

## Efficient Delineation of Curvilinear Networks from Biological Images

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*Delineating networks of curvilinear structures is a challenging problem with numerous applications in the neuroscience, medical and biometrics fields. The large quantities of high-dimensional data produced by today's acquisition systems creates a growing demand for efficient data-mining and recognition algorithms to analyze these networks. The goal of this project is to develop a range of data-agnostic delineation tools that are simple, fast and require minimal user interaction.*

Curvilinear networks, such as blood vessels and neurons, are ubiquitous in biology. Reconstructing them digitally is of great importance in the field of neuroscience to quantitatively analyze neuronal connectivity patterns, and in the medical sciences to study vascular pathologies or to assist surgeons in image-guided planning and navigation. However, despite many years of sustained efforts, existing solutions require extensive manual intervention that is both time-consuming and tedious.

We have developed a set of delineation algorithms that require minimal user interaction and can handle both tree-like and loopy networks in a variety of imaging modalities, such as confocal/bright-field micrographs and MRA/CT scans. The software supports visualising and processing a wide range of data including 2D images and 3D image stacks of various bit-depths as well as time-lapse sequences and color imagery.

The new delineation tools range from manual and interactive techniques that give the user full control over the results to automated ones that require only a few user clicks. This allows the user to take the most efficient approach depending on the data characteristics, such as spatial resolution, signal-to-noise-ratio and contrast.

A common feature of the tools is a novel "virtual mouse" algorithm, which estimates the 3D center location and radius of a curvilinear structure from a user-defined 2D point on the computer screen. The algorithm has no tunable parameters but involves a fast preprocessing step, which typically takes a few seconds for a 1 GB image stack on a modern laptop.

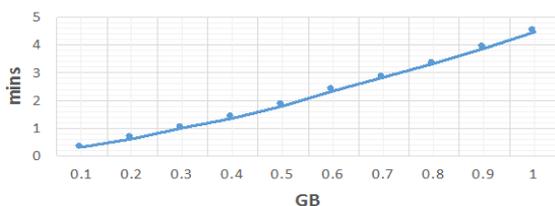


Figure 1: Image size versus tubular path preprocessing time.

Another preprocessing step common to the developed tools is the computation of tubular paths between all pairs of image locations. The computation and storage of the paths requires only  $O(N)$  memory space, where  $N$  is the total number of image pixels. Furthermore, the running time of this step grows almost linearly with the image size as depicted by Figure 1.

The software operates mainly in four different delineation modes, namely manual, sliding-path, endpoint and one-click modes. The manual mode allows the user to sequentially connect points with tubes either with the help of the virtual

mouse algorithm or by manually picking the points in 3D. In the sliding-path mode, the user traces the filaments interactively by moving the mouse over them on the render window. The tool then automatically finds the most relevant 3D points and connects them with a smooth tubular path.

Unlike these two modes and existing solutions on the market, which require specifying intermediate points along the filaments, the endpoint tool finds a number of globally optimal paths connecting a given point (usually filament endpoints) to the delineation. The software then allows the user to view and select the best path on the render window. Finally, the one-click mode requires only a single point to be provided for each connected curvilinear network in the image.

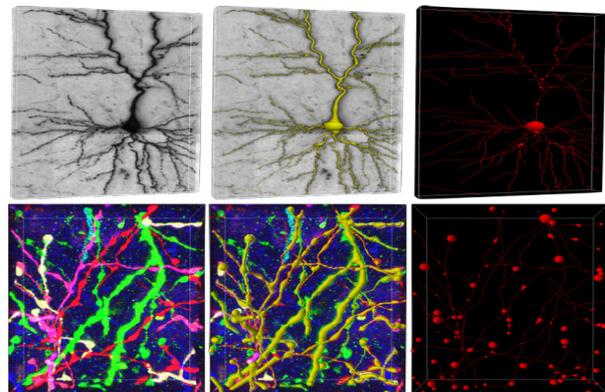


Figure 2: Neural structures delineated in the sliding-path and endpoint modes one at a time. Top: Brightfield micrograph of a biocytin-stained neuron. Bottom: Neurites acquired by the brainbow technique [1]. From left to right, intensity projections of the raw image stacks, delineations overlaid in yellow, and centerlines in red.

The combination of the sliding-path and endpoint tools represents a powerful strategy, which can handle both imaging noise and discontinuities along faint curvilinear filaments as shown in Figure 2. However, on cleaner data, such as high-resolution images of blood vessels, the one-click tool provides the most time-efficient approach (Figure 3).

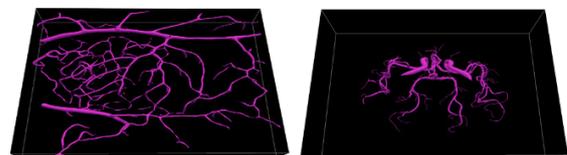


Figure 3: Two loopy networks produced in the one-click mode. Left: Reconstruction from a confocal image stack of blood vessels; Right: Reconstruction of a cerebral vasculature from an MRA scan.

[1] J. Livet, T. Weissman, H. Kang, R. Draft, J. Lu, R. Bennis, J. Sanes, J. Lichtman, "Transgenic strategies for combinatorial expression of fluorescent proteins in the nervous System," Nature, 450 (2007)