Time-Domain Quantitation with a Metabolite Basis Set

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Synopsis

A *time-domain* quantitation algorithm based on a metabolite basis set obtained by quantum mechanical simulation is proposed. This non-linear least squares algorithm fits a time domain model function, combination of (quantum-mechanically simulated) metabolite signals, to low-SNR *in vivo* data. The metabolite basis set was created with NMR-SCOPE which can handle various experimental protocols. The present work investigates through Monte Carlo studies the ability of the algorithm to quantify strongly overlapping spectral components in presence of (residual) water and a macromolecule spectrum. Quantitation of short echo-time ^{1}H human brain signals at 1.5T is demonstrated as well as quantitation of ^{31}P signals.

Method

Fitting of model functions to low-SNR *in vivo* data with strongly overlapping peaks needs invocation of ever more prior knowledge about the model parameters. The fit can be performed in the frequency [1] or time [2] domain using measured spectra of selected metabolite solutions as numerical model functions. Alternatively, one can compute theoretical metabolite signals/spectra quantum-mechanically for the measurement protocol used by a scanner and fit in the frequency domain [3].

The proposed algorithm QUEST (QUantitation based on QUantum ESTimation) fits a combination of (quantum-mechanically simulated) signals of metabolites directly to the *in vivo* data at hand, in the *time-domain* domain. QUEST is based on

- A non-linear least squares algorithm aiming at finding the model parameters that minimize the distance between the raw signal and the model function. This algorithm allows to automatically compensate for distortions due to the magnetic field heterogeneities with the ideal signals of the metabolite basis set. This has been done by using small extra damping factors and frequency shifts in the fit procedure.
- A metabolite basis set. Signals of the metabolites were computed by quantum mechanics with NMR-SCOPE [4] using the spin Hamiltonian parameters given in [5]. NMR-SCOPE, based on the product-operator formalism, can handle various NMR pulse sequences.

As for preprocessing, QUALITY deconvolution is applied first (if reference signal available), then water suppression using HLSVD [6] and macromolecule removal by weighting/truncation [7] or correction [8] of initial samples. The quantitation errors are estimated by computing the Cramér-Rao lower bounds. Note, that our CRBs are too small because we have not included the water/macromolecules in the model function.

Results

QUEST performances are assessed through Monte-Carlo studies, see Fig.1. Then, *in vivo* ^{1}H short echo-time signals of human brain at 1.5T obtained with STEAM were quantified with QUEST, see Fig.2. Signals of aspartate (Asp), choline (Cho), GABA, glucose, glutamate (Glu), glutamine (Gln), lactate (Lac), myo-inositol (Ins), N-acetylaspartate (NAA), phosphocreatine (PCr), creatine (Cr), taurine (Tau), plus signals modelling the lipids at 0.9 and 1.3 ppm were included in the QUEST fits. Quantitation of a ^{31}P signal is shown in Fig.3.

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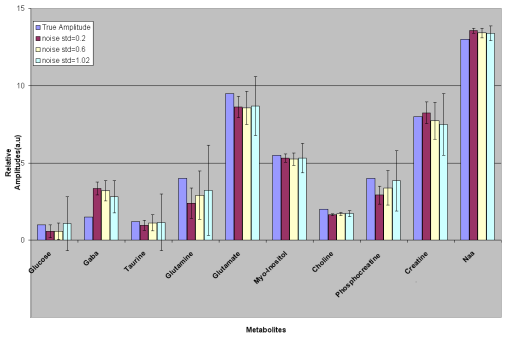

Fig.1. Monte Carlo study: quantitation with QUEST after water suppression with HLSVD of simulated ^{1}H short echo-time signals at 1.5T comprising eleven metabolites plus a water peak modelled by five exponentially damped sinusoids. The mean values of the metabolite estimated amplitudes and the mean values of the corresponding estimated 2 CRBs were obtained from 256 realizations of the signal for noise standard deviations equal to 0.2, 0.6 and 1.02 respectively.

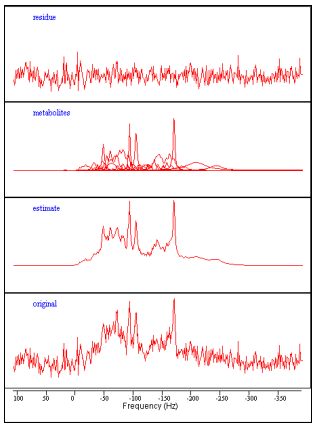

Fig.2. ^{1}H spectra of a human brain at 1.5T obtained with STEAM with an echo-time of 30 ms; quantified with QUEST. From bottom to top, raw spectrum, estimated spectrum, spectra of the metabolites and the residue.

Discussion

This work demonstrates that automatic quantitation of ^{31}P signals and short echo-time ^{1}H human brain signals at 1.5T is possible with QUEST without preliminary experiments for acquiring signals of *in vitro* metabolite solutions. Nevertheless, to get reliable results, 1) the amplitudes of metabolites with low concentrations must not be too small compared to the noise standard deviation and 2) the damping factor differences between metabolites and the background components must be large enough. When fitting either in the time or in the frequency domain, one has to cope with the water/macromolecule signals. In the frequency domain, water/macromolecules lead to a baseline which has to be accounted for. In the time domain, SVD-based techniques enable automatic processing/removal of the water/macromolecule signals. An other advantage is that missing of initial and/or final data points need not hamper the procedure. In particular, omission or weighting of initial data points is a simple way to reduce the detrimental influence of macromolecules [7]. QUEST coupled with preprocessing algorithms allows easy handling of prior knowledge.

Acknowledgements

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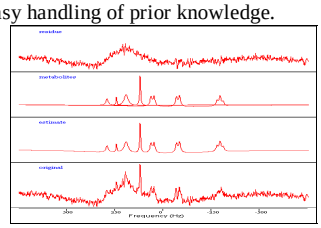

Fig.3. ^{31}P spectra of a human brain at 1.5T**,** quantified with QUEST. From bottom to top, raw spectrum, estimated spectrum, spectra of the metabolites and the residue showing the broad PDE