

Colloidal Synthesis of Semiconductor Quantum Dots toward Large-Scale Production: A Review

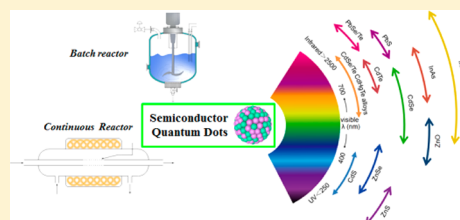
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ABSTRACT: The development of green synthetic approaches is one of the key materials challenges in moving toward semiconductor quantum dots (QDs) for large-scale production and commercial applications. This article presents a comprehensive overview on the synthesis of colloidal QDs prepared via chemical approaches in solution phase, with emphasis on green routes which possess the advantages of environment-friendly raw materials, simple operation process, and robust mass-scale production. The approaches for the synthesis of QDs in batch reactors are summarized, including hot-injection organometallic synthesis, noninjection organometallic synthesis, aqueous synthesis and biosynthesis approaches, with some of the concerns on their limitations for scale-up, followed by some continuous synthetic methods aiming for reproducible and large-scale production. Current advances in continuous synthesis of QDs by microfluidic devices, high-gravity reactors, and spray-based techniques are briefly introduced. We also provide some insights into challenges and opportunities based on our own understanding of this field.



1. INTRODUCTION

Fluorescence is the emission of light by a substance that has absorbed light or other electromagnetic radiation after a brief interval called fluorescence lifetime, which has many practical applications such as chemical sensing,^{1–3} biological imaging,^{4–6} antifake labeling,^{7,8} and light-emitting diode (LED) displaying devices.^{9,10} Organic dyes have been the most commonly used fluorescent agents since the mid-19th century.¹¹ However, they are limited due to a number of drawbacks, such as narrow excitation spectrum, inherent susceptibility to proteolytic enzymes, and poor photostability, especially for advanced applications in bioimaging, lighting, and displaying.¹² The development of nanotechnology has opened up new frontiers in material science and engineering by creating new materials with aforementioned properties.^{11–17} Semiconductor quantum dots (QDs), also known as semiconductor nanocrystals (NCs), are among the most frequently reported nanomaterials in the past two decades both from the fundamental point of view and for their exploitation as emerging materials for varieties of applications.^{11,12,18–24}

Classical QDs are nanoparticles or nanocrystals of a semiconducting material with diameters in the range of a few nanometers, in which the quantum confinement effects originate, leading to a widening of the band gap.²² Accordingly, the state of free charge carriers within the dot is quantized and the spacing of the discrete energy states is linked to the size of the dot.²³ Therefore, the emission color of QDs can be tuned by controlling their size and composition.²⁴ By choosing suitable core material with a desirable band gap and tuning the size of the QDs, their emission wavelength can cover the

ultraviolet (UV), visible, and near-infrared (NIR) regions (Figure 1). In comparison with organic dyes, QDs have similar quantum yields but extinction coefficients that are 10–50 times

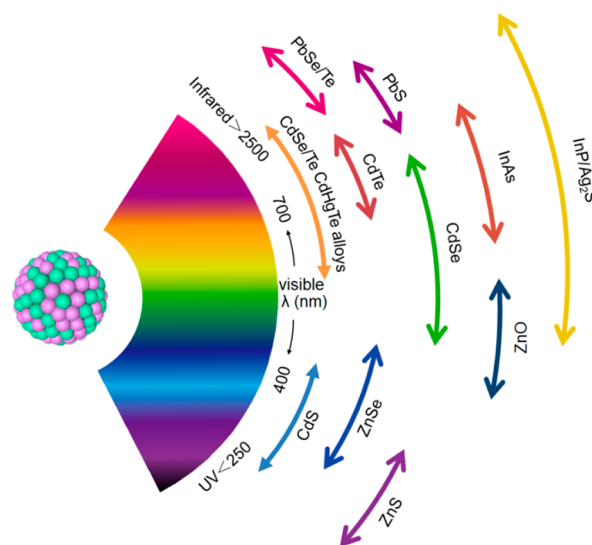


Figure 1. Representative QDs core materials scaled as a function of their emission wavelength superimposed over the spectrum.

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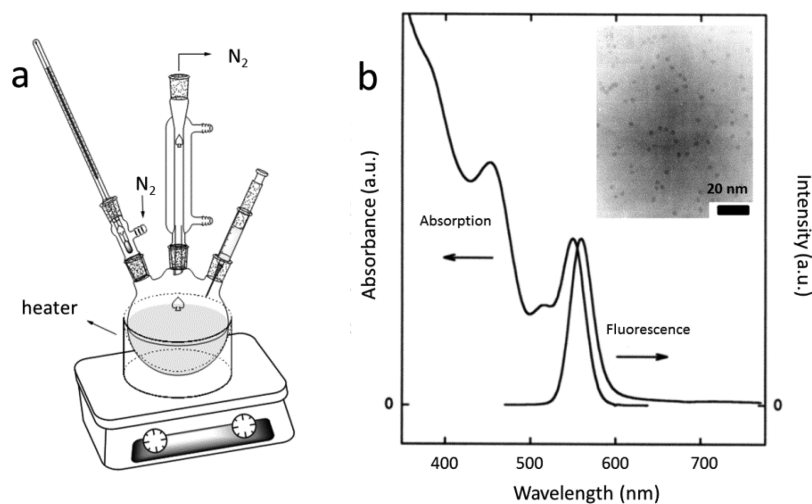


Figure 2. (a) Schematic diagram for a hot-injection organometallic synthesis of QDs; (b) typical room temperature band edge luminescence and absorption spectra for 3.5 nm CdSe QDs (inset: a typical TEM imaging of well dispersed CdSe QDs averaging 3.5 nm \pm 5% with no aggregation). Adapted with permission from ref 51. Copyright (1993) American Chemical Society.

larger and significantly more reduced photobleaching rates, exhibiting 10–20 times brighter fluorescence and 100–200 times better photostability.^{25,26} To date, the most popular QDs are CdSe and CdTe QDs, which offer appealing optical properties in the range of the visible spectrum from 400 to 700 nm.^{27,28} Meanwhile, the QDs with NIR emission properties, such as CuInSe,²⁹ PbS,³⁰ and Ag₂S³¹ QDs, have also attracted much attention due to the advantages of NIR light for *in vivo* animal imaging studies. More recently, there has been growing interest in perovskite QDs owing to their potential applications for high efficient photoelectric devices.³² It was noted that in many recent publications various carbon-based nanoparticles were named as carbon QDs or graphene QDs. However, a closer look at the data often reveals that those particles are more like fluorescent organic dots.^{33–36} In this article, we focus on the QDs composed of semiconductor nanocrystals.

The QD synthesis methodologies have progressed substantially in the past two decades, and various synthetic approaches have been developed for the synthesis of QDs, ranging from liquid-phase methods to vapor phase epitaxial growth.^{25,37} Although the vapor phase epitaxial growth methods have been successfully used on the preparation of size-tunable QDs, there are some inherent drawbacks such as the use of expensive instruments and difficulty in separation from the substrates.^{38,39} The liquid-phase methods have the potential to produce highly dispersed QDs in various solutions with less energy-demanding processes. Generally, the liquid-phase synthesis routes involve preparation of colloidal QDs via hot-injection organometallic synthesis, noninjection organometallic synthesis, aqueous synthesis, and biosynthesis approaches in batch reactors. From the view of scale-up, various types of continuous reactors have been applied, including microchannels,^{40,41} high-gravity reactors,^{42,43} and spray-based techniques.⁴⁴ Tens of thousands of literature reports have been published in recent years concerning the colloidal synthesis of semiconductor QDs,^{45–47} and it is unrealistic to cover all these studies, but our intention is rather to give some useful concepts here.

In this article, we will present a focused review on the synthesis of colloidal QDs prepared via chemical approaches in solution phase, with emphasis on the green synthetic routes toward reproducible large-scale production of QDs. It should

be noted that the large-scale synthesis of QDs is a relative concept, hard to define by quality or number of the production. In literature, some authors mentioned “large-scale synthesis” with the production of several grams while others refer to the production of several hundreds of grams.^{48–50} To our minds, a potential large-scale synthesis route for QDs should, at the least, operate under mild conditions and can be easily scaled up, regardless of the yield value in one batch reaction. In such a context, the approaches for the synthesis of QDs in batch reactors will be first introduced, including hot-injection organometallic synthesis, noninjection organometallic synthesis, aqueous synthesis, and biosynthesis approaches, with some concerns regarding their limitations for scale-up. Then, some continuous synthesis methods aiming for reproducible and large-scale production of QDs will be given. Finally, some challenges and opportunities for large-scale production and commercialization of QDs are provided based on our own understanding of this field.

2. SYNTHETIC APPROACHES IN BATCH REACTORS

The liquid-phase synthesis of colloidal QDs involves a series of chemical reactions. Therefore, the chemical reactor in which the chemical reaction takes place is of primary consideration. The chemical reactors can be divided into two broad categories, which are batch reactors and continuous reactors. Batch reactors are used for most of the synthetic approaches of colloidal QDs carried out in a laboratory.

2.1. Hot-Injection Organometallic Synthesis of QDs. A traditional approach for the synthesis of QDs relies on the heating of specific organic solvents and injection of semiconductor precursors, which was pioneered by Murray et al. in 1993.⁵¹ As the schematic diagram shown in Figure 2,⁵¹ in a typical preparation approach of CdSe QDs, the Cd precursor and Se precursor solutions are first prepared by mixing Cd(CH₃)₂ and elemental Se in liquid tri-*n*-octylphosphine (TOP) solutions respectively, which are then rapidly injected into heated trioctylphosphine oxide (TOPO) solution under an inert atmosphere in a batch reactor (typically, a three-neck round-bottom flask).⁵¹ The TOPO serves as the stabilizing agent and high boiling solvent, which allows the mixture to reach high reaction temperatures (up to 320 °C). A series of

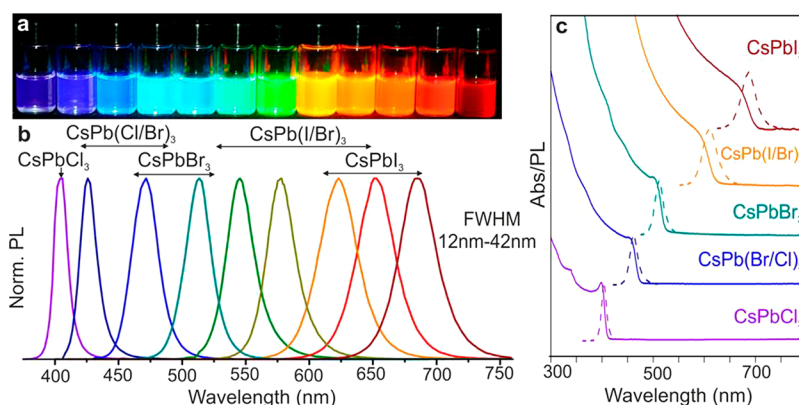


Figure 3. Colloidal perovskite CsPbX_3 QDs ($X = \text{Cl}, \text{Br}, \text{I}$) exhibit size- and composition-tunable band gap energies covering the entire visible spectral region with narrow and bright emission: (a) colloidal solutions in toluene under UV lamp ($\lambda = 365 \text{ nm}$); (b) representative fluorescence spectra ($\lambda_{\text{exc}} = 400 \text{ nm}$ for all but 350 nm for CsPbCl_3 samples); (c) typical optical absorption and fluorescence spectra. Adapted with permission from ref 73. Copyright (2015) American Chemical Society.

QDs with different sizes from 1.5 to 11.5 nm could be obtained over a period of a few hours by controlling the growth temperature.⁵¹

This synthetic scheme was considered to be an inspiring example and model system for the synthesis of high quality CdSe QDs, as well as other CdS QDs and CdTe QDs. However, the reactant $\text{Cd}(\text{CH}_3)_2$ is extremely toxic, expensive, and explosive, which makes this route impractical for large-scale preparation of QDs. One milestone in the hot-injection synthesis of QDs was the greener route of Peng et al., who used inexpensive and little toxic CdO instead of $\text{Cd}(\text{CH}_3)_2$ to produce CdSe NCs, with no decrease in the quality in the final QDs.^{52,53} It should be noted that the elementary compositions of Cd, Pb, etc. do not allow the use of completely nontoxic precursors of several kinds of QDs, such as CdSe, CdS, PbS, and PbSe. However, these QDs still have their unique research and application value at this stage. In this article, we focus on the “green synthesis” of QDs with less hazardous chemicals, safer solvents, and high efficiency chemical processes.⁵⁴ Following these principles, researchers have made much effort to develop “green” hot-injection approaches.^{55,56} The use of noncoordinating solvent octadecene (ODE) instead of coordinating solvent TOPO has been well-developed,^{57,58} and the final QDs exhibit no decrease in the quality after optimization of the synthesis parameters.⁵⁹ Thereafter, Deng et al. chose paraffin liquid and oleic acid as the reaction medium instead of TOP/TOPO, which significantly simplified the reaction for green and low-cost synthesis of the CdSe QDs.⁶⁰ By the suitable choice of source and synthetic parameters,⁵⁹ the hot-injection approach has been extended to the preparation of many types of semiconductor QDs, such as PbS,^{61,62} PbSe,⁶³ InP,⁶⁴ Ag_2S ,⁶⁵ and Ag_2Se .^{66,67} The synthesis of highly luminescent perovskite colloidal QDs has been extensively studied in recent years.^{68–74} By injecting a cesium oleate precursor solution into a PbX_2 ($X = \text{Cl}, \text{Br}, \text{I}$) precursor solution, Kovalenko et al.⁷³ first synthesized all inorganic CsPbX_3 ($X = \text{Cl}, \text{Br}, \text{I}$) perovskite nanocrystals in an ODE solution (Figure 3). The fluorescence properties of as-prepared CsPbX_3 ($X = \text{Cl}, \text{Br}, \text{I}$) perovskite QDs are comparable to those of highly luminescent CdSe QDs.⁷³ Wang et al.⁷⁴ have developed a facile solution-phase hot-injection approach for shape-controlled synthesis of lead-free and stable single-crystalline perovskite derivative Cs_2SnI_6 QDs, which open up

new opportunities to synthesize and rationally control the shape of new types of perovskite QDs.

2.2. Noninjection Organometallic Synthesis of QDs.

As described above, the hot-injection approaches require the rapid injection of a solution of one or more organometallic precursor solutions into a hot mixture of organic solvents in the batch reactor, followed by a fast and complete mixing of the mixture solution. These processes seem to be the best to produce high-quality QDs with optimal physical and chemical characteristics in laboratory scale by precise control of the reaction parameters such as precursor injection speed, stirring rate, and temperature. However, it is difficult to control the reaction temperature upon the injection of precursor solution, which leads to low batch-to-batch reproducibility. This problem will become more prominent in the large-scale production (e.g., tens to hundreds of kilograms). Therefore, a number of noninjection organometallic synthesis strategies have been developed, aiming to make QDs in large quantities. Efrima et al.⁷⁵ reported a simple and versatile method for the controlled production of high-quality tunable metal sulfide nanoparticles using a generic precursor in a single-pot, low temperature process. By heating the metal xanthate in a strong electron-donating solvent (e.g., hexadecylamine (HDA)), the metal sulfide particles form at a temperature as low as $70 \text{ }^\circ\text{C}$.⁷⁵ The synthesis process follows the classical colloid La Mer behavior,⁷⁶ and QDs of various sizes could be obtained by adjusting the reaction temperature. Later, Cao et al.⁷⁷ developed a one-pot colloidal synthesis method for high-quality CdS nanocrystals, based on the concept of controlling the thermodynamics and kinetics of the nanocrystal nucleation stage. By introducing nucleation initiators in the reaction system, the separation between nucleation and growth is automatically achieved, and the quality of the CdS QDs produced is comparable to that made by hot-injection approaches.^{77,78} The one-pot noninjection organometallic synthesis methods have been extended to other types of QDs, such as CdSe,^{79,80} CdTe,⁸¹ Cu_7S_4 ,⁸² PbS,^{83,84} and Ag_2S .^{85,86} In particular, Liu et al.⁸³ developed a noninjection and low temperature approach to small PbS QD ensembles with the band gap in wavelengths shorter than 900 nm and with a narrow bandwidth. The growth temperature for PbS QDs can be as low as room temperature, and the resulting QDs exhibited a desirable emission in the range of 700–900 nm by different growth temperatures, growth periods, acid-to-Pb feed molar

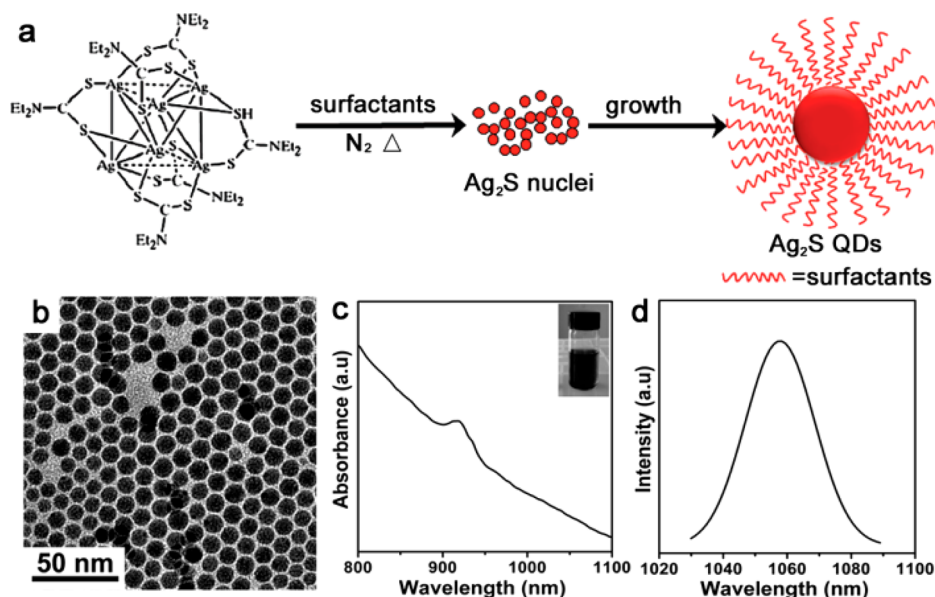


Figure 4. (a) Schematic diagram for the synthesis of Ag_2S QDs from a single source precursor of silver diethyldithiocarbamate; (b) a typical TEM image of the Ag_2S QDs; (c) NIR absorption spectrum of the Ag_2S QDs; the inset is a photograph of Ag_2S dispersed in cyclohexane. (d) NIR fluorescence emission spectrum of Ag_2S QDs at room temperature under excitation 785 nm light. Adapted with permission from ref 86. Copyright (2010) American Chemical Society.

ratios, feed reactant concentrations, and Pb-to-S feed molar ratios,⁸³ allowing them to be favorable candidates as bioimaging agents in animals.⁸⁴ Du et al.⁸⁶ reported the first NIR-emission Ag_2S QDs via the pyrolysis of a single source precursor of silver diethyldithiocarbamate $[(\text{C}_2\text{H}_5)_2\text{NCS}_2\text{Ag}]$ in a mixture of oleic acid, octadecylamine, and ODE. In their approach, the combination of different capping ligands and solvents was found to play a key role in obtaining monodisperse Ag_2S QDs.⁸⁶ Monodisperse Ag_2S QDs were formed in a mixed solvent of oleic acid, octadecylamine, and ODE while the sole use of oleic acid as the capping ligand and solvent produced soluble but aggregated Ag_2S nanoparticles.⁸⁶ The crystallite size of the as-obtained Ag_2S QDs could be tuned mainly by altering the solution composition.⁸⁶ In particular, the monodisperse Ag_2S QDs with an average size of 10 nm exhibited NIR emission at 1058 nm under 785 nm light excitation (Figure 4) and may act as biocompatible QDs for *in vivo* bioimaging.^{86–88} As for the synthesis of perovskite colloidal QDs, Chen et al.⁴⁹ have demonstrated the one-pot synthesis of perovskite CsPbX_3 QDs by direct heating of precursors in ODE in air. The emission wavelengths of the QDs are completely tunable in the UV to NIR range through simple changes in the sizes and compositions of the particles. Since the noninjection approach does not require precursor injection, it can be easily scaled-up to yield high quality CsPbX_3 QDs products on the gram scale.⁴⁹

2.3. Aqueous Synthesis of QDs. Although organometallic synthesis (either hot-injection or noninjection approaches) exhibits certain advantages for the preparation of high-quality QDs, in which high quality generally refers to high crystallinity, narrow size distribution, and high fluorescence quantum yield. However, for some applications, especially biological and clinical applications, the QDs obtained by organometallic synthesis approaches usually require additional phase transfer steps to be well-dispersed in water. On the other hand, the disposal of organic solvents used in organometallic synthesis processes is a serious environmental problem, when scale-up of production is required. As compared to many other organic

solvents, water is a much “greener” solvent. Direct synthesis of QDs in water offers the following advantages: (1) surface functionalization with water-soluble ligands occurs during the synthesis, which is suitable for biological applications; (2) it uses less toxic organic reagents and lower reaction temperatures (usually $<100\text{ }^\circ\text{C}$) that are beneficial for scale-up production. Therefore, the aqueous synthesis of QDs has become an interesting alternative to the common organometallic synthesis approaches. In fact, the water-based synthesis of QDs is the oldest approach to the colloidal QDs, as pioneered reported by Henglein⁸⁹ and Brus and co-workers⁹⁰ in the early 1980s, when they documented the size dependence of the optical band gap of CdS QDs. Vossmeier et al.⁹¹ then demonstrated the size-dependent UV–vis absorption of CdS QDs obtained by the aqueous synthesis approach using $\text{Cd}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$, H_2S , and 1-thioglycerol. However, no photoluminescence properties were reported.⁹¹ The first report on the aqueous synthesis of QDs that exhibited comparable fluorescence properties to those obtained by organometallic routes were provided by Weller and co-workers.⁹² Typically, for instance, the synthesis of CdTe QDs in an aqueous solution was based on the reaction between Cd^{2+} and NaHTe and required reflux at $96\text{ }^\circ\text{C}$ for hours to obtain the photoluminescence emission.⁹² Thereafter, the aqueous synthesis of II–VI QDs, such as CdTe,^{93,94} CdSe,⁹⁵ HgTe,⁹⁶ CdHgTe,^{97,98} and PbS,⁹⁹ has been extensively studied and several improvements of the aqueous synthetic method have been reported including hydrothermal synthesis,¹⁰⁰ microwave irradiation,¹⁰¹ and ultrasonic treatment.¹⁰² For instance, very recently, Yakoubi et al.¹⁰³ reported a facile, mild, and low cost aqueous-based synthesis for the production of high quality CdZnS and Cu-doped CdZnS QDs. Highly emissive Cu:CdZnS QDs could be produced using 3-mercaptopropionic acid (MPA) or *N*-acetylcysteine (NAC) as capping ligand.¹⁰³ The fluorescence of the Cu:CdZnS QDs could be tuned in the whole visible spectrum via the stoichiometric ratio of Cd/Zn precursors in the host CdZnS QDs and by tuning the particle size (Figure 5).¹⁰³

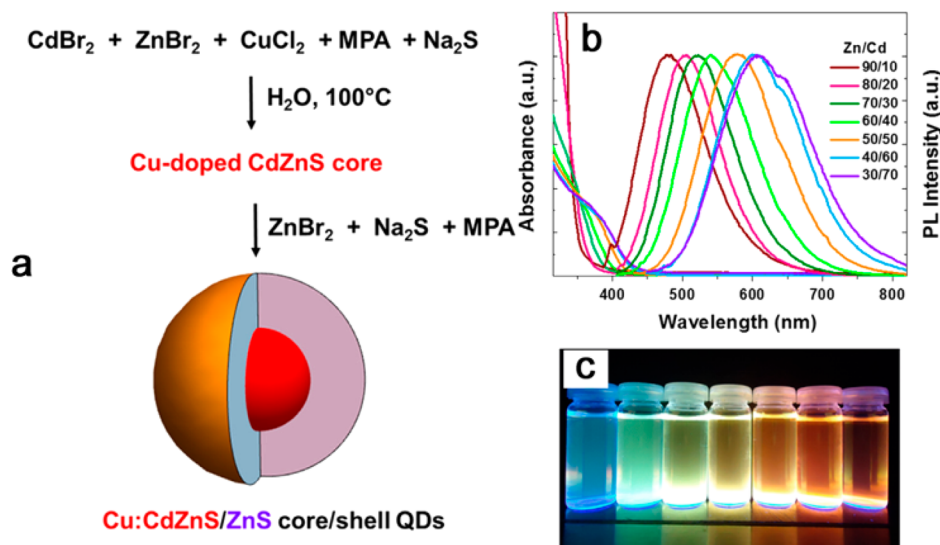


Figure 5. (a) A schematic illustration of the synthesis of Cu: CdZnS/ZnS QDs; (b) UV–visible absorption and fluorescence spectra of Cu-doped $\text{Cd}_x\text{Zn}_{1-x}\text{S}$ QDs; (c) digital photograph of aqueous dispersions of Cu: CdZnS/ZnS QDs under UV light irradiation (from the left to the right, x varies from 0.1 to 0.7). The excitation wavelength is 350 nm. Adapted with permission from ref 103. Copyright (2016) Elsevier.

However, practical and large-scale applications of these QDs have been hampered by the high toxicity of the QDs constituents such as Cd, Hg, and Pb. Several kinds of greener, nonheavy-metal QDs, such as ZnSe,¹⁰⁴ ZnO,¹⁰⁵ and ZnS,¹⁰⁶ have been produced in aqueous processes, which usually emit in the blue range. In the past decade, near-infrared fluorescent QDs have been attracting significant scientific interest due to their potential application for deep-tissue *in vivo* animal imaging.¹⁰⁷ In particular, Ag_2S QDs have emerged as novel NIR fluorescent probes with low toxicity to organisms.¹⁰⁸ Yang et al.¹⁰⁹ reported the aqueous synthesis of Ag_2S QDs by using bovine serum albumin (BSA) as the capping agent. The synthetic approach involves the incubations of AgNO_3 with BSA for the initial heterogeneous nucleation, followed by a slow injection of Na_2S solution and agitation for Ag_2S crystallization.¹⁰⁹ The obtained Ag_2S QDs exhibited ultrasmall sizes (<10 nm) and size-dependent emission wavelengths from 1050 to 1294 nm, by tuning the precursor molar ratio of Ag to S.¹⁰⁹ Wang et al.¹¹⁰ developed a one-step approach to prepare water-soluble Ag_2S QDs using glutathione as the capping reagent and a sulfur–hydrazine hydrate complex as the S^{2-} source, respectively. By adjusting the amount of glutathione and the ratio of Ag^+ to $\text{S-N}_2\text{H}_4\cdot\text{H}_2\text{O}$, Ag_2S QDs with tunable fluorescence in the range of visible red (624 nm) to NIR (724 nm) were obtained.¹¹⁰

2.4. Biosynthesis of QDs. Biosynthesis or biomanufacturing¹¹¹ using the intrinsic enzymatic machinery of microorganisms provides another route for the synthesis of QDs, especially for metal sulfide QDs, such as CdS,^{112,113} ZnS,^{114–116} PbS,^{117,118} and Ag_2S .¹¹⁹ The biosynthesis of metal sulfide QDs usually requires two sources of metal and sulfide ions as precursors. In one strategy (i.e., intracellular synthesis), these ions can enter the cell cytoplasm through the magnesium or manganese transport system and be converted into nanocrystals by the intracellular enzymes located in the cytoplasm.¹²⁰ The other route is extracellular synthesis, in which the formation of QDs caused by the enzymes occurs on the cell membrane or excreted to the medium.¹²¹ Li et al.¹²² produced a single size of CdSe QDs within yeast cells through genetic engineering of intracellular redox conditions, illustrating the potential for

cellular engineering to regulate nanocrystal biosynthesis. Gallardo et al.¹²³ demonstrated that psychrotolerant, oxidative stress-resistant bacteria from Antarctic microorganisms are able to biosynthesize CdS QDs at low temperature in the presence of Cd and S precursors. Recently, McIntosh et al.^{124–127} developed a general approach for the reproducible biosynthesis of CdS and PbS QDs using an engineered strain of *Stenotrophomonas maltophilia* (SMCD1) that has been specifically evolved to control particle size. For instance, the SMCD1 is capable of the direct extracellular biomineralization of CdS quantum dot nanocrystals from a buffered aqueous solution of cadmium acetate and L-cysteine without the addition of a chemically reactive precursor (Figure 6).¹²⁷ The

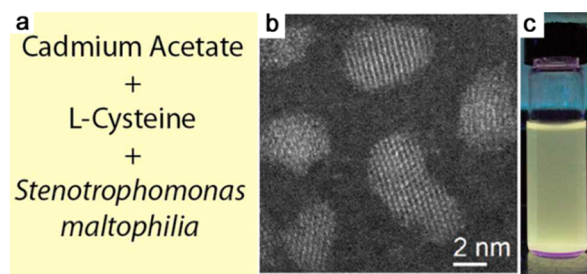


Figure 6. (a) A schematic illustration for the biosynthesis of CdS QDs; (b) a typical high-resolution TEM image of the CdS QDs; (c) a photograph of the visible fluorescence from the CdS QDs under UV illumination. Adapted with permission from ref 127. Copyright (2016) American Chemical Society.

observed trends are consistent with L-cysteine acting as both a sulfur source and nanocrystal capping agent. Enzymatic turnover of L-cysteine by a putative cystathionine γ -lyase forms a reactive sulfur in solution, removing the requirement for addition of reactive sodium sulfide typical of most other biomineralization approaches.¹²⁷ The optical properties can be controlled and tuned by varying the growth conditions, especially the growth time.¹²⁷ In contrast to typical chemical synthesis schemes, biosynthesis offers a route to low temperature, aqueous phase synthesis of crystalline materials, perhaps

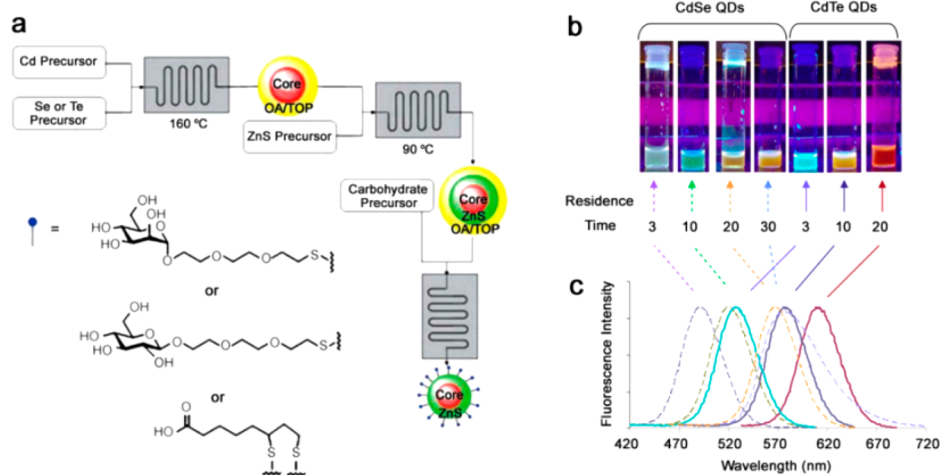


Figure 7. (a) Microreactor setup for the continuous-flow synthesis of functionalized QDs (OA: oleic acid; TOP: tri-*n*-octylphosphine); (b) selected samples of CdSe and CdTe nanoparticles under UV lamp; (c) normalized luminescence spectra of CdSe (---) and CdTe (—) nanoparticles after 3, 10, 20, 30 min. Adapted with permission from ref 133. Copyright (2010) John Wiley and Sons.

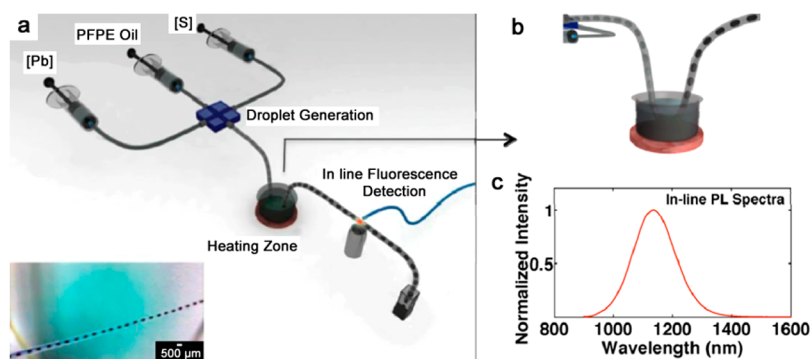


Figure 8. (a) Schematic of the droplet-based microfluidic reactor used for synthesis of PbS QDs synthesis, including an in-line NIR fluorescence detection system (bottom inset: Image of generated droplets containing synthesized PbS QDs); (b) schematic of the color change of the generated droplets after transport through the heating section; (c) in-line fluorescence characterization of the synthesized particles. Adapted with permission from ref 137. Copyright (2014) American Chemical Society.

in structures or morphologies that may not be accessible through purely chemical routes.¹²⁷ This intrinsically greener synthesis route has the potential to reduce production cost and lead to materials with new or improved functionality.¹²⁷

3. SYNTHETIC APPROACHES IN CONTINUOUS REACTORS

As for the synthesis of QDs, the reaction process control parameters, such as temperature, stirring rate, precursor injection position, and mixing are critical for the quality of the final products. With precise control of the synthesis procedures, gram-scale or even subkilogram-scale synthesis of QDs has been realized in batch reactors. For instance in 2006, Kim and Lee⁴⁸ published a subkilogram-scale synthesis of QDs, with 0.2 kg of dried core/shell CdSe/ZnSe QDs produced in one batch. The key to the success of their approach is a quick injection, under temperature-controlled conditions, of a shell precursor possessing suitable reactivity.⁴⁸ More recently, Bang et al.⁵⁰ reported the gram-scale preparation of InP QDs in one batch. The white P (P_4) was used as the P precursor, and InP QDs with tunable sizes were obtained by varying the reaction parameters such as the reaction time and temperature, and the type of precursors.⁵⁰ In their work, the large-scale production of InP@ZnS QDs was demonstrated by yielding more than 6 g of

QDs per one-batch reaction.⁵⁰ The successful scaling up of the batch reaction for InP QDs was attributed to the slow reaction of P_4 precursor with indium halides.⁵⁰ However, complete control of the reaction parameters and conditions is hard to achieve in traditional batch reactors for those QDs synthesized by quick reaction, especially when large volumes of solution are involved.¹²⁸ An alternative to a batch reactor is a continuous reactor, in which the reactants are continuously fed into the reactor and emerge as a continuous stream of product. The product tends to be of a more consistent quality from a continuous reactor because the reaction parameters (e.g., residence time, temperature and pressure) are better controlled than in batch operations.

3.1. Synthesis of QDs in Microfluidics. Microfluidics are typical continuous reactors which are integrated with heaters and fluid control elements, offering much higher levels of reaction process control than those that can be achieved in conventional macroscale batch-type reactors.¹²⁹ Microfluidic reactors have emerged as an attractive technology for nanocrystal synthesis since the earliest reports in 2002.^{129–137} Many efforts have been focused toward the synthesis of semiconductor QDs in microfluidic reactors,¹³⁴ and we are just giving a few examples here. Figure 7a shows a typical setup reported by Kikkeri and co-workers¹³⁵ to synthesize surface-

functionalized CdSe and CdTe QDs. The chemical reactions in the whole process are similar to that of an organometallic synthesis of QDs in batch reactors as mentioned above.¹³⁵ However, the required temperatures (160 °C) in the flow process are much lower than those in batch processes (250–300 °C).¹³⁵ Both the formation of the CdSe/CdTe core and ZnS shell can be performed in the continuous-flow microchannels.¹³⁵ The sizes of the QDs were tunable by simply varying the reaction time in the reactor.¹³⁵

Viscous drag at the channels walls is one of the common issues of microfluidic reactors, which lead to a spread of fluid velocities in the channel, resulting in polydispersity and poorly defined particle properties. Especially for the synthesis of QDs involving high viscosity long-chain solvents, the viscous drag can be a serious problem.¹³⁶ Jensen and co-workers¹³⁶ have demonstrated the supercritical continuous microfluidic synthesis of QDs at high pressure to overcome the limitations of viscous drag. The use of supercritical hexane leads to higher supersaturation compared to squalane, producing more nuclei and narrowing the size distribution.¹³⁶ In addition, by incorporation of “in-line” analytical platforms to feed information back to reaction controllers, real-time tuning and optimization of products can be achieved in the microfluidic devices.¹³⁷ Lignos et al.¹³⁷ have demonstrated the synthesis of monodisperse PbS and PbSe QDs over a wide range of experimental conditions, with real-time assessment and fine-tuning of material properties, which were achieved by rapid in-line NIR fluorescence spectroscopy characterization (Figure 8).¹³⁷

3.2. Synthesis of QDs by High-Gravity Technique. The high-gravity (Higee) technology, as one of the cutting-edge process intensification technologies, was originally invented by Ramshaw et al. in 1979,^{138–140} by using a rotating packed bed (RPB) to simulate the high gravitational field to intensify the mass transfer.¹⁴¹ In the RPB reactor, the aqueous reactants going through the packing were spread or split into micro- or nanodroplets, threads, or thin films.^{142,143} Therefore, the mass transfer and micromixing could be significantly intensified compared to those in conventional batch reactors.¹⁴⁴ In 1994, the first RPB reactor was designed to produce nanoparticles by Chen et al.,¹⁴⁵ and calcium carbonate nanoparticles of 15–30 nm in mean size with a very uniform particle size distribution was obtained. Figure 9 shows the basic structure of the RPB. The key part of the RPB is a packed rotator, which is installed

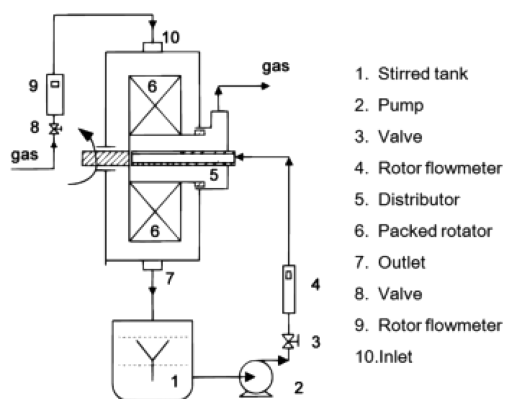


Figure 9. Schematic of experimental setup for nanomaterials synthesis using a RPB reactor. Adapted with permission from ref 138. Copyright (2000) American Chemical Society.

inside the fixed casing and rotates at the speed of several hundreds to thousands rpm.¹³⁸ A liquid solution or slurry is introduced into the eye space of the rotator from the liquid inlet pipe and then sprayed by the slotted pipe distributor onto the inside edge of the rotator.¹³⁸ The liquid entered the bed flows in the radial direction under centrifugal force, passing the packing and outside space between the rotator and shell, finally collecting and leaving the equipment through the liquid exit.¹³⁸ The gas is introduced from an outside source (gas cylinder) through the gas inlet, flows inward counter currently to the liquid in the packing of the rotator, and finally goes out through the gas exit under the force of the pressure gradient.¹³⁸ Following up with Chen’s work, many researchers have demonstrated that RPB is an essential tool for process intensification in nanomaterials syntheses.¹³⁸ Along with others, we have demonstrated the preparation of a variety of inorganic and organic nanomaterials in high-gravity RPB reactors due to the intensified mixing and mass transfer.^{146–148} Several kinds of semiconductor nanoparticles such as ZnO^{149,150} and ZnS¹⁵¹ have also been reported. However, the sizes of those semiconductor nanoparticles were mainly dozens of nanometers and their photoluminescence properties were absent.^{149–151}

Using a so-called spinning disc processor (SDP), Hartlieb et al.¹⁵² synthesized ZnO QDs with average sizes of less than 3 nm (Figure 10). Typically, the SDP makes use of centrifugal acceleration to create very thin films of fluid (1 to 200 μm) on a surface by supplying solutions to the surface of a rapidly rotating disc (300–3000 rpm), thus creating conditions of high mass and heat transfer, which is similar to the enhancement mechanism of those in an RPB reactor.^{140,152}

In high gravity reactors such as RPB and SDP, the liquid–liquid mixing and mass transfer can be intensified by several orders of magnitude, which guarantee highly homogeneous reaction conditions to all reactants, overcoming many limitations related to batch reactors and microreactors. The scale-up for the synthesis of QDs is also easily realized in theory. However, according to our knowledge, there have been no public reports on the synthesis of other types of high quality QDs using high gravity reactors, which will be an interesting topic for follow-up studies beyond the scope of the present work.

3.3. Thermospray Synthesis of QDs. As for the synthesis of QDs in either approach mentioned above, the use of organic ligands is necessary during the synthesis process. The ligands coated on the surface of nanoparticles prevent the aggregation of QDs to make them highly dispersed in liquid solutions or solid composites. On the other hand, the ligands also weaken both mechanically and chemically any available assemblies and limit the scientific research and technological applications involving electron transport or energy transfer between QDs. Amirav and co-workers¹⁵³ have developed a spray-based method for the production of high quality semiconductor QDs to overcome the limitations exhibited by the conventional liquid-phase synthesis methods.¹⁵³ Typically, as shown in Figure 11, aqueous or organic solutions of precursors (i.e., semiconductor salts) are first sprayed via a thermospray nebulizer into monodispersed droplets.¹⁵¹ As the droplets move forward, the precursor reach over saturation and salts condensation spontaneously occur due to the evaporation of the solvents.¹⁵³ Followed by the complete vaporization of the solvent, each semiconductor dot is produced from a single spray droplet, and the QDs are free-standing, unsupported, and

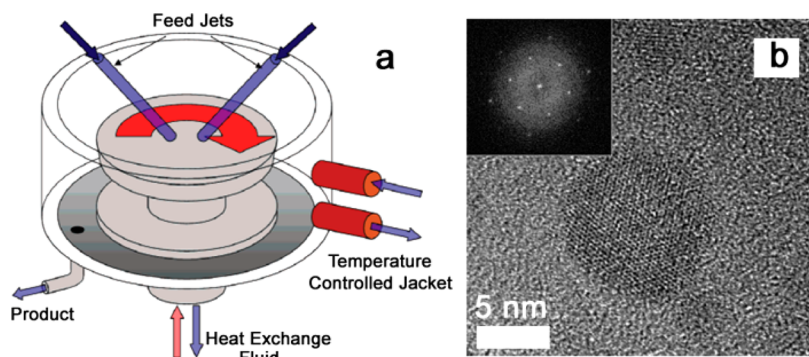


Figure 10. (a) Schematic of a spinning disc processor; (b) high-resolution TEM image of aged ZnO QDs prepared using Zn:KOH:PVP10 1:2:0.05 wt % at 25 °C and 2000 rpm (inset: Fourier transform of central particle). Adapted with permission from ref 152. Copyright (2007) American Chemical Society.

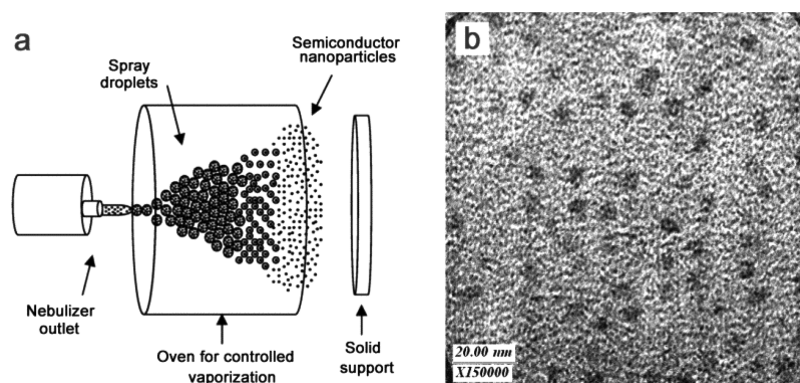


Figure 11. Illustration of the production of a stream of unsupported cadmium sulfide nanocrystals upon vaporization of the solvent from the spray droplets; (b) a typical TEM image of CdS QDs produced by pneumatically assisted thermospray with an average size of 5.1 nm. Adapted with permission from ref 153. Copyright (2005) American Chemical Society.

uncoated.¹⁵³ The nanocrystals obtained using spray-based methods have been extended to II–VI semiconductor QDs such as CdS, ZnS, and MnS; the IV–VI semiconductor QDs PbS; and the metal sulfide MoS₂.^{154–156} For all sorts of applications where films of uncapped and packed QDs are required, the thermospray synthetic approach is very promising.¹⁵³

4. SUMMARY AND PROSPECT

Semiconductor QDs have attracted tremendous attention and found promising applications in many fields, including biomedical, energy and optoelectronic devices. Although there have been several kinds of QD products in the market, the QDs remain expensive, costing hundreds of dollars per gram, and ranging up to ten thousands of dollars per gram.^{157,158} Broad application of QDs will not be realized if there is no low-cost and large-scale fabrication capability for them with a well-defined size and shape. The development of robust mass-scale nanoparticle synthesis methods has been identified as one of the five key materials challenges in *Science* by Molly et al.¹⁵⁹ However, the “chemical engineering part” of the QD story has only just begun. Due to the extraordinary number of levers that chemical engineering affords, there will be a growing dialogue between chemical engineers and researchers in other fields (such as chemists, physics, and materials) who, otherwise, might only have worked with QDs in laboratory scale. We have presented a focused review from a chemical engineering standpoint on the liquid-phase synthesis of colloidal QDs in both batch and continuous reactors, with

emphasis on green routes which possess advantages of environment-friendly raw materials, a simple operation process, and robust mass-scale production. With so many synthetic approaches already reported, and more to be developed, there will be many opportunities for developing various new synthetic approaches for QDs with well-defined properties desirable for tailor-made products and devices. Some important issues remain to be addressed.

- (1) The use of green raw materials without expensive or unnecessary dangerous compounds has become an everlasting pursuit. The elementary compositions of heavy metals in some QDs allow no completely green precursors. There are concerns about the possible side effects (e.g., environmental toxicity and pollution characteristics) derived from the use of QDs, especially heavy-metal based QDs. Discovery of novel QDs that are completely green in elementary composition may provide an alternative.
- (2) The development of green processes for the synthesis of QDs with precise control of all reaction parameters for multistep procedures is still at an early stage. It is difficult to determine which type of reactor or technology is favored for the synthesis of QDs. The quality of the product and the cost should be taken into account for practical application. In our opinion, process intensification based on microchannels devices and/or high gravity RPB reactors is promising for continuous production of QDs. Introduction of built-in analytical and feedback

mechanisms for real-time tuning and optimization of products is required.

Many researchers have made great efforts regarding QDs, conducting active and beneficial exploration. We believe that more researchers will be involved in this exciting platform, and we hope that this short review can stimulate new ideas and inspire new endeavors to promote QDs for large-scale commercial application.

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Notes

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