Non-Rigid Registration and Atlases in Medical Image Analysis

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Uses for Non-Rigid Registration

- Correcting/Accounting for Imaging Distortions
  - Scanner Induced Geometric changes
- Correcting Tissue Deformations
  - Subject Related Anatomical Changes
- Capturing Tissue Growth or Loss within a Subject
  - Studying Dementia or Tissue Growth: Deformation Based Morphometry
- Resolving Differences Between Subjects:
  - Spatial Normalization to Compare Image Data Across Populations

Non-Rigid Registration in Medical Image Analysis

- Where is Non-rigid registration needed in Medical Imaging?
- How do we describe image deformations?
  - Global Parametric Approaches
  - Dense Fields Approaches:
    - 'Physical' Models
    - Large Deformation Models:

With and Without Gradient Correction: No Movement, Positioned Centrally in Magnet
Correction of Larger Scale Geometric and Intensity Distortion

Reference T1 Anatomical MRI
Spin Echo EPI (Rigid Registration)

Using a Model of Spin Echo Signal Conservation and Intensity Distortion when Estimating Registration

\[ I_{\text{rec}}(x,y,z) = I_{\text{sel}}(x,y,z) / J_{\text{dist}}(x,y,z) \]

So, if we have a spatial registration estimate of EPI to anatomy, we can use its Jacobian to estimate an EPI intensity correction.

- Collecting data from different individual anatomies is not trivial.
- Need to locate corresponding location in atlas for a given measurement in the subject anatomy.
- Need a template (in atlas space) to match subject anatomy to a given subject anatomy.
- How do we derive a correspondence or mapping?
  - Estimate the warp that takes us from template to subject.
  - Need a non-rigid registration algorithm.

Spatial Normalisation: Bringing Image data into a Common Coordinate System

- Components of a non-rigid registration algorithm:
  - Model or parameterization of the Transformation $T$
    - What structural differences we can resolve.
  - Registration (similarity) measure $S(T)$
    - Provide an absolute or relative measure of the quality of match.
  - Geometric Constraints $C(T)$
    - Prevent unwanted or physically meaningless deformations.

- Optimization Method
  - Continuous refinement of many parameters.
  - Often high-dimensional search space.
  - Constrained by corresponding spatial structures.

Non Rigid Registration

Mathematical Models for Spatial Transformations of Image Data

- Global Affine
- Non-Linear Global Parameterizations
- Spatially Local Parameterizations
- Dense Field Techniques

Deformation Models For Non-Rigid Registration

- Simplest Methods:
  - Use Global Linear or Affine model.
  - Describing only global:
    - Translations, Rotations.
  - Scaling and Shear.
Deformation Models For Non-Rigid Registration

- More complex deformations:
  - Globally Parameterize the Deformation Field:
    - e.g. Polynomial function of location (here 1D)
    \[ T(x) = a_x x + b_y y^2 + c_x x + d \]
  - Modify Parameters \( a, b, c \) and \( d \) so global similarity \( F(T) \) maximized

- Radial Basis Functions
  - Given a set of corresponding landmarks, what happens between?
  - An RBF estimates mapping for points not at landmarks
  - For a given point \( x \), it combines mappings from neighboring landmarks \( i \), weighted by a function of distance
    \[ y(x) = \sum_{i=1}^{N} u_i \phi(||x - c_i||), \]
  - Where the basis function determines the form of the warp:
    \[ \phi: \mathbb{R}^2 \rightarrow \mathbb{R} \]

- Properties of RBF
  - Many of the common forms (e.g. thin plate) provide optimally smooth deformations
  - Generally stable to estimate weights for many different configurations of points.
  - Change location of any landmark and whole deformation field changes:
    - Expensive to re-evaluate whole image match

- Deformation Models For Non-Rigid Registration
  - Cosine Basis Functions
    \[ T(x) = \frac{1}{\sqrt{2\pi M}} \sum_{m=1}^{M} \sum_{j=1}^{J} b_{ij} \cos \left( \pi (2m-1)(j-1)/2M \right) \]
    \( i = 2, ..., J, m = 1, ..., M \)
  - Gaussian:
    \[ \phi(r) = e^{-r^2/2} \]
  - Multiquadric:
    \[ \phi(r) = \sqrt{r^2 + c^2} \]
  - Thin Plate Spline:
    \[ \phi(r) = r^2 \ln(r) \]

- Limitations of Global Parameterizations
  - \( T(x) = f(x, a, b, c) \)
    - Each Parameter \( a, b, c, ... \) Modifies entire image
      - Expensive to evaluate gradients of \( T \) wrt parameters
    - Complex Brain shape differences requires a fine scale deformation
    - Fine Scale deformation requires MANY parameters
      - High spatial frequencies for Cosine parameters
      - or: high order polynomial
    - So… Need a way to simplify problem

- Different forms of Radial Basis Function:
  - Thin Plate Spline:
    \[ \phi(r) = r^2 \ln(r) \]
  - Gaussian:
    \[ \phi(r) = e^{-r^2/2} \]
  - Multiquadric:
    \[ \phi(r) = \sqrt{r^2 + c^2} \]
Alternatives: Local Models

- Rather than have:
  - Many parameters
  - Where each influences the image deformation over the whole space:
- Need parameters that have localized influence on the deformation
  - Faster to Evaluate Image Match
- Forms of Spline can provide spatially localized deformation control

Spline Based Deformations with local support

- Thin-Plate splines can be adapted to have local support:
  - Mike Fornefett, Karl Rohr, and H. Siegfried Stiehl, Elastic Registration of Medical Images Using Radial Basis Functions with Compact Support, Computer Vision and Pattern Recognition, 1999
  - Other forms using Specialized regular control knots can provide faster evaluation:

B-Spline Models For Registration

- B-Spline Model:
  \[ f(x) = \sum_{r=0}^{N} P_{i+r} B_r(x-x_p) \]
  Sum of contributions from local knots \( r=0..N \) only
- The Basis functions \( B_r(t) \) are specific polynomials eg Cubic
  - \( B_0(t) = (1-t)^3/6 \)
  - \( B_1(t) = (3t^3-6t^2 +4)/6 \)
  - \( B_2(t) = (-3t^3+3t^2 +3t+1)/6 \)
  - \( B_3(t) = t^3/6 \)
- Move one knot and deformation changes only within A given range of knot locations.
- A B-Spline Approximates: it does not interpolate!
  - Functions does not have to pass through knot values

B-Spline Models For Registration

- B-Spline Transformation Model
  \[ T(x) = x + \sum_{r=0}^{N} P_{i+r} B_r(x-x_p) \]
  B-Spline can Still Fold! (e.g. multiple \( x \)'s map to the same value of \( T(x) \))
  - Can Test for Folding based on distance between knot values.
  - Can Prevent folding by adding a smoothness penalty term

Extend to 3D Displacement Along 3 Axes

- Describe Transformation \( T(x) \) in directions \( x, y \) and \( z \) for each point in \( x, y, z \)
- Parameterized by a Lattice of control parameters (knots)
  \[ Q_{x,y,z} = \sum_{p=0}^{P} \sum_{q=0}^{Q} \sum_{r=0}^{R} m_{pq} \]
Extend to 3D Displacement Along 3 Axes
Using 3D lattices of control knots

Maximize Image Similarity $Y()$ w.r.t. $Q_{pqr}$

\[ R(Q_{pqr}) = Y(Q_{pqr}) - \lambda \sum_i \frac{T(x, Q_{pqr})}{\partial x_i} \]

Registration Criteria: Regularization Penalty

Example Group Spatial Normalization
(Studholme et al, Proc. SPIE Medical Imaging 2001)

Capturing More Detail...
Dense Field Models

Dense Field Methods
- Derive a voxel by voxel force field making images more similar
  - (local gradient of similarity measure with respect to individual voxel location)
- Move in the direction of the force field and re-evaluate

Deformation Models for Registration
- Early approach applied to 3D brain images:
  Elastic Registration [Bajcsy, JCAT, 1983]
  - Applying a marked template to a new individual
  \[ T(x) = x + u(x) \]
- Find a displacement field $u(x)$ which balances the elastic energy of $u(x)$ with the registration criteria $S(x)$
- So the Elastic Deformation Model then is given by:
  \[ \mu \nabla^2 u(x) + (\lambda + \mu) \nabla \cdot u(x) = S(x) \]

$\mu$ and $\lambda$ are Lame's elasticity constants
Deformation Models for Registration

- $\mu \nabla^2 u(x) + (\lambda + \mu) \nabla (\nabla^T u(x)) = S(x)$

$\mu$ and $\lambda$ relate applied forces to the resulting strains, by the Poisson’s Ratio:

- $\sigma = \lambda/(\lambda + \mu)$

$\Rightarrow$ Ratio of Lateral Shrink to Extensional Strain.

Generally for registration $\lambda = 0$

So registration force in one axis does not influence other axes.

Elastic Deformation for Registration

$\mu \nabla^2 u(x) + (\lambda + \mu) \nabla (\nabla^T u(x)) = S(x)$

Key Idea: The Force balancing registration criteria is a function of the derivatives of the deformation field $[\nabla^T u(x)]$ etc.

...Rates of change of displacements $u(x)$ w.r.t. location $x$:

Example Elastic Warping of Brain Anatomy: Template (MNI)

Example Elastic Warping of Brain Anatomy: Subject (affine)

Example Elastic Warping of Brain Anatomy: Subject (Elastic Warp)
Elastic Deformation for Registration

- Can be used to prevent Singularities or Folding…
- But as displacement field evolves:
  - Deformation Energy builds up
- For extreme differences in anatomies:
  - deformation energy will prevent complete registration

Limits of Elastic Matching

Regularization and Large Deformations

\[ \mu \nabla^2 u(x) + (\lambda + \mu) \nabla (\nabla^T u(x)) = S(x) \]

One Step  Multiple Steps: Regridding

Mapping between Anatomies:
Describing Correspondence

Track Evolution over Curved Manifold

Christensen, Miller et al,
IEEE trans Image Processing, 1996
Curved Diffeomorphic Mapping: Describing Large Deformations

Discrete Diffeomorphic Mapping: Composing Sequences of Small deformations

Deformation Models For Registration
- Best known approach is a Viscous Fluid Deformation Model [Christensen,TIP,1996] and [Freeborough&Fox98]
- For current deformation, evaluate Velocity Field:
  \[ \mu \nabla^2 v(x) + (\lambda + \mu) \nabla(\nabla^T v(x)) = S(u(x)) \]
  \( \mu \) is Shear Modulus, \( \lambda \) is Lame's Modulus
- Evaluate a fractional update (\( \Delta t \) 'seconds') of the displacement field along current velocity field:
  \[ u'(x) = u(x) + R \Delta t \]
  where
  \[ R = v(x) - v(x) [\partial u / \partial x]^T \]
  - Then update the Force Field \( S(u(x,t)) \) and iterate

Example Large Deformation

Sparse Registration Force Field Driving Points into Better Alignment

In Regions of misaligned Tissue Force \( > 0 \)

Velocity Field Smooth and Well Behaved i.e. no singularity points or folding

Then: Update displacement estimate \( u(x) \) along \( v(x) \)

Deformation Models For Registration
i) Evaluate Velocity Field \( v(x) \) for Current Force
ii) Propagate mapping along Velocity Field (update \( u(x) \))
iii) Update Force Field \( F(u(x,t)) \) for Current Deformation
Key Idea: The fluid model ensures that the deformation preserves topology at each step: i.e. two points don’t map to one point.
Can Resolve Complex Deformations:
Even many cortical structures deformed (intensities/tissue... look the same) BUT: not necessarily registered!

Fluid registration can be dangerous...
Can be critically dependent on initialization: pre-registration and constraints on region applied to.
Key factor: Lots of engineering rather than mathematics

Atlases and Templates for Spatial Normalization of Anatomies

An Atlas
In practice we might say an Atlas is:
A map or spatial record of what we know about a region

Overview
- What is an Atlas?
- Templates for Spatial Normalisation

Types of Atlas
Characteristics of an Atlas:
1. The type information we record in it
2. How we place that information within the atlas
3. How we display/project/extract that information
1. An Atlas usually refers to an (often probabilistic) model of a population of spatial data (images).

2. Parameters determining the model are learned from a set of training data.
   - One or more subjects: eg atlas of brain regions
3. Simplest form is a template or average intensity.
   - Eg: Mean grey matter density, Mean PET tracer uptake

4. More complex forms capture
   - Higher order statistics: Variance, or other Model of Distribution
   - Complex parameterized models: eg Age

How do we place information into an atlas?

**Independent Modalities**

- Use 'structure' to place 'functional' measurements within the atlas
- Use MRI to normalize subject anatomy to a template anatomy
- Apply anatomical transformations to bring functional measurements in a subject into the atlas

**Same Modality**

- Use neighboring structure to locate and place measurements within an atlas of the same type of measurements
  - How accurately do we place that information?
  - How does that neighboring information influence placement?
Warping in Atlas Mapping

- Collecting data from different individual anatomies is not trivial.
- Need to locate corresponding points in atlas for a given measurement in the subject.
- Need a Template (in atlas space) to match each subject to.
- How do we derive a correspondence or mapping?
  - Warp from template to subject?
  Need a [non-rigid] Registration algorithm for Spatial Normalisation.

Templates for Atlas Mapping

- What structure do we use as a target or template?
- Needs to contain information relevant to the problem:
  - Where are the ports along a coastline?
  - Where are the gyri delineating functional brain regions?
- Needs to Exclude irrelevant information:
  - Template should not contain a tumor if studying normal anatomy.
- Need to have a representative shape:
  - Don’t use a brain with rare sulcal patterns to study normal anatomy.

Templates and Atlases

- Early Atlases for presentation/visualization:
  - Were often manually drawn
    - Broadmann[1]
  - ‘Idealized’ anatomies created by sketching features of interest
    - Difficult to compare results
- Modern Templates -> for Spatial Normalisation:
  - Can be optimized for use with registration method


Optimizing Templates

- Contrast/Intensity Properties
  - High signal to noise (average brain of MNI Colin27??)
    - Show imaging structures of interest:
      - T1W template for T1W matching -> structure
      - T2W template for T2W matching -> fMRI?
- Resolution
  - High isotropic resolution
    - Minimize loss of fine structure/tissue boundary
- Spatial Mathematical Properties:
  - Average ‘Shape’ of anatomies studied
    - Aid in visualization of results
    - Improve registration algorithm?

Optimal Templates for Matching

- Average Intensity? (older SPM/VBM analyses)
  - Register a set of MRI’s to a single subject MRI:
    - and average intensities to form a new template:

Single subject MRI  "Average" subject MRI

• Since images imperfectly aligned:
  - there is a Fundamental problem:
  - Resulting ‘average’ image is not necessarily an example of a real anatomy which has been blurred.
  - May even be topologically different: (eg sulci covered over)
  - So... deforming an individual to it may be impossible!
Average Shape Between a Cube and a Sphere:
The need for local deformations

- Template is most similar in shape to a given group being studied
- Makes registration easier?

**Linear Averaging: 'Unbiased Atlases'**

Evaluate a common space such that the average displacements of a given point to a set of subjects is zero.

Can do this

1. Group-Iteratively during registration:
   - register group to template
   - warp template to linear average
   - re-warp subject to template
   - Collectively during group-wise registration
     - Use distance as a constraint

2. Collectively during group-wise registration

\[ \sum_{X} \sum_{i} d_{i} \rightarrow 0 \]

**Optimal Templates for Matching**

- Improving Average through fine scale registration

**Linear Averaging: ‘Unbiased Atlases’**

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**Elastic averaging of group (driven by entropy)**

Starting Population

- (No Knowledge of Underlying Average Shape or Contrast Differences)

Populations Deformed Toward Each other

- Subpopulation with internal features Collectively Aligned

Studholme et al, A template free approach to spatial normalisation of brain anatomy Pattern Recognition Letters, vol 29(10), July, 2005
Non-Linear Shape Averaging

- The shape distance problem (same as in regularization):
  - Simple Case
  - More Complex Case

Average Shape
Measure distances along a curved manifold

Large Deformation Non-Linear Average Shape Between a Cube and a Sphere

Distance measured along curved Manifold: Then Averaged Over Population

Example Symmetric Warping between Developing Anatomies

Warp Image Pair into Alignment

Average Anatomical Space Scanned Anatomy

Example Symmetric Warping between Developing Anatomies

Average Anatomical Space Scanned Anatomy

Example Symmetric Warping between Developing Anatomies

Average Anatomical Space Scanned Anatomy

Linear and Non-linear Averages of 23 Subjects

Summary

- Many Different factors in atlas based analysis
- Critical issues is registration algorithm
  - how accurately can you relate individuals to atlas?
    - for atlas construction and atlas use
      - importance depends on application.
- Very active area of research