Impact of the mono-exponential signal decay approximation on the numerically predicted spatial BOLD specificity for spin echo sequences

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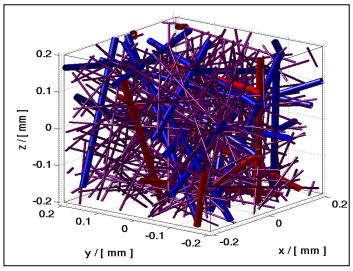
Introduction:

To study the BOLD effect numerically, blood vessels are often modelled as infinite cylinders [1] (infinite cylinder model, ICM). To simplify analytical calculations, signal dephasing resulting from spins diffusing around these infinite cylinders is then usually further approximated as a mono-exponential signal decay as suggested by Ogawa et al.[1]. Although for a wide range of parameters this mono-exponential approximation (MEA) is a good approximation for the signal resulting from the ICM it is known to increasingly deviate for increasing radii of the cylinders and when using spin echoes instead of gradient echoes [2]. In high resolution fMRI studies, however, spin echoes are sometimes used to increase the ratio R between the BOLD signal stemming from micro-vascular and macro-vascular tissue and thus increase the spatial specificity of the acquired activation (see e.g. [3]). For spin echoes, this ratio R has recently been investigated by Uludag et al. [2] for a wide parameter range using an analytical model for the BOLD signal which relied on the aforementioned MEA. To investigate the impact of the MEA on the predicted BOLD spatial specificity, we implemented the ICM into our general purpose MRI simulator JEMRIS [4]. JEMRIS solves the resulting Bloch equations using the numerical ordinary equation solver CVODE [5] and is thus capable of calculating the complete signal resulting from the ICM without further approximations such as the MEA.

Methods:

The ICM was implemented into JEMRIS as follows: in a bounding box of definable size, infinite cylinders of random orientation are placed until the cerebral blood volume (CBV) is reached. Each cylinder is defined as capillary, arteriole or venule according to the relative cerebral blood volume (rCBV) of each compartment. A typical micro-vascular environment generated by this approach is shown on the right. Spins are then placed randomly inside the micro-vascular environment. Spins placed inside a cylinder are assigned the T_1/T_2 values of blood while extra-vascular spins have parameters defined for tissue. During the simulation of the pulse sequence, the extra-vascular spins diffuse inside the micro-vascular environment thus experience different magnetic field shifts, ΔB, over time. These shifts induced by the blood vessels are calculated at each point in space as a superposition of the contributions of all cylinders. To permit a comparison of the results with the analytical model proposed by Uludag et al. [2] all simulation parameters are chosen in accord with that paper, including CBV, rCBV for each compartment, vessel radii, vessel oxygenation, $T_{1/2}(B_0,Y)$, diffusion constant. As in [2], the macro-vascular environment is modelled by a single vein with r=100µm oriented at 90° to the main magnetic field.



Results:

The resulting BOLD signals $\Delta S=S_{act}-S_{bl}$ are shown in Figure 1 together with the corresponding results from the MEA (extra-vascular signal only; circles: simulation, lines: MEA; light/dark gray: micro-/macro-vasculature; B_0=16T). For mono-exponential decay the maximum BOLD signal is located at $TE=T_2$ whilst using the signal from the ICM without further approximations shows a vessel radius dependent delay of the extra-vascular BOLD signal to higher echo times and thus a high ratio R for echo times shorter than T_2. To investigate this further, R was calculated at multiple B_0 for multiple TE using the full micro-vasculature model as described in the methods. The results are shown in Figure 2 using the analytical model from Uludag et al. [2] (left) and using the simulations without the MEA (right). Obviously, the predicted optimal signal ratio is considerably different if the signal resulting from the ICM is not approximated by a mono-exponential decay. This difference is mainly attributed to different results from the macro-vascular model.

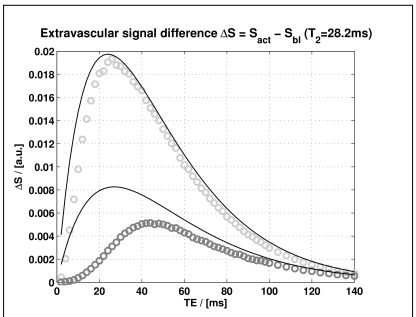


Figure 1

Discussion:

The simulation shows that for large vessels using spin echoes the MEA is no longer a good approximation for the extra-vascular signal resulting from the ICM. Using the full signal of the ICM reveals a vessel radius dependent initial delay of the BOLD signal which is not observable if the MEA is used to simplify the calculation. This initial delay can be exploited to increase BOLD specificity by using echo times shorter than T_2. The intra-vascular BOLD signal which was not shown in Figure 1 compromises the BOLD signal ratio for very short echo times (Figure 2, right). At very high magnetic fields, however, the intra-vascular BOLD signal decays rapidly due to the very short T_2 of blood, and thus a considerable BOLD signal ratio is again predicted. Diffusion gradients are sometimes used to increase R by suppressing the intra-vascular BOLD signal [6]. This approach could be combined with the shown results by additionally using an echo time shorter than T_2 an thereby potentially further increase R.

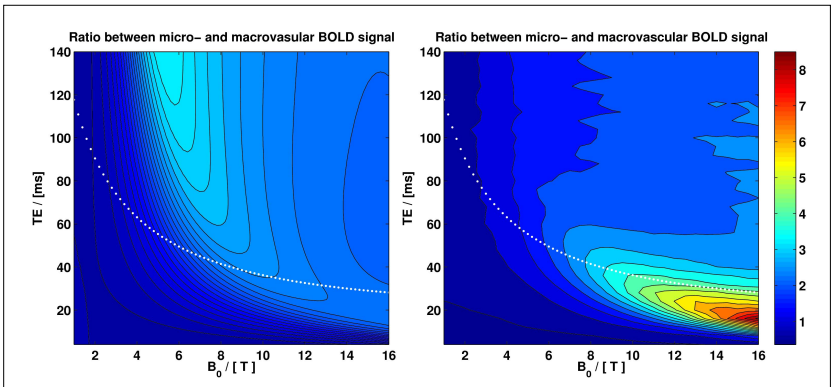


Figure 2: BOLD signal ratio R with (left) and without (right) the MEA, same color scale. White dots: $T_2(B_0)$ used in simulation (see [2]).

References: [1] Ogawa et al. (1993) Biophys. J. 64:803-812. [2] Uludag et al. (2009) NeuroImage 48:150-165. [3] Harel et al. (2006) J. Mag. Res. Imag. 23:945-957. [4] Stoecker et al. MRM, *submitted; www.jemris.org* [5] Cohen, Hindmarsh (1996) Comput. Phys. 10:138-143. [6] Yacoub et al. (2003) MRM 49:655-664.