

Handling arbitrary unknown line-shape without introducing extra parameters.

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Introduction

Although the technique of shimming is steadily progressing [1], distorted signal-decay (line-shape) can still occur. Lack of information about the decay function complicates MRS metabolite quantitation. In the absence of line overlap, complications can be avoided by integrating the individual lines, this requiring no knowledge of the decay function. In the presence of overlap, availability of a suitable reference line brings solace [2] under the condition that all individual spectral components have the same shape. When lines overlap and no reference line is available, the line-shape can be estimated from the metabolite signals themselves: Under the same condition as mentioned above, division of the MRS signal by an estimated *non*-decaying version -- *i.e.*, no relaxation -- of that signal yields a 'raw' noisy estimate of the decay [3]. The raw decay can be improved by modelling it with splines, wavelets, or exponentials [4]. However, such modelling requires estimation of extra parameters on top of the regular MRS model parameters. The present work avoids modelling with splines, wavelets, or exponentials so that *no extra parameters* need be estimated. This simplifies metabolite quantitation and reduces its errors.

Methods

A raw estimate of the decay is obtained from division of the noisy MRS signal by a noiseless, non-decaying version of that MRS signal. The non-decaying MRS signal can be obtained from a non-decaying metabolite signal database, calculated with a quantum-mechanical simulation package, plus starting values of the metabolite concentrations and actual frequencies. Apart from noise, the estimated raw decay should look smooth. However, spurious high-frequency features (see Fig. 1c) arise when the starting values are not optimal. Reduction of these features can be achieved in two ways:

- 1) Improve the starting values of the non-decaying version of the MRS signal, or
- 2) Model the raw decay with splines, wavelets, or exponentials.

Here, option 1 is applied. It hinges on the fact that proper adjustment of the concentrations and frequencies of the metabolites suffices to eliminate the spurious features in the decay. In fact, the values of the metabolite parameters that optimally smooth the decay are the true ones of the MRS signal. Should sufficient computing power be available, the wanted adjustment could simply be accomplished by an exhaustive search through the metabolite-parameter space. Instead, we devised a search with a dual set of gradients. The first set of gradients equals that of the usual Non-Linear Least-Squares (NLLS) fit procedure which minimises the residue of the fit. The second set of gradients comprises the derivatives of the raw line-shape w.r.t. the *same* parameters as those used in the usual NLLS fit. The latter gradients force the line-shape toward zero beyond some frequency region $-v_{\text{threshold}} < v < v_{\text{threshold}}$ based on *a priori* knowledge. The two gradient sets were made to *operate in tandem*, each satisfying its own criterion. Thus, the NLLS-fit residue is minimised while nulling the line-shape everywhere beyond $\pm v_{\text{threshold}}$. Alternatively, one could say: The line-shape is nulled everywhere beyond $\pm v_{\text{threshold}}$ while minimising the NLLS-fit residue. Starting values of the concentrations and frequencies of the metabolites were obtained from conventional NLLS fitting using exponential decay (Lorentz line-shape).

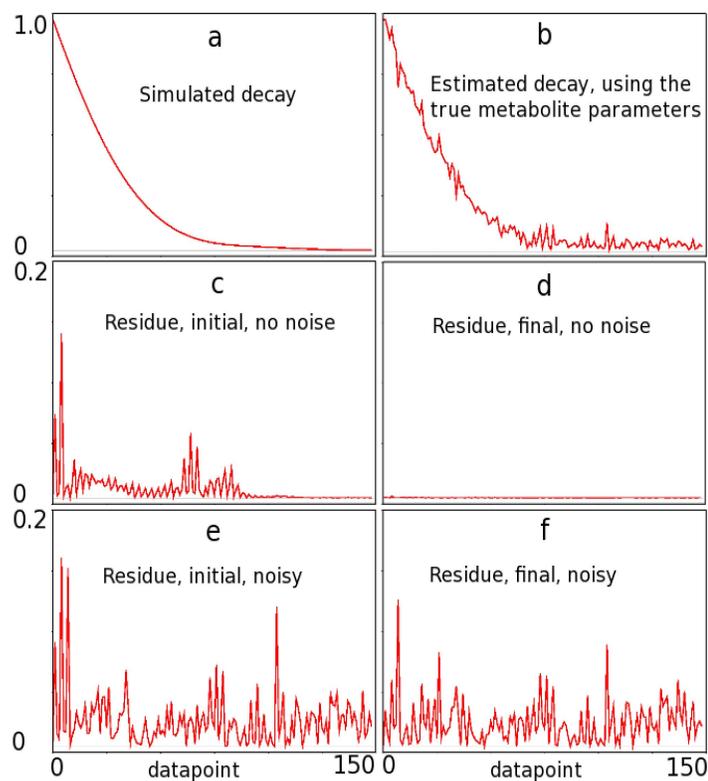


Figure 1. Simulated decay, estimated decay, residues for various cases. See text in Sec. Results. Note the difference in vertical scale between a,b and c,d,e,f.

Results

The method was tested on a simulated noisy MRS signal comprising three fictitious metabolite signals, two of whom overlap heavily. Thousand different noise realisations were used. The simulated line-shape was asymmetric and perturbed by eddy current effects.

Fig. 1 summarises results obtained with the dual gradient-set search indicated in Sec. Methods. Each sub-figure shows the absolute value of the item in question as a function time. 150 data points were used for estimating the raw decay.

a) True simulated decay. **b)** Raw decay, *i.e.*, obtained through division of the noisy MRS-signal by a non-decaying noiseless version using the *true* values of the concentrations and frequencies. We emphasise that the probability that both the real and imaginary parts of a non-decaying MRS-signal simultaneously approach zero is negligibly small. Therefore, the division poses no numerical problems down to the very end of the signal. **c)** Residue [abs(raw decay) - abs(true decay)] in the case that the non-decaying version of the signal is obtained from suboptimal starting values of the concentrations and frequencies. The MRS signal is chosen noise-free so as to ensure clear visibility of the ensuing spurious features. **d)** As **c)** but now after 14 iterations of the dual gradient-set search. The spurious features have been strongly reduced. **e)** As **c)** but now with noise added to the MRS signal. **f)** As **d)** but now with noise added to the MRS signal and 37 iterations.

So far, estimation errors in the metabolite concentrations incurred with the dual gradient-set search were significantly smaller than those incurred after modelling the raw decay with exponentials.

For the sake of comparison, availability of a strong reference signal was also investigated. This yielded lower errors only for one of the three metabolites.

Conclusion

We proved in principle that handling arbitrary, unknown decay (line-shape) without introducing extra parameters is possible. The method searches through the regular metabolite parameter space with a dual gradient set. The attendant metabolite quantitation errors compare favourably with those of various other methods.

Acknowledgement

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