A Step-by-Step Guide to Cortical Surface Modeling of the Nonhuman Primate Brain Using FreeSurfer

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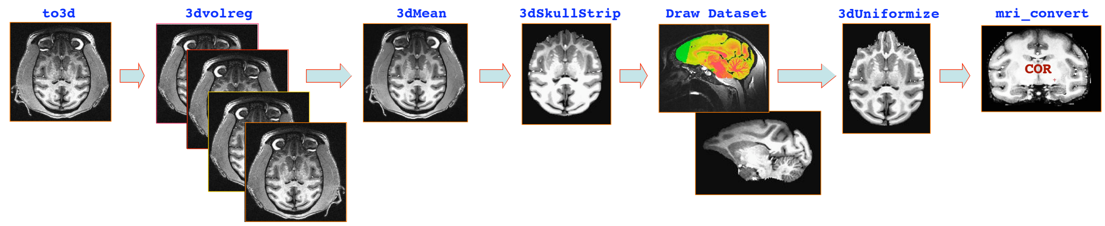
INTRODUCTION

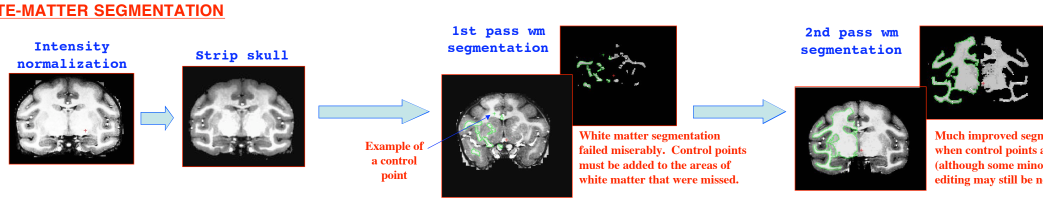
The cortical reconstruction of nonhuman primate volumes presents some unique challenges not seen in human surface modeling. For instance, a vital step in cortical reconstruction is to correct for intensity non-uniformities in the volume. This step results ina sharper distinction between the tissue classes, which leads to a better white matter segmentation. The segmented volume is then used to reconstruct a cortical surface. In primates, a large mass of muscle attached to the skull appears as high intensity voxels in the 3D volume, which can cause the non-uniformity correction to fail. As such, the skull and muscle in non-human primate volumes must be removed prior to performing the non-uniformity correction. The thin lines of white matter in the primate brain also make segmentation difficult, resulting in more manual editing than with human volumes. Finally, some of the newer features in FreeSurfer that attempt to automatically correct flaws on human surface models cannot be applied to primate volumes, thereby requiring greater manual editing by the user.

VOLUME PRE-PROCESSING



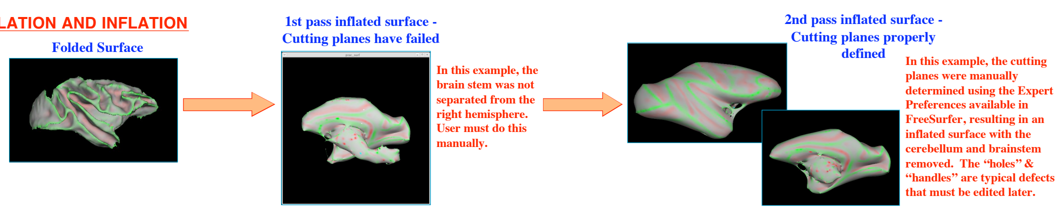
- The pre-processing stream is somewhat involved for primate volumes. As with human volumes, the primate volumes are first assembled in AFNI using **`to3d`**. The volumes are then aligned using **`3dvolreg`**, and averaged together with **`3dMean`**.
- At this point, the skull is removed with the AFNI program **`3dSkullStrip`**. The large volume of muscle attached to the skull shows up as high intensity voxels in the volume, which can cause 3dUniformize to fail if the intensity normalization is done *prior* to skull stripping.
- Any cortex that was inadvertently removed by 3dSkullStrip must be added back manually, using the **`Draw Dataset`** plugin in AFNI
- **`3dUniformize`** can now be implemented, followed by FreeSurfer's COR-formatting program **`mri_convert`**.

WHITE-MATTER SEGMENTATION



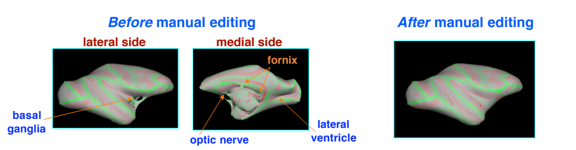
- Although a non-uniformity correction was already performed outside of FreeSurfer using the AFNI program **`3dUniformize`**, FreeSurfer nonetheless performs another one internally. The program then takes the corrected volume and strips the skull using a watershed algorithm (this is not really necessary with the monkey volume because the skull has already been removed, but the program is nonetheless useful because it will remove additional skull "debris" that may not have been picked up before with 3dSkullStrip). The next step is segmentation of the white matter.
- Due to fine strands of white matter in the primate brain, the automated segmentation program in FreeSurfer often misses many of the white matter voxels within those strands. Therefore, "control points" must always be added to primate volumes to help the program locate most white matter voxels.
- Even with control points, the user must manually insert white matter voxels that were missed by the program. The segmented volume can then be reconstructed into a surface model.

TESSELATION AND INFLATION



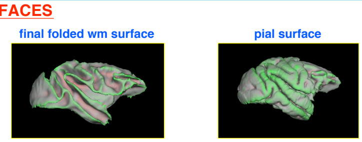
- Surface tesselation and inflation for primates is similar to that of humans. One possible problem, however, is that the cutting planes (done after *white* matter segmentation) may fail for primate volumes, resulting in a surface that contains the cerebellum and/or brain stem.
- If cutting planes fail, they must be manually defined by the user, either in command line mode, or via the "Expert Preference" menu in the FreeSurfer graphical interface. Once the planes have been correctly defined, the next step is to re-inflate the surface.

MANUAL EDITING



- This step is necessary to correct for segmentation errors and anatomical defects, which appear as "holes" and "handles" on the surface.
- Problem areas typically include the **fornix**, **lateral ventricles**, **basal ganglia**, and **optic nerve**.
- Manual edits are done with the volumetric data. These edits are then applied to the surface when it is re-inflated.
- The more accurate the white matter segmentation, the less manual editing that needs to be done. This is another reason why proper segmentation is so important.

FINAL SURFACES



- FreeSurfer Menu: `Subject Tools ---> Make Final Surfaces`
- The last step in cortical reconstruction of nonhuman primate volumes is to create the final surfaces, which are free of topological defects, and are (hopefully) topologically correct.
- These final surfaces include a folded surface, an inflated surface, and a gray matter "pial" surface
- At this stage, one can also use the following additional FreeSurfer tools: (1) cut & flatten surface to make flat maps (of an entire hemisphere or just portions of it), (2) create spherical surfaces and register them to a template of 40+ averaged brains (humans only, no primate version available), and (3) overlay functional data onto the surfaces.

CONCLUSION

FreeSurfer is very capable of creating cortical models of nonhuman primate volumes. However, the processing of primate volumes involves some unique challenges that the user must attend to. For instance, the muscle mass in monkey volumes must be removed prior to running a non-uniformity correction on the volume, and since the gray/white matter distinction is not well defined at this stage, the skull-stripping program may also remove some cortex, which much be manually drawn back before processing the volume any further. Furthermore, primate white matter tends to be thinner and finer than that of human white matter, making segmentation of those white matter voxels difficult. Control points must be added to the primate volume in order for FreeSurfer's segmentation program to adequately distinguish between gray and white matter voxels in these problem area. Finally, since primate volumes cannot be placed into Talairach coordinates (as is done with human volumes), the program in FreeSurfer that divides the two hemispheres and removes the cerebellum and brainstem may fail, thus requiring the user to manually define the cutting planes. Although the process of creating surfaces for nonhuman primates is a bit more involved than for human surfaces, the future may hopefully bring computer applications that will facilitate (and automate) this process.