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DOCTORAL DISSERTATION

Development of Polymer Grafting Methodologies for Advanced Surface Engineering

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Many things are looked upon as quite impossible, until they have been actually effected.

Pliny the Elder

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List of Abbreviations

AA	acrylic acid
abs.	absolute
AETMAC	[2-(acryloyloxy)ethyl] trimethylammonium chloride
AIBN	azobis(isobutyronitril)
AFM	atomic force microscopy
AOI	angle of incidence
at%	atomic percent
ATRC	atom transfer radical coupling
ATRP	atom transfer radical polymerization
b	block
В	magnetic field
ВА	butyl acrylate
Вос	tert-butyloxycarbonyl
C ₁₁ -alkyl	<i>n</i> -undecyl
СМР	copper-mediated radical polymerization
со	copolymer
СТА	chain transfer agent
d	diameter
DAPA	3-(dimethylamino)propyl acrylate
DCM	dichloromethane
DLS	dynamic light scattering
DLW	direct laser writing
DMAP	4-(dimethylamino)pyridine

DMF	dimethyl formamide
DMPA	2,2-dimethoxy-2-phenylacetophenone
DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
DoPAT	2-(dodecylthiocarbonothioylthio)propionic acid
DP	degree of polymerization
Ð	dispersity
EDC	1-ethyl-3-(3-dimethylaminopropyl)carbodiimide
EGMA	ethylene glycol dimethacrylate
EHA	2-ethylhexyl acrylate
EPR	electron paramagnetic resonance
ESCP	enhanced spin capturing polymerization
ESI-MS	electrospray ionization mass spectrometry
ESR	electron spin resonance
EtOAc	ethyl acetate
EtOH	ethanol
FWHM	full width at half maximum
(GA)ATR-FTIR	(grazing angle) attenuated total reflection Fourier-
	transform infrared
GMA	glycidyl methacrylate
GPC	gel permeation chromatography
HEA	2-hydroxyethyl acrylate
HEMA	2-hydroxyethyl methacrylate
НМРА	N-2-hydroxypropyl methacrylamide
HPLC	high performance liquid chromatography
ICAR	initiators for continuous activator regeneration

IUPAC	International Union of Pure and Applied Chemistry
LED	light-emitting diode
M ²	beam propagation ratio
МА	methyl acrylate
MALDI	matrix-assisted laser desorption/ionization
МСТ	mercury cadmium telluride
Me ₆ TREN	tris(2-aminoethyl)amine
MeCN	acetonitrile
MeOEGA	oligo(ethylene glycol) methyl ether acrylate
MeOGEMA	oligo(ethylene glycol) methyl ether methacrylate
[M]	monomer concentration
MHKS	Mark-Houwink-Kuhn-Sakurada
MIP	molecularly imprinted polymer
ММА	methyl methacrylate
Mn	number-average molecular weight
M _w	weight-average molecular weight
nBA	n-butyl acrylate
NHS	N-hydroxysuccinimide
NIPAAm	N-isopropyl acrylamide
NMP	nitroxide-mediated polymerization
NMP2	photoinduced NMP
NMR	nuclear magnetic resonance
NMRC	nitrone-mediated radical coupling
NP	nanoparticle
OGEMA	oligo(ethylene glycol) methacrylate
p.a.	pro analysi

PBN	<i>N-tert-</i> butyl- <i>a-</i> phenylnitrone
PDI	polydispersity index, used for \mathcal{D} in the past
PEG	poly(ethylene glycol)
PET	photoinduced electron transfer
PFA	perfluoroalkoxy alkane
PGSE	pulsed-gradient spin echo
photoATRP	photoinduced ATRP
photoCMP	photoinduced CMP
photoNMP	photoinduced NMP
photoRDRP	photoinduced RDRP
PMDETA	N, N, N', N'', N''-pentamethyldiethylenetriamine
ppm	parts per million
рру	2-phenylpyridin
PS	polystyrene
PTFE	polytetrafluoroethylene
PTZ	10-phenylphenothiazine
RAFT	reversible addition fragmentation (chain) transfer
	(polymerization)
RDRP	reversible deactivation radical polymerization
RI	refractive index
Rq	roughness parameter
SAM	self-assembled monolayer
SEC	size exclusion chromatography
SET-LRP	single electron transfer living radical polymerization
SI	surface-initiated
SIMS	secondary ion mass spectrometry

SPMA	3-sulfopropyl methacrylate
STXM	scanning transmission X-ray microscopy
tBA	tert-butyl acrylate
tBMA	tert-butyl methacrylate
TEMPO	2,2,6,6-tetramethylpiperidinyloxyl
TEOS	tetraethoxysilane
TFEMA	2,2,2-trifluoroethyl methacrylate
TGA	thermogravimetric analysis
THF	tetrahydrofuran
ToF	time of flight
UV	ultraviolet light
VE	elution volume
wt%	weight percent
x	conversion
XPS	X-ray photoelectron spectroscopy
δ	chemical shift
ρ	density
σ	surface coverage
Τ	delay time
T _{pulse}	pulse duration

Chapter 1

Introduction



Parts of this chapter have been published in

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1.1 What is a polymer?

The word "polymer" finds its linguistic roots in the Greek words "*poly*" and "*meros*" which together mean "many parts". IUPAC defines a polymer as a macromolecule of which "a part, or the whole of the molecule has a high relative molecular mass and essentially comprises the multiple repetition of units derived, actually or conceptually, from molecules of low relative molecular mass".^[1] The bare existence of polymers remained controversial until the 1930s when Staudinger could convincingly demonstrate their existence via viscometry.^[2]

Natural polymers such as cellulose or DNA are essential for life on earth. The first synthetic polymer was a resin from phenol and formaldehyde and first patented in 1907 by Leo Baekeland who called it Bakelite.^[3-5] Nowadays, polymers are almost omnipresent and used in coatings, paint, insulation, construction, medical devices and many more. The versatility of polymers is also reflected in an annual production of more than 320 million tons worldwide and an annual turnover of more than 340 billion euros in Europe alone.^[6]

1.2 Classes of polymerization

There are two classes of polymerizations: step-growth polymerization and chaingrowth polymerization which itself is divided into uncontrolled chain-growth and living chain-growth polymerization. Each of them possesses a distinct evolution of molecular weight with conversion, depicted in **Figure 1.1**.

Step-growth polymerization proceeds via a cascade of dimerization reactions. Often triggered by a catalyst, monomers first form dimers, then tetramers and so on. In consequence, only at high conversions, actual polymers with high molecular weight are formed. This is the reason that impurities such as defects in chain end functionality easily suppress the formation of polymers. Nevertheless, stepgrowth polymerizations of endgroup-protected polymer precursors are very attractive thanks to their good processability and are, for example, used for construction foam. Prominent examples of step-growth polymerizations are most polycondensation reactions and polyadditions, resulting in polyesters, polycarbonates, polyurethanes.

In contrast to step-growth, uncontrolled chain-growth polymerization such as free radical polymerization reaches high molecular weights at lowest conversions. Chain-growth polymerizations usually employ monomers of rather low reactivity and therefore require an initiator or external activation such as heat or light. When activated, the initiator features a functionality of high reactivity that allows for addition of monomers upon which the reactive site is transferred to the new chain end. The individual growth of each chain is readily terminated once two growing chains meet each other or once the reactive site is transferred to



Figure 1.1. Molecular weight vs. conversion of uncontrolled chain-growth, living chaingrowth, and step-growth polymerization. Adapted from reference [7].

a present molecule, e.g. solvent, monomer or another polymer chain. All four stages – initiation, propagation, termination and chain transfer – happen simultaneously and the respective rate constants determine the outcome of the otherwise purely statistical process depending on the respective concentrations.

"Living" polymerization is a special type of chain-growth polymerization that "does not involve a termination step" (M. Szwarc) and therefore allows for the formation of block copolymers.^[8] Essential conditions for "living" polymerizations were early described by Flory: (1) there is no chain transfer or termination, (2) the reactivity of active terminal sites is the same throughout the polymerization and polymerization only occurs via these active sites, which are preserved in absence of monomer and therefore allow for block copolymer formation; and finally (3) all active sites must be introduced at the beginning of the reaction.^[9] Once these conditions are met, the chain length of the growing chains becomes a Poisson distribution that shifts linearly to higher molecular weights with increasing monomer conversion. Deviation from these strict conditions inevitably leads to a much broader distribution and since these deviations are present very often, already a dispersity D below 1.5 is considered as "controlled" since 1.5 is the minimum that can be reached in uncontrolled chain-growth polymerizations.^[9] Various polymerization methodologies meet the three requirements described above to a high extent, among which reversible deactivation radical polymerization presents probably the most versatile.[10-15]

1.3 Reversible deactivation radical polymerization

Reversible deactivation radical polymerization (RDRP) is one of the most intensively investigated fields in polymer science with nitroxide-mediated radical polymerization (NMP), atom transfer radical polymerization (ATRP), and reversible addition fragmentation chain transfer radical polymerization (RAFT) as its bestknown representatives. Further, iniferter polymerization has gained considerable attention, especially for surface grafting.

In contrast to living polymerization as defined by Szwarc, RDRP reduces irreversible transfer reactions to a negligible quantity and either reduces the termination rate (ATRP and NMP) or distributes the propagation probability over all chains (RAFT). Consequently, there are two types of control in RDRP: reversible termination and degenerative chain transfer.

Reversible termination offers control by significantly reducing the radical concentration. Since the termination rate is proportional to the second order of the radical concentration and the propagation rate only has a first order correlation, the termination rate is affected much more severely. Quasi-living behavior is obtained when reversible termination reduces the overall (irreversible) termination rate to a negligible quantity. In contrast to that, the degenerative chain transfer mechanism leaves the radical concentration untouched, but distributes the radical over a large number of growing chains. In consequence, propagation and termination events are also distributed, reducing the termination probability of every individual chain, yet keeping overall termination rate the same as in free radical polymerization. Quasi-living behavior is achieved when the growing chains strongly outnumber the dead chains.

After consumption of all present monomers, reversibly terminated chains and built-in chain transfer agent are preserved and therefore allow for block copolymerization upon addition of another monomer or endgroup modification. The quasi-living behavior and a great tolerance towards other chemical functionalities make RDRP an ideal tool to access materials with complex function. Since recently, most RDRP protocols also exist as a photoinduced or photomediated version.^[16] PhotoRDRP allows for reactions at room temperature and therefore are more energy efficient. Next to this economic advantage, photoRDRP often features temporal control and allows for direct patterning of surfaces (1.4 Photoinduced RDRP for surface modifications). However, photoRDRP's efficiency is strongly depending on the optical path lengths, requiring special set-ups for optimized reaction conditions.

1.3.1 Nitroxide-mediated polymerization

Nitroxide-mediated polymerization effectively suppresses termination reactions via an equilibrium of a thermolabile alkoxyamine – the NMP initiator – and its corresponding thermolysis products – i.e. a nitroxide radical and a carbon-centered radical (**Scheme 1.1**).^[17]



Scheme 1.1. Nitroxide-mediated polymerization. Growing chains are predominantly present in dormant state (left), whereas active growing chains periodically undergo short phases of free radical polymerization before they are recaptured by the present nitroxide (right).

This equilibrium lays completely on the side of the alkoxyamine at room temperature. At elevated temperatures, the alkoxyamine reversibly dissociates into a nitroxide and a carbon-centered radical. The carbon-centered radical then undergoes propagation – so in principle a short free radical polymerization – before it is recaptured by the present nitroxide. Addition of excess nitroxide therefore leads to better control as it further shortens the free radical phase, yet also slows down the reaction.

As the equilibrium in NMP is strongly dependent on the stability of both formed radicals, first successful examples of NMP have been reported for styrene. Only later on, alkoxyamines suitable for acrylates and – in the presence of small amounts of styrene – also methacrylates have been reported. Nowadays, NMP-initiators for a broad range of monomers exist, yet at limited commercial availability and often at very high prices.

Recently, photoinduced NMP, also called NMP2, has been reported. In photoNMP, photosensitive alkoxyamines have to favor dissociation of the carbon-oxygen bond over the normally preferred dissociation of the nitrogen-oxygen bond upon exposure to UV light. Next to this prerequisite, photoNMP follows the same mechanism as thermal NMP.

1.3.2 Atom transfer radical polymerization

In atom transfer radical polymerization (ATRP), control is achieved via suppression of termination reactions by reduction of the free radical concentration via a redox equilibrium (**Scheme 1.2**).^[18]

A radical precursor P_n -X – called dormant species where X often is an alkyl halide – is reduced by a transition metal complex Mt^{m+}/L – the activator – to give the



Scheme 1.2. Atom transfer radical polymerization is controlled by a redox equilibrium.

free radical P_n and the respective oxidized transition metal complex X-Mt^{(m+1)+}/L, also called deactivator. L typically denotes an amine ligand such as N, N, N', N'', N''pentamethyldiethylenetriamine (PMDETA) or tris[2-(dimethylamino)ethyl]amine (Me₆TREN). The formed radical P_n can then undergo propagation for a short amount of time before it is reversibly deactivated by the deactivator X-Mt^{(m+1)+}/L. During the propagation phase, termination reactions and transfer reactions can occur just as in normal free radical polymerization. However, the redox equilibrium is significantly shifted towards the dormant side, which is why only a few monomer additions happen during each free radical phase and the radical concentration is strongly reduced. Since termination reactions are proportional to the second order of the radical concentration and the propagation rate only has a first order correlation, termination is effectively diminished compared to propagation. As undesired consequence, however, ATRP reactions are much slower than the corresponding free radical reactions.

The most common version of ATRP is mediated by a copper catalyst. There has been some controversy about the mechanism of copper-mediated ATRP. There is strong evidence that copper(I) acts as activator in nonpolar solvents such as toluene. However, the fast disproportionation to copper(0) and copper(II) in polar solvents is the reason that many people are convinced that copper(0) is the actual activating species and therefore prefer the term single-electron transfer living radical polymerization (SET-LRP) or just copper-mediated radical polymerization (CMP). Besides copper, many other transition metals such as iron, nickel, osmium, rhodium and ruthenium have been reported, yet sometimes require other ligands such as phosphines.^[19] In general, ATRP is limited to monomers that do not react with the catalyst – thus the transition metal and its ligands. Therefore, coordinating nitrogen-containing or acidic monomers are very challenging to polymerize via thermal ATRP.

ATRP can also be conducted as photopolymerization (**Scheme 1.3**). In fact, the effect of light on classical copper-mediated ATRP was first mentioned in 2000.^[20] A strongly enhanced rate of polymerization was then observed under the influence of light; however, it took more than 10 years before this observation was further investigated.



Scheme 1.3. General reaction scheme for a photoATRP reaction with a copper(II) catalyst. In contrast to thermal CMP, the activating copper(0) or copper(I) species is formed in-situ from copper(II) salts upon exposure to light in the presence of an excess of amine ligand, often PMDETA^[21-24] or Me₆TREN.^[25, 26] A very broad variety of acrylate esters has been polymerized via photoCMP,^[24-36] even fluorinated monomers.^[37] A less diverse situation is found for methacrylates for which most studies focused on methyl methacrylate.^[21-25, 27, 35, 36, 38-43]

Figure 1.2 shows the results for the model polymerization of methyl acrylate with [MA]:[ethyl *a*-bromoisobutyrate]:[Me₆TREN]:[Cu^{II}Br₂] = 50:1:0.12:0.02 in DMSO (50%, v/v). Molecular weight M_n increased linearly with conversion and



Figure 1.2. (left) Molecular weight characteristics of the polymerization of methyl acrylate (MA) under UV ($\lambda_{max} \approx 360$ nm) irradiation with [MA]:[ethyl *a*-bromo-isobutyrate]:[Me₆TREN]:[Cu^{II}Br₂] = 50:1:0.12:0.02 in DMSO (50%, v/v). (right) MALDI-ToF-MS confirms high endgroup fidelity. (Reproduced from reference [25], with permission from the American Chemical Society.)

concomitantly the dispersity \mathcal{D} approached 1.05. Almost no deviation from the theoretic values was observed and reinforced by very high endgroup fidelity (right side of **Figure 1.2**). This excellent endgroup fidelity makes photoCMP very attractive for block copolymerization.^[28, 31, 32, 36, 44]

The molar ratio of copper(II) salt to ligand has significant impact on the polymerization and use of ligand in excess has been reported most frequently. However, good results were also obtained for equimolar ratios,^[23] yet very slow conversion rates and higher susceptibility to inhibition by oxygen were observed.^[35, 45] In fact, higher ligand to copper(II) molar ratios significantly speeded up the reaction and reduced the inhibition through oxygen such that degassing of monomer and solvent became unnecessary.^[35, 45]

The photoCMP mechanism was target of several investigations.^[24-26, 46] Generally, a reductive quenching cycle was proposed (**Scheme 1.4**). Reductive quenching proceeds via reduction of the photoexcited copper(II) species by some free amine ligand, which explains why equimolar ligand to copper(II) conditions only gave



Scheme 1.4. Reductive quenching cycle in photoCMP. (Adapted from reference [16], with permission from Elsevier.)

very slow polymerizations, if at all.^[26] Detailed mass spectrometry studies revealed that photochemical reduction of copper(II) by the free amine represents the major pathway for radical (re)generation. Direct photoactivation of the initiator and other processes were reported to have little impact.^[26, 46]

PhotoCMP has been successfully conducted for a variety of light sources with respect to wavelength and intensity. Besides an essential overlap of absorbance and emission spectra of complex and lamp, photoCMP is only induced when photons possess enough energy to induce a ligand to metal charge transfer.^[24] Consequently, no conversion was observed for green and red light or in complete absence of any light, while blue and ultraviolet light led to full conversion.^[24, 25] Interestingly, change of light intensity only had influence on conversion rate and inhibition period, yet not on the control over molecular characteristics.^[45]

One of the most important features of photoreactions is temporal control. Photomediated reactions such as [2+2] cycloadditions only work when exposed to light.^[47] Photoinduced reactions, however, only require light for the generation of a reactive species that actually triggers the reaction. Therefore, temporal



Figure 1.3. Assessment of temporal control for the polymerization of methyl acrylate with (left) six fold Me₆TREN excess to copper(II) (Reproduced from reference [25], with permission from the American Chemical Society.) and (right) the discrete copper complex $[Cu(Me_6TREN)(O_2CH)](ClO_4)]$. (Reproduced from reference [34], with permission from the Royal Society of Chemistry.)

control in photoinduced reactions is determined by the lifetime of the reactive species and generally assessed via intermittent light-dark cycles for alternating periods. Typical behavior of photoCMP in such experiment can be seen on the left side of **Figure 1.3**. High conversion rates are observed whenever exposed to light, yet in the dark, the conversion rate does not drop to zero.^[23-26, 31, 32, 48] In contrast, the right side of **Figure 1.3** depicts the thus far only example of perfect temporal control of photoCMP.^[34] Instead of a Cu(II) bromide with six fold excess of Me₆TREN ligand, the discrete complex [Cu(Me₆TREN)(O₂CH)](ClO₄)] was employed that further was stable over more than 6 months in a non-degassed vial exposed to visible light.

In our group, photoCMP was investigated for single-unit insertion reactions to target short protein-mimicking polymer chains.^[49] Also multiblock copolymerization in batch was investigated (**Figure 1.4**).^[31] Further, photoCMP was successfully employed in flow.^[48, 50] Acrylates and methacrylates and



Figure 1.4. Molecular weight distributions of the intermediate block copolymer products in the synthesis of decablock copolymers from sequential monomer addition of acrylates. (Reproduced from reference [31], with permission from the American Chemical Society.)

their block copolymers have been reported.^[36, 44] Moreover, multiblock star polymers were created^[44] and finally, photoCMP was employed for surface modification (Chapter 2 and 3).

Next to copper, a variety of transition metals is used in photoATRP of which iridium and iron have received most attention over the past recent years. Iridiumcatalysts, especially fac-[Ir(ppy)₃], have been used for the polymerization of various methacrylates^[51-53] including 2,2,2-trifluoroethyl methacrylate^[54] and even methacrylic acid^[51] under visible light. Acrylates were also polymerized, yet control was readily lost for acrylic acid of which only copolymerization with low acrylic acid content could be realized with low dispersities.^[55]

Iron's natural abundance, low toxicity and cheap price give it an exposed role among the transition metals.^[56] Iron-mediated photoATRP has been successfully carried out for a variety of methacrylates^[57-61]. A remarkable evolution has taken place for iron-mediated photoATRP going from photoinduced ICAR ATRP towards ligand- and initiator-free photoATRP that uses the oxidized monomer as initiator (**Scheme 1.5**).^[61] The oxidized monomer features two bromine groups of which only one acts as initiator for the ATRP process. However, only around 40% of FeBr₃ were converted into FeBr₂ and 2,3-dibromoisobutyrate initiator and more importantly, tailing in chain extension reactions was more pronounced than in comparable reactions. Nevertheless, this very simple and cheap protocol represents an important step towards larger scale production of well-defined polymers.

Organocatalyzed, metal-free ATRP is a current trend in photoATRP that circumvents the limitations of metal-mediated ATRP. Among other photoredox catalysts, 10-phenylphenothiazine (PTZ) was used in photoRDRP of methacrylates^[62, 63] and acrylonitrile,^[64] resulting in good control over molecular weight and narrow dispersities. A linear increase of molecular weight $M_{n, NMR}$ with conversion was found and excellent temporal control for several subsequent on-off irradiation cycles. Given the absence of a copper catalyst, even (dimethylamino)ethyl methacrylate^[62] and methacrylic acid^[63] were successfully polymerized with good dispersities. Chain extension experiments further underpinned the controlled nature of PTZ-catalyzed metal-free ATRP.^[62]



Scheme 1.5. Photoinduced Fe-mediated ATRP of methacrylates in the presence of only monomer and catalyst. (Reproduced from reference [61], with permission from the American Chemical Society.)

1.3.3 Iniferter polymerization

Iniferter is one of the oldest RDRP techniques. The term "iniferter" is derived from *ini*tiator-trans*fer* agent-*ter*minator, describing already the core of the control mechanism.^[65] When exposed to light or higher temperatures, iniferter agents homolytically dissociate into carbon- and sulfur-centered radicals and initiate a polymerization, yet also reversibly endcap growing chains. This process is similar to the persistent radical effect of ATRP and NMP. Simultaneously, chain ends are susceptible to degenerative chain transfer reactions like in reversible addition fragmentation chain transfer (Section 1.3.4). *N*,*N*-diethyldithiocarbamates are very typical (photo)iniferter agents and various vinyl monomers including styrene, methyl methacrylate, and methyl acrylate were successfully polymerized.^[66-68] Even though mechanistically more related to NMP, iniferter agents are closely related to RAFT agents or can actually be employed as such.

1.3.4 Reversible addition fragmentation chain transfer polymerization

Reversible addition fragmentation chain transfer (RAFT) polymerizations use a degenerative chain transfer agent (CTA) that allows for a rapid equilibrium between active and dormant chains. The high ratio of growing chains versus dying chains is obtained via two fast equilibria – called pre- and main equilibrium (**Scheme 1.6**). Both equilibria are very similar with the difference that initial, polymer-free RAFT agent takes part in the pre-equilibrium, whereas the main equilibrium already includes the RAFT agent with a polymer chain. The choice of CTA is strongly depending on the used monomer. Typically, CTAs possess a thiocarbonyl thio group with a stabilizing group Z and a leaving group R as substituents. Common CTAs are trithiocarbonates, which are best suited for



Scheme 1.6. RAFT mechanism: a) pre-equilibrium and b) main equilibrium.

acrylates and styrene, dithiobenzoates, which work well especially for methacrylates, and dithiocarbamates that work for very reactive monomers such as vinyl esters and amides. A wide range of (meth)acrylates can be covered with switchable CTAs.

Effectively, the radical is shared among a large number of growing chains during its lifetime, and hence propagation and termination are shared. Since termination is not suppressed, a continuous radical supply is necessary, e.g. by a thermal initiator such as AIBN. In contrast to ATRP and NMP, RAFT allows for acidic functionalities such as in (meth)acrylic acid.^[69-71]

PhotoRAFT exists in several versions. First, with the use of a photoinitiator, photoRAFT is directly accessible as long as the RAFT agent itself does not absorb light in the same range as the photoinitiator. Often, no complete separation of absorption ranges can be realized, due to which a balanced selection of photoinitiator and RAFT agent has to be made. Loss of control has been observed for longer reaction times which led to discoloring of the solution and hence loss of controlling RAFT agent.^[72] The use of blue-shifted trithiocarbonates results in low decomposition rates and therefore good control even at high conversion.^[73] Second, similar to photoiniferter, photoRAFT can also be conducted without

additional photoinitiator.^[72] Here it is, however, essential that iniferter-like initiation via decomposition of the photoRAFT agent is sufficiently slow to not disturb the RAFT equilibrium.^[16] Third, photoelectron-transfer (PET)-RAFT employs a photosensitizer that activates the RAFT agent and therefore allows for polymerization. Porphyrins,^[74] tertiary amines,^[75] Eosin Y,^[76] and other photosensitizers^[77-80] have been reported.

1.4 Photoinduced RDRP for surface modifications

The need for polymer-patterned surfaces has been growing over the past twenty years as interactions between two materials are largely determined by their surface characteristics.^[81] Polymer brushes on surfaces often allow for good control over optical and mechanical surface properties and are usually obtained via two pathways: Grafting-from or grafting-to approaches.^[82] Grafting-to reactions proceed via efficient conjugation reactions and attach the preformed polymer on the surface, which leads to lower grafting densities due to sterical hindrance.^[83-85] The employed polymers can be synthesized in solution and therefore excellent control over the grafted material can be obtained. Grafting-from reactions build the polymeric structures from the surface and allow for good control over film thickness, composition and architecture while concomitantly yielding high grafting densities.^[86] However, surface-initiated polymerization kinetics can differ from solution-based reactions^[87] and with the inherently more challenging characterization, grafting-from usually leads to less defined polymer structures.

Precise control over chain length, dispersity and chemical functionalities is an essential but not sufficient feature to obtain well-defined polymer patterns. Spatial control on flat substrates can be realized via various techniques:^[88] microcontact

printing,^[89] dip pen^[90] and polymer pen lithography,^[91, 92] lithography with photomask and resist,^[93]or light-induced reactions^[16] to only mention a few. Light-induced reactions are especially interesting thanks to simple procedures and good scalability.

Combining good control over material properties and spatial control via the use of light, photoRDRP has become a powerful tool for surface engineering.^[16] Photopolymerizations can be used to directly grow polymer brushes in specific patterns following RDRP protocols. Linearly increasing film thickness with reaction time, reinitiation and block copolymer formation are typical characteristics of RDRP reactions on surfaces.

1.4.1 PhotoATRP for surface modifications

The first reported copper-mediated photoATRP for surface-initiated polymerization used TiO₂ as photosensitizer.^[94] Various hydrophilic, or even ionic, methacrylates such as (oligo(ethylene glycol) methyl ether) methacrylate (MeOGEMA), *N*-isopropyl acrylamide (NIPAAm) and 3-sulfopropyl methacrylate (SPMA) were



Figure 1.5. PhotoATRP grafting of 3-sulfopropyl methacrylate from thiol-patterned gold substrate. (A) Film thickness vs. time evolution at different light intensities in comparison with conventional ATRP. (B) Comparison of film thicknesses for various light intensities for exposure times of 20 and 30 min. (C) Evolution of film thickness with TiO₂ particle concentration at 1.25 mW·cm⁻² illumination for 20 min. (Reproduced from reference [94] with permission from the American Chemical Society.)

grafted from a flat gold substrate or titanium nanowires with water-methanol mixtures as solvent at low light intensities. Poly(methyl acrylate) films grew linearly with time and reached more than 200 nm in thickness (**Figure 1.5**). Increased thicknesses were found with increased light intensities, whereas the TiO₂ concentration has no influence once a certain level was exceeded.

Polymer brush patterns were generated via combination of microcontact printing and photoATRP.^[94] More recently, TiO₂ particles were imprinted with a dye, yielding faster reactions.^[95] Remarkable nanoscale-resolved patterns were generated with anodized aluminum oxide as a photomask. Recently, the grafting from a nanocomposite of TiO₂ and reduced graphene oxide as photosensitizer was reported in combination with tetrasulfonated copper phthalocyanine.^[40] The resulting PMMA brushes were cleaved in a saponification reaction over 7 days and showed a dispersity of around 1.3 and $M_n = 25000 \text{ g} \cdot \text{mol}^{-1}$.^[40]

The first photoCMP grafting without photosensitizer was described for methyl methacrylate (MMA) from silicon substrates.^[42] Successful block copolymer formation with *t*-butyl methacrylate (tBMA) and micropatterning indicated the controlled nature of the initial grafting-from polymerization and exemplified the full potential of photoATRP grafting. Photosensitizer-free photoCMP of acrylates was first reported to graft methyl acrylate from cellulose substrates.^[96] PhotoCMP grafting of various acrylates from silicon substrates was investigated (Chapter 2).^[97] *N*-2-hydroxypropyl methacrylamide (HMPA) and a broad variety of methacrylates was grafted from silicon substrate under photoCMP conditions.^[98]

Besides Cu- and Ir-based catalysts, Fe^[60] and Mn-mediated^[100] photoATRP grafting protocols were also reported. MMA, oligo(ethylene glycol) methacrylate



Figure 1.6. (A) Optical micrograph and (B) AMF image of nanoscale-inclined plane formed from polymer brushes upon light exposure through a shadow mask with optical density gradient. (C) Height along dashed line across feature as shown in (A). (Reproduced from reference [101], with permission from Wiley.)

(OEGMA) and various fluorinated methacrylates were polymerized via Ir-mediated photoATRP and yielded film thicknesses between 60 and 120 nm within one-hour brush polymerization time (**Figure 1.6**).^[101, 102] Ionic monomers such as 2-methacryloyloxyethyl phosphorylcholine and sulfobetaine methacrylate formed only very thin layers, even with trifluoroethanol as co-solvent.^[102] The linear relationship between irradiation time, light intensity and film thickness and performed chain extension reactions confirmed the controlled nature of the reported grafting-from procedures.^[101, 102]

This gave a direct access to 3D architectures on the surface via use of photomasks with areas of different optical densities.^[101] Due to short diffusion path lengths of the excited Ir-catalyst species, patterns with µm resolution were readily accessible. On-off experiments confirmed good temporal control.

The sequential use of Ir-mediated photoATRP with thermal Cu-mediated ATRP gave access also to ionic monomers.^[102] The generated micron-scale patterns were investigated with optical microscopy, scanning transmission X-ray microscopy (STXM) and secondary ion mass spectrometry (SIMS). Ir-mediated photoATRP was also reported for the modification of membranes with antifouling
polymers such as poly(2-hydroxyethyl methacrylate) (polyHEMA), poly(glycidyl methacrylate) (polyGMA) and polyOEGMA.^[103]

Recently, a visible-light mediated phenothiazine-catalyzed metal-free ATRP was extended to fabricate well-defined polymer brushes from flat, curved surfaces and particle surfaces.^[104] Single-layer patterns, gradient structures as well as block copolymer architectures could be readily obtained under irradiation from compact fluorescent lamps and natural sunlight. A linear relationship between brush height and irradiation time was observed, confirming the "living" nature of the whole process. Moreover, chain-extension of a uniform PMMA brush (~30 nm) with 2,2,2-trifluoroethyl methacrylate (TFEMA) increased the brush thickness by 26 nm, indicating a good retention of active chain ends. In a following work, 2-bromo-2-phenylacetate based tetherable initiators were prepared and gave better initiation efficiency and performance in 10-phenylphenothiazine-catalyzed metal-free surface-initiated-ATRP.^[105]

1.4.2 Photoiniferter and photoRAFT for surface modifications

The first photoiniferter grafting methodology was reported in 1996.^[106] Various monomers such as MMA, styrene and dimethylaminopropyl acrylamide were grafted from polymer substrates armed with 30 mol% diethyldithiocarbamate functionalities. Triblock copolymers were grafted in a controlled manner, visualized via fluorescence microscopy after staining, and film thicknesses up to 420 nm were reached.^[106] Photomask and neutral-density filters were employed to generate complex 3D structures, **Figure 1.7**.^[106, 107] More elaborated patterns with polymer grafting including formation of a gradient in film thicknesses were generated with x-y-adjustable photomasks.^[108] Further, a methodology for the generation of 2D and 3D patterned polymer substrates was developed.^[109-111]

Patterns of second^[110] or even third^[111] generation hyperbranched brushes on glass slides were prepared from poly(*p*-chloromethylstyrene) brushes functionalized with additional iniferter initiators (**Figure 1.7**).

The investigation of the kinetics of photoiniferter surface grafting showed a linear evolution of film thickness with time only for short reaction times, followed by a decrease in polymerization rate indicating the presence of termination events.^[112] This behavior is expected for any surface-initiated RDRP.^[113] The addition of a diethyldithiocarbamate functionality was suggested to suppress chain transfer events and to improve the polymerization control.^[114-116] The effect of diethyldithiocarbamates on the grafting kinetics was investigated^[117] and the reinitiation ability dependence of the concentration of the diethyldithiocarbamate tetraethylthiuram disulfide was modeled in a subsequent study.^[118] Furthermore, it was suggested that an increase in the concentration of deactivating species could improve the livingness.^[112]



Figure 1.7. (left) Fluorescence micrograph of photoiniferter grafting by UV irradiation through a stripe-patterned projection metal mask and a neutral-density filter and subsequently stained with rose bengal, and the three-dimensional image (b) of the distribution of the fluorescence intensity in the area shown in (a). (Reproduced from reference [106], with permission from the American Chemical Society.) (right) Schematic drawing of first generation to n-th generation graft architectures. (Reproduced from reference [111], with permission from the American Chemical Society.)

Hydrophilic,^[119, 120] ionic,^[121] and carboxybetaine^[122-126] monomers were employed for the preparation of antifouling coatings on gold, polymers and silicon substrates via photoiniferter grafting-from reactions. The combination of short poly(carboxybetaine) brushes with long brushes for specific protein antibody binding enabled access to antifouling films with concomitantly good binding characteristics for the desired protein.^[124-126]

Recently, initiator-free photoRAFT was employed to graft PMA brushes from crosslinked poly((ethylene glycol) diacrylate) particles.^[127] An initiation efficiency of 95% was determined for the embedded trithiocarbonate RAFT agent. No additional photoinitiator was used since radicals were directly generated from the transfer agent 2-(((butylthio)carbonothiolyl)thio)propanoic acid upon exposure to blue LED-light. PhotoRAFT was employed to graft poly(acrylic acid) (PAA)^[128, 129] and PHEMA^[130] from polypropylene microporous membranes, although only a few repeating units were attached in the presence of chain transfer agent in solution. Subsequently, a PNIPAAm block was grafted via thermal RAFT to yield block copolymers.^[128, 130] Further control experiments were not performed. These modifications of the membrane were conducted by initially exposing the surface to high power UV light in the presence of benzophenone, which subsequently formed surface-bound semipinacol radicals to initiate the polymerization in the presence of a chain transfer agent.

The potential of photoRAFT for the production of molecularly imprinted polymers (MIP)-SiO₂ composite beads was demonstrated.^[131] Photoiniferter and photoRAFT, activated with a surface-bound azoinitiator in the presence of a RAFT agent, were compared. PhotoRAFT and photoiniferter surface functionalization were carried out at 15 °C. L-Phenylalanine anilide was imprinted on a poly(MAA-

23

co-EGMA) matrix. A loss of sulfur concentration was observed for both systems, indicating a loss of control potentially due to recombination events. However, the same result was found in an earlier study where photoiniferter was reported to allow successful formation of various layers.^[132] In contrast to a photoiniferter procedure, the photoRAFT system maintained the pore size distribution of the original silica particles.^[131] Furthermore, particles modified with the photoRAFT featured a more homogenous polymer film. With respect to enantioselectivity and retention in column chromatography, photoRAFT surface functionalization was superior to photoiniferter grafting. Silica particles functionalized via photoiniferter grafting were not able to separate racemic mixtures of phenylalanine anilide, whereas the respective particles, after photoRAFT grafting, featured good separation for film thicknesses beyond 1 nm, which was attributed to the formation of more homogenous films. Retention factor and enantioselectivity were linearly dependent on the graft density for photoRAFT, in contrast to the results of photoiniferter grafting-from reactions where a bell shaped curve was observed.

1.4.3 PhotoNMP for surface modifications

The development of novel photosensitive alkoxyamines extended the use of NMP processes to many applications such as photolithography, microfluidics, data storage devices, 3D-printing, biochips, etc. For example, a homogeneous acrylate-based multilayered film with a thickness close to 50 nm and a good spatial resolution could be prepared by using photosensitive alkoxyamines.^[133] The living character of photoinduced NMP enabled reinitiation of the polymerization producing multi-layered objects with nanometric scale thickness. The photoinduced NMP process was also proposed and developed for fabrication of functional micropatterns complex with structures such as hydrophilic/hydrophobic or luminescent surfaces simply by using a mask ($\ensuremath{\textit{Figure}}$

1.8).^[134]



Figure 1.8. Schematic representation of fabrication of micropatterned films via photomediated NMP processes by combination of homogeneous and local irradiations. (Reproduced from reference [16], with permission from Elsevier.)

1.4.4 Direct laser writing

Three dimensional printing is one of the current trends in materials science.^[135] Stereolithography and direct laser writing (DLW) allow for manufacturing of µm-resolved surfaces.^[136] These techniques are based on very fast photoinitiation and crosslinking monomers such as multiacrylates or epoxy-based photoresists.^[136] Stepping further towards truly functional structures, direct laser writing (DLW) with photoinduced controlled radical polymerization was first reported for photomediated NMP.^[133] Line widths of 1.5 µm were achieved with a 375 nm laser (16 mW) and an inverted microscope objective with piezoelectronically positioned sample. Polymeric microstructures of up to 2 µm height were grafted from the surface of a crosslinked polymer film featuring suitable alkoxyamine groups with only 30 ms irradiation time. The structure height was proportional to the irradiation time for the first 10 ms. Recently, microstructure grafting via direct laser writing on Ir-mediated photoATRP was reported (**Figure 1.9**).^[138]



Figure 1.9. Direct laser writing with Ir-mediated photoATRP using a Nd:YAG microlaser (523 nm, 0.6 ns) with a ×40-microscope objective. (left) Control of line height with laser power of 5 ms irradiation. (right) Logo created with 130 μ W, 10 ms. (Reproduced from reference [138], with permission from the Royal Society of Chemistry.)

An almost linear dependence of the structure height on the power of the employed Nd:YAG microlaser (532 nm) was reported. In contrast to photomediated NMP, Ir-mediated photoATRP was reported for significantly higher laser powers and structure heights were limited to less than 350 nm.

1.5 Conjugation techniques

Since the introduction of the 'click chemistry' concept by Sharpless in 2001,^[139] modular approaches for molecular design have received significant attention.^[140, 141] To allow for efficient conjugation reactions with 'click' characteristics, Sharpless and colleagues proposed a set of criteria that has later been expanded towards a use in polymer chemistry (**Scheme 1.7**).^[139, 142] Figuratively, Sharpless and colleagues described 'click' reactions a "*'spring-loaded' single [reaction] trajectory*". In this term, orthogonality, chemoselectivity, fast time-scale, and high yields combined. Further criteria are a modular nature, wide in scope, stable products and simple, non-chromatographic purification. In polymer science, simple (large-scale) purification is basically limited to selective precipitation and evaporation of volatile compounds. Therefore, the 'click' requirements are stricter and extended to equimolarity, which is especially important for modular approaches that do not allow for any purification method.



Scheme 1.7. The 'click' criteria by Sharpless and colleagues (blue) and their necessary extension (green) to deal with the very limited purification methods in polymer science. (Reproduced from reference [142] with permission from Wiley.)

1.5.1 Nitrone-mediated radical coupling

Nitrones received most attention in synthetic organic chemistry for their use in [2+3] cycloadditions^[143-145] and as radical spin-traps,^[146-148] yet only little in the context of polymer chemistry.^[149] Initially nitrones were assessed as control agents in enhanced spin capturing polymerization^[150-153] and further as coupling reagent in nitrone-mediated radical coupling (NMRC; **Scheme 1.8**) that allows for the introduction of a new mid-chain alkoxyamine functionality,^[154, 155] e.g. to construct dendrimers,^[156] star polymers,^[157] and other architectures.^[158, 159] More recently, NMRC has also been used to couple polymers derived from reverse iodine-transfer polymerization, further underpinning that any precursor of non-persistent radicals can be employed.^[160] The closely connected nitroxide-mediated





radical coupling is essentially the second half of NMRC and consequently yields asymmetric products.^[161]

Similar to atom transfer radical coupling, ATRP-derived polymers can be directly employed for nitroxide radical coupling or nitrone-mediated radical coupling.^[161] Atom transfer radical coupling (ATRC) leads to the irreversible formation of a symmetric polymer via a carbon-carbon bond and is only well suited for polystyrene. In contrast, both nitroxide- and nitrone-mediated radical coupling result in an asymmetric and symmetric alkoxyamine, respectively, and function well with polyacrylates.^[161]

Additionally, nitrones give direct access to nitroxide radicals when the reaction is stopped after the addition of one radical (**Scheme 1.8**), making nitroxide-equipped particles directly accessible. The potential of such nitroxide-containing particles has recently been demonstrated for overcoming multidrug resistance in epidermoid cancers.^[162] The second addition is generally reversible at higher temperature and leads to the formation of an internal alkoxyamine (**Scheme 1.8**). In principle, the formed alkoxyamine allows for block copolymer formation via nitroxide-mediated polymerization if the formed nitroxide either does not possess

any proton in a-position to the nitrogen^[163, 164] or is sufficiently sterically hindered.^[165]

1.5.2 Thiol-ene reactions

The addition of a thiol group to an ene functionality is called thiol-ene reaction (**Scheme 1.9**).^[166] Thiol-ene reactions require the presence of a radical initiator or a catalyst, respectively.



Scheme 1.9. The addition of a thiol to an ene is called thiol-ene reaction.

Radical thiol-ene reactions are very commonly used in polymer science, yet they do not fulfill Sharpless' click criteria^[167] since side reactions can only be neglected at high concentrations which cannot be reached with polymers.^[168] Thermal and photoinitiators can be employed and even self-initiation via photodissociation is an option, yet significantly slower.

Radical thiol-ene reactions proceed via three steps: (1) initiation, (2) addition, and (3) transfer (**Scheme 1.10**).^[168] Initiation leads to the presence of thiyl radicals, which can subsequently add to an ene functionality. Finally, the formed carbon-centered radical abstracts a hydrogen atom from a thiol group to complete the reaction cycle. Radical-radical couplings are not part of the desired reaction, yet potential side reactions and are best avoided via low radical concentrations concomitantly with high thiol and ene concentrations. While high reactant concentrations lead to good coupling efficiencies, polymers in particular often have low limiting concentrations. Further, the bimolecular nature of the thiol-ene reactions disfavors the coupling reaction compared to unimolecular initiator



Scheme 1.10. Mechanism of radical thiol-ene reactions. Initiation of the thiol, either by light or a radical initiator, is followed by a repetitive addition-transfer cycle.^[168]

decomposition and quasi unimolecular transfer to solvent side reactions. In consequence, radical thiol-ene reactions are a great tool for synthetic organic chemistry of small molecules and when the quenching alkene can be used in high excess – e.g. for endgroup modification, yet usually falls far short from click characteristics for polymer-polymer conjugation.^[167] Exceptions were found for the very reactive endgroup norbornene with a redox catalyst such as ammonium persulfate as radical source.^[169] In this case, coupling efficiencies up to 91% were reported for the conjugation of two endgroup functionalized PEG polymers of 5000 g·mol⁻¹.

In contrast to radical thiol-ene reactions, catalyzed nucleophilic thiol-ene reactions require an electrophilic target such as a Michael-acceptor, yet otherwise follow the same three steps, i.e. initiation, addition, and transfer (**Scheme 1.11**). Common catalysts are trialkylphosphines or bases such as hexylamine.^[170] While the radical version does not show click characteristics, nucleophilic thiol-ene reactions are

quasi-orthogonal and therefore suited for step-growth polymerizations.^[171] Linear,^[172] branched,^[173] and crosslinked^[174] polymers have been realized.



Scheme 1.11. Nucleophile-mediated thiol-ene addition to a Michael system using a phosphine catalyst.^[170]

1.6 Aim and outline of research

Surface properties determine the interaction of two materials. Methodologies that allow for tunable surface properties consequently possess a high importance in materials science. With the rise of thermal reversible deactivation radical polymerizations such as ATRP, RAFT, or NMP, polymers with almost any desired architecture and composition have become accessible. However, these thermal techniques either lack spatial control on surface in 'grafting-from' approaches or require post-polymerization modification when employed in 'grafting-to' approaches. The main goal of the work presented in this thesis was to overcome these two constraints. The present doctoral thesis consequently targets the development of new methodologies for polymer grafting. Surface-initiated photoinduced copper-mediated radical polymerization of acrylate monomers from silicon substrates at extremely low copper concentrations is described in **Chapter 2** for conventional UV-B light sources and photomasks.

Chapter 3 translates the methodology of Chapter 2 into a mask-free 2Dphotolithography protocol that combines a pulsed excimer laser with a 2D galvo scanner.

With the grafting-to via nitrone-mediated radical coupling for flat silicon substrates and nanoparticles in **Chapter 4**, a grafting-to methodology that does not require post-polymerization modifications for polymers with bromine terminus is presented. Two different approaches are presented and subsequently discussed.

Furthermore, the (preliminary) results of two side projects are presented in Chapter 5 and 6. Both chapters are not directly linked to surfaces, yet show techniques that could have impact on future surface science applications.

Chapter 5 targets the synthesis of polyzwitterionic polymers via thiol-ene Michael addition of cysteinyl cysteine and diacrylates.

Conversion rates of radical thiol-ene reactions in milli- and microflow reactions are compared with respect to light intensities in **Chapter 6**.

Chapter 7 provides all relevant analytical and experimental procedures.

A summary and outlook are presented in Chapter 8.

All chapters are written in manuscript-style. Chapter 2 has been published. Chapter 3 and 4 have been submitted to peer-reviewed journals.

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Chapter 2

Surface Grafting via Photoinduced

Copper-Mediated Radical

Polymerization at Extremely Low

Catalyst Concentrations



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2.1 Abstract

Surface-initiated photoinduced copper-mediated radical polymerization was employed to graft a wide range of polyacrylate brushes from silicon substrates at extremely low catalyst concentrations. This is the first time the controlled nature of the reported process has been demonstrated via block copolymer formation and reinitiation experiments. In addition to unmatched copper catalyst concentrations in the range of few ppb, film thicknesses up to almost 1 µm were achieved within only one-hour illumination time.

2.2 Introduction

Polymer-patterned surfaces have received significant attention over the past twenty years as a tool to produce surfaces with complex functions.^[1] Well-defined structures can be directly attached to the surface in a 'grafting-to' approach, often achieved via ligation chemistry.^[2-4] Alternatively, increased grafting densities can be achieved via 'grafting-from' approaches which however may suffer from less control over the obtained surface properties due to confined spaces on the surface.^[5, 6]

Easy to conduct and with the widest range of usable monomers, reversible deactivation radical polymerization (RDRP) techniques represent the first choice for the generation of complex architectures on the surface.^[7] Each SI-RDRP has its distinct advantages and disadvantages: SI-CMP features surface-confined grafting and low reaction temperatures, whereas the use of copper in higher concentrations can be a disadvantage.

All methodologies have in common that the polymer layer thicknesses are usually limited by the reaction efficiency and layer thicknesses beyond 300 nm have been Surface Grafting via PhotoCMP at Extremely Low Catalyst Concentrations rarely reported.^[8, 9] In addition, sophisticated polymer patterns require more than control over the polymerization itself and spatial resolution on the substrate can only be achieved via techniques such as microcontact printing,^[10] dip pen^[11] and polymer pen^[12, 13] lithography, lithography using photomask and a resist,^[14, 15] or light-induced reactions.^[2-4, 16-19] The use of light is both readily accessible and scalable and photoinduced grafting is hence an ideal tool for advanced surface engineering.

Herein, we report the grafting of up to unmatched 950 nm thick polymer brushes from silicon wafers under direct photoCMP conditions for a broad range of acrylate monomers under the use of extremely low copper catalyst concentrations. The reported reactions were very efficient and concomitantly very fast, even with unmatched catalyst loadings of 0.0082 – 8.9 ppm Cu. Excellent control over the polymerization was achieved as underpinned by block copolymer brush formations and the ability to generate well-defined patterns on planar surfaces. The reduction of the copper concentration opens pathways to very economical light-triggered grafting procedures and permits the use of the grafted substrates for biomedical applications.

2.3 Results and discussion



Scheme 2.1. Surface-initiated photoCMP of acrylates.

The grafting of polymer brushes via photoCMP comprises a two-step process: the formation of a self-assembled monolayer of a suitable initiator, and the grafting of the polymer brushes. Both steps are equally important to ensure a stable, homogeneous surface after the grafting. The selected initiator 2-1 is a trichlorosilane, featuring an undecyl spacer ensuring an efficient formation of the self-assembled monolayer. Other initiators based on trialkoxysilanes have led to ill-defined SAMs with the concomitant detachment of large areas of brushes.^[8] Starting from the initiator layer, a variety of polyacrylates was grafted: methyl acrylate (MA), 2-hydroxyethyl acrylate (HEA), 3-(dimethylamino)propyl acrylate (DAPA), oligo(ethylene glycol) methyl ether acrylate (MeOEGA), n-butyl acrylate (nBA), 2-ethylhexyl acrylate (EHA), [2-(acryloyloxy)ethyl] trimethylammonium chloride (AETMAC), and t-butyl acrylate (tBA). Since acrylates were reported to work readily in photoCMP in solution, a controlled polymerization was also expected in the grafting-from process.^[20, 21] Grafting was achieved by immersing the surfaces in a solution of the acrylate monomer, copper dibromide and tris[2-(dimethylamino)ethyl] amine in dimethyl sulfoxide, followed by subsequent exposure to UV light irradiation at ambient temperature (Scheme 2.1).

The evolution of the film thickness versus time for surface-initiated photoCMP was utilized for the assessment of the control. *t*BA was chosen as a model monomer to study the polymerization. Various catalyst concentrations were investigated, the lowest being 8.2 ppb of Cu (10⁻⁵ mol% with respect to monomer), and thus well below initiators for continuous activator regeneration (ICAR) ATRP levels.^[22] A close-to-linear relation between film thickness and time – thus a constant rate – was observed in all cases for the first 30 min and partially longer for lowest catalyst concentrations (**Figure 2.1**).



Figure 2.1. Dry ellipsometric thickness of poly(*t*-butyl acrylate) brushes grafted from Si-substrate functionalized with 11-(trichlorosilyl)undecyl 2-bromo-2-methylpropanoate. Effect of Cu concentration. Black [Cu]₀ = 137 μ M (8.2 ppm), red [Cu]₀ = 13.7 μ M (0.82 ppm), blue [Cu]₀ = 1.37 μ M (82 ppb), brown [Cu]₀ = 0.137 μ M (8.2 ppb). [Me₆TREN]₀ = 6·[Cu]₀, [M]₀ = 1.40 M. The insert depicts a 5 x 5 μ m² AFM height image of 549±6 nm thick poly(*t*-butyl acrylate) brushes.

While a slight dependence of thickness evolution with the catalyst concentration might exist, it is a remarkable observation that very similar layer thicknesses were reached irrespective of the catalyst concentration. To date, no CMP process has been described with comparatively low catalyst amounts. In contrast, a reduction of the monomer concentration to one fifth led to an almost linear drop in film thickness over time.^[23]

Excluding either light, initiator or catalyst from the reaction system prevented any grafting reaction, evidencing that the grafting reaction did follow a photoCMP mechanism, highlighting the confinement of the polymerization to the surface.

The chemical and physicochemical properties of the brushes were assessed via dynamic water contact angle (**Table S2.1**), grazing angle attenuated total reflection Fourier-transform infrared (GAATR-FTIR) spectroscopy, X-ray photoelectron spectroscopy (XPS), and time of flight secondary ion mass spectrometry (ToF-SIMS). The C 1s XPS spectra of the grafted initiator and the grafted poly(*t*BA) are well in line with successful silanization and subsequent grafting.^[23] The identified carbon peak ratios correspond well to the particular carbon ratios in both the initiator and the poly(*t*BA) (**Figure 2.2**). It should be noted that the film thickness reached up to 750 nm within one-hour reaction time. The surface thickness was homogeneous as evidenced by the very low standard deviation of the thickness. Atomic force microscopy was used to test the homogeneity at the nanometer level (insert in **Figure 2.1**). The mean square roughness R_q of 549±6 nm thick poly(*t*BA) brushes was determined to be only 7.8±0.2 nm.

In the following, a range of acrylates was photografted (for monomers, see list above). From solution polymerization, it is known that the photoCMP process is most efficient for acrylate monomers. Methacrylates^[24] or (meth)acrylamides^[25] are, however, also in principle accessible.

The chemical composition of all polyacrylate brushes was assessed by XPS. The C 1s XPS spectra of all grafted polymer brushes are depicted in **Figure 2.2**. The peak at 285.0 eV is assigned to hydrocarbon (C–C, C–H), while the one at a separation of 3.9 eV (i.e. centered at 288.9 eV) is assigned to the COO moiety of the acrylate ester group. The presence of C–O moiety of ester and ether side chains, the C–N moiety of tertiary and quaternary amines, as well as the C–Br distal endgroup give rise to the contribution at about 286.5 eV.^[26]



Figure 2.2. Comparison of the C 1s XPS spectra: (A) after silanization with 11-(trichlorosilyl)undecyl 2-bromo-2-methylpropanoate, (B) poly(*t*-butyl acrylate), (C) poly(methyl acrylate), (D) poly(2-hydroxyethyl acrylate), (E) poly(3-(dimethylamino)propyl acrylate), (F) poly[oligo(ethylene glycol) methyl ether acrylate], (G) poly(*n*-butyl acrylate), (H) grafted poly{[2-(acryloyloxy)ethyl]trimethylammonium chloride}, and (I) poly(2-ethylhexyl acrylate). Peak heights have been normalized to maximum intensity. The measured XPS spectra (points) were fitted/deconvoluted (red curve) with 3 contributions centered at 285.0, 286.8, and 288.9 eV arising from the C–C and C–H (black curve), C–O (blue curve) and COO (green curve) moieties (**Table S2.3** for integration ratios).

The presence of the grafted initiator was confirmed by the presence of bromine and by the expected ratio of the peaks in the C 1s envelope. The close matching between the theoretical and the measured/fitted values within the contributions of the C 1s envelope further confirms the covalent structure of the polymer (Table **S2.3** for integration ratios). The poly(t-butyl acrylate) and poly(n-butyl acrylate) brushes were evidenced by the expected 1:1:5 ratio for their integrated C 1s peak intensities, matching well with the corresponding integrated O 1s intensities. The poly(methyl acrylate), poly(2-hydroxyethyl acrylate), same way, and poly(2-ethylhexyl acrylate) successfully confirmed. For were poly(3-(dimethylamino)propyl acrylate), the intensity of the C-O, C-N peak is underestimated, yet the present nitrogen and the atomic concentration ratios of O 1s, N 1s and C 1s signals evidence the successful grafting. The intense C-O signal accompanied with the close to 1:2 ratio of two remaining signals confirmed convincingly the presence of for poly[oligo(ethylene glycol) methyl ether acrylate] brushes. Both chlorine and nitrogen peaks together with a matching carbon and oxygen ratio successfully evidenced poly{[2-(acryloyloxy)ethyl] trimethylammonium chloride} brushes.

Additional ToF-SIMS^[23] (**Table S2.2**) and GAATR-FTIR (**Figure 2.3**) were performed to obtain more information about the chemical structure. All investigated polymer brushes showed an intense C=O stretching vibration band at around 1732 cm⁻¹ as well as intense bands at around 1160 cm⁻¹, 1270 cm⁻¹, and 1450 cm⁻¹ due to the C–O–C symmetric stretching vibration, the C–O–C asymmetric stretching vibration, and CH₂ scissoring, respectively. A weak band due to C–H stretching vibration was found at around 2950 cm⁻¹ that was shifted to 3024 cm⁻¹ in case of poly{[2-(acryloyloxy)ethyl]trimethylammonium chloride}.

poly{[2-(acryloyloxy)ethyl]trimethylammonium chloride} sample is well in line with the absorption of water in the polymer layer. The vibration band at 1481 cm⁻¹ indicates the asymmetric deformation vibration of *N*-bound CH₃. 2767 cm⁻¹ and 2819 cm⁻¹ represent symmetric C–H stretching vibrations of *N*-bound CH₃ in poly(3-(dimethylamino) propyl acrylate).



Figure 2.3. GAATR-FTIR spectra. (1) poly(*t*-butyl acrylate); (2) poly(2-hydroxyethyl acrylate); (3) poly(*n*-butyl acrylate); (4) poly(2-ethylhexyl acrylate); (5) poly([2-(acryloyloxy)ethyl]trimethylammonium chloride); (6) poly(3-(dimethylamino) propyl acrylate); (7) poly[oligo(ethylene glycol) methyl ether acrylate]; (8) poly(methyl acrylate).

For poly[oligo(ethylene glycol)methyl ether acrylate], the symmetric C–O–C stretching vibration of the ether functions overlaid the symmetric C–O–C stretching vibration of the ester group. At 2871 cm⁻¹ the intense vibration band was due to the C–H stretching vibration of the O–CH₂ groups in oligo(ethylene glycol) side chains and a very weak shoulder towards lower wavenumbers originating from the methoxy terminating group.

A marked change in the wettability of the films was observed for different brushes water.^[23] and corresponds well to their ability to bind or repel The film thickness evolution for each monomer over time is given in **Figure 2.4**. Within the first 30 min, the growth rate remained close to constant for each investigated monomers, reaching thicknesses unmatched by SI-ATRP.^[8] Typically, for thicknesses between 150 – 750 nm are reached within this time. Forlonger reaction times, a reduction in growth rate was observed. This decrease in grafting rate towards longer reaction times is also known from conventional SI-RDRP.^[9] Interestingly, less sterically demanding acrylates resulted in the formation of thinner films, whereas the more bulky polyEHA films grew not only faster compared to the other monomers, but also reached almost 1 µm brush thickness which is exceptionally large for an end-grafted polymer. In addition, the grafting of almost 0.5 µm thick films of ionic polyAETMAC underlines the versatility of photoCMP. In contrast to the extremely thick films found for poly(tBA), significantly thinner films were determined for poly(*n*BA). A possible explanation for this effect might be reduced termination rates due to less accessible radical centers as a result of higher excluded volume interactions. Such an assumption is well in line with the more linear film thickness evolution for bulky monomers, suggesting a constant grafting density along the grafting direction.



Figure 2.4. Dry ellipsometric thickness of various polyacrylate brushes grafted from Si-substrate functionalized with 11-(trichlorosilyl)undecyl 2-bromo-2-methylpropanoate using $[Cu]_0 = 137 \,\mu$ M, $[Me_6TREN]_0 = 862 \,\mu$ M and $[M]_0 = 1.40 \,\mu$ M in DMSO. (*carried out in trifluoroethanol ** carried out in DMSO : water (93 : 7))

DAPA showed no significant growth in pure DMSO after an initial layer of 20 nm had been formed, which may be explained by a loss of reaction efficiency due to amine-complexation of the catalyst to the graft itself. Replacing DMSO with trifluoroethanol, a solvent shown to be beneficial in SET-LRP,^[27] resulted in a more linear thickness evolution, yet also in this case only yielding thin brushes.

The good correlation between film growth and time for all monomers suggests the presence of a successful photoCMP process. Yet, at this stage, it might be possible that only chain initiation was light triggered, while the polymerizations themselves could proceed without any chain-length control. PhotoCMP polymerizations in solution with similarly low amounts of copper catalyst lack precise chain-length control. Thus, further experiments were required to investigate the livingness of the grafting process.



Figure 2.5. (left) Reinitiation experiment. Dry ellipsometric film thickness evolution versus cumulative time. Poly(*t*-butyl acrylate) was grafted for 0, 5, 10 and 15 min (black) and then reinitiation for 15 min (red). (right) XPS depth profile of poly(*t*-butyl acrylate-*b*-2-hydroxyethyl acrylate): Evolution of the relative contribution of poly(*t*-butyl acrylate) (red) and poly(2-hydroxyethyl acrylate) (black) to the C 1s XPS spectrum etch depth.

Thus, reinitiation experiments were performed where polymerizations were stopped and resumed after an extended period (**Figure 2.5**). If the chains carried the required bromine end-functionality, such reinitiation must be achievable for a well-controlled process. Indeed, reactions could be resumed and took place with the same grafting rate, showing a linear evolution of the film thickness over time before as well as after the reinitiation. In fact, the determined film thicknesses matched those for the continuous grafting for the same illumination time, suggesting that a large proportion of the chains was end-capped with bromine and that termination was minimal. Such an observation is in line with recent findings for SET-LRP showing excellent chain-end functionality compared with other CMP.^[28]

In addition, the potential to form block copolymers is usually seen as proof of livingness. Thus, block copolymers were generated. PolyEHA was grafted from the chain-end of poly(tBA) brushes of various film thicknesses, showing a linear film thickness evolution also for the second block after a short initiation period. The

Surface Grafting via PhotoCMP at Extremely Low Catalyst Concentrations block structure of the resulting films was characterized via XPS depth profiling (right side of **Figure 2.5**). The change of the relative contributions of poly(*t*-butyl acrylate) and poly(2-hydroxyethyl acrylate) to the XPS C 1s spectrum over the etch depth is displayed. Near to the substrate, a clear region with a composition close to pure poly(*t*BA) is observed (120 nm etch depth). This is followed by a gradual shift in the composition, which evolved to the top region with a preferential content of polyEHA (<36 nm). The gradual shift is well in line with the partial backcoiling of the chains.

Analysis of the bromine distribution in ToF-SIMS depth profiling with C₆₀⁺ and Cs⁺ sputtering showed two well-separated regions (**Figure 2.6**). Significant bromine concentrations are found at the silicon/polymer interface (unreacted initiator)^[29] and on the top of the brushes, indicating living chain ends. For sputtering with Cs⁺, the implantation of Cs into the sample matrix enhanced the ionization efficiency of negatively charged secondary ions.

This effect and the rapid removal of airborne contaminations at the earliest stage of the sputtering experiment are responsible for the first maximum of Br⁻



Figure 2.6. ToF-SIMS depth profiling using (left) C_{60}^+ and (right) Cs^+ sputtering. The distributions of both bromine isotopes and of some characteristic silicon (oxides) ions as well as of the C_6^- fragment of the used C_{60}^+ are displayed.

intensities at the surface of the polymer layer (right side of **Figure 2.6**). Reaching deeper layers of the polymer, the bromine content decreases and reaches a second local maximum at the polymer-silicon interface.

Temporal control was investigated via on-off experiments. It must, however, be noted that the temporal control was not perfect. In principle, no reaction should occur in the dark. Still, growth at reduced reaction rate was observed during the "off" period if the reaction had already been exposed to light (**Figure 2.7**). Similar behavior was found in literature^[30] and in fact there has been only one complex for which excellent temporal control was obtained.^[31] As it is unlikely that radicals remain active for several minutes, it may be speculated that low amounts of Cu⁰ were formed by catalyst disproportionation, which would inevitably lead to conventional SET-LRP processes.^[20, 21, 28]



Figure 2.7. Dry ellipsometric film thickness evolution of poly(*t*-butyl acrylate) brushes. After 15 min, the UV light was turned off for 10 min. A reduced growth rate during the "off" period was found.



Figure 2.8. (left) Silicon wafer after photoCMP using a shadow mask.^[2-4] A pattern is visible to the bare eye after a reaction time of a few minutes. (right) Profilometry of a small part of the pattern confirmed the resolution on a micrometer level.

Spatial control can be achieved by photoCMP simply by selecting the illuminated areas (**Figure 2.8**). After only a few minutes reaction time, photoCMP resulted in a patterned surface structure visible to the naked eye. Profilometry confirmed the obtained resolution on a micrometer level.

2.4 Summary and conclusions

In conclusion, photoCMP is a powerful technique for the grafting of polymer brushes of a wide range of acrylic monomers. Unmatched low copper catalyst concentrations achieved good control over the grafting reaction, allowing for the growth of films of up to 1 μ m. Such thickness have been never achieved before for polymer brushes. Furthermore, basic spatial and temporal control was successfully demonstrated.

2.5 Supporting information

 Table S2.1. Advancing and receding water contact angles.

Coating	Advancing	Receding			
Initiator	81.3	65.9			
Poly(t-butyl acrylate)	88.3	80.9			
Poly(methyl acrylate)	79.9	31.9			
Poly(2-hydroxyethyl acrylate)	53.5	11.6			
Poly(3-(dimethylamino)propyl acrylate)	49.6	29.0			
Poly[oligo (ethylene glycol) methyl ether acrylate]	43.8	24.6			
Poly(n-butyl acrylate)	100.5	48.9			
Poly{[2-(acryloyloxyethyl]trimethylammonium	8.9	8.8			
chloride}					
Poly(2-ethylhexyl acrylate)	106.8	54.4			
Sample	Characteristic fragments				
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	Positive polarity	Negative polarity ^[*]			
Initiator	[¥]	Br ⁻ (m)			
Poly(t-butyl acrylate)	C ₄ H ₉ + (vs)	C₄H9O⁻ (s)			
Poly(methyl acrylate)	[¥]	CH₃O⁻ (vs)			
Poly(2-hydroxyethyl acrylate)	$C_2H_5O^+$ (vs)	C ₂ H ₅ O ₂ - (vs)			
		CH ₃ O⁻ (s)			
Poly(3-(dimethylamino)	$C_{2}H_{6}N^{+}$ (vs)	CN⁻ (vs)			
propyl acrylate)	$C_3H_8N^+$ (vs)	CNO⁻ (vs)			
	C ₄ H ₁₀ N ⁺ (m)	SO3 ⁻ (vs) [†]			
	$C_5H_{10}N^+$ (s)				
Poly[oligo(ethylene glycol)	$C_2H_5O^+$ (vs)	C₂H₃O⁻ (vs)			
methyl ether acrylate]		$C_2H_5O_2^-$ (vs)			
		CH ₃ O⁻ (s)			
Poly(n-butyl acrylate)	C ₄ H ₉ + (vs)	C₄H ₉ O⁻ (s)			
Poly{[2-(acryloyloxy)-	$C_3H_8N^+$ (vs)	Cl⁻ (vs)			
ethyl]trimethylammonium	C ₄ H ₁₀ N ⁺ (m)	HCl ₂ - (w)			
chloride}	$C_5H_{12}N^+$ (s)	CN⁻ (s)			
		CNO⁻ (s)			
		SO ₃ ⁻ (vs) ^[‡]			
Poly(2-ethylhexyl acrylate)	C ₄ H ₉ + (vs)	[¥]			
	C ₅ H ₉ + (s)				
	C ₅ H ₁₁ ⁺ (s)				

Table	52.2	ToF-SIMS	surface	snectra	of all	orafted	nolvacr	vlates	and the	initiator
Iavie	32.2	101-31113	Suitace	specia	u an	graiteu	pulyaci	ylates	and the	initiator.

vs = very strong, s = strong, m = medium, w = weak

[*] All polymer sample showed intense signals for $C_3H_3O_2^-$.

^[¥] only unspecific hydrocarbon fragments detected

[†] Contamination

Chapter 2

Sample	Atomic ratio*					
	C 1s		Ν	0 1s		Cl
	С-С, С-О,		1s		0.0.0	2p ³
	C-H	C-N		L-0-L	0-0=0	
Initiator	12.2	2.3	-	[±]	[±]	-
Poly(<i>t</i> -butyl acrylate)	5.1	1.1	-	1.0	1.1	-
Poly(methyl acrylate)	2.1	1.0	-	0.9	0.9	-
Poly(2-hydroxyethyl	2.1	2 1		1.6	1 2	-
acrylate)	2.1	2.1		1.0	1.2	
Poly(3-(dimethylamino)	57	13	0 9	1 1	0.8	
propyl acrylate)	5.7	1.5	0.5	1.1	0.0	
Poly[oligo(ethylene glycol)	15	133	_	7 0	04	_
methyl ether acrylate]	1.5	15.5		7.0	0.4	
Poly(n-butyl acrylate)	4.8	1.0	-	0.9	0.9	-
Poly{[2-(acryloyloxy)-						
ethyl]trimethylammonium	2.9	5.1	0.9	1.1	0.8	1.0
chloride}						
Poly(2-ethylhexyl acrylate)	9.0	1.2	-	0.9	1.0	-

Table S2.3. Ratio of atomic concentrations of the fitted contributions assigned in the corresponding XPS spectra.

* Normalized to COO = 1

 $^{[\pm]}$ Intense SiO_2 background prevented integration of the O 1s signal of initiator

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Chapter 3

2D-Direct Laser Writing on Silicon Substrates via Photoinduced Copper-

Mediated Radical Polymerization



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3.1 Abstract

Today's needs for complex functions and steady miniaturization of devices challenge materials scientists towards constant improvement. Despite reversible deactivation radical polymerization's ability to generate complex functions and architectures, there is a lack of protocols to translate this ability towards surface patterning. Here we present the first direct laser writing protocol for controlled grafting of polymer brushes. Poly(t-butyl acrylate), poly(2-hydroxyethyl acrylate), poly(oligo(ethylene glycol) methyl ether acrylate), and poly([2-(acryloyloxy)ethyl] trimethylammonium chloride) were grafted from silicon substrates via laser-induced copper-mediated radical polymerization. Film thicknesses up to 39 nm were reached within 125 µs of exposure to UV laser light (351 nm). Successful block copolymerization underpinned the controlled nature of the grafting methodology. The resolution of a small structure of grafted poly(2-hydroxyethyl acrylate) was assessed to be approximately 270 µm and is limited by the type of laser used in the study. Further, a checkerboard pattern of poly(t-butyl acrylate) and poly(oligo(ethylene glycol) methyl ether acrylate) was produced and imaged via time of flight secondary ion mass spectrometry (ToF-SIMS), and X-ray photoelectron spectroscopy (XPS).

3.2 Introduction

The need for polymer-patterned surfaces has been growing over the past twenty years as interactions between two materials are largely determined by their surface characteristics.^[1] Grafting of polymer brushes onto surfaces hereby often provides good control over optical and mechanical surface properties and is hence ideal to tailor surface properties in a wide range of applications. Polymer brushes are typically obtained via two pathways: Grafting-from or grafting-to approaches.^[2] Grafting-to reactions proceed via efficient conjugation reactions and attach a preformed polymer to the surface. While overall quite versatile, grafting-to often leads to comparatively low grafting densities due to steric congestion.^[3-5] On the other side, the employed polymers can be synthesized in solution and therefore excellent control of the grafted material is obtained. Grafting-from reactions build the polymeric structures from the surface and provide good control over film thickness, composition and architecture while concomitantly yielding high grafting densities.^[6] However, grafting-from usually leads to less defined polymer microstructures because surface-initiated polymerization kinetics can differ significantly from solution-based reactions.^[7] Additionally, surface characterization is inherently more challenging, which often leaves doubts about the exact composition and structure of grafted-from brushes.

With the discovery of living and controlled polymerization protocols, well-defined and tailor-made polymeric architectures have become accessible.^[8] Especially reversible deactivation radical polymerization (RDRP) with its high tolerance towards chemical functionalities and the availability of straightforward reaction protocols has become the tool of choice for surface engineering.^[6, 9] The three most widely used RDRPs are reversible addition fragmentation transfer radical polymerization (RAFT),^[10, 11] nitroxide-mediated polymerization (NMP)^[12], and atom transfer radical polymerization (ATRP) which is often – but not exclusively – conducted with copper catalyst.^[13] Precise control over chain length, dispersity and chemical functionalities is an essential but not sufficient feature to obtain welldefined polymer patterns. Spatial control on flat substrates is equally important and can be realized via various techniques,^[14] such as microcontact printing,^[15] dip pen^[16] or polymer pen lithography,^[17, 18] conventional lithography with a photomask and resist,^[19] or light-induced reaction^[20] to only mention a few. Light-induced reactions are especially interesting thanks to simple procedures, good scalability, and additional temporal control.

Combining tunable material properties together with spatial control via the use of light, photoRDRP has become a powerful tool for surface engineering.^[20] PhotoRDRP was successfully employed to graft polymer brushes of different length and block copolymers of methacrylates, using iridium catalysts^[21, 22] and metal-free systems.^[23, 24] Photoinduced copper-mediated radical polymerization (photoCMP) has been reported for grafting both silicon^[25-28] and cellulose substrates.^[29] Films up to almost 1 µm thickness of polyacrylates were produced at lowest catalyst concentrations.^[27] Up to now, spatial control was achieved via the use of conventional photomasks. Even though some very convincing examples of spatial control have been reported recently for iridium catalysts combined with inkjet-printed photomasks in a stop-flow cell,^[22] photomask-free procedures are more versatile and allow for fast adaptions.

A prominent example of photomask-free methodologies is three dimensional printing, one of the current trends in materials science.^[30] Stereolithography and direct laser writing (DLW) allow for manufacturing of µm-resolved surface patterns.^[31] These techniques are based on very fast photoinitiation and crosslinking monomers such as multiacrylates or epoxy-based photoresists, yet are limited to random copolymers as they mostly rely on free radical polymerization.^[31, 32]

To date, there are only few examples that combine direct laser writing on flat surfaces and RDRP. Very recently, polymer brushes with sub-100 nm resolution

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were grafted in a two-step procedure: stimulated-emission depletion was exploited in laser lithography to graft an ATRP initiator, which was followed by thermal surface-initiated CMP.^[33] Using photoRDRP, also one-step methodologies towards very well resolved polymer structures were reported; yet actual photoRDRP characteristics (controlled chain growth and endgroup fidelity) have never been confirmed. PhotoNMP of di- and triacrylates was employed to graft a multilayered, µm-resolved network structure from a crosslinked polymer film.^[34] Control over film thickness was hereby obtained by adjustment of the exposure time on a millisecond scale. RDRP-like behavior was only indirectly indicated via AFM and the technique was not tested for brush-like (hence non-crosslinking monomers) structures. More recently, the same group reported an iridium-based system to graft micrometer-resolved structures via direct laser writing from crosslinked polymer films.^[35] Good control over film thickness was achieved by variation of laser power for a constant exposure time of 5 ms. However, no information on the used monomer and no proof of RDRP-like behavior were unfortunately provided.

Herein, we pioneer the combination of photoCMP with direct laser writing, specifically for grafting-from of polymer brushes. RDRP-like behavior was convincingly demonstrated: Following a general grafting of polymer brushes for various acrylates, the kinetics for the grafting of poly(*t*-butyl acrylate) brushes are investigated. Successful block copolymerization is evidenced via X-ray photoelectron spectroscopy (XPS) and grazing angle attenuated total reflection Fourier-transform infrared (GAATR-FTIR). Finally, the creation of different surface patterns is described and the resolution is assessed via time of flight secondary ion mass spectrometry (ToF-SIMS).

3.3 Results and discussion

The formation of polymer brushes on surfaces comprises a two-step procedure: first, formation of a self-assembled monolayer of a covalently bonded suitable initiator and secondly the grafting-from polymerization. Stable self-assembled monolayers that lead to high grafting densities of polymer brushes are generally obtained for initiators with undecyl spacers between anchor group and initiating site.^[6] We have further chosen work with the trichlorosilane to 11-(trichlorosilyl)undecyl 2-bromo-2-methylpropanoate to avoid poorly defined monolayers that are often obtained for triethoxysilanes.^[36] PhotoCMP direct laser writing was carried out with a pulsed excimer laser of 351 nm wavelength and a galvo scanner with focus lens to graft patterns of polymer onto modified flat silicon substrates (Scheme 3.1).



Scheme 3.1. (top) A pulsed excimer laser ($\lambda = 351 \text{ nm}$, $\tau_{\text{pulse}} = 4 - 6 \text{ ns}$) was used for photoinduced copper-mediated radical polymerization from flat silicon substrates. The laser light was sent through a prism to obtain a squared beam before it was directed in the galvo scanner and then focused on the substrate. The substrate was placed in an airtight chamber under nitrogen atmosphere. (bottom) Photoinduced copper-mediated radical polymerization for surface grafting of polyacrylates.

The excimer laser was operated at 500 Hz with an energy of 1.5 mJ per pulse of 4 - 6 ns. Laser light was first sent through a prism to obtain a rectangle beam of $6 \text{ mm} \times 8 \text{ mm}$ and through a reflective filter that reduced the intensity by a factor 100 to approximately 1.56 mW·cm⁻². A software-operated galvo scanner redirected the laser light through a focus lens onto the flat silicon substrate to obtain the desired pattern. The substrate was placed in a Teflon container under nitrogen atmosphere. We found the reaction to be oxygen sensitive, but insensitive towards water impurities. The lower part of Scheme 3.1 depicts the performed grafting reaction. Starting from a silicon substrate coated with a monolayer of ATRP initiator, acrylate monomers were polymerized in the presence of copper(II) bromide and tris[2-(dimethylamino)ethyl] amine (Me_6TREN) in DMSO as solvent upon exposure to laser light. The writing speed was set to 0.02 m·s⁻¹ for an assumed spot size of 250 μ m × 250 μ m to achieve a more or less homogenous light exposure despite the pulsed nature of the laser. A range of acrylate monomers from hydrophobic t-butyl acrylate (tBA) over more hydrophilic 2-hydroxyethyl acrylate (HEA) and oligo(ethylene glycol) methyl ether acrylate (OEGA) towards very hydrophilic [2-(acryloyloxy)ethyl] trimethylammonium chloride (AETMAC) was grafted.

At first, the general feasibility of laser-induced copper-mediated radical polymerization was assessed. The above listed acrylates were grafted homogenously on a silicon substrate. The polymer grafts were characterized via XPS. **Figure 3.1** shows the C 1s XPS spectra of poly(*t*-butyl acrylate) (PtBA), poly(2-hydroxyethyl acrylate) (PHEA), poly(oligo(ethylene glycol) methyl ether acrylate) (POEGA), and poly(2-acryloyloxyethyl trimethylammonium chloride) PAETMAC. Three different peaks corresponding to O=C-O (288.9 eV), C-O, C-N

(~286.6 eV), and C-C, C-H (285.0 eV) were fitted.^[27] (C-O, C-N)/O=C-O ratios were calculated for all polymers and are in good to excellent agreement with the expected values. There were little deviations from the theoretical C-C, C-H contributions in the case of PHEA and PAETMAC, however, these were also found for photoCMP grafting with standard UV light^[27] and stem in all likelihood from small surface contaminations. Besides the observed shift of the C-O peak (286.8 eV) towards smaller binding energy (286.4 eV) corresponding to the additional presence of C-N groups, PAETMAC also showed the expected positively charged nitrogen and chlorine signals.



Figure 3.1. C 1s XPS spectra of grafted polymers after direct laser writing. a: poly(*t*-butyl acrylate), b: poly(2-hydroxyethyl acrylate), c: poly(oligo(ethylene glycol) methyl ether acrylate), d: poly(2-acryloyloxyethyl trimethylammonium chloride).

Additional ToF-SIMS and GAATR-FTIR measurements confirmed the XPS results (**Table S3.1**) and hence underpin the successful grafting of polymer chains.

Subsequently, the grafting kinetics of PtBA were investigated. **Figure 3.2** shows on its right side the pattern that we used to assess the film thickness evolution. Five rectangles at increasing distance were placed along 6 mm on a silicone substrate. Each rectangle was 250 μ m in width and consisted of 6 lines at a distance of 50 μ m. For simplistic reasons and to account for non-ideal focus adjustment, we assume a focused beam size of 250 μ m × 250 μ m. AFM was measured in the middle of each structure to assess film height. Exposure times were calculated from writing speed, frequency, and spot size, assuming that each line in the center of the structure was exposed 5 times per writing cycle. On its left side, **Figure 3.2** shows the film thickness evolution of PtBA as a function of exposure time to laser light.



Figure 3.2. (left) Evolution of PtBA film thickness with exposure time to laser light. Film thicknesses were determined via AFM scratch tests. (right) Scheme of structure used to assess film thickness evolution.

Film thicknesses range from 0 nm after 8 μ s up to 39 nm after 125 μ s of laser light. The film thickness evolution follows a linear slope, yet a short inhibition period of 8 μ s is observed. Linear film thickness evolutions is usually seen as indication for the livingness of the grafting process. A constant growth rate corresponds to a constant number of growing chains and hence control.

The induction period of 8 µs was potentially caused by oxygen, given the high oxygen sensitivity of the photoCMP process and similar observations in literature.^[35] Consequently, no film was grafted in the areas not exposed to direct laser light according to AFM.

While linear evolution with film thickness is a good indication of controlled chain growth, block copolymer formation is typically considered as further proof as it is used to assess reinitiation capabilities (and hence retention of the active chain end). Here, a rectangle ($8 \times 8 \text{ mm}^2$) of PtBA was grafted onto a silicon substrate and subsequently a smaller rectangle $(4 \times 4 \text{ mm}^2)$ of PHEA was grafted in the middle of the larger one. A clearly visible change of hydrophilicity was observed during the subsequent washing procedure according to the grafted structure. The GAATR-FTIR spectra of the employed polymers PtBA and PHEA as well as the diblock copolymer PHEA-b-PtBA are shown on the left side of **Figure 3.3**. All three polymers show the expected C=O stretching vibration at 1732 cm⁻¹ and the asymmetric C-O-C stretching at 1160 cm⁻¹. The spectrum of the diblock copolymer grafts show the symmetric CH_3 bending vibration at 1367 cm⁻¹ very prominently in both PtBA and PHEA-b-PtBA. The C-O stretching vibration of the primary alcohol of PHEA was found at 1079 cm⁻¹, prominently in pure PHEA and little in the diblock copolymer. Also found in the PHEA spectrum was the SiO_2 background peak at 1225 cm⁻¹ due to the low film thickness.



Figure 3.3. (left) Grazing angle attenuated total reflection Fourier-transform infrared (GAATR-FTIR) spectra of poly(2-hydroxyethyl acrylate) (PHEA), poly(*t*-butyl acrylate) (PtBA), and poly(2-hydroxyethyl acrylate)-*b*-poly(*t*-butyl acrylate) (PHEA-*b*-PtBA) on silicon substrate. (right) C 1s XPS spectrum of PHEA-*b*-PtBA.

The weak contribution of the C–O stretching vibration of the primary alcohol to the diblock copolymer's spectrum is associated with the relatively low surface area of only 25% that was functionalized. Moreover, it is known from literature that even for a fully functionalized substrate of 120 nm PHEA-*b*-PtBA as diblock (with only 47 nm PtBA as first block), the respective peak remained rather low.^[27] As both polymers are not phase separating, the XPS spectrum of the diblock copolymer shows a mixture of both polymers (right side of **Figure 3.3**) accordingly. A carbon ratio C–O / O–C=O of 1.24 was found which corresponds to a mixture of ~56% PtBA and ~44% PHEA within the uppermost 8 – 10 nm. Our calculations are based on the XPS results of the homopolymers grafts as they give a more realistic picture than the theoretical values: indeed this ratio shows a value of 0.9 to 1.0 for pure PtBA and a value of 1.7 for pure PHEA. The 120 nm-thick PHEA-*b*-PtBA graft reported in literature showed only 60% PHEA contribution to the XPS C 1s spectrum.^[27] Therefore, we conclude that diblock copolymerization was successful also for direct laser writing. Moreover, ToF-SIMS confirmed the

presence of both PtBA and PHEA (**Table S3.1**), which again is only possible upon successful reinitiation of chains.

Finally, the resolution of the grafted polymer was assessed with a control structure that is typically used in photolithography: Starting from a small rectangle of 236 μ m × 236 μ m in the upper left corner, a series of rectangles with increasing size and inter-rectangle distances along the respective x- and y-axes was created. Thus, we are able to monitor not only the lateral resolution, yet also the influence of the structure size, which is linked to the total exposure time of each structure. As before, all rectangles were filled with lines with 50-µm line spacing. Each structure was exposed to direct laser light for 9 µs per surface area and 2-hydroxyethyl acrylate was used as monomer.

Figure 3.4 depicts the combined intensity patterns of the sum of CH_3O^- and $C_2H_5O^-$ fragments from the PHEA of the whole structure on the left and of its smallest spot in the middle. The leftmost image is obtained under static SIMS condition without significant sample damage. Here, the SIMS probing depth is a few nanometers only. The image of the smallest patterned spot in the middle of



Figure 3.4. ToF-SIMS data of patterns of PHEA. Intensity patterns of sum of PHEA characteristic CH_3O^- and $C_2H_5O_2^-$ secondary ions of (left) the whole structure and (middle) of its smallest spot. (right): The pseudo profile of the smallest spot from dual beam depth profiling with argon cluster ion erosion. The full width at half maximum (*FWHM*) of the Gaussian fit is 270 µm.

Figure 3.4 is obtained from a dynamic SIMS experiment. Therefore, in addition to the imaging Bi primary ion beam an Ar₁₆₀₀, 5 keV, beam was applied to erode the polymer layer down to the silicon wafer. The obtained, depth-integrated signals of CH_3O^- and $C_2H_5O^-$ fragments are a measure of the thickness of the deposited polymer spot. The rightmost graph in Figure 3.4 shows the combined intensity of CH_3O^- and $C_2H_5O^-$ across the center of the smallest structure. The intensity profile has a Gaussian shape and no sharp edges were found. The full width at half of the maximum intensity (FWHM) of the Gaussian fit is around 270 µm. Even though all target structures were rectangles, sharp edges were completely replaced by round edges. This smoothing was most pronounced for the smallest structure, which was turned into a circle (Figure 3.4, middle). Increasing the size of the rectangles or grafting of subpatterns in the center of a larger pattern led to a loss of lateral resolution, which can probably be assigned to some low intensity optical artifacts that we observed due to undesired reflections. Furthermore, larger structures showed much higher intensities in ToF-SIMS, indicating thicker polymer layers. In contrast to 2-photon DLW that gains a large portion of its remarkable resolution from the non-linearity of optical susceptibility and light intensity, 2D single photon DLW completely relies on the beam quality parameter M^2 of the employed laser. The beam quality parameter M^2 gives the deviation factor from a perfectly focusable, thus diffraction limited laser. The excimer laser we used featured a 6 mm × 4 mm laser beam (FWHM values) with divergences of 2 and 1 mrad respectively, which results in M^2 of around 54 and 18. A prism doubles the 4 mm size shortly after leaving the laser. At a distance to lens (56 mm focal length) of around 65 cm with a wavelength of 351 nm, the minimal theoretical spot size ranges around 185 μ m \times 96 μ m. Given this limitation and the size of the target structure of 236 μ m \times 236 μ m, a FWHM-

size of only 270 μ m is surprisingly good. Therefore, it is more likely that the resolution of small structures at short exposure times is actually limited by the inhibition by oxygen (**Figure 3.2**).

Our current resolution is approximately 270 μ m, less than twice the minimal theoretical spot size to which the beam quality $M^2 = 54$ is proportional. Since many commercially available laser such as diode-pumped Nd:YAG solid-state micro laser have $M^2 < 1.5$, resolutions in the range of 10 μ m can probably be expected for the presented methodology.

In another experiment, a checkerboard pattern of PtBA and POEGA was produced. All squares were of equal size and PtBA was grafted first with 16 μ s exposure time per surface area. **Figure 3.5** shows the corresponding ToF-SIMS images. The left side of **Figure 3.5** depicts the C₄H₉O⁻ intensity pattern that corresponds to the squares of grafted PtBA. The intensity pattern of C₂H₃O⁻ for POEGA is depicted in the middle and their overlay on the right side. From the latter two it appears that the secondly grafted POEGA formed a better-resolved and more pronounced pattern. In general, the lateral resolution within the checkerboard was much lower than at its borders. This loss of lateral resolution probably led to formation of block



Figure 3.5. ToF-SIMS spectra of a checkerboard pattern of PtBA and POEGA with the intensity patterns of $C_4H_9O^-$ (left), $C_2H_3O^-$ (middle) and their overlay (right).

copolymers in the center of the pattern with likely longer inhibition times as similar observations were made for diblock copolymer formation with non-laser UVlight.^[27] Inhibition might also be the reason the structures of the first block were more pronounced in the center of the pattern, whereas the second block was more at its borders. Contrarily to lateral resolution, film thicknesses close to the edges of the checkerboard pattern seemed much lower than at the center as evidenced by the presence of silicon signal in XPS mapping (**Figure 3.6**). Similar to the ToF-SIMS results, XPS mapping evidences a much better resolution for the secondly grafted POEGA at the edges of the checkerboard pattern and concomitantly a much higher presence of PtBA in the center of the checkerboard.



Figure 3.6. XPS mapping of a checkerboard pattern of PtBA, POEGA, and silicon, obtained after principal component analysis of the C 1s and Si 2p spectra.

3.4 Summary and conclusions

We introduce the direct grafting of polymer chains in predefined patterns using a focused laser to initiate and control chain growth. Specifically, laser-induced copper-mediated radical polymerization was employed to graft various acrylate monomers from silicon substrates. XPS, ToF-SIMS, and GAATR-FTIR evidenced the successful grafting. A linear dependence of the film thickness on direct exposure time to laser light was observed and the reaction was found to be very fast, reaching almost 40 nm after 125 µs of laser light exposure. The controlled nature of the grafting was further demonstrated via block copolymer formation. Moreover, a checkerboard pattern was produced and imaged via ToF-SIMS and XPS. The present methodology is strongly influenced by beam quality of the employed laser and resolutions in the range of 300 µm could be realized according to ToF-SIMS. Better optical set-ups and UV laser with higher beam quality should significantly improve the resolution.

3.5 Supporting information

Table S3.1. ToF-SIMS surface spectra of the initiator, all grafted polyacrylates and their diblock copolymer.

Sample	Characteristic fragments			
	Positive polarity	Negative polarity ^[*]		
Initiator	[¥]	Br ⁻ (m)		
Poly(t-butyl acrylate)	C ₄ H ₉ + (vs)	C₄H ₉ O⁻ (s)		
Poly(2-hydroxyethyl acrylate)	C ₂ H ₅ O ⁺ (vs)	$C_2H_5O_2^-$ (vs)		
		CH ₃ O⁻ (s)		
Poly[oligo(ethylene glycol)	C ₂ H ₅ O ⁺ (vs)	C ₂ H ₃ O ⁻ (vs)		
methyl ether acrylate]		C ₂ H ₅ O ₂ ⁻ (vs)		
		CH₃O⁻ (s)		
Poly{[2-(acryloyloxy)-	C ₃ H ₈ N ⁺ (vs)	Cl ⁻ (vs)		
ethyl]trimethylammonium chloride}	C ₅ H ₁₂ N ⁺ (s)			
Poly(2-hydroxyethyl	C ₄ H ₉ + (vs)	$C_2H_5O_2^-$ (m)		
acrylate)-b-poly(t-butyl acrylate)		C₄H ₉ O⁻ (m)		

vs = very strong, s = strong, m = medium

 $[\ast]$ All polymer sample showed intense signals for $C_3H_3O_2^{\text{-}}.$

 $\ensuremath{^{[\mathtt{Y}]}}$ only unspecific hydrocarbon fragments detected

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Chapter 4

Reversible Surface Engineering via

Nitrone-Mediated Radical Coupling



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4.1 Abstract

Efficient and simple polymer conjugation reactions are critical for introducing functionalities on surfaces. For polymer surface grafting, post polymerization modifications are often required, which can impose a significant synthetic hurdle. Here, we report two strategies that allow for reversible surface engineering via nitrone-mediated radical coupling (NMRC). Macroradicals stemming from activation of polymers generated by copper-mediated radical polymerization are grafted via radical trapping with a surface-immobilized nitrone or a solution-borne nitrone. Since the product of an NMRC coupling features an alkoxyamine linker, the grafting reactions can be reversed or chain insertions be performed via nitroxide mediated polymerization (NMP). Poly(*n*-butyl acrylate) $(M_n = 1570 \text{ g} \cdot \text{mol}^{-1}, D = 1.12)$ with bromine terminus was reversibly grafted to planar silicon substrates or silica nanoparticles as successfully evidenced via X-ray photoelectron spectroscopy (XPS), time of flight secondary ion mass spectrometry, and grazing angle attenuated total reflection Fourier-transform infrared spectroscopy (GAATR-FTIR). NMP chain insertions of styrene is evidenced via GAATR-FTIR. On silica nanoparticles, an NMRC grafting density of close to 0.21 chains per nm^2 was determined by dynamic light scattering and thermogravimetric analysis. Concomitantly, a simple way to decorate particles with nitroxide radicals with precise control over the radical concentration is introduced. Silica microparticles and zinc oxide, barium titanate, and silicon nanoparticles were successfully functionalized.

4.2 Introduction

The need for polymer-coated surfaces with unique properties has remained unbroken over the past twenty years.^[1-4] There are two general methodologies to graft polymers onto a surface: 'grafting-from' and 'grafting-to'.^[5-8] Grafting-from approaches allow for high grafting densities as small molecules are directly attached to the surface followed by chain growth, yet precise tuning of polymer properties is challenging since imperfections of the growth mechanism in the confined space on the surface are irreversibly encoded. Further, the characterization of the grafted chains is challenging.^[9] In contrast, grafting-to approaches attach preformed chains to the surface. Therefore, these methods often rely on very efficient conjugation reactions such as (hetero) Diels-Alder, thiol-ene (Michael additions), nitrile imine tetrazole-ene cycloadditions,^[10] coppercatalyzed azide–alkyne cycloadditions,^[5] and oxime ligations^[11] to name a few prominent examples. Nevertheless, grafting densities are often below the respective grafting-from approaches due to steric congestion on the binding sites.^[12]

Grafting-to reactions rely on an efficient conjugation processes. However, these conjugation reactions in most cases require specific functional groups that are not a priori present in the target molecule and postpolymerization modifications might become necessary – either to introduce or to unprotect the required chemical functionality.^[13, 14] The high endgroup fidelity of reversible deactivation radical polymerization hereby provides a good starting point for the introduction of the desired functionality. However, these modifications do not only require at least one other reaction step, yet may lead to unwanted side products and impurities.^[15] If the polymerization conditions and the target endgroup chemistry

are orthogonal, the desired functionality can be readily attached to the initiator or chain transfer agent, respectively.^[14] However, even the robust copper-catalyzed azide–alkyne cycloadditions are subject to a loss of orthogonality with many monomers during radical polymerization since monomers can slowly react with the azide moiety, especially at extended reaction times.^[16] While RAFT polymers in principle allow for direct hetero Diels-Alder reactions,^[17] ATRP polymers can be directly employed in radical-radical coupling reactions such as atom transfer radical coupling, nitroxide radical coupling or nitrone-mediated radical coupling (**Scheme 4.1** and Chapter 1.5.1).^[18] Atom transfer radical coupling (ATRC) leads to the irreversible formation of a symmetric polymer via a carbon-carbon bond and is only well suited for polystyrene. In contrast, both nitroxide- and nitrone-mediated radical coupling result in an asymmetric and symmetric alkoxyamine, respectively, and functions well with polyacrylates.^[18]

$$\mathbb{R}^{1} + \mathbb{R}^{2} \xrightarrow{\mathsf{N}^{0}}_{\mathbb{R}^{2}} \mathbb{R}^{3} \xrightarrow{\mathsf{1}^{\text{st}} \text{ additon}} \mathbb{R}^{2} \xrightarrow{\mathsf{N}^{1}}_{\mathbb{R}^{2}} \mathbb{R}^{3} \xrightarrow{\mathbb{R}^{4}}_{\mathbb{R}^{2}} \xrightarrow{\mathsf{R}^{4}}_{\mathbb{R}^{2}} \mathbb{R}^{1} \xrightarrow{\mathsf{N}^{1}}_{\mathbb{R}^{2}} \mathbb{R}^{3}$$

Scheme 4.1. General reaction scheme for nitrone-mediated radical coupling (NMRC). Furthermore, nitrones give direct access to nitroxide radicals when the reaction is stopped after the addition of one radical (**Scheme 4.1**), making nitroxideequipped particles directly accessible. The second addition is generally reversible at higher temperature and leads to the formation of an internal alkoxyamine (**Scheme 4.1**). In principle, the formed alkoxyamine allows for block copolymer formation via nitroxide-mediated polymerization if no a-H is present that would facilitate elimination reactions.^[18, 19]

Alkoxyamines further allow for radical crossovers at higher temperatures,^[20] which has been exploited for the formation of graft polymers,^[21] crosslinking systems,^[22] star polymers,^[23] and side-chain modification on surfaces.^[24, 25] However, strong excluded volume effects led to low degrees of crossover on surfaces and a scaffolding polymer backbone was always required. Nevertheless, alkoxyamine-based crossovers give direct access to dynamic covalent surface chemistry, which can only be achieved by very few other methodologies such as triazolinedione conjugation,^[26] reversible disulfide formation,^[27, 28] and β -cyclodextrin host-guest systems^[29, 30] and few others.^[31-34]

We herein exploit both key features of NMRC, i.e. dynamic covalent reversibility and post-coupling NMP, for surface grafting. We have selected two approaches on flat surfaces and further on particles for quantification. First, the precursor of a radical – here an ATRP initiator – was grafted to a planar silicon substrate and subsequently subjected to nitrone-mediated radical coupling with a brominecapped polyacrylate and the nitrone in solution. The reversibility of the NMRC coupling was demonstrated via both a degrafting experiment and nitroxidemediated polymerization with styrene. Similarly, our second approach employed nitrones grafted to a surface and their subsequent use in nitrone-mediated radical coupling, degrafting experiments and nitroxide-mediated radical polymerization. The grafting density of the latter approach was assessed on silica nanoparticles. Finally, silica particles with tunable radical concentration were produced and characterized. The methodology was further extended to silicon, BaTiO₃, and ZnO nanoparticles, of which the latter two are very interesting compounds for second harmonic imaging microscopy.



Scheme 4.2. (Top row) Nitrone-mediated radical coupling with the nitrone species in solution. **4-1**: silicon substrate decorated with an ATRP initiator. **4-2** represents the of product nitrone-mediated radical coupling of **4-1** and poly(*n*-butyl acrylate). Sample **4-2** was subjected to degrafting in the presence of tributyltin hydride to yield **4-3**. (Bottom row): Nitrone-mediated radical coupling with the nitrone species grafted onto the surface, **4-4**. Poly(*n*-butyl acrylate) grafted by nitrone-mediated radical coupling, resulting in **4-5**. **4-6** consitutes the degrafting product of **4-5**.

4.3 Results and discussion

4.3.1 Nitrone-mediated radical coupling to flat surfaces

Reversible nitrone-mediated radical coupling with the nitrone species in solution requires generation of a transient radical on the surface. The key advantages of this approach are its full reversibility and higher accessibility based on readily available and broadly used bromine-carrying silanes, which can be combined with commercially available nitrones. As depicted on the top row of **Scheme 4.2**, an ATRP initiator with a long alkyl spacer was selected as precursor for the surface radical and was grafted in a silanization reaction, yielding a deactivated radical on substrate **4-1**. A C₁₁-alkyl spacer was selected to ensure the formation of a self-

assembled monolayer.^[35] Consequently, а poly(*n*-butyl acrylate) $(M_n=1570 \text{ g}\cdot\text{mol}^{-1}, D=1.12)$ with bromine terminus and a 10-fold excess of nitrone were used to conduct the nitrone-mediated radical coupling under SET-LRP conditions. A polymer-coated substrate 4-2 was obtained, indicating inprinciple the success of the reaction. Yet - as pointed out above - absence of competing atom transfer radical coupling still had to be proven. Degrafting experiments were conducted to reverse the grafting, exploiting the thermolabile carbon-oxygen bond of the alkoxyamine. If the nitrone is built-in efficiently, these bonds will open, allowing for cleavage of the polymer grafts. ATRC coupling, in contrast, would not allow for such reversible grafting. Therefore, **4-2** was heated to 130 °C in the presence of tributyltin hydride as hydrogen donor. After hydrogen-capturing, the cleaved polymer-grafts remained in solution, leaving only structure **4-3** on the surface.

Figure 4.1 depicts XPS and ToF-SIMS images of substrates **4-1** to **4-3**. On the right in **Figure 4.1**, the ToF-SIMS spectra of two characteristic poly(*n*-butyl acrylate) fragments, $C_4H_7O^-$ and $C_4H_9O^-$ as well as $C_2H_4NO^-$ and SiO₃⁻ are depicted. The absence of $C_4H_7O^-$ and $C_4H_9O^-$ before the nitrone-mediated radical coupling on both the blank (not displayed) and **4-1** shows – as expected – the absence of poly(*n*-butyl acrylate) prior to NMRC grafting. After NMRC grafting, both fragments appear with significant intensity. Since the control sample – a blank substrate exposed to NMRC conditions – did not show any increase of the respective intensities, physisorption can be ruled out. The substrate fragment SiO₃⁻ behaved contrary to the C₄ fragments and clearly lost intensity after grafting, indicating a polymer layer thickness above the SIMS probing depth of a few nanometers.



Figure 4.1. (left) C 1s XPS spectra of a silicon substrate, after silanization **4-1**, after nitronemediated radical coupling with poly(*n*-butyl acrylate) **4-2**, and after degrafting with tributyltin hydride **4-3**. (right) $500 \times 500 \ \mu\text{m}^2$ ToF-SIMS images of steps **4-1** to **4-3**. Intensity maps of the characteristic fragments of the grafted poly(*n*-butyl acrylate), C₄H₇O⁻ and C₄H₉O⁻; C₂H₄NO⁻ and SiO₃⁻ from the substrate.

The almost complete absence of $C_2H_4NO^-$ is associated with the instability and/or low ionization yield of this fragment in ToF-SIMS. Presence of the alkoxyamine is demonstrated via the above-described degrafting experiment that relies on radical crossover at elevated temperatures. The degrafted sample **4-3** indicates almost complete disappearance of the characteristic polymer signals $C_4H_7O^-$, $C_4H_9O^-$ and an increase in the substrate signal SiO₃⁻ (**Figure 4.1**, right). In conclusion, there is no poly(*n*-butyl acrylate) remaining after degrafting, evidencing that all polymer was reversibly removed from the substrate, and hence was grafted in the first place via the desired NMRC mechanism.

XPS experiments were performed to add quantitative information to the qualitative ToF-SIMS results (**Figure 4.1**, left). For the grafted initiator **4-1**, XPS showed the presence of bromine covalently bound to a carbon atom (Br 3d_{5/2} at

70.1 eV^[34], here not shown) and the expected C1s component ratios as previously reported.^[36] After nitrone-mediated radical coupling, the presence of poly(*n*-butyl acrylate) has been evidenced by the clear increase of the O=C-Ocarbon signal at 288.9 eV.^[37] The quantitative analysis of all spectra allows for an approximation of the film thickness. The quantitative analysis reveals a contribution of the substrate (silicon and corresponding oxygen) of close to 65 at%, whereas approx. 28 at% total carbon was detected. With respect to the information depth of the method of about 8-10 nm and under the assumption of a homogenous, closed layer, the XPS results suggest a layer thickness of close to 3 – 4 nm at the maximum. This film thickness is fully in line with the SIMS data showing a significant decrease of the SiO_3^- intensity for **4-2** as compared to **4-1**. However, the small film thickness is no surprise, given the average DP of 10 of the polymer. This length corresponds - in its stretched state - only to approximately 2.5 nm. After degrafting, XPS indicates a strong decrease of the O=C-O species which supports the degrafting of the polymer, yet the surface coverage with carbon remained the same and the total surface coverage even increased. This increase was probably due to the presence of tributyltin on the substrate 4-3 and the corresponding control sample since a significant amount of tin was found. The presence of tributyltin on the substrate accounts for the rather constant surface coverage with carbon, while ToF-SIMS shows the complete removal of the poly(*n*-butyl acrylate).

Moreover, GAATR-FTIR spectroscopy was employed to complement the characterization (**Figure 4.2**). As expected, the blank sample indicates the absence of specific functionalities as there was no peak besides the major SiO₂ signal that is found in all spectra. The silanized ATRP initiator in **4-1** was chosen



Figure 4.2. GAATR-FTIR spectra of the blank sample (**blank**), the grafted ATRP initiator **4-1**, the grafted poly(*n*-butyl acrylate) after the NMRC reaction **4-2**, the degrafted sample **4-3** and finally the NMP-modified sample **NMP A**. Poly(*n*-butyl acrylate) was evidenced by the presence of a carbonyl peak at 1730 cm⁻¹. The NMP-modified sample **NMP A** shows three characteristic polystyrene peaks at 1600, 1494, and 1455 cm⁻¹ and a very small carbonyl peak of remaining poly (*n*-butyl acrylate).

to form a well-defined and consequently very thin monolayer, featuring only a little peak for its C=O stretch vibration at 1730 cm⁻¹. The grafted poly(*n*-butyl acrylate) of **4-2** features sufficient carbonyl groups to give a signal at around 1735 cm⁻¹. The reaction in solution above the substrate can give an indication for the coupling efficiency on the surface. For the solution reaction, a coupling

efficiency of 65% is calculated from SEC results. After degrafting, no carbonyl peak was observed, further underpinning the XPS and ToF-SIMS results, which indicate that the majority of polymer chains was coupled via reversible NMRC.

Finally, the NMRC-grafted substrate **4-2** was subjected to nitroxide-mediated polymerization (NMP) with styrene (**Scheme 4.3**). In this NMP reaction, styrene monomers are inserted when the thermolabile carbon-oxygen bond is reversibly cleaved into a carbon-centered radical on the surface and a nitroxide radical in solution. However, the nitroxide readily diffuses into the solution and consequently cannot be reused for reversible spin trapping. Thus, some polystyrene obtained from enhanced spin capturing polymerization (ESCP-polymer; 1.00 equiv.) and free stable free nitroxide TEMPO (0.12 equiv.) were added along with the monomer to allow for the swift reversible deactivation of the surface radical. The ESCP-polymer of PBN was used to have the very same nitroxide in solution and on the surface.



Scheme 4.3. Nitroxide-mediated polymerization was employed for chain insertion of styrene at 110 °C in the presence of 1.00 equivalent polystyrene obtained from enhanced spin capturing polymerization with PBN and 0.12 equivalents TEMPO, leading to **NMP A**. Chain extension in solution increased the molecular weight from $M_n = 2300$ to 37000 g·mol⁻¹. TEMPO endgroups are not displayed, yet they represent around 12% of all endgroups.

Furthermore, the addition of TEMPO was necessary to suppress any non-controlled polymerization via autoinitiation of styrene at 110 °C. Instead of TEMPO, an alternative free nitroxide can be used, yet TEMPO was chosen for its ready availability. TEMPO-based alkoxyamines, however, feature higher thermostability than PBN-based ones and are therefore primarily incorporated, leading to around 12% TEMPO-capped polymer chains. As the entire process represents an equilibrium, the high amount of ESCP-polystyrene polymer in solution compared to poly(*n*-butyl acrylate) on the surface clearly dominates the nitroxide exchange.^[38] Consequently, poly(*n*-butyl acrylate) was expected to be completely exchanged for polystyrene from ESCP polymer in **NMP A**.

The successful grafting of polystyrene was evidenced by the appearance of three characteristic aromatic C–H stretching vibrations at 1600 cm⁻¹, 1494 cm⁻¹, and 1455 cm⁻¹ as well as a small peak of the aromatic C–H deformation vibration at 1020 cm⁻¹ (**Figure 4.2**). As expected, no poly(*n*-butyl acrylate) remained on the surface due to the equilibrium with the ESCP polymer in solution. Blank samples exposed to the same reaction conditions showed no polystyrene signals, ruling out physisorption during NMP grafting. Further evidence for a successful NMP process was obtained from the solution above the silicon substrates. The molecular weight increased from *M*_n = 2300 to 37000 g·mol⁻¹ with a moderate rise of dispersity to 1.19 from 1.41 which is associated with constant initiation from the autopolymerization of styrene (**Figure 4.3**).


Figure 4.3. Size-exclusion chromatography of the reaction mixture obtained after the grafting of polystyrene via an NMP reaction shows a chain extension from 2300 to $37000 \text{ g} \cdot \text{mol}^{-1}$.

In a first conclusion, the NMRC of surface radicals with nitrones in solution allowed for successful grafting of the surface with polyacrylates chains. Degrafting or exchange with another type of polymer may in future proof to be very useful when the technique is combined, for example, with methods of spatiotemporal control such as photoNMP.

4.3.2 Nitrone-mediated radical coupling on flat surfaces

Our second approach reverses the above procedure in that the nitrone-species is immobilized on the surface and both radical reactants are located in the solution (bottom row of **Scheme 4.2**). The second approach requires more synthetic effort, yet has its charm in a potential combination with widely used [3+2] cycloadditions.^[39] However, nitrones are rather sensitive molecules, which readily undergo hydrolysis in the presence of acids,^[40] and further exhibit some sensitivity towards light that leads to intramolecular cyclization and eventually to the formation of amides.^[41] Given the low overall nitrone concentration present in a

surface monolayer, precautions are required when working with nitrones on surfaces. A specifically designed reactor is thus employed to avoid any exposure to light or acids (**Figure 7.3**).

To attach the nitrone onto the surface, a nitrone-carrying triethoxysilane was grafted in the dark under nitrogen atmosphere. In order to reduce photo degradation reactions, the functionalized substrates **4-4** were kept in a custom-made reactor flushed with copious amounts of dry solvents of different polarities before the NMRC reaction. Due to its sensitivity towards light and hydrolysis, the nitrone-functionalized substrate **4-4** could not be isolated as degradation occurs before analysis is possible. In contrast to the well-defined monolayers in **4-1**, triethoxysilanes generally lead to less well-defined yet thicker layers.^[42]

Subsequently, a poly(*n*-butyl acrylate) with bromine terminus was introduced in the presence of copper and PMDTA. Nitrone-mediated radical coupling subsequently proceeded via spin-trapping of radicals from solution. Here, in principle an alkoxyamine with two poly(*n*-butyl acrylate) arms to either side should be formed (structure **4-5**), in contrast to the first approach with the nitrone in solution, where only one arm is attached per nitrone moiety (**Scheme 4.2**). Degrafting experiments were performed in the presence of tributyltin hydride at 130 °C, leading to sample **4-6**.

As noted above, with the nitrone on the surface, the substrate has to be handled in the dark under nitrogen atmosphere and was hence used directly to obtain substrate **4-5**. The successful grafting of the nitrone-species (**4-4**) has been indirectly evidenced by the grafting of poly(*n*-butyl acrylate) proved via XPS (**Figure 4.4**, left). The C 1s spectrum of **4-5** shows a clear peak at 288.9 eV (O– C=O), associated with the polymer since the nitrone silane does only entail one urethane carbon. Moreover, a carbon ratio O-C=O : C-O, C-N : C-C, C-H. of 1 : 1.5 : 6.5 was found. While poly(*n*-butyl acrylate) alone shows a peak ratio of 1 : 1 : 5, the differences can be explained by the short chain length (*DP* = 10) of the employed poly(*n*-butyl acrylate) and the long spacer used for the nitrone in **4-4**. Further, a significant increase of the nitrogen concentration could be observed, which is associated with the successful grafting of the nitrone silane (**4-4**). Compared to the first approach with the nitrone in solution, qualitatively a higher surface coverage is obtained with around 36 at% total carbon in the XPS spectrum and a slightly higher contribution of the specific O-C=O component stemming from the polymer which shows here 3.8 at% compared to 2.5 at% in the case of the coupling in solution. However, the higher grafting density might also be associated with the less well-defined monolayer of the nitrone silane in **4-4** rather than with a better grafting of polymer in **4-5**. ToF-SIMS measurements



Figure 4.4. (left) C 1s XPS spectra of a **blank**, the PnBA-coated, **4-5**, and the degrafted, **4-6**, silicon substrates. (right) $500 \times 500 \ \mu\text{m}^2$ ToF-SIMS images of the respective steps from blank to degrafted sample are displayed. Intensity maps of the characteristic fragments of the grafted poly(*n*-butyl acrylate), C₄H₇O⁻ and C₄H₉O⁻, as well as of C₂H₄NO⁻ and SiO₃⁻.

further underpin the XPS results as depicted in **Figure 4.4** (right). While both blank and control samples (not displayed) do not show any poly(*n*-butyl acrylate) fragments, the NMRC-functionalized substrate **4-5** shows both the characteristic poly(*n*-butyl acrylate) signals $C_4H_7O^-$ and $C_4H_9O^-$ and the nitroxide-derivative $C_2H_4NO^-$.

Degrafting experiments (**4-6**) reduced the surface coverage with carbon in XPS from 36 at% to 20 at%, yet again left some tin compounds behind which are known to add to nitroxide radicals.^[43] Surprisingly, XPS showed again the removal of most of the O=C–O species, hence of the poly(*n*-butyl acrylate). This has been rather unexpected since the NMRC grafting with the nitrone on the surface involves the addition of two (polymeric) radicals of which only one is linked via a thermolabile carbon-oxygen bond. ToF-SIMS indicated almost no signal for $C_{4}H_{9}O^{-}$ and no signal for $C_{2}H_{4}NO^{-}$, suggesting removal of almost all poly(*n*-butyl acrylate) and nitroxides. $C_{4}H_{7}O^{-}$ fragments, however, were found and even less of the substrate fragment SiO₃⁻ was observed. It is possible that these $C_{4}H_{7}O^{-}$ fragments arise from the nitrone silane grafted in the previous step or from the attachment of tributyltin derivatives.

The GAATR-FTIR spectra show a carbonyl peak at 1730 cm⁻¹, the C–O–C asymmetric stretching vibration at 1263 cm⁻¹, and the C–O–C symmetric stretching vibration at 1105 cm⁻¹, evidencing the presence of poly(*n*-butyl acrylate). The absence of the respective peaks on the blank and the control samples demonstrates successful NMRC grafting (**Figure 4.5**). In addition, GAATR-FTIR shows the complete removal of the carbonyl species at 1730 cm⁻¹



Figure 4.5. GAATR-FTIR of the substrate after nitrone-mediated radical coupling (**4-5**), the degrafted NMRC-functionalized substrate (**4-6**), the NMP block formation with styrene in **NMP B**, and the degrafted NMP-sample **NMP Q**.

and most of the C–O–C asymmetric stretching vibration at 1263 cm $^{-1}$, thus successful degrafting.

Similar to the approach described above, sample **4-5** was subjected to chain insertion via nitroxide-mediated polymerization of styrene with ESCP-polystyrene and 12 mol% TEMPO as mediators, **Scheme 4.4**. In contrast to the NMP reaction described above in **Scheme 4.3**, the controlling nitroxide remained on the surface, potentially covered by some poly(*n*-butyl acrylate). Hence, steric

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hindrance can be of significant influence. For successful grafting, the growing polystyrene radicals need to able to access the surface, which becomes less likely with increasing chain length and grafting density. Steric hindrance may also be seen as the reason why there is almost no literature for this type of NMP-grafting.^[38] Finally, degrafting was performed at 130 °C in the presence of tributyltin hydride, giving **NMP Q**.

The NMP reaction and subsequent degrafting were investigated via GAATR-FTIR (**Figure 4.5**). The aromatic C–H stretching vibrations at 1600 cm⁻¹, 1494 cm⁻¹, and 1455 cm⁻¹ plus a small peak of the aromatic C–H deformation vibration at 1020 cm⁻¹ demonstrate the presence of grafted polystyrene.



Scheme 4.4. Nitroxide-mediated polymerization on **4-5** for chain exchange-insertion of styrene (pink) to give structure **NMP B**. Subsequent degrafting led to **NMP Q**.

Reversible Surface Engineering via Nitrone-Mediated Radical Coupling Because insufficient washing can lead to false positive results due to physisorption, control experiments on blank substrates were carried out to confirm the effectiveness of the washing procedure.

As expected, some poly(*n*-butyl acrylate) remained on the surface, as reflected by the C=O stretch vibration at 1735 cm⁻¹. After degrafting, no C=O stretch vibration was observed, yet the three characteristic peaks of polystyrene at 1600 cm⁻¹, 1494 cm⁻¹, and 1455 cm⁻¹. Thus, only the removal of poly(*n*-butyl acrylate) was successful, yet not of grafted polystyrene, indicating that grafting was rather uncontrolled despite the high concentration of added TEMPO radicals.

In conclusion, NMRC via surface-grafted nitrones allowed for grafting of poly(*n*-butyl acrylate) onto flat silicon substrates. Even though unexpected, the reaction seems to be fully reversible as shown via degrafting experiments. Subsequent NMP grafting provided a simple way to introduce a second functionality, yet NMP-grafting was not reversible.

4.3.3 Nitrone-mediated radical coupling on particles

While grafting-to reactions usually allows for the grafting of very well defined polymers, they often suffer from lower grafting densities due to steric hindrance. Based on the inherently very low overall concentrations in thin layers, it is very challenging to assess the grafting density on planar substrates. Higher amounts of grafted materials are obtained when particles instead of flat surfaces are employed due to the much higher total surface area. In addition, the higher amount of grafted nitrone reduces the problems of undesired degradation due to light or acids.



Scheme 4.5. NMRC grafting of poly(*n*-butyl acrylate) onto silica nanoparticles with surfacebound nitrone. a: silanization of a nitrone silane onto silica nanoparticles, b: NMRC grafting of poly(*n*-butyl acrylate) (blue).

Therefore, NMRC with surface-grafted nitrones was carried out on monodisperse silica particles with 60 nm in diameter (**Figure 4.6**) and a surface area of close to $50 \text{ m}^2 \cdot \text{g}^{-1}$ (**Scheme 4.5**). Monodisperse nanoparticles were produced from tetraethoxysilane and functionalized with nitrone silane prior to washing. Subsequently, poly(*n*-butyl acrylate) was grafted under NMRC conditions. The high surface area of the nanoparticles allowed for the use of thermogravimetric analysis (TGA). While XPS was used to confirm the presence of the grafted nitrone and poly(*n*-butyl acrylate) (**Table 7.2** for integration ratios), respectively, the combination of DLS and TGA gives a good indication of the grafting density.

In order to prevent centrifuge- and ultrasound-induced aggregation prior to DLS measurements, the particles were dialyzed to remove excess reagents after grafting. The pore-size of the used semipermeable membrane was chosen to allow for the complete removal of both small silane aggregates and polymer species. In addition, all particles were centrifuged three times prior to TGA. **Figure 4.7** shows the TGA results for the nitrone-coated (left) and the polymer-coated silica nanoparticles (right), respectively. Both relative weight loss (solid black line) and



Figure 4.6. (left) Dynamic light scattering of before and after nitrone-mediated radical coupling. (right) Corresponding autocorrelation functions.

its derivative (dashed blue line) are depicted. Note that not all weight loss could be associated with loss of thermolysis of organic material. The blank silica nanoparticles indicated a constant weight loss until around 600 °C, which is associated with condensation reactions and leads to a relative mass loss of approx. 10% at 600 °C. Nitrone-coated particles showed four mass loss events: the first at around 100 °C, the second at around 200 °C, the third (small) one at 300 °C and finally the fourth one (broad) at around 500 °C. The first peak is associated with the loss of solvent. The nitrone-functionalized particles are prone to undergo degradation at higher temperature and were therefore dried for 2 days in high vacuum only at room temperature prior to TGA. Traces of remaining solvent and potential water absorption due to their high hygroscopicity were consequently associated with the first peak. The second and third mass loss are also associated with the grafted nitrone species as TGA of the pure nitrone silane shows them very prominently (Figure 4.8, left side). The fourth peak at around 500 °C, however, does not match the TGA result of the pure nitrone silane. It is ascribed to the loss of silanol groups that were rapidly formed from ethoxy groups in basic (aqueous) solutions during the sol-gel synthesis.[44, 45]



Figure 4.7. Thermogravimetric analysis of silica nanoparticles (left) functionalized with a nitrone silane and (right) functionalized via NMRC with poly(*n*-butyl acrylate). Relative weight loss in black, differential weight loss in blue.

The polymer-coated nanoparticles showed four different mass losses: narrow peak at 50 °C and two broad ones at 200 and 400 °C, respectively. The first one at around 50 °C was again assigned to the loss of solvent. In contrast to the nitronecoated nanoparticles, the polymer-coated ones were dried at 70 °C in high vacuum and therefore only showed little loss of solvent, probably water absorbed from air. The second peak at 200 °C is much broader than for the nitrone-coated particles. It actually entails two contributions, first of the nitrone around 190 °C, and a second closer towards 230 °C from the poly(*n*-butyl acrylate) (**Figure 4.8**, right side). The third peak at 400 °C entails a very high portion of poly(*n*-butyl acrylate) degradation.

In contrast to the previous step, no mass loss at 500 °C was observed. Potential explanations could be a more advanced condensation reaction in non-aqueous solutions and the complexation of silanol by copper(II) ions,^[46] which also explains the light blue color of the particles.

To calculate an approximate grafting density, we consider the weight loss between 225 °C and 450 °C, which minimizes the contribution of the silanol condensation

and covers the entire decomposition range of pure poly(*n*-butyl acrylate). The difference in mass loss between nitrone@SiO₂ and PnBA@SiO₂ is 2.77 %. Based on a diameter of around $d_{\text{DLS}} = 60$ nm and silica density $\rho = 2.0$ g·cm⁻³, a grafting density $\sigma = 0.21$ nm⁻² is estimated.

Very efficient grafting-to reaction afford grafting densities in the range of 0.1 – 0.6 (thiol-ene)^[47], 0.3 – 1.2 (Huisgen Cycloaddition),^[48] and 0.1 chains·nm⁻² (hetero-Diels-Alder)^[49, 50]. In addition, most grafting-from reactions do not yield higher grafting densities. Pre-synthesized RAFT agents for surface-modification often lead to grafting densities below 0.8 initiators·nm⁻² and typical ATRP initiators yield between 1 and 5 initiators·nm⁻².^[12, 51] However, after subsequent grafting-from reactions, the grafting density of the polymer brushes is often only 0.1 – 0.5 chains·nm⁻² as just small fraction of the initiator sites is actually used for surface-initiated ATRP.^[12, 51] Thus, our grafting density of $\sigma = 0.21$ nm⁻² is in the range of other efficient grafting-to procedures and of many reported grafting-from protocols.^[12]



Figure 4.8. Thermogravimetric analysis of (left) the employed nitrone silane and (right) of the employed poly(*n*-butyl acrylate).

4.3.4 Particles with tunable radical concentration on their surface

Particles featuring a tunable amount of nitroxide radicals are accessible via a variation of the nitrone-mediated radical coupling approach described above. When the only provided radical source, e.g. an ATRP initiator, is covalently anchored to the surface of a particle, the NMRC reaction stops at the nitroxide stage if the radicals are trapped by a nitrone before they undergo radical annihilation reactions. We have chosen silica microparticles of 63 – 200 µm in diameter as very readily processable model substrate for our investigations. Later on, the same methodology was also applied to ZnO-, BaTiO₃-, and silicon nanoparticles of which the first two are very interesting for second harmonic imaging microscopy.^[52-54]



Scheme 4.6. NMRC on silica microparticles. a: Silanization with a suitable ATRP initiator trichlorosilane. b: Formation of nitroxide radicals on the surface via NMRC without counterpart.

The microparticles were washed, activated with piranha solution and subsequently dried in high vacuum. The dry particles were immersed in a concentrated solution of an ATRP silane (**Scheme 4.6**). After the reaction, the particles were extensively washed and used for the same NMRC grafting as described on the top row of **Scheme 4.2**, yet without a polymer counterpart in solution. Consequently, the reaction stops at the nitroxide stage, yielding surface-bound radicals. In **Figure 4.9**, the EPR spectra of silica microparticles carrying a nitroxide exposed to different amounts of nitrone in otherwise the same reaction mixture are shown on the left-hand side. As expected, if the experiment is carried out in absence of

nitrone no detectable EPR signal is observed. With increasing nitrone concentration in the reaction mixture, the EPR signal increased, too. Double integration of the recorded EPR signals yields in principle the radical concentration when referenced against a TEMPO calibration curve. TEMPO calibrations are often used in EPR, yet in our case we have to stress that the comparison of surface-bound nitroxides with nitroxides in solution is a good tool for comparison of different measurements, yet might not be a perfect fit for the determination of absolute concentrations.

The right side of **Figure 4.9** shows the radical concentration is linearly dependent on the employed nitrone concentration, giving access to particles with a tunable radical concentration. The thermal stability of these nitroxide-carrying microparticles was assessed under nitrogen atmosphere at ambient temperature, 7 °C and –15 °C, respectively, over the course of 82 days (**Figure 4.10**, left side).



Figure 4.9. (left) EPR spectra of silica microparticles treated with different amounts of PBN. (right) double integrated EPR spectra referenced against a TEMPO calibration curve. The evolution radical concentration in mmol as function of the used mass ratio of PBN to silica microparticles is shown.

In the freezer, the nitroxide concentration remained almost constant over the entire observation period, whereas already in the fridge, 25 % was lost within the first 40 days and even 65 % at room temperature.

When used for ZnO-, $BaTiO_3$ -, and silicon nanoparticles, silicon showed the strongest, $BaTiO_3$ the weakest nitroxide concentration, suggesting that silanization worked more effectively on silicon than on $BaTiO_3$ (**Figure 4.10**, right side).^[52, 55]



Figure 4.10. (left) Thermal stability of the nitroxide species on silica microparticles at 22, 7, and -15 °C. (right) EPR spectra of nitroxide-decorated nanoparticles: silicon (black), zinc oxide (red), and barium titanate (blue). The signal intensity was normalized to mass of the respective nanoparticles.

4.4 Summary and conclusions

Nitrone-mediated radical coupling is exploited to reversibly graft poly(n-buty)acrylate) via an alkoxyamine that allows for subsequent NMP. Two routes were explored, once with the nitrone species in solution and once on the surface. Both approaches resulted in grafted poly(n-butyl acrylate) on planar silicon substrates. Degrafting experiments indicate that nitrone coupling can be used for reversible grafting of surfaces and concomitantly ruled out a potentially concurrent atom transfer radical coupling for both approaches. Subsequent modification via nitroxide-mediated radical polymerization, however, functioned better for the route with the nitrone initially in solution. In addition, the grafting density of the grafted-nitrone approach was assessed on silica particles to be close to 0.21 chains per nm², placing NMRC in the range of other efficient grafting-to and many grafting-from techniques.^[12] Critically, particles with tunable radical concentration were generated and characterized via EPR. In summary, we demonstrate that reversible nitrone-mediated radical coupling is a powerful alternative for surface modification and for the introduction of surface-bound radicals, which recently have been shown to possess potential for overcoming drug resistance in epidermoid cancers.^[56]

4.5 References

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Chapter 5

Synthesis of Polyzwitterionic Polymers via Thiol-Ene Michael Addition of Cysteinyl Cysteine



5.1 Abstract

A novel approach for the synthesis of polyzwitterions with charges along the polymer backbone is presented. Nucleophilic thiol-ene Michael addition was employed to polymerize the dipeptide cysteinyl cysteine and tetra(ethylene glycol)diacrylate in a step-growth polymerization. ¹H-NMR and SEC evidenced the successful polymerization and pH-responsive behavior was underpinned by DLS. Amphiphilic ABA triblock copolymers were synthesized via subsequent thiol-ene Michael addition of poly(benzyl acrylate) with thiol endgroup. Aggregate sizes of 250 nm in diameter were obtained from DLS and pH responses were observed at pH below 3 and above 12. Concomitantly, an optimized synthesis procedure for cysteinyl cysteine was developed.

5.2 Introduction

Synthetic polymers carrying ionic groups are of great importance for many applications, e.g. as superabsorber in diapers or antifouling coatings. Even more than non-ionic hydrophilic polymers, polyzwitterionic polymers strongly bind water and are therefore better suited for antifouling coatings as dehydration of both adsorbent and surface are necessary steps in any adsorption process.^[1, 2]

Polyzwitterions are sometimes also called "polybetaines", yet the term is inconsistently used in literature.^[1, 3-5] Both terms refer to structures with both positive and negative charges. IUPAC further defines that "polybetaines cannot be presented without formal charges".^[6] In the present chapter, only the term (poly)zwitterion is used to refer to all structures with both positive and negative charges. Besides polyzwitterions, there are polyelectrolytes as class of charged materials that carry either positive or negative charges. Positive charges are often Polyzwitterionic Polymers via Thiol-Ene Michael Addition of Cysteinyl Cysteine introduced by secondary and tertiary amines or quaternary ammonium, whereas negative charges can come from carboxylates, phosphonates and sulfonates.^[3]

Interestingly, polyelectrolytes and polyzwitterions feature opposite behavior upon addition of a low molecular weight electrolyte.^[3] In polyelectrolytes, repulsive electrostatic forces are then effectively shielded off which leads to a polymer coil shrinkage and is called polyelectrolyte effect.^[3] Polyzwitterions, however, may react with coil expansion upon shielding off attractive electrostatic forces, therefore named as antipolyelectrolyte effect.^[3] Antipolyelectrolyte effects are structure-dependent and usually obtained for polyzwitterions with near charge balances, while block structures with large charge balance rather behave like polyelectrolytes.^[3] This potential change of morphology is especially important since polyelectrolytes do not possess antifouling properties but rather facilitate protein adhesion.^[7, 8]

When polyzwitterions are made via ATRP,^[9, 10] a hydrophobic carbon chain, the polymer backbone, is built up and zwitterions can only be present in the side chain. Moreover, monomers with short carbon spacers between ionic groups possess better antifouling properties than those with longer spacers.^[11] With respect to these findings, a polyzwitterionic polymer with a high density of alternating cat- and anionic groups along the backbone should feature an even higher antifouling potential.

As alternative for radical polymerization that result in a hydrophobic polymer backbone, highly efficient conjugation reactions such as nucleophile-catalyzed thiol-ene Michael addition can be used for step-growth polymerization that does not necessarily have a hydrophobic backbone.^[12] Linear polymers made from dithiols and diacrylates were reported with molecular weights up to

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10400 g·mol⁻¹.^[13] Control over molecular weight was achieved by adjustment of the stoichiometry. In contrast to polymers obtained by radical polymerization, the formed poly(β -thioesters)s were degradable, potentially under physiological conditions. Insoluble networks were produced when the diacrylate was exchanged for a multifunctional crosslinker.^[14] Addition of only 10 mol% crosslinker to the diacrylate resulted in soluble hypercrosslinked polymers of a molecular weight up to 10^6 g·mol⁻¹. Successful degradation was observed in acidic and basic environment. The same approaches was employed for the formation of functional nanoparticles^[15] and for a photoinduced version for photopatterning and temporal control over network formation.^[16]

Instead of low molecular weight building blocks, also macromonomers obtained from RAFT polymerization of bifunctional RAFT agents can be employed.^[17] The combination of RAFT polymerization and thiol-ene Michael addition allowed for the synthesis of polymeric structures whose properties were strongly determined by the macromonomers, yet showed biodegradability.^[17]

Herein, a novel approach to access polyzwitterions is presented. Nucleophilecatalyzed thiol-ene Michael additions was employed to polymerize the zwitterion and dithiol cysteinyl cysteine with tetra(ethylene glycol)diacrylate in a stepgrowth polymerization. ¹H-NMR and SEC results evidence the successful polymerization and pH-responsive behavior was observed by DLS. Amphiphilic ABA triblock copolymer structures were generated by conjugation of thiolendcapped poly(benzyl acrylate) and DLS was employed to shed light on the aggregation behavior upon change of pH. Concomitantly, an improved protocol for the synthesis of cysteinyl cysteine is presented. The project is still ongoing and preliminary results are presented.

5.3 Results and discussion

As for other dipeptides,^[18-20] the synthesis of cysteinyl cysteine requires the use of protection groups and a multistep procedure (**Scheme 5.1**). We based our synthesis on a protocol described in literature^[21] and developed it further to circumvent column chromatography, avoiding protection of the carboxyl group and therefore allowing for a shorter protocol. Therefore, the reaction can readily be upscaled.

First, the thiol group of cysteine **5-1** was protected with a triphenylmethyl protection group, followed by protection of the amine with a Boc-group. Afterwards, the carboxyl group was activated to give a reactive NHS-ester **5-4**. The protected dipeptide **5-5** was formed by the reaction of **5-2** and **5-4**. The desired product **5-6** was ultimately reached after removal of the protection groups with trifluoroacetic acid and subsequent precipitation in hexane to yield the salt-free **5-6**.



Scheme 5.1. Synthesis procedure from cysteine to cysteinyl cysteine. a: *S*-protection using triphenylmethanol, b: *N*-protection via Boc₂O, c: formation of a reactive *N*-hydroxysuccinimide ester via EDC coupling, d: dipeptide formation from **5-4** and **5-2**, e: deprotection of *S*- and *N*- groups in trifluoroacetic acid.

Characterization of the intermediate steps is challenging because of impure intermediate products and only the final product **5-6** could clearly be identified via ¹H-NMR (**Figure 5.1**). Due to low solubility of neutral **5-6**, some trichloroacetic acid was added and subsequently removed under reduced pressure. The residue was characterized via ¹H-NMR. Coupling constants and integration values matched well, however the signal assigned to the proton in a-position (magenta) to the COOH group showed 0.5 protons too much which could not be explained. The signals of the thiol protons were shifted to 3.38 and 3.17 ppm, respectively, which is attributed to their interaction in water.



Figure 5.1. ¹H-NMR of cysteinyl cysteine **5-6**. All peaks have been assigned via peak integration (above color label) and comparison of coupling constants. red: J = 4.3, 7.9 Hz, magenta: J = 4.3, 5.5 Hz, orange: J = 4.3, 15.2 Hz, grey: J = 7.9, 15.2 Hz, green: J = 5.6, 15.2 Hz, blue: J = 4.3, 15.2 Hz.



Figure 5.2. Titration curve of cysteinyl cysteine **5-6** dissolved in 0.1 M HCl upon addition of 0.1 M NaOH solution. Equivalence points at pH = 5.13 and 10.13 determined from first derivative.

Cysteinyl cysteine **5-6** was titrated against 0.1 M NaOH solution to obtain both the equivalence points and the isoelectric point. Two equivalence points were observed at 5.13 and 10.13, respectively. For (slightly) acidic dipeptides such as cysteinyl cysteine, the first equivalence point also corresponds to the isoelectric point at which the molecule has zero net charge.^[22] At the isoelectric point, the solubility is strongly reduced and can be improved by addition of salt due shield off contracting opposite charges.





To get the target polyzwitterionic structure, **5-6** was subjected to thiol-ene Michael addition with a diacrylate (**Scheme 5.2**). Due to the very low solubility of **5-6** in organic solvents, the slightly water-soluble tetra(ethylene glycol)diacrylate was chosen. High degrees of polymerization in step-growth polymerizations can only be reached for high conversions (**Figure 1.1**). Therefore, stoichiometric concentrations have to be chosen for both reactants. Since it was probable that some trifluoroacetate salt remained in **5-6**, **5-6** was dissolved in water at pH = 9 and a small excess of diacrylate in ethanol/water was added dropwise. Dropwise addition was such that the added diacrylate solution was continuously diluted to approach (and exceed) the actual concentration of **5-6** very slowly. Upon addition of the diacrylate, the polymer precipitated directly to form a sticky solid on the magnetic stirrer.

The polyaddition product was characterized via ¹H-NMR (**Figure 5.3**). The presence of the ethylene glycol protons indicates the successful formation of the desired polyzwitterion **5-7**. The almost complete disappearance of the vinylic protons indicates high molecular weights of the precipitated polymer since the diacrylate was employed in access. Alternatively, the precipitation of **5-7** could have stopped the reaction at low conversion after the addition of few **5-6** units, explaining the missing acrylate endgroups. Because of the very low solubility of **5-6** in water at pH = 7, **Figure 5.3** shows the corresponding trichloroacetate which is therefore shifted towards the low field compared to the respective peaks of polyzwitterion **5-7**.



Figure 5.3. ¹H-NMR spectra of $H(5-6)^+$ CCl₃COO⁻ (black), tetra(ethylene glycol)diacrylate (red), and their addition product **5-7** after thiol-ene Michael addition (blue) in D₂O. a: CH-NH₃, b: CH-COOH, c: SH, d: CH₂–S, e: vinylic protons, f: CH₂–COO, g: CH₂–C–COO, h: O–CH₂–CH₂–O, i: S–CH₂–C–COO, j: S–C–CH₂–COO.

Size-exclusion chromatography of the formed polymer **5-7** was performed in water or DMF. It is very challenging to get a good idea of the molecular weight because of strong aggregation. **Figure 5.4** shows the DMF-SEC elugram of a **5-7**-type polyzwitterion. A bimodal distribution is shown. To get an indication about the actual molecular weight, different calibration files were used and their results are given in the table on the right side of **Figure 5.4**. Molecular weights range from 1400 g·mol⁻¹ (PEG calibration) to 2400 g·mol⁻¹ (PS calibration), suggesting the formation of oligomers. Dispersities ranged between 1.25 and 1.31. As for step-growth polymerization, dispersity is directly linked to the conversion *x* in the



Figure 5.4. (left) Elution volume of **5-7** on DMF-SEC. (right) Results for M_n , M_w and D for different sets of MHKS parameters.

relation $\mathcal{D} = 1 + x$,^[23] the low obtained dispersities suggest a likewise low conversion in contrast to ¹H-NMR. However, the polymer **5-7** precipitated rapidly upon formation. It is possible that only the higher molecular weight fractions precipitated, while the first addition products remained soluble and were not characterized.

Complementary information was obtained via pulsed-gradient spin echo (PGSE) ¹H-NMR. Measurements were performed in D₂O and methanol-d₄ and both gave a very similar diffusion coefficient factor of around $2.17 \cdot 10^{-10}$ and $2.26 \cdot 10^{-10}$ m²s⁻¹. With viscosity values for D₂O and methanol-d₄ taken from literature, ^[24, 25] Stokes-Einstein's equation translates these results into hydrodynamic radii of only 0.80 nm in D₂O and 1.80 nm deuterated methanol, further supporting the DMF-SEC results depicted in **Figure 5.4**. The observed solvent dependence could indicate different aggregation behavior or solubility in D₂O and methanol-d₄.

Other batches of **5-7**, however, showed very different molar masses (on water-SEC), even though the same protocols were used. The left side of **Figure 5.5**



Figure 5.5. Elugrams on water-SEC with UV (red) and RI (black) detectors of two samples prepared with the same protocol. (left) broad, multimodal distribution of a sample of low molecular weight (right) sample of high molecular weight.

shows two multimodal molar mass distributions with an elution volume $V_{\rm E}$ of 7.4 – 9.2 mL and 9.4 – 9.9 mL, translating into molar masses (with MHKS parameters of PS) from 25000 to 2000 g·mol⁻¹ and from 1500 to 500 g·mol⁻¹, respectively.

RI and UV signals overlap quite well, indicating a potentially low degree of aggregation.^[26] Another sample of type **5-7** shows a more condensed signal shifted to lower elution volumes, 6.6 mL in UV and 6.8 mL in RI detection (right side of **Figure 5.5**). Based on the MHKS parameters of PS, molar masses were in the range of 10⁵ g·mol⁻¹. The differences in UV- and RI-signals indicate also that the polymer chains were aggregating to some extent.

A solubility gap between pH = 10.8 and 12 has been evidenced via turbidity measurements (**Figure 5.6**, left side). When an aqueous solution of 5 mg·mL⁻¹ of **5-7** with molecular weight in the range of 10^5 g·mol⁻¹ (MHKS parameters of PS) was titrated with NaOH, a strong increase in turbidity was found around pH = 10.8, quantified via a photospectrometer (λ = 650 nm) connected to a

titration set-up via a photoflow cell. The solution turned milky before it formed rather discrete flakes that were inhomogeneously distributed in the solution, which increased the scattering of the data points. Flake formation was probably due to bad or soft mixing inside the flow cell and tubing. Upon further addition of NaOH, the solution became clear again and the flakes redissolved. At concentrations of approximately 1 mg·mL⁻¹ of **5-7** in water, no precipitation upon increase of pH above 10.8 was found. The bare presence of the solubility gap at pH = 10.8 is counterintuitive as no polyzwitterions should be present and repulsive electrostatic forces should break up aggregates effectively. At pH = 10.8, the ammonium group gets deprotonated, leaving only the negative charges of carboxylate groups and thus an electrostatic repulsive force.

Moreover, a pronounced antipolyelectrolyte effect is observed. While the product is hardly soluble at pH = 7, it becomes soluble upon addition of NaCl – either directly or as part of a titration cycle. Hence, repeated crossing of pH = 10.8 does not lead to a repeated precipitation.



Figure 5.6. (left) Light absorption (650 nm) of a solution of high molecular weight **5-7** upon increase of pH from 8 to 11. (right) Number average diameter of low molecular weight **5-7** determined via DLS at different pH.

Polyzwitterionic Polymers via Thiol-Ene Michael Addition of Cysteinyl Cysteine Additionally, DLS was used to determine aggregate sizes of the sample depicted in **Figure 5.4** at different pH (**Figure 5.6**, right side). All diameters are given as number average values and the approximate concentration of **5-7** in water was 1 mg·mL⁻¹.

Strong aggregation (diameter above 10 μ m) was observed around neutral pH, so close to the isoelectric point of the monomer **5-6**, **Figure 5.2**. However, **5-7** dissolved readily in water without traces to the naked eye, whereas **5-6** was insoluble at pH = 7 without addition of salt. At pH = ~1 and ~12, the polyzwitterion **5-7** formed aggregates of 38 and 62 nm, respectively. Otherwise, no aggregation was observed, which is ascribed to the low concentration.

Finally, **5-7** was conjugated to poly(benzyl acrylate) **PBnA-RAFT** with thiol endgroup obtained from RAFT polymerization and its subsequent aminolysis of the

DoPAT RAFT-agent (**Scheme 5.3**). The RAFT polymer was employed together with some drops of tributylphosphine to prevent disulfide formation. For DLS measurements, the reaction mixture was used without prior purification. For SEC characterization, the solvent was removed under reduced pressure. **PBnA-RAFT** featured $M_n = 9800 \text{ g} \cdot \text{mol}^{-1}$ and $\mathcal{D} = 1.11$.



Scheme 5.3. Thiol-ene Michael addition of **5-7** and poly(benzyl acrylate) with thiol endgroup **PBnA-RAFT** to give the ABA triblock copolymer **5-8**.



Figure 5.7. (left) Molecular weight distributions from DMF-SEC for **5-7** (red) and **5-8** (black) and from THF-SEC for **PBnA-RAFT** (blue). **5-8** also shows the peak of **PBnA-RAFT** as it was measured without any purification. (right) DLS measurement of **5-8**: Number-average diameter plotted against pH.

Figure 5.7 depicts the SEC and the DLS results of **5-8**. SEC traces of **5-7** (red), the RAFT polymer **PBnA-RAFT**, and **5-8** (black) are depicted. **5-7** and **5-8** were measured on the same DMF-SEC, while **PBnA-RAFT** was obtained on a THF-SEC. To allow for comparison, molecular weights obtained from calibration with polystyrene standards are compared. **5-8** shows a bimodal distribution with a maximum at a slightly higher mass than **PBnA-RAFT**, indicating the addition of only one RAFT polymer to **5-7**. The second peak of **5-8**, however, comes at a molecular weight that is more than double of **PBnA-RAFT**, evidencing the desired addition of two RAFT polymers to **5-7**.

On the right side of **Figure 5.7**, the number-average diameters (DLS) are plotted against the pH. Aggregate sizes ranged from 180 to 1500 nm and were pH-dependent. Below pH = 3 and above pH = 12, aggregates of more than 250 nm in diameter were formed. While fully hydrophilic **5-7** showed almost no aggregation besides very low solubility at neutral pH and at pH = 10.8, the

Polyzwitterionic Polymers via Thiol-Ene Michael Addition of Cysteinyl Cysteine amphiphilic structure of **5-8** did not allow for complete dissolution, yet also seemed to prevent the solubility gap. It appears that conjugation to poly(benzyl acrylate) stabilizes the aggregates and reduces the susceptibility towards precipitation. Only below pH = 3 and above pH = 13, aggregate sizes increased up to 1500 nm.

5.4 Summary and conclusions

A novel approach for the synthesis of polyzwitterionic polymers from the dipeptide cysteinyl cysteine and tetra(ethylene glycol)diacrylate via nucleophilic thiol-ene Michael addition was presented. ¹H-NMR showed the disappearance of the acrylate endgroups and indicated the formation of a polymer. SEC, however, showed only oligomers in DMF which was supported by PGSE ¹H-NMR. For other samples of the polymer molar masses up to more than 20 kg·mol⁻¹ were found. The aggregation behavior was investigated via DLS and pH responsiveness that could be underpinned via turbidity measurements that showed a solubility gap for pH > 10.8 for solutions of more than 5 mg·mL⁻¹.

ABA triblock copolymers were formed via conjugation to poly(benzyl acrylate) with a thiol endgroup and featured stable aggregates over the entire pH scale.

5.5 References

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Chapter 6

Influence of Light Intensity on Photo-

Induced Radical Thiol-Ene Reactions



6.1 Abstract

Photoinduced coupling reactions have been employed for many years, yet often little or no information on light intensities has been reported. We investigated the influence of light intensity on ene conversion of photoinduced radical thiol-ene reactions of 3-butenol (0.1 M) and 1-octanethiol (0.1 M) with DMPA (0.001 M). Light intensities ranged from 0.93 to 12.2 mW·cm⁻² in milliflow and from 20 to 40 mW·cm⁻² in microflow. After only a few minutes reaction time, the lowest light intensities gave the highest conversions for both reactors, ultimately however, almost identical conversions were obtained. Even though the beneficial character of lower light intensities decreased with increasing reactant concentration, the reaction at 0.25 mol·L⁻¹ and 3.01 mW·cm⁻² yielded higher ene conversion than the one at 0.5 mol·L⁻¹ and 12.2 mW·cm⁻² at almost no cost of reaction speed. Similarly, higher photoinitiator concentrations reduced the efficiency gain of lower light intensities. Consequently, decreased light intensity might be a very straightforward way to deal with less concentrated solutions.

6.2 Introduction

Thriving for more complex architectures and functions, efficient conjugation reactions have gained significant attention since the introduction of the 'click' concept by Sharpless and Finn.^[1, 2] Nucleophilic thiol-ene additions to Michael acceptors are highly efficient conjugation reactions^[3] and are well-suited for stepgrowth polymerizations (also Chapter 5).^[4-6] However, also radical thiol-ene reactions have often been handled as 'click'-type reactions in literature, especially for the conjugation of small molecules.^[7-10] The 'click' attribute is however misleading for radical thiol-ene couplings as they are not orthogonal. Step-growth polymerizations were reported to result in homopolymerization of the
Influence of Light Intensity on Photoinduced Radical Thiol-Ene Reactions (meth)acrylate species and only little formation of the desired thiol-ene coupling product.^[11] A more detailed study shed light on the limitations of radical thiol-ene coupling for polymer-polymer conjugation.^[12] While conjugation of polymers with an excess of small molecules gave near quantitative yields, detailed study of products obtained for polymer-polymer conjugation revealed only 25% coupling efficiency. Neither longer reaction times nor change in radical flux (= use of other light sources) nor 5-fold excess concentration of one of the reactants led to a significant improvement in yield. Instead, random biradical termination products dominated. Detailed kinetic investigations elucidated the reasons behind this loss of efficiency for polymer-polymer coupling.^[13] Simulations showed an increasing amount of side reactions with decreasing reactant concentrations because of the bimolecular nature of the chain transfer mechanism of the radical thiol-ene couplings (Chapter 1.5.2) in contrast to the unimolecular decomposition of the radical initiator.^[13] Consequently, near-quantitative coupling efficiencies were only observed for high reactant concentrations ($>0.1 \text{ mol} \cdot L^{-1}$) and simultaneously low radical concentrations (<0.05 mol·L⁻¹).^[13] As polymers cannot reach such high concentrations, radical concentrations would have to be strongly reduced, leading to unfeasibly low reaction rates. A very recently published report, however, contradicts the conclusion of very inefficient polymer-polymer conjugation.^[14] Coupling efficiencies up to 91% were reported for the conjugation of norborneneterminated PEG with thiol-functionalized PEG using an ammonium persulfate as redox catalyst. Both the ene endgroup and the radical source had significant impact on the conjugation product yield.

With the strong influence of the radical concentration on the coupling efficiency, the decomposition rate of the initiator moves into the focus of attention. While there is much data about the decomposition rates of thermal initiators, the influence of light intensity on the decomposition of photoinitiators is hardly known. In an early study, a reaction rate proportional to the square root of the light intensity was reported for radical thiol-ene reactions.^[15] However, due to the close connection of light intensity and illumination efficiency, reactor design plays a crucial role for any kinetic investigation.

Continuous milliflow reactors with defined dimensions can help to ensure comparable conditions.^[16] Continuous flow has been used for a long time in industrial chemistry, yet has only slowly found its way into lab scale and fine chemical synthesis.^[17] For the past 20 years, especially microreactor technology has gained significant attention, both in organic synthesis and polymer chemistry.^[18, 19] Improved heat transfer, on- and in-line characterization,^[20-22] straightforward scalability,^[23] and multi-step synthesis in a single reactor^[24, 25] are some of the distinct advantages that can be exploited in continuous reaction set-ups.^[16, 26] On the other side, precipitation, viscosity, and other parameters pose more severe limitations in flow compared to batch, making a careful case-to-case decision necessary.^[27]

One of the biggest constraints of photoreactions is the low illumination efficiency arising from the optical density of the reaction mixture. From the Beer-Lambert law, it is known that light intensity decreases exponentially within a light-absorbing liquid. To overcome this limitation, photoreactions can be carried out in continuous flow reactors that provide shorter path lengths than batch reactors (**Figure 6.1**).^[16, 26, 28] The significant impact of efficient illumination in flow reactors is best visualized by the speed-up of otherwise very slow [2+2]

Influence of Light Intensity on Photoinduced Radical Thiol-Ene Reactions cycloadditions, which can be accelerated from several hours to a minute reaction time when switching from batch to flow operation.^[29, 30]

The present chapter sheds light on the influence of light intensity on the ene conversion of the radical thiol-ene reaction of 3-butenol and 1-octanethiol with DMPA as photocatalyst. The reaction was carried out in milli- and microflow reaction set-ups and for 0.1, 0.25, and 0.5 M reactant concentrations. Finally, two different DMPA concentrations were compared.



Figure 6.1. Light intensity profile in a batch reactor (left), a tubular flow reactor (right), and Beer-Lambert law (middle). Reproduced from reference [28] with permission from The Royal Society of Chemistry.

6.3 Results and discussion

Our goal was to test the hypothesis that the fast and complete decomposition of the photoinitiator limits the ene conversion, as the chain transfer reaction requires an initiator to abstract the hydrogen atom of the thiol.

For our study, both milli- and microflow reactors were employed. Milliflow reactors were illuminated with a 15 W fluorescent tube, whereas microflow reactors were operated with an OmniCure UV source with both 365 nm as emission maxima. The light intensities were assessed via a photometer and adjusted by changing

the distance from the fluorescent lamp (milliflow) and by changing the iris opening of the OmniCure system (microflow).

As starting point, we chose conditions that were found to yield quantitative ene conversion in simulation studies.^[13] First, the radical thiol-ene reaction of 0.1 M 3-butenol and 0.1 M 1-octanethiol with 0.01 equivalents DMPA was carried out in acetonitrile (**Scheme 6.1**).



Scheme 6.1. Radical thiol-ene reaction of 3-butenol and octanethiol with DMPA as photoinitiator upon exposure to UV light of 365 nm.

For our first reaction in milliflow, a light intensity of 12.2 mW·cm⁻² was chosen, while 2 mW·cm⁻² were reported for the kinetics study in literature.^[13] As illumination efficiencies are rather low in batch reactors according to the Beer-Lambert law, the actual light intensities with respect to the average volume segment of the batch reactor used in literature were probably significantly lower.

Figure 6.2 depicts the conversions obtained for various reaction times in a milliflow reactor. Conversions were determined by ¹H-NMR spectroscopy and suffer from an uncertainty due to challenging baseline adjustment because of high solvent peaks. Nevertheless, they provide a good indication of the trend. The graph reflects two phases of the reaction. The reaction showed very high conversion rates that decreased rapidly to almost 0, yielding an ene conversion of approximately 72% within the first minute. The second phase was dominated by a plateau of very low conversion. Eventually, roughly 86% conversion was reached after 20 min.



Figure 6.2. Ene conversion versus reaction time for photoinduced radical thiol-ene reaction of octanethiol and 3-butenol under equimolar conditions at $0.1 \text{ mol} \cdot \text{L}^{-1}$ in milliflow upon exposure to light of 365 nm in the presence of 0.001 mol·L⁻¹ DMPA. The light intensity was 12.2 mW·cm⁻².

On first sight, our hypothesis seems to be confirmed, even though the reaction did not stop completely after decomposition of the initiator. Consequently, light intensities were systematically screened for the thiol-ene reaction of 3-butenol and 1-octanethiol. Different light intensities were obtained by varying the distance of the fluorescent lamp to the milliflow reactor. The reaction was carried out for reaction times ranging from 2 s to 360, **Figure 6.3** on the left side. For the lowest light intensity of 0.93 mW·cm⁻², an induction period, probably due to oxygen contamination, and the lowest initial conversion within the first 10 s rate were found. Similarly for 3.01 mW·cm⁻², a very small induction period was observed, followed by a significantly faster conversion rate within the first 10 s. No induction period was observed at 6.41 and 12.2 mW·cm⁻² as small oxygen contaminations had little influence on the light radical flux achieved at higher light intensities.



Figure 6.3. Radical thiol-ene reaction of octanethiol and 3-butenol. 3-Butenol conversions versus reaction time at various light intensities are displayed (left) in milliflow reactor and (right) in microflow.

For the higher light intensities of 6.41 and 12.2 mW·cm⁻² no significant difference in conversion rate was found for the first 10 s. However, the drop in conversion rate was much less significant at 6.41 mW·cm⁻² and therefore higher conversions were achieved. For lower light intensities of 3.01 and 0.93 mW·cm⁻², the same behavior of high initial rates and a fast drop to low rates was observed, yet less pronounced at 0.93 mW·cm⁻². In consequence, light intensities of 6.41 mW·cm⁻² and below led to higher conversion for reactions of more than 120 s, even though conversion rates at 12.2 mW·cm⁻² did not drop to 0 and extended reaction times showed a steady increase in conversion for at least 20 min (**Figure 6.2**). Eventually, all light intensities assumably end at the same conversion.

With respect to these findings, we conclude that our hypothesis was true for the first few minutes of the reaction, yet false for significantly longer reaction times as it seems that there was further photoinitiation.

Influence of Light Intensity on Photoinduced Radical Thiol-Ene Reactions In order to investigate the behavior of the ene conversion at higher light intensities, the same reaction was investigated in a microflow reactor (**Figure 6.3**, right side). In contrast to the milliflow set-up, no tubular fluorescent lamp was employed but a powerful OmniCure system with a light guide.

Similar to the results from milliflow, conversions at different light intensities, here 20, 30, and 40 mW·cm⁻², reached a conversion plateau after an initial steep increase. Because of the reactor's pressure limitation, reaction times below 15 s could not be monitored. Interestingly, even though light intensities in microflow were much higher not only due to the stronger lamp but also due to shorter optical path lengths, conversion rates did not exceed those obtained for the much lower light intensities in milliflow. In fact, differences in conversion rate for light intensities above 6.41 mW·cm⁻² were minimal for the first minute. It appeared that a photo saturation was reached and consequently tuning of light intensity is only effective below the saturation limit. Further supporting our hypothesis, the lowest light intensity led to the higher plateau level also in microflow. However, with longer reaction times, the differences became negligibly small. As observed before, it seems that there is another type of photoinitiation as conversions rises slowly after the initial burst of radicals.

Radical thiol-ene reactions have also been reported to work without photoinitiator at high light intensities and for long reaction times.^[31] To rule out any contribution of self-initiation of the thiol, a blank sample with no photoinitiator added was subjected to 40 mW·cm⁻² for up to 1200 s (right side of **Figure 6.3**). No conversion was observed after 300 s and even after 1200 s, almost no alkene was converted. The slow but steady increase in conversion after reaching the plateau level is therefore – most likely – not related to photoinitiator-free self-initiation of

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the thiol species. It appears that the employed photoinitiator DMPA (fast decomposition, type I) has been consumed very fast, yet potentially its decomposition products – e.g. with benzophenone substructures – could act as slow photoinitiators (type II).^[10]

Figure 6.4 shows the respective conversions for three concentrations, 0.1, 0.25, and 0.5 M, in both reactants at 12.2 mW·cm⁻² on the left side and the right side at $3.01 \text{ mW}\cdot\text{cm}^{-2}$. At $12.2 \text{ mW}\cdot\text{cm}^{-2}$, higher concentrations led to higher conversions at any given time – as expected from literature,^[13] even though they approached each other very slowly with increasing reaction time. After 360 s, the total conversions were 75% for 0.1 M, 90% for 0.25 M, and 96% for 0.5 M.

In contrast to that, differences in conversion decreased much faster at $3.01 \text{ mW} \cdot \text{cm}^{-2}$ (right side of **Figure 6.4**). While there was still a significant difference between 0.25 and 0.1 M, almost no difference was found between 0.25 and 0.5 M after only 120 s. Interestingly, the advantage gained by higher concentration was completely diminished by the use of lower light intensity as both for 0.25 and 0.5 M solutions 95% ene conversion was found.



Figure 6.4. Ene conversion for reaction times up to 360 s and different reactant concentrations: 0.1 M (black), 0.25 M (blue), and 0.5 M (red). The left side shows data acquired at 12.2 mW·cm⁻² and the right side at 3.01 mW·cm⁻² light intensity.

To compare the effect of light intensity at the respective concentrations, graph in **Figure 6.5** was constructed by subtraction of the ene conversion obtained at $12.2 \text{ mW} \cdot \text{cm}^{-2}$ from the ene conversion obtained at $3.01 \text{ mW} \cdot \text{cm}^{-2}$. Y-Values above 0 consequently depict higher conversion at $3.01 \text{ mW} \cdot \text{cm}^{-2}$ and below 0 higher ene conversion at $12 \text{ mW} \cdot \text{cm}^{-2}$. All three curves show higher initial conversion at higher light intensity due to higher initial radical flux. However, while at 0.5 M it was always beneficial to use $12 \text{ mW} \cdot \text{cm}^{-2}$, both 0.25 and 0.1 M showed an advantage for $3.01 \text{ mW} \cdot \text{cm}^{-2}$ for reaction times of more than 40 and 50 s, respectively. Reactions at $3.01 \text{ mW} \cdot \text{cm}^{-2}$ at 0.1 M concentration were up to 8% more efficient with respect to conversion after 120 s. For longer reaction times, the differences became smaller which is ascribed to the non-zero conversion rate at the conversion plateau. However, for 0.25 M, no such decrease was found, yet this could also be due to inaccuracies of ¹H-NMR that was used to determine the conversion. Within the constraints from above, our hypothesis seems to be true for concentrations below 0.5 M.



Figure 6.5. Advantage in conversion of a light intensity of $3.01 \text{ mW} \cdot \text{cm}^{-2}$ over a light intensity of $12.2 \text{ mW} \cdot \text{cm}^{-2}$ for a radical thiol-ene reaction of 3-butenol and 1-octanethiol for 0.1 (black), 0.25 (blue), and 0.5 M (red) reactant concentrations. Values above 0% correspond to higher conversion at $3.01 \text{ mW} \cdot \text{cm}^{-2}$, whereas the reaction at $12.2 \text{ mW} \cdot \text{cm}^{-2}$ shows higher conversion for values below 0%.



Figure 6.6. (left) Ene conversion of radical thiol-ene reaction of 3-butentol and 1-octanethiol for both 3.01 mW·cm⁻² (blue and black) to 12.2 mW·cm⁻² (pink and red) light intensity with 0.01 and 0.05 equivalents DMPA, respectively. (right) Difference in ene conversion obtained by subtraction of 12.2 mW·cm⁻² from 3.01 mW·cm⁻² to for 0.01 (red) and 0.05 (blue) equivalent DMPA. Values above 0% correspond to higher conversion at 3.01 mW·cm⁻², whereas the reaction at 12.2 mW·cm⁻² shows higher conversion for values below 0%.

Figure 6.6 displays on its left side the ene conversion at different DMPA concentrations for reactions times up to 110 s at light intensities of 3.01 mW·cm⁻² and 12.2 mW·cm⁻², respectively. At 0.01 equivalent DMPA, 3.01 mW·cm⁻² led to a clearly slower reaction yet resulted in a higher conversion of 71%, in contrast to only 64% for 12.2 mW·cm⁻². It took around 50 s until 3.01 mW·cm⁻² reached a higher conversion than the reaction at 12.2 mW·cm⁻² (right side of **Figure 6.6**). Interestingly, the reaction rate at 3.01 mW·cm⁻² after 110 s was significantly higher than for 12.2 mW·cm⁻² which was close to 0.

The same reaction at 0.05 equivalent DMPA showed a stronger increase in rate at 12.2 mW·cm⁻² than at 3.01 mW·cm⁻² for the first few seconds, yet afterwards less pronounced differences in both conversion rate and conversion compared to the lower photoinitiator concentration. Conversions of 80% for 12.2 mW·cm⁻² and 84% for 3.01 mW·cm⁻² were reached, and after only 30 s, 3.01 mW·cm⁻² already yielded higher conversions than 12.2 mW·cm⁻².

It appears that the positive effect of lower light intensities, i.e. our hypothesis, is much more pronounced for low concentrations of photoinitiator. It is likely that the higher photoinitiator concentration effectively counters the lower decomposition rate, either by prolongation of the decomposition or by a higher radical flux.

6.4 Summary and conclusions

The influence of light intensities on the photoinduced radical thiol-ene reaction of 3-butenol and 1-octanethiol in milli- and microflow was investigated to shed light on the hypothesis that high light intensities lead to lower conversions. Our findings show that our hypothesis was partially true and in line with literature.^[13] At high light intensity, high initial ene conversion rates and their fast drop to almost zero within a few seconds were observed. In contrast, lower light intensities were found to have lower initial conversion rates that dropped only slowly with increasing reaction time. In consequence, higher conversions were reached at low light intensities already after short reaction time. However, the respective final conversions after a long reaction time were very similar, potentially because of continuous photoinitiation of the DMPA's decomposition products.

The advantage of low light intensities was most prominent at low concentrations and almost diminished at 0.5 M concentrations. Similarly, higher photoinitiator concentrations reduced the advantage of higher light intensities with respect to conversions. Remarkably was however that the use of lower light intensities effectively countered the advantage gained by higher concentrations.

Even though there was no effectively limiting influence of high concentrations on the ene conversion, we have demonstrated lower light intensities are beneficial unless very high reactant concentrations are chosen. Contrary to a widely shared perception, batch reactors might consequently deliver better results for radical thiol-ene reactions than flow reactors as high illumination efficiency harms more than it helps. Moreover, the use of less intense light might be a more practical solution to achieve a low radical flux than the repeated addition of small quantities of photoinitiator as suggested in literature.^[13] For a complete picture, our study has to be extended to product yields since conversion alone can readily mislead.

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Chapter 7

Experimental Details



7.1 Materials

7.1.1 Chapter 2

t-Butyl acrylate (98%), n-butyl acrylate (99%), methyl acrylate (99%), 2-hydroxyethyl acrylate (96%), 3-(dimethylamino)propyl acrylate (95%), oligo(ethylene glycol) methyl ether acrylate ($M_n = 480 \text{ g} \cdot \text{mol}^{-1}$), 2-ethylhexyl acrylate (98%), [2-acryloyloxy)ethyl]trimethylammonium chloride (80 wt% in H₂O), CuBr₂ (99.999% trace metal basis), tris[2-(dimethylamino)ethyl]amine $(Me_6TREN, 97\%), 2,2,2$ -trifluororethanol (99%), triethylamine (99%), 10-undecen-1-ol (98%), a-bromoisobutyryl bromide (98%), trichlorosilane (99%), platinum(0)-1,3-divinyl-1,1,3,3-tetramethyldisiloxane complex solution (Karstedt's catalyst, ~2% Pt in xylene) were acquired from Sigma-Aldrich, Czech Republic. Extra-dry solvents (over molecular sieves) toluene (99.85%) and dimethyl sulfoxide (99.7%, DMSO) were purchased from Acros, Czech Republic. Solvents ethanol (99.8%), acetone (99.5%), tetrahydrofuran (THF, 99.5%), toluene (99%), and DMSO (99%) were purchased from Lach-Ner, Czech Republic. Deionized water was obtained from a Milli-Q system (Merck-Millipore, Czech Republic). Silicon wafers were purchased from ON Semiconductor, Czech Republic. All monomers were passed through a basic alumina column immediately before use to remove the inhibitor. Triethylamine was refluxed over CaH₂ overnight, distilled, and stored under argon atmosphere in dark. THF was dried over sodium and freshly distilled before use.

7.1.2 Chapter 3

Sulfuric acid (95%, Analytical Reagent Grade), hydrochloric acid (37%, Analytical Reagent Grade), ammonia (25% Laboratory Reagent Grade), absolute ethanol (Analytical Reagent Grade), dimethyl sulfoxide (Analytical Reagent Grade), and

toluene (Analytical Reagent Grade) were purchased from Fisher. Hydrogen peroxide (35 wt%), triethylamine (99+%), 2-bromoisobutyryl bromide (98%), sodium sulfate (99+%), and copper dibromide (99+%) were purchased from Acros. 10-Undecan-1-ol (>98%) and 2-hydroxyethyl acrylate (>95%) were purchased from TCI. *t*-Butyl acrylate (98%), oligo(ethylene glycol) methyl ether acrylate, [2-(acryloyloxy)ethyl]trimethylammonium chloride solution 80 wt% in water, and trichlorosilane (99%) were purchased from Sigma Aldrich. Tetrahydrofuran (HPLC grade) bought from VWR, was and tris[2-(dimethylamino)ethyl]amine (99+%) from Alfa Aesar. All monomers were passed through basic alumina prior to use. All other chemicals were used as purchased.

7.1.3 Chapter 4

Deuterated chloroform (99.80% D) was purchased from Eurisotop, deuterated methanol-d₄ (99.80% D) was purchased from Cambridge Isotope Laboratories Inc. Dimethyl sulfoxide (DMSO), toluene, absolute ethanol, dimethyl formamide (DMF), hydrochloric acid (37%), and sulfuric acid (>95%) were purchased in Analytical Reagent Grade from Fisher. Dichloromethane (>99%, Laboratory Reagent Grade), chloroform (>99%, Laboratory Reagent Grade), and ammonia solution (25% in water) were purchased from Fisher. Xylenes (mixed isomers with ethylbenzene, 96%), potassium iodide (>99%), 11-bromoundecan-1-ol (97%), magnesium sulfate (99%, extra pure, dried), *n*-butyl acrylate (>99%, stabilized), copper(II) bromide (>99%, extra pure, anhydrous), hydrogen peroxide (35 wt% in water, stabilized), and tributyltin hydride (97%) were purchased from Acros. TEMPO (for ESR spectroscopy), 4-hydroxybenzaldehyde (98%), dibutyltin dilaurate (95%), *N*,*N*,*N*'',*N*'',*P*''-pentamethyldiethylenetriamine (99%; PMDTA),

zinc oxide (particle size < 100 nm), tetraethoxysilane (>99%; TEOS), and basic aluminum oxide were purchased from Sigma Aldrich. 3-(TriethoxysilyI)propyl isocyanate (95%) was purchased from ABCR. *N-tert*-butylhydroxylamine hydrochloride (>97%) was purchased from TCI. Ethyl α-bromoisobutyrate (>97%) was purchased from Fluka. Methanol (>98.5%) was purchased from VWR. AIBN was purchased from Glentham Life Sciences. Barium titanate nanoparticles (50–60 nm, 99%) were purchased from Alfa Aesar. Copper powder (<63 μm, >99.7%) was purchased from Merck. Silica microparticles (40–63 μm diameter) were purchased from Grace GmbH. Dry and oxygen-free solvents (dichloromethane, diethyl ether, dimethyl formamide, tetrahydrofuran, and toluene) were obtained from an MBraun SPS800 system equipped with HPLC grade solvents from Sigma Aldrich. Water was provided by a Sartorius arium 611 UV system with Sartopore® 2 150 filter with 0.2 μm pore size.

7.1.4 Chapter 5

L-cysteine (99%) was purchased from Merck. Triphenylmethanol (>99%) and di*tert*-butyldicarbonate (95%) were purchased from TCI. Trifluoroacetic acid was purchased from Fluorochem. Diethyl ether (technical), sodium hydroxide, ethyl acetate (Laboratory Reagent Grade), and tetrahydrofuran (HPLC grade) were purchased from VWR. Potassium carbonate (99+%), magnesium sulfate (99%), 4-dimethylamino pyridine (99%), pyridine (99+%), triethylamine (99+%), sodium hydrogencarbonate (99.5%), triethylsilane (99%), tri-*n*-butyl phosphine (95%), and hexylamine (99%) was purchased from Acros. Absolute ethanol (Analytical Reagent Grade), dioxane (Analytical Reagent Grade), hydrochloric acid (37%, Analytical Reagent Grade), and chloroform (Laboratory Reagent Grade) were purchased from Fisher. 2,2'-Azobis(2-methylpropionitrile) was purchased from Glentham Life Sciences.

7.1.5 Chapter 6

Octanethiol (97%), 2,2-dimethoxy-2-phenylacetophenone (99%), and hydroquinone (99%) were purchased from Acros. Dodecanethiol (>95%) and 3-buten-1-ol (>98%) were purchased from TCI. 1-Octene (98%) was purchased from Sigma Aldrich. Acetonitrile (HPLC grade) was purchased from Fisher.

7.2 Characterization

7.2.1 Instruments used across all chapters

7.2.1.1 Time of flight secondary ion mass spectrometry

ToF-SIMS (time of flight secondary ion mass spectrometry) was performed on a TOF.SIMS5 instrument (ION-TOF GmbH, Münster, Germany. This spectrometer is equipped with a Bi cluster primary ion source and a reflectron type time of flight analyzer. UHV base pressure was $< 5 \cdot 10^{-9}$ mbar. For high mass resolution the Bi source was operated in the "high current bunched" mode providing short Bi₃+ primary ion pulses at 25 keV energy, a lateral resolution of approx. 4 µm, an a target current of 0.4 pA. The short pulse length of 1.1 ns allowed for high mass resolution. The primary ion beam was rastered across a 500 × 500 µm² field of view on the sample, and 128 × 128 data points were recorded. Primary ion doses were kept below 10¹¹ ions·cm⁻² (static SIMS limit). If charge compensation was necessary, an electron flood gun providing electrons of 21 eV was applied and the secondary ion reflectron was tuned accordingly. Spectra were calibrated on the omnipresent C⁻, C₂⁻, C₃⁻, or on the C⁺, CH⁺, CH₂⁺, and CH₃⁺ peaks. Based on these datasets the chemical assignments for characteristic fragments were determined.

For depth profiling several dual beam analyses were performed using either C_{60}^+ , Cs^+ , or Ar_{1600}^+ sputter ions. For C_{60}^+ depth profiling the primary ion source was again operated in "high current bunched" mode with a scanned area of 500 \times 500 μ m² (10 frames with 128 × 128 data points) and a sputter gun (operated with C_{60}^+ ions, 20 keV, scanned over a concentric field of 750 \times 750 μ m², target current 1.3 nA) was applied to erode the sample for 2.8 s followed by a 0.2 spause (non-interlaced mode). Thereby, the sputter ion dose density was >100 times higher than the Bi ion dose density. For Cs⁺ depth profiling the Bi_{3^+} primary ion source was rastered over 300 \times 300 μ m², while interlaced sputter beam erosion was performed on a field of 500 \times 500 μ m² applying a 500 eV, 47 nA, Cs beam. For argon cluster depth profiling, a sputter gun (operated with Ar_{1600}^+ ions, 5 keV, scanned over a concentric field of 750 \times 750 μ m², target current 0.3 nA) was applied to erode the sample for 2 scans followed by a 0.5 s pause. This approach allows the argon cluster ion dose density to be >250 times higher than the Bi ion dose density and is preserving molecular structures in the sample during erosion and is therefore highly suited for polymeric materials.

7.2.1.2 X-ray photoelectron spectroscopy

X-ray Photoelectron Spectroscopy (XPS) measurements were performed using a K-Alpha XPS spectrometer (ThermoFisher Scientific, East Grinstead, UK). Data acquisition and processing using the Thermo Avantage software is described elsewhere.^[1] All samples were analyzed using a microfocused, monochromated Al K_{α} X-ray source (400 µm spot size). The K-Alpha charge compensation system was employed during analysis, using electrons of 8 eV energy, and low-energy argon ions to prevent any localized charge build-up. The spectra were fitted with one or more Voigt profiles (binding energy uncertainty: <u>+</u>0.2 eV) and Scofield

sensitivity factors were applied for quantification.^[2] All spectra were referenced to the C 1s peak attributed to C–C, C–H at 285.0 eV binding energy which has been controlled by means of the well-known photoelectron peaks of metallic Cu, Ag, and Au, respectively. The K-alpha+ snapmap option was used to image an area of 3 mm × 3 mm with an X-ray spot of 300 μ m. (10 iterations were run in order to reach a better statistic). A principal component analysis of the spectra was conducted.

7.2.1.3 Grazing angle attenuated total reflection Fourier-transform infrared (GAATR-FTIR) spectroscopy

Grazing angle attenuated total reflection Fourier-transform infrared (GAATR-FTIR) spectra were obtained from the dry polymer layers using a Frontier FTIR spectrometer (PerkinElmer) equipped with an MCT detector and a Veemax III attachment (PIKE Technologies). For the collection of the spectra, a resolution of 4 cm⁻¹ was selected.

7.2.1.4 Nuclear magnetic resonance (NMR) spectroscopy

¹H-NMR spectra were recorded in deuterated chloroform and methanol, respectively, applying a pulse delay of 15 s with Oxford Instruments Ltd. NMR spectrometers (300 and 400 MHz).

7.2.1.5 Size-Exclusion Chromatography (SEC)

Analytical size-exclusion chromatography (SEC) was performed on a Tosoh EcoSEC HLC-8320GPC, comprising an autosampler, a PSS guard column SDV (50 mm × 7.5 mm), followed by three PSS SDV analytical linear XL (5 μ m, 300 mm × 7.5 mm) columns thermostated at 40 °C (column molecular weight range: 10² to 10⁶ g·mol⁻¹), and a differential refractive index detector (Tosoh EcoSEC RI) using THF as the eluent with a flow rate of 1 mL·min⁻¹. Toluene was

used as a flow marker. Calibration was performed using linear narrow polystyrene (PS) standards from PSS Laboratories in the range of $470 - 7.5 \cdot 10^6 \text{ g} \cdot \text{mol}^{-1}$.

7.2.1.6 Electrospray ionization mass spectrometry (ESI-MS)

Electrospray ionization mass spectrometry (ESI-MS) was performed on an LCQ Fleet mass spectrometer (ThermoFischer Scientific) equipped with an atmospheric pressure ionization source operating in the nebulizer-assisted electrospray mode. The instrument was calibrated in the *m*/*z* range 220–2000 using a standard solution containing caffeine, MRFA, and Ultramark 1621. A constant spray voltage of 5 kV was used, and nitrogen at a dimensionless auxiliary gas flow rate of 3 and a dimensionless sheath gas flow rate of 3 was purged. The capillary voltage, the tube lens offset voltage, and the capillary temperatures were set to 25 V, 120 V, and 275 °C, respectively. A 250 µL aliquot of polymer solution with a concentration of 10 µg·mL⁻¹ was injected. A mixture of THF and methanol (THF : MeOH = 3 : 2), all HPLC grade, was used as solvent.

7.2.1.7 Electron paramagnetic resonance (EPR) spectroscopy

Subsequently, a freely chosen, but small and known amount of material was introduced into 3 mm outer and 2 mm inner diameter Suprasil quartz ESR tubes (Wilmad, USA and the tubes were sealed and placed in an ESR cavity of a Magnettech MiniScope MS400 at room temperature. Spectra were measured with a 60 s sweep time, 3368.7 G B₀-field, 250 G sweep width, and 2 G modulation amplitude. To obtain accurate concentration-intensity relationships, the system was calibrated with 10^{-1} , 10^{-2} , 10^{-3} , and 10^{-4} molar solutions of TEMPO in before the respective experiments.

7.2.1.8 Thermogravimetric analysis (TGA)

An SDT Q600 device of TA-Instruments is used for the TGA-analysis. All samples were measured under nitrogen atmosphere, which was established during 30 min of purging prior to heating. Heating was performed at a rate of 10 K·min⁻¹ from room temperature to 580 °C.

7.2.1.9 Atomic force microscopy

The atomic force microscopy (AFM) measurements were performed on a Dimension Icon instrument (Bruker) using an ASYELEC tip. Tip dimensions were 28 ± 10 nm in radius and $14 \pm 4 \mu$ m in height. The resonance frequency was 70 kHz. Topography was measured in tapping mode. To locally remove the polymer, the same tip was used in contact mode with higher push force. The process was repeated multiple times for a complete removal of the polymer in the area of interest.

7.2.1.10 Dynamic light scattering

The particle size was determined by dynamic light scattering (DLS) (Brookhaven Zetapals/90Plus) using suspension of less than 1 mg·mL⁻¹ in absolute ethanol as solvent.

7.2.2 Instruments only for Chapter 2

7.2.2.1 Atomic force microscopy

All images were acquired with a *Multimode Atomic Force Microscope NanoScope IIIa* (*Digital Instruments*) as topological scans in tapping mode in air, using silicon probes *OTESPA-R3* (*Bruker*) with a nominal spring constant of 26 N·m⁻¹ and a tip radius of 7 nm. Areas of $5 \times 5 \ \mu\text{m}^2$ (512 × 512 pixels) were scanned at a rate of 1 Hz. The scans were analyzed using *Gwyddion* software.

7.2.2.2 Dynamic water contact angle

The wettability of the surfaces was measured by the dynamic water contact angle using the sessile drop method with a *DataPhysics OCA 20* instrument. A 5 μ L drop was deposited on the surface and its volume was increased up to 15 μ L and decreased back to 5 μ L at a flow rate of 0.5 μ L·s⁻¹. The drop profile was recorded during the process and was fitted with a circular algorithm, from which the advancing and receding contact angles were extracted.

7.2.2.3 Grazing angle attenuated total reflection Fourier-transform infrared (GAATR-FTIR) spectroscopy

Grazing angle attenuated total reflection Fourier-transform infrared (GAATR-FTIR) spectra were obtained from the dry polymer layers using a Nicolet Nexus 870 FTIR spectrometer (ThermoFisher Scientific) equipped with a VariGATR attachment (Harrick Scientific Products) under continuous purging with dry air. For the collection of the spectra, 256 scans were taken at a resolution of 2 cm⁻¹.

7.2.2.4 NMR spectroscopy

¹H-NMR spectra were acquired on a 300 MHz Bruker NMR spectrometer in CDCl₃, using TMS as an internal standard at 0 ppm.

7.2.2.5 Single wavelength variable angle ellipsometry

The dry thickness of the polymer layers was measured with an imaging autonulling ellipsometer EP³-SE (Nanofilm Technologies GmbH, Germany). The ellipsometric data was acquired in air at ambient temperature using a laser λ = 532 nm at angles of incidence (AOI) of 60, 65, and 70°. The fitting was performed with the *EP4Model* analysis software using multilayer models, fitting simultaneously for the polymer thickness and refractive index. Each chip was measured in three spots to confirm sample uniformity and the values are reported as mean and standard deviation.

7.2.2.6 Stylus profilometry

Stylus profilometry was performed using Tencor P-10 Surface Profiler (Texas, USA). Topographic scans over areas of $600 \times 700 \ \mu\text{m}^2$ were acquired at speed of 20 $\mu\text{m}\cdot\text{s}^{-1}$ and sampling rate of 100 Hz. The stylus force was set at 0.01 N.

7.2.2.7 X-ray photoelectron spectroscopy

The XPS depth profiling was performed utilizing a K-Alpha+ spectrometer with the MAGCIS source operated in small cluster ion mode at 8000 eV. The cluster ion sputtering was performed for 20 s per cycle over areas of $2 \times 1 \text{ mm}^2$. These conditions provided profiling of the block copolymer layer at a sputtering rate of 0.19 nm·s⁻¹. XPS spectra acquired in between etch cycles allowed quantitative determination of the moieties present in the block copolymer layer.

7.3 Syntheses and procedures

7.3.1 Syntheses and procedures of Chapter 2

7.3.1.1 Synthesis of undec-10-en-1-yl 2-bromo-2-methylpropanoate



Scheme 7.1. Synthesis of undec-10-en-1-yl 2-bromo-2-methylpropanoate.

To a solution of undec-10-en-1-ol (15 mL, 75 mmol) and triethylamine (13.5 mL, 90 mmol) in dry THF (75 mL) was added dropwise a solution of *a*-bromoisobutyryl bromide (10.7 mL, 84.8 mmol) in 30 mL of dry THF at 0 °C. The reaction mixture

was kept under argon stirring overnight at ambient temperature. Hexane (150 mL) was subsequently added to the mixture and it was washed twice with 2 M HCl, twice with brine and water, and dried over sodium sulfate. After removal of the solvent under vacuum, the product was purified by vacuum distillation. ¹H-NMR (300 MHz, CDCl₃) δ (ppm): 1.21–1.43 (m, 12H), 1.61–1.73 (m, 2H), 1.93 (s, 6H), 2.03 (q, 2H, *J* = 7.2 Hz), 4.16 (t, 2H, *J* = 6.6 Hz), 4.87–5.04 (m, 2H), 5.72–5.9 (m, 1H).

7.3.1.2 Synthesis of 11-(trichlorosilyl)undecyl 2-bromo-2-methyl propanoate^[3,4]



Scheme 7.2. Hydrosilylation of undec-10-en-1-yl 2-bromo-2-methylpropanoate.

To an Ar-filled dry flask containing 10-undecen-1-yl-2-bromo-2-methylpropionate (8.15 g, 25.5 mmol) and trichlorosilane (25.3 mL, 251 mmol), 1.24 mL Karstedt's catalyst (xylene, Pt ~2 %; 0.05 mol%) was added and kept under argon stirring to react overnight. The mixture was rapidly passed through a plug of silica to remove the catalyst and the remaining trichlorosilane was removed under reduced pressure. The product **2-1** was purified by Kugelrohr distillation at 190 °C. ¹H-NMR (300 MHz, CDCl₃) δ (ppm): 1.21–1.47 (m, 16H), 1.51–1.74 (m, 4H), 1.93 (s 6H), 4.16 (t, 2H, *J* = 7 Hz).

7.3.1.3 Grafting of ATRP initiator 2-1



Scheme 7.3. Grafting of a monolayer of initiator 2-1.

Silicon substrates (cut size $\sim 1 \times 1 \text{ cm}^2$) were rinsed with EtOH (abs.), then MilliQ water, followed by EtOH (abs.) and finally MilliQ water. The substrates were dried with nitrogen and placed in a Petri dish. All substrates were exposed to air plasma for 20 min. A freshly prepared solution of 1 mg·mL⁻¹ **2-1** in toluene was added to the freshly activated silicon substrates. Subsequently, the Petri dish was covered with another Petri dish, and placed in a desiccator. The reaction was allowed to proceed for 3 h at ambient temperature. After that period, the Petri dish was removed from the desiccator and the substrates were rapidly removed from the Petri dish, shaken in toluene (p.a.) to remove the silane, and then placed in a Petri dish filled with toluene (p.a.). Subsequently, the substrates were rinsed with acetone, followed quickly by EtOH (abs.) and MilliQ water, EtOH (abs.) again, and finally MilliQ water. The substrates were dried with nitrogen and placed in a storage container. The thickness of the silane was determined via ellipsometry. A 1.6 nm thick silane monolayer was measured on the silicon substrates bearing 1.5 nm thick films of silicon oxide.





Scheme 7.4. PhotoCMP grafting of acrylates.

A stock solution of 3.9 mM CuBr₂ and 23.4 mM Me₆TREN in DMSO was freshly prepared and kept in the dark. 273.5 µL of the stock solution was added to a 10 mL round bottom flask wrapped in aluminum foil containing 6.15 mL DMSO (giving solution 1). Both solution 1 and the acrylate monomer were purged with argon for 30 min. Subsequently, solution 1 and 10.83 mmol acrylate monomer were combined, giving solution 2. Using gastight syringes, solution 2 was transferred to glass vials containing silicon substrates functionalized with a SAM of initiator **2-1** under argon atmosphere. The vials were sealed and quickly taped to the "UV reactor", a nail-curing device with four 9 W lamps with an emission maximum at 365 nm, followed by exposure to UV light for 5, 10, 15, 20, 25, 30, and 60 min, respectively. The temperature in the UV reactor was kept close to ambient temperature, using a big ventilator.

After the desired time had passed, the samples were quickly removed from the UV reactor, and 5 mL DMSO was added to quench the reaction, and the substrates were removed from the reaction solution (within less than 20 s after removal from the "UV reactor"). The substrates were washed with DSMO, acetone, THF, and EtOH (abs.). Subsequently, the substrates were dried with nitrogen and placed in a storage container.

The above procedure was used for *t*-butyl acrylate, *n*-butyl acrylate, methyl acrylate, 2-ethylhexyl acrylate, 2-hydroxyethyl acrylate, 3-(dimethylamino)propyl acrylate, [2-(acryloyloxy)ethyl]trimethylammonium chloride (carried out in DMSO : water 93 : 7), and oligo(ethylene glycol) methyl ether acrylate. For the grafting of poly(*t*-butyl acrylate) brushes under reduced catalyst and monomer concentration, the CuBr₂ and Me₆TREN concentration were simultaneously reduced by factor 10, 100, and 1000, and the monomer concentration was reduced by factor 5, respectively. For the grafting of 3-(dimethylamino)propyl acrylate in 2,2,2-trifluoroethanol solution 1 was replaced by 4.5 mg CuBr₂ (0.020 μ mol) and 31.25 μ L Me₆TREN (0.117 μ mol) in 5 mL 2,2,2-trifluoroethanol.

All samples were characterized via dynamic water contact angle, ellipsometry, GAATR-FTIR, XPS, and ToF-SIMS measurements.

7.3.1.4.1 Grafting of poly(t-butyl acrylate) with reinitiation

Poly(*t*-butyl acrylate) brushes were grafted for 0, 5, 10, and 15 min following the protocol given above. The dry film thickness was determined via ellipsometry. Subsequently, the same samples were reinitiated for 15 min.

7.3.1.4.2 Grafting of homopolymer brushes with interrupted irradiation

The experiment was carried out as described above. After 15 min, the UV light was turned off for 10 min. While light was a strict requirement to start the reaction, reduced chain growth was observed when the light was turned off after an initial exposure to light.

7.3.1.5 Proving livingness: poly(*t*-butyl acrylate)-*b*-poly(2-hydroxyethyl acrylate)

A first block of poly(*t*-butyl acrylate) was grafted for 6 min, yielding a dry ellipsometric film thickness of 46.6 ± 2.32 nm. The same samples were reinitiated using 2-hydroxyethyl acrylate for 10, 15, and 20 min, respectively.

7.3.1.6 Control experiments

All control experiments were carried out with *t*-butyl acrylate following the procedure described above with the following changes: a) without irradiation, b) without a self-assembled monolayer of initiator, c) without catalyst.

a) Without irradiation

Samples were kept in the dark, i.e. wrapped in aluminum foil, for 10 and 60 min, 48 hours. One sample was exposed to light after being kept one hour in the dark. There was no chain growth in complete absence of light. The period in the dark preceding to irradiation had almost no influence on the film thickness (**Table 7.1**).

b) Irradiation of substrates lacking SAM of initiator

Instead of a silicon wafer featuring a self-assembled monolayer of the initiator, a clean, blank silicon wafer was used. All samples were subjected to irradiation for 10 and 60 min, respectively, giving a film thickness of 0.00 ± 0.00 nm. Thus, no material was grafted.

c) Without catalyst

No catalyst – which comprised 1 equiv. $CuBr_2$ and 6 equiv. Me_6TREN – was added. The sample was exposed to UV irradiation for 2 hours. After irradiation a negligible thickness was observed (less than 2 nm) which can be attributed to contamination of the surface by physisorption of monomer.

period in the dark	Average thickness / nm
10 min	0.4±0.1
	0.4±0.1
60 min	351.3
+ subsequent irradiation for 30 min	
0 min in the dark + subsequent irradiation for 30 min	383.9
48 h	<2

Table 7.1. Dry ellipsometric film thickness of samples lacking exposure to UV light, or beingkept in the dark preceding exposure to UV light, respectively.

7.3.1.7 Patterning via photoCMP

The experiment was carried out in an analogous fashion as described for the grafting of the whole surface with the only exception being the silicon wafer mounted on the shadow mask holder and covered with a shadow mask featuring a meander line pattern (**Figure 7.1**). The wafer was exposed to UV light for 5 min. Subsequently, the shadow mask was removed and the patterned wafer exhaustively rinsed with various solvents. The grafted pattern was visible with the naked eye and was further characterized via profilometry.



Figure 7.1. Shadow mask with a meander line pattern in a shadow mask holder for $1.00 \times 1.00 \text{ cm}^2$ substrates.^[3]

7.3.2 Syntheses and procedures of Chapter 3

7.3.2.1 Silanization

Silicon wafers were placed in a 1 to 1 solution of H_2SO_4 and H_2O_2 . After 15 min, the wafers were taken out, rinsed with H_2O and placed in 1M HCl for another 15 min. Then the wafers were again taken out, rinsed with H_2O and placed in a 1 to 1 solution of NH₃ (25%) and H_2O_2 for 15 min. The substrates were rinsed with H_2O and blown dry with nitrogen. Whenever H_2O_2 was used, samples were only handled with PTFE tweezers.



Scheme 7.5. Grafting of a monolayer of initiator 2-1.

A freshly prepared solution of 5 mg·mL⁻¹ 11-(trichlorosilyl)undecyl 2-bromo-2-methylpropanoate (for synthesis, Section 7.3.1.2) in dry toluene was added to the freshly activated silicon substrates inside the glove box (**Scheme 7.5**). Subsequently, the Petri dish was covered with another Petri dish and the reaction was allowed to proceed for 3 h at ambient temperature. After that period, the substrates were removed from the Petri dish, shaken in dry toluene to remove the silane, and then placed in a Petri dish filled with dry toluene before they were removed from the glove box. Subsequently, the substrates were rinsed with toluene (p.a.) and tetrahydrofuran (p.a.), followed quickly by EtOH (abs.) and MilliQ water. The substrates were blown dry with nitrogen and placed in a storage container. N.B. It is important that the substrates do not dry between the rinsing steps.

7.3.2.2 Direct laser writing

0.23 mg CuBr₂ and 3.5 mL DMSO were mixed in a glass vial equipped with a stirring bar. Subsequently, 1.7 μ L Me₆TREN was added and the vial was wrapped in aluminum foil. Then the mixture was purged with nitrogen for 30 min. Simultaneously, pure, inhibitor-free monomer was purged with nitrogen for 30 min. Afterwards, 10.3 mmol monomer was added to the DMSO solution. The new mixture was stirred for 10 min in the dark.



Scheme 7.6. (top) General set-up used for direct laser writing. A XeF excimer laser ($\lambda = 351$ nm, 4–6 ns pulses, 1.5 mJ per pulse) was combined with a software-controlled galvo scanner. Laser light was first sent through a prism to double the shorter side of the beam from 4 to 8 mm before it passed a reflective filter to reduce its intensity by factor 100. Finally, the light was guide into the galvo scanner where it was redirect onto a silicon substrate that was placed in an airtight chamber under nitrogen atmosphere. (bottom) General reaction scheme for the grafting of polyacrylates via photoCMP.



Figure 7.2. Direct Laser Writing (DLW) Chamber made from stainless steel with a PTFE insert and a quartz glass window.

A silanized silicon substrate was placed in the PTFE-insert of a custom-made DLWchamber. The chamber was airtight and equipped with a quartz glass window (**Figure 7.2**). The DLW chamber filled with the substrate was purged with nitrogen for 30 min. Then the windows was covered with aluminum foil and 0.7 mL of the prepared monomer solution was added rapidly. Subsequently, the sample was subjected to direct laser writing at 351 nm.

For direct laser writing, a pulsed XeF excimer laser (ATLEX 1000-I, ATL Lasertechnik GmbH) and a galvo scanner (SCANcube III, Scanlab GmbH) were employed. Pulse energy was set to 1.5 mJ per pulse of around 4–6 ns. The frequency was set to 500 Hz. Moreover, the laser energy was reduced by factor 100 by a reflective filter. LaserDESK Software (Scanlab GmbH) was used for control of laser and galvo scanner and to design all target structures, which were filled with straight lines with 0.05 mm line spacing.

After completion of the writing process, the substrate was further kept in the dark while the DLW chamber was opened. A few milliliter of a good solvent for the monomer was added before the chamber was opened. Afterwards, the substrate was exhaustively rinsed with toluene, tetrahydrofuran, absolute ethanol and water. For [2-acryloyloxy)ethyl]trimethylammonium chloride, absolute ethanol and water were employed for washing before the full sequence from toluene to water was used.

7.3.3 Syntheses and procedures of Chapter 4

7.3.3.1 Enhanced spin capturing polymerization (ESCP) of polystyrene

280 mg PBN (1.58 mmol, 1.0 equiv.), 350 mg AIBN (2.13 mmol, 1.35 equiv.), and 1.8 mL styrene (1.64 g, 15.2 mmol, 9.9 equiv.) were dissolved in 5 mL dry toluene. The mixture was purged with argon for 20 min and subsequently heated to 60 °C overnight. Next, the formed polymer was precipitated in cold methanol, stored in the freezer overnight and then filtered off. Consequently, the obtained white powder was redissolved in a small amount of toluene and precipitated and collected a second time as described above. The dried product was characterized via size-exclusion chromatography, giving $M_{n, SEC} = 2300 \text{ g} \cdot \text{mol}^{-1}$, $\mathcal{D} = 1.19$.

7.3.3.2 Synthesis of 4-((11-hydroxyundecyl)oxy)benzaldehyde^[4]

0.50 g 4-hydroxybenzaldehyde (4.02 mmol, 1.00 equiv.), 1.06 g 11-bromoundecan-1-ol (4.18 mmol, 1.04 equiv.), 0.05 g potassium iodide (0.3 mmol, 0.07 equiv.), and 2.9 g potassium carbonate (21 mmol, 5.2 equiv.) were mixed in 10 mL dimethyl sulfoxide. The mixture was stirred for 3 days at 90 °C. Subsequently, the potassium carbonate was filtered off and 100 mL dichloromethane was added to the filtrate. The organic phase was washed three times with water and brine to remove all dimethyl sulfoxide. Next, the organic phase was dried over magnesium sulfate before the dichloromethane solvent was removed under reduced pressure. 1.06 g (90%) of 4-((11-hydroxyundecyl)oxy) benzaldehyde was obtained. ¹H-NMR (400 MHz, CDCl₃) δ (ppm): 9.84 (s, 1H), 7.79 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.7 Hz, 2H), 4.00 (t, *J* = 6.5 Hz, 2H), 3.60

(t, J = 6.6 Hz, 2H), 1.88 (br. s, 1H), 1.82 – 1.73 (m, 2H), 1.58 – 1.49 (m, 2H), 1.47 – 1.39 (m, 2H), 1.37 – 1.23 (m, 12H).

7.3.3.3 Synthesis of *N-tert*-butyl-1-(4-((11-hydroxyundecyl)oxy) phenyl)methane imine oxide S1

2.00 g 4-((11-hydroxyundecyl)oxy)benzaldehyde (6.85 mmol, 1.00 equiv.), 0.86 g *N-tert*-butylhydroxylamine hydrochloride (6.85 mmol, 1.00 equiv.), and 0.70 mL pyrrolidine (0.60 g, 8.39 mmol, 1.23 equiv.) were mixed in 20 mL dry dichloromethane and subsequently stirred for 4 days at ambient temperature. The organic phase was subsequently extracted 3 times with water and brine before it was dried over magnesium sulfate. After removal of the solvent under reduced pressure, 2.2 g (88%) of **S1** was isolated. ¹H-NMR (400 MHz, CDCl₃) δ (ppm): 8.29 – 8.24 (m, 2H), 7.51 (s, 1H), 6.95 – 6.89 (m, 2H), 4.00 (t, *J* = 6.6 Hz, 2H), 3.63 (t, *J* = 6.6, 2H), 1.83 – 1.74 (m, 2H), 1.61 (s, 9H), 1.60 – 1.52 (m, 2H), 1.50 – 1.40 (m, 2H), 1.39 – 1.23 (m, 12H).

7.3.3.4 Synthesis of *N-tert*-butyl-1-(4-((4,4-diethoxy-9-oxo-3,10-di-

oxa-8-aza-4-silahenicosan-21-yl)oxy)phenyl)methanimine oxide S2

2.00 g **S1** (5.50 mmol, 1.00 equiv.) and 14.3 mg dibutyltin dilaurate (0.14 mmol, 0.03 equiv.) were added to a glass vial. The vial was subsequently moved into the glove box and then 7 mL dry tetrahydrofuran was added, followed by 1.36 mL 3-(triethoxysilyl)propyl isocyanate. The mixture was stirred at ambient temperature for 6 hours. Full conversion of the isocyanate species was confirmed via ATR-FTIR. The reaction mixture was then removed from the glove box and dried in high vacuum overnight. The product was obtained as a bright yellow solid in quantitative yield.
¹H-NMR (400 MHz, CDCl₃) δ (ppm): 8.33 – 8.20 (m, 2H), 7.45 (s, 1H), 6.97 – 6.80 (m, 2H), 4.89 (br.s, 1H), 4.02 (t, *J* = 6.6 Hz, 2H), 3.98 (t, *J* = 6.6 Hz, 2H), 3.81 (q, *J* = 7.0 Hz, 6H), 3.16 (dd, *J* = 12.9, 6.5 Hz, 2H), 1.85 – 1.71 (m, 2H), 1.68 – 1.51 (m, 2H), 1.59 (s, 9H), 1.48 – 1.39 (m, 2H), 1.34 – 1.25 (m, 14H), 1.21 (t, *J* = 7.0 Hz, 9H), 0.68 – 0.55 (m, 2H).

¹³C(APT)-NMR (75 MHz, CDCl₃) δ (ppm): 160.57 (s, quart. C), 156.94 (s, quart. C), 130.84 (s, CH), 129.72 (s, CH), 123.90 (s, quart. C), 114.36 (s, CH), 70.13 (s, CH₂), 68.18 (s, CH₂), 64.96 (s, quart. C), 58.57 (s, CH₂), 43.47 (s, CH₂), 29.95
28.94 (m, CH₂), 28.43 (s, CH₃), 26.12 (s, CH₂), 26.01 (s, CH₂), 23.43 (s, CH₂), 18.41 (s, CH₃), 7.73 (s, CH₂).

7.3.3.5 Synthesis of tris[2-(dimethylamino)ethyl]amine

Me₆TREN was synthesized according to literature.^[5] Additional purification was carried out via Kugelrohr distillation.

7.3.3.6 Synthesis of poly(*n*-butyl acrylate) with bromine terminus^[6]

1.5 mL ethyl *a*-bromoisobutyrate (10.2 mmol, 1.0 equiv.), 15 mL *n*-butyl acrylate (104 mmol, 10.2 equiv.), 47 mg CuBr₂ (0.21 mmol, 0.02 equiv.), and 0.33 mL Me₆TREN (1.24 mmol, 0.12 equiv.) were added to 23 mL dimethyl sulfoxide and subsequently purged for 30 min with argon. The polymerization was carried out in a continuous photoflow reactor constructed from a 22.5 m perfluoroalkoxy (PFA) tubing (Advanced Polymer Tubing GmbH; outer diameter, 1/16"; inner diameter, 0.75 mm; reactor volume, 10 mL) wrapped around a Vilber Lourmant 15 W UV-light tube ($\lambda_{max} = 365$ nm). A syringe pump (Chemyx Fusion 100) was used to inject the reaction solutions into the reactor. The flow rate was set to 0.25 mL·min⁻¹, thus 40 min reaction time and 90 % conversion according to ¹H-NMR. The dimethyl sulfoxide solvent was removed via repeated extraction with

dichloromethane and water. The solvent was subsequently removed to afford 13.25 g of poly(*n*-butyl acrylate). The obtained polymer was characterized with size-exclusion chromatography (M_n =1570 g·mol⁻¹, D = 1.12) and close to 100% endgroup fidelity was confirmed via ESI-MS.

7.3.3.7 Activation and cleaning of silicon substrates

Silicon wafers were placed in a 1 to 1 solution of H_2SO_4 and H_2O_2 . After 15 min, the wafers were taken out, rinsed with H_2O and placed in 1 M HCl for another 15 min. The wafers were then removed again, rinsed with H_2O and placed in a 1 to 1 solution of NH₃ (25%) and H_2O_2 for 15 min. The substrates were rinsed with H_2O and dried in a nitrogen stream. Whenever H_2O_2 was used, samples were only handled with PTFE tweezers.

7.3.3.8 Nitrone-mediated radical coupling for surface modification with nitrone in solution

Silanization with 11-(trichlorosilyl)undecyl 2-bromo-2-methylpropanoate (for synthesis, Section 7.3.1.2) was carried out as described in Section 7.3.2.1 to obtain substrate **4-1**. Eight substrates **4-1** were placed in a large PTFE reactor and then the reactor was inserted into the glove box. A suspension of 130 mg poly(*n*-butyl acrylate) with bromine terminus ($M_n = 1570 \text{ g} \cdot \text{mol}^{-1}$; for synthesis 7.3.3.6), 130 mg *N*-tert-butyl-*a*-phenylnitrone (PBN), 20 mg Cu powder, and 70 µL PMDTA in 4 mL dry DMF was injected into the reactor. The NMRC reaction was allowed to proceed overnight at 50 °C. Subsequently, the reactor was flushed with 25 mL DMF and the reaction mixture was collected for further characterization with size-exclusion chromatography (2300 g $\cdot \text{mol}^{-1}$, $\vartheta = 1.24$). All

samples were removed from the reactor and thoroughly rinsed with toluene, THF, absolute ethanol, and H_2O before they were dried in nitrogen stream giving **4-2**.



Scheme 7.7. Nitrone-mediated radical coupling with the nitrone species in solution. First a flat silicon substrate was silanized with an ATRP initiator, resulting in **4-1**, to provide a deactivated radical on the surface, second nitrone-mediated radical coupling with poly(*n*-butyl acrylate) was performed, giving **4-2**. The polymer-functionalized surface was subsequently subjected to quenching in the presence of tributyltin hydride to reverse the nitrone-mediated radical coupling, which resulted in **4-3**. In addition, product **4-2** was subjected to nitroxide-mediated polymerization of styrene, leading to **NMP A**.

7.3.3.9 Nitrone-mediated radical coupling for surface modification with

the nitrone on the surface

The freshly activated substrates were placed in a reactor (~2 mL total volume; made from PTFE and glass, **Figure 7.3**) and inserted into the glove box (N₂ atmosphere). A solution of 70 mg nitrone silane **S2** (for synthesis, Section 7.3.3.3) in 4 mL dry toluene was injected into the reactor. The silanization was allowed to take place overnight at 50 °C to give **4-5**. After 12 h, the reactor was flushed with 75 mL dry toluene, 75 mL dry THF, and 75 mL dry DMF. The reactor

was not opened and kept inside the glove box to prevent degradation of the nitrone due to light.

Subsequently, a suspension of 250 mg poly(*n*-butyl acrylate) with bromine terminus ($M_n = 1570 \text{ g} \cdot \text{mol}^{-1}$; for synthesis, Section 7.3.3.6), 20 mg Cu powder, and 70 µL PMDTA in 4 mL dry DMF was injected into the reactor. The NMRC reaction was allowed to take place overnight at 50 °C. Consequently, the reactor was flushed with 25 mL DMF and the reaction mixture was collected for further



Scheme 7.8. Nitrone-mediated radical coupling with the nitrone species on the surface. The nitrone was grafted in a silanization reaction to give sample **4-4**. Subsequently, poly(*n*-butyl acrylate) was grafted in a nitrone-mediated radical coupling, resulting in **4-5**. In a nitroxide-mediated polymerization of styrene, the controlling group remains on the surface, thus some polystyrene is grafted while some poly(*n*-butyl acrylate) is still present (**NMP B**). With the alkoxyamine on the surface, quenching with tributyltin hydride can only remove half of the grafted poly(*n*-butyl acrylate) and polystyrene, leading to sample **4-6** and **NMP Q**, respectively.

characterization with size-exclusion chromatography to check for radical coupling in solution ($M_{n, after NMRC} = 1430 \text{ g} \cdot \text{mol}^{-1}$, $\mathcal{D} = 1.37$). All samples were removed from the reactor and thoroughly rinsed with toluene, THF, absolute ethanol, and H₂O before they were blown dry with N₂ to finally give **4-5**.



Figure 7.3. Custom-made reactor for nitrone-mediated radical coupling on $1.0 \text{ cm} \times 1.0 \text{ cm}$ silicon substrates in the glove box. An in- and outlet for 1.58 mm outer-diameter tubing allowed for efficient solvent exchange without exposing the substrates to light or air. The reactor was wrapped in aluminum foil and placed on heating block with an inclined plane to make sure that no potentially formed air bubbles interfere with the substrates.

7.3.3.10 Quenching of alkoxyamines for degrafting

The respective substrate, **4-2**, **4-5** or **NMP B**, was placed in a glass vial with a mixture of 0.5 mL tributyltin hydride and 1 mL xylene and subsequently heated to 130 °C for 5 h. Next, the sample was removed from the glass vial and thoroughly rinsed with toluene, THF, absolute ethanol and H_2O before being blown dry with N₂. The same procedure was also conducted with a blank Si-wafer.

7.3.3.11 Nitroxide-mediated radical polymerization

An alkoxyamine-carrying sample – **4-2** or **4-5** – and a blank sample were placed in individual glass vials under nitrogen atmosphere. To each vial, 3 mL of an

oxygen-free solution of 5 mg TEMPO, 11 mL styrene, 16 mL xylene and 800 mg polystyrene with alkoxyamine functionality ($M_n = 2300 \text{ g} \cdot \text{mol}^{-1}$, D = 1.19; for synthesis, Section 7.3.3.1). The vials were connected to a mini-Schlenkline with argon to allow for pressure release and then they were heated to 110 °C for 5 hours. Subsequently, NMR and SEC samples were taken and 5 mL of xylene was added to each vial. The xylene was removed and replaced with fresh xylene before all substrates were thoroughly rinsed with toluene, THF, absolute ethanol, and H₂O before being blown dry with N₂.

7.3.3.12 Sol-gel synthesis of silica nanoparticles

8 mL tetraethoxysilane (TEOS), 4 mL H_2O , 5 mL NH_3 (25 wt% in H_2O), and 192 mL EtOH were mixed and stirred over the weekend. 50 mL of the obtained solution was taken away as reference, dialyzed in 4–6 cycles in 500 mL EtOH and finally the dialyzed suspension was dried in high vacuum at 70 °C for 2 days. The remaining 150 mL of suspended nanoparticles in EtOH were directly used in the following step.

7.3.3.13 Silanization of silica nanoparticles

750 mg of the nitrone silane **S2** (for synthesis, Section 7.3.3.3) was added to the formed nanoparticles and the mixture was further stirred overnight. Next, the product mixture was subjected to 4–6 dialysis cycles in 1000 mL of ethanol over the course of one week. The dialyzed particles were characterized via dynamic light scattering before they were centrifuged a few times. Subsequently, the particles were dried for 2 days at ambient temperature in high vacuum. The successful silanization was evidenced via ¹H-NMR in methanol-d₄ and XPS (**Table 7.2**).

7.3.3.14 Nitrone-mediated radical coupling on silica nanoparticles

To 20 mL fully dialyzed suspension of silanized nanoparticles, 330 mg poly(*n*-butyl acrylate) with bromine terminus, and 120 µL PMDETA as ligand was added and the mixture was purged for 30 min with argon. Consequently, 50 mg of Cu powder and 70 mL dry DMF was added to a Schlenk flask inside the glove box. To this flask, the purged mixture of suspended nanoparticles and polymer was added under argon atmosphere. The obtained reaction mixture was purged for another 30 min with argon before being heated to 50 °C overnight.

The product mixture was subsequently dialyzed in DMF/EtOH mixtures and then characterized via dynamic light scattering. Subsequently, a part of the obtained dialyzed solution was centrifuged and the particles were then dried for 2 days at 70 °C in high vacuum before they were characterized via TGA. The dried particles were also characterized via XPS (**Table 7.2**).

Name	Relative Concentration		
	Pure nitrone S2	Nitrone@SiO ₂	PnBA@SiO₂
С-С, С-Н	18.0	15.4	7.56
C-O, C-N	5.67	5.54	2.66
0=C-0	1	1	1
N	1.65	1.52	0.70

Table 7.2: XPS integration ratios.

XPS integration ratio show a good match for the pure and the grafted nitrone silane. After nitrone-mediated radical coupling with poly(n-butyl acrylate), the O=C-O contribution rises by more than factor 2.

7.3.3.15 Activation and cleaning of silica microparticles

10 g of fine silica powder (Mesh 60) was suspended and stirred in 40 mL of a mixture of H_2SO_4 and H_2O_2 for 30 min and then washed with water. Subsequently, the mixture was stirred in 1 M HCl for another 30 min, followed by another washing step and before it was finally stirred in a mixture of NH_3 (25 wt% in water) and H_2O_2 for half an hour. To remove all reagents, the silica powder was washed again with water. Note that all washing steps occur via a ceramic filter with copious amounts of water. The cleaned silica powder was dried at 40 mbar with a heat gun before it was stored in the glove box under nitrogen atmosphere.

7.3.3.16 Functionalization of silica microparticles with an ATRP initiator

3.5 g of the activated and dry silica particles and a large excess of 6 g of 11-(trichlorosilyl)undecyl 2-bromo-2-methylpropanoate (for synthesis, Section 7.3.1.2) was mixed in 100 mL dry toluene inside the glove box. The mixture was stirred overnight inside the glove box before it was passed over a filter to remove the liquid reaction mixture. The solid residue was washed with 500 mL dry toluene and subsequently removed from the glove box. The functionalized silica particles were then washed with large amounts of methanol, acetone, abs. ethanol, and water before they were dried in high vacuum overnight.

A similar procedure was employed to functionalize nanoparticles of BaTiO₃, ZnO, and silicon. The corresponding nanoparticles were centrifuged three times for purifications after each reaction step, i.e. activation, silanization.

7.3.3.17 Decoration of silica microparticles with nitroxide

50 mg of the silica microparticles functionalized with an ATRP initiator, varying amounts of PBN (1 – 20 mg), and 3 cm copper wire was suspended in 1.5 mL of a mixture of 160 μ L Me₆TREN and 9 mL dimethyl sulfoxide in a small glass vial.

The mixture was purged with argon for 1 hour and was subsequently stirred inside the glove box at 40 °C for the desired reaction time, mostly 6 hours. Reaction times longer than 6 hours led to no further increase or even a decrease in radical concentration. Afterwards, the functionalized particles were washed with acetone, methanol, water, and again acetone before they were dried in high vacuum overnight.

A similar procedure was employed to decorate nanoparticles of BaTiO₃, ZnO, and silicon, which were previously functionalized with an ATRP initiator. Subsequently, the decorated nanoparticles were purified via repeated centrifuging and redispersion in suitable solvents DMSO and THF. Eventually, EPR spectroscopy was used for characterization.

7.3.3.18 Long-term EPR investigation of nitroxide-carrying microparticles

Approximately 30 mg of silica microparticles equipped with nitroxides on the surface was transferred into the glove box. Under nitrogen atmosphere, three Suprasil quartz ESR tubes (3 mm outer and 2 mm inner diameter) of known weight were filled with approximately 10 mg of microparticles before they were sealed in an airtight manner. Subsequently, all tubes were removed from the glove box to be stored in an air-conditioned room at 22 °C, in the fridge at 7 °C, and in the freezer at -15 °C for a period of 84 days. Frequently, the remaining nitroxide concentration was assessed via EPR spectroscopy, calibrated against at least three TEMPO solutions of different concentrations for each series of measurements.

7.3.4 Syntheses and procedures of Chapter 5

7.3.4.1 Protection of the thiol group of cysteine 5-1



Scheme 7.9. Protection of the thiol group of cysteine **5-1** with a triphenylmethyl protection group, giving **5-2**.

Cysteine **5-1** (30 g, 248 mmol, 1.00 equiv.) and triphenylmethanol (64.6 g, 248 mmol, 1.00 equiv.) were dissolved in 230 mL trifluoroacetic acid. The reaction mixture was stirred for 45 min at room temperature. Diethyl ether (200 mL) and ice (200 mL) was added. The mixture was placed in an ice bath. Trifluoroacetic acid was neutralized with K_2CO_3 until a white precipitate formed. The precipitate was filtered off and washed with cold water and EtOH. The product was taken up in diethyl ether was filtered again. The product **5-2** was dried under high vacuum overnight and used without further purification.

7.3.4.2 Protection of the amine group of 5-2



Scheme 7.10. Protection of the amine group of 5-2 with a Boc group, giving 5-3.

Di-*tert*-butyl dicarbonate (16.8 g, 77 mmol, 1.1 equiv.) was dissolved in 28 mL 2.5 M NaOH, 100 mL H₂O, and 150 mL dioxane. Subsequently the mixture was cooled to 0 °C with an ice bath. Triphenylcysteine **5-2** (25.4 g, 70 mmol, 1.0 equiv.) was added to the cold mixture. The reaction mixture was stirred overnight while being allowed to reach room temperature. HCl (1M) was added slowly to adjust pH to 3. Ethyl acetate was added and the aqueous phase was extracted three times. The pooled organic phase was washed with water and subsequently dried over MgSO₄. The solvent was removed under reduced pressure. Product **5-3** was used without further purification.





Scheme 7.11. Formation of the *N*-hydroxysuccinimide (NHS) ester **5-4** via EDC coupling of NHS and **5-3**.

N,*S*-protected cysteine **5-3** (10.0 g, 21.6 mmol, 1.00 equiv.) was dissolved in 400 mL cold EtOAc and cooled to 0 °C with an ice bath. EDC (4.6 g, 24 mmol, 1.1 equiv.), DMAP (270 mg, 2.2 mmol, 0.10 equiv.), NHS (2.7 g, 24 mmol, 1.1 equiv.), and pyridine (1.9 mL, 25 mmol, 1.1 equiv.) were added. The mixture was stirred overnight while being allowed to reach room temperature. The solvent was removed under reduced pressure. Diethyl ether (400 mL) was added. The organic phase was washed twice with each 100 mL brine, once with 100 mL water,

and subsequently dried with MgSO₄. The solvent was removed under reduced pressure. Product **5-4** was used without further purification.



7.3.4.4 Synthesis of protected cysteinyl cysteine 5-5

Scheme 7.12. Dipeptide formation via NHS coupling of 5-2 and 5-4 to 5-5.

NHS-cysteine **5-4** (9.34 g; 16.7 mmol; 1.00 equiv.) was dissolved in 150 mL chloroform. Triphenylcysteine **5-2** (6.05 g; 16.7 mmol; 1.00 equiv.) was added, followed by 2.5 mL triethylamine (2.7 mL; 19.5 mmol; 1.2 equiv.). The reaction mixture was stirred overnight. The solvent was removed and the residue was redissolved in ethyl acetate. Water (50 mL) and saturated NaHCO₃ solution (80 mL) were added. The organic phase was washed with saturated NaHCO₃ solution (twice) and brine (twice). The organic phase was dried over MgSO₄. The product **5-5** was freed from solvent under reduced pressure and used without further purification.

7.3.4.5 Deprotection of cysteinyl cysteine 5-5



Scheme 7.13. Removal of protection groups of 5-5, yielding 5-6.

N,*S*-protected cysteinyl cysteine **5-5** (~10 g) was dissolved in 150 mL dry DCM and cooled to 0 °C. HSiEt₃ (20 mL) was added. Subsequently, trifluoroacetic acid (75 mL) was added dropwise. After 2 hours, the solvent was removed under reduced pressure at room temperature. Diethyl ether (100 mL) and water (100 mL) were added. The water phase was washed two more times with diethyl ether. The water solvent was removed under reduced pressure at room temperature. The water solvent was redissolved in methanol (<20 mL) and precipitated in diethyl ether (>500 mL) to get the pure product **5-6**. ¹H-NMR (400 MHz, D₂O) δ (ppm): 4.12 (dd, *J* = 4.3, 7.9 Hz, 1H), 3.98 (dd, *J* = 4.3, 5.5 Hz, 1H), 3.38 (dd, *J* = 4.3, 15.2 Hz, 1H), 3.17 (dd, *J* = 7.9, 15.2 Hz, 1H), 3.09 (dd, *J* = 5.6, 15.2 Hz, 2H), 3.00 (dd, *J* = 4.3, 15.2 Hz, 2H).

7.3.4.6 Thiol-ene Michael addition polymerization to 5-7

6.18 mg cysteinyl cysteine **5-6** (1.83 mmol, 1.00 equiv.) was dissolved in 9 mL water and 1.1 mL 2.5 M NaOH solution (2.75 mmol, 1.50 equiv.). To this solution 0.55 mL tetra(ethylene glycol)diacrylate (2.02 mmol, 1.11 equiv.) in 7.5 mL ethanol and 3 mL water was added in the following manner. About two third of the mixture was added fast. The remaining third was diluted with a water/ethanol mixture and half of this mixture was added dropwise. The remaining half was again diluted and one half of the new mixture was added dropwise. Finally, these dilution cycles were repeated 3 times before all remaining diacrylate was added with the 4th cycle. Eventually, the excess diacrylate was removed from the reaction mixture by dropwise addition to a mixture of 150 mL petroleum spirit and 30 mL ethyl acetate. Then the polymer was precipitated in ethanol.

7.3.4.7 Synthesis of poly(benzyl acrylate) with thiol endgroup

Benzyl acrylate (5.0 mL, 33 mmol, 76 equiv.), 2-(dodecylthiocarbonothioylthio) propionic acid (DoPAT; 150 mg, 0.43 mmol, 1.00 equiv.), and AIBN (11 mg, 0.067 mmol, 0.16 equiv.) were mixed in toluene (7 mL), then purged with argon and stirred at 40 °C for 3 days. The solvent was removed under reduced pressure.

1.46 g poly(benzyl acrylate) was then added to 1.0 mL hexylamine and 50 μ L P(nBu)₃ in 20 mL dichloromethane. The mixture was stirred for 2 h. The polymer was precipitated in cold methanol and subsequently dried. The product was characterized via SEC ($M_n = 9800 \text{ g} \cdot \text{mol}^{-1}$ and $\mathcal{D} = 1.11$).

7.3.4.8 Thiol-ene Michael addition for ABA triblock copolymer 5-8

To 160 mg of **5-7**, 280 mg of poly(benzyl acrylate) with thiol endgroup was added. The mixture was stirred in a mixture of THF, MeOH, and some H₂O to ensure at least partial solubility of both reactants. A few small drops of $P(nBu)_3$ was added to prevent disulfide formation. The mixture was stirred overnight at 25 °C before the solvent was removed under reduced pressure.

7.3.5 Syntheses of procedures of Chapter 6

7.3.5.1 Determination of light intensity

To get a tunable light intensity for both milli- and microflow reactors, two different lamps had to be used to guarantee homogenous illumination. For milliflow reactors, a 30 cm long fluorescent lamp had to be used, whereas the microflow reactor could be operated with an OmniCure system.

A UV-Radiometer (RM12-UV, Groebel GmbH) with a calibration for light of 365 nm was employed to measure light intensities in steps of 0.5 cm from the fluorescent

tube (15 W, 365 nm emission maximum), **Figure 7.4**. Light intensities were limited to around 12 mW·cm⁻².

For the OmniCure system, the light intensities were determined in the same way at 100% iris opening, however, eventually a fixed distance of 6.3 cm was chosen to obtain good illumination and the actual light intensity per reaction adjusted via the iris opening. Light intensities up to 40 mW·cm⁻² were readily reached at 6.3 cm distance.



Figure 7.4. Intensity versus Distance from Lamp curve for a fluorescent tube of 15 W.

7.3.5.2 Radical thiol-Ene in milliflow and microflow



Scheme 7.14. Radical thiol-ene reaction of 3-butenol and octanethiol with DMPA as photoinitiator in acetonitrile upon exposure to UV light of 365 nm.

Octanethiol and 3-butenol were purged separately for 5 min with argon. 0.03 and 0.15 mmol DMPA was added to 30 mL acetonitrile, respectively, and the solution was purged in the dark for 30 min with argon. 3.0 mmol of both thiol and alkene

were added to the acetonitrile solution. The mixture was injected into a flow reactor of around 0.5 m PFA tubing (1.54 mm outer diameter, 0.75 mm inner diameter) of which 15.5 cm was exposed to UV light and the rest carefully covered with aluminum foil **Scheme 7.15**. Flow rates were adjusted via a syringe pump (*Chemyx*) to give the desired reaction times. Reaction products were collected in a GPC vial filled with 30 μ L of 0.1 wt% hydroquinone in acetonitrile and subsequently characterized via ¹H-NMR in the dark.

Microreactions were performed on the Labtrix® Start R2.2 system (*Chemtrix BV*, *NL*), equipped with a glass microreactor (reactor volume = 19.5μ L and 1μ L, respectively) Reaction times between 1 s and 1200 s were targeted.



Figure 7.5. Microreactor Labtrix 3227 with 19.5 μ L reactor volume.



Scheme 7.15. Milliflow reactor at certain distances from a 15 W fluorescent lamp (365 nm emission maximum). The reactor was installed vertically on a metal grid and could be shifted horizontally to adjust the desired light intensity. The reactor was built from around 0.5 m PFA tubing of 0.75 mm inner diameter of which only 15.5 cm were exposed to light, while the rest of the reactor was carefully covered with aluminum foil.

7.4 References

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Chapter 8

Summary and Outlook



8.1 Summary

Surface properties determine the interaction of two materials. Tuning surface properties such as wettability and refractive index, potentially in a stimuliresponsive way, gives access to advanced materials with complex functions.^[1] Polymers with almost any desired architecture and composition can be accessed via thermal reversible deactivation radical polymerizations such as ATRP, RAFT, or NMP. However, these thermal techniques either lack spatial control on surface in 'grafting-from' approaches or require post-polymerization modification when employed in 'grafting-to' approaches.

The main goal of the work presented in this thesis was to overcome these two constraints. Both a 'grafting-from' and a 'grafting-to' methodology were explored to exploit the full potential of copper-mediated radical polymerization for surface engineering.

First, surface-initiated photoinduced copper-mediated radical polymerization (SI-photoCMP) was employed to graft a wide range of polyacrylate brushes from silicon substrates at extremely low catalyst concentrations. This was the first time the controlled nature of the reported process has been demonstrated via block copolymer formation and reinitiation experiments. In addition to unmatched copper catalyst concentrations in the range of few ppb, film thicknesses up to almost 1 µm were achieved within only one hour illumination time. Spatial resolution was achieved by the use of photomasks.

For a photomask-free methodology, the UV light source was replaced by a XeF excimer laser that was connected to a galvo scanner set-up. This laser-induced SI-photoCMP was employed to graft various polyacrylates from silicon substrates in arbitrarily patterns. XPS, ToF-SIMS, and GAATR-FTIR evidenced the successful

grafting. A linear dependence of film thickness on direct exposure time to laser light was observed. The reaction was found to be extremely fast, reaching almost 40 nm after 125 μ s of direct laser light. In addition, the controlled nature of the grafting was demonstrated via block copolymer formation. Resolutions in the range of 300 μ m could be realized according to ToF-SIMS, however, the present methodology was strongly influenced by beam quality of the employed laser.

Besides the two previous 'grafting-from' protocols, also a new 'grafting-to' methodology has been developed that allows for direct use of polymers with a bromine endgroup. Nitrone-mediated radical coupling was exploited to reversibly graft poly(*n*-butyl acrylate) via an alkoxyamine that allows for subsequent NMP. Two routes were explored, one with the nitrone species in solution and one on the surface. Both approaches resulted in grafted poly(*n*-butyl acrylate) on planar silicon substrates. Degrafting experiments indicated that nitrone coupling could be used for reversible grafting of surfaces for both approaches. Subsequent modification via nitroxide-mediated radical polymerization, however, functioned better for the route with the nitrone initially in solution. In addition, the grafting density of the grafted-nitrone approach was assessed on silica nanoparticles to be close to 0.21 chains per nm², placing NMRC in the range of other efficient 'grafting-to' and many 'grafting-from' techniques.^[2] Critically, particles with tunable radical concentration were generated and characterized via EPR.

Furthermore, a novel approach for the synthesis of polyzwitterionic polymers from the dipeptide cysteinyl cysteine and tetra(ethylene glycol)diacrylate via nucleophilic thiol-ene Michael addition was presented. ¹H-NMR and SEC evidenced the formation of a polymer. The aggregation behavior was investigated via DLS and pH responsiveness that could be underpinned via turbidity measurements.

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ABA triblock copolymers were formed via conjugation to poly(benzyl acrylate) with a thiol endgroup and featured stable aggregates over the entire pH spectrum.

Finally, the influence of light intensities on the photoinduced radical thiol-ene reaction of 3-butenol and 1-octanethiol in milli- and microflow was investigated to shed light on the hypothesis that higher light intensities actually lead to lower conversions. Our findings show that our hypothesis was partially true. Higher conversions were reached at low light intensities already after short reaction times. However, the respective final conversions after a long reaction time were very similar to those of higher light intensities. The advantage of low light intensities was most prominent at low concentrations of reactant and photoinitiator. Remarkably, the use of lower light intensities effectively outcompeted the general advantage gained by higher concentrations. Therefore and contrary to a widely shared perception, batch reactors might consequently deliver better results for radical thiol-ene reactions than flow reactors as high illumination efficiency harms more than it helps. Moreover, the use of low radical flux than the repeated addition of small quantities of photoinitiator as suggested in literature.^[3]

8.2 Nederlandse samenvatting

De eigenschappen van een oppervlak of interface bepalen de interactie van twee verschillende materialen. Het tunen van eigenschappen zoals de brekingsindex en bevochtigbaarheid, al dan niet als respons op een specifieke stimulus, bieden de mogelijkheid om geavanceerde materialen met complexe functies te bekomen.^[1] Via thermisch geïnitieerde, reversibele gedeactiveerde radicaal polymerisaties, zoals ATRP, RAFT, of NMP kunnen polymeren worden geproduceerd van bijna elke gewenste samenstelling en architectuur. Thermische technieken hebben echter een povere ruimtelijke controle wanneer zij worden gebruikt in een "graftingfrom" methode. Ook voor de "grafting-to" methode zijn post-polymerisatie modificaties vereist.

Het overwinnen van deze twee hindernissen was het hoofddoel van mijn doctoraatsonderzoek. Zowel de "grafting-from" als de "grafting-to" methode werden onderzocht om het volledige potentieel van de koper gemedieerde radicaal polymerisatie te demonstreren.

Ten eerste werd er een oppervlak-geïnitieerde, foto-geïnduceerde, kopergemedieerde radicaal polymerisatie (ook SI-FotoCMP) aangewend om polyacrylaat strengen te groeien op silicium substraten, met extreem lage concentraties aan koper. Dit proces vond plaats op een gecontroleerde wijze zoals aangetoond werd door de synthese van blokcopolymeer en reinitiatie experimenten. Daarbij was het mogelijk om met deze ongeëvenaard lage koper concentratie een polymeer film te groeien tot bijna 1 µm dik na 1 uur illuminatie. Ruimtelijke resolutie kon worden bekomen door het gebruik van fotomasks.

Voor een fotomask-vrije methode werd de eerder gebruikte UV-lichtbron vervangen door een XeF excimer laser die werd verbonden aan een galvo 2D scanner set-up. Met deze laser-geïnduceerde SI-fotoCMP konden verschillende polyacrylaten groeien op silicium substraten in willekeurige patronen. XPS, ToF-SIMS en GAATR-FTIR toonden het succes van deze techniek aan. Een lineair verband werd waargenomen tussen de blootgestelde tijd aan de UV-laser en de dikte van de polymeerfilm. Deze reactie vond snel plaats waarbij diktes van 40 nm na 125 µs blootstelling vastgesteld werden. Ook hier was er sprake van controle als gevolg van de vorming van blokcopolymeren. Via ToF-SIMS kon een resolutie

van 300 μ m bekomen worden. Deze methode is echter sterk afhankelijk van de kwaliteit van de laserstraal.

Naast de twee besproken 'grafting-from' methoden werd ook een 'grafting-to' methode ontwikkeld die toeliet broom-getermineerde polymeren direct te gebruiken. Nitron-gemedieerde radicale koppeling werd aangewend om poly(*n*-butyl acrylaat) reversibel te koppelen via een alkoxyamine. Dit laat toe om vervolgens een NMP uit te voeren. Twee verschillende routes werden daarbij onderzocht, waarbij de nitronen enerzijds in oplossing en anderzijds gekoppeld aan een oppervlak (silicium substraat) voorkwamen. Beide manieren resulteerden in poly(*n*-butyl acrylaat) op het substraat. Zogenaamde 'degrafting' experimenten tonen aan dat het met deze techniek mogelijk is om de polymeren reversibel aan de substraten te koppelen. Een hierop volgende modificatie via NMP werkte beter met de nitronen in oplossing. Verder werd de "grafting" densiteit bepaald op silica nanopartikels, hetgeen resulteerde in een densiteit van 0.21 polymeerketens per nm². Dit maakt NMRC evenwaardig aan andere efficiënte "grafting-to" methoden en veel "grafting-from" technieken.^[2] Partikels met een afstembare radicaal concentratie werden geproduceerd en vervolgens gekarakteriseerd via EPR.

Een nieuwe strategie werd ontwikkeld voor de synthese van polyzwitterionische polymeren via de nucleofiele thiol-een Michael additie vanuit het dipeptide cysteinyl cysteïne en tetra(ethyleen glycol)diacrylaat. ¹H-NMR en SEC toonden het succes van de reactie aan. Aggregatie werd onderzocht via DLS en de troebelheid werd gemeten via bepaling van de pH responsiviteit. ABA triblokcopolymeren werden gevormd via de conjugatie van poly(benzylacrylaat) met een thiol eindgroep. Dit gaf stabiele aggregaten voor alle pH waarden. Tenslotte werd de invloed van lichtintensiteit op de foto-geïnduceerde radicalaire thiol-een reactie onderzocht in milli-en microflow voor de koppeling van 3-butanol en 1-octaanthiol. De hypothese hierbij was dat hogere lichtintensiteit leidt tot lagere conversies. Deze hypothese werd gedeeltelijk waargenomen in onze experimenten. Er werd al bij lage intensiteit een hoge conversie gehaald na korte tijd. De uiteindelijke conversie, bereikt na langdurige reactie, was echter erg gelijkaardig aan deze bij hogere lichtintensiteit. Het voordeel van lage intensiteit werd vooral behaald bij lage concentratie van reactant en foto-initiator. Het was daarbij opmerkelijk dat het tijdsvoordeel bij hoge concentraties werd overtroffen door het voordeel van de lage lichtintensiteit. Dit wil zeggen dat bij radicale thiol-een reacties een goede blootstelling aan licht, zoals het geval is bij het gebruik van flow, eerder een nadeel wordt dan een voordeel. Het gebruik van lagere lichtintensiteit is bijgevolg een meer praktische methode om een lagere flux aan radicalen te bekomen dan de reeds eerder gepubliceerde methodes waarbij herhaaldelijk kleine hoeveelheden aan foto-initiator worden toegevoegd.^[3]

8.3 Outlook

Over the last four years, there has been a rapid development of tools for surface engineering. PhotoRDRP gives straightforward access to patterning with material of well-defined properties. Recently, iron- and especially organocatalyzed photoRDRP have moved into the center of attention. Up to now, copper- and iridium-mediated ATRP still yield better results with respect to control over molecular weight characteristics and especially endgroup fidelity. However, it can be expected that new organocatalysts will improve and soon achieve the same level of control.

While sequence-controlled and even sequence-defined polymerizations have become available for polymerizations in solution,^[4-6] multiblock copolymerization from surfaces has only received little attention.^[2] Grafting multiple stimuliresponsive multiblock copolymers might give access to readily switchable surfaces and is definitely worth of being investigated.

Excellent spatial control has become more a question of optical equipment than of chemical reactions as recently demonstrated.^[7] Currently, spatial control is usually obtained by use of photomasks, which allows for high-throughput yet also limits the choice of patterns to the availability of the respective photomasks. Photomask-free approaches such as the 2D direct laser writing presented in this thesis will probably gain more attention in the future. It could be worthwhile to investigate other photoRDRP techniques, including photoiniferter, for 2D and eventually 3D direct laser writing.

Very interesting might be the combination of spatially resolved 'grafting-from' and spatially resolved 'grafting-to' methodologies, potentially in λ -orthogonal reactions.

Last but not least, promising results have been presented in Chapters 5 and 6.

While Chapter 5 could potentially be extended to surfaces, research based on

Chapter 6 probably should focus on the decomposition rates of photoinitiators and

to what extend decomposition products themselves can act as photoinitiating species.

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List of Publications

1) "Surface Grafting via Photoinduced Copper-mediated Radical Polymerization at Extremely Low Catalyst Concentrations"

J. Laun, M. Vorobii, A. de los Santos Pereira, O. Pop-Georgievski, V. Trouillet,
A. Welle, C. Barner-Kowollik, C. Rodriguez-Emmenegger, T.
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- "Photomediated Controlled Radical Polymerization"
 X. Pan, M. A. Tasdelen, J. Laun, T. Junkers, Y. Yagci, K. Matyjaszewski, Prog. Polym. Sci. 2016, 62, 73-125.
- "Reversible Surface Engineering via Nitrone-Mediated Radical Coupling"
 J. Laun, W. Marchal, V. Trouillet, A. Welle, A. Hardy, M.K. Van Bael, C. Barner-Kowollik, T. Junkers, **2017**, submitted.
- 4) "2D Laser Lithography on Silicon Substrates via Photoinduced Copper-Mediated Radical Polymerization"

J. Laun, Y. De Smet, E. Van de Reydt, A. Krivcov, V. Trouillet, A. Welle, H. Möbius, C. Barner-Kowollik, T. Junkers, **2017**, submitted.

Conferences and Presentations

Oral presentations

- "Surface Grafting via Photoinduced Copper-Mediated Radical Polymerization at Extremely Low Catalyst Concentrations"
 J. Laun, M. Vorobii, A. de los Santos Pereira, O. Pop-Georgievski, V. Trouillet, A. Welle, C. Barner-Kowollik, C. Rodriguez-Emmenegger, T. Junkers, *KNMF User Meeting* **2016**, Karlsruhe (Germany).
- 2) "Surface Grafting via Photoinduced Copper-Mediated Radical Polymerization at Extremely Low Catalyst Concentrations"

J. Laun, M. Vorobii, A. de los Santos Pereira, O. Pop-Georgievski, V. Trouillet, A. Welle, C. Barner-Kowollik, C. Rodriguez-Emmenegger, T. Junkers, *Chemistry Conference for Young Scientists (ChemCYS)* **2016**, Blankenberge (Belgium). *** Best Oral Presentation, 2nd Prize ***

3) "Surface Grafting via Photoinduced Copper-Mediated Radical Polymerization at Extremely Low Catalyst Concentrations"
J. Laun, M. Vorobii, A. de los Santos Pereira, O. Pop-Georgievski, V. Trouillet,
A. Welle, C. Barner-Kowollik, C. Rodriguez-Emmenegger, T. Junkers, Winter School "Functional Coatings, 2016, Diepenbeek (Belgium).
*** Best Oral Presentation ***

Poster presentations

- "Exploiting Nitrone Chemistry for Surface Patterning"
 J. Laun, A. Welle, C. Barner-Kowollik, T. Junkers, Annual Meeting of the Belgian Polymer Group **2014**, Gent (Belgium).
- 2) "Surface Grafting via Photoinduced Copper-Mediated Radical Polymerization at Extremely Low Catalyst Concentrations"
 J. Laun, M. Vorobii, A. Pereira, O. Pop-Georgievski, V. Trouillet, A. Welle, C. Barner-Kowollik, C. Rodrigues-Emmenegger, T. Junkers, Annual Meeting of the Belgian Polymer Group **2015**, Houffalize (Belgium).
- 3) "Grafting-to via Nitrone-Mediated Radical Coupling"
 J. Laun, C. Barner-Kowollik, T. Junkers, Annual Meeting of the Belgian 4) Polymer Group 2016, Hasselt (Belgium).
- "Toolbox PhotoATRP Contributions to Access Complex Functions in Solution and on Surfaces"

J. Laun, G. Ramakers, B. Wenn, J. Vandenbergh, C. Barner-Kowollik, T. Junkers, *European Polymer Federation* **2017**, Lyon (France).

Curriculum Vitae

Joachim Frieder Laun was born on 2 June 1988 in Schwäbisch Hall, Germany. After finishing high school in 2008, he studied pure Chemistry at the Karlsruhe Institute of Technology (KIT) in Germany. The Konrad-Adenauer-Foundation supported Joachim's undergraduate studies with a full study scholarship and Joachim received two prizes for outstanding course achievements at the KIT before he graduated summa cum laude in 2013 under supervision of prof. Christopher Barner-Kowollik (KIT) and co-supervision of prof. Tanja Junkers (University of Hasselt, Belgium) on the topic "Photo-Induced Patterning of Surfaces via Nitrone-Mediated Chemistry". In the beginning of 2014, Joachim started his PhD on the "Development of Polymer Grafting Methodologies for Advanced Surface Engineering" at the University of Hasselt in Hasselt, Belgium, under supervision of prof. Tanja Junkers and co-supervision of prof. Christopher Barner-Kowollik. Joachim obtained two awards for his oral presentations at international conferences. The Research Foundation - Flanders (FWO) and the University of Hasselt financially supported his research that eventually led to various scientific contributions, which are presented in this dissertation.

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