Advanced Medical Image Registration Techniques

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Outline

• Introduction to Image Registration
• Symmetric Image Registration
• Jacobian of a Transformation
• Large Deformation Diffeomorphic Image Registration
• Currents
• Applications

Registration Framework

Target Image

Source Image

Similarity Metric

Optimizer

Interpolator

Transform

Transformation direction

I₁ Source

I₂ Target
A transformation establishes a unique correspondence between each \((y_1, y_2)\) coordinate in the original image with a point \((x_1, x_2)\) in the deformed/transformed image.

There are two types of transformations that produce the same deformed image:
- A push-forward transformation pushes an intensity from \((y_1, y_2)\) to \((x_1, x_2)\).
- A pullback transformation pulls an intensity from \((y_1, y_2)\) to \((x_1, x_2)\).

Push-forward and pullback transformations are inverses of each other.

It is convenient to use a push-forward transformation when describing how an image transforms from its original to its deformed shape.

However, a pullback transformation is used to compute the deformed image.
**Push-forward Transformation**

A push-forward transformation is a vector valued function \( \varphi \) that maps a point \((y_1, y_2)\) in the original image to a point \((x_1, x_2)\) in the deformed image.

\[
\begin{align*}
x_1 &= \varphi(y_1, y_2) \\
x_2 &= \varphi(y_1, y_2)
\end{align*}
\]

- Original/Moving
- Transform Direction
- Deformed/Target

Directly using the push-forward transform may not work as you would expect...

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**Pullback Transformation**

- A pullback transformation is a vector valued function \( \varphi^{-1} \) that maps a point \( x \) to \( y \).
- It is used to pull back the intensity value at \( y \) to \( x \) to create the deformed image.

\[
\begin{align*}
x &= \varphi^{-1}(y) \\
y &= \varphi^{-1}(x)
\end{align*}
\]

- Original/Moving \( I(y) \)
- Transform Direction
- Deformed/Target \( I(x) = I(h(x)) \)

Suppose we want to actually apply a transform to an image. How should we do it?
Suppose we want to actually apply a transform to an image. How should we do it?

Now let’s see what happens using the pullback transformation.
Symmetric Image Registration

- Many image registration algorithms are not symmetric. That is, registering $T$ to $S$ (called the forward direction) gives a different correspondence than registering $S$ to $T$ (called the reverse direction).
- The inverse consistency error measures the error in the correspondence between the forward transformation $\varphi$ and the reverse transformation $\psi$.

The determinant of the push-forward transformation Jacobian describes the pointwise expansion or contraction produced by the transformation at y.

\[
J(y) = \left| \frac{\partial \psi(x)}{\partial y} \right| = \begin{bmatrix}
\frac{\partial \psi_{1}}{\partial y_1} & \cdots & \frac{\partial \psi_{m}}{\partial y_1} \\
\vdots & \ddots & \vdots \\
\frac{\partial \psi_{1}}{\partial y_m} & \cdots & \frac{\partial \psi_{m}}{\partial y_m}
\end{bmatrix} = \text{Push-forward Jacobian}
\]

Example interpretations of the push-forward Jacobian determinant:

- \( \det(J) = 0 \) \( \Rightarrow \) transformation is singular (no inverse)
- \( 0 < \det(J) < 1 \) \( \Rightarrow \) area becomes smaller
- \( \det(J) = 1 \) \( \Rightarrow \) area is preserved
- \( \det(J) > 1 \) \( \Rightarrow \) area becomes larger

NOTE: The Jacobian determinant is occasionally referred to as "the Jacobian."

The determinant of the pullback transformation Jacobian describes the pointwise expansion or contraction produced by the transformation at x.

\[
J(x) = \left| \frac{\partial \psi^{-1}(x)}{\partial y} \right| = \begin{bmatrix}
\frac{\partial \psi_{1}}{\partial y_1} & \cdots & \frac{\partial \psi_{m}}{\partial y_1} \\
\vdots & \ddots & \vdots \\
\frac{\partial \psi_{1}}{\partial y_m} & \cdots & \frac{\partial \psi_{m}}{\partial y_m}
\end{bmatrix} = \text{Pullback Jacobian}
\]

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NOTE: The matrix inverse of the push-forward Jacobian matrix is the Jacobian matrix of the pullback transformation if the transformation is a diffeomorphism.
Inhalation

Exhalation

Jacobian Maps

- Jac > 1: Expansion (purple)
- Jac < 1: Contraction (red)
- Jac = 1: No volume change

An obvious dorsal to ventral gradient is noticed

Vessels have small volume change.

Diffeomorphism

Definition: A diffeomorphism is a differentiable transformation from $\mathbb{R}^n$ to $\mathbb{R}^n$, a bijection (a one-to-one and onto map) and its inverse is differentiable.

Transforming an image with a diffeomorphism ensures that

- Objects do not rip apart.
- Neighborhood structure is maintained.
- Objects/structures change size but do not disappear or get turned inside out.

Example:

$\eta(x) = \left[ x_1 + \frac{1}{5} \sin(2x_1 + x_2), x_2 \right]$ for $x \in \Omega = [0,1]^2$ is not a diffeomorphism.

Parameterizing Diffeomorphisms

In the large-deformation setting:

- A diffeomorphic transformation is most often parameterized by a velocity field.
Parameterizing Diffeomorphisms

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- A diffeomorphic transformation is most often parameterized by a velocity field.
- A flow \( \phi_t \) is computed from a given time-dependent velocity vector field \( v_t \) using the evolution equation:
  \[
  \frac{d}{dt} \phi_t(x) = v_t(\phi_t(x)) \quad 0 \leq t \leq 1
  \]
- The solution to this equation is a flow \( \phi_t \), with initial point \( \phi_0 = \text{identity map} \) and ending point \( \phi_1 \) = desired transformation \( \psi \).


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- The solution to this equation is a flow \( \phi_t \), with initial point \( \phi_0 = \text{identity map} \) and ending point \( \phi_1 \) = desired transformation \( \psi \).
- Thus, the goal is to find the velocity field \( \psi \) that generates the diffeomorphism \( \psi \) that registers the moving image to the target image.


Simple Flow Example

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LDDMM = Large Deformation Diffeomorphic Metric Mapping

The goal is to find $\psi$ that minimizes

$$C(\psi) = \int_0^1 (I_0 \circ \psi^{-1} - I_1)^2 dx + \alpha \int \|\nabla \psi\|^2 dx$$

Such that

$$\frac{d}{dt} \psi_t(x) = \xi_t(\psi_t(x))$$

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**Registration Framework**

**Target Image** ----> **Similarity Metric** ----> **Optimizer** ----> **Transform** ----> **Source Image**

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**Similarity Metrics**

- Intensity-based similarity metrics
  - SSD  --- Sum of Squared intensity Difference
  - MI  --- Mutual Information
  - SSTVD  --- Sum of Squared Tissue Volume Difference/
    Mass preserving image registration
  - SSTVD  --- Sum of Squared Vesselness Measure Difference
- Curve and Surface-based similarity metric:
  - Currents
- 4D similarity metric
  - Group SSD

Consider CT intensity change due to different air content during respiration!

In 2005, J. Glaunès and M. Vaillant introduced the concept of currents in the field of Computational Anatomy.

The currents similarity measure does not assume point correspondence between meshes or polygonal curves.

They proposed to use the framework of reproducing kernel Hilbert spaces (RKHS) to give a tractable formula of this metric as well as its derivatives.


Points and line segments

Points, line segments and tangents

How do we define correspondence between two lines?

Pointwise?

What if there are a different number of points?

One solution is to use currents to represent a curve.

Currents do not assume correspondence between curves

But, what is a current?
Vessel Tree Currents

The current of a curve $L$ is defined as the path integral of a vector field $\omega$ along the curve $L$ and is given by

$$L(\omega) = \int_L \omega(x) \cdot v(x) \, ds(x)$$

where $v$ is the tangent to $L$ at $x$ and $ds$ the Lebesgue measure on $L$.

- Think of the object $L$ as the current.
- $L$ is acting on $\omega$ to produce a real number.

- Abuse of notation:
  - $L$ represents the curve.

Lung Surface Currents

The current of a surface $S$ is defined by the flux of a vector field $\omega$ through $S$ and is given by

$$S(\omega) = \int_S \omega(x) \cdot n(x) \, dA(x)$$

where $n$ is the normal to $S$ at $x$ and $dA$ the Lebesgue measure on $S$.

- From Gorbunova et al., Curve- and Surface-Based Registration of Lung CT Images Via Currents. 2nd International Workshop on Pulmonary Image Analysis, 2009
Reproducing Kernel Hilbert Space

- Let $W$ denote the space of test functions which is the set of square integrable functions convolved with a smoothing kernel.
- Formally, $W$ is defined as a Reproducing Kernel Hilbert Space (RKHS).
- Assume a Gaussian kernel: $K_W(x, y) = \exp(-\|x - y\|^2/\lambda_W^2)/d_4$.

The RKHS of vector fields $W$ have two important properties:

- $W$ is the closed span of the vector fields of the form $u(x) = K_W(x, y)\beta$ for any fixed points $y$ and vector $\beta$. The pair $(y, \beta)$ is called momentum.

Example with momentum $= (y, \beta) = (1, 0, 3, 1, 3)$, kernel: $\lambda_W = 2.2$.

- $u(x) = \frac{\beta_1}{\lambda_W} \exp\left(-\frac{\|x - y\|^2 + \|x - y\|^2}{\lambda_W^2}\right)$.

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Example 2:
- momentum $= (y, \beta) = (1, 10, 10, 0, 0)$, kernel: $\lambda_W = 3.0$.

- $u(x) = \sum_{i=1}^{\beta} \beta_i \exp\left(-\frac{\|x - y\|^2}{\lambda_W^2}\right)$.
Reproducing Kernel Hilbert Space

Red = Y-shaped object
Blue = vector field representation of Y-shaped object via a linear combination of Gaussian kernel basis functions.
Circle = location of a momentum
standard deviation of Gaussian kernel = 1.2

Let $W$ denote the space of test functions which is the set of square integrable functions convolved with a smoothing kernel.

Formally, $W$ is defined as a Reproducing Kernel Hilbert Space (RKHS).

Assume a Gaussian kernel: $K^W(x, y) = \exp(-|x - y|^2/\lambda^2)$.

The RKHS of vector fields $W$ have two important properties:

- $W$ is the closed span of the vector fields of the form $u(x) = K^W(x, y)\beta$ for any fixed points $y$ and vector $\beta$. The pair $(y, \beta)$ is called momentum.

- $W$ is provided with an inner product defined by

\[
\langle u, v \rangle_W = \int \frac{1}{\lambda^2} \exp(\frac{-(x-y)^2}{\lambda^2}) du \int \frac{1}{\lambda^2} \exp(\frac{-(x-y)^2}{\lambda^2}) dv
\]

Example:

\[
\langle u, v \rangle_W = \int \frac{1}{\lambda^2} \exp(\frac{-(x-y)^2}{\lambda^2}) du \int \frac{1}{\lambda^2} \exp(8) dv
\]

which is called the "reproducing property".
Reproducing Kernel Hilbert Space

\[ W = \text{RKHS} \]

Basis \( \omega = \mathcal{K}^W(\cdot, \cdot) \)

Smooth vector fields

\[ \langle \omega, \omega' \rangle_W \]


Dual Space = Space of Currents

\[ W = \text{RKHS} \]

Basis \( \omega = \mathcal{K}^W(\cdot, \cdot) \)

Smooth vector fields

\[ \mathcal{L}_W \]

\[ W^* = \text{Dual Space of } W = \text{Space of Currents} \]


Currents Basis

\[ W = \text{RKHS} \]

Basis \( \omega = \mathcal{K}^W(\cdot, \cdot) \)

Smooth vector fields

\[ \mathcal{L}_W \]

\[ W^* = \text{Dual Space of } W = \text{Space of Currents} \]

Basis \( \mathcal{L}_W = \mathcal{L}_W(\mathcal{K}^W(\cdot, \cdot)) \)

Linear functionals
Discrete Vessel Tree Currents

The discrete approximation of the current \( L \) is given by

\[
L(\omega) = \int \omega(x)^t \nu(x) \, dA(x) = \sum_{k} U_k(\omega) = \sum_{k} \omega(x_k)^t \nu_k
\]

where \( \nu_k \) is the tangent to \( L \) at \( x_k \).

Momentsa corresponding to vessel tree centerlines

From Gorbunova et al., Curve-and Surface-based Registration of Lung CT images Via Currents. 2nd International Workshop on Pulmonary Image Analysis, 2009

Discrete Lung Surface Currents

The discrete approximation of the current \( S \) is given by

\[
S(\omega) = \int s(\omega)^t \nu(\omega) \, dA(\omega) = \sum_{k} W_k(\omega) = \sum_{k} \omega(x_k)^t \nu_k
\]

where \( \nu_k \) is the normal to \( S \) at \( x_k \).

Momentsa corresponding to the lung surface

From Gorbunova et al., Curve-and Surface-based Registration of Lung CT images Via Currents. 2nd International Workshop on Pulmonary Image Analysis, 2009

Currents Inner Product

\[
W = \text{RKHS} \quad \text{Basic } \omega = K^W(\cdot, \cdot) \quad \text{Smooth vector fields}
\]

\[
<\omega,\omega'>_W
\]

\[
W^* = \text{Dual Space of } W \quad \text{Basic } k^*_W = \mathcal{L}_W(K^W(\cdot, \cdot)) \quad \text{Linear functionals}
\]

\[
<\kappa^*_W,\kappa^*_W>_{W^*}
\]
Currents Inner Product

\[ W = \text{RKHS} \]
\[ \text{Basis } w = K^W(\cdot, y) \]
\[ \text{Smooth vector fields} \]
\[ < w, w' >_W \]
\[ L^w \]
\[ L^w_\perp \]

\[ W^* = \text{Dual Space of } W \]
\[ \text{Space of Currents} \]
\[ \text{Basis } K^W(\cdot, \cdot) \]
\[ \text{Linear functionals} \]
\[ < K^W(\cdot, \cdot), K^W(\cdot, \cdot) >_W \]
\[ = < K^W(\cdot, \cdot), K^W(\cdot, \cdot) >_W \]
\[ = a_K^W(\cdot, \cdot) \delta \]

Induced Currents Norm

\[ W = \text{RKHS} \]
\[ \text{Basis } w = K^W(\cdot, y) \]
\[ \text{Smooth vector fields} \]
\[ < w, w' >_W \]
\[ \| w \|_W = < w, w >_W \]
\[ L^w \]
\[ L^w_\perp \]

\[ W^* = \text{Dual Space of } W \]
\[ \text{Space of Currents} \]
\[ \text{Basis } K^W(\cdot, \cdot) \]
\[ \text{Linear functionals} \]
\[ < K^W(\cdot, \cdot), K^W(\cdot, \cdot) >_W \]
\[ = < K^W(\cdot, \cdot), K^W(\cdot, \cdot) >_W \]
\[ = a_K^W(\cdot, \cdot) \delta \]
\[ \| T \|_W = < T, T >_W \]

Current Similarity Cost Function

The joint cost function for registering both line and surface currents from source currents \( (L_1, S_1) \) to target currents \( (L_2, S_2) \) is defined by

\[
C(v) = \| a(L_1 - L_2) \|_{L^2_2}^2 + \| a(S_1 - S_2) \|_{L^2_2}^2 + \beta \int_0^1 \| v \|_W^2 \, dv
\]

(1)

where the transformation \( v = \psi \) satisfies

\[
\frac{d}{dt} \psi(x) = v(\psi(x))
\]

(2)
**Current Similarity Cost Function**

The joint cost function for registering both line and surface currents from source currents \( (L_1, S_1) \) to target currents \( (L_2, S_2) \) is defined by

\[
C(c) = \| \sigma_1 L_1 - L_2 \|_{W_2}^2 + \| \sigma_1 S_1 - S_2 \|_{W_2}^2 + \beta \int_0^1 \| \sigma \|_{W_1}^2 \, dt
\]

(1)

where the transformation \( \varphi = \rho_1 \) satisfies

\[
\frac{d}{dt} \rho_1(x) = v_1(x) \rho_1(x)
\]

(2)

- Curve: push-forward action is given by: \( \varphi_* L_1 = \frac{d}{dt} \rho_1(x) \)
- Surface: push-forward action is given by: \( \varphi_* S_1 = \int v_1(x) \rho_1(x) \, dt \)

**Mechanical Analysis**

**Deformation of a Continuum Body**

- \( \phi \) is the transformation from the undeformed configuration to the deformed configuration
- \( x = \phi(X) = X + u(X) \) where \( u \) is the displacement field
- \( F = \nabla \phi(X) = I + \nabla u(X) \) is the deformation gradient tensor
- \( F \) is the Jacobian of \( \phi \)

\[
F = \nabla \phi(X) = \begin{bmatrix}
\frac{\partial x_1}{\partial X_1} & \frac{\partial x_1}{\partial X_2} & \frac{\partial x_1}{\partial X_3} \\
\frac{\partial x_2}{\partial X_1} & \frac{\partial x_2}{\partial X_2} & \frac{\partial x_2}{\partial X_3} \\
\frac{\partial x_3}{\partial X_1} & \frac{\partial x_3}{\partial X_2} & \frac{\partial x_3}{\partial X_3}
\end{bmatrix}
\]
Max Principal Strain & Direction

- Linear Strain Tensor

\[ \epsilon = \begin{bmatrix} \epsilon_{xx} & \epsilon_{xy} & \epsilon_{xz} \\ \epsilon_{yx} & \epsilon_{yy} & \epsilon_{yz} \\ \epsilon_{zx} & \epsilon_{zy} & \epsilon_{zz} \end{bmatrix} = \frac{1}{2} \left( \nabla \nabla^T \right) \]

- Apply SVD on strain tensors to get
  Principal Strains: \( \lambda_1, \lambda_2, \lambda_3 \)
  Principal Directions: \( d_1, d_2, d_3 \)

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Anisotropic Deformation Index (ADI)

\[ ADI = \frac{1 + \text{Max Principal Strain}}{1 + \text{Min Principal Strain}} \]

Tissues around fissures have more anisotropic deformation.

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Summary of mechanical parameters

- Jacobian — Specific volume change
- Strain Tensors — Geometric information (Def. magnitude, direction and pattern)
- Max prin. strain
- prin. direction
- ADI
RT Applications

- Biomechanical analysis of lung motion using mechanical measures (PI Reinhardt, HL079406, Iowa)
- Tracking cumulative dose in pulmonary RT in presence of tumor regression and atelectasis (PI Hugo, CA166119, VCU and Iowa)
- 4DCT reconstruction using 4D B-spline registration (PI Hugo, CA166119, VCU and Iowa)
- Modeling and predicting dose response in pulmonary RT using pretreatment Jacobian determinant (PI Bayouth, CA166703, Wisconsin and Iowa)
- Starting Aug 2016 at Wisconsin, treating patients with Pulmonary RT plans that spare healthy lung tissue based on pretreatment Jacobian determinant (PI Bayouth, CA166703, Wisconsin and Iowa)

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