Introduction

Quantum dots (QDs) are semiconductor particles that contain hundreds to many thousands of atoms (the particle diameter is typically in the range of 1 to 10 nm), which are often composed of atoms from group II-VI (e.g. CdSe, CdTe, CdS, and ZnSe) or III-V (e.g. InP, InAs, GaP, and GaAs) elements in the periodic table. [1,2] Because of their novel optical and electrochemical properties, which will be discussed in the next section, quantum dots are of current interest for chemical, physical and biological research.

Optical properties [1-4]

Semiconductors have an energy gap between the valence band and the conduction band. As the size of a semiconductor is reduced to the nanometer scale, the edges of the bands become discrete and band-gap energy becomes larger (Figure 1, left). [1] Therefore, the fluorescent emission energy increases, which means that quantum dots have various fluorescent colors depending on particle size as shown in Figure 2. [3] More interestingly, these quantum dots can be excited simultaneously by a single wavelength due to their broad excitation spectrum while conventional organic dyes have narrow excitation peaks (Figure 1,
right), [3] thus multicolor experiments are possible with a single light source. Quantum dots are also extremely stable against photobleaching, as the fluorescent colors last for hours while conventional dyes last only for several minutes. [2]

**Figure 1.** (Left) Density of state in metal (A) and semiconductor (B) (Right) Comparison of (a) the excitation and (b) the emission profiles between rhodamine 6G (red) and CdSe QDs (black).

**Figure 2.** Ten distinguishable emission colors of ZnS-capped CdSe QDs excited with a near-UV lamp. From left to right (blue to red), the emission maxima are located at 443, 473, 481, 500, 518, 543, 565, 587, 610, and 655 nm.
Synthesis

Before 1993, Quantum dots were normally prepared in aqueous solution with stabilizing agents. Quantum dots from this method were of low quality (poor fluorescence quantum yields and large size variations). In 1993, Bawendi et al. [5] developed a simple route to produce of high-quality CdSe quantum dots through a high-temperature organometallic procedure. These particles have narrow size variation (5% RSD in diameter) and nearly perfect crystal structures, but the quantum yields were still low (~10%). In 1996 and 1997, several research groups [6] introduced core-shell type composite quantum dots which improved the fluorescent quantum yield up to 30-50%. ZnS, which has a wider band gap than CdSe but similar bond length was deposited on CdSe quantum dot. Most recently, Peng et al. [7] reported alternative routes to production of Cd quantum dots (CdTe, CdSe and CdS) by using CdO as a precursor instead of using the organomatetallic compound, Cd(CH₃)₂, which is extremely toxic, expensive and unstable at room temperature. This new method is reproducible, simple and more environmentally benign. Moreover, large-scale syntheses are possible because of the mild reaction conditions.

Applications to biosensing

In 1998, two research groups [8,9] reported using quantum dots as fluorescent biological stains in cells. The first problem they encountered was how to make their quantum dots soluble in aqueous solution, a critical condition for biological labeling. Alivisatos and coworkers [8] used a silica/siloxane coating as a
third layer on ZnS-capped CdSe QDs. They linked biotin onto the silica surface by a covalent linking reaction, and then used these QDs to label filaments of actin protein in mouse fibroblast cells. The second group [9], Nie and coworkers, prepared water-soluble QDs by directly adsorbing bifunctional ligands such as mercaptoacetic acid on the QD surface. These dots were then labeled with protein and immunomolecules to detect specific antibodies and antigens. Since these original papers, QDs have been used as biological dyes by many other groups.

As was mentioned earlier, quantum dots can be used in multicolor fluorescent experiments with a single excitation light source. Nie and coworkers [10] reported multicolor optical coding of biomolecules by embedding multicolor quantum dots (ZnS-capped CdSe) inside polystyrene microbeads (1.2µm) at precisely controlled ratios (Figure 3). The use of six colors and ten intensity combinations can theoretically encode up to one million nucleic acid or protein sequences. They covalently linked several probe DNA molecules to the multicolor beads and used these beads to detect target DNA simultaneously at the single bead level. Alivisatos’ group [11] also reported multicolor analysis using quantum dots having different emission colors. They covalently immobilized four different sequences of DNA to four kinds of quantum dots. By using the complementary DNA of each, quantum dot-tagged DNA was sorted and detected with a single excitation light source.

As a real biological application of quantum dots, Dubertret et al. [12] introduced quantum dots encapsulated in phospholipid micelles that are more biocompatible. The micelle-encapsulated quantum dots were stable and nontoxic
(<5 \times 10^9 \text{ nanocrystals per cell}) after injected into Xenopus embryos and they were confined exclusively to the injected cells and the progeny of the injected cells.

Besides these applications of quantum dots as fluorescent dyes, they have also been attached on electrode surfaces for photoelectrochemical sensing of enzyme inhibitors by Pardo-Yissar and coworkers. [13] In this work, they prepared monolayers consisting of a CdS quantum dots/acetylcholine esterase hybrid system which was used to detect enzyme inhibitors.

References

3. Chan, WC. W.; Maxwell, D.J.; Gao, X.; Bailey, R.E.; Han, M.; Nie, S. Current Opinion in Biotechnology 2002, 13, 40-46


