

Spherical Nucleic Acids: Integrating Nanotechnology Concepts into General Chemistry Curricula

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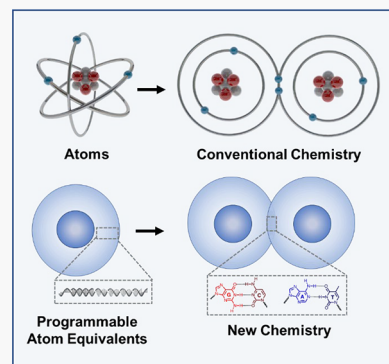
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ABSTRACT: Nanoscience and technology research offer exciting avenues to modernize undergraduate-level General Chemistry curricula. In particular, spherical nucleic acid (SNA) nanoconjugates, which behave as “programmable atom equivalents” (PAEs) in the context of colloidal crystals, are one system that one can use to reinforce foundational concepts in chemistry including matter and atoms, the Periodic Table, Lewis dot structures and the octet rule, valency and valence-shell electron-pair repulsion (VSEPR) theory, and Pauling’s rules, ultimately leading to enriching discussions centered on materials chemistry and biochemistry with key implications in medicine, optics, catalysis, and other areas. These lessons connect historical and modern concepts in chemistry, relate course content to current professional and popular science topics, inspire critical and creative thinking, and spur some students to continue their science, technology, engineering, and mathematics (STEM) education and attain careers in STEM fields. Ultimately, and perhaps most importantly, these lessons may expand the pool of young students interested in chemistry by making connections to a broader group of contemporary concepts and technologies that impact their lives and enhance their view of the field. Herein, a way of teaching aspects of General Chemistry in the context of modern nanoscience concepts is introduced to instructors and curricula developers at research institutions, primarily undergraduate institutions, and community colleges worldwide.

KEYWORDS: First-Year Undergraduate/General, Inorganic Chemistry, Analogies/Transfer, Colloids, Nanotechnology, Materials Science



INTRODUCTION

In 2012, the President’s Council of Advisors on Science and Technology (PCAST) highlighted that a significant increase to the rate at which STEM professionals are produced was needed for the US to remain competitive in science and technology (an approximate 34% increase in STEM bachelor’s degrees needed, approximately 1 million more over the next decade).¹ This call-to-action is particularly relevant to General Chemistry, a common gateway course for an interdisciplinary student body pursuing education in the physical sciences, engineering, and medicine. Curricula developers, textbook authors, and instructors alike must acknowledge this breadth of student interest and work to engage a diverse student body. At Northwestern University, we have worked to integrate advances in nanoscience and technology research into our General Chemistry curriculum. We propose that this deeper integration of nanotechnology into this curriculum is one of several possible strategies to drive an increase in student retention and the production of STEM professionals, albeit multiple strategies in the context of nanotechnology, including those that rely on experiments,^{2,3} service,⁴ research groups,⁵ or other methods,^{6,7} must be implemented to comprehensively answer the call-to-action by the PCAST.

Nanoscience and technology involve the study and manipulation of matter on the 1–100 nm length scale.^{8,9}

Objects with such small dimensions (approximately one billionth of a meter or a millionth of a millimeter) display dramatically different properties (e.g., chemical, electrical, optical, thermal, mechanical) compared to materials of identical composition but with macroscopic dimensions.¹⁰ Nanochemistry, in particular, encompasses research dedicated to the synthesis and understanding of building blocks with properties that are size-, composition-, and shape-dependent (Figure 1).^{11,12} Recent developments in nanoscience, and specifically nanochemistry, research are enabling exciting scientific breakthroughs in medicine,^{13–16} materials science,¹⁷ advanced manufacturing,^{18,19} and energy and environmental sciences.^{20–23} In our curriculum, we have paralleled teachable concepts in nanochemistry alongside the evolution of foundational principles in General Chemistry as a key component of multiple course lectures, with understanding evaluated via quiz and test questions in certain cases, and in 2021, through integration with the NUCHEM Videos project (<https://youtu>).

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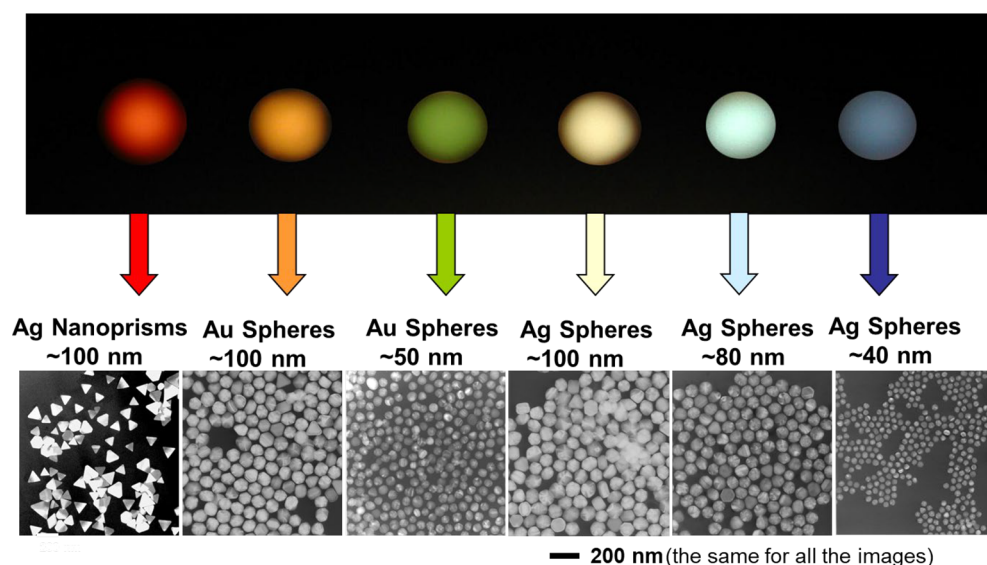


Figure 1. Optical properties (like Rayleigh scattering (top)) are dependent on the size, composition, and shape (seen in electron microscopy images (bottom)) of the corresponding nanoparticles. Reprinted with permission from ref 12. Copyright 2005 John Wiley and Sons.

be/8djmHmIFlhA). Indeed, we envision two key strategies to teaching through the lens of nanoscience: (1) by enhancing the 1–2 week advanced or modern materials or biochemistry modules typically taught at the end of General Chemistry courses to include a more in-depth discussion comparing topics in nanochemistry to their classical counterparts and (2) by integrating the content throughout the course in several lectures (minutes per lecture) (see link to sample lecture slides in the Notes).

Herein, we detail how nanoscience can be introduced throughout the course to reinforce, *not replace*, foundational General Chemistry topics (strategy 2). Brief surveys of Northwestern General Chemistry students have indicated that the deeper integration of contemporary nanotechnology research into their General Chemistry education increased their understanding of what nanoscience is and why it is important, augmented their grasp of the connection between historical and modern concepts in the field of chemistry, and reinforced their understanding of introductory chemistry principles (see Figures S1 and S2). Furthermore, we have found that teaching through the lens of nanoscience allows us to engage some students in discussions that relate class material to current academic and industrial research in addition to topics in the popular media. By mindfully bringing nanotechnology examples to the center of General Chemistry, we also propel students to develop as critical and informed scientific thinkers regardless of their intended career path and, in some cases, motivate them to pursue continued education and research in STEM disciplines (see Figures S1 and S2). We envision that many other institutions of higher education, including research institutions, primarily undergraduate institutions, and community colleges, could similarly map nanoscience or other areas of modern research onto their established General Chemistry curricula, use it to teach first-year seminars for chemically savvy students, or employ it as the foundation of advanced special topics courses at the undergraduate (or even graduate) level. These discussions do not necessarily require instructors to have expertise in nanochemistry or nanoscience and follow directly from classical

topics in General Chemistry in many cases (see link to sample lecture slides in the Notes).

We elaborate on our motivation for launching this initiative and report on the similarities and differences we emphasize between traditional General Chemistry principles and some of the most recent discoveries in nanoscience and technology using the spherical nucleic acid (SNA) nanoconjugate,²⁴ a type of programmable atom equivalent (PAE), as a model system. SNAs are hybrid, or multicomponent, materials that typically consist of a nanoparticle core and a densely functionalized and highly ordered nucleic acid shell (Figure 2). These nanoconjugates are structurally different than 1D (linear) and 2D (circular) forms of nucleic acids found in nature and exhibit unique chemical and physical properties. The original SNA structure, first introduced in 1996,²⁵ consists of a gold nanoparticle core and a single-stranded DNA shell (a “Koosh ball” structure), and it has been one of the most highly studied

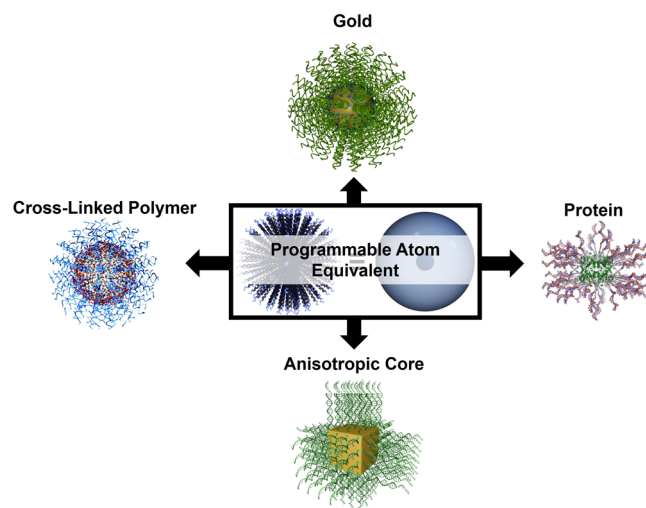


Figure 2. Types of programmable atom equivalents (core component listed). The prototypical spherical nucleic acid (SNA) with a spherical gold nanoparticle core and a radially oriented and densely packed single-stranded DNA shell is shown at the top.

forms despite the development of several other versions with different cores and shells (Figure 2).^{26–32} While many other nanotechnology examples also lend themselves to incorporation in General Chemistry curricula, to name a few, molecular machines and the mechanical bond (a discovery that was recognized with the 2016 Nobel Prize in Chemistry),³³ supramolecular chemistry and coordination chemistry-based approaches to biomimicry,^{34–37} and porous materials,³⁸ such as metal–organic frameworks (MOFs)^{39,40} (one of the most intensely researched areas in modern chemistry today and an example of an important class of modern materials with uses in energy and environmental science, water, sustainability, catalysis, and other fields), we have focused on SNAs because of the breadth of General Chemistry concepts that they can be used to reinforce in the context of modern nanoscience. Indeed, SNAs can be applied to bolster concepts, including those pertaining to matter, atoms, the Periodic Table, chemical bonding, Lewis dot structures, valence-shell electron-pair repulsion (VSEPR) theory, phase diagrams, Pauling's rules, equilibria, and solution chemistry.^{41,42}

■ EDUCATIONAL APPROACH

Matter and Measurement

Many General Chemistry curricula begin by defining matter and, subsequently, delineating how scientists measure and classify it.^{41,42} Given that nanoscale materials, for example, the gold nanoparticles that form the core of the prototypical SNA structure, display significantly different properties compared to macroscopic samples of identical substances, we can immediately draw examples from nanoscience into our General Chemistry classroom as well as introduce the SNA to students. For instance, the nanoparticle cores of SNAs provide an excellent model for demonstrating the size-dependent properties of nanoscale matter.⁴³ The surface area-to-volume ratio of a gold nanoparticle that serves as a SNA core is much larger than that of a macroscopic sample of gold.⁹ (This is important because, in nanoparticles, atoms at the surface are more reactive than atoms in the bulk and have a greater weighted contribution to the overall properties of such materials; thus, nanoparticles in many cases are more effective at catalyzing chemical reactions than bulk materials, for example). In our courses, we have led students to this conclusion through both conceptual and numerical inquiry-based problems involving dimensional analysis.

Atoms, Molecules, and Ions

With an established foundation in classifying matter, General Chemistry curricula typically delve into a discussion of the building blocks of matter, namely, atoms and ions, and the arrangement and assembly of those building blocks through chemical bonds to form molecules and atomic and ionic crystals.^{41,42} Extensive work in modern academic chemistry laboratories has shown that SNAs behave as a type of PAE to build higher order colloidal crystals (Figure 3). This research has allowed us to draw analogies between atomic bonding and PAE bonding in our courses.^{41,42,44–47} With PAEs based on SNAs, we present the spherical nanoparticle core as the nucleus and core electrons of an “atom”, while the DNA strands in the shell form the “bonding elements” like the unpaired valence electrons do in atomic systems. The structure of the DNA strands in the shell governs the bonding and assembly of PAEs, paralleling how the electronic structure of

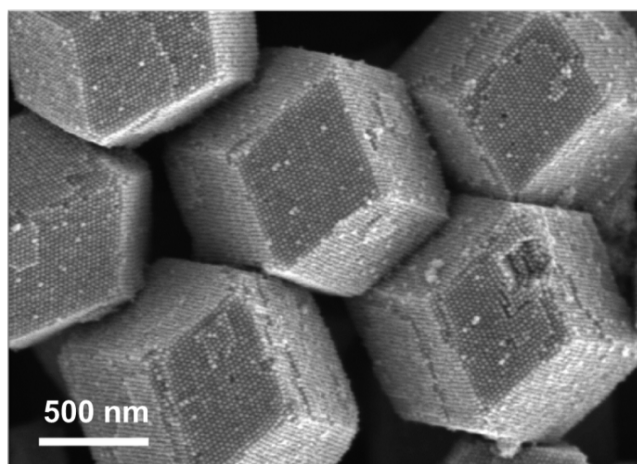


Figure 3. Scanning electron microscopy (SEM) image of rhombic dodecahedron-shaped colloidal crystals prepared from programmable atom equivalents comprised of gold nanoparticle cores and DNA shells. Reprinted with permission from ref 87. Copyright 2019 John Wiley and Sons.

an atom or ion predicts favorable and permissible bonding events.

To further enrich this analogy, we also liken ionic interactions between positively and negatively charged ions with the complementary base pair interactions that occur during the hybridization of two complementary DNA strands. While electrostatic interactions drive the assembly of cations and anions into crystalline lattices in ionic solids, we emphasize that weaker hydrogen-bond interactions between certain nucleobases of DNA, although they are a different type of interaction, are capable of driving the assembly of PAEs into crystalline lattices of similar structural types. To illustrate this, we compare NaCl, a prominent example of an ionic compound in General Chemistry (which features a face-centered cubic (FCC) arrangement of sodium ions and chloride ions), with assemblies of PAEs arranged in an FCC lattice.^{41,42,44–47}

The Periodic Table

Another mainstay of General Chemistry is the Periodic Table, and we can introduce a similar table of PAEs (Figure 4a) in our classes. This table of PAEs has been introduced in the modern chemistry literature to allow researchers to catalog and discern trends pertaining to these nanostructures.⁴⁸ Elements are arranged in the Periodic Table according to their electronic configuration.⁴⁹ PAEs have been arranged and organized based on the size, shape, and composition of their core (Figure 4a);⁴⁸ however, one could also imagine a table that arranges PAEs based on the length, sequence, density, flexibility, and backbone of the nucleic acid strands and the density of the nucleic acid shell (which also dictate binding properties) or a combination of core and shell features. We can use the table of PAEs to introduce to our students the idea that there are other ways that matter can be organized, especially as length scales change, using foundational concepts in General Chemistry as a template. Indeed, SNAs, and thus PAEs, come in dozens of forms^{45,48} and PAEs exist that possess anisotropic (e.g., nonspherical) cores.^{47,50} Importantly, unlike atoms in the Periodic Table, with electronic structures, and hence bonding patterns, fixed by nature, the structures of PAEs are highly adjustable, and therefore scientists can precisely tune PAE bonding. The table of nanoscale PAEs could have a near-

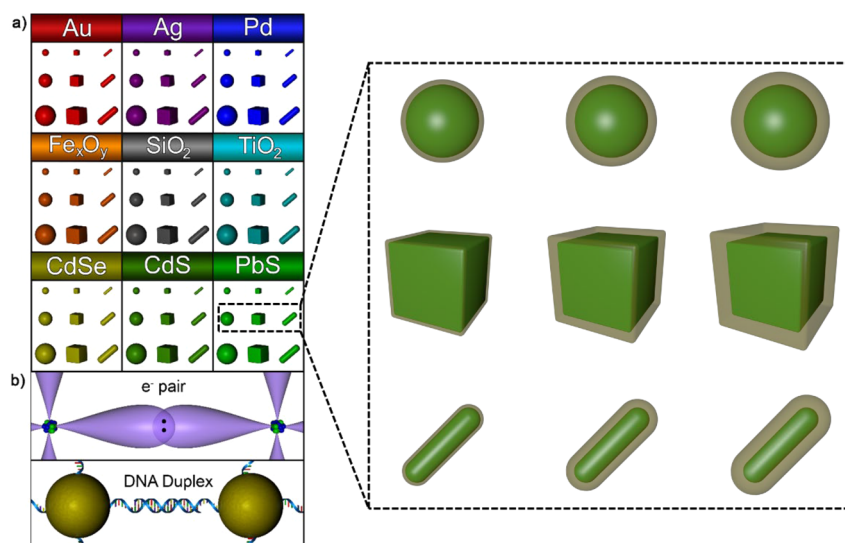


Figure 4. (a) Table of Programmable Atom Equivalents (PAEs). Note this is one example based on PAE core; others could be prepared based on PAE shell characteristics (e.g., length, right). For each entry, a near-infinite number of shell configurations exist, owing to the rich chemistry of DNA. (b) Bonding between atoms involves electrons (top) whereas bonding between PAEs involves nucleic acids (bottom); however, analogies can be drawn between the two types of bonding. Adapted with permission from ref 48. Copyright 2013 John Wiley and Sons.

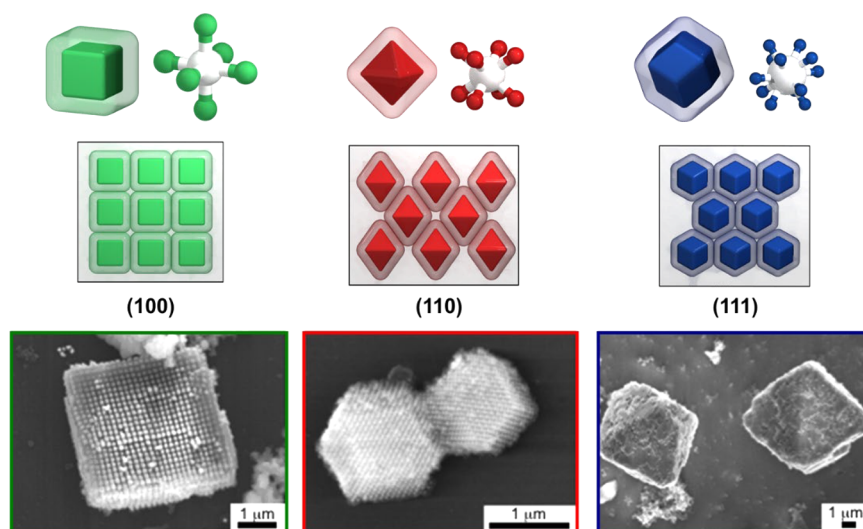


Figure 5. Distinct crystallographic facets of anisotropic nanoparticles enable directional bonding (hybridization) interactions that can be used to dictate hierarchical organization. The use of cube, octahedron, and rhombic dodecahedron nanoparticle building blocks (left to right) lead to colloidal crystals with cube, rhombic dodecahedron, and octahedron crystal habits, respectively. The top row shows the PAE structure (left) and its molecular equivalent (right), and the middle row shows the different closest-packed planes. Reprinted with permission from ref 88. Copyright 2016 American Chemical Society.

infinite number of entries, but interestingly, since the DNA shell dictates bonding, all PAEs, regardless of core identity, bond according to the same set of design rules.^{45,48} This is a fundamental departure from conventional chemistry, where the choice of atomic building blocks is linked to possible modes of bonding (see below).

Chemical Bonding and Molecular Geometry

With a foundational understanding of atoms, molecules, and ions, we continue to utilize the SNA-based PAE to underpin core concepts pertaining to chemical bonding in General Chemistry, revealing the similarities and *key differences* between atomic bonding and PAE bonding. With atoms, the electron is the fundamental bonding unit—with the valence electrons of multiple atoms interacting via donating, accepting,

or sharing to constitute the chemical bond.^{41,42} In General Chemistry, students learn that, according to the octet rule, atoms generally form bonds to attain a maximum of eight valence electrons. In a PAE-based system, surface-bound unpaired DNA strands on a nanoparticle core function as the fundamental bonding units—with the formation of hydrogen-bonding interactions (duplex interactions) between DNA strands on the surface of particles constituting the PAE bond.²⁵ Similar to atoms, PAEs seek to maximize the number of DNA duplex interactions between the DNA “sticky ends” of their nearest neighbors. This observation is the basis for the Complementary Contact Model (CCM), which we frame as analogous to the octet rule for PAE assemblies.⁵¹ Further extending the relationship between electrons and surface-bound DNA bonding elements, we draw analogies to Lewis

symbols, in which the hybridized DNA “sticky ends” are likened to the paired electrons between atomic nuclei (Figure 4b).

Critically, for atoms, the nature of bond formation, identity, and strength intrinsically relate to the bonding atom's identity via its electronic structure—a fundamental lesson of General Chemistry.^{41,42} For example, multiple bonds occur when the sharing of two or more pairs of electrons between atomic nuclei is possible, increasing both the bond strength and bond order while decreasing the bond length (i.e., a triple bond is stronger and shorter than a double bond which is stronger and shorter than a single bond). However, a key difference is that, with PAEs, the nature of the bonds formed is independent of the nanoparticle core. This is a unique feature of PAEs that allows for immense control over bonding characteristics and, therefore, materials design.^{44,45,48} For example, through the judicious choice of DNA sequence, length, and surface density, which dictate the nature of the DNA base pair interactions that occur, the lengths, strengths, and the overall number of bonds between PAEs can be tuned.^{52–54} Returning to the analogy from the previous paragraph, we can teach that the atomic symbols, or the centers, in Lewis dot structures dictate the surrounding electron “dots”; with SNAs, however, the “center symbol” is entirely independent of the “sticky ends” surrounding it.

Many General Chemistry curricula move from discussing chemical bonding to examining molecular geometry and the VSEPR model.^{41,42} The 3D molecular shape of a group of bonded atoms results from the directional overlap of atomic orbitals, and the VSEPR model allows us to predict this shape based on electron domains around the central atom. For PAEs, researchers have achieved directional bonding by employing anisotropic cores, such as cubes, triangular prisms, or disks,⁵⁵ or even proteins with tunable bond distributions,⁵⁶ to induce bonding domains analogous to the electron domains seen with Lewis structures and the VSEPR model (Figure 5). For example, we stress that according to the CCM, one expects face-to-face interactions between DNA-functionalized nanoparticles because these maximize the number of DNA duplex interactions.⁵¹ Indeed, PAEs prepared using a triangular prism and/or disk nanoparticle core assemble into a 1D stack to maximize the number of face-to-face interactions (Figure 6).^{55,57} Using this example, we also underscore an analogy between the directional bonding in a trigonal bipyramidal molecular geometry and with trigonal prism-based PAEs to our undergraduate students. The similarities and differences between atomic interactions and PAE-based interactions can be used to bolster basic concepts of chemical bonding and highlight the exciting aspects of PAE-based assemblies. For example, PAE crystals are being explored as programmable optical (e.g., metamaterials, photonic materials) and catalytic materials.^{58–60}

Intermolecular Forces and Phase Diagrams

In a General Chemistry course's discussion of intermolecular forces, phase diagrams illustrate the equilibrium between solid, liquid, and gaseous states of a given pure substance with pressure on the *y*-axis and temperature on the *x*-axis.^{41,42} To enrich this discussion, we also can incorporate phase diagrams representing the equilibria between different states of nano-scale matter. For example, we show and explain phase diagrams with PAEs to understand their assembly into superlattices. By plotting the DNA linker ratio—the ratio of the number of

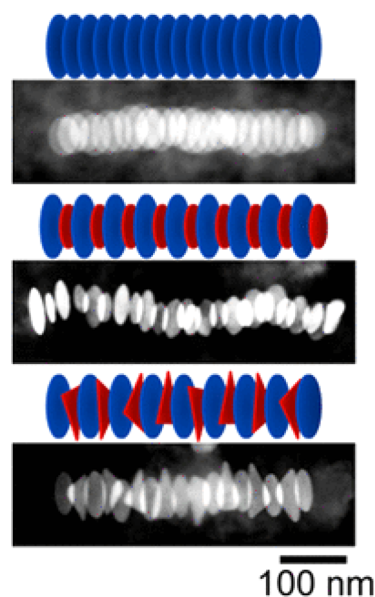


Figure 6. Schematic illustrations of the orientation of crystallized nanodisks or nanoprisms are shown above high-magnification transmission electron microscopy (TEM) images of nanodisks and/or nanoprisms in 1D, columnar arrangements. Reprinted from ref 57. Copyright 2017 American Chemical Society.

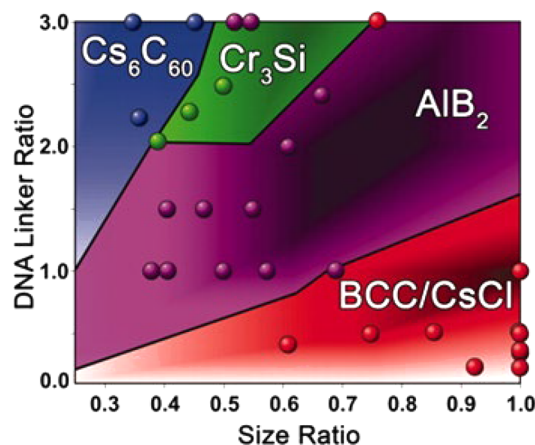


Figure 7. Phase diagram showing the types of lattices expected for programmable atom equivalents with different DNA linker ratios and size ratios. Reprinted with permission from ref 51. Copyright 2011 American Association for the Advancement of Science.

DNA linker strands on each of the two PAE types—versus the size ratio—the ratio of the size (here, defined as the radius of the core of the PAE plus the DNA linker length) of each of the two PAEs—instead of pressure and temperature in traditional phase diagrams, one can construct a phase diagram of the predicted crystalline phases of PAE assemblies (Figure 7).⁵¹ By incorporating such an example, we expose students to a sample of the other types of phase diagrams that can be constructed, broadening their awareness of this topic. This section also continues to deepen the discussion of PAE-based materials. Note that, because of the qualitative nature of this work, problem sets have been designed based on these concepts.

Solids and Modern Materials

General Chemistry texts traditionally feature nanomaterials primarily within their “Solids” or “Modern Materials” sections.^{41,42} By weaving nanoscience concepts through many

course elements as is discussed herein, using SNAs, and more generally PAEs, as model systems, we significantly advance what is possible with these discussions. For instance, when discussing the close packing of spheres in metallic and ionic solids, we can now accentuate the strong similarities to PAE assembly. The atoms in metallic and ionic solids pack closely to maximize the interactions between their valence electrons to efficiently share them throughout the system, and the most stable lattice of PAEs maximizes the number of all types of possible sequence-specific DNA duplex interactions (via the CCM, a key model governing PAE assembly).⁵¹ In the simplest cases, this means that for PAEs that are all the same size (particle diameter plus DNA length) and covered with *self-complementary* DNA strands, FCC lattices, one of the densest, most efficient packing arrangement of spheres of a single size, form, and if two sets of PAEs with *complementary* DNA strands are used, a body-centered cubic (BCC) lattice forms. By varying the size and linker ratio of the PAEs in the assembly, DNA design, or other thermal conditions of growth according to the design rules, scientists have also isolated PAE lattices with simple cubic, hexagonal close-packed (HCP), CsCl, AlB₂, and other crystal structures typically introduced in General Chemistry (Figure 8).⁵¹ However, we emphasize that a

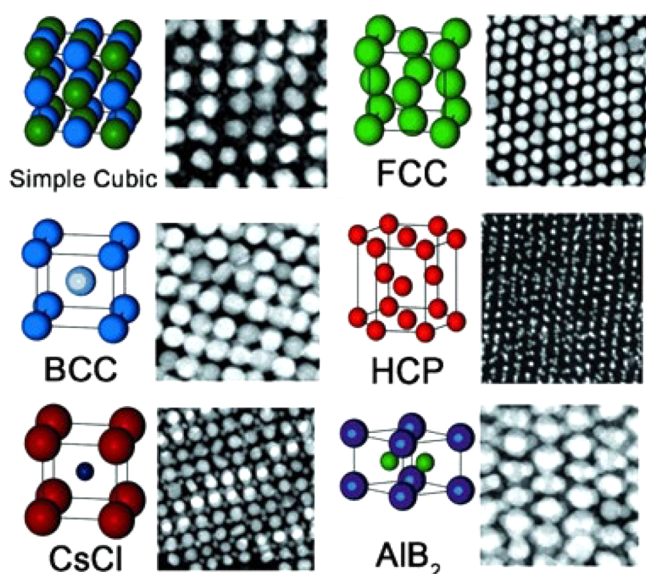


Figure 8. Examples of crystal symmetries that can be made with PAEs (over 50 have been prepared thus far, including ones not seen in nature), with their corresponding transmission electron microscopy (TEM) images. Reprinted with permission from ref 51. Copyright 2011 American Association for the Advancement of Science.

difference between PAEs and ionic and metallic solids is the strength of the interaction between particles as compared to atoms. Due to the much weaker hydrogen-bond interactions central to PAE–PAE bonding, PAE lattices exhibit much lower melting temperatures than many of their metallic and ionic solid counterparts. Nevertheless, we can still describe PAE lattices in terms of the unit cell and their lattice parameters. Therefore, the General Chemistry student can learn about the structures of PAE assemblies alongside those of traditional solid systems.

Unlike with metallic and ionic solids, PAEs crystallize according to the same set of rules regardless of the nanoparticle core's identity (i.e., size and composition), yet another key

difference. As mentioned above, another basic design rule dictates that the overall size of the PAE rather than the lengths and diameters (or compositions) of the individual oligonucleotide and nanoparticle components, respectively, dictates PAE assembly behavior.⁵¹ Effectively, that means that PAEs with two different core sizes (or compositions) and DNA lengths could exhibit similar packing behavior, permitting the synthesis of exotic alloys and hybrid crystals composed of nanoparticles of more than one size or composition.^{61–63} Thus, the rules governing PAE assembly⁵¹ are ultimately more predictive than Pauling's rules for inorganic solids, which simply provide a basis for understanding why particular structures form. The tenets of PAE assembly can be used to design and synthesize targeted structures with desired emergent properties, a major goal of chemists who want to use science to understand and then control aspects of the natural world.

A unique feature of metallic solids is that valence electrons delocalize over the entire structure—the electron-sea model. Recent work has shown “electron-like” PAEs mimic the movement of electrons within metallic solids.⁶⁴ These PAEs, referred to as “electron equivalents” (EE), are smaller in size, possess a lower density of surface-bound DNA compared to their traditional PAE counterparts, and can diffuse freely throughout a larger PAE lattice, stabilizing various compound phases. By introducing the concept of EEs alongside a discussion of metallic structure, we highlight another similarity between atomic and PAE bonding.

Finally, another common feature of modern materials discussions in General Chemistry is a section on polymers. Nucleic acids, one of the fundamental building blocks of SNAs, are an important biological polymer, and in relation to PAEs, we present nucleic acids as a smart “glue” in materials chemistry, not just a biological entity. Because this is a key concept foundational to many fields of modern chemistry research, this concept is important to introduce to General Chemistry students. Note that we also can make an analogy between SNAs and another modern, spherical material familiar to General Chemistry students—a fullerene, a three-dimensional, spherical form of carbon⁶⁵ (like carbon, nucleic acids come in many forms).

Properties of Solutions and Equilibria

In terms of their materials classification, solutions of SNAs, and many other types of nanoparticles, are sols—colloids where the dispersing substance is a liquid and the dispersed substance is a solid.^{25,41} Therefore, solutions of SNAs serve as an example along with other common examples of sols highlighted in General Chemistry, like paint. As is touched upon in General Chemistry texts, charge is very important when discussing many types of colloids, and colloids with highly charged particles are often stable. As-synthesized gold nanoparticles, the cores of classic SNAs, are negatively charged because their surfaces are stabilized by citrate ions (sodium citrate is a reducing agent/stabilizer in gold nanoparticle synthesis).⁶⁶ DNA is a polyanionic molecule, and when thiolated forms are chemically linked to a gold nanoparticle to form a SNA, it displaces the more weakly bound citrate molecules.²⁵ Thus, the particle conjugate becomes more negatively charged than the gold nanoparticle that is not functionalized with DNA.⁶⁷ Practically, then, the SNA is more stable than the citrate-functionalized gold particle, and this concept helps explain why SNAs are stable in saline solutions, buffers, biological, cellular, and other complex environments and solvent systems, while as-

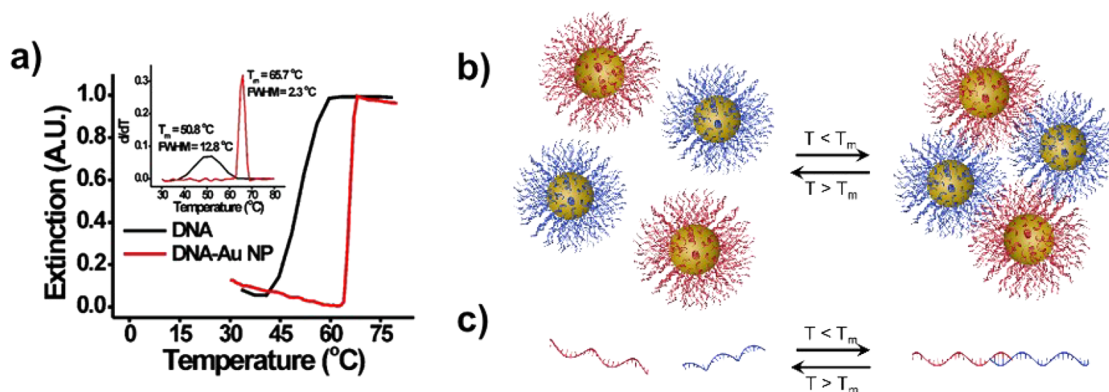


Figure 9. Melting transitions (a) for assemblies of spherical nucleic acids (red) (b) and linear duplex DNA (black) (c) of the same sequence. The inset shows the first derivatives of these transitions, which can be utilized to determine the melting temperature. Reprinted from ref 75. Copyright 2008 American Chemical Society.

synthesized gold nanoparticles are not.^{25,68,69} This lesson can be coupled with classroom or laboratory activities that explore the effect of adding strong electrolytes (like NaCl) to gold nanoparticle solutions.⁷⁰ This route also gives us an inroad to considering the applications of SNAs in medicine,^{71–73} an interesting discussion for many General Chemistry students.

In General Chemistry, students spend several chapters becoming familiar with equilibria of all types, including chemical equilibrium, acid–base equilibria, and other aqueous equilibria (including titrations).^{41,42} We incorporate SNAs as a modern model to demonstrate shifting chemical and solubility equilibria. Solubility, the capacity for a solute to dissolve in a solvent, is a prominent topic in General Chemistry, as well as the factors that influence it, like temperature, common ions, pH, and complexing ions. We can modernize this discussion in the context of nanoscience and technology and SNAs to show how solubility is important in real-world situations, such as in biology and biomedicine, a major student interest. For example, small molecules (i.e., the drug paclitaxel) that are typically insoluble in aqueous solution become significantly more soluble when conjugated to the surface of a gold nanoparticle using DNA.⁷⁴ This is one example where nanoscale modification or encapsulation, for instance, can change the solubility of a molecular moiety, thereby enhancing functionality or performance.

Biochemistry

Lastly, many General Chemistry courses feature a section, often toward the end, introducing the chemistry of biomolecules, like proteins, carbohydrate, lipids, and nucleic acids.^{41,42} This unit serves to introduce General Chemistry students to the field of biochemistry, useful for those who are continuing their studies in chemistry and the life sciences and those planning to continue to medical school (a large fraction of the General Chemistry student body). Regarding the subsection on nucleic acids, there is an opportunity to enhance student learning by integrating concepts pertaining to SNAs. As discussed above, SNAs have different forms and functions than other nucleic acids found in nature; melting behavior is a key property that differs. For example, SNA assemblies prepared from two different sets of particles functionalized with complementary DNA have a higher melting temperature (an indicator of enhanced stability) and a sharper melting transition (an indicator of cooperative binding) than the same sequences duplexed when not on a particle surface (Figure 9).⁷⁵ Furthermore, thermodynamics experiments have also

shown that DNA strands immobilized on a nanoparticle surface bind incoming complementary DNA strands more tightly (orders of magnitude) than the same strand free in solution⁷⁶ (an enthalpic effect resulting from DNA surface confinement).⁷⁷ Unlike other forms of oligonucleotides, SNAs also can enter cells directly, without the use of cationic transfection agents despite their negative charge.^{30,68,78–83} These properties along with their enhanced stability, and other factors mentioned above, have led to the extensive use of SNAs in biology, biomedicine, and the life sciences as probes, gene regulation agents, and immunotherapies (they can bind targets more effectively and are therefore more potent).^{16,84–86} This is an active area in modern chemistry research and featuring these ideas could pique the interest of some students, including the large medical school contingent, in General Chemistry.

CONCLUSION

In this article, we described a novel educational idea focused on engaging undergraduate students in General Chemistry through integration of nanoscience and technology concepts using the SNA as a model system or proof-of-concept. We envision pairing the classroom-focused concepts described here with General Chemistry laboratory experiments and in-class demos focused on nanoscience and technology, and this has been done at Northwestern. We hope that others will adopt such a strategy and that the outcomes of such a new teaching method will (1) attract the interest of a wider subset of the student body, (2) engage students who are not necessarily chemistry majors, such as engineering, premed, biology, and liberal arts students with scientific curiosities, (3) create a venue for developing inquiry/persistence in STEM that will serve society broadly, and (4) nudge more students toward pursuing STEM degrees and research opportunities by exposing them to these modern topics. We anticipate that more parallels and illustrative differences to General Chemistry concepts will be able to be drawn as modern research progresses and that a rigorous discussion of them will benefit General Chemistry instruction and students and ultimately society as a whole.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available at <https://pubs.acs.org/doi/10.1021/acs.jchemed.1c00441>.

Survey data and Sample quiz/test questions (PDF)

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Notes

The authors declare no competing financial interest.

Sample course lecture 1: Polymers and Sample course lecture 2: Nanomaterials can be downloaded at <https://www.iinano.org/education/undergraduate-education/> in PDF or PPTX format.

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