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Gel Materials

High-Tech Applications of Self-Assembling Supramolecular Nanostructured Gel-Phase Materials: From Regenerative Medicine to Electronic Devices

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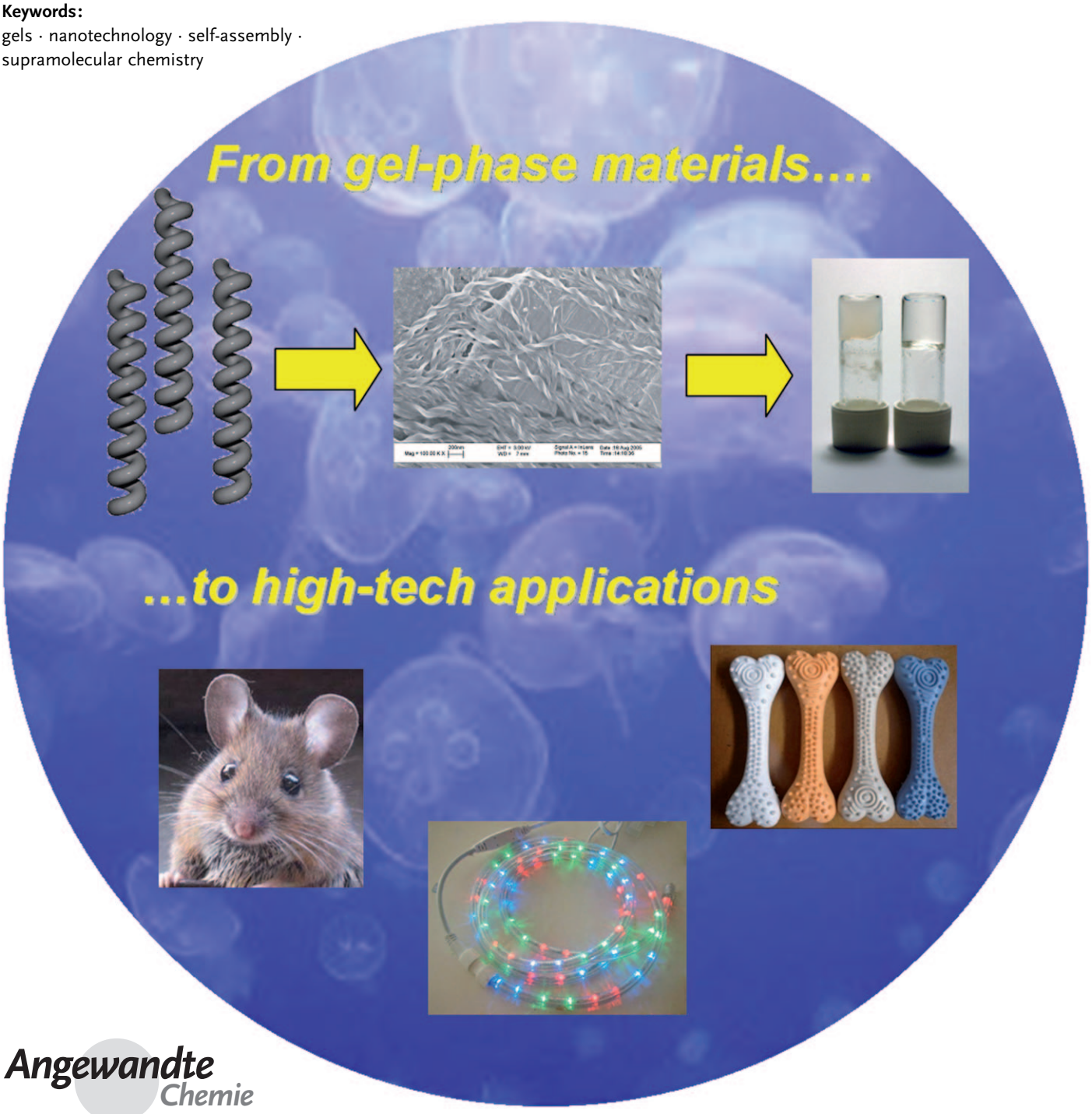

It is likely that nanofabrication will underpin many technologies in the 21st century. Synthetic chemistry is a powerful approach to generate molecular structures that are capable of assembling into functional nanoscale architectures. There has been intense interest in self-assembling low-molecular-weight gelators, which has led to a general understanding of gelation based on the self-assembly of molecular-scale building blocks in terms of non-covalent interactions and packing parameters. The gelator molecules generate hierarchical, supramolecular structures that are macroscopically expressed in gel formation. Molecular modification can therefore control nanoscale assembly, a process that ultimately endows specific material function. The combination of supramolecular chemistry, materials science, and biomedicine allows application-based materials to be developed. Regenerative medicine and tissue engineering using molecular gels as nanostructured scaffolds for the regrowth of nerve cells has been demonstrated in vivo, and the prospect of using self-assembled fibers as one-dimensional conductors in gel materials has captured much interest in the field of nanoelectronics.

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1. Introduction

The use of molecular building blocks capable of forming self-assembled structures is a fundamental construction principle for biological materials. This approach is employed in various systems, ranging from double-stranded DNA to complex structures, such as the tobacco mosaic virus.[1] Molecular-scale information guides the organization of complexity, which is expressed at the materials level in terms of a specific function.[2] The observation of self-assembled structures inherent in the cell (e.g. lipid assemblies, folded proteins, protein complexes, or structured nucleic acids), or the organization of fiber-like polymers and membrane ion channels, provides an insight into the key role of this process in biological systems.[3] To develop new technologies based on self-assembly, the ideal material should have a simple synthesis which is amenable to molecular design and which can be tailored for a broad range of applications. Supramolecular chemistry, involving an understanding of the noncovalent interactions between molecular building blocks, forms the foundation for the development of designed, self-assembling materials.[4] Thus, this approach aims to mimic nature's remarkable ability to self-assemble functional complex shapes or patterns with nanoscale precision. In this way, supramolecular chemistry, biology, and materials engineering are cleverly harnessed to create self-assembling materials that imitate biological microstructures, achieve mechanical action, or generate molecular electronic or sensor devices.

Intense activity has recently been devoted to applying molecular recognition processes to control the formation of gel-phase materials from simple molecular building blocks.[5,6] Gels are a colloidal state of matter in which a small amount of a solid-like network is able to immobilize the bulk flow of a larger amount of liquid-like phase. Many everday commercial gels employ a polymeric solid-like network; however, there is increasing interest in gelation systems based on low-molecular-weight building blocks. In such systems, the solid-like phase typically has a fibrillar structure, which forms an extended sample-spanning network. In the case of molecular gels, these fibers are formed by the self-assembly of molecular building blocks by complementary noncovalent interactions in a quasi one-dimensional manner. By controlling the organization of supramolecular structures in this way, specific physical and/or chemical properties may be expressed at the macroscopic level. On the molecular level, the solvent is mobile within the gel-phase network; however, the flow of the bulk solvent is only prevented as a consequence of capillary forces and some solvent–gelator interactions. Depending on the nature of the liquid-like phase, gels can be classified as either organogels (i.e., the liquid phase is an organic solvent) or hydrogels (in which the liquid phase is water). This Review highlights current design strategies used to fabricate gel-phase systems with high-tech applications, in which their function is underpinned by chemically programmed molecular self-assembly. These developments are illustrated using a selection of articles and reviews.

2. Biomaterials

The development of artificial biological scaffolds that store or attract cells and then direct cell proliferation and differentiation is of critical importance in regenerative medicine.[7] Small-molecule hydrogels are a regenerative medicine strategy capable of restoring biological and mechan-

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ical function to tissue.[8] In addition to the ability of a gel structure to support cells by acting as a relatively inert matrix, it is also possible to modify self-assembling molecules to contain biologically active motifs, for example, cell adhesive or protease-sensitive sequences. In this way, small-molecule hydrogels may be designed to imitate the tissue's natural extracellular matrix (ECM). This area of medical technology therefore uses tailored small-molecule gels to create a platform to mediate the growth of tissues and organs for regenerative medicine, thus exploring the conceptually exciting interface between materials chemistry and the ability to repair human biology.[9]

2.1. Regenerative Medicine

Recently, self-assembling peptide nanofiber scaffolds have been developed for brain repair and axon regeneration, the specific objective being optic tract regeneration and functional recovery of vision.[10] The constituents of the hydrogel scaffold are individual fibers (ca. 10 nm in diameter) composed of amphiphilic oligopeptides. Typically, these molecules have alternating repeat units of positively charged residues (lysine, Lys or arginine, Arg) and negatively charged residues (aspartate, Asp and glutamate, Glu) separated by hydrophobic residues (alanine, Ala or leucine, Leu). The peptide therefore contains 50% charged residues, and it has periodic repeats of alternating ionic hydrophilic and uncharged hydrophobic amino acids. These peptides self-assemble under physiological conditions (Figure 1), and even in human cerebral spinal fluid (CSF). Zhang and co-workers demonstrated that the application of one of the nanoscaffolds underpinned by a gelator with a peptide repeat unit of Arg-Ala-Asp-Ala enabled reconnection of nerve tissue after the optical tract in the hamster midbrain had been surgically severed.[10c] Injection of a 1% peptide solution resulted in the regeneration of the optic tract and functional return of vision. In contrast, for an untreated hamster, no axonal regeneration was observed. It is proposed that the hydrogel material is capable of assembling in irregular voids, such as those found in the damaged optic nerve, and thus intimate contact between the self-assembled nanofibers and the extracellular matrix can facilitate cell–scaffold interactions, which promote healing. Importantly, over a period of 6 months, no evidence of prion-like substances or fibril entanglements were found in animals that had been treated with the gel.

During the neurosurgical procedure described above, it was also discovered that the self-assembling peptide gel achieved complete hemostasis in 15 seconds when applied to a wound. Furthermore, this ability to rapidly achieve hemostasis was not tissue-specific, and was successfully demonstrated in the brain, spinal cord, femoral artery, liver, and skin of mammals. This approach demonstrates that bleeding can be stopped without the application of heat, pressure, platelet activation, use of adhesive, or desiccation. Additionally, no pyrogenicity or systemic coagulation, which was observed with other hemostatic agents, was found. This discovery could revolutionize bleeding control during surgery and trauma: as

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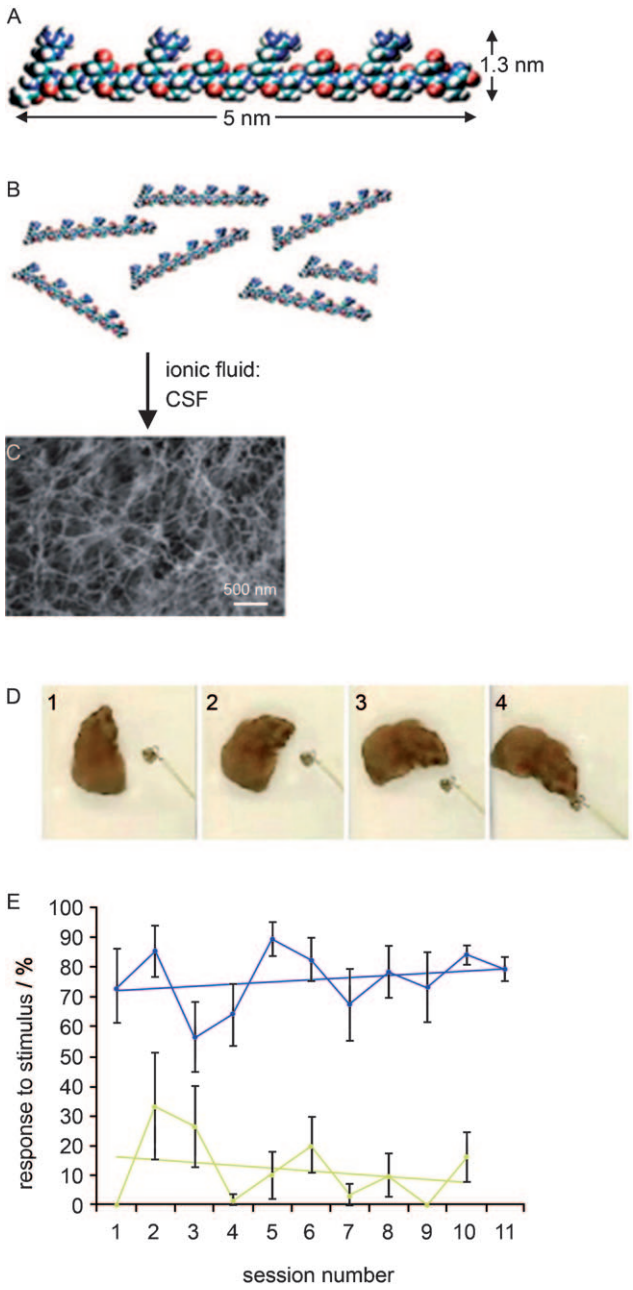


Figure 1. Peptide hydrogelators assemble into a fibrillar network as a consequence of hydrophobic and hydrogen bond interactions (A–C). When applied to the damaged optic nerve of hamsters blinded in their right eye, vision is regenerated and the hamster responds to stimulus (D). The data in (E) indicate that treated hamsters (blue) regained ca. 80% of vision, whereas untreated animals (yellow) regained less than 20%. Reproduced from reference [10c] with permission of the National Academy of Sciences (USA).

much as 50% of surgical time can be spent packing wounds to reduce or control bleeding.[11]

Stupp and co-workers have demonstrated the extraordinary chemical versatility of this approach to regenerative medicine by designing a library of peptide–amphiphile molecules that self-assembled into nanofibrillar networks and formed hydrogels.[12] One of these peptide–amphiphile gelators was modified by the incorporation of the pentapeptide epitope isoleucine-lysine-valine-alanine-valine (Ile-Lys-Val-Ala-Val), which is known to promote the growth and direction of murine neural progenitor cells (NPCs), which are central nervous system cells in mice. The self-assembly of the gel network was triggered by injection of peptide solutions (10–80 μL of 1 wt% solutions) in vitro into enucleated rat eye preparations and in vivo into rat spinal cords. On contact with tissue, hydrogelation was triggered, providing a material which places the bioactive pentapeptide epitope at the surface of high-aspect-ratio nanofibers. Thus, the three-dimensional network maximizes signal presentation to cells in a three-dimensional geometry.[13] Astonishingly, after six weeks, preliminary results revealed that paralysed mice, injected with this peptide solution, regained at least partial use of their rear legs. Dissection of the damaged spinal columns revealed regenerated neural tissue across the severed cord. This work is currently being expanded as a possible regenerative platform for other debilitating illnesses, including Parkinson's disease.[14]

A different strategy was developed for cartilage repair by Kisiday, Grodzinsky and co-workers, and used a self-assembling peptide hydrogel as a three-dimensional encapsulation material.[15] During four weeks of culture in vitro, chondrocytes seeded within the peptide hydrogel developed a network rich in glycosaminoglycans and type II collagen, which indicates the progressive growth of the cartilage-like extracellular matrix (ECM). Time-dependent accumulation of this ECM was paralleled by increased material stiffness, which indicates mechanically functional cartilage tissue. Furthermore, using the same hydrogel, liver progenitor cells embedded within nanofibers adopted properties including binucleation and expression of cytochrome P450s that suggested hepatocyte maturation.[16]

Co-cultures of endothelial cells (cells that line the circulatory system) and cardiac myocytes (heart muscle cells) have also been seeded into a small-molecule peptide hydrogel. Interestingly, rapid organization of cells was reported, with cardiac cells assembling around capillary-like channels of endothelial cells. This result suggests that self-assembling peptide hydrogels are well-suited for the assembly of myocardium-like structures, that is, muscular heart tissue.[17] This work has been taken further by Lee and co-workers, who demonstrated that injection of peptide hydrogels into the left ventricular free wall of mice created a nanofibrous environment within the myocadium. Vascular smooth muscle cells were recruited to the gel network, thus promoting the formation of functional vascular structures.[18]

Fisher and co-workers have developed an alternative strategy towards the development of new injectable joint lubricants for osteoarthritis (OA). A range of de novo peptides were compared with hyaluronic acid (HA), which is a charged linear polymeric carbohydrate and the main component of healthy synovial fluid, and plays an important role in joint lubrication.[19] Encouragingly, peptides with systematic alterations of charge and hydrophilicity were found to self-assemble under physiological conditions, mimicking the behavior of HA. However, the results indicated that even the best self-assembling peptide was a less efficient

lubricant than HA. Nonetheless, the results suggested that a strategy based on self-assembling peptides could be developed as a new viscosupplementation treatment for early-stage OA.

Stupp and co-workers have recently focused on the development of bioactive scaffold materials using branched peptide amphiphiles bearing variations of the Arg-Gly-Glu-Ser (RGDS) adhesion epitope.[20] Although these systems assembled into fibrillar nanoscale architectures, they did not actually form gels. These amphiphiles were coated onto a scaffold, which was then investigated for the growth of bladder cells. Primary human bladder smooth muscle cells showed greater initial adhesion to epitope-functionalized scaffolds than to those which were untreated, or to those which were coated with a simple linear peptide amphiphile.

Angiogenesis, the process of forming new blood vessels, is essential for wound healing, and plays a crucial role in regenerative medicine, as materials developed for tissue regeneration need to ensure an adequate blood supply for cell survival. Stupp and co-workers have designed an α-helical peptide amiphiphile that self-assembles into β-sheet nanostructures upon the addition of heparin (with and without angiogenic growth factors, FGF-2 and VEGF) to give a biopolymer that binds angiogenic growth factors.[21] These β-sheet nanostructures underpin gelation, generating a network of fibers 6–7.5 nm in width and several micrometers in length. The presence of polyanionic heparin screens repulsive charges between the peptide molecules, triggering self-assembly. Isothermal titration calorimetry (ITC) proved the strong binding ($K_a = (1.1 \pm 0.03) \times 10^7\ mol^{-1}\ m^3$) between the peptide amphiphile and heparin.[22] In combination with growth factors, heparin-binding nanostructures promoted significant neovascularization compared with samples based on collagen gels, and as such may have applications in tissue engineering.

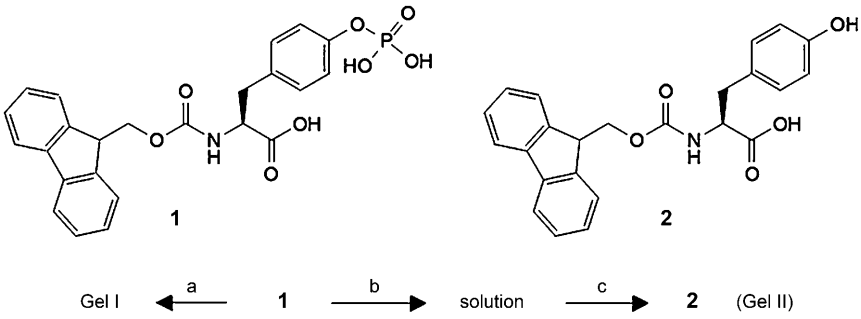
Xu and co-workers have developed a hydrogel to treat simulated uranium-contaminated wounds. This system employs two amino acid derivatives with anti-inflammatory activity and a bisphosphonate that coordinates UO_2^{2+}, thus reducing its toxicity. Complementary self-assembly of these molecules leads to a network of nanofibers that underpin a hydrogel whilst the therapeutic activity of the molecular components is maintained. This process was demonstrated by administrating the hydrogel to wound sites on the skin of mice that had been contaminated with (non-radioactive) uranyl nitrate. The control group of mice (wounds contaminated but untreated) weighed 35% less after eight days than mice treated with the hydrogel, or even died.[23] This work was extended by designing a hydrogel based on D-glucosamine, a naturally occurring aminosaccharide found in cartilage matrix, synovial fluid, and as a component of wound healing. Application of the hydrogel to mice wound sites resulted in faster wound healing and, significantly, minimal scar tissue compared to a control group.[24]

Self-assembling hydrogel biomaterials constructed from low-molecular-weight species, such as those described above, have several advantages over currently available traditional polymer biomaterials that are applied in this area. Firstly, the nanofiber networks that assemble are of a similar scale to the native extracellular matrix, and therefore provide a pseudo in-vivo environment for cell growth, migration, and differentiation. Secondly, the material is readily broken down over time into its molecular constituents (and their metabolism products) and ultimately excreted in urine. Finally, these materials appear to be immunologically inert, thus avoiding potential problems of tissue rejection.

2.2. Enzyme-Responsive Hydrogels

A new approach to create functional hydrogels with biological applications is to design small molecules in which self-assembly and gelation is enzymatically controlled.[25] Typically, an enzymatic reaction is used to regulate the balance between hydrophobicity and hydrophilicity; therefore, precursor molecules can be converted into self-assembling hydrogelators, or vice versa.

Xu and Yang employed commercially available Fmoc-tyrosine phosphate **1**, which dissolves in dilute aqueous alkali solutions. The addition of alkaline phosphatase enzyme to the solution then converted **1** into a more hydrophobic compound **2**, which is a hydrogelator, forming a macroscopic gel (Scheme 1).[26] An inhibitor of the phosphatase enzyme should prevent the formation of the hydrogelator and thus macroscopic gelation; therefore Xu and co-workers utilized this approach to provide a visual assay for screening the activities of inhibitors for the acid phosphatase enzyme. However, it should be noted that, compared to existing colorimetric or fluorescent assays, this system requires further optimization to determine accurate enzyme IC_{50} values.

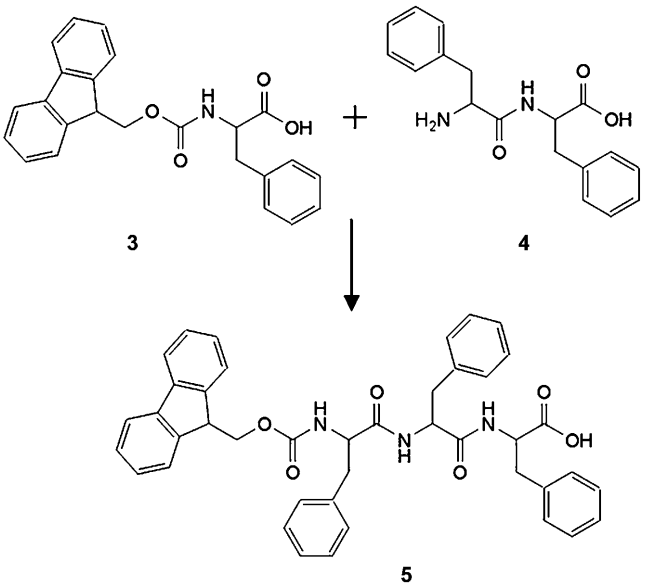


Scheme 1. Structures of compounds **1** and **2**, and mechanism of hydrogelation. Conditions of hydrogelation: a) 40 mM, pH 2.5; b) Na_2CO_3, pH 6.0; c) enzyme in buffer, 37 °C. Reproduced from reference [26] with permission of the Royal Society of Chemistry.

Unlike phosphatases, which catalyze a bond-breaking reaction, thermolysin, a protease produced by bacteria, can

catalyze the formation of a covalent bond by the condensation of two amino acids. Ulijn and co-workers used thermolysin (or chymotrypsin) to connect two compounds **3** and **4** to produce hydrogelator **5**, which self-assembles, forming optically transparent hydrogels (Scheme 2).[27] This approach may offer a new model for the in-situ formation of nanostructured hydrogel scaffolds for tissue growth.

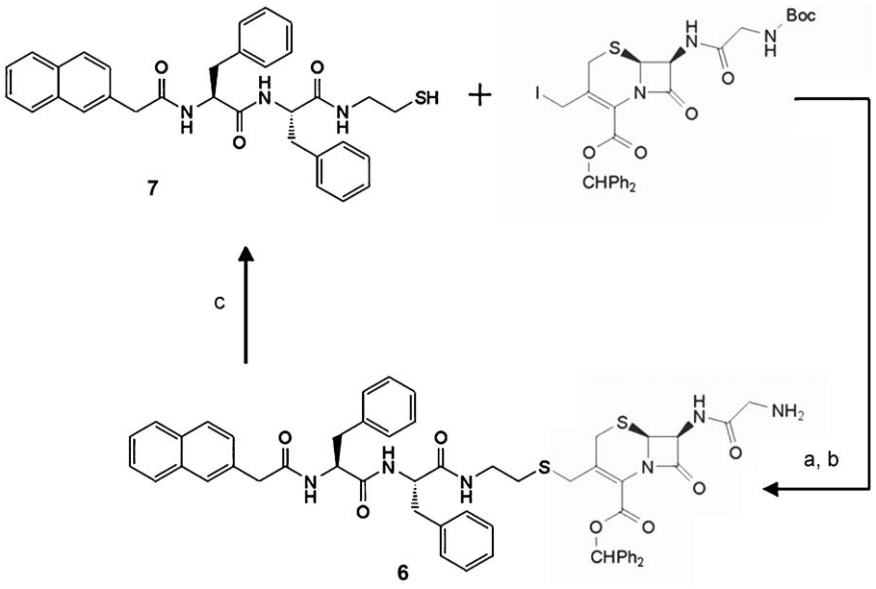
In a related approach, Xu and co-workers synthesized a β-lactam conjugate **6**, which could be converted into a hydrogelator **7** by a β-lactamase (Scheme 3).[28] The enzyme, which is responsible for penicillin resistance in some bacteria, catalyses the opening of the β-lactam precursor, with the subsequent rearrangement releasing the active hydrogelator and leading to macroscopic gelation. Interestingly, the precursor also responded to the lysates of *E. coli* bacteria containing different types of β-lactamases. Conversely, enzymatically induced hydrogelation was also able to assay β-lactamase inhibitors; indeed, the assay had a higher reporting threshold than the conventional nitrocefin assay. Therefore, this general approach may have practical applications, for example, in selectively detecting resistant bacteria in a clinical setting.



Scheme 2. Molecules **3** and **4** used to develop hydrogelator **5** by thermolysin-catalysed bond formation. Reproduced from reference [27] with permission of the American Chemical Society.

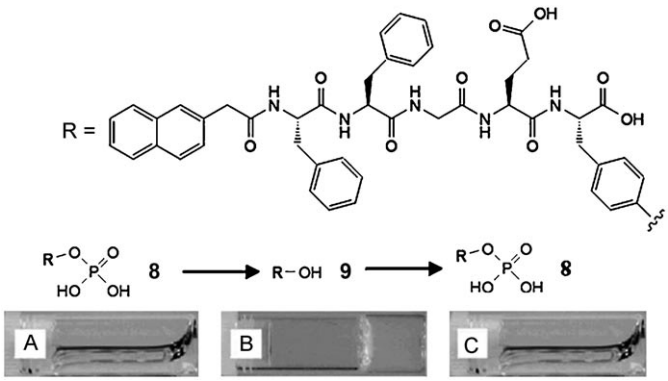
One possible disadvantage of using α-amino acid derivatives or α-peptides is their relatively high biodegradability owing to peptidase-catalyzed amide hydrolysis events. Obviously, this can be beneficial in terms of ultimate clearance of a material, but in some cases, a bioscaffold with greater in-vivo stability may be desirable. Xu and co-workers have therefore designed and synthesized a precursor molecule based on a β-peptidic structure that is known to resist a variety of peptidases.[29] A tripeptide derivative consisting of two β-amino acids was synthesized (that is, β^3-homophenylglycine and an α-amino acid, tyrosine phosphate). Self-assembly and macroscopic gelation were triggered by the presence of phosphatase. Interestingly, the morphology of the network structure and rate of hydrogelation were dependent on the amount of enzyme present: high levels of enzyme resulted in greater fiber polydispersity. Importantly, the β-peptide-based hydrogels had longer half-lives than α-peptide hydrogels when implanted in the subcutaneous environment of mice.[30]

The examples highlighted above describe enzymatically controlled hydrogelation based on a single enzyme. However, in nature it is common for a pair of enzymes to work together to regulate protein function in biological systems. This strategy has been cleverly incorporated into a hydrogel (Scheme 4). The precursor molecule **8** undergoes dephosphorylation in the presence of phosphatases, and a sol–gel transition was observed as a self-assembling hydrogel based on the pentapeptidic hydrogelator **9** was formed.[31] Gelator **9** is the substrate of a tyrosine kinase, and in the presence of this enzyme and ATP, the hydrogel undergoes a gel–sol transition as the compound is phosphorylated, giving precursor molecule **8**. This is an exciting example of molecular hydrogelation based on a reversible phosphatase/kinase switch. Furthermore, in-vivo enzymatic hydrogelation confirmed the biocompatibility of this approach.



Scheme 3. Synthesis of the β-lactam conjugate **6**. In the presence of β-lactamase, it is converted into hydrogelator **7**. Conditions: a) $NaHCO_3$, DMF; b) TFA, anisole, CH_2Cl_2; c) β-lactamase, pH 8.0. Reproduced from reference [28] with permission of the American Chemical Society.

In biomedical applications, enzyme-catalyzed, in-situ reversible self-assembly and gelation of hydrogelators may be advantageous because it allows the hydrogel to respond to the expression of specific enzymes. Furthermore, an investigation of the enzymatically regulated self-assembly may



Scheme 4. A pentapeptidic hydrogelator system based on the reversible phosphatase/kinase switch. Optical images (A–C) indicate how the properties of the material are changed by the enzyme switch. Reproduced from reference [31] with permission of the American Chemical Society.

help provide an understanding of the behavior of supramolecular hydrogels in a biological environment in which multiple enzymes are present.

2.3. Enzyme–Hydrogel Hybrid Materials

A supramolecular hydrogel based on a glycosylated amino acid ester applied as a semi-wet peptide/protein gel array was compatible with enzyme assays and the screening of enzyme inhibitors.[32] Aqueous cavities created in the gel matrix provided a suitable semi-wet reaction medium for an enzyme, whereas the hydrophobic domain of the fibrillar gel network provided a way of monitoring the subsequent enzymatic reaction. In a proof-of-principle experiment, lysyl endopeptidase (LEP) was used as the enzyme catalyst. A pentapeptide substrate for LEP was designed bearing Lys and a fluorescent environmentally sensitive probe DANsen, which acts as a hydrophobic moiety at the C terminal. In principle, when LEP cleaves the peptide bond adjacent to the DANsen, the environmentally sensitive DANsen molecule should shift from the aqueous environment of the hydrogel cavity to the hydrophobic fibrillar network, inducing a fluorescence change. The assay was constructed by spotting a glass plate with hydrogel followed by the injection of various protein substrate solutions and the corresponding enzymes. Before hydrolysis, the emission maximum of DANsen was at 540 nm, which is comparable to that in an aqueous solution. After enzymatic cleavage, the emission maximum shifted to 508 nm and the emission intensity increased twofold. This was accompanied by a visible color change of the hydrogel from pinkish-yellow to light green. The results indicate that the peptide/hydrogel array can indicate the enzyme based on its catalytic proficiency.

The findings described above stimulated Hamachi and co-workers to immobilize a fluorescent zinc(II) sensor in an analogous hydrogel, developing a semi-wet molecular recognition chip for the high-throughput analysis of metal cations.[33] Typically, a heated solution (10 μL) of gelator **10** and probe **11** was spotted onto a glass plate prior to gelation, and allowed to stand for one hour to yield a hydrogel array (Figure 2). After different cations were added to each hydrogel spot, strong blue emissions were only observed on the spots to which the zinc(II) and the cadmium(II) solutions were added. In contrast, a very weak emission was observed in the hydrogels containing Na^+, K^+, Mg^{2+}, Ca^{2+}, Fe^{3+}, Co^{2+}, or Ni^{2+} ions. The next stage was to integrate four different probes in a single hydrogel spot to enable the simultaneous identification of mixtures of a phosphorylated peptide, zinc(II), calcium(II), and hydroxide (i.e., pH value) at different concentrations. Lanes 3–5 in Figure 2 clearly show weaker spots, which correspond to the missing components (Ca^{2+}, Zn^{2+}, or phosphorylated peptide, respectively). This work highlights the feasibility of using a molecular hydrogel as a platform for the high-throughput sensing of mixed analytes. There has been great interest in the development of sensor gels, not only using enzymes, but also using chemical sensors. For example, Shinkai and co-workers have designed a colorimetric detection material based on an organogel, which differentiated different classes of electron-rich naphthalene compounds.[34]

The design of semi-wet molecular recognition chips has been further extended to selectively sense and discriminate between various phosphate derivatives, that is, phosphate,

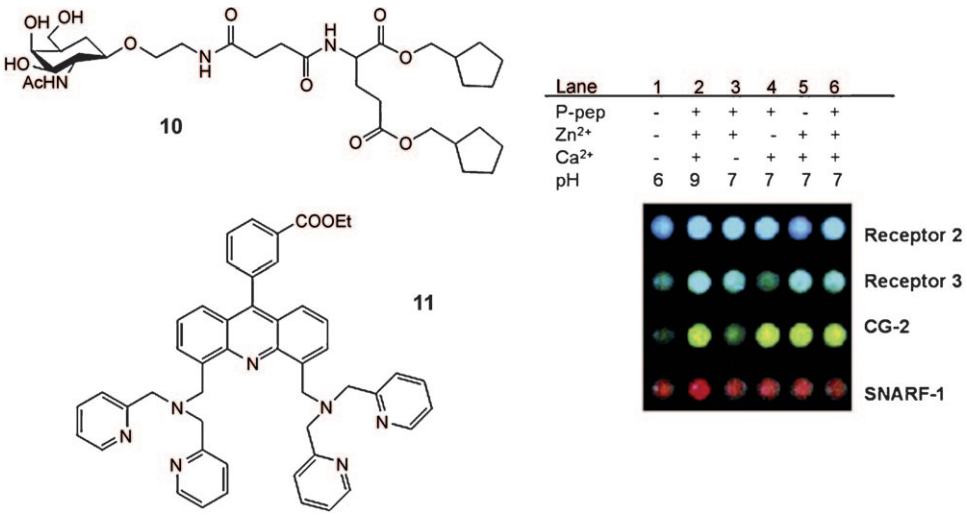


Figure 2. Representation of the components of the hydrogel and a photograph of an integrated hydrogel chip, showing the sensing patterns for mixed solutions. Reproduced from reference [33] with permission of the American Chemical Society.

phosphotyrosine, phenyl phosphate, and adenosine triphosphate (ATP), based on a combination of a fluorescence wavelength shift, ratiometric fluorescence change, and simple fluorescence.[35] Furthermore, Bhuniya and Kim synthesized a monosaccharide-based fluorescent pyrene-containing hydrogelator with the ability to sense insulin.[36] In the presence of insulin, the emission spectrum of the hydrogel at 393 nm, corresponding to the pyrene moiety, decreased. The authors suggested intercalation of insulin within the fibrous network structure perturbed aggregation of the pyrene moieties. As a result, upon sensing insulin, the originally deep-blue hydrogel turned green–blue.

Xu and co-workers have developed molecular gels containing encapsulated enzymes to catalyse reactions.[37a] One such system incorporated hemin, which is a ubiquitous enzyme that catalyses the peroxidation of pyrogallol to purpurogallin.[37b] Hemin chloride was mixed into the hydrogel, which was formed by the self-assembly of equimolar equivalents of two amino acid derivatives and two equivalents of sodium carbonate. Transmission electron microscopy (TEM) and energy-dispersive X-ray spectroscopy (EDX) confirmed a network structure, which consists of 20 nm diameter fibers in which hemin molecules were localized on the nanofiber surface. Furthermore, using UV/Vis spectroscopy, the authors suggested that, in analogy with literature data,[38] the localized enzyme was monomeric hemin chloride. The molecular gel was observed to provide a scaffold that both immobilizes and enhances the catalytic activity of hemin chloride for peroxidation in water.

Hydrogel-immobilized enzyme catalysis has also been used as a delivery model for hydrophobic drugs. John and co-workers reported an enzyme-triggered curcumin release mechanism based on amygdalin derivatives.[39] Gel degradation occurred owing to the cleavage of ester bonds in the gelator. Manipulating the enzyme concentration and/or the temperature controlled the release of the encapsulated curcurmin. Other examples employing a similar approach include the enyzme-mediated hydrolysis of (*S*)-(+)-ibuprofen-based hydrogelator,[40] enzyme- and pH-triggered release of oligonucleotides from a biotin-based hydrogel,[41] and an enzymatically cleavable gelator–drug conjugate capable of releasing a model drug molecule, 6-aminoquinoline.[42] Other molecular gels have also been developed to entrap and release biologically important molecules, including quinoline derivatives often used as antimalarial and antileishmanial drugs,[43] leuprolide associated with prostate cancer and endometriosis,[44] and vitamin B_{12}.[45]

Stupp and co-workers reported the synthesis and in-vitro magnetic resonance (MR) images of a self-assembling peptide amphiphile appended with a gadolinium(III)-complexed tetraazamacrocycle. This strategy allows the biomaterial scaffold to be imaged in vivo, providing vital information on the fate of the self-assembled material.[46]

2.4. Biomineralization

Organisms have been producing mineralized skeletons for the past 550 million years. In nature, the key components for biomineralization are proteins, lipid structures, and larger macromolecular frameworks, which are intimately involved in controlling the nucleation, growth, and shape of the inorganic phase, as well as adapting its mechanical properties.[47] In this way, self-assembled organic components are used to direct the hierarchical organization of inorganic matter. This process has attracted scientists, not only for the development of new inorganic materials, but also as a biomimetic process of mineralization. One way to accomplish this in artificial systems is to prepare an organic template based on a small molecule gelator that can, after self-assembly, control crystal nucleation and growth. This approach potentially offers a new nanofabrication process for the construction of organized synthetic materials.

This principle was first demonstrated by Shinkai and co-workers using a cholesterol-based gelator as a template to prepare hollow fibrillar silica.[48a] In this example, the cholesterol derivatives gelated tetraethoxysilane (TEOS), which was used to produce silica by a sol–gel polymerization process. This strategy afforded hollow fibrillar structures composed of silica, with the organogel fibers acting as a template in the TEOS polymerization process. After calcination, hollow tubes were formed.[48b–d] This ground-breaking work was furthered by the discovery that the chirality present in the gel–fiber template could be transcribed into the silica; in one example, a right-handed helical orientation was templated into the fibrous silica.[49,50] Additionally, different families of small-molecule gelators have been used as templates to direct the growth of anisotropic inorganic objects (hollow fibers, ribbons, tubes, helices, etc.) of silica,[51] metal oxides,[52] or other non-oxide materials,[53] such as copper(II) sulfide.

Stupp and co-workers designed a nanostructured organic template to study the mineralization of biologically relevant apatite crystals, namely bone material.[54] This system was based on the self-assembly of a dendron rod–coil (DRC) peptide amphiphile **12** (Figure 3). This self-assembling compound contains five structural regions: region 1 is a long alkyl tail that conveys hydrophobic character, endowing the molecule with amphiphilicity; region 2 consists of four cysteine residues that can form disulfide bonds upon oxidation; region 3 is a linker of three glycine residues to provide flexibility; region 4 is a phosphorylated serine group designed to interact with calcium ions and direct crystallization; and region 5 displays the cell adhesion ligand RGD. After cysteine cross-linking, the fibers were able to direct the mineralization of hydroxyapatite to form a biocomposite in which the crystallographic *c* axes of hydroxyapatite were aligned with the long axes of the fibers, which is analogous to the alignment observed between collagen fibers and hydroxyapatite crystals in bone.

Mann and co-workers have demonstrated that hydrogels produced by enzymatic dephosphorylation of *N*-(fluorenylmethoxycarbonyl)tyrosine phosphate can be used as organic templates for the mineralization of calcium phosphate.[55] The dephosphorylation of **13** in water produces compound **14**, which helically self-assembles by π stacking of the fluorenyl end groups (Figure 4). The resultant hydrogels consist of interconnecting bundles of coaligned fibers that are about

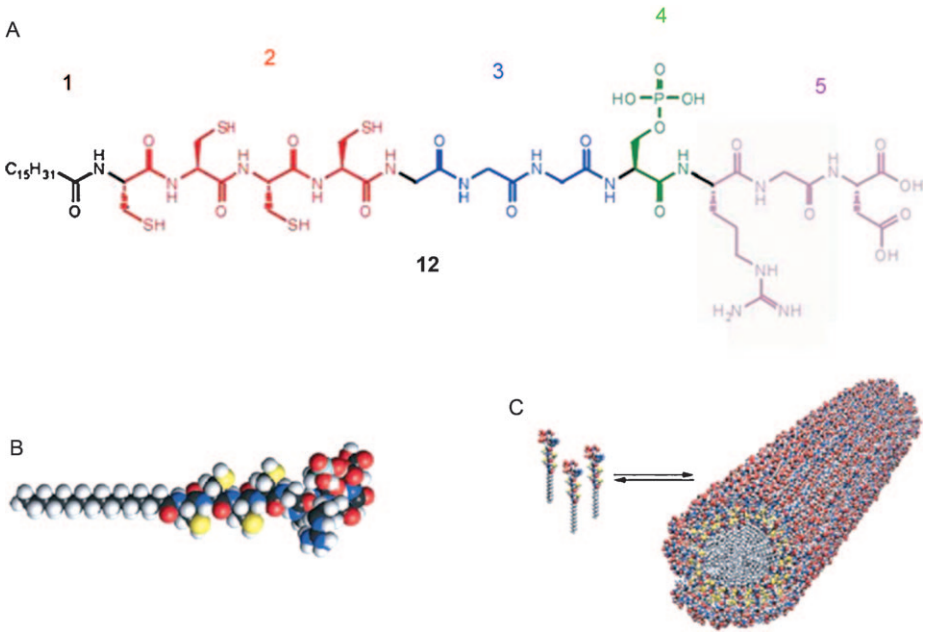


Figure 3. A) Chemical structure of the DRC **12**, with the five structural features indicated by color (see text). B) Molecular model of the DRC. C) Self-assembly of the DRC into a cylindrical micelle. Reproduced from reference [54] with permission of the American Association for the Advancement of Science.

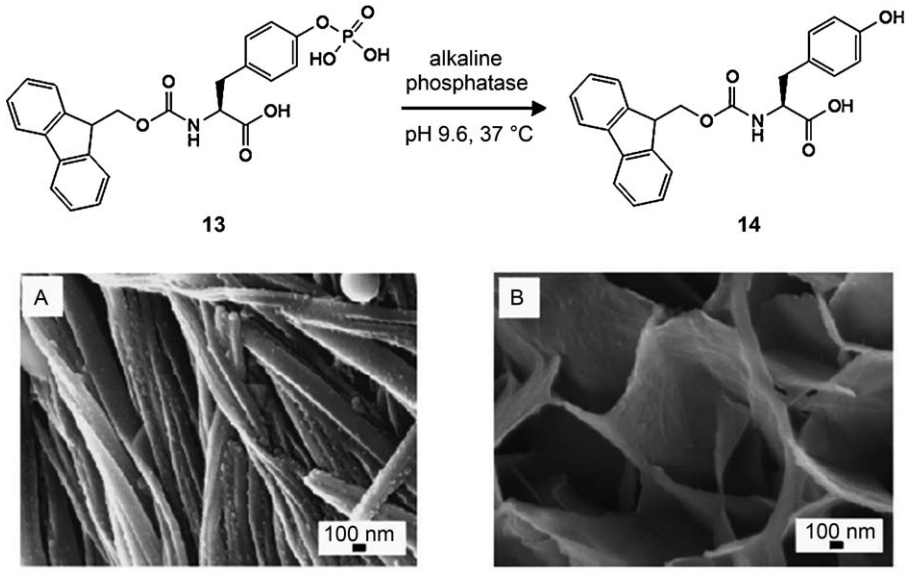


Figure 4. Hydrogel formation by alkaline phosphatase-catalyzed dephosphorylation. A) Image indicates discrete calcium phosphate nucleation sites across the fiber surface. B) Intact macroporous calcium phosphate network after disassembly of the self-assembled matrix.[55]

100 nm wide. Soaking the phosphate-containing hydrogels in calcium chloride solution (12–18 h, 1 mM $CaCl_2$) led to relatively low levels of mineralization, producing gels that consisted of a network of well-defined mineralized fibers. High-magnification scanning electron microscopy (SEM) suggested that mineralization of the self-assembled fibers occurred at multiple nucleation points on the fiber surface (Figure 4A). Corresponding TEM images of mineralized films showed regular arrangement of needle-like hydroxyapatite crystals, suggesting that both nucleation and growth of calcium phosphate were influenced by the presence of self-assembled fibers. Extensive mineralization of the hydrogel (one week, 0.1 M $CaCl_2$) produced hardened composites. Viscoelasticity measurements showed that increased levels of mineralization enhanced thermal stability, stiffness, and resistance to breakage under tension, suggesting that hybrid composites with different properties can be readily prepared. Washing these samples with water dissolved the self-assembled gel network to produce a sample-spanning macroporous inorganic network. (Figure 4B). Significantly, deposition of calcium phosphate in the absence of the self-assembled gel network produced only dense hydroxyapatite aggregates.

Hamilton and co-workers used a self-assembled hydrogel[56] to provide a microenvironment for calcite crystallization.[57] The gel network created by the self-assembly of a carboxylate-bearing molecule offers the potential of providing fibrous structures with calcium(II) binding sites. In this case, however, the gel network provided a nonspecific template for the adsorption and growth of calcite crystals. Nonetheless, the results suggested that during the growth of calcite crystals, the gel network became occluded into the crystalline lattice, and this in turn modified the dissolution properties of the crystals. These results highlight the complexity of mineralization processes, in which the template may have several roles, including specific adsorption onto growing crystal faces, intercalation into the crystalline matrix, and the presentation of ordered binding-site arrays.

3. Using Gels to Create Modified Smart Materials

The self-assembly of gelators provides an easy method for the generation of inherent nanostructures on surfaces and within materials. As such, gel modification offers an interesting approach for the synthesis of a new class of nanostructured smart materials.

3.1. Surface Modification with Gels

The development of highly hydrophobic surfaces is usually achieved using polymers.[58] However, in a recent study, Nakano and co-workers have demonstrated that

supramolecular polymer gel materials can also be used to achieve large effects on surface mofification.[59] The surface roughness of glass plates, and hence their hydrophobicity, was modified by treatment with perfluoroalkyl gelators mixed with volatile solvents, which evaporated to leave a thin-film dried xerogel. The packing of gelator fibers on the dried glass surface led to the surfaces having water contact angles greater than 150 degrees, which is a significant degree of modification using such a simple approach.

Figure 5. Hard and rubbery materials formed by polymerization under the same conditions: pure polystyrene (left); gel-derived polystyrene using 1 wt% DRC (middle); and gel-derived poly(2-ethylhexylmethacrylate) using 1 wt% DRC (right). The rubbery material (right) was mechanically deformed by hand before the image was taken.[61]

3.2. Polymer Modification with Gels

In 1997, pioneering work by a number of groups initiated the investigation of polymer gel hybrid materials.[60] In this work, solvents capable of being polymerized, such as methyl methacrylate or styrene, were mixed with an appropriate low-molecular-weight gelator and immobilized. Polymerization of the solvent was then initiated to yield a hybrid polymeric material with an embedded gel network that can exhibit modified material properties. In these early studies it was further demonstrated that removal of the self-assembled gelator from the polymer was possible, leaving porous materials that contained mesoscopic channels of submicrometre dimensions.

Stupp and co-workers built on this early research and reported some particularly remarkable results. They used a self-assembled DRC molecular scaffold to modify bulk polymer properties. They used their DRC gelator to structure polymerizable solvents, such as styrene or acrylates. Subsequent polymerization should, in principle, capture the self-assembled gel nanoscaffold. Figure 5 illustrates how the presence of the gelator has a visible macroscopic effect on the properties of the resultant polymer. TEM micrographs of thin films of the polystyrene, stained with osmium tetroxide, provided some evidence for the presence of ribbon-like morphologies within the polymer.[61] This work has been further extended, and the presence of the DRC gelator within drawn polystyrene gave rise to higher orientational order and significantly improved impact strength. We have recently reported polymeric materials with embedded gel-phase nanostructures, which contain reactive pripheral groups, and demonstrated that these groups can be selectively reacted within the polymer matrix.[62] This offers a new approach to the fabrication of modified multifunctional nanomaterials.

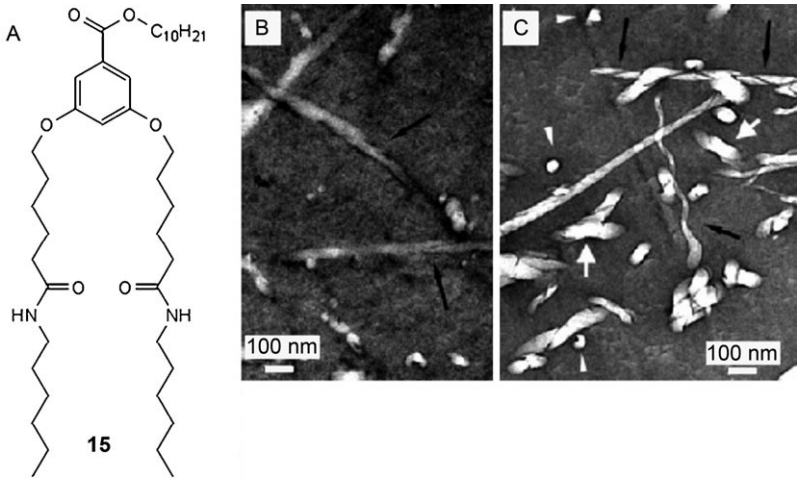


Figure 6. A) The structure of the gelator **15** (BHPD). B) TEM image of the templated polymer. Black arrows indicate helical tapes. C) TEM image with the template removed. White arrows indicate helical pores. Reproduced from reference [63b] with permission of the American Chemical Society.

Mésini and co-workers showed that 3,5-bis(5-hexylcarbamoylpentoxy)benzoic acid decyl ester (BHPB, **15**; Figure 6) formed gels in various organic solvents, including the polymerizable solvent ethylene glycol diacrylate (EGDA).[63] UV irradiation of a BHPD/EGD mixture in the presence of an initiator resulted in a transparent, glassy material.[63b] Extraction of the self-assembled scaffold using dichloromethane led to oblate objects with widths between 30 and 50 nm and lengths between 500 nm and 1 μm. It was argued that these were voids left after dissolution of the templates corresponding to helical pores (Figure 6C). Furthermore, N_2 adsorption isotherms obtained for systems containing 50 wt% template were recorded and showed the specific area increased dramatically after the washing process, from 0.5 $m^2 g^{-1}$ to 50 $m^2 g^{-1}$, once again indicating the removal of the self-assembled template and the formation of nanostructured voids. Such materials may have potential applications in separation science or catalysis.

3.3. Gel-Phase Materials with Applications in Optical Technologies

The ability of gel materials to respond to light has been of intense interest since the early work of Shinkai and co-workers demonstrated that the incorporation of an azoben-

zene unit into a cholesterol-based gelator could yield soft materials with a degree of photoresponse.[64] The transition of the azobenzene unit from *trans* to *cis* drives the transition from gel to sol, and this process could be repeated numerous times. The gel–sol–gel transition was monitored by circular dichroism spectroscopy and simple visual observation of the macroscopic properties. The general strategy of employing a molecular unit, which responds to photoirradiation, is a powerful way of building photoaddressability into gel materials. This strategy has since been employed by a range of researchers and demonstrated to modify the gel–sol transition characteristics.[65]

To generate highly responsive materials, Feringa, Duppen, van Esch et al. designed an amide-appended dithienylcyclopentene gelator capable of light-induced reversible switching between an assembled and a nonassembled state and macroscopically expressed as a reversible sol–gel phase transition.[66] This feature was exploited to generate spatially confined gel objects in solution by selective irradiation ($\lambda = 330$ nm) of the sample through an optical mask. Nonassembled molecules that diffused into the irradiated area were captured to create the assembled gel network. Interestingly, the self-assembled structure was erased with visible light ($\lambda = 420$ nm). The cycle of gel formation/erasure was repeated several times, and thus the gel therefore clearly demonstrates the process of an optically-induced read–write cycle. Finally, a toluene solution (1.5 mM) in a 1 mm cell was simultaneously irradiated with a diffraction grating of $\lambda = 330$ nm and a homogeneous beam at $\lambda = 500$–600 nm. This method allowed patterns in the same sample to be both formed and disassembled, enabling the generation of patterns that can be created, changed, or replaced.

Kato and co-workers have also developed a photoresponsive liquid-crystalline gel applicable as a rewritable information recording material (Figure 7).[67] This composite gel consists of a chiral diamide gelator (**16**) based on two azobenzene moieties in a nematic liquid crystal (LC) phase (**17**). Reversible structural changes between LC nematic gel and LC cholesteric solutions were induced by *trans–cis* photoisomerization of the gelator azobenzene groups. The cholesteric LC phase was induced by the chirality of the gelator with *cis*-azobenzene units dissolved in the nematic phase. Upon UV irradiation using a template (that is, photopatterning), these two different LC states coexist. Therefore, the photopatterning process was applied as a method of photon-mode rewritable information recording. Figure 7B shows a polarized image of the stored lattice pattern (200 μm). The regions of the nematic gels with fine domains and the cholesteric solution state with characteristic structures are arranged alternately. Excitingly, Figure 7C shows the photoinduced pattern prepared by UV irradiation through a photomask. This result shows that micrometer-scale patterns can be recorded based on this gel-phase composite material. The rewritable patterns are stable at room temperature for more than one year, and importantly, the patterns can be erased by heating the material to the isotropic temperature, rendering the material amenable to a new patterning cycle.

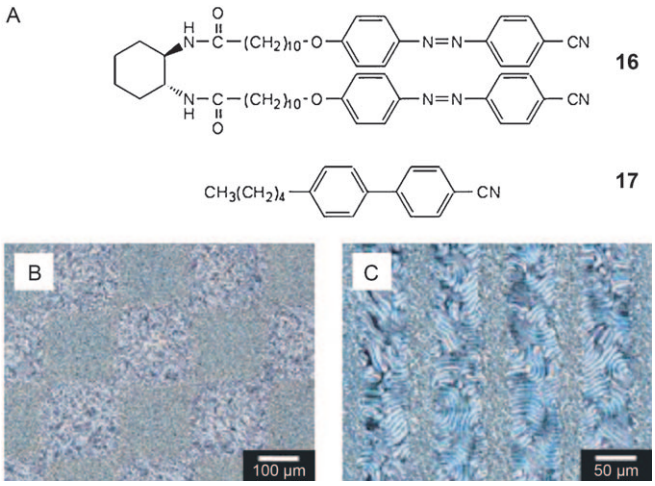


Figure 7. A) Molecular structures of the photoresponsive hybrid material—gelator **16** and LC mesogen (anisotropic structure-ordering unit) **17**. B) Polarized photomicrograph of a patterned sample prepared by UV radiation through a photomask with a 200 μm lattice. C) Polarized photomicrograph of a patterned sample prepared by UV radiation through a photomask of 50 μm lines and spaces.[67]

3.4. Metallogels

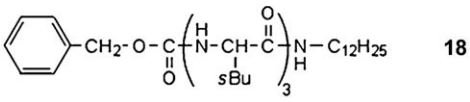
The combination of molecular self-assembly and coordination chemistry provides a powerful design tool for the development of gel-phase materials.[68] Many metal chelates have long-lived excited triplet states that emit strongly in the visible region. Metallogelators are therefore ideal for luminescence-based technologies, photovoltaics, and photocatalysis. This design principle has been demonstrated by Aida and co-workers.[69] Based on a trinuclear gold(I) pyrazolate metallacycle gelator, room-temperature phosphorescence could be recorded in the gel phase. Doping/undoping with silver(I) induced a reversible red–green–blue luminescence. This model was exploited to generate security inks for the preparation of rewritable phosphorescent paper.[70]

Metallogels, in which the self-assembled networks incorporate palladium, catalyze the oxidation of benzyl alcohol to benzaldehyde.[71] Recently, Tu, Dötz and co-workers showed that a palladium–CNC pincer bis(imidazolylidene) complex appended with two C_{16} alkyl chains forms gels in a variety of protic and aprotic solvents.[72] The catalytic activity of the material towards the double Michael addition of α-cyanoacetate to methyl vinyl ketone was investigated—palladium pincer carbene complexes are known catalysts for this reaction.[73] The DMSO-based gel revealed a higher catalytic activity than that based on DMF. To ensure that the self-assembled gel was responsible for the observed catalytic activity, a saturated solution of the palladium complex in dichloromethane was also applied as the catalyst. Under these conditions, the double Michael addition was comparable to a blank test. This study reveals that incorporating organometallic compounds into self-assembling gel systems may yield accessible, tunable materials with promising catalytic activity.

3.5. Alignment of Gel Fibers

Meijer and co-workers have used a magnetic field to align the fibrillar self-assembly of 2,3-bis-*n*-decyloxyanthracene gelator molecules during organogel preparation.[74] This remarkable effect occurs because of the diamagnetic susceptibility of organic molecules when placed in a magnetic field. In a normal solution-phase sample, thermal effects and Brownian motion prevent complete alignment; however, in a self-assembled gel, the magnetic field is able to overcome these weakened forces and thus align fibers. The fibrous network was orientated perpendicular to the magnetic field direction and the aligned organogel system even maintained its stability after removal of the field. This molecular material had a fiber orientation order parameter of 0.85, a large linear birefringence, and fluoresence dichrosim. Further examples of this approach have included the alignment of peptide amphiphiles appended with polymerizable diacetylene moities.[75] In this case, it was necessary to cool the sample from above its T_{gel} value (90 °C) whilst applying the magnetic field. Subsequent polymerization of the peptide amphipihiles by the diacetylene units of the alkyl chain provided a mechanism for transferring the birefringence properties of the gel to a bulk material. An alternative approach to generating magnetically responsive gels involved the incorporation of superparamagnetic iron oxide nanoparticles into a gel.[76]

Kato and co-workers have taken a different approach to achieve alignment by developing liquid-crystalline physical gels. These systems are based on the liquid-crystal phase previously described (**17**) as a hybrid material, with the incorporation of self-assembled fibers based on small molecule gelators (**18**).[77] Interestingly, these composite materials have two independent thermoreversible transitions based on the gel network and the liquid crystal phase. Therefore, two types of structural changes are possible. If the thermally reversible sol–gel transition ($T_{sol-gel}$) of the gel network is higher than the isotropic–anisotropic transition temperature (T_{iso-Ic}) of the liquid crystal component, a type I material is formed. This system has a randomly dispersed gel network is formed in the isotropic LC phase. Conversely, if $T_{sol-gel}$ is lower than T_{iso-Ic}, then a type II material is formed, in which the liquid crystal acts as a template and induces the formation of an oriented self-assembled gel network. Type II systems have been exploited to develop materials with a light-scattering, high-contrast electrooptical switch in reverse mode (i.e., transparent in the off-state and turbid in the on-state).[78] Such switching is desirable for applications in which the transparent state is present in the absence of an applied voltage, and would be advantageous for switchable coatings for windows and large-area and projection displays. As shown in Figure 8A, the homeotropically oriented system is formed by the template effect of the LC media on the gel network. In this case, the material was optically transparent. Application of an electric field (80 V) resulted in the random alignment of the LC molecules within the nontemplated, disordered gel network, leading to the formation of randomly orientated polydomains of liquid crystals (Figure 8B). The material then scatters the incident light, and a turbid material was observed. Such materials have potential applications in, for example, electrically switchable pricvacy windows.



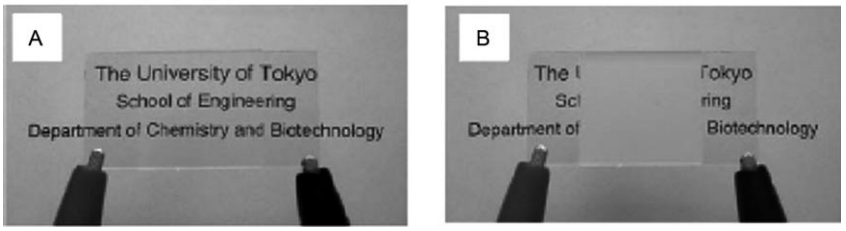


Figure 8. A) The gelator molecule (**18**) employed in a hybrid material. A, B) Photographs of a liquid-crystal cell incorporating the nematic gel of LC **17** and gelator **18**: A) light transmission state; B) light scattering state.[77a]

4. Electronic Devices

There is currently intense interest in the development of molecular electronic devices, and particularly the facile construction of effective molecular wires or conductive architectures.[79] These architectures are synthetic nanometer-sized materials that are capable of directional, long-range electron transport. Using chemically programmed self-assembly, nanowires may be created from almost any polymeric and oligomeric π-conjugated system.[80] Synthetic components that are among the most promising candidates to create (opto)electronic devices include conjugated oligomers,[81] polythiophenes,[82] phthalocyanines,[83] (Pcs) and tetrathiafulvalenes[84] (TTFs). However, the properties and performance of these materials not only depend on the electronic structure of the molecules themselves, but also the precise spatial organization of components with well-defined geometries with respect to their neighbor.[85] Given the versatility of chemical synthesis used in forming the individual components and the one-dimensional fibrillar nature of gel-phase materials, attention has naturally begun to focus on the ability of self-assembled gels to facilitate energy transfer processes.[86] In this way, molecular gels may ultimately provide an approach for the nanofabrication of miniaturized devices with high-tech electronic applications.

4.1. Assembly of Electroactive Organic Building Blocks

A early example of the assembly of electroactive building blocks to form gel nanofibers was presented by van Esch and co-workers in 1999.[87] They employed their widely investigated bisurea gelation motif and functionalized it with mono- and bithiophene units. The self-assembled fibers which result exhibit efficient intermolecular charge transport as a consequence of the noncovalent organization of the electro-

active molecular building blocks. The assembly of this type of building block was further studied at the liquid–solid interface using scanning tunnelling microscopy.[88] The hydrogen-bond interactions controlled the spatial alignment, whereas the π-systems were partially overlapping, providing a potential pathway for charge transport.

Extensive studies by Meijer and co-workers later showed that suitably functionalized oligo(*p*-phenylvinylene)s (OPVs) have the capability to self-assemble, and can provide efficient excitation energy donors to suitable acceptors.[89] Recently, this concept was applied to create luminescent organogelators that self-assemble into controlled nanoscale architectures.[90] Ajayaghosh and co-workers have demonstrated the ability to encapsulate an energy-accepting molecule (< 2 mol %) within the organogel scaffold of OPV donors, thereby facilitating energy transfer in the gel state.[90d] Energy transfer is only feasible in the gel phase and occurs exclusively from the donor OPV gel network as a result of fast and efficient exciton migration. These results open up the possibility of developing artificial light-harvesting gel materials.

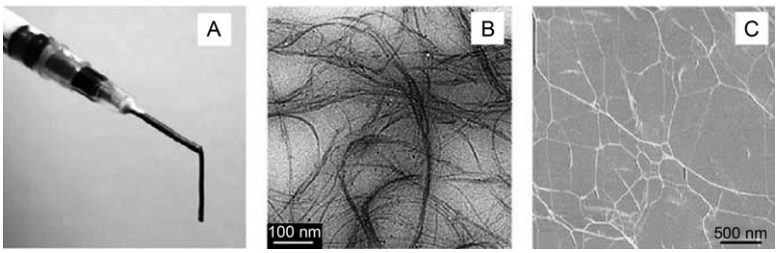


Figure 9. A) SWNT-based gel. B) TEM image of SWNTs obtained by dispersion of a gel (in $BMIBF_4$) in deionized water. C) AFM phase image of the surface of a SWNT-based plastic film prepared by free-radical polymerization of a methacrylate derivative of an imidazolium-ion-based SWNT–gel system. Reproduced from reference [95c] with permission of Royal Society Publishing.

A recent example by Meskers, Schenning and co-workers used a template approach, in which gold nanoparticles are bound to tape-like structures of self-assembled OPV organogelators.[91] This approach offers a potential design strategy for creating optoelectronic materials based on the immobilization of gold nanoparticles on the periphery of semiconducting π-conjugated gelator systems. In this case, the proximity of the metal particles to the π-conjugated tapes facilitates electronic communication.

Amabilino and co-workers prepared electroactive fibrillar nanowires from an amide-functionalized TTF-based organogel.[92] The xerogel was prepared on a glass surface and oxidized with iodine vapor. The resultant material had a room-temperature conductivity $\sigma = 3\text{–}5 \times 10^{-3}\ \Omega^{-1}\,cm^{-1}$. The temperature dependence (200–300 K) of the resistance also indicated semiconductor-like properties, with an activation energy $E_{act} = (170 \pm 15)$ meV. Annealing the xerogel allowed the formation of robust TTF nanowires on different substrates, generating an electrically conducting thin film. Shinkai and co-workers also developed a TTF-based gelation system composed of one-dimensional fibers that were unusually highly aligned in one direction.[93] If doped with iodine, the mixed-valence state of the TTF stack had a characteristic absorption band in the NIR region, which is a necessary prerequisite for conductivity. Kato and co-workers have combined electroactive TTF-derived gelators with their liquid-crystal approach outlined in Section 3.5 and generated oriented gel fibers with interesting electrical conductivities.[94]

Aida and co-workers observed that sonication and grinding of a suspension of single-walled carbon nanotubes (SWNTs) in a variety of imidazolium-based ionic liquids led to the formation of gel materials.[95] In contrast to conventional molecular gels, these materials could be easily processed by extrusion from a syringe (Figure 9A). TEM was employed to demonstrate network formation of the SWNTs (Figure 9B), and Raman and electronic absorption spectroscopy showed that the SWNTs were not modified chemically. Differential scanning calorimetry, X-ray diffraction, and rheological measurements indicated that gelation was underpinned by a large number of weak physical cross-links between SWNT fiber bundles. Employing in-situ free-radical polymerization of gels based on acrylate- and methacrylate-appended ionic liquids generated a plastic film with embedded gelated SWNTs. These materials exhibited interesting electronic behavior; for example, a plastic film prepared from a methacrylate-appended ionic liquid and with 7 wt % content of SWNTs had a conductivity as large as $1\ S\,cm^{-1}$. Furthermore, the Young's modulus increased 120-fold. Such a large enhancement of the tensile modulus of SWNTs had never previously been reported for SWNT-doped polymeric materials, and indicates that the network formation of the nanotubes through gelation must be playing an active role in controlling the properties of the material. AFM showed that the plastic film contained a network structure composed of SWNTs (Figure 9C). This approach was extended to develop the first dry actuator.[96] The actuator film was fabricated by layer-by-layer casting of the electrode and electrolyte components. The electrode layer was composed of 13 wt % SWNTs, 54 % $BMIBF_4$ (1-butyl-3-methylimidazolium tetrafluoroborate), and 33 wt % of a 4-methyl-2-pentanone solution of vinylidene difluoride–hexafluoropropylene coplymer (PVdF(HFP)). The electrolyte layer contained 67 wt % $BMIBF_4$ and 33 wt % PVdF(HFP). Upon applying an electric potential of ± 3.5 V with a frequency of 0.01 Hz, the actuator underwent a bending motion towards the anode with a maximum displacement of 5 mm. The actuator also responded to an alternating voltage of ± 3.0 V, even at a much higher frequency of 30 Hz. The actuation process (± 2.0 V, 0.1 Hz) could be repeated for at least 8000 cycles in air. This elegant example thus clearly demonstrates the connection between molecular structure, nanoscale assembly, and macroscopic behavior.

Attention has also focussed on the fabrication of highly elongated materials based on gelator components with terminal polymerizable units.[97] Shinkai and co-workers introduced diacetylene units that are capable of being photopolymerized into an alkylamide-tethered tetraphenylporphyin gelator.[98] Using a decalin-based gel, this material was photopolymerized to fabricate unimolecularly segregated

polydiacetylene. Casting the gel onto highly orientated pyrolytic graphite (HOPG) and subsequent washing with cyclohexane to remove solvent before photopolymerization produced a network structure of fibers. AFM revealed that the photoirradiated sample consisted of unimolecular 3 nm fibrils, which were several micrometers in length without defects. This system thus offers a strategy for generating discrete unimolecularly stacked arrays that are applicable to the generation of conducting nanowires.

4.2. Organization of Metal Nanostructures Using Gels

Controlling the spatial organization of metal nanoparticle assemblies is one potential strategy for fabricating nanoscale electronic and optical devices.[99] Indeed, biological substrates,[100] such as viruses,[101] fungi,[102] and DNA[103] have been applied as scaffolds for the one-dimensional assembly or growth of nanoparticles. Recently, one-dimensional arrangements of metal nanoparticles were realized using gel composites[104] and fibers,[105] highlighting the possibility of fabricating metal-containing nanowires by molecular means using gel materials.

Stupp and co-workers templated cadmium sulfide using a gel-phase material based on helical nanoribbons formed from DRCs.[105a] Figure 10 shows a TEM image of mineralized nanoribbons formed from a gel based on ethyl methacrylate (EMA). In this case, the cadmium sulfide was isolated from a 1 wt% DRC gel, to which a solution of cadmium nitrate in THF had been added prior to exposure to hydrogen sulfide gas. The inorganic structures formed had a pitch of approximately 40–50 nm and were several microns in length. Additional electron-diffraction studies coupled with high resolution TEM confirmed that the polycrystalline mineral had the CdS zinc blende structure, as seen by rings corresponding to {111}, {220} and {311} reflections, and had a grain size of 4–8 nm. The authors proposed that the nanoribbons acted as a template in which the cadmium(II) ions were bound to the hydroxy groups of the DRC molecules, producing a supersaturation of ions around the ribbon, and leading to nucleation and crystal growth on exposure to H_2S gas.

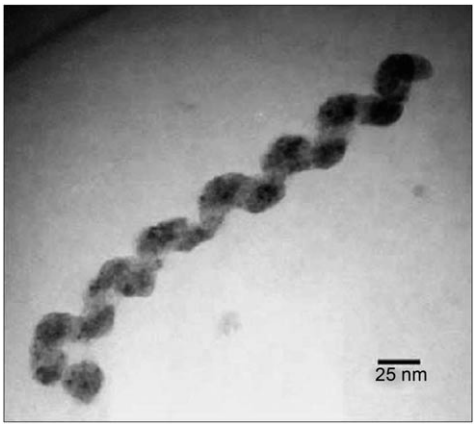


Figure 10. TEM micrograph of gels based on EMA in which CdS was precipitated.[97a]

Shirai, Kimura and co-workers designed a gelator based on a *trans*-1,2-bis(alkylamide)cyclohexane unit containing two thiol units.[105c] The two thiol units served as anchoring points for octanethiol-stabilized gold nanoparticles. FTIR spectroscopy showed that broad bands at about 3284 and 1637 cm^{-1} could be assigned to N–H and C=O stretch vibrations that pertain to intermolecular hydrogen bonding. The gelator was added to a degassed toluene solution (1.0 mL) of gold nanoparticles (50 mg) and heated above 60 °C. After cooling, a transparent brown-colored gel was formed. The gel was filtered, separating a brown solid from a colorless filtrate, suggesting that most of the gold nanoparticles had reacted with the thiol groups of the gelator. Furthermore, TEM images indicated that the fibrillar gel network consisted of spatially organized gold nanoparticles. Importantly, a system having a gelator lacking thiol groups showed no organization effects, indicating that the gold nanoparticles are linked to the self-assembled fiber by the site-exchange reaction between the nanoparticle and the thio-functionalized network structure. A similar approach has also been employed recently by Banerjee and co-workers.[105d]

5. Conclusions and Outlook

This Review demonstrates the power of synthetic chemistry to generate low-molecular-weight gelators with added functionality, which makes them of interest for high-tech applications. For a long time, molecular gels have been employed in relatively low-cost bulk applications, such as in lubricants, grease, and personal care products. However, with a clear understanding of nanoscale self-assembly processes, gelators can be designed to generate or exhibit unique forms of biological activity or materials behavior. Clearly, many challenges remain in this field. There will be an increasing need for well-designed molecular gelators with smart functionality, which results from the structural features programmed-in at the molecular level using synthetic chemistry. Furthermore, this field of research will continue to be supported by fundamental studies which provide greater insight into the mode and mechanism of gelation, and the development of models which allow the effective prediction of gel behavior. Building on this firm groundwork, it seems increasingly likely that such designer gel materials will reach the market for pharmaceutical or electrooptical applications, thus being a clear example of the way in which chemical synthesis and an understanding of the interactions between molecular building blocks will underpin the nascent field of nanofabrication.

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