Investigating Neuron Trajectories with Splines

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Introduction

Understanding neuromorphology is central to the Brain Initiative Cell Census's goals, but popular morphological statistics are limited to macroscopic features such as branching frequency and connectivity between regions [4]. However, with the advent of high-throughput neuron tracing, it is becoming possible study the geometry of neurons themselves. Many neuron traces are stored as points in space, with edges connecting them and thus neuron geometry is reduced to a piecewise linear structure. In this work, we consider the points as a sampling of a continuous curve that we approximate with b-splines.

B-spline Background

Given a sequence of nondecreasing numbers, $\xi = \{\xi_i\}_{i=1}^n$, called *knots*, and an integer k, called the *order*, one can construct a set of polynomials that are piecewise over ξ called normalized b-splines. This set is in fact a basis for the space of such piecewise polynomials, and general splines can be constructed with linear combinations of them.

A spline can be fit to a set of points in space in a way that is both efficient, and emphasizes "smoothness" [1].

An important advantage of b-splines is that the continuity of their derivatives can be controlled, through their knots, and their derivatives can be computed in closed form. These properties allow for the computation of curvature and torsion which, through the Frenet-Serret formulas of differential geometry, completely characterize continuous differentiable curves in three-dimensional Euclidean space, up to rigid motion [2].

Materials

Our work is uses data from the Mouselight Project at HHMI Janelia [4]. The dataset involves a single mouse brain with 176 neuron traces reviewed by a trained tracer.

Summary

- **Motivation:** Current neuromorphological features do not adequately capture the geometry of how neurons curve through space.
- **Method:** Split neuron traces into segments then fit with b-splines in order to study their differential geometry.
- **Result:** On a dataset of neurons traced in a mouse brain, there was a statistically significant inverse relationship between neuronal segment length, and its curvature and torsion.

Methods

Given a set of points organized in a tree structure (such as a neuron trace in a .swc file), we:

1. Split the tree into segments by recursively identifying the longest root to leaf path (Fig. 1a).
2. Fit an interpolating b-spline to each segment (Fig. 1b) [3].

The resulting splines pass through all points in the original trace, and are three times continuously differentiable for segments that are composed of 5 or more points.

For each segment, points were sampled every 1 μm, then curvature and absolute value of torsion were computed. The distributions of segment length, mean curvature, and mean absolute torsion are non-negative with long tails, so, after values of zero were excluded, Pearson correlation tests were applied to their logarithms.

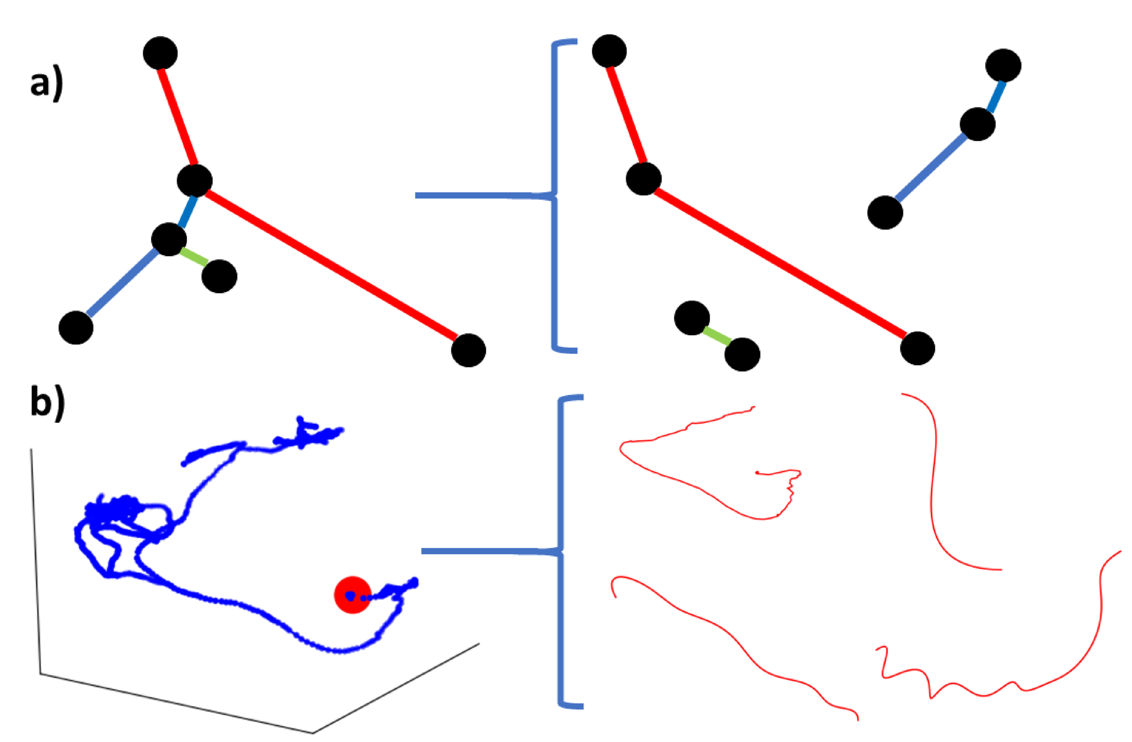

Figure 1: **a)** Cartoon demonstrating how a tree is split into paths by identifying the longest root to leaf paths. **b)** Example neuron trace (soma in red) and some of the splines that were fit to its segments.

Results

Pearson's correlation test yielded a statistically significant negative correlation between both log segment length and log mean curvature (two-sided p-value $\leq 10^{-11}$) and log segment length and log mean torsion (two-sided p-value $\leq 10^{-11}$). The figures below demonstrate these inverse relationships.

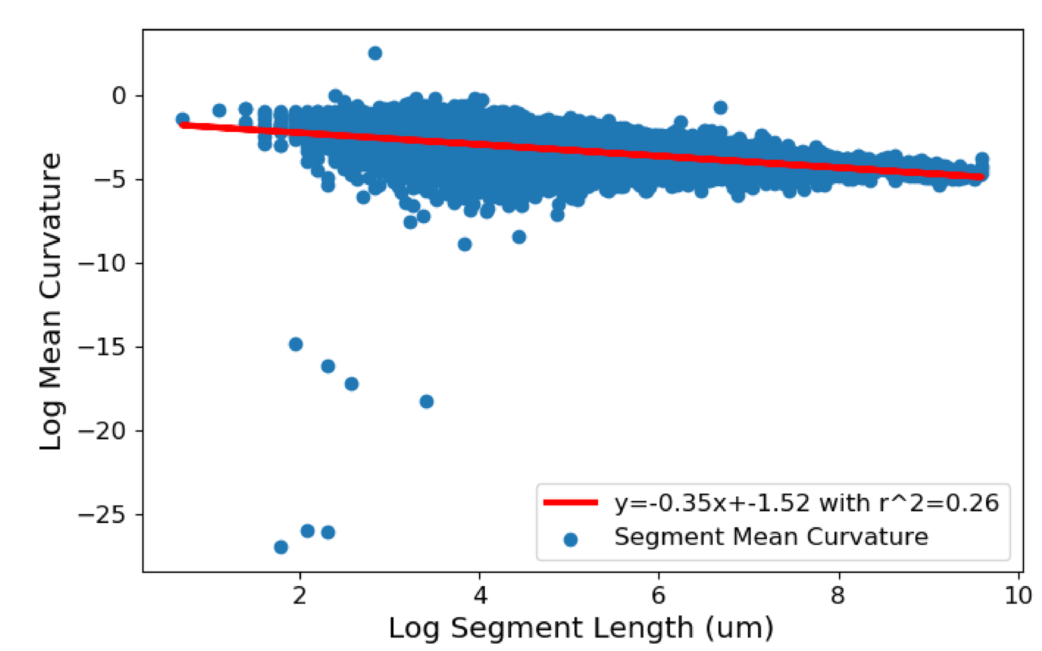

Figure 2: Curvature vs. Segment Length in 19701 segments, with a linear regression.

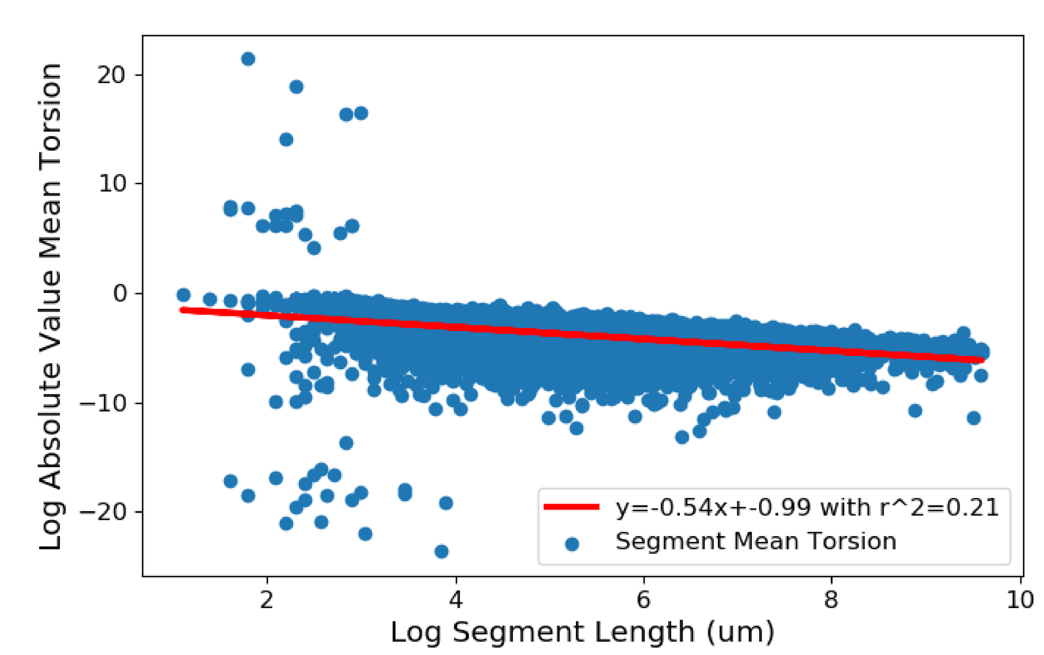

Figure 3: Torsion vs. Segment Length in 16025 segments, with a linear regression.

Conclusion

Our work makes it possible to construct a continuous representation of neuron morphology from point-based traces using b-slines. This representation allows for the study of neuronal geometry as it travels through space, such as by computing curvature and torsion in closed form. A look at 176 neurons in a mouse brain suggested that there is a power law relationship between neuronal segment length and both curvature and torsion. This suggests that long neuronal segments that traverse the brain have a quantitatively different geometry than short segments found in axonal arbors.

References

[1] Paul Dierckx.
Algorithms for smoothing data with periodic and parametric splines.
Computer Graphics and Image Processing, 20(2):171–184, 1982.

[2] Ulf Grenander and Michael I Miller.
Pattern theory: from representation to inference.
Oxford university press, 2007.

[3] F. Pedregosa et al.
Scikit-learn: Machine learning in Python.
Journal of Machine Learning Research, 12:2825–2830, 2011.

[4] Johan Winnubst et al.
Reconstruction of 1,000 projection neurons reveals new cell types and organization of long-range connectivity in the mouse brain.
Cell, 179(1):268–281, 2019.

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