Applications of Laplacian eigenfunctions and heat kernels in computational anatomy


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2D to 3D imaging

Thomas Eakins, The Agnew Clinic, 1889

Modern radiograph (2D)

Modern CT (3D)

Modern MRI (3D)
Modern Imagers can “see”, but not quantify, measure or “understand”

- Future imaging systems will be “intelligent” - delivering detailed inferences regarding observed anatomical structure and function.

- Understanding will be via established statistical limits of variability in normal state and disease.

- Computational Anatomy – Quantifying shape changes from medical images.
Brain Diseases show pathology-specific evolution

http://www.alz.org

Our Preliminary Results

Brettschneider et al.
Acta Neuropathol (2014)

N=34

Goedert et al.
Neurology Nature Rev., 2013

N=30

Mathias et al.
Nature, 2013

N=8

VBM+TBM

N=19
3D Imaging of the Eye: Computational Retina Anatomy

2D Fundus image

3D OCT Image
Computational Retinal Anatomy
Computational Retinal Anatomy

Mean Thickness (mm)

Glaucome

T-values

p-values

NFL

Choroid

OD

OS (re-oriented)
2D to 3D imaging to Anatomical Models
Extrinsic approach

- Shape represented via diffeomorphic deformation $\phi^{(i)}$: $M^{(i)} = \Phi^{(i)}(M^{(atlas)})$
- Signal $f^{(i)}$ mapped onto $M^{(atlas)}$ via $\Phi^{(i)}$
- Atlas selection is an open problem
- Sensitive to the accuracy of the estimated $\Phi^{(i)}$
Intrinsic approach

- Without using an extrinsic template
- Set of scalars as shape and signal features:
  - Shape parameterization using spherical harmonics [Gerig 01]
  - (Shape-DNA) - Laplacian eigenvalue spectrum [Reuter 05]
  - Partition functions on $M$ for regional signal statistics [Qiu 08]
Laplacian eigenfunctions

• Laplace-Beltrami problem for the manifold $M$:

$$\Delta_M \psi(u) + \lambda \psi(u) = 0$$

$$\int_M |\psi(u)|^2 \, dM = 1 \quad < \nabla_M \psi(u), n > |_{\partial M} = 0$$

- Eigenvalues: $0 \leq \lambda_1 \leq \lambda_2 \ldots \infty$
- Eigenfunctions: $\psi_1, \psi_2, \psi_3, \ldots$

- Eigenfunctions form orthogonal basis and eigenvalues are isometric invariant

• Solution methods:
  - Finite Element Method (FEM) [Reuter 06] [Qiu 08]
  - Commuting with an integral operator [Saito 07]
SPHARM parameterization

- SPHARM are eigenfunctions of a sphere
- Map surface to a unit sphere and parameterize:
  \[ v(\theta, \phi) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} c_l^m Y_l^m(\theta, \phi) \]
  - \( l \) - degree, \( m \) - order
  - \( c = (c_0^0, c_{-1}^1, c_1^0, \ldots) \) are the shape features

[Gerig 01] contd...
• Hippocampus shape features for AD classification:
  23 AD and 25 controls (CN)
• SPHARM of degree 20 chosen
• AD vs CN classification accuracy 94% (leave-one-out) using SVM and t-test based feature selection
Laplacian eigenvalue features

• Eigenvalues directly as a shape feature (Shape-DNA): [Niethammer 08]
  ▪ normalized using surface area for scale invariance
  ▪ Caudate surfaces
  ▪ Group-wise differences between Schizotypal personality disorder and control subjects

• Eigenvalue ratios as pose/scale invariant shape features: [Beg 04]
  \[Z_1 = \left( \frac{\lambda_1}{\lambda_2}, \frac{\lambda_1}{\lambda_3}, \ldots \right)\]
  \[Z_2 = \left( \frac{\lambda_1}{\lambda_2}, \frac{\lambda_2}{\lambda_3}, \ldots \right)\]
  \[Z_3 = \left( \frac{\lambda_1}{\lambda_2} - \frac{d_1}{d_2}, \frac{\lambda_1}{\lambda_3} - \frac{d_1}{d_3}, \ldots \right)\]

▪ Binary hippocampal volumes
▪ Group-wise differences between AD and controls
Partitioning anatomical manifolds

- Nodal lines: zero-level sets of eigenfunctions
- Lower order eigenfunction nodal lines partition domain in a geometrically meaningful manner
- Signal statistics in each partition are comparable across different subjects

contd...
Partitioning anatomical manifolds

• Normalized signal in the $k^{th}$ partition of $n^{th}$ eigenfunction as a feature:

$$\bar{f}_{nk}^{(j)} = \frac{\int_{M(j)} f^{(j)}(x) \psi_{nk}^{(j)}(x) ds(x)}{\int_{M(j)} \psi_{nk}^{(j)}(x) ds(x)}$$

• Cortical thickness function in cingulate gyrus

• Group wise differences found between Schizophrenia and control subjects

contd…
Partitioning anatomical manifolds

- Recursively partition Freesurfer cortical labels using $2^{nd}$ eigenfunctions
- Mean cortical thickness in a partition as a signal feature
- Outperforms Freesurfer labels in an AD vs CN classification task

[Lebed thesis 2013]

contd...
Partitioning anatomical manifolds (4)

- Mandible shape modeling:
  - 100 level contours of the 2nd eigenfunctions
  - Connect centroids of level contours to get centerline
  - Length $l_c$ and angle $\theta_c$ as shape features
- Regression model between shape features and age + gender.

[Seo 2011] contd…
Heat Kernels

• Initial value diffusion PDE on a manifold $M$:
  $$\frac{\partial u}{\partial t} = \Delta_M u, \quad u(x, 0) = f(x)$$

• $K_\sigma \ast f$ is the solution at $t = \frac{\sigma^2}{2}$ where:
  $$K_\sigma (x, y) = \sum_{j=0}^{\infty} e^{-\lambda_j \sigma} \psi_j(x)\psi_j(y)$$
Cortical thickness smoothing

- Iterative smoothing by decomposing into smaller band width kernels:
  
  $$K^{(k)}_\sigma \times f = K_{\sqrt{k}\sigma} \times f$$

- Assuming sufficiently small $\sigma$, discrete implementation is:

  $$\tilde{W}_\sigma \times f(p) = \sum_{i=0}^{m} \tilde{W}_\sigma(p, q_i) f(q_i)$$

  $$\tilde{W}_\sigma(p, q_i) = \frac{\exp\left(-\frac{||p-q_i||}{2\sigma^2}\right)}{\sum_{j=0}^{m} \exp\left(-\frac{||p-q_i||}{2\sigma^2}\right)}$$

[Chung 2005] Part of Freesurfer package
Solution using Laplacian eigen basis

- Finite eigenfunction expansion:
  \[ f(x) \approx \sum_{j=0}^{k} \beta_j \psi_j(x) \]

- Estimate \( \beta_j \) via solving a least squares problem using iterative residual fitting algorithm

- Then, heat kernel smoothing is given by:
  \[ K_\sigma * f(p) = \sum_{j=0}^{k} e^{-\lambda_j \sigma} \beta_j \psi_j(p) \]

• Mandible *shape* smoothed

[Chung 2011]
Smoothing on subcortical manifolds

- Heat kernel Smoothing implemented using the finite eigenfunction expansion approach
- Hippocampus and amygdala surfaces
- Shape and signal (surface displacements) were smoothed
- Regression model between displacements and age + gender
Open problems

• Richer measures to capture cortical structure beyond thickness?

[Chung 2005]

www.frontalcortex.com

[www.frontalcortex.com](http://www.frontalcortex.com)

atlassnc.uniurb.it

[www.frontalcortex.com](http://www.frontalcortex.com)

contd...
• Shape features for vasculature in the retina?

Speckle variance optical coherence tomography (OCT) images of retina in the eye