BMI/STAT-768
Statistical Methods for Medical Image Analysis

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Volume to surface
Jacobian determinants
Tensor-based morphometry
Tensor-Based Morphometry
How to quantify brain growth and atrophy at voxel level?
Deformable shape model
D’Arcy Thompson 1860-1948

figuratively speaking, the "

Fig. 178. Co-ordinates of figures in the Cartesian plane.

Fig. 179. Skull of chimpanzee.

Fig. 180. Skull of baboon.

On Growth and Form
D’Arcy Thompson

I have sh is obviou differs or anthrop...
Deformable shape modeling framework

MRIs will be warped into a template and anatomical differences can be compared at a common reference frame.
Deformation vector field on the template

The deformation field match the homologous anatomy across two different images.
Visualizing Deformation

Red: tissue expansion
Blue: tissue shrinking
Yellow: deformation change
Tensor-based Morphometry (TBM)

- It uses higher order spatial derivatives of deformation fields to construct morphological tensor maps.
- From these tensor maps, 3D statistical parametric maps (SPM) are created to quantify the variations in the higher order change of deformation.
- More sensitive and powerful than voxel-based morphometry.
How to compute Jacobian determinant

\[ d_1, d_2, d_3 = d(x_1, x_2, x_3) \]

target position \hspace{1cm} Initial position

\[ U(x_1, x_2, x_3) = d(x_1, x_2, x_3) - (x_1, x_2, x_3) \]

Displacement vector

Jacobian determinant

\[ J(x) = \det \frac{\partial d(x)}{\partial x} = \det \left( \frac{\partial d_j}{\partial x_i} \right) \]
Examples. How to compute Jacobian determinant

- **1D:**
  \[ x' = 2x + 1 \]
  \[ J(x) = 2 \]

- **2D:**
  \[ x' = 2x + y + 1 \]
  \[ y' = x + 2y \]
  \[ J(x, y) = 4 - 1 = 3 \]
Jacobian determinant in 3D

\( x + u \)

displacement vector

JD

S.-G. Kim, Seoul National University
The effect of affine registration

- For affine registration $p' = Ap + B$, the Jacobian determinant is $\det(A)$.

- Every voxel will have the same scalar value.

- Affine registration based TBM only detect global size difference.
Interpretation of Jacobian determinant (JD)

- JD measures the volume of the deformed unit-cube after registration.

- A voxel can be considered a unit-cube.

- JD measures how voxel volume changes after registration.
Hard example:

**Jacobian determinant for surface deformation**

Surface parameterization:

\[ u = (u^1, u^2) \rightarrow X(u) \]

Riemannian metric tensor:

\[ g_{ij} = \left\langle \frac{\partial X}{\partial u^i}, \frac{\partial X}{\partial u^j} \right\rangle \]

\[ \sqrt{\det g} \]

Chung et al. 2003 NeuroImage 18:198-213
Generalization of Jacobian determinant in arbitrary manifold
= determinant of Riemannian metric tensors
= local volume (surface area) expansion
Normality of JD

\[ d(p) = p + U(p) \]

\[ \frac{\partial d(p)}{\partial p'} = I + \frac{\partial U(p)}{\partial p'} \]

\[ J(p) \equiv 1 + tr \left( \frac{\partial U}{\partial p'} \right) = 1 + \frac{\partial U_1}{\partial p_1} + \frac{\partial U_2}{\partial p_2} + \frac{\partial U_3}{\partial p_3} \]

Note that we modeled displacement \( U \) to be a Gaussian random field. Any linear operation (derivative) on a Gaussian random field is again Gaussian. So \( J \) is approximately a Gaussian random field.
Statistical properties of JD

- $J(p) > 0$ for one-to-one mapping
- $J(p) > 1$ volume increase; $J(p) < 1$ volume decrease
- Due to symmetry, the statistical distribution of $J(p)$ and $1/J(p)$ should be identical.
Lognormality of JD

- Domain \(-\infty < \log J(p) < \infty\)
- If \(J(p) = 1\), \(\log J(p) = 0\)
- Symmetry: \(\log [J^{-1}(p)] = -\log J(p)\)
- These 3 properties show that JD can be modeled as \emph{lognormal distribution}. 
Lognormal distribution

- Random variable $X$ is log-normally distributed if $\log X$ is normally distributed.
- For $E \log X=0$, the shape of density:

Some lognormal distribution looks normal so how do we check if data follows normal or lognormal?
Testing normality of data

• How do we check if JD is normal or lognormal emphatically?

• Quantile-quantile (QQ) plot can be used. For given probability $p$, the $p$-th quantile of random variable $X$ is the point $q$ that satisfies $P(X < q) = p$.

• See supplementary lecture material.

Read /reading/lecture03-quantile.pdf
QQ-plot compares quantiles

\[ P(Y < t) \]

\[ P(X < t) \]
QQ-plots
Plots are generated by R-package http://www.r-project.org
Normal probability plot

Sample quantiles

Quantiles from $N(0,1)$

The sample has longer tails.
Normal probability plot showing asymmetric distribution

Longer tail
Fisher’s Z transform on correlation

Tricks for increasing normality of correlation
Increasing normality of surface-based smoothing

Thickness  50 iterations  100 iterations

QQ-plot  QQ-plot  QQ-plot
Tensor-Based Morphometry Applications
A Unified Statistical Approach to Deformation-Based Morphometry

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Brain growth in children
Red: Tissue growth  $p < 0.025$
Blue: Tissue loss  $p < 0.025$
Yellow: Structure displacement  $p < 0.05$
Statistically significant regions of local volume change
JD > 1 volume increase, JD < 1 volume decrease over time
Early Stress Is Associated with Alterations in the Orbitofrontal Cortex: A Tensor-Based Morphometry Investigation of Brain Structure and Behavioral Risk

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Hanson et al., 2010. Journal of Neuroscience 30:7466-7472
oFC cluster that was smaller in physically abused children compared to controls and that there is a significant negative relationship between oFC development and the occurrence of family stress.
Behavioral/Systems/Cognitive

Structural Variations in Prefrontal Cortex Mediate the Relationship between Early Childhood Stress and Spatial Working Memory

Jamie L. Hanson,¹ Moo K. Chung,¹ Brian B. Avants,² Karen D. Rudolph,³ Elizabeth A. Shirtcliff,⁴ James C. Gee,¹ Richard J. Davidson,¹ and Seth D. Pollak¹

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Hanson et al., 2012. Journal of Neuroscience 32:7917-7925
PFC white matter negatively correlated with stress
positively correlated with executive function
Multivariate-TBM
Multivariate vector = Group + Brain + Age + Noise

Multivariate general linear model (MGLM):

\[ P_{n \times 3} = X_{n \times p} B_{p \times 3} + Z_{n \times r} G_{r \times 3} + U_{n \times 3} \Sigma_{3 \times 3} \]

Multivariate vector = Group + Brain + Age + Noise

*Chung et al., 2010 NeuroImage 53:491-505*
Massive univariate vs. multivariate

Massive univariate hypothesis:

\[ H_0 : \lambda_1(x) = \lambda_2(x) \text{ for all } x \]
\[ H_1 : \lambda_1(x) \neq \lambda_2(x) \text{ for some } x \]

Multivariate relational hypothesis:

\[ H_0 : \lambda_1(x) = \lambda_2(y) \text{ for all } x \text{ and } y \]
\[ H_1 : \lambda_1(x) \neq \lambda_2(y) \text{ for some } x \text{ and } y \]
Massive univariate vs. multivariate

Region A

Group 1

Region B

Group 2

univariate

multivariate
Data

• T1-weighted MRI were collected using a 3T GE SIGNA scanner.

• 23 maltreated children who have been post-institutionalized (PI) in orphanages in East Europe and China but later adopted to the families in US.

• Age-matched 31 normal control subjects.

• Age: PI: 11.26 +- 1.71, Controls: 11.58 +- 1.61 years.

• Gender PI: 10 boys and 13 girls, Controls: 18 boys and 13 girls.
Jacobian determinant (tissue volume change) with respect to the template
MATLAB Demo/Data
Homework 2
Determine Gaussianness of Jacobian surface data

Due: 2 weeks from now
Checking normality on surface data

Suggested output: Chung et al. 2003 NeuroImage
Multivariate-TBM analysis flow for single seed

Jacobian Determinant

Seed voxels

Connectivity Maps

Z-statistic
Seed-based (genu) correlation map of Jacobian determinants
Seed-based (genu) correlation map of Jacobian determinants
T-stat map on correlation map difference (seed= genu)
1856 preselected nodes

Multiregion correlation map of Jacobian determinants

Correlation maps
Graph representation of thresholded correlation

0.9

PI
Controls
Graph representation of thresholded correlation

PI

Controls
Graph representation of thresholded correlation

Interpretation: PI is more homogenous than the controls.
Z-statistic map of group difference (PI- controls)
Dendrogram representation of correlations
Lecture 4

Surface to networks
Correlations
Sparse inverse covariance matrix estimation

Read

Special guest lecture on sparse regression

Time: September 18 Tuesday 10:00-10:40am

Speaker: Sijian Wang
Assistant Professor
Department of Biostatistics and Medical Informatics
University of Wisconsin-Madison

Title: Sparse Integrative Clustering of Multiple “Omic” Data Sets

Abstract: High resolution microarray and next-generation sequencing platforms are powerful tools to investigate genome-wide alterations in gene expression, DNA copy number, DNA methylation, and other genomic events associated with a disease. An integrated genomic profiling approach measuring these “omic” data types simultaneously in the same set of samples would further reveal disease mechanisms that would not be otherwise detectable with a single data type. In this talk, I will present a joint data analysis approach for subtype discovery and associated biomarkers. Building upon the connection between principal component analysis (PCA), K-means clustering, and Gaussian mixture model, we formulated a novel integrative clustering method for integrating “omic” data sets. Sparse solutions are derived using regularization methods exploiting genomic data structures to yield “grouping” effects for highly correlated features and to impose smoothness along chromosomal positions.