VIRUS CAPSIDS: CONSTRAINED ORGANIC ARCHITECTURES FOR NANOMATERIALS SYNTHESIS

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In nature, proteins orchestrate the formation of elaborate inorganic 'biomineralized' structures. The single-celled algae, *Emiliania huxleyi*, form intricate calcium carbonate ($CaCO_3$) structures called coccoliths (Figure 1A) whereas synthetic preparations of $CaCO_3$ result in a far more limited range of morphologies, by comparison. Coccolith formation is controlled by proteins that direct the nucleation and assembly of crystallites into intricate 3D assemblies. The degree of control exhibited by this and other natural biomineral systems is an inspiration for material scientists.

Viral capsids are also naturally occurring, intricate assemblies that serve to house, protect, and deliver nucleic acid genomes to specific host cells. Their structures must be robust enough to survive diverse conditions yet sufficiently dynamic to release their genome into host cells. Proteins are the building blocks of viral capsids and protein-protein interactions dictate their 3D structure. Typically, protein motifs on the interior are involved in packaging nucleic acid whereas those on the exterior are involved with cell recognition and attachment. Viral capsids devoid of their nucleic acid genomes can be thought of as "nanocontainers" [1]. The diversity of these nanocontainers is seemingly endless, since viruses are ubiquitous with life. An illustration of this functional organic architecture is the *Sulfolobus* turreted icosahedral virus (STIV), isolated from the acidic hot (>90°C) springs of Yellowstone National Park (YNP), which presents elaborate turret-like structures on its exterior [2] (Figure 1B). Both the coccolith and the archaeal virus are examples of naturally occurring 3D assemblies whose architecture is dictated by protein. Inspired by nature, we have selected a bio-mimetic approach to nanomaterials synthesis utilizing protein cage architectures to serve as size constrained reaction vessels and chemical building blocks [3-5].

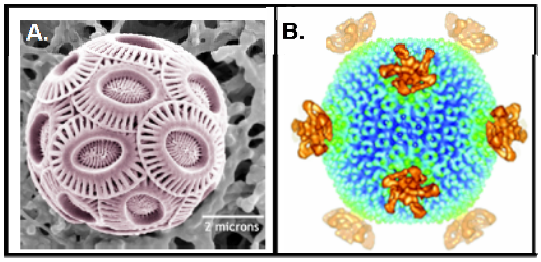

Figure 1. Biological Assemblies. A. *Emiliania huxleyi* formed $CaCO_3$ coccolith structures arranged in a coccosphere, ~ 6 mM in diameter. **B.** Cryo TEM image reconstruction of the ~ 74 nm diameter STIV capsid with turret-like projections extending from each of the 5-fold vertices.

Protein cage architectures, 10-100 nm diameter, are self-assembled hollow spheres derived from viruses and other biological cages including heat shock proteins (Hsp), DNA binding proteins from starved cells (Dps), and ferritins. These architectures play critical and biological roles and are similar in that they are all essentially proteinaceous containers with three distinct surfaces (interior, exterior, and subunit interface) to which one can impart synthetic function by design. Through a combination of genetic and chemical modifications the cages can be used to direct the nucleation of specific inorganic phases, the covalent attachment of organics, and the packaging of polymers in a size constrained manner. This has resulted in the formation of materials

with novel magnetic, catalytic and therapeutic properties. This presentation will highlight the demonstrated utility of protein cage architectures in nanotechnology with applications including magnetic nanoparticle synthesis and the development of targeted therapeutic and imaging delivery agents [6-10] (Figure 2).

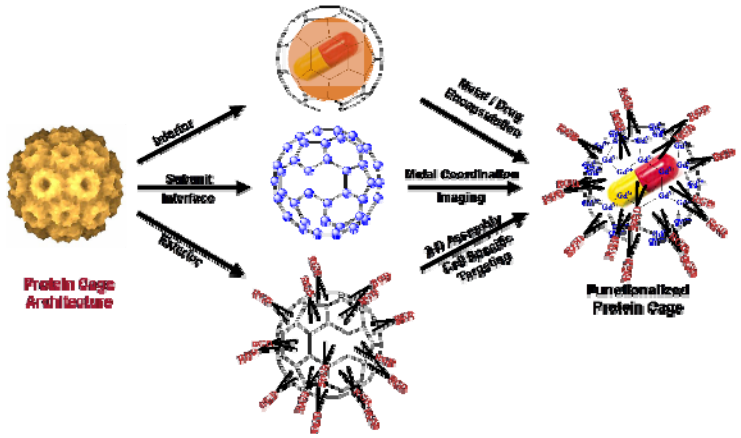

Figure 2. Schematic Representation of Protein Cage Functionalization. Protein cage architectures have three surfaces (interior, subunit interface, and exterior) amenable to both genetic and chemical modification.

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