Chem Soc Rev

TUTORIAL REVIEW

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Cite this: DOI: 10.1039/c7cs00246g

Dissipative out-of-equilibrium assembly of man-made supramolecular materials

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Received 5th April 2017

DOI: 10.1039/c7cs00246g

rsc.li/chem-soc-rev

The use of dissipative self-assembly driven by chemical reaction networks for the creation of unique structures is gaining in popularity. In dissipative self-assembly, precursors are converted into self-assembling building blocks by the conversion of a source of energy, typically a photon or a fuel molecule. The self-assembling building block is intrinsically unstable and spontaneously reverts to its original precursor, thus giving the building block a limited lifetime. As a result, its presence is kinetically controlled, which gives the associated supramolecular material unique properties. For instance, formation and properties of these materials can be controlled over space and time by the kinetics of the coupled reaction network, they are autonomously self-healing and they are highly adaptive to small changes in their environment. By means of an example of a biological dissipative self-assembled material, the unique concepts at the basis of these supramolecular materials will be discussed. We then review recent efforts towards man-made dissipative assembly of structures and how their unique material properties have been characterized. In order to help further the field, we close with loosely defined design rules that are at the basis of the discussed examples.

Key learning points

– Out-of-equilibrium assemblies are characterized by a net loss of energy into their environment.
– Several types of out-of-equilibrium assemblies exist including metastable assemblies and dissipative assemblies.
– Dissipative self-assembly is the process of out-of-equilibrium self-assembly driven by irreversible chemical reactions.
– In order to design assemblies formed *via* dissipative self-assembly, one must not only take the thermodynamics into account, but also the kinetics.
– Molecular dissipative assemblies differ mainly in the energy source used (light *vs.* chemical fuel-driven) and the coupling of the energy source to the assembly process (direct *vs.* indirect).
– The properties of biological out-of-equilibrium materials, like spatial and temporal control over assembly, adaptivity and self-healing can also be reached with man-made counterparts.

1. Introduction

Most man-made materials reside in equilibrium, where the forward and backward rates of assembly and bond formation are balanced. At equilibrium, we understand many of the processes at play. Furthermore, because we understand, we are able to control the properties of existing materials or even create new materials with new functions.[1] Structures and materials may also exist out-of-equilibrium in which there is a net exchange of matter and energy with their environment. In fact, life and the structures it comprises, are thermodynamically unstable and can therefore not exist in-equilibrium. For instance, the cytoskeletal networks, parts of the extracellular matrix, and the mitotic spindle[2] are all biomolecular structures that consume energy and materials *via* irreversible processes to sustain their structure and function. While the out-of-equilibrium nature of these structures gives the resulting biological materials unique properties, the development of analogous man-made out-of-equilibrium supramolecular materials is still in its infancy. In this review, we illustrate the opportunities that dissipative out-of-equilibrium structures bring, we demonstrate recent efforts towards man-made counterparts and we lay out

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the challenges on the road towards man-made out-of-equilibrium supramolecular materials.

The boundaries of this tutorial review are set to energy dissipating structures on the molecular scale, and we limit the driving force to irreversible chemical reactions. Within that framework, we will mostly focus on man-made out-of-equilibrium structures. In this review, we will use the term dissipative self-assembly (DSA) for the process of out-of-equilibrium self-assembly driven by irreversible chemical reactions. Other terms, including dynamic self-assembly,[3,4] have been used to describe the same or very similar processes. Since dynamic self-assembly does not exclude all forms of in-equilibrium assemblies, *e.g.* the rapid exchange of surfactants between micelles and bulk solution, we prefer the term dissipative self-assembly in the context of our boundary conditions. We will include examples of colloidal assembly driven by chemical reaction networks, even though, strictly speaking, this is not molecular assembly. The choice to include them was made as they follow similar design principles as dissipative molecular self-assembly and their collective work has provided important insights into the field of molecular DSA.

In this review, we will give an overview of recent examples and extract the general features in their molecular design. We will define the differences between in-equilibrium and out-of-equilibrium structures, and we will give a flavor of why out-of-equilibrium assembly can lead to unique material properties, demonstrated by pioneering examples of applications. In order to aid the further development of the field, we close with loosely defined design rules that are at the basis of the discussed examples.



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Susan van Rossum obtained her Bachelor in Chemistry (2012) and her Master in Nanomaterials: Chemistry and Physics (2014), both at the University of Utrecht. During her research projects in the groups of Willem Kegel and Daniël Vanmaekelbergh she focussed on self-assembly of polymer and semiconductor colloids. During her Master she also did an internship about self-healing polymers in the Croda company. She is currently a PhD researcher in the group of Rienk Eelkema and Jan van Esch at Delft University of Technology. Her research focuses on the design of dissipative self-assembly systems activated by chemical fuels.



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2. Out-of-equilibrium assembly: energy landscapes and an example from biology

Self-assembly of artificial (synthetic) molecules is an active research area with many highlights over its half a century of history. Based on the thermodynamic and kinetic stability of precursors, building blocks, and self-assembled structures, one can identify three different types of self-assembly processes which we compare in terms of their energy landscapes (Fig. 1).

In equilibrium self-assembly, the self-assembled structure resides in the global minimum of the energy landscape (Fig. 1B, left). The state associated with non-assembled building blocks is slightly higher in that landscape, and it is thus thermodynamically favorable to assemble the building blocks. The population distribution between assembled and non-assembled state depends on their difference in energy level and available free energy, and is thus determined thermodynamically. In equilibrium self-assembly, exchange between the two states is possible, meaning that building blocks can escape the assemblies and dissolved building blocks can enter assemblies, but this happens with equal rates. As a result, there is no net flow of energy and matter and the assembly is thus in equilibrium.

The assemblies can also reside somewhat higher in the energy landscape, in a local, but not the global minimum of the thermodynamic energy landscape (Fig. 1B, middle).[5] Depending on the height of the activation barriers around this minimum, two states are possible. Either the energy barrier towards surrounding minima is high and the structure does not exchange matter or energy with its surrounding. In this state, referred to as "kinetically trapped", the self-assembled state has an infinite lifetime. Technically, an infinite lifetime is immeasurable, so the more common definition is a lifetime that is greater than the time of the experiment. If, on the other hand, the energy barrier towards a surrounding lower minimum is relatively low, building blocks in the self-assembled state can "escape" towards that state. This conversion of building blocks towards a lower energy state implies that the self-assembled state has a finite lifetime, and is thus metastable. It also means that this state is not in equilibrium. These so called metastable states are extensively reviewed by Hermans, De Greef and coworkers.[6]

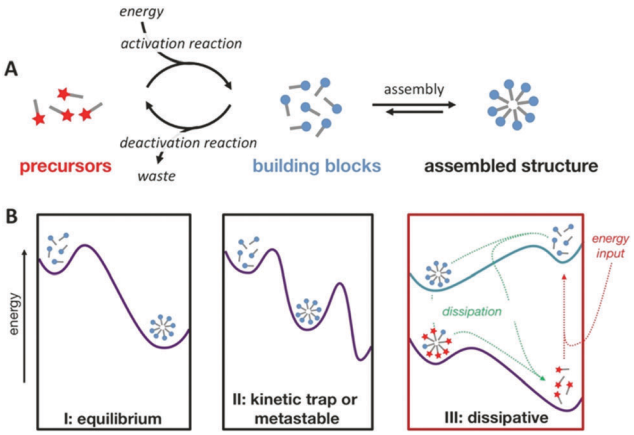

Fig. 1 Comparison of the free energy landscapes of static self-assembly and dissipative self-assembly. (A) Definition of the participants in a self-assembly process. In equilibrium self-assembly and in kinetically trapped and metastable self-assembly, only the building blocks and assembled structures take place in the assembly process. In dissipative non-equilibrium self-assembly, the assembly of building blocks is coupled to an energy-driven chemical reaction network. It is important to note that deactivation of the building blocks can either occur in solution or in the assembled structure. (B) One can identify three types of self-assembly based on the relative stability of the self-assembled structure, the building blocks and precursors. In equilibrium self-assembly, the assembly resides in the global minimum (left). Kinetically trapped assemblies reside in a local minimum and cannot escape to the global minimum. In contrast, metastable assemblies can escape that minimum and thus have a finite lifetime (middle). In dissipative self-assembly (right), the assemblies reside high in the energy landscape and can only be sustained by continuous input of external energy (*e.g.* fuel molecule or a photon). Dissipative self-assembly is the major subject of this review.

The focus of this review is on a self-assembled state that is higher in the energy landscape than the states mentioned so far. In this scenario, which we call "dissipative self-assembly" or DSA, the self-assembly of a building block is coupled to a chemical reaction network, *i.e.* a network of at least two irreversible chemical reactions that control the activation and deactivation of building blocks (Fig. 1A). In the chemical reaction network, a non-assembling precursor, that is at the global minimum in the energy landscape, is converted into a building block by an activation reaction (Fig. 1B, right). This reaction is driven by the irreversible conversion of a high-energy entity that "pushes" the precursor into a high-energy building block state. After this activation, self-assembly of multiple building blocks can take place leading to larger structures or even materials. Crucially, a second chemical reaction in the network deactivates the high-energy building blocks and reverts them into their original precursors. In this step, the high-energy building block dissipates the energy it absorbed during the activation reaction into the environment as it deactivates to its original precursor. This deactivation process can either happen in solution or in the assembled structure.[7] Hence, the building blocks in the



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self-assembled state reside out of thermodynamic equilibrium and the structures are thermodynamically labile. Following the Second Law of Thermodynamics, structures formed through DSA can only be maintained by a constant conversion of energy that keeps them out-of-equilibrium, as nature strives to reach equilibrium. When a finite amount of energy is added as a batch, assembly will take place for as long as the energy source is available to the system. After removal or depletion, the formed unstable structures will start to disintegrate, having the system return to the non-assembled state. In contrast, when there is a continuous supply of energy to sustain the assemblies, the system can in principle reach a non-equilibrium steady state where assembled and non-assembled structures coexist and are continuously converted into each other. It is in this scenario that emergent phenomena such as chaotic behavior, oscillations and bifurcations can occur, depending on the kinetics of the chemical reaction network. For a more in-depth discussion of the energetics of such processes, we refer to a book by Casas-Vazquez.[8]

Within the boundary conditions of this Tutorial Review, the energy source driving DSA is a chemical reaction that uses a high-energy entity (photon or fuel molecule) to convert a molecular precursor into a building block that is now activated for an assembly process. The term ''chemical reaction'' should be taken somewhat loosely here. For instance, we will discuss classical chemical reactions that drive self-assembly, such as *cis–trans* isomerization of an azobenzene group driven by UV-light, but also processes that involve non-covalent ATP-complexation to activate self-assembly. Whether these reactions are classical chemical reactions that make and break covalent bonds or supramolecular processes that form non-covalent bonds, similar principles hold: a high-energy source drives the conversion of a molecular precursor into a building block for assembly. We will also discuss examples of chemical reaction networks that drive morphological transition from one self-assembled state to another and even examples of self-assembled structure that are disassembled by their chemical reaction network. Strictly, these examples fall out of the definition of DSA as depicted in Fig. 1B. We chose to include them, because, from a supramolecular material's points of view, the exact nature of the precursor state is irrelevant as long as the externally applied energy induces a transient change in material properties.

A particularly illustrative example of biological structure formed *via* DSA is the guanosine triphosphate (GTP)-driven DSA of microtubules.[9] Microtubules are part of the cytoskeleton and are vitally important in maintaining the structure of the cell. Besides scaffolding, the microtubule network is involved in intracellular transport of vesicles, organelles and other macromolecules. The network also assists in the process of cell migration and is the major component of the mitotic spindle, which is the complex cell machinery responsible for separation of the chromosomes in eukaryotic mitosis. To perform any of these functions, a dynamic material is required that can rapidly remodel on demand to adapt its morphology to the required tasks. Microtubules are endowed with the required dynamics because their dissipative self-assembly is coupled to a chemical reaction network that activates precursors and deactivates building blocks. The chemical reaction network, in turn, is driven by the hydrolysis of GTP.

Microtubules are self-assembled from tubulin dimers that consist of two tubulin segments, α- and β-tubulin. Each segment can bind one molecule of GTP in its GTP-binding site, and doing so activates tubulin for self-assembly. Assembly occurs in a head-to-tail fashion with the α-domain binding the β-segment of the adjacent dimer resulting in tubes with a diameter of roughly 25 nm. While α-subunit-bound GTP is chemically stable, the β-subunit catalyzes the hydrolysis of GTP to guanosine diphosphate (GDP) in its binding site. Moreover, the hydrolytic activity is drastically higher for tubulin in the assembled state compared to activated tubulin in solution, as self-assembly of tubulin activates its GTPase.[10] Hydrolysis of the GTP bound to β-tubulin destabilizes the microtubule, but only if all GTP at the end-cap of the microtubule has hydrolyzed to GDP, the microtubule rapidly disassembles, referred to as the catastrophe phase. Taken together, the dissipative self-assembly of microtubules is driven by the hydrolysis of GTP, and as long as addition of activated tubulin outcompetes deactivation of assembled tubulin, self-assembly will take place. As soon as the opposite is the case, the tubules will collapse. The competition between both processes result in a dynamic ensemble referred to as dynamic instability. It is these dynamics driven by the chemical reaction network that allow for rapid morphological transitions when required.

As is clear from the example above, coupling the self-assembly of materials to chemical reaction networks comes with unique properties. One of those is the ability to control assembly both in space and time by controlling the kinetics of the chemical reaction network at play. In the case of the microtubules, this is clearly demonstrated by the ability of tubulin to take place in many processes at different times throughout a cell's life cycle. Even during mitosis of eukaryotic cells, the tubulin precursors play very diverse roles ranging from the formation of the mitotic spindle to the formation of microtubule-asters that help with the spatial and temporal organization of the organelles. Both structures are required at very specific times and very specific locations in the process of mitosis, and that spatial and temporal control is in part regulated by gradients of GTP and in part regulated by microtubule-associated proteins. Thus, the kinetics of the chemical reaction network, in part, determine where and when microtubules carry out their function. It is this autonomous control of material function in space and time that is unique to DSA and can be attractive to materials science.

Besides the possibility to control dynamic assembly in space and time, these assemblies can be extremely adaptive towards changes in their environment such as fuel levels or the presence of entities that change the kinetics of one of the pathways in the chemical reaction network (*e.g.* the microtubule-associated proteins). Spatial fluctuations in these parameters can favor assembly at one place and favor disassembly at other places. Because of the dynamic nature of DSA, the system can rapidly adapt by forming a new assembly while breaking down the

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old one. One extreme case of adaptivity is the ability of the assemblies to repair themselves after externally applied damage. Provided that the chemical reaction network remains intact, the system can recover its self-assembled state even if all building blocks were converted. For instance, researchers have placed microtubules under externally applied mechanical stress for several cycles. With increasing numbers of cycles, the persistence length of the fibers decreased, which is a typical sign of material fatigue. When the system was given the time to repair between stress cycles, typically in the range of 100 seconds, the material fatigue was not observed. By means of microscopy, the healing process was shown to take place by incorporation of active tubulin dimers in defect sites along the microtubule, a process that was not observed in undamaged microtubules.[11]

Because of the sensitivity of the assemblies to local fluctuations in fuel fluxes, structures that are formed *via* DSA have the ability to self-organize, *i.e.* to form dynamic patterns of the assemblies at much greater length-scales than the original building blocks. Although the exact requirements for such emerging phenomena is not fully understood, the patterns can only exist under non-linear energy dissipating conditions where the assembly exerts feedback on its own chemical reaction network. As an example, the abovementioned microtubules can organize into patterns including asters, vortices and cortical bundles, depending on kinetic parameters,[12] but also on physical confinement.[13] For materials science and especially microelectronics, controlling the formation of patterns of macroscopic sizes while retaining structure at the molecular level has been a longstanding challenge.

Taken together, even though creating structures *via* DSA costs energy and comes with demanding requirements, it has certain unique properties that can be beneficial to materials science. These benefits include spatial and temporal control over function, adaptive and self-healing behavior of the material and self-organization into patterns. Inspired by biological DSA, scientists have started to explore some of these unique features in the recent past. In the next sections, we will show examples of molecular DSA that explore the concept for control over material behavior, and come with design rules to aid further development.

3. Trends in non-biological approaches towards DSA

The dynamic self-assembly of microtubules shows that materials formed *via* DSA can be endowed with unique material properties. Fortunately, DSA is not limited to biological structures, but can also be man-made. In this section, we give an overview of synthetic structures formed *via* DSA. We categorize the various DSA systems by the energy source that drives their chemical reaction network, which can either be light or chemical fuels. Within this division, we further distinguish the way the conversion of energy is coupled to structure formation, be it direct, *i.e.* where the precursors and assemblers are directly coupled to the chemical reaction network, or indirect, *i.e.* where the precursors and assemblers respond to a change in their environment induced by the chemical reaction network.

3.1. Energy sources

Within our boundary conditions, DSA is driven by chemical reaction networks. In these chemical reaction networks, a precursor is converted into a building block at the expense of an energy source (Fig. 1A). A second reaction deactivates the building block to form the original precursor. The energy source in these networks is a crucial element. We will discuss chemical energy sources in which a fuel molecule gets converted into waste products and thermal energy, and we will give examples of reaction networks that use light as energy source, in which light is converted to thermal energy.

Fuel-driven chemical reaction networks that are used to drive DSA will lead to the formation of waste products, *e.g.* GDP in the microtubule example. These waste products can have significant consequences for repeated operation of a dissipative self-assembled system and in some cases, result in failure.[14,15] In contrast, chemical reaction networks that are driven by light can often perform many DSA cycles,[16,17] as they typically dissipate their energy *via* thermal relaxation. A current complication of using chemical fuels to drive chemical reaction networks is their challenging design and their restriction in suitable chemical reactants and reactions. Finally, the choice of energy source affects the lifetime of the supramolecular structures. When a finite amount of fuel is added, the system will continue the formation of building blocks until all fuel has reacted, *i.e.* the fuel can serve as some sort of buffer of energy. In contrast, when the system is irradiated with a finite amount of light, the activation reaction stops immediately after removing the source of energy.

3.1.1. Light-driven chemical reaction networks. UV-light has been used as a source of energy in many other DSA systems including gelators[18] and the assembly of nanoparticles.[16] A particular example has been described by Sleiman and coworkers.[19] They used a system containing carboxylic acid-derived azobenzenes, which are prone to form extended linear tapes held together by hydrogen bonds between the carboxylic acids (Fig. 2). UV-light irradiation of the azobenzene precursors led to the formation of hydrogen-bonded cyclic structures that subsequently stacked to form larger aggregates. The *cis*-form reverted to the more stable *trans*-form over time by thermal relaxation, leading to the formation of linear tapes once the irradiation source was removed. Notably, the system could be reactivated by re-irradiation with UV-light.

3.1.2. Fuel-driven chemical reaction networks. Despite the vast amount of known chemical reactions, chemical reactions networks that drive dissipative self-assembled systems remain rare. The basic requirements for such networks are that all reactions have to take place within a single environment, that is under the same conditions (*e.g.*, temperature, solvent, ionic strength). Moreover, the activation and deactivation reactions should proceed through two different pathways. Finally, it is important that the reagents involved in the activation and deactivation reaction do not react with one another, or at least

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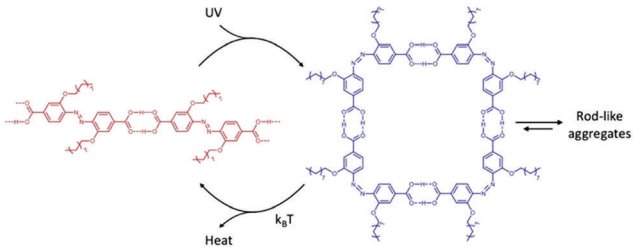

Fig. 2 The *trans*-azobenzene molecules (in red) formed linear tapes. Under UV-light the isomerization from the *trans*- to the activated *cis*-conformation molecules (in blue) led to the formation of cyclic structures, which stack into rod-like aggregates. The *cis*-form reverted back to the more stable *trans*-form over time, resulting in the disassembly of the rod-like aggregates. Adapted from ref. 19. Copyright 2003, John Wiley and Sons.

at low rates compared to the activation reaction, to ensure limited unwanted background reaction.

An example of a dissipative self-assembled system activated by a chemical fuel is the membrane transport system designed by Fyles and coworkers, which is based on dynamic thioester–thiol exchange chemistry.[20] In this system, a thioester was used as chemical fuel, which underwent a thiol–thioester exchange with the precursor (Fig. 3). This reaction led to the formation of the building blocks which assembled to form a transient membrane pore. Meanwhile the building block gradually reacted through an intramolecular thioester displacement, resulting in the formation of the precursor and a ring-closed waste product. Clearly, the activation and deactivation proceeded *via* two different pathways. Moreover, the deactivation by intramolecular rearrangement results in the formation of a stable cyclic amide product that can thus not interfere with the activation reaction.

We would like to mention that, although strictly not DSA by our definition, fuel-driven chemical reaction networks can also induce disassembly of a self-assembled precursor. From a dissipative supramolecular material's point of view, the result is the same, *i.e.* the chemical reaction network induces a transient change in material properties driven by the addition of fuel. Recently, Hermans and coworkers described such a system in which a redox reaction was coupled to the collapse and growth

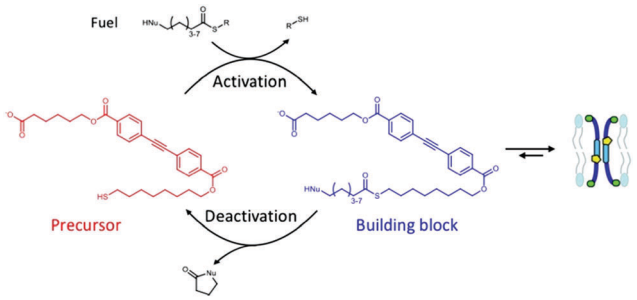

Fig. 3 Thioester-driven dissipative assembly of membrane pores. The thioester (fuel, Nu═O, NH) undergoes a thiol–thioester exchange with the precursor (red) to form a building block that can form pores in a supramolecular membrane. The building block (blue) reacts intramolecularly to form the precursor and a waste product. Adapted from ref. 20. Copyright 2014, The Royal Society of Chemistry.

of supramolecular fibers.[21] In that system, neutral perylene-diimide molecules assembled to form long fibers in thermodynamic equilibrium. When these fibers were allowed to grow for an extended period they irreversibly precipitated out of solution. However, when the fibers were still in solution, the fiber length could be controlled using redox chemistry. When the reductant sodium dithionite was added as fuel, the fibers started to break apart into smaller fibers. Here, reduction with dithionite led to the formation of negatively charged precursors, which resulted in an increase in electrostatic repulsion and thus the breaking of the fibers. Nevertheless, as the negatively charged molecules were unstable, they were slowly oxidized back to the neutral building blocks, again resulting in the formation of long fibers.

3.2. Direct *vs.* indirect DSA

In the fuel-driven example mentioned above, the precursor reacts directly with the energy source to form the building block. We introduce the term "direct DSA" for these examples. In contrast, the energy source can also indirectly result in the conversion of precursors to building blocks. For instance, the energy source can induce a change in pH, that will be reverted when all energy has been dissipated. In such cases, self-assembly can be coupled to that oscillation in pH, in which case we speak of "indirect DSA". In indirect self-assembly, the energy source is responsible for the assembly process, but it does not react directly with the precursor.

Additional complexity can be introduced by the use of chemical oscillators in which one reactant with oscillating concentration induces a morphological transition of a supramolecular material. Both the direct and indirect methods using light-driven or fuel-driven chemical reaction networks have been described to obtain transient supramolecular materials.

3.2.1. Direct DSA. In the assemblies formed *via* direct DSA, the precursor reacts directly with the energy source, which can be light or a chemical fuel, and the examples mentioned in Sections 3.1.1. and 3.1.2. are thus examples of direct self-assembly. In recent literature, we can find examples of supramolecular structures that are obtained using direct DSA, such as aggregated colloids, fibers, gels, and surfactant based structures.[7,15,16,21]

3.2.2. Indirect DSA. For indirect dissipative self-assembled systems, the precursor does not directly react with the fuel, but an intermediate reagent is first generated by reaction with the energy source. Subsequently, the intermediate species reacts with the precursor to form the building block, leading to self-assembly of the building blocks through non-covalent interactions. Examples of liquid crystals, nanoparticles, gels or dynamic monolayers can be found in literature.[17,22–24] Among them, the most abundant examples of indirect dissipative self-assembled systems are found in the light-driven reorganization of liquid crystals. In these systems, a dopant, dissolved in the liquid crystal matrix, undergoes a reversible isomerization upon irradiation with UV-light.[22,25,26] This change induces a reorganization of the liquid crystal matrix. After removal of the light source, these systems revert to the initial organization

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resulting from the thermally activated reversal of the dopant to its most stable state. The conformation of the dopant is only changed upon a continuous energy input which leads to the rotation of the liquid crystal matrix. Thus, the supramolecular structure is not only in an out-of-equilibrium state, but the conformation of the dopant is as well.

Klajn and coworkers designed a system in which the assembly[17] of non-light responsive nanoparticles is indirectly coupled to irradiation with light. In this system, a spiropyran derivative in solution released a proton upon light-driven ring closure, leading to protonation of the negative functional groups on the nanoparticles and subsequent aggregation. Importantly, the switches were not attached to the nanoparticle building blocks; they remained in solution throughout the entire process. This design makes the system more versatile, because different nanoparticles can be used for transient aggregation. When protons would be directly added to the system, it would not lead to transient aggregates, but it would just re-position thermodynamic equilibrium. Thus, the use of the spiropyran switches is crucial to obtain an out-of-equilibrium state.

Besides light as an energy source, chemical fuels can also be used to drive indirect DSA. A distinctive example is devised by Miravet and coworkers,[23] in which hydrogel formation was indirectly fueled by sucrose conversion (Fig. 4). Sucrose was converted to ethanol and carbon dioxide using yeast. In water, the produced carbon dioxide is in equilibrium with bicarbonate, subsequently releasing a proton. Protonation of a soluble negatively charged amide surfactant resulted in surfactant assembly and the formation of a fibrous network. Remarkably, the aforementioned chemical equilibrium formed the basis for the indirect dissipative self-assembled system as the gaseous carbon dioxide gradually left the system. Hence, over time the chemical equilibrium shifted to the carbon dioxide side and the protons were gradually removed from the fibers, resulting in the collapse of the hydrogel. When protons instead of sucrose would be added to the surfactants the hydrogel was indefinitely stable.

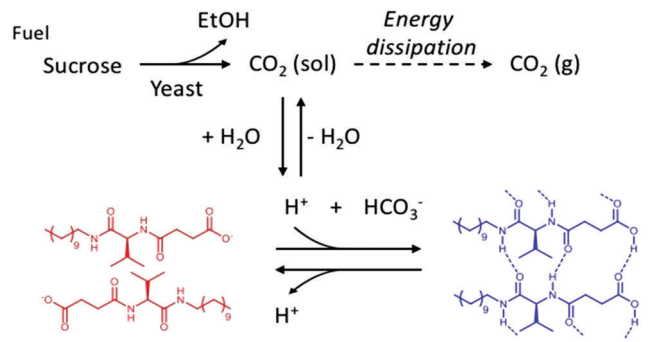

Fig. 4 Dissipative assembly of hydrogels indirectly fueled by the oxidation of sucrose. The sucrose fuel was converted to CO_2 by yeast, amongst other molecules, which in turn formed a chemical equilibrium with a proton and bicarbonate. Protonation converted the negatively charged precursor molecule (red) into a self-assembling building block (blue), resulting in the formation of fibers and consequently hydrogelation. The hydrogel was only transiently stable because the CO_2 left the system, inducing a shift in the chemical equilibrium away from the protonated building block. Adapted from ref. 23. Copyright 2016, The Royal Society of Chemistry.

3.2.3. Oscillations. Chemically fueled oscillators, like the well-known Belousov-Zhabotinsky reaction, are chemical reaction networks in which the concentration of one or more reactants changes in a periodic fashion. Naturally, oscillators are out-of-equilibrium systems driven by the conversion of chemical fuel. Their periodically changing reactant concentrations can be used to drive self-assembly in a process that we classified as indirect DSA. The oscillation enables the system to go through multiple self-assembly cycles without any human intervention. Furthermore, when using an open system, the oscillation frequency can be controlled by the flow rate, which is a straightforward method to control material lifetimes.[27]

Two examples of oscillating dissipative self-assembled systems are reported by Grzybowski and coworkers. In these systems, supramolecular structure formation was controlled by the methylene glycol–sulfite–gluconolactone (MGSG) chemical oscillator.[28,29] This oscillator periodically changed the pH of the solution. They used this oscillation for two systems: firstly, the oscillation of nanoparticle aggregation and secondly, the oscillation of a micelle-to-vesicle transition. In the first, gold nanoparticles were coated with 2-fluoro *para*-mercaptophenol ligands that are neutral at low pH and negatively charged at high pH.[28] Over time the oscillation reaction shifted the pH leading to the oscillatory aggregation of the nanoparticles at low pH and dispersion at high pH. With this oscillatory behavior, the authors were able to obtain more than ten aggregation cycles without any signs of fatigue. In the second system, the supramolecular structure was based on the assembly of oleic acid based surfactants.[29] These surfactants formed micelles when they were negatively charged and vesicles when partially neutralized. Again, the MGSG oscillation regulated the pH of the solution and therefore the assembly behavior could be controlled. This system showed a pH oscillation that led to a two-minute micelle–vesicle–micelle cycle.

Zhang and coworkers used the IO_3^-–NH_3OH^+–OH^- chemical oscillator to control amphiphilic copolymer assembly.[30] The oscillator controls the iodine concentration, which was coupled to the assembly of a PEG-functionalized polymer (Fig. 5). In the

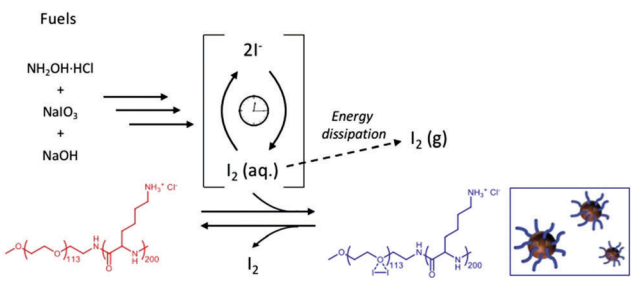

Fig. 5 The use of a chemical oscillator for indirect DSA. An iodate based chemical oscillator shows oscillation between iodide and iodine. The formed iodine can bind to a hydrophilic polyethylene glycol based polymer (precursor in red) leading to an increase in hydrophobicity (blue) and its subsequent aggregation. Over time, the iodine escaped as gas resulting in the redispersion of the polymer. Adapted from ref. 30. Copyright 2016, The Royal Society of Chemistry.

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absence of iodine in solution, the polymer was hydrophilic and well-soluble. After initiation of the oscillation, the transiently formed iodine binds to the PEG-chains resulting in an increase in its hydrophobicity and the subsequent assembly of the amphiphiles. A decrease of the iodine concentration during an oscillation led to release of iodine from the polymer and subsequent dissolution of the assemblies. An open system was used to remove the waste products, thereby extending the time the oscillator could operate. However, it was found that the assembly was not completely reversible, as not all iodine was removed from the PEG-chains in the deactivation reaction.

4. Exploration of the unique properties of structures formed *via* DSA

In Section 2, we used the GTP-driven assembly of microtubules to illustrate that materials formed *via* DSA have unique properties as a result of their dynamic nature. Unfortunately, the use of microtubules as materials or other biologically derived dissipative structures is hampered by their availability, price, complexity, versatility and scalability. However, as we demonstrated in the previous section, more and more examples of man-made structures formed *via* DSA have become available in recent years. As a result of their dissipative nature, these structures possess some of the unique features that arise from the dynamic nature of their building blocks. In this section, we will discuss these unique characteristics and we will demonstrate each with prominent man-made examples. These properties include control over where and when an assembly is formed and disassembled, the ability to adapt to a change in its environment, the ability to be re-used and the ability to self-heal. While initially the focus will be on the unique properties of the self-assembled architectures, we will emphasize, in a later section, the implication of these unique features on material properties.

4.1. Temporal control over supramolecular structure formation

Temporal and spatial control over assemblies represents a major challenge in the design of smart materials. As an example, supramolecular materials that release bioactive cues, like growth factors and anti-inflammatory agents, at prespecified sites with predefined rates is key in the successful regeneration of lost or damaged tissue.[31] Likewise, supramolecular structures that aid microfluidic guidance[32,33] or assemble to form self-erasing inks[16,34] require both spatial and temporal control over assembly and disassembly. Although disassembly of architectures can be encoded in the design of in-equilibrium assemblies, they inherently require a trigger that changes the environment, and thus the energy landscape, to induce disassembly, referred to as responsive self-assembly.[35] Changing the environment of an assembly is not always possible (*i.e.* changes in pH or temperature *in vivo*). In contrast, structures formed *via* DSA are kinetically controlled by where and when fuel is present and can thus be controlled over space and time, simply by only locally applying a finite amount of fuel. Using a DSA approach to control materials over time and space does not require an externally induced change of the environment, which in some cases can be advantageous. Here we list a few examples where supramolecular structures are controlled over time using a DSA approach.

When a finite amount of fuel is added to the precursors, it will induce their assembly resulting in the desired supramolecular material. Inherently, these materials will exist transiently and disappear as the system reaches equilibrium. Typically, equilibrium is reinstated sometime after all fuel has been converted. Understanding the kinetics at play allows the user to predetermine the lifetime of the material by the amount of fuel added. To that end, Van Esch, Eelkema and coworkers[7,36] reported the first example of a chemically driven formation of an assembly and showed the possibility to tune the lifetimes of the assemblies by altering the rate of the chemical reactions involved. To do so, a water-soluble dicarboxylate precursor was converted into its corresponding methyl ester by reaction with a methylating agent (methyl iodide or dimethyl sulfate, Fig. 6). As the methyl ester existed in an aqueous environment, it was thermodynamically unstable. Thus, simultaneous to the activation of building blocks, hydrolysis of the ester back to its soluble dicarboxylate precursor took place (Fig. 6A). The ester building blocks were molecularly engineered to assemble into fibers that, in turn, formed a dense network which entrapped the aqueous environment forming a hydrogel (Fig. 6B). Crucially, the lifetime of the gels could be controlled by the kinetics of the reactions involved. For instance, the nature of the fuel could be used as a parameter to control the activation reaction. Methyl iodide, a relatively weak electrophile, showed slow activation and thus low yields of building blocks, prohibiting gel formation. In contrast, dimethyl sulfate, a more reactive methylating agent compared to methyl iodide, enabled the system to reach sufficient concentrations of methyl esters, leading to gel formation. The lifetimes of these gels could be further modified by changing the pH of the media, thereby altering the hydrolytic deactivation reaction. Using a buffered solution at pH 9 gave gels that persisted for

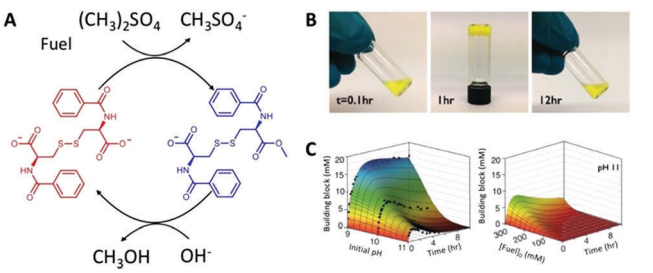

Fig. 6 Fuel-driven direct DSA to control the lifetime of a material. (A) Reaction cycle describing the activation and deactivation reactions. The precursor (carboxylate in red) reacted with the fuel (dimethylsulfate) producing the active building block (methyl ester in blue) which self-assembled into fibrous structures. Hydrolysis of methyl esters resulted in the formation of the original inactive precursor. (B) Transient hydrogel formation in a typical reaction cycle. (C) Kinetics of transient hydrogelator formation at different pH values (left) and different initial fuel concentrations (right) as measured by HPLC (markers) and calculated by a kinetic model. Adapted from ref. 7. Copyright 2015, American Association for the Advancement of Science.

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more than a week, while at pH 11 gels were only present for hours. Alternatively, the concentration of fuel could be increased to give higher relative yields and thus greater lifetimes (Fig. 6C). The possibility of repeating the out-of-equilibrium assembly process was assessed by adding a second batch of fuel. The concentration of methyl ester obtained was the same as during the first cycle, however the scattering intensity of the assemblies reached lower values than in the first cycle, because of the presence of waste products from the first cycle such as methanol, which disturbed the fiber formation.

Transient hydrogel formation driven by a batch of chemical fuel was also reported by Ulijn and coworkers.[14,37] They showed the dissipative formation of hydrogels in which both the activation and the deactivation reaction rate could be controlled by the same enzyme. This hydrogel formation was driven by an enzyme catalyzed peptide coupling between a methyl ester of an amino acid as fuel and an amine as precursor (Fig. 7). Meanwhile, the hydrolysis of the resulting peptide building block coupling was catalyzed by the same enzyme, albeit at a lower rate. Over time the methyl ester fuel was consumed and the hydrolysis towards the amine precursor took over leading to the collapse of the hydrogel. As both reactions were catalyzed by the same enzyme, tuning the lifetime of the material was not straightforward. The activation reaction showed limited dependence on the concentration enzyme when greater than 0.5 mg mL^{-1}, which gave the authors the possibility to tune the deactivation reaction by varying the amount of enzyme, while the activation reaction remained mostly unaffected. For instance, at 0.5 mg mL^{-1} enzyme, the transformation of gel to liquid occurred after 16 hours, while the gel state was sustained for only 3 hours at 3 mg mL^{-1}. Likewise, control over the deactivation reaction was achieved by varying the pH. At more alkaline pH values, the hydrolysis rate increased and thus the lifetime of the gels decreased. Finally, varying the amount of fuel allowed for tuning the lifetime of the assemblies from minutes to hours. Addition of new fuel batches gave the possibility of repeated transient gel formation up to three cycles. After more than three fuel additions, the dipeptide conversion could not reach the minimum gelation concentration, most likely due to the accumulation of waste product. The latter two examples of temporal control over self-assembly by means of DSA illustrate that for repeated or continuous operation, waste management is essential.

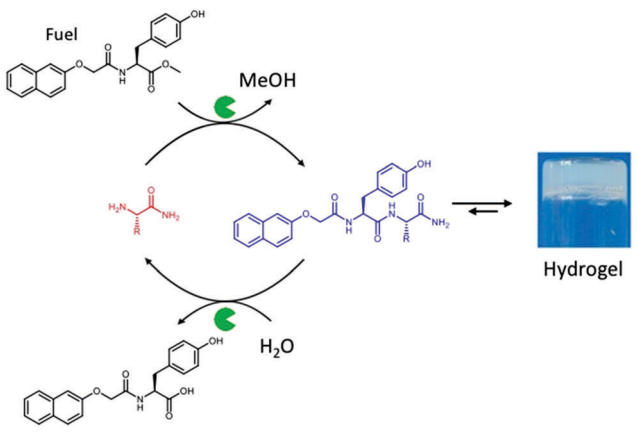

Fig. 7 Enzyme catalyzed dissipative assembly of a hydrogel. The precursor (red) is activated by the enzyme-catalyzed reaction with the fuel (black). This reaction leads to the formation of a building block (dipeptide in blue) which self-assembles into fibers that eventually form a hydrogel. The hydrogel is unstable as the enzyme also catalyzes the hydrolysis of the building block leading to the collapse of the gel and the release of the precursor and a waste product. Adapted from ref. 14. Copyright 2013, American Chemical Society.

A fine-tuned example of indirect DSA of which the lifetimes could be controlled was recently described by Walther and coworkers.[32,38] They developed a clever concept of indirect DSA in which self-assembly of a plethora of building blocks is coupled to a transient jump in the pH value. In this work, a reactant rapidly changed the environment (promoters or activators), thereby inducing assembly, while a second class of reactants (dormant deactivators) slowly brings the environment back to the original state, thereby inducing disassembly. This unique approach required simultaneous injection of both reagents leading to the rapid formation of the transient species and a slow deactivation. Crucially, deactivators were generated in a kinetically controlled manner from the dormant deactivator. For instance, the urease-catalyzed conversion of urea into CO_2 and NH_3 progressively increased the pH value back to the initial stage while the spontaneous hydrolysis of ester-containing molecules released acid decreasing, therefore, the pH value. Changing the ratio between activator, typically an acid or basic buffer, and dormant deactivator, the duration of the transient non-equilibrium state was successfully tuned from minutes to days. When this chemical network was coupled to pH sensitive building blocks, different temporary supramolecular assemblies were achieved.

In the examples we described, a chemical fuel is added batch-wise to create a transient self-assembled structure. The lifetime of this transient assembled species can be controlled by tuning the rates of the reactions involved. When light is used to drive the formation of assemblies, similar principles hold. The lifetime can be increased by longer exposure times or by greater intensity of light, both subjecting the precursors to a greater number of photons. In the case of nanoparticles functionalized with photo-responsive azobenzene molecules, UV-light triggers the formation of assemblies by inducing an isomerization from the *trans*- to *cis*-azobenzene configuration.[16] Longer UV-light exposure times afforded a larger conversion from *trans* to *cis*, and thus a greater number of dipole moments on the nanoparticle. Analogous to the chemically fueled temporal control over structures, the lifetime of the UV-light induced self-assembled state can be decreased by an increased building block deactivation rate. In one example, the deactivation rate was increased by exposing the azobenzene functionalized particles to visible light or by running the experiment at a higher temperature.[16] Particularly in the case of nanoparticles, the lifetime of the assemblies can also be significantly tuned by adjusting the surface concentration of the light-sensitive molecules.[16,39] In general, the times required to achieve full disassembly increased with increasing coverage of the switches

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on the nanoparticles. Tuning of the lifetime is not limited to azobenzene functionalized nanoparticles, as a recent report by Klajn and coworkers showed spiropyran functionalized nanoparticles that self-assembled upon UV-light irradiation.[39] This system is based on the isomerization of spiropyran to the highly polar merocyanine isomer. The polarity of the solvent was chosen such that the polar merocyanine was insoluble and thus led to aggregation of the particles. Crucially, after switching off the UV-light, the disassembly process started immediately but completed within different times depending on the surface concentration of spiropyran. For instance, half-lives ranging from 9 to 72 seconds were observed increasing the molar content of spiropyran from 0.6 to 0.9 units, where 1 is full coverage and 0 is no coverage.

4.2. Spatiotemporal control over structure formation

Local availability of an energy source can lead to the formation of a reaction diffusion gradient that dictates the concentration of activated building blocks and thus the material properties in space. Similar to the examples above, if this gradient is created using a finite amount of fuel, the locally formed out-of-equilibrium material will show a finite lifetime and will cease to exist once equilibrium is reached. We would like to emphasize that the unique aspect of DSA is the ability to control structures both over space and time simultaneously.

In order to achieve such simultaneous temporal and spatial control over the DSA process, the energy supply needs to satisfy specific requirements. The energy source should be applied locally thus creating a gradient of activated building blocks in solution. Light, as source of energy, can be delivered locally and remotely and thus allows instant application and removal. These features make light a successful energy source to create spatial shapes and patterns.

As an example, Klajn and coworkers[34] demonstrated the self-assembly of nanoparticles in transient patterns in response to an energy source. Gold nanoparticles functionalized with acidic groups and spiropyran light sensitive molecules were embedded into a thin film of polyethylene glycol gel in methanol. Under ambient conditions these gels are yellow as a result of the self-assembled nanoparticles. However, when exposed to blue light the gels become red following the dispersion of the assembled clusters into single particles. The dispersion is caused by the spiropyran molecules, which released a proton upon light-driven ring closure, leading to protonation of functional groups on the nanoparticles. As the particles could only be free in solution under constant irradiation, the gels turned yellow upon removing the light source. Similarly, when the gel was irradiated with blue light *via* a mask, only the exposed areas turned red. The images self-erased and could be rewritten at least a hundred times without deterioration of the material. It is worth to note that this is, strictly speaking, not an example of DSA, as the assembled state is thermodynamically favored while the out-of-equilibrium state is disassembled. We chose to describe the example because it does demonstrate an energy dissipating change in material property that can be used to achieve spatial and temporal control over material properties.

UV-light switchable organic molecules have also been used to induce order and disorder transitions when placed into liquid crystal mixtures. Typically, these organic molecules exhibit photo-induced conformational changes which lead to order-increasing or decreasing changes in the liquid crystal arrangement. In this manner, when the energy source is supplied locally, only the exposed areas undergo a transition.[25,40] Liquid crystals have the ability to amplify the response of a dopant to external stimuli, which is at the basis of the following examples of indirect DSA. In these examples, a UV-light switchable organic molecule is dissolved in a liquid crystal. Upon switching the molecule, it destabilizes the liquid crystal arrangement and thus induces a morphological transition. As the activated state of the dopant is thermodynamically unfavored it relaxes back to its starting point configuration upon ceasing the energy flux, in this case UV-light, thereby allowing the liquid crystal to revert to its original state. Besides earlier work by Feringa,[26,41] this strategy was applied by Bunning and coworkers[25] using a naphthopyran-based compound dissolved into a liquid crystal mixture. In its closed form, the switch destabilized the liquid crystal to give an isotropic phase at room temperature. Upon light-induced ring opening, the naphthopyran molecules became elongated and planar, stabilizing the liquid crystal phase and thus inducing a phase change from isotropic to liquid crystalline (Fig. 8A). Again, a mask was used to drive the indirect DSA in local areas. As expected, upon exposure, only the illuminated areas underwent a transition from the isotropic to the nematic phase (Fig. 8B). Once the energy influx was ceased, the naphthopyran compound reverted back to its closed form in minutes thereby undoing the morphological transition of the liquid crystals. Hedge and coworkers[40] applied a similar strategy to trigger a transition

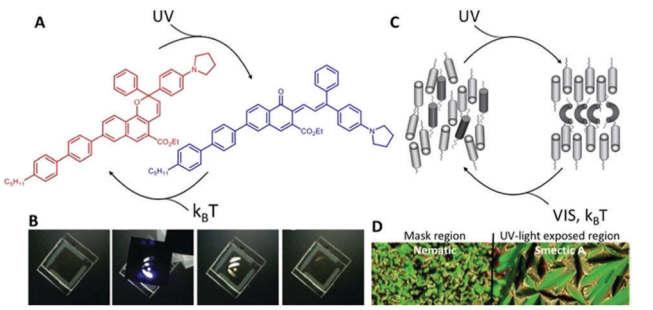

Fig. 8 Light-driven liquid crystal reorganization. (A) Activation and deactivation chemical reactions of the naphthopyran derivative dopant. UV-light triggered the isomerization from the precursor (closed naphthopyran form in red) to the building block (open naphthopyran form in blue). Upon removal of UV-light irradiation, the open form reverted back to the original precursor. (B) Spatially controlled transition from isotropic to nematic liquid crystal phases upon UV-light irradiation using a mask. Adapted from ref. 25. Copyright 2012, Nature publishing group. (C) Schematic representation showing an order inducing phased transition triggered by UV-light irradiation. When UV-light is absent, the *trans*-form of the dopant (dark grey cylinder) coexisted with the host liquid crystal (light grey cylinder). Upon UV-light radiation the bent *cis*-isomer dopant segregated from the liquid crystal host giving rise to the ordered smectic A phase. (D) Spatially controlled transition from a nematic to a smectic A phase induced by UV-light irradiation through a mask. Adapted from ref. 40. Copyright 2005, John Wiley and Sons.

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from nematic to smectic A liquid crystal phases, using a photo-induced *trans*- to *cis*-isomerization of azobenzene dopants. In the absence of UV-light the *trans*-azobenzene dopant was dissolved in the nematic host (Fig. 8C). Under UV-light irradiation, the dopant molecules isomerized to the *cis*-form. The bent shape of *cis*-isomer was less compatible with the liquid crystal host, leading to segregation of the dopant and the host and the appearance of a layered smectic A phase. When the azobenzene-doped liquid crystals were locally exposed to UV-light, fan-shaped focal conical structures typical of a smectic A phase were found only at the irradiated regions (Fig. 8D).

4.3. Adaptivity

A promising feature of structures formed *via* DSA is their adaptivity to external stimuli. In this context, adaptivity is defined as the ability of the assembly to respond to changes in their environment.[3] As structures formed *via* DSA require a continuous supply of energy to sustain, a small fluctuation in this energy flow can dramatically affect the assembly process. We would like to emphasize that adaptivity can be encoded into in-equilibrium assemblies as well, *e.g.* in pH-responsive assemblers. Still, the diversity of morphological transitions is far richer for out-of-equilibrium assemblies, *e.g.* microtubules can self-assemble into asters, vortices, or a homogeneous network of fibers, all in response to different fuel flows.[12,13] In terms of adaptivity in man-made materials formed *via* DSA, there may be an opportunity here. We are not aware of examples with similar sophisticated responses to small changes in the environment as those observed in microtubules.

In one example of adaptivity in DSA, light was used as an energy source to induce spatially controlled assembly of small molecules in organic solvents. Van Esch and coworkers[18] designed a diarylethene photochromic switch that could undergo ring-closure upon absorption of UV-light. In toluene, the open form of this diarylethene switch was well soluble. However, when energy was supplied in the form of UV-light, a reversible interconversion from the open to closed form induced self-assembly into fibers (Fig. 9A). These fibers entrapped the toluene eventually resulting in formation of an organogel. Subsequent irradiation with visible light resulted in the diarylethene derivatives switching back to their open state which destabilized the assemblies and consequently resulted in the collapse of the gel state. When UV (activation) and visible light (deactivation) were applied simultaneously, a dynamic ensemble was obtained. A mask was used to locally expose the solution with UV-light while the entire solution was exposed to visible light. In this setup, gel formation only took place in the illuminated regions. The patterning was successfully achieved because the formation and immobilization of the assembly was faster than diffusion of molecules to the non-UV-light irradiated area (Fig. 9B). The adaptivity of the light-driven dynamic structures was demonstrated by rotating the UV-light irradiation grating (Fig. 9C). Changing the UV-light grating angle changed the local availability of energy to the system. The assemblies adapted to that change by reassembling the structure to match the new irradiation pattern. In the locations where the system was shielded from UV-light, the structures disappeared, while new fibers appeared in areas that were previously not irradiated. In other words, the self-assembled state could adapt to the change in energy availability.

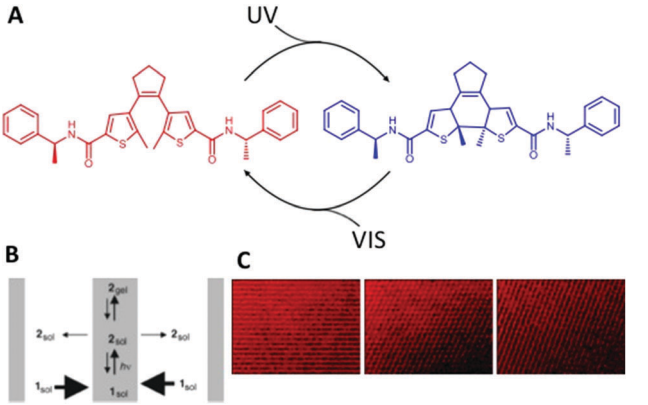

Fig. 9 Light controlled dynamic pattern formation. (A) Reaction cycle describing the activation and deactivation chemical reactions. The open state of the diarylethene (precursor in red) converted into the building block (blue) by an electrocyclization driven by UV-light. The building block (blue) reverted back to the precursor (red) with visible light. (B) Diagram representing the kinetic scheme for the diffusion mechanism. Grey areas indicated UV-light irradiation and the thickness of the arrow indicated the dominance of the process. (C) Dynamic and spatially controlled self-assembly in time. Assemblies adapted to changes in the UV-light irradiation grating angle. Adapted from ref. 18. Copyright 2005, John Wiley and Sons.

4.4. Self-healing

One form of adaptivity of dynamic assemblies is their ability to respond to externally induced damage. Provided that the damage does not affect the chemical reaction network, the self-assembled states can restore the damage as the self-assembled structures are continuously formed and broken down in the presence of an energy source. Materials that are in or close to equilibrium are typically only self-healing in exceptional cases, for instance when the building block exchange dynamics are relatively fast. Prominent examples of such self-healing materials are viscoelastic networks formed by worm-like micelles that, even under equilibrium conditions, can self-heal their viscoelastic nature.[42] In the case of DSA, the monomer exchange dynamics are coupled to the dynamics of the chemical reaction network, and such materials are thus autonomously self-healing driven by energy conversion.

Examples of self-healing materials formed *via* DSA remain relatively scarce. Van Esch, Eelkema and coworkers[7] showed the self-regenerative behavior of the above described hydrogel materials driven by methylating agents (Fig. 6). By means of rheometry, the authors demonstrated that a gel could be liquefied by applying a high strain. Next, the recovery of the gel was followed. Typically, similar low molecular weight gels that are in- or close to- equilibrium do not restore after such damage, mainly due to slow monomer-fiber exchange and even slower fiber–fiber reconnection. In contrast, the authors described that the gels were formed *via* DSA did recover after damage. Moreover, they tested how the self-healing behavior scaled with the availability

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of fuel. When the gels were disrupted early in the reaction cycle and thus contained relatively high amounts of fuel, they recovered their original state within minutes and then continued their cycle relatively unaffected by the damage. In contrast, when the gels were disrupted at later stages of a dissipative cycle, as most fuel had reacted, the original gel stiffness did not recover and regenerative behavior was akin to in-equilibrium gels.

5. Transient control over the function of supramolecular materials

We have shown that DSA endows the structures it forms with unique properties as a result of their dynamic and out-of-equilibrium nature. Biology uses these features to its advantage to control function of materials over space and time, uses its adaptivity to rapidly adjust between self-assembled states or to heal damaged tissue. Here we will discuss recent man-made attempts to molecularly engineer similar control over material properties into materials formed *via* DSA, including control over chemical reactivity, optical properties and directional motion.

5.1. Temporal control over chemical reaction rates

Grzybowski and coworkers developed a dissipative self-assembled system that reversibly controlled catalytic activity using light-driven assembly of azobenzene-functionalized nanoparticles that aggregated upon irradiation with UV-light.[43] These nanoparticles were catalytically active in their dispersed state, but self-assembly led to a decreased catalytic activity due to a reduction in available surface area per particle. When the UV-light was switched off, *i.e.* when the fuel source was removed, the particles redispersed leading to an increase in catalytic activity. The authors were able to switch from a conversion of ~1% in the aggregated state to a conversion of 40% in 25 minutes in the dispersed state.

Another example of an out-of-equilibrium structure controlling chemical reaction rates used the transient assembly of nanoparticles of different nature (gold, silica, magnetite) functionalized with azobenzene groups.[44] Irradiation with UV-light drove the assembly of the dispersed apolar nanoparticles into aggregates. This aggregation was caused by the isomerization of the azobenzene groups to the polar *cis*-conformation. When hydrophilic reactants were added to the samples, the reactants were confined within the hydrophilic cavities of the aggregates leading to a higher reaction rate compared to non-aggregated system (Fig. 10A). Crucially, removing the source of UV-light led to redispersal of the nanoparticles and stopped the chemical reaction between the hydrophilic precursors. Light-driven assembly not only increased the reaction rate, but also afforded control over the stereochemistry of the product. Without nanoparticles, the dimerization of anthracene would lead to the *anti*-product while the *syn*-product was obtained using nanoparticle aggregates (Fig. 10B). The addition of a chiral ligand to the nanoparticles also made it possible to separate enantiomers in the aggregated state (Fig. 10C).

Prins and coworkers described the dissipative assembly of vesicles, that were able to increase the rate of a chemical

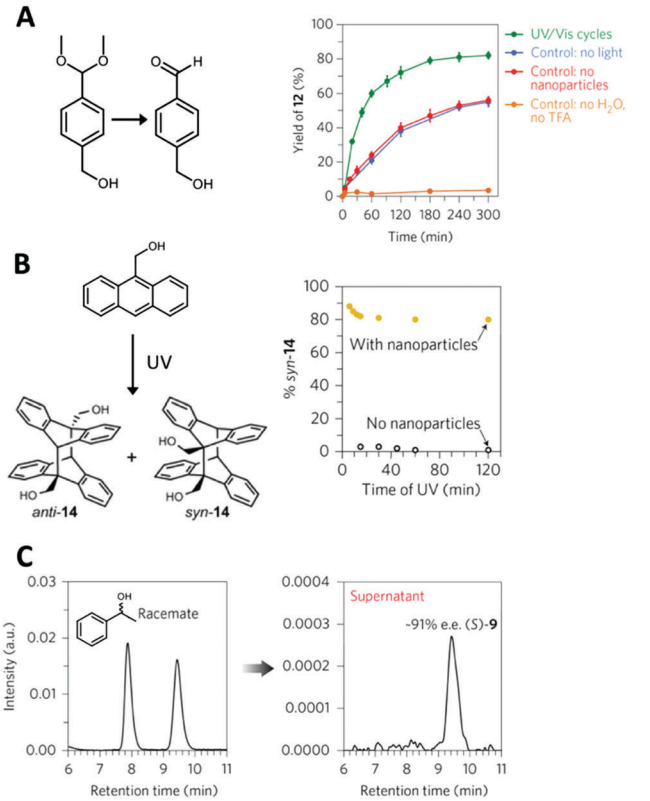

Fig. 10 Control over reaction rates using transiently assembled nanoparticle structures. (A) Increased yield of the acetal hydrolysis in the presence of nanoparticle aggregates. (B) A chemical reaction in which the *anti*-product was obtained when the particles were dispersed and the *syn*-product was obtained in the presence of nanoparticle aggregates. (C) Separation of a racemate using aggregated chiral nanoparticles. Adapted from ref. 44. Copyright 2015, Nature Publishing Group.

reaction.[15] The assembly of these vesicles was driven by the electrostatic complexation of anionic ATP to cationic surfactants. Introduction of the enzyme potato apyrase, that hydrolyses ATP, induced breakdown of the formed vesicles and allowed control over their lifetime (Fig. 11A). The transient presence of the vesicles was used to accelerate a chemical reaction of two hydrophobic precursors within the hydrophobic domain of the vesicle bilayer (Fig. 11B). The authors show that the conversion of the reaction increases with increasing vesicle concentration (Fig. 11C and D). An advantage of such catalysts is that the duration of the chemical reaction can be controlled by the kinetics of fuel conversion, which are subsequently affected by the ATP and potato apyrase concentrations. Moreover, this system could in principle be applied for many chemical reactions, because the only requirement is the hydrophobicity of the reactants.

5.2. Controlling motion

DSA is a promising approach to introduce energy-driven motion or actuation in soft materials. To that end, Klajn and coworkers designed a system in which directional motion only occurred in the dissipative self-assembled state.[33] Silica colloids were mixed with smaller azobenzene functionalized iron oxide particles. Upon irradiation with UV-light the dipole moment of the

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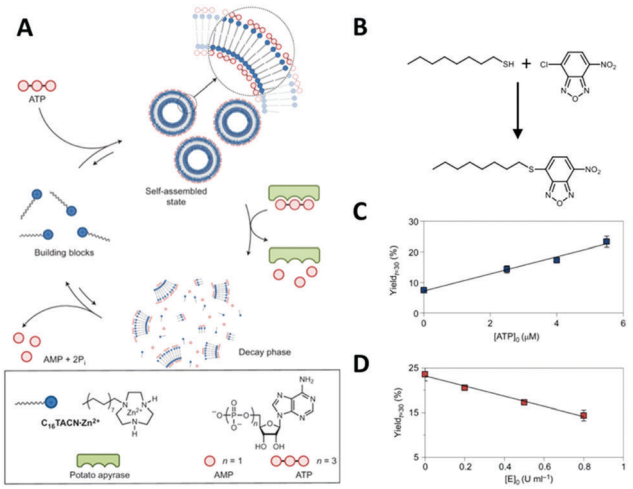

Fig. 11 Overview of ATP-driven dissipative self-assembly of vesicles. (A) Schematic representation of the ATP-activated assembly of cationic surfactants and the potato apyrase catalyzed breakdown of their formed structures. (B) The alkylation reaction performed within the vesicle bilayer. (C) Relation between the ATP concentration and the yield of the alkylation. (D) Relation between the enzyme concentration and the yield of the alkylation. Adapted from ref. 15. Copyright 2016, Nature Publishing Group.

azobenzene groups was enlarged caused by the *trans*-to-*cis* configuration. This shift of the dipole moment subsequently resulted in the association of iron oxide particles with the larger silica colloid (Fig. 12A). When a magnetic field was introduced to the system, the hybrid colloids assembled into elongated chains. Only the hybrid colloids were influenced by the magnetic field, as the externally applied magnetic field was insufficient to affect the unassembled iron oxide particles. The elongated chains could be directed to move to a specific location by controlling the direction of the magnetic field (Fig. 12B and C). When the supramolecular structure reached its destination, the UV-light was switched off and the assembly fell apart. Using this method, apolar diamagnetic particles, such as silica and gold particles, can be captured and transported to a specific location to be released again.

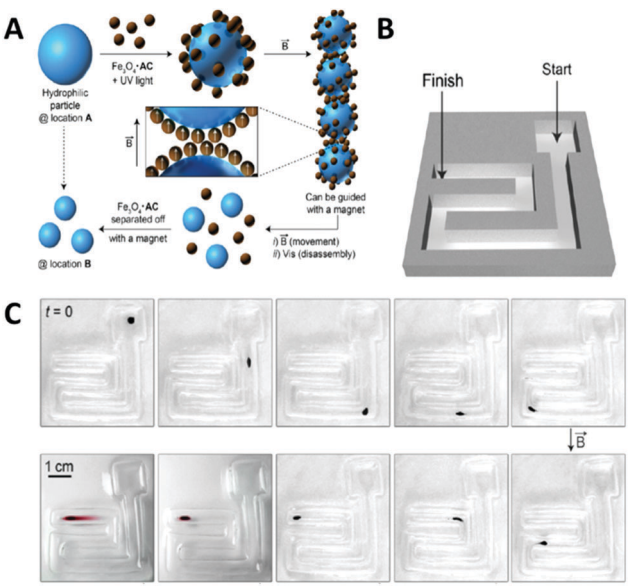

Fig. 12 DSA and directed motion of particles. (A) Schematic overview of the system. Silica and iron oxide particles assemble upon UV-light irradiation. These assemblies can be further aligned with an externally applied magnetic field. Upon removal of the UV-light the assemblies fall apart. (B) The setup for the transport experiment. (C) Directed transport of the assembly upon a directional change in the magnetic field as imaged by microscopy. Adapted from ref. 33. Copyright 2012, American Chemical Society.

Directional motion can also be generated using dissipative liquid crystal systems. Takeda and coworkers recently reported an example of a macroscopic system that performed oscillatory motion in response to DSA driven by light.[45] Thin crystalline assemblies made of a mixture of oleic acid and azobenzene derivatives were able to bend and unbend repetitively in an autonomous manner under continuous irradiation of blue light. The blue light increased the amount of *cis*-isomer of the azobenzene which induced instability of the original phase and thereby a morphological transition. As a consequence of this molecular rearrangement, a change in the photoisomerization quantum yield decreased the population of *cis*-isomer. When the amount of *trans*-isomer reached a threshold, the assembly reverted to its original morphology. This mechanical bending–unbending motion observed in this example was then achieved due to the combination of a change of photoisomerization efficiency and phase transitions of the assembly. The frequency of the movement could be tuned by changing the intensity of the light.

Two examples in which the conformation of liquid crystal director depended on irradiation with UV-light were developed by Feringa and coworkers[41,46] and Tamaoki and coworkers.[22] In these systems, a liquid crystal was mixed with a chiral dopant: a molecular motor or switch. A few weight percentage of the chiral dopant induced a helical cholesteric order in the liquid crystal material. Irradiation with UV-light led to a conformational change in the dopant and an associated change in helical twisting power. This in turn led to a change in the pitch of the cholesteric liquid crystal, thus giving a change in supramolecular assembly. When confined in a thin film, this change in pitch caused a stress in the liquid crystal that was relaxed by the rotational reorganization of the entire film. If a solid object was added on top of the liquid crystal film, it rotated along the liquid crystal rotation (Fig. 13). After continued UV-light irradiation, the motor or switch dopant reached its photostationary state and the rotational reorganization of the liquid crystal ceased. At this point, the liquid crystal was in a steady state that can only be maintained by continuous UV-light irradiation. When the UV-light was

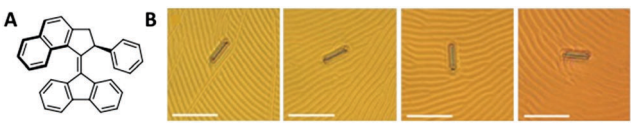

Fig. 13 (A) UV-light active chiral dopant used by the group of Feringa. (B) Rotation of a microscale object and reorganization of a liquid crystal upon UV-light irradiation. Adapted from ref. 46. Copyright 2006, Nature Publishing Group.

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switched off, the liquid crystal relaxed back to its original configuration as the chiral dopant fell back to its most stable configuration in a heat activated process. Again, the solid object rotated (counter clockwise) along with the liquid crystal rotation. These examples show that a UV-light driven process can induce a rotational reorganization of a supramolecular structure that can exert a force large enough to rotate and move a microscale object.

Self-oscillating gels can also be used to obtain a directional motion, which in turn can be used for artificial motors and micropumps. Ichijo and coworkers developed a *N*-isopropylacrylamide (IPAAm) polymer gel functionalized with $Ru(bpy)_3$ groups.[47] They were able to periodically change the oxidation state of the ruthenium from 2+ to 3+ with the Belousov-Zhabotinsky (BZ) reaction. As the Ru-catalyst was only present inside the gel, the oscillation only occurs inside the gel. The authors observed a self-oscillating pattern of 6 mm throughout the gel, caused by the diffusion of the reactants through the gel. The pattern changed in color, redox state and volume over time and space. When the shape of the gel was cut smaller than the pattern wavelength of the oscillation (<6 mm), the gel was homogeneously oscillating between the swollen and the shrunken state. Moreover, by changing the shape of the gel and by changing the period of the chemical oscillator the mechanical motion could be changed. Maeda and coworkers were then able to use this system to create a real micropump using microfluidics.[48] They observed that particles near the gel move about 200–400 μm caused by the swelling and shrinking of the gel.

5.3. Transient images

Grzybowski and coworkers designed self-erasing inks based on the DSA of *trans*-azobenzene-functionalized gold and silver nanoparticles that isomerize to *cis*-azobenzene in response to UV-light.[16] The *cis–trans* isomerization served as an activation reaction as it induced a significant increase of the dipole moment which mediated attractive interactions between nanoparticles resulting in their assembly (Fig. 14A and B). Crucially, in the absence of UV-light, the thermodynamically unfavored *cis*-azobenzene isomerized back to its *trans*-constituent, thereby losing the increased dipole moment. In turn, the nanoparticles disassembled to recover their initial dispersed state. In order to achieve spatial and temporal control over the self-assembled state, the nanoparticles were embedded into a thin and flexible organogel. When patterned UV-light was applied *via* a photomask or by using a laser pen (Fig. 14C), only the area exposed to the UV-light showed signs of the assembly process. Multiple color inks could be obtained by changing the size of the nanoparticle aggregates. Gold nanoparticle dispersions changed color upon UV-light irradiation from red to blue, while the silver nanoparticle dispersions transformed from yellow to red and purple upon UV-light exposure. Additionally, the color of the ink could be controlled by the intensity of UV-light irradiation.

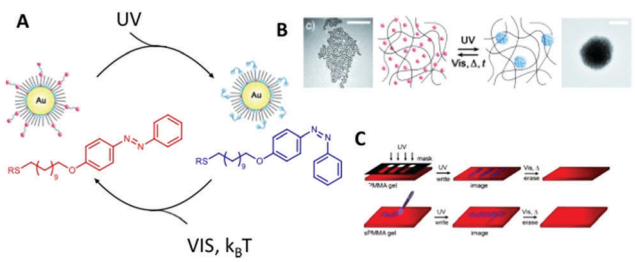

Fig. 14 Light-driven dissipative self-assembly of nanoparticles. (A) Reaction cycle describing the activation-deactivation chemical reactions. The azobenzene *trans*-isomer on gold nanoparticles (red) isomerized to the *cis*-isomer (blue) when UV-light irradiation was applied. The *cis*-isomer reverted to the *trans*-form either spontaneously or upon irradiation with visible light or by heating. (B) TEM images and schematic representation of dispersed functionalized nanoparticles (in red) and spherical assemblies of *cis*-azobenzene nanoparticles (in blue). (C) Schematic representation of a photomask and a light pen used to create patterns of nanoparticles' assemblies upon UV-light irradiation. Adapted from ref. 16. Copyright 2009, Wiley and Sons.

6. Can DSA form the materials of the future?

DSA holds great potential for use in dynamic and responsive materials. Due to their dynamics, these structures are endowed with unique properties that open the door to self-healing and adaptive materials that have a level of autonomy that cannot be obtained in equilibrium. Examples from biology verify the importance of dissipative structures for the creation of materials with applications ranging from the diverse functions of the cytoskeleton to self-healing organs. However, the number of man-made materials formed *via* DSA remains limited to proof-of-concept studies until now. Probably the most explored feature of DSA is the spatial and temporal control over structure formation and associated properties, while the potential for self-healing or adaptive materials has only been explored superficially.

6.1. Design rules for DSA

Besides being a relatively new research area, a reason for the mismatch between what possibly can be achieved, and what has been achieved may be the lack of clear design rules for DSA. In contrast to DSA, materials formed *via* static self-assembly are widely used and the number of examples of applications and new material properties is continuously growing. This success can be partly attributed to the availability of clear design rules. In contrast, the field of DSA is still in an era of serendipity, even though the notion of DSA to create materials is established. One of the major drawbacks of structures formed *via* DSA is their relatively complicated design that comes with a large set of criteria. Not only should the thermodynamics of the entire system be taken into account, the kinetics of the system also have to match. Based on the experience from our own labs and observations from examples in the literature, we draw here some preliminary design rules that could aid the further development of materials formed by DSA. We anticipate that these rules will further crystallize in the years to come as the field is developing.

First, a reversible transition in supramolecular structure should be engineered between the thermodynamically favored

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precursor and the out-of-equilibrium building blocks. To obtain this reversible transition, the non-covalent attractive and repulsive interactions between the building blocks have to be balanced to favor assembly upon chemical activation, but favor disassembly upon deactivation. Moreover, the attraction–repulsion balance should be controlled by the chemical reaction network. A successful way to satisfy these criteria is the use of reaction networks that alter the ionization state of precursors, thereby changing electrostatic repulsion or attraction and thus inducing self-assembly. Other strategies include changing a dipole moment or activating the ability to form hydrogen bonds. As a result of the vast literature on responsive assemblies, this design criterion is relatively easy to satisfy.

A far more challenging design feature of DSA involves the matching of the kinetics of the chemical reactions involved, such that dissipative assembly is favored. In cases where the reaction network only comprises a building block activation and a deactivation reaction, satisfying this criterion is relatively straightforward, *i.e.* activation needs to be faster than deactivation to accumulate an amount of building block that is greater than its critical aggregation concentration and that survives for a long enough time to self-assemble. When a finite amount of fuel or a continuous input of fuel is applied, building blocks will be created and the deactivation reaction will commence. Since deactivation is slower than activation, building blocks will accumulate transiently in the case of batch addition, or building blocks will accumulate until the deactivation matches the activation rate and a steady state arises. In the case of photochemical reactions, the network often only comprises an activation and deactivation step. In such cases, a photon is absorbed and induces an isomerization while a thermal reaction drives the isomerization back to the starting point. If thermal relaxation is sufficiently slow, the high-energy building blocks accumulate and a steady state is formed where building blocks can assemble. In the case of chemical fuels to drive DSA, the networks get more complicated. In such networks, side reactions of the fuel allow for dissipation of energy *via* non-assembling pathways. For instance, in the case of ATP-driven self-assembly, ATP will spontaneously hydrolyze to ADP, with a half-life in the order of days at room temperature and neutral pH,[49] while in the case of dimethylsulfate-driven self-assembly the half-life of the fuel is in the range of hours.[7] In the latter case, the activation reaction needs to outcompete both the deactivation and the background hydrolysis of the fuel which further complicates the design of the chemical reaction network. Taken together, when DSA is driven by photochemical reaction networks, thermal relaxation, *i.e.* deactivation, should be sufficiently slow to accumulate adequate amount of building blocks. When DSA is driven by chemical reaction networks, a fuel should be chosen that is sufficiently stable towards auto-deactivation (*via* non-assembling pathways) but adequately reactive towards precursors in order to outcompete the deactivation reaction.

Satisfying the criteria above does not have to be a matter of trial and error. In our experience, kinetic modelling of chemical reaction networks can be extremely helpful to predict the feasibility of the networks, without performing a single kinetic experiment. Many chemical reaction rates, including the above-mentioned dimethylsulfate hydrolysis (background reaction), but also its reaction with carboxylates (activation) and the methyl ester hydrolysis (building block deactivation), can be found in the vast literature on chemical reaction kinetics. Simply implementing these rate constants in a kinetic model can determine whether a chemical reaction network follows the above criteria, and can form significant amounts of building block in response to fuel addition. The use of kinetic models that predict the kinetic parameters needed to achieve DSA using chemical reaction networks will therefore become a crucial tool to the further development of materials formed *via* DSA. For further information on the design of complex molecular systems we refer to a recent review by Taylor and coworkers.[50]

6.2. Technical challenges

The design rules above are written for the development of systems capable of dissipative assembly, which is not necessarily analogous to a useful material. Even though these structures possess unique features, their use as materials might not be directly obvious. For instance, self-healing materials formed *via* DSA can be desirable from a material's point of view, *e.g.* a self-healing car tire or bumper, but these features require a constant supply of chemical energy to be sustained. This requirement implies that the material needs to be connected to a constant influx of fuel. Biology's solution to this problem is *in situ* regeneration of the fuel, but even that strategy requires, ultimately, the influx of some sort of energy carrier and building blocks, as well as an efflux of waste products. Until now, this challenge has mostly been ignored and all materials mentioned above deal with finite amounts of fuel that drive transient material formation, until fuel has been consumed and equilibrium is reinstated. To make use of all unique features of DSA, we should start thinking about approaches to overcome the technical challenges of continuous fuel input, *e.g.* by means of carriers that release large amounts of fuel or by use of fuels that are abundantly available in the environment such as certain metabolites or light.

7. Conclusions

Although common in biology, we are only now starting to see the development of the first man-made assemblies formed *via* DSA, driven directly by light or by chemical reagents, as well indirectly by energy dissipating processes. The variety of assemblies that has been formed *via* DSA is rich and includes fibers, nanoparticle clusters, vesicles and liquid crystals. These developments have opened the door to functional materials formed *via* DSA, and thus exploration of the unique properties that such materials possess. Indeed, some materials have been described that display properties unique to DSA, including self-erasing inks and patterns, self-healing supramolecular gels and catalysts with a tunable lifetime and activity. Even though the list of DSA materials remains rather short, the number of successful examples is ramping up and we foresee exciting new applications for DSA in the future.

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Acknowledgements

The authors thank Dr Thomas Hermans (ISIS, University of Strasbourg) for valuable discussions. RE and SR acknowledge funding from the Netherlands Organisation for Scientific Research, through a VIDI grant. JHvE acknowledges funding from the Netherlands Organisation for Scientific Research, through an ECHO grant. JB and MTS acknowledge funding by the Technische Universität München – Institute for Advanced Study, funded by the German Excellence Initiative and the European Union Seventh Framework Programme under grant agreement no. 291763 and the International Research Training Group ATUMS (IRTG 2022).

Notes and references

1 M. R. Chierotti and R. Gobetto, *Supramolecular Chemistry: From Molecules to Nanomaterials*, 2012.
2 E. Karsenti, *Nat. Rev. Mol. Cell Biol.*, 2008, **9**, 255–262.
3 M. Fialkowski, K. J. M. Bishop, R. Klajn, S. K. Smoukov, C. J. Campbell and B. A. Grzybowski, *J. Phys. Chem. B*, 2006, **110**, 2482–2496.
4 B. A. Grzybowski, C. E. Wilmer, J. Kim, K. P. Browne and K. J. M. Bishop, *Soft Matter*, 2009, **5**, 1110.
5 F. Tantakitti, J. Boekhoven, X. Wang, R. V. Kazantsev, T. Yu, J. Li, E. Zhuang, R. Zandi, J. H. Ortony, C. J. Newcomb, L. C. Palmer, G. S. Shekhawat, M. O. de la Cruz, G. C. Schatz and S. I. Stupp, *Nat. Mater.*, 2016, **15**, 469–476.
6 A. Sorrenti, J. Leira-Iglesias, A. J. Markvoort, T. F. A. de Greef and T. M. Hermans, *Chem. Soc. Rev.*, 2017, DOI: 10.1039/C7CS00121E.
7 J. Boekhoven, W. E. Hendriksen, G. J. M. Koper, R. Eelkema and J. H. van Esch, *Science*, 2015, **349**, 1075–1079.
8 G. Lebon, D. Jou and J. Casas-Vázquez, *Understanding Non-equilibrium Thermodynamics*, 2008.
9 G. M. Cooper and R. E. Hausman, *The Cell: A Molecular Approach*, 2nd edn, 2007.
10 S. Roychowdhury and M. M. Rasenick, *Biochemistry*, 1994, **33**, 9800–9805.
11 L. Schaedel, K. John, J. Gaillard, M. V. Nachury, L. Blanchoin and M. Thery, *Nat. Mater.*, 2015, **14**, 1156–1163.
12 F. J. Nédélec, T. Surrey, A. C. Maggs and S. Leibler, *Nature*, 1997, **389**, 305–308.
13 M. Pinot, F. Chesnel, J. Z. Kubiak, I. Arnal, F. J. Nedelec and Z. Gueroui, *Curr. Biol.*, 2009, **19**, 954–960.
14 S. Debnath, S. Roy and R. V. Ulijn, *J. Am. Chem. Soc.*, 2013, **135**, 16789–16792.
15 S. Maiti, I. Fortunati, C. Ferrante, P. Scrimin and L. J. Prins, *Nat. Chem.*, 2016, **8**, 725–731.
16 R. Klajn, P. J. Wesson, K. J. M. Bishop and B. A. Grzybowski, *Angew. Chem., Int. Ed.*, 2009, **48**, 7035–7039.
17 D. Samanta and R. Klajn, *Adv. Opt. Mater.*, 2016, **4**, 1373–1377.
18 J. J. D. de Jong, P. R. Hania, A. Pugžlys, L. N. Lucas, M. de Loos, R. M. Kellogg, B. L. Feringa, K. Duppen and J. H. van Esch, *Angew. Chem., Int. Ed.*, 2005, **44**, 2373–2376.
19 F. Rakotondradany, M. A. Whitehead, A. M. Lebuis and H. F. Sleiman, *Chem. – Eur. J.*, 2003, **9**, 4771–4780.
20 A. K. Dambenieks, P. H. Q. Vu and T. M. Fyles, *Chem. Sci.*, 2014, **5**, 3396–3403.
21 J. Leira-Iglesias, A. Sorrenti, A. Sato, P. A. Dunne and T. M. Hermans, *Chem. Commun.*, 2016, **52**, 9009–9012.
22 Y. Kim and N. Tamaoki, *J. Mater. Chem. C*, 2014, **2**, 9258–9264.
23 C. A. Angulo-Pachón and J. F. Miravet, *Chem. Commun.*, 2016, **52**, 5398–5401.
24 S. O. Krabbenborg, J. Veerbeek and J. Huskens, *Chemistry*, 2015, **21**, 9638–9644.
25 T. Kosa, L. Sukhomlinova, L. Su, B. Taheri, T. J. White and T. J. Bunning, *Nature*, 2012, **485**, 347–349.
26 T. van Leeuwen, T. C. Pijper, J. Areephong, B. L. Feringa, W. R. Browne and N. Katsonis, *J. Mater. Chem.*, 2011, **21**, 3142–3146.
27 K. Kovacs, R. E. McIlwaine, S. K. Scott and A. F. Taylor, *Phys. Chem. Chem. Phys.*, 2007, **9**, 3711–3716.
28 I. Lagzi, B. Kowalczyk, D. Wang and B. A. Grzybowski, *Angew. Chem., Int. Ed.*, 2010, **49**, 8616–8619.
29 I. Lagzi, D. Wang, B. Kowalczyk and B. A. Grzybowski, *Langmuir*, 2010, **26**, 13770–13772.
30 G. Wang, B. Tang, Y. Liu, Q. Gao, Z. Wang and X. Zhang, *Chem. Sci.*, 2016, **7**, 1151–1155.
31 J. Boekhoven and S. I. Stupp, *Adv. Mater.*, 2014, **26**, 1642–1659.
32 T. Heuser, E. Weyandt and A. Walther, *Angew. Chem., Int. Ed.*, 2015, **54**, 13258–13262.
33 O. Chovnik, R. Balgley, J. R. Goldman and R. Klajn, *J. Am. Chem. Soc.*, 2012, **134**, 19564–19567.
34 P. K. Kundu, D. Samanta, R. Leizrowice, B. Margulis, H. Zhao, M. Börner, T. Udayabhaskararao, D. Manna and R. Klajn, *Nat. Chem.*, 2015, **7**, 646–652.
35 A. Wang, W. Shi, J. Huang and Y. Yan, *Soft Matter*, 2015, **12**, 337–357.
36 J. Boekhoven, A. M. Brizard, K. N. K. Kowlgi, G. J. M. Koper, R. Eelkema and J. H. van Esch, *Angew. Chem., Int. Ed.*, 2010, **49**, 4825–4828.
37 C. G. Pappas, I. R. Sasselli and R. V. Ulijn, *Angew. Chem., Int. Ed.*, 2015, **54**, 8119–8123.
38 T. Heuser, A.-K. Steppert, C. Molano Lopez, B. Zhu and A. Walther, *Nano Lett.*, 2015, **15**, 2213–2219.
39 P. K. Kundu, S. Das, J. Ahrens and R. Klajn, *Nanoscale*, 2016, **8**, 19280–19286.
40 S. K. Prasad, G. G. Nair and G. Hegde, *Adv. Mater.*, 2005, **17**, 2086–2091.
41 R. Eelkema, M. M. Pollard, N. Katsonis, J. Vicario, D. J. Broer and B. L. Feringa, *J. Am. Chem. Soc.*, 2006, **128**, 14397–14407.
42 J.-F. Berret, *Molecular Gels*, Springer, 2005, pp. 235–275.
43 Y. Wei, S. Han, J. Kim, S. Soh and B. A. Grzybowski, *J. Am. Chem. Soc.*, 2010, **132**, 11018–11020.
44 H. Zhao, S. Sen, T. Udayabhaskararao, M. Sawczyk, K. Kučanda, D. Manna, P. K. Kundu, J. Lee, P. Král and R. Klajn, *Nat. Nanotechnol.*, 2016, **11**, 82–88.
45 T. Ikegami, Y. Kageyama, K. Obara and S. Takeda, *Angew. Chem., Int. Ed.*, 2016, **55**, 8239–8243.

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46 R. Eelkema, M. M. Pollard, J. Vicario, N. Katsonis, B. S. Ramon, C. W. M. Bastiaansen, D. J. Broer and B. L. Feringa, *Nature*, 2006, **440**, 163.
47 B. R. Yoshida, T. Takahashi, T. Yamaguchi and H. Ichijo, *Adv. Mater.*, 1997, 175–178.
48 K. Takahashi, S. Nagasawa and S. Maeda, *IEEE Int. Conf. Intell. Robot. Syst.*, 2013, 4040–4045.
49 H. R. Hulett, *Nature*, 1970, **225**, 1248–1249.
50 G. Ashkenasy, T. M. Hermans, S. Otto and A. F. Taylor, *Chem. Soc. Rev.*, 2017, **46**, 2543–2554.

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