Reconstructing Neural Structures from Sparse User Scribbles

Mike Roberts* Harvard University
Won-Ki Jeong* Harvard University
Amelio Vázquez-Reina* Harvard University
Markus Unger† Graz University of Technology
Horst Bischof† Graz University of Technology
Jeff Lichtman‡ Harvard University
Hanspeter Pfister* Harvard University

Abstract

We present a novel semi-automatic method for segmenting neural structures in large, highly anisotropic EM (electron microscopy) image stacks. Our method takes advantage of sparse scribble annotations provided by the user to guide a 3D variational segmentation model, thereby allowing our method to globally optimally enforce 3D geometric constraints on the segmentation. Moreover, we leverage a novel algorithm for propagating segmentation constraints through the image stack via optimal volumetric pathways, thereby allowing our method to compute highly accurate 3D segmentations from very sparse user input. We evaluate our method by reconstructing 16 neural structures in a $1024 \times 1024 \times 50$ nanometer-scale EM image stack of a mouse hippocampus. We demonstrate that, on average, our method is 68% more accurate than previous state-of-the-art semi-automatic methods.

1 Introduction

Mapping neural circuitry is an important ongoing challenge in neurobiology. Current approaches to this task involve tracing neural structures through segmented nanometer-scale EM (electron microscopy) image stacks of brain tissue. Since our understanding of neural circuitry is often limited by our ability to reconstruct neural structures from EM image stacks, accurately segmenting neural structures is an important open problem in the biological image analysis community.

Dense reconstruction algorithms [3, 5, 6] generally rely on supervised learning methods to automatically classify every pixel in an image stack according to the type of cellular structure to which it belongs. However, no dense reconstruction algorithm can reliably produce segmentations that are completely free of topological errors. In practice, these methods often require significant user effort to correct errors in the automatically generated segmentations.

On the other hand, *sparse reconstruction algorithms* generally rely on the user to interactively guide the segmentation of individual neural structures. Most existing sparse algorithms compute 3D reconstructions as sequences of locally optimal 2D segmentations after the user provides an initial 2D contour [4, 10]. However, these approaches do not optimally enforce 3D geometric consistency constraints on the resulting segmentation, and can require frequent user intervention. The recent *Markov Surfaces* algorithm [7] requires user-defined 2D contours on the first and last slices of an image stack. This algorithm automatically tessellates a set of globally optimal paths between these contours, relying on 2D Bézier interpolation to produce smooth surfaces. However, since Bézier interpolation does not take into account the underlying image data, the resulting segmentations may ignore important image features.

2 Our Method

We observe that the problem of reconstructing neural structures through highly anisotropic EM image stacks is conceptually similar to the problem of tracking moving objects in video sequences.

*e-mail: {mroberts,wkjeong,amelio,pfister}@seas.harvard.edu
†e-mail: {bischof,unger}@icg.tugraz.at
‡e-mail: jeff@mcb.harvard.edu

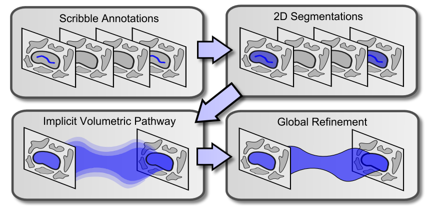

Figure 1: Overview of our method. We assume that we are given scribble annotations indicating a neural structure of interest on the first and last slices of an image stack (top left). We compute 2D segmentations that contain the scribble annotations and align with strong image edges; these 2D segmentations define hard constraints on our 3D segmentation (top right). We propagate the 2D segmentations through the image stack according to an implicitly represented volumetric pathway, which we compute based on the dense optical flow between image slices; the interior level sets of this volumetric pathway define soft constraints on our 3D segmentation (bottom left). We compute the final 3D segmentation by globally refining the volumetric pathway according to an anisotropic variational segmentation model that aligns with strong in-plane image edges and enforces 3D smoothness (bottom right).

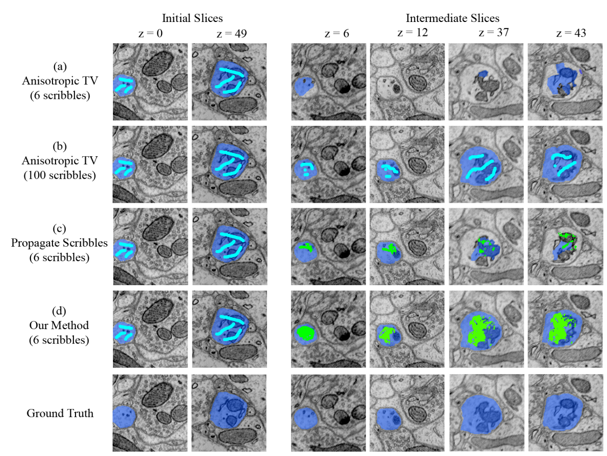

Figure 2: Key observations motivating our method. Anisotropic Total Variation [8] fails to segment this neural structure from sparse scribble annotations (a), but succeeds if scribble annotations are given on every slice (b). Our method only requires scribble annotations on the first and last slices because we automatically propagate segmentation constraints through the image stack. However, propagating user scribbles as segmentation constraints results in a significant under-segmentation of this neural structure (c). Instead, we compute 2D segmentations from the scribbles and propagate the 2D segmentations; this results in a more accurate segmentation of this neural structure (d). Scribble annotations are shown in light blue, segmentations are shown in dark blue, and automatically propagated segmentation constraints are shown in green.

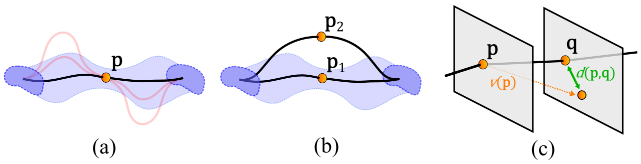

Figure 3: Computing the cost volume. There are many possible paths through the image stack (shown in red) that connect the 2D segmentations on the first and last slices (shown in dark blue) via $\mathbf{p}$, but there is only one shortest path (shown in black); we set the cost of each pixel in the cost volume to be the length of this path (a). For example, $\mathbf{p}_2$ will be assigned a higher cost than $\mathbf{p}_1$, since the length of its shortest path is longer; this means $\mathbf{p}_2$ is less likely to belong to the neural structure of interest than $\mathbf{p}_1$ (b). When computing the length of each path, we model the distance between pixels $\mathbf{p}$ and $\mathbf{q}$ on adjacent slices (shown in green) as a function of the optical flow vector originating at $\mathbf{p}$ (shown in orange) (c). In this formulation, paths through the image stack that agree strongly with the optical flow field will have very short lengths, and the pixels belonging to these paths will be assigned very low costs. Thus, the cost volume implicitly defines a volumetric pathway containing pixels that are likely to belong to the neural structure of interest.

Based on this observation, our work is inspired by the recent *Anisotropic Total Variation* model proposed by Unger *et al.* [8], which tracks objects through video sequences based on sparse constraints provided by the user. However, the absence of color information in EM image data and poor spatial continuity across EM image slices prevent the direct application of this method to neural structure reconstruction (Figure 2). To account for these additional challenges, we propose the following novel segmentation method.

Input. We assume that the user marks the neural structure of interest with a few foreground and background scribbles on the first and last image slices.

Computing 2D segmentations. We compute 2D segmentations of the neural structure of interest using the variational segmentation model of Unger *et al.* [9]. This results in 2D segmentations that respect the user-provided scribble annotations and align with strong image edges. The foreground and background regions of these 2D segmentations define hard foreground and background constraints on our 3D segmentation, respectively.

Computing an Optimal Volumetric Pathway. Once we have obtained hard constraints on the first and last slices of our image stack, we generate soft constraints on all the other slices by automatically propagating the previously computed 2D segmentations through the stack. We accomplish this by defining an optimal volumetric pathway through the image stack that connects the previously computed 2D segmentations and encloses the pixels that are most likely to belong to the neural structure of interest. In this formulation, the optimal volumetric pathway is given by the interior level sets of a *cost volume* that encodes the probability of each pixel in the image stack belonging to the neural structure of interest (Figure 3). The interior level sets of this cost volume define soft foreground constraints on our 3D segmentation.

Computing the 3D Segmentation. Once we have obtained hard constraints on the first and last slices of the image stack, and soft constraints on all other slices, we obtain the final 3D segmentation by using the using the anisotropic variational segmentation model of Unger *et al.* [8]. We demonstrate the accuracy of our method in Figures 4 and 5.

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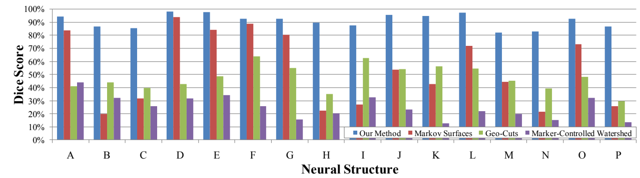

Figure 4: Accuracy of our method, Markov Surfaces [7], Geo-Cuts [1], and Marker-Controlled Watersheds [2] while segmenting 16 neural structures in an annotated $1024 \times 1024 \times 50$ mouse hippocampus EM image stack. On average, our method is 68% more accurate than Markov Surfaces [7], 91% more accurate than Geo-Cuts [1], and 263% more accurate than Marker-Controlled Watersheds [2].

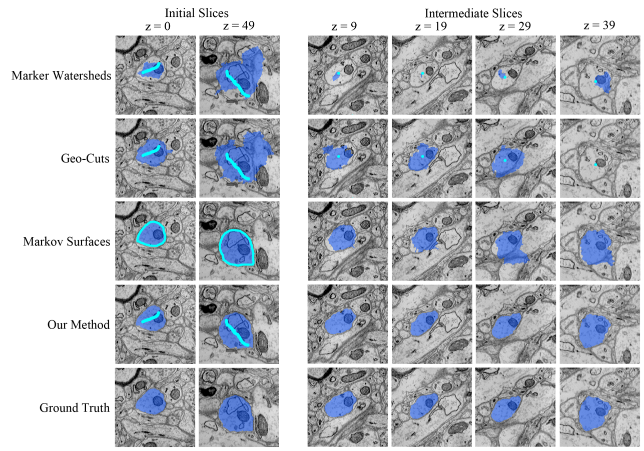

Figure 5: Segmentation results from our method, Markov Surfaces [7], Geo-Cuts [1], and Marker-Controlled Watersheds [2] on various slices of a $1024 \times 1024 \times 50$ mouse hippocampus EM image stack. Bright blue regions indicate the user-provided annotations used to initialize the algorithms, dark blue regions indicate the resulting segmentations.

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