Maximum Likelihood Estimation of T1 Relaxation Parameters Using VARPRO

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INTRODUCTION

Accurate T_1 relaxation time parameter estimation is essential for a wide variety of quantitative MR applications; for example, obtaining accurate T_1 values can be crucial in problems such as quantitative contrast enhanced imaging studies, image segmentation and tissue characterization, and absolute metabolite quantification in NMR spectroscopy. Typical experiments designed specifically for T_1 estimation often involve acquiring multiple datasets, with the timings within the experiment chosen differently for each dataset. T_1 can then be estimated by a parametric fitting of the data with signal intensity formulas derived from the physics of the MR experiment. Despite the wide variety of possible T_1 measurement schemes [1], the resulting model signal intensity function often takes the following simplified form (assuming proper phase cycling and/or crushing and that the RF pulse flip angles might be different from their nominal values) [2]:

$$S(\tau_n, A, B, C, T_1) = \frac{A + B\exp(-\tau_n/T_1)}{1 - C\exp(-\tau_n/T_1)}, \quad n \in \{1, \ldots, N\}, \tag{1}$$

where N is the number of experimental datasets acquired with different timings, and the parameter C will be small if the RF pulse flip angles are close to perfect. For a long time, it has been argued that statistically-motivated criterion perform better than more heuristic methods [3]. Using maximum likelihood (ML) estimation, for example, yields a standard nonlinear least-squares (NLS) problem:

$$\{T_1^*, A^*, B^*, C^*\} = \underset{\{T_1, A, B, C\}}{\arg\min}\, J(A, B, C, T_1), \quad \text{where} \quad J(A, B, C, T_1) = \sum_{n=1}^{N} \left|S(\tau_n, A, B, C, T_1) - d[n]\right|^2, \tag{2}$$

with the d[n] values representing the collection of acquired data. Many authors have solved this 4-parameter curve-fitting problem directly using standard iterative methods, such as Levenberg-Marquardt or Gauss-Newton algorithms. However, iterative approaches can be problematic, particularly in cases when the data is very noisy; this is because the NLS problem is not convex everywhere, meaning that iterative algorithms can miss finding globally optimal solutions. Another problem is that direct optimization of (2) can sometimes yield non-physical and/or improbable parameter values. Specifically, the coefficients A, B, and C all are related to physically meaningful experimental parameters and cannot take on arbitrary real values. Thus, there is a large amount of prior information that is not captured by the unconstrained NLS formulation of the problem. While a constrained NLS formulation of the problem can guarantee reasonable fitted parameter values, the constrained problem is more difficult to solve than the unconstrained problem, and a good initial starting guess for the parameter values is essential for accurate results.

PROPOSED METHOD

To mitigate some of the above problems, we use the *variable projection* (VARPRO) algorithm for separable least squares problems [4] to reduce the four-dimensional minimization problem (2) to a two dimensional maximization problem, noting that the least-squares optimal values of A and B have a closed form expression if N>2 for fixed values of C and T_1 (for nominal RF pulses, VARPRO reduces the optimization to a one-dimensional maximization problem since C can be fixed at 0). Through brute force evaluation of the simplified cost function for a range of potential C and T_1 values, we can generate images of the cost function such as that shown in Figure 1, which was simulated according to (1) using A=1, B=-0.9, C=0.05, and T_1=800ms, for 6 different times τ. The shape shown in the figure is very representative of those we have seen in T_1 estimation; empirically, fitting data of this type has consistently yielded cost functions with a curved ridge-like structure oriented as in the figure (though the curvature and the width of the ridge change as the A, B, C, T_1 and τ values are changed), and the NLS T_1 value consistently is found on top of this ridge. As the noise level increases and the cost function changes, it becomes common to find the NLS T_1 and C estimates at unrealistic points on the ridge; for example, it is common to find C estimated within the range of 0.8-0.9 and a correspondingly large value of T_1 when the simulated noise standard deviation is on the order of 0.1. This large estimated value directly goes against the prior knowledge that C should be close to 0 if the RF pulses are near their desired values. Moreover, if attention is restricted to that range of the cost where C is close to 0, the most likely values of T_1 fall into a much narrower range than if C were allowed to grow unrealistically large. Many other possibilities for incorporating prior information are possible, and the particular choices will depend both on the strength of the prior information and the resulting computational complexity. The approach presented here is fast and efficient, rather than exploiting the full range of prior information that might be available. Simulations indicate that this approach estimating parameter values can be more accurate that standard unconstrained NLS. Some i*n vivo* results are shown in Figure 2.

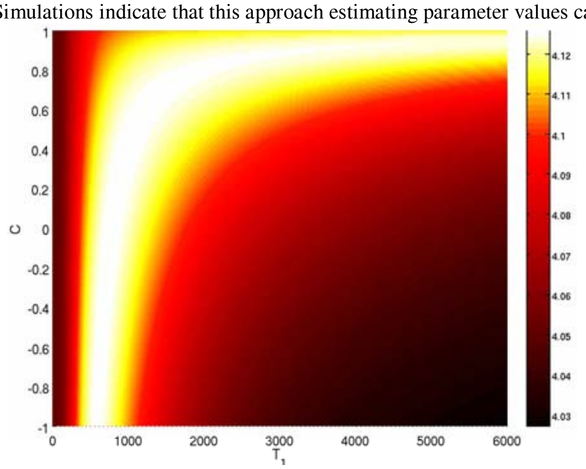

Fig. 1: Cost function for simulated data. ML optimization finds the T_1 and C that maximize this function, and the maximum will be found along the bright ridge. However, noise can easily perturb the optimal solution to correspond to overly large values of C, while we should expect C to be near 0.

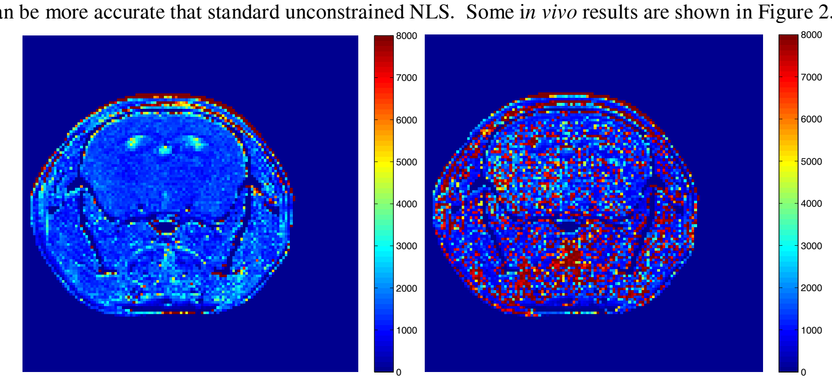

Fig. 2: Experimental T_1 parameter estimates (in ms) from an *in vivo* mouse brain shown reconstructed using VARPRO with a restricted range of C (left) and with unconstrained least-squares (right). The restriction to reasonable values of C greatly improves the stability and quality of the estimate, which is poor in the unconstrained case because of the behavior of the least-squares cost function. The large T_1 estimates near object boundaries in both images are artifacts from motion during the experiment.

CONCLUSION

The VARPRO algorithm provides a fast and efficient method for finding meaningful T_1 estimates (or reasonable initial guess values for constrained NLS fits) within a realistic range of possible values, even with noisy data for which traditional unconstrained NLS fits can provide physically unrealistic answers.

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