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Recent advances in DNA nanotechnology

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DNA is a powerful guiding molecule to achieve the precise construction of arbitrary structures and high-resolution organization of functional materials. The combination of sequence programmability, rigidity and highly specific molecular recognition in this molecule has resulted in a wide range of exquisitely designed DNA frameworks. To date, the impressive potential of DNA nanomaterials has been demonstrated from fundamental research to technological advancements in materials science and biomedicine. This review presents a summary of some of the most recent developments in structural DNA nanotechnology regarding new assembly approaches and efforts in translating DNA nanomaterials into practical use. Recent work on incorporating blunt-end stacking and hydrophobic interactions as orthogonal instruction rules in DNA assembly, and several emerging applications of DNA nanomaterials will also be highlighted.

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Introduction

DNA nanotechnology has provided a powerful tool to create objects with arbitrary control of size and shape as well as high templating potential [1•]. From a structural perspective, the rigid, well-defined DNA duplex makes it suitable as a building block for nanoscale to microscale constructions with high spatial resolution. Importantly, the hybridization between DNA single strands is sequence-dependent and highly selective, allowing the programmable connection of DNA duplexes into a user-defined pattern. The unique sequences of DNA strands that constitute a DNA object also provide a precise 'address' to site-specifically position functional materials with high precision on the nanometer scale.

It is of note that Watson–Crick base-pairing is employed as the only assembly language in most of DNA nanomaterials. Because it is limited to four DNA bases, more complicated designs require a large number of unique DNA sequences for their construction. In addition to issues of cost, scalability and complexity for *in vivo* applications, this can result in increased assembly errors, potentially lowering product yields. As chemists, a powerful approach to address this limitation is to combine the toolbox of supramolecular chemistry with DNA nanotechnology. This has expanded the repertoire of DNA assembly languages and resulted in new structural and functional complexity without the need to increase the number of assembly components [1•,2].

Over the past 30 years, the fascinating aspects of DNA nanomaterials altogether have allowed their use to greatly advance research in many fields. The scope of this review is to provide a brief overview of the most recent trends in DNA assembly's design and scalability, followed by the recent progress in incorporating additional supramolecular interactions (blunt-end stacking and hydrophobic interactions) as orthogonal assembly languages in DNA assembly. In the last section, some selected applications of DNA nanotechnology will be covered.

Structural DNA assembly

New approaches for DNA nanostructure assembly

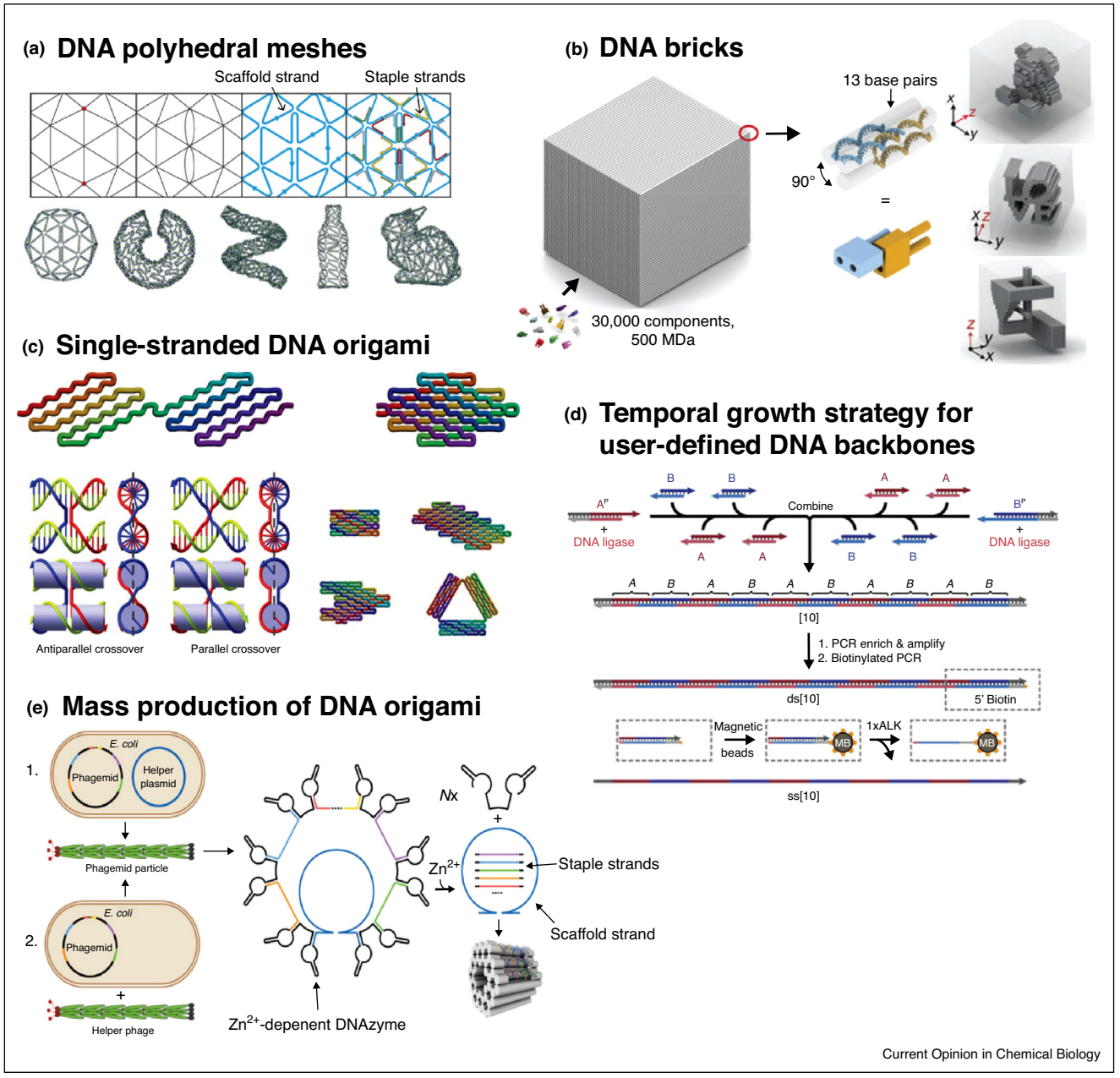
Following the lead of the first DNA objects reported by Seeman and co-workers in 1991 [3], an enormous library of well-defined DNA structures ranging from monodisperse discrete DNA nanostructures to extended DNA arrays has been generated, along with the development of new DNA assembly approaches. Recent trends have attempted to expand the complexity of an object that one can create. We direct the readers who are interested in a detailed progress to the more comprehensive reviews [1•,4•].

The invention of DNA origami by Rothemund in 2006 has revolutionized the field by offering an opportunity to create large, arbitrary 2D DNA-dense nanostructures [5••]. This approach is based on the folding of a long DNA single strand into a specific shape, guided by hundreds of short DNA single strands. Since then, progress towards 3D construction has been made, which significantly increased the complexity of DNA nanostructures and allowed DNA origami to be one of the most widely used approaches by many research groups [4•]. As an interesting example of new folding strategies, Högberg and co-workers applied graph theory to create wireframe DNA origami, where a 3D desired object (e.g., a Stanford bunny) was converted into a polyhedral triangulated

mesh [6]. A long DNA scaffold was routed on this 3D mesh, which was then folded by multiple short, unique DNA single strands, thus replacing all polygonal edges by DNA helices (Figure 1a).

Yin and co-workers introduced a scaffold-free concept called DNA bricks assembly [7•] and they recently demonstrated that up to 1 giga-dalton DNA nanostructures can be assembled from ~10^4 unique brick components, the highest complexity achieved to date [8]. These bricks are DNA single strands with four binding domains designed to form staggered duplexes with neighboring DNA bricks, creating 3D DNA arrays (Figure 1b). Analogous to Lego bricks, this approach allows a user to create an object by selecting a set of DNA bricks that define the overall shape of the target structure.

Figure 1



Structural DNA assembly. **(a)** Scaffold-based assembly of 3D wireframe origami based on polyhedral-mesh strategy [6]. **(b)** Scaffold-free 3D assembly by using multiple unique DNA brick components [8]. **(c)** The folding of 2D DNA origami from a long DNA single strand, following the parallel crossover design principle [9]. **(d)** Temporal growth strategy for the production of long DNA single strands with user-defined sequence patterns [15]. **(e)** Bacteriophage-based mass production of DNA-strand components for DNA origami assembly [21•].