approach well-known in computer graphics. The algorithm routes the scaffold along the Eulerian meshwork and adds the staple strands to the design. Before the actual 'staple strand' sequences are computed, a physical model is generated to understand whether there is undesirable steric strain in the structure that requires relaxation. The authors showed the feasibility of their semi-automated '3D printing' technique by producing several fascinating DNA structures with spherical topologies, such as the nanosized 'Stanford bunny'. Recently, the same laboratory extended their method by creating two-dimensional DNA shapes derived from the flat-sheet triangulated meshes[8].

Now, in the next step, Bathe and colleagues[1] present an algorithm that reduces human input to a minimum and can create DNA nanostructures with a greater diversity of sizes, edge lengths and topologies. The fully automated procedure is named DAEDALUS (DNA origami sequence design algorithm for user-defined structures) after the virtuoso craftsman and the creator of labyrinths in Greek mythology.

In brief, the procedure starts by representing the target structure as a polyhedral mesh and computing the corresponding 3D graph (step i) and the 'spanning tree' (step ii). The spanning tree algorithm routes the linear scaffold strand through the target shape with an Eulerian circuit (step iii) and finally generates staple strand sequences (step iv) for sealing the origami structure (**Fig. 1a**). The wireframe motif is based on two interconnected DNA double helices (i.e., double-crossover (DX) molecules), allowing more structural robustness than the previously reported top-down objects with single duplex edges[7]. After designing the shape and obtaining the sequences, researchers fabricate the structures using standard annealing routines. The DAEDALUS software (http://daedalus-dna-origami.org/) not only generates a list of staple strands but also produces atomistic models of the designed structures, whereas the CanDo software (http://cando-dna-origami.org/)[5,6] can be used to simulate shapes of the objects in aqueous solution.

Bathe and colleagues[1] demonstrate the power of DAEDALUS by creating numerous Platonic, Archimedean, Johnson and Catalan solids as well as objects with higher structural complexity, such as asymmetric constructs and polyhedra with non-spherical topologies (**Fig. 1b**). They also show how to produce linear scaffold strands of the required sequence and length by a facile asymmetric PCR. The scaffolds they use are shorter or longer than the conventional M13 phage DNA—a circular strand that has a proven track record as a suitable scaffold[3] but that is strictly fixed in size (7,249 nucleotides). Custom-length scaffolds that minimize the excess of single-stranded DNA may help increase folding yields and structural integrity in low-salt conditions.

The authors verify that 45 different shapes are correctly folded using atomic force microscopy and single-particle cryo-electron microscopy, further supported by 3D reconstruction compared to model predictions. These studies also reveal detailed structural features, such as the chirality of the vertex twist. The scaffold routing is counter-clockwise around each face due to the preference of the DNA major groove to point inwards at vertices, and indeed, the cryo-electron microscopy reconstructions confirm this expected geometry. Interestingly, the objects can be folded in the presence of low concentrations of cations (magnesium or sodium) and in phosphate-buffered saline alone. The reported constructs are stable in phosphate-buffered saline and in other cell-compatible buffers (e.g., Dulbecco's Modified Eagle Media with fetal bovine serum) for up to 6 h, an important prerequisite for any biological application[9].

Although the above results indicate that relatively stable wireframe DNA objects can be designed and synthesized, a goal for future work will be to increase the durability of structures for certain implementations. Along these lines, the authors speculate that further generalizations of their technique could include edge design with arbitrary cross-sections. This feature would make structures mechanically sturdier and help in obtaining closed-surface topologies, which are needed, for example, to encapsulate cargo in DNA containers[10]. Another intriguing route toward *in vivo* applications would be to develop automated methods for genetically encoding DNA nanostructures in order to synthesize them in living cells.

Overall, the work of Bathe and colleagues[1] adds to a growing body of research that is broadening the structural diversity of DNA nanostructures. Various applications of the technology are already beginning to emerge. For example, the structural similarities between rigid, cage-like DNA nanostructures and virus particles or other protein cages suggest approaches in which nanostructures decorated with appropriate targeting peptides are used to deliver drugs to particular cell types or to trigger immune responses[9,10] (**Fig. 1c**).

But it is perhaps in the area of materials engineering that the majority of near-term applications lie. Rigid, closed DNA nanostructures might serve, for instance, as 'molds' for the production of custom-shaped metal nanoparticles[11] (**Fig. 1c**). In fact, because they offer such an astoundingly high degree of structural order—similar to that found in proteins[3]—DNA nanostructures may also find use as scaffolds for precisely positioning other pivotal molecules, such as catalytic enzymes. As methods such as DAEDALUS move us closer to the *in silico* design of ever more complex DNA nanostructures at atomic resolution, the era of fully programmable nanoscale materials comes increasingly into view[4].

COMPETING FINANCIAL INTERESTS
The authors declare no competing financial interests.

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