Spatial Control of Chemistry on the Inside and Outside of Inorganic Nanocrystals

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ABSTRACT The ability to make inorganic nanocrystals of controlled size, shape, and composition is well-established for some elements and compounds, but by no means has been generalized to the entire periodic table. A new paper in this issue of *ACS Nano* offers a route to explore more of the periodic table with increased control over both composition and position for inorganic nanostructures. This Perspective provides a snapshot of the major challenges in controlling the positions of atoms and molecules both in the cores and on the surfaces of inorganic nanocrystals.

See the accompanying Article by Leonard *et al.* on p 940.

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The readers of *ACS Nano* are likely familiar with the many emerging applications of inorganic nanocrystals, for example, gold nanocrystals of controlled size and shape for biomedical imaging and photothermal therapeutics;[1−9] zinc oxide and other II−VI semiconductor nanocrystals of controlled size and shape for next-generation solar cells[10−13] and light emission;[14−17] iron oxide nanocrystals for magnetic resonance imaging and drug delivery;[18−20] and platinum nanocrystals of controlled size, shape, and orientation for catalysts.[21−24] In some applications, the nanocrystals are best used as a colloidal dispersion (*e.g.*, for biological imaging/tracer experiments); in others, the nanocrystals are best used when supported on a solid substrate or immobilized in a matrix (*e.g.*, as electronic devices or heterogeneous catalysts). Even though progress in the synthesis of elemental, and metal oxide, sulfide, selenide, or telluride nanocrystals has been extraordinary, there is a relative dearth of methods for making inorganic nanocrystals with arbitrary compositions from the entire periodic table. Solid-state chemists routinely discover new compounds with new properties in the bulk that are not readily predictable, for example, the yttrium barium copper oxide family of superconductors,[25] the more recent excitement over magnesium boride superconductors,[26] and the nickel−titanium family of "memory metals" that convert from one macroscopic structure to another *via* a thermal phase transition. The effect of nanoscale particle size on these material properties is an interesting problem to consider, but the preparation of nanocrystals of controlled size, shape, and composition at this scale remains difficult. Even if the composition is correct, in the sense that the proper ratio of elements is present, the question would remain as to whether all the atoms were arranged in the proper structure. Would they alloy, arrange as core−shell, or phase separate within an individual nanoparticle (Figure 1)? For systems like iron hydroxide/oxides, where there are multiple phases (hematite, goethite, magnetite), the situation is even more complex.[27,28] To the extent that properties depend on atomic arrangements within the particle, spatial control of composition is critical.

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The paper by Schaak and co-workers in this issue offers a route to achieve compositional and spatial control of inorganic nanostructures. In this paper, the Schaak team screened a large number of reactions across the periodic table to map out conditions to generate new inorganic nanocrystals selectively.[29] In one example from their paper, a mixture of nickel and platinum nanoparticles was selectively converted to Ni_3Sn_4 and PtPb nanoparticles, respectively, in one pot.[29] The team also found conditions at lower temperature than the bulk for previously unreported nanocrystals, with unusual compositions such as RhSb, RhBi, PdBi, Pd_8Sb_3, and Pd_5Pb_3.[29] These last nanomaterials are potential catalysts, but the lack of a good synthetic method to make them has naturally hampered catalytic studies. The Schaak team also demonstrated spatial control of composition by putting

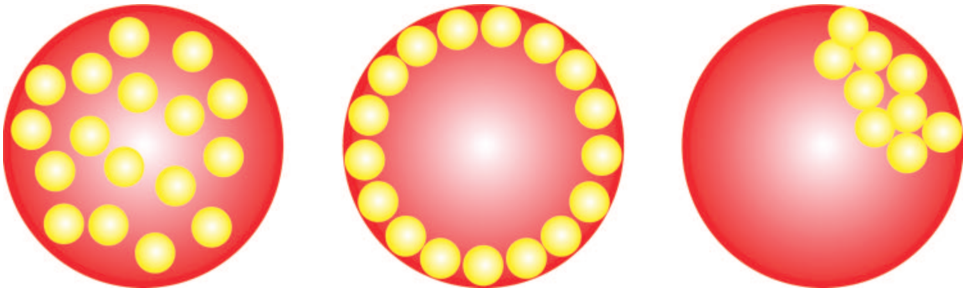

Figure 1. Schematic of spatial control of chemistry within inorganic nanocrystals: alloy (left), core−shell (center), and phase-separated (right). Different colors denote different phases, compositions, or atoms depending on scale.

their selective reactions to work on striped multimetallic nanowires and lithographically patterned surfaces.[29] In one example, they were able to convert elemental silver to silver sulfide, with the silver sulfide product retaining the nanoscale position of its original silver precursor.[29] Another group also recently reported the reaction of silver to silver sulfide with nanoscale spatial control.[30]

Schaak and his team were able to make their materials in sufficient quantities and grain sizes, starting from 5−25 nm diameter colloidal metal nanocrystals or preformed striped metal nanowires, such that X-ray diffraction and elemental mapping by energy dispersive X-ray spectroscopy in a scanning electron microscope, respectively, were good characterization tools for each type of particle. The production of compositionally and spatially controlled nanostructures at smaller scales is still a great challenge. For example, the growth of gold nanocrystals on the tips of cadmium selenide nanorods and tetrapods is sufficiently difficult that the result was big news only several years ago.[31,32] Also noteworthy are galvanic replacement reactions on the nanoscale, such as

$$\mathrm{Au(s)} + 3\mathrm{Ag}^{+}\mathrm{(aq)} \rightarrow \mathrm{Au}^{3+}\mathrm{(aq)} + 3\mathrm{Ag(s)}$$

which have been performed in organic dendrimer "reactors"[33] or on solid gold nanocrystals to produce hollow silver shells that retain the overall shape of the original core structure.[34] Conversion of metal nanocrystals to hollow metal oxides or chalcogenides, relying on differential diffusion rates of atoms and ions within the nanocrystal,[35] is another route to chemical control of nanocrystal composition that could, in principle, be used for spatial control. Complex metal oxides have been prepared by numerous groups,[36−40] typically starting from simple elemental or metal salt precursors, although there are occasional examples of one type of nanocrystal conversion to another (*e.g.*, 11 nm iron nanospheres oxidized to 11 nm iron oxide nanospheres[41]).

In their paper, Schaak and his team point out that organic chemists have decades of a head start in atomic-level placement of elements in organic compounds with high spatial precision, compared to solid-state inorganic chemists. Their paper gives us inorganic chemists hope that we too will have standard named reactions for nanocrystal synthesis! In the immediate future, however, there are interesting questions that the Schaak paper[29] stimulates:

1. What degree of product nanocrystal size and shape control is possible with these solid-state-like reactions?
2. Can the composition of the final product be predicted from bulk phase diagrams?
3. How thermodynamically stable are these unusual nanocrystals?
4. Is it possible to have multiple phases within one nanocrystal (and be able to prove it)?
5. Can a protecting group strategy be used, similar to organic chemistry, to functionalize inorganic nanocrystals asymmetrically?[32]
6. What is the chemical nature of the nanocrystal surface?

This last question is of vital interest to many subcommunities in nanoscience. For example, passivation of semiconductor surfaces has been known for decades to eliminate surface trap states and dangling bonds that otherwise might trap charge carriers.[42] One important reason for the success of silicon in the microelectronics industry is the fact that its insulating oxide, SiO_2, forms excellent thin films on Si upon air exposure that passivate the surface. The same concept holds for quantum dots: typically a wide band gap semiconductor such as ZnS or ZnO is grown epitaxially on colloidal CdSe or CdS to passivate the surface so excitonic emission, not deep trap emission, is promoted.[14−17,43]

Another community within nanoscience is exploring biological applications with colloidal nanocrystals.[1−9,14−16,18−20] A typical procedure is to prepare the colloidal inorganic core and to coat the surface with organic molecules that both stabilize the particles against aggregation and also give them specificity in biological interactions (*e.g.*, DNA−DNA, small molecule−protein, antibody−antigen). The chemistry to attach biological molecules to nanoparticle surfaces is well-advanced, but even here surprises are found; a recent *ACS Nano* paper provides evidence that the footprint size of molecules on nanocrystals is influenced by nanocrystal curvature.[44,45]

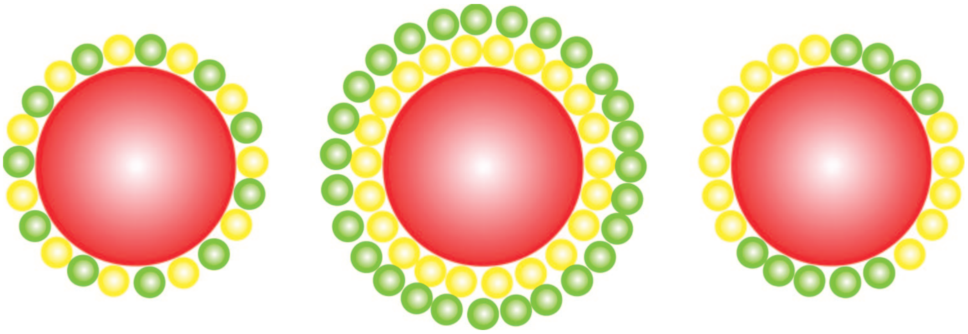

Figure 2. Schematic of spatial control of chemistry on the surface of inorganic nanocrystals: alloy (left), core−shell (center), and phase-separated (right). Different colors of spheres on the surface represent different adsorbed molecules. The interior of the inorganic nanocrystal, of course, may be internally alloy, core−shell, or phase-separated, as shown in Figure 1.

The introduction of multiple chemical groups to the surfaces of nanocrystals can produce a variety of spatially distinct characters to the final products: "alloy" in which the adsorbed molecules are intimately and randomly mixed; "core−shell," or layer-by-layer, in which layers of adsorbed molecules are deposited sequentially;[46] and phase-segregated, in which there are patches of different chemical functionalities at the surface on an individual nanoparticle, in principle, driven by weak forces between adsorbed ligands but also by surface curvature (Figure 2). This last type of nanocrystal is perhaps the most difficult to design and to demonstrate adsorbate spatial control.[47−52] The relative positions of adsorbed molecules on a nanoscale surface can influence their properties; for example, self-assembled monolayers of carboxylic acids, with the acid groups facing the solvent, can have pK_a values closer to 10 rather than the usual 5, due to lateral hydrogen bonding in the monolayer.[53]

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In a true biological or environmental system, proteins, peptides, hormones, nucleic acids, salts, carbohydrates, fatty acids, natural organic matter, and so forth are present and can adsorb to nanocrystal surfaces, potentially blocking the recognition molecules that the chemist has so painstakingly engineered there.[54−58] Moreover, these adsorbates might change over time as abundant weak binders are displaced by strong binders to the surface.[54−58] These issues have been recognized for decades in biomaterial interfaces[54] but only recently have nanocrystal chemists begun to address them, with the additional complication of potential intrinsic curvature effects on molecular adsorption and adsorbate conformation. A recent example is a fascinating study of the exposure of commercial polystyrene nanospheres of two different sizes (50 nm, 100 nm) and three different initial surface groups ("plain", meaning a few sulfonate groups; carboxylic acids; amines) to human plasma.[59] The authors were able to extract 50+ components from what they call "the protein corona" that surrounds the nanospheres upon exposure, and the relative concentrations of these components varied both as a function of nanoparticle size and initial nanoparticle surface charge.[59] Thus, the nanobiotechnology and nanomedicine communities are left with the uncomfortable realization that the mechanism of action they might propose for nanoparticle-based drug delivery or therapy might be completely different from what they imagine based on initial surface chemistry. However, even for nanocrystals in which the originally distinct surfaces have all apparently been overcoated with the same protein, differential cellular uptake suggests that there are some remnants of the original surface properties that can be exploited for cellular targeting.[60]

Overall, the challenges in nanocrystal syntheses are moving past the point of simple size control of single-metal nanocrystals. The Schaak paper in this issue of *ACS Nano* points the way to inorganic nanocrystal synthetic strategies across the entire periodic table.

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