Synthesis and Assembly of Nano-Building Blocks and Their Bio-Medical Applications

Current technologies including informational, biological, and medical technology have their bases mainly on classical mechanics. The ever growing demands for the fabrication of smaller devices used in daily life and faster operation are pushing the limits of current classical mechanics based-technologies to meet the demands from both the general public and industry. Nanoscience and nanotechnology utilizing inorganic nanocrytals have recently emerged as a promising candidate to overcome many of the limitations of the currently available technologies. Although nanoscience and nanotechnology have potentials with the new possibilities for the significant improvements in many scientific and industrial areas, current studies still lie in the initial stage. This is mainly due to limited development of nano-building blocks and poor understanding of novel chemical and physical nanophenomena. Therefore, it is important to develop a general synthetic protocol for the fabrication of inorganic nano-building blocks with nanoscale controllability. The ability to synthetically tune the materials properties of nanocrystals in terms of size, shape, and composition allows one to observe and systematically control their enhanced optical, magnetic, and electronic properties, which finally make them useful for the futuristic informational and bio-medical device applications.

During my graduate research program, I have pursued to have a general understanding of colloidal inorganic nanocrystals in both synthetic and application aspects. At the beginning of my research, I have focused on the development of a general synthetic protocol which can produces a variety type of inorganic nanocrystals with controlled geometry in terms of size, shape, composition, and surface states. The shape guiding mechanism of various nanomaterials, which includes semiconductors (CdS, MnS, PbS, GaP), electronic ceramics (TiO_2, Mn_3O_4, $W_{18}O_{49}$), and magnetic materials (Co, CoPt, Fe_3O_4), were systematically investigated. At the last two years of my graduate research program, I moved my interest into the biomedical applications of nanocrystals, especially magnetic materials. I and my colleague developed a novel type of magnetic nanocrystal probes and successfully utilized them for *in vitro* and *in vivo* breast cancer diagnosis through dynamic targeting and magnetic resonance imaging (MRI).

My research is started from the shape control of semiconductor CdS nanocrystals. Since CdS possesses two distinct crystalline structures which include isotropic zinc blende and anisotropic wurtzite, CdS can be a good model system to investigate crystalline phase effects of nuclei on the final geometry of the nanocrystals. We found that the crystalline phase of the nuclei is controllable by changing synthetic parameters (e.g. growth temperature, monomer concentration) and is crucial for determining the final geometry of the nanocrystal. The shape of nanocrystals obtained systematically evolves from 1-dimensional (1-D) rods to tetrapods through bipods and tripods, as the growth temperature decreases (Fig. 1). Systematic structural analyses including high resolution transmission electron microscopy (HRTEM) and X-ray diffraction analyses (XRD) reveal that 1-D rods are formed as a result of preferential growth of nanocrystals along the *c*-axis of wurtzite nuclei, while tetrapods are resulted from epitaxial growth of wurtize arms from four {111} faces of zinc blende nuclei. Our multipod structures of bipods and tripods are some of the first pioneering works in the research area of nanocrystal synthesis. We reported this result in JACS (2001) and this article has been cited many times during last three years by other following researches (times cited: 78).

We extended our study to a magnetic semiconductor nanocrystal, MnS, which have the diverse crystallographic structures from zinc blende to wurtzite, and rock salt. In consistent with the CdS nanocrystal case, control of the crystal

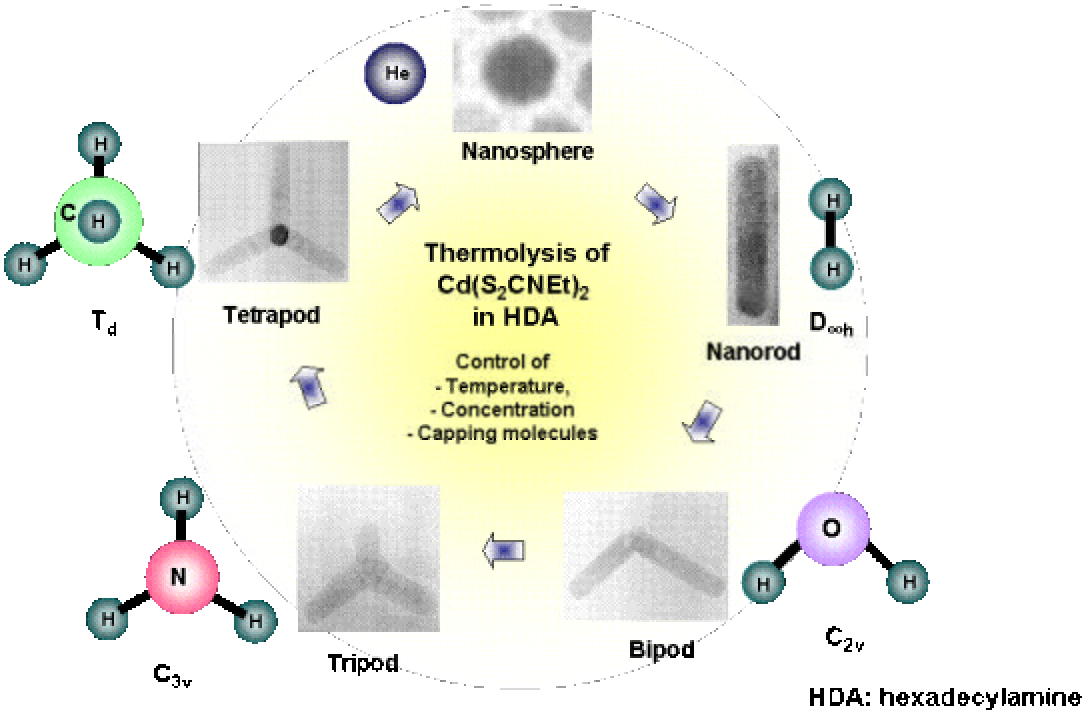

Fig. 1. CdS nano-architectures with various symmetries.

growth parameters results in systematic variation of nanocrystal shapes which include monowires, branched nanowires (bi-, tri-, and tetra-pods), rods, spheres, and cubes. Shape dependent optical and magnetic properties of MnS nanocrystals obtained were elucidated. Obtained nanowires exhibit enhanced optical and magnetic properties compared to those of 0-D nanospheres.

Based on the shape controlled synthesis of CdS and MnS, we further investigated the synthesis of diluted magnetic semiconductor (DMS) $Cd_{1-x}Mn_xS$ nanocrystals. DMS nanocrystals are of great interest in materials science since the use of both the spin and the charge of electrons in semiconductors has long been thought as an ideal components for the storage and processing of information for electronic devices. Proper choice of molecular precursors which can generate stable monomers and kinetically driven low-temperature growth afford dopant controlled 1-D $Cd_{1-x}Mn_xS$ nanorods with homogeneous doping of Mn at high levels (up to 12 %), which is supported by XRD and electron paramagnetic resonance (EPR) results. This work was reported in JACS (2002) and this is the first report of the homogeneous doping of magnetism in quantum rod.

To have better understanding the shape evolution processes of nanocrystals from 0-D to 1-D structures, we investigating the PbS nanocrystal system. By carefully controlling the nanocrystal growth regime between thermodynamically controlled growth and kinetically controlled growth regimes, we accomplished the first synthesis of the highly symmetric star-shaped nanocrystals as a transient species between 0-D cubes and 1-D rod based multi-pods was synthesized (Fig.2.). This result was published in JACS (2002) and highlighted in various scientific media such as Science and Chemweb.com.

Further studies in the shape-controlled synthesis of nanocrystals were performed with metal oxide nanocrystals. In this study, we focused on the role of a capping molecule which selectively binds to a specific crystallographic face. This

strategy resulted in the systematic nanocrystal shape control from bullet and diamond structures to rods and branched rods

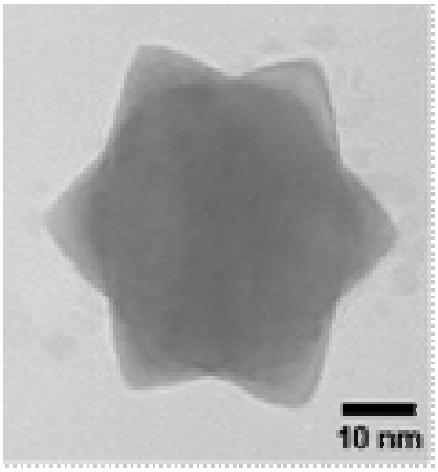

Fig. 2. Highly symmetric PbS star-shaped nanocrystals.

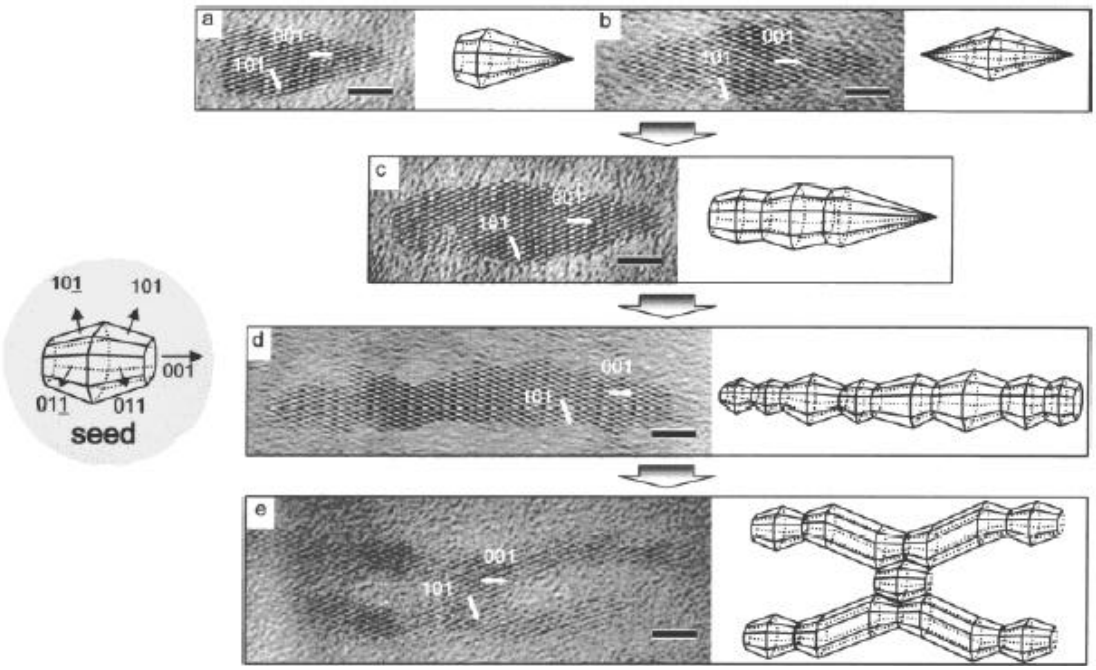

Fig. 3. Shape evolution of TiO_2 nanocrystals. (a) a bullet, (b) a diamond, (c) a short rod, (d) a long rod, and (e) a branched rod. The long axes of the nanocrystals are parallel to the *c*-axis of the anatase structure, while the nanocrystals are faceted with {101} faces along the short axes. Hexagon shapes (the [010] projection of a truncated octagonal bipyramid) truncated with two {001} and four {101} faces are observed either at the one end or at the center of the nanocrystals. The branched shape is a result of the growth along [101] directions starting from the hexagon shape. Scale bar) 3 nm.

(Fig. 3). We found that the modulation of surface energies of the different crystallographic faces through the use of a surface selective surfactant also act as a key parameter for the shape control.

As well as nanocrystals described above, we have synthesized other nanocrystals including ZnSe, ZnTe, GaP, Mn_3O_4, $W_{18}O_{49}$, Co, CoPt, and Fe_3O_4 with well-defined size and shapes. Shape controlled synthesis including these works were reported in world renown journals including JACS and summarized as an invited review paper in Coordination Chemistry Reviews (2005 in press) and two book chapters.

With these nanocrystals synthesized, I have interested in the utilization of the nanocrystals for bio-medical sciences. Among various nanocrystals that I have, magnetic Fe_3O_4 nanocrystals which exhibit unique properties arising from superparamagnetism were chosen. Before utilizing them for bio-medical applications, we investigated nanoscale size effect that correlates magnetism, induced nuclear spin relaxation processes, and MR signals. By elucidation of nanoscale size effect, we developed unique magnetic nanocrystals with multiple capabilities such as well-defined and strong magnetism, high bio-compatibility, and the possession of active functionality for desired receptors. Our magnetic nanocrystals lead to the development of high performance magnetic nanocrystal probe systems for magnetic resonance imaging (MRI). Upon conjugation to a targeting antibody, these nanocrystal conjugates are utilized as MRI probes not only for *in vitro* diagnosis of cancer cell lines but also for the monitoring of *in vivo* dynamic targeting events of human cancer cells implanted in live mice by taking advantage of their exceptional properties (e.g. strongest magnetism for MR effect reported so far, high colloidal stability, and high binding selectivity). This study demonstrates the first successful *in vivo* MRI diagnosis of cancer through direct cancer marker recognition processes of magnetic nanocrystal probes.

In conclusion, during the past four years I have developed novel shapes of inorganic nanocrystals with the systematic elucidation of nanocrystal growth processes and demonstrate their utilization for medical diagnostic systems. Our synthetic strategy for the nanocrystal fabrication can be extended to other nanomaterials and the nanocrystals obtained will be the key components for the futuristic nanodevices. Furthermore, I believe that our research can be extended to the development of a smart nanohybrid system such as an artificial nanocrystal-based immune system which can perform simultaneous detection, pin-pointing therapy, and maintenance after the therapy inside a living system. In my future research, I am pursuing to develop this smart nanohybrid system by combining the unique properties of nanocrystals and chemical or biological functional molecules.