

# Increased T2-sensitivity in BOLD fMRI using stimulated echoes: A Monte-Carlo simulation

U. Goerke<sup>1</sup>, K. Ugurbil<sup>1</sup>

<sup>1</sup>CMRR/University of Minnesota, Minneapolis, Minnesota, United States

## Introduction:

It has previously been shown that the relative BOLD signal changes in a stimulated echo sequence are larger than in a spin echo experiment [1, 2]. In the presented study, the relative signal changes are calculated using Monte-Carlo simulations as a function of echo and mixing time. The shortening of the extravascular  $T_2$  due to diffusion of water molecules in the presence of magnetic field gradients in the vicinity of capillaries, venules, and small veins was computed. The simulations are compared with experimental results [2].

## Simulation:

In the Monte-Carlo simulation, artificial vessel networks were generated for a variety of vessels of different diameters and vessel densities obtained from ref. [3] for the human cortex. Vessels were arranged on a face-centered cubic lattice. The spacing between vessels was determined from the relative blood volume fraction. Three different network structures were simulated based physiological vessel structures which are predominate in different vascular layers [3]: random orientations in three dimensions, random orientations in a plane, and a preferential orientation of vessels. Each simulated vessel network contained vessels of a fixed diameter forming one kind of network structure with constant vessel density. Vessel networks with pial veins, branching venules, or capillaries were simulated. Capillaries were assumed to be permeable [4].

For each set of parameters, four network structures were generated. In each artificial vascular network, 250 spins performed a random walk with an apparent diffusion coefficient of  $D = 10^{-3}$  mm<sup>2</sup>/s. Changes of the local static magnetic field distortion in the extravascular space due to variations of the blood oxygenation level were calculated using the model and physiological parameters in ref. [5]. A main magnetic field strength of 7 T was assumed. The magnetic field variations, which the spins experience during their random walks through the vascular network, were computed. As diffusion distances are much longer for stimulated echoes compared to gradient-echo or spin-echo sequences, the field distortions of neighboring vessels were taken into account.

The signal phase of each diffusing spin was calculated for the primary (PRE) and the stimulated echo (STE) in a stimulated echo sequence and averaged over all possible orientations relative to the main magnetic field direction. In a spin ensemble, the phase distribution is broadened since each spin starts and ends at a different location within in the magnetic field distribution created by the vascular network. The echo signal intensity is attenuated depending on the spread of the spin phases.

Each simulation represents a fixed vessel size in one kind of network structure with a constant vessel density. They were combined to a representative voxel of 2x2x2 mm<sup>2</sup> including all vascular layers at a ratio simulating the microanatomical structure in human gray matter [3]. Relative signal changes were computed for two limiting cases. In the multi-compartment (mc) approximation, the diffusion distance is shorter than the thickness of the individual vascular layers described by the simulated network structures. The different pools of water molecules do not exchange. For long diffusion times, water molecules diffuse long distances and exchange between different regions with different network structures and vessel types. In this limiting case, the average signal attenuation was calculated using the single compartment (sc) approximation. For both cases, the relative signal changes were calculated for the primary and the stimulated echo as a function of mixing ( $T_M$ ) and echo time ( $T_E$ ).

## Experimental:

Experiments were performed on a 7 T varian scanner using a quadrature surface radio-frequency coil. The presented visual stimulus consisted of 30 s of flashing checkerboard alternated with 39 s of resting condition. For the fMRI experiments, a stimulated echo sequence with EPI readout was used [2]. In the first study, the mixing time was varied ( $T_M = 75$  ms, 325 ms, 575 ms, and 825 ms) keeping the echo time  $T_E = 60$  ms constant. In the second study, the echo time was incremented (PRE: 25 ms, 40 ms, 60 ms, and 80 ms; STE: 21 ms, 40 ms, 60 ms, and 80 ms) at constant  $T_M = 575$  ms. In each study, six healthy volunteers participated. Relative signal changes were calculated for ROI in the primary visual cortex, and the group averages of the relative signal changes were computed.

## Results and discussion:

Figure 1 shows the relative signal changes, which were obtained from the simulations and the experiments. The simulations predict an increase of the relative signal change as a function of echo and mixing time. Furthermore, the relative signal changes of the STE are larger than the ones of the PRE. These findings are consistent with the experimental observations. The experimental results are closer to the single-compartment model indicating an efficient exchange of water molecules between different vascular layers as expected for long diffusion times. It is concluded that the increase of relative BOLD signal changes of the STE predominately originate from an enhancement of  $T_2$ -sensitivity as a result of a more efficient dynamic averaging of the STE compared to the PRE.

## References and acknowledgments:

[1] Goerke U, Moller HE, Time course of transient changes of the apparent self-diffusion coefficient during task activation, ISMRM Kyoto (Japan) 2004; [2] Goerke U, Van de Moortele P-F, Ugurbil K, Increased T2-sensitivity in BOLD fMRI using stimulated echoes, ISMRM Miami (Florida, USA) 2005; [3] Duvernoy HM, Delon S, Vanson JL, Cortical blood vessels of the human brain. *Brain Res. Bulletin* 7: 519 (1981); [4] Regan DG, Kuchel PW. Mean residence time of molecules diffusing in a cell bounded by a semi-permeable membrane: Monte Carlo simulations and an expression relating membrane transition probability to permeability. *European Biophysics Journal* 29: 221 (2000); [5] Fujita N, *MRM* 46: 723 (2001).

Financial support by the MIND Institute, the KECK Foundation, and the grant BTRR P41 008079 is acknowledged.

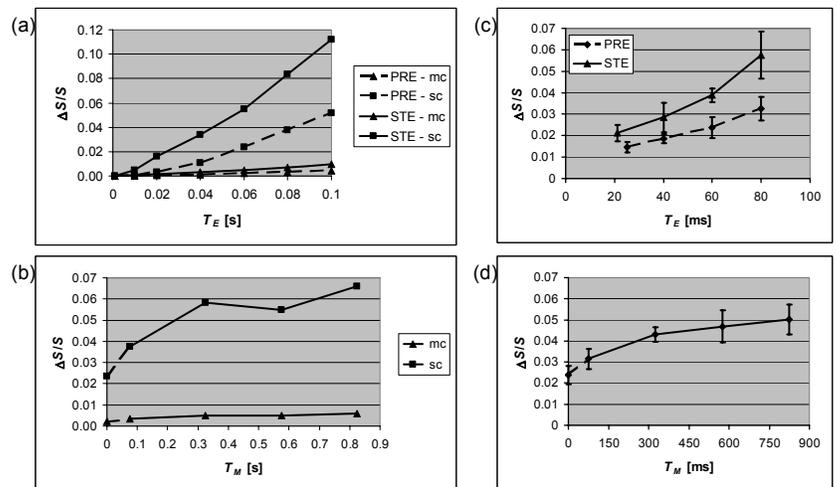


Figure 1: Relative signal changes as a function of (a), (c) echo and (b), (d) mixing time. (a), (b) Monte-Carlo simulations for a representative voxel. (c), (d) Experimental results. PRE: primary echo, STE: stimulated echo; mc: multi-compartment model, sc: single compartment model; (b), (d)  $T_M = 0$  s represents PRE.