Inspiration (and Perspiration) from Biology

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ABSTRACT The exquisite structures produced by biological systems provide inspiration for the fabrication of nanomaterials. We sometimes forget, however, that Nature can provide muscle while serving as a Muse—a wide array of nanosystems are produced biologically that can be used for the design of functional materials. At the 2007 Materials Research Society Fall Meeting in Boston, Symposium MM (Biomolecular and Biologically Inspired Interfaces and Assemblies) highlighted the synergy between researchers using biomaterials and those using nature as a model for synthetic and quasi-synthetic systems. The symposium was organized by Vincent Rotello, Paula Hammond, Molly Stevens, Jeffrey Tok, and Darrin Pochan, with support provided by the U.S. Army Research Office and the RSC journal *Soft Matter*, and featured over 70 talks and 75 posters.

Proteins provide an excellent example of a material that can serve both inspirational and utilitarian purposes. Proteins can be obtained directly from natural sources as well as through biotechnological methods, and they are hence readily available and quite "green". Moreover, proteins are inherently nanoscopic entities that can be employed for a variety of structural and functional purposes. As an example, there are a number of viruses and protein assemblies that provide hollow cages. These cages can be used for a wide variety of applications, including imaging, delivery, and the synthesis of functional nanomaterials.[1] Douglas and co-workers at Montana State University have demonstrated the use of ferritin as a highly efficient catalyst for the reduction of protons to hydrogen gas, a very promising process for the creation of "clean" fuels. Hydrogen production was provided by a multistep photoctalytic process, with proton reduction occurring on Pt clusters in the protein cage of ferritin. A key feature of this system was the stability of the ferritin catalyst, which could be employed at 85 °C with no loss of structure or activity.

The enormous variety of structures formed by proteins has made these biomolecules prototypes for a wide range of

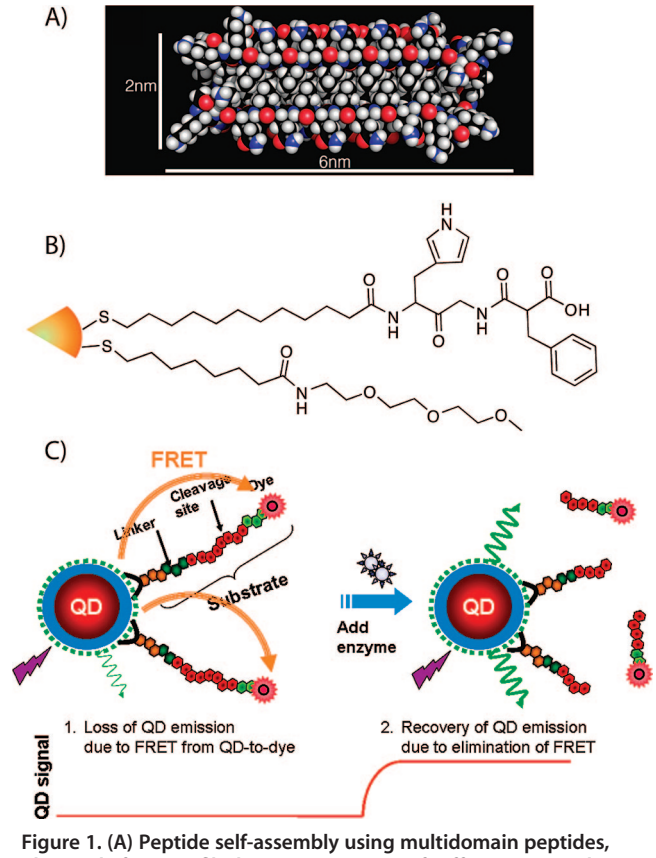

Figure 1. (A) Peptide self-assembly using multidomain peptides, ultimately forming fibrils. Image courtesy of Jeffrey Hartgerink. (B) Esterase model based on a peptide-functionalized nanoparticle scaffold. Image courtesy of Lucia Pasquato. (C) Sensing of protease activity using quantum dot−peptide−quencher assemblies. Image courtesy of Hedi Mattoussi.

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peptide-based and peptidomimetic systems. These systems can mimic extended structures such as collagen or discrete soluble proteins. Hartgerink and co-workers at Rice University have explored the self-assembly of short peptides into fibril hydrogels[2] that can be used to support cell proliferation and direct cell differentiation.[3] These multidomain peptides (Figure 1A) generate a hydrophobic stack of peptides in extended conformations that hydrogen bond with one another in β-sheet fashion to form extended fibrils. Nowick and co-workers from the University of California, Irvine, took an alternate path, engineering structural components common to both discrete soluble proteins and extended structures such as amyloid plaques. These studies used macrocyclic peptides featuring 54-membered rings that folded into *discrete* β-sheet structures that closely mimic native protein structure.[4]

In addition to their structural role, peptides can serve as both catalysts (*i.e.*, enzymes) and substrates for catalysis. An important feature of enzymatic catalysis is the highly evolved spatiotemporal proximity of the multiple functionalities required to effect the required transformations. Pasquato and co-workers from The University of Trieste have developed and characterized efficient catalysts that mimic esterase activity (Figure 1B). These systems feature peptide-functionalized side chains that exploit the pre-organization provided by the self-assembled monolayer to imitate the pre-organization of enzyme active sites.[5]

Proteases cleave peptides and are biomarkers for a number of diseases, including cancer. As such, peptides provide a logical starting point for the creation of protease sensors. The key is transducing the cleavage event. Mattoussi and colleagues at the Naval Research Laboratories used peptides as substrates to create extremely sensitive sensors for proteases (Figure 1C).[6] In these sensors, cleavage of the peptide releases the quencher from the quantum dot, generating fluorescence and providing a "turn-on" sensor.

VIRUS-BASED NANOASSEMBLIES

Viral capsids are large cages formed *via* self-assembly of proteins. Normally, the virus coat proteins assemble around nucleic acids, either DNA or RNA. Appropriate engineering of nanoparticle monolayers can be used to "trick" the protein subunits to assemble into capsids around nanoparticles instead of the normal anionic nucleic acid payload,[7] providing virus-like particles (VLPs). Dragnea and co-workers at Indiana University have used these VLPs to organize nanoparticles into crystalline arrays (Figure 2A).[8] They are exploring the application of VLPs in surface-enhanced Raman spectroscopy (SERS), a highly sensitive technique capable of identifying single molecules. The metallo-dielectric crystals formed from encapsidated gold nanoparticles exhibit surface-enhanced Raman emission when illuminated with a laser at 510 nm. However, as opposed to traditional SERS, the crystals emit uniformly from every location, with no random "hot spots" involved (Figure 2B), making them promising candidates for SERS-based sensors.

Moving from three dimensions to one, De Yoreo and co-workers at Lawrence Livermore National Laboratories described an effective strategy for the organization of genetically modified cow pea mosaic virus on linear templates. This strategy integrates top-down fabrication (scanning probe lithography) with bottom-up self-assembly (Figure 3). Interaction between the virus and the substrate was provided by nickel coordination between a histidine tag on the virus and a nitrilotriacetic acid ligand-functionalized alkanethiol on gold. The reversibility of the interaction results in a high degree of uniformity in viral packing relative to the authors' previous covalent linkage strategy,[9] opening up applications requiring structured one-dimensional assemblies.

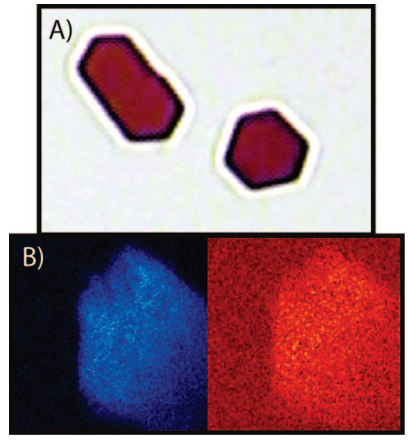

Figure 2. (A) 3D crystals of virus-like particles. (B) Scanning confocal Raman microscopy showing homogeneous emission from the entire sample, as opposed to "hot spots" found in standard SERS substrates. Images courtesy of Bogdan Dragnea.

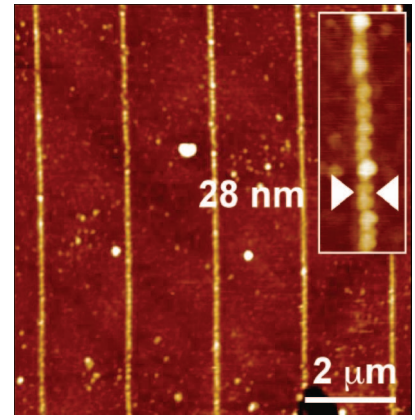

Figure 3. One-dimensional array of cow pea mosaic virus on a gold substrate patterned *via* scanning probe lithography. Image courtesy of Jim De Yoreo.

DNA-MEDIATED ASSEMBLIES

The high information content and unique structural properties of DNA make these systems attractive building blocks for materials. Seeman and colleagues at New York University demonstrated the use of a simple DNA motif to create a highly regular alternating array of 5 and 10 nm particles (Figure 4).[10] DNA is both a structural element and a therapeutic material for gene therapy. Lynn and co-workers at the University of Wisconsin elegantly integrated these two functions, describing new approaches to the assembly of ultrathin multilayered films.[11] These films provide tunable control over film erosion and thus control over the release of incorporated agents such as DNA in physiologically relevant environments.

A particularly elegant and effective approach to the creation of DNA-based

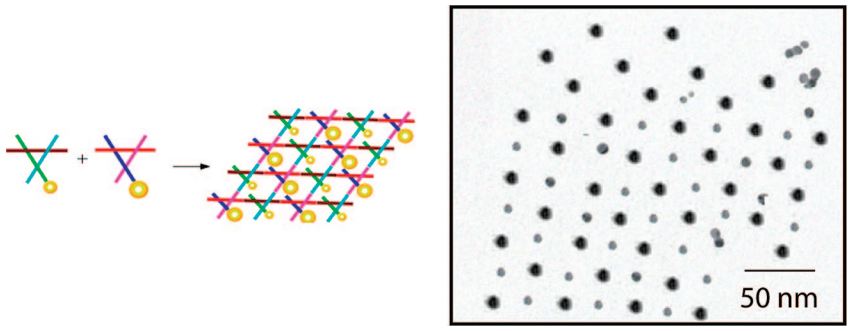

Figure 4. Alternating array of 5 and 10 nm nanoparticles formed *via* DNA-mediated self-assembly. Image courtesy of Nadrian Seeman.

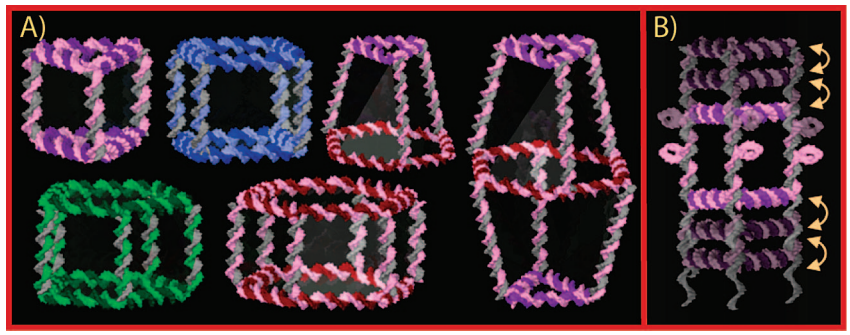

Figure 5. (A) Assembly of DNA polyhedra. (B) Adjustable prismatic cage whose length can be reversibly modulated from 5.2 to 8.9 nm through "unlooping". Image courtesy of Hanadi Sleiman.

dynamic nanostructures was provided by Sleiman from McGill University.[12] These cage-like structures used internal loops in the vertices in the polyhedral structures to create a system where multiple cage geometries and cage size could readily be switched, as demonstrated by fluorescence resonance energy transfer between appended fluorophores (Figure 5).

From these selected highlights, one can get a feel for the evolution of the interface between biology and nanoscience. Biomolecules provide both structural and functional elements that can be used to create new materials and devices. These systems also provide a level of complexity and preorganization that can be emulated using the tools of synthesis and self-assembly. As these two approaches mature and intermingle, other exciting methods and phenomena will undoubtedly emerge. The prospect of integrating synthetic and biological systems has already fueled a generation of science fiction writers; soon, we will be able to leave the "fiction" out and just have the science.

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