**Introduction**

- **Goal:** develop algorithms to trace neuron fibers in variety of 3D imageries for connectivity analysis.

- Neuron connection maps could be used to create computer simulations of neural circuits involving tens of thousands of neurons with biologically realistic connections and potentially be used to model neuro-degenerate diseases such as Alzheimer or Parkinson.

- Challenges of tracing neurons:
  - low resolution in one dimension
  - high interactions between neuronal structures

- Approach: develop a tracing method suitable for different imagery techniques without ad-hoc heuristics
  - Principal Curves
  - first proposed by Hastie and Stuetzle
  - can be used for dimensionality reduction, OCR, etc

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**Principal Curve Tracing**

Given Probability Density Function:
Follow the eigenvectors of the local covariance to project data points onto principal curve

Red – gradient direction (leads to local maxima)
Blue – greatest eigenvector local covariance (projects onto principal curve)
Green – principal curve

Summary of Principal Curve Tracing Algorithm for Image Datasets
1. At iteration $t=0$ initialize $x$, and the direction of the curve $\gamma_0$.
2. At iteration $t$ evaluate the wKDE mean shift update $ms(x(t))$
3. Evaluate the gradient, the Hessian, and perform the eigendecomposition of $\Sigma^{-1}(x) = VTV$, where $V_{1:n}$ are the eigenvectors with corresponding eigenvalues $\Gamma = \text{diag}(\lambda_1 \leq \lambda_2 \leq \cdots \leq \lambda_n)$.
4. Let $V_1$ and $V_{2:n}$ be the eigenvectors that consequently span $S_H(x)$, and $S_L(x)$, such that $ms_H(x) = \eta_1(x)\eta_1(x)^T ms(x)$, and $ms_L(x) = V_{2:n}V_{2:n}^T ms(x)$.
5. Evaluate the new curve direction vector $\gamma_t = sign(\gamma_{l-1}^T ms_H(x))ms_H(x)$
6. If $x$ is outside the image boundary stop, else $x(t+1) = \arg \min_{x \in T_x} (\gamma_t^T (x_k - x))$. Here $T_x$ is the connected neighborhood of the $x$ composed of 26 voxels in 3D.

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**Image Datasets**

- Cerebellar Climbing
- Neocortical Layer 6
- Hippocampal CA3
- Neuromuscular Projection
- Olfactory Projection

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**Results**

- Algorithm is tested on Brainbow image stack
  - Image stack has 31 slices each having 1024x1024 pixel resolution
  - Spacing: 0.64 x 0.11 x 0.11 μm
  - Centerline obtained using the proposed method is compared with the result obtained from a shape driven GCM approach

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**Conclusion**

- Principal curve tracing can be used to trace neuronal structures from different imagery techniques
- They provide reliable, fast and robust tracing results that can be used to create connectivity maps
- Bifurcation detection is simpler
- Future work includes obtaining more quantitative results and estimation of volume of neuronal structures.