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Artificial synthesis of supramolecular protein structures

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Large multi-subunit protein complexes self-assemble spontaneously yet do not prematurely form unwanted aggregates. Static snapshots of intact complexes or component parts provide little insight into how this occurs. We combine high-resolution crystal structures combined with small-angle X-ray scattering and in vivo biochemical crosslinking, to elucidate a structural and thermodynamic mechanism for the controlled synthesis of the bacterial flagellar motor, a biological motor consisting of hundreds of subunits that can rotate at over 1300 Hz. The mechanism describes how a structural template can trigger and guide the self-polymerisation of one subunit via a domain-swap mechanism during assembly. Here we describe our efforts to replicate this process in vitro by replacing the natural scaffold with synthetic scaffolds constructed from DNA origami. By observing the kinetics of artificial synthesis with bulk and single molecule methods, we can probe fundamental questions about supramolecular protein complex assembly in biology.

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