

# Solid-State NMR Characterization of Biodegradable Shape-Memory Polymer Networks

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**Summary:** Copolymer networks synthesized from dilactide and diglycolide were characterized by solid-state  $^{13}\text{C}$  CPMAS NMR in terms of composition, cross-link density, and rate of cross-linking by UV irradiation. The latter is directly evident by a signal at 44 ppm in the  $^{13}\text{C}$  NMR spectrum. Comparison of solid-state NMR data with the determination of the gel content revealed that this NMR method is sensitive to the chemical cross-link density whereas the gel content is also influenced by physical constraints such as entanglement. Furthermore, these copolymer networks show a shape-memory effect, i.e. a temporary macroscopic shape can be programmed by heating the network above its glass transition temperature together with fixation during cooling. Reheating without fixation recovers the permanent shape. The recovery of the permanent shape could be followed by  $^1\text{H}$  DQ NMR buildup curves for a sample that was stretched by 80%.

**Keywords:**  $^{13}\text{C}$  CPMAS; lactide-glycolide copolymers; shape-memory effect; solid-state NMR

## Introduction

Polymers or copolymers containing lactide and glycolide units are known to be biodegradable.<sup>[1–4]</sup> Therefore, these materials are of considerable interest for dental,<sup>[4]</sup> orthopaedic as well as drug-delivery applications.<sup>[5,6]</sup> Commercially available suture materials from poly(glycolide) or copolymers are already available, known as Dexon<sup>®</sup> and Vicryl<sup>®</sup>, respectively. Our approach focusses on the synthesis of copolymer networks with permanent covalent bonds. For this, lactide-glycolide copolymers were prepared by ring-opening polymerization of *L,L*-dilactide and diglycolide with ethylene glycole as initiator.<sup>[7]</sup> In order to obtain fully amorphous copolymers, transesterification was induced using long reaction times and dibutyltin

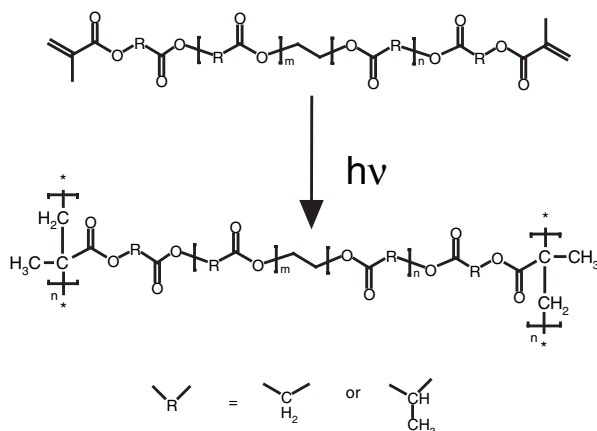
oxide as catalyst. The resulting macrodiols were reacted with methacryloyl chloride to yield copolymers with olefinic end groups. These were cross-linked by UV light without the need for an initiator to obtain copolymer networks. The chemical structures of the dimethacrylate and the final polymer network are illustrated in Scheme 1. Different segment chain lengths were obtained by varying the ratio of ethylene glycole to dilactide/diglycolide. The resulting copolymer networks are fully amorphous and have a glass transition temperature ( $T_g$ ) of around 50 °C. Interestingly, the  $T_g$  is fairly independent of the segmental chain length of the network precursor.

Since these copolymer networks are insoluble, structural characterization is demanding. Solid-state NMR is able to characterize these materials in detail by  $^{13}\text{C}$  CPMAS<sup>[8]</sup> spectra with respect to composition, cross-link density, and completeness of UV cross-linking.

An interesting feature of these networks is the fact that they show the shape-memory effect,<sup>[9]</sup> i.e. a temporary macroscopic shape can be programmed by heating the

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### Scheme 1.

Chemical structures of the dimethacrylate precursor and the final polymer network after irradiation with UV light.

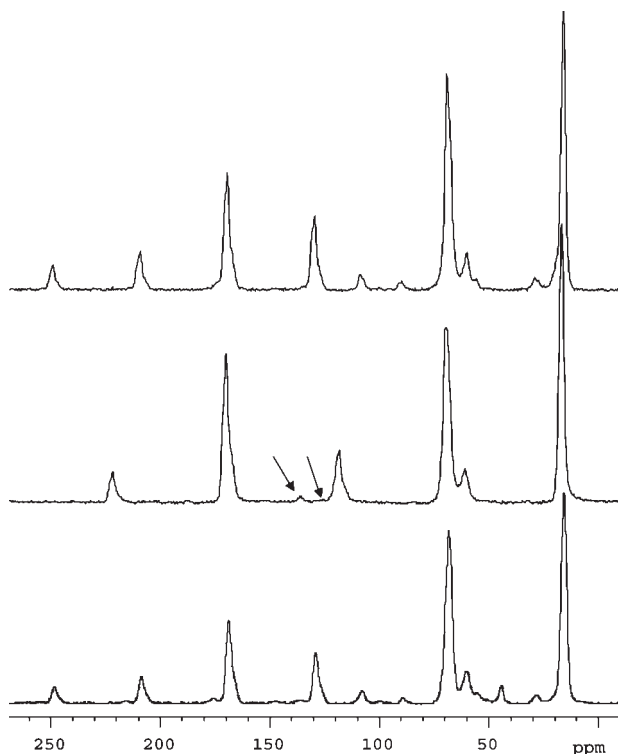
samples above  $T_g$  and fixing this shape during cooling. By reheating above  $T_g$  without fixing, the permanent shape can be recovered. This effect could be exploited for instance in minimal-invasive surgery in a way that the network in the temporary shape is compressed during the implantation process and expands at body temperature to its permanent shape. Furthermore, the copolymer networks can be equipped with drugs and serve as matrices for drug-delivery, thereby releasing the drug uniformly during the degradation of the network.

## Structural Assignment

To characterize the intermediate copolymers and the final network,  $^{13}\text{C}$  cross-polarization magic angle spinning (CPMAS<sup>[8]</sup>) experiments were performed. The results are shown in Figure 1. A fairly good separation of the individual functional groups – methyl groups at 17 ppm, methylene and methine carbon signals at 61 and 69 ppm, respectively, and carbonyl carbon signals at 170 ppm – is obtained. From the macrodiol to the macrodimethacrylate only small variations are visible, i.e. small intensity signals at 125 and 136 ppm corresponding to the olefinic carbons of the

chain ends are present. The methyl group of the methacrylate has the same chemical shift as the methyl group from the lactide unit. In the copolymer network the olefinic signals are absent but a signal at 44 ppm is visible that corresponds to the quaternary carbon signal of the cross-linking point. This was clarified by dipolar dephasing experiments<sup>[10]</sup> and comparison with published data. Apart from this signal also small signals at 177 ppm for the carbonyl group and at 52 ppm for the methylene group of the methacrylate are visible that indicate the spectroscopic changes due to cross-linking. But the striking feature is that the signal at 44 ppm is a direct indicator of the cross-linking point and therefore is a measure of the cross-link density. Furthermore, it is well separated from other signals and therefore only simple signal integration is necessary to quantify the cross-link density as will be shown below.

Copolymer networks with different ratios of lactide to glycolide were studied by  $^{13}\text{C}$  CPMAS NMR as well. From the signal intensities of the methine groups at 69 ppm for lactide and of the methylene groups at 61 ppm for glycolide the composition in the final network could be determined by spectral deconvolution. The results were in good agreement with the synthesis input (data not shown).



**Figure 1.**

$^{13}\text{C}$  CPMAS spectra of the network precursor and the final network. Top: macrodiol, middle: macrodimethacrylate, bottom: final network. The arrows indicate the small intensity of the olefinic carbon signals. Contact time in all experiments was 1 ms, the spinning speed was 5 kHz for the top and bottom spectrum and 6 kHz for the middle spectrum to prevent signal overlap of the olefinic carbons with a spinning sideband of the carbonyl carbons.

It has to be mentioned that cross-polarization is in general not a quantitative method since the  $^{13}\text{C}$  signal intensity depends on the efficiency of magnetization transfer from the nearby protons coupled through space and the loss of magnetization due to relaxation processes.<sup>[11]</sup> The cross-polarization behavior can be checked by so-called variable contact time experiments. Here, the signal intensities first increase due to the magnetization transfer and finally decrease due to the relaxation. Moreover, the signal buildup is proportional to the dipolar coupling between the carbon nucleus under investigation and the nearby protons, a higher dipolar coupling will lead to a faster signal buildup. For the determination of the composition for samples with

varying lactide to glycolide ratio, both methine and methylene groups showed almost identical contact time behavior. This means that within a spectrum the relative composition of lactide to glycolide can be obtained directly by signal integration and a quantification from CPMAS spectra is justified. Furthermore, the agreement with the synthesis input proves that during cross-linking no or only small changes occur to the segmental chains. On the other hand, in a sample series measured under identical NMR parameters a comparison of the signal intensity of one signal in different samples is valid under the assumption that the different samples show the same behavior in the cross-polarization process which was also clarified by studying

the variable contact time behavior.<sup>[11]</sup> This will be used in the next section to evaluate the cross-link density from CPMAS data.

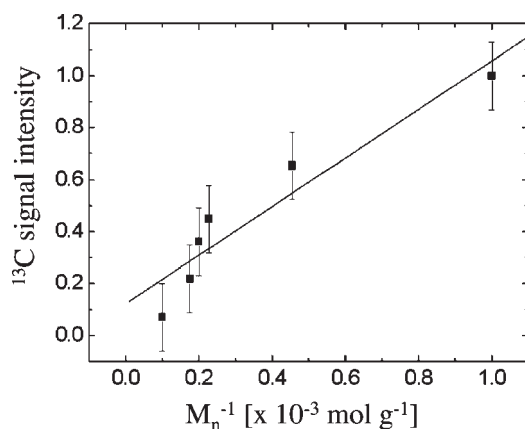
## Cross-Link Density

Because the signal at 44 ppm of the quaternary carbon in the  $^{13}\text{C}$  spectrum stems from the cross-linking position, a direct determination of the cross-link density in these copolymer networks is possible. In Figure 2 the intensity of the signal at 44 ppm is plotted versus the inverse number average molecular weight and with that the segment chain length of the network precursor determined from  $^1\text{H}$  NMR of the dimethacrylate precursor in solution. The signal intensities of the individual samples were measured using identical experimental parameters by scaling to the intensities of the signals that do not change with cross-link density since different amounts of sample were used for the measurements.

It can be seen that a good linear correlation exists between the  $^{13}\text{C}$  signal intensity and the inverse molecular weight of the precursor which is directly related to the cross-link density. Slight deviations from the linear correlation occur for the longest chain segments only, i.e. smallest

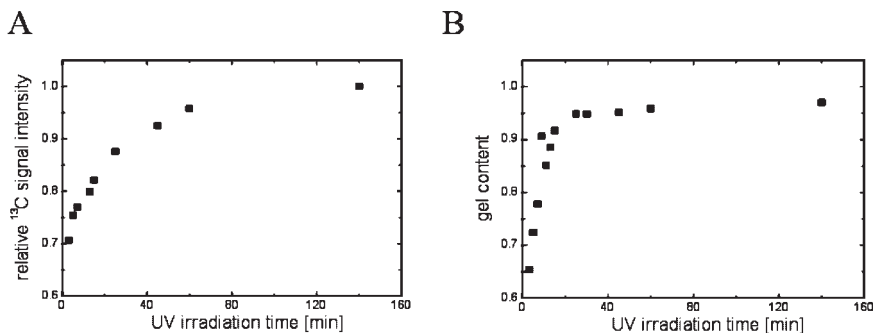
values of  $1/M_n$  and with that smallest cross-link density. This is not too surprising since it is not unlikely for these longest chain segments that the cross-linking is incomplete because due to their length not all chain-ends find a reaction partner for cross-linking.

In a further investigation the rate of cross-linking by UV irradiation was followed on the one hand by measuring the gel content and on the other hand with our established  $^{13}\text{C}$  NMR method. The gel content is determined by the ratio of the weight of the dried sample after swelling – by which unreacted dimethacrylate chains are removed – and the weight of the sample before swelling. The results are shown in Figure 3. In the first few minutes most of the cross-linking has already taken place. Nevertheless, at longer irradiation times the gel content increases more rapidly than the 44 ppm signal intensity. This reflects that the gel content is not only affected by the amount of chemical cross-links but also from the presence of physical constraints like entanglements of uncross-linked chain segments or segments that have only reacted at one end. The NMR signal intensity on the other hand is only sensitive to the chemical cross-link density and is increasing even up to 140 minutes of total UV-irradiation time.



**Figure 2.**

$^{13}\text{C}$  signal intensity at 44 ppm as a function of inverse number average molecular weight of the network precursor. Intensities are scaled with respect to the highest intensity.



**Figure 3.**

A: signal intensity of the 44 ppm  $^{13}\text{C}$  signal as a function of UV irradiation time. The intensity is scaled relative to the intensity after 140 minutes of UV irradiation. B: gel content as a function of UV irradiation time. The gel content was determined by the ratio between the weight after swelling and before swelling.

## Shape-Memory Effect

To study the shape-memory effect of these networks by NMR, one sample was programmed by stretching it by 80%. With this, the degree of order of the chain segments was increased due to elongation. Segmental chain order can be studied by different NMR methods like linewidth, spin-spin relaxation time measurements,<sup>[12]</sup> or multiple quantum buildup curves.<sup>[13,14]</sup> We choose the latter since it is the most sensitive method. The parameter underlying these methods is the dipolar coupling which is inversely proportional to the cube of the distance of two coupled spins or nuclei. But the more important in this case is the fact that it is also depending on the mobility of the polymer chain segments which is fast on the time scale of an NMR experiment. The more restricted the mobility, the higher is the dipolar coupling.  $^1\text{H}$  DQ buildup curves reflect this mobility via the dipolar couplings in such a way as the relative intensity, i.e. the efficiency of the excitation of a double quantum coherence, and also the position of the maximum indicate the strength of the dipolar coupling. A maximum is obtained by two concurring processes, the one is the pumping of double quantum coherence and the other the loss of coherence due to relaxation processes. The higher the relative intensity – scaled by the intensity of a one-pulse spectrum – and the smaller

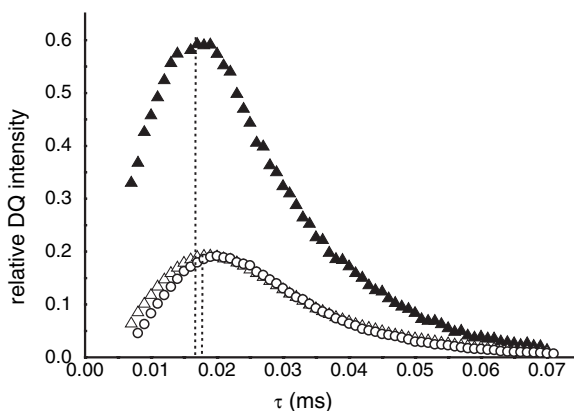
the time at maximum intensity, the higher is the dipolar coupling and with that the more restricted is the segmental chain mobility.

Figure 4 shows the DQ buildup curves of a sample at three different stages of the shape-memory process, before stretching, stretched by 80%, and after reheating above  $T_g$  and thereby releasing the stress.

It can be seen that for the stretched sample a higher relative intensity and a slightly shorter time at maximum intensity is observed due to a higher degree of chain order. Whereas the position of the maximum is qualitatively a good indicator, the influence of relaxation processes might be different for the stretched and unstretched sample. For quantification, one has to take into account these relaxation processes. Nevertheless, Figure 4 also shows that the recovery of the permanent shape is almost fully reversible since the two buildup curves before stretching and after reheating are almost identical. Therefore, the shape-memory effect can be well studied by solid-state NMR methods even if the sample elongation was limited to 80%. This is the maximum elongation possible before the sample breaks.

## Conclusions

It has been shown that solid-state NMR is well-suited to characterize biodegradable



**Figure 4.**

$^1\text{H}$  DQ buildup curves measured at room temperature at three different stages of a copolymer network: Permanent shape before stretching (open circles), temporary shape after stretching the sample by 80% above  $T_g$  and fixing the shape down to room temperature (solid triangles), recovery of permanent shape after reheating above  $T_g$  without fixation (open triangles).

copolymer networks from dilactide and diglycolide that are hard to analyze otherwise. Of special importance is the fact that from the  $^{13}\text{C}$  CPMAS spectra the cross-link density can be determined directly which is an important parameter for the application of these copolymer networks for medical applications as temporary implants or as a matrix for drug-release. By following the rate of UV cross-linking it became evident that NMR is sensitive to the chemical cross-link density whereas the gel content is also influenced by physical constraints such as entanglements. This is an important aspect with regard to the question if uncross-linked chain segments are present in the network and NMR is the more reliable method. Furthermore, it could be shown that the shape-memory effect of these networks could be followed by  $^1\text{H}$  DQ NMR spectroscopy due to an increase of chain order by stretching the sample by 80%. From the different results it can therefore be concluded that the methodology presented here could be also useful for other polymer networks.

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