Spatiotemporal Anatomical Atlas Building

Population Shape Regression For Random Design Data

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Population Shape Regression

Regression in Vector Space

Regression on a Shape Manifold

[84 Healthy Individuals]

Mortemet et al.
Detailed Anatomical Regression

- Infer average structural changes
- Improve understanding of anatomy
- Indicated in disease detection, understanding

[Diagrams of brain scans across different ages]
Related Work

- **Large-deformation Diffeomorphic 3D Image Matching**
  - Younes, Trouve, Joshi, Beg, Avants, Gee, Miller

- **Longitudinal shape change models for individuals**
  - Beg, Miller [03, 04]; Clatz et al. [05]; Tompson, Toga eg. [00]

- **Large-deformation Intrinsic Mean Images**
  - Avants & Gee [04]; Davis, Lorenzen, Joshi [04,05]; Pennec [06]

- **Regression of scalar function on manifold**
  - Nilsson, Sha, Jordan [07]

- **Regression of spherical data**
  - Jupp & Kent [87]
Our Work

• Average anatomical change for population, not individual
• Anatomical change via large-deformation diffeomorphic transformations
• Predictor: vector space (e.g., time); Response: point on manifold
Outline

• Anatomical Shape Change Via Image Mapping
  – Manifold, Intrinsic Mean
• Nadaraya-Watson Regression Estimator
• Manifold Kernel Regression
• Synthetic example
• Application: Healthy brain aging
Review: Capturing Anatomical Shape Change

- Detailed local changes via diffeomorphic transformations of underlying coordinate system $\Omega \subset \mathbb{R}^3$
- Diffeomorphism: smooth mapping with smooth inverse

$\text{Diff}(\Omega)$
• Manifold structure, not vector space: addition is not defined

\[ \forall h_1, h_2 \in \text{Diff}(\Omega) : g = h_1 + h_2 \notin \text{Diff}(\Omega) \]

• Form a group under composition

\[ \forall h_1, h_2 \in \text{Diff}(\Omega) : g = h_1 \circ h_2 \in \text{Diff}(\Omega) \]

• Example: Rotations
Review: Capturing Anatomical Shape Change

- Metric structure on $\text{Diff}(\Omega)$
  - Integrate flow of velocity fields

\[
h_t(x) = x + \int_0^t v_s(h_s(x)) \, ds
\]

- Induce a metric via Sobolev norm on velocity fields

\[
d_{\text{Diff}(\Omega)}^2(\text{Id}, h) = \min_{v:\dot{h}_s = v_s \circ h_s} \int_0^1 \int_{\Omega} \| L v_t(x) \|^2 \, dx \, dt
\]
Review: Capturing Anatomical Shape Change

• Implies a metric \( d_\mathcal{I} \) on anatomical images: captures “severity” and “amount” of shape change required to match images

\[
d_\mathcal{I}^2(I, J) \equiv \min_{v: h_s = v_s \circ h_s} \int_0^1 \int_\Omega \|Lv_s(x)\|^2\,dx\,ds + \frac{1}{\sigma^2} \int_\Omega (I(h^{-1}(x)) - J(x))^2\,dx
\]
Review: Nadaraya-Watson Regression

• Observations \( \{x_i, y_i\}, x_i, y_i \in \mathbb{R} \)

\[ y_i = m(x_i) + \varepsilon_i \]

Regression estimator:

\[ m(x) \equiv E(Y|X = x) = \int y \frac{f(x, y)}{f_X(x)} \, dy \]
Review: Nadaraya-Watson Regression

- Replace unknown densities with kernel density estimates

\[
\hat{f}_X^h(x) \equiv \frac{1}{N} K_h \left( \frac{x - x_i}{h} \right)
\]

- Joint density estimate via product kernel

\[
\hat{f}_{g,h}(x, y) \equiv \frac{1}{N} K_h \left( \frac{x - x_i}{h} \right) K_g \left( \frac{y - y_i}{g} \right)
\]
Review: Nadaraya-Watson Regression

\[ \hat{m}_h(x) = \frac{\sum_{i=1}^{N} K_h(x - x_i) y_i}{\sum_{i=1}^{N} K_h(x - x_i)} \]

- Assume symmetric kernels
- Weighted mean of response variables
- Weights depend on predictor variables
Manifold Kernel Regression

• How do we define regression on a manifold?

\[ m(x) \equiv E(Y \mid X = x) = \int y \frac{f(x, y)}{f_X(x)} \, dy \]

• Use Fréchet expectation to define intrinsic mean via the metric \( d \)

\[ \mu = \arg\min_{q \in \mathcal{M}} \frac{1}{N} \sum_{i=1}^{N} d^2(q, p_i) \]
Frechet Mean: “Averaging Anatomies”

Motivation:

- Map population into common coordinate space
- Learn about normal variability
- Describe difference from normal
- Use as normative atlas for segmentation

Figure 1. Template Construction Framework

Manifold Kernel Regression

• Image observations and associated age measurements \( \{t_i, I_i\} \)

• Manifold Kernel Regression estimator via Fréchet expectation

\[
\hat{m}_h(t) = \arg\min_{I \in \mathcal{I}} \left( \frac{\sum_{i=1}^{N} K_h(t - t_i) d_{\mathcal{I}}^2(I, I_i)}{\sum_{i=1}^{N} K_h(t - t_i)} \right)
\]
Manifold Kernel Regression

**Predictor:** \( t_i \in \mathbb{R} \)

**Response:** \( \text{Diff}(\Omega) \)
Manifold Kernel Regression

- Weighted Intrinsic Mean

Predictor: $t_i \in \mathbb{R}$

Response: $\text{Diff(}\Omega\text{)}$

$$\sum_i^{N} \frac{K_h(t - t_i) d^2_I(I, I_i)}{\sum_i^{N} K_h(t - t_i)}$$
Manifold Kernel Regression

• Solution
  – Compute weighted, large-deformation Fréchet mean at each age
    • Iterative greedy method
    • Alternately optimize deformations, mean image
      [Davis, Lorenzen, Joshi ISBI 2004, NeuroImage 2004]
  – Coarse-to-fine
Manifold Kernel Regression

- Linear in number of observations
- Multithreaded implementation
- 5-80 minutes (per predictor)
  - 2-68 256³ images
  - 8x2-core 3 GHz Processors
  - 64 GB memory
Example: Regression with Known Ground Truth

- **Observations:**
  - 100 2D “bullseye” images
  - random predictor values
  - $r_i(t)$ nonlinear, independent

- **Structural Noise:** i.i.d. Gaussian noise added to radii

- **Goal:** Recover radii functions from images alone via regression
Example: Regression with Known Ground Truth

- Observations (sorted by $t$)
Example: Regression with Known Ground Truth

- Regressed Images
- Ground Truth Overlay (colored)
Application: Aging Brain

- How does the brain change over time?
- Regress image as function of age
- 84 3T-MR T1 volumes from healthy adults
- Ages 20-72
- Preprocessing:
  - Intensity calibration
  - Skull stripping
  - Rigid alignment
- Kernel Bandwidth: 6 years
- Available Online
Quantifying Change

• Dense collection regressed images
• Infer diffeomorphic transformation $h_t$ that encodes change of average anatomy over time
Diffeomorphic Growth Model

- Individual represented by observations $I_t$
  
  \[
  \int_0^1 \|v_t\|^2_V \, dt + \frac{1}{\sigma^2} \int_0^1 \|I_t - I_0 \circ h_t^{-1}\|^2_{L_2} \, dt
  \]

  Measure shape change via Sobolev norm

  Deformed template matches image observations $I_0$

[motivation] [methods] [application] [conclusion]  
Davis, Fletcher, Bullitt, Joshi
Diffeomorphic Growth Model

- Individual represented by observations $I_t$
  
  $\int_0^1 \|v_t\|^2_V dt + \frac{1}{\sigma^2} \int_0^1 \|I_t - I_0 \circ h_t^{-1}\|_{L^2}^2 dt$

- Apply to population via Fréchet Expectation

$\int_0^1 \|v_t\|^2_V dt + \frac{1}{\sigma^2} \int_0^1 \|E(I|T = t) - I_0 \circ h_t^{-1}\|_{L^2}^2 dt$
Quantifying Change

30 34 38 42

Expansion

46 50 54 58

Contraction
Quantifying Change

\[ \log |D (Id(x) + v_t(x))| > 0 \]

Expansion:

Contraction:

\[ \log |D (Id(x) + v_t(x))| < 0 \]
Kernel Bandwidth
Kernel Bandwidth

- “Goldie Locks”: Too smooth; Too rough; Just right!
- Cross-Validation based on MISE

Female20 K02  Female20 K06  Female20 K32
Conclusion

• Anatomical change via regression
• Manifold Kernel Regression estimator within diffeomorphic image mapping framework
• Apply to study aging brain via 3D MR image database
Future Work

- Predictors
- Compare populations
- Analyze new observations

- Kernel Regression
  - Parametric; Robust; convergence?

- Shape Spaces/Metrics
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Questions?

Image database may be downloaded from this URL:

www.insight-journal.org/midas/view_community.php?communityid=21

Or email:

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