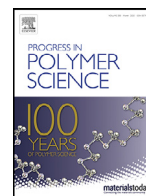Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Design of materials with supramolecular polymers

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ABSTRACT

One hundred years ago Hermann Staudinger was strongly criticized by his scientific peers for his macromolecular hypothesis, but today it is hard to imagine a world without polymers. His hypothesis described polymers as macromolecules composed of large numbers of structural units connected by covalent bonds. In the 1990s the concept of supramolecular polymers emerged in the scientific literature as discrete entities of large molar mass comparable to that of classical polymers but built through non-covalent bonds among monomers. Supramolecular polymers exist in biological systems, and potentially blend the physical properties of covalent polymers with unique features such as high degrees of internal order within the polymeric structure, defined shapes, and novel dynamics. This trend article provides a summary of seminal contributions in supramolecular polymerization and provides recent examples from the Stupp laboratory to demonstrate the potential applications of an exciting class of materials composed fully or partially of supramolecular polymers. In closing, we provide our perspective on future opportunities provided by this field at the onset of a second century of polymers. It is our objective here to demonstrate that this second century could be as prosperous, if not more so, than the preceding one.

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1. Introduction

When Hermann Staudinger first discussed the concept of "high molecular weight products" in 1920 [1], the mainstream view of these products was that they consisted of aggregates or micelles of small, well-defined molecules which could in turn crystallize. Holding on to his hypothesis was indeed bold at the time, as many scientists detested the idea of "very large molecules," resulting in Staudinger facing intense criticism from his colleagues [2]. Staudinger's insight one hundred years ago has led to great advances in our understanding of macromolecules, the birth of the field of "polymer science" embedded now in materials science, physics, and chemistry and the growth of a multibillion-dollar industry worldwide. Polymer products have completely transformed our lives with their use in consumer goods, protective equipment so critically important during the COVID-19 pandemic, biomedical materials and devices, transportation enabling the operation of large aircraft and ground transportation, and our food supply, among many other functions. Polymer science has also made critical contributions to our understanding of living organisms, and it

is remarkable that just a century ago when Staudinger's work was proceeding in full force the critical role of macromolecules in biology remained unknown.

The term "polymer" is of Greek origin, *polus* meaning "many" and *meros* which translates to "part or piece", hence in its most basic form the term polymer refers to "many parts." The International Union of Pure and Applied Chemistry (IUPAC) defines a macromolecule as a "molecule of high relative molecular mass, the structure of which essentially comprises the multiple repetition of units derived, actually or conceptually, from molecules of low relative molecular mass" [3]. With the additional clarification that a "molecule can be regarded as having a high relative molecular mass if the addition or removal of one or a few of the units has a negligible effect on the molecular properties." This definition is inclusive of almost all polymer molecules with the exception of certain natural polymers such as proteins or DNA, where although large in relative molecular weight, the loss of even one building block can significantly change function and properties. In comparison IUPAC defines an oligomer as having an intermediate relative molecular mass, where properties "significantly vary with the removal of one or a few of the units" [3]. These definitions allow us to demarcate what a covalent polymer is in a classical context. IUPAC, the notion of "relative size" clearly matters, and it is in-

Abbreviations

BMP-2	Bone morphogenetic protein 2
Cy 3	Cyanine 3
Cy 5	Cyanine 5
DNA	Deoxyribonucleic acid
DPP	Diketopyrrolopyrrole
ECM	Extra cellular matrix
IUPAC	International Union of Pure and Applied Chemistry
1D	One dimensional
PA	Peptide amphiphile
SAXS	Small angle x-ray scattering
SEM	Scanning electron microscopy
2D	Two dimensional
0D	Zero dimensional

deed this size of macromolecules that enables a number of advantageous characteristics of polymers. Supramolecular polymers [4], the topic of this brief article, are systems in which the many recurring parts have the full chemical structure of monomers since a chemical reaction is not involved in their formation. They are instead aggregates of molecules interacting through non-covalent bonds, but the same IUPAC definitions of covalent polymers apply, namely high molar mass with negligible impact on its value if a few monomers are removed. We reflect here on the exciting potential of these polymers as soft materials based on the rapidly growing scientific and industrial activity in this area.

The field of supramolecular polymers, in which monomers are bonded non-covalently, is now an established branch of polymer chemistry owing to the discovery that physical properties similar to those of covalent macromolecules as well as novel ones can be achieved with supramolecular systems [4]. An early example of 2D supramolecular polymers using chiral monomers was reported by Stupp *et al.* in 1993 as part of a study that utilized these assemblies as precursors to synthesize 2D covalent polymers [5]. However, experimental evidence of supramolecular polymers as discrete aggregates of molecules with a collective molar mass that meets the IUPAC definition of polymers mentioned above was first reported by Stupp *et al.* [6] and Meijer *et al.* [7]. Most importantly, these systems were found to emulate the physical properties normally associated with covalent polymers, namely transparent plastic films [6] and elastomers [7]. Conceptually supramolecular polymers were introduced by an earlier paper by Fouquey *et al.* [8] reporting on liquid crystals formed by the non-covalent association of triply hydrogen-bonded monomers. However, in this inspiring early work, there was no evidence of polymeric molar mass or physical properties associated with solid polymers in the supramolecular systems reported. Work in 1988 by Inoue *et al.* [9] reported on structures consisting of aggregated porphyrins and Ducharme and Wuest [10] on aggregates of hydrogen bond acceptors and donors. Though, in this early work again there is no experimental evidence of polymer-like properties or collective molar mass in the size range of polymers.

Since the early work on supramolecular polymers, many contributions followed exploring structures and physical properties [11–15]. One remarkable characteristic of these systems is the self-healing of supramolecular polymer networks, first reported by Cordier *et al.* in 2008 [16]. In this work, monomers were polymerized and crosslinked through multiple hydrogen bonds to create a supramolecular polymer network. These materials demonstrated full strain recovery after extension under load and, in contrast to covalent rubbers, the capability for repeated self-healing at room temperature without loss of function [16]. Further work from Leibler and coworkers on reversible covalent bonding, as

demonstrated in vitrimers, are also an exciting opportunity for the processability and reusability of materials for a range of applications [17]. The realization of supramolecular interfacial polymerization, pioneered by Zhang and coworkers, and the control this provides in fabricating supramolecular polymeric materials can lead to supramolecular materials with well-defined properties [18–20]. For a thorough review of the topic of controlling supramolecular polymerizations we direct the reader to a review published earlier this year by Qin *et al.* [21].

The field of covalent polymer chemistry has explored over the past few decades functional opportunities in macromolecular architectures beyond linear chains such as dendrimers [22–24], 2D polymers [5,25–28], and polymers with star, comb, ladder, and ring architectures [29,30]. Similar interesting directions exist for supramolecular polymers but are not yet fully developed. Firstly, one may ask what the equivalent functional opportunities in supramolecular polymers are compared to those offered by the architectural diversity in covalent polymer backbones. The first one is the dimensionality of the non-covalent aggregates (0D, 1D, 2D), secondly the possibility of forming crystalline assemblies throughout an entire polymeric aggregate (very difficult to achieve in covalent polymers and functionally important, for example, in the movement of excitons [31]) and lastly, the definition of polymer shape which brings polymers structurally closer to inorganic nanoparticles [32]. With expansion in the types and bonding energies available for the design of supramolecular polymers, dimensionality could be controlled and expanded into the 3D regime of micron scale and even macroscopic structures. With respect to supramolecular polymers, the directionality of non-covalent bonds such as hydrogen bonding and π-π stacking gives rise to assemblies that are nanoparticles of low symmetry (0D) [6], filament-like with many morphologies possible (1D) or sheet-like (2D) in architecture [5].

We anticipate that advances in the design of novel materials with supramolecular polymers will be related to the very "lively" and tunable dynamics of monomers connected non-covalently. This dynamic character was already shown to result in the formation of materials with reversible hierarchical structures [33]. Both dynamics enabling reconfiguration of structures and hierarchical order are unique features of soft matter in living organisms. Structures with non-covalently coupled monomers can contribute to sustainable materials since at least partial replacement of covalent bonds for non-covalent ones will create more easily processable and recyclable materials. These hybrid materials are also of interest as stimuli-responsive materials for robotic and sensing applications to use either the dynamic nature of supramolecular polymers to enhance the time scales of responsive behavior or their ordering capacity to create anisotropic structures [4,34–36]. The partial replacement is in fact extremely important in order to create materials that combine the robustness of covalent polymers with dynamics and order of supramolecular polymers. We referred earlier to these systems as "hybrid bonding polymers" which chemically integrate covalent and supramolecular polymers [37]. Supramolecular polymers are definitely attractive as biomaterials in areas such as regenerative medicine and drug delivery since bioactive supramolecular scaffolds and drug vehicles could be designed to biodegrade rapidly after their function has been performed [4,38]. The research laboratory of the authors has in fact extensively investigated the use of supramolecular polymers as biomaterials for tissue regeneration and therapeutic applications [39–50]. We anticipate many novel supramolecular biomaterial opportunities given the possibility of easily controlling their non-covalent bonds with monomer structure and architecture [51,52], pH [53], and the presence of enzymes [54]. Using examples from the authors' laboratory, we review the evolution of architectures and hierarchical structures in supramolecular polymers, and also illustrate the potential
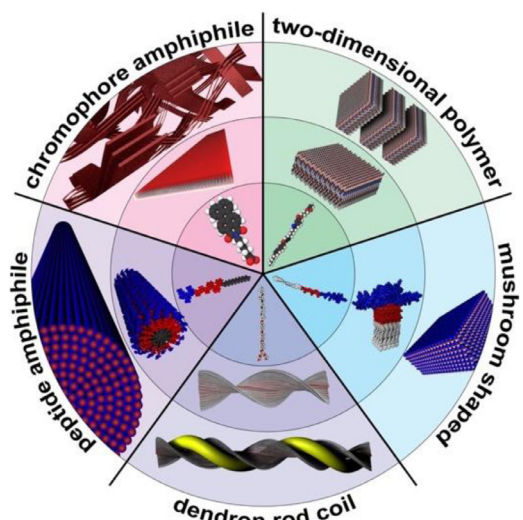
Fig. 1. Examples of hierarchical supramolecular polymers with the monomer (inner circle), supramolecular polymers (middle circle), and hierarchical assembly (outer circle) in each case schematically represented. Clockwise from the top, two-dimensional (2D) polymers that form single-crystal stacks, asymmetric 0D supramolecular polymers which form polar stacks, dendron rod coil monomers that assemble into twisted nanoscale ribbons used to template CdS crystal growth, peptide amphiphile monomers that form filament-like supramolecular polymers which can bundle and interact intimately with cells, and most recently chromophore amphiphile monomers that self-assemble into crystalline supramolecular polymers with enhanced photocatalytic properties. [5], Copyright 1993. Reproduced with permission from the American Association for the Advancement of Science. [6], Copyright 1997. Reproduced with permission from the American Association for the Advancement of Science. [60], Copyright 2001. Reproduced with permission from the American Chemical Society. [63], Copyright 2002. Reproduced with permission from Wiley-VCH. [65], Copyright 2001. Reproduced with permission from the American Association for the Advancement of Science. [55], Copyright 2014. Reproduced with permission from the Nature Publishing group.

of these exciting materials in applications ranging from regenerative medicine to energy materials. We also demonstrate, through recent examples, the importance of supramolecular polymers in a range of applications from tissue regeneration through to solar energy devices.

2. Self-assembled supramolecular polymers and their hierarchical structures

Fig. 1 summarizes strategies utilized by the Stupp laboratory over the past few decades to generate architectures and hierarchical structures with supramolecular polymers of the kind that have significant degrees of internal order. In our view this variety of supramolecular polymers, which we previously described as "self-assembling supramolecular polymers" or "internally ordered supramolecular polymers", are the ones that differ most from classical covalent polymers that typically feature entropy-driven conformational disorder. The structures of internally ordered supramolecular polymers can be crystalline, which is not common but examples were discovered recently in our laboratory [55–57], or non-crystalline but with order parameters comparable to those observed in liquid crystals. The first example of these from the authors' laboratory was a bilayer 2D supramolecular polymer formed by self-assembly of the monomers [5,25]. These 2D supramolecular polymers could be doubly cross-linked at three different planes of the assemblies through a combination of a polymerizable functional group (acrylate) and a chiral center with a reactive dipole (nitrile) to create 2D covalent polymers (Fig. 1) [5]. This method was the first example of a bulk pathway to synthesize 2D polymers at a time when there was not strong interest in such structures, before graphene and cova-

lent organic frameworks. In this case, monomers interacted non-covalently through chiral, dipolar, π-π stacking, and hydrophobic forces to create 2D assemblies of high collective molar mass. This early example is further evidence of the potential for supramolecular polymers to have architectures beyond one-dimensional assemblies of molecules [5,25]. The hierarchical structure that emerged here was the highly ordered stacking of 2D assemblies as characterized by electron diffraction.

In 1997, oligomer-sized "rodcoil" monomers, so-called because of their structure containing molecularly rigid and flexible domains, were reported to self-assemble into zero-dimensional supramolecular polymers [6]. From an architectural perspective, the mushroom-shaped aggregates of high collective molar mass, on the order of 10^5 daltons, are supramolecular polymer equivalents to dendrimers, proteins, and nanoparticles in general; hence their description as zero-dimensional objects (Fig. 1). The formation of the mushroom-shaped supramolecular polymers was mediated by the nanoscale crystallization of identical rigid rod-like segments in the monomers limited by sterics and the entropy of subtly diverse coil-like molecular segments containing two distinct blocks of oligostyrene and oligoisoprene [6]. After evaporation of solvent, these structures self-assembled into a transparent material that could have been mistaken as a plastic film, containing hundreds of layers of the supramolecular polymers stacked in a polar arrangement. As a result of the polar hierarchical structure and the contrasting chemistry of the mushroom stem and its cap, the films displayed adhesive tape-like properties with one non-adhesive hydrophobic surface and a hydrophilic sticky one (Fig. 1) [6]. The ability of these supramolecular polymers to self-order into polar arrangements offers many functional opportunities for materials that require macroscopic polarity such as piezoelectricity, second harmonic generation, self-assembly of adhesive films with useful chemistry on exposed surfaces for bioactivity or lubrication, among others [6,58,59].

The addition of a bulky dendritic segment to rodcoil monomers was found to change the supramolecular structure from mushroom-shaped nanostructures to 1D twisted nanoribbons [60]. These dendron rodcoil monomers interacted through hydrogen bonding and π-π stacking and self-assembled into supramolecular polymers shaped as nanoscale ribbons with well-defined width and thickness. (Fig. 1) [60–62]. These assemblies were applied as a template to provide the first example of a nanoscale helical morphology of cadmium sulfide which was grown on the supramolecular nanoribbons [63]. Further, dendron rodcoil molecules were able to self-assemble in the presence of vinyl monomers which following covalent polymerization resulted in both hard and soft gels that contained significant order resulting from the inclusion of only a small fraction of the self-assembling molecules [64]. Other examples of dendron rodcoil monomers containing stereocenters led to left- and right-handed helical structures, in which monomeric R and S enantiomers yielded supramolecular polymers that were mirror images of each other [32].

In 2001, the Stupp laboratory reported on self-assembling supramolecular polymers based on peptide amphiphile (PA) monomers consisting of a peptide sequence attached to a single alkyl segment (Fig. 1) [65,66]. In an aqueous environment hydrophobic collapse of the aliphatic tails and intermolecular hydrogen bonding among the peptide segments drive these monomers to form supramolecular polymers with one-dimensional architecture and internal sub-structures that contain β-sheet secondary structure [67,68]. The key structural features in PA monomers that led to the discovery that these molecules can form one-dimensional supramolecular polymers were the single alkylation of the peptide segment, and the use of peptide domains with a propensity to form β-sheets within the supramolecular polymer. In fact, PAs were known before 2001 which had double alkylated tails

and different peptide sequences that could order at air-water interfaces or form micelles [69–72]. Depending on polymerization pathways and peptide sequences, the filament-shaped polymers can have extremely high aspect ratios with persistence lengths never observed in common covalent polymers that easily reach into the size scale of microns. In fact, theoretical work has shown that infinite supramolecular polymerization can be expected in certain monomers under the right solvent conditions [68]. Also depending on peptide sequence and solvent conditions, the amphiphilic monomers can form a range of architectures that include spherical micelles [73], cylindrical fibers [65], flat belts [74], and twisted ribbons [75]. These primarily filamentous structures are highly reminiscent of structures present in the natural extracellular matrix (ECM) of cells and as demonstrated by extensive research over the past two decades an ideal platform to create supramolecular polymers for cell signaling in regenerative medicine through the presentation of biological cues by the peptide-based terminal segment of monomers [40–44,46–49,52,65,76–79].

These versatile, non-covalent, supramolecular structures have found a diverse range of applications beyond regenerative medicine including drug release [80–83], cancer therapies [84], nucleation of inorganic nanoparticles [85], enhanced magnetic resonance imaging contrast agents [86], and thermally and light-responsive actuation [34,35]. The ability to co-polymerize PA molecules within these systems provides a unique potential to integrate multiple functions over a range of densities within these supramolecular polymers [87]. Furthermore, due to the non-covalent nature of bonding among the monomers, their positions within the polymer are not necessarily fixed depending on the strength of inter-structural unit interactions. This would in turn allow spatial rearrangements that might be functionally useful, an opportunity not available with covalent polymers [88].

The full crystallization of macromolecules in synthetic materials is a major challenge, yet many potential functions benefit from crystalline lattices including ferroelectrics, photovoltaics, exciton movement in photocatalysis, and quantum computing in the future, among many others. In this context it has been interesting to find that supramolecular polymers can indeed form highly crystalline structures, while remaining discrete structures that could physically behave as covalent polymers [89]. In 2014 the Stupp laboratory reported on internally crystalline supramolecular polymers that led to enhanced light-harvesting capabilities [31,55–57,68,90–92]. These systems were inspired by the internal structure of photosynthetic organelles in plants that can colocalize molecules involved in light absorption, charge transport, and the catalysis used to create chemical bonds from the energy provided by sunlight [55]. In our system, the supramolecular polymers of perylene monoimide amphiphiles can crystalize and gel in the presence of electrolyte charge screening resulting in enhanced electronic coupling among the monomers. In the first examples reported, the supramolecular polymers are able to electrostatically attract a nickel-based catalyst to the surface of the gels for effective light harvesting and photocatalytic hydrogen gas production (Fig. 1) [55]. We can expect many new developments in the field of crystalline supramolecular polymers and possibly their integration with covalent polymers to achieve the required functions and mechanical robustness.

3. Reversible superstructure formation resulting from dynamic exchange in supramolecular polymers

A key opportunity offered by supramolecular polymers is the ability for monomers in these systems to escape the assemblies where they initially reside and create new supramolecular polymers in which monomeric composition is changed [88]. This process is analogous to how the ECM in biology, which contains many protein supramolecular polymers, can dynamically reorganize to display biological cues presented to cells to instruct a range of cellular processes with temporal control. We have demonstrated earlier that this dynamic nature of monomers can be used to drive the formation of reversible hierarchical superstructures [33,93]. This was demonstrated in supramolecular polymers containing monomers with complementary DNA sequences or others consisting of zwitterionic PA monomers designed for self-complementary electrostatic interactions. Using the latter monomers, the size scale of the hierarchical structures was tunable and dependent on the spacing between charged regions of the monomers (Fig. 2a). Furthermore, these structures were found to be reversible with changes in pH, altering the complementarity of these electrostatic interactions (Fig. 2b) [33]. At pH 4 and 10, when only basic or acidic residues of the zwitterionic monomer are charged, the hierarchical bundling of the nanofibers does not occur. This was evident in small-angle X-ray scattering (SAXS) with a slope of approximately -1 in the low q region, indicating a cylindrical morphology (Fig. 2c). At pH 7, both the acidic and basic residues of the monomer are charged, resulting in favorable electrostatic interactions leading to bundling. This again was evidenced in SAXS by a slope of -2.5 in the low q region of the pattern indicative of the formation of larger structures (Fig. 2c). Through coarse-grained simulations, it was determined that as long as the strength of non-covalent bonds in the supramolecular polymer is low enough to allow monomers to escape from their original assemblies then there is potential for the formation of hierarchical structures driven by the possibility of forming highly favorable inter-polymer interactions [33].

In supramolecular polymers formed by PA molecules with specific amino acid sequences, bonding among the monomers includes multiple interactions which in some cases includes strong intermolecular β-sheet hydrogen bonding. In a recent study, we investigated the strength of these interactions on hierarchical structure formation [93]. When supramolecular polymers of differing surface charge contained weak cohesive forces among the monomers, monomeric escape from the polymers was possible allowing the molecular re-arrangement into hierarchical assemblies [93]. The addition of hydrophobic peptide residues to enhance strong β-sheet hydrogen bonding among molecules, in turn, suppressed or limited the monomeric escape. Furthermore, increasing the charge and resulting intermolecular repulsion within the supramolecular polymers accelerated exchange to create favorable electrostatic interactions and thus the formation of bundles of supramolecular polymers [93]. These findings introduce new opportunities to design novel structures and properties based on the ability of monomers in supramolecular polymers to equilibrate into thermodynamically favorable structures and at the same time create strategies to make them reversible.

4. Supramolecular polymers for regenerative medicine

Peptide amphiphile monomers that create filament-like supramolecular polymers, were reported by our laboratory in 2001 [65], and continue to provide unique opportunities for biomedical applications [39,40,42,44,46,48–50,77,79,94–97] and development of novel materials that include robotic soft materials [34,35]. In one recent example, we demonstrated the importance of dynamic behavior in supramolecular polymers to enhance bioactivity, by developing sulfated glycopeptide amphiphile monomers. The intent was to create filamentous supramolecular polymers that emulate the highly functional and complex biopolymer active in cell signaling known as heparan sulfate. More than 300 secreted or membrane-bound proteins have been found to bind to this highly
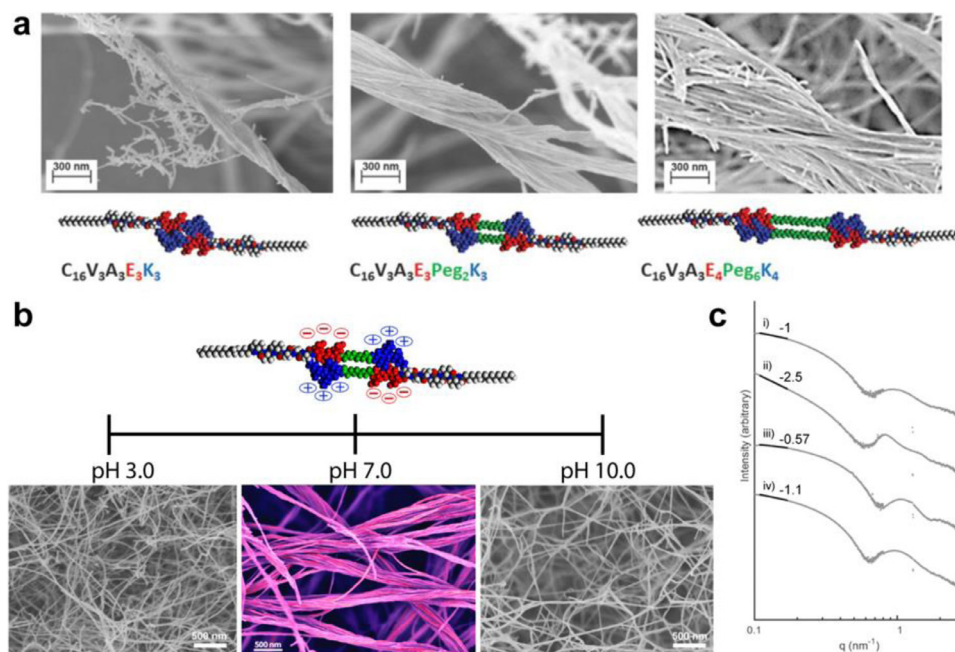
Fig. 2. Reversible hierarchical assembly of supramolecular polymers. a) Representative scanning electron microscopy (SEM) images of the hierarchical assembly with molecular graphics demonstrating molecular interaction of $C_{16}V_3A_3E_3K_3$ (left), $C_{16}V_3A_3E_3\text{-PEG}_2\text{-}K_3$ (middle), and $C_{16}V_3A_3E_4\text{-PEG}_6\text{-}K_4$ (right). b) Representative SEM images of $C_{16}V_3A_3E_3\text{-PEG}_2\text{-}K_3$ at pH 3, 7, and 10. The SEM micrograph for pH 7 has been false-colored to emphasize the hierarchical superstructure formation. c) Small-angle X-ray scattering (SAXS) patterns of $C_{16}V_3A_3E_3\text{-PEG}_2\text{-}K_3$ monomer annealed at i) pH 4, ii) pH 7, iii) pH 10, and iv) $C_{16}V_3A_3E_3$ monomer annealed at pH 7. [33], Copyright 2018. Reproduced with permission from the American Association for the Advancement of Science.
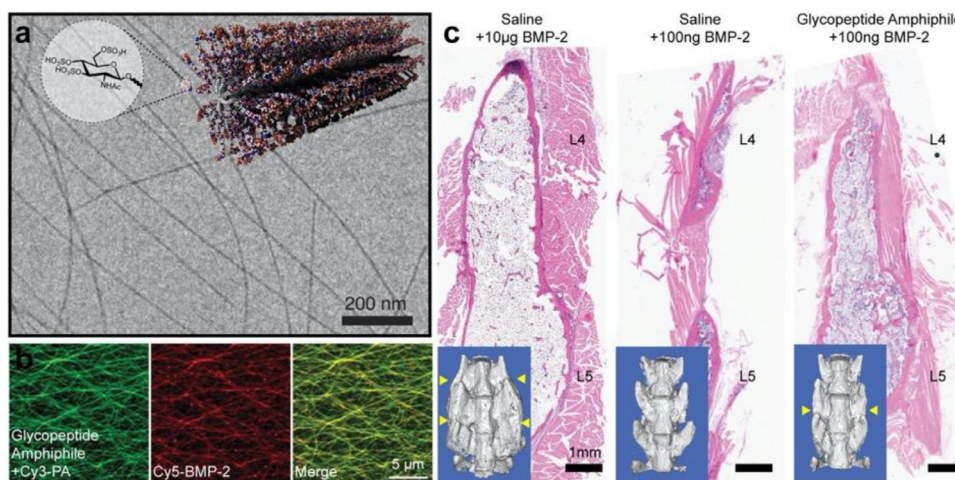

Fig. 3. Glycopeptide supramolecular polymer for tissue regeneration. a) cryogenic transmission electron micrograph of the sulfated glycopeptide amphiphile which forms filamentous nanofibers, with molecular graphic overlay of the assembled nanofiber. b) Confocal microscopy images of Cy-3 fluorescently labeled glycopeptide amphiphile assembly (left) and after mixing with Cy-5 labeled BMP-2 (middle). The merged image (right) demonstrates the colocalization of the protein with the supramolecular polymers. c) Representative sagittal cross-sectional images of L4-L5 posterolateral spine specimens with hematoxylin and eosin staining following treatment in a rat spinal fusion model. Insets are representative volume renderings from micro-computed tomography analysis with yellow arrows indicating bone fusion. [39], Copyright 2017. Reproduced with permission from the Nature Publishing Group.

sulfated and aperiodic polymer ubiquitous in extracellular matrices. Binding of proteins through their so-called "heparin-binding domains" to specific regions of this aperiodic polymer mediate biological functions including cell differentiation, organogenesis, blood coagulation, lipid metabolism, inflammation, response to injury, and many others [39]. Interestingly, the sulfated glycopeptide supramolecular polymer, which utilizes a single monomer displaying at one terminus a trisulfated monosaccharide, was able to bind a number of critical growth factors in both development and regeneration (Fig. 3a). All these growth factors have different heparin-binding domains, yet the supramolecular polymer was able to bind most of them suggesting that its dynamic structure allows it to rearrange structurally to recognize multiple targets [39]. The importance of this system was demonstrated using *in vitro* experiments and an *in vivo* model of bone regeneration. The binding of bone morphogenetic protein 2 (BMP-2), which promotes bone regeneration, by the glycopeptide supramolecular polymer (Fig. 3b) led to greatly enhanced activation of the growth factor relative to heparin *in vitro* and was able to achieve spinal fusion through bone growth in a murine model using a BMP-2
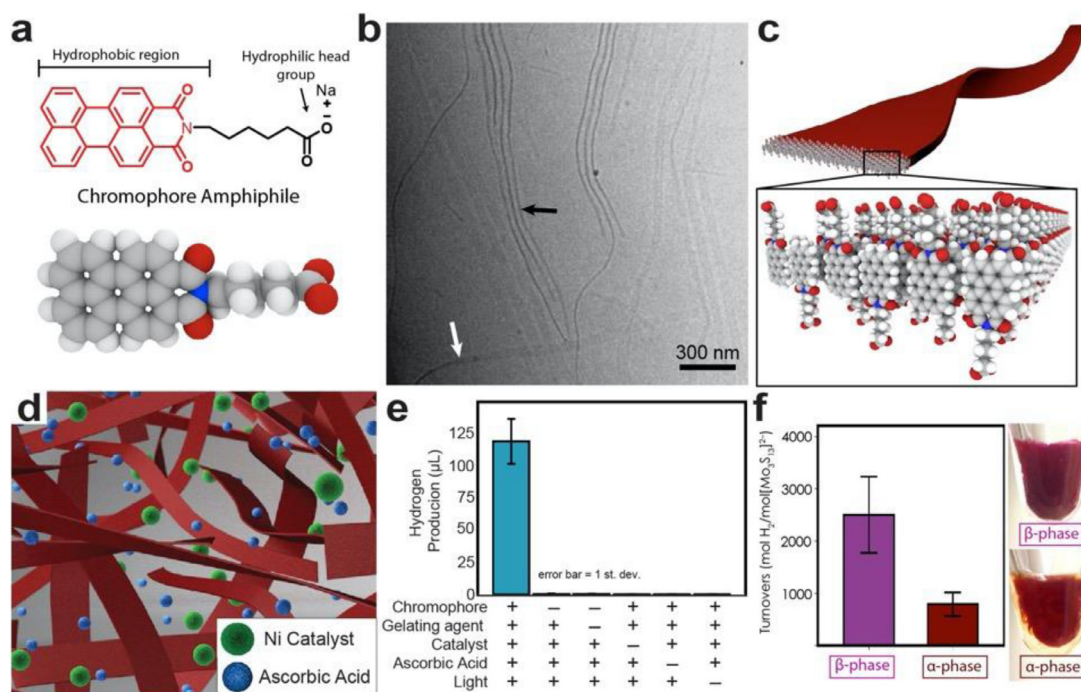
Fig. 4. Crystalline supramolecular polymers for hydrogen production. a) Molecular structure and space-filling model of the chromophore amphiphile monomers. b) Cryogenic transmission electron micrograph of the crystalline supramolecular polymers which are approximately 40 nm in width; differences in contrast are a result of the ribbon orientation either face-on (white arrow) or edge-on (black arrow). c) Schematic representation of the antiparallel packing of monomers to form the interdigitated supramolecular polymer ribbons. d) Schematic representation of the porous photocatalytic hydrogel for photoinduced H₂ production containing crystalline supramolecular polymers (red), with entrapped nickel catalyst (green) and the sacrificial electron donor, ascorbic acid (blue). Water molecules have been omitted from the schematic for clarity. e) Plot of the amount of H₂ produced in the presence of the photocatalytic hydrogel. H₂ is not generated when chromophore, catalyst, sacrificial reagent or light is absent in the photocatalytic system (error bar = 1 s.d., n = 12 trials (or n = 3 for each control experiment). f) Plot of the catalytic turnovers of H₂ produced from the β-phase helices compared to α-phase structures in the presence of a $Mo_3S_{13}^{2-}$ proton reduction catalyst with corresponding photographs of the β-phase and α-phase gels. [55], Copyright 2014. Reproduced with permission from the Nature Publishing Group. [56], Copyright 2017. Reproduced with permission from the American Chemical Society. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

concentration that was 100-fold lower compared to controls (Fig. 3c) [39]. We suggest that the enhanced dynamic nature of supramolecular polymers is likely to lead to the development of highly bioactive biomaterials in the future.

5. Supramolecular polymers for energy applications

The Stupp laboratory in 2014 first reported on crystalline supramolecular polymers with the ability to catalyze light-driven hydrogen production in an aqueous environment [55]. This work was inspired by the photosynthetic organelles found in plants, which are able to colocalize molecules involved in light absorption, charge transport and catalysis for energy production. The monomers used were chromophore amphiphiles consisting of a hydrophobic perylene core conjugated to a hydrophilic carboxylated alkyl tail (Fig. 4a). The π–π interactions among chromophores in these systems drive self-assembly of these molecules in water to form crystalline supramolecular polymers in the presence of electrolytes that screen repulsive electrostatic interactions (Fig. 4b-c) [31,55,56,68,89–91,98,99]. These supramolecular polymers photosensitize reactions by serving as light-harvesting assemblies, and their crystallization improves the size and lifetime of the resulting charge transfer excitons participating in the photocatalysis [31]. The addition of screening polyelectrolytes rather than simply salts leads to the formation of hydrogels in which photocatalysis can be activated by encapsulated catalysts, with supramolecular polymers entrapped by crosslinked covalent polyelectrolytes [98].

Due to the high surface charge, favorable electrostatic interactions with a positively charged nickel-based catalyst can result in catalyst entrapment within a hydrogel that allows free diffusion of

reactants and products (Fig. 4d) [55,90]. The charge-transfer excitons formed upon irradiation with light causes photocatalytic production of hydrogen (H₂) in the presence of a sacrificial electron donor [31,55,90]. Appreciable H₂ production was not observed in control experiments where the supramolecular polymer, catalyst, or sacrificial donor were omitted from the system, indicating the importance of each of these in the photocatalytic function of the hydrogels. (Fig. 4e). Furthermore, gels which were kept in the dark did not produce H₂, indicating that the catalyst requires photoactivation by the π-bonded supramolecular polymers. In follow up work, the photocatalytic hydrogen production was compared between a kinetically trapped α-phase to that of a highly crystalline, thermodynamically favorable β-phase achieved through thermal annealing and salt charge screening effects of chromophore amphiphiles consisting of an alkyl substituted perylene core [56]. This thermodynamically favored product produced a scroll like morphology which could form charge transfer excitons and was superior to the α-phase for the production of H₂ in the presence of a different molybdenum-based proton reducing catalyst (Fig. 4f). This work clearly demonstrated the importance of crystalline packing of monomers within the supramolecular polymer for photocatalysis [56]. More recently, additional modifications to the chromophore amphiphile monomers have been investigated to elucidate the relationship between molecular structure, supramolecular polymerization, and functional application of these catalytic systems [31,55,56,90–92], which have recently been reviewed elsewhere [89]. The opportunity for soft organic materials, which can intimately incorporate the components required for catalysis is an exciting prospect, made possible by these crystalline supramolecular polymers and their ability to efficiently photosensitize catalysts for solar fuel production.
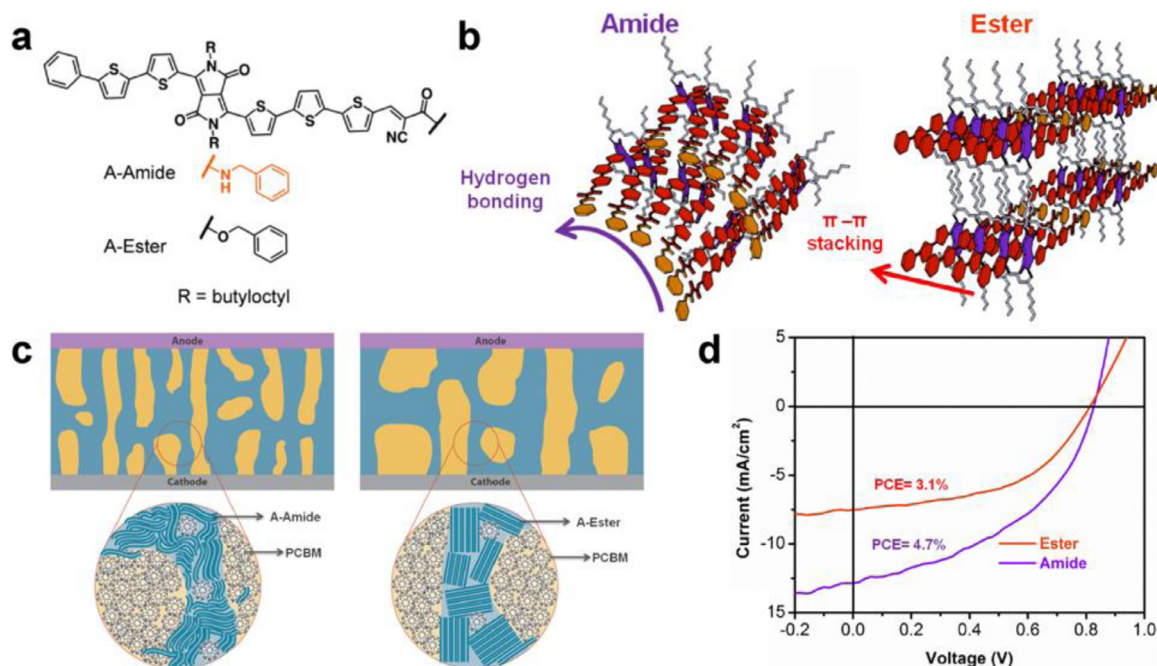
Fig. 5. Control over morphology of supramolecular polymers formed by electron donor monomers affects photovoltaic device performance. (a) Diketopyrrolopyrrole (DPP)-based asymmetric electron donor molecule design with variations in the hydrogen bonding capabilities at one end of the molecule. (b) Molecular graphic representation demonstrating the formation of supramolecular polymers using DPP monomers with amide versus ester bonds. (c) Schematic representation demonstrating how the effective competition of hydrogen bonding over extensive $\pi-\pi$ stacking results in supramolecular polymer morphologies that lead to higher photovoltaic efficiencies. (d) Current-voltage (I-V) sweep curves of bulk heterojunction solar cells containing either the DPP ester or amide supramolecular polymers with [6,6]-phenyl-C_{71}-butyric acid methyl ester as the electron acceptor. [102], Copyright 2015. Reproduced with permission from the American Chemical Society.

6. Supramolecular polymers in photovoltaic devices

The use of supramolecular polymers in organic solar cells has also been investigated in the Stupp laboratory [100–105]. One of these studies at the time of publication held the efficiency record for small molecule organic photovoltaic devices resulting from ordered molecular packing and exceptional hole mobility within the active layer [105]. Understanding the role supramolecular polymers can play in the active layer of these devices led to improved solar cell efficiencies. An example of this work investigated the effects of hydrogen bonding on active layer morphology through comparing two asymmetric derivatives, one containing an amide bond capable of forming hydrogen bonds with one having an ester bond in the same position, which allowed for greater crystallinity and $\pi-\pi$ stacking (Fig. 5a and b) [102]. The amide derivative formed short fiber-like supramolecular aggregates with much smaller domain sizes and less order compared to the long-range crystallinity and $\pi-\pi$ stacking of the ester derivative (Fig. 5c). While maintaining similar optoelectronic properties, controlling the active layer morphology resulted in a 50% increase in power conversion of devices formed with the amide derivative relative to the ester derivative (Fig. 5d) [102]. This increase in performance is attributed to the ability of the hydrogen bonding amide derivative to produce short fiber-like structures which are interconnected over longer distances and allow enhanced charge transport across the film.

Supramolecular assembly can also be used to control the effectiveness of electron donors in organic photovoltaic devices. In other work exploring this effect, electron rich tripodal aromatic monomers were designed to consist of either branched alkyl groups or linear side chains where the alkyl groups inhibited the self-assembly of supramolecular polymers while the latter resulted in bundled one-dimensional nanowires [103]. The formation of the supramolecular polymers and their bundling resulted in a 50% increase in power conversion efficiency relative to the branched alkyl side chains owing to significant gains in the fill factor of the device [103]. From these examples, it is clear that opportunities exist in both the understanding of supramolecular assembly and the combination of supramolecular polymers in energy devices for enhanced function.

7. Concluding remarks

In this trend article, we aimed to demonstrate the unique functionalities of supramolecular polymers and how these can be harnessed to create novel materials. Given their non-covalent bonding among monomers, one of the opportunities with supramolecular polymers is the possibility to create dynamic and reversible superstructures that are not attainable with covalent polymers. In living organisms, we observe complex structures in which the synergy between supramolecular and covalent polymers are combined to create high-value functions. An example is skeletal muscle where supramolecular polymers of actin and myosin are linked to the giant protein covalent polymer known as titin to make-up the highly aligned structure of the sarcomere. We believe there is great promise in the combination of supramolecular and covalent polymers, and termed these systems in an earlier publication as hybrid bonding polymers [37]. In recent publications we also demonstrated the functional value of hybrid bonding polymers aiming at the development of robotic soft materials [34,35]. As this recent work shows the interplay between covalent and non-covalent interactions will provide the opportunity for materials to take on responsive behavior characteristic of living organisms.

From an environmental standpoint, we see a great challenge currently facing the polymer community. Covalent polymers owing to their inherent high kinetic and thermodynamic stability, a trademark of many of their useful applications, is now resulting in a burgeoning challenge as plastic waste in the environment reaches critical levels. To tackle this problem we need to consider

the partial replacement of covalent for non-covalent bonds and design materials as hybrid bonding polymers as has been recently explored [106]. Such systems may provide avenues to circumvent the plastic pollution problems our world faces currently. Furthermore, as explained above we also see the opportunity for supramolecular polymers to contribute to our use of renewable resources for energy production and to human health as well.

In recent decades there has been great progress in our ability to control molecular weight distribution and sequence in covalent polymers. Supramolecular polymers on the other hand are at an earlier stage in structure control. Further progress on the control of shape, size distribution and sequence in supramolecular polymers will certainly enable new functional opportunities for soft materials. One defining difference of supramolecular polymers versus their covalent counterparts is the ability for monomers to dynamically exchange between polymeric structures. Although we know this phenomenon can result in interesting hierarchical assemblies, the actual mechanisms of this process and its full functional potential is still in an early phase. Further understanding of this process, which clearly occurs in biological systems, will point us in new directions for the next 100-years of polymer science.

Credit statement

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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