Laminar time course extraction over extended cortical areas

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Target Audience: Brain researchers that are interested in (high resolution) laminar fMRI in humans.
Purpose: The human cerebral cortex consists of maximally six histological layers. As these layers are associated with different functions, it is of great interest to extract laminar signal from functional MRI volume signals. However, as the cortex is on average only 3 mm thick and its layers only a fraction of this, it is almost unfeasible to distinguish the different layers with fMRI, especially since the acquisition of very small voxels using EPI is associated with severe distortions and such high spatial resolution implies extremely low SNR. Here we propose a method to reliably extract time courses from a cortical area, despite having a voxel size larger than the layer thickness.
Methods: Hitherto, laminar signals have been deduced by integration of the MR signal over a cortical area, interpolated at a given cortical depth (e.g. [2,3,4,5]). Instead of interpolating, we propose to decompose the laminar signal by means of a General Linear Model[6]. This leads to much cleaner and more interpretable laminar signals.

The signal in each voxel can be considered as a linear combination of the signals contributed by different layers, which can be quantified in the form of a spatial design matrix (layer volume distribution). The layer volume distribution is based on the level set approach[7], yielding layer boundaries. We extended this to a quantification of the contribution of each layer to the voxel signal. If it is assumed that the underlying laminar signal is constant throughout the region of interest (ROI), then the voxel signals of the ROI can be regressed against this design matrix, yielding the estimated laminar signals from the ROI.

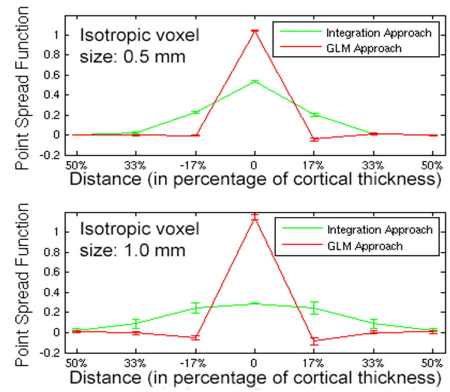

Figure 1: The Point Spread Function of our GLM approach (red) and the integration approach (green) for different voxel sizes. The sharp peak means that laminar signals can be more accurately disentangled from an fMRI signal.

For validation of the extraction of cleaner signals, we computed signal leakage for the integration approach and our proposed GLM approach, in the form of a Point Spread Function (PSF). In the absence of a gold standard model of how the histological laminae are folded in the brain, we simulated a cortical area by means of a spring-mass system. An important property of the cortex is preservation of layer volume ratio, independent of the curvature, which has become known as the Bok principle[7,8]. Six equi-volume layers were simulated in a piece of cortex that was positively and negatively curved, to simulate gyri and sulci respectively. Note that these layers are not equivalent to histological layers. Using the simulation, the spatial PSF for the extracted layer signal can be determined. Treating the simulated layers as a gold standard, the signal leakage between layers can be determined. The PSF of both methodologies is determined by simulating volumes in which one layer is given the value one; the remainder are set to zero. The extent to which this one layer signal leaks to other layers gives the PSF. The simulated layers were analysed at two isotropic resolution levels, one with a voxel size of 0.5 mm, the other 1.0 mm. The cortex was assumed to be 2.5 mm thick.

In addition, we examined the cortical profile of 11 subjects of a T1-weighted MP2RAGE, acquired at a 7T scanner, 1.0^3 mm^3, TR/TE/TI1/TI2 = 5000ms/1.89ms/900ms/3200ms, of the calcarine sulcus. The MP2RAGE was chosen for its homogeneous contrast and sharp transition from white to grey matter, such that the blurring effect could be investigated.

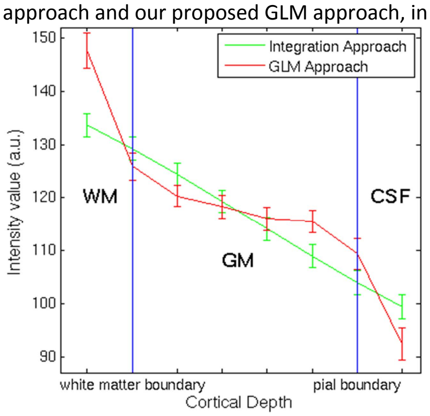

Figure 2: Grey matter signal extracted from an MP2RAGE, as determined by the integration approach (green) and our GLM approach (red). The GLM approach is significantly more flat in grey matter.

Results: The PSFs for both approaches are shown in Figure 1. For the integration approach, the signal clearly leaks to the neighbouring layers, becoming worse with increased voxel size. The proposed GLM approach for extraction of the laminar signal shows a much cleaner retrieval of the original signal. This shows that laminar signals can be better identified using a regression approach. The grey matter profiles of the MP2RAGE, shown in Figure 2, are expected to be straight if the grey matter signal is constant. This is almost achieved by the GLM approach, whereas the signal in the integration approach shows a smooth transition from the signal intensity of the white matter to the CSF.
Discussion: Our proposed method gives an accurate method of obtaining laminar time courses that is less confounded by leakage from neighbouring layers. In addition to the increased distinguishing power, the framework of the GLM allows for estimations of uncertainty in the obtained signals. Both methods come with assumptions: the laminar signals in the ROI are assumed to be constant. For our approach, normality of errors is assumed. The method allows for variable layer thickness, which can be useful in order to match the histological layer thickness. Care must be taken, as this may introduce a bias towards the thicker layers as they contribute more to the squared error. Even though our approach does not resolve the problems such as subject motion, distortions in the functional images or physiological noise, their effects may be reduced as larger voxel sizes are allowed.
Conclusion: Our proposed method is a reliable and accurate way to extract laminar time courses from fMRI data. This may help to overcome the severe SNR and distortion problems of traditional laminar analysis, by allowing larger voxel sizes to extract a laminar signal.
References: [1]Hawkins J, Blakeslee S. On Intelligence. Times Books 2004 [2]Koopmans, PJ et al. Layer-specific BOLD activation in human V1, Human Brain Mapping 2010. [3]Polimeni JR et al. Laminar analysis of 7T BOLD using an imposed spatial activation pattern in human V1, NeuroImage 2010 [4]Olman CA et al. Layer-specific fmri reflects different neuronal computations at different depths in human V1, PLoS ONE 2012 [5]Martino FD et al. Cortical depth dependent functional responses in humans at 7T: Improved specificity with 3D GRASE, PLoS ONE 2013. [6] Friston KJ et al. Statistical Parametric Maps in Functional Imaging: A General Linear Approach. Human Brain Mapping 1995;2:189-210 [7]Waehnert MD et al. Anatomically motivated modeling of cortical laminae. NeuroImage 2013 [8]Bok ST. Der Einfluss der in denFurchen und Windungen auftretenden Krommungen der Grohirnrinde auf die Rindenarchitektur, Z. Gesamte Neurol Psychiatr 1929