Bayesian Monte Carlo Analysis of mcDESPOT

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Target Audience: scientists interested in the Multi-component Driven Equilibrium Single Pulse Observation of T_1 and T_2 (mcDESPOT) approach to tissue analysis and Bayesian inference for parameter estimation.

Purpose: mcDESPOT has been proposed as a rapid approach for multicomponent relaxometry [1]. It has been applied to map myelin-bound water in brain [2] and proteoglycan-associated water in knee cartilage [3]. However, even for 2-pool models, the dimensionality of fit parameter space remains relatively high. This renders parameter estimation difficult due to the presence of multiple local minima and the flattening of the fit residual energy surface. Stochastic region contraction (SRC) has been proposed as an efficient approach to the extraction of system parameters from mcDESPOT data [4]. However, the SRC algorithm is very sensitive to initial parameter conditions in the presence of a complex structure of local minima, especially at low-to-moderate signal-to-noise ratios (SNR). Several previous studies have established the potential benefit of the Bayesian probability approach in parameter estimation [5-6]. Indeed, unlike non-linear least squares-based approaches, Bayesian inference does not require initial estimates and provides a natural framework for the incorporation of prior knowledge when available. These characteristics arise fundamentally from the process of marginalization over nuisance parameters, defined as parameters besides the one under current consideration. In this study, we investigated the accuracy and precision of component fraction determination from a bicomponent mcDESPOT model using two Bayesian methods, and compared the results with those derived using the SRC algorithm.

Theory and Methods: *Bayesian Monte Carlo mcDESPOT (BMC-mcDESPOT):* mcDESPOT uses a combination of L SPGR and M bSSFP images obtained at different flip angles. bSSFP images are typically acquired for two different radiofrequency (RF) phase cycles (bSSFP_1, bSSFP_2). Under the assumption of two on-resonance non-exchanging pools, and by normalizing the SPGR, bSSFP_1 and bSSFP_2 datasets by their respective mean values, the vector, $\boldsymbol{\Lambda}$, of free system parameters to be obtained is given by $\boldsymbol{\Lambda} = \left(f_s\ T_{2,s}\ T_{2,l}\ T_{1,s}\ T_{1,l}\right)$, where the subscripts s and l stand for the short (rapidly relaxing) and long (slowly relaxing) tissue components. The formal statement of Bayes theorem for the probability distribution of the unknown parameters is $\mathrm{P}(\boldsymbol{\Lambda} \mid \mathbf{S}, \sigma) = \mathrm{P}(\boldsymbol{\Lambda})\ L(\mathbf{S} \mid \boldsymbol{\Lambda}, \boldsymbol{\sigma})/\mathrm{P}(\mathbf{S})$, where $\mathrm{P}(\boldsymbol{\Lambda}) \propto 1/\boldsymbol{\Lambda}$ represents *a priori* parameter distributions given by the Jeffreys prior, $L(\mathbf{S} \mid \boldsymbol{\Lambda}, \boldsymbol{\sigma}) \propto \prod_{l=1}^{L} exp\left(-\frac{\left(S^l_{SPGR} - M^l_{SPGR}(\boldsymbol{\Lambda})\right)^2}{2\sigma^2_{SPGR}}\right) \prod_{m=1}^{M} exp\left(-\frac{\left(S^m_{bSSFP_1} - M^m_{bSSFP_1}(\boldsymbol{\Lambda})\right)^2}{2\sigma^2_{bSSFP_1}} - \frac{\left(S^m_{bSSFP_2} - M^m_{bSSFP_2}(\boldsymbol{\Lambda})\right)^2}{2\sigma^2_{bSSFP_2}}\right)$ is the likelihood function for obtaining the vector of the measured signal $\mathbf{S} = \left(S_{SPGR}\ S_{bSSFP_1}\ S_{bSSFP_2}\right)$ given $\boldsymbol{\Lambda}$ and $\boldsymbol{\sigma} = \left(\sigma_{SPGR}\ \sigma_{bSSFP_1}\ \sigma_{bSSFP_2}\right)$, the vector of known standard deviations of the noise in each experiment, and $\mathrm{P}(\mathbf{S}) = \int \mathrm{P}(\boldsymbol{\Lambda})\ L(\mathbf{S} \mid \boldsymbol{\Lambda}, \boldsymbol{\sigma})\ \mathrm{d}\boldsymbol{\Lambda}$ is a normalization constant. An estimate, $\widehat{f_s}$, of the short fraction, f_s and hence $f_l = (1 - f_s)$ as well, can be derived as the maximum posterior probability (MAP) given by $\hat{f}_s = \arg\max_{f_s}\{\mathrm{P}(f_s \mid \mathbf{S}, \boldsymbol{\sigma})\} = \arg\max_{f_s}\left\{\int\int\int\int \mathrm{P}(\boldsymbol{\Lambda})\ L(\mathbf{S} \mid \boldsymbol{\Lambda}, \boldsymbol{\sigma})\ \mathrm{d}T_{2,s}\mathrm{d}T_{2,l}\mathrm{d}T_{1,s}\mathrm{d}T_{1,l}\right\}$, or as the MEAN of the posterior probability given by $\hat{f}_s = \int f_s\, \mathrm{P}(f_s \mid \mathbf{S}, \boldsymbol{\sigma})\ \mathrm{d}f_s = \int f_s \int\int\int\int (\mathrm{P}(\boldsymbol{\Lambda})\ L(\mathbf{S} \mid \boldsymbol{\Lambda}, \boldsymbol{\sigma})/\mathrm{P}(\mathbf{S}))\ \mathrm{d}T_{2,s}\mathrm{d}T_{2,l}\mathrm{d}T_{1,s}\mathrm{d}T_{1,l}\mathrm{d}f_s$. As can be seen, short fraction estimation using either MAP or MEAN methods requires a high dimensional lengthy integration of the posterior distribution. To overcome this difficulty, rather than standard deterministic (fully sampled) integrations, we explored the possibility of using Monte Carlo (MC) integration consisting of averaging the posterior probability distribution values calculated on a finite random set of parameter combinations.

Input parameters: For all simulations, the following underlying input parameters were used: $T_{2,s}$ = 15 ms, $T_{2,l}$ = 90 ms, $T_{1,s}$ = 350 ms, $T_{1,l}$ = 1400 ms, $TR_{SPGR} = TR_{bSSFP}$ = 6 ms, α_{SPGR} = [2 4 6 8 10 12 14 16 18 20]°, α_{bSSFP} = [2 6 14 22 30 38 46 54 62 70]°, and bSSFP RF phase cycling of 0° and 180°. The boundary conditions for the SRC algorithm were $0 \le f_s \le 0.4$, 2 ms $\le T_{2,s} \le$ 45 ms, 60 ms $\le T_{2,l} \le$ 200 ms, 200 ms $\le T_{1,s} \le$ 500 ms and 500 ms $\le T_{1,l} \le$ 3000 ms. These boundary conditions were also used as limits of the integrals used in the Bayesian-based methods and as ranges for the random sampling needed in the MC integration. Signals were generated with added white noise to investigate results across a range of SNR (*i.e.* SNR = S_0 / σ where S_0 represents the signal amplitude at echo time of 0 ms).

Comparisons of the MC and deterministic integration techniques: The MC and deterministic integration techniques for the estimation of f_s were compared at SNR values of 500, 1000 and 2000 for $f_s = 0.15$. For each SNR, results are presented as the mean and standard deviation of the estimated f_s over 400 noise realizations, using MAP and MEAN methods described above. Uniform sampling was used for the MC integration. All numerical calculations were performed using MATLAB (MathWorks, Natick, MA, USA).

Comparison of the SRC algorithm and Bayesian-based methods: The performance of the SRC algorithm and Bayesian-based methods (MAP and MEAN) for the estimation of f_s was evaluated for different SNR values of 500, 1000 and 2000, and for different f_s values of 0.05, 0.1, 0.15, 0.2 and 0.3. The comparison consisted of calculating the relative bias, a measure of accuracy, defined as $100 * |f_s - \bar{\hat{f}}_s|/f_s$, and the relative dispersion, a measure of precision, defined as the relative standard deviation, $100 * \mathrm{SD}(\hat{f}_s)/f_s$, over 1000 noise realizations.

Results and Discussion: Fig.1 shows that MC integration provides very comparable results to those obtained with deterministic integration. Although the number of uniform random samples used in the MC integration was relatively high (*i.e.* N = 300,000), the processing time was greatly reduced (several minutes instead of several hours). Further exploration of MC sampling strategies may further define the required number of sampled points to maximize accuracy while maintaining short integration times. Fig.2 shows the relative bias and dispersion in the estimation of f_s. Overall, both bias and dispersion decrease with increasing SNR or f_s. The Bayesian-based methods (MEAN or MAP) demonstrate a substantial reduction of both bias and dispersion compared to the SRC algorithm. At low SNR and very small short fractions, the MAP method showed more bias but less dispersion than the MEAN method. At high SNR, the SRC was able to perform almost as well as the Bayesian MEAN and MAP methods, especially for $f_s \ge 0.15$. However, in all cases, the two Bayesian methods out-performed the SRC method.

Conclusions: Estimation of the short fraction of a bicomponent system from mcDESPOT was markedly improved through use of Bayesian analysis. Further work will extend the BMC-mcDESPOT analysis to the estimation of the other system parameters and will include exchange between pools.

References: [1] Deoni SCL *et al*. MRM 2008;60:1372-1387. [2] Deoni SCL *et al*. MRM 2013;70:147-154. [3] Fang L *et al*. JMRI 2014;39:1191-1197. [4] Berger FM *et al*. IEEE Trans Signal Process 1991;39:2377-2386. [5] Neil JJ and Bretthorst GL. MRM 1993;29:642-647. [6] Bouhrara M *et al*. MRM 2014 (DOI: 10.1002/mrm.25457).

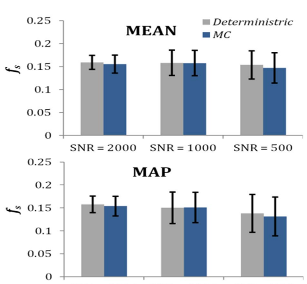

Fig.1. Mean and standard deviation of f_s obtained using deterministic or MC integration for three different SNRs.

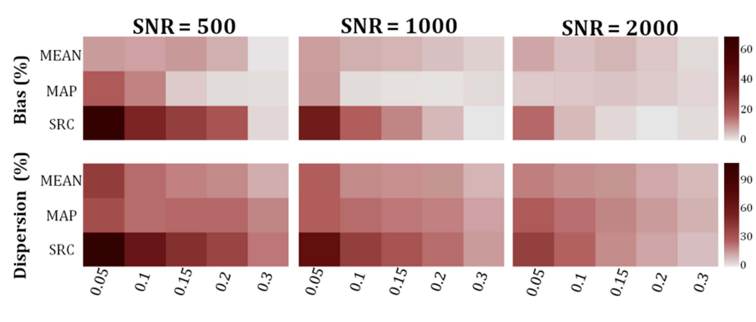

Fig.2. Relative bias and dispersion in the estimation of f_s using the MEAN, MAP and SRC methods. Results are presented for several combinations of SNR and f_s values.