Lipoic acid/ethyl lipoate as cleavable comonomers for synthesis of degradable polymer networks

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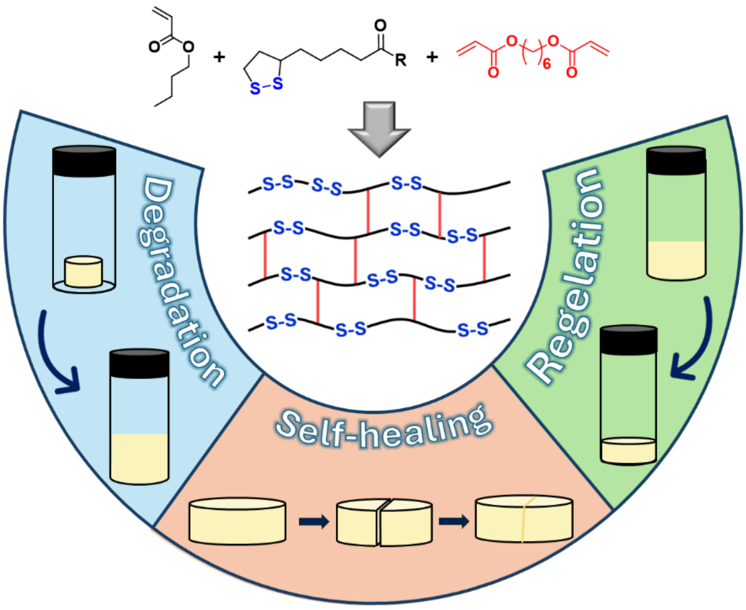


Abstract

α-Lipoic acid, and its derived ester ethyl lipoate, can copolymerise with *n*-butyl acrylate to install labile disulfide bonds within the polymer backbone. Covalently crosslinked gel networks containing these comonomers were synthesised by conventional (FRP) and reversible addition fragmentation chain transfer (RAFT) polymerisation. Gels synthesised by both methods and using both comonomers could be degraded by thiol-disulfide exchange to form soluble polymer fragments. The critical comonomer loading for degradation was lower for RAFT synthesised gels due to their more homogenous network structure. As these fragments where thiol functional, they could be oxidised in air with a base catalyst to reform a solid network. However, the presence of the carboxylic acid and the relatively low dispersity of the fragments act to prevent regelation. Therefore, only the gels containing the minimum amount of ethyl lipoate synthesised by RAFT could successfully regel as these fragments had no acid functionality and the highest dispersity value. We suggest that uniform comonomer incorporation leading to lower dispersity of the degraded fragments can be detrimental for the efficient reformation of the degraded network. However, the large amounts of the lipoate comonomer allow the dynamic exchange properties of the disulfide bonds within the polymer backbone, in the presence of DBU catalyst, to impart the networks with self-healing ability with no external pressure or heat.

Introduction

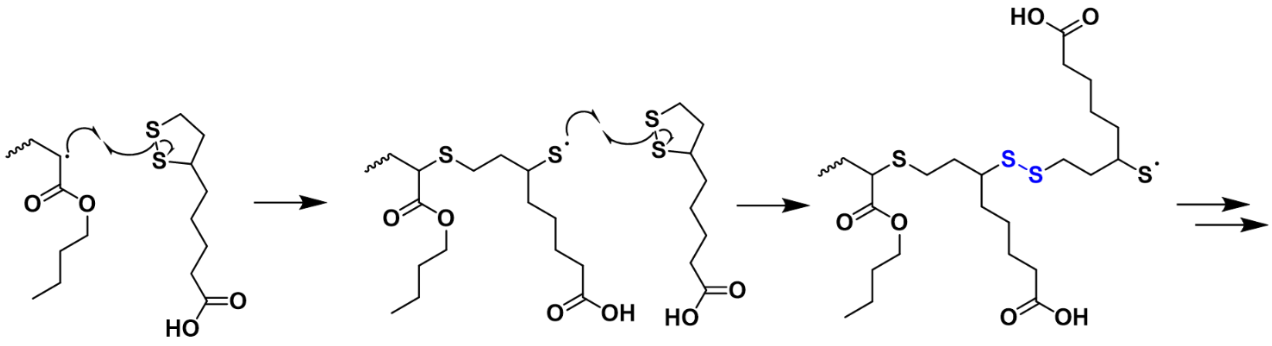
Crosslinked polymer networks are inherently difficult to recycle but are widely used in a variety of applications due to their superior mechanical properties and thermal stability.[1–4] Efforts to improve the sustainability of polymer materials has increased research into modifying these materials to more be readily degraded and/or recycled. One strategy that has been explored for both crosslinked and non-crosslinked materials is the incorporation of chemically labile bonds into the polymer chains, which can be cleaved by some external stimulus, breaking the polymer down into smaller fragments.[5–8] A theoretical and experimental study from Johnson *et al.*, [8] as well as our recent work,[9] have shown that networks with cleavable units within the polymer strands are more readily degradable than when the cleavable units are within the crosslinks. Not only are the presence of these labile bonds beneficial for recycling processes, but they also could be useful in biomedical applications such as drug delivery[10] or for self-healing materials.[11–13]

An effective method to install labile bonds into the polymer backbone is by radical ring-opening (co)polymerisation (rROP) of vinyl monomers with cyclic comonomers[6,14,15] such as cyclic ketene acetals[16,17], allyl sulfide lactones[18] and thionolactones such as dibenzo[c,e]-oxepane-5-thione (DOT).[19–23] The ring opening of the DOT comonomer implements a labile thioester bond which can be cleaved by aminolysis, and the copolymerisation is compatible with both conventional free radical polymerisation (FRP) and reversible deactivation radical polymerization techniques (RDRP). We have previously shown that DOT can be used to degrade crosslinked poly(butyl acrylate) networks to soluble polymer fragments, using both FRP[24] and reversible addition fragmentation chain transfer polymerisation (RAFT).[9] Macroscopic degradation (i.e., full solubilisation) of the gel occurred at a critical DOT:crosslinker loading of 4:1 for FRP-made networks, which decreased to 1.5:1 for RAFT-made networks, highlighting the more homogeneous structure of networks synthesised using RDRP.

Although effective at affording degradability to both linear and crosslinked polymers at low comonomer loadings, one disadvantage of DOT, as well as other comonomers classes, is the multi-stage synthesis required to produce the comonomer, sparking interest in more sustainable alternatives.[20,25] The dietary supplement α-lipoic acid (LA) has been considered as attractive alternative due to its commercial availability, low cost and biocompatibility. LA can undergo rROP through the scission of the disulfide bond present within the 1,2 dithiolane motif, and the carboxylic acid group can act as a functionalisation site allowing for a variety of modifications.[26,27] The polymerisation of LA can be triggered by heat[11,28,29] or UV light[12,30,31] , either directly or through an external source of radicals.[26,27,32,33] This reaction will produce polymers containing dynamic disulfide bonds, which can be cleaved by reduction,[33] thiol-disulfide exchange [9,34] or directly depolymerised.[35]

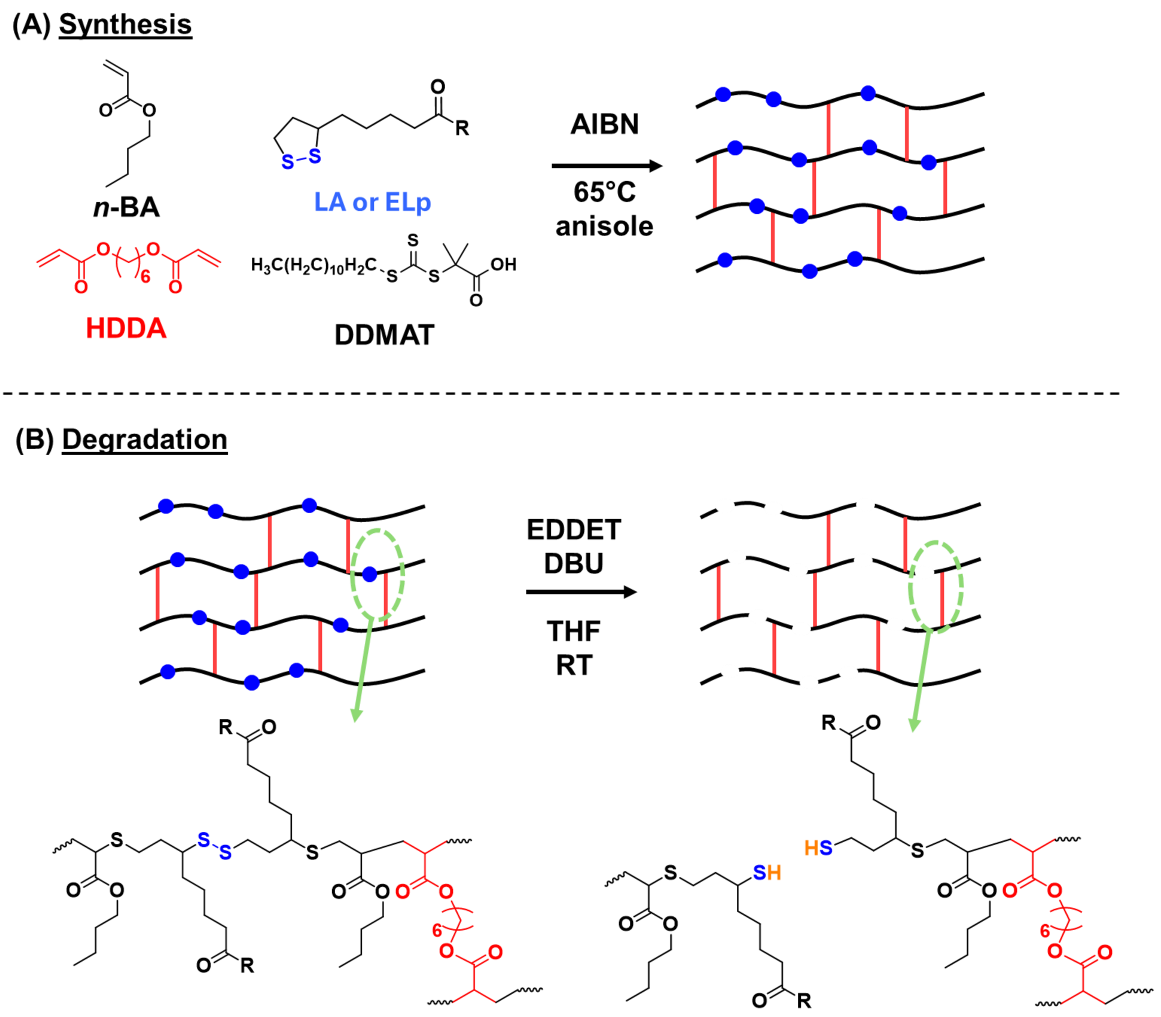
The polymerisation of LA has previously been used to synthesise polymer networks. For example Sieredzinka *et al.* grafted LA to pendant amines on a polydimethylsiloxane (PDMS), which was then cured with UV to achieve crosslinking through the photopolymerization of the 1,2 dithiolane group without a photoinitator present.[31,35] Pendant 1,2 dithiolane groups have also been utilised in the formation of dynamic hydrogels from ABA triblock copolymers. With the addition of a dithiol, the pendant 1,2 dithiolane and thiols can reversibly react to form dynamic crosslinks, allowing the gel to be self -healable and shear thinning.[36] Choi *et al*. used PDMS-LA macromonomers to synthesise soft bottle-brush elastomers through photopolymerization, with these networks having a full poly(disulfide) backbone.[12] This allowed for efficient self-healing under UV light and degradation of the network through heating at 180°C, as well as via base or reducing agent. This highlights the low ceiling temperature of LA based polymers, also reported by Tsarevsky and Nicolay for the esterified form of lipoic acid, ethyl lipoate (ELp).[26] Similarly, Zheng *et al.* also synthesised bottlebrush elastomers using a LA-PDMS macromonomer, with these networks synthesised through thermal self-polymerisation of the macromonomer. [29]

When LA or its derivatives copolymerise with vinyl monomers, the labile disulfide bond that imparts degradability to the polymer is only formed when two LA units polymerise sequentially, forming a dyad (**Scheme 1**). Tang and Tsarevsky reported the copolymerisation of ELp with ethyl acrylate, with the presence of disulfide bonds confirmed by the reduction in the molecular weight of the polymer under reductive conditions.[37] They continued to show the homopolymerisation of a vinyl functional LA derivative to form degradable branched polymers. In their study of ELp and LA-based pressure sensitive adhesives, Albanese *et al*. reported that in the copolymerisation of ELp with *n*-BA, dyad formation can be promoted by low temperature and high [M] reaction conditions due to the reversible propagation the ELp monomer.[27] This work showed both LA and ELp could polymerise with *n*-BA using conventional FRP with a thermal radical initiator. After light crosslinking, these high molecular weight copolymers produced comparable pressure sensitive to acrylic acid/butyl acrylate-based analogues. These materials were degradable under reducing conditions and the fragments were successfully recycled using oxidation with I_2/pyridine. Albanese *et al.* also showed the compatibility of LA copolymerisation with acrylate and acrylamide monomers using RAFT polymerisation to synthesis degradable, linear polymers.[33] They found that no copolymerisation occurred with methacrylate, a result that Endo *et al.* also reported in their early work on the polymerisation of lipoamide with vinyl monomers.[38] Interestingly, Endo *et al*. report that lipoamide did not homopolymerize with AIBN, whereas Raeisi and Tsaerevsky[26] show this is possible for ELp, which indicates that the functionalisation of LA derivatives would impact their polymerisation kinetics.



Scheme 1: Copolymerisation of lipoic acid with *n*-butyl acrylate by radical ring-opening polymerisation. 2 sequential additions of lipoic acid to the polymer forms a disulfide bond within the chain.

Recent examples of LA-based networks have utilised rROP of the 1,2 dithiolane group to incorporate disulfide bonds into the network structure: either within the polymer backbone[12,13,35], the crosslinks[31,36] or in both.[39] In this work, the LA and the esterified form ELp are used as cleavable comonomers with *n*-butyl acrylate to form covalently crosslinked gel networks with 0-30 mol% LA or ELp (**Scheme 2**). Degradation of these gels by thiol-disulfide exchange is investigated to find the critical comonomer loadings for macroscopic degradation to soluble fragments. Both FRP and RAFT polymerisation were implemented to illustrate how network topology would affect the degradation of these materials. The self-healing and recycling ability is also explored.



Scheme 2: (A) Synthesis of PBA networks containing LA or ELp comonomer synthesised by either RAFT polymerisation (DDMAT present) or FRP (no DDMAT). (B) Degradation of synthesised gel networks by thiol-disulfide exchange using 2,2'-(ethylenedioxy)diethanethiol (EDDET) with 1,8-diazabicyclo[5.4.0]undec-7- ene (DBU) catalyst.

Results and discussion

Kinetics of lipoic acid/ethyl lipoate RAFT copolymerisation with *n*-butyl acrylate

The copolymerisation of *n*-butyl acrylate and lipoic acid has been shown to be compatible with both conventional FRP and RAFT polymerisation, using a trithiocarbonate RAFT agent dodecylthiocarbonothioylthio)-2-methylpropionic acid (DDMAT).[40] Lipoic acid (LA) was functionalised with ethanol by Steglich esterification to form the comonomer ethyl lipoate (ELp). Before synthesising crosslinked networks containing these two comonomers, the RAFT polymerisation kinetics for comparable non-crosslinked reactions were studied. In this case a targeted degree of polymerisation of 150 was chosen with [BA]:[LA or ELp]:[AIBN]:[CTA] of 120:30:0.4:1. BA and comonomer conversions were monitored by ^{1}H NMR **(Figures 1A, 1B, 2A** and **2B**). The reaction kinetics of BA with both comonomers were very similar, with the comonomer being incorporated only slightly faster into the polymer than the BA, suggesting that the comonomer, and thus the disulfide bonds, are incorporated in a uniform distribution throughout the polymer chains. This directly contrasts the copolymerisation of DOT and BA, where the DOT was incorporated significantly faster into the polymer than BA, leading to a gradient microstructure of the polymer chains.[9,20,23,24,41] The differing distribution of cleavable sites within the polymers will affect the structure of the products of degradation, which was modelled in recent work from Lundberg *et al*.[42]

Both the BA-LA and BA-ELp copolymerisation reached ~80% conversion in 120 minutes, with the comonomer functionality having little effect on the reaction kinetics. Samples were also analysed by GPC (**Figures S1**, **S2** and **Tables S1**, **S2**), and the measured M_n values were close to the calculated theoretical values from the conversion measurements, although the dispersity values were slightly elevated, with both systems approaching $Đ$ = 1.40 at high monomer conversions **(Figures 1A, 1B, 2A and 2B)**. This is most likely due to increased termination from the slightly higher [AIBN] than used in other literature studies, which was required to produce fully developed gel networks under these conditions (vide infra). The PBA-LA system showed better correlation to theoretical M_n values than the PBA-ELp system; however, this could be due to how closely the polystyrene calibration correlates to the copolymer.

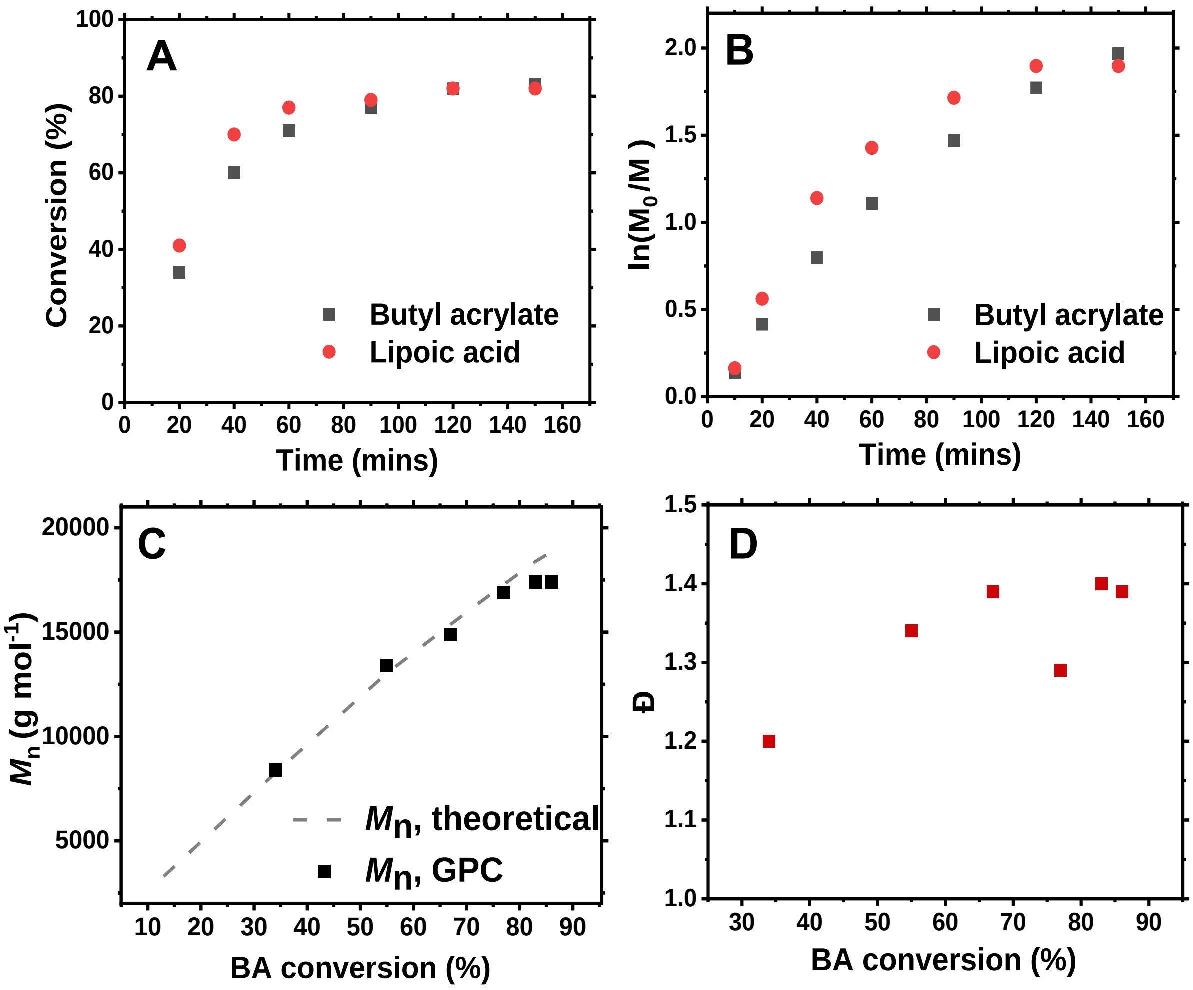


Figure 1: Conversion plots (A) and first-order semi-logarithmic kinetic plots (B) for RAFT copolymerisation of *n*-butyl acrylate with lipoic acid comonomer. [BA]:[LA]:[AIBN]:[CTA] 120:30:0.4:1. BA:anisole 1:1 v/v, T = 65 °C. M_n (C) and *Đ* (D) measured by THF GPC, and monomer conversions and theoretical M_n measured from ^{1}H NMR.

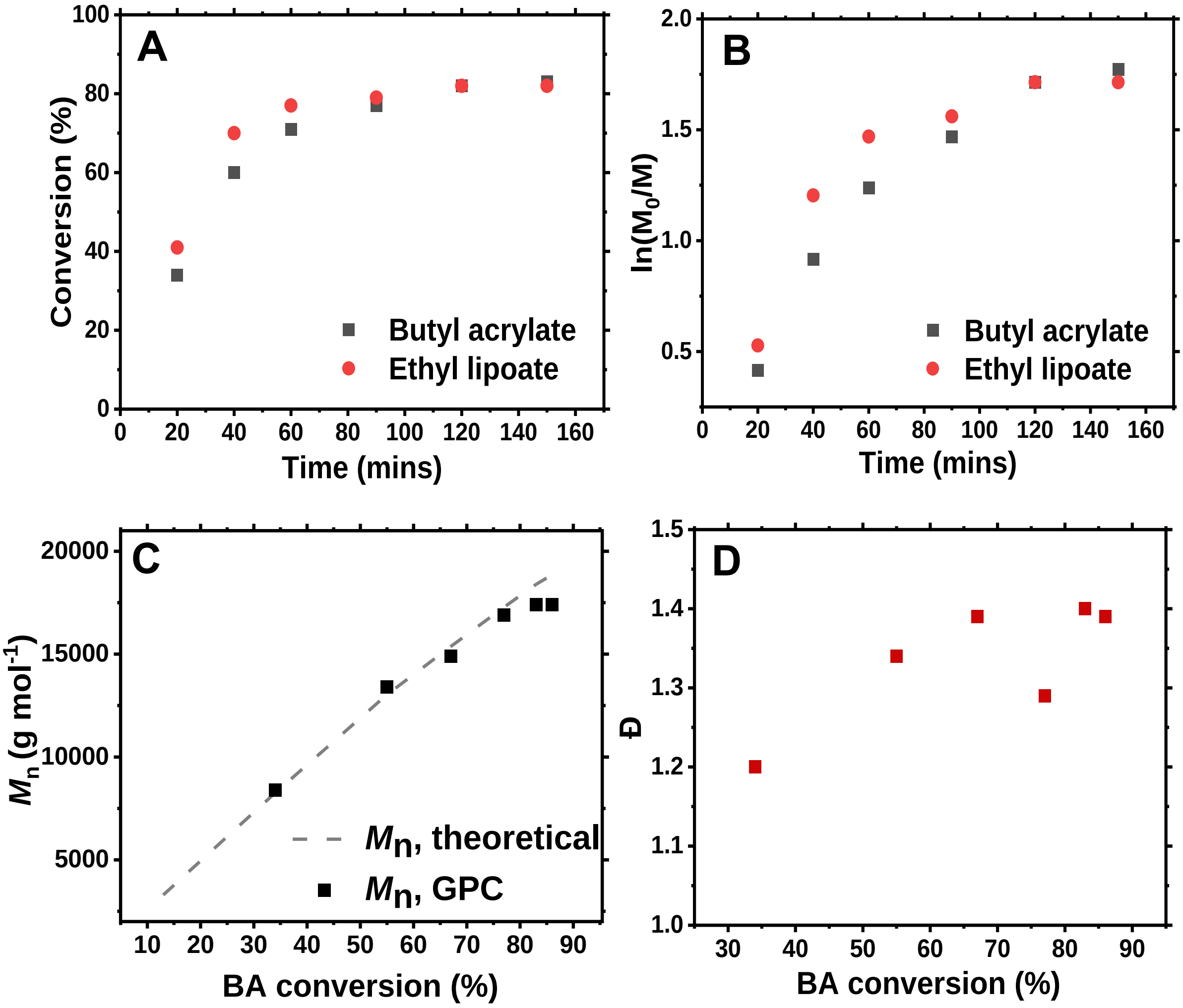


Figure 2: Conversion plots (A) and first-order semi-logarithmic kinetic plots (B) for RAFT copolymerisation of *n*-butyl acrylate with ELp comonomer. [BA]:[ELp]:[AIBN]:[CTA] 120:30:0.4:1. BA:anisole 1:1 v/v, T = 65 °C. M_n (C) and $Đ$ (D) measured by THF GPC. Monomer conversions and theoretical M_n measured from ^{1}H NMR.

Thermomechanical properties of PBA-LA and PBA-ELp gels

Gel networks were synthesised by both FRP and RAFT with varying amounts of LA or ELp between 0-30 mol%. When synthesis of crosslinked networks with relatively low radical initiator amount ([BA]:[AIBN] = 100:0.1) was attempted by RAFT polymerisation, the gels produced were very soft and not suited for mechanical analysis due to the slow reaction rate. Therefore, the amount of initiator was elevated ([BA]:[AIBN] = 100:0.4) to make defined gels on a practical timescale, which led to a slight loss of control at high monomer conversions in reactions without crosslinkers (Figs 1 and 2).

When designing a degradable polymer network, the aim is to install degradable units into the network without compromising the material's mechanical properties. In our previous work on PBA-DOT gels, the small amount of additive had no effect on the ESRs, gel fractions or storage modulus of the gels.[9,24] In contrast, significantly more LA or ELp would be required to impart similar degradability as two units of comonomer are required to form a single disulfide linkage. Therefore, these physical properties may be more affcted by the comonomer addition.

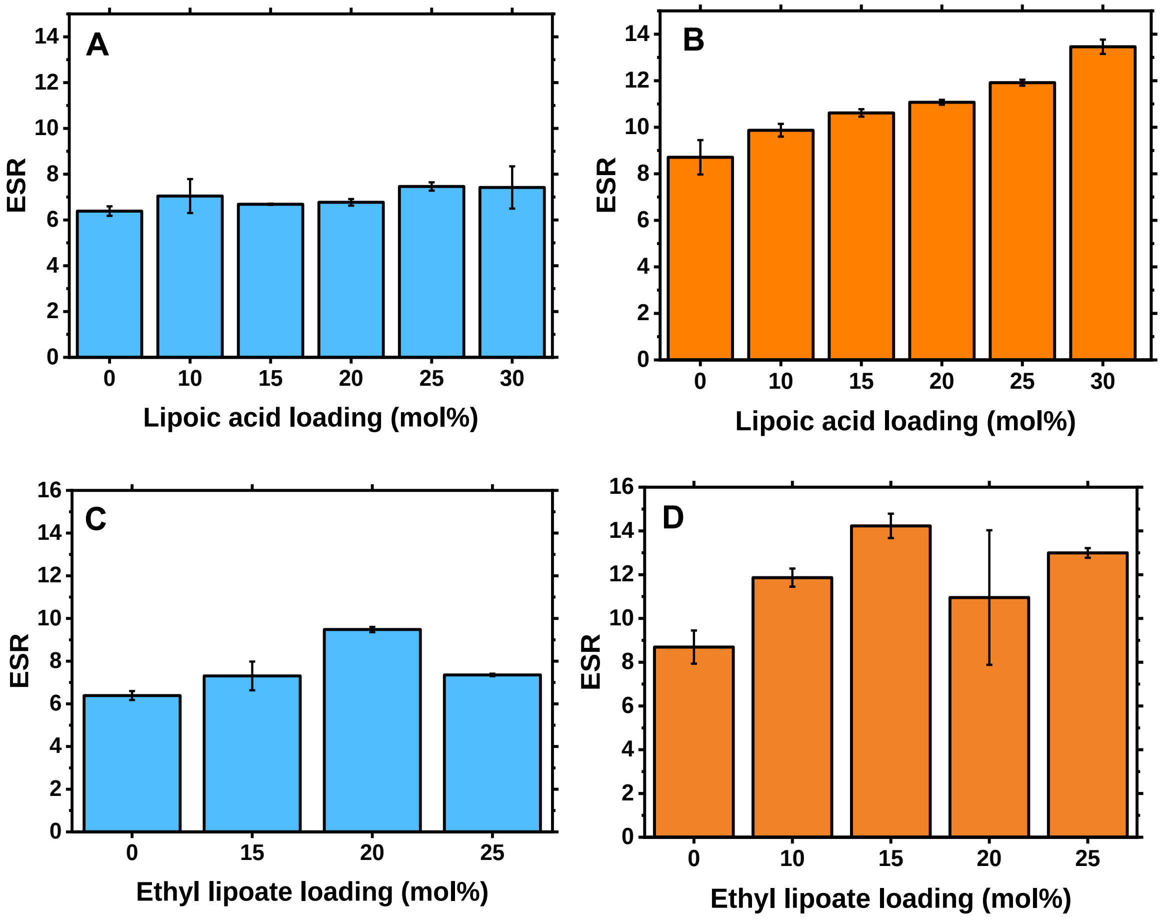


Figure 3: Equilibrium swelling ratios for (A, B) PBA-LA and (C, D) PBA-ELp gels synthesised by FRP (A, C) and RAFT polymerisation (B, D).

The equilibrium swelling ratio (ESR) and gel fraction % for these gels were measured in THF (**Figure 3**, **Figure S3**). When synthesised using FRP, the ESR does not significantly change with addition of either comonomer, and the gel fraction remains at > 90%. For the RAFT synthesised gels, the addition of both comonomers reduces the gel fraction and increases the ESR. The ESR increases from 8.7±0.7 to 13.5±0.3 for 30 mol% LA sample and to 13.0±0.2 for ELp. It is commonly observed that gels synthesised by RAFT polymerisation display higher ESR values and lower gel fraction percentages compared to gels synthesised by FRP.[9,34] This is due to the very different mechanism of network formation, with RAFT polymerisation producing homogenous networks containing chains with a lower degree of polymerisation.[4,43,44]

The difference in the gels synthesised by RAFT and FRP is also apparent in the oscillatory rheology data (**Figure 4** and **Figure S4**). As commonly observed, RAFT synthesised gels have lower and more frequency-dependent storage moduli compared to FRP synthesised gels.[34,45] Although all the phase angles recorded are < 45° indicating the gels behave more elastically than viscously overall, the RAFT synthesised gels consistently show greater phase angle values than the FRP synthesised gels, indicating that there is a larger contribution from viscous flow for these samples (**Figure S4**). The polymer chains for the RAFT made gels are much shorter than for the FRP gels, and so are not entangled, which leads to the lower G' value. The frequency dependence displayed is likely due to gradual stress relaxation of the high concentration of dangling ends and higher sol fraction in these gels.[46] For FRP synthesised gels with no comonomer added, the storage modulus (G') value is 7.3 kPa at 1 rad s^{-1} which rises to 26.2 kPa and 12.2 kPa with 25 mol% LA and ELp loadings respectively. Previous reports on materials based on homopolymerized LA show the presence of hydrogen bonding between the pendant carboxylic acid groups, which act as non-covalent crosslinks between chains.[11,47] The increase in G' value for the PBA-LA gels could be due to these additional physical crosslinks contributing to the elastic response of the material. For the RAFT synthesised gels, the effect of the comonomer on G' is much less apparent, especially for the PBA-ELp gels, despite the ESRs increasing with comonomer addition. The contribution to the storage modulus from the additional LA comonomer may be competing with the effect of the increased sol fraction for gels with high comonomer loading.

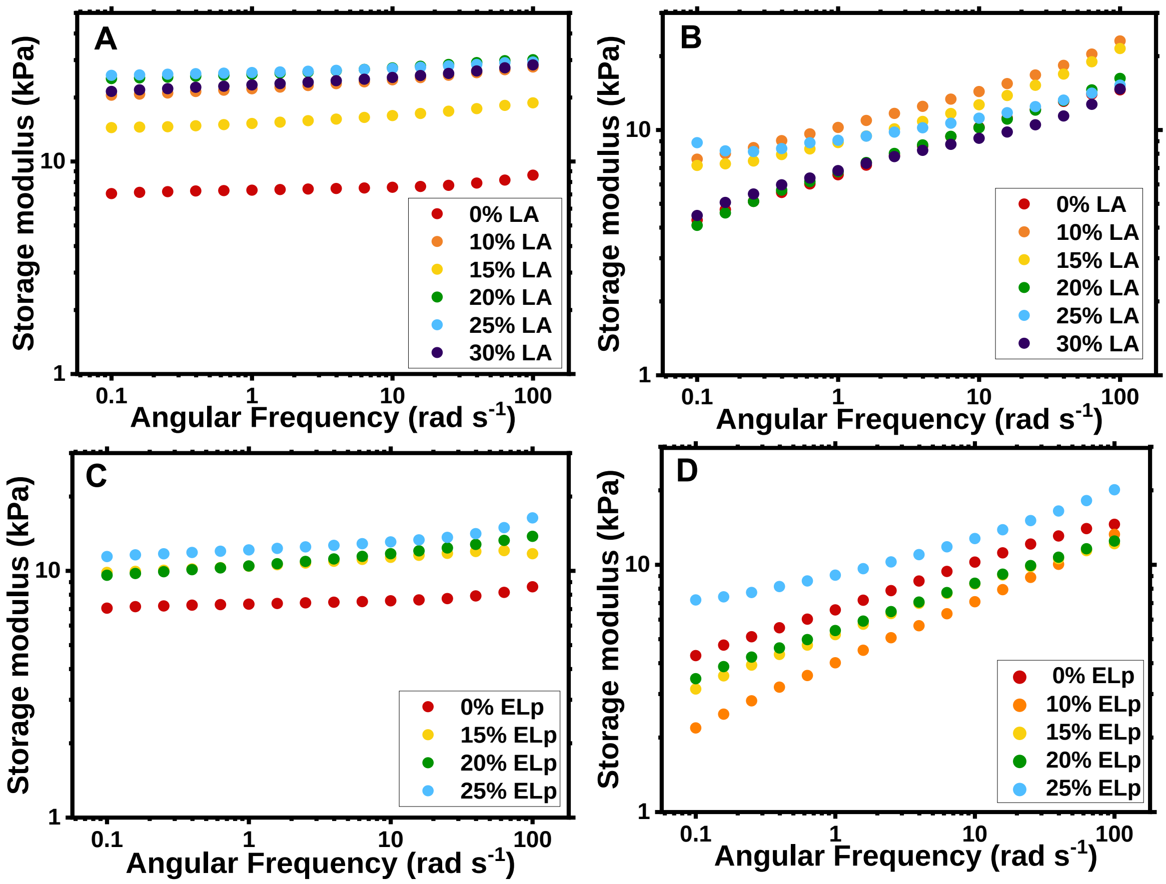


Figure 4:Oscillatory rheology frequency sweep of (A, B) PBA-LA and (C, D) PBA-ELp gels synthesised by FRP (A, C) and RAFT (B,D).

The thermal properties of the PBA networks are also affected by the addition of LA/ Elp comonomer. Through thermogravimetric analysis (TGA) the thermal degradation profiles were measured for PBA networks containing no comonomer, 25% LA and 25% ELp synthesised by both RAFT and FRP (**Figure S5** and **Table S3**). Addition of either comonomer reduced the degradation onset and the peak rate of degradation temperatures of the networks, due to the presence of weaker disulfide and thioether bonds within the polymer backbone. This reduction of thermal stability is consistent with other reports of disulfide-containing polymer materials.[48,49] Through differential scanning calorimetry (DSC) the glass transition temperatures (T_g) of these networks were also measured (**Figure S6** and **Table S4**). Compared to an unmodified PBA network (T_g = −40 °C for PBA-0%LA-RAFT), addition of 25 mol% ELp comonomer slightly reduced the measured T_g of the material (T_g= −47 °C) and LA addition significantly elevated the T_g (T_g= −23 °C). This increase is expected due to the presence of hydrogen bonding between lipoic acid groups reducing mobility of polymer chains leading to an increase in T_g.[50] Addition of both comonomers affect the thermal stability of the networks, and LA addition significantly impacts the T_g. In contract, we have previously shown that using DOT comonomer does not affect thermal properties,[24] so it is important that these effects are noted when using comonomers in certain applications.

Degradation of lipoic acid/ ethyl lipoate containing gels

As synthesized gels were degraded using 2,2'-(ethylenedioxy)diethanethiol (EDDET, 3 equiv. to comonomer) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 1 equiv. to comonomer) in THF at room temperature (**Scheme 2B**). Both FRP and RAFT gels successfully degraded into soluble fragments at some LA or ELp loading, indicating a significant number of disulfide bonds incorporated into the polymer structure. Generally, the critical comonomer loading required for full degradation was 5 mol% lower for ELp compared to LA, and it was also 5 mol% lower for RAFT gels compared to FRP **(Table 1** and **Table 2)**. It is consistent that RAFT networks require fewer cleavable bonds present to fully degrade, due to their more homogenous network structure. The gel sample that fully degraded with the lowest comonomer loading was the 15 mol% ELp gel synthesised by RAFT polymerisation. This is still significantly higher than the critical DOT loading we have previously reported[9] for a comparable gel (3 mol%) which is expected due to the reversibility of the LA/ELp propagation and the necessity to form dyads to produce disulfide linkages.

Table 1: Degradation of PBA-LA gel networks synthesised by RAFT polymerisation and FRP.

Sample	Macroscopic degradation[a]	Mass loss %[b]
PBA-0% LA-RAFT	No	0.45±0.7
PBA-10% LA-RAFT	No	16.9±0.6
PBA-15% LA-RAFT	No	74.9±1.1
PBA-20% LA-RAFT	Yes	100
PBA-25% LA-RAFT	Yes	100
PBA-30% LA-RAFT	Yes	100
PBA-0% LA-FRP	No	-1.32±0.9
PBA-10% LA-FRP	No	21.7 ±11.3
PBA-15% LA-FRP	No	26.6 ±0.6
PBA-20% LA-FRP	No	68.9 ±8.5
PBA-25% LA-FRP	Yes	100
PBA-30% LA-FRP	Yes	100

[a] Macroscopic degradation determined visually when no solids remain. [b] Measured gravimetrically by washing and drying remaining solids after degradation. When full macroscopic degradation was observed, the mass loss was assumed to be 100%.

Table 2: Degradation of PBA-ELp gel networks synthesised by RAFT polymerisation and FRP.

Sample	Macroscopic degradation[a]	Mass loss %[b]
PBA-0% ELp-RAFT	No	0.45±0.7
PBA-10% ELp-RAFT	No	69.4±7.3
PBA-15% ELp-RAFT	Yes	100
PBA-20% ELp-RAFT	Yes	100
PBA-25% ELp-RAFT	Yes	100
PBA-0% ELp-FRP	No	-1.32±0.9

PBA-15% ELp-FRP	No	62.1±3.2
PBA-20% ELp-FRP	Yes	100
PBA-25% ELp-FRP	Yes	100

[a] Macroscopic degradation determined visually when no solids remain. [b] Measured gravimetrically by washing and drying remaining solids after degradation. When full macroscopic degradation was observed, the mass loss was assumed to be 100%.

The fragments of the fully degraded PBA-LA and the PBA-ELp gels synthesised by RAFT polymerisation were analysed by GPC (**Figure 5**). These traces were broad and multimodal, indicating significant branching. The molecular weights decrease with increasing comonomer loading, which is expected for gels with higher numbers of labile bonds within the backbone. The dispersity of these fragments also decreases with increasing comonomer loading and seems to approach $Đ = 2$, reflecting the uniform incorporation of both comonomers seen in kinetics experiments. Indeed, the degradation of polymer networks with cleavable comonomers was modelled by Johnson *et al.* who found that for the ideally random copolymerisation of a cleavable comonomer into a crosslinked network the dispersity of the degraded fragments were ~2.[8] Compared to PBA-DOT gels synthesised by RAFT polymerisation,[9] the degraded fragments for the PBA-LA and PBA-ELp gels were also less multimodal and their measured dispersities were significantly lower. Whereas the DOT-BA copolymerisation formed a distinct gradient structure, the degraded fragment analysis corroborates the linear polymerisation kinetics study to suggest that the LA/ELp dyads are distributed more evenly throughout the network.

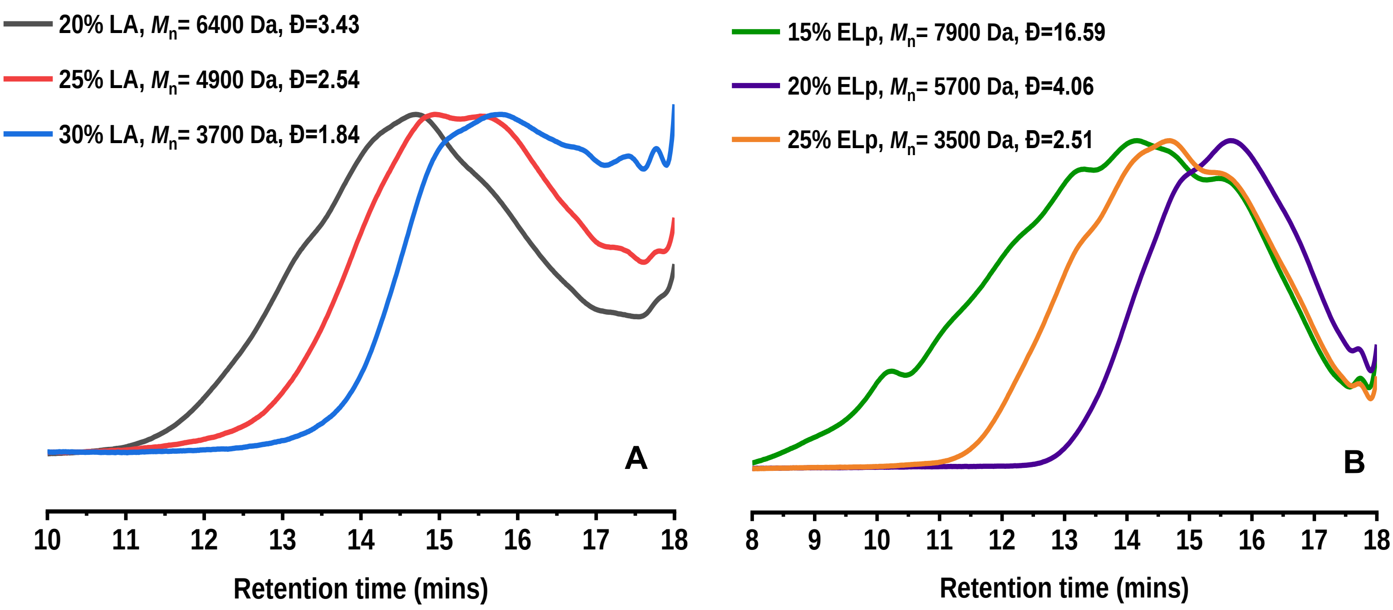


Figure 5: GPC traces of the degraded gel fragments for (A) PBA-LA gels and (B) PBA-ELp gels synthesised by RAFT polymerisation.

Regelation

We have previously shown that thiol-functional degraded gel fragments can be oxidised in air in the presence of base to reform disulfide linkages and reform a solid network.[9] The polymer fragments formed upon degradation of these PBA-LA and PBA-ELp networks also are thiol functional, and Albanese *et al.* have also shown the repolymerisation of linear PBA-ELp using thiol oxidation.[27] Therefore, reformation of these networks after degradation should be possible. After degradation with a small amount of EDDET (1.5 equiv. to comonomer) and DBU (1 equiv. to comonomer) in THF, AcOH (1.5 equiv) was added to quench the thiol groups on the fragments. The fragments were precipitated in methanol/water 90:10 and then transferred to a small vial. In order to facilitate disulfide formation, additional pyridine (5 equiv. to comonomer) and DMF were added to the degraded fragments before heating in air, as polar aprotic solvent and base are known to promote thiol oxidation in air.[51] Degradation- regelation was attempted for all samples listed in **Tables 1** and **2** which macroscopically degraded. The samples were left for 1 week to form the maximum number of disulfides.

In our previous study on PBA-DOT networks, the regelation of gels with 3-5 mol% DOT synthesised by RAFT was relatively easy, whereas gels made by FRP the regelation could not occur. A similar result was observed here, where neither FRP-made gel could successfully form a solid network. Surprisingly however, reformation of these LA and ELp gels synthesised by RAFT polymerisation also was difficult to accomplish. All attempts led to an increase in fragment viscosity to varying extents, however the only successful sample to fully regel to a solid network was the PBA-15%ELp-RAFT gel (**Figure 6** and **Figure S7**). Likely, there are two reasons for this behaviour. First, as the oxidation of thiols is base-mediated, reaction with the acid groups in the LA-containing gels may be competing with the thiol oxidation reaction, making the PBA-ELp gels more suitable for regelation. Furthermore, the structure of the fragments is clearly affecting the ease of relation. Notably, the PBA-15% ELp fragments had a significantly higher dispersity than any other sample ($Đ = 16.59$, Fig. 5B), which indicates that fragment dispersity is key to reforming networks. The other fragments have much lower dispersity values, which were also lower than any of the PBA-DOT gel fragments which successfully regelled in our previous study.[9] These results suggest that the regelation success depends on the presence of acid groups (chemical contribution), and the dispersity of the fragments (structural contribution). Interestingly, this would indicate that uniform distribution of the cleavable groups in the backbone, which is typically a sought-after feature that improves degradation by producing low dispersity fragments, might be detrimental if the network is designed to also reform after deconstruction.

While this effect may at first seem counterintuitive, it can be rationalised by referring to the Flory-Stockmayer theory, where larger dispersity of crosslinking polymer chains results in lower number of crosslinks needed to reach the gel point.[45,52] On the other hand, low dispersity enhances degradation, whether through cleavable comonomers/strands[8] or crosslinks[53], and therefore the opposite relationship should be expected when reforming the degraded network.

Nevertheless, regelation of the PBA-15%ELp-RAFT sample led to a well-defined material that could be analysed by swelling and oscillatory rheology (**Figure 7**). There was only a very slight increase in ESR value from 14 to 16 before and after the degradation/regelation process suggesting small reduction in network connectivity. This was confirmed by oscillatory rheology which showed a slight decrease in *G'* value compared to the original sample, indicating that the disulfide reformation, while still high, was not 100% complete. The *G'* was also less frequency dependent and the *G"* was lower for the regelled sample compared to the original, as the latter was measured as synthesised and contained a significant sol fraction.

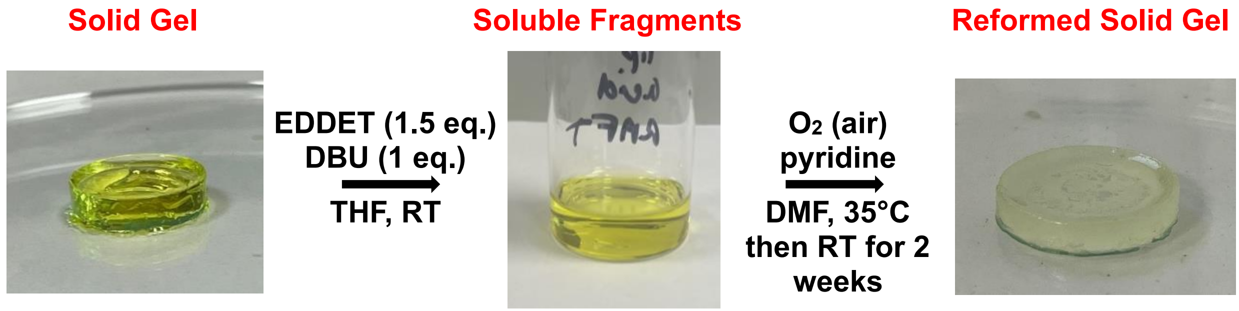


Figure 6: Degradation and regelation of PBA-15% ELp RAFT gel.

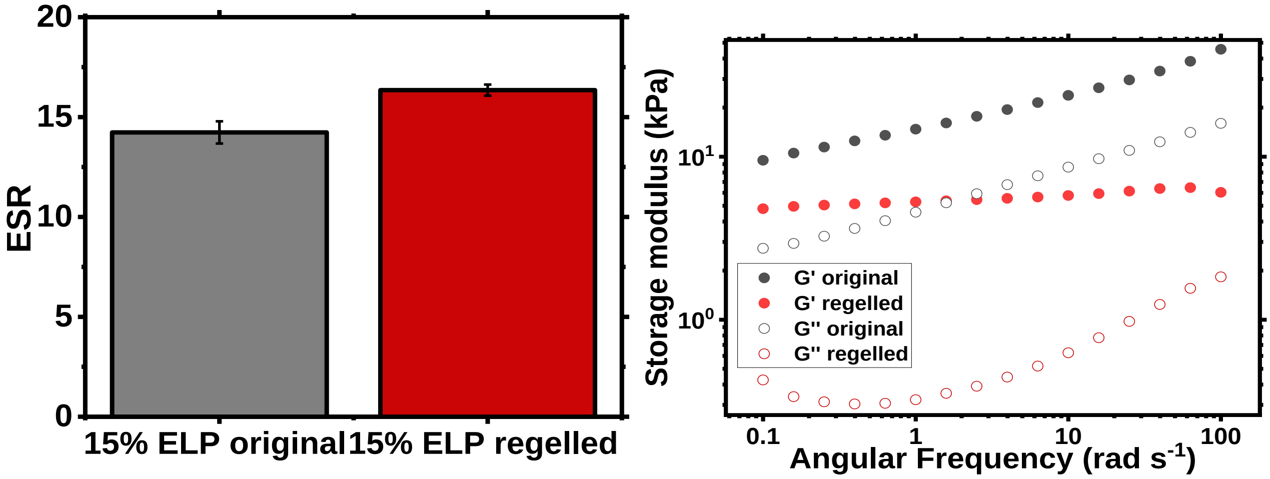


Figure 7: (Left) Equilibrium swelling ratio and (Right) oscillatory rheology frequency sweep of PBA-15%ELp gels before and after degradation/regelation process.

Self-healing

The presence of dynamic disulfide bonds in a polymer network is often utilised for some form of self-healing behaviour[11–13,47,54]. Usually this is in response to heat, light or other stimulus but can also be spontaneous if the concentration of disulfide is high enough. When the network is cut, the disulfide bonds can rearrange across the fracture. Choi *et al.* produced crosslinked 3D-printed objects from the photopolymerization of a PEF-LA macromonomer to form super-soft bottlebrush networks.[13] The dynamic exchange of the network was tested by crushing the objects and reprocessing under pressure with heat or light. It was also shown that cut portions of the material could be reattached upon the addition of DBU, acting as a strong base to facilitated disulfide rearrangement. A similar approach was very recently utilised by Han *et al*. for healing of 3D-printed resins containing disulfide bonds within the network's backbone and crosslinks.[39] This method was used to test the PBA-LA and PBA-ELp gels, to see if a similar healing behaviour could be observed in materials with significantly fewer disulfide linkages.

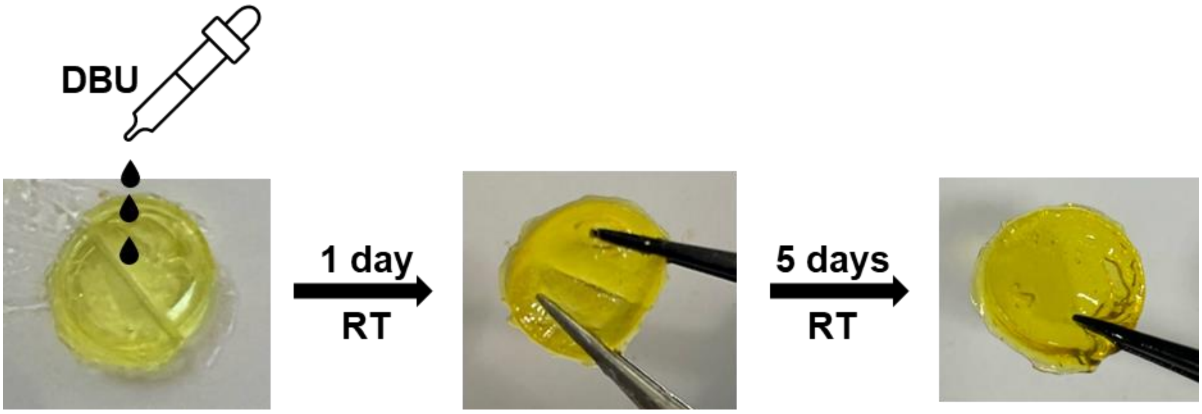


Figure 8: Healing of cut PBA-25% ELp-RAFT gel using DBU catalyst.

Gels with 25 mol% comonomer loading were tested, with the PBA-25%ELp-RAFT gel healing enough to hold the disc together, even with light amounts of pulling apart, after 24 hours which improved after 5 days (**Figure 8**). Once again, the ELp gels were more successful than the LA gels due to the competing reaction of the DBU with the carboxylic acid groups. The RAFT-made gels were also more successful as they were softer and, as the previous rheology data shows (**Figures 4** and **S4**), have more viscous flow behaviour due to shorter chains and higher sol fraction. Since the gel pieces are placed next to each other with no external pressure, this flow allows for greater contact across the fracture allowing for disulfide exchange to occur between chains within the two pieces. If the comonomer loading was increased, this healing behaviour possibly would become more effective, however at the expense of influencing other properties of the gel.

Conclusions

We have shown that α-lipoic acid and its ester ethyl lipoate can be used as a comonomer to impart macroscopic degradability to poly(*n*-butyl acrylate) crosslinked networks, at loadings as low as 15 mol% (vs monomer). Disulfide bonds are evenly distributed throughout the chains where two comonomer units copolymerise sequentially to form dyads which can be cleaved by thiol-disulfide exchange. Whereas networks synthesised by RAFT have been shown before to readily degrade using both cleavable comonomers and cleavable crosslinkers, gels synthesised by FRP are not as easily degraded. Here LA and ELp comonomers successfully produce degradable PBA networks synthesised by FRP, requiring slightly higher loadings of comonomer than their corresponding RAFT-synthesised networks. It is possible to reform networks after degradation, however due to competing reaction with acid groups and low fragment dispersity this is difficult, and only possible when the networks are made using RAFT polymerisation. Low dispersity of the polymer chains has been shown to make degradation more efficient, however here we show that this can negatively impact network reformation. These relationships could be utilised to control the degradation/regelation properties of a material, modifying the dispersity to make a material moderately degradable but easily reprocessable. The dynamic disulfide bonds located in the backbones also allow these networks to heal in the presence of DBU catalyst, at comonomer loadings of only 25 mol%. Lipoic acid comonomers could be utilised in making degradable and healable crosslinked materials for use in medical or cosmetic products due to its non-toxicity and biocompatibility.

Acknowledgments

This work was supported by the EPSRC New Investigator Award grant no. EP/W034778/1. Analytical equipment was provided by the Chemical Characterisation Facility at the University of Bath. The authors thank Dr Martin Levere for help with the GPC measurements.

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