

## Sub millimiter coregistration of functional maps across imaging sessions

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**Introduction** – fMRI is ideally suited for longitudinal studies of structural and functional brain plasticity. It is now feasible to collect functional brain maps with spatial resolutions of  $\sim 100 \mu\text{m}$  in ultra-high field systems. While these data sets are intrinsically coregistered for studies collected within a session from immobilized animals, the accuracy of coregistration across imaging sessions (or within, in the presence of head motion) is limited by the accuracy with which structural and functional images can be coregistered. The goal of this study is to develop an accurate and reliable registration process for longitudinal acquisitions of functional MRI scans providing partial brain coverage at very high resolution in order to quantify functional and structural changes across time.

**Methods** – Structural and functional images were collected from five squirrel monkeys across multiple sessions separated by weeks to months. In each session, three types of image volumes were acquired: a) BOLD and/or CBV-weighted functional echo planar images (EPI) runs, centered on the somato-sensory cortex, comprising 4 contiguous slices oriented obliquely with respect to the scanner frame of reference (in-plane resolution  $0.27 \times 0.27 \text{ mm}$ , 2 mm slice thickness); b) a high resolution anatomical slab of 4 slices covering the same space, having the same orientation as the functional slab (in-plane resolution  $68.5 \times 68.5 \mu\text{m}$ , slab thickness 2 mm); c) an anatomical image covering the whole head (resolution:  $0.5 \times 0.5 \times 0.5 \text{ mm}$ ). All images were acquired with the same 3 cm surface coil on anesthetized monkeys under an IACUC approved protocol. Focal single activations were generated in area 3b of primary somatosensory cortex by delivering seven 30 sec duration blocks of vibrotactile stimulation, alternated with 30 sec rest periods, to digits 1 and 3.. We assume that geometric distortion is minimal for the anatomical slabs. The various transformations required to register these images are thus all rigid body transformations. The easiest approach would be to simply register slabs acquired during different sessions to each other with a standard intensity-based algorithm. However incomplete overlap of slabs across sessions led to unsatisfactory performance with intensity-based techniques. The solution we developed to address these issues involved four main steps: (1) register the anatomical slab to the full head volume acquired during the same session; (2) register full head volumes across sessions; (3) apply distortion correction to the functional maps; (4) apply the overall transformation computed to the distortion corrected functional maps.

Using a combination of mutual information [1] intensity-based rigid-body registration [2] with information retrieved from the scanner (Euler angles used to acquire the scan and center of the volume) as a starting point, we were able to accurately register the anatomical slab to the full head scan. Since signal attenuation is severe with the surface coils, and because the coil is not placed at the exact same position relative to the brain from acquisition to acquisition, regions of the brain show

variable signal attenuation across acquisitions and direct intensity based registration between full head scans was unreliable. We therefore generated gradient images, and used mutual information on these gradient images of the full head scans to register them together between the two timestamps

Since the EPI data sample the same volume as the anatomical slab, the overall transform from anatomical slab 1 to anatomical slab 2 was used on functional maps computed from the average of the three EPI runs without, and then with distortion correction

**Results** – Fig. 1a-c show the two original anatomical slabs before registration and the result of registration. The green lines represent landmarks from slab 1 (sulci, vessels, etc.) projected on slab 2 after registration. Anatomic coregistration of the slab across two sessions in five monkeys was accurate to  $30 \mu\text{m}$  (s.d.  $15 \mu\text{m}$ ). Fig. 1d-g show the same slice of both slabs with the BOLD functional maps overlaid before registration and following registration of raw and distortion-corrected functional maps. Fig. 1h-k present the equivalent results for the CBV-base functional maps. As shown in Fig. 1 f, j, this rigid body coregistration of raw functional maps, while accurate to  $\sim 1 \text{ mm}$  across sessions, was nonetheless significant, and presumably reflects the effects of residual distortion in the EPI images. Correction of these residual distortions led to excellent ( $< 100 \mu\text{m}$ ) coregistration of the activation centers maps obtained by BOLD and CBV mapping.

**Discussion/Conclusion** – To the best of our knowledge, this is the first registration method proposed for the longitudinal registration of ultrahigh resolution functional maps with sub-millimeter coregistration accuracy. Furthermore, these results suggest that high resolution fMRI mapping has the capability to identify functional reorganization in cortex with sub-millimeter accuracy in longitudinal studies.

Figure 1 – Results of registration. From left to right: Session 1, session 2 and result of registration of session 1 images to session 2. Top panel: anatomical slabs. Middle panel: BOLD maps. Bottom panel: CBV maps. Colors lines on right column images are features from Day 1 projected on Day 2 images after registration.

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**References** – [1] Studholme, C., Hill, D. and Hawkes, D., "An overlap invariant entropy measure of 3D medical image alignment," *Pattern Recognition* 32, 71-86 (1999). [2] Maes, F., Collignon, A., Vandermeulen, D., Marchal, G. and Suetens, P., "Multimodality image registration by maximization of mutual information," *IEEE Transactions on Medical Imaging* 16(2), 187-198 (1997).