DirEct Complex signAl Fitting (DECAF) for multi-compartment analysis in white matter

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Target audience: Researchers interested in multi-compartment analysis in white matter or quantitative myelin imaging.

Purpose: Recent studies have demonstrated that signals from three water compartments-myelin, axonal, and extracellular water-in white matter have different B_0 orientation dependent frequency offsets[1-4]. This observation improved data fitting results in GRE-based MWI by using complex signal fitting as compared to magnitude signal fitting[2,5]. However, the complex signal fitting approaches applied in the previous studies[1,3,4] required several pre-processing steps including a nonlocal background field removal step. Therefore, the results were strongly influenced by them. In this study, we propose a new fitting method that does not require a prior background field removal step. This method shows improvement in parameter estimation.

Methods: The three pool complex signal is modeled as follow:

$$S(t) = (A_{my}e^{-(1/T^*_{2,my}+i2\pi\Delta f_{my})t} + A_{ax}e^{-(1/T^*_{2,ax}+i2\pi\Delta f_{ax})t} + A_{ex}e^{-(1/T^*_{2,ex}+i2\pi\Delta f_{ex})t})\, e^{-(i2\pi\Delta f_{bg})t}\, e^{-(i\emptyset_0)},$$

where A_i, $T^*_{2,i}$, Δf_i: relative amplitude, relaxation time, and frequency offset of each compartment (i = my: myelin, ax: axonal, and ex: extracellular water), Δf_{bg}: nonlocal background frequency offset, $\emptyset_0$: a phase offset from transmit B_1. In the previous studies[1,3,4], the background frequency and phase offset terms (Δf_{bg} and $\emptyset_0$) were estimated and removed before data fitting. In our method, these terms were estimated during the fitting as follows: First, Δf_{bg} was merged into the frequency offset terms of each pool ($S(t) = (A_{my}e^{-(1/T^*_{2,my}+i2\pi\Delta f_{my+bg})t} + A_{ax}e^{-(1/T^*_{2,ax}+i2\pi\Delta f_{ax+bg})t} + A_{ex}e^{-(1/T^*_{2,ex}+i2\pi\Delta f_{ex+bg})t})\, e^{-(i\emptyset_0)}$ where $\Delta f_{my+bg} = \Delta f_{my} + \Delta f_{bg}$, $\Delta f_{ax+bg} = \Delta f_{ax} + \Delta f_{bg}$, and $\Delta f_{ex+bg} = \Delta f_{ex} + \Delta f_{bg}$). Then, this new model was fitted to complex data using an iterative non-linear curve fitting algorithm (*lsqnonlin* in MATLAB). The initial values and ranges for the fitting parameters are listed in Table 1. After estimating all parameters, Δf_{my} and Δf_{ax} were approximated by $\Delta f_{my+bg} - \Delta f_{ex+bg}$ and $\Delta f_{ax+bg} - \Delta f_{ex+bg}$, respectively. These approximations were supported by a recent observation that the frequency offset of the extracellular water pool is close to zero[4]. Eleven volunteers (IRB-approved) were scanned at 3T (Siemens). A 3D GRE was acquired with following parameters: TR = 120 ms, # echoes = 32, TE_1 = 2.1 ms, ΔTE = 1.9 ms, flip angle = 30˚, BW = 1502 Hz/px, 2 mm isotropic voxel, and 72 slices. DTI was acquired. For comparison, the fitting was also performed for complex data with high-pass filtered phase with different kernel sizes (Gaussian; σ = 2, 4, 8 mm).

	Myelin water (my)			Axonal water (ax)			Extracellular water (ex)			Offset
	A_{my} (a.u.)	$T_{2,my}^*$ (ms)	Δf_{my+bg} (Hz)	A_{ax} (a.u.)	$T_{2,ax}^*$ (ms)	Δf_{ax+bg} (Hz)	A_{ex} (a.u.)	$T_{2,ex}^*$ (ms)	Δf_{ex+bg} (Hz)	$\emptyset_0$(rad)
Initial value	$0.1\times\lvert S_1\rvert$	10	$\Delta f_{bg,init}$	$0.6\times\lvert S_1\rvert$	64	$\Delta f_{bg,init}$	$0.3\times\lvert S_1\rvert$	48	$\Delta f_{bg,init}$	$\angle S_1$
Lower bound	0	3	$\Delta f_{bg,init}$ -75	0	24	$\Delta f_{bg,init}$ -25	0	24	$\Delta f_{bg,init}$ -25	-π
Upper bound	$2\times\lvert S_1\rvert$	24	$\Delta f_{bg,init}$ +75	$2\times\lvert S_1\rvert$	150	$\Delta f_{bg,init}$ +25	$2\times\lvert S_1\rvert$	150	$\Delta f_{bg,init}$ +25	π

Table 1. Initial values and search boundary. $S_1 = S(TE_1)$. $\Delta f_{bg,init} = \angle\{\sum_{n=1}^{17} S_n^* S_{n+1}\}/(2\pi\Delta TE)$: initial Δf_{bg}.

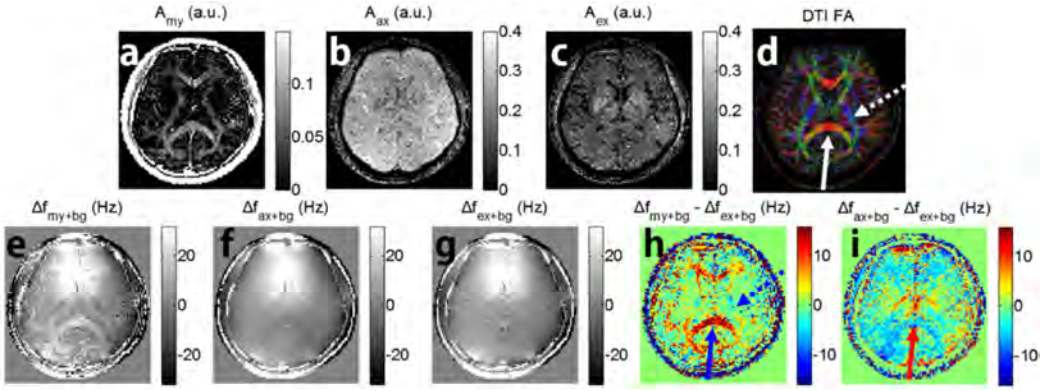

Figure 1. Estimated parameters using the proposed method

Results: Figure 1 shows the estimated parameters from the proposed complex signal model. Despite Δf_{bg} terms merged in each frequency offset maps (Fig. 1e, f, g), microstructural frequency contrasts are observable for the myelin and axonal water compartments. The approximated Δf_{my} map (Fig. 1h) indicates large positive values in the perpendicular fibers (solid blue arrow) and relatively small values in the parallel fibers (dashed blue arrow). In the approximated Δf_{ax} map (Fig. 1i), negative values are observed in the perpendicular fibers (solid red arrow). These contrasts are in accordance with those from the previous studies[3,4]. The results from the high-pass filtered phase data (Fig. 2) demonstrates that the background field estimation process has significant effects on the parameter estimation, which confirms the advantage of our new method.

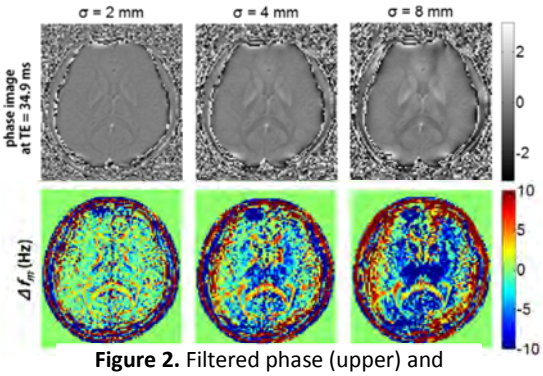

Figure 2. Filtered phase (upper) and Δf_{my} (lower) images

Discussion & Conclusion: We demonstrated that the proposed method is effective in the multi-compartment analysis of complex GRE data. As shown in Figure 2, imperfect filtering before the model fitting leads to incorrect parameter estimation. Although more sophisticated processing may reduce these errors[1,3,4], it still pertains residual errors that could be significant during the sensitive data fitting process.

References: 1. Schweser, ISMRM 2011, p4527; 2. Van Gelderen, MRM 67, 2012; 3. Wharton PNAS, 2012; 4. Sati, Neuroimage, 2013; 5. Nam, ISMRM 2014, p337