# Theory of Susceptibility Induced Transverse Relaxation in the Capillary Network.

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## Introduction

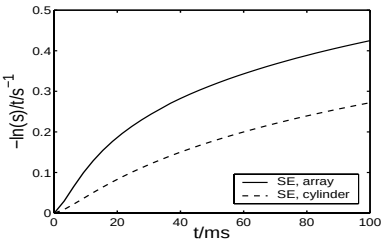
A deeper insight into the physics of MR signal formation in living tissues may provide methods to glean information about biological structures much below the achievable MRI resolution. Conversely, the manner in which mesoscopic structure (a few micrometres) may affect the net transverse relaxation is crucial, for example, in quantifying the BOLD-fMRI in terms of physiological parameters. The compartmentalization of paramagnetic deoxyhaemoglobin in red blood cells (RBCs) is hence commonly neglected in analytical models of BOLD effect. Deoxyhaemoglobin is considered to be evenly distributed over the vessel volume, which might be advocated as a reasonable assumption for large vessels, but not necessarily for capillaries. This simplification may particularly affect measurements with the spin echo (SE) and Carr-Purcell-Meiboom-Gill (CPMG) sequences, due to their enhanced sensitivity to the microvasculature. In the present analytical study, the effect of deoxyhaemoglobin compartmentalization in the capillary network is clarified in the diffusion-narrowing regime, which holds for the native blood paramagnetism at moderate fields up to about 1.5 T (1).

## Theoretical Results

The generic form for the relaxation effect of arbitrary shaped mesoscopic paramagnetic objects (1) is adapted to two models of capillaries, which are simulated either as infinitely long homogeneously magnetized cylinders or as infinitely long arrays of spheres simulating the individual RBCs. Calculations require a proper regularization of divergent quantities. In the model, the vessels are randomly placed and oriented and a free diffusion of spin bearing molecules is assumed. The blood occupies a volume fraction $\zeta$. The signal change, $s$, due to the capillary network takes the form $s = \exp(-\zeta \cdot f)$ where the $f$-function for the cylinder and array of spheres was derived to be

$$f_{cylinder}(\tau) = \frac{8\delta\omega^2 R^4}{45D^2}\int_0^\infty g(q^2\tau)J_1^{\,2}(q)\frac{dq}{q^5} \qquad [1]$$

$$f_{array}(\tau, R/l) = \frac{8\delta\omega^2 R^5}{15lD^2}\sum_{m=-\infty}^{\infty}\int_0^\infty g(\bar{q}^2\tau)\left(\sin(\bar{q})-\bar{q}\cos(\bar{q})\right)^2\frac{qdq}{\bar{q}^{10}} \qquad [2]$$




Here $R$ is the radius of the cylinder and spheres; $D$ is the diffusion constant; $t_D$ is the diffusion time to pass one object; $\tau = t/t_D$ is a dimensionless time; $\delta\omega$ is given by $\delta\omega = 4\pi\chi\omega_L$, where $\chi$ is the susceptibility of the objects and $\omega_L$ is the Larmor frequency; $\bar{q} = \sqrt{q^2 + (2\pi mR/l)^2}$, where $l$ is the distance between the centers of spheres. The $g$-function is known for the free induction decay (FID), SE and the CPMG sequences (1). The integral in [1] and the sum in [2] are numerically found and tabulated as functions of $\tau$ [1-2] and of $R/l$ [2].

## Physiological Applications and Discussion

The results are in good agreement with earlier Monte Carlo simulations (3) and coincide with analytical expressions derived for special objects (1,2). By their analytical nature, the obtained equations [1-2] have the advantage of displaying the complete parameter dependence of the susceptibility-induced relaxation rate including the scaling rules for parameter variation. In this way the effect of haemoglobin compartmentalization can be studied. For example, reducing the haematocrit from 40% to 30%, accompanied by a compensating increase in deoxyhaemoglobin concentration results in an up to 0.14 $s^{-1}$ increase in the capillary-induced relaxation rate. This demonstrates a sensitivity of the transverse relaxation to the haematological effects in in-vivo experiments. As the main result of this study it is shown that the commonly used model of homogeneously magnetized cylinders underestimates the capillary-induced relaxation rate by up to 0.15 $s^{-1}$ (see figure) for realistic parameters involved in the SE relaxation at 1.5 T, and by up to 0.17 $s^{-1}$ for the FID. For echo-times between t=20 ms and t=100 ms, this constitutes respectively 55%-36% and 36%-28% of the capillary-induced relaxation rate. Theses contributions are noticeable in the variation of the total relaxation rate during the brain activation, which is about 0.55 $s^{-1}$ for the SE and 0.70 $s^{-1}$ for the FID (4, 5). The contribution of veins should be less subjected to the compartmentalization of deoxyhaemoglobin, since the span of induced magnetic field is of the order of vein diameter, which is larger than the RBC size. The present refinement of the relaxation theory should significantly modify the quantifying of physiological parameters based on BOLD fMRI.

**References:** (1) Kiselev, Novikov; *Phys. Rev. Lett.* **89**: 278101, 2002. (2) Kiselev, Posse, *Phys. Rev. Lett.* **81**:5696–5699, 1998. (3) Boxerman *et al; MRM.* **34**:555-566, 1995. (4) Bandettini *et al*; *NMR Biomed.* **7**:12-20, 1994. (5) Jones; *NMR Biomed.* **12**:299-308, 1999.