



Computational Neuroscience

Skull-stripping with machine learning deformable organisms

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HIGHLIGHTS

- Our segmentation plan framework adapts to any segmentation problem and dataset.
- A novel definition of deformable organisms that work to segment an image.
- Example using a plan for brain segmentation or skull-stripping.
- Compared with manual segmentations and methods specific for skull-stripping.

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ABSTRACT

Background: Segmentation methods for medical images may not generalize well to new data sets or new tasks, hampering their utility. We attempt to remedy these issues using deformable organisms to create an easily customizable segmentation plan. We validate our framework by creating a plan to locate the brain in 3D magnetic resonance images of the head (skull-stripping).

New method: Our method borrows ideas from artificial life to govern a set of deformable models. We use control processes such as sensing, proactive planning, reactive behavior, and knowledge representation to segment an image. The image may have landmarks and features specific to that dataset; these may be easily incorporated into the plan. In addition, we use a machine learning method to make our segmentation more accurate.

Results: Our method had the least Hausdorff distance error, but included slightly less brain voxels (false negatives). It also had the lowest false positive error and performed on par to skull-stripping specific method on other metrics.

Comparison with existing method(s): We tested our method on 838 T1-weighted images, evaluating results using distance and overlap error metrics based on expert gold standard segmentations. We evaluated the results before and after the learning step to quantify its benefit; we also compare our results to three other widely used methods: BSE, BET, and the Hybrid Watershed algorithm.

Conclusions: Our framework captures diverse categories of information needed for brain segmentation and will provide a foundation for tackling a wealth of segmentation problems.

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1. Introduction

Deformable organisms label objects in images by integrating high level control mechanisms into a segmentation plan. More recent implementations have incorporated a variety of processes such as sensing, knowledge representation, reactive behavior, and proactive planning; a set of organisms may also cooperatively segment an image. Deformable organisms were introduced

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into medical imaging by [McInerney et al. \(2002\)](#) who combined ideas from artificial life ([Steels, 1993](#)) and deformable models ([McInerney and Terzopoulos, 1996](#); [Terzopoulos et al., 1987](#)). Since their introduction, deformable organisms have been used for limb delineation ([McIntosh et al., 2007](#)), and segmentation of the spinal cord ([McIntosh and Hamarneh, 2006b](#)), vasculature ([McIntosh and Hamarneh, 2006c](#)), and corpus callosum in the brain ([Hamarneh and McIntosh, 2005](#)). [McIntosh and Hamarneh \(2006a\)](#) created a deformable organisms framework using the Insight Toolkit (ITK) ([Ibanez et al., 2005](#)), but we did not use it here, as we developed our own representation along with a set of behaviors to govern its development. Our deformable organisms attempt to segment the brain by incorporating high-level knowledge and expectations regarding image data by leveraging the interaction of multiple deformable models that cooperatively use low-level image processing and computer vision techniques for brain segmentation. In contrast to several brain segmentation methods that work with low-level image processing and computer vision techniques, our deformable organisms can incorporate high-level knowledge and expectations regarding image data.

Our contribution in the method presented here is to specify in detail the way organisms should be initialized, how they can be used to interpret an image, adapt physically in the image space, and follow a unique high-level goal-oriented plan specified by a researcher. In addition to our definition of deformable organisms we explored using a machine learning step to deal with the discrepancies that may arise from a high-level segmentation plan and the fine boundaries of functional regions in the brain. We chose a wrapper ([Wang et al., 2011](#)) based on the Adaboost algorithm that learns the errors made by our algorithm from training data. We evaluated and compared our organisms based on their performance on one specific neuroimaging segmentation problem (skull-stripping), which we detail here. Even so, they offer a rich toolbox to construct a plan for any type of segmentation. The ability to adapt this toolkit to different segmentation problems could make it ideal for a wide range of standard neuroimaging tasks.

In our experiments, we evaluate our deformable organisms framework by segmenting the entire brain boundary from non-brain regions in whole head images. Segmenting brain from non-brain tissues (such as the eyes, skull, scalp, and neck) in magnetic resonance imaging (MRI) images of the head is a vital pre-processing step for many types of image analysis tasks. Accurate masks of the brain are helpful for longitudinal studies ([Resnick et al., 2003](#)), for multi-subject analyses of brain structure and function ([Thompson et al., 2003](#)), and as a pre-processing step prior to cortical surface modeling ([Thompson et al., 2004](#)), surgical planning ([Gering et al., 2001](#)), and brain registration ([Woods et al., 1999](#)).

The process of segmenting brain versus non-brain tissue in MRI is commonly referred to as “skull-stripping” (although, strictly speaking, the skull generates almost no signal on T1-weighted MRI and the scalp and meninges are the main tissues removed). This has traditionally been done manually by trained experts, or by automated methods that are subsequently corrected by hand. Manually-created masks may also be used as gold standard delineations to validate performance of skull-stripping methods based on different principles. Many approaches have been developed for this task, but time consuming manual clean-up of these generated masks is almost always required. Many published methods do not perform well on all datasets, making improvements on existing methods an active area of research.

There are a variety of existing skull-stripping methods. The brain extraction tool (BET) ([Smith, 2002](#)) evolves a deformable model to find the boundary of the brain. It provides a robust way to find the boundary in unclear regions but does not incorporate prior knowledge of the brain’s shape. The brain surface extractor (BSE) ([Shattuck and Leahy, 2002](#)) uses edge detection and

morphological operations to find the brain/non-brain boundary. BSE quickly extracts the brain from an image but may include extra material in the mask, as it sometimes fails to remove connections between the brain and surrounding tissue. The Hybrid Watershed Algorithm (HWA) ([Segonne et al., 2004](#)) uses the watershed algorithm to find the brain region, then fits a deformable model to the region, and finally deforms it based on a statistical atlas and geometric constraints. These methods have also been analyzed in ([Boesen et al., 2004](#)). We chose these methods as they are among the most widely used and are part of larger neuroimaging toolkits. Our goal was to assess whether a deformable organism framework and accompanying plan of segmentation could result in delineations at least comparable with existing problem specific algorithms.

We present a detailed definition of deformable organisms for brain segmentation and incorporate them into a segmentation plan that governs a collection of organisms to segment different parts of the head and brain. The organisms evolve dynamically in the images. They cooperatively compute an accurate and robust segmentation of the brain. We then use a learning method to analyze the errors in our method, and incorporate information on it into the models. We evaluate how effective this additional error correction step is, in improving our segmentation. We test our method with 630 T1-weighted MRI images from healthy young adults along with another dataset of 208 older adults with Alzheimer’s disease. We compare our approach to three widely used methods and we validate our results using distance, overlap, and error metrics. The current study builds on our preliminary work that used simpler deformable models and had less extensive experiments ([Prasad et al., 2011a,b](#)).

2. Methods

Our deformable organisms method aims to segment and model the brain in T1-weighted MRI images of the head. We describe our deformable organism definitions for any type of general segmentation of the brain, a way to learn and correct errors in our method, validation metrics to compare our results to the gold standard and to other widely-used methods, and in our experiments we propose and evaluate a plan for skull-stripping.

2.1. Deformable organisms

Deformable organisms are organized in five different layers that combine control mechanisms and different representations to segment an image. We adapt this general approach for segmenting the brain.

2.1.1. Geometry and physics

We represent each organism as a 3D triangulated mesh. These meshes are initialized on a standard brain template image. Our template was selected from the 40 images in the LONI Probabilistic Brain Atlas (LPBA40) ([Shattuck et al., 2008](#)), which have corresponding manual segmentations for 56 structures, and have manual delineations of the brain boundary. In the image we selected from this set, the voxels lying in each of our regions of interest are labeled. We fit our organisms to these labels to create a mesh using a marching cubes method ([Lorenson and Cline, 1987](#)) that goes through the image. The mesh is made up of polygons representing the border of the regions, which are then fused together. These meshes deform to fit the 3D region that their corresponding organism is modeling. This iterative process moves each of the mesh’s vertices along its normal direction with respect to the mesh surface. The surface is smoothed at every iteration using curvature weighted smoothing ([Desbrun et al., 1999](#); [Ohtake et al., 2002](#)). This

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