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Statistical Computing on Manifolds for Computational Anatomy

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:
- Anatomophysics
- Microscopy, histology

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

Voxel-Man, U. Hamburg, 2001

- From dissection to in-vivo in-situ imaging
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® (Flaute 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
- Normalization, interpretation, modeling
- Computer assisted medicine
- Statistical analysis
- Knowledge inference
- Generative models
- Computational models of the human body
- Anatomy
  - Physics
  - Physiology
- Images, signals, clinics, genetics, etc.
- Individual
- Population
- Identification
- Personalization

Methods of computational anatomy

Structural variability of the cortex

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 [Aubamer, Arsigny, Miller, Trouve, Younes…]

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 and tensors

Morphometry of the Brain
- Statistics on curves to model the cortex variability
- Local statistics on local deformations
- Towards global statistics on (some) diffeomorphisms

Challenges of Computational Anatomy

The geometric framework: Riemannian Manifolds

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

Unfolding (log), folding (exp):

<table>
<thead>
<tr>
<th>Operator</th>
<th>Euclidean space</th>
<th>Riemannian manifold</th>
</tr>
</thead>
<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) = |xy|)</td>
</tr>
<tr>
<td>Gradient descent</td>
<td>(x_\epsilon = x - \epsilon \nabla f(x))</td>
<td>(x_\epsilon = \exp_x(-\epsilon \nabla f(x)))</td>
</tr>
</tbody>
</table>
**Statistical computing on manifolds**

First statistical tools
- Fréchet / Karcher mean: minimize variance
- Covariance Higher order moments in the exponential chart
- Intrinsic vs. extrinsic [Oller & Corcuera 95, Battacharya & Patrangenaru 2002 ]

Distributions and tests : practical approximations
- Gaussian maximizes entropy knowing mean and covariance
  \[ N(y) = k \exp \left( \frac{-1}{2} y \Gamma y \right) \]
  \[ \text{avec} \quad \Gamma = \Sigma^{-1} - \frac{1}{2} \text{Ric} + O(\sigma^2) + \epsilon(\sigma/r) \]
- Mahalanobis distance follows a chi2 law
  \[ \mu^2(x) = \Sigma x \Sigma^{-1} x - x^2 + O(\sigma^2) + \epsilon(\sigma/r) \]

Intrinsic Riemannian computing
- Interpolation (bi- tri-linear), filtering (e.g. Gaussian): weighted means
- Harmonic / anisotropic regularization: Laplace-Beltrami
  \( \Rightarrow \) Trivial numerical scheme in the exponential chart
  [ Pennec, NSIP’99, JMIV 25(1) 2006, Pennec et al, IJCV 66(1) 2006]

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**Statistical Analysis of the Scoliotic Spine**

[ J. Boisvert et al., ISBI’06, to appear in IEEE TMI, 2007]

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 rotation var. around anterior-posterior axis

PCA of the Covariance
- 4 first variation modes have clinical meaning
**Statistical Analysis of the Scoliotic Spine**

- 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)

[ J. Boisvert et al., ISBI’06, to appear in IEEE TMI, 2007]

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**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, Comp. Anim. & Virtual World 2005, MICCAI’07]

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**Metrics for Tensor computing**

- **Affine invariant metric** (curved space – Hadamard)
  - Geodesics: \( \exp_p(\Sigma \Psi) = \Sigma^{1/2} \exp(\Sigma^{1/2} \Sigma \Psi \Sigma^{-1/2}) \Sigma^{1/2} \)
  - Distance: \( \text{dist}(\Sigma, \Psi) = \left( \Sigma \Psi \Sigma^{-1} \right)^{1/2} = \| \log(\Sigma) - \log(\Psi) \| \)


- **Log-Euclidean metric** (vector space)
  - Geodesics: \( \exp_p(\Sigma \Psi) = \exp(\Sigma \Psi) \)
  - Distance: \( \text{dist}(\Sigma, \Sigma') = \| \log(\Sigma) - \log(\Sigma') \| \)

[ 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 ]

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**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

[Penec et al, IJCV 66(1) 2006, Fillard et al, ISBI’06 and IEEE TMI, in press]

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**Freeware Announcement**

**MedINRIA**

*Processing and Visualization of Medical Images:*
- Powered by ITK and VTK
- **DTI Track Module:**
  - Demonstration of Log-Euclidean* DTI Processing
  - Interactive fiber bundling
  - DT-MRI – fMRI fusion

Contact: Pierre Fillard, medinria@lists-sop.inria.fr

http://www-sop.inria.fr/asclepions/software/MedINRIA

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*X. Pennec Computational Anatomy*
Outline

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Statistical computing on manifolds
- The geometrical and statistical framework
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Morphometry of the Brain
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Challenges of Computational Anatomy

Morphometry of the Cortex from Sugal Lines

1/ Mean curve: Alternated minimization of the variance on matches / position
2/ Computation of the covariance tensor at each point of the mean
3/ Extrapolation to the whole volume: harmonic diffusion of tensors

\[ C(\Sigma) = \frac{1}{2} \int \sum_{i=0}^{N} G(x\cdot x) \text{dist}(\Sigma(x), \Sigma)^2 \, dx + \frac{1}{2} \|
\n\text{Silvian fissure}

[ Fillard et al., IPMI 2005, Neuroimage 34(2), 2007, Extension later today!]
Comparison with a diffeomorphic approach

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

Difference between

- Matching, then extrapolation [Fillard, NeuroImage 34(2) 2007]
- Extrapolation of speed vectors and trajectory integration

Method

- Global space diffeomorphism parameterized by a finite number of point
- Distance between lines using currents [J. Glaunès, M. Vaillant: IPMI 2005]

Advantages

- Generative model of deformations
- Retrieve the tangential deformation component.

Variability for what?

Several methods with different assumptions:

- Similar results at some locations, different results at other places
- Vary assumptions and discover truth by consensus

Learning / modeling phase (anatomy / neurosciences)

- Goal: analyze and understand the population variability
- Identify anatomical differences between populations
  - Can be computationally intensive,
  - Relies on good quality observations and “mild pathologies”

Use in a clinical / medical workflow: Personalization of atlases

- Anatomical prior to compensate for incomplete / noisy / abnormal (pathological) observations.
  - How to use statistics as a regularizer in registration?
  - Need robust methods, should be very fast (at least efficient)
One example use of variability information:
better constrain the atlas to subject registration

- Deform the atlas anatomy (without tumor) towards the patient one
- Segment the structures of interest in the patient image
- Minimize irradiation in areas at risk.

[Commowick, et al, MICCAI 2005]

Introducing local variability and pathologies
in non-linear registration

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

- 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:**
- No regularization model is more justified than others
- Learning statistically the variability from a population
  [Thompson 2000, Rueckert TMI 2003, Fillard IPMI 2005]

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## 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)

\[
\text{Statistics on the deformation field} \quad \sum_{i=1}^{N} \Phi(x) = \sum_{i=1}^{N} \text{abs}(\log(\nabla \Phi_i(x)))
\]

\[
\sum(x) = \frac{1}{2} \sum \text{abs}(\log(\Sigma(x)))
\]

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

- Idea: Replace the Euclidean by the Log-Euclidean metric

\[
\text{Reg}(\Phi) = \int \mu \text{Tr}((\Sigma - I)^2) + \frac{\lambda}{2} \text{Tr}(\Sigma - I)^2
\]

\[
\Sigma = \nabla \Phi^t \nabla \Phi
\]

\[
\text{dist}_{LE}(\Sigma, I)^2 = \left\| \log (\Sigma) \right\|^2
\]

- Statistics on strain tensors: Mean, covariance, Mahalanobis computed in Log-space

\[
\text{Reg}(\Phi) = \int \text{Cov}((\text{log}(\Sigma - W))^2, \text{Cov}(\text{log}(\Sigma - W))
\]

Using Riemannian Elasticity as a metric (TBM)

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

[ Natsha Lepore + Caroline Brun + Paul Thompson, Equipe Associee Brain Atlas with UCLA]
### 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. Filiard, 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., NeuroImage, 04]
- [Durrieu 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?**
- [Bossa, MICCAI’07, Vercauteren MICCAI’07, Ashburner NeuroImage 2007]
- Mathematical problems but efficient numerical methods!

### Statistics on geometrical objects

A consistent statistical computing framework on Riemannian manifolds 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?

**Infinite dimensional manifolds**
- Curves and surfaces
- Space of diffeomorphisms

**How to chose or estimate the metric?**
- Invariance, reachability of boundaries, learning the metric
- Families of anatomical deformation metrics (models of the Green’s function)
- Spatial correlation between neighbors… and distant points
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]
- Topological changes
- Evolution: growth, pathologies

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

Couple modeling and statistical learning
- Variability estimation / structure inference / model validation and refinement
- Use models as a prior for inter-subject registration / segmentation:
  Validation by better statistics on populations (e.g. functional)
- Need large database and distributed processing/algorithms

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