# 8th BigBrain Workshop - Challenges of Multimodal Data Integration



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# Adaptation of FreeSurfer v7.4 pipeline for automated volumetric parcellation and cortical surface extraction of BigBrains 1 and 2

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## Introduction:

In 2013, we published BigBrain1 (BB1), a high-resolution ( $20\mu m^3$ ) histological 3D-reconstructed model of the human brain (Amunts et al., 2013). Over the past several years, progress has also been made on BigBrain2 (BB2) (Mohlberg et al., 2022; Lepage et al., 2023), with preliminary reconstruction and segmented volumes [white matter (WM) and gray matter (GM)] now available ( $100\mu m^3$ ).

Here, we utilize the segmented volumes as input to an MRI simulator, which can then be used as input to an adapted FreeSurfer (FS) v7.4 pipeline.

Outputs of this pipeline include:

(1) FS white and gray cortical surface extractions for BB1 and BB2, which may improve multimodal surface matching (MSM) surface registration (Robinson et al., 2018). Although MSM was developed and parameterized on FS surfaces, we (Lewis et al., 2023) have used it in the past to register (CIVET-extracted) BigBrain surfaces to structural MRI-derived population average surfaces that serve as important reference frames for multimodal data integration, e.g. FS'fsaverage (Fischl 2012) and Human Connectome Project's (HCP) fs\_LR (Van Essen et al., 2012). FS-extracted surfaces possess tessellation and medial cut methodologies expected to be more compatible with MSM surface registration.

(2) Initial automated FS volumetric parcellations (wmparc.mgz) of BB1 and BB2, which can provide regions of interest for higher-resolution analyses, such as FS'hippocampal subfield segmentation (Iglesias et al., 2015).

### Methods:

We created 2 versions each of segmented volumes ( $200\mu$ m<sup>3</sup>) of BB1 and BB2. In both versions, we premasked the hippocampus and amygdala as GM. In version (A), we additionally masked all other subcortical gray regions as WM (to improve subsequent cortical surface extraction). This version was used as input to mrisim (Kwan et al., 1996; modified to allow high-resolution input and output) to create a simulated T1weighted volume ( $200\mu$ m<sup>3</sup>) which was then used as input to Freesurfer (FS) v7.4. In version (B), we did not pre-mask the subcortical gray regions. Version (B) was used as input to mri\_synthseg (Billot et al., 2023), as described below.

The simulated T1 volumes were submitted to a modified version of the FS -hires ( $200\mu m^{3}$ ) pipeline, with the following most notable changes. Instead of the default mri\_ca\_label, we used mri\_synthseg (v1), which we found was superior for our subcortical masking needs (both in terms of quality and efficiency). For surface extraction, we additionally modified recon-all to produce high-resolution surfaces (~500k vertices per hemi).

While the white surfaces were of decent quality, we found that the pial surfaces were severely underexpanded for high-resolution surfaces (~500k vertices). Thus we had to additionally modify: mris\_autodet\_gwstats; mrisurf\_mri.cpp; mris\_place\_surface.cpp.

### **Results:**

Fig 1A shows examples of FS white and gray surface extractions for BB2.

Fig 1B shows automated FS volumetric parcellation (wmparc.mgz) for both BB1 and BB2 (200 $\mu$ m^3).

Fig 1C shows the FS hippocampal subfield segmentation output when the histological intensity volume (113 $\mu$ m^3) is input to mimic a T2-weighted volume.

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