
Microgel-Polymer Composite Fibres

VON DER FAKULTÄT FÜR MATHEMATIK, INFORMATIK UND NATURWISSENSCHAFTEN
DER RWTH AACHEN UNIVERSITY
ZUR ERLANGUNG DES AKADEMISCHEN GRADES EINES DOKTORS DER
NATURWISSENSCHAFTEN GENEHMIGTE DISSERTATION

VORGELEGT VON

M.SC. DOMINIC KEHREN

AUS

NEUSS, NRW, DEUTSCHLAND

BERICHTER:

UNIVERSITÄTSPROFESSOR DR. ANDRIJ PICH
UNIVERSITÄTSPROFESSOR DR. JOACHIM MAYER

TAG DER MÜNDLICHEN PRÜFUNG: 03.09.2014

DIESE DISSERTATION IST AUF DEN INTERNETSEITEN DER HOCHSCHULBIBLIOTHEK
ONLINE VERFÜGBAR.

Contents

List of Figures	V
List of Tables	VIII
List of Abbreviations	VIII
Introduction	1
General Theoretical Introduction	5
1 Microgels	6
1.1 Synthesis Methods	8
2 Electrospinning/Nanofibres	12
2.1 Nano- and Microfibres	12
2.2 Electrospinning	13
2.3 Nanofibres/Electrospinning with Microgels	18
PVA - Nanofibres	20
1 Introduction	21
2 Experimental Part	23
2.1 Materials	23
2.2 Microgel Synthesis	23
2.3 Preparation of Spinning Solutions	24
2.4 Fibre Fabrication	24
2.5 Fibre Crosslinking	25
2.5.1 Physical Crosslinking	25
2.5.2 Chemical Crosslinking	25
2.6 Characterisation Methods	26
2.6.1 Dynamic Light Scattering (DLS)	26
2.6.2 Atomic Force Microscopy (AFM)	26
2.6.3 Field Emission Scanning Electron Microscopy (FESEM)	26
2.6.4 Rheology	26
2.6.5 Thermo Gravimetric Analysis (TGA)	27
2.6.6 Differential Scanning Calorimetry (DSC)	27
2.6.7 Water Adsorption/Desorption	27

Contents

2.6.8	Raman Spectroscopy	28
2.6.9	Infrared Spectroscopy (IR)	28
2.6.10	Toxicity Tests	28
3	HEA Modified Microgels	29
4	Fibre Fabrication	32
4.1	Viscosity of the Spinning Solutions	32
4.2	Fibre Formation	33
4.3	Influence of the Process Parameters on the Fibre Formation	37
5	Fibre Crosslinking	39
5.1	Physical Crosslinking	39
5.2	Chemical Crosslinking	41
6	Fibre Characterisation	44
7	Summary/Conclusions	50
	 Polycaprolactone - Microfibres	 51
1	Introduction	52
2	Experimental Part	54
2.1	Materials	54
2.2	Microgel Synthesis	54
2.3	Preparation of Spinning Solutions	54
2.4	Degradation of the Fibres	56
2.5	Characterisation Methods	56
2.5.1	Contact Angle Measurements	56
2.5.2	Sedimentation Analysis	56
2.5.3	X-Ray Diffraction	57
3	Investigation of Microgels and Spinning Solutions	58
3.1	Microgel Behaviour in Different Solvent Systems	58
3.2	Preparation and Analysis of the Spinning Solutions	61
4	Fibre Fabrication	68
4.1	Fibres Spun from Methanol/Toluene	68
4.2	Fibres Spun from Chloroform/DMF	70
5	Fibre Characterisation	72

5.0.1	Fibre Properties	72
5.0.2	XRD studies of PCL-microgel fibres	79
5.0.3	Degradation	82
6	Summary/Conclusions	86
 Degradable Microgels with Hydrophobic Pockets		87
1	Introduction	88
2	Experimental Part	90
2.1	Materials	90
2.2	Synthesis of xPCL Crosslinker	90
2.3	Synthesis of Microgels	91
2.4	Degradation of Microgel Particles	93
2.5	Immobilisation of Hydrophobic Dye: Nile Red	93
2.6	Immobilisation and Release of (RS)-2-(4-(2-methylpropyl)phenyl)propanoic acid (Ibuprofen)	93
2.7	Characterisation Methods	93
2.7.1	Ultraviolet-Visible Spectroscopy (UV/Vis)	94
2.7.2	Nuclear Magnetic Resonance Spectroscopy (NMR)	94
3	Synthesis Process: Miniemulsion?	95
4	Incorporation of xPCL Crosslinker into Microgels	98
5	Microgel Analysis	101
5.1	Microgel Degradation	105
5.2	Immobilisation of Hydrophobic Substances	109
6	Outlook: xPCL-microgels in fibres	113
7	Summary/Conclusions	115
 Poly lactide - Microfibres		116
1	Introduction	117
2	Experimental Part	118
2.1	Materials	118
2.1.1	VIm-Microgel Synthesis	118

Contents

2.2	Preparation of Spinning Solutions	119
2.3	PLA-Fibre Degradation	120
2.4	Characterisation Methods	120
2.4.1	Potentiometric Titration	120
3	VIm-Microgel Characterisation	121
4	Fibre Fabrication	123
5	Fibre Characterisation	125
5.1	Fibre Degradation	129
6	Summary/Conclusion	131
Introductory Studies/Outlook		132
1	Introduction	133
2	Experimental Part	134
2.1	Materials	134
2.2	Particle Synthesis	134
2.2.1	Phosphazene Microspheres	135
2.2.2	Iron(III) oxide Nanoparticles	135
2.3	Preparation of Spinning Solutions	136
2.3.1	Preparation of Hollow Fibre Membranes	137
2.4	Characterisation Methods	139
3	Composite Microfibre Variations	140
3.1	Introduction	140
3.2	PCL-Fibres with Iron Oxide Nanoparticles	140
3.3	PCL-fibres with Phosphazene Microspheres	143
3.4	Summary/Conclusion	145
4	Microgels as Additives for Hollow Fibre Membranes	146
4.1	Introduction	146
4.2	Fabrication and Characterisation	146
4.3	Summary/Conclusion	151
Summary and Conclusion		152
Bibliography		155

List of Figures

1	Scheme of the phase transition of a thermo-responsive polymer at the LCST .	6
2	Example of a temperature depended DLS measurement	7
3	Scheme of a minieemulsion polymerisation	9
4	Scheme of the particle growth mechanism	10
5	Examples for nanofibres	13
6	Horizontal standard electrospinning set-up used in this thesis	14
7	Taylor cone and initiation of the jet [1]	15
8	Instabilities occuring during electrospinning	16
9	Assumed crosslinking mechanism	25
10	Microscopy of HEA microgels	29
11	DLS results of HEA microgels	30
12	Raman spectra of HEA microgels	31
13	Viscosity of different microgel/polymer solutions	33
14	Fibre formation	34
15	Inhomogenous PVA-microgel fibres	35
16	Comparison PVA fibres with microgel fibres	36
17	PVA-microgel fibres after contact with water	39
18	Physically crosslinked microgel fibres	40
19	Chemically crosslinked microgel fibres	41
20	IR-spectra for the chemical crosslinking reaction	42
21	DSC measurements of microgels, PVA and PVA-microgel fibres	44
22	TGA measurements of PVA fibres, microgels and composite fibres	46
23	Water sorption measurements of PVA and microgel fibres	47
24	Harkins-Jura plot of PVA-microgel fibres	48
25	Toxicity test of microgels and PVA-microgel fibres	49
26	Microgel size distribution in selected solvent mixtures	59
27	Microgel behaviour in different solvent systems	60
28	Sedimentation analysis of the spinning solutions	63
29	Films cast from the spinning solutions	65
30	Scheme of the solidification processes	67
31	PCL-microgel fibres spun from Me/To	69
32	PCL-microgel fibres spun from Ch/DMF	70
33	PCL-microgel fibre type C cross-section	71
34	Determination of material ratios by means of TGA	73

List of Figures

35	Degree of swelling of PCL-microgel fibres	74
36	Contact angle measurements of PCL-microgel fibres	75
37	Water sorption measurements of PCL-microgel fibres	76
38	Harkins-Jura plot of PCL-microgel fibres	77
39	DSC measuerements of PCL-microgel fibres	78
40	XRD measurements of PCL-microgel fibres	80
41	XRD measurements of swollen and molten PCL-microgel fibres	81
42	Degradation of the PCL-microgel fibres	83
43	Particle size distribution of from the fibres released microgels	84
44	Mass loss during the fibre degradation	85
45	xPCL synthesis scheme	91
46	Scheme of the microgel synthesis by miniemulsion polymerisation	92
47	Emulsion stability over time measured by means of DLS	96
48	NMR-spectra of xPCL and microgels	98
49	NMR spectra of microgels with various xPCL types/concentrations	99
50	FT-IR spectra of microgels with xPCL	100
51	Size distributions of microgels with xPCL	101
52	Micrographs of microgels with xPCL	102
53	Sedimentation profiles of microgels with 0.3 g xPCL	104
54	Degree of swelling of microgels with different xPCL contents	105
55	FESEM study of the microgel degradation	106
56	Degradation of xPCL microgels followed by DLS	107
57	Scheme of the degradation mechanism	108
58	NMR spectrum of the microgel degradation products	109
59	Loading of microgels with Nile RED	110
60	Uptake and release behaviour	111
61	Type S fibres spun with xPCL-microgels	113
62	Drug release from fibres with xPCL microgels	114
63	DLS measuremnts of VCL/AAEM/VIm microgels	122
64	PLA-microgel fibres	124
65	DSC measurement of PLA-microgel fibres	125
66	Degree of swelling of PLA-microgel fibres	126
67	Contact angle measurements of PLA-microgel fibres	127
68	Water droplet absorbtion on PLA-microgel fibres	128
69	Water sorption measurements of PLA-microgel fibres	129
70	Degradation of PLA-microgel fibres	130

List of Figures

71	FESEM micrograph of Phosphazene microspheres	135
72	FESEM micrograph of iron(III) oxide nanoparticles	136
73	PCL-microfibres with iron(III)oxide nanoparticles	141
74	PCL-microfibres with iron(III) oxide nanoparticles on the surface	142
75	Photo of PCL-microfibres with iron(III) oxide nanoparticles	143
76	PCL-microfibres with phosphazene microspheres	144
77	PES hollow fibre membrane	147
78	PES hollow fibre membranes with microgel agglomerates	148
79	PES hollow fibre membranes with microgels	149
80	TGA measurement of a PES/MG hollow fibre membrane	150

List of Tables

1	Ingredients used for the microgel synthesis	24
2	Influence of the electrospinning parameters on the fibre diameter	38
3	Results of the Harkins-Jura plot for PVA-microgel fibres	49
4	Spinning solutions prepared for PCL-microgel fibres	55
5	Properties of solvents used for the electrospinning	55
6	Refractive indices regarding microgel swelling	61
7	Results of the Harkins-Jura plot for PCL-microgel fibres	77
8	Used materials in the xPCL modified microgel synthesis	92
9	Overview of the analysis of the polymerisation process	95
10	Information about the crosslinker variations used	99
11	Analysis data of various xPCL microgels	103
12	Summary of VCL/AAEM/VIm microgel synthesis	118
13	Spinning solutions for PLA-microgel fibres	119
14	Spinning solutions of PCL fibres with iron(III) oxide nanoparticles and phosphazene microspheres	137
15	Spinning solutions for the fabrication of hollow fibre membranes	138

List of Abbreviations

• AAEM	acetoacetoxyethyl methacrylate
• AFM	atomic force microscope
• AUC	analytical ultracentrifugation
• AMPA	azobis methylpropionamidin dihydrochlorid
• BIS	methylen-bis-acrylamide
• bPEI	branched polyethylimine
• cTAB	cetyl trimethylammonium bromide
• DLS	dynamic light scattering
• DMF	dimethylformamide
• DSC	differanial scanning calorimetry
• FESEM	field emission - scanning electron microscope
• HCCP	hexachlorocyclotriphosphazene
• HEA	hydroxyethylacrylate
• IR	infra-red
• LCST	lower critical solution temperature
• MG	microgel
• Me/To	methanol/toluene
• NIPAAM	n-Isoprpylacrylamide
• NMP	n-methyl-pyrrolidone
• NMR	nuclear magnetic resonance
• NP	nano particle
• PBS	phosphate buffered saline
• PCL	polycaprolactone
• PES	polysulfone
• PLA	polylactide
• PVA	polyvinylalkohol
• PVP	polyvinylpyrrolidone
• SEM	scanning electron microscope
• TEA	triethylamine
• TGA	thermogravimetric analysis
• THF	tetrahydrofuran
• UCST	upper critical solution temperature
• UV/Vis	ultraviolet/visible
• VCL	N-vinylcaprolactam
• VIm	N-vinylimidazole
• VPTT	volume phase transition temperature
• xPCL	star-shaped acrylate-functionalised poly(ϵ -caprolactone) crosslinker
• XRD	x-ray diffraction

Introduction

I

In the centre of this thesis stands the idea of composite materials, of the combination of different materials to enhance properties or to overcome drawbacks of single materials or even to gain new properties in the synergy of the combination. Composite materials are common in nature and are used by humans since ancient times. Wood is a composite of cellulose fibres in a lignin matrix; muscles are also fibres embedded in tissue. One of the first advances in constructions was the development of cob bricks from the normal mud bricks, which is basically a fibre (straw) reinforced clay. A common example nowadays, which is still using the same idea, is ferro-concrete. These examples show already that one of the most common composite combinations is the fibre reinforcement, but also different geometries of additives or co-compounds or layered composites are used. An example is cemented carbide, where spherical carbide (tungsten carbide or titanium carbide) particles of a few micrometres in diameter are dispersed in a metal matrix, leading to very hard materials. Sometimes the change in the material's properties are so tremendous that completely new fields open for its application. A curious example is pykrete; ice with 14% of sawdust. Due to the sawdust, pykrete has a much lower melting rate, and toughness close to concrete, and since it is made out of ice and wood it still has a lower density than water, so it floats. It was actually invented during the Second World War in a program of the British navy to build an unsinkable aircraft carrier.

In this work nano- or micrometre sized polymer fibres, which are macroscopic in one dimension, but nanoscopic in the others having extra high surface areas, will be combined with thermo-sensitive microgels. The composite material will have the dimension related properties of the fibres, the material related properties of the fibre polymer and additionally the properties of the microgel polymer or polymers, since the microgel itself can also be a composite material if it is based on more than one polymer. This kind of material combination has applications in a broad range of scientific fields, due to the various possibilities in the material properties: Every property known for polymers is possible, from conductive to bio-degradable.

The first step of creating such fibres is the actual fabrication focussing on the process and parameters, which was not done before in a systematic manner. The fabrication process chosen in this work is electrospinning, which is a favourable way to fabricate nano- and micrometre sized fibres. The main idea of this thesis is the reproducible fabrication of homogenous microgel based microfibres. Reproducible in the sense that the effects of the parameters involved in the process are understood and that the achieved fibres can be produced always with the same quality in a continuous process. Furthermore, the idea was to include the unique features of thermo-sensitive microgels, which have switchable swelling or water uptake properties, to create smart or interactive materials, addressable in a macroscopic way (fibre nonwovens), without losing the microscopic properties (microscopic fibres). Microgels are usually found as dispersion, but as a co-compound in a fibrous composite material they are given a solid form. However, not only the fabrication of this new composite material was the aim of this work, but also to investigate their properties and show some possible combinations of properties.

This work is structured in seven parts, most of them with several chapters. The first part

after the introduction is a general theoretical introduction of the basic topics of this thesis. The synthesis and properties of microgels are described and the electrospinning process is explained in detail, including a general description of nano- and microfibres. Furthermore, the questions why these materials are used and why they are interesting will be addressed in more detail than in this introduction.

The results are presented in the parts three to seven, each with its own introduction in the specific questions and ideas for the presented studies, an experimental part describing all experiments and analyses done, and a conclusion. All the introductions, including this one, are meant to guide through this thesis, they are consecutive in the outline of the idea of this work and try to merge the aim and idea of this work throughout the different chapters.

Part three is about microgel-polyvinyl alcohol composite fibres. In this study the basic fabrication principles for the microgel based fibres are investigated, using well known materials, always considering possible medical application that arise from the biocompatibility of the materials and water based synthesis. Furthermore, the fibres are analysed in detail, showing that the interactive feature of the microgels can be retained in the fibre structure.

In part four pre-eminently the fibre polymer is changed to polycaprolactone, a degradable and hydrophobic polymer. Microgel-polycaprolactone composite fibres were fabricated. Changing the polymer from a water soluble to a not water soluble one also means to change the solvent system, but it gives new opportunities regarding the fibre morphology through phase separation during the electrospinning process. Fibres with microgels only on the surface or only in the fibre core are achieved. Furthermore, the combination of the hydrophobic polymer with the hydrophilic microgels, given by the straight forward one step electrospinning process, shows to be an elegant way to modify or change completely the fibre properties. The fabrication, as well as the analysis of the fibre properties was performed in detail.

The fifth part is not directly related to microgel based fibres, but describes the synthesis of a new microgel with properties that should prove very useful for fibre systems, like they are shown in part four. Thermo-sensitive microgels have been created, which are degradable and have hydrophobic domains that are able to immobilise hydrophobic substances like drugs. Since the degradation process is the same as for polycaprolactone, completely degradable fibres could be fabricated with these microgels. Furthermore, immobilised drugs in the microgels, which are located on the fibre surface, can be released targeted at a specific place. The synthesis of these microgels was achieved by a tailor made crosslinker using a modified variant of a miniemulsion polymerisation, with the molten monomer. Again the synthesis as well as the analysis is described in detail.

Results part six addresses the fabrication and characterisation of polylactide-microgel composite fibres. It is a preliminarily study for a bigger project targeting on the creation of new polylactide based implants or suture material, where microgels modified with vinylimidazole

are used to suppress the acidic degradation of polylactide. This acidic degradation causes problems in the form of immune reaction, when polylactide is used as implant, stent or suture material, and this new combination of materials could be a possibility to overcome this problem. Furthermore, the combination of microgels with a hydrophobic polymer leads to new properties in the composite material regarding the uptake of water.

The last results shown in this thesis are a short summary of introductory studies, which constitute an outlook for the on-going research in the broad field of composite fibres and microgel composite materials. This part seven is named “Introductory studies/Outlook”. The first small study shows the possibilities of the fabrication process described in part four, which produces fibres with microgels exclusively located on the fibre surface. In this case iron(III) oxide nanoparticles and phosphazene microspheres are used. These two materials also give access to different properties, namely magnetism and flame retardant behaviour. Furthermore, this study helps to learn more about the mentioned process. In the second small study some introductory results are shown for microgels used in hollow fibre membranes. These fibres are not spun via electrospinning but via a wet spinning process enlarging the possible ways to use microgels as co-compound in composite materials. The last part of this thesis is an overall summary and conclusion emphasising the achievements of the studies.

General Theoretical Introduction

II

1 Microgels

There is no straightforward definition for microgels yet to find in literature. One definition would be: Microgels are colloidal stable particles based on hydrogels also exhibiting similar properties [2]. Another one is: “Polymer Microgels are crosslinked particles with network structure that are swollen in solvents” [3]. The second definition is much broader, since it includes the swelling in different solvents other than water. Microgels can be synthesised in so many different ways, for example precipitation polymerisation or emulsion polymerisation, and they can be based on so many different polymers and their combinations, that their size (50 nm to 5 μm [4]) and properties vary so much that a very precise definition does not seem possible. Therefore, this theoretical overview will focus on the specific class of thermo-sensitive microgels that has been used in this work. This overview is far from complete, but it is supposed to give an insight in the field of thermo-sensitive or thermo-responsive microgels for a better understanding of this research work and its intentions.

Thermo-responsive microgels, are polymer network particles based on monomers/polymers that exhibit a lower critical solution temperature (LCST). Most prominently and best studied example is poly(N-isopropylacrylamide) (NIPAAm) [5, 6, 4] in water. Polymers that have a LCST are in an expanded random coil state below this temperature. The hydrophilic groups of the polymer chain form hydrogen bonds with the water molecules; the solvent-polymer interactions are stronger than the polymer-polymer interactions. When the temperature increases above the LCST the hydrogen bonds break and the polymer-polymer interactions become stronger than the solvent-polymer interactions. The polymer chains form a globular structure to reduce the surface area of their hydrophobic groups with the surrounding water. The form changes from a coil state to a globular state and a phase separation of the polymer occurs; therefore the solvation is switchable by the temperature. This is schematically shown in Figure 1. The LCST of NIPAAm is 32 °C [5, 6] and is therefore in a physiological range.

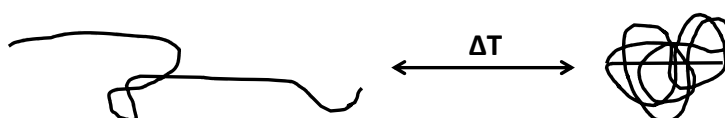


Figure 1: Scheme of the phase transition of a thermo-responsive polymer at the LCST

The above described effect also takes place in the crosslinked polymer network form, microgels or hydrogels, of these polymers, but since microgels are dispersed colloidal particles and not single polymer chains the transition makes a different appearance. Microgels do not have a LCST but a volume phase transition temperature (VPTT), which can differ from the LCST of the polymer the microgels are based on [3, 4]. Below the VPTT microgels are swollen with water, hydrogen bonds are formed and the polymer-solvent interaction prevails. Above

the VPTT the hydrogen bonds break, the polymer-polymer interaction increases, water gets pushed out and the network shrinks. The volume of the particles, and therefore their diameter, changes below or above the VPTT. An example for this transition measured by means of dynamic light scattering (DLS) can be seen in Figure 2. The hydrodynamic radius (R_h), the radius which corresponds to the radius of the solute plus the solute surrounding shell that diffuses with the same rate, is plotted against the temperature for each measurement. Below the VPTT the hydrodynamic radius is big, the particle is swollen, above the VPTT the particle is collapsed and the R_h is smaller. The transition is not as sharp as for the polymer or a macroscopic hydrogel [7]. This can be explained by the higher heterogeneity of the chain lengths in the microgel network, than in a polymer solution for example. Shorter sub-chains will collapse at slightly higher temperatures than longer sub-chains, due to a different hydrophobicity/hydrophilicity [2]. Another difference to macroscopic hydrogels is the shorter time, less than a second, which is needed to reach the other steady-state. In hydrogels the way from inside to outside has a different scale and additionally the shrinking of the outer layers hinders the water transport from the inner layers[4].

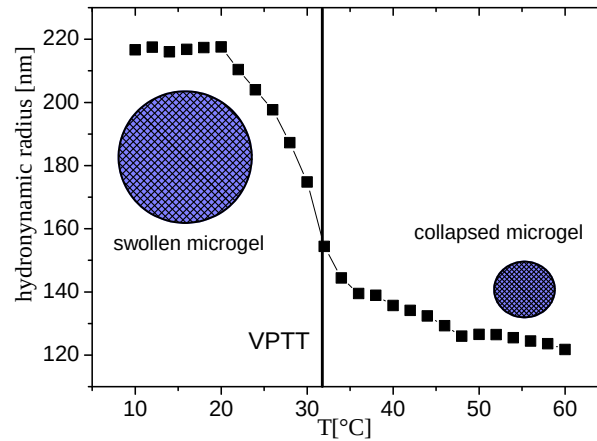


Figure 2: Example of an temperature depended DLS measurement of the hydrodynamic radius of a VCL/AAEM microgel

Polymers and can also have an upper critical solution temperature (UCST), which leads to a phase separation at low temperatures and a solvation at higher temperatures. The same basic mechanisms of polymer-polymer and polymer-solvent interactions induce this behaviour. For microgels based on these polymers this means a small diameter at temperature below the VPTT and a larger diameter above the VPTT. Microgels can also be dispersed and sometimes also swollen in other solvents than water, like alcohols, having different diameters, smaller or larger than in water, depending on the solvent [8].

Like it was mentioned already above, NIPAAm is the most common monomer for thermo-responsive microgels. Another known example is N-isopropylmethacrylamide (NIPMAAm), which has in difference to NIPAAm an additional methyl group, but due to a smaller chain mobility [2] the LCST/VPTT is shifted to 45 °C [9]. All microgels in this thesis are based on N-vinylcaprolactam (VCL). VCL is a member of the vinylamide family, having a lactam ring with 6 carbon atoms and one nitrogen atom; seven-member ring. It has a LCST/VPTT of 32 °C, which is basically the same as for NIPAAm and which is in the physiological range. VCL is stable against hydrolysis [10, 11] and biocompatible [12]. Even though it is stable against hydrolysis it will eventually hydrolyse, but due to the position of the amid group in the lactam ring, no toxic low molecular weight amides are formed. This is the basis of its good biocompatibility, below and above the LCST [13] and it gives an advantage over the discussable biocompatibility of NIPAAm [14, 13].

One of the major advantages of responsive microgels is their material flexibility, the combination of various monomers, co-monomers and additives in one particle. Therefore, their properties and possibilities are diverse as well. They can carry reactive groups [15] or charges [16] or they can be degradable [17]. As composites with nanoparticles or proteins they can even be magnetic [18], conductive [19] or catalytic [20]. Furthermore, their switch ability is not limited to temperature; microgels can also be sensitive to pH [21], light [22] or solvent type [8] changes. Moreover, nearly any kind of combinations of these properties can be synthesized. This wide range of properties gives microgels access to many different kinds of applications in cosmetics, food-industry, industrial polymer processing, coatings, agriculture and most prominently medicine [4, 23].

Another way to extent microgel properties is to modify their morphology or their macroscopic structuring. Core-shell microgels [24], as an example for different microgel morphology, can be made of a non sensitive and a sensitive monomer, two temperature sensitive monomers with different VPTTs or even of monomers with different trigger attributes, like temperature and pH value. To achieve the core-shell architecture usually a two step process is required, where first the core is synthesized which is then used in the second step as seed for the shell. The macroscopic structuring of microgels includes films [25], colloidal crystals [26, 27] or microgel chains [28].

1.1 Synthesis Methods

Microgels can be synthesized in various ways, by physical or chemical crosslinking in micro-droplets, in water-in-oil emulsions or oil-in-water emulsions, via miniemulsion polymerisation or in microfluidic devices, but probably the most common way is the precipitation polymerisation [23].

In this short overview only a brief summary of the miniemulsion technique, as well as of the precipitation polymerisation will be given, since these are the techniques used in this work. In either way, the method is a heterophase polymerisation, a free radical or controlled radical polymerisation, in the presence of a crosslinking molecule [23]. The method of choice is often conditioned by the monomers or co-monomers used. For example many bio-molecules can not stand the elevated temperatures usually used in precipitation polymerisations, while completely water insoluble molecules can not be synthesised in water based processes.

In a miniemulsion polymerisation two not miscible solvents, toluene and water for example, are mixed with high shear rates and stabilised by surfactants to form stable dispersions. All monomers and the crosslinker are added before the mixing to the dispersed phase. The usual miniemulsion would consist of water as the continuous phase and “oil” as the dispersed phase; if water is the dispersed phase and the “oil” is the continuous phase it is called inverse miniemulsion. The emulsions are kinetically stable, usually stable for several days and the particles sizes are only about a few hundred nm. Water or oil soluble initiators can be used and the particles formation takes place in the droplets. Therefore, the particle size is mainly depending on the droplet size, which in turn is depending on the surfactant concentration and on the shear rate used during the emulsification. The latter can for example be done by stirring, mixing, shaking, ultrasound or microfluidics. One major disadvantage of this technique in comparison to precipitation polymerisation is the usage of organic solvents, which have to be removed after the synthesis and can be toxic. A scheme of a miniemulsion polymerisation can be found in Figure 3.

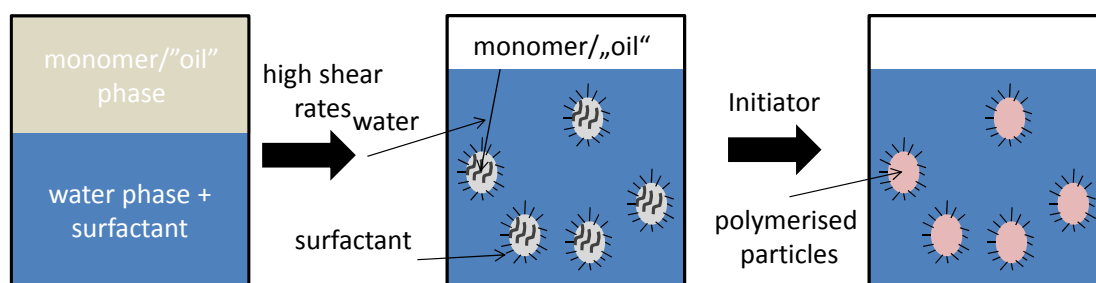


Figure 3: Scheme of a minieemulsion polymerisation

In the precipitation polymerisation all components, monomers, crosslinker, additives, such as surfactants, and an initiator are dissolved in water, which is the only solvent. The reaction temperature is usually a bit elevated (50-70 °C) due to a better solvation of the components and to activate the radicalisation of the initiator. Free radicals cause radical propagation; chain growth. Polymers with a LCST will collapse, due to a reaction temperature higher than the LCST, after a certain chain length is reached and the globular chains serve as precursor particles for the on-going reaction. The particles growth mechanism can be an aggregation of

the precursor particles to polymer particles, a deposition on already existing polymer particles or an addition of monomers and oligomers [23]. Due to charges from the initiator, the formed polymer particles are at this stage of the synthesis electrostatically stabilised, and even though they are in their collapsed state (temperature above the VPTT) they still contain water. After the reaction is finished and the temperature decreases below the VPTT, the particles will swell and form a “hairy” or “fuzzy” spherical polymer network, which is sterically stabilised. A scheme of the particle growth mechanism can be seen in Figure 4.

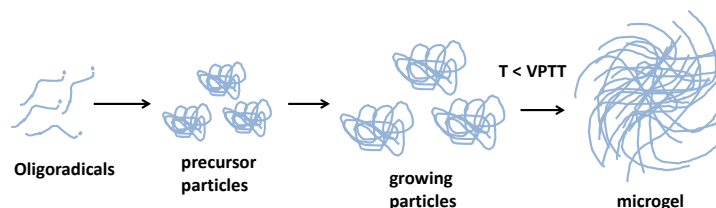


Figure 4: Scheme of the particle growth mechanism

Precipitation polymerisation can be carried out as a surfactant-free synthesis, because particles can be electrostatically stabilised by the ionic initiator residues, but this limits the size of the microgels. To synthesise smaller microgels many small precursor particles are needed instead of faster growing, bigger precursor particles, but the large surface area of many small particles can not be covered by the initiator residues; therefore the use of surfactants is needed. Surfactants can stabilise a bigger amount of small particles and prevent them from aggregation, which is one of the growth mechanisms. The size of NIPAAm based microgels for example can be reduced by a factor of 10 with the use of sodium dodecyl sulphate [29].

Precipitation polymerisation is a very straightforward method to synthesise microgels, and can furthermore be used to achieve microgels with core-shell morphology. One way for achieving microgels with core-shell morphology is to use two monomers with either a different reactivity or with a different hydrophobicity. In the first case the core will mainly consist of the faster consumed monomer and the shell of the slower consumed one [30]. In the second case the more hydrophilic compound will most likely be arranged closer to the surface of the microgels, closer to the surrounding water phase [31, 32]. Another method to synthesise core-shell microgels is the simple addition of the shell monomer in a later state of the reaction. All components except of the shell monomer are added as usual and the reaction is started by the initiator; after some minutes when a first turbidity occurs the shell monomer is added and can therefore only be integrated in the outer part of the microgel. The seed polymerisation follows the same principles as described before, but has two stages: at first all components are placed in the reactor and the whole reaction is carried out achieving a microgel or in general a polymeric colloid. In a second step the second monomer and again crosslinker and initiator are added and a second synthesis takes place, but the already fabricated particles will serve as

seeds and a core-shell architecture will be achieved [33, 24]. Using these techniques, properties from different monomers can not only be included into the same microgel, but also placed specifically where there are needed, like a reactive group for further modifications is more useful at the surface of the microgel.

In addition to post modifications of microgels by a post synthesis addition and incorporation of nanoparticles or small molecules, like drugs, the precipitation polymerisation offers *in-situ* methods to create hybrid microgels and opens the possibility to use the microgels as reaction centres. As an example, nanoparticles can be added to the reaction mixture before the initiation and serve as seeds for the microgel formation [34, 35]. Other methods are the simultaneous synthesis of polymer particles and inorganic particles or the use of microgels as reaction centres: Microgels with a co-monomer, which is used as a reduction agent during the nanoparticle formation [36, 37, 38].

This overview of the synthesis pathways for microgels and the possibilities of the precipitation polymerisation is far from being complete but should be sufficient as an introduction of this topic, for the better readability of this research work.

2 Electrospinning/Nanofibres

2.1 Nano- and Microfibres

Fibres are one of the most common and oldest products of mankind. This includes Stone Age times (animal hair for clothing), as well as preindustrial (loom), early industrial (steam and electrical powered looms) and modern times. Their usage ranges from ropes and clothing to specialist medical products (patches, stents) and to fibre composite materials for aircrafts or space shuttles. Even micro and nanometre sized fibres are common in our daily usage. The best known, but infamous example is asbestos, which consists of thin fibrous silicate crystals.

Nanofibres, which will include for this chapter also fibres with a few micrometres in diameter, are, as opposed to macroscopic fibres, only macroscopic in one dimension and nanoscopic in the other two. This causes extremely high surface areas and ratios between surface and volume, not rarely more than $100 \text{ m}^2/\text{g}$ [39]. Besides their dimensions the fibre properties depend on the material they are based on and their morphology. Polymer-nanofibres have been shown to be conductive, fluorescent or degradable [40, 41, 42]. Combinations of different polymers in one fibre will lead to combinations of each of their properties. Polymer based composite fibres with carbon nanotubes [43], metallic or ceramic nanoparticles [44, 45] or proteins and other biomaterials [46, 47, 48] broaden the range of possibilities of these fibre further (magnetic [49], antibacterial [50]). The other way around, fibres can also be used to reinforce other materials, like concrete or plastics. Therefore, the possible range of applications is the same as for common fibres, from clothing (smart, conductive textiles) and medical applications (patches, tissue engineering) to microelectronics and constructions (insulation). The most common application nowadays is probably in filtering.

The usual morphology for nanofibres, fabricated by electrospinning, is a smooth surface and a spherical cross-section. Fibres with pores or undulations of the diameter can be achieved by special material combinations (phase separations) or with post-process treatments, for example one of two components could be etched out [51]. Special coaxial nozzles can be used to create core-shell or hollow fibres [52]. In figure 5 A electrospun PVA nanofibres are shown as a general example for nanofibres to get a perception of how nanofibres look like and how they are laying on the target after the electrospinning process. The micrographs from Figure 5 B and C show examples for the different morphologies and options possible with nanofibres. Poly(vinylpyrrolidone) fibres, with iron oxide nanoparticles inside, are presented in micrograph B and porous polylactide fibres in micrograph C.

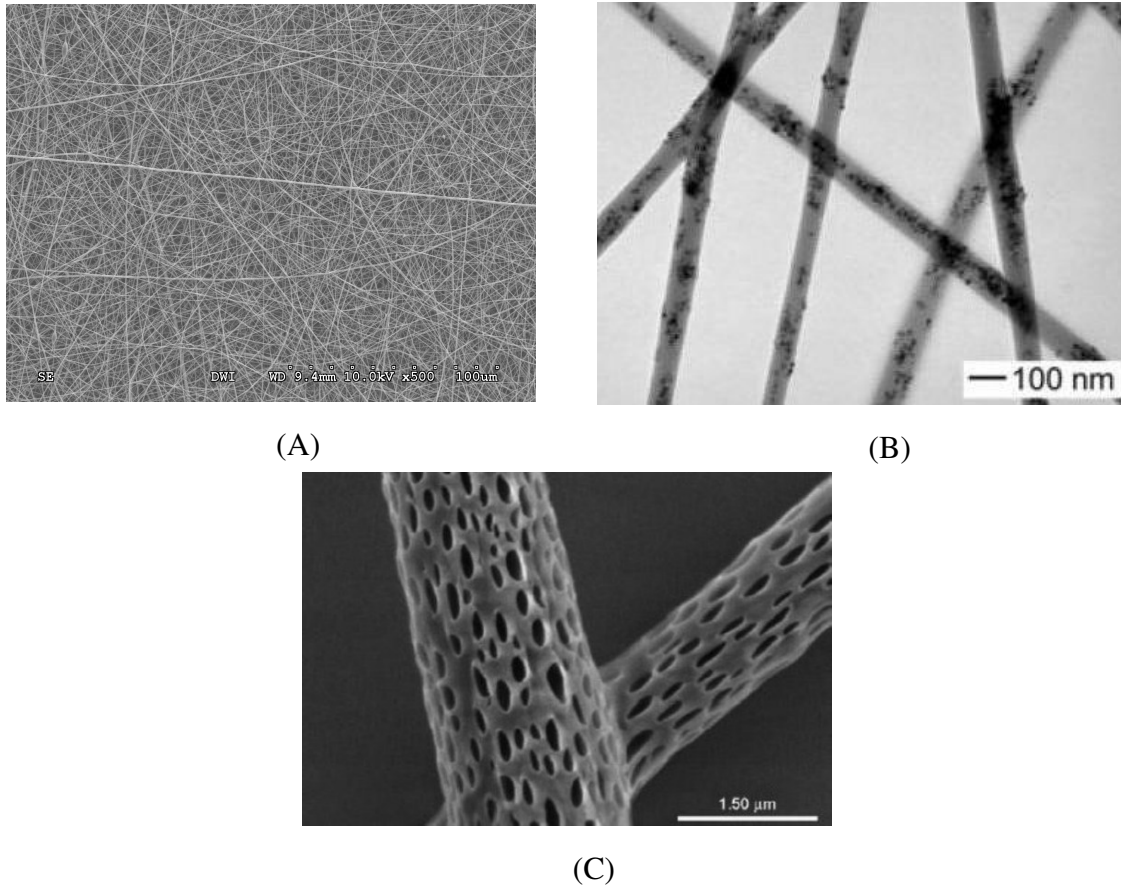


Figure 5: Electrospun PVA nanofibres (A), poly(vinylpyrrolidone) nanofibres with iron oxide nanoparticles [53] (B) and porous polylactide nanofibres [54] (C)

2.2 Electrospinning

Electrospinning is a surprisingly old process used to produce nano- and micrometre scaled materials. The technique is known and used since the beginning of the twentieth century and it is based on conventional spinning of fibres as well as on the work of Lord Rayleigh. He described the influence of electric fields on liquids [55, 56]. Early machines did what today is called electrospraying, which is basically the same process, but instead of fibres, small droplets are sprayed on a target [57]. Artificial silk was done with the help of electric fields in 1929 by Hagiwaba [58] and the first patent about electrospinning of polymers came in 1934 by Anton Formhals [59, 60]. Nevertheless it was only in the 1990s that a bigger scientific focus was put on electrospinning, with main contributions from Reneker and his group [61]. Electrospinning gives the possibility to produce nano- and micrometre scaled materials in a

relatively simple process obtaining a macroscopically usable product: a nonwoven consisting of thin fibres. The advantages of thin fibres were already described in the previous chapter and make instantly clear why this technique is valuable for natural scientist, as well as for engineers and physicists. The one drawback of the electrospinning process is the maximum output that is needed for large scale industrial products.

The simplicity of the electrospinning process comes from a simple set-up and a straightforward process itself. However, the theory behind it is not as simple. An example set-up is shown in Figure 6. It consists of a syringe with a metal nozzle or cannula, where the material is pressed through the syringe by a syringe pump. The cannula is one electrode and a metal target is the other one connected to a high voltage generator. The liquid spinning solution will exit from the cannula and on the target, dry, solvent free fibres deposit. More complicated or industrial set-ups still consist of the same parts; just the parts will have some extra features, like a moveable or rotating collector instead of a metal plate as target, or better controllable pumping equipment than a simple syringe pump. The set-up shown in Figure 6 is a horizontal set-up and is the one used to fabricate all samples shown in this thesis.

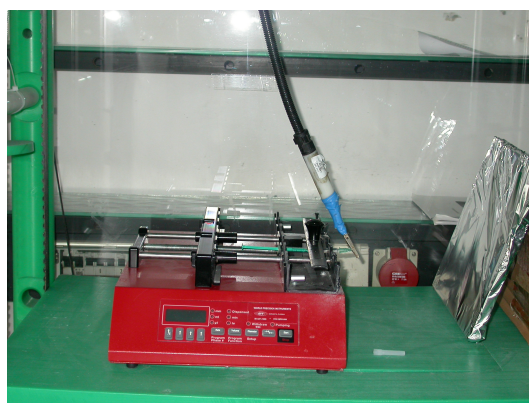


Figure 6: Horizontal standard electrospinning set-up used in this thesis

Following the process step by step, everything starts with a droplet. When a fluid is pressed through a nozzle at the tip of the nozzle, a droplet or better said a pendant drop, will be formed. The shape is spherical since the surface tension will favour smaller surface areas. Besides the surface tension, the gravitation and the viscosity of the liquid play a major role in the droplet shape. Applying a high voltage will induce charges in the liquid, evenly distributed on the surface, and the electrostatic repulsion of these charges as well as the coulomb forces from the external field will influence the droplet [53]. The result of the electrostatic forces is the Taylor cone; the droplet will morph into a conical shape. Even stronger electric fields will overcome the surface tension and a stream of liquid, the jet, will be expelled from the Taylor cone. Acceleration, due to the Coulomb forces between the charges on the surface of the jet and the target electrode, takes place; the jet will be stretched and thinned in the beginning

followed by different instability forces, which continue the thinning until the target is reached. In Figure 7 the change in the droplet morphology from its original spherical shape until the initiation of the jet is shown.

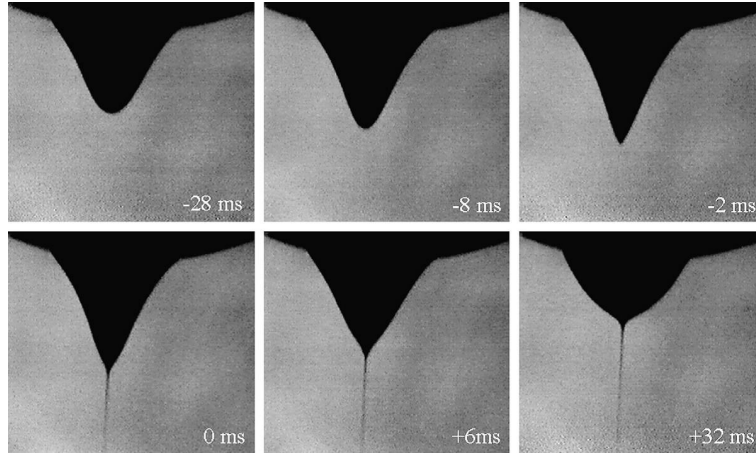


Figure 7: Taylor cone and initiation of the jet [1]

A jet of a low molecular liquid, like water, just pumped out of a fountain for example, without any electric field, will fall apart after a certain distance due to the Rayleigh instabilities. This is an every day phenomenon, which can be observed at fountains or just at a tap. The basic driving force for the Rayleigh instabilities is the minimisation of the surface energy and their reason are undulations or perturbations in the jet's diameter [55, 56]. If the perturbation is sinusoidal and has a wavelength $\lambda < 2\pi r$, it will reduce the surface energy, grow and lead to the disintegration of the jet [56]. Different influences, like the viscosity, the molecular weight, or factors from outside, like airstreams, affect this disintegration. Liquids containing molecules with molecular weights of a few tens of thousands g/mol, like a polymer solution, undergoing the electrospinning process will also experience the Rayleigh instabilities, but intramolecular interactions, the entanglement of the polymer chains, counteract the disintegration, and fibre formation is possible. However, beside the Rayleigh instabilities the jet will experience other instabilities caused by the applied electric field, most prominently the axisymmetric instabilities and the whipping instabilities. The axisymmetric instabilities are caused by undulations and perturbations of the fibre diameter. Differences in the diameter lead to differences in the density of the surface charges and the repulsing forces of the charges do not work anymore in the direction of the jet, since the surface of the perturbation area is not parallel to the direction of the jet [1]. This means that axisymmetric instabilities amplify the disintegration of the jet in droplets, or if not possible the bead building of the fibre. Figure 8 A shows a scheme of the formation of axisymmetric instabilities. The whipping instabilities are in a way the most important instabilities, since they are one reason for the possibility to produce fibres with diameters in the nanometre scale. They are caused by the fact that charges of the same type,

linearly ordered along an elastic line, are very instable against lateral deflection [62]. If the jet is deflected on one position, the repulsing forces will amplify the deflection, like it is shown in Figure 8 B. Considering all charges in the jet and the forces, like they are shown in the Figure 8 B, the result is a jet that is bending and whipping, forming loops on its way to the target. Furthermore, the bending occurs also in higher orders, when the loops interfere with each other. As a results of the whipping and bending, the jet gets stretched and additionally the way between nuzzle and target is much longer than the straight way, which gives even more time for the stretching [1]. This entails the possibility to fabricate nanometre scaled fibres with a very simple practical process and equipment.

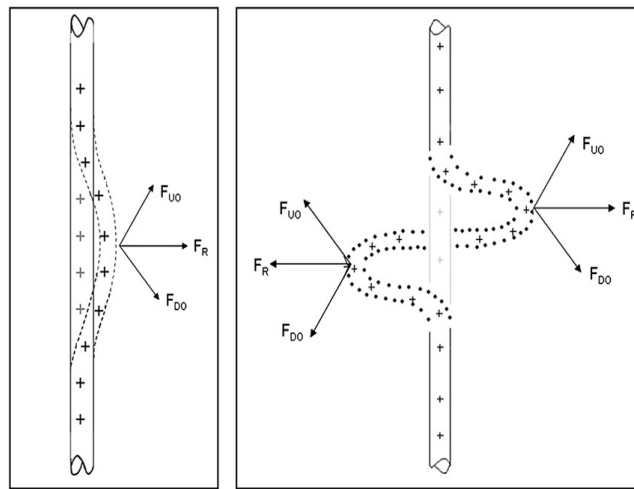


Figure 8: Scheme of axisymmetric instabilities (left) and whipping instabilities (right) [1]

Overall, the electrospinning process has three phases: The initiation of the jet, the elongation, and the solidification or fibre formation. The first two are already described above, the solidification in most simple systems, containing of a solvent and a polymer, means just the evaporation of the solvent and the strong stretching of the solidifying fibres. The material in the jet needs circa 0.1 seconds from the nuzzle to the target, while the formation of the fibre structure takes place already in 0.01 seconds [57]. Since the surface of the jet is very high, and the way to the target relatively long, the short time is, depending on the vapour pressure of the solvents, enough for the evaporation. The short solidification time can lead to chilled fibres, aging process of the material or different degrees of crystallisation; for example small crystallites with defects [63]. The strong stretching and the fast stretching velocity, together with the short solidification time can lead to highly oriented chains. These factors can influence the fibres properties like hardness, E-Modulus or degradation. In systems consisting of different solvents or different polymers, the solidification can also be more complicated. In systems like two non miscible polymers spun from one solvent, or one or more polymers spun

from a solvent system, phase separation can take place during the evaporation of the solvents. Especially when the system has a miscibility gap, spinodal or binodal morphologies of the fibre interior can occur [57]. A spinodal separation induces a morphology with two intermixing separate phases and a binodal separation conducts a morphology where one phase is dispersed in a matrix of the other phase.

The product made by electrospinning is a nonwoven; a fabric of fibres where the single fibres are not interweaved, neither mechanically nor chemically. A common example for a nonwoven fabric is felt. The fibres fabricated during the process get one after the other placed on the target and after a while on top of each other. Therefore, the fibres are not oriented and their anisotropic properties are less prominent. However, the usage of special target electrodes or for example a rotating collector [64] allows the fabrication of aligned fibres, to use the full potential of possible anisotropic properties.

Considering the simple set-up of an electrospinning process, the process has surprisingly many parameters that can influence the fibre formation, the fibre diameter or the morphology of the fibres. There are four different categories of parameters: molecular parameters, solution parameters, process parameters and environmental parameters. The latter includes the humidity and the temperature, which can have a big influence for example on the evaporation of the solvent, but they can not be controlled in a simple set-up such as the one used in this work, therefore no detailed description will be given. Molecular parameters are for example the molecular weight, the solvation of the polymer in the solvent or the crystallisation velocity. A polymer that does not dissolve in the solvent can not be spun and a polymer that is only soluble in one of two solvents of a solvent mixture will probably undergo a phase separation. The molecular weight influences the viscosity of the solution and the ability of the polymer chains for the entanglement. If the molecular weight is too low, no entanglement occurs and no fibre formation takes place.

The flow rate of the liquid through the syringe, the applied voltage, the target distance or the diameter of the cannula are examples for process parameter. These parameters are also the ones that can be varied the easiest. The target distance influences the stretching of the fibres and the evaporation time for the solvent. In general it can be said, that a longer target distance will lead to thinner fibres, because the jet gets stretched more. The flow rate regulates the amount of liquid that gets pressed through the nozzle and into the jet, therefore, higher flow rates lead to thicker fibres [53], but higher flow rates also increase the stress on the solution. The applied voltage can also lead to thicker fibres, because more material is sucked into the jet, but its major influence is regarding the homogeneity of the fibre diameter; higher voltages lead to less undulations in the fibre diameter [57].

Solution parameters are derived from the composition of the solutions, like polymer concentration, viscosity, surface tension or the conductivity. A higher polymer concentration leads to thicker fibres with less undulations, since more entanglement is ensured. The other way

around, lower polymer concentrations lead to thinner fibres until no entanglement is possible and no fibre formation takes place [57]. The polymer concentration is directly connected to the viscosity. Higher polymer concentrations induce higher viscosities and therefore high viscosities induce thicker fibres as well. But liquids with high viscosities also have due to stronger cohesion effects higher surface- or interfacial tensions, which counteract the formation of the Taylor cone and the jet initiation. Moreover, even though most polymer solutions are Newtonian liquids, the solutions can be shear thinning or rheopectic; showing different behaviours with the stress induced by the flow rate.

Two other aspects or variations of the process should be mentioned. First many of the parameters, especially the solution parameters can further be influenced by additives, like salts or surfactants. Salts lead to a higher conductivity, a higher density of the surface charges, therefore the stretching effect of the electric field gets stronger, and thinner fibres can be achieved [65]. Surfactants lower the surface tension and facilitate the formation of the Taylor cone and the jet initiation. The second point to mention is the formation of multiple jets, which is usually caused by inhomogeneities in the solution or the process. When controlled it can lead to thinner fibres, since the jet is split up, but mostly it leads to inhomogeneous fibre morphologies and diameters [64].

As it is obvious by considering some of the parameter examples given, many parameters influence each other, so that an easy conclusion about their direct influence on the process or the fibres is not possible. Furthermore, there are many parameters that can not be influenced at all, since they are given by the materials desired. Due to the vast amount of parameters a choice is made usually, regarding which ones are to vary towards the ones that seem most likely to be important for the specific system. And even though literature and experience from different studies can give some hints about the parameters' values and the effect of their variation, the electrospinning of a new material system is based on a lot of trial and error, due to the vast amount of parameters and their interleave. However, as it was mentioned already in the beginning of this chapter electrospinning is a simple and straight forward process to try new material combinations of nanometre scale fibres, which can lead to a great variety of possible applications.

2.3 Nanofibres/Electrospinning with Microgels

As it was already mentioned, electrospun fibres can also be modified with various additives and co-compounds. A big majority of publications about nanofibres with particles as co-compounds focus on inorganic particles like carbon nanotubes, metal oxides or metal nanoparticles. Work on polymeric colloids and electrospinning was done too, but much less intensive. One example is a work on poly(vinylpyrrolidone) fibres with NIPAAm microgels [66]. In

this work fibres with incorporated microgels were spun, but it was mainly a proof of principle with some additional characterisations of the optical properties. From the picture provided in the cited study it comes forth that the fibres themselves are not homogenous, show beads and the microgels are also not homogenously spread, but mainly located in the beads. In another example microgels based on N,N-dimethylacrylamide and acrylamidoethylsulfonic acid have been electrospun without a matrix polymer [67]. These microgels are not thermo-responsive but can bind metals. Again it was basically a proof of principle; no focus was laid on the process, on the parameters or on the actual properties of the fibres. Also a work about PVA with polystyrene particles can also be found [68], in which the particles are fluorescently labelled in order to observe them inside of the fibres. But again no parameter study or intensive characterisation of the fibres is presented, and the fibres shown in the cited study show again inhomogeneities.

This short review of the literature is of course far from being complete, but it gives an impression about the major differences between works that have already been done about microgel-polymer fibres and the work done in this thesis. The present work focusses not only on the fabrication of nanofibres with microgels, but on the detailed description, the reproducible fabrication of homogenous fibres with also homogenously distributed microgels and the explicit analysis of their properties. For a more detailed image regarding the differences between the fabricated fibres shown in this thesis and the fibres shown in the cited works, a look into them is suggested.

Polyvinyl alcohol - Nanofibres

III

1 Introduction

The basic idea of this work, like it was outlined in the general introduction, is to create a material that combines the properties and possible applications of nano- or micrometre sized polymer fibres with the “smart” or sensitive properties of microgels. Especially the option to make the usually dispersed microgels accessible in the macroscopic scale, while keeping nanoscopic properties is very interesting and promising.

One aim of this study is not only the fabrication, but also the understanding of the fabrication process for reproducible fibres of good quality and the possible transfer of the acquired experiences to various other materials. Since this combination of materials is not remarkably common in literature and the works found [67, 66, 68] do not focus directly on the fabrication of homogenous fibres, the first experiments of this work had to be done with materials common in their specific fields. This means the basic polymer needed to be well known in the field of electrospinning, while also providing some key properties like biocompatibility, or water solubility. Therefore, the choice was made to use polyvinyl alcohol (PVA). In the case of the microgels the choice for the main monomer was N-vinylcaprolactam (VCL), which provides the microgels with the thermo sensitive swelling behaviour, and which is also known to be biocompatible. 2-(methacryloyloxy)ethyl acetoacetate (AAEM) was chosen as a co-monomer, because it gives the microgels a higher stiffness. The combination of VCL and AAEM, their synthesis and properties, are well known, which made these microgels good candidates for this work. 2-hydroxyethylacrylate (HEA) was chosen to be added as second co-monomer to the microgels. HEA adds hydroxyl groups to the microgel network, which later can be used for different crosslinking reactions, which are needed to prevent the fibres from dissolution in water, due to the water solubility of PVA. However the water solubility of PVA has the advantage that no organic solvents need to be used throughout the whole synthesis and fabrication process, which means no elaborated cleaning of the samples and less possibilities to have toxic substances in the achieved material, making them desirable for medical application. The downside is that the fibres will also be water soluble and need to be crosslinked at some point during their fabrication, physically or chemically.

High surface areas, a high and temperature tuneable degree of swelling and biocompatibility, which are some of the key properties that can be achieved with this materials combination, are also important for possible applications in fields like medicine or filtration. Furthermore, the combination of two materials may lead to synergy effects or to an amplification of a property that is inherent for both materials, like in this case their hydrophilicity. Besides the motivation of creating a new composite material, this study is also supposed to be the first step into the field of microgel based fibres and level the way regarding the process conditions for other similar material combinations.

The following part of the thesis is divided in five chapters, besides the introduction and the conclusion. The experimental part will provide all necessary information about the synthesis

and fabrication procedures to recapitulate the results as well as the analytical experiments. Afterwards, the HEA-modified VCL/AAEM microgels are described and analysed, followed by the detailed description of the fibre fabrication. The latter is focussing not only on the results of the procedure but on a detailed review on the influences of the process and solution parameters of the electrospinning process of microgels and PVA. The chapter “Crosslinking” describes physical as well as chemical crosslinking possibilities of the achieved fibres. In the chapter “Fibre Characterisation” the fibre properties are analysed by means of thermal analysis (TGA, DSC), water moisture sorption analysis and toxicity testing to investigate properties like the degree of swelling or their biocompatibility.

The synthesis and analysis of the HEA modified VCL/AAEM microgels and the fibre fabrication (not the characterisation) was already part of my master thesis [69]. These experiments and results are only part of this work to give, firstly, a detailed overview of the whole work that I have done on microgel-polymer composite fibres, and, secondly, because a thesis can not be started in the middle of the results. Furthermore, most of this part of the thesis has been published in a peer-reviewed paper [70], written by me and also me being the first author of the paper. Nevertheless, the texts in this work have been rewritten.

2 Experimental Part

In the following sections the description of all syntheses and fabrication processes of the samples and materials, as well as the description of all experiments and analyses that have been done with these samples, are described in detail. All parameters of the experiments will be defined and explained. First mentioned will be the materials used, followed by the microgel synthesis and the description of the electrospinning. Afterwards the various analysis methods will be specified.

2.1 Materials

Poly(vinyl alcohol) (PVA, MW=146.000-186.000 g/mol, 98-99% hydrolysed, Sigma-Aldrich), 2,2'-Azobis[2-methylpropionamidine] dihydrochloride (AMPA, 97%, Aldrich), N,N'-methylenebis-(acrylamide) (BIS, 99%, Sigma-Aldrich), 2-hydroxyethylacrylate (HEA, 96%, Aldrich), distilled water. All these materials are used as delivered without having undergone any other cleaning procedures. 2-(methacryloyloxy)ethyl acetoacetate (AAEM, 95%, Aldrich) and methacryloyl chloride (97%, Aldrich) have been purified from stabilisers before use. N-Vinylcaprolactam (VCL, 98%, Aldrich) was purified by vacuum distillation under nitrogen before use.

2.2 Microgel Synthesis

The synthesis of VCL/AAEM and VCL/AAEM/HEA-microgels was performed on the basis of previous works [30, 21]. The reaction was set in a double-wall glass reactor equipped with a stirrer, reflux condenser and was purged with nitrogen. The monomer solution was added into the reactor and stirred for 8 h at 70 °C, the initiator (0.05 g (0.268 mmol)) was added after 20 min, when all monomers were dissolved. The microgel dispersions were purified for 72 hours by dialysis (Millipore Labscale TFF System). The recipes for the various microgels synthesised are presented in Table 1.

Table 1: Ingredients used for the microgel synthesis

Sample	VCL [g] (mmol)	AAEM [g] (mmol)	HEA [g] (mmol)	BIS [g] (mmol)	AMPA [g] (mmol)	Water [g]
VCL/AAEM	1.874 (13.46)	0.341 (1.59)		0.06 (0.38)	0.05 (0.26)	150
VCL/AAEM/HEA(1%)	1.853 (13.31)	0.338 (1.57)	0.017 (0.14)	0.06 (0.38)	0.05 (0.26)	150
VCL/AAEM/HEA(3%)	1.805 (12.96)	0.331 (1.54)	0.052 (0.44)	0.06 (0.38)	0.05 (0.26)	150
VCL/AAEM/HEA(5%)	1.779 (12.78)	0.324 (1.51)	0.087 (0.74)	0.06 (0.38)	0.05 (0.26)	150

2.3 Preparation of Spinning Solutions

The spinning solutions are based on aqueous PVA solutions of 6 wt%. Freeze-dried microgel powder is added in various amounts/ratios to these solutions. The mixtures are stirred with a magnetic stirrer until a homogenous solution is achieved (approximately 2-3 hours). The variations of the microgel/polymer ratios that have been prepared are summarized in table 2.

2.4 Fibre Fabrication

The aperture used for the fibre fabrication was a horizontal set-up consisting of an Eltex KNH34 generator, an automatic syringe pump (Al 6000-20Z World Precision Instruments) and 1 mL disposable syringes with metal tip cannulas (0.8 mm diameter). Depending on the subsequent experiments aluminium foil or glass specimen served as targets. The parameters varied during the fabrication process were the target distance, the applied voltage, and the flow rate through the syringe.

2.5 Fibre Crosslinking

The crosslinking of the fibres to prevent them from dissolving in water was tried using different methods. For example by adding a photo-crosslinker or by modifying the PVA with methacryloyl groups. In the following sections only the two methods that have shown to be successful will be described as they will also be part of the results.

2.5.1 Physical Crosslinking

Physical crosslinking was achieved by a combination of a drying process in a vacuum drying oven and heat treatment. The fibres dry 4 hours in the vacuum drying oven until they reach constant weight; afterwards they are put into an oven at 155 °C for 10 minutes.

2.5.2 Chemical Crosslinking

Figure 9 shows the idea of a chemical crosslinking reaction. The procedure is based on the reaction of the hydroxyl groups which are available both in PVA and microgels (HEA) with methacryloyl chloride. Afterwards a temperature induced reaction of vinyl groups will form covalent bonds. In this way microgels and PVA chains become crosslinked with each other and with themselves. This crosslinking experiment was typically done with 0.5 g of fibre material which was immersed into pure methacryloyl chloride (1.5 g) at 75 °C for 30 minutes. The reaction temperature in the oven was 120 °C for 10 minutes. The crosslinked fibres were cleaned by washing with water for 4 cycles to remove non-reacted methacryloyl chloride and other by-products.

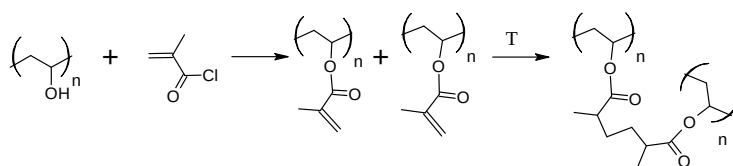


Figure 9: Assumed mechanism for the polyvinyl alcohol crosslinking with methacryloyl chloride

2.6 Characterisation Methods

In this section the characterisation methods and analyses of the samples are described. They are both described in general and in specific details for these samples. In the later parts of this thesis this section will be reduced to the specific details, for general information a reference will be made to this section.

2.6.1 Dynamic Light Scattering (DLS)

DLS measurements have been carried out with an ALV/LSE-5004 Light Scattering Multiple Tau Digital Correlator and Electronics with the scattering angle set at 90° . Size measurements at 15°C as well as temperature dependent size measurements (from 10°C to 60°C) have been done. The temperature fluctuations were below 0.1°C . Two droplets of the microgel sample diluted with doubly distilled water (2 mL) were used for these measurements.

2.6.2 Atomic Force Microscopy (AFM)

AFM images were taken with a Dimension Atomic Force Microscope icon ScanAsyst. Nanoscope 8.10 (Build R1.60476) software and OTESPA cantilevers with resonance frequencies of 284-338 kHz and spring constants of 12-103 N/m were used. The deposition of the microgels was done by spin coating on a silicon wafer and the investigation took place in dry state.

2.6.3 Field Emission Scanning Electron Microscopy (FESEM)

A Hitachi FE-SEM S4800 was used to analyse the fibres. Samples were cut out of the aluminium target and used without further preparation (for example sputtered with gold) after the electrospinning.

2.6.4 Rheology

Rheological measurements of the spinning solutions were carried out on a Rheometric Scientific DSR with plate/plate geometry. The lower plate was connected to a temperature control device and set to 20°C . 1 mL for each sample was placed in the instrument.

2.6.5 Thermo Gravimetric Analysis (TGA)

The instrument used for TGA measurements was the TG 209c by Netzsch. It was used to determine the degree of swelling; the amount of water the fibres are able to take up. The samples have been placed in water to swell isothermally (at 25 °C and 50 °C, respectively) until equilibrium. Afterwards they were wiped with dust-free paper to remove any water that is attached from the outside to the nonwoven fibre network. The measurements were run in alumina crucibles with 2 K/min under nitrogen draft of 20 mL/min in a temperature range from room temperature to 150 °C. The measured mass loss was used to calculate the degree of swelling according to the equation: $Q = \frac{F - F_d}{F_d}$, where F is the weight of the swollen fibres and F_d the weight of the dry fibres.

2.6.6 Differential Scanning Calorimetry (DSC)

The instrument used was a DSC 204 by Netzsch. It was used to make the temperature depending transition of the microgels visible and to investigate in this way if the volume change of the microgels at the VPTT still takes place in the fibres. The samples were weighted and placed in aluminium pans. 50 μ L of D_2O was added before the pans were closed. An empty aluminium crucible was used as reference. The nitrogen draft to wash the pans was 20 mL/min. Cycles of heating-cooling-heating between 10 °C and 60 °C were done with a rate of 2 K/min.

2.6.7 Water Adsorption/Desorption

Water sorption/desorption measurements have been done using an isothermal gravimetric moisture sorption analyser (IGAsorp) (Hidden Analytical). They were performed at 25 and 50 °C respectively. The device is based on a gravimetric controlled analysis of moisture sorption which takes place in a controlled humidity chamber at a constant temperature. Fibre samples are placed in the sample holder and the humidity inside the chamber increases/decreases stepwise (each step 10% up to 95% and back to 5%; equilibration time for each step is 60 minutes). Their changing weight by absorbing/desorbing the moisture is continuously measured. The device provides isothermal kinetic data (mass or humidity change per time). This data, especially the slope between the single steps, is used to calculate the adsorption or desorption rates. Rate constants k of a first order sorption/desorption kinetics were determined by plotting $-\ln(1 - \alpha)$ versus sorption time t ($\alpha = \frac{m_t - m_{t=0}}{m_{max} - m_{t=0}}$) with m_t being the weight of the fibre at time t , $m_{t=0}$ the weight of the fibre at $t = 0$ and m_{max} the weight of the fibre at equilibrium.

2.6.8 Raman Spectroscopy

Small amounts of freeze-dried microgels were measured with a Bruker RFS 100/S. Raman spectroscopy was chosen for this samples instead of infrared spectroscopy, because the signal of the small amount of HEA was overlaid by VCL and especially the similar AAEM in the infrared spectra. Raman spectroscopy offered the possibility to see the double bond present in HEA and therefore distinguish it from the other components.

2.6.9 Infrared Spectroscopy (IR)

Infrared spectroscopy was performed on a Thermo Nicolet Nexus 470 Fourier transform infrared spectrometer. The dried samples have been embedded in a Potassium bromide matrix before measuring.

2.6.10 Toxicity Tests

To test the toxicity of the fibres a CytoTox-ONETM Homogeneous Membrane Integrity Assay by Promega was used. This test gives first hints of the biocompatibility of the new material or better said the new material combination. An detailed description of this test can be found in [71].

3 HEA Modified Microgels

Due to the reasons mentioned in the introduction of this part of the thesis, PVA was chosen to be the first matrix polymer for the fabrication of microgel/polymer composite fibres. Since PVA is water soluble it was clear from the beginning that the later achieved fibres would need to be stabilised against water for any possible application. Therefore, the idea came up to modify the standard VCL/AAEM microgels with hydroxyl ethyl acrylate (HEA), which is chemically close enough to AAEM that no bigger changes in the synthesis need to be expected, and provides additionally hydroxyl groups. Hydroxyl groups are also present in the PVA and thus made it reasonable that any OH based crosslinking reaction of the PVA would also include the OH groups of the microgels. 1, 3 and 5 mol% of HEA were copolymerised with VCL and AAEM in a precipitation polymerisation, like it is described in 2.2, based on previous works [30, 21]. The obtained microgels were monodisperse and stable. In Figure 10A an AFM micrograph and in 10B a FESEM micrograph of microgels with 5 mol% HEA are shown; their monodispersity is clearly visible.

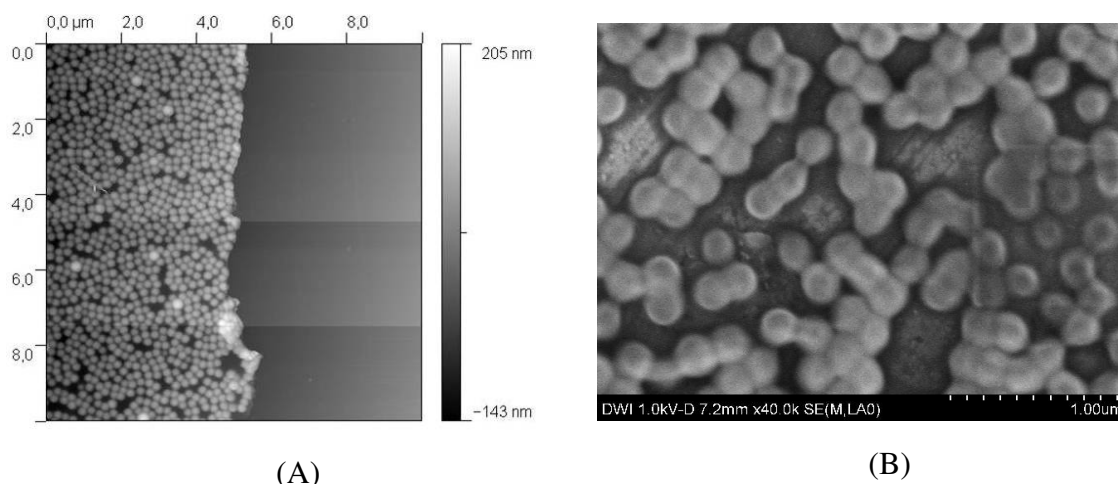


Figure 10: AFM micrograph (A) and FESEM micrograph (B) of microgels with 5 mol% HEA

The examination of the pictures shows that the microgels have a diameter of around 150 nm in dried state. In their water swollen state the diameter is more than twice this size, around 380 nm, the hydrodynamic radius is 190 nm. This was measured by DLS at 15-20 °C. The R_h is also depending on the HEA content in the microgel. DLS measurements that show this fact are shown in Figure 11 A. With increasing HEA content the microgel radius decreases. It was shown that microgels with increasing amounts of AAEM show the same trend. VCL/AAEM microgels show a core-shell structure with AAEM mainly in the core and VCL mainly in the shell. AAEM is more reactive than VCL and therefore forms the core; with higher amounts of AAEM the core gets more and more dense and the microgel particle gets smaller and its degree of swelling decreases. The latter is also due to the higher hydrophobicity of AAEM

compared to VCL. Since HEA has a similar chemical structure and is an acrylate like AAEM it should cause the same effect. The difference between the two microscope measurements and the DLS results comes from the fact that the microgels are swollen in water during the DLS analysis. At 15 °C they are in swollen state, and even at 50 °C, which is above the VPTT and the microgels are in the collapsed state, they still contain a residual amount of water. That is why they show bigger radii than in the completely dry state, which can be seen in the microscope analysis.

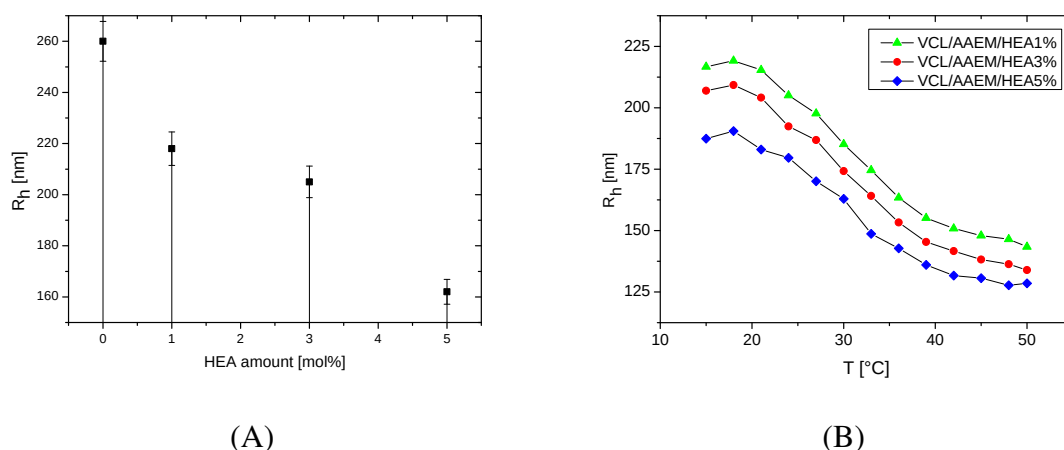


Figure 11: Size dependency of the microgels with the HEA content (A); temperature trend measurement of microgels with different amounts of HEA (B)

Figure 11 B shows temperature dependent DLS measurements. The hydrodynamic radius is measured at different temperatures to show the thermo-responsive behaviour of the microgels. The inflection point of this graph marks the VPTT. The VPTT of all microgels with HEA was determined to be 32-33 °C, which is also the VPTT of pure VCL microgels. The inclusion of HEA in the microgels does not influence the VPTT.

To prove the incorporation of HEA into the microgels, spectroscopic methods (infrared and Raman) have been used. The identification of HEA in the VCL/AAEM/HEA microgels proved slightly problematic, since AAEM and HEA are both acrylates and have a similar chemical structure and the big amount of VCL additionally overlays many of their signals. The unique OH group of HEA in this system could also not be used, because the microgel is hydrophilic and binds even in dry state to water molecules from the air, making it impossible to see the OH band in the spectra. Therefore, the identification of HEA was only successful in an indirect way. Figure 12 shows the Raman spectra of microgels with 0, 5 and 10 mol% HEA (A) and a zoom of these spectra in the region of the carbonyl band (B). It is shown that with increasing amount of HEA the intensity of the carbonyl band also increases. The amount of AAEM in the

microgels with increasing HEA is indeed decreasing but the total ratio of the carbonyl bonds in relation to the VCL is increasing, therefore the increasing amount of HEA in the microgels is indirectly proven.

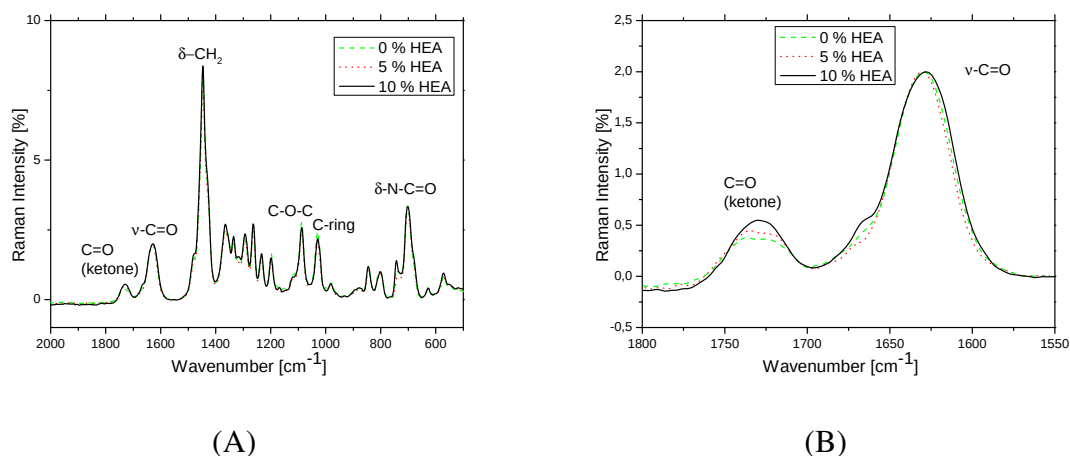


Figure 12: Raman spectra of VCL/AAEM/HEA microgels with 0, 5 and 10 mol% (A); zoom at the carbonyl band of these spectra (B); the increasing intensity with an increasing amount of HEA is observable

4 Fibre Fabrication

In the following sections the fabrication procedure of homogenous and reproducible microgel/PVA composite fibres via an electrospinning process is described in detail. Like mentioned before, the process depends on a variety of parameters, most notably the viscosity of the spinning solutions, the general composition of the spinning solutions and process parameters like the flow rate or the target distance. All these influences will be addressed and it will be shown that fibres of good and reproducible quality can only be obtained by using a certain set of parameters. The pictures shown in this section are all from fibres prepared with this set of parameters, which is as follows: microgel/polymer ratio of 70:30 wt%, target distance of 16 cm, applied voltage of 30 kV and flow rate of 1 mL/h.

4.1 Viscosity of the Spinning Solutions

The Viscosity of the spinning solutions is of great importance for the whole process. This can easily be seen by taking a look at two possible “extreme” situations. If the viscosity is too low the process will be more like elctrospraying than spinning and no fibre formation occurs. If the viscosity is too high no Taylor cone can be formed and the process does not even start; and all kinds of intermediate states are also possible. In a simple polymer solution the viscosity can be adjusted by using a certain amount of polymer that gives good conditions for the process. The system used in this work is more complicated in the way that two different polymers, a linear one and a coil, particle like one is used, whereas the latter one is also swellable and deformable in the solvent. To understand the used system rheological investigations have been undertaken. Figure 13 shows the results of these measurements. The first observation to be noted is that pure solutions of the linear polymer, PVA, and the globular polymer, microgel, show completely different behaviours. The PVA solution (6 wt% in water) shows a Newtonian behaviour: The viscosity is not changing with the shear rate. The microgel solutions (22 wt% in water) show a shear thinning behaviour: The viscosity decreases with increasing shear rate. This shear thinning behaviour was also observed for PNIPAAm microgels [72, 73]. Explanations for this behaviour are on one hand that the microgels are soft and will be deformed to an anisotropic form (ellipsoidal) at higher shear rates, showing the same effect like red blood cells for example. On the other hand water can be pressed out of the water swollen microgels, which will also lower the viscosity.

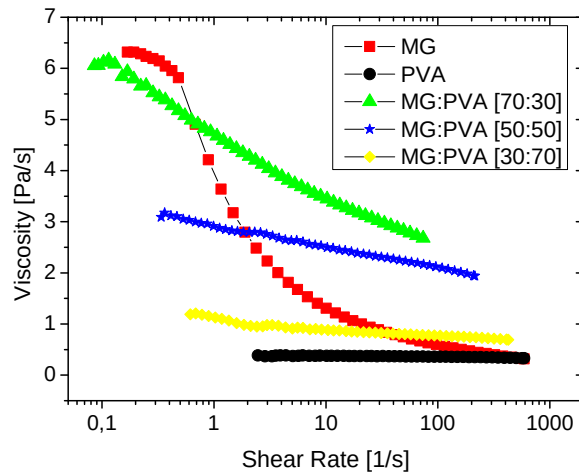


Figure 13: Viscosity of different microgel/polymer solutions. The shear thinning behaviour of the microgels gets more and more dominant in the spinning solutions with increasing microgel content.

The mixtures of PVA and microgels show rheological properties that can be seen as a mixture of the two components. With an increasing amount of microgels in the solutions the starting viscosity also increases, but also their shear thinning property becomes more obvious. These results have to be taken into account in other experiments, because the shear thinning behaviour will have an influence on other parameters. For example higher flow rates would generally increase the fibre diameter since more material gets transported through the jet, but higher flow rates also increase the shear rate and thus decrease the viscosity (for samples with microgels), which would lead to smaller fibre diameters.

4.2 Fibre Formation

The fibre formation is mainly depending on the materials in the spinning solution and the solution's properties. The process parameters which will be addressed in the next section are more related to the fibre diameter and the continuity of the process. The solutions in this case consist of three materials: Water, PVA and microgels. 6 % of PVA in water was chosen to be the basic solution for this fibres, because fewer amounts of PVA and water are not viscous enough to form fibres and higher amounts will already have a viscosity that would be too high, after the microgels are added. Nevertheless, also solutions without any PVA have been tested, to explore the possibility of fabricating pure microgel fibres. Figure 14 shows the results of

spinning attempts from solutions with an increasing amount of PVA (a-d). Without any PVA in the spinning solutions no fibre formation takes place. Not even at a microgel content of 22 wt%; above the solutions become too viscous. To form fibres via electrospinning the polymers have to entangle with each other. Linear polymers of high enough molecular weights are able to do this, but the microgels seem not to be able to perform this entanglement, since they have a globular form and their chain length is not sufficient.

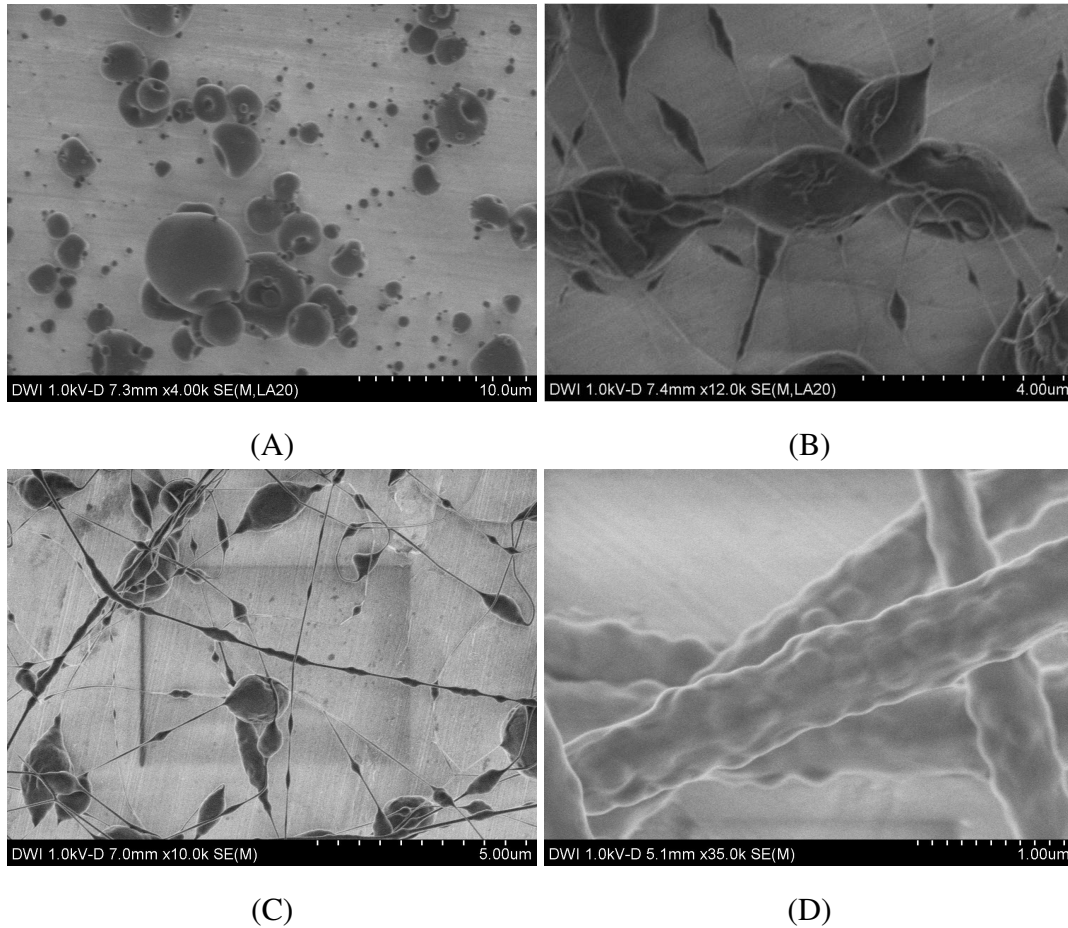


Figure 14: Results of fibre fabrication with increasing PVA content (A) 0 wt%, (B) 10 wt%, (C) 20 wt%, (D) 30 wt%; homogenous fibres can be achieved with a microgel content of 30 wt%

Already with 10 wt% PVA the fibre formation partially takes place (Figure 14B), big microgel beads are connected by small PVA fibres. The structures get more and more fibre like with an increasing amount of PVA, and at a ratio of 30 wt% PVA and 70 wt% microgels homogenous composite fibres are formed (Figure 14D). The microgels are clearly visible in the fibres, which also makes the fibre surface rough in comparison to pure PVA fibres. Even higher

polymer concentrations can also lead to a fibre formation, but the formed fibres are not as homogenous or the microgels are not spread as homogeneously through the fibres as in the fibres with 30 wt% PVA. This can be seen in Figure 15. 15A shows fibres with a microgel/polymer ratio of 50:50. A fibre with evenly distributed microgels is presented in the center, but in the upper left corner a fibre without microgels is to see. Additionally an inlay shows a rope of pearls like structure of microgels and PVA which was found in the same sample. Figure 15 shows a sample with a microgel/polymer ratio of 30:70, where there are noticeable also fibres without microgels and a fibre in the centre with microgels only at the surface. Both examples reveal again that only a specific ratio leads to a homogenous and reproducible fibre quality.

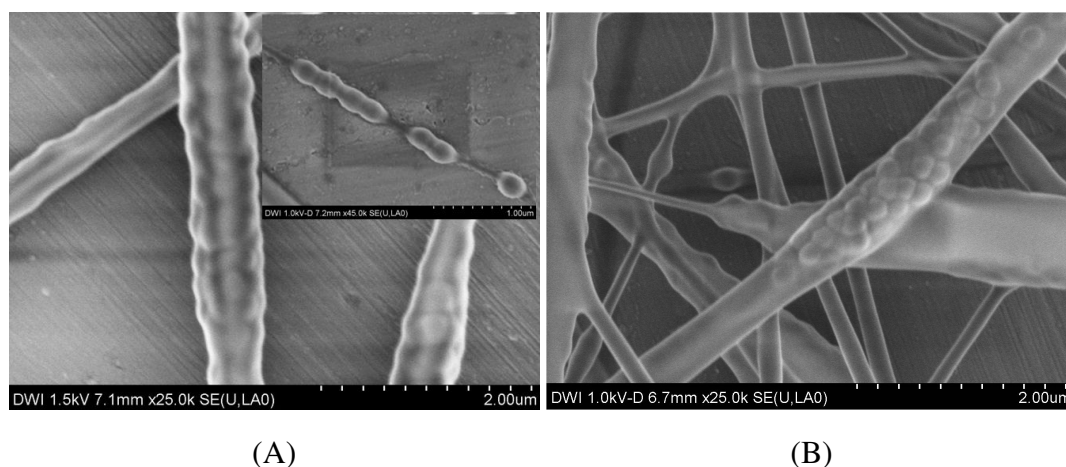


Figure 15: Fibres with a microgel/polymer ratio of 50:50 (A); fibres with a microgel/polymer ratio of 30:70 (B); fibres deviating from the 70:30 ratio show a less homogenous morphology

In Figure 16 pure PVA fibres (A, C and E) are compared with composite fibres with a microgel/polymer ratio of 70:30 (B, D and F). A and B show the fibre nonwoven at relatively low magnifications to emphasise the homogenous fibres. C and D show pictures of single fibres at higher magnifications, to show the different morphology: PVA has a smooth surface; the microgel fibres are rougher due to the clearly visible microgels. E and F show cross-sections of the fibres. These cross-sections have been done by freezing the nonwoven in liquid nitrogen and cutting them with a razor knife. The cuts were scanned with the FE-SEM until a spot was found where the fibre interior was revealed. PVA fibres show a homogenous interior, since they consist just of one material. Figure 16F shows that the microgels are distributed through the whole fibre diameter. The microgels are not only located close to the surface, they are evenly distributed in a PVA matrix and therefore forming a more porous structure. This morphology results from the phase separation that takes place during the solidification process. The matrix-like structure, one phase is dispersed in the other, can often be found in systems with binodal segregation [57]. Binodal segregation can usually only be found in a narrow range of

the ratios of the materials; it is strongly depended on the phase ratios. If the ratio is not in that particular range or the mixture is not homogenous, the segregation will not take place or at least not in the entire sample.

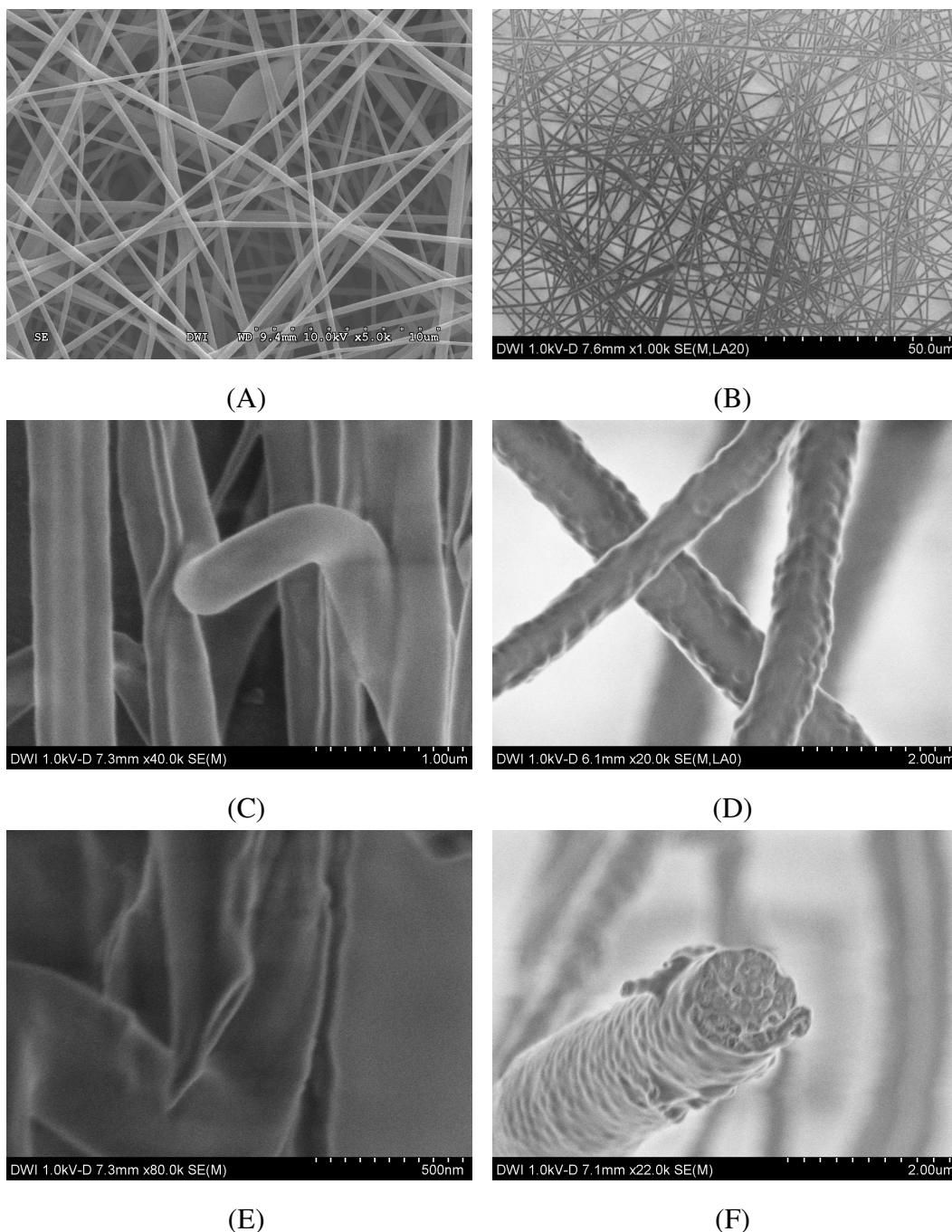


Figure 16: Comparison of PVA fibres (left) with PVA-microgel fibres with a MG:polymer ratio of 70:30 (right)

A concluding remark for this section is that fibres of a homogenous and reproducible quality can only be obtained at the specific microgel/polymer ratio of 70:30 wt%.

4.3 Influence of the Process Parameters on the Fibre Formation

In this section the influence of the process parameters, namely the flow rate, the target distance, the voltage and the diameter of the cannula are investigated. These parameters should not have a general influence on the fibre morphology, but they influence the process in its homogeneity and continuity; moreover they can change the fibre diameter. Table 2 shows the variations that have been done and their results. To be able to compare these results all variations have been made with a spinning solution with a microgel/polymer ratio of 70:30 wt% (compare with section 4.2, part III). With an increasing target distance the fibre diameter is decreasing. This can be expected since a longer way to the target increases the elongation time, the time in which the whipping instabilities can influence the fibres. Nevertheless, the influence is not big, since a tripled distance only reduces the diameter by 50 nm. The applied voltage does not show a recognisable influence, likewise does the diameter of the cannula. The parameter that shows a big influence is the flow rate. In theory with an increasing flow rate more material is pushed into the jet and therefore the fibre diameter is supposed to increase. Comparing a low flow rate of 0.1 mL/h to 1 mL/h the diameter increases like expected, but at a flow rate of 5 mL/h the diameter is decreased and at 8 mL/h it is increased again in comparison to 5 mL/h, but still smaller than at 1 mL/h. This shows an effect that was mentioned already in section 4.1, or better to say shows two competing effects. The viscosity of the solutions is reduced with increasing shear rates and increasing shear rates are caused in this case by higher flow rates. Therefore, increasing flow rates will lead to smaller diameters, since decreasing viscosities have this effect. But increasing flow rates will also push more material into the jet and therefore cause bigger diameters. The two effects compete in their influence on the fibre diameter, which leads to the non linear results for the fibre diameter with increasing flow rates.

Table 2: Influence of the electrospinning parameters on the fibre diameter

Sample	Target distance [cm]	Voltage [kV]	cannula diameter [mm]	Flow rate [mL/h]	Fibre diameter [nm]
PVA 6 wt%	16	30	0.4	1	240
MG:PVA [70:30]	16	30	0.4	1	788
MG:PVA [70:30]	8	30	0.4	1	803
MG:PVA [70:30]	24	30	0.4	1	748
MG:PVA [70:30]	16	15	0.4	1	760
MG:PVA [70:30]	16	20	0.4	1	780
MG:PVA [70:30]	16	30	0.8	1	772
MG:PVA [70:30]	16	30	0.4	0.1	572
MG:PVA [70:30]	16	30	0.4	5	392
MG:PVA [70:30]	16	30	0.4	8	489

The set of parameters that fabricates the most homogenous and best reproducible fibres is, as mentioned before, the following: microgel/polymer ratio of 70:30 wt%, a target distance of 16 cm, an applied voltage of 30 kV and a flow rate of 1 mL/h. All characterisation shown below is made with fibres prepared with this set of parameters.

Like it was shown in chapter 3 the size of the microgels depends on the HEA content. The size of the microgels could also have an influence on the fibre diameter, therefore fibres with the mentioned parameter set and microgels with 0, 3 and 5 mol% of HEA were prepared, but no influence is determined (Table 2). All fibres used in the chapters below have been prepared with microgels with 3 mol% of HEA.

5 Fibre Crosslinking

PVA is a water soluble polymer and therefore the PVA based composite fibres are also water soluble. In contact with water the PVA matrix will disintegrate and the microgels will be set free into the surrounding medium. This will happen in a few minutes. Figure 17 shows how some of the microgels are still bound in some residual PVA on the aluminium target. This quick dissolution of the fibre structure is counterproductive for any possible application, which is why the fibres have to be crosslinked. Additionally the crosslinking is needed for further analyses like the degree of swelling or the water adsorption. Different ways to crosslink the fibre have been tried, for example a modification of the PVA with methacryloyl groups or a reaction with divenylylsulfon, which is commonly used to crosslink PVA hydrogels. In the two following sections two succesful procedures are presented.

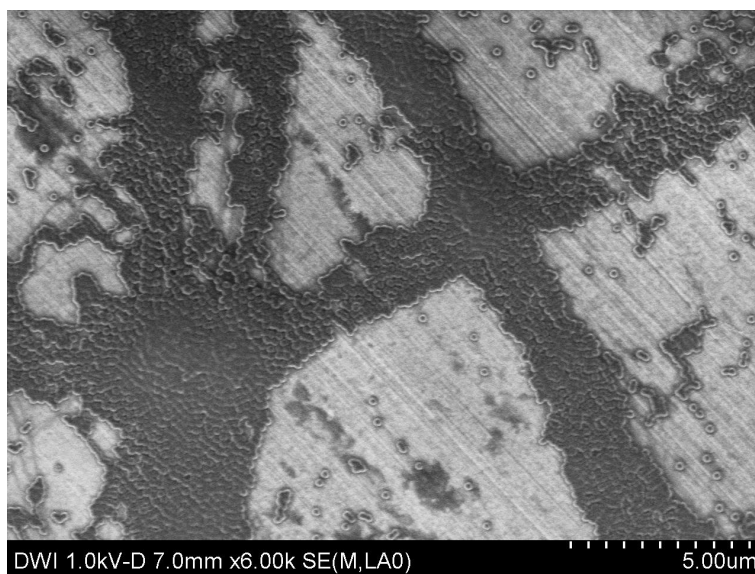


Figure 17: PVA-microgel fibres after contact with water. The PVA dissolved and microgels stick to the sample holder surface

5.1 Physical Crosslinking

After some draw backs in the chemical crosslinking methods, physical crosslinking has been explored and shown to be successful. Generally heat treatment is a well known method to stabilise pure PVA fibres in water [74, 75, 76]. An explanation for the stabilisation due to heat treatment is that the fibres undergo physical crosslinking due to a rearrangement of the polymer chains, crystallisation and decrease of the interplanar spacing of the (100) plane. The heat treatment removes any residual water in the fibres and the structural changes occur.

This leads to more intermolecular hydrogen bonds, which will not break later when the fibres swell again with water, ensuring that no fibre dissolution occurs [75, 76]. A literature value that shows good results for macroscopic PVA fibres is a temperature of about 235 °C. The microgel fibres with a diameter of about 780 nm are not stable at such high temperatures, but PVA nanofibres are shown to be physically crosslinked at temperatures close to 150 °C and a treatment time of 10 minutes [77, 78]. For the composite fibre this treatment does not work, since the microgels can also be seen as defects in the PVA matrix, which prevent the matrix from higher crystallisation rates, that are needed for the stabilisation against water. Additionally the residual water that is brought into the fibre structure by the microgels, even in their dried state, might not be totally removed during the 10 minutes of treatment. This water would then increase the interplanar spacing and hinder the PVA chains from forming hydrogen bonds with each other, making the crosslinking not effective. An extended increase of the treatment time would damage the fibres and it is not an option to solve this problem. Therefore, the fibres were dried in a vacuum drying oven until constant weight was reached, followed by the heat treatment in the oven at 150 °C for 10 min. The combination of 4 hours drying at moderate temperature with a heat treatment of 10 minutes at 150 °C achieves the stabilisation of the microgel fibres against dissolution in water. The theory behind this physical crosslinking is also confirmed by the crystallinity of the fibres, which was calculated from DSC measurements. It is 0.12 for fibres without the drying step in the vacuum oven and 0.53 with the drying step. The latter is a value known in literature for water stable PVA fibres [79]. Figure 18 shows fibres, which are physically crosslinked by the above described treatment after 72 hours of immersion in 60 °C warm water. The fibres show some changes in their morphology due to the swelling and softening, but the general fibre structure is retained.

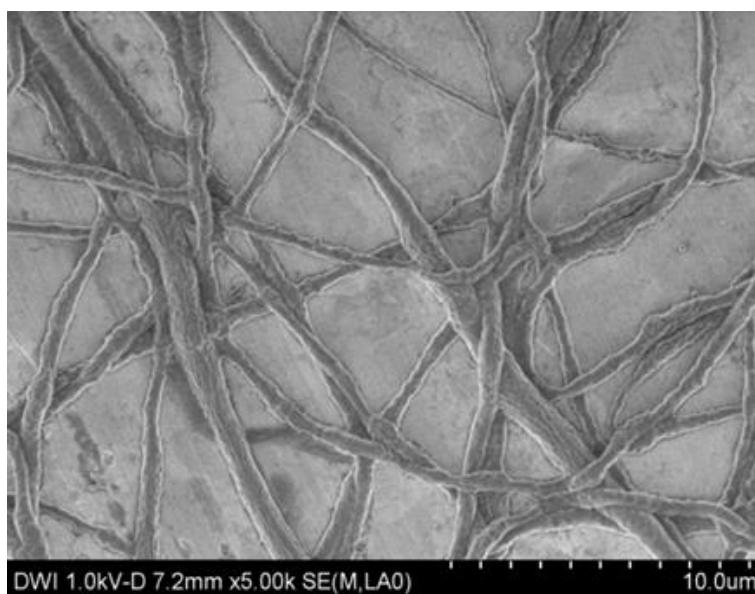


Figure 18: Physically crosslinked microgel fibres after 72 hours immersion in water (60 °C), the fibre structure is still intact

5.2 Chemical Crosslinking

As it is mentioned above, the first tries for a chemical crosslinking of the fibres were not successful. The method that was developed and proved to be successful (described in section 2.5.2) was a reaction of the available OH groups in both the PVA and the microgels due to the use of HEA as co-monomer, with methacryloyl chloride, see also Figure 9. Figure 19 shows the chemical crosslinked fibres after 72 hours of immersion in water at 60 °C. The fibres show, similar to the physically crosslinked ones, some change in morphology mainly due to softening, but retain basically their fibrous structure.

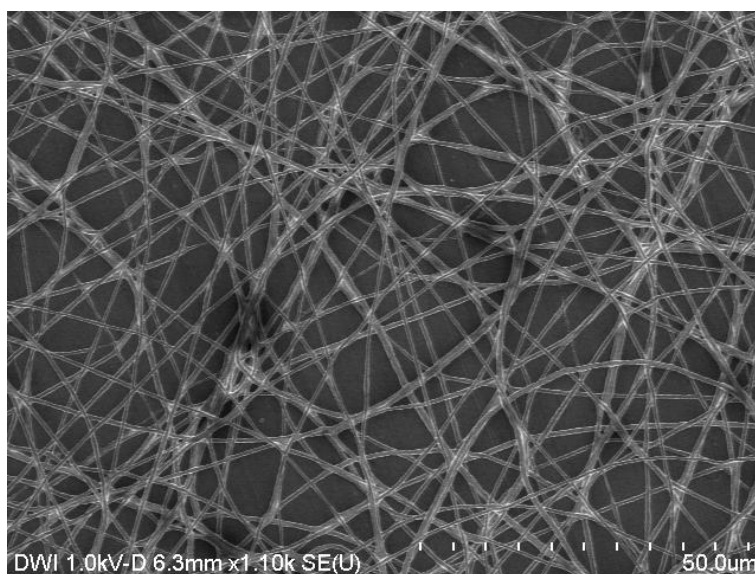


Figure 19: Chemically crosslinked microgel fibres after 72 hours immersion in water (60 °C), the fibre structure is still intact

To prove the crosslinking reaction IR-spectroscopy was used. This investigation was not possible for the fibres themselves, due to the strong overlap of the PVA and the microgel signal in the spectra. An investigation like this was also not possible for the microgels, because the amount of HEA and therefore the low amount of OH groups in the microgels only is not sufficient for a successful crosslinking reaction. Therefore PVA films without microgels have been used as replacements. The reaction was done in the same way as for the fibre samples. Figure 20 shows IR spectra of untreated PVA (A), PVA reacted with methacryloyl chloride (B), and the film after the heat treatment (C). The specific peaks of methacryloyl chloride are observable in the spectra after its addition. Most notable are the C=O bond that appears at 1820 cm^{-1} , which represents the not reacted methacryloyl chloride, and the peak of the C=O bond next to the C-O-C group at 1700 cm^{-1} , which makes the connection to the PVA chain.

The C=C double bond of the methacryloyl chloride appears at 1643 cm^{-1} . After the heat treatment, which removes/evaporates the not reacted methacryloyl chloride, only the C=O signal at 1700 cm^{-1} is observable to prove this fact. Furthermore, the signals of the C=C double bonds are gone, indicating that the crosslinking was successful. This proves that PVA and the PVA-microgel fibres can be crosslinked by this esterification with methacryloyl chloride followed by a thermal induced crosslinking. Moreover, it is reasonable to believe that the OH groups of the HEA modified microgels also take part in this reaction and the microgels become covalently bound into the PVA matrix.

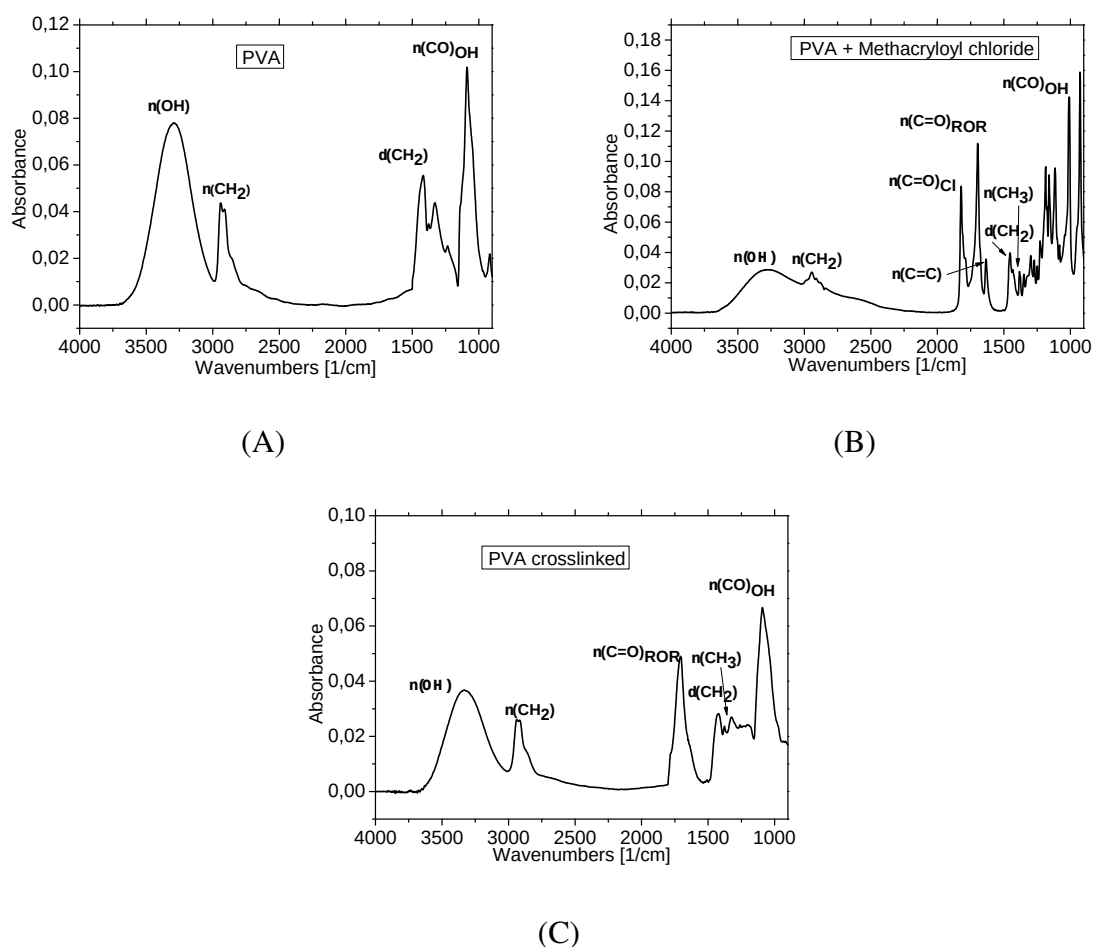


Figure 20: IR spectra of PVA (A), PVA with methacryloyl chloride (B) and PVA crosslinked with the methacryloyl chloride (C)

This reaction could be refined for example by the adjustment of the methacryloyl chloride concentration and with it the crosslinking density could be controlled, but it is in any case more laborious than the physical crosslinking and it adds a possibly toxic component to the

system. Furthermore, the degree of swelling of the chemically crosslinked fibres was measured to be lower than the one of the physically crosslinked fibres (3.9 to 5.9; compare chapter 6, part III). This reduction of the degree of swelling might be caused by a higher crosslinking density in the chemically crosslinked fibres, where an additional physical crosslinking could occur in the evaporation step. All these reasons led to the decision to focus on the physically crosslinked fibres and to continue the further analysis with these fibres. Nevertheless, the availability of this chemical crosslinking method might also be valuable for some applications.

6 Fibre Characterisation

Since PVA is a well known and often used polymer for the fabrication of nanofibres, the characterisation of the newly achieved microgel/polymer composite fibres is basically focused on the advancements or changes introduced by the addition of the microgels. As it was already shown in the sections above the microgels influence the spinning process and the fibre morphology. The latter is influenced in the way that the fibre surface is not smooth but more rough. But the main attribute of the microgels is their thermo responsive swelling behaviour. DSC can be used to measure the volume phase transition of microgels; therefore it was used to evaluate the transition of the microgels inside of the microgel fibres. Experiments were done with three heating and two cooling cycles; the effect is endothermal at heating and is mirrored by an exothermal effect at cooling, proving the reversibility of the phase-transition. The data shown in Figure 21 were taken from the second heating cycles, since the first heating cycle often removes some residual stress from the samples. Only the region close to the VPTT is shown to make the generally small effect good visible. The curves clearly show that the thermo-responsive behaviour of the microgels is preserved in the PVA matrix from the fibre structure. Pure PVA fibres expectedly do not show any transition in that region, but the composite fibres reflect the behaviour of microgel particles.

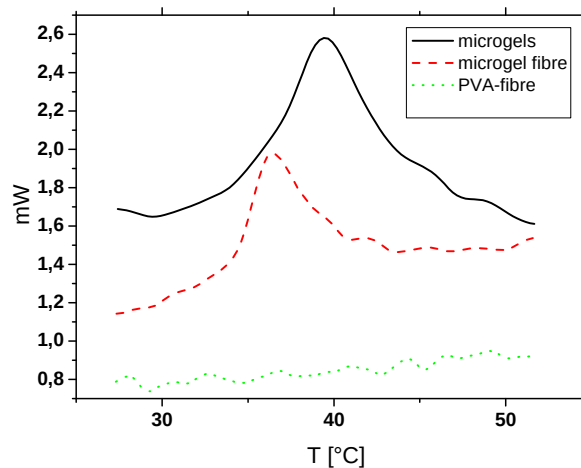


Figure 21: DSC measurements of microgels, PVA and PVA-microgel fibres. The volume phase transition is also observable in the composite material

The peaks indicate the VPTT and show in all cases a shift to higher temperatures compared to the 32 °C measured by DLS for these microgels (compare section 3, part III). These shifts have different reasons. For once D₂O was used in the DSC measurements, because it improves the recorded signals, due to stronger hydrogen bonds compared to H₂O [80]. Stronger hydrogen

bonds have a higher energetic barrier for breaking. A higher energy needed gives stronger peaks, but it also means a higher temperature needed, which induces the shift of the VPTT peak. Nevertheless, this effect would not explain the even further shifted peak of the pure microgels or the different on-set temperatures of the pure microgel (28.3 °C) and the composite fibres (26.6 °C). But this can be explained by the different morphologies: the microgels were freeze-dried before the measurement and therefore are closely packed and agglomerated; they will hinder themselves in dispensing the water. The microgels inside of the fibres are distributed in the PVA matrix and can dispense the water into some possible free space/free volume around them and into the soft and swellable PVA. The idea of some free volume around the microgel in the fibre matrix is based on assumptions and conclusions drawn from the results of the DSC, TGA and water sorption measurements and will be discussed more in the following paragraphs. The peak areas relate to the enthalpy of the transition. The value determined for the pure microgels is 6.1 J/g and for the microgel fibres it is 3.7 J/g. These differences reflect to some extent the microgel content in the samples, but it does not display the exact mass ratios. This is probably because the PVA matrix interacts with the microgels and overlays to some extent the transition.

The degree of swelling of the fibres was investigated by means of TGA. Figure 22 shows the results for the degree of swelling calculated from the TGA data. The measurements were done with samples that have been swollen in water at 25 °C (A) and above the VPTT, at 50 °C (B). Pure PVA fibres, pure microgels and composite fibres with 70 and 50 wt% were compared. It is shown that the composite fibres can uptake more water than either of the pure materials and a higher amount of microgels increases this effect further. Reasons for this are probably related to the inner morphology of the fibres. Since the microgels are “defects” or inclusions in the PVA matrix, it is assumable that some free volume exists around these inclusions. This diminutive free volume could be occupied by water molecules, leading to a higher degree of swelling. The assumption regarding the free volume is supported by the porous structure of the inner fibre (compare Figure 16 F) and the information from the water sorption analysis below. Furthermore this assumption is also supported by the TGA results at 50 °C. At 50 °C, which is above the VPTT, the microgels are in their collapsed, more hydrophobic state and will not absorb as much water as at temperatures below the VPTT. For the pure microgels the degree of swelling got nearly reduced to half, for the fibres the effect is not that distinctive. This decrease in the effect could be explained by the free volume, occupied by water independently from the volume phase temperature transition. Additionally, the free volume gets bigger, when the microgels shrink above the VPTT and can be occupied by more water, thus diminishing the decrease of the degree of swelling, as shown by the TGA data. The enlarging free volume compensates partially the loss in water absorption. In contrast to the composite fibres, the pure PVA fibres do not show any difference in the degree of swelling at different temperatures. Therefore the TGA results confirm the ones from the DSC in the fact that the microgels retain their thermo-responsive behaviour when incorporated in the fibre structure.

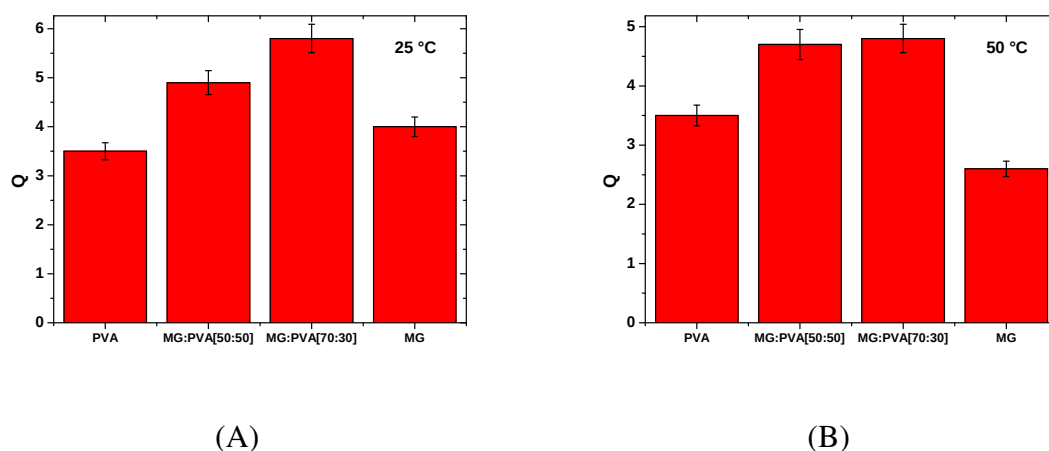


Figure 22: TGA measurements of PVA, microgel fibres with 70 and 50 wt% microgels at 25 °C (A) and 50 °C (B); the degree of swelling increases with the addition of the microgels

Besides the degree of swelling, moisture sorption is another important property of fibres and materials in general that are intended for medical applications. Moisture sorption kinetics can provide interesting information about materials in different environmental conditions. The water sorption analysis in this work was done with pure PVA fibres as well as with the microgel composite fibres (70 wt% microgels). Isothermal moisture sorption and desorption measurements at 25 and 50 °C were done, and the adsorption and desorption rates derived from the kinetic measurements are shown in Figure 23. The adsorption rate (Figure 23A) generally decreases with an increasing humidity. An increasing saturation of the fibres hinders further moisture uptake. Pure PVA fibres show independently on the temperature basically the same adsorption and desorption rates; as it is expected. In comparison to the PVA values the microgel fibres exhibit higher adsorption and desorption rates, by almost a factor of 4. This also indicates a more porous structure (compare Figure 16 F and the paragraph about the TGA results above). The assumed free volume around the microgels in the PVA matrix, which allows an easy occupation by water, is also again indicated. Moisture adsorption requires the breaking of polymer-polymer interaction and a creation of free volume for water molecules. Moisture desorption is antithetic to the adsorption process and is induced by the breaking of the polymer-water interactions and the formation of a denser structure. The results presented indicate that the increase of the moisture uptake and release in the composite fibres is enhanced compared to pure PVA fibres, due to the presence of the microgels. The adsorption as well as the desorption rates for the microgel fibres are much higher at 50 °C than at 25 °C. This can on one hand be explained by the Arrhenius dependency of the rate constant on temperature and on the other hand by the formation of a more open structure in the fibre interior due to the shrinkage of the microgels above the VPTT. At a humidity of 50-70 % the adsorption rates of

the microgel fibres show a significant increase, which was similarly observed for biodegradable polyester/polyether resins [81]. It can be assumed that the reason is a rearrangement of the internal fibre structure at this humidity towards a more open inner structure. After this increase the decrease due to the mentioned saturation and the change in diffusion continues.

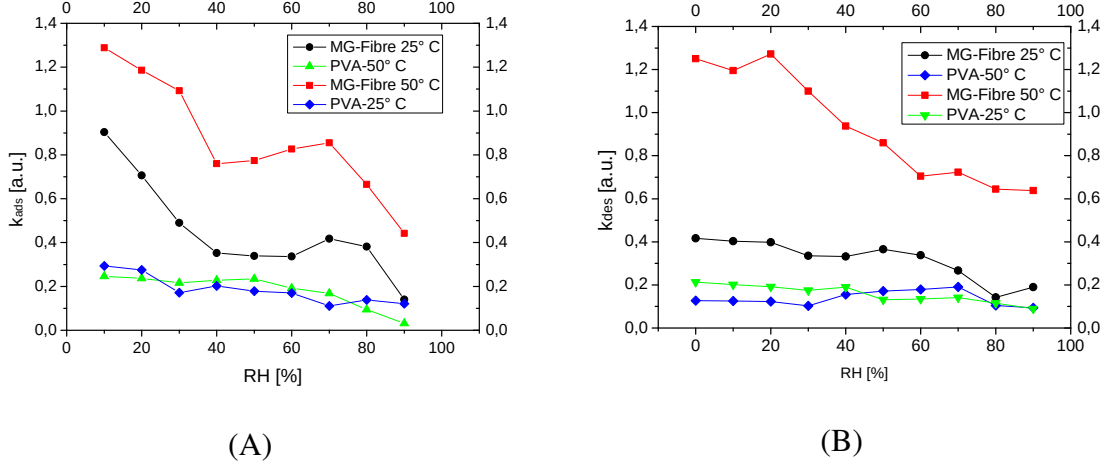


Figure 23: Water sorption measurements of pure PVA fibres and microgel fibres at 25 and 50 °C (RH = relative humidity); water adsorption (A) and water desorption (B)

The TGA results as well as the analysis of the kinetic moisture sorption data indicate some free volume around the particles and an opening of the inner structure, therefore the isotherm of the moisture sorption data was analysed by the method of Harkins and Jura [82, 83]. In this method the isothermal data is plotted according to the following equation:

$$\log \frac{p}{p_0} = B - \frac{A}{v^2} \quad (6.1)$$

$\frac{p}{p_0}$ relative pressure (relative humidity)

A, B constants

v the absorbed mass

A, the slope of the straight line given by this equation, is:

$$A = \frac{a10^{20}S^2V_M^2}{2RTN_a} \quad (6.2)$$

S specific surface area	R gas constant
V_M molar gas volume	T temperature
N_a Avogadro constant	a constant

A is related to the surface area coverable by moisture through $S = KA^{\frac{1}{2}}$, where K is a proportionality constant depending only on the adsorbate independently from the adsorbent [83]. For water moisture it is $K = 3.83$. The Method of Harkins and Jura can be used to determine the surface area of a material by fitting the isothermal data with the above given equations. Figure 24 shows an example of this plot for the PVA-microgel fibres at 25 °C. It is not possible to fit all data points with the Harkins-Jura equation with an acceptable accuracy at once. Therefore, two fits with two different values for A are needed to fit all data points accurately. The chosen lines represent the fits with the highest correlation coefficients (R^2). The intersection of the two lines represents the region of the relative humidity in which the adsorption behaviour changes (about 40 % in this example), since two lines with two different values of A also imply different surface areas: according to $S = KA^{\frac{1}{2}}$ the surface area changes with different values for A . This means that at a relative humidity of about 40 % the surface area of the PVA-microgel fibres increases from 155.1 m²/g to 488.38 m²/g (factor 3.1). This proves the indicated structural opening, leading to an increased moisture uptake in the following measurement steps (50-70 %).

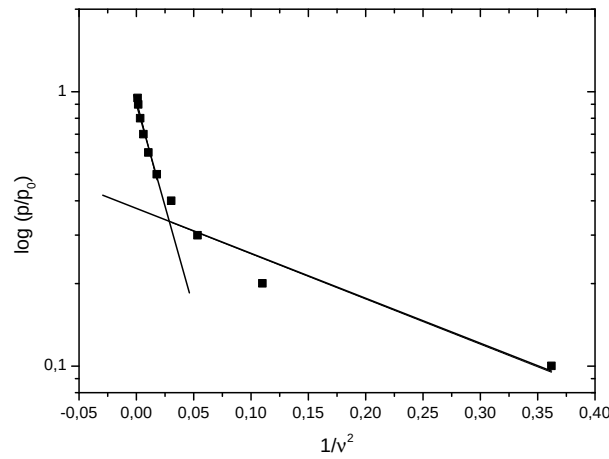


Figure 24: Harkins-Jura plot of the moisture adsorption isotherme of PVA-microgel fibres at 25 °C; the two regions indicate a change in the adsorption behaviour

In Table 3 the results for A and the surface area S for PVA and PVA-microgel fibres at 25 and 50 °C are shown. The structural change happens independently of the fibre type and

temperature, but at 50 °C the PVA-microgel fibres have a significantly higher difference in the surface area before and after the structural change. This is probably due to the collapsed, smaller, state of the microgels. However, the structural opening and the higher surface area can explain the increase in the moisture adsorption rate.

Table 3: Results of the Harkins-Jura plot for PVA-microgel fibres

Sample	A ₁	S ₁ [m ² /g]	R ²	A ₂	S ₂ [m ² /g]	R ²	$\frac{S_1}{S_2}$
PVA fibre [25 °C]	15.6	478.36	0.967	1.76	160.67	0.941	2.97
PVA fibre [50 °C]	16.1	485.97	0.970	1.79	162.04	0.939	2.99
PVA-MG-fibre [25 °C]	16.26	488.38	0.964	1.64	155.1	0.926	3.184
PVA-MG-fibre [50 °C]	11.26	406.4	0.969	0.76	105.58	0.934	3.849

As mentioned already several times, PVA was selected also because of its biocompatibility and non-toxic properties. To approve these properties for the new microgel/PVA composite fibres the CytoTox-ONETM Homogeneous Membrane Integrity Assay by Promega [71] was used. In this test dead cells will be identified by the release of lactate dehydrogenase from cells with damaged membranes (dead cells). More dead cells cause more released lactate dehydrogenase and therefore a higher measured fluorescence intensity. More dead cells obviously also indicate a higher toxicity. Figure 25 A shows the toxicity test for a microgel solution and Figure 25 B shows the test for the microgel fibres. Intentionally damaged cells as control value (positive control) and a value for a known non-toxic medium (negative control) are shown in both cases. Both samples demonstrate that the materials do not show toxicity in the applied test. Therefore it can be said that the microgels do not reduce the biocompatibility of the PVA.

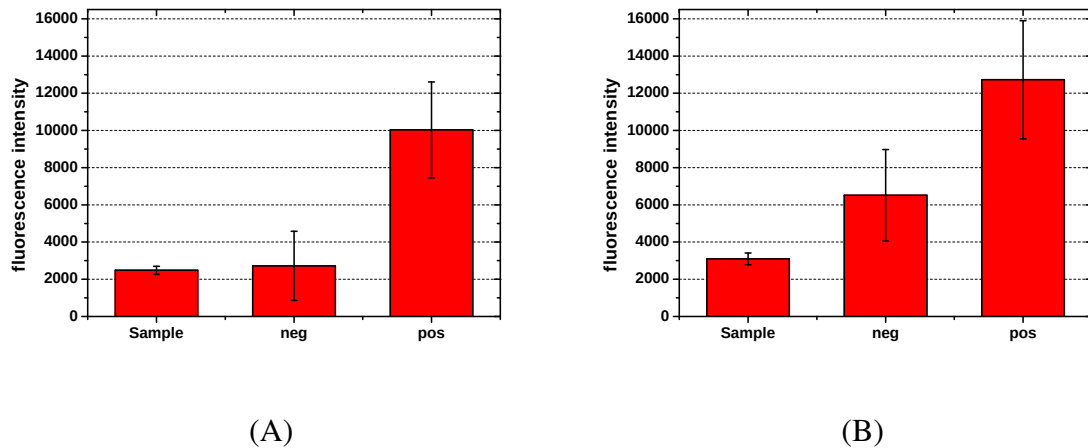


Figure 25: Toxicity test of microgels (A) and PVA-microgelfibres (B); both materials do not show toxic behaviour in this test

7 Summary/Conclusions

In this Part of the thesis microgel-PVA composite fibres have been successfully fabricated by means of a simple one step electrospinning process. The fibres have defined diameters and morphology, are homogenous, and the electrospinning process is continuous. The fibres have a PVA matrix with the microgels homogeneously spread inside. An ideal set of parameters was defined to achieve the fabrication of homogenous fibres of reproducible good quality. During the parameter study it was found that the viscosity of the spinning solution and the flow rate through the needle-tip has the biggest influence on the fibre diameter and the process itself. These parameters also influence each other, since the microgels will deform at higher shear rates (higher flow rates), which will reduce the viscosity; therefore no linear trend for these parameters can be observed. Since PVA is water soluble the fibres need to be crosslinked, which was successfully done chemically with methacryloyl chloride and physically by a combination of careful drying and heating at 155 °C for 10 minutes. The physical crosslinking was the chosen method for all further experiments, because it is simple and lacks the use of toxic chemicals.

TGA and DSC results show that the microgels retain their thermo-sensitive behaviour inside the fibres. Furthermore, they enhance the swelling properties of the fibres, which are also tuneable by temperature change. Water moisture sorption analysis shows that the sorption and desorption rate are also enhanced and switchable by the addition of the microgels to the fibres. It also shows a structural change during the moisture uptake, leading to higher surface areas (pores, free volume around the microgels, which are impurities in the PVA matrix). Due to the intended medical use, toxicity tests of the microgels and the PVA-microgel fibres have been done and show that both are non-toxic.

As a conclusion to this part, it can be stated that microgel polymer composite fibre can successfully and reproducibly be fabricated in a straight forward process. The combination of microgels and PVA give the fibres enhanced and tuneable swelling properties and the fibres retain their non toxic features, therefore making them suitable for medical applications. The only draw back is the need for crosslinking as a post fabrication step, which even though it can be achieved in two fairly simple ways, it is still less effective than a water insoluble polymer. However, this study was a good and successful first step into a relatively new field of microgel-polymer fibres.

Polycaprolactone - Microfibres

IV

1 Introduction

In this part of the thesis the work that has been done with the PVA-microgel fibres was continued and redefined. The results achieved with the PVA-microgel fibres are good and promising, but these fibres also show a small drawback: the water solubility. The initial idea was to avoid any kind of organic solvent and therefore bypass elaborated cleaning steps, which is good especially for medical applications. Nevertheless, for water-soluble polymers like PVA, additional crosslinking is necessary. As it was shown in the previous part, the chemical crosslinking is an elaborated fabrication step, while the physical crosslinking is effective and not time consuming, but energy (and therefore money) intensive and the fibres will still decompose in a short period of time. For some applications this might still be a good option, but for many others, like suture- or patch materials it is not. Therefore, another polymer, polycaprolactone (PCL), was chosen for the further fabrication of microgel-polymer composite fibres. PCL is hydrophobic and not water soluble, therefore bypasses the necessity for crosslinking, moreover, it is biocompatible [84] and biodegradable [85, 86]. As microgel standard VCL/AAEM microgels have been used, since for the fabrication no special properties of the microgels are needed. In order to achieve different fibre morphologies, different solvents and solvent mixtures have been used.

In the previous part the properties of microgels and PVA have been combined and in some cases synergy effects have been found, but in this part of the work a hydrophobic and a hydrophilic material will be combined, therefore the changes in properties are expected to be much more significant. In general it could be said, that the aim of this study is the development of a one step process to fabricate hydrophilic modified PCL fibres, which exhibit a controlled swelling and degradation behaviour. The control of the fibres hydrophilicity and swelling behaviour is especially of importance for tuneable cell growth or adhesion on these fibres [87, 88]. Other possible applications are, like mentioned before, in the medical field, like sutures, patches, implants or in tissue engineering.

Another aim of this study is the exploitation of the possibilities of the electrospinning process. Since there is no restriction in this case on only one solvent, different solvents and solvent systems can be used for the fibre fabrication. This opens the way to different possible fibre morphologies, also regarding the microgel distribution in the fibres (on the surface or in the fibre core). Morphology and microgel distribution will be shown to be essential for fibre properties like surface roughness, degree of swelling or degradation, which are key properties for the mentioned applications. This all shows the motivation in the combination of PCL and microgels using the electrospinning technique.

The following part of this thesis is, besides introduction and conclusion, structured in four chapters. The experimental part will give information about all syntheses, fabrication and characterisation done, detailed enough to recreate each experiment. However, it is to state that for some descriptions this would be the same as the ones in the PVA part, in these cases only

references to the according sections are given. In the chapter “Investigation of the Spinning Solutions” the microgel behaviour in the solvents used for the spinning solutions, as well as the properties of the spinning solutions are analysed. Afterwards the fibre fabrication itself will be discussed in detail. The chapter “Fibre Characterisation” focusses on the investigation of the fibre properties by means of thermal analysis (TGA, DSC) and water moisture sorption analysis concentrating on the interaction with water (for example the degree of swelling); and on the investigation of the fibre degradation by means of DLS, gravimetric analysis and NMR. DLS is used to follow the release of the microgels out of the fibre structure during the degradation process.

Most of the results presented in this part of the thesis are also part of a peer-reviewed paper [89], written by me and with me being the first author of the paper. Some results/experiments regarding the fibres spun from chloroform/DMF were done by Astrid Catalina Molano Lopez as a bachelor-student under my supervision. Nevertheless the texts have been rewritten for this thesis.

2 Experimental Part

The following sections present only the descriptions of the synthesis and fabrication processes of the samples and materials, as well as the description of the experiments and analyses that have been done with these samples which can not be found in one of the previous chapters of this thesis. In cases of specific changes in the experiments, these changes will be mentioned and the remaining description will be referred to. This is done to avoid unnecessary repetitions.

2.1 Materials

2,2'-Azobis[2-methylpropionamidine] dihydrochloride (AMPA, 97%, Aldrich), chloroform (99.5%, VWR), dimethylformamide (DMF, 99.8%, VWR), methanol (99.8%, VWR), N,N'-methylene-bis-(acrylamide) (BIS, 99%, Sigma-Aldrich), phosphate buffered saline (PBS, Aldrich), poly(caprolactone) (PCL, MW=70.000-90.000 g/mol, Aldrich), toluene (99.5%, VWR), and distilled water were used as received without having undergone any other cleaning procedures. 2-(methacryloyloxy)ethyl acetoacetate (AAEM, 95%, Aldrich) has been purified before use. N-Vinylcaprolactam (VCL, 98%, Aldrich) was purified by vacuum distillation under nitrogen before use.

2.2 Microgel Synthesis

In this part of the thesis only VCL/AAEM microgels have been used. The synthesis is done exactly like it was described in 2.2. The recipe was as following: VCL - 1.877 g (13.40 mmol); AAEM - 0.338 g (1.579 mmol); BIS (crosslinker) - 0.06 g (0.389 mmol) and water 150 g the initiator (0.05 g (0.268 mmol)).

2.3 Preparation of Spinning Solutions

The spinning solutions for all PCL fibres in this work are based on two different solvent systems, one is methanol/toluene and chloroform/DMF. In both cases mixtures with different ratios of the solvents and different amounts of PCL have been prepared. Afterwards varying amounts of freeze-dried microgels were added and the solutions were mixed with an Omni TH homogeniser (Omni International) for 5 minutes at 10000 rpm. A detailed list of all

prepared solutions can be found in Table 4. Since the solvent mixtures and their properties are an important parameter for the fibre formation and therefore the fibre morphology, table 5 provides the most important physical constants of the used solvents.

Table 4: Samples that were prepared for electrospinning. Depending on the viscosity of the sample not all parameter variations are possible for the electrospinning process

Methanol/Toluene	MG:Polymer	PCL in solution	DMF/Chloroform	MG:Polymer	PCL in solution
30:70	60:40	8 wt%	30:70	60:40	8 wt%
30:70	20:80	12 wt%	30:70	30:70	10 wt%
30:70	30:70	12 wt%	30:70	40:60	10 wt%
30:70	20:80	18 wt%	30:70	30:70	12 wt%
50:50	30:70	8 wt%	50:50	40:60	8 wt%
50:50	60:40	8 wt%	50:50	60:40	8 wt%
50:50	20:80	12 wt%	50:50	30:70	10 wt%
50:50	30:70	12 wt%	50:50	40:60	10 wt%
50:50	50:50	12 wt%	50:50	50:50	10 wt%
50:50	20:80	18 wt%	50:50	30:70	12 wt%
50:50	30:70	18 wt%	50:50	40:60	12 wt%
70:30	30:70	8 wt%	70:30	40:60	8 wt%
70:30	60:40	8 wt%	70:30	60:40	8 wt%
70:30	20:80	12 wt%	70:30	30:70	10 wt%
70:30	30:70	12 wt%	70:30	40:60	10 wt%
70:30	20:80	18 wt%	70:30	30:70	12 wt%
70:30	30:70	18 wt%	70:30	40:60	12 wt%

Table 5: Properties of solvents used for the electrospinning

Solvent	Molar mass [g/mol]	Boiling point [°C]	Density [g/cm ³]	Dipole moment (Debye)	Solubility parameter
Chloroform	119.4	61.2	1.470	1.15	19.0
DMF	73.1	153.0	0.940	3.86	24.0
Methanol	32	64.7	0.790	1.7	29.7
Toluene	92	111	0.857	0.375	18.5

The fibre fabrication and the electrospinning setup is equal to the one in section 2.4.

2.4 Degradation of the Fibres

The fibre degradation was investigated by using 2 cm² of the nonwoven fibre samples placed in 10 mL phosphate buffered saline (PBS) (0.01 M). PBS was used to simulate the human body fluids. After certain time intervals parts of these samples were analysed by means of electron microscopy to investigate the degree of degradation and erosion effects on the fibre surface. The degradation media was analysed by DLS to detect possible release of microgels from the fibre into the solution. Additionally the mass loss of the samples was studied gravimetrically. The mass loss was calculated according to the following equation: $massloss[\%] = \frac{m - m_f}{m} \times 100$, where m is the initial mass and m_f is the mass of degraded fibre.

2.5 Characterisation Methods

In this section only the characterisation methods that have not been mentioned before in this thesis are described. The descriptions for DLS, SEM, TGA, DSC and moisture sorption analysis can be found in 2.6.1, 2.6.3, 2.6.5, 2.6.6 and 2.6.7.

2.5.1 Contact Angle Measurements

The contact angle on different nonwoven fibre samples of 1 cm² was measured with a Krüss G2/DSA II. A droplet of distilled water was placed on the sample; pictures were taken in time intervals of a few seconds. Droplet shape and contact angles were analysed using the device software.

2.5.2 Sedimentation Analysis

Studies of the sedimentation behaviour of the microgels in methanol/toluene as well as in chloroform/DMF and of the spinning solutions were done by using a separation analyser, LUMiFuge (LUM GmbH, Germany). The device measures in particular the sedimentation velocity of particles in solutions, which leads to conclusions about the stability of the dispersions. The samples have been measured in quartz glass cuvettes at an acceleration velocity of 2000 rpm.

2.5.3 X-Ray Diffraction

X-ray diffraction (XRD) measurements have been done with an Empyrean X-ray diffractometer (PANalytical). The samples were placed on the sample stage after peeling off from the aluminium target. The sample stage can be temperature controlled and for some experiments the samples were swollen with some droplets of water.

3 Investigation of Microgels and Spinning Solutions

This part of the thesis, as it was mentioned before, is based on the experiences with the PVA fibres. Therefore, the basic set of process parameters, the flow rate (1 mL/h), the target distance (16 cm) and the applied voltage (30 kV) were used again. Only the solution parameters like the ratio between microgels and polymer have been varied, and, since PCL is not water soluble, water was not applicable as solvent. As promising solvent combinations methanol/toluene (Me/Te) and chloroform/DMF (Ch/DMF) were chosen, their ratios have also been varied. Both versions will be discussed in separate sections. Like before with the PVA/microgel fibres, in both cases one specific set of parameters will be defined for a reproducible good fibre quality and will be used for all further analyses. For the PCL/microgel fibres microgels with VCL/AAEM were used. HEA, like in the PVA/microgel fibres was not needed.

3.1 Microgel Behaviour in Different Solvent Systems

The solvent systems that have been chosen to fabricate PCL/microgel fibres had to fulfill at least two criteria: PCL has to be soluble and the microgels have to be well dispersible. The latter and the overall behaviour of microgels in the two solvent systems, Me/To and Ch/DMF, will be addressed in the following. The freeze-dried microgels were re-dispersed in the various solvent mixtures by heavy stirring and an ultra sound probe and analysed by means of DLS and sedimentation analysis. In general they were well dispersible in all solvent mixtures, no agglomerates were detected and the PDI showed mostly values below 0.1. In Figure 26 the size distribution curves taken by DLS are shown for three selected samples. All three show a narrow size distribution indicating the low PDI and no agglomerates. The selected samples are representative for any other sample and were chosen, because these solvent mixtures will later be shown to be the relevant ones.

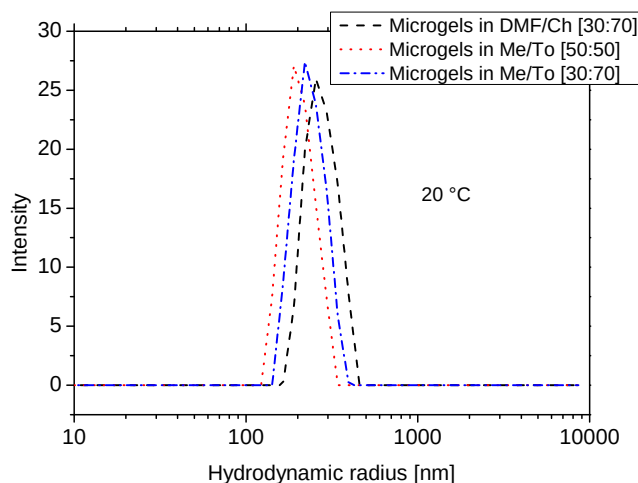


Figure 26: Microgel size distribution in selected solvent mixtures indicating that an agglomerate free re-dispersion is possible

Two important parameters of the microgel behaviour are the microgel size in the different solvents, which reflects the swelling and the colloidal stability. The first one is shown in Figure 27 A. Hydrodynamic radii are plotted against the percentages of methanol and DMF, respectively, in the mixtures. The horizontal line shows the microgel size in water. All measurements were done at 20 °C and the radius of the dried microgels determined by electron microscopy is about 100 nm. In the case of Me/To the microgel size increases with an increasing methanol content. In pure methanol the radius is about 250 nm and in pure toluene about 150 nm. At a ratio of 50:50 the microgels have the same radius like in water; about 200 nm. The stronger swelling of VCL based microgels in alcohols (methanol, ethanol) compared to water has been reported previously [90]. In the Ch/DMF mixtures the radius is in all cases higher than in water, and shows a slight but not significant increase with an increasing amount of chloroform. However, both cases show that the microgels are not only well dispersable (no agglomerations and good PDI, mentioned above) in the solvent mixtures; they also swell since their size is higher than the radius of the dried/collapsed microgels. This observation is also important for the spinning solutions, because microgels that swell more will uptake more solvent and reduce therefore the viscosity of the solutions.

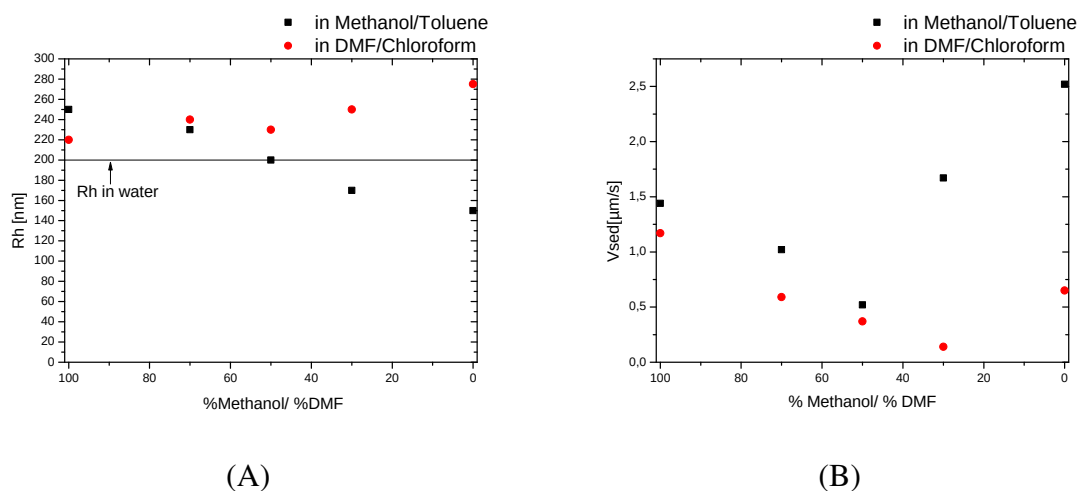


Figure 27: DLS measurements of the hydrodynamic radius of microgels in different solvent mixtures (20 °C)(A); The colloidal stability regarding the sedimentation velocity of microgels in different solvent mixtures (B)

The mentioned increase in size with the methanol fraction leads to the assumption that the microgels swell preferably with methanol and therefore more methanol should be present in the microgel interior. An approach to verify this fact was the determination of the refractive index. 1 mL solutions of different solvent mixtures have been prepared and 0.05 g freeze dried microgel was added. After some minutes the swollen microgel was removed by centrifugation and the refractive index of the supernatant was measured and compared to the one before the microgels were added. This method is not very exact and the results have big errors; nevertheless, the methanol amount in the solvent after the separation process was always found to be significantly reduced, considering the values of the refractive indices. The measured values can be seen in Table 6 and show that this is indeed an indication of more methanol than toluene present in the microgels. A similar effect for the Ch/DMF mixtures was not found, which is in agreement with the DLS results that also show no significant dependency on the solvent composition in the Ch/DMF mixtures.

Table 6: Changes of the refractive index in the solvent mixtures caused by microgels

Me/To [%Me]	n	n(supernatant)	Ch/DMF [%DMF]	n	n(supernatant)
100	1.326		100	1.43	
90	1.353		90	1.431	
70	1.409	1.471	70	1.434	1.432
50	1.443	1.485	50	1.437	1.439
40	1.453		40	1.439	
30	1.467	1.489	30	1.440	1.439
10	1.487		10	1.443	
0	1.494		0	1.445	

The colloidal stability is the second mentioned important parameter of the microgel behaviour. Instable microgels, microgels with a quick sedimentation, could cause problems during the electrospinning process, since the composition of microgels and polymer would not be homogenous in the syringe throughout the whole fabrication time. In Figure 27 B the sedimentation velocity, representing the colloidal stability of dispersions, of the microgels in different solvent mixtures is shown. A faster sedimentation means a less stable system. In general all values show quite good stabilities. However, the sedimentation velocity changes in both systems with the solvent composition and in both cases a minimum can be found. In the case of Me/To the sedimentation velocity decreases in the beginning with a decreasing methanol content. The microgels get smaller and denser. At a ratio of 50:50 the minimum is reached and the sedimentation velocity increases again having its maximum for pure toluene. For Ch/DMF mixture the behaviour is similar, but the minimum is reached at a ration of 70:30 and the maximum is in pure chloroform.

3.2 Preparation and Analysis of the Spinning Solutions

After the microgel behaviour in the different solvent mixtures was investigated, the next step was the preparation of the actual spinning solutions consisting of the solvents, microgels and PCL. The parameters varied were the ratio of the two solvents to each other, the ratio between microgel and polymer and the basic amount of the PCL. Table 4 shows the prepared spinning solutions for Me/To and for Ch/DMF. First electrospinning tests of the solutions showed some interesting differences in the fibre morphology. For a ratio of Me/To of 50:50 the microgels were found on the surface of the fibre, while for other ratios and for Ch/DMF this was not

the case. It was also never found in the PVA-microgel fibres. Therefore, some more detailed investigations of the spinning solutions have been done and will be shown in the following.

Since the formation of the fibre morphology in electrospun fibres depends mainly on separation processes, the sedimentation behaviour of the spinning solutions has been investigated. The exact same samples that are also used for the electrospinning, with the same amounts and compositions and viscosities are used to perform the sedimentation analysis. This analysis is in general a centrifugation, which accelerates the natural sedimentation process of the sample, combined with an observation of the sample's light transmittance. In an usual sedimentation process the dispersed phase will sediment slowly to the bottom of the container and the liquid phase will clear up, thus the light transmittance will increase. Figure 28 shows three sedimentation profiles of typical spinning solutions. The transmittance is plotted against the position in the cuvette. The Me/To 50:50 and the Ch/DMF are the solutions, which are used to prepare the fibres in the following sections. Figure 28 A shows the sedimentation profile of Ch/DMF 70:30 with 10 wt% PCL, and a microgel/polymer ratio of 40:60. In the beginning the whole sample is turbid, since everything is well mixed and dispersed. With time (each curve represents the transmittance profile at a certain time) the transmittance in the upper part of the cuvette increases, meaning that the dispersed phases start to sediment and the upper part of the sample gets clearer. At the end of the measurement most of the cuvette is clear; microgels and polymer are only at the bottom, displayed in slick layers. This is a good example for a usual sedimentation. Figure 28 B shows the sedimentation profile of Me/To 70:30, 12 wt% PCL and a microgel/polymer ratio of 30:70. In general the behaviour is the same like in Figure 28 A, just that the sample is more stable and therefore the curves, representing the different times in the measurements, are closer together. At the end of the measurement not all material has sedimented. The sedimentation profile of Me/To 50:50, 12 wt% PCL and a microgel/polymer ratio of 30:70, that is shown in Figure 28 C, gives a completely different result and it is the only sample of all tested mixtures that gives this result. At the end of the measurement the top part of the cuvette is still turbid, the middle part is basically clear and the bottom is turbid again. One part of the dispersed phase settled down and one part showed a creaming effect, rising up to the surface of the sample, like oil would do in water. A separated analysis of these phases makes clear that the creamed phase basically consists of the microgels and the sediment consists basically of PCL.

To sum up these results: The only spinning solution that produces fibres with microgels on the surface is also the only spinning solution that shows a creaming effect of the microgels instead of sedimentation. And since the only changed parameter in the two Me/To examples shown is the ratio between methanol and toluene, the reason for this effect has to be related to it.

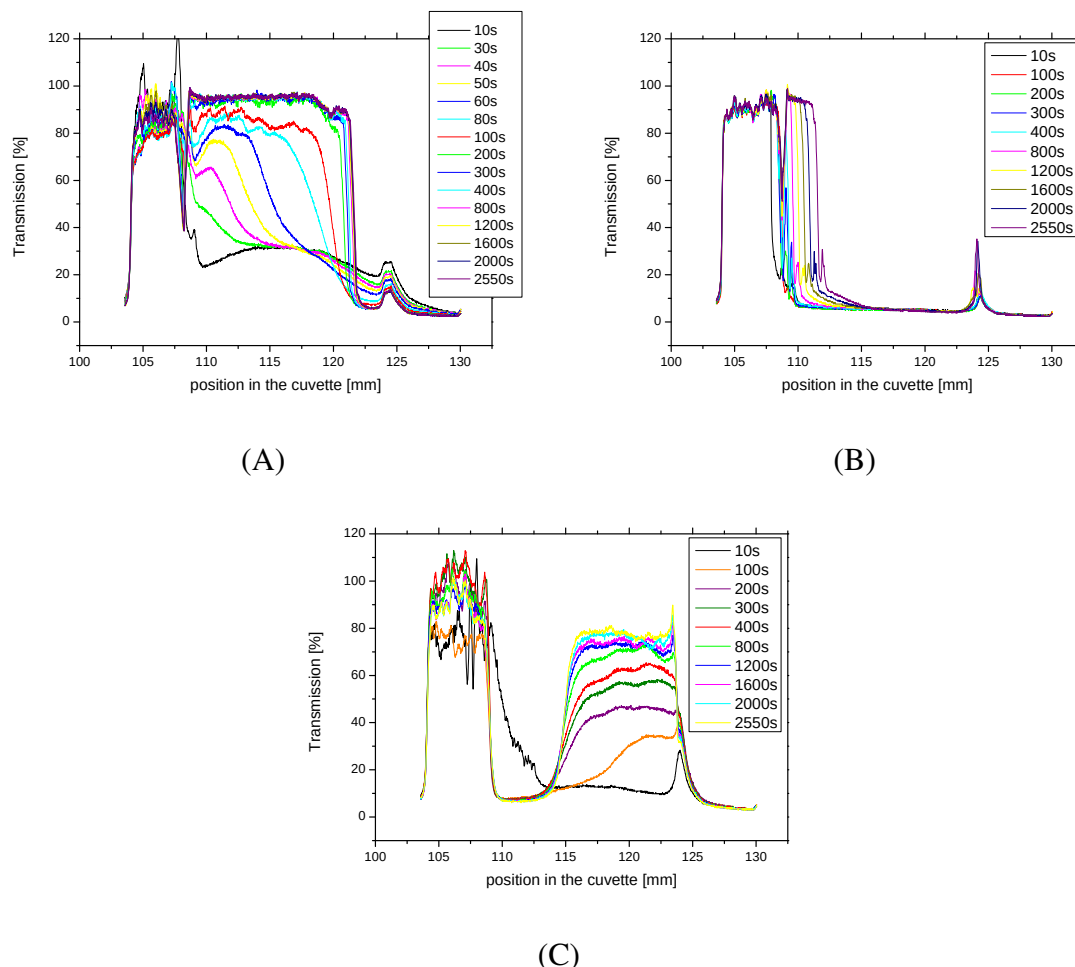


Figure 28: Sedimentation profiles of microgels in Ch/DMF 70:30, 10 wt% PCL and a microgel/polymer ratio of 40:60 (A); microgels in Me/To 70:30, 12 wt% PCL and a microgel/polymer ratio of 30:70 (B) and microgels in Me/To 50:50, 12 wt% PCL and a microgel/polymer ratio of 30:70 (C)

To further investigate this effect and to see if it is reproducible with a different method than electrospinning, and therefore exclude other reasons, like the applied voltage, films from the spinning solutions were prepared. The exact same solutions that were used for the electrospinning were slowly dried at room temperature until all solvents evaporated and a film was formed. These films were analysed by means of electron microscopy to visualise their surfaces and interiors. Figure 29 shows the electron micrographs of the same three samples taken as examples also in the sedimentation analysis paragraph above. From each sample the surface and a cross-section (cut with a razor blade in liquid nitrogen) is shown. Again all samples show in general the same morphology: a more or less smooth (microgel free) surface and

microgels distributed throughout the film interior, like it is shown in Figure 29 A-D. The only exception is the Me/To 50:50 mixture with a microgel/polymer ratio of 30:70 (Figure 29 E-F), which shows some layers of microgels at the surface and a smooth and homogenous interior. The pictures E and F even indicate that a clear phase separation takes place and the microgels are not only on the surface, but exclusively found on the surface. However, the investigations of the films confirm the results of the electrospinning (compare section 5, part IV) and the sedimentation analysis.

The explanation for these different behaviours during the film formation or the electrospinning from different Ch/DMF and Me/To solutions has to consider many system parameters, like the microgel behaviour in these solutions, but also of the PCL chains and the general properties of the solvent mixtures. The main components of the microgels are PVCL chains, their intramolecular mobility in water and various organic solvents can be investigated by polarised luminescence to measure the relaxation time t_w , reflecting the intramolecular mobility of the chains [91]. From this measurements t_w for PVCL is 21 ns in water and 7.4, 7.4 and 7.3 ns in methanol, chloroform and toluene, respectively, all much smaller than for water. For DMF t_w is with 2.8 ns even smaller. The mobility of PVCL in water is hindered by the extensive formation of hydrogen bonds. Additionally it has to be noted that all four solvents are good solvents for PVCL [92] even though they have different dipol moments (compare Table 5) and solubility parameters. Considering these facts and taking into account also the DLS and sedimentation data shown in section 3.1, it can be concluded that the PVCL based microgels should not show specific interactions with the solvents and should stay in their solvated state independently from the solvent composition. The other component in this system, PCL, is soluble in chloroform and toluene, but DMF and methanol are non-solvents for it [93]. Nevertheless different boiling points and evaporation rates (compare Table 5) can influence the solubility of PCL in the mixtures during the drying process, which happens during the solidification process present in electrospinning, as well as in the film formation. These could lead to different morphologies after the solidification, but in general all mixtures show a similar morphology, with the single exception of a Me/To ratio of 50:50. Alcohols such as methanol are found in contrast to toluene, in solutions in an associated form; the methanol molecules appear in small molecular clusters [94]. This will influence the intermolecular interactions in methanol/toluene mixtures. Moreover, the excess molar volumes, the difference between the real and the ideal volume of mixtures, V_E , are negative in Me/To mixtures, having a minimum at a ratio of 50:50 [95]. In the case of Me/To the negative V_E is related to changes in the free volume induced by electron donor-acceptor interactions between the two solvents (toluene is a p-electron donor) [94]. Additionally the viscosity as well as the surface tension is related to enhanced molecular interactions increased in methanol/toluene mixtures with mol fractions of toluene between 0.4 and 0.7 mol, which includes the 50:50 mixtures. Nothing similar was found to be reported in Ch/DMF mixtures.

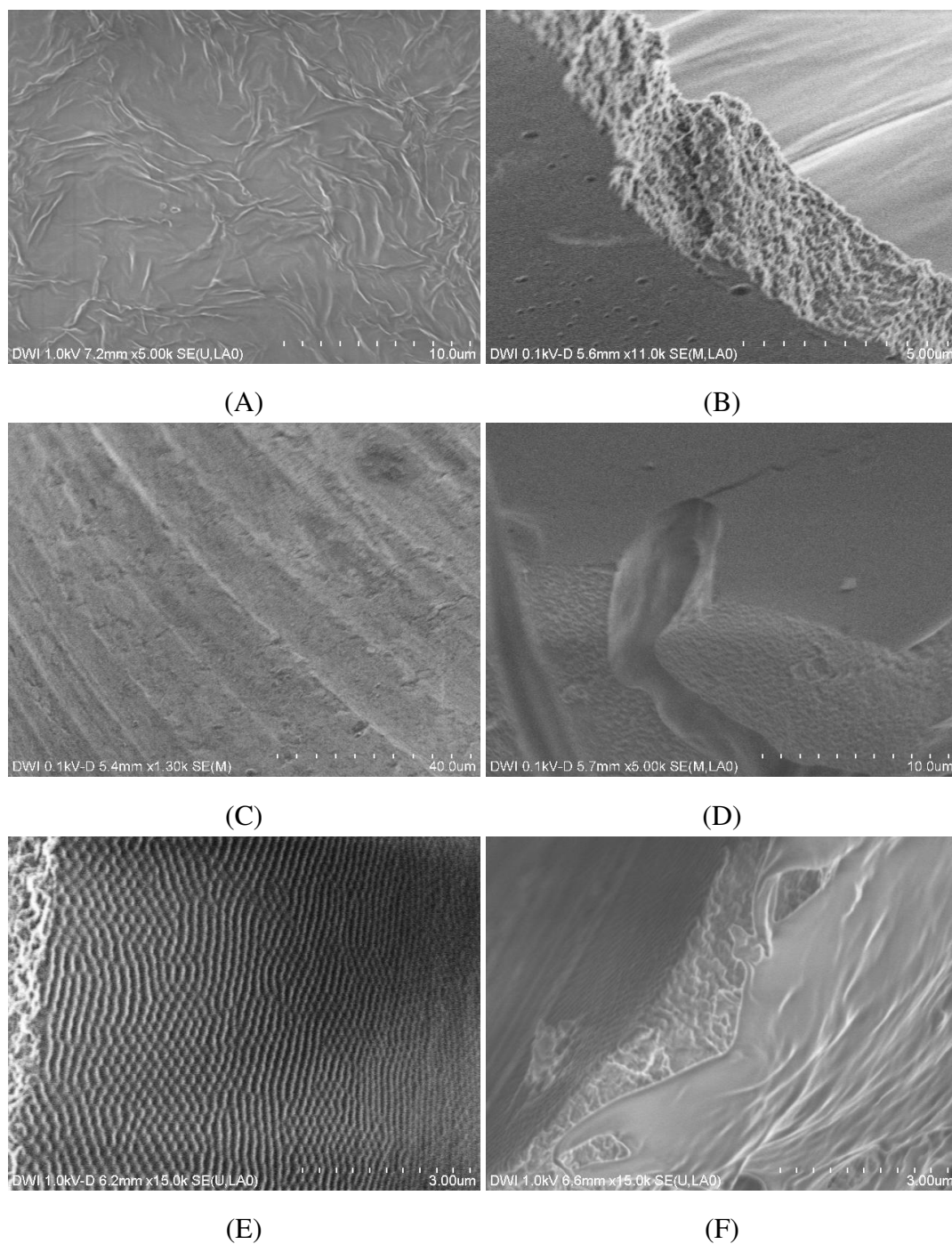


Figure 29: FE-SEM micrographs of microgel/PCL films prepared from different spinning solutions: surface (A) and cross-section (B) of a film cast from Ch/DMF 70:30 and a microgel/polymer ratio of 40:60; surface (C) and cross-section (D) of a film cast from Me/To 70:30 and surface (E) and cross-section (F) of a film cast from Me/To 50:50 both with a microgel/polymer ratio of 30:70

Based on the discussion above and the fact that a methanol/toluene ratio of 50:50 has some anomalous properties it is reasonable to believe that the special morphology of the PCL-microgel fibres is caused by these circumstances. However, an actual theory or explanation was not sufficiently devised. The preferable theory induced by the combination of facts shown above will be described shortly: in Me/To the microgels are in a swollen state and they are mostly swollen with methanol. Therefore, the bulk density of the microgels, the density of the porous particle plus the density of its interpenetrating media, will be closer to the density of methanol, which is lower than the one of toluene, than to the toluene density. Creaming would occur when the bulk density of the dispersed particles is smaller than the density of the medium (solvents plus polymer). It could now be possible that the bulk density of the microgels fulfils this criterion exactly at the Me/To ratio of 50:50, this is especially suggested by the anomalous properties of this ratio. This theory could be proven by analytical ultracentrifugation (AUC) experiments and the calculation of the exact particle density by using the following equation, which is based on the Lamm equation, the basic equation of all AUC experiments:

$$\frac{v_{sed}}{c_{acc}} = S = \frac{1}{18} \cdot \frac{1}{\eta_0} \cdot D^2 \cdot (p_p - p_0) \quad (3.1)$$

v_{sed} sedimentation velocity
 c_{acc} centrifugational acceleration
 η_0 viscosity of the continuous phase
 D diameter of the particles
 S sedimentation coefficient
 p_p density of the particles
 p_0 density of the continuous phase

The particle density p_p can be calculated from this equation and if it would be especially smaller only at a Me/To ratio of 50:50 in the spinning solutions, the morphology phenomenon would be explained. Nevertheless AUC experiments have not been possible and this theory could not be proven in this work. Nevertheless, the separation takes place and the microgels arrange themselves exclusively in one spinning solution at the surface.

In Figure 30 the film formation process is shown schematically to illustrate the separation during the solidification, that was mentioned in the above discussion. In the beginning PCL chains and microgels are homogeneously distributed in the solution. In the case of most Me/To and all Ch/DMF mixtures no special separation processes take place during the evaporation of the solvents, and always enough free solvent is available to solvate PCL and microgels until the mixtures solidify. In the case of Me/To mixtures the microgels are preferentially swollen with methanol and PCL is only soluble in toluene and at the 50:50 ratio the bulk density of the particles will drive them to the surface, forming a kind of bilayer structure.

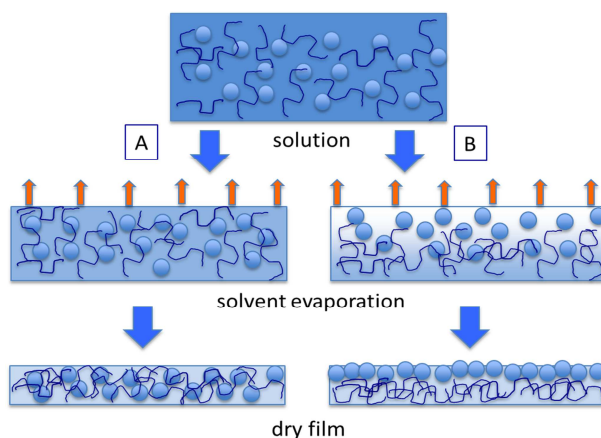


Figure 30: Scheme of the solidification processes

4 Fibre Fabrication

As it is mentioned above fibres were spun from two different solvent mixtures: methanol/toluene and chloroform/DMF. In the following sections their fabrications will be described separately and for each an ideal set of parameters for reproducible fibres of good quality will be defined.

4.1 Fibres Spun from Methanol/Toluene

Table 4 in section 3.2 shows the spinning solutions that have been prepared. All these solutions have been used to fabricate fibres and were investigated by means of electron microscopy. The process parameters, such as the flow rate, the target distance and the applied voltage were used regarding the experience gained with the PVA-microgel fibres. After a first examination of the spun fibres these parameters were carefully adjusted for the most promising spinning solutions. In the end it turned out, that Me/To mixtures with a ratio of 50:50 not only produce fibres of a good quality, but also with the already discussed unique morphology, which consists of microgels exclusively spread on the surface of the fibres. Additionally it is notable that the colloidal stability of the microgels (compare Figure 27 B) for this mixture was the best; therefore, it could be stated that for colloidal stability, which means less aggregation and sedimentation, it is important to obtain a homogenous and continuous electrospinning process. In Figure 31 electron micrographs of fibres spun from a Me/To 50:50 solution, with a PCL concentration of 12 wt% and a microgel/polymer ratio of 30:70 wt% with different process parameters, are shown. 31 A and B show fibres spun at a flow rate of 3 mL/h, a target distance of 16 cm and an applied voltage of 30 kV. Microgels are clearly visible at the surface of the fibres, but they are not homogeneously spread. Also the fibre diameter of the two fibres shown is completely different, which shows the inhomogeneous spinning process with these parameters. Nevertheless, it is clear that the fibres are exclusively found at the surface and that they are bound to the fibre by some polymer film. The latter can also explain why the microgels are actually fixed on the surface and will not fall off, for example in contact with water.

Figure 31 C and D show fibres from the same spinning solution like the ones in pictures A and B with the same spinning parameters, just that the flow rate is 1 mL/h. Picture D shows an overview to emphasize that the fibres are homogenous, and picture C shows that with this set of parameters the microgels also are spread homogeneously and cover every spot on the fibres surface. The average fibre diameter, calculated with the software of the electron microscope, is 3 μm .

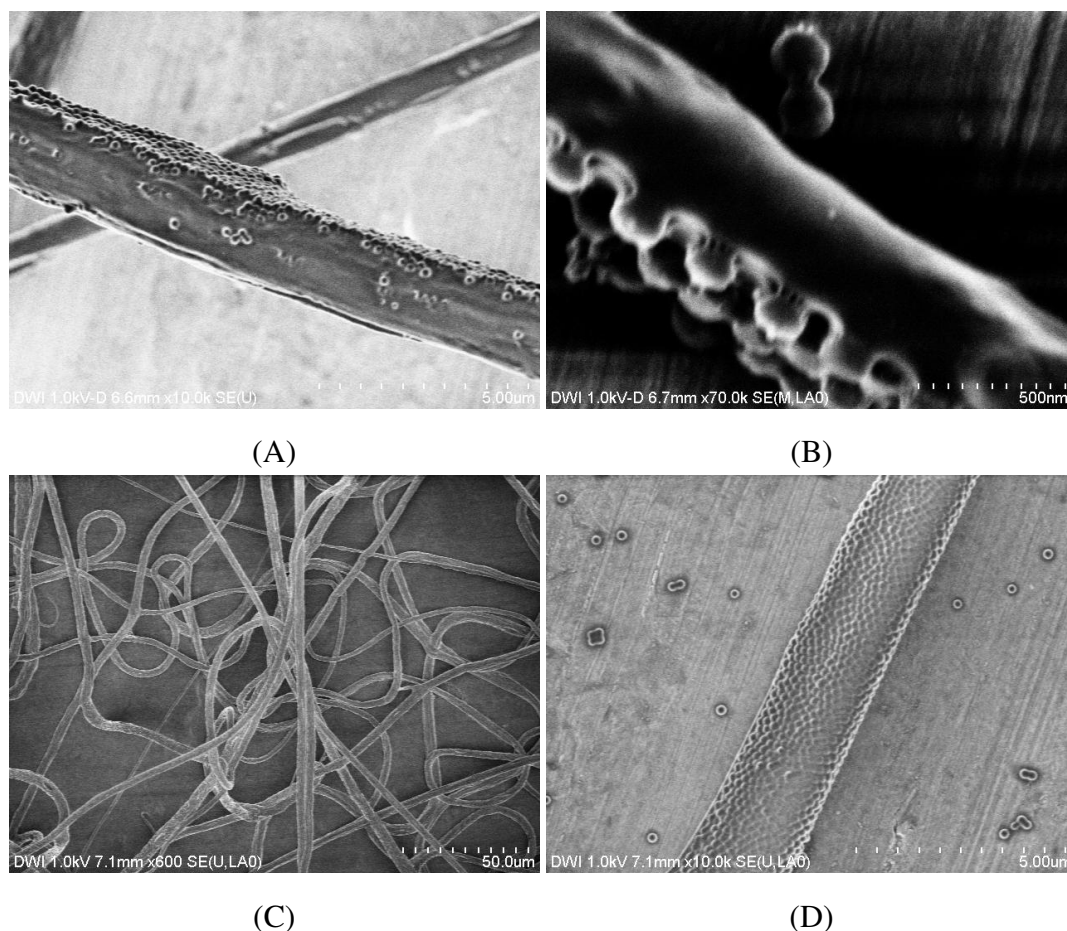


Figure 31: Fibres spun from a Me/To 50:50 solution, with a PCL concentration of 12 wt% and a microgel/polymer ratio of 30:70 wt% with a flow rate of 3 mL/h (A) and (B) and a flow rate of 1 mL/h (C) and (D); the latter ones showing the homogenous fibres that can be achieved

It can be concluded that fibres with microgels exclusively and homogeneously spread on the surface, additionally to a good general fibre quality, can only be obtained by using Me/To 50:50 spinning solutions with 12 wt% of PCL and a microgel/polymer ratio of 30:70 wt%. The parameters have to be set to a flow rate of 1mL/h, a target distance of 16 cm and an applied Voltage of 30 kV. All analyses of these fibres that will be shown in the next chapter have been done with fibre spun from this solution with this set of parameters. Fibres with microgels on the surface will be referred to as type S fibres. It is also to mention that the best set of process parameters is exactly the same that was found for the PVA-microgel fibres, even when the solution itself is completely different, having a different solvent and different microgel/polymer ratio. The average fibre diameter is about 3 μm .

4.2 Fibres Spun from Chloroform/DMF

Chloroform/DMF is the second solvent system that was used. The spinning solutions prepared are presented also in Table 4 in section 3.2. As it was done with the Me/To solutions, the set of parameters known from the PVA-microgel fibres was used to screen spinning solutions and the obtained fibres were analysed with the electron microscope. The spinning solution for the best fibre quality turned out to be a Ch/DMF ratio of 70:30 with 10 wt% of PCL and a microgel/polymer ratio of 40:60 wt%. Like in the experiments before in Me/To the most homogenous fibres and the most continuous electrospinning process is adjusted at the Ch/DMF ratio in which the microgels show the best colloidal stability (compare Figure 27 B). The colloidal stability of the microgel has a big influence on the process stability, due to agglomeration and sedimentation in the spinning solutions, and when the stability is higher, the process is more continuous. The set of process parameters for these fibres is again similar to the one of the PVA-microgel fibres. The flow rate is 1 mL/h and the applied voltage is 30 kV, but the target distance needed to be increased to 25 cm. This leads to smaller fibre diameter besides other factors; the average diameter determined with the electron microscope software is about 1 μm . This increase in the target distance was needed, because the evaporation of the solvents was not completely finished at a distance of 16 cm; the fibres were still wet and “amorphous”. The mentioned parameters in this paragraph are the ones used for all fibres spun from Ch/DMF that are analysed and shown in the next chapter. These fibres will be referred to as type C fibres.

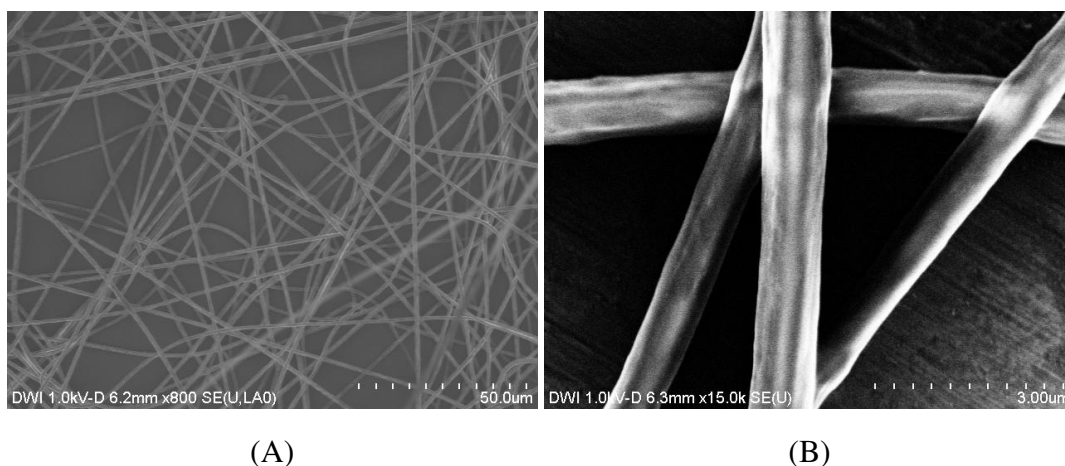


Figure 32: Fibres spun from a Ch/DMF 70:30 solution with 10 wt% PCL and a microgel/polymer ratio of 40:60 wt%

Figure 32 shows the fibres described above; micrograph A shows an area of the nonwoven displaying the homogenous quality of the fibres and micrograph B shows a close-up of the

fibre surface. In contrast to the type S fibres and also to the PVA-microgel fibres, the surface of the fibres from type C is smooth, no microgels are visible. The microgels are all spread exclusively in the interior of the fibres. This can be concluded by the fact that nearly no microgels can be found on the target, and also by the results of the subsequent analysis of the fibres. The fibre morphology also correlates with the results from the film formation and the sedimentation analysis (compare section 3.2, part IV).

Even though all indirect proofs in the fibre fabrication as well as in the analysis of the fibre properties and the degradation analysis, which will be shown in the following sections, lead to the un-doubtable conclusion that the microgels are located in the fibre core, attempts to visualise these fact have been made. Cutting or breaking the fibres in liquid nitrogen was not successful, because the cutting edges were closed when investigated by electron microscopy and no view inside of the fibres was possible. Therefore, the fibres have been cut by an ultra-microtome in slights of 80 nm. The electron microscope investigation was done with the SU9000 SEM (Hitachi). Figure 33 shows a fibre cross section, the circular shape of the fibre and its interior is visible. Nevertheless, no microgels can be seen, which can be explained by the fact that the microgels as well as the matrix is a polymer and no obvious difference like with an inorganic compound inside of the fibres is given. The microtome cuts right through the microgels and no easy interpretable differentiation between matrix and microgels can be made. However, like it was mentioned before the proof of the location of the microgels in the fibre core is given by the other data presented in this part.

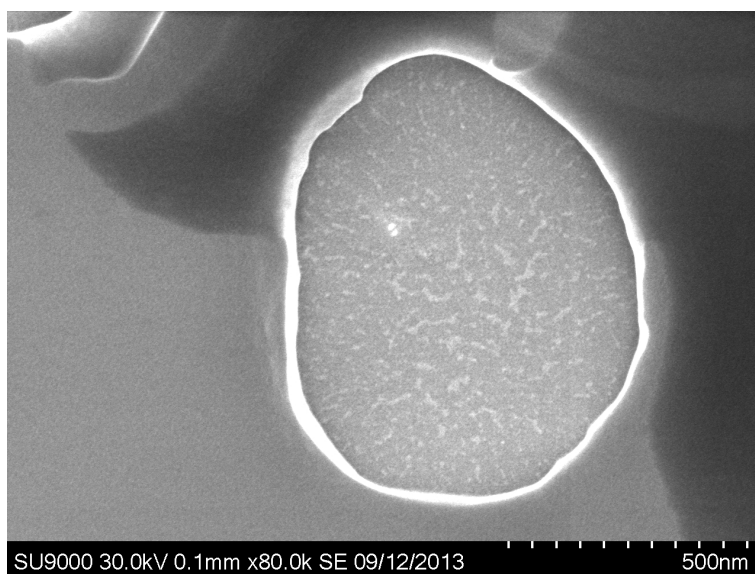


Figure 33: PCL-microgel fibre type C cross-section, cut by a microtome (80 nm slights). The fibre interior is visible, but the microgels can not be differentiated from the PCL polymer matrix

5 Fibre Characterisation

As it was shown in the previous chapter fibres with two completely different morphologies have been obtained by electrospinning from two different solvent systems. Type S has the microgels attached exclusively at the surface and in type C the microgels are located only in the fibre interior. Therefore, different behaviour in terms of swelling or degradation can be expected. In the following sections the analysis for both fibre types will be presented, compared and discussed.

5.0.1 Fibre Properties

In all following results the fibre types defined above will be compared, but their comparability has one issue that has to be addressed before, namely their microgel content. The spinning solutions have a different microgel content 30:70 and 40:60 wt% respectively. To compare results, like the degree of swelling for example, where the amount of microgels will certainly be of importance, it is necessary to know the exact amount of microgels in both fibre types, to differentiate between effects from the fibre structure and the materials composition. For the determination of the microgel amount in the fibres TGA measurements have been done. Figure 34 shows the results of these measurements. Since the temperature of the thermal decomposition of PCL and the microgels differs, two distinctive mass-loss steps can be seen. From the mass-percentages that are lost in these steps the amount for each material can be calculated. For the type S fibres spun from methanol/toluene the effective microgel/polymer ratio is 20:80 wt% and for type C fibres spun from Ch/DMF the effective microgel/polymer ratio is 22.5:77.5. Even though the microgel/polymer ratio before the spinning process is not the same, afterwards it is considering the margin of error. For the comparison of the following analysis this is convenient, since all differences in the results can be explained by the structural differences of the fibres, but in general it is a sign that the process is not working perfectly. 10 respectively 20 wt% of the microgels are lost during the process.

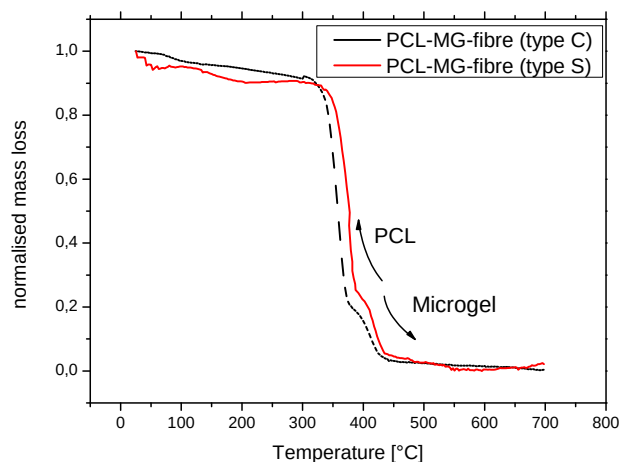


Figure 34: TGA measurements of the different fibre types showing the two step thermal decomposition of the fibres, which can be used to determine the actual material composition

The first property to be investigated is the degree of swelling of the PCL-microgel fibres measured by TGA. Figure 35 A shows the equilibrium degree of swelling for both fibre types at 25 and 50 °C. The pure PCL fibres show a very low degree of swelling of 1.7 independent of the temperature. This is to be expected since PCL is hydrophobic and exhibits a very weak water uptake. Furthermore, the determined value is connected to water captured between the fibres in the nonwoven due to capillary forces and is not caused by water uptake into the fibres. Therefore, the degree of swelling in this case is basically an artefact, which can also be seen by the immediate and rapid decrease of weight in the measurements compared to the one of the microgel modified fibres. This is shown in an example comparison between pure PCL fibres and the type S fibres swollen at 20 °C in Figure 35 B. The type S fibres have, even though they are also based on hydrophobic PCL, due to the microgels at the surface, a much higher degree of swelling of 3.9 at 25 °C. The microgels, which more or less form a shell around a PCL core, take up most of the water and the PCL core remains mostly dehydrated. The degree of swelling decreases to 2.4 at 50 °C, a temperature above the VPTT, because the microgels collapse and are in their less hydrophilic form. They will still uptake water but in a smaller degree, which is also shown by the fact, that a degree of swelling of 2.4 is still higher than the one from pure PCL fibres.

Fibres from type C exhibit a degree of swelling of 5.7, which is even higher than the one of the type S fibres. The surface of the type C fibres consists of hydrophobic PCL, since the microgels are assumed to be only in the fibre interior. These results show not only that this assumption has to be true, because otherwise there should not be any water uptake, but they

also permit the assumption of the formation of pores that can lead the water into the fibres to the water uptaking microgels. Due to the fact that the degree of swelling is even higher than that for the type S fibres, while having the same amount of microgels, the idea of a free volume around the microgels formulated for the PVA-microgel fibres is reinforced. A decrease of the degree of crystallisation (compare the DSC results) also supports this assumption. At 50 °C, above the VPTT, the degree of swelling decreases to 2.5, which is similar to the type S fibres. However, the TGA results show that the microgels change the fibre properties from hydrophobic to in some extent hydrophilic and the degree of swelling can be controlled by the fibre morphology, depending on the position of the microgels in the fibre. Furthermore, the dependency of the degree of swelling on the temperature shows that the thermo-sensitive properties of the microgels remain intact in the fibre structure.

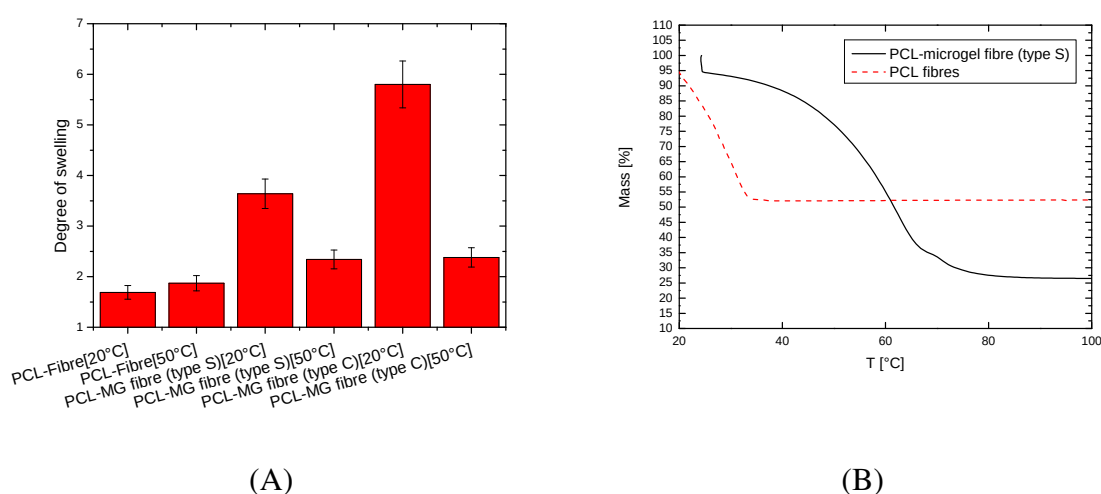


Figure 35: Degree of swelling of both types PCL-microgel fibres determined by means of TGA (A) and two example TGA measurements (B)

The TGA measurements show that an uptake of water is possible, therefore the PCL-microgel fibres seem to be hydrophilic modified; the modification influences the hydrophilic/hydrophobic balance on the fibre surface. To address this property in more detail contact angle measurements have been done. Figure 36 show the pictures taken during these measurements. Pictures A and B show the water droplet on the PCL fibres directly after the dripping and after ten minutes. The droplet does not show any change after 10 minutes except of some evaporation. The contact angles are $120 \pm 5.8^\circ$ and $119 \pm 5.9^\circ$, indicating the hydrophobicity of PCL, correlating with the literature data [87]. Figure 36 C and D show the same experiment for type C fibres and E and F for type S fibres. In both cases the first picture was made directly after the dripping of the droplet and the second just one second later. The water droplet is absorbed by the fibres, since the microgels modified them in the way that they get hydrophilic and that they can absorb the water. The surface properties of the fibres are completely changed. The time

the droplet needs to be absorbed is for the type C fibres slightly higher, which can be expected because the microgels are, in contrast to the type S fibres, not at the surface but in the fibre interior and the water has to pass first through pores into the more hydrophilic fibre interior.

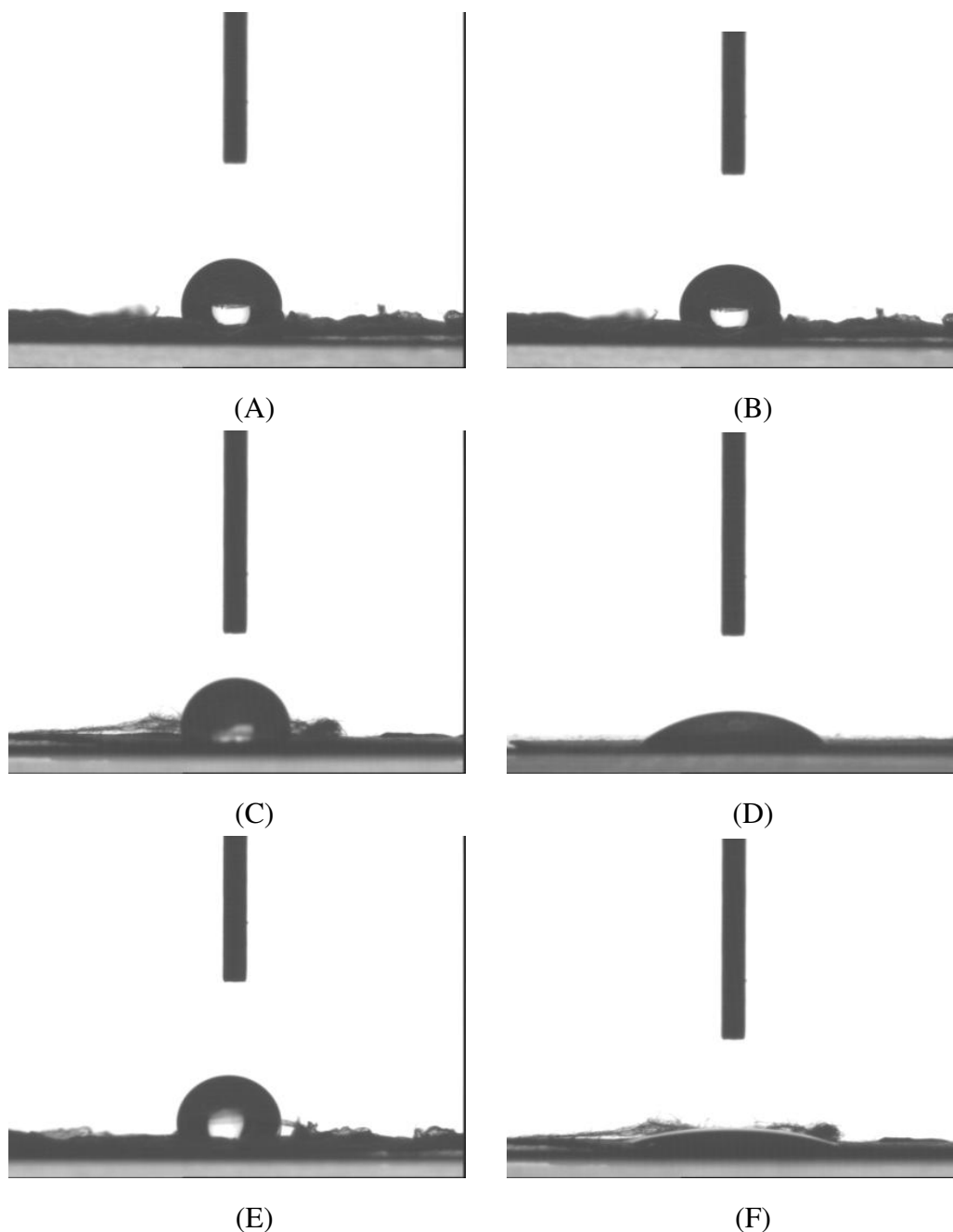


Figure 36: Water droplets on the surface of fibre mats of different samples. (A) PCL fibres after dripping, (B) after 10 minutes; (C) fibres type C after dripping, (D) after one second; (E) fibres type S after dripping, (F) after one second

The fibres have also been analysed regarding to their moisture sorption properties. Figure 37 shows the sorption (A) and desorption (B) rates of water moisture for both fibre types. Pure PCL fibres are not displayed, since no reasonable values can be obtained (explanation will be given in the next paragraph). The adsorption is in general decreasing with increasing humidity, because the increasing saturation hinders further moisture uptake. The desorption is antithetic to this behaviour. No noticeable difference can be seen between the two fibre types as well as between the two temperatures used.

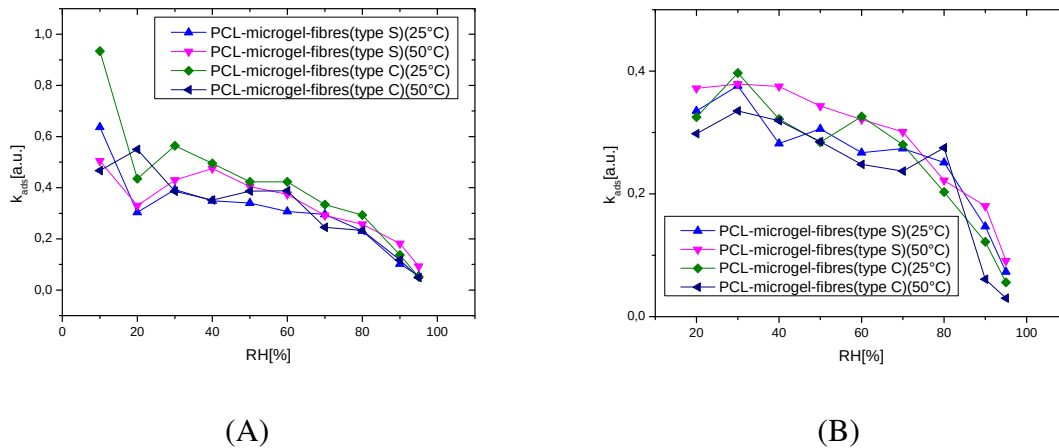


Figure 37: Water moisture sorption (A) and desorption (B) measurements of both fibres types at 25 and 50 °C

Taking into account the sorption analysis of the PVA-microgel fibres (compare section 6, part III) and the TGA results, especially for the type C fibre, an increase for 50 °C was expected due to a possible structural opening. However, the Harkins-Jura plot of the isothermal data (compare section 6, part III) shows that this is not the case for PCL based fibres, since the whole data range can be plotted by one straight line, like it is shown in Figure 38. Even though the plot only works for a relative humidity above 10 %. The fact that no structural opening occurs on the PCL-microgel fibres explains that no difference between the two different temperatures can be seen. Table 7 shows the results for the analysis with the Harkins-Jura method. The plotting of the data of pure PCL fibres gives very low correlation coefficients. Harkins and Jura state that if this linear plot is not possible the adsorbate is not suitable for the adsorbent, therefore the data for the sorption analysis did not give reasonable values for pure PCL fibres. The microgel modified PCL fibres can be plotted with this method; the microgels make the fibres suitable for water moisture.

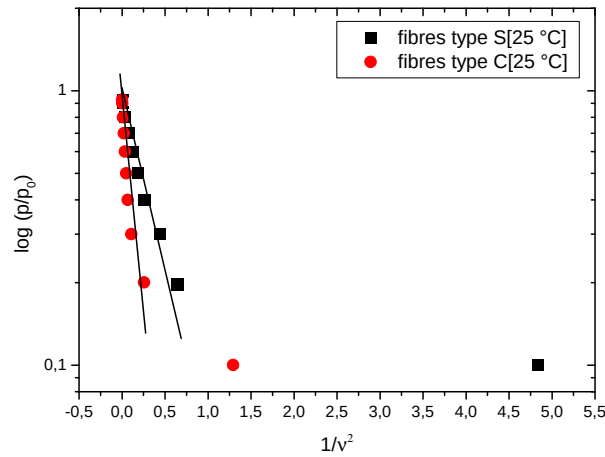


Figure 38: Harkins-Jura plot of the moisture adsorption isotherme of both types PCL-microgel fibres at 25 °C; the data points can be fitted by on straight line for relative himidities above 10%

The values for the surface area calculated with the Harkins-Jura method show a difference of 120 m²/g between the two fibre types. Since the microgels in type S fibres are only at the surface, no pores are formed in contrast to the microgels in the fibre core of the type C fibres, which can explain in some extent, additionally to the crystallisation degree, the higher water uptake shown in the TGA results.

Table 7: Results of the Harkins-Jura plot for PCL-microgel fibres

Sample	A	S [m ² /g]	correlation coefficients
PCL fibres [25 °C]	—	—	0.832
fibre type S[25 °C]	1.17	131	0.973
fibres type S [50 °C]	1.07	125.2	0.946
fibres type C [25 °C]	4.76	264.2	0.98
fibres type C [50 °C]	4.94	269.19	0.963

DSC measurements have been done to show the volume phase transition of the microgels and therefore prove that their thermo-sensitive properties are retained in the fibre structure. The measurements were done in a temperature range of 25-50 °C and the fibres were swollen with D₂O; the results are shown in Figure 39 A. As expected the pure PCL fibres do not show any transition in this temperature range. The graph of the pure microgels was already shown in

Figure 21 . It shows a broad peak reflecting the volume phase transition, and the VPTT is found at 40 °C. The general VPTT for PCVL is 32 °C; the shift is due to stronger hydrogen bonds with the D₂O and the agglomeration of the freeze-dried microgels, which represents a hindrance for the polymer chains. Both types of microgel modified fibres show a transition; 34 and 36 °C for type S and type C, respectively. The shift to lower temperatures can be explained on one hand by the interactions of the hydrophobic CH₂ segments of the VCL rings with the PCL chain, which reduces the chain mobility and solvation by water molecules. A similar effect was observed for PNIMPAAM microgels with incorporated hydrophobic co-monomers [96]. On the other hand the microgels are also less hindered, especially on the fibre surface, which is also shown by the lower VPTT of both fibre types, than in the agglomerated pure microgel sample. Concluding it can be said that the thermo-sensitive properties are proven to be retained in the fibre structure and due to the reversible nature of the volume phase transition, the swelling of the fibres can be tuned by temperature, considering the TGA results.

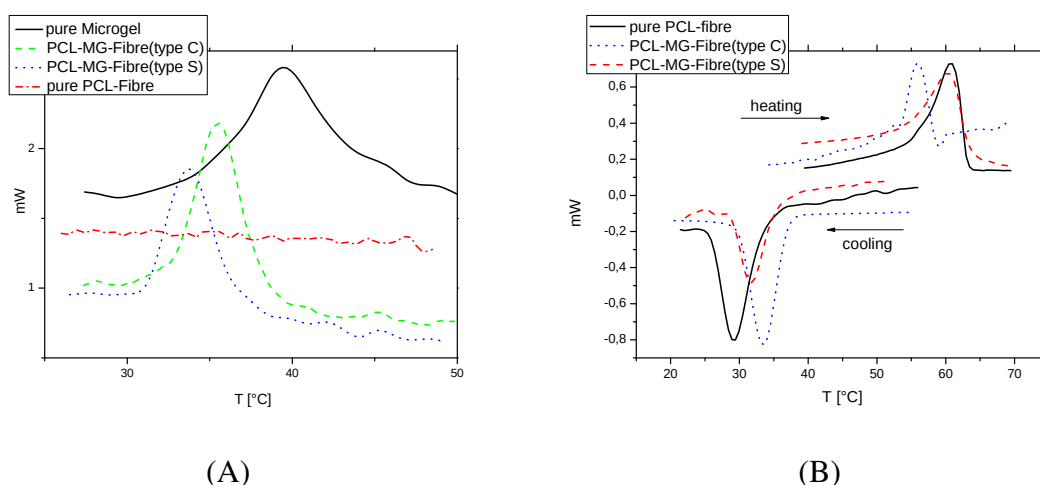


Figure 39: DSC measurements of pure PCL fibres, pure microgels and both PCL-microgel fibre types (A); Heating and cooling runs of the DSC spectra for the determination of the crystallinity (B)

Figure 39 B shows the DSC spectra of dry measured fibres, without D₂O, to investigate the crystallinity of the fibres. Heating and cooling runs in the temperature range of 20 -70 °C have been performed. PCL is in general a crystalline polymer, having a melting point of 60 °C [97]. The pure PCL fibres show expectedly also this melting temperature in the DSC measurement. The type S fibres show the same melting point, since the microgels are exclusively at the surface and the PCL does not undergo any change in its properties. In contrast to that the melting point for the type C fibres is decreased to 56 °C. The reason for that is found in the results of the crystallisation process during the cooling run. The crystallisation temperature shifts for the type C fibres to higher values, probably because the microgels in the fibre interior

act as nucleation centres promoting the crystallisation process. The peak area of the heating run indicates the energy needed to melt the material and represents its crystallinity in the way that literature states for 100 % crystalline PCL 139 J/g [85, 98]. The deviation from this value shows the variance in crystallinity. Pure PCL fibres have a crystallinity of 53.2 %, the type S fibre a slightly reduced one of 40.3 %, which can be seen also in the shift in the cooling run. This might indicate that some single microgels are trapped in the fibre interior here as well. For the type C fibres the crystallinity is decreased to 25.8 %. The microgels in the interior are defects in the structure causing pores and reduce the crystallinity, acting as nucleation centres in the crystallisation process. The decreased crystallinity of the type C fibres confirms in some extent the TGA results for the increased degree of swelling.

5.0.2 XRD studies of PCL-microgel fibres

X-ray diffraction measurements have been done to further investigate the effects of the microgels on the internal structure of the fibres. Even though the crystallinity was already determined by means of DSC measurements (compare section 5.0.1 part IV) X-ray diffraction can lead to new insights. The results gained in this investigation were nevertheless unexpected. Figure 40 A shows the XRD spectra of both fibre types. In both spectra the double peak represents the semi-crystalline PCL, which has an amorphous (broader hill) part and a crystalline part (peaks). The spectra are shifted in their intensity to be compared more easily in one graph. The fibres type S spectra does not show any other peaks, the microgels influence could only be seen in the degree of crystallisation (compare section 5.0.1 part IV) and since the microgels are exclusively on the fibre surface no bigger influence was expected. The spectrum of the type C fibres, which is also shown in Figure 40 B in a more detailed scale, shows in addition to the PCL peaks more and periodic peaks. The periodicity of the peaks in this spectrum represents perfectly the periodicity of a body-centred cubic lattice, which means the peak reappears the first time after $\sqrt{2}$ times the first position followed by $\sqrt{3}$, 2, $\sqrt{5}$, $\sqrt{7}$ and so on times the first position.

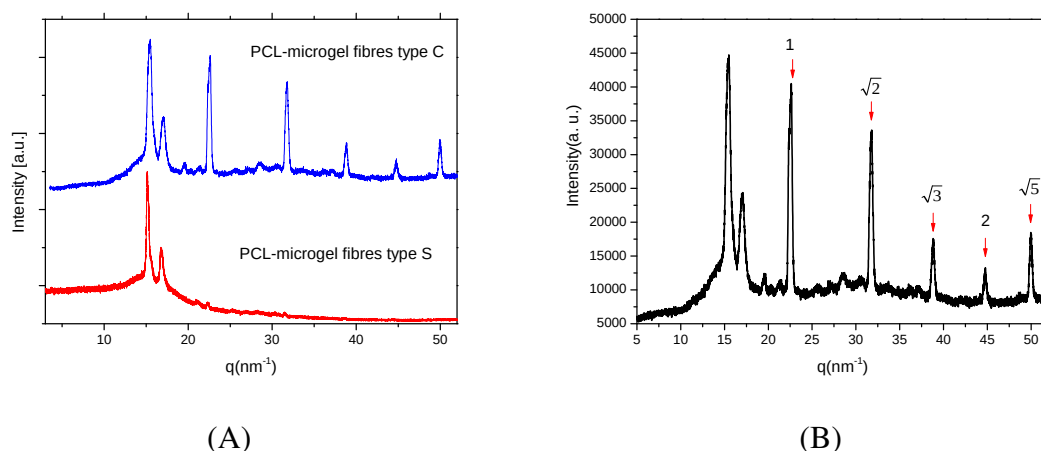


Figure 40: XRD spectra of both types of PCL-microgel fibres (A), a detailed look at the spectrum of the fibre type C (B), which shows a periodic appearing peak representing a body-centred cubic lattice

The first explanation for this peaks that comes to mind is a ordered and periodic arrangement of the microgels in the fibre core, but a simple approximation of the full width at half height of the first peak gives a crystal size of some few nm and the microgels themselves have already a diameter of several 100 nm, which excludes the first idea. Right now this phenomenon is not yet fully understood but nevertheless the results above and the ones following allow a hypothesis.

Since this result is quite astonishing the experiment was repeated several times. The same sample gave always the same result. Samples prepared in the same way, also gave usually the same results, but it seemed to depend on the state of drying of the samples, which means fibres with residue solvents (problem during the fabrication, for example humidity in the laboratory) did not show as good results as fibres without. Pure PCL fibre, fibres from type S or fibres made in the same way as fibres type C, but with slightly different process parameters (less homogenous, fibres of lower quality) did not show these results. Also films prepared as shown in section 3.2 part IV did not show these results. Therefore, the conclusion has to be drawn that the appearance of these peaks is special for exactly this fibre type, with specific fabrication conditions. Due to the connection of residue solvents and the appearance of the peaks in the spectra experiments with swollen fibres have been done. The dried fibre sample was measured and afterwards water droplets were placed on the sample, directly on the sample stage, to swell the fibres, which than were measured again. After letting them dry out completely a third measurement was performed. The results of these measurements can be seen in Figure 41 A. The peaks disappear in the wet and swollen state of the fibres and reappear when the fibres are dry again. In the swollen state water penetrates into the fibres and the microgels

swell, since they are the hydrophilic compound in this composite material. The vanishing of the peaks in the swollen state and their reappearing after the evaporation of the water leads to the conclusion that the peaks originate from a confinement effect in or in the closer area around the microgels, for example a confinement of PCL chains. Figure 41 B shows again spectra of a sample in different stages. First again after the sample preparation, but the second spectrum was recorded after the sample stage was heated up to 75 °C, which is slightly above the melting temperature of PCL (60 °C). Afterwards the sample was slowly cooled down to 35 °C and than back to room temperature. In the molten state the peaks disappear again and during the cool down or better to say during the re-crystallisation they reappear. Even though the microgels are not affected too much by the elevated temperatures, the peaks disappear in the molten state of the PCL, where the PCL chains exhibit a higher mobility, which in turn confirms in some extent the idea of the PCL chain confinement close or even inside of the microgels.

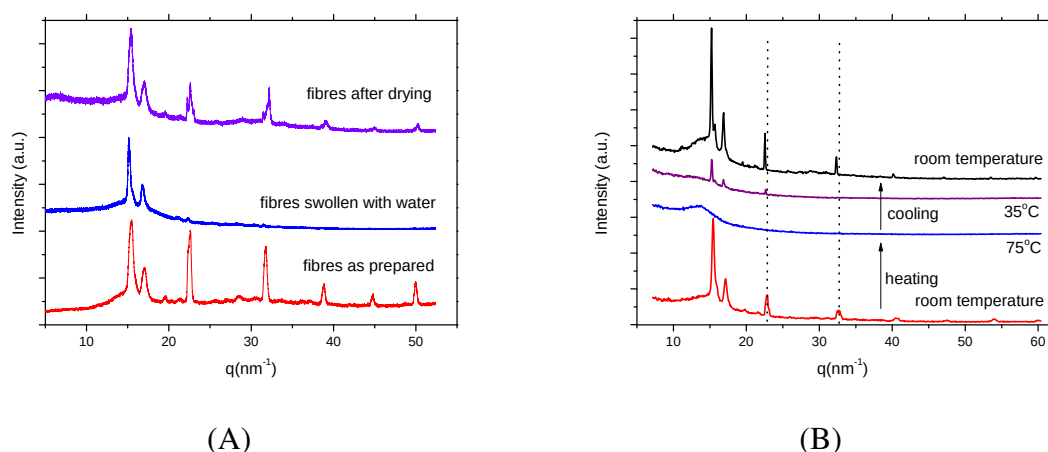


Figure 41: XRD spectra of fibres type C before, during and after swelling with water (A); XRD spectra of fibres type C before, during and after melting at 75 °C (B); both times the peaks disappear in the changed state and reappear afterwards again

The results presented in this section let assume that a confinement in or close to the microgels takes place, but no proof of this effect is given and an explanation could not be found. However, similar effects can be found in literature for interactions of colloids and polymers [99]. In this literature example it is shown that confinement, can lead to solidification and different phases in polymer colloid mixtures, due to an increased interparticle attraction. In the case of the PCL-microgel fibres this could mean a localised confinement induced periodicity of the PCL or PVCL chains.

5.0.3 Degradation

One of the key properties of PCL for any bio/medical application is its degradability, therefore the investigation of this property in these new composite materials is essential. The degradation of PCL itself, the decomposition of its polymer chains, can occur by hydrolytic or enzymatic pathways [85, 86] and it is a well understood phenomenon, but the microgels inside or at the surface of the fibres might have an influence on the fibre degradation. Both fibres types were placed in PBS buffer and the degradation process was followed by means of electron microscopy, DLS and gravimetrically. These investigation have been done in certain time intervals. The DLS investigation was focused on the degradation media, to analyse if the microgels are released into it during the degradation and decomposition of the fibre matrix material. Figure 42 shows the change in the fibre morphology upon the degradation of both fibre types (A and B for type S fibres and C and D for type C fibre) as well as pure PCL fibres (E and F). The fibres before the degradation were shown already in Figure 31 and Figure 32. Figure 42 A,C and E show the fibres after 4 weeks in PBS. The pure PCL fibre do not show a change in their morphology, but a slight reduction in their diameter. In contrast to that the type S fibres show a release of the microgels, which can be seen because the fibres are not completely covered anymore by microgels and there are microgels present on the microscope sample holder. In Figure 31 A and B it is shown how the microgels are bond by a polymer film to surface of the fibres. It is to expect that this polymer film degraded within the first weeks and the microgels were set free into the surrounding medium. Type C fibres also show a change in their morphology after four weeks. The fibre structure is less homogenous and there are microgels present on the micrograph. On one hand this confirms again the existence of the microgels in the fibre interior, since they are noticable after the surface degrades to some extent and before they were not; and on the other hand it also shows that the microgels will be set free in the medium, probably just slower than from the type S fibres.

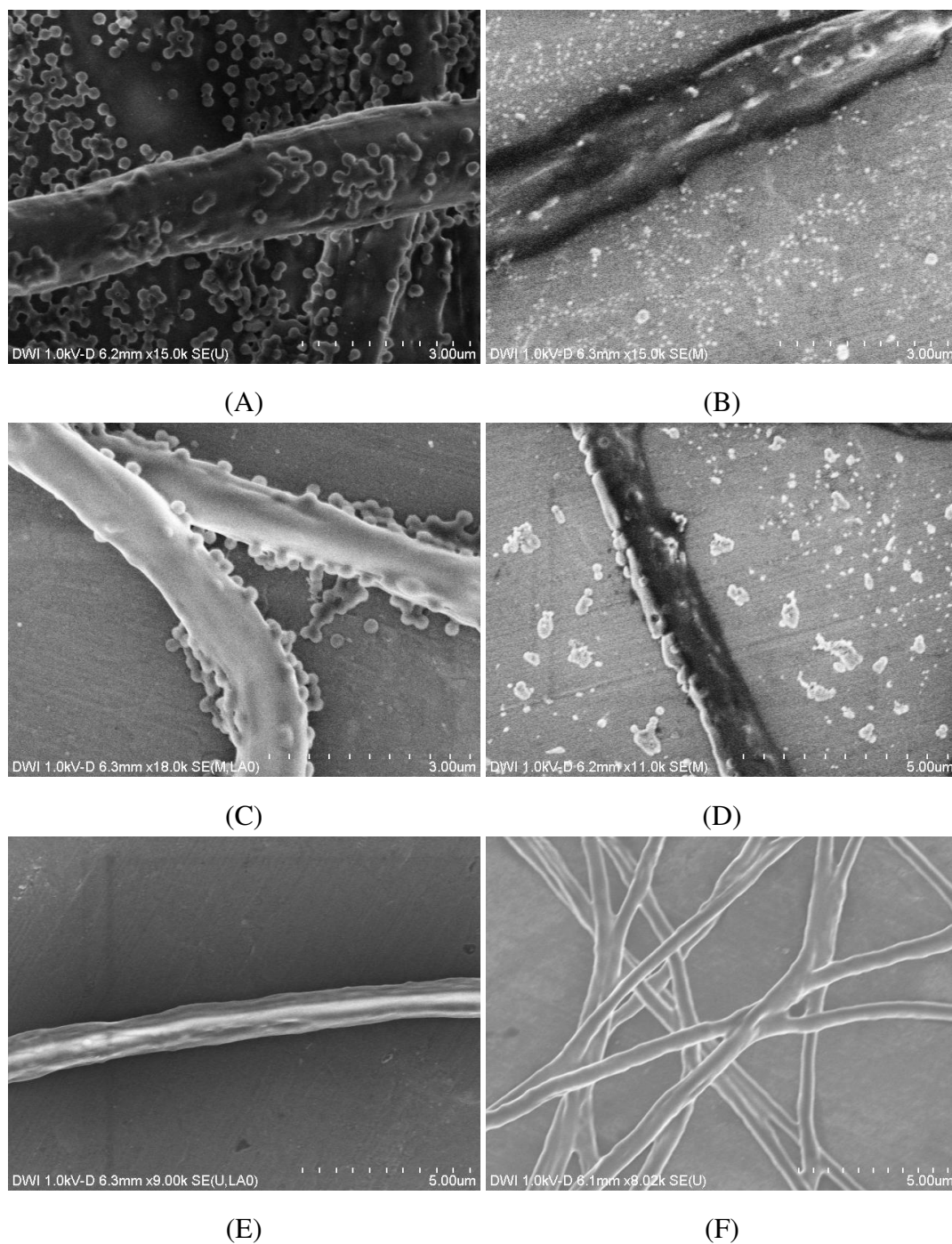


Figure 42: FESEM micrographs of the degradation process of the type S fibres after 4 weeks (A) and after 28 weeks (B); of the type C fibres after 4 weeks (C) and after 18 weeks (D) and of pure PCL fibres after 4 weeks (E) and after 28 weeks (F)

DLS measurements of the medium have been done to prove the release of microgels from the fibres into the medium during the degradation process. Figure 43 shows the particle size distribution of the particles found in the degradation media after 12 weeks for both fibre types and a size distribution of the standard microgel after synthesis and dialysis. These measurements clearly prove the release of the microgels even though the size distribution in comparison to the standard is broadened. This broadening has different reasons: some microgels might be aggregated after the spinning process and additionally some PCL residue could be connected to the particles. Another reason is the PBS itself, which influences the measurements due to its composition.

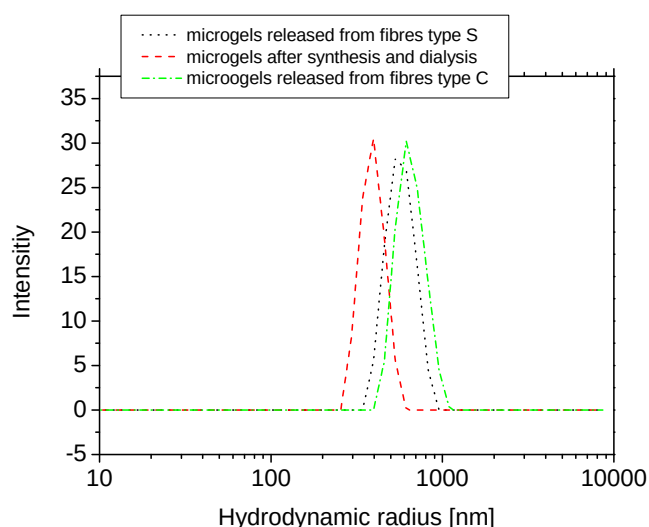


Figure 43: DLS measurements of the degradation media showing the particle size distribution of the microgels released from the fibres

Figure 42 B, D and F show the different fibres after 28, 18 and again 28 weeks, respectively. Type S fibres are completely degraded after 28 days, type C fibres already after 18 weeks. The white and slightly crystalline structures visible on both micrographs are salt crystals that grew during the degradation consisting of NaCl and KCl, which is present in the PBS. In contrast to the PCL-microgel fibres the pure PCL fibres are still recognisable as fibres after 28 weeks. The fibres look less homogeneous and the diameter decreased, but they are still present. The composite fibres degrade remarkably faster. To confirm the FESEM data the degradation was followed by gravimetric analysis of the mass loss. The results are presented in Figure 44. The data show that the microgel modified fibres degrade faster than the pure PCL fibres, like it was shown already in the FESEM pictures. The enhanced or accelerated degradation is a consequence of the water uptake, which was achieved by the incorporation of the microgels into the fibres. The hydrolysis rate depends logically on the contact of water with the ester bonds, which in pure PCL fibres will basically only occur at the surface. The composite fibre

can uptake water which also leads to hydrolysis inside of the fibre at the same time. The comparison of the two composite fibre types shows that in the first 8 weeks the mass loss is similar and afterwards the type C fibres show a faster decrease in their mass. During the degradation the type S fibres will release in the early stages the microgels from their surface, which will be part of the mass loss, afterwards the mass loss is slower because the rest of the fibre is mostly only PCL. In contrast to that, the type C fibres have a basically homogenous cross section and show a linear loss in mass. Since they can uptake more water than the type S fibres (compare the TGA results in section 5.0.1, part IV) and, due to the fact that the microgels in their interior will spread the water homogenously throughout the whole fibre, the hydrolysis rate is highest in the type C fibres. Another reason for the faster degradation of the type C fibres is their lower degree of crystallinity (compare DSC results in section 5.0.1, part IV). A structure of higher crystallinity, is less penetrable for water, which was also already shown in the PVA-fibre chapter. However, the mass loss investigation is in good agreement with the microscopy data and confirms the interpretations given above. Overall the data presented in this section indicates that the degradation process of the PCL-microgel fibres can be tuned by the incorporation of microgels and their localisation in the fibre structure.

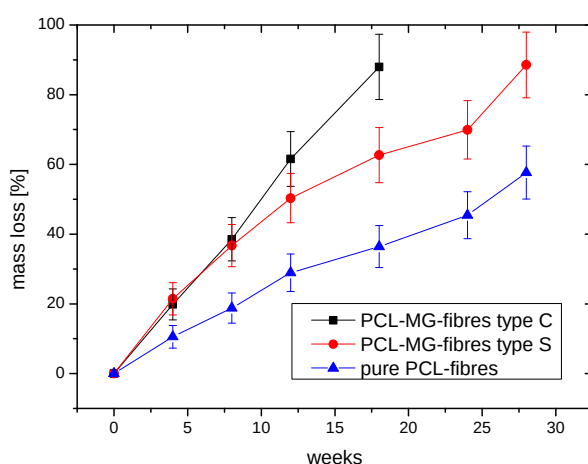


Figure 44: Mass loss during the fibre degradation determined by means of gravimetical analysis, showing different degradation times of the several fibre types

6 Summary/Conclusions

This part of the thesis was focused on improving the idea of microgel-polymer composite fibres, by using water insoluble and degradable PCL and achieving different fibre morphologies. To achieve the latter different solvents and solvent systems have been tried, to find methanol/toluene and chloroform/DMF as most promising. For both solvent systems an ideal set of solution and process parameters was defined to fabricate homogenous and reproducible fibres of a good quality, with a defined fibre diameter by a continuous one step electrospinning process. Fibres spun from methanol/toluene, uniquely at a mass ratio of 50:50, have a morphology with microgels exclusively on the fibre surface, whereas fibres spun from chloroform/DMF show a morphology with microgels exclusively in the fibre core.

The combination through this straight forward one step process of hydrophobic PCL with hydrophilic microgels leads to a radical change in the fibre properties. While pure PCL fibres are not able to swell with water the composite fibres with microgels are hydrophilic, can swell with water and can adsorb water moisture. Furthermore, the degree of swelling is tuneable by temperature, since the microgels retain their thermo-sensitive properties, which was also proven by DSC measurements. The moisture sorption analysis also shows that the fibres with microgels in the fibre core have a larger surface area, due to pores, which are caused by the microgel. The degradation process is shown to take place in a time scale of three to four months, whereas the fibres with microgels in the fibre core degrade faster due to a lower degree of crystallisation and because water is taken into the fibre interior. Therefore, the degradation depends on the fibre morphology and is in general faster than in pure PCL fibres. Furthermore, the microgels are set free into the water during the degradation.

Concluding it can be stated that the electrospinning of microgel-PCL composite fibres is a simple and fast way to hydrophilically modify PCL fibres. This combination of materials leads to new fibre properties regarding swelling in water and moisture uptake and the degradation behaviour is also influenced. The fact that two possible morphologies can be achieved broadens the application possibilities of these fibres, especially in the combination with further modified microgels or even completely different colloids or inorganic nanoparticles.

*Degradable Microgels with Hydrophobic
Domains*

v

1 Introduction

During the work on the PCL-microgel fibres, while the results became more and more promising, the general idea of this work, to combine the special properties of polymer micro-fibres and microgels, was in some way extended. Microgel-polymer composite microfibrils were already successfully fabricated with two different polymers and in the case of PCL also in different morphologies. But the microgels in the fibres were standard microgels, which are thermo sensitive and give the fibres the ability to swell with water. However, microgels have a wide range of possible modification by simply adding co-monomers or other additives to the synthesis, they give a big opportunity to further improve the fibres for possible applications (for example in medicine). As it was shown for the PCL-microgel fibres, the microgels are released into the water during the degradation, which could also mean into the human body. Therefore, the obvious idea is to have microgels that are degradable as well. The most obvious medical application would be the uptake and release of drugs, which are often hydrophobic substances. In this context the topic of this part of the thesis is the synthesis of degradable microgels with hydrophobic domains.

Degradable microgels have been synthesised before, in different ways. Some examples are the inverse microemulsion polymerisation with an acidic degradable crosslinker [100], dextran-hydroxethyl methacrylate microgels (7 μm), which degrade by hydrolysis [101], a slightly complicated precipitation polymerisation with a degradable azo-aromatic crosslinker [102], or even microgels crosslinked with hydrazone fabricated in microfluidic chips [103]. Microgels have also already been investigated regarding their abilities as drug delivery systems [104, 105, 106, 107]. Examples for this are polysaccharide-based microgels [106, 108] and different approaches with poly(N-isopropylacrylamide)(pNIPAAm) [107]. NIPAAm combined with acrylamide [109] and hydrophobic co-monomers like hexylacrylate or hexafluorobutylpolymethacrylate [110] were used to achieve drug uptake and release properties. However, in contrast to these examples, the idea for the microgels described in this part of the thesis was the combination of degradability, hydrophobic domains and thermo-sensitivity. VCL was chosen over NIPAAm to synthesise these microgels because of the discussed disadvantages in the field of biocompatibility of NIPAAm [14, 13], and to stay closer to the microgels systems used until now. The degradability, as well as the hydrophobic domains, will both be introduced into the microgels by the crosslinker, keeping the synthesis in this way as simple as possible, having only one monomer and a crosslinker. The crosslinker is a star-shaped acrylate functionalised poly(ϵ -caprolactone) [81, 111, 112], which is degradable at its caprolactone repeating units. These units are also the hydrophobic domains. Furthermore, the degradation mechanism is exactly the same as in the PCL-fibres, since both consist of caprolactone. However, because the crosslinker is hydrophobic and therefore not soluble in water, a usual precipitation polymerisation is not possible. The synthesis route chosen is a miniemulsion polymerisation of the monomer melt in water. No toxic solvents were used during the whole process and better size distribution can be achieved.

Recapitulating, the idea of this part of the thesis is the synthesis of thermo-sensitive, degradable microgels with hydrophobic domains using just one monomer (VCL, thermo-sensitive) and a crosslinker (degradable and hydrophobic) by a straightforward miniemulsion polymerisation, excluding any organic solvents. Possible applications for this kind of microgels, besides using them with the microgel fibres, are in the textile industry as carriers of insecticides or dyes and also in medicine as targeted or smart drug delivery system.

Besides introduction and conclusion this part of the thesis is divided in six chapters. The experimental part will give all information needed to replicate all syntheses, experiments and analyses described in the work. For the descriptions that would be similar to the ones in a previous part of this thesis, only references to the according sections are given. Afterwards the synthesis procedure is investigated in detail, because even though the idea of an emulsion of the monomer melt in the solvent sounds simple, questions occur due to the solubility of VCL in water. The chapter “Microgel Analysis” deals with the study of the synthesised microgels regarding the incorporation of the crosslinker or their swelling behaviour in water and stability. The investigation of the degradation process and the immobilisation of hydrophobic substances and their release behaviour is discussed in an extra chapter following the general analysis of the microgels.

Most of the results presented in this part are going to be published in a peer-reviewed paper, which is still in the writing phase. This paper will be written by me and with me being the first author. Some of the experiments/results have been done by Astrid Catalina Molano Lopez and Ann-Katrin Steppert during their bachelor and research work, respectively, under my supervision. Some first preliminary tests have also been done by Florian Konstantin Störmann during his diploma thesis. Nevertheless, everything has been rewritten for this thesis.

2 Experimental Part

In the following sections are presented only the descriptions of synthesis and fabrication processes of the samples and materials, as well as the description of experiments and analyses that have been done with these samples, which can not be found in one of the previous chapters of this thesis. In cases of specific changes in the experiments, these changes will be mentioned and the remaining description will be referred to. This is done to avoid unnecessary repetitions.

2.1 Materials

Acetone (99.9%, VWR), 2,2'-Azobis[2-methylpropionamidine] dihydrochloride (AMPA, 97%, Aldrich), cetyl trimethylammonium bromide (CTAB, 99.9%, Aldrich), 9-diethylamino-5-benzo[α] phenoxazinone (Nile-Red, 98%, Aldrich), N,N'-methylen-bis-(acrylamide) (BIS, 99%, Sigma-Aldrich), phosphate buffered saline (PBS, Aldrich), (RS)-2-(4-(2-methylpropyl)phenyl)propanoic acid (Ibuprofen, 98%, Aldrich), tetrahydrofuran (THF, 99.9% VWR), distilled water. All these materials are used as delivered without having undergone any other cleaning procedures. N-Vinylcaprolactam (VCL, 98%, Aldrich) was purified by vacuum distillation under nitrogen before use.

2.2 Synthesis of xPCL Crosslinker

The star-shaped acrylate-functionalised poly(ϵ -caprolactone) crosslinker (xPCL) was synthesised by following a procedure presented in a previous work [81, 111, 112]. The synthetic pathway is shown in Figure 45. In this work xPCL with 4 or 6 arms was used and the number of caprolactone repeating units was 5 and 15. Di(trimethylolpropane) or di(pentaerythritol) were dissolved in 3-caprolactone and $\text{Zn}(\text{oct})_2$ was added. The mixture was stirred for 24 h at 130 °C; the polymer was recovered by precipitation in cold hexane. The precipitate (PCL) was separated by decantation and dried in vacuum at 40 °C until constant weight was reached. The star-shaped PCL was dissolved in dichloromethane and acryloylchloride was added. Afterwards everything was stirred for 5 h at 60 °C and then precipitated in cold hexane. The separation of the precipitate was done by decantation. Afterwards the precipitate was dried in vacuum at room temperature until constant weight. Characterisation data for most frequently used crosslinker in this study (xPCL having 4 arms and 5 repeating units): yield: >97%. $M_{n,SEC} = 4900$ g/mol with repeating units $n = 5$. ^1H NMR (CDCl_3): δ (ppm) $\frac{1}{4}$ 0.80-0.92 (m, H4); 1.32-1.48 (m, H3, H9); 1.58-1.72 (m, H8, H10); 2.31 (tr, H7); 3.22-3.36 (m, H1); 3.96-4.10 (m, H5, H11); 4.10-4.20 (tr, H11E) 5.82 (d, H14); 6.11 (dd, H13); 6.40 (d, H14).

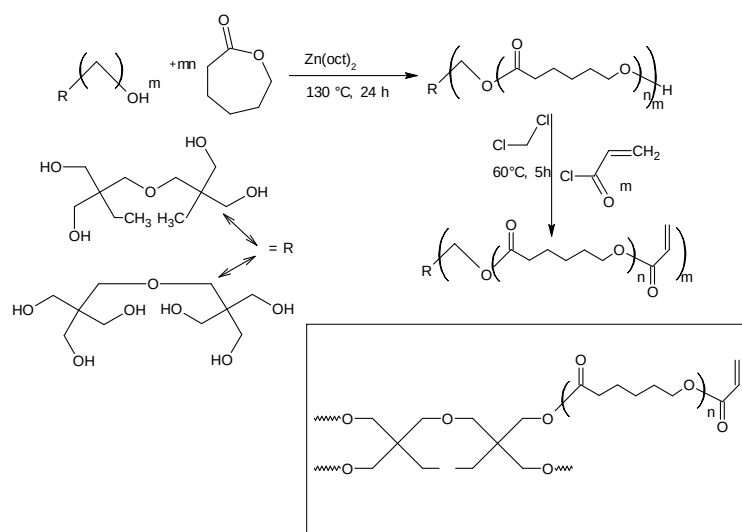


Figure 45: Synthetic pathway to the various xPCL crosslinker; in the frame an example with 4 arms is shown

2.3 Synthesis of Microgels

As it is shown in Figure 46 the synthesis of the microgels in this part is divided in three steps. In the first step the surfactant cTAB was dissolved in 100 mL of distilled water, which was then heated to 70 °C. In another flask the monomer N-vinylcaprolactam (VCL) was melted at 70 °C and the crosslinker xPCL was dissolved in the monomer melt under nitrogen atmosphere. These two mixtures are mixed in the second step while keeping the temperature constant at 70 °C. First a pre-emulsion is prepared by simple stirring with a magnetic stirrer, then this pre-emulsion is improved by an additional emulsifying step using the MRT-CR5 microfluidizer (Microfluidics corp., USA) (1800 bar, 8 cycles) to form a more stable emulsion. The obtained miniemulsion was then transferred into a double-wall glass reactor preheated to 70 °C which was equipped with a stirrer, reflux condenser and was again purged with nitrogen. In the third step the water-soluble initiator AMPA was added and the polymerisation continued for 6 h under continuous stirring at 70 °C. A detailed list of the ingredients used for all microgel synthesis is provided in Table 8. The microgel dispersions were purified for 72 hours by dialysis (Millipore Labscale TFF System) using a regenerated cellulose membrane with MWCO 10.000 g/mol. Additionally, for some samples precipitation polymerisation was performed. This was done with the standard procedure, which was described in 2.2 part III.

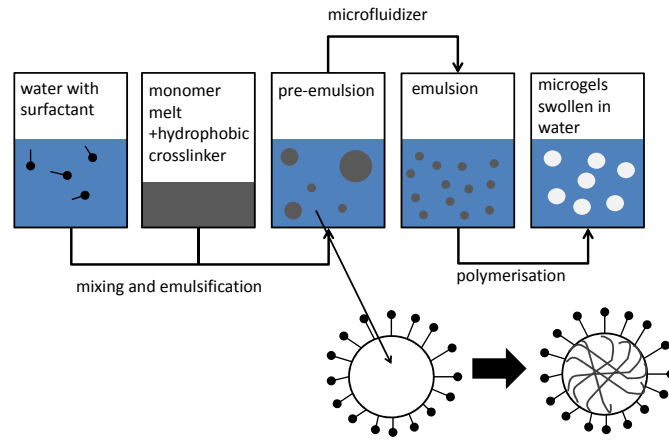


Figure 46: Scheme of the microgel synthesis by miniemulsion polymerisation

Table 8: Used materials in the xPCL modified microgel synthesis

VCL [g]	xPCL(type) [g]	BIS [g]	AMPA [g]	cTAB [g]	water [mL]
1	0.07 (405)	0	0.05	0.005	100
1	0.07 (410)	0	0.05	0.005	100
1	0.07 (415)	0	0.05	0.005	100
1	0.07 (605)	0	0.05	0.005	100
1	0.07 (610)	0	0.05	0.005	100
1	0.1 (405)	0	0.05	0.005	100
1	0.2 (405)	0	0.05	0.005	100
1	0.3 (405)	0	0.05	0.005	100
1	0.1 (410)	0	0.05	0.005	100
1	0.1 (605)	0	0.05	0.005	100
1	0.07 (405)	0	0.05	0.01	100
1	0.07 (405)	0	0.05	0.05	100
1	0.035 (405)	0.035	0.05	0.005	100
1	0.0525 (405)	0.0175	0.05	0.005	100
1	0.07 (405)	0.07	0.05	0.005	100
1	0.12 (405)	0.08	0.05	0.005	100
1	0.0924 (405)	0.0462	0.05	0.005	100
1	0.084 (405)	0.056	0.05	0.005	100
1	0.0462 (405)	0.0231	0.05	0.005	100
1	0.042 (405)	0.028	0.05	0.005	100

2.4 Degradation of Microgel Particles

The degradation behaviour of the microgels was studied in diluted solutions (8 mg/mL). The degradation itself was achieved by adding 15 mg of *Candida rugosa* (Sigma, EC 3.1.1.3, 2 U/mg). The degradation would happen also in water, but the enzyme accelerates the process. The solution was kept at pH 7 and 37 °C, which are the optimal conditions for the enzyme. Samples were taken in several time intervals and investigated by DLS and FESEM.

2.5 Immobilisation of Hydrophobic Dye: Nile Red

To determine the microgel ability to immobilise hydrophobic substances the water insoluble fluorescent dye Nile Red was used. Due to its well known behaviour we used it as a model substance. Nile Red was dissolved in a mixture of acetone/THF (2:1) with a concentration of 0.3 mg/mL and 10 μ L and then successively added to the microgel dispersion (20 mg/mL). The uptake of the dye by the microgels was followed by means of UV/Vis spectroscopy. An aqueous microgel solution without dye was used as reference sample.

2.6 Immobilisation and Release of (RS)-2-(4-(2-methylpropyl)phenyl)propanoic acid (Ibuprofen)

The same procedure as described in 2.5 was used to study the immobilisation of Ibuprofen. Ibuprofen is poorly soluble in water and was used as a cheap and easy to handle drug example. After the immobilisation the samples have been freeze dried, to prevent any release. To study the release of Ibuprofen the microgels were re-dispersed in water and measured in time intervals of 10 minutes using UV/Vis spectroscopy.

2.7 Characterisation Methods

In this section only the characterisation methods that have not been mentioned before in this thesis are described. The descriptions for DLS, sedimentation analysis, Infrared spectroscopy and SEM can be found in 2.6.1, 2.5.2, 2.6.9 and 2.6.3.

2.7.1 Ultraviolet-Visible Spectroscopy (UV/Vis)

The UV/Vis spectroscopy investigations have been done with a Jasco V-630 photometer. This device is a double beam instrument; therefore each sample was measured against a reference. The data was analysed with the device software.

2.7.2 Nuclear Magnetic Resonance Spectroscopy (NMR)

^1H NMR spectra were measured with a Bruker AV 400 FT-NMR spectrometer at 400 MHz. The solvent used was deuterated chloroform (CDCl_3) and tetramethylsilane (TMS) was the internal standard.

3 Synthesis Process: Miniemulsion?

The polymerisation process used to prepare the microgels in this chapter is very similar to miniemulsion polymerisation. In a usual miniemulsion a water insoluble monomer is forcefully emulsified and stabilised in water. In the inverse method water droplets are formed in another solvent and within these droplets particles are formed. The difference to these methods is that VCL is soluble in water at the process temperature of 70 °C (also in the concentrations used) and, nevertheless, a stable emulsion is formed, as it will be shown in the following paragraphs. Experiments were performed to prove the presumed polymerisation process like it was shown in section 2.3 and furthermore to answer the following questions: -Is the VCL/water emulsion stable? -How much monomer/polymer is lost to the water phase? -Can a precipitation be excluded? For these experiments a series of microgels have been prepared by miniemulsion polymerisation using xPCL (405) or xPCL and BIS in a 1:1 ratio (details about the additional use of BIS will be given in chapter 5) and with the same educts as a precipitation polymerisation used as comparing standard. All samples have been analysed regarding their size, PDI, monomer concentration before the polymerisation and the concentration of the linear polymer after the polymerisation in the water phase. The data is presented in Table 9.

Table 9: Overview of the analysis of the polymerisation process

MG sample	R_h [nm] of the emulsion (PDI)	monomer in water phase before polymerisation	R_h [nm] the MG (PDI)	polymer in water phase after polymerisation
BIS/xPCL[50:50] (0.07 g, 3 mol%)	98.5 (0.09)	10.5 % of the whole monomer ammount	200 (0.09)	9.3 % of the whole monomer ammount
BIS/xPCL[50:50] (0.14 g, 6 mol%)	101(0.11)	11.2 % of the whole monomer ammount	350 (0.09)	10.4 % of the whole monomer ammount
BIS (0.07 g, 6 mol%)	96.5 (0.09)	17.3 % of the whole monomer ammount	175 (0.08)	14.1 % of the whole monomer ammount
xPCL(0.3 g, 1.5 mol%)	102 (0.12)	12.9 % of the whole monomer ammount	420 (0.2)	11.2 % of the whole monomer ammount
Microgel BIS(0.07 g, 6 mol%) precipitation polymerisation	—————	100 %	360 (0.05)	8 % of the whole monomer ammount

In order to answer the first question mentioned above, the time dependent behaviour of VCL/water emulsions was investigated by means of DLS. Figure 47 shows the measured droplet size of the emulsions measured every 10 minutes for four hours at 70 °C, no initiator was added. It is shown that the droplet size remains constant above the whole time and for all investigated samples. The droplet size also remains independent of the crosslinker amount. Like it is shown in Table 9 the diameter of the microgels after the polymerisation is two to three times higher than the diameter of the emulsion droplets, which can be explained by the fact that the microgel formation takes places in the molten monomer, excluding any water, and above the VPTT. After the polymerisation and microgel formation is completed the dispersion is cooled down to room temperature (below the VPTT) and the microgels will swell with water, increasing in size. However, the diameter of the droplets correlates with the diameter of the collapsed microgels at temperatures above the VPTT.

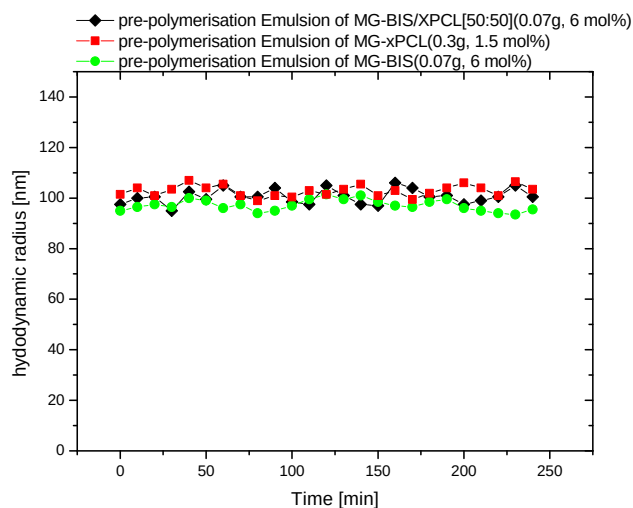


Figure 47: Emulsion stability over time measured by means of DLS, showing a stable droplet size over several hours

The stability of the emulsion droplets shows that there is no agglomeration or Ostwald ripening, which would lead to bigger particles over time, as well as no considerable loss of monomer into the water phase, which would lead to a decreasing droplet size. The amount of monomer and polymer found in the water phase, before and after the polymerisation, was analysed to investigate the possible loss. Before the polymerisation the VCL phase of the emulsion was separated by centrifugation and the supernatant (water phase) was freeze-dried to determine the amount of VCL. The amount of VCL found, shown in Table 9, varies between 10 and 13 % of the total monomer amount. Only the sample without xPCL, but only BIS, shows a higher amount of 17 %. After the polymerisation the amount of non-reacted monomer and non-crosslinked polymer chains was separated by dialysis and determined to be between 9

and 14 % which is in good correlation with the amount of monomer found. Especially to mention is that the sample prepared by precipitation polymerisation shows also a similar amount of non-crosslinked polymers. Even though this method has a considerable error margin, the data supports strongly the given hypothesis that the VCL remains in the droplets during the polymerisation and the process is basically a miniemulsion polymerisation. Nevertheless, the process used is different, since the monomer is not hydrophobic, and also no organic solvent is used as oil phase for the monomer. The whole droplet polymerises and swells later on with water forming a stable dispersion.

4 Incorporation of xPCL Crosslinker into Microgels

The approach to synthesise microgels with the hydrophobic crosslinker xPCL via a special miniemulsion polymerisation works, therefore in the next step the actual incorporation of xPCL has to be shown. The best method to show the integration of xPCL into the microgel network was in this case NMR spectroscopy. Figure 48 shows the ^1H -NMR spectra of the pure crosslinker (405; 4 arms and 5 PCL repeating units) and the microgels synthesised with xPCL. Since the crosslinker is only present in a few mol% and the VCL peaks overlap with the one of xPCL, most of its peaks are covered by the VCL peaks. Nevertheless, the double bond peaks, which are in a non overlapping region are not present in the microgel, indicating that they are consumed during the polymerisation and the crosslinking took place. The methyl-group (number 4 in structure B) at 0.81 ppm is also visible in the microgel spectrum indicating the presence of xPCL in the microgel network. The VCL peaks in general are broadened due to a reduced chain mobility in the crosslinked form of a microgel network. However, the NMR analysis of the fabricated microgels shows a successful incorporation and crosslinking of microgels with xPCL.

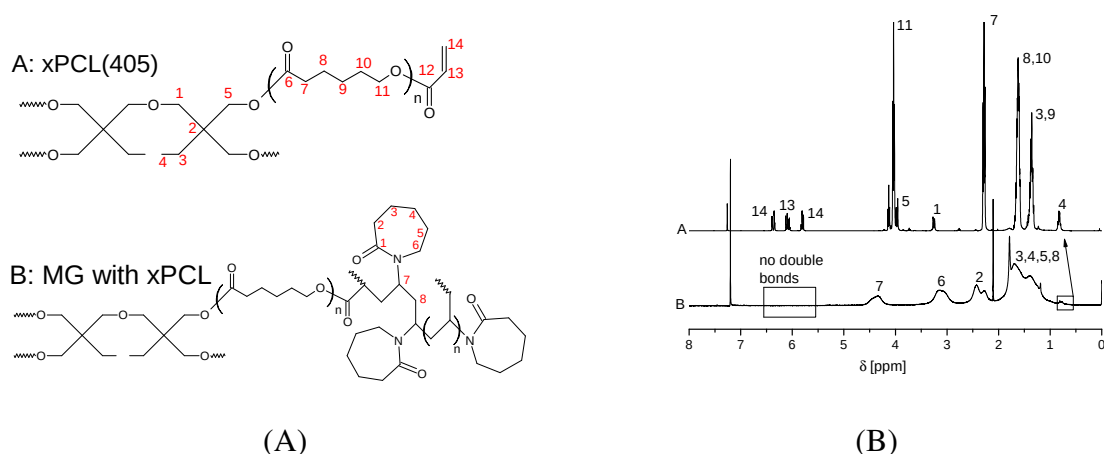


Figure 48: ^1H -NMR spectra of PVCL microgel crosslinked by xPCL(405) and of the crosslinker molecule xPCL(405) (B) indicating the successful crosslinking by the vanishing double bonds; schemes of the molecules for both spectra with the marked peak positions are provided as well (A)

xPCL was synthesised with varying arm numbers (4 and 6) and different numbers of caprolactone repeating units (5 and 15). Both have an influence on the molecular weight of the crosslinker. The synthesis was carried out with the variations shown in Table 10 and the influence on the synthesis and the polymerisation yield were investigated. xPCL (405) granted

the best synthesis results, which is also reflected by the highest measured yield. In general the yield decreases with an increasing molecular weight (repeating units or arm number). The high molecular weight might cause some restriction of the mobility of the crosslinker in the monomer mixture leading to crosslinking inhomogeneity and higher fractions of non crosslinked linear polymer chains. The latter will be removed by dialysis.

Table 10: Information about the crosslinker variations used

crosslinker	number of arms	caprolactone repeating units	$M_{n,NMR}$	yield of the microgel synthesis [%]
405	4	5	2749.37	73.1
415	4	15	7315.07	17.9
605	6	5	4002.83	6.7

After analysing the yield NMR spectra of the synthesised microgel variations have also been done. Figure 49 shows the spectra of microgels synthesised with xPCL(405; 4 arms, 5 repeating units) with a varying concentration from 0.05 g – 0.3 g (0.25 – 1.5 mol%), as wells as synthesised with xPCL(605; 6 arms 5 repeating units) and xPCL(415; 4 arms, 15 repeating units), both with 1 g (0.5 mol%) of crosslinker.

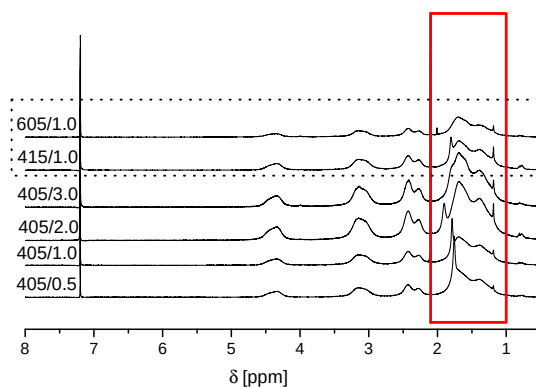


Figure 49: NMR spectra of microgels with various xPCL types (frame shows the region where the broadening of the signals is observed)

The analysis of these spectra shows a broadening of the signal assigned to the protons of the caprolactam ring with an increasing crosslinker concentration. Peak broadening is caused

by a reduction of the chain mobility, which is in this case due to an increasing crosslinking density with an increasing amount of crosslinker. A comparison of all three xPCL types with the same crosslinker concentration used shows no further considerable broadening in the calculated integrals of the mentioned peak. Due to the low yields and taking into account the above shown NMR analysis, a lower incorporation efficiency of the xPCL with higher molecular weights (arm number and repeating units) can be assumed. Therefore, xPCL(405) was exclusively used in all following analysis and investigations.

The samples were analysed by means of FTIR spectroscopy to show the incorporation of different concentrations of xPCL crosslinker. Figure 50 A shows a spectrum of a microgel with a xPCL concentration of 0.1 g (0.5 mol%); the spectrum is normalised to the amide band. Residual water and uptake of air moisture into the microgels leads to the $\nu(\text{OH})$ peak at 3450 cm^{-1} . $\nu(\text{CH}_2, \text{CH}_3)$ peaks are present at 2927 and 2856 cm^{-1} and $\nu(\text{CN})$ at 1479 cm^{-1} . The amide peak at 1636 cm^{-1} is labelled in the spectra and it indicates the polymerisation of VCL, leading to PVCL being the strongest peak, since it is the main component. Moreover, at 1735 cm^{-1} the carbonyl peak of the ester is labelled, which confirms the incorporation of xPCL, like it was already shown in the NMR analysis. The area of this carbonyl peak is magnified in Figure 50 B and the peak intensity is increasing with an increasing crosslinker concentration. Therefore, the incorporation of the crosslinker was not only confirmed by the IR studies, but it is also shown that increasing amounts of xPCL can be incorporated. This can easily be achieved by increasing amounts of xPCL in the reaction mixture.

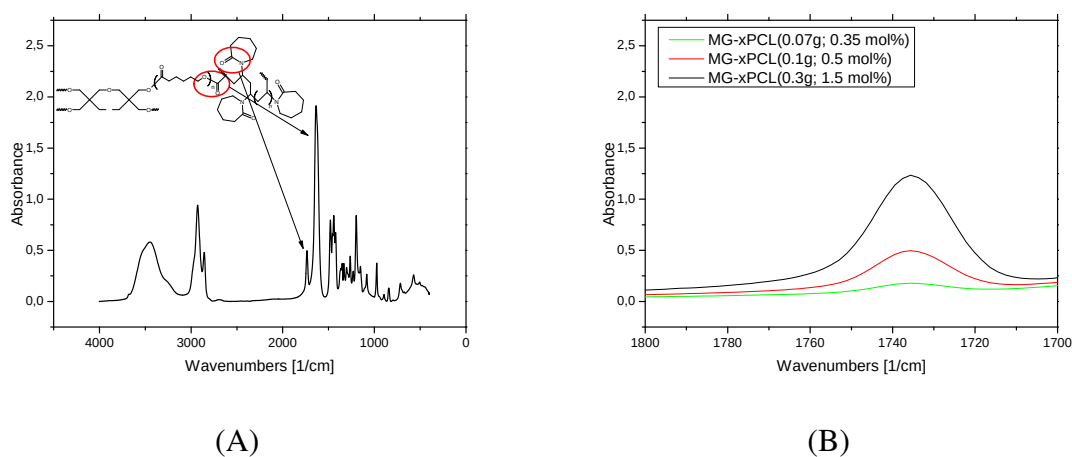


Figure 50: FT-IR spectrum of microgels synthesised with 0.1 g (0.5 mol%) xPCL(405) (A); magnification of the increasing xPCL carbonyl peak of the ester) (B)

5 Microgel Analysis

The fabricated microgels with incorporated xPCL were further analysed by means of DLS, FESEM, DSC and sedimentation analysis to investigate their properties, especially regarding the influence of xPCL on the particle behaviour. Figure 51 A shows the size distribution of microgels synthesised with different xPCL concentrations. At low concentration the size distribution has a multimodal shape, with an increasing crosslinker concentration (up to 0.3 g/1.5 mol%) the size distribution is monomodal and becomes more and more narrow. This is also shown in the FESEM micrographs in Figure 52 A and B. In micrograph A a broad range of particle sizes is visible, confirming the multimodal size distribution at low crosslinker concentrations, and in micrograph B a monomodal and not too broad size distribution for 1.5 mol% xPCL is recognisable. Both pictures prove that no agglomeration of the particles occurs. Since the size distribution of these new microgels is not as narrow as from the standard VCL/AAEM microgels crosslinked by BIS, additional syntheses with combinations of xPCL and BIS have been done, to investigate if any further improvement of the particles could be achieved. Figure 51 B shows the particle size distributions of microgels with different BIS/xPCL ratios. The obtained particles show a narrower size distribution than microgels crosslinked only by xPCL, and even close to size distributions of microgels synthesised by precipitation polymerisation. Best results can be achieved in BIS/xPCL ratios of 50:50 wt%. Figure 52 C shows the uniform sized particles of a sample with a BIS/xPCL ratio of 50:50 and 0.14 g of total crosslinker amount. Furthermore, the addition of BIS into the synthesis leads to yields up to 90 % for the 50:50 ratio, which is 20 % higher than without BIS (compare Table 10). Therefore it can be stated that the addition of BIS leads to a certain improvement of the synthesis, but since it is not degradable and does not form hydrophobic pockets it also might interfere with the basic idea of these microgels. This question will be addressed later in detail.

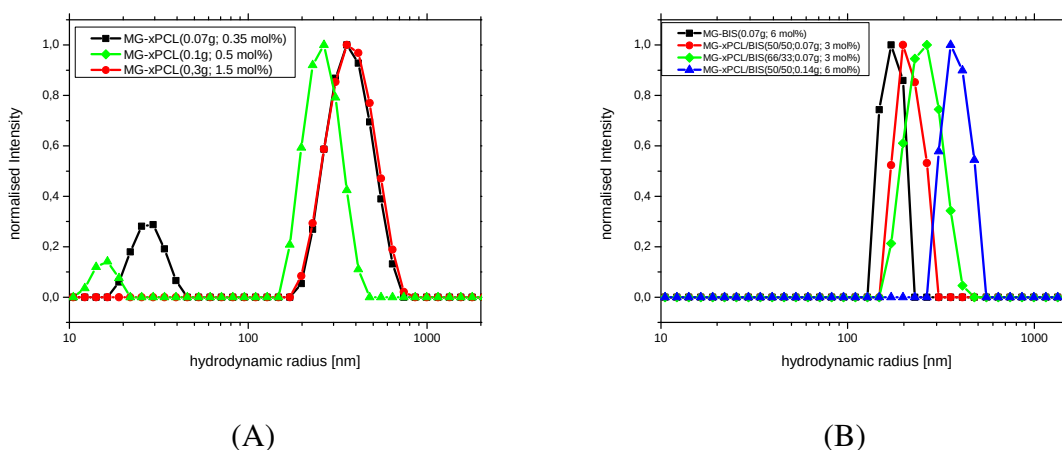


Figure 51: Dependency of the particle size distribution on the xPCL content (A) and on the BIS/xPCL ratio (B)

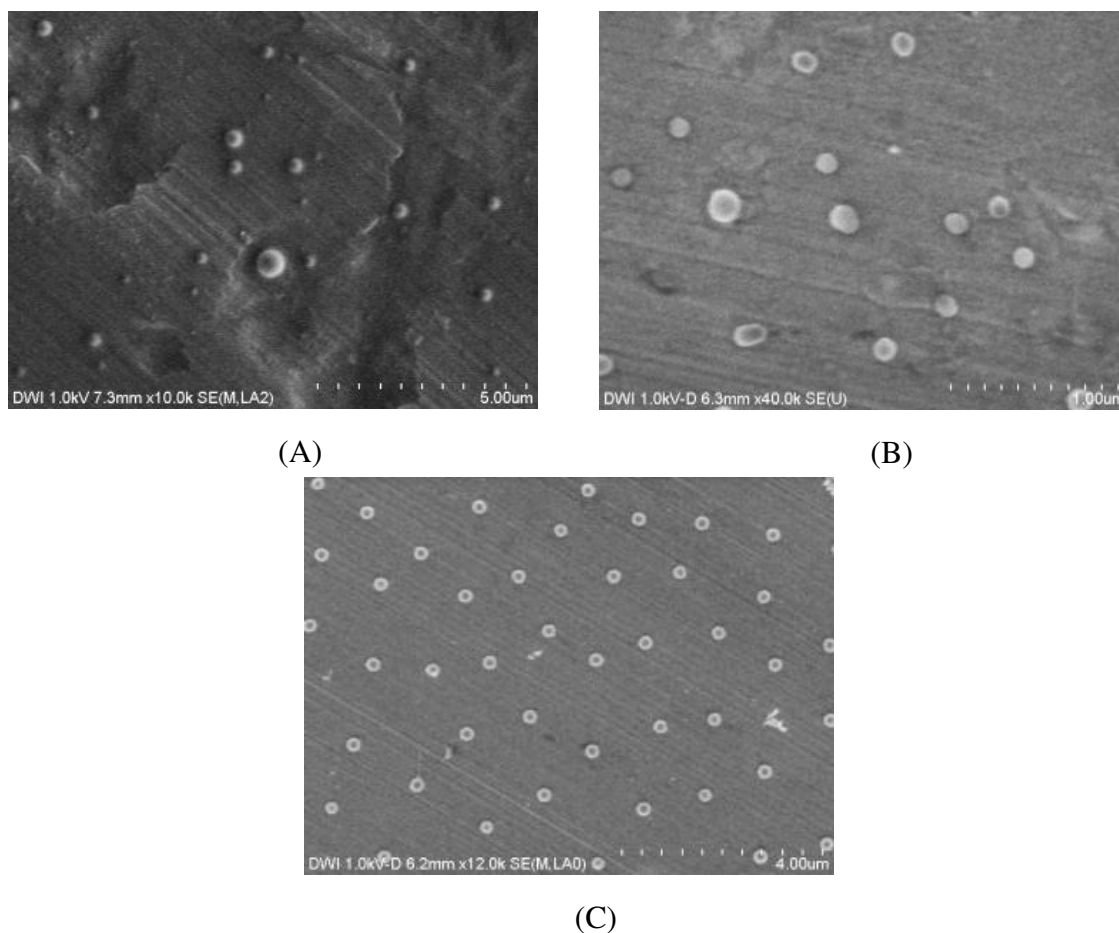


Figure 52: FESEM micrographs of microgels with a low amount (0.07 g; 0.35 mol%) of xPCL (A), with a high amount (0.3 g; 1.5 mol%) of xPCL and with a 50:50 ratio of BIS and xPCL(0.07 g; 3 mol%) (C)

The size of the microgel particles and their swelling depends on different factors, like the crosslinking density (referring to BIS) for example. An increasing crosslinking density leads to stiffer particles, since the polymer network is better connected and the ability of the particle to swell in a solvent and therefore increase in its size is hindered by this bonds. Therefore, a higher crosslinking density leads to a poorer swelling. The crosslinking density is increased by using a higher amount/concentration of the crosslinker. A higher amount of crosslinker leads to an increasing particle size [113], because it offers more possibilities to connect monomers/polymers to the particle during its synthesis. In the special case of xPCL, a crosslinker of a relatively high molecular weight, which is also hydrophobic, even more factors have to be taken into account. Similar amounts of xPCL in weight are of course not the same amounts in mol%, ergo not obtaining the same crosslinking density as with BIS. The chain length of the crosslinker molecules might also have an influence on the stiffness of the

particles and with it an influence on their swelling behaviour. The hydrophobicity of xPCL leads to more hydrophobic particles, which means that they will swell less good in water, but in their collapsed state the repelling of the water will be enhanced due to the hydrophobic domains [114, 115]. A stronger water repulsion implicates a smaller particle size in collapsed state. In Table 11 the hydrodynamic radius, the polydispersity index (which was already discussed above), the sedimentation velocity and the VPTT (measured by DSC) are summarised for different samples. A comparison of samples with the same crosslinker concentrations (2-3 or 4-6) shows that the particle size increases with the amount of xPCL, whereas the broadening particle size distribution (increasing PDI) has also to be taken into account. The samples with only xPCL (7-9) show an even more obvious increase in size, especially because the PDI decreases, but in this case it should be noted that the total amount of crosslinker increases, which leads to bigger particles. Nevertheless, a comparison of the samples 4-6, with 6 mol% crosslinker with sample 1, with the same crosslinker concentration but synthesised only with BIS, shows an obvious influence of xPCL on the particle size (increasing).

Table 11: Analysis data of various xPCL microgels

No.	sample	R_h [nm]	PDI	sedimentation velocity [$\mu\text{m/s}$]	VPTT measured by DSC [$^{\circ}\text{C}$]
1	MG-BIS (0.07 g, 6 mol%)	175	0.08	0.8	32.5
2	MG-xPCL/BIS[50:50] (0.07 g, 3 mol%)	200	0.09	1.1	32.8
3	MG-xPCL/BIS[66:33] (0.07 g, 3 mol%)	275	0.2	1.4	32.6
4	MG-xPCL/BIS[50:50] (0.14 g, 6 mol%)	350	0.09	1.7	33.1
5	MG-xPCL/BIS[66:33] (0.14 g, 6 mol%)	375	0.3	2.1	33.3
6	MG-xPCL/BIS[70:30] (0.14 g, 6 mol%)	400	0.36	4.8	33.2
7	MG-xPCL (0.07 g, 0.035 mol%)	325	0.9	5.3	32.8
8	MG-xPCL (0.1 g, 0.5 mol%)	350	0.75	4.8	33.1
9	MG-xPCL (0.3 g, 1.5 mol%)	420	0.2	7.5	32.0

The sedimentation velocity which is also shown in Table 11 was measured to investigate the colloidal stability of the microgels and the influence of xPCL on it. All measured samples

show a good colloidal stability, the values are overall very low, and they do not sediment in several months or in the accelerated sedimentation process (4000 rpm), which was used to measure the sedimentation velocity. This is also shown as an example for the sample with 0.3 g (1.5 mol%) of xPCL in the sedimentation profiles in Figure 53 (an explanation for the interpretation of these data was already given in section 3.2). After one hour of accelerated sedimentation the microgels just begin to sediment. However, the sample with only BIS shows the lowest sedimentation velocity and the velocity increases with an increasing xPCL concentration. Reasons for this are mainly related to the increasing particle size with increasing amounts of xPCL and to the differences in the PDI. Smaller and therefore lighter particles are in general more stable, as well as monodisperse solutions are more stable than polydispers ones.

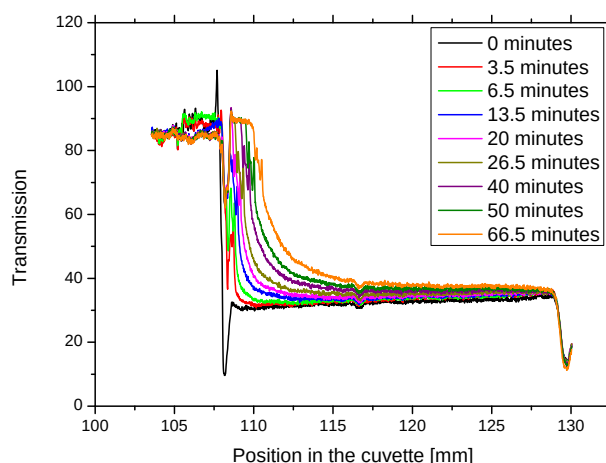


Figure 53: Sedimentation profiles of microgels with 0.3 g xPCL indicating a slow sedimentation process

Temperature triggered swelling is one of the key properties of VCL based microgels, therefore the influence of xPCL on the VPTT and the swelling had to be investigated. The VPTT can be determined by the inflection point of temperature depending DLS measurements or by means of DSC, which shows the endothermic or exothermic energy changes. Table 11 shows the DSC results, stating that xPCL, even though it is hydrophobic, does not shift the VPTT to lower temperatures. This would have been expected because a more hydrophobic microgel interior would make the polymer-polymer interactions preferable. Figure 54 shows the results of the temperature dependent DLS measurements by showing the degree of swelling of three different samples. The degree of swelling is the hydrodynamic radius R_h divided by the hydrodynamic radius at 50 °C (R_{h0}) of each sample. On one hand these data shows that the microgels are still thermo-sensitive even with 0.3 g of xPCL incorporated, thereby the

DSC results are also confirmed. On the other hand it is shown that both presented samples with xPCL have a higher degree of swelling compared to the sample without xPCL. The incorporation of hydrophobic molecules into the microgel network should in general lead to a decreased swelling property, but like it was mentioned above several factors have to be taken into account regarding the swelling of the particles. The sample with a xPCL/BIS ratio of 50:50 wt% and the same crosslinker concentration as the sample without xPCL has, due to its higher hydrophobicity, a stronger water repelling behaviour, and therefore a smaller radius in the collapsed state [114, 115], which is used for the calculation of the degree of swelling. This is also, or even more true for the sample with 0.3 g (1.5 mol%) of xPCL, but in this case the crosslinking density is also lower and therefore the particles are less stiff.

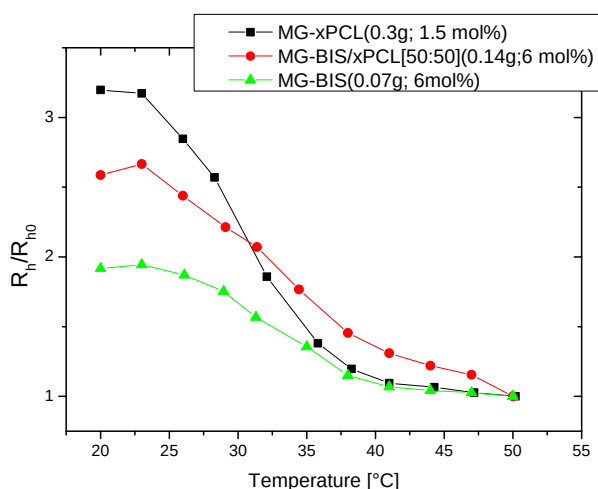


Figure 54: Degree of swelling of microgels with different xPCL contents

As a short conclusion: the incorporation of xPCL is successful, it does not influence any properties of the microgels in a negative way, and it even enhances some, like the degree of swelling. Moreover, the overall particle quality is very good, considering the PDI and the colloidal stability.

5.1 Microgel Degradation

One of the ideas for these microgels is their degradability, which originates from the degradability of the PCL backbone of the crosslinker. The hydrolysis, which will happen over time, in water or PBS, was in this case accelerated by the addition of an enzyme (*candida rugosa*) into

the microgel dispersions. Changes in morphology and size were followed by means of DLS and electron microscopy. In Figure 55 the micrographs of microgels with 0.3 g (1.5 mol%) xPCL (A and B), with a 50:50 ratio of BIS/xPCL (C), and only with BIS (D) are shown. Even after 40 days of exposure to the enzyme, the BIS crosslinked microgels do not show any visual changes; like expected they do not degrade. However, the microgels crosslinked only by xPCL (A and B) lose their structure and spherical shape during the degradation and show also some coagulation with each other. The microgels crosslinked with both, xPCL and BIS, also degrade to some extent (C), which is understandable since only the xPCL crosslinked polymer chains will lose their bonds to the microgel network. Furthermore, the micrograph permits the assumption that the crosslinking does not take place statistically during the synthesis, because a degrading shell and a stable core can be observed. A faster crosslinking reaction with BIS could be the reason for this. Anyhow, this is only an assumption based on an interpretable micrograph and therefore it needs further investigations in the future.

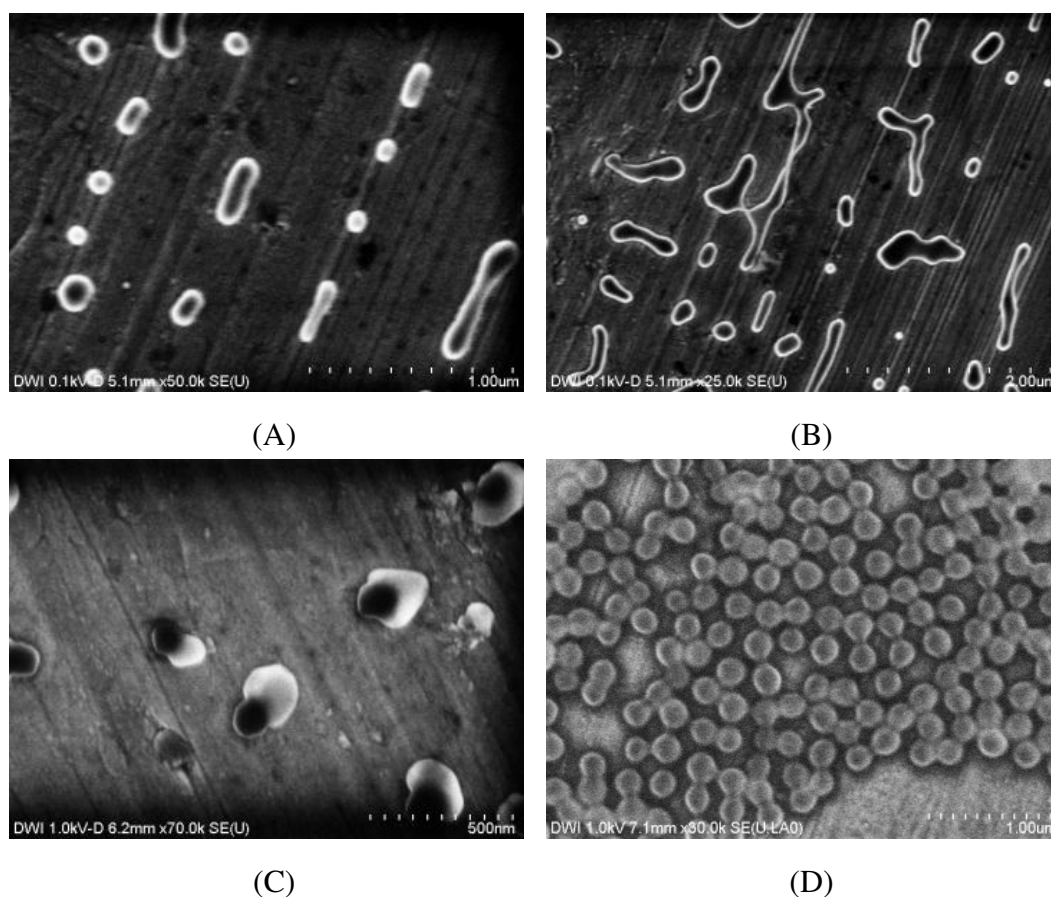


Figure 55: FESEM micrographs of the degradation of different microgels: microgels with xPCL (0.3 g, 1.5 mol%) after 11 days (A) and after 30 days (B); microgels with a BIS/xPCL ratio of 50:50 wt% (6 mol%) after 12 days (C) and microgels only with BIS (0.07 g, 6 mol%) after 40 days (D)

Another more detailed way to follow the degradation process is through DLS measurements of the samples at different time intervals. Figure 56 shows size distributions of a microgel sample with 0.3 g (1.5 mol%) xPCL at different times during the enzymatic degradation. In the beginning the size distribution is monomodal and narrow, after a couple of days the peak begins to broaden, and a secondary peak at smaller radii appears, making the distribution bimodal. In the continuing degradation, the original peaks decrease in intensity and the intensity at smaller radii increases, followed by the appearance of another peak at 10 nm. After 33 days the main peak has disappeared, only a peak below 1 nm can be seen, which will also disappear after around 40 days. The degradation shown by the xPCL microgels is different from particles completely consisting of a degradable polymer, which would show a continuous decrease of the particle size due to a stepwise degradation of the surface [116, 117, 118]. In contrast to that, the xPCL crosslinked microgels consist of a non-degradable polymer, whose chains are crosslinked by a degradable polymer. As described the degradation process shows peak broadening as well as newly appearing and vanishing peaks; no simple shift to smaller sizes can be seen. Figure 57 shows a proposed mechanism for this kind of degradation compared to the simple one. Nevertheless, the DLS measurements prove the complete degradation of the microgels crosslinked with xPCL.

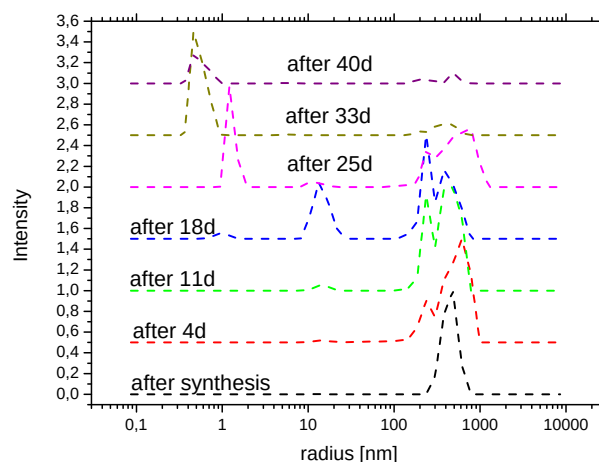


Figure 56: Degradation of xPCL microgels (0.3 g, 1.5 mol%) followed by DLS over 40 days showing the decrease of the main peak and the appearance of peaks at smaller radii

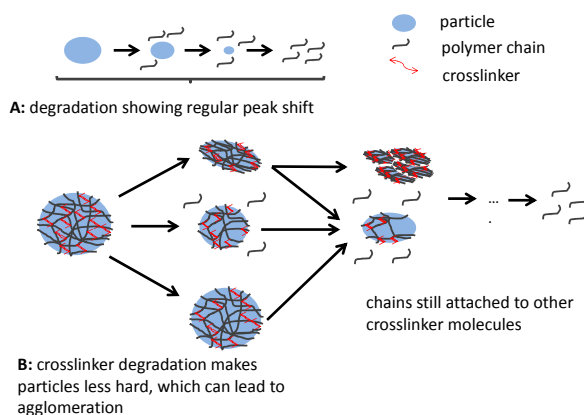


Figure 57: Mechanism of a usual degradable particle made of a degradable material (A); Proposed degradation behaviour of xPCL crosslinked microgels(B)

The degradation products were analysed with NMR spectroscopy as further investigation and proof of the degradation. Figure 58 B shows the spectrum of the degradation products of microgel synthesised with 0.3 g of xPCL. The broad PVCL peaks of a microgel network (compare Figure 48) are gone, but narrow PVCL oligomer/polymer peaks reappeared. The spectrum does not show VCL monomers, since the VCL double bond, which is consumed during the polymerisation, is missing in this spectrum. The peaks are also not as narrow as the ones shown in the VCL monomer spectrum in Figure 58 A and also not as broad as the ones of the linear PVCL shown in the same figure. The xPCL signals are still mainly covered by the dominant VCL signals, just that the backbone signal at 0.84 ppm can be seen. Nevertheless, this shows that the degradation of the microgel network down to its building blocks took place.

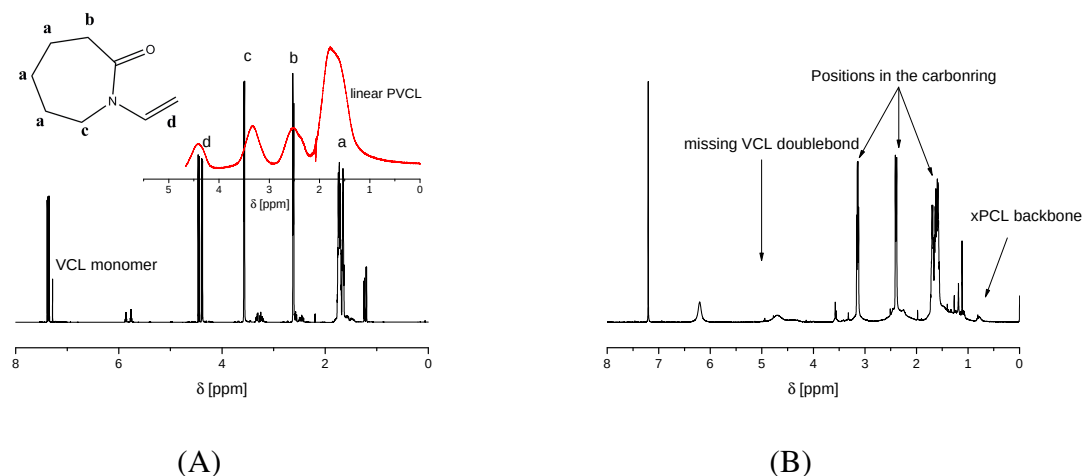


Figure 58: NMR spectra of VCL monomer and linear PVCL polymer to compare with the degradation Product (A) NMR spectrum of the microgel degradation products showing narrow oligomer/polymer peaks instead of the broad peaks of crosslinked microgels or linear polymers (B)

5.2 Immobilisation of Hydrophobic Substances

The second aim related to the properties of these microgels is the immobilisation of hydrophobic substances, mainly drugs for medical applications. As with the degradation, this property will also be achieved by the incorporation of xPCL. To show the immobilisation and to prove the existence of the assumed hydrophobic pockets or domains, built up by the caprolactone repeating units of the xPCL, the microgels were loaded with hydrophobic substances. As a first experiment Nile Red, a completely water insoluble dye, was used. Afterwards (RS)-2(4-(2-methylpropyl)phenyl)propanoic acid (Ibuprofen) was used as an example drug with a pH-dependent solubility in water. Figure 59 shows the successively loading of microgels (0.3 g, 1.5 mol% of xPCL) with Nile Red. The loading was followed by UV/Vis spectroscopy measurements. After the addition of each droplet of Nile Red solution a measurement was done and the increase of intensity in the absorbance can be seen in Figure 59. This kind of measurement was done for several different samples but only this one is shown as an example. These measurements were used to determine the loading capacity of the microgels.

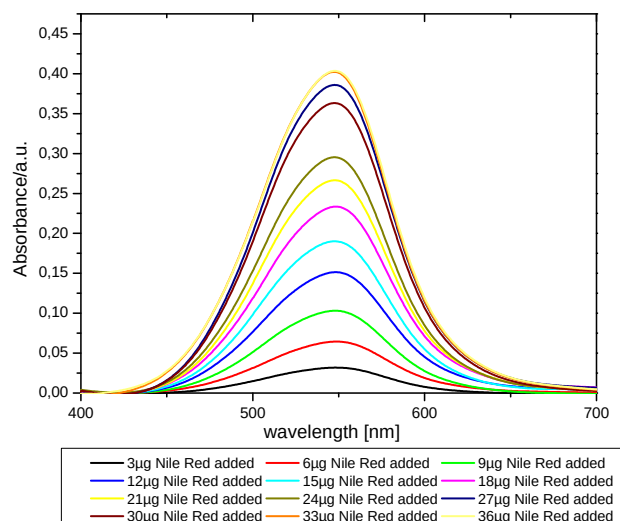


Figure 59: Example of the microgel (0.3 g xPCL) loading with Nile Red followed by UV/vis spectroscopy

Figure 60 A and B show the loading capacity of the microgels with Nile Red and Ibuprofen, respectively, in both cases depending on the xPCL concentration. As reference, microgels crosslinked by BIS, without xPCL, were used. The loading with Nile Red shows a clear trend of an increasing immobilisation capacity with an increasing xPCL concentration, by the increase of the saturation concentration. The BIS crosslinked microgels show basically no uptake of the dye. However, the efficient immobilisation of Nile Red is a good evidence for the generation of hydrophobic pockets in the microgel network. For the Ibuprofen loading the same situation is found. The saturation concentration increases with an increasing xPCL concentration in the microgels, therefore the loading capacity increases as well. In contrast to the Nile Red uptake, the reference sample without xPCL can immobilise a small amount of Ibuprofen, probably due to the low but existent solubility in water. However, the presented data proves that the incorporation of xPCL in the microgels gives them the possibility to immobilise hydrophobic substances, due to the generation of hydrophobic pockets in the microgel network.

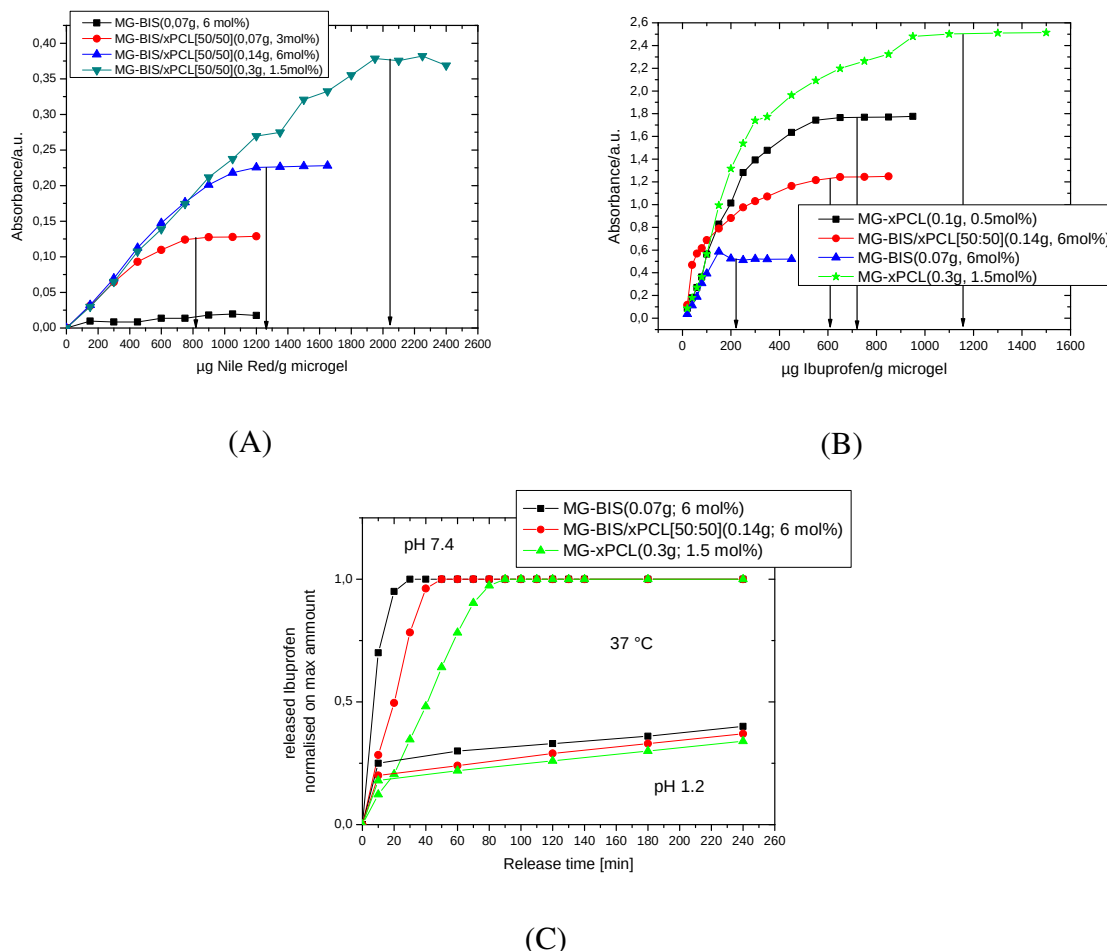


Figure 60: Loading capacity of microgel samples, with different xPCL concentrations, with Nile Red (A) and Ibuprofen (B); release of Ibuprofen from the microgels at pH 7.4 and pH 1.2 at 37 °C (C)

After the uptake, a drug such as Ibuprofen should be also released. The release from the microgels was investigated at pH of 1.2 and 7.4, each at 37 °C. The first reflects gastric and the second intestinal conditions. Figure 60 C shows the release behaviour at both conditions over time. For the interpretation of these data it should be mentioned in detail again, that Ibuprofen has a pH depended water solubility. At pH 1.2 the solubility is about 10^{-4} mol/L and at pH 7.4 it is about 10^{-2} mol/L [119]. In both cases the solubility is, even though it is still quite low, higher than the loaded amount of Ibuprofen in 15 mg of microgels, which is the mass used in 2 mL water for the UV/Vis measurements. Higher microgel concentrations in the cuvettes would not be appropriate for the measurements. The release at pH 7.4, as it is shown in figure 60 C, shows overall a linear release and an increasing release time with an

increasing xPCL concentration. The release time is tripled in relation to microgels without any xPCL, and the complete release of Ibuprofen is reached after 90 minutes for microgels with 0.3 g (1.5 mol%) xPCL. These values are in a similar time range like it was already shown in other studies [120, 121, 122]. However, the incorporation of xPCL reduces the release rate and increases the time until the complete release. The release behaviour at pH 1.2 is different in the way that before the linear release a burst release of about 20 % of the Ibuprofen takes place. The following linear release is much slower, compared to pH 7.4 . It should be mentioned that the incorporation of xPCL leads to a smaller burst in the beginning and to a generally slower release compared to the behaviour of microgels without xPCL. The difference between the two different xPCL concentrations is too small to make out an obvious trend. After four hours about 40 % Ibuprofen is released; the extrapolation of the curves (slope) results in a period of 10 to 14 hours until a complete release is reached. The difference between the release at pH 7.4 and pH 1.2 can be explained by the difference in the solubility of Ibuprofen [120]. Even though the sink conditions were kept throughout the whole experiment, the higher solubility at pH 7.4 will increase the release/diffusion of Ibuprofen in water. However, the immobilisation as well as the release was successful and also improved by the incorporation of xPCL. Nevertheless, it should be stated that an improvement is observable in comparison to microgels without xPCL but not in comparison to other methods, and that the improvement is not as high as hoped or intended for, since a release time of 90 minutes is for many applications still too fast.

6 Outlook: xPCL-microgels in fibres

The idea to create microgels as they are presented in this part of the thesis, was from the beginning connected to the fabrication of microgel based fibres with a specific use in medical applications, like it was described in the introduction to this part. Therefore, even though these experiments are still in an early stage, an outlook will be given at this stage to the use of microgels crosslinked by the xPCL crosslinker.

Figure 61 shows fibres spun with the same parameters and conditions like the type S fibres shown in chapter 4.1 part IV, but with xPCL microgels (0.3 g of xPCL) instead of VCL/AAEM microgels. As it is shown in the previous sections the xPCL microgels do not vary extremely from the standard VCL/AAEM microgels regarding their size and swelling behaviour. Therefore, it was expected to achieve the same morphology with microgels only at the surface of the fibres, which is shown in Figure 61 B. The average fibre diameter is about 3 μm , which is the same as for the type S fibres with VCL/AAEM microgels.

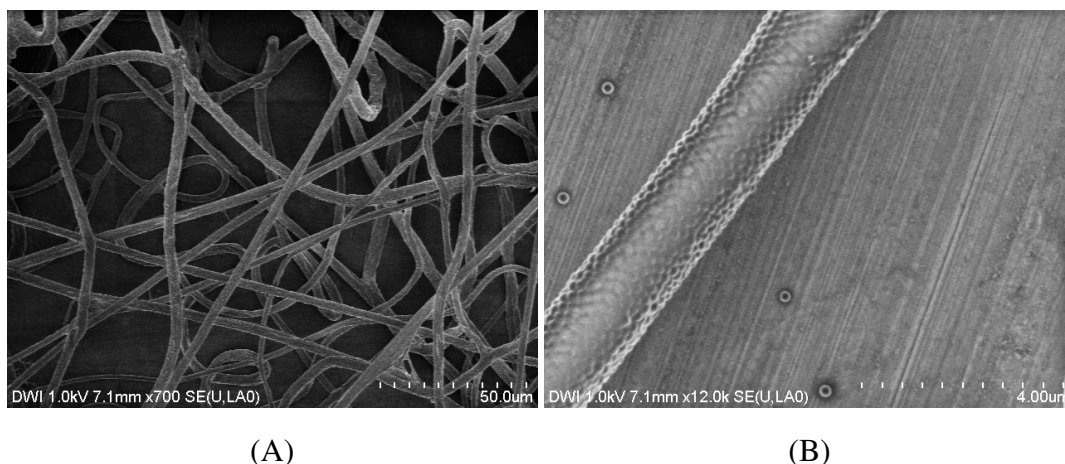


Figure 61: FESEM micrographs of type S fibres spun with xPCL-microgels. An overview of the sample (A) shows the uniformity of the fibres and a close-up view (B) shows the fibre morphology with microgels at the fibre surface

In Figure 62 the release of the drug sulfamethoxazole, a hydrophobic bacteriostatic antibiotic, from a 100 mg fibre sample is shown. The drug was introduced in the microgels (xPCL microgels with 0.3g of xPCL) during the synthesis by adding it to the monomer melt (compare section 2.3). The release was followed by UV/Vis measurements at 37 $^{\circ}\text{C}$, pH 7.4 and under sink conditions over several days. The results show a promising release over two days. However, it must be stated that the synthesis of xPCL microgels with a drug present during the synthesis is not yet fully analysed and understood, these results are only an outlook to show the potential of microgels with hydrophobic pockets for drug uptake and release in combination with fibres for localised treatment.

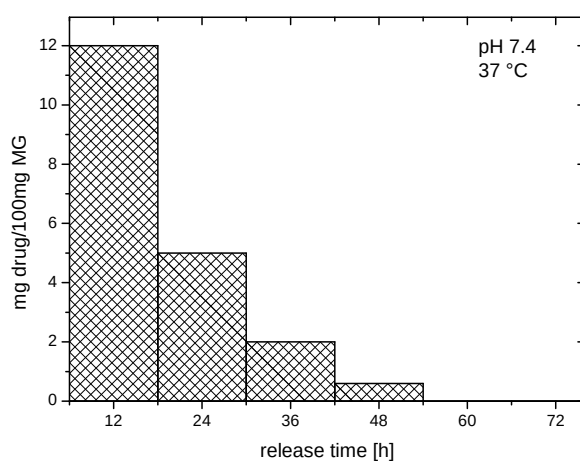


Figure 62: Release of Sulfamethoxazole from PCL-MG(0.3gxPCL) fibres type S over two days at 37 °C, pH 7.4 and under sink conditions

7 Summary/Conclusions

This part of the work presents the synthesis of VCL based microgels crosslinked with a star-shaped acrylate functionalised poly(ϵ -caprolactone) crosslinker via an miniemulsion polymerisation process of the molten monomer. The integration of xPCL was done to achieve degradable microgels with hydrophobic domains. The synthesis was special in the way that, although VCL is water soluble at the process temperature of 70 °C, it was shown that the emulsion of the molten VCL was stable and that the reaction is a miniemulsion polymerisation. Generally the synthesis was successful, although particles with a narrow particle size distribution were only achieved with high amounts of xPCL or in the combination with BIS. The particle size depends on the crosslinker content in general and also specifically on the xPCL content and varies between 180 and 400 nm. The particles show a thermo-sensitive swelling behaviour, due to the VCL and the VPTT is not changed by the incorporation of xPCL. The degradation process of the particles was followed by means of DLS and SEM and it takes place within 40 days. The mechanism is not a gradual decrease of the particle size, since VCL, the microgels' main component, is not degradable. Nevertheless, the process can be shown. Microgels with a combination of BIS and xPCL do not degrade completely, only the xPCL crosslinked part degrades. The existence of hydrophobic domains is proven on one hand by the increased water repulsion above the VPTT and on the other hand by the immobilisation of Nile Red and Ibuprofen. Both Nile Red and Ibuprofen can be immobilised by the xPCL modified microgels. An increasing amount of xPCL allows more immobilised substance. The release of Ibuprofen was studied as well, and an enhancement of the release time in comparison to microgels without xPCL can be seen. Nevertheless, the achieved results are not better than results gained by other methods and moreover they show that all material was released already in about 90 minutes.

The aim of this part of the thesis was to synthesise thermo-sensitive microgels that are degradable and possess hydrophobic domains, which was successfully done. These microgels could be used in medicine as drug carriers or in textile industry for dyes or insecticides. Moreover, regarding to this thesis, they can be used for PCL fibres with microgels on the surface, like they were shown in the previous chapter. Such fibres would be fully degradable, since the microgels released from them would degrade due to the same mechanism as the fibres. Furthermore, these fibres could uptake drugs, dyes or insecticides and could be applied on surfaces or textiles. In conclusion, even though the idea of degradable microgels or microgels with hydrophobic domains is not new, the combination of these properties in one particle with additional thermo-sensitive properties while using only two components and a simple synthesis, is an elegant way to achieve a smart or interactive microgel. The similarity of the degradation process of xPCL and PCL is also a nice feature for fully degradable fibres. Therefore, it can be stated that these microgels constitute an improvement also for the field of microgel-polymer composite fibres.

Polylactide - Microfibres

VI

1 Introduction

In this part of the thesis another new polymer is chosen for the fabrication of polymer-microgel composite fibres: polylactide (PLA). PLA is like PCL a hydrophobic and bio-degradable polymer. It has applications as packing material, in agriculture (plastic mulch) and in food related products like cups or drinking straw. In all these applications a major role is played by its degradability and recyclability, or the possibility to be composted. Nevertheless, probably the most interesting application field of PLA is in medicine as implants, stents or sutures; but the degradation of PLA in the human body causes inflammations, due to dropping the pH values in the surrounding area [123, 124], which is a big drawback in the development of these implants. Different attempts to buffer the pH during the degradation process have already been developed [125, 126] using alkaline additives. A cooperation between different institutes in Aachen (a.o. DWI, ITA, UKA) started a project with the aim to develop a fibre based PLA-stent with a neutral degradation behaviour by the addition of specially modified microgels. This study was on one hand a preliminary work for this project, to get some first information about the important factors in the fabrication process of PLA-microgel fibres and the change in the PLA-fibre properties. On the other hand the electrospinning of fibres is also a faster and less material intensive method to try new ideas (for example different microgels). The fabrication of PLA-microgel fibres with vinylimidazole (VIm) modified microgels for a neutral degradation gives new facets to the field of microgel based polymer fibres. Furthermore, PLA/microgels are a combination of a hydrophobic and a hydrophilic materials, just like PCL/microgels presented in part four. Therefore, the analysis of the composite fibres will provide new insights in this specific change of properties. This part is on one hand only an introduction for a bigger study/project and therefore not as detailed as the other parts of this thesis. But on the other hand it is also a continuation of the basic aim of this thesis to fabricate microgel based fibres.

This part is structured in the three sections, besides the summary and conclusion. First the VIm modified microgels are characterised concerning their swelling behaviour and their VPTT. Afterwards the fibre fabrication is described in detail. In the chapter “Fibre Characterisation” the fabricated fibres are investigated regarding for example their swelling behaviour and more importantly their degradation behaviour.

Some of the experiments/results were made by Magnus Kruse during his research work under my supervision.

2 Experimental Part

The following sections present only the descriptions of the synthesis and fabrication processes of the samples and materials, as well as the description of the experiments and analyses that have been done with these samples, which were not explained already in one of the previous chapters of this thesis. In cases of specific changes in the experiments, these changes will be mentioned and the rest of the description will be referred to. This is done to avoid unnecessary repetitions.

2.1 Materials

Acetone (HPLC grade, Th.Geyer), chloroform (99.5%, VWR), 2,2'-Azobis[2-methylpropionamidine] dihydrochloride (AMPA, 97%, Aldrich), methanol (99.8%, VWR), N,N'-methylen-bis-(acrylamide) (BIS, 99%, Sigma-Aldrich), polylactide (PLA, MW = 115000 g/mol and 650000 g/mol Boehringer Ingelheim AG & Co. KG), vinylimidazole (VIm, 99% Aldrich) and distilled water were used as received without having undergone any other cleaning procedures. 2-(methacryloyloxy)ethyl acetoacetate (AAEM, 95%, Aldrich) has been purified before use. N-Vinylcaprolactam (VCL, 98%, Aldrich) was purified by vacuum distillation under nitrogen before use.

2.1.1 VIm-Microgel Synthesis

VCL/AAEM microgels have been used as reference in chapter 2.2 and in general in chapter 4. The synthesis is done exactly like it was described in 2.2. The recipe was as following: VCL - 1.877 g (13.40 mmol); AAEM - 0.338 g (1.579 mmol); BIS (crosslinker) - 0.06 g (0.389 mmol) and water 150 g the initiator (0.05 g (0.268 mmol)). The same synthesis was used for the vinylimidazole modified microgels (VCL/AAEM/VIm microgels). VIm is added in the same way and at the same time like the other monomers. In Table 12 all synthesised VCL/AAEM/Vim microgels are summed up.

Table 12: Summary of VCL/AAEM/VIm microgel synthesis

VIm amount [mol%]	VCL [g] (mmol)	AAEM [g] (mmol)	VIm [g] (mmol)	BIS [g] (mmol)	AMPA [g] (mmol)	water [g]
0	1.83 (13.1)	0.33 (1.54)	0	0.06 (0.389)	0.05 (0.268)	150
2	1.83 (13.1)	0.33 (1.54)	0.033 (0.3)	0.06 (0.389)	0.05 (0.268)	150
5	1.83 (13.1)	0.33 (1.54)	0.071 (0.75)	0.06 (0.389)	0.05 (0.268)	150
8	1.83 (13.1)	0.33 (1.54)	0.125 (1.33)	0.06 (0.389)	0.05 (0.268)	150

2.2 Preparation of Spinning Solutions

Generally the spinning solutions are made as in the chapters before, too. Solutions of the polymer and a solvent or solvent mixture are prepared and freeze dried particles are added in certain ratios. In Table 13 the prepared spinning solutions for PLA-microgel fibres are shown. The values were chosen taking into account the experience gained with the PVA- and PCL-microgel fibres. The PLA with a molecular weight of 115000 g/mol (PLA115) was chosen, since it is a standard value in literature and also comparable to the molecular weights from the PVA and PCL used in this work. Additionally PLA with a molecular weight of 650000 g/mol (PLA650) was chosen, because the first tests with PLA 115 were not so promising. Spinning solutions with PLA650 exhibit much smaller concentrations of PLA, since the viscosity would be otherwise too high for the electrospinning process. In the beginning of these experiments all fibres were fabricated with VCL/AAEM microgels without Vim. In the later states of this study, the spinning solutions, which produce fibres of the best quality were prepared anew with VCL/AAEM/Vim microgels with varying amounts of Vim.

Table 13: Spinning solutions for PLA-microgel fibres

Polymer	PLA in solution [wt%]	PLA:MG [wt%]	solvent
PLA115	8	50:50	chloroform
PLA115	9	50:50	chloroform
PLA115	12	50:50	chloroform
PLA115	8	70:30	chloroform
PLA115	9	70:30	chloroform
PLA115	12	70:30	chloroform
PLA115	9	70:30	chloroform/methanol (90:10)
PLA115	9	70:30	chloroform/methanol (80:20)
PLA115	9	70:30	chloroform/methanol (70:30)
PLA650	3	70:30	chloroform
PLA650	4	70:30	chloroform
PLA650	4	50:50	chloroform
PLA650	5	70:30	chloroform
PLA650	4	70:30	chloroform/methanol (90:10)
PLA650	4	70:30	chloroform/methanol (80:20)
PLA650	4	50:50	chloroform/methanol (80:20)

2.3 PLA-Fibre Degradation

For the degradation study of the PLA-microgel fibres 3 cm² of each sample was placed in 10 mL distilled water (pH 7.4) at 37 °C. Once per week the pH values were measured by a metrohm 704 (Mettler-Toledo). Due to an unexpected long degradation time *candida antarctica* lipase B was added in excess to accelerate the degradation.

2.4 Characterisation Methods

In this section only the characterisation methods that have not been mentioned before in this thesis are described. The descriptions for DLS, SEM, TGA, DSC, contact angle measurements and moisture sorption analysis can be found in 2.6.1, 2.6.3, 2.6.5, 2.6.6, 2.5.1 and 2.6.7.

2.4.1 Potentiometric Titration

To determine the real incorporated amount of VIm in the microgels potentiometric titration measurements have been done. 250 mg freeze dried microgels were re-dispersed in distilled water. The pH value of the dispersion was set to 10.5 by addition of NaOH (equilibration time 2 hours). The titration is done at room temperature with 1 molar HCl. The measurement ends at a pH of 3 and the equivalence points are automatically calculated by the device software.

3 VIm-Microgel Characterisation

The VCL/AAEM/VIm microgels are synthesised based on a previous work [21]. Nevertheless, it is necessary to analyse the synthesised microgels in detail for all following characterisations of the fabricated fibres. The PDI of all synthesised samples is below 0.1, which shows that they have a narrow size distribution and no aggregation takes place. Figure 63 shows DLS measurements at 15 °C (A), where the microgels are in completely swollen state, and the results of temperature trend measurements (B). The measurements have been performed at a constant pH value of 7.4 to prevent an influence of the pH value of the solution to the particle size [21]. The hydrodynamic radius of the microgels increases with an increasing amount of VIm, which is shown by Figure 63 A. The reason for this is that the hydrophilic VIm increases the overall hydrophilicity of the microgels, therefore more water can be bound and the particles swell to bigger sizes, which is shown by Figure 63 B. The temperature trend measurements also show the phase transition of the microgels triggered by the VPTT. The incorporation of VIm does not influence the temperature sensitive properties of the microgels in general, but the VPTT itself is changed. The VPTT is the inflection point in the temperature trend curves and was calculated to be 34 °C for 2 mol% of VIm, 36 °C for 5 mol% VIm and 41 °C for 8 mol% VIm. For VCL based microgels without VIm the VPTT is 32 °C. The incorporation of VIm into the microgel network leads to higher VPTTs with an increasing amount of VIm. Again the reason is the increasing hydrophilicity, because more energy is needed to shift towards a favourable polymer-polymer interaction instead of the polymer-water interaction. High amounts of VIm in the microgels are probably needed for the neutral degradation of the PLA fibres, but high amounts of VIm also shift the VPTT above body temperature, which could be of importance in medical applications and needs to be kept in mind for the design of the fibres. However, the change in size, degree of swelling and VPTT proves the incorporation of VIm into the microgel network and shows furthermore qualitatively the increasing incorporation with an increasing amount used.

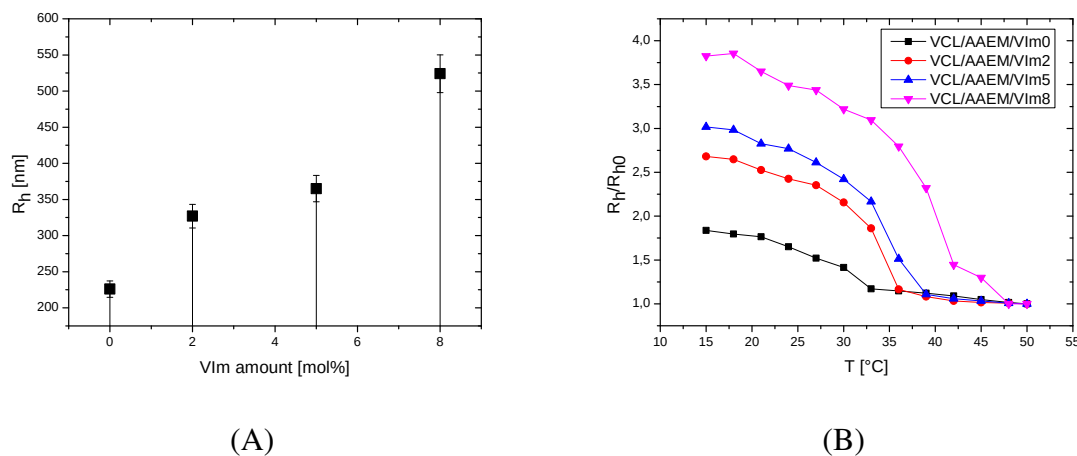


Figure 63: Hydrodynamic radius dependency of the VIm amount in the microgels (A) and the degree of swelling of the various VIm modified microgels depending on the temperature (B) at pH 7.4

To determine the real amount of VIm incorporated in the microgels potentiometric titration was used. For small amounts up to 5 mol% about 90 % of the VIm will be incorporated, which was also already shown in [127]. For the sample with 8 mol% VIm the yield was about 76 %, which leads to a real amount of only 6 mol%. This information is necessary for the degradation test, the test of buffer efficiency in the PLA-fibres.

4 Fibre Fabrication

Table 13 in section 2.3 shows all the spinning solutions that were prepared for this system. All of these spinning solutions were used to spin fibres and were characterised by means of microscopy. The process parameters (applied voltage, target distance and flow rate) have been varied regarding the experiences of the PVA- and PCL-microgel fibre fabrication, for the most promising samples an adjustment in detail of these parameters was done too. Even without microgels no continuous process or homogeneous fibres were obtained by using the PLA115 (115000 g/mol). The fibre diameter of rather good samples still have a diameter variation of some hundred nm to 3 μm , and trials with microgels, added to the solutions, resulted in even less homogenous samples, with big beads and big droplets on the target. Therefore, all other investigations have been done with PLA650 (650000 g/mol). As it is shown in Table 13 the chosen solvent is chloroform, but with chloroform only, the spinning process was found to be not continuous enough to fabricate homogenous fibres. This is because chloroform is a non polar solvent and electrospinning is a process based on charges. To overcome this problem methanol was added as a polar solvent, but since it is not a solvent for PLA its addition is limited. The best results were achieved with the following parameters: a solvent mixture of chloroform/methanol 80:20 wt%, an applied voltage of 20 kV, a target distance of 15 cm, a flow rate of 5 mL/h and a polymer content in the solution of 4 wt%, and a polymer:microgel ratio of 70:30 wt%. All fibres in the following analyses were fabricated with these parameters, just the VIm content in the microgels was changed. Additionally fibres with a microgel/polymer ratio of 50:50 wt% were fabricated, with all other parameters kept the same. Figure 64 shows electron micrographs of pure PLA fibres fabricated with the above mentioned parameters (A and B) and PLA-microgel fibres (70:30 wt%) (C and D). The pure PLA fibres are uniform and homogenous with an average fibre diameter of 2 μm . A close-up of the fibre surface (B) shows a rough surface structure, which is well known for electrospun PLA fibres [54].

The PLA-microgel fibres in Figure 64 C and D show a different, but still rough surface and the average fibre diameter is reduced to about 1 μm in comparison to the pure PLA fibres. Microgels can not be seen on or in the fibres, which leads to the conclusion that they are in the core of the fibres, like in the PCL-microgel fibres spun from Chloroform/DMF solutions (compare section 4.2, part IV). Due to the fact that no microgels can be found on the aluminium target and due to the results of the following fibre analysis the microgels have to be located in the fibre core.

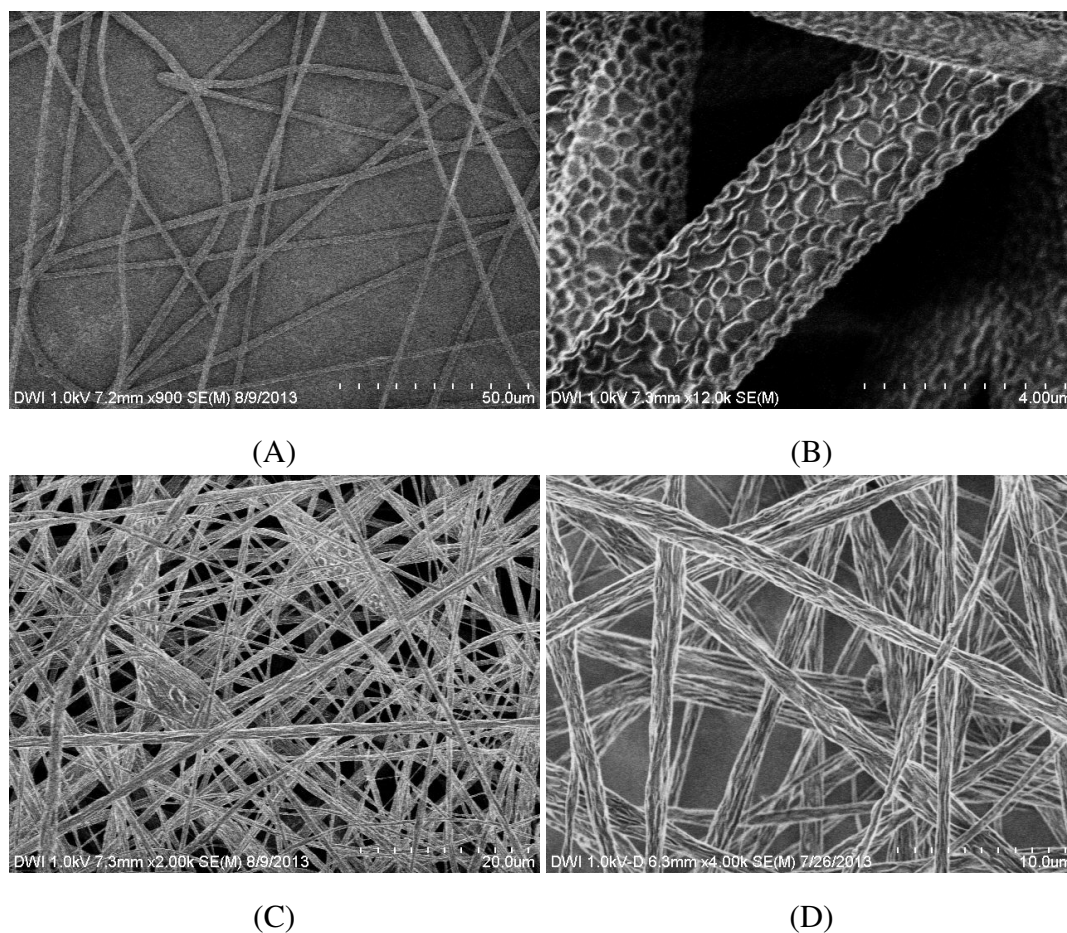


Figure 64: Pure PLA fibre (A and B) and PLA-microgel fibres (polymer:microgel ratio 70:30 wt% (C and D) spun from chloroform/methanol (80:20 wt%)

As mentioned above the PLA-microgel fibres have been spun with microgels with varying VIm contents (0, 2, 5 and 8 mol%). The VIm amount in the microgels, even though it has a big influence on the microgel size (compare section 3, part VI), it does not influence the fibre diameter, like it was already shown with the PVA-microgel fibres. Also the fibres with a polymer:microgel ratio of 50:50 wt% do not have a different morphology and only a slightly higher fibre diameter of about $1.2 \mu\text{m}$, due to the higher overall polymer content in the solution.

5 Fibre Characterisation

The main idea of these fibres is the pH buffering during the degradation process, which is needed in medical applications, for example as stent material or in wound suture. Another important property in this area is for example the swelling in water, which might be influenced by the microgels in the fibres. The DSC measurement presented in Figure 65 shows that the microgels are located inside of the fibres. The measurement was done in the temperature range of 5 to 60 °C, to investigate the VPTT of the microgels, although the temperature range from 35 to 45 °C is presented to make the transition better visible. Expectedly, the pure PLA does not show any transition in that area. The PLA-microgel fibres do show a transition at 40.7 °C, which reflects the VPTT of the microgels. The microgels used in the example shown have 5 mol% VIm and therefore a VPTT of 36 °C (compare section 3, part VI). The shift in the VPTT comes from the usage of D₂O and the hindrance of the microgels inside of the fibre matrix, as it was already shown for the PVA- and PCL-microgel fibres. However, the results prove that the microgels are inside of the fibres, even though they are not visible on the micrographs, and furthermore that the thermo sensitive behaviour is still present inside of the fibres.

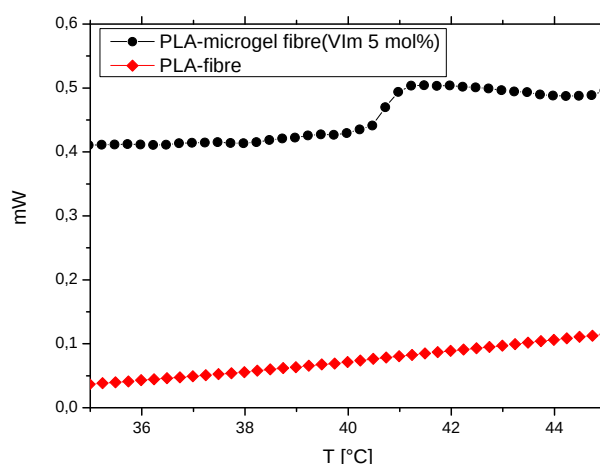


Figure 65: DSC measurement of PLA-microgel fibres showing the volume phase transition in the composite fibres

Figure 66 A shows the equilibrium degree of swelling measured by TGA for pure PLA fibre and for PLA-microgel fibres (VIm 8 mol%) at 25 and 50 °C. After executing the TGA experiments exactly like with the PVA or PCL fibres, it is showed that the swelling of the PLA-microgel fibres needs some time and is not completed after a few seconds; therefore the fibres were kept in water for 5 minutes, until weight constancy was reached. The results show that the pure PLA fibres have a very low degree of swelling at both temperatures, which

furthermore is due to water that was trapped in the fibre nonwoven by capillary forces and that was not adsorbed by the fibres. PLA is a hydrophobic polymer, therefore this results was expected. Figure 66 B shows example TGA measurements of pure PLA fibres and PLA-microgel fibres swollen at 20 °C. The difference between water bond by capillary forces and water adsorbed into the fibres can be seen by the difference in the slope of the mass loss during the measurement. The degree of swelling of the PLA-mircogel fibres is with 8.4 significantly higher. This proves again that the microgels are inside of the fibres and additionally shows a tremendous change in the fibre properties from hydrophobic to hydrophilic. At 50 °C, a temperature above the VPTT of the microgels, the PLA-microgel fibres show a half reduced degree of swelling of 4.1, which shows that the thermo sensitive behaviour is still active in the microgels, supporting the DSC results. Nevertheless, 4.1 is still four times higher than the degree of swelling of the pure PLA fibres, which is due to the fact that the microgels, even in their collapsed state are able to take up water, indicating that the incorporation of the microgels into the PLA matrix made the fibres easier accessible for water through pores for example.

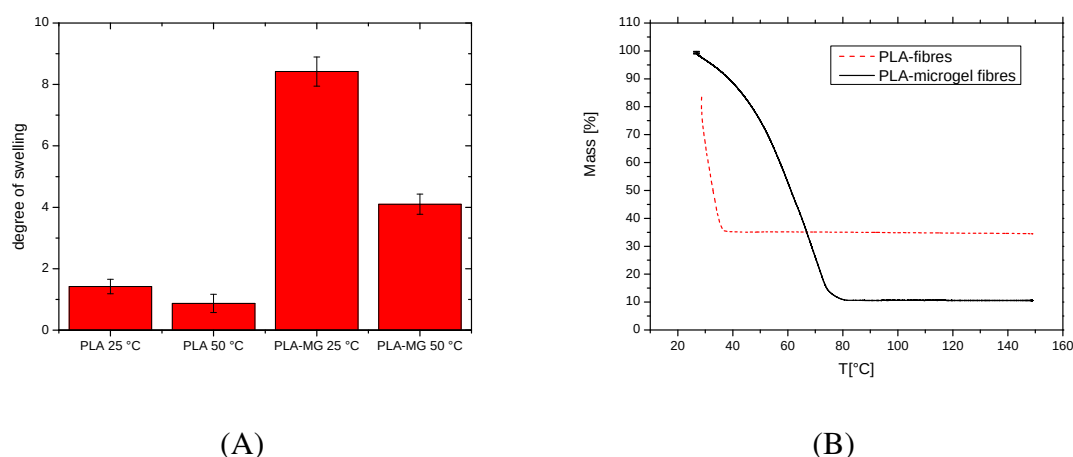


Figure 66: Degree of swelling of PCL-microgel fibres determined by means of TGA at 25 and 50 °C (A) and two example TGA measurements (B)

Contact angle measurements were used for two purposes: first, to investigate the change in the fibres surface properties by adding the microgels to their matrix, and second, to further investigate the time depending swelling that was observed during the TGA measurements. Figure 67 shows the contact angles for different fibre samples depending on the time. The hydrophobic pure PLA fibres do not show a change in the contact angle, the droplet stays on the non woven until it evaporates. In contrast to that, all microgel modified fibres show a time depending contact angle, because the water is absorbed by the fibres and water swollen environment has a reducing hydrophobicity. The starting contact angle is for all samples

basically the same, just the PLA-microgel fibres with a polymer:microgel ratio of 50:50 wt% show in the beginning of the measurements already a reduced contact angle of 110 instead of 127. The higher amount of microgels inside of the fibres increases the probability of microgels located closer to the surface, which would reduce the hydrophobicity. These fibres also take up water faster than the other samples, which can be expected due to the higher amount of hydrophilic microgels in the fibres. The VIm content also has an effect on the water uptake: with an increasing VIm concentration in the microgels, which are embedded in the fibres, the contact angle decreases faster, even though the effect for 5 mol% VIm is less evident compared to microgels without VIm.

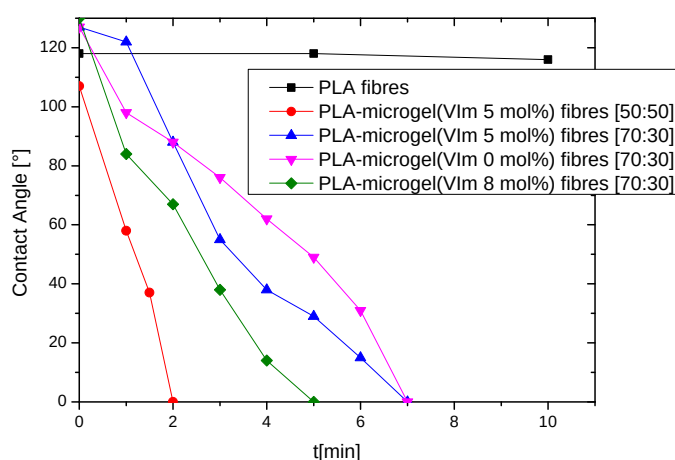


Figure 67: Contact angle measurements of PLA-microgel fibres indicating a not instantaneous uptake of the water droplet

Figure 68 shows an illustrating example of the water uptake on the fibre nonwovens. On the left hand side fibres with microgels without VIm are shown, and on the right hand side fibres with a 50:50 ratio of microgels and PLA and 5 mol% VIm are shown. The fast reducing droplet size and therefore the contact angle indicate faster water uptake. However, these experiments prove once more the change in the fibre and fibre surface properties. The incorporation of the microgels makes the fibres more hydrophilic and makes it possible to absorb water. This has to be taken into account for the degradation studies as well as for any application tests.

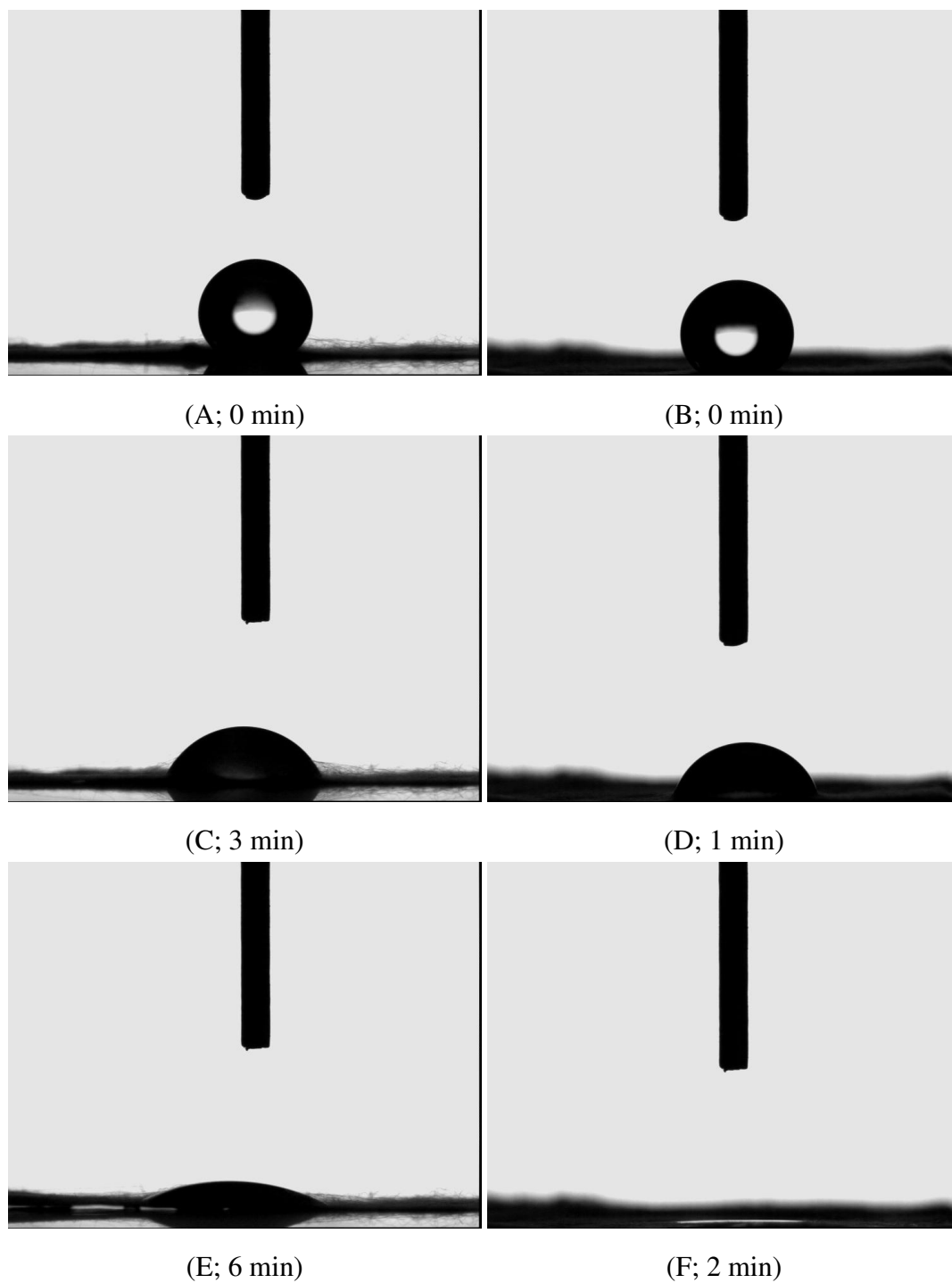


Figure 68: Water droplets and their absorption by time on PLA fibres with a 70:30 wt% ratio of polymer:microgel(VIm 0 mol%) (A,C and E) and on PLA fibres with a 50:50 ratio of polymer:microgel(VIm 5 mol%) (B,D and F)

The PLA-microgel fibres have also been analysed regarding their moisture sorption properties. Figure 69 shows the water moisture adsorption (A) and desorption (B) for PLA-microgel fibres with different microgels. As for the pure PCL, pure PLA does not give reasonable values, again explainable by a non suitable adsorbate-adsorbent combination (compare section 5.0.1, part IV), proven by a very low correlation coefficient of the Harkins-Jura plot of 0.821. The sorption and desorption rates shown in Figure 69 do not show any significant differences. The sorption rate is decreasing with increasing saturation, hindering further uptake and the desorption is antithetic to that.

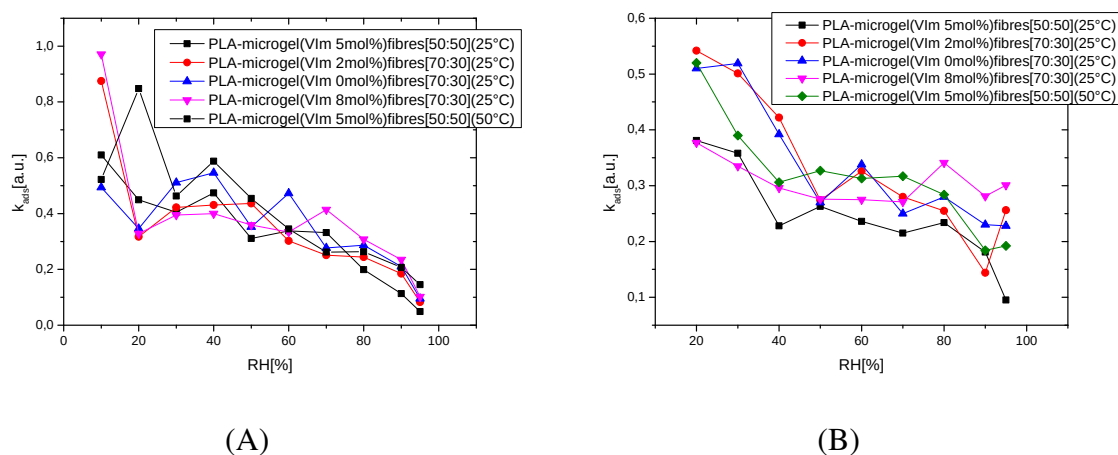


Figure 69: Water moisture sorption (A) and desorption (B) measurements of PLA-microgel fibres with different microgels at 25 and 50 °C

The values for the surface area calculated by the Harkins-Jura method also do not show a trend or interesting new insights for the PLA-microgel fibres. The values are between 120 and 145 m²/g with or without microgels in the fibres. The microgels in the PLA matrix seem therefore not to lead to high surface areas, like in case of the PCL fibres type C. No extra pores or free volume around the particles are caused by the incorporation of the microgels. Nevertheless, water and water moisture uptake is possible in the composite fibres.

5.1 Fibre Degradation

In order to analyse the degradation behaviour the PLA microgel fibres were prepared as described in section 2.3 of this part. The analysis was performed by measuring the pH values. After 7 month no signs of degradation, in particular no change in the pH value was observed

neither for the fibres with microgels nor for the pure PLA fibres. Therefore, a negative influence of the microgels can be excluded. An explanation for this inconsistency can not be given. Moreover, the experiments need to be repeated and will be prepared again. Due to the minimum time frame of the degradation of several months they can not be part of this thesis. Nevertheless, the degradation is an essential part of this study, therefore, an attempt to accelerate the degradation by the addition of *candida antarctica* lipase B was done. Figure 70 shows the pH value of the immersion medium depending on the degradation time after the addition of the lipase for pure PLA fibres and PLA-microgel fibres with a polymer:MG ratio of 70:30 and two different VIm contents in the microgels. The pure PLA fibres, without any buffering microgels show fast decrease of the pH value compared to the microgel modified fibres, which is a promising result. The VIm modified microgels in the PLA-microgel fibres are able to act as buffer for this degradation system and a higher amount of VIm in the microgels leads to a higher buffer capacity. However, this accelerated degradation does not mirror the condition of a degradation process in the human body, but the results shown display that the aim of this study can be achieved.

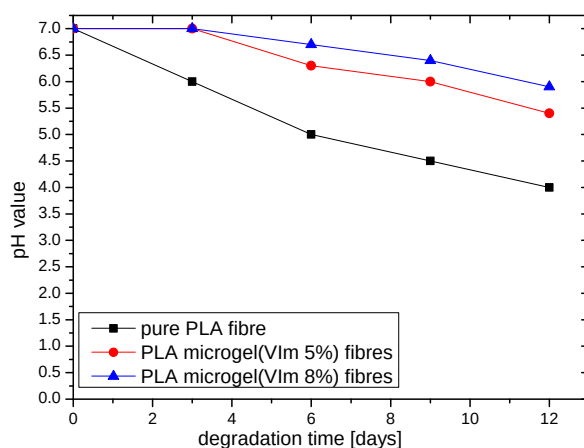


Figure 70: pH value of the immersion medium depending on the degradation time after the addition of the lipase for pure PLA fibres and PLA-microgel fibres with a polymer:MG ratio of 70:30 and two different VIm contents in the microgels

6 Summary/Conclusion

In this study microgel polylactide composite fibres have been successfully fabricated via electrospinning, where the microgels are modified with vinylimidazole. The idea was to achieve neutral degradation behaviour, a degradation without a drop of the pH value, which would be the usual case for PLA, through the microgel modification. However, at first it can be said that the PLA fibre modification with VCL/AAEM/VIm microgels was possible without problem due to the experience gained with PVA- and PCL-microgel fibres. The fibres are uniform, homogenous and the process is continuous; the morphology is similar to the one of microgel-PCL fibres spun from chloroform/DMF with microgels in the fibre core. The microgels retain their thermo-sensitive swelling properties inside of the PLA fibres, which is shown by means of DSC. The hydrophobic PLA is hydrophilically modified and the fibres are able to swell in water and to absorb water moisture. As with the other investigated fibres in this work the water swelling is tuneable by temperature. The switching temperature depends on the VIm concentration in the microgels, because higher amounts of the hydrophilic VIm in the microgel networks increase the VPTT. An increase above body temperature has to be kept in mind for the design of fibres for medical applications.

Although the main aim, the neutral degradation of the fibres, could not be shown in detail, because the normal degradation experiments failed, the accelerated degradation showed promising results. Depending on the VIm content of the microgels in the fibres the pH decrease is slowed down and the neutral degradation might be achievable with this system. New degradation studies are already prepared and the results will be available in a few month.

Introductory Studies/Outlook

VII

1 Introduction

As the title of this part of the thesis suggests, not only one topic will be addressed in this part, but two studies in different stages of progress are summarised. Each has its own introduction in which the aim and motivation for this particular study will be presented. Even though these studies are still in some extent far from being complete, they are interesting, show new opportunities for microgel based fibres and give new insights in the results of the previous parts of this thesis. Therefore, they are worth to be presented in this work and help to give an extended and more exhaustive view on my work done.

Both studies are also intended as an outlook in the on-going research regarding the possibilities of composite fibre fabrication via electrospinning and microgel based composite materials in general. The first study shown, extends the work done with the PCL-microgel fibres to ironoxide nanoparticles and phosphazene microspheres, in order to give these fibres even more possible properties (magnetic, flame-retardant). The other study is a first glance on the wet spinning of polymer hollow fibre membranes with microgels as additives. However, the experimental parts are merged into one chapter at the beginning to decrease the amount of repetitions.

2 Experimental Part

The following sections present only the descriptions of the synthesis and fabrication processes of the samples and materials, as well as the description of the experiments and analyses that have been done with these samples, which were not explained already in one of the previous chapters of this thesis. In cases of specific changes in the experiments, these changes will be mentioned and the rest of the description will be referred to. This is done to avoid unnecessary repetitions. In contrast to the other parts, this one will address different studies and like mentioned above all experiments and synthesis will be described in this chapter.

2.1 Materials

Acetonitrile (LCMS grade, Th.Geyer), chloroform (99.5%, VWR), dimethylacetamide (99.5%, Fluka), 1-Methyl-2-pyrrolidinone (NMP, 99%, Aldrich), 2,2'-Azobis[2-methylpropionamidine] dihydrochloride (AMPA, 97%, Aldrich), iron(III)chloride (97%, Aldrich), methanol (99.8%, VWR), N,N'-methylen-bis-(acrylamide) (BIS, 99%, Sigma-Aldrich), poly(caprolactone) (PCL, MW = 70.000-90.000 g/mol, Aldrich), polysulfone (PES, MW = 15.000 g/mol, Aldrich), polyvinylpyrrolidone (PVP, K90, 360.000 g/mol, Aldrich), sodium phosphate monobasic (98%, Aldrich), toluene (99.5%, VWR), triethylamine (TEA, 99.5%, Aldrich) and distilled water were used as received without having undergone any other cleaning procedures. Branched polyethylimine (bPEI, 50 wt% aqueous solution, BASF) was freeze dried before use. N-Vinylcaprolactam (VCL, 98%, Aldrich) was purified by vacuum distillation under nitrogen before use. 2-(methacryloyloxy)ethyl acetoacetate (AAEM, 95%, Aldrich) has been purified before use. Hexachlorocyclotriphosphazene (HCCP, 99%, Aldrich), was purified by sublimation and stored under nitrogen.

2.2 Particle Synthesis

For the different studies different kinds of particles were used. VCL/AAEM microgels were used as standard microgels as additives for the hollow fibre membranes. These microgels were used before in this thesis and their synthesis can be found in section 2.2. Additionally particles based on phosphazenes and magnetic iron(III) oxide were synthesised and their synthesis are presented in the following sections.

2.2.1 Phosphazene Microspheres

The phosphazene microspheres based on hexachlorocyclotriphosphazene (HCCP) and branched polyethylimine (bPEI) are based on another work in the research group [128]. The synthesis will be described shortly. The referred publication should be consulted for further information and analysis of these particles. bPEI ($M_n = 1200$ g/mol, 0.207 g, 4.806 mmol) was dissolved in 40 mL acetonitrile before 2 mL of TEA was added. HCCP (0.1 g, 0.288 mmol) dissolved in acetonitrile (10 mL) was mixed with the bPEI solution. The reaction took place in an ultrasonic bath for 3 h at 50 °C. The synthesised particles were separated by centrifugation and washed with distilled water before freeze-drying. Figure 71 shows an electron micrograph of the particles, dried and slightly agglomerated on aluminium paper, with an average diameter in dried state of 400 nm.

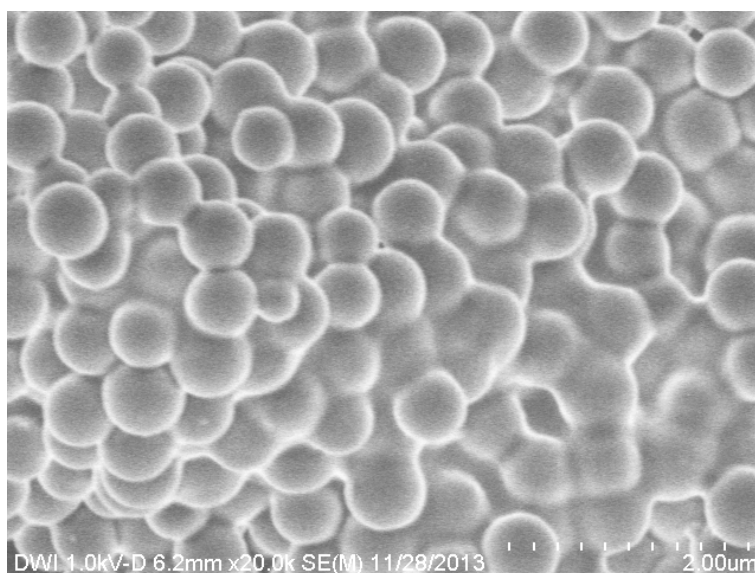


Figure 71: FESEM micrograph of Phosphazene microspheres

2.2.2 Iron(III) oxide Nanoparticles

The iron(III) oxide nanoparticles (α -Fe₂O₃) have been prepared following the idea of forced hydrolysis of ferric chloride [129]. A short description of the procedure is presented below. The referred publication should be consulted for more details. The synthesis itself was carried out in a 2 L flask with reflux condenser under nitrogen. 1 L of distilled water was pre-heated to 100 °C, then 5409 mg (29.9 mol) iron(III)chloride and 0.024 g (0.2 mmol) monosodium phosphate were added. The solution was heated with an oil bath at 130 °C to keep it always

boiling and the reaction was carried out for 48 h. Figure 72 shows an electron micrograph of the particles dried on aluminium paper, with an average length of 200 nm.



Figure 72: FESEM micrograph of iron(III) oxide nanoparticles

2.3 Preparation of Spinning Solutions

Generally the spinning solutions are made as in the chapters before. Solutions of the polymer and a solvent or solvent mixture are prepared and freeze dried particles are added in certain ratios. The re-dispersability of iron(III)oxide as well as of the VCL/AAEM microgels in NMP are not sufficient for a homogenous fabrication process. Therefore, these particles were re-dispersed in the solvent before the polymer was added and additionally the dispersion was enhanced by using an UIP1000hd transducer (hielscher Ultrasound Technology) with 18000 kHz. This device was just used as a very powerful ultrasound probe.

Table 14 shows the prepared spinning solutions for the PCL fibres modified with iron(III) oxide nanoparticles and phosphazene microspheres. The general solution was always methanol and toluene with a ratio of 50:50 wt% and a PCL concentration of 12 wt% like it was used in section 4.1 part IV, since the idea is to repeat these experiments with different co-compounds.

Table 14: Spinning solutions of PCL fibres with iron(III) oxide nanoparticles and phosphazene microspheres

Co-compound	PCL:particle [wt%]	PCL in solution [wt%]	Me/To ratio [wt%]	Ultrasound applied
Nanoparticle	50:50	12	50:50	no
Nanoparticle	70:30	12	50:50	no
Nanoparticle	70:30	12	50:50	yes
Nanoparticle	30:70	12	50:50	no
Nanoparticle	30:70	12	50:50	yes
Nanoparticle	20:80	12	50:50	no
Nanoparticle	20:80	12	50:50	yes
Nanoparticle	10:90	12	50:50	yes
Phosphazene	50:50	12	50:50	no
Phosphazene	20:80	12	50:50	no
Phosphazene	80:20	12	50:50	no
Phosphazene	70:30	12	50:50	no
Phosphazene	30:70	12	50:50	no

The fibre fabrication and the electrospinning setup is the same as the one described in section 2.4 part III, therefore no extra section will be included to describe the setup and procedure.

2.3.1 Preparation of Hollow Fibre Membranes

The method used to fabricate hollow fibre membranes with microgels as co-compounds was a wet spinning process or wet-phase inversion spinning process. The set-up was a simple self made one, because commercial available set-ups are usually too big and need too high minimal amounts of solution to work, which is a problem for the amount of microgels that can be prepared in reasonable times. The set-up consisted of two syringe pumps for the two different fluids and tubes. These parts were connected to a spinneret and to the water bath that belong to a bigger commercial set-up.

Two different fluids need to be prepared to fabricate hollow fibre membranes with this process: a dope-fluid and a bore-fluid. The dope-fluid contains the later membrane material, in this case the VCL/AAEM microgels and PES as main component; as solvent NMP was used and 5 wt% of water as pore forming agent. The bore-fluid is used to flow through the developing fibre to keep a channel in the middle open and free of material, therefore the fibre will be hollow in the end. The bore-fluid contains NMP (78 wt%), distilled water (19 wt%) and PVP (3 wt%)

as additional stabiliser. Each fluid is separately pumped by one of the syringe pumps through the spinneret; the dope-fluid in the outer part and the bore-fluid in the inner part. The exiting fibre is led into the water bath (coagulation or precipitation bath) where it solidifies. NMP is water soluble and gets washed out by the water, PES is not soluble in water and “precipitates”, solidifies in the given form of fibre, with a hollow core due to the bore-fluid. In this case the question arises if the microgels, which are well dispersible in water will stay in the fibre or get washed out during the solidification. Presumably the solidification is fast enough to trap the microgels inside.

In Table 15 the compositions of the solutions are summarised. Experience values gained in previous studies have been used for the process parameters. Their variation was kept as small as possible, due to the new material system. The air gap between the spinneret and the bath was always 1 cm, the flow rate of the dope-fluid was 1.5, 1.8 or 2.0 mL/min, and the flow rate of the bore-fluid was 0.5, 0.7, 0.85 or 0.9 mL/min. All possible variations of the two flow rates have been tried. Most of these parameter combinations have been tried with all of the different dope-solutions that are shown in Table 15.

Table 15: Spinning solutions for the fabrication of hollow fibre membranes

PES in solution [wt%]	MG:PES ratio [wt%]	solvent	Ultrasound applied
14	9:91	NMP	no
14	9:91	NMP	yes
14	15:85	NMP	no
14	15:85	NMP	yes
11	15:85	NMP	yes
14	33:66	NMP	no
14	33:66	NMP	yes
11	33:66	NMP	yes
17	33:66	NMP	yes
14	43:57	NMP	no
14	43:57	NMP	yes
11	43:57	NMP	yes
17	43:57	NMP	yes
14	50:50	NMP	no
14	50:50	NMP	yes
11	50:50	NMP	yes

The dope-fluids have been prepared by dissolving PES in NMP and adding a certain amount of freeze-dried microgels. The first fabricated hollow fibre membrane showed mainly aggregated microgels inside, therefore, procedure was changed in the way that the microgels were

re-dispersed first in the solvent, with the additional use of a UIP1000hd transducer (Hielscher Ultrasound Technology) with 18000 kHz as a ultrasound probe for a more homogenous dispersion. Afterwards PES was dissolved.

2.4 Characterisation Methods

In this part no characterisation methods that have not been mentioned before in this thesis were used. All descriptions of the methods used can be found in the characterisation methods section of the other parts.

3 Composite Microfibre Variations

3.1 Introduction

The results that have been obtained with microgels and PCL spun from methanol/toluene with microgels exclusively on the fibre surface, are encouraging to make similar fibres with other additives to gain access to completely different properties. Two interesting options were chosen to use this newly established technique: phosphazene microspheres with flame-retardant properties [130, 131, 128] and magnetic iron oxide nanoparticles. The possibility to homogeneously decorate fibre surfaces in a simple one step process with flame-retardant particles seems an interesting use of the established technique. Magnetic iron oxide nanoparticles (iron(III)oxide, Fe_2O_3) are used as an inorganic additive, to further broaden the field of particles used with this technique. Furthermore, iron(III) oxide is also known in catalytic application, as pigment, or in filtration (for example arsenate removal from water [132]), which are all applications that would benefit from the combination of the nanoparticle properties with the high surface areas of microfibres. However, the idea of this study is not only the fabrication of fibres with different interesting properties but also the investigation of the process itself: it should be shown that the process works also with other kinds of particles and not only with microgels. Furthermore, more insights in the question why the phase separation occurs could be found.

This chapter is divided in two sections, each addressing the fabrication of PCL fibres with one of the mentioned composite compounds and a general summary and conclusion. Some of the experiments/results were made by Fabian Christopher Gladisch during his research work under my supervision.

3.2 PCL-Fibres with Iron Oxide Nanoparticles

The fabrication of PCL microfibres with iron(III) oxide nanoparticles was mainly done to further investigate the possibilities of the electrospinning of PCL microfibres from methanol/toluene (50:50 wt% ratio), and to obtain fibres with co-compounds homogeneously spread on the fibre surface. Therefore, the basic spinning solution was set to be methanol and toluene in a ratio of 50:50 with 12 wt% PCL, and only the ratio polymer to nanoparticles was varied (compare Table 14). Furthermore, the process parameter such as target distance, flow rate and applied voltage were varied to achieve fibres with the best possible quality. In Figure 73 an overview (A) and a close-up (B) of the most homogenous fibres that have been achieved are shown. The ratio between polymer and nanoparticles is 50:50 wt%, the flow rate was 1 mL/h, the applied voltage 30 kV and the target distance 16 cm. The values for the process parameters are exactly

the same as for the PCL-microgel fibres. The fibres have an average diameter of 4 μm . As it is observable in Figure 73 B the nanoparticles align along the fibres, and are embedded in the PCL matrix. Some are located close to the surface, but they are also found inside of the fibres. A combination of parameters that would lead to fibres with the nanoparticles exclusively on the surface was not found. Nevertheless, fibres of a good quality, which have a homogeneous morphology and with homogeneously spread nanoparticles were achieved. A possible reason for the different morphology in comparison to the PCL-microgel fibres is discussed in the next section.

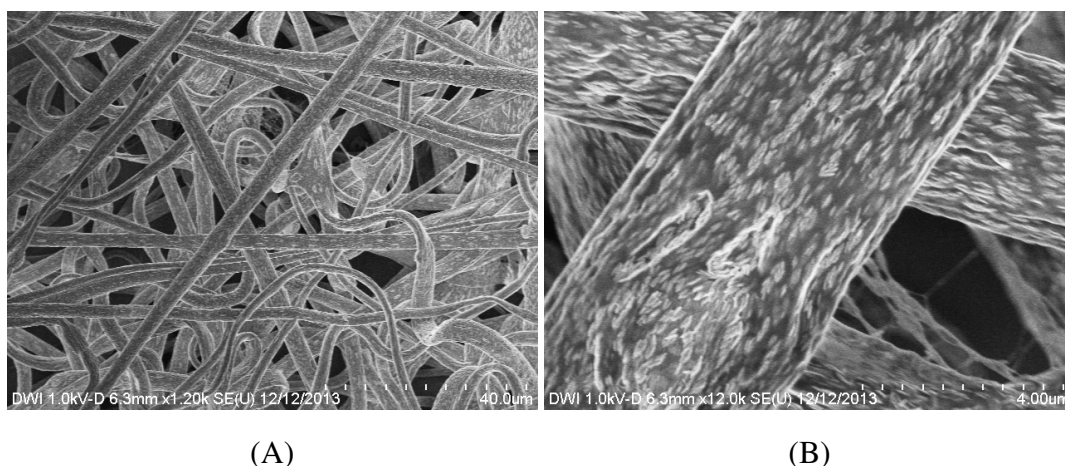


Figure 73: PCL-fibres spun from methanol/toluene (50:50), with a polymer:nanoparticle ratio of 50:50 wt% showing homogeneously spread particles, which are aligned in the fibre axis

As an attempt to achieve fibres with nanoparticles mainly on the surface, the ratio between polymer and nanoparticles was shifted so much to the side of the nanoparticles, that the polymer would only be used for the entanglement of the particles with each other. In Figure 74 fibres spun with the same process parameter as mentioned before, but with a polymer:nanoparticles ratio of 20:80 wt% are shown. Fibres with nanoparticles on the surface are presented, but the comparison of the two micrographs shows already a big difference in the fibre diameter. Furthermore, many fibres that are present in a sample like this are also empty of any particles, and on the target itself big areas consisting only of nanoparticles are found. The reason is most probably an inhomogeneous spinning process where big portions of the polymer are spun without nanoparticles entangled and later on portions of only particles are sprayed on the fibres. If the fibres are not completely dry when the particle spraying occurs, the particles will be added to the surface. Even though this would be the fibre morphology that was aimed for, the process is inhomogeneous and not continuous and the achieved fibres are not homogeneous as well. Therefore, this study was not successful from the point of view that no fibres with nanoparticles exclusively on the fibre surface could be fabricated. Never-

theless, the study was successful from the point of view that homogenous PCL-iron(III)oxide nanoparticle composite fibres were fabricated and new insights in this process were gained (presented in the next section).

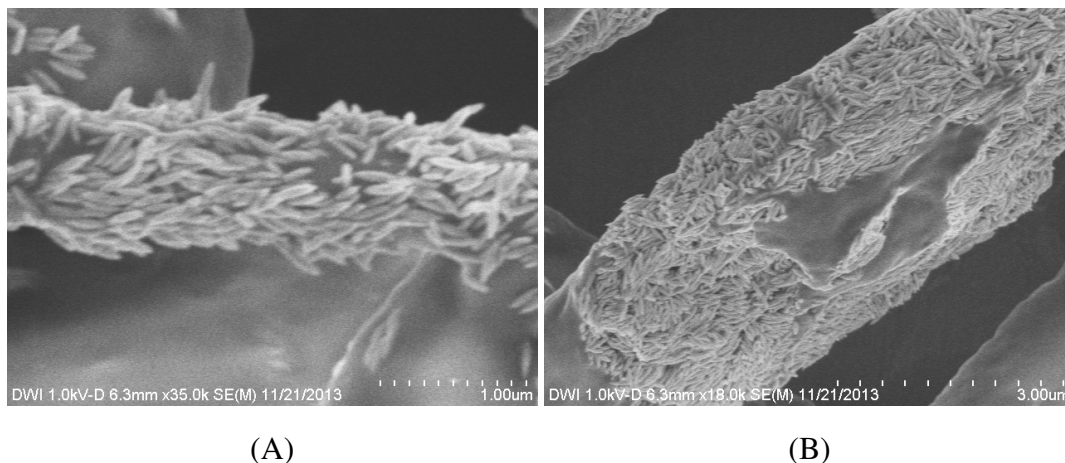


Figure 74: PCL-fibres spun from methanol/toluene (50:50), with a polymer:nanoparticle ratio of 20:80 wt%. The fibres have particles mainly on the surface but are in general not homogeneous

Another aspect of this study can be seen in Figure 75. A photograph of PCL fibres with iron(III) oxide nanoparticles is shown and it is obvious that the fibres imbibe the red colour of the nanoparticles. Iron(III) oxide is already used as pigment in cosmetics and embedded inside of polymer fibres it can easily serve as pigment for these kind of materials. Furthermore, surface related applications (for example catalysis) are also possible, since the particles are also located at the surface of the fibres, even though they are not exclusively located at the surface.



Figure 75: Photo of PCL-microfibres with iron(III) oxide nanoparticles; the red colour of the fibres due to the pigmentation with the nanoparticles is clearly visible

3.3 PCL-fibres with Phosphazene Microspheres

As in the section before, the fabrication of PCL fibres with phosphazene microspheres was done from methanol/toluene solutions with a ratio of 50:50 wt% and 12 wt% PCL in the solution in the attempt to create composite fibres with these microspheres exclusively on the fibre surface. The polymer:microsphere ratio was the main factor that was varied, besides the process parameters. For the latter the best choice is 30 kV applied voltage, 0.5 mL/h flow rate and 20 cm target distance. The polymer:microsphere ratio for the most homogenous fibres is 20:80. Figure 76 shows electron micrographs of fibres spun with the above mentioned parameters in an overview (A) and a close-up (B). The microspheres are, as intended, homogeneously spread on the fibre surface. The average fibre diameter is 4.5 μm .

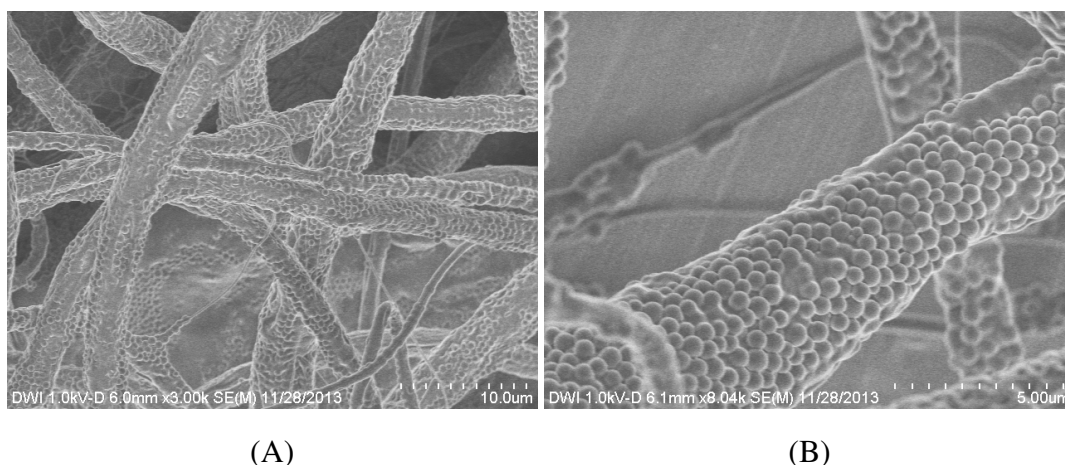


Figure 76: PCL-fibres spun from methanol/toluene (50:50), with a polymer:microsphere ratio of 20:80 wt%

Taking into account the results of this study with both materials, the iron(III) oxide nanoparticles and the phosphazene microspheres, and the results of the PCL-microgel fibres and films it can be said that the proposed theory about a bulk density depending creaming/sedimentation process in the spinning solutions (compare section 3.2, part IV) is most likely true. The nanoparticles do not swell in the solvent and have obviously a higher density than the solvent mixture, therefore they will sediment in the spinning solution and also during the spinning process, forming a morphology with the nanoparticle embedded in the PCL. The phosphazene microspheres are able to swell in the solvent mixture and like DLS measurements show, they swell favourable in toluene (the R_h in methanol is 400 nm and the R_h in toluene is 750 nm). A look at equation 3.1 (Part IV) shows that higher radii lead to smaller bulk densities and therefore the unique circumstances at the methanol/toluene ratio of 50:50 induce the shown fibre morphology. However, the proposed explanation is not proven, but seems to be likely true, due to the presented data.

It has also to be stated that tests of the flame-retardant properties have been done, but without any success; cotton fibres coated with the PCL-phosphazene composite fibres or without, burned both already after a few seconds. However, since no proper equipment for these tests was accessible, the tests have to be repeated with this equipment.

3.4 Summary/Conclusion

In this study composite PCL fibres with iron oxide nanoparticles and phosphazene based colloids have been fabricated using the same technique as for the PCL-microgel fibres type S. In both cases homogenous fibres were obtained. In the case of the phosphazene particles the intended structure with particles on the fibre surface was achieved, with the iron oxide NP this was not possible; the particles are spread in the PCL matrix. This results support the conclusion of the proposed theory in section 3.2 part IV, that the bulk density of the particles depending on the preferred solvent (swelling with methanol or toluene; iron oxide does not swell at all) leads to a creaming of the particles in the spinning solution. Nevertheless, it is still no proof for it and AUC measurements need to be done.

It can be concluded that the electrospinning of PCL from methanol/toluene mixtures with a 50:50 ratio of the solvents is an adequate technique to fabricate fibres with different kind of colloidal particles exclusively on the fibre surface. This offers many possibilities to specifically modify the fibre surface of PCL microfibres for different needs and applications. The particles presented in this study could provide flame retardant, magnetic or specifically absorbent properties to the materials created. Moreover, this study shows that through an easy one step process a wide range of colloids and other particles can be integrated/combined with polymer composite fibres with controlled morphology.

4 Microgels as Additives for Hollow Fibre Membranes

4.1 Introduction

In this study the possibility to use microgels as additives or co-compounds in other kinds of fibres or spinning processes is addressed. In all other studies the fibres are fabricated via electrospinning, which is a one step process with a rapid solidification. In contrast to that wet spinning, which is used in this study, is a process with more parameters, where the fibres solidify slower due to a precipitation or coagulation in a non solvent for the matrix polymer. For the standard polymer used, PES, this is water, which of course is a medium where microgels disperse well. However, this process gives new challenges for the homogenous incorporation of microgels, but it also offers new opportunities for microgel applications. Hollow fibre membranes with microgels as additives are the basic aim of this study. Membranes in general are used in separation processes and, in contrast to distillation or sublimation for example, they are not a thermally driven process and therefore more energy efficient. Membrane separation is used in many important markets like medicine (artificial kidney), food industry or in fuel cells, one upcoming market is the waste water treatment [133]. In the latter especially ultra- and microfiltration is needed to remove small molecules (drugs), nanoparticles or pathogenic agents. Microgels, which can also be seen as a nano-porous network that can be specifically modified with reactive groups, which can filter particular targets could be an advancement for this technology, when they are integrated in the common membrane structure. A first step in this direction will be shown in the following chapter.

Some of the measurements/results have been done by Carsten Stobbe during his research work done under my supervision.

4.2 Fabrication and Characterisation

The set-up used to fabricate the hollow fibre membranes in this study was half self built; therefore, the first experiments were done without microgels to find the right parameters to fabricate homogenous fibres. Additionally these fibres serve as reference for the investigation of the newly achieved fibre morphologies. Figure 77 shows an overview picture of a PES fibre (A) and a close-up on the fibre wall (B). The hollow fibre core is clearly recognisable and the wall is porous but homogenous, only a few voids are recognisable. Other irregularities are due to the preparation (break under liquid nitrogen) of the crosscut. The fibres shown have been prepared with an air gap of 1 cm, a dope-fluid flow rate of 1.5 mL/min and a bore-fluid flow

rate of 0.85 mL/min. The fluids themselves were the same as for the later test just without microgels, the polymer concentration was 14 wt%.

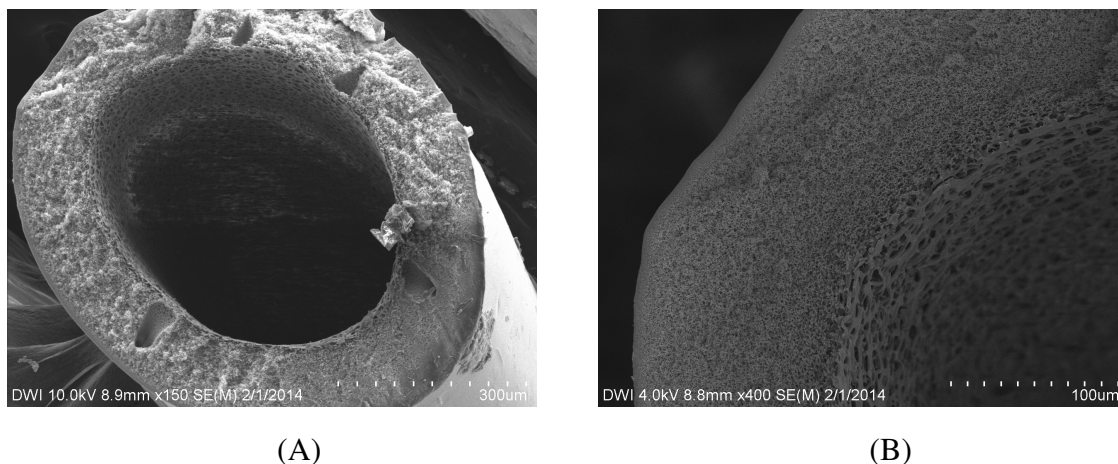


Figure 77: Overview of a PES hollow fibre membrane (A) and close-up of the fibre wall (B) showing the homogenous structure

The first tests made with microgels in the dope-fluid showed that the microgels are not very well dispersed in the viscous liquid and are agglomerated. Nevertheless, in Figure 78 some micrographs of these samples are shown. One reason is that in contrast to the later shown pictures with well dispersed microgels, the microgels are actually visible in these pictures, but the main reason is to show how the microgels are built into the PES matrix. Figure 78 A and B show microgel agglomerations close to the outer skin of the membrane fibre. This would be a desirable position for the microgels and the functionality of the membrane separation processes, but the agglomeration and the free volume around the microgels are not desirable. The free volume around the particles is additionally interesting considering the results of the PVA- and PCL microgel fibres, where many indications but no visible proof for these kind of free volume was found. Of course these pictures are again no proof, since it is a different material system, a different process, a different size scale and the microgels are agglomerated. Nevertheless, it is an additional and this time visual hint in the same direction: microgels incorporated in a polymer matrix tend to have a certain free volume around them.

The micrographs C and D of Figure 78 show a region with a higher concentration of microgel particles close to the inner skin of the fibre. The particles are also agglomerated which can be seen as a disturbance of the desired structure. Furthermore, it has to be said that this region is an exception and not present everywhere in the samples. The sample were prepared with a PES concentration of 14 wt% and a MG:PES ratio of 9:91 wt%. The dope-fluid flow rate was 1.5 mL/min and the bore-fluid flow rate 0.85 mL/min.

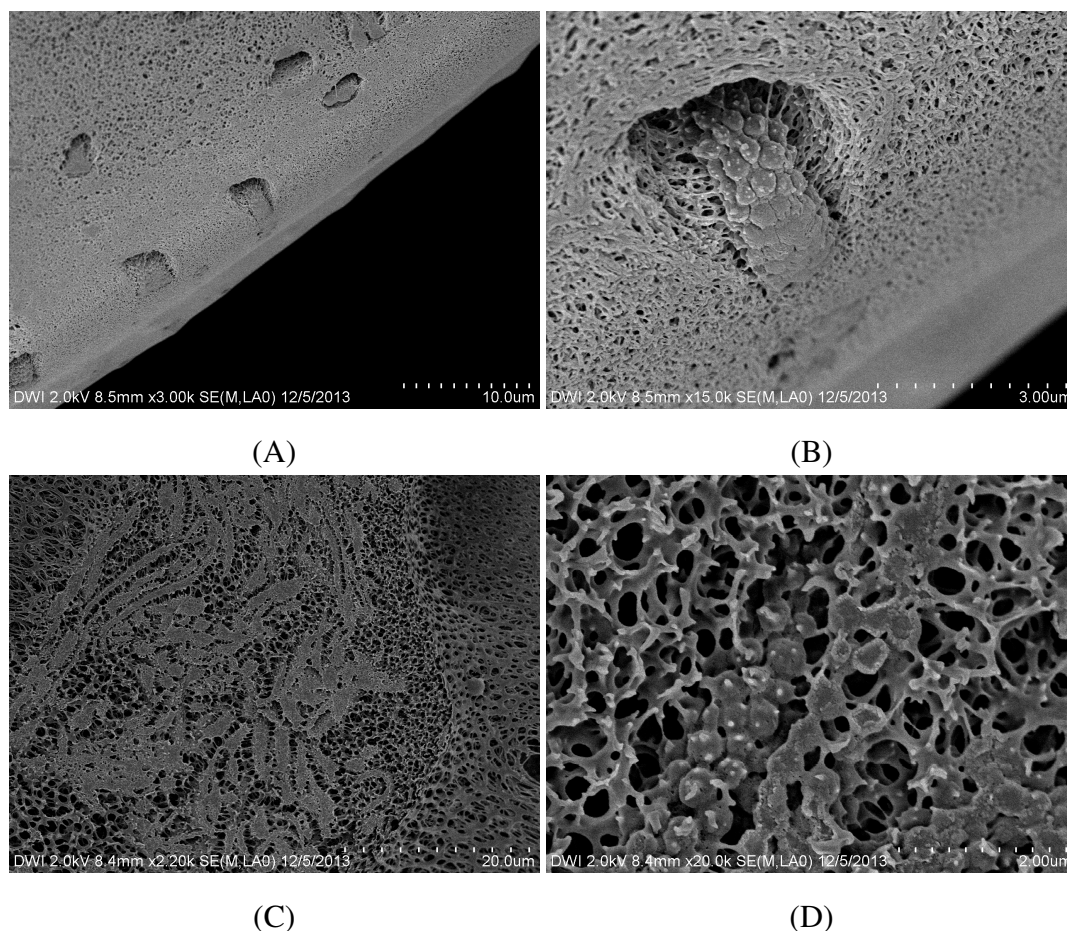


Figure 78: PES hollow fibre membranes with microgel agglomerations close to the outer skin (A and B) and a region with a higher microgel concentration close to the inner skin (C and D)

When the microgels were added into the solution before the PES and the samples were prepared with the additional use of strong ultrasound (compare section 2.3.1, part VII), than the microgels are well dispersed in the solution and there are no agglomerations in the fibres. However, all hollow fibre membranes prepared with microgels show big voids in the wall structure like it is presented in Figure 79 A and B. These voids are unwelcome since they may cause mechanical failures, and may lead to irregularities in the fibre properties. This problem has its reason in the viscosity of the solutions. The addition of microgels changes the viscosity of the solutions, which is additionally dependend on the stress that is put on the microgels, since they have a sheer thinning behaviour instead of a linear, Newtonian behaviour as most linear polymers (compare section 4.1, part III). Therefore, the adaption of the solution and the process parameters needs to be done in more detail, like it was done in the case of the electrospun microgel-polymer composite fibres. The fibre shown in Figure 79 A was spun

with a dope-fluid flow rate of 1.5 mL/min and a bore-fluid flow rate of 0.8 mL/min, the PES concentration was 14 wt% and the MG:PES ratio 9:91 wt%. The fibre shown in figure 79 B and C was spun with a dope-fluid flow rate of 1.8 mL/min and a dope-fluid flow rate of 0.9 mL/min, the PES concentration was again 14 wt%, but the MG:PES ratio was 50:50 wt%.

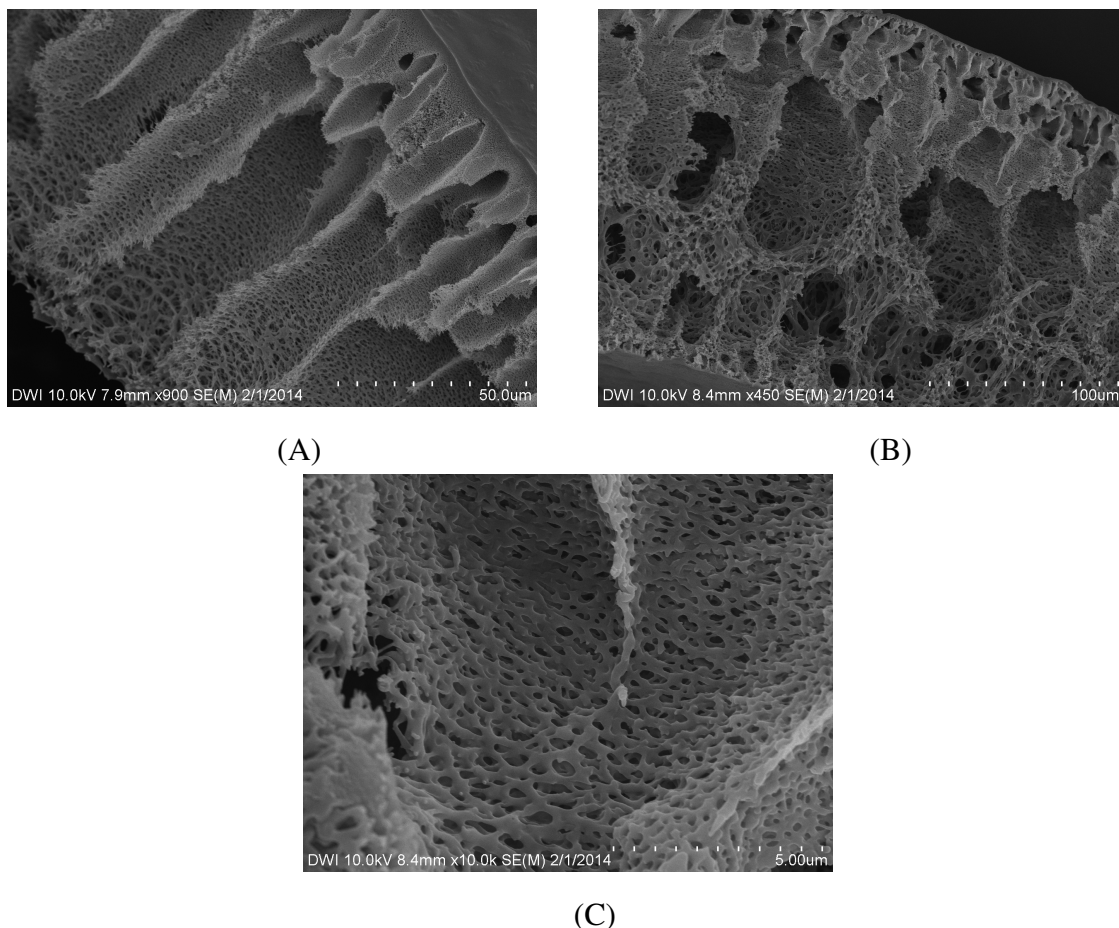


Figure 79: Two different PES hollow fibre membranes with microgels spread in the fibre structure. A and B show each an overview of the fibre wall of each fibre with voids, C shows a close-up of the porous membrane structure

Microgel agglomerations are not visible in Figure 79, but also in general microgels are difficult to spot in these micrographs. In the close-up of the membrane structure in Figure 79 C, especially in the lower left region, some spherical structures, which are most likely microgels, are observable. They are supposed to be all over this structure, but a clear view of them is not given, and additionally they do not display the given MG:PES ratio of 50:50 wt% in this sample. Therefore, different attempts to prove the existence of the microgels in the fibres were made, similar to the ones for the electrospun microgel based fibres. DSC was

one option, which additionally could have shown the thermo-sensitive behaviour of the microgels. Unfortunately, and in contrast to electrospun fibres, DSC measurements were not successful; no transition was seen. Most probably the fibre dimensions are the reason and DSC was not sensitive enough for the in comparison with the electrospun fibres thick membrane fibres. The TGA investigation of the fibres was successful, which is shown in Figure 80. PES and the microgels decompose at completely different temperatures; therefore, two relatively distinct steps in the mass loss can be seen. The membrane without microgels does not show the second step in the decomposition, which proves that the second step can be assigned to the microgels (compare also Figure 34). The measurements have been done under nitrogen atmosphere, therefore unburned carbon residue is found in the crucible, shown in the curves in Figure 80 approximately below 40 wt%. The fibres used for this measurement had a theoretical MG:PES ratio of 50:50 wt%, the calculation of the data shown leads to the same ratio with an error margin of $\pm 5\%$. It can be stated that the microgels are integrated in the fibre structure and that nearly no microgel loss occurs during the fibre formation process. This also means that, if no microgels are lost and therefore all microgels are in the fibres, and additionally only a few microgels are seen on the FESEM micrographs, the microgels have to be really integrated in the fibre structure, which would be the desired morphology of hollow fibre membranes composites with microgels.

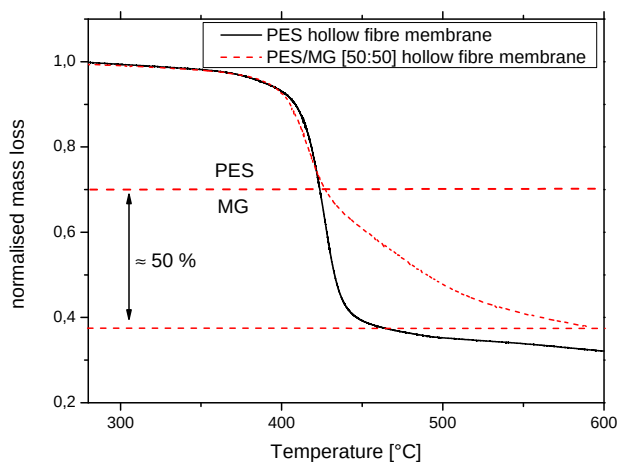


Figure 80: TGA measurement of a PES and a PES/MG hollow fibre membrane. In the latter the two step thermal decomposition can be observed. The data is used to determine the actual material composition

It is shown that hollow fibre membranes with microgels as co-compounds can be fabricated, even though some advancements in the fibre homogeneity have still to be achieved. Fibres can be produced continuously, nearly without any loss of microgels during the process and

with the microgels homogenously spread throughout the whole fibre. The next steps should test the functionality of these membranes as well as investigate a possible influence of the membrane properties by the thermo-sensitive properties of the microgels. Since these tests are still on-going and are done in cooperation with another institute they are not part of this thesis.

4.3 Summary/Conclusion

In this study it was shown that the fabrication of hollow fibre membranes with microgels as co-compounds is possible, microgels are spread in the fibres and no loss of microgels occurs during the fabrication process. Nevertheless, this study is basically only a proof of principle, since the membrane walls show voids and no ideal set of solution and process parameters are yet found. Furthermore, no tests of the membrane functionality are shown, but as it was mentioned they are on-going. It is also only a proof of principle because the main idea is to give additional properties to the membranes by using specifically designed microgels, which can for example bind target molecules. All this needs to be done to show the possibilities for microgel composite hollow fibre membranes. Anyhow this study is a first step in this direction and shows promising results about the possibilities for different microgel composite materials. The study gives additionally a new hint on the way microgels are built into a polymer matrix, stating again, as in many of the previous parts of this thesis, that the microgels are surrounded by a certain free volume, which can be accessed by water.

Summary and Conclusion

VIII

In this thesis some novel ideas and advancements in the field of polymer composite fibres, specifically microgel-based polymer composite fibres have been achieved. The main task was to investigate and understand the electrospinning process of microgels and polymers and the interplay of parameter influences, in order to fabricate reproducible and continuously homogeneous composite fibres. The main aim was to fabricate a composite material which combines the special properties of polymer fibres and thermo-sensitive microgels, as well as properties given by the specific choice of the fibre polymer and the microgels co-monomers. Furthermore, these fibres are supposed to enable a macroscopic access to the microgel properties, because their usual dispersion state is not applicable for many tasks, but a macroscopic fibre nonwoven consisting of microscopic fibres decorated with nanoscopic microgels will provide this opportunity, without losing the “nano” aspect. In a first step, using PVA it was already shown that the microgels retain their thermo-sensitive, smart swelling properties in the fibre structure, which gives the fibres tuneable swelling properties as well. Additional ways to crosslink these fibres chemically or physically are shown. In the next step, PCL, a polymer with more special properties (hydrophobic, degradable), was chosen to achieve fibres with these properties and to show how much these properties can be influenced by the addition of microgels. Moreover, different fibre morphologies have been fabricated, fibres with microgels located only in the core and fibres with microgels located only on the surface, which not only show differences in the tuneable swelling behaviour and the degradation process, but it also opens opportunities to more specific applications. The different morphologies were achieved by using different solvent systems: methanol/toluene and chloroform/DMF. Additionally, it should be mentioned that the simple one step electrospinning process of hydrophilic microgels and hydrophobic PCL gives access to an elegant way to completely change the hydrophobicity of the general polymer fibres.

To give a possibility for a better exploitation of the newly achieved PCL fibres with microgel exclusively on the fibre surface, microgels with a special property combination have been created: microgels, crosslinked with a star-shaped acrylate-functionalised poly(ϵ -caprolactone) crosslinker, that are degradable due to the same functionality as PCL, having additionally hydrophobic domains to immobilise hydrophobic drugs. The synthesis was done via a specialised miniemulsion polymerisation and uptake as well as release of ibuprofen was shown. Fibres with these microgels on the surface could deliver drugs targeted to specific places and are completely degradable under physiological conditions.

The results of a preliminary study for a project with the aim of creating PLA based stents, with a neutral degradation process for a higher tolerance in the human body. A combination of VIm modified microgels with polylactide fibres was chosen to achieve this. The fibres are successfully realised and analysed regarding their swelling properties, in the same manner as the other composite fibres presented in this work. The initial degradation studies showed no observable results and need to be repeated, but accelerated degradation studies showed promising results of an inhibited pH drop depending on the VIm content in the microgels inside the PLA fibres. Nevertheless, the effect of the microgels on the pH value during the

degradation process needs to be assessed in detail in a repetition of the degradation studies.

Two small preliminary studies about different topics, which are still in an early stage, but that already show promising results are also presented in this thesis. Fibres with iron(III) oxide nanoparticles and phosphazene microsphere have also been fabricated using the same technique shown for the PCL-microgel fibres with microgel exclusively on the surface. These fibres give an insight in the process and show its limitations and possibilities. Furthermore, hollow fibre membranes with microgels as additive have been prepared using a wet spinning process, to show other options to fabricate composite materials with microgels, accessing the field of filtration and separation.

Overall, it can be said that the research goals set have been reached. New composite materials have been created and the electrospinning process was optimised for the different needs of each composite fibre system. The fibres have been analysed in detail for their properties and interesting, new or changed properties in the composite fibres are reported. All this was done while keeping an eye on medical applications. Many syntheses and processes have been done exclusively with water as solvent and the microgels containing hydrophobic domains were tested due to their uptake and release behaviour of ibuprofen. However, no actual applications are yet shown and should be in the focus of the next steps of this research. In this perspective many opportunities for possible application are shown and the newly created microgel-polymer composite fibres present a promising option for various applications.

Bibliography

- [1] RENEKER, DARRELL H. and ALEXANDER L. YARIN: *Electrospinning jets and polymer nanofibers*. Polymer, 49(10):2387–2425, May 2008.
- [2] NAYAK, SATISH and L. ANDREW LYON: *Weiche nanotechnologie mit weichen nanopartikeln*. Angewandte Chemie, 117(47):7862–7886, 2005.
- [3] SAUNDERS, BRIAN R. and BRIAN VINCENT: *Microgel particles as model colloids: theory, properties and applications*. Advances in Colloid and Interface Science, 80(1):1–25, February 1999.
- [4] PELTON, ROBERT: *Temperature-sensitive aqueous microgels*. Advances in Colloid and Interface Science, 85, September 2000.
- [5] HESKINS, M. and J. E. GUILLET: *Solution properties of poly(n-isopropylacrylamide)*. Journal of Macromolecular Science: Part A - Chemistry, 2(8):1441–1455, 1968.
- [6] SCHILD, H. G.: *Poly(n-isopropylacrylamide): experiment, theory and application*. Progress in Polymer Science, 17(2):163–249, 1992.
- [7] WU, CHI and SHUIQIN ZHOU: *Volume phase transition of swollen gels: discontinuous or continuous*. Macromolecules, 30(3):574–576, February 1997.
- [8] CROWTHER, H. M. and B. VINCENT: *Swelling behavior of poly n-isopropylacrylamide microgel particles in alcoholic solutions*. Colloid and Polymer Science, 276(1):46–51, January 1998. WOS:000071801000007.
- [9] DURACHER, D., A. ELAISSARI, and C. PICHOT: *Characterization of cross-linked poly(n -isopropylmethacrylamide) microgel latexes*. Colloid & Polymer Science, 277(10):905–913, October 1999.
- [10] EISELE, MICHAEL and WALTHER BURCHARD: *Hydrophobic water-soluble polymers, 1. dilute solution properties of poly(1-vinyl-2-piperidone) and poly(n-vinylcaprolactam)*. Die Makromolekulare Chemie, 191(1):169–184, 1990.
- [11] LAU, ANDY C. W. and CHI WU: *Thermally sensitive and biocompatible poly(n-vinylcaprolactam): Synthesis and characterization of high molar mass linear chains*. Macromolecules, 32(3):581–584, February 1999.
- [12] VIHOLA, HENNA, ANTTI LAUKKANEN, JOUNI HIRVONEN, and HEIKKI TENHU: *Binding and release of drugs into and from thermosensitive poly(n-vinyl caprolac-*

- tam*) nanoparticles. *European Journal of Pharmaceutical Sciences*, 16(1–2):69–74, July 2002.
- [13] VIHOLA, HENNA, ANTTI LAUKKANEN, LAURI VALTOLA, HEIKKI TENHU, and JOUNI HIRVONEN: *Cytotoxicity of thermosensitive polymers poly(n-isopropylacrylamide), poly(n-vinylcaprolactam) and amphiphilically modified poly(n-vinylcaprolactam)*. *Biomaterials*, 26(16):3055–3064, June 2005.
- [14] DIMITROV, IVAYLO, BARBARA TRZEBICKA, AXEL H.E. MÜLLER, ANDRZEJ DWORAK, and CHRISTO B. TSVETANOV: *Thermosensitive water-soluble copolymers with doubly responsive reversibly interacting entities*. *Progress in Polymer Science*, 32(11):1275–1343, November 2007.
- [15] SA, SHENG-SHU, BAO-HUA ZHANG, QING YANG, XIA-QIN WANG, and ZHI-PING MAO: *Application of reactive acrylate microgels in water-base coatings*. *Journal of Shanghai University (English Edition)*, 13(1):67–71, March 2009.
- [16] MOHANTY, P. S. and W. RICHTER: *Structural ordering and phase behavior of charged microgels*. *The Journal of Physical Chemistry B*, 112(47):14692–14697, November 2008.
- [17] MURTHY, N., M. C. XU, S. SCHUCK, J. KUNISAWA, N. SHASTRI, and J. M. J. FRECHET: *A macromolecular delivery vehicle for protein-based vaccines: Acid-degradable protein-loaded microgels*. *Proceedings of the National Academy of Sciences of the United States of America*, 100(9):4995–5000, April 2003. WOS:000182612600008.
- [18] KHAN, ASLAM: *Preparation and characterization of magnetic nanoparticles embedded in microgels*. *Materials Letters*, 62(6-7):898–902, March 2008.
- [19] LIN, C. L. and W. Y. CHIU: *Polypyrrole/poly(n-isopropylacrylamide-co-acrylic acid) thermosensitive and electrically conductive composite microgels*. *Journal of Polymer Science Part a-Polymer Chemistry*, 44(5):1648–1659, March 2006. WOS:000235526500009.
- [20] AGRAWAL, MUKESH, ANDRIJ PICH, SMRATI GUPTA, NIKOLAOS E. ZAFEIROPOULOS, JORGE RUBIO-RETAMA, FRANK SIMON, and MANFRED STAMM: *Temperature sensitive hybrid microgels loaded with ZnO nanoparticles*. *Journal of Materials Chemistry*, 18(22):2581, 2008.
- [21] PICH, ANDRIJ, ANNE TESSIER, VOLODYMYR BOYKO, YAN LU, and HANS-JUERGEN P. ADLER: *Synthesis and characterization of poly(vinylcaprolactam)-based*

- microgels exhibiting temperature and pH-Sensitive properties.* Macromolecules, 39(22):7701–7707, October 2006.
- [22] KLINGER, DANIEL and KATHARINA LANDFESTER: *Photo-sensitive PMMA microgels: light-triggered swelling and degradation.* Soft Matter, 7(4):1426, 2011.
- [23] PICH, ANDRIJ and WALTER RICHTERING: *Microgels by precipitation polymerization: Synthesis, characterization, and functionalization.* In PICH, ANDRIJ and WALTER RICHTERING (editors): *Chemical Design of Responsive Microgels*, volume 234, pages 1–37. Springer Berlin Heidelberg, Berlin, Heidelberg, 2010.
- [24] RICHTERING, WALTER and INGO BERNDT: *Doubly temperature sensitive core-shell microgels.* Macromolecules, 36(23):8780–8785, 2003.
- [25] SERPE, M. J., K. A. YARMEY, C. M. NOLAN, and L. A. LYON: *Doxorubicin uptake and release from microgel thin films.* Biomacromolecules, 6(1):408–413, February 2005. WOS:000226344300052.
- [26] DEBORD, J. D. and L. A. LYON: *Thermoresponsive photonic crystals.* Journal of Physical Chemistry B, 104(27):6327–6331, July 2000. WOS:000088156500001.
- [27] LYON, L. A., J. D. DEBORD, S. B. DEBORD, C. D. JONES, J. G. MCGRATH, and M. J. SERPE: *Microgel colloidal crystals.* Journal of Physical Chemistry B, 108(50):19099–19108, December 2004. WOS:000225695100007.
- [28] HILTL, STEPHANIE, MARCO-PHILIPP SCHÜRINGS, ANDREEA BALACEANU, VERONIKA MAYORGA, CLEMENS LIEDEL, ANDRIJ PICH, and ALEXANDER BÖKER: *Guided self-assembly of microgels: from particle arrays to anisotropic nanostructures.* Soft Matter, 7(18):8231–8238, September 2011.
- [29] MCPHEE, WAYNE, KAM CHIU TAM, and ROBERT PELTON: *Poly(*n*-isopropylacrylamide) latices prepared with sodium dodecyl sulfate.* Journal of Colloid and Interface Science, 156(1):24–30, March 1993.
- [30] BOYKO, VOLODYMYR, ANDRIJ PICH, YAN LU, SVEN RICHTER, KARL-FRIEDRICH ARNDT, and HANS-JUERGEN P. ADLER: *Thermo-sensitive poly(*n*-vinylcaprolactam-co-acetoacetoxyethyl methacrylate) microgels: 1—synthesis and characterization.* Polymer, 44(26):7821–7827, December 2003.
- [31] YIN, XIANGCHUN and HARALD D. H. STÖVER: *Hydrogel microspheres formed by complex coacervation of partially MPEG-Grafted poly(styrene-alt-maleic anhydride)*

- with PDADMAC and cross-linking with polyamines.* Macromolecules, 36(23):8773–8779, November 2003.
- [32] QIU, XINGPING and SVETLANA A. SUKHISHVILI: *Copolymerization of n-vinylcaprolactam and glycidyl methacrylate: Reactivity ratio and composition control.* Journal of Polymer Science Part A: Polymer Chemistry, 44(1):183–191, 2006.
- [33] HOARE, TODD and DANIEL MCLEAN: *Kinetic prediction of functional group distributions in thermosensitive microgels.* The Journal of Physical Chemistry B, 110(41):20327–20336, October 2006.
- [34] PICH, ANDRIJ, FENBAO ZHANG, LEI SHEN, SEBASTIAN BERGER, OLGA ORNATSKY, VLADIMIR BARANOV, and MITCHELL A. WINNIK: *Biocompatible hybrid nanogels.* Small, 4(12):2171–2175, 2008.
- [35] ZHANG, QING-SONG, LIU-SHENG ZHA, JING-HONG MA, and BO-RUN LIANG: *Synthesis and characterization of novel, temperature-sensitive microgels based on n-isopropylacrylamide and tert-butyl acrylate.* Journal of Applied Polymer Science, 103(5):2962–2967, 2007.
- [36] LU, YAN, JIAYIN YUAN, FRANK POLZER, MARKUS DRECHSLER, and JOHANNES PREUSSNERS: *In situ growth of catalytic active au - pt bimetallic nanorods in thermoresponsive core - shell microgels.* Acs Nano, 4(12):7078–7086, December 2010. WOS:000285449100007.
- [37] PALIOURA, D., S. P. ARMES, S. H. ANASTASIADIS, and M. VAMVAKAKI: *Metal nanocrystals incorporated within pH-responsive microgel particles.* Langmuir, 23(10):5761–5768, May 2007. WOS:000246071800081.
- [38] SUZUKI, DAISUKE and HARUMA KAWAGUCHI: *Stimuli-sensitive core/shell template particles for immobilizing inorganic nanoparticles in the core.* Colloid and Polymer Science, 284(12):1443–1451, September 2006. WOS:000240058600008.
- [39] DERSCH, ROLAND, ANDREAS GREINER, MARTIN STEINHART, and JOACHIM H. WENDORFF: *Nanofasern und nanoröhrchen: Bausteine aus polymeren.* Chemie in unserer Zeit, 39(1):26–35, 2005.
- [40] MACDIARMID, A.G., W.E. JONES JR., I.D. NORRIS, J. GAO, A.T. JOHNSON JR., N.J. PINTO, J. HONE, B. HAN, F.K. KO, and H. OKUZAKI: *Electrostatically-generated nanofibers of electronic polymers.* Synthetic Metals, 119(1-3):27–30, March 2001.

- [41] WANG, XIANYAN, CHRISTOPHER DREW, SOO-HYOUNG LEE, KRIS J. SENEAL, JAYANT KUMAR, and LYNNE A. SAMUELSON: *Electrospun nanofibrous membranes for highly sensitive optical sensors*. Nano Letters, 2(11):1273–1275, November 2002.
- [42] YOSHIMOTO, H., Y. M. SHIN, H. TERAII, and J. P. VACANTI: *A biodegradable nanofiber scaffold by electrospinning and its potential for bone tissue engineering*. Biomaterials, 24(12):2077–2082, May 2003. WOS:000181758200010.
- [43] KO, F., Y. GOGOTSI, A. ALI, N. NAGUIB, H. YE, G.L. YANG, C. LI, and P. WILLIS: *Electrospinning of continuous carbon nanotube-filled nanofiber yarns*. Advanced Materials, 15(14):1161–1165, July 2003.
- [44] LI, DAN and YOUNAN XIA: *Direct fabrication of composite and ceramic hollow nanofibers by electrospinning*. Nano Letters, 4(5):933–938, May 2004.
- [45] LU, X., Y. ZHAO, and C. WANG: *Fabrication of PbS nanoparticles in polymer-fiber matrices by electrospinning*. Advanced Materials, 17(20):2485–2488, October 2005.
- [46] GENSHEIMER, MARCO, ASTRID BRANDIS-HEEP, SEEMA AGARWAL, RUDOLF K. THAUER, and ANDREAS GREINER: *Polymer/Bacteria composite nanofiber nonwovens by electrospinning of living bacteria protected by hydrogel microparticles*. Macromolecular Bioscience, 11(3):333–337, March 2011.
- [47] TOWNSEND-NICHOLSON, ANDREA and SUWAN N. JAYASINGHE: *Cell electrospinning: a unique biotechnique for encapsulating living organisms for generating active biological microthreads/scaffolds*. Biomacromolecules, 7(12):3364–3369, December 2006.
- [48] ZENG, JUN, ACHIM AIGNER, FRANK CZUBAYKO, THOMAS KISSEL, JOACHIM H. WENDORFF, and ANDREAS GREINER: *Poly(vinyl alcohol) nanofibers by electrospinning as a protein delivery system and the retardation of enzyme release by additional polymer coatings*. Biomacromolecules, 6(3):1484–1488, May 2005.
- [49] LI, D., T. HERRICKS, and Y. N. XIA: *Magnetic nanofibers of nickel ferrite prepared by electrospinning*. Applied Physics Letters, 83(22):4586–4588, December 2003. WOS:000186787100040.
- [50] XU, XIAOYI, QINGBIAO YANG, YONGZHI WANG, HAIJUN YU, XUESI CHEN, and XIABIN JING: *Biodegradable electrospun poly(l-lactide) fibers containing antibacterial silver nanoparticles*. European Polymer Journal, 42(9):2081–2087, September 2006. WOS:000241091300016.

- [51] MCCANN, JESSE T., MANUEL MARQUEZ, and YOUNAN XIA: *Highly porous fibers by electrospinning into a cryogenic liquid*. Journal of the American Chemical Society, 128(5):1436–1437, February 2006.
- [52] LI, D., J. T. MCCANN, and Y. N. XIA: *Use of electrospinning to directly fabricate hollow nanofibers with functionalized inner and outer surfaces*. Small, 1(1):83–86, January 2005. WOS:000229117700011.
- [53] LI, D. and Y. XIA: *Electrospinning of nanofibers: Reinventing the wheel?* Advanced Materials, 16(14):1151–1170, July 2004.
- [54] BOGNITZKI, M., W. CZADO, T. FRESE, A. SCHAPER, M. HELLWIG, M. STEINHART, A. GREINER, and J. H. WENDORFF: *Nanostructured fibers via electrospinning*. Advanced Materials, 13(1):70–72, 2001.
- [55] RAYLEIGH, JOHN WILLIAM STRUTT: *On the equilibrium of liquid conducting masses charged with electricity*. Philosophical Magazine, 14, May 1882.
- [56] RAYLEIGH, JOHN WILLIAM STRUTT: *On the instability of jets*. Proceedings of the London Mathematical Society, 10, October 1878.
- [57] GREINER, ANDREAS and JOACHIM H. WENDORFF: *Elektrospinnen: eine faszinierende methode zur präparation ultradünnner fasern*. Angewandte Chemie, 119(30):5770–5805, July 2007.
- [58] HAGIWARA, KIYOHICO: *Process for manufacturing artificial silk and other filaments by applying electric current*. US1699615 A, 1929. US-Klassifikation 204/483, 264/178.00F, 204/553, 204/499; Internationale Klassifikation D01D5/06; Unternehmensklassifikation D01D5/0046; Europäische Klassifikation D01D5/00E2D4.
- [59] FORMHALS, ANTON: *Artificial thread and method of producing same*. US Patent 2349950, 1934.
- [60] FORMHALS, ANTON: *Process and apparatus for preparing artificial threads*. US Patent 2187306, 1940.
- [61] RENEKER, D. H. and I. CHUN: *Nanometre diameter fibres of polymer, produced by electrospinning*. Nanotechnology, 7(3):216–223, September 1996. WOS:A1996VL33100010.

- [62] RENEKER, DARRELL H., ALEXANDER L. YARIN, HAO FONG, and SUREEPORN KOOMBHONGSE: *Bending instability of electrically charged liquid jets of polymer solutions in electrospinning*. Journal of Applied Physics, 87(9):4531, 2000.
- [63] WUNDERLICH, B.: *Macromolecular Physics, Volume 1: Crystal Structure, Morphology, Defects*. Academic Press, 1973.
- [64] HUANG, ZHENG-MING, Y. Z. ZHANG, M. KOTAKI, and S. RAMAKRISHNA: *A review on polymer nanofibers by electrospinning and their applications in nanocomposites*. Composites Science and Technology, 63(15):2223–2253, November 2003.
- [65] ZUSSMAN, E., A. YARIN, and D. WEIHS: *A micro-aerodynamic decelerator based on permeable surfaces of nanofiber mats*. Experiments in Fluids, 33(2):315–320, August 2002.
- [66] DIAZ, JUAN ESTEBAN, ANTONIO BARRERO, MANUEL MARQUEZ, ALBERTO FERNANDEZ-NIEVES, and IGNACIO G. LOSCERTALES: *Absorption properties of microgel-PVP composite nanofibers made by electrospinning*. Macromolecular Rapid Communications, pages NA–NA, November 2009.
- [67] PIPERNO, SILVIA, LEVI A. GHEBER, PATRIZIA CANTON, ANDRIJ PICH, GITA DVO-RAKOVA, and ANDREA BIFFIS: *Microgel electrospinning: A novel tool for the fabrication of nanocomposite fibers*. Polymer, 50(26):6193–6197, December 2009.
- [68] FRIEDEMANN, KATHRIN, ANDREY TURSHATOV, KATHARINA LANDFESTER, and DANIEL CRESPI: *Characterization via two-color STED microscopy of nanostructured materials synthesized by colloid electrospinning*. Langmuir, 27(11):7132–7139, June 2011.
- [69] KEHREN, DOMINIC: *Herstellung und Charakterisierung Mikrogel-modifizierter Kompositfasern*. PhD thesis, RWTH Aachen, 2010.
- [70] KEHREN, DOMINIC and ANDRIJ PICH: *Fabrication and characterisation of Microgel/Polymer composite microfibrils*. Macromolecular Materials and Engineering, 298(12):1282–1293, 2013.
- [71] COOPERATION, PROMEGA: *CytoTox-ONE™ homogeneous membrane integrity assay*. <http://www.ebiotrade.com/buyf/productsf/Promega/tb306.pdf>, 2010.
- [72] SENFF, H. and W. RICHTER: *Temperature sensitive microgel suspensions: Colloidal phase behavior and rheology of soft spheres*. The Journal of Chemical Physics, 111(4):1705, 1999.

- [73] SENFF, H. and W. RICHTERING: *Influence of cross-link density on rheological properties of temperature-sensitive microgel suspensions*. Colloid & Polymer Science, 278(9):830–840, September 2000.
- [74] SAKURADA, I.: *Fasern aus polyvinylalkohol*. Kolloid-Zeitschrift and Zeitschrift Fur Polymere, 139(3):155–163, 1954.
- [75] KAWAKAMI, HIROSHI, NOBORU MORI, HIDESHI SATO, and AKIRA MIYOSHI: *X-ray studies on polyvinyl alcohol fiber*. Sen'i Gakkaishi, 16(3):155–162, 1960.
- [76] LEWIN, MENACHEM: *Handbook of Fiber Chemistry, Third Edition*. CRC Press, November 2006.
- [77] KANG, YUN OK, IN-SOO YOON, SO YOUNG LEE, DAE-DUK KIM, SEUNG JIN LEE, WON HO PARK, and SAMUEL M. HUDSON: *Chitosan-coated poly(vinyl alcohol) nanofibers for wound dressings*. Journal of Biomedical Materials Research Part B: Applied Biomaterials, 92B(2):568–576, 2010.
- [78] DING, BIN, HAK-YONG KIM, SE-CHUL LEE, CHANG-LU SHAO, DOUK-RAE LEE, SOO-JIN PARK, GYU-BEOM KWAG, and KYUNG-JU CHOI: *Preparation and characterization of a nanoscale poly(vinyl alcohol) fiber aggregate produced by an electrospinning method*. Journal of Polymer Science Part B: Polymer Physics, 40(13):1261–1268, 2002.
- [79] SAKURADA, I., NUKUSHINA, Y., and MORI, N.: *Determination of the degree of crystallinity of polyvinyl alcohol fibres with an x-ray counter*. Kobunshi Kagaku, 12:302–311, 1955.
- [80] NEMETHY, GEORGE and HAROLD A. SCHERAGA: *Structure of water and hydrophobic bonding in proteins. IV. the thermodynamic properties of liquid deuterium oxide*. The Journal of Chemical Physics, 41(3):680, 1964.
- [81] THEILER, STEFAN, STEFANOS E. DIAMANTOUROS, STEFAN JOCKENHOEVEL, HELMUT KEUL, and MARTIN MOELLER: *Synthesis and characterization of biodegradable polyester/polyether resins via michael-type addition*. Polymer Chemistry, 2(10):2273, 2011.
- [82] HARKINS, WILLIAM D. and GEORGE JURA: *Surfaces of solids. XII. an absolute method for the determination of the area of a finely divided crystalline solid*. Journal of the American Chemical Society, 66(8):1362–1366, August 1944.

- [83] HARKINS, WILLIAM D. and GEORGE JURA: *Surfaces of solids. XIII. a vapor adsorption method for the determination of the area of a solid without the assumption of a molecular area, and the areas occupied by nitrogen and other molecules on the surface of a solid.* Journal of the American Chemical Society, 66(8):1366–1373, August 1944.
- [84] DASH, TAPAN K. and V. BADIREENATH KONKIMALLA: *Poly-epsilon-caprolactone based formulations for drug delivery and tissue engineering: A review.* Journal of Controlled Release, 158(1):15–33, February 2012.
- [85] PITT, C. G., F. I. CHASALOW, Y. M. HIBIONADA, D. M. KLIMAS, and A. SCHINDLER: *Aliphatic polyesters. i. the degradation of poly(epsilon-caprolactone) in vivo.* Journal of Applied Polymer Science, 26(11):3779–3787, 1981.
- [86] LIU, L. J., S. M. LI, H. GARREAU, and M. VERT: *Selective enzymatic degradations of poly(l-lactide) and poly(epsilon-caprolactone) blend films.* Biomacromolecules, 1(3):350–359, 2000. WOS:000168755100010.
- [87] MA, M. L., Y. MAO, M. GUPTA, K. K. GLEASON, and G. C. RUTLEDGE: *Superhydrophobic fabrics produced by electrospinning and chemical vapor deposition.* Macromolecules, 38(23):9742–9748, November 2005. WOS:000233225600044.
- [88] HAN, NING, JED K. JOHNSON, PATRICK A. BRADLEY, KUNAL S. PARIKH, JOHN J. LANNUTTI, and JESSICA O. WINTER: *Cell attachment to hydrogel-electrospun fiber mat composite materials.* Journal of Functional Biomaterials, 3(4):497–513, July 2012.
- [89] KEHREN, DOMINIC, ASTRID CATALINA MOLANO LOPEZ, and ANDRIJ PICH: *Nanogel-modified polycaprolactone microfibres with controlled water uptake and degradability.* Polymer, 55(9):2153–2162, April 2014.
- [90] PICH, ANDRIJ, YAN LU, VOLODYMYR BOYKO, SVEN RICHTER, KARL-FRIEDRICH ARNDT, and HANS-JUERGEN P. ADLER: *Thermo-sensitive poly(n-vinylcaprolactam-co-acetoacetoxyethyl methacrylate) microgels. 3. incorporation of polypyrrole by selective microgel swelling in ethanol–water mixtures.* Polymer, 45(4):1079–1087, February 2004.
- [91] ANUFRIEVA, YV, MR RAMAZANOVA, VB LUSHCHIK, TN NEKRASOVA, TV SHEVELEVA, TM KARAPUTADZE, YE KIRSH, and MG KRAKOVYAK: *Intramolecular mobility of poly-n-vinyl amides in water and organic-solvents.* Vysokomolekul-yarnye Soedineniya Seriya B, 28(8):573–576, August 1986. WOS:A1986E239400006.
- [92] KIRSH, YE: *Water-soluble poly(n-vinylamides) - microstructure, solvation, conformational state and complex-formation in aqueous-solutions.* Progress in Polymer Science,

- 18(3):519–542, 1993. WOS:A1993LW22900004.
- [93] JEUN, JOON PYO, YOUN MOOK LIM, and YOUNG CHANG NHO: *Study on morphology of electrospun poly(caprolactone) nanofiber*. Journal of Industrial and Engineering Chemistry, 11(4):573–578, 2005.
- [94] NIKAM, PANDHARINATH S., BAPU S. JAGDALE, ARUN B. SAWANT, and MEHDI HASAN: *Densities and viscosities of binary mixtures of toluene with methanol, ethanol, propan-1-ol, butan-1-ol, pentan-1-ol, and 2-methylpropan-2-ol at (303.15, 308.15, 313.15) K*. Journal of Chemical & Engineering Data, 45(4):559–563, July 2000.
- [95] WANCHOO, R. K. and J. NARAYAN: *Excess properties of (methanol + toluene or p-xylene) binary liquid mixture*. Physics and Chemistry of Liquids, 25(1):15–26, 1992.
- [96] DEBORD, JUSTIN D. and L. ANDREW LYON: *Synthesis and characterization of pH-Responsive copolymer microgels with tunable volume phase transition temperatures*. Langmuir, 19(18):7662–7664, September 2003.
- [97] WANG, XIAOFENG, HAIBIN ZHAO, LIH-SHENG TURNG, and QIAN LI: *Crystalline morphology of electrospun poly(epsilon-caprolactone) (PCL) nanofibers*. Industrial & Engineering Chemistry Research, 52(13):4939–4949, April 2013.
- [98] WILLIAMSON, MATTHEW R. and ALLAN G.A. COOMBES: *Gravity spinning of polycaprolactone fibres for applications in tissue engineering*. Biomaterials, 25(3):459–465, February 2004.
- [99] SPANNUTH, MELISSA and JACINTA C. CONRAD: *Confinement-induced solidification of colloid-polymer depletion mixtures*. Physical Review Letters, 109(2):028301, July 2012.
- [100] MURTHY, N.: *Inaugural article: A macromolecular delivery vehicle for protein-based vaccines: Acid-degradable protein-loaded microgels*. Proceedings of the National Academy of Sciences, 100(9):4995–5000, April 2003.
- [101] DE GEEST, B. G., C. DEJUGNAT, G. B. SUKHORUKOV, K. BRAECKMANS, S. C. DE SMEDT, and J. DEMEESTER: *Self-rupturing microcapsules*. Advanced Materials, 17(19):2357–+, October 2005. WOS:000232625900014.
- [102] BROMBERG, L., M. TEMCHENKO, V. ALAKHOV, and T. A. HATTON: *Kinetics of swelling of polyether-modified poly(acrylic acid) microgels with permanent and degradable cross-links*. Langmuir, 21(4):1590–1598, February 2005. WOS:000226962100064.

- [103] KESSELMAN, LEAH R. B., SIAWASH SHINWARY, P. RAVI SELVAGANAPATHY, and TODD HOARE: *Synthesis of monodisperse, covalently cross-linked, degradable "Smart" microgels using microfluidics*. *Small*, 8(7):1092–1098, April 2012. WOS:000302471100020.
- [104] MALMSTEN, MARTIN: *Microgels in drug delivery*. In FERNANDEZ-NIEVES, ALBERTO, HANS M. WYSS, JOHAN MATTSSON, and DAVID A. WEITZ (editors): *Microgel Suspensions*, pages 375–405. Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, February 2011.
- [105] MALMSTEN, MARTIN: *Soft drug delivery systems*. *Soft Matter*, 2(9):760–769, August 2006.
- [106] OH, JUNG KWON, RAY DRUMRIGHT, DANIEL J. SIEGWART, and KRZYSZTOF MATYJASZEWSKI: *The development of microgels/nanogels for drug delivery applications*. *Progress in Polymer Science*, 33(4):448–477, April 2008. WOS:000255666400003.
- [107] SOPPIMATH, K. S., T. M. AMINABHAVI, A. M. DAVE, S. G. KUMBAR, and W. E. RUDZINSKI: *Stimulus-responsive "smart" hydrogels as novel drug delivery systems*. *Drug Development and Industrial Pharmacy*, 28(8):957–974, 2002. WOS:000178590400007.
- [108] OH, JUNG KWON, DO IK LEE, and JONG MYUNG PARK: *Biopolymer-based microgels/nanogels for drug delivery applications*. *Progress in Polymer Science*, 34(12):1261–1282, December 2009. WOS:000272129900001.
- [109] DINARVAND, R. and A. DEMANUELE: *The use of thermoresponsive hydrogels for on-off release of molecules*. *Journal of Controlled Release*, 36(3):221–227, October 1995. WOS:A1995TB21400004.
- [110] LOWE, T. L., J. VIRTANEN, and H. TENHU: *Interactions of drugs and spill probes with hydrophobically modified polyelectrolyte hydrogels based on n-isopropylacrylamide*. *Polymer*, 40(10):2595–2603, May 1999. WOS:000078290700014.
- [111] THEILER, STEFAN, MICHAEL TESKE, HELMUT KEUL, KATRIN STERNBERG, and MARTIN MÖLLER: *Synthesis, characterization and in vitro degradation of 3D-microstructured poly(epsilon-caprolactone) resins*. *Polymer Chemistry*, 1(8):1215, 2010.
- [112] THEILER, STEFAN, PETRA MELA, STEFANOS E. DIAMANTOUROS, STEFAN JOCKENHOEVEL, HELMUT KEUL, and MARTIN MÖLLER: *Fabrication of highly*

- porous scaffolds for tissue engineering based on star-shaped functional poly(epsilon-caprolactone)*. Biotechnology and Bioengineering, 108(3):694–703, March 2011.
- [113] BALACEANU, ANDREEA, DAN E. DEMCO, MARTIN MÖLLER, and ANDRIJ PICH: *Microgel heterogeneous morphology reflected in temperature-induced volume transition and 1H high-resolution transverse relaxation NMR. the case of poly(n-vinylcaprolactam) microgel*. Macromolecules, 44(7):2161–2169, April 2011.
- [114] YI, FANGPING and SIXUN ZHENG: *Effect of hydrophobic polystyrene microphases on temperature-responsive behavior of poly(n-isopropylacrylamide) hydrogels*. Polymer, 50(2):670–678, January 2009.
- [115] MU, JIANGFENG and SIXUN ZHENG: *Poly(n-isopropylacrylamide) nanocrosslinked by polyhedral oligomeric silsesquioxane: temperature-responsive behavior of hydrogels*. Journal of colloid and interface science, 307(2):377–385, March 2007. PMID: 17196603.
- [116] AGRAWAL, GARIMA, JINGBO WANG, BERIT BRÜSTER, XIAOMIN ZHU, MARTIN MÖLLER, and ANDRIJ PICH: *Degradable microgels synthesized using reactive polyvinylalkoxysiloxanes as crosslinkers*. Soft Matter, 9(22):5380–5390, May 2013.
- [117] GHUGARE, SHIVKUMAR V., ESTER CHIESSI, BARBARA CERRONI, MARK T. F. TELLING, VICTORIA GARCÍA SAKAI, and GAIO PARADOSSI: *Biodegradable dextran based microgels: a study on network associated water diffusion and enzymatic degradation*. Soft Matter, 8(8):2494–2502, February 2012.
- [118] VAN THIENEN, T. G., B. LUCAS, F. M. FLESCHE, C. F. VAN NOSTRUM, J. DE-MEESTER, and S. C. DE SMEDT: *On the synthesis and characterization of biodegradable dextran nanogels with tunable degradation properties*. Macromolecules, 38(20):8503–8511, October 2005.
- [119] AVDEEF, A, C M BERGER, and C BROWNELL: *pH-metric solubility. 2: correlation between the acid-base titration and the saturation shake-flask solubility-pH methods*. Pharmaceutical research, 17(1):85–89, January 2000. PMID: 10714613.
- [120] YANG, YOU QIANG, LING SHAN ZHENG, XIN DONG GUO, YU QIAN, and LI JUAN ZHANG: *pH-Sensitive micelles self-assembled from amphiphilic copolymer brush for delivery of poorly water-soluble drugs*. Biomacromolecules, 12(1):116–122, January 2011.
- [121] WANG, LIN, DONGDONG CHEN, and JUNQI SUN: *Layer-by-layer deposition of polymeric microgel films on surgical sutures for loading and release of ibuprofen*. Lang-

- muir: the ACS journal of surfaces and colloids, 25(14):7990–7994, July 2009. PMID: 19326871.
- [122] QIU, XINGPING, STEFANO LEPORATTI, EDWIN DONATH, and HELMUTH MÖHWALD: *Studies on the drug release properties of polysaccharide multilayers encapsulated ibuprofen microparticles*. Langmuir, 17(17):5375–5380, August 2001.
- [123] LI, SUMING and STEPHEN MCCARTHY: *Further investigations on the hydrolytic degradation of poly (DL-lactide)*. Biomaterials, 20(1):35–44, January 1999.
- [124] HEIDEMANN, WOLFGANG, STEPHANIE JESCHKEIT, KURT RUFFIEUX, JÜRGEN HARTMUT FISCHER, MATHIAS WAGNER, G KRÜGER, ERICH WINTERMANTEL, and KLAUS LOUIS GERLACH: *Degradation of poly(d,l)lactide implants with or without addition of calciumphosphates in vivo*. Biomaterials, 22(17):2371–2381, September 2001.
- [125] HEIDEMANN, WOLFGANG, STEPHANIE JESCHKEIT-SCHUBBERT, KURT RUFFIEUX, JÜRGEN HARTMUT FISCHER, HEDDA JUNG, GERHARD KRUEGER, ERICH WINTERMANTEL, and KLAUS LOUIS GERLACH: *pH-stabilization of predegraded PDLLA by an admixture of water-soluble sodiumhydrogenphosphate—results of an in vitro- and in vivo-study*. Biomaterials, 23(17):3567–3574, September 2002.
- [126] SCHILLER, CARSTEN and MATTHIAS EPPLE: *Carbonated calcium phosphates are suitable pH-stabilising fillers for biodegradable polyesters*. Biomaterials, 24(12):2037–2043, May 2003.
- [127] GÖTZ, ANDREA: *Geladene Mikrogele als Träger für antimikrobielle Enzyme*. PhD thesis, RWTH Aachen, 2012.
- [128] KOEHLER, JENS, SEBASTIAN KUEHL, HELMUT KEUL, MARTIN MOELLER, and ANDRIJ PICH: *Synthesis and characterization of polyamine-based cyclophosphazene hybrid microspheres*. Journal of Polymer Science Part a-Polymer Chemistry, 52(4):527–536, February 2014. WOS:000329171900010.
- [129] OZAKI, MASATAKA, STANKA KRATOHVIL, and EGON MATIJEVIĆ: *Formation of monodispersed spindle-type hematite particles*. Journal of Colloid and Interface Science, 102(1):146–151, November 1984.
- [130] MATHEW, D., C. P. R. NAIR, and K. N. NINAN: *Phosphazene-triazine cyclomatrix network polymers: some aspects of synthesis, thermal- and flame-retardant characteristics*. Polymer International, 49(1):48–56, January 2000. WOS:000084755800005.

- [131] GLERIA, M. and R. DE JAEGER: *Polyphosphazenes: A review*. In MAJORAL, J. P. (editor): *New Aspects in Phosphorus Chemistry V*, volume 250, pages 165–251. Springer-Verlag Berlin, Berlin, 2005. WOS:000230596500006.
- [132] KILIANOVA, MARTINA, ROBERT PRUCEK, JAN FILIP, JAN KOLARIK, LIBOR KVITEK, ALES PANACEK, JIRI TUCEK, and RADEK ZBORIL: *Remarkable efficiency of ultrafine superparamagnetic iron(iii) oxide nanoparticles toward arsenate removal from aqueous environment*. Chemosphere, 93(11):2690–2697, November 2013.
- [133] MELIN, THOMAS and ROBERT RAUTENBACH: *Membranverfahren*. Springer London, Limited, January 2007.

Publications

published:

KEHREN, DOMINIC and ANDRIJ PICH: *Fabrication and characterisation of Microgel/Polymer composite fibres*. Macromolecular Materials and Engineering, 298(12):1282-1293, 2013.

KEHREN, DOMINIC, ASTRID CATALINA MOLANO LOPEZ, and ANDRIJ PICH: *Nanogel-modified polycaprolactone microfibres with controlled water uptake and degradability*. Polymer, 55(9):2153-2162, April 2014

in progress:

KEHREN, DOMINIC, FLORIAN STOERMANN, ASTRID CATALINA MOLANO LOPEZ, STEFAN THEILER, HELMUT KEUL, ANDRIJ PICH: *Multicompartment aqueous microgels with degradable hydrophobic domains*. in progress.