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Muonium formation and magnetic relaxation in dextran and iron–dextran

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ABSTRACT: Zero- and longitudinal field muon spin relaxation was used to study muonium formation in dextran and an iron–dextran complex. The temperature dependence of the reduced hyperfine coupling constant, A', was determined for both samples. In addition, superparamagnetic relaxation processes associated with the iron–dextran cores were characterized. The resulting zero-field muon spin relaxation is found to be stretched exponential in form, indicating a broad distribution of correlation times for the internal magnetic fields, whilst the temperature dependence of the muon relaxation rate provides evidence that the superparamagnetic relaxation follows a thermally activated Arrhenius behaviour with a characteristic activation energy $E_a/k = 84$ K.

KEYWORDS: muon spin relaxation; iron–dextran complex; superparamagnetism

INTRODUCTION

Iron is essential for all forms of life, and is stored by both plants and animals in the form of ferritin. These naturally occurring ferritins consist of a spherical iron-mineral core of a ferrihydrite-like composition ~8 nm in diameter surrounded by a protein shell approximately 2 nm thick.[1] Iron–dextrans, complexes of iron(III) hydroxide and dextran, are pharmaceutically important as synthetic substitutes for ferritin and are used in the treatment of iron deficiency anaemias. Dextran is a polymer, $(C_6H_{10}O_5)_n$, of anhydroglucose having mainly α-D-(1 → 6) linkages with some unusual 1,3-glucosidic linkages at branching points, whilst the complexes are composed of an iron-based core ~6 nm in diameter surrounded by a dextran coat 2–15 nm thick.[2] Mössbauer spectroscopic and d.c. magnetization measurements on a freeze-dried iron–dextran complex over the temperature range 5–300 K have shown that the magnetic properties of iron–dextran and ferritin are remarkably similar.[3] The coercivity is 0.33 and 0.35 T for ferritin and iron–dextran, respectively, at 5 K, whilst the high- and low-temperature Mössbauer spectra from the two materials are comparable.[3] However, substantial differences are observed in the temperature dependence of the Mössbauer spectra: although both samples behave superparamagnetically the onset of superparamagnetic blocking in iron–dextran occurs at 120 K with a mean superparamagnetic blocking temperature $\langle T_B \rangle \approx 60$ K, whereas in ferritin the onset is at ~60 K with $\langle T_B \rangle \approx 35$ K.[3,4] Analysis of the powder x-ray diffraction pattern obtained at 300 K from a sample of freeze-dried iron–dextran complex has shown that the cores are crystalline and similar in structure to akaganéite (β-FeOOH) with a monoclinic crystal cell (space group $I2/m$) with dimensions $a = 10.594(4)$ Å, $b = 3.019(1)$ Å, $c = 10.299(3)$ Å and $\beta = 88.98(5)$ Å.[5] Both the Mössbauer spectroscopic results and the x-ray diffraction data indicate that there are two non-equivalent Fe^{3+} sites in this structure, each of which is surrounded by a distorted octahedron of oxygen atoms.

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Zero-field muon spin relaxation

μSR is an acronym for muon spin rotation, relaxation and resonance. This powerful and widely used technique is discussed in detail elsewhere.[6,7] Only a brief description of muon spin relaxation is included here.

When spin polarized muons are implanted in a sample, the local magnetic environment dictates the subsequent precession of the muon spins. The muons decay with a time constant of ~2.2 μs, emitting a positron preferentially in the direction of the muon spin according to the expression $W_0 = 1 + a_0 \cos\theta$, where θ is the angle between the muon spin and the direction of positron emission. In muon spin relaxation, detectors are positioned in front of and behind the sample, along the beam direction. Relaxation spectra $a(t)$ are determined from the forward $F(t)$ and backward $B(t)$ time-dependent positron count rates in these detectors using the expression

$$a(t) = \frac{F(t) - \alpha B(t)}{F(t) + \alpha B(t)} \quad (1)$$

where α is a calibration term to account for the relative efficiencies of the counters in the forward and backward detectors; α is determined for each sample from room temperature spectra measured in a small transverse magnetic field of 2 mT.

Muon repolarization

When positive muons, μ^+, are deposited in a chemical sample, at least three possible events can occur:

(i) μ^+ sits in the sample and decays with its characteristic lifetime of 2.2 μs;
(ii) μ^+ combines with an electron to form a muonium atom, Mu, a radioactive light isotope of hydrogen;
(iii) Mu reacts with the substrate to form a muonium-substituted radical, or resides in a diamagnetic environment.

Muons in state (i) should retain their full spin polarization. If Mu is formed, as in case (ii), 50% of the polarization is initially lost, although this polarization is restored by the application of a magnetic field in a direction longitudinal to the spin polarization, as the muon and electron spins become decoupled by the applied magnetic field. In case (iii) more than 50% of the initial polarisation is lost on molecular formation.

For comparison with protium species, it is useful to cite muon–electron hyperfine coupling constants, A_μ, in a reduced form, $A'_\mu = A_\mu(\mu_p/\mu_\mu) = 0.3141A_\mu$, where μ_p is the magnetic moment of a proton and μ_μ is the muon magnetic moment. Preliminary experiments on the deposition of positive muons in ferritin and the iron-depleted protein apoferritin have shown evidence for a muonium-substituted species common to both proteins.[8] In apoferritin an estimate for the reduced isotropic muon–electron hyperfine coupling constant, A', at 270 K is 168 ± 39 MHz. In ferritin A' is 164 ± 37 MHz at 280 K. In this paper, we present the results of an investigation of the behaviour of μ^+ deposited in samples of dextran and iron–dextran over the temperature range 15–250 K using zero-field muon spin relaxation and applied field repolarization techniques.

EXPERIMENTAL

Our experiments were performed on a freeze-dried iron(III) hydroxide–dextran complex from Sigma-Aldrich. Muon spin relaxation measurements were conducted on the EMU spectrometer at the ISIS Pulsed Muon Facility, Rutherford Appleton Laboratory, UK.[9] Approximately 2 g of sample were placed in a silver sample holder and mounted on the cold stage of a closed-cycle refrigerator. Spectra were collected over a time range of 0.1–16 μs in an applied longitudinal magnetic field between 0 to 400 mT for a selection of temperatures between 14 and 270 K. Relaxation spectra $a(t)$ were determined for each sample using Eqn (1).

RESULTS AND DISCUSSION

Zero-field measurements

Dextran. Figure 1(a) shows an example of the muon spin relaxation spectra obtained in zero field for dextran.

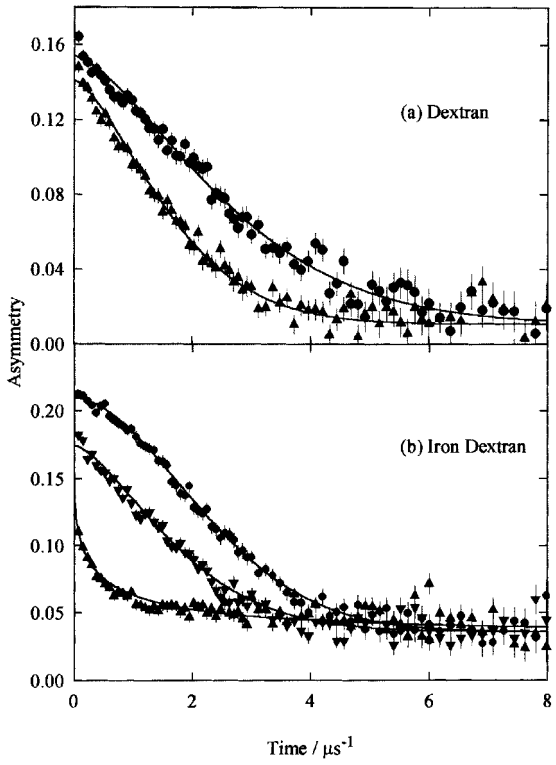

Figure 1. Zero-field muon spin relaxation spectra for (a) dextran at (▲) 14 and (●) 270 K and (b) iron–dextran at (▲) 14, (▼) 120 and (●) 215 K. The solid lines are fits to the data as described in the text.

These zero-field data were fitted at all temperatures over the range 0.1–10 μs using a phenomenological stretched exponential relaxation function:[10,11]

$$G_z(t) = a_0 \exp(-\lambda t)^\beta + BG \qquad (2)$$

where a_0 is the initial asymmetry at time $t = 0$, λ is the relaxation rate in μs^{-1} and BG is a temperature-independent background term arising from muons stopped in the silver mask. In zero field the muon relaxation rate λ is related to the second moment of the magnetic field distribution width $\langle B^2 \rangle$ and the characteristic correlation time, τ_c, of the internal fields at the muon site by the relation

$$\lambda = \gamma_\mu^2 \langle B^2 \rangle \tau_c \qquad (3)$$

The initial fits of the dextran data to Eqn (2) were carried out with a_0, λ, β and BG as temperature-dependent variables. However, these fits suggested that β and BG are constants with values of 1.5 and 0.0105, respectively, and therefore the data were refitted with these parameters fixed at these values. Examples of the final fits are shown as solid lines in Fig. 1(a).

The temperature dependence of the initial asymmetry and the relaxation rate obtained from these fits is shown in Fig. 2. It is clear from this figure that the parameters are relatively independent of temperature. The initial asymmetry a_0 drops from a value of 0.1434(9) at 270 K to 0.1304(9) at 14 K, while the relaxation rate, λ, increases smoothly from 0.3319(6) to 0.5286(6) μs^{-1} over the same temperature range.

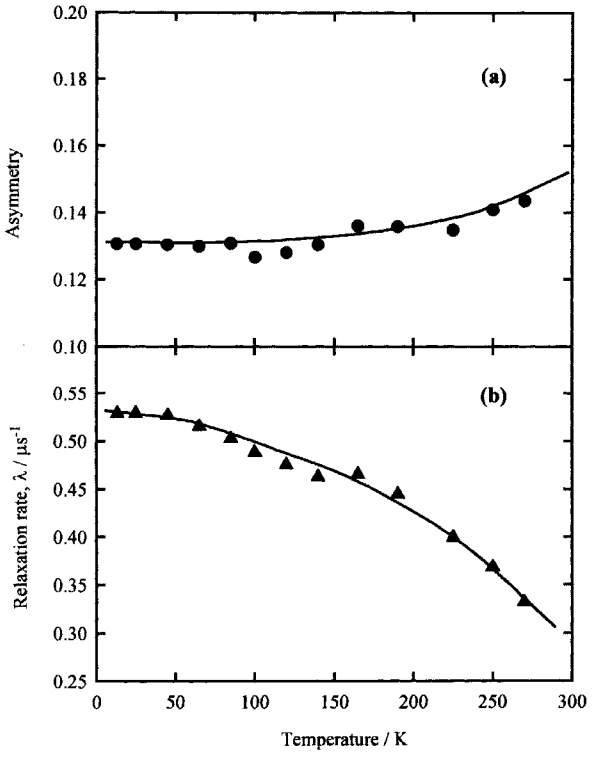

Figure 2. Temperature dependence of a_0 and λ obtained from fitting Eqn (2) to the dextran data as described in the text. The solid lines are guides to the eye.

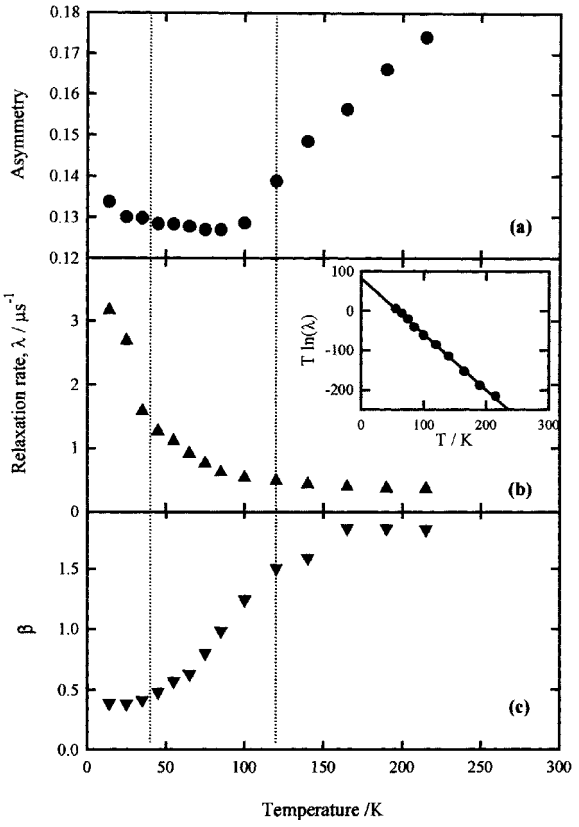

Figure 3. Temperature dependence of a_0, λ and β obtained from fitting Eqn (2) to the iron–dextran data as described in the text. The dotted lines indicate the onset of superparamagnetic blocking and the temperature at which the iron cores are fully blocked as determined from the Mössbauer spectroscopic data.

Iron–dextran. Figure 1(b) shows examples of the muon relaxation spectra obtained from iron–dextran in zero field over the temperature range 14–215 K. Again the phenomenological model of Eqn (2) provided an excellent description of the data, as can be seen by the best-fit lines in the figure.

The parameters obtained from these fits are shown in Fig. 3. It can be seen in Fig. 3(a) that the initial asymmetry, a_0, decreases smoothly with decreasing temperature: as the temperature decreases from 215 to 100 K, a_0 falls from 0.1740(7) to 0.1280(1). Below 100 K, a_0 is approximately constant at 0.128. This pronounced reduction in a_0 may be due in part to the development of intense static magnetic fields and hence muon precessional rates beyond the experimental window at ISIS.

As shown in Fig. 3(b), the muon relaxation rate, λ, increases smoothly with decreasing temperature, indicating a pronounced increase in the correlation time, τ_c, associated with the local fields. Interestingly, this temperature dependence is extremely well represented by Arrhenius behaviour, indicative of thermally activated relaxation processes, at least down to 50 K at which magnetization measurements suggest the onset of hysteresis.[3] From the modified Arrhenius plot[10] of $T\ln(\lambda)$ against T shown in the inset in Fig. 3(b), it is possible to assign [from the intercept on the $T\ln(\lambda)$ axis] an effective activation temperature, $T_a = E_a/k$, of 84 K. This value is significantly lower than that of 318 K found for ferritin.[4]

The temperature dependence of the exponent β, depicted in Fig. 3(c), is also of some interest. Stretched exponential relaxation is normally associated with concentrated spin glass systems[11] in which β rises from 1/3 at the glass temperature, T_g, reaching unity at $\sim 4T_g$, and has been attributed to a broad distribution of magnetic relaxation rates. In the case of iron–dextran, β takes a value close to 1/3 at 50 K, that is, at the onset of magnetic hysteresis, rising to 1.8 at the highest temperatures.

Within the general framework of this spin glass-like model, we can therefore assume that the muons localize close to the superparamagnetic moment associated with the iron–dextran cores, thereby sensing an apparently concentrated magnetic system in which there is a broad distribution of thermally activated magnetic relaxation rates. The onset of hysteretic behaviour appears to be analogous to an effective spin glass freezing at which the superparamagnetic moments become static on the timescale of the muons' response.

The fact that β rises above unity at high temperatures is not inconsistent with this model. It simply implies that the Gaussian-distributed ($\beta = 2$) magnetic fields arising from the nuclear moments provide an increasingly significant relaxation mechanism at higher temperatures where those fields associated with the superparamagnetic moments are increasingly motionally narrowed. Such behaviour has been observed in several other concentrated spin glass-like systems.[12]

These μSR results are fully consistent with those obtained from Mössbauer spectroscopy.[3] Our μSR measurements show distinct changes in a_0, λ and β close to

110 and 40 K, while Mössbauer spectroscopy indicates that the onset of superparamagnetic blocking occurs at 120 K and that all the iron cores are fully blocked below 40 K. A similar agreement is seen between the ZF-μSR and Mössbauer measurements on ferritin: Cristofolini *et al.*[13] observed changes in the μSR lineshape at 60 and 11 K, while Mössbauer spectroscopic measurements showed the onset of superparamagnetic blocking occurring at ~60 K, with all ferritin cores blocked below 10 K.[3] It is not unreasonable to suggest, therefore, that the changes observed in the μSR parameters are a direct result of the blocking or freezing of the superparamagnetic moments as the temperature is decreased.

Applied field measurements

Repolarization curves were obtained from the applied field spectra by fitting the first 0.1–1 μs of all the time-dependent relaxation spectra to a simple exponential function:

$$G_z(t) = a_0 \exp(-\lambda t) \quad (4)$$

where λ is the relaxation rate and a_0 is the initial asymmetry at time zero. Although this expression does not always describe the data well at long times (>5 μs), only the value of the asymmetry extrapolated to $t = 0$ is necessary to determine the repolarization curve. Table 1 collates values for a_0 determined from these fits for dextran and iron–dextran at selected temperatures in the range 14–250 K. Repolarization curves were constructed for all of the samples using the values of a_0 for silver noted in Table 1.

Figure 4 shows the variation of a_0 with applied longitudinal field and temperature over a range of values. It is immediately evident that unlike the dextran substrate, the initial asymmetry for positive muons stopped in iron–dextran displays a strong temperature dependence and that the field dependence at the higher fields studied is different than that for μ^+ in dextran.

To check the experimental set-up for the detection of muonium, a spectrum was collected at ambient temperature using a quartz plate. Figure 5 shows the repolarization of muonium in quartz in applied longitudinal fields, B, ranging from 10 to 400 mT. If all μ^+ which stop in the sample convert to muonium the resulting polarization P is simply

$$P = \frac{1}{2}\left(1 + \frac{x^2}{1+x^2}\right) \quad (5)$$

where x represents the reduced applied magnetic field B/B_{eff} and B_{eff} is the hyperfine field. If a component p

Table 1. Initial asymmetry a_0 for positive muons stopped in silver (Ag), dextran (Dex) and iron–dextran (Fedex) for some applied longitudinal fields B and a range of temperatures T[a]

	B (mT)									
	8	16	24	32	50	100	150	200	300	400
Ag, 290 K	0.2259	0.2257	0.2256	0.2255	0.2251	0.2228	0.2226	0.2218	0.2188	0.2146
Dex, 13 K	0.1619	0.1693	0.1781	0.1803	0.1858	0.1973	0.2061	0.2129	0.2204	0.2122
Dex, 165 K	0.1589	0.1699	0.1733	0.1792	0.1827	0.1928	0.2033	0.2078	0.2154	0.2160
Dex, 250 K	0.1567	0.1679	0.1677	0.1675	0.1823	0.1929	0.2006	0.2057	0.2139	0.2121
Fedex, 25 K	0.113	0.126	0.134	0.141	0.146	0.159	0.171	0.177	0.187	0.193
Fedex, 65 K	0.140	0.147	0.154	0.156	0.161	0.169	0.176	0.185	0.194	0.199
Fedex, 100 K	0.170			0.177	0.176	0.185	0.190	0.197	0.199	0.203
Fedex, 190 K	0.217			0.219	0.218	0.222	0.227	0.227	0.226	0.228

[a] The standard error for a_0 is ±0.002.

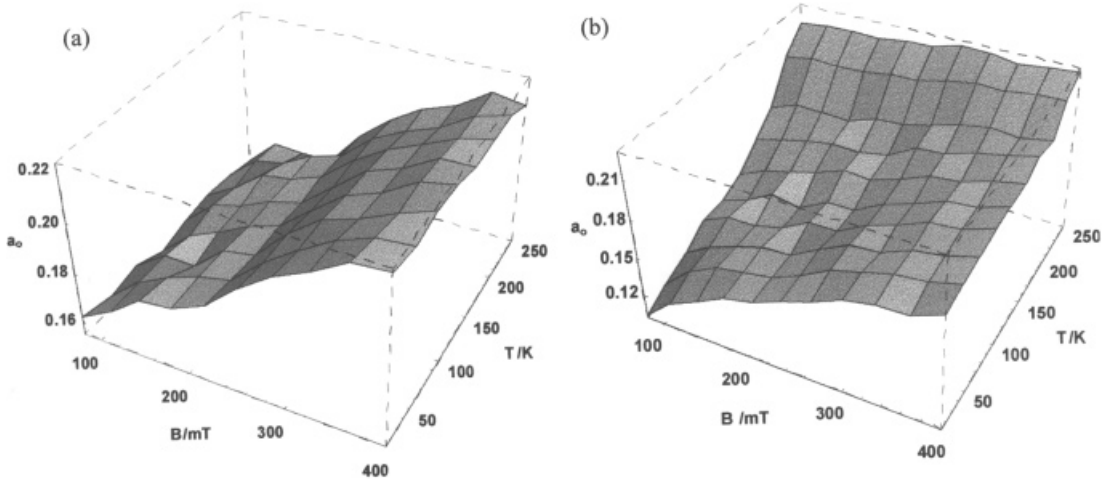

Figure 4. Variation of the initial asymmetry a_0 with applied longitudinal field, B (mT), and temperature, T (K), over the range of values observed for a_0: (a) for μ^+ stopped in dextran; (b) for μ^+ stopped in iron-loaded dextran. The standard error is ±0.002.

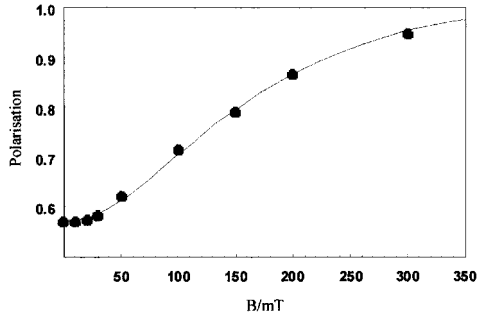

Figure 5. Repolarization curves for μ^+ stopped in quartz at room temperature.

of the stopped muons remains as μ^+ then we have

$$P = p + C\left(1 + \frac{x^2}{1+x^2}\right) \tag{6}$$

Using Eqn (6), a least-squares fit of the points in Fig. 5 was made, giving the full line shown. We can note from Eqn (6) that at zero applied field the polarization P is $p + C$ whereas at high fields P tends to $p + 2C$. The value of p which derives from stray muons in these quartz observations is 0.074 ± 0.010. C has a value of 0.496 ± 0.010 and the hyperfine field B_{eff} is 163.4 ± 0.057 mT. The field B_{eff} and A, the unreduced value of the hyperfine coupling constant, are related by $B_{\text{eff}} = A/(\gamma_\mu + \gamma_e)\hbar$. One finds then a reduced muon–electron isotropic hyperfine coupling constant A' of 1446 ± 50 MHz here for Mu in quartz. Transverse field muon spin rotation studies on muonium in quartz provide a more accurate value of 1416 ± 0.9 MHz for A'.[7] From these observations on quartz we conclude that the experimental arrangement is well aligned to study any muonium formation in dextran and iron-loaded dextran.

μ^+ in dextran. Figure 6 illustrates the repolarization curve measured at 190 K for muons stopped in dextran. Similar curves were obtained at all temperatures. The parameters p and C obtained by fitting the repolarization curves with Eqn (6) display little temperature dependence. This is evident from Fig. 7, where the variations with temperature of these parameters, together with the initial and total polarizations, are shown. Table 2 lists values of p and C determined at each temperature. At 45 K,

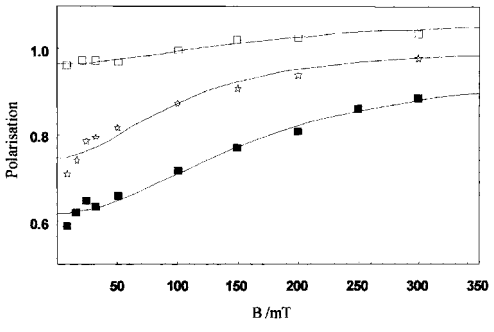

Figure 6. Repolarization curves for μ^+ stopped in dextran and iron-loaded dextran: (*) dextran at 190 K; (■) iron–dextran at 45 K; (□) iron–dextran at 190 K.

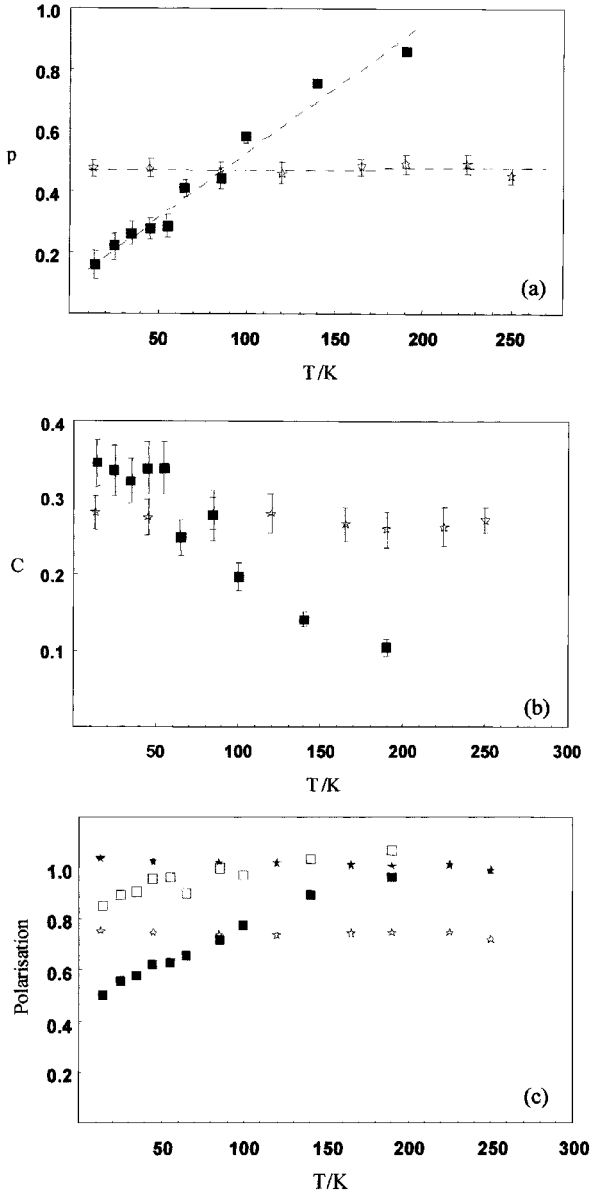

Figure 7. (a) Variation of the parameter p with temperature, (*) dextran, (■) iron dextran; (b) variation of the parameter C with temperature, (*) dextran, (■) iron dextran; and (c) variation of the initial polarization, $p + C$, (*) dextran, (■) iron–dextran, and final polarization, $p + C$, (*) dextran, (□) iron–dextran, with temperature.

for example, we see that p is 0.473 and C is 0.274, giving an initial polarization of $p + C = 0.747$ and a final polarization of $p + 2C = 1.021$.

Clearly, p is no longer representative of a few stray muons, as in the case of quartz, but indicates a significant component of muons residing at sites in the dextran, complemented by a certain amount of muonium formation. The value of the reduced hyperfine coupling constant, A', at 45 K is 895 ± 174 MHz. We see at once that the values for A' obtained here are only rough estimates for this quantity, but they are sufficiently accurate to show that the muonium hyperfine coupling constant is significantly lower than for muonium in quartz, and recalls the lower values observed, for example, for muonium in sulphur.[14] In that case it was concluded that Mu occupies a site on

Table 2. Optimum values for the parameters p and C, and for A' (MHz), the reduced hyperfine coupling constant, for dextran at various temperatures

	T(K)							
	13	45	85	120	165	190	225	250
p	0.473	0.473	0.462	0.457	0.480	0.490	0.486	0.450
C	0.280	0.274	0.278	0.279	0.265	0.258	0.261	0.270
A'	927	895	897	865	928	898	992	804

an intermolecular vector between two S_8 molecules in the unit cell.[15] It is possible that in dextran the muonium atom takes a similar position, between two molecules in the vicinity of the lone pair of electrons at an oxygen atom. We also see in Fig. 8 that there is only a slight variation with temperature of A' when muonium is formed in dextran.

μ^+ in iron–dextran. In Fig. 6 we contrast the repolarization curves obtained from the iron–dextran complex at 45 and 190 K with the repolarization obtained for dextran at 190 K. It is clear that the situation for the iron–dextran is more complicated than that for dextran itself. We have already seen (Fig. 4) that zero-field muon spin relaxation studies indicate a strong temperature dependence of the initial asymmetry, which may be partly attributed to a progressive blocking of superparamagnetic clusters which leads in turn to strong but random static fields at the muon site. In the following analysis we assume with reasonable confidence that the applied magnetic field has relatively little effect on the 'lost' initial asymmetry arising from these static fields.

The parameters p, C and A', obtained from analysis of the field and temperature dependence of the initial asymmetry of the iron dextran complex, using Eqn (6), are presented in Table 3. The pronounced temperature dependence of these parameters is evident. At 14 K the value for p is 0.157, rising to 0.862 at 190 K. Correspondingly, there is a large muonium component at 14 K with $C = 0.345$, decreasing to 0.102 at 190 K. At low temperatures A' has a value similar to that found for dextran, whilst the values of A' of 1451 ± 221 MHz at 45 K and 1390 ± 262 MHz at 190 K are close to the value expected for muonium in quartz.

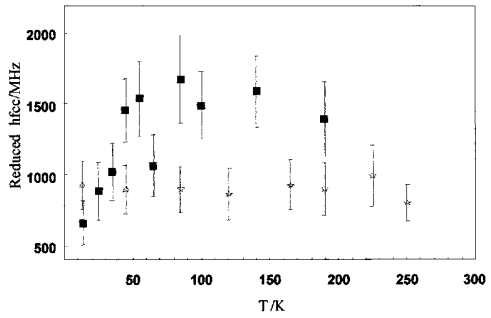

Figure 8. Variation of the reduced hyperfine coupling constant A' (MHz) with temperature T (K) for dextran (*) and iron–dextran (■).

The temperature dependences of the parameters p and C are shown in Fig. 7 together with the same parameters obtained from the repolarization of dextran. It can be seen that for iron–dextran p exhibits a slight inflection at 55 K, close to the superparamagnetic blocking temperature of 50 K determined by our muon spin relaxation measurements, whilst C rises to a plateau of approximately 0.33 at the same temperature. The significance of these results is not yet fully understood. To our knowledge, this is the first combined study of muon repolarization and relaxation in a magnetic system, and further systematic studies are necessary. However, the results do provide clear evidence of interplay between the field-dependent behaviour of muonium in iron–dextran and the magnetic relaxation associated with the superparamagnetic cores.

In comparison with similar studies of μ^+ in ferritin and apoferritin,[8] where at most temperatures about two-thirds of the muons stop in the protein shell and the remainder stop in the vicinity of the iron core, we find here different behaviour with the muon fraction in iron–dextran increasing almost linearly with temperature, at the expense of the muonium formation; however, in ferritin we also observed muonium radical formation which is precluded here by the saturated structure of the substrate.

CONCLUSIONS

Our muon spin relaxation and muon spin repolarization measurements have provided a useful insight into the nature of muonium in dextran and an iron–dextran complex, whilst also providing detailed information on thermally activated superparamagnetic relaxation associated

Table 3. Optimum values for the parameters p and C and for A' (MHz), the reduced hyperfine coupling constant, for iron–dextran at various temperatures

	T(K)									
	14	25	35	45	55	65	85	100	140	190
p	0.157	0.219	0.261	0.280	0.287	0.409	0.443	0.575	0.753	0.862
C	0.345	0.335	0.322	0.338	0.339	0.247	0.276	0.196	0.140	0.102
A'	661	888	1021	1451	1540	1065	1675	1487	1586	1390

with the iron–dextran cores. Indeed, in this respect we have shown that μSR can be entirely complementary to both magnetic and Mössbauer spectroscopic measurements in the study of magnetic phenomena in complex magnetic systems.

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