Can We Hear the Shape of Neurons?

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Outline

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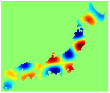
Announcement: IPAM Workshop Feb. 9–13, 2009

INSTITUTE FOR PURE AND APPLIED MATHEMATICS

Los Angeles, California



Laplacian Eigenvalues and Eigenfunctions: Theory, Computation, Application

February 9 – 13, 2009

ORGANIZING COMMITTEE: Denis Grebenkov (Ecole Polytechnique), **Peter Jones** (Yale), **Naoki Saito** (UC Davis)

Scientific Overview

The investigation of eigenvalues and eigenfunctions of the Laplace operator in a bounded domain or a manifold is a subject with a long history, yet it is still a central area in mathematics, physics, engineering, and computer science. Activity has increased dramatically in the past twenty years for several reasons:

• a discovery of many fascinating properties of the Laplacian eigenfunctions such as the localization in small regions of a complicated domain and scarring in quantum chaotic billiards;

• the use of Laplacian eigenfunctions as a natural tool for a broad range of data analysis tasks, e.g., dimensionality reduction of high dimensional data via diffusion maps, or analysis of fMRI data for understanding functionality of brain regions;

• the use of the underlying Laplacian eigenvalues as natural "fingerprints" to identify geometrical shapes, e.g., copyright protection, database retrieval, quality assessment of digital data representing surfaces and solids, and the related inverse spectral problems;

• the spectral analysis of the Laplace operator for a better interpretation of nuclear magnetic resonance measurements of diffusive transport, e.g., experimental determination of the surface to volume ratio in porous media through the asymptotic properties of the heat kernel;

• numerical computation of the Laplacian eigenfunctions and eigenvalues in irregular, often multiscale domains (or sets, or graphs) that still remains a challenging problem demanding for new numerical techniques.

This short-term workshop will be an exciting opportunity to discuss these new or long-standing problems with experts in mathematics, physics, biology, and computer sciences.

Invited Speakers

Carlos J. S. Alves Instituto Superior Tecnico, **Nalini Anantharaman** Ecole Polytechnique, **Alex Barnett** Dartmouth, **Krzysztof Burdzy** University of Washington, **Ronald Coifman** Yale, **Denis Grebenkov** Ecole Polytechnique, **Ilya Gruzberg** University of Chicago, **Michel Lapidus** UC Riverside, **Mauro Maggioni** Duke, **Francois Meyer** University of Colorado, **Martin Reuter** MIT, **Naoki Saito** UC Davis, **Pabitra Sen** Schlumberger-Doll Research, **Terence Tao** UCLA

Participation

Additional information about this workshop, including links to register and to apply for funding, can be found on the webpage listed below. Encouraging the careers of women and minority mathematicians and scientists is an important component of IPAM's mission, and we welcome their applications.

www.ipam.ucla.edu/programs/le2009

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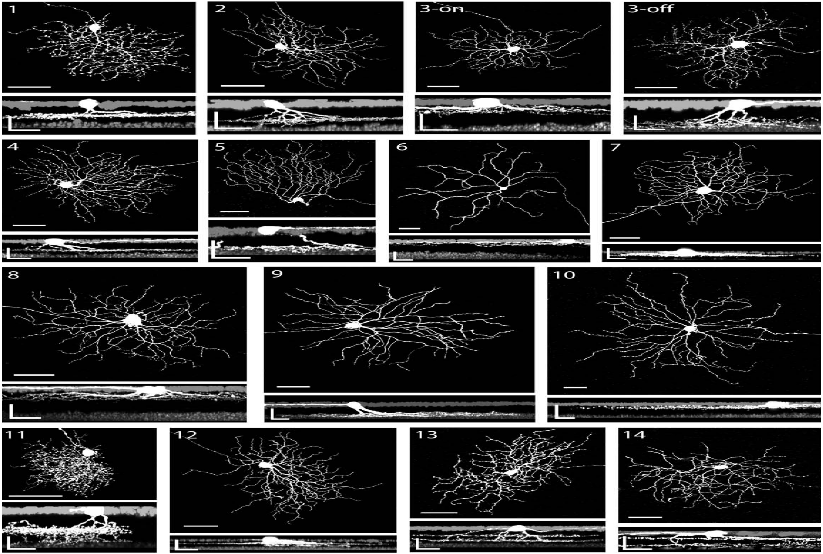
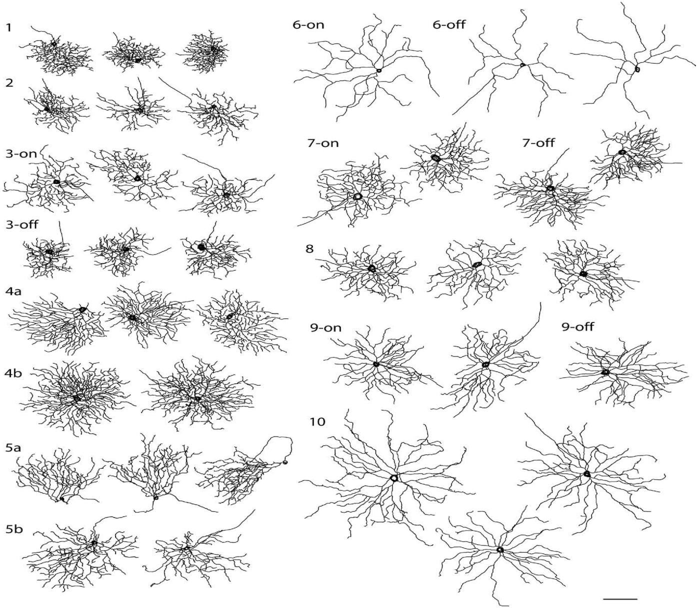
Clustering Mouse Retinal Ganglion Cells . . . 3D Data



Clustering Mouse's Retinal Ganglion Cells

- Objective: To understand how the structural/geometric properties of mouse retinal ganglion cells (RGCs) relate to the cell types and their functionality
- Why mouse? $\Longrightarrow$ great possibilities for genetic manipulation
- Data: 3D images of dendrites of RGCs
- State of the Art $\Longrightarrow$ a manually intensive procedure using specialized software:
    - Segment dendrite patterns from each 3D cube;
    - Extract geometric/morphological parameters (totally 14 such parameters);
    - Apply the conventional bottom-up "hierarchical clustering" algorithm
- The extracted morphological parameters include: somal size; dendric field size; total dendrite length; branch order; mean internal branch length; branch angle; mean terminal branch length, etc.
- It takes half a day per cell with a lot of human interactions!

Clustering Results by the Manually Intensive Method



Outline

Why Laplacian Eigenfunctions/Eigenvalues?

- The Laplacian eigenfunctions defined on the domain Ω provides the orthonormal basis of $L^2(\Omega)$.
- The Laplacian eigenvalues encode geometric information of the domain $\Omega \Longrightarrow$ "Can we hear the shape of a drum?" (Mark Kac, 1966).
- Consider the Laplacian eigenvalue problem in $\Omega \in \mathbb{R}^d$ with the Dirichlet boundary condition:

$$\begin{cases} -\Delta u = \lambda u & \text{in } \Omega \\ u = 0 & \text{on } \partial\Omega. \end{cases}$$

- Let $0 < \lambda_1 < \lambda_2 \leq \lambda_3 \leq \cdots \leq \lambda_k \leq \cdots \to \infty$ be the sequence of eigenvalues of the above Dirichlet-Laplace eigenvalue problem.
- Kac showed (based on the work of Weyl, Minakshisundaram-Pleijel):

$$\sum_{k=1}^{\infty} \mathrm{e}^{-\lambda_k t} = (4\pi t)^{-\frac{d}{2}} \left\{ \mathrm{Vol}_d(\Omega) - \sqrt{\frac{\pi t}{4}} \mathrm{Vol}_{d-1}(\partial\Omega) \right\} + o\left(t^{\frac{1-d}{2}}\right) \quad \text{as } t \downarrow 0.$$

Universal (or Payne-Pólya-Weinberger) Inequalities

For $m = 1, 2, \ldots$

- $\lambda_{m+1} - \lambda_m \le \frac{4}{md} \sum_{j=1}^{m} \lambda_j.$
- $\frac{\lambda_{m+1}}{\lambda_m} \le 1 + \frac{4}{d}.$
- $\sum_{j=1}^{m} \frac{\lambda_j}{\lambda_{m+1} - \lambda_j} \ge \frac{md}{4}$ (Hile-Protter).
- $\sum_{j=1}^{m} (\lambda_{m+1} - \lambda_j)^2 \le \frac{4}{d} \sum_{j=1}^{m} \lambda_j (\lambda_{m+1} - \lambda_j)$ (Yang).
- $\lambda_{m+1} \le \left(1 + \frac{4}{d}\right) \cdot \frac{1}{m} \sum_{j=1}^{m} \lambda_j$ (Yang).

Isoperimetric Inequalities

- $\lambda_1 \geq \left(\frac{\mathrm{Vol}_d(B_1)}{\mathrm{Vol}_d(\Omega)} \right)^{\frac{2}{d}} j^2_{\frac{d}{2}-1,1}$ (Faber-Krahn)
- $\frac{\lambda_2}{\lambda_1} \leq \frac{j^2_{\frac{d}{2},1}}{j^2_{\frac{d}{2}-1,1}} \approx 2.5387$ if $d = 2$ (Ashbaugh-Benguria)
- $j_{k,1}$ is the first zero of the Bessel function of order k, i.e., $J_k(j_{k,1}) = 0$. In the above inequalities, the equality is attained iff Ω is a unit ball in $\mathbb{R}^d$ in the first case while that is attained iff Ω is a ball of arbitrary radius in $\mathbb{R}^d$ in the second case.

Other Properties

- Domain monotonicity property:
  If $\Omega_1 \subset \Omega_2$, then

$$\lambda_k(\Omega_1) \geq \lambda_k(\Omega_2), \quad k \in \mathbb{N}.$$

- Scaling property:

$$\lambda_k(\alpha\,\Omega) = \frac{\lambda_k(\Omega)}{\alpha^2}, \quad \alpha > 0,\ k \in \mathbb{N}.$$

  This implies:

$$\frac{\lambda_k(\alpha\,\Omega)}{\lambda_m(\alpha\,\Omega)} = \frac{\lambda_k(\Omega)}{\lambda_m(\Omega)}, \quad k,\ m \in \mathbb{N}.$$

  From this, we see that the ratios of Laplacian eigenvalues are scale invariant.
- Laplacian eigenvalues are translation and rotation invariant.
- Note the related work on "Shape DNA" by Reuter et al. (2005), and classification of tree leaves by Khabou et al. (2007).

Eigenfunctions of Laplacian . . . Difficulties

- The key difficulty is to compute such eigenfunctions; directly solving the Helmholtz equation (or eigenvalue problem) on a general domain is tough.
- Unfortunately, computing the Green's function for a general Ω satisfying the usual boundary condition (i.e., Dirichlet, Neumann) is also very difficult.

Outline

Integral Operators Commuting with Laplacian

- The key idea is to find an integral operator commuting with the Laplacian without imposing the strict boundary condition a priori.
- Then, we know that the eigenfunctions of the Laplacian is the same as those of the integral operator, which is easier to deal with, due to the following

Theorem (G. Frobenius 1878?; B. Friedman 1956)

Suppose $\mathcal{K}$ and $\mathcal{L}$ commute and one of them has an eigenvalue with finite multiplicity. Then, $\mathcal{K}$ and $\mathcal{L}$ share the same eigenfunction corresponding to that eigenvalue. That is, $\mathcal{L}\varphi = \lambda\varphi$ and $\mathcal{K}\varphi = \mu\varphi$.

Integral Operators Commuting with Laplacian ...

- Let's replace the Green's function $G(\mathbf{x}, \mathbf{y})$ by the fundamental solution of the Laplacian:

$$K(\mathbf{x}, \mathbf{y}) = \begin{cases} -\frac{1}{2}|x - y| & \text{if } d = 1, \\ -\frac{1}{2\pi} \log |\mathbf{x} - \mathbf{y}| & \text{if } d = 2, \\ \frac{|\mathbf{x}-\mathbf{y}|^{2-d}}{(d-2)\omega_d} & \text{if } d > 2. \end{cases}$$

- The price we pay is to have rather implicit, non-local boundary condition although we do not have to deal with this condition directly.

Integral Operators Commuting with Laplacian ...

- Let $\mathcal{K}$ be the integral operator with its kernel $K(\mathbf{x}, \mathbf{y})$:

$$\mathcal{K}f(\mathbf{x}) \triangleq \int_\Omega K(\mathbf{x}, \mathbf{y}) f(\mathbf{y})\, \mathrm{d}\mathbf{y}, \quad f \in L^2(\Omega).$$

Theorem (NS 2005)

The integral operator $\mathcal{K}$ commutes with the Laplacian $\mathcal{L} = -\Delta$ with the following non-local boundary condition:

$$\int_\Gamma K(\mathbf{x}, \mathbf{y}) \frac{\partial \varphi}{\partial \nu_\mathbf{y}}(\mathbf{y})\, \mathrm{d}s(\mathbf{y}) = -\frac{1}{2}\varphi(\mathbf{x}) + \ \mathrm{pv}\int_\Gamma \frac{\partial K(\mathbf{x}, \mathbf{y})}{\partial \nu_\mathbf{y}} \varphi(\mathbf{y})\, \mathrm{d}s(\mathbf{y}),$$

for all $\mathbf{x} \in \Gamma$, where φ is an eigenfunction common for both operators.

Integral Operators Commuting with Laplacian ...

Corollary (NS 2005)

The integral operator $\mathcal{K}$ is compact and self-adjoint on $L^2(\Omega)$. Thus, the kernel $K(\mathbf{x}, \mathbf{y})$ has the following eigenfunction expansion (in the sense of mean convergence):

$$K(\mathbf{x}, \mathbf{y}) \sim \sum_{j=1}^{\infty} \mu_j \varphi_j(\mathbf{x}) \overline{\varphi_j(\mathbf{y})},$$

and $\{\varphi_j\}_j$ forms an orthonormal basis of $L^2(\Omega)$.

Outline

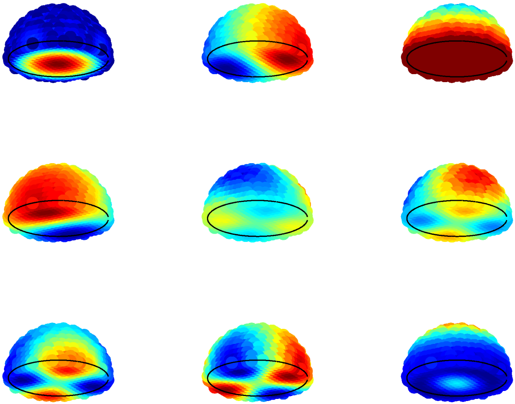
Discretization of the Problem

- Assume that the whole dataset consists of a collection of data sampled on a regular grid, and that each sampling cell is a box of size $\prod_{i=1}^{d} \Delta x_i$.
- Assume that an object of our interest Ω consists of a subset of these boxes whose centers are$\{\mathbf{x}_i\}_{i=1}^{N}$.
- Under these assumptions, we can approximate the integral eigenvalue problem $\mathcal{K}\varphi = \mu\varphi$ by the following simple quadrature rule (i.e., the midpoint rule) with accuracy $O(N^{-2/d})$:

$$\sum_{j=1}^{N} w_j K(\mathbf{x}_i, \mathbf{x}_j)\varphi(\mathbf{x}_j) = \mu\varphi(\mathbf{x}_i), \quad i = 1, \ldots, N, \quad w_j = \prod_{i=1}^{d} \Delta x_i.$$

- Let $K_{i,j} \triangleq w_j K(\mathbf{x}_i, \mathbf{x}_j)$, $\varphi_i \triangleq \varphi(\mathbf{x}_i)$, and $\boldsymbol{\varphi} \triangleq (\varphi_1, \ldots, \varphi_N)^T \in \mathbb{R}^N$. Then, the above equation can be written in a matrix-vector format as: $K\boldsymbol{\varphi} = \mu\boldsymbol{\varphi}$, where $K = (K_{ij}) \in \mathbb{R}^{N \times N}$. Under our assumptions, the weight w_j does not depend on j, which makes K symmetric.

- Consider the unit ball Ω in $\mathbb{R}^3$. Then, our integral operator $\mathcal{K}$ with the kernel $K(\mathbf{x}, \mathbf{y}) = \frac{1}{4\pi|\mathbf{x}-\mathbf{y}|}$.
- Top 9 eigenfunctions cut at the equator viewed from the south:

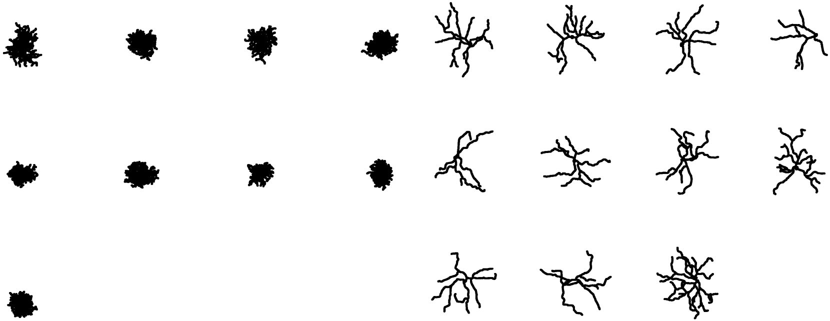


Outline

Preliminary Study on Mouse Retinal Ganglion Cells

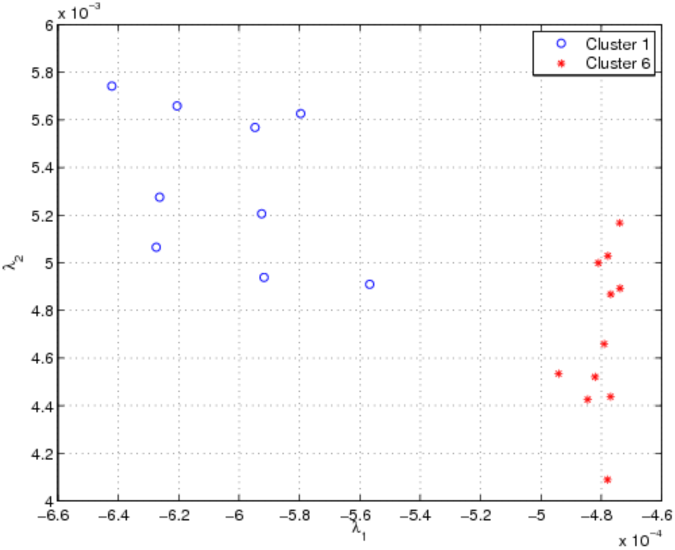
- Use either 2D plane projection data or full 3D data
- Compute the smallest k Laplacian eigenvalues using our method (i.e., the largest k eigenvalues of $\mathcal{K}$) for each image
- Construct a feature vector per image
- Possible feature vectors reflecting geometric information: $\mathbf{F}_1 = (\lambda_1, \ldots, \lambda_k)^T$; $\mathbf{F}_2 = (\mu_1, \ldots, \mu_k)^T$; $\mathbf{F}_3 = (\lambda_1/\lambda_2, \ldots, \lambda_1/\lambda_k)^T$; $\mathbf{F}_4 = (\mu_1/\mu_2, \ldots, \mu_1/\mu_k)^T$.
- Do visualization and clustering

Preliminary Study on Mouse RGCs . . .

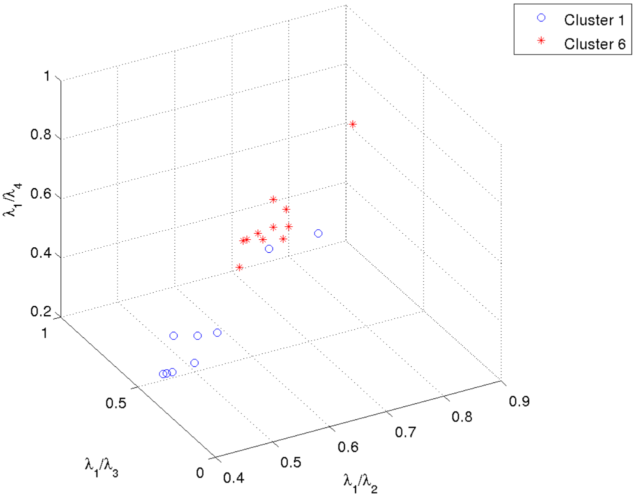


(a) Cluster 1 (b) Cluster 6

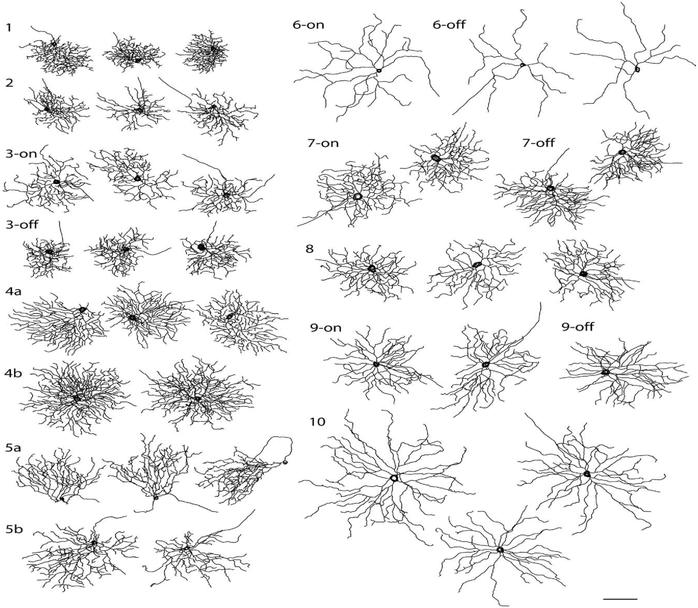
(λ_1, λ_2) of 2D Dataset



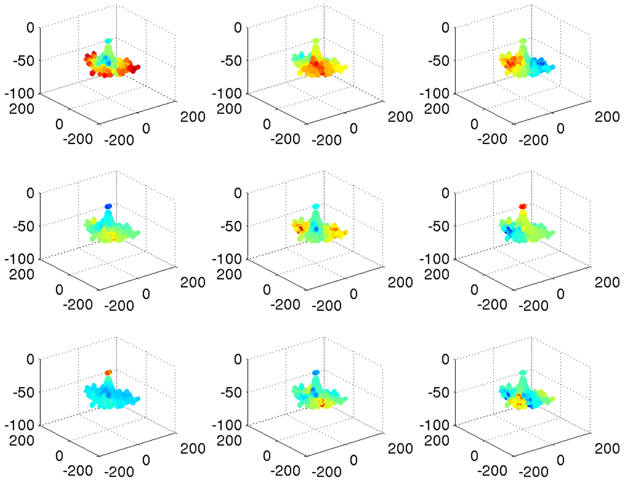
$(\lambda_1/\lambda_2, \lambda_1/\lambda_3, \lambda_1/\lambda_4)$ of 3D Dataset



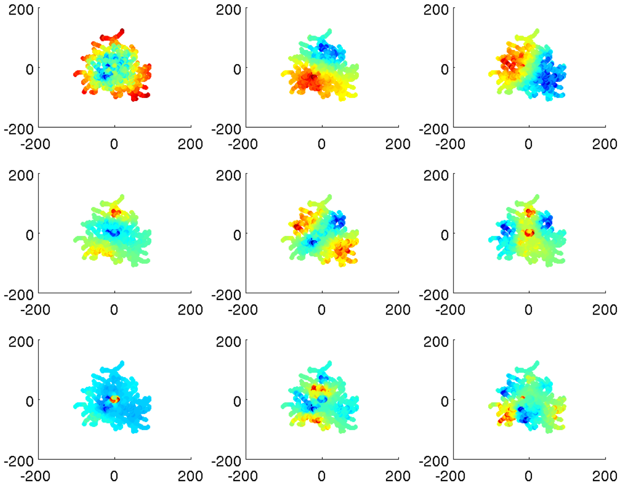
Clustering Results by the Manually Intensive Method



Laplacian Eigenfunctions on a Mouse RGC



Laplacian Eigenfunctions on a Mouse RGC ...



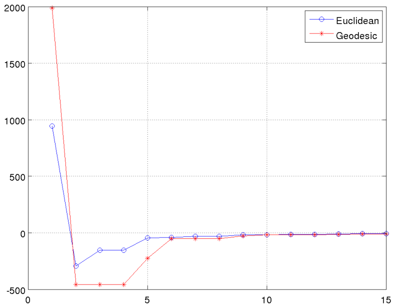
Outline

Challenges to Mouse Retinal Ganglion Cell Analysis

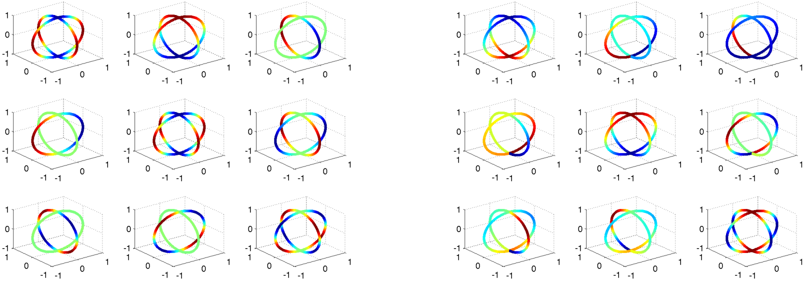
- A big issue is how to encode the domain.
- Interpretation of our eigenvalues are not yet fully understood compared to the Dirichlet-Laplacian case that have been well studied: Payne-Pólya-Weinberger; Faber-Krahn; Ashbaugh-Benguria, etc.
- How to use eigenfunctions
- Reduce computational burden $\Longrightarrow$ The Fast Randomized Algorithm of Martinsson-Rokhlin-Tygert
- Heat propagation/random walks on the dendrites may give us interesting and useful information; after all the dendrites are network to disseminate information via chemical reaction-diffusion mechanism.
- Construct actual graphs based on the connectivity and analyze them directly via spectral graph theory and diffusion maps $\Longrightarrow$ the Cheeger constant of a graph is related to the time to transmit "information" among its nodes! (T. Sunada)
- Automatic segmentation of the dendrite patterns is needed.

An Issue on Domain Encoding: An Example

- Consider two great circles perpendicularly crossing at both the north and south poles on the unit sphere in $\mathbb{R}^3$.
- Let our domain consist of such two great circles minus the south pole.
- Then the four endpoints around the south pole are further apart although the Euclidean distances among them are small.
- Use the connectivity (or geodesic) distances for constructing the kernel matrix rather than the Euclidean distances.



Effect of Different Distances on Eigenfunctions



(a) Euclidean (b) Geodesic

Outline

References

- Laplacian Eigenfunction Resource Page http://www.math.ucdavis.edu/~saito/lapeig/ contains
  - All the talk slides of the minisymposium "Laplacian Eigenfunctions and Their Applications, " which Mauro Maggioni and I organized for ICIAM 2007 at Zürich; and
  - My Course Note (elementary) on "Laplacian Eigenfunctions: Theory, Applications, and Computations"
- The following article is available at http://www.math.ucdavis.edu/~saito/publications/

  - N. Saito: "Data analysis and representation using eigenfunctions of Laplacian on a general domain," *Applied & Computational Harmonic Analysis*, vol. 25, no. 1, pp. 68–97, 2008.

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Thank you very much for your attention!