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Using Symmetry to Design Self-Assembling Protein Cages and Nanomaterials on the Mid-Nanometer Scale

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Self-assembling molecular structures having diverse cellular functions are widespread in nature. Some of the largest and most sophisticated types are built from many copies of the same or similar protein molecules arranged following principles of symmetry. A long-standing engineering goal has been to design novel protein molecules to self-assemble into geometrically specific structures similar to the extraordinary structures that have evolved in Nature. Practical routes to this goal have been developed by using ideas in symmetry to articulate the minimum design requirements for achieving various types of symmetric architectures, including cages, extended two-dimensional layers, and three-dimensional crystalline materials. The key requirement is that two distinct self-associating interfaces, each conferring one element of rotational symmetry, have to be engineered into the protein molecule (or molecules), following particular geometric specifications. The main principle is that combining two separate symmetry elements into a single molecular entity produces a molecule that necessarily assembles into an architecture dictated by a symmetry group that is the product of the two simpler contributing symmetries. Recent experiments have demonstrated success using a variety of symmetry-based strategies. Strategic variations are emerging that differ from each other with respect to biophysical features such as flexibility vs rigidity in the assembled structures, and with respect to design aspects such as whether the protein interfaces are inherited from natural oligomeric proteins or are designed de novo by advanced computational methods. The success of these strategies has been proven by determining crystal structures of several giant, self-assembling protein cages and clusters (10-25 nm in diameter), created by design. The ability to create sophisticated supramolecular structures from designed protein subunits opens the way to broad applications in synthetic biology and nanotechnology.