Hierarchical assembly is more robust than egalitarian assembly in synthetic capsids

Seth Fraden

1. Abstract

Self-assembly of complex and functional materials remains a grand challenge in soft material science. Efficient assembly depends on a delicate balance between thermodynamic and kinetic effects, requiring fine-tuning affinities and concentrations of subunits. By contrast, we introduce an assembly paradigm that allows large error-tolerance in the subunit affinity and helps avoid kinetic traps. Our combined experimental and computational approach uses a model system of triangular subunits programmed to assemble into T=3 icosahedral capsids comprising 60 units. The experimental platform uses DNA origami to create monodisperse colloids whose 3D geometry is controlled to nanometer precision with two distinct bonds whose affinities are controlled to k_BT precision, quantified in situ by static light scattering. The computational model uses a coarse-grained representation of subunits, short-ranged potentials, and Langevin dynamics. Experimental observations and modeling reveal that when the bond affinities are unequal, two distinct hierarchical assembly pathways, in which the subunits first form dimers in one case, and pentamers in another, produce complete capsids faster. Such hierarchical pathways are more robust against affinity variation than egalitarian pathways, in which all binding sites have equal strengths. This finding suggests that hierarchical assembly may be a general engineering principle for optimizing self-assembly of complex target structures.