

# Direct Estimation of Model Parameters in MR Spectroscopic Imaging using Deep Neural Networks

Dhritiman Das<sup>1,4</sup>, Eduardo Coello<sup>2,4</sup>, Anjany Sekuboyina<sup>1,3</sup>, Rolf F. Schulte<sup>4</sup>,  
Bjoern H. Menze<sup>1</sup>

<sup>1</sup>Department of Computer Science, Technical University of Munich, Germany

<sup>2</sup>Department of Physics, Technical University of Munich, Germany

<sup>3</sup>Klinikum rechts der Isar, Munich, Germany <sup>4</sup>GE Healthcare, Munich, Germany

**Abstract.** We introduce a deep-learning based framework based on a multilayer perceptron for estimation of the output parameters of a model-based analysis of MR spectroscopy data. Our proposed framework: (1) learns the spectral features from a training set comprising of different variations of synthetic spectra; (2) uses this learning and performs non-linear regression for the subsequent metabolite quantification. Experiments involve training and testing on simulated and in-vivo human brain spectra. We estimate parameters such as metabolite-concentration ratios and compare our results with that from the LCModel.

## 1 Introduction

Quantification of MR Spectroscopy (MRS) signals generates metabolic maps which show the concentration of metabolites in the sample being investigated. Accurate quantification of these metabolites is important for diagnosis of brain tumor and other in-vivo diseases. For this purpose, non-linear model-fitting tools are widely used (such as the LCModel [4], TARQUIN [8], AMARES [6] and ProFit [5]). The LCModel is widely regarded as the gold-standard fitting tool. However, some of its drawbacks include: (1) prior knowledge-tuning and long fitting times, and (2) high estimation error for noisy data. Prior work has also focused on using machine-learning for metabolite-quantification [2]. In this study, we present an alternative to the non-linear model fitting using a deep-learning approach.

## 2 Methods

A multilayer perceptron(MLP)[7] is a fully-connected, feedforward deep-neural network comprising of three or more layers of non-linearly activated nodes. The nodes in each layer are connected to the next layer with certain weights and a supervised learning technique (backpropagation)[3] is used for training. Weights are updated after each backward-pass and the error (loss function) is computed

after each iteration. Once the error reduces and achieves convergence, the learning stops.

In MRSI, The time-domain complex signal of a nucleus is given by:

$$S(t) = \int p(\omega) \exp(-i\Phi) \exp(-t/T_2^*) dw. \quad (1)$$

, and the corresponding frequency-domain spectrum is given by  $S(\omega)$ .

Using the MLP-framework, we perform the inverse signal modeling where we have a training dataset  $D = (S_i(\omega), Y_i)$ ,  $i \in [1, N]$ , where  $N$  is the total number of synthetic training spectra.  $S_i(\omega)$  represents the synthetic training spectral data while  $Y_i$  represents the corresponding multi-parameter training labels. As a preliminary study, for our model, we consider the concentrations (with respect to Creatine) for the major metabolites - NAA and Choline. Therefore, for a given spectrum  $S_i(\omega)$ ,  $Y_i = [NAA_i, Cho_i]$ .

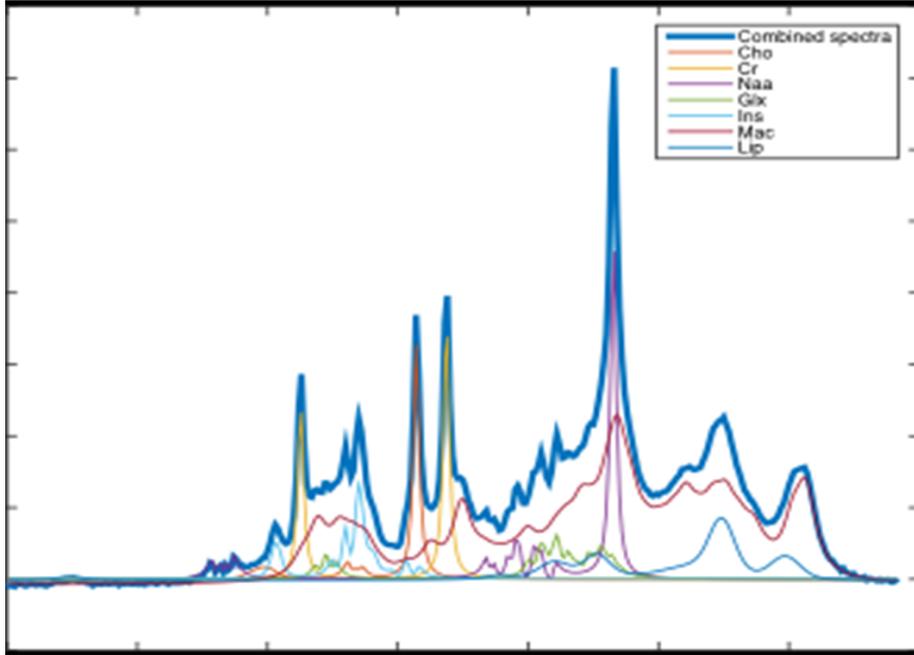
A five-layered perceptron network was constructed to work as a regressor mapping the  $S_i(\omega)$  to the  $Y_i$ . Each layer consisted of 300 neurons with rectified linear unit (ReLU) activation. The training data consisted of  $N=1$ -million spectra with their corresponding parameters. The randomly initialized network was trained to predict the parameters by iteratively minimizing the squared-error loss between the predicted and actual parameters using gradient descent with a learning rate of 1e-3. For faster convergence, Adam optimizer with a Nesterov’s momentum of 0.9 was employed. As the data is mostly well-behaved, the ‘early stopping’ convergence check was utilized on 0.1

To check the ability of our network to predict the parameters, we use two test-sets: synthetic and real CSI. The predicted concentrations are denoted by  $\hat{Y}_j$ . The corresponding LCMoel fitted concentration labels  $Y_j$  serve as the ground-truth,  $j \in [1, M]$  where  $M$  is the total number of test spectra.

**Error Calculation.** For our experiments, given the estimate  $\hat{Y}_j$  and the testing label  $Y_j$ , the estimate error for the parameter  $Y_j$  can be calculated as,

$$\hat{E}_j = \|\hat{Y}_j - Y_j\| / \|Y_j\| \quad (2)$$

**Data.** A metabolite basis set was generated by using the data provided by the ISMRM MRS Fitting Challenge 2016. An example has been shown in 1. Over 1 million spectra were simulated with variations in NAA, Cho, Cr concentrations, macro-molecular baseline, lipids, t2 values (for changes in linewidth) and signal-to-noise ratio (SNR) to account for changes in spectral quality. For testing, we acquire a standard phase-encoded 2D brain MRSI data of a healthy human volunteer on a 3T scanner using a point-resolved spin-echo localization sequence (PRESS) with voxel size = 10x10x15 mm<sup>3</sup>, TE/TR=35/1000 ms, spectral width = 2000 Hz, number of points = 400. For testing purposes, we use 96 spectra from the inner-region of the brain which serves as the region of interest. For peak alignment, ppm-cropping and signal-normalization of the training and test spectra, a pre-processing step is performed.

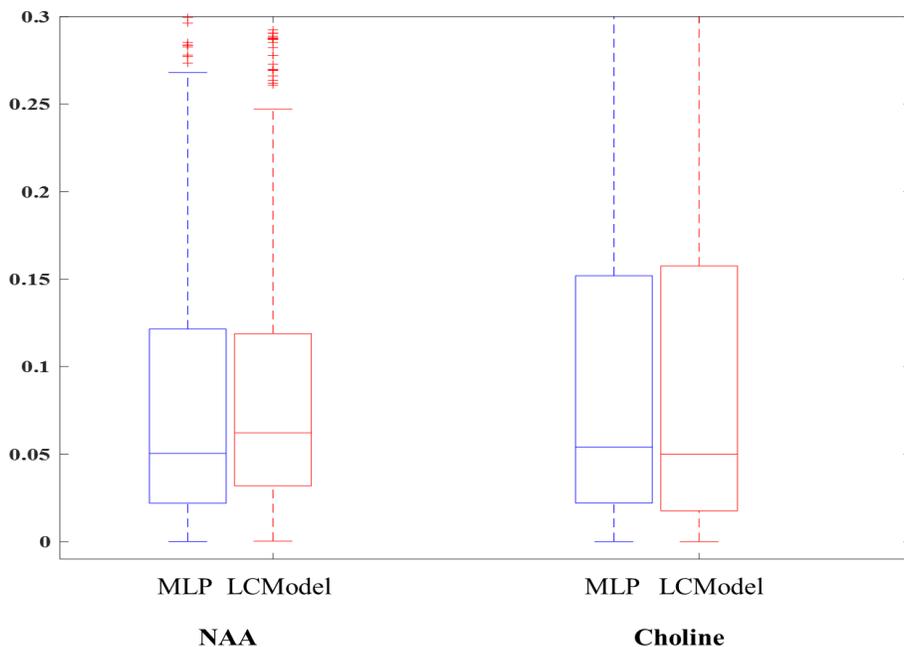


**Fig. 1.** An example spectra generated using the basis sets provided by the ISMRM MRS Fitting Challenge 2016. Using the same basis sets, over **1 million** spectra are generated with variations in NAA, Cho, Cr and other metabolite concentrations along with changes in macro-molecular baseline, lipids, linewidth ( $t_2$ ) and SNR.

## 2.1 Results

As a direct comparison of both the MLP and LCModel methods, we use the synthetic test dataset to generate the error distribution shown in Fig. 2. For both NAA/Cr and Cho/Cr, the MLP shows a lower median error than the LCModel. Using the Bland-Altman method [1], we observe a strong correlation between the LCModel and RF estimates for a sample patient (Fig. 3).  $\hat{E}_j$  for the same sample patient are within the acceptable range (especially for the major metabolites such as NAA, Choline and Creatine). Fig. 4 shows the resulting concentration distribution from both the MLP and LCModel methods for both NAA/Cr and Cho/Cr. The mean relative errors over the LCModel for NAA/Cr and Cho/Cr are 0.31 and 0.12 respectively.

**Speed:** Training time for the synthetic data is 10 minutes using the MLP. While the LCModel takes 10 minutes for the in-vivo metabolite quantification, our proposed network, after training, takes only 10 seconds leading to a 60x improvement in speed.



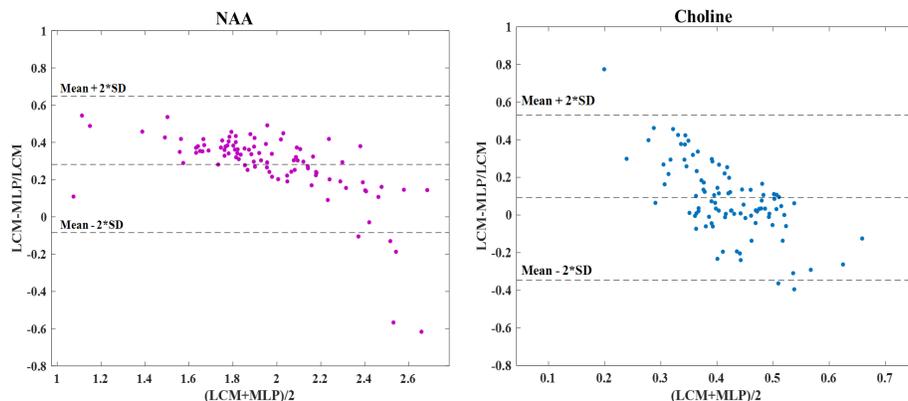
**Fig. 2.** Estimation error for different metabolite concentration ratios in a synthetic spectra test-set. Whiskers span the [min max] values. Median error values are represented by the red line and are as follows: NAA/Cr MLP = 0.050, LCMoDel = 0.065, Cho/Cr MLP = 0.0505, LCMoDel = 0.050.

### 3 Discussion and Conclusion

While the synthetic test-results gave a lower error compared to the LCMoDel, the in-vivo testing gave a slightly higher relative error. A larger training set with more training labels and a stronger network would solve this issue by providing a robust classification of real data. In our proposed method, testing and concentration estimation happens in only a few seconds and is considerably faster than the LCMoDel fitting. The deep neural-networks may be used directly, or indirectly by initializing LCMoDel fits thereby improving their results in the presence of noise and speeding up convergence.

Future work would involve using a more diverse network with layer-wise training of spectral features to improve the accuracy of parameter estimation. Once a framework has been established, further work can be done on combining these networks with global decisions about predicting spectral quality especially in the presence of artifacts.

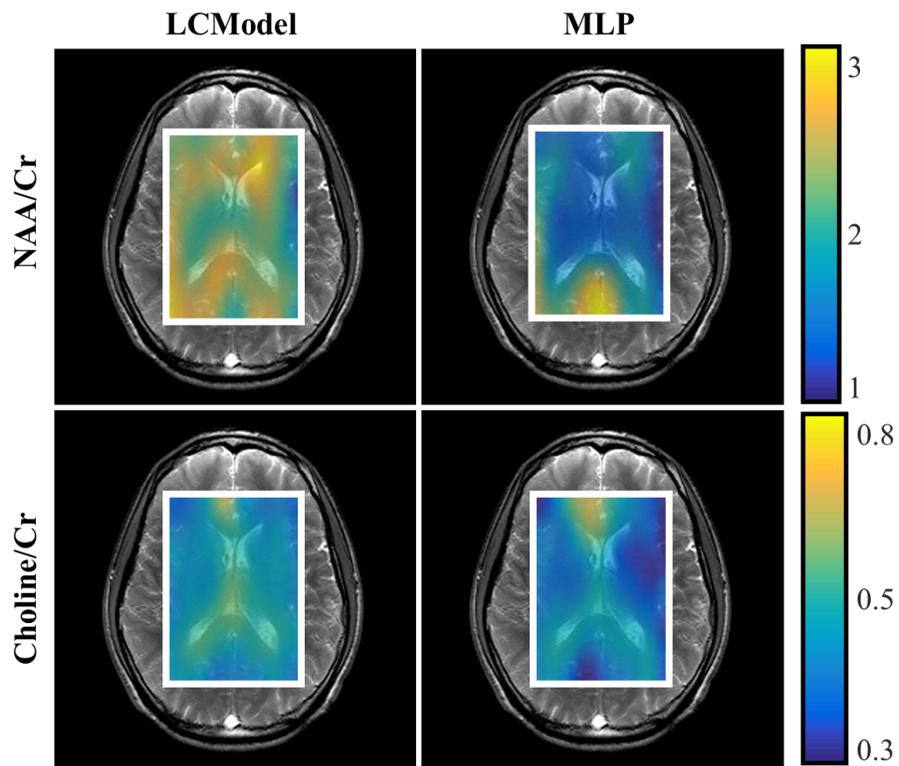
**Acknowledgements.** The research leading to these results has received funding from the European Union’s H2020 Framework Programme (H2020-MSCA-ITN-2014) under grant agreement n 642685 MacSeNet.



**Fig. 3.** Bland-Altman plots [1] representing LCMModel and Multi-Layer Perceptron (MLP) estimates of spectra for the real CSI dataset. The X-Axis is the mean of the LCMModel and MLP estimate, while the Y-Axis represents the relative error of the MLP estimate over the LCMModel. Bland-Altman plots for: **(Left)**: NAA and **(Right)**Choline. Both plots show a good correlation with very few outliers.

## References

1. Bland, J.M., Altman, D.: Statistical methods for assessing agreement between two methods of clinical measurement. *The Lancet* 327(8476), 307 – 310 (1986), <http://www.sciencedirect.com/science/article/pii/S0140673686908378>, originally published as Volume 1, Issue 8476
2. Das, D., Coello, E., Schulte, R.F., Menze, B.H.: Quantification of Metabolites in Magnetic Resonance Spectroscopic Imaging Using Machine Learning, pp. 462–470. Springer International Publishing, Cham (2017), [https://doi.org/10.1007/978-3-319-66179-7\\_53](https://doi.org/10.1007/978-3-319-66179-7_53)
3. Hecht-Nielsen, R.: Theory of the backpropagation neural network. In: International 1989 Joint Conference on Neural Networks. pp. 593–605 vol.1 (1989)
4. Provencher, S.W.: Estimation of metabolite concentrations from localized in vivo proton NMR spectra. *Magnetic Resonance in Medicine* (6), 672–9
5. Schulte, R.F., Lange, T., Beck, J., Meier, D., Boesiger, P.: Improved two-dimensional J-resolved spectroscopy. *NMR in Biomedicine* 19(2), 264–270 (2006)
6. Vanhamme, L., van den Boogaart, A., Huffel, S.V.: Improved method for accurate and efficient quantification of mrs data with use of prior knowledge. *Journal of Magnetic Resonance* 129(1), 35 – 43 (1997), <http://www.sciencedirect.com/science/article/pii/S1090780797912441>
7. Widrow, B., Lehr, M.A.: 30 years of adaptive neural networks: perceptron, madaline, and backpropagation. *Proceedings of the IEEE* 78(9), 1415–1442 (Sep 1990)
8. Wilson, M., Reynolds, G., Kauppinen, R.A., Arvanitis, T.N., Peet, A.C.: A constrained leastsquares approach to the automated quantitation of in vivo 1h magnetic resonance spectroscopy data. *Magnetic Resonance in Medicine* 65(1), 1–12 (1 2011), <http://dx.doi.org/10.1002/mrm.22579>



**Fig. 4.** NAA/Cr and Cho/Cr concentration distribution estimates from **(Left)**LCModel fit and **(Right)** multi-layer perceptron (MLP). The mean relative errors are 0.31 for NAA/Cr and 0.12 for Cho/Cr.