

## Bioinspired Construction of Light-Harvesting Systems via Protein Self-Assembly Strategies

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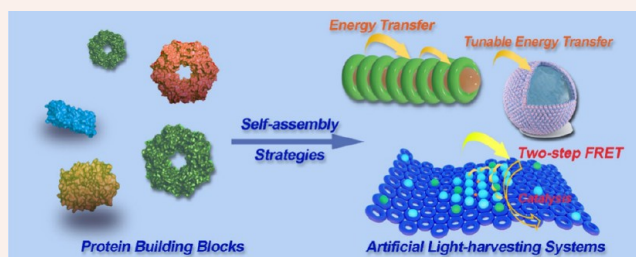
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**CONSPECTUS:** Photosynthesis is a vital process that sustains life on Earth, and its energy transfer mechanism can be elucidated by fluorescence resonance energy transfer (FRET), a process in which fluorescence donors and acceptors provide energy transfer through long-range dipole–dipole interactions. Constructing artificial light-harvesting systems (ALHSs) assists in the exploration and mimicry of natural light-harvesting systems (LHSs) and is expected to provide a potential solution to the energy crisis. Structures fabricated by the self-assembly of proteins provide ideal templates and skeletons for the construction of ALHSs, as they enable the orderly arrangement of chromophores and effectively prevent the aggregation-induced quenching effect of dyes. The programmability and designability of the proteins and their flexible assembly strategies allow for diverse and functionalized protein-based template construction, making them ideal template nanomaterials for constructing ALHSs.

In this Account, dealing with the strategy and the structural diversity of protein self-assemblies, we will first introduce the driving forces and assembling strategies of protein self-assembly. Then, based on our long-term research on protein self-assemblies, we will summarize our work on the development and exploration of ALHSs constructed in our laboratory in recent years, using polymorphic protein-assembly structures as templates. We will discuss the specific effects of different protein templates on energy transfer. Finally, the challenges and proposed possible strategies for the design of future LHSs by integrating proteins with nanotechnology interface science are presented.

Considering the highly codable and designable nature of proteins, as well as the definite and delicate structure of their assemblies on the nanoscale, we propose the strategy of “using protein assemblies as templates to construct ALHSs”. Protein template backbones can be constructed through both noncovalent (electrostatic, metal-chelation, host–guest interactions) and covalent interactions. Furthermore, the dynamic processes of protein assembly and disassembly are important, as we believe that flexible protein assembly and construction strategies can mimic the self-regulatory functions of the adaptive natural photosynthetic system.

Based on the “energy funneling” step flow transfer mechanism, different dimensions of protein self-assembly show their specific characteristics in the construction of ALHSs. One-dimensional (1D) protein self-assemblies feature linearly arranged chromophore molecules with linear energy transfer, mimicking light-harvesting antennas. In comparison, two-dimensional (2D) protein backbones provide more multidirectional energy transfer paths for chromophores or pigment molecules, avoiding overall transfer interruption from individual position defects. We found that the diverse assembly strategies among proteins allow the assembly structure to be regulated by a stimulus-responsive mechanism. This mechanism can modulate the efficiency of energy transfer, which further controls the catalytic performance of the ALHS in model reactions. In summary, protein self-assemblies not only achieve stabilization and orderly arrangement of chromophores but can also control energy transfer by manipulating their degree of assembly.



### 1. INTRODUCTION

Photosynthesis is one of the most pivotal biological processes in nature. Sunlight, as both the energy source and driving force behind photosynthesis, is harnessed by photosynthetic pigments and subsequently transferred to the reaction center, where it triggers charge separation, initiating a cascade of intricate photochemical reactions.<sup>1–6</sup> Within light-harvesting complexes, the mechanism of energy transfer can be elucidated by fluorescence resonance energy transfer (FRET). This process entails the transfer of energy between two fluorophores through

dipole–dipole coupling when they are in close proximity, typically within a range of 1–10 nm.<sup>7,8</sup> During FRET, the

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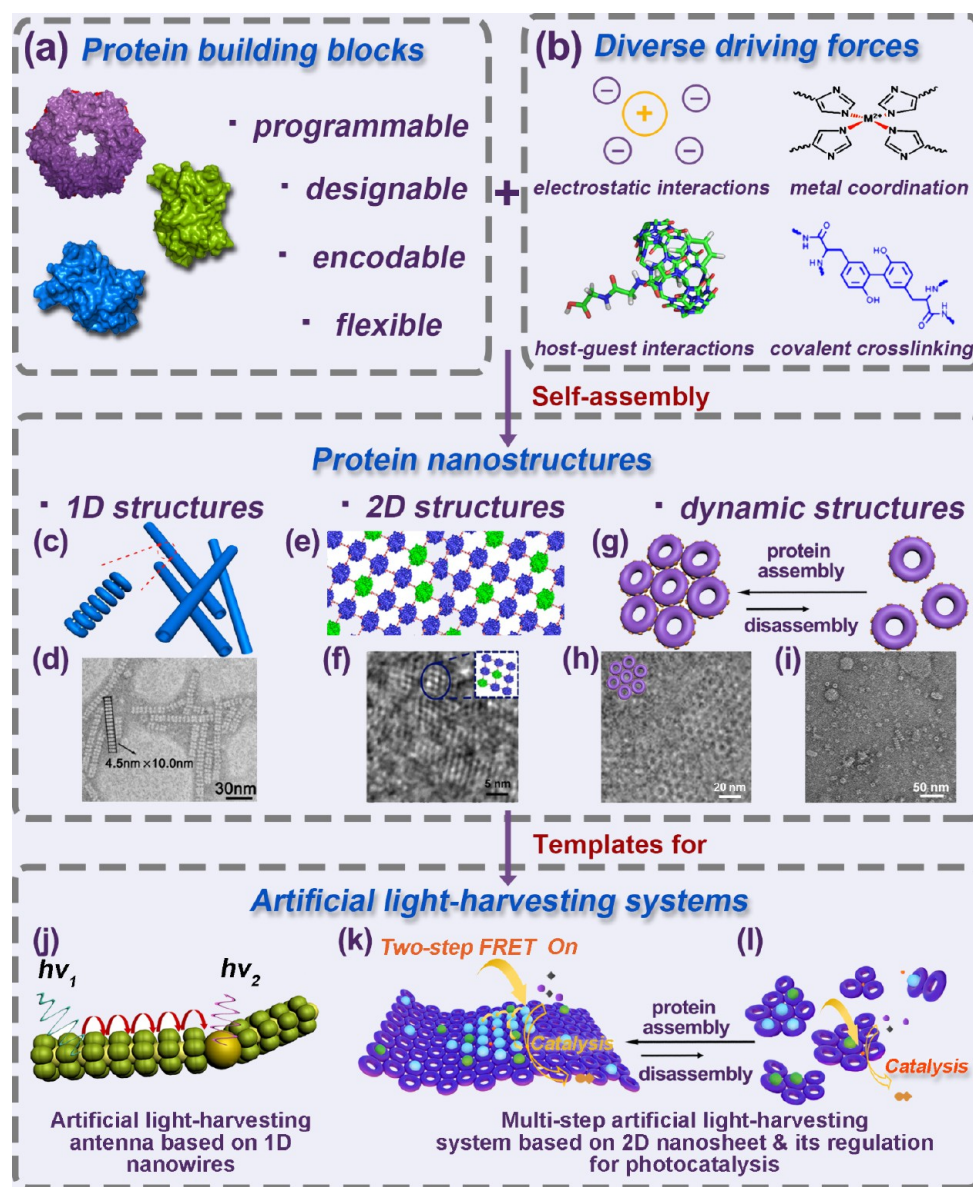


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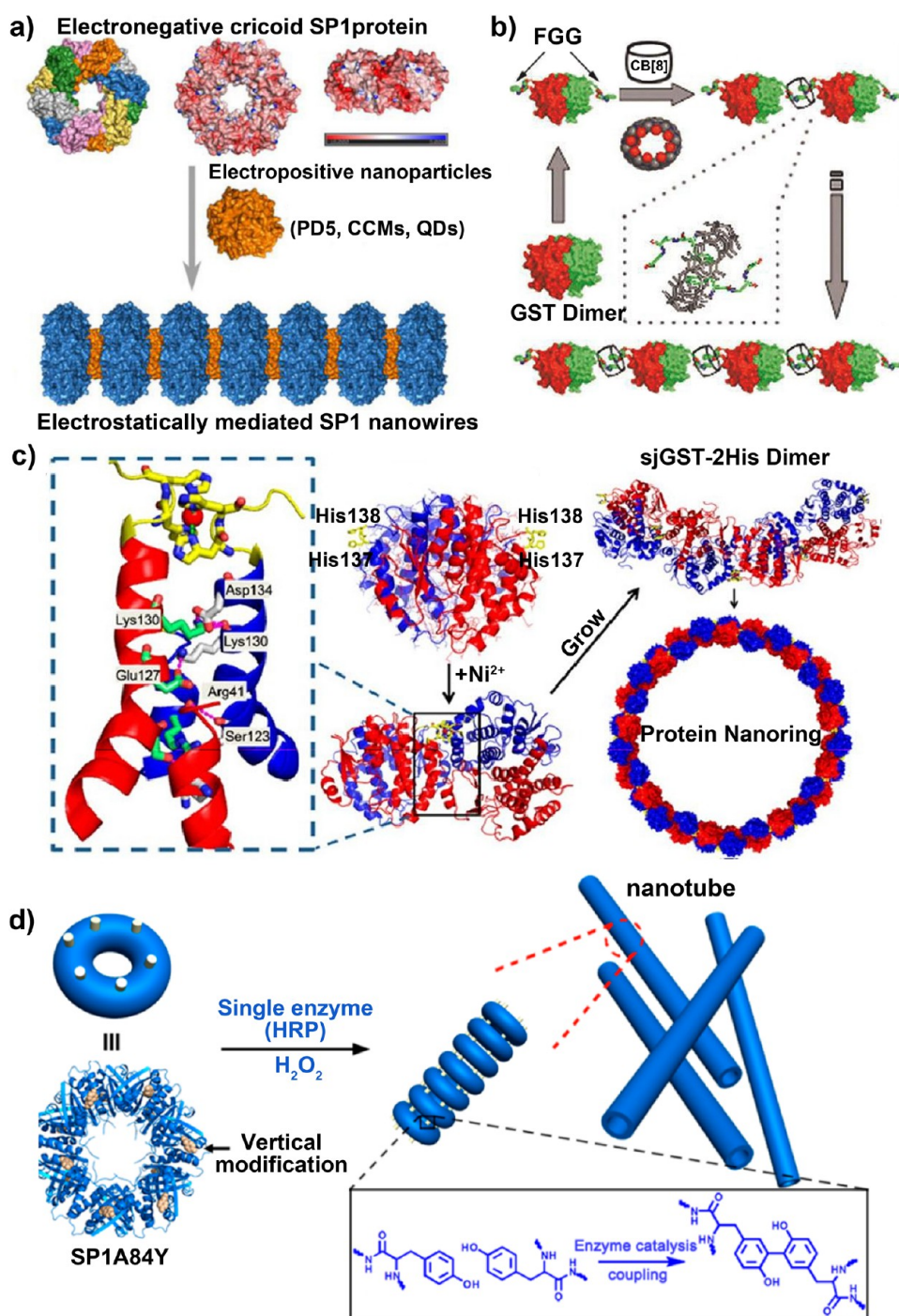
**Figure 1.** Design strategies for protein-assembly-based ALHs. (a) Protein building blocks and their unique characteristics. (b) Diverse driving forces for protein self-assembly in our studies. (c–i) Structures of the protein assemblies and their TEM images obtained in our studies. (j) 1D protein-nanowire-based artificial light-harvesting antenna. (k) 2D protein-nanosheet-based multistep ALHs for photocatalytic model reaction and (l) its disassembling process. Reprinted with permission from refs 1–3 and 31. Copyright 2014, 2017, 2019, and 2022 American Chemical Society.

emission intensity of the fluorescent donor decreases as a result of transferring its energy to the fluorescent acceptor through long-range dipole–dipole interactions.

In natural light-harvesting complexes, chromophores are regularly and tightly arranged. When a chromophore absorbs light, the excitation energy propagates in a unidirectional manner among the chromophore molecules until it reaches the reaction center, initiating long-lasting charge separation. The elegance and efficiency of natural light-harvesting systems (LHSs) have inspired scientists to explore biomimicry in the development of artificial light-harvesting systems (ALHSs),<sup>9–11</sup> which have found applications in various areas such as photocatalysis, biosensors, or nanomedicine.<sup>12–15</sup> In many ALHSs, chromophores typically exist in an aggregated form, which can impact the stability of these systems and result in aggregation-induced quenching.<sup>16–18</sup> An efficient and stable LHS typically requires the ordered arrangement of chromo-

phores on the nanoscale at appropriate distances. In some cases, templates should be designed to facilitate the regular arrangement of chromophores.

Self-assemblies have attracted increasing attention for the fabrication of ALHSs due to their ability to spatially organize chromophores in an orderly manner.<sup>19–21</sup> This organization is essential for controlling energy transfer processes, thus influencing the effectiveness of light-harvesting devices. Significant advancements have been made in utilizing non-covalent interactions, including metal coordination, electrostatic interaction, and hydrophobic interactions, as well as covalent interactions, to construct self-assemblies for designing ALHSs.<sup>17,22,23</sup> Protein self-assemblies, capable of arranging protein monomers in an orderly manner, serve as optimal platforms for crafting ALHSs. They can structurally and functionally mimic natural LHSs, offering a biomimetic strategy for the design and fabrication of ALHSs.



**Figure 2.** (a) Model of a SP1 nanowire formed by electrostatic interactions of SP1 nanoring subunits (blue) and PD5, CCMs, QDs (orange). (b) Nanowires obtained via the host–guest interactions between FGG-fused GST and cucurbit[8]uril. (c) Protein nanorings based on metal coordination between His<sub>6</sub>-tags and Ni<sup>2+</sup>. (d) SP1-based nanotubes via covalent coupling between Tyr in the presence of substrates H<sub>2</sub>O<sub>2</sub> and HRP. Reprinted with permission from refs 32, 37, 39, and 3. Copyright 2015 American Chemical Society, 2013 John Wiley and Sons, 2013 and 2017 American Chemical Society.

This Account introduces our recent work on protein assemblies, covering one-dimensional (1D), two-dimensional (2D), and dynamic protein assemblies obtained via covalent or noncovalent interactions (Figure 1). We present the ALHSs derived from these protein assemblies. The photocatalytic application of our protein-assembly-based LHSs is discussed. Finally, the challenges and proposed strategies for the design of future LHSs by integrating proteins with nanotechnology interface science are presented. We believe that constructing

ALHSs based on protein assembly can provide insights into the exploration and reconstruction of natural photosynthetic systems.

## 2. SCAFFOLDS AND TEMPLATES BASED ON PROTEIN SELF-ASSEMBLY

Protein self-assemblies show their unique advantages compared to other types of supramolecular assembly systems, such as host–guest-based assemblies,<sup>24,25</sup> supramolecular poly-

mers,<sup>26,27</sup> supramolecular organic frameworks (SOFs),<sup>28</sup> in many artificially constructed templates and skeletons of LHSs. First, proteins are translated by gene coding, which enables highly flexible design. By using genetic engineering technology, amino acids with specific functions can be introduced at any desired location to realize the activation of functional sites, facilitating the construction of protein assemblies. Second, protein assemblies have clear and fine structures at the nanometer scale, and their precise arrangement of protein monomers benefits reasonable dispersion of fluorescent chromophores, which can simulate natural LHSs in terms of structure and function. In addition, the photosynthetic system has developed self-protection functionality to adapt to the external extreme environment, and such controllable functions can also be realized through flexible protein assembly strategies. Therefore, one can anticipate using the protein-assembly strategy to explore and simulate natural LHSs from the aspects of structure, energy transfer process, and substance transformation. While protein-assembly-based LHSs offer unique advantages, certain challenges remain. For instance, the relatively large size of proteins can result in lower energy transfer efficiency compared to small-molecule assemblies. Additionally, the intrinsic instability of natural proteins may affect the tunability and scalability of these systems.

### 2.1. Driving Forces of Protein Self-Assembly

The most representative way in which chemical-strategy-based driving forces induce protein assembly is through supramolecular interactions.<sup>29</sup> Supramolecular assembly strategies can utilize driving forces such as electrostatic interactions, metal coordination, and host–guest interactions to induce the formation of ordered protein nanostructures by interacting with monomers in a novel way. The rise of supramolecular chemistry has greatly promoted the development of protein assemblies, not only enriching the methodology of assemblies but also diversifying their structure and function.

Electrostatic interactions play an important role in regulating the formation of hierarchical structures from natural proteins while simultaneously stabilizing the protein nanostructure.<sup>30</sup> Proteins with specific isoelectric points exhibit different electric charges depending on pH conditions. The cyclic dodecameric protein “stable protein one” (SP1) has attracted much attention in the field of protein assembly due to its high thermal stability, special  $C_6$  symmetry structure, and high negative surface charge. Our research group has made considerable progress in using SP1 to construct functional nanostructures through electrostatic interactions (Figure 2a).<sup>31–33</sup> A representative example is the construction of nanowire structures by electrostatic assembly of mutant SP1 and dendritic molecules.<sup>32</sup> We synthesized a series of amino dendrimers and finally found that the fifth-generation dendrimers can assemble along the protein axis to form a regular nanowire structure due to their good spatial complementarity and multivalent charge effect with SP1.

Host–guest interaction is a type of small-molecule-based driving force with high binding strength and high selectivity and is also reversible. It has been widely used in constructing ideal protein nanostructures in recent years.<sup>34–36</sup> The host molecule utilizes strong interactions to capture a guest molecule into its cavity, leading to recognition and inducing protein assembly. Cucurbit[8]uril (CB[8]) and the phe-gly-gly (FGG) tripeptide, a host–guest recognition pair, was used as a backbone, and our group extended its application in the field of protein assembly from the construction of protein dimers to functional 1D protein

assemblies.<sup>37</sup> FGG was fused to the symmetrical N-terminus of the dimeric GST protein by genetic engineering (Figure 2b). The GST mutant (GST-FGG) could easily be assembled into highly ordered protein nanowires in the presence of CB[8] to form flexible 1D protein skeletons.

The strong binding force and geometric specificity of metal coordination also play an important role in stabilizing the structure of supramolecular protein assemblies. Traditional  $Ni^{2+}$  ligand His<sub>6</sub>-tags were introduced via gene fusion into the N-terminal of glutathione S-transferase (GST) to realize the application of metal ion chelation.<sup>38</sup> Protein nanowires and protein network structures were successfully constructed based on metal coordination between His<sub>6</sub>-tags and  $Ni^{2+}$ . Subsequently, our research group achieved further precise prediction and regulation of assembly behavior through the synergistic effect of metal chelation and protein–protein interactions and constructed protein nanorings of highly uniform size.<sup>39</sup> GST was introduced as a building block with two metal chelating sites in the vertical direction of its  $C_2$  symmetry axis, forming a V-shaped His-tagged dimer (Figure 2c). Computer simulations revealed that the designed sites realize a good synergistic effect with the nonspecific interaction of the protein. According to this design method, nanoring structures with almost identical diameters can be obtained.

Covalent interaction is another force that drives proteins into highly ordered nanostructures, which is not limited to proteins with special properties and is more universal and versatile compared with supramolecular interaction. Recently, our research group developed a novel and mild enzyme-catalyzed induction method of protein covalent assembly.<sup>3</sup> Since horseradish peroxidase (HRP) can catalyze the efficient coupling of tyrosine (Tyr) *in vitro*,<sup>40</sup> we used SP1 as a template and introduced Tyr on its top and bottom surfaces to obtain SP1-A84Y mutants, which grew along the axial directions to form 1D protein nanotubes after covalent coupling of Tyr in the presence of hydrogen peroxide and HRP (Figure 2d).

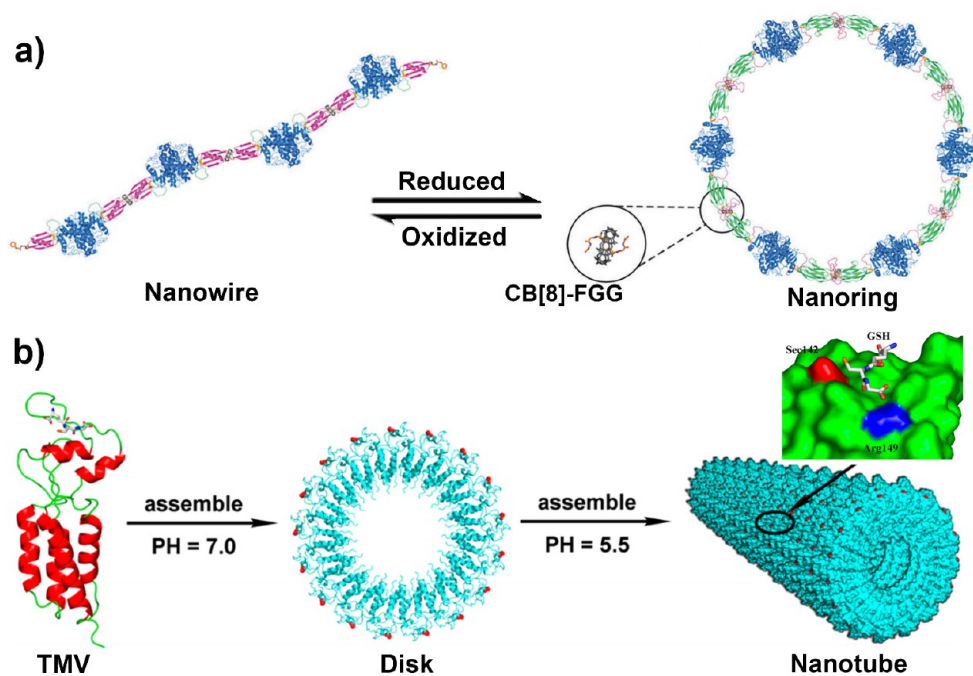
Covalently cross-linked protein nanostructures are significantly more stable than those induced by noncovalent interactions, which will benefit the development of light-harvesting templates that require specific stability. In general, the combined use of multiple assembly strategies is expected to promote the rapid development of protein assembly science, providing continuous inspiration for the preparation of more diversified protein nanomaterials.

### 2.2. Various Structures of Protein Assemblies

#### 2.2.1. One-Dimensional Protein Assembly Structures.

In general, a 1D structure usually refers to a structure formed by an object extending in one direction. The interactions between proteins can form regular linear “strings”, which can further connect end-to-end to form nanorings, spiral nanotubes, or microtubular structures.

Scientists have made numerous attempts to demonstrate that binary or multiple proteins can form alternating nanowires through dual specific recognition design. Our group tried to construct 1D protein structures based on supramolecular assembly methods. As mentioned in Section 2.1, 1D nanowires were obtained based on the host–guest interactions between GST-FGG building blocks and CB[8].<sup>37</sup> Furthermore, we used SP1 to construct a series of linearly structured 1D protein-nanoparticle hybrids via electrostatic assembly strategies. Various nanostructures with positive charges, such as poly-amidoamine dendrimers (PAMAM dendrimers, PDS),<sup>32</sup>



**Figure 3.** (a) 1D controllable protein self-assembly based on the ring chain competition mechanism. (b) 1D nanotube based on TMV and regulated by pH. Reprinted with permission from refs 42 and 43. Copyright 2017 Royal Society of Chemistry and 2012 American Chemical Society.

polymer micelles,<sup>33</sup> and quantum dots (QDs),<sup>31</sup> can induce the self-assembly of cricoid SP1 into 1D supramolecular nanowires.

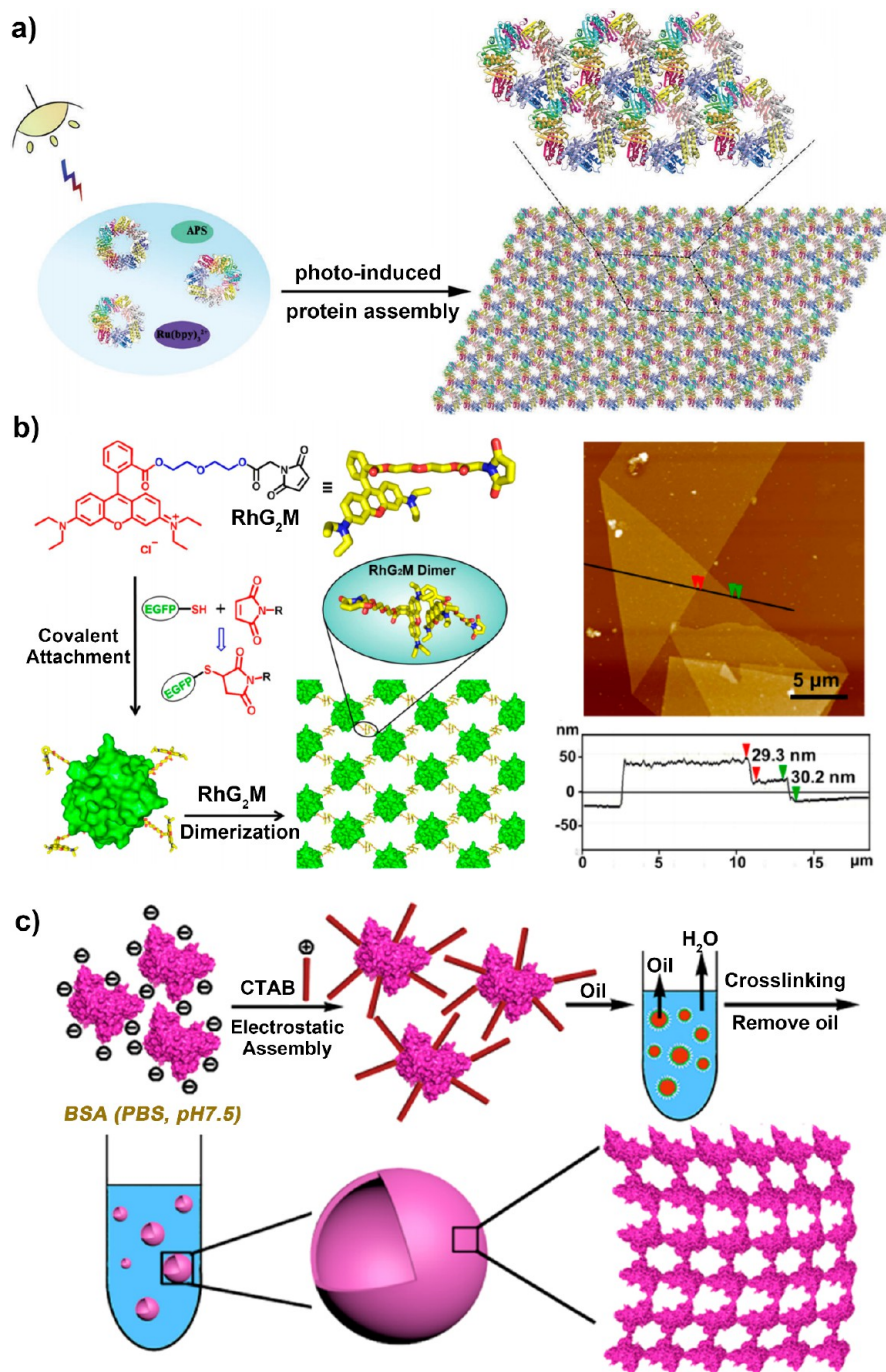
Apart from the linear growth control of proteins, protein building blocks can also be manipulated to form closed rings with controlled curvature. We constructed a controllable protein self-assembly based on the ring chain competition mechanism, where the transition between nanowires and nanorings can be controlled by protein concentration.<sup>41</sup> At low protein concentrations, proteins tend to form nanorings by head-to-tail binding, while at high concentrations, they assemble into nanowires. A redox approach could regulate this transformation in the FGG-tagged fusion protein FGG-G-I-GST (FGIG). Under oxidation conditions, FGIG forms nanowires, while under reduction conditions, expanded FGIG forms nanorings (Figure 3a).<sup>42</sup> It remains challenging to construct uniform large nanorings because of the need for precise protein–protein interactions and orientation control. Inspired by this difficult synthesis strategy, we reported the precise control of protein orientation and self-assembly into protein nanorings through the collaboration of metal ion chelation interactions and nonspecific protein–protein interactions.<sup>39</sup> “His” V-shaped GST can cooperate with Ni<sup>2+</sup> and self-assemble in a specific bending process to form highly ordered large nanorings with diameters of  $367 \pm 10$  nm.

Next to the discussed nanowire and nanoring, the nanotube is another 1D structure of protein assembly. However, designing well-organized tubular structures requires more complex protein–protein interactions. We followed many approaches to overcome this difficulty and found that the natural tube-like virus TMV can first assemble through pH regulation into a disc-shaped structure, which then grows linearly in the vertical direction to form a nanotube structure (Figure 3b).<sup>43</sup> Besides this method, we also developed a simple strategy for constructing highly ordered protein nanotubes by utilizing electrostatic interactions and “zero-length” cross-linking induced by the small molecule ethylenediamine.<sup>44</sup>

### 2.2.2. Two-Dimensional Protein Assembly Structures.

Inspired by nature, 2D protein self-assembly has attracted much attention due to the structural complexity, functional diversity, and inherent biological affinity of building blocks. The nanotechnology used in the construction of 2D assemblies has advanced significantly, enabling the precise regulation of protein assembly to form regular 2D nanosheet arrays.

The formation of 2D layered protein structures can be achieved by the programmable arrangement of proteins on a plane. Our group utilized a strategy of integrating light stimulation and covalent coupling to construct a size-adjustable 2D protein structure with ordered ring-shaped stacking patterns through remote photocontrol.<sup>45</sup> Using tris(2,2′-bipyridine)-ruthenium(II) cation (Ru(bpy)<sub>3</sub><sup>2+</sup>) as a photosensitizer, SP1 was redesigned and self-assembled into nanosheets through efficient oxidative protein cross-linking reaction in the presence of ammonium persulfate (APS) (Figure 4a). On this basis, we also achieved the precise manipulation of EGFP-4C, an enhanced green fluorescent protein (EGFP) variant with four cysteine residues, which underwent self-assembly through redesigned, maleimide-functionalized rhodamine B moieties (RhG<sub>2</sub>M) (Figure 4b).<sup>46</sup> In this process, an ultralarge 2D array was constructed based on the binding of site-specific RhG<sub>2</sub>M-modified EGFP-4C via the dimerization of RhG<sub>2</sub>M. We also fabricated ultrathin protein membranes using proteins and polymers based on hydrophilic and hydrophobic interactions at the oil–water interface.<sup>47,48</sup> 2D protein membranes do not always exhibit sheet-like structures and can bend into curved surfaces in some cases, further growing into giant spherical vesicles (Figure 4c). Inspired by this process, we combined the amphiphilic molecule cetyltrimethylammonium bromide (CTAB) with the negatively charged bovine serum albumin (BSA) protein through electrostatic interaction and then constructed a giant proteasome based on an interface assembly strategy.<sup>49</sup>

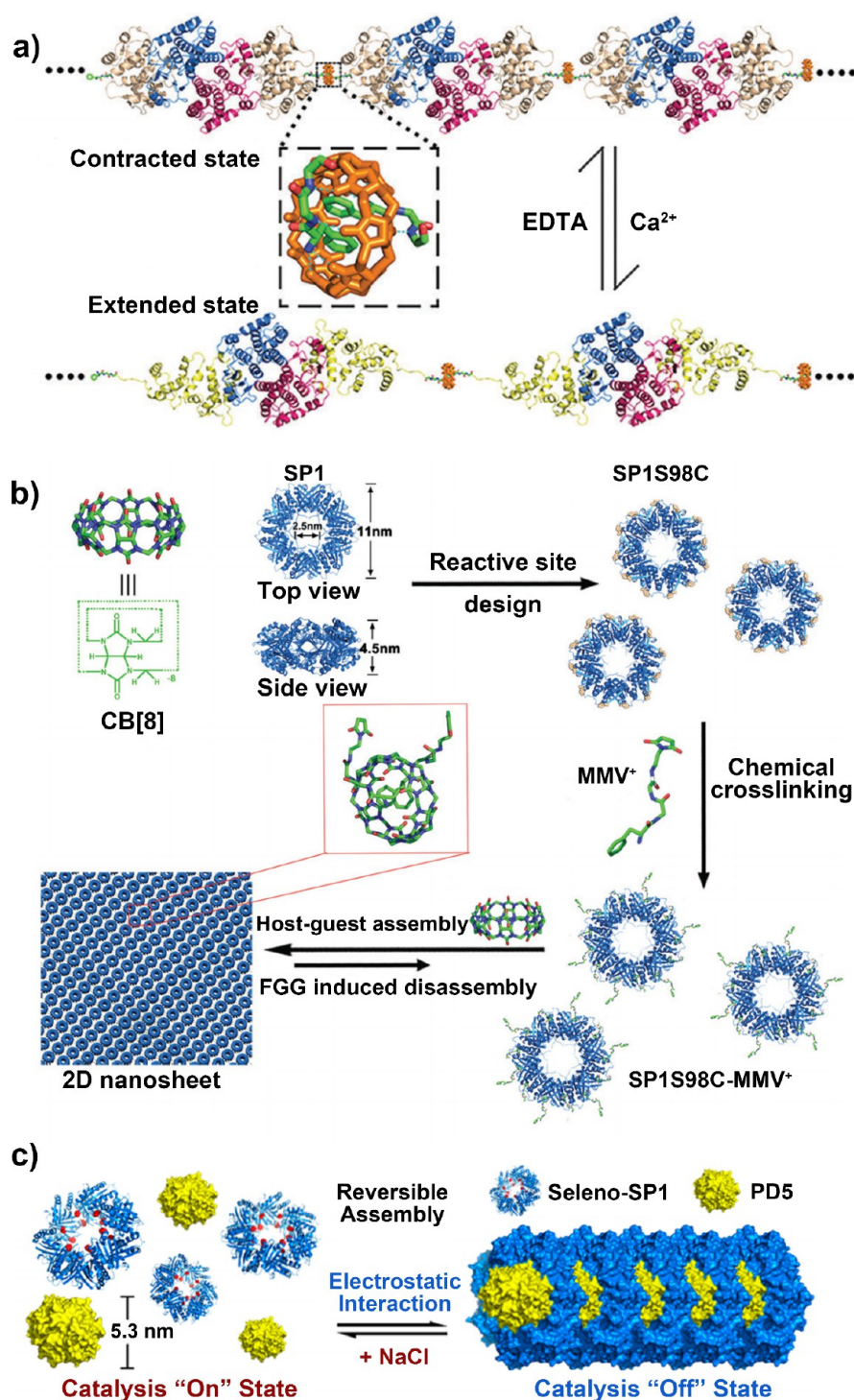


**Figure 4.** (a) 2D SP1-based nanosheet via protein cross-linking reaction in the presence of APS. (b) Nanosheets based on fluorescent proteins via covalent cross-linking between proteins and linkers. (c) Giant spherical vesicles based on proteins and polymers via hydrophobic interactions. Reprinted with permission from refs 45, 46, and 49. Copyright 2018 Royal Society of Chemistry, 2021 and 2019 American Chemical Society.

**2.2.3. Dynamic Protein Assembly Structures.** One of the most important stimulus-responses involves the process of protein assembly and disassembly, which plays a crucial role not only in cellular growth and apoptosis but also in the physiological activities of organs.<sup>50,51</sup> The dynamic protein assembly can benefit ALHSs by adaptively optimizing chromophore arrangements in response to environmental changes, fine-tuning energy transfer to minimize losses, and facilitating self-repair to prolong lifespan. Dynamic regulation of ALHSs becomes particularly crucial in scenarios such as fluctuating light environments (e.g., maintain efficiency amid

intensity/wavelength variations), multifunctional systems (e.g., switching roles between light-harvesting and catalysis), and biocompatible applications (e.g., responding to cellular signals). The ability to respond specifically to external stimuli is a key factor in the construction of intelligent materials.<sup>52</sup> Inspiringly, the development of dynamically controllable structures has become a promising direction in protein assembly research.

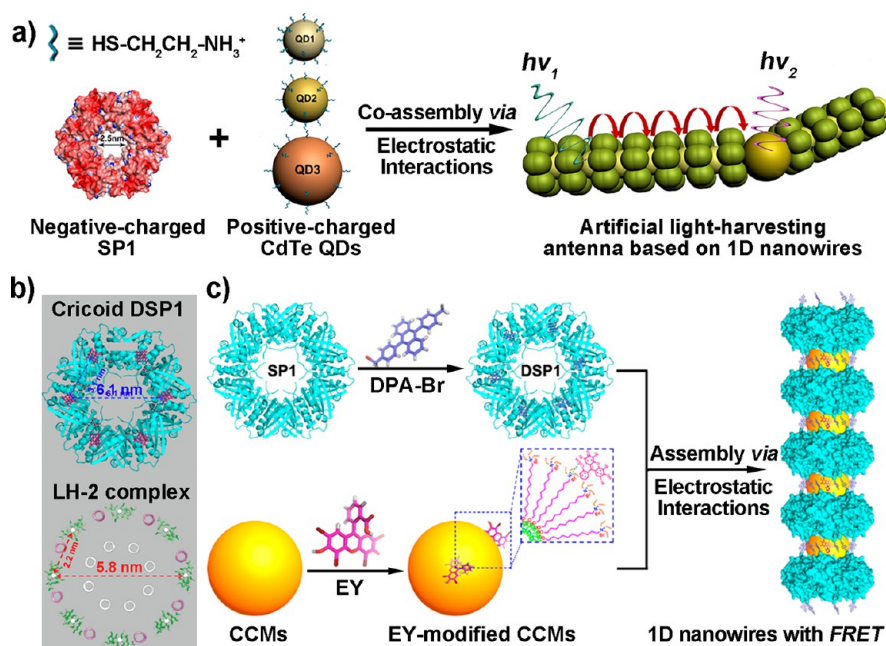
Our team has developed a series of dynamically regulated protein assemblies. A self-assembled protein nanospring was constructed via the host–guest interaction of the fusion protein FGG-recoverin-GST and CB[8] (Figure 5a).<sup>53</sup> The nanospring



**Figure 5.** (a) Dynamic nanospring based on FGG-recoverin-GST and cucurbit[8]uril by binding or unbinding of  $\text{Ca}^{2+}$ . (b) Dynamically controllable protein nanosheet regulated by the competition mechanisms of guests. (c) Protein nanowires of SP1 tuned by charge shielding effects. Reprinted with permission from refs 53, 54, and 55. Copyright 2016 and 2021 Royal Society of Chemistry, 2020 American Chemical Society.

underwent structural changes in response to  $\text{Ca}^{2+}$  stimuli, in which its assembly structure altered during contraction and expansion to achieve a spring-like movement, maintaining excellent performance after multiple switches. Subsequently, we designed a dynamically controllable protein nanosheet, which was assembled based on supramolecular interactions between CB[8] and the modified protein SP1S98C-MMV<sup>+</sup> (MMV<sup>+</sup> is a guest molecule for CB[8]) and could then be disassembled by introducing FGG as competitive guest molecule (Figure 5b).<sup>54</sup>

We also successfully constructed an efficient and switchable selenium-containing antioxidant system based on SP1, the activity of which can be turned off by forming protein nanowires through electrostatic assembly with polyamine dendrimers (PD5) and then be turned on by charge shielding-induced disassembly (Figure 5c).<sup>55</sup> The giant proteinosome based on BSA and CTAB, mentioned in Section 2.2.2, can be further regarded as a smart "breathing" vesicle.<sup>49,56</sup> These protein structures with unique advantages are of great significance for



**Figure 6.** 1D protein-nanowire-based artificial light-harvesting antenna based on between SP1 and (a) different sized QDs and (b) CCMs. Reprinted with permission from refs 31 and 33. Copyright 2014 and 2016 American Chemical Society.

the development of functional stimulus-responsive smart nanomaterials.

### 3. ALHSS INSPIRED BY PROTEIN SELF-ASSEMBLY

Because of their well-defined structures and high degree of order, the various and diverse nanostructures synthesized via hierarchical protein self-assembly are a perfect match for the requirements of constructing ALHSSs. The energy transfer process in natural light-harvesting complexes can usually be described by the FRET theory, which requires the interchromophore distance to be strictly controlled between 1 and 10 nm; while protein self-assembly processes are usually affected by the size of their building blocks and the driving forces for their assembly, these dimensions can satisfy the requirements of regular self-assembly. Precisely arranged protein arrays can not only mimic the structure of the natural photosynthetic system, dispersing pigment or chromophore molecules in an orderly manner and thereby preventing their aggregation-induced quenching, but are also expected to hinder electrostatic-induced irregular aggregation and deposition of chromophores by stabilizing the structure and properties of chromophores to mimic the pigment–protein-complex-enhanced energy transfer of natural LHSs. In addition, the stimulus-responsive mechanism of protein assembly behavior can offer the possibility of dynamic regulation of the constructed ALHSSs, which in turn is expected to realize the artificial control of the energy transfer process.

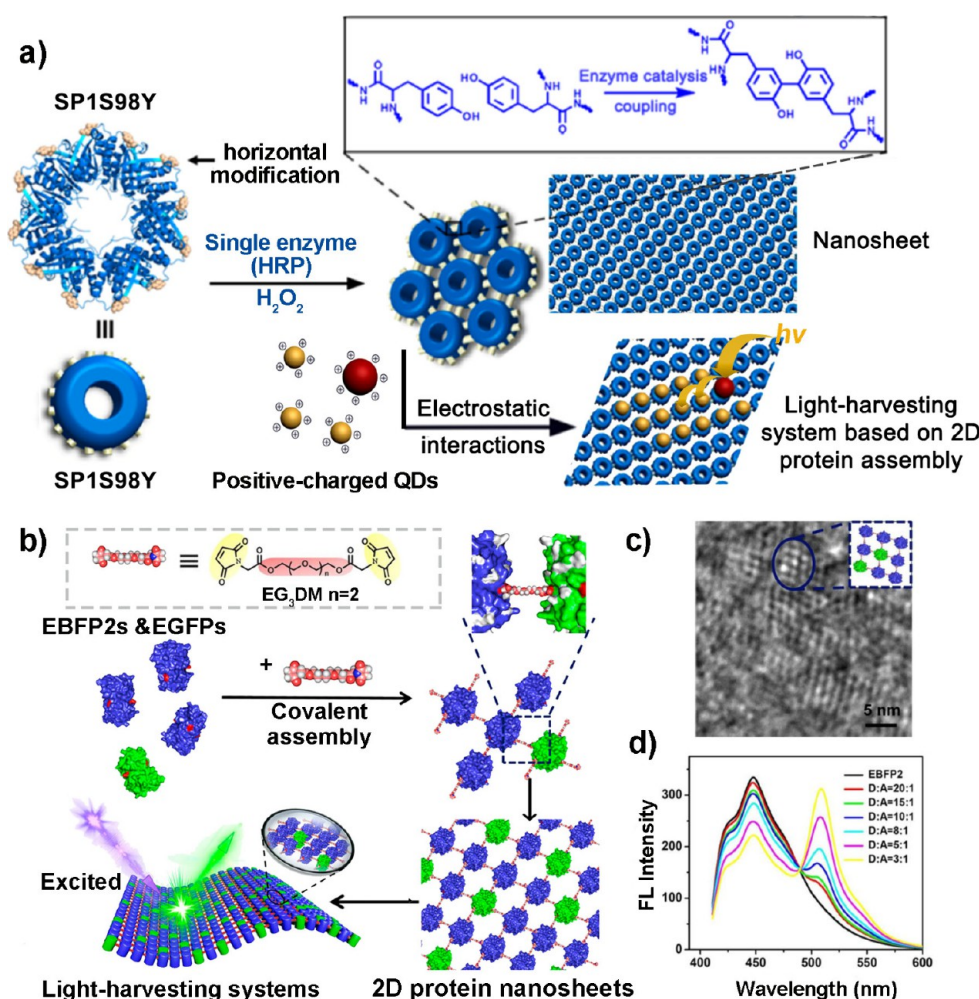
Based on the “energy funneling” step flow transfer mechanism, protein self-assemblies of different dimensions exhibit their characteristics in the construction of ALHSSs. 1D protein self-assemblies are scaffold-distributed chromophore molecules that are mostly linearly arranged. Consequently, their energy transfer paths follow a linear pattern, and the assemblies function like light-harvesting antennas. 2D protein backbones, however, offer more multidirectional energy transfer paths for chromophores or pigment molecules. Compared to the single path of 1D protein assemblies, in which energy transfer might be

interrupted due to defects in the path structure, the 2D assemblies can circumvent such interruptions due to the existence of multiple energy transfer pathways. There are multiple noncovalent interactions in the structure of the protein building blocks, and this structure can be altered by denaturants (e.g., urea, GuHCl). Additionally, the diverse intermolecular assembly strategies of proteins allow the structure of the assemblies to be modulated by the stimulus-responsive mechanisms of their driving forces, which motivates attempting the construction of an adaptive ALHS.

#### 3.1. Artificial Light-Harvesting Antennas Based on 1D Protein Assembly

1D linear protein self-assemblies can provide directional energy flow paths to their dispersed chromophore molecules. Based on the electrostatic interactions between surface-negative-charge-enriched SP1 and positively charged chromophores, we have prepared a variety of artificial light-harvesting antennas with 1D protein nanowires as the scaffolds. The negatively charged surfaces and the concave hydrophobic central cavity of SP1 (Figure 6a)<sup>31</sup> provide a structural basis both for the acceptance of size-matched chromophores and the possibility for self-assembly with positively charged chromophores. Two different positively charged and spectrally well-overlapped CdTe QDs (within 6 nm) have been selected as donor and acceptor chromophores and assembled with SP1 into 1D linear nanowires for FRET process. Notably, the straight linear assembly behavior is directionally distorted when the size of QDs increased ( $\sim 10$  nm), resulting in branched structures rather than linear ones. However, the branched structures can modulate the distance between the chromophores, which holds promise for artificially modulating the energy transfer efficiency of this light-harvesting antenna.

Furthermore, our investigations inspired by nature revealed that the ring structure of SP1 highly mimics the LH-2 light-trapping complexes of photosynthetic bacteria (Figure 6b).<sup>33</sup> 9-[4-(Bromomethyl)-phenyl]-10-(4-methylphenyl)anthracene (DPA-Br) and eosin-5-isothiocyanate (EY) were covalently



**Figure 7.** 2D protein-nanosheet-based ALHSs based on (a) SP1 and (b) fluorescent proteins. (c) TEM images of the 2D protein nanosheets in (b). (d) The energy transfer process of the template-free ALHSs. Reprinted with permission from refs 3 and 2. Copyright 2017 and 2019 American Chemical Society.

modified at the periphery of the SP1 rings as donor chromophores or as acceptor chromophores on positively charged core-cross-linked micelles (CCMs), respectively. The modified proteins and CCMs were electrostatically self-assembled to form 1D protein supramolecular nanoarrays, and the distance between the donor and acceptor molecules was within 2 nm, which further enhanced the efficiency of FRET and constructed a more efficient artificial light-harvesting antenna (Figure 6c). The strategy of modifying the protein nanoscaffolds further avoided the randomness of the donor–acceptor chromophore distribution.

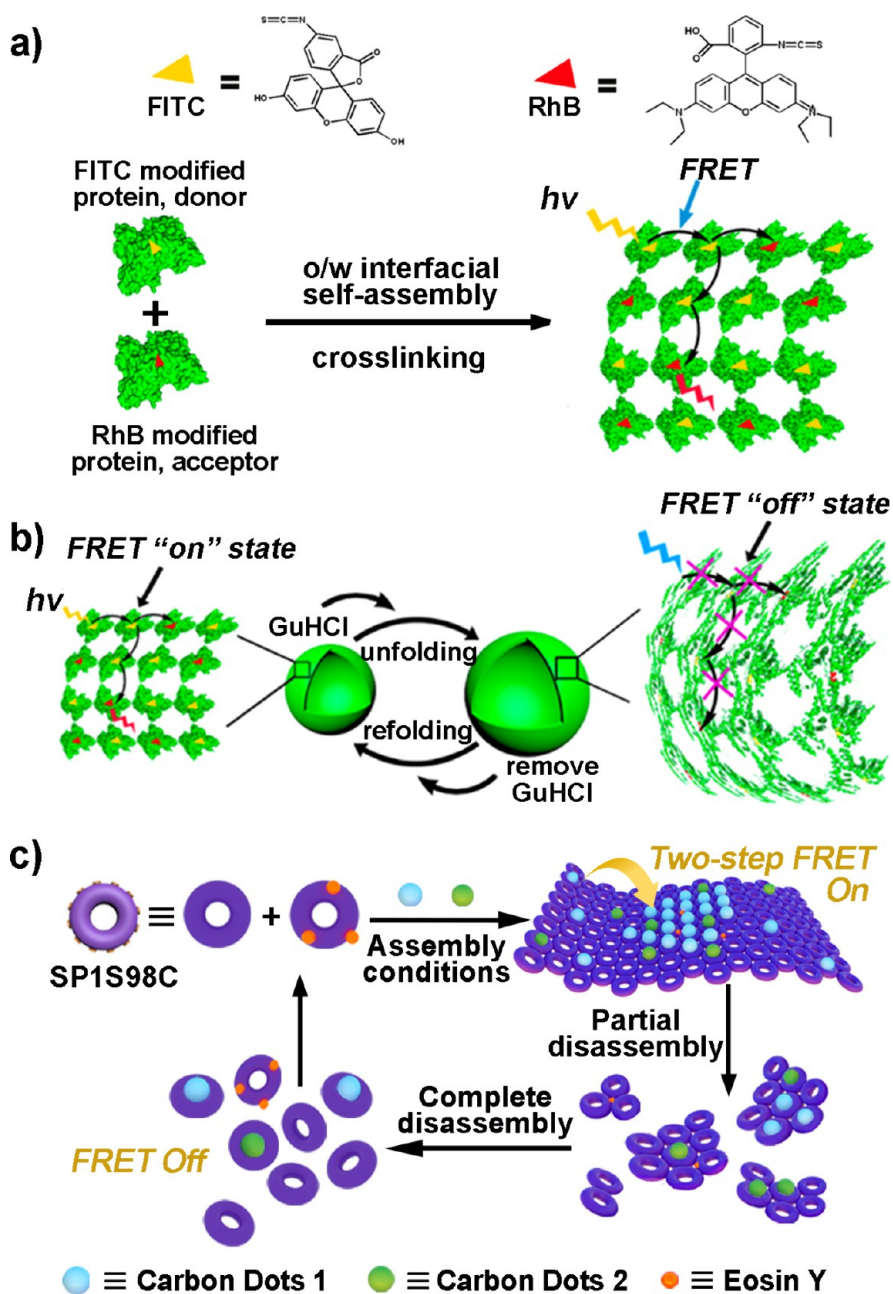
The artificial light-capturing antenna based on 1D protein assembly realizes the fixation and arrangement of donor–acceptor chromophore molecules and energy capture and transfer to a certain extent. However, at the same time, it also has its disadvantages: the linear energy transfer is easily interrupted by the local defects or improper arrangement of chromophores, which leads to the complete disruption of FRET and the failure of the light-harvesting process. The application of a higher-dimensional protein scaffold is expected to solve this problem.

### 3.2. ALHSs Based on 2D Protein Assembly

To address the problem of interrupted energy transfer, we further chose to arrange chromophores using 2D protein self-

assemblies as templates. In natural chloroplasts, chromophores are distributed in highly ordered arrays on the protein substrates of 2D thylakoid membranes, and this network of pigment–protein complexes plays a crucial role in efficient energy transfer. Compared with 1D protein nanostructures, the ALHSs constructed with 2D protein nanosheets as the scaffold are not only structurally more closely aligned with the natural photosynthetic system but also provide multidirectional energy transfer pathways to avoid interruption of the energy transfer process due to defects at a single location. We modified SP1 by gene fusion to introduce Tyr into the peripheral surface of its protein ring. Under HRP-catalyzed oxidation, the mutant protein grew alongside its plane and formed monolayers, separated due to electrostatic repulsion into single-layer nanosheet structures (Figure 7a).<sup>3</sup> Importantly, the orderly arrangement of the pore-ring structure of SP1 provided regular and tightly packed binding sites for donor and acceptor chromophores (CdTe QDs), which led to the well-ordered assembly of the chromophores in the nanoarrays and the realization of the light-harvesting process. The FRET phenomenon of the constructed ALHSs was evident, and the energy transfer efficiency was as high as 56%.

In addition, we have developed a template-free strategy for constructing a 2D ALHS, which utilized fluorescent proteins

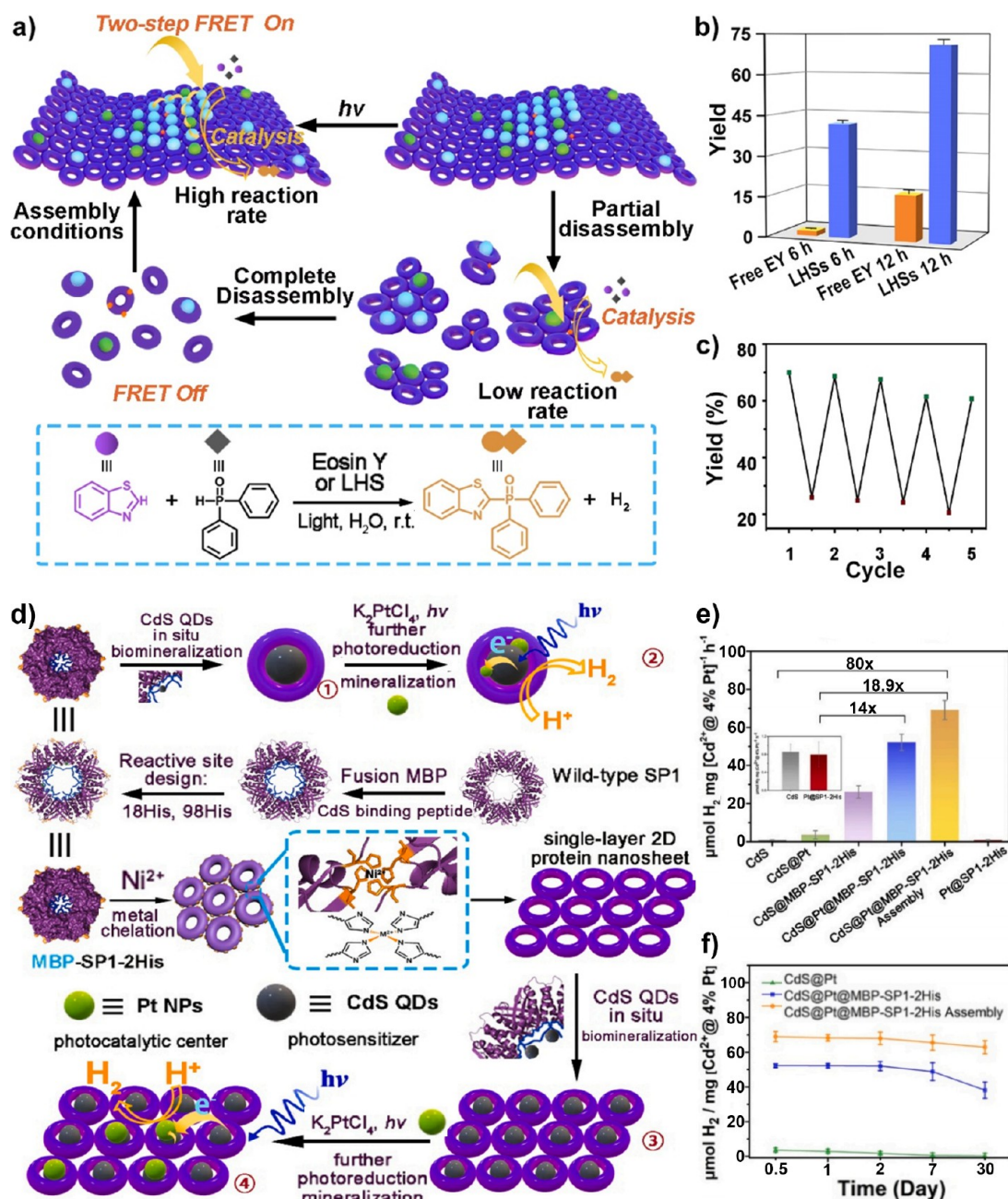


**Figure 8.** Controllable ALHSs regulated by (a) the folding and unfolding of protein structures with a denaturant and (b) the redox stimulus response of the 2D protein nanosheet template. Reprinted with permission from refs 56 and 1. Copyright 2019 and 2022 American Chemical Society.

directly as chromophores without the additional introduction of inorganic QDs. The blue fluorescent protein (EBFP2) and green fluorescent protein (EGFP) were used as donor and acceptor chromophores, respectively, and their barrel structure was genetically designed with four cysteines (Cys) as covalent functional sites. By covalently cross-linking the building block proteins with the small molecule PEG-bismaleimide (EG3DM) as the linker, protein nanosheets were obtained, and intermolecular energy transfer was realized. The template-free protein-based covalently self-assembled 2D ALHS was successfully constructed (Figure 7b).<sup>2</sup> The donor and acceptor chromophores obtained by this strategy were homogeneously arranged into well-structured nanoarrays (Figure 7c). The maximum energy transfer efficiency of this system reached 33.2%, which may be attributed to the nanoscale size of the

protein shell, leading to an increase in the intermolecular distance between its inside-protected chromophores (Figure 7d). Nonetheless, this construction strategy of directly covalently assembling protein chromophores without templates provides a reasonable and open idea for constructing ALHSs based on protein assemblies.

Three-dimensional (3D) self-assemblies have demonstrated great potential for developing ALHSs, featuring hierarchical, spatially ordered architectures and high structural complexity. They support densely packed pigment arrays with multidirectional energy transfer pathways and allow nanoscale positioning of photoactive molecules,<sup>57,58</sup> enhancing light absorption and enabling more efficient energy funneling compared to 1D or 2D systems.



**Figure 9.** (a) Regulation of the photocatalytic model reaction by our controllable ALHs. (b) Histogram of the contrast yield of the model reaction with photocatalysis activities between the free EY and our LHSs. (c) The yield of the photocatalytic performance of the LHSs controlled by the interconversion of the protein assembly process. (d) Construction of the photocatalytic system based on protein assembly. (e) H<sub>2</sub> production rate of CdS@Pt@MBP-SP1-2His system (free and assembly) and other control groups. (f) Stability evaluation of hydrogen production performance. Reprinted with permission from refs 1 and 59. Copyright 2022 American Chemical Society and 2025 Elsevier.

### 3.3. Regulation of ALHs Based on Protein Assembly–Disassembly Processes

As scaffolds for ALHs, the structure of proteins and their assemblies are expected to respond to external stimuli as a strategy to modulate the energy transfer process. We successfully achieved the folding and unfolding of protein structures with a denaturant (GuHCl) to obtain fluorescent on/off light-capturing protein vesicles and also realized the process of regulating the sequential multistep FRET process with the assembly driving forces, i.e., the redox stimulus-response of disulfide bonds.

#### 3.3.1. Energy Transfer Process Regulated by Changing the Structure of Protein Assemblies.

Protein vesicles were formed by self-assembly at the oil–water interface of an emulsion through an interfacial assembly strategy. Such protein capsules can be regarded as ordered layer structures to reduce the distance between acceptor and donor. We modified the donor and acceptor chromophores, fluorescein isothiocyanate (FITC) and isothiocyanate rhodamine B (RhB), respectively, on protein monomers, and successfully constructed an LHS based on protein vesicles with such modified proteins (Figure 8a).<sup>56</sup> By adding GuHCl, the structure of the protein became loose, leading to an increase in the molecular distance between

**Table 1. Structural Characteristics and Size-Related Parameters of the Proteins Involved in the Development of ALHSs**

| Key components         | Driving forces             | Assembly structures | Dynamic properties               | References  |
|------------------------|----------------------------|---------------------|----------------------------------|-------------|
| SP1 (dodecamer, 11 nm) | electrostatic interactions | 1D nanowire         | none                             | refs 31, 33 |
|                        | electrostatic interactions | 2D nanosheet        | none                             | ref 3       |
|                        | covalent interactions      | 2D nanosheet        | protein assembly and disassembly | ref 1       |
|                        | metal coordination         | 2D nanosheet        | none                             | ref 59      |
| EGFP (monomer, 2.4 nm) | covalent interactions      | 2D nanosheet        | none                             | ref 2       |
| BSA (monomer, 7 nm)    | interfacial assembly       | 2D vesicle          | protein unfolding and refolding  | ref 56      |

the donor–acceptor chromophores and an interruption of energy transfer. In contrast, the refolding of the protein structure when the denaturant was removed by slow dialysis resatisfied the requirements for FRET (Figure 8b).

**3.3.2. Multistep Energy Transfer Processes Controlled by the Degree of Protein Assembly.** The natural light-harvesting process is always accompanied by multistep sequential energy transfer rather than relying only on single-step transfer of the captured sunlight. 2D monolayer sheet protein scaffolds offer the possibility of constructing more complex ALHSs. Inspired by nature, we introduced Cys on the side surface of cyclic SP1 and constructed single-layer protein nanosheets (Figure 8c) by driving the reversible covalent self-assembly of mutant proteins through the disulfide bond formed between Cys.<sup>1</sup> The carbon dots CD1 and CD2 as donors and acceptors, respectively, could be precisely distributed on the surface of the protein nanosheets by electrostatic interactions. Further, upon anchoring EY as the second acceptor, the constructed ALHS could sequentially transfer energy between the CDs and toward the center of EY with a high efficiency of 84%. The FRET process of this system could be reversibly switched between “on/off” states by the redox-regulated assembly and disassembly of the SP1 building block. Thus, this regulable multistep ALHS based on protein assembly mimics the natural LHS structurally and functionally and provides direction to explore adaptive ALHSs.

### 3.4. Protein-Assembly-Based ALHSs for Catalyzing Model Reactions

Having successfully constructed an energy-cascading ALHS based on protein nanosheets, we envisioned that the photocatalytic properties of the EY chromophore could be fully utilized by combining the oxidation–reduction stimulation response properties of the protein scaffolds with the catalytic properties of the system to control catalytic performance. EY acts as a photocatalyst to catalyze the model reaction of the photocatalytic coupling of benzothiazole with diphenylphosphine oxide for hydrogen production. However, EY has a small range of spectral utilization due to its narrow absorption band. Using our ALHS to catalyze the reaction, the light energy captured by CD1 and CD2 would be finally delivered to the second receptor and reaction center, EY, which broadens the spectral availability and thus improves catalytic performance (Figure 9a).<sup>1</sup> After 12 h of irradiation, the yield obtained under catalysis by the complete ALHS was as high as 71% compared with the yield of 17% of the reaction catalyzed with free EY, demonstrating significant improvement in reaction efficiency (Figure 9b). The switchable “on/off” FRET state, regulated by the assembly disassembly process of the protein templates, could modulate the catalytic activity of the system accordingly, changing between high and low activity over at least five cycles (Figure 9c). In addition, we designed and developed an efficient artificial photocatalytic hydrogen production system based on protein genetic engineering and self-assembly strategies,

achieved via the in situ biosynthesis of peptide-anchored protein–semiconductor hybrid materials (Figure 9d).<sup>59</sup> A metal-binding peptide (MBP) was fused to the N-terminus of SP1, and histidine was introduced into the lateral surface of the fused SP1 through point mutation, resulting in the mutant protein MBP-SP1-2His. This protein can provide spatial confinement for the in situ growth of CdS QDs, and the formed CdS@MBP-SP1-2His hybrid exhibited excellent dispersibility. To enhance the photocatalytic performance, a mild method was utilized to load Pt nanoparticles onto the surface of CdS, forming CdS@Pt@MBP-SP1-2His. The loading of Pt effectively suppressed the recombination of photogenerated electron–hole pairs, significantly boosting the photocatalytic hydrogen production rate. The hydrogen production rate of CdS@Pt@MBP-SP1-2His assembly reached an impressive 69,100  $\mu\text{mol h}^{-1} (\text{g Cd}^{2+})^{-1}$ , which was 80 times that of free CdS (Figure 9e). This enhanced performance stemmed from the precisely ordered assembly architecture, which prevented random aggregation-induced encapsulation and deactivation of catalytic centers, thereby maximizing accessible active sites and facilitating accelerated electron transfer. We further evaluated the real-time photocatalytic hydrogen production performance after Pt doping, the degree of hydrogen evolution rate attenuation in each photocatalytic system directly correlated with its precipitation extent. The photocatalytic systems exhibited sustained hydrogen evolution efficiencies of 6.5% for free CdS@Pt, 73.1% for CdS@Pt@MBP-SP1-2His, and 91.2% for CdS@Pt@MBP-SP1-2His assembly at 30th day (Figure 9f).

Table 1 summarizes the structural characteristics and size-related parameters of the proteins involved in ALHSs development, providing a clearer understanding of their roles in the assembly and function.

## 4. CONCLUSION AND PERSPECTIVE

Due to the advantages of ordered arrangement, biocompatibility, and defined structures, protein-assembly-based ALHSs could mimic natural LHSs in both structure and function, thus attracting significant attention in the development of ALHSs. In this Account, we introduced the covalent or noncovalent driving forces for fabricating protein assemblies, as well as the different assembly structures. These various protein assemblies provide suitable platforms for the fabrication of efficient ALHSs. Building upon the foundation of ALHSs based on protein assemblies, we explored their applications in photocatalysis for model reactions.

The main challenges in the fabrication of protein-assembly-based ALHSs include the following points. (1) Large sizes of protein monomers often lead to relatively long distances between donors and acceptors, potentially reducing energy transfer efficiency compared to systems using small molecules. For scenarios requiring extremely high energy transfer efficiency, one feasible strategy is to modify a single protein monomer with both donor and acceptor molecules prior to assembly, rather

than attaching them to separate protein monomers. Alternatively, a protein-small molecule synergy approach can be employed. These strategies effectively reduce the distance between chromophores, thereby enhancing energy transfer efficiency (2) Noncovalent interactions involved in the formation of complex spatial structures of proteins and their assemblies can render ALHSs sensitive to the microenvironment. Selecting stable protein monomers and utilizing immobilized scaffolds may help to improve stability. (3) The irreversibility of covalent bonds may result in defects in protein assemblies, leading to low energy transfer efficiency in ALHSs. Slowing down the speed of protein assembly, such as assembling at low temperatures or concentrations, or exploring alternative assembly conditions may mitigate this issue. (4) For the application of ALHs based on protein assemblies, it is necessary to explore other applications such as photodynamic therapy for biomedical use, and carbon or nitrogen fixation. (5) Efforts should also be made toward mimicking the complete natural photosynthetic cascade, including charge separation and electron transfer, within protein-assembly-based ALHSs. We aim to further investigate this complex system and believe that valuable insights can be gained through the rational design of protein functional sites combined with computer-aided simulations. (6) The integration of proteins with hybrid or multifunctional systems, such as inorganic nanomaterials, or catalytic components, offers an opportunity to build multifunctional assemblies for energy conversion and reactive oxygen species (ROS) control.

In conclusion, this Account describes our group's recent progress in constructing ALHSs using protein assemblies. Given the diversity of protein monomers and the range of involved noncovalent and covalent driving forces, we anticipate the emergence of new ALHSs based on protein assemblies in the coming years. Our research group will continue to explore the development of more efficient and stable protein-assembly-based ALHSs and investigate additional applications of such technologies.

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## Notes

The authors declare no competing financial interest.

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## REFERENCES

- (1) Li, Y. J.; Xia, C. L.; Tian, R. Z.; Zhao, L. L.; Hou, J. X.; Wang, J. Q.; Luo, Q.; Xu, J. Y.; Wang, L.; Hou, C. X.; Yang, B.; Sun, H. C.; Liu, J. Q. "On/Off" Switchable Sequential Light-Harvesting Systems Based on Controllable Protein Nanosheets for Regulation of Photocatalysis. *ACS Nano* **2022**, *16*, 8012–8021.

- (2) Li, X. M.; Qiao, S. P.; Zhao, L. L.; Liu, S. D.; Li, F.; Yang, F. H.; Luo, Q.; Hou, C. X.; Xu, J. Y.; Liu, J. Q. Template-Free Construction of Highly Ordered Monolayered Fluorescent Protein Nanosheets: A Bioinspired Artificial Light-Harvesting System. *ACS Nano* **2019**, *13*, 1861–1869.
- (3) Zhao, L. L.; Zou, H. X.; Zhang, H.; Sun, H. C.; Wang, T. T.; Pan, T. Z.; Li, X. M.; Bai, Y. S.; Qiao, S. P.; Luo, Q.; Xu, J. Y.; Hou, C. X.; Liu, J. Q. Enzyme-Triggered Defined Protein Nanoarrays: Efficient Light-Harvesting Systems to Mimic Chloroplasts. *ACS Nano* **2017**, *11*, 938–945.
- (4) Mirkovic, T.; Ostroumov, E. E.; Anna, J. M.; van Grondelle, R. Light Absorption and Energy Transfer in the Antenna Complexes of Photosynthetic Organisms. *Chem. Rev.* **2017**, *117*, 249–293.
- (5) Croce, R.; van Amerongen, H. Natural Strategies for Photosynthetic Light Harvesting. *Nat. Chem. Biol.* **2014**, *10*, 492–501.
- (6) Kundu, S.; Patra, A. Nanoscale Strategies for Light Harvesting. *Chem. Rev.* **2017**, *117*, 712–757.
- (7) Wu, L.; Huang, C.; Emery, B. P.; Sedgwick, A. C.; Bull, S. D.; He, X.-P.; Tian, H.; Yoon, J.; Sessler, J. L.; James, T. D. Förster Resonance Energy Transfer (FRET)-Based Small-Molecule Sensors and Imaging Agents. *Chem. Soc. Rev.* **2020**, *49*, 5110–5139.
- (8) Prevo, B.; Peterman, E. J. Förster Resonance Energy Transfer and Kinesin Motor Proteins. *Chem. Soc. Rev.* **2014**, *43*, 1144–1155.
- (9) Teunissen, A. J.; Pérez-Medina, C.; Meijerink, A.; Mulder, W. J. Investigating Supramolecular Systems Using Förster Resonance Energy Transfer. *Chem. Soc. Rev.* **2018**, *47*, 7027–7044.
- (10) Peng, H.-Q.; Niu, L.-Y.; Chen, Y.-Z.; Wu, L.-Z.; Tung, C.-H.; Yang, Q.-Z. Biological Applications of Supramolecular Assemblies Designed for Excitation Energy Transfer. *Chem. Rev.* **2015**, *115*, 7502–7542.
- (11) Park, J. M.; Hong, K.-I.; Lee, H.; Jang, W.-D. Bioinspired Applications of Porphyrin Derivatives. *Acc. Chem. Res.* **2021**, *54*, 2249–2260.
- (12) Tan, Y. X.; Zhang, X.; Wang, Y. B.; Yao, J. N. Molecular Assembly of Functional Motifs for Artificial Photosynthesis. *Acc. Mater. Res.* **2024**, *5*, 1377–1387.
- (13) Jiao, H. M.; Wang, C.; Xiong, L. Q.; Tang, J. W. Insights on Carbon Neutrality by Photocatalytic Conversion of Small Molecules into Value-Added Chemicals or Fuels. *Acc. Mater. Res.* **2022**, *3*, 1206–1219.
- (14) Qiu, X.; Xu, J.; Cardoso Dos Santos, M.; Hildebrandt, N. Multiplexed Biosensing and Bioimaging Using Lanthanide-Based Time-Gated Förster Resonance Energy Transfer. *Acc. Chem. Res.* **2022**, *55*, 551–564.
- (15) Zhang, L.; Gao, J.; Qi, A.; Gao, Y. A Novel DRET and FRET Combined Fluorescent Molecule and its Applications in Sensing and Bioimaging. *Sensor. Actuat. B-Chem.* **2020**, *320*, No. 128457.
- (16) Zhang, M.; Lu, M.; Lang, Z. L.; Liu, J.; Liu, M.; Chang, J. N.; Li, L. Y.; Shang, L. J.; Wang, M.; Li, S. L. Semiconductor/Covalent-Organic-Framework Z-Scheme Heterojunctions for Artificial Photosynthesis. *Angew. Chem., Int. Ed.* **2020**, *132*, 6562–6568.
- (17) Hao, M.; Sun, G.; Zuo, M.; Xu, Z.; Chen, Y.; Hu, X. Y.; Wang, L. A Supramolecular Artificial Light-Harvesting System with Two-Step Sequential Energy Transfer for Photochemical Catalysis. *Angew. Chem., Int. Ed.* **2020**, *132*, 10181–10186.
- (18) Bryant, D. A.; Canniffe, D. P. How Nature Designs Light-Harvesting Antenna Systems: Design Principles and Functional Realization in Chlorophototrophic Prokaryotes. *J. Phys. B-At. Mol. Opt.* **2018**, *51*, No. 033001.
- (19) Ensslen, P.; Wagenknecht, H.-A. One-Dimensional Multichromophore Arrays Based on DNA: From Self-Assembly to Light-Harvesting. *Acc. Chem. Res.* **2015**, *48*, 2724–2733.
- (20) Kumar, A.; Saha, R.; Mukherjee, P. S. Self-assembled Metal-supramolecular Cages towards Light Harvesting Systems for Oxidative Cyclization. *Chem. Sci.* **2021**, *12*, 5319–5329.
- (21) Liu, Y.; Jin, J.; Deng, H.; Li, K.; Zheng, Y.; Yu, C.; Zhou, Y. Protein-Framed Multi-Porphyrin Micelles for a Hybrid Natural–Artificial Light-Harvesting Nanosystem. *Angew. Chem., Int. Ed.* **2016**, *55*, 7952–7957.
- (22) Guo, S.; Song, Y.; He, Y.; Hu, X. Y.; Wang, L. Highly Efficient Artificial Light-Harvesting Systems Constructed in Aqueous Solution Based on Supramolecular Self-Assembly. *Angew. Chem., Int. Ed.* **2018**, *57*, 3163–3167.
- (23) Chen, P. Z.; Weng, Y. X.; Niu, L. Y.; Chen, Y. Z.; Wu, L. Z.; Tung, C. H.; Yang, Q. Z. Light-Harvesting Systems Based on Organic Nanocrystals To Mimic Chlorosomes. *Angew. Chem., Int. Ed.* **2016**, *55*, 2759–2763.
- (24) Shi, B.; Li, X.; Chai, Y.; Qin, P.; Zhou, Y.; Qu, W.-J.; Lin, Q.; Wei, T.-B.; Sun, Y.; Stang, P. J. Platinum Metacycle-Based Molecular Recognition: Establishment and Application in Spontaneous Formation of a [2]Rotaxane with Light-Harvesting Property. *Angew. Chem., Int. Ed.* **2023**, *62* (31), No. e202305767.
- (25) Li, H.; Yang, J.; Li, D.; Li, X.; Li, J.; He, C. Host-Guest Approach to Promoting Photocatalysis Based on Consecutive Photo-Induced Electron-Transfer Processes via Efficient Förster Resonance Energy Transfer. *Angew. Chem., Int. Ed.* **2024**, *63* (37), No. e202409094.
- (26) Han, Y.; Zhang, X.; Ge, Z.; Gao, Z.; Liao, R.; Wang, F. A bioinspired sequential energy transfer system constructed via supramolecular copolymerization. *Nat. Commun.* **2022**, *13* (1), 3546.
- (27) Mu, B.; Hao, X.; Luo, X.; Yang, Z.; Lu, H.; Tian, W. Bioinspired polymeric supramolecular columns as efficient yet controllable artificial light-harvesting platform. *Nat. Commun.* **2024**, *15* (1), 903.
- (28) Wang, Y.; Ma, C.-Q.; Li, X.-L.; Dong, R.-Z.; Liu, H.; Wang, R.-Z.; Yu, S.; Xing, L.-B. A novel strategy of constructing an artificial light-harvesting system based on a supramolecular organic framework for photocatalysis. *J. Mater. Chem. A* **2023**, *11* (6), 2627–2633.
- (29) Bai, Y.; Luo, Q.; Liu, J. Q. Protein Self-Assembly via Supramolecular Strategies. *Chem. Soc. Rev.* **2016**, *45*, 2756–2767.
- (30) Nakamura, H. Roles of Electrostatic Interaction in Proteins. *Q. Rev. Biophys.* **1996**, *29*, 1–90.
- (31) Miao, L.; Han, J.; Zhang, H.; Zhao, L.; Si, C.; Zhang, X.; Hou, C.; Luo, Q.; Xu, J.; Liu, J. Q. Quantum-Dot-Induced Self-Assembly of Cricoid Protein for Light Harvesting. *ACS Nano* **2014**, *8*, 3743–3751.
- (32) Sun, H.; Miao, L.; Li, J.; Fu, S.; An, G.; Si, C.; Dong, Z.; Luo, Q.; Yu, S.; Xu, J.; Liu, J. Q. Self-Assembly of Cricoid Proteins Induced by “Soft Nanoparticles”: An Approach To Design Multienzyme-Cooperative Antioxidative Systems. *ACS Nano* **2015**, *9*, 5461–5469.
- (33) Sun, H.; Zhang, X.; Miao, L.; Zhao, L.; Luo, Q.; Xu, J.; Liu, J. Q. Micelle-Induced Self-Assembling Protein Nanowires: Versatile Supramolecular Scaffolds for Designing the Light-Harvesting System. *ACS Nano* **2016**, *10*, 421–428.
- (34) Hu, Q.-D.; Tang, G.-P.; Chu, P. K. Cyclodextrin-Based Host–Guest Supramolecular Nanoparticles for Delivery: From Design to Applications. *Acc. Chem. Res.* **2014**, *47*, 2017–2025.
- (35) Guo, D.-S.; Liu, Y. Calixarene-Based Supramolecular Polymerization in Solution. *Chem. Soc. Rev.* **2012**, *41*, 5907–5921.
- (36) Liu, Z. X.; Chen, J. Y.; Li, C. J. Biphenylarene-Based Supramolecular Materials. *Acc. Mater. Res.* **2025**, *6*, 765–778.
- (37) Hou, C.; Li, J.; Zhao, L.; Zhang, W.; Luo, Q.; Dong, Z.; Xu, J.; Liu, J. Q. Construction of Protein Nanowires through Cucurbit[8]uril-based Highly Specific Host–Guest Interactions: An Approach to the Assembly of Functional Proteins. *Angew. Chem., Int. Ed.* **2013**, *52*, 5590–5593.
- (38) Zhang, W.; Luo, Q.; Miao, L.; Hou, C.; Bai, Y.; Dong, Z.; Xu, J.; Liu, J. Q. Self-assembly of Glutathione S-Transferase into Nanowires. *Nanoscale* **2012**, *4*, 5847–5851.
- (39) Bai, Y.; Luo, Q.; Zhang, W.; Miao, L.; Xu, J.; Li, H.; Liu, J. Q. Highly Ordered Protein Nanorings Designed by Accurate Control of Glutathione S-Transferase Self-Assembly. *J. Am. Chem. Soc.* **2013**, *135*, 10966–10969.
- (40) Wang, X.; Hu, J.; Zhang, G.; Liu, S. Highly Selective Fluorogenic Multianalyte Biosensors Constructed via Enzyme-Catalyzed Coupling and Aggregation-Induced Emission. *J. Am. Chem. Soc.* **2014**, *136*, 9890–9893.
- (41) Li, X.; Bai, Y.; Huang, Z.; Si, C.; Dong, Z.; Luo, Q.; Liu, J. Q. A Highly Controllable Protein Self-Assembly System with Morphological Versatility Induced by Reengineered Host–Guest Interactions. *Nanoscale* **2017**, *9*, 7991–7997.

- (42) Wang, R.; Qiao, S.; Zhao, L.; Hou, C.; Li, X.; Liu, Y.; Luo, Q.; Xu, J.; Li, H.; Liu, J. Q. Dynamic Protein Self-Assembly Driven by Host–Guest Chemistry and the Folding–Unfolding Feature of a Mutually Exclusive Protein. *Chem. Commun.* **2017**, 53, 10532–10535.
- (43) Hou, C.; Luo, Q.; Liu, J.; Miao, L.; Zhang, C.; Gao, Y.; Zhang, X.; Xu, J.; Dong, Z.; Liu, J. Q. Construction of GPx Active Centers on Natural Protein Nanodisk/Nanotube: A New Way to Develop Artificial Nanoenzyme. *ACS Nano* **2012**, 6, 8692–8701.
- (44) Miao, L.; Fan, Q.; Zhao, L.; Qiao, Q.; Zhang, X.; Hou, C.; Xu, J.; Luo, Q.; Liu, J. Q. The Construction of Functional Protein Nanotubes by Small Molecule-Induced Self-Assembly of Cricoid Proteins. *Chem. Commun.* **2016**, 52, 4092–4095.
- (45) Zhao, L.; Li, Y.; Wang, T.; Qiao, S.; Li, X.; Wang, R.; Luo, Q.; Hou, C.; Xu, J.; Liu, J. Q. Photocontrolled Protein Assembly for Constructing Programmed Two-Dimensional Nanomaterials. *J. Mater. Chem. B* **2018**, 6, 75–83.
- (46) Li, X.; Tian, R.; Ji, Y.; Liu, S.; Jiang, X.; Li, F.; Luo, Q.; Hou, C.; Xu, J.; Liu, J. Q. Construction of Ultralarge Two-Dimensional Fluorescent Protein Arrays via a Reengineered Rhodamine B-Based Molecular Tool. *ACS Macro Lett.* **2021**, 10, 307–311.
- (47) Wang, T.; Fan, X.; Li, R.; Xu, J.; Liu, J. Q. Multi-Enzyme-Synergetic Ultrathin Protein Nanosheets Display High Efficient and Switch on/off Antibacterial Activities. *Chem. Eng. J.* **2021**, 416, No. 129082.
- (48) Li, R.; Xu, J.; Wang, T.; Wang, L.; Li, F.; Liu, S.; Jiang, X.; Luo, Q.; Liu, J. Q. Dynamically Tunable Ultrathin Protein Membranes for Controlled Molecular Separation. *ACS Appl. Mater. Interfaces* **2021**, 13, 12359–12365.
- (49) Wang, T.; Xu, J.; Fan, X.; Yan, X.; Yao, D.; Li, R.; Liu, S.; Li, X.; Liu, J. Q. Giant “Breathing” Proteinosomes with Jellyfish-like Property. *ACS Appl. Mater. Interfaces* **2019**, 11, 47619–47624.
- (50) Zhang, R.; Lee, D. M.; Jimah, J. R.; Gerassimov, N.; Yang, C.; Kim, S.; Luvsanjav, D.; Winkelman, J.; Mettlen, M.; Abrams, M. E.; Kalia, R.; Keene, P.; Pandey, P.; Ravoux, B.; Kim, J. H.; Ditlev, J. A.; Zhang, G.; Rosen, M. K.; Frost, A.; Alto, N. M.; Gardel, M.; Schmid, S. L.; Svitkina, T. M.; Hinshaw, J. E.; Chen, E. H. Dynamin Regulates the Dynamics and Mechanical Strength of the Actin Cytoskeleton as a Multifilament Actin-Bundling Protein. *Nat. Cell Biol.* **2020**, 22 (6), 674–688.
- (51) Xiao, Y.; Zhang, T.; Zhou, M.; Weng, Z. Disassembly of 2D Vertical Heterostructures. *Adv. Mater.* **2019**, 31, No. 1805976.
- (52) Pena-Francesch, A.; Jung, H.; Demirel, M. C.; Sitti, M. Biosynthetic Self-Healing Materials for Soft Machines. *Nat. Mater.* **2020**, 19, 1230–1235.
- (53) Si, C.; Li, J.; Luo, Q.; Hou, C.; Pan, T.; Li, H.; Liu, J. Q. An Ion Signal Responsive Dynamic Protein Nano-Spring Constructed by High Ordered Host–Guest Recognition. *Chem. Commun.* **2016**, 52, 2924–2927.
- (54) Li, Y.; Zhao, L.; Chen, H.; Tian, R.; Li, F.; Luo, Q.; Xu, J.; Hou, C.; Liu, J. Q. Hierarchical Protein Self-Assembly into Dynamically Controlled 2D Nanoarrays via Host–Guest Chemistry. *Chem. Commun.* **2021**, 57, 10620–10623.
- (55) Pan, T.; Liu, Y.; Sun, H.; Xu, J.; Liu, J. Q. Reversible Switch of a Selenium-Containing Antioxidant System Regulated by Protein Assembly. *ACS Catal.* **2020**, 10, 9735–9740.
- (56) Wang, T. T.; Fan, X. T.; Xu, J. Y.; Li, R. Y.; Yan, X.; Liu, S. D.; Jiang, X. J.; Li, F.; Liu, J. Q. Giant Proteinosomes As Scaffolds for Light Harvesting. *ACS Macro Lett.* **2019**, 8, 1128–1132.
- (57) Heater, B.; Yang, Z.; Lee, M.; Chan, M. K. In Vivo Enzyme Entrapment in a Protein Crystal. *J. Am. Chem. Soc.* **2020**, 142, 9879–9883.
- (58) McCoy, K.; Uchida, M.; Lee, B.; Douglas, T. Templated Assembly of a Functional Ordered Protein Macromolecular Framework from P22 Virus-Like Particles. *ACS Nano* **2018**, 12, 3541–3550.
- (59) Li, Y. J.; Tian, R. Z.; Xu, J. Y.; Wang, T. T.; Fan, X. T.; Liu, J. Q. Engineered Self-Assembled Protein Nanosheets for in Situ Biosynthesis of Peptide Anchored Protein-Semiconductor Hybrids for Efficient Hydrogen Production. *Appl. Catal. B Environ.* **2025**, 362, No. 124764.



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