AGND Traitement d’images médicales:
du voxel aux atlas numériques
Strasbourg, 2 au 6 juin 2008

Xavier Pennec

Computational Anatomy & Atlases
Anatomy

Science that studies the structure and the relationship in space of different organs and tissues in living systems [Hachette Dictionary]

Antiquity
- Animal models
- Philosophical physiology

Renaissance:
- Dissection, surgery
- Descriptive anatomy

17-20e century:
- Anatomo-physiology
- Microscopy, histology

1990-2000:
- Explosion of imaging
- Computer atlases
- Brain decade

- From dissection to in-vivo in-situ imaging
- From representative individual to population
- From descriptive atlases to interactive and generative models (simulation)
The revolution of medical imaging

In vivo observation of living systems
- A large number of modalities to image anatomy and function
  - Growing spatial resolution (molecules to whole body)
  - Multiple temporal scales

Non invasive observations
- Emergence of large databases
- From representative individual to population

Extract and structure information
- 50 to 150 MB for a clinical MRI
- Computer analysis is necessary
- From descriptive atlases to interactive and generative models (simulation)
  - Bone Morphing® (Fleute et al, 2001)
Algorithms to Model and Analyze the Anatomy

- Estimate representative organ anatomies across species, populations, diseases, aging, ages…
- Model organ development across time
- Establish normal variability

To understand and to model how life is functioning

- Classify pathologies from structural deviations (taxonomy)
- Integrate individual measures at the population level to relate anatomy and function

To detect, understand and correct dysfunctions

- From generic (atlas-based) to patients-specific models
- Quantitative and objective measures for diagnosis
- Help therapy planning (before), control (during) and follow-up (after)
Modeling and image analysis: a virtuous loop

Integrative models for biology and neurosciences

Population

Computational models of the human body

Anatomy

Physics

Physiology

Individual

Normalization, Interpretation, Modeling

Images, Signals, Clinics, Genetics, etc.

Identification

Personalization

Prevention

Diagnosis

Therapy

Statistical analysis

Knowledge inference

Generative models

Computer assisted medicine
Methods of computational anatomy

Hierarchy of anatomical manifolds (structural models)
- Landmarks [0D]: AC, PC [Talairach et Tournoux, Bookstein], functional landmarks
- Curves [1D]: crest lines, sulcal lines [Mangin, Barillot, Fillard…]
- Surfaces [2D]: cortex, sulcal ribbons [Thompson, Mangin, Miller…],
- Images [3D functions]: VBM, Diffusion imaging
- Transformations: rigid, multi-affine, local deformations (TBM), diffeomorphisms [Asburner, Arsigny, Miller, Trouve, Younes…]

Structural variability of the cortex

Groupwise correspondances in the population

Model observations and its structural variability

→ Statistical computing on Riemannian manifolds
Outline

Goals and methods of Computational anatomy

Statistical computing on manifolds
- The geometrical and statistical framework
  - Examples with rigid body transformations
- Extending the framework to manifold-valued images
  - Building a statistical atlas of the hear fibers

Computational neuro-anatomy
- Morphometry of sulcal lines on the brain
- Statistics of deformations for non-linear registration

Conclusion and challenges
**Statistical analyses on manifolds**

**Medical image analysis: Noisy geometric measures**

- Feature extracted from images
  - Lines, oriented points
  - Extremal points: semi oriented frames
  - Tensors from DTI

- Transformations in registrations
  - Rigid, Affine, locally affine, families of deformations

**Goal:**

- Deal with noise consistently on these non-Euclidean manifolds
- A consistent computing framework
Probabilités et statistiques simples

Objets géométriques :

- Primitives, Transformations : Variétés différentielles

Mesure :

* vecteur aléatoire $x$ de densité $p_x(z)$

Approximation :

* $x \sim (\bar{x}, \Sigma_{xx})$

Propagation :

* $y = h(x) \sim \left( h(\bar{x}), \frac{\partial h}{\partial x} \cdot \Sigma_{xx} \cdot \frac{\partial h^T}{\partial x} \right)$

Modèle de bruit : additif, gaussien...

Distance statistique : Mahalanobis et $\chi^2$
Quelques problèmes avec la géométrie

Moyenne de rotations 3D : Définition intrinsèque (indép. de la carte)

\[
\mathbf{R} = \frac{1}{n} \sum_i \mathbf{R}_i \\
\mathbf{q} = \frac{1}{n} \sum_i \mathbf{q}_i \\
\mathbf{r} = \frac{1}{n} \sum_i \mathbf{r}_i
\]

Bruit IID sur les rotations : invariance par un groupe de transfo.

\[
\Sigma_1 = \Sigma \\
\Sigma_2 = \Sigma
\]

\[
\Sigma = \sigma^2 \begin{bmatrix} 0 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}
\]

\[
\Sigma_1' = \frac{8}{\pi^2} \Sigma \\
\Sigma_2' = \frac{\pi^2}{8} \Sigma
\]
Riemannian Manifolds: geometrical tools

Riemannian metric:
- Dot product on tangent space
- Speed, length of a curve
- Distance and geodesics
  - Closed form for simple metrics/manifolds
  - Optimization for more complex

Exponential chart (Normal coord. syst.):
- Development in tangent space along geodesics
- Geodesics = straight lines
- Distance = Euclidean
- Star shape domain limited by the cut-locus
- Covers all the manifold if geodesically complete
### Computing on Riemannian manifolds

<table>
<thead>
<tr>
<th>Operation</th>
<th>Euclidean space</th>
<th>Riemannian manifold</th>
</tr>
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<tbody>
<tr>
<td>Subtraction</td>
<td>( xy = y - x )</td>
<td>( xy = \log_x (y) )</td>
</tr>
<tr>
<td>Addition</td>
<td>( y = x + xy )</td>
<td>( y = \exp_x (xy) )</td>
</tr>
<tr>
<td>Distance</td>
<td>( \text{dist} (x, y) = |y - x| )</td>
<td>( \text{dist}(x, y) = \left| xy \right|_x )</td>
</tr>
<tr>
<td>Gradient descent</td>
<td>( \Sigma_{t+\epsilon} = \Sigma_t - \epsilon \nabla C(\Sigma_t) )</td>
<td>( \Sigma_{t+\epsilon} = \exp_{\Sigma_t} (-\epsilon \nabla C(\Sigma_t)) )</td>
</tr>
</tbody>
</table>
**Statistical tools on Riemannian manifolds**

**Metric -> Volume form (measure)**

\[ dM(x) \]

**Probability density functions**

\[ \forall X, P(x \in X) = \int_X p_x(y).dM(y) \]

**Expectation of a function \( \phi \) from \( M \) into \( R \):**

- **Definition:**
  \[ E[\phi(x)] = \int_M \phi(y).p_x(y).dM(y) \]

- **Variance:**
  \[ \sigma_x^2(y) = E[\text{dist}(y, x)^2] = \int_M \text{dist}(y, z)^2.p_x(z).dM(z) \]

- **Information (neg. entropy):**
  \[ I[x] = E[\log(p_x(x))] \]
Statistical tools: Moments

Frechet / Karcher mean minimize the variance

\[ \mathbb{E}[x] = \operatorname{argmin}_{y \in M} \left( \mathbb{E}[\operatorname{dist}(y, x)^2] \right) \quad \Rightarrow \quad \mathbb{E}[\overline{xx}] = \int_{M} \overline{xx}.p_x(z).dM(z) = 0 \quad [P(C) = 0] \]

Geodesic marching

\[ \overline{x}_{t+1} = \exp_{\overline{x}_t}(v) \quad \text{with} \quad v = \mathbb{E}[\overline{yx}] \]

Covariance et higher moments

\[ \Sigma_{xx} = \mathbb{E} \left[ \left( \overline{xx} \right) \left( \overline{xx} \right)^T \right] = \int_{M} \left( \overline{xz} \right) \left( \overline{xz} \right)^T . p_x(z).dM(z) \]

[ Pennec, JMIV06, RR-5093, NSIP'99 ]
Example with 3D rotations

Exp chart at Id: rotation vector: \( r = \theta . n \)

Distance: \( \text{dist}(R_1, R_2) = \left\| r_1^{(-1)} \right\| o r_2 \)

Frechet mean:
\[
\bar{R} = \arg \min_{R \in SO_3} \left( \sum_i \text{dist}(R, R_i) \right)
\]

Centered chart:
mean = barycenter
Distributions for parametric tests

Uniform density:
- maximal entropy knowing $X$
  \[ p_x(z) = \text{Ind}_X(z) / \text{Vol}(X) \]

Generalization of the Gaussian density:
- Stochastic heat kernel $p(x,y,t)$ / Wrapped Gaussian
- Maximal entropy knowing the mean and the covariance
  - From Dirac to uniform (on compact manifolds)
  \[
  N(y) = k \cdot \exp\left(\left(\frac{x}{\mu}\right)^T \Gamma \left(\frac{x}{\mu}\right) / 2\right) \quad \text{with} \quad \Gamma = \Sigma^{(-1)} - \frac{1}{3} \text{Ric} + O(\sigma) + \varepsilon(\sigma / r)
  \]

Mahalanobis D2 distance / test:
- \[
  \mu^2_x(y) = \langle\overrightarrow{x}y\rangle \cdot \Sigma_{xx}^{(-1)} \cdot \overrightarrow{x}y
  \]
- Any distribution:
  \[
  E[\mu^2_x(x)] = n
  \]
- Gaussian:
  \[
  \mu^2_x(x) \propto \chi_n^2 + O(\sigma^3) + \varepsilon(\sigma / r)
  \]

[ Pennec, JMIV06, NSIP’99 ]
Validation of the rigid registration accuracy

Comparing two transformations and their Covariance matrix:

\[ \mu^2(T_1, T_2) \approx \chi^2_6 \]

Mean: 6, Var: 12
KS test

Intra-echo: \( \mu^2 \approx 6 \), KS test OK
Inter-echo: \( \mu^2 > 50 \), KS test failed, Bias!

**Bias estimation**: (chemical shift, susceptibility effects)
- \( \sigma_{rot} = 0.06 \) deg (not significantly different from the identity)
- \( \sigma_{trans} = 0.2 \) mm (significantly different from the identity)

Inter-echo with bias corrected: \( \mu^2 \approx 6 \), KS test OK

[ X. Pennec et al., Int. J. Comp. Vis. 25(3) 1997, MICCAI 1998 ]
Validation using Bronze Standard

Best explanation of the observations (ML):
- LSQ criterion
- Robust Fréchet mean
- Robust initialization and Newton gradient descent

Result
\[ T_{i,j}, \sigma_{\text{rot}}, \sigma_{\text{trans}} \]


Derive tests on transformations for accuracy / consistency
Liver puncture guidance using augmented reality

3D (CT) / 2D (Video) registration
- 2D-3D EM-ICP on fiducial markers
- Certified accuracy in real time

Validation
- Bronze standard (no gold-standard)
- Phantom in the operating room (2 mm)
- 10 Patient (passive mode): < 5mm (apnea)

[S. Nicolau, PhD’04 MICCAI05, ECCV04, IS4TM03, Comp. Anim. & Virtual World 2005]
Statistical Analysis of the Scoliotic Spine

[ J. Boisvert et al. ISBI’06, AMDO’06 and IEEE TMI 27(4), 2008 ]

Database

- 307 Scoliotic patients from the Montreal’s Sainte-Justine Hospital.
- 3D Geometry from multi-planar X-rays

Mean

- Main translation variability is axial (growth?)
- Main rot. var. around anterior-posterior axis
Statistical Analysis of the Scoliotic Spine

[ J. Boisvert et al. ISBI’06, AMDO’06 and IEEE TMI 27(4), 2008 ]

PCA of the Covariance:
4 first variation modes have clinical meaning

- Mode 1: King’s class I or III
- Mode 2: King’s class I, II, III
- Mode 3: King’s class IV + V
- Mode 4: King’s class V (+II)
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Conclusion and challenges
Diffusion Tensor Imaging

Covariance of the Brownian motion of water
-> Architecture of axonal fibers

**Very noisy data**

- Tensor image processing
  - Robust estimation
  - Filtering, regularization
  - Interpolation / extrapolation

- Information extraction (fibers)

**Symmetric positive definite matrices**

- Convex operations are stable
  - mean, interpolation
- More complex operations are not
  - PDEs, gradient descent…

**Intrinsic computing on Manifold-valued images?**
A Riemannian Framework on tensors

**Affine-invariant Metric** (Curved space – Hadamard)

- Action of the linear group $\text{GL}_n$  
  \[ A * \Sigma = A \Sigma A^T \]

- Dot product  
  \[ \langle V | W \rangle_{\Sigma} = \langle AVA^T | AW A^T \rangle_{A^T \Sigma A} = \langle \Sigma^{-1/2} V \Sigma^{-1/2} | \Sigma^{-1/2} W \Sigma^{-1/2} \rangle_{Id} \]

- Geodesics:  
  \[ \Gamma_{Id,W}(t) = \exp(tW) \]

- Exponential map:  
  \[ \exp_{\Sigma}(\Sigma \Psi) = \Sigma^{1/2} \exp(\Sigma^{-1/2} \Sigma \Psi \Sigma^{-1/2}) \Sigma^{1/2} \]

- Log map:  
  \[ \overrightarrow{\Sigma \Psi} = \log_{\Sigma}(\Psi) = \Sigma^{1/2} \log(\Sigma^{-1/2} \Psi \Sigma^{-1/2}) \Sigma^{1/2} \]

- Distance  
  \[ \text{dist}(\Sigma, \Psi)^2 = \langle \overrightarrow{\Sigma \Psi} | \overrightarrow{\Sigma \Psi} \rangle_{\Sigma} = \left\| \log(\Sigma^{-1/2} \Psi \Sigma^{-1/2}) \right\|_{L_2}^2 \]

[ Pennec, Fillard, Ayache, IJCV 66(1), 2006, Lenglet JMIV’06, etc]
Metrics for Tensor computing

Affine-invariant Metric (Curved space – Hadamard)

- Dot product
  \[ \langle V | W \rangle_{\Sigma} = \langle AVA^T | AW A^T \rangle_{A\Sigma A^T} = \langle \Sigma^{-1/2} V \Sigma^{-1/2} | \Sigma^{-1/2} W \Sigma^{-1/2} \rangle_{Id} \]

- Geodesics
  \[ \exp_{\Sigma} (\Sigma \Psi) = \Sigma^{1/2} \exp(\Sigma^{-1/2} \Sigma \Psi \Sigma^{-1/2}) \Sigma^{1/2} \]

- Distance
  \[ \text{dist}(\Sigma, \Psi)^2 = \langle \Sigma \Psi | \Sigma \Psi \rangle_{\Sigma} = \| \log(\Sigma^{-1/2} \cdot \Psi \cdot \Sigma^{-1/2}) \|_{L_2}^2 \]


Log-Euclidean similarity invariant metric (vector space)

- Transport Euclidean structure through matrix exponential

- Dot product
  \[ \langle V | W \rangle_{\Sigma} = \langle \partial V \log(\Sigma) | \partial W \log(\Sigma) \rangle_{Id} \]

- Geodesics
  \[ \exp_{\Sigma} (\Sigma \Psi) = \exp(\log(\Sigma) + \partial_{\Sigma \Psi} \log(\Sigma)) \]

- Distance
  \[ \text{dist}(\Sigma_1, \Sigma_2)^2 = \| \log(\Sigma_1) - \log(\Sigma_2) \|_{L_2}^2 \]

[ Arsigny, Pennec, Fillard, Ayache: Fast and Simple Calculus on Tensors in the Log-Euclidean Framework, MICCAI’05, SIMAX 29(1) 2007, MRM 52(6) 2006 ]
Geodesic shooting in tensors spaces

- Geodesics starting from the same tensor with the same tangent vector

- Undefined (non positive)

- Euclidean metric

- Choleski metric

- Affine-invariant / Log-Euclidean metrics
Tensor interpolation

**Geodesic walking in 1D**

\[ \Sigma(t) = \exp_{\Sigma_1} (t \Sigma_1 \Sigma_2) \]

**Weighted mean in general**

\[ \Sigma(x) = \min_{\Sigma} \sum w_i(x) \cdot \text{dist}(\Sigma, \Sigma_i)^2 \]
Gaussian filtering: Gaussian weighted mean

\[ \Sigma(x) = \min \sum_{i=1}^{n} G_{\sigma}(x - x_i) \cdot \text{dist} (\Sigma, \Sigma_i)^2 \]
Intrinsic Riemannian Computing

Integral or sum in $M \rightarrow$ minimize an intrinsic functional

- Interpolation
  - Linear between 2 elements: interpolation geodesic $x(t) = \exp_{x_i}(t \overrightarrow{x_1x_2})$
  - Bi- or tri-linear in images: weighted means

- Gaussian filtering
  - Gaussian weighted Mean weighted

Regularization: the exponential map (partially) accounts for curvature

- Harmonic
  \[ \text{Reg}(\Sigma) = \int \|\nabla \Sigma(x)\|_{L^2(x)}^2\, dx \]
  - Gradient: Laplace-Beltrami operator $\Delta \Sigma(x) = \frac{1}{\varepsilon} \sum_{u \in S} \Sigma(x) \Sigma(x + \varepsilon u) + O(\varepsilon^2)$

- Anisotropic
  - Perona-Malik 90 / Gerig 92
    \[ \Delta_w \Sigma(x) = \sum_w w\left(\|\nabla_x \Sigma(x)\|_{L^2(x)}\right) \Delta_x \Sigma(x) \]
  - Robust functions
    \[ \text{Reg}(\Sigma) = \int \Phi\left(\|\nabla \Sigma(x)\|_{L^2(x)}^2\right) dx \]

- Trivial intrinsic numerical schemes thanks to the exponential maps!

Filtering and anisotropic regularization of DTI

Raw

Coefficients $\sigma=2$

Riemann Gaussian $\sigma=2$

Riemann anisotropic
**DTI-based Anatomical models**

**Diffusion tensor IRM**
- Covariance of the water Brownian motion
  - Estimation, filtering, interpolation
  - Fiber extraction: architecture of axons tracts

**Atlas of the heart fibers**
- 7 DTI of dogs hearts
- Fibers and sheets structure

---

[ Pennec et al, IJCV 66(1) 2006, Fillard et al, ISBI’06 and IEEE TMI, 26(11), 2007 ]

Cardiac Fiber Architecture

Myocardial fibers

Laminar sheets

This geometric structure of the myocardium

- Controls propagation of electrical potential
- Controls Mechanical contraction
- Is needed for patient-specific applications
  - Electromechanical simulations (for therapy planning)
  - Image analysis (motion tracking, strain analysis, …)
Cardiac Fiber Architecture

Myocardial fibers

Laminar sheets

Correlation with DTI eigenvectors

[Scollan, 1998] [Helm, 2005]

- primary as fiber orientation
- secondary as orthogonal to fibers in the sheet plane
- tertiary as normal to sheet plane

DTI = Direct 3D description:
- Build a statistical atlas of fibers from DTI?
A Computational Framework for the Statistical Analysis of Cardiac Diffusion tensors

Jean Marc Peyrat (Asclepios, INRIA and Siemens SCR, Princeton)

- Use of the whole diffusion tensor?
- Use a population for atlas building?
Groupwise Registration

Register the DTI images to an average geometry

- Use Tensor images => bias in the statistical analysis
- Use anatomical MRIs = baseline (B0) image of the DT-MRI acquisition (coacquired in the same reference frame)

Shape and intensity average model [Guimond, 1999]

- Iterative process
  - Mean deformation (atlas geometry)
  - Mean intensity (atlas image)
Tensor reorientation (transforming DT-MRIs)

- **Eigenvalues are preserved**
  - Intrinsic properties of the tissues

- **Eigenvectors are modified**
  - Linked to the reference frame that is locally transformed

- **Transformation of diffusion tensors**
  = rotation of the original diffusion tensor

  \[ A \ast D = R \cdot D \cdot R^t \]

- **Two common reorientation strategies [Alexander,2001]**
  - Finite Strain (FS) => preferred here
  - Preservation of Principal Direction (PPD)
Statistics on Diffusion Tensors

Diffusion tensor space is not a vector space

- Use the Log-Euclidean metric [Arsigny, 2005]

Mean and covariance at each voxel [Pennec, IJCV 2006]

\[
\overline{D}_{\log}(X) = \exp\left(\frac{1}{N} \sum_{i=1}^{N} \log(D_i(X))\right)
\]

\[
\Sigma(X) = \frac{1}{N-1} \sum_{i=1}^{N} \text{vec}(\Delta D_i(X)) \cdot \text{vec}(\Delta D_i(X))^t
\]

where \( \Delta D_i = \log(D_i) - \log(\overline{D}_{\log}) \)

\[
\text{vec}(D) = (D_{11}, \sqrt{2}D_{12}, D_{22}, \sqrt{2}D_{31}, \sqrt{2}D_{32}, D_{33})^t
\]

- Mean tensor gives mean fiber and laminar sheet orientation

- 21x21 covariance matrix measures variability of the mean tensor components: Interpretation in terms of cardiac fiber architecture?
Mean Geometry and Fiber Orientation

- 9 normal ex vivo canine hearts [Helm, 2005]

- High resolution DT-MRI
  \~256 \times 256 \times 128 with
  \~0.3 \times 0.3 \times 0.9 \text{ mm}^3 \text{ per voxel}

Variability of Diffusion Tensors

Norm of the Covariance Matrix

\[ \sqrt{\text{Tr}(\Sigma)} \]

\[ \sim 10\% \]

Covariance Matrix Analysis

Projection of the Covariance Matrix

- Eigenvalues Variability
  \[ E(\delta\lambda_1^2) = \text{vec}(\mathbf{W}_1)^\text{T} \cdot \Sigma \cdot \text{vec}(\mathbf{W}_1) \]
  \[ E(\delta\lambda_2^2) = \text{vec}(\mathbf{W}_2)^\text{T} \cdot \Sigma \cdot \text{vec}(\mathbf{W}_2) \]
  \[ E(\delta\lambda_3^2) = \text{vec}(\mathbf{W}_3)^\text{T} \cdot \Sigma \cdot \text{vec}(\mathbf{W}_3) \]

- Eigenvectors Variability
  \[ E(\varepsilon_{23}^2) = \frac{1}{2(\lambda_2 - \lambda_3)^2} [\text{vec}(\mathbf{W}_4)^\text{T} \cdot \Sigma \cdot \text{vec}(\mathbf{W}_4)] \]
  \[ E(\varepsilon_{13}^2) = \frac{1}{2(\lambda_1 - \lambda_3)^2} [\text{vec}(\mathbf{W}_5)^\text{T} \cdot \Sigma \cdot \text{vec}(\mathbf{W}_5)] \]
  \[ E(\varepsilon_{12}^2) = \frac{1}{2(\lambda_1 - \lambda_2)^2} [\text{vec}(\mathbf{W}_6)^\text{T} \cdot \Sigma \cdot \text{vec}(\mathbf{W}_6)] \]

where the \( \{\mathbf{W}_i\}_{i=1,2,3} \) form an orthonormal frame of the tangent space at the mean diffusion tensor:

\[ \mathbf{W}_1 = \mathbf{v}_1 \cdot \mathbf{v}_1^\text{T} \quad \mathbf{W}_4 = \frac{1}{\sqrt{2}}(\mathbf{v}_3 \cdot \mathbf{v}_3^\text{T} + \mathbf{v}_2 \cdot \mathbf{v}_2^\text{T}) \]
\[ \mathbf{W}_2 = \mathbf{v}_2 \cdot \mathbf{v}_2^\text{T} \quad \mathbf{W}_5 = \frac{1}{\sqrt{2}}(\mathbf{v}_1 \cdot \mathbf{v}_1^\text{T} + \mathbf{v}_3 \cdot \mathbf{v}_3^\text{T}) \]
\[ \mathbf{W}_3 = \mathbf{v}_3 \cdot \mathbf{v}_3^\text{T} \quad \mathbf{W}_6 = \frac{1}{\sqrt{2}}(\mathbf{v}_2 \cdot \mathbf{v}_2^\text{T} + \mathbf{v}_1 \cdot \mathbf{v}_1^\text{T}) \]

Statistics on Eigenvalues

1\textsuperscript{st} Eigenvalue

2\textsuperscript{nd} Eigenvalue

3\textsuperscript{rd} Eigenvalue

Statistics on Eigenvectors

1\textsuperscript{st} & 2\textsuperscript{nd} Eigenvectors (around 3\textsuperscript{rd})
(mode of std dev: 7.9 degrees)

1\textsuperscript{st} & 3\textsuperscript{rd} Eigenvectors (around 2\textsuperscript{nd})
(mode of std dev: 7.7 degrees)

2\textsuperscript{nd} & 3\textsuperscript{rd} Eigenvectors (around 3\textsuperscript{rd})
(mode of std dev: 22.7 degrees)
Inter-species comparison with a human heart

1\textsuperscript{st} eigenvector

Angular difference

Mahalanobis distance

2\textsuperscript{nd} eigenvector

3\textsuperscript{rd} eigenvector
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Statistical computing on manifolds
  □ The geometrical and statistical framework
  □ Examples with rigid body transformations and tensors

Computational neuro-anatomy
  □ Morphometry of sulcal lines on the brain
  □ Statistics of deformations for non-linear registration

Conclusion and challenges
Hierarchy of anatomical manifolds

- Landmarks [0D]: AC, PC (Talairach)
- **Curves** [1D]: crest lines, sulcal lines
- Surfaces [2D]: cortex, sulcal ribbons
- Images [3D functions]: VBM
- **Transformations**: rigid, multi-affine, diffeomorphisms [TBM]
Morphometry of the Cortex from Sulcal Lines

Associated team Brain-Atlas (2001-2006)
- LONI (UCLA): P. Thompson et al.
- ASCLEPIOS (INRIA): V. Arsigny, N. Ayache, P. Fillard, X. Pennec

Neuroanatomical reference:
- 72 sulcal lines manually extracted and labeled
- 700 subjects

Alternative
- Automatic extraction
  JF. Mangin, D. Rivière, 2003, SHFJ-CEA
**Morphometry of the Cortex from Sulcal Lines**

**Computation of the mean sulci: Alternate minimization of global variance**
- Dynamic programming to match the mean to instances
- Gradient descent to compute the mean curve position

**Extraction of the covariance tensors**

Currently:
- 80 instances of 72 sulci
- About 1250 tensors

Collaborative work between Asclepios (INRIA) and LONI (UCLA) P. Thompson
Compressed Tensor Representation

Representative Tensors (250)  Reconstructed Tensors (1250)  (Riemannian Interpolation)
Extrapolation by Diffusion

\[ C(\Sigma) = \frac{1}{2} \int \sum_{i=1}^{n} G_{\sigma}(x-x_i) \text{dist}(\Sigma(x), \Sigma_i)^2 \, dx + \frac{\lambda}{2} \int \| \nabla \Sigma(x) \|^2_{\Sigma(x)} \]

\[ \nabla C(\Sigma)(x) = - \sum_{i=1}^{n} G_{\sigma}(x-x_i) \Sigma(x) \Sigma_i - \lambda(\Delta \Sigma)(x) \]
Full Brain extrapolation of the variability

\[ C(\Sigma) = \frac{1}{2} \int_{\Omega} \sum_{i=1}^{n} G_\sigma(x - x_i) \text{dist}(\Sigma(x), \Sigma_i)^2 \, dx + \frac{\lambda}{2} \int_{\Omega} \|\nabla \Sigma\|_{\Sigma(x)}^2 \]
Comparison with cortical surface variability

Consistent low variability in phylogenetical older areas
  (a) superior frontal gyrus

Consistent high variability in highly specialized and lateralized areas
  (b) temporo-parietal cortex

Asymmetry
  Maximale : aire de Broca (langage), cortex pariétal; minimale : aires somatomotrices primaires
  [Fillard, Arsigny, Pennec, Thompson, Ayache, IPMI 2005, NeuroImage 34(2), 2007]
Local and distant structural correlation

Left central sulcus

Unexpected distant correlation

Local correlation

Correlation to the symmetric point

Left inferior temporal sulcus

Local correlation

Unexpected distant correlation

Correlation to the symmetric point

Enumeration: Modeling the Green’s function

[Fillard, Pennec, Thompson, Thompson, Evaluating Brain Anatomical Correlations via Canonical Correlation Analysis of Sulcal Lines, MICCAI Workshop on stat. Atlases, 2007]
Asymmetry Measures

\[ \text{dist}(\Sigma, \Sigma')^2 = \left( \Sigma \Sigma' | \Sigma \Sigma' \right)_\Sigma = \left\| \log(\Sigma^{-1/2} \cdot \Sigma' \cdot \Sigma^{-1/2}) \right\|^2_{L_2} \]

w.r.t the mid-sagittal plane.

w.r.t opposite (left-right) sulci

<table>
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<th>Lowest asymmetry</th>
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<td>Primary sensorimotor areas</td>
</tr>
</tbody>
</table>
Symmetry of the variability between groups

[Fillard, Pennec, Thompson, Thompson, Evaluating Brain Anatomical Correlations via Canonical Correlation Analysis of Sulcal Lines, MICCAI Workshop on stat. Atlases, 2007]
An alternative approach with diffeomorphisms

[ S, Durrleman, X. Pennec, A. Trouvé, N. Ayache, MICCAI 2007 ]

Does the method influence results?
- Matching, then extrapolation
  [Fillard, NeuroImage 34(2) 2007]
- Extrapolation of speed vectors and trajectory integration

Method
- Global space diffeomorphism
  (integration of time varying vector fields)
  [Trouve, Younes, Miller, etc]
- Distance between lines using currents
  [J. Glaunès, M. Vaillant: IPMI 2005]

Advantages
- Generative model of deformations
- Retrieve some tangential deformation component.
Comparison with a diffeomorphic approach

The aperture problem

- Tangential variability is minimized on purpose with Fillard's method
- The global diffeomorphism performs a spatially consistent integration

[S, Durrleman et al. MICCAI 2007]  [Fillard et al., Neuroimage 34(2), 2007]
Outline

Goals and methods of Computational anatomy

Statistical computing on manifolds
- The geometrical and statistical framework
- Examples with rigid body transformations and tensors

Computational neuro-anatomy
- Morphometry of sulcal lines on the brain
- Statistics of deformations for non-linear registration

Conclusion and challenges
Use of the variability information?

Learning / modeling phase (anatomy / neurosciences)

- Goal: analyze and understand the population variability
- Methods can be computationally intensive, experiments relies on good quality observations
- Fact: Methods have different assumptions
  - Similar results at some locations, different results at other places
  - Each method is based on partial observations
  - Each method is biased by its assumptions
- Vary assumptions / data, and discover “truth” by consensus

Personalization of atlases (use in a clinical / medical workflow)

- Anatomical prior to compensate for incomplete / noisy / abnormal (pathological) observations.
- Need robust and efficient methods
- Use variability statistics as a regularizer to robustify registration?
Atlas-based segmentation for Radiotherapy planning

Structures to segment

- Tumor (to maximize irradiation)
- Organs at risk (to minimize irradiation)
  - Registering an atlas segments all structures at once
One example use of variability information: better constrain the atlas to subject registration

- Atlas = artificial MRI (MNI simulator) + segmented structures of interest (P-Y Bondiau, MD, CAL, Nice)
- Deform the atlas anatomy (without tumor) towards the patient one
- Use result as a prior to segment the structures in the patient image

Introducing local variability and pathologies in non-linear registration

\[ E(T) = E_{\text{sim}}(I, J(T)) + \lambda E_{\text{reg}}(T) \]

- Non stationary regularization: anatomical prior on the deformability
- Non stationary image similarity / regularization tradeoff: takes pathologies into account

Regularization in dense non-linear registration

Physically based regularizations
- Elastic [Bajcsy 89]
- Fluid [Christensen TMI 97]
- Right-invariant distance [LDDMM, Beg IJCV 05]

Efficient regularization methods
- Gaussian filtering [Thirion Media 98, Modersitzki 2004]
- Isotropic but non stationary [Lester IPMI'99]
- Towards anisotropic non stationary regularization [Stefanescu MedIA 2004]

Observation:
- **Inter-subject**: no regularization model is more justified than others
- **Idea**: learning statistically the variability from a population
  [Thompson 2000, Rueckert TMI 2003, Fillard IPMI 2005]
Statistics on the deformation field

- Objective: planning of conformal brain radiotherapy (O. Commowick, Dosisoft)
- 30 patients, 2 to 5 time points (P-Y Bondiau, MD, CAL, Nice)

\[
\overline{\text{Def}}(x) = \frac{1}{N} \sum_i \text{abs}(\log(\|\nabla \Phi_i(x)\|))
\]

\[
\overline{\Sigma}(x) = \frac{1}{N} \sum_i \text{abs}(\log(\Sigma_i(x)))
\]

\[
D(x) = (\text{Id} + \lambda \overline{\Sigma}(x))^{-1}
\]

Introducing deformation statistics into RUNA

Heuristic RUNA stiffness  Scalar statistical stiffness  Tensor stat. stiffness (FA)

Riemannian elasticity: a well posed framework to introduce statistics in non-linear elastic regularization


**Gradient descent** \( C(\Phi) = \text{Sim}(\text{Images}, \Phi) + \text{Reg}(\Phi) \)

**Including statistics in Regularization**

- St Venant Kirchoff elastic energy
  - Elasticity is not symmetric
  - Statistics are not easy to include
  \[ \text{Reg}(\Phi) = \int \mu \text{Tr}(\Sigma - I)^2 + \frac{1}{2} \text{Tr}(\Sigma - I)^2 \]
  \[ \Sigma = \nabla \Phi' \cdot \nabla \Phi \]

- Idea: Replace the Euclidean by the Log-Euclidean metric
  \[ \text{Tr}(\Sigma - I)^2 \rightarrow \text{dist}_{LE}(\Sigma, I)^2 = \| \log(\Sigma) \|^2 \]

- Statistics on strain tensors:
  Mean, covariance, Mahalanobis computed in Log-space
  \[ \text{Reg}(\Phi) = \int \text{Vect} [\log(\Sigma) - \overline{W}]^T \cdot \text{Cov}^{-1} \cdot \text{Vect}[\log(\Sigma) - \overline{W}] \]

**Using Riemannian Elasticity as a metric (TBM)**

- The mean provides an unbiased atlas
- Better constraining the deformation should give better results in TBM

[N. Lepore et al, MICCAI’07, C. Brun et al, MICCAI’07 Atlas Workshop, UCLA associated team]
Isotropic Riemannian Elasticity Results

Roi 186x124x216 voxels, $\lambda=\mu=0.2$, 12 PC 2Gh.

- Larger computation times 3h vs 1h
- Slightly larger and better deformation of the right ventricle

without any statistical information yet…

Using Riemannian Elasticity as a metric (TBM)

- Register all subjects and controls to template
- Statistical analysis to find significantly different deformations (at the population level)

\[
\sqrt{\text{det}(\Sigma)} \quad \rightarrow \quad \text{dist}_{LE}(\Sigma, I)^2 = \|\log(\Sigma)\|^2
\]

[ N. Lepore et al, MICCAI’06]
Multivariate statistics give additional (more sensitive measures) for genetic studies.

Mean absolute difference in regional volume

Standard TBM:
Determinant of the Jacobian
\[ \sqrt{\text{det}(\Sigma)} \]

Tangent of the Geodesic Anisotropy
\[ GA(\Sigma) = (\text{Trace}(\log(\Sigma) - \langle \log(\Sigma) \rangle I)^2)^{1/2} \]

[ N. Lepore et al, MICCAI’07, C. Brun et al, MICCAI’07 Atlas Workshop, UCLA associated team ]
A valid measure of anatomical resemblance

Distance from each of the twins to all others

- Minimize this distance to find the unbiased atlas
- Couple statistics in registration to improve statistical power?
Statistics on which deformations feature?

Local statistics on local deformation (mechanical properties)
- Gradient of transformation, strain tensor
- [Riemannian elasticity, TBM, N. Lepore + C. Brun]

Global statistics on displacement field or B-spline parameters
- [Rueckert et al., TMI, 03], [Charpiat et al., ICCV’05],
- [P. Fillard, stats on sulcal lines]
- Simple vector statistics, but inconsistency with group properties

Space of “initial momentum” [Quantity of motion instead of speed]
- [Vaillant et al., Neurolmage, 04, Durrleman et al, MICCAI’07]
- Based on left-invariant metrics on diffeos [Trouvé, Younes et al.]
- Needs theoretically a finite number of point measures
- Computationally intensive

An alternative: log-Euclidean statistics on diffeomorphisms?
- [Arsigny, MICCAI’07]
- [Bossa, MICCAI’07, Vercauteren MICCAI’07, Ashburner Neurolmage 2007]
- Mathematical problems but efficient numerical methods!
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Computing on manifolds: a summary

The Riemannian metric easily gives
- Intrinsic measure and probability density functions
- Expectation of a function from M into R (variance, entropy)

Integral or sum in M: minimize an intrinsic functional
- Fréchet / Karcher mean: minimize the variance
- Filtering, convolution: weighted means
- Gaussian distribution: maximize the conditional entropy

The exponential chart corrects for the curvature at the reference point
- Gradient descent: geodesic walking
- Covariance and higher order moments
- Laplace Beltrami for free

Statistics on geometrical objects

A consistent framework with important applications in
- Medical Image Analysis (registration evaluation, DTI)
- Building models of living systems (spine, brain, heart...)

Is the Riemannian metric the minimal structure?
- No bi-invariant metric but bi-invariant means on Lie groups [V. Arsigny]
  Change the Riemannian metric for the symmetric Cartan connection?

Computational framework for infinite dimensional manifolds
- Curves and surfaces: statistics on currents?
- Efficient framework for some spaces of diffeomorphisms?

How to chose or estimate the metric?
- Invariance, reacheability of boundaries, learning the metric
- Families of anatomical deformation metrics (models of the Green’s function)
Challenges of Computational Anatomy

Build models from multiple sources
- Curves, surfaces [cortex, sulcal ribbons]
- Volume variability [Voxel/Tensor Based Morphometry, Riemannian elasticity]
- Diffusion tensor imaging [fibers, tracts, atlas]

Compare and combine statistics on anatomical manifolds
- Each method is biased by its assumptions (fewer data than unknowns)
- Validate methods and models by consensus

From modeling to personalized medicine
- Topological changes
- Evolution: growth, pathologies
- Couple statistical learning / modeling and use of models as prior for inter-subject registration / segmentation

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References

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Statistics on Manifolds


Tensor Computing


Applications in Computational Anatomy