

# UNIVERSITY OF BIRMINGHAM

## Research at Birmingham

### Rheological studies of polycaprolactone in supercritical CO<sub>2</sub>

Kelly, Catherine; Murphy, Shona; Leeke, Gary; Howdle, Steven M.; Shakesheff, Kevin M.; Jenkins, Michael

DOI:

[10.1016/j.eurpolymj.2012.11.021](https://doi.org/10.1016/j.eurpolymj.2012.11.021)

License:

Creative Commons: Attribution-NonCommercial-NoDerivs (CC BY-NC-ND)

*Document Version*

Peer reviewed version

*Citation for published version (Harvard):*

Kelly, C, Murphy, SH, Leeke, G, Howdle, SM, Shakesheff, KM & Jenkins, M 2013, 'Rheological studies of polycaprolactone in supercritical CO<sub>2</sub>', *European Polymer Journal*, vol. 49, no. 2, pp. 464-470. <https://doi.org/10.1016/j.eurpolymj.2012.11.021>

[Link to publication on Research at Birmingham portal](#)

#### **Publisher Rights Statement:**

NOTICE: this is the author's version of a work that was accepted for publication in *European Polymer Journal*. Changes resulting from the publishing process, such as peer review, editing, corrections, structural formatting, and other quality control mechanisms may not be reflected in this document. Changes may have been made to this work since it was submitted for publication. A definitive version was subsequently published in *European Polymer Journal*, [VOL 49, ISSUE 2, Feb 2013] DOI:10.1016/j.eurpolymj.2012.11.021  
Eligibility for repository: Checked 02/06/2015

#### **General rights**

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

#### **Take down policy**

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact [UBIRA@lists.bham.ac.uk](mailto:UBIRA@lists.bham.ac.uk) providing details and we will remove access to the work immediately and investigate.

## Rheological studies of polycaprolactone in supercritical CO<sub>2</sub>

Catherine A. Kelly<sup>1</sup>, Shona H. Murphy<sup>2</sup>, Gary A. Leeke<sup>1</sup>, Steven M. Howdle<sup>3</sup>, Kevin M. Shakesheff<sup>4</sup>, Mike J. Jenkins<sup>2\*</sup>

<sup>1</sup>*School of Chemical Engineering, University of Birmingham, Edgbaston, Birmingham. B15 2TT, UK*

<sup>2</sup>*School of Metallurgy and Materials, University of Birmingham, Edgbaston, Birmingham. B15 2TT, UK*

<sup>3</sup>*School of Chemistry, University of Nottingham, University Park, Nottingham. NG7 2RD. UK*

<sup>4</sup>*School of Pharmacy, University of Nottingham, University Park, Nottingham. NG7 2RD, UK*

*Correspondence should be sent to Mike Jenkins*

m.j.jenkins@bham.ac.uk tel: +44 (0)121 414 2841 fax: +44 (0)121 414 7468

### Abstract

A high pressure parallel plate rheometer is utilised to probe the rheological properties of polycaprolactone (PCL) over a range of temperatures (80 to 120 °C) and CO<sub>2</sub> pressures (atmospheric to 100 bar). Interpretation of storage/loss modulus against angular frequency plots show that the reptation time of PCL can be significantly reduced by the addition of 60 bar CO<sub>2</sub>. This reduction is equivalent to heating the polymer by 20 °C. Application of a time/temperature superposition, coupled with the Arrhenius equation, shows that the addition of CO<sub>2</sub> also lowers the activation energy to flow from 31.3 to approximately 21 kJ mol<sup>-1</sup>.

**Keywords:** reptation; rheology; supercritical CO<sub>2</sub>; polycaprolactone

### 1. Introduction

Polycaprolactone (PCL) is a semi-crystalline polymer possessing glass transition and melting temperatures of -60 and 60 °C, respectively. It is commonly used in a wide range of medical applications, for example tissue engineering [1-2] and drug delivery [3], as a result of its biocompatible and biodegradable nature coupled with a high compressive strength. In the melt phase, PCL displays a high viscosity, which results in elevated temperatures (above 140 °C) being required to process it [4]. This is a major problem when trying to incorporate thermally sensitive drugs or cells for biomedical applications; often causing them to denature or degrade [5].

Supercritical CO<sub>2</sub> (scCO<sub>2</sub>) is becoming increasingly used to facilitate the processing of high viscosity polymers [6-7]. We have previously highlighted the ability of high pressure and supercritical CO<sub>2</sub> to absorb into PCL [8] and the depression of the melting point that occurs as a result [9]. The gas-like viscosity of scCO<sub>2</sub> enables it to diffuse into the free volume within amorphous regions of polymers. Once inside, it takes part in Lewis acid/base interactions with the carbonyl groups of PCL, weakening the intermolecular interactions between the individual polymer chains and increasing the free volume [10]. As a result, the chains experience greater mobility thereby reducing the viscosity of the polymer matrix [11-12]. This phenomenon is analogous to heating the polymer and therefore enables processing to occur at lower temperatures.

There are numerous publications on the thermal and physical effects experienced by polymers, and in particular PCL, on the addition of scCO<sub>2</sub> [9, 13-16]. However, there has been little research into what occurs at a molecular level. The reptation model, formulated by de Gennes [17] and developed further by Doi and Edwards [18], enables the chain dynamics of highly entangled polymers to be probed thereby providing an insight into its viscous flow and dynamic properties. This model focuses on the topological constraints on individual polymer chains, bestowed by the surrounding bulk polymer, which effectively constricts the chain to an imaginary tube. As a result, movements can only occur laterally with a “snake-like” motion. The reptation time is given by the time it takes for the polymer chain to diffuse through one length of the imaginary tube. Development of this theory enables the reptation time to be determined as the reciprocal angular frequency at the point where the storage and loss moduli intersect during oscillation experiments [18-22]. In addition, repetition of these studies at various temperatures or stresses leads to calculation of the respective shift factors, allowing predictions to be made at further time decades [23]-[24].

To the authors knowledge no reptation studies have been conducted on polymers in the presence of scCO<sub>2</sub>. Therefore, the aim of the current study is to understand the effect of high pressure and supercritical CO<sub>2</sub> on the reptation time of a PCL grade with a molecular weight above the critical entanglement molecular weight. Rheological experiments are performed over a range of temperatures (80 to 120 °C) and CO<sub>2</sub> pressures (atmospheric to 100 bar), below the CO<sub>2</sub> saturation limit within PCL [8], using a high pressure parallel plate rheometer. From these results the reptation times at each condition are analysed and compared. In addition a time-temperature superposition is applied to the rheological data at each pressure enabling the activation energy to flow to be calculated using the Arrhenius equation and the effects of pressure to be further probed.

### **1.1 Materials**

Polycaprolactone (CAPA 6800) (M<sub>w</sub> 120 kDa; PDI 1.74 as specified by the manufacturer) was supplied in pellet form by Perstorp UK Ltd. (Warrington, UK). CO<sub>2</sub> (purity 99.9 %v/v) was obtained from BOC (Manchester, UK) and used as received.

### **1.2 Production of PCL plaques**

Plaques (150 x 150 x 1 mm) of PCL were produced by compression moulding using a Moore E1127 hydraulic hot press (George E. Moore & Sons Ltd, Birmingham, UK) which was preheated to 200 °C. Briefly, the polymer pellets (30 g) were placed into a mould (150 x 150 x 1 mm) which was then inserted into the press. The mould was allowed to warm for 5 minutes before applying a load of 10 kN for a further 5 minutes. The plaques were removed from the press and allowed to cool to room temperature. During cooling recrystallisation occurred, restoring the original crystallinity of the pellets (~60 %). Discs, with a radius of 10 mm, were then cut from the plaques for use in the rheometer.

### **1.3 Reptation analysis**

Rheological analyses were performed using a Physica MCR301 rheometer (Anton Paar, Hertford, UK) with a high pressure parallel plate geometry of 20 mm in diameter and with a 1 mm gap (PP20/pr). In a typical experiment, a polymer disc was added to the lower plate of the preheated rheometer, to fill the 1 mm gap between the plates. The rheometer was then sealed and CO<sub>2</sub> charged into the vessel, using an ISCO high pressure syringe pump Model 2400 (Teledyne ISCO, Lincoln, NE, USA) to generate the desired pressure. The disc was allowed to soak for 5 minutes, prior to analysis, to allow the CO<sub>2</sub> to diffuse into the polymer. Oscillation tests were performed in which the angular frequency was varied on a log scale over 14 data points from 0.2 to 100 rad.s<sup>-1</sup>. At each angular frequency the torque was allowed to stabilise, without any time constraints, prior to recording any data. Typically, each analysis took 14 minutes.

Initial viscosity analyses showed that the Newtonian region of PCL occurred between a shear rate of 0.02 and 0.32 s<sup>-1</sup> (data not shown). A series of strain sweeps were therefore performed over a range of angular frequencies to determine the strain required to obtain a shear rate within the Newtonian region. In light of this analysis, the strain was also adjusted from 100 to 0.2 % throughout the experiment to maintain a shear rate within the viscoelastic region. The storage ( $G'$ ) and loss ( $G''$ ) moduli were determined for a range of temperatures (80 to 120 °C) above the melting point of PCL and CO<sub>2</sub> pressures (atmospheric to 100 bar). Three analyses were performed for each condition to give data confidence and the average  $G'$  and  $G''$  values were then plotted against angular frequency ( $\omega$ ). The error bars on the plots represent  $\pm 1$  standard deviation from the mean.

### **1.4 Statistical Analysis**

Statistical analyses were performed on either the angular frequencies at the intersection of the storage and loss moduli or the calculated reptation times, using Microsoft Excel. Analyses were

calculated using ANOVA and the Least Significant Difference (LSD) at the 5 % confidence level. Any differences in the results were considered significant if the p-value was less than 0.05.

## 2. Results and Discussion

### 2.1 Effect of temperature on the atmospheric rheological properties of PCL

Frequency sweeps were performed on PCL at atmospheric pressure over a range of temperatures (80-120 °C) above the melting point (~60 °C). Oscillation analyses were repeated three times for each condition and the average storage ( $G'$ ) and loss ( $G''$ ) moduli plotted against the angular frequency ( $\omega$ ) (Figure 1). The error bars in the figure are given by  $\pm 1$  standard deviation from the mean.

Each of the conditions analysed generated typical responses of linear polymers with narrow polydispersity indexes (PDI) as governed by the Maxwell model (Figure 1) [25]. This model gives rise to two equations for the storage and loss moduli:

$$G'(\omega) = (G_p \omega^2 \tau^2) / (1 + \omega^2 \tau^2) \quad (1)$$

$$G''(\omega) = (G_p \omega \tau) / (1 + \omega^2 \tau^2) \quad (2)$$

where  $G_p$  is the plateau modulus,  $\omega$  is the angular frequency and  $\tau$  is the reptation time of the polymer.

The Maxwell model states that at low angular frequencies  $G'$  is proportional to  $\omega^2$  and  $G''$  is proportional to  $\omega$  for linear polymers with low PDIs [26]. A plateau in  $G'$  is also observed at high frequencies as the material becomes inflexible and rigid under rapid motion.

The results of the frequency sweeps at a range of temperatures (Figure 1) clearly show a horizontal shift along the angular frequency axis as the temperature of the polymer is increased. This shift is created by a decrease in both  $G'$  and  $G''$  at a given frequency for low angular

frequencies. As these values make up the real and imaginary parts of the dynamic shear modulus ( $G^*$ ), respectively [27], this property needs to be evaluated in order to determine the cause of the horizontal shift. In an oscillation analysis a constant shear strain is applied to the polymer at a set angular frequency. The resultant shear stress required to produce this strain is then recorded and  $G^*$  is calculated as:

$$G^* = \text{Shear stress} / \text{shear strain} \quad (3)$$

Above the melting point of a crystalline polymer short range motions of the polymer segments occur rapidly however, long range translation motion is restricted by entanglements between neighbouring chains. On increasing the temperature of the polymer, thermal expansion occurs which increases the free volume of the polymer and as a result enables more translational movement [28]. In addition, more energy is supplied to the polymer chains, increasing their mobility. These two factors reduce the force and therefore stress required to shear the material and consequently the dynamic shear modulus is also reduced. This phenomena gives rise to the reduction in both the storage and loss moduli and therefore the apparent horizontal shift in the traces (Figure 1). Horizontal shifts observed on increasing the experimental temperature are well characterised and leads to calculation of the activation energy to flow via a time-temperature superposition as discussed later [29].

The Maxwell equations (Equations 1 and 2) can also be used to calculate the reptation time of a polymer. Equating these two equations at the point where the storage and loss moduli curves intersect leads to the following expression for the reptation time:

$$\tau = 1 / \omega_{(G'=G'')} \quad (4)$$

where  $\tau$  is the reptation time of the polymer and  $\omega_{(G'=G'')}$  is the angular frequency at the point where  $G'$  and  $G''$  intersect.

Calculation of the reptation time at each of the conditions shows an almost 50 % reduction on heating from 80 to 100 °C and a 30 % reduction on heating the material by a further 20 °C. This reduction occurs for two reasons. At temperatures just above the melting point of the polymer, the individual chains remain tightly packed together restricting the tube diameter through which the polymer chain will reptate. In addition, the energy of the chain will be relatively low, slowing its movement. Due to the thermal expansion of materials, heating the polymer causes the free volume between the polymer chains to increase thereby expanding the tube diameter and facilitating reptation. In addition, the rise in temperature will supply the polymer chain with more energy, increasing its mobility. These two factors aid reptation and therefore the reptation time of the polymer is reduced on heating.

The temperature dependence on the rheological properties of polymers is often assessed using a time-temperature superposition in which each of the curves are shifted along the horizontal axis to a reference temperature [23]. In this case, a reference of 100 °C was chosen as this temperature is most commonly used by other researchers when performing rheological studies on PCL [30-31]. The shift factors required to transpose each curve were then calculated as the ratio between the two angular frequencies:

$$\text{Shift factor}(a_T) = \omega_{\text{Experimental}} / \omega_{\text{Reference}} \quad (5)$$

where:  $\omega_{\text{Experimental}}$  is the angular frequency at the experimental temperature; and  $\omega_{\text{Reference}}$  is the angular frequency at the reference temperature.

As the isotherms have identical shapes the time-temperature superposition was found to be successful with similar shift factors obtained for each of the viscoelastic properties. On plotting the temperature dependence of the shift factors, Arrhenius behaviour was observed for this data set (data not shown). Use of the Arrhenius equation (Equation 6) then enabled an



activation energy to flow of  $31.3 \text{ kJ mol}^{-1}$  to be obtained for PCL. This value is consistent with results published previously in which activation energies of between  $32$  and  $41 \text{ kJ mol}^{-1}$  were obtained, using the same method, for a range of different molecular weight PCL grades at atmospheric pressure [30-32].

$$\ln a_T = (E_a/R)[(1/T)-(1/T_0)] \quad (6)$$

where:  $E_A$  is the activation energy to flow;  $R$  is the universal gas constant ( $8.314 \text{ J mol}^{-1} \text{ K}^{-1}$ );  $T_0$  is the reference temperature (K); and  $T$  is the experimental temperature (K).

## **2.2 Effect of CO<sub>2</sub> pressure on the rheological properties of PCL**

Similar frequency sweeps were performed at 80, 100 and 120 °C over a range of pressures in order to evaluate the effect of CO<sub>2</sub> pressure on the reptation time of PCL. Three analyses were again performed for each condition, to generate confidence in the data, and the average  $G'$  and  $G''$  values are plotted against angular frequency (Figure 2). The error bars in the figure are given by  $\pm 1$  standard deviation from the mean.

Responses typical of linear polymers were again generated at each condition as was to be expected (Figure 2). Comparison of the curves generated at atmospheric pressure and in the presence of 60 bar CO<sub>2</sub> show a distinct shift towards higher angular frequencies on the addition of the CO<sub>2</sub>. This shift is similar to that seen on increasing the temperature (Figure 1) and indicates a decrease in the dynamic shear modulus of the polymer created by a reduction in the torque required to produce a given strain (Equation 2). It is well understood that raising the pressure imparted on a polymer increases the dynamic shear modulus as the free volume between the chains becomes compressed thereby restricting the movement of the polymer

chains [28]. However, in this situation, the opposite occurs showing it to be an effect of the CO<sub>2</sub> addition alone rather than a pressure effect.

The ability of CO<sub>2</sub> to diffuse into the amorphous regions of PCL, whereupon it undergoes Lewis acid/base interactions with the carbonyl groups in the polymer chain, is well characterised [8, 10]. This weakens the intermolecular interactions between the individual polymer chains, increasing the free volume of the polymer and also the mobility of the chains. As a result of these factors, less force is required to cause the polymer to flow and therefore the dynamic shear modulus is reduced, along with the storage and loss moduli, leading to the horizontal shift in the traces.

Although a horizontal shift in the traces is observed on the addition of 60 bar CO<sub>2</sub>, there is little movement as the pressure is increased further. We have previously shown that as the CO<sub>2</sub> pressure is elevated the concentration dissolved within PCL also increases [8]. This excess should expand the free volume further leading to large reductions in the dynamic shear modulus, however this is not observed here. As mentioned above, the addition of pressure generated by non-soluble gases causes compression of the polymer matrix and therefore a reduction in the free volume, leading to increased shear moduli. As the CO<sub>2</sub> pressure is increased above 60 bar it is therefore likely that the two effects compete against each other with the CO<sub>2</sub> absorption mildly dominating, leading to only a subtle horizontal shift.

Calculation of the reptation time at each pressure (Table 2) shows a significant decrease upon the addition of CO<sub>2</sub>. This reduction is analogous to heating the polymer from 80 to 100 °C (Table 1) and suggests that the addition of 60 bar CO<sub>2</sub> can reduce the processing temperature of PCL by 20 °C leading to a more economical process and reducing the likelihood of any bioactives degrading. As mentioned in the previous section, CO<sub>2</sub> is able to penetrate into the amorphous regions of polymers where it expands the free volume and increases the mobility of the polymer chains. Both of these processes contribute to the reduction in reptation time as enlarging the

free volume of the polymer reduces the tortuous nature of the reptation path, whilst enhancing the mobility of the chains, allowing their faster transient motion through the bulk polymer.

Despite the large reduction in the reptation time observed on the addition of CO<sub>2</sub>, raising the pressure further had little effect (Table 2). As discussed above, previous CO<sub>2</sub> absorption experiments on PCL have shown that a greater concentration of CO<sub>2</sub> becomes dissolved in the polymer on raising the pressure [8]. This increase in CO<sub>2</sub> absorption will enhance the effects discussed, leading to a greater free volume and chain mobility and therefore a reduced reptation time. However, the increase will also raise the pressure surrounding the polymer, forcing the chains closer together again [33]. This hinders the expansion of the free volume, diminishing the effect of the absorbed CO<sub>2</sub> on the reptation time.

A large reduction in the reptation time on the addition of CO<sub>2</sub> coupled with a negligible effect as the pressure was increased further was also experienced at both 100 and 120 °C (Figure 3). It can be seen however, that the effect of the CO<sub>2</sub> addition diminishes as the experimental temperature is increased with only a 29 % reduction observed at 120 °C compared to a 49 % reduction at 80 °C. The results from the previous two sections have illustrated how both temperature and CO<sub>2</sub> pressure can enhance the free volume of the polymer, reducing the tortuous nature of the reptation pathway, whilst also increasing the mobility of the polymer chains. We have also discussed how both of these factors contribute to the observed reductions in the reptation times. It therefore follows that at high temperatures, as the polymer has already undergone thermal expansion and the chains possess a greater mobility, the effects generated by the addition of CO<sub>2</sub> become less dominant.

As the frequency sweeps were performed over a temperature range for each of the pressures a time-temperature superposition, to a reference temperature of 100 °C, was applied to the data sets. Each of the isotherms could be superimposed onto the reference trace and similar shift factors were obtained for each rheological parameter (Equation 4) (data not shown). The

temperature dependence of the shift factors displayed Arrhenius behaviour and therefore the activation energy to flow at each pressure could be calculated from the Arrhenius equation (Equation 5).

The activation energy to flow of PCL at atmospheric pressure was calculated previously as  $31.3 \text{ kJ mol}^{-1}$ , however, on the addition of 60 to 100 bar  $\text{CO}_2$ , the energy required was considerably reduced to between  $20.7$  and  $22.2 \text{ kJ mol}^{-1}$ , respectively (Table 3). This reduction is created by the increased free volume and chain mobility afforded by the polymer on the absorption of  $\text{CO}_2$  which reduces the energy required for the polymer chains to move and therefore the polymer to flow.

### **3. Conclusions**

The rheological properties of PCL over a range of temperatures (80 to 120 °C) and  $\text{CO}_2$  pressures (atmospheric to 100 bar) have been evaluated. On increasing the temperature there is an obvious shift along the horizontal axis to higher angular frequencies leading to a significant reduction in the reptation time of PCL. The time-temperature superposition of these plots, in line with the Arrhenius equation, led to the calculation of an activation energy of flow of  $31.3 \text{ kJ mol}^{-1}$ , which is consistent with those values reported in the literature. Upon the addition of 60 to 100 bar  $\text{CO}_2$  a reduction in the reptation time of PCL was again observed, however varying the pressure had little effect. The activation energy to flow also reduced by approximately  $10 \text{ kJ mol}^{-1}$  on the addition of  $\text{CO}_2$  but again pressure displayed little effect.

### **Acknowledgements**

The authors are grateful for the funding received from the European Union; FP7, project number 232145. K. M. Shakesheff also thanks the European Research Council for his Advanced Grant.

## Figures

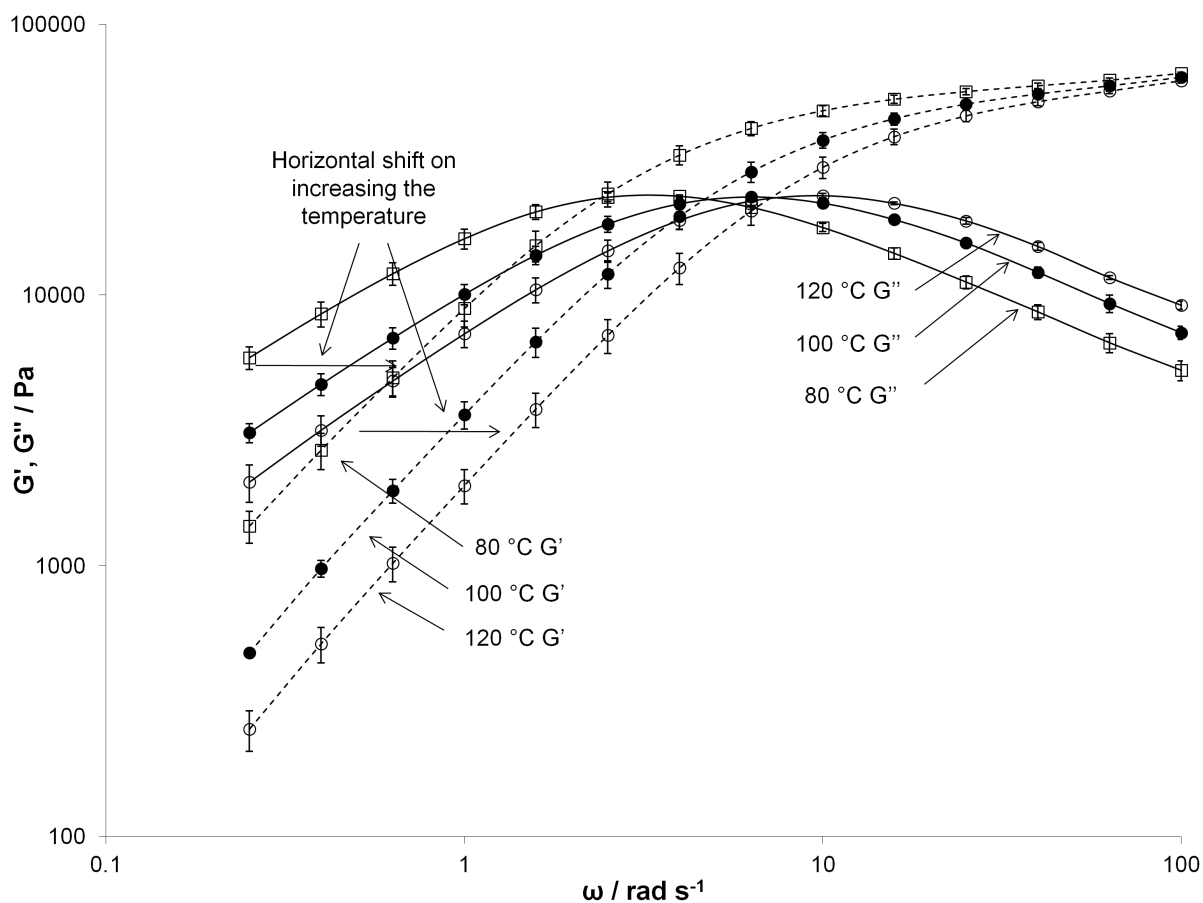


Figure 1: Plots of the storage modulus ( $G'$ ) and loss modulus ( $G''$ ) against angular frequency for PCL at atmospheric pressure over a range of temperatures. The results show a clear horizontal shift to higher angular frequencies as the temperature is raised, indicating a reduction in the reptation time.  $p < 0.0001$ , 5 % LSD =  $0.94 \text{ rad s}^{-1}$ .

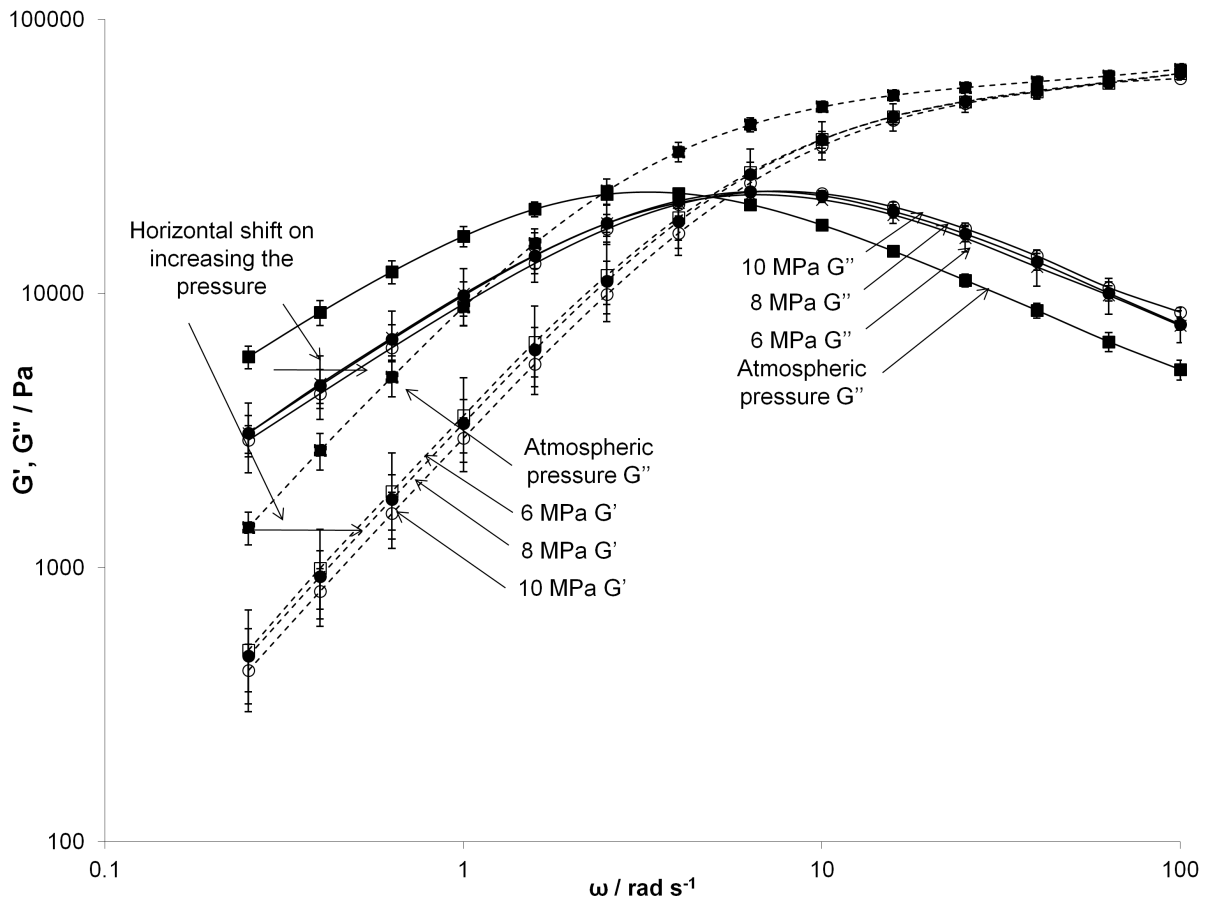


Figure 2: Plots of the storage modulus ( $G'$ ) and loss modulus ( $G''$ ) against angular frequency for PCL at 80 °C over a range of CO<sub>2</sub> pressures. The results show a clear horizontal shift to higher angular frequencies on raising the pressure indicating a reduction in the reptation time.  $p = 0.0044$ , 5 % LSD = 1.50  $\text{rad s}^{-1}$ .

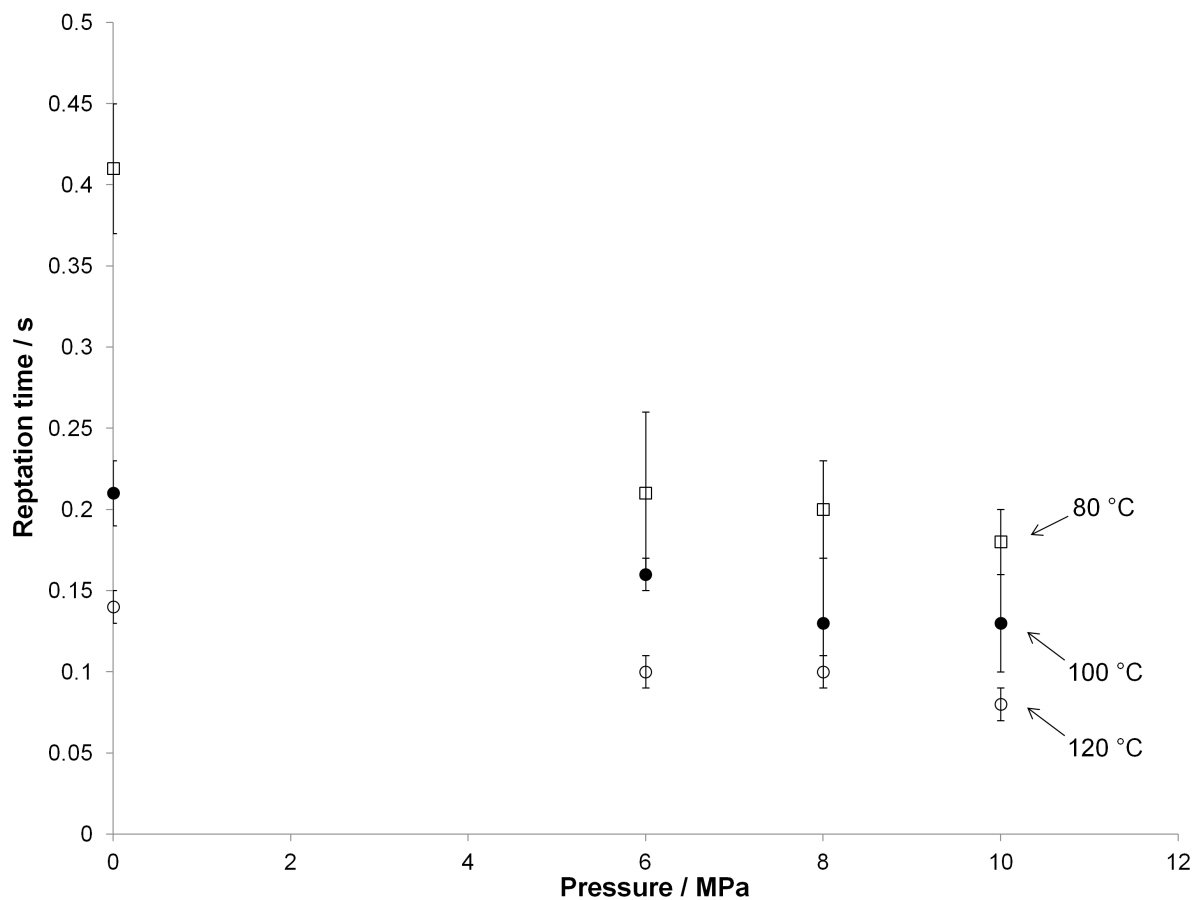


Figure 3: Change in reptation time on varying the pressure at a range of temperatures. As the experimental temperature is increased the effect of the addition of CO<sub>2</sub> becomes less significant. 80 °C  $p < 0.0001$  5 % LSD = 0.07 s; 100 °C  $p = 0.0499$  5 % LSD = 0.0499 s; and 120 °C  $p = 0.001$  5 % LSD = 0.0218 s.

## Tables

Table 1: The reptation times of PCL over a range of temperatures. Raising the temperature of the polymer significantly reduces the reptation time.

Temperature (°C)	G' G'' crossover frequency (rad s <sup>-1</sup> )	Reptation time (s)
80	2.4	0.41 ± 0.05
100	4.6	0.21 ± 0.03
120	7.2	0.14 ± 0.01

Significant difference between conditions  $p < 0.0001$ , 5 % LSD = 0.94 rad s<sup>-1</sup>

Table 2: Calculation of the reptation time of PCL at 80 °C over a range of pressures. The addition of scCO<sub>2</sub> significantly reduces the reptation time and a general trend of decreasing reptation time with increased pressure is observed.

Conditions		G' G'' crossover frequency (rad s <sup>-1</sup> )	Reptation time (s)
Temperature (°C)	Applied CO <sub>2</sub> Pressure (bar)		
80	-	2.44	0.41 ± 0.05
80	60	5.03	0.21 ± 0.06
80	80	5.17	0.20 ± 0.03
80	100	5.95	0.18 ± 0.03

Significant difference between conditions  $p = 0.0044$ , 5 % LSD = 1.50 rad s<sup>-1</sup>



Table 3: Activation energy to flow of PCL over a range of pressures. The addition of CO<sub>2</sub> reduces the activation energy to flow.

Applied CO <sub>2</sub> Pressure (bar)	Activation energy to flow (kJ mol <sup>-1</sup> )	R <sup>2</sup> value of Arrhenius plot
Atmospheric	31.3	0.9899
60	20.7	0.9587
80	20.7	0.9896
100	22.2	0.9692

## References

- [1] Hutmacher DW. Scaffolds in tissue engineering bone and cartilage. *Biomaterials*. 2000;21(24):2529-2543.
- [2] Ginty PJ, Barry JJA, White LJ, Howdle SM, Shakesheff KM. Controlling protein release from scaffolds using polymer blends and composites. *European Journal of Pharmaceutics and Biopharmaceutics*. 2008;68(1):82-89.
- [3] Waknis V, Jonnalagadda S. Novel poly-DL-lactide-polycaprolactone copolymer based flexible drug delivery system for sustained release of ciprofloxacin. *Drug Delivery*. 2011;18(4):236-245.
- [4] Kapoor B, Bhattacharya M. Transient shear and extensional properties of biodegradable polycaprolactone. *Polymer Engineering and Science*. 1999;39(4):676-687.
- [5] Costantino HR, Carrasquillo KG, Cordero RA, Mumenthaler M, Hsu CC, Griebenow K. Effect of excipients on the stability and structure of lyophilized recombinant human growth hormone. *Journal of Pharmaceutical Sciences*. 1998;87(11):1412-1420.
- [6] Jordan F, Naylor A, Kelly CA, Howdle SM, Lewis A, Illum L. Sustained release hGH microsphere formulation produced by a novel supercritical fluid technology: In vivo studies. *J Control Release*. 2010;141(2):153-160.
- [7] Kelly CA, Naylor A, Illum L, Shakesheff KM, Howdle SM. Supercritical CO<sub>2</sub>: A Clean and Low Temperature Approach to Blending PDLLA and PEG. *Advanced Functional Materials*. 2012;22(8):1684-1691.
- [8] Leeke GA, Cai JG, Jenkins M. Solubility of supercritical carbon dioxide in polycaprolactone (CAPA 6800) at 313 and 333 K. *Journal of Chemical and Engineering Data*. 2006;51(5):1877-1879.
- [9] Kelly CA, Harrison KL, Leeke GA, Jenkins MJ. Detection of melting point depression and crystallization of polycaprolactone (PCL) in scCO<sub>2</sub> by infrared spectroscopy. *Polym J*. 2012.

- [10] Kazarian SG, Vincent MF, Bright FV, Liotta CL, Eckert CA. Specific intermolecular interaction of carbon dioxide with polymers. *Journal of the American Chemical Society*. 1996;118(7):1729-1736.
- [11] Tai H, Upton CE, White LJ, Pini R, Storti G, Mazzotti M, et al. Studies on the interactions of CO<sub>2</sub> with biodegradable poly(DL-lactic acid) and poly(lactic acid-co-glycolic acid) copolymers using high pressure ATR-IR and high pressure rheology. *Polymer*. 2010;51(6):1425-1431.
- [12] Kelly CA, Jenkins MJ, Howdle SM, M. SK, Leeke GA. Viscosity studies of Poly(DL-lactic acid) in supercritical CO<sub>2</sub>. *Journal of Polymer Science Part B: Polymer Physics* 2012; In press.
- [13] Shieh YT, Su JH, Manivannan G, Lee PHC, Sawan SP, Spall WD. Interaction of supercritical carbon dioxide with polymers .2. Amorphous polymers. *J Appl Polym Sci*. 1996;59(4):707-717.
- [14] Shieh YT, Su JH, Manivannan G, Lee PHC, Sawan SP, Spall WD. Interaction of supercritical carbon dioxide with polymers .1. Crystalline polymers. *J Appl Polym Sci*. 1996;59(4):695-705.
- [15] Lian ZY, Epstein SA, Blenk CW, Shine AD. Carbon dioxide-induced melting point depression of biodegradable semicrystalline polymers. *J Supercrit Fluids*. 2006;39(1):107-117.
- [16] Liao X, Wang J, Li G, He JS. Effect of supercritical carbon dioxide on the crystallization and melting behavior of linear bisphenol A polycarbonate. *Journal of Polymer Science Part B- Polymer Physics*. 2004;42(2):280-285.
- [17] de Gennes PG. *Scaling Concepts in Polymer Physics*. Ithaca, New York: Cornell University Press; 1979.
- [18] Doi M, Edwards S. *The Theory of Polymer Dynamics*. New York: Oxford University Press; 1986.
- [19] Elder J. *PMMA Clay Nanocomposites*. Durham: Durham University; 2009.
- [20] Martins JA, Zhang W, Brito AM. Saturation of shear-induced isothermal crystallization of polymers at the steady state and the entanglement-disentanglement transition. *Macromolecules*. 2006;39(22):7626-7634.
- [21] Rahalkar RR. Correlation between the crossover modulus and the molecular-weight distribution using the Doi-Edwards theory of reptation and the Rouse theory *Rheologica Acta*. 1989;28(2):166-175.
- [22] Likhtman AE, McLeish TCB. Quantitative theory for linear dynamics of linear entangled polymers. *Macromolecules*. 2002;35(16):6332-6343.
- [23] Ferry JD. *Viscoelastic Properties of Polymers*. 3rd Edition ed. New York: Wiley; 1980.
- [24] Brostow W. Reliability and prediction of long term performance of polymer-based materials. *Pure and Applied Chemistry*. 2009;81:417.
- [25] Mezger TG. *The Rheology Handbook - For Users of Rotational and Oscillatory Rheometers*. Second ed. Hannover: Vincentz Network; 2006.
- [26] Vega JF, Rastogi S, Peters GWM, Meijer HEH. Rheology and reptation of linear polymers. Ultrahigh molecular weight chain dynamics in the melt. *J Rheol*. 2004;48(3):663-678.
- [27] Barnes HA, Hutton JF, Walters K. *An Introduction to Rheology*. Oxford: Elsevier Ltd.; 1989.
- [28] Osswald T, Hernandez-Ortiz JP. *Polymer Processing: Modelling and Simulation*. Ohio, US: Hanser Gardner Publications Inc; 2006.
- [29] Dealy J, Plazek D. Time temperature superposition - A users guide. *Rheology Bulletin*. 2009;78(2):16-31.

- [30] Noroozi N, Thomson J, Noroozi N, Schafer L, Hatzikiriakos S. Viscoelastic behaviour and flow instabilities of biodegradable poly ( $\epsilon$ -caprolactone) polyesters. *Rheologica Acta*. 2011:1-14.
- [31] Ramkumar DHS, Bhattacharya M. Steady shear and dynamic properties of biodegradable polyesters. *Polymer Engineering and Science*. 1998;38(9):1426-1435.
- [32] Gimenez J, Cassagnau P, Michel A. Bulk polymerization of epsilon-caprolactone: Rheological predictive laws. *J Rheol*. 2000;44(3):527-547.
- [33] Nalawade SP, Nieborg VHJ, Picchioni F, Janssen L. Prediction of the viscosity reduction due to dissolved CO<sub>2</sub> of and an elementary approach in the supercritical CO<sub>2</sub> assisted continuous particle production of a polyester resin. *Powder Technology*. 2006;170(3):143-152.