DNA-PROTEIN NANOSTRUCTURES SELF-ASSEMBLED WITH MOLECULAR PRECISION

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Self-assembly is a fundamental feature of biological systems, but has been difficult to replicate in synthetic structures, which typically form under near-equilibrium, diffusion-limited, conditions. DNA-mediated self-assembly is a powerful method with which to build multi-functional, molecularly-addressable nanostructures of arbitrary shape. Recent developments in DNA nanostructure fabrication have expanded the design space, but fabrication based on DNA alone can suffer from low yields and is constrained by the need to strike a balance between mechanical rigidity and size. We have developed a two-stage, hierarchical self-assembly process, to create structures that are otherwise impossible to make. We first use DNA polymerase to create double-stranded DNA sections on a single-stranded template. Single-stranded DNA sections are then folded into a mechanically flexible skeleton by the origami method. This process directs the large-scale geometry and shapes the structure at the nanoscale. The DNA skeleton subsequently guides the cooperative assembly of RecA protein filaments, which provide rigidity at the micrometer scale. The self-assembly toolbox is thus expanded by blending sequence-specific and structure-specific elements, enabling us to produce micrometer-scale, rigid, molecularly-addressable structures. Our results indicate that, more generally, the scale of finite-size self-assembling systems can be increased by minimizing the number of unique components and instead relying on generic components to construct a framework that supports the functional units.

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