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## IDEAS FOR BRAIN SHAPE ANALYSIS

Here are a few ideas that came to my mind after reading your R01 grant proposal. Your proposal has very ambitious and very exciting goals! I listed below some suggestions to do things differently based on my experience in industry and academia. Please consider them as brainstorming notes that we would throw on the whiteboard before deciding on the best strategy and diving into the postdoc adventure. I do not guarantee that these alternative methods would work better; only a test-driven approach will tell. At Kitware we used to say: 'If it is not tested, it doesn't work!' I would be very interested to hear your opinion next week if you are available.

### 1. Automated extraction of brain structures

A 3D approach is definitely what we need to shoot for. However my experience with skeleton extraction is that it is not robust to noise (spurious details at the boundary of a structure could create ghost features). As an alternative, I would extract the brain folds based on a curvature analysis. I would differentiate the sulci and the gyri using the mean curvature and the local normal. I would build on my previous work in shape characterization [1] and extend it with the recent results on curvature computation using optimal point sampling over the boundary surface of the anatomical structures [2]. A point based method could lead to a very efficient implementation, which could turn critical to gain an order of magnitude acceleration.

### 2. Parametric shape analysis

During my PhD, I tried fitting a surface in a brain volume using an active surface ('snake'). I realized that pushing the active surface deep inside the brain folds while these folds are only one or two voxel(s) apart was not trial. A careful numerical analysis showed that balancing the terms of the Mumford-Shah functional would be practically impossible and difficult to reproduce across different clinical data sets. The macroscopic MRI artifacts (particularly partial volume effect, susceptibility artifact, and chemical shift) blur the brain fold interfaces and smooth out the distinction between background voxels and brain voxels. That is what motivated my research on topology correction of cortical surfaces [3]. I have always followed the research in the meshing community and particularly the developments in parameterization of surfaces [4]. I believe that coupling the ITK mesh structure and some Open Source numerical libraries (e.g. GOTO BLAS) could lead to a very efficient implementation of surface parameterization algorithms for brain shape analysis.

### 3. Geometric shape analysis

In addition to the geometric measurements (volume, boundary surface area, direction in a stereotactic frame), I would like to increase the set of metrics with a cortical thickness measurement along the lines of my IEEE paper [5]. A major finding in this publication is that the boundary of the bladder exhibits a variable thickness and that a mesh-based algorithm can automatically discriminate between pathological and normal thickness. To achieve this study, I

developed a novel algorithm to perform a local thickness measurement and create a statistical atlas of the local thickness across a cohort of 3D images. I am confident that the same principle could be applied to brain shape analysis and I would love to create the first thickness atlas for the cortex.

#### 4. Editing of cortical surfaces

Currently no computer tool provides the flexibility to edit a surface for annotation and/or geometric correction. Recent developments with Slicer within the NA-MIC community try to address this issue [6]. Based on my 10 year overview of medical imaging platforms, I can say that the software package BrainSuite developed by Professor Shattuck is one of a kind in its ability to trace in real-time sulcal creases and ridges. Such a tool would be useful for reducing the time burden during manual delineation and editing of brain ROIs. At Siemens I developed for the CT scanner platform (I'm sorry to say I did some closed source development!) a surface editing tool based on contour tracing and surface reconstruction. I believe that a similar result could be achieved using subdivision surfaces or cubic Hermite patches... and made available Open Source in MindBoogle! Besides, a graph editor would be a wonderful contribution to allow for the creation of hierarchical representations of the brain.

#### 5. Statistical analysis of anatomical structures

Related to your vision of statistical modeling of brain shapes for automated segmentation, I would like to investigate the statistical variability of brain structure orientation, in a similar fashion as my analysis of cardiac fiber orientation [7]. This work could be complemented with my recent work on segmentation and tracking of spinal nerves [8] to create a stochastic tractography tool for brain structures orientations. I am very enthusiastic to pursue this research direction as it brings together my experience with statistical modeling [9], efficient algorithm implementation and visualization of high dimensional data!

#### 6. Brain parcellation

The idea I would promote to tackle brain parcellation would be to use a wavelet decomposition on meshes [10]. This paper, which I wrote during my internship with Professor Schroder at Caltech, was the first to bring the concept of wavelets on meshes to the medical imaging area. The problem I wanted to address at that time was atlas-based surface registration for brain labelling. The idea was to first decompose an atlas brain surface into its wavelet components. Since the large features (e.g. central sulcus) can be reliably detected across subjects, this method offers a robust gross alignment. Then I iteratively added the smaller features (secondary and tertiary sulci) and aligned the brain surface at every level of the progressive refinement. Once the atlas surface was registered at its finest resolution (smallest wavelets components), the labels from the atlas surface can simply be transferred to the subject brain surface by a local neighborhood search. This neighborhood segmentation can easily be replaced by a ROI segmentation to enhance the brain parcellation in Mindboogle. My wavelet on meshes method could favorably extend the current ITK implementation, which is limited to spherical representations. Since mapping to the sphere introduces local shape distortion that are difficult to control, a wavelet framework for irregular surfaces would be extremely beneficial for the shape analysis of the brain and its highly folded pattern.

## 7. New trends in software design

Since the beginning of my PhD work, I have been an active member of the Open Source community. I package the code of my thesis into what I called the OpenTopology toolkit [3]. When I joined Siemens Corporate Research, I immediately configured the eXtensive Imaging Platform (XIP is an imaging library built on top of OpenInventor) using CMake and made the first cross-platform releases and automated builds of XIP [11]. Thanks to the commitment that Siemens made to win the NIH NCI grant (<https://cabig.nci.nih.gov>), I was authorized to run Windows, Linux and MacOS on my desktop! At Kitware had the chance to be the main developer to port the NVidia GPU language CUDA in the VTK libraries [12]. At the Brigham and Women's Hospital, I focus on multi-threading programming to take advantage of multi-core computer architectures and generate real time segmentation results during image guided surgery. Parallel algorithms and multi-core aware implementations will be critical for Mindboogle to scale up to a massively large number of anatomical feature comparisons.

## 8. Untouched research avenues

The analysis of topology for brain surfaces [13] has been an area that has been practically untouched until now. I would speculate that the reason is that a change of mindset from the Image Processing and Computer Vision community is necessary to move from a pixel-centric approach to a more Mathematical approach. The concepts of Discrete Topology and Computational Geometry are challenging to grasp and the current algorithms are not amenable to an easy translation. Besides the data structures, libraries and visualization tools are only available for some specific domains (CGAL for modeling, Catia for industrial design, 3DStudio for animation) and need to be ported to the Computational Neuroscience domain by scientists and engineers with an expertise in mesh processing. Based on my interaction with scientists at Caltech Computer Science Department and MIT Applied Math Department, I believe the Neuroscience community would tremendously benefit from concepts in Discrete Topology and Computational Geometry.

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