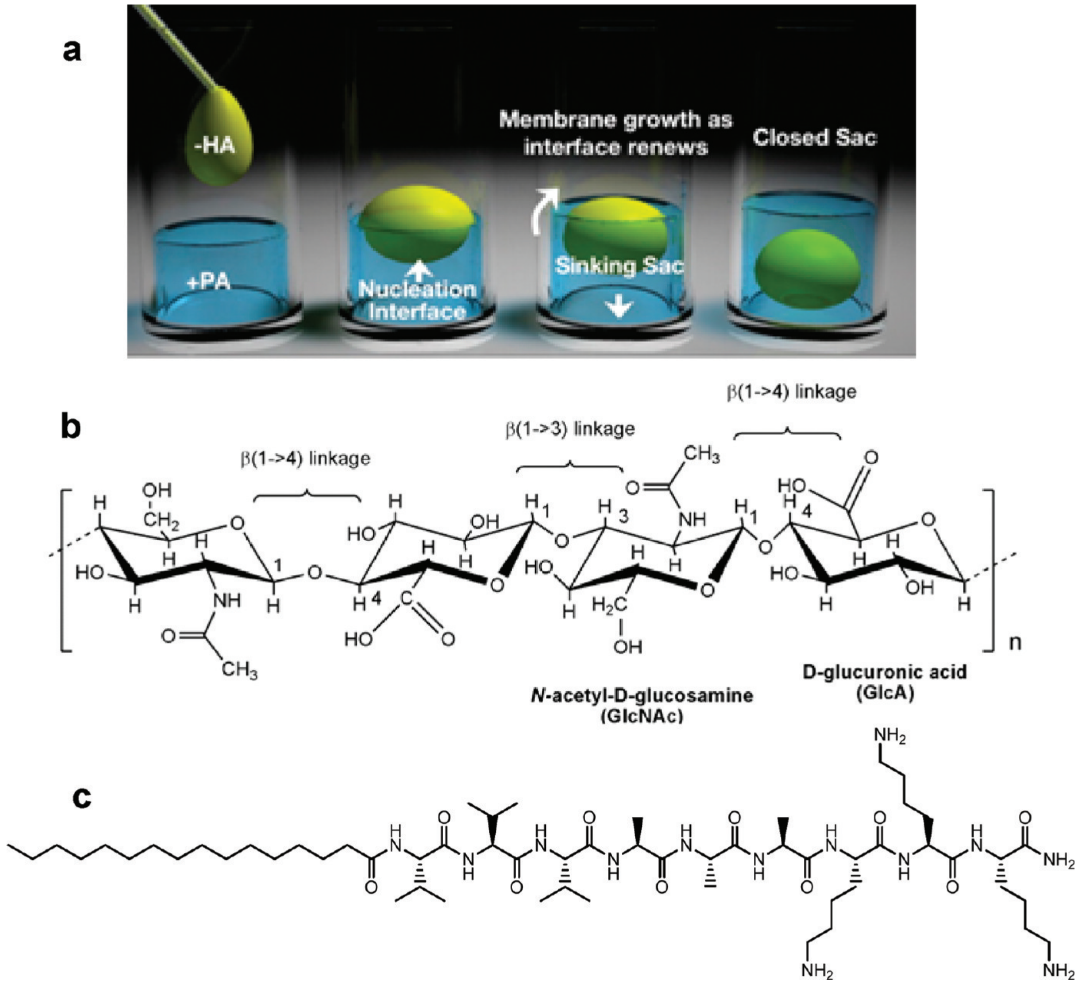

Figure 15. (a) One of the methods to form a self-sealing closed sac. A sample of the denser negatively charged HA biopolymer solution is dropped onto a positively charged peptide amphiphile (PA) solution. (b) Chemical structure of the hyaluronic acid (HA) polysaccharide. HA had an average molar mass of 1.76 MDa. (c) Chemical structure of the $C_{16}V_3A_3K_3$ (PA) used to make sac and membrane. Adapted with permission from ref 18. Copyright 2008 American Association for the Advancement of Science.

nature the membranes can be *fully recycled* (*via* dissolving by an organic solvent such as THF or ethanol, followed by solvent evaporation, redissolving in water and deposition on a standard commercial filter), while the material that is caught by the filter (large nanoparticles) can be easily separated by centrifugation or extraction and recycled as well (Figure 13i,j). These findings demonstrate feasibility of a *self-assembling functional material based on water that is both robust enough for practical applications and easily recyclable*, suggesting a versatile and environmentally friendly alternative to covalent systems.[173]

Judicious choice of a self-assembly pathway has been shown to produce multilayered gel structures: manipulating a chitosan-based gel leads to creation of strongly bonded systems intermittent with weakly bonded ones (Figure 14).[174] In this system, first, a gel is formed from a chitosan solution in a 50/50 water/1,2-propanediol (other alcohols can be used as well) following water evaporation. Second, neutralization in a sodium hydroxide solution and subsequent washings in water yield a physical hydrogel that contains mostly water (over 95 wt %) and chitosan in the free amine form (Figure 14). Here switching from hydrophilic (charged) to more hydrophobic neutral polymers produces a stable membrane, where the polymer chains are held together by strong hydrophobic interactions. The formation of intermembrane spaces (interphases) was achieved by slowing down the neutralization (by removing the gel from the neutralization bath or by washing with water). Remarkably, simple fabrication, where the number and thickness of the layers can be controlled by neutralization/washing sequences, results in tailor-made multimembrane structures (Figure 14). Free "intermembrane" spaces appear to be useful for cell or drug introduction.[174] Apparently, the system can be disassembled by the addition of acid.

A combination of electrostatic and hydrophobic interactions was utilized to assemble macroscopic supramolecular sacs.[18] When hyaluronic acid (HA, linear negatively charged macromolecule containing

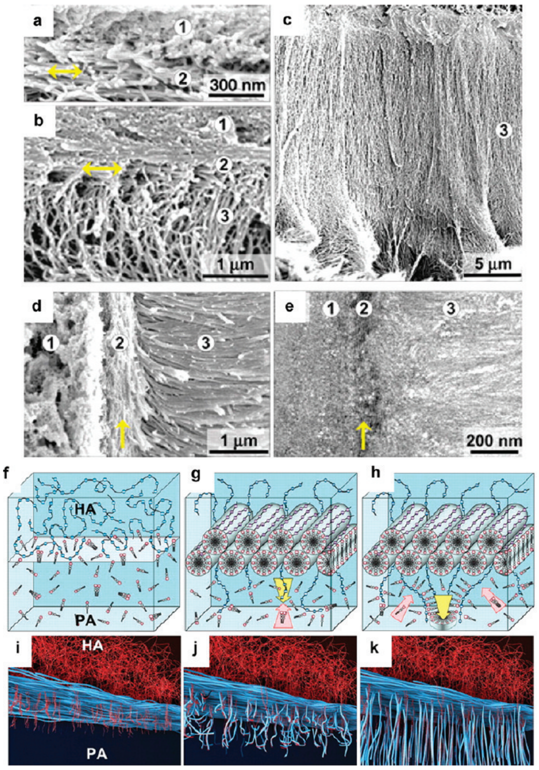

Figure 16. (a−c) SEM of the sac membrane as it forms over time (HA solution side on top, PA solution side on bottom): (a) 1 min, (b) 30 min, and (c) 4 days. (d) SEM and (e) TEM of a cross-sectional slice of the membrane. The parallel fiber region (arrow) between the amorphous and perpendicular fiber zones correspond to region 2. Region 3 comprises PA/HA fiber hybrids (see panels j,k). Darker contrast in region 2 (e) indicates positive staining of HA by uranyl acetate. (f−k) Schematic illustration of the model for membrane formation. (f) Initial mixing at the interface. (g) Formation of nanofibers at the interface composed of small molecules (due to electrostatic screening by the negatively charged polymer) creates a physical barrier between the two solutions, followed by reptation of macromolecules through the barrier and into the small-molecule solution (yellow arrow). (h) Nucleation of nanofibers perpendicular to the interface by polymer strands crossing the barrier (yellow arrow). Pink arrows indicate attraction of PA monomer or their aggregates to polymer strands as they cross the barrier. (i−k) Schematic representation of polymer stubs (red) penetrating the diffusion barrier and inducing nanofiber assembly. Adapted with permission from 18. Copyright 2008 American Association for the Advancement of Science.

a disaccharide repeat unit) was mixed with a positively charged peptide amphiphile (PA, PAs are widely utilized to form stable nanofibers[175]), a solid membrane localized at the interface between the two liquids is formed (Figure 15). A simple method that involves injecting one solution directly into the bulk of the other leads to either HA-filled or PA-filled sacs. Charge compensation plays an important role in the self-assembly process, as robust membranes are obtained when the HA and PA solutions have high zeta potentials with opposite charges. The structure of the membranes as revealed by electron microscopy is highly ordered, a consequence of (probably cooperative) electrostatic and hydrophobic interactions. Thus, first, an amorphous layer (region 1, Figure 16) is formed due to a rapid diffusion of the relatively small PA molecules and their electrostatic interaction with HA. This triggers the formation of parallel fibers (region 2) self-assembled from PAs that further interact as a result of electrostatic screening of the HAs. In the self-assembly of sacs, the charge of their hydrophilic surface is decreased by HA molecules, creating a hydrophobic interface that induces fiber ordering and assembly. Then ordered growth of PA-based nanofibers perpendicular to the interface gives rise to a layer that reaches 1.5 μm thickness in just 30 min, and can grow further (*e.g.*, 20 μm in 4 days, Figure 16). Evidently, hydrophobic interactions following charge compensation as well as those responsible for the formation of PA fibers play a critical role in the self-assembly of macroscopic sac membranes. These are mechanically robust in both dry and hydrated states, are permeable to proteins, and have the capability to self-seal defects instantly.[18]

STRONG NONCOVALENT INTERACTIONS AND NANOSCALE DESIGN: UNDERSTANDING THE BASICS AND DEVELOPING THE METHODOLOGIES

How to rationally design a nanostructure based on strong noncovalent interactions? Although some principles have been developed, rational design in supramolecular chemistry remains very challenging.[13] Normally, noncovalent synthesis is based on the idea that the system rapidly equilibrates forming a single thermodynamic product, whose structure is defined ("encoded") by the structure of the primary covalent building block. This is not the case for systems with strong noncovalent bonds, where kinetic trapping may result in several stable assemblies based on a single primary building block. This complicates rational design, but enables achieving pathway-encoded self-assembly, in which the minima on the supramolecular reaction profile correspond to *different* stable structures based on a single building block (Figure 17). Furthermore, if switching of equilibrium and nonequilibrium modes is feasible, it may enable controlled modification of noncovalent assemblies.

Kinetic Control and Mechanisms. Kinetically controlled pathway-dependent self-assembly has been observed for some amphiphilic block copolymers, where strong hydrophobic interactions and slow dynamics of polymer chains result in the formation of kinetic products.[143,177,178] Nonequilibrium self-organization has also been employed for self-assembling inorganic nanoscale objects and organic/inorganic hybrids.[95,179,180]

Usually, noncovalent assemblies based on *well-defined molecular units* equilibrate rapidly under ambient conditions as they are held together by relatively weak noncovalent forces, inadequate for achieving efficient kinetic trapping. However, if *strong noncovalent interactions are involved, kinetic control becomes an important factor* regulating the assembly process.

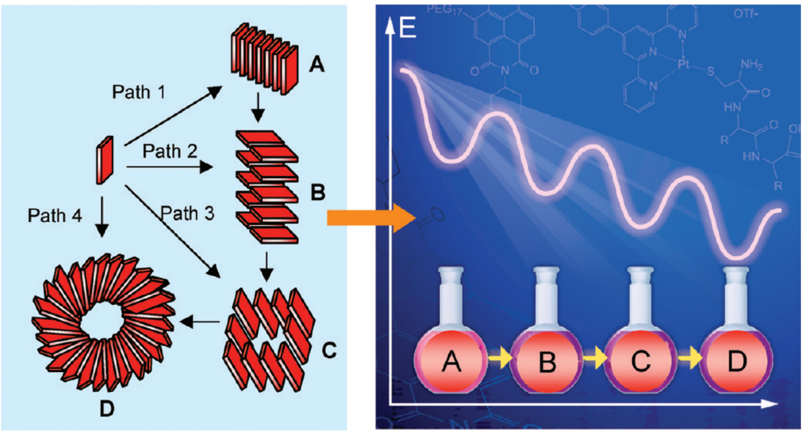

Figure 17. Kinetic control and pathway-dependent self-assembly leading to diversity. Diverse structures (A–D) can be assembled from a single building block (*e.g.*, using different energy inputs in each pathway). Controlled conversion toward lower energies (A→B→C→D) may take place since the assemblies correspond to kinetic minima (and stable kinetic products) along the supramolecular reaction profile. Adapted with permission from ref 176. Copyright 2011 Wiley.

Thus, strong multiple hydrogen bond interactions can lead to stable kinetic assemblies.[102,181–184] Kinetic control was observed in the case of self-assembly based on strong dipolar interactions of merocyanine dyes[185–188] and squarine dyes.[189] Kinetically controlled processes in host–guest systems have been also reported.[190–194] Kinetically controlled self-organization of relatively small molecular amphiphiles in water has been recently shown to control self-replication in dynamic combinatorial libraries.[195,196] Pathway-dependent alignment of supramolecular fibrils over macroscopic scales in aqueous medium has been demonstrated.[197] Pathway-controlled nanoscale self-assembly based on kinetic trapping can represent a powerful tool in noncovalent synthesis,[198] yet it remains largely unexplored especially for well-defined, low molecular weight building blocks. An ability to generate *diverse* stable structures based on a *single molecular unit,* as well as regulating supramolecular transformations in these structures *via* the assembly path would significantly enrich the methodology of noncovalent synthesis.

Slow kinetics of self-assembly in water allowed direct observation of morphological transitions leading to formation of helical ribbons from peptide-based amphiphiles[199] and supramolecular nanotubes from a chiral bolaamphile (Figure 18).[200] Hydrophobic interactions play a key role in these processes. The slow kinetics allows unique insight into the self-assembly through observation of multiple intermediate structures. The evolution and ordering of the assemblies may proceed through Ostwald ripening, which favors the growth of larger elements over the small ones, and occurring *via* exchange of individual monomers between fibers and ribbons.[200,201] Alternatively, the growth may proceed through the fusion of fibers and ribbons. Elucidating the exact mechanism of such assembly processes would be of primary importance for developing rational design strategies toward nanoscale assemblies.

Mechanistic self-assembly studies in equilibrium systems usually rely on concentration or temperature dependence of the self-assembly process.[120,202,203] Significant progress has been made in this area; however, involvement of multiple assembly stages as well as difficulty in obtaining direct structural information at each stage allow only partial mechanistic insight. Yet, experimental and theoretical frameworks for distinguishing cooperative from noncooperative processes have been developed,[204] and the importance of solvent-mediated transformations has been demonstrated.[203] Kinetically controlled processes are beneficial regarding mechanistic research, enabling studies of individual supramolecular transformation steps,[183,188,205] which is not possible in rapidly equilibrating systems. In general, kinetic mechanistic studies of noncovalent self-assembly processes are scarce, while representing a basis for mechanistic understanding in covalent chemistry.

An insight into the mechanism of noncovalent self-assembly was obtained in a kinetic study of merocyanine dye aggregation.[185–188] It was shown that achiral bis(merocyanine) dye **M**[a] (having substantial zwitterionic character) self-assembles into well-defined nanorods through hierarchical supramolecular polymerization (also leading to gelation) based on strong dipolar/π-stacking interactions between the dyes in nonpolar solvents (Figure 19).[206,207] Chiral bis(merocyanine) derivative (*R*,*R*)-**M** results in helical rods as evidenced by atomic force microscopy (AFM) and circular dichroism (CD).[186] Chiral dye **M** exhibited rare supramolecular stereomutation in the course of a complex transition process from initial kinetically self-assembled nanorods (H1) into thermodynamic nanorods (H2).[186] The kinetic studies together with employing "majority rules" methodology (aggregates are coassembled from enantiomeric **M**, (*R*,*R*) and (*S*,*S*), of various enantiomeric excess (ee)) provided an insight into the mechanism of self-assembly processes (Figure 19).[188] The first step involves the self-assembly

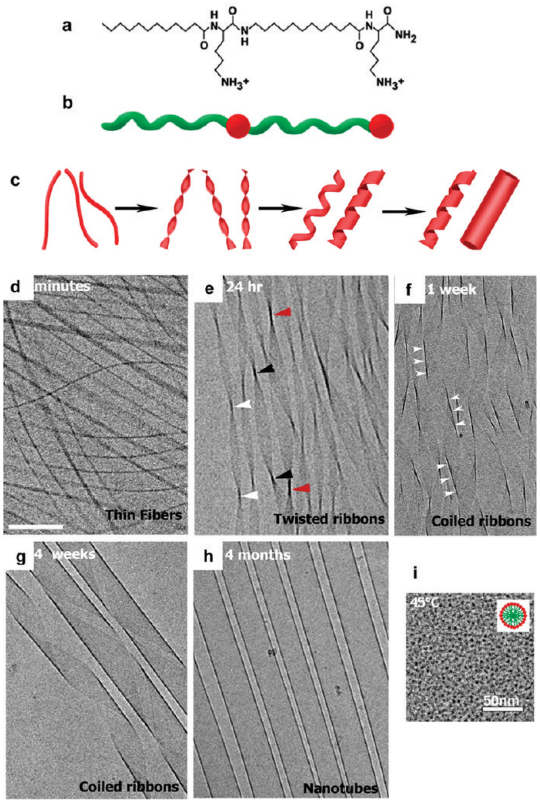

Figure 18. Pathway to nanotubes. (a) Chemical structure of the primary building block. (b) Schematic of the bolaamphiphile unit (red, hydrophilic groups; green, hydrophobic tails) (c) Schematic illustration of the structures. (d–i) Time-evolution cryo-TEM images of the 1-D supramolecular structures forming at 25 °C. Bars =100 nm. (d) Thin micrometer-long fibrils in fresh solution. (e) Twisted ribbons of various widths dominate after 24 h. Colored arrowheads that follow the periodicity along the ribbons length show that the pitch unit of a single ribbon is fairly uniform, and increases with an increase in the ribbon width. (f) Helically coiled ribbons start to form with aging and comprise the dominant nanostructure between 1 week (f) and 4 weeks (g). Alternating arrowheads follow the helical turn and highlight the cylindrical curvature, as opposed to the Gaussian curvature that characterizes the twisted ribbons shown in panel e. The gaps between coils close over time, and (h) after 4 months nanotubes prevail. (i) Spherical micelles of ∼4 nm at 45 °C. Adapted from ref 200. Copyright 2011 American Chemical Society.

of H1-type aggregate precursors (H1*) from the instantly formed unordered oligomer species D. In the subsequent step, the initial H1* precursors grow into elongated H1 nanorods. The kinetics of the coupled two-step self-assembly sequence D→H1*→H1 was evaluated by nonlinear curve fitting. The two steps could be decoupled and analyzed independently, indicating an *autocatalytic nucleation–growth mechanism* in D→H1* process, involving the spontaneous formation of a "critical" nucleus. In the second step H1*→H1, "majority-rules"-directed chiral amplification also occurs through autocatalytic mechanism (the slow kinetics of stereomutation H1→H2 was not studied in detail). These studies underline the importance of autocatalysis and the initial nucleation steps, which define the structure of the assemblies and the rate of self-assembly processes. Thus, understanding the nucleation process in kinetically controlled systems would significantly advance our ability to control the self-assembly outcome. Importantly, kinetic studies on autocatalytic bacteriochlorophyll aggregation allowed for estimation of a critical nucleus size (∼14 molecules),[205] although its structural analysis was not accessible. On the whole, a self-assembly process involves both adding new units to the growing aggregate and internal reorganization of the assembly, while solvent plays an important role in these processes. The complex balance between these parameters necessitates mechanistic research based on kinetics, structural studies, and theory, addressing the course of assembly evolution and the structure of intermediates and transition states.

Recently fluorescence microscopy and computer simulations have been employed to study the surface diffusion mechanisms of multivalent host–guest systems: the spreading of mono-, di-, and trivalent ligand molecules (guest: Ad) on a receptor-functionalized surface (host: CD) of molecular printboards.[208] Kinetic and thermodynamic studies in combination with Monte Carlo simulations showed that the spreading is directional (along a developing gradient of vacant receptor sites) and is strongly dependent on ligand valency and concentration of a competing monovalent receptor in solution. Multiple surface diffusion mechanisms have been identified: walking (binding events without full detachment, involving the closest available receptor), hopping (the same as walking, involving more remote receptors), and flying (full detachment and subsequent rebinding). These findings provide an insight into interfacial recognition mechanisms, underscoring the complexity of noncovalent dynamics.

An important example indicating the importance of kinetic trapping involves formation of hydrogels from synthetic foldamers upon heating. The foldmers that have pleated structure in water driven by the complementary electrostatics and hydrophobics of alternating electron-rich 1,5-dialkoxynapthalene (DAN) and electron-deficient 1,4,5,8-napthalenetetracarboxylic acid diimide (NDI) aromatic units are stable at ambient conditions.[209] However, upon heating to 80 °C irreversible formation of ordered hydrogels was observed, indicating that the DAN-NDI foldamers represent kinetic products that can be converted into more stable ordered networks.[209] Interestingly, conceptually similar unfolding and aggregation of proteins (naturally folded arrays) are responsible for amyloid formation in biological systems.[210]

How to distinguish kinetic form thermodynamic self-assembly? Several observations may indicate formation of kinetically trapped noncovalent assemblies: (1) they undergo change with heating; (2) more

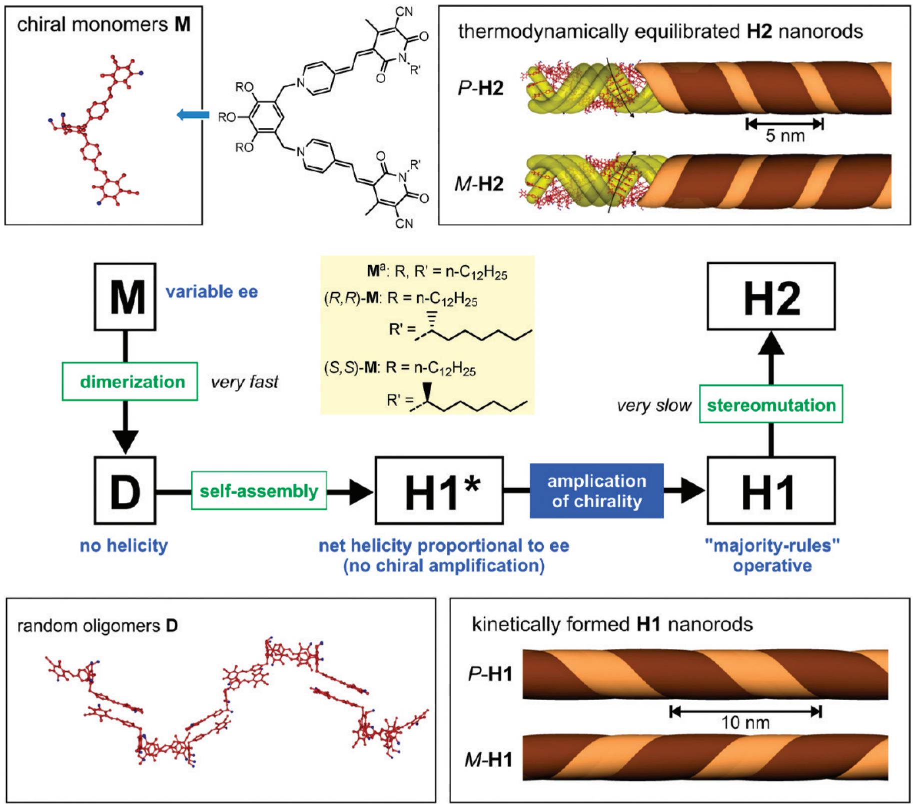

Figure 19. Self-assembly sequence of chiral bis(merocyanine) dyes M into helical nanorods. Instantaneous dimerization of the chromophores leads to oligomeric species D without helical preference, which self-assemble into nanorod precursors H1*, showing a net helicity that is proportional to the ee values of the monomer mixtures. Directed by the "majority-rules" effect, the H1* precursors assemble into H1 nanorods with supramolecular homochirality. Thermodynamically equilibrated H2 nanorods are formed under stereomutation from H1 nanorods in the course of several days. Adapted with permission from ref 188. Copyright 2008 Wiley.

ordered system forms upon addition of a disaggregating solvent; (3) disordered system is formed from well-defined primary building block; (4) more than one stable product is formed; (5) the outcome of the assembly depends on the self-assembly pathway.

Pathway-Dependent Self-Assembly. HBr addition to double bonds normally proceeds according to Markovnikov rule (hydrogen is added to the most substituted carbon); however, when peroxides are added to the reaction, it proceeds by a radical mechanism affording anti-Markovnikov products. Can we manipulate supramolecular transformations in a similar way? In principle, it should be possible if strong noncovalent bonds are involved, resulting in kinetic trapping of different assemblies, whose formation may be regulated through the assembly path. Several systems we described above (sacs and layered gels) owe their complex structure to a particular self-assembly sequence. It was suggested that this synthetic concept can be viewed as "synchronized self-assembly":[198] in such process the final noncovalent assembly structure depends on the sequence of the self-assembly steps, rather than on the thermodynamic end point. Notably, the structures of LBL-deposited systems also depend on assembly sequences that take advantage of strong interactions between oppositely charged electrolytes (see above), or other types of multivalent interactions. Pathway-dependent self-assembly has been also reported for amphiphilic block copolymer systems.[177,211] What is about well-defined *molecular* systems? Apparently, also in this case, if sufficiently strong noncovalent interactions are involved, kinetically controlled and pathway-dependent self-assembly processes are prevalent.

We have demonstrated that well-defined amphiphilic molecular systems based on perylene diimide/peptide conjugates exhibit kinetically controlled self-assembly in aqueous medium, enabling pathway-dependent assembly sequences, in which different organic nanostructures are evolved in a stepwise manner from *a single building block*.[176] Upon assembly of **PDI-[Pt]-CFF** (CFF = cystein−phenylalanine−phenylalanine) in a water/THF = 95:5 (v/v) mixture (10^{-4} M), a weak signal in the CD spectrum is observed, and cryo-TEM reveals the formation of unordered structures (Figure 20). To evolve the system and then induce kinetic trapping, the water/THF = 80:20 (v/v) solution of **PDI[Pt]-CFF** was kept for 40 h at room temperature (disaggregating THF induces equilibration), followed by dilution with water to the conditions identical to the ones used to

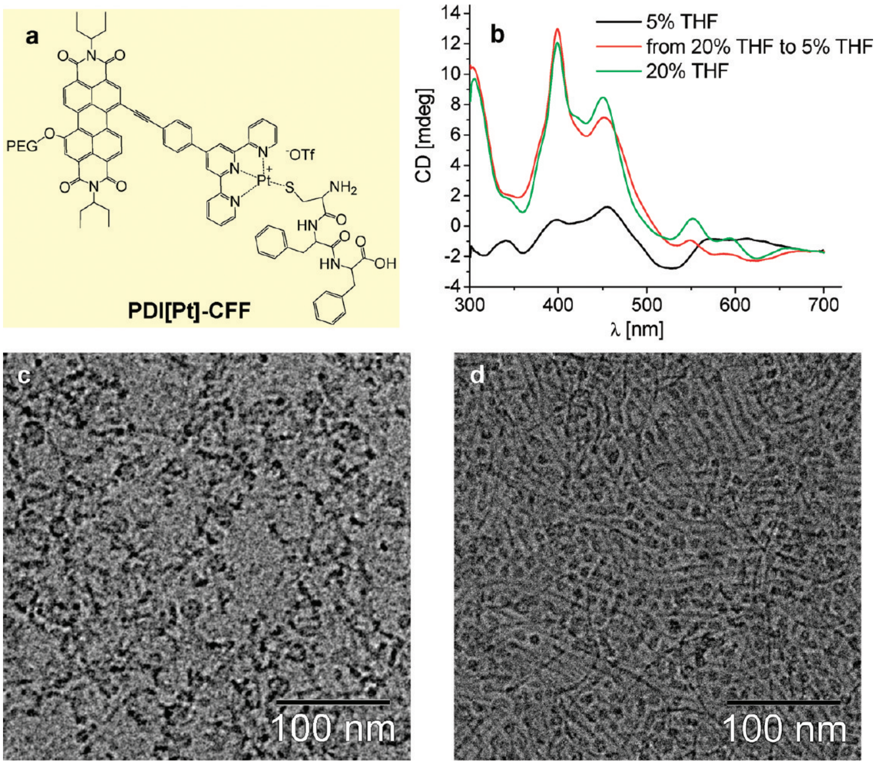

Figure 20. (a) Chemical structure of PDI[Pt]-CFF. (b) CD spectra of 10^{-4} M aqueous solutions of PDI[Pt]-CFF with various THF contents. Black line corresponds to image c, red one to image d. (c) Cryo-TEM image of PDI[Pt]-CFF solution (10^{-4} M) in water/THF = 95:5 (v/v). (d) Cryo-TEM image of PDI[Pt]-CFF solution (10^{-4} M) in water/THF = 95:5 (v/v) following addition of water to water/THF = 80:20 (v/v) PDI[Pt]-CFF solution kept at room temperature for 40 h. Adapted with permission from ref 176. Copyright 2011 Wiley.

form the disordered system described above (95:5 = water/THF, 10^{-4} M). The evolved assembly exhibits a strong signal in the CD spectrum (Figure 20b). The cryo-TEM images reveal the formation of two dominant structural motifs: long fibers, 4.6 ± 0.7 nm in diameter, and at least 200 nm in length, aligned to form ordered arrays (with interfiber distances of 4.7 ± 0.8 nm), and spherical micelles with a diameter of 10.1 ± 1.0 nm (Figure 20d). Both evolved (Figure 20d) and nonevolved (Figure 20c) systems are stable (kinetically trapped), showing no change in structure for at least two months. The similar system with cystein–alanine–alanine (CAA) ligand exhibited formation of various fiberlike structures that can be kinetically trapped, allowing evolution of nanofibers from short disordered ones into long ordered ones.[176] The addition of THF to the kinetically trapped systems leads to the evolution toward a more ordered system. This process can be stopped by the addition of water, and set off again by the addition of THF. Such a lock/unlock sequence can be viewed as a supramolecular reaction that transforms less ordered assemblies into more ordered ones and can be triggered and stopped at any point of evolution.

Pathway-dependent alignment of supramolecular fibrils over macroscopic scales has been controlled through heat treatment: the preheated self-assembled peptide amphiphile fibers form large domains of aligned bundles to afford mechanically stable string gels, while unheated samples do not show gel formation.[197] It was suggested that partial dehydration upon heating is responsible for fusion of the fibers, apparently driven by interfiber hydrophobic interactions.

Kinetic switching between two modes of bisurea surfactant self-assembly has been employed to control the morphology of the aggregates *via* the assembly pathway.[212] Pathway-dependent self-assembly has been also shown to operate in combinatorial libraries involving aromatic macrocycle/peptide conjugates capable of hydrophobic interactions, leading to different products depending on whether the system was shaken or stirred.[195] Such unique mechanoselective chemistry underlines the utility of strong noncovalent bonds for entailing pathway-dependent processes.

Complexity. If we aim at complex functions, structural complexity is required. Hierarchical noncovalent self-assembly addresses this challenge through encoding multiple interaction modes into a primary covalent building block.[3,213] In the case of strong noncovalent interactions, the structure of the system can be encoded also through the assembly pathways (see above). We review here systems based on strong interactions in aqueous media (particularly advantageous in terms of adaptivity and molecular recognition[147]) that exemplify both the challenges and opportunities related to the design of complex noncovalent systems.

For amphiphilc systems in water, Israelachvili packing parameters ($p = \nu/al$, where ν is hydrophobic volume, a is interfacial area at the water interface, and l is chain length normal to the surface per molecule) can be used to predict the structure of the self-assembled systems such as spherical micelles ($p \approx {}^1/_3$), cylindrical micelles ($p \approx {}^1/_2$) and vesicles ($p \approx 1$).[214] However, these parameters were developed for equilibrium systems, and may not adequately describe the nonequilibrium ones. Furthermore, specific structure of the amphiphiles may significantly influence the geometry of the assemblies, resulting in complex structures that cannot be adequately described by the classical "micelle–rod–vesicle–lamella" paradigm.

Recent studies on amphipilic block copolymers revealed that their self-assembly may result in nonclassical structures such as disk-like, toroidal, bicontinuous, and compartmentalized micelles, and an excellent recent review on this topic is available.[145] In particular,

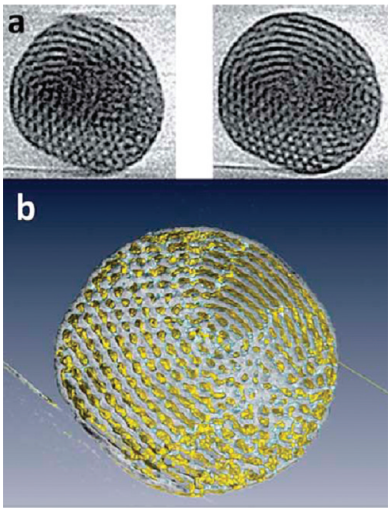

Figure 21. Cryo-EM images: (a) z slices and (b) computer visualization of a 3D reconstruction (using cryo-EM tomography) of a bicontinuous PEO-PODMA particle, 300 nm in diameter, formed at 4 °C. Adapted with permission from refs 145 **and** 219**. Copyright 2011 Royal Society of Chemistry and 2010 American Chemical Society, respectively.**

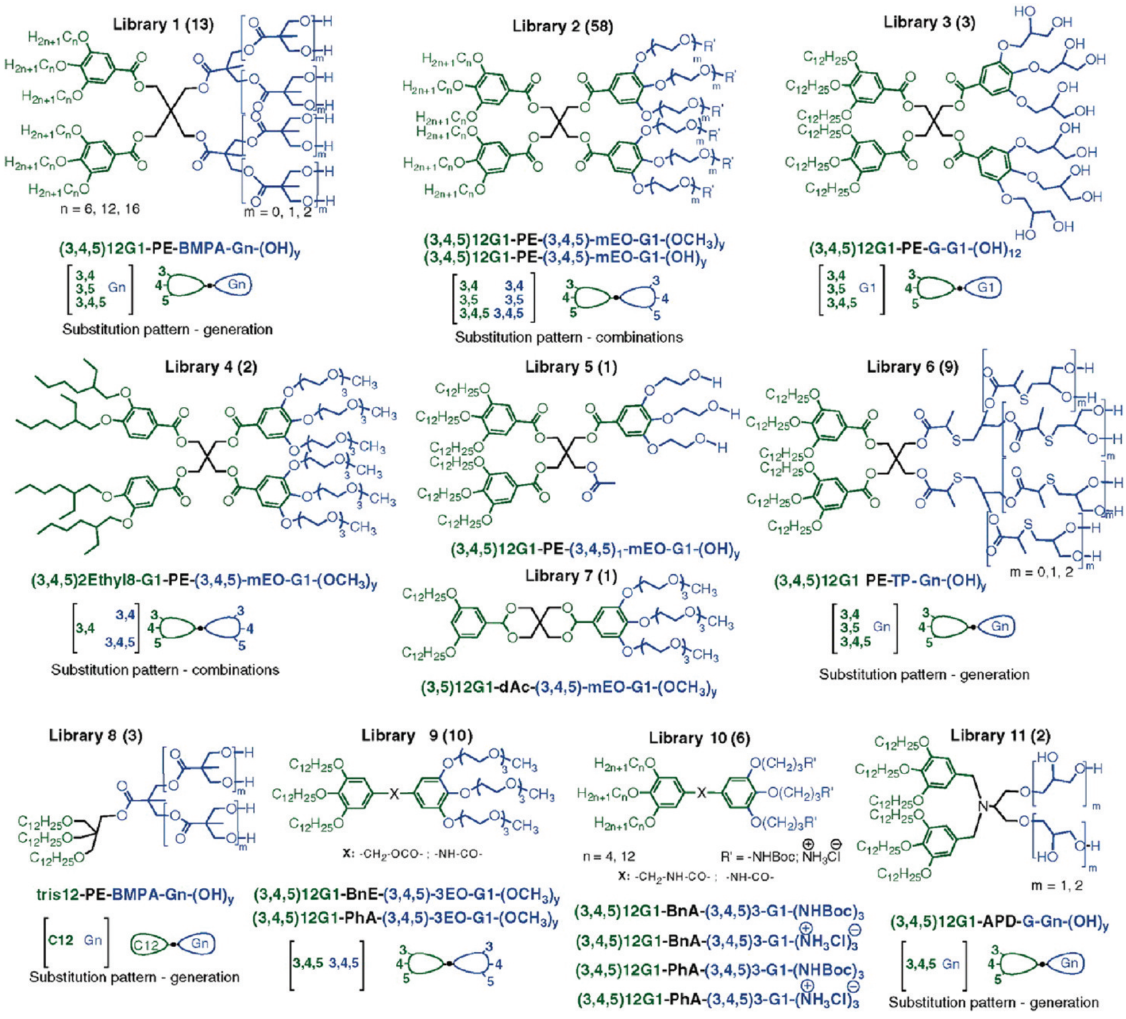

Figure 22. Libraries of amphiphilic Janus dendrimers. Adapted with permission from ref 222. Copyright 2010 American Association for the Advancement of Science.

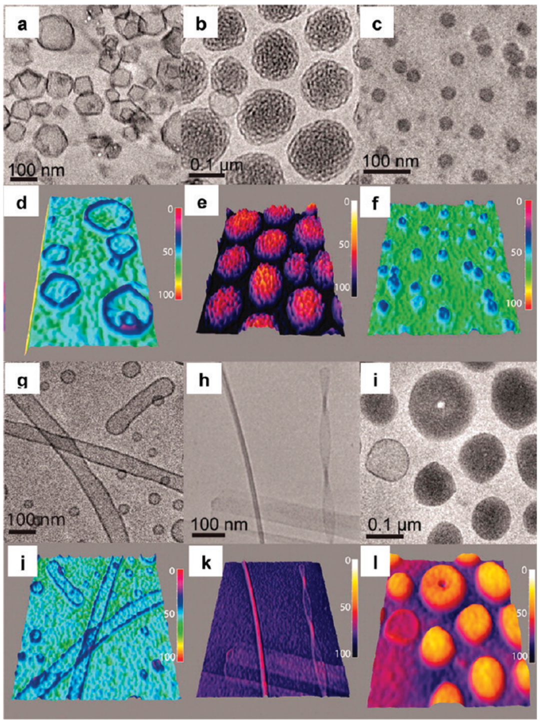

Figure 23. Cryo-TEM and 3D intensity profiles of (a and d) polygonal dendrimersomes from (3,4)12G1-PE-(3,4)-3EO-G1-$(OMe)_4$. (b and e) Bicontinuous cubic particles coexisting with low concentration of spherical dendrimersomes from (3,5)12G1-PE-(3,4,5)-2EO-$(OMe)_6$. (c and f) Micelles from (3,4,5)12G1-PE-BMPA-G2-$(OH)_8$. (g and j) Tubular dendrimersomes from (3,5)12G1-PE-(3,4,5)-3EO-$(OMe)_6$. (h and k) Rodlike, ribbon and helical micelles from *tris*12-PE-BMPA-G2-$(OH)_8$. (i and l) Disklike micelles and toroids from (3,4,5)12G1-PE-(3,5)-3EO-$(OMe)_4$. Adapted with permssion from ref 222. Copyright 2010 American Association for the Advancement of Science.

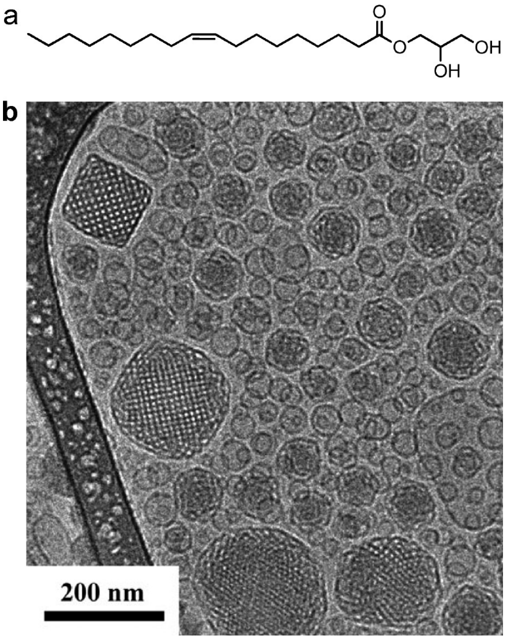

Figure 24. (a) Chemical structure of glycerol mono-olein. (b) Cryo-TEM image of cubosomes, which are the square and rounded particles with internal cubic lattices; also seen are conventional vesicles. Adapted with permission from refs 228 and 229.Copyright 2005 Elsevier and 2001 American Chemical Society, respectively.

multicompartment micelles having core—shell—corona morphology can self-assemble from linear ABC block copolymers, where A is the hydrophilic block and B and C are hydrophobic blocks of poor compatibility that eventually phase-separate.[142] More complex "hamburger" (sandwiched lamellas), segmented, and "raspberry" (small spheres embedded in larger ones) morphologies were achieved with miktoarm and star block coplymers.[142,215−218] Remarkably complex, ordered structures were observed in bicontinuous systems. Thus, the semicrystalline AB(C) comb-like block copolymer poly(ethylene oxide)-*block*-poly(octadecyl methacrylate) (PEO_{39}-*b*-$PODMA_{17}$, PEO-PODMA)[219] forms bicontinuous spherical structures by the slow addition of water to THF solutions and subsequent dialysis against water. Highly ordered systems were observed at 4 °C, and their 3D structure was revealed by cryo-TEM tomography (Figure 21). The structure was rationalized using thermodynamic arguments and a modified packing parameter model.

Kinetic control was employed to create complex one-dimensional structures (multicompartment cylinders with phase-separated cores and the cylindrical nanostructures with alternating nanostructured gold/organic layers) based on linear poly(acrylic acid)-*block*-poly(methyl acrylate)-*block*-polystyrene (PAA-*b*-PMA-*b*-PS) triblock copolymer.[143] The block copolymers are assembled *via* specific assembly pathways through a combination of solvent mixing and the complexation of a charged, hydrophilic block with divalent, organic counterions. The resultant assemblies are kinetically trapped, yet stable, because strong noncovalent interactions (electrostatic and hydrophobic) prevent the system from thermodynamic equilibration.

"Nonclassical" self-assembly is not limited to polymers. Well-defined small amphiphilic molecules are also able to self-assemble into complex structures. For example, it was shown that aromatic amphiphiles may give rise to a high degree of order in aqueous systems due to their well-defined rigid geometry and the ability to create both face-to-face and T-stacked motifs.[220,221] Recently, it has been shown that relatively uniform complex structures (dendrimerosomes) self-assemble from aromatic dendrimer amphiphiles (Figures 22, 23).[222] Libraries of dendritic amphipiles with systematically varied structures (Figure 22) allowed access to a vast structural space, which resulted from the aqueous assembly of well-defined building blocks (Figure 23). Apparently, a relatively rigid 3D structure of the dendrimers is responsible for the observed structural diversity, reflecting more complex assembly modes than could be predicted based on packing parameters and spontaneous curvature arguments. Formation of more than one type of assemblies (Figure 23g–l) may indicate involvement of kinetically controlled self-assembly in some of the described systems. Although at present the assembly outcome in dendrimer systems is difficult to predict from the molecular structure, it is evident that self-assembly in aqueous medium that involves rigid well-defined building blocks leads to complex noncovalent nanoarrays, enabling an entry into a new class of complex systems based on relatively small molecules. Such systems proved to possess unique functionalities: complex self-assembled channel structures based on π-stacking/hydrophobic interactions of well-defined aromatic amphiphiles have been utilized in artificial photosynthetic systems[223,224] and in water/proton transferring pores.[225,226] Switchable supramolecular nanotubes have been reported to self-assemble from peptide–dendron hybrids.[227]

Aqueous self-assembly of polyalcohol-based amphiphiles such as glycerol mono-olein or phytantriol leads to cubosomes—bicontinuous nanostructures having cubic morphology created by bilayers with complex periodic structures (Figure 24).[228,229] These systems exemplify both the questions and opportunities in aqueous self-assembly: while the mechanism of the assembly process is yet to be elucidated, the possibility to obtain complex structures based on simple molecular units is tantalizing. Kinetic control has been suggested to play an important role in cubosome formation.[228] Hexasomes have been also shown to self-assemble from several polyalcohol-based amphiphiles.[230]

As summarized by Holder and Sommerdijk, "Whilst the Israelachvili packing parameter model is still of considerable use and can be utilized in the design of aggregates... tailored chemical and physical interactions in the self-assembled structures can over-ride this model and induce aggregate morphologies that might otherwise remain inaccessible".[145]

Complexity can be also achieved by self-assembly of more than one component. Dynamic combinatorial libraries and systems chemistry address self-assembly in multicomponent systems[231,232] Understanding of such systems is only starting to emerge, yet, ultimately, they provide powerful framework for achieving complexity. For example, self-sorting in multicomponent systems[192,233–235] may provide means for creating well-defined diverse coexisting assemblies and separating incompatible reagents.

The importance of nonequilibrium self-assembly for achieving complexity is evident from the above-mentioned examples, and far-from-equilibrium self-assembly may lead to even more complex systems.[95,236] Systematic research strategies addressing far-from-equilibrium molecular self-assembly involving predesigned energy dissipation are yet to be developed.

There is growing evidence that noncovalent systems, more complex and robust than previously thought, result from self-assembly in aqueous medium. The factors leading to complexity include rigid well-defined structure of building blocks, internal phase separation, and kinetic trapping. Notably, a high degree of structural complexity and diversity is achievable through simple manipulation of building block chemistry and self-assembly pathways.

CONCLUSIONS AND PROSPECTS

Multiple noncovalent interactions can reach significant strengths, retaining adaptive properties characteristic of noncovalent bonding. Noncovalent materials based on multiple host–guest interactions exhibit mechanical properties similar to the ones of conventional polymers.[83] Multiple electrostatic interactions between organic and inorganic moieties resulted in exceptionally mechanically robust yet self-healing hydrogels.[19] Hydrophobic interactions are sufficiently strong to hold together an ultrafiltration membrane, whose performance is similar to its covalent counterparts.[20] Furthermore, organic noncovalent nanostructures can compete in stiffness with steel.[132]

While robustness of noncovalent materials has been unequivocally demonstrated, their rational design is challenging. Multiple bonding modes, low degree of directionality, and complex interactions with solvents preclude accurate retrosynthetic analysis. Also, mechanistic information is not readily available for self-assembly processes, while constituting a basis for rational design in covalent chemistry. In this respect, strong noncovalent bonding, resulting in slow kinetics, is beneficial for mechanistic studies. Recent studies of relatively slow self-assembly processes allowed observation of intermediates in noncovalent nanofiber,[176] nanoribbon,[199] and nanotube[200] formation. Kinetic studies also revealed the importance of the autocatalysis and nucleation–growth mechanism.[188] The complexity of transformations in self-assembled systems calls for an adequate mechanistic description that is currently lacking. A number of key mechanistic aspects must be addressed: structure of intermediates and transition states, solvent influence, identification of rate-determining steps, and structure of the initially formed nucleus. Importantly, the advances in electron microscopy techniques, and especially in cryo-TEM,[237–239] have significantly enhanced our ability to directly image noncovalent structures in solution, and observe them as they evolve,[176,199,200] which is critical for adequate mechanistic research.

Kinetically controlled self-assembly appears to be a rather general phenomenon in the case of strong noncovalent bonding. This is of primary importance, introducing a paradigm shift in the field of noncovalent synthesis—a departure from a conventional equilibrium methodology, where a single thermodynamic assembly is expected. Nonequilibrium self-assembly presents both challenges and opportunities: on one hand, kinetically trapped systems are difficult to design, and complex mixtures of kinetic products are difficult to analyze; on the other hand, diverse nanoarrays may be assembled from a single building block and the self-assembly outcome may be regulated *via* its pathway.[198] Furthermore, switching of kinetic and thermodynamic regimes enables triggering and interrupting self-assembly processes leading to controlled evolution of noncovalent arrays.[176] Thus, noncovalent synthesis traditionally benefiting from the reversibility of the assemblies can also take advantage of kinetic trapping, analogously to covalent methods. Pathway-dependent self-assembly has been successfully implemented in a number of systems, emerging as a powerful methodology of noncovalent synthesis at the nanoscale.[18,143,174,176,197]

Systems self-assembled in aqueous medium and based on multiple noncovalent interactions can form nanoscale arrays with astonishingly complex structures.[7,145,228] The interplay of kinetic and thermodynamic factors leading to such complexity is yet to be understood, but the ability to assemble complex systems from relatively simple building blocks is appealing. Water, bringing about strong hydrophobic interactions as well as unique molecular recognition,[9,139−141,147] is an especially advantageous medium (and active component) for creating complex, robust, and adaptive systems.[240] Water-based biological systems are inspiring, while the large variety of artificial building blocks unavailable to living organisms may lead to systems superior in robustness and having functions not present in nature.

Self-assembled noncovalent systems have been successfully utilized in a variety of biomedical applications.[165,175,241−244] Recent examples suggest that additional applications are possible, where noncovalent nanostructured systems may perform as well as (or better than) conventional polymer-based materials. For example, noncovalent systems have been utilized as stimuli-responsive polymeric materials,[2,12,15,110,245] macroscopic sacs,[18] and filtration membranes.[20] Recyclable, self-healing, multifunctional noncovalent materials enable unique applications and may replace some conventional covalent systems.

There are several key challenges that we need to address in order to rationally design and synthesize robust noncovalent nanomaterials. Mechanistic insight would be important to create a general framework for systematic synthetic approaches to complex noncovalent arrays. In this respect, understanding and controlling nucleation in kinetically controlled processes appear to be critical for efficient structural design, necessitating detailed kinetic studies, trapping and characterization of the nuclei, and theoretical simulations. Developing approaches to pathway-dependent self-assembly where a supramolecular reaction can be activated and stopped, resulting in the desired outcome would enable a rich palette of synthetic strategies. Studying mechanical properties and correlating them with the assembly structure and the noncovalent bond strength will result in better understanding of molecular mechanisms related to macroscopic robustness. Finally, identifying and targeting applications and functions where noncovalent materials can outperform the covalent ones is key to the emerging paradigm shift related to adaptive multifunctional and recyclable materials. Strong noncovalent interactions are beneficial in regards to all the above-mentioned aspects.

Robust yet adaptive supramolecular systems create a new paradigm: fully recyclable materials with practically unlimited life-span, and multifunctionality that can be controlled by external stimuli. The range of potential applications is enticing, and the following questions exemplify exciting prospects in the field. Is it possible to fabricate a coating that will self-heal upon damage, change color on demand, and be permeable only to certain types of molecules? Can we produce supramolecular plastic-type materials that are recycled within minutes? Can one create a universal membrane with reversibly tunable pore size that can be employed to separate molecules, nanoparticles, and (bio)-polymers? In targeting these applications, water-based materials are especially appealing as they are environmentally friendly and take advantage of unique properties of water. Ultimately, robust water-based noncovalent arrays that can be evolved (possibly far from equilibrium) into a multitude of nanoscale architectures may lead to synthetic materials having complexity and functionality akin or superior to those of biological systems.

Acknowledgment. This work was supported the Gerhardt M. J. Schmidt Minerva Center for Supramolecular Architectures, Israel Science Foundation, and the Helen and Martin Kimmel Center for Molecular Design. I am grateful to C. Faul, D. Reinhoudt, F. Würthner, D. Danino, C. Schmuck, M. Grinstaff, R. Klajn, and I. Rousso for providing their original artwork, to E. Krieg and R. Klajn for critical reading of the manuscript, and to H. Weissman for his help with the graphics. B. R. is the incumbent of the Abraham and Jennie Fialkow Career Development Chair.

REFERENCES AND NOTES

1. Stupp, S. I.; LeBonheur, V.; Walker, K.; Li, L. S.; Huggins, K. E.; Keser, M.; Amstutz, A. Supramolecular Materials: Self-Organized Nanostructures. *Science* **1997**, *276*, 384–389.
2. Brunsveld, L.; Folmer, B. J. B.; Meijer, E. W.; Sijbesma, R. P. Supramolecular Polymers. *Chem. Rev.* **2001**, *101*, 4071–4097.
3. Elemans, J. A. A. W.; Rowan, A. E.; Nolte, R. J. M. Mastering Molecular Matter. Supramolecular Architectures by Hierarchical Self-Assembly. *J. Mater. Chem.* **2003**, *13*, 2661–2670.
4. Reinhoudt, D. N.; Crego-Calama, M. Synthesis Beyond the Molecule. *Science* **2002**, *295*, 2403–2407.
5. Lehn, J.-M. Toward Self-Organization and Complex Matter. *Science* **2002**, *295*, 2400–2403.

6. Whitesides, G. M.; Grzybowski, B. Self-Assembly at All Scales. *Science* **2002**, *295*, 2418–2421.
7. Rosen, B. M.; Wilson, C. J.; Wilson, D. A.; Peterca, M.; Imam, M. R.; Percec, V. Dendron-Mediated Self-Assembly, Disassembly, and Self-Organization of Complex Systems. *Chem. Rev.* **2009**, *109*, 6275–6540.
8. Chatzia, E. G.; Koeniga, J. L. Morphology and Structure of Kevlar Fibers: A Review. *Polym.-Plast. Technol.* **1987**, *26*, 229–270.
9. Ball, P. Water as an Active Constituent in Cell Biology. *Chem. Rev.* **2008**, *108*, 74–108.
10. Carlisle, J. R.; Weck, M., Functional Materials *via* Multiple Noncovalent Interactions. In *Functional Organic Materials: Syntheses, Strategies and Applications*; Müller, T. J. J., Bunz, U. H. F., Eds.; Wiley-VCH: Weinheim, Germany, 2007; pp 261−294.
11. Mulder, A.; Huskens, J.; Reinhoudt, D. N. Multivalency in Supramolecular Chemistry and Nanofabrication. *Org. Biomol. Chem.* **2004**, *2*, 3409–3424.
12. Wojtecki, R. J.; Meador, M. A.; Rowan, S. J. Using the Dynamic Bond To Access Macroscopically Responsive Structurally Dynamic Polymers. *Nat. Mater.* **2011**, *10*, 14–27.
13. Stoddart, J. F. Thither Supramolecular Chemistry? *Nat. Chem.* **2009**, *1*, 14–15.
14. Sijbesma, R. P.; Beijer, F. H.; Brunsveld, L.; Folmer, B. J. B.; Hirschberg, J. H. K. K.; Lange, R. F. M.; Lowe, J. K. L.; Meijer, E. W. Reversible Polymers Formed from Self-Complementary Monomers Using Quadruple Hydrogen Bonding. *Science* **1997**, *278*, 1601–1604.
15. Greef, T. F. A.; Meijer, E. W. Materials Science—Supramolecular Polymers. *Nature* **2008**, *453*, 171–173.
16. Zimmerman, S. C.; Zeng, F.; Reichert, D. E. C.; Kolotuchin, S. V. Self-Assembling Dendrimers. *Science* **1996**, *271*, 1095–1098.
17. Ling, X. Y.; Reinhoudt, D. N.; Huskens, J. From Supramolecular Chemistry to Nanotechnology: Assembly of 3D Nanostructures. *Pure Appl. Chem.* **2009**, *81*, 2225–2233.
18. Capito, R. M.; Azevedo, H. S.; Velichko, Y. S.; Mata, A.; Stupp, S. I. Self-Assembly of Large and Small Molecules into Hierarchically Ordered Sacs and Membranes. *Science* **2008**, *319*, 1812–1816.
19. Wang, Q.; Mynar, J. L.; Yoshida, M.; Lee, E.; Lee, M.; Okuro, K.; Kinbara, K.; Aida, T. High-Water-Content Mouldable Hydrogels by Mixing Clay and a Dendritic Molecular Binder. *Nature* **2010**, *463*, 339–343.
20. Krieg, E.; Weissman, H.; Shirman, E.; Shimoni, E.; Rybtchinski, B. A Recyclable Supramolecular Membrane for Size-Selective Separation of Nanoparticles. *Nat. Nanotechnol.* **2011**, *6*, 141–146.
21. Burnworth, M.; Tang, L. M.; Kumpfer, J. R.; Duncan, A. J.; Beyer, F. L.; Fiore, G. L.; Rowan, S. J.; Weder, C. Optically Healable Supramolecular Polymers. *Nature* **2011**, *472*, 334–U230.
22. Hofmeier, H.; Schubert, U. S. Recent Developments in the Supramolecular Chemistry of Terpyridine−Metal Complexes. *Chem. Soc. Rev.* **2004**, *33*, 373–399.
23. Dobrawa, R.; Würthner, F. Metallosupramolecular Approach toward Functional Coordination Polymers. *J. Polym. Sci., Part A* **2005**, *43*, 4981–4995.
24. Friese, V. A.; Kurth, D. G. From Coordination Complexes to Coordination Polymers through Self-Assembly. *Curr. Opin. Colloid Interface* **2009**, *14*, 81–93.
25. Yang, S. K.; Ambade, A. V.; Weck, M. Main-Chain Supramolecular Block Copolymers. *Chem. Soc. Rev.* **2011**, *40*, 129–137.
26. Fox, J. D.; Rowan, S. J. Supramolecular Polymerizations and Main-Chain Supramolecular Polymers. *Macromolecules* **2009**, *42*, 6823–6835.
27. Corbett, P. T.; Leclaire, J.; Vial, L.; West, K. R.; Wietor, J. L.; Sanders, J. K. M.; Otto, S. Dynamic Combinatorial Chemistry. *Chem. Rev.* **2006**, *106*, 3652–3711.
28. Tennyson, A. G.; Norris, B.; Bielawski, C. W. Structurally Dynamic Conjugated Polymers. *Macromolecules* **2010**, *43*, 6923–6935.
29. Prins, L. J.; Scrimin, P. Covalent Capture: Merging Covalent and Noncovalent Synthesis. *Angew. Chem., Int. Ed.* **2009**, *48*, 2288–2306.
30. Macgillivray, L. R.; Papaefstathiou, G. S.; Friscic, T.; Hamilton, T. D.; Bucar, D. K.; Chu, Q.; Varshney, D. B.; Georgiev, I. G. Supramolecular Control of Reactivity in the Solid State: From Templates to Ladderanes to Metal−Organic Frameworks. *Acc. Chem. Res.* **2008**, *41*, 280–291.
31. Faul, C. F. J.; Antonietti, M. Ionic Self-Assembly: Facile Synthesis of Supramolecular Materials. *Adv. Mater.* **2003**, *15*, 673–683.
32. Rehm, T. H.; Schmuck, C. Ion-Pair Induced Self-Assembly in Aqueous Solvents. *Chem. Soc. Rev.* **2010**, *39*, 3597–3611.
33. Zhang, T.; Brown, J.; Oakley, R. J.; Faul, C. F. J. Towards Functional Nanostructures: Ionic Self-Assembly of Polyoxometalates and Surfactants. *Curr. Opin. Colloid Interface* **2009**, *14*, 62–70.
34. Wathier, M.; Grinstaff, M. W. Synthesis and Properties of Supramolecular Ionic Networks. *J. Am. Chem. Soc.* **2008**, *130*, 9648–9649.
35. Wathier, M.; Grinstaff, M. W. Synthesis and Creep-Recovery Behavior of a Neat Viscoelastic Polymeric Network Formed through Electrostatic Interactions. *Macromolecules* **2010**, *43*, 9529–9533.
36. Craig, S. L. From Ionic Liquids to Supramolecular Polymers. *Angew. Chem., Int. Ed.* **2009**, *48*, 2645–2647.
37. Schneider, H. J. Linear Free-Energy Relationships and Pairwise Interactions in Supramolecular Chemistry. *Chem. Soc. Rev.* **1994**, *23*, 227–234.
38. Grawe, T.; Schrader, T.; Zadmard, R.; Kraft, A. Self-Assembly of Ball-Shaped Molecular Complexes in Water. *J. Org. Chem.* **2002**, *67*, 3755–3763.
39. Zadmard, R.; Schrader, T.; Grawe, T.; Kraft, A. Self-Assembly of Molecular Capsules in Polar Solvents. *Org. Lett.* **2002**, *4*, 1687–1690.
40. Fiammengo, R.; Timmerman, P.; de Jong, F.; Reinhoudt, D. N. Highly Stable Cage-like Complexes by Self-Assembly of Tetracationic Zn(II) Porphyrinates and Tetrasulfonatocalix-[4]arenes in Polar Solvents. *Chem. Commun* **2000**, 2313–2314.
41. Corbellini, F.; Di Costanzo, L.; Crego-Calama, M.; Geremia, S.; Reinhoudt, D. N. Guest Encapsulation in a Water-Soluble Molecular Capsule Based on Ionic Interactions. *J. Am. Chem. Soc.* **2003**, *125*, 9946–9947.
42. Oshovsky, G. V.; Reinhoudt, D. N.; Verboom, W. Triple-Ion Interactions for the Construction of Supramolecular Capsules. *J. Am. Chem. Soc.* **2006**, *128*, 5270–5278.
43. Decher, G. Fuzzy Nanoassemblies: Toward Layered Polymeric Multicomposites. *Science* **1997**, *277*, 1232–1237.
44. Ikkala, O.; Ten Brinke, G. Hierarchical Self-Assembly in Polymeric Complexes: Towards Functional Materials. *Chem. Commun.* **2004**, 2131–2137.
45. Voets, I. K.; de Keizer, A.; Stuart, M. A. C. Complex Coacervate Core Micelles. *Adv. Colloid Interface Sci.* **2009**, *147*−*48*, 300–318.
46. Gröhn, F. Soft Matter Nanoparticles with Various Shapes and Functionalities Can Form through Electrostatic Self-Assembly. *Soft Matter* **2010**, *6*, 4296–4302.
47. Zhang, X.; Chen, H.; Zhang, H. Y. Layer-by-Layer Assembly: From Conventional to Unconventional Methods. *Chem. Commun.* **2007**, 1395–1405.
48. Schlenoff, J. B. Retrospective on the Future of Polyelectrolyte Multilayers. *Langmuir* **2009**, *25*, 14007–14010.
49. Ma, Y. J.; Hempenius, M. A.; Vancso, G. J. Electrostatic Assembly with Poly(ferrocenylsilanes). *J. Inorg. Organomet. Polym. Mater.* **2007**, *17*, 3–18.
50. Srivastava, S.; Kotov, N. A. Composite Layer-by-Layer (LBL) Assembly with Inorganic Nanoparticles and Nanowires. *Acc. Chem. Res.* **2008**, *41*, 1831–1841.
51. Guldi, D. M.; Prato, M. Electrostatic Interactions by Design. Versatile Methodology towards Multifunctional Assemblies/Nanostructured Electrodes. *Chem. Commun.* **2004**, 2517–2525.

52. Podsiadlo, P.; Kaushik, A. K.; Arruda, E. M.; Waas, A. M.; Shim, B. S.; Xu, J. D.; Nandivada, H.; Pumplin, B. G.; Lahann, J.; Ramamoorthy, A.; Kotov, N. A. Ultrastrong and Stiff Layered Polymer Nanocomposites. *Science* **2007**, *318*, 80–83.
53. Mandal, S.; Lee, M. V.; Hill, J. P.; Vinu, A.; Ariga, K. Recent Developments in Supramolecular Approach for Nanocomposites. *J. Nanosci. Nanotechnol.* **2010**, *10*, 21–33.
54. Cohen Stuart, M. A.; Huck, W. T. S.; Genzer, J.; Muller, M.; Ober, C.; Stamm, M.; Sukhorukov, G. B.; Szleifer, I.; Tsukruk, V. V.; Urban, M.; Winnik, F.; Zauscher, S.; Luzinov, I.; Minko, S. Emerging Applications of Stimuli-Responsive Polymer Materials. *Nat. Mater.* **2010**, *9*, 101–113.
55. Guan, Y.; Antonietti, M.; Faul, C. F. J. Ionic Self-Assembly of Dye-Surfactant Complexes: Influence of Tail Lengths and Dye Architecture on the Phase Morphology. *Langmuir* **2002**, *18*, 5939–5945.
56. Faul, C. F. J.; Antionietti, M. Facile Synthesis of Optically Functional, Highly Organized Nanostructures: Dye-Surfactant Complexes. *Chem.—Eur. J.* **2002**, *8*, 2764–2768.
57. Willerich, I.; Gröhn, F. Switchable Nanoassemblies from Macroions and Multivalent Dye Counterions. *Chem.—Eur. J.* **2008**, *14*, 9112–9116.
58. Guan, Y.; Yu, S. H.; Antonietti, M.; Bottcher, C.; Faul, C. F. J. Synthesis of Supramolecular Polymers by Ionic Self-Assembly of Oppositely Charged Dyes. *Chem.—Eur. J.* **2005**, *11*, 1305–1311.
59. Shelnutt, J. A.; Medforth, C. J.; Wang, Z. C.; Martin, K. E.; Song, Y. J.; Jacobsen, J. L. Self-Assembled Porphyrin Nanostructures. *Chem. Commun.* **2009**, 7261–7277.
60. Schmuck, C.; Wienand, W. Highly Stable Self-Assembly in Water: Ion Pair Driven Dimerization of a Guanidiniocarbonyl Pyrrole Carboxylate Zwitterion. *J. Am. Chem. Soc.* **2003**, *125*, 452–459.
61. Rehm, T.; Schmuck, C. How to Achieve Self-Assembly in Polar Solvents Based on Specific Interactions? Some General Guidelines. *Chem. Commun.* **2008**, 801–813.
62. Rehm, T.; Stepanenko, V.; Zhang, X.; Würthner, F.; Gröhn, F.; Klein, K.; Schmuck, C. A New Type of Soft Vesicle-Forming Molecule: An Amino Acid Derived Guanidiniocarbonyl Pyrrole Carboxylate Zwitterion. *Org. Lett.* **2008**, *10*, 1469–1472.
63. Rodler, F.; Linders, J.; Fenske, T.; Rehm, T.; Mayer, C.; Schmuck, C. pH-Switchable Vesicles from a Serine-Derived Guanidiniocarbonyl Pyrrole Carboxylate Zwitterion in DMSO. *Angew. Chem., Int. Ed.* **2010**, *49*, 8747–8750.
64. Wang, Y. F.; Weinstock, I. A. Cation Mediated Self-Assembly of Inorganic Cluster Anion Building Blocks. *Dalton Trans.* **2010**, *39*, 6143–6152.
65. Yin, P. C.; Li, D.; Liu, T. B. Counterion Interaction and Association in Metal-Oxide Cluster Macroanionic Solutions and the Consequent Self-Assembly. *Isr. J. Chem.* **2011**, *51*, 191–204.
66. Bishop, K. J. M.; Wilmer, C. E.; Soh, S.; Grzybowski, B. A. Nanoscale Forces and Their Uses in Self-Assembly. *Small* **2009**, *5*, 1600–1630.
67. Ofir, Y.; Samanta, B.; Rotello, V. M. Polymer and Biopolymer Mediated Self-Assembly of Gold Nanoparticles. *Chem. Soc. Rev.* **2008**, *37*, 1814–1823.
68. Lim, S. I.; Zhong, C. J. Molecularly Mediated Processing and Assembly of Nanoparticles: Exploring the Interparticle Interactions and Structures. *Acc. Chem. Res.* **2009**, *42*, 798–808.
69. Nie, Z. H.; Petukhova, A.; Kumacheva, E. Properties and Emerging Applications of Self-Assembled Structures Made from Inorganic Nanoparticles. *Nat. Nanotechnol.* **2010**, *5*, 15–25.
70. Klajn, R.; Stoddart, J. F.; Grzybowski, B. A. Nanoparticles Functionalised with Reversible Molecular and Supramolecular Switches. *Chem. Soc. Rev.* **2010**, *39*, 2203–2237.
71. Walther, A.; Bjurhager, I.; Malho, J. M.; Ruokolainen, J.; Berglund, L.; Ikkala, O. Supramolecular Control of Stiffness and Strength in Lightweight High-Performance Nacre-Mimetic Paper with Fire-Shielding Properties. *Angew. Chem., Int. Ed.* **2010**, *49*, 6448–6453.
72. Rao, J. H.; Lahiri, J.; Isaacs, L.; Weis, R. M.; Whitesides, G. M. A Trivalent System from Vancomycin−D-Ala-D-Ala with Higher Affinity than Avidin-Biotin. *Science* **1998**, *280*, 708–711.
73. Badjic, J. D.; Nelson, A.; Cantrill, S. J.; Turnbull, W. B.; Stoddart, J. F. Multivalency and Cooperativity in Supramolecular Chemistry. *Acc. Chem. Res.* **2005**, *38*, 723–732.
74. Ravoo, B. J.; Voskuhl, J. Molecular Recognition of Bilayer Vesicles. *Chem. Soc. Rev.* **2009**, *38*, 495–505.
75. Rao, J. H.; Lahiri, J.; Weis, R. M.; Whitesides, G. M. Design, Synthesis, and Characterization of a High-Affinity Trivalent System Derived from Vancomycin and L-Lys-D-Ala-D-Ala. *J. Am. Chem. Soc.* **2000**, *122*, 2698–2710.
76. Crespo-Biel, O.; Ravoo, B. J.; Reinhoudt, D. N.; Huskens, J. Noncovalent Nanoarchitectures on Surfaces: From 2D to 3D nanostructures. *J. Mater. Chem.* **2006**, *16*, 3997–4021.
77. Huskens, J.; Deij, M. A.; Reinhoudt, D. N. Attachment of Molecules at a Molecular Printboard by Multiple Host−Guest Interactions. *Angew. Chem., Int. Ed.* **2002**, *41*, 4467–4471.
78. Nijhuis, C. A.; Huskens, J.; Reinhoudt, D. N. Binding Control and Stoichiometry of Ferrocenyl Dendrimers at a Molecular Printboard. *J. Am. Chem. Soc.* **2004**, *126*, 12266–12267.
79. Huskens, J.; Ling, X. Y.; Reinhoudt, D. N. Reversible Attachment of Nanostructures at Molecular Printboards through Supramolecular Glue. *Chem. Mater.* **2008**, *20*, 3574–3578.
80. Wolf, H.; Ling, X. Y.; Malaquin, L.; Reinhoudt, D. N.; Huskens, J. An *in Situ* Study of the Adsorption Behavior of Functionalized Particles on Self-Assembled Monolayers *via* Different Chemical Interactions. *Langmuir* **2007**, *23*, 9990–9999.
81. Crespo-Biel, O.; Dordi, B.; Reinhoudt, D. N.; Huskens, J. Supramolecular Layer-by-Layer Assembly: Alternating Adsorptions of Guest- and Host-Functionalized Molecules and Particles Using Multivalent Supramolecular Interactions. *J. Am. Chem. Soc.* **2005**, *127*, 7594–7600.
82. Ling, X. Y.; Phang, I. Y.; Maijenburg, W.; Schonherr, H.; Reinhoudt, D. N.; Vancso, G. J.; Huskens, J. Free-Standing 3D Supramolecular Hybrid Particle Structures. *Angew. Chem., Int. Ed.* **2009**, *48*, 983–985.
83. Ling, X. Y.; Phang, I. Y.; Schonherr, H.; Reinhoudt, D. N.; Vancso, G. J.; Huskens, J. Freestanding 3D Supramolecular Particle Bridges: Fabrication and Mechanical Behavior. *Small* **2009**, *5*, 1428–1435.
84. Nijhuis, C. A.; Wimbush, K. S.; Reus, W. F.; van der Wiel, W. G.; Reinhoudt, D. N.; Whitesides, G. M.; Velders, A. H. Control over Rectification in Supramolecular Tunneling Junctions. *Angew. Chem., Int. Ed.* **2010**, *49*, 10176–10180.
85. Mulder, A.; Auletta, T.; Sartori, A.; Del Ciotto, S.; Casnati, A.; Ungaro, R.; Huskens, J.; Reinhoudt, D. N. Divalent Binding of a Bis(adamantyl)-Functionalized Calix[4]arene to β-Cyclodextrin-Based Hosts: An Experimental and Theoretical Study on Multivalent Binding in Solution and at Self-Assembled Monolayers. *J. Am. Chem. Soc.* **2004**, *126*, 6627–6636.
86. Ravoo, B. J.; Vico, R. V.; Voskuhl, J. Multivalent Interaction of Cyclodextrin Vesicles, Carbohydrate Guests, and Lectins: A Kinetic Investigation. *Langmuir* **2011**, *27*, 1391–1397.
87. Falvey, P.; Lim, C. W.; Darcy, R.; Revermann, T.; Karst, U.; Giesbers, M.; Marcelis, A. T. M.; Lazar, A.; Coleman, A. W.; Reinhoudt, D. N.; Ravoo, B. J. Bilayer Vesicles of Amphiphilic Cyclodextrins: Host Membranes that Recognize Guest Molecules. *Chem.—Eur. J.* **2005**, *11*, 1171–1180.
88. Ravoo, B. J.; Jacquier, J. C.; Wenz, G. Molecular Recognition of Polymers by Cyclodextrin Vesicles. *Angew. Chem., Int. Ed.* **2003**, *42*, 2066–2070.
89. Lim, C. W.; Crespo-Biel, O.; Stuart, M. C. A.; Reinhoudt, D. N.; Huskens, J.; Ravoo, B. J. Intravesicular and Intervesicular Interaction by Orthogonal Multivalent

Host−Guest and Metal-Ligand Complexation. *Proc. Natl. Acad. Sci.U.S.A.* **2007**, *104*, 6986–6991.

90. Lim, C. W.; Ravoo, B. J.; Reinhoudt, D. N. Dynamic Multivalent Recognition of Cyclodextrin Vesicles. *Chem. Commun.* **2005**, 5627–5629.
91. Lee, H. K.; Park, K. M.; Jeon, Y. J.; Kim, D.; Oh, D. H.; Kim, H. S.; Park, C. K.; Kim, K. Vesicle Formed by Amphiphilc Cucurbit[6]uril: Versatile, Noncovalent Modification of the Vesicle Surface, and Multivalent Binding of Sugar-Decorated Vesicles to Lectin. *J. Am. Chem. Soc.* **2005**, *127*, 5006–5007.
92. Jung, H.; Robison, A. D.; Cremer, P. S. Multivalent Ligand-Receptor Binding on Supported Lipid Bilayers. *J. Struct. Biol.* **2009**, *168*, 90–94.
93. Appel, E. A.; Biedermann, F.; Rauwald, U.; Jones, S. T.; Zayed, J. M.; Scherman, O. A. Supramolecular Cross-Linked Networks *via* Host−Guest Complexation with Cucurbit[8]uril. *J. Am. Chem. Soc.* **2010**, *132*, 14251–14260.
94. Min, Y. J.; Akbulut, M.; Kristiansen, K.; Golan, Y.; Israelachvili, J. The Role of Interparticle and External Forces in Nanoparticle Assembly. *Nat. Mater.* **2008**, *7*, 527–538.
95. Grzybowski, B. A.; Wilmer, C. E.; Kim, J.; Browne, K. P.; Bishop, K. J. M. Self-Assembly: From Crystals to Cells. *Soft Matter* **2009**, *5*, 1110–1128.
96. Ewers, T. D.; Sra, A. K.; Norris, B. C.; Cable, R. E.; Cheng, C.-H.; Shantz, D. F.; Schaak, R. E. Spontaneous Hierarchical Assembly of Rhodium Nanoparticles into Spherical Aggregates and Superlattices. *Chem. Mater.* **2005**, *17*, 514–520.
97. Zhuang, J.; Wu, H.; Yang, Y.; Cao, Y. C. Supercrystalline Colloidal Particles from Artificial Atoms. *J. Am. Chem. Soc.* **2007**, *129*, 14166–14167.
98. Mirkin, C. A. The Polyvalent Gold Nanoparticle Conjugate-Materials Synthesis, Biodiagnostics, and Intracellular Gene Regulation. *MRS Bull.* **2010**, *35*, 532–539.
99. Bang, J.; Jeong, U.; Ryu, D. Y.; Russell, T. P.; Hawker, C. J. Block Copolymer Nanolithography: Translation of Molecular Level Control to Nanoscale Patterns. *Adv. Mater.* **2009**, *21*, 4769–4792.
100. Klajn, R.; Olson, M. A.; Wesson, P. J.; Fang, L.; Coskun, A.; Trabolsi, A.; Soh, S.; Stoddart, J. F.; Grzybowski, B. A. Dynamic Hook-and-Eye Nanoparticle Sponges. *Nat. Chem.* **2009**, *1*, 733–738.
101. Sijbesma, R. P.; Meijer, E. W. Self-Assembly of Well-Defined Structures by Hydrogen Bonding. *Curr. Opin. Colloid Interface Sci.* **1999**, *4*, 24–32.
102. Prins, L. J.; Reinhoudt, D. N.; Timmerman, P. Noncovalent Synthesis Using Hydrogen Bonding. *Angew. Chem., Int. Ed.* **2001**, *40*, 2382–2426.
103. Lehn, J. M. Supramolecular Polymer Chemistry—Scope and Perspectives. *Polym. Int.* **2002**, *51*, 825–839.
104. Fathalla, M.; Lawrence, C. M.; Zhang, N.; Sessler, J. L.; Jayawickramarajah, J. Base-Pairing Mediated Non-covalent Polymers. *Chem. Soc. Rev.* **2009**, *38*, 1608–1620.
105. De Greef, T. F. A.; Smulders, M. M. J.; Wolffs, M.; Schenning, A. P. H. J.; Sijbesma, R. P.; Meijer, E. W. Supramolecular Polymerization. *Chem. Rev.* **2009**, *109*, 5687–5754.
106. Rebek, J. Molecular Behavior in Small Spaces. *Acc. Chem. Res.* **2009**, *42*, 1660–1668.
107. Zeng, H. Q.; Miller, R. S.; Flowers, R. A.; Gong, B. A Highly Stable, Six-Hydrogen-Bonded Molecular Duplex. *J. Am. Chem. Soc.* **2000**, *122*, 2635–2644.
108. Boal, A. K.; Ilhan, F.; DeRouchey, J. E.; Thurn-Albrecht, T.; Russell, T. P.; Rotello, V. M. Self-Assembly of Nanoparticles into Structured Spherical and Network Aggregates. *Nature* **2000**, *404*, 746–748.
109. Such, G. K.; Johnston, A. P. R.; Caruso, F. Engineered Hydrogen-Bonded Polymer Multilayers: From Assembly to Biomedical Applications. *Chem. Soc. Rev.* **2011**, *40*, 19–29.
110. Bosman, A. W.; Sijbesma, R. P.; Meijer, E. W. Supramolecular Polymers at Work. *Mater. Today* **2004**, 34–39.
111. Cordier, P.; Tournilhac, F.; Soulie-Ziakovic, C.; Leibler, L. Self-Healing and Thermoreversible Rubber from Supramolecular Assembly. *Nature* **2008**, *451*, 977–980.
112. Valkama, S.; Kosonen, H.; Ruokolainen, J.; Haatainen, T.; Torkkeli, M.; Serimaa, R.; Ten Brinke, G.; Ikkala, O. Self-Assembled Polymeric Solid Films with Temperature-Induced Large and Reversible Photonic-Bandgap Switching. *Nat. Mater.* **2004**, *3*, 872–876.
113. Zhao, Y.; Thorkelsson, K.; Mastroianni, A. J.; Schilling, T.; Luther, J. M.; Rancatore, B. J.; Matsunaga, K.; Jinnai, H.; Wu, Y.; Poulsen, D.; Frechet, J. M. J.; Alivisatos, A. P.; Xu, T. Small-Molecule-Directed Nanoparticle Assembly towards Stimuli-Responsive Nanocomposites. *Nat. Mater.* **2009**, *8*, 979–985.
114. Grimme, S. Do Special Noncovalent $\pi-\pi$ Stacking Interactions Really Exist? *Angew. Chem., Int. Ed.* **2008**, *47*, 3430–3434.
115. Sinnokrot, M. O.; Sherrill, C. D. Highly Accurate Coupled Cluster Potential Energy Curves for the Bnzene Dimer: Sandwich, T-shaped, and Parallel-Displaced Configurations. *J. Phys. Chem. A* **2004**, *108*, 10200–10207.
116. Lewis, M.; Watt, M. W., M.; Hardebeck, L. K. E.; Kirkpatrick, C. C. Face-to-Face Arene−Arene Binding Energies: Dominated by Dispersion but Predicted by Electrostatic and Dispersion/Polarizability Substituent Constants. *J. Am. Chem. Soc.* **2011**, *133*, 3854–3862.
117. Salonen, L. M.; Ellermann, M.; Diederich, F. Aromatic Rings in Chemical and Biological Recognition: Energetics and Structures. *Angew. Chem., Int. Ed.* **2011**, *50*, 4808–4842.
118. Hunter, C. A.; Sanders, J. K. M. The Nature of $\pi-\pi$ Interactions. *J. Am. Chem. Soc.* **1990**, *112*, 5525–5534.
119. Wheeler, S. E.; Houk, K. N. Substituent Effects in the Benzene Dimer Are Due to Direct Interactions of the Substituents with the Unsubstituted Benzene. *J. Am. Chem. Soc.* **2008**, *130*, 10854–10855.
120. Chen, Z.; Lohr, A.; Saha-Moller, C. R.; Würthner, F. Self-Assembled π-Stacks of Functional Dyes in Solution: Structural and Thermodynamic Features. *Chem. Soc. Rev.* **2009**, *38*, 564–584.
121. Hoeben, F. J. M.; Jonkheijm, P.; Meijer, E. W.; Schenning, A. P. H. J. About Supramolecular Assemblies of π-Conjugated Systems. *Chem. Rev.* **2005**, *105*, 1491–1546.
122. Schenning, A. P. H. J.; Meijer, E. W. Supramolecular Electronics; Nanowires from Self-Assembled π-Conjugated Systems. *Chem. Commun.* **2005**, 3245–3258.
123. Watson, M. D.; Fechtenkotter, A.; Müllen, K. Big is beautiful—"Aromaticity" Revisited from the Viewpoint of Macromolecular and Supramolecular Benzene Chemistry. *Chem. Rev.* **2001**, *101*, 1267–1300.
124. Zang, L.; Che, Y. K.; Moore, J. S. One-Dimensional Self-Assembly of Planar π-Conjugated Molecules: Adaptable Building Blocks for Organic Nanodevices. *Acc. Chem. Res.* **2008**, *41*, 1596–1608.
125. Cockroft, S. L.; Perkins, J.; Zonta, C.; Adams, H.; Spey, S. E.; Low, C. M. R.; Vinter, J. G.; Lawson, K. R.; Urch, C. J.; Hunter, C. A. Substituent Effects on Aromatic Stacking Interactions. *Org. Biomol. Chem.* **2007**, *5*, 1062–1080.
126. Hunter, C. A.; Lawson, K. R.; Perkins, J.; Urch, C. J. Aromatic Interactions. *J. Chem. Soc., Perk. Trans. 2* **2001**, 651–669.
127. Yang, X.; Dou, X.; Rouhanipour, A.; Zhi, L.; Rader, H. J.; Müllen, K. Two-Dimensional Graphene Nanoribbons. *J. Am. Chem. Soc.* **2008**, 4216–4217.
128. Pisula, W.; Feng, X. L.; Müllen, K. Charge-Carrier Transporting Graphene-Type Molecules. *Chem. Mater.* **2011**, *23*, 554–567.
129. Dossel, L.; Gherghel, L.; Feng, X. L.; Müllen, K. Graphene Nanoribbons by Chemists: Nanometer-Sized, Soluble, and Defect-Free. *Angew. Chem., Int. Ed.* **2011**, *50*, 2540–2543.
130. Fasel, R.; Cai, J. M.; Ruffieux, P.; Jaafar, R.; Bieri, M.; Braun, T.; Blankenburg, S.; Muoth, M.; Seitsonen, A. P.; Saleh, M.; Feng, X. L.; Müllen, K. Atomically Precise Bottom-Up Fabrication of Graphene Nanoribbons. *Nature* **2010**, *466*, 470–473.

131. Feng, X.; Marcon, V.; Pisula, W.; Hansen, M. R.; Kirkpatrick, J.; Grozema, F.; Andrienko, D.; Kremer, K.; Müllen, K. Towards High Charge-Carrier Mobilities by Rational Design of the Shape and Periphery of Discotics. *Nat. Mater.* **2009**, *8*, 421–426.
132. Adler-Abramovich, L.; Kol, N.; Yanai, I.; Barlam, D.; Shneck, R. Z.; Rousso, I.; Gazit, E. Self-Assembled Organic Nanostructures with Metallic-like Stiffness. *Angew. Chem., Int. Ed.* **2010**, *49*, 9939–9942.
133. Kol, N.; Adler-Abramovich, L.; Barlam, D.; Shneck, R. Z.; Gazit, E.; Rousso, I. Self-Assembled Peptide Nanotubes Are Uniquely Rigid Bioinspired Supramolecular Structures. *Nano Lett.* **2005**, *5*, 1343–1346.
134. Percec, V. Bioinspired Supramolecular Liquid Crystals. *Philos. Trans. R. Soc. A* **2006**, *364*, 2709–2719.
135. Lee, M.; Cho, B. K.; Zin, W. C. Supramolecular Structures From Rod−Coil Block Copolymers. *Chem. Rev.* **2001**, *101*, 3869–3892.
136. Elemans, J. A. A. W.; Van Hameren, R.; Nolte, R. J. M.; Rowan, A. E. Molecular Materials by Self-Assembly of Porphyrins, Phthalocyanines, and Perylenes. *Adv. Mater.* **2006**, *18*, 1251–1266.
137. Wasielewski, M. R. Self-Assembly Strategies for Integrating Light Harvesting and Charge Separation in Artificial Photosynthetic Systems. *Acc. Chem. Res.* **2009**, *42*, 1910–1921.
138. Burattini, S.; Colquhoun, H. M.; Fox, J. D.; Friedmann, D.; Greenland, B. W.; Harris, P. J. F.; Hayes, W.; Mackay, M. E.; Rowan, S. J. A Self-Repairing, Supramolecular Polymer System: Healability as a Consequence of Donor-Acceptor $\pi-\pi$ Stacking Interactions. *Chem. Commun.* **2009**, 6717–6719.
139. Blokzijl, W.; Engberts, J. B. F. N. Hydrophobic Effects. Opinions and Facts. *Angew. Chem., Int. Ed.* **1993**, *32*, 1545–1579.
140. Southall, N. T.; Dill, K. A.; Haymet, A. D. J. A View of the Hydrophobic Effect. *J. Phys. Chem. B* **2002**, *106*, 521–533.
141. Chandler, D. Interfaces and the Driving Force of Hydrophobic Assembly. *Nature* **2005**, *437*, 640–647.
142. Li, Z.; Kesselman, E.; Talmon, Y.; Hillmyer, M. A.; Lodge, T. P. Multicompartment Micelles from ABC Miktoarm Stars in Water. *Science* **2004**, *306*, 98–101.
143. Cui, H.; Chen, Z.; Zhong, S.; Wooley, K. L.; Pochan, D. J. Block Copolymer Assembly *via* Kinetic Control. *Science* **2007**, *317*, 647–650.
144. Discher, D. E.; Eisenberg, A. Polymer Vesicles. *Science* **2002**, *297*, 967–973.
145. Holder, S. J.; Sommerdijk, N. A. J. M. New Micellar Morphologies From Amphiphilic Block Copolymers: Disks, Toroids and Bicontinuous Micelles. *Polym. Chem.* **2011**, *2*, 1018–1028.
146. Ryu, J. H.; Hong, D. J.; Lee, M. Aqueous Self-Assembly of Aromatic Rod Building Blocks. *Chem. Commun.* **2008**, 1043–1054.
147. Oshovsky, G. V.; Reinhoudt, D. N.; Verboom, W. Supramolecular Chemistry in Water. *Angew. Chem., Int. Ed.* **2007**, *46*, 2366–2393.
148. Hill, J. P.; Jin, W.; Kosaka, A.; Fukushima, T.; Ichihara, H.; Shimomura, T.; Ito, K.; Hashizume, T.; Ishii, N.; Aida, T. Self-Assembled Hexa-peri-hexabenzocoronene Graphitic Nanotube. *Science* **2004**, *304*, 1481–1483.
149. Zhang, G.; Jin, W.; Fukushima, T.; Kosaka, A.; Ishii, N.; Aida, T. Formation of Water-Dispersible Nanotubular Graphitic Assembly Decorated with Isothiouronium Ion Groups and Its Supramolecular Functionalization. *J. Am. Chem. Soc.* **2007**, *129*, 719–722.
150. Hartgerink, J. D.; Beniash, E.; Stupp, S. I. Peptide−Amphiphile nanofibers: A Versatile Scaffold for the Preparation of Self-Assembling Materials. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 5133–5138.
151. Ostrander, J. W.; Mamedov, A. A.; Kotov, N. A. Two Modes of Linear Layer-by-Layer Growth of Nanoparticle−Polylectrolyte Multilayers and Different Interactions in the Layer-by-Layer Deposition. *J. Am. Chem. Soc.* **2001**, *123*, 1101–1110.
152. Dill, K. A.; Fennell, C. J.; Kehoe, C. Oil/Water Transfer Is Partly Driven by Molecular Shape, Not Just Size. *J. Am. Chem. Soc.* **2010**, *132*, 234–240.
153. Finney, J. L. Water? What's So Special About It? *Philos. Trans. R. Soc. B* **2004**, *359*, 1145–1163.
154. Mal, P.; Breiner, B.; Rissanen, K.; Nitschke, J. R. White Phosphorus Is Air-Stable within a Self-Assembled Tetrahedral Capsule. *Science* **2009**, *324*, 1697–1699.
155. Pluth, M. D.; Raymond, K. N.; Bergman, R. G. Proton-Mediated Chemistry and Catalysis in a Self-Assembled Supramolecular Host. *Acc. Chem. Res.* **2009**, *42*, 1650–1659.
156. Fujita, M.; Yoshizawa, M.; Klosterman, J. K. Functional Molecular Flasks: New Properties and Reactions within Discrete, Self-Assembled Hosts. *Angew. Chem., Int. Ed.* **2009**, *48*, 3418–3438.
157. Ziv, A.; Grego, A.; Kopilevich, S.; Zeiri, L.; Miro, P.; Bo, C.; Müller, A.; Weinstock, I. A. Flexible Pores of a Metal Oxide-Based Capsule Permit Entry of Comparatively Larger Organic Guests. *J. Am. Chem. Soc.* **2009**, *131*, 6380–6382.
158. Giles, M. D.; Liu, S. M.; Emanuel, R. L.; Gibb, B. C.; Grayson, S. M. Dendronized Supramolecular Nanocapsules: pH Independent, Water-Soluble, Deep-Cavity Cavitands Assemble *via* the Hydrophobic Effect. *J. Am. Chem. Soc.* **2008**, *130*, 14430–14431.
159. Liu, S.; Gibb, B. C. High-Definition Self-Assemblies Driven by the Hydrophobic Effect: Synthesis and Properties of a Supramolecular Nanocapsule. *Chem. Commun.* **2008**, 3709–3716.
160. Jong, J.; Feringa, B.; Esch, J., Responsive Molecular Gels. In *Molecular Gels*; Springer: Dordrecht, Germany, 2006; pp 895−927.
161. Hirst, A. R.; Escuder, B.; Miravet, J. F.; Smith, D. K. High-Tech Applications of Self-Assembling Supramolecular Nanostructured Gel−Phase Materials: From Regenerative Medicine to Electronic Devices. *Angew. Chem., Int. Ed.* **2008**, *47*, 8002–8018.
162. Sangeetha, N. M.; Maitra, U. Supramolecular Gels: Functions and Uses. *Chem. Soc. Rev.* **2005**, *34*, 821–836.
163. Xie, P.; Zhang, R. Liquid Crystal Elastomers, Networks and Gels: Advanced Smart Materials. *J. Mater. Chem.* **2005**, *15*, 2529–2550.
164. Ajayaghosh, A.; Praveen, V. K.; Vijayakumar, C. Organogels as Scaffolds for Excitation Energy Transfer and Light Harvesting. *Chem. Soc. Rev.* **2008**, *37*, 109–22.
165. Peppas, N. A.; Hilt, J. Z.; Khademhosseini, A.; Langer, R. Hydrogels in Biology and Medicine: From Molecular Principles to Bionanotechnology. *Adv. Mater.* **2006**, *18*, 1345–1360.
166. Estroff, L. A.; Hamilton, A. D. Water Gelation by Small Organic Molecules. *Chem. Rev.* **2004**, *104*, 1201–18.
167. Steed, J. W. Supramolecular Gel Chemistry: Developments over the Last Decade. *Chem. Commun.* **2011**, *47*, 1379–1383.
168. Dawn, A.; Shiraki, T.; Haraguchi, S.; Tamaru, S.; Shinkai, S. What Kind of "Soft Materials" Can We Design from Molecular Gels? *Chem. Asian J.* **2011**, *6*, 266–282.
169. Fairclough, J. P. A.; Norman, A. I. Structure and Rheology of Aqueous Gels. *Annu. Rep. Sect. C* **2003**, *99*, 243–276.
170. Dastidar, P. Supramolecular Gelling Agents: Can They Be Designed? *Chem. Soc. Rev.* **2008**, *37*, 2699–2715.
171. Krieg, E.; Shirman, E.; Weissman, H.; Shimoni, E.; Wolf, S. G.; Pinkas, I.; Rybtchinski, B. Supramolecular Gel Based on a Perylene Diimide Dye: Multiple Stimuli Responsiveness, Robustness, and Photofunction. *J. Am. Chem. Soc.* **2009**, *131*, 14365–14373.
172. See, for example, technical specifications of Koch Membrane Systems HFM-100/180, HFK-131, or GE Osmonics KN1CP04700.
173. Schmuck, C. Robust Materials from Weak Forces. *Nat. Nanotechnol.* **2011**, *6*, 136–137.
174. Ladet, S.; David, L.; Domard, A. Multimembrane Hydrogels. *Nature* **2008**, *452*, 76–80.

175. Cui, H. G.; Webber, M. J.; Stupp, S. I. Self-Assembly of Peptide Amphiphiles: From Molecules to Nanostructures to Biomaterials. *Biopolymers* **2010**, *94*, 1–18.
176. Tidhar, Y.; Weissman, H.; Wolf, S. G.; Gulino, A.; Rybtchinski, B. Pathway-Dependent Self-Assembly of Perylene Diimide/Peptide Conjugates in Aqueous Medium. *Chem.—Eur. J.* **2011**, *17*, 6068–6075.
177. Lee, S.; Arunagirinathan, M. A.; Bates, F. S. Path-Dependent Morphologies in Oil/Water/Diblock Copolymer Mixtures. *Langmuir* **2010**, *26*, 1707–1715.
178. Zhang, L.; Eisenberg, A. Thermodynamic *vs* Kinetic Aspects in the Formation and Morphological Transitions of Crew-Cut Aggregates Produced by Self-Assembly of Polystyrene-*b*-poly(acrylic acid) Block Copolymers in Dilute Solution. *Macromolecules* **1999**, *32*, 2239–2249.
179. Bigioni, T. P.; Lin, X. M.; Nguyen, T. T.; Corwin, E. I.; Witten, T. A.; Jaeger, H. M. Kinetically Driven Self-Assembly of Highly Ordered Nanoparticle Monolayers. *Nat. Mater.* **2006**, *5*, 265–270.
180. Mann, S. Self-Assembly and Transformation of Hybrid Nano-objects and Nanostructures under Equilibrium and Non-equilibrium Conditions. *Nat. Mater.* **2009**, *8*, 781–792.
181. Prins, L. J.; De Jong, F.; Timmerman, P.; Reinhoudt, D. N. An Enantiomerically Pure Hydrogen-Bonded Assembly. *Nature* **2000**, *408*, 181–184.
182. Prins, L. J.; Neuteboom, E. E.; Paraschiv, V.; Crego-Calama, M.; Timmerman, P.; Reinhoudt, D. N. Kinetic Stabilities of Double, Tetra-, and Hexarosette Hydrogen-Bonded Assemblies. *J. Org. Chem.* **2002**, *67*, 4808–4820.
183. de Greef, T. F. A.; Ligthart, G. B. W. L.; Lutz, M.; Spek, A. L.; Meijer, E. W.; Sijbesma, R. P. The Mechanism of Ureido-pyrimidinone:2,7-Diamido-naphthyridine complexation and the Presence of Kinetically Controlled Pathways in Multicomponent Hydrogen-Bonded Systems. *J. Am. Chem. Soc.* **2008**, *130*, 5479–5486.
184. Jonkheijm, P.; Miura, A.; Zdanowska, M.; Hoeben, F. J. M.; De Feyter, S.; Schenning, A. P. H. J.; De Schryver, F. C.; Meijer, E. W. π-Conjugated Oligo-(*p*-phenylenevinylene) Rosettes and Their Tubular Self-Assembly. *Angew. Chem., Int. Ed.* **2004**, *43*, 74–78.
185. Lohr, A.; Gress, T.; Deppisch, M.; Knoll, M.; Würthner, F. Synthesis of Merocyanine Dye Nanorods: The Importance of Solvent, Kinetic and Thermodynamic Control, and Steric Effects on Self-Assembly. *Synthesis* **2007**, 3073–3082.
186. Lohr, A.; Lysetska, M.; Würthner, F. Supramolecular Stereomutation in Kinetic and Thermodynamic Self-Assembly of Helical Merocyanine Dye Nanorods. *Angew. Chem., Int. Ed.* **2005**, *44*, 5071–5074.
187. Lohr, A.; Würthner, F. Time-Dependent Amplification of Helical Bias in Self-Assembled Dye Nanorods Directed by the Sergeants-and-Soldiers Principle. *Chem. Commun.* **2008**, 2227–2229.
188. Lohr, A.; Würthner, F. Evolution of Homochiral Helical Dye Assemblies: Involvement of Autocatalysis in the "Majority-Rules" Effect. *Angew. Chem., Int. Ed.* **2008**, *47*, 1232–1236.
189. Jyothish, K.; Hariharan, M.; Ramaiah, D. Chiral Supramolecular Assemblies of a Squaraine Dye in Solution and Thin Films: Concentration-, Temperature-, and Solvent-Induced Chirality Inversion. *Chem.—Eur. J.* **2007**, *13*, 5944–5951.
190. Badjic, J. D.; Cantrill, S. J.; Stoddart, J. F. Can Multivalency be Expressed Kinetically? The Answer Is Yes. *J. Am. Chem. Soc.* **2004**, *126*, 2288–2289.
191. Dyck, A. S. M.; Kisiel, U.; Bohne, C. Dynamics for the Assembly of Pyrene-γ-Cyclodextrin Host−Guest Complexes. *J. Phys. Chem. B* **2003**, *107*, 11652–11659.
192. Mukhopadhyay, P.; Zavalij, P. Y.; Isaacs, L. High Fidelity Kinetic Self-Sorting in Multicomponent Systems Based on Guests with Multiple Binding Epitopes. *J. Am. Chem. Soc.* **2006**, *128*, 14093–14102.
193. Oshikiri, T.; Takashima, Y.; Yamaguchi, H.; Harada, A. Kinetic Control of Threading of Cyclodextrins onto Axle Molecules. *J. Am. Chem. Soc.* **2005**, *127*, 12186–12187.
194. Jiang, W.; Schafer, A.; Mohr, P. C.; Schalley, C. A. Monitoring Self-Sorting by Electrospray Ionization Mass Spectrometry: Formation Intermediates and Error-Correction during the Self-Assembly of Multiply Threaded Pseudorotaxanes. *J. Am. Chem. Soc.* **2010**, *132*, 2309–2320.
195. Carnall, J. M. A.; Waudby, C. A.; Belenguer, A. M.; Stuart, M. C. A.; Peyralans, J. J. P.; Otto, S. Mechanosensitive Self-Replication Driven by Self-Organization. *Science* **2010**, *327*, 1502–1506.
196. Cougnon, F. B. L.; Au-Yeung, H. Y.; Pantos, G. D.; Sanders, J. K. M. Exploring the Formation Pathways of Donor−Acceptor Catenanes in Aqueous Dynamic Combinatorial Libraries. *J. Am. Chem. Soc.* **2011**, *133*, 3198–3207.
197. Zhang, S. M.; Greenfield, M. A.; Mata, A.; Palmer, L. C.; Bitton, R.; Mantei, J. R.; Aparicio, C.; de la Cruz, M. O.; Stupp, S. I. A Self-Assembly Pathway to Aligned Monodomain Gels. *Nat. Mater.* **2010**, *9*, 594–601.
198. Moore, J. S.; Kraft, M. L. Chemistry—Synchronized Self-Assembly. *Science* **2008**, *320*, 620–621.
199. Pashuck, E. T.; Stupp, S. I. Direct Observation of Morphological Tranformation from Twisted Ribbons into Helical Ribbons. *J. Am. Chem. Soc.* **2010**, *132*, 8819–8821.
200. Ziserman, L.; Lee, H. Y.; Raghavan, S. R.; Mor, A.; Danino, D. Unraveling the Mechanism of Nanotube Formation by Chiral Self-Assembly of Amphiphiles. *J. Am. Chem. Soc.* **2011**, *133*, 2511–2517.
201. Ziserman, L.; Mor, A.; Harries, D.; Danino, D. Curvature Instability in a Chiral Amphiphile Self-Assembly. *Phys. Rev. Lett.* **2011**, 238105.
202. Smulders, M. M. J.; Nieuwenhuizen, M. M. L.; de Greef, T. F. A.; van der Schoot, P.; Schenning, A. P. H. J.; Meijer, E. W. How to Distinguish Isodesmic from Cooperative Supramolecular Polymerisation. *Chem.—Eur. J.* **2010**, *16*, 362–367.
203. Jonkheijm, P.; van der Schoot, P.; Schenning, A. P. H. J.; Meijer, E. W. Probing the Solvent-Assisted Nucleation Pathway in Chemical Self-Assembly. *Science* **2006**, *313*, 80–83.
204. Hunter, C. A.; Anderson, H. L. What is Cooperativity? *Angew. Chem., Int. Ed.* **2009**, *48*, 7488–7499.
205. Balaban, T. S.; Leitich, J.; Holzwarth, A. R.; Schaffner, K. Autocatalyzed Self-Aggregation of (3^1*R*)-[Et,Et]Bacteriochlorophyll c_F Molecules in Nonpolar Solvents. Analysis of the Kinetics. *J. Phys. Chem. B* **2000**, *104*, 1362–1372.
206. Würthner, F.; Yao, S.; Beginn, U. Highly Ordered Merocyanine Dye Assemblies by Supramolecular Polymerization and Hierarchical Self-Organization. *Angew. Chem., Int. Ed.* **2003**, *42*, 3247–3250.
207. Yao, S.; Beginn, U.; Gress, T.; Lysetska, M.; Würthner, F. Supramolecular Polymerization and Gel Formation of Bis(merocyanine) Dyes Driven by Dipolar Aggregation. *J. Am. Chem. Soc.* **2004**, *126*, 8336–8348.
208. Perl, A.; Gomez-Casado, A.; Thompson, D.; Dam, H. H.; Jonkheijm, P.; Reinhoudt, D. N.; Huskens, J. Gradient-Driven Motion of Multivalent Ligand Molecules along a Surface Functionalized with Multiple Receptors. *Nat. Chem.* **2011**, *3*, 317–322.
209. Bradford, V. J.; Iverson, B. L. Amyloid-like Behavior in Abiotic, Amphiphilic Foldamers. *J. Am. Chem. Soc.* **2008**, *130*, 1517–1524.
210. Dobson, C. M. Protein Folding and Misfolding. *Nature* **2003**, *426*, 884–890.
211. Hayward, R. C.; Pochan, D. J. Tailored Assemblies of Block Copolymers in Solution: It Is All about the Process. *Macromolecules* **2010**, *43*, 3577–3584.
212. Vos, M. R. J.; Leclere, P. E. L. G.; Meekes, H.; Vlieg, E.; Nolte, R. J. M.; Sommerdijk, N. A. J. M. Kinetic Switching between Two Modes of Bisurea Surfactant Self-Assembly. *Chem. Commun.* **2010**, *46*, 6063–6065.
213. Palmer, L. C.; Velichko, Y. S.; Olvera de la Cruz, M.; Stupp, S. I. Supramolecular Self-Assembly Codes for Functional Structures. *Phil. Trans. R. Soc. A* **2007**, *365*, 1417–1433.
214. Israelachvili, J. N. In *Intermolecular and Surface Forces*; Academic Press: London, 1992.

215. Lutz, J. F.; Laschewsky, A. Multicompartment Micelles: Has the Long-Standing Dream Become a Reality? *Macromol. Chem. Phys.* **2005**, *206*, 813–817.
216. Li, Z. B.; Lodge, T. P.; Hillmyer, M. A. Morphologies of Multicompartment Micelles Formed by ABC Miktoarm Star Terpolymers. *Langmuir* **2006**, *22*, 9409–9417.
217. Marsat, J. N.; Heydenreich, M.; Kleinpeter, E.; Berlepsch, H. v.; Bottcher, C.; Laschewsky, A. Self-Assembly into Multicompartment Micelles and Selective Solubilization by Hydrophilic−Lipophilic−Fluorophilic Block Copolymers. *Macromolecules* **2011**, *44*, 2092–2105.
218. von Berlepsch, H.; Bottcher, C.; Skrabania, K.; Laschewsky, A. Complex Domain Architecture of Multicompartment Micelles From a Linear ABC Triblock Copolymer Revealed by Cryogenic ElectronTomography. *Chem. Commun.* **2009**, 2290–2292.
219. McKenzie, B. E.; Nudelman, F.; Bomans, P. H. H.; Holder, S. J.; Sommerdijk, N. A. J. M. Temperature-Responsive Nanospheres with Bicontinuous Internal Structures from a Semicrystalline Amphiphilic Block Copolymer. *J. Am. Chem. Soc.* **2010**, *132*, 10256–10259.
220. Whitten, D. G.; Chen, L. H.; Geiger, H. C.; Perlstein, J.; Song, X. D. Self-Assembly of Aromatic-Functionalized Amphiphiles: The Role and Consequences of Aromatic−Aromatic Noncovalent Interactions in Building Supramolecular Aggregates and Novel Assemblies. *J. Phys. Chem. B* **1998**, *102*, 10098–10111.
221. Song, X. D.; Geiger, C.; Farahat, M.; Perlstein, J.; Whitten, D. G. Aggregation of Stilbene Derivatized Fatty Acids and Phospholipids in Monolayers and Vesicles. *J. Am. Chem. Soc.* **1997**, *119*, 12481–12491.
222. Percec, V.; Wilson, D. A.; Leowanawat, P.; Wilson, C. J.; Hughes, A. D.; Kaucher, M. S.; Hammer, D. A.; Levine, D. H.; Kim, A. J.; Bates, F. S.; *et al.* Self-Assembly of Janus Dendrimers into Uniform Dendrimersomes and Other Complex Architectures. *Science* **2010**, *328*, 1009–1014.
223. Bhosale, S.; Sisson, A. L.; Talukdar, P.; Furstenberg, A.; Banerji, N.; Vauthey, E.; Bollot, G.; Mareda, J.; Roger, C.; Würthner, F. ; *et al.* Photoproduction of Proton Gradients with π-Stacked Fluorophore Scaffolds in Lipid Bilayers. *Science* **2006**, *313*, 84–86.
224. Bhosale, S.; Sisson, A. L.; Sakai, N.; Matile, S. Synthetic Functional π-Stack Architecture in Lipid Bilayers. *Org. Biomol. Chem.* **2006**, *4*, 3031–3039.
225. Percec, V.; Dulcey, A. E.; Peterca, M.; Adelman, P.; Samant, R.; Balagurusamy, V. S. K.; Heiney, P. A. Helical Pores Self-assembled from Homochiral Dendritic Dipeptides Based on L-Tyr and Nonpolar α-Amino Acids. *J. Am. Chem. Soc.* **2007**, *129*, 5992–6002.
226. Kaucher, M. S.; Peterca, M.; Dulcey, A. E.; Kim, A. J.; Vinogradov, S. A.; Hammer, D. A.; Heiney, P. A.; Percec, V. Selective Transport of Water Mediated by Porous Dendritic Dipeptides. *J. Am. Chem. Soc.* **2007**, *129*, 11698–11699.
227. Shao, H.; Parquette, J. R. Controllable Peptide-Dendron Self-Assembly: Interconversion of Nanotubes and Fibrillar Nanostructures. *Angew. Chem., Int. Ed.* **2009**, *48*, 2525–2528.
228. Spicer, P. T. Progress in Liquid Crystalline Dispersions: Cubosomes. *Curr. Opin. Colloid Interface Sci.* **2005**, *10*, 274–279.
229. Spicer, P. T.; Hayden, K. L.; Lynch, M. L.; Ofori-Boateng, A.; Burns, J. L. Novel Process for Producing Cubic Liquid Crystalline Nanoparticles (Cubosomes). *Langmuir* **2001**, *17*, 5748–5756.
230. Boyd, B. J.; Rizwan, S. B.; Dong, Y. D.; Hook, S.; Rades, T. Self-Assembled Geometric Liquid-Crystalline Nanoparticles Imaged in Three Ddimensions: Hexosomes Are Not Necessarily Flat Hexagonal Prisms. *Langmuir* **2007**, *23*, 12461–12464.
231. Ludlow, R. F.; Otto, S. Systems Chemistry. *Chem. Soc. Rev.* **2008**, *37*, 101–108.
232. Lehn, J.-M. From Supramolecular Chemistry Towards Constitutional Dynamic Chemistry and Adaptive Chemistry. *Chem. Soc. Rev.* **2007**, *36*, 151–160.
233. Pal, A.; Karthikeyan, S.; Sijbesma, R. P. Coexisting Hydrophobic Compartments through Self-Sorting in Rodlike Micelles of Bisurea Bolaamphiphiles. *J. Am. Chem. Soc.* **2010**, *132*, 7842–7843.
234. Ghosh, S.; Li, X.-Q.; Stepanenko, V.; Würthner, F. Control of H- and J-Type π-Stacking by Peripheral Alkyl Chains and Self-Sorting Phenomena in Perylene Bisimide Homo- and Heteroaggregates. *Chem.—Eur. J.* **2008**, *14*, 11343–11357.
235. Wu, A. X.; Isaacs, L. Self-Sorting: The Exception or the Rule? *J. Am. Chem. Soc.* **2003**, *125*, 4831–4835.
236. Bishop, K. J. M.; Tretiakov, K. V.; Grzybowski, B. A. Additivity of the Excess Energy Dissipation Rate in a Dynamically Self-Assembled System. *J. Phys. Chem. B* **2009**, *113*, 7574–7578.
237. Cui, H.; Hodgdon, T. K.; Kaler, E. W.; Abezgauz, L.; Danino, D.; Lubovsky, M.; Talmon, Y.; Pochan, D. J. Elucidating the Assembled Structure of Amphiphiles in Solution *via* Cryogenic Transmission Electron Microscopy. *Soft Matter* **2007**, *3*, 945–955.
238. Friedrich, H.; Frederik, P. M.; de With, G.; Sommerdijk, N. A. J. M. Imaging of Self-Assembled Structures: Interpretation of TEM and Cryo-TEM Images. *Angew. Chem., Int. Ed.* **2010**, *49*, 7850–7858.
239. Nudelman, F.; de With, G.; Sommerdijk, N. A. J. M. Cryo-Electron Tomography: 3-Dimensional Imaging of Soft Matter. *Soft Matter* **2011**, *7*, 17–24.
240. Krieg, E.; Rybtchinski, B. Noncovalent Water-Based Materials: Robust Yet Adaptive. *Chem.—Eur. J.* **2011**, *33*, 9016–9026.
241. Truong, W. T.; Su, Y. Y.; Meijer, J. T.; Thordarson, P.; Braet, F. Self-Assembled Gels for Biomedical Applications. *Chem. Asian J.* **2011**, *6*, 30–42.
242. Dvir, T.; Timko, B. P.; Kohane, D. S.; Langer, R. Nanotechnological Strategies for Engineering Complex Tissues. *Nat. Nanotechnol.* **2011**, *6*, 13–22.
243. Langer, R.; Tirrell, D. A. Designing Materials for Biology and Medicine. *Nature* **2004**, *428*, 487–492.
244. Zhang, S. G. Fabrication of Novel Biomaterials through Molecular Self-Assembly. *Nat. Biotechnol.* **2003**, *21*, 1171–1178.
245. Russew, M. M.; Hecht, S. Photoswitches: From Molecules to Materials. *Adv. Mater.* **2010**, *22*, 3348–3360.