Medical Image Analysis

Instructor: Moo K. Chung
mchung@stat.wisc.edu

Lecture 18.
Review of Medical Image Analysis
and Other Issues

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Medical Image Analysis Flow

**Image Acquisition**
- MRI, fMRI, PET, CT, EEG, MEG etc.

**Importing Image into computer**
- DIACOM, MINC, ANALYZE, BRIK

**Image Segmentation**
- Image intensity based segmentation:
  - Gaussian mixture with EM algorithm and a Bayesian prior

**Deformable curve and surface**:
- Active contour, snakes, deformable surface model, level set, thin-plate spline

**Image Registration**

**Topics not covered**

**Topics covered**

**Numerical methods for PDE**
Motivation for using partial differential equation (PDE) based approaches

• PDE models a continuous physical process
• The solution of PDE provides a continuous solution

Applications:
Image segmentation (active contours, level set)
Image registration (elastic or fluid dynamics equation)
Image smoothing (diffusion smoothing)
Cortical thickness estimation (Laplace equation)
Anatomical surface parameterization (conformal mapping)
Image Registration

Similarity measure

$$\rho(x, y) = \rho\left(I_1(x), I_2(y)\right)$$

Variational approach

$$\min_d \left[ \int_{x \in \Omega} \rho\left(x, x + d(x)\right) \, dx + \lambda \int_{x \in \Omega} \left\| \frac{\partial d}{\partial x} \right\| \, dx \right]$$

PDE approach

$$\alpha(x) \cdot \frac{\partial^2 d}{\partial x^2} + \beta(x) \cdot \frac{\partial d}{\partial x} + \gamma(x) = 0$$
Solving ODE in 1D

Heat diffusion:

\[ \frac{\partial f}{\partial t} = \frac{\partial^2 f}{\partial x^2} \]

with initial data \( f(x, t) = Y(x) \)

Finite difference:

\[ f(x, t_{j+1}) = f(x, t_j) + \delta t \frac{\partial^2 f}{\partial x^2}(x, t_j) \]

iteration step size \( \delta t = t_{j+1} - t_j \) is fixed
Finite Difference Method (FDM)

\[ \frac{\partial^2 f}{\partial x^2}(x, t_j) = \frac{\frac{f(x + \delta x, t_j) - f(x, t_j)}{\delta x} - \frac{f(x, t_j) - f(x - \delta x, t_j)}{\delta x}}{\delta x} \]

\[ = \frac{[f(x - \delta x, t_j) - 2f(x, t_j) + f(x - \delta x, t_j)]}{\delta x^2} \]
Simulation result
Convergence of FDM

• FDM converges for sufficiently small time step.

• Maximum principal: diffused signal should be between the maximum and the minimum of the previous time step.

Assuming positive data

\[
\begin{align*}
  f(x_i, t_{j+1}) &= f(x, t_j) + \delta t \frac{\partial^2 f}{\partial x^2}(x, t_j) \\
  \leq \max [f(x_{i-1}, t_j), f(x_i, t_j), f(x_{i+1}, t_j)]
\end{align*}
\]

\[
\delta t \leq \max \left[ \left| \frac{f(x_{i-1}, t_j) - f(x_i, t_j)}{\frac{\partial^2 f}{\partial x^2}} \right|, \left| \frac{f(x_{i+1}, t_j) - f(x_i, t_j)}{\frac{\partial^2 f}{\partial x^2}} \right| \right]
\]
Solving PDE in 2D Mesh

Heat diffusion: \[ \frac{\partial F}{\partial t} = \Delta F \]

with initial condition \[ F(x, t = 0) = f(x) \]

Numerical computation requires the combination of finite element method (FEM) + the finite difference method (FDM).
Basic idea of FEM

FEM is a numerical technique for setting up a PDE on triangle mesh.

Solution is approximated as a linear combination of step functions defined on triangle elements.
Finite Element Method (FEM)

\[ G, F \in PL\left( \bigcup_{i=1}^{N} T_i \right) \quad \text{space of piecewise continuous linear functional} \]

\[ N = 82190 \]

For an arbitrary test function \( G \), we have

\[ \int_{T_i} G \frac{\delta F}{\delta t} \, dT = \int_{T_i} G \Delta F \, dT = -\int_{T_i} \langle \nabla F, \nabla G \rangle \, dT. \]

Solving this for every triangles, we obtain a system of ODE

\[ \frac{d[F]}{dt} = -[A]^{-1}[C][F] \]

40962 x 40962 sparse matrix

FDM is used to solve ODE via iteration.
Laplace-Beltrami Operator (Graph Laplacian)

The Laplacian on graph can be estimated via computer algebra package (Maple, Mathematica).

Matrix inversion via Maple

\[
\Delta \hat{F}(p) = \sum_{i=1}^{m} w_i \left( F(p_i) - F(p) \right)
\]

\[
w_i = \frac{\cot \theta_i + \cot \phi_i}{\sum_{i=1}^{m} |T_i|}
\]
Finite Difference Scheme

\[
\frac{\partial F}{\partial t} = \Delta F
\]

\[
\frac{F(x, t_{n+1}) - F(x, t_n)}{t_{n+1} - t_n} = \Delta F(x, t_n)
\]

Stability condition (maximal principle):

\[
\min_i F(p_i, t_n) \leq F(p, t_{n+1}) \leq \max_i F(p_i, t_n)
\]

Convergence condition for time step:

\[
t_{n+1} - t_n \leq \min \left( \left| \frac{\max_i F(p_i, t_n) - F(p, t_n)}{\Delta F(p, t_n)} \right|, \left| \frac{\min_i F(p_i, t_n) - F(p, t_n)}{\Delta F(p, t_n)} \right| \right)
\]
2D mesh simulation result

5mm FWHM filter size

Noisy data

20 iterations

100 iterations
Medical Image Analysis Flow

Image Segmentation

Image Registration

Similarity measures
- correlations, mutual information
- Kullback-Leibler (KL) distance

Curve registration
- dynamic time warping
- Functional data analysis

Image registration
- Intensity-based, PDE-based

Curve modeling:
- modeling of landmarks (markers)
- along anatomical boundary

Model building
15 markers are located at the major joints of the human body and their movements are recorded continuously for 40 subjects (1400 measurements over time while walking)

Data: 3 coordinates x 15 makers = 45 dim. vector $\mathbf{p}$. 
Principal components analysis (PCA)

1400 posture vectors will give a set of PC for each subject. The bars denote the s.d. of PC over 40 subjects.

The first four components explain 98% of the overall variability.
Modeling on posture vector $\mathbf{p}$

$$\mathbf{p} = \mathbf{p}_0 + \sum_{i} c_i \mathbf{p}_i$$

average posture

weighted linear combination of the first four PCA
PC change over time of a single subject

Four principal components over time

Model fit using sine functions
R-square values: 0.99, 0.95, 0.94, 0.90
Model for posture (single subject)

\[ p(t) = p_0 + p_1 \sin(\omega t) + p_2 \sin(\omega t + \phi_2) \]
\[ + p_3 \sin(2\omega t + \phi_3) + p_4 \sin(2\omega t + \phi_4) \]

\( j \)-th subject

\[ p_j(t) = p_{j,0} + p_{j,1} \sin(\omega_j t) + p_{j,2} \sin(\omega_j t + \phi_{j,2}) \]
\[ + p_{j,3} \sin(2\omega_j t + \phi_{j,3}) + p_{j,4} \sin(2\omega_j t + \phi_{j,4}) \]
Subpixel Curvature Estimation of the Corpus Callosum via Splines and its Application to Autism

Thomas J. Hoffmann\textsuperscript{1}, Moo K. Chung\textsuperscript{1,2,3}, Kim D. Dalton\textsuperscript{3}, Andrew L. Alexander\textsuperscript{3,4,5}, Grace Wahba\textsuperscript{1,2}, Richard J. Davidson\textsuperscript{3,4,6}

\textsuperscript{1}Department of Statistics, \textsuperscript{2}Department of Biostatistics and Medical Informatics, \textsuperscript{3}Keck Laboratory for Functional Brain Imaging and Behavior, Waisman Center

\textsuperscript{4}Department of Psychiatry, \textsuperscript{5}Department of Medical Physics, \textsuperscript{6}Department of Psychology

University of Wisconsin, Madison, WI 53706

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Level set segmentation

Spline smoothing
Level set segmentation

- The anatomical boundary is modeled as the zero level set of a function $\phi(x,y,t)$.

$\text{Red} = \phi(x,y,0) = \text{anatomical boundary}$

$$\frac{\partial \phi}{\partial t} + F |\nabla \phi| = 0$$

boundary propagation velocity
Fast marching cube method is used to incrementally propagate the boundary (level set).
Fast Marching Cube

(i)

(ii)

(iii)

(iv)
Level set simulation
Artery segmentation
Microscopic image segmentation
White matter segmentation
Level set segmentation produces noisy boundary

\[
\min_g \frac{1}{n} \sum_{j=1}^{n} [Y_j - g(t_j)]^2 + \lambda \int [g'''(t)]^2 \, dt
\]

Spline is used to obtain smooth boundary
Curvature estimation
Curve registration via curvature matching

Find smooth deformation field $d$ by minimizing

$$
\frac{1}{n} \sum_{j=1}^{n} \|X(t_j) - X(d(t_j))\| + \lambda \int |\kappa_1(t) - \kappa_2(d(t))| \, dt
$$

positional difference curvature difference
Visualization of displacement vector
P-value map (uncorrected) of group difference
Medical Image Analysis Flow

**Image Segmentation**
- Voxelwise Morphometry
  - Voxel-based morphometry (VBM)
  - Deformation-based morphometry (DBM)
  - Tensor-based morphometry (TBM)
  - Surface-based morphometry (SBM)

**Image Registration**

**Model Building**
- Surface measures
  - Cortical thickness
  - Surface curvatures
  - Area element
  - Riemannian metric tensors
- Volume measures
  - Tissue density
  - Jacobian determinant

**Functional-MRI**
- AR-model
- HRF estimation
- Whitening process

**Image Smoothing**
• Morphometry


• Anatomical boundary segmentation/parameterization


Cortical thickness analysis


Cortical thickness vs. gray matter density

• Validation is difficult since cortical thickness is obtained from 2D surface mesh while gray matter density is obtained from 3D whole brain image.

• **Solution:** convert 2D cortical mesh data to 3D volume data using distance map
Distance map

• At each voxel position $x$,

$$
\text{dist}(x) = \min_{y\in\text{surface}} \| x - y \|
$$

• Optimization is performed using the nearest neighbor search algorithm on an optimized k-D tree (MATLAB)

• Given inner and outer surfaces, we can compute the average distance map.
From surface mesh, we obtain distance map

Contour plot of average distance map

Density map as a function of distance map

Kernel smoothing
Counter-intuitive result showing negative correlation between cortical thickness and gray matter density
Thickness and density do not correlate well near tissue boundary

Fig. 11. Top: gray matter density projected onto inner, mid and outer surfaces. On the inner surface, the deep sulcal regions show the low density while the gyral ridges show high density. On the outer surface, this is opposite. The deep sulcal regions show high density while the gyral ridges show lower density. The middle surface shows high density. Bottom: Scatter plot of gray matter density over thickness. They show negative correlations.
Gray matter density does not necessarily measure the amount of gray matter. Cortical thickness is only 1D measure defined on 2D surface. It will not completely quantify the amount of gray matter (3D measure).

Fig. 13. Simple 2D schematic showing the negative correlation between thickness and gray matter density. Gray colored pixels are gray matter. The black circle is the contour of heat kernel. There are more gray matter pixels in region (a) than region (c) although the thickness in region (c) is thicker than that of region (a). The gray matter density in the middle of the gray matter (b) is 1 for almost all subject indicating very small between-subject and between-group variability. Because of the small between-group variability, VBM does not usually detect signal in the middle of the gray matter. Most of significant signal detected in VBM is near the tissue boundary where the between-group variability is high.
**Surface-based morphometry**


Focal Decline of Cortical Thickness in Alzheimer’s Disease Identified by Computational Neuroanatomy

36 subjects (17 controls, 19 AD)
Mini Mental State Examination (MMSE) score
Age
T1 weighted MRI (three scans per subject)

\[ Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + e \]

- **Group variable**: 0 control, 1 AD
- **Scan variable**: 1, 2, 3
- **Age**
- **MMSE**
Cortical thickness Analysis pipeline

20mm FWHM diffusion smoothing (Chung et al., 2003) was used

Figure 1. An overview of the steps involved in cortical thickness analysis. First, the images are non-uniformity corrected and registered into stereotaxic space. They are then classified (1) and fit with a white matter surface (2). The gray surface is found by expanding out from the white (3). Cortical thickness is measured at every vertex (4), and blurred using a 20 mm surface-based kernel (5).
Statistical parametric maps

Figure 5. Regional analysis using the cortical thickness methodology in AD versus normal controls displaying differences in the entorhinal cortex. The four cortical views show: (a) the probability maps of the entorhinal and perirhinal cortices in this population; (b) the t-statistics of the MMSE regression; (c) the group analysis; and (d) the time difference from baseline. The color scales are the same as in Figures 2–4, 6 and 7 respectively. The graphs illustrate the effects at the vertex indicated by the black lines. Atrophy of the PHG is clearly implicated in each of the three analyses shown.
• Surface data smoothing


Medical Image Analysis Flow

**Image Smoothing**
- Anisotropic smoothing
  - Anisotropic diffusion smoothing
  - Edge preserving smoothing
  - Vector fields smoothing
    (vector spline)

**Kernel smoothing**
- Gaussian kernel smoothing
- Heat kernel smoothing
- Iterative kernel smoothing

**Diffusion smoothing**
- Diffusion equations

**Surface smoothing**

**Random fields**
- Covariance functions
- Isotropic field

**General linear model (GLM)**
- Multiple regression
- Logistic regression
- (discriminant analysis)
- Correlation analysis

**Statistical Issues**
- Gaussianess
- QQ-plot

**Statistical Analysis**

**Multiple comparison correction**
Surface smoothing

• Motivation: segmented anatomical surfaces are noisy.

A Signal Processing Approach To Fair Surface Design

Gabriel Taubin
IBM T.J. Watson Research Center

• Taubin’s surface fairing approach extend this idea: surface signal is decomposed into the linear combination of eigenfunction of surface Laplacian.
Taubin’s surface fairing

Weights are determined from the discrete surface Laplacian

\[ v'_i = v_i + \{\lambda, \mu\} \sum_{j \in i^*} w_{ij} (v_j - v_i) \]
Smoothing is applied iteratively
Smoothing closed curve

1. Iterated kernel smoothing of corpus callosum boundary
2. Gaussian white noise is added to curve 2.
3. X-coordinate function and its iterated kernel smoothing
4. Simulated curve obtained from smoothing curve 2.
Smoothing cortical boundary
Anisotropic surface smoothing

- Extension of edge preserving smoothing in 2D image
- This requires anisotropic boundary information
Anisotropic Boundary Information

Direction of Anisotropy

\[ C(p) = \sum_{i=1}^{n} (v_i - c)(v_i - c)^T \]

where \( v_i \) is the location of the surface point on the neighborhood and \( c \) is the centroid of the neighborhood.

Corner: all eigenvalues are nearly equal
Edge: one dominating eigenvalue
Planar: two eigenvalues nearly equal and larger than the third
• Surface Smoothing/fairing


Medical Image Analysis Flow

Validation and Simulation
• In statistical literature, simulation is widely used as a way to demonstrate the correctness of proposed methodologies.
• In imaging literature, simulation is somewhat limited due to the difficulty of simulating realistic images.
• Multiple comparison corrections


Comparative analysis


Permutation test