# Brain tumour classification using short echo time $^1$H MRS. Objective comparison of classification techniques (LDA, LS-SVM).

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## Introduction

Magnetic Resonance Spectroscopy (MRS) is a non-invasive technique, that can give detailed metabolic information of suspected brain tumours. Several studies have reported differences in metabolite concentrations between normal and cancerous tissue. Here we present an objective comparison of several classification techniques, for binary and multiclass classification of short echo time $^1$H spectra. The influence of several factors (e.g. normalization method, or complete spectra versus selected regions versus peak integrated values) on the performance is tested [2].

## Materials and Methods

The dataset was provided by 6 centres [1], four classes of common brain tumour types are considered: glioblastomas (*gbm*, 87 data), meningiomas (*mng*, 57), metastases (*met*, 39) and astrocytomas grade II (*astII*, 22). All data passed a quality control and validation process [1].

Three techniques were compared for classification: Principal Component Analysis (PCA) prior to Linear Discriminant Analysis (LDA), Least Squares Support Vector Machines (LS-SVM) with a linear kernel and LS-SVM with a Radial Basis Function (RBF). LS-SVM is a kernel-based technique that is able to learn and generalize in high dimensional input spaces without dimensionality reduction. Data were either normalized to the tumour water signal or to the area under the complete spectrum (L2-normalization). A comparison was also made of using the complete spectra (real and magnitude), selected frequency regions or peak integrated values corresponding to signals from known metabolites (lipids, *Lac*, *Ala*, *NAA*, *Glx*, *Cr*, *Cho*, *mI*, *Tau*, *Gly*). Multiclass classification is carried out in two steps; step one considers *gbm* and *met* as one class of aggressive tumours and separates *mng*, *astII* and aggressive tumours, while step two further separates the aggressive tumours into *gbm* and *met* (Figure 1). The performance for binary and multiclass classification was measured respectively by Receiver Operating Characteristic (ROC) curve analysis and the accuracy.

## Results

Based on the complete L2-normalized MRS spectra, binary classifiers are able to reach a mean area under the ROC curve (AUC) of at least 0.95, except for the most difficult binary classification to discriminate *gbm/met*. Table 1 shows the average performance based on the complete magnitude spectra after L2-normalization. All classification techniques, linear as well as nonlinear, perform well and based on the available data no significant differences were found between any of the applied techniques. Table 2 mentions the average performance based on the water normalized spectra. Comparison between L2- and water normalization yields in a few cases (e.g. *gbm*/*mng* when using PCA/LDA and LS-SVM with a linear kernel) a significantly lower performance for water normalization.

For the binary discrimination of *gbm/mng*, the following mean AUCs were obtained (test data): 0.973 (complete spectra), 0.973 (selected frequency regions) and 0.971 (peak integrated values), using LS-SVM RBF applied to the L2-normalized magnitude spectra. For multiclass classification based on the complete, L2-normalized, magnitude spectra, PCA/LDA, LS-SVM lin and LS-SVM RBF respectively reached a mean accuracy (test data) of 85.088%, 87.279% and 86.632% after step one, and 67.618%, 69.412% and 68.544% after step two. Although a quite good performance is obtained after step one, the separation of *gbm*/*met* clearly deteriorates the performance after step two.

## Conclusions

Similar results are obtained whether complete spectra, or selected frequency regions or peak integrated values are used. This indicates that the selected frequency regions and peak integrated values cover most of the available information and can be used to categorize brain tumour types. Based on our investigation all classification techniques reached a similar performance. However, due to the limited amount of data, the nonlinear technique (LS-SVM RBF) could not fully exploit its advantage to draw an optimal nonlinear separating boundary. The results also indicate that L2 normalization may provide a metabolite profile that is less dependent on changes in cellular density and tissue water than water normalization, but other normalizations such as quantitative analysis of the individual metabolite components must still be investigated.

**Table 1. Binary classification of L2-normalized spectra. Average test performance (mean AUC and its pooled standard error).**

| Classes | PCA/LDA | LS-SVM lin | LS-SVM RBF |
|---|---|---|---|
| *gbm* vs. *mng* | 0.956 ± 0.028 | 0.973 ± 0.021 | 0.973 ± 0.020 |
| *gbm* vs. *met* | 0.591 ± 0.097 | 0.592 ± 0.094 | 0.587 ± 0.094 |
| *gbm* vs. *astII* | 0.966 ± 0.029 | 0.964 ± 0.031 | 0.962 ± 0.031 |
| *mng* vs. *met* | 0.954 ± 0.044 | 0.977 ± 0.026 | 0.978 ± 0.025 |
| *mng* vs. *astII* | 0.997 ± 0.009 | 0.996 ± 0.010 | 0.990 ± 0.017 |
| *met* vs. *astII* | 0.986 ± 0.025 | 0.992 ± 0.018 | 0.990 ± 0.019 |

**Table 2. Binary classification of water normalized spectra.**

| Classes | PCA/LDA | LS-SVM lin | LS-SVM RBF |
|---|---|---|---|
| *gbm* vs. *mng* | 0.840 ± 0.061 | 0.929 ± 0.040 | 0.958 ± 0.028 |
| *gbm* vs. *met* | 0.549 ± 0.094 | 0.592 ± 0.093 | 0.595 ± 0.094 |
| *gbm* vs. *astII* | 0.949 ± 0.040 | 0.956 ± 0.034 | 0.960 ± 0.033 |
| *mng* vs. *met* | 0.892 ± 0.062 | 0.962 ± 0.047 | 0.970 ± 0.031 |
| *mng* vs. *astII* | 0.743 ± 0.120 | 0.993 ± 0.014 | 0.979 ± 0.030 |
| *met* vs. *astII* | 0.978 ± 0.030 | 0.976 ± 0.039 | 0.984 ± 0.028 |

## References

[1] http://carbon.uab.es/INTERPRET/.

[2] Devos, A. et al. Classification of brain tumours using short echo time $^1$H MRS spectra, *Journal of Magnetic Resonance.* submitted, http://www.esat.kuleuven.ac.be/scd/

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**Figure 1. Multiclass classification in two steps.**