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Magnetic Resonance Spectroscopy Signal Analysis Based on Fingerprinting Dictionary Approaches

Iurii Venglovskyi[1,2]
[1]Institute of Scientific Instruments of the CAS
Královopolská 147, Brno, Czech Republic
iurii@isibrno.cz; Iurii.Venglovskyi@vutbr.cz
[2]Department of Biomedical Engineering, Brno University of Technology
Technická 12, Brno, Czech Republic

Abstract **-** Magnetic resonance spectroscopy (MRS) is a technique applicable in medical diagnosis or research, which has the unique capability to give non-invasive access to the biochemical content (metabolites) of scanned organs. Up to recent times, all the proposed methods solved metabolite quantification as an optimization problem attempting to minimize the difference between the data and a given parameterized model function. This paper proposes quantification of metabolites in MR spectroscopic imaging using a fingerprinting method, whose function is based on the creation of a dictionary of linear combinations of metabolite signals. Experimental results demonstrate the accuracy of the proposed method, compared to data obtained by a standard quantification method (QUEST), on concentration estimates of 8 metabolites from signals with macromolecule background and noise. The prototype results indicate that the concept of MR fingerprinting dictionary, useful also for preparing data for machine learning, can serve as an alternative method for metabolite quantification by NMR signal analysis.

Keywords**:** magnetic resonance spectroscopy, fingerprinting dictionary, spectroscopic imaging, artificial intelligence

1. Introduction

The method of *in vivo* proton magnetic resonance spectroscopy (^{1}H MRS), which allows studying the metabolic composition in local isolated tissue areas in live organisms in normal conditions and in different kinds of disorders that are accompanied with various pathological changes, has been actively developing since the late 1980s [1]. Nevertheless, the long acquisition and the complex analysis procedure compared to standard magnetic resonance imaging (MRI) and the lack of standardized protocols have led to the fact that even after 30 years, many radiologists evaluate *in vivo* ^{1}H MRSI as a research method whose clinical use is limited [2]. A crucial step for a better function of MRSI and its wider usage, especially in live tissues, is improvement of the quantification methods.

One of such possibilities is fingerprinting – metabolite quantification based on the creation of a specific dictionary formed as a list of metabolite signal patterns. This method relies on direct identification of similar patterns (fingerprints) in the massive signal dictionary instead of using some kind of generalized knowledge as in functionally similar artificial intelligence method [3], drawing on training cases, or an accurate signal model as in classical curve fitting. In MRI, such approach has demonstrated its ability to cope well with irregular artefacts resulting from irregular undersampled MR scanning, thus enabling an acceleration of quantitative imaging. Both methods demonstrate a trend to eliminate the need of a definite mathematical model and to use massive computation for handling data obtained under various irregular conditions. Such experience suggests that the fingerprinting method may show its efficiency also in handling MRSI data and lead to rapid spectroscopic data analysis of even large data sets, improving the applicability of *in vivo* MRSI [4].

2. Subject and Methods

MRS signals are acquired in the time domain, but are commonly inspected in the frequency domain since metabolites are characterized by specific identifiable spectral patterns [5]. It is a notable aspect of MRS that the signal amplitude resulting from each specific molecule type is directly proportional to the concentration of these molecules. Signals acquired with short echo time may contain several (up to 20) discernible metabolite contributions superimposed on a macromolecular background. The MRS signal $s(t) = x(t) + y(t) + e$ can be classified as parametric (metabolite part $x(t)$) and non-parametric

parts (macromolecular part *y(t)* and random *e* noise) – *x(t)* is defined as a linear combination However, it still requires further investigation and refinement in improvement of the process of spectrum's identification and also optimization the storage memory to fulfil all the needed tasks, such as the exploration and preservation a huge number of linear spectrums combinations.

2.1. Principle of Fingerprinting

The NMR metabolite fingerprint dictionary is based on the concept of creation of the different spectrum list from known concentrations of metabolites. Thus, the comparing the identification of the unknown spectrum to the spectral data from the data set in the dictionary lies down in the base of the dictionary functioning ad it is shown on the Fig. 1.

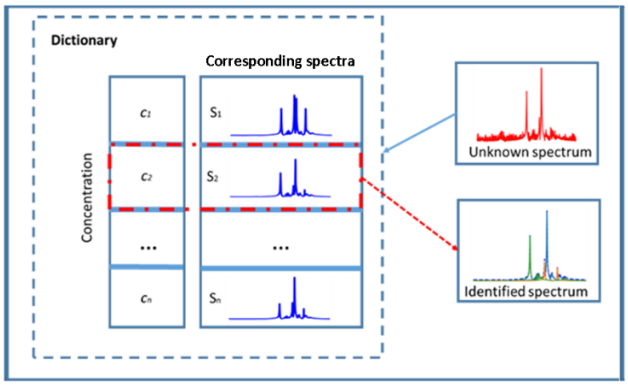

Fig. 1: Schematic representation of the dictionary as a set of concentrations and corresponding spectra for identification of the unknown spectrum

2.2. Dictionary Generation

The idea of creating one all-encompassing dictionary not divided to partitive sub-dictionaries was rejected because of difficulties to operate large amounts of data (when the quantity of metabolites exceeds 3) what caused runtime errors in work of described program. Another problem was the impossibility to store all necessary spectrum parameters from a large number of linear combinations. All this together leads to a slowdown in the search and identification of the relevant spectrum. That is why the solving of described problems has led to the decision to construct separate sub-dictionaries and combine them together when needed.

The task was to create sub-dictionaries of spectra's list got by the method of linear combination of acquired individual metabolites spectra, which were described in the previous chapter. The spectra were achieved by operating with the simulation method.

All of these sub-dictionaries are bound together into one single dictionary with the help of Pandas DataFrame, data processing toolbox in Python [6]. Extracts are shown on the fig. 2.

A DataFrame is a 2-dimensional data structure that can store data of different types (including characters, integers, floating point values, categorical data and more) in columns. Pandas provides various facilities for easily combining Series or DataFrame with various kinds of set logic for the indexes and relational algebra functionality in the case of join/merge-type and search/compare operations.

Dictionary

	Concentration	Spectral data
0	[0.1 0.1 0.1]	[(1.2237815524040987-0.3878558546250981j), (1....
1	[0.1 0.2 0.1]	[(1.2238484028713608-0.3892737720492625j), (1....
2	[0.1 0.3 0.1]	[(1.2239168181184343-0.39068800599345654j), (1...
3	[0.1 0.4 0.1]	[(1.2239868405712215-0.3920982240075099j), (1....
4	[0.1 0.5 0.1]	[(1.2240585145988858-0.39350408100764517j), (1...

Sub - dictionary

	Concentration	Spectral data
0	[0.11 0.11 0.11]	[(1.3461597076445084-0.42664144008760785j), (1...
1	[0.11 0.12 0.11]	[(1.3713320329028553-0.4395413112882874j), (1....
2	[0.11 0.13 0.11]	[(1.396504358161202-0.452441182488967j), (1.39...
3	[0.11 0.14 0.11]	[(1.4216766834195487-0.4653410536896465j), (1....
4	[0.11 0.15 0.11]	[(1.4468490086778953-0.4782409248903261j), (1....

Fig.2. Fragment example of the dictionary (left) and correspond sub – dictionary (right)

2.3. Data Simulation

All obtained data were received by the method of obtaining simulation spectra for basis set of metabolite with the usage of the NMRScopeB plugin in the jMRUI software, which is a software package for advanced time-domain analysis of magnetic resonance spectroscopy and MRSI data [7]. The NMRScopeB plugin provides simulation of the evolution of coupled spin systems during an NMR experiment and its main purpose is to calculate the experiment-specific signals expected from each metabolite that can be detected, which then form a basis set used in jMRUI for signal decomposition and metabolite quantitation.

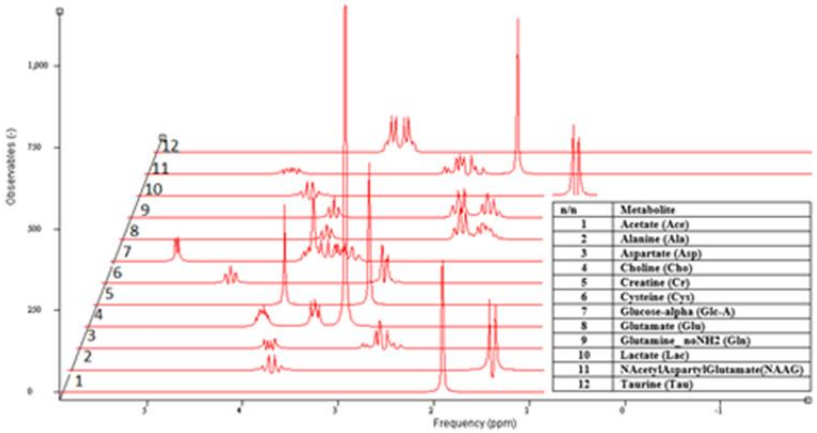

Fig. 2. Simulated selected basis set of metabolites

Fig. 2 shows the list of selected most commonly used metabolites and their corresponding spectral curves in NMR for spectroscopy analysis. All simulations were done on a PC with video adapter NVIDIA GeForce RTX 2060 and CPU Intel Core i3-8100 3.60 GHz for PRESS (Point RESolved Spectroscopy) excitation [8].

3. Results

Exploring method of fingerprinting, basic set of eight metabolites was used, the spectra of which were generated by linear combination. The dictionary of over than 100,000 spectra was created for eight components. Each spectrum has a specific identification number that corresponds to the relative concentration of the component. The identification of spectra from a dictionary acts like a simple task, because the only one, what is needed, is to compare signals without noise. Meanwhile, it becomes more complicated while detecting spectra with noise and background. Nevertheless, if the dictionary is well executed, the noise and other additional parameters do not significantly impact the identification process, as the algorithm compares each point of unknown spectra to already existing spectra in the dictionary and selects the one which is the best match of given criteria of search.

For comparing the effectiveness of the suitability of the fingerprinting method for analysing the spectral data, the experimental measured spectrum, obtained with the help of the method PRESS, was implemented. The characteristics of PRESS method, what were used, are B_0= 9.4 T, short echo time TE=16.5 ms and repetition time TR= 2500 ms with water signal suppression. The all pre-processing was performed with the help of Nmrglue module for working with NMR data in Python. Nmrglue provides a robust environment for the rapidly developing new methods for processing, analysing, and visualizing NMR data. Nmrglue also provides a framework for connecting existing NMR software packages [9].

The grafical visualisation of the obtained spectrum data in the experimental spectrum is to be shown on fig. 4, where the upper plot (a) demonstrates the detection of the estimated spectrum from the original measured spectrum and its devision to the “real” parametric methabolic part (b) and nonparametric part, such as noise and macromolecular background (c).

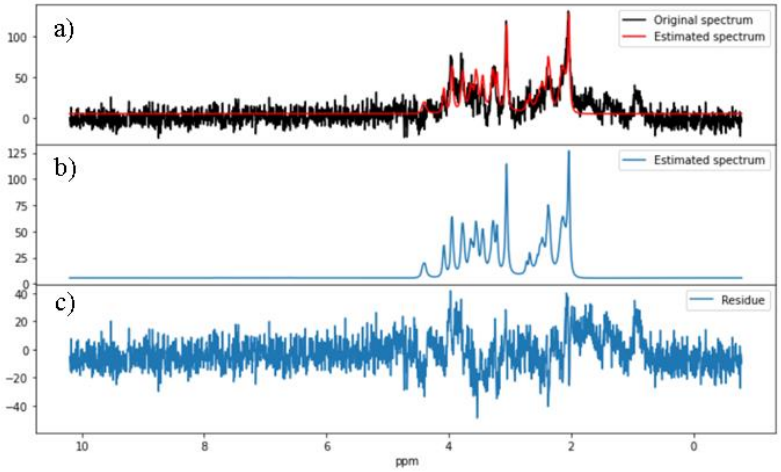

Fig.4 The grafical visualisation of obtained spectrum data in the experimental spectrum

For better visualisation of the efficiency of the fingerprint method, all obtained experimental measured spectrum data, which are subscribed above, are compared with the data, obtained with the help of the other method of quantification, such as QUEST [10], in what the mathematical models serve as the clue. The all compared figures are to be shown in the tabl.1.

Table 1. Comparison values of amplitude, obtained with the help of fingerprinting method and QUEST method

	Fingerprinting			QUEST		
Metabolite	Amplitude	dLW, Hz	sd Ampl.	Amplitude	dLW, Hz	sd Ampl.
Choline (Cho)	0.047	8.11	4.53E-03	0.048	8.11	5.53E-03
Creatine (Cr)	0.21	11.6	0.0516	0.2653	12.73	0.0556
Glutamate (Glu)	0.62	11.5	0.038	0.6573	12.73	0.048
Glutamine_withNH2 (Gln)	0.30	12.73	0.0656	0.3164	12.73	0.0556
MyoInositol (m-Ins)	0.32	12.73	0.017	0.2514	12.73	0.017
NAcetylAspartate (NAA)	0.43	11.53	0.0272	0.4612	11.53	0.0172
Phosphocreatine (PCr)	0.24	12.53	0.0557	0.2654	12.73	0.0557
Taurine (Tau)	0.25	5.91	0.0119	0.2234	6.01	0.0179

4. Conclusion

Magnetic Resonance Spectroscopy Imaging (MRSI) enables detection and localization of spectra from several spatially distributed voxels. After each voxel signal quantification procedure, it obtains spatially resolved, non-invasive and non-ionizing, and therefore non-harmful for the live object metabolic information about the body's condition. The quantification process is performed by analysing the acquired spectra in order to estimate the metabolite concentrations, one of the indicators of the functioning of living cells and tissues.

Up to recent times, all the proposed quantification methods solve an optimization problem attempting to minimize the difference between the data and a given parameterized model function. Most available methods employ local minimization and, in the case of short echo time, metabolite parameters are usually estimated by a non-linear least squares fit (in the time or the frequency) of the model using a known basis set of the metabolite signals. Despite the numerous proposed fitting methods (eg, QUEST), the robust, reliable and accurate quantification of brain metabolite concentration remains difficult. The major problems are: 1) strong overlapping metabolite spectral pattern, 2) low signal-to-noise ratio, 3) unknown background and peak line shape.

Meanwhile, the usage of the fingerprinting method helps avoiding such difficulties and/or minimize the influence of the following factors. Moreover, the method of fingerprinting is quite reliable; as it is seen from the data in the tab.1, the parameters that are detected and combined with the help of the fingerprinting method, are quite similar to the data obtained by the QUEST method. And the other great advantage of the method is its quite simpleness in usage. However, it still requires further investigation and refinement in improvement of the spectrum's identification process, as well as optimization the storage memory to fulfil all the needed tasks, such as the exploration and preservation a huge number of linear spectrums combinations.

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