JOURNAL OF MATERIALS SCIENCE: MATERIALS IN MEDICINE **14** (2003) 783–787

Rheological properties of poly(2-hydroxyethyl methacrylate) (pHEMA) as a function of water content and deformation frequency

J. R. MEAKIN*, D. W. L. HUKINS
Department of Bio-Medical Physics and Bio-Engineering, University of Aberdeen, UK
E-mail: j.meakin@biomed.abdn.ac.uk

R. M. ASPDEN
Department of Orthopaedic Surgery, University of Aberdeen, UK

C. T. IMRIE
Department of Chemistry, University of Aberdeen, UK

Poly(2-hydroxyethyl methacrylate) (pHEMA) hydrogels have been used, or suggested for use, in a wide range of biomedical applications. In many of these applications, the mechanical properties of the gel are important for its proper functioning. These properties are influenced by a number of factors, including water content. In this study the storage and loss shear moduli were measured as a function of frequency for gels with water contents ranging from 22% to 48% at a temperature of 37 °C. At low frequencies and high water contents, deformation frequency had little effect. However, at higher frequencies and lower water contents, both moduli increased markedly with increasing frequency. This can be explained by the gels approaching a glass transition. The curves describing the behavior of each gel were combined to form a master curve, using a method analogous to the time–temperature superposition principle. This master curve can be used to predict the shear moduli for gels with a wide range of water contents and loading frequencies. For example, for a gel with a water content of 47.8% (as a percentage of the mass of gel), the curve provides shear moduli values over a frequency range of 10^{-2}–10^{4} Hz.

Introduction

Hydrogels, polymers that absorb water, are potentially useful for a wide range of applications, including the field of biomedical implants [1]. Poly(2-hydroxyethyl methacrylate) (pHEMA) hydrogels, in particular, have been used or proposed for use in contact lenses [2], corneal replacement [3], as a synthetic dural prosthesis [4], as an artificial skin for wound dressing [5], as an artificial articulating surface for joint prostheses or osteochondral defect repair grafts [6], as a cement to stabilize implants [7], as an intervertebral disc prosthesis [8], and as a drug delivery system [9].

For many of these applications, the mechanical properties of the gels are important. They can be directly important, such as in replacement tissues which are load-bearing, or indirectly important, such as when the mechanical properties are related to the transport properties of the gel (e.g. in drug delivery applications). The mechanical properties, however, are likely to be influenced by a number of factors, in particular the frequency of deformation, the temperature, and the water content [10]. Other factors include the cross-link density [11], the molar mass [12], and any additional constituents such as other polymers [12] or fibers [5]. In this study uncrossed-linked pHEMA was used in order not to introduce an additional variable into the experimental design.

Hydrogels are viscoelastic, meaning that the stress resulting from an applied strain is a function of time, and hence deformation frequency. This viscoelasticity has important implications [13, 14], which are described in this paragraph. If a viscoelastic material is subjected to an oscillating strain, the resulting stress will lag behind it. Two moduli can be used to describe the properties of the material: the storage modulus (also called the elastic or real modulus) which is in phase with the applied strain and is measured at the point of the highest strain, and the loss modulus (also called the viscous or imaginary modulus) which is 90° out of phase with the applied strain and is measured at the point of the highest strain rate. The typical behavior of a polymer as a function of frequency is shown in Fig. 1.

In the rubbery region (at the lower frequency range) and in the glassy region (at the higher frequency range)

---

*Author to whom all correspondence should be addressed.

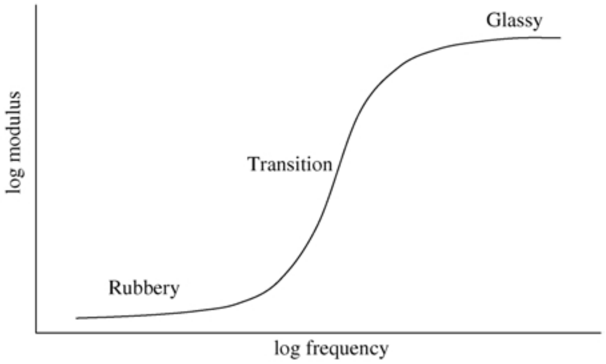

Figure 1 Schematic diagram showing how the material properties of a polymer change with frequency of deformation.

the modulus of the material changes little with frequency. In the transition region, however, a small change in frequency can give rise to a dramatic change in modulus. Likewise, temperature affects the storage and loss moduli of polymers. Increasing the temperature, for example, has the effect of shifting the curve shown in Fig. 1, to the right. For a linear viscoelastic material the amount of shift is related to the temperature by an equation known as the WLF (Williams, Landel, Ferry) equation [15]. This principle, known as time–temperature superposition (or time–temperature correspondence) is useful as it allows data recorded at different frequencies and temperatures to be reduced to a more manageable form. It can also extend the frequency range that can be investigated experimentally. This is done by performing experiments in a limited frequency range at different temperatures, and then fitting the separate curves together to form a master curve.

For hydrogels, the third influencing factor on mechanical properties is the quantity of water present in the gel [10]. Water acts as a plasticizer and has a similar effect to temperature, with increasing water content acting analogously to increasing temperature. For other polymers diluted with plasticizers, it has been shown that time and concentration are interrelated in a similar way to time and temperature and that concentration-dependent shift factors can be determined [15].

The effects of loading frequency and water content have implications for the behavior of medical implants made from pHEMA. During normal daily activities such as walking or travelling in a motor vehicle, the body is subjected to vibrations with frequencies ranging over several decades (mainly in the range of about 0.1–100 Hz) [16]. The use of power tools can also subject the body to vibrations that have components of frequency up to a few kilo hertz [16]; high frequency components are also associated with the sudden application of load. In addition, implants are likely to experience a change in water content due to sustained loading or physiological factors.

For pHEMA hydrogels, a previous study has investigated the effect of water content and temperature on the frequency-dependent properties [17], but only in the range from 2% to 28% water. For applications as a biological implant it is likely that higher water contents will be more relevant but that the effects of temperature are less important. Therefore, in this study, we investigated uncrosslinked pHEMA gels with water contents ranging from 22% to 48%, at a fixed temperature of 37 °C. Both the shear storage and loss moduli were measured as a function of frequency and water content, and the results combined to construct a master curve for the behavior of pHEMA.

Methods

Materials

Uncrosslinked pHEMA with an average molecular weight of 300,000 was obtained from Aldrich (Aldrich Chemical Company Ltd., Milwaukee, WI, USA) and used without further purification or modification. Gels were prepared by soaking 0.3 g of the polymer in deionized water for at least a week. The fully hydrated gel samples were then placed under a 5 kg mass for about 2 h to form flat discs of about 25 mm diameter and 0.5 mm thickness. These discs were then stored in deionized water.

To obtain gels with lower water contents, the hydrated discs of gel were dried in air until they had reached a pre-calculated mass. They were then placed in a double layer of heat sealed plastic wrap for about 48 h to help ensure that the water was evenly distributed throughout the sample. Experimental studies on the sorption behavior of pHEMA suggest that this length of time would be sufficient for equilibrium to occur [18].

Testing

The hydrogels were tested in shear using a stress rheometer (SR5, Rheometric Scientific Ltd, Leatherhead, Surrey, UK) shown schematically in Fig. 2. The lower fixture consisted of a Peltier plate that allowed the temperature of the sample to be controlled. The upper part consisted of a 25 mm diameter plate which applied the shear stress to the samples. The samples were mounted onto the Peltier plate at a temperature of 20 °C. The upper plate was then lowered until it registered a resistance of 10 N. Any excess gel surrounding the perimeter of the upper plate was then trimmed away using a scalpel blade. A humidity cover, lined with pads of paper dampened with water, was placed around the sample to help reduce evaporation of water from its exposed edges. Once the set-up was completed, the temperature was raised to 37 °C. To allow the whole gel sample to reach thermal equilibrium at

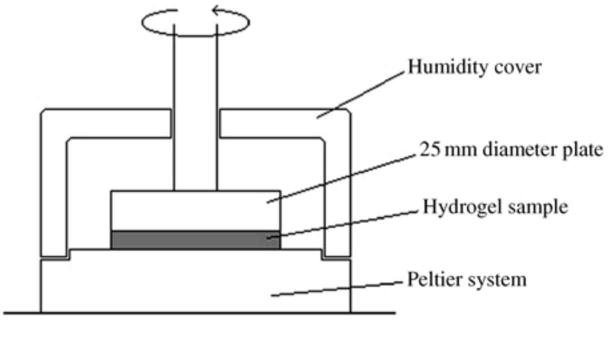

Figure 2 Schematic diagram of the rheometer showing the sample placed on the Peltier plate, for temperature regulation, and the upper plate which is lowered onto the sample and through which a torsional strain is applied.

37 °C, a time of 30 s was allowed to elapse before starting the tests.

Two sets of tests were performed. The first set investigated the dynamic stress–strain behavior of the gels. This was to see if the gels behaved linearly and to determine a suitable strain to use in the subsequent set of tests. A total of five gels, with a range of water contents, were tested. A sinusoidal oscillating shear strain was applied to the gels at a frequency of 1 Hz. The amplitude of this strain was increased from 0.1% to 2%, and the amplitude of the resulting oscillating stress was recorded.

The second set of tests investigated the frequency-dependent viscoelastic shear properties of the gels as a function of water content. Six gels, again with a range of water contents, were tested. This time the strain was fixed and the frequency was increased from 0.08 to 80 Hz for five of the gels and between 0.008 and 0.8 Hz for the remaining gel. The shear storage modulus (G') and loss modulus (G'') were recorded at each frequency together with tan δ, which is the ratio of the moduli (G''/G').

Immediately after testing, the water content of the hydrogel samples was determined. Each sample was wrapped in a pre-weighed piece of Aluminum foil and its wet mass determined. It was then dried in an oven at 105 °C for at least 48 h. It has previously been shown, using a thermogravimetric analyzer linked to a mass spectrometer, that this temperature does not cause the polymer to decompose [19]. The dry mass was then measured, and the water content calculated as a percentage of the wet gel mass.

Results

Stress–strain behavior

The dynamic stress–strain curves for the five gels tested are given in Fig. 3, together with the water contents of these gels. It can be seen that all five gels appeared to exhibit linear behavior in the strain range used, with the exception of the gel with a water content of 43.9% which tailed off at 1.12% strain. Linear regression analysis, with the intercept fixed to be zero, gave the correlation coefficients given in Table I.

For the gel with 43.9% water, no data could be obtained above a strain of 1.12%. On removing this sample from the rheometer, it was observed that a fine film of water had formed between the gel and the Peltier plate. This presumably caused some slippage between the sample and Peltier plate which prevented a stress from being registered. This may also explain the non-linearity in the stress–strain curve at this strain. From the results of these tests, it was decided to use a strain of 1% for the subsequent tests to investigate the frequency dependence.

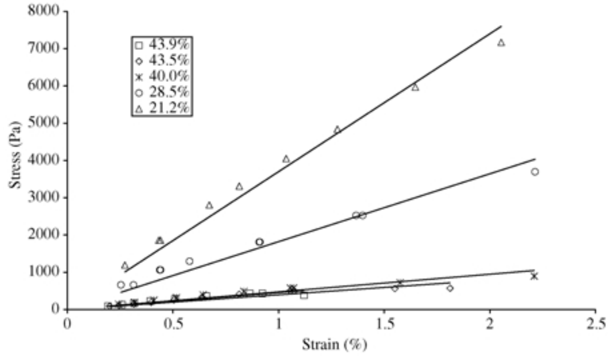

Figure 3 Stress–strain behavior of pHEMA hydrogels tested in shear at 1 Hz. Linear regression lines with a zero intercept are also plotted.

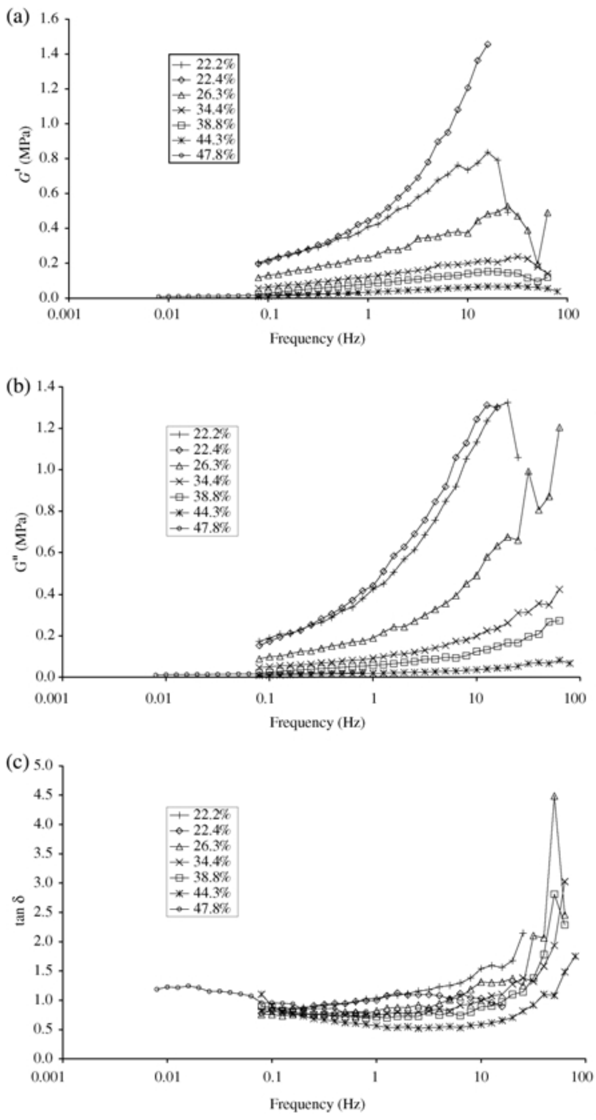

Figure 4 Behavior as a function of frequency of pHEMA hydrogels with a range of water contents: (a) shear storage modulus (G'); (b) shear loss modulus (G''); (c) tan δ.

Frequency behavior

Fig. 4(a)–(c) show the shear storage modulus (G'), loss modulus (G'') and tan δ (G''/G') as a function of frequency for each gel tested. It can be seen that the gels with the higher water content had a low modulus which varied little over the range of frequencies used. The

TABLE I Linear correlation coefficients for the regression analysis on the data given in Fig. 3

Water content of gel (%)	Correlation coefficient
21.2	0.99
28.5	0.98
40.0	0.94
43.5	0.91
43.9	0.90

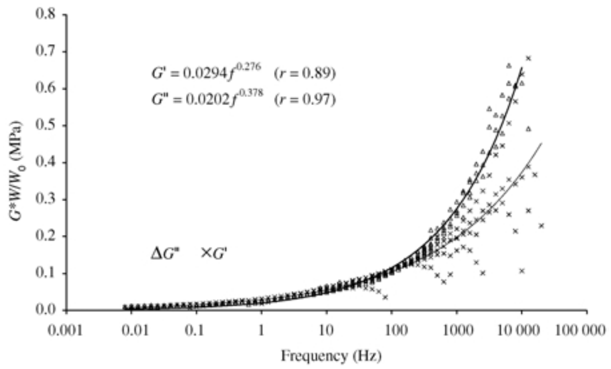

Figure 5 Master curve for the storage and loss modulus of a pHEMA hydrogel with a water content of 47.8% (note that the modulus values have been scaled with reference to this water content, see text for more details). The equations fitted to these curves are shown together with the correlation coefficients (r values) describing how well the data fits these equations.

lowest water content gels showed more variation, rising steeply with increasing frequency. The tailing off in some of the curves at the highest frequencies may be due to some loss of water at the edges of the sample.

As described in the introduction, the plasticising effect of water was hypothesized to have a similar form to that of raising temperature on the behavior of pHEMA. The curves shown in Fig. 4 were therefore combined to produce a master curve for both G' and G''. To do this, the gel with the highest water content (47.8%) was first chosen as the reference gel. The modulus values of each curve were then scaled by a factor W/W_0, where W was the water content of the gel for that curve and W_0 was the water content of the reference gel (in this case 47.8%); in this paper all water contents are expressed as a percentage of the mass of the gel. Modulus values were scaled in this way to take into account the effects of different water contents on the free volume of the pHEMA [15].

Fig. 5 shows master curves for G' and G'' together with the equations which were fitted to the data using IDL software (IDL 5.3, Research Systems Inc., Boulder, CO., USA). To create the master curve for G', each curve in Fig. 4(a) (apart from the reference curve for the 47.8% gel) was shifted along the logarithmic frequency axis until it formed a smooth continuation of one of the other curves. As a result, there was considerable overlap between some curves, i.e. results from different samples at different frequencies contained equivalent information. The master curve for G'' was created in the same way, using results from Fig. 4(b). The shift used for each curve is referred to as the shift factor ($\log a_w$) and is plotted in Fig. 6, as a function of the gel water content. A linear equation was fitted to both sets of shift factors; this is also shown in Fig. 6. A linear equation was used to provide a simple comparison of the two sets of shift factors, and was found to give a reasonable fit ($r > 0.9$). In principle, the relationship between the shift factors and the water content may be non-linear because of the form of the WLF equation used for time–temperature superposition [15].

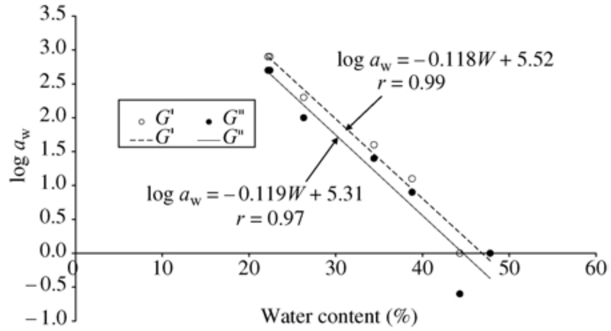

Figure 6 Shift factors ($\log a_w$) used to construct the master curves in Fig. 5 plotted against the corresponding water content showing similar behavior for both storage and loss moduli. Linear regression lines are shown for G' (dashed) and G'' (continuous).

Discussion

The results of this study have shown that for a frequency of 1 Hz, pHEMA gels with a water content between 21% and 44% are linearly viscoelastic up to a strain of about 2%. It has also been shown that the storage and loss moduli of pHEMA gels are a function of both water content and deformation frequency.

For gels of high water content, storage and loss moduli showed little dependence on frequency over the range tested (Fig. 4(a) and (b)). This result was consistent with the gels being in the rubbery region (Fig. 1). Indeed, the behavior of pHEMA gels with a high water content and deformed at a slow rate (analogous to a low frequency deformation) has previously been described using classical rubber elasticity theory [20] (where the shear modulus is determined solely by the intrinsic properties of the gel, and not by time or frequency of loading [21]).

For gels of lower water content, the moduli showed more variation over the frequencies used, rising sharply at the high frequency end for the driest gels. This was consistent with the gels approaching the transition region (Fig. 1). This result is consistent with thermal analysis of pHEMA having a glass transition at 37 °C when it has a water content of 12% [19]. However, this comparison is only semi-quantitative because thermal detection of glass transitions is performed at effectively a much lower frequency.

Using the same principles applied to time–temperature superposition, the individual curves were combined to construct a master curve for a gel with a water content of 47.8%. The shift factors, describing how this master curve moves along the logarithmic frequency axis for gels with different water contents, were found to be similar for both G' and G'' (the mean difference in the shift factors was 0.2). For materials that are linearly viscoelastic, the shift factors should be the same for all the material properties [13]. Hence, the similarity in the shift factors for G' and G'' is consistent with the linear behavior shown in the first part of this study.

The construction of a master curve allowed more of the frequency-dependent behavior of pHEMA to be investigated than would have otherwise been possible. In this study, the frequency range that was tested experimentally was 0.008–80 Hz. The upper limit of 80 Hz was imposed by the maximum frequency that the rheometer could apply, the lower limit by the drying out of gel samples for tests that took a long time to perform.

The master curve in Fig. 5, however, spans over six decades of frequency.

Once constructed the master curve can also be used, together with the shift factors, to predict the behavior of a pHEMA gel with a water content other than 47.8%. This is done by first finding the shift factor for that gel and calculating a ''look up'' frequency, *F*, using Equation 1.

$$\log(F) = \log(f) + \log a_{W_1} \qquad (1)$$

where W_1 is the water content of the gel and f is the frequency of interest.

The look up frequency is then used on the master curve to find a value for the modulus, which is scaled by the relative water content as shown in Equation 2.

$$G(W_1,f) = \frac{W_0}{W_1} G(W_0,F) \qquad (2)$$

As an example, consider a gel with a water content of 30% for which the storage modulus is required at a frequency of 5 Hz. The shift factor for this gel is 1.98 (from the linear equation given in Fig. 6), giving a look up frequency of 477 Hz. From the equation given in Fig. 5, this gives a storage modulus of 0.16 MPa, which, once scaled for water content, gives a prediction that this gel would have a shear storage modulus of 0.26 MPa. Comparing this with the data shown in Fig. 4(a) demonstrates that this prediction is about right.

The predictive properties of the master curve and shift factors are particularly useful in the design of a pHEMA implant which has a mechanical function, such as an intervertebral disc prosthesis, and which is subjected to a range of different frequencies in everyday life (such as occur in walking, during sitting in a moving vehicle or using a power tool) [16]. Throughout the course of a day, the loads on the implant are likely to squeeze some of the water out of the gel. The effect of this drying will be, as shown in this study, to shift its viscoelastic behavior along the frequency axis. Therefore, a gel which was soft and rubbery when implanted, will become stiffer and may even exhibit glassy behavior during higher frequency activities. This may then have the effect of damaging surrounding tissues as the load distribution changes suddenly. Knowing the frequency and water content dependent mechanical properties of pHEMA is therefore an important consideration.

Conclusions

The conclusions from this study are that:

- at a frequency of 1 Hz, pHEMA gels with a water content between 21% and 44% are linearly viscoelastic up to a strain of about 2%,
- the storage and loss moduli of pHEMA gels are a function of both water content and deformation frequency,
- the influence of water on the frequency-dependent behavior of pHEMA can be expressed using shift factors which depend on water content.

Acknowledgments

We thank the Engineering and Physical Sciences Research Council (UK) for funding this research (grant number GR/M42732/01) and the Medical Research Council for a Senior Fellowship for RMA.

References

1. P. H. CORKHILL, C. J. HAMILTON and B. J. TIGHE, *Biomaterials* **10** (1989) 3.
2. T. T. MCMAHON and K. ZADNIK, *Cornea* **19** (2000) 730.
3. G. J. CRAWFORD, T. V. CHIRILA, S. VIJAYASEKARAN, P. D. DALTON and J. J. CONSTABLE, *J. Refract. Surg.* **12** (1996) 525.
4. S. BHATIA, P. R. BERGETHON, S. BLEASE, T. KAMPER, A. ROSIELLO, G. P. ZIMBARDI, C. FRANZBLAU and E. L. SPATZ, *J. Neurosurg.* **83** (1995) 897.
5. C. D. YOUNG, J. R. WU and T. L. TSOU, *Biomaterials* **19** (1998) 1745.
6. V. P. BAVARESCO, C. A. DE CARVALHO ZAVAGLIA, M. DE CARVALHO REIS and S. M. MALMONGE, *Artif. Organs* **24** (2000) 202.
7. P. A. NETTI, J. C. SHELTON, P. A. REVELL, C. PIRIE, S. SMITH, L. AMBROSIO, L. NICOLAIS and W. BONFIELD, *Biomaterials* **14** (1993) 1098.
8. L. AMBROSIO, P. A. NETTI, S. IANNACE, S. J. HUANG and L. NICOLAIS, *J. Mat. Sci. Mater. Med.* **7** (1996) 251.
9. L. FERREIRA, M. M. VIDAL and M. H. GIL, *Int. J. Pharmaceutics* **194** (2000) 169.
10. J. VINCENT, in ''Structural Biomaterials'', revised edn. (Princeton University Press, Princeton, 1990) p. 25.
11. J. V. CAUISH-RODRIGUEZ, W. DEB and R. SMITH, *J. Mat. Sci. Mater. Med.* **7** (1996) 349.
12. D. I. PERERA and R. A. SHANKS, *Polymer Int.* **36** (1995) 303.
13. A. V. TOBOLSKY, in ''Properties and Structure of Polymers'' (Wiley, New York, 1960) p. 136.
14. J. J. AKLONIS and W. J. MACKNIGHT, in ''Introduction to Polymer Viscoelasticity'' (Wiley, New York, 1983) p. 36.
15. J. D. FERRY, in ''Viscoelastic Properties of Polymers'', 2nd edn. (Wiley, New York, 1970) p. 518.
16. M. J. GRIFFIN, in ''Handbook of Human Vibration'' (Academic Press, London, 1990) p. 553.
17. S. R. LUSTIG, J. M. CARUTHERS and N. A. PEPPAS, *Polymer* **32** (1991) 3340.
18. Y. M. SUN and H. L. LEE, *ibid.* **37** (1996) 3915.
19. J. R. MEAKIN, C. T. IMRIE, D. W. L. HUKINS and R. M. ASPDEN, *J. Mater. Sci. Med.* **14** (2003) 9.
20. C. MIGLIARESI, L. NICODEMO, L. NICLOAIS and P. PASSERINI, *J. Biomed. Mater Res.* **15** (1981) 307.
21. L. R. G. TRELOAR, in ''The Physics of Rubber Elasticity'', 3rd edition (Clarendon Press, Oxford, 1975) p. 64.

Received 11 March
and accepted 23 December 2002