Simple Correction of Chemical Shift Changes in Quantitation

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Introduction

High-resolution magic angle spinning (HRMAS) ^{1}H spectroscopy is playing an increasingly important role for diagnosis. This technique enables setting up metabolite profiles of *ex vivo* pathological and healthy tissue, see *e.g.* [1]. Automatic quantitation of HRMAS signals will provide reliable reference profiles to monitor diseases and pharmaceutical follow-up [2]. Nevertheless, for several metabolites chemical shifts often slightly differ according to the microenvironment in the tissue or cells, in particular with its pH [3]. This hampers accurate estimation of the metabolite concentrations mainly when using quantitation algorithms based on a metabolite basis-set [2, 4]. In this work, we propose a user-friendly way to circumvent this problem.

Method

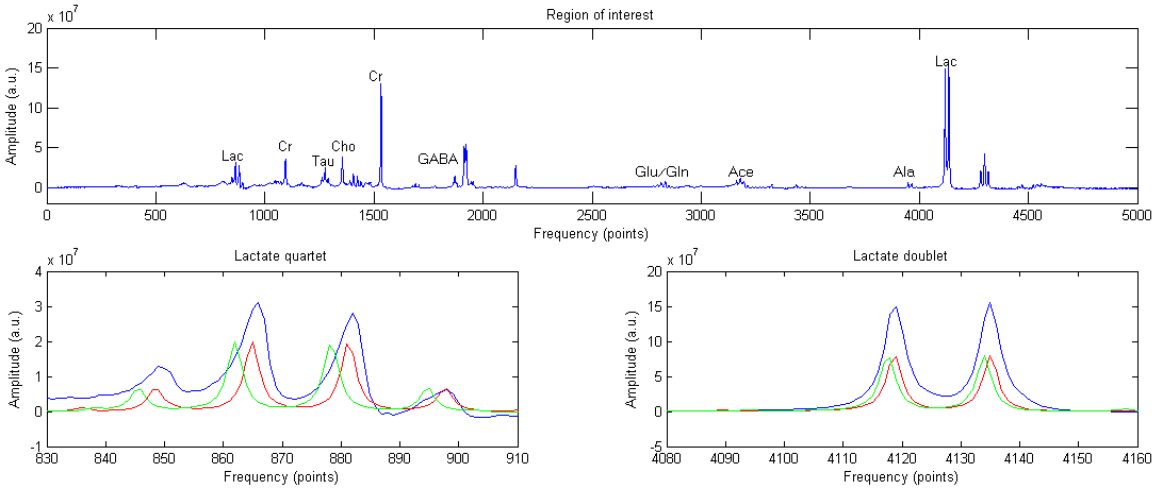
The complex-valued time-domain model signal is written as a linear combination of the M weighted metabolite model $\hat{x}^m$ of the basis-set:

$$\hat{x} = \exp(i\phi 0) \sum_{m=1}^{M} \left\{ c_m \; \hat{x}^m \exp(\Delta\alpha_m t + i\Delta\omega_m t) \exp(i\Delta\phi_m) \right\}$$

c_m is proportional to the concentration of the metabolite m, $\Delta\alpha_m$, $\Delta\omega_m$, $\Delta\phi_m$ are small extra damping factors, angular frequency shifts and phase shifts enabling to automatically compensate for distortions due to the magnetic field heterogeneities with respect to the ideal signals of the metabolite basis-set. We propose to modify the metabolite basis-set signals $\hat{x}^m$, sensitive to pH changes, by just slightly stretching (expansion/contraction) the corresponding spectrum. This is justified by the fact that to 1st order approximation a change of pH can produce a linear change of the width of the spectrum of a metabolite of an AB and AX system. Stretching can easily be done by introducing a frequency scaling parameter κ_m and by directly using the inverse scale change of the $\hat{x}^m_\kappa$ time-domain signals (frequency scale expansion results in contraction of the time scale and vice versa). This avoids splitting of the metabolite basis-set signals of given metabolites into basis sub-components according to chemical groups and adding appropriate constraints (prior knowledge) to the parameters of the groups. Either κ_m can be estimated prior to quantitation by maximizing the correlation between the *ex vivo* signal and $\hat{x}^m$ or by introducing κ_m in the quantitation procedure.

Results

Results are illustrated on an HRMAS signal from a tissue sample of a human brain with an oligodendroglioma, acquired at 11.7T. The lactate signal of the basis set was automatically stretched prior to the quantitation procedure as mentioned above. It can easily be seen that thanks to stretching one can independently "shift" the different multiplets of the spectrum. This enables us to adapt artificially the chemical shifts variations due to pH.



Top: Region of interest of an HRMAS spectrum from a tissue sample of a human brain with an oligodendroglioma, acquired at 11.7T; Bottom: zoom in on the lactate quadruplet and doublet regions (blue: raw spectrum; green: original lactate basis-set spectrum; red: stretched lactate basis-set spectrum).

Conclusions

We proposed a very simple method to account for chemical shift changes related to pH in quantitation methods based on a metabolite basis-set and used for quantitation of HR-MAS or high resolution signals. It is well suited to improve quantitation of AB and AX spin systems like citrate, lactate, creatine, ethanolamine, *etc.*. For the more complicated spin systems like glutamate and glutamine, the method is less suited but still improves the quantitation results. A more accurate method based on Quantum Mechanics is under development.

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