

A DROPLET-BASED MICROFLUIDIC REACTOR FOR SILICA NANOPARTICLE SYNTHESIS AND POST PROCESSING OF QUANTUM DOTS

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By
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A Droplet-based Microfluidic Reactor For Silica Nanoparticle Synthesis
and Post Processing of Quantum Dots

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We certify that we have read this thesis and that in our opinion it is fully adequate,
in scope and in quality, as a thesis for the degree of Master of Science.

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ABSTRACT

A DROPLET-BASED MICROFLUIDIC REACTOR FOR SILICA NANOPARTICLE SYNTHESIS AND POST PROCESSING OF QUANTUM DOTS

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M.S. in Mechanical Engineering

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The unique properties of nanoparticles mainly depend on their size and morphology; thus, it is of the utmost importance to synthesize them monodispersely to be useful in an application. Microfluidic reactors enable a monodisperse nanoparticle synthesis through a precise control over the reaction conditions such as temperature, residence time, and reactant concentrations. Droplet-based microreactors facilitate the rapid mixing of reactants with a reduced diffusion length, while maintaining a uniform residence time because of the circulating flow profile in contrast to the parabolic flow profile in continuous flow microreactors. In this thesis, a droplet-based silicon microreactor was fabricated and used for silica nanoparticle synthesis. Silica nanoparticles were obtained with a size range of 25.0 ± 2.7 nm. Considering the shorter processing time and the decreased amount of materials used alongside the comparable size range and monodispersity, this method was later implemented to be used for silica coating of quantum dot semiconductors. Silica coating of quantum dots maintain their photostability and preserve their optical properties. This thesis is the first attempt to coat *CdSe/CdS* core/shell quantum dots with a silica layer inside a microreactor. The accurate control over the reaction could enable the adjustable size and size distribution of the synthesized nanoparticles. The initial results are presented as part of this thesis.

Keywords: Microfluidics, Droplet-Based Microreactor, Silica Nanoparticles, Silica Coating, Quantum Dot Nanoparticles.

ÖZET

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Nanoparçacıkların özgün özellikleri onların boyut ve morfolojilerine dayalı olduğu için, parçacıkların bir örnek olarak sentezlenmesi kullanılacakları uygulamaların yararlılığı açısından büyük önem taşımaktadır. Mikroakışkan reaktörlerde reaksiyon koşullarının (sıcaklık, süre ve konsantrasyon) hassas olarak kontrol edilebilmesinden dolayı bir örnek üretim mümkün olmaktadır. Damlacık temelli akışa sahip mikroakışkan reaktörlerde ise damlaların içerisindeki dairesel akış hareketleri sebebiyle kimyasalların hızlı karıştırılması ve kanal içerisinde kalış sürelerinin eşit olması sağlanabilmektedir. Bu tezde damlacık temelli silisyum bir mikroakışkan sistem içerisinde silisyum dioksit (silika) nanoparçacıklar sentezlenmiş ve 25.0 ± 2.7 nm'lik bir boyut dağılımı elde edilmiştir. Bu metot kullanılan geleneksel seri bazlı üretime göre daha kısa sürmüş ve parçacıkların boyut dağılımı da istenilen aralıkta elde edilmiştir. Bu metot daha sonra optik özellikleri ile ön plana çıkan kuantum noktaların silika kabuk ile kaplanmaları için geliştirilmiştir. Kuantum noktaların özgün optik özelliklerinin korunabilmesi ve kararlı kalabilmesi için silika ile kaplanma işlemi yine seri bazlı üretim ile literatürde yapılmaktadır. Bu tezde de literatürde ilk defa nanoparçacıkların kanal içerisinde kaplanma çalışmalarına başlanmıştır. Böylelikle reaksiyon koşullarını kontrol ederek kabuk boyutlarının daha titiz bir şekilde kontrol edilmesi hedeflenmiştir. Sonuçlar bu tez kapsamında sunulmuştur.

Anahtar sözcükler: Mikroakışkan sistemler, damlacık tabanlı mikroreaktör, silisyum dioksit nanoparçacıklar, silisyum dioksit kaplama, quantum noktalar.

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Chapter 1

Introduction

Microfluidic devices have a wide variety of applications in the fields of biology, biotechnology, chemistry and material science. Microfluidic reactors (Microreactors) offer various advantages compared to the conventional nanomaterial synthesis methods. The large surface to volume ratio available in these micron-sized reactors accelerates heat and mass transport. The reaction within the microreactor allows the use of smaller amounts of toxic materials and provides uniform heating and mixing inside the microchannels; enabling a higher yield and reactant conversion. Microfluidic reactors have shown great progress in the monodisperse nanoparticle generation by controlling reaction parameters such as temperature, concentration of reagents and residence time [1, 2, 3]. Since the nanoparticle properties depend heavily on their size and morphology, uniform synthesis of nanomaterials with high yield is essential for them to be used in an application. Due to the ability to control reaction parameters precisely, microreactors can be utilized in nanoparticle synthesis, heat treatment of nanomaterials and coating of nanoparticles with other materials. Scaling down the reaction and a better control over the reaction parameters in microfluidic devices also attract other biological applications such as DNA detection and DNA amplification through polymer chain reaction (PCR) and biomedical separation [4].

Microreactors can be fabricated in a variety of materials such as metal, glass,

polymer, and silicon; each of these materials has different advantages for controlling the reaction [5]. Active and passive control are easily reachable in all kinds of microreactor substrates. Active control includes applying external forces such as electric field and magnetic field while the passive control consists of the control over channel geometry and reagent concentration and flow rates [6]. Among the different flow types available in microfluidic devices, continuous flow and droplet-based or segmented flow have been widely used in microreactors. While the continuous flow microreactors are usually easier to handle and control, the droplet-based microreactors overcome the shortcomings of continuous flow as they provide a more uniform residence time and prevent channel clogging caused by nanoparticle deposition on the channel walls.

The advantages of the microfluidic devices have been promising for chemical synthesis; however, post processing of existing nanoparticles has not been shown in such reactors yet. This thesis is one of the first attempts to use a microreactor for functionalizing nanoparticles.

1.1 Microreactor Substrate Materials

Different materials can be used as the substrate of the microreactor. Here is a quick review of the material properties which demonstrates the advantages and disadvantages of each material.

1. **Polydimethylsiloxane (PDMS):** The main advantages offered by PDMS devices are cheap price and a relatively easy fabrication procedure. The fabrication and preparation of PDMS devices usually include the fabrication of a master mold via soft lithography with a negative photoresist. This mold will be used to cast the PDMS, which would be later peeled off and bonded to the glass. Although PDMS microreactors face a limited operating temperature and pressure range alongside a quite low chemical resistance, they remain one of the top options for the microreactor substrates as they provide a cheap platform for microreactor prototypes [5].

2. **Flouropolymer:** The devices fabricated with flouropolymer offer an excellent chemical compatibility compared to PDMS microreactors; however, their application at high pressure is mainly limited due to a poor glass bonding [7, 8].
3. **Metal-based substrates:** This kind of substrates offers a good thermal resistance as well as the ability to perform under high heat and exposure to toxic chemicals [9, 10]. However, it is not possible to track the flow within these reactors due to their opaque nature.
4. **Glass/glass substrates:** Glass substrates have low thermal conductivity and limited pressure range; however, they also have a lot of applications due to their good optical properties [11].
5. **Silicon and Pyrex:** In this class of microreactors, channels are fabricated through etching of the silicon substrate and later anodic bonding to a Pyrex substrate for encapsulation. As they provide a good chemical and thermal resistance as well as optical access through the Pyrex side, they have been widely used for nanoparticle synthesis [12].

1.2 Flow Types in Microreactors

There are two possible flow types inside the microreactors based on the fluid characteristics. In the case of continuous flow, the system could be counted as one distinct fluid passing through the channels with a parabolic velocity profile. On the other hand, immiscible fluids result in two phase flow, which is often referred to as segmented or droplet-based microreactors.

1.2.1 Continuous Flow

The micro scale channel size range results in low Reynolds number; hence, the flow inside the microchannels follows the laminar flow characteristics. The fully

developed laminar flow inside the microchannel has a parabolic velocity profile obtained from the coupled solution of the momentum and the continuity equation. Figure 1.1 shows the parabolic velocity profile inside a microchannel with continuous flow. The flow profile in these channels is given as:

$$U(y) = \frac{dP}{dx} \frac{y(d-y)}{2\mu} \quad (1.1)$$

, where $\frac{dP}{dx}$ represents the pressure gradient alongside the channel length, while y shows the distance from the channel center line and d is the channel diameter. In this equation, μ indicates the fluid viscosity. As illustrated in the Figure 1.1 and based on the equation 1.1, the no-slip boundary condition on the channel walls, results in uneven material transport. This causes non-uniform residence time for fluid particles, which is a problem for nanomaterial processing as this would lead to non-uniform size distribution and therefore non-uniform properties. On the other hand, since the fluid contacts with the channel walls, when there is a chemical synthesis, this may cause clogging in the channel.

Considering the limitations of continuous flow in obtaining even residence time in nanoparticle synthesis and the probable channel clogging, the continuous flow microreactors would result in polydisperse size distributions and therefore would not be very suitable for nanomaterial processing.

1.2.2 Droplet-Based Flow

A variety of advantages, such as higher throughput, uniform residence time and rapid mixing, are offered by droplet-based microreactors. Two immiscible fluids form a segmented flow inside the main microchannel in which a carrier fluid carries out the droplet phase. The mixing in the channel is facilitated by circulation of fluid particles inside the droplet as illustrated in Figure 1.2 and Figure 1.3. On the other hand, since reactants can be carried in droplets, clogging due to channel wall interaction will be prevented.

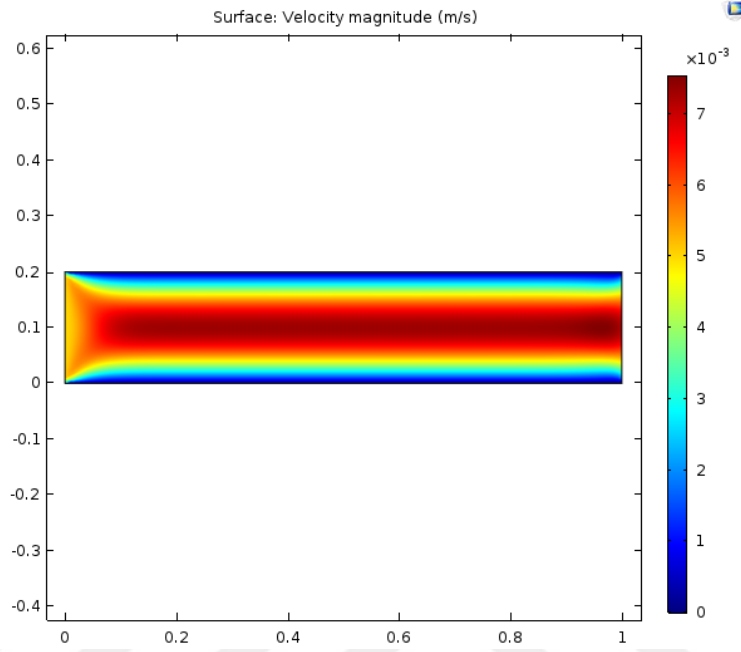


Figure 1.1: Continuous flow simulation in a microchannel (simulation is performed by using COMSOL Multiphysics)

T-junction and flow focusing are the two common geometries which could be used to generate droplets [13, 14, 15, 16, 17, 18, 19].

The governing parameters which characterize the droplet formation dynamics are:

- Channel geometry
- Fluid properties
- Operating parameters (flow rates, flow rate ratios, pressure, etc.)

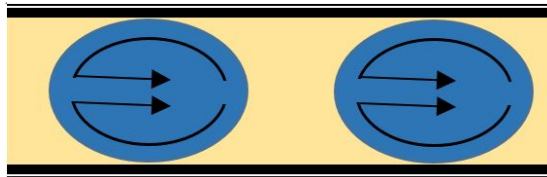


Figure 1.2: Flow profile in droplet-based microreactor

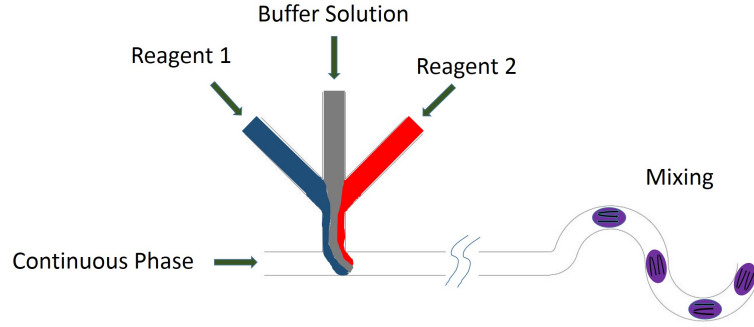


Figure 1.3: Particle mixing inside the droplets in segmented flow microreactor

To further discuss the typical flow regimes in droplet-based microreactors, a summary of the two-phase flow basics is presented in the next section.

1.2.3 Fundamentals of Two-phase Flow

Droplet-based microreactors depend on channel geometry, flow conditions, and fluid properties. The droplet formation mechanism could be explained via the involved forces analysis, such as gravitational forces, interfacial forces, and viscous forces. The different flow characteristics and regimes available in droplet-based flow can be categorized based on the three main dimensionless numbers that are presented below:

- **Reynolds Number**

As shown in the equation 1.2, the Reynolds number represents the ratio of inertial forces with respect to the viscous forces.

$$Re = \frac{\rho du}{\mu} \quad (1.2)$$

In this equation, ρ indicates the fluid density in $[\frac{kg}{m^3}]$, d represents the channel characteristic length in $[m]$, u stands for the flow velocity in $[\frac{m}{s}]$, and μ indicates the dynamic viscosity in $[Pa.s]$.

- **Bond Number**

The bond number can be represented as the ratio between the gravitational

forces and the interfacial forces.

$$Bo = \frac{\Delta\rho g d^2}{\sigma} \quad (1.3)$$

As illustrated in the equation 1.3, $\Delta\rho$ indicates the fluid density difference, while g is the gravitational acceleration and σ shows the surface tension of the two fluids in contact.

Because of the micron-size geometries in microreactors, Re and Bo numbers are usually below 1.0 and the interfacial and viscous forces are dominant in micro-scale.

- **Capillary Number**

The third dimensionless number which characterizes the flow regimes in microreactors can be represented as in equation 1.4, where it shows the viscous forces with respect to interfacial tension forces.

$$Ca = \frac{\mu u}{\sigma} \quad (1.4)$$

Based on the Ca number, the flow regimes can be categorized in three modes:

1. **Squeezing Regime:**

If the $Ca < 0.01$, the shear stress and viscous forces can be neglected with respect to surface tension, so the pressure drop dominates the droplet breakup, and as a result, the droplet size is only a function of continuous and dispersed flow rate ratio.

2. **Dripping Regime:**

For the $Ca > 0.01$ the shear force starts to affect the droplet breakup and the droplet size becomes a reverse function of Ca number. As the flow rates or the carrier fluid viscosity increase, the size of the droplet decreases [20].

3. **Jetting Regime:**

If the $0.01 < Ca < 0.75$, the droplets would be generated with a diameter less than the channel height [21, 22]. Within these limits, the viscous forces applied by the continuous phase alongside the increased interfacial instability, cause the droplet generation.

1.3 Microreactors for Nanoparticle Synthesis

Microreactors are being used for the synthesis of nanoparticles due to their advantages over conventional batch-wise nanomaterial synthesis methods [3, 23, 24, 25, 26]. The precise control over reaction parameters leads to monodispersed size distribution while maintaining rapid mixing of the reagents with rapid heat transport. The main important parameter to obtain the monodisperse nanoparticle synthesis is the separation of nucleation and growth zones [2, 6]. This can be achieved in microreactors as reported by Erdem et al. [2]. Fast mixing of two reagents is also effective in achieving uniform particle generation for room temperature synthesis such as in the reactor reported by Frenz et al. [27] where the iron oxide synthesis in a PDMS droplet-based microreactor resulted in higher quality of materials through fast mixing.

Iron oxide nanoparticle synthesis in droplet-based microreactors has been further investigated by Abou Hassan et al. [28, 29], Zhang et al. [30], and Kimar et al. [31] who reported multistep continuous flow microreactor to generate iron oxide core/shell nanoparticles.

As a vital building block for drug delivery nanoparticles [32], the synthesis of chitosan nanoparticles has attracted a lot of attention in the field of microfluidics. Çetin et al. [33] has utilized a continuous flow PDMS microreactor that could enhance synthesis rate of chitosan nanoparticles while reducing the nanoparticle clogging inside the channels.

Semiconductor nanoparticles and quantum dots could be synthesized using microfluidic reactors as well [34]. While Shestopalov et al. [35] reported a PDMS reactor that enables the direct reagent injection to synthesize *CdSe* nanoparticles, high-temperature synthesis of *CdSe* quantum dots has been investigated by Chen et al. [36] in a droplet-based microreactor and by Yen et al. [37] in a multiple temperature microreactor that separates the nucleation and growth zones.

While the continuous flow method for metal oxides, polymers, and colloidal nanoparticles has shown a great progress and enhancement of the reaction,

droplet-based microreactors were promising to solve the problems faced in continuous form such as clogging, uneven residence time and reagent mixing [1, 38]. This thesis presents a viable method to coat the colloidal quantum dots with silica precursors.

1.3.1 Silica Particle Formation With Microreactors

The controlled growth of silica particles has been reported by Stöber [39] back in 1968. In this method, the size and size distribution of the silica spheres could be well controlled in a reaction, which includes the hydrolysis of tetraethoxysilane (*TEOS*). The alternative methods based on the micro-emulsions still face the problems such as the large amount of required materials.

To overcome this problem, several combined and semi-batch methods have been reported to form the silica nanoparticles, which resulted in a narrower size distribution and a better control over the size and shape [40, 41, 42]. Min Su [43, 44] reported a combined micromixer/microreactor/batch reactor system which includes microchannels for the reactant mixing and a batch reactor for the growth of the silica nanoparticles. The synthesis was performed both for single phase laminar flow and two-phases segmented gas-liquid flow and resulted in an increased yield and enhanced the spherical shape of the nanoparticles. The use of hydrodynamic micromixers for silica nanoparticle formation enables an adjustable particle size and size distribution as reported by Gutierrez et al. [42], Yujuan He et al. [45], and Ping He et al. [46].

Modified Stöber methods have been used for the synthesis of mesoporous silica microspheres. Yano et al. [47] have reported a modified Stöber method to gain a controlled synthesis of monodispersed mesoporous silica particles. Lee et al. [48] generated the mesoporous silica particles through a one-step in situ method in a microfluidic device. They combined a microfluidic emulsification and a rapid solvent diffusion and reported controlled size, shape, and surface morphology. Carroll and coworkers [49] used a droplet-based microreactor for silica microspheres synthesis. The silica precursor and surfactant were contained

in the droplets which were suspended in the continuous oil phase flow. Khan et al. [50] reported a comparison between microfluidic synthesis of colloidal silica in laminar flow and segmented flow reactors and examined the residence time effect on the particle size distribution. The segmented flow reactors can eliminate the axial dispersion and enable a thorough investigation of growth mechanism. Moreover, De Matteis et al.[51] used a combined reactor to prepare hydrophilic organic coatings of silica. In the reported microreactor, a segmented flow reactor was used for the injection of the reactants and the aging was enabled inside the tubular reactor.

The post processing of the nanoparticles with silica spheres has been reported by Knossalla et al. [52] in which a gas-liquid segmented flow tubular reactor has been used to generate mesoporous core/shell spheres and encapsulate gold particles with silica shells ($Au@SiO_2$). This continuous synthesis could be potentially used for coating other materials with silica nanostructures.

Table 1.1 presents a summary of recent microfluidic approaches for silica nanoparticle formation and the size ranges obtained based on each synthesis method. For all cases, the reactants are prepared with ethanol or a polar solvent; however, in order to use the method for silica encapsulation of $CdSe/CdS$ quantum dots, a nonpolar solvent such as cyclohexane must be used as the synthesis approach implemented in this thesis.

Table 1.1: Silica nanoparticle formation with microreactors

Author	Microreactor Type (Flow Type)	Reactants	Residence Time	Temperature	Average Size
Khan et al. [50]	Laminar Flow	0.1 M TEOS 1.0 M NH_3	6.5 min	RT	281 nm , σ = 20%
			16 min	RT	321 nm , σ = 9%
	Segmented Flow	0.1 M TEOS, 1.0 M NH_3	10 min	RT	277 nm , σ = 9.5%
			20 min	RT	390 nm , σ = 8.7%
	Segmented Flow	0.2 M TEOS 2.0 M NH_3	9 min	RT	407 nm , σ = 7.1%
			14 min	RT	540 nm , σ = 4.5%
Carroll et al. [49]	Flow Focusing Emulsification & Batch Reactor	TEOS, Ethanol, N-hydrochloric acid	120 min	80°C	30 μm
Lee et al. [48]	Flow Focusing Rmulsification & Solvent Diffusion	TEOS, Ethanol, Hydrochloric acid	120 min	RT	19.4 $\pm$ 0.6 μm
Min Su et al. [43, 44]	Laminar Flow Reactor Batch Reactor Semi-Batch Reactor Micromixer/Miromreactor /Batch Reactor	TEOS, Ethanol, Ammonium - hydroxide	120 min	78°C	Size & PDI 58 nm , 0.064 18 nm , 0.227 20 nm , 0.203 87 nm , 0.05
			180 min	78°C	
			120 min	78°C	
			120 min	75°C	
			120 min	75°C	
Gutierrez et al. [42]	Micromixer/Batchreactor	TEOS, Ethanol, Ammonium - hydroxide	90 min	40°C	298 nm , 0.036
			30 min	40°C	276 nm , 0.011

1.4 Quantum Dot Nanoparticles

Quantum dots are nanometer-scale conjugated semiconductors with a wide variety of applications in biological labeling and detection, imaging, and biosensing [53, 54]. The optical properties of these artificial atoms mainly depend on their size and shape. Due to the quantum confinement of electrons, the unique optical and electrical properties of quantum dot nanoparticles have a huge advantage over the organic dyes and fluorescent proteins [55, 56, 57]. Their longer photostability and narrower emission and absorption spectra have been utilized by Wang et al. [58] for magnetic separation and cell detection via formation of Fe_2O_3 nanocomposites. Alongside the ligand exchange [59, 60] and micelle formation [61, 62], silica coating [63, 64, 65] could enhance the quantum dots stabilization. Silica encapsulation for different kinds of quantum dots, such as $CdSe$, InP , ZnP , ZnS , and $ZnSe$, increases the compatibility as their optical properties degrades under the UV exposure [66, 67, 68, 69].

This thesis presents a method for generation of silica nanoparticles inside a droplet-based microreactor, which could be later used as a suitable method to coat the $CdSe$ quantum dots. Next section reviews the basic method for silica generation and recent attempts to synthesize these nanoparticles in microfluidic devices.

1.5 Silica Coating of Nanoparticles

The transparent and chemically inert silica shells have been widely used to prevent the oxidation of nanoparticles. In the case of quantum dot nanoparticles, silica encapsulation would enhance the photostability and enable the water solubility [70, 71, 72, 73]. Silica coating could be performed in two different methods: microemulsion synthesis for thin silica coating ($< 10nm$) and the microemulsion method for coating inorganic nanoparticles with monodispersed smooth silica surfaces [74, 75].

In Stöber method, initially, the hydrophobic nanoparticles have to be surrounded by hydrophilic micelle that can enable the silica growth. This process requires a surface exchange in which hydrophilic ligands are substituted on the surface. Cyclohexane and IGEPAL are used to synthesize the micelles and ammonium hydroxide forms a reverse microemulsion and as tetraethyl orthosilicate (TEOS) is added, the encapsulation of silica shells occurs via hydrolysis [76, 77]. Although this method would seem to be problematic in preparation steps and difficulty in coating nanoparticles with nonpolar ligands, it has been a popular method for silica coating of metallic nanoparticles [78, 79] and quantum dot semiconductors [80, 81], such as *CdSe/ZnS* [82], *PbSe* [83], and *CdTe* [84].

Overall, as the silica coating enhances the optical and chemical properties of quantum dots, it is a critical step in their biomedical applications. The silica synthesis method presented in this thesis could be a step towards the silica coating of quantum dots inside the microreactor.

1.6 Thesis Overview

The emerging of microfluidic reactors has provided a precise control over the chemical reactions. Microreactors have enabled an accurate understanding of the reaction control parameters and their effect on the resultant size and shape of the nanoparticles. A chemically robust silicon microreactor was employed to synthesize silica nanoparticles in a droplet-based reaction. This process could potentially be utilized to coat quantum dot nanoparticles to enhance their optical properties.

Chapter 2, reviews the conventional materials used in microreactor fabrication. Two different methods for nanofabrication of the microfluidic devices are presented in this chapter and the fabrication steps are mentioned. Finally, the characteristics of two silicon microreactor are presented.

Chapter 3, starts with the description of the silica nanoparticle synthesis process. Batch-wise synthesis of silica nanoparticles is initially described as the reference method. Later on, an extensive explanation of the proposed droplet-based reaction is presented and the experimental results of the droplet-based reaction are compared to the reference results from the batch synthesis.

Chapter 4, introduces the batch synthesis for silica encapsulation of quantum dots. Experimental results obtained for the droplet-based encapsulation of *CdSe/CdS* quantum dots are presented following the optimum conditions from Chapter 2.

Chapter 5, presents a summary of the results and outcomes of the thesis. The concluding remarks are followed by the proposed recommendations to enhance the synthesis process.

Chapter 2

Microreactor Design and Fabrication

Different materials could be used to prepare microreactors. Each type of material offers various characteristics, therefore choosing the proper material is highly based on the application. Polymers such as Polydimethylsiloxane (PDMS) and PMMA (Poly (methyl methacrylate)) are among the most popular materials used in microreactor fabrication. These polymers offer an easy fabrication procedure. Different techniques could be used in their fabrication processes such as micro-machining, photolithography, and injection molding. Despite the low cost of polymer-based microreactor fabrication, they offer a poor resistance to chemicals and are not suitable for high temperature processes. On the other hand, silicon substrate microreactors are chemically robust and suitable for high temperature reactions. However, this fabrication procedure is more expensive than polymer based methods which might be counted as the disadvantage of silicon substrate microreactors.

In this thesis, PDMS and silicon substrate reactors have been fabricated to perform the silica nanoparticle synthesis. In this chapter, the design and fabrication steps for each microreactor have been presented respectively.

2.1 PDMS Substrate Microreactors

Polymer based microreactors require a simple and low cost fabrication. Among the popular fabrication methods, micromachining, photolithography, and injection molding are usually used to prepare microreactors with PDMS and PMMA. Since the surface quality of the microreactor is an important factor, microfabrication methods have a clear advantage over the micromachining techniques. Microfabrication methods in Cleanroom offer precise geometries and junction profiles points while maintaining a smooth surface. A detailed review of the polymer-based microreactors could be found by Becker et al. [85].

PDMS microreactors can be fabricated by the soft lithography technique. The choice of photoresist is often based on the desired characteristics and applications of the microreactors. The thickness of the photoresists could be controlled based on the tables provided by the manufacturer and different channel geometries could be obtained by the mask design in the photolithography process.

In this thesis, initially, a PDMS reactor was fabricated with soft lithography technique to provide a prototype to simulate the experimental conditions. The fabrication steps are presented in the next section.

2.2 Fabrication Steps of the PDMS Microreactor

The design parameters and microchannel geometries are based on the reported study by Ozkan et al. [86]. The CAD design of the microchannels is shown in the Figure 2.1.

This design includes a total channel length of 237 *mm* and the channel cross section is designed to be 200 $\mu m \times 200 \mu m$. The microfabrication steps are shown in Figure 2.2. This flowchart represents the fabrication procedure, starting from

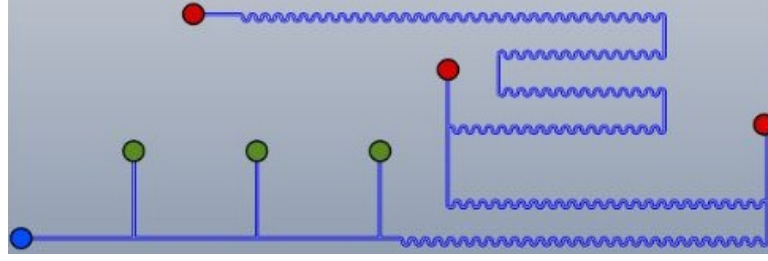


Figure 2.1: CAD drawing of the microchannel design [87]: The blue dot represents the continuous phase inlet, the green marks show the inlets for the dispersed phase and red dots indicate three different outlets to examine the effect of residence time.

a bare silicon wafer to the PDMS bonding to the glass slide.

1. Starting from a bare silicon wafer, the wafer should be rinsed with acetone, Isopropanol (IPA) and deionized (D.I.) water. Later the wafer was dried by a blow dry and kept in the oven for 7 minutes at 110°C to completely get rid of the water droplets on the surface.
2. To let the substrate reach the room temperature, it should be kept in the ambient between 4-5 minutes before any fabrication procedure.
3. In order to create the desired channel geometry on the silicon master mold, initially, a layer of HMDS and negative photoresist should be coated on the wafer. HMDS increases the adhesion between the photoresist and the

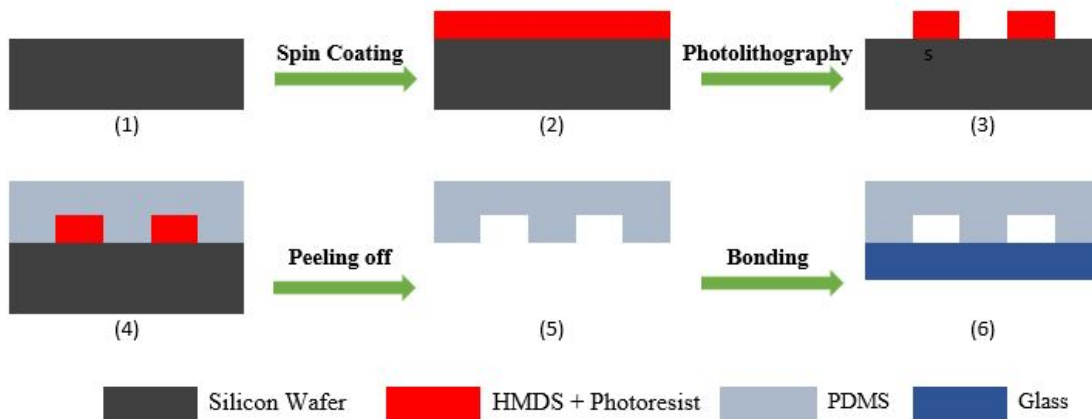


Figure 2.2: Photolithography fabrication steps for the PDMS microreactor

wafer. The photoresist spin coating parameters are chosen based on the required thickness of $200\text{ }\mu\text{m}$:

- **HMDS Spin Coating:** $v_H = 5000\text{ rpm}$, $a_H = 2000\text{ rpm/s}$, and $t_H = 40\text{ s}$
- **Photoresist Spin Coating:** *SU-8:2050* was used as the negative photoresist to create the microchannel geometries. Due to its high viscosity, a two-step recipe should be used for the spin coating in order to obtain a uniform layer.
 - (i) **Spreading:** $v_{Spread} = 500\text{ rpm}$, $a_{Spread} = 100\text{ rpm/s}$, and $t_{Spread} = 10\text{ s}$
 - (ii) **Spinning:** $v_{Spin} = 1000\text{ rpm}$, $a_{Spin} = 300\text{ rpm/s}$, and $t_{Spin} = 30\text{ s}$

This recipe followed by the presented baking steps would result in a photoresist layer with $200\mu\text{m}$ thickness. After the spin coating, the photoresist residues should be removed from the wafer perimeter using acetone.

4. A soft-bake process should be performed after the photoresist spin coating to prevent the cracks on the surface. The procedure includes a two-step bake at 65°C for 7 minutes, followed by a 33 minute bake at 95°C . To prevent the wafer from sticking to the mask in the photolithography process, the baked photoresist on the wafer should be rested for at least 4 hours.
5. Considering the standard parameters for the mask and wafer thickness (mask thickness = $2.3\text{ }\mu\text{m}$ and wafer thickness = $500\text{ }\mu\text{m}$), the UV-exposure was performed for a $200\text{ }\mu\text{m}$ layer of *SU-8 :2050* under 275 mJ/cm^2 power with a $500\text{ }\mu\text{m}$ proximity.
6. The post-bake step after the UV exposure in the soft lithography includes a two-step baking at 65°C for 5 minutes and at 95°C for 13 minutes. The precise post-bake would ensure a strong bonding between the photoresist and the substrate.
7. Before the photoresist development process, the baked wafer should be cooled down in the ambient. The special *SU-8:2000* developer was used

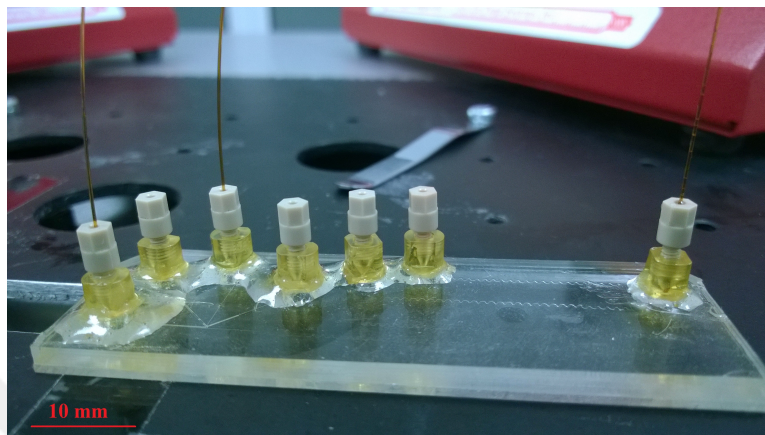


Figure 2.3: PDMS microreactor with the attached fittings and capillary tubing.

to sink the wafer. Since a negative photoresist was used, the exposed areas in the lithography step would become less soluble in the developer solution. The developing process was performed under the continuous shaking for 16 minutes.

8. As the final step before the PDMS casting, the developed substrate was rinsed with IPA and D.I. water and dried with N_2 .
9. The PDMS cast was prepared following the steps presented in the Appendix A. Figure 2.3 shows the fabricated PDMS microreactor with attached fittings to use the capillary tubing.

2.3 Silicon Substrate Microreactor

Considering the ease of fabrication and low cost process, polymer-based microreactors are a proper choice for the simple synthesis process. However, as they offer a poor chemical and thermal resistance, they cannot be utilized for more complicated chemical processes. In the case of nanoparticle synthesis inside the microreactors, the precise control over the temperature is highly important as many of the reactions are thermally activated. Silicon substrate reactors provide a chemically robust and thermally resistant platform for the nanoparticle

synthesis.

Silicon is considered as the workhorse of microfabrication. It is fairly cheap, abundant and has a default compatibility with microfabrication equipment. Silicon wafers in different sizes could be used to prepare the microreactors with a proper thermal and chemical resistance. Silicon provides a flexible and smaller channel design compared to other types of microreactors.

The key step in nanoparticle synthesis is to separate the nucleation and growth zones and this could be easily achieved in silicon substrates to perform different thermal treatments for each zone. Erdem et al, [2] reported a two-phase silicon microreactor, with two thermally isolated regions that could synthesize monodispersed nanoparticles. Chan et al. [36] used a droplet-based microreactor for the high temperature synthesis of *CdSe* nanoparticles. Utilizing a droplet-based microreactor prevents the residence time distribution and reduces the clogging problem in the microchannels.

In order to perform the silica nanoparticle synthesis, a silicon microreactor was fabricated to provide proper chemical resistance.

2.4 Fabrication Steps of the Silicon Substrate Microreactor

Conventional microfabrication techniques were used to prepare the silicon microreactor. The channel design was based on the CAD design shown in Figure 2.1. The fabrication steps flowchart is presented in Figure 2.4.

The microreactor includes a total channel length of 237 mm with a cross section area of $200\ \mu\text{m} \times 200\ \mu\text{m}$. Multiple T-junctions implemented in the design (Figure 2.1) enable the droplet generation and sequential supply of reagents, while three different outlets provide different residence times for the reaction. The microfabrication steps are listed below:

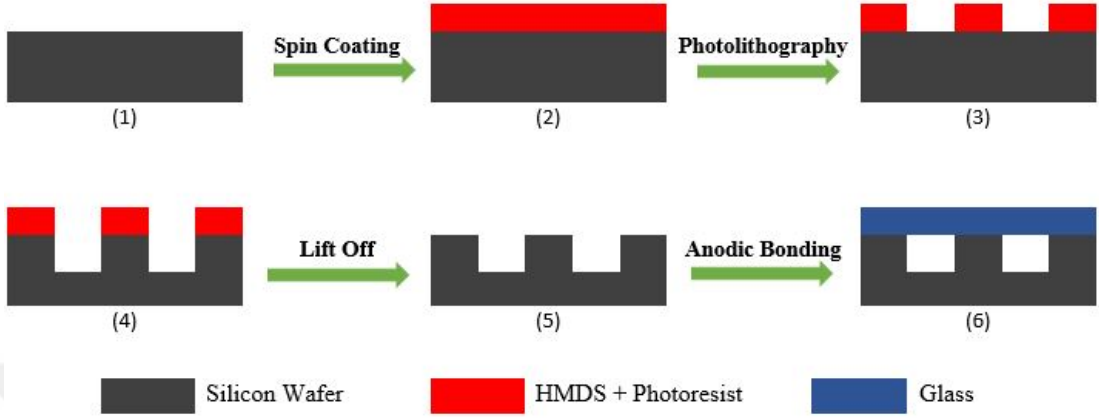


Figure 2.4: Microfabrication steps for silicon substrate microreactor.

1. Starting from a bare silicon wafer, the wafer should be rinsed with acetone, Isopropanol (IPA) and D.I. water. Later the wafer was dried by a blow dry and kept in the oven for 7 minutes at 110°C to completely get rid of the water droplets on the surface.
2. To let the substrate reach the room temperature, it should be kept in the ambient between 4-5 minutes before any fabrication procedure.
3. In order to create the desired channel geometry on the silicon wafer, initially, a layer of HMDS and positive photoresist should be coated on the wafer. HMDS increases the adhesion between the photoresist and the wafer. The photoresist spin coating parameters are chosen based on the required thickness ($1.4\mu m$):

- **HMDS Spin Coating:** $v_H = 5000 \text{ rpm}$, $a_H = 2000 \text{ rpm/s}$, and $t_H = 40 \text{ s}$
- **Photoresist Spin Coating:** AZ 5462 was used as the positive photoresist to create the microchannel geometries. $v_{Spin} = 1000 \text{ rpm}$, $a_{Spin} = 300 \text{ rpm/s}$, and $t_{Spin} = 30 \text{ s}$.

This recipe followed by the presented baking steps would result in a photoresist layer with $1.4 \mu m$ thickness.

4. The pre-bake process for this positive photoresist includes heating for up to 50 seconds at 110°C on a hot plate.

5. Considering the standard parameters for the mask and wafer thickness (mask thickness = $2.3\ \mu m$ and wafer thickness = $500\mu m$), the UV-exposure was performed for a $1.4\ \mu m$ layer of *AZ 5462* under $200\ mJ/cm^2$ power with a $500\ \mu m$ proximity.
6. After the UV exposure, the post-bake step was performed at $110^\circ C$ for up to 50 seconds on a hot plate.
7. Before the photoresist development process, the baked wafer should be cooled down in the ambient. To prepare the *AZ 4000* development solution, it was diluted with D.I. water with 1 : 4 ratio. Later on, the photoresist was developed for 50 seconds. To maintain the photoresist pattern, a precise control over the development time is required. This step was followed by rinsing the wafer in IPA and D.I. water. At this stage, acetone would dissolve the photoresist pattern and must be avoided.
8. Deep reactive ion etching (DRIE) process based on parameters in Bosch Process [88] as listed in Table 2.1 was performed for 4 hours to obtain the desired $200\mu m$ channel depth. DRIE provides a very good selectivity, high aspect ratio and nearly vertical walls in the etching process [89, 90].
9. After the DRIE step, the photoresist protective layer was removed by sinking the substrate in acetone. This lift-off process took about 10 minutes in the ultrasonic bath.
10. Finally, the patterned silicon wafer was bonded to Pyrex using anodic bonding at METU MEMS.
11. Micromilling technique using a Poly Crystalline Diamond (PCD) with a $0.7\ mm$ diameter was used to drill the channel inlets, under the spinning speed of $600\ rpm$ and $20\ mm/min$ feed rate.

The resultant silicon microreactor is shown in Figure 2.5.

This microreactor (Figure 2.5) was used for the initial rounds of experiments; however, it was not sufficient to provide long residence times. Therefore a second

Table 2.1: Bosch process parameters for DRIE

	Passivation	Etching
Cycle Time	7 <i>seconds</i>	10 <i>seconds</i>
Pressure	20 <i>mTorr</i>	35 <i>mTorr</i>
C_4F_8 Flow	70 <i>sccm</i>	—
SF_6 Flow	—	80 <i>sccm</i>
O_2 Flow	—	5 <i>sccm</i>
Bias Power	—	13 <i>W</i>
Bias Frequency	—	13.56 <i>MHz</i>
Coil Power	400 <i>W</i>	400 <i>W</i>
Heater Temperature	—	45°C
Chinner Temperature	20°C	20°C
Platen Matching	Load 35, Tune 50	Load 35, Tune 50
Coil Matching	Load 40, Tune 50	Load 40, Tune 50

silicon microreactor was used during the silica nanoparticle synthesis as shown in Figure 2.6. This multi-temperature silicon microreactor was previously used by Erdem et al.[2] to synthesize TiO_2 metal oxide nanoparticles in a two-step reaction. The multi-temperature silicon microreactor consists of 2 meters long microchannel with a $200\ \mu m \times 200\ \mu m$ cross section area. As shown in Figure 2.6, the T-junction enables the droplet generation and two outlets provide different residence times for the reaction. Both of these silicon microreactors were used with different configuration and experiment conditions to reach the optimum recipe for silica nanoparticle synthesis.

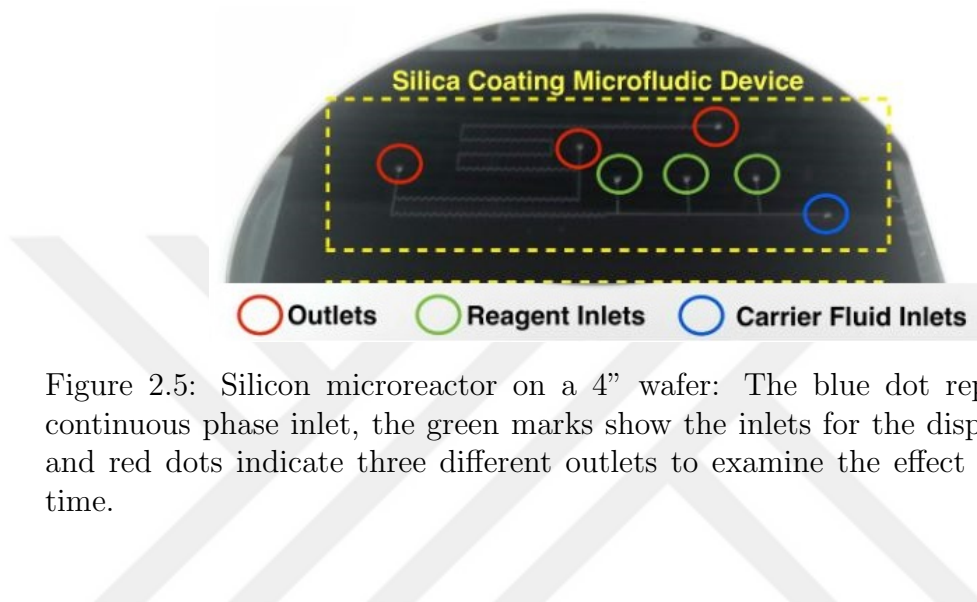


Figure 2.5: Silicon microreactor on a 4" wafer: The blue dot represents the continuous phase inlet, the green marks show the inlets for the dispersed phase and red dots indicate three different outlets to examine the effect of residence time.

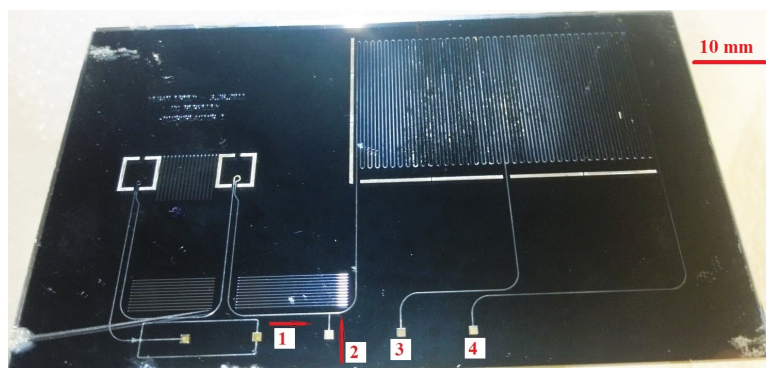


Figure 2.6: Multi-temperature zone silicon microreactor: Arrow 1 indicates the direction of continuous phase flow, while arrow 2 shows the dispersed phase flow direction. There are two outlets (3&4) to examine the effect of different residence time. A total length of 2 m is provided for the synthesis. The channel cross section area is $200\ \mu m \times 200\ \mu m$

Chapter 3

Silica Nanoparticle Formation

Silica nanoparticles and hollow silica structures provide a very good biocompatibility with controllable surface areas. The chemical inertness and thermal stability of these nanoparticles [43, 91] could be potentially used in various fields and applications such as sensors [92], drug delivery [93], chromatography [94], and coating [95]. Among the several different methods that could be implemented to synthesize two dimensional and three-dimensional silica structures, a microfluidic approach based on the reverse micelle method reported by Stöber et al.[39] could provide a uniform size distribution and solve the reproducibility issues faced in the conventional batch synthesis [96]. Stöber and coworkers [39] has achieved a well-controlled growth of micron-sized silica spheres via silicic acid hydrolysis. The presence of the surfactant at the interface can stabilize the dispersion of two immiscible fluids [97, 98]. In the reported Stöber method, IGEPAL is the non-ionic surfactant and ammonium hydroxide (NH_4OH) plays the catalyst role and triggers the silica encapsulation process.

Microfluidic approach for silica particle synthesis includes a wide range of combined microreactors for silica nanoparticle synthesis. Su et al.[43, 46] has reported a microfluidic synthesis of silica nanoparticles via a combined micromixer/microreactor and compared the results for single phase and two-phase segmented flow microreactors . Yujuan He et al.[45] and Ping et al.[46] obtained

the adjustable size distribution of hollow silica nanoparticles with a hydrodynamic focusing micromixer and a microreactor fabricated with PEEK Y-shaped connectors and EFTE tubings that could provide a wide range of reaction residence time. Similarly, Gutierrez et al. [42] have reported a narrow size synthesis of silica nanoparticles with micromixer microreactor. Controlled synthesis of mesoporous silica particles inside microreactors has been reported with a modified Stöber method [47, 48, 49, 50].

Previous research is mainly focused on the generation of mesoporous silica microspheres inside the microreactors. In all of the reported microfluidic approaches for silica synthesis based on the Stöber method, the reactants were prepared in ethanol or a polar solvent. However, as the ultimate goal of this thesis, a special case of synthesis had to be introduced that could be later used for the silica coating of *CdSe/CdS* quantum dots. The choice of solvents throughout the experiments was made with regards to the potential encapsulation of hydrophobic quantum dot nanoparticles. In this thesis, a droplet-based microfluidic device has been investigated for silica coating of quantum dot nanoparticles. Initially, the growth of silica nanoparticles was examined based on Stöber method. Once the optimum recipe and conditions were obtained compared to the batch-wise synthesis method, the process was investigated for the *CdSe* quantum dots post processing.

3.1 Silica Nanoparticle Formation: Batch-wise Synthesis

In order to obtain the optimum conditions inside the microreactor, initially, the batch-wise synthesis results of the silica nanoparticle synthesis dots were studied (**Experiment 3.1**).

Silica nanoparticle generation was carried out by the following recipe reported

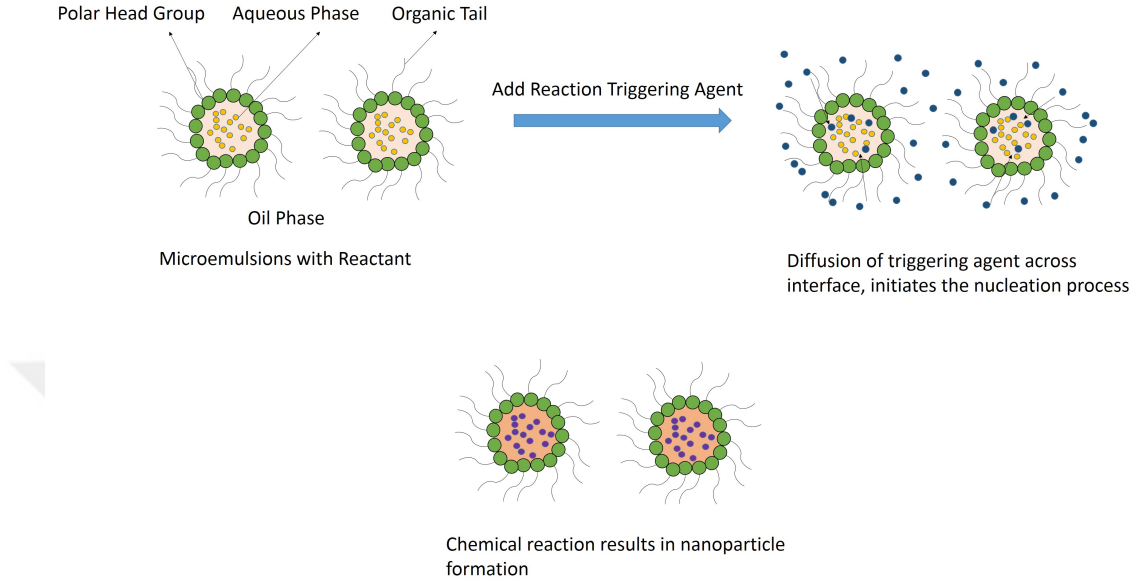


Figure 3.1: Typical reverse micelle system and steps involved in one microemulsion process [100]

by Popovic et al. [99]. Initially, using a round bottom flask, 1.3 ml *IGEPAL CO-520* and 10 ml of anhydrous cyclohexane were mixed and stirred for 15 minutes. After that, 80 μl of tetraethyl orthosilicate (*TEOS*) was added, and the mixture in the flask was stirred for 30 minutes. Finally, 150 μl ammonium hydroxide (28% in water) was added and the stirring continued for 48 hours. At last, the silica nanoparticles were dissolved in the mixture of water and 20 μl of 2 M *NaOH* and preserved at 4 °C (Table 3.1).

The schematic of the reverse micelle procedure is shown in Figure 3.1 and the TEM results are presented in Figure 3.2.

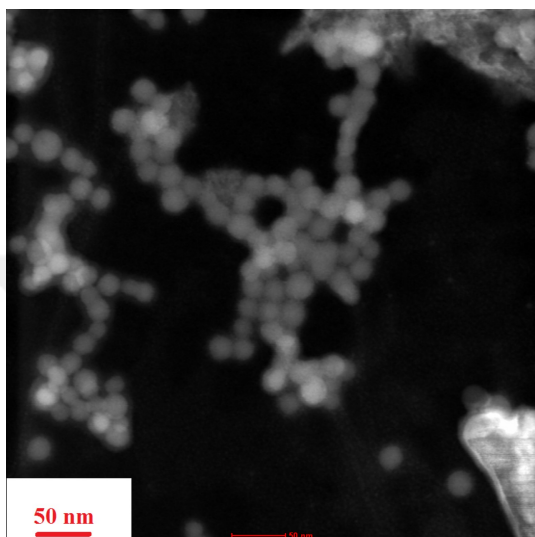
As illustrated in Figure 3.2 and Table 3.1, the batch-wise synthesis of silica

Table 3.1: Silica nanoparticle synthesis: Batch-wise reaction: Experiment 3.1

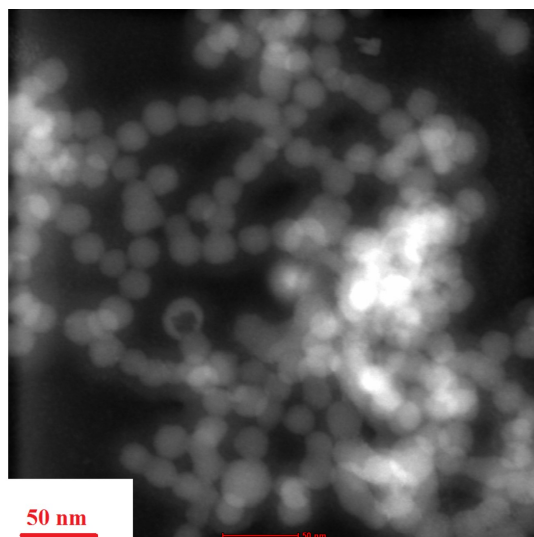
Batch synthesis	
Reaction Time	48 hours
Nanoparticles Average Size	18.25 ± 2.2 nm
Number of Measured Particles	45 (Table B.1)

nanoparticles takes about 48 hours and results in nanoparticles with a size range of 18.25 ± 2.2 nm. Although the size range would not remain constant for different batches, the size range achieved by from this batch synthesis was targeted throughout the droplet-based synthesis.

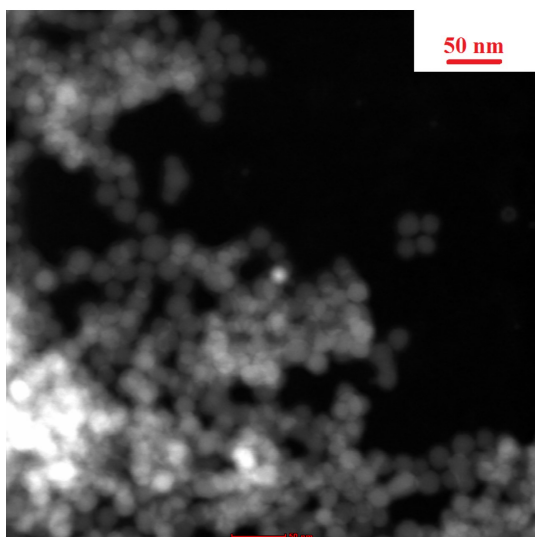




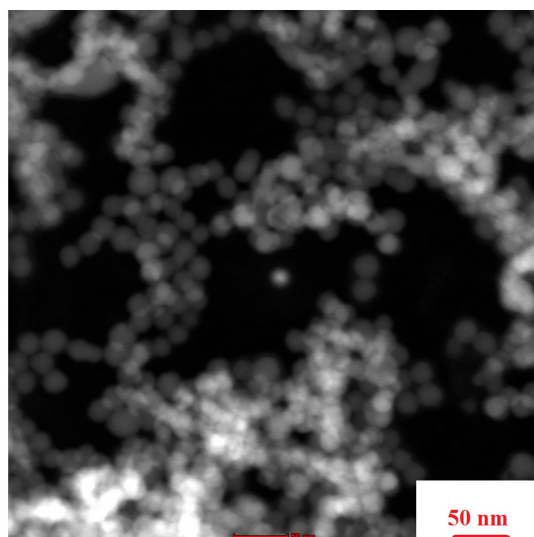
(a)



(b)



(c)



(d)

Figure 3.2: TEM results for batch-wise synthesis of silica nanoparticle (Experiment 3.1) with an average size of $18.25 \pm 2.2\text{nm}$.

3.2 Materials and Synthesis Method

Three different droplet-based microreactors were prepared to perform the synthesis as illustrated in Chapter 2. As the PDMS microreactor could not provide a proper chemical resistance to the chemicals, the experiments had to stop after 10 minutes because of the device failure [87]. To ensure a reliable experiment platform, two silicon microreactors were used to enable a steady run of synthesis. The channel cross section in both silicon microreactors was $200\ \mu m \times 200\ \mu m$; however, the available channel length and hence, the maximum residence times were different. The first silicon microreactor (Figure 2.5) provides a total channel length of $140\ mm$ for the synthesis, while the second microreactor has a total channel length of $2\ m$ as illustrated in Figure 2.6 [12].

The essential step in the synthesis is to generate the steady droplets containing the reagents that could be carried away in a continuous flow. As the case for all the droplet-based microreactors, the dispersed phase (containing the reaction reagents) and the continuous flow (which enables the droplet generation) must be immiscible. However, considering the choice of materials and the solutions which are necessary for the process, a single continuous phase, which is immiscible with all of the reagents could not be found. The best choice for the continuous phase was N-Methylformamide (*NMF*) with the chemical formula of C_2H_5NO . *NMF* is immiscible with cyclohexane and *TEOS*, but could be mixed with ammonium hydroxide. Lee et al. [48] have reported a case of the precursor solution diffusion from the droplets into the continuous oil phase. The fast diffusion of dispersed phase solvents results in forming an interfacial sub-phase and loss of the reactants inside the droplet. The dispersion of ammonium hydroxide inside the *NMF* could be controlled with the total concentration of ammonium hydroxide through the synthesis and reactions.

3.2.1 Materials

Usually, the reagents are supplied through the dispersed phase and mixed inside the generated droplets. Two different configurations could be investigated throughout based on the supply condition of ammonium hydroxide. Each one of these two methods required different materials preparation. However, to enable the supply of the exact amount of desired ammonium hydroxide, it was used within the dispersed phase.

In this method, pure *NMF* is supplied as the carrier fluid and induces the droplet break-up, while all the reagents are mixed inside the droplet as shown in Figure 3.3. Two different solutions were prepared and supplied through individual entries. To prepare the first solution, 1.3 ml of *IGEPAL CO-520* was mixed with 10 ml of anhydrous cyclohexane and stirred for 15 minutes. After that, 80 μl of tetraethylorthosilicate (TEOS) was added and stirred for 15 min. To prepare the second solution, 150 μl of ammonium hydroxide (28% in water) was added to 10 ml of anhydrous cyclohexane and stirred for 15 minutes.

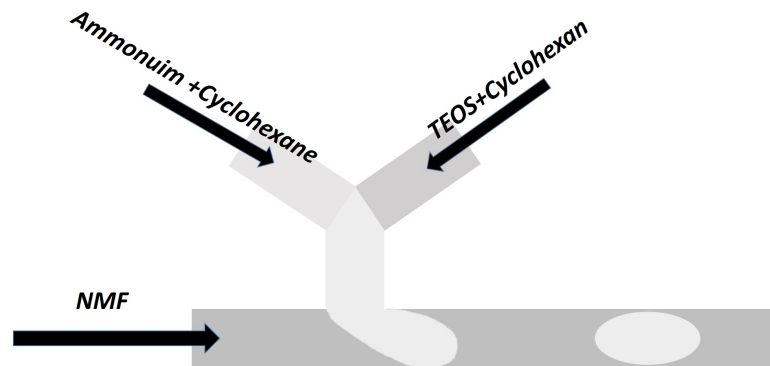


Figure 3.3: Silica nanoparticle synthesis with supplying the ammonium hydroxide within the dispersed phase: The pure *NMF* is supplied through the horizontal channel and enables the droplet break-up of the dispersed phase which contains all the reagents.

3.2.2 Synthesis Control Parameters

Microfluidic devices offer a precise control over the reaction parameters. The small amount of reactants used inside the microchannels could be well controlled in terms of concentration and temperature. The residence time can be controlled via the reactant flow rates. The control parameters that were studied during the experiments to obtain the optimum conditions are:

(i) Temperature

The temperature of the reaction can be easily controlled since silicon microreactors provide a good thermal conductive platform. The batch-wise synthesis is performed at room temperature; however, heating is possible by utilizing a hot plate or ceramic heaters.

(ii) Residence Time

The residence time of the reactants inside the microchannels is mainly based on the continuous phase flow rate. While the reagents are mixed inside the droplets, they are carried away by the carrier fluid. Throughout this thesis, two microreactors with different channel lengths were used. Considering the constant channel length for each reactor, carrier fluid flow rate determines the residence time in each experiment.

(iii) Reactant Concentration

The initial concentrations mentioned in the material preparation are based on the assigned concentration in Stöber method [39]. Since the concentration for *TEOS* is constant for the batch-wise synthesis, only the ammonium hydroxide concentration was changed during the experiments in order to achieve the optimum conditions.

3.3 Experimental Set-up

The experimental set-up for the first and second silicon microreactors are presented in Figure 3.4 and Figure 3.5 respectively.

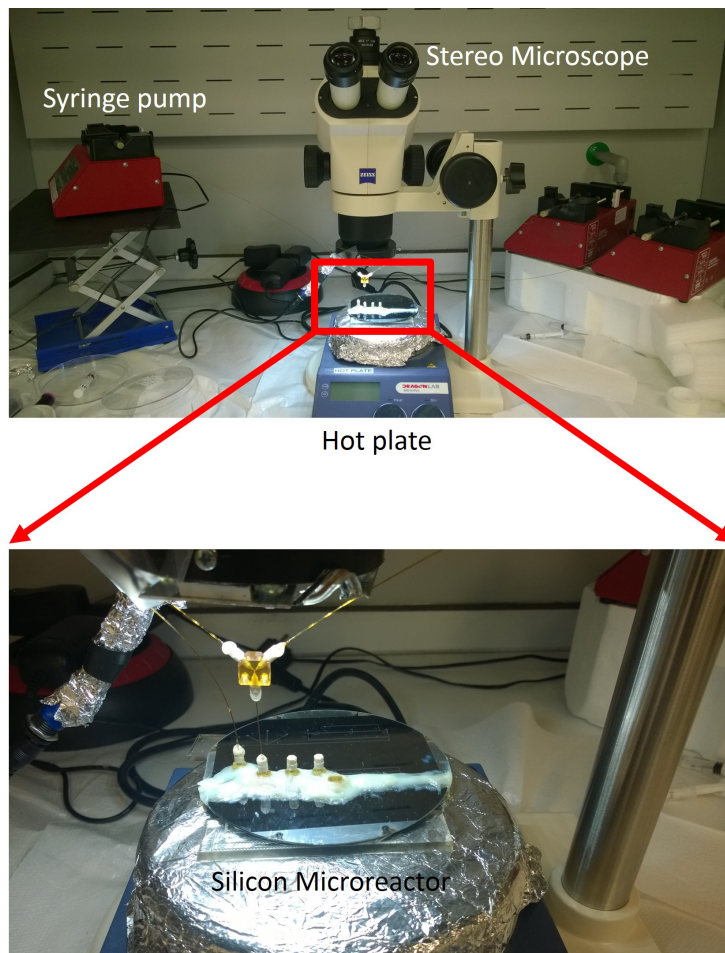


Figure 3.4: Experimental setup for the first microreactor: Solutions are pumped by the syringe pumps through the capillary tubing. A constant monitoring of the channels is available through the microscope and heating is possible by the hot plate.

As shown in Figure 3.4 for the first silicon microreactor, the solutions are pumped with syringe pumps and are supplied to the microchannels via capillary tubings attached to the inlets. A conventional stereomicroscope was used to constantly monitor the microchannels during the experiments. Live time images could be stored with a camera attached to the microscope via the *ToupView*

software. A hot plate was used to control the temperature of the microreactor.

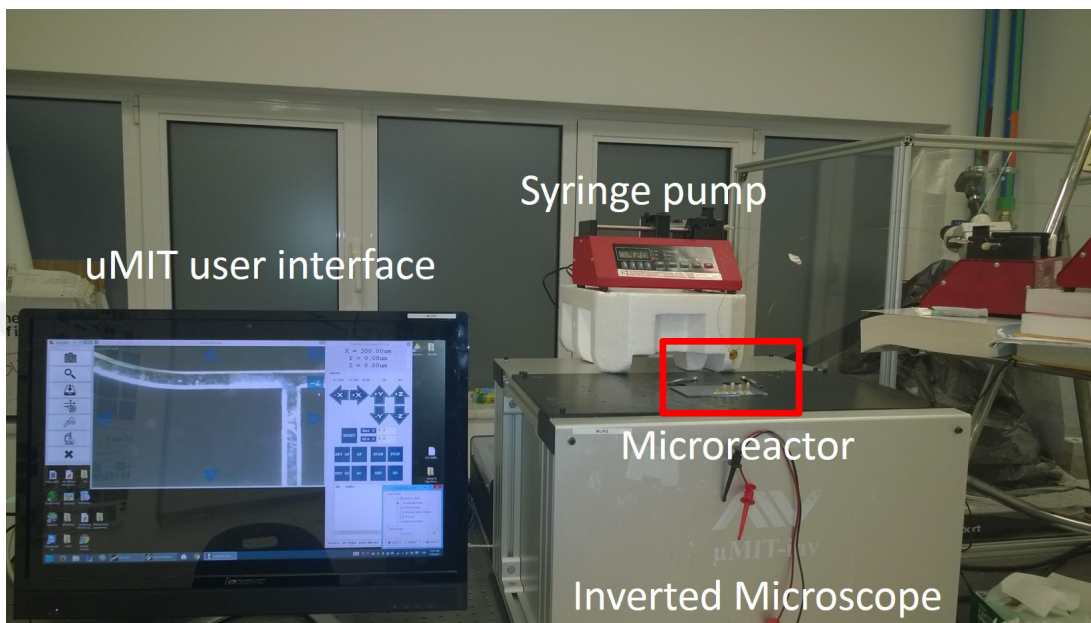


Figure 3.5: Experimental set-up for the multi-temperature zone silicon microreactor: Solutions are pumped by the syringe pumps through the capillary tubing. An inverted microscope enables the constant channel monitoring via the μ MIT user interface.

Figure 3.5 represents the experimental set-up for the second microreactor. Since in this microreactor the ports were not attached to the Pyrex side, in order to ensure the constant droplet generation, an inverted microscope was used to monitor the microchannels and the T-junction as shown in Figure 3.6. For this microreactor, the heating is possible by utilizing the Peltier heaters.

As shown in Figure 3.6, the droplet break-up occurs at the T-junction and the carrier fluid carries the droplets through the microchannels. Considering the fact that in ordinary laboratory condition all of the solutions are transparent, the droplet interface would not be completely distinguished compared to the conventional water-in-oil droplets.



Figure 3.6: Droplet generation images at the T-junction. Arrow 1 shows the flow direction of *NMF* as the carrier fluid with a flow rate of $9.5 \mu\text{L}/\text{min}$. Arrow 2 indicates the direction of reagents with a total flow rate of $4.0 \mu\text{L}/\text{min}$.

3.4 Results and Discussion

In this section, the experimental results are presented following the methods explained earlier. The experiments were aimed to generate silica nanoparticles inside the microreactor. To find a comparable result with the batch-wise synthesis, a series of reactions were performed with different characteristics. Generation of silica nanoparticles was optimized with adjustment of the control parameters (temperature, residence time, and ammonium hydroxide concentration). A successful synthesis of silica nanoparticles inside the microreactor would indicate the correct parameters for the actual encapsulation of quantum dot nanoparticles.

In order to prepare the samples for TEM inspection, the collected samples were mixed with pure ethanol with 1 : 1 ratio and centrifuged at the speed of 14500 *rpm* for 15 minutes. The deposited particles were dissolved in D.I. water. To ensure a thorough investigation of the nanoparticles, alongside the centrifuged solution, the main solution was inspected as well. The size measurements were performed using *Adobe illustrator CC* based on the TEM results. Considering the low number of particles obtained in each experiment because of the unstable reagents, and the possible agglomeration after the sample preparation, DLS inspection (Dynamic light scattering) did not provide a reliable size distribution. The size measurements reported in Appendix B are obtained using manual measurements with *Adobe illustrator CC*.

3.4.1 Silica Nanoparticle Synthesis With Ammonium Hydroxide in The Dispersed Phase

As illustrated in Figure 3.3, droplet-based synthesis of silica nanoparticles was performed based on the Stöber method. NMF was supplied as the carrier fluid and two reagents were prepared following the recipe in the materials section.

The results represented below show the progress in the droplet-based synthesis. Based on the TEM images obtained in each trial, the control parameters (ammonium concentration, residence time, and temperature) were altered to reach the desired size range.

(i) Experiment 3.2:

According to Table 3.2, reagents were supplied with a 0.5 $\mu\text{l}/\text{min}$ rate and formed the droplets which were carried by the carrier fluid with 12.0 $\mu\text{l}/\text{min}$ flow rate. Based on the results represented in Figure 3.7, the formed nanoparticles were very small compared to the targeted size range. Since the silicon microreactor in this experiment, did not provide enough channel length, long residence times were not achievable. Further experiments with reduced carrier fluid flow rates, did not improve the result; hence, all the

Table 3.2: Silica Nanoparticle Droplet-base Synthesis: Experiment 3.2

Experiment 3.2	Carrier Fluid	Reagent 1	Reagent 2
Contents	NMF	TEOS + Cyclohexane	NH_4OH + Cyclohexane
Flow rate	12.0 $\mu l/min$	0.5 $\mu l/min$	0.5 $\mu l/min$
Ammonium Hydroxide	—	—	0.38 M (150 μl in 10 ml)
Channel Length	140 mm		
Residence Time	28 seconds		
Nanoparticles Average Size	1.98 ± 0.5 nm		
Number of Measured Particles	30 (Table B.2)		

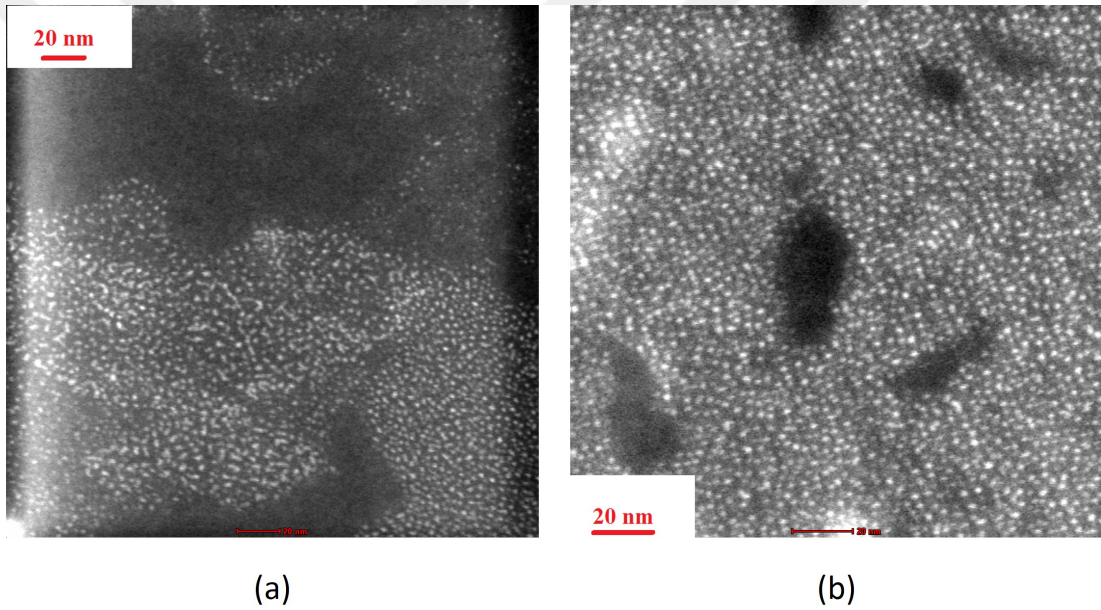


Figure 3.7: TEM results of silica nanoparticle synthesis: Experiment 3.2 (Table 3.2) with an average size of 1.98 ± 0.5 nm.

experiments after this point were completed with the multi-temperature silicon microreactor.

(ii) Experiment 3.3:

In this experiment, reagents were supplied with an equal flow rate of 1.2 $\mu l/min$. The TEM results of Experiment 3.3 (Table 3.3) in Figure 3.8 indicate little signs of improvement in the nanoparticle size range. At this stage, the concentrations were kept constant and only the effect of residence time was studied. Further increase in residence time is possible via decreasing the carrier fluid flow rate.

Table 3.3: Silica Nanoparticle Droplet-base Synthesis: Experiment 3.3

Experiment 3.3	Carrier Fluid	Reagent 1	Reagent 2
Contents	NMF	TEOS + Cyclohexane	NH_4OH + Cyclohexane
Flow rate	$19.5 \mu l/min$	$1.2 \mu l/min$	$1.2 \mu l/min$
Ammonium Hydroxide	—	—	0.38 M (150 μl in 10 ml)
Channel Length	2 m		
Residence Time	250 seconds		
Nanoparticles Average Size	3.35 ± 0.45 nm		
Number of Measured Particles	40 (Table B.3)		

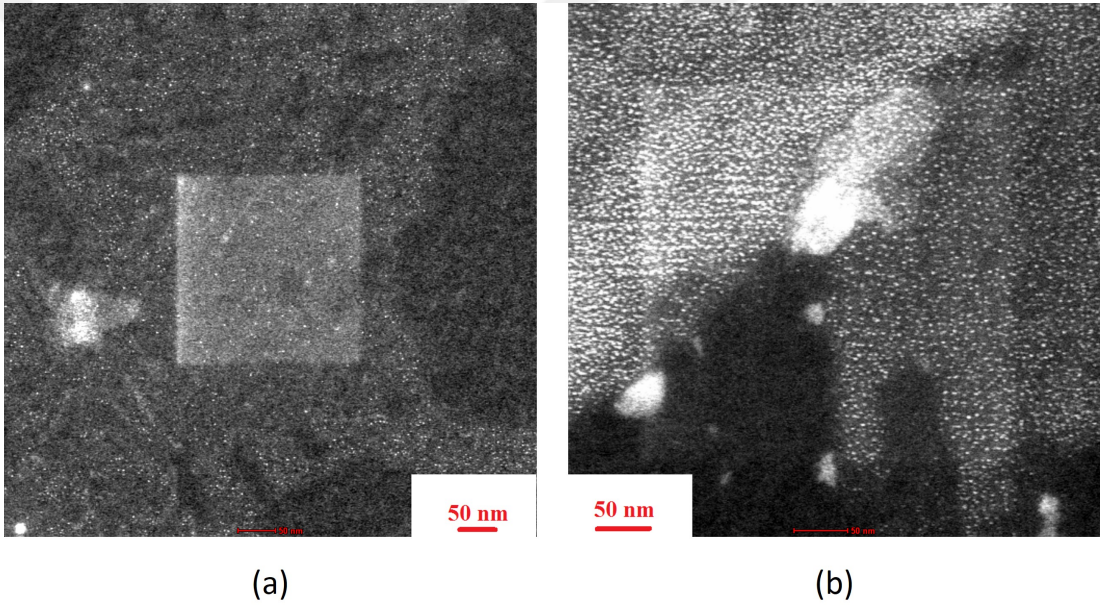


Figure 3.8: TEM results of silica nanoparticle synthesis: Experiment 3.3 (Table 3.3) with less than 4 nm average size.

(iii) Experiment 3.4:

At this stage, the carrier fluid flow rate was decreased to $9.5 \mu l/min$ and the 1:1 ratio between the reagents was kept to examine the direct effect of residence time. The total reagent flow rates supplied to the T-junction was $2.4 \mu l/min$ with 1:1 ratio. Figure 3.9 shows no increase in nanoparticle sizes as the residence time is double (510 seconds compared to 250 seconds).

Table 3.4: Silica Nanoparticle Droplet-base Synthesis: Experiment 1.3

Experiment 3.4:	Carrier Fluid	Reagent 1	Reagent 2
Contents	NMF	TEOS + Cyclohexane	NH_4OH + Cyclohexane
Flow rate	$9.5 \mu l/min$	$1.2 \mu l/min$	$1.2 \mu l/min$
Ammonium Hydroxide	—	—	0.38 M (150 μl) in 10 ml
Channel Length	2 m		
Residence Time	510 seconds		
Nanoparticles Average Size	3.30 ± 0.8 nm		
Number of Measured Particles	30 (Table B.4)		

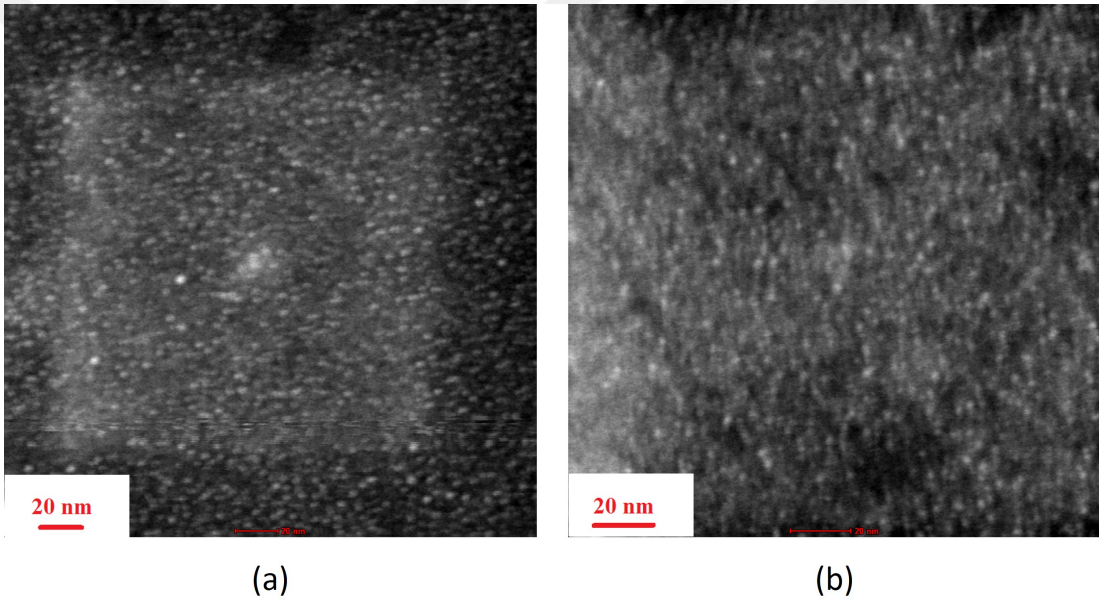


Figure 3.9: TEM results of silica nanoparticle synthesis: Experiment 3.4 (Table 3.4) with less than 4 nm average size.

(iv) Experiment 3.5:

To check the effect of reagent flow ratios, in this experiment, the flow rate of reagent 2, containing ammonium hydroxide was increased while keeping a constant total reagent flow rate. A slight increase in the carrier fluid flow rate was observed as the viscosity of the dispersed phase changed.

The results shown in Figure 3.9 did not indicate a significant progress in the silica nanoparticle growth. Since the ammonium hydroxide concentration was the only unchanged parameter throughout experiment 3.2 and experiment 3.5, to enhance the silica nanoparticle growth the concentration of the ammonium was double starting from experiment 3.6.

Table 3.5: Silica Nanoparticle Droplet-base Synthesis: Experiment 3.5

Experiment 3.5	Carrier Fluid	Reagent 1	Reagent 2
Contents	NMF	TEOS + Cyclohexane	NH_4OH + Cyclohexane
Flow rate	$9.6 \mu l/min$	$0.8 \mu l/min$	$1.6 \mu l/min$
Ammonium Hydroxide	—	—	0.38 M (150 μl in 10 ml)
Channel Length	2 m		
Residence Time	510 seconds		
Nanoparticles Average Size	3.23 ± 0.26 nm		
Number of Measured Particles	30 (Table B.5)		

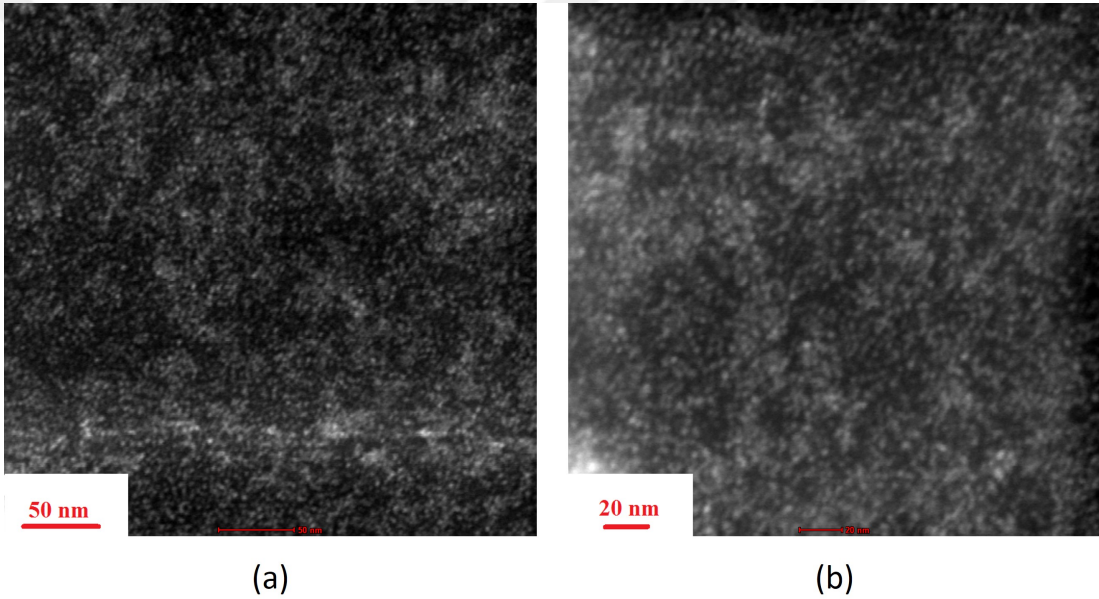


Figure 3.10: TEM results of silica nanoparticle synthesis: Experiment 3.5 (Table 3.5) with less than 4 nm average size.

(v) Experiment 3.6:

At this stage, the ammonium concentration in the reagent 2, was doubled. The reagents were supplied with equal flow rates and the residence time was around 525 seconds. As the results in Figure 3.11 show, the particle size has enhanced significantly and reached 32.7 ± 6.9 nm. Because of the high size deviation, the main solution (centrifuge residual) was inspected as well (Figure 3.12). The size distribution obtained for this solution was 3.7 ± 1.2 nm. This proves that during the sample preparation, a portion of the nanoparticles was washed in the centrifuge process.

Table 3.6: Silica Nanoparticle Droplet-base Synthesis: Experiment 3.6

Experiment 3.6	Carrier Fluid	Reagent 1	Reagent 2
Contents	NMF	TEOS + Cyclohexane	NH_4OH + Cyclohexane
Flow rate	$9.2 \mu l/min$	$1.9 \mu l/min$	$1.9 \mu l/min$
Ammonium Hydroxide	—	—	0.76 M (300 μl in 10 ml)
Channel Length	2 m		
Residence Time	525 seconds		
Nanoparticle Average Size	First Test 32.66 ± 6.9 nm	Centrifuge Residual 3.93 ± 0.75 nm	Second Test 25.0 ± 2.7 nm
Number of Measured Particles	7	20	140
Table of Measurements	Table B.6	Table B.7	Table B.8

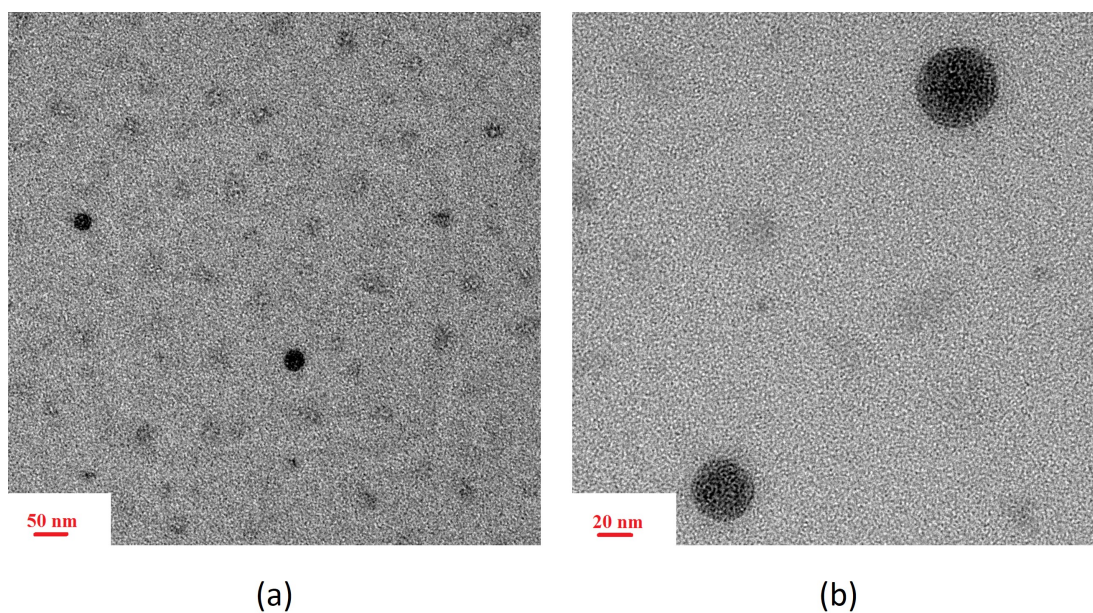


Figure 3.11: TEM results of silica nanoparticle synthesis: Experiment 3.6 (Table 3.6) with an average size of 32.7 ± 6.9 nm.

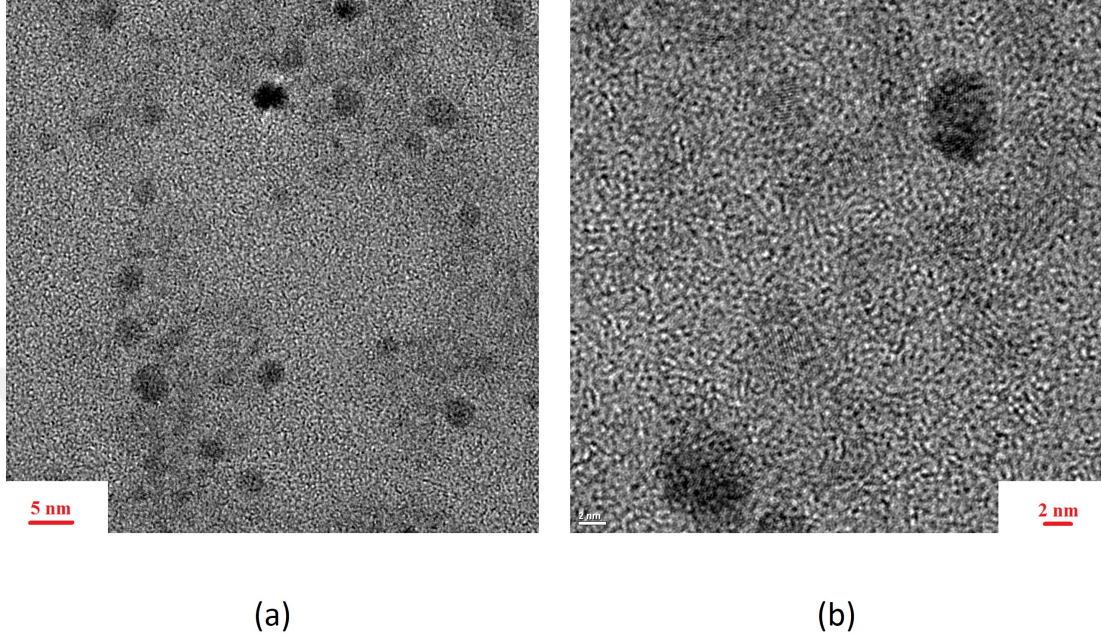


Figure 3.12: TEM results of silica nanoparticle synthesis: Experiment 3.6 (Table 3.6) from the centrifuge residual with an average size of 3.9 ± 0.75 nm.

(vi) Experiment 3.7:

As the results of Experiment 3.6 seemed promising in terms of size and shape, the experiment was repeated with similar conditions following the conditions mentioned in Table 3.6. Figure 3.13 shows the results from the repeated experiment 3.6. TEM images indicate the silica nanoparticle growth with a size distribution of 25.0 ± 2.7 nm. As shown in Figure 3.14, the EDX quantification results of this sample represent a low percentage of silica (silicon and oxygen) in the sample due to the flow rate ratios assigned in the experiment.

Since the final results of Experiment 3.7, indicate a comparable size range with the batch-wise synthesis, this configuration, and experimental conditions were assigned as the optimum for silica nanoparticle growth. In theory, the silica encapsulation of quantum dots should follow the similar steps, so the parameters of Experiment 3.7 were chosen to investigate the silica coating of quantum dots.

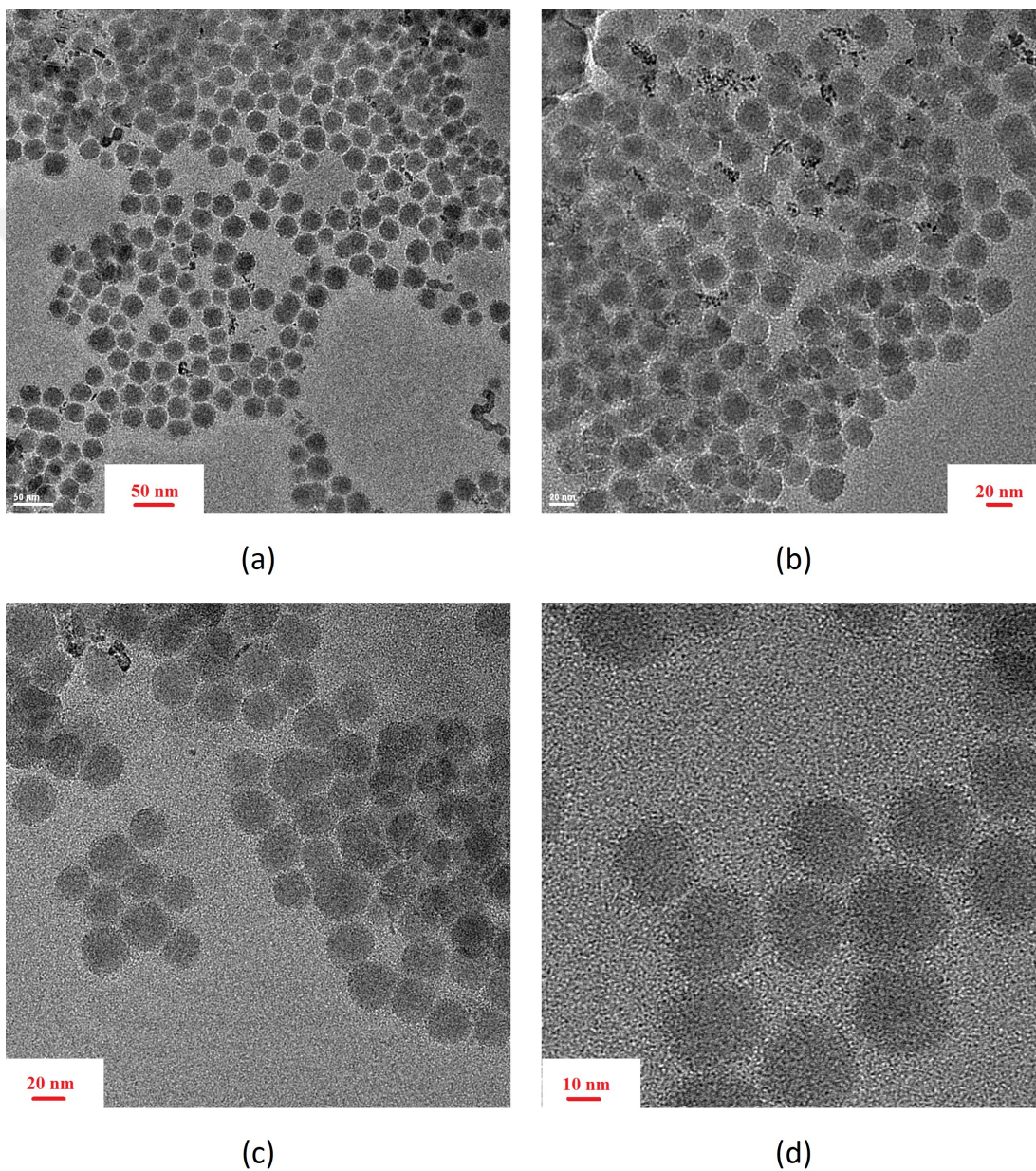


Figure 3.13: TEM results of silica nanoparticle synthesis: Experiment 3.7 (Table 3.6) with a size range of 25.0 ± 2.7 nm.

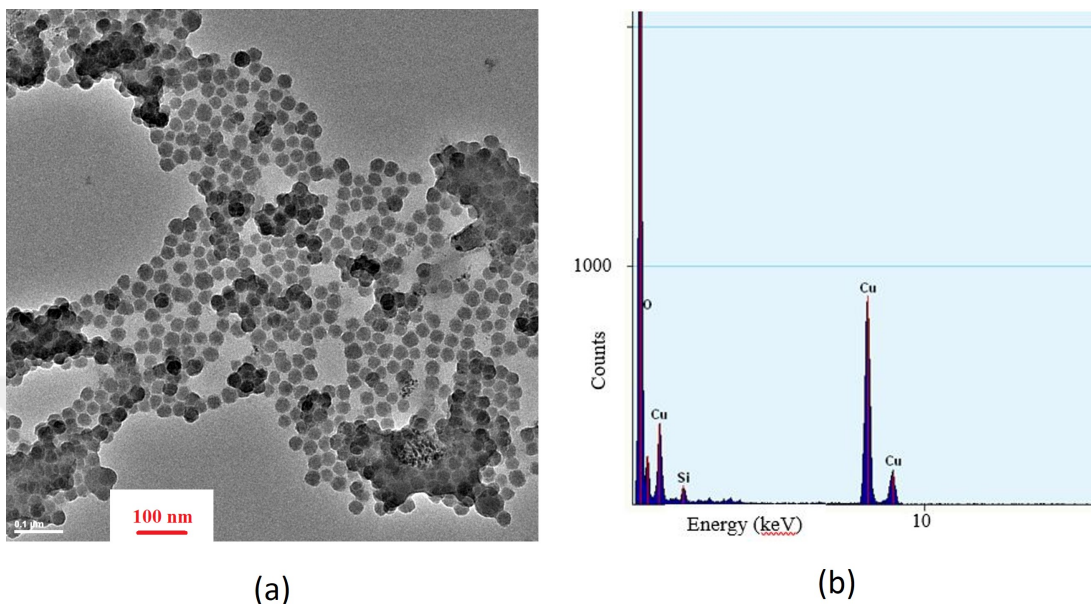


Figure 3.14: TEM results of silica nanoparticle synthesis: Experiment 3.7 (Table 3.6) and the assigned EDX quantification results. The low percentage of silicon and oxygen are mainly due to the assigned flow rate ratios in the experiment.

Although both experiments 3.6 and 3.7 were conducted with the same configuration and same flow rates, a slight difference between the results is observed. This difference could be explained by the fact that reagent 1 (containing silica precursors in TEOS) is unstable as the particles tend to agglomerate after two hours past preparation. The time difference between the reagent preparation and performing the experiments has proven to be decisive as observed in experiments 3.6 and 3.7; however, since repeating the experiment 3.6 lead to acceptable results, the same conditions could be investigated for the silica encapsulation process.

3.5 Conclusion

The high amount of Cu and C observed in the EDX results in Figure 3.14 is due to the materials used in the TEM grid. The low amount of Si could be explained because of the low flow rates applied for the reagents throughout the experiments. Particle sizes could be measured from the TEM images using *Adobe Illustrator CC*.

Table 3.7 represents the comprehensive experimental results for silica nanoparticle formation inside the droplet-based microreactor. Although a linear relation could not be observed based on the residence time and reactant concentration, the final conditions could be potentially used for silica encapsulation of quantum dots.

Table 3.7: Comprehensive experimental results for silica nanoparticle synthesis

	Ammonium Hydroxide Concentration	Carrier Fluid Flow Rate	Residence Time	Number of Measurements	Average Size
Experiment 3.1 Batch-wise Synthesis	0.38 M (150 μ l)	-	48 hours	45 Table B.1	18.25 $\pm$ 2.2 nm
Experiment 3.2	0.38 M (150 μ l in 10 ml Cyclohexane)	12 μ l/min	28 seconds	30 Table B.2	1.98 $\pm$ 0.5 nm
Experiment 3.3	0.38 M (150 μ l in 10 ml)	19.5 μ l/min	250 seconds	40 Table B.3	3.35 $\pm$ 0.45 nm
Experiment 3.4	0.38 M (150 μ l in 10 ml)	9.5 μ l/min	510 seconds	30 Table B.4	3.30 $\pm$ 0.8 nm
Experiment 3.5	0.38 M (150 μ l in 10 ml)	9.6 μ l/min	510 seconds	30 Table B.5	3.23 $\pm$ 0.26 nm
Experiment 3.6 Main solution	0.76 M (300 μ l in 10 ml)	9.2 μ l/min	525 seconds	7 Table B.6	32.66 $\pm$ 6.9 nm
Experiment 3.6 Centrifuge Residual	0.76 M (300 μ l in 10 ml)	9.2 μ l/min	525 seconds	20 Table B.7	3.93 $\pm$ 0.75 nm
Experiment 3.7	0.76 M (300 μ l in 10 ml)	9.2 μ l/min	525 seconds	140 Table B.8	25.0 $\pm$ 2.7 nm

Chapter 4

Silica Coating of CdSe/CdS Quantum Dots

Silica coating of nanoparticles enhances the colloidal stability of nanoparticles. In the case of quantum dot semiconductors, based on the desired shell size, different methods can be used to stabilize their size-dependent optical properties [76]. Stöber and coworkers [39] has achieved a well-controlled growth of micron-sized silica spheres via silicic acid hydrolysis. The presence of the surfactant at the interface can stabilize the dispersion of two immiscible fluids [97, 98]. In the reported Stöber method, IGEPAL is the nonionic surfactant and ammonium hydroxide (NH_4OH) plays the catalyst role and triggers the silica encapsulation process.

The size and shape of coated nanoparticles could potentially define the characteristics of the quantum dots. Batch-wise methods tend to face the problem of heterogeneous coating and reproducibility because of the non-uniform distribution of reactant concentration and thermal gradient in the bulk mixture. Considering the importance of monodispersed coating, this thesis represents one of the first attempts to use a droplet-based microreactor to silica coat *CdSe/CdS* quantum dots via Stöber method.

4.1 Batch-wise Synthesis

Initially, the batch-wise synthesis for silica encapsulation of quantum dot nanoparticles was investigated to obtain the desired results. The batch synthesis consists of two steps following the methods of Popovic et al.[99] and Selvan et al.[76] and was carried out by our collaborator Dr. Yusuf Keleştemur:

4.1.1 Synthesis of New Generation CdSe/CdS Core/Shell Colloidal Quantum Dots

This process starts with the synthesis of *CdSe* cores. Cadmium myristate and selenium dioxide are dissolved in octadecene and evacuated at room temperature for 15 minutes. The nucleation of *CdSe* cores starts when the solution is heated to 240°C for 10 minutes. At this stage, the size of the *CdSe* cores is controlled with residence time. After the heating step, as-synthesized *CdSe* cores are dissolved in hexane after precipitation with acetone.

After the formation of *CdSe* cores in a four-neck flask, they are mixed with 3ml of octadecane and 3ml of oley amine. At 240°C, cadmium precursor and sulfur precursor are delivered with a rate of 3 ml/min. The solutions are heated up to 300°C and the *CdS* shells are formed after two hours under the argon atmosphere. Finally, *CdSe/CdS* core/shell colloidal quantum dots are dissolved in hexane after precipitation with acetone [99].

4.1.2 Silica Encapsulation of New Generation CdSe/CdS Core/Shell Colloidal Quantum Dots

Popovic et al. has reported the recipe for silica coating of *CdSe/CdS* core/shell CQDs [99]. Initially, 2 nmol of *CdSe/CdS* core/shells is dissolved in 1 ml of anhydrous cyclohexane. In a flask, 1.3 ml IGEPAL CO-520 and 10 ml of anhydrous

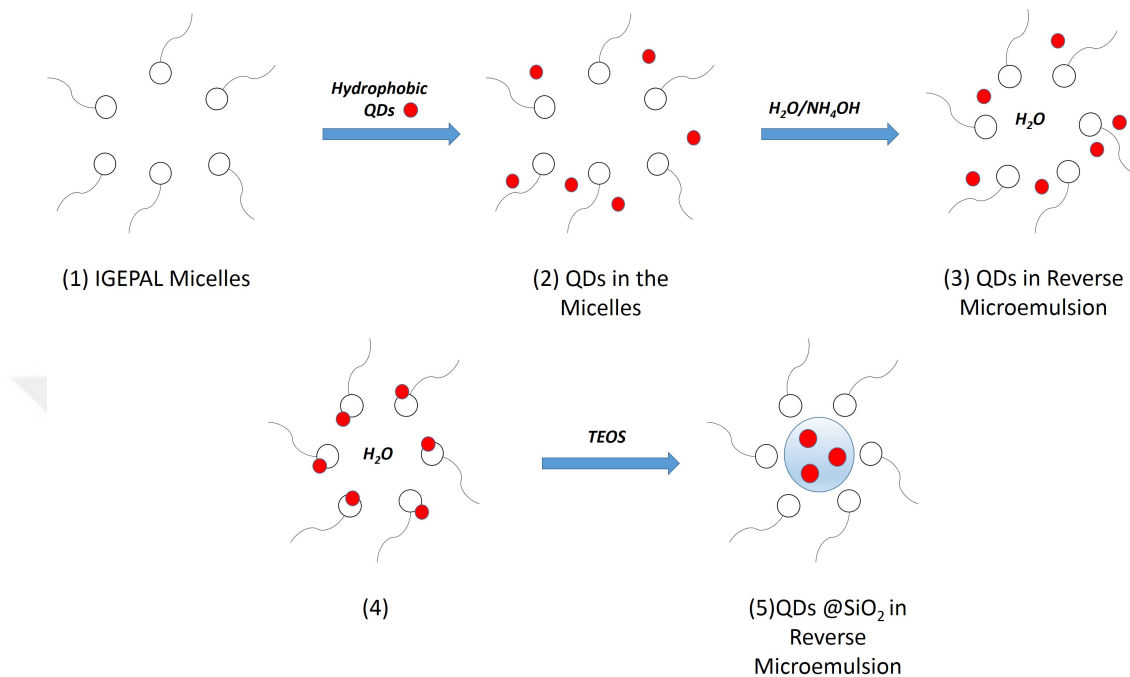


Figure 4.1: Schematic representation of silica encapsulation of hydrophobic quantum dots via reverse micelle [76]

cyclohexane are mixed and stirred for 15 minutes. Later on, the solution with *CdSe/CdS* core/shells is added to the mixture and it is stirred for 15 minutes. After that, 80 μl of tetraethyl orthosilicate (*TEOS*) is added, and the mixture in the flask is stirred for 30 minutes. Finally, 150 μl ammonium hydroxide (28% in water) is added and the stirring continues for 48 hours. At last, the silica coated colloidal quantum dots are dissolved in the mixture of water and 20 μl of 2 *M NaOH* and preserved at 4 °C.

The schematic of the reverse micelle procedure is shown in Figure 4.1.

Since the size range and size distribution of each batch would be different, the assigned batch results will be represented at each step to compare the results from the droplet-based synthesis.

4.2 Droplet-Based Method

Two different configurations were investigated for silica coating of quantum dot nanoparticles. The first one follows the results obtained from the silica nanoparticle synthesis in Chapter 3. The second proposed method was solely investigated to fully observe the ammonium hydroxide concentration effect.

4.2.1 Ammonium Hydroxide Within The Dispersed Phase

In this method, pure *NMF* is supplied as the carrier fluid and induces the droplet break-up, while all the reagents are mixed inside the droplet as shown in Figure 4.2. Two different solutions were prepared and supplied through individual entries. The first solution was prepared based on the reactant concentrations in batch synthesis as 1.3 ml of *IGEPAL CO-520* was mixed with 10 ml of anhydrous cyclohexane and stirred for 15 minutes. After that, 1 ml of *CdSe/CdS* core/shell *CQDs* (2 nmol) dissolved in anhydrous cyclohexane was added and stirred for 15 min. Finally, 80 μ l of tetraethyl orthosilicate (TEOS) was added and stirred for 15 min. To prepare the second solution, 300 μ l of ammonium hydroxide (28% in water) was added to 10 ml of anhydrous cyclohexane and stirred for 15 minutes. The concentration of the second reagent was based on the results obtained from the silica nanoparticle synthesis in Chapter 3. These solutions are shown under the UV-light illumination in Figure 4.3.

The desired size range for the silica nanoparticles, obtained with the droplet-based synthesis, could be used for silica encapsulation of quantum dot nanoparticles. Initially, the characteristics of the *CdSe/CdS* cores were inspected. The TEM results shown in Figure 4.4 indicate the average size of 8.43 ± 1.7 nm for quantum dot nanoparticles.

Since only one batch synthesis was performed to prepare the quantum dot nanoparticles, the size range in Figure 4.4 could be used for further investigations

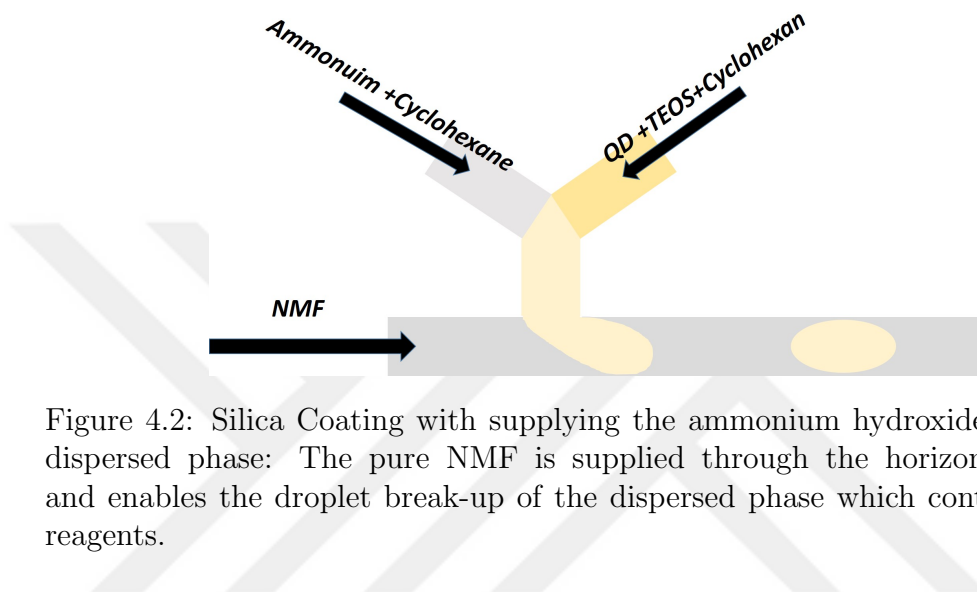


Figure 4.2: Silica Coating with supplying the ammonium hydroxide within the dispersed phase: The pure NMF is supplied through the horizontal channel and enables the droplet break-up of the dispersed phase which contains all the reagents.

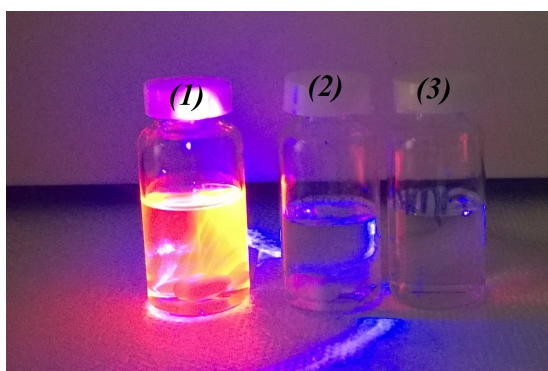


Figure 4.3: Chemical solutions under the UV-light illumination: Bottle number (1) is the mixture of reagents containing the CdSe/CdS quantum dot nanoparticle, bottle number (2) shows the mixture of ammonium hydroxide and cyclohexane and bottle number (3) is the pure NMF.

during all the silica encapsulation experiments.

The silica nanoparticle synthesis reaction could be potentially used for the quantum dot encapsulation. Based on the results obtained in experiment 3.7 (Figure 3.13) the following experiments were performed in order to coat the quantum dot nanoparticles.



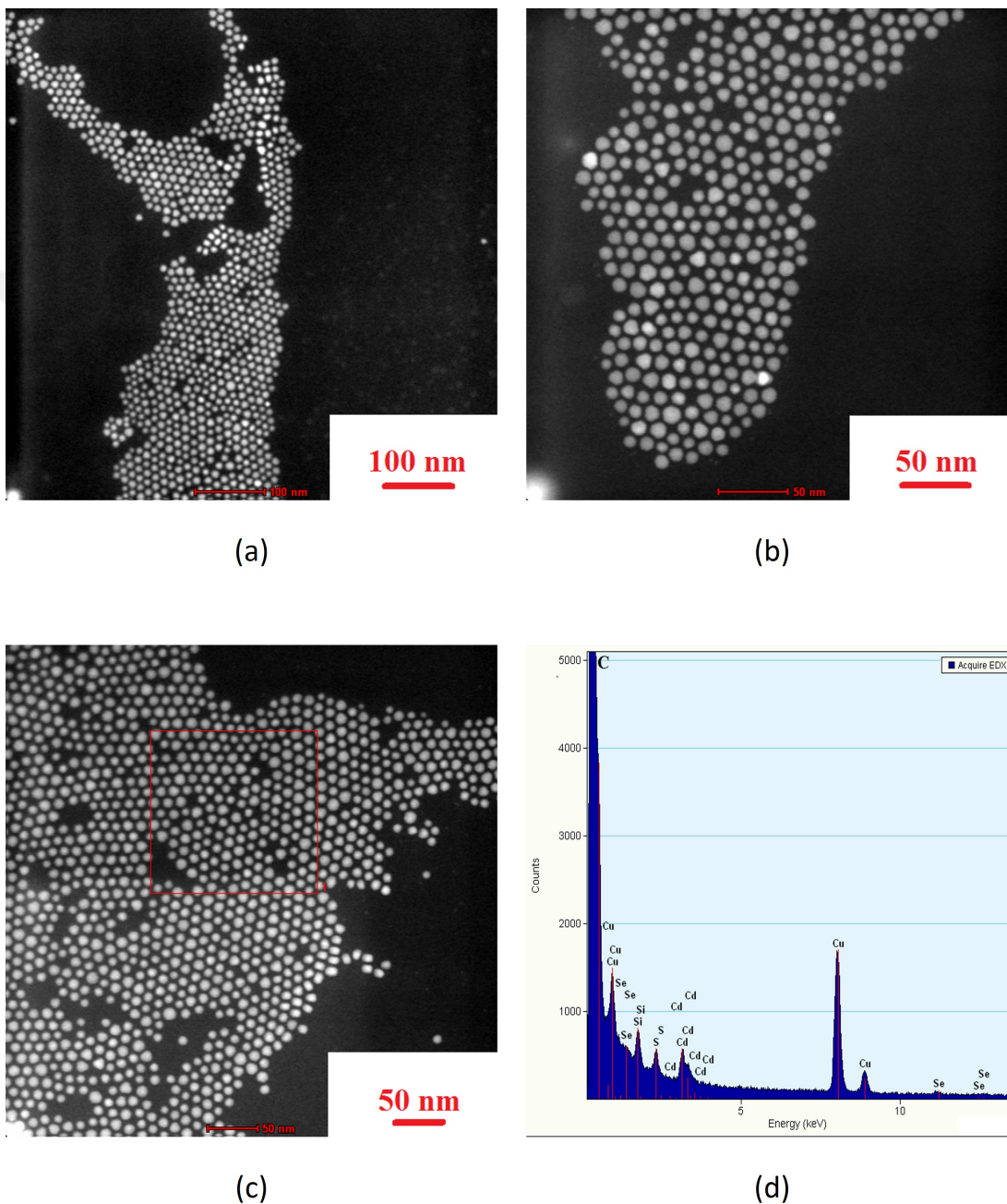


Figure 4.4: TEM images of CdSe/CdS quantum dot nanoparticles. The particles in (a),(b), and (c) indicate an average size of nanoparticles is 8.43 ± 1.7 nm (Table B.9 with 75 particles measured). Part (d) shows the EDX result of the specified area in (c).

(i) Experiment 4.1

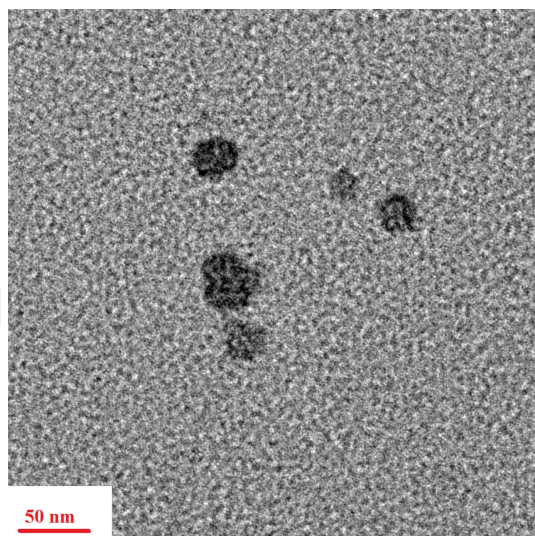
For this experiment, the solutions were prepared based on the default concentrations mentioned in the batch synthesis following the Stöber method. The only difference was the increased concentration of ammonium hydroxide, which was obtained in Experiment 3.7 (Table 3.6).

Table 4.1: Silica Coating of Quantum Dots: Experiment 4.1

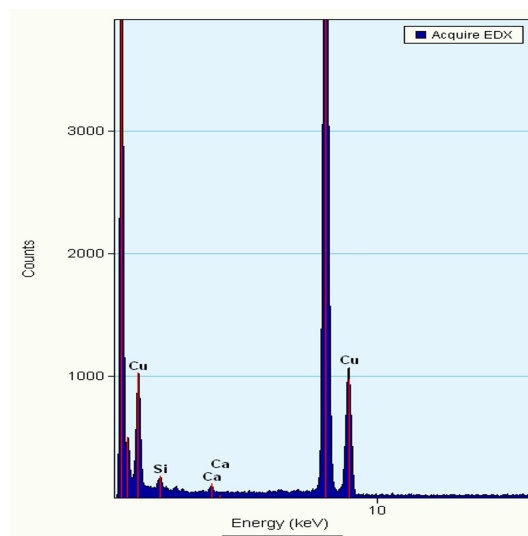
Experiment 4.1	Carrier Fluid	Reagent 1	Reagent 2
Contents	NMF	QD+ TEOS + Cyclohexane	NH_4OH + Cyclohexane
Flow rate	$9.5 \mu l/min$	$2.0 \mu l/min$	$2.0 \mu l/min$
Ammonium Hydroxide	—	—	0.76 M (300 μl in 10 ml)
Channel Length	2 m		
Residence Time	510 seconds		
Nanoparticles Average Size	28.8 ± 3.0 nm		
Number of Measured Particles	13 (Table B.10)		

Figure 4.5 shows the synthesized nanoparticles; however, based on the EDX results assigned, there is no trace of $CdSe/CdS$ in the images. This indicates that although the synthesis method has worked well to generate full grown silica nanoparticles, quantum dots were not captured inside the silica precursors.

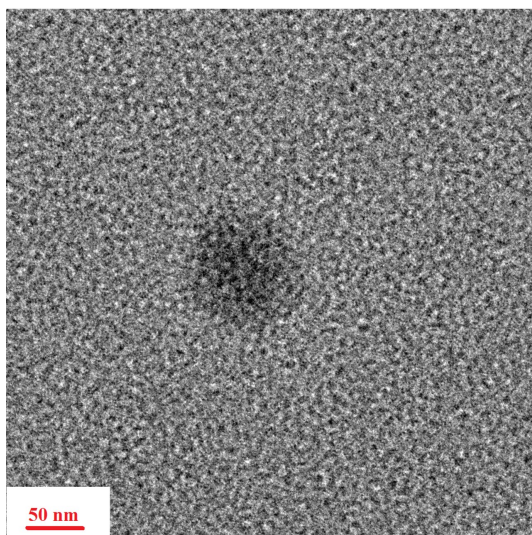
Figure 4.6 shows the TEM result of a wider area. As we zoom out, bigger clusters of silica are found. Moreover, based on the EDX result presented in Figure 4.6.(b), the elements Cd , Se , and S are found in the picture. Table 4.2 presents the EDX quantification results of Figure 4.6. The small amounts of Cd , Se , and S are not clearly and individually surrounded by the silica precursors.



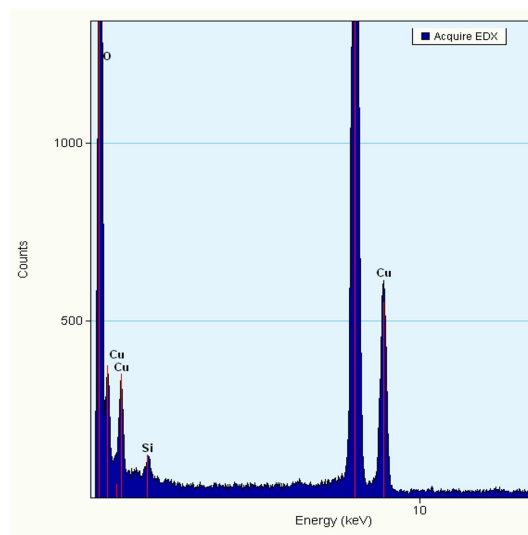
(a)



(b)



(c)



(d)

Figure 4.5: TEM results of silica encapsulation of quantum dots: Experiment 4.1. Figure (a) and (c) indicate an average size of 28.8 ± 3.8 nm. Based on the EDX results in (b) and (d), the nanoparticles observed, do not contain the quantum dots.

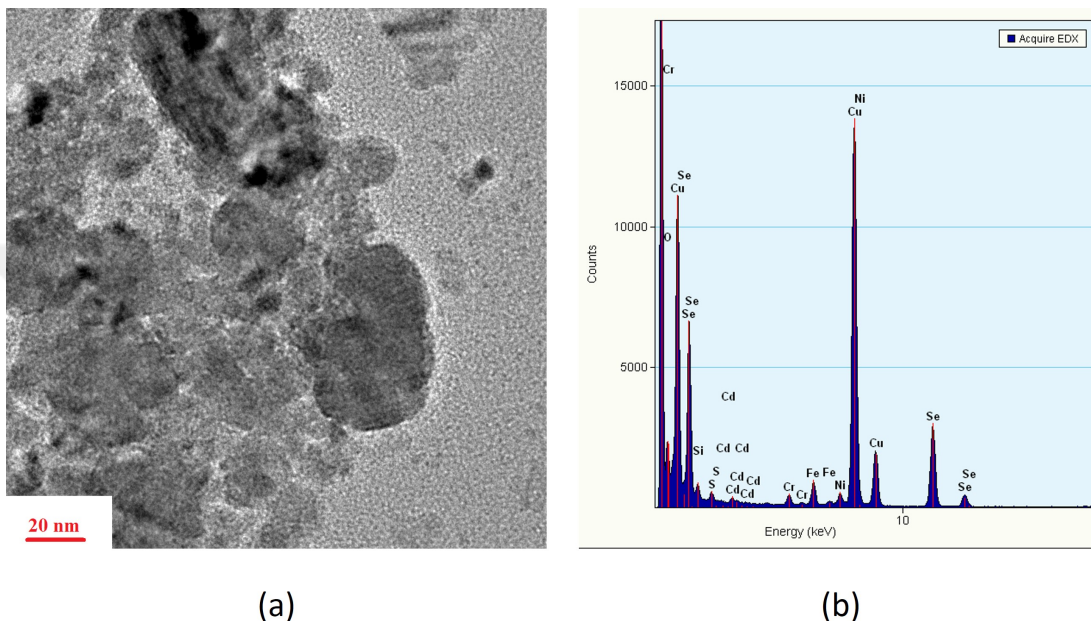


Figure 4.6: TEM results of silica encapsulation of quantum dots: Experiment 4.1. Based on the EDX result in (b), the nanoparticles observed are surrounded inside the big silica clusters.

Table 4.2: EDX quantification results for Experiment 4.1

Element	Weight %	Atomic %	Uncertainty %	Detector Correction	K-Factor
O	19.29	51.0	0.20	0.49	2.008
Si	3.22	4.93	0.05	0.92	1.000
S	2.20	2.99	0.04	0.93	1.015
Se	71.27	38.77	0.35	1.00	2.312
Cd	3.99	1.52	0.12	0.97	6.498

(ii) Experiment 4.2

Keeping the conditions of experiment 4.1, the process was once again examined to check the previous results. Both reagents were supplied with the flow rate of $1.8 \mu\text{l}/\text{min}$ and the droplets were carried by the continuous flow of NMF with a flow rate of $10.0 \mu\text{l}/\text{min}$. These flow rates resulted in 8 minutes of residence time inside the microchannels.

Table 4.3: Silica Coating of Quantum Dots: Experiment 4.2

Experiment 4.2	Carrier Fluid	Reagent 1	Reagent 2
Contents	NMF	QD+ TEOS + Cyclohexane	NH_4OH + Cyclohexane
Flow rate	$10.0 \mu\text{l}/\text{min}$	$1.8 \mu\text{l}/\text{min}$	$1.8 \mu\text{l}/\text{min}$
Ammonium Hydroxide	—	—	0.76 M (300 μl in 10 ml)
Channel Length	2 m		
Residence Time	490 seconds		
Nanoparticles Average Size	$8.6 \pm 0.8 \text{ nm}$		
Number of Measured Particles	45 (Table B.11)		

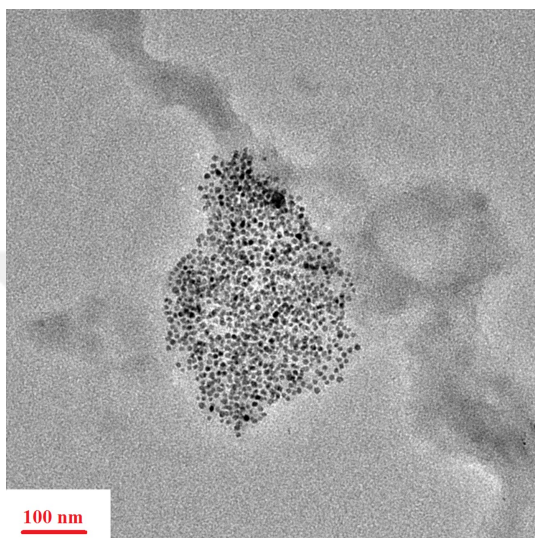
As illustrated in Figure 4.7, quantum dot nanoparticles in (a) and (d) are surrounded by the silica clusters. The size distribution of $8.6 \pm 0.8 \text{ nm}$, indicates no apparent sign of individual coating among the quantum dots.

(iii) Experiment 4.3

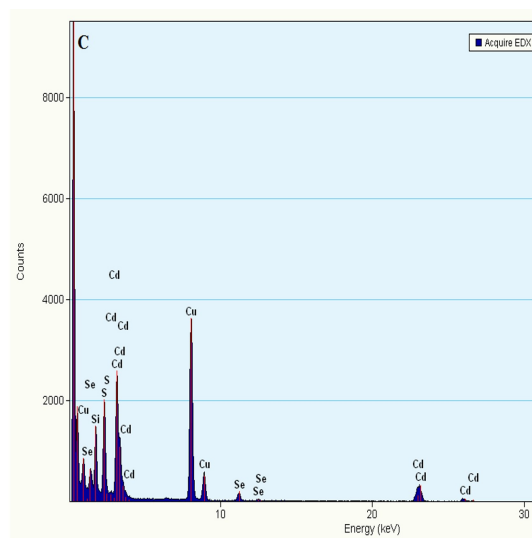
In order to examine the residence time effect, the carrier fluid flow rate was decreased to half, which eventually decreased the reagents flow rates as well. The new configuration enables an average of 14 minutes residence time in the microchannels. TEM results are presented in Figure 4.8. The particles have an average size of $11.3 \pm 2.4 \text{ nm}$.

Table 4.4: Silica Coating of Quantum Dots: Experiment 4.3

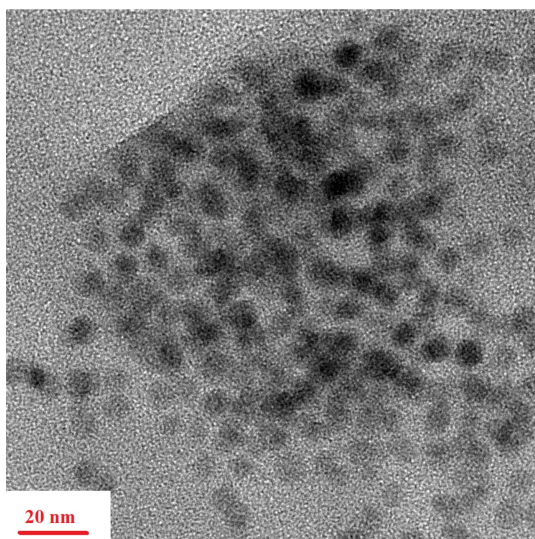
Experiment 4.3	Carrier Fluid	Reagent 1	Reagent 2
Contents	NMF	QD+ TEOS + Cyclohexane	NH_4OH + Cyclohexane
Flow rate	$5.0 \mu\text{l}/\text{min}$	$1.0 \mu\text{l}/\text{min}$	$1.0 \mu\text{l}/\text{min}$
Ammonium Hydroxide	—	—	0.76 M (300 μl in 10 ml)
Channel Length	2 m		
Residence Time	980 seconds		
Nanoparticles Average Size	$11.3 \pm 2.4 \text{ nm}$	—	—
Number of Measured Particles	100 (Table B.12)		



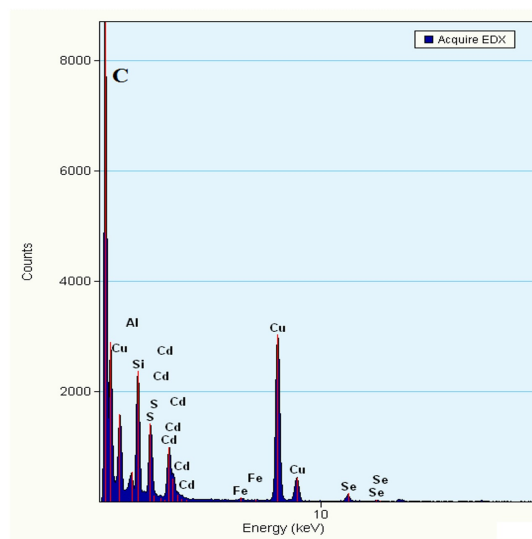
(a)



(b)



(c)



(d)

Figure 4.7: TEM results of silica encapsulation of quantum dots: Experiment 4.2. Based on the Figure (a) and (c) the particles have an average size of 8.6 ± 0.8 nm. Figures (b) and (d) represent the EDX result of the (a) and (c) respectively.

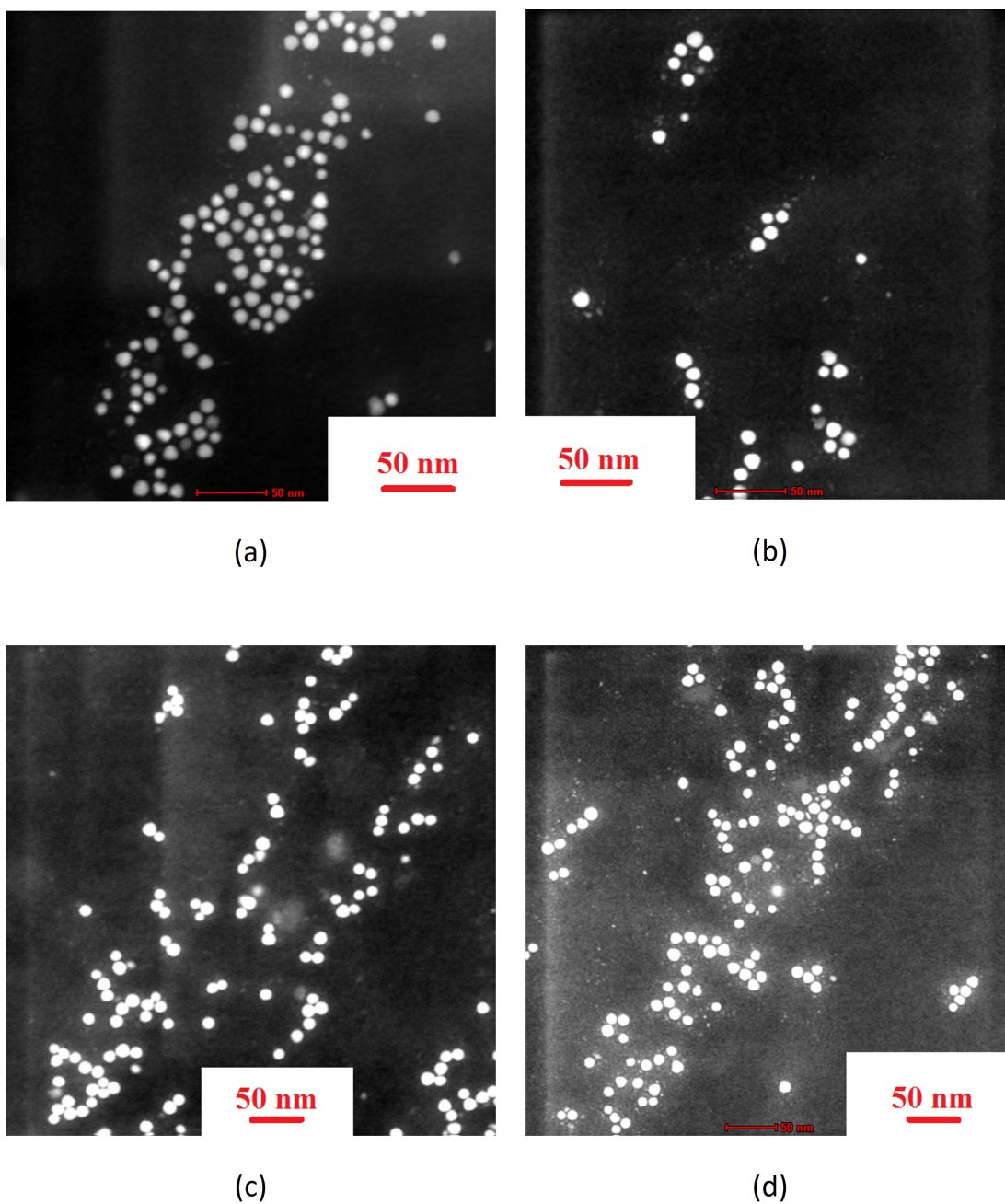


Figure 4.8: TEM results of silica encapsulation of quantum dots: Experiment 4.3. The particles have an average size of 11.3 ± 2.4 nm.

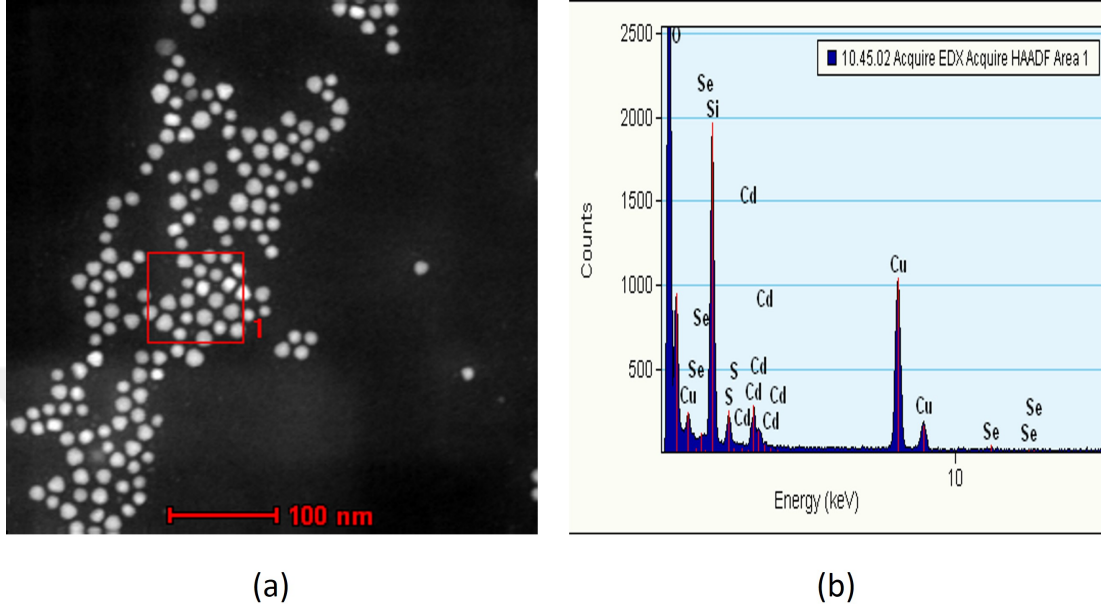


Figure 4.9: TEM results of silica encapsulation of quantum dots: Experiment 4.3. The particles have an average size of 11.3 ± 2.4 nm.

Table 4.5: EDX quantification results for Experiment 4.3

Element	Weight %	Atomic %	Uncertainty%	Detector Correction	K-Factor
O	25.23	45.67	0.37	0.49	2.008
Si	26.70	29.34	0.25	0.92	1.000
S	1.89	1.82	0.05	0.93	1.015
Cu	35.20	17.09	0.34	0.99	1.601
Se	0.38	0.15	0.05	1.00	2.312
Cd	10.56	2.90	0.29	0.97	6.498

Figure 4.9 represents the TEM result for experiment 4.3 and the EDX result for the specified area. Figure 4.8.(a) and Table 4.4 prove the presence of quantum dot nanoparticles alongside the silica precursors.

To summarize the results obtained from the silica coating of quantum dots, based on the slight increase in the nanoparticles sizes, especially for experiment 4.3, a slim shell around the nanoparticles is thought to have formed around the particles. EDX result also verifies the existence of Silica in the sample. However, the wide size distribution for experiment 4.3 (11.3 ± 2.4) clearly shows the poor

encapsulation rate as a large number of particles have remained unchanged in the process. To overcome this problem, further experiments are required in which the reagents are supplied with lower flow rates in order to acquire a narrower nanoparticle size distribution.

4.2.2 Ammonium Hydroxide Within the Continuous Phase:

The schematic configuration of this method is illustrated in Figure 4.10. The mixture of reagents containing the silica precursors and quantum dot nanoparticles are supplied through the vertical channel. Ammonium hydroxide and NMF are supplied via the horizontal channel and induce the droplet break-up at the T-junction. To prepare the proper solutions for this method, 1.3 ml of *IGEPAL CO-520* was mixed with 10 ml of anhydrous cyclohexane and stirred for 15 minutes. After that, 1 ml of *CdSe/CdS* core/shell *CQDs* (2 nmol) dissolved in anhydrous cyclohexane was added and stirred for 15 min. Finally, 80 μ l of tetraethylorthosilicate (TEOS) was added and stirred for 15 min. For the second solution (continuous phase), 150 μ l of ammonium hydroxide (28% in water) was added to 10 ml of N-methyl formamide (NMF) and stirred for 15 min. These solutions are shown in Figure 4.11 under the UV-light illumination.

Based on the TEM results in Figure 4.12 and the EDX quantification results presented in Figure 4.12 and Table 4.7, due to the high concentration of silica, it was hard to clarify the silica shells around the particles (quantum dot nanoparticles were from a different batch; hence, the size distribution does not match with the results shown in Figure 4.4). Since in this method, the carrier fluid flow rate was higher than the dispersed phase's flow rate, the amount of ammonium hydroxide supplied to the channels was higher compared to the amount of quantum dots. Decreasing the ammonium concentration lead to a decrease in the carrier fluid viscosity; however, further investigations following this method did not provide any progress in the silica coating of quantum dots.

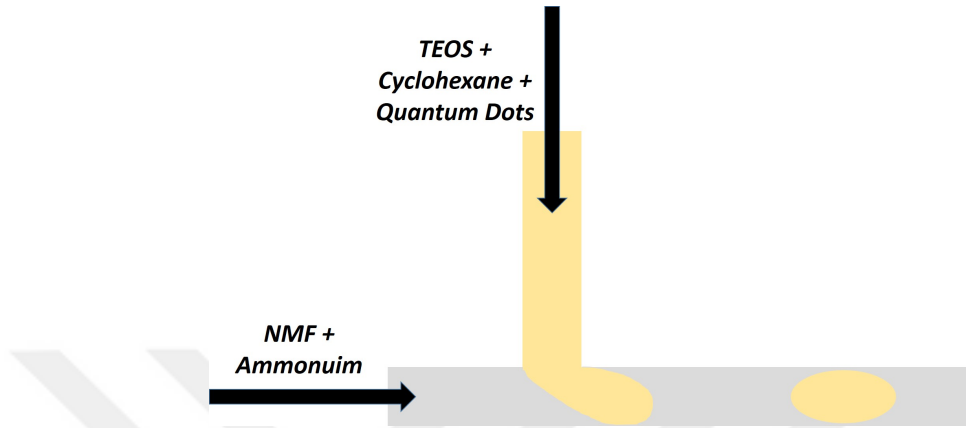


Figure 4.10: Synthesis with supplying the ammonium hydroxide within the continuous phase: The mixture of the NMF and ammonium hydroxide is supplied through the horizontal channel and enables the droplet break-up of the dispersed phase which contains the reagents.

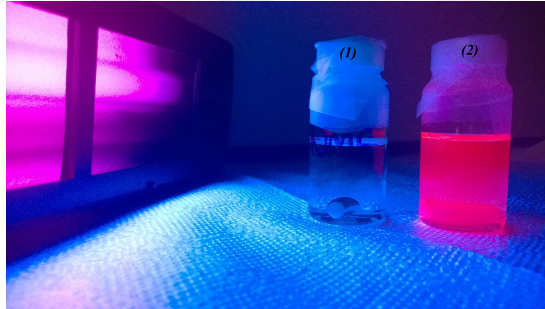


Figure 4.11: Chemical solutions under the UV-light illumination: Bottle number (1) is the mixture of the NMF and ammonium hydroxide as the continuous phase and bottle number (2) shows the mixture of reagents containing the CdSe/CdS quantum dot nanoparticle.

Table 4.6: Silica Encapsulation of Quantum Dots

Test 1	Carrier Fluid	Dispersed Phase
Contents	NMF + NH_4OH	QD + TEOS + Cyclohexane
Flow rate	24.0 $\mu\text{L}/\text{min}$	2.0 $\mu\text{L}/\text{min}$
Ammonium Hydroxide	0.38 M (150 μL in 10 ml)	—
Channel Length	140 mm	
Residence Time	14 seconds	
Nanoparticles Average Size	3.42 ± 0.55 nm	
Number of Measured Particles	30 (Table B.13)	

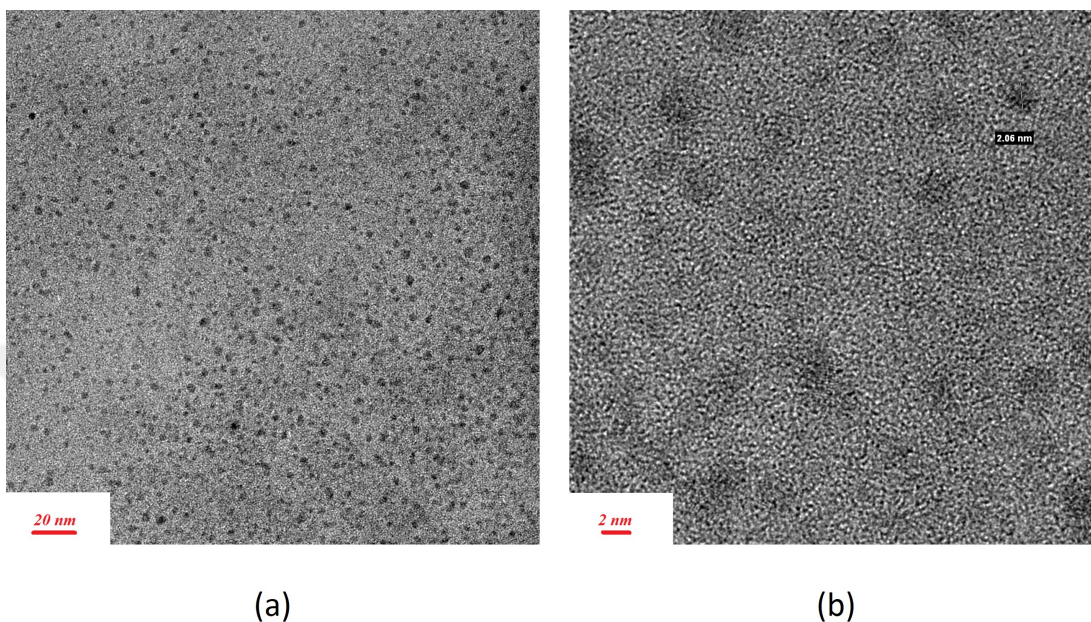


Figure 4.12: TEM results of the silica encapsulation of quantum dots for experiment 4.4. The average particle size is 3.42 ± 0.55 nm; the quantum dots are within the clusters of silica precursor.

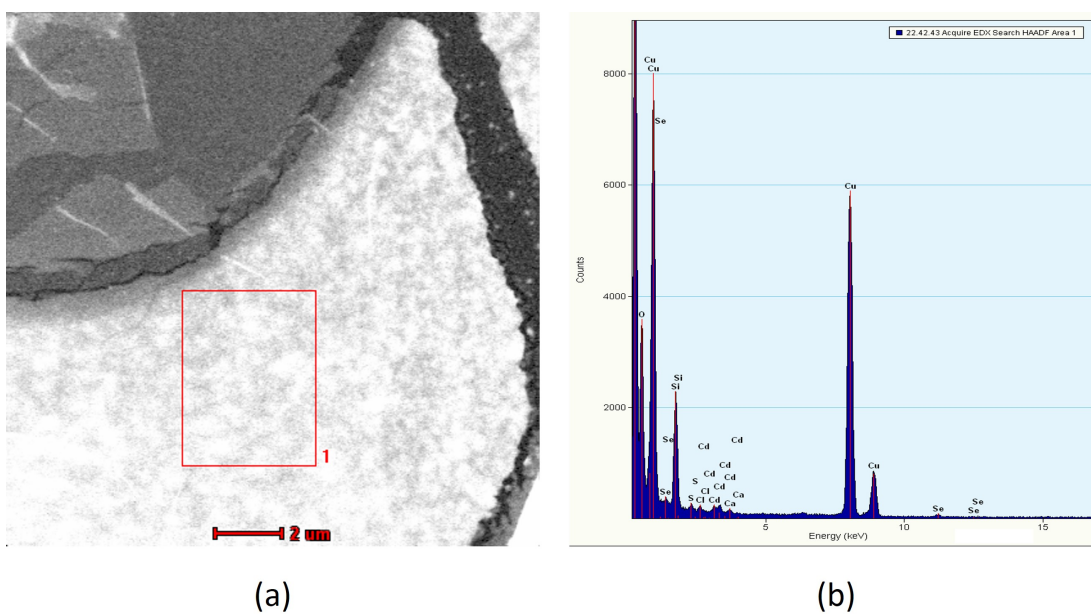


Figure 4.13: EDX result of experiment 4.4. The high amount of silica observed is due to the high carrier flow rate applied.

Table 4.7: EDX quantification results of Experiment 4.4

Element	Weight %	Atomic %
Si	78.43	91.90
S	1.55	1.59
Se	5.14	2.14
Cd	14.86	4.35

4.2.3 Temperature Control

The batch-wise synthesis of silica nanoparticles and silica encapsulation of *CdSe/CdS* quantum dots based on the Stöber method [39] are performed at room temperature. Initially, the conditions of the droplet-based reaction were completely based on the parameters in batch synthesis. Since the early results were not comparable, different parameters such as reactant concentration, residence time and temperature, were altered in order to enhance the reaction. At each stage, the reaction was performed at room temperature and then at a higher temperature to investigate the effect of higher temperatures. To heat the silicon microreactor, based on the reactor, which was being used, a hot plate or Peltier heaters were implemented to enable a higher surface temperature in the region of 40-50 °C. In all cases, the increased surface temperature of the reactor did not show any progress in the resultant nanoparticles. Especially, in experiments 4.1 to 4.3, the increased temperature leads to losing the nanoparticles in the TEM inspection step as shown in Figure 4.15. As the temperature of the reactor was raised the quantum dot nanoparticles may have dissipated on the channel wall since the nanoparticle aggregation speeds up at higher temperatures. Overall, since the temperature increase failed to make any impact on the process, it was ruled out of the optimization factors and the reactions were mainly based on the control of concentration and residence time.

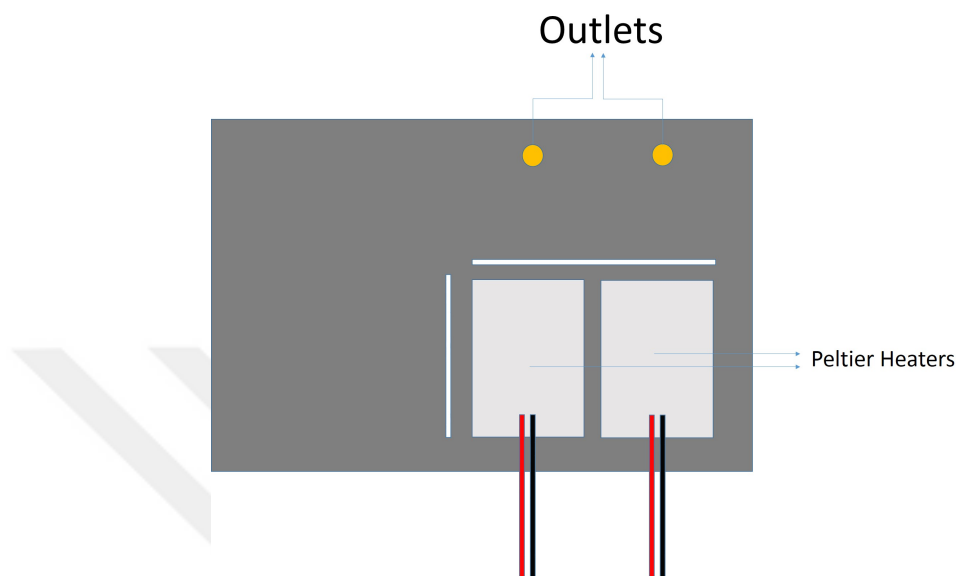


Figure 4.14: Schematic of Peltier heaters and their attachment to the microreactor. The picture is not drawn to scale.



Figure 4.15: TEM results of the silica encapsulation of quantum dots: Experiment 4.3 at 50 °. Quantum dot nanoparticles could not be detected while the silica clusters indicate the particle agglomeration.

4.3 Conclusion

Table 4.8 shows the comprehensive results for quantum dot silica coating experiments. Based on the increased average size in Experiment 4.3, slight encapsulation of scattered particles could be comprehended. Considering the low number of particles obtained from each sample, the FTIR inspection could not provide a valid indication of silica encapsulation. The increased average size in Experiment 4.3 compared to the bare quantum dots could be interpreted as a random and scarce coating of quantum dots; However, further analysis is required to completely investigate the control parameters to capture the individual quantum dots and generate the desired shell thickness around them.

Table 4.8: Comprehensive experimental results for silica coating of quantum dot nanoparticles

	Ammonium Hydroxide Concentration	Carrier Fluid Flow Rate	Residence Time	Number of Measurements	Average Size
Quantum dot nanoparticles Batch-wise synthesis	-	-	48 hours	75 Table B.9	8.43 ± 1.7 nm
Experiment 4.2	0.76 M (300 μ l in 10 ml)	10.0 μ l/min	490 seconds	45 Table B.11	8.60 ± 0.8 nm
Experiment 4.3	0.76 M (300 μ l in 10 ml)	5.0 μ l/min	980 seconds	100 Table B.12	11.30 ± 2.4 nm

Chapter 5

Conclusion and Recommendations for Future Work

Microfluidic reactors were prepared using photolithography and Bosch process to create near vertical channel walls. The silicon microreactor enabled chemically robust platform with a precise control over the reaction parameters such as temperature, reagent concentrations, and the reaction residence time. Optimizing these parameters leads to a control over the size and size distribution of synthesized nanoparticles. Firstly, silica nanoparticle synthesis was investigated in droplet-based reaction. The promising results from the silica nanoparticle synthesis were comparable with the batch results in terms of shape and size distribution. The batch-wise synthesis of silica nanoparticles takes about 2 days; on the other hand, the droplet-based reaction represented in this thesis had a maximum residence time of 10 minutes. Considering the significant decrease in reaction time inside the microreactor, this method could replace the time consuming conventional methods while enabling an accurate study on the detailed reaction parameters.

The optimized method of silica nanoparticle synthesis was later implemented

to encapsulate the *CdSe/CdS* quantum dot nanoparticles. Silica coating of quantum dots enhances their photostability and maintain their size-dependent optical properties, so any progress to enhance the reaction is highly desirable. The droplet-based microreactor could potentially allow a detailed monitoring of the reaction with a significant reduction in the time and amount of required materials. Although the results of the silica encapsulation process showed a slight increase in the nanoparticle diameters, it proved that the silica coating of the particles could be accomplished inside the microreactor by a modified method. The final results of the thesis showed a trend as the nanoparticle diameters increased with the increased residence time.

Further investigations are required to fully examine the relationship. The multi-temperature silicon microreactor used in the synthesis provided a quite long channel length; however, even longer microchannels may enable the further increase in the synthesized nanoparticle diameter. One of the problems which prohibit the residence time increase in the microreactor is the fact that the quantum dot solution prepared as the reagent 1, is highly unstable as the particles agglomerate in 2-3 hours. In batch-wise synthesis, the solution is constantly mixed and as the micelles are formed, the aggregation of quantum dots is limited. However, in the droplet-based synthesis, only a very small amount of solution is supplied through the channel and this would make it difficult to maintain a steady reaction for longer periods of time to collect a significant amount of sample. The experiments in this thesis were performed in 2-3 hours time spans since the reagent containing the quantum dots degraded significantly after a couple of hours. This limited time interval meant that the amount of collected sample was mainly based on the applied flow rates, so only a small amount of sample was collected for each test (around 1 ml). Collecting larger amounts of the sample may result in better understanding of the control parameters affecting the reaction.

One of the most important issues in quantum dot silica coating is to prepare the individually coated quantum dots. Due to their small size and considering the conventional channel dimensions in microreactors, it is fairly impossible to enable the access to the individual quantum dots. Nevertheless, flow focusing geometries could be implemented to reach a narrower stream of quantum dots and this may

lead to a better encapsulation of the individual nanoparticles. Designing a system that facilitates this narrow stream of reagents could be achieved by adapting different geometries such as tapered channels and a sequential method to add the reagents.

To maintain a steady reaction inside the droplets, the reagents should be immiscible with the carrier fluid; however, considering the nature of the nanoparticles used in the process, the choice for a proper carrier fluid was limited. NMF provided most of the characteristics of a suitable continuous phase except for the fact that ammonium hydroxide is soluble in NMF. This fact resulted in the diffusion of ammonium hydroxide to the carrier fluid and lead to a much higher concentration of ammonium hydroxide. Further analysis of the exact required concentration of ammonium hydroxide could be performed by introducing sequential streams of reagents and revising the choice of carrier fluid.

Bibliography

- [1] C.-H. Chang, B. K. Paul, V. T. Remcho, S. Atre, and J. E. Hutchison, “Synthesis and post-processing of nanomaterials using microreaction technology,” *Journal of Nanoparticle Research*, vol. 10, no. 6, pp. 965–980, 2008.
- [2] E. Y. Erdem, J. C. Cheng, F. M. Doyle, and A. P. Pisano, “Multi-temperature zone, droplet-based microreactor for increased temperature control in nanoparticle synthesis,” *small*, vol. 10, no. 6, pp. 1076–1080, 2014.
- [3] C.-X. Zhao, L. He, S. Z. Qiao, and A. P. Middelberg, “Nanoparticle synthesis in microreactors,” *Chemical Engineering Science*, vol. 66, no. 7, pp. 1463–1479, 2011.
- [4] K. Mullis, F. Faloon, S. Scharf, R. Saiki, G. Horn, and H. Erlich, “Specific enzymatic amplification of dna in vitro: the polymerase chain reaction,” in *Cold Spring Harbor symposia on quantitative biology*, vol. 51, pp. 263–273, Cold Spring Harbor Laboratory Press, 1986.
- [5] S. Marre and K. F. Jensen, “Synthesis of micro and nanostructures in microfluidic systems,” *Chemical Society Reviews*, vol. 39, no. 3, pp. 1183–1202, 2010.
- [6] L.-H. Hung and A. P. Lee, “Microfluidic devices for the synthesis of nanoparticles and biomaterials,” *Journal of Medical and Biological Engineering*, vol. 27, no. 1, p. 1, 2007.

- [7] W. H. Grover, M. G. von Muhlen, and S. R. Manalis, “Teflon films for chemically-inert microfluidic valves and pumps,” *Lab on a Chip*, vol. 8, no. 6, pp. 913–918, 2008.
- [8] P. A. Willis, B. D. Hunt, V. E. White, M. C. Lee, M. Ikeda, S. Bae, M. J. Pelletier, and F. J. Grunthaner, “Monolithic teflon® membrane valves and pumps for harsh chemical and low-temperature use,” *Lab on a Chip*, vol. 7, no. 11, pp. 1469–1474, 2007.
- [9] K. Jähnisch, V. Hessel, H. Löwe, and M. Baerns, “Chemistry in microstructured reactors,” *Angewandte Chemie International Edition*, vol. 43, no. 4, pp. 406–446, 2004.
- [10] S. Marre and K. F. Jensen, “Synthesis of micro and nanostructures in microfluidic systems,” *Chemical Society Reviews*, vol. 39, no. 3, pp. 1183–1202, 2010.
- [11] R. M. Tiggelaar, F. Benito-López, D. C. Hermes, H. Rathgen, R. J. Egberink, F. G. Mugele, D. N. Reinhoudt, A. van den Berg, W. Verboom, and H. J. Gardeniers, “Fabrication, mechanical testing and application of high-pressure glass microreactor chips,” *Chemical Engineering Journal*, vol. 131, no. 1, pp. 163–170, 2007.
- [12] E. Y. Erdem, *Microfluidic Reactors for the Controlled Synthesis of Nanoparticles*. University of California, Berkeley, 2013.
- [13] T. Nisisako, S. Okushima, and T. Torii, “Controlled formulation of monodisperse double emulsions in a multiple-phase microfluidic system,” *Soft Matter*, vol. 1, no. 1, pp. 23–27, 2005.
- [14] S. Van der Graaf, M. Steegmans, R. Van Der Sman, C. Schroën, and R. Boom, “Droplet formation in a t-shaped microchannel junction: a model system for membrane emulsification,” *Colloids and Surfaces A: Physico-chemical and Engineering Aspects*, vol. 266, no. 1, pp. 106–116, 2005.
- [15] P. Garstecki, M. J. Fuerstman, H. A. Stone, and G. M. Whitesides, “Formation of droplets and bubbles in a microfluidic t-junction: scaling and mechanism of break-up,” *Lab on a Chip*, vol. 6, no. 3, pp. 437–446, 2006.

- [16] J. Xu, S. Li, J. Tan, Y. Wang, and G. Luo, "Preparation of highly monodisperse droplet in a t-junction microfluidic device," *AIChE journal*, vol. 52, no. 9, pp. 3005–3010, 2006.
- [17] Q. Xu and M. Nakajima, "The generation of highly monodisperse droplets through the breakup of hydrodynamically focused microthread in a microfluidic device," *Applied Physics Letters*, vol. 85, no. 17, pp. 3726–3728, 2004.
- [18] L. Yobas, S. Martens, W.-L. Ong, and N. Ranganathan, "High-performance flow-focusing geometry for spontaneous generation of monodispersed droplets," *Lab on a Chip*, vol. 6, no. 8, pp. 1073–1079, 2006.
- [19] B. D. Hamlington, B. Steinhaus, J. J. Feng, D. Link, M. J. Shelley, and A. Q. Shen, "Liquid crystal droplet production in a microfluidic device," *Liquid Crystals*, vol. 34, no. 7, pp. 861–870, 2007.
- [20] J. Xu, S. Li, J. Tan, and G. Luo, "Correlations of droplet formation in t-junction microfluidic devices: from squeezing to dripping," *Microfluidics and Nanofluidics*, vol. 5, no. 6, pp. 711–717, 2008.
- [21] A. S. Utada, A. Fernandez-Nieves, H. A. Stone, and D. A. Weitz, "Dripping to jetting transitions in coflowing liquid streams," *Physical review letters*, vol. 99, no. 9, p. 094502, 2007.
- [22] J. Xu, S. Li, J. Tan, Y. Wang, and G. Luo, "Preparation of highly monodisperse droplet in a t-junction microfluidic device," *AIChE journal*, vol. 52, no. 9, pp. 3005–3010, 2006.
- [23] J. d. Mello and A. d. Mello, "Focusmicroscale reactors: nanoscale products," *Lab on a Chip*, vol. 4, no. 2, pp. 11N–15N, 2004.
- [24] I. Lignos, R. Maceiczkyk, and A. J. deMello, "Microfluidic technology: Uncovering the mechanisms of nanocrystal nucleation and growth," *Accounts of Chemical Research*, 2017.

- [25] J. Ma, S. M.-Y. Lee, C. Yi, and C.-W. Li, "Controllable synthesis of functional nanoparticles by microfluidic platforms for biomedical applications—a review," *Lab on a Chip*, vol. 17, no. 2, pp. 209–226, 2017.
- [26] R. L. Hartman and K. F. Jensen, "Microchemical systems for continuous-flow synthesis," *Lab on a Chip*, vol. 9, no. 17, pp. 2495–2507, 2009.
- [27] L. Frenz, A. El Harrak, M. Pauly, S. Bégin-Colin, A. D. Griffiths, and J.-C. Baret, "Droplet-based microreactors for the synthesis of magnetic iron oxide nanoparticles," *Angewandte Chemie International Edition*, vol. 47, no. 36, pp. 6817–6820, 2008.
- [28] A. A. Hassan, O. Sandre, V. Cabuil, and P. Tabeling, "Synthesis of iron oxide nanoparticles in a microfluidic device: preliminary results in a coaxial flow millichannel," *Chemical Communications*, no. 15, pp. 1783–1785, 2008.
- [29] A. Abou-Hassan, R. Bazzi, and V. Cabuil, "Multistep continuous-flow microsynthesis of magnetic and fluorescent γ - Fe_2O_3 @ SiO_2 core/shell nanoparticles," *Angewandte Chemie International Edition*, vol. 48, no. 39, pp. 7180–7183, 2009.
- [30] T. Zhang, X. Zhang, X. Yan, L. Kong, G. Zhang, H. Liu, J. Qiu, and K. L. Yeung, "Synthesis of Fe_3O_4 @ ZIF-8 magnetic core-shell microspheres and their potential application in a capillary microreactor," *Chemical engineering journal*, vol. 228, pp. 398–404, 2013.
- [31] K. Kumar, A. M. Nightingale, S. H. Krishnadasan, N. Kamaly, M. Wylenzinska-Arridge, K. Zeissler, W. R. Branford, E. Ware, *et al.*, "Direct synthesis of dextran-coated superparamagnetic iron oxide nanoparticles in a capillary-based droplet reactor," *Journal of Materials Chemistry*, vol. 22, no. 11, pp. 4704–4708, 2012.
- [32] F. S. Majedi, M. M. Hasani-Sadrabadi, S. H. Emami, M. A. Shokrgozar, J. J. VanDersarl, E. Dashtimoghadam, A. Bertsch, and P. Renaud, "Microfluidic assisted self-assembly of chitosan based nanoparticles as drug delivery agents," *Lab on a Chip*, vol. 13, no. 2, pp. 204–207, 2013.

- [33] B. Cetin, M. D. Asik, and S. Taze, “Design and fabrication of a microfluidic device for synthesis of chitosan nanoparticles,” *Journal of Nanotechnology in Engineering and Medicine*, vol. 4, no. 3, p. 031004, 2013.
- [34] A. M. Nightingale and J. C. de Mello, “Microscale synthesis of quantum dots,” *Journal of Materials Chemistry*, vol. 20, no. 39, pp. 8454–8463, 2010.
- [35] I. Shestopalov, J. D. Tice, and R. F. Ismagilov, “Multi-step synthesis of nanoparticles performed on millisecond time scale in a microfluidic droplet-based system,” *Lab on a Chip*, vol. 4, no. 4, pp. 316–321, 2004.
- [36] E. M. Chan, A. P. Alivisatos, and R. A. Mathies, “High-temperature microfluidic synthesis of cdse nanocrystals in nanoliter droplets,” *Journal of the American Chemical Society*, vol. 127, no. 40, pp. 13854–13861, 2005.
- [37] B. K. Yen, A. Günther, M. A. Schmidt, K. F. Jensen, and M. G. Bawendi, “A microfabricated gas–liquid segmented flow reactor for high-temperature synthesis: The case of cdse quantum dots,” *Angewandte Chemie*, vol. 117, no. 34, pp. 5583–5587, 2005.
- [38] R. L. Hartman and K. F. Jensen, “Microchemical systems for continuous-flow synthesis,” *Lab on a Chip*, vol. 9, no. 17, pp. 2495–2507, 2009.
- [39] W. Stöber, A. Fink, and E. Bohn, “Controlled growth of monodisperse silica spheres in the micron size range,” *Journal of colloid and interface science*, vol. 26, no. 1, pp. 62–69, 1968.
- [40] H. S. Fogler *et al.*, “Elements of chemical reaction engineering,” 1999.
- [41] K. Do Kim and H. T. Kim, “Formation of silica nanoparticles by hydrolysis of teos using a mixed semi-batch/batch method,” *Journal of sol-gel science and technology*, vol. 25, no. 3, pp. 183–189, 2002.
- [42] P. He, G. Greenway, and S. J. Haswell, “Microfluidic synthesis of silica nanoparticles using polyethylenimine polymers,” *Chemical engineering journal*, vol. 167, no. 2, pp. 694–699, 2011.

- [43] M. Su, "Synthesis of highly monodisperse silica nanoparticles in the microreactor system," *Korean Journal of Chemical Engineering*, vol. 34, no. 2, pp. 484–494, 2017.
- [44] M. Su, H. Su, B. Du, X. Li, G. Ren, and S. Wang, "The properties of silica nanoparticles with high monodispersity synthesized in the microreactor system," *Journal of sol-gel science and technology*, vol. 72, no. 2, pp. 375–384, 2014.
- [45] Y. He, K.-J. Kim, and C.-H. Chang, "Continuous, size and shape-control synthesis of hollow silica nanoparticles enabled by a microreactor-assisted rapid mixing process," *Nanotechnology*, vol. 28, no. 23, p. 235602, 2017.
- [46] P. He, G. Greenway, and S. J. Haswell, "Microfluidic synthesis of silica nanoparticles using polyethylenimine polymers," *Chemical engineering journal*, vol. 167, no. 2, pp. 694–699, 2011.
- [47] K. Yano and Y. Fukushima, "Particle size control of mono-dispersed super-microporous silica spheres," *Journal of Materials Chemistry*, vol. 13, no. 10, pp. 2577–2581, 2003.
- [48] I. Lee, Y. Yoo, Z. Cheng, and H.-K. Jeong, "Generation of monodisperse mesoporous silica microspheres with controllable size and surface morphology in a microfluidic device," *Advanced Functional Materials*, vol. 18, no. 24, pp. 4014–4021, 2008.
- [49] N. J. Carroll, S. B. Rathod, E. Derbins, S. Mendez, D. A. Weitz, and D. N. Petsev, "Droplet-based microfluidics for emulsion and solvent evaporation synthesis of monodisperse mesoporous silica microspheres," *Langmuir*, vol. 24, no. 3, pp. 658–661, 2008.
- [50] S. A. Khan, A. Günther, M. A. Schmidt, and K. F. Jensen, "Microfluidic synthesis of colloidal silica," *Langmuir*, vol. 20, no. 20, pp. 8604–8611, 2004.
- [51] V. De Matteis, L. Rizzello, M. P. Di Bello, and R. Rinaldi, "One-step synthesis, toxicity assessment and degradation in tumoral ph environment of sio2@ ag core/shell nanoparticles," *Journal of Nanoparticle Research*, vol. 19, no. 6, p. 196, 2017.

- [52] J. Knossalla, S. Mezzavilla, and F. Schüth, “Continuous synthesis of nanostructured silica based materials in a gas–liquid segmented flow tubular reactor,” *New Journal of Chemistry*, vol. 40, no. 5, pp. 4361–4366, 2016.
- [53] M. Mahajan, R. Dubey, and J. Mahajan, “Characteristics and properties of cdse quantum dots,” *Int. J. Latest Res. Sci. Tech*, vol. 2, pp. 457–459, 2013.
- [54] W. Y. William, E. Chang, R. Drezek, and V. L. Colvin, “Water-soluble quantum dots for biomedical applications,” *Biochemical and biophysical research communications*, vol. 348, no. 3, pp. 781–786, 2006.
- [55] T. Jamieson, R. Bakhshi, D. Petrova, R. Pocock, M. Imani, and A. M. Seifalian, “Biological applications of quantum dots,” *Biomaterials*, vol. 28, no. 31, pp. 4717–4732, 2007.
- [56] W. C. Chan, D. J. Maxwell, X. Gao, R. E. Bailey, M. Han, and S. Nie, “Luminescent quantum dots for multiplexed biological detection and imaging,” *Current opinion in biotechnology*, vol. 13, no. 1, pp. 40–46, 2002.
- [57] B. Guzelturk, Y. Kelestemur, K. Gungor, A. Yeltik, M. Z. Akgul, Y. Wang, R. Chen, C. Dang, H. Sun, and H. V. Demir, “Stable and low-threshold optical gain in cdse/cds quantum dots: An all-colloidal frequency up-converted laser,” *Advanced Materials*, vol. 27, no. 17, pp. 2741–2746, 2015.
- [58] D. Wang, J. He, N. Rosenzweig, and Z. Rosenzweig, “Superparamagnetic fe₂o₃ beads- cdse/zns quantum dots core- shell nanocomposite particles for cell separation,” *Nano Letters*, vol. 4, no. 3, pp. 409–413, 2004.
- [59] W. C. Chan and S. Nie, “Quantum dot bioconjugates for ultrasensitive nonisotopic detection,” *Science*, vol. 281, no. 5385, pp. 2016–2018, 1998.
- [60] S. F. Wuister, I. Swart, F. van Driel, S. G. Hickey, and C. de Mello Donegá, “Highly luminescent water-soluble cdte quantum dots,” *Nano Letters*, vol. 3, no. 4, pp. 503–507, 2003.

- [61] B. Dubertret, P. Skourides, D. J. Norris, V. Noireaux, A. H. Brivanlou, and A. Libchaber, “In vivo imaging of quantum dots encapsulated in phospholipid micelles,” *Science*, vol. 298, no. 5599, pp. 1759–1762, 2002.
- [62] H. Fan, E. W. Leve, C. Scullin, J. Gabaldon, D. Tallant, S. Bunge, T. Boyle, M. C. Wilson, and C. J. Brinker, “Surfactant-assisted synthesis of water-soluble and biocompatible semiconductor quantum dot micelles,” *Nano Letters*, vol. 5, no. 4, pp. 645–648, 2005.
- [63] M. Bruchez, M. Moronne, P. Gin, S. Weiss, and A. P. Alivisatos, “Semiconductor nanocrystals as fluorescent biological labels,” *science*, vol. 281, no. 5385, pp. 2013–2016, 1998.
- [64] D. E. Gómez, I. Pastoriza-Santos, and P. Mulvaney, “Tunable whispering gallery mode emission from quantum-dot-doped microspheres,” *Small*, vol. 1, no. 2, pp. 238–241, 2005.
- [65] A. L. Rogach, D. Nagesha, J. W. Ostrander, M. Giersig, and N. A. Kotov, “raisin bun-type composite spheres of silica and semiconductor nanocrystals,” *Chemistry of materials*, vol. 12, no. 9, pp. 2676–2685, 2000.
- [66] M. A. Correa-Duarte, M. Giersig, and L. M. Liz-Marzán, “Stabilization of cds semiconductor nanoparticles against photodegradation by a silica coating procedure,” *Chemical Physics Letters*, vol. 286, no. 5, pp. 497–501, 1998.
- [67] Y. Zheng, Z. Yang, Y. Li, and J. Y. Ying, “From glutathione capping to a crosslinked, phytochelatins-like coating of quantum dots,” *Advanced Materials*, vol. 20, no. 18, pp. 3410–3415, 2008.
- [68] W. Zhang, X.-W. He, W.-Y. Li, and Y.-K. Zhang, “Thermo-sensitive imprinted polymer coating cdte quantum dots for target protein specific recognition,” *Chemical Communications*, vol. 48, no. 12, pp. 1757–1759, 2012.
- [69] Y. Chen and Z. Rosenzweig, “Luminescent cdse quantum dot doped stabilized micelles,” *Nano Letters*, vol. 2, no. 11, pp. 1299–1302, 2002.

- [70] D. K. Yi, S. T. Selvan, S. S. Lee, G. C. Papaefthymiou, D. Kundaliya, and J. Y. Ying, "Silica-coated nanocomposites of magnetic nanoparticles and quantum dots," *J. Am. Chem. Soc.*, vol. 127, no. 14, pp. 4990–4991, 2005.
- [71] Z. Zhelev, H. Ohba, and R. Bakalova, "Single quantum dot-micelles coated with silica shell as potentially non-cytotoxic fluorescent cell tracers," *Journal of the American Chemical Society*, vol. 128, no. 19, pp. 6324–6325, 2006.
- [72] A. Guerrero-Martínez, J. Pérez-Juste, and L. M. Liz-Marzán, "Recent progress on silica coating of nanoparticles and related nanomaterials," *Advanced materials*, vol. 22, no. 11, pp. 1182–1195, 2010.
- [73] N. R. Jana, C. Earhart, and J. Y. Ying, "Synthesis of water-soluble and functionalized nanoparticles by silica coating," *Chemistry of Materials*, vol. 19, no. 21, pp. 5074–5082, 2007.
- [74] M. Darbandi, R. Thomann, and T. Nann, "Single quantum dots in silica spheres by microemulsion synthesis," *Chemistry of materials*, vol. 17, no. 23, pp. 5720–5725, 2005.
- [75] I. Gorelikov and N. Matsuura, "Single-step coating of mesoporous silica on cetyltrimethyl ammonium bromide-capped nanoparticles," *Nano letters*, vol. 8, no. 1, pp. 369–373, 2008.
- [76] S. T. Selvan, "Silica-coated quantum dots and magnetic nanoparticles for bioimaging applications (mini-review)," *Biointerphases*, vol. 5, no. 3, pp. FA110–FA115, 2010.
- [77] R. Koole, M. M. van Schooneveld, J. Hilhorst, C. de Mello Donegá, D. C. t. Hart, A. van Blaaderen, D. Vanmaekelbergh, and A. Meijerink, "On the incorporation mechanism of hydrophobic quantum dots in silica spheres by a reverse microemulsion method," *Chemistry of Materials*, vol. 20, no. 7, pp. 2503–2512, 2008.
- [78] Y. Kobayashi, H. Katakami, E. Mine, D. Nagao, M. Konno, and L. M. Liz-Marzán, "Silica coating of silver nanoparticles using a modified stöber

- method,” *Journal of colloid and interface science*, vol. 283, no. 2, pp. 392–396, 2005.
- [79] P. Mulvaney, L. Liz-Marzan, M. Giersig, and T. Ung, “Silica encapsulation of quantum dots and metal clusters,” *Journal of Materials Chemistry*, vol. 10, no. 6, pp. 1259–1270, 2000.
- [80] Y. Yang, L. Jing, X. Yu, D. Yan, and M. Gao, “Coating aqueous quantum dots with silica via reverse microemulsion method: toward size-controllable and robust fluorescent nanoparticles,” *Chemistry of materials*, vol. 19, no. 17, pp. 4123–4128, 2007.
- [81] R. Koole, M. M. van Schooneveld, J. Hilhorst, C. de Mello Donegá, D. C. t. Hart, A. van Blaaderen, D. Vanmaekelbergh, and A. Meijerink, “On the incorporation mechanism of hydrophobic quantum dots in silica spheres by a reverse microemulsion method,” *Chemistry of Materials*, vol. 20, no. 7, pp. 2503–2512, 2008.
- [82] D. Gerion, F. Pinaud, S. C. Williams, W. J. Parak, D. Zanchet, S. Weiss, and A. P. Alivisatos, “Synthesis and properties of biocompatible water-soluble silica-coated cdse/zns semiconductor quantum dots,” *The Journal of Physical Chemistry B*, vol. 105, no. 37, pp. 8861–8871, 2001.
- [83] T. T. Tan, S. T. Selvan, L. Zhao, S. Gao, and J. Y. Ying, “Size control, shape evolution, and silica coating of near-infrared-emitting pbse quantum dots,” *Chemistry of Materials*, vol. 19, no. 13, pp. 3112–3117, 2007.
- [84] A. Wolcott, D. Gerion, M. Visconte, J. Sun, A. Schwartzberg, S. Chen, and J. Z. Zhang, “Silica-coated cdte quantum dots functionalized with thiols for bioconjugation to igg proteins,” *The Journal of Physical Chemistry B*, vol. 110, no. 11, pp. 5779–5789, 2006.
- [85] H. Becker and C. Gärtner, “Polymer microfabrication technologies for microfluidic systems,” *Analytical and bioanalytical chemistry*, vol. 390, no. 1, pp. 89–111, 2008.

- [86] A. Özkan and E. Y. Erdem, “Numerical analysis of mixing performance in sinusoidal microchannels based on particle motion in droplets,” *Microfluidics and Nanofluidics*, vol. 19, no. 5, pp. 1101–1108, 2015.
- [87] A. Özkan, *Droplet-based microfluidic systems for silica coating and synthesis of conjugated polymer nanoparticles*. PhD thesis, bilkent university, 2015.
- [88] M. J. Madou, *Fundamentals of microfabrication: the science of miniaturization*. CRC press, 2002.
- [89] J. Quero, F. Perdigones, and C. Aracil, “10-microfabrication technologies used for creating smart devices for industrial applications,” *Smart Sensors and Mems*, pp. 281–304, 2014.
- [90] J. X. Zhang and K. Hoshino, *Molecular Sensors and Nanodevices: Principles, Designs and Applications in Biomedical Engineering*. William Andrew, 2013.
- [91] B. Lin and S. Zhou, “Poly (ethylene glycol)-grafted silica nanoparticles for highly hydrophilic acrylic-based polyurethane coatings,” *Progress in Organic Coatings*, vol. 106, pp. 145–154, 2017.
- [92] H. Yang and Y. Zhu, “Size dependence of sio 2 particles enhanced glucose biosensor,” *Talanta*, vol. 68, no. 3, pp. 569–574, 2006.
- [93] M. Liong, B. France, K. A. Bradley, and J. I. Zink, “Antimicrobial activity of silver nanocrystals encapsulated in mesoporous silica nanoparticles,” *Advanced materials*, vol. 21, no. 17, pp. 1684–1689, 2009.
- [94] C. J. Brinker and G. W. Scherer, *Sol-gel science: the physics and chemistry of sol-gel processing*. Academic press, 2013.
- [95] S.-F. Wang, Y.-F. Hsu, T. C. Yang, C.-M. Chang, Y. Chen, C.-Y. Huang, and F.-S. Yen, “Silica coating on ultrafine α -alumina particles,” *Materials Science and Engineering: A*, vol. 395, no. 1, pp. 148–152, 2005.
- [96] S. Zhou, X. Yao, and T. Fan, “Confined synthesis of three-dimensionally ordered arrays of multilamellar silica nanoparticles as a gold catalyst support,” *RSC Advances*, vol. 6, no. 104, pp. 102258–102263, 2016.

- [97] T. Aubert, F. Grasset, S. Mornet, E. Duguet, O. Cador, S. Cordier, Y. Molard, V. Demange, M. Mortier, and H. Haneda, "Functional silica nanoparticles synthesized by water-in-oil microemulsion processes," *Journal of colloid and interface science*, vol. 341, no. 2, pp. 201–208, 2010.
- [98] J. H. Schulman, W. Stoeckenius, and L. M. Prince, "Mechanism of formation and structure of micro emulsions by electron microscopy," *The Journal of physical chemistry*, vol. 63, no. 10, pp. 1677–1680, 1959.
- [99] Z. Popović, W. Liu, V. P. Chauhan, J. Lee, C. Wong, A. B. Greytak, N. Insin, D. G. Nocera, D. Fukumura, R. K. Jain, *et al.*, "A nanoparticle size series for in vivo fluorescence imaging," *Angewandte Chemie*, vol. 122, no. 46, pp. 8831–8834, 2010.
- [100] C. Dhand, N. Dwivedi, X. J. Loh, A. N. J. Ying, N. K. Verma, R. W. Beuerman, R. Lakshminarayanan, and S. Ramakrishna, "Methods and strategies for the synthesis of diverse nanoparticles and their applications: a comprehensive overview," *Rsc Advances*, vol. 5, no. 127, pp. 105003–105037, 2015.

Appendix A

PDMS Microreactor Preparation Using Soft Lithography

To prepare the PDMS microreactor:

1. Initially, the PDMS mixture was prepared using the curing agent with 1:10 mass-based ratio. The mixture should be stirred for at least 3 minutes to obtain a homogeneous state.
2. The PDMS mixture was poured into the petri dish containing the silicon master mold and was placed in a vacuum chamber in a desiccator for 25-30 minutes to get rid of the air bubbles.
3. The mold was baked at 80°C for 70 minutes. This baking time depends on the material used for the master mold.
4. After the baking, the mold should reach the ambient temperature in order to ensure a complete and spotless peeling off process.
5. Required holes for the inlets and outlets of the microreactor were created with a puncher.
6. The PDMS mold was cleaned with tape to remove all the dust and extra particles.

7. The oxygen plasma was used for the bonding. Initially, the PDMS mold and the glass lamel were placed inside the chamber. The plasma light was turned on and as the purple light became visible, the PDMS mold and the lamel were exposed for 45 seconds.
8. Bonding was completed by putting the PDMS mold on the glass lamel and exerting a mild pressure.



Appendix B

Nanoparticle Size Measurements

B.1 Silica Nanoparticle Synthesis Size Measurements

- Experiment 3.1

Table B.1: Size measurements for Experiment 3.1

No.	Size (nm)	No.	Size (nm)	No.	Size (nm)
1	14.881	16	17.241	31	19.200
2	14.881	17	17.241	32	19.600
3	14.943	18	17.241	33	19.600
4	15.476	19	17.262	34	20.000
5	15.476	20	17.262	35	20.115
6	16.000	21	17.262	36	20.238
7	16.071	22	17.262	37	20.400
8	16.400	23	17.262	38	20.690
9	16.400	24	17.816	39	20.690
10	16.667	25	18.000	40	21.600
11	16.667	26	18.000	41	21.839
12	17.200	27	18.391	42	25.595
13	17.200	28	18.400	43	25.862
14	17.200	29	18.452	44	18.966
15	17.241	30	18.452	45	18.320

• **Experiment 3.2**

Table B.2: Size measurements for Experiment 3.2

No.	Size (nm)	No.	Size (nm)	No.	Size (nm)	No.	Size (nm)
1	1.340	11	1.667	21	1.942	31	2.500
2	1.381	12	1.667	22	2.029	32	2.500
3	1.381	13	1.667	23	2.062	33	2.917
4	1.443	14	1.856	24	2.083	34	3.333
5	1.443	15	1.856	25	2.083		
6	1.443	16	2.583	26	2.083		
7	1.505	17	2.899	27	2.203		
8	1.505	18	1.856	28	2.292		
9	1.505	19	1.913	29	2.292		
10	1.598	20	1.917	30	2.474		

• **Experiment 3.3**

Table B.3: Size measurements for Experiment 3.3

No.	Size (nm)	No.	Size (nm)	No.	Size (nm)	No.	Size (nm)
1	2.353	11	3.059	21	3.353	31	3.706
2	2.529	12	3.059	22	3.471	32	3.706
3	2.665	13	3.059	23	3.529	33	3.765
4	2.706	14	3.059	24	3.529	34	3.765
5	2.706	15	3.118	25	3.529	35	3.824
6	2.806	16	3.176	26	3.529	36	3.824
7	2.824	17	3.353	27	3.647	37	4.000
8	2.824	18	3.353	28	3.706	38	4.059
9	3.059	19	3.353	29	3.706	39	4.118
10	3.059	20	3.353	30	3.706	40	4.176

- **Experiment 3.4**

Table B.4: Size measurements for Experiment 3.4

No.	Size (nm)	No.	Size (nm)	No.	Size (nm)
1	1.771	11	2.833	21	3.529
2	2.479	12	2.875	22	3.529
3	2.500	13	2.941	23	3.706
4	2.529	14	2.941	24	4.000
5	2.542	15	2.941	25	4.000
6	2.667	16	3.063	26	4.294
7	2.765	17	3.125	27	4.588
8	2.792	18	3.265	28	4.706
9	2.813	19	3.324	29	4.824
10	2.833	20	3.529	30	5.176

- **Experiment 3.5**

Table B.5: Size measurements for Experiment 3.5

No.	Size (nm)	No.	Size (nm)	No.	Size (nm)
1	2.500	11	3.061	21	3.485
2	2.625	12	3.125	22	3.500
3	2.625	13	3.152	23	3.542
4	2.875	14	3.208	24	3.545
5	2.909	15	3.212	25	3.625
6	2.917	16	3.212	26	3.625
7	2.958	17	3.231	27	3.625
8	2.970	18	3.250	28	3.636
9	3.000	19	3.333	29	3.750
10	3.042	20	3.424	30	3.939

- **Experiment 3.6**

Table B.6: Size measurements for Experiment 3.6 (main solution)

No.	Size (nm)
1	25.111
2	27.302
3	29.603
4	33.492
6	36.563
7	47.188

Table B.7: Size measurements for Experiment 3.6 (centrifuge residual)

No.	Size (nm)	No.	Size (nm)
1	2.667	11	4.684
2	2.788	12	4.684
3	3.030	13	4.937
4	3.061	14	5.190
5	3.121	15	5.190
6	3.278	16	4.051
7	3.418	17	4.177
8	3.544	18	4.177
9	3.606	19	4.342
10	3.636	20	4.430

- **Experiment 3.7**

Table B.8: Size measurements for Experiment 3.7

No.	Size (nm)	No.	Size (nm)	No.	Size (nm)	No.	Size (nm)
1	15.625	36	23.125	71	25.000	106	26.250
2	19.375	37	23.125	72	25.000	107	26.250
3	20.000	38	23.125	73	25.000	108	26.250
4	20.000	39	23.125	74	25.000	109	26.250
5	20.625	40	23.125	75	25.000	110	26.494
6	20.625	41	23.750	76	25.000	111	26.494
7	21.250	42	23.750	77	25.000	112	26.494
8	21.250	43	23.750	78	25.000	113	26.875
9	21.250	44	23.750	79	25.000	114	26.875
10	21.250	45	23.750	80	25.000	115	26.875
11	21.250	46	23.750	81	25.000	116	26.875
12	21.250	47	23.750	82	25.000	117	26.875
13	21.429	48	23.750	83	25.000	118	27.273
14	21.429	49	23.750	84	25.325	119	27.273
15	21.875	50	23.750	85	25.325	120	27.273
16	21.875	51	23.766	86	25.625	121	27.500
17	21.875	52	23.766	87	25.625	122	27.500
18	21.875	53	24.156	88	25.625	123	27.500
19	21.875	54	24.156	89	25.625	124	27.500
20	22.500	55	24.375	90	25.625	125	27.500
21	22.500	56	24.375	91	25.625	126	27.663
22	22.500	57	24.375	92	25.625	127	27.663
23	22.500	58	24.375	93	25.625	128	28.052
24	22.500	59	24.375	94	25.625	129	28.125
25	22.500	60	24.375	95	25.625	130	28.125
26	22.500	61	24.375	96	25.625	131	28.125
27	22.500	62	24.375	97	25.714	132	28.125
28	22.598	63	24.375	98	25.714	133	28.125
29	22.598	64	24.375	99	25.714	134	28.125
30	23.125	65	24.375	100	26.104	135	28.750
31	23.125	66	24.375	101	26.250	136	28.750
32	23.125	67	24.375	102	26.250	137	28.750
33	23.125	68	24.375	103	26.250	138	28.750
34	23.125	69	24.546	104	26.250	139	28.750
35	23.125	70	24.935	105	26.250	140	29.375

B.2 Quantum Dot Post Processing Size Measurements

- Quantum Dot Nanoparticles

Table B.9: Size measurements for quantum dot nanoparticles

No.	Size (nm)	No.	Size (nm)	No.	Size (nm)	No.	Size (nm)
1	6.017	26	7.712	51	9.130	76	10.435
2	6.441	27	7.797	52	9.130	77	10.435
3	6.522	28	7.826	53	9.130	78	10.593
4	6.522	29	7.826	54	9.130	79	10.739
5	6.522	30	7.881	55	9.130	80	10.739
6	6.522	31	7.966	56	9.130	81	10.870
7	6.525	32	8.261	57	9.130	82	10.870
8	6.610	33	8.261	58	9.237	83	11.017
9	6.780	34	8.305	59	9.322	84	11.304
10	6.783	35	8.305	60	9.322	85	11.304
11	6.783	36	8.475	61	9.348	86	11.304
12	6.949	37	8.475	62	9.348	87	11.304
13	6.949	38	8.475	63	9.492	88	12.609
14	6.957	39	8.565	64	9.565	89	12.609
15	6.957	40	8.565	65	9.565	90	12.610
16	6.992	41	8.644	66	9.565		
17	7.288	42	8.696	67	9.565		
18	7.288	43	8.696	68	9.565		
19	7.415	44	8.729	69	9.565		
20	7.415	45	8.729	70	9.826		
21	7.458	46	8.898	71	9.826		
22	7.458	47	8.898	72	10.000		
23	7.458	48	9.130	73	10.000		
24	7.542	49	9.130	74	10.000		
25	7.627	50	9.130	75	10.254		

- **Experiment 4.1**

Table B.10: Size measurements for Experiment 4.1

No.	Size (nm)	No.	Size (nm)	No.	Size (nm)
1	24.818	6	27.941	11	32.353
2	26.277	7	27.941	12	35.294
3	27.007	8	27.941	13	36.765
4	27.206	9	29.412		
5	27.372	10	30.882		

- **Experiment 4.2**

Table B.11: Size measurements for Experiment 4.2

No.	Size (nm)	No.	Size (nm)	No.	Size (nm)	No.	Size (nm)
1	6.75	16	8.25	31	8.80	46	9.38
2	6.81	17	8.25	32	8.80	47	9.39
3	7.00	18	8.35	33	8.80	48	9.52
4	7.01	19	8.38	34	8.84	49	9.60
5	7.41	20	8.40	35	8.87	50	9.82
6	7.70	21	8.40	36	8.92	51	9.97
7	7.73	22	8.41	37	8.94	52	10.00
8	7.77	23	8.43	38	9.02	53	10.00
9	7.99	24	8.45	39	9.09	54	10.21
10	8.00	25	8.48	40	9.10		
11	8.00	26	8.50	41	9.15		
12	8.00	27	8.56	42	9.20		
13	8.04	28	8.60	43	9.20		
14	8.11	29	8.60	44	9.24		
15	8.14	30	8.80	45	9.24		

• **Experiment 4.3**

Table B.12: Size measurements for Experiment 4.3

No.	Size (nm)	No.	Size (nm)	No.	Size (nm)	No.	Size (nm)
1	7.328	26	9.655	51	11.000	76	11.983
2	7.375	27	9.741	52	11.034	77	12.069
3	8.103	28	9.741	53	11.207	78	12.500
4	8.448	29	9.914	54	11.207	79	12.500
5	8.621	30	9.914	55	11.207	80	12.586
6	8.750	31	10.125	56	11.207	81	12.845
7	8.750	32	10.259	57	11.207	82	12.931
8	8.793	33	10.259	58	11.207	83	12.931
9	8.836	34	10.259	59	11.207	84	12.931
10	9.052	35	10.259	60	11.207	85	12.966
11	9.052	36	10.345	61	11.293	86	13.103
12	9.052	37	10.345	62	11.313	87	13.276
13	9.095	38	10.345	63	11.379	88	13.305
14	9.138	39	10.345	64	11.379	89	13.559
15	9.138	40	10.345	65	11.438	90	13.729
16	9.224	41	10.466	66	11.525	91	14.407
17	9.224	42	10.603	67	11.603	92	14.483
18	9.267	43	10.625	68	11.625	93	15.254
19	9.310	44	10.690	69	11.638	94	15.678
20	9.310	45	10.750	70	11.724	95	16.017
21	9.375	46	10.776	71	11.724	96	16.102
22	9.397	47	10.776	72	11.767	97	17.373
23	9.483	48	10.938	73	11.875	98	17.966
24	9.483	49	10.948	74	11.897	99	18.644
25	9.569	50	10.948	75	11.931	100	20.339

- **Experiment 4.4**

Table B.13: Size measurements for Experiment 3.5

No.	Size (nm)	No.	Size (nm)	No.	Size (nm)
1	2.060	11	3.412	21	3.765
2	2.655	12	3.412	22	3.812
3	2.673	13	3.435	23	3.835
4	2.706	14	3.435	24	3.835
5	2.778	15	3.435	25	3.882
6	2.824	16	3.459	26	3.906
7	2.894	17	3.576	27	4.000
8	2.905	18	3.647	28	4.235
9	2.941	19	3.647	29	4.235
10	3.280	20	3.694	30	4.282

- **Standard deviation**

For each experiment, the standard deviation was calculated based on the measurements presented in the respective table using the Equation B.1.

$$\sigma = \sqrt{\frac{1}{N-1} \sum_{i=1}^N (x_i - x_{avg})^2} \quad (\text{B.1})$$