

Morphological design and structure evaluation of poly(divinylbenzene)-based particles

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„Und am nächsten Tag geht die Sonne wieder auf.“

(Dr. Dirk Strauch)

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1 Abstract

This thesis focuses on advancing the synthesis of polydivinylbenzene (PDVB) microparticles via precipitation polymerization and swelling techniques, aiming to tailor their morphological features for enhanced applications, particularly in size exclusion chromatography (SEC).

The first part focuses on the synthesis of core-shell particles via precipitation polymerization, consisting of a non-porous core and a porous shell, intended as column material for SEC. Monodisperse, non-porous core particles were reliably produced using cost-efficient standard laboratory equipment in place of specialized devices. Next to shell growth, it could be shown that low-molecular-weight porogens common for suspension polymerization do not yield pores suitable for SEC in precipitation polymerization under the tested conditions. This could be explained by the lack of confined space during particle formation in precipitation polymerization. The synthesized particles proved effective for hydrodynamic chromatography (HDC) and can be used as size standards for analytical applications like particle size analyzers.

The second part presents an approach to PDVB particle synthesis by combining precipitation polymerization with a template-swelling technique. Three distinct strategies involving different polystyrene templates were explored, resulting in particles with intricate morphologies, including surface grooves and hollow cores. SEM analysis revealed the impact of template architecture on the particle morphology. The resulting particles with adjustable void sizes hold promise for various applications, like catalysis and delivery systems. This work provides a proof of concept, and future research may further extend control over the nanoarchitecture and explore other templating methods.

The third part explores an alternative route to create a porous shell on a highly crosslinked PDVB core particle, utilizing the template swelling method with macromolecular porogen aiming at pore sizes larger than 10 nm. The two-step swelling method sought to integrate the PS porogen into the precursor particle shells and subsequently remove it to leave behind the desired porous structure. However, despite successful incorporation of the PS template during the initial swelling stage, the subsequent removal of the porogen did not lead to the expected porous structure. Excessive, unintended crosslinking, possibly due to chain transfer reactions or residual double bonds in the PDVB system, appears to have hindered the removal of the PS template. While the procedure still seems promising, further research needs to be done to lower the crosslinking degree of the precursor particle shell.

The findings contribute to the ongoing efforts to enhance the versatility of PDVB particles for diverse applications, like for example for HDC chromatography or in the biomedical field, emphasizing the importance of combining and tailoring synthesis methods to achieve specific morphological features. Parts of this thesis were performed in collaboration with PSS GmbH, Mainz and LiNaCon Dr. Ingo Lieberwirth, Mainz.

2 Zusammenfassung

Diese Arbeit beschäftigt sich mit der Weiterentwicklung der Synthese von Polydivinylbenzol (PDVB)-Mikropartikeln mittels Fällungspolymerisation und Quelltechniken, um deren morphologische Eigenschaften gezielt anzupassen – insbesondere für Anwendungen in der Größenausschlusschromatographie (GPC).

Der erste Teil befasst sich mit der Synthese von Kern-Schale-Partikeln, bestehend aus einem unporösen Kern und einer porösen Schale, durch Fällungspolymerisation welche als Säulenmaterial für die GPC eingesetzt werden sollen. Monodisperse, unporöse Kernpartikel konnten zuverlässig mit kostengünstiger Standardlaborausrüstung anstelle von speziellem Equipment hergestellt werden. Neben dem Schalenwachstum konnte gezeigt werden, dass niedrigmolekulare Porogene, wie sie häufig in der Suspensionspolymerisation verwendet werden, unter den getesteten Bedingungen in der Fällungspolymerisation keine für die GPC geeigneten Poren erzeugen. Dies lässt sich durch die fehlende Begrenzung des Reaktionsraumes während der Partikelbildung bei der Fällungspolymerisation erklären. Die hergestellten Partikel eignen sich jedoch für die hydrodynamische Chromatographie (HDC) und als Größenstandards in analytischen Anwendungen wie Partikelgrößenanalysatoren.

Im zweiten Teil wird Fällungspolymerisation mit einer Templat-Quelltechnik kombiniert. Drei Strategien mit verschiedenen Polystyroltemplaten führten zu Partikeln mit komplexer Morphologie, etwa Oberflächenrillen oder hohlen Kernen. Elektronenmikroskopische Aufnahmen zeigen dabei den Einfluss der Templatarchitektur auf die entstehende Partikelmorphologie. Die erhaltenen Partikel erscheinen vielversprechend für Anwendungen in Katalyse oder Wirkstofftransport. Die Ergebnisse belegen die prinzipielle Machbarkeit und bieten Ansätze zur weiteren Kontrolle der Feinstruktur.

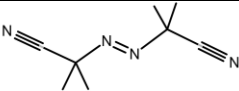
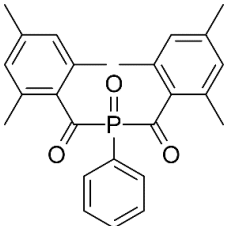
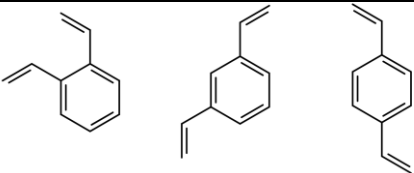
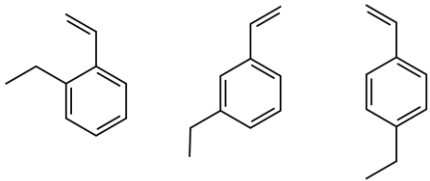
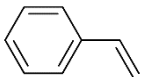
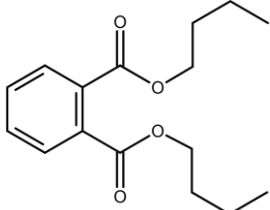
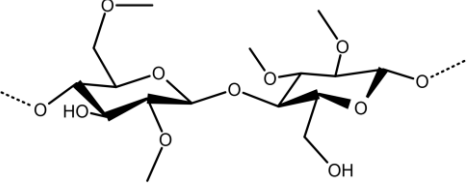
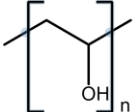
Im dritten Teil wird ein alternativer Ansatz zur Erzeugung poröser Schalen auf hochvernetzten PDVB-Kernen mittels makromolekularer Porogene und Templat-Quellmethode verfolgt, mit dem Ziel, Porengrößen über 10 nm zu erzielen. In einem zweistufigen Quellverfahren sollte das PS-Porogen zunächst in die Schale der Präkurspartikel eingebracht und anschließend entfernt werden, um die gewünschte poröse Struktur zu erzeugen. Obwohl das PS-Porogen erfolgreich in die Partikelschale eingebracht wurde, gelang die Entfernung nicht wie erwartet. Wahrscheinlich verhinderte eine unbeabsichtigte Übervernetzung, etwa durch

Kettenübertragungen oder verbleibende Doppelbindungen, die Porenbildung. Der Ansatz bleibt jedoch vielversprechend und erfordert weitere Optimierung des Vernetzungsgrads.

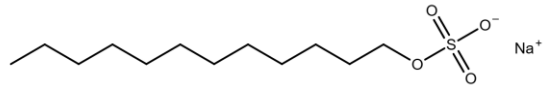
Die Ergebnisse dieser Doktorarbeit leisten einen Beitrag zur Weiterentwicklung vielseitig einsetzbarer PDVB-Partikel, beispielsweise für die HDC-Chromatographie oder Anwendungen im biomedizinischen Bereich, und demonstrieren, wie wichtig es ist, Synthesemethoden zur Erzielung spezifischer morphologischer Merkmale zu kombinieren und aufeinander abzustimmen. Teile der Arbeit wurden in Zusammenarbeit mit PSS GmbH, Mainz, und LiNaCon Dr. Ingo Lieberwirth, Mainz, durchgeführt.

3 Structures and Abbreviations

3.1 Structures

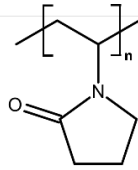
Compound role	Structure	Name
Initiators		
AIBN		azobisisobutyronitrile
BAPO/ Irgacure 819		bis(2,4,6-trimethylbenzoyl)- phenylphosphineoxide
Monomers		
DVB		divinylbenzene (isomeric mixture)
EVB		ethylvinylbenzene (isomeric mixture)
Sty		styrene
Swelling Agent and Stabilizers		
DBP		dibutyl phthalate
Methocel		methyl cellulose
PVA		polyvinyl alcohol

SDS



sodium dodecyl sulfate

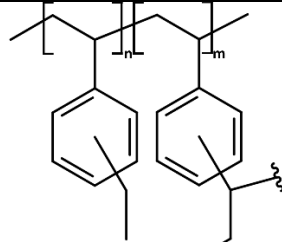
PNVP



poly-*N*-vinylpyrrolidone

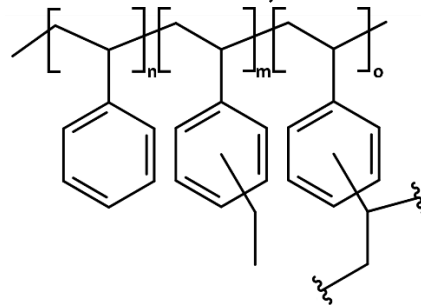
Polymers

PDVB



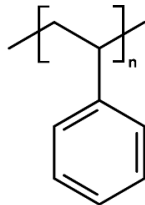
poly(divinylbenzene)
including EVB units

P(DVB-co-Sty)



copolymer composed of DVB and
Sty units
including EVB units

PS



poly(styrene)

3.2 List of Abbreviations

Table 1: List of abbreviations

Abbreviation	Explanation / Name	Abbreviation	Explanation / Name
ACN	acetonitrile	min	minute
AIBN	azobisisobutyronitrile	P(DVB-co-Sty)	poly(divinylbenzene-co-styrene) = copolymer composed of DVB and Sty subunits
ATRP	atom transfer radical polymerization	PAAm	Polyallylamine
BAPO	bis(2,4,6-trimethylbenzoyl)-phenyl phosphine oxide	PDVB	poly(divinylbenzene)
BSE	backscattered electron	PNVP	poly-N-vinylpyrrolidone
DBP	dibutyl phthalate	PP	polypropylene
DVB	divinylbenzene	PSD	particle size distribution
ESI	electronic supporting information	PS	poly(styrene)
EtOH	ethanol	PVA	polyvinyl alcohol
EVB	ethyl vinylbenzene	RAFT	reversible addition–fragmentation chain-transfer polymerization
GMA	2,3-epoxypropyl methacrylate	RI	refractive index
GPC	Größenausschluss-chromatographie	s	second
h	hour	SDS	sodium dodecyl sulfate
HDC	hydrodynamic chromatography	SE	secondary electron
HPLC	high pressure liquid chromatography	SEC	size exclusion chromatography
HMDS	hexamethyldisilazane	SEM	scanning electron microscopy
KOH	potassium hydroxide	Sty	styrene
LALS	static low angle light scattering	TEM	transmission electron microscopy
LM	light microscopy (optical microscopy)	THF	tetrahydrofuran
MALS	multi angle light scattering	UV	ultraviolet radiation (wavelengths of 10–400 nm)
Methocel	methyl cellulose		

4 General Introduction

In the past decades, the necessity for polymer particles in the research fields of biomedicine and chromatography has risen.¹⁻³ Polymer particles are playing a vital part in biomedical applications like drug delivery systems, catalysts, and as sorbent materials.⁴⁻⁹ Compared to inorganic particles they offer a much wider variety of inherent properties, like better chemical stability in acidic conditions, and can be tailored to be less brittle than silica.^{10,11} Aside from polyethylene, polystyrene-based particles are the most common type of polymer used in biomedical applications such as cell sorting and immunoprecipitation.¹²

Polydivinylbenzene-based (PDVB) particles are chemically related to polystyrene but generate a much higher crosslinking degree within the particle because of the additional vinyl group of the DVB monomer. Thus, they add chemical, thermal and mechanical stability to the properties of styrene-based systems.^{4,11,13} Furthermore, fully porous particles based on Poly(styrene-co-divinylbenzene) are a common material used as stationary phase in different types of chromatography.¹⁴⁻¹⁷

These polymer particles can be synthesized via a wide range of methods like precipitation polymerization,^{18,19} emulsion polymerization,²⁰ suspension polymerization²¹ and swelling techniques,²²⁻²⁵ with each of these methods having their own variety of advantages and disadvantages for the resulting properties of the yielded particle.^{26,27} Dimension control, for example, is well achievable with precipitation polymerization and emulsion polymerization, while suspension polymerization and swelling methods offer many possibilities to introduce certain properties to the particle, like porosity for size exclusion chromatography (SEC) for example. In such manner, non-porous PDVB particles by precipitation polymerization offer good mechanical stability and can serve as the basis for further surface modification, but the introduction of significantly large pores to separate macromolecules effectively was explored with varying results so far.^{10,28-30}

Porous particles, on the other hand, are well established as stationary phase materials in SEC and show better separation efficiency the smaller the particles are.¹⁴ Unfortunately, the applicable size of these particles has a lower limit since higher packing densities of smaller particles lead to higher back pressures and damage to the analyte molecules through shear stress.^{14,31-33}

To improve or tailor the properties of PDVB-based polymer particles, more complex structures, like core-shell particles, have been explored in addition to the simpler fully porous or non-porous architectures.^{4,26,34–36} For the example of SEC, a core-shell particle with a non-porous core and a porous shell would solve the problem of separation efficiency vs. shear stress by offering a comparatively small pore volume per particle. This lowers the overall diffusion pathway accessible for the analytes without reducing the size of the particle further.³⁷

Employing different existing synthesis methods in sequence is a promising approach to achieve new forms of PDVB-based polymer particles which combine the advantages of the different simple architectures in one particle or may even lead to unexpected properties.

5 Aim and Outline of the Thesis

This thesis explores different synthetic procedures to enhance control over polydivinylbenzene (PDVB) particle architecture.

In the first part (chapter 7.1), the aim is to synthesize core-shell PDVB particles via precipitation polymerization, featuring a stable, highly crosslinked core and a porous shell suitable for macromolecule separation in size exclusion chromatography (SEC). An alternative synthesis route to incubator bottles is developed and optimized in terms of reagents and reaction conditions for the given lab environment. Next, the particle shell growth in precipitation polymerization is explored and the introduction of low-molecular-mass porogens to the shell synthesis is studied. The particle sizes are monitored by light microscopy (LM), while scanning electron microscopy is used to study the particle morphology and porosity. SEC column performance tests are used to assess the particle's suitability as separation media.

The second part (chapter 7.2) presents PDVB-based particles created by combining precipitation polymerization and a template-swelling technique.³⁸ The study examines the impact of template architecture on the morphology of the resulting PDVB particle, using three different polystyrene templates. Swelling and polymerization processes are monitored by LM, while SEM of particle cross-sections provide detailed morphological insights.

In the final part (chapter 7.3), an alternative method to create a porous shell on a highly crosslinked PDVB core (from chapter 7.1) is explored using template swelling with a macromolecular porogen. The goal is to create a precursor PDVB particle with a swellable shell. The shell of the precursor particle should then be swollen with styrene followed by polymerization to create the template. In the last step, a PDVB network is formed and the template is removed, creating pores in the shell structure. LM is used to track particle sizes, and SEM to characterize morphology and porosity.

6 Theoretical Background

6.1 PDVB in the Field of Particle Research

Divinylbenzene (DVB) is chemically similar to styrene but can be used as a crosslinking unit during polymerization due to the one additional polymerizable vinyl group per benzene ring compared to styrene with only one vinyl group. Therefore, polymer networks can be created with DVB, while styrene results mostly in linear chains when polymerized. Because of the chemical similarity, divinylbenzene can easily be added to styrene polymerizations without the need for large adaptations in the synthesis setup and thus is a favored crosslinker in styrene-based systems.^{39–42} The higher the percentage of the used DVB during polymerization, the higher the crosslinking degree in the product will be and the lower the swellability will be.

In the field of particle research, this relation is used to alter existing polystyrene-based systems with DVB to create various particle architectures ranging from (highly crosslinked) non-porous spheres to porous or hollow particles which all have a relatively homogeneous composition. More complex architectures where the composition varies in different domains of the particle are composite particles like Janus particles, core-shell structures, or less symmetrical shapes such as crescent-shaped composite particles, for example. An overview about these architectures is given in Figure 1. While there are some advances in the nano particle regime (1-100 nm) as well, this thesis focuses mainly on microspheres and thus this chapter will highlight the state-of-the-art knowledge for particles ranging from 1-1000 μm .

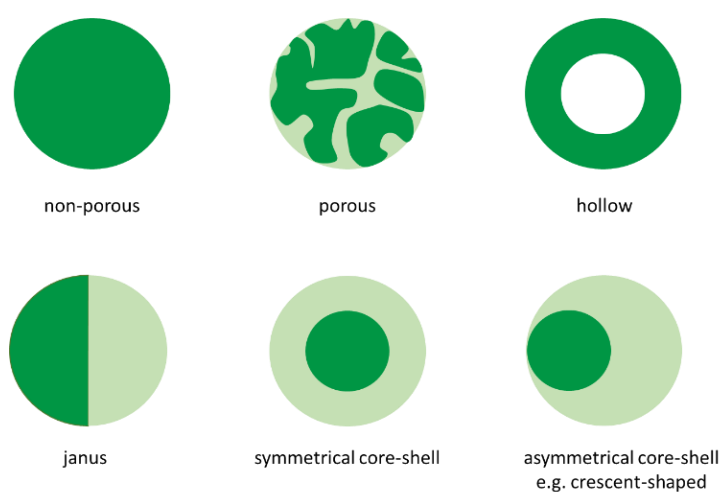


Figure 1: Schematic depiction of different possible particle architectures involving divinylbenzene

Non-porous microspheres are uniform, solid spherical particles that do not possess any pores and are made of a single polymer or a combination of polymers, like styrene and divinylbenzene. Such particles can be synthesized with a narrow size distribution and a high percentage of divinylbenzene via stabilizer-free precipitation polymerization.^{19,43–45} Due to the absence of stabilizers, these microspheres have a very clean surface and the high percentage of DVB results in residual unreacted vinyl groups being present on the particle surface giving access to further modifications.^{9,10,46–49} For example, functionalization with first poly(allylamine) (PAAm) and nanodiamond layers by layer-by-layer deposition and then further modification with C18 chains results in a thermally and pH-stable material for high pressure liquid chromatography (HPLC).¹¹ More specific modifications can be done by grafting to or grafting from methods with for example hydrophilic polymers to yield specialized materials for HPLC or cation-exchange materials for protein separations.^{50–53}

In comparison to solid microspheres, particles with a **porous** structure possess some important features which can be exploited in the following specific applications:

Firstly, the pores create a much higher surface area, which can be used for chemical reactions or interactions. Therefore, porous particles are often applied as ion exchangers,^{29,54} support material for catalysts,^{29,55–57} or as sorbent materials.^{7,29,48,58} Furthermore, pores can be reversibly loaded with molecules as active agents creating carrier particles for biomedical application such as in the field of controlled drug release.^{3,5,6,29}

An important sector where porous particles can be applied is liquid chromatography.^{14,29,59} Here, materials with a significant DVB content are common since highly crosslinked materials are needed to avoid swelling of the stationary phase which would result in clogging of the column. Size exclusion chromatography (SEC, see also chapter 6.4.3) in organic solvents needs stationary phase that is chemically close to the solvent to avoid unwanted interactions of the stationary phase and the analyte. This requirement is usually fulfilled by using porous particles made from styrene and DVB.^{14,59–61} These porous poly(styrene-co-divinylbenzene) particles are also a valued stationary phase for HPLC columns when further functionalized for the respective purpose, for example by chloromethylation.^{54,62–64}

As diverse as their applications are, the synthesis methods for porous particles are equally numerous. They can be prepared by precipitation, suspension, dispersion, and emulsion

polymerization as well as more complex methods like swelling techniques (seeded growth), via microfluidics, or electrospraying.^{28,29,59,65–67} Some of these methods will be covered in more detail in the succeeding chapter (6.2).

Hollow particles, also termed capsules, contain a singular void inside the sphere, usually in the center of the particle. When this void is filled with air, such particles possess a lower density compared to solid microspheres. This architecture can be achieved by either direct polymerization (suspension polymerization)²¹ or by the removal of the core component (etching or dissolution) of a core-shell particle.^{68,69} The void in the center of the particle stemming from this procedure can then serve as a reservoir for other molecules making such particle architectures interesting as controlled release materials.^{70,71} Multi-hollow particles are a variation of hollow particles, consisting of multiple inner voids and a closed surface, which are usually obtained through seeded polymerizations or post-treatment processes.⁷² The separated voids enable the particles to encapsulate different reagents which makes them a more sophisticated material for multi-drug delivery.^{73,74}

Janus particles are spheres with two distinct hemispheres or regions, each with different properties or compositions.^{75–77} More asymmetrical shapes include two spheres of different properties fused together creating either dumbbells, when the spheres are of the same size, or snowman-like architectures, if one of the spheres is smaller than the other.^{78,79} These two different sides make them very useful for applications requiring asymmetry such as catalysis, solid surfactants (Pickering emulsions) and building blocks for self-assembling systems.^{79–83} One application example which involves DVB on one side of the Janus particle is the creation of superhydrophobic coatings by a controlled orientation of the DVB side to the top of the surface while the silica side of the particle is used for chemical bonding to the substrate.⁸⁴

Core-shell particles are a very versatile category of spheres. Rudimentarily, they consist of a core compound and a shell surrounding it. Various architectures can emerge depending on the type of synthesis and the ratio of the used core and shell compounds.⁴ The most common type is the symmetrical core-shell particle with one core sitting in the center of the

particle.^{34,37,85} The core and shell can have different properties, providing versatility in applications like, for example, drug delivery systems, catalysts, sensors, surface coatings and pollution control devices.^{4,85–89}

The most common way to synthesize core-shell polymers is in 1-3 steps using precipitation, dispersion, or emulsion polymerization as for example seeded polymerization (two stages) or crosslinking reactions in micelles.^{4,36} Usually, DVB is used as a crosslinker in either the core or the shell part of the particle,⁴ but some applications, like liquid chromatography, require such a high crosslinking degree that DVB is used as the main monomer.⁸⁵ With the core-shell approach, proven systems in chromatography like glass beads can be combined with other materials such as styrene and divinylbenzene, thus expanding the possibilities of their uses. For instance, a poly(styrene-co-divinylbenzene) shell on a glass bead can be further modified to create ion exchangers with a mechanically stable glass core.^{37,90,91}

When used as the main monomer for the core, DVB creates particles with residual double-bonds on the particle surface.^{43,85} This feature can be utilized to graft a lightly-crosslinked shell layer onto the highly-crosslinked core by reversible addition–fragmentation chain-transfer (RAFT) or atom transfer radical polymerization (ATRP) with the possibility to change the hydrophilicity of the particle depending on the chosen monomer for the shell.^{36,50,51,92} In precipitation polymerization, these double-bonds are used as well to grow a shell of the same kind or other properties on the particle core.^{35,43}

If the shape of a core-shell particle is not symmetrical, morphologies such as **crescent-shaped** structures are described where the core is asymmetrically displaced from the particle center and may touch the outer perimeter of the particle. This can be achieved in styrene/divinylbenzene systems via seeded emulsion polymerization, where the crosslinking degree directly influences the resulting architecture: with an increasing crosslinking degree in the seed particle, the resulting core-shell morphology changes from a symmetrical core-shell to a crescent-shaped structure.^{4,39,93} Further increase of the crosslinking degree again results in more symmetrical particle architectures again such as snowman-like or raspberry shapes. The versatility of this specific system makes it a perfect test model for colloidal research.³⁹

6.2 Free Radical Polymerization Techniques for Polymer Particles

Free radical polymerization is a very versatile polymerization technique thanks to its broad applicability to a broad range of monomer types and different reaction setups. This chapter will give a brief overview of the most common types used for particle production: precipitation-, dispersion-, suspension-, emulsion- and seeded polymerization.

In terms of size ranges, the various polymerization methods discussed here cater to a diverse spectrum of particle sizes as shown in Figure 2.^{27,57,94,95} Precipitation and dispersion polymerization typically yield particles in the nanometer to micrometer range, suitable for applications requiring finely tuned control over the particle size. On the other end of the size spectrum, suspension polymerization offers versatility in producing particles across the micrometer scale and extends into the millimeter range but yields particles with a broader size distribution. Emulsion polymerization covers the production of polymer particles with sizes below one micrometer down to a few tens of nanometers and provides a narrow size distribution for the resulting particles. Lastly, seeded polymerization allows for precise control over particle size and yields particles in the submicron and micrometer range depending on the size of the employed seed particle. In the following, the respective methods are presented and compared to each other in terms of their advantages and disadvantages.

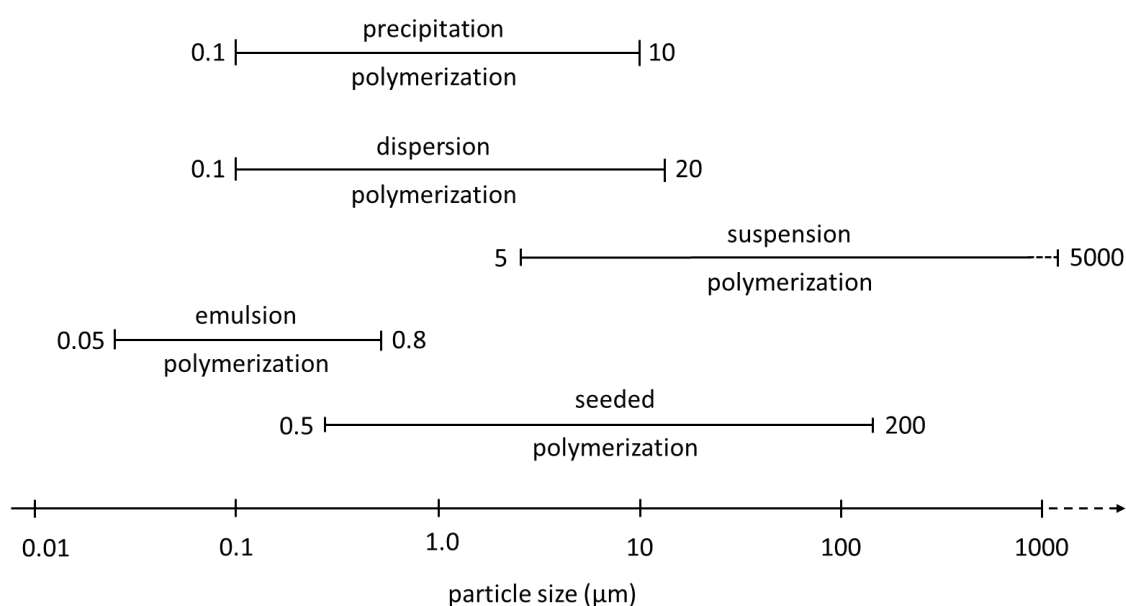


Figure 2: Schematic diagram of approximate size ranges of polymer particles made by free radical polymerization techniques according to literature^{27,57,94,95}

Precipitation Polymerization

In precipitation polymerization, the monomer and initiator are typically soluble in the reaction medium at the beginning of the process. As polymerization proceeds, the solubility of the growing polymer chains decreases, leading to their precipitation when reaching a critical size. Particles are then formed by the aggregation of the precipitated polymer chains and can grow further by adding new precipitates to their surfaces.^{18,96}

Precipitation polymerization does not require colloidal stabilizers, like sodium dodecyl sulfate (SDS) and poly-*N*-vinylpyrrolidone (PNVP). Therefore, the difficulties of removing the stabilizer from the particle post-polymerization are eliminated.^{19,95} The absence of stabilizers makes the polymerization process more difficult to handle, though, because the system becomes more sensitive to disturbances which can lead to agglomeration. The product particles can be easily separated from the reaction medium by sedimentation or centrifugation and rarely need many purification steps since residual oligomers and educts are easily removed with the reaction medium and a few extra washing steps with suitable solvents.^{18,19}

Precipitation polymerization allows for precise control over the size and morphology of the polymer particles via the concentration of the monomer and initiator as well as environmental factors such as reactor geometry, stirring conditions, temperature, and reaction time.^{27,65,97,98} This makes this method suitable for applications where uniformity is crucial. The uniform growth is beneficial to synthesize symmetrical core-shell particles with a centered core, for example.^{43,85} However, the applicability of this method is rather narrow since it requires a precise solvent-monomer-polymer-matching (θ solvent) which is not available for all types of polymers.⁹⁹

In recent years, various optimizations or alternative setups to the standard precipitation polymerization process were established to overcome polymerization challenges: with distillation precipitation polymerization reaction time can be reduced^{44,65} and photoinduced precipitation polymerization avoids heat-induced particle stickiness and thus creates a lower risk for agglomeration.⁴⁵ Other examples are reflux precipitation polymerization, solvothermal precipitation polymerization, controlled “living” radical precipitation polymerization and self-stabilized precipitation polymerization.¹⁸

Dispersion Polymerization

Dispersion polymerization is a special form of precipitation polymerization, as it also starts from a homogeneous monomer solution and the resulting polymer precipitates during the polymerization leading to a dispersion of monosized polymer particles.^{95,96}

Unlike regular precipitation polymerization, dispersion polymerization relies on the use of stabilizers to maintain the dispersion of polymer particles and prevent them from sticking together or agglomerating.^{100,101} Common steric stabilizers used for dispersion polymerization range from homopolymers and macromonomers to graft- or block copolymers.^{95,100,102–105} In addition to the parameters that also influence the outcome of precipitation polymerizations, in dispersion polymerization the particle size is controlled by the type and concentration of the stabilizer. While stabilizers facilitate the handling of dispersion polymerization during the reaction step by preventing particle agglomeration, they present a challenge during the subsequent purification phase. In the purification process, the stabilizers need to be removed from the polymer product, which requires additional effort. This is due to stabilizers interfering with the desired properties or applications of the polymer, and their presence might be undesirable in the final product.

Complete removal of the stabilizer may not be entirely achievable, as some of the stabilizer becomes bound to the particle during the radical polymerization process like it is the case for PNVP in the production of polystyrene particles in ethanol.¹⁰⁵ This yields particles with altered properties on the particle surface compared to their pure counterparts such as changing hydrophobic polystyrene particles to hydrophilic ones with PNVP. However, this phenomenon can be used to deliberately incorporate functionalities on the particle surface.

As for precipitation polymerization, the used reaction medium needs to be matched carefully with the monomer and polymer as well as the stabilizer: monomer, initiator and stabilizer need to be soluble in the reaction medium, while the polymer needs to be insoluble. Accordingly, the range of application is limited to these parameters.⁹⁴

Suspension Polymerization

As outlined by IUPAC,⁹⁶ suspension polymerization is a process where the polymer is formed within monomer droplets which are dispersed in a continuous, liquid phase that is a non-solvent for both the monomer and the polymer. This two-phased system is prevented from coalescence by stabilizers, and the initiator is usually located in the monomer phase.

Since water is a non-solvent for many monomers and polymers, it is a commonly used continuous phase and makes this type of reaction relatively cheap, well scalable and environmentally friendly compared to dispersion polymerization.^{14,100}

The reaction mechanism is similar to bulk polymerizations as the conditions in each droplet are equal. Yet, the heat from exothermal reactions is more efficiently dissipated in this setup as the surface-to-volume ratio of the droplets is advantageous for heat dissipation compared to bulk reactors and water serves as a good heat conductor. In consequence, higher polymerization rates can be tolerated without risking to evaporate the educts or thermal runaway.^{57,100} The resulting particle size is dependent on the droplet size of the monomer phase. With parameters as the stirring speed, the type and concentration of the stabilizers used, the volume fraction of the monomer and the viscosities of both phases, the droplet sizes during polymerization can be adjusted.¹⁰⁰ Other properties of the resulting particles, like for example the porosity, can be tuned by the addition of good or poor solvents to the monomer phase.^{27,106}

Similar to the particle production processes, the overall separation of product and liquid phases can easily be done by sedimentation, centrifugation, and filtration, but the removal of the used stabilizers can be problematic. Common stabilizers for this type of process are natural gums, cellulose ethers, PNVP and polyvinyl alcohol (PVA).²⁷ Unfortunately, as coalescence and separation of droplets occurs steadily during the polymerization process, the size distribution that can be achieved by this technique is relatively broad compared to aforementioned processes.¹⁴ However, for industrial uses this problem can be partially alleviated after isolation of the particles from the reaction medium by mechanically sorting the particles according to their size with sieving or classifying devices at the cost of the overall yield.^{29,95}

Emulsion Polymerization

Similar to suspension polymerization, the reaction setup in emulsion polymerization is an inhomogeneous system consisting of more than one phase which are stabilized.⁹⁶ But in contrast to suspension polymerization, the initiator is dissolved in the continuous (usually aqueous) phase instead of the monomer phase.²⁷ A prominent example for this “classical” emulsion polymerization is the synthesis of polystyrene particles.

Next to bigger monomer droplets, the monomer is also located in small, surfactant stabilized micelles and at very low concentrations dissolved in the continuous phase.¹⁰⁷ Initiation starts in the continuous phase, where the initiator is dissolved.^{27,107} These initial radicals can react with the small amount of dissolved monomer in the continuous phase and create oligomers with active radical sites. These oligo radicals can further react in several ways: they either terminate in the continuous phase by combination or disproportionation or add further monomer molecules from the continuous phase until the polymer chains precipitate or are adsorbed by a micelle where the oligo radical proceeds growing into a polymer chain. Starting from the latter case, a particle can form from each micelle. While chain growth is active in the micelle, more monomer can diffuse into it from the continuous phase which is fed by the bigger monomer droplets to maintain equilibrium. This growth is only dependent on the available monomer supply and can exceed the original size of the micelle. Thus, the particle size in emulsion polymerization is not dependent on the micellar size at the beginning of the reaction but rather on every parameter that dominates the polymerization rate.^{27,107} In consequence, it can be well controlled by factors such as solubility of the monomer in the continuous phase, the initiator and surfactant concentrations and the polymerization temperature.^{27,107} Particles that grow above the original size of their micelle also need further surface stabilization and thus adsorb more surfactants from the continuous phase or scavenge them from micelles that have not reacted yet. In this way, the overall emulsifier concentration, and with it the initial number of micelles, is another factor to control particle sizes here.^{107,108}

Analogous to suspension polymerization, the advantage of emulsion polymerization is the high percentage of water in the reaction mixture, which provides a good heat transfer. The high water percentage is also more environmentally friendly than methods that rely on organic solvents, like precipitation polymerization.¹⁰⁷ The need for stabilizers, though, comes with the same advantages and disadvantages as discussed before. Stabilizers may be avoided

by using emulsifier-free emulsion polymerization techniques, where the growing particle is stabilized by its own polymer chain, or more specifically by the surfactant-like chain end containing the initiator. This method also yields very narrow particle size distributions.⁹⁵

Swelling Techniques

During seeded polymerizations or swelling techniques, seed particles derived from emulsion or dispersion polymerization are grown further by swelling them with monomer followed by polymerization. The most well-known type of is the seeded emulsion polymerization, where seed particles are added to the reaction mixture at the beginning which generally leads to particle growth instead of new particle formation.⁹⁶

For the classical swelling technique, the monomer, initiator, stabilizers, and seed particles are mixed with a continuous phase that is a non-solvent for the monomer. The low solubility of the monomer in the continuous phase facilitates its absorption into the particles, causing them to swell.^{95,109} To avoid phase separation and deformation, it is necessary to use the same type of monomer for swelling as the monomer used to build the seed particle.⁹⁵ Yet, in certain cases such as the production of core-shell particles, phase separation is desired and can be controlled by the hydrophilicity of the monomer compared to the seed.³⁴ The amount of emulsifier needs to be high enough to prevent the swollen and thus sticky particles from coagulating but low enough to allow absorption of monomer. If the stabilization of the monomer droplets is too effective, secondary nucleation can occur in the subsequent polymerization step.⁹⁵ Other parameters that can be adjusted to avoid secondary nucleation are the number of seed particles per volume and the concentration of the initiator.²⁷ If the particles do not coagulate, the size distribution of the seed particles determines the size distribution of the grown particle.⁹⁵

For the classical swelling approach, the diameter increase only lies around a factor of two. However, adding an organic compound with low molar mass or oligomers as an activator before or during the swelling process can significantly enhance swelling, reaching 100 - 5000 times the seed volume.^{27,61,95} The activator acts as a stabilizing agent of the oil phase to prevent Ostwald ripening of the hydrophobic droplets (see also chapter 6.3 “Internal Particle Growth”).¹¹⁰ Due to the high monomer load and the resulting increased tendency of particle coalescence, stabilizing the mixture is of high importance in this “activated swelling” process.

This technique is also suitable to introduce pores into the particle: the seed is swollen with a crosslinkable monomer, and the seed polymer serves as a template for the later pores. After the polymerization of the swelling monomer, the seed polymer can be removed with a suitable solvent yielding pores.²² The pore sizes are controllable by the molar mass of the seed polymer and by the choice of the activator molecule.⁹⁵

Swelling can also be achieved in a more dynamic manner:⁹⁵ Initially, seeds and monomer are combined in a solvent for the monomer, followed by the gradual addition of a non-solvent for the monomer. The decreasing solubility of the monomer in the medium forces the monomer to partition preferentially into the seed particles which slowly swells them.¹¹¹ Alternatively, reducing the temperature of the reaction mixture can be employed to achieve this dynamic swelling process. Nevertheless, this process is more suitable for polymerizations that do not rely on thermal initiation or needs to be coupled with the above described solubility-based approach afterwards.²⁵

Overall, these particle swelling methods are applicable for a wide range of polymer-monomer mixtures and can thus meet the requirements for a range of applications.^{27,95} However, due to the many swelling steps that can be involved during the synthesis, this technique is rather time consuming and therefore expensive.⁵⁷

6.3 Particle Growth Mechanisms

Particle growth mechanisms can be roughly characterized by two categories as shown in Figure 3: internal growth or external growth. On one hand, growth can happen inside the particle via swelling with monomer and consecutive polymerization. On the other hand, growth can happen on the outside of the particle by processes like oligomer scavenging/precipitation to the surface and particle coalescence via collision.

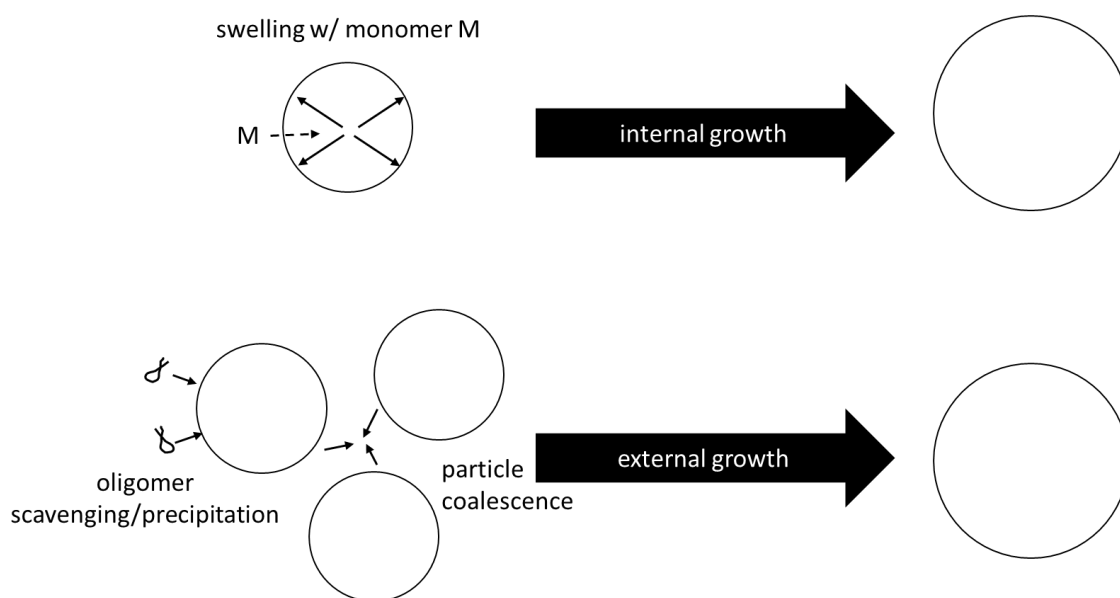


Figure 3: Schematic depiction of the two particle growth mechanism categories: internal growth via monomer swelling and external growth via oligomer scavenging/precipitation or particle coalescence.

Internal Particle Growth

Internal particle growth is the main process during swelling methods like seeded polymerizations. Here, polymeric seed particles are swollen with a monomer-initiator mixture which is then polymerized inside the particle, as discussed in the section above.⁹⁵ The monomer acts as a solvent for the polymer and at least partially dissolves the polymer chains, rendering them mobile again.⁵⁹ This process can be enhanced with the addition of compounds

with low molar masses that do not take part in the following polymerization reaction but (partially) dissolve the polymer chains.¹¹⁰

The swelling process and dissolution of the polymer inside the seeds can go as far as transforming the particles back into emulsifier-stabilized droplets.^{59,110} The present stabilizer concentration needs to be high enough to keep these droplets stable but low enough to prevent the formation of smaller droplets and, thus, new particles. The use of compounds with low molar masses was found to increase the swelling capacity for polystyrene-based seed particles.¹¹⁰ As a slightly water-soluble compound, styrene typically diffuses in small amounts through the water phase during the swelling period. This causes smaller droplets to lose styrene in favor of larger droplets (Ostwald ripening) and might even lead to disruption of the stability of the emulsion. Apparently, already small amounts of water or insoluble small organic molecules hinder this diffusion and keep styrene inside the swollen particle.¹¹⁰

In a sufficiently swollen particle, the mobile polymer chains can rearrange before and during the polymerization. Depending on the monomer that was used for swelling, phase separation can take place that can result in many different particle morphologies such as raspberry, sandwich-like and core-shell structures.^{34,112} If the seed polymer is more hydrophilic than the swelling monomer, for example, the seed polymer chains will gather at the outside of the particle towards the aqueous phase and the newly forming polymer will gather towards the center of the particle.³⁴ This rearrangement can be blocked by a highly crosslinked layer inside the particle acting as a diffusion barrier.³⁴

In case of crosslinkable monomers like DVB, the forming PDVB polymer network inside the particle can induce phase separation upon crosslinking of the growing polymer chains: when a certain degree of crosslinking is reached for a cluster of polymer chains, they precipitate and can form smaller globules inside the droplet.^{9,22} Although these globules might interconnect when they grow larger and touch each other, they will stay separate due to their high crosslinking density.^{9,61} The mobile seed polymer chains are displaced by this process and rearrange around the globules and can be used as a macromolecular pore-forming agents (porogens) to produce pores when washed out with a suitable solvent.^{59,61} Higher average molar masses of the porogenic polymer (the seed particle) were found to enlarge the generated pores, but also increase the risk of binding the porogen chains permanently to the

particle by entanglement and grafting by chain transfer.^{41,59} Thus, the nature of the seed particle has a high influence on the resulting particle.²²

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External Particle Growth

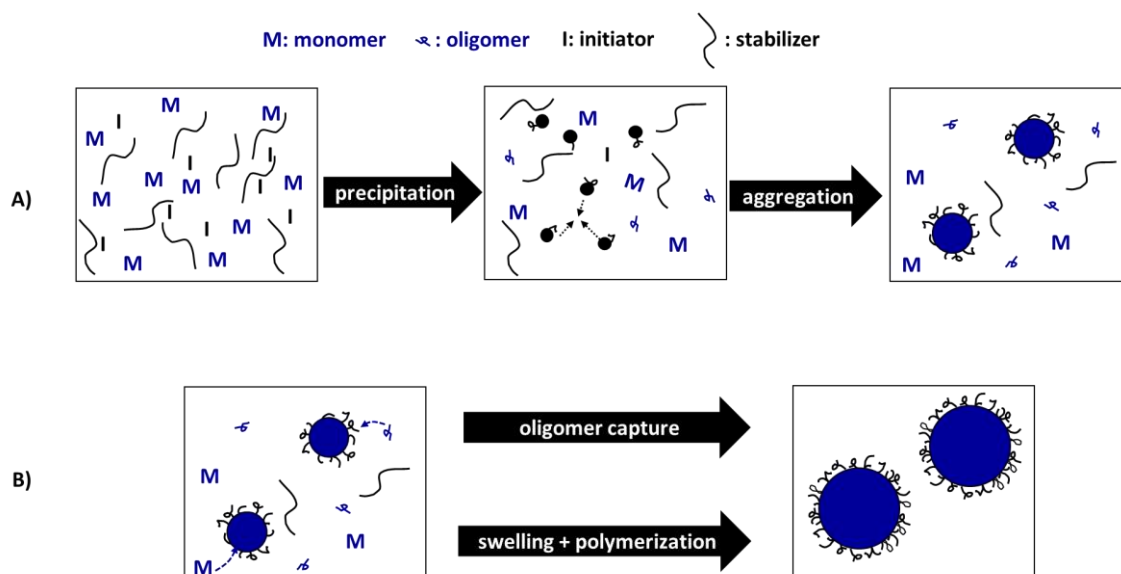


Figure 4: Particle formation mechanism during dispersion polymerization via a nucleation stage (A) and a growth stage (B).

The image was adapted from literature.¹¹³

Particle growth in dispersion polymerization starts with the formation of oligomers (Figure 4A). Depending on their solubility in the respective solvent, the oligomers precipitate out of the solution at a certain degree of polymerization. These first nuclei then aggregate through collision with larger particles having stabilizers adsorbed on their surface (nucleation stage).⁹⁵ If the crosslinking density is low or no crosslinkers are used, monomer and initiator can be absorbed into the particle and further particle growth can happen from within the particle (Figure 4B).⁹⁸ In addition to that, particle growth on the surface of the particle happens by the capture of newly forming oligomers before they can precipitate. Both processes can be summarized as the growth stage. In both cases, enough stabilizer needs to adsorb on the particle surface from the solution to keep the particle stable. The amount of stabilizer in the solution plays a major role here:¹⁰⁰ if the concentration is too low, the adsorption might be too slow or insufficient, which results in agglomeration. If the stabilizer concentration is too high, newly formed oligomers may be stabilized before they can be captured by larger

particles. Secondary nucleation and a broad particle size distribution would result in this case.¹⁰⁰

Since the growing particles compete equally for monomer absorption and oligomer capture, the resulting particle diameter depends on the number and size of stable seed particles at the beginning of the growing process.^{95,100} The resulting particle diameter is thus determined by factors such as initiator concentration, reaction temperature, and monomer load.⁹⁵ For the latter, oligomers precipitate later due to a higher solubility with higher monomer loads and thus larger nuclei form. A higher reaction temperature or initiator concentration increases the concentration of nuclei in the medium which then leads to higher collision rates and larger stable seed particles.

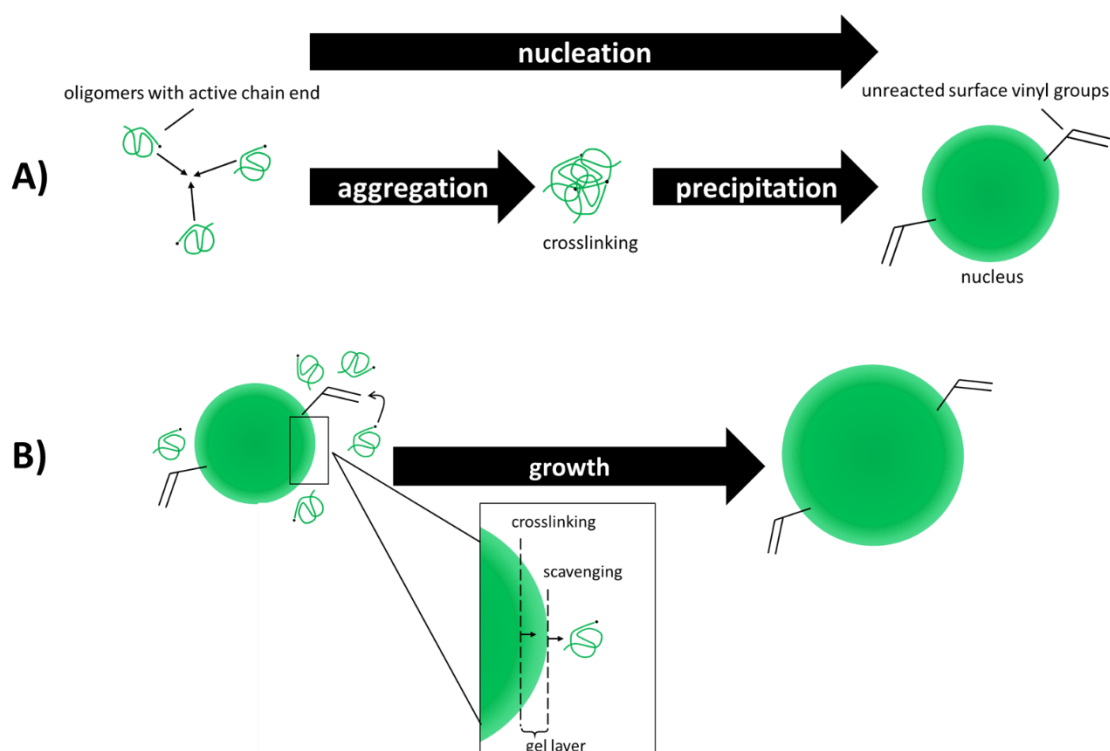


Figure 5: Particle formation mechanism during precipitation polymerization of PDVB as proposed by Downey and Stöver.⁴³ The particle formation mechanism includes a nucleation stage (A) and a growth stage (B). The image was adapted from literature.⁴³

Precipitation polymerization is a process that does not rely on stabilizing agents added to the reaction mixture. Downey and Stöver proposed the following mechanism and explain PDVB particle stability:^{19,43}

At the start of the polymerization reaction, growing oligomers that are still soluble aggregate in solution to form swollen microgels. When they desolvate, they form the first particle nuclei

(nucleation stage). The reason for desolvation of the first aggregates was not stated in the original studies^{19,43} but other groups argue that the aggregated oligomers exceed the solubility limit in the medium quickly after the first crosslinks form. The oligomers thus become one molecule with a high degree of polymerization that precipitates.⁹⁸ Due to the frequent crosslinking happening in PDVB precipitation polymerization, particle swelling and growth from within the particle is not possible after a short while. Growth rather happens on the particle surface by capturing soluble oligomers from the solution.⁴³

For PDVB systems specifically, it was shown that this growing process includes a reactive mechanism where residual double bonds on the particle surface are actively taking part in binding oligomers to the particle before they precipitate compared to mere precipitation and adsorption of oligomers on the surface. The scavenging of oligomers before they precipitate seems to be crucial: when those residual double bonds were blocked by hydrogenation for example, secondary nucleation and broadening of particle size distributions were observed instead of monodisperse particles yielded from DVB polymerization. If the growing process would rely on precipitation alone, it would not be influenced to this extent by the availability of surface double bonds.^{43,98} This formation mechanism was also supported by other groups⁹⁷ who observed the formation of raspberry like particles stemming from nuclei collision in the early stages of the reaction. These irregular shaped particles were then observed to even out over time as more material was added to the particle surface.

Stabilization in this system is provided by the outer layer of the forming particle:^{29,43} before the crosslinking density is high enough to promote desolvation, a swollen gel layer forms, which stabilizes the particle. Newly added soluble oligomers extend this layer from the outside, while the crosslinking process shrinks the layer simultaneously from the inside. Apparently, the gel layer is influenced by the oligomer solubility in the system and has an optimum thickness for stabilization. Lowering the solubility of the oligomer, and consequently reducing the thickness of the gel layer by switching the solvent to acetic acid instead of acetonitrile, resulted in the production of less uniform particles.⁹⁷ On the other hand, higher chances for agglomeration were observed for an increased oligomer solubility caused by the utilization of higher monomer loads.¹⁹ The latter observation can also stem from higher chances of collision between particles, as with higher monomer load, the nuclei concentration also rises.⁹⁸ In addition to stabilization by the gel layer, the particles undergo self-stabilization

at the end of the reaction through the crosslinking process, creating a stable network and a rigid surface that prevents particles from sticking together.^{19,98} Thus, a high concentration of crosslinkable monomer is crucial for this type of stabilization and probably the reason why crosslinker-free systems need to rely on external stabilizing agents more.⁹⁸

6.4 Characterization Methods for Particle Systems

6.4.1 Light Microscopy

Light microscopy (also called optical microscopy) is a widely used non-damaging imaging technique that employs light from the visible spectrum and a system of optical lenses to magnify objects. This gives access to structural details of specimen which are too small for the bare eye.

In general, each microscope technique can reach a certain resolution, where resolution refers to the minimum distance between two points at which they can be distinguished by the observer as two points. Using the Rayleigh criterion, this resolution is defined by:

$$R = \frac{0.61\lambda}{NA} \quad (1)$$

with λ being the wavelength of the used light and NA the numerical aperture, which is defined by:

$$NA = n \cdot \sin \alpha \quad (2)$$

where n is the refractive index of the used medium between the specimen and objective lens. The angle α is defined as half of the light-collecting angle of the used objective. From this equation it becomes apparent that the resolution is higher when short wavelengths are used. Thus, for the visible light spectrum, the resolution is finite. However, the resolution can also be improved by changing the medium between the objective lens and objective to a higher refractive index as for example from air ($n = 1$) to oil ($n = 1.5$). Since the resolution limit with air in the visible spectrum of light is about $0.2 \mu\text{m}$, the bin size for all shown particle size histograms in this thesis is $0.2 \mu\text{m}$, too.^{114,115}

Another important factor to achieve sharp images is the depth of field or DOF. The DOF is the layer thickness in which a specimen is still displayed sharply and is defined by

$$DOF = \frac{1.22\lambda}{NA \cdot \tan \alpha} \quad (3)$$

meaning that a higher NA, for example resulting from measurements in oil, will result in a lower DOF.^{114,115} Only samples that are positioned within this DOF will be displayed sharply. Therefore, if the size of a specimen is close to the size of the DOF, the specimen should be fixed in position to avoid parts of it being displayed blurry. If a specimen is even larger than the DOF, as it can happen for very large droplets or particles, the specimen will never appear fully sharp in the resulting image.

In this thesis, a microscope using wide field- and trans-illumination is used since the observed polymer particles (PS and PDVB), organic droplets and their dispersion media are transparent and colorless. The particles or organic droplets are still visible because their refractive indices are sufficiently different from the chosen dispersion medium, which creates a good contrast and outlines the objects. From these outlines, particle sizes or droplet sizes can be determined, and the size distribution within a sample can be displayed in a particle size distribution (PSD) diagram.

However, in the case where polystyrene particles are added to an emulsion of organic droplets (consisting mainly of the swelling monomer) in water, the particles cannot be distinguished optically from the organic droplets due to their similar optical transparency and lack of color. PSD diagrams can thus only be created from images of purified particles dispersed in a homogeneous liquid.¹¹⁶

6.4.2 Scanning Electron Microscopy and Ultramicrotomy

Scanning electron microscopy (SEM) is another imaging technique besides light microscopy. Here, the interactions of accelerated electrons with the sample material are exploited to create images instead of using light from the visible spectrum. This results in a much lower resolution limit due to the far shorter wavelength of electrons (c.f. chapter 6.4.1) and thus gives access to characterization of nanostructured materials.

Upon contact with the specimen surface, electrons are scattered by the specimen atoms, resulting in either inelastic or elastic scattering. In inelastic scattering, incoming electrons transfer kinetic energy to specimen electrons, causing them to leave the specimen if their energy is sufficiently high, producing secondary electrons (SEs). Conversely, in elastic

scattering, incoming electrons are scattered without significant loss of kinetic energy, leading to the generation of backscattered electrons (BSEs). Since SE are of lower energy, they can only escape from smaller depths or the surface of the sample (5 - 50 nm), as shown in Figure 6. Thus, SE is commonly used for topographical analysis of the specimen surface as performed in this thesis. The higher energy of BSE electrons on the other hand enables them to escape the sample from much deeper specimen layers (50 - 300 nm). Therefore, the detection of BSE electrons can be used for a more detailed analysis of the sample, including differentiation of various elements.^{114,117}

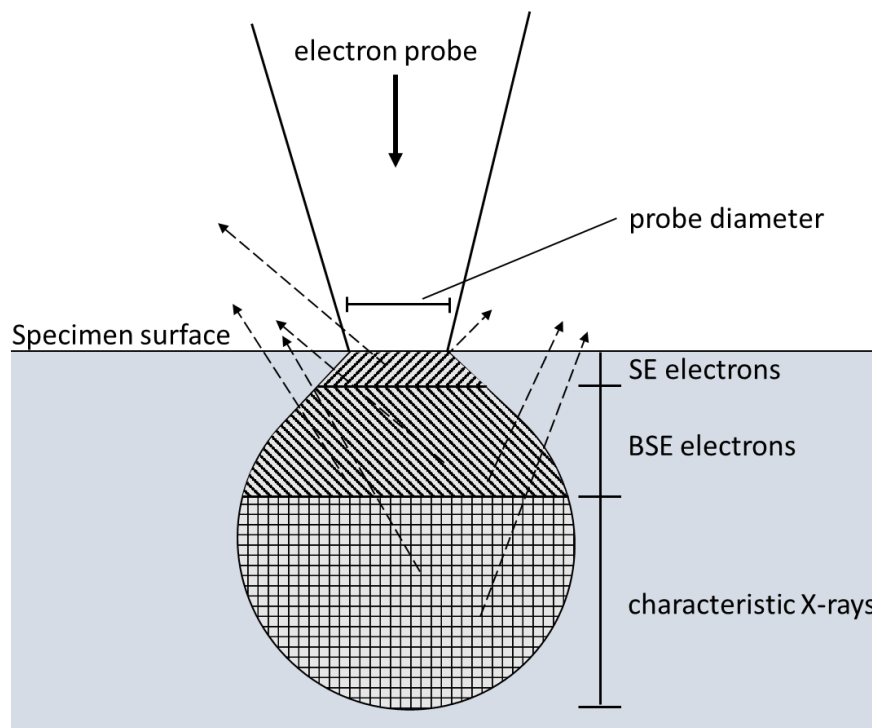


Figure 6: Pear shaped interaction zone of electrons and specimen atoms during an SEM measurement. The image was adapted from literature.¹¹⁴

The contrast creation during SEM imaging depends on the number of electrons measured by the detector while the focused ion beam rasters over the sample surface. The measured electron intensities are mostly influenced by two effects: the trajectory effect and the electron number effect. The trajectory effect occurs when scattered electrons leave the specimen from a surface that is not facing the detector, leading to a lower chance of reaching the detector and thus resulting in a lower signal, which appears darker on the created image ("shadowing effect"). The electron number effect occurs when an electron hits an edge, or an exposed feature of a specimen, as schematically indicated in Figure 7. Due to the pear-shaped

interaction field, electrons hitting these topographies have a higher chance of escaping the specimen compared to electrons hitting a flat, bulky surface. This leads to stronger signals being detected from edges, spheres, or grooved surfaces which makes them appear brighter in the image.

The resolution in SEM imaging is primarily dependent on the probe diameter, with a small diameter leading to a higher resolution. Among others, a small probe diameter can be achieved by increasing the acceleration voltage of the instrument. For this reason, older SEM instruments equipped with thermionic electron guns usually use relatively high acceleration voltages around 25kV. However, this leads to a few disadvantages for the sample: In the best case, the higher voltage leads to more charging effects of samples which are not sufficiently conductive. In the worst case, though, the high voltage can cause structural damage to the specimen.¹¹⁸

To prevent charging, samples which are not electrically conductive by nature, e.g. PDVB particles, need to be covered with a thin layer (5-20 nm) of a conductive material like gold or carbon in a process called sputter coating. During sputtering, gold atoms are dislodged from a target source (cathode) by bombarding it with high-energy ions and then adhere to the sample surface (anode).¹¹⁴ Unfortunately, depending on the layer thickness of the applied conductive layer, this can lead to hiding of features and thus lower the imaging quality, especially when fine structures like small pores need to be assessed. Another way to achieve a small probe diameter is to utilize brighter electron sources. The development of field emission guns led to a tremendous increase of brightness (> 1000x) compared to thermionic guns.^{114,119} As a result, instruments equipped with this first type of electron source can operate at a much lower acceleration voltage in the range of several hundred volts to 5 kV.^{114,119} This does not only lead to much less specimen damage but also gives access to measuring non-conductive samples without the requirement for sputtering beforehand.¹²⁰ Therefore, not only a high resolution can be achieved with much lower acceleration voltages but features which usually get hidden by a sputter-coating can also be made visible.

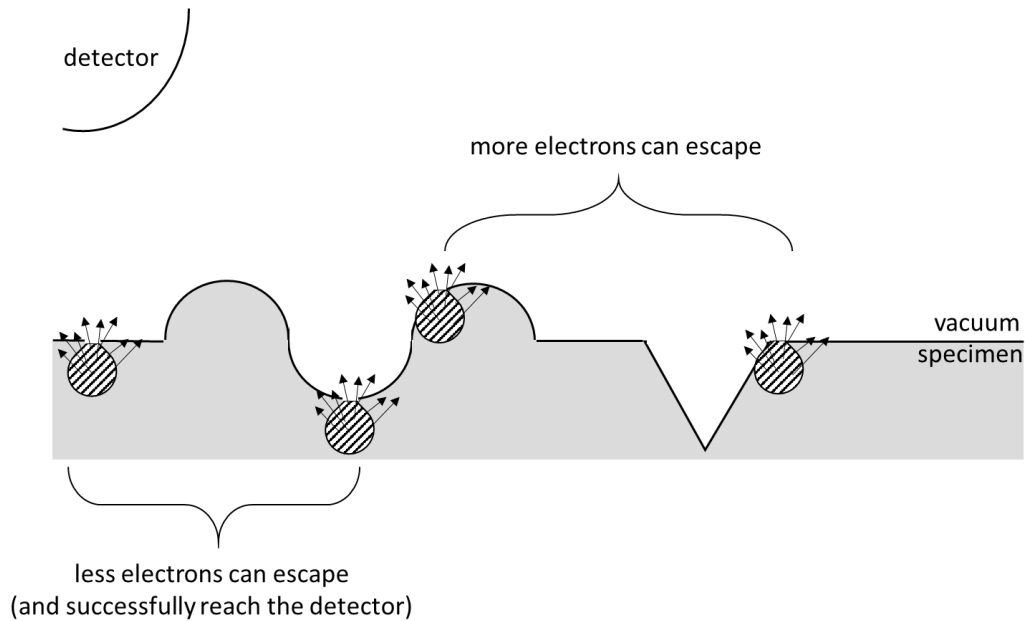


Figure 7: Electron number effect during SEM measurements. More secondary electrons and back scattered electrons can escape the specimen from edges or exposed features due to the pear-shaped interaction field. The image was adapted from literature.¹¹⁴

Since SEM imaging using SE detectors is not suitable to investigate the inner structure of the sample, microtomy is used to reveal a cross-section view of samples and provides insights into the architecture below the surface. The process involves embedding a specimen in a resin block (commonly epoxy resins),¹²¹ which is then sliced into ultra-thin sections (typically 30-100 nm thick) with a sharp diamond knife. For this, the specimen is placed into a holder which gradually moves towards the up and down moving knife. The specimen is sectioned as it passes the edge of the knife blade, and the thin sections are collected on a water surface and can be transferred to specialized grids for measurement. One disadvantage of the embedding technique, though, is the possibility of masking parts of the sample feature. If the resin and the sample are too similar in nature, the contrast in the resulting SEM image might be too low to detect fine structures and the resin can obscure details of the sample like pores. In those cases, either cutting the sample without prior embedding or staining of the sample can be used alternatively.^{114,122,123}

6.4.3 Size Exclusion Chromatography

Size exclusion chromatography (SEC), also called gel permeation chromatography (GPC), is an analytical method based on liquid column chromatography and is employed to investigate macromolecules. With this technique, the molar mass average and molar mass distribution can be determined, or it can be used to separate macromolecules preparatively according to their hydrodynamic radii. In general, SEC can be applied to analyze synthetic polymers as well as natural macromolecules like proteins and DNA.^{31,124}

For the analysis of the molar mass distribution of a polymer sample, a diluted solution of polymer is added to a moving stream of solvent (mobile phase), which flows through a column packed with a stationary phase consisting of a porous material, like, for example, polymer particles. The pores of the stationary phase vary in their sizes within the material. A schematic depiction of the separation mechanism in SEC is shown in Figure 8.

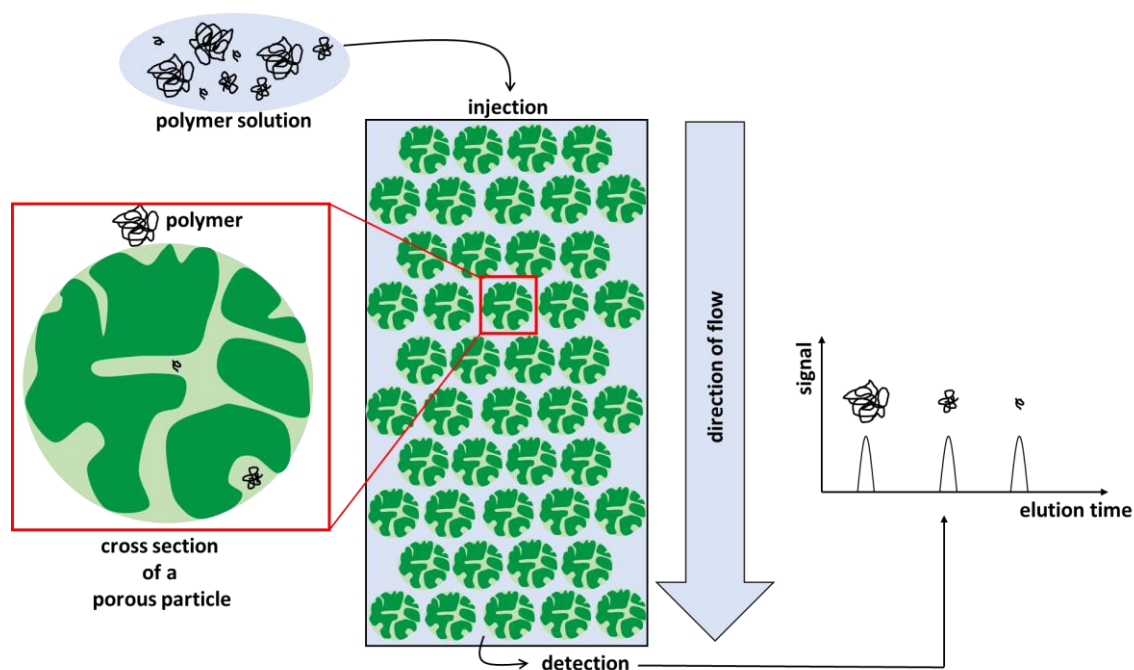


Figure 8: Schematic depiction of the polymer separation within a SEC column: polymers with a smaller hydrodynamic volume can enter more pores of the stationary phase while traveling through the column. This extends their overall diffusion pathway and leads to a later elution than polymers with a larger hydrodynamic volume.

The hydrodynamic radius, or hydrodynamic volume, of a polymer is a property that describes the dimensions of the polymer coil when in solution. A higher hydrodynamic radius results from a better solubility of the macromolecule in the solvent and its increased chain length. So,

depending on the hydrodynamic radius of the polymer in solution, the polymer chains can enter fewer or more pores of the stationary phase. The higher the number of pores which are accessible to the polymer, the longer the diffusion path through the column becomes for the polymer chain. As a consequence, the polymer leaves the column later than polymers which can only enter very few pores leading to a later elution signal in the detector. Therefore, molecules with a larger hydrodynamic volume will elute first, followed by molecules with decreasing hydrodynamic radii. Since the hydrodynamic radius of a polymer directly depends on its molar mass, the elution time of a polymer can be correlated to this property.

Ideally, both mobile and stationary phases are chosen in such a way that the analytes do not enthalpically interact with the wall of the stationary phase and are solely separated according to the above-mentioned hydrodynamic radius, making this process entirely entropically driven. Typical stationary phases are densely packed porous particles or porous monoliths which can be either organic/polymeric or inorganic (silica).¹⁴ Pore sizes are usually a mixture of mesopores (2–50 nm) and small macropores (>50 nm).^{14,125} For porous particles, packings of small particles up to 5 μm in diameter provide enhanced resolution and are more efficient in separation. However, they also generate higher back pressures and shear stress which can damage the analyte molecules. Oppositely, columns packed with porous particles above 5 μm exhibit heightened sensitivity to sample impurities.³¹

The most frequently used detectors can be roughly categorized into concentration-sensitive and molar mass-sensitive detectors.³¹ Concentration sensitive detectors measure either the property of the whole eluate, like refractive index (RI) detectors, or the property of the solute (this can be the analyte or any impurities), like UV detectors and IR detectors. While these detectors are relatively easy to handle, their disadvantage is that the analytes have to be UV- or IR-active, and the mobile phase needs to be sufficiently transparent for the respective detector to not disturb the analyte signal. Molar mass detectors are usually either dynamic light scattering detectors, static low angle or multi angle light scattering (LALS or MALS), or viscosimeters. A huge advantage of viscosimeters is the possibility to measure the intrinsic viscosity of a polymer solution. When coupled with a concentration detector (usually RI), it gives access to the universal calibration for SEC measurements: While classical calibrations need a standard of the same type of polymer as the analyte polymer (e.g. PS standard for PS samples), it is possible to use a different type of polymer as the standard compared to the

analyte polymer (e.g. PS standards for PMMA samples). With this calibration technique it is also possible to analyze unknown polymer samples and more complex structures than linear polymers.^{32,33,126}

The concept of SEC can also be used in reverse: instead of the determination of the unknown molar mass distribution of a polymer sample with the help of a stationary phase with known pore size distribution, a polymer standard with a known molar mass distribution can be used to determine the pore size distribution and separation capacities of a unknown stationary phase. The column performance tests (also called “inverse SEC”) can be used to analyze porous polymer particles. As with the regular SEC technique, the mobile phase is chosen in such a way to minimize the interaction between the polymer and stationary phase.^{32,127} Next to mercury intrusion porosimetry, nitrogen sorptometry and scanning electron microscopy, inverse SEC is another tool to further analyze pore size distributions of porous material like polymer particles.¹²⁷

If a column is packed with non-porous particles, though, another separation mechanism is observed which was used to develop hydrodynamic chromatography (HDC).^{128–130} A schematic depiction of the separation mechanism in HDC is shown in Figure 9. The separation is still dependent on the hydrodynamic volume of the analyte molecule, but due to the absence of pores the separation only takes place in the interstitial volume between the packed particles of the column.¹³¹ This interstitial space can be seen as a system of capillaries in which solvent and analyte flow.¹²⁸ The smaller the hydrodynamic radii of a molecule, the closer it can get to the “walls” of this capillary system where the flow velocity is slower. Consequently, the average flow rate of small molecules is lower compared to larger molecules, which only experience the faster flow velocities in the center. Additionally, the smaller the molecule, the better it can enter the small crevices between particles with the lowest flow rates. Therefore, smaller molecules elute slower than larger ones. Hence, this technique can complement size exclusion chromatography, especially for samples with high molecular mass which suffer a lot of damage from shear stress in SEC.^{129,132,133} However, due to the absence of pores in the stationary material, hydrodynamic chromatography still remains a low resolution chromatography technique.^{128–131,134}

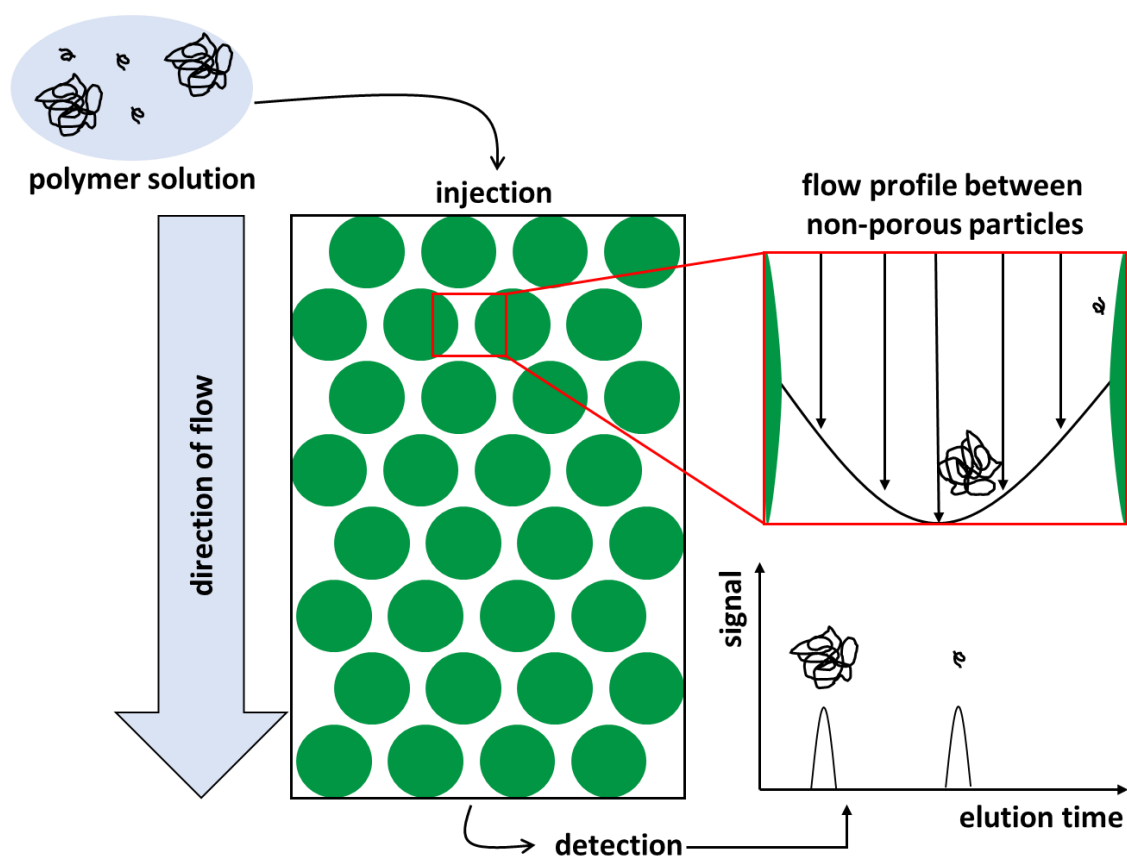


Figure 9: Schematic depiction of the polymer separation within a HDC column: polymers with a smaller hydrodynamic volume experience the whole range of the flow profile, while larger polymers only experience the fast flow rates in the center. Thus, the larger the hydrodynamic volume of a polymer, the faster it eludes.

7 Results and Discussion

7.1 Polydivinylbenzene Particles via Precipitation Polymerization

Stabilizer-free precipitation polymerization is a common approach to synthesize poly(divinylbenzene) (PDVB) particles.^{19,28,35,43,50,85,97} Here, the monomer and initiator are soluble in the reaction solvent, but the formed polymer is not. Once a critical degree of polymerization is reached, the polymer chains precipitate, coil up, and form nuclei. These nuclei subsequently grow by coalescence with other nuclei and by addition of monomers to active centers or oligomer adsorption on the particle surface (see chapter 6.2 for a more detailed description). This process often involves using a heating system with incubator bottles, where glass bottles are placed into a preheated reactor (incubator) and rotated around their horizontal axis during polymerization.^{19,97}

Figure 10 shows the general reaction scheme of precipitation polymerization with divinylbenzene in acetonitrile (a) and a schematic laboratory setup (b) illustrating the particle formation.

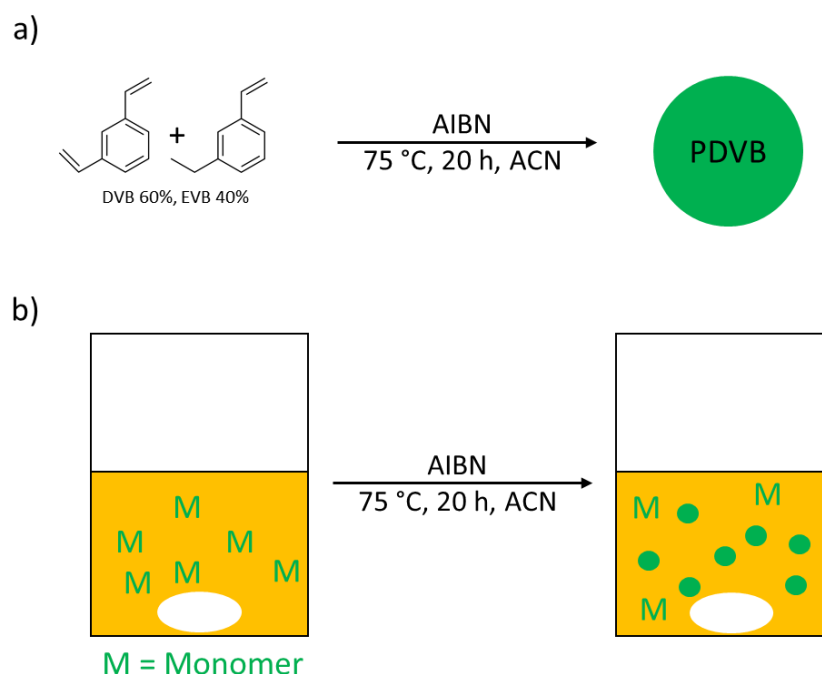


Figure 10: Depiction of a) the reaction scheme and b) the schematic laboratory setup of a common precipitation polymerization of DVB in acetonitrile. The white object depicts a stirring bar.

In this chapter, this synthesis route is studied in detail and systematically modified in an attempt to produce PDVB particles with a core-shell architecture, intended for application in size exclusion chromatography (SEC). The target is to generate monodisperse particles with diameters in the range of 3–5 μm , consisting of a highly crosslinked, mechanically stable core and a porous shell capable of size-based separation of macromolecules. To establish a reliable and reproducible synthesis protocol without the use of incubator bottles, a new reaction setup using standard laboratory equipment is developed and optimized. The reaction behavior for non-porous PDVB particles is investigated in this context (chapters 7.1.1 to 7.1.3). Subsequently, shell growth is explored, starting with non-porous shells and followed by efforts to introduce porosity through the incorporation of low-molecular-weight porogens such as toluene (chapters 7.1.4 and 7.1.5).

Particle size distributions are monitored by light microscopy, while scanning electron microscopy is employed to analyze particle morphology and porosity. Finally, the synthesized particles are evaluated in SEC column performance tests to assess their suitability as stationary phase materials for macromolecular separations.

7.1.1 Establishing a Reliable Experimental Setup for Non-Porous Particles

While precipitation polymerization of DVB is already known in literature,^{18,19,28,35,43,50,51,85} many details about the reaction conditions vary from paper to paper or are not described in sufficient detail for successful reproduction. In order to assess the suitability of standard laboratory equipment to replace the commonly used but specialized incubator heating systems¹⁹, it was necessary to design an alternative reaction setup for this thesis. Thus, this chapter will focus on selecting a suitable reaction vessel, developing a heating method based on generally available equipment, determining feasible agitation conditions, establishing a light microscopy-based particle size analysis method capable of evaluating a high number of particles, and identifying the required reagent quality to achieve the formation of single particles. Studies on the influence of different reaction parameters, such as reaction temperature and reagent concentration, on the resulting particle sizes within the established reaction setup will be discussed afterwards.

7.1.1.1 Selection and Pretreatment of the Reaction Vessel

In studies about precipitation polymerization the most common container materials are glass flasks,^{35,135} glass vials^{97,98,136} and bottles made from polyethylene or polypropylene.^{19,43,50,85} The latter are mainly used for the aforementioned reactor setup with rotation around the long bottle axis, which was intended to be substituted within this thesis.

This chapter will discuss the pretreatment of reaction vessels made from glass and compare different treatment techniques in terms of their influence on agglomeration during precipitation polymerization of DVB. The goal is to achieve stable reaction conditions which ensure single particle formation instead of agglomeration. Additionally, the reusability of each setup will be tested. Precipitation polymerization is very sensitive towards impurities and neat conditions are required for every reaction. Therefore, a reliable cleaning method for the used vessel setup needs to be established. First, pristine glass flasks were tested with a standard recipe that uses 98vol% acetonitrile (ACN), 2v% divinylbenzene (DVB) and 16mol% azobisisobutyronitrile (AIBN) at a reaction temperature of 75°C for 20 h. Those new flasks were used several times with only rinsing out the flask with neat ACN in between experiments.

A thin turbid film remained on the glass walls after each reaction. Removing the remaining film from the glass walls by mechanical force and soap resulted in strong agglomeration in the following experiments and was therefore omitted as a cleaning procedure.

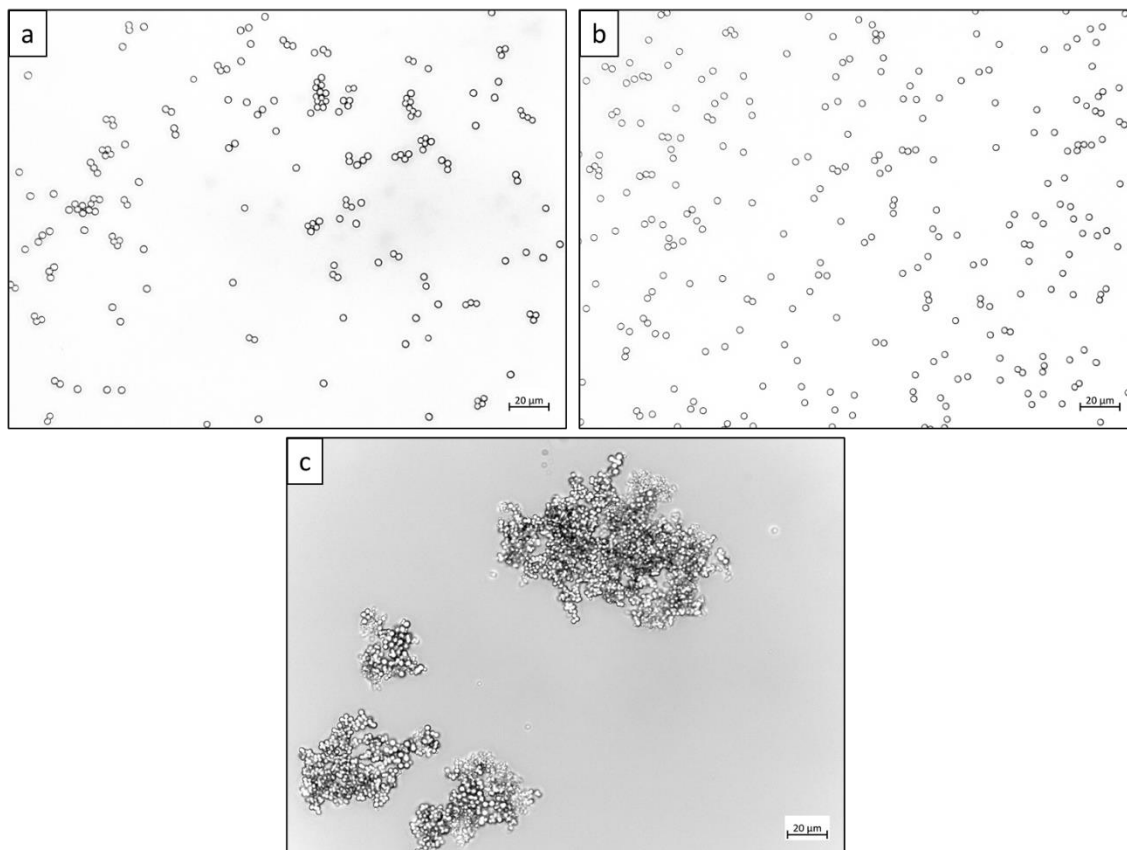


Figure 11: LM images of PDVB particle reaction mixture after precipitation polymerization. The used flasks were in the following conditions: a) first usage of newly bought flask, b) second usage, and c) third usage. The flask was rinsed with neat ACN between usages.

Figure 11 shows light microscope (LM) images of the reaction mixtures after one, two or three consecutive precipitation polymerization experiments with rinsing in between. The first two experiments yielded uniform single particles that do not agglomerate. After the third consecutive experiment, however, strong agglomeration can be observed in the reaction mixture. This is likely a result of the thin polymer film building up on the glass wall of the flask with every polymerization reaction. The polymer film on the glass wall does not seem to interact or hinder the particle formation in the second repetition of the experiment, because the film stays intact. But usually by the third repetition, the built-up polymer film apparently begins to lose integrity, which is also visible by macroscopic fractures or partially loose

polymer bits. These loosened polymer residues can cause contamination of the reaction mixture and result in agglomeration.

Chemical treatment of the flasks to remove the built-up film and other impurities after precipitation polymerization was done by either immersing the flasks in a concentrated potassium hydroxide (KOH) solution or a strong oxidizing agent consisting of sulfuric acid and hydrogen peroxide (also known as Caro's acid) overnight and rinsing with water followed by neat ACN. In both cases, the film was removed but during the following precipitation polymerization experiments, agglomeration was observed (see Figure S 1 in the appendix). Apparently, the chemical treatment altered the glass surface in such a way that it was interfering with the precipitation polymerization afterwards.

In another experiment series, the glass wall of the reactions vessels was hydrophobized with HMDS to mimic polypropylene (PP) bottles. This treatment method was chosen because PP bottles as reaction vessels showed good results for precipitation polymerization of PDVB particles in literature.¹⁹ While some particle formation during precipitation polymerization was found, the treatment did not completely prevent agglomeration (see Figure S 2 in the appendix). Thus, the hydrophobic surface of the PP bottles seems not to be the most crucial factor for single particle formation. In consequence, this flask treatment method was not pursued further.

Since removing the film with mechanical or chemical treatment of the glass leads to agglomeration in the following experiments, pyrolysis was tested for film removal. After thermally treating the flasks, they were rinsed with neat ACN before further usage. With this combined method, no residual polymer or any other contaminant should be left in the flask. Additionally, scratching the glass, which could also interfere with particle formation, is avoided.

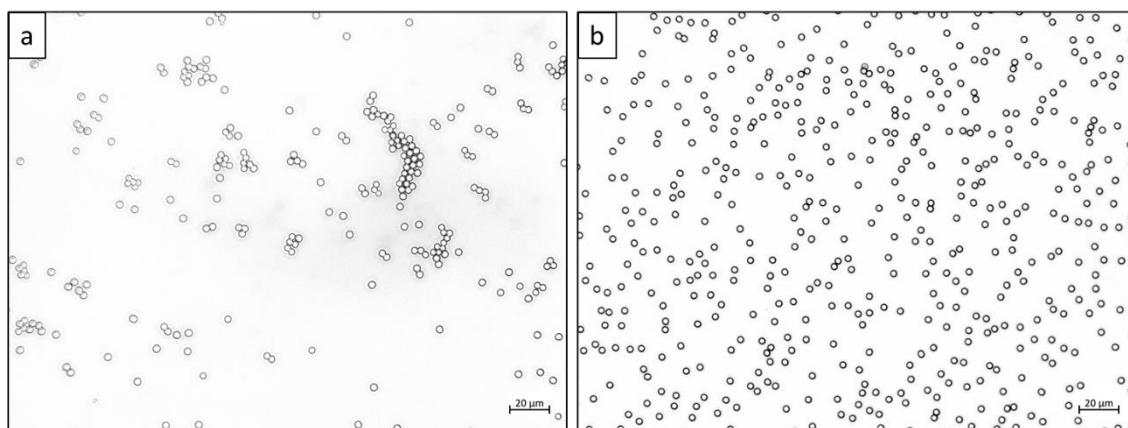


Figure 12: LM images of the particle reaction mixture after precipitation polymerization of PDVB particles in a newly bought flask (a) or in the same flask that was thermally treated before repeated usage to remove any organic residues from prior experiments (b)

Figure 12 shows a comparison of two reaction mixtures after precipitation polymerization of PDVB particles: one using a new flask and one using the same flask three consecutive times for the same reaction followed by thermal treatment. In the second case, the flask had been used for three consecutive precipitation experiments, and agglomeration occurred during the third run. However, after thermal treatment of the same flask, the subsequent polymerization produced well-dispersed single particles again (Figure 12b), comparable in quality to those obtained with a new flask. This shows that thermal treatment of the flasks is a reliable option to fully remove any organic residues from the glass wall and restoring the flask's surface to ensure stable reaction conditions for the following precipitation polymerization. This set of experiments also showed that a glass surface, which comes close to its pristine manufacturing state, benefits single particle formation during precipitation the most. However, this cleaning method is very time and energy consuming and thus makes it only economically feasible for very large flasks (2 L and more) which are too expensive to replace frequently on a small laboratory scale.

In summary, the best results in terms of absent agglomeration can be achieved with glass reaction containers which are in pristine condition. For smaller scale experiments this can be achieved by always using new flasks, which is not cost efficient, or to employ "single-use" glass vials with screw caps as a more economic approach. Both approaches lead to single particle formation with only negligible amounts of agglomeration as can be seen in Figure 13.

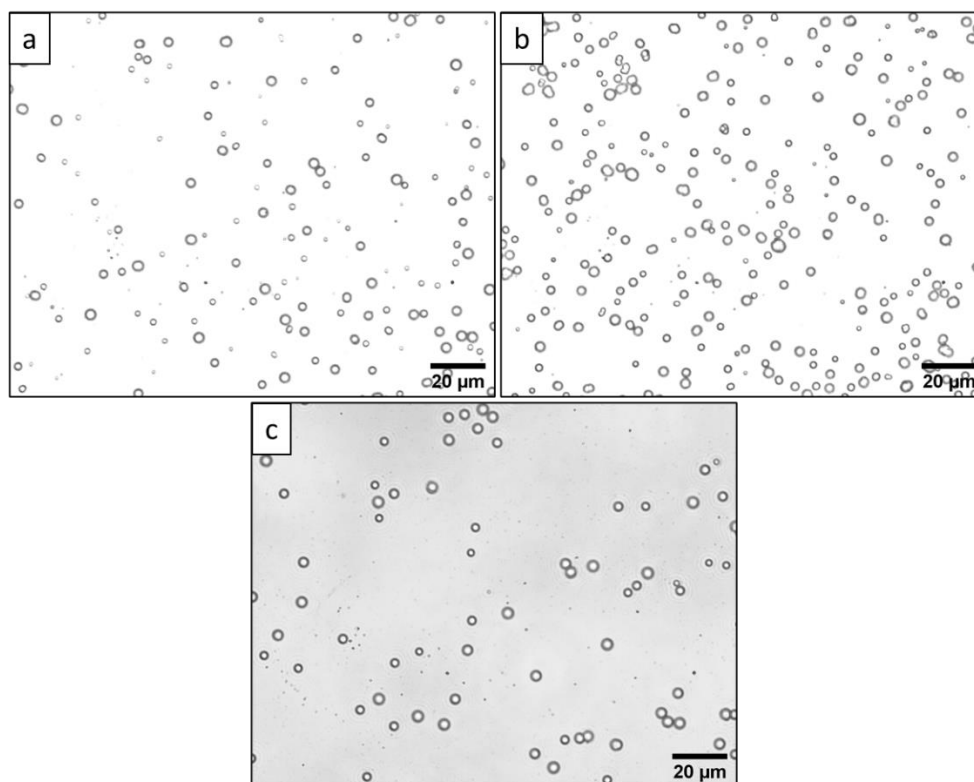


Figure 13: LM images of the particle reaction mixture after precipitation polymerization of PDVB particles in “single-use” glass vials (a and b) or a newly bought flask (c)

7.1.1.2 Development of a Controlled Heating Setup for Glass Vials

Single-use screw cap glass vials proved to be a cost efficient and reliable reaction container, but their relatively low volume limits the number of particles that can be made within one reaction. In addition to that, the reaction time of at least 20 h is another bottle-neck factor for optimizing the reaction and developing new modifications. For this reason, the ability to perform more than one reaction in parallel would be highly beneficial for optimization and development.

While it is possible to place multiple glass vials into a conventional oil bath heating setup, the positioning by hand is time consuming and not precisely reproducible from experiment series to experiment series. Furthermore, using bulky clamps to secure the glass vials imposes a maximum of about three to four vials per experiment series.

Hence, a new heating setup was created, consisting of a cylindrical block of aluminum with cavities for the glass vials. The base area matches the size of the heating plate commonly used in the given lab environment. Seven evenly distributed cylindrical holes for the glass vials and one for the thermometer of the heating plate could be added without losing mechanical integrity of the block. The hole diameters were chosen to minimize air volume between the glass and aluminum while maintaining vial mobility. The depth is sufficient to cover most of the glass vial without the screw cap touching the aluminum block when inserted. A schematic depiction of the aluminum block and single-use screw cap vials is shown in Figure 14.

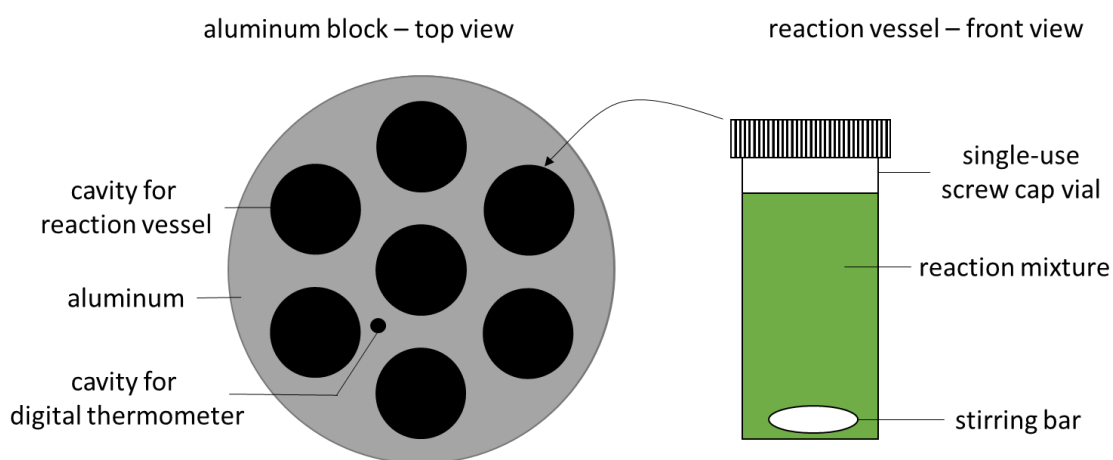


Figure 14: Schematic depiction of a reaction setup using screw cap vials as reaction vessels and an aluminum block as heating system. Please note that the components are not drawn to a uniform scale.

Aluminum was chosen over steel alloys or copper because of its good thermal conductivity, low cost, low density and good workability. The metal allows for precise hole drilling and results in a finished product that can still be carried easily by one person, whereas choosing steel or copper would result in an object three times heavier. The good thermal conductivity ensures a fast and uniform distribution of heat from the heating plate towards all inserted samples. This was tested with water-filled vials at different positions which resulted in all samples reaching thermal equilibrium at 75 °C after 30 min matching the preheating time during the reaction setup.

The choice of stirring bars had to be adjusted, because six out of seven vial positions are not centered over the heating plate causing irregular movement and insufficient mixing. Thus, the stirring bar size was reduced significantly to minimize wobbling while ensuring sufficient mixing throughout the entire liquid column, given the cylindrical vessel geometry. General discussions about stirring conditions can be found in chapter 7.1.1.3.

Compared to the conventional oil bath setup the aluminum block ensures reproducible positioning of the samples across different experiment series. Additionally, it offers improved handling by eliminating the need to clean reaction vessels from oil or to prevent oil contamination. The reaction vessels can also be checked quickly and easily during preheating with minimal system disturbance. Furthermore, the aluminum block needs less maintenance as it retains its properties over time and is easy to clean. In contrast, oil baths degrade or become contaminated over time, requiring frequent replacement or risking altered heating properties.

Since neither the oil bath nor the aluminum block change their optical appearance when heated, external indication is still needed for safety.

A disadvantage of the aluminum block compared to the oil bath is its lower flexibility for different reaction vessels. The oil bath can accommodate various vessel sizes and geometries whereas the aluminum block can only be used for fixed vessel geometries and sizes. This limitation was partially mitigated by manufacturing small aluminum inserts for the cavities, allowing shorter vessels with the same diameter to be used.

The heating system using an aluminum block proved to be reliable across various experiment series, showing only small variations in particle sizes within each series, as can be seen in Figure S 17. In this example, the resulting particles from five experiment series, each consisting

of six parallel experiments, were combined and the most frequent particle size range of 3.8 – 4.2 μm remained relatively narrow.

Therefore, the aluminum block heating system was the preferred setup for experiments described in chapter 7.1.4 and thereafter because of its reliable heating, easy handling, and the possibility to run several experiments in parallel.

7.1.1.3 Comparison of Reaction Conditions Involving Mild Agitation versus Quiescent Conditions (Stirring versus no Stirring)

In literature, gentle agitation by rotating incubator bottles is the most common method to ensure agglomeration-free precipitation polymerization.^{19,43,50,97,98} There, glass vials or PE bottles are placed horizontally into a heated reactor and are then slowly rotated around their horizontal axis during polymerization.

For the developed aluminum block setup, discussed in the previous chapter, the slight agitation typically employed in incubator setups would translate to gentle stirring using small magnetic stirring bars inside the vials. For comparison, quiescent conditions during the reaction, which are successfully used with distillation-driven precipitation polymerization,^{135,137} were also tested. Distillation-driven precipitation polymerizations are processes in which polymer precipitation occurs due to concentration increase from solvent evaporation during polymerization. The resulting PDVB particle reaction mixtures are shown in Figure 15.

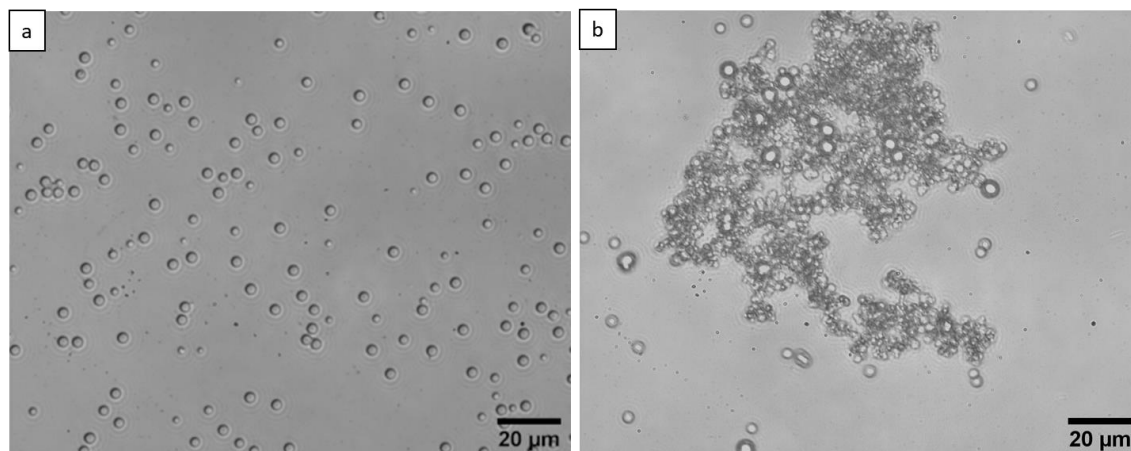


Figure 15: LM image of PDVB particle reaction mixture after precipitation polymerization carried out with stirring at 300 rpm (a) or without stirring (b). The reaction mixture in b was mixed (shaken) before pictures were taken to include the sedimented parts of the reaction mixture in the image.

During precipitation polymerization with gentle stirring at 300 rpm, single particles with consistent sizes were predominantly formed, and there were no agglomerated particles visible (as depicted in Figure 15a). Additionally, there was no sedimentation observed.

For the samples which were not stirred during the reaction (cf. Figure 15b), single particle formation in the main volume of the reaction mixture was observed besides sedimentation with the sediment mostly consisting of agglomerates.

While literature suggests that particle collision of few particles at a time is needed to ensure formation of larger particles,^{43,98} particle contact for a longer time period and of many particles simultaneously, like during sedimentation, results in fusion of larger amounts of particles. Due to the longer contact time, chemical bonds have time to form at the particle interfaces which consequently creates agglomerates. In the above mentioned publications with quiescent reaction conditions^{135,137} this effect could probably be avoided by the relatively short reaction times of 1.5 h that is needed for distillation-driven precipitation polymerization.

From the given data it can be concluded that stirring up to 300 rpm is important to avoid agglomeration and thus gentle stirring was applied to all precipitation polymerization reactions henceforth. Overall, the absence of stabilizing agents in precipitation polymerization rises the difficulty of keeping the system from agglomerating.

7.1.1.4 Light Microscopy-Based Particle Size Analysis

This chapter will discuss the process of particle size measurements with light microscopy and how obtained images were converted to yield particle size distribution (PSD) histograms.

Light microscopy was chosen for its simplicity and efficiency, which allows to rapidly scan particle dispersions even from the reaction mixture if needed. In contrast, SEM would require significantly more preparation steps per measurement, increasing both time and complexity. Thus, SEM was chosen only for selected particle samples and for more detailed morphological analysis. Dynamic light scattering would provide fast scans of particle dispersions as well but is not suitable for particle sizes over 1 μm . Since most of the obtained particles in this thesis are in a range of 1-10 μm , light microscopy is the preferred method here. Since bright field transillumination provided the highest contrast, it was used for all particle dispersions.

A 50x magnification objective was selected for most images as it represented the best compromise between measurement accuracy and the number of particles captured per image. At 100x magnification, the depth of field was too shallow, causing most particles to fall out of focus, either by moving entirely out of the focal plane or being too large to fit within it. In contrast, magnifications lower than 50x provided a greater depth of field, ensuring that most particles remained in focus, and included more particles per image. However, the lower resolution would reduce the precision of size measurements and edge detection during image processing. Unfortunately, image stacking was not possible to mitigate the limitations given by the depth of field as the particles were constantly moving during image acquisition, preventing multiple images of the same particle in the same position from being captured. To compensate for size measurement inaccuracies caused by focusing limitations, each PSD histogram was based on at least 1000 particles from 10 different images.

To prepare the acquired images to be suitable for the implemented size measurement tool of ImageJ, the following steps were taken as shown in Figure 16 and Figure 17: The greyscale images were converted to 8bit images with only black and white properties (Figure 16 a to b). The resulting black rings on white backgrounds were then filled in to obtain circles which can be analyzed by the built-in particle analysis tool of ImageJ (Figure 16 b to c). If particles are out of focus in the original image, they are usually not fully transformed into circles after these steps, which helps with exclusion of these unwanted objects from the

measurement. On some occasions, when rings were too close together, their filling resulted in bigger black objects of irregular shape. To ensure accurate interpretation by the analysis tool, these objects had to be separated again into individual round shapes using white lines (Figure 16 c to Figure 17 a). This prevented the tool from either counting several clustered particles as one single large object or excluding them due to the irregularity of the combined shape. The tool then proceeded to measure all given circular areas, excluding all circles that were cut by the edge of the image, yielding a list of area values and an output image that displayed all included circles as shown in Figure 17 b. This list was then converted into a PSD diagram using the data analysis add-in for Excel.

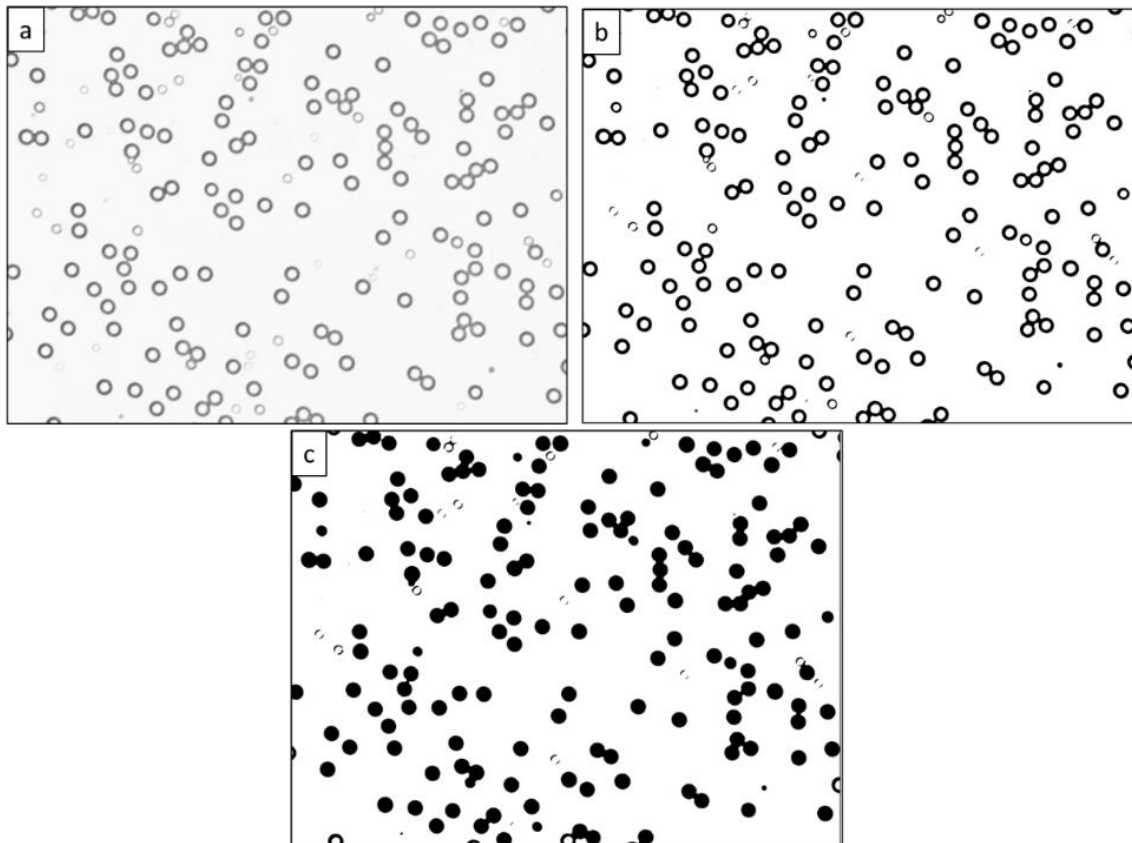


*Figure 16: Part one of processing light microscopy images of particle dispersions for particle size measurement with ImageJ:
a) original image, b) 8bit black and white image and c) image with filled in circles and larger irregular objects.*

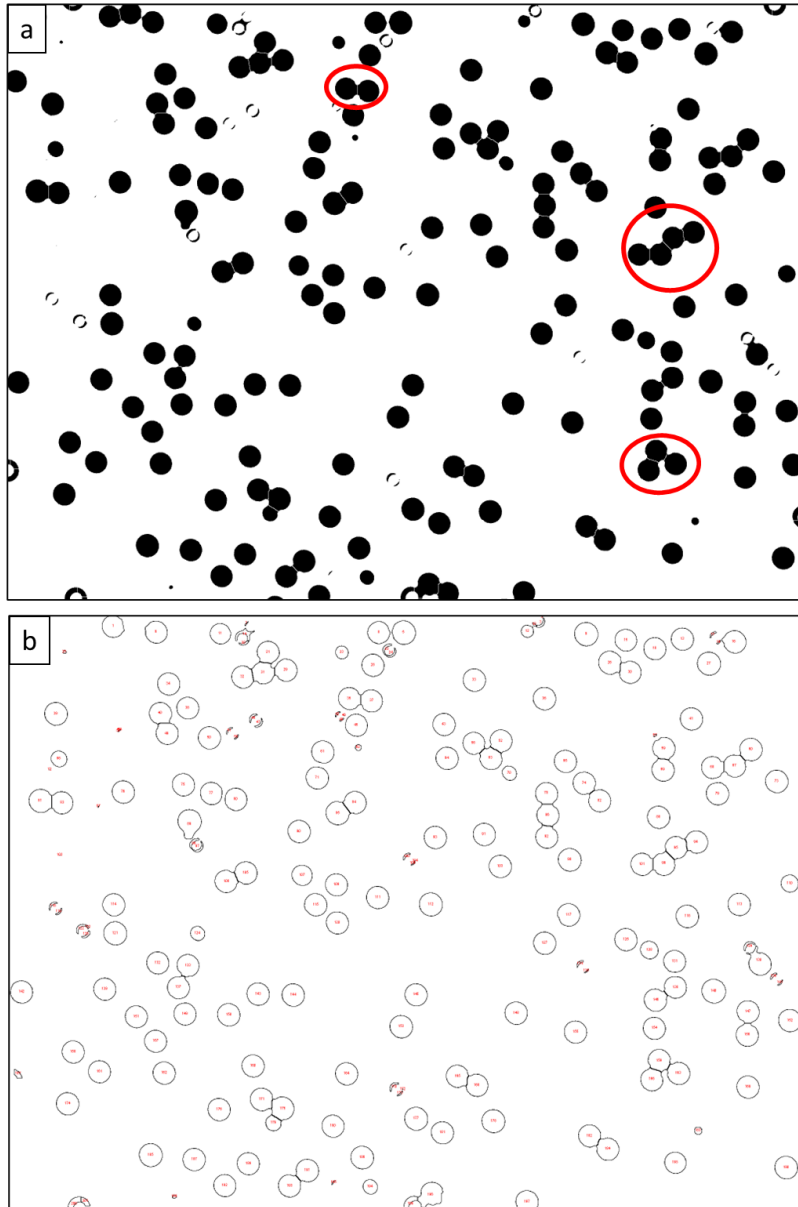


Figure 17: Part two of processing light microscopy images of particle dispersions for particle size measurement with ImageJ:
a) image with filled in circles and separated larger objects highlighted by the red line b) example output image by ImageJ
showing which circle was taken into account for the particle size analysis (including all values for “size” and “circularity”)

Since including all circularity and size values would also include artifacts, like incorrectly separated aggregates, small impurities, and incompletely filled circles (Figure 17b), adjustments were made. To exclude small impurities (like dirt on the “old” camera lens that could not be removed) areas below $0.5 \mu\text{m}^2$ were disregarded. Irregular shapes introduced by the image processing steps were filtered by considering only objects with a circularity between 0.5 and 1.0, where 1.0 denotes a perfect circle and 0.0 represents highly elongated or irregular forms. A circularity of 0.5 would still include slightly elongated ellipses and rounded polygons,

such as hexagons, for comparison. Nevertheless, even with these adjustments, errors such as counting agglomerates as single particles or including artifacts can still occur, which is why a large sample size was chosen to compensate.

While the previous steps focused on optimizing image processing, a technical change in the setup also affected the measurements and needs to be discussed: the replacement of the camera system led to systematic differences in apparent particle sizes as can be seen in Figure 18. The initial image acquisition was performed using an older camera system, which became unusable due to the irreversible failure of the connected computer. Thus, a new camera setup was used starting from chapter 7.1.3 and thereafter. While the replacement camera offered improved resolution and higher contrast resulting in better image quality, it also led to changes in apparent particle sizes even after the same scaling standard was used to calibrate the new camera system.

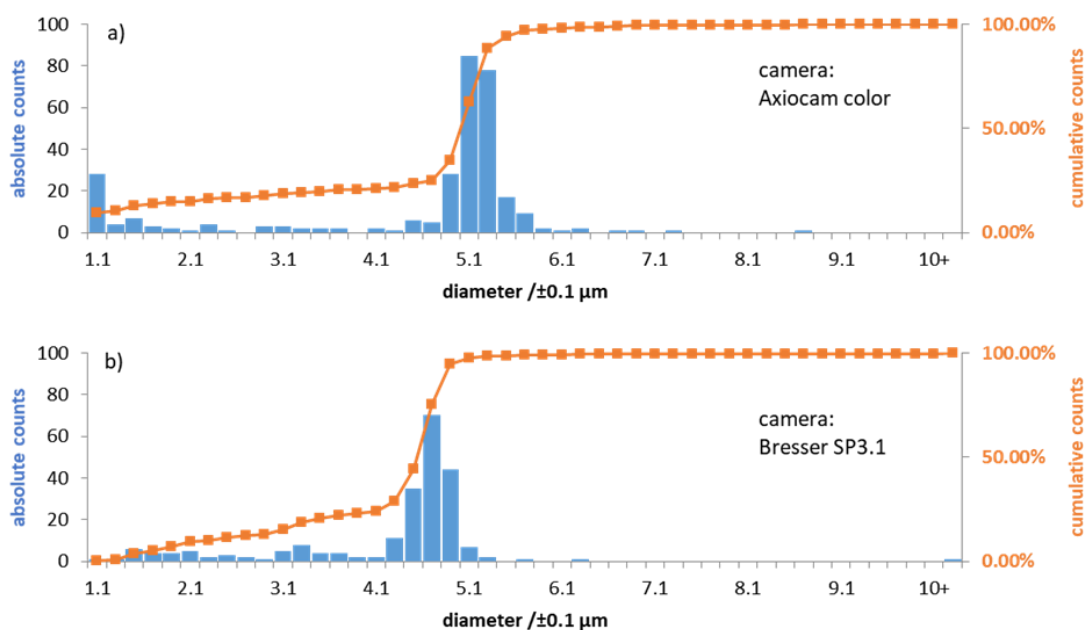


Figure 18: Comparison of PSD diagrams of PDVB particles made with the “standard recipe” (2v% DVB, 16mol% AIBN with respect to monomer content, 75 °C reaction temperature). The light microscopy images used for histogram a) were captured with the old camera setup (Axiocam color) and the ones for histogram b) were captured with the new camera setup (Bresser SP3.1).

One possible explanation for this observation is that the better image quality of the new camera enhances contrast and reduces noise, creating sharper particle boundaries. Additionally, the camera software likely employs more advanced methods for noise reduction,

gamma correction or dynamic range handling to improve image quality further. These factors can produce steeper edge gradients, which, after black-and-white conversion, may result in thinner rings and thus smaller filled circle areas. This effect may contribute to the observed reduction in apparent particle size, even though the actual particles remain unchanged.

Similar reasoning can be applied to the calibration process: Since the new camera setup provides better resolution and contrast, the edges of the scaling standard lines can be identified more accurately and in smaller increments which improved precision during the calibration process. However, this can lead to a slightly altered calibration factor ($\mu\text{m}/\text{pixel}$) compared to the old camera setup even after the better resolution is accounted for. In both cases, the better-defined edges lead to more precise, but not necessarily identical, measurement outcomes.

As a result of the systematic shift, particle sizes should only be compared within a single experiment series. The trends observed within one series remain valid, while particles from different experiment series should not be compared even when the same synthesis procedure was applied as the apparent particle size differs between camera setups. In the future, AI-assisted imaging analysis tools could be considered to further improve particle identification for the particle size distribution analysis.

7.1.1.5 Influence of the Chemical Quality of the Reagents

Besides the environmental conditions, the quality of the used reagents has an influence on the particle formation during precipitation polymerization. In this chapter, the influence of the reagent quality on the resulting particles will be discussed.

To achieve single PDVB particles without agglomerates present after precipitation polymerization, the following versions of acetonitrile (ACN) were tested: distilled technical grade ACN, ACN which was used in a successful PDVB precipitation reaction before and then distilled, and pristine HPLC-grade ACN. Each ACN version was used in the same standard recipe using 98v% ACN, 2v% DVB and 16mol% AIBN with respect to monomer content. The mixture was stirred gently for 20 h at 75 °C. LM images of PDVB particle reaction mixtures after precipitation polymerization using one of the above mentioned ACN versions are depicted in Figure 19.

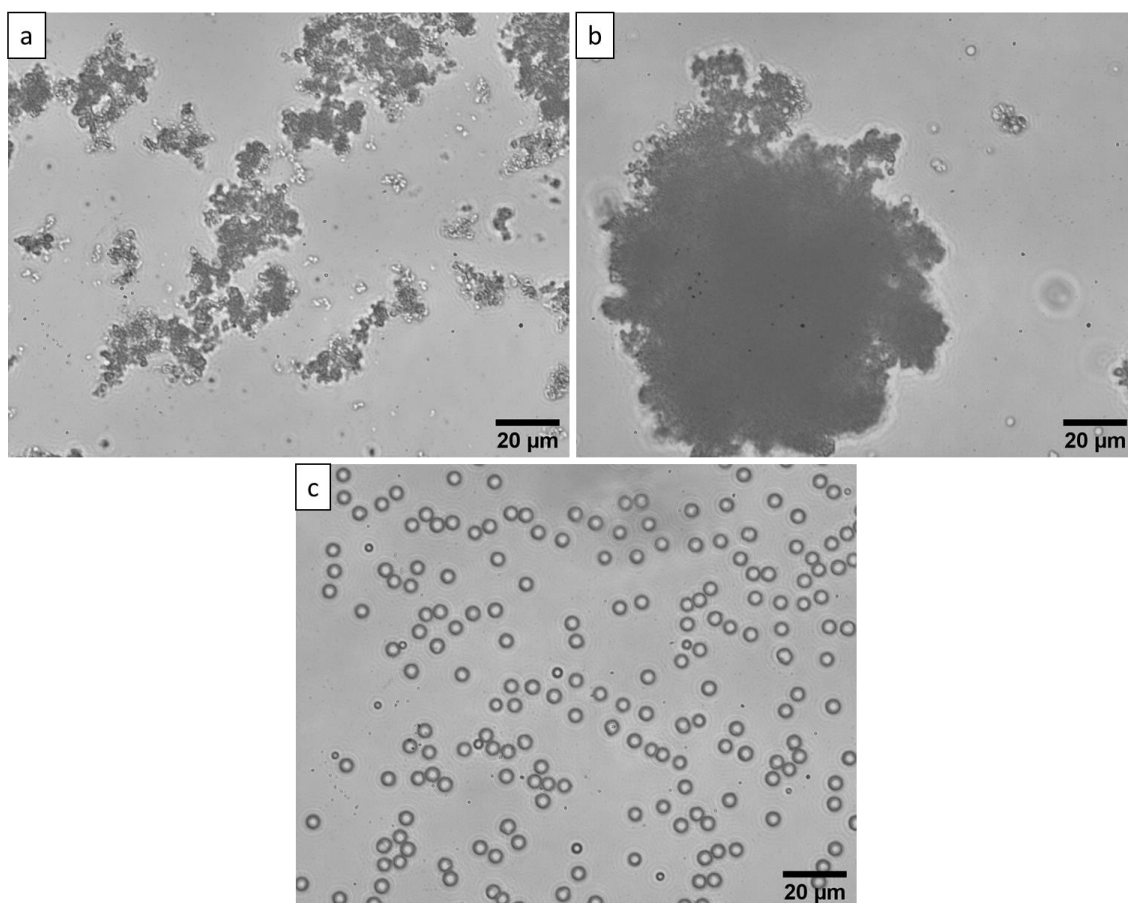


Figure 19: LM image of PDVB particle reaction mixture after precipitation polymerization using distilled technical grade ACN (a) or from previous precipitation reaction recycled ACN (b), which both lead to agglomeration, versus using pristine HPLC-grade ACN out of the bottle (c)

If distilled, technical grade ACN was used for the synthesis (Figure 19a), the resulting particle mixtures showed agglomeration as well as single particle formation. In Figure 19b it can be seen that reusing ACN for a second precipitation polymerization after recycling it also led to strong agglomeration in the resulting particle mixture. Only HPLC-grade ACN proved to be a reliable reaction medium yielding spherical particles without agglomeration (Figure 19c). These results provide further support for the idea that already small impurities can lead to agglomeration during the particle formation process and distillation of ACN is not sufficient in removing those impurities.

Since with HPLC-grade ACN reproducible results were obtained during the experiments, the nature of the impurities was not further investigated. However, water that might be codistilled with the ACN phase during recyclization or distillation of technical grade ACN can be excluded as a cause for agglomeration. It will be shown in later chapters (7.1.5.2 and following) that controlled addition of water to the reaction mixture did not lead to agglomeration.

AIBN, which was used throughout all precipitation reactions, is a common thermal initiator in the field of free radical polymerizations¹²⁶ and is often employed for particle synthesis with a major application in PDVB precipitation polymerization.^{14,18,43,138} For economic reasons it was important to determine whether the quality of the received AIBN is sufficient or if purification prior to usage is necessary due to unwanted agglomeration caused by impurities in the initiator batch.

The standard formula used for this set of experiments utilizes 16mol% of AIBN with respect to the monomer contents in the reaction mixture, which were kept constant. Figure 20 compares LM images of PDVB reaction mixtures after carrying out the precipitation polymerization with either AIBN, which was used as received (Figure 20a) or recrystallized (Figure 20b).

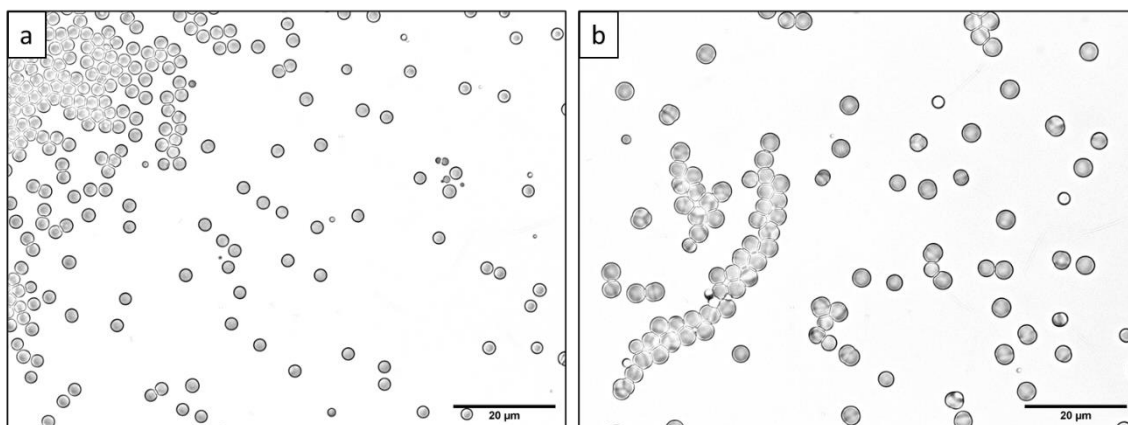


Figure 20: LM pictures of PDVB particle reaction mixtures after precipitation polymerization using AIBN as received (a) or AIBN which was recrystallized twice (b)

As visible from the images, both reactions yielded spherical particles and no agglomeration is present. Also, for both reactions, the particle size distribution is rather narrow. Therefore, the purity of AIBN has no significant influence on the agglomeration tendency of PDVB particles during precipitation polymerization within the tested concentration and AIBN can be used as received without further purification.

However, the particles resulting from initiation with recrystallized AIBN have higher diameters than the ones obtained from initiation with AIBN which was used as received (for detailed PSD diagrams see Figure S 3 in the appendix). This stems from the fact that for a given mass of used AIBN, the recrystallized AIBN contains more of the active reagent due to the absence of impurities than if it was used as received. Thus, the actual concentration of AIBN in the reaction mixture is lower when AIBN is used as received compared to reactions where the initiator was recrystallized before usage. This result is consistent with findings discussed in chapter 7.1.2.2 where PDVB particle sizes increased with higher amounts of initiator being employed.

When the monomer was used as received, no agglomeration was observed after other parameters, like the vessel condition, were optimized. Nevertheless, the used batches of DVB changed over the course of the thesis. This resulted in significant changes in PDVB particle sizes depending on the employed monomer batch, as will be discussed below. A comparison of three different PDVB particle size distribution diagrams is presented in Figure 21.

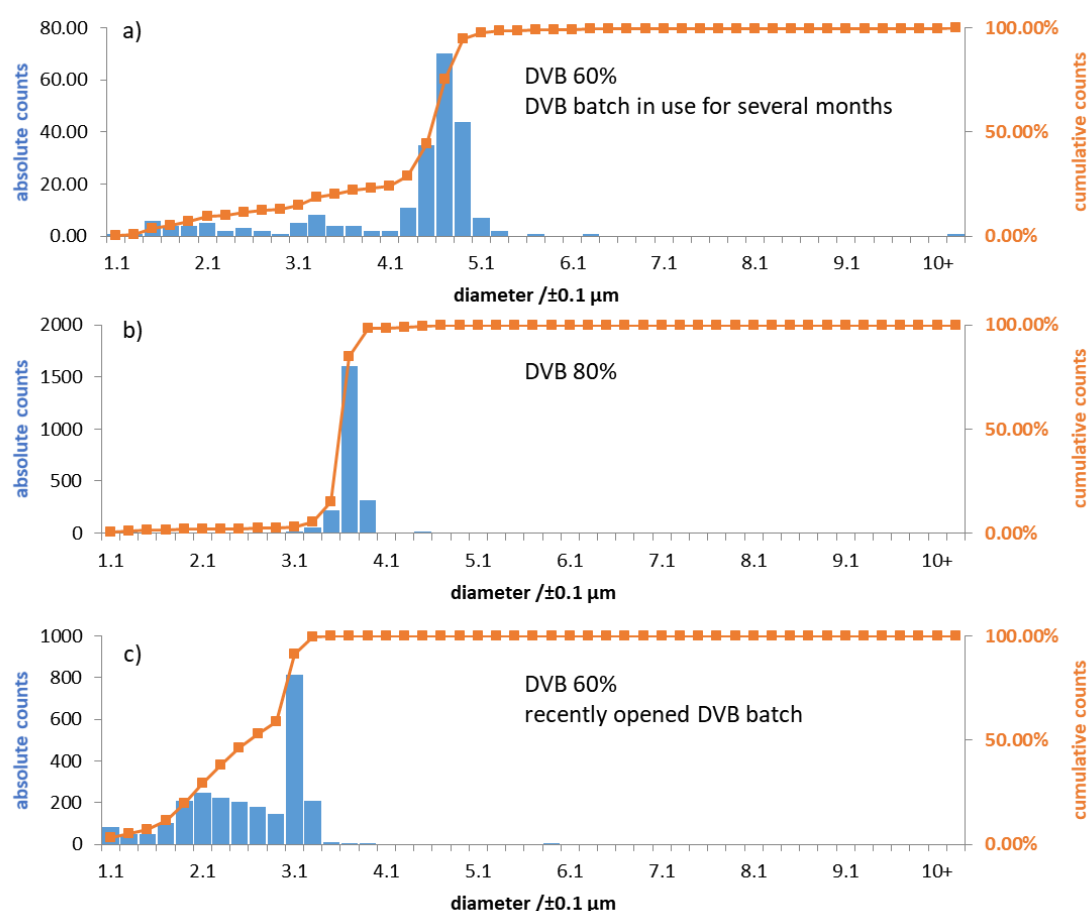


Figure 21: PSD diagrams of PDVB particles synthesized via precipitation polymerization using different batches of DVB. a) The used batch of 60% DVB (40% EVB) was already in use for several months, b) the used batch contained 80% DVB (20% EVB), and c) the used batch of 60% DVB (40% EVB) was opened recently and probably reduced impurities.

The monomer mixture containing 60% of DVB and 40% of ethylvinylbenzene (EVB) resulted in larger particles (Figure 21a) compared to experiments where the monomer mixture with 80% DVB and 20% EVB was used (Figure 21b). The PDVB particle size changes significantly if another type of monomer mixture is used because the overall crosslinking degree in the obtained particles varies and should be higher for the particles that were synthesized with 80% DVB in the monomer mixture. Additionally, significant changes in particle sizes were obtained within the same DVB:EVB composition if the duration of monomer usage in the laboratory varied. Particle sizes obtained from a recently opened DVB container were about 3.1 μm compared to the 4.7 μm large particles obtained from a monomer batch that was already in use for several months. So, possible impurities, like formed oligomers for example, that accumulate over time during usage of a monomer batch seem to influence the particle sizes as well.

As a consequence, experimental data on particle sizes can only be compared within an experiment series that uses the exact same type of DVB but not between usage of different DVB batches (the recently opened DVB batch was used for experiments in chapter 7.1.5 and thereafter).

7.1.2 Assessment of Key Influences on Non-Porous Particle Sizes

7.1.2.1 Evaluation of the Influence of Reaction Temperature on PDVB Particle Sizes

The size of the resulting PDVB particles plays a critical role in determining their properties which can then be tailored to match their potential application. Therefore, in this chapter the influence of the reaction temperature on the resulting PDVB particle size will be discussed. In literature, the influence of temperature on particle sizes was tested for acetic acid-based reactions.⁹⁷ To avoid additional influences of temperature changes during heating, most of the solvent and all of the monomer were preheated before addition of the initiator, which was predissolved in a small portion of the reaction solvent. This method should ensure simultaneous initiation and provide the same temperature conditions for every growing particle.

The tested reaction temperatures range between 50 °C and 75 °C, which is the commonly used temperature range for AIBN.¹³⁹ But most importantly the upper temperature limit is still safe to use with acetonitrile in closed screw-cap glass vessels as acetonitrile has a boiling point of 82 °C under normal pressure (the choice of reaction container is discussed in chapter 7.1.1.1). The light microscope images in Figure 22 exemplarily show the resulting particles after precipitation polymerizations performed at 50 °C and 70 °C. The resulting particles exhibit significantly differing sizes depending on the temperature. At higher temperatures, larger particles were obtained compared to particles from polymerizations operated at lower temperatures.

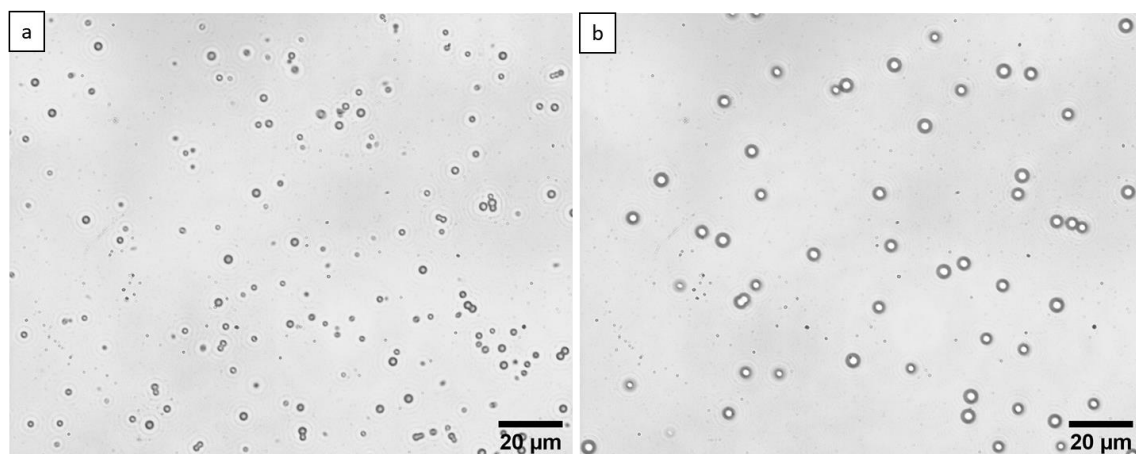


Figure 22: LM images of PDVB particle reaction mixtures after precipitation polymerization at reaction temperatures of 50 °C (a) or 70 °C (b).

This observation persists across most of the tested reaction temperatures, as illustrated in the overview diagram in Figure 23. The figure shows two experimental series, conducted on different days as part of an intended set of replicates. One series is marked in orange, the other in blue. An overall trend of decreasing particle sizes with lower reaction temperatures is visible. These observations are similar to the trends reported for precipitation polymerizations in acetic acid.⁹⁷ For the experiment series displayed in blue, the particles resulting from the reaction temperature of 50 °C were too small to be measured by light microscopy. At higher temperatures, the polymerization reaction occurs more rapidly, and the overall particle movement is enhanced. This results in larger particles being formed due to an enhanced polymerization rate^{97,107} and more frequent collision and coalescence processes which lead to larger particles.⁹⁸ Additionally, at higher temperatures the initiator decays faster leading to more radicals being present and starting chain growth at the same time. This results in more particles forming simultaneously that can collide. According to the literature, particle growth also happens by oligomer-capturing on the PDVB particle surface.⁴³ Therefore, long polymer chains, which usually occur from lower radical concentrations, are not necessary for the formation of large particles. The influence of the initiator concentration on the resulting PDVB particle size is further discussed in chapter 7.1.2.2.

However, some of the experimental results do not follow the observed trend. This can be due to the quite broad particle size distribution diagrams that occurred for many of the carried-out experiments. An example can be found in Figure S 5 in the appendix. From this broader distribution, only the most frequent particle size was displayed in the overview diagram in

Figure 23. Thus, the overall broader size distribution might also have an influence on the most frequent particle size as the distribution is not necessarily gaussian shaped.

Furthermore, although attempts were made to maintain consistency among all other parameters during a series of experiments, the synthesis route was not fully optimized at this point. For example, glass flasks and oil bath heating were used during these experiment series which turned out to be less reliable than the aluminum block setup with single-use glass vials. Thus, some variations from other parameters may have occurred and led to a change in particle sizes.

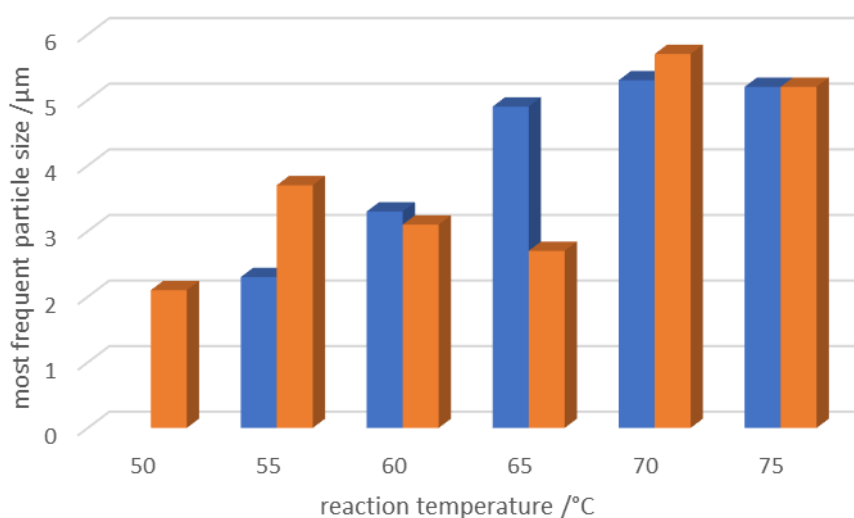


Figure 23: Resulting PDVB particles sizes depending on the reaction temperature during the precipitation polymerization. Two experimental series, conducted on different days, are shown in orange and blue, respectively. Please note that the resulting particles of the blue experiment series conducted at 50 °C were too small to be analyzed quantitatively by light microscopy (<1 μm).

It should be noted that the particle sizes observed after reactions at 75 °C in this experiment series are also much higher (around 5 μm) than particle sizes obtained from experiments done with the same procedure discussed later in chapter 7.1.3 (about 3.5 μm). Additionally, apart from a change in monomer quality which was discussed in chapter 7.1.1.5, the camera used in the microscope setup changed starting from chapter 7.1.3 and measuring techniques were optimized for the experiments discussed. When measured again with the improved equipment and technique, the apparent particle sizes from the current experiment series decreased significantly as can be seen in Figure S 4 in the appendix and was discussed in chapter 7.1.1.4. Thus, while resulting apparent particle sizes can be compared within one

series of experiments, this cannot be necessarily extrapolated to other experiment series with similar reaction procedures in this work. Nevertheless, the trends observed within one experiment series should remain valid, as the influence of parameter changes is expected to follow the same direction despite the presence of systematic errors.

Overall, it can be concluded that the particle size can be influenced by the reaction temperature with higher temperatures leading to larger particles. This can be utilized to optimize and tailor PDVB particle sizes according to their intended application.

7.1.2.2 Influence of the Chemical Composition

Another way to influence PDVB particle sizes in precipitation polymerization according to literature is to vary the chemical composition, like the initiator concentration or the monomer feed.^{19,97} Given the differences in experimental setup, particularly the absence of incubator bottles as used in traditional setups, this chapter seeks to confirm whether the established findings remain valid within the context of standard lab equipment, like glass flasks and oil bath heating.

For the monomer feed, volume concentrations of 1v% to 7v% were tested while keeping all other ratios constant. In Figure 24 the resulting particle sizes are displayed in relation to the used monomer concentration. The particle sizes were measured from light microscopy images and the corresponding pictures and PSD diagrams can be found in Figure S 6 and Figure S 7 in the appendix. Strong agglomeration was obtained for all samples where the added monomer volume was above 2v%, while reaction mixtures starting with a monomer load of 2v% or lower yielded single particles. Furthermore, a trend towards smaller particles is visible when the employed monomer volume is lower. This trend of larger particle sizes with higher monomer feed as well as the observed agglomeration after a certain monomer feed threshold is consistent with the reaction behavior reported in the literature.^{19,97,98}

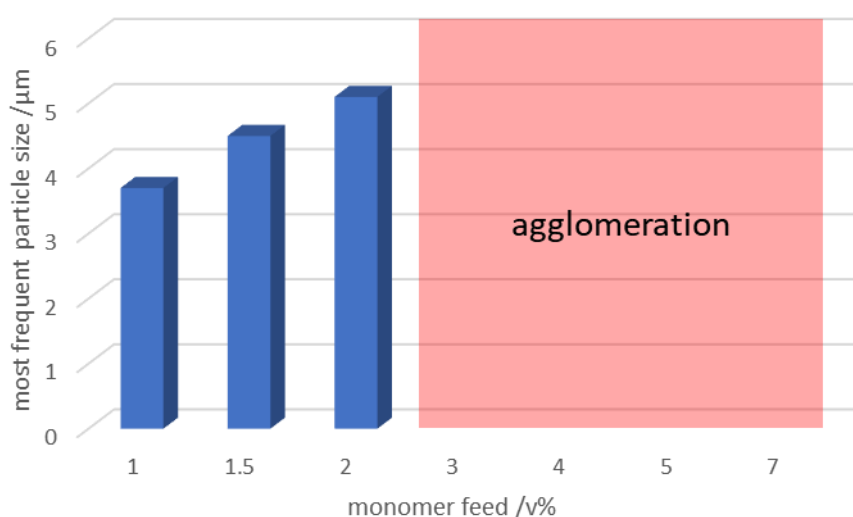


Figure 24: Influence of monomer feed (v% with respect to total monomer content) on PDVB particle sizes.

With higher monomer concentration and therefrom resulting higher concentration of particles, the frequency of particle collisions is increased.⁹⁸ While larger particles may form as a result of the more frequent collisions, there is also a higher risk of coagulation. Additionally, as the monomer acts as a solvent for the polymer, higher amounts of monomer in the reaction mixture increase the solubility limit of the growing oligomers.⁹⁸ This can have two effects: firstly, oligomers precipitate at higher degrees of polymerization when forming the initial nuclei yielding larger nuclei at the nucleation stage. Furthermore, the average degree of polymerization of captured oligomers can be longer compared to lower monomer loads and thus create a thicker gel-like layer on the surface of the growing particle. Thicker gel layers with still mobile chains tend to promote more entanglement between particles (stickiness) and thus increase chances for agglomeration.¹⁹

In another series of experiments, **the initiator concentration** was modified to investigate the influence of the initiator on the particle dimensions and overall reaction behavior for the given reaction environment. The amount of initiator used ranged from 1mol% to 16mol% with respect to the fixed amount of monomer that was used (2v%).

Figure 25 shows a comparison of light microscope images of PDVB particles after precipitation polymerization with 1mol% (a) or 10mol% (b) added. As observed with the monomer feed, the particle sizes are larger with a higher amount of initiator added at the beginning of the reaction.

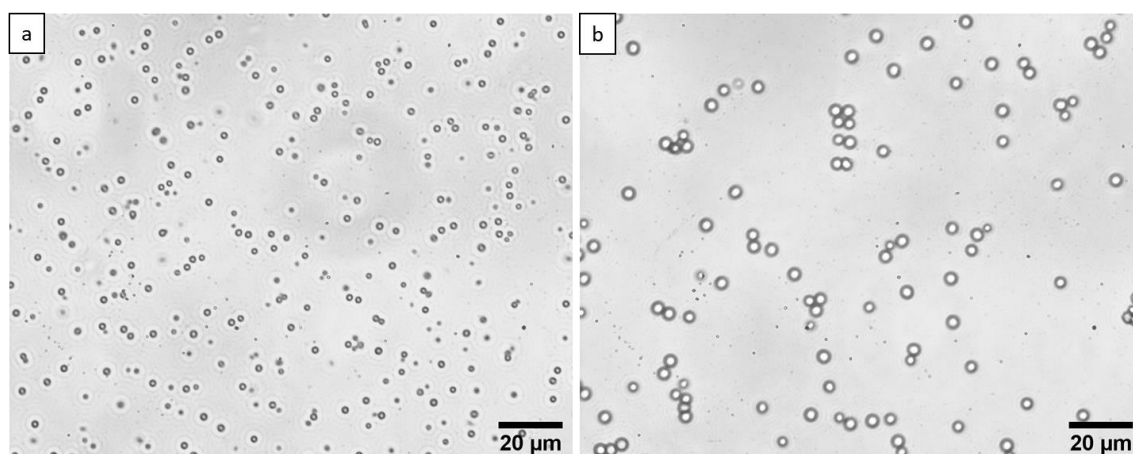


Figure 25: LM images of PDVB particle reaction mixtures after precipitation polymerization with 1mol% (a) or 10mol% (b) AIBN.

This trend can be observed for all tested initiator concentrations as shown in Figure 26, where the most frequent particle size is displayed in relation to the added initiator. The figure shows two experimental series, conducted on different days as part of an intended set of replicates. One series is marked in orange, the other in blue. The most frequent particle size for each experiment was determined from particle size distribution diagrams and can be found exemplarily for the blue experiment series in Figure S 4 and Figure S 8 in the appendix. The size distributions of the experiment series displayed in orange were similar.

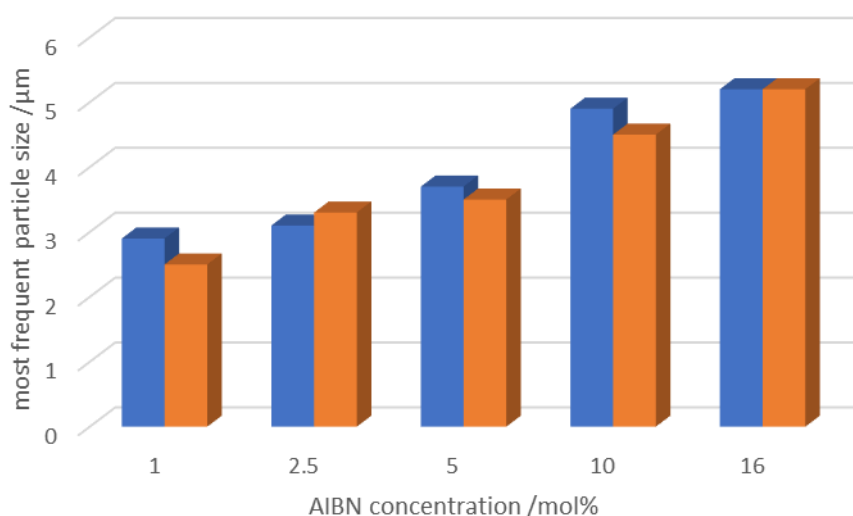


Figure 26: Resulting PDVB particles sizes depending on the AIBN concentration during the precipitation polymerization. Two experimental series, conducted on different days, are shown in orange and blue, respectively.

With a higher initiator concentration at the beginning of the reaction, more small particles can form at the same time during the nucleation stage.⁹⁸ The higher concentration of small particles in the reaction mixture then enhances the collision rate leading to larger particles in consequence. This trend is in accordance to findings reported in literature.^{19,97}

Based on these findings, the amount of monomer and initiator are valuable tools to tailor the resulting PDVB particle size. For the amount of monomer, however, careful adjustment is required to prevent agglomeration. One approach to avoid agglomeration while adding more monomer is the stepwise addition over time. This will be discussed in chapter 7.1.4.1 with a specific focus on particle growth.

7.1.3 Morphological Analysis of Non-Porous PDVB Particles

In the previous chapters (7.1.1) key parameters were identified which are required to establish a robust and reproducible PDVB precipitation polymerization protocol in the given laboratory environment. In particular, single-use screw cap vials used alongside an aluminum block heating setup, pristine ingredients and gentle stirring proved essential for achieving consistent results. Based on these optimized conditions, the following chapter focuses on the morphological characterization of the resulting polymer particles. This data set serves as a reference for upcoming modifications of this synthesis approach as well as for other approaches later in this work.

In Figure 27 the particle size distribution diagram and a light microscope image of the PDVB particles are shown which formed using the “standard reaction mixture” for non-porous PDVB particles: With respect to the total reaction volume a monomer feed of 2v% DVB was chosen (in 98v% acetonitrile respectively) combined with an initiator concentration of 16mol% of AIBN with respect to the amount of monomer. With the employed monomer and initiator ratios, monodisperse PDVB particles of $3.5\ \mu\text{m} \pm 0.1\ \mu\text{m}$ formed at a reaction temperature of 75 °C. The size distribution is narrow and no secondary nucleation (formation of smaller particles) or agglomeration is present. From the light microscope images, it is visible that the particles exhibit a spherical structure and only single particles formed which are uniform. Furthermore, for a more detailed look at the actual particle morphology and the surface topography, SEM imaging was performed on these reference particles.

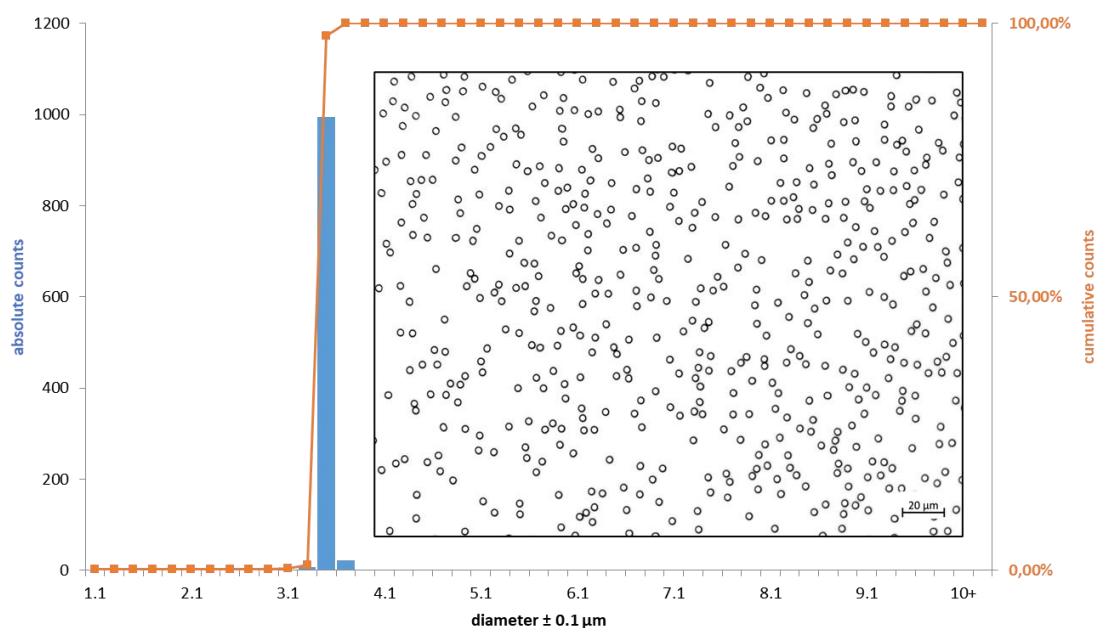


Figure 27: PSD diagram and light microscope image (50x magnification) of monodisperse non-porous PDVB particles synthesized via precipitation polymerization with optimized reaction parameters in ACN; (2v% DVB, 98v% ACN, 16mol% AIBN with respect to monomer content)

Figure 28 shows a SEM overview picture of three PVB particles (a) and a close-up on the particle surface to display the details (b). As already assumed from the light microscope images, the SEM overview images depict a spherical and uniform shape. However, the higher resolution now reveals some grooves on the surface of some particles.

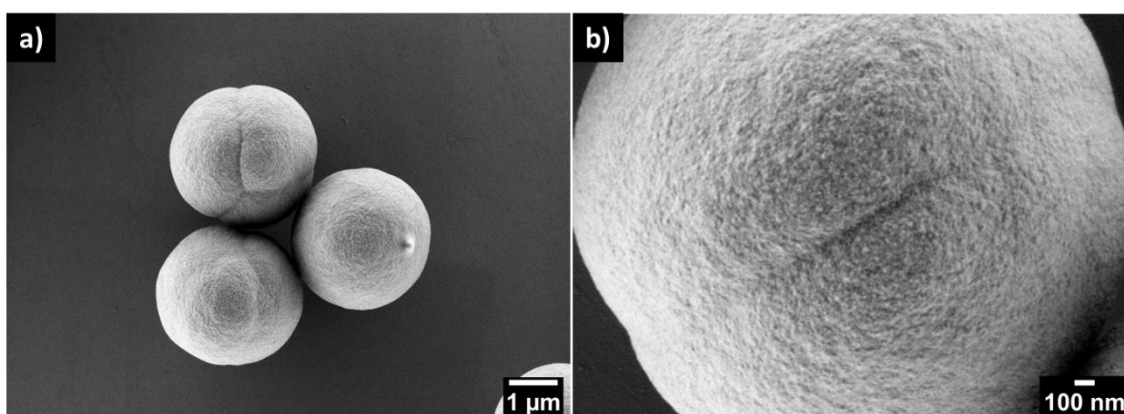


Figure 28: SEM images of PDVB particles synthesized via precipitation polymerization with optimized reaction parameters. a) overview image and b) detailed depiction of the particle surface without large pores. The measurements were conducted without sputtering the samples and under low voltage (Leo Gemini 1530).

These grooves derive from collisions of smaller primary particles which lead to aggregation of these smaller particles. When these aggregates grow by capturing more monomer or oligomers, the grooves are evened out.⁴³ As reported in the literature, this effect is even more pronounced when acetic acid is used as reaction solvent compared to acetonitrile due to acetic acid being a poorer solvent for the forming polymer chains.⁹⁷ This, in turn, leads to precipitation of shorter chains and to the formation of more and smaller primary particles. Therefore, more particle collisions happen leading to increasingly raspberry-like surfaces. As expected, the particles exhibit a relatively smooth surface and do not show any pores (the resolution limit is at least about 10 nm here) compared to PDVB particles derived from e.g. suspension polymerization (cf. Figure S 9 in the appendix). These observations obtained from the synthesis setup using an aluminum block and stirring are in similar to the findings from literature which utilized incubator bottles and rolling systems.^{19,97} Thus, the reaction setup established in this work functions equivalently to the already published systems. Still, the more detailed image (Figure 28 b) shows a slightly granular structure that likely derives from the particle formation process where smaller nuclei fuse through collision. Other high-resolution images of non-porous PDVB particles can be found in chapter 7.3.1. Only a selected and limited number of particle samples was measured with the high-resolution SEM within the collaboration with LiNaCon Dr. Ingo Lieberwirth, Mainz, while all particle systems were measured on the in-house SEM by the author.

Within the collaboration with PSS GmbH, Mainz, the particles were also tested for their porosity and ability to separate polymeric samples of different chain lengths when packed into a size exclusion chromatography (SEC) column. As expected from the SEM images, which showed no porous particle surfaces, the particles show no size exclusion separation ability for polymer samples in the sense of separation via a porous surface (cf. Figure S 10 in the appendix). Only a hydrodynamic chromatography (HDC, see also chapter 6.4.3) separation mechanism can be detected which might be enhanced by the slightly granular surface.

7.1.4 PDVB Particle Shell Growth

So far, the synthesis of PDVB particles has been successfully established under the given conditions using a simple and reproducible approach. Building upon this basis, the upcoming aim is to develop a more sophisticated core-shell architecture, with tunable properties. The introduction of a PDVB shell layer around the PDVB core seeks to enhance control over particle size and functionality.

While the core particle synthesis allows for tunable particle sizes, it might be more precise to achieve certain particle diameters by shell growth since this process can be interrupted at any time to stop growth at the desired size or can be repeated until the desired size is reached.⁸⁵ In addition to that, the feasibility for PDVB particle shell growth under the conditions described in this work (aluminum block setup instead of incubator heating setup⁸⁵) is a prerequisite for the design of PDVB shells with different properties.

For applications in size-exclusion chromatography (SEC), the desired core-shell architecture would be a combination of a rigid, non-porous PDVB core with a porous PDVB shell. This design would facilitate improved separation efficiency while minimizing shear stress.¹⁴ Thus, the second part of this chapter will focus on the introduction of pores to the PDVB particle shell.

7.1.4.1 Particle Size Alterations using DVB

This chapter introduces the first modification to the standard PDVB particle procedure described in chapter 7.1.3: the formation of a PDVB shell through the addition of monomer and initiator to an existing particle suspension in a second reaction step. This approach, schematically illustrated in Figure 29, is meant to enable controlled particle size increase as suggested by literature.^{43,85} Transferring and controlling this concept of PDVB particle shell growth to the reaction environment established in this work, which operates without incubator bottles, is necessary for further modifications of the PDVB particle shell.

In the first reaction step, PDVB particles are formed by precipitation polymerization as discussed before. In the following reaction step, the particles are supposed to grow further since new DVB monomer and initiator are added which in turn restarts the polymerization and precipitation process. Without further addition of other ingredients, this newly formed layer

of PDVB is intended to be of the same characteristics as the core particle: highly crosslinked and non-porous.

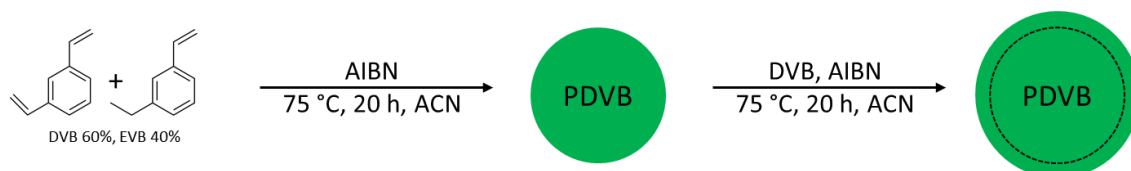


Figure 29: Schematic depiction of a common precipitation polymerization of DVB in acetonitrile followed by PDVB non-porous shell growth by addition of new monomer and initiator to the reaction mixture.

The amount of the newly added DVB and AIBN is the same as in the first step. Therefore, the volume of the particles is expected to double which corresponds to an estimated shell growth of 0.9 μm (from 3.5 μm to 4.4 μm). However, since it is assumed that residual, unreacted monomer from the first reaction step is still present in the mixture, the overall DVB concentration is now higher than 2v% of the total reaction volume which could lead to slightly higher volumes and diameters. This change in concentration can be avoided by converting the one-pot approach into a two-step process, where the initial core particles are purified before further modification. Then a new reaction mixture with exact measures can be used to precisely control the reaction conditions. Within this work, both approaches were used with similar results. For simplification only the two-step process with particle purification in between steps is discussed here.

The particle size distribution diagrams of core PDVB particles, formed in the first reaction step, and of PDVB particles after the shell formation step are compared in Figure 30. On the right side of the figure, the corresponding light microscope images from the reaction mixture are given.

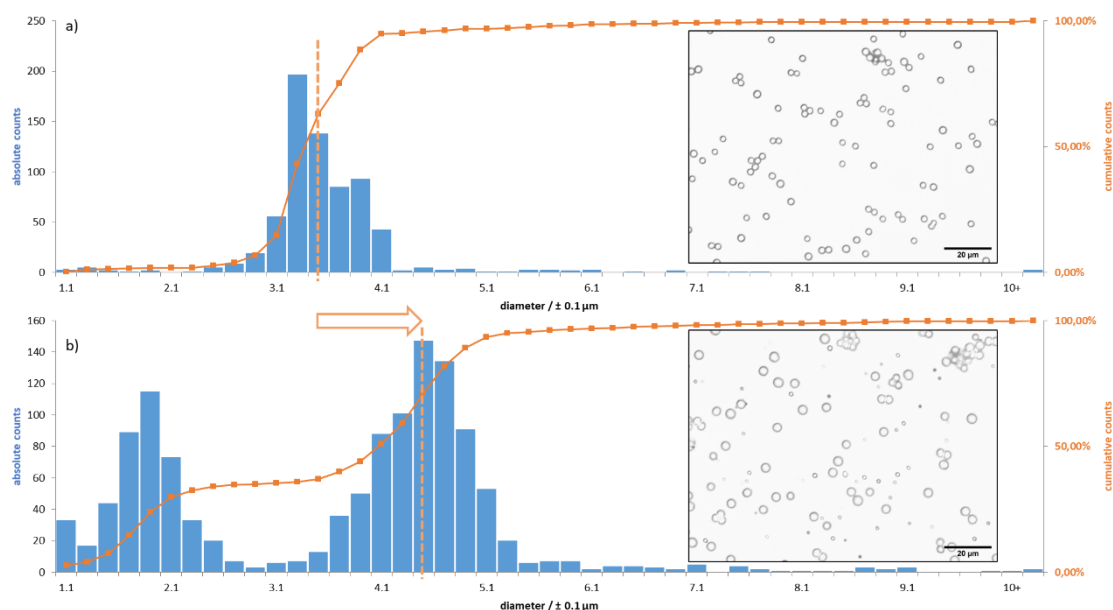


Figure 30: PSD diagrams and their corresponding light microscope images from the reaction mixture showing shell growth via polymer precipitation: particle size distributions of PDVB non-porous core particles in acetonitrile (a) and particle size distribution of the same particles after shell growth by addition of new monomer and initiator (b)

The particle size distribution diagrams of PDVB core particles indicate a narrow size range of 3.3 to 3.5 μm (Figure 30a). After the second reaction step, the particles grow to sizes between 4.3 and 4.7 μm , as highlighted by the orange arrow in Figure 30. This shell growth of approximately 1 μm aligns with expectations. However, next to these grown particles smaller particles with sizes of 1.7 to 2.1 μm are also present in the reaction mixture (Figure 30b). So, while in theory precipitating polymer chains should be preferentially captured by the already existing core particles and thus increase their size, secondary nucleation is also a possible phenomenon. Here, the formed polymer chains form new nuclei which do not combine with the already existing particles.

Overall, these observations suggest that more polymer precipitates during the second reaction step compared to the core synthesis. This could be attributed to polymer scavenging by the larger particles in the reaction mixture. Since their surfaces contain residual double bonds, they can actively participate in polymerization reaction, binding shorter polymer chains to their surfaces that would otherwise be unable to precipitate on their own under these

conditions. While secondary nucleation cannot completely be avoided, the smaller particles can be separated from the desired large particles by centrifugation.

It is to note that the grown particles retain their overall size distribution compared to the core particles. Thus, the core particles can be used as a template for the size distribution with the final size being adjustable by particle growth. Also, very homogeneous precipitation can be assumed, since the particles retain their spherical and uniform shape. The possibility of this uniform growth resulting from particle swelling (and growth from within) can be ruled out, since the high crosslinking density of the core particle is supposed to prevent significant particle swelling (see also chapter 6.3).

In the following, SEM images of non-porous PDVB particles and PDVB core – PDVB shell particles are shown in Figure 31 to compare their surfaces topographies with the focus on the particle porosity.

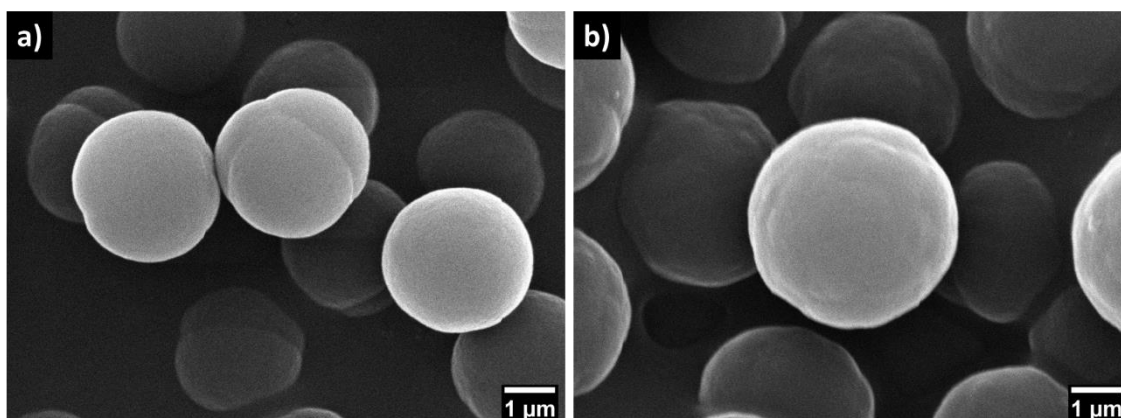


*Figure 31: SEM images of PDVB non-porous particles (a) and PDVB non-porous core – PDVB non-porous shell particles (b).
The samples were coated with a gold layer (thickness: 10 nm) and measured under a high voltage (CamScan24).*

As assumed before, the core-shell variant of these PDVB particles does not exhibit a more porous surface than the core particles because it was synthesized without additional pore-forming agent (porogen). However, the surface is more structured, which probably stems from smaller particle collisions in one of the reaction steps.

With this data, it can be confirmed that particle growth by further addition of monomer and initiator is possible under the reaction conditions established in this work and can be used to

fine tune the particle size of PDVB particles via the amount of added monomer or number of growing steps or used as a base for further customizations.

7.1.4.2 Particle Size Alterations using Styrene

Just as PDVB was precipitated onto the surface of a PDVB particle, it would be interesting to explore whether a similar approach using styrene could yield a polystyrene shell as depicted in Figure 32a. This shell might then be utilized to create pores using a dynamic swelling technique.^{22,59,140} PDVB core particles alone cannot be used for a swelling technique since they are not swellable with a polymeric porogen.

Since polystyrene is soluble in acetonitrile, the standard precipitation technique that was used so far needs to be adjusted. The formation of a polystyrene shell requires a reaction medium that effectively dissolves styrene monomers and short polymer chains but gradually becomes a worse solvent as the polymer chains grow longer, eventually leading to their precipitation. In contrast to acetonitrile (ACN), isopropyl alcohol (iPrOH) is a bad solvent for polystyrene and both solvents mix well. Therefore, a mixture of both solvents could possibly be utilized to fine-tune the solvency conditions for the growing polystyrene chains. As shown in Figure 32b, different solvent mixtures ranging from 100v% iPrOH to 100v% ACN were tested as liquid reaction media for precipitation polymerization of polystyrene. The experiment series covers ACN contents in 20% increments as well as an experiment with a 50:50v% iPrOH:ACN mixture. As a result, one of the two observations were made for all of the experiments:

In the first case, the formed PS chains are not soluble in the liquid medium with high iPrOH contents and thus precipitate onto the preexisting particles. The styrene monomer, however, is soluble in the formed PS shell and can swell it, which results in a mobile and thus sticky coating. This leads to particle agglomeration, which is amplified by the fact that PDVB particles already have a tendency to remain in close proximity during the reaction, since iPrOH, as a polar solvent, is not an ideal dispersing medium for these nonpolar particles. Agitation of the reaction medium did not resolve any of these phenomena.

In the second case, for experiments with higher ACN contents in the reaction medium, better PDVB particle dispersion was observed. However, after the polymerization reaction was carried out, no change in particle sizes could be measured as shown in Figure S 11 in the

appendix. This can be explained by the high ACN content leading to such good solubility of the growing PS chains that no precipitation occurs regardless of chain length during polymerization. Only in pure acetonitrile as reaction medium agglomeration is observed again. In this instance, it is possible that some PS chains become grafted onto the PDVB surface, for example via chain transfer reactions. These surface-bound chains remain solvated and may entangle with other PS chains in solution, promoting particle aggregation through bridging interactions. Under slightly poorer solvent conditions, such interactions might be suppressed because the poorer solvent quality may cause grafted chains to collapse into more compact coils, limiting their accessibility for said interactions.

In conclusion, this route does not seem to be a suitable method to prepare polystyrene shells on highly crosslinked PDVB core particles. The addition of small amounts of DVB as a crosslinking monomer could help to force precipitation through the generation of networks with high molecular masses. This approach will be explored in 7.3.1.

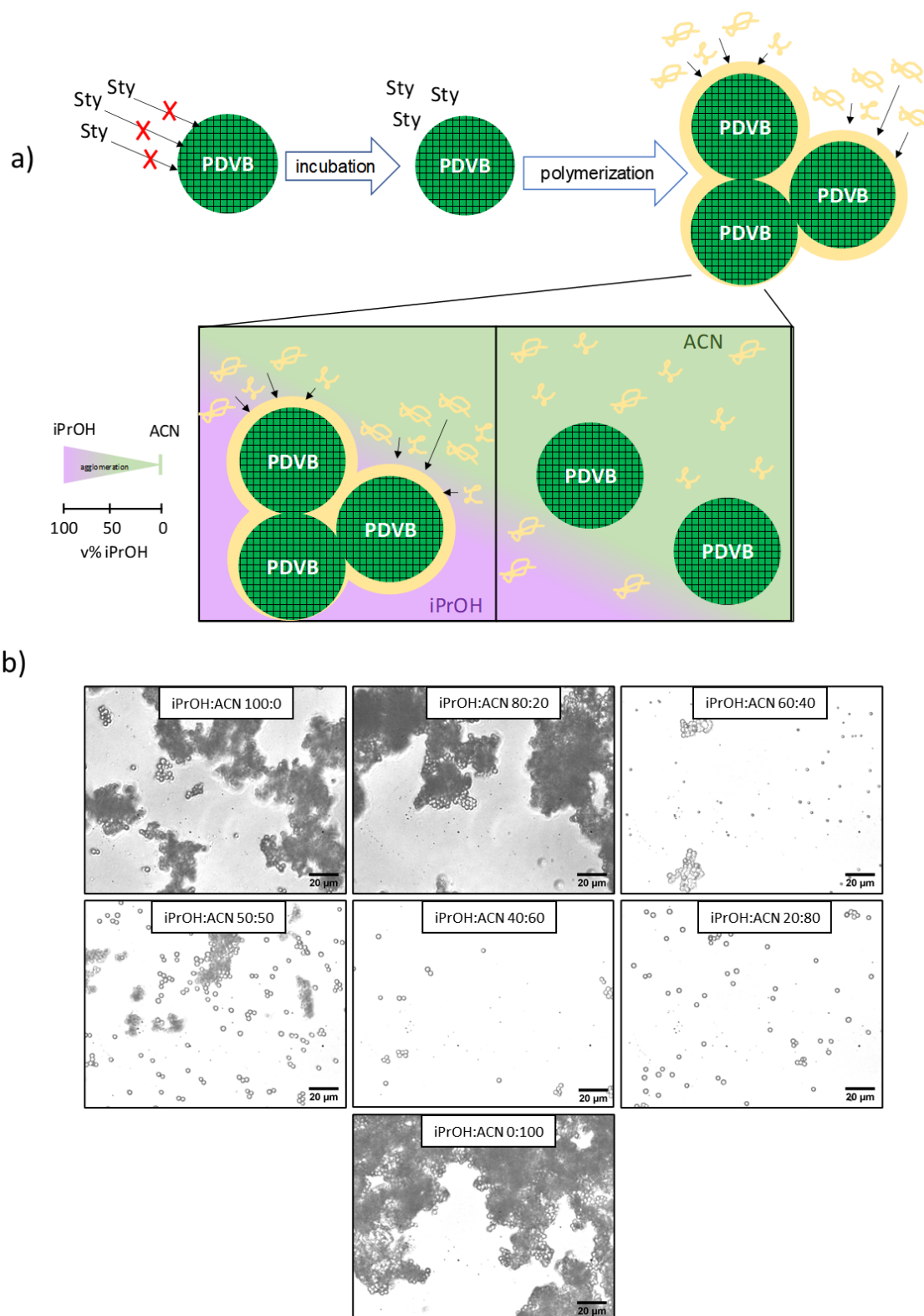


Figure 32: a) Schematic reaction pathway for growing a PS shell on highly crosslinked PDVB particles via precipitation polymerization. b) Light microscopy pictures of the reaction mixture after precipitation polymerization of PS onto PDVB particles in different solvent mixtures of isopropyl alcohol (iPrOH) and acetonitrile (ACN). The specific volume fractions of the solvents used are given in each picture. Scaling is indicated in the bottom right of each picture displayed.

7.1.4.3 Attempts to Introduce Pores into the PDVB Particle Shell

Building upon the knowledge gained from the synthesis of core-shell particles with a non-porous shell, the introduction of pores into the shell will be attempted in the following.

A particle that has a porous shell could be used in many different fields of research like chromatography, selective adsorption, and as catalysts.^{14,18,28,141} As mentioned at the beginning of chapter 7.1.4, the main target for the PDVB particles discussed here is to function as separation material in SEC which operates with materials containing mixtures pore sizes between roughly 2 and 100 nm.^{14,125}

The porous shell should be achievable by addition of a pore-forming agent, also called a porogen,¹⁴² to the reaction mixture of the second reaction step as schematically can be seen in Figure 33. Literature suggests that the porogen can be a good solvent for the polymer, like the used toluene in this chapter, or a non-solvent.^{10,29,85} When a good solvent is used, the pores are supposed to form from small amounts of solvent being trapped in the particle during the precipitation process. This should occur at higher degrees of polymerization compared to experiments with acetonitrile alone due to the improved solubility of the polymer under these conditions.²⁸



Figure 33: Schematic depiction of precipitation polymerization of DVB in acetonitrile followed by the attempt to PDVB porous shell growth by addition of a porogen in the second reaction step as suggested by literature (here: toluene).⁸⁵

While all other ratios in the reaction mixture were kept the same, the solvent mixture was altered as suggested by the literature from neat acetonitrile to an ACN:toluene mixture of 60:40 v/v by addition of the appropriate amount of toluene to the mixture.⁸⁵ The polymerization process was then again started by addition of monomer and initiator as shown before.

The light microscope images of the resulting reaction mixtures after the first and second reaction step can be seen in Figure 34. Both of the reaction mixtures do not show agglomerates. However, the particle sizes do only change for a very small portion of the visible particles (indicated by red arrows in Figure 34) while most particles keep their diameter at around 4.3 μm (see also particle size distribution diagrams in Figure S 12 in the appendix). Additional to the light microscope imaging, the purified particles are tested for porosity in SEC column tests (cf. Figure S 10 in the appendix) where they exhibit similar characteristics as the non-porous PDVB particles from chapter 7.1.2.2.

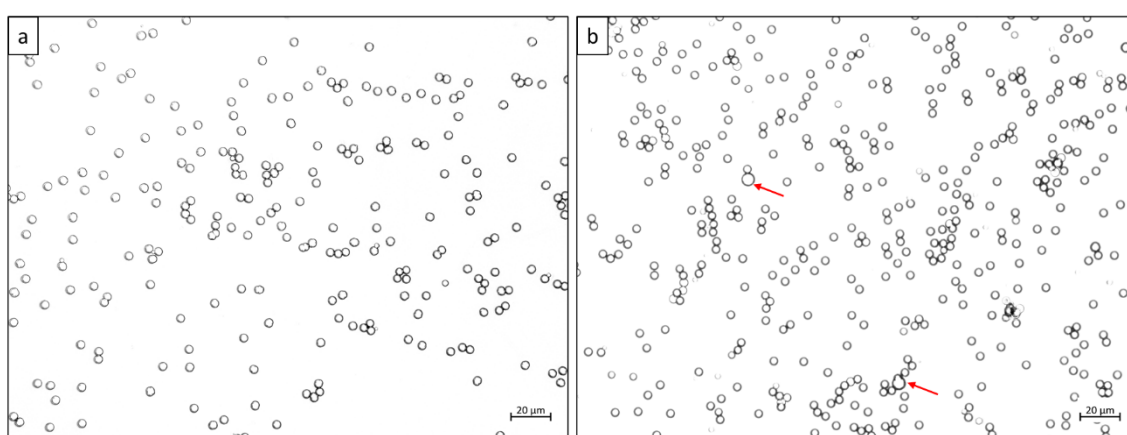


Figure 34: Light microscope images of the core particle reaction mixture (a) and the core-shell particle reaction mixture (b). The red arrows indicate the few particles that grew larger than particles in the first reaction step.

These data lead to the assumption that either no shell growth occurred or, if it happened, the shell thickness lies below the detection limit of the microscope (particle size distribution diagram bin size: 200 nm). In both cases, though, no porous shell was achieved by applying this amount of toluene. However, a fine precipitate was observed during purification after the second reaction step. Therefore, a polymerization apparently has taken place.

One explanation for these findings could be that the used amount of toluene is high enough to prevent the growing polymer chains from precipitating until the chains crosslink with each other. The so induced formation of large, crosslinked polymer chain clusters then leads to precipitation of submicron objects which are self-stabilized by the crosslinks and rigid (secondary nucleation), but not visible with light microscopy.

To efficiently investigate the cause for missing pores and sufficient shell growth, the synthesis of fully porous particles by precipitation polymerization in one reaction step will be discussed in the following chapter before transferring a more successful version of the recipe to the core-shell concept.

Taking all findings into account, the following statements about PDVB core – PDVB shell particle synthesis can be made so far:

The particle size of non-porous PDVB particles can be increased by simple addition of new monomer and initiator to the already existing particle mixture. This method can be used in the form of an easy to handle one-pot synthesis or, if more accuracy is needed within the ingredient ratios, in a two-step synthesis where the core particles are purified before further usage. Next to the possibility of further tailoring the particle size, this method might also be used to alter the shell surface by adding other comonomers next to divinylbenzene. The introduction of pores into the shell could not be achieved under the present conditions by addition of toluene as suggested by the literature⁸⁵ and needs to be further investigated by synthesizing fully porous particles via precipitation polymerization first.

7.1.5 Investigating Low-Molecular-Weight Porogens for Pore Formation

It is reported in the literature that the addition of pore-forming agents (porogens) to a precipitation polymerization of DVB will lead to pore formation in the resulting particles.^{10,28,29,97}

Since pore formation was not attained during the PDVB shell deposition on a PDVB core in the previous chapter, this chapter explores the use of porogens within the less complex core particle synthesis approach that was developed until chapter 7.1.3. The feasibility of transferring literature-reported results with various low-molecular-weight porogens under the reaction conditions established for this synthesis will be examined. To this end, porogens will be introduced during PDVB core synthesis (Figure 29), while the shell formation step is omitted. The resulting “fully porous” particle will then be analyzed for pore formation. If one of the used porogens leads to a porous architecture, this recipe will be transferred back to the shell formation step to achieve the initial goal of a porous shell on a solid core.

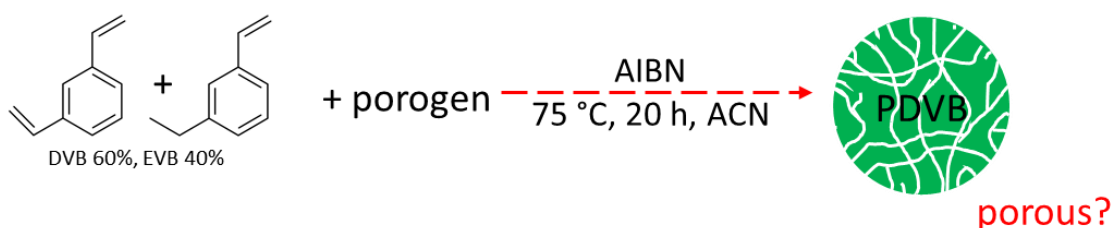


Figure 35: Schematic depiction of the reaction for PDVB particle synthesis via precipitation under presence of porogen(s) in the mixture. Solvents for DVB, non-solvents or mixtures thereof were tested as low-molecular-weight porogens.

As suggested by literature, the low-molecular-weight porogens added to the reaction mixture are supposed to create pores in the formed particle by a locally limited demixing of the solvents in the mixture. The solvents are then captured by the forming particles during precipitation. Thus, small regions of better or poorer solubility of DVB are supposed to be created which results in pore formation in the final particle.^{9,10,28} As good solvents for DVB, toluene and THF were tested, because their Hildebrand solubility parameters, 18.2 MPa^{1/2} and 18.6 MPa^{1/2}, are close to the one given for styrene-like systems (19.0 MPa^{1/2}).^{40,143} Water was chosen because it is a non-solvent for DVB (Hildebrand solubility parameter: 47.9 MPa^{1/2}).¹⁴³

The solvents or non-solvents are added separately to the reaction mixture in varying concentrations and the polymerization reaction is carried out as described in chapter 7.1.3. In addition to using one porogen at a time, particles synthesized in the presence of porogen mixtures were assessed in the same way.

7.1.5.1 Investigation of Good DVB Solvents as Low-Molecular-Weight Porogen

Good solvents are the first group of porogens to be further investigated in this work, since toluene was already used for the shell recipe. After the formation of a porous shell was not achieved in the previous chapter, the objective is now to investigate the cause for the pore formation issues by introducing pore formation into the less complex core particle synthesis and establish a reliable process that can be transferred to the shell formation step afterwards.

To confirm the effects observed in the previous chapter, 40v% of toluene was added to the core particle synthesis. Additionally, it remained unclear whether the quantity of toluene utilized impeded the precipitation of polymer chains in any way. If this was the case, then no polymer particles should form during this synthesis.

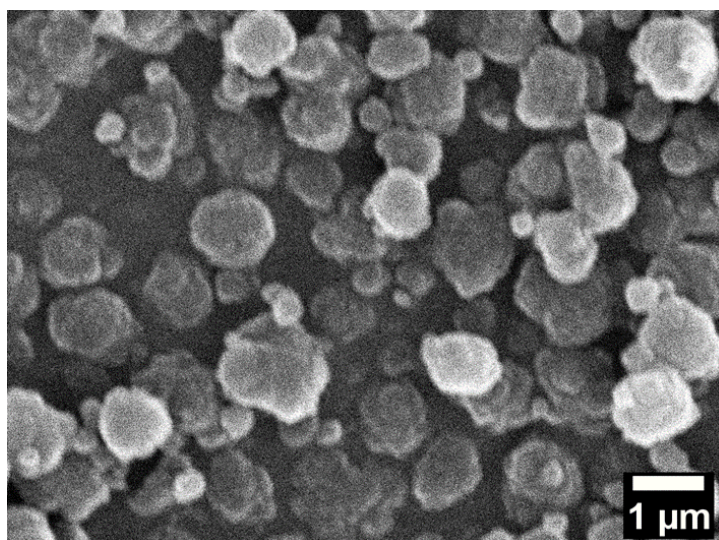


Figure 36: SEM image of PDVB core particles with 40v% toluene present in the reaction mixture. The samples were coated with a gold layer (thickness: 10 nm) and measured under a high voltage (CamScan24).

As can be seen exemplary in Figure 36, all syntheses with 40v% toluene in the reaction mixture resulted in PDVB particles of 1 μm or smaller compared to the 3.5 μm particles yielded from the porogen-free synthesis. Since these sizes could not be measured reliably with light microscopy anymore, SEM imaging was used to analyze the particle characteristics instead. The shown particles are up to 1 μm but only roughly spherical. This leads to the assumption that the used quantity of toluene somehow disturbs particle growth beyond the shown size. In addition to that, no pores can be seen with SEM imaging.

One reason for this phenomenon could be that even long polymer chains cannot precipitate due to the high concentration of a good solvent (in this case: toluene). This might continue until a large polymeric network develops through crosslinking, with many high-molecular-weight polymer fragments being involved in the process. Only the large network then precipitates and forms the first nuclei. The high crosslinking degree, which already exists when these first particles form, could then prevent surface softening by toluene that is needed for particle coalescence via collision (self-stabilization). Although no secondary nucleation was seen with the shell growth experiment before, secondary nucleation might have occurred there as well with the newly formed particles being too small for detection with light microscopy imaging. So, while the precipitation of polymer chains is not completely prevented by the utilized amount of toluene, the formation of larger particles is hindered.

With these findings, it is unlikely that this quantity of toluene is suitable for pore formation or shell growth.

In consequence to these results, the quantity of the used amount of toluene was lowered to 20v% of the total reaction volume to enable particle formation again. The particle size distribution diagram and the corresponding light microscope image of the resulting PDVB particles can be seen in Figure 37.

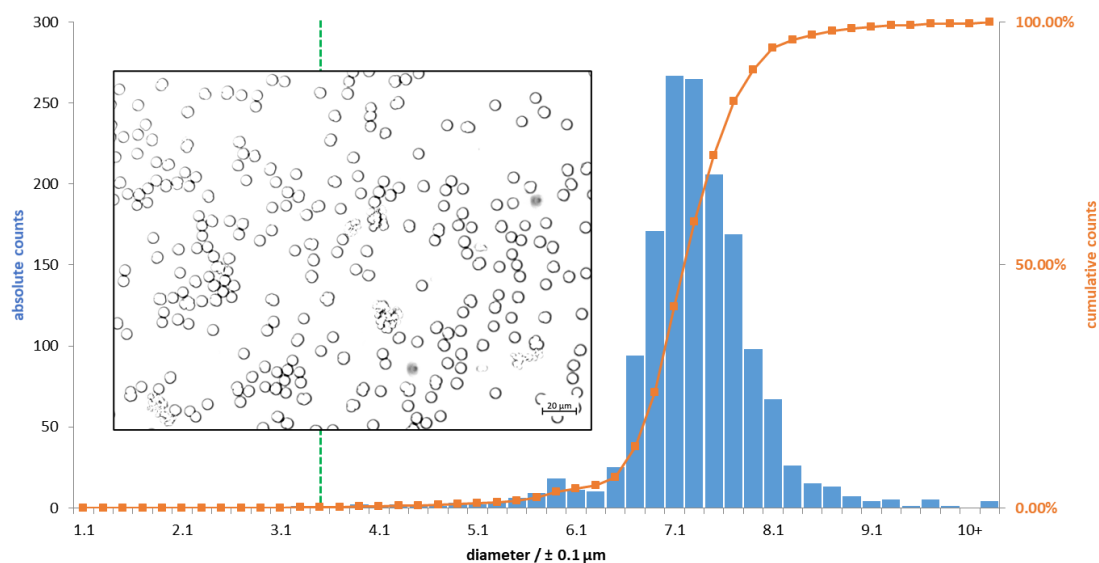


Figure 37: PSD diagram and light microscope image of PDVB particles synthesized via precipitation polymerization in ACN with 20v% toluene present in the reaction mixture. For comparison, the PDVB particle sizes from the porogen free standard synthesis are indicated by the dotted green line.

For the shown example, the resulting particles are found to be much larger in size after the polymerization (about 7 μm) compared to core particles synthesized without addition of porogen (about 3.5 μm). Some agglomeration can be seen, but to a negligible degree. In addition to the large particles found in the shown example, some experiments also yielded a broader size distribution with particles between 1 and 8 μm (cf. Figure S 13). Yet, most of the syntheses involving 20v% toluene resulted in particle mixtures with high percentages of particles being larger than 3.5 μm (>70%).

Compared to the porogen-free systems, polymer chains can grow longer until they precipitate creating larger nuclei in the first place as it was also discussed for high monomer loads before (chapter 7.1.2.2). These particles can then grow further by particle collision and oligomer scavenging as indicated by the SEM images presented in Figure 38. The average size of the captured oligomers may also be larger due to the higher solubility limit. All of the large particles in the overview image (Figure 38a) consist of smaller particles which fused together and are still discernible by thin grooves separating them.

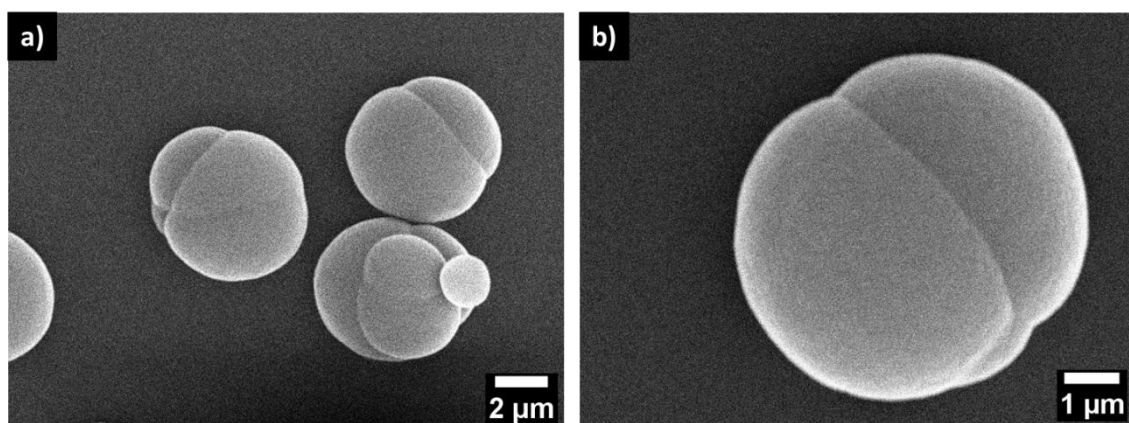


Figure 38: SEM images of PDVB particles synthesized with 20v% toluene present in the reaction mixture. a) overview image and b) detailed depiction of the particle surface without pores. The samples were coated with a gold layer (thickness: 10 nm) and measured under a high voltage (CamScan24).

The presence of toluene has probably helped in this process since it can soften the particle surface due to the good solvent quality in the same way as monomer residues in the reaction mixture do (cf. chapter 7.1.2.2) but without being consumed in the polymerization process. Therefore, the particle surfaces might stay stickier for longer, facilitating coalescence until a threshold in the crosslinking density is reached. This high crosslinking density then prevents swelling and thus softening of the surface.

The SEM image, which provides a more detailed view of the topographical characteristics (Figure 38b) compared to the previous overview image, reveals the absence of discernible pores. However, due to the resolution limit of 10 nm under optimal conditions for the used SEM and the possibility that smaller pores are hidden by the 10 nm thick gold layer from sputtering, supplementary tests were conducted employing SEC column performance tests (cf. Figure S 10).

As observed before with the PDVB particles obtained from the porogen-free synthesis and the non-porous core - “porous” shell approach, the PDVB core particles with 20v% toluene present in the reaction mixture do not exhibit a SEC separation mechanism that can be linked to a porous surface. Since this finding is in congruence to the SEM imaging data, it can be assumed that no pores of a significant size formed during the precipitation polymerization.

One reason for this could be that the characteristics of toluene and acetonitrile are not different enough to support local demixing. Also, with the given high solvency of toluene for DVB it is more likely that toluene swells the forming particle by homogenously permeating it, which should not create pores.

Thus, with the given data, it is evident that 20v% of toluene does not prevent particle growth like it was observed with 40v% toluene in the reaction mixture. Instead, particle growth beyond 3.5 μm is even favored.

PDVB particle syntheses with 20v% of tetrahydrofuran (THF) instead of toluene yielded similar results as the ones obtained for toluene addition. The particle sizes increased to about 5 μm compared to porogen-free syntheses (cf. Figure S 14), which is smaller than seen with toluene addition though. Furthermore, no pore formation was detectable during SEC column performance tests with the observed separation behavior aligning with the previously discussed particle variants. Similar findings were reported in the literature for photoinitiated polymerizations of DVB and GMA (2,3-epoxypropyl methacrylate) with added THF.³⁰

Overall, it can be said that the addition of good solvents like toluene and THF to a certain volume percentage leads to increased particle sizes compared to a porogen-free synthesis. Nevertheless, under the tested conditions both investigated good solvents do not lead to pore formation in the resulting particles in contrast to the suggestion in literature.²⁸ Higher amounts of toluene even lead to small and non-spherical particle clusters instead of uniform and smooth particles.

7.1.5.2 Assessment of Water - a Non-Solvent for DVB - as a Porogen

Apart from good solvents for DVB, also non-solvents have been studied as low-molecular-weight porogens in the literature.^{9,29} In suspension polymerization, the pore formation is achieved by partial phase separation of non-solvents for DVB in the organic droplets in the same way as was discussed for good solvents before. The main difference with non-solvents is that the growing nuclei are reported to barely swell due to the lower solvent affinity. Thus, transferring these observations from suspension polymerization, water as a strong non-solvent for DVB¹⁴³ will be evaluated for suitability as porogen in precipitation polymerization in this chapter.

As before, the porogen was added to PDVB core particle synthesis before polymerization. When 10v% water with respect to the total reaction volume was added, agglomeration

occurred. Therefore, only volume percentages of water lower than this were further investigated.

In the following, Figure 39 shows light microscope images and the corresponding particle diagrams of PDVB particle reaction mixtures after polymerization with 1v%, 2v% or 5v% water (with respect to total reaction volume) added to the reaction mixture.

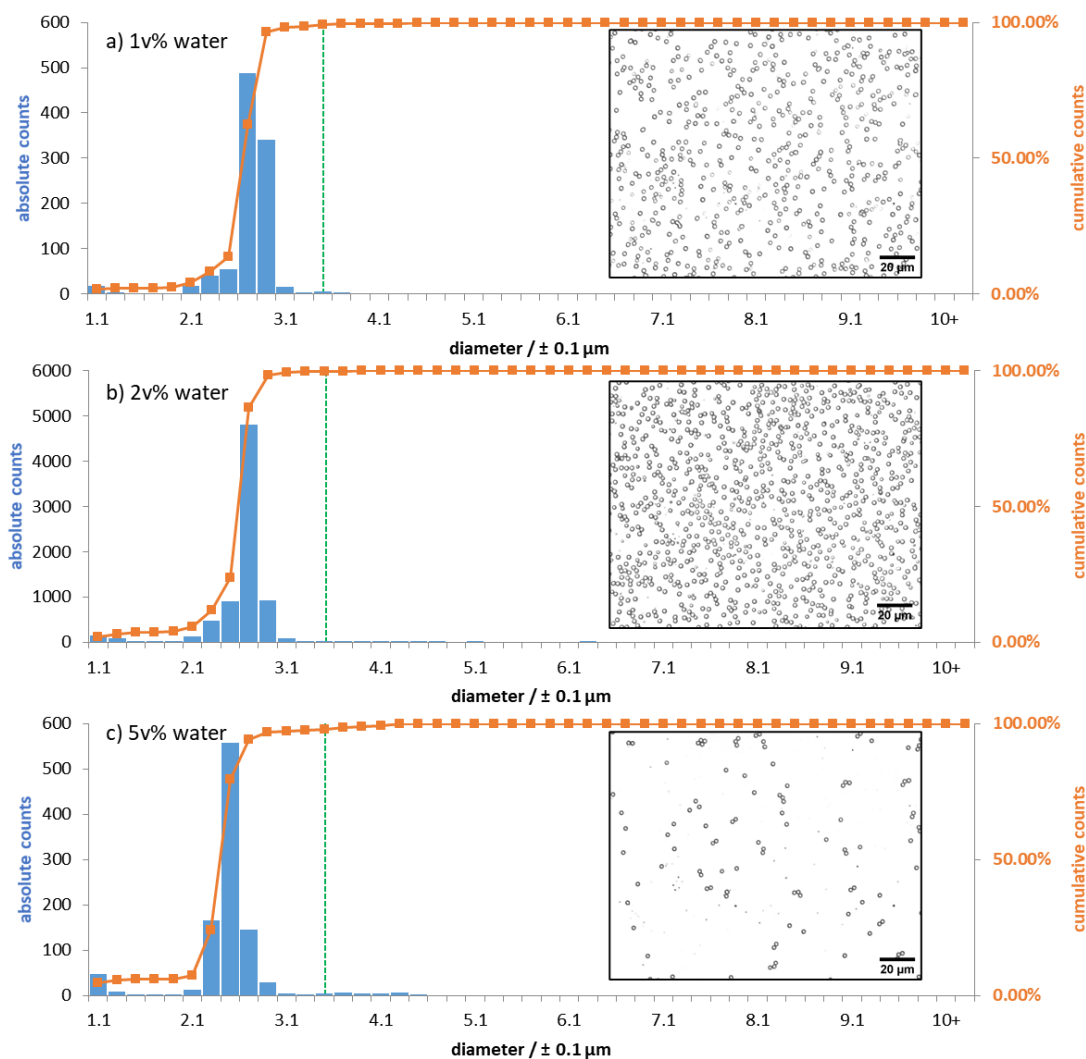


Figure 39: PSD diagram and light microscope images (50x magnification) of PDVB particles synthesized via precipitation polymerization in ACN with presence of different amounts of water in the mixture: a) 1v%, b) 2v% and c) 5v%. For comparison, the PDVB particle sizes from the porogen free standard synthesis are indicated by the dotted green lines.

For all three tested variants no or negligible agglomeration could be observed, and the resulting particle sizes are between 2.4 μm and 3.0 μm . Thus, the overall addition of water

results in a slight reduction in PDVB particle sizes compared to porogen-free precipitation polymerizations, where particles with an average size of 3.5 μm were obtained. The higher the volume percentage of water in the reaction mixture, the smaller the resulting particle sizes get. Thus, as a non-solvent for DVB, water influences particle growth in the opposite way as was observed for the good solvents like toluene. This could be explained with the same hypothesis about solubility behavior as discussed before: The presence of non-solvent for DVB (in this case: water) reduces the affinity of growing polymer chains to remain in solution, leading to their earlier precipitation compared to porogen-free syntheses.⁹⁷ Therefore, the starting nuclei are smaller as well as the average size of the oligomers in solution which can be added to the particle surface during growth. Additionally, the smaller nuclei can only undergo growth through coalescence as long as there is sufficient monomer present to soften the particle surface. Assuming the monomer is consumed at a similar rate as in porogen-free syntheses, the particles have a comparable time frame for growth. However, since the nuclei were smaller initially, this results in smaller particles in the end.

According to pore formation, the particles shown in the SEM images in Figure 40 look quite similar to particles formed in porogen-free syntheses and do not display any pores of significant size regardless of the amount of water that was used. SEC performance tests confirmed this finding for particles made with 2v% water, as the observed behavior was similar to the particle variants discussed before (cf. chapter 7.1.5.1). The absence of pores cannot be attributed to uniform particle swelling, as PDVB particles do not exhibit any tendency for swelling in water.

In consequence to the obtained data, it can be said that also water as a non-solvent for DVB is not suitable as a pore formation agent (porogen). However, it can be used to achieve slightly smaller PDVB particles compared to porogen-free precipitation polymerizations in acetonitrile yielding a tool for size adjustment in such polymerizations.

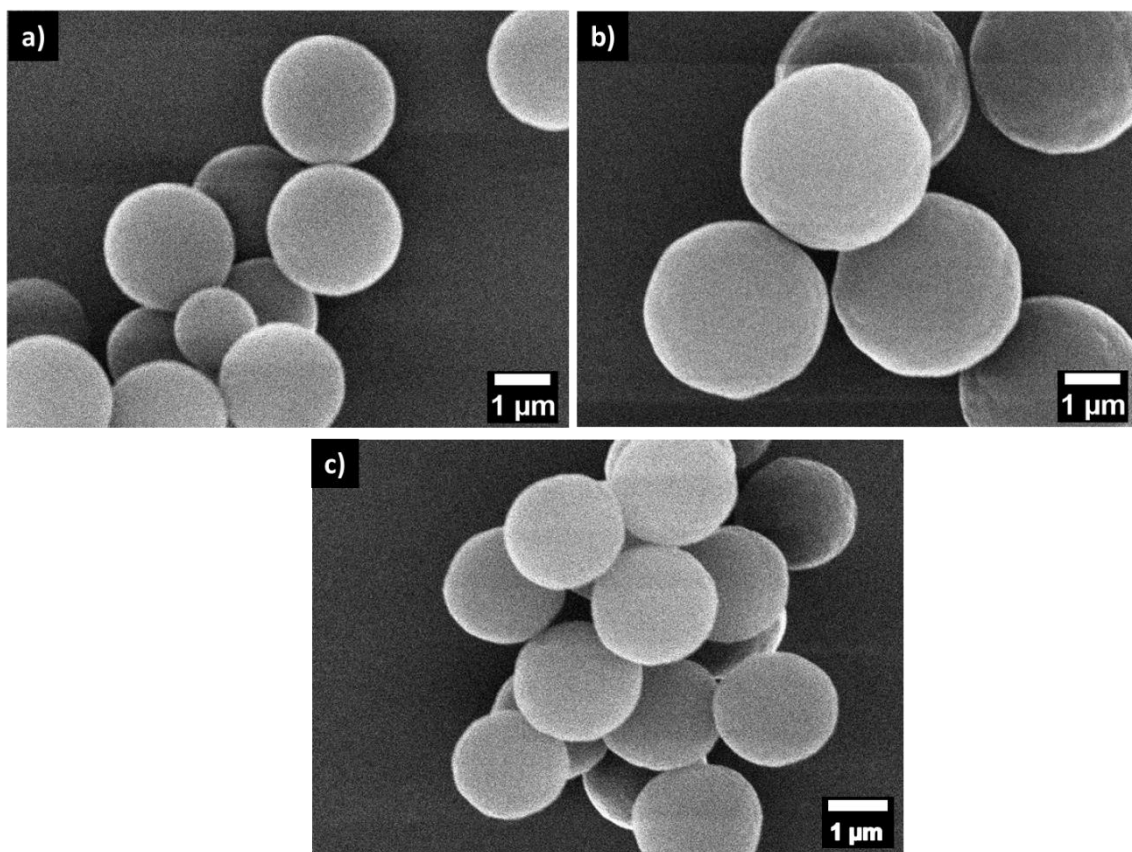


Figure 40: SEM images of PDVB particles synthesized via precipitation polymerization in ACN with presence of different amounts of water in the mixture: a) 1v%, b) 2v% and c) 5v%. The samples were coated with a gold layer (thickness: 10 nm) and measured under a high voltage (CamScan24).

7.1.5.3 Evaluation of Low-Molecular-Weight Porogen Mixtures

After studying the low-molecular-weight porogens individually, several questions concerning mixtures of porogens arise: Firstly, and of utmost importance, do these mixtures influence pore formation differently than individual porogens? Does the different nature and immiscibility of toluene and water facilitate local demixing which is supposed to be responsible for pore formation according to literature?^{9,28} Secondly, given that good solvents, like toluene, have been observed to increase resulting particle sizes and water, as a non-solvent, has been shown to reduce them, it would be valuable to explore the combined impact of a good solvent and a non-solvent on the particle size.

As a consequence, the influence of toluene and water in tertiary mixtures with acetonitrile was investigated further. To keep the reaction comparable to the individual porogen additions, toluene was kept at 20v% as with the individual addition described above. For water, either 2v% or 5v% were added.

Figure 41 displays the PSD diagram and the corresponding LM image of the reaction mixture after the formation of PDVB particles, where toluene (20v%) and water (2v%) were present.

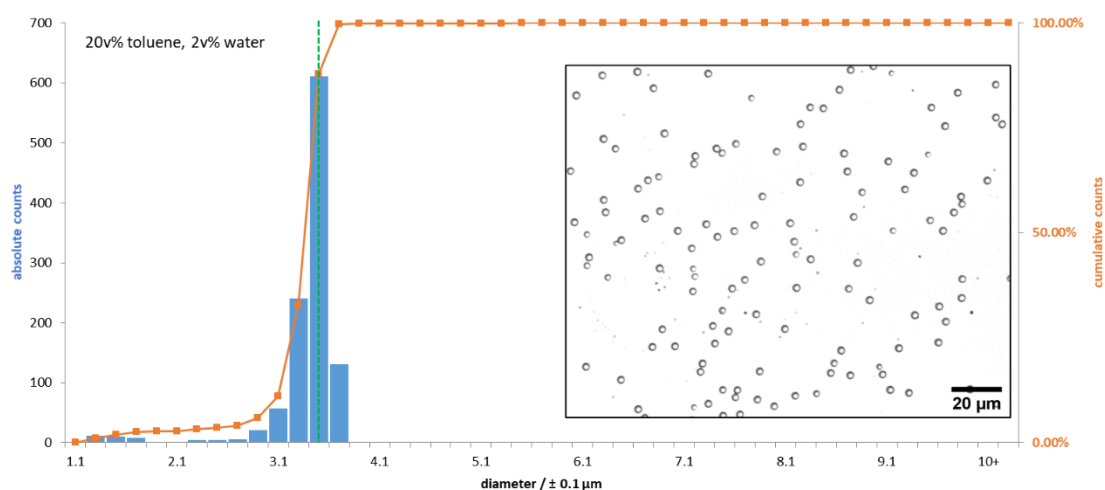


Figure 41: PSD diagrams and light microscope images (50x magnification) of PDVB particles synthesized via precipitation polymerization in ACN with presence of 20v% toluene and 2v% water in the mixture. For comparison, the PDVB particle sizes from the porogen free standard synthesis are indicated by the dotted green line.

The resulting, agglomeration-free particle mixtures exhibit particle sizes around 3.5 μm with a narrow size distribution like it was observed for the porogen-free syntheses. So, while the

individual porogens have opposite effects on the particle size, the combination of both seems to cancel out these effects. Using 5v% water instead of 2v% yielded slightly smaller particles again (around 3.3 μm), as can be seen in Figure S 15 in the appendix. Hence, as with water as the only porogen, an increase in water content leads to a slight decrease in particle size. With 5v% water, more aggregates were observed in the reaction mixture after polymerization. However, these aggregates could be separated again during the purification step.

In the following, a set of SEM images is shown (Figure 42) to compare the influence of toluene and water alone on the resulting topography of the PDVB particle surface and how they affect the particle morphology in combination. Without porogens added to the mixture (Figure 42a), the particles display a smooth surface. However, some still show signs of coalescence, as indicated by sectoring through long grooves extending from pole to pole. The same was observed for particles made with toluene present in the reaction mixture (Figure 42b), but with larger diameters forming at the end. With water added individually to the reaction mixture, the resulting particles exhibit a slightly rougher surface with a tendency toward a raspberry-like morphology (Figure 42c). This structure arises from the coalescence of significantly smaller particles compared to those in cases (a) and (b). However, if toluene and water are added in combination, this structure cannot be observed anymore. Instead, the particle surface is smooth and does not show any grooves from particle coalescence (Figure 42d and Figure S 16 in the appendix for overview images). So, with the combined addition of toluene and water, the resulting particles can be improved in terms of particle smoothness and uniformity.

Unfortunately, no pore formation can be observed for particles synthesized in tertiary mixtures of toluene, water, and acetonitrile under the tested compositions, similar to the binary solvent mixtures involving these porogens. Since the particles in Figure 42d show an even smoother surface than particles analyzed with SEC column performance testing before, it was assumed that it was not likely that significant-sized pores capable of polymer separation were formed. Therefore, no further SEC column testing was performed since it was very unlikely to yield any new results.

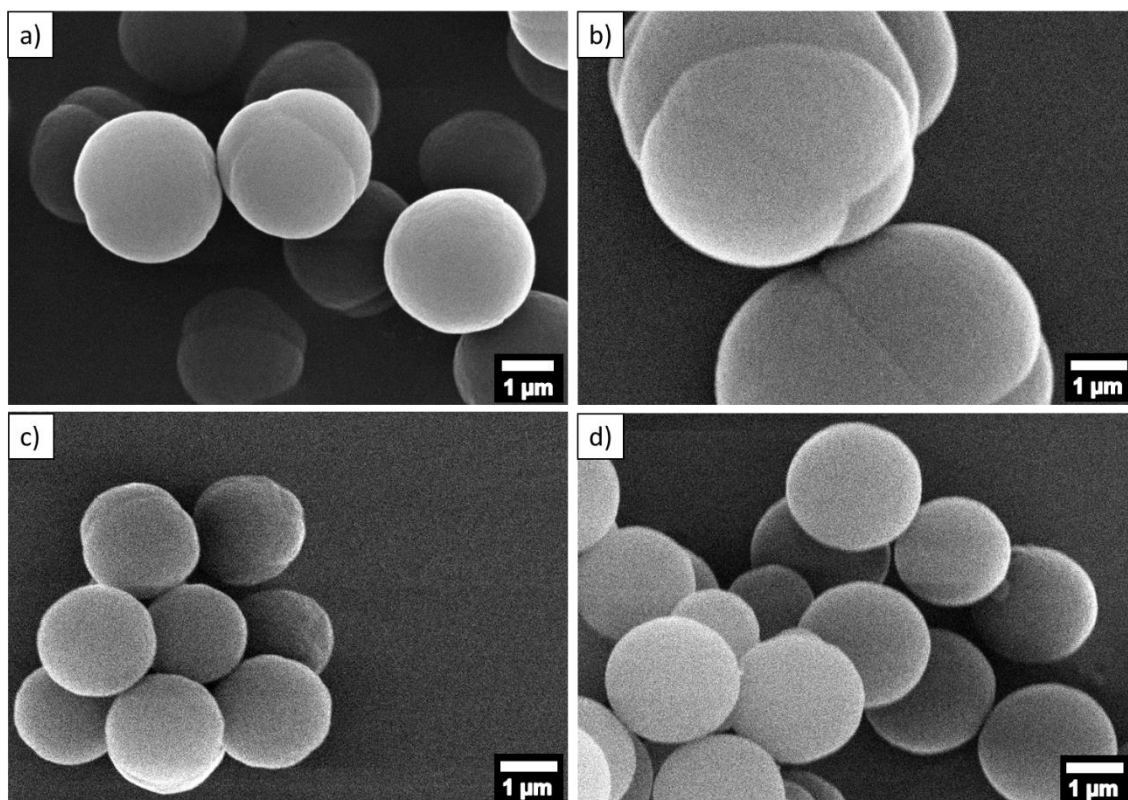


Figure 42: SEM images of PDVB particles synthesized via precipitation polymerization in neat ACN (a) or with presence of different amounts of porogens added to the mixture: b) 20v% toluene, c) 5v% water and d) 20v% toluene and 5v% water.

The samples were coated with a gold layer (thickness: 10 nm) and measured under a high voltage (CamScan24).

So, while the utilization of two porogens with opposing solvent characters, water and toluene, revealed that no pores of significant size were formed on the particle surface, it is documented in literature that a combination of toluene and dodecanol as porogens is sufficient to form pores on PDVB particles during precipitation polymerization.¹⁰ Dodecanol is another common porogen for the synthesis of porous beads.^{9,14,138} For precipitation polymerization, it is suggested in literature that due to the larger size of the dodecanol molecule, compared to toluene, larger pore volumes are formed when dodecanol is inserted.^{10,28}

Experiments with dodecanol as the only porogen (20v% of total reaction volume) yielded PDVB particles with sizes between 3.8 μm - 4.2 μm or smaller (cf. Figure S 17 in the appendix) but did not lead to any pore formation visible with SEM imaging (cf. Figure S 18 in the appendix). These particles behaved in the same way during SEC column performance tests like all other types of particles documented before (e.g. chapter 7.1.5.1) confirming the observations made with SEM imaging.

It is suggested in the literature¹⁰ that toluene is necessary to make the PDVB particles accessible for dodecanol by partially swelling and softening the forming particles so that dodecanol can be inserted more easily. Therefore, a combined addition of toluene and dodecanol was investigated although the data obtained from the individual additions did not result in pore formation in PDVB particles.

The reported recipe¹⁰ was adapted to the synthesis developed in this thesis as described in chapter 7.1.3 to ensure an agglomeration-free process: Instead of 3v% monomer load (literature), 2v% DVB were used and the AIBN concentration was kept at 16mol% in the reaction mixture or 2wt% with respect to the used amount of monomer (literature: 3wt%). As suggested by the publication, the solvent mixture used for the synthesis was changed to contain 15v% of each porogen with the rest of the solvent mixture being acetonitrile.

The resulting particle sizes measured with light microscopy (Figure S 19 in appendix) increased slightly to 4.1 μm compared to porogen-free synthesis. This is roughly the same increase as observed with particles resulting from the individual addition of dodecanol (Figure S 17 in the appendix).

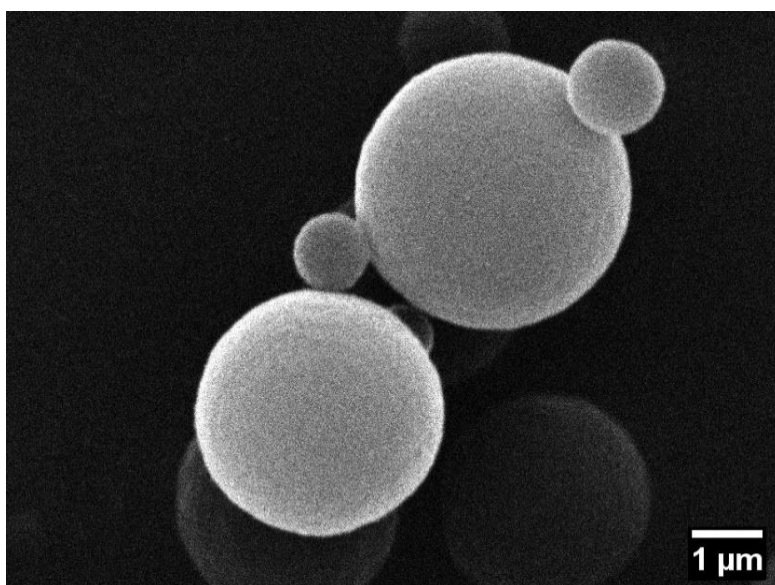


Figure 43: SEM images of PDVB particles synthesized via precipitation polymerization in ACN with presence of 15v% toluene and 15v% dodecanol (with respect to total reaction volume) in the reaction mixture. The samples were coated with a gold layer (thickness: 10 nm) and measured under a high voltage (CamScan24).

Still, when the particle surface is checked with SEM imaging (cf. Figure 43), no pore formation or other substantial changes in the particle surface can be detected compared to smooth-surfaced particles made without added porogen. The surface may display a very fine granular structure. However, this observation cannot be definitively distinguished from measurement artifacts. Compared to SEM images given in literature¹⁰, pores should be significantly visible at the used magnification, if they formed. Since this is not the case in this instance, no further SEC column performance tests were issued.

The effect of adding 20v% of each porogen was investigated as well but resulted in either agglomerates or shapeless particles with sizes $<1\ \mu\text{m}$ (cf. Figure S 20 in the appendix). These results are similar to the ones from 40v% toluene addition. Since dodecanol also has a similar Hildebrand solubility parameter ($21.3\ \text{MPa}^{1/2}$) as styrene-like systems ($19.0\ \text{MPa}^{1/2}$) and toluene ($18.2\ \text{MPa}^{1/2}$), the combined addition of toluene and dodecanol (40v% in total) might have the same effect as toluene alone (40v%).^{40,143–145}

With these findings, the suggested pore formation after a combined addition of toluene and dodecanol during precipitation polymerization of DVB could not be confirmed under the tested reaction conditions.

In summary, no pores could be found when any of the above investigated low-molecular-weight porogens were added. Changes in particle size were found for some of the solvents compared to the standard recipe. For some porogens the reaction mixtures collapsed and resulted in agglomerated particles as a primary result, especially when higher volume fractions of the porogen were used.

One possible explanation for this phenomenon may be rooted in the contrasting mechanisms of suspension polymerization and precipitation polymerization: in suspension polymerization, the formed nuclei slowly interconnect and grow together in a confined space and thus can trap cosolvents which are also confined to the monomer droplet in the case of nonpolar solvents. On the other hand, nuclei in precipitation polymerization can grow individually without necessarily touching each other and cosolvents can move freely in the reaction mixture. This leads to less entrapping of the cosolvent(s) (or non-solvents) even if local demixing occurs, since the solvents might have enough freedom to leave the growing particle due to the lack of confinement. This might explain why regardless of the nature of solvents or

the combined addition of more than one species pore formation was not observed in the tested environment. Nevertheless, the addition of cosolvents to the precipitation polymerization of DVB can be used to alter, and thus tailor, the resulting particle sizes while still receiving narrow particle size distributions.

7.1.6 Chapter Conclusion and Outlook

In chapter 7.1, the PDVB particle synthesis via precipitation polymerization was explored using standard laboratory equipment, replacing the more complex incubator bottle method. For small-scale experiments, a setup consisting of single-use screw cap vials and aluminum block heating was developed. Pyrolysis-cleaned glass flasks and oil bath heating were used for large-scale experiments. Both setups reliably provided monodisperse particles. Gentle agitation and HPLC-grade solvent were required to avoid agglomeration. The initiator and monomer could be used as received, with purity influencing only the particle size. Reaction parameters such as temperature, initiator concentration, and monomer load influenced particle size, with higher temperature and monomer load increasing size, whereas higher initiator concentration decreased it. However, increasing the monomer load beyond 2v% caused agglomeration. The non-porous core PDVB particles (3.5 μm in diameter) displayed a smooth surface in SEM imaging and showed the expected HDC separation in SEC column tests. Non-porous shell growth was achieved using the same monomer and initiator amounts as the core synthesis, increasing the diameter by 1 μm . Investigations of pore formation during shell growth or the core synthesis with low-molecular-weight porogens resulted in particles with no significant pores suitable for application in SEC, as shown by SEM and column performance tests. This can be attributed to the lack of confined space during particle formation in precipitation polymerization. Applying macromolecular porogens and a confined polymerization process may address this issue, as explored in later chapters. Nonetheless, low-molecular-weight porogens influenced particle size, offering a simple way to adjust dimensions without additional reaction steps. The resulting PDVB particles, with high mechanical stability and narrow size distribution, are suitable for HDC and could serve as particle size standards for analytical applications like particle size analyzers.

7.2 Morphological design of PDVB-based particles

Data from this chapter was included in the publication

S. Freese, G. Glasser, M. Susewind, I. Lieberwirth, T. Hofe, U. Jonas, Morphological design of PDVB-based particles, NanoSelect, 2024, 5, 2300064, DOI: <https://doi.org/10.1002/nano.202300064>.

In the field of size exclusion chromatography (SEC), sorbents, or delivery systems porous particles are a well-established class of materials.^{6,7,10,14,28,61,138,146,147} Usually, due to the larger volume demand in such applications, microspheres with dimensions in the 1 to 1000 micrometer range are favored over nanoparticles (approx. 1 - 100 nm).^{1,12,67} However, achieving such advanced functionalities relies on the precise design of the particle's internal nanoarchitecture.¹⁴⁸ For this, a wide range of preparation methods for polymer particles exists which allow specific control over the particle size, morphology and architecture.^{4,14,19,29,106,149} On the one hand, particle sizes can be well tailored by precipitation and emulsion polymerization.^{43,150} On the other hand, pore architectures can be introduced by suspension polymerization or by template swelling techniques.^{14,22,41,106} However, the suspension polymerization typically results in polymer particles with a broad size dispersion while narrow particle size distributions can be retained by swelling template particles with monomer. The swelling method and precipitation polymerization technique, which are commonly used to achieve specific particle sizes and morphologies in polystyrene (PS) and polydivinylbenzene (PDVB) systems, are schematically illustrated in Figure 44.

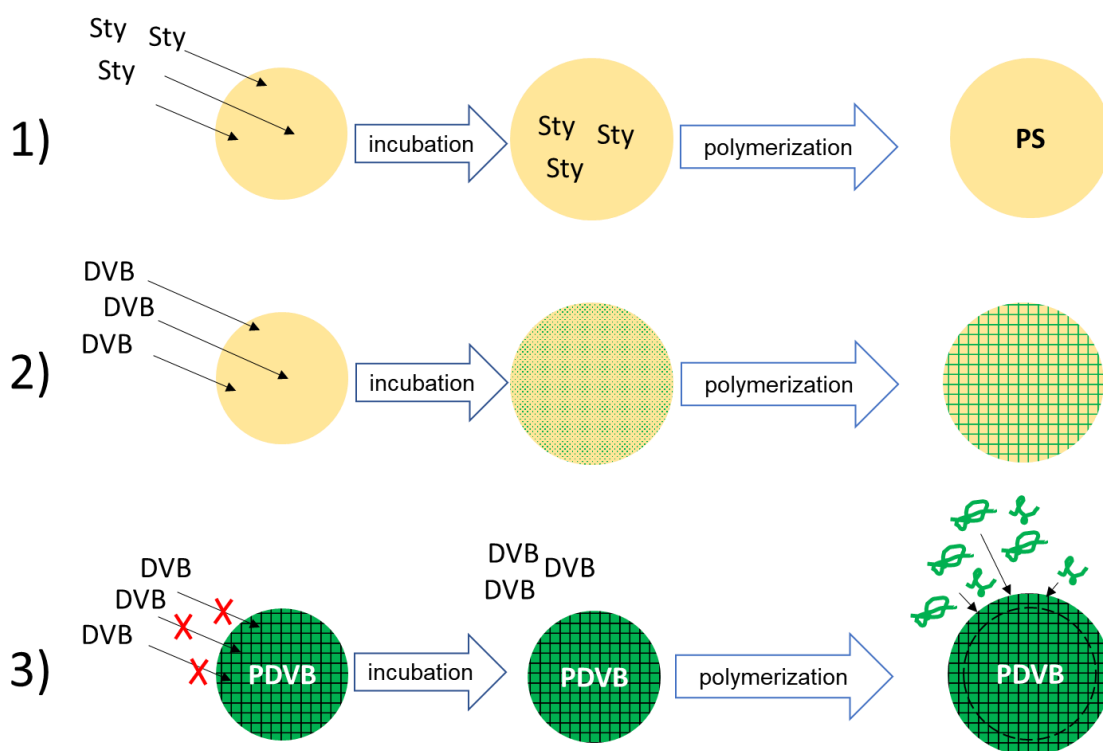


Figure 44: Comparison of swelling and precipitation mechanisms: Swelling of polystyrene (PS) particles with either 1) styrene (Sty) or 2) divinylbenzene (DVB) or 3) precipitation of polydivinylbenzene (PDVB) chains on PDVB particles.

Non-crosslinked polymer particles (like PS latex) are composed of single chain entities and can be utilized as soluble templates for monomer swelling followed by polymerization. By this procedure, the particle size can be increased in a well-defined manner, and pores can be introduced after dissolution of the template material through swelling with a crosslinking monomer.^{22,60,61}

The emulsion polymerization technique is commonly employed to prepare the PS template. However, this method typically limits particle diameters to a maximum of around 1 μm .⁵⁹ To further increase the particle size, an additional reaction step is needed, which involves swelling the PS matrix with extra styrene monomer, followed by polymerization (reaction pathway 1 in Figure 44). When DVB is introduced as a crosslinking monomer into these non-crosslinked PS template particles, subsequent polymerization creates a PDVB network interspersed with mobile PS chains within the particle (pathway 2 in Figure 44). The resulting phase separation between the PDVB network and the PS template can generate porous particles upon dissolution of the PS template using an appropriate solvent.^{22,60}

Precipitation polymerization using a crosslinking monomer such as DVB leads to the formation of highly crosslinked particles that are no longer swellable with monomer.¹⁹ Continued

precipitation polymerization leads to shell growth through the deposition of newly formed polymer onto the particle surface (pathway 3 in Figure 44), whereby the shell becomes indistinguishable from the core.^{43,85} To introduce porosity into such fully crosslinked PDVB particles following pathway 3, several methods have been reported in the literature,^{10,28,30} albeit with varying degrees of success.

Combining such particle formation methods provides a promising way to harness the unique advantages of each technique and bring together the architectural features attained with each method. Yet, these combinations do not always produce the expected outcomes from simply adding individual effects. Instead, new properties may arise from the synergy between the applied techniques.^{34,68,70,151,152} Therefore, this chapter explores how the combination of precipitation polymerization and particle swelling influences the morphology of PDVB particles. Three different PDVB architectures derived from PS templates with varying crosslinking levels will be examined, and the role of PS in the formation of grooves and pores will be discussed.

7.2.1 Preparation of crosslinked particles with grafted polystyrene chains (PDVB-gPS) from non-crosslinked seed templates (tPS^{nc})

The synthetic route of forming a porous shell via precipitation polymerization, by changing the monomer and continuing the growth in a one-pot reaction, was investigated in previous chapters:

As discussed in chapters 7.1.4.3 and 7.1.5, model experiments with toluene or other low-molecular-weight porogens did not yield discernible separation behavior in SEC under the tested conditions. Moreover, chapter 7.1.4.2 describes the attempt to create a non-crosslinked PS shell on a PDVB core through precipitation polymerization, with the aim of subsequently creating a porous structure via PS templating. However, this approach proved unsuccessful, with one of two outcomes being observed: either the particles agglomerated, or the shell material remained dissolved after the reaction, and no measurable increase in particle size was found. Based on these findings, this strategy was considered unsuitable for porous shell formation. As a consequence, three different strategies based on the combination of precipitation polymerization with template swelling were developed.

As a first route, the swelling method described in the literature was implemented: a non-crosslinked PS template particle was swollen with DVB, the crosslinker was polymerized, and the PS template was subsequently removed by dissolution from the resulting PDVB network (see Figure 45). In the literature,⁵⁹ this swelling process is carried out using a non-crosslinked PS template, an excess of a monomer mixture (monomer mass : PS particle mass of 2:1 for an equal monomer mixture of Sty:DVB = 1:1), and the plasticizer dibutyl phthalate as swelling aid. The resulting spherical particles were reported to have a diameter of 7.4 μm and a porous structure with an average pore diameter of 49 nm, when starting from a PS template with molar masses of $M_n = 4.1 \times 10^3 \text{ g/mol}$ and $M_w = 9.0 \times 10^3 \text{ g/mol}$.

To obtain larger pores, the literature procedure was adapted by reducing the DVB amount relative to the PS template to a ratio of 0.2:1 and omitting styrene entirely. As the lower monomer ratio required less swelling of the template, the experiment was conducted without the swelling aid. The morphological evolution during each process step was monitored by analyzing the particles after each stage. Particle dimensions were measured by light microscopy (LM), and, except for the DVB swelling step, scanning electron microscopy (SEM)

was used to examine the surface morphology and internal pore structure after microtome sectioning.

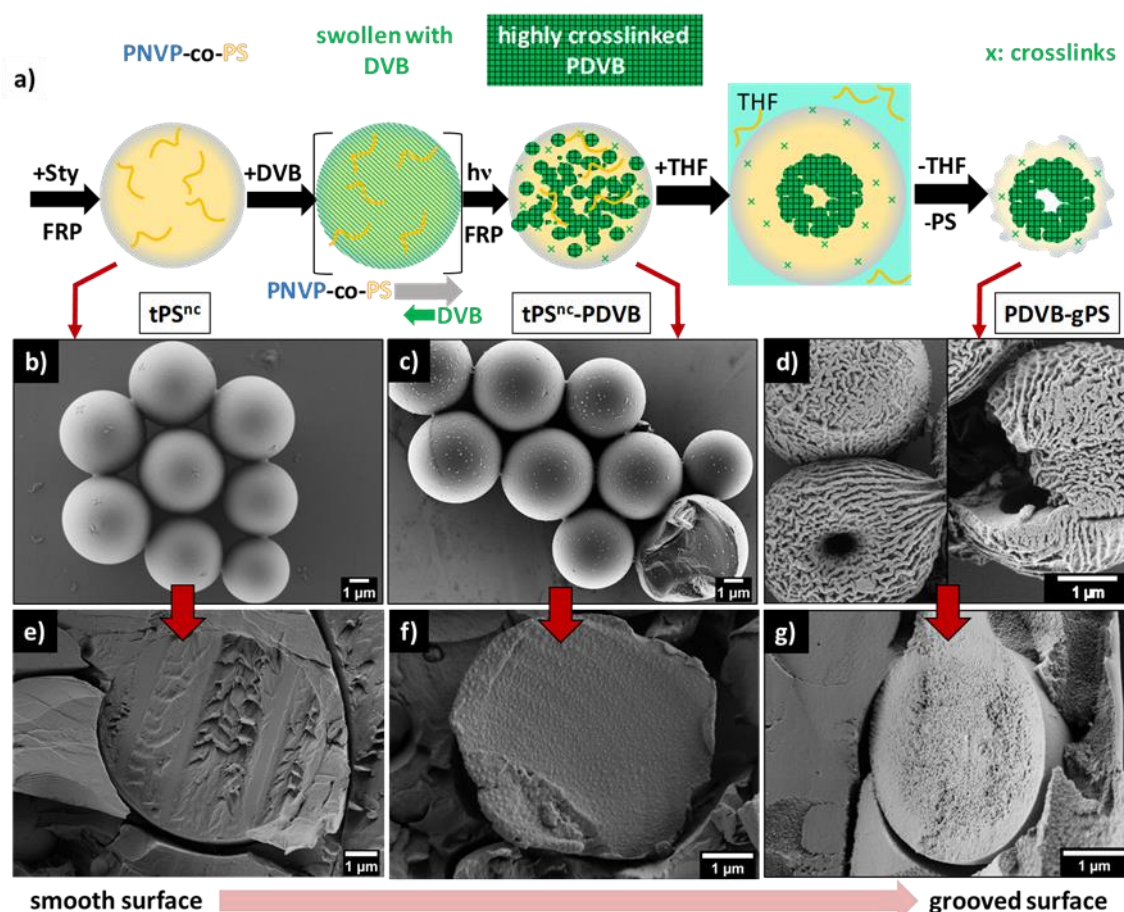


Figure 45: a) Schematic of the three-step procedure: PS-template swelling followed by photoinitiated polymerization to prepare crosslinked PDVB-gPS particles with a grooved surface. Green “x”s indicate crosslinks. SEM images of b) non-crosslinked PS template particles (tPS^{nc}) obtained via precipitation polymerization, with PNVP-rich phases at the outer particle rim labeled as PNVP-co-PS, c) PS particles with a semi-penetrating network of PDVB inside (tPS^{nc}-PDVB), and d) fully crosslinked PDVB-gPS particles after extraction of non-crosslinked PS: intact sphere (top left), indented particle (bottom left), and fractured shell with visible hollow core (right). e–g) SEM images of particle cross sections.

Figure 45a schematically illustrates the swelling procedure, which involves 1.) swelling of the template particle with a crosslinkable monomer and initiator, 2.) photoinitiated polymerization of the monomer, and 3.) extraction of the template polymer using a suitable solvent. In these experiments, THF was used for extraction. Non-crosslinked PS particles (referred to as tPS^{nc}) synthesized via precipitation polymerization in ethanol served as templates (Figure 45b and e). In contrast to the literature,⁵⁹ the preliminary swelling step with styrene to enlarge the particles was omitted, as the PS particles obtained by precipitation

polymerization already exhibited diameters above 3 μm and a narrow size distribution below 10%.

Poly-N-vinylpyrrolidone (PNVP) was used as a stabilizer during the synthesis of the PS templates and apparently remains associated with the particles, resulting in a hydrophilic surface. Two possible scenarios for the PNVP attachment can be considered, which may also coexist: i) PNVP chains may be entangled with the PS phase, or ii) PS side chains may be grafted onto the PNVP backbone via chain transfer reactions during styrene polymerization. Throughout this work, the resulting PNVP-rich region is referred to as PNVP-co-PS.

It was found that thermally initiated polymerization of DVB-swollen tPS^{nc} particles at 75 $^{\circ}\text{C}$ caused coalescence of the template particles, leading to a broadening of the particle size distribution. Therefore, to avoid temperature-induced coalescence, photoinitiation at room temperature was used for all particle preparations described in this chapter. LM images and particle size distribution (PSD) diagrams for both photoinitiated and thermally initiated polymerizations are shown in Figure S 21 in the appendix. For the setup of the photoinitiated polymerization a photograph is provided in Figure S 25 in the appendix.

A comparison of the particle size distributions before and after DVB swelling (based on LM analysis shown in Figure S 22 in the appendix) revealed an average diameter increase of 0.6 μm , from 4.9 μm to 5.5 μm . Prior to swelling, the tPS^{nc} particles exhibited a smooth surface and a homogeneous, pore-free interior (Figure 45b). The stripes visible in the cross section in Figure 45e are cutting artifacts caused by deformation and tearing of the soft PS material during sectioning. After DVB swelling and subsequent polymerization, resulting in the tPS^{nc} -PDVB particles, a granular particle structure became apparent across both the cross sections and the particle surfaces (Figure 45c and f). The crosslinking polymerization of DVB is expected to form a semi-penetrating PDVB network that encloses non-crosslinked PS chains. This network seemingly enhances the mechanical robustness of the particles, as evidenced by the reduced cutting artifacts compared to the tPS^{nc} reference.

Following THF extraction and drying, the crosslinked particles with grafted PS chains (PDVB-gPS) exhibit deeply grooved surfaces (Figure 45d), differing notably from the reported pore structure described in a comparable fabrication method.⁵⁹ Top-view SEM images reveal three dominant particle morphologies: approximately 60–70% intact spheres and 30–40% indented particles (both shown in Figure 45d, left), as well as 5–10% fractured shells with visible hollow

interiors (Figure 45d, right). These observations confirm the hollow nature of the particles after extraction. The widespread occurrence of these morphologies is clearly visible in the SEM overview images (Figure S 27) and the particle gallery (Figure S 28) in the appendix. The relative abundances of the different particle morphologies were quantified from multiple SEM overviews containing well-resolved structural details. Since the deep indentations seen in Figure S 26 to Figure S 28 emerge only after THF extraction, they likely result from the collapse of the hollow core during drying.

The prominent groove pattern on the surface is especially remarkable, as such a topological feature has not been reported for particles produced by similar methods.^{22,59,68,70} In contrast, the cross section of a matrix-embedded PDVB-gPS particle (Figure 45g) shows a uniformly porous core region surrounded by a dense shell with few or no visible pores. To enable cross sectioning, the fragile particles were embedded in a matrix. The liquid resin precursor used to create the matrix evidently penetrated the shell and filled the internal cavities. As a result, after resin curing and microtoming, structural details such as pores and hollow cores were masked by the infused matrix.

To interpret the observed morphology, several mechanisms proposed in the literature for this type of particle synthesis can be considered, with one of the most often described processes being phase separation during swelling of the template particles.⁶⁸ When swollen with DVB and a photo-initiator, the PS chains become partially solvated, increasing their mobility. According to previous reports, this results in phase separation into three distinct components: a PNVP-rich phase (I), which remains at the particle-water interface due to the hydrophilicity of the PNVP chains,^{34,152} and two similarly hydrophobic phases, DVB (II) and PS (III), which are expected to migrate toward the particle center.¹⁵¹ The spatial arrangement of these phases becomes fixed during subsequent polymerization and concurrent crosslinking.

Accordingly, the PNVP-rich phase (I) can be attributed to the outermost region of the particles. In contrast, the inner sections of the PDVB-gPS particles appear inhomogeneous, exhibiting prominent voids near the particle center after THF extraction. These voids manifest as large central indentations in the SEM images. The distribution behavior of DVB molecules (II) and PS chains (III) during phase separation appears to differ. Despite their comparable hydrophobic character, the PS chains (III) tend to accumulate more strongly in the particle

center than the formed PDVB network. Similar trends have been reported in previous studies involving the swelling of PS particles with DVB.^{68,70}

According to the literature, phase separation effects become more pronounced with increasing mobility of the involved species, which is relevant for both the monomeric DVB (II) and the PS chains (III).¹⁵¹ Prior to polymerization, DVB is a low-molar-mass liquid with high mobility. It enters the particles from the outside and diffuses inward through the PS template. This creates a concentration gradient, with higher DVB content in the outer regions of the core and decreasing levels toward the center. In addition, DVB plasticizes the PS chains, thereby increasing their mobility. Similarly, the initiator molecules, which are dissolved in the DVB phase, enter the particle through the surface and diffuse into the PS matrix.

Upon initiation by UV irradiation, DVB molecules undergo chain growth via free radical polymerization to form a PDVB network whose translational mobility significantly decreases as the network expands. Therefore, monomer addition to the radical sites located at the network periphery can proceed only via reaction diffusion of the monomer to the network.¹⁰⁷ During this diffusion process, a PS chain adjacent to the reaction center exchanges positions with an incoming DVB molecule, which subsequently incorporates into the network, causing it to grow. Hence, this mechanism causes the PS template to be displaced by the newly formed PDVB material.

Since the light intensity and potentially the initiator concentration are highest at the particle surface and decrease inward, PDVB network formation is expected to start predominantly at the outer region of the tPS^{nc} particles and progress toward the center. This results in an accumulation of the PS phase in the particle center. Consequently, the crosslinking polymerization produces a shell composed of a PDVB-rich network surrounding a PS-rich core. During this process, the PDVB phase may also grow around individual PS chains, forming a semi-penetrating network. Following THF extraction of the mobile PS chains, the particle center is left hollow.

The grooves observed on the PDVB-gPS particles after THF extraction most likely originate from the drying process of THF-saturated particles, indicating a highly swollen outer shell. Since the PDVB network is highly crosslinked, it is not expected to exhibit such a high degree of swelling. At the same time, the non-crosslinked PS chains are expected to dissolve completely in THF. However, a weakly crosslinked network, which would be required to

account for the highly swollen shell, must contain longer chain segments between crosslinks. These segments can only be provided by the PS template. The necessary crosslinking may have resulted from chain transfer reactions involving the PS backbone during the free radical polymerization of the PDVB network. As this occurs throughout the entire PS phase, a weakly crosslinked PS network forms alongside non-crosslinked PS chains within the final PDVB-gPS particle. This loosely crosslinked network remains chemically bonded to the more densely crosslinked PDVB phase and is therefore referred to as a grafted PS network, abbreviated as “gPS” in the particle acronym. When exposed to a good solvent such as THF, both the weakly crosslinked PS shell and the PNVP-rich outer layer swell, creating a gel corona around the particle. As the solvent evaporates, this swollen corona contracts and folds, producing the characteristic convoluted structure with grooves observed on PDVB-gPS particle surfaces. The presence of a swollen gel corona around the particles in a good solvent introduces challenges during column packing in SEC experiments: The PDVB-gPS particles could be readily loaded into the SEC column when dispersed in a more polar solvent such as acetone. Nevertheless, after exchanging the solvent to THF, which is a good solvent for PS, the column backpressure increased sharply due to blockage of the interstitial volume by the THF-swollen corona. Particle rupture from the applied pressure was ruled out since the particles remained intact upon extraction from the column. These findings suggest that PDVB-gPS particles are unsuitable for use as SEC stationary phase in organic solvents capable of swelling PS, though their applicability in aqueous systems may differ. Further support for the presence of a PS gel corona comes from the inability to redisperse the dried PDVB-gPS particles in ethanol after THF treatment and drying. In contrast, tPS^{nc}-PDVB particles could be dispersed in ethanol prior to extraction. This irreversible agglomeration is likely caused by the coalescence of the swollen PS corona during drying, which promotes chain entanglement. Evidence for this mechanism can be seen in the capillary necks connecting particles (Figure S 26 in the appendix, middle image, bottom row).

The results demonstrate how a complex property profile can emerge from combining two different procedures, yielding microparticles with a hollow core, a rigid shell, and a very soft corona when suspended in good solvents for PS, as well as a convoluted surface topography formed upon drying.

7.2.2 Crosslinked particles with grafted polystyrene chains (PDVB-gPS^{xl}) from slightly crosslinked seed templates (tPS^{xl})

To reduce the formation of the gel corona described previously, the procedure was modified by incorporating a low crosslink density into the PS template particles. Although a higher crosslink density could suppress the gel corona more effectively, it would also limit the swelling capacity with DVB. Therefore, a modest crosslink density of approximately 5% network junctions connecting the linear PS chain segments was aimed for.

To synthesize the tPS^{xl} template particles successfully, the volume ratio of DVB to styrene was limited to a maximum of 4:96 v/v during precipitation polymerization in ethanol. Using higher DVB amounts led to significant particle agglomeration. The obtained slightly crosslinked tPS^{xl} template particles were then subjected to the same swelling procedure as used for the tPS^{nc} particles. A schematic representation of the mechanism, along with SEM images illustrating the particle morphologies at various reaction stages, is presented in Figure 46 (additional images can be found in Figure S 29 in the appendix).

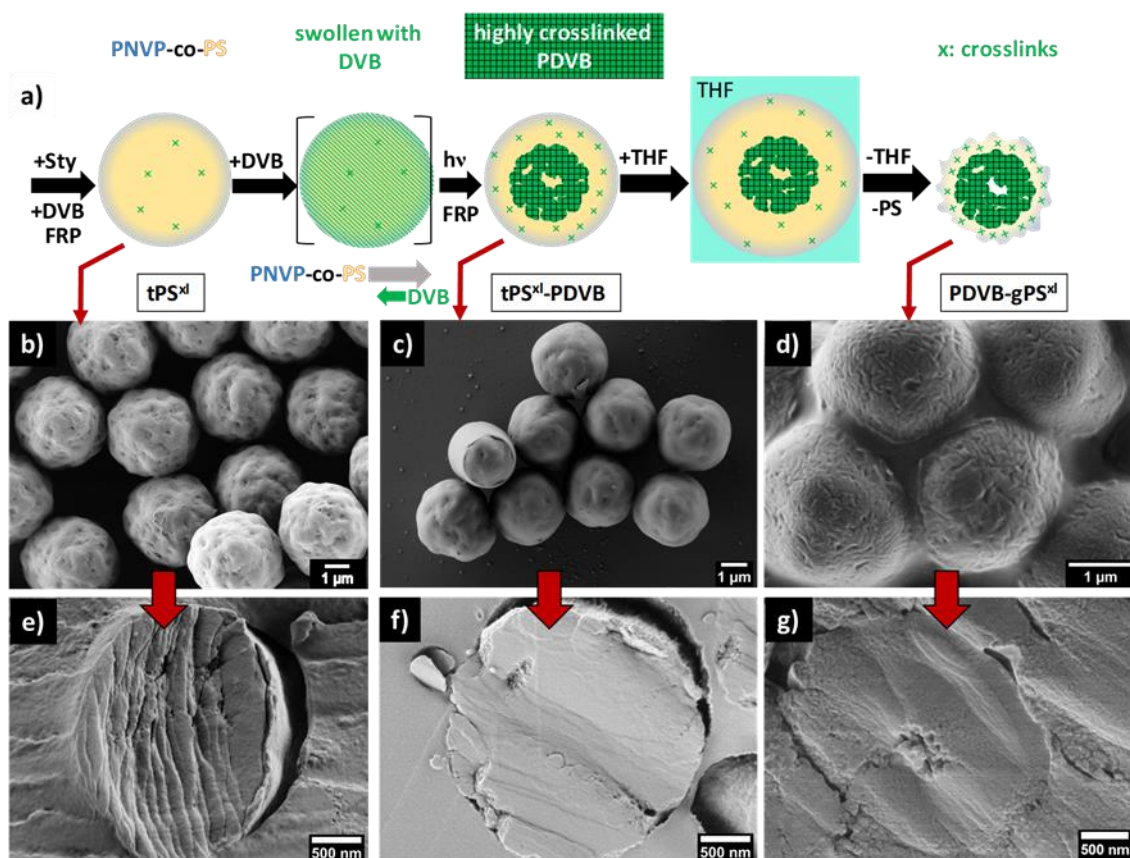


Figure 46: a) Schematic of the three-step procedure: PS-template swelling and photoinitiated polymerization to prepare crosslinked PDVB-gPS^{xl} particles from slightly crosslinked templates (tPS^{xl}). Green “x”s indicate crosslinks. SEM images of b) slightly crosslinked PS template particles (tPS^{xl}) obtained via precipitation polymerization, with PNVP-rich phases at the outer rim labeled as PNVP-co-PS, c) PS particles with a semi-penetrating network of PDVB inside (tPS^{xl}-PDVB), and d) fully crosslinked PDVB-gPS^{xl} particles after extraction of non-crosslinked PS. e-g) SEM images of particle cross sections.

The slightly crosslinked template particles (tPS^{xl}) shown in Figure 46b exhibit a more irregular overall shape compared to the non-crosslinked tPS^{nc} templates. Their surface displays a distinctly corrugated topography, with a tendency towards a raspberry-like appearance. Particle cross-sections after microtoming (Figure 46e) reveal largely compact particles with only minimal indications of internal porosity. Still, as discussed for the tPS^{nc} particles, it cannot be ruled out that potential pores were filled with matrix material during sample preparation (see also Figure S 33 for a direct comparison of the template types).

Swelling of the tPS^{xl} template particles with DVB followed by polymerization resulted in an average diameter increase of approximately 0.4 μm. Light microscopy data on particle size distribution and swelling are provided in the appendix (Figure S 23). Compared to the non-crosslinked tPS^{nc} particles, this diameter increase is less pronounced, which can be attributed

to the pre-crosslinking of the tPS^{xl} templates. As observed previously for the tPS^{nc} system, both particle dimensions and size distribution remain largely unchanged between the swelling and photopolymerization steps.

The tPS^{xl}-PDVB particles exhibit a smoother topography in the SEM images (Figure 46c) after swelling and polymerization. However, they remain more irregular compared to the spherical tPS^{nc}-PDVB particles from the initial approach (Figure 45c; see also Figure S 34 for a direct comparison at this reaction stage). SEM cross sections (Figure 46f) reveal a uniform particle morphology without discernible phase differences. As before, subtle indications of a porous structure are present, though penetration of the particles by matrix material during microtome embedding cannot be ruled out.

Removal of the PS template with THF yielded PDVB-gPS^{xl} particles characterized by a grooved surface, a granular internal structure, and a central void (Figure 46d and g). Notably, the cross-sectional SEM analysis was conducted on dried samples that were microtome-sectioned without prior matrix embedding. Unlike the previous samples, these particles exhibited sufficient mechanical robustness to allow sectioning without the use of an embedding matrix.

In comparison to the PDVB-gPS sample from the initial approach (Figure 45d), the surface grooves of the PDVB-gPS^{xl} particles are considerably less pronounced. The particles are coated with a diffuse layer, and the interstitial spaces are filled by a homogeneous phase that connects the individual spheres. In SEM overview images, the characteristic deep indentations, which were frequently observed in the PDVB-gPS particles, are absent on the PDVB-gPS^{xl} particles.

In the cross-section images of Figure 46g, smaller granule-filled voids are visible within the cores of the PDVB-gPS^{xl} particles (see also Figure S 35, middle row, right image, in the appendix). As no embedding procedure was applied to the PDVB-gPS^{xl} samples prior to microtome cutting, matrix infusion can be excluded, allowing a clearer observation of the internal particle morphology. Additional examples of particles with voids are provided in Figure S 30 in the appendix.

The morphological features of the PDVB-gPS^{xl} particles can be explained by the same phase separation mechanisms described earlier for the PDVB-gPS system. However, a major difference lies in the pre-crosslinking of the tPS^{xl} templates, which substantially reduces PS

chain mobility and thereby affects the details of PS phase separation during PDVB network formation. Consequently, the reduced chain mobility limits the inward migration of PS during phase separation, leading to a lower concentration in the particle core and, after THF extraction, a correspondingly smaller void.

As discussed for the PDVB-gPS particles, radical chain transfer occurs during the DVB polymerization step. In the case of the pre-crosslinked tPS^{xl} templates, this leads to the formation of additional crosslinks. As a result, the gel corona with a higher crosslinking degree swells less in THF and, in turn, forms less distinct surface folds after drying than those observed for the corona of the PDVB-gPS particles. Once dried, the corona on PDVB-gPS^{xl} particles appears as a diffuse surface layer that obscures finer structural features and creates interconnecting necks between adjacent particles.

A greater number of PS chain segments remain attached to the PDVB-gPS^{xl} particles after washing with THF due to the higher crosslink density compared to the PDVB-gPS particles. The involvement of free PS chains in forming the diffuse surface layer can be ruled out, as Soxhlet extraction over two days was used during the washing process. Consequently, the PDVB-gPS^{xl} system is unsuitable as an SEC stationary phase for PS solvents like THF, since the soft, swollen corona occupies the interstitial volume, which blocks the SEC column. Using lightly crosslinked PS template particles in this second approach results in particles characterized by a relatively smooth surface and reduced free volume in the core, making them distinctly different from those produced in the first approach with non-crosslinked PS templates.

The results indicate that modifying the crosslinking density within the PS template provides a means to control the morphology of the resulting PDVB particles.

7.2.3 Crosslinked particles with grafted polystyrene chains (PDVB-gPS^{xl+nc}) from slightly crosslinked seed templates containing additional mobile chains (tPS^{xl+nc})

Since the two previous approaches yielded markedly different particle structures, a third strategy was investigated that combines crosslinked PS templates with mobile PS chains. As shown in Figure 47a-I, the process began by swelling the slightly crosslinked tPS^{xl} template particles (from the second approach) with styrene, followed by thermally initiated free radical polymerization (FRP). This extra step was necessary to introduce non-crosslinked PS chains into the PS^{xl} matrix. The resulting composite PS^{xl+nc} template particles were then swollen with DVB (Figure 47a-II) and polymerized. While maintaining the same absolute number of crosslinks as the tPS^{xl} templates, the PS^{xl+nc} particles now also contain additional mobile PS chains. This modification is expected to increase the free volume within the particles after extraction of the mobile PS chains with THF.

Figure 47b-g show SEM images corresponding to various stages of the process leading to the formation of PDVB-gPS^{xl+nc} particles from this third approach. Supplementary images are provided in Figure S 31 in the appendix.

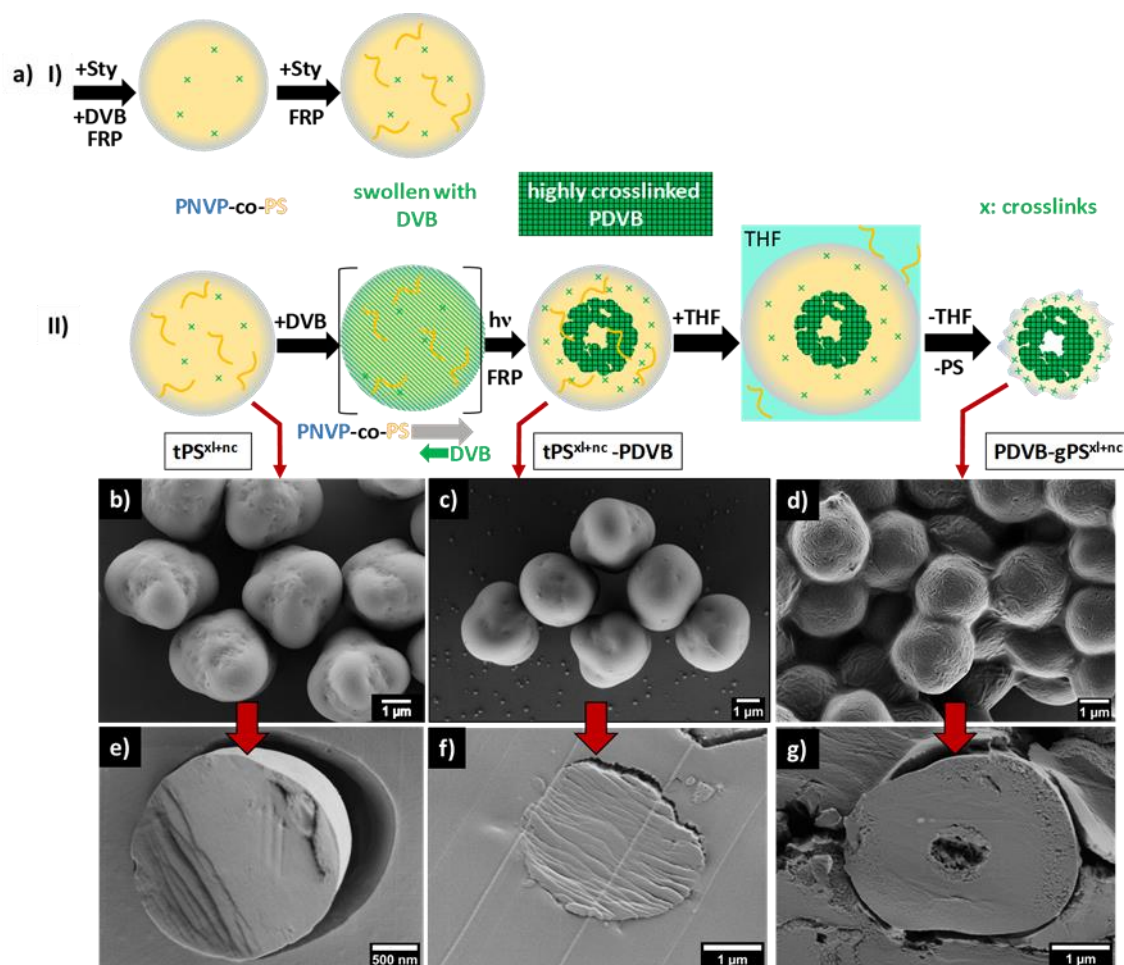


Figure 47: Schematics of a-I) the procedure for modifying slightly crosslinked PS template particles (tPS^{xl}) by swelling with styrene and subsequent thermally initiated free-radical polymerization (FRP) to form composite templates containing non-crosslinked PS chains (tPS^{xl+nc}), and a-II) the three-step procedure involving PS-template swelling and photoinitiated polymerization to prepare $PDVB-gPS^{xl+nc}$ particles from tPS^{xl+nc} templates. Green "x"s indicate crosslinks. SEM images of b) slightly crosslinked PS template particles with additional non-crosslinked chains (tPS^{xl+nc}) obtained via precipitation polymerization, with PNVP-rich phases at the outer rim labeled as PNVP-co-PS, c) PS particles with a semi-penetrating network of PDVB ($tPS^{xl+nc}-PDVB$), and d) fully crosslinked $PDVB-gPS^{xl+nc}$ particles after extraction of mobile PS chains. e-g) SEM images of corresponding particle cross sections.

The SEM images of the tPS^{xl+nc} template particles reveal fewer surface corrugations (Figure 47b) compared to the tPS^{xl} templates (Figure 46b). Subsequent swelling with DVB followed by polymerization further smoothens these surface features (Figure 47c). Cross-sectional images of both particle types display homogeneous bulk structures without visible voids or pores (Figure 47e and f). Still, as noted previously for the tPS^{nc} and $tPS^{nc}-PDVB$ particles, the embedding matrix used for microtome sectioning may obscure any granular or porous internal structures, rendering them indistinguishable in these images.

LM observations show an overall particle size increase of approximately 0.2 μm during DVB swelling (see Figure S 24 in the appendix), with particle dimensions remaining stable throughout the polymerization step.

After template extraction, the PDVB-gPS^{xl+nc} particles exhibit a grooved surface (Figure 47d) resembling the topography of the PDVB-gPS^{xl} particles, although the surface features are less pronounced compared to the PDVB-gPS samples from the first strategy (see also Figure S 35, left column, for comparison). Thus, incorporating additional mobile PS chains into the template did not drastically influence the swelling behavior of the gel corona. It appears that the primary factor governing corona swelling is the absolute number of crosslinks in the template particle, as provided by the tPS^{xl} system. Due to the presence of a swellable corona, these PDVB-gPS^{xl+nc} particles are likewise unsuitable as an SEC stationary phase when using PS solvents. Once dried, the corona forms a connective layer around the PDVB-gPS^{xl+nc} particles, similar to the coverage observed for PDVB-gPS^{xl} particles described earlier.

The SEM cross-sectional image in Figure 47g reveals a large central cavity with micrometer-scale dimensions, reminiscent of the smaller, granule-filled voids previously observed in the PDVB-gPS^{xl} particles (Figure 46g).

The cavity walls are composed of well-defined granules with diameters below 100 nm (Figure S 36 in the appendix), forming a porous structure, but with greater free volume than seen in the PDVB-gPS^{xl} system. Additional cross-sectional SEM images illustrating these voids are provided in the gallery in Figure S 32. In the specific cross-section shown in Figure 47g, a porous outer shell approximately 0.6 μm thick is visible, while the intermediate region between the central void and the outer shell (measuring about 0.9 μm) is compact and lacks visible pores. The overall void volume in the PDVB-gPS^{xl+nc} particles exceeds that of the PDVB-gPS^{xl} particles, which is attributed to the dissolution of the additional mobile PS chains introduced into the tPS^{xl+nc} template. This observation is supported by the SEM images in Figure S 35 (rightmost images in the second and third rows).

Comparison of the morphological features of PDVB-gPS^{xl+nc} particles (third strategy) and PDVB-gPS^{xl} particles (second strategy) reveals that the void volume in the particle core can be directly tuned by incorporating additional mobile PS chains into slightly crosslinked templates.

7.2.4 Chapter Conclusion and Outlook

In this chapter, precipitation polymerization was combined with particle swelling and photopolymerization techniques to develop three distinct strategies for fabricating complex colloidal architectures.

The first approach employed non-crosslinked polystyrene template particles, producing PDVB-gPS particles characterized by pronounced surface grooves and a hollow core, which is an unexpected morphology when swelling non-crosslinked PS templates from precipitation polymerization. The second strategy utilized slightly crosslinked PS templates, resulting in particles with shallower grooves and diminished core voids due to the pre-existing crosslinks within the template. The third approach introduced additional mobile PS chains into the slightly crosslinked PS templates, which increased the hollow core volume in the resulting PDVB microspheres. These findings illustrate the capability to tailor void sizes in contrasting ways, emphasizing the versatility of the method presented. While SEM analysis enabled detailed observation of morphological features, embedding particles in a matrix for microtome sectioning posed challenges, as it may have obscured internal structures in non-extracted particles. To address this, sectioning was performed on dried films of extracted particles, allowing successful visualization of nanoscopic morphological details by SEM.

The unique combination of preparation techniques yielded microspheres featuring a soft corona, a robust shell, and a hollow core, offering potential for diverse applications including size exclusion chromatography, surface functionalization, catalysis, and delivery systems. Moreover, these advanced colloidal architectures, feasible by tailored templating and swelling, provide promising model systems for investigating particle interactions, aggregation, and structure formation within colloidal physics.

As this set of experiments serves as a proof of concept with a limited parameter range, future work could offer further insight into how to achieve extended control over the nanoarchitecture. The principles developed here may also be transferable to other swelling-based templating approaches, broadening their potential applicability.

7.3 Studies of Template Swelling Methods to Prepare PDVB Non-Porous Core - Porous Shell Particles

In this chapter, an alternative strategy of introducing pores into a PDVB particle shell will be explored. Low-molecular-weight pore formation agents (porogens), like solvents or non-solvents for DVB, yielded pores below a suitable size for size exclusion chromatography (SEC) of macromolecules (chapter 7.1.5). Polymer separation in SEC is predominantly performed using porous materials that comprise a mixture of mesopores (2–50 nm) and small macropores (>50 nm).^{14,125} Therefore, polystyrene (PS) will be studied as a macromolecular porogen in the following chapter. This type of porogen is known to generate meso- and macropores, attributable to its greater molar mass compared to that of small solvent or non-solvent molecules typically used for DVB.^{41,59,153,154}

This concept was explored in literature^{153–155} and pore formation in particles could be demonstrated by employing template swelling methods with polystyrene as a porogen reaching pore diameters usually in the range of 10-100 nm.^{22,59,61,156} In the process documented in the literature, a polymer particle is swollen with a matching plasticizer and the monomer corresponding to the macromolecular porogen. During a thermally initiated polymerization within the particle, a polymer forms, and acts as a template for the pores: When the macromolecular porogen is extracted with a suitable solvent, it leaves cavities in the particle. The porous particles obtained in this manner are suggested for use as sorbents, catalysts and separation media for HPLC or SEC depending on their surface chemistry.^{6–8,14,15,41,55,56,157}

While this swelling method is close to the swelling method presented in chapter 7.2, the PS/DVB ratio and the used stabilizers vary. Additionally, a plasticizer is used to improve swelling of the particles. The detailed differences will be discussed in chapter 7.3.2 where the concept is transferred to PDVB particles and evaluated for its suitability within this system. For SEC specifically, it would be beneficial to develop a particle with a solid core and a porous shell to reduce the overall diffusion pathway in the particle. This would reduce the time an analyte would spend in a pore and thus shorten measurement time. With this, larger particles could be used in columns without increasing the diffusion pathway too much, and thus mimic the efficiency of smaller particles.^{14,37} Analytes with high molar masses are also less prone to

shear stress in columns with larger particles due to larger interstitial volumes and reduced back pressures compared to SEC columns packed with smaller particles.^{158–160}

In order to transfer the template swelling concept described in the literature,^{22,59} chapter 7.3.1 will focus on the development of precursor particles based on the PDVB core-PDVB shell architecture previously discussed in chapter 7.1.4.1. The strategy involves modifying the highly crosslinked and thus non-swelling core-shell particles to meet specific criteria: they should have a shell that can readily swell with styrene and DVB, while maintaining a solid, highly crosslinked core that remains unaffected by the swelling process.

In the subsequent chapter (7.3.2), the concept of template swelling from literature will be adapted to fit the PDVB core-shell precursor particles.⁵⁹ The objectives here are a) to introduce pores larger than 10 nm in diameter suitable for macromolecular separation with SEC and b) creating these pores exclusively within the particle shell, preserving a solid core. If this new PDVB particle architecture is achieved, it could be applied as a separation medium in SEC to improve measurements.

7.3.1 Synthesis and Characterization of Precursor Particles

In this chapter, the synthesis and characterization of core-shell precursor particles with a highly crosslinked core and a slightly crosslinked shell will be discussed. A slightly crosslinked shell is essential to permit monomer swelling within it, making it applicable for the template swelling method to create pores large enough for SEC separation. The synthesis method is based on the precipitation polymerization and shell growth concept discussed in chapter 7.1.4.1, but will be adapted to create a swellable shell as a replacement for a highly crosslinked one.

Since the swellability of the shell increases with fewer crosslinks existing in it, a fully non-crosslinked shell would be most beneficial for this approach. Accordingly, a complete substitution of the crosslinking monomer DVB with the non-crosslinking monomer styrene would be the most straight forward strategy. However, experiments to grow a PS shell on a PDVB core via precipitation polymerization resulted in either no precipitation of PS on the PDVB core or aggregation of the core particles (see also chapter 7.1.4.2). Therefore, a mixture of styrene and DVB will be used to create a slightly crosslinked shell instead.

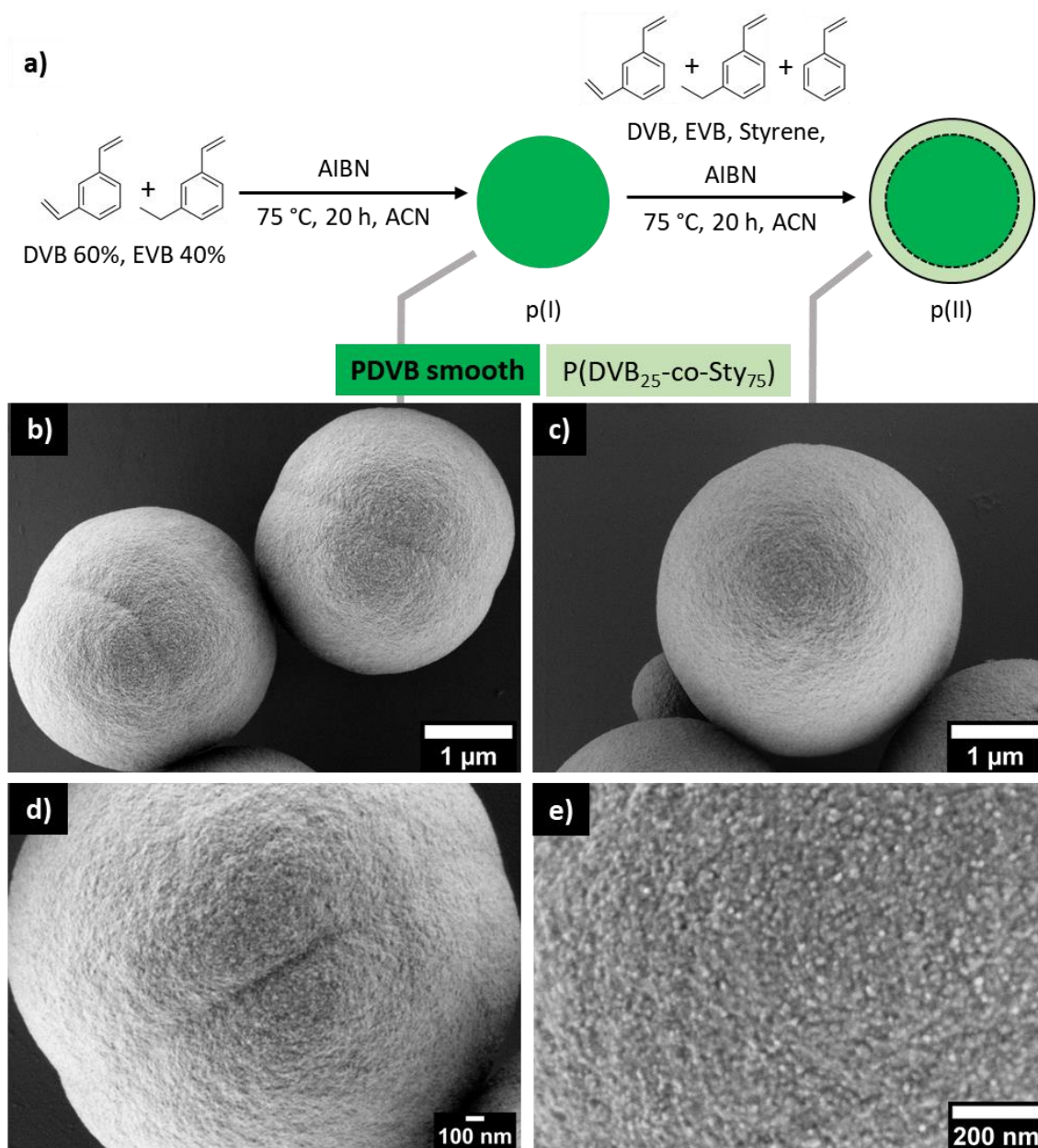


Figure 48: Schematic depiction of the production process of PDVB core – P(DVB₂₅-co-Sty₇₅) shell particles (a)) and SEM pictures of the PDVB core (overview: b) and zoom-in: d)) and the core-shell particle (overview: c) and zoom-in: e)). The measurements were conducted without sputtering the samples and under low voltage (Leo Gemini 1530).

As displayed in Figure 48a, the synthesis of the partially swellable precursor particle consists of two steps in a one-pot approach: First, the solid, highly crosslinked core (p(I)) is synthesized via precipitation polymerization of DVB in acetonitrile as discussed in chapter 7.1.1. In the second step, the core-shell particle (p(II)) is created by adding a mixture of monomers (75v% styrene and 25v% DVB) along with an initiator to start another precipitation polymerization. In contrast to the synthesis of a highly crosslinked shell (chapter 7.1.4.1), the volume

percentage of styrene is significantly higher than DVB here. This composition is chosen to reduce the crosslinking density when compared to shells made entirely of PDVB which in turn facilitates the swelling of the shell.

Experiments aimed at shell formation using monomer ratios with even lower DVB content did not result in noticeable shell growth. This outcome is likely attributed to solubility issues similar to those observed with pure styrene monomer (cf. chapter 7.1.4.2): the polymer formed, characterized by a very high PS content, does not reach the solubility limit in acetonitrile necessary to precipitate onto the particle shell. Furthermore, the low DVB content significantly limits the formation of crosslinks, reducing the likelihood of larger polymer clusters forming and precipitating.

In the PSD histograms of Figure 49, the particle sizes before and after the shell formation step are displayed. In Figure 49a, the core particles have a dimension of about 3.3 μm which increases to 4.3 μm after the shell deposition step (Figure 49b). This increase of about 1 μm is similar to the shell growth observed for shells made entirely of PDVB (chapter 7.1.4.1).

SEM imaging was done on the core particles as well as the core-shell particles to characterize the particle surfaces before pore introduction is done via the swelling method. Figure 48b and d (close up) show the core particle surfaces which do not exhibit any porous or rough structure. This finding was also supported by SEC column performance tests as discussed in chapter 7.1.2.2.

As expected at this stage, the core-shell particle surface looks similar to the core particle surface with no pores of significant size being visible with SEM imaging (Figure 48c and e). The only visible difference is the even more uniform particle surface. The slight grooves which are often visible on the core particle surfaces are not present for most of the core-shell particles (c.f. Figure S 37 in the appendix). Such grooves are probably filled up by the precipitating polymer during the shell formation step.

Overall, the shell deposition could be confirmed by LM imaging and the particle surface looks smooth as it was expected at this stage. The swellability of the particle shell will be discussed in the following chapter.

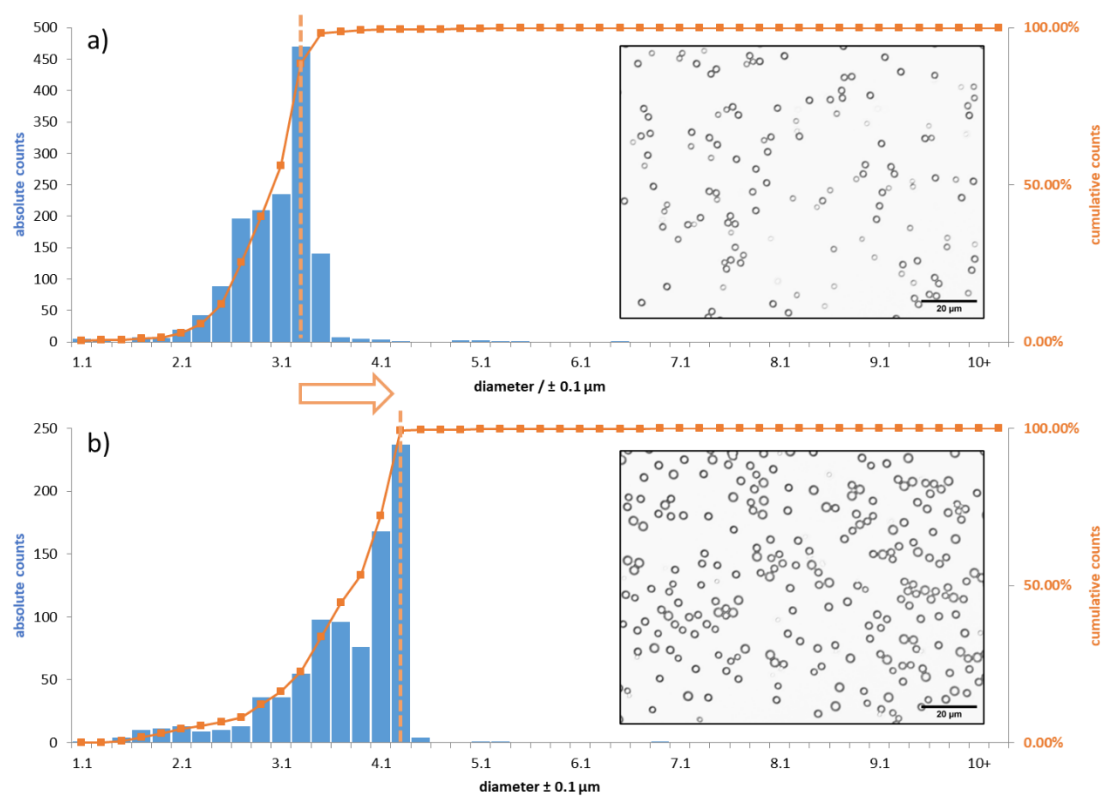


Figure 49: PSD diagrams and the corresponding LM images of a) PDVB core particles and b) PDVB core - P(DVB₂₅-co-Sty₇₅) shell particles. The particle growth due to the shell deposition is depicted by the orange arrow and markings.

7.3.2 Investigating Pore Formation with Macromolecular Porogens

This chapter explores a template swelling strategy^{22,59} transferred to the framework of PDVB core-shell particle systems. Polystyrene (PS), a macromolecular porogen, is intended to be introduced into a swellable particle shell, serving as a placeholder for the desired pores. This approach seeks to produce pores larger than 10 nm in diameter, enabling the formation of mesoporous and macroporous structures required for effective SEC separation of macromolecules. Since polystyrene was found to create pores in the regime of 10-100 nm using a template swelling strategy,^{22,59} this should address the limitations of low-molecular-weight porogens, which did not result in pores large enough for this purpose.

The template swelling strategy is divided into two main processes: First, the PS template would be introduced into the precursor particle shell. Given that the precursor particles predominantly contain chemically bound PS chains in their shells, additional removable PS chains would need to be incorporated to function as a pore template (macromolecular porogen). This could potentially be achieved by swelling the shell of the precursor particle with a suitable monomer (e.g. styrene) followed by polymerization. In the second process, a network around the PS porogen would be formed, and the macromolecular porogen could then be removed using an appropriate solvent like THF. This process would ideally result in pores at the locations previously occupied by the porogen (templating technique).

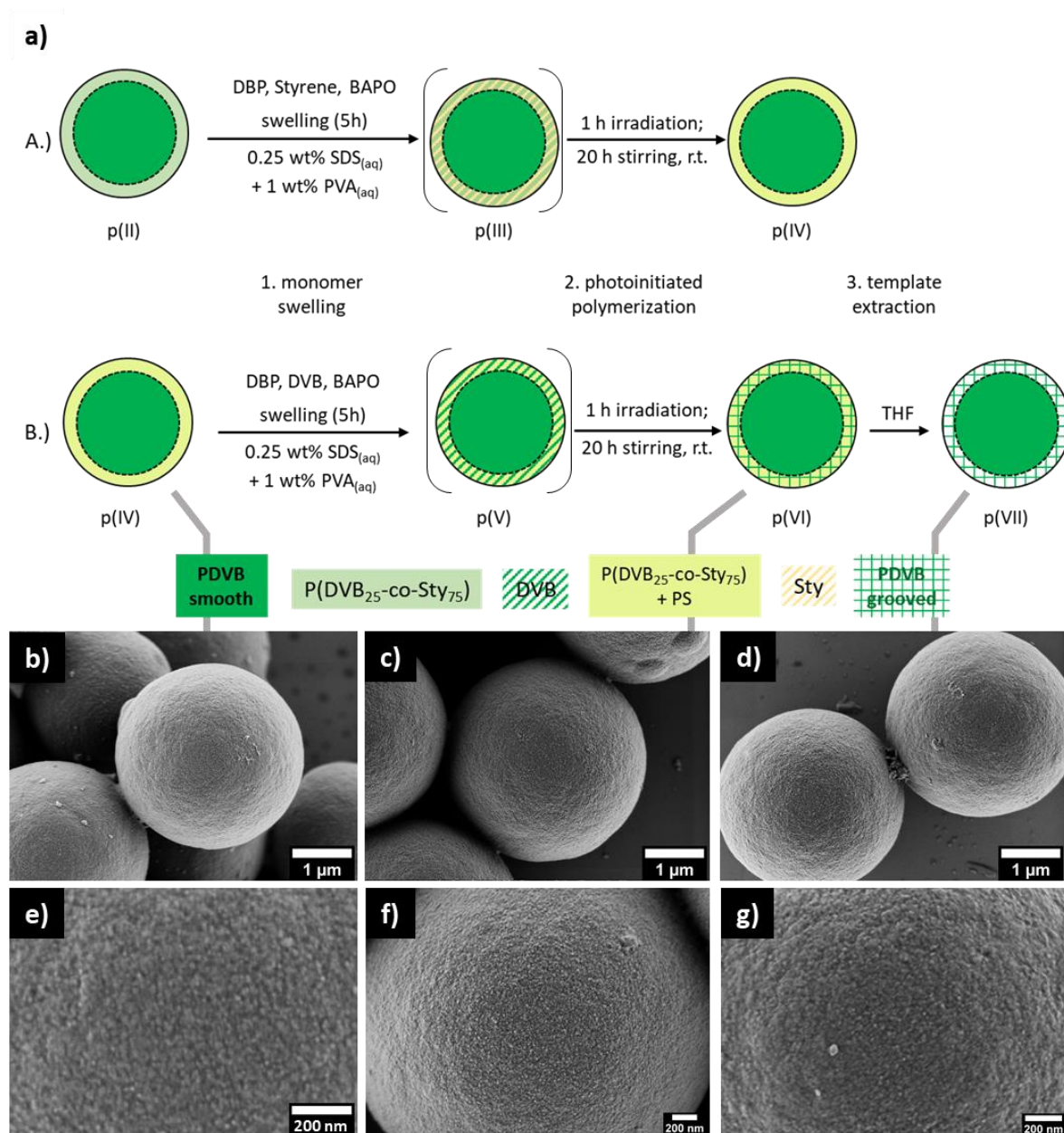


Figure 50: Schematic depiction of the procedure to get solid PDVB core – porous PDVB shell particles in two steps (a). In step A) the PS porogen is introduced into the swellable P(DVB₂₅-co-Sty₇₅) shell of the precursor particle p(II) and in step B) a PDVB network is introduced before the porogen is removed again. SEM pictures of the templated particles containing PS (p(IV), b) and zoomed-in: d), templated particles with the porogen and a newly formed network of PDVB inside, (p(VI), c) and zoomed-in: f)) and the final particles after the removal of the porogen template (p(VII), d) and zoomed-in: g)). The measurements were conducted without sputtering the samples and under low voltage (Leo Gemini 1530). Abbreviations used: BAPO - bis(2,4,6-trimethylbenzoyl)-phenylphosphineoxide, DBP - dibutyl phthalate, PVA - polyvinyl alcohol, SDS - sodiumdodecylsulfate.

In Figure 50a, the detailed, schematic procedures of the porogen introduction (A) and the network formation with subsequent porogen removal (B) are displayed. For the porogen introduction to the precursor particle p(II), the particles undergo swelling by mixing them with an w/o emulsion (p(III)). When the organic phase of the emulsion comes into contact with the particles, the monomer (styrene) corresponding to the porogen (PS), a plasticizer (dibutyl phthalate, DBP) and the photo initiator (Bis(2,4,6-trimethylbenzoyl)-phenylphosphineoxide, BAPO) can enter the swellable part of the precursor particle. The plasticizer is used in combination with the monomer to soften the shell and make it more accessible for the monomer. For this specific swelling mechanism, it is reported to significantly improve the amount of monomer that can be absorbed in the particle when the plasticizer is added before or with the monomer.¹⁴⁰ This is needed due to the relatively high amount of monomer used per precursor shell (monomer:shell 1:2 wt) compared to the swelling process presented in chapter 7.2 (monomer:shell 1:5 wt). As suggested by the literature,⁵⁹ the emulsion is stabilized by Sodium dodecyl sulfate (SDS) and poly(vinyl alcohol) (PVA) due to the reliable stabilizing effects this specific mixture offers. Dispersion tests where only SDS was used as stabilizing agent resulted in more agglomeration compared to experiments that combined both stabilizers. The swelling process is allowed for several hours before the polymerization is initiated by irradiation, resulting in mobile, removable PS chains being incorporated into the particle shell (p(IV)).

The thermally initiated polymerization reported in the literature^{22,59,140} was modified to a photoinitiated one due to agglomeration occurring during heating. As it was also observed with the PDVB systems presented in chapter 7.2, the heat probably causes the particle surface to soften and thus become more tacky. For precursor particles that consist solely of PS, as it was done in literature,⁵⁹ the particle size distribution also drastically changes during the polymerization step (c.f. p(III) and p(IV) in Figure S 38 in the appendix). This supports the theory that the non-crosslinked parts of the particles soften or even liquify (in case of neat PS) during heating which causes particle coalescence and separation in the case of neat PS and tackiness and agglomeration with PDVB-based systems. To avoid this phenomenon, photoinitiation at room temperature was chosen over thermal initiation and performed as described in chapter 7.2.

A comparison of particle sizes before swelling the precursor particles (p(II)) and after the polymerization (p(IV)) can be found in Figure S 40 in the appendix. The most frequent particle sizes change from 3.8 - 4.2 μm to 4.0 - 4.4 μm indicating a small increase in particle dimensions. With this finding, it can be assumed that the precursor particle shell is swellable to a certain degree. Since only the shell is supposed to be swellable and still contains a quite high amount of crosslinking monomer (25mol%), the small change in particle dimension is still within expectations.

In the second process (B) displayed in Figure 50a, the network around the PS template is created. For this, the templates particles (p(IV)) are subjected to swelling again. While most of the emulsion ingredients are kept the same as for process A, the monomer (DVB) used here is capable of forming crosslinks and thus can form a network upon polymerization.

The polymerization is carried out in the same way as described for process A and is intended to result in particles which contain both the template and a newly formed network inside the shell.

LM images and PSD diagrams of particles p(IV) before swelling with DVB and the particles p(VI) after polymerization can be found in Figure S 41 in the appendix. In this instance, it is surprising that the particle sizes remained constant during the swelling and polymerization steps while swelling was observed with the model particles at this stage before (cf. Figure S 39 in the appendix).

The following explanations are possible for this result: Firstly, DVB might not have entered the particle shell. For this to happen either the swelling capacity of the shell is too low now or all available space was already occupied by the template. Secondly, a very minor swelling with DVB and consecutive polymerization might have led to a negligible effect on the particle sizes due to shrinking of the polymer volume during polymerization. For the last step, the PS template is removed with a suitable solvent (THF) to obtain particles p(VII) with a solid core and a porous shell.

PSD diagrams from LM pictures were only taken before swelling and after polymerization and not during the intermediate stages due to the following limitations with this technique: Swollen particles and droplets containing the organic phase cannot be distinguished with light microscopy (cf. Figure S 42 in the appendix). Thus, these organic droplets made it difficult to accurately assess particle sizes, leading to unreliable data. To narrow down the possible

explanations to the absent particle swelling, SEM images of the different reaction stages will be discussed below:

In Figure 50 b-g, SEM images of the particles from different stages of the DVB swelling process are displayed with images b-d showing an overview of the particles and images e-g having a closer focus on the surface structure. The templated particles p(IV) obtained from the styrene swelling step can be seen in Figure 50 b and e. They show an overall smooth surface structure that is spotted with small granules. Furthermore, no pores are visible as expected at this stage. The particles are uniform and spherical supporting the data derived from light microscope imaging. SEM overview images of these particles can be found in Figure S 43 in the appendix. Here, it can be observed that some particles are interconnected.

After the DVB swelling and polymerization step, the obtained particles p(VI) are still spherical and uniform with a smooth surface structure. In this instance, no small granules can be observed on the particle surface anymore. In the SEM overview images (cf. Figure S 44 in the appendix), only a small portion of particles are still interconnected. Most particles are separated.

Upon completion of the template removal step, during which the macromolecular porogen is intended to be washed out with THF, the surface of the resulting p(VII) particles exhibited no significant change (Figure 50 g). Compared to the particles before the porogen removal p(VI) and to the original solid, non-porous PDVB core particles p(I), the particles obtained here look similar in terms of surface smoothness and porosity. A slightly granular morphology is observed, suggesting the presence of small pores (<10 nm), while larger pores are absent. If pores larger than 10 nm in diameter formed, as observed in the model particles from the literature (Figure 51), they should be detectable by SEM at this stage, as the resolution limit of the SEM used is at least 10 nm. As observed before, in the overview images (cf. Figure S 45 in the appendix) it becomes apparent that most particles are separated. If a connection between two particles is visible, the connective material is more porous than before (cf. Figure 50d) leading to the assumption that at least some parts of it contained mobile PS chains.

Since the SEM images do not reveal a porous structure with pore sizes larger than 10 nm, and the particles appear similar to the PDVB core particles p(I), it is reasonable to assume that the column performance tests for the particles after template removal (p(VIII)) would yield the same separation behavior as the non-porous PDVB particles (p(I)). Taking the results from the

SEM images into account, the removal of the macromolecular porogen has not resulted in the porosity expected from the model system (10-100 nm, cf. Figure 51).⁵⁹ Apparently, the inserted PS chains were fixed to the particle and could not be removed anymore.

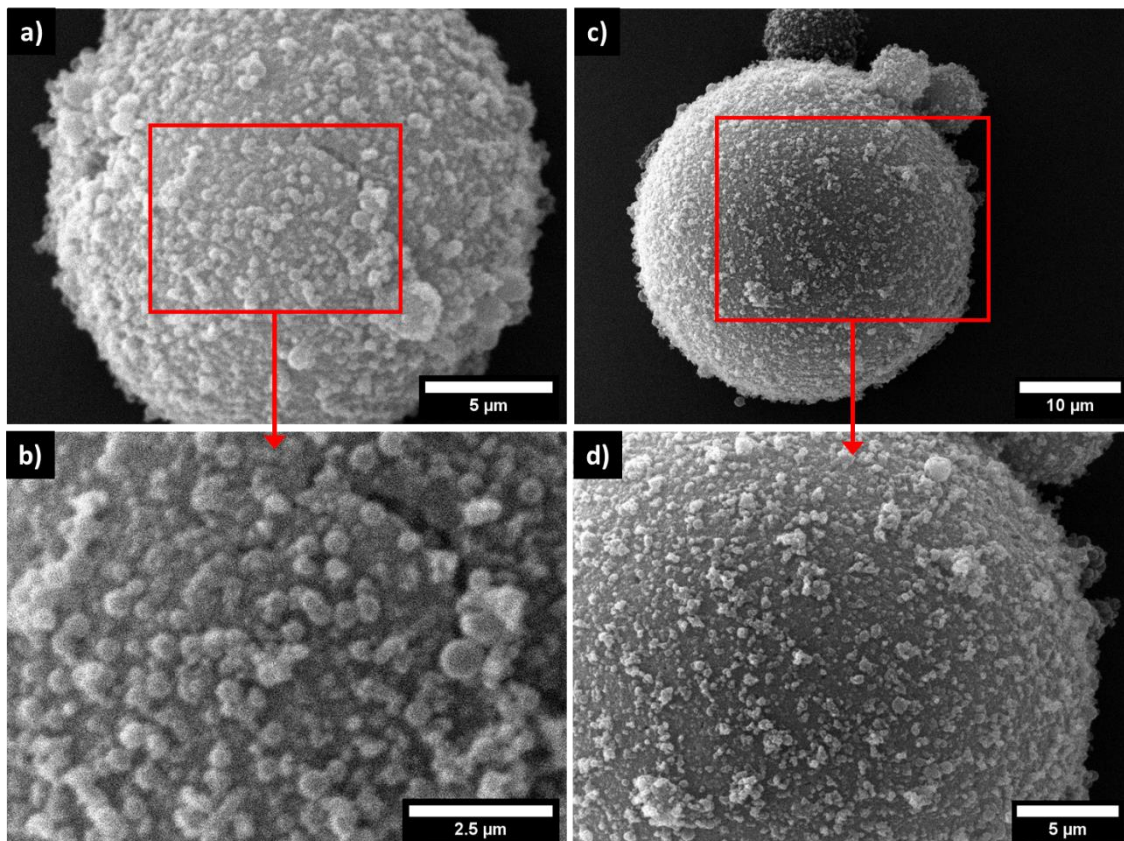


Figure 51: SEM images of PDVB model particles, synthesized here according to a template-swelling procedure for poly(styrene-co-divinylbenzene) particles from literature.⁵⁹ The particles are shown before the PS template extraction with THF (a) and b)) and afterwards (c) and d)). The samples were coated with a gold layer (thickness: 10 nm) and measured under a high voltage (CamScan24).

One possible reason for this could be that the inserted DVB in the second step has caused so many crosslinks in the newly developed network, that the present PS chains were trapped inside the particle. In the second swelling process B), only DVB and a plasticizer were used for swelling instead of a mixture of styrene and DVB as was reported in literature.⁵⁹ This might have caused too many crosslinks leading to the formation of an impermeable network and covalent binding of the mobile PS chains to the particle. Taking the absent particle swelling with DVB in the second process (B) into account, something in the first process (A) might have altered the particle shell in such a way that swelling is not possible anymore in the second process. This is likely caused by some sort of additional crosslinking in the shell. On one hand,

additional crosslinking can develop during the free radical polymerization due to chain transfer reactions. They can occur at the backbone of either the polymer network or the mobile PS chains and either create an unwanted crosslink or graft the mobile PS chains to the network. On the other hand, it is reported that PDVB particle systems tend to carry free double-bonds on the particle surface when they were synthesized via precipitation polymerization.^{36,43,50} Since a significant amount of DVB still had to be used to form the particle shell in the precursor synthesis, the residual double-bonds might have aided in the formation of unwanted crosslinking via by taking part in the polymerization reaction during process A). The so obtained higher crosslinking density in the particle shell would prevent further swelling with DVB and the plasticizer in process B) and thus explain the observations made with light microscopy and SEM imaging.

In summary, while the two-step swelling method showed promise in incorporating mobile PS chains into particle shells which could act as macromolecular porogen, unexpected challenges likely due to unwanted crosslinking prevented the porogen removal and thus the desired porous structure.

7.3.3 Chapter Conclusion and Outlook

A macromolecular porogen (polystyrene) was investigated to introduce pores into the shell of PDVB core-shell particles using a template swelling technique aiming to generate pores in the regime of 10-100 nm. Precursor particles with a swellable shell were synthesized with 75v% styrene in the shell ensuring shell growth without agglomeration. Swelling with styrene and polymerization increased the particle sizes slightly, confirming the shell's swellability. However, in the final swelling and polymerization step using DVB as monomer, no significant increase in particle size occurred. Additionally, SEM images showed that no pores larger than 10 nm were formed after the template removal. These findings can likely be attributed to excessive crosslinking during polymerization. This unintended crosslinking, possibly due to chain transfer reactions or residual double bonds in the PDVB system, appears to have hindered the removal of the porogen. Furthermore, the preexisting network in the precursor shell might have amplified this effect as observed in chapter 7.2.

To address this, the precursor particle's crosslinking degree could be reduced further. Future experiments should focus on optimizing solvent/cosolvent combinations to enable higher styrene concentrations. Additionally, transitioning to a more stable precipitation-based system, like dispersion polymerization, would be possible. Here, the stabilizer type and concentration must be carefully matched to the solvent and monomer to avoid secondary nucleation or agglomeration. Moreover, the stabilizer should not increase the hydrophilicity of the particle to maintain the particles' suitability as an SEC stationary phase, adding another layer of complexity to the stabilizer-solvent selection. For the template removal step, harsher conditions like higher temperatures, other solvents and sonication could be explored.

8 Overall Conclusion

This thesis explored various synthetic approaches to design and control the morphology of PDVB-based particles, aiming to create a core-shell structure with a stable, non-porous core and a porous shell for size exclusion chromatography.

In chapter 7.1, precipitation polymerization and low-molecular-weight porogens were examined. A newly developed reaction setup yielded monodisperse, non-porous particles as a basis for later shell growth, which was successful, though pores above 10 nm could not be introduced. The limited confined space during the reaction likely prevented the formation of larger pores. Still, the particle size was tunable by varying the porogens.

Chapter 7.2 focused on PDVB particles with hollow cores and surface grooves obtained by combining precipitation polymerization with template swelling. As shown in three approaches, the extent of the grooves and core size was tunable by adjusting the template crosslinking density. Despite this, the internal porous structure was unsuitable for SEC applications.

With the knowledge from the first two parts, chapter 7.3 aimed to generate larger pores using macromolecular porogens. To enable swelling, the PDVB particle shell from chapter 7.1 was modified. However, after the template swelling process, pores above 10 nm were not observed likely due to the formation of unwanted crosslinks leading to the permanent incorporation of the porogen.

Overall, this work demonstrates different methods to design and control the morphology of PDVB particles, with potential applications in HDC chromatography or as model systems in colloidal analysis. Since the system allows versatile surface modification, the particles also offer promising potential as drug carriers in medical contexts and as functional supports for catalysts.

9 Experimental Part

9.1 Materials

AIBN (azobis(isobutyronitril), 98.0%, Fluka Analytical), ACN (acetonitrile, HPLC grade 99.9%, Chemsolute) or ACN (technical grade, $\geq 99\%$, VWR chemicals), BAPO (Bis(2,4,6-trimethylbenzoyl)-phenylphosphineoxide, also known as Irgacure 819, Acrylat Shop), DBP (dibutyl phthalate, $>98\%$, Fluka), DVB (divinylbenzene, stab., 60.0-65.0 %, with 34.0-39.0% ethylvinyl benzene, Merck), dodecanol (98%, Alfa Aesar), ethanol (EtOH, absolute, 99.98%, VWR chemicals), hydrogen peroxide (H_2O_2 30%, stabilized, Carl Roth GmbH), isopropyl alcohol (iPrOH, HPLC grade, VWR chemicals), Methocel (K100, methyl cellulose), PNVP (polyvinylpyrrolidone, $M_w = 40\,000$ g/mol, Alfa Aesar), potassium hydroxide (KOH, $\geq 85\%$, in pellets, Carl Roth GmbH), sulfuric acid (H_2SO_4 , 95%, analytical reagent grade, Fisher Scientific), styrene (Sty, stab., 99%, Alfa Aesar), toluene (analytical grade, Fisher Scientific), THF (tetrahydrofuran, ACS grade, VWR chemicals) and water (ultrapure (Type 1) or sourced from a local tap supply). If not stated otherwise, the chemicals were used as received.

9.2 PDVB Particles via Precipitation Polymerization

For a small scale experiment in a single-use screw-cap vial with aluminum block heating the following synthesis was done adapted from literature¹⁹:

To a preheated solution (75 °C) of acetonitrile (ACN, HPLC grade, 29.4 mL, 98v% of the total reaction volume) and divinylbenzene (DVB, 0.6 mL, 2v% of the total reaction volume, (60% DVB, 40% EVB)), azobisisobutyronitrile (AIBN, used as received, 0.011 g, 16mol% with respect to monomer content, dissolved in 1 mL of ACN from the initial ACN amount) was added. The reaction mixture was stirred at 75 °C for 20 h at 300 rpm.

Purification was done five times either by centrifugation (4k rpm, 15 min) or sedimentation (4 h or overnight) with the supernatant being substituted with fresh acetonitrile after each step. The isolated particles were dried overnight under ambient conditions.

The yield was 168 mg (29%). The theoretical yield (100%) was calculated from the masses of the monomer and initiator combined.

This recipe was used for all PDVB precipitation polymerization reactions if not stated otherwise and will be referred to as “standard recipe for precipitation polymerization of PDVB” in the following.

9.2.1 Establishing a Reliable Experimental Setup for Non-Porous Particles

Selection and Pretreatment of the Reaction Vessel

In the first experiment series, new glass flasks and oil bath heating were used for “the standard recipe for precipitation polymerization of PDVB” (cf. chapter 9.2) and the experiment was repeated several times in the same flask. Between each experiment the flask was rinsed with neat acetonitrile.

In the second experiment series, the inside of the used glass flasks were coated with HMDS before the “standard recipe for precipitation polymerization of PDVB” was carried out. For this, HMDS (2-5 mL) was inserted into the flask and spread by tilting and rotating the flask by hand for 5 min or until the residual HMDS had evaporated.

In the third experiment series, the used glass flasks were either immersed into a freshly prepared KOH bath (saturated solution in isopropyl alcohol) or filled with Caro's acid (70v% sulfuric acid and 30v% hydrogen peroxide) and kept overnight under ambient conditions. After the flasks were rinsed with water and dried the "standard recipe for precipitation polymerization of PDVB" was carried out.

Experiment series two and three were conducted by Samar Diraoui in the course of a SHK project under supervision of the author of this thesis.

For large flasks (2 L or more), thermal treatment was employed between each synthesis. During thermal treatment, the flask was immersed into an oven, heated to 900 °C or more and was kept at this temperature overnight. The carbon residues were rinsed out with neat acetonitrile before the flask was used for synthesis again.

For small scale experiments either new flasks or single-use screw-cap vials the "standard recipe for precipitation polymerization of PDVB" (cf. chapter 9.2) were used. The vials were disposed after the experiments.

Comparison of Reaction Conditions Involving Mild Agitation versus Quiescent Conditions

While keeping the ingredient ratios and reaction temperature like the “standard recipe for precipitation polymerization of PDVB” (cf. chapter 9.2), the stirring speed was altered in this experiment series. The experiments were conducted in screw cap vials using aluminum block heating.

When 300 rpm stirring speed was employed, single particles formed with a yield of 127 mg (23%). If no stirring was applied, agglomeration occurred and thus no yield was calculated.

Influence of the Chemical Quality of the Reagents

For the following experiments, the “standard recipe for precipitation polymerization of PDVB” (cf. chapter 9.2) was used and either the quality of the employed acetonitrile, AIBN or DVB was altered at the same time (see Table 2) while all other parameters and the ingredient ratios were kept constant. Reactions, where the employed ACN or DVB was changed, were conducted in flasks using oil bath heating. The experiment series around changing the type of AIBN was conducted in screw cap vials using aluminum block heating.

The most frequent particle diameters were evaluated from PSD histograms of light microscopy images from the reaction mixture after polymerization. “Most frequent” includes the bin with the highest particle count and all other bins that have at least half of this value.

Table 2: Ingredient qualities that were changed during precipitation polymerization of PDVB particles and the resulting particle sizes (or agglomeration) and yields.

Ingredient name	Employed quality	most frequent particle diameter / μm	Yield / mg (%)
ACN	tech. grade, distilled before usage*	agglomeration	-
	recycled**	agglomeration	-
	HLPC grade	4.7 μm	313 (28)
AIBN	as received	2.7 μm	183 (33)
	2x recrystallized	3.9 μm	175 (31)
DVB	60v% DVB, 40v% EVB batch in use for months	4.7 μm	313 (28)
	80v% DVB, 20v% EVB	3.7 μm	12100 (41)
	60v% DVB, 40v% EVB recently opened batch	3.1 μm	168 (29)

* This experiment series was conducted by Samar Diraoui in the course of a SHK project under supervision of the author of this thesis.

** This experiment series was conducted by Clinton Richard Victor Thiagarajan as part of his master thesis under supervision of the author of this thesis.

9.2.2 Assessment of Key Influences on Non-Porous Particle Sizes

Evaluation of the Influence of the Reaction Temperature on PDVB Particle Sizes

For this series of experiments, the “standard recipe for precipitation polymerization of PDVB” (cf. chapter 9.2) was carried out in new glass flasks using oil bath heating at different reaction temperatures, as follows:

Table 3: Different reaction temperatures used during a precipitation polymerization experiment series and the resulting particle sizes and yields.

Reaction temperature / °C	most frequent particle diameter / µm	Yield / mg (%)
75	5.2	461 (41)
	5.2	439 (39)
70	5.3	427 (38)
	5.7	371 (33)
65	4.9	337 (30)
	2.7	326 (29)
60	3.3	225 (20)
	3.1	270 (24)
55	2.3	169 (15)
	3.7	169 (15)
50	could not be measured (< 1.0)	-
	2.1	11 (1)

This experiment series was conducted by Renée Hoffmann as part of a research lab course under supervision of the author of this thesis.

Influence of the Chemical Composition

In the following two experiment series the “standard recipe for precipitation polymerization of PDVB” (cf. chapter 9.2) was carried out in glass flasks using oil bath heating and either the concentration of the monomer (DVB, see Table 4) or the initiator (AIBN, see Table 5) was altered while the other parameters were kept constant.

Table 4: Different monomer feed concentration used during precipitation polymerization and the resulting particle sizes and yields.

DVB / v%*	most frequent particle diameter / μm	Yield / g (%)
7	agglomeration	-
5	agglomeration	-
4	agglomeration	-
3	agglomeration	-
2	5.1	0.31 (28)
1.5	4.5	8.63 (26)
1	3.7	0.27 (33)

*with respect to total reaction volume

This experiment series was conducted by Clinton Richard Victor Thiagarajan as part of his master thesis under supervision of the author of this thesis.

Table 5: Different initiator concentrations used during precipitation polymerization and the resulting particle sizes and yields.

AIBN / mol%*	most frequent particle diameter / μm	Yield / mg (%)
16	5.2	461 (41)
	5.2	439 (39)
10	4.9	349 (31)
	4.5	382 (34)
5	3.7	247 (22)
	3.5	225 (20)
2.5	3.1	146 (13)
	3.3	157 (14)
1	2.9	11 (1)
	2.5	12 (1)

* with respect to total monomer content

This experiment series was conducted by Renée Hoffmann as part of a research lab course under supervision of the author of this thesis.

9.2.3 PDVB Particle Shell Growth

Particle Size Alterations using DVB

For the first reaction step the “standard recipe for precipitation polymerization of PDVB” was carried out as stated above (cf. chapter 9.2). The particles were purified as stated above before further usage. The experiments were carried out in screw-cap vials using aluminum block heating.

In the second reaction step, a dispersion consisting of acetonitrile (ACN, HPLC grade, 29.4 ml, 98v% of total volume), divinylbenzene (DVB, 0.6 mL, 2v% of the total reaction volume, (60% DVB, 40% EVB)) and the polydivinylbenzene (PDVB) particles from the first reaction step (0.220 g $\triangleq$ 40% yield from core synthesis) was preheated to 75 °C. To this mixture, azobisisobutyronitrile (AIBN, used as received, 0.011 g, 16mol% with respect to monomer content, dissolved in 1 mL of ACN from the initial ACN amount) was added and the mixture was stirred at 130 rpm for 20 h at 75 °C.

Purification was done five times by either centrifugation (4k rpm, 15 min) or sedimentation (4 h or overnight) with the supernatant being substituted with fresh acetonitrile after each step. The isolated particles were dried overnight under ambient conditions. Yield: 416 mg (58%)

Preliminary experiments to optimize this shell growth reaction and one-pot experiments were done by Clinton Richard Victor Thiagarajan (Master thesis, 11th March 2019) under supervision of the author of this thesis.

Particle Size Alterations using Styrene

A dispersion consisting of a liquid medium (isopropyl alcohol (iPrOH) : acetonitrile (ACN) mixture, 15 mL, 98v% of the total reaction volume, both HPLC grade, see Table 6 for exact ratios), styrene (Sty, 0.3 mL, 2v% of the total reaction volume) and polydivinylbenzene (PDVB) core particles (90 mg) was preheated to 75 °C. To this mixture, azobisisobutyronitrile (AIBN, used as received, 0.006 g, 16mol% with respect to monomer content, dissolved in 1 mL of ACN from the initial ACN amount) was added and the mixture was stirred at 130 rpm for 20 h at 75 °C.

Purification was done five times by sedimentation in ethanol (for 4 h or overnight) with the supernatant being substituted with fresh ethanol after each step. The isolated particles were dried for 3 days under ambient conditions.

The yield and most frequent particle diameters can be found in Table 6. The most frequent particle diameters were evaluated from PSD histograms of light microscopy images from the isolated particles after purification and dispersion in isopropyl alcohol. “Most frequent” includes the bin with the highest particle count and all other bins that have at least half of this value.

Table 6: Liquid medium ratios used for precipitation polymerization of styrene onto PDVB cores and the corresponding resulted particle properties.

iPrOH mL / v% of liquid medium	ACN mL / v% of liquid medium	most frequent particle diameter	Yield / mg (%)
15 / 100	0 / 0	agglomerates	103 (25)
12 / 80	3 / 20	agglomerates	90 (22)
9 / 60	6 / 40	agglomerates	72 (17)
7.5 / 50	7.5 / 50	3.4 µm - 4.0 µm	77 (18)
6 / 40	9 / 60	3.4 µm - 4.0 µm	72 (17)
3 / 20	12 / 80	3.4 µm - 4.0 µm	74 (18)
0 / 0	15 / 100	agglomerates	96 (23)

Attempts of Porogen Introduction During the Shell Formation

First step: Acetonitrile (ACN, HPLC grade, 800 mL, 98 v% of the total reaction volume) and divinylbenzene (DVB, 16 mL, 2v% of the total reaction volume, (80% DVB, 20% EVB)) were combined and purged with argon for 60 min at 300 rpm. AIBN (used as received, 320 mg, 16mol% with respect to monomer content) was added and the mixture was purged with argon for another 30 min. The mixture was put into a preheated incubator and was slowly turned around its horizontal axis for 20 h at 60 °C.

Second step: To half of the reaction mixture from the first reaction step, a prepurged (5 min, Argon) mixture of ACN and toluene (60:40, 240 mL ACN, 160 mL toluene) was added and the mixture was purged for further 30 min before adding DVB (16 mL, 2v% of the total reaction volume, (80% DVB, 20% EVB)). After purging for additional 5 min, AIBN (used as received, 320 mg, 16mol% with respect to monomer content) was added and the mixture was put into a preheated incubator and was slowly turned around its vertical axis for 20 h at 60 °C.

Purification was done by filtration and washing the gained particles with acetone five times. The isolated particles were dried overnight under ambient conditions. Yield: 5.10 g (24%)

9.2.4 Investigating Low-Molecular-Weight Porogens for Pore Formation

To a preheated solution (75 °C) of acetonitrile (ACN, HPLC grade, (29.4- X_1 - X_2) mL, (98- Y_1 - Y_2)v% of the total reaction volume), the porogen(s) (X mL, Y v% of the total reaction volume, see also Table 7 for detailed numbers) and divinylbenzene (DVB, 0.6 mL, 2v% of the total reaction volume, (60% DVB, 40% EVB)), azobisisobutyronitrile (AIBN, used as received, 0.011 g, 16mol% with respect to monomer content, dissolved in 1 mL of ACN from the initial ACN amount) was added. The reaction mixture was stirred at 75 °C for 20 h at 300 rpm. All experiments were carried out in screw-cap vials using aluminum block heating.

Purification was done five times either by centrifugation (4k rpm, 15 min) or sedimentation (4 h or overnight) with the supernatant being substituted with fresh acetonitrile after each step. The isolated particles were dried overnight under ambient conditions.

The yield and most frequent particle diameters can be found in Table 7. The most frequent particle diameters were evaluated from PSD histograms of light microscopy images from the reaction mixture after polymerization. “Most frequent” includes the bin with the highest particle count and all other bins that have at least half of this value.

Table 7: Different porogens and porogen mixtures used in the formation of PDVB particles via precipitation polymerization in acetonitrile.

porogen 1 (X ₁ , Y ₁)	mL / v% of total volume	porogen 2 (X ₂ , Y ₂)	mL / v% of total volume	most frequent particle diameter	Yield / mg (%)
toluene	12 / 40 6.0 / 20	/		< 1 µm or agglomerates 6.8 µm - 7.8 µm*	239 (43) 225 (40)
THF**	6.0 / 20	/		4.8 µm - 5.2 µm	231 (41)
water	0.3 / 1 0.6 / 2 1.5 / 5 3.0 / 10	/		2.6 µm - 3.0 µm 2.6 µm - 2.8 µm 2.4 µm - 2.6 µm agglomerates	183 (33) 207 (37) 195 (35) 202 (36)
dodecanol**	6.0 / 20	/		3.8 µm - 4.2 µm	270 (48)
toluene	6.0 / 20 6.0 / 20	water	0.6 / 2 1.5 / 5	3.4 µm - 3.6 µm 3.0 µm - 3.6 µm	211 (38) 204 (36)
toluene	4.5 / 15 20	dodecanol	4.5 / 15 20	3.8 µm - 4.2 µm < 1 µm non- spherical objects	199 (35) 196 (35)

*some experiments show a broad size distribution of 1-8 µm, with <70% of particles being larger than 3.5 µm

** The syntheses of these particles were conducted by Aliia Ibragimova in the course of a SHK project under supervision of the author of this thesis.

9.3 Morphological design of PDVB-based particles

9.3.1 PS template particles

Non-crosslinked PS^{nc} template

Adapted from literature,¹⁶¹ non-crosslinked PS particles were prepared as follows: styrene (8.3v% of the total reaction volume), PNVP ($M_w = 40\,000$ g/mol, 25 mol% wrt. monomer content) and AIBN (3mol% wrt. to monomer content) were dissolved in ethanol (absolute, 91.7v% of the total reaction volume) in a round bottom flask. In a preheated oil bath, the reaction was carried out at 75 °C for 20 h at a stirring speed of 130 rpm. For purification, the particles were centrifuged, and the supernatant liquid was replaced by fresh ethanol. This step was repeated at least 5 times before the particles were dried under ambient conditions for 24 h.

Slightly crosslinked PS^{xl} template

The procedure for PS^{xl} template particles was carried out in the same way as the procedure for non-crosslinked PS template particles but with a mixture of styrene and DVB (Sty:DVB 96:4 v/v) instead of neat styrene.

Combined PS^{xl+nc} template

PS^{xl} template particles were dispersed in a solution consisting of ethanol (absolute, 99v% of total volume), styrene (4v% of total volume, PS:Sty = 1:1), PNVP ($M_w = 40\,000$ g/mol, 50mol% wrt. PS particles) and AIBN (3mol% wrt. to monomer) and stirred for 2 h at room temperature. The reaction was carried out in a preheated oil bath at 75 °C for 20 h at a stirring speed of 130 rpm. For purification, the particles were centrifuged, and the supernatant liquid was replaced by fresh ethanol. This step was repeated at least 5 times before the particles were dried under ambient conditions for 24 h.

9.3.2 Synthesis of PDVB-gPS, PDVB-gPS^{xl}, and PDVB-gPS^{xl+nc} particles

PS template particles (see Table 8, 300 mg) were evenly dispersed in an aqueous Methocel solution (18.6 g/L, 7.5 mL) before a solution of DVB (65 μ L, 60 mg; PS:DVB 5:1 wt) and Irgacure 819 (6 mol% wrt. monomer, 11.5 mg) in ethanol (1 mL) was added dropwise under fast stirring at 0 °C. To ensure a stable dispersion, the mixture was stirred for 2 h under aforementioned conditions and then stored overnight at 7 °C without stirring. After the mixture was irradiated under mild stirring for 1 h (Nichia UV LED lamp NVSU333A 365 nm, 3.64 W; mode: 4.2 V, 3.8 A), it was slowly stirred under light exclusion at room temperature for additional 20 h.

For purification, the particles were centrifuged, and the supernatant liquid was replaced by water. This step was repeated at least 5 times or until the supernatant liquid was as viscous as water. The same process was repeated once each with ethanol:water 1:3, 1:1, 3:1 and ethanol before the particles were dried under ambient conditions for 24 h.

The template extraction with THF was carried out in a Soxhlet extractor for 2 days.

Table 8: Details about the particle types used in the three different preparation methods to obtain the product particles PDVB-gPS, PDVB-gPS^{xl}, and PDVB-gPS^{xl+nc}, with the particle diameter of different reaction stages measured using pictures from light microscopy (template and monomer swollen particle dispersed in the reaction medium) and SEM (dried particles after THF extraction).

product particle	template particle	template particle diameter / $\pm 0.1 \mu\text{m}$	swollen template diameter / $\pm 0.1 \mu\text{m}$	dried particle diameters after THF extraction
PDVB-gPS	tPS ^{nc}	4.9 μm	5.5 μm	2.8 - 3.1 μm
PDVB-gPS ^{xl}	tPS ^{xl}	3.3 μm	3.7 μm	2.8 - 3.1 μm
PDVB-gPS ^{xl+nc}	tPS ^{xl+nc}	3.7 μm	3.9 μm	2.6 - 2.9 μm

9.4 Studies of Template Swelling Methods to Prepare PDVB Non-Porous Core - Porous Shell Particles

Precursor Particle Synthesis

The precursor particle synthesis was carried out in a two-step process as a one-pot reaction: The core particles were synthesized according to the PDVB core particle synthesis described in chapter 9.2 and all experiments were carried out in screw-cap vials using aluminum block heating:

To a preheated solution (75 °C) of acetonitrile (ACN, HPLC grade, 29.4 mL, 98v% of the total reaction volume) and divinylbenzene (DVB, used as received, 0.6 mL, 2v% of the total reaction volume, (60% DVB, 40% EVB)), azobisisobutyronitrile (AIBN, used as received, 0.011 g, 16mol% with respect to monomer content, dissolved in 1 mL of ACN from the initial ACN amount) was added. The reaction mixture was stirred at 75 °C for 20 h at 300 rpm.

The shell formation step was carried out as follows:

To a preheated reaction mixture of the core formation, styrene (used as received, 0.45 mL, 0.5v% of the total reaction volume, Sty:DVB 75:25 v/v), divinylbenzene (DVB, used as received, 0.15 mL, 1.5v% of the total reaction volume, (60% DVB, 40% EVB)), and azobisisobutyronitrile (AIBN, used as received, 0.011 g, 16mol% with respect to monomer content, dissolved in 1 mL of ACN) were added. The reaction mixture was stirred at 75 °C for 20 h at 300 rpm.

Purification was performed five times by centrifugation (4k rpm, 15 min) with the supernatant being substituted with fresh acetonitrile after each step. The isolated particles were dried overnight under ambient conditions.

The isolated particles appear as a white power with a yield of 168 mg (29%). The theoretical yield (100%) was calculated from the masses of the monomer and initiator combined.

Investigating Pore Formation with Macromolecular Porogens

Model systems utilizing non-crosslinked PS particles as starting material were synthesized according to literature.⁵⁹

The swelling method was carried out in two separate processes A and B:

Swelling process A (styrene):

To a dispersion of precursor particles (36 mg) in an aqueous SDS solution (5 mL, 0.25 wt% SDS) an emulsion of DBP (23 μL^* , 28.1 mg, DBP:particle shell mass 1.4:1), styrene (11 μL^* , 10 mg, Styrene:particle shell mass 1:2) and BAPO (2 μg^* , 6mol% with respect to monomer) and aqueous SDS (5 mL, 0.25 wt% SDS) was added and well mixed by vigorous stirring. From an aqueous PVA solution (5wt%) enough was added to the mixture to obtain a 1 wt% solution in the final mixture. The mixture was stirred for at least 3 h at room temperature before subjected to irradiation with light for 1 h (Nichia UV LED lamp NVSU333A 365 nm, 3.64 W; mode: 4.2 V, 3.8 A) at room temperature during mild stirring. The mixture was then stirred again under light exclusion for several hours at room temperature to ensure full conversion.

*The organic compounds were added via an ethanolic stock solution (given amounts are per 1 mL of Ethanol).

For purification, the particles were centrifuged, and the supernatant liquid was replaced by water. This step was repeated at least 5 times or until the supernatant liquid showed the same viscosity as water. The same process was repeated once each with ethanol:water 1:3, 1:1, 3:1 and ethanol before the particles were dried under ambient conditions for 24 h.

The isolated particles appear as a white power with a yield of 13 mg (28%). The theoretical yield was calculated from the monomer masses and educt particles.

Swelling process B (DVB):

The swelling process B and the polymerization step was carried out in the same way as described in process A with styrene being substituted by the same amount of DVB.

Purification was done in the same way as described for process A. After the particles were isolated, the template was extracted with THF via a Soxhlet extractor for 2 days. After the extraction process, the particles were dried under ambient conditions overnight.

The isolated particles before the THF extraction step appear as a white power with a yield of 12 mg (26%). The theoretical yield was calculated from the monomer masses and educt particles.

This experiment series was conducted by Nazih Dagher as part of a research lab course under supervision and experimental design of the author of this thesis.

9.5 Equipment and Methods

Light microscopy

Before each measurement, a droplet of the sample dispersion was dropped onto a glass microscope slide, and a cover slip was applied. The specific dispersion medium is given in the caption for each image.

Light microscopy was performed with a Zeiss Axioskop 50 microscope and either an “old” camera setup using Axiocam color (Software: Axio-Vision version 2.0.5.3; 1999) or a Bresser MikroCam SP 3.1 camera (Software: MikroCamLabII version 3.7.13814.20190120 (64 bit)) referred to as “new camera setup” (employed for chapter 7.1.3 and thereafter with the exception of chapter 7.1.4.2). The bright field transillumination mode was used for all shown LM pictures. Used objectives were a.) Zeiss Epiplan-Neofluar 50x magnification with NA = 0.75. Scaling was done with a microscope slide using a micrometer-scale standard with known spacing.

The resulting images were processed with ImageJ version 1.52i (running with Java 1.8.0_271 (64 bit)). For the particle size distribution (PSD) diagrams at least 1000 particles from 10 different images were measured with the implemented “analyze particles” function of ImageJ. To be processible, each image was transformed with ImageJ following this order: transformation to an 8bit image, converting to a black and white image with the “threshold” command, making particles countable and distinguishable with the “filling holes” and “watershed” commands. The resulting images were then processed with the “Analyze Particle” command implemented in ImageJ including circles with the following properties: 1.) a circularity between 0.5 and 1.0, b) area values larger than $0.5 \mu\text{m}^2$ and c) every circle that is not cut by the edge of the image. From the resulting list of circle areas, PSD diagrams were generated via the analysis tool pack (“Analyse-Funktionen” add-in) for data analysis of “Excel for Office 365 MSO” (16.0.12527.20260 32-bit) using a bin size of $0.2 \mu\text{m}$ (width of one histogram bar).

Scanning electron microscopy

The SEM images in chapter 7.1 (except Figure 28) and the sample shown in Figure 51 in chapter 7.3.2 were recorded by the author in the following way:

A small amount of the dry sample was spread on an aluminum foil and then transferred to a carbon adhesive tab by stamping the foil and sample. Before measurement, the sample was coated with a 10 nm thin gold layer (Edwards sputter coater S150B, 2×10^{-1} mbar). The SEM images were recorded with a Camscan24 (1990, Cambridge Scanning Company, Cambridge, England) scanning electron microscope (100 mA, wolfram cathode) using a SE detector, an acceleration voltage of 25 kV and 27-35 mm working distance for all samples. The software used for recording the images was Olympus Scandium (Version 5.2, Build 6076, for Windows 7) which also provided scaling.

All other SEM images were kindly provided by Gunnar Glasser within the collaboration with LiNaCon Dr. Ingo Lieberwirth, Mainz and were created in the following way:

For SEM analysis, a small volume of the particle dispersion was deposited onto a silicon wafer and left to dry at room temperature. The dried samples were analyzed without any additional coating using a LEO Gemini 1530 microscope (Zeiss, Oberkochen, Germany), operating at an accelerating voltage of 700 V (Schottky field-emission gun) and a probe current in the range of 15 to 70 pA.

To prepare cross-sectional samples, multiple drops of the dispersion were placed on a pre-cured Epofix resin substrate (Agar Scientific, Stansted, UK). Once fully dried, the samples were covered with a second layer of Epofix and subsequently cured. The matrix-embedded specimens were sectioned into slices with a thickness of 2 μm using an ultramicrotome (UCT 7, Leica, Germany) equipped with a diamond knife (Diatome, Switzerland). Afterwards, the sections were transferred to a silicon wafer. The resin-embedded particles were cut into 2 μm thick sections in an ultramicrotome (UCT 7, Leica, Germany) using a diamond knife (Diatome, Switzerland) and then transferred to a silicon wafer. SEM imaging of the cross sections was carried out with the LEO Gemini 1530 under the same operational settings as described above.

SEC Column Performance Tests

SEC column performance tests were kindly provided by Moritz Susewind and Thorsten Hofe during the collaboration with PSS GmbH, Mainz.

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12 Appendix

12.1 PDVB Particles via Precipitation Polymerization

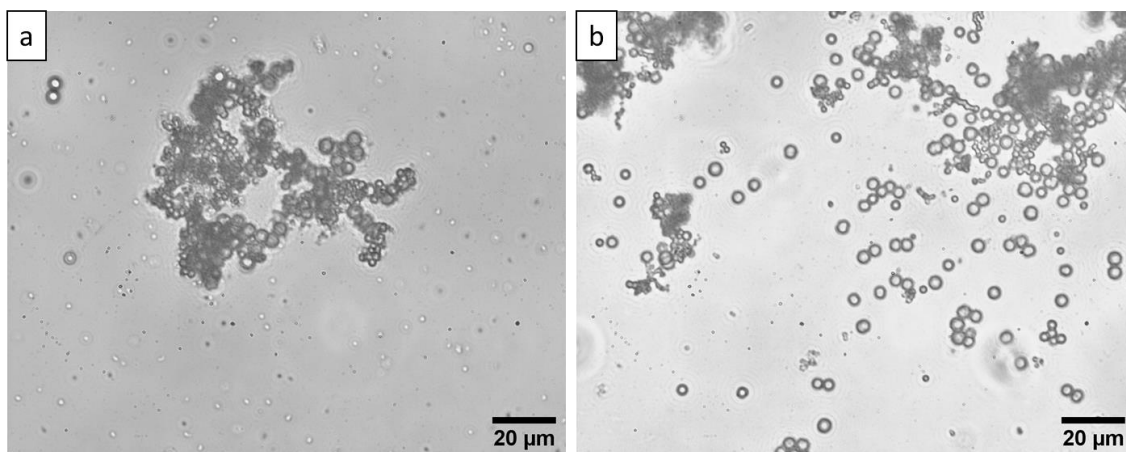


Figure S 1: LM images of PDVB particle reaction mixtures after precipitation polymerization, with the reaction vessel being treated with caro's acid (a) or KOH (b) before usage.

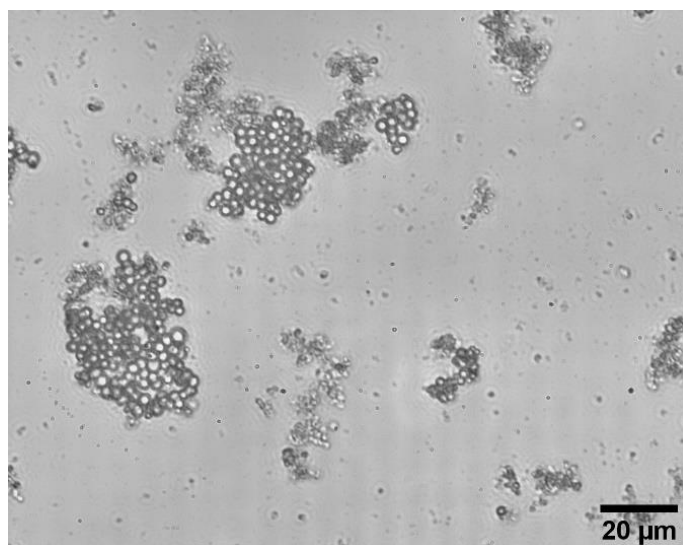


Figure S 2: LM images of PDVB particle reaction mixture after precipitation with the vessel being hydrophobized with HMDS before usage to mimic PP bottles.

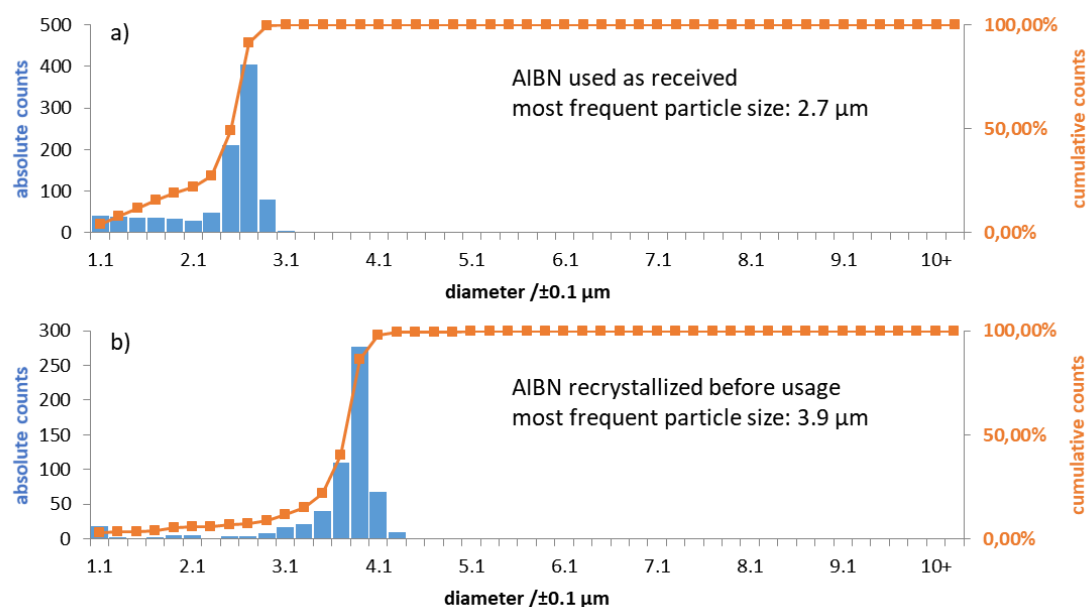


Figure S 3: PSD diagrams of PDVB particle reaction mixtures after precipitation polymerization with AIBN, which was used as received (a), or recrystallized AIBN (b)

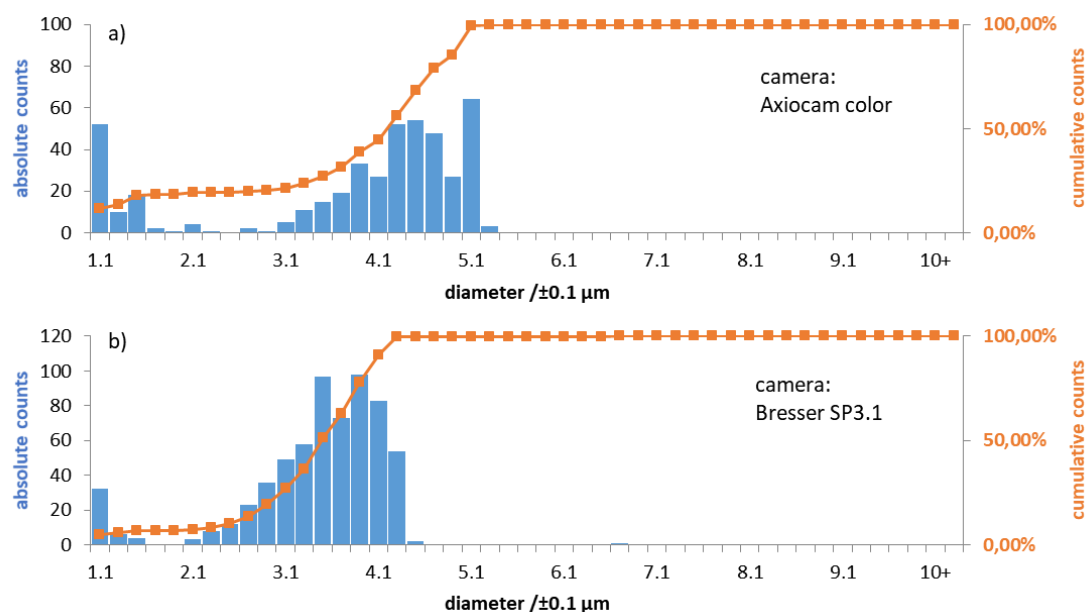


Figure S 4: PSD diagrams for comparison of the PDVB benchmark experiment (2v% DVB, 16mol% AIBN with respect to monomer content, 75 °C reaction temperature) captured with the old camera (Axiocam color) (a) and the new camera (Bresser SP3.1) (b) which shows a systematic shift in apparent particle sizes with the new camera setup.

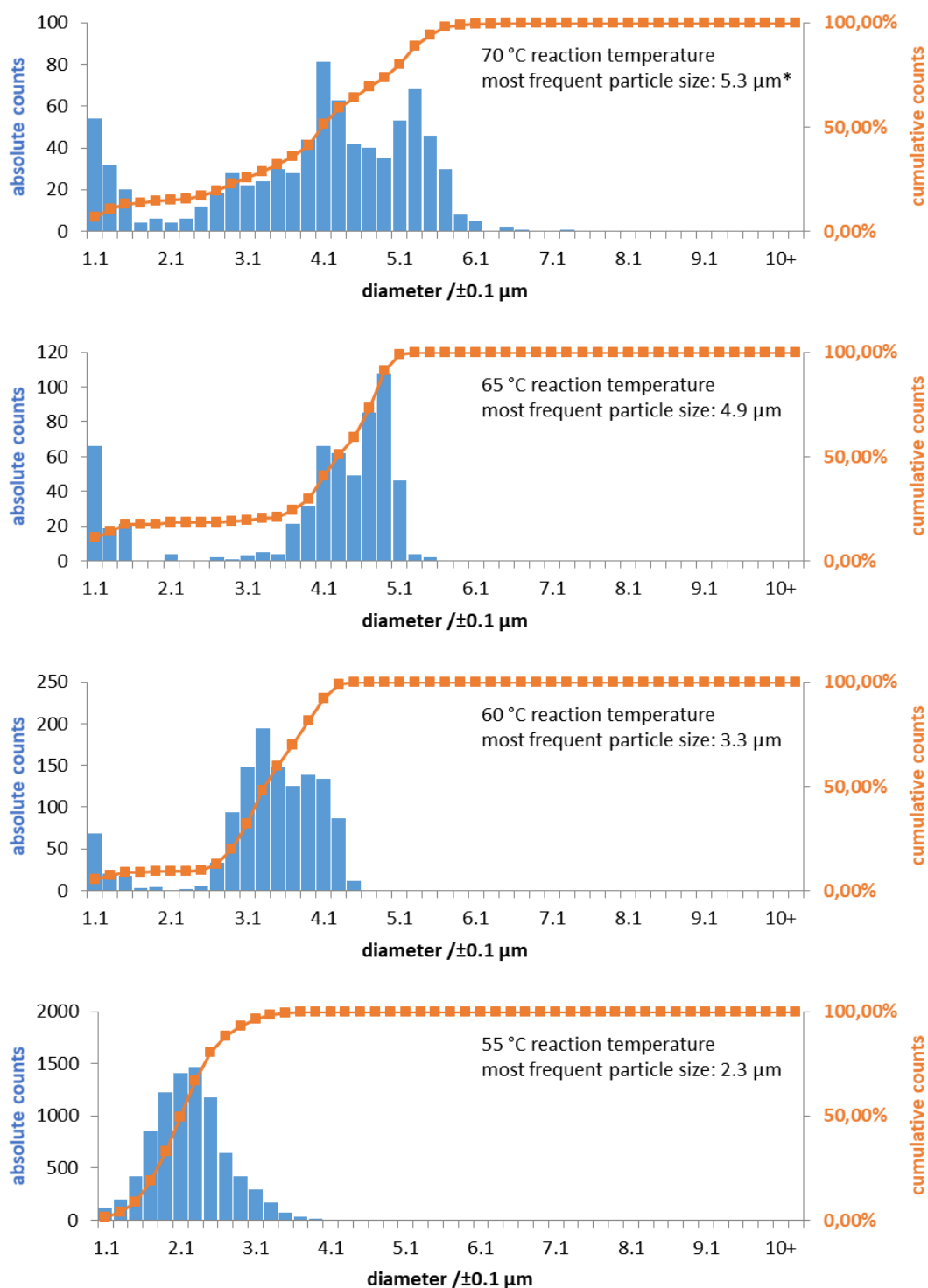


Figure S 5: Particle size distribution diagrams of PDVB particles made at different temperatures (first batch of samples). Please note that the resulting particles of the experiment conducted at 50 °C were too small to be analyzed quantitatively by light microscopy (<1 μm). For all other PSD diagrams, the analysis was done on light microscope 10 images from the reaction mixture after polymerization. *bimodal distribution, with the higher value displayed

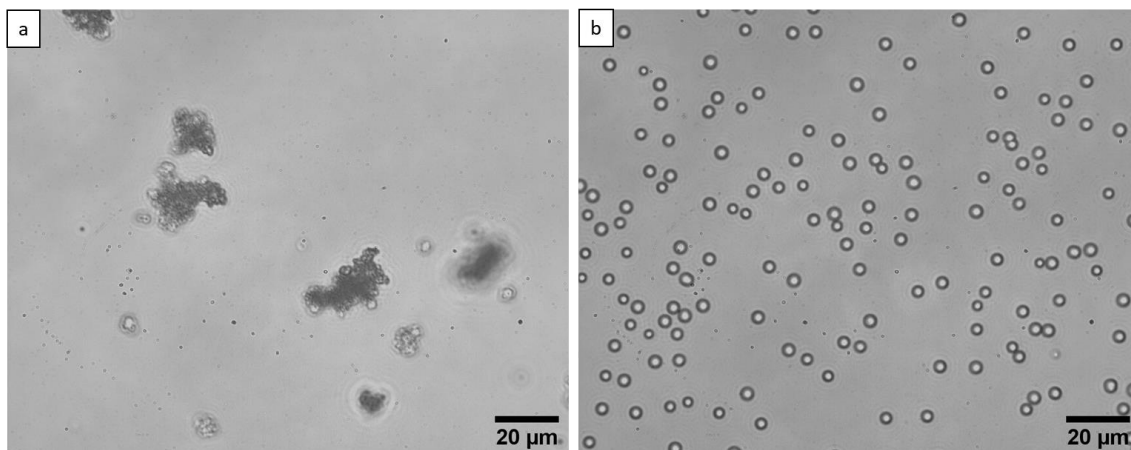


Figure S 6: LM images of PDVB particle reaction mixtures after precipitation polymerization with monomer feed of 4v% (a) showing agglomeration (this was observed for all samples with monomer feed higher than 2v%) and 1v% (b) showing single particle formation. Volume percentages are with respect to total reaction volume.

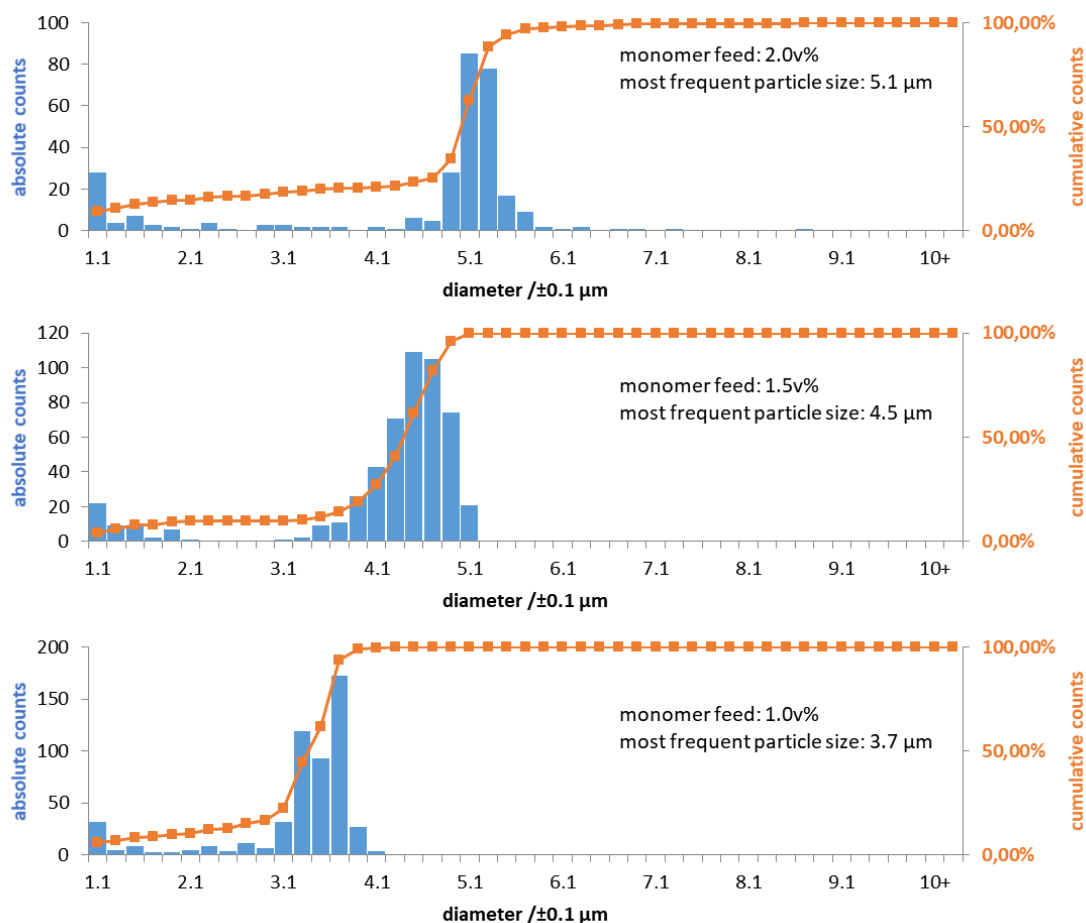


Figure S 7: Particle size distribution diagrams of PDVB particles made with different monomer concentrations. The particles sizes were calculated from 10 light microscope images of the reaction mixture after polymerization.

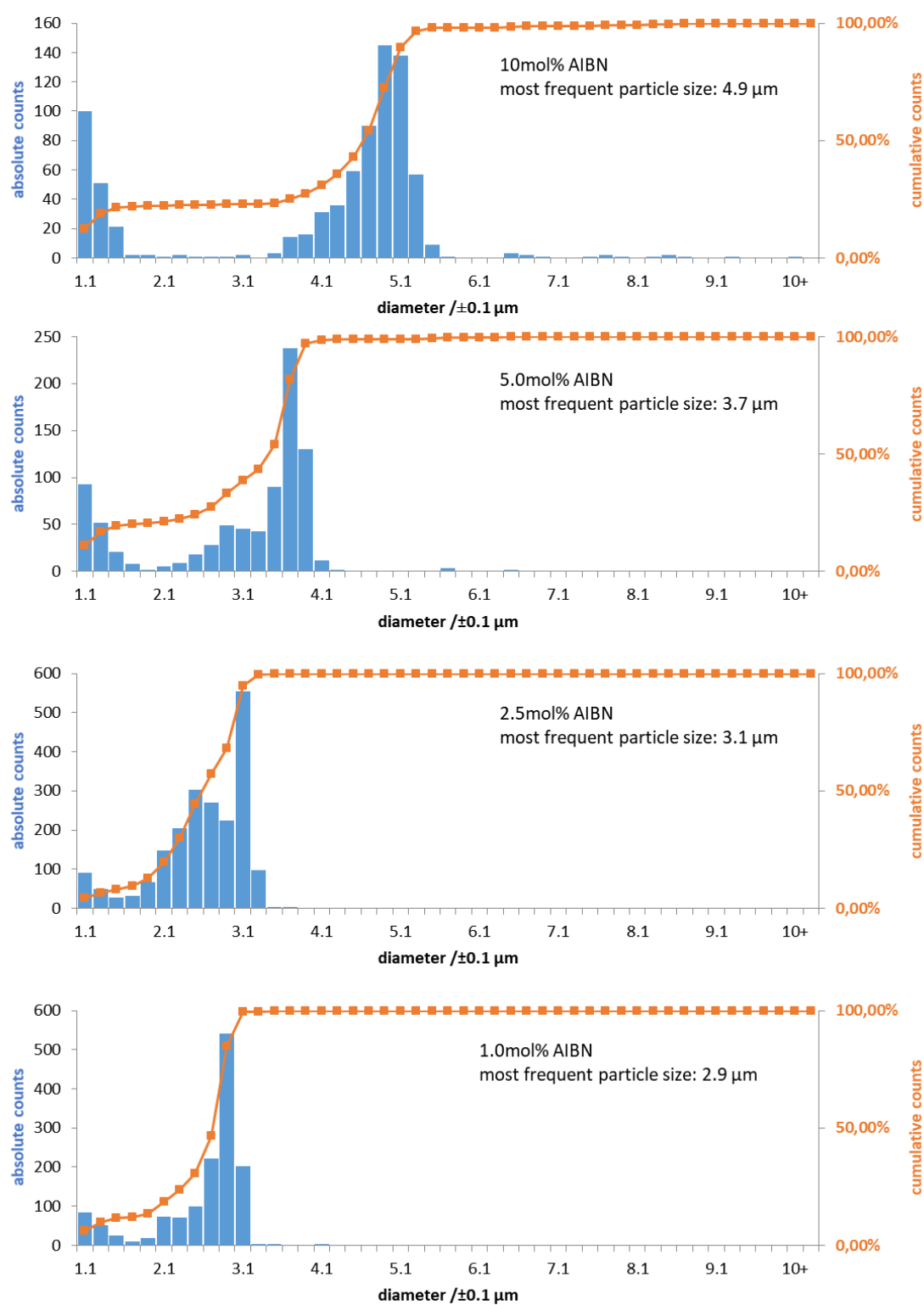


Figure S 8: Particle size distribution diagrams of PDVB particles made with different AIBN concentrations (first batch). The particles sizes were calculated from 10 light microscope images of the reaction mixture after polymerization.

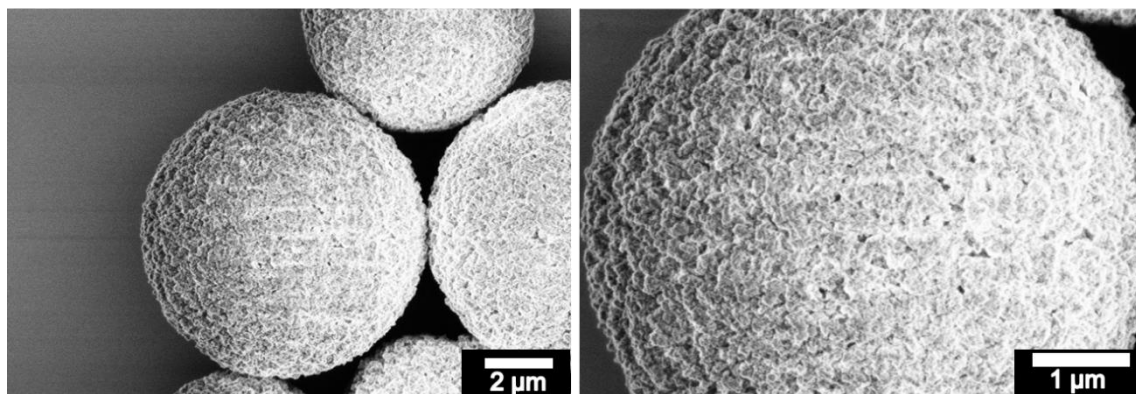


Figure S 9: SEM images of porous PDVB particles (10^4 Å) derived from suspension polymerization. These particles were kindly provided by PSS GmbH, Mainz.

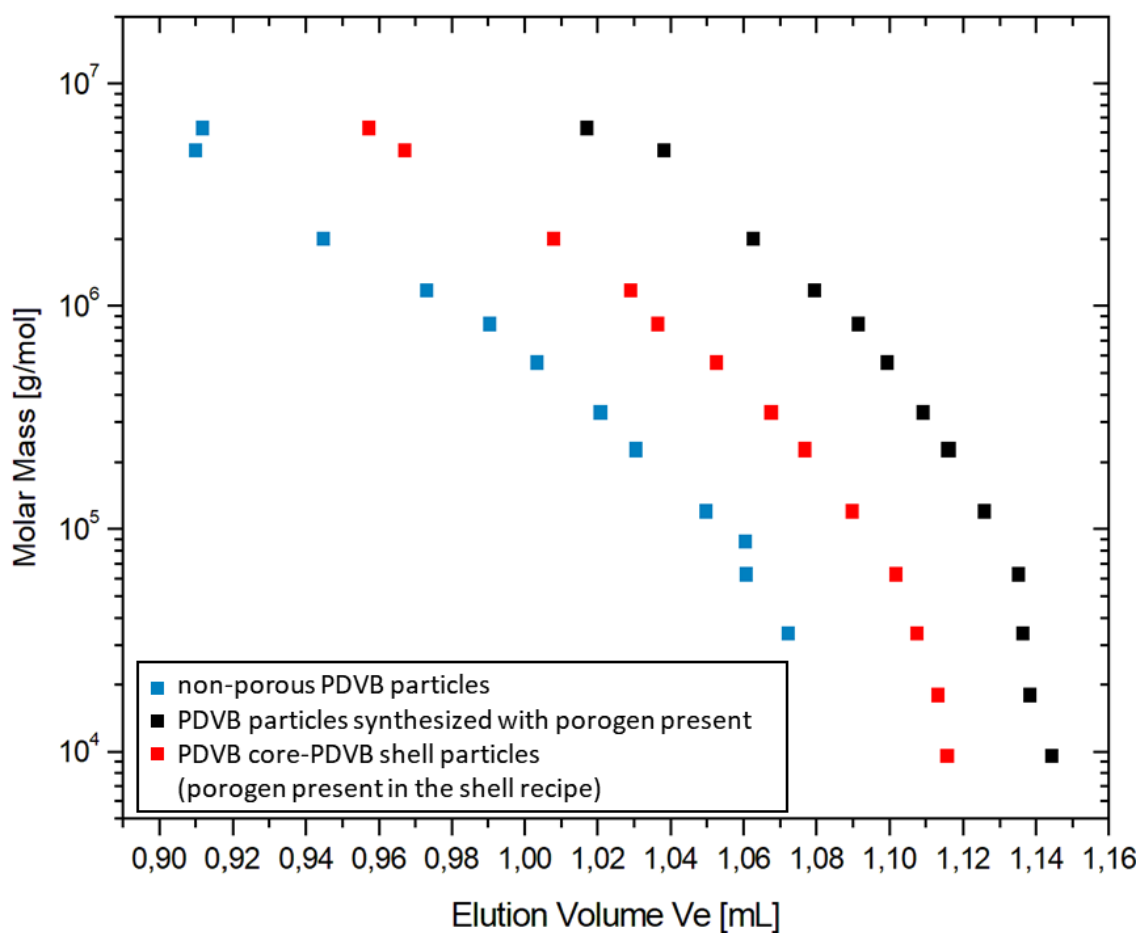


Figure S 10: Molecular mass calibration curves for SEC columns filled with non-porous PDVB particles (blue), PDVB particles synthesized with porogen present (black) and PDVB core-PDVB shell particles, with porogen present in the shell recipe (red). All curves show that there is no apparent separation within pore volumes. This diagram was kindly provided by PSS GmbH, Mainz.

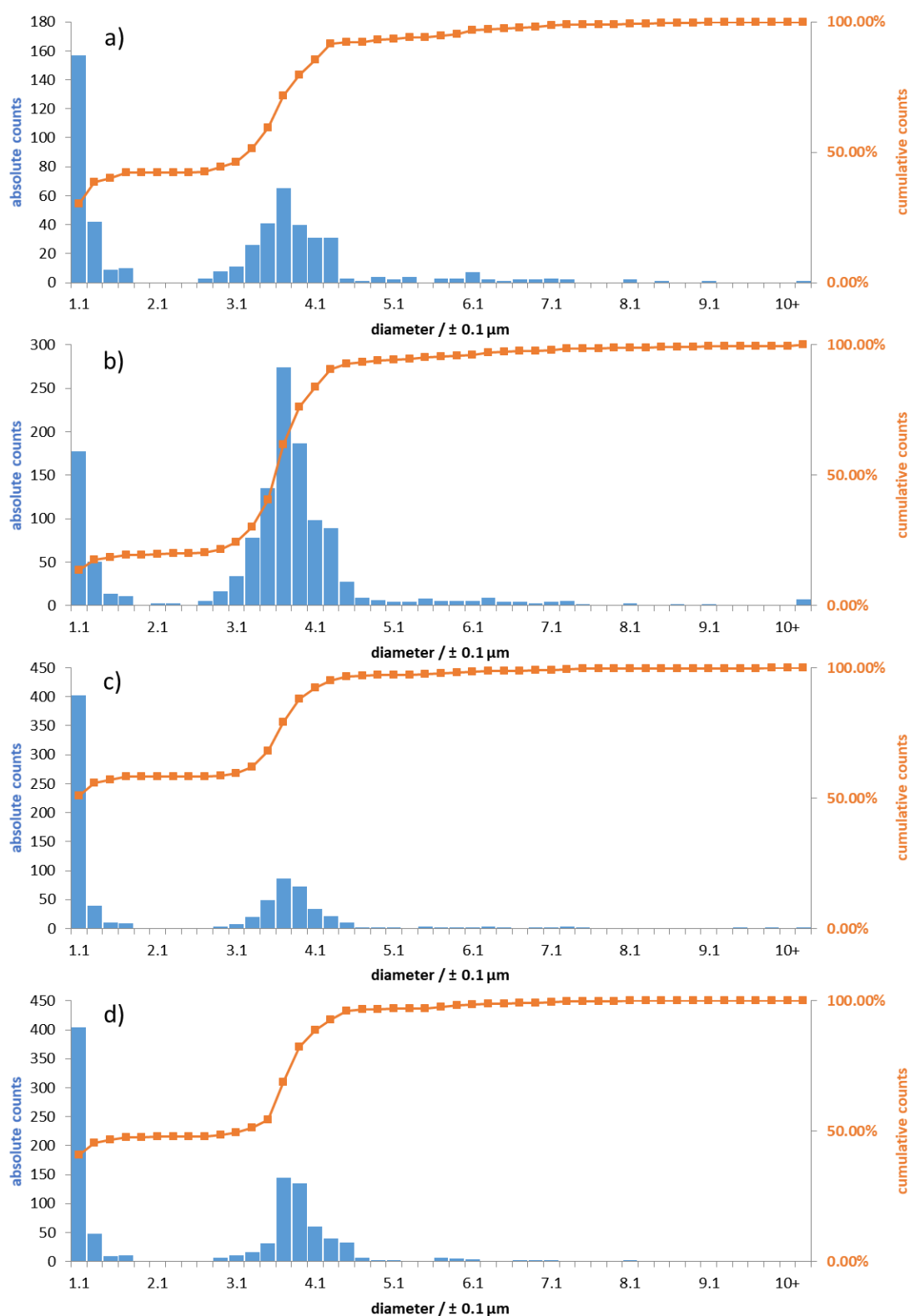


Figure S 11: Isolated particles dispersed in *i*PrOH after precipitation polymerization of styrene onto a PDVB core in different liquid media: a) PDVB core particles before polymerization, b) *i*PrOH:ACN 50:50v%, c) *i*PrOH:ACN 40:60v%, and d) *i*PrOH:ACN 20:80v%

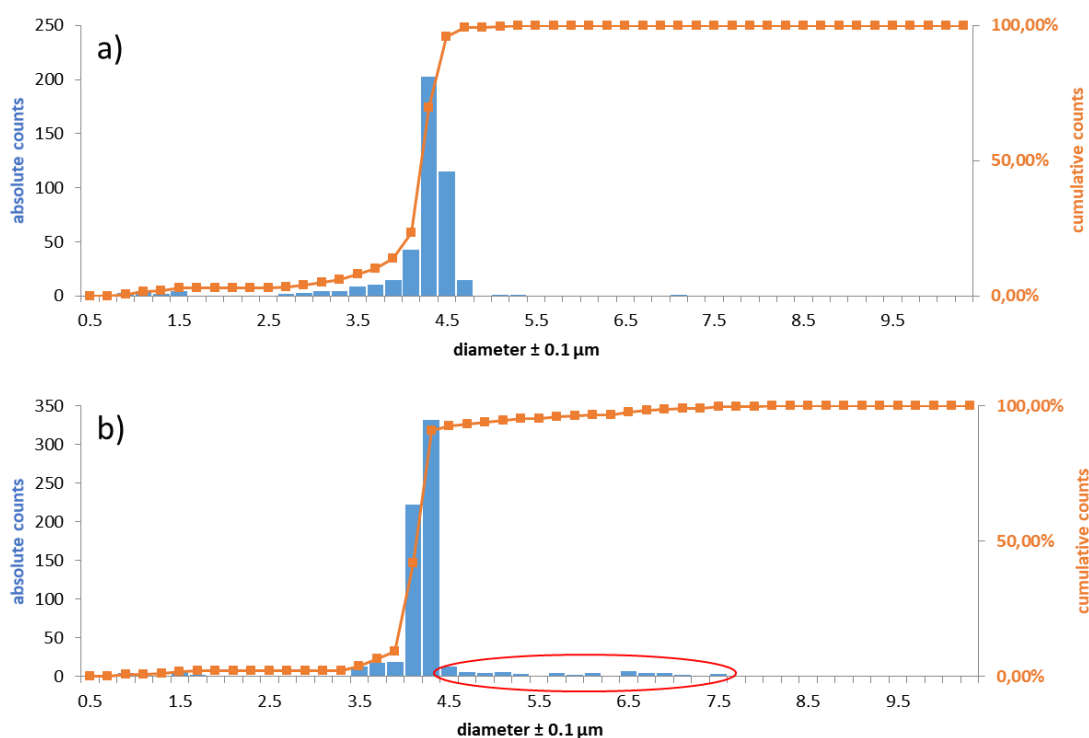


Figure S 12: PSD diagram of PDVB particle reaction mixtures after the first reaction step (core, a) and the second reaction step (core-shell, b). The red circle indicates the small number of particles that grew compared to the first reaction step.

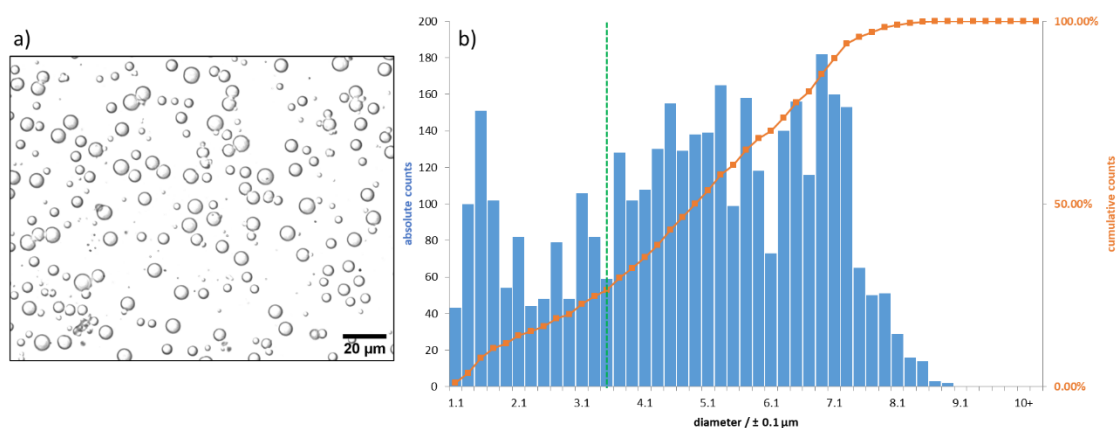


Figure S 13: Light microscope image a) and the corresponding PSD diagram of PDVB particles synthesized with 20v% toluene (with respect to total reaction volume) present in reaction mixture. For comparison, the PDVB particle sizes from the porogen free standard synthesis are indicated by the dotted green line.

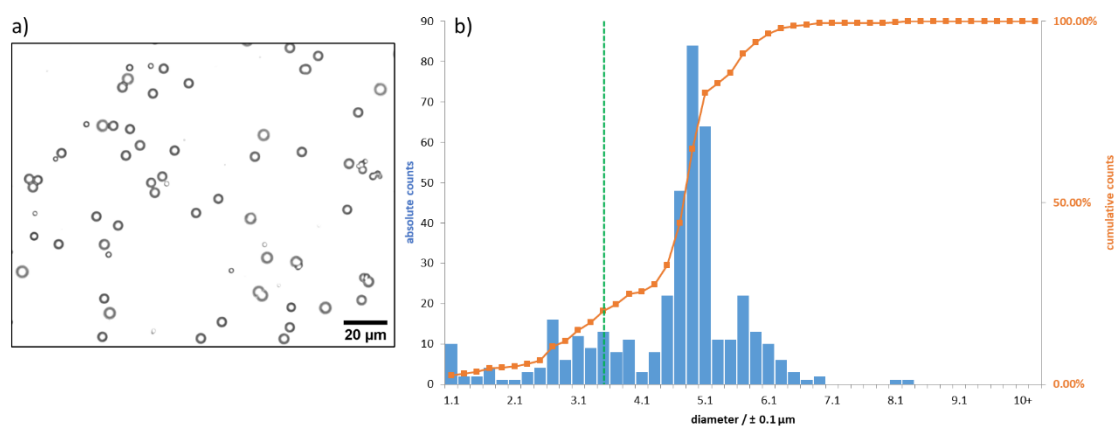


Figure S 14: Light microscope image a) and the corresponding PSD diagram of PDVB particles synthesized with 20v% THF (with respect to total reaction volume) present in reaction mixture. For comparison, the PDVB particle sizes from the porogen free standard synthesis are indicated by the dotted green line.

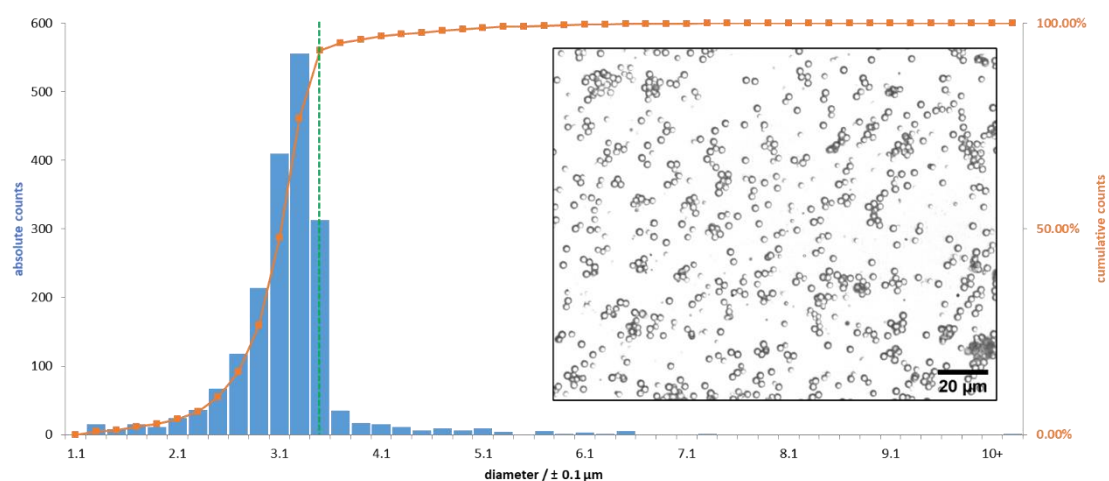


Figure S 15: PSD diagrams and light microscope images (50x magnification) of PDVB particles synthesized via precipitation polymerization in ACN with presence of 20v% toluene and 5v% water (with respect total reaction volume) in the mixture. The aggregates could be resolved during purification. For comparison, the PDVB particle sizes from the porogen free standard synthesis are indicated by the dotted green line.

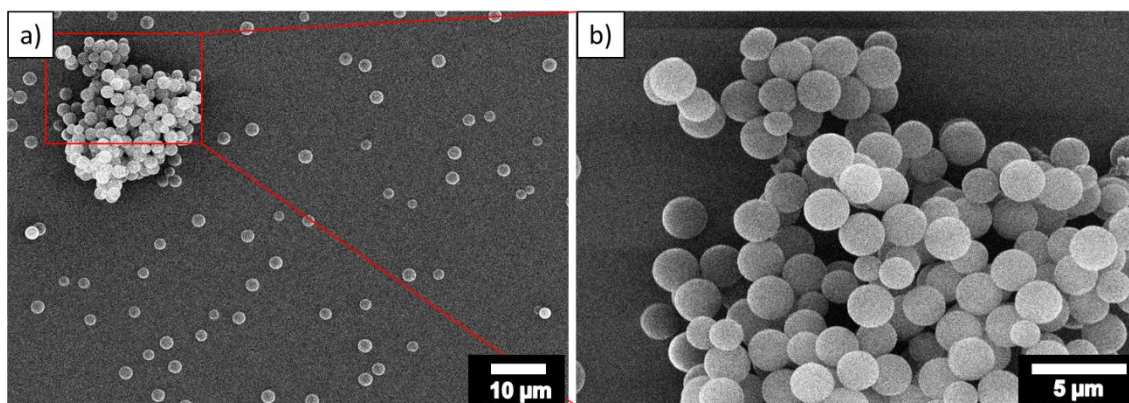


Figure S 16: SEM overview images of PDVB particles made with 20v% toluene and 5v% water in the reaction mixture. The samples were coated with a gold layer (thickness: 10 nm) and measured under a high voltage (CamScan24).

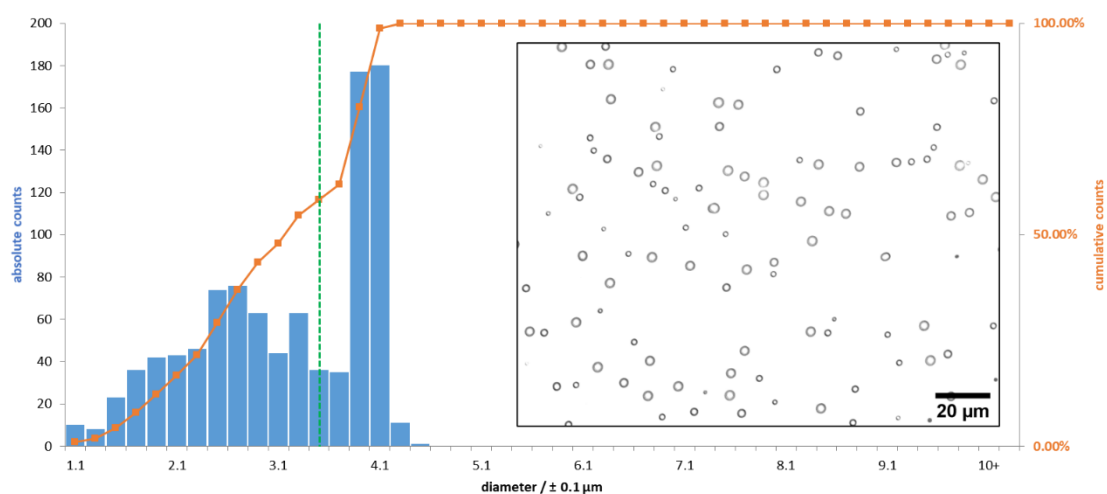


Figure S 17: Particle size distribution diagram and the corresponding light microscope image of PDVB particle reaction mixtures with 20v% dodecanol (with respect to total reaction volume) present in the reaction mixture. For comparison, the PDVB particle sizes from the porogen free standard synthesis are indicated by the dotted green line.

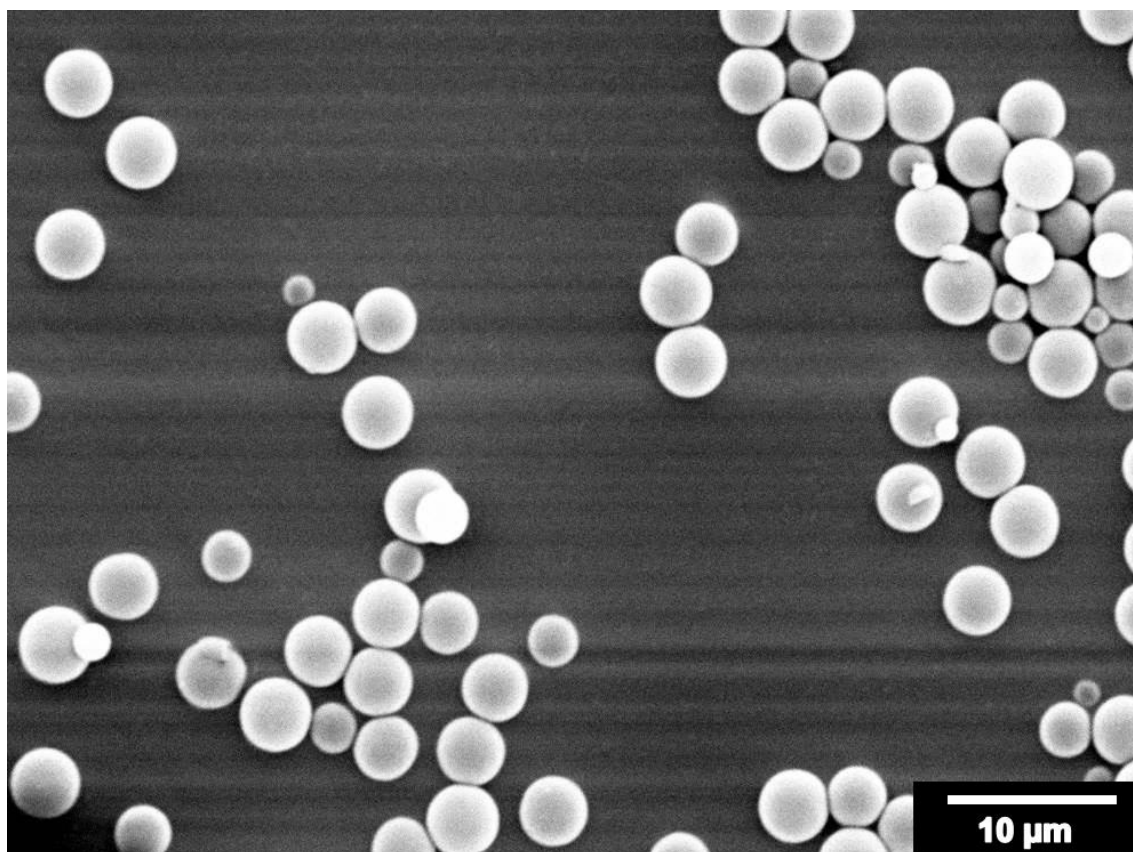


Figure S 18: SEM overview image of PDVB particles made with 20v% dodecanol being present in the reaction mixture. The samples were coated with a gold layer (thickness: 10 nm) and measured under a high voltage (CamScan24).

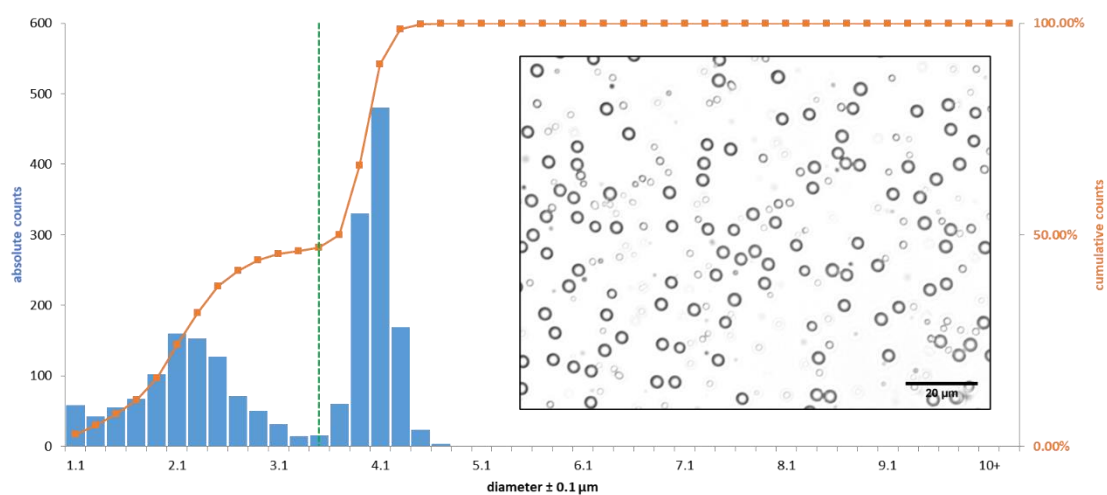


Figure S 19: Particle size distribution diagram and the corresponding light microscope image of PDVB particle reaction mixtures with 15v% toluene and 15v% dodecanol (with respect to total reaction volume) present in the reaction mixture.

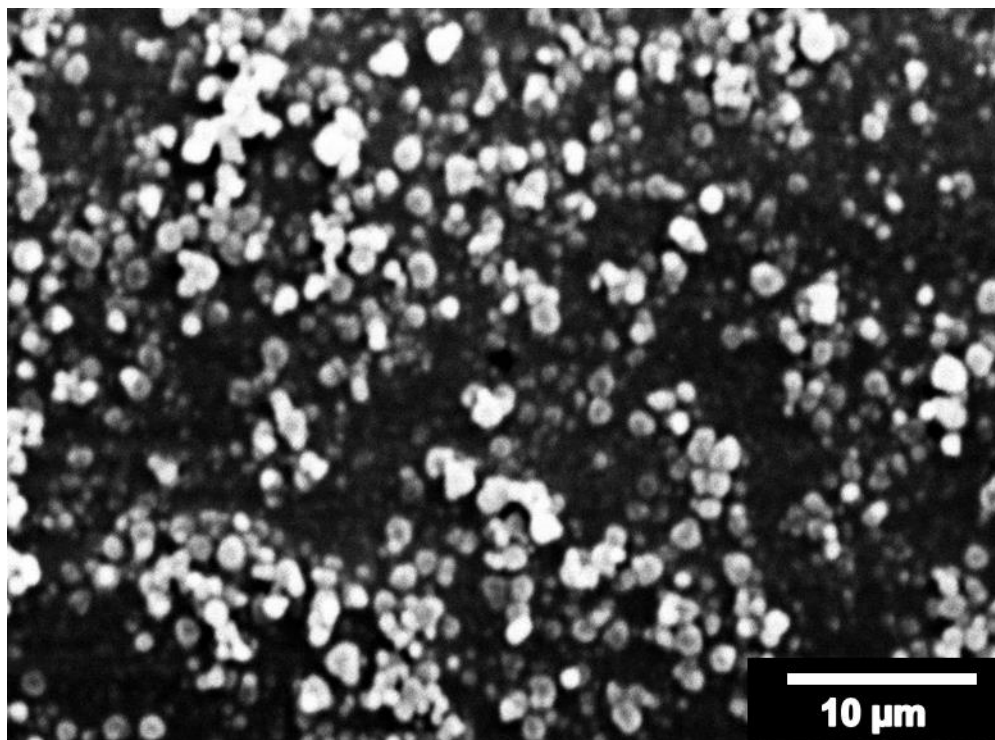


Figure S 20: SEM overview image of PDVB particles made with 20v% toluene and 20v% dodecanol being present in the reaction mixture. The samples were coated with a gold layer (thickness: 10 nm) and measured under a high voltage (CamScan24). Object sizes were too small to be measured with light microscopy.

12.2 Morphological design of PDVB-based particles

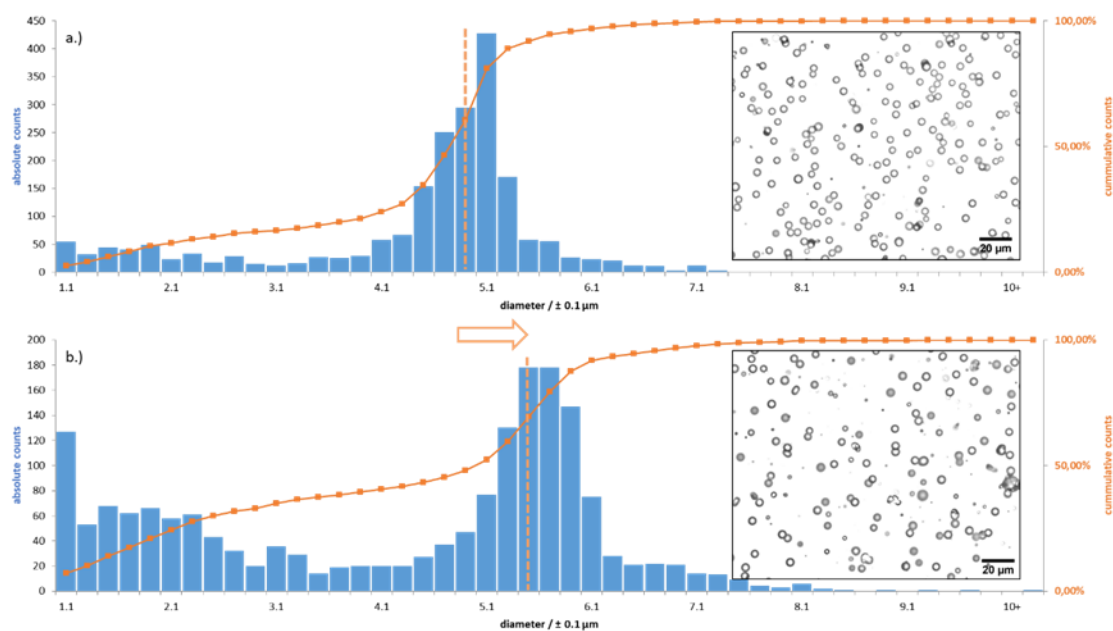


Figure S 21: PSD diagrams with corresponding light microscope images showing $t\text{PS}^{\text{nc}}$ template swelling with DVB: template particles in aqueous Methocel solution a.) before swelling with monomer and b.) after swelling and polymerization

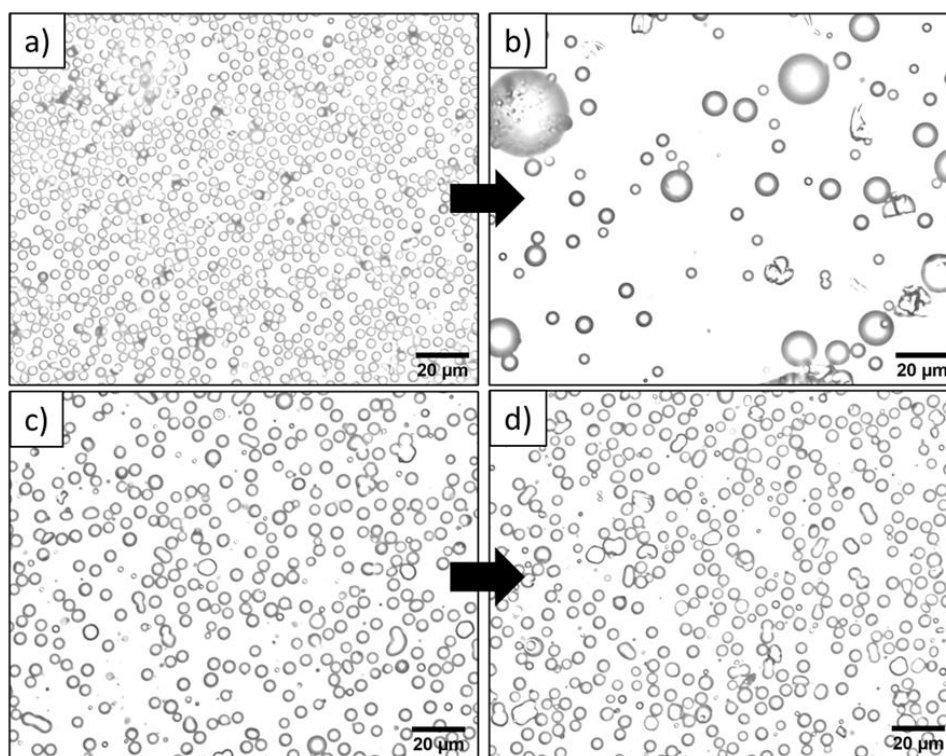


Figure S 22: Comparison between thermally initiated (a, b) and photoinitiated (c, d) polymerization of DVB-swollen $t\text{PS}^{\text{nc}}$ particles. Images were taken before (a, c) or after polymerization (b, d).

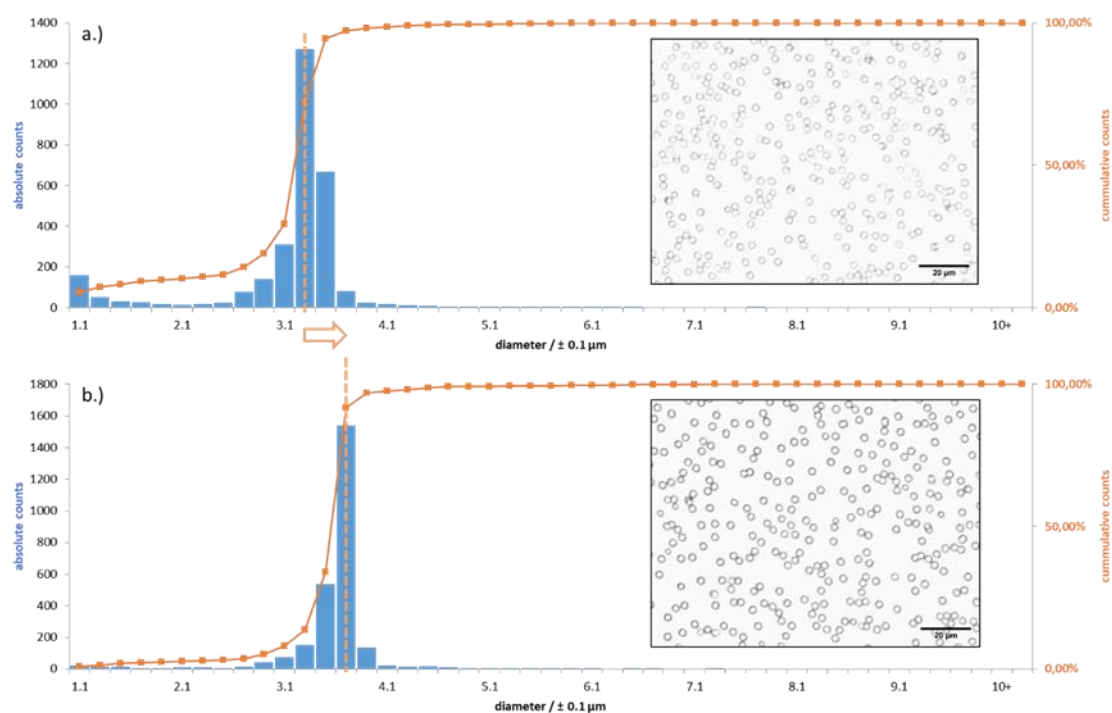


Figure S 23: PSD diagrams with corresponding light microscope images showing tPS^{xl} template swelling with DVB: template particles in aqueous Methocel solution a.) before swelling with monomer and b.) after swelling and polymerization

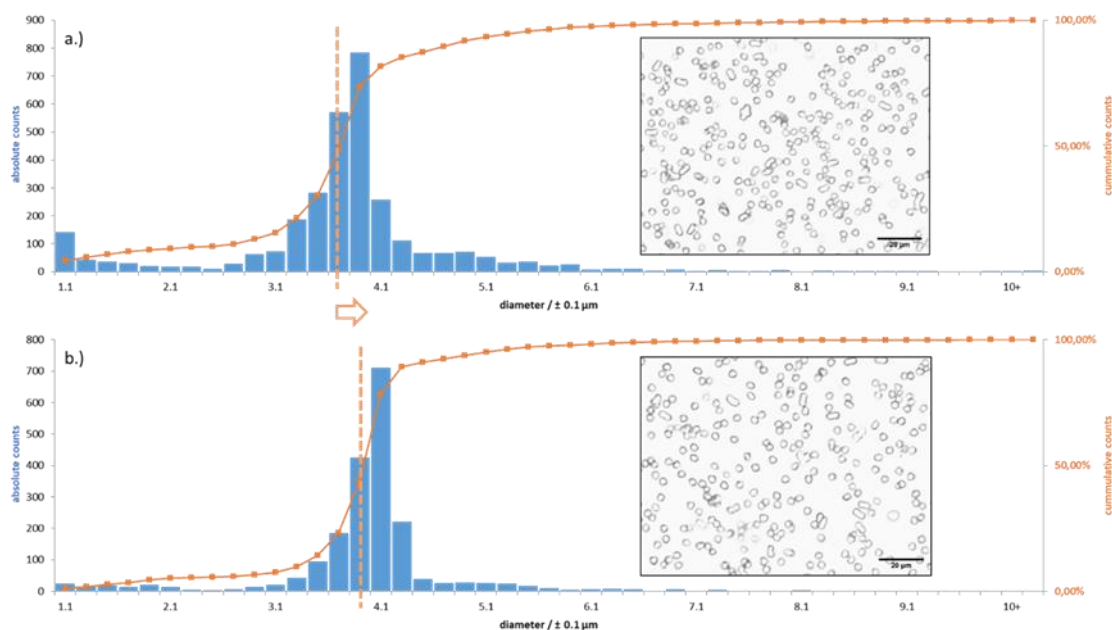


Figure S 24: PSD diagrams with corresponding light microscope images showing tPS^{xl+nc} template swelling with DVB: particles in aqueous Methocel solution a.) before swelling with monomer and b.) after swelling and polymerization.

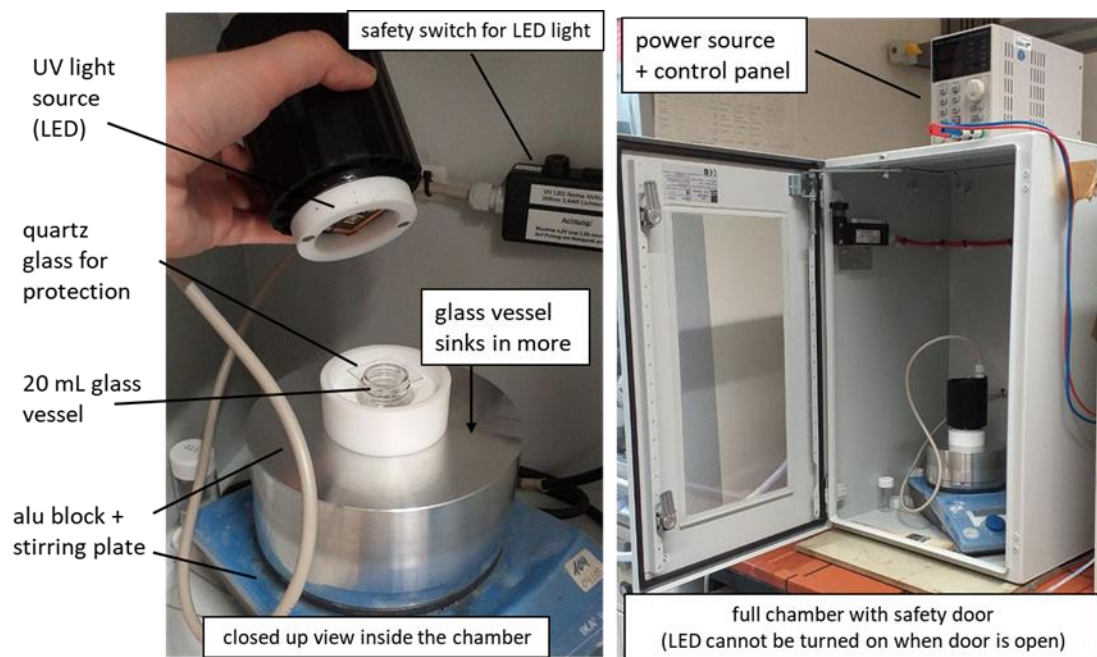


Figure S 25: Overview of the photo initiation chamber setup used for DVB polymerization following template particle swelling. Key components and safety features are highlighted in the images.

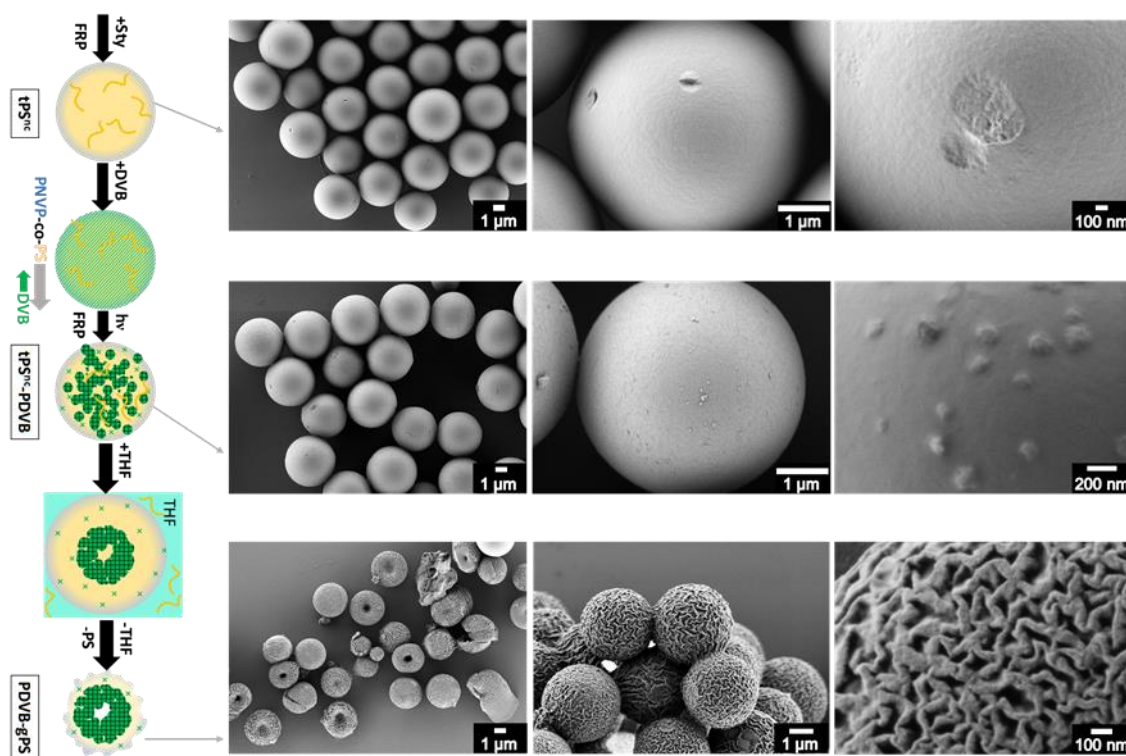


Figure S 26: SEM images of particles at various stages of the swelling process leading to PDVB-gPS formation. Grey arrows on the left mark the corresponding reaction stage shown in each row.

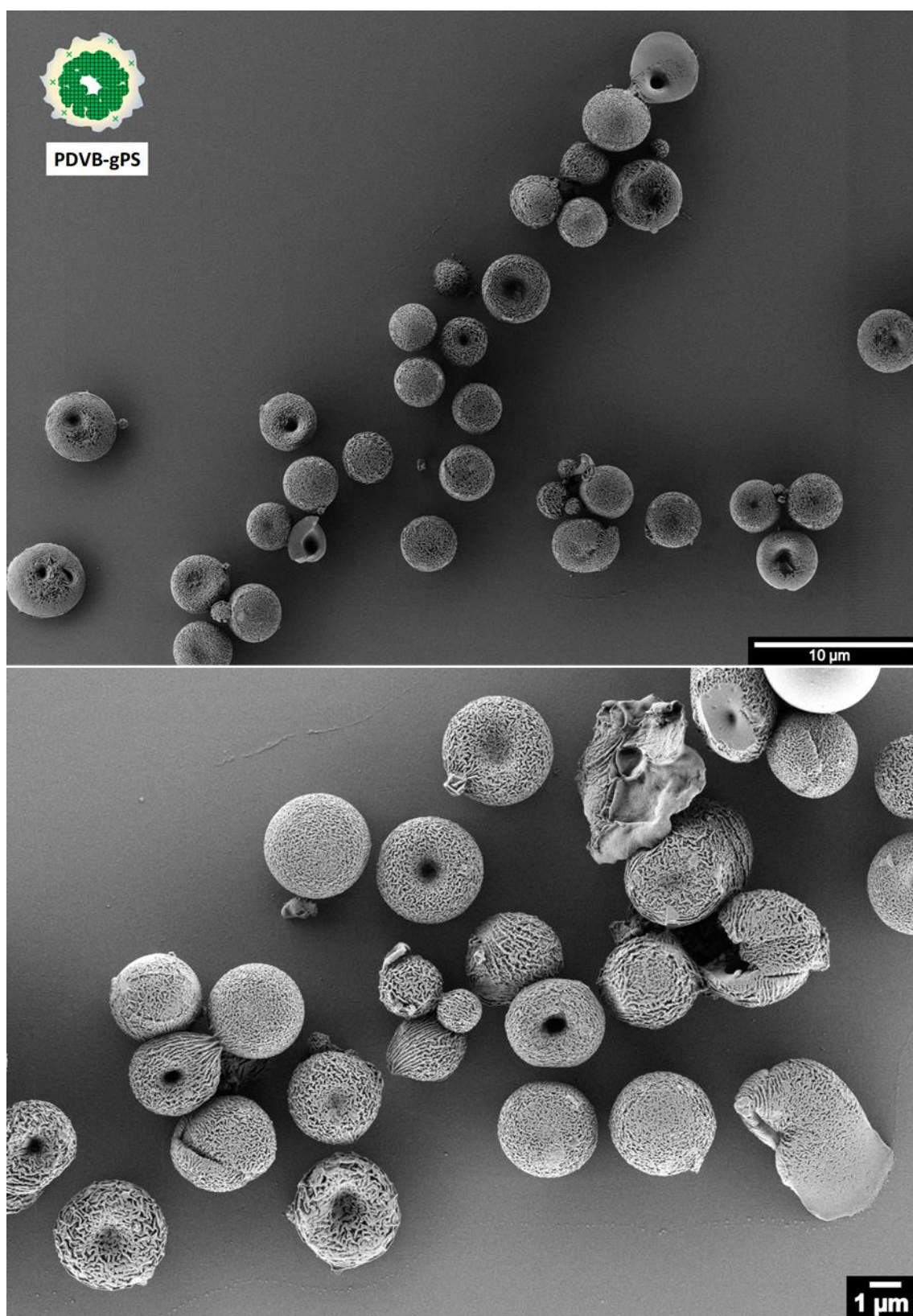


Figure S 27: Overview SEM images of PDVB-gPS particles displaying intact spheres alongside indented and fractured shells.

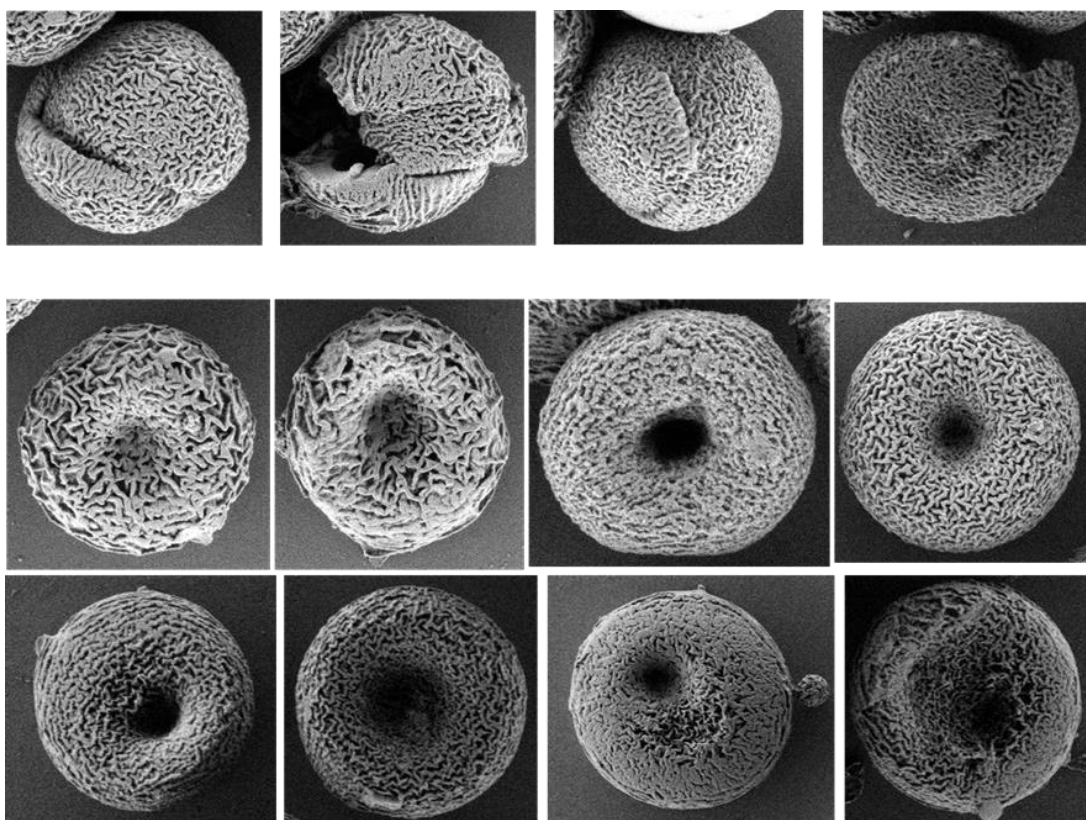


Figure S 28: SEM image gallery of individual PDVB-gPS particles. Top row: fragmented shells, appearing in approximately 5–10% of all particles. Middle and bottom rows: indented particles, representing about 30–40% of the total particle population. Particle diameters range from 3 to 4 μm .

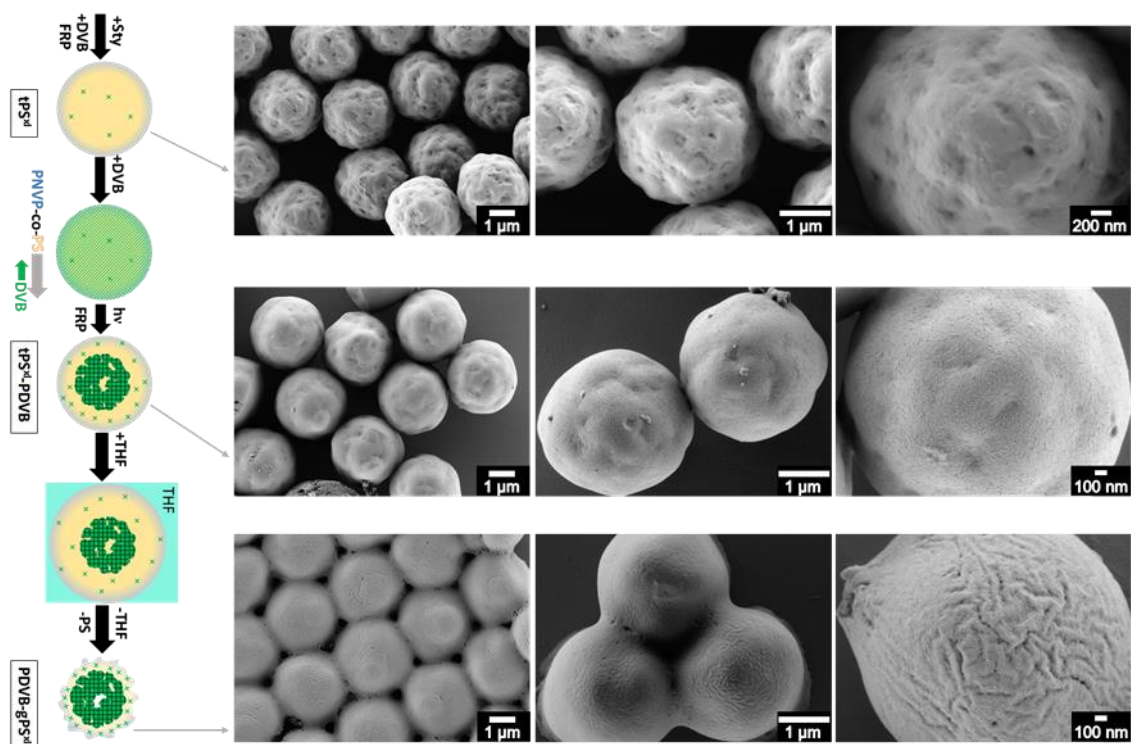


Figure S 29: SEM images of particles at various stages of the swelling process leading to PDVB-gPS^{xl} formation. Grey arrows on the left mark the corresponding reaction stage shown in each row.

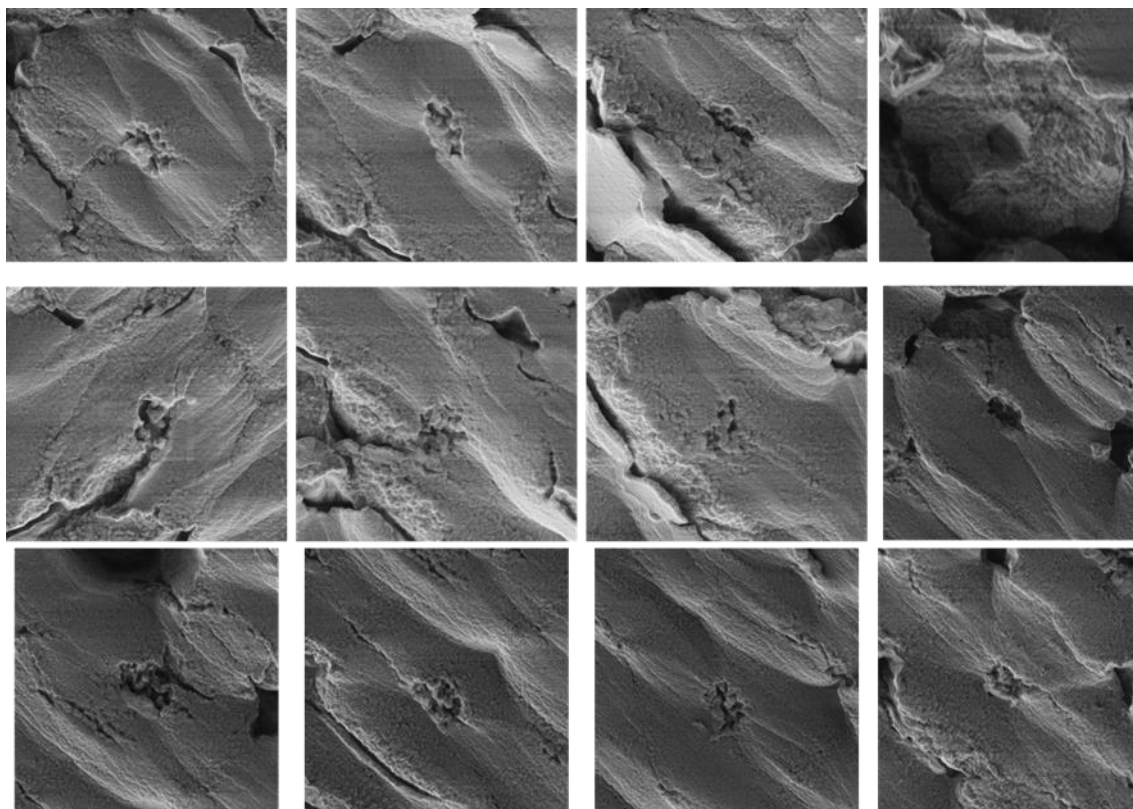


Figure S 30: SEM image gallery of individual PDVB-gPS^{xl} cross-sections. The particle diameters range from 3 to 4 μm.

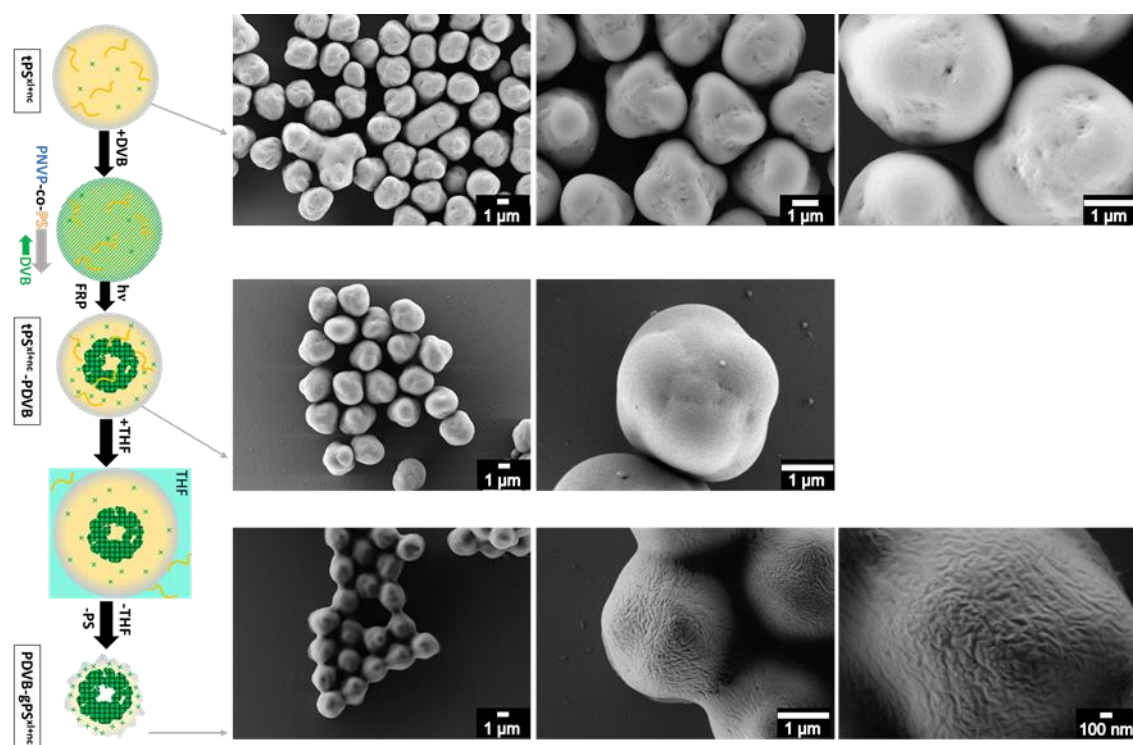


Figure S 31: SEM images of particles at various stages of the swelling process leading to PDVB-gPS^{xl+nc} formation. Grey arrows on the left mark the corresponding reaction stage shown in each row.

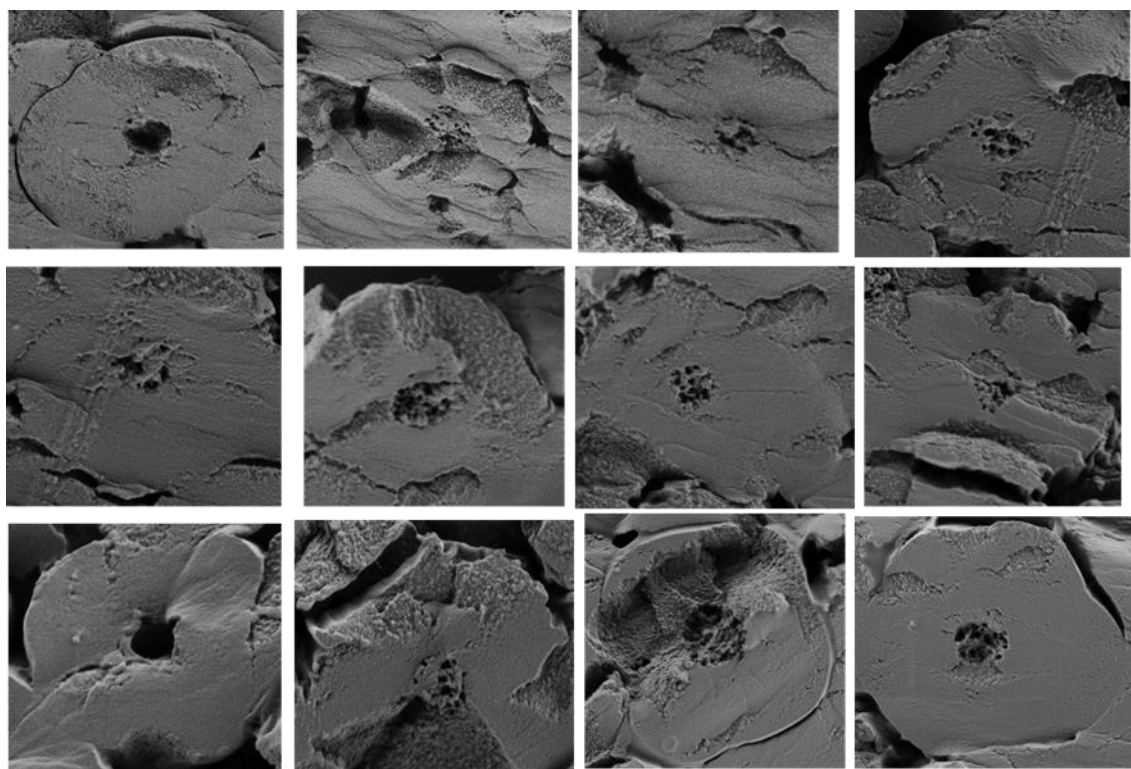


Figure S 32: SEM image gallery of individual PDVB-gPS^{xl+nc} cross-sections. The particle diameters range from 3 to 4 μm.

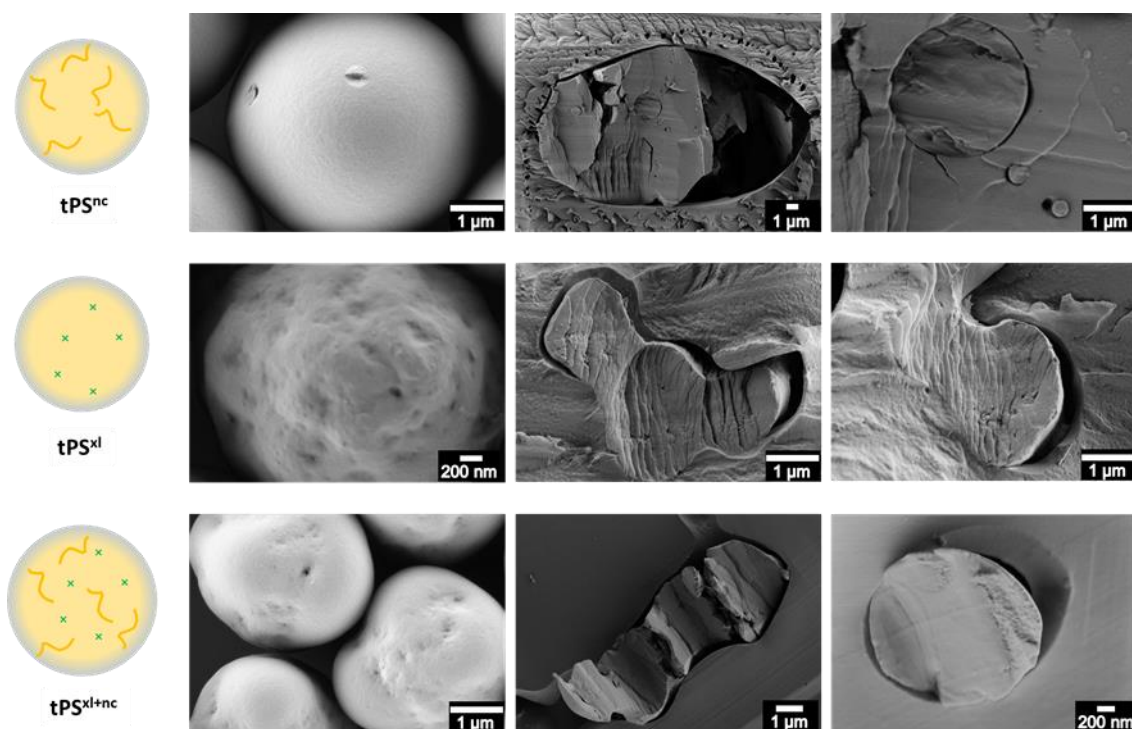


Figure S 33: SEM images of intact and cross-sectioned template particles before swelling: comparison of tPS^{nc} (top row), tPS^{xl} (middle row), and tPS^{xl+nc} (bottom row)

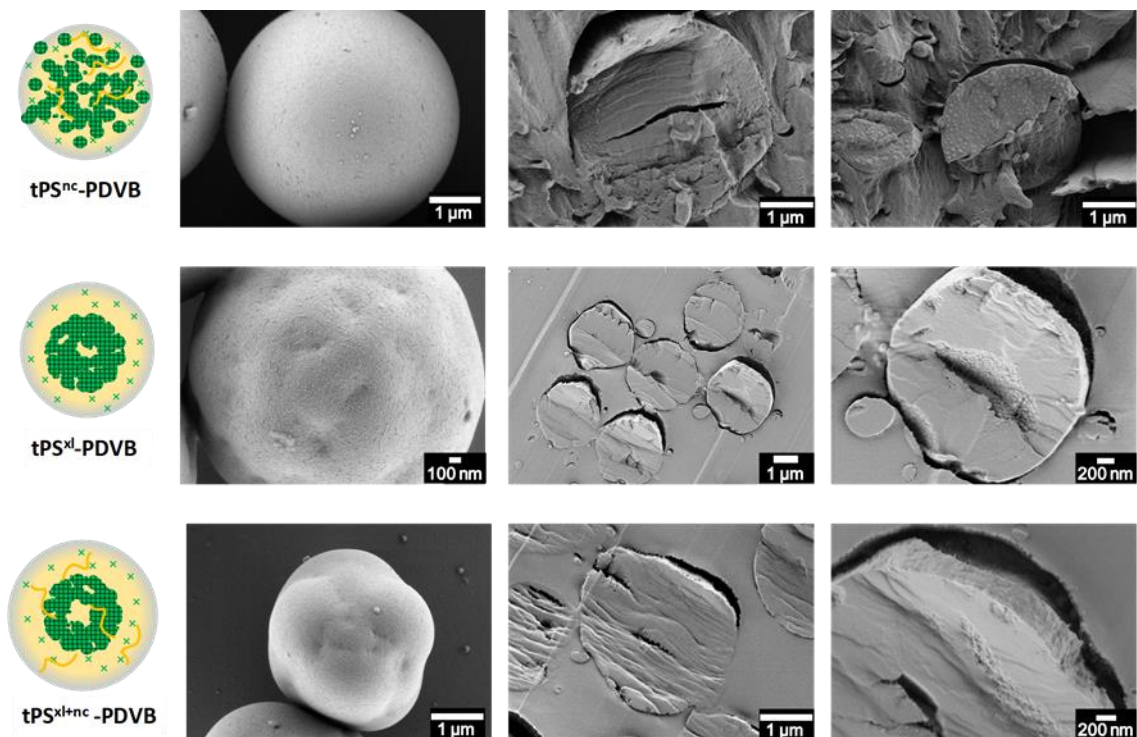


Figure S 34: SEM images of intact and cross-sectioned particles after DVB swelling and subsequent polymerization: comparison of tPS -PDVB (top row), tPS^{xl} -PDVB (middle row), and tPS^{xl+nc} -PDVB (bottom row)

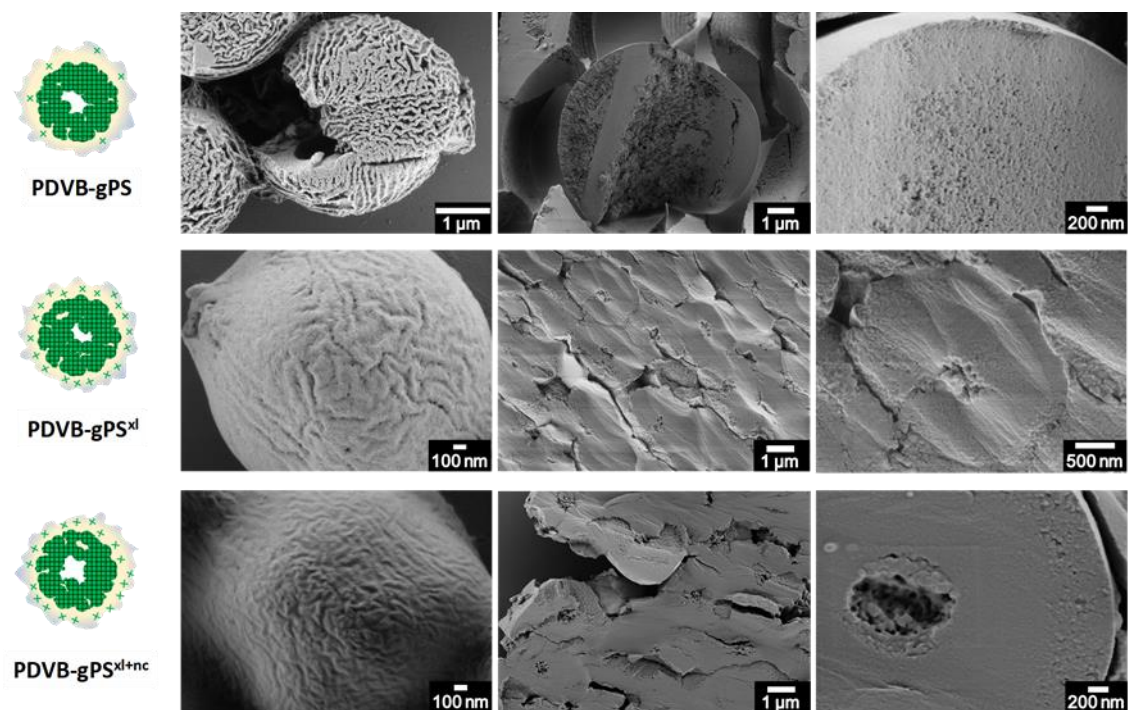


Figure S 35: SEM images of intact and cross-sectioned product particles after PS template removal with THF: PDVB-gPS (top row), PDVB-gPS^{xl} (middle row), and PDVB-gPS^{xl+nc} (bottom row)

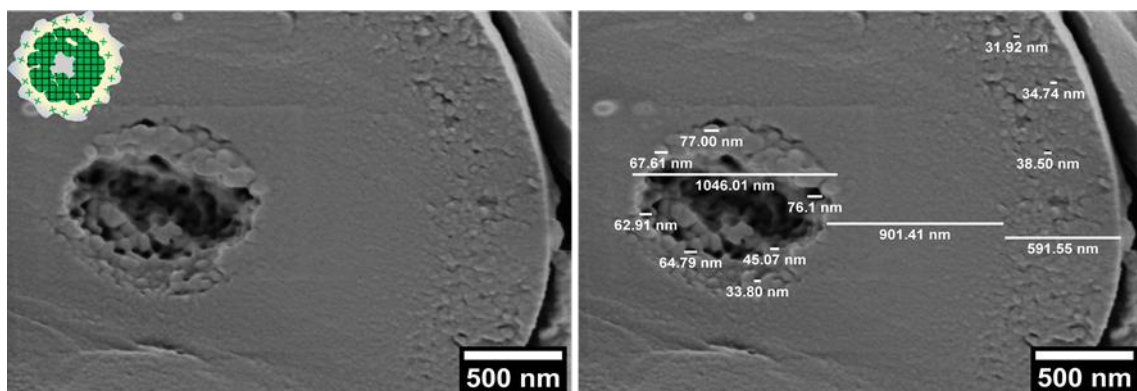


Figure S 36: SEM cross-section image of PDVB-gPS^{xl+nc} particles with scaling indicating layer thicknesses, granule sizes, and pore dimensions.

12.3 Studies of Template Swelling Methods to Prepare PDVB Non-Porous Core - Porous Shell Particles

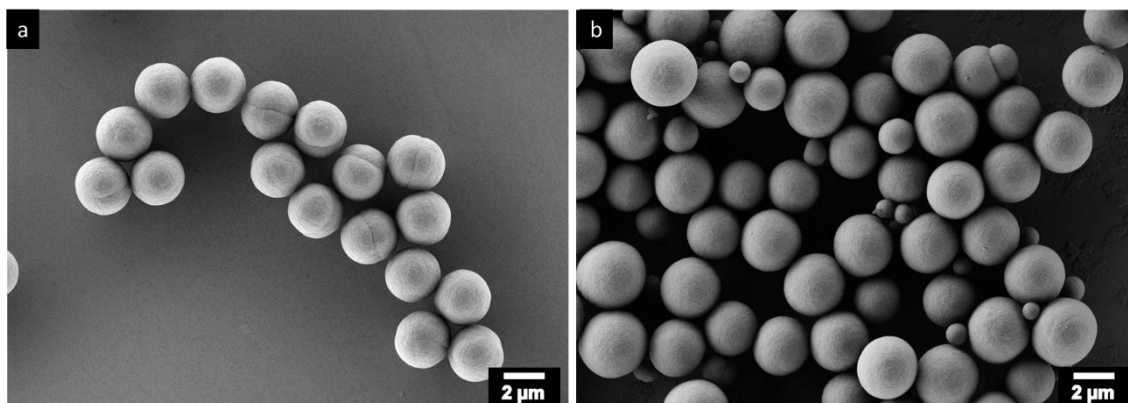


Figure S 37: SEM overview images of PDVB core (a) and PDVB core – P(DVB₂₅-co-Sty₇₅) shell particles (b). The measurements were conducted without sputtering the samples and under low voltage (Leo Gemini 1530).

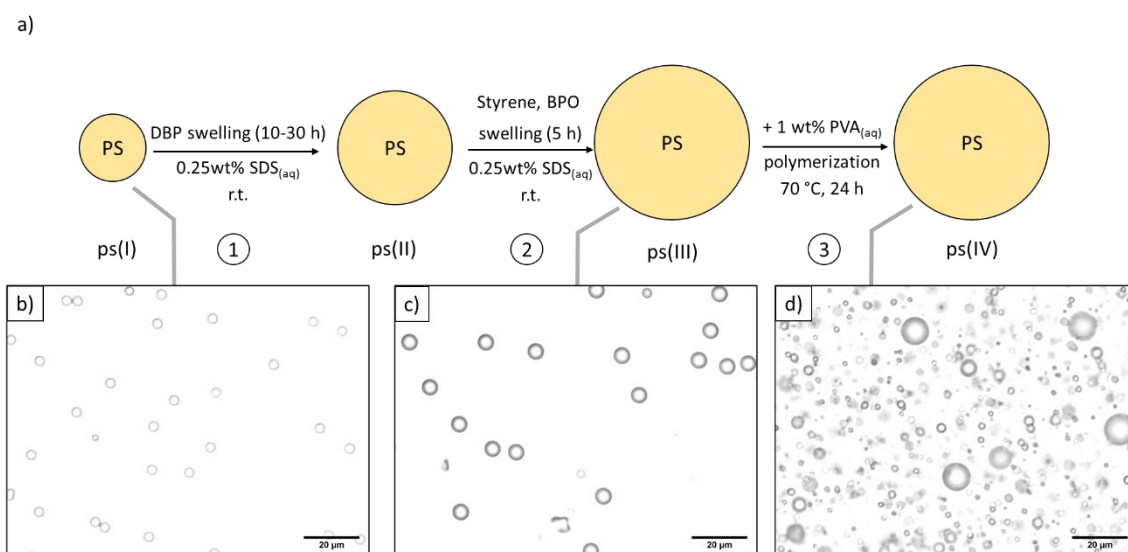


Figure S 38: Schematic depiction of reaction procedure to produce large PS template particles from smaller monodisperse PS particles (a) and light microscopy images of b) PS particles by precipitation polymerization (ps(I)), c) template particles swollen styrene, DBP and initiator (ps(III)), and d) PS particles after polymerization (ps(IV)). During polymerization, the monodispersity of the particles is lost due to particle coalescence. These particles were synthesized here according to a procedure from literature.⁵⁹

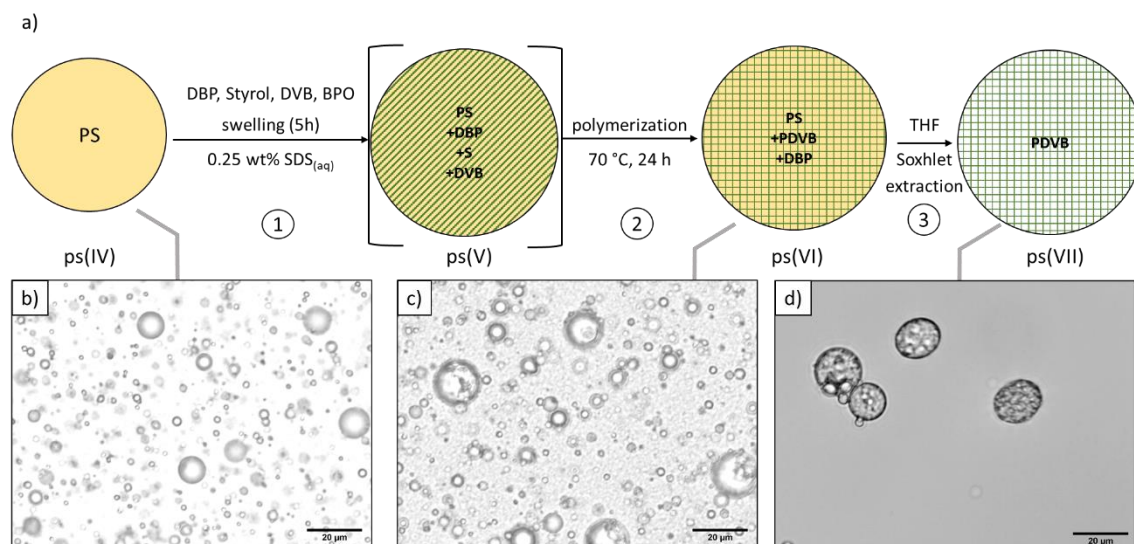


Figure S 39: Schematic depiction of reaction procedure to produce porous PDVB particles (ps(VII), a)) and light microscopy images of b) enlarged PS template particles (ps(IV)), c) template particles with a semi-penetrating network of PDVB (ps(VI)), and d) fully crosslinked PDVB particles with varying porosities after extraction of the PS template (ps(VII)). These particles were synthesized here according to a procedure from literature.⁵⁹

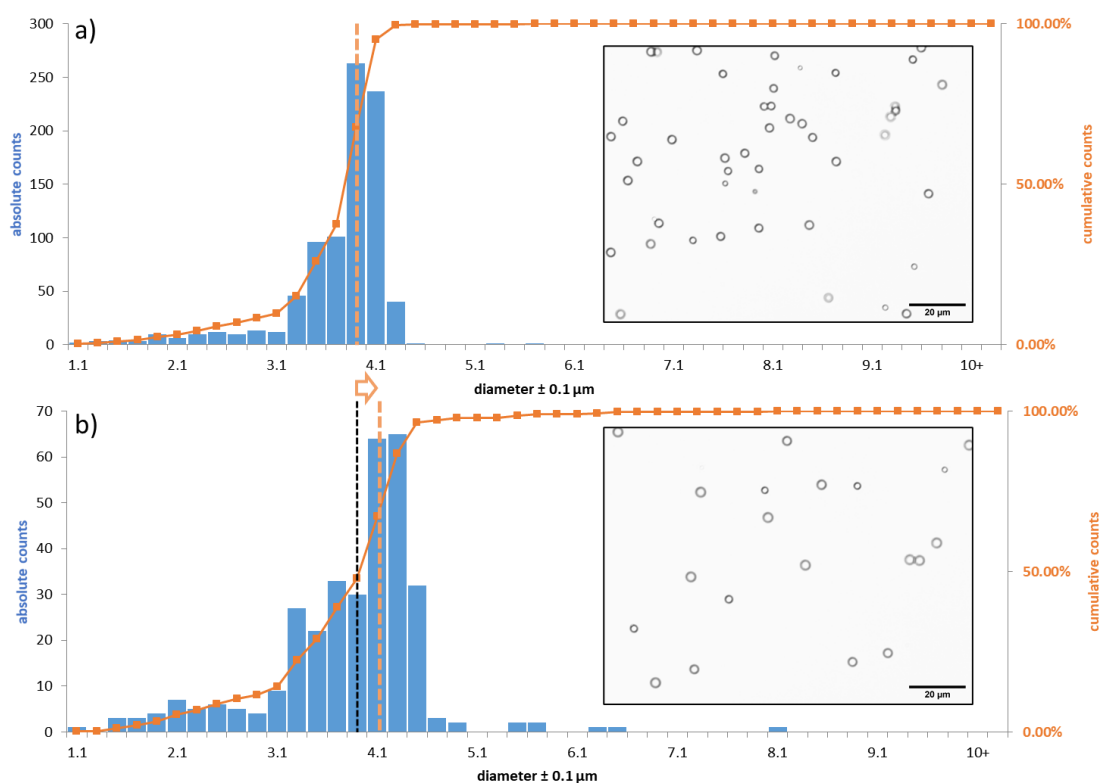


Figure S 40: PSD diagrams and the corresponding LM images of a) the precursor particles (p(III)) and b) the resulting particles after the styrene swelling and polymerization step (A.) of the template swelling method (p(IV)). In both cases the particles were purified and dispersed in an aqueous SDS solution.

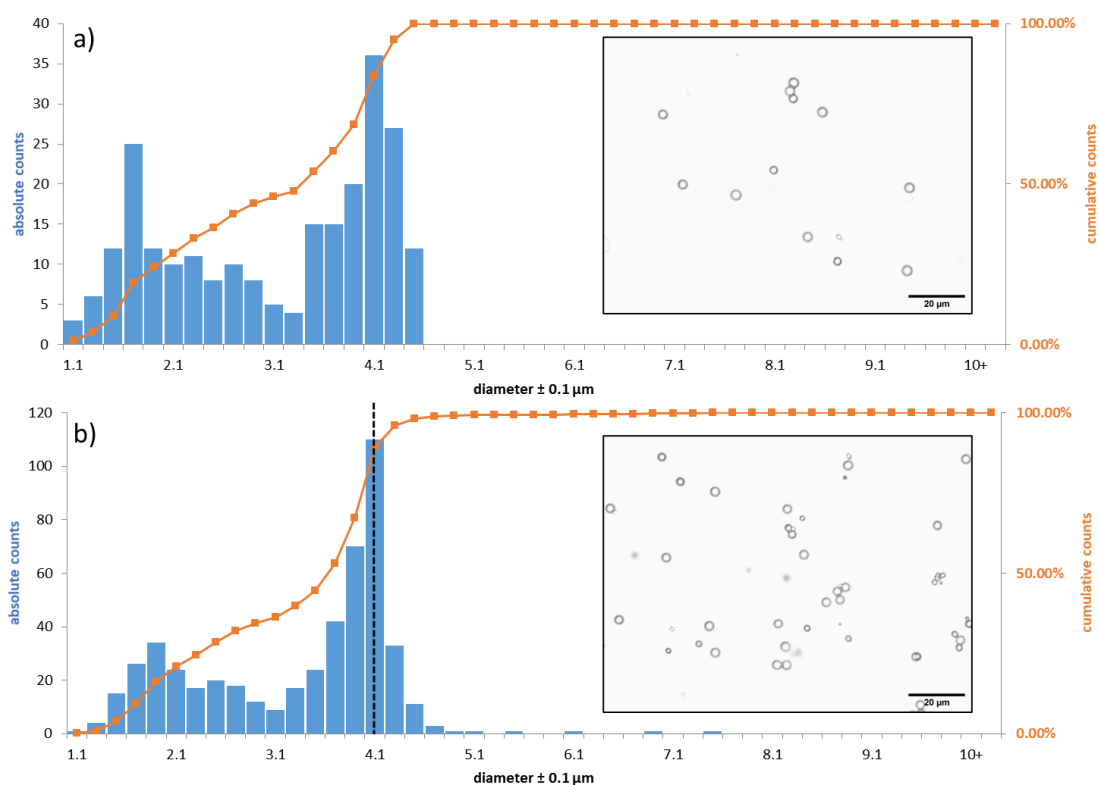


Figure S 41: PSD diagrams and the corresponding LM images of a) the particles containing template PS (p(IV)) from step A.) and b) the resulting particles after the DVB swelling and polymerization (p(VI)) from step (B.) of the template swelling method. In both cases the particles were purified and dispersed in an aqueous SDS solution. The template was not yet removed with THF in b).

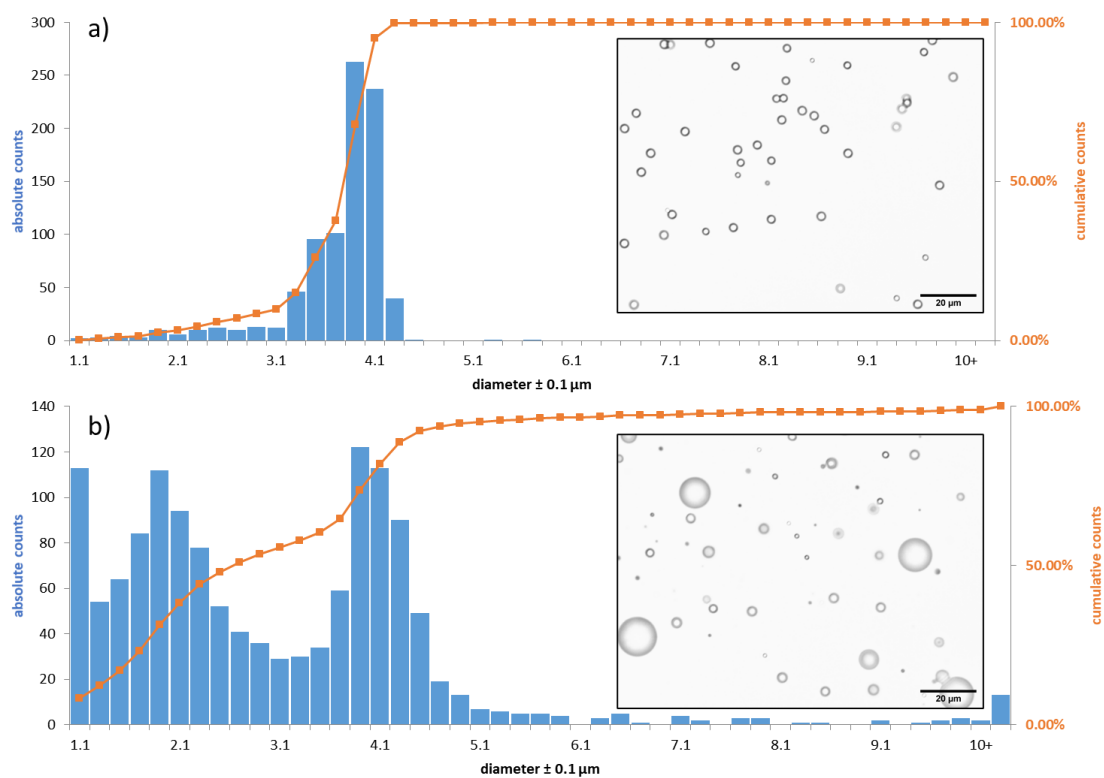


Figure S 42: PSD diagrams and the corresponding LM images of a) the precursor particles dispersed in an aqueous SDS solution and b) the particles after the first swelling step with styrene, DBP and an initiator before polymerization. Particles and organic droplets cannot be distinguished.

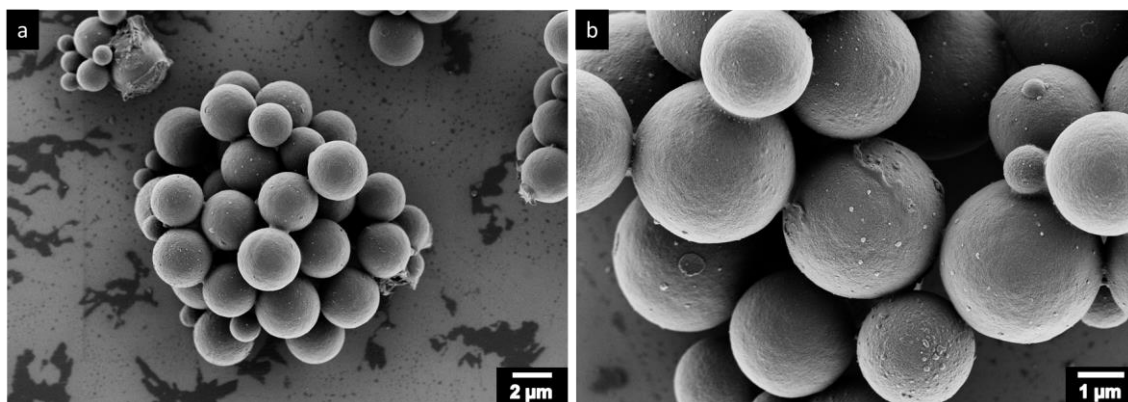


Figure S 43: SEM overview images of templated PDVB particles p(IV) obtained after the styrene swelling process A). The measurements were conducted without sputtering the samples and under low voltage (Leo Gemini 1530).

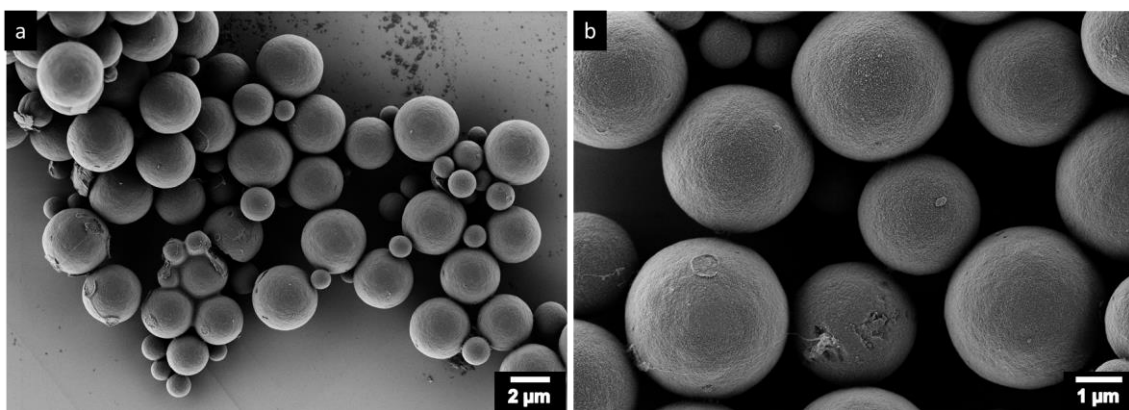


Figure S 44 SEM overview images of PDVB particles p(VI) obtained after the DVB swelling process B) before the template was removed. The measurements were conducted without sputtering the samples and under low voltage (Leo Gemini 1530).

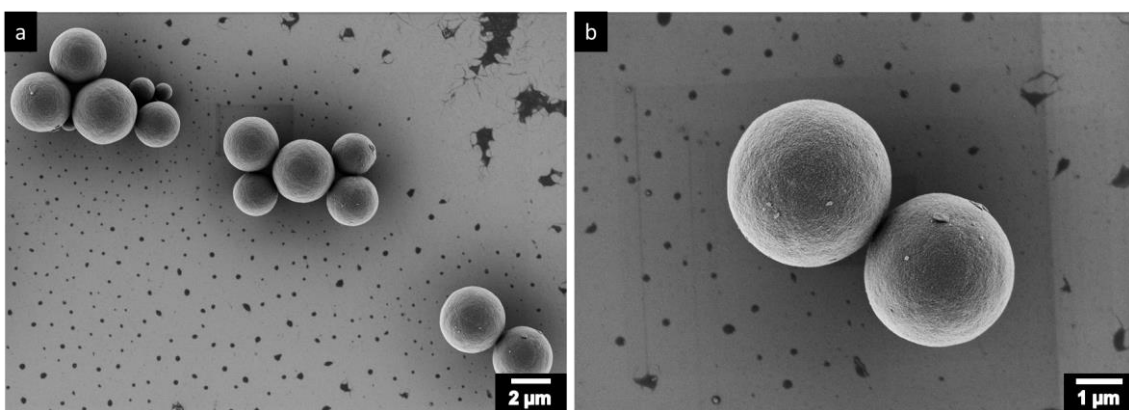


Figure S 45 SEM overview images of PDVB particles obtained after the DVB swelling process B) after the template was removed p(VII). The measurements were conducted without sputtering the samples and under low voltage (Leo Gemini 1530).