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Catalysis of Supramolecular Hydrogelation

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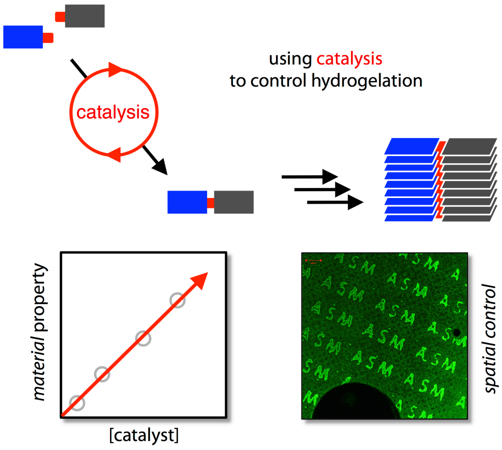
CONSPECTUS



One often thinks of catalysts as chemical tools to speed up a reaction, or to have a reaction run under more benign conditions. As such, catalysis has a role to play in the chemical industry and in lab scale synthesis that is not to be underestimated. Still, the role of catalysis in living systems (cells, organisms) is much more extensive, ranging from the formation and breakdown of small molecules and biopolymers, to controlling signal transduction cascades and feedback processes, motility and mechanical action. Such phenomena are only recently starting to receive attention in synthetic materials and chemical systems. 'Smart' soft materials could find many important applications ranging from personalized therapeutics to soft robotics, to name but a few. Until recently, approaches to controlling the properties of such materials were largely dominated by thermodynamics, for instance looking at phase behavior and interaction strength. However, kinetics play a large role in determining the behavior of such soft materials, for instance in the formation of kinetically trapped (metastable) states, or the dynamics of component exchange. As catalysts can change the rate of a chemical reaction, catalysis could be used to control the formation, dynamics and fate of supramolecular structures, when the molecules making up these structures contain chemical bonds whose formation or exchange are susceptible to catalysis.

In this *Account*, we describe our efforts to use synthetic catalysts to control the properties of supramolecular hydrogels. Building on the concept of synthesizing the assembling molecule *in the self-assembly medium* from non-assembling precursors, we will introduce the use of catalysis to change the kinetics of assembler formation, and thereby the properties of the resulting material. In particular, we will focus on the synthesis of supramolecular hydrogels where the use of a catalyst provides access to gel materials with vastly different appearance and mechanical properties, or controls localized gel formation and the growth of gel objects. As such, catalysis will be applied to create molecular materials that exist outside of chemical equilibrium. In all, using catalysts to control the properties of soft materials constitutes a new avenue for catalysis, far beyond the traditional use in industrial and lab scale synthesis.

1. INTRODUCTION

This Account deals with the development of a supramolecular hydrogelator system where the properties, rate of formation and spatial distribution of hydrogel materials are determined using catalysis, by controlling the rate of formation of the hydrogelator molecules. Catalysis is historically considered to be an indispensable tool in the synthesis of both simple and highly complex molecules and polymers, ranging from milligram lab-scale to multi-ton industrial processes. As catalysts can also be used to amplify a signal[1], they are also widely applied in sensing, for instance through the ELISA protocol. The role of catalysis in living systems is even more elaborate, ranging from the formation and breakdown of small molecules and biopolymers, to signal transduction cascades, and controlling motility and mechanical changes in cells. A catalyst is defined as a chemical species that can increase the rate of a chemical reaction without being consumed itself. As such, catalysis could be used to control the formation, dynamics and fate of supramolecular structures, when the molecules making up these structures contain chemical bonds whose formation or exchange are susceptible to catalysis. This concept, although common in nature, has so far found little attention in synthetic molecular systems.

2. TIMELINE

Around 2010, the Advanced Soft Matter group at Delft University of Technology developed a major research program on the *in situ* formation and assembly of surfactants from soluble and non-assembling building blocks. There, surfactant formation is based on the spontaneous and reversible formation of imine bonds in aqueous solvents, starting from soluble amine-functionalized hydrophobic tails and typically a charged hydrophilic head group functionalized with an aldehyde moiety.[2,3,4] This concept was later also applied to the formation of dynamic covalent gels[5] and conjugated polymers.[6] Importantly, in all these systems, the imine formation equilibrium is reached rapidly after mixing of the precursors and the properties of the final system are largely determined by the chemical structure of the formed surfactants and thermodynamic parameters such as the equilibrium constant of imine formation, and the surfactant critical aggregation concentration. One of the questions we had was whether changing the rate of formation or exchange of such dynamic covalent bonds would impact on the behavior of such assemblies and materials.

At the time, we noticed the work of Rein Ulijn (City University in New York), and Bing Xu (Brandeis University). In their work, they use enzyme-catalyzed transformations of peptide-based gelators to control gelator assembly.[7,8,9,10] In our group, we also used enzymatic catalysis to control break-down kinetics of supramolecular gels.[11,12] Enzymes rank among the most active and efficient catalysts known. Still, enzymes can be limited in substrate scope, reaction types, stability, solvents and operating conditions. Also, their size can be both a blessing and a burden in terms of diffusive mobility. Although typically less active than many enzymes, synthetic catalysts such as transition metal complexes and organocatalysts can catalyze a seemingly unlimited range of molecular transformations, with broad substrate scope and under widely differing reaction conditions. Having worked on transition metal catalysis, both in polymer synthesis[13] and aimed at applications in enantioselective synthesis[14,15], we were then inspired to use non-enzymatic catalysis to control the formation and properties of supramolecular materials. As such, this should provide a versatile handle to start using reaction kinetics instead of thermodynamic stability as a design parameter in synthetic supramolecular materials. Two main types of supramolecular structures were studied in the group at the time, namely surfactant assemblies and supramolecular fiber-based gelatinous materials.[16,17] We chose supramolecular gels as our first assembly type to subject to catalytic control.

3. CONCEPT & MOTIVATION

The last decades have witnessed great advances in the design, application and understanding of soft, supramolecular materials. Historically, approaches to controlling the properties of such materials were largely dominated by thermodynamics, by investigating parameters such as phase behavior, melting temperatures and association constants (interaction strength). Although often ignored, kinetics play a large role in determining the behavior of soft materials, for instance in the formation of kinetically trapped (metastable) states, or the dynamics of component exchange. Kinetic parameters are now finally starting to receive the attention they deserve.[18,10] Still, control over the kinetics of self-assembly processes can be difficult to achieve, as the formation of the weak, non-covalent interactions holding these materials together is typically (nearly) without an activation energy barrier. Conversely, the formation of stronger covalent bonds generally carries an appreciable activation energy. Catalysis offers a fairly simple tool to speed up a given chemical reaction by lowering its activation energy. Thus, incorporation of catalysis-susceptible covalent bonds in key locations in supramolecular materials will enable catalysis as a tool to control the rates of their formation, breaking and exchange.

From the start, we have had multiple reasons for wanting to incorporate a catalytically controlled step in a self-assembly process. In principle, the *in situ* synthesis of a molecule prior to self-assembly, and control over the rate of that last synthetic step using a catalyst, opens up a number of possibilities. When the kinetics of the self-assembly process are similar or faster than those of the synthesis step, controlling the rate of bond formation will allow control over the rate of material formation. Because the rate of assembler formation depends on catalyst activity, controlling catalyst activity in space or time will also control when and where a material is formed. In particular, spatio-temporal control over gel formation will enable on demand *in situ* phase changes. Also, many supramolecular materials reside in local minima on the thermodynamic energy landscape. The self-assembly pathways on such energy landscapes are controlled by kinetics, i.e. the rate of a self-assembly process can have a large impact on the properties and structure of the obtained materials.[19] Catalysis may control such a rate, and thereby provide controlled access to certain metastable states of a supramolecular material. Also, the rate of exchange of a so-called dynamic covalent bond (a reversible covalent bond) might be controlled using a catalyst. Drastically increasing the rate of exchange[20] of such a bond in a material could induce remodeling of a supramolecular material, as for instance Leibler demonstrated for polymer networks in his "vitrimer" concept.[21] Besides this, catalysis can be used to achieve homeostasis in dynamic soft materials.[22] We were also particularly interested to apply catalysis to control the rates of certain reactions in the chemical reaction networks driving active soft materials, and to introduce feedback loops.[23,24]

4. DESIGN

The general design of any molecular system capable of self-assembling after *in situ* formation of the assembler molecule is based on the following considerations (Figure 1):

1) the building blocks should all be soluble in the reaction solvent, or should be able to react at a phase boundary;

2) the separate building blocks should not assemble by themselves;

3) the building blocks should carry the functional groups necessary to construct the final covalent bond through a chemical reaction;

4) the final bond forming reaction should be compatible with the conditions (solvent, temperature, concentration, ions, pH) of the self-assembly process, and vice versa.

We now added a fifth design principle[25]:

5) use a catalyst to enhance the rate of the final bond forming reaction leading to formation of the assembling molecule.

To various degrees, these principles have been applied to controlling self-assembly through enzymatic catalysis[26,27,28,29,30,31] and synthetic catalysis[32,33].

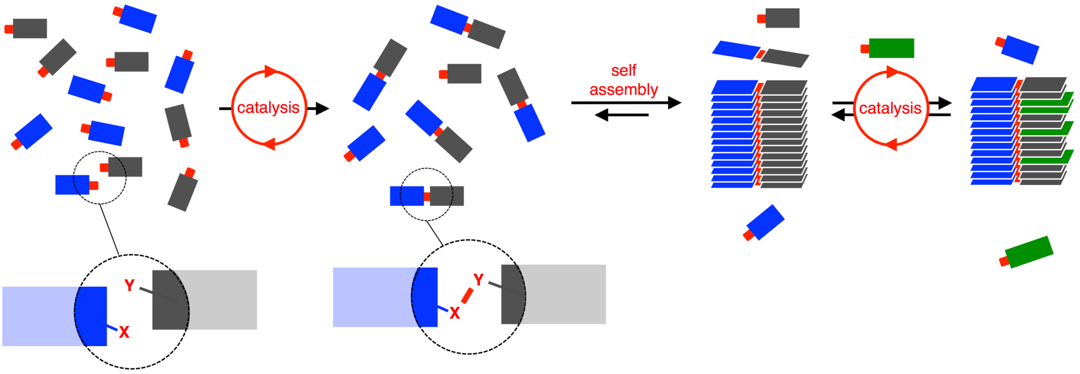


Figure 1. Catalysis-controlled self-assembly. Non-assembling building blocks (blue and dark grey) can form an assembly-prone molecule through covalent bond formation (red) using a catalyst, subsequently triggering assembly to form a molecular material (left). If a somewhat reversible covalent bond is used, catalysis can also impact on the rate of component exchange (with the green building block), even at equilibrium (right). In the work described in this *Account*, we have mostly focused on formation.

From 2004 onwards, our group has gained significant experience in the design and synthesis of new supramolecular hydrogelators (i.e., low molecular weight hydrogelators).[34,35] The general design of these molecules was based upon the use of a central *cis,cis*-cyclohexanetrisamide moiety, functionalized with one or several amino acid groups, often decorated with short oligoethylene oxide chains. The central cyclohexane trisamide provides a rigid, discotic platform to direct 1D supramolecular polymerization[36] through hydrogen bonding to the next gelator molecule. The side chains of the amino acid groups provide hydrophobic shielding of the H-bonding groups (e.g. using phenylalanine or methionine). The oligoethylene oxide chains can block side-on assembly of gelator molecules, thus preventing 3D crystallization.

To create a catalysis-controlled supramolecular material, we designed a multi-component hydrogelator along rules 1-5, based on the previously described class of cyclohexanetrisamide-based gelators. While retaining the cyclohexane core, we replaced the amide bonds by hydrazone bonds. Similar to amides, the hydrazone group can act as both a hydrogen bond donor and an acceptor. Hydrazone bonds can form spontaneously in aqueous solution by condensation of a hydrazide with an aldehyde. This reaction proceeds very slowly in the pH 7-10 window, but is significantly accelerated using either Brønsted-Lowry acid catalysis (pH 3-6), or nucleophilic aniline catalysis[37,38], suggesting that we can use multiple types of catalysis to control the formation of these gelators. Moreover, in certain pH windows or catalyst concentration, they are considered dynamic covalent bonds[39,40] and the rate of exchange can be controlled using a catalyst.

Mainly for solubility reasons, we initially fitted the cyclohexane core with three hydrazide groups (Figure 2). The peripheral amino acids in the original trisamide-gelators were replaced by benzaldehyde derivatives functionalized with solubilizing oligoethylene glycol chains. The phenyl group in these compounds should then provide shielding of the H-bonds between hydrazone groups, while also leading to additional stabilization of the fibers through π–π interactions, dispersion forces and the hydrophobic effect. We also reduced the original amino acid functionality to a simple benzaldehyde derivative to allow straightforward and large-scale synthesis. In all, the design comprises three benzaldehydes reacting with a cyclohexanetrishydrazide core to form a thrishydrazone gelator molecule, which should then assemble to form fibers. These fibers should subsequently crosslink to form a network, gelling the solvent. The rate of gelator formation can be controlled through catalysis of hydrazone condensation.

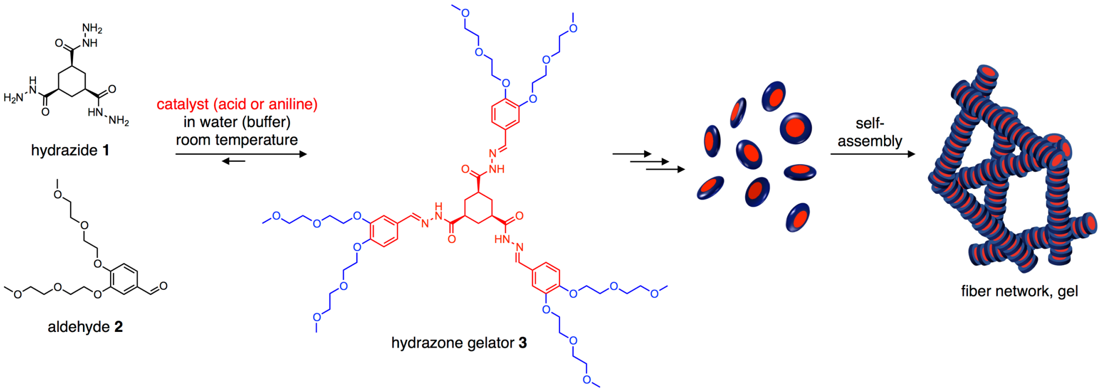


Figure 2. Catalytic formation of a supramolecular hydrazone gel. Acid or aniline catalyzed threefold condensation of hydrazide **1** with aldehyde **2** gives hydrazone gelator **3**, which subsequently assembles into fibers and eventually a network, gelling the solvent.

5. RESULTS

5.1 THE GELATION SYSTEM

Cyclohexanetrishydrazide **1** and benzaldehyde **2** are both soluble in aqueous solvents. Individually, they do not show self-assembly when in solution. Mixing these solutions leads to the synthesis of gelator **3** though hydrazone formation. Above a certain threshold concentration (the *critical gelation concentration* or CGC), assembly of **3** into a fibrous network leads to gelation of the surrounding solvent. We typically observed the formation of macroscopic gels with an appearance ranging from opalescent to opaque (Figure 3). These gels consist of fairly monodisperse, yet sometimes bundled or branched fibers of around 5.5 nm in diameter. Up until now, the precise packing of molecules within these fibers has not been fully elucidated. These gels are commonly shear thinning and display no significant mechanical recovery after failure.[41]

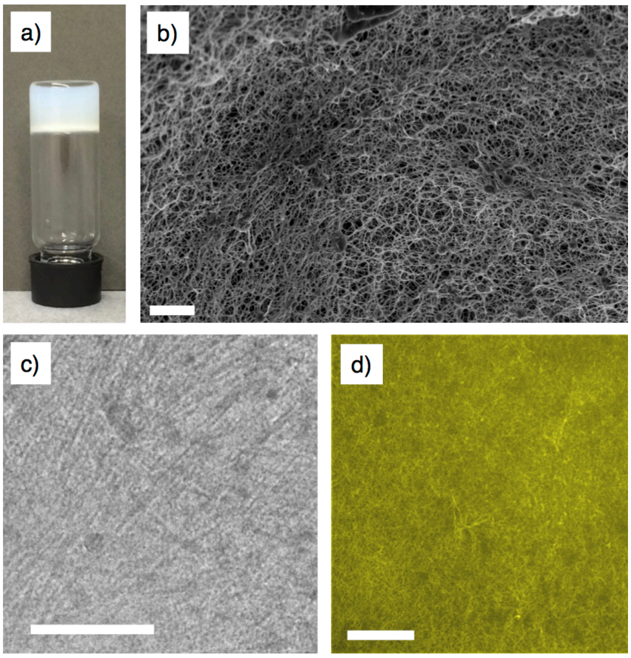


Figure 3. Macro- and microscopic structure of supramolecular hydrazone gels. a) A photograph of an acid catalyzed gel; b) a scanning electron micrograph (scale bar is 500 nm), c), a cryo-transmission electron micrograph (scale bar is 150 nm) and d) a confocal fluorescence micrograph (scale bar is 20 μm) of a gel made using aniline as a catalyst. Adapted with permission from ref. 45. Copyright 2013 Nature Publishing Group.

We exploited the modular nature of the gelator design to either change the bulk properties of the obtained gels, or to create simple methodology for functionalizing the gel fibers with all sort of chemical tags.[42] Using a number of fluorophores with a benzaldehyde functionality, we achieved multi-color imaging of these gels using confocal fluorescence microscopy (Figure 4). Simply mixing a small amount of such fluorophores with the common aldehyde and hydrazide followed by reaction and gelation leads to the formation of gels with fluorescently labeled fibers. Herein also lies the strength of this approach: these is no need to fully synthesize and purify fluorescently labeled gelator molecules, as these labeled gelators will form spontaneously in the gelation mixture. We also showed that this method can be used to simultaneously decorate the fibers with a range of functionalities including click handles, sugars and proteins. Alternatively, changing the structure of the aldehyde or the hydrazide entirely can have a profound impact on the properties of bulk gels, such as CGC, mechanical properties, or fiber morphology.[42]

In a recent collaboration, the Lloyd group (Heriot Watt University) demonstrated hydrogelation through hydrazone formation between an aldehyde functionalized core and hydrazide peripheral groups.[43] The Becker group (University of Akron) showed that these principles also hold for oxime formation in polymer gels.[44]

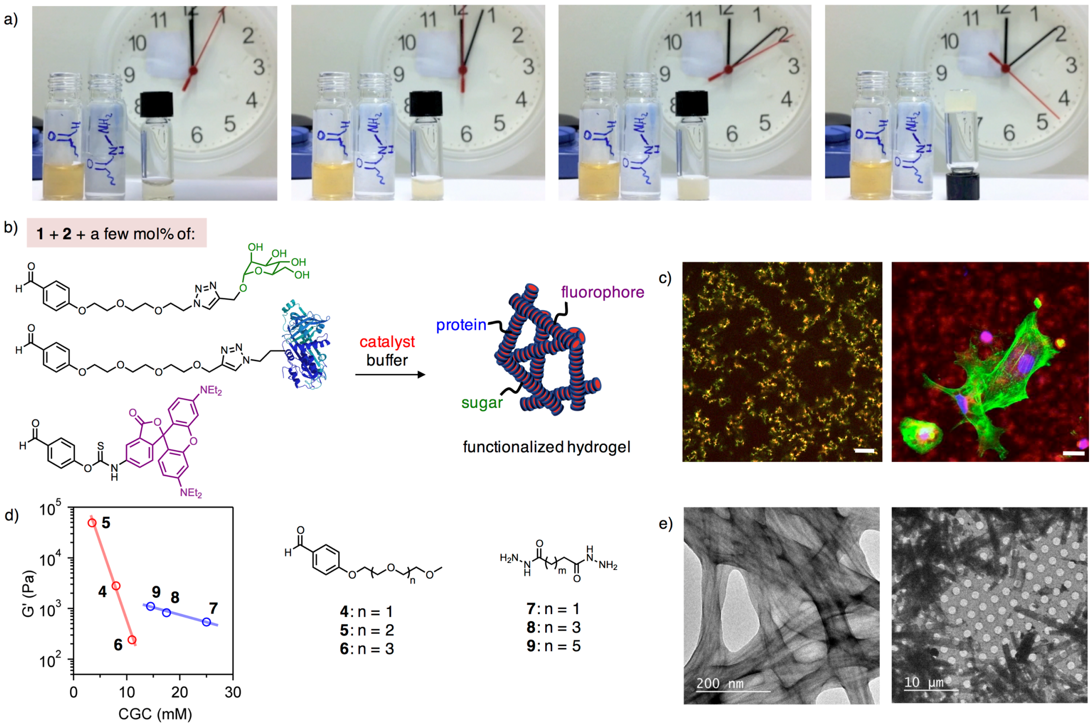


Figure 4. Formation and functionalization of supramolecular hydrazone gels. a) Movie stills showing increased opacity during formation of a gel, after mixing solutions of **1** and **2**. b) Functionalization of gel fibers using functional aldehydes. c) Confocal fluorescence micrographs show a gel functionalized with a rhodamine-derived aldehyde and a mannose-derived aldehyde binding to FITC-Concanavalin A (left, scale bar is 20 μm), and fixed mouse astrocytes (with stained actin filaments and nucleus) on a rhodamine-derived gel (red, scale bar is 20 μm, right). d) The structure of the aldehyde or hydrazide building blocks influence CGC and stiffness. Red line: **1**+(**4**/**5**/**6**)), blue line: (**7**/**8**/**9**)+**4**). e) Transmission electron micrographs show very large

differences between **1**+**4** gels (left) and **9**+**4** gels (right). Adapted with permission from ref.42. Copyright 2016 Royal Society of Chemistry.

5.2 CATALYSIS

At the core of the concept detailed in this *Account* is a catalyst capable of accelerating covalent bond formation. The rate of hydrazone bond formation is increased by either acid catalysis or nucleophilic aniline catalysis. Acid catalysis is generally much more efficient than aniline catalysis. Still, in some applications, especially those in biological environments, acid catalysis cannot be used because it operates outside of the allowed (physiological) pH window. For those purposes, nucleophilic catalysis could be useful. In the gelation experiments described in this *Account*, we investigated both types.

The rate of gelation of **1** and **2** is drastically increased under the influence of a catalyst. Where gelation will take up to six hours at pH 7.0, it is completed in less than ten minutes at pH 5.0, or using an aniline catalyst (Figure 5). In all these experiments, the final yield of gelator **3** is >95%, independent of the type and concentration of catalyst.

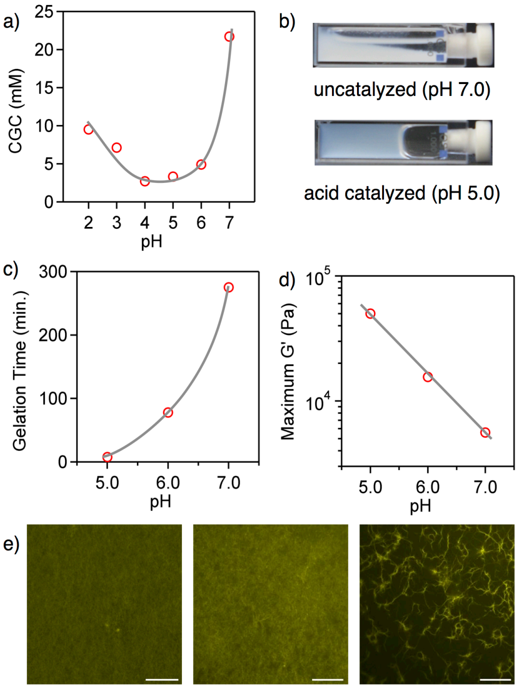


Figure 5. The impact of catalysis on gel properties. a) The CGC depends on acid catalyst concentration (pH). b) Gelation experiments performed at fixed concentrations of **1**+**2**, but different catalyst concentration. c) The time needed to reach the final G' value (maximum gelation time) is drastically reduced with increasing acid catalyst content. d) Performing the gelation experiment at pH 5 results in an order of magnitude increase in G', vs. pH 7. e) From left to right: CLSM images of gels made using acid, aniline or no catalyst. Scale bars are 20 μm. Adapted with permission from ref.45. Copyright 2013 Nature Publishing Group.

5.3 KINETIC CONTROL

We observed that the appearance of the materials obtained from reaction of **1** and **2** depends on the presence of a catalyst during the reaction-gelation process. Either acid or the aniline led to the formation of gels. Without a catalyst (pH 7.0), instead a precipitate was obtained at concentrations below 20 mM **1** (Figure 5).[45] The CGC shows a large variation with the catalyst concentration in the system. For instance, using acid catalyst, the lowest CGCs are obtained in the pH 4-6 window. Below pH 4, the equilibrium of the hydrazone shifts back to the starting materials, leading to a decreased yield of gelator and an increased CGC. Above pH 6, acid catalysis no longer plays a role and a drastic increase of the CGC is observed.

Also mechanical properties such as the storage modulus (G') of the gels depend on catalyst content. Using acid catalysis leads to an order of magnitude increase in G', to 50 kPa (Figure 5). Similar effects were observed for aniline catalyzed gels. As these gels will all have the same gelator content, differences in mechanical properties and appearance imply that by changing the kinetics of gelator and gel formation using a catalyst, we are able to address various different metastable or kinetically trapped states on the thermodynamic energy landscape, each with different macroscopic properties. As such, catalysis is used as a form of kinetic control over supramolecular structure formation.[45]

At the origin of these differences in macroscopic properties lies a change in the morphology of the network that depends on the rate of network formation. Using microscopy techniques such as confocal laser scanning fluorescence microscopy (CLSM) or scanning electron microscopy (SEM), we observed dense, well connected networks when a catalyst was used during formation, whereas uncatalyzed gels consisted of a much less dense, poorly connected network of bundled fibers (Figure 5). In a nutshell, the fibers that are formed at a faster rate have a higher tendency to branch during formation. Branching leads to the formation of a network with a much larger number of crosslinks, and less bundling of fibers, overall leading to stiffer gel materials.

5.4 SPATIAL CONTROL

Once material formation is coupled to a chemical reaction, it becomes possible to control the spatial distribution of material formation and create soft matter objects. Locally increasing the rate of assembler formation will lead to local assembly of a soft material, as long as the rate of assembly is faster than the rate of diffusion of the formed assemblers. Catalysts can cause a local increase in rate, but for this purpose we need to either localize an active catalyst, or locally activate a catalyst. We pursued both options to achieve spatial control over gel formation.

To limit catalytic action to a certain micrometer or nanometer scale domain, the diffusional mobility of the catalyst should be restricted. One way of achieving this is to immobilize the catalyst on a surface [27], a microparticle or in a gel mesh. In a first attempt to create a localized acid catalyst, we made microscale patterns of acid catalysts on a macroscale surface (Figure 6). In aqueous solution, negatively charged surfaces will attract protons from the bulk solution because of electrostatic interactions, lowering the pH near the charged surface. Using microcontact printing, we patterned a glass slide with sulfonic acid groups. We estimated that the pH near these patterns would be 1-1.5 pH points below the bulk pH, depending on the ionic strength of the medium. Upon applying a solution containing **1** and **2** over these patterns, we observed the formation of fiber networks near the surface, before eventual gelation of the bulk solution. On the surface, the formed gel patches follow the shape of the microcontact printed catalyst patterns (Figure 6). Moreover, for reasons yet unknown to us, the fibers grown on the patterns had a preferential orientation perpendicular to the surface.[46]

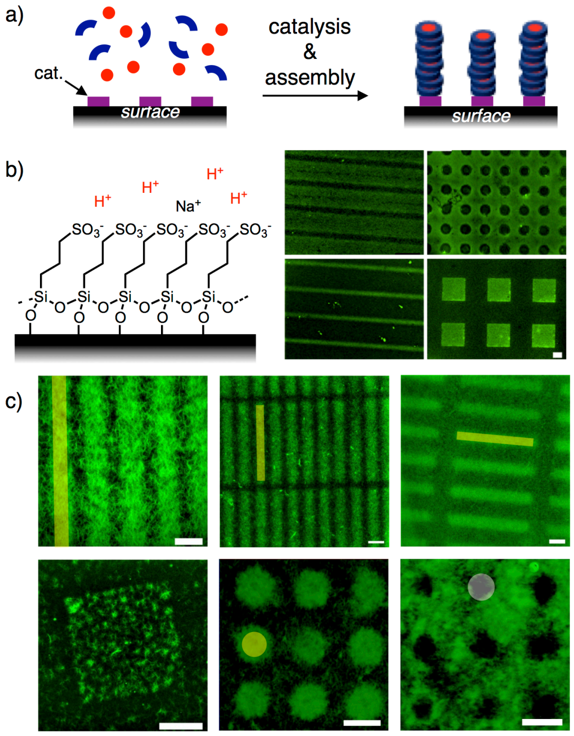


Figure 6. Spatial control over fiber formation using a patterned surface confined catalyst. a) Gelator formation near the surface confined catalyst will lead to local fiber formation. b) Using microcontact printing, we made patterns (right, CLSM) of sulfonic acid groups (left) on a glass surface. Scale bar is 20 μm. c) Gel patterns obtained on top of a printed catalyst surface. The imposed light areas indicate the dimensions of the catalyst pattern. Scale bars are 20 μm. Adapted with permission from ref.46. Copyright 2014 Wiley Interscience.

Besides surface-confined catalysts, one could also use solution phase catalysts that are activated by some sort of local stimulus. We briefly investigated the use of irreversible photoacid[47] catalysts, but then quickly turned to the use of switchable catalysts. Although commonplace in nature, only a few examples of artificial switchable catalysts have been described.[48] We found that spiropyran based photoswitchable acids[49] can act as acid catalysts for the hydrazone formation reaction. In aqueous solution, switches such as **10** can ring-close upon irradiation with visible light, leading to release of a proton, thereby lowering the pH of the solution. Very important to our work is the relative instability of the ring-closed form. When irradiation is stopped, the switch will open up again in a few minutes at room temperature, driven by thermal energy. This means that upon removal of the stimulus or outside of the zone of irradiation, the pH of the solution will rapidly return to its original value, deactivating the catalyst. Initial experiments using this switch as an acid catalyst for gel formation showed that irradiation of the switch leads to accelerated gel formation, and that the obtained gels have enhanced mechanical properties compared to the non-irradiated samples.[50] Local irradiation should lead to a local activation of an acid catalyst, providing spatial control over gel formation. When irradiating gelation samples through photomasks with sub-millimeter feature dimensions, we observed the formation of structured gels (Figure 7). The shape and dimensions of the formed gel structures followed those of the masks, showing that local catalyst activation can be used to control local structure formation, even in solution. Because switch **10** quickly reverts back to the open form, no catalyst is generated outside of the irradiated zones, limiting initial gel formation to the irradiated areas. Moreover, as there is a large difference in diffusive mobility between the gelation building blocks **1** and **2**, and the gelator in the aggregated state, we observed an appreciable degree (>50%) of mass transfer from the dark zones to the irradiated gel zones. In all, this shows that local catalyst activation can be used to control the local formation and spatial distribution of soft materials.

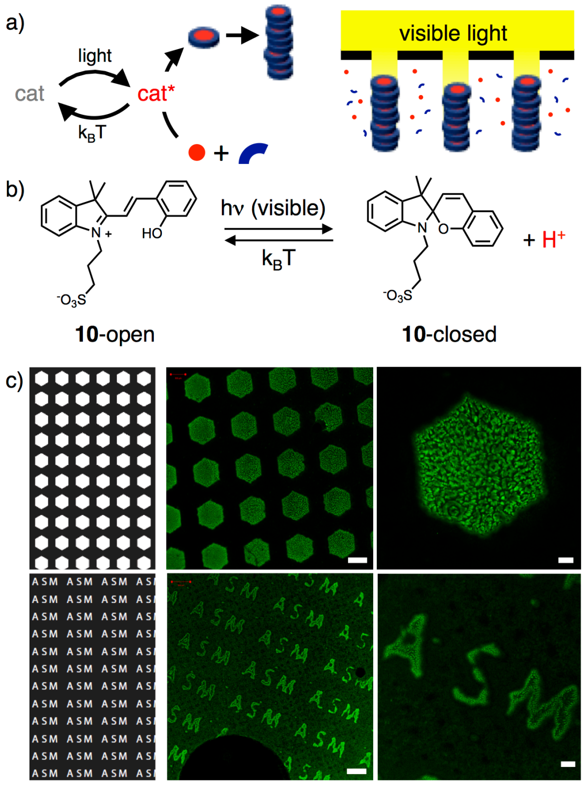


Figure 7. Spatial control using light-switchable catalyst **10**. a) Light-driven activation of a catalyst leads to (local) gelator and fiber formation. b) Switch **10** will release a proton upon light-induced ring closure. c) Gel structures (middle, right) obtained when irradiating a solution of **1**, **2** and **10** through a mask (left). Scale bars are 500 μm (middle) and 100 μm (right). Adapted with permission from ref.50. Copyright 2015 Wiley Interscience.

6. CONCLUSIONS AND FUTURE DIRECTIONS

Controlling the rate of a chemical reaction using a catalyst allows control over the formation of soft, supramolecular materials in time and space. Moreover, changing the kinetics of material assembly using a catalyst provides access to kinetically trapped states on the self-assembly energy landscape. As such, catalysis can be applied to create molecular materials that exist outside of chemical equilibrium. In the past years, we have demonstrated these concepts using a modular gelator that is formed in the self-assembly medium by a catalytically controlled reaction between a hydrazone and an aldehyde building block. Changing the rate of gelator formation using a catalyst has a large impact on the properties of the resultant materials. By localizing a catalyst either on a surface or locally activating a catalyst in solution, the spatial distribution of gel formation can be controlled. In all, using catalysis to control the properties of soft materials constitutes a new avenue for catalysis, on top of the traditional use in industrial and lab scale synthesis. In living systems, catalysis plays a vital role in performing and controlling all sorts of cellular processes, far beyond the mere production of chemicals. The future role of catalysis in soft materials lies in achieving and controlling life-like behavior such as homeostasis, propulsion[51,52], actuation, signaling, control over exchange dynamics, and the introduction of feedback mechanisms in active, fuel-driven materials. Advantages of the current hydrazone system are the facile synthesis of its components, the straightforward formation of gel materials by simple mixing and reaction under ambient conditions, and the easy chemical functionalization of the gel materials by incorporation of functionalized building blocks. Besides investigating new forms of catalysis, we are currently looking into application of this concept in reaction diffusion systems and compartmentalization, and in biomedical materials[53,54], in self-healing materials[55], and for signaling and sensing purposes.

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Notes

The authors declare no competing financial interest.

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Fanny Trausel graduated in chemistry from Leiden University, where she did research in organometallic chemistry in the group of Lies Bouwman. She is currently working on her PhD under the supervision of Rienk Eelkema. Her main research interest is to use catalysis to control soft materials.

Frank Versluis obtained his PhD with Alexander Kros (Leiden University), working on a supramolecular system capable of inducing membrane fusion. Currently, he is a postdoctoral researcher in the laboratory of Rienk Eelkema at TU Delft. His main focus is on supramolecular hydrogels and their biological applications.

Chandan Maity received his MSc from the Indian Institute of Technology, Bombay. In 2011, he obtained his PhD from Humboldt-Universität zu Berlin working with Stefan Hecht. Since 2012, he has been working as a postdoctoral researcher with Rienk Eelkema at TU Delft. His research interests include the application of organic chemistry in responsive functional materials.

Jos Poolman received his MSc from Leiden University in 2011, specialized in organic synthesis. He is currently a PhD student in the group of Jan van Esch at TU Delft. His interests include the tuning and functionalizing of self-assembling hydrogelator systems by incorporating novel molecules.

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Jan van Esch is professor of chemistry at TU Delft, and he chairs the Advanced Soft Matter group. After a PhD with Roeland Nolte (Nijmegen) he did postdoctoral stays with Helmut Ringsdorf and Ben Feringa. His research focuses on directed self-assembly and far-from-equilibrium phenomena in molecular systems, and to exploit such systems in smart materials and biomedical applications.

Rienk Eelkema is an assistant professor of chemistry at TU Delft. After a PhD with Ben Feringa (University of Groningen) and a postdoctoral fellowship with Harry Anderson (Oxford University), he assumed a tenure track position at TU Delft in 2008 and obtained tenure in 2013. His main research interests are to couple chemical reactions to self-assembly processes, and the application of organic chemistry in physics, biology and engineering.

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