Nanoscience under Glass: The Versatile Chemistry of Silica Nanostructures

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ABSTRACT Silica nanoparticles and nanostructures provide an unprecedented materials platform to accomplish many nanoscale functions, and they offer a practical method for introducing multiple functionalities into the same nanoparticle. Much of the advances in silica nanochemistry are based on the condensation of tetraethylorthosilane, known as the Stöber synthesis. We discuss some unusual approaches for modifying and ultimately controlling the growth of silica nanostructures, from microgravity studies to advances in biomimetic synthesis and a novel peptide-based templating approach.

Silane-based chemistry may be one of the lesser-sung heroes of nanoscience, but undeservedly so. When compared to many types of nanostructures that have become the essential components of the nanoassembler's toolkit, such as semiconductor quantum dots, plasmonic nanostructures, carbon nanotubes, and magnetic nanoparticles, silica, by comparison, may seem rather mundane. As a highly transparent, dielectric material, its most valuable uses, at least macroscopically, typically depend on what it does *not* do—absorb light or conduct electrons. As an inert host, it provides a matrix, enabling the production of macroscopic materials into which nanoparticles and nanostructures can be doped, imparting the nanoparticle's properties to the material as a whole (Figure 1). On the nanoscale, silica plays this same role, but it also does much more. Silica nanoparticles can be synthesized as highly monodisperse, highly spherical nanoparticles, forming the basis for much beautiful work on colloidal crystal arrays and inverse opal structures.[1] Silica nanoparticles and epilayers are also often used to define the shape or the space between other nanoscale structures, as in plasmonic nanoparticles,[2] where metallic cores or shell layers are grown onto the silica structures. Just like its macroscopic analogue, silica nanostructures can serve as a practical host for more functional nanomaterials. In this issue, Insin *et al.* make full use of the versatility of silica chemistry to "nanoengineer" two disparate functionalities into the same nanoparticle—fluorescence and magnetism—for the formation of monodisperse, highly regular structures able to respond to both optical excitation and manipulation in magnetic fields.[3]

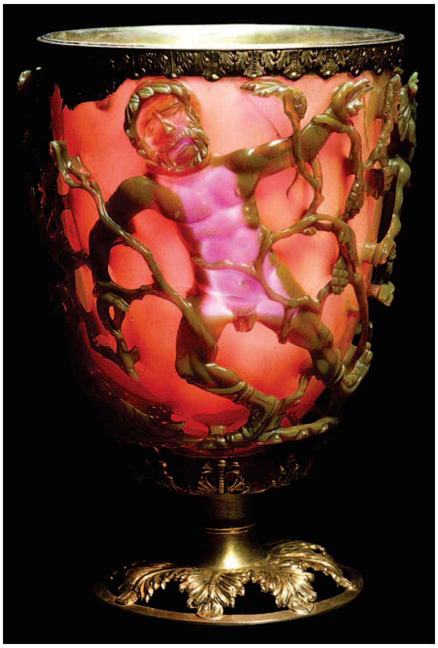

Figure 1. The Lycurgus Cup, an example of nanochemistry under glass from antiquity, where glass serves as a host for functional nanoparticles, *e.g.*, gold colloid. Copyright Trustees of the British Museum.

ⓦ A movie is available showing the color change that occurs when the cup is illuminated from the inside, demonstrating the nanoscale properties of the gold particles embedded within the glass.

The Stöber Method. Silica nanoparticles can be formed by polymerization of silicic acids in an aqueous system, or through hydrolysis and condensation of silicon alkoxides, known as the Stöber synthesis.[4] These two routes are distinguished from one another by the mechanism of particle formation. Comparison of nuclear magnetic resonance (NMR) spectra from commercial aqueous silicates (Ludox) and acid-catalyzed silicon alkoxides showed that the former are dominated by monomers and tetrafunctionalized species, whereas di- and trifunctionalized species dominate for alkoxides.[5] Comparison of small-angle X-ray scattering (SAXS) measurements of Ludox and acid- and base-catalyzed alkoxides shows that only aqueous silicate sols are uniform, whereas alkoxides generate fractal particles.[6] These results illustrate that sols derived from aqueous silicates by standard

See the accompanying article by Insin *et al.* on p 197.

ⓦ This paper contains enhanced objects available on the Internet at http://pubs.acs.org/journals/ancac3.

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> As a highly transparent, dielectric material, silica's most valuable uses depend on what it does *not* do—absorb light or conduct electrons.

chemical methods are fully hydrolyzed and grow by classical monomer addition, resulting in uniform polymeric particles. Stöber particles, on the other hand, grow through cluster aggregation and retain a fractal inner morphology, even while the particles coarsen through surface tension reorganization. Two distinct regimes characterize particle growth: diffusion-limited, in which the transport of mass to the growing structure is the dominant growth limitation, and reaction-limited, in which the efficiency of attachment limits the growth process. In general, diffusion-limited conditions result in a reduction in the growth rate since the collisional frequency of the reactant species is reduced. Species that do collide do not have the chance to attach in a manner that minimizes surface energy, favoring external sites and resulting in disordered morphologies. As a result, aggregates formed in diffusion-limited conditions are distinguished by lower fractal dimensions. Reaction-limited growth, on the other hand, is characterized by more compact structures. The sticking coefficient is small enough that species are able to sample attachment sites for energetically favorable configurations.

The Stöber synthesis was the first method reported for making highly spherical, highly monodisperse silica nanoparticles of high enough quality to condense into arrays with long-range order or to form the foundation for uniform, layered functional or multifunctional nanoparticles. Typically, ethanol, ammonium hydroxide, and sometimes a small amount of water are mixed together, and then tetraethylorthosilicate, also called tetraethoxysilane (TEOS), is introduced into the mixture, with subsequent stirring. The reaction proceeds as a condensation of the $-OH$ groups, resulting in the formation of a $Si-O-Si$ network with H_2O as a reaction product. The size of the particles is controlled by the reactant concentrations. The monodispersity can be influenced by numerous factors, in particular ensuring that the TEOS has been handled in an inert environment prior to Stöber synthesis, to prevent polymerization of TEOS molecules, which serve as nucleation sites for nanoparticle growth, resulting in a significant size distribution of the final nanoparticle product. Subsequent to the initial papers describing this synthesis, there have been many reports that describe improvements on this technique, variations that result in control of size, monodispersity, and morphology, and additional studies, including quantitative models of the growth mechanism. More recently, the introduction of surfactants into the reaction has been explored to develop methods for controlling the product morphology.[7] It is quite stunning that the condensation of TEOS at acidic pH results in the formation of macroscopic sol–gel materials,[8] but at the highly basic pH of this reaction, highly uniform spherical silica nanoparticles result.

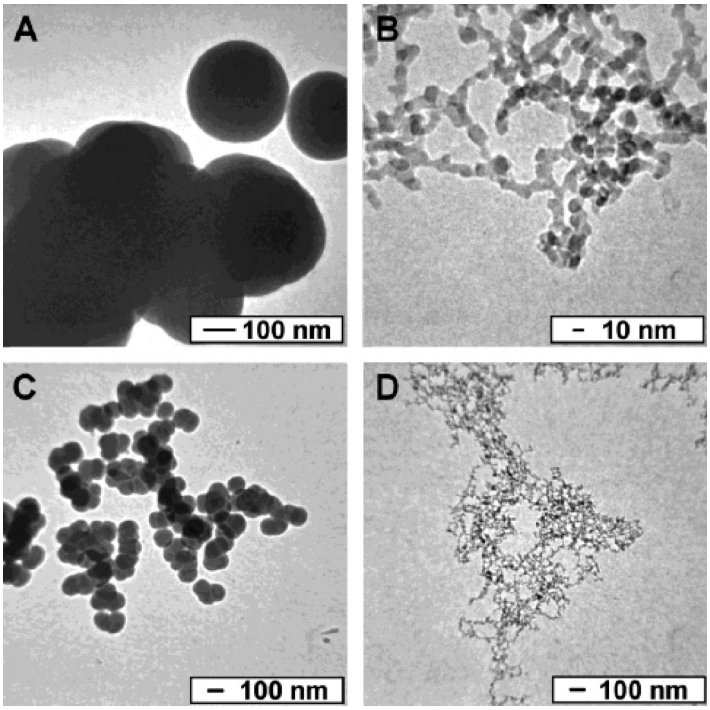

Figure 2. Transmission electron microscopy images of silica Stöber particles formed using two distinct protocols, R1 (A,B) and R2 (C,D). R1: 0.14 mL of TEOS, 4.21 mL of EtOH, and 0.654 mL of NH_4OH (30% NH_3). R2: 0.153 mL of TEOS, 4.59 mL of EtOH, and 0.245 mL of NH_4OH (30% NH_3). The particles in panels A and C were grown under terrestrial conditions; those in panels B and D were grown in microgravity. Reprinted with permission from ref 9. Copyright 2000 American Chemical Society.

Silica Nanoparticle Synthesis in Space: The Final Frontier? A few years ago, our research group had the opportunity to examine the Stöber growth process for silica nanoparticles by performing the Stöber synthesis in microgravity, in a set of experiments flown on a NASA space shuttle.[9] Under microgravity conditions, buoyancy-driven convection is eliminated, and many processes, from protein or colloid crystallization to embryonic development, can be profoundly affected. Microgravity allows diffusion-limited reaction conditions to persist for systems that would be reaction-limited under terrestrial conditions. We anticipated that, under microgravity conditions, the Stöber synthesis may well result in variations in nanoparticle size or morphology. For microgravity Stöber growth, nanoparticles smaller than are achievable in the laboratory for the same reactant mixtures would be anticipated, since the elimination of buoyancy-driven convection would be expected to slow the rate of formation of the nanoparticles. So we embarked upon answering the question: Could the Stöber synthesis work better in outer space?

To perform these experiments, four variations in the Stöber protocol were chosen, each yielding silica nanoparticles with different properties under normal laboratory conditions: (a) the "standard" protocol (R1), which produces highly monodisperse silica nanoparticles nominally of 100 nm in diameter; (b) a protocol that produces very small nanoparticles (R2); (c) one that typically results in a bimodal distribution of silica nanoparticles; and (d) one that results in large, mis-shapen nanoparticles.

Reaction vessels were needed that required an isolation of the reactants so that mixing could be performed in an entirely sealed environment by one of the mission specialists of the flight, not necessarily trained in chemistry. For the space-flight experiment, each 5 mL recipe was divided into two parts and loaded into coupled polyurethane (Hydex) syringes separated by a breakable Parafilm seal to enable mixing of the reactants. The first part consisted of TEOS and half the ethanol, while the second part consisted of water, ammonium hydroxide (30% NH_3), and the remaining ethanol. Each batch was also divided into ground and space samples, which were stoichiometrically identical. The only difference in the growth conditions between the ground and space samples was the presence or absence of gravity. The designated space samples (12 total, 3 per recipe) were then placed in the Gelation of Sols, Applied Microgravity Research (GOSAMR) hardware and activated aboard the space shuttle orbiter (Mission STS-95) after microgravity conditions had been established. The GOSAMR hardware, built by 3M Corporation and refurbished for this experiment, consists of a set of modules, each of which contain eight coupled syringe cartridges. Upon activation, a battery-powered, motor-driven lead screw with a reversing actuator drives the syringe cartridges back and forth, mixing the solutions after breaking the barrier seals between them. On Mission STS-95, the Stöber synthesis experiments were performed by former U.S. Senator John Glenn in his celebrated return to space after 36 years, making him quite likely the only U.S. Senator (thus far) to attempt a nanoparticle synthesis. Upon return of the flight samples, an ultraprobe sonicator was used to obtain diluted suspensions of the samples in ethanol, and these were allowed to evaporate onto carbon-coated copper TEM grids for image characterization.

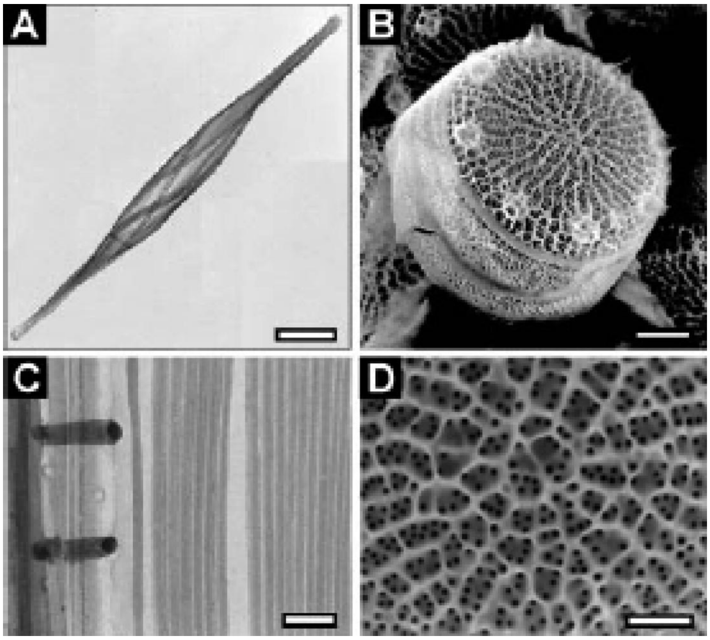

Figure 3. Examples of biosilica from diatoms. (A,C) Transmission electron microscopy images of *Cylindrotheca fusiformis* cell wall. (B,D) Scanning electron microscopy images of *Thalassiosira pseudonana* cell wall. Scale bars: (A) 5 μm, (B) 1 μm, (C,D) 200 nm. Reprinted with permission from ref 12. Copyright 2004 American Society for Biochemistry and Molecular Biology.

We discovered that microgravity affects the Stöber synthesis of silica nanoparticles profoundly (Figure 2). Instead of the formation of highly spherical particles, long, thin fractal aggregate structures were formed. Under two of the reaction conditions, some silica particles did, in fact, form along with the fractal structures. These beautiful fractal networks are likely snapshots of the early stages of terrestrial Stöber nanoparticle formation. Although microgravity does not yield highly regular nanoparticles in this case, the morphologies and the aspect ratios of the structures formed are unique to microgravity conditions. Perhaps in the hands of future generations of scientists, the Stöber synthesis will again return to space as Senator John Glenn did, older and wiser, to examine further in what ways chemists can control and modify the unique nanostructures formed under these conditions.

The Future of Silica Nanoparticle Synthesis: In Mother Nature's Hands. Perhaps the most promising direction

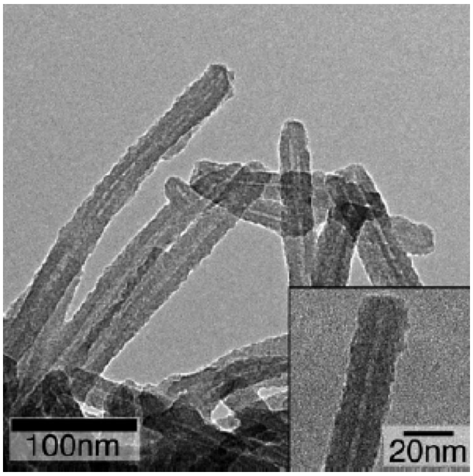

Figure 5. Peptide amphiphiles direct the synthesis of hollow silica nanotubes. Reprinted with permission from ref 19. Copyright 2007 American Chemical Society.

for advancing silica nanostructure chemistry to new morphologies and increased functionality and control comes from the recent advances in understanding how bio-organisms produce silica nanostructures (Figure 3).[10–13] Biomineralization, defined as the growth of inorganic materials by organisms, is widespread in nature in both plant and animal phyla. Silica is the second most abundant biomaterial, surpassed only by calcium carbonate.[14] Although practiced by a wide variety of species, including mammals, silica biomineralization occurs most dominantly in small aquatic life forms.[15] The two groups of organisms that have been the focus of significant studies of this process have been diatoms, unicellular organisms that produce silica-based exo- and endoskeletons accounting for most of their body mass, and multicellular sponges that produce silica spicules. For understanding how organisms control the growth morphology of silica in nanoscale structures, diatoms offer an array of remarkably intricate patterns in their cell walls at the nanoscale (and microscale). Since the intricate silica nanoscale patterns formed by these organisms are species-specific, it follows that the directed growth process must be encoded in the genome of the organism and that certain proteins expressed must play important species-specific directing roles in the controlled growth of silica nanostructures. When first analyzed, it was apparent that biomineralized silica is not a purely inorganic material but instead contains a small but significant percentage of organic molecules, but their role in the growth and patterning processes remained obscure.[16] More recently, the proteins and other organic molecules associated with the growth of biosilica have been identified and characterized extensively, and our knowledge of the cell-biologic aspects of silica growth has been significantly advanced.

It is currently understood that certain proteins, most specifically silaffins, isolated from the cell walls of the diatom *Cylindrotheca fusiformis*, play integral roles in controlled biosilica growth.[13] Long-chain polyamines (LCPAs), extracted from the diatom *S. turris*, are also present in relatively high quantities.[17] Although other proteins are present in biosilica, the silaffins and the LCPAs, in various species-specific forms, appear to be the molecules most actively directing the growth process. Both of these classes of molecules have been shown to precipitate silica from aqueous solutions *in vitro*, with the LCPA-assisted precipitates forming nanospheres with a narrow size distribution (Figure 4).[18] In subsequent research inspired by these observations, a number of synthetic amino acids, peptides, and polyamines have been shown to precipitate silica from aqueous solutions. As more details of this complex process become known, there will be numerous opportunities to adapt methods originating in biological systems to grow silica nanoparticles and nanostructures into new morphologies, and also under gentler chemical conditions than the traditional Stöber method.

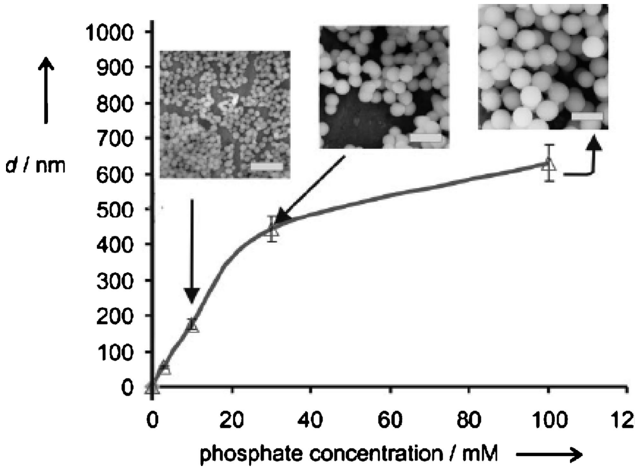

Figure 4. Diameters of silica nanospheres produced under the guidance of the polyamine/phosphate system as a function of the phosphate concentration. The polyamine/phosphate ratio strictly controls the diameters of the precipitating silica nanospheres. Insets: scanning electron microscopy images of the corresponding silica precipitates (scale bars are 1 μm for all images). Reprinted with permission from ref 18. Copyright 2003 Wiley-VCH Verlag GmbH & Co. KGaA.

Another potentially important adaptation of bioassembly principles to the growth of silica nanostructures utilizes proteins at a higher level of organization as templates for silica deposition into controlled morphologies. Recently, engineered peptides were developed specifically for this purpose.[19] Peptide amphiphiles are structures that organize into long, stable cylindrical nanofibers in aqueous solution and present many opportunities to direct surface or templating chemistry by variation of their surface functional groups. These structures can be used as templates for TEOS polymerization. Condensation of TEOS onto the nanoscale-diameter peptide fibrils, followed by calcination, yields a unique route to hollow, long silica nanotubes (Figure 5). Considering the multiplicity of morphologies and functions available with engineered proteins and peptides, this general approach offers many exciting possibilities for the fabrication of controlled, complex, 3D silica-based nanostructures by design.

As we pursue the development of complex, multifunctional nanostructures, it is clear that silica nanochemistry will continue to offer important capabilities, limited only by our imaginations. Perhaps future scientists will design and assemble structures at the nano- and microscales with complexities equivalent to diatoms but with functionalities designed by the researchers themselves.

REFERENCES AND NOTES

1. van Blaaderen, A.; Ruel, R.; Wiltzius, P. Template-Directed Colloidal Crystallization. *Nature* **2003**, *385*, 321–324.
2. Wang, H.; Brandl, D. W.; Nordlander, P.; Halas, N. J. Plasmonic Nanostructures: Artificial Molecules. *Acc. Chem. Res.* **2007**, *40*, 53–62.
3. Insin, N.; Tracy, J. B.; Lee, H.; Zimmer, J. P.; Westervelt, R. M.; Bawendi, M. G. Incorporation of Iron Oxide Nanoparticles and Quantum Dots into Silica Microspheres. *ACS Nano* **2008**, *2*, 197–202.
4. Stöber, W.; Fink, A.; Bohn, E. Controlled Growth of Monodisperse Silica Spheres in Micron Size Range. *J. Colloid Interface Sci.* **1968**, *26*, 62–69.
5. Brinker. C. J. In *The Colloid Chemistry of Silica*; Bergna, H. E., Ed.; American Chemical Society: Washington, D.C., 1994; pp 31.
6. Schaefer, D. W.; Martin, J. E.; Keefer, K. D. In *Physics of Finely Divided Matter*; Bocarra, N., Daoud, M., Eds.; Springer-Verlag: Berlin, 1985; p. 31.
7. Shimura, N.; Ogawa, M. Preparation of Surfactant Templated Nanoporous Silica Spherical Particles by the Stober Method. Effect of Solvent Composition on the Particle Size. *J. Mater. Sci.* **2007**, *42*, 5299–5306.
8. Pienaar, C. L.; Chiffoleau, G. J. A.; Follens, L. R. A.; Martens, J. A.; Kirschhock, C. E. A.; Steinberg, T. A. Effect of Gravity on the Gelation of Silica Sols. *Chem. Mater.* **2007**, *19*, 660–664.
9. Smith, D. D.; Sibille, Z.; Cronise, R. J.; Hunt, A. J.; Oldenburg, S. J.; Wolfe, D.; Halas, N. J. Effect of Microgravity on the Growth of Silica Nanostructures. *Langmuir* **2000**, *16*, 10055–10060.
10. Sumper, M.; Brunner, E. Learning from Diatoms: Nature's Tools for the Production of Nanostructured Silica. *Adv. Funct. Mater.* **2006**, *16*, 17–26.
11. Poulsen, N.; Sumper, M.; Kroger, N. Biosilica Formation in Diatoms: Characterization of Native Silaffin-2 and its Role in Silica Morphogenesis. *Proc. Natl. Acad. Sci.* **2003**, *21*, 12075–12080.
12. Poulsen, N.; Kroger, N. Silica Morphogenesis by Alternative Processing of Silaffins in the Diatom *Thalassiosira Pseudonana*. *J. Biol. Chem.* **2004**, *279*, 42993–42999.
13. Sumper, M.; Kroger, N. Silica Formation in Diatoms: The Function of Long-Chain Polyamines and Silaffins. *J. Mater. Chem.* **2004**, *14*, 2059–2065.
14. Davis, S. A.; Dujardin, E.; Mann, S. Biomolecular Inorganic Materials Chemistry. *Curr. Opin. Solid State Mater. Chem.* **2003**, *7*, 273–281.
15. Treguer, P.; Nelson, D. M.; Van Bennekom, A. J.; DeMaster, D. J.; Leynaert, A.; Queguiner, B. The Silica Balance in the World Ocean: A Reestimate. *Science* **1995**, *268*, 375–379.
16. Swift, D. M.; Wheeler, A. P. Evidence of an Organic Matrix from Diatom Biosilica. *J. Phycol.* **1992**, *28*, 202–209.
17. Sumpfer, M. Biomimetic Patterning of Silica by Long-Chain Polyamines. *Angew. Chem., Int. Ed.* **2004**, *17*, 2251–2254.
18. Sumper, M.; Lorenz, S.; Brunner, E. Biomimetic Control of Size in the Polyamine-Directed Formation of Silica Nanospheres. *Angew Chem., Int. Ed.* **2003**, *42*, 5192–5195.
19. Yuwono, V. M.; Hartgerink, J. D. Peptide Amphiphile Nanofibers Template and Catalyze Silica Nanotube Formation. *Langmuir* **2007**, *23*, 5033–5038.