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Nanoscience

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From Chemistry to Nanoscience: Not Just a Matter of Size[**]

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Chemistry is the science of the structure, properties, and transformation of matter. Its significant development during the past 125 years shows that this branch of scientific knowledge has played a crucial role in producing novel materials, developing applications, and improving our quality of life. Meanwhile, chemistry is one of the central sciences and contributes to the development of many other scientific fields such as physics, materials science, biology, and nowadays nanoscience.

Nanoscience is the science of matter that occurs in systems with at least one dimension on the 1–100 nm scale. Nano is about as small as it gets in the world of regular chemistry (although chemistry can start on the angstrom, i.e., subnanometer scale), materials science, biology, and electronics, and nanoscience is thus strongly related to these research fields and serves as a multidisciplinary interface for all of them.

Nanoscience is concerned with the size of matter. On the nanoscale, materials show some unique properties that bulk materials do not have, such as quantum-size and surface effects. When the particle size is on the nanoscale, properties such as melting point, fluorescence, electrical conductivity, magnetic permeability, and chemical reactivity change as a function of the size of the particle. Nanoscale materials have much larger surface areas than similar masses of larger-scale materials. As the surface area per unit mass of a material increases, a greater amount of the material can come into contact with surrounding materials, thus affecting reactivity.

The rapid development of nanoscience has gained strong support from chemistry. Historically, chemistry itself has provided a plentiful resource of nanomaterials, such as colloids, micelles, and polymers. Supramolecular chemistry and chemical self-assembly provide many ways of forming nanostructures and nanosized materials. Moreover, chemistry provides a powerful method for the production of the nanomaterials in a controlled manner. On one hand, chemistry provides the most straightforward methods to generate nanomaterials, be it top-down or bottom-up. On the other hand, on account of their high surface area and large surface energy, nanomaterials tend to aggregate and fuse with each other when their surfaces are uncoated, leading to the loss of their unique properties. It is usually necessary, therefore, to modify the surface with functional groups or stabilizers in order to increase the stability and maintain the specific properties of nanomaterials. When we look at nanoscience from a chemical viewpoint, it is not only a matter of size; there are many other factors to also take into account.

On the occasion of the 125 anniversary of *Angewandte Chemie*, which has recorded many great achievements in chemistry, we look into future of chemistry with the belief that new frontiers will bring about new opportunities for chemistry. Indeed, there is a great increase in nano-related research in chemical journals, and many new areas related to chemistry, such as the chemistry of nanoparticles, hollow nanostructures, nanocatalysts, nanomedicine are emerging. These trends show the indivisible relationship between chemistry and nanoscience. Herein, we would like to share some of our thoughts on chemistry and nanoscience from the viewpoint of size and beyond.

1. Chemistry as a Contributor to the Rapid Development of Nanoscience

The power of chemistry is its ability to create new forms of matter and/or nanostructures. Both the covalent and noncovalent bond have proved to be effective in fabricating nanostructures. In addition, through understanding the kinetics and thermodynamics of many fundamental chemical processes, various nanosized molecules and nanomaterials have been produced, thus leading to the discovery of new phenomena. Figure 1 illustrates some synthetic nanosized molecules or assembled nanostructures, and the size-dependent properties of quantum dots and organic nanoparticles to show some examples how chemistry can contribute to nanoscience.

Chemical Synthesis. Chemical synthesis has played a major role in the development of new compounds and materials. The advantage of chemical synthesis is its versatility in

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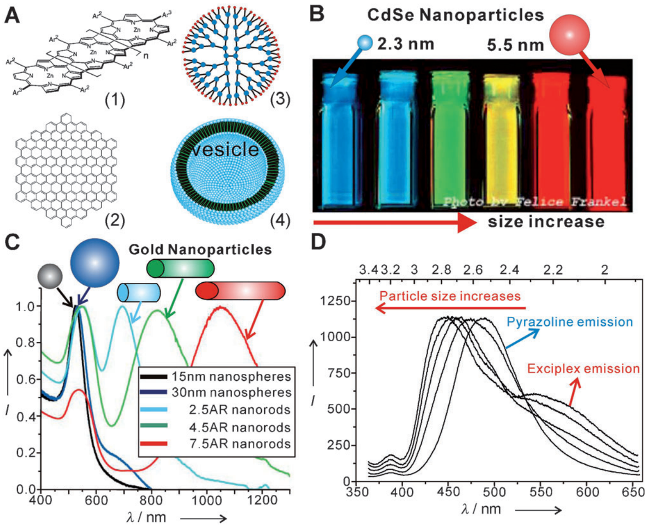

Figure 1. A) Some nanosized molecules and assemblies: 1) fused porphyrins, 2) molecular graphene, 3) dendrimers, and 4) a self-assembled vesicle. B) Fluorescence emission of CdSe quantum dots with different sizes. C) Absorption spectra of gold nanoparticles with various sizes and shapes. D) Fluorescence emission spectra of organic nanoparticles with different sizes. (Figures redrawn from references [6b] and [7a]; AR = aspect ratio.)

producing new materials with the understanding how they assemble on an atomic and molecular level and the effects on their macroscopic properties.

Researchers have synthesized a huge number of compounds from simple molecules to complicated macromolecules, and from small molecules to nanosized molecules. For example, Osuka and co-workers[1] have synthesized fused tape-shaped porphyrin arrays, which have extremely red-shifted absorption bands and can be potentially used as molecular wires. They have prepared the longest reported meso–meso-linked porphyrin arrays containing 1024 monomers with a molecular length of approximately 840 nm. Müllen and co-workers[2] have synthesized a series of molecular graphene analogues, including a giant graphite disc comprising 91 fused benzene rings. In contrast to the popular methods for preparing graphene, the structure of this molecular graphene analogue is controlled at the atomic level, and it is expected to perform well in organic electronic devices. The power of synthesizing larger-sized molecules is also shown by polymerization, a means through which various functional materials have been developed. Although functional molecules with precise molecular weights cannot be generated by most routes for conventional polymerization, they can be effectively obtained by dendrimer synthesis.[3] Recently, Schlüter and co-workers[4] have synthesized a dendrimer that has a diameter of 10 nm and a mass equal to 200 million hydrogen atoms, which is about the same size as the tobacco mosaic virus. This molecule could be the largest stable synthetic molecule ever made. With its nanometer scale and its unique structure, this dendrimer is potentially useful as a carrier for drugs or catalysts.

Chemical synthesis is not only just a matter of forming covalent bonds, it also allows thermodynamics, reaction kinetics, phase equilibria, and crystallization processes to influence the formation and properties of the formed nanomaterials. Now various chemical means have been established to produce nanomaterials of controlled size, such as quantum dots, which could be potentially used in displays, solar power, and biological imaging.[6] For example, the fluorescent CdSe quantum dots with controlled sizes can be obtained by using these synthetic techniques (Figure 1 B). The control of shape, which affects the properties of the nanoparticles, is also possible. Gold nanoparticles with various sizes and shapes show totally different UV/Vis spectra.[6b]

Besides inorganic nanoparticles, organic nanoparticles also show size-dependent effects on their properties (Figure 1 D). Although the electron confinement effect is relatively weak for organic nanoparticles because of the covalent bonding in organic molecules, the remarkable size effects on the optical properties of organic nanoparticles could also be detected.[7] However, the size range is completely different from those of metal or metal oxide nanoparticles and quantum dots. For many organic nanoparticles, aromatic molecules have been used as building blocks, and fluorescence enhancements as well as exciplex emissions have been disclosed as a function of particle sizes (Figure 1 D).

Self-Assembly. Noncovalent bonding interactions are also important for obtaining nanomaterials through supramolecular chemistry and self-assembly. With a knowledge of noncovalent bonding and self-assembly, various kinds of surfactants, amphiphiles, polymers, or even nanomaterials can be used as building blocks for the formation of the large assemblies with control of function, shape, and structural organization. The variety of the available building blocks and the full utilization of noncovalent bonding interactions provides many opportunities to obtain nanosized structures, such as vesicles (Figure 1 A) and nanotubes in a controlled manner. For example, with the rational molecular design of amphiphiles, discrete and homogeneous cylindrical hollow tubes with inner diameters of 10–1000 nm, such as organic nanotubes, can be fabricated. These structures are not only beautiful but also have tremendous potential in biology since many biological systems have similar tubular structures.[5] These systems have provided easy ways to obtain nanostructured materials and may be regarded as an important part of nanoscience.

2. Chemistry on the Nanoscale: More than Size Alone

Chemistry has contributed to the development of nanoscience, and in turn, nanoscience has also provided many opportunities for chemistry. Since the beginning of nanoscience, there has been an increasing tendency for more nano-related topics to appear in chemistry journals. Several years ago, IUPAC surveyed the impact of nanotechnology on chemistry by using publications related to nanotechnology in chemistry journals.[8] We added the data for the period 2010–2011 and combined the data in Figure 2. There is an apparent overall trend towards a growing share of nanotechnology papers in almost all chemistry journals. In particular cases,

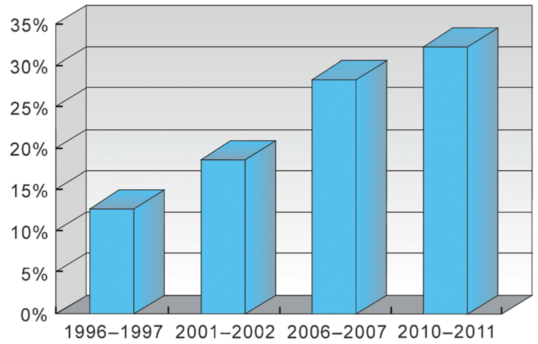

Figure 2. Proportion of nanotechnology papers in chemistry journals in different time intervals. (Part of the data is adapted from reference [8])

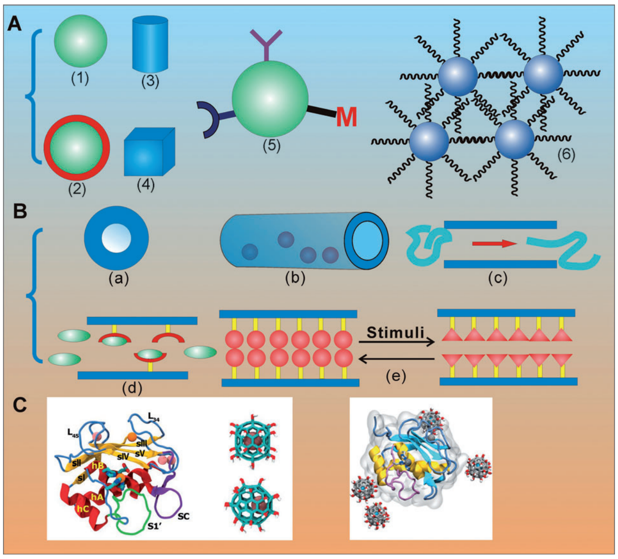

Figure 3. Nanoparticles, nanotubes/nanochannels, and nanomedicine. A) Nanoparticles with different shapes (1, 3, 4), nanoshell or core/shell nanoparticles (2), nanoparticles with various modifications (5), assembly of nanoparticles (6); B) nanopore (a), nanotube and the confinement of a catalyst (b), nanochannel for transportation of biomaterials (c), nanochannel for recognition (d), stimuli-responsive nanochannel (e). All of these channels were modified by chemical or biological compounds on their interior. C) Gd@C82$(OH)_{22}$ nanoparticles bound to matrix metalloproteinases (MMP9) as a nanomedicine. (Illustrations c–e in part B are redrawn from reference [13]; part C is from reference [18b].)

this proportion has been more than 30% in recent years. The trend forces us to consider why chemistry is so closely related to nanoscience and what nanoscience can bring to chemistry. When chemistry is performed at the nanoscale, what new phenomena or properties could emerge? What is the difference between chemistry and nanoscience? To answer these questions, an important approach is to compare traditional chemistry with that at nanoscale. While traditional chemistry focuses on reactions in solutions or in the gas phase, without considering the regime of nanostructures, chemistry at the nanoscale relates to the nanostructures as well as their sizes. It does not stop there. Surface modification, assembly, hierarchical structural evolution, and multifunction design, which are important for nanomaterials, are required of precise chemistry at nanoscale. Figure 3 illustrates several examples of nanoparticles, hollow nanostructures such as nanopores, nanochannels, and nanotubes, nanocatalysts and nanomedicine, in which new science and technology can emerge from the combination of chemistry and nanoscience, and lead nanoscience past being just about size.

Nanoparticles: Beyond the Issue of Size

Nanoparticles have been widely investigated in the fields of nanoscience. Both their size and shape effects are well known. The properties of nanoparticles, however, are not only dependent on their size and shape, but are also determined by surface modification. It is not always clear which factor, that is, if the size or the surface modifier really determines the properties of the nanoparticles. For instance, Nakashima et al.[9] have synthesized CdS, CdSe, and CdTe nanoparticles, which exhibit absorption peaks at approximately 320, 470, and 540 nm, respectively. When these nanoparticles were capped with D- and L-methylcysteine (MeCys), respectively, they showed mirror-image circular dichroism (CD) spectra. Interestingly, the CD profiles for all three nanoparticles are the same, regardless of their different absorptions. This result indicates that the optical activity of nanoparticles originates not from the CdTe core but from the surface shell of chiral capping molecules.

Tang and co-workers[10a,b] have explored the fact that, although nanomaterials have the same shapes and sizes, when their stabilizers are changed from hydrophilic thioglycolic acid to amphiphilic 2-(diethyl-amino)ethanethiol, their self-assembled structures will spontaneously alter from one-dimensional nanowires to two-dimensional nanosheets, regardless if they are noble metals or semiconductor nanomaterials. Further studies demonstrate that these self-assembled nanomaterials with different structures show different optical and electrical properties. Meanwhile, even though the stabilizers are the same, differences in the conformation of the stabilizers also gives rise to a pronounced influence on both the properties and the applications of the nanomaterials. Taking glutathione-modified CdTe nanoparticles as an example, when all the other conditions remain the same for both nanoparticles (e.g., the shapes and sizes of nanoparticles, and the number of stabilizers), the L-glutathione-protected CdTe nanoparticles are much more toxic than the D-glutathione-protected ones, an observation that is ascribed to the fact that the L-glutathione-protected CdTe NPs can be more easily phagocytosed by biological cells than the D-glutathione protected analogue.[10c]

It is clear that the properties of nanoparticles are more dependent on their surface stabilizers rather than on their size. Therefore, the challenge remains of how to control the type, number, and conformation of the stabilizers on the nanoparticle surfaces when considering their target applications. Chemistry will, no doubt, contribute to the modification of the nanoparticle surface. Such modification will not stop at simple syntheses, since many of the functional groups can be attached to the surfaces of nanoparticles, and multifunctional nanoparticles can be realized by modifying them with different functional groups, something that cannot be done with molecules. In addition, their further assembly and patterning will create new properties for further applications. Nanoparticles are one of the most important entities in nanoscience research and many new applications in materials and biology can be anticipated.

Hollow Nanostructures: Chemistry in Confined Spaces and Beyond

Nanoscience, to some extent, has grown along with the advent of fullerene and carbon nanotube research. Interestingly, both these molecules have hollow structures. While the initial interest in these materials was related to their unique electronic properties, an interest in hollow nanostructures for their own sake began to capture the imagination of researchers. Many hollow nanostructures, such as nanopores, nanochannels, and nanotubes, have been studied recently and their applications have been investigated extensively. Nanopores can be defined as pores with diameters in the range 1–100 nm, with the pore diameter being larger than its depth. If the pore depth is much larger than the diameter, the structure is generally referred to as a nanochannel.[11] In contrast to solid nanoparticles, hollow nanostructures offer several unique properties, such as the controlled transport of molecules. In addition, their inner surfaces can be modified, while the thickness of their walls and their volumes can all be controlled by chemical or physical means. These confined spaces and their tailor-made surfaces provide many opportunities for chemistry, and enrich it in many different ways, thus leading to the emergence of new functions or the mimicking of biological systems. For example, the emerging nanopore analysis technique, which involves driving molecules through nanoscale pores in a membrane between two electrolytes, and monitoring how the ionic current through the nanopore changes as single molecules pass through it, is fast becoming a new technique for DNA sequencing.[12] On the other hand, when chemical motifs are introduced into nanochannels, greater flexibility in terms of shape and size, superior robustness, and surface properties addressing desired functions can be enhanced. For example, chemical modification (Figure 3B) of the interior surfaces of nanochannels with functional molecules can result in the mimicking of the gating mechanisms of biological channels and may provide a highly efficient means to control ionic or molecular transport through nanometer-scale openings in response to stimuli that lead to a conformational change, molecular recognition, and reversible gating.[13] By designing more complex functional molecules, these nanochannels could be used to build smart biomimetic structures with more precisely controlled functions in the near future.

Hollow nanostructures provide a special and confined space where the size resembles that of carbon nanotubes. Many organic nanotubes can form confined spaces of this size through the act of self-assembly. When atoms or molecules are confined in such a small space, their properties change. A typical example is the water trapped in a reversed micelle or a microemulsion, which show different properties from those of their bulk states. Within attoliter (10^{-18} L) space, many unusual applications, such as specific gene carriers and capillary transport, can be expected.[14]

We can expect hollow nanostructrues to play a more and more important role in the development of nanoscience. With precise chemical modification and controlled fabrication, these nanomaterials are not limited by their sizes and their applications in functional materials, diagnostics, sensing, drug carriers, or delivery systems can be anticipated. At the interdisciplinary interfaces between chemistry, biology, and physics, more hollow-structured nanomaterials will emerge with greater frequency en route to finding more real-life applications.

Nanocatalysts: In Search of More Efficiency and Selectivity

Catalysis is an extremely important chemical process and most of the modern chemical industry would not exist if there were no catalysts. One of the principal challenges in chemical catalysis is the development of methods for the control and manipulation of the activities, selectivities, and specificities of catalytic systems. Although the field of surface science has contributed significantly to our fundamental understanding of catalysis at a molecular, and even atomic, level, most commercial catalysts are still produced by a process of "mixing, stirring, and baking" that involves multiple components without any control of their nanostructures, a detail which might be very important. Nanostructured materials often have increased surface areas and improved reactivities, and so can possibly lead to better catalysts. Nanocatalysis, which involves the use of nanomaterials as catalysts, is currently experiencing an explosive growth for a variety of applications in homogeneous and heterogeneous catalysis. One can expect catalysis using engineered nanostructured materials to impact on the oil and chemical industries, and our daily lives. For example, more efficient catalytic converters in cars will reduce the toxicity of the vehicle exhausts. Nanoengineered batteries, fuel cells, and catalysts can potentially rely on enhanced reactivity at the nanoscale to produce cleaner, safer, and more affordable modes of energy production and storage. The activity and selectivity of nanocatalysts can be increased by controlling their pore size and particle characteristics. In addition, the replacement of precious-metal catalysts by catalysts tailored at the nanoscale can be anticipated. The control of active sites and the immobilization of catalysts in nano-confined spaces as well as their exposed surfaces will dramatically increase their efficiency and selectivity.[15a] We continue to expand our knowledge of nanocatalysts. For example, Bao and co-workers[15b] have reported a striking enhancement of the catalytic activity of Rh particles when they are confined inside carbon nanotubes for the conversion of CO and H_2 to ethanol. They found that the overall rate of formation of ethanol inside the nanotubes exceeds that on the outside of the nanotubes by more than an order of magnitude, even though the latter offers much more accessible space for the catalytic reaction. This kind of synergetic confinement indicates that nanostructures can provide a new platform for more efficient or selective chemical reactions.

When traditional chemical catalysts are transformed into nanocatalysts, which take the form of nanostructured materials, it is necessary that we deepen our basic understanding of their mechanisms, as well as controlling fabrication by better processing. We predict that nanocatalysts will raise the stature of nanoscience and also win a large commercial market.

Nanomedicine: Towards Biology from the Interface of Chemistry and Nanoscience

Nanomedicine can be defined as "the use of materials, of which at least one of their dimensions that affects their function is in the scale range of 1–100 nm, for specific diagnosis or therapeutic purpose".[16]

The design and synthesis of precisely tailor-made nanostructures are essential for the development of nanomedicine. In short, chemistry is the basis for successful nanodrug development. For example, therapeutic nanodrugs originating from "engineered nanomaterials" can be designed and synthesized by chemists. By using such man-made nanodrug carriers, traditional therapeutic compounds can be delivered to diseased areas with significantly lower dosages and considerably less side effects, especially when compared to highly toxic antitumor chemotherapeutic agents, which have disadvantages in that they can damage healthy tissues and the immune system of patients.[17]

More recently, it has been demonstrated that nanomaterials themselves can be used directly as novel therapeutic agents.[18] These intelligent materials do not need to carry any traditional drugs to realize highly efficient antitumor therapy, and, more importantly, with low or no toxicity. Zhao and coworkers have reported, on the basis of experiments in cells, tissues, and animals, that the endohedral metallofullerenol $Gd@C82(OH)_{22}$ can inhibit neoplastic activity (Figure 3C).[18] The compound $Gd@C82(OH)_{22}$ effectively blocks tumor growth in human pancreatic cancer xenografts in a nude mouse model.

For diagnostic applications, nanomaterials are usually prepared by wet chemistry methods or by nanofabrication in the case of nanodevices. Even although highly developed nanodevices can be produced by physical manufacturing, they still need further surface functionalization with nanosurface chemistry in order to achieve a specific biomedical function for diagnosis.[19] There is an urgent need to develop effective and efficient collaborative research frameworks and platforms to attract scientists from chemistry, biology, materials science, medicine, and engineering to produce nanomedicines for our society: chemistry will surely play a crucial role in this mission.

When medicinal chemistry meets up with nanomedicine, the science goes far beyond the use of nanosized materials: its biocompatibility, safety, and bioeffects need to be considered. It is necessary to assemble all the knowledge of chemistry, life sciences, and medical practice. Indeed, it is a very active research field, not only because of the nanofabrication of sophisticated diagnostics and therapeutics into a more efficient and new system, but also because of the expectations for the development of nanomaterials with completely new medicinal actions. In any case, there is still a long way to go to develop nanomedicine for we should take everything into consideration for its safety and long-term bioeffects.

Summary and Future Challenges

Chemistry has demonstrated its power in creating nanomaterials with controlled size, shape, morphology, and surface modifications. Nanoscience provides an open platform for chemistry at the nanoscale, on nanosurfaces, and in nanospace. Chemistry is entering into more precise and more complicated systems. It faces many challenges at the nanoscale. For example, how can we probe chemical processes on the nanoscale? The development of new instruments and methods are needed. With STM, we can see and even manipulate atoms and nanostructures.[20] The challenge remains, however, of how to probe chemical processes as they relate to structure and reactivities on the nanoscale. Secondly, we have observed many new phenomena at the nanoscale and in nanomaterials. The theoretical understanding of nanoscale processes, such as the catalytic, enzymatic, and biological effects of nanoparticles, still remains unclear. Thirdly, when we focus on nanosize, in fact, microsize cannot be neglected. In many cases, the functions can only be realized with the support of microsystems. When we are considering the functions of cells, we need to think about how to combine hierarchical structures from the molecular and nanoscale all the way up to the microscale. It is still a challenge to fabricate materials in a controlled manner through various hierarchical levels.

The 20th century has witnessed some enormous benefits in the well-being of humankind brought about by chemistry, despite its well-publicized shortcomings. The question now is, can we look forward to "better living through nanoscience" in the 21st century? We have discussed the developments in nanoparticles, hollow nanostructures, nanocatalysts, and nanomedicine, as well as their potential applications in the materials industry and human health. Insofar as nanoscience is concerned, we still have areas, such as nanoelectronics and nanobiotechnology, all of which are witnessing rapid development. There is no doubt that nanoscience will result in a better quality of life for us—even our lifestyles in the future will experience radical change. However, just as the development of chemistry resulted in the concept of green chemistry and sustainability in order to solve environmental problems, nanoscience also has to develop in a green manner. Therefore, we should call for the green development of nanoscience and make sure that there are regulations that are observed worldwide.

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