RESEARCH ARTICLE

Quantitative MRI by nonlinear inversion of the Bloch equations

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Purpose: Development of a generic model-based reconstruction framework for multiparametric quantitative MRI that can be used with data from different pulse sequences.

Methods: Generic nonlinear model-based reconstruction for quantitative MRI estimates parametric maps directly from the acquired k-space by numerical optimization. This requires numerically accurate and efficient methods to solve the Bloch equations and their partial derivatives. In this work, we combine direct sensitivity analysis and pre-computed state-transition matrices into a generic framework for calibrationless model-based reconstruction that can be applied to different pulse sequences. As a proof-of-concept, the method is implemented and validated for quantitative T1 and T2 mapping with single-shot inversion-recovery (IR) FLASH and IR bSSFP sequences in simulations, phantoms, and the human brain.

Results: The direct sensitivity analysis enables a highly accurate and numerically stable calculation of the derivatives. The state-transition matrices efficiently exploit repeating patterns in pulse sequences, speeding up the calculation by a factor of 10 for the examples considered in this work, while preserving the accuracy of native ordinary differential equations solvers. The generic model-based method reproduces quantitative results of previous model-based reconstructions based on the known analytical solutions for radial IR FLASH. For IR bSSFP it produces accurate T1 and T2 maps for the National Institute of Standards and Technology (NIST) phantom in numerical simulations and experiments. Feasibility is also shown for human brain, although results are affected by magnetization transfer effects.

Conclusion: By developing efficient tools for numerical optimizations using the Bloch equations as forward model, this work enables generic model-based reconstruction for quantitative MRI.

KEYWORDS
Bloch equations, model-based reconstruction, nonlinear inversion, quantitative MRI, sensitivity analysis, state-transition matrix

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1 | INTRODUCTION

Conventional quantitative MRI is based on a two-step process, where first intermediate images are reconstructed and then physical models are fitted pixel-wisely to obtain parameter maps. Acquiring a sufficient amount of high-quality images with carefully designed contrasts is required for achieving a good fit. For this reasons, these methods are too slow for many clinical applications. In contrast, nonlinear model-based reconstruction methods formulate image reconstruction as a single inverse problem. They exploit a physical model of the measurement process and directly estimate quantitative parameter maps from k-space. Thus, they make optimal use of the available data and enable highly efficient parameter mapping from signals acquired with sequences that make use of transient magnetization dynamics. These techniques have two problems: They are computationally demanding and they need to be specially designed for each application.

Alternatively, fingerprinting uses a lookup dictionary obtained by Bloch simulations to map the pixels of intermediate images computed directly from undersampled data to quantitative parameter maps. This enables multiparametric mapping with high acceleration in a flexible and computationally efficient framework, but is not optimal due to its lack of a least-squares data consistency term. Subspace models can be exploited for a more efficient mapping by approximating the physical signal with a larger linear subspace. They reduce the computational demand of the reconstruction very efficiently, but are still not optimal because a linear subspace is used to approximate the manifold of possible signals. For complicated spin dynamics a larger number of subspace coefficients may be needed to accurately represent the signal, rendering subspace methods less efficient.

The aim of this work is to develop a generic framework for nonlinear model-based reconstruction with accurate signal models for different MRI sequences even with complicated spin dynamics. The generalization of the forward model then allows the use of optimized sequences for which no analytical expression for their signal can be derived. Fundamentally, such a generic method requires efficient techniques to compute the partial derivatives of the Bloch equations. So far, two different methods were used in MRI. First, symbolic derivatives can be calculated for analytical solutions of the Bloch equations for special sequences and this can be generalized to chains of small blocks using automatic differentiation. These methods require idealized assumptions such as hard pulse approximation and perfect inversion. In more complicated scenarios with long pulses or imperfect inversion they require high discretization rates or suffer from errors. Second, derivatives can be estimates using difference quotients (DQ). This method fully exploits the generality of full Bloch simulations, but is computational expensive and requires careful tuning to balance accuracy and noise amplification.

To overcome these limitations, this work uses a direct sensitivity analysis to compute the derivatives of the Bloch equations for arbitrary sequences with high accuracy by solving an extended system of ordinary differential equations (ODE). The technique is validated using an analytical model of an IR bSSFP sequence and is compared to results obtained from DQ methods. To further improve computation speed, precomputed state-transition matrices (STMs) are applied to arbitrary initial conditions solving the required ODEs for all repeating parts of an MRI sequence efficiently. They are validated by comparing them to the direct application of a Runge-Kutta ODE solver. We further integrate both techniques in a nonlinear model-based reconstruction with integrated calibration-less parallel imaging. For IR FLASH, we show that the methods reproduce the results of an analytical model. In a numerical and measured phantom study with an IR bSSFP sequence we refine the flexible forward model of the generic model-based reconstruction to include realistic simulations with slice-selective excitations and hyperbolic secant inversion pulses. Thus, we show that the reconstruction quality benefits much from the more physically accurate modeling leading to accurate T1 and T2 parameter maps. Finally, we test the developed technique on in vivo brain data from a healthy volunteer.

Parts of this work have been published in References 20-23.

2 | THEORY

In the following, we briefly explain the concepts of a direct sensitivity analysis and its application to the Bloch equations (SAB). We then describe how STMs can be used to accelerate the solution of the ODEs. Afterwards, both methods are integrated into a nonlinear model-based reconstruction method.

2.1 | Sensitivity analysis of the Bloch equations

We consider the temporal evolution of a magnetization vector $\mathbf{M}(c, t)$ depending on a vector of parameters $c$ and time $t$. The temporal behavior of its components $M_i(c, t)$ is described by the Bloch equations as a system of ODEs
where \( f \) defines the dynamics. The partial derivative of the component \( M_i \) with respect to the parameter \( c_j \) defines the \((i,j)\)th entry

\[
Z_{ij}(t) = \frac{\partial M_i(c, t)}{\partial c_j},
\]

(2)

of the sensitivity matrix \( Z(t) \).

Using direct sensitivity analysis \(^{19} \) one obtains \( Z(t) \) by solving an additional set of ODEs. Assuming that the partial and ordinary differential equations interchange, the time derivative of the \((i,j)\)th entry of \( Z \) is

\[
\frac{d}{dt} Z_{ij}(t) = \frac{d}{dt} \left( \frac{\partial M_i(c, t)}{\partial c_j} \right) = \frac{\partial}{\partial c_j} \left( \frac{dM_i(c, t)}{dt} \right). \tag{3}
\]

Substituting \( \frac{dM_i(c, t)}{dt} \) then yields

\[
\frac{d}{dt} Z_{ij}(t) = \frac{\partial}{\partial c_j} f_i(M(c, t), c, t). \tag{4}
\]

With the chain rule, the resulting ODE becomes

\[
\frac{d}{dt} Z_{ij}(t) = \frac{\partial f_i(M(c, t), c, t)}{\partial c_j} + \sum_j \frac{\partial f_i(M(c, t), c, t)}{\partial M_j} \frac{dM_j(c, t)}{dt} Z_{ij}, \tag{5}
\]

where \( \frac{\partial f_i(M(c, t), c, t)}{\partial M_j} \) describes the \((i,j)\)th element of the Jacobian \( J_{ij} \). This can be written compactly for the sensitivity matrix \( Z(t) \) as

\[
\frac{d}{dt} Z(t) = f_z(M(c, t), c, t) + J(M(c, t), c, t) \cdot Z(t). \tag{6}
\]

If a direct sensitivity analysis is applied to the Bloch equations for the parameters \( R_1 \), \( R_2 \), and \( B_1 \), the ODE in Equation (6) describing the temporal evolution of the sensitivities becomes

\[
\frac{d}{dt} Z = \begin{bmatrix}
0 & -M_x & -\gamma \sin \phi M_x \\
0 & -M_y & \gamma \cos \phi M_z \\
M_0 - M_z & 0 & \gamma (\sin \phi M_x - \cos \phi M_y) \\
-\gamma B_2 & -R_2 & -\gamma \sin \phi B_1 \\
\gamma \sin \phi B_1 & -\gamma \cos \phi B_1 & -R_1
\end{bmatrix} \cdot Z. \tag{7}
\]

depending on the \( x \), \( y \), and \( z \) components of the magnetization \( M \), the magnetic fields \( B_2 \) and \( B_1 \) as well as the radiofrequency (RF) pulse phase \( \phi \). Equation (7) is solved jointly with the Bloch Equation (1) which provide the time-dependent solutions for \( M_x \), \( M_y \), and \( M_z \).

### 2.2 State transition matrices

By embedding the magnetization vector into a four-dimensional space

\[
M(c, t) = \begin{bmatrix}
M_x(c, t) \\
M_y(c, t) \\
M_z(c, t) \\
1
\end{bmatrix}, \tag{8}
\]

we obtain a formulation of the Bloch Equation (1) as a system of homogeneous ODEs

\[
\frac{dM(c, t)}{dt} = f(M(c, t), c, t) = A(c, t) M(c, t), \tag{9}
\]

with the system matrix

\[
A(c, t) = \begin{bmatrix}
-R_2 & \gamma G_z(t) \cdot r & -\gamma B_z(t) & 0 \\
-\gamma G_z(t) \cdot r & -R_2 & \gamma B_z(t) & 0 \\
\gamma B_y(t) & -\gamma B_z(t) & -R_1 & M_0 R_1 \\
0 & 0 & 0 & 0
\end{bmatrix}. \tag{10}
\]

at location \( r \) depending on time \( t \), the \( z \)-gradient \( G_z \) and the magnetic fields \( B_{xy} \).

The Bloch equations can be solved directly for time-dependent coefficients \( A(t) \) using standard ODE solvers. Here we describe the precomputation of STMs as more efficient way to solve the equations for MRI sequences with repeating patterns. A STM \( S_{t_i \rightarrow t_2} \) describes the evolution of an arbitrary starting magnetization \( M(c, t_1) \) for the time span from \( t_1 \) to \( t_2 \) including all effects from relaxation and time-dependent external RF fields. This compresses the temporal evolution to a single matrix multiplication

\[
M(c, t_2) = S_{t_i \rightarrow t_2} M(c, t_1). \tag{11}
\]

The computation of \( S_{t_i \rightarrow t_2} \) is based on derivation of Equation (11)

\[
\frac{dM(c, t_2)}{dt_2} = \frac{d}{dt_2} \left( S_{t_i \rightarrow t_2} M(c, t_1) \right). \tag{12}
\]

Using the Bloch Equations (9) to replace the time derivative on the left side and using \( \frac{dM(c, t_1)}{dt_1} = 0 \) for the right, we obtain

\[
A(t_2)M(c, t_2) = \left( \frac{d}{dt_2} S_{t_i \rightarrow t_2} \right) M(c, t_1). \tag{13}
\]

By using Equation (11) and switching both sides we obtain

\[
\frac{d}{dt_2} S_{t_i \rightarrow t_2} M(c, t_1) = A(t_2)S_{t_i \rightarrow t_2} M(c, t_1). \tag{14}
\]
As this holds for arbitrary \( M(c, t_1) \) and by renaming \( t_2 \) as \( t \) a system of ODEs
\[
\frac{d}{dt} S_{t_1 \rightarrow t} = A(t)S_{t_1 \rightarrow t},
\]
for the entries of the STM is derived. This ODEs (15) can be solved for estimating \( S_{t_1 \rightarrow t} \) column-wisely with an ODE solver\(^{24,25} \) with initial conditions
\[
S_{t_1 \rightarrow t_1} = 1 .
\]

The solution of the state-transition ODE in Equation (15) can be formally defined as a time ordered exponential
\[
S_{t_1 \rightarrow t_2} = \prod_{t_1}^{t_2} e^{A(r) \Delta r} \equiv T \left\{ e^{\int_{t_1}^{t_2} A(r) \, dr} \right\} .
\]
\[
\equiv \lim_{N \to \infty} \left( e^{A(t_N) \Delta t} e^{A(t_{N-1}) \Delta t} \ldots e^{A(t_1) \Delta t} \right) .
\]

This links the proposed technique to approximation methods based on matrix-exponentials computed using discretized sampling\(^{26,27} \).

This technique is not limited to the Bloch equations, but can be extended to also include the sensitivity analysis for the three partial derivatives \( R_1, R_2, \) and \( B_1 \). This is further described in Appendix A.

### 2.3 Bloch model-based reconstruction

In the following, we integrate the generic Bloch operator \( B \) into a nonlinear model-based reconstruction framework with non-Cartesian, calibrationless, parallel imaging and compressed sensing as illustrated in Figure 1. The reconstruction method solves the nonlinear inverse problem for the maps \( x = (x_p \, x_c)^T \) with the physical parameters \( x_p = (R_1 \, R_2 \, M_0 \, B_1)^T \) and coil sensitivities \( x_c = (c_1 \ldots c_N)^T \) by optimizing
\[
\hat{x} = \arg\min_x \| y - A(x) \|^2_2 + a Q(x_c) + \beta R(x_p) .
\]

Equation (19) includes the forward-operator \( A \), the measured data \( y \), the Sobolev norm \( Q \) with its regularization parameter \( a \) to enforce the smoothness of coil profiles\(^{28} \) and \( B_1 \) maps. A joint sparsity constraint \( R \) is applied to the other parameter maps.\(^{29,30} \) The full forward operator is \( A = PF CB \). It is solved by the Iteratively Regularized Gauss-Newton Method (IRGNM)
\[
\hat{x}_{n+1} = \arg\min_x \| D_A(x_n)(x - x_n) + A(x_n) - y \|^2_2
+ a_n Q(x_c) + \beta_n R(x_p),
\]

with the Jacobian \( D_A(x_n) \) and the regularization parameters \( a_n = a_0 \cdot q^n \) and \( \beta_n = \beta_0 \cdot q^n \) at the \( n \)th iteration step. Here, \( C \) is the nonlinear parallel imaging operator combining the signal with the coil profiles, \( F \) represents the Fourier operator, \( P \) the sampling pattern. The generic operator \( B \) takes information about the applied sequence and outputs the simulated signal based on the STM technique. The partial derivatives of \( B \) are calculated using the direct sensitivity analysis. The derivatives of \( A \) are described in Appendix B.

### 3 METHODS

#### 3.1 Implementation

All simulations and reconstructions are implemented in the Berkeley Advanced Reconstruction Toolbox (BART) using single-precision floating point arithmetic.\(^{31} \) The Bloch operator \( B \) is implemented in BARTs nonlinear operator framework.\(^{32} \) The calibrationless model-based reconstruction is based on an IRGNM-FISTA following Wang et al.\(^{13} \) and we refer to this work for further details. The Bloch operator includes a pixel-wise calculation of the signal evolution using STMs (Section 2.2) and of the partial derivatives with SAB (Section 2.1). ODEs are solved using the a Runge–Kutta algorithm (RK54) with adaptive step-sizes. The error tolerances are chosen to be \( 10^{-7} \) for the simulation comparisons in Sections 2.1 and 2.2 as well as \( 10^{-6} \) for further reduced computational costs in the Bloch model-based reconstructions. The Runge–Kutta solver exploits weights published by Dormand and Prince.\(^{33} \) For balancing the relative scaling of the partial derivatives during the optimization of Equation (19) pre-conditioning following Wang et al.\(^{13} \) is used. The initial wavelet regularization is set to \( a_0 = \beta_0 = 1 \) and decreased by \( q = 1/2 \) in each Newton iteration. The output of the Bloch model operator \( B \) is scaled according to Section D. As a globalized Newton method, the IRGNM does not require fine tuning of initial values. Here, the maps are initialized with the constants \( R_1 = 1 \) Hz, \( R_2 = 1 \) Hz, \( M_0 = 1 \), \( B_1 = 0 \) and the coil profiles are initialized with zero.

For comparison, we also implemented the reparameterized Look-Locker model from Equation (C4) in the same model-based reconstruction framework following Wang et al.\(^{13} \)

#### 3.2 Validation of Bloch simulation

The accuracy of the SAB technique is validated with an IR bSSFP sequence for tissue with \( T_1/T_2 = 1250/45 \) ms. An
\[ \hat{x} = \arg\min_{x_c, x_p} (\| y - \mathcal{PFC}(x_c, \mathcal{B}(x_p)) \|^2_2 + \alpha q(x_c) + \beta r(x_p)) \]

\[ y \xrightarrow{\mathcal{B}} \]

\[ \frac{dM}{dt} = \left( \begin{array}{cccc} -R_2 & \gamma B_z & -\gamma \sin \phi B_1 & 0 \\ -\gamma B_z & -R_2 & -\gamma \cos \phi B_1 & 0 \\ 0 & 0 & -R_1 & R_1 M_0 \\ 0 & 0 & 0 & 1 \end{array} \right) \left( \begin{array}{c} M_x \\ M_y \\ M_z \\ 1 \end{array} \right) \]

\[ \frac{dZ}{dt} = \left( \begin{array}{cccc} 0 & -M_x & -\gamma \sin \phi M_z & 0 \\ -M_y & 0 & \gamma \cos \phi M_z & 0 \\ M_0 - M_z & 0 & 0 & \gamma (\sin \phi M_x - \cos \phi M_y) \end{array} \right) + \left( \begin{array}{cccc} -R_2 & \gamma B_z & -\gamma \sin \phi B_1 \\ -\gamma B_z & -R_2 & -\gamma \cos \phi B_1 \\ \gamma \sin \phi B_1 & -\gamma \cos \phi B_1 & -R_1 \end{array} \right) \cdot Z \]

**Figure 1** Illustration of the operators used in the Bloch model-based reconstruction. The bottom part presents the ODEs for the signal and the derivatives.

Analytical solution for the IR bSSFP signal can be derived from the Bloch equations\(^\text{34}\) assuming hard pulses, a perfect inversion and a perfect nonselective excitation. The symbolic partial derivatives with respect to the parameters \(R_1, R_2, M_0,\) and \(B_1\) are calculated in Appendix F and are used as ground truth. For validation of the derivatives the ODE simulation parameters are chosen to be close to the assumptions of the analytical model. The ODE solution for the derivatives is also compared to the DQ techniques calculated using two simulations \(M_{t,p}\) and \(M_{t,p+h}\) differing by a small perturbation \(h\) for all parameters \(p \in (T_1, T_2, M_0, B_1)\) and time points \(t:\)

\[ \frac{dM_{t,p}}{dp} \approx \frac{M_{t,p+h} - M_{t,p}}{h}. \]  

(21)

The size of the perturbation is decreased until numerical noise dominates.

To validate the STM approach in the presence of RF pulses, gradients, and relaxation, a slice-selective excitation of a Hamming-windowed sinc-shaped inversion pulse with \(T_{RF} = 1\) ms, BWTP = 1, \(\Delta z = 10\) mm, \(G_z = 10\) mT/m is simulated. Relaxation parameters are selected based on typical human white matter values at 3 T: \(T_1/T_2 = 832/80\) ms.\(^\text{35}\) The STM simulation is computed with the Runge–Kutta solver and the magnetization just before the slice rewinder is compared to a direct simulation exploiting the same solver. For comparison a traditional Bloch simulation technique based on temporal discretization with rotational matrices (ROT) is performed using a discretization rate of 1 MHz. According to the analysis shown in Figure S3, a sampling rate of 1 MHz is required for ROT to accurately model complex spin dynamics that include slice-selective RF pulses.

The simulation speed is analyzed for a FLASH sequence with \(FA = 8^\circ\), pulse repetition time/echo time (TR/TE) = 3.1/1.7 ms and \(T_{RF} = 1\) ms simulated for 101 isochromats homogeneously distributed along a slice of 0.02 m width and using a slice-selection gradient of 12 mT/m. The tissue parameters are set to relaxation times of white matter at 3 T. The simulations were executed on a single Intel(R) i7-8565U CPU core at 1.80 GHz.

### 3.3 Validation of reconstruction

To validate the model-based reconstruction we further perform validations on numerical and experimental
phantoms as well as in vivo data for both single-shot IR FLASH and IR bSSFP sequences with tiny golden-angle-based radial sampling. The IR bSSFP sequence includes a prior $a/2$-TR/2 pulse to achieve a smooth signal evolution during the transient state. To be able to decouple the information of $T_1$ and $T_2$ for an IR bSSFP sequence (see Section E) a $B_1$ map is acquired on the same slice using a vendor protocol based on rapid $B_1$ estimation with preconditioned RF pulses and Turbo-FLASH readout. All sequence parameters are shown in Table F1.

Phantom data for an IR FLASH sequence published by Wang et al. was downloaded from Zenodo. This data was measured on a 3 T Magnetom Skyra by Siemens Healthcare with a 20-channel head-coil. The measured phantom is a commercial reference phantom (Diagnostic Sonar LTD, Eurospin II, gel 3, 4, 7, 10, 14, and 16) consisting of six tubes with known $T_1$ relaxation values surrounded by water. A digital phantom of the dataset is created with the same sequence and acquisition characteristics as the downloaded measurement. The relaxation parameters were set to the estimated reference $T_1$ and $T_2$ values from previous studies. Additional phantom data for a radial single-shot IR bSSFP sequence was acquired on the $T_2$ spheres of a National Institute of Standards and Technology (NIST) phantom on the same scanner and the same 20-channel head-coil. For comparison gold-standard maps of $T_1$ and $T_2$ are estimated on the same slice of the NIST phantom used for decoupling the information of $T_1$ and $T_2$ for an IR FLASH sequence published by Wang et al. The measured $T_2$-spheres of the NIST geometry are corrected in both cases using the correction published by Deichmann et al.

The method is numerically validated using a digital phantom of the $T_2$ sphere of the NIST phantom (model version 130) implemented in BART. The multicoil phantom is simulated in the frequency domain with the same sequence parameters as the measurement. The eight coils are compressed to four virtual coils using a singular-value decomposition (SVD). Complex Gaussian noise is added before coil compression to further avoid an inverse crime. To ensure realistic physical conditions the simulated signal model includes a nonselective hyperbolic secant inversion pulse and slice-selective excitations using multiple isochromats distributed over equally spaced slice-selection gradient positions.

While analytical solutions of the Bloch equations require the assumption of perfect inversions and ideal non-selective excitation, the generic simulation of the Bloch model-based reconstruction technique can simulate more realistic signal models. We show how stepwise improvements to the model allow more accurate modeling of actual measurements. This is demonstrated on the numerical and measured NIST phantom datasets by performing reconstructions with various different assumptions about the signal model. The first reconstruction uses a model close to the analytical formula by assuming a perfect inversion and a nonselective excitation. We then add a realistic slice-selective excitation simulated as mean signal of various homogeneously spaced isochromats along the slice-selection gradient. To also model the effect of nonoptimal inversion efficiency, the final reconstruction includes an extended model with realistic nonselective hyperbolic secant inversion.

The radial single-shot IR bSSFP in vivo data is reconstructed using the most realistic model. For comparison, the single-shot IR FLASH measurement was acquired on the same slice and reconstructed with the Bloch model-based reconstruction assuming a realistic IR FLASH signal model with nonselective hyperbolic...
secant inversion and gradient-based slice-selective excitation model to estimate a $T_1$ map.

Details about the measurements can be found in Table F1.

4 | RESULTS

4.1 | Validation of Bloch simulation

Figure 2 shows the partial derivatives for an IR bSSFP sequence with respect to $R_1$, $R_2$, and $B_1$ for the analytical reference, the SAB technique and DQ techniques with different perturbations $h$ on the left. On the right Figure 2 presents the differences of DQ and SAB to the analytical reference.

As expected, the error of DQ decreases for small perturbations until numerical noise starts to dominate for very small $h$.

The SAB technique demonstrates a high accuracy and precision of estimating partial derivatives without requiring tuning of the perturbation level.

Figure 3A compares the simulation results of a Hamming-windowed sinc-shaped inversion pulse using...
The slice-selection gradient based simulation for a Hamming-windowed sinc-shaped inversion pulse simulated with the RK54 framework is shown (left). The point-wise errors of the RK54 (top), the STM technique (center) and the ROT method (bottom) with sampling rate 1 MHz are plotted for the x-, y- and z-component of the magnetization. Note that the errors are scaled by large factors for visualization.

B: The runtime of the STM technique is compared to the reference RK54 method and a ROT simulation performed with a sampling rate of 1 MHz. The simulation is performed for 101 isochromats homogeneously distributed along a slice-selection gradient during a FLASH sequence for various numbers of repetitions. The maximum of 1000 is chosen to cover about 4 s of acquisition, required to measure enough data points for mapping high T1 values. A more detailed version of this figure has been added to the Supplementary Section S3.

the Runge–Kutta 54 method with Dormand–Prince weights (RK54)STM, and ROT technique.

The error of the STM simulation is dominated by numerical noise due to limited floating point precision. With the parameters used here, the STM technique has substantially lower point-wise errors than ROT.

It demonstrates that STM reproduces the RK54 technique for finding solutions to the Bloch equations extremely well, while ROT is affected by errors due to the discretization with fixed sampling rate and its nature of being a first order method constrained to single floating point precision here. The computational cost of ROT increases linear with higher sampling rates. The STM has higher initial costs than the other techniques which reflect the initial calculation of the STMs. The other methods are therefore faster for a small number of repetitions. For more repetitions, the STM becomes much faster as it requires only a few matrix multiplications per TR. A detailed comparison of the computational cost and accuracy of the RK54, STM, and ROT techniques for various error tolerances and sampling rates can be found in Section S3 and Figure S3.

4.2 Validation of reconstruction

The Bloch model-based reconstruction was compared to the Look-Locker model-based version for simulated (Figure 4A) and measured single-shot IR FLASH phantom data (Figure 4B). Both methods recover high quality T1 maps with small differences. Values for the same Regions-of-Interests (ROIs) are very similar leading to their position on the diagonal of the Bloch versus Look-Locker plot on the most right of Figure 4A,B. The reconstructed tubes are very homogeneous in both reconstructions leading to low standard deviations. Reconstructions using different regularization parameters or no regularization are shown in Figures S4 and S6, respectively.

In the difference map between the T1 maps of the two methods only the water background shows areas with
FIGURE 4  Reconstructed $T_1$ parameter maps for radial single-shot IR FLASH data acquired from a numerical (A) and measured phantom (B) as well as a human brain (C). The Bloch model-based reconstruction and the differences between the two methods are shown in the middle. The difference map is scaled up by a factor of 20 to improve visualization. On the right the $T_1$ values of the color-coded ROIs (arrows) of the Bloch reconstruction vs. Look-Locker reconstruction are plotted together with standard deviations. Besides the in vivo $T_1$ map presented in C, the Bloch model-based technique reconstructs a complex valued $M_0$ map, a relative flip angle map and complex coil sensitivities shown in D.
minor differences. This probably results from small differences in the Sobolev regularization on the flip angle map in both techniques. At the walls of the inner tubes there is not enough signal and the $T_1$ maps are not well defined. Results for the radial single-shot in vivo IR FLASH data are shown in Figure 4C. The parameter maps are visually indistinguishable except for minor artifacts in the areas of the head with flow related effects, which are not modelled by both signal models. The $T_1$ values in the marked ROIs for representative white and gray matter areas show a very good correspondence. The homogeneity within the white matter is high corresponding to a small SD.

The complex $M_0$ parameter map in Figure 4D reconstructed with the Bloch model-based reconstruction is of good quality showing no artifacts and a homogeneous phase. Only in border regions phase changes are present which are most likely caused by fat. The relative flip angle map is globally lower than one. It combines the effect of an imperfect slice-selective excitation and the present $B_1$ field. The intensity and phase of the estimated singular-value decomposition-compressed virtual coil sensitivities is comparable to intensity and phase of sensitivities estimated with ESPIRiT (results not shown).

Figure 5 shows the reconstructed $T_1$ and $T_2$ maps of the digital NIST phantom (Figure 5A) and the measurement (Figure 5B) using the radial single-shot IR bSSFP acquisition for different models compared to the reference values in Bland–Altman plots. The most simplistic model assumes a perfect inversion and an ideal non-selective excitation (Perfect Inversion) and shows inaccuracies in the $T_1$ and $T_2$ estimation. By integrating a slice-selective excitation (Slice) the errors in $T_2$ are significantly reduced leaving an offset in $T_1$. Adding a realistic hyperbolic secant inversion pulse to the forward model (Pulse+Slice) corrects for the $T_1$ offset leading to an accurate estimation of the relaxation parameters. These effects are present in both: the simulation and the measured data reconstructions. Important to note is that the NIST phantoms contain some spheres with extreme $T_1$ and $T_2$ parameters, which were excluded from the Bland–Altman analysis in Figure 5A,B for improved visualization. In particular, the three highest $T_2$ values (1.450, 0.388, and 0.271 s) were removed for the reconstruction from simulated data and the highest and lowest $T_2$ values (1.450, 0.006 s) for the measured data. Especially the simple model has difficulties in finding the correct relaxation parameters in the reconstruction of the measured data, so that the mean value is outside the plotted region. A direct comparison of reference and estimated parameters in a diagonal plot can be found in Figure S1. A Bland–Altman plot with all data points is shown in Figure S2.

Reconstructed $T_1$ and $T_2$ parameter maps for the two single-shot IR bSSFP scans of a human brain are shown in Figure 6. For comparison, a map with the Look-Locker model-based reconstruction of the IR FLASH scan of the same slice is added. Both IR bSSFP reconstructions show large offsets in $T_1$ compared to the IR FLASH reference. The relaxation values for the two analyzed ROIs are listed in Table F2. The differences are smaller for the longer TE and longer RF pulse duration $T_{RF}$ compared to the short pulse protocol. This is likely due to the magnetization transfer effect (MT) that affects the IR bSSFP sequence but is not included in the current study.

The reconstruction times depend on the complexity of the forward model. The reconstruction of the IR FLASH datasets took about 80 s on an AMD EPYC 7662 64-Core CPU and a Nvidia A100-SXM-80GB GPU. The reconstruction of the simple forward model of the IR bSSFP NIST phantom dataset took 60 s, while the most complex model reconstruction took 38 min. The longest reconstruction times were required for the in vivo IR bSSFP dataset with short RF pulse. The strong slice-selection gradient prolonged the reconstruction to about 75 min.

5 | DISCUSSION

A nonlinear model-based reconstruction framework can be used in combination with well-crafted sequences and their analytical signal representations to accelerate quantitative MRI. This work presents a generalization of this well-known approach to arbitrary MRI sequences by exploiting the Bloch equations directly as forward model. This method becomes computationally feasible by including a direct sensitivity analysis of the Bloch equations. It allows us to use a generic ODE solver to compute the derivatives required by efficient nonlinear optimization algorithms such as the IRGNM. In comparison to techniques based on DQ it produces highly stable and accurate partial derivatives without the need of fine-tuning perturbation levels. This was shown by estimating partial derivatives of an IR bSSFP experiment with the mentioned techniques and by comparing their results to the underlying analytical reference.

To further reduce computational demand, we exploit precomputed STMs. They are used to solve the Bloch equations and the system describing their sensitivities simultaneously for arbitrary initial conditions for a given time span. They reduce the spin dynamics even in the presence of external fields, gradients, and relaxation to single matrix multiplications. It dramatically speeds up
the reconstruction whenever the MRI sequence contains repeated patterns as it is often the case. In the presented example of the FLASH sequence with 101 isochromats along a slice and simulated for 1000 repetitions, the run-time of the simulation was reduced by a factor of 10 from 5 s down to 0.5 s in comparison to a regular Runge–Kutta ODE solver. Even in the presence of gradients, RF pulses and relaxation the slice-profile analysis showed the high accuracy of the STM technique in reproducing the ODE solver results.

Experimentally we confirmed that the Bloch model-based reconstruction reproduces the Look-Locker model as a special case. A comparison between both techniques showed only minor differences in the T1 maps reconstructed from the single-shot phantoms and single-shot in vivo data.

The integration of a generic Bloch simulation into the reconstruction adds the flexibility to analyze a broad variety of sequences. As an initial example, we applied the technique to IR bSSFP sequence and validated it using a
FIGURE 6 The $T_1$ parameter map reconstructed from a radial single-shot IR FLASH in vivo dataset with a Look-Locker model-based reconstruction is shown on the left. It also shows the reconstructed $T_1$ parameter maps of a radial single-shot IR bSSFP in vivo dataset acquired on the same brain slice for short RF pulses ($T_{RF}: 1$ ms, $TR: 4.88$ ms) on the top and long RF pulses ($T_{RF}: 2.5$ ms, $TR: 10.8$ ms) on the bottom reconstructed with the Bloch model-based reconstruction. In the center column the difference maps are shown. The values corresponding to the colored ROIs are listed in Table F2. On the right the $T_2$ parameter maps for the short and long RF pulse experiments are shown reconstructed from the IR bSSFP sequence.

numerical and measured NIST phantom dataset. By correctly modeling the slice-selective excitation and a nonselective hyperbolic secant inversion pulse highly accurate $T_1$ and $T_2$ maps could be obtained.

For a human brain, $T_1$ maps estimated from an IR bSSFP sequence were compared to Bloch model-based reconstructions of an IR FLASH acquisition of the same slice both including nonselective hyperbolic inversion and a slice-selective excitation. Here, differences could be observed which are likely caused by MT. This hypothesis is supported by the fact that prolonging the RF pulse duration and increasing the TR reduced the differences, but preliminary results (Section S5) suggest that this does not explain the complete discrepancy and that other effects may also play a role. The NIST phantom measurement is not affected by MT effects, because it is based on water. The IR FLASH measurement is assumed to be unaffected by MT because of its small flip angle.

At this stage, the most relevant practical limitation is the need to manually tune the scaling factors used for preconditioning. For each analyzed sequence the relative scaling between the partial derivatives needs to be balanced manually to ensure smooth convergence. Future work is going to investigate automatic scaling techniques.

Further extensions could be the application to hybrid state free precession sequences, multi-echo inversion-recovery sequences, and MT models.

6 | CONCLUSION

This work developed a generic framework for model-based reconstruction using the Bloch equations. The approach is validated numerically and tested experimentally using phantom and in vivo scans.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interests.
DATA AVAILABILITY STATEMENT
The data of this work was uploaded to Zenodo @doi:10.5281/zenodo.7654462. The scripts reproducing all figures of this manuscript are published at Github @mrirecon/bloch-moba. The reconstruction code is implemented in BART with commit 0e847a2. A tutorial about the usage of the Bloch model-based reconstruction with BART can be found at Github @mrirecon/bloch-tutorial.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher’s website.

Figure S1: Reconstructed T1 and T2 parameter maps and the corresponding ROI values for numerical radial single-shot IR bSSFP data of a digital multicoil reference object simulated in k-space.

Figure S2: A: Reconstructed T1 and T2 parameter maps and all corresponding ROI values for simulated radial single-shot IR bSSFP data.

Figure S3: Simulation accuracy.

Figure S4: Reconstructed T1 parameter maps similar to Figure 4B for varying wavelet regularization strength β0 for the Bloch model-based reconstruction (upper row).

Figure S5: Influence of the magnetization transfer effect.

Figure S6: Bloch model-based reconstruction of an in vivo single-shot IR bSSFP dataset acquired with 1-ms long RF pulses.

Table S1: Table listing the fitting parameters estimated for Figure S5.

Table S2: Table listing the sequence parameters for the analysis in Figure S5.

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The system matrix $A(t)$ in Equation (10) can be extended to include the sensitivity analysis for the three partial derivatives $R_1, R_2,$ and $B_1$:

$$
\begin{bmatrix}
-R_1 & \gamma R_1 & -\gamma R_1 & 0 & 0 & 0 & 0 & 0 & 0 \\
-R_2 & -\gamma R_2 & -\gamma R_2 & 0 & 0 & 0 & 0 & 0 & 0 \\
-\gamma R_1 & -\gamma R_2 & R_1 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
\end{bmatrix}
$$

with its corresponding parameter vector from Equation (9):

$$
\mathbf{M}(t) \rightarrow \mathbf{x}(t) =
\begin{pmatrix}
M_x(t) \\
M_y(t) \\
M_z(t) \\
Z_{R_1,x}(t) \\
Z_{R_1,y}(t) \\
Z_{R_1,z}(t) \\
Z_{R_2,x}(t) \\
Z_{R_2,y}(t) \\
Z_{R_2,z}(t) \\
Z_{B_1,x}(t) \\
Z_{B_1,y}(t) \\
Z_{B_1,z}(t) \\
1
\end{pmatrix}
$$
**APPENDIX B. FORWARD MODEL DERIVATIVES**

The derivative of $A$ in Equation (19) follows by exploiting the Jacobi matrix and the product rule similar to: \(^{13,28}\)

The adjoint of the derivative becomes

\[
DA(x) = \begin{pmatrix}
\frac{dR_1}{dR_2} \\
\frac{dM_0}{dM_2} \\
\frac{dc_1}{dc_2} \\
\vdots \\
\frac{dc_N}{dc_N}
\end{pmatrix}
\]

\[
P^F \left( dc_1 M_{i_1} + c_1 \left[ \frac{\partial M_i}{\partial R_1} dR_1 + \frac{\partial M_i}{\partial R_2} dR_2 + \frac{\partial M_i}{\partial M_0} dM_0 + \frac{\partial M_i}{\partial B_1} dB_1 \right] \right)
\]

\[
\vdots
\]

\[
P^F \left( dc_N M_{i_N} + c_N \left[ \frac{\partial M_i}{\partial R_1} dR_1 + \frac{\partial M_i}{\partial R_2} dR_2 + \frac{\partial M_i}{\partial M_0} dM_0 + \frac{\partial M_i}{\partial B_1} dB_1 \right] \right)
\]

\[
DA^H(x) = \begin{pmatrix}
y_{1,1} \\
y_{2,1} \\
\vdots \\
y_{n,N}
\end{pmatrix}
\] = \begin{pmatrix}
\frac{dR_1}{dR_2} \\
\frac{dM_0}{dB_1} \\
\frac{dc_1}{dc_2} \\
\vdots \\
\frac{dc_N}{dc_N}
\end{pmatrix}
\]

\[
= \begin{pmatrix}
\sum_{j=1}^{N} \sum_{k=1}^{n} \frac{\partial M_i}{\partial R_1} \cdot c_j \cdot F^{-1} \left[ p^H y_{k,j} \right] \\
\vdots \\
\sum_{j=1}^{N} \sum_{k=1}^{n} \frac{\partial M_i}{\partial B_1} \cdot c_j \cdot F^{-1} \left[ p^H y_{k,j} \right] \\
\sum_{j=1}^{N} \sum_{k=1}^{n} \frac{\partial M_i}{\partial M_0} \cdot c_j \cdot F^{-1} \left[ p^H y_{k,j} \right] \\
\vdots \\
\sum_{j=1}^{N} \sum_{k=1}^{n} \frac{\partial M_i}{\partial R_1} \cdot c_j \cdot F^{-1} \left[ p^H y_{k,j} \right] \\
\vdots \\
\sum_{j=1}^{N} \sum_{k=1}^{n} \frac{\partial M_i}{\partial B_1} \cdot c_j \cdot F^{-1} \left[ p^H y_{k,j} \right] \\
\vdots \\
\sum_{j=1}^{N} \sum_{k=1}^{n} \frac{\partial M_i}{\partial M_0} \cdot c_j \cdot F^{-1} \left[ p^H y_{k,j} \right]
\end{pmatrix}
\]

\[
\text{by the effective flip angle } \alpha_{\text{eff}}. \quad \text{(C1)}
\]

\[
M_z(M_0, R_1, R_1', t, \alpha_{\text{eff}})
\]

\[
= M_0 \left( \frac{R_1}{R_1 + R_1'} - \left( 1 + \frac{R_1}{R_1 + R_1'} \right) \cdot e^{-[R_1 + R_1']^t} \right).
\]

\[
\text{APPENDIX C. LOOK-LOCKER REPARAMETERIZATION}
\]

The Look-Locker model represents a special solution of the Bloch equations for an IR FLASH sequence. \(^{51}\) It assumes a perfect inversion, a small flip angle and short repetition times compared to the relaxation effects. Initial relaxation effects between the inversion and the first echo can be compensated analytically. \(^{43}\) The original formulation of the Look-Locker model with the parameters $M_0, M_{ss}$, and $R_1$ is

\[
M_z(M_{ss}, M_0, R_1, t) = M_{ss} - (M_{ss} + M_0) \cdot e^{-R_1' \cdot t}. \quad \text{(C1)}
\]

These parameters are related to the underlying physical parameters $M_0$, $R_1$, and $\alpha_{\text{eff}}$. With the assumption of short repetition times\(^{52}\)

\[
\frac{M_0}{M_{ss}} = \frac{R_1'}{R_1}. \quad \text{(C2)}
\]

**APPENDIX D. SCALING FACTORS**

The output of the forward operator $B$ in Equation (19) is the strength of the signal estimated by the Bloch simulation and its partial derivatives. The strength of the

\[
R_1' = R_1 + \frac{1}{TR} \ln \cos \alpha_{\text{eff}}. \quad \text{(C3)}
\]
signal depends on the sequence and especially the applied flip angle. Therefore, the signal's output differs for classical FLASH or bSSFP sequences influencing the weighting between the data fidelity and regularization terms changing the optimization behavior.

A generic reconstruction aims for robustness against variations of the sequence parameters. It requires a scaling of the signal and its partial derivatives simulated within $B$. The implemented scaling is motivated by the Look-Locker model assumption that the longitudinal magnetization $M_z$ in Equation (C4) is proportional to the measured signal $M_{xy}$ and scaled to 1. Thus, the signal of a simulation with an initial magnetization of length 1 requires scaling of the simulated signal output $M_{xy}$ by the applied flip angle $\alpha$ and the relaxation effect $e^{-\frac{\Delta t}{T_1}}$ during the echo time interval $\Delta t_{TE}$:

$$M_z = \frac{e^{-\frac{\Delta t}{T_1}}}{\sin \alpha} \cdot M_{xy}. \quad (D1)$$

Because of the short echo times of the sequences used in this work, the $T_2$ relaxation effect can be neglected. This assumption avoids additional $T_2$ dependencies of the estimated derivatives. The final scaling factor $\frac{1}{\sin \alpha}$ increases the robustness of the forward operator $B$ in Equation (19) to the choice of the applied flip angle in FLASH based sequences. For a bSSFP type sequence the flip angle in Equation (D1) needs to be halved to take its dynamics on the $\alpha/2$ cone into account.\textsuperscript{35}

**APPENDIX E. IR bSSFP INFORMATION ENCODING**

The IR bSSFP signal behavior is described by a limited exponential growth similar to the IR FLASH sequence.\textsuperscript{34} A single inversion recovery can encode information for estimating three parameters. While the IR FLASH sequence is sensitive to exactly three parameters, the IR bSSFP is also sensitive to $T_2$, leading to four parameters in total. With a single limited exponential growth this additional parameter can not be encoded and two parameters need to be coupled. For bSSFP sequences the relaxation parameters $T_1$ and $T_2$ are coupled. Prior knowledge about $B_1$ can be used to decouple both relaxation parameters.\textsuperscript{34,56,57}

**APPENDIX F. SYMBOLIC DERIVATIVES OF IR bSSFP**

The analytical signal model for an IR bSSFP can be derived from the Bloch equations with the assumptions of hard RF pulses, a perfect inversion and an ideal $\alpha/2 - TR/2$ magnetization preparation.

The signal is modeled by:\textsuperscript{34}

$$M(M_{ss}, M_0^*, R_1^*, t) = M_{ss} - (M_0^* + M_{ss}) \cdot e^{-R_1^* t} \quad (F1)$$

with

$$R_1^* = R_1 \cos^2 \left( \frac{\alpha}{2} \right) + R_2 \sin^2 \left( \frac{\alpha}{2} \right)$$

$$M_{ss} = \frac{M_0(1 - E_1) \sin \alpha}{1 - (E_1 - E_2) \cos \alpha - E_1 E_2}$$

$$M_0 = \frac{M_0}{R_0} \left( \frac{R_1}{R_2} + 1 \right) - \cos \alpha \cdot \left( \frac{R_1}{R_1 - 1} \right)$$

$$M_0 = M_0 \sin \left( \frac{\alpha}{2} \right) \quad (F2)$$

for

$$E_{1,2} = e^{-R_{1,2} t}. \quad (F3)$$

This can be reparameterized to the physical parameters $R_1$, $R_2$, $M_0$ and $\alpha$:

$$M(R_1, R_2, M_0, \alpha, t) = \frac{M_0 \sin \alpha}{R_0^\alpha + 1 - \cos \alpha \left( \frac{R_2}{R_1} - 1 \right)}$$

$$- M_0 \sin \alpha \cdot e^{-R_1 \cos^2 \left( \frac{\alpha}{2} \right) t - R_2 \sin^2 \left( \frac{\alpha}{2} \right) t}$$

$$- M_0 \sin \left( \frac{\alpha}{2} \right) \cdot e^{-R_2 \cos^2 \left( \frac{\alpha}{2} \right) t - R_2 \sin^2 \left( \frac{\alpha}{2} \right) t} \quad (F4)$$

with its symbolic derivatives:

$$\frac{\partial M(R_1, R_2, M_0, \alpha, t)}{\partial R_1}$$

$$= -M_0 R_2 \sin \alpha \cdot (\cos \alpha - 1) \cdot \frac{1 - C(R_1, R_2, \alpha, t)}{B^3(R_1, R_2, \alpha)}$$

$$+ M_0 R_1 \sin \alpha \cos \left( \frac{\alpha}{2} \right) \cdot \frac{C(R_1, R_2, \alpha, t)}{B(R_1, R_2, \alpha)}$$

$$+ M_0 \sin \left( \frac{\alpha}{2} \right) \cos^2 \left( \frac{\alpha}{2} \right) \cdot C(R_1, R_2, \alpha, t) \quad (F5)$$

$$\frac{\partial M(R_1, R_2, M_0, \alpha, t)}{\partial R_2}$$

$$= M_0 R_2 \sin \alpha \cdot (\cos \alpha - 1) \cdot \frac{1 - C(R_1, R_2, \alpha, t)}{B^3(R_1, R_2, \alpha)}$$

$$+ M_0 R_2 \sin \alpha \sin^2 \left( \frac{\alpha}{2} \right) \cdot \frac{C(R_1, R_2, \alpha, t)}{B(R_1, R_2, \alpha)}$$

$$+ M_0 \sin \left( \frac{\alpha}{2} \right) \cdot C(R_1, R_2, \alpha, t) \quad (F6)$$
Table listing the sequence parameters for the performed measurements of this work.

| Sequence | IR FLASH | IR bSSFP | Turbo FLASH | Spin-echo |
|----------|----------|----------|-------------|-----------|
|          | phantom  | In vivo  | phantom | In vivo | phantom | In vivo |
| Figure   | 4B       | 4C, 4D, 6B | 5       | 6       | 6        | 5       | 6       | 5       |
| TR/TE (ms) | 4.1/1.84 | 4.1/2.58 | 4.88/2.44 | 4.88/2.44 | 10.8/5.4 | 2000/2.14 | 2000/2.14 | 8000/15 | 8000/15 (15:40:455) |
| FA (°)   | 6        | 6        | 45       | 45       | 45       | 8        | 8        | —       | —       |
| T_{RF} (ms) | 1       | 1        | 1        | 1        | 2.5      | —       | —       | —       | —       |
| Nominal slice thickness (mm) | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Repetitions | 1020 | 1000 | 1000 | 1000 | 500 | 1 | 1 | 1 | 1 |
| Coils    | 20       | 20       | 20       | 20       | 20       | 20       | 20       | 20       | 20       |
| BWTP     | 4        | 4        | 4        | 4        | 4        | —       | —       | —       | —       |
| BR       | 256      | 256      | 192      | 256      | 256      | 192      | 256      | 256      | 256      |
| FoV (mm) | 192      | 200      | 200      | 200      | 200      | 200      | 200      | 200      | 200      |
| Duration (min:s) | 0:04   | 0:04     | 0:05     | 0:05     | 0:06     | 0:04     | 0:04     | 34:16    | 34:16    |
| others   | #tiny GA = 7 | #tiny GA = 7 | #tiny GA = 7 | #tiny GA = 7 | #tiny GA = 7 | T_{inv} = 30:250:2530 ms |
### Table F2

Table listing the single-shot in vivo IR bSSFP region-of-interest (ROI) analysis results presented in Figure 6.

|       | T₁,IR FLASH (s) | T₁,IR bSSFP, short (s) | T₁,IR FLASH, long (s) | T₂,IR bSSFP, short (s) | T₂,IR bSSFP, long (s) |
|-------|-----------------|-------------------------|-----------------------|------------------------|------------------------|
| ROI 1 | 0.737 ± 0.016   | 1.35 ± 0.019            | 1.061 ± 0.019         | 0.024 ± 0.001          | 0.033 ± 0.001          |
| ROI 2 | 1.736 ± 0.299   | 2.434 ± 0.413           | 2.226 ± 0.456         | 0.066 ± 0.02           | 0.096 ± 0.088          |

\[ \frac{\partial M(R_1, R_2, M_0, \alpha, t)}{\partial \alpha} = \frac{M_0 R_1 \sin^2 \alpha (R_2 - R_1) \cdot (C(R_1, R_2, \alpha, t) - 1)}{B^2(R_1, R_2, \alpha)} - \frac{M_0 R_1 \sin \alpha \cdot C(R_1, R_2, \alpha, t) \sin \left( \frac{\alpha}{2} \right) \cos \left( \frac{\alpha}{2} \right) (R_1 - R_2)}{B(R_1, R_2, \alpha)} - \frac{M_0 \cos \left( \frac{\alpha}{2} \right) \cdot C(R_1, R_2, \alpha, t)}{B(R_1, R_2, \alpha)} - M_0 \sin^2 \left( \frac{\alpha}{2} \right) \cos \left( \frac{\alpha}{2} \right) (R_1 - R_2) \cdot C(R_1, R_2, \alpha, t) t, \quad (F7) \]

\[ \frac{\partial M(R_1, R_2, \alpha, t)}{\partial M_0} = \frac{\sin \alpha}{R_2 \cdot R_1 + 1 - \cos \alpha \left( \frac{R_2}{R_1} - 1 \right)} - \frac{\sin \alpha \cdot e^{-R_1 \cos^2 \left( \frac{\alpha}{2} \right) t - R_2 \sin^2 \left( \frac{\alpha}{2} \right) t}}{R_2 \cdot R_1 + 1 - \cos \alpha \left( \frac{R_2}{R_1} - 1 \right)} - \sin \left( \frac{\alpha}{2} \right) \cdot \exp \left( -R_1 \cos^2 \left( \frac{\alpha}{2} \right) t - R_2 \sin^2 \left( \frac{\alpha}{2} \right) t \right), \quad (F8) \]

with

\[ B(R_1, R_2, \alpha) = (R_1 - R_2) \cos \alpha + R_1 + R_2 \]

\[ C(R_1, R_2, \alpha, t) = \exp \left( -R_1 \cos^2 \left( \frac{\alpha}{2} \right) t - R_2 \sin^2 \left( \frac{\alpha}{2} \right) t \right). \quad (F9) \]