# DNA-Functionalized Supramolecular Polymers: Dynamic Multicomponent Assemblies with Emergent Properties

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ABSTRACT: Recent years have witnessed an increasing interest in hybrid molecular systems in which the programmability of DNA hybridization is used to introduce enhanced molecular control in synthetic systems. The first examples of DNA-functionalized supramolecular polymers have been reported only recently, but have already revealed structural and functional properties that are not easily obtained in either synthetic supramolecular polymers or DNA-only based systems. In this Topical Review, we provide an overview of the various forms of additional control offered by DNA hybridization for different types of supramolecular polymers and discuss how orthogonal supramolecular interactions in these hybrid systems can give rise to emergent structural and functional properties.
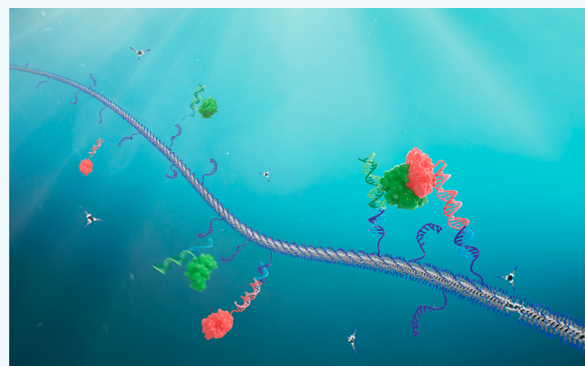
INTRODUCTION

At the cellular level, life is predominantly built from aqueous, dynamic molecular assemblies.[1,2] The transient nature of these complex multicomponent systems introduces adaptability and allows for rapid response to biological triggers with great efficiency.[3−5] In the quest to understand and emulate these natural systems, supramolecular chemistry has become a topical research field in which supramolecular polymers play a prominent role.[6] Although the first synthetic supramolecular polymers were designed to assemble in organic solvents, many water-soluble variants exist today, providing an interesting platform for the development of molecular systems and materials with life-like properties.[7] Extensive studies using a wide variety of biophysical approaches have provided detailed insight into the assembly mechanisms and exchange dynamics of several of these water-soluble supramolecular polymers.[8−12] These studies have revealed a subtle interplay between various noncovalent interactions that together govern their structural and dynamic properties, but also showed that tuning these properties and introducing functionality in these dynamic systems can be challenging. The latter is important as future applications would require these systems to specifically interact with other components, materials, cells, or tissues. However, synthesis of these building blocks is not straightforward.

DNA has rapidly emerged as a highly versatile molecular building block for the construction of precise nanometer structures and sophisticated molecular machines and networks. In contrast to synthetic supramolecular interactions, the programmability of DNA hybridization enables the modular assembly of structures and reaction cascades with great precision and structural control.[13] Recent years have witnessed an increasing interest in hybrid molecular systems.[14,15] For example, DNA functionalization of covalent polymers provides an additional level of control on the structure and macroscopic properties of materials, allowing the construction of stimuli-responsive materials such as hydrogels and other nanomaterials, DNA-surfactants that can be applied as responsive drug delivery systems, and materials for optoelectronic devices.[16−22] Only recently have the first examples of DNA-functionalized supramolecular polymers been reported. In this Topical Review, we provide an overview of the various forms of additional control offered by DNA hybridization for different supramolecular polymers and discuss how orthogonal supramolecular interactions in these hybrid systems can give rise to emergent structural and functional properties.

AROMATIC OLIGOMERS

Some of the first examples of DNA-functionalized supramolecular polymers were reported by the group of Häner. In their pioneering work, DNA-grafted supramolecular polymers consisting of oligomers of aromatic compounds and oligonucleotides were constructed and used to study how DNA can be used to gain control over the structural characteristics of supramolecular polymers.[23] One class of hybrid supramolecular building blocks consists of phospho-diester-linked pyrene oligomers modified with oligonucleotides via solid-phase phosphoramidite chemistry (Figure 1a). The supramolecular assembly of these monomers is initiated by the formation of stair-like arrangements of the pyrenes within the
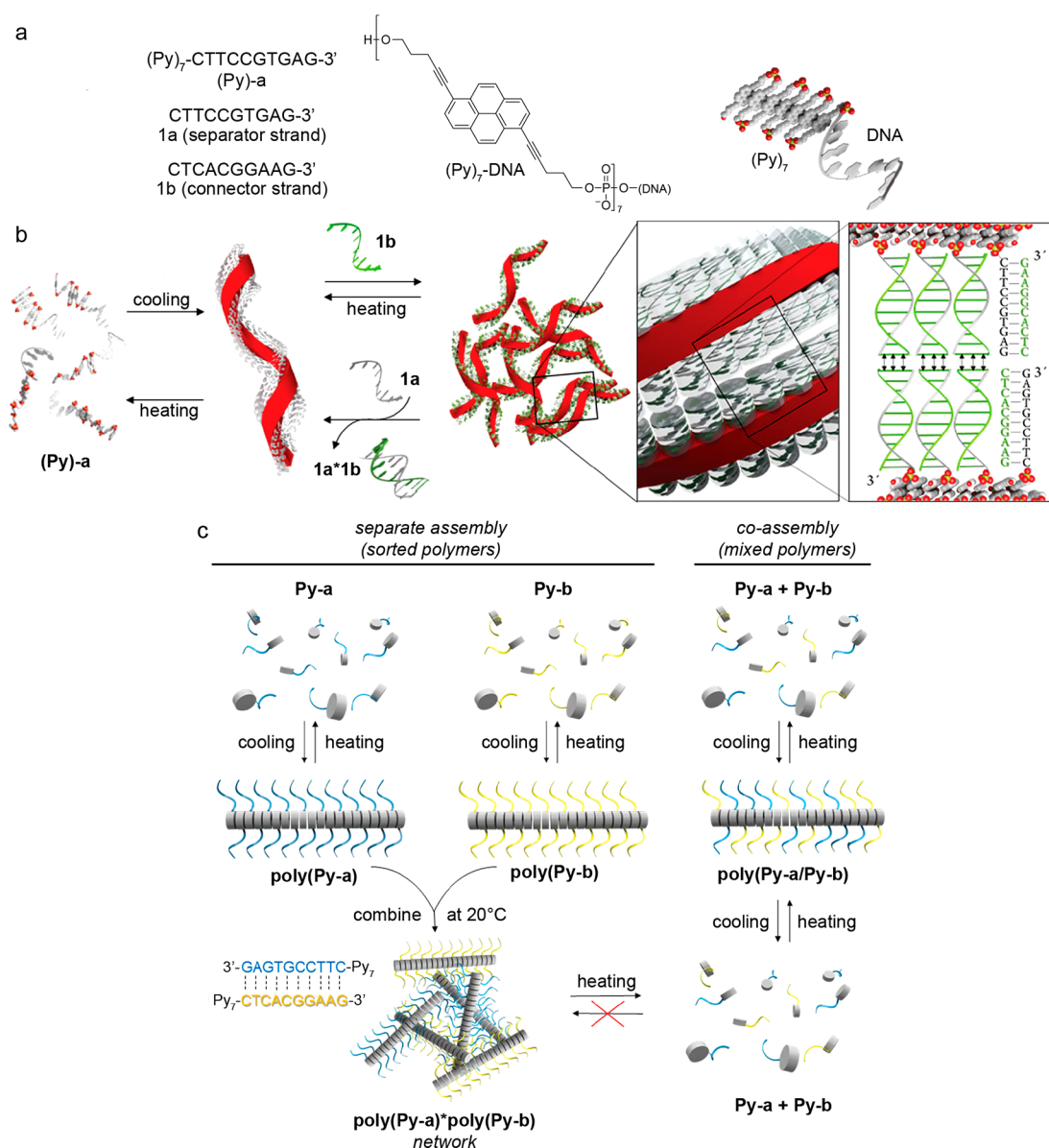
Figure 1. Using DNA to reversibly control the structural characteristics of supramolecular polymer assemblies. (a) Structure and schematic representation of a DNA-modified heptapyrene monomer with the sequences of the grafted, separator, and connector oligonucleotides. (b) DNA-modified heptapyrene monomers are assembled into DNA-grafted ribbons in water. Hybridization of the oligonucleotide on the heptapyrene with a complementary handle (1b) results in the formation of fibrous networks driven by the blunt-end stacking of the grafted DNA helices. This process is reversible via disruption of the hybridized oligonucleotides, either by thermal denaturation or by addition of an excess of a separator strand (1a). Adapted and reproduced with permission from ref 25. (c) Schematic representation of the assembly pathways of pyrene monomers functionalized with complementary oligonucleotides (Py-a and Py-b). The monomers separately assemble into supramolecular polymers which form networks upon mixing due to hybridization of the complementary grafted oligonucleotides. Thermal disruption of these networks or mixing of the different monomers leads to the formation of mixed polymers which do not form networks. Adapted and reproduced with permission from ref 26.

monomers and subsequent assembly of multiple monomers. The balance between the lengths of the oligopyrenes and oligonucleotides directed the morphology of the supramolecular assemblies. Oligopyrenes containing 7 pyrenes and 10 base oligonucleotides reversibly formed fibers with lengths up to several hundreds of nanometers, while no fibrous structures could be observed for oligopyrenes containing 4 or 1 pyrene unit(s).[23] Additionally, hepta-oligopyrene functionalized with a single nucleotide assembled into 2D nanosheets, whereas micrometers to tens-of-nanometers-long ribbons were formed when using DNA handles containing 2 or more nucleotides, respectively.[24] Addition of an oligonucleotide

complementary to that on the hepta-oligopyrene units resulted in the formation of micrometer-size fibrous networks due to cross-links formed by blunt-end stacking of the grafted double-stranded DNA (Figure 1b).[9] The formation of these networks was reversible by thermal denaturation of the double-stranded DNA or by the addition of a scavenger oligonucleotide which separates the strand complementary to the grafted handle via a strand displacement reaction. The formation of cross-linked networks could also be achieved by mixing supramolecular DNA-oligoperylene polymers grafted with complementary strands (Figure 1c).[26] Increasing the temperature first disassembled the resulting networks followed by full disruption
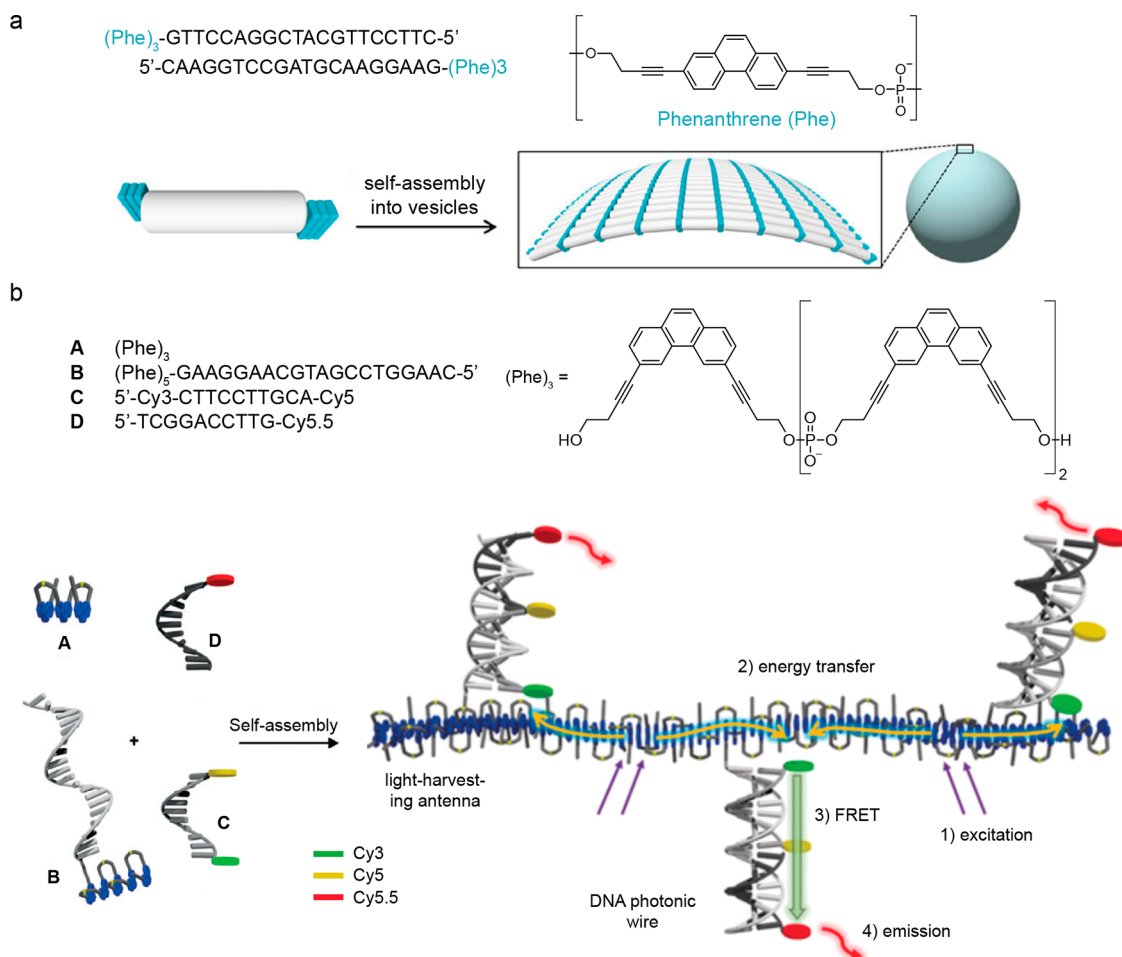
Figure 2. Combining the intrinsic light harvesting properties of phenanthrene based polymers to transfer energy toward a DNA photonic wire. (a) Vesicles are formed by the assembly of two triphenanthrenes modified with complementary oligonucleotides. Adapted and reproduced with permission from ref 27. (b) Supramolecular polymers are assembled by mixing triphenanthrene (A) with DNA-modified pentaphenanthrene (B) monomers. By addition of labeled oligonucleotides complementary to the phenanthrene grafted oligonucleotide (C and D), a photonic wire is constructed. After excitation of the phenanthrenes, the harvested energy is transferred along the supramolecular polymers toward the photonic wires where it is transferred via FRET between the cyan dyes to the final Cy5.5 acceptor. Adapted and reproduced with permission from ref 28. Copyright 2018, Wiley-VCH.

of the supramolecular polymeric assemblies at higher temperatures. Interestingly, subsequent cooling of the mixture did not result in the reformation of networks, but instead yielded one-dimensional polymer stacks containing mixtures of the grafted strands. It was hypothesized that in these mixed polymers, electrostatic repulsion between noncomplementary oligonucleotides prevented hybridization of complementary strands between fibers, and that the initial network formed by mixing preformed supramolecular polymers with complementary strands represented a metastable state. These findings illustrate the importance of pathway complexity on the structural and functional properties of supramolecular polymers containing orthogonal assembly motifs.

A second example of hybrid supramolecular-building blocks introduced by the Häner group consists of DNA-modified tri- and pentaphenanthrenes, which were also synthesized using phosphoramidite chemistry. When two triphenanthrenes modified with complementary oligonucleotides of 20 bases are mixed, the supramolecular interaction is dominated by DNA hybridization resulting in the formation of 20 nucleotide dsDNA containing phenanthrene overhangs at both ends. Hydrophobic interactions between the phenanthrene "sticky ends" promoted the formation of sheets and 50−200 nm vesicles in the presence of spermine, which counteracts the electrostatic repulsion between the dsDNA units (Figure 2a).[27] The same building blocks could also be used to construct micrometers-long polymers grafted with ss-DNA-handles by mixing unmodified triphenanthrene monomers with pentaphenanthrene monomers modified with only one of the oligonucleotides (Figure 2b).[28] In these systems supramolecular polymerization is driven by hydrophobic interactions between the phenanthrene groups, while the oligonucleotides serve as handles grafted on the supramolecular polymer to introduce additional functionalities. The light-harvesting properties of the oligophenanthrenes were used to construct photonic wires in which the energy harvested by light absorption in the oligophenanthrenes was channeled via a cascade of (Förster) energy transfer steps through precisely spaced cyanine dyes on complementary oligonucleotides to finally excite a NIR Cy5.5 acceptor dye.

SQUARAMIDE BOLA-AMPHIPHILES

Several other examples have been reported where DNA hybridization is used to recruit DNA-modified molecular cargo
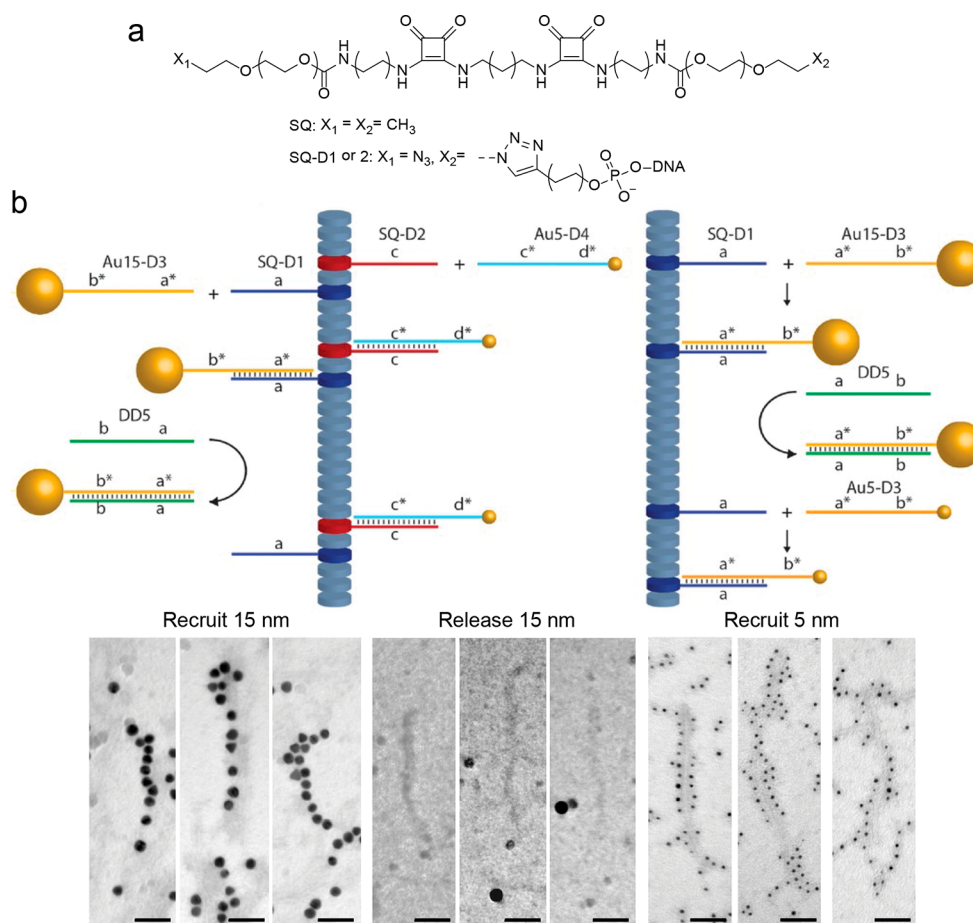
Figure 3. Selective and reversible recruitment of cargo on supramolecular polymers mediated by DNA hybridization. (a) Structures of an inert and a DNA-modified squaramide bola-amphiphile. (b) Supramolecular copolymers of squaramide derivatives were assembled containing two monomers grafted with DNA handles with different sequences (a and c). This enabled the selective recruitment of two gold particles of 5 and 15 nm functionalized with DNA handles containing a sequence complementary to one of the DNA-grafted squaramides (a* and c*). By addition of an oligonucleotide (b,a) fully complementary to the handle on one of the gold nanoparticles, the DNA handle on the polymer is displaced, which selectively releases the particle. Using these techniques, the system allows the sequential recruitment and release of the 15 nm particles after which the 5 nm particles can be recruited. Scale bars represent 50 nm. Adapted and reproduced with permission from ref 30. Copyright 2017, Wiley-VCH.

on supramolecular polymers. Both the Häner group and the group of Kieltyka demonstrated reversible recruitment of DNA-functionalized gold nanoparticles along supramolecular polymers.[29,30] The latter group used squaramide based bola-amphiphiles to form hundreds-of-nanometers-long supramolecular assemblies, driven by hydrogen bonding and hydrophobic interactions. Squaramide monomers were decorated with 16 nucleotide DNA-handles via copper mediated cyclo-addition reactions and mixed with inert monomers to obtain DNA-grafted squaramide polymers (Figure 3a). By using unique handle sequences for particles with a diameter of 5 or 15 nm in combination with two squaramide monomers decorated with complementary handles, the system enabled the specific recruitment of one or both gold particles (Figure 3b). The DNA-based tethering of the particles also allowed subsequent release of the particles by using toehold-mediated strand displacement. By sequential addition of the DNA-modified particles and displacer strands, sequential loading and release of gold nanoparticles was shown, demonstrating a high level of control over the recruitment and release of components on the polymer scaffold.

PEPTIDE AMPHIPHILES

A particularly impressive demonstration of the ability to reversibly and rationally control the formation of super-structured networks was recently reported by Stupp and co-workers through introducing DNA handles on peptide amphiphile (PA) based supramolecular polymers. PA monomers consist of an aliphatic chain and an amino acid sequence containing a β-sheet forming region and a hydrophilic region. To obtain DNA-modified PA derivatives, amine-functionalized oligonucleotides with lengths from 10 to 45 nucleotides were functionalized with dibenzocyclooctyne-sulfo-N-hydroxylsucci-nimidyl (DIBAC-NHS) and subsequently conjugated to an azide-modified PA using strain promoted alkyne azide click chemistry (Figure 4a).[31] Mixing of DNA-modified and inert PAs resulted in the formation of 10−15-nm-wide, one-dimensional nanofibers containing a stoichiometric distribution of DNA handles driven by hydrophobic interactions and β-sheet formation. Pure DNA-modified PA's did not form fibers but assembled into spherical micelles, probably due to steric and electrostatic repulsion between the DNA handles.

Mixing fibers decorated with complementary oligonucleotides resulted in the formation of hydrogels, which could be
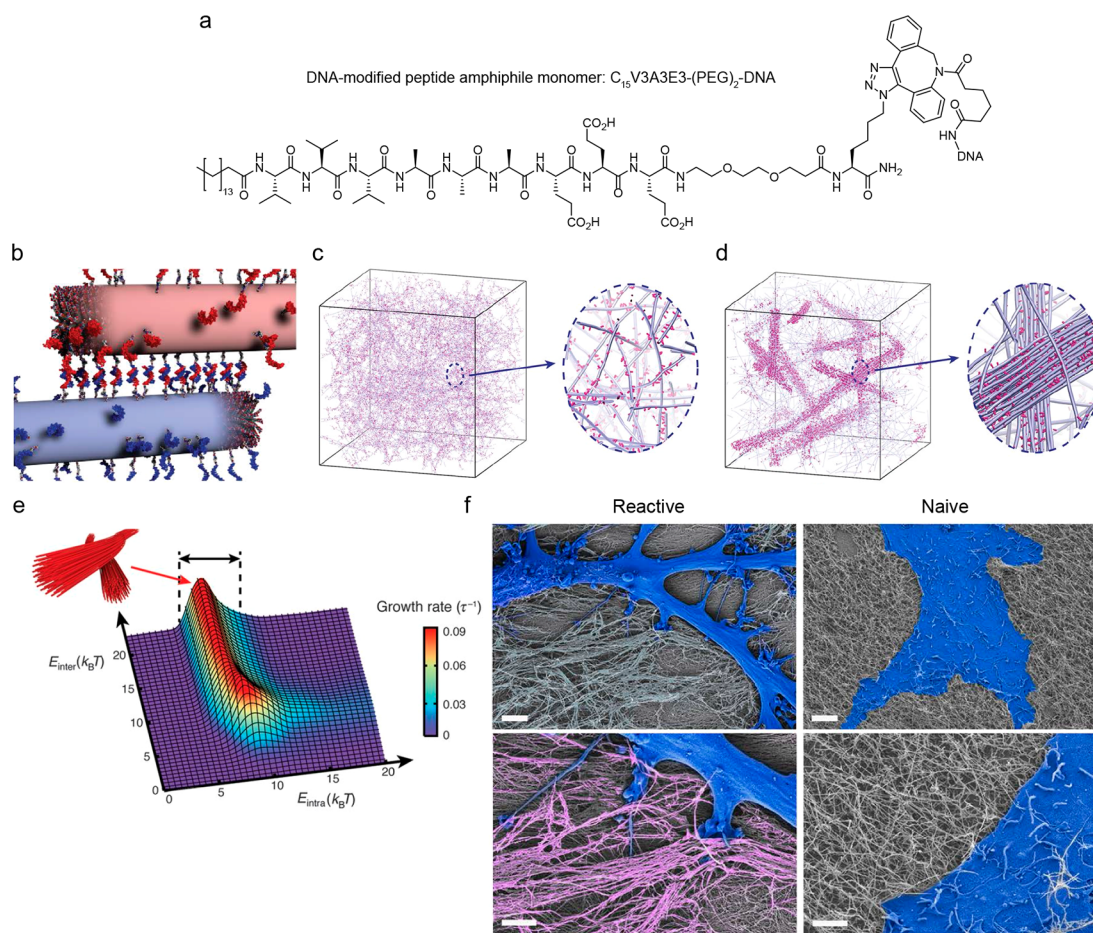
Figure 4. Reversible formation of superstructures in peptide amphiphile−DNA networks. (a) Structure of a peptide amphiphile (PA) monomer modified with oligonucleotides via DIBAC conjugation. (b) PA copolymers of inert and DNA-modified monomers cross-link due to hybridization of complementary grafted oligonucleotides which subsequently cluster within the fibers. (c) Simulations show that homogeneous hydrogels are obtained when molecular exchange of DNA monomers between PA fibers is prohibited. The magnified view shows individual fibers (blue) with a stochastic distribution of DNA monomers (pink) along the fibers. (d) When molecular exchange is allowed, the simulations result in the formation of bundled fibers. The magnified view shows a bundle of fibers (blue) enriched with DNA (pink) in a matrix of individual fibers depleted of DNA monomers. (e) Simulations showing that the bundle growth rate is a function of the molecular attraction between monomers and the interfiber hybridization of the grafted oligonucleotides (respectively, the intra- and interfiber energies (E_{intra}, E_{inter})). Bundles form within the energy range 5 $k_B T < E_{intra}$. (f) SEM micrographs of astrocytes cultured on cross-linked, bundled (left), and individual (right) PA-DNA fibers. The cells display a reactive phenotype on the bundled fibers while a naive phenotype is observed on the individual fibers. Cells are falsely colored in blue and bundled PA-DNA fibers in pink. The magnified view (lower images) shows the cell−substrate interaction. Scale bars represent 5 μm (upper images) and 2 μm (lower images). Adapted and reproduced with permission from ref 31. Copyright 2018, American Association for the Advancement of Science.

reversed by breaking the DNA-mediated interaction between fibers using toehold-mediated strand displacement (Figure 4b). Structural analysis of the gels using scanning electron microscopy (SEM) showed a superstructure consisting of large, micrometer-sized bundles of fibers segregated within a network of individual nanoscale fibers. Coarse-grained simulations of this system suggested that the formation of these superstructures relies on the formation of clusters of cross-linked DNA-modified monomers within the fibers. The cross-linked fibers then intertwine to form bundles which subsequently intertwine with each other to form the observed superstructures. Confocal microscopy revealed that the formation of the cross-linked fibers was complete in 10 min and was accompanied by clustering of the DNA-modified PA within the fiber. It was shown experimentally and by simulations that it is crucial that the interactions between the PA monomers are sufficiently strong to form stable fibers but not too strong to prevent dynamic redistribution of the DNA-grafted monomers to form the bundled structures (Figure

4c,d). Additionally, the hybridization interactions need to be strong enough to maintain the cross-links between the fibers. Taken together, these simulations showed that the bundles can form when the balance between the intra- and interfiber interactions lies in a remarkably narrow distribution (Figure 4e). The density of DNA-PA also proved important for the formation of the cross-linked superstructures. Very low densities did not support the formation of sufficient cross-links, but at too high DNA-PA densities the system formed a three-dimensional gel before the formation of the cross-linked fibers could occur. The formation of cross-linked fibers in the gel increased the stiffness of the gels and could be tuned in a predictable manner by changes in the length and GC content of a cross-linker DNA strand, salt concentration, and the length of the aliphatic chain and type of amino acids in the PA monomers. Additionally, the DNA cross-links and the subsequent formation of the highly bundled fibrous structures could be disrupted in a reversible fashion via thermal disruption or toehold-mediated strand displacement. This
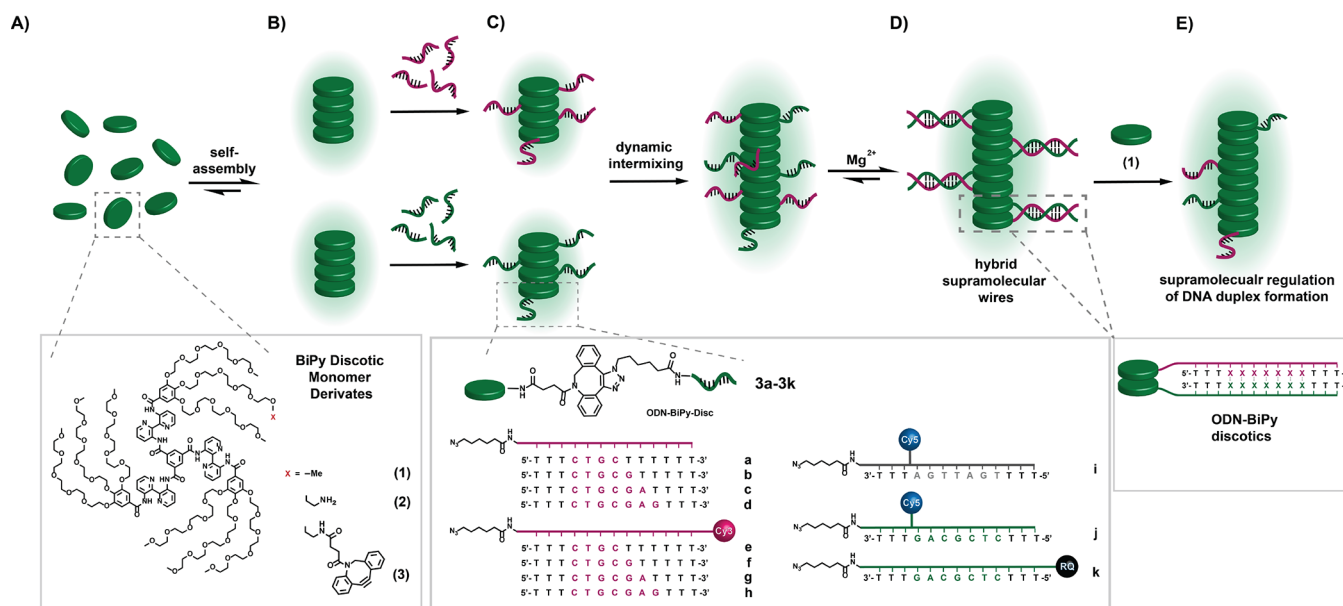
Figure 5. (a) Inert and DBCO-modified bis-pyridine decorated BTA derivatives are mixed and (b) subsequently form coassemblies. (c) Oligonucleotides with various sequences are then added to react with the DBCO-modified monomers. (d) After mixing BTA assemblies grafted with complementary oligonucleotides, the addition of magnesium results in hybridization of the complementary DNA-handles enabled by the dynamic rearrangement of the BiPy-BTA monomers. (e) Subsequent addition of inert monomers leads to dilution of the DNA-grafted monomers over the assemblies and disruption of the hybridized handles and redistribution of the monomers. Reproduced with permission from ref 33. Copyright 2018, Wiley-VCH.

ability to switch the structural properties of the fibrous networks was subsequently used to study the response of neural cells (astrocytes) to changes in their environment. When the cells were cultured in the PA-DNA hydrogels containing the higher order bundles, a reactive phenotype was observed while naive cells were observed in hydrogels existing from individual fibrous networks (Figure 4f). Interestingly, the phenotype of the cells could be switched from reactive to naive or visa versa by addition of an invader or anti-invader strand to, respectively, disrupt or reform the DNA cross-links in the network.

BENZENE-1,3,5-TRICARBOXAMIDE (BTA) POLYMERS

In the work described so far, DNA hybridization either served to recruit DNA-cargo on a supramolecular polymer, or was used to control the formation of networks and other superstructures. However, DNA hybridization and supramolecular polymerization can also enhance each other when two complementary DNA strands are attached to the same supramolecular polymer in an antiparallel orientation. This phenomenon was studied by Brunsveld and co-workers using C3 symmetric amphiphiles consisting of a bis-pyridine benzene-1,3,5-tricarboxamide (BiPy-BTA) core decorated with water-soluble ethylene glycol (EG) tails (Figure 5a). Driven by hydrophobic interactions and intermolecular hydrogen bonds between the monomer cores, these BiPy-BTA-EG monomers assemble into stable fluorescent polymers.[32] DNA-functionalized BiPy-DNA monomers were obtained by conjugation of azide-modified oligonucleotides to bis-pyridine decorated BTA derivatives (BiPy-BTA) modified with a single dibenzocyclooctyne (DBCO) via strain-promoted cycloaddition.[33] To systematically study the effect of supramolecular templating on DNA hybridization, a 13 nucleotide template strand was conjugated via its 3′ end,

whereas a series of 13 base DNA sequences containing between 4 and 7 complementary bases was conjugated to the BiPy-BTA via their 5′-end (Figure 5c). Supramolecular-templated hybridization was monitored using FRET between Cy3- and C5-dyes conjugated to each strand and compared to the nontemplated interaction. Supramolecular templating enhanced DNA hybridization by at least 6 kcal/mol, equivalent to the effect of 4 additional base pair interactions. The increased interaction strength can be understood by the high local concentration of the DNA-strands, which was estimated to be between 2 and 20 mM. Using the dynamic nature of the assemblies, the hybridization of the grafted oligonucleotides with 4 complementary bases could subsequently be reversed via addition of inert monomers which insert between the DNA-modified monomers in the assemblies, thus decreasing the local concentration of DNA strands on the supramolecular polymer (Figure 5e). Time-dependent studies showed that the rearrangement process took about 2 h and was determined by the kinetics of monomer exchange.

The work by Brunsveld and co-workers shows the potential of using supramolecular polymers as a dynamic platform to enhance molecular interactions by increasing their effective local concentration, a strategy that is also frequently used in biology to control signal transduction and increase the efficiency of metabolic reaction cascades. Our group recently showed that DNA-mediated recruitment of proteins on another type of supramolecular BTA polymer can efficiently promote protein–protein interactions. The BTA system used in these studies consisted of a BTA core containing three amphiphilic dodecyl-EG4 side-arms that shield the hydrogen bonds in the core from water, while facilitating water solubility of the assembled polymer. BTA-DNA monomers were obtained by conjugation of a 10 base alkyne-functionalized oligonucleotide to an azide-functionalized BTA via a copper-mediated alkyne–azide cycloaddition reaction (Figure 6a).[34] Copolymer
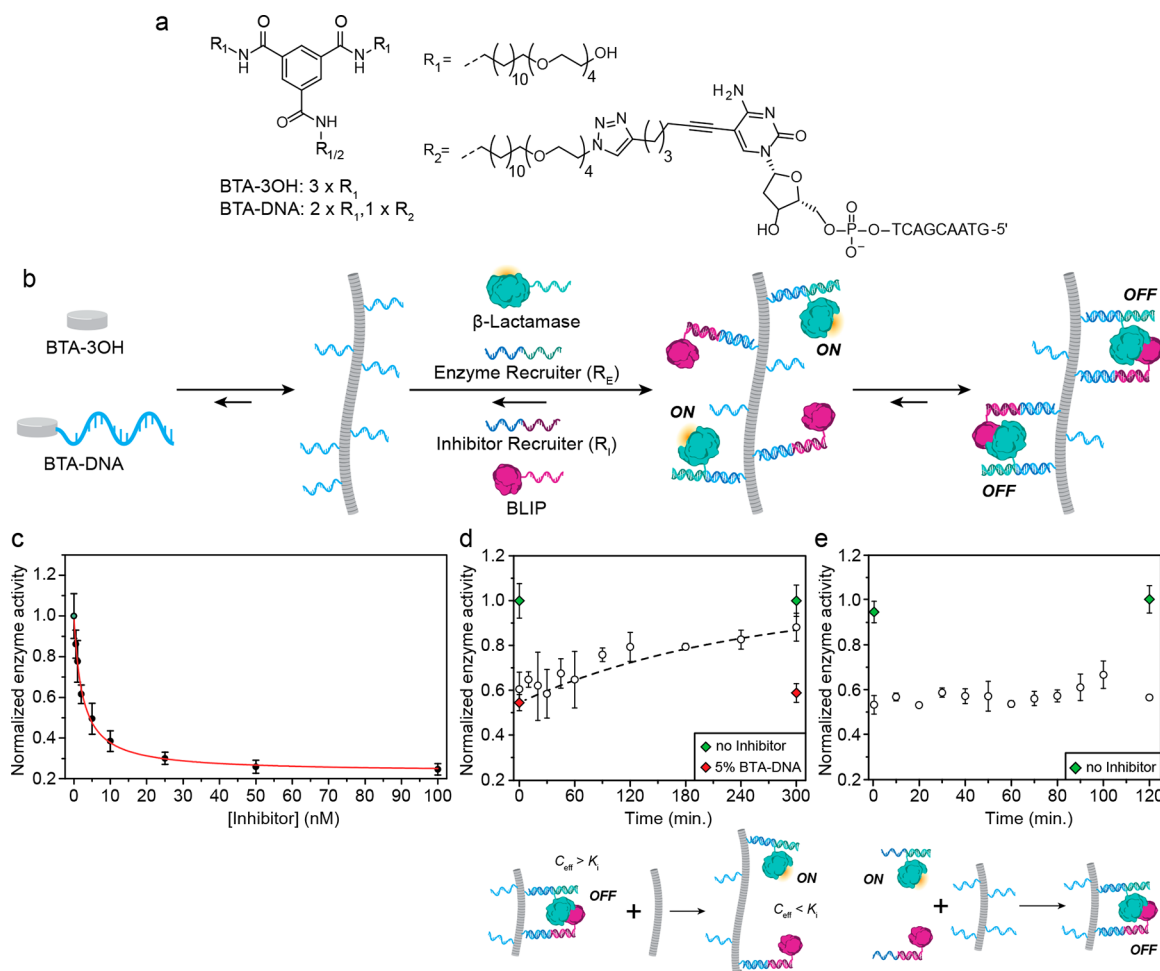
Figure 6. Controlling protein activity by dynamic recruitment on a supramolecular polymer platform. (a) Chemical structures of an inert BTA monomer and a DNA-modified monomer obtained via copper mediated cyclo-addition. (b) Supramolecular polymers are obtained by assembly of inert and DNA-modified BTAs. A DNA-modified enzyme and inhibitor protein can be selectively recruited driven by the hybridization of specific recruiter strands with the oligonucleotides on the BTA and the proteins. The high local protein concentration results in protein complex formation and subsequently a decrease in enzyme activity. (c) Normalized enzyme activity as a function of inhibitor concentration (black dots). The fitting of the enzymatic activities was derived from a Michaelis–Menten model for competitive inhibition, yielding an apparent inhibition constant ($K_{i,app}$) of 2.3 ± 0.2 nM (red line). (d) Upon the addition of inert BTA monomers, dynamic exchange of BTAs results in dilution of the recruited proteins and subsequently an increase of the total protein activity. (e) Upon addition of the DNA-grafted BTA polymers to the proteins and recruiter strands, the equilibrium of protein inhibition is reached within minutes. Adapted and reproduced with permission from ref 34. Copyright 2018, Springer Nature.

assembly of BTA and BTA-DNA resulted in the formation of μm-long 1D supramolecular BTA polymers. These polymers were found to be remarkably robust, even with a high percentage of DNA-functionalized BTA. To study specific recruitment of proteins to the BTA polymers, TEM1-β-lactamase was used as a reporter enzyme along with its inhibitor protein BLIP. Each protein was functionalized with a specific 21-base oligonucleotide, which allowed recruitment on the BTA-polymer in the presence of specific recruiter strands that are complementary to the DNA-strands on the BTA and on one of the proteins (Figure 6b).

Recruitment of both proteins on the BTA-scaffold resulted in inhibition of enzyme activity at low nanomolar concentrations of the inhibitor protein, representing a 1000-fold increase in apparent inhibition constant compared to the K_d of 1.5 μM obtained in solution (Figure 6c). The increased apparent affinity could be quantitatively understood by the increased local concentration of the proteins on the BTA polymer scaffold, which could be tuned by changing the

density of DNA handles on the polymer. Indeed, enzyme activity could be restored by the addition of excess inert BTA monomers to dilute the BTA-DNA density from 5% to 0.25%. The restoration of enzyme activity by BTA-dilution took several hours, which is in accordance with the kinetics known for dynamic exchange of the BTA monomers (Figure 6d). Remarkably, recruitment of the DNA-modified proteins on the BTA template and subsequent formation of the enzyme–inhibitor complex was found to be fast, reaching equilibrium within minutes (Figure 6e). Since this process is much faster than the kinetics of BTA-monomer exchange, protein complex formation on the BTA-scaffold was hypothesized to involve rapid association and dissociation between DNA-duplexes along the polymer. The 10-nucleotide interaction between the DNA strand on the BTA polymer and the recruiter strand thus allows rapid exchange of DNA-conjugated proteins ($k_{diss} \sim 1$ s^{-1}),[35] while also providing sufficient thermodynamic driving force to recruit proteins and increase their effective local concentration.
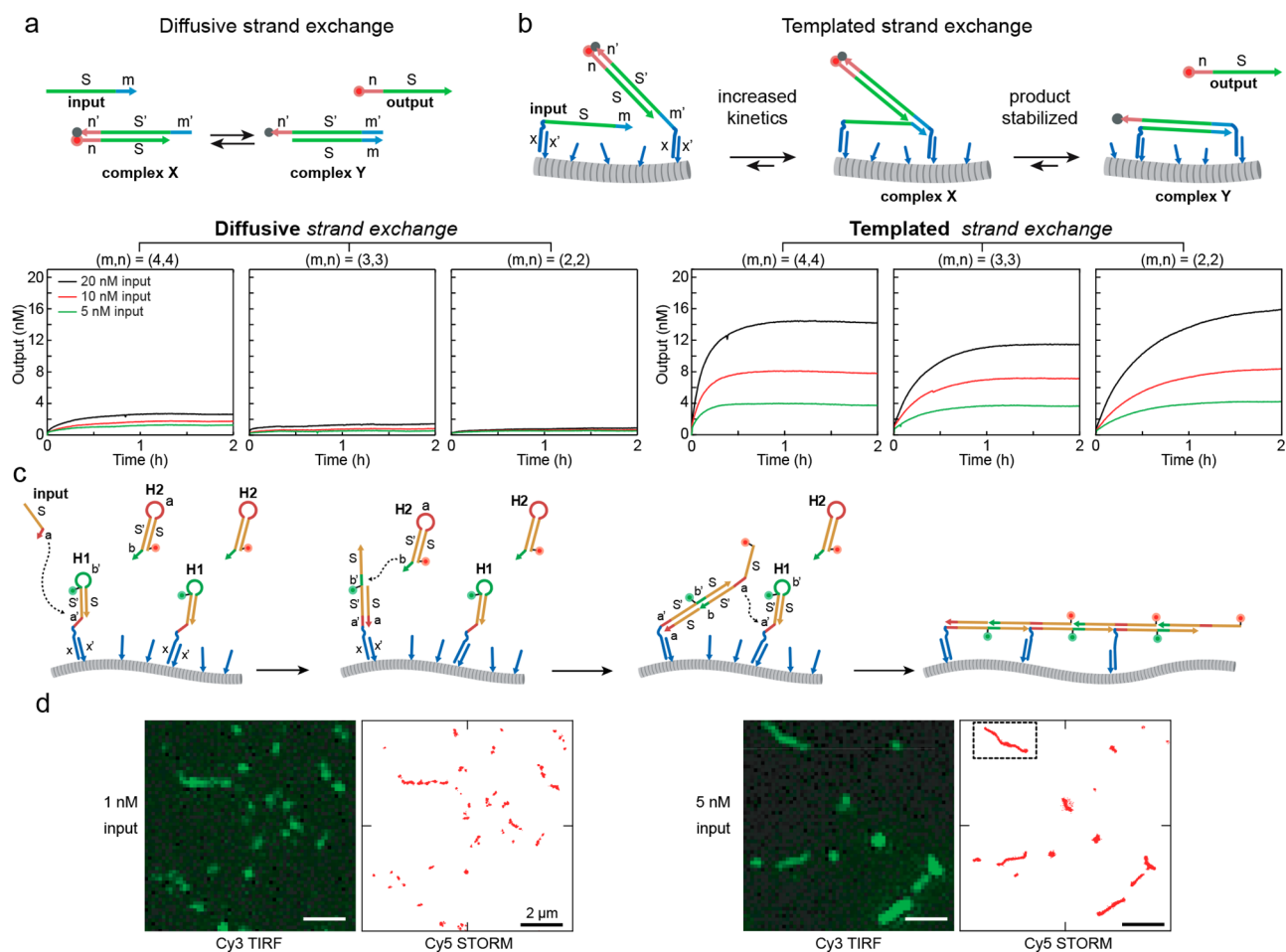
Figure 7. Acceleration of DNA-based computing on supramolecular polymers. (a) Schematic representation of a strand exchange reaction using freely diffusing oligonucleotide reactants with the kinetic characterization of a reaction with toeholds of various lengths. (b) Schematic representation of a strand exchange reaction templated by a BTA polymer. The reactants are recruited to the polymer via the hybridization of a sequence complementary to the oligonucleotide on the BTA. This results in a high local concentrations which consequently increases the association kinetics of toehold binding. Additionally, due to the multivalent anchoring of the product to the supramolecular polymer, the product is stabilized resulting in increased operation yields. (c) Schematic representation of a hybridization chain reaction (HCR) templated by the BTA polymers. Starting upon the addition of an input, the sequential opening of two labeled metastable hairpin strands results in the formation of a polymeric DNA assembly. (d) TIRF images of immobilized BTA polymers containing Cy3 labeled monomers with corresponding STORM images of the HCR product containing Cy5 labeled oligonucleotides after the HCR was initiated by addition of, respectively, 1 and 5 nM input strand. The scale bars represent 2 μm. Adapted and reproduced with permission from ref 36.

The remarkable efficiency of DNA-functionalized BTA polymer to template the formation of protein−protein interactions, suggested that they might also provide attractive scaffolds to enhance the speed of DNA-based molecular circuits.[36] These circuits typically consist of a series of sequential toehold-mediated strand exchange reactions, using low nanomolar concentrations of individual reactants to avoid background and nonintended side reactions. As the reaction rates of the DNA networks depend on the concentration of the reactants, the operations are slow, taking several hours or even days, hampering their translation into practical applications. The speed of DNA-based molecular computing has been increased by confining the reactants on the surfaces of DNA-functionalized nanoparticles or DNA-origami scaffolds. However, immobilizing oligonucleotide reactants on a DNA origami scaffold requires careful positioning of the circuit components to facilitate efficient interaction between reactants. To explore whether DNA-functionalized supramolecular polymers could provide a more dynamic and operationally more simple alternative platform, we first tested whether

confinement of DNA reactants on the BTA-polymer could enhance the kinetics of toehold-mediated strand displacement and strand exchange reactions, two fundamental reactions in DNA computing. DNA reactants were extended with a sequence complementary to the 10 bases of the BTA-DNA conjugate (Figure 7a,b). Recruitment of these components on the BTA-DNA polymers increased the speed of single displacement and exchange reactions up to a 100-fold. The templated strand exchange reaction was also favored thermodynamically by multivalent interactions with the polymer template. The general applicability of the BTA-DNA scaffold to increase the speed of DNA-based computing was subsequently demonstrated for three well-known and practically important DNA-computing operations: multi-input AND gates, catalytic hairpin assembly (CHA), and hybridization chain reactions (HCR). The product of the latter amplification reaction is of a polymer of alternating, partially overlapping DNA strands (Figure 7c). Dual color imaging of Cy3-labeled BTAs and Cy5-labeled reaction product using a combination of total internal reflection (TIRF) and stochastic

optical reconstruction microscopy (STORM) indeed showed a clear overlap between the DNA polymer product and the BTA-polymer backbone, consistent with the BTA-polymer acting as template of the HCR reaction (Figure 7d).

SUMMARY AND CONCLUSIONS

DNA hybridization is arguably the most studied and best understood natural supramolecular interaction, but hybrid systems that combine synthetic supramolecular polymers with DNA-based assembly have only recently been reported. Nonetheless, these studies have already revealed interesting emerging properties that are not easily obtained in either synthetic supramolecular polymers or DNA-only based systems. A relatively straightforward application of grafting DNA-strands on supramolecular polymers is to allow the functionalization of supramolecular polymers with DNA-modified molecular cargo such as small molecules, proteins, and nanoparticles. The reversible nature of DNA hybridization and the ability to precisely tune both its affinity and dynamics provides much higher control than using other forms of noncovalent or covalent interactions. DNA-based interactions can also be easily controlled externally, both generally using salt concentration or temperature, and specifically using DNA-displacement reactions. Interactions between complementary strands on different polymers can be used to create networks and other higher order superstructures. The formation of these structures is not only determined by the relative thermodynamic strengths of orthogonal supramolecular interactions, but also by their dynamics, giving rise to kinetically trapped states and pathway complexity. DNA hybridization and supramolecular polymerization can also reinforce each other, with supramolecular polymerization stabilizing the interactions between complementary strands within the same polymer, and DNA-interactions steering internal ordering in supramolecular polymers. Vice versa, by dynamically confining DNA reactants on their surface, supramolecular polymers can act as adaptive templates to increase the kinetics and efficiency of DNA-based molecular computing. The reversibility and ability to tune the dynamics of both supramolecular polymerization and DNA hybridization provides access to modular and uniquely tunable systems that can already emulate some of the adaptivity and specificity of their natural counterparts. While these studies have mainly focused on understanding fundamental properties, they also provide a first glimpse of possible applications, such as the development of responsive materials in tissue engineering, controlled drug delivery, molecular sensors and the construction of synthetic signaling cascades.

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Notes
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