The future of poly(2-oxazoline)s

Richard Hoogenboom

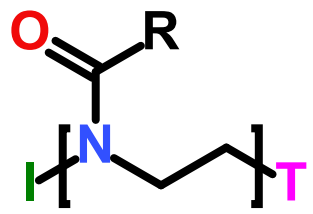
Supramolecular Chemistry Group, Centre of Macromolecular Chemistry (CMaC), Department of Organic and Macromolecular Chemistry, Krijgslaan 281-S4, B-9000 Ghent, Belgium

Email: Richard.hoogenboom@ugent.be

Abstract:

Poly(2-oxazoline)s have gained significant interest in the past decade, especially driven by their high potential for biomedical applications, amongst others to substitute poly(ethylene glycol). Within this perspective article the emerging trends in the area of poly(2-oxazoline)s are discussed with a focus on synthetic advances, including the development of high molar mass polymers, the broadening of the cyclic imino ether monomer range, and the development of degradable poly(2-oxazoline) derivatives. Furthermore, emerging trends in the use of poly(2-oxazoline)s will be highlighted, including their use to study basic fundamental polymer properties, specific biomedical applications, including drug delivery and 3D scaffolds, as well as other applications as interlayers in organic devices and polymer gel electrolytes. Finally, this perspective article provides a discussion on the future vision for the area of poly(2-oxazoline)s.

Graphical abstract:



Keywords: Polymers; cationic ring-opening polymerization; living polymerization; biomaterials; drug delivery

1. Introduction

The use of polymers has strongly contributed to modern society. Despite that the concept of polymers was only discovered about hundred years ago by Staudinger, they have had a tremendous impact on a wide range of applications from disposable plastics, via light-weight construction materials and high-strength composites to biomedical devices and drug therapy. Current times are sometimes even referred to as the 'Polymer Age'.[1]

About 55 years ago, poly(2-oxazoline)s were first reported based on the living cationic ring-opening polymerization (CROP) of 2-oxazoline monomers as shown in Figure 1.[2-6] This polymerization proceeds via nucleophilic attack of the monomer onto the initiator leading to the formation of a 2-oxazolinium group while the leaving group of the initiator ends up as counter-ion. Subsequent nucleophilic attack of the next monomer on the carbon on the 5-position of the 2-oxazolinium ring leads to the ring-opened poly(2-oxazoline)s, while the incoming monomer ends up as the 2-oxazolinium chain end. This monomer addition process continues until all monomer is consumed, after which another monomer can be added to make block copolymers or a nucleophile can be added to terminate the polymerization and to introduce a functional end-group.[7-9] Depending on monomer nucleophilicity and the counter-ion stability, there may be an equilibrium between 2-oxazolinium cationic propagating species and covalent dormant propagating species in which the anionic leaving group is attached to the chain end.[10] The properties of the resulting poly(2-oxazoline)s can be controlled by variation of the 2-substituent of the 2-oxazoline monomer, which becomes the side-chain of the polymer.[7,8] This variability of the side-chain provides access to a wide range of polymer properties ranging from hydrophilic, via hydrophobic to fluorophilic and from highly flexible polymers, via semi-crystalline to rather rigid polymers as well as responsive polymers.[10-12]

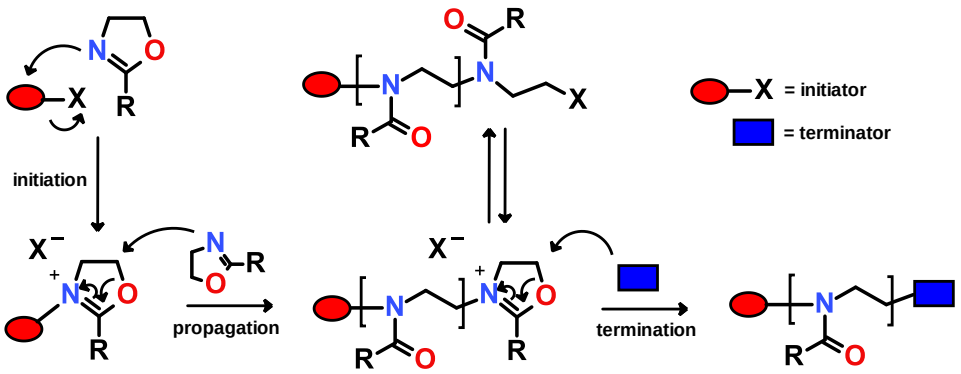


Figure 1. Simplified schematic representation of the living cationic ring-opening polymerization of 2-oxazolines leading to poly(2-oxazoline)s.

After the discovery of poly(2-oxazoline)s, the majority of early publications focused on the polymerization mechanism as well as expanding the monomer scope.[7] However, despite that the CROP of cyclic imino ethers is not limited to 2-oxazolines, the vast majority of publications only focused on the polymerization of 2-substituted-2-oxazolines. Furthermore, the physicochemical properties of the resulting poly(2-oxazoline)s were studied in detail enabling in depth understanding of how the side-chains influence the physicochemical properties of the polymers. In the early years, the application potential of poly(2-oxazoline)s was mostly evaluated for bulk applications, such as compatibilizers, surfactants and polymer networks.[7] To date, only poly(2-ethyl-2-oxazoline) (PEtOx) has found wide-spread applications in such bulk applications and is marketed under the tradename Aquazol® by Polymer Chemistry Innovations.[13]

Nowadays, the major field of research on poly(2-oxazoline)s focuses on their potential use in biomedical applications, such as biomedical devices, tissue engineering and drug delivery.[14,15,16] This interest is inspired by the seminal work of Zalipsky who was the first to demonstrate enhanced blood circulation for PEtOx and poly(2-methyl-2-oxazoline) (PMeOx) decorated liposomes, with similar blood circulation times compared to poly(ethylene glycol) (PEG) decorated liposomes.[17] These results indicated that PMeOx and PEtOx have similar ability to shield non-specific interactions with proteins and cells as PEG. However, it should be noted that more and more evidence arises that a large percentage of Western population has antiPEG antibodies, which may induce an allergic response upon treatment with PEGylated formulations, including COVID-19 vaccines,[18,19] further stimulating research on alternative polymers that suppress non-specific interactions,[20-22] including poly(2-oxazoline)s. Even though there are no approved biomedical applications of poly(2-oxazoline)s yet, Serina Therapeutics has reported that a poly(2-oxazoline)-drug conjugate is safe and well-tolerated in a preliminary clinical trial with 19 human patients.[23] In addition, they demonstrated that once-a-week subcutaneous administration of the poly(2-oxazoline)-drug conjugate led to continuous blood plasma levels of the drug. More recently, a poly(2-oxazoline) based hemostatic patch, as developed by GATT technologies, also entered human clinical trials.[24] Even though to date there are no therapeutics or medical devices based on poly(2-oxazoline)s approved for the clinic, the approval to start these clinical trials implies that poly(2-oxazoline)s have been demonstrated to be non-toxic in multiple animal models and can reproducibly be manufactured in sufficient purity.

Within this perspective article, the emerging trends in the synthesis of poly(2-oxazoline)s will be first addressed, mostly focusing on recent synthetic advances that contributed to their, biomedical, application potential. Secondly, the emerging trends in the properties and application potential of poly(2-oxazoline)s will be discussed. Finally, a personal view on the future of poly(2-oxazoline)s will be provided.

2. Emerging trends in the synthesis of poly(2-oxazoline)s

The synthesis of a wide-variety of poly(2-oxazoline)s with various (functional) side-chains and end-groups is well-established and is continuously being further expanded with both new monomers as well a new functionalization strategies and protocols.[9-11] This section will, however, not focus on these continuous improvements, but rather aims to discuss recent emerging trends in the synthesis of poly(2-oxazoline)s that have enabled the preparation of previously unattainable and/or unexplored poly(2-oxazoline)s and poly(2-oxazoline)-derivatives.

One of the main challenges for the development of poly(2-oxazoline)s by CROP of 2-oxazolines (Figure 2a) has been the occurrence of intrinsic chain transfer side reactions during the CROP that obstruct the reproducible synthesis of defined high molar mass polymers, which is required for their use in applications where polymer chain entanglements are required to enhance the mechanical properties, such as pharmaceutical excipients or additive manufacturing. It is believed that the lack of straightforward access to high molar mass poly(2-oxazoline)s is one of the main reasons why they have been abandoned for use in bulk polymer applications. It should be noted that Aquazol is available with a mass average molar mass up to 500 kg/mol, but the number average molar mass (M_n) of this Aquazol 500 is limited to 120 kg/mol,[25] indicating that a broad molar mass distribution is obtained during production, likely due to chain transfer and polymer coupling side reactions. Only very recently, our team reported a methodology for preparing defined high molar mass poly(2-oxazoline)s with a M_n up to 287 kg/mol and a dispersity of ~ 1.15.[26] This was achieved by stringent purification of all reagents, in combination with selecting chlorobenzene as a non-interfering, rate accelerating solvent that allowed polymerization at 40 °C. It was rationalized that this low temperature was required to suppress intrinsic chain transfer side-reactions that were ascribed to tautomerization of the 2-oxazolinium cationic chain end to an enamine form. The access to defined high molar mass poly(2-oxazoline)s enabled the discovery of phase separation in blends of PEtOx with poly(2-*n*-propyl-2-oxazoline) (P*n*PrOx)[27] and the development of thermogelling P*n*PrOx-*b*-PEtOx-*b*-P*n*PrOx triblock copolymers.[28] It should be noted, however, that the use of low polymerization temperatures (40 °C) leads to a significant increase in polymerization time up to 28 days to obtain a M_n of 300 kg/mol, severely limiting industrial applications. In this regard, the future use of sulfolane or trifluoromethylbenzene could be considered as solvents for the preparation of high molar mass poly(2-oxazoline)s, as these solvents were demonstrated to accelerate the CROP of 2-oxazolines.[29,30]

In recent years, there is an increasing interest in expanding the monomer scope of cyclic imino ethers beyond the common 2-substituted-2-oxazolines with alkyl or aryl substituents.[31] The polymerization of the six-membered cyclic 4,5-dihydro-1,3-oxazines, commonly referred to as 2-oxazines, has gained interest as the resulting poly(2-oxazine)s have an additional methylene group in the main chain resulting in higher flexibility, i.e. lower glass transition temperature, and slightly higher hydrophobicity compared to poly(2-oxazoline)s with the same side chain (Figure 2b).[32] Interestingly, the statistical copolymerization of 2-oxazolines and 2-oxazines leads to the

spontaneous formation of gradient copolymers, whereby the 2-oxazine is incorporated faster than the 2-oxazoline providing straightforward access to amphiphilic gradient copolymers.[33] The poly(2-oxazine)s are gaining interest for biomedical applications as the higher chain mobility has been demonstrated to lead to improved antifouling properties compared to poly(2-oxazoline)s and PEG[34] while also being beneficial for drug delivery.[35,36] However, recently it was demonstrated that core-crosslinked micelles coated with poly(2-methyl-2-oxazine) and poly(2-ethyl-2-oxazine) revealed more interactions with blood immune cells than core-crosslinked micelles coated with PEtOx and, especially, PMeOx.[37] These results demonstrate that antifouling behavior and biocompatibility depends on the investigated polymer as well as the formulation indicating the importance of in depth comparative studies. Furthermore, the incorporation of poly(2-oxazine) structures has been demonstrated to be beneficial for the development of thermoresponsive hydrogels that can be used for 3D printing and for melt-electrospinning writing.[38,39]

Further increasing the cyclic imino ether ring-size to the 7-membered 4,5,6,7-tetrahydro-1,3-oxazepine structure, commonly referred to as 2-oxazepines, has been proven to be very challenging, despite that the 2-(1-pyrridinyl)-2-oxazepine monomer was already reported by Saegusa in 1997.[40] However, the presence of the pyridinyl side-chain leads to the formation of polyureas, which could be obtained using methyl triflate as initiator while the use of benzyl chloride led to the exclusive isomerization to 1,1'-carbonyl-di-pyrrolidine. Only some years ago, our group demonstrated the successful synthesis of the second 2-oxazepine monomer, namely 2-phenyl-2-oxazepine, and its polymerization, which was found to be more than 500 times slower than the CROP of the corresponding 2-phenyl-2-oxazoline monomer (Figure 2c).[41] The slower polymerization of the 2-oxazepine monomer was ascribed to the non-planarity of imino ether moiety obstructing its isomerization to the final tertiary amide of the resulting polymers.

In 2019, Wu and Swager introduced 2-ethylthio-2-oxazoline as versatile monomer for the living CROP resulting in defined poly(2-ethylthio-2-oxazoline) (Figure 2d).[42] Subsequent oxidation of the ethylthio side chains of this polythiocarbamate activates the side chain for mild nucleophilic substitution with a broad range of thiol and amine containing nucleophiles leading to diverse functional poly(2-oxazoline) analogues with thiocarbamate and urea functionalities, respectively. It should be noted that similar polyurea analogues can also be prepared through hydrolysis of poly(2-oxazoline)s to linear polyethyleneimine (PEI) followed by full amidation with isocyanates,[43] which, however, is much less elegant and is limited by the availability and reactivity of the isocyanates.

A final 2-oxazoline monomer that is receiving more and more attention in recent years is 2-isopropenyl-2-oxazoline (iPOx) (Figure 2e).[44] Both the CROP and radical polymerization of iPOx were first reported by Kagiya and Matsuda in 1972.[45] The CROP of iPOx is rather challenging as the conjugated side-chain vinyl group induces significant chain transfer and termination side-reactions leading to the formation of short oligomers with broad molar mass distributions. Therefore, current interest is focused on the polymerization of the vinyl group of iPOx, which can

be achieved by (controlled) radical polymerization,[46-48] anionic polymerization[46,49,50] or group transfer polymerization.[51] The renewed interest in PiPOx is inspired by the work of Kronek and coworkers who demonstrated the good biocompatibility of this hydrophilic polymer.[52,53] More recently, we demonstrated the high stability of PiPOx in phosphate buffered saline.[54] Furthermore, PiPOx has 2-oxazoline side chains that can be easily modified by reaction with carboxylic acids providing straightforward access to a wide range of functional polymers through post-polymerization modification reactions,[46-51,55] which also enabled the straightforward preparation of hydrogels and networks through crosslinking with dicarboxylic acids.[56-58]

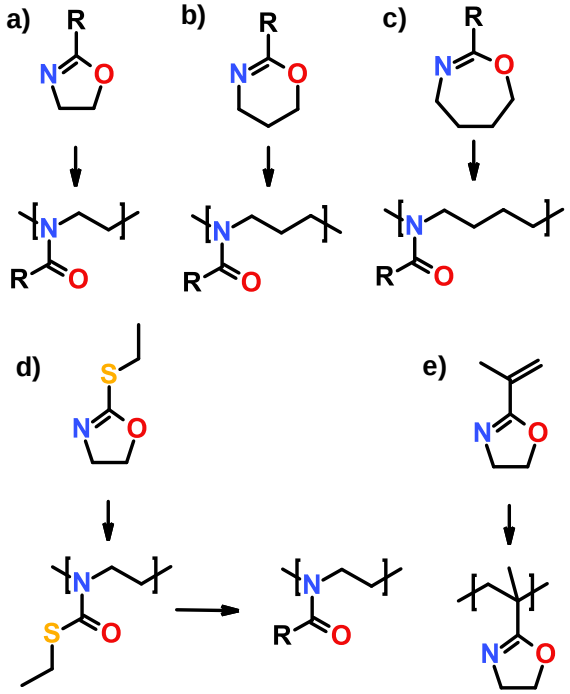


Figure 2. Schematic representation of 2-oxazoline (a), 2-oxazine (b), 2-oxazepine (c), 2-ethylthio-2-oxazoline (d) and 2-isopropenyl-2-oxazoline (e) monomers and the corresponding polymers, respectively.

One of the intrinsic limitations of poly(2-oxazoline)s is that they are non-biodegradable, even under the strong acidic conditions that are present in the stomach.[59] Oxidative degradation of poly(2-oxazoline)s has been reported under oxidative stress, but this is only relevant for mid- and long-term applications and is rather uncontrolled.[60] In recent years, this limitation has been addressed by developing degradable poly(2-oxazoline) analogues. Schubert and coworkers reported a synthetic method to convert poly(2-oxazoline)s into poly(2-oxazoline)-polyglycine copolymers as shown in Figure 3a.[61] The glycine units could be introduced by first hydrolyzing PEtOx to obtain linear PEI. Subsequent partial oxidation provided access to a copolymer of PEI and glycine, which was transformed back to the poly(2-oxazoline) by acylation of the secondary amine groups of linear PEI. The introduced secondary amide units are susceptible to enzymatic degradation by proteases enabling the degradation of the polymer backbone into shorter oligomer fragments. These degradable poly(2-oxazoline) analogues were also incorporated as

hydrophilic block into amphiphilic block copolymers with poly(2-*n*-nonyl-2-oxazoline) or polycaprolactone as hydrophobic block.[62]

A poly(2-oxazoline)-inspired degradable polymer was developed by Wang and Hadjichristidis.[63] Therefore, cyclic *N*-acylated-1,4-oxazepan-7-one monomers were developed having both an ester and a tertiary amide in the ring-structure. Subsequent organocatalyzed ring-opening polymerization of the ester units led to the formation of the poly(2-oxazoline)-inspired poly(ester amide)s that are degradable through hydrolysis of the ester units (Figure 3b).

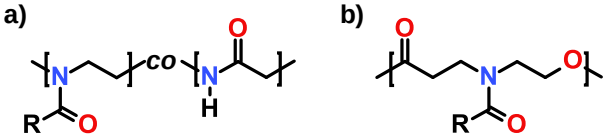


Figure 3. Chemical structures of poly(2-oxazoline)s with degradable secondary amide (a) or ester (b) groups in the main chain.

3. Emerging trends in the properties and applications of poly(2-oxazoline)s

This section will discuss some of the emerging trends in the properties and applications of poly(2-oxazoline)s that were reported in recent years, ranging from fundamental insights in polymer properties, via biomedical applications to other applications. This perspective article does not intend to be a comprehensive review of recent progress in properties and applications of poly(2-oxazoline)s, but rather aims to provide an insight in some important emerging recent trends, from the perspective of the author.

At first, some emerging trends will be discussed for the use of poly(2-oxazoline)s as research tool to gain fundamental insights in polymer properties in general. In this regard, poly(2-oxazoline)s have provided a platform for the in depth evaluation of effect of cyclic polymer topology on their properties.[64] The synthesis of cyclic poly(2-oxazoline)s was first reported by Grayson through copper(I)-catalyzed azide-alkyne cycloaddition of α-alkyne-ω-azido-functionalized poly(2-oxazoline)s, as basis for the preparation of cyclic polyethyleneimines.[65] A similar methodology was adapted by the group of Benetti to demonstrate the superior antifouling and lubrication behavior of cyclic polymer coated substrates[66,67] as well as enhanced stability of cyclic polymer coated nanoparticles,[68] based on a direct comparison of linear and cyclic poly(2-oxazoline) coatings as illustrated in Figure 4 for polymer-coated iron oxide nanoparticles. In addition, it was demonstrated that the polymer topology of the polymer coating determines the formation of a protein-corona on polymer coated iron oxide nanoparticles.[69] Furthermore, Jang reported the synthesis of linear and cyclic poly(2-*iso*propyl-2-oxazoline)s as basis to evaluate the effect of polymer topology on the thermoresponsive lower critical solution temperature (LCST) behavior of the polymers.[70] It was found that the cyclic polymer topology increases the cloud point temperature of the polymer solutions and that intermediate cloud point temperatures could be achieved by mixing of linear and cyclic polymers. Similarly, it was demonstrated by Reimhult that the flocculation temperature of iron oxide nanoparticles coated with cyclic thermoresponsive

poly(2-*iso*propyl-2-oxazoline) was higher compared to linear polymer analogues.[71] Cyclic poly(2-oxazoline)s with reactive side chains were also used for the fabrication of the first reported covalent cyclic polymer hydrogel.[72] The cyclic polymer hydrogel showed unique properties, such as an increase in swelling degree when prepared at higher polymer concentration while linear polymer hydrogels generally show the opposite behavior. The difference was ascribed to the higher steric constraints in the cyclic polymer hydrogels, which also led to a higher storage modulus for the cyclic polymer hydrogel compared to linear polymer analogues.

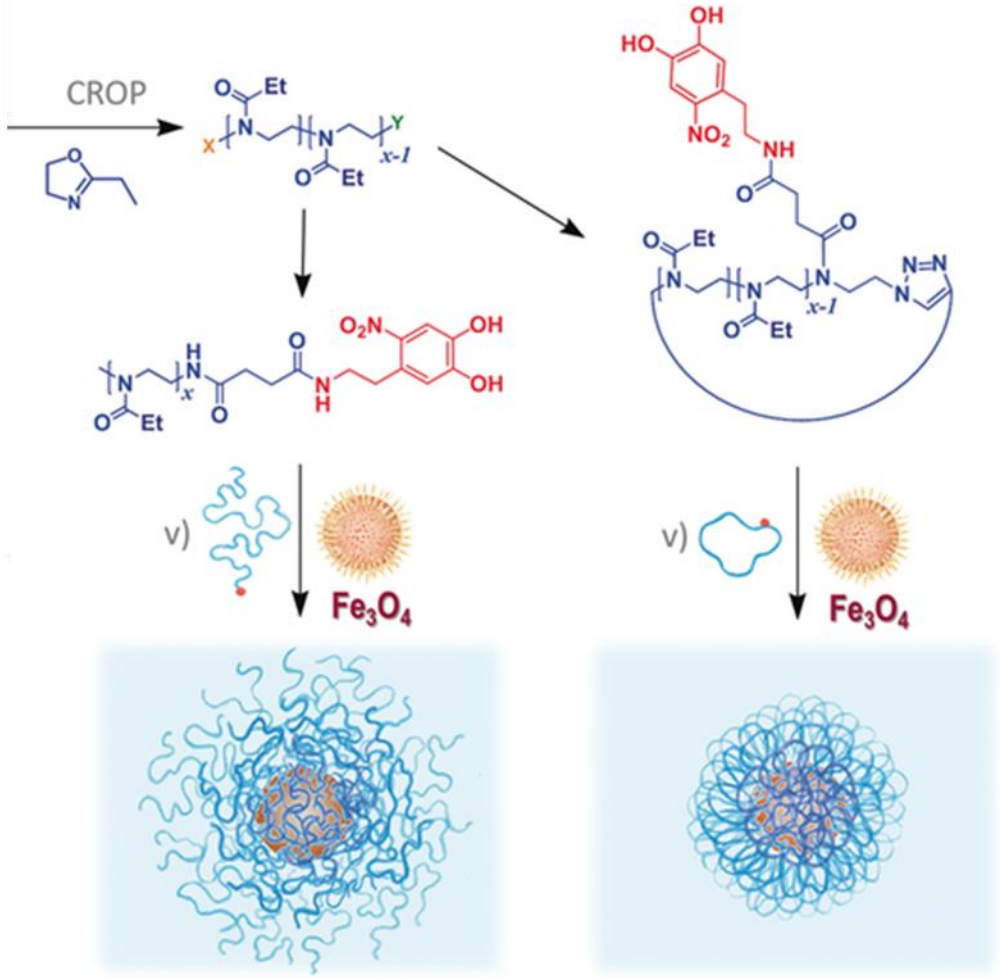


Figure 4. Schematic representation of the synthesis of linear and cyclic poly(2-ethyl—2-oxazoline)s and their use for coating of iron oxide nanoparticles. Reprinted with permission from ref 68.

Poly(2-oxazoline)s have also been widely used to study fundamentals and structure-property relations of thermoresponsive polymers.[12,73] Some recent highlights in this area will be discussed here, as a full coverage of this area is beyond the scope of this perspective article. Tiller reported a systematic investigation on the effect of the comonomer structures on the LCST phase

diagram of the corresponding copolymers.[74] This is an important contribution to the area of LCST polymers as, nowadays, phase diagrams are only sporadically reported. The study revealed that copolymers with similar LCST show differences in the LCST phase diagrams depending on the (non-)similarity of the hydrophilic-hydrophobic balance of the utilized comonomers, whereby a lower concentration dependence of the cloud point temperatures was observed if the comonomers have similar hydrophilic-hydrophobic balance. This observation was translated to hydrogels in which it was demonstrated that a normal thermal transition could only be obtained when the cloud point temperature of the polymer building blocks are independent of concentration.[75] Becer also demonstrated that the variation of the linker in between the poly(2-oxazoline) backbone and a side-chain sugar functionality can be used to tune the cloud point temperature of the copolymers.[76] Furthermore, the lectin-binding of these glycopolymers was also found to depend on the length of the linker. Thermoresponsive poly(2-oxazoline) block copolymers were also used by Kjoniksen to study the effect of temperature and concentration on the self-assembly behavior.[77] The group of Mulhaupt exploited thermoresponsive poly(2-oxazoline)s with LCST behavior to gain thermal control over the aggregation and dispersion behavior of silver nanoparticles and graphene oxide, providing opportunities for efficient catalyst recycling by a mild increase of temperature.[78,79] Furthermore, it was demonstrated that thermoresponsive poly(2-oxazoline)-coated particles with LCST behavior could be shuttled between water and ethyl acetate by variation of the temperature allowing efficient transport of a loaded cargo in between the phases of this biphasic solvent system.[80] Similar shuttling of poly(2-oxazoline) block copolymer micelles has previously also been demonstrated in biphasic water-ionic liquid systems.[81,82]

Another interesting fundamental aspect of poly(2-oxazoline)s is their crystallization behavior that was discussed in full detail in a review by Oleszko-Torbus.[83] Especially crystallization of poly(2-isopropyl-2-oxazoline) (PiPrOx) from an aqueous solution that is annealed above the cloud point temperature is quite unique, as first reported by Demirel and Schlaad.[84] The presence of PiPrOx crystals in a PiPrOx coated substrate has been demonstrated to promote proliferation of human dermal fibroblasts by Dworak.[85] The PiPrOx crystallization process has also been utilized for heating-induced irreversible formation of micelles and nanorods with a crystalline core from MeOx-*b*-PiPrOx block copolymers by Taton and Lecommandoux,[86] and very recently for the living, heat-induced crystallization of MeOx-*b*-PiPrOx block copolymers into defined stealthy nanorods by Davis and Kempe.[87,88] However, the potential irreversible crystallization of thermoresponsive poly(2-oxazoline)s from aqueous solution can also interfere with potential applications. Therefore, reports appeared on thermoresponsive poly(2-oxazoline) copolymers in which statistical comonomer distributions, e.g. in PiPrOx-PnPrOx copolymers and PEtOx-poly(2-nonyl-2-oxazoline) copolymers, lead to absence of crystallinity as reported by Dworak and Oleszko-Torbus.[89,90]

Poly(2-oxazoline)s are receiving significant interest for various drug delivery and therapeutic applications, including matrix for formulations, polymer-drug conjugates, polymer-protein conjugates, micellar carriers for drug loading, shielding of drug delivery vehicles and antimicrobial

polymers.[35,36,91-94] The progress in each of these areas is significant and selected recent examples will be discussed to illustrate this emerging area.

Even though the first use of PEtOx as matrix excipient for the preparation of oral drug formulation was reported in 2012,[95] this area only strongly expanded in recent years with reports on the use of PEtOx as matrix excipient for drug formulation for oral drug delivery through tablets[96] or an inhaler,[97] ocular drug delivery[98] as well as buccal drug delivery.[99] Furthermore, poly(2-oxazoline)s have been demonstrated for the formation of amorphous solid dispersions of various drugs, thereby enhancing the solubilization of poorly water-soluble drugs by suppression of drug crystallization.[100-102]

Covalent drug-conjugation to polymers through cleavable linkers is a popular strategy for drug delivery as it enables stimuli-controlled or slow release of the active drug, while the polymer-drug conjugate usually is inactive.[103] This concept has been used by Serina Therapeutics for the development of injectable slow release formulations of rotigotine based on a rotigotine-PEtOx conjugate that revealed stable blood plasma concentration of the drug in humans upon once a week subcutaneous injection.[23] More recently it was proposed that these slow release kinetics are driven by shielding of the degradable ester linkage by the polymer chain, thereby slowing down the enzymatic drug release kinetics.[104] Our group demonstrated that the nature of the utilized poly(2-oxazoline) is important as it determines the maximum hydrophobic drug loading capacity while retaining sufficient aqueous solubility required for intravenous administration, whereby the more hydrophilic PMeOx allows higher covalent drug loading than PEtOx.[105,106] For depot formulations, more hydrophobic poly(2-oxazoline)s lead to longer-term release kinetics[107] while the use of hydrophobic polymer-drug conjugates with dynamic cloud point temperatures enables longer term near-zero-order release kinetics due to enhancement of polymer hydration upon partial release of the conjugated hydrophobic drug.[108] An interesting concept was reported by Liu, Li and coworkers who demonstrated that PEtOx end-functionalized with temozolomide self-assembled into micellar drug carriers, thereby enhancing the blood circulation time and increasing the accumulation in and inhibition of glioblastoma.[109] Ashjari reported a poly(2-oxazoline)-based block copolymer drug conjugate consisting of a hydrophilic PEG block and a thermoresponsive PiPrOx block having doxorubicin conjugated through pH-degradable hydrazine linkers to the poly(2-oxazoline) chain end.[110] This provides a dual-responsive micellar drug delivery vehicle for which it was demonstrated that most efficient drug release occurred at slightly elevated temperature and a low pH of 5, as is the case in a tumor microenvironment.

Recently, Sengstock, Klostermeier, Tiller and coworkers reported the synthesis of amphiphilic block copoly(2-oxazoline)s end-capped with ciprofloxacin as polymer-antibiotic conjugates.[111] It was demonstrated that these copolymers showed activities against various bacterial strains, including ciprofloxacin-resistive bacteria. It was hypothesized that this enhanced activity is related to the concentration of the amphiphilic polymers in the bacterial cytoplasm, which delicately depends on the hydrophilic-hydrophobic balance of the poly(2-oxazoline) block

copolymer carrier. In recent years, the group of Liu also introduced peptide mimicking poly(2-oxazoline)s as antimicrobial agents Figure 5).[112] Poly(2-aminomethyl-2-oxazoline) (Gly-POX) was demonstrated to be a potent antimicrobial agent, that was even effective against bacterial strains that are highly resistant against antibiotics.[113] Importantly, it was demonstrated that multiple treatments with Gly-POX did not induce any resistance. The introduction of a longer alkyl spacer in poly(4-aminopropyl-2-oxazoline) (GABA-POX) was demonstrated to lead to a different mode of action, also enabling potent antimicrobial activity.[114] The mode of action of the more hydrophobic GABA-POX was ascribed to membrane-targeting, while mode of action of the more hydrophilic Gly-POX was associated to DNA targeting (Figure 5). More recently, the amino-groups of the GABA-POX were transformed into guanidine groups, which was shown to induce potent antifungal activity by fungal cell membrane penetration followed by organelle disruption.[115] These poly(2-guanidine-propyl-2-oxazoline)s were very selective against fungi and did not induce antifungal resistance.

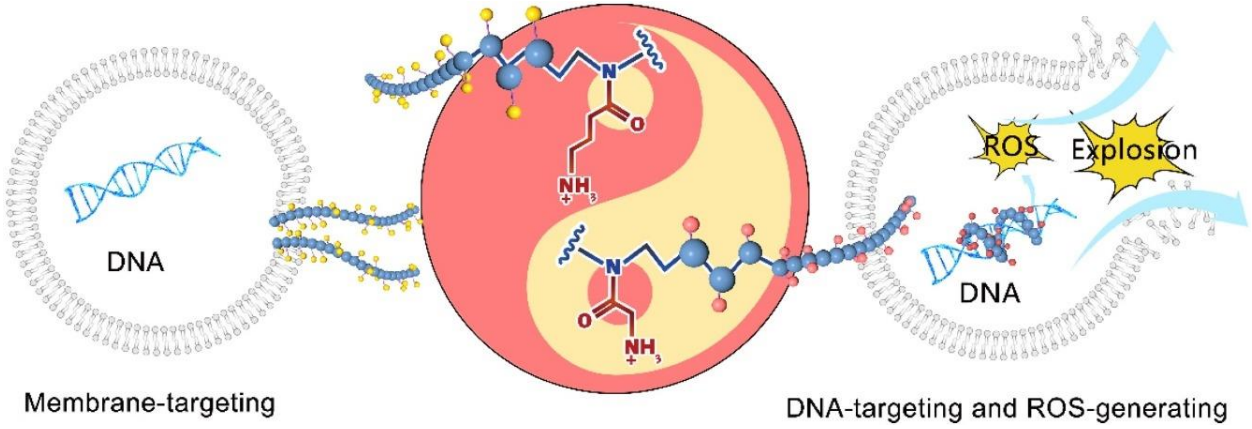


Figure 5. Schematic representation of the development of poly(2-oxazoline)s with pendent glycine (Gly-POX) and γ-aminobutyric acid (GABA) groups as antimicrobial agents, together with their proposed DNA-targeting and membrane-targeting mechanisms, respectively. Reprinted with permission from ref 114.

Amphiphilic ABA triblock copoly(2-oxazoline) micelles have been developed by Jordan, Luxenhofer and Kabanov who demonstrated their potential as excellent carriers for various hydrophobic drugs, enabling very high drug loading.[116] These systems have been further developed, amongst others, for treatment of ovarian and breast cancer through codelivery of cisplatin and paclitaxel,[117] as well as for lung adenocarcinoma through immunotherapy with resiquimod,[118] which were both demonstrated to be effective in *in vivo* using mice models. More recently, Kabanov and coworkers also reported the use of such ABA triblock copoly(2-oxazoline)s as stabilizer for a Remdesivir formulation for aerosol treatment of COVID-19.[119] Finally, an in depth preclinical bioequivalence study using standardized protocols revealed that a paclitaxel loaded ABA triblock copoly(2-oxazoline) nanoformulation had comparable pharmacokinetic

profiles as Abraxane®.[120] Systematic studies on variation of the polymer structure and micellar formulation of various drugs by Luxenhofer and coworkers provided fundamental understanding of the effects of the hydrophilic corona-forming and hydrophobic core-forming blocks on the drug loading and solubilization.[121-123] In addition to ABA triblock copoly(2-oxazoline)s, amphiphilic gradient copoly(2-oxazoline)s are receiving increasing interest as potential drug carriers for hydrophobic drugs, driven by the straightforward one-step synthesis of spontaneously formed gradient copolymers when selecting comonomers with sufficiently different reactivity.[33,124] Pispas, Demetzos and coworkers were the first to report the use of poly(2-oxazoline) gradient copolymers based on MeOx and 2-phenyl-2-oxazoline (PhOx) for the micellar formulation of hydrophobic drugs,[125,126] which was later extended towards coformulation with phospholipids[127,128] as well as the complexation of nucleotides using partially hydrolyzed gradient copolymers.[129] More recently, comparative studies between block and gradient copolymers revealed higher drug loading efficiency of rifampicin for gradient copolymers of MeOx and PhOx or MeOx and 2-(4-butylphenyl)-2-oxazoline[130] while similar loading capacity of curcumin was found for block and gradient copolymers of MeOx and PhOx.[131] Amphiphilic gradient copolymers consisting of 2-methyl-2-oxazine and 2-*n*-propyl-2-oxazoline or 2-*n*-butyl-2-oxazoline were also demonstrated as carriers for hydrophobic drug loading, revealing similar loading capacity as the corresponding block copolymers.[33,132] Such spontaneously formed gradient copolymers with similar loading capacity as block copolymers might still be beneficial over the block copolymers as they are more easy, and thus more economical, to prepare with higher anticipated reproducibility, albeit the latter has not been reported in detail to date.

Besides drug delivery and therapeutic applications, poly(2-oxazoline)s also gained significant interest for the development of hydrogels and scaffolds for tissue engineering.[133,134] The interest in poly(2-oxazoline)s for these applications are driven by their high biocompatibility, easy functionalization as well as good processability. Noteworthy recent developments include the development of poly(2-oxazoline)s for 3D printing[38,135,136] and 2-photon-polymerization[137,138] as well as its use for electrospinning[25,139] and melt-electrowriting.[39,140] These reports indicate that poly(2-oxazoline)s can be processed through various additive manufacturing methods for the creation of 3D structures. Poly(2-oxazoline) hydrogels that actively interact with living matter are also emerging as tissue adhesive hemostatic materials[24,141,142] and bone adhesives[143] as well as for cell scaffolds for tissue engineering and protein sensors based on the introduction of peptide crosslinkers that can be cleaved by matrix metalloproteinases.[133,144,145]

Finally, there are some exciting emerging applications of poly(2-oxazoline)s for technological , rather than biomedical, applications. Kim, Bradley and Kim introduced PEtOx as dipole interlayer that enhanced the efficiency of bulk heterojunction solar cells.[146] This pioneering work was followed by a significant number of reports that demonstrated improved solar cell efficiency upon application of PEtOx interlayers for various types of solar cells, field effect transistors and light emitting diodes.[147-154] In the area of batteries, it has been demonstrated that effective gel

electrolytes can be prepared based on cationic poly(2-oxazoline) macromonomers as gel elctrolytes for lithium ion batteries.[155]

4. Future vision

The area of poly(2-oxazoline)s has seen major progress in the last decade, ranging from significant advances in the synthesis of defined high molar mass, block and gradient copolymers as well as functional poly(2-oxazoline)s and related poly(cyclic imino ethers). Furthermore, specific polymers have been designed for a wide variety of biomedical applications and the first poly(2-oxazoline)s materials, namely a polymer drug conjugate and a hemostatic patch, have entered clinical trials. Moreover, poly(2-oxazoline)s remain important materials for studying basic concepts in polymer science, such as cyclic polymers and thermoresponsive materials. Finally, we have seen major progress in the construction of poly(2-oxazoline)-based hydrogels and 3D-materials, as well as in previously unanticipated applications as electronic interlayers in devices and as lubricants in oil. However, these applications are believed to be just the initial steps towards the broader application potential of poly(2-oxazoline)s, as we are at the beginning of broader biomedical use of poly(2-oxazoline)s.

The synthetic versatility of poly(2-oxazoline)s is believed to continue to support their use as functional polymers for developing proof-of-concept studies for a wide-range of biomedical applications, to gain fundamental understanding of structure property relationships and to investigate novel concepts in polymer science. Remaining synthetic challenges are the development of high molar mass poly(2-oxazoline)s in shorter times as well as the synthesis and polymerization of 2-oxazepines. The properties and application potential of poly(2-oxazine)s also remains to be further explored, as their application potential only seems to be limited by the imagination of the involved scientist. As example, the CROP of cyclic imino ethers provides a tunable platform for designing and preparing a wide range of amphiphilic gradient copolymers that deserve to be further explored as easily accessible alternatives for amphiphilic block copolymers. Moreover, functional amino-side chains were recently demonstrated to lead to very high potential antimicrobial agents, and many other side chains remain unexplored today.

Once the first poly(2-oxazoline)-construct is approved for use in the clinic, this is expected to further boost the interest from both academia and industry for this class of polymers. Important challenges for biomedical use of poly(2-oxazoline)s remain the in depth evaluation of biocompatibility and potential immune-response, which should be performed for different poly(2-oxazoline)-derivatives, different types of medical devices and implants as well as drug carriers.

For the coming decade, it is believed that the use of poly(2-oxazoline)s will go beyond their use in biomedical applications, including for example for cosmetics and personal care. However, for these type of applications it will be crucial to develop degradable analogues, being one of the emerging areas. An important challenge remain the development of straightforward synthetic

protocols for developing degradable poly(2-oxazoline)-analogues. For more technical applications, it will be important to develop scalable production methods for poly(2-oxazoline)s enabling straightforward and economical access to larger quantities of polymers, as has been developed for PEtOx by Polymer Chemistry Innovations.[13]

Altogether, I believe that we are at an important moment for poly(2-oxazoline)s as they are about to breakthrough for biomedical applications and I expect that the interest in these polymers will strongly increase in the coming decade.

Conflict of interest statement

RH is one of the founders of Avroxa BV that commercializes poly(2-oxazoline)s as Ultroxa® and has been listed as inventor on a range of patent families dealing with poly(2-oxazoline)s.

5. References

1. M. Sutton, 'The birth of the Polymer age', Chemistry World, **2020** https://www.chemistryworld.com/features/the-birth-of-the-polymer-age/4011418.article (last accessed 17 March 2021).
2. D.A. Tomalia, D.P. Sheetz, Homopolymerization of 2-alkyl- and 2-aryl-2-oxazolines, J. Polym. Sci. Part A-1 Polym. Chem. 4 (1966) 2253–2265.
3. W. Seeliger, E. Aufderhaar, W. Diepers, R. Feinauer, R. Nehring, W. Thier, H. Hellmann, Recent Syntheses and Reactions of Cyclic Imidic Esters, Angew. Chemie Int. Ed. English. 5 (1966) 875–888.
4. T.G. Bassiri, A. Levy, M. Litt, Polymerization of cyclic imino ethers. I. Oxazolines, J. Polym. Sci. Part B Polym. Lett. 5 (1967) 871–879.
5. T. Kagiya, S. Narisawa, T. Maeda, K. Fukui, Ring-opening polymerization of 2-substituted 2-oxazolines, J. Polym. Sci. Part B Polym. Lett. 4 (1966) 441–445.
6. R. Hoogenboom, 50 years of poly(2-oxazoline)s, Eur. Polym. J. 88 (2017) 448-450.
7. K. Aoi, M. Okada, Polymerization of oxazolines, Prog. Polym. Sci. 21 (1996) 151-208.
8. B. Verbraeken, B. D. Monnery, K. Lava, R. Hoogenboom, Eur. Polym. J. 88 (2017) 451-469.
9. G. Delaittre, Telechelic poly(2-oxazoline)s, Eur. Polym. J. 121 (2019) 109281.
10. E. Rossegger, V. Schenk, F. Wiesbrock, Design Strategies for Functionalized Poly(2-oxazoline)s and Derived Materials, Polymers 5 (2013) 956-1011.
11. M. Glassner, M. Vergaelen, R. Hoogenboom, Poly(2-oxazoline)s: A comprehensive overview of polymer structures and their physical properties, Polym. Int. 67 (2018) 32-45.
12. S. Jana, M. Uchman, Poly(2-oxazoline)-based stimulus-responsive (Co)polymers: An overview of their design, solution properties, surface-chemistries and applications, Prog. Polym. Sci. 106 (2020) 101252.
13. https://www.polychemistry.com (last accessed 20 July 2021)

14. R. Luxenhofer, Y. Han, A. Schulz, J. Tong, Z. He, A.V. Kabanov, R. Jordan, Poly(2-oxazoline)s as polymer therapeutics, Macromol. Rapid Commun. 33 (2012) 1613-1631.
15. T. Lorson, M. M. Lübtow, E. Wegener, M. S. Haider, S. Borova, D. Nahm, R. Jordan, M. Sokolski-Papkov, A. V Kabanov, R. Luxenhofer, Poly(2-oxazoline)s based biomaterials: A comprehensive and critical update, Biomaterials 178 (2018) 204-280.
16. T. Dargaville, J.-R. Park, R. Hoogenboom, Poly(2-oxazoline) Hydrogels: State-of-the-Art and Emerging Applications, Macromol. Biosci. 18 (2018) 1800070.
17. S. Zalipsky, C. B. Hansen, J. M. Oaks, T. M. Allen, Evaluation of Blood Clearance Rates and Biodistribution of Poly(2-oxazoline)-Grafted Liposomes, J. Pharm. Sci. 85 (1996) 133-137.
18. https://www.sciencemag.org/news/2020/12/suspicions-grow-nanoparticles-pfizer-s-covid-19-vaccine-trigger-rare-allergic-reactions (doi:10.1126/science.abg2359; last accessed 20 July 2021).
19. M. A. Bruusgaard-Mouritsen, J. D. Johansen, L. H. Garvey, Clinical manifestations and impact on daily life of allergy to polyethylene glycol (PEG) in ten patients, Clin. Exp. Allergy 51 (2021) 463-470.
20. K. Knop, R. Hoogenboom, D. Fischer, U. S. Schubert, Poly(ethylene glycol) in Drug Delivery: Pros and Cons as Well as Potential Alternatives, Angew. Chem. Int. Ed. 49 (2010) 6288-6308.
21. M. Barz, R. Luxenhofer, R. Zentel, M. J. Vicent, Overcoming the PEG-addiction: well-defined alternatives to PEG, from structure–property relationships to better defined therapeutics, Polym. Chem. 2 (2011) 1900-1918.
22. T. T. H. Thi, E. H. Pilkington, D. H. Nguyen,J. S. Lee, K. D. Park, N. P. Truong, The Importance of Poly(ethylene glycol) Alternatives for Overcoming PEG Immunogenicity in Drug Delivery and Bioconjugation, Polymers 12 (2020) 298.
23. C. W. Olanow, D. G. Standaert, K. Kieburtz, T. X. Viegas, R. Moreadith, Once-Weekly Subcutaneous Delivery of Polymer-Linked Rotigotine (SER-214) Provides Continuous Plasma Levels in Parkinson's Disease Patients. Mov. Disord. 35 (2020) 1055-1061.
24. https://www.clinicaltrials.gov/ct2/show/NCT04819945 (last accessed 8 July 2021).
25. B. Stubbe, Y. Li, M. Vergaelen, S. Van Vlierberghe, P. Dubruel, K. De Clerck, R. Hoogenboom, Aqueous electrospinning of poly(2-ethyl-2-oxazoline): Mapping the parameter space, Eur. Polym. J. 88 (2017) 724-732.
26. B. Monnery, V. V. Jerca, O. Sedlacek, B. Verbraeken, R. Cavill, R. Hoogenboom, Defined high molar mass poly(2-oxazoline)s, Angew. Chem. Ind. Ed. 57 (2018) 15400-15404.
27. E. Schoolaert, R. Merckx, J. Becelaere, M. Everaerts, J. F. R. Van Guyse, O. Sedlacek, B. G. De Geest, G. Van den Mooter, D. R. D'hooge, K. De Clerck, R. Hoogenboom, Immiscibility of Chemically Alike Amorphous Polymers: Phase Separation of Poly(2-ethyl-2-oxazoline) and Poly(2-*n*-propyl-2-oxazoline), Macromolecules 53 (2020), 7590-7600 .
28. B. Monnery, R. Hoogenboom, Thermoresponsive hydrogels formed by poly(2-oxazoline) triblock copolymers, Polym. Chem. 10 (2019) 3480-3487.

29. M. Vergaelen, B. Verbraeken, B.D. Monnery, R. Hoogenboom, Sulfolane as common rate accelerating solvent for the cationic ring-opening polymerization of 2-oxazolines, ACS Macro Lett., 4 (2015) 825-828.
30. B. Pásztóia, T. M.Trötschler, Á. Szabó, B. Kerscher, H. Tenhu, R. Mülhaupt, B. Iván, Quasiliving cationic ring-opening polymerization of 2-ethyl-2-oxazoline in benzotrifluoride, as an alternative reaction medium, Polymer 212 (2021) 123165.
31. M. M. Bloksma, U. S. Schubert, R. Hoogenboom, Poly(cyclic imino ether)s Beyond 2-Substituted-2-oxazolines, Macromol. Rapid Commun. 32 (2011), 1419-1441.
32. Z. Varanaraja, J. Kim, C. R. Becer, Poly(2-oxazine)s: A comprehensive overview of the polymer structures, physical properties and applications, Eur. Polym. J. 147 (2021), 110299.
33. O. Sedlacek, K. Lava, B. Verbraeken, S. Kasmi, B. G. De Geest, R. Hoogenboom, Unexpected Reactivity Switch in the Statistical Copolymerization of 2-Oxazolines and 2-Oxazines Enabling the One-Step Synthesis of Amphiphilic Gradient Copolymers, J. Am. Chem. Soc. 141 (2019) 9617-9622.
34. G. Morgese, B. Verbraeken, S. N. Ramakrishna, Y. Gombert, E. Cavalli, J.-G. Rosenboom, M. Zenobi-Wong, N. D. Spencer, R. Hoogenboom, E. M. Benetti, Chemical Design of Non-Ionic Polymer Brushes as Biointerfaces: Poly(2-oxazine)s Outperform Both Poly(2-oxazoline)s and PEG, Angew. Chem. Int. Ed. 57 (2018) 11667-11672.
35. A. Zahoranova, R. Luxenhofer, Poly(2-oxazoline)- and Poly(2-oxazine)-Based Self-Assemblies, Polyplexes, and Drug Nanoformulations—An Update, Adv. Healthcare Mater. 10 (2021), 2001382.
36. O. Sedlacek, R. Hoogenboom, Drug Delivery Systems Based on Poly(2-Oxazoline)s and Poly(2-Oxazine)s, Adv. Therap. 3 (2020), 1900168.
37. M. N. Leiske, M. Lai, T. Amarasen, T. P. Davis, K. J. Thurecht, S. J. Kent, K. Kempe, Interactions of core cross-linked poly(2-oxazoline) and poly(2-oxazine) micelles with immune cells in human blood, Biomaterials 274 (2021) 120843.
38. L. Hahn, M. Maier, P. Stahlhut, M. Beudert, V. Flegler, S. Forster, A. Altmann, F. Töppke, K. Fischer, S. Seiffert, B. Böttcher, T. Lühmann, R. Luxenhofer, Inverse Thermogelation of Aqueous Triblock Copolymer Solutions into Macroporous Shear-Thinning 3D Printable Inks, ACS Appl. Mater. Interf. 12 (2020) 12445-12456.
39. D. Nahm, F. Weigl, N. Schaefer, A. Sancho, A. Frank, J. Groll, C. Villmann, H.-W. Schmidt, P. D. Dalton, R. Luxenhofer, A versatile biomaterial ink platform for the melt electrowriting of chemically-crosslinked hydrogels, Mater. Horiz. 7 (2020) 928-933.
40. M. Miyamoto, K. Aoi, T. Saegusa, Ring-opening polymerization of six- and seven-membered cyclic pseudoureas, J. Polym. Sci., Part A: Polym. Chem. 35 (1997) 933-945.
41. B. Verbraeken, J. Hullaert, J. Van Guyse, K. Van Hecke, J. Winne, R. Hoogenboom, The Elusive Seven-Membered Cyclic Imino Ether Tetrahydrooxazepine, J. Am. Chem. Soc. 140 (2018) 17404-17408.
42. Y.-C. Wu, T. M. Swager, Living Polymerization of 2-Ethylthio-2-oxazoline and Postpolymerization Diversification, J. Am. Chem. Soc. 141 (2019) 12498-12501.

43. M. A. Mees, R. Hoogenboom, Full and partial hydrolysis of poly(2-oxazoline)s and the subsequent post-polymerization modification of the resulting polyethylenimine (co)polymers, Polym. Chem. 9 (2018) 4968-4978.
44. B. Kopka, B. Kost, M. Basko, Poly(2-isopropenyl-2-oxazoline) as a reactive polymer for materials development, Polym. Chem. 13 (2022) advance article, doi: 10.1039/D2PY00660J.
45. T. Kagiya, T. Matsuda, Selective Polymerization of 2-Isopropenyl-2-oxazoline and Cross-linking Reaction of the Polymers, Polym. J. 3 (1972) 307-314.
46. N. Zhang, S. Huber, A. Schulz, R. Luxenhofer, R. Jordan, Cylindrical Molecular Brushes of Poly(2-oxazoline)s from 2-Isopropenyl-2-oxazoline, Macromolecules 42 (2009) 2215-2221.
47. C. Weber, T. Neuwirth, K. Kempe, B. Ozkahraman, E. Tamahkar, H. Mert, C. R. Becer, U. S. Schubert, 2-Isopropenyl-2-oxazoline: A Versatile Monomer for Functionalization of Polymers Obtained via RAFT, Macromolecules 45 (2012), 20-27.
48. V. Raus, A. Hološ, J. Kronek, J. Mosnáček, Well-Defined Linear and Grafted Poly(2-isopropenyl-2-oxazoline)s Prepared via Copper-Mediated Reversible-Deactivation Radical Polymerization Methods, Macromolecules 53 (2020) 2077-2087.
49. H. Feng, M. Changez, K. Hong, J. W. Mays, N.-G. Kang, 2-Isopropenyl-2-oxazoline: Well-Defined Homopolymers and Block Copolymers via Living Anionic Polymerization, Macromolecules 50 (2017) 540-62.
50. F. A. Jerca, V. V. Jerca, A. M. Anghelache, D. M. Vuluga, R. Hoogenboom, Poly(2-isopropenyl-2-oxazoline) as a versatile platform towards thermoresponsive copolymers, Polym. Chem. 9 (2018) 3473-3478.
51. N. Zhang, S. Salzinger, B. S. Soller, B. Rieger, Rare Earth Metal-Mediated Group-Transfer Polymerization: From Defined Polymer Microstructures to High-Precision Nano-Scaled Objects, J. Am. Chem. Soc. 135 (2013) 8810-8813.
52. Z. Kroneková, M. Mikulec, N. Petrenčíková, E. Paulovičová, L. Paulovičová, V. Jančinová, R. Nosál', P. S. Reddy, G. D. Shimoga, D. Chorvát Jr., J. Kronek, Ex Vivo and In Vitro Studies on the Cytotoxicity and Immunomodulative Properties of Poly(2-isopropenyl-2-oxazoline) as a New Type of Biomedical Polymer, Macromol. Biosci. 16 (2016) 1200-1211.
53. E. Paulovičová,Z. Kroneková, L. Paulovičová, M. Majerčíková, J. Kronek, Cell-Mediated Immunoreactivity of Poly(2-isopropenyl-2-oxazoline) as Promising Formulation for Immunomodulation, Materials 14 (2021) 1371.
54. M. N. Leiske, A. M. Mahmoud, N. M. Warne, J. A. C. M. Goos, S. Pascual, V. Montembault, L. Fontaine, T. P. Davis, M. R. Whittaker, K. Kempe, Poly(2-isopropenyl-2-oxazoline) – a structural analogue to poly(vinyl azlactone) with Orthogonal Reactivity, Polym. Chem. 11 (2020) 5681-5692.
55. F. A. Jerca, V. V. Jerca, R. Hoogenboom, In Vitro Assessment of the Hydrolytic Stability of Poly(2-isopropenyl-2-oxazoline), Biomacromolecules 22 (2021) 5020-5032.
56. F. A. Jerca, A. M. Anghelache, E. Ghibu, S. Cecoltan, I.-C. Stancu, R. Trusca, E. Vasile, M. Teodorescu, D. M. Vuluga, R. Hoogenboom, V. V. Jerca, Poly(2-isopropenyl-2-oxazoline) Hydrogels for Biomedical Applications, Chem. Mater. 30 (2018) 7938-7949.

57. B. Kopka, B. Kost, K. Rajkowska, A. Pawlak, A. Kunicka-Styczyńska, T. Biela, M. Basko, A simple strategy for efficient preparation of networks based on poly(2-isopropenyl-2-oxazoline), poly(ethylene oxide), and selected biologically active compounds: Novel hydrogels with antibacterial properties, Soft Matter 17 (2021) 10683-10695.
58. M. Ceglowski, V. V. Jerca, F. A. Jerca, R. Hoogenboom, Reduction-Responsive Molecularly Imprinted Poly(2-isopropenyl-2-oxazoline) for Controlled Release of Anticancer Agents, Pharmaceutics 12 (2020) 506.
59. H. P. C. Van Kuringen, J. Lenoir, E. Adriaens, J. Bender, B. G. De Geest, R. Hoogenboom, Partial Hydrolysis of Poly(2-ethyl-2-oxazoline) and Potential Implications for Biomedical Applications? Macromol. Biosci. 12 (2012) 1114-1123.
60. J. Ulbricht, R. Jordan, R. Luxenhofer, On the biodegradability of polyethylene glycol, polypeptoids and poly(2-oxazoline)s, Biomaterials 35 (2014) 4848-4861.
61. N. E. Göppert, M. Kleinsteuber, C. Weber, U. S. Schubert, Degradable Poly(2-oxazoline) Analogues from Partially Oxidized Poly(ethylene imine), Macromolecules 53 (2020) 10837-10846.
62. N. E. Göppert, M. Dirauf, C. Weber, U. S. Schubert, Block copolymers comprising degradable poly(2-ethyl-2-oxazoline) analogues via copper-free click chemistry, Polym. Chem. 12 (2021) 5426-5437.
63. X. Wang, N. Hadjichristidis, Organocatalytic Ring-Opening Polymerization of N-Acylated-1,4-oxazepan-7-ones Toward Well-Defined Poly(ester amide)s: Biodegradable Alternatives to Poly(2-oxazoline)s, ACS Macro Lett. 9 (2020) 464-470.
64. B. Verbraeken, R. Hoogenboom, Cyclic polymers: from scientific curiosity to advanced materials for gene delivery and surface modification, Angew. Chem. Int. Ed. 56 (2017) 7034-7036.
65. M. A. Cortez, W. T. Godbey, Y. Fang, M. E. Payne, B. J. Cafferty, K. A. Kosakowska, S. M. Grayson, The Synthesis of Cyclic Poly(ethylene imine) and Exact Linear Analogues: An Evaluation of Gene Delivery Comparing Polymer Architectures, J. Am. Chem. Soc. 137 (2015) 6541-6549.
66. G. Morgese, L. Trachsel, M. Romio, M. Divandari, S. N. Ramakrishna, E. M. Benetti, Topological Polymer Chemistry Enters Surface Science: Linear versus Cyclic Polymer Brushes, Angew. Chem. Int. Ed. 128 (2016) 15812-15817.
67. G. Morgese, E. Cavalli, J.-G. Rosenboom, M. Zenobi-Wong, E. M. Benetti, Cyclic Polymer Grafts That Lubricate and Protect Damaged Cartilage, Angew. Chem. Int. Ed. 130 (2018) 1637-1642.
68. G. Morgese,B. S. Shaghasemi, V. Causin, M. Zenobi-Wong, S. N. Ramakrishna, E. Reimhult, E. M. Benetti, Next-Generation Polymer Shells for Inorganic Nanoparticles are Highly Compact, Ultra-Dense, and Long-Lasting Cyclic Brushes,
69. M. Schroffenegger, N. S. Leitner, G. Morgese, S. N. Ramakrishna, M. Willinger, E. M. Benetti, E. Reimhult, Polymer Topology Determines the Formation of Protein Corona on Core–Shell Nanoparticles, ACS Nano 14 (2020) 12708-12718.

70. Y. Jung, J.-H. Kim, W.-D. Jang, Linear and cyclic poly(2-isopropyl-2-oxazoline)s for fine control of thermoresponsiveness, Eur. Polym. J. 88 (2017) 605-612.
71. M. Willinger, E. Reimhult, Thermoresponsive Nanoparticles with Cyclic-Polymer-Grafted Shells Are More Stable than with Linear-Polymer-Grafted Shells: Effect of Polymer Topology, Molecular Weight, and Core Size, J. Phys. Chem. B 125 (2021) 7009-7023.
72. L. Trachsel, M. Romio, M. Zenobi-Wong, E. M. Benetti, Hydrogels Generated from Cyclic Poly(2-Oxazoline)s Display Unique Swelling and Mechanical Properties, Macromol. Rapid Commun. 42 (2021) 2000658.
73. R. Hoogenboom, H. Schlaad, Thermoresponsive poly(2-oxazoline)s, polypeptoids, and polypeptides, Polym. Chem. 8 (2017) 24-40.
74. M. Hijazi, M. Schmidt, H. Xia, J. Storkmann, R. Plothe, D. Dos Santos, U. Bednarzick, C. Krumm, J. C.Tiller, Investigations on the thermoresponsive behavior of copoly(2-oxazoline)s in water, Polymer 175 (2019) 294-301.
75. D. Segiet, A. Stockmann, J. Sadowski, F. Katzenberg, J. C. Tiller, Insights in the Thermal Volume Transition of Poly(2-oxazoline) Hydrogels, Macromol. Chem. Phys. 222 (2021) 2100157.
76. G. Yilmaz, V. Uzunova, M. Hartweg, V. Beyer, R. Napier, C. R. Becer, The effect of linker length on ConA and DC-SIGN binding of S-glucosyl functionalized poly(2-oxazoline)s, Polym. Chem. 9 (2018) 611-618.
77. L. T. Che, M. Hiorth, R. Hoogenboom, A.-L. Kjøniksen, Complex Temperature and Concentration Dependent Self-Assembly of Poly(2-oxazoline) Block Copolymers, Polymers 12 (2020) 1495.
78. A. Kozur, L. Burk, R. Thomann, P. J.Lutz, R. Mülhaupt, Graphene oxide grafted with polyoxazoline as thermoresponsive support for facile catalyst recycling by reversible thermal switching between dispersion and sedimentation, Polymer 178 (2019) 121553.
79. S. Wiedmann, B. Kerscher, C. Lienert, D. Böcherer, R. Mülhaupt, Tailoring Poly(2-oxazoline)-Based Polymeric Ionic Liquids as Thermoresponsive Molecular Brushes and Programmable Dispersants for Silver Nanoparticles, Macromolecules 53 (2020) 6703-6710.
80. S. Wiedmann, M. Luitz, B. Kerscher, J-F. Lutz, R. Mülhaupt, Programmable Thermoresponsive Micelle-Inspired Polymer Ionic Liquids as Molecular Shuttles for Anionic Payloads, Macromolecules 52 (2019) 8672-9681.
81. C. Guerrero-Sanchez, J.-F. Gohy, C. D'Haese, H. Thijs, R. Hoogenboom, U. S. Schubert, Controlled thermoreversible transfer of poly(oxazoline) micelles betweenan ionic liquid and water, Chem. Commun. (2008) 2753-2755.
82. C. Guerrero-Sanchez, D. Wouters, S. Hoeppener, R. Hoogenboom, U. S. Schubert, Micellar dye shuttle between water and an ionic liquid, Soft Matter 7 (2011) 3827-3831.
83. N. Oleszko-Torbus, A. Utrata-Wesołek, M. Bochenek, D. Lipowska-Kur, A. Dworak, W. Wałach, Thermal and crystalline properties of poly(2-oxazoline)s, Polym. Chem. 11 (2020) 15-33.
84. A. L. Demirel, M. Meyer, H. Schlaad, Formation of Polyamide Nanofibers by Directional Crystallization in Aqueous Solution, Angew. Chem. Int. Ed. 46 (2007) 8622-8624.

85. N. Oleszko, W. Wałach, A. Utrata-Wesołek, A. Kowalczuk, B. Trzebicka, A. Klama-Baryła, D. Hoff-Lenczewska, M. Kawecki, M. Lesiak, A. L. Sieroń, A. Dworak, Controlling the Crystallinity of Thermoresponsive Poly(2-oxazoline)-Based Nanolayers to Cell Adhesion and Detachment, Biomacromolecules 16 (2015), 2805-2813.
86. C. Legros, M.-C. De Pauw-Gillet, K. C. Tam, D. Taton, S. Lecommandoux, Crystallisation-driven self-assembly of poly(2-isopropyl-2-oxazoline)-block-poly(2-methyl-2-oxazoline) above the LCST, Soft Matter 11 (2015) 3354-3359.
87. J. R. Finnegan, E. H. Pilkington, K. Alt, Md. A. Rahim, S. J. Kent, T. P. Davis, K. Kempe, Stealth nanorods via the aqueous living crystallisation-driven self-assembly of poly(2-oxazoline)s, Chem. Sci. 12 (2021) 7350-7360.
88. J. R. Finnegan, T. P. Davis, K. Kempe, Heat-Induced Living Crystallization-Driven Self-Assembly: The Effect of Temperature and Polymer Composition on the Assembly and Disassembly of Poly(2-oxazoline) Nanorods, Macromolecules 55 (2022) 3650-3660.
89. A. Dworak, A. Utrata-Wesołek, N. Oleszko, W. Wałach, B. Trzebicka, J. Anioł, A. L. Sieroń, A. Klama-Baryła, M. Kawecki, Poly(2-substituted-2-oxazoline) surfaces for dermal fibroblasts adhesion and detachment, J. Mater. Sci.: Mater. Med. 25 (2014) 1149-1163.
90. N. Oleszko-Torbus, W. Wałach, A. Utrata-Wesołek, A. Dworak, Control of the Crystalline Properties of 2-Isopropyl-2-oxazoline Copolymers in Condensed State and in Solution Depending on the Composition, Macromolecules 50 (2017) 7636-7645.
91. L. Simon, N. Marcotte, J. M. Devoisselle, S. Begu, V. Lapinte, Recent advances and prospects in nano drug delivery systems using lipopolyoxazolines, Int. J. Pharm. 585 (2020) 119536.
92. O. Sedlacek, V. R. De la Rosa, R. Hoogenboom, Poly(2-oxazoline)-protein conjugates, Eur. Polym. J. 120 (2019) 109246.
93. A. Zahoranová, R. Luxenhofer, Adv. Healthcare Mater. 10 (2021) 2001382.
94. L. Benski, J. C. Tiller, Telechelic biocidal poly(2-oxazoline)s and polycations, Eur. Polym. J. 120 (2019) 109233.
95. B. Claeys, A. Vervaeck, C. Vervaet, J.-P. Remon, R. Hoogenboom, B. G. De Geest, Poly(2-ethyl-2-oxazoline) as Matrix Excipient for Drug Formulation by Hot Melt Extrusion and Injection Molding, Macromol. Rapid Commun. 33 (2012) 1701-1707.
96. R. I.Moustafine, A. S.Viktorova, V. V.Khutoryanskiy, Interpolymer complexes of carbopol® 971 and poly(2-ethyl-2-oxazoline): Physicochemical studies of complexation and formulations for oral drug delivery, Int. J. Pharm. 558 (2019) 53-62.
97. M. Z. R. Sabuj, T. R. Dargaville, L. Nissen, N. Islam, Inhaled ciprofloxacin-loaded poly(2-ethyl-2-oxazoline) nanoparticles from dry powder inhaler formulation for the potential treatment of lower respiratory tract infections, PLOS One 16 (2021) e0261720.
98. G. K. Abilova, D. B. Kaldybekova, E. K. Ozhmukhametova, A. Zh.Saimova, D. S. Kazybayeva, G. S. Irmukhametova, V. V.Khutoryanskiy, Chitosan/poly(2-ethyl-2-oxazoline) films for ocular drug delivery: Formulation, miscibility, in vitro and in vivo studies, Eur. Polym. J. 116 (2019) 311-320.

99. L. Ruiz-Rubio, M. L. Alonso, L. Pérez-Álvarez, R. M. Alonso, J. L. Vilas, V. V. Khutoryanskiy, Formulation of Carbopol®/Poly(2-ethyl-2-oxazoline)s Mucoadhesive Tablets for Buccal Delivery of Hydrocortisone, Polymers 10 (2018) 175.
100. O. Policianova, J. Brus, M. Hruby, M. Urbanova, A. Zhigunov, J. Kredatusova, L. Kobera, Structural Diversity of Solid Dispersions of Acetylsalicylic Acid As Seen by Solid-State NMR, Mol. Pharmaceutics, 11 (2014) 516-530.
101. E. Boel, A. Smeets, M. Vergaelen, V. R.De la Rosa, R. Hoogenboom, G. Van den Mooter, Comparative study of the potential of poly(2-ethyl-2-oxazoline) as carrier in the formulation of amorphous solid dispersions of poorly soluble drugs, Eur. J Pharm. Biopharm. 144 (2019) 79-90.
102. X. Shan, M. A. Moghul, A. C. Williams, V. V. Khutoryanskiy, Mutual Effects of Hydrogen Bonding and Polymer Hydrophobicity on Ibuprofen Crystal Inhibition in Solid Dispersions with Poly(N-vinyl pyrrolidone) and Poly(2-oxazolines), Pharmaceutics, 13 (2021) 659.
103. I. Ekladious, Y. L. Colson, M. W. Grinstaff, Polymer–drug conjugate therapeutics: advances, insights and prospects, Nat. Rev. Drug Discovery 18 (2019) 273-294.
104. J. M. Harris, M. D. Bentley, R. W.Moreadith, T. X. Viegas, Z. Fang, K. Yoon, R. Weimer, B. Dizman, L. Nordstierna, Tuning drug release from polyoxazoline-drug conjugates, Eur. Polym. J. 120 (2019) 109241.
105. O. Sedlacek, B. D. Monnery, J. Mattova, J. Kucka, J. Panek, O. Janouskova, A. Hocherl, B. Verbraeken, M. Vergaelen, M. Zadinova, R. Hoogenboom, M. Hruby, Poly(2-ethyl-2-oxazoline) conjugates with doxorubicin for cancer therapy: In vitro and in vivo evaluation and direct comparison to poly[N-(2-hydroxypropyl)methacrylamide] analogues, Biomaterials, 146 (2017) 1-12.
106. O. Sedlacek, A. Van Driessche, A. Uvyn, B. G.De Geest, R. Hoogenboom, Poly(2-methyl-2-oxazoline) conjugates with doxorubicin: From synthesis of high drug loading water-soluble constructs to in vitro anti-cancer properties, J. Controlled Release 326 (2020) 53-62.
107. J.-R. Park, J. F. R. Van Guyse, A. Podevyn, E. C. L. Bolle, N. Bock, E. Linde, M. Celina, R. Hoogenboom, T. R.Dargaville, Influence of side-chain length on long-term release kinetics from poly(2-oxazoline)-drug conjugate networks, Eur. Polym. J. 120 (2019) 109217.
108. J.-R. Park, M. Sarwat, E. C. L. Bolle, M. A. de Laat, J. F. R. Van Guyse, A. Podevyn, R. Hoogenboom, T. R. Dargaville, Drug–polymer conjugates with dynamic cloud point temperatures based on poly(2-oxazoline) copolymers, Polym. Chem. 11 (2020) 5191-5199.
109. K. Xu, L. Zhang, Y. Gua, H. Yang, B. Du, H. Liu, Y. Li, Increased the TMZ concentration in brain by poly(2-ethyl-2-oxazoline) conjugated temozolomide prodrug micelles for glioblastoma treatment, Eur. Polym. J. 145 (2021) 110232.
110. M. Ashjari, M. Kazemi, M. N. Abi, M. Mohammadi, S. Rafiezadeh, Poly(isopropyl-oxazoline) micelle nanocarrier as dual-responsive prodrug for targeted doxorubicin delivery, J. Drug Deliv. Sci. Technol. 59 (2020) 101914.
111. A. Romanovska, J. Keil, J. Tophoven, M. F. Oruc, M. Schmidt, M. Breisch, C. Sengstock, D. Weidlich, D. Klostermeier, J. C. Tiller, Conjugates of Ciprofloxacin and Amphiphilic Block

Copoly(2-alkyl2-oxazolines)s Overcome Efflux Pumps and Are Active against CIPResistant Bacteria, Mol. Pharm. 18 (2021) 3532-3543.
112. M. Zhou,W. Jiang, J. Xie, W. Zhang, Z. Ji, J. Zou, Z. Cong, X. Xiao, J. Gu, R. Liu, Peptide-Mimicking Poly(2-oxazoline)s Displaying Potent Antimicrobial Properties, ChemMedChem 16 (2021) 309-315.
113. M. Zhou,Y. Qian, J. Xie, W. Zhang, W. Jiang, X. Xiao, S. Chen, C. Dai, Z. Cong, Z. Ji, N. Shao, L. Liu, Y. Wu, R. Liu , Poly(2-Oxazoline)-Based Functional Peptide Mimics: Eradicating MRSA Infections and Persisters while Alleviating Antimicrobial Resistance, Angew. Chem. Int. Ed. 59 (2020) 6412-6419.
114. C. Dai, M. Zhou, W. Jiang, X. Xiao. J. Zou, Y. Qian, Z. Cong, Z. Ji, L. Liu, J. Xie, Z. Qiao, R. Liu, Breaking or following the membrane-targeting mechanism: Exploring the antibacterial mechanism of host defense peptide mimicking poly(2-oxazoline)s, J. Mater. Sci. Technol. 59 (2020) 220-226.
115. W. Jiang, M. Zhou, Z. Cong, J. Xie, W. Zhang, S. Chen, J. Zou, Z. Ji, N. Shao, X. Chen, M. Li, R. Liu, Short Guanidinium-Functionalized Poly(2-oxazoline)s Displaying Potent Therapeutic Efficacy on Drug-Resistant Fungal Infections, Angew. Chem. Int. Ed. in press (2022) doi: 10.1002/anie.202200778.
116. R. Luxenhofer, A. Schulz, C. Roques, S. Li, T. K. Bronich, E. V. Batrakova, R. Jordan, A. V. Kabanov, Doubly amphiphilic poly(2-oxazoline)s as high-capacity delivery systems for hydrophobic drugs, Biomaterials 31 (2010) 4972-4979.
117. X. Wana, J. J. Beaudoin, N. Vinoda, Y. Min, N. Makita, H. Bludau, R. Jordan, A. Wang, M. Sokolsky, A. V.Kabanov, Co-delivery of paclitaxel and cisplatin in poly(2-oxazoline) polymeric micelles: Implications for drug loading, release, pharmacokinetics and outcome of ovarian and breast cancer treatments, Biomaterials 192 (2019) 1-14.
118. N. Vinod, D. Hwang, S. H.Azam, A. E. D. Van Swearingen, E. Wayne, S. C. Fussell, M. Sokolsky-Papkov, C. V. Pecot, A. V. Kabanov, High-capacity poly(2-oxazoline) formulation of TLR 7/8 agonist extends survival in a chemo-insensitive, metastatic model of lung adenocarcinoma, Sci. Adv. 6 (2020) eaba5542.
119. J. D. Ramsey, I. E. Stewart, E. A. Madden, C. Lim, D. Hwang, M. T. Heise, A. J. Hickey, A. V. Kabanov, Nanoformulated Remdesivir with Extremely Low Content of Poly(2-oxazoline)-Based Stabilizer for Aerosol Treatment of COVID-19, *Macromol. Biosci.* **2022**, 2200056.
120. D. Hwang, N, Vinod, S. L. Skoczen, J. D. Ramsey, K. S.Snapp, S. A. Montgomery, M. Wang, C. Lima, J. E. Frank, M. Sokolsky-Papkov, Z. Li, H. Yuan, S. T.Stern, A. V.Kabanov, Bioequivalence assessment of high-capacity polymeric micelle nanoformulation of paclitaxel and Abraxane® in rodent and non-human primate models using a stable isotope tracer assay, *Biomaterials* **2021**, *278*, 121140.
121. L. Hahn, M. M. Lübtow, T. Lorson, F. Schmitt, A. Appelt-Menzel, R. Schobert, R. Luxenhofer, Investigating the Influence of Aromatic Moieties on the Formulation of Hydrophobic Natural Products and Drugs in Poly(2-oxazoline)-Based Amphiphiles, Biomacromolecules 19 (2018) 3119-3128.

122. M. M. Lübtow, M. S. Haider, M. Kirsch, S. Klisch, R Luxenhofer, Like Dissolves Like? A Comprehensive Evaluation of Partial Solubility Parameters to Predict Polymer–Drug Compatibility in Ultrahigh Drug-Loaded Polymer Micelles, Biomacromolecules 20 (2019) 3041-3056.
123. M. S. Haider, M. M. Lübtow, S. Endres, S. Forster, V. J. Flegler, B. Böttcher, V. Aseyev, A.-C. Pöppler, R. Luxenhofer, Think Beyond the Core: Impact of the Hydrophilic Corona on Drug Solubilization Using Polymer Micelles, ACS Appl. Mater. Interf. 12 (2020) 24531-24543.
124. R. Hoogenboom, H. M. K. Thijs, M. W. M. Fijten, B. M. Van Lankvelt, U. S. Schubert, One-Pot Synthesis of 2-Phenyl-2-oxazoline-Containing Quasi-Diblock Copoly(2-oxazoline)s under Microwave Irradiation, J. Polym. Sci., Part A: Polym. Chem. 45 (2007) 416-422.
125. Y. Milonaki, E. Kaditi, S. Pispas, C. Demetzos, Amphiphilic gradient copolymers of 2-methyl- and 2-phenyl-2-oxazoline: self-organization in aqueous media and drug encapsulation, J. Polym. Sci., Part A: Polym. Chem. 50 (2021) 1226-1237.
126. A. Chroni, T. Mavromoustakos, S. Pispas, Poly(2-oxazoline)-Based Amphiphilic Gradient Copolymers as Nanocarriers for Losartan: Insights into Drug–Polymer Interactions, Macromol 1 (2021) 177-200.
127. N. Pippa, M. Merkouraki, S. Pispas, C. Demetzos,DPPC:MPOx chimeric advanced Drug Delivery nano Systems (chi-aDDnSs): Physicochemical and structural characterization, stability and drug release studies, Int. J. Pharm. 450 (2013) 1-10.
128. N. Pippa, E. Kaditi, S. Pispas, C. Demetzos, DPPC/poly(2-methyl-2-oxazoline)-grad-poly(2-phenyl-2-oxazoline) chimeric nanostructures as potential drug nanocarriers, J. Nanoparticle Res. 15 (2013) 1685.
129. E. Vlassi, S. Pispas, Solution Behavior of Hydrolyzed Gradient Methyl/Phenyl Oxazoline Copolymers and Complexation with DNA, Macromol. Chem. Phys. 216 (2015) 873-883.
130. L. Loukotová, P. Švec, O. Groborz, T. Heizer, H. Beneš, H. Raabová, T. Bělinová, V. Herynek, M. Hrubý, Direct Comparison of Analogous Amphiphilic Gradient and Block Polyoxazolines, Macromolecules 54 (2021) 8182-8194.
131. O. Sedlacek, V. Bardoula, E. Vuorimaa-Laukkanen, L. Gedda, K. Edwards, A. Radulescu, G. A. Mun, Y. Guo, J. Zhou, H. Zhang, V. Nardello-Rataj, S. Filippov, R. Hoogenboom, Influence of Chain Length of Gradient and Block Copoly(2-oxazoline)s on Self-Assembly and Drug Encapsulation, Small, early view, doi: 10.1002/smll.202106251.
132. D. Babuka, K. Kolouchova, L. Loukotova, O. Sedlacek, O. Groborz, A. Skarkova, A. Zhigunov, E. Pavlova, R. Hoogenboom, M. Hruby, P. Stepanek, Self-Assembly, Drug Encapsulation, and Cellular Uptake of Block and Gradient Copolymers of 2-Methyl-2-oxazine and 2-n-Propyl/butyl-2-oxazoline, Macromolecules 54 (2021) 10667-10681.
133. T. R. Dargaville, J.-R. Park. R. Hoogenboom, Poly(2-oxazoline) Hydrogels: State-of-the-Art and Emerging Applications, Macromolecular Bioscience, 18 (2018) 1800070.
134. L. Trachsel, M. Zenobi-Wang, E. M. Benetti, The role of poly(2-alkyl-2-oxazoline)s in hydrogels and biofabrication, Biomat. Sci. 9 (2021) 2874-2886.

135. L. Trachsel, C. Johnbosco, T. Lang, E. M. Benetti, M. Zenobi-Wong, Double-Network Hydrogels Including Enzymatically Crosslinked Poly-(2-alkyl-2-oxazoline)s for 3D Bioprinting of Cartilage-Engineering Constructs, Biomacromolecules 20 (2019) 4502-4511.
136. L. B. Bronzeri, C. Gauche, L. Gudimard, E. -J. Courtial, C. Marquette, M. I. Felisberti, Amphiphilic and segmented polyurethanes based on poly(ε-caprolactone)diol and poly(2-ethyl-2-oxazoline)diol: Synthesis, properties, and a preliminary performance study of the 3D printing, Eur. Polym. J. 151 (2021) 110449.
137. T. Wloka, S. Czich, M. Kleinsteuber, E. Moek, C. Weber, M. Gottschaldt, K. Liefeith, U. S. Schubert, Microfabrication of 3D-hydrogels via two-photon polymerization of poly(2-ethyl-2-oxazoline) diacrylates, Eur. Polym. J. 122 (2020) 109295.
138. S. Czich, T. Wloka, H.Rothe, J. Rost, F. Penzold, M. Kleinsteuber, M. Gottschaldt, U. S. Schubert, K. Liefeith, Two-Photon Polymerized Poly(2-Ethyl-2-Oxazoline) Hydrogel 3D Microstructures with Tunable Mechanical Properties for Tissue Engineering, Molecules 25 (2020) 5066.
139. O. I. Kalaoglu-Altan, Y. Li, R. McMaster, A. Shaw, Z. Hou, M. Vergaelen, R. Hoogenboom, T. R. Dargaville, K. De Clerck, Crosslinking of electrospun and bioextruded partially hydrolyzed poly(2-ethyl-2-oxazoline) using glutaraldehyde vapour, Eur. Polym. J. 120 (2019) 109218.
140. G. Hochleitner, J. F. Hümmer, R. Luxenhofer, J. Groll, High definition fibrous poly(2-ethyl-2-oxazoline) scaffolds through melt electrospinning writing, Polymer 55 (2014) 5017-5023.
141. M. A. Boerman, E. Roozen, M. José Sánchez-Fernández, A. R. Keereweer, R. P. Félix Lanao, J. C. M. E. Bender, R. Hoogenboom, S. C. Leeuwenburgh, J. A. Jansen, H. Van Goor, J. C. M. Van Hest, Next Generation Hemostatic Materials Based on NHS-Ester Functionalized Poly(2-oxazoline)s, Biomacromolecules 18 (2017) 2529-2538.
142. M. A. Boerman, E. A. Roozen, G. M. Franssen, J. C. M. E. Bender, R. Hoogenboom, S. C. G. Leeuwenburgh, P. Laverman, J. C.M.van Hest, H. van Goor, R. P.Félix Lanao, Degradation and excretion of poly(2-oxazoline) based hemostatic materials, Materialia 12 (2020) 100763.
143. M. J. Sánchez-Fernández, J. Rutjes, R. P. Félix Lanao, J. C. M. E. Bender, J. C. M. van Hest, S. C. G. Leeuwenburgh, Bone-Adhesive Hydrogels Based on Dual Crosslinked Poly(2-oxazoline)s, Macromol. Biosci. 21 (2021) 2100257.
144. N. Ahmad, B. Colak, M. J. Gibbs, D.-W. Zhang, J. E. Gautrot, M. Watkinson, C. R. Becer, S. Krause, Peptide Cross-Linked Poly(2-oxazoline) as a Sensor Material for the Detection of Proteases with a Quartz Crystal Microbalance, Biomacromolecules 20 (2019) 2506-2514.
145. Y. You, K. Kobayashi, B. Colak, P. Luo, E. Cozens, L. Fields, K. Suzuki, J. Gautrot, Engineered cell-degradable poly(2-alkyl-2-oxazoline) hydrogel for epicardial placement of mesenchymal stem cells for myocardial repair, Biomaterials 269 (2021) 120356.
146. S. Nam, J. Seo, S. Woo, W. H. Kim, H. Kim, D. D. C. Bradley, Y. Kim, Inverted polymer fullerene solar cells exceeding 10% efficiency with poly(2-ethyl-2-oxazoline) nanodots on electron-collecting buffer layers, Nat. Commun. 6 (2015) 8929.

147. W. Chen, G. Zhang, L. Xu, R. Gu, Z. Xu, H. Wang, Z. He, Low temperature processed, high-performance and stable NiOx based inverted planar perovskite solar cells via a poly(2-ethyl-2-oxazoline) nanodots cathode electron-extraction layer, Mater. Today Energy 1-2 (2016), 1-10.
148. W. Chen, Y. Zhu, Y. Yu, L. Xu, G. Zhang, Z. He, Low Cost and Solution Processed Interfacial Layer Based on Poly(2-ethyl-2-oxazoline) Nanodots for Inverted Perovskite Solar Cells, Chem. Mater. 28 (2016) 4879-4883.
149. J. Seo, Y. Moon, S. Lee, C. Lee, D. Kim, H. Kim, Y. Kim, High efficiency tandem polymer solar cells with MoO3/Ni/ZnO:PEOz hybrid interconnection layers, Nanoscale Horiz. 4 (2019) 1221-1226.
150. J. Seo, S. Nam, H. Kim, D. D. C. Bradley, Y. Kim, Nano-crater morphology in hybrid electron-collecting buffer layers for high efficiency polymer:nonfullerene solar cells with enhanced stability, Nanoscale Horiz. 4 (2019) 464-471.
151. D. Huang, T. Goh, L. McMillon-Brown, J. Kong, Y. Zheng, J. Zhao, Y. Li, S. Zhao, Z. Xu, A. D. Taylor, PEOz-PEDOT:PSS Composite Layer: A Route to Suppressed Hysteresis and Enhanced Open-Circuit Voltage in a Planar Perovskite Solar Cell, ACS Appl. Mater. Interf. 10 (2018) 25329-25336.
152. S. Nam, V. R. de la Rosa, Y. Cho, R. Hamilton, S. Cha, R. Hoogenboom, D. D. C. Bradley, Poly(2-alkyl-2-oxazoline) electrode interlayers for improved n-type organic field effect transistor performance, Appl Phys. Lett. 115 (2019) 143302.
153. S. Nam, D. Khim, G. T. Martinez, A. Varambhia, P. D. Nellist, Y. Kim, T. D. Anthopoulos, D. D. C. Bradley, Significant Performance Improvement in n-Channel Organic Field-Effect Transistors with C60:C70 Co-Crystals Induced by Poly(2-ethyl-2-oxazoline) Nanodots, Adv. Mater. 33 (2021) 2100421.
154. H. Lin, L. Zhu, H. Huang, C. J. Reckmeier, C. Liang, A. L. Rogach, W. C. H. Choy, Efficient near-infrared light-emitting diodes based on organometallic halide perovskite–poly(2-ethyl-2-oxazoline) nanocomposite thin films, Nanoscale 8 (2016) 19846-19852.
155. M. Drews, T. Trötschler, M. Bauer, A. Guntupalli, W. Beichel, H. Gentischer, R. Mülhaupt, B. Kerscher, D. Biro, Photocured Cationic Polyoxazoline Macromonomers as Gel Polymer Electrolytes for Lithium-Ion Batteries, ACS Appl. Polym. Mater. 4 (2022) 158-168.