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Transverse water relaxation in whole blood and erythrocytes at 3T, 7T, 9.4T, 11.7T and 16.4T; Determination of intracellular hemoglobin and extracellular albumin relaxivities

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Abstract

Blood is a physiological substance with multiple water compartments, which contain water-binding proteins such as hemoglobin in erythrocytes and albumin in plasma. Knowing the water transverse (R_2) relaxation rates from these different blood compartments is a prerequisite for quantifying the blood oxygenation level-dependent (BOLD) effect. Here, we report the Carr-Purcell-Meiboom-Gill (CPMG) based transverse (R_{2CPMG}) relaxation rates of water in bovine blood samples circulated in a perfusion system at physiological temperature in order to mimic blood perfusion in humans. R_{2CPMG} values of blood plasma, lysed packed erythrocytes, lysed plasma/erythrocyte mixtures, and whole blood at 3 T, 7 T, 9.4 T, 11.7 T and 16.4 T were measured as a function of hematocrit or hemoglobin concentration, oxygenation, and CPMG inter-echo spacing (τ_{cp}). R_{2CPMG} in lysed cells showed a small τ_{cp} dependence, attributed to the water exchange rate between free and hemoglobin-bound water to be much faster than τ_{cp} . This was contrary to the tangential dependence in whole blood, where a much slower exchange between cells and blood plasma applies. Whole blood data were fitted as a function of τ_{cp} using a general tangential correlation time model applicable for exchange as well as diffusion contributions to R_{2CPMG} , and the intercept $R_{20blood}$ at infinitely short τ_{cp} was determined. The $R_{20blood}$ values at different hematocrit and the R_{2CPMG} values of lysed erythrocyte/plasma mixtures at different hemoglobin concentration were used to determine the relaxivity of hemoglobin inside the erythrocyte (r_{2Hb}) and albumin (r_{2Alb}) in plasma. The r_{2Hb} values obtained from lysed erythrocytes and whole blood were comparable at full oxygenation. However, while r_{2Hb} determined from lysed cells showed a linear dependence on oxygenation, this dependence became quadratic in whole blood. This possibly suggests an additional relaxation effect inside intact cells, perhaps due to hemoglobin proximity to the erythrocyte membrane. However, we cannot exclude that this is a consequence of the simple tangential model used to remove relaxation contributions from

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exchange and diffusion. The extensive data set presented should be useful for future theory development for the transverse relaxation of blood.

Keywords

lysed blood in vitro; transverse relaxation; relaxivity; hematocrit; oxygenation; hemoglobin concentration

INTRODUCTION

During BOLD functional MRI measurements, the transverse relaxation rate in tissue changes due to changes in the oxygenation fraction (Y) of blood in capillaries, venules, and veins [1–4]. In order to understand the spin echo and gradient echo BOLD effects it is therefore necessary to first know the effects of oxygenation changes on the transverse relaxation rate $R_2 = 1/T_2$ of blood water. In addition, the hematocrit fraction (Hct) differs between these blood vessels [5, 6] and may affect the relaxation rate. Blood is a complex system with multiple sources of water transverse relaxation, including the individual transverse relaxation rates of water spins in the intracellular (erythrocytes, R_{2ery}) and extracellular (plasma, $R_{2plasma}$) compartments. The water inside each compartment interchanges rapidly (very fast on the MR time scale) between free and bound water inside the hydration shell of protein molecules [7, 8], of which hemoglobin in the erythrocytes and albumin in plasma are the major components. The electronic structure of heme iron in hemoglobin changes with oxygenation fraction (Y), affecting not only R_{2ery} , but also causing a change in the bulk magnetic susceptibility (χ_{ery}) of the donut-shaped cell. Any difference in susceptibility (χ) with plasma creates a magnetic field difference, which causes additional relaxation effects [9–20]. A first possible contribution is due to water molecules continuously exchanging between the two compartments through the erythrocyte membrane, and attaining a different phase in each compartment. The lifetime of water inside the erythrocyte is on the order of 6.5 – 9.6 ms [21–23], and the exchange regime for exchange between compartments may be fast or slow depending on the frequency difference between the two compartments ($\omega = \gamma B_0 \chi$), which depends on the hemoglobin oxygenation state and the magnetic field strength. A second possible transverse relaxation contribution is that from translational diffusion through the generated magnetic field gradients that depend on the shape of the erythrocyte and the field strength [10, 14, 24, 25]. Both effects can be visualized by varying the inter-echo spacing (τ_{cp}) in a Carr-Purcell-Meiboom-Gill (CPMG) multi-echo experiment. The exchange and diffusion contributions increase with the square of magnetic field strength B_0 because the frequency difference between plasma and erythrocytes ($\omega = \gamma B_0 \chi$) determines the magnitude of the proton dephasing that causes transverse relaxation [11, 13, 14, 24–27]. While the transverse relaxation of fully oxygenated blood is determined by diamagnetic effects primarily related to cellular and plasma protein contents, there also is a small diamagnetic susceptibility difference that affects transverse relaxation as explained above.

It has been suggested that the presence of the erythrocyte membrane may cause an additional increase in blood relaxivity above diffusional and exchange effects [12, 28, 29]. The goal of

this study was to measure the intrinsic intracellular (lysed erythrocyte) and extracellular (plasma) contributions to R_{2CPMG} and to determine whether there are any additional relaxation contributions just from within these compartments when a membrane is present. To gain insight into the intrinsic relaxation properties of each blood compartment, we studied the individual R_{2CPMG} values of blood plasma, lysed packed erythrocytes, and lysed erythrocyte/plasma mixtures as a function of hemoglobin concentration, oxygenation fraction (Y) and inter-echo spacing τ_{cp} at 3 T, 7 T, 9.4 T, 11.7 T, and 16.4 T. Since the changes in R_{2ery} are caused mostly by hemoglobin, its property as an endogenous contrast agent affecting the relaxation rate of water protons was expressed in terms of the relaxivity r_{2Hb} . In order to study any additional effect of compartmentalization on the rates within the erythrocyte and the plasma, we also measured R_{2CPMG} of whole blood as a function of Hct and oxygenation fraction at these five magnetic field strengths. This was done as a function of inter-echo spacing τ_{cp} and the data fitted using a general correlation time model applicable for exchange as well as diffusion contributions to R_2 to determine the intercept $R_{20blood}$ at infinitely short τ_{cp} , where these relaxation mechanisms are expected to be nonexistent. This intercept was then used to determine the relaxivity of hemoglobin r_{2Hb} in the presence of a membrane and compared with the number from lysed erythrocytes to evaluate the effect of the membrane to intrinsic relaxation. The studies of lysed erythrocyte/plasma mixtures and whole blood as a function of hemoglobin concentration and Hct, respectively, also allowed determination of the relaxivity of albumin.

MATERIALS AND METHODS

Theory

In whole blood, water spins may move through the plasma or erythrocyte interior or through the membranes between them. So we will treat the system as a two-compartment system with water exchange between two protein solutions. One is the plasma with albumin (Alb, 50 g/L = 0.75 mM [19]), the other is the erythrocyte with hemoglobin (Hb, 332 g/L = 5.15 mM tetramer, ABL700 Series Reference Manual). Treating these as solutions in a buffered liquid with very fast exchange of water between solution and the hydration sphere of the protein, we can write:

$$R_{2ery} = R_{2buffer} + [Hb(5.15 mM)] \cdot r_{2Hb}(Y) + R_{2membrane} \quad (1)$$

$$R_{2plasma} = R_{2buffer} + [Alb(0.75mM)] \cdot r_{2Alb} \quad (2)$$

In which $r_{2HB}(Y)$ and r_{2Alb} are the millimolar relaxivities ($mM^{-1}s^{-1}$) of the proteins, of which the one for hemoglobin is oxygenation dependent. A membrane term is added to the erythrocyte to account for water exchanging with the membrane hydration sphere inside the erythrocyte. Water in plasma on the other hand can exchange with the membrane hydration sphere on the outside of the erythrocyte. Since the definition of the plasma water relaxation is without a membrane, as we measure this on a centrifuged sample with the cells removed, we need to account for this membrane term in the two-compartment system. For the plasma

water, the amount of membrane interacted with depends on the number of cells and thus scales with the Hct, while the amount of water in plasma reduces with Hct. This can be accounted for by a term $f_{plasma} \cdot Hct \cdot R_{2membrane}$. Therefore, for just two isolated compartments, i.e. without water exchange through the membrane and without relaxation due to field gradients around the membrane, the transverse relaxation rate of water in blood would be:

$$\begin{aligned} R_{20blood} &= f_{plasma} \cdot R_{2plasma} + f_{ery} \cdot R_{2ery} + f_{plasma} \cdot Hct \cdot R_{2membrane} \\ &= R_{2plasma} + Hct \cdot R_{2membrane} + f_{ery}(R_{2ery} - R_{2plasma} - Hct \cdot R_{2membrane}) \end{aligned} \quad (3)$$

As explained in previous papers [19, 30], since we are looking at water proton relaxation, the contributions of the relaxation terms for erythrocyte and plasma need to be proportional not to Hct and 1-Hct, respectively, but to the actual water fractions f_{ery} and f_{plasma} ($= 1 - f_{ery}$). These are determined by the water volume remaining after accounting for the presence of high concentrations of Hb and Alb, which occupy 30% and 5% of the erythrocyte and plasma volumes, respectively:

$$f_{ery} = \frac{0.7Hct}{0.7Hct + (1-Hct) \cdot 0.95} \quad \text{and} \quad f_{plasma} = \frac{0.95(1-Hct)}{0.7Hct + (1-Hct) \cdot 0.95} \quad (4)$$

Using Eqs. (1), (2) and (4), Eq. (3) can be rewritten as

$$\begin{aligned} R_{20blood} &= R_{2buffer} + [Alb(0.75mM)] \cdot r_{2Alb} + Hct \cdot R_{2membrane} \\ &+ f_{ery} \{ [Hb(5.15mM)] \cdot r_{2Hb}(Y) - [Alb(0.75mM)] \cdot r_{2Alb} + (1-Hct)R_{2membrane} \} \end{aligned} \quad (5)$$

If a mixture of erythrocytes and plasma would be prepared and subsequently lysed, the relaxation rate would not include the membrane hydration sphere contribution:

$$R_{20lysed} = R_{2buffer} + [Alb(0.75mM)] \cdot r_{2Alb} + f_{ery} \{ [Hb(5.15mM)] \cdot r_{2Hb}(Y) - [Alb(0.75mM)] \cdot r_{2Alb} \} \quad (6)$$

Thus experimental determination of $R_{20blood}$ and $R_{20lysed}$ will provide information about possible relaxation contributions from the membrane. In the above, any effect of white blood cells is neglected. When measuring $R_{20lysed}$ as a function of f_{ery} , the intercept and slope should allow us to determine $r_{2Hb}(Y)$ and r_{2Alb} , which can be confirmed by measurement of pure plasma and packed erythrocytes. The relaxation rate of PBS (phosphate buffered saline) can be used for $R_{2buffer}$.

While the determination of $R_{20lysed}$ is relatively straightforward, this is not the case for $R_{20blood}$. This is a result of additional relaxation mechanisms that contribute to transverse relaxation, including exchange through the membrane [10, 13, 14, 18, 31] and diffusion

through field gradients [20, 24, 32–34] around the membrane. These effects actually make the transverse relaxation time dependent on the echo time TE, for instance when using a single 180° pulse and increasing TE to measure such a rate. When using a Carr-Purcell-Meiboom-Gill multi-echo experiment, the signal decay is again exponential, but the rate R_{2CPMG} will depend on the inter-echo spacing τ_{cp} :

$$S(TE, \tau_{cp}) = S_0 e^{-R_{2,blood}^{CPMG}(\tau_{cp})TE} \quad (7)$$

S_0 is the equilibrium magnetization. Our interest is the baseline relaxation rate of blood water ($R_{20blood}$), which can be determined from the intercept at infinitely short τ_{cp} of the dependence of R_{2CPMG} on $1/\tau_{cp}$. The question is which model to use for this fit. Fortunately, the exchange and diffusion models are similar. Jensen and Chandra [24] suggested that the $1/\tau_{cp}$ dependencies for compartmental exchange or diffusion can actually both be regarded as cases of the motion of spins through an inhomogeneous magnetic field, namely a restricted diffusion in discontinuous fields with a correlation time around 8 ms (exchange effect) or an unrestricted diffusion in continuous fields with a correlation time around 2 ms (diffusion effect). Under the weak field approximation, which is suitable in the blood case, the temporal correlation function about the field fluctuation experienced by spins during exchange is usually approximated as a mono-exponential decay function [35, 36] and the R_2 enhancement based on exchange effect can be derived using a model [37] similar to the Luz-Meiboom model based on Anderson-Weiss mean field theory [35, 36]. However, the temporal correlation function for spins diffusing in the continuous inhomogeneous field has been found to be better characterized by more complicated functions [24, 32]. To our knowledge, there currently is not a single analytical model that can accurately describe the correlation function for these two types of motion together. Several studies at different fields have compared the Luz-Meiboom model for exchange and the Jensen or Ziener models for diffusion [20, 33, 34]. The diffusion model always gives a statistically superior fit, but the $1/\tau_{cp}$ curves for the two models are actually difficult to distinguish. As our goal is to accurately determine just the intercept at negligible τ_{cp} , we therefore used a general tangential relaxation equation modified from Luz-Meiboom model [38], but without constraining the τ_{cor} and model-based coefficient A:

$$R_{2,blood}^{CPMG}(\tau_{cp}) = R_{20blood} + A \tau_{cor} \{1 - (2\tau_{cor}/\tau_{cp}) \tanh(\tau_{cp}/2\tau_{cor})\} \quad (8)$$

τ_{cor} is a general correlation time for magnetic field fluctuations that can relate to diffusion through field gradients or exchange over the cell membrane. The contributions $R_{20,blood}$, A (an arbitrary constant) and τ_{cor} were fitted as variables for all data at different Y , Hct and B_0 with the sole goal of getting a close to perfect fit of the data for the purpose of properly determining the transverse relaxation rate of blood at infinitely fast refocusing ($R_{20blood}$), i.e. when water spin movement is negligible on the cellular exchange and translational diffusion time scales. We therefore did not assign a physical meaning to them and will not interpret their values.

In lysed erythrocytes, due to the absence of a membrane and the presence of very fast exchange (relative to τ_{cp}) of water between the protein hydration sphere and the solution, the τ_{cp} dependence is much smaller and it is difficult to attain high accuracy using the general Eq. (8) to fit this dependence. As a good approximation, we therefore used the relaxation rate at the shortest τ_{cp} to approximate $R_{20lysed}$.

Blood sample preparation

Bovine blood was used in all experiments, because of similar transmembrane water permeability and hemoglobin properties of bovine and human erythrocytes. Fresh blood was bought from a local slaughterhouse. The blood was collected into a 1-gallon container containing ~300 mL of a water solution of the anticoagulant trisodium citrate to give a final concentration of 25 mM after mixing. All blood samples were stored at 4°C and used within 8 days after delivery. Whole blood samples at different hematocrit fractions (Hct = 0.30 – 0.78) were prepared by separating red blood cells and plasma through centrifugation at 10,000 g for 15 min at 4°C, and mixing the fractions of each to achieve different blood hematocrit values. Oxygenation fractions (Y) at different Hct were varied over a range of 0.45 – 1. Hct, pH and methemoglobin (MetHb) fractions (f_{metHb}), together with the blood oximetry parameters sO_2 (oxygen saturation), pO_2 (oxygen partial pressure) and pCO_2 were measured with a blood gas analyzer (Radiometer ABL 700 series, Radiometer, Copenhagen, Denmark). This analyzer calculates Hct based on total hemoglobin concentration in the blood (ctHb) according to an empirical relationship $Hct = 0.00301 (L/g) \times ctHb (g/L)$ (reference manual of the ABL700 blood analyzer). This corresponds to a hemoglobin concentration in erythrocytes (mean corpuscular hemoglobin concentration, MCHC) of 332 g/L [39]. In this analyzer, $sO_2 (=100\% \times Y)$ is calculated from the ratio between oxygenated hemoglobin concentration and total hemoglobin concentration (the sum of oxygenated and deoxygenated hemoglobin concentration).

Lysed blood samples at physiological hemoglobin concentration (~33 g/dL) and different oxygenation values were prepared by centrifuging whole blood at different oxygenations and removing the plasma fraction. Such packed blood cells were sonicated on ice (300 mL in aliquots of 100 mL) for 6 min with an amplitude of 45% in cycles of 10 sec “on” and 5 sec “off”, using a flat tip horn by Branson Ultrasonics (Danbury, CT, USA). Cell debris was removed by centrifugation at 10,000 g for 15 min at 4°C, and the cell lysate was immediately used for NMR measurements. The concentration of hemoglobin in lysed packed erythrocytes was in the range of 32.7 – 34.6 g/dL, i.e. similar to the concentration of hemoglobin in an erythrocyte. In addition to the packed cells, we also prepared several samples at lower than physiological hemoglobin concentration. These samples were prepared similar to whole blood samples at different hematocrit, namely by mixing plasma with cells. For lysed blood, we then lysed these mixtures, meaning that we then have a mixture of hemoglobin and albumin in solution, which has to be accounted for in the data fitting. For all samples, it was important to keep the time between cell lysis and data acquisition as short as possible, because of increased formation of paramagnetic methemoglobin in lysed blood. Cell lysis triggers mechanisms that significantly slow down natural methemoglobin reduction to oxygen-carrying hemoglobin [40] and these effects are even greater in bovine blood [41]. However, while the effect of MetHb is large for $R_{I,blood}$ it

has been reported to be negligible with respect to $R_{2,blood}$ if metHb levels can be kept to a few percent or less [25, 42]. Except for the 3T experiment at ctHb = 11.9 g/dL and $Y = 1$, where the methemoglobin fraction was 2.8 %, all of the measured MetHb levels in lysed blood were between 1.8 – 2.4 %.

The relaxation rate of PBS was measured at 3.0 T and 11.7 T to estimate $R_{2,buffer}$ in Eqs. (1, 2). In addition, to check whether addition of salt substantially affects the transverse relaxation, we also measured R_2 on a sample of 25 mM trisodium citrate solved in PBS at 37 °C on 3 T.

Blood perfusion apparatus

A home-built perfusion apparatus (Fig. 1, modified from [15, 27]) was used to provide a continuous flow of blood samples from the gas mixing chamber to the NMR - compatible flow chamber (cylinder shaped, 1 cm diameter and 10 cm length) placed vertically inside the RF coil, and back to the chamber. About 300 – 350 ml of oxygenated whole blood or lysed blood at different oxygenations was injected into a gas mixing chamber. A reduction of whole blood oxygenation level was established with a slow gas flow (mixture of N_2 , O_2 and CO_2) through the mixing chamber. Simultaneous rotation of mixing discs within the chamber maintained a high blood surface area, which is necessary for efficient exchange of gasses and also for preventing blood sedimentation. A peristaltic pump system (Masterflex, Cole-Parmer, USA) was used to circulate the blood through gas impermeable tubing with an inner diameter of 3.1 mm (Cole-Parmer, USA). All samples were placed vertically within the MRI scanner. The blood was circulated continuously during each NMR acquisition to prevent settling of erythrocytes. During R_2 measurements the flow velocity was ~ 30 mL/min (or 0.5 cm/s), which is sufficiently slow to avoid signal loss (and thus apparent increase in relaxation rate) during the measurements. The oxygenation of the system was monitored by an NMR compatible needle - encased fiber optic oxygen sensor (Oxford Optronix, Oxford, UK) inserted into the flowing blood in the tubing at the entrance of the magnet bore. This was done before and after the series of R_2 measurements as a function of τ_{cp} . If the oxygenation values before and after the series differed by more than 3 % ($dY > 0.03$) data were not included in the final tables.

Maintaining temperature stability was crucial for the experiments. Therefore, a section of the tubing between the mixing chamber and the NMR tube was jacketed and perfused with hot water from the water bath, while another section was thermally isolated by a foam insulator. This temperature calibration required the water bath temperature to be set to 38 – 41 °C to generate a blood temperature of ~37°C at the entrance of the magnet bore, which was continuously measured by a temperature sensor (Oxford Optronix, Oxford, UK). Blood samples (200 μ l) were collected at the tubing sampling point before and after each experiment for measurement of blood parameters by the blood gas analyzer.

MR acquisition

Relaxation measurements were conducted at five magnetic field strengths (3, 7, 9.4, 11.7, and 16.4 T). Experiments at 3 T and 7 T were performed using human MRI scanners (Philips Medical Systems, Best, The Netherlands) each equipped with a quadrature head coil

for RF transmission and reception. The sample tube was positioned vertically in the horizontal bore of the magnet. Additional saline bags were placed around the sample tube to load the coil. A single slice (10 mm thick) in the center region of the tube was imaged [43]. The transverse relaxation rates of water spins in blood were measured using a T2prep module right before the acquisition. The T2prep pulse sequence was similar to the one in [43], but now with hard pulses (See Table 1). A single-shot gradient-echo EPI was used (FOV = 64×64 mm², matrix = 32×32) for acquisition after the CPMG T2prep module. At 3 T, the imaging TE was 11 ms and, after acquisition, a non-selective BIR-4 [44] saturation pulse with 3 s delay was used to achieve steady-state before each T2prep block. At 7 T, imaging employed a half-scan factor of 0.6, TE = 3 ms and, after acquisition, a non-selective tailored hard-pulse saturation pulse train (65° , 83° , 143° , 162°) [45] with 4 s delay was used to achieve steady-state before each T2prep block.

Experiments at 9.4, 11.7, and 16.4 T were performed using Bruker Avance spectrometers (Bruker BioSpin, Billerica, MA, USA). Each spectrometer was equipped with a micro2.5 imaging probe with 20 mm RF coil inserts positioned vertically to the magnetic field. To suppress spuriously excited signals from regions outside the coil that may cause bias in CPMG experiments, an outer-volume suppression pre-pulse was applied using a dual frequency saturation scheme [46] to select the center part of the tube (about 1 cm). A conventional Carr-Purcell Meiboom-Gill (CPMG) sequence ($90_x \{-\tau_{cp}/2 - (180_y) - \tau_{cp}/2 -\}_n$) with variable inter-echo spacing was used to measure R_2 at different τ_{cp} values. Due to the increase in relaxation rate with field strength, lower values of τ_{cp} were used at higher field. A possible issue in the accuracy of measured relaxation rates is deviation of the 180° pulses from an actual 180° , an effect that worsens when more 180° pulses are added to lengthen TE and keep τ_{cp} constant. We tested this initially by looking at a PBS sample with very long T_2 to see if the signal remained constant, which it was for the TE value ranges used in our studies. In addition, since we selected only a small volume in the center of the tube, we expect the 180° pulses not to deviate much from the correct value.

We also studied lysed samples at 16.4 T just before switching the scanner permanently to 17.6 T. However, the data could not be interpreted and thus we have no values for this field strength.

Data analysis

Data were analyzed with Matlab (Mathworks, Natick, MA, USA) and Python (www.python.org). The signal intensity S was calculated by averaging the measured magnitude intensities in a ROI (3 T, 7 T) or the selected volume (9.4 T, 11.7 T, 16.4 T) for each inter-echo time (τ_{cp}) and total echo time (TE). $R_{2,blood}^{CPMG}$ at each τ_{cp} was determined by applying nonlinear-least-square curve-fitting of the signal decay curve to a mono-exponential function using Eq. (7). At high magnetic fields and low oxygenations, the signal decay was fast and the water resonance at longer TE was contaminated with some underlying signal components that appeared to relax slower. In these cases we used less echo times for the fit (only until signal was about $1/e$ times S_0), to avoid contamination.

Using equation 8, data for $R_{2,blood}^{CPMG}$ at each field, Hct and Y were subsequently fitted as a function of τ_{cp} for whole blood to determine $R_{20blood}$. For lysed erythrocyte/plasma mixtures (“lysed blood”) this dependence was minimal and the $R_{2,blood}^{CPMG}$ value at shortest was used to determine $R_{20lysed}$. Using the dependence of $R_{20lysed}$ at full oxygenation on f_{ery} , Eq. (6) and the measured $R_{2buffer}$ were used to determine $r_{2Hb}(Y=1)$ and r_{2Alb} from the slope and intercept, and these numbers were confirmed by measurement of pure plasma and packed erythrocytes. The slopes from the f_{ery} dependence of $R_{20blood}$ at full oxygenation (Eq. (5)) was subsequently compared to the slope from the lysed erythrocyte/plasma samples (Eq. (6)) to evaluate whether there are any additional relaxation components induced by the membrane presence that are not related to the exchange and translational diffusion effects. When performing the fit to Eq. (5) for oxygenated lysed erythrocyte/plasma mixtures, we consistently found the fitted $R_{2plasma}$ to be within error of the one measured for pure plasma. On the other hand, we did not have such low f_{ery} values for whole blood and we therefore included the measured $R_{2plasma}$ in the fit of Eq. (5) to obtain a more accurate slope.

We subsequently used $R_{20blood}$ at low oxygenation fractions to calculate $r_{2Hb}(Y)$ for each oxygenation using the previously determined $R_{2plasma}$ and r_{2Alb} . The oxygenation dependence of the data obtained from whole blood, $r_{2Hb}(whole)$, and from lysed erythrocytes, $r_{2Hb}(lysed)$, was subsequently compared to evaluate the presence of any additional relaxation effects at lower oxygenations.

RESULTS AND DISCUSSION

Using the CPMG sequence, the R_2 of PBS buffer ($R_{2buffer}$) was measured to be $0.362 \pm 0.013 \text{ s}^{-1}$ at 3 T and 0.364 ± 0.010 at 11.7 T. For buffer with 25 mM trisodium citrate this was 0.371 ± 0.021 , which is the same within error and we conclude that we can reasonably assume the salt to not substantially affect the relaxation times of the blood samples.

$R_{2,blood}^{CPMG}$ values of whole blood water obtained at different inter-echo times τ_{cp} for all hematocrits, oxygenation ratios at different magnetic fields are shown in Table 2a, Table 2b, Table 2c, Table 2d, Table 2e, and Fig. 2. The data at Hct = 0.01 (value determined by blood gas analyzer, with an error of ± 0.01) are for isolated plasma samples. These plasma data show a small to negligible τ_{cp} dependence and we used the value at the shortest τ_{cp} as an estimate for $R_{2plasma}$ at each field. Fits of $R_{2,blood}^{CPMG}$ as a function of $1/\tau_{cp}$ using Eq. (8) are shown in Fig. 2, while the resulting parameters A, τ_{cor} , and $R_{20blood}$ are shown in Table 3a, Table 3b, Table 3c, Table 3d, Table 3e. $R_{20blood}$ represents the transverse relaxation rate of blood in the absence of diffusion or exchange contributions. The $R_{2,lysed}^{CPMG}$ values of lysed erythrocyte/plasma mixtures (“lysed blood”) measured as a function of τ_{cp} at multiple oxygenations and hemoglobin concentrations at four fields are listed in Table 4a, Table 4b, Table 4c, Table 4d. The data as a function of τ_{cp} at different field strengths are visualized in Figs. 3a–d. Contrary to the data for whole blood, a tangential dependence can hardly be identified for lysed erythrocytes. The reason is that the only relevant correlation time in a protein solution is that of exchange between the free and hydration layer water, which is

much faster than the inter-echo spacing. Since this dependence is so small, we used $R_{2,blood}^{CPMG}$ at the shortest τ_{cp} as an estimate for $R_{20lysed}$.

In Figs. 4a and 4b, the dependencies of $R_{20lysed}$ and $R_{20blood}$ on f_{ery} are compared for the data at full oxygenation ($Y > 0.97$). Fig. 4c shows that the field dependence for the relaxation rates is linear and comparable. In the first two result columns of Table 5, the measured $R_{2plasma}$ and $R_{2plasma}$ determined from the intercept of the lysed blood fit in Fig. 4a are compared for each field strength. These values are the same within measurement error, in agreement with the definitions in Eqs. (2) and (6). We then fitted the whole blood values without including $R_{2plasma}$ to see whether we could make any conclusions regarding the term $Hct \cdot R_{2membrane}$ in Eq. 5 (third column in Table 5). However, these values were both larger and smaller than the measured $R_{2plasma}$ from isolated samples, indicating a larger error, which is not unexpected in an intercept when the lowest f_{ery} values are about 0.25. We therefore included the experimental $R_{2plasma}$ in the fits in Fig. 4b for a more accurate determination of the slopes and the subsequent calculation of the protein relaxation rates. The intercepts of these whole blood curves are in the 4th column of Table 5.

In Table 6, the slopes resulting from the linear fits in Fig. 4 are given together with the $r_{2Hb}(Y=1) = r_{2oxyHb}$ and r_{2Alb} values calculated from these, the lysed intercept data in Table 5, and the R_2 of PBS buffer ($R_{2buffer}$), which was measured to be $0.362 \pm 0.013 \text{ s}^{-1}$ at 3 T and 0.364 ± 0.010 at 11.7 T and assumed to be 0.36 s^{-1} in the calculations. At 16.4 T, due to the lack of lysed blood R_2 data, the measured $R_{2plasma}$ and whole blood intercept data were used to calculate r_{2oxyHb} and r_{2Alb} . It can be seen that these slopes for whole blood and lysed blood are the same within error, indicating that the membrane relaxation contribution is at most very small and most likely negligible. Thus, in the future, Eqs. (1), (3) and (5) can be simplified to:

$$R_{2ery} = R_{2buffer} + [Hb(5.15 \text{ mM})] \cdot r_{2Hb}(Y) \quad (1a)$$

$$R_{20blood} = R_{2plasma} + f_{ery}(R_{2ery} - R_{2plasma}) \quad (3a)$$

$$R_{20blood} = R_{2buffer} + [Alb(0.75 \text{ mM})] \cdot r_{2Alb} + f_{ery} \{ [Hb(5.15 \text{ mM})] \cdot r_{2Hb}(Y) - [Alb(0.75 \text{ mM})] \cdot r_{2Alb} \} \quad (5a)$$

Of these, Eq. (3a) has of course been used before, but the current data provide a basis for excluding any additional significant contributions due to relaxation enhancement of water binding to the membrane.

Finally, using the determined relaxivities for albumin (Table 6), the calculated $R_{2plasma}$ from lysed blood (Table 5) and $R_{2buffer}$, the relaxivities of hemoglobin ($r_{2Hb}(Y)$) at different oxygenations were determined using Eq. (5a) for whole blood (Table 7a, Table 7b, Table 7c, Table 7d, Table 7e) and Eq. (6) for lysed blood (Table 8). The measured $R_{2plasma}$ was used to calculate the relaxivities of hemoglobin at 16.4 T due to the lack of lysed blood R_2 data on 16.4 T. When plotting these as a function of deoxygenation (1-Y) in Fig. 5, it is again clear that the intercept between whole and lysed blood is very similar, but that the transverse relaxivity increases approximately quadratically with deoxygenation for whole blood while it is linear with a small positive slope for lysed blood. In Fig. 5, we therefore fitted these $r_{2Hb}(Y)$ values coming from lysed and whole blood using the below equations:

$$r_{2Hb}(\text{lysed}) = r_{2oxyHb} + r_{2deoxyHb}(1-Y) \quad (9)$$

$$r_{2Hb}(\text{whole}) = r_{2oxyHb} + r_{2deoxyHb}(1-Y)^2 \quad (10)$$

where r_{2oxyHb} and $r_{2deoxyHb}$ are the oxyhemoglobin and deoxyhemoglobin relaxivity, respectively. Notice that (i) $r_{2oxyHb} = r_{2Hb}(Y=1)$, so we used the values from Table 6 for these fits to obtain the results in Table 9; (ii) the approach here is very different from other papers on R_2^* and R_2 [15, 16, 18, 47–49], that typically decompose relaxation contributions into linear and quadratic terms for (1-Y). The main part of the quadratic term in those analyses is determined by the diffusion and exchange effects. Here, through removing these contributions using Eq. 8, we separate out actual hemoglobin relaxivity contributions to the intercept $R_{20,blood}$.

The discrepancy in oxygenation dependence measured between the transverse relaxivities for whole blood and lysed blood is contradictory to what was found for the longitudinal relaxivities [30]. This may be due to several potential effects, about which one can speculate. First of all, there may be cellular changes that give an additional transverse relaxation term for lower oxygenations, e.g. involvement of the membrane in conformation changes in the hemoglobin tetramer upon deoxygenation. Alternatively, it could be that the intercepts determined from extrapolation of the tangential curve fits using Eq. (8) are inaccurate, an effect that would increase with field strength. A design of more advanced theories taking into accounts both diffusion and exchange is probably needed to account for these effects. The data presented in this paper should be a useful basis for developing such theories.

CONCLUSION

Using CPMG relaxation data from whole blood and lysed blood, we determined the transverse relaxivities of oxyhemoglobin, deoxyhemoglobin and Albumin at five magnetic field strengths. Interestingly, while the oxyhemoglobin relaxivities were comparable as determined from lysed and whole blood, this was not the case for deoxyhemoglobin relaxivities. The data presented are expected to be useful as a basis set for the development of further theories of the transverse relaxation of blood, which ultimately may help elucidate

the complex transverse relaxation measured in whole blood that affects the signal in BOLD MRI.

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Fig. 1.

Fig. 2a

Fig. 2b

Fig. 2c

Fig. 2d

Fig. 2e

Fig. 2.

Fig. 3a

Fig. 3b

Fig. 3c

Fig. 3d

Fig. 3.

Fig. 4.

Fig. 5.

Table 1

Experimental parameters for CPMG experiments of whole blood, lysed erythrocyte/plasma mixtures and plasma.

B ₀ /T	Sample	delay/s	ds	p1/ μ s	p2/ μ s
3.0	all	3	0	300	600
7.0	all	4	0	400	800
	Whole	8.6	2	47 – 54	94 – 108
9.4	Lysed	8.6	2	48 – 56	96 – 112
	Plasma	8.6 – 23.6	2	50 – 54	98 – 108
	Whole	9.6	0	30 – 31	60 – 62
11.7	Lysed	9.6	0	30 – 31.5	60 – 64
	Plasma	18.6 – 20.6	0	33 – 34	66 – 68
	Whole	9.6	4	50	100
16.4	Lysed	N/A	N/A	N/A	N/A
	Plasma	9.6	4	50	100

ds = number of dummy scans; delay = recovery time. On Bruker scanner this consisted of d1 on scanner + time for data storage each scan; τ_{cp} = inter-echo time; p1 = 90° pulse; p2 = 180° pulse.

N/A: not applicable.

Table 2a

Measured whole blood relaxation rates ($R_{2,blood}^{CPMG}$) at different Hct, oxygenation fraction, and inter-echo time at 3.0 T

Hct	Y	$R_{2,blood}^{CPMG}$ (s ⁻¹) at 3 Tesla												
		τ_{ep} (ms)	2.0	2.5	3.0	4.0	5.0	6.0	8.0	10	14	20		
0.01	1.00		2.23	2.15	2.39	2.66	2.31	2.53	2.36	2.53	2.60	2.63		
0.31	1.00		4.73	4.62	4.75	4.77	4.91	4.80	5.10	5.12	5.33	5.62		
	0.80		5.60	5.65	6.13	5.93	6.44	6.65	6.80	7.19	7.63			
	0.68		7.25	7.71	7.98	8.58	8.99	9.30	10.1	10.7	11.5	12.6		
	0.58		8.72	9.51	9.86	11.0	11.6	12.3	13.3	14.4	16.3	17.2		
	0.58		8.56	9.25	9.73	10.6	11.3	11.9	13.0	13.7	15.2	17.1		
	0.54		14.0	14.4	16.0	20.0	21.1	21.4	25.1					
0.45	0.97		5.90	5.88	6.22	6.17	6.17	6.34	7.07	7.25	8.03	7.64		
	0.79		7.29	7.43	8.01	8.47	8.87	9.46	10.8	11.6	12.0	12.9		
	0.72		9.11	8.50	9.19	10.2	10.6	11.2	12.9	14.6				
	0.63		10.8	10.4	11.5	12.7	13.9	15.3	16.2	17.5				
	0.52		13.7	13.2	15.7	18.5	21.4	21.9						
0.56	0.99		7.08	6.69	6.89	7.04	6.93	7.54	7.70	8.27	8.69			
	0.80		8.34	8.12	8.42	8.84	8.83	10.1	10.6	10.0	12.5	13.5		
	0.71		10.0	9.82	10.4	11.1	12.5	12.9	14.8	16.4				
	0.61		11.9	11.7	13.0	14.5	15.6	17.7	19.9	20.8				
	0.54		14.0	14.4	16.0	20.0	21.1	21.4	25.1					
0.67	0.98		7.34	7.61	7.66	7.79	7.92	8.12	8.21	8.42	8.70	9.00		
	0.88		8.00	8.11	8.24	8.51	8.5	8.7	8.7	9.0	9.3	9.68		
	0.73		9.69	10.2	10.5	11.2	11.7	12.2	12.9	15.0				
	0.63		11.1	12.0	12.4	13.4	14.3	14.9	16.0	17.9	19.4			
	0.50		13.6	14.6	15.7	17.4	18.4	20.0	21.6	23.7				

Table 2b

Measured whole blood relaxation rates ($R_{2,blood}^{CPMG}$) at different Hct, oxygenation fraction, and inter-echo time at 7.0 T.

Hct	Y	$R_{2,blood}^{CPMG}$ (s^{-1}) at 7 Tesla												
		τ_{cp} (ms)	2.2	3.0	4.0	5.0	6.0	8.0	10	15	20	30	40	
0.01	1.00		5.18	5.24	5.41	5.38	5.41	5.29	5.35	5.49	5.35	5.29		
0.31	1.00		9.90	10.1	10.3	10.5	10.8	11.4	12.0	12.3	13.3			
	0.88		11.5	11.8	12.5	12.8	13.3	14.1	14.5	15.4	16.4			
	0.74		18.2	19.6	21.3	23.3	23.8	25.6	27.0	27.8	30.3			
	0.62		27.8	31.3	34.5	37.0	38.5	41.7	43.5	47.6				
	0.51		38.5	45.5	50.0	55.6	55.6	62.5	66.7	76.9				
0.46	1.00		12.8	13.2	13.7	13.9	14.1	15.4	15.9	18.5	17.9			
	0.79		18.2	18.9	20.0	20.8	21.3	22.7	23.8	25.6	27.8			
	0.75		22.7	25.0	26.3	28.6	29.4	32.3	34.5	37.0	40.0			
	0.61		38.5	41.7	47.6	50.0	55.6	55.6	58.8					
	0.50		50.0	55.6	58.8	62.5	66.7	76.9	83.3					
0.56	1.00		14.9	14.9	15.6	15.9	16.4	17.5	18.5	19.6	20.4			
	0.81		20.8	22.2	23.3	24.4	25.0	27.8	28.6	31.3	33.3			
	0.68		32.3	35.7	38.5	41.7	43.5	47.6	50.0	55.6	58.8			
	0.58		43.5	47.6	52.6	55.6	58.8	66.7	71.4	76.9				
	0.45		62.5	66.7	76.9	83.3	83.3	90.9	100					
0.63	1.00		15.9	15.9	16.4	16.9	17.5	17.5	17.5	19.2	20.8	23.8		
	0.87		18.2	18.9	19.2	20.0	20.4	21.3	21.7	23.3	23.8			
	0.76		26.3	27.8	28.6	30.3	32.3	34.5	35.7	40.0	45.5			
	0.63		38.5	41.7	45.5	47.6	50.0	55.6	58.8	62.5				
	0.50		50.0	55.6	62.5	71.4	76.9	83.3	90.9					
0.75	1.00		18.5	18.9	19.2	20.0	20.8	21.7	22.7	23.3	24.4	25.0		
	0.86		21.7	22.2	22.7	23.3	23.8	24.4	24.4	25.6	27.0			
	0.71		31.3	34.5	35.7	37.0	38.5	40.0	40.0	43.5				
	0.63		41.7	43.5	45.5	47.6	50.0	52.6	55.6					

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Hct	Y	$R_{2, blood}^{CPMG}$ (s ⁻¹) at 7 Tesla				
	0.50	55.6	58.8	62.5	66.7	71.4

Table 2c

Measured whole blood relaxation rates ($R_{2,blood}^{CPMG}$) at different Hct, oxygenation fraction, and inter-echo time at 9.4 T.

Hct	Y	$R_{2,blood}^{CPMG}$ (s ⁻¹) at 9.4 Tesla															
		τ_{ep} (ms)	0.8	0.9	1.1	1.3	1.6	2.1	3.1	4.1	6.1	8.1	12.1	16.1	20.1		
0.01	1.00				5.92		6.04	6.31	6.31	6.61	6.57	6.80	6.44	6.43	6.45		
1.00			5.32	5.41	5.63	5.78	5.95	6.36	6.76	6.98	6.77	6.68	7.04	7.13			
1.00			5.04	5.30	5.59	5.63	6.08	6.43	6.64	6.49	6.55	6.61	7.01	6.95			
1.00			5.43	5.59	5.62	5.93	5.99	6.07	6.24	6.87	7.43	7.68	7.30	7.31			
0.30	0.98		12.2	12.0	12.4	12.8	13.0	13.6	14.0	13.5	14.7	15.0	15.7	16.7	17.5		
	0.88		13.4	13.7	14.6	14.8	15.9	17.2	17.6	18.7	20.5	20.9	22.5	23.7	24.7		
	0.77		18.1	18.4	19.7	21.0	22.5	25.3	28.8	31.2	34.4	37.1					
	0.62		26.7	27.3	29.5	33.2	37.0	43.6	53.1	60.1							
	0.51		35.5	37.4	43.3	48.3	52.7	64.3	79.8	89.1							
0.39	0.99		13.7	14.1	14.4	14.4	14.9	15.2	15.8	15.6	16.7	17.5	18.9	20.4			
	0.83		18.8	19.3	20.3	21.0	22.0	23.6	25.9	26.1	27.7	29.2	31.5	32.6			
	0.76		21.7	22.6	24.6	25.9	28.0	30.9	35.2	38.3	40.8	44.7					
	0.66		28.8	30.6	33.4	37.0	40.7	46.4	53.9	58.5	65.5	72.5					
	0.56		35.8	38.5	43.3	47.7	54.3	63.3	74.5	82.4	92.4						
0.44	0.99		15.2	15.4	15.8	16.0	16.3	16.7	17.4	17.7	18.4	19.1	21.0	22.6			
	0.86		18.4	18.9	19.7	20.1	21.5	22.3	23.7	24.8	26.1	27.4	29.3	30.7			
	0.74		24.5	25.4	28.0	29.3	32.0	36.4	41.2	44.1	48.7	52.8					
	0.63		33.4	35.2	38.8	42.2	48.2	54.5	64.3	69.4	79.4						
	0.48		50.3	54.0	60.5	67.9	77.2	87.2	108								
0.54	0.98		17.4	17.8	17.8	18.0	18.2	18.9	19.9	20.1	21.4	22.5	24.4	26.4			
	0.81		23.7	24.3	25.4	26.1	27.6	29.1	32.3	33.8	36.9	39.1	42.9				
	0.73		28.4	30.1	32.2	33.5	36.0	39.6	45.4	47.6	52.7	56.8					
	0.63		34.8	37.4	41.3	44.8	49.8	57.0	67.5	72.9	82.5						
	0.55		42.0	44.8	50.1	56.2	62.6	72.9	87.6	94.9	106						
0.64	0.99		20.0	20.1	20.7	21.0	21.6	21.8	22.0	22.4	25.4	26.2	28.0	30.2			

Hct	Y	$R_{2, blood}^{CPMG}$ (s ⁻¹) at 9.4 Tesla															
	0.83	25.7	26.4	27.5	28.7	30.7	31.6	33.5	35.9	38.6	41.7	45.6					
	0.73	33.2	34.8	37.5	39.3	44.2	47.4	52.3	56.4	61.6							
	0.63	42.6	45.9	50.5	52.9	57.7	69.2	76.2	83.5	92.9							
	0.51	57.8	62.3	67.2	73.7	82.5	95.3	107	114								
0.75	0.98	23.9	24.3	24.7	24.9	25.1	25.9	25.7	25.5	29.3	31.2	34.0	36.1				
	0.84	28.7	29.3	30.4	31.3	32.3	33.8	34.5	35.9	41.6	44.1	48.9					
	0.73	34.5	35.8	37.9	39.7	41.6	42.9	47.8	54.2	60.9	66.5						
	0.65	41.1	42.9	46.3	48.5	51.1	59.1	67.3	71.8	81.9							
	0.53	52.9	55.9	60.8	64.9	69	80	96	103								

Table 2d

Measured whole blood relaxation rates ($R_{2,blood}^{CPMG}$) at different Hct, oxygenation fraction, and inter-echo time at 11.7 T.

Hct	Y	$R_{2,blood}^{CPMG}$ (s ⁻¹) at 11.7 Tesla																		
		τ_{cp} (ms)	0.50	0.60	0.70	0.80	1.00	1.20	1.40	1.50	1.60	1.70	2.00	2.50	3.00	4.00	5.00	6.00	8.00	10.0
0.01	1.00	7.29	7.59	7.90	8.27	8.60	8.64		8.85			8.94	9.01	8.86	9.21		9.44	9.50	9.21	
		τ_{cp} (ms)	0.56	0.66	0.76	0.86	0.91	1.06	1.26	1.46	1.66	1.86	2.06	2.56	3.06	3.56	4.06	5.06	6.06	
0.31	1.00	14.2	14.6	14.9	15.1		15.4	15.5	15.7	15.8		16.0	16.3	16.4		16.9	17.1	17.2		
	0.87	16.4	16.9	17.4	17.9		18.7	19.4	20.1	20.7		21.7	22.9	23.7		25.1	26.2	27.1		
	0.78	20.4	21.8	23.1	24.2		26.5	28.5	30.6	32.4		35.8	38.6	41.3		45.7	49.0	52.0		
	0.60	27.6	30.5	33.1	35.8		40.8	44.4	48.5	52.2		57.8	65.4	70.8		78.5	86.6			
0.38	1.00	16.3	16.7	17.1	17.2		17.4	17.8	17.9	18.1		18.5	18.6	18.9		19.5	19.8	20.3		
	1.00	15.5	15.7	15.9	16.2		16.5	16.8	16.8	17.0		17.4	17.5	17.7		18.2		18.8		
	0.91	18.1	18.7	19.1	19.5		20.1	20.9	21.3	21.9		22.7	23.4	24.1		25.3	26.1	26.8		
	0.80	20.4	21.7	22.7	23.5		25.2	26.7	27.9	29.2		31.5	33.7	36.1		40.1		47.4		
	0.70	24.9	26.9	28.9	30.8		34.2	37.0	39.9	43.2		47.9	53.1	58.8		67.9		76.6		
	0.50	45.0	50.1	54.1	59.9		69.2	75.6	83.1	89.5		97.4	110	119						
0.42	0.99	17.6	17.9	18.1	18.5		18.7	18.8	19.2	19.1		19.5	19.6	20.1	20.3	20.4	20.9			
	0.63	36.8	40.6	44.2	47.6		54.0	59.0	65.4	69.9	73.6	76.8	85.5	92.0						
0.45	0.98	18.5	18.9	19.2	19.4		19.7	20.0	20.3	20.4		20.7	20.9	21.3		22.0		23.0		
	0.98	18.4	18.8	19.2	19.4		19.8	20.0	20.2	20.4		20.6	20.8	21.1		21.8		22.9		
	0.85	21.5	22.2	22.9	23.4		24.4	25.3	26.1	26.7		28.0	29.2	30.7		32.9		37.0		
	0.73	28.0	30.2	31.6	33.0		36.2	39.2	42.0	45.5		48.5	52.4	56.7		63.4		68.9		
	0.69	30.7	33.2	35.2	37.4		41.6	45.8	49.6	53.2		59.4	65.6	72.3		81.4				
	0.63	34.8	37.8	40.3	43.0		48.1	52.6	57.1	62.9		67.9	74.9	82.8						
	0.54	41.9	46.2	50.0	53.9		62.4	69.1	75.7	84.6		92.1	105							
0.53	1.00	20.0	20.5	20.9	21.0		21.6	21.8	22.0	22.1		22.5	22.8	23.1		23.9		24.7		
	0.86	23.8	24.5	24.9	25.7		27.0	28.0	28.9	29.9		31.8	33.1	34.8		37.9		43.5		
	0.69	33.2	35.1	36.3	38.4		42.0	44.9	48.1	50.9		54.7	61.0	64.9		73.0				

Hct	Y	$R_{V_2, blood}^{CPMG} (s^{-1})$ at 11.7 Tesla															
	0.98	21.4	21.9	22.2	22.4	22.9	23.3	23.5	23.7	24.3	24.4	24.9	25.9	27.6			
	0.80	29.1	30.8	32.0	33.0	35.1	37.0	38.9	40.2	43.0	45.2	47.6	51.8	58.5			
	0.61	48.1	52.9	57.1	60.5	69.0	76.0	82.7	87.9	98.0	107	119	133				
	0.52	56.7	61.6	67.3	72.7	83.0	91.7	100	106	117	132	143					
0.64	0.99	24.3	24.8	25.1		25.6	25.9	26.2	26.4	26.5	27.0	27.2	27.4				
	0.80	31.2	32.5	33.9		35.5	37.0	39.1	40.9	42.5	45.8	48.9	52.5	57.7	69.8		
	0.68	39.0	41.4	43.5		46.6	49.3	52.4	56.0	59.1	64.1	70	75	86	104		
	0.54	50.2	53.0	56.7		61.4	66.1	73.2	80.5	86.9	95.9	107	116	131			
		0.51	0.56	0.61	0.66	0.76	0.86	0.96	1.06	1.26	1.46	1.66	2.06	2.56	3.06	4.06	5.06
		$\tau_{cp} (ms)$															
0.71	0.99	27.0	27.4	27.6	27.9	28.3	28.4	28.7	29.4	29.4	30.0	30.3	30.6	31.2	32.4	33.2	
	0.85	31.5	32.1	32.7	33.3	34.0	34.8	35.5	36.5	37.2	38.9	39.6	41.0	42.5	44.5	48.3	51.6
	0.78	35.0	35.6	36.9	37.4	38.3	39.1	40.7	42.1	43.9	45.7	47.0	50.0	52.6	55.3	60.8	66.9
	0.66	42.7	44.2	45.8	47.2	49.5	51.3	54.5	56.7	60.9	65.0	68.3	74.3	80.9	87.8	100	111

Table 2e

Measured whole blood relaxation rates ($R_{2,blood}^{CPMG}$) at different Hct, oxygenation fraction, and inter-echo time at 16.4 T.

Hct	Y	$R_{2,blood}^{CPMG}$ (s ⁻¹) at 16.4 Tesla																	
0.01	1.00	τ_{cp} (ms)	0.5	0.8	1.0	1.3	1.5	2.0	3.0	4.0	6.0	8.0	10.0						
			11.2	11.8	12.0	12.2	12.4	12.7	12.5	12.6	12.6	12.7	12.4						
		τ_{cp} (ms)	0.50	0.75	1.00	1.25	1.50	1.75	2.00	2.25	2.50	2.75	3.00	3.50	4.00	6.00	8.00	10.0	
0.32	1.00		21.1	22.0	22.3	21.6	22.6	23.1	23.1	23.3	23.7	24.8	25.6	26.7					
		0.80		29.8	34.1	37.8	40.3	44.0	47.7	47.7	54.7	59.6							
		0.74		33.4	40.5	46.0	50.3	54.6	58.8	62.3	66.0	68.8	71.4	73.4	77.5				
0.44	1.00	0.57		53.5	70.9	84.4	98.7	109	117	127									
		0.85		25.8	26.4	26.8	26.7	27.1	27.3	27.3	27.9	28.6	29.7	31.3	32.9				
		0.76		31.2	33.8	36.1	37.9	39.5	42.4	42.4	46.4	50.0	55.0						
0.55	1.00	0.65		40.7	47.8	53.1	58.0	62.2	65.7	68.5	71.7	74.1	76.8						
		0.54		58.3	72.7	85.4	95.3	104	112	118	125	130							
		0.84		77.6	102	123	141	157	170	182									
0.73	1.00		30.8	32.2	32.6	32.8	33.1	33.0	33.0	33.2	34.3	35.8	37.7						
		0.63		38.7	42.4	45.2	47.8	49.8	53.6	53.6	60.2	62.9							
		0.55		52.4	62.5	70.4	77.5	83.7	88.3	92.2	96.3	99.7	105						

Table 3aTangential fitting results for the whole blood R_2 at 3.0 T.

Hct	Y	A (s⁻²)	τ_{cor} (ms)	$R_{20\text{blood}}$(s⁻¹)
0.31	1.00	433	3.91	4.60
0.31	0.80	1540	6.38	5.60
0.31	0.68	2884	2.48	7.17
0.31	0.58	4893	2.13	8.27
0.45	0.97	1600	18.8	5.90
0.45	0.79	3767	2.08	6.70
0.45	0.72	4804	4.08	8.42
0.45	0.63	7258	1.77	9.14
0.45	0.52	16480	1.44	9.74
0.56	0.99	1740	10.2	6.70
0.56	0.80	2239	4.04	8.06
0.56	0.71	5424	3.02	9.19
0.56	0.61	9185	1.95	10.1
0.56	0.54	16525	1.30	10.2
0.67	0.98	956	2.14	7.30
0.67	0.88	804	2.78	8.00
0.67	0.73	3000	2.71	9.70
0.67	0.63	5415	2.38	10.8
0.67	0.50	9850	1.74	12.2

Table 3bTangential fitting results for the whole blood R_2 at 7.0 T.

Hct	Y	A (s⁻²)	τ_{cor} (ms)	$R_{20\text{blood}}$(s⁻¹)
0.31	1.00	2660	20.00	9.90
0.31	0.88	3280	15.09	11.50
0.31	0.74	9982	1.59	16.15
0.31	0.62	19388	1.48	23.89
0.31	0.51	27236	1.97	35.65
0.46	1.00	2775	3.11	12.49
0.46	0.79	4579	2.90	17.92
0.46	0.75	10381	2.20	21.53
0.46	0.61	35877	1.07	28.54
0.46	0.50	27291	2.79	47.49
0.56	1.00	2995	2.84	14.34
0.56	0.81	6660	2.56	20.27
0.56	0.68	16924	2.09	30.19
0.56	0.58	26243	1.97	39.13
0.56	0.45	41732	1.54	53.36
0.63	1.00	1986	7.66	15.90
0.63	0.87	4760	19.66	18.20
0.63	0.76	7793	3.71	26.25
0.63	0.63	19865	1.85	35.04
0.63	0.50	45843	1.62	40.04
0.75	1.00	3649	2.31	17.83
0.75	0.86	2547	2.66	21.59
0.75	0.71	8700	1.81	31.02
0.75	0.63	12813	2.11	39.58
0.75	0.50	16849	2.20	53.44

Table 3cTangential fitting results for the whole blood R_2 at 9.4 T.

Hct	Y	A (s⁻²)	τ_{cor} (ms)	$R_{20\text{blood}}$(s⁻¹)
0.30	0.98	3824	1.45	12.00
0.30	0.88	10729	1.07	13.40
0.30	0.77	31291	0.80	16.32
0.30	0.62	80585	0.76	21.17
0.30	0.51	135926	0.69	26.50
0.39	0.99	4080	1.97	13.70
0.39	0.83	16671	0.88	18.48
0.39	0.76	40707	0.72	19.51
0.39	0.66	74168	0.74	25.08
0.39	0.56	129493	0.62	26.92
0.44	0.99	4520	1.95	15.20
0.44	0.86	12784	1.01	18.40
0.44	0.74	50477	0.72	21.67
0.44	0.63	99000	0.66	26.84
0.44	0.48	190458	0.60	36.51
0.54	0.98	5280	2.16	17.40
0.54	0.81	20255	1.09	23.55
0.54	0.73	46855	0.77	26.45
0.54	0.63	102785	0.66	28.39
0.54	0.55	151651	0.61	31.04
0.64	0.99	6040	2.19	20.00
0.64	0.83	20121	1.13	25.70
0.64	0.73	70378	0.57	28.06
0.64	0.63	113531	0.62	35.23
0.64	0.51	199616	0.49	40.49
0.75	0.98	7220	2.42	23.86
0.75	0.84	16389	1.61	28.70
0.75	0.73	36271	1.25	34.50
0.75	0.65	75327	0.77	37.18
0.75	0.53	127102	0.70	44.96

Table 3dTangential fitting results for the whole blood R_2 at 11.7 T.

Hct	Y	A (s^{-2})	τ_{cor} (ms)	$R_{20blood}(s^{-1})$
0.31	1.00	9123	0.39	13.95
0.31	0.87	21730	0.63	15.91
0.31	0.78	60435	0.67	19.15
0.31	0.60	126429	0.63	24.50
0.38	1.00	8264	0.47	15.24
0.38	1.00	8131	0.55	16.30
0.38	0.91	18582	0.58	17.71
0.38	0.80	41680	0.86	20.40
0.38	0.70	91811	0.76	23.56
0.38	0.50	254651	0.47	33.73
0.42	0.99	8275	0.48	17.43
0.42	0.63	185921	0.49	28.97
0.45	0.98	8467	0.60	18.50
0.45	0.98	8781	0.56	18.40
0.45	0.85	24733	0.87	21.50
0.45	0.73	83385	0.67	26.23
0.45	0.69	119666	0.65	27.32
0.45	0.63	148614	0.54	29.07
0.45	0.54	232666	0.51	31.88
0.53	1.00	9920	0.53	19.99
0.53	0.98	10462	0.69	21.40
0.53	0.86	29259	0.92	23.80
0.53	0.80	52032	0.71	28.73
0.53	0.69	92982	0.65	30.57
0.53	0.61	212807	0.59	41.59
0.53	0.52	282981	0.51	44.94
0.64	0.99	5480	0.60	24.30
0.64	0.80	55665	0.96	31.20
0.64	0.68	96460	0.94	39.00
0.64	0.54	197287	0.63	43.22
0.71	0.99	15021	0.46	26.82
0.71	0.85	36745	0.71	31.50
0.71	0.78	56703	0.75	34.86
0.71	0.66	123049	0.77	42.08

Table 3eTangential fitting results for the whole blood R_2 at 16.4 T.

Hct	Y	A (s⁻²)	τ_{cor} (ms)	$R_{20\text{blood}}$(s⁻¹)
0.32	1.00	5334	1.22	21.14
0.32	0.80	80629	0.52	27.62
0.32	0.74	124696	0.54	30.33
0.32	0.57	369899	0.39	37.17
0.44	1.00	6582	1.31	25.80
0.44	0.85	43822	0.68	30.97
0.44	0.76	130886	0.46	36.29
0.44	0.65	300763	0.41	45.81
0.44	0.54	526299	0.39	54.68
0.55	1.00	7544	1.09	30.79
0.55	0.84	66999	0.52	36.88
0.55	0.73	194608	0.43	45.12
0.55	0.63	373610	0.37	54.52
0.55	0.55	519702	0.36	60.42

Measured lysed blood transverse relaxation rates ($R_{2,lysed}^{CPMG}$) at different oxygenation fraction (Y), hemoglobin concentration (ctHb) and inter-echo spacing (τ_{cp}) at 3.0 T.

Table 4a

ctHb (g/dl)	Y	$R_{2,lysed}^{CPMG}$ (s ⁻¹)									
		τ_{cp} (ms)	2.0	3.0	4.0	5.0	6.0	8.0	10	15	20
11.9	1.00		4.51	4.70	4.72	4.79	4.91	5.20			
23.0	1.00		6.72	6.81	7.00	7.09	7.00				
33.7	0.99		9.71	10.0	10.2	10.1	10.2	10.4	10.3	10.4	10.3
33.4	0.87		9.43	9.62	10.0	10.1	10.1	10.1	10.1	10.1	10.1
33.9	0.72		10.2	10.4	10.6	10.6	10.6	10.8	10.8	10.8	10.8
33.9	0.70		10.4	10.8	10.9	11.0	10.9	11.1	10.9	11.1	11.1
32.7	0.68		9.90	10.2	10.2	10.2	10.3	10.4	10.3	10.3	10.4
33.2	0.58		10.9	11.2	11.2	11.2	11.1	11.5	11.5	11.4	11.5

Measured lysed blood transverse relaxation rates ($R_{2,lysed}^{CPMG}$) at different oxygenation fraction (Y), hemoglobin concentration (ctHb) and inter-echo spacing (τ_{cp}) at 7.0 T.

Table 4b

ctHb (g/dl)	Y	$R_{2,lysed}^{CPMG}$ (s ⁻¹)									
		τ_{cp} (ms)	2.2	3.0	4.0	5.0	6.0	8.0	10	15	20
24.8	1.00	17.9	18.2	17.9	17.5	17.2	18.2	18.5	18.5	18.5	18.2
14.9	1.00	12.5	12.5	12.5	12.7	12.5	12.7	12.7	12.7	12.1	10.6
7.6	1.00	8.85	8.85	8.93	8.93	8.93	8.93	8.93	8.85	9.17	8.47
33.0	1.00	23.8	23.8	22.7	22.7	22.7	23.8	24.4	24.4	24.4	23.3
31.8	0.88	23.8	23.8	23.8	24.4	23.3	23.3	22.7			
34.6	0.79	26.3	26.3	26.3	26.3	27.0	26.3	27.0	26.3		
33.8	0.72	25.6	26.3	26.3	27.0	26.3	27.0	26.3	26.3	26.3	
33.6	0.57	27.0	27.8	27.0	27.8	27.8	27.8	27.8	27.8	27.8	27.8

Table 4c

Measured lysed blood transverse relaxation rates ($R_{2,lysed}^{CPMG}$) at different oxygenation fraction (Y), hemoglobin concentration (ctHb) and inter-echo spacing (τ_{cp}) at 9.4 T.

ctHb (g/dl)	Y	$R_{2,lysed}^{CPMG}$ (s ⁻¹)									
		1.1	1.6	2.1	3.1	4.1	6.1	8.1	12.1	16.1	20.1
		τ_{cp} (ms)									
34.8	1.00	32.4	32.4	32.5	33.3	33.0	33.9	34.8	35.6		
25.4	1.00	24.0	24.3	24.7	25.1	25.2	25.4	25.9	26.1	26.0	26.1
15.1	1.00	15.9	16.1	16.2	16.5	16.2	16.5	17.0	17.2	17.5	
34.2	0.99	31.7	31.6	31.4	32.4	33.0	32.1	31.7	33.0	32.4	
33.6	0.78	34.7	35.2	35.6	36.1	36.7	36.9	36.6	35.7	36.0	
33.4	0.61	37.2	37.9	38.5	38.4	39.0	39.6	39.5	39.1	39.5	
		τ_{cp} (ms)									
		0.8	0.9	1.1	1.3	1.6	2.1	3.1	4.1	6.1	8.1
24.6	1.00	23.5	23.9	24.8	25.7	24.4	25.2	25.3	24.9	24.8	24.6
15.5	1.00	16.5	16.7	17.3	17.5	17.6	18.0	18.2	17.7	18.2	19.5
7.4	1.00	10.5	10.8	10.8	11.3	11.2	11.7	12.0	12.4	13.0	12.8
34.0	0.99	32.0	32.3	33.6	34.5	34.8	34.5	35.1	35.5	36.0	36.1
33.7	0.89	32.4	34.1	33.9	33.1	34.3	34.2	35.8	35.5	35.9	36.1
34.3	0.86	35.2	35.8	36.5	36.8	36.9	37.5	38.5	39.4	38.8	39.1
33.8	0.75	34.9	36.0	36.4	35.3	37.3	38.1	38.4	38.3	39.0	39.1
34.5	0.66	39.3	39.3	40.1	40.0	40.8	40.8	42.4	42.3	42.8	43.1
32.7	0.53	38.4	38.8	39.2	38.9	39.2	36.5	36.7	40.4	41.7	42.4
33.1	0.50	37.6	38.9	40.2	40.6	40.4	40.7	41.7	41.6	42.1	42.3
34.6	0.42	40.5	41.0	41.7	41.7	42.9	42.0	43.5	43.1	43.8	44.4
33.6	0.40	40.1	40.6	40.8	40.2	41.5	42.2	42.9	42.4	43.5	43.3
32.9	0.38	38.6	38.1	39.0	39.4	39.7	40.0	41.1	40.9	41.6	41.2
32.7	0.25	39.9	40.2	40.8	40.6	41.9	41.9	42.8	43.4	43.4	44.2
31.8	0.24	37.7	38.4	38.7	38.7	39.5	39.6	41.4	40.9	41.2	42.1

Measured lysed blood transverse relaxation rates ($R_{2,lysed}^{CPMG}$) at different oxygenation fraction (Y), hemoglobin concentration (ctHb) and inter-echo spacing (τ_{cp}) at 11.7 T.

Table 4d

B ₀ (T)	ctHb (g/dl)	Y	$R_{2,lysed}^{CPMG}$ (s ⁻¹)													
			τ _{cp} (ms)	0.56	0.66	0.76	0.91	1.06	1.26	1.46	1.66	2.06	2.56	3.06	4.06	6.06
11.7	22.9	1.00	27.6	28.2	28.7	29.2	29.8	30.1	30.3	30.5	30.8	30.9	31.1	31.4	31.5	
	14.6	1.00	19.7	20.0	20.0	20.6	21.0	22.4	22.2	21.8	21.8	22.1	22.9	22.3	22.3	
	6.2	1.00	11.9	12.1	12.4	12.8	13.3	13.5	13.7	13.3	13.4	13.7	13.8	13.8	14.2	
	33.5	0.95	40.3	41.1	41.9	42.7	43.2	43.4	44.0	44.0	44.7	45.5	45.3	45.5		
	15.2	0.90	21.2	21.9	21.8	22.6	22.8	22.5	23.1	24.2	23.8	23.5	23.5	23.5	24.2	
	34.1	0.86	45.4	46.0	46.8	47.4	48.2	48.5	48.9	49.2	49.5	49.2	49.2	48.9	49.8	
	34.1	0.81	45.0	45.5	46.0	46.8	47.4	47.4	47.8	48.2	48.6	48.5	48.8	49.5	49.6	
	33.4	0.80	44.2	44.7	45.6	46.1	46.8	46.8	47.5	47.5	47.8	47.7	48.0	48.7	48.9	
	21.5	0.79	29.1	29.7	30.2	30.8	31.0	31.5	32.2	32.2	32.5	32.7	32.7	32.9	32.3	
	32.0	0.78	41.7	42.4	43.2	43.6	44.2	44.0	44.7	45.0	45.4	45.3	45.5	46.0	46.3	
			43.3	44.2	44.9	45.4	46.1	46.5	47.3	47.4	47.8	47.8	48.1	48.1		
			35.6	36.5	37.1	37.6	38.2	38.6	39.3	39.5	39.8	39.8	40.4	39.8		
			49.0	49.9	50.5	51.4	51.9	52.4	52.7	52.9	53.2	52.9	52.9	52.8	53.8	
			50.5	51.6	52.3	52.6	53.4	53.6	53.4	54.2	54.4	54.6	54.9	54.9		
			34.1	0.54												
			32.5	0.49												

Table 5

Comparison between the measured $R_{2\text{plasma}}$ and fitted intercepts of the lysed and whole blood fits in Fig. 4.

B0 (T)	Measured $R_{2\text{plasma}}$ (s^{-1})	Fitted Intercept (s^{-1})		
		Lysed blood	Whole blood without including $R_{2\text{plasma}}$	Whole blood including $R_{2\text{plasma}}$
3.0	2.23	2.27 $\pm$ 0.28	2.84 $\pm$ 0.37	2.38 $\pm$ 0.21
7.0	5.18	5.52 $\pm$ 0.17	5.44 $\pm$ 0.31	5.26 $\pm$ 0.16
9.4	5.26	6.03 $\pm$ 0.24	5.04 $\pm$ 0.43	5.17 $\pm$ 0.27
11.7	7.29	7.28 $\pm$ 0.28	5.88 $\pm$ 0.57	6.69 $\pm$ 0.42
16.4	11.2		9.59 $\pm$ 0.43	11.0 $\pm$ 0.41

Table 6

The fitted slopes from $R_{20lysed}$ and $R_{20blood}$ at $Y = 1$ (Fig. 4), determined albumin relaxivities (r_{2Alb}), and calculated hemoglobin relaxivities (r_{2Hb}) at full oxygenation.

B_0 (T)	Slope (s^{-1})		r_{2Alb} (s^{-1}/mM)	r_{2oxyHb} (s^{-1}/mM)
	Whole blood	Lysed blood		
3.0	8.67 $\pm$ 0.54	7.35 $\pm$ 0.39	2.54 $\pm$ 0.37	1.80 $\pm$ 0.13
7.0	18.6 $\pm$ 0.4	18.3 $\pm$ 0.3	6.88 $\pm$ 0.22	4.56 $\pm$ 0.08
9.4	26.7 $\pm$ 0.7	25.9 $\pm$ 0.3	7.56 $\pm$ 0.3	6.14 $\pm$ 0.11
11.7	30.8 $\pm$ 1.0	33.0 $\pm$ 0.5	9.23 $\pm$ 0.4	7.75 $\pm$ 0.14
16.4	41.0 $\pm$ 1.3		14.1 $\pm$ 0.5	10.5 $\pm$ 0.3

Table 7a

Calculated hemoglobin relaxivities from $R_{20blood}$ at 3.0 T.

Hct	Y	r_{2Hb} (Y) (s^{-1}/mM)
0.31	1.00	2.19
0.31	0.80	2.97
0.31	0.68	4.19
0.31	0.58	5.06
0.45	0.97	2.25
0.45	0.79	2.66
0.45	0.72	3.55
0.45	0.63	3.92
0.45	0.52	4.23
0.56	0.99	2.15
0.56	0.80	2.70
0.56	0.71	3.15
0.56	0.61	3.50
0.56	0.54	3.54
0.67	0.98	2.00
0.67	0.88	2.23
0.67	0.73	2.78
0.67	0.63	3.13
0.67	0.50	3.58

Table 7bCalculated hemoglobin relaxivities from $R_{20blood}$ at 7.0 T.

Hct	Y	$r_{2Hb}(Y)$ (s^{-1}/mM)
0.31	1.00	4.42
0.31	0.88	5.67
0.31	0.74	9.31
0.31	0.62	15.4
0.31	0.51	24.5
0.46	1.00	4.51
0.46	0.79	7.25
0.46	0.75	9.07
0.46	0.61	12.6
0.46	0.50	22.2
0.56	1.00	4.54
0.56	0.81	6.92
0.56	0.68	10.9
0.56	0.58	14.5
0.56	0.45	20.2
0.63	1.00	4.63
0.63	0.87	5.43
0.63	0.76	8.24
0.63	0.63	11.3
0.63	0.50	13.1
0.75	1.00	4.48
0.75	0.86	5.54
0.75	0.71	8.20
0.75	0.63	10.6
0.75	0.50	14.5

Table 7cCalculated hemoglobin relaxivities from $R_{20blood}$ at 9.4 T.

Hct	Y	$r_{2Hb}(Y)$ (s^{-1}/mM)
0.30	0.98	5.93
0.30	0.88	7.07
0.30	0.77	9.43
0.30	0.62	13.4
0.30	0.51	17.7
0.39	0.99	5.75
0.39	0.83	8.65
0.39	0.76	9.28
0.39	0.66	12.7
0.39	0.56	13.8
0.44	0.99	5.96
0.44	0.86	7.66
0.44	0.74	9.39
0.44	0.63	12.1
0.44	0.48	17.3
0.54	0.98	5.86
0.54	0.81	8.44
0.54	0.73	9.66
0.54	0.63	10.5
0.54	0.55	11.6
0.64	0.99	5.89
0.64	0.83	7.84
0.64	0.73	8.65
0.64	0.63	11.1
0.64	0.51	12.9
0.75	0.98	6.13
0.75	0.84	7.50
0.75	0.73	9.13
0.75	0.65	9.89
0.75	0.53	12.1

Table 7dCalculated hemoglobin relaxivities from $R_{20blood}$ at 11.7 T.

Hct	Y	r_{2Hb} (Y) (s^{-1}/mM)
0.31	1.00	6.55
0.31	0.87	8.08
0.31	0.78	10.6
0.31	0.60	14.8
0.38	1.00	6.32
0.38	1.00	6.98
0.38	0.91	7.86
0.38	0.80	9.54
0.38	0.70	11.5
0.38	0.50	17.9
0.42	0.99	7.01
0.42	0.63	13.5
0.45	0.98	7.14
0.45	0.98	7.09
0.45	0.85	8.69
0.45	0.73	11.1
0.45	0.69	11.7
0.45	0.63	12.6
0.45	0.54	14.1
0.53	1.00	6.78
0.53	0.98	7.39
0.53	0.86	8.42
0.53	0.80	10.5
0.53	0.69	11.3
0.53	0.61	16.0
0.53	0.52	17.5
0.64	0.99	7.18
0.64	0.80	9.54
0.64	0.68	12.2
0.64	0.54	13.7
0.71	0.99	7.25
0.71	0.85	8.66
0.71	0.78	9.67
0.71	0.66	11.9

Table 7e

Calculated hemoglobin relaxivities from $R_{20blood}$ at 16.4 T.

Hct	Y	$r_{2Hb}(Y)$ (s^{-1}/mM)
0.32	1.00	9.61
0.32	0.80	14.5
0.32	0.74	16.5
0.32	0.57	21.7
0.44	1.00	9.80
0.44	0.85	12.6
0.44	0.76	15.4
0.44	0.65	20.4
0.44	0.54	25.1
0.55	1.00	10.1
0.55	0.84	12.6
0.55	0.73	16.0
0.55	0.63	19.9
0.55	0.55	22.3

Table 8The calculated $r_{2\text{Hb}}(\text{Y})$ from the lysed blood data.

B0 (T)	ctHb (g/dL)	Y	R_2 (s^{-1})	$r_{2\text{Hb}}(\text{Y})$ (s^{-1}/mM)
3.0	11.9	1.00	4.51	1.86
3.0	23.0	1.00	6.72	1.75
3.0	33.7	0.99	9.71	1.78
3.0	33.4	0.87	9.43	1.74
3.0	33.9	0.72	10.2	1.87
3.0	33.9	0.70	10.4	1.91
3.0	32.7	0.68	9.90	1.88
3.0	33.2	0.58	10.9	2.05
7.0	7.6	1.00	8.85	4.55
7.0	14.9	1.00	12.5	4.62
7.0	24.8	1.00	17.9	4.51
7.0	33.0	1.00	23.8	4.58
7.0	31.8	0.88	23.8	4.76
7.0	34.6	0.79	26.3	4.81
7.0	33.8	0.72	25.6	4.81
7.0	33.6	0.57	27.0	5.10
9.4	7.4	1.00	10.5	6.08
9.4	15.1	1.00	15.9	6.13
9.4	15.5	1.00	16.5	6.28
9.4	24.6	1.00	23.5	6.10
9.4	25.4	1.00	24.0	6.04
9.4	34.8	1.00	32.4	5.90
9.4	34.2	0.99	31.7	5.89
9.4	34.0	0.99	32.0	5.98
9.4	33.8	0.89	32.4	6.12
9.4	34.3	0.86	35.2	6.52
9.4	33.6	0.78	34.7	6.58
9.4	33.8	0.75	34.9	6.57
9.4	34.5	0.66	39.3	7.23
9.4	33.4	0.61	37.2	7.10
9.4	32.7	0.53	38.4	7.52
9.4	33.1	0.50	37.6	7.26
9.4	34.6	0.42	40.5	7.43
9.4	33.6	0.40	40.1	7.61
9.4	32.9	0.38	38.6	7.50
9.4	32.7	0.25	39.9	7.81
9.4	31.8	0.24	37.7	7.62
11.7	6.2	1.00	11.9	7.54
11.7	14.6	1.00	19.7	7.93

B0 (T)	ctHb (g/dL)	Y	R₂ (s⁻¹)	r_{2Hb}(Y) (s⁻¹/mM)
11.7	15.2	0.90	21.2	8.39
11.7	22.9	1.00	27.6	7.70
11.7	21.5	0.79	29.1	8.71
11.7	26.4	0.76	35.6	8.77
11.7	33.5	0.95	40.3	7.68
11.7	34.1	0.86	45.4	8.48
11.7	34.1	0.81	45.0	8.41
11.7	33.4	0.80	44.2	8.46
11.7	32.0	0.78	41.7	8.37
11.7	31.5	0.77	43.3	8.85
11.7	33.9	0.64	49.0	9.22
11.7	34.1	0.54	50.5	9.44
11.7	32.5	0.49	50.0	9.88

Table 9

Linear and quadratic fitting results of the deoxygenation dependence of the hemoglobin relaxivities based on Eqs. (9) and (10).

B0(T)	Lysed blood	Whole blood
	$r_{2\text{deoxyHb}}$ (s^{-1}/mM)	$r_{2\text{deoxyHb}}$ (s^{-1}/mM)
3.0	0.40 $\pm$ 0.09	11.3 $\pm$ 1.2
7.0	1.39 $\pm$ 0.31	53.5 $\pm$ 3.3
9.4	2.55 $\pm$ 0.16	41.1 $\pm$ 2.0
11.7	4.00 $\pm$ 0.18	41.0 $\pm$ 1.5
16.4		69.2 $\pm$ 4.5