Defining and Measuring Cortical Thickness: Histology and MRI

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Introduction

- MRI data has been used for estimation of cortical thickness in vivo [Fischl 2000, Hutton 2008].
- The gray matter (GM) - white matter (WM) boundary is strictly defined only by cytoarchitecture.
- However, MRI contrast mostly derives from the presence of myelin, so that images show myeloarchitecture.
- Investigation of brain sections stained alternately for myelin and neuronal cell bodies may provide detailed criteria for determining the GM-WM boundary from MR images.

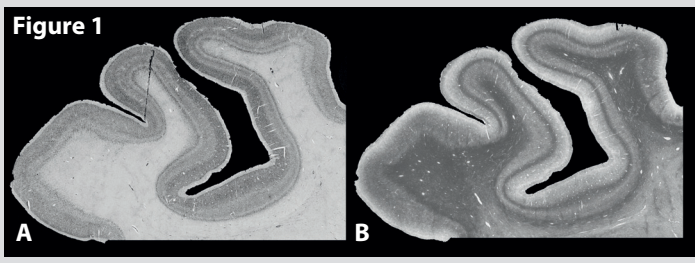
Methods

- We sectioned the visual cortex of a human postmortem brain at 30 µm and stained alternately for cell bodies (Merker silver impregnation, fig. 1a) and myelin (Gallyas stain, fig. 1b).
- The images from adjacent section pairs were masked and co-registered. Linear registration (fig. 2a) was followed by unwarping, non-linear registration (fig. 2b) using AIR 5 (Automated Image Registration, RP Woods), since sections can undergo significant mutual distortion during sectioning, mounting, and staining.
- Laplace equation approach: [Jones 2000, Annese 2004, Hutton 2008]
  - Preliminary boundaries: pial boundary and the GM-WM boundary obtained by thresholding the cell-body stained section.
  - Apply relaxation method to solve the Laplace equation and obtain isocontour lines (fig. 3a).
  - Take gradients of solution to compute 1280 individual cortical traverses (fig. 3c).
- cortical profiles:
  - Extend traverses at both ends to ensure that pial and GM-WM boundaries and plateaus representing WM are reflected in profiles.
  - Take gray values at 100 equidistant points (to ensure normalization) along identical traverses from pictures of cell and myelin stained section (fig. 3c, fig. 3d) to construct 1280 individual cortical profiles.
  - Use a sliding average of 70 neighboring profiles to construct final average profiles (fig. 4).

Results

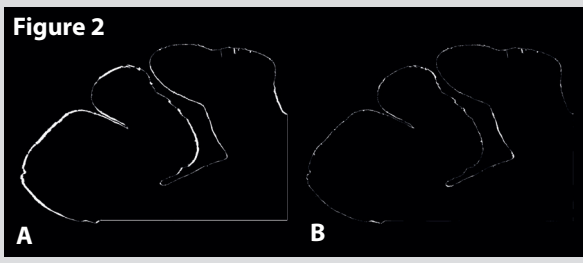
- Cortical traverses (fig. 3c, fig. 3d) derived using the Laplace equation are more realistic than the straight lines used in earlier studies [Schleicher, 2005]. These do not intersect, and they strike the cortical boundaries perpendicularly [Annese, 2004]. They are often consistent in direction with the larger intracortical blood vessels (fig. 5a, circle), which implies that in several regions the plane of section was parallel to the vertical organization of the cortical columns [Schleicher, 2005]. In the myelin-stained section at 5 µm/pixel resolution (not shown), in these regions, the myelin fibers can be seen along their whole length across the cortex.
- Final pial boundary and GM-WM boundary derived from profiles of cell stained section (fig. 4, blue line):
  - The final pial boundary is identified as the maximum in the left half of each average profile (fig. 4, green dashed line).
  - The final GM-WM boundary is identified in the region just before the plateau representing the consistently lower cell density of WM (fig. 4, blue +). It is the point of intersection (fig. 4, red x) between the so called cell criterion and the profile. The cell criterion is the percentage of the gray value of WM (fig. 4, blue x) which gives the most reasonable GM-WM boundary when being plotted onto the cell stained section (fig. 5a).
  - Found cell criterion for this section of visual cortex is 93% of its value in WM. Standard deviation of location of final GM-WM boundary over all average profiles: 3%.
- Cortical thickness: The lengths of six different traverses in between the final boundaries are 2.53 mm, 2.29 mm, 2.04 mm, 3.31 mm, 2.16 mm and 2.32 mm (fig. 5a and b, dark blue lines from left to right). The changes of cortical thickness may be due to a variation of the cutting angle.
- Behavior of myelin stained sections at final pial and GM-WM boundaries:
  - Plotting the boundaries at exactly the same location onto the myelin stained section (fig. 5b) was possible because of the registration and corresponds to the boundaries seen here.
  - Average profiles of the myelin stained section (fig. 4 , black line) [Eickhoff, 2005]: The myelin criterion (fig. 4, orange x) is the gray value of the profile at the final GM-WM boundary, expressed in percent of the gray value of WM (fig. 4, gray +). Mean of myelin criterion over all averaged profiles: 118 %, Standard deviation: 10%.

Figure 1



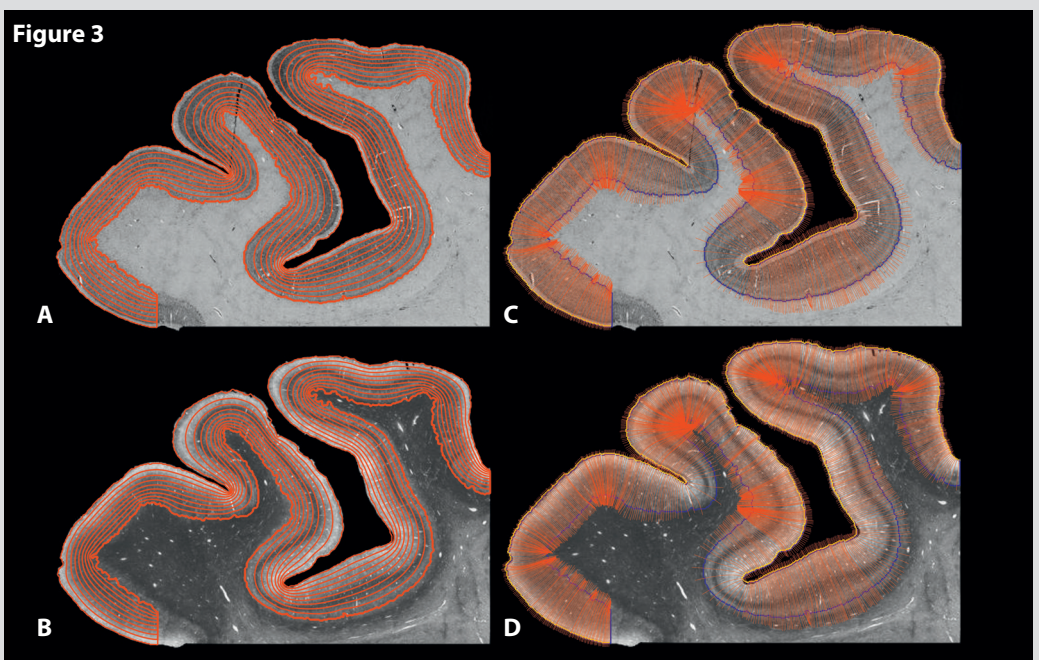
Part of the occipital lobe of a human postmortem brain including a length of the stria of Gennari.
Resolution: 10.32 µm/pixel.
A: Cell stained section (standard picture).
B: Myelin stained section.

Figure 2



In order to evaluate registration, the difference was constructed between conversions into 1bit images, where the background was set to 0 and the image was set to1. A: Differences between the cell stained and the linearly registered myelin stained section (1.9%). B: Differences between the cell stained section and the unwarped myelin stained section (0.6%).

Figure 3

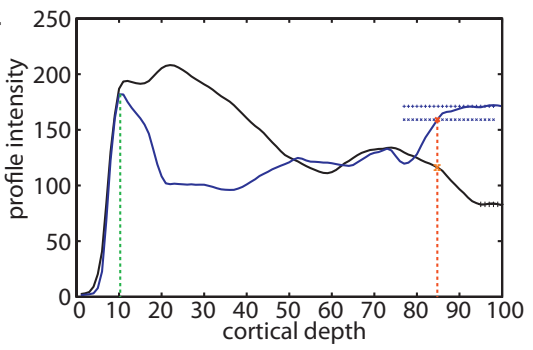


Resolution 51.6 µm/pixel

A: Isocontour lines of Laplace equation solution.
B: Contours from fig. 3A plotted onto the unwarped myelin stained section.

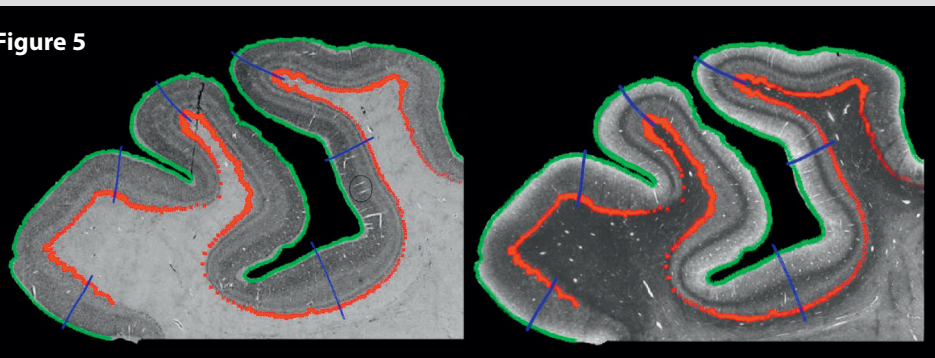
C: Extended traverses (red lines) and their starting points (yellow line), reflecting and end points (blue line).
D: Traverses and boundaries from fig. 3C plotted onto the unwarped myelin stained section.

Figure 4



Example of two corresponding average profiles from the cell stained section (blue line) and the myelin stained section (black line). Cell WM: blue +. Cell criterion: blue x. Final GM-WM boundary: red x. Myelin WM: gray +. Myelin criterion: orange x. Final pial boundary: green line.

Figure 5



Green line: Final pial contour. Red line: Final GM-WM boundary. Blue lines: The parts of the traverses that are between the final boundaries represent cortical thicknesses.

Conclusions

The question to be answered here was, how does the GM-WM boundary determined by cytoarchitecture look in the myeloarchitecture? Since staining a section for both modalities at once is impossible, precise registration of two nearby sections was vital. For this section we deduced a 93% cell criterion from the extended cell profiles, describing at how many percent of the cell WM plateau one finds the GM-WM boundary. This was checked by plotting the resulting GM-WM boundary onto the cell stained section.
The crucial point in this work was to analyze the myeloarchitecture at the so found GM-WM boundary w.r.t. the myelin WM plateau. We found that the GM-WM boundary occurs at 118% percent of the WM plateau gray value. Taking this myelin criterion enables us to deduce the location of the cell GM-WM boundary from myeloarchitecture alone, e.g. from T1 MRI pictures. We plan to extend this to a more robust and quantitative definition of the boundary criterion in high resolution (200 µm/pixel) MR images of postmortem and living human brains. This should enable anatomically much more valid in vivo mapping of cortical thickness.

References

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