Fully Bayesian Multi-model Inference for Parameter Estimation in DCE-MRI

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Target Audience: Researchers and clinicians who want to improve the accuracy and reliability of parameter estimates from Dynamic Contrast Enhanced MRI. **Introduction:** Pharmacokinetic models are widely used for the data analysis of DCE-MRI[1]. They vary in complexity and the set of underlying assumptions. The use of data-driven model selection and combined estimates from different models has been proposed previously. However, assessment of the performance of such methods yielded inconclusive results[2]. The study at hand is a first approach to exploit Bayesian methods, in order to find a maximum likelihood estimate across a joint model space with models of varied complexity. Unlike previous work, this approach incorporates information not only about the maximum likelihood estimate but also about the posterior likelihood distribution, that is, the entire probability distribution of the parameters given the model and the data. The advance of Markov Chain Monte Carlo methods allows for efficient sampling from the posterior likelihood. The hypothesis underlying this study is that the incorporation of this additional information enables multimodel estimates that feature an overall higher accuracy than any single model. For this initial characterization of the method proposed here, it is instructive to observe how data-driven model selection prefers a more complex model, provided sufficient SNR supports that choice. This is why we examine this fully Bayesian multi-model approach using a known ground truth fit with two models of differing complexity. **Methods:** In particular, this means that the data is generated with the two-compartment exchange model (*2CXM*, 4 free parameters) and fit with the extended Tofts Model (*ETM*, 3 free parameters), as well as with the ground truth model, *2CXM*, itself. This allows to isolate and examine the effect of fitting an overly complex model. We expect a regime for lower data quality where the *ETM* provides more accurate estimates than the ground truth model. For the purpose of this study we vary the acquisition time between 40s and 100s, while the SNR (noise standard deviation = 0.015 units) and the sampling rate (4s) are kept constant. Data simulation is based on the analytic approximation of an arterial input function that was measured across a population of mice[3]. The peak of this AIF is normalized to have a magnitude of 1 unit. Uptake curves are simulated for all combinations of the following parameter values: Volume transfer constant K^{trans} = 0.25, 0.45 min^{-1}; extracellular extravascular volume fraction v_e = 0.45; plasma volume fraction v_p = 0.02, 0.08; blood flow F_p = 1.5, 2.5 min^{-1}. An adaptive Metropolis algorithm within the PyMC python package is used for Markov Chain Monte Carlo sampling. The parameter priors are uniform, all parameters are restricted to be larger than zero, the partial volumes to be smaller than 1, K^{trans} and F_p to be smaller than 8 min^{-1}. The sampling procedure for each parameter set is carried out 50 times with different realizations of random noise. $5x10^5$ samples are drawn, the first $5x10^3$ are discarded as burn in. Convergence is assured by visual examination of the autocorrelation within each parameter chain. Eventually, the equilibrium likelihood distributions for every data point allow for calculation of the *Watanabe-Akaike information criterion* (WAIC)[4], which is a fully Bayesian approximation to leave-one-out cross validation. Probability weights for each model are calculated from the WAIC score[5]. **Results:** Fig. 1 shows that WAIC weighted estimates are more or as accurate as the best of the single models. In the regime around 50s acquisition time it is observed that the 2CXM is not able to produce reliable estimates and quickly surpasses a mean absolute bias of 50% for shorter times. Even though the ETM, as expected, is more accurate in this regime, it is outperformed by the WAIC weighted estimate. Fig. 2 depicts the precision in the parameter estimates. While it is very similar for longer acquisition times, ETM again, surpasses the precision of 2CXM for very short times. The WAIC weighted estimates retain this higher precision. **Discussion and Conclusion:** Ground truth data in this study was simulated by one of the candidate models. Even though ground truth data is absent in a realistic experimental situation, this approach offers the most fundamental and least distorted benchmark for the ability to improve parameter estimates. We have shown that the proposed, fully Bayesian model mixing procedure is able to pick the more accurate K^{trans} estimate for different tissues types, while it retains the precision of the best model. Thus, in the absence of other prior knowledge, this method is superior to any single model choice. WAIC enables fruitful model weighting among models of different complexity. However, due to the limited scope of this study, further validation is paramount. Applying this method to models of the same complexity but with different underlying assumptions would allow for the mixing of model assumptions rather than model complexity. Furthermore, more realistic ground truth data could be simulated based on tracer kinetic models that mimic the behaviour of tissue and thus the real-world performance of this method in more detail.

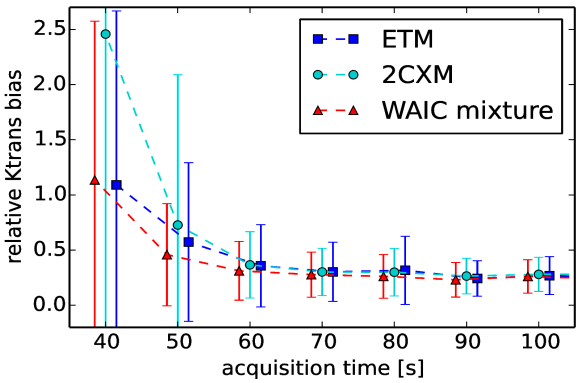

Fig 1: ***Accuracy*** *- Mean relative absolute deviation from the true K^{trans} value under variation of the acquisition time. The mean is taken across parameter sets and random iterations. The small horizontal shift within each group of data points is only for visibility.*

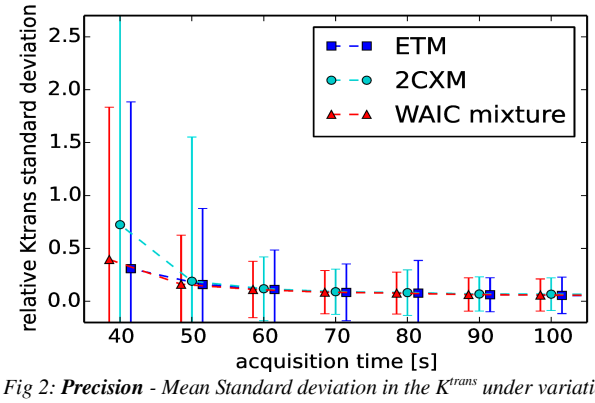

Fig 2: ***Precision*** *- Mean Standard deviation in the K^{trans} under variation of the acquisition time. The mean is taken across parameter sets and random iterations.The small horizontal shift within each group of data points is only for visibility.*

References:
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