DNA-PROTEIN NANOCOMPOSITES: MICROSCALE STRUCTURES WITH MOLECULAR PRECISION

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DNA is unique in its programmability and addressability. The ability of complementary sequences of DNA to recognize and bind to each other makes it an almost universal tool for controlling the assembly of nanoscale objects over small distances. DNA origami [1] is a particularly powerful self-assembly approach, serving to create breadboards on which to assemble nanostructures, but is limited to length scales below 100 nm. Attempts to extend its spatial scale lead to structures that assemble with poor yields, and for which size and mechanical rigidity must be traded off against one another. Here, we present a new paradigm for producing large, micrometer-scale structures, whilst maintaining the precision and programmability offered by DNA. We show that poor yields are a result of having too many unique components in the self-assembling system [2], and that poor mechanical rigidity is an intrinsic limitation of DNA. We overcome these limitations by using *RecA*, a DNA-binding protein, to increase the stiffness of our DNA nanostructures. The composite *RecA*-DNA structure has a persistence length almost an order of magnitude greater than that of double-stranded DNA (dsDNA) alone. *RecA* also acts as a generic component in our self-assembly scheme, since it binds in a non-sequence specific way to dsDNA. In addition, once one *RecA* monomer binds to dsDNA, the binding probability for other monomers increases. This cooperative binding feature means that any region of dsDNA becomes completely and uniformly coated with protein with almost perfect yield. We can thus build large, rigid structures in this way. To maintain our ability to address the structure with molecular precision, we create small origami breadboards at specific locations within the larger structure. In this way, we minimize the number of unique components involved in the assembly process, and therefore the number of pathways by which an incorrect structure can form. Our approach enables us to create micrometer-scale structures with molecular precision [4].

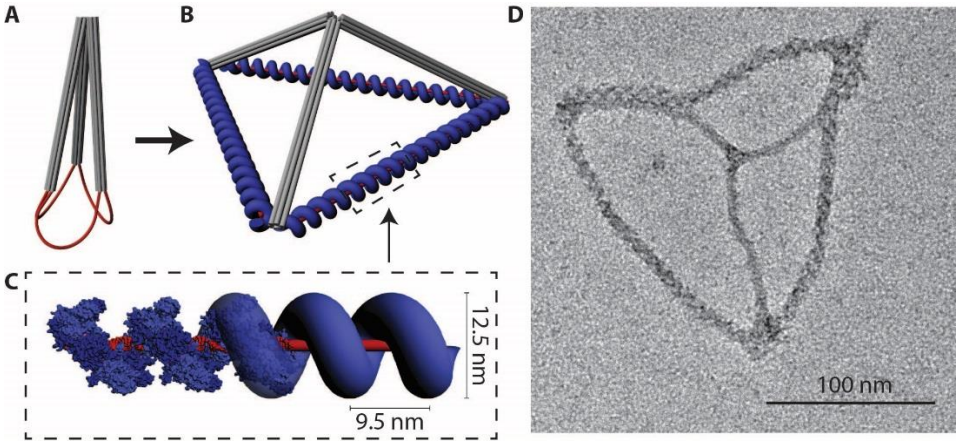

Figure 1. Tetrahedron formation by RecA protein filament assembly. 3D model of a DNA tripod before (A) and after (B) RecA assembly. (C) RecA filament model based on crystal structure from protein data bank entry 3CMX. [3] (D) TEM image of RecA rigidified tetrahedron.

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