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Quantum Dots-Based Biological Fluorescent Probes for *In Vitro* and *In Vivo* Imaging

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1. Introduction

The 2008 Nobel Prize in chemistry was awarded to three distinguished scientists who discovered and developed the green fluorescent protein (GFP), which has proved to be a powerful and versatile fluorescent probe for biological and biomedical researches [1]. High-performance fluorescent biological probes are expected to possess several important properties including excellent water-dispersibility, high photoluminescent quantum yield (PLQY), robust photostability, and favorable biocompatibility. A consensus has been reached that the GFP and organic dyes, recognized as the well-established fluorescent probes, are to some extent inappropriate for long-time in bioimaging because of their photobleaching property (Figure 1). In this respect, II-VI QDs have attracted intensive attentions due to their unique optical and electronic properties (e.g. size-tunable emission, broad photoexcitation, narrow and symmetrical emission spectra, strong fluorescence, and robust photostability). Indeed, the QDs are currently considered as most promising fluorescent probes, which open new opportunities for real-time and long-term monitoring and imaging both *in vitro* and *in vivo* [2].

1.2 Synthesis of II-VI QDs

It is well-known that there are two rudimentary approaches to prepare II-VI QDs: one is the organometallic route, the other is the aqueous method.

The organic synthesized QDs (orQDs) with excellent spectral properties have been achieved through the well-established organic strategy in elegant work [3]. As far as 1993, Bawendi's group developed a simple strategy, which was based on the pyrolysis of organometallic reagents by injection into a hot coordinating solvent, to production of serial highly monodispersed II-VI QDs (e.g., CdS, CdSe, and CdTe QDs). Such resultant QDs possessed uniform size, shape, and sharp absorption and emission features [3a]. Alivisatos et al. studied the growth kinetics of the CdSe QDs in a detailed way, providing a useful guidance for testing theories of quantum confinement, and also for designing high-quality QDs of controllable shapes [3b]. Peng and coworkers, by using CdO as precursor, developed more

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green-chemistry methods to prepare II-VI QDs [3c]. On the basis of which, they further optimized experiment conditions to synthesiz CdSe QDs with excellent optical properties, whose PLQY value reached 85% [3d]. Thereafter, different kinds of core-shell structured QDs (e.g., CdTe-CdS and CdTe-ZnS QDs) were achieved via organic synthesis [3e,f]. It is worth noting that, these orQDs cannot be directly used in bioapplications due to their hydrophobic character. A general strategy is to transfer the hydrophobic nanocrystals from the organic phase to aqueous solution by wrapping an amphiphilic polymer around the particles [4]. Although this method is efficient, it is relatively complicated and requires addition steps. Another effective strategy is to substitute the hydrophilic molecules, which have strong polar groups such as carboxylic acid or reactive groups such as Si-O-R, for surface-binding TOPO [5]. Nevertheless, in addition to relatively complicated manipulations, the treatment may depress optical properties and stability of the QDs (e.g, the PLQY may decrease when the orQDs are transferred into water because the polarity of water is too strong to break various equilibriums related to the nanocrystals) [6].
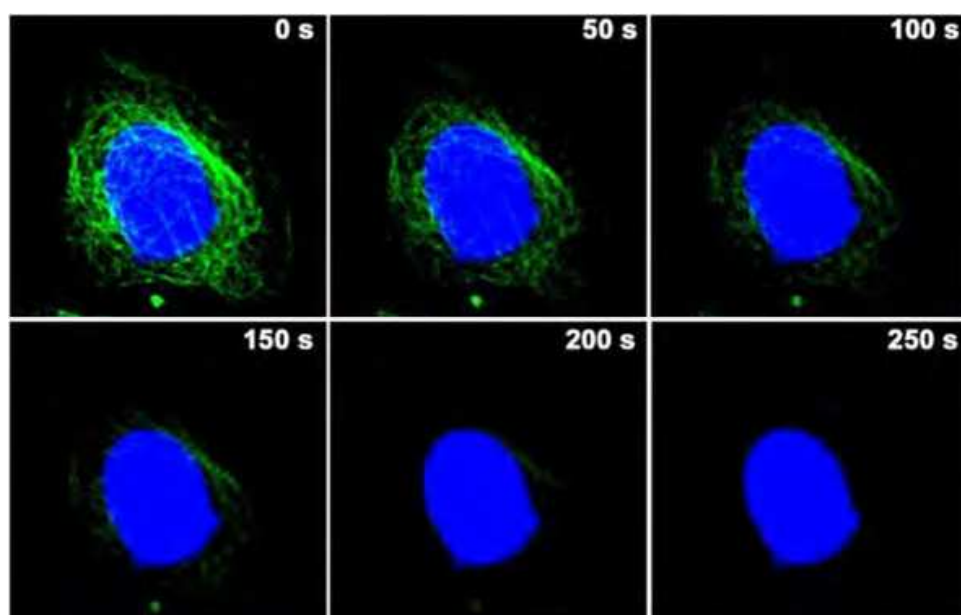

Fig. 1. Photobleaching of organic dyes. Microtubules were labeled with fluoresceinisothiocyanate (FITC, one typical kind of commercial organic dyes). Green fluorescence signals of FITC were rapidly disappeared in 250-s irradiation owing to severe photobleaching.

Aqueous synthesis is an alternative strategy to directly prepare water-dispersed QDs, which is relatively simpler, cheaper, less toxic, and more environmentally friendly. More importantly, the aqueous synthesized QDs (aqQDs) are naturally water-dispersed without any posttreatment due to a large amount of hydrophilic ligand molecules (e.g., 3-Mercaptopropionic acid, thioglycolic acid, et al.) covered on their surface. Rogach and coworkers reported aqueous synthesis of CdTe aqQDs those are directly prepared in water by using thiol molecules as ligands. However, the PLQY of aqQDs was generally lower than 30% [7]. Systematic investigations reveal that, large amount of surface defects, which are often generated due to the long reaction time in aqueous phase, results in low PLQY [8]. Tremendous effort has been devoted to improve the spectral properties of QDs directly prepared in the aqueous phase. Zhang et al developed a hydrothermal method

for synthesis of highly luminescent aqQDs (PLQY: ~50%). Notably, the growth rate of QDs was greatly accelerated under high reaction temperature (e.g, 200 °C), leading to effective reduce of surface defects [9].

More recently, microwave-assisted method has been developed as novel promising strategies for synthesizing high-quality QDs. Compared with conventional heating method, there are four main advantages about microwave irradiation as heating method: (a) temperature can be rapidly raised due to the high utilization factor of microwave energy, and the kinetics of the reaction are increased by 1-2 orders of magnitude, (b) stirring effect on molecular level can be realized through microwave irradiation, which are favorable for uniform heating, (c) stagnant phenomenon can be effectively avoided compared with traditional heating method because microwave energy vanishes once closing microwave device, and (d) the initial heating is rapid which can lead to energy savings [10]. Ren et al reported CdTe aqQDs with PLQY of 40-60%, which were rapidly prepared via microwave synthesis [11]. He and coworkers developed a facile microwave-assisted method for synthesizing a variety of highly luminescent aqQDs (e.g., CdTe/CdS core-shell QDs, CdTe/CdS/ZnS core-shell-shell QDs). Notably, such resultant aqQDs feature excellent optical properties (PLQY: ~50-80%) due to the above-mentioned unique merits of microwave irradiation (Figure 2) [12]. Very recently, they further synthesized the near-infrared (NIR)-emitting QDs via microwave synthesis. Significantly, the prepared NIR-emitting QDs possessed excellent aqueous dispersibility, ultrasmall size (~4 nm), robust storage-, chemical-, and photo-stability, and finely-tunable emission in the NIR range (700-800 nm) [13].

1.3 II-VI QDs for biological fluorescence imaging

Biological fluorescence imaging is one of most important and interdisciplinary research involving chemistry, biology, life science, and biomedicine, which has been widely used for various *in vivo* and *in vitro* studies [1]. Particularly, fluorescent biological probes are essential tools for bioimaging. For optimum imaging and tracking of biological cells, these probes should be water-dispersible, anti-bleaching, luminescent, and biocompatible. In the last century, organic dyes and fluorescent proteins were mostly used as fluorescent probes in biological research; however they suffer from severe photobleaching that restricts their applications for long-term *in vitro* or *in vivo* cell imaging. This shortcoming has led to the intense interest in II-VI QDs due to their many unique merits. Particularly, compared to fluorescent dyes, QDs possess the unique advantages such as size-tunable emission color, broad photoexcitation, narrow emission spectra, strong fluorescence, and high resistance to photobleaching. Consequently, QDs have been widely used as a new class of fluorescent probes in biological research, particularly for *in vitro* and *in vivo* imaging [1,2].

In 1998, the groups of Alivisatos and Nie independently reported the first examples of QDs-based bioprobes, suggesting great promise of II-VI QDs for cell imaging [14]. Thereafter, the II-VI QDs have been extensively developed and optimized to be a kind of well-established fluorescent biological probes for a variety of bioimaging studies. Wu et al used CdSe/ZnS QDs liked to immunoglobulin G (IgG) and streptavidin to label the breast cancer marker Her2 on the surface of fixed and live cancer cells, to stain actin and microtubule fibers in the cytoplasm, and to detect nuclear antigens inside the nucleus. Notably, taking advantage of the emission flexibility of QDs, one single cell was dual-color labeled the QDs of different
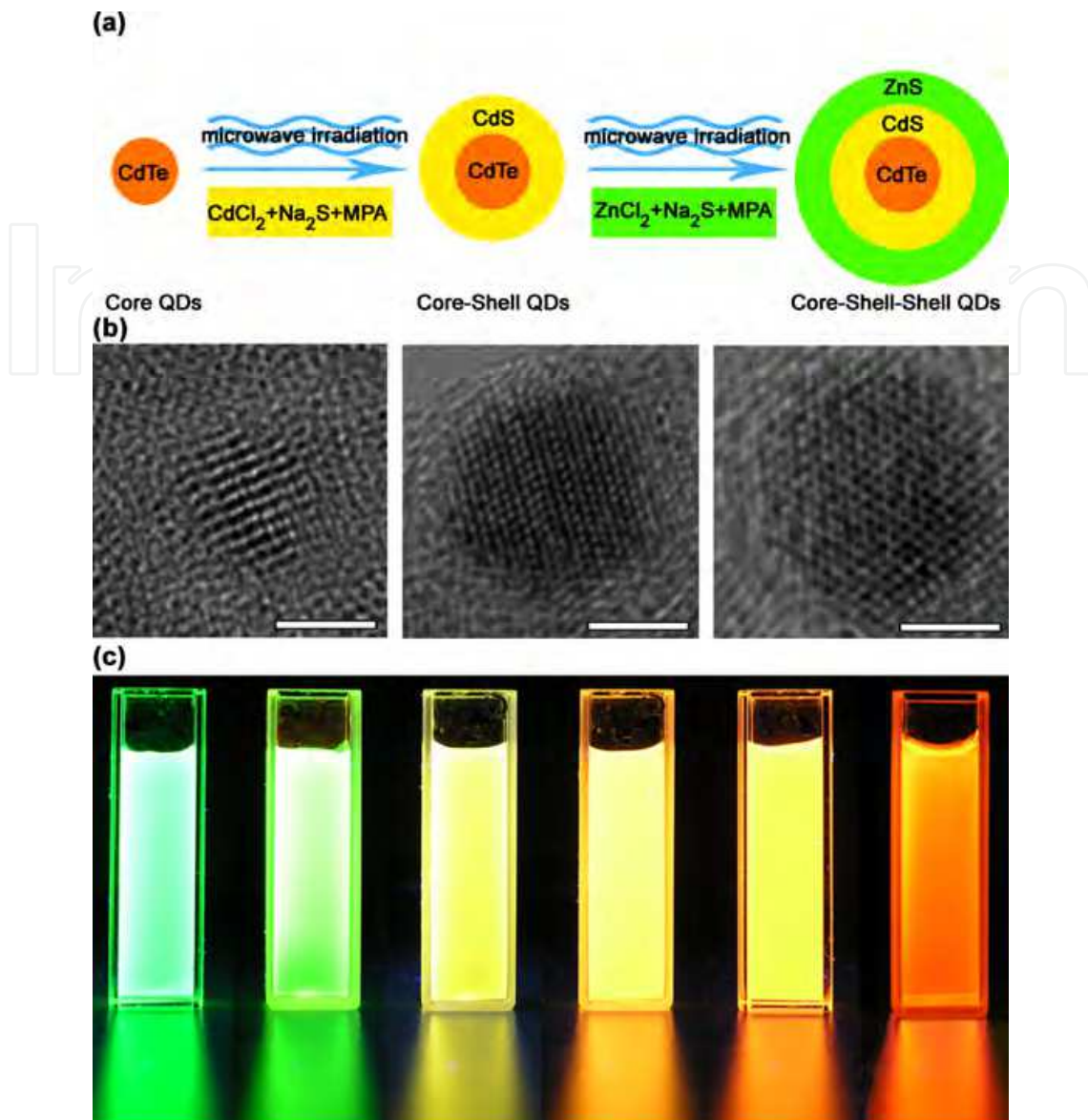
Fig. 2. (a) Schematic illustration of microwave-assisted synthesis of aqQDs. (b) High-resolution transmission electron microscopy (HRTEM) images of CdTe (left), CdTe-CdS core-shell (middle), CdTe-CdS-ZnS core-shell-shell (right) aqQDs. (c) Photograph of the wide spectral range of bright luminescence from aqQDs aqueous solution under irradiation with 365-nm ultraviolet light from a UV lamp. (Reprinted with permission from [12d], 2008 Wiley).

luminescence. They further compared the photostability of the QDs and Alexa 488 (one kind of commercial organic dyes). Significantly, labeling signals of Alexa 488 faded quickly and became undetectable within 2 min; in striking contrast, the QDs preserved stable and bright fluorescence for 3 min illumination period, which provides powerful demonstration of superior photostability of QDs compared to organic dyes [15]. Meanwhile, Simon and coworkers developed procedures for using QDs to label live cells and demonstrated their use for long-term multicolor imaging of live cells. The live cells were labeled via two approaches, i.e., (1) endocytic uptake of QDs and (2) selective labeling of cell surface proteins with antibodies-conjugated QDs. The QDs-labeled cells were readily long-time

monitored via tracking QDs fluorescence due to robust photostability of QDs [16]. Wang et al employed aqQDs-based nanospheres for *in vitro* imaging, demonstrating that the aqQDs were superbly efficacious for long-term and high-specificity immunofluorescent cellular labeling, and multi-color cell imaging [12e]. Based on progresses of QDs-based cellular imaging, the QDs bioprobes were further utilized for *in vivo* imaging. Typically, Nie et al designed a triblock polymer-encapsulated and bioconjugated QDs with excellent aqueous dispersibility and strong luminescence. The prepared QDs were effectively targeted tumors both by the enhanced permeability and retention (EPR) of tumor sites and by antibody binding to cancer-specific cell surface biomarkers. Moreover, multicolor fluorescence imaging of cancer cells under *in vivo* conditions was achieved by using both subcutaneous injection of QD-tagged cancer cells and systemic injection of QD probes. Their studies offer high promise for ultrasensitive and multiplexed imaging of tumor targets *in vivo* [17]. It is worthwhile to point out that, near-infrared (NIR) fluorescence imaging is widely recognized as an effective method for high-resolution and high-sensitivity bioimaging due to minimized biological autofluorescence background and increased penetration of excitation and emission light through tissues in the NIR wavelength window (700-900 nm) [18]. More recently, He et al developed a kind of NIR-emitting, ultrasmall-sized aqQDs, and further employed the prepared QDs for highly spectrally and spatially resolved imaging in cells and animals. The NIR QDs were specifically highly accumulated in the tumor region through a passive targeting process caused by an enhanced permeability and retention (EPR) effect. Significantly, the fluorescent signals of QDs were distinctively bright, clearly spectrally and spatially resolved, despite the strong autofluorescence background in mouse. This study clearly demonstrates the advantages of NIR QDs for in-vivo imaging for which the QDs fluorescence and biological autofluorescence of the mouse are spectrally separated, and that the NIR-emission is less absorbed by tissues as compared to visible luminescence [13].

1.4 Biosafety assessment of II-VI QDs

While fluorescent II-VI QDs are recognized as novel high-performance biological probes and at the forefront of nano-biotechnology research, sufficient and objective assessment of QDs-relative biosafety is necessary for their wide ranging bioapplications. To meet requirement of practical biological and biomedical applications, a large amount of studies on biosafety assessment of the QDs have been carried out.

Bhatia et al shown that surface oxidation of QDs led to the formation of reduced Cd on the QD surface and release of free cadmium ions, and correlated with cell death [19]. Yamamoto et al found that the cytotoxicity of QDs was not only caused by the nanocrystalline particle itself, but also by the surface-covering molecules of QDs, i.e., surface-covered functional groups (e.g., -NH2 and -COOH) covering on the surface of QDs [20]. Parak et al demonstrated that, in addition to the release of Cd ions from the surface of QDs, QDs precipitation on the cell surface could also impaire cells. They further suggested that cytotoxic effects were different in the case that QDs are ingested by the cells compared to the case that QDs were just present in the medium surrounding the cells [21]. Fan et al presented systematic cytotoxicity assessment of a series of aqQDs, i.e., thiols-stabilized CdTe, CdTe/CdS core-shell structured and CdTe/CdS/ZnS core-shell-shell structured QDs. They demonstrated that the CdTe aqQDs were highly toxic for cells; epitaxial growth of a CdS layer reduced the cytotxicity of QDs; and the presence of a ZnS outlayer greatly improved the biocompatibility of aqQDs (Figure 4) [22]. In their following investigation,

they further revealed relationship between the cytotoxicity of aqQDs and free cadmium ions. Significantly, they found that the CdTe aqQDs were more cytotoxic than $CdCl_2$ solutions even when the intracellular Cd^{2+} concentrations were identical in the treated cells, implying the cytotoxicity of aqQDs cannot be attributed solely to the toxic effect of free Cd2+, but also dependent on the concentration of total aqQDs ingested by cells [23]. These studies are useful for understanding the *in vitro* toxicity of QDs, and for systematical assassment of cytotxicity of QDs.
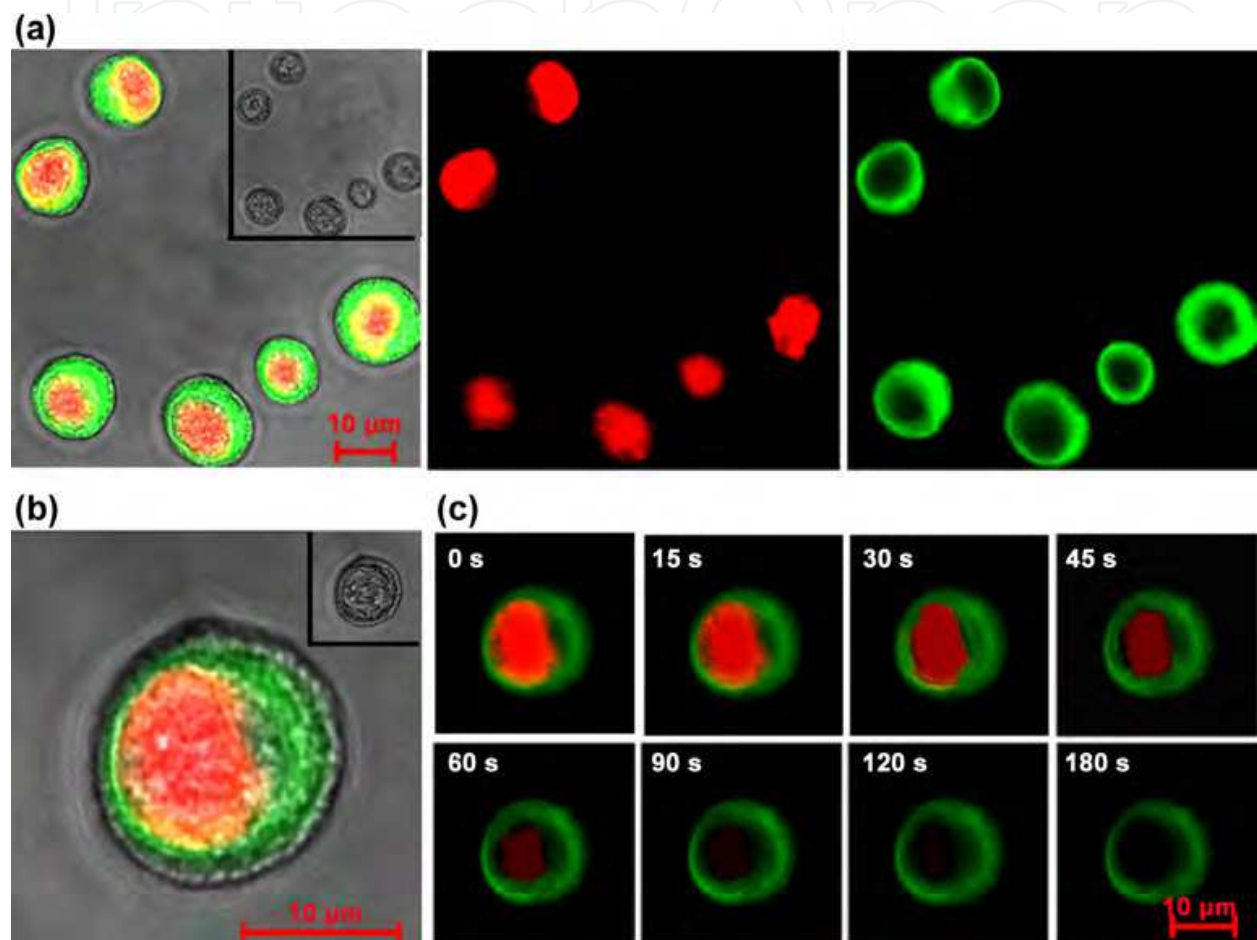
Fig. 3. Two-color staining of fixed cells. a, Fluorescent microscopy images of leukaemia K562 cells stained with the aqQDs-based nanospheres and PI dye. b, Fluorescent microscopy image of a single K562 cell labeled with the aqQDs-based nanospheres and PI dye. Inset displays the corresponding bright-field image. c, Temporal evolution of fluorescent signals of the K562 cells labeled with the aqQDs-based nanospheres (green fluorescent signal) and PI (red fluorescent signal). Images are captured with a cooled CCD camera at 15 s intervals automatically. Images at 0, 15, 30, 45, 60, 90, 120, and 180 s are shown. (Reprinted with permission from [12e], 2011 Biomaterials).

Such *in vitro* achievements are useful for biosafety assessment of the QDs; notwithstanding, comprehensive studies concerning *in vivo* toxicity are superior, since the results will assist in pinpointing the potential target organ and cells involved [24]. As a result, in the past several years, *in vivo* toxicity of QDs has been extensively studied. Particularly, Chan's group presented the first quantitative report on the *in vivo* biodistribution of QDs in 2006 [25]. In their

latest study, they further systematically studied short- and long-term toxicity, animal survival, hematology, biochemistry, and organ histology of the QDs. Significantly, they demonstrated that the QDs did not cause appreciable toxicity *in vivo* even over long-term periods (e.g., 80 days), which differs from *in vitro* results (e.g, obvious QDs-induced cytotoxicity) [26]. Besides, Choi et al recently revealed that *in vivo* behavior of QDs are greatly dependent on their hydrodynamic diameters. Of particularle note, they found that, compared
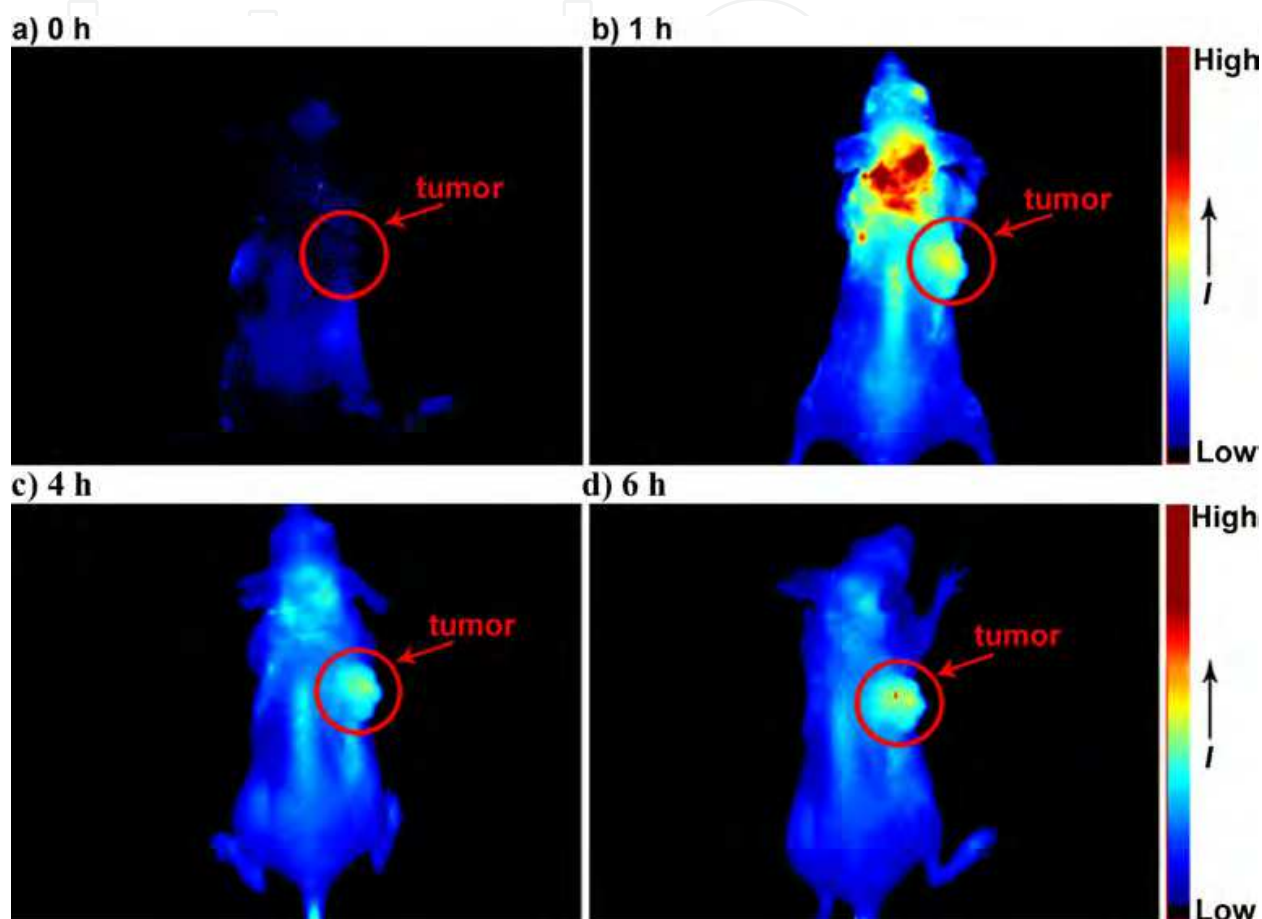

Fig. 4. *In vivo* tumor targeting of NIR QDs. Spectrally unmixed *in vivo* fluorescence images of KB tumor bearing nude mice at 0, 1 h, 4 h, and 6 h post injection of the prepared QDs. Mouse autofluorescence was removed by spectral unmixing in the above images. High tumor uptake of QDs was observed for the tumor models. (Reprinted with permission from [13], 2011 Wiley).

to those of large hydrodynamic diameter (> 15 nm), the QDs with smaller hydrodynamic diameter were more rapidly and efficiently eliminated from the mice through renal clearance. On the basis of which, they suggested that QDs with final hydrodynamic diameter < 5.5 nm produce feeble *in vivo* toxicity, and thus are more favorable for further bioapplications [27]. It is worthwhile to point out that, the QDs studied in all these mentioned publications are prepared via organometallic routes (organic synthesized QDs, orQDs). By using CdTe aqQDs as models, He et al carried out a comprehensive investigation on *in vivo* behaviors of the aqQDs, including their short- and long-term *in vivo* biodistribution, pharmacokinetics, and toxicity. They found that the biodistribution was largely dependent on hydrodynamic diameters of the QDs, blood circulation time, and types of organs. Based on histological and

biochemical quantitative analysis, and real-time body weight measurement, we further revealed that, the aqQDs produced no overt adverse effect to mice [28]. These studies are important for understanding the *in vivo* toxicity of QDs, and for designing QDs with acceptable biocompability for biomedical applications.
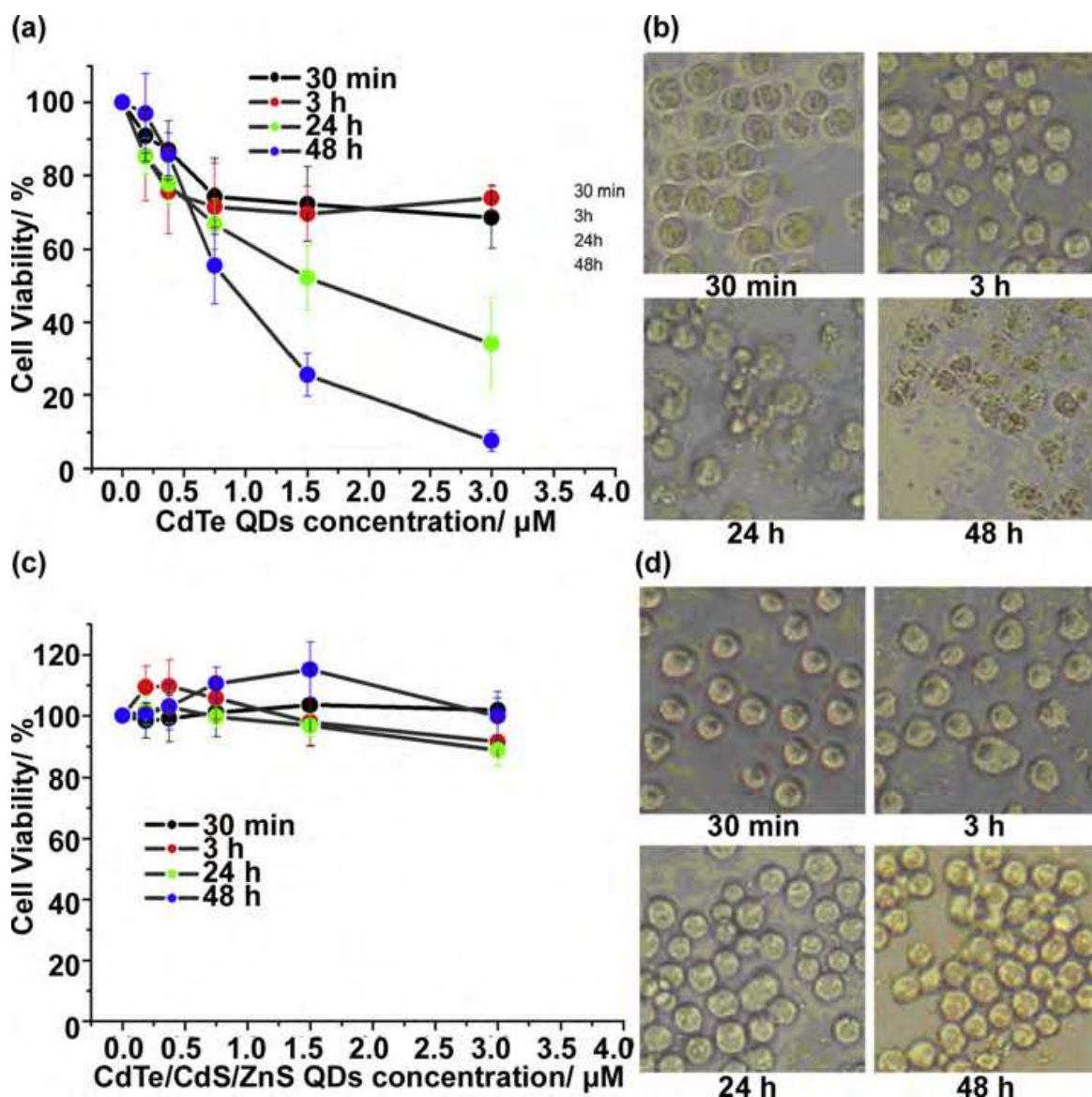

Fig. 5. Cytotoxicity of CdTe QDs (a,b) and CdTe-CdS-ZnS (c,d) QDs with different concentrations and incubation time with K562 cells. (a,c) Viability of K562 cells after treat with CdTe (a) and CdTe-CdS-ZnS (c) QDs. (b,d) Morphology of K562 cells after incubated with 3 μM CdTe (b) and CdTe-CdS-ZnS (d) QDs for 0.5, 3, 24, 48 h, respectively. (Reprinted with permission from [22], 2009 Biomaterials).

2. Carbon/silicon quantum dots-based biological fluorescent probes

2.1 Introduction

Two kinds of fluorescent QDs, i.e., carbon QDs (CQDs) and silicon QDs (SiQDs), have been recently developed as promising fluorescent biological probes for *in vivo* and *in vitro*

imaging. Carbon/silicon-based nanostructures, such as nanoribbons, nanowires, nanotubes, and nanodots, are being intensely investigated and utilized for various applications ranging from electronics to biology [29]. Particularly, the quantum confinement phenomenon in CQDs and SiQDs is the focus of research since it would increase the probability of irradiative recombination via indirect-to-direct band gap transition, leading to enhanced fluorescent intensity and the prospect of long-awaited optical applications. In the past several years, exciting progress on development of CQDs/SiQDs-based fluorescent biological probes have been achieved.

2.2 Carbon quantum dots-based biological fluorescent probes

Carbon nanostructures, such as fullerenes, carbon nanotubes (CNTs), graphene, and carbon quantum dots (CQDs) have been utilized in a broad range of technological applications due to their many attractive advantages, including high natural abundance of carbon, low specific weight, favorable biocompatibility, as well as the chemical and thermal robustness, et al [30]. Of particular note, recent report revealed that CQDs could produce fluorescence in some specific conditions, which is attributed to passivated defects on the surface of carbon nanostructures acting as excitation energy traps [31]. As a result, CQDs have been extensively explored as novel fluorescent bioprobes owing to their strong fluorescence and low toxicity.

Sun's group reported a kind of carbon nanodots that were produced via laser ablation of carbon target in the presence of water vapor with argon as carried gas. The prepared nanodots yield bright luminescence (PQLY: 4-10%) upon the surface passivation by attaching organic species to their surface. such resultant carbon nanodots preserved stable fluorescence with respect to photoirradiation, exhitiging no meaningful reduction in the observed intensities under continuously long-time excitations [32]. On the basis of which, they further developed the carbon nanodots exhibiting strong luminescence with two-photon excitation. The prepared nanodots were thus utilized for cell imaging with two-photo luminescence microscopy. The labeled cell membrane and the cytoplasm of MCF-7 cells showed distinct green signals of the nanodots [33]. Liu et al presented multicolor fluorescent, ultrasmall (sizes: < 2 nm) and water-dispersible CQDs obtained from the combustion soot of candles. The CQDs fluoresce with different color (the emission-peak wavelengths ranging from 415 (violet) to 615 nm (orange-red)) under a single-wavelength UV excitation. Moreover, the CQDs contain carboxylic acid groups on their surface, allowing functionalization with biomolecules through N-hydroxysuccinimide (NHS) chemistry to construct CQDs-based bioprobes [34]. Thereafter, Sun et al demonstrated the first study of carbon nanodots for optical imaging *in vivo*. Particularly, the nanodots injected in various ways (e.g., subcutaneous injection, interdermal injection, and intravenous injection) into mice remain strongly fluorescent *in vivo* (Figure 7). They further revealed that no animal exhibited any sign of acute toxicological responses due to favorable biocompatibility of CQDs [35]. More recently, Lee's group developed a facile one-step alkali-assisted electrochemical fabrication of highly luminescence (PLQY: ~12%) CQDs. The CQDs with sizes of 1.2-3.8 nm displayed controllable fluorescence via adjustment of current density. In addition to the strong and size-controllable luminescence, the prepared CQDs featured excellent aqueous dispersibility and upconversion luminescence properties, offering great potential for optical bioimaging and related biomedical applications [36].
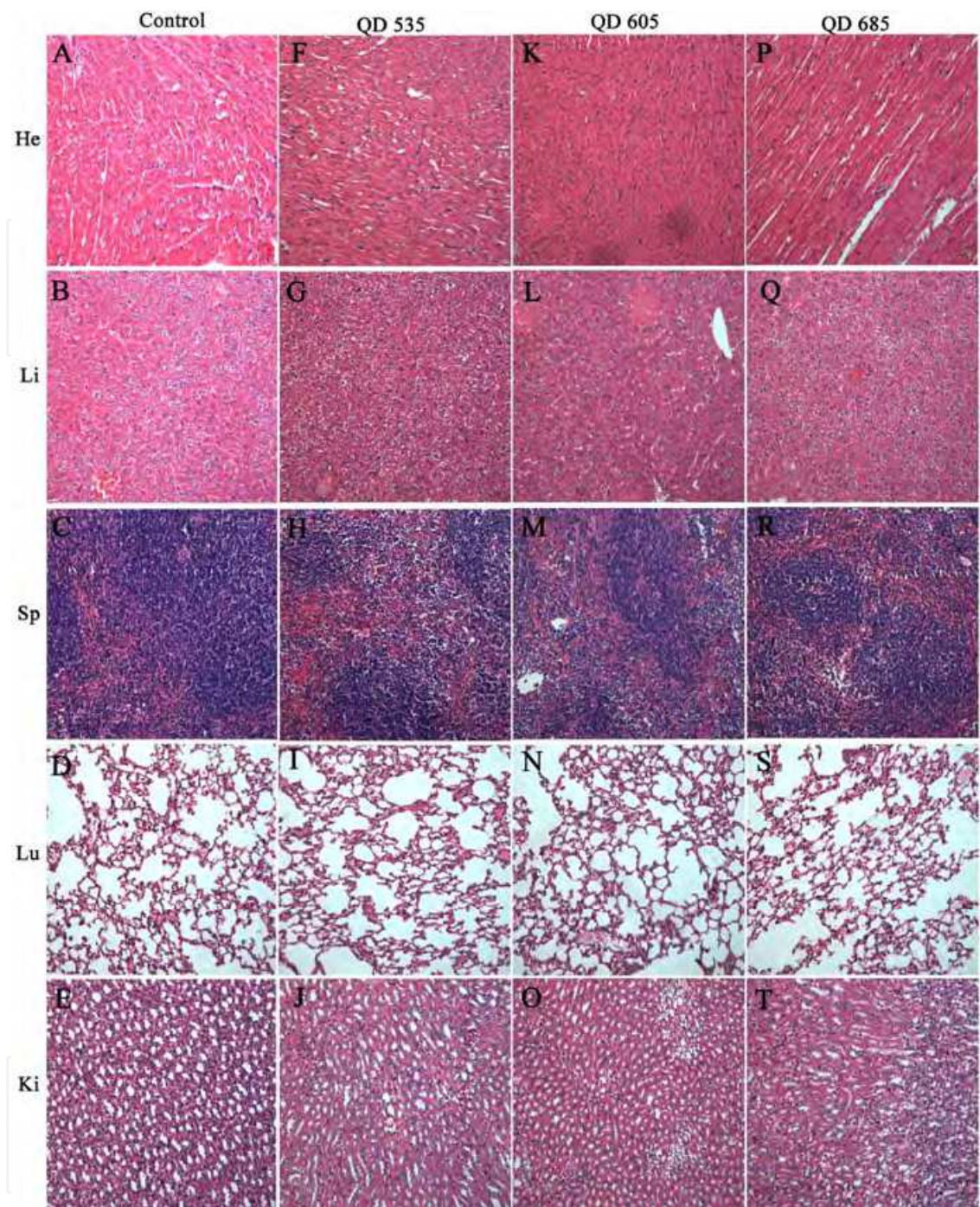
Fig. 6. Representative organ histology for control and treated animals. For control (A-E) and injected with aqQD535 (F-J), aqQD605 (K-O) and aqQD685 (P-T) animals, heart (He), liver (Li), spleen (Sp), lung (Lu) and kidney (Ki) are shown. Our analysis shows that organs did not exhibit signs of toxicity. (Reprinted with permission from [28], 2011 Biomaterials).

On the other hand, fluorescent nanodiamons, as another typical kind of carbon nanostructures, have also been explored as promising fluorescent biomarkers for *in vitro* and *in vivo* studies. Due to page limitation, this chapter will not discuss their bioimaging applications in a detailed way. The corresponding progresses could be referred in previous reports [37-39].
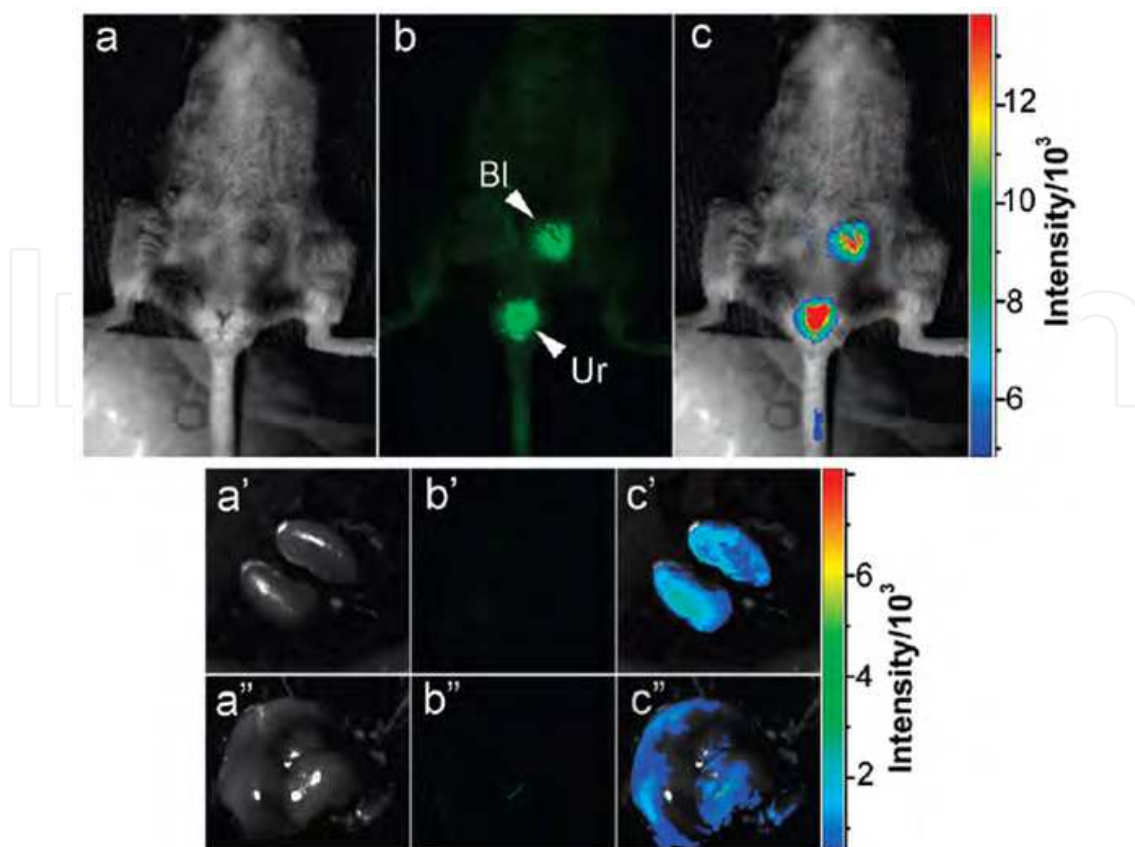
Fig. 7. Intravenous injection of fluorescent carbon nanodots: (a) bright field, (b) as-detected fluorescence (Bl, bladder; Ur, urine), and (c) color-coded images. The same order is used for the images of the dissected kidneys (a' – c') and liver (a'' – c''). (Reprinted with permission from [35], 2009 American Chemical Society).

2.3 Silicon quantum dots-based biological fluorescent probes

Silicon nanomaterials are a type of important nanomaterials with attractive properties including excellent electronic/mechanical properties, favorable biocompatibility, huge surface-to-volume ratios, surface tailorability, improved multifunctionality, as well as their compatibility with conventional silicon technology [29,40]. Consequently, there has been great interest in developing functional silicon nanomaterials for various applications ranging from electronics to biology. To meet increasing demands of silicon-based applications, silicon materials of various nanostructures (e.g., nanodot [41], nanowire [29a,42], nanorod [43], and nanoribbon [44]) have been developed. Particularly, previous research reveal that quantum confinement phenomenon in SiQDs can increase the probability of irradiative recombination via direct band gap transition [45], leading to improvement of fluorescent intensity and the prospect of optical applications. Due to their excellent biocompatibility and noncytotoxic property, SiQDs are considered as promising fluorescent biological probes for *in vivo* and *in vitro* imaging.

Since the first reports of room-temperature light emission from porous silicon in the early 1990s [46], a variety of fabrication techniques have been developed for preparation of silicon quantum dots, including solution-phase reductive [47], plasma-assisted aerosol precipitation [48], microemulsion [49], mechanochemical [50], laser ablation [51], and

sonochemical synthesis [52]. While luminescent intensity of silicon is enhanced at the nanoscale, SiQDs usually possess inferior optical properties (quantum yield < 10%) to semiconductor II-VI QDs (e.g. CdSe, CdSe/ZnS QDs) with direct band gaps (quantum yield 80-90%) [3,12]. Recent theoretical studies reveal that optical properties of SiQDs are significantly influenced by surface oxidation. Particularly, oxygen bonded to the surface of silicon quantum dots often reduces the band gap and limits luminescent emission, resulting in low quantum yield [53]. Consequently, it is essential to avoid surface oxidation to improve the quantum yields of SiQDs [53,54]. Indeed, Kortshagen et al. recently reported successful preparation of SiQDs with remarkably high ensemble quantum yields exceeding 60% by using plasma-assisted synthesis with strict removal of oxygen and elaborate surface passivation [48b], which provides an excellent example. It demonstrates that SiQDs could possess quantum yields as high as II-VI QDs under optimum conditions. Lee et al. recently developed a polyoxometalate-assisted electrochemical etching method for synthesizing SiQDs with controllable luminescent colors (e.g., blue, orange, and red) (Figure 8) [55].

Despite these progresses on SiQDs synthesis, most as-prepared SiQDs are not well water-dispersible since their surfaces are covered by hydrophobic moieties (e.g., styrene, alkyl, and octene). Extensive efforts have been undertaken to realize aqueous dispersibility of SiQDs. In 2004, Ruckenstein and Li developed a UV-induced graft polymerization for surface modification of SiQDs [56]. These SiQDs became well water-dispersible with the grafting of a water-soluble poly (acrylic acid) (PAAc) layer. In addition, the grafted PAAc also improved the photoluminescence stability of the SiQDs. Moreover, high density of carboxylic acid moieties of PAAc could be used to immobilize biomolecules (e.g., protein). Photostability comparison of SiQDs and four types of organic dyes (e.g., Alexa 488, Cy5, fluorescein isothiocyanate (FITC), and laser dye styryl (LDS751)) demonstrated superior resistance to photobleaching than the conventional organic dyes. Such modified SiQDs with quantum yield of 24% were employed as biological probes for cell imaging, suggesting potential bioimaging applications of modified SiQDs. Tilley and co-workers later reported a room-temperature synthesis for preparing water-dispersed SiQDs that exhibited strong blue photoluminescence [57]. In their method, a platinum chemical was utilized as catalyst for initiating reaction between Si-H surface bonds of the SiQDs and C=C bonds of allylamine. The resultant blue-emitting SiQDs became hydrophilic because their surfaces were modified with allylamine. In addition to the good aqueous dispersibility as well as relatively high quantum yield (~10%), the allylamine-capped SiQDs possessed robust storage- and photo-stability. They kept stable optical properties for several-month and long-time (more than 1 h) UV irradiation. As a comparison, the photoluminescence from rhodamine 6G dropped by 60% under the same illumination conditions. Sato and Swihart utilized photoinitiated hydrosilylation to successfully attach propionic acid (PA) to the surface of SiQDs, thereby producing water-dispersible, PA-terminated SiQDs with average diameter of less than 2.4 nm [58]. Compared to the former two reports showing water-dispersed SiQDs of a single emission color (red or blue), this work is significant because the size and corresponding PL emission color of SiQDs could be controlled by varying conditions. PA-terminated SiQDs with continuous luminescent color from yellow to green were readily synthesized in their work. Recently, Erogbogbo, Swihart et al. revealed that most of the modified SiQDs often showed obvious PL degradation especially in biological media with different pH, despite their high storage- and photo-stability in water [59]. Low pH stability would severely hinder their broad applications in biology. For example, conjugation of SiQDs with antibodies

would be technically difficult if they were instable at neutral and alkaline pH environment. They further developed a new kind of SiQDs encapsulated by phospholipid micelles. Significantly, such micelle-encapsulated SiQDs kept stable optical properties under various biologically relevant conditions of pH values (4-10) and temperatures (20-70 ºC) [59]. The micelle-encapsulated SiQDs were further used in multiple cancer-related *in vivo* applications, including tumor vasculature targeting, sentinel lymph node mapping, and multicolor imaging in live mice [60]. Tilley and coworkers systematically investigated the chemical reactions on molecules attached to the surface of SiQDs, and further developed a multi-stepped chemical method for surface modification of SiQDs [61]. This stepwise approach offers new opportunities to prepare the SiQDs with diverse and desirable functionalities. This study sheds new insight into biological applications of silicon quantum dots.
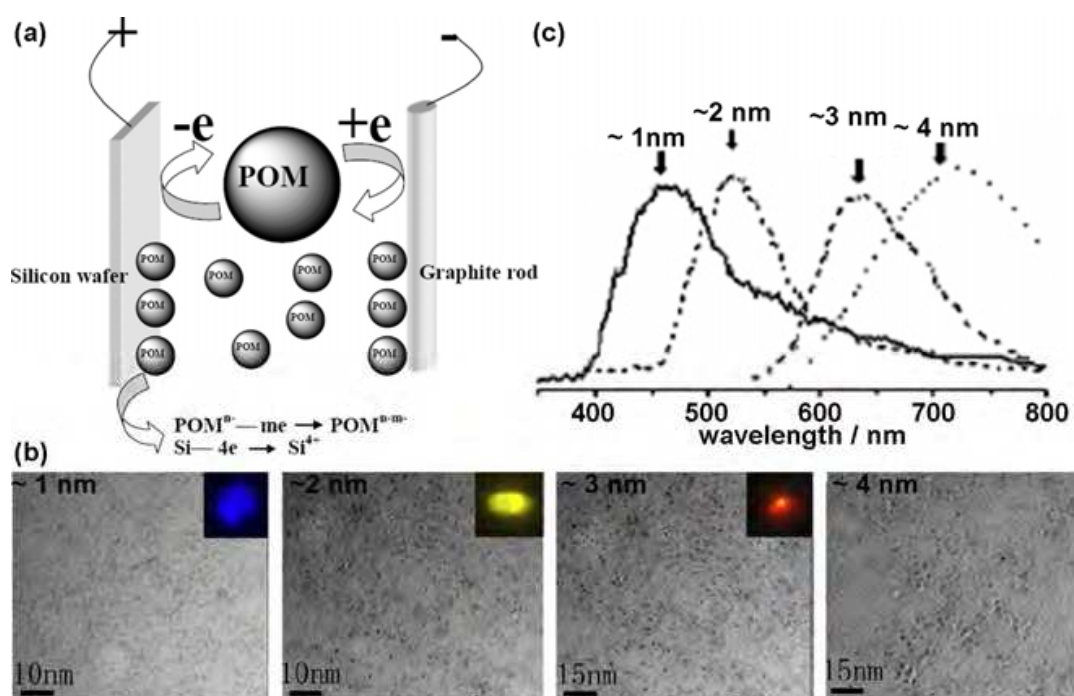

Fig. 8. (a) Schematics for the POMs-assisted electrochemical etching process. (b) TEM picture of serial sizes of SiQDs and their corresponding luminescence colors under UV irradiation (inset). (c) Typical PL spectra of SiQDs with sizes from ~1 to ~4 nm. (Reprinted with permission from [55], 2007 American Chemical Society.)

Lee and coworkers recently presented an EtOH/H2O2-assisted oxidation method to synthesize water-dispersed Si/SiOxHy core/ shell quantum dots with a Si core of different controlled diameters [62]. Significantly, this method allows for fine tuning emission wavelengths of QDs, producing seven luminescent colors from blue to red. On the basis of such studies [55,62] and theoretical prediction [63], they developed a new class of fluorescent silicon nanospheres (SiNSs) that each containing several hundreds of SiQDs (Figure 5). The as-prepared nanospheres, featuring excellent aqueous dispersibility, strong fluorescence, robust photo stability, and favorable biocompatibility, were further utilized for long-term cellular imaging [64]. Very recently, they developed a new microwave-assisted method for one-pot

synthesis of high-quality SiQDs, which were facilely and rapidly prepared in short reaction times (e.g. 15 min). Remarkably, the ~4 nm SiQDs featured excellent aqueous dispersibility, robust photo- and pH-stability, strong fluorescence (PLQY: ~15%), and favorable biocompatibility (Figure 9). They further demonstrated that the prepared SiQDs were suitable for long-term immunofluorescent cellular imaging as biological probes. Particularly, the SiQDs-labeled microtubules yielded very stable fluorescent signals during continuous 240-min observation. In sharp contrast, the signals of the control groups using CdTe QDs (recognized as photostable fluorescent labels) or FITC (one typical kind of conventional fluorescent dyes) as fluorescent labels almost completely disappeared in 25-min irradiation under the same conditions (Figure 10) [65]. These studies well demonstrated the great promise for real-time and long-term bioimaging with the SiQDs-based fluorescent probes.
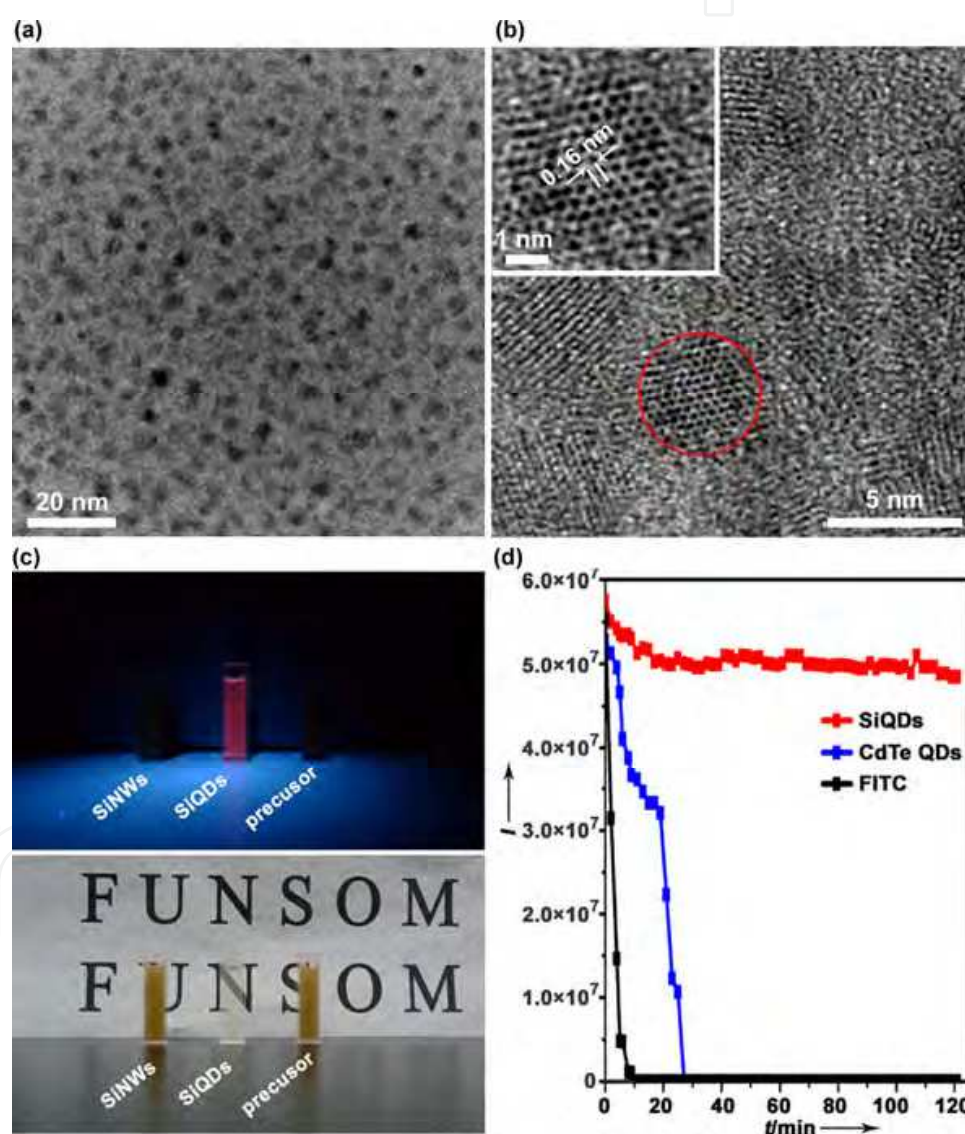

Fig. 9. TEM and HRTEM images (a,b), Inset in (b) presents the HRTEM image of a single SiQD. (c) Temporal evolution of fluorescence of the SiQDs under various pH values. (d) Photostability comparison of FITC, CdTe QDs, and as-prepared SiQDs. All samples are continuously irradiated by a 450 W xenon lamp. (Reprinted with permission from [65], 2011 American Chemical Society.)
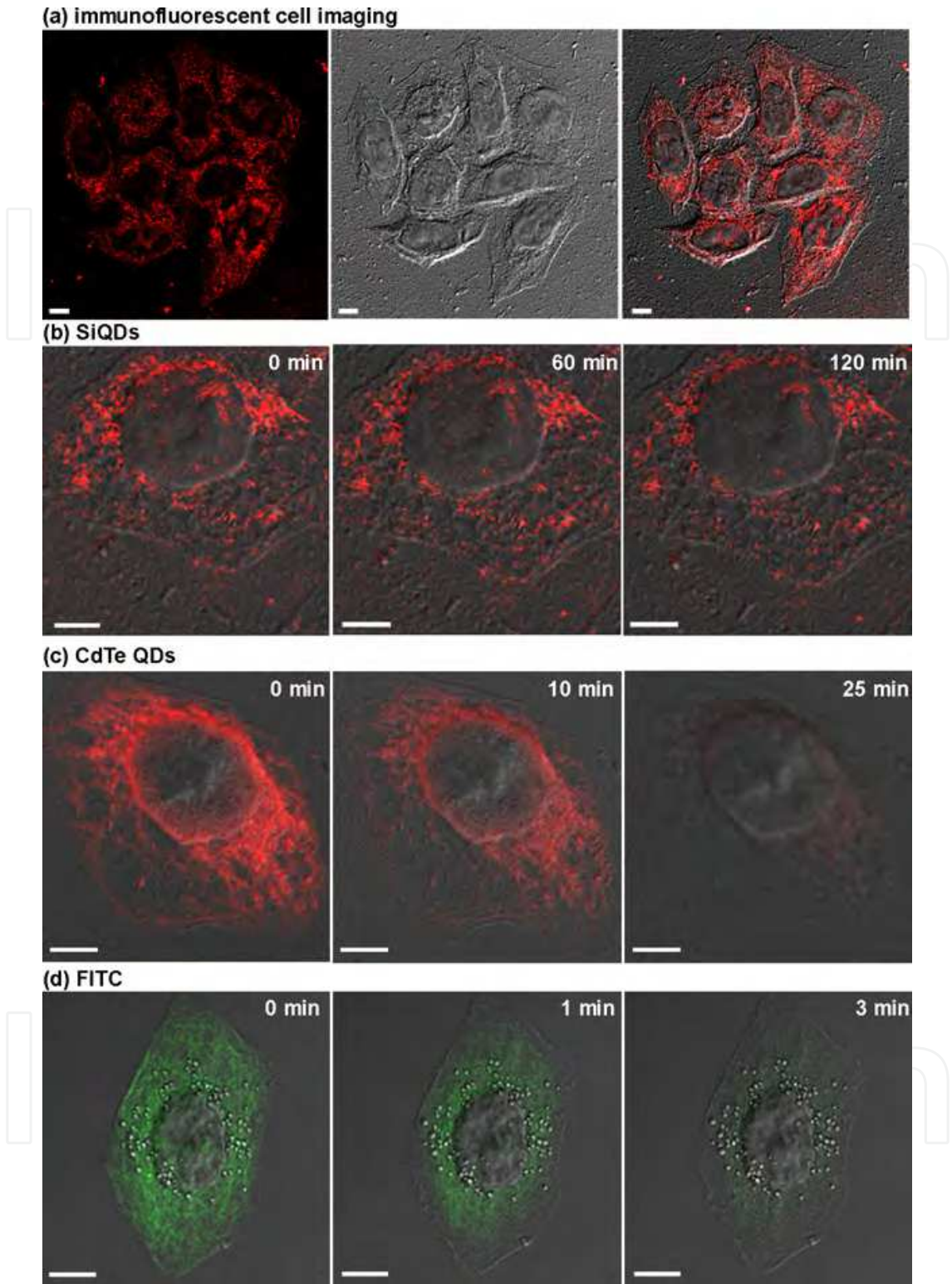
Fig. 10. Photos of immunofluorescent cell imaging captured by laser-scanning confocal microscopy. (a) Left: microtubules of Hela cells are distinctively labeled by the SiQDs/protein bioconjugates. Middle: bright field image. Right: superposition of fluorescence and transillumination images. (b)-(d) Stability comparison of fluorescence signals of Hela cells labeled by SiQDs (b), CdTe QDs (c), and FITC (d). Scale bar = 5 μm. (Reprinted with permission from [65], 2011 American Chemical Society.)

3. Conclusion and perspectives

In the past two decades, there have been considerable advances in the development of QDs-based fluorescent biological probes. Various kinds of high-quality QDs, i.e., II-VI QDs, CQDs, and SiQDs, have been developed for biological imaging.

II-VI QDs, serving as high-performance bioprobes, have been widely used for a variety of bioimaging applications, such as cell labeling, and tracking cell migration, tumor targeting, ect. Along with wide ranging bioapplications, concerns about their biosafety have attracted increasingly intensive attentions. *In vitro* studies have suggested that cytotoxicity of QDs is ascribed to release of toxic metals, production of reactive oxygen species, and hydrodynamic size of the QDs, which could be largely alleviated by surface modification (e.g., epitaxial growth of ZnS shell). On the other hand, *in vivo* experiments indicate that QDs of proper concentrations were not toxic to the animals (e.g., No apparent histopathological abnormalities or lesions are observed in QDs-treated mice). Therefore, while II-VI QDs are not completely innocuous, a safe range likely exists in which they can accomplish their task without major interference with the process under study. Notwithstanding, to meet requirement of practical biological and biomedical applications, further efforts are still urgently required to fully address the potential toxicity problem of the II-VI QDs, including the evaluation of QDs composition, surface chemistry, diameter, as well as the effect of their byproducts on biodistribution, toxicity, and pharmacokinetics.

The inherent problems, i.e. severe photobleaching or potential toxicity, associated with the traditional dyes or the fluorescent II/VI QDs remain completely unsolved, and have fueled a continual and urgent pursuit for new fluorescent bioprobes that are more photostable and biocompatible. Despite exciting progress on this area, extensive efforts (e.g., systematical assessment of QDs-relative biosafety, optimizing optical properties of CQDs/SiQDs, enhancing photo/chemical stability of QDs, investigating QDs behaviors in complicated biological environment, etc) are necessary to fit the demands of biological and biomedical applications. While there have been several exciting reports on the utility of CQDs/SiQDs for biological imaging, further efforts are necessary to modify and tailor CQDs/SiQDs architectures to fit the demands of biological and biomedical applications. One big challenge remaining is the development of economic and facile strategies for the large-scale synthesis of highly luminescent CQDs/SiQDs with controllable colors, which is the fundamental basis for their widespread bioapplications. Furthermore, effective methods of surface modification are required to further improve aqueous dispersibility and optical properties of CQDs/SiQDs. Moreover, a number of biological parameters have to be satisfactorily addressed before eventual *in vivo* and *in vitro* applications. While carbon and silicon are expected to be biocompatible, it is critically important to carry out systematic studies to assess their biosafety, including biodistribution and interactions between CQDs/SiQDs and biomolecules, cells and animals for *in vivo* bioimaging [1,2,66].

Key Words: Quantum dots; Fluorescent biological probes; Bioimaging; Silicon; Carbon

4. References

[1]   G. U. Nienhaus, *Angew. Chem. Int. Ed.* 2008, *47*, 8992-8994.
[2]   a) M. P. Bruchez, M. Moronne, P. Gin, S.Weiss, A. P. Alivisatos, *Science* 1998, *281*, 2013-2016. b) W. C. W. Chan, S. Nie, *Science* 1998, *281*, 2016-2018. c) X. Y. Wu, H. J. Liu, J.

Q. Liu, K. N. Haley, J. A. Treadway, J. P. Larson, N. F. Ge, F. Peale, M. P. Bruchez, *Nature Biotech*. 2003, *21*, 41-46. d) X. Michalet, F. F. Pinaud, L. A. Bentolila, J. M. Tsay, S. Doose, J. J. Li, G. Sundaresan, A. M. Wu, S. S. Gambhir, S. Weiss, *Science* 2005, *307*, 538-544.

[3] a) C. B. Murray, D. J. Noms, M. G. Bawendi, *J. Am. Chem. Soc.* 1993, *115*, 8706-8715. b) X. G. Peng, L. Manna, W. D. Yang, J. Wickham, E. Scher, A. Kadavanich, A. P. Alivisatos, *Nature* 2000, *404*, 59-61. c) Z. A. Peng, X. G. Peng, *J. Am. Chem. Soc.* 2001, *123*, 183-184. d) L. H. Qu, X. G. Peng, *J. Am. Chem. Soc.* 2002, *124*, 2049-2055. e) J. J. Li, Y. A. Wang, W. Z. Guo, J. C. Keay, T. D. Mishima, M. B. Johnson, X. G. Peng, *J. Am. Chem. Soc.* 2003, *125*, 12567-12575. f) J. M. Tsay, M. Pflughoefft, L. A. Bentolil, S. Weiss, *J. Am. Chem. Soc.* 2004, *126*, 1926-1927.

[4] T. Pellegrino, L. Manna, S. Kudera, T. Liedl, D. Koktysh, A. L. Rogach, S. Keller, J. Radler, G. Natile, W. J. Parak, *Nano Lett.* 2004, *4*, 703-707.

[5] a) D. Gerion, F. Pinau, S. C. Williams, W. J. Parak, D. Zanchet, S. Weiss, A. P. Alivisatos, *J. Phys. Chem. B* 2001, *105*, 8861-8871. b) H. Borchert, D. V. Talapin, N. Gaponik, C. McGinley, S. Adam, A. Lobo, T. Mo1ller, H. Weller, *J. Phys. Chem. B* 2003, *107*, 9662-9668.

[6] a) S. F. Wuister, I. Swart, F. V. Driel, S. G. Hickey, C. D. M. Donega, *Nano Lett.* 2003, *3*, 503-507. b) H. B. Bao, Y. J. Gong, Z. Li, M. Y. Gao, *Chem. Mater.* 2004, *16*, 3853-3859. c) Y. Wang, Z. Y. Tang, M. A, C. Duarte, I. P. Santos, M. Giersig, N. A. Kotov, L. M. L. Marza, *J. Phys. Chem. B* 2004, *108*, 15461-15469.

[7] N. Gaponik, D. V. Talapin, A. L. Rogach, K. Hoppe, E. V. Shevchenko, A. Kornowski, A. Eychmu1ller, H. Weller, *J. Phys. Chem. B* 2002, *106*, 7177-7185.

[8] a) M. T. Crisp, N. A. Kotov, *Nano Lett.* 2003, *3*, 174-177. b) J. Guo, W. L. Yang, C. C. Wang, *J. Phys. Chem. B* 2005, *109*, 17467-17473.

[9] H. Zhang, L. P. Wang, H. M. Xiong, L. H. Hu, B. Yang, W. Li, *Adv. Mater.* 2003, *15*, 1712-1715.

[10] a) D. M. P, Mingos, D. R. Baghurst, *Chem. SOC. Rev.* 1991, *20*, 1-47. b) S. A. Galema, *Chemical Society Reviews* 1997, *26*, 233-238. c) H. Grisaru, O. Palchik, A. Gedanken, V. Palchik, M. A. Slifkin, A. M. Weiss, *Inorganic Chemistry* 2003, *42*, 7148-7155. d) D. J. Brooks, R. Brydson, R. E. Douthwaite, *Adv. Mater.* 2005, *17*, 2474-2477. e) V. Swayambunathan, D. Hayes, K. H. Schmidt, Y. X. Liao, D. Meisel, *J. Am. Chem. Soc.* 1990, *112*, 3831-3837. f) J. A. Gerbec, D. Magana, A. Washington, G. F. Strouse, *J. Am. Chem. Soc.* 2005, *127*, 15791-15800.

[11] L. Li, H. F. Qian, J. Ren, *Chem. Commun.* 2005, 528-530.

[12] a) Y. He, H. T. Lu, L. M. Sai, W. Y. Lai, Q. L. Fan, L. H. Wang, W. Huang, *J. Phys. Chem. B* 2006, *110*, 13352-13356. b) Y. He, H. T. Lu, L. M. Sai, W. Y. Lai, Q. L. Fan, L. H. Wang, W. Huang, *J. Phys. Chem. B* 2006, *110*, 13370-13374. c) Y. He, L. M. Sai, H. T. Lu, M. Hu, W. Y. Lai, Q. L. Fan, L. H. Wang, W. Huang, *Chem. Mater.* 2006, *19*, 359-365. d) Y. He, H. T. Lu, L. M. Sai, Y. Y. Su, M. Hu, C. H. Fan, W. Huang, L. H. Wang, *Adv. Mater.* 2008, *20*, 3416-3421. e) Y. He, H. T. Lu, Y. Y. Su, L. M. Sai, M. Hu, C. H. Fan, L. H. Wang, *Biomaterials* 2011, *32*, 2133-2140.

[13] Y. He, Z. H. Kang, Q. S. Li, Chi Him A. Tsang, C. H. Fan, S. T. Lee, *Angew. Chem. Int. Ed.* 2009, *48*, 128-132.

[14] a) M. B. Jr, M. Moronne, P. Gin, S. Weiss, A. P. Alivisatos, *Science* 1998, *281*, 2013-2016. b) W. C. W. Chan, S. Nie, *Science* 1998, *281*, 2016-2018.

[15] X. Y. Wu, H. J. Liu, J. Q. Liu, K. N. Haley, J. A. Treadway, J. P. Larson, N. F. Ge, F. Peale, M. P. Bruchez, *Nat. Biotechnol.* 2003, *21*, 41-46.

[16] J. K. Jaiswal, H. Mattoussi, J. Mattoussi, J. M. Mauro, S. M. Simon, *Nat. Biotechnol.* 2003, *21*, 47-51.

[17] X. H. Gao, Y. Y. Cui, Richard M Levenson, L. W. K. Chung, S. Nie, *Nat. Biotechnol.* 2004, *22*, 969-976.

[18] a) R. Weissleder, Nat. Biotechnol. 2001, 19, 316-317. b) R. Weissleder, V. Ntziachristos, *Nat. Med.* 2003, *9*, 123-128. c) S. Lee, E. J. Cha, K. Park, S. Y. Lee, J. K. Hong, I. C. Sun, S. Y. Kim, K. Choi, I. C. Kwon, K. Kim, C. H. Ahn, *Angew. Chem. Int. Ed.* 2008, *47*, 2804-2807.

[19] A. M. Derfus, W. C. W. Chan, S. N. Bhatia, *Nano Lett.* 2004, *4*, 11-18.

[20] A. Hoshino, K. Fujioka, T. Oku, M. Suga, Y. F. Sasaki, T. Ohta, M. Yasuhara, K. Suzuki, K. Yamamoto, *Nano Lett.* 2004, *4*, 2163-2169.

[21] C. Kirchner, T. Liedl, S. Kudera, T. Pellegrino, A. M. J. H. E. Gaub, S. Stolzle, N. Fertig, W. J. Parak, *Nano Lett.* 2005, *5*, 331-338.

[22] Y. Y. Su, Y. He, H. T. Lu, L. Sai, Q. N. Li, W. X. Li, L. H. Wang, P. P. Shen, Q. Huang, C. H. Fan, *Biomaterials* 2009, *30*, 19-25.

[23] Y. Y. Su, M. Hub, C. H. Fan, Y. He, Q. N. Li, W. X. Li, L. H. Wang, P. P. Shen, Q. Huang, *Biomaterials* 2010, *31*, 4829-4834.

[24] J. Edward, B. S. J, C. Meghan, D. A. M, V. Yuri, G. k. Y. K, K. N. A, *ACS Nano* 2008, *2*, 928-932.

[25] H. C. Fischer, L. C. Liu, K. S. Pang, W. C. W. Chan, *Adv. Funct. Mater.* 2006, *16*, 1299-1305.

[26] T. S. Hauck, R. E. Anderson, H. C. Fischer, S. Newbigging, W. C. W. Chan, *Small* 2010, *1*, 138-144.

[27] H. S. Choi, W. H. Liu, P. Misra, E. Tanaka, J. P. Zimmer, B. I. Ipe, M. G. Bawendi, J. V. Frangioni, *Nat. Biotechnol.* 2007, *25*, 1165-1170.

[28] Y. Y. Su, F. Peng, Z. Y. Jiang, Y. L. Zhong, Y. M. Lu, X. X. Jiang, Q. Huang, C. H. Fan, S. T. Lee, Y. He, *Biomaterials* 2011, *32*, 5855-5862.

[29] a) D. D. D. Ma, C. S. Lee, F. C. K. Au, S. Y. Tong, S. T. Lee, *Science* 2003, *299*, 1874-1877. b) F. Lu, L. Gu, M. J. Meziani, X. Wang, P. G. Luo, L. M. Veca, L. Cao, Y. P. Sun, *Adv. Mater.* 2009, *21*, 139-152. c) Y. He, C. H. Fan, S. T. Lee, *Nano Today* 2010, *5*, 282-295. d) Y. He, S. Su, T. T. Xu, Y. L. Zhong, J. A. Zapien, J. Li, C. Fan, S. T. Lee, *Nano Today* 2011, *6*, 122-130. e) Y. He, Y. L. Zhong, F. Peng, X. P. Wei, Y. Y. Su, S. Su, W. Gu, L. S. Liao, S. T. Lee, *Angew. Chem. Int. Ed.* 2011, *50*, 3080-3083.

[30] T. N. Hoheisel, S. Schrettl, R. Szilluweit, H. Frauenrath, *Angew. Chem. Int. Ed.* 2010, *49*, 6496-6515.

[31] X. Y. Xu, R. Ray, Y. L. Gu, H. J. Ploehn, L. Gearheart, K. Raker, W. A. Scrivens, *J. Am. Chem. Soc.* 2004, *126*, 12736-12737.

[32] Y. P. Sun, B. Zhou, Y. Lin, W. Wang, K. A. S. Fernando, P. Pathak, M. J. Meziani, B. A. Harruff, X. Wang, H. F. Wang, P. G. Luo, H. Yang, M. E. Kose, B. Chen, L. M. Veca, S. Y. Xie, *J. Am. Chem. Soc.* 2006, *128*, 7756-7757.

[33] L. Cao, X. Wang, M. J. Meziani, F. Lu, H. F. Wang, P. G. Luo, Y. Lin, B. A. Harruff, L. M. Veca, D. Murray, S. Y. Xie, Y. P. Sun, *J. Am. Chem. Soc.* 2007, *129*, 11318-11319.

[34] H. Liu, T. Ye, C. Mao, *Angew. Chem. Int. Ed.* 2007, *46*, 6473-6475.

[35] S. T. Yang, L. Cao, P. G. Luo, F. Lu, Xin Wang, H. F. Wang, M. J. Meziani, Y. F. Liu, G. Qi, Y. P. Sun, *J. Am. Chem. Soc.* 2009, *131*, 11308-11309.

[36] H. T. Li, X. D. He, Z. H. Kang, H. Huang, Y. Liu, J. L. Liu, S. Y. Lian, C. H. A. Tsang, X. B. Yang, S. T. Lee, *Angew. Chem. Int. Ed.* 2010, *49*, 4430-4434.

[37] S. J. Yu, M. W. Kang, H. C. Chang, K. M. Chen, Y. C. Yu, *J. Am. Chem. Soc.* 2005, *127*, 17604-17605.

[38] C. C. Fu, H. Y. Lee, K. Chen, T. S. Lim, H. Y. Wu, P. K. Lin, P. K. Wei, P. H. Tsao, H. C. Chang, W. Fann, *PNAS* 2007, *104*, 727-732.

[39] N. Mohan, C. S. Chen, H. H. Hsieh, Y. C. Wu, H. C. Chang, *Nano Lett.* 2010, *10*, 3692-3699.

[40] a) L. Pavesi, L. D. Negro, C. Mazzoleni, G. Franzo, F. Priolo, *Nature* 2000, *408*, 440-444. b) Z. F. Ding, B. M. Quinn, Haram, K. P. Santosh, E. Lindsay, Korgel, A. Brian, A. JBard, *Science* 2002, *296*, 1293-1298. c) J. E, Allen, E. R. Hemesath, D. E. Perea, J. L. Lenschfalk, Z. Y. Li, F. Yin, M. H. Gass, P. Wang, A. L. Bleloch, R. E. Palmer, L. J. Lauhon, *Nature nanotechnology* 2008, *3*, 168-173. d) G. F. Grom, D. J. Lockwood, J. P. McCaffrey, H. J. Labbé, P. M. Fauchet, J. B. White, J. Diener, D. Kovalev, F. Koch, L. Tsybeskov, *Nature* 2000, *407*, 358-361.

[41] a) J. D. Holmes, K. J. Ziegler, R. C. Doty, L. E. Pell, K. P. Johnston, B. A. Korge, *J. Am. Chem. Soc.* 2001, *123*, 3743-3748. b) M. Cavarroc, M. Mikikian, G. Perrier, L. Boufendi, *Appl. Phys. Lett.* 2006, *89*, 013107−013110.

[42] V. Schmidt, J. V. Wittemann, S. Senz, U. Gosele, *Adv. Mater.* 2009, *21*, 2681-2702.

[43] a) J. G. Fan, X. J. Tang, Y. P. Zhao, *Nanotechnology* 2004, *15*, 501-504. b) Hawker, T. P. Russell, M. Steinhart, U. Gosele, *Nano Lett.* 2007, *7*, 1516-1520.

[44] a) A. J. Baca, M. A. Meitl, H. C. Ko, S. Mack, H. S. Kim, J. Y. Dong, P. M. Ferreira, J. A. Rogers, *Adv. Funct. Mater.* 2007, *17*, 3051-3062. b) H. C. Ko, A. J. Baca, J. A. Rogers, *Nano Lett.* 2006, *6*, 2318−2324.

[45] a) W. L. Wilson, P. F. Szajowski, L. E. Brus, *Science* 1993, *262*, 1242-1244. b) N. M. Park, C. J. Choi, T. Y. Seong, S. J. Park, *Phys. Rev. Lett.* 2001, *86*, 1355-1357.

[46] a) Canham, L. T. *Appl. Phys. Lett.* 1990, *57*, 1046-1048. b) Cullis, A. G.; Canham, L. T. *Nature* 1991, *335*, 335-338.

[47] a) C. S. Yang, R. A. Bley, S. M. Kauzlarich, H. W. H. Lee, G. R. Delgado, *J. Am. Chem. Soc.* 1999, *121*, 5191-5195. b) R. K. Baldwin, K. A. Pettigrew, E. Ratai, M. P. Augustine, S. M, Kauzlarich, *Chem. Commun.* 2002, 1822-1823.

[48] a) L. Mangolini, E. Thimsen, U. Kortshagen, *Nano Lett.* 2005, *5*, 655-659. b) D. Jurbergs, E. Rogojina, *Appl. Phys. Lett.* 2006, *88*, 233116-1-233116-2.

[49] R. D. Tilley, K. Yamamoto, *Adv. Mater.* 2006, *18*, 2053-2056.

[50] A. S. Heintz, M. J. Fink, B. S. Mitchell, *Adv. Mater.* 2007, *19*, 3984-3988.

[51] D. Riabinina, C. Durand, M. Chaker, F. Rosei, *Appl. Phys. Lett.* 2006, *88*, 073105-1-073105-3.

[52] N. A. Dhas, C. P. Raj, A. Gedanken, *Chem. Mater.* 1998, *10*, 3278-3281.

[53] Z. Zhou, L. Brus, R. Friesner, *Nano Lett.* 2003, *3*, 163-167.

[54] A. Puzder, A. J. Williamson, J. C. Grossman, G. Galli, *J. Am. Chem.Soc.* 2003, *125*, 2786-2791.

[55] Z. H. Kang, C. H. A. Tsang, Z. D. Zhang, M. L. Zhang, N. B. Wong, J. A. Z. Shan, S. T. Lee, *J. Am. Chem. Soc.* 2007, *129*, 5326-5327.

[56] Z. F. Li, E. Ruckenstein, *Nano Lett.* 2004, *4*, 1463-1467.

[57] J. H. Warner, A. Hoshino, K. Yamamoto, R. D. Tilley, *Angew. Chem. Int. Ed.* 2005, *44*, 4550-4554.

[58] S. Sato, M. T. Swihart, *Chem. Mater.* 2006, *18*, 4083-4088.

[59] F. Erogbogbo, K. T. Yong, I. Roy, G. X. Xu, P. N. Prasad, M. T. Swihart, *ACS Nano* 2008, *2*, 873-878.

[60] F. Erogbogbo, K. T. Yong, I. Roy, R. Hu, W. C. Law, W. W. Zhao, H. Ding, F. Wu, R. Kumar, M. T. Swihart, P. N. Prasad, *ACS Nano* 2011, *5*, 413-423.

[61] A. Shiohara, S. Hanada, S. Prabakar, K. Fujioka, T. H. Lim, K. Yamamoto, P. T. Northcote, R. D. Tilley, *J. Am. Chem. Soc.* 2010. *132*, 248-253.

[62] Z. H. Kang, Y. Liu, C. H. A. Tsang, D. D. D. Ma, X. Fan, N. B. Wong, S. T. Lee, *Adv. Mater.* 2009, *21*, 661-664.

[63] a) Q. S. Li, R. Q. Zhang, S. T. Lee, T. A. Niehaus, T. Frauenheim, *Appl. Phys. Lett.* 2008, *92*, 053107-1-053107-3. b) Q. S. Li, R. Q. Zhang, T. A. Niehaus, T. Frauenheim, S. T. Lee, *J. Chem. Theory Comput.* 2007, *3*, 1518-1526. c) X. Wang, R. Q. Zhang, T. A. Niehaus, T. Frauenheim, *J. Phys. Chem. C* 2007, *111*, 2394-2400.

[64] a) Y. He, Z. H. Kang, Q. S. Li, C. H. A. Tsang, C. H. Fan, S. T. Lee, *Angew. Chem. Int. Ed.* 2009, *48*, 128-132. b) He, Y. Y. Su, X. B. Yang, Z. H. Kang, T. T. Xu, R. Q. Zhang, C. H. Fan, S. T. Lee, *J. Am. Chem. Soc.* 2009, *131*, 4434-4438.

[65] Y. He, Y. L. Zhong, F. Peng, X. P. Wei, Y. Y. Su, Y. M. Lu, S. Su, W. Gu, L. S. Liao, S. T. Lee, *J. Am. Chem. Soc.* 2011, *133*,14192-14195.

[66] S. P. Song, Y. Qin, Y. He, Q. Huang, C. H. Fan, H. Y. Chen, *Chem. Soc. Rev.* 2010, *39*, 4234-4243.
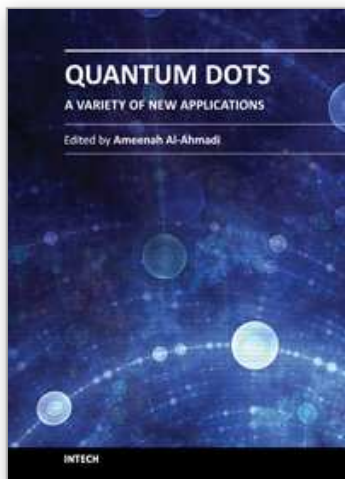
Quantum Dots - A Variety of New Applications

Edited by Dr. Ameenah Al-Ahmadi

The book "Quantum dots: A variety of a new applications" provides some collections of practical applications of quantum dots. This book is divided into four sections. In section 1 a review of the thermo-optical characterization of CdSe/ZnS core-shell nanocrystal solutions was performed. The Thermal Lens (TL) technique was used, and the thermal self-phase Modulation (TSPM) technique was adopted as the simplest alternative method. Section 2 includes five chapters where novel optical and lasing application are discussed. In section 3 four examples of quantum dot system for different applications in electronics are given. Section 4 provides three examples of using quantum dot system for biological applications. This is a collaborative book sharing and providing fundamental research such as the one conducted in Physics, Chemistry, Biology, Material Science, Medicine with a base text that could serve as a reference in research by presenting up-to-date research work on the field of quantum dot systems.

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