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## Three-Dimensional Vascular Reconstruction and Centerline Extraction from 1 $\mu\text{m}$ Histological Slice Images

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High-resolution 3D reconstructions not only provide insights into the geometric and topological properties of vascular networks but also enable quantitative analysis essential for disease diagnosis, surgical planning, and personalized therapeutic strategies. Within the framework of the BigBrain project, which seeks to generate ultra-high-resolution models of the human brain at 1  $\mu\text{m}$  isotropic resolution, vascular reconstruction is particularly significant for refining anatomical context, supporting multimodal data integration, and advancing computational modeling of cerebrovascular function.

In this work, we present a robust methodology for reconstructing vascular structures and extracting their centerlines from a set of 100 consecutive 1  $\mu\text{m}$ -thick vascular slice images, each with a resolution of 512 $\times$ 512 pixels and a spacing of one voxel along the z-axis. Our approach combines classical image processing techniques with modern data-driven modeling to address the challenges posed by noise, irregular boundaries, and inter-slice variability. First, each 2D slice is preprocessed through grayscale normalization, binarization, denoising, and morphological operations to identify the largest connected vascular region. The maximum inscribed circle within this region is then determined, providing an estimate of both the slice-specific radius and the geometric center. By stacking the geometric centers across slices, we generate a discrete trajectory of vascular centroids in 3D space.

To model the vascular centerline, we initially employ polynomial curve fitting across x-z and y-z coordinates. After evaluating multiple orders, a sixth-order polynomial is selected as the optimal balance between smoothness and accuracy, yielding coefficients of determination ( $R^2$ ) above 0.99 and mean absolute errors below 5 pixels. While polynomial fitting effectively captures the global trajectory, it exhibits sensitivity to local noise and oscillatory artifacts (Runge's phenomenon). To overcome these limitations, we further apply a machine learning-based regression strategy using random forests. This approach preserves both local geometric detail and global smoothness, reducing fitting error by approximately 40% compared to polynomial models. The random forest-based method achieves  $R^2$  values above 0.998 for both x- and y-coordinates, demonstrating superior robustness and denoising capability.

The reconstructed vascular radius averages approximately 30.1 pixels ( $\approx 30 \mu\text{m}$  in real scale), with only minor fluctuations across slices. Orthogonal projections of the 3D centerline onto XY, YZ, and ZX planes provide an intuitive visualization of vascular curvature and spatial continuity. Moreover, the proposed methodology enables the generation of realistic vascular tube models by extruding the fitted radius along the reconstructed centerline. These models enhance interpretability and facilitate integration into multimodal brain atlases such as BigBrain, where vascular context is indispensable for accurate localization and functional annotation.

Our contributions are threefold: (1) a mathematically principled framework for radius estimation and centerline modeling from serial 1  $\mu\text{m}$  histological sections; (2) the introduction of machine learning-based regression to improve stability and robustness of centerline fitting; and (3) comprehensive quantitative evaluation using MAE, RMSE, and  $R^2$  metrics, validating the accuracy and reproducibility of the reconstruction. Future work will extend this methodology to larger-scale vascular networks within the 1  $\mu\text{m}$  BigBrain dataset and explore integration with multimodal imaging modalities such as MRI and micro-CT.

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