

## Classification of cortical layers at sub-pixel resolution

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**Introduction:** Imaging of the brain's micro-structures became extremely popular with the development of techniques that can quantify features such as the axon diameter distribution through diffusion imaging<sup>1</sup> or the myelin water fraction through relaxometry<sup>2</sup>. The ability of MRI to detect such small features of the tissue turns MRI into a virtual microscope. However, MRI seems to fall short in detecting other features of tissue micro-structure such as the cellular architecture (cortical layers). While the imaging of such micro-structures can be resolved by increasing the image resolution to 200-300 microns, such conditions can only be met at high field MRI with lengthy acquisition times. Recently, inversion recovery MRI was shown to have high contrast and distinct  $T_1$  range for different layers of the cortex<sup>3</sup>. However, the implementation of this method is limited due to the partial volume artifacts in conventional imaging setup. In this work we introduce a post processing method which resolves the partial volume problem of cortical layer imaging. Using statistical learning and the IR data we compute for each voxel the sub-voxel layer composition. In addition, we use the sub-voxel composition to reconstruct enhanced resolution images of the layers.

**Methods:** (1) **Acquisition:** Subjects (aged 25-35) underwent MRI in a 3T scanner (GE). The protocol included IR-FSE acquired at resolution of  $0.43 \times 0.43 \times 1.5 \text{ mm}^3$  covering the entire hemisphere in the sagittal plane. The inversion time (TI) varied from 230 to 1380 ms.

(2) **Image analysis:** From the IR data set,  $T_1$  maps were calculated. Histogram of the  $T_1$  values revealed a multi-class pattern within the range of gray matter values (Fig. 1).

(3) **Statistical Learning:** The training set is calculated by fitting a Gaussian mixture model to the  $T_1$  data (Fig.1). For each class, we sampled the IR data for voxels in which the posterior distribution is high ( $>0.4$ ). Using this training set, we fit a classification model (logistic regression) that predicts (based on principal component analysis (PCA) of the IR data) the probability that a new voxel belongs to each of the classes. This analysis results in probability maps for each class (Fig. 2).

(4) **Resolution enhancement:** The sub-voxel composition, reflected by the classes' probability maps, is used to enhance the image resolution by solving a regularized optimization problem in which each voxel is divided to 4 sub-voxels such that their mean value has minimum deviation from the original voxel value. The regularization function used is total variation, which preserves the edges in the image. The optimization problem is solved by using the recently introduced FISTA algorithm<sup>4</sup>.

**Results & Discussion:** Using the classification model, we computed probability maps of each  $T_1$  class revealing a layer pattern across the cortex (Fig. 2). Such analysis overcomes the partial volume effects as it computes the sub-voxel composition based on the acquired data without imposing a single-component model on the data. Using the composition probability for each class in each voxel, and by calculating the enhanced resolution images, it is possible to minimize the partial volume artifact. Indeed, such analysis enables to reveal layer class that was masked by other more prominent classes in the same voxel. Example for that is shown in Fig. 3, where the enhanced resolution probability majority vote (hard classification) image (Fig. 3C) identifies layers (class 2 and 4) that could not be resolved in the original resolution (Fig. 3B). In addition, the enhanced resolution images have sufficient information to allow the visualization of the border between different cortical regions by inspecting the change in layer composition. Fig. 4 shows an example for such border definition, where the width of layer class 1 and 2 (see Figs. 4B and 4C) change at the border between the two adjacent regions (as predicted by the Free-Surfer cortical segmentation, Fig. 4A).

**Conclusions:** IR MRI enables robust classification and quantification of different layers within the cortex using a statistical learning approach. The layer class probability maps imply on the sub-voxel composition, which can be used to compute enhanced resolution images of cortical layer classes. Using the statistical learning approach described here, it is possible to explore and characterize the in-vivo cortical layer composition while minimizing partial volume artifacts without the need for extreme resolution acquisition.

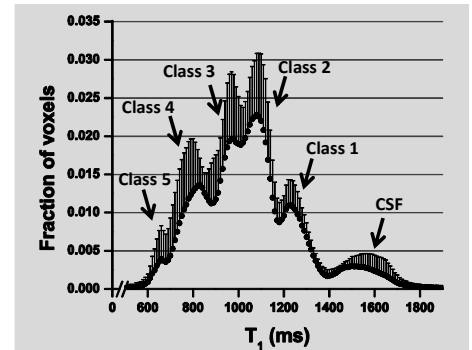


Fig. 1 – Histogram of  $T_1$  values of the cortex

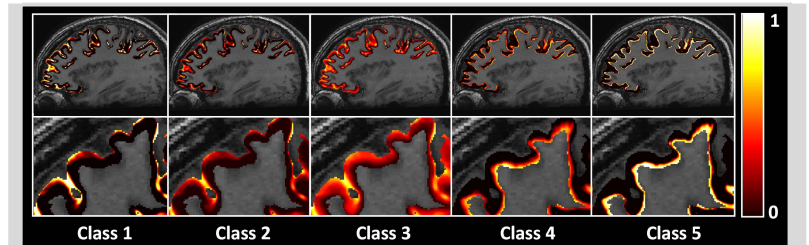


Fig. 2 – The different class probability maps. Color scale represents the probability of each class.

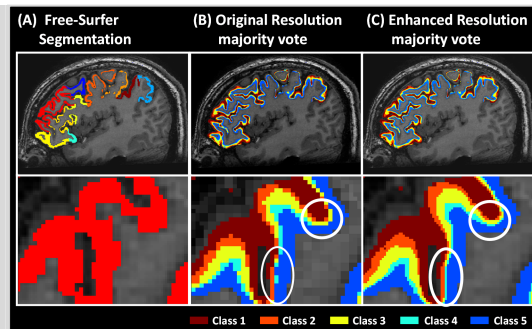


Fig. 3 – Revealing layer composition of the cortex

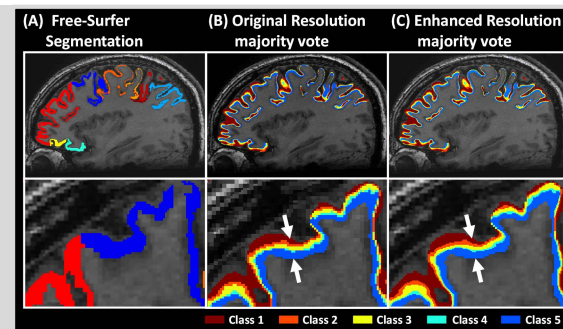


Fig. 4 – Identifying the border between cortical regions

**References:** 1. Barazany D, Basser PJ, Assaf Y. *Brain* 2009. 2. Du YP, Chu R, Hwang D, et al. *Magn Reson Med* 2007. 3. Barazany D, Assaf Y. *Cereb Cortex* 2011. 4. Beck A, Teboulle M. *IEEE Trans Image Process* 2009