Xavier Pennec

Asclepios team, INRIA Sophia-Antipolis – Méditerranée, France

With contributions from Vincent Arsigny, Pierre Fillard, Marco Lorenzi, Christof Seiler, Jonathan Boisvert, Nicholas Ayache, etc

Statistical Computing on Manifolds for Computational Anatomy 1:

Simple Statistics on Riemannian Manifolds

Infinite-dimensional Riemannian Geometry with applications to image matching and shape analysis
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

Galien (131-201) Vésale (1514-1564) Sylvius (1614-1672) Gall (1758-1828) : Phrenology
Paré (1509-1590) Willis (1621-1675) Talairach (1911-2007)

Revolution of observation means (1988-2007) :
- From dissection to in-vivo in-situ imaging
- From representative individual to population
- From descriptive atlases to interactive and generative models (simulation)
Computational Anatomy

- Design Mathematical Methods and Algorithms to Model and Analyze the Anatomy

  - Statistics of organ shapes across species, populations, diseases…
  - Model organ development across time (heart-beat, growth, ageing, ages…)
  - To understand and to model how life is functioning
    - Classify structural deviations (taxonomy), Relate anatomy and function
  - To detect, understand and correct dysfunctions
    - From generic (atlas-based) to patients-specific models
  - Very active topic in medical image analysis
    - Keyword of Medic Image Computing and Computer Assisted Intervention (MICCAI)
Statistical Analysis of Geometric Features

Noisy Geometric Measures
- Tensors, covariance matrices
- Curves, tracts
- Surfaces

Transformations
- Rigid, affine, locally affine, diffeomorphisms

Goal:
- Deal with noise consistently on these non-Euclidean manifolds
- A consistent statistical (and computing) framework
Morphometry through Deformations

Measure of deformation [D’Arcy Thompson 1917, Grenander & Miller]
- Observation = “random” deformation of a reference template
- Reference template = Mean (atlas)
- Shape variability encoded by the deformations

Statistics on groups of transformations (Lie groups, diffeomorphism)?
Consistency with group operations (non commutative)?
Methods of computational anatomy

Remodeling of the right ventricle of the heart in tetralogy of Fallot

- Mean shape
- Shape variability
- Correlation with clinical variables
- Predicting remodeling effect

Shape of RV in 18 patients
**Longitudinal deformation analysis**

Dynamic observations

How to transport longitudinal deformation across subjects?
What are the convenient mathematical settings?
Statistical Computing on Manifolds for Computational Anatomy

Simple Statistics on Riemannian Manifolds

Manifold-Valued Image Processing

Metric and Affine Geometric Settings for Lie Groups

Analysis of Longitudinal Deformations
Statistical Computing on Manifolds for Computational Anatomy

Simple Statistics on Riemannian Manifolds
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Manifold-Valued Image Processing
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Basic probabilities and statistics

Measure: random vector \( \mathbf{x} \) of pdf \( p_x(z) \)

Approximation: \( \mathbf{x} \sim (\overline{x}, \Sigma_{xx}) \)

- Mean:
  \[ \overline{x} = \mathbb{E}(\mathbf{x}) = \int z.p_x(z).dz \]

- Covariance:
  \[ \Sigma_{xx} = \mathbb{E}[(\mathbf{x} - \overline{x}).(\mathbf{x} - \overline{x})^T] \]

Propagation:

\[ \mathbf{y} = h(\mathbf{x}) \sim \left( h(\overline{x}), \frac{\partial h}{\partial \mathbf{x}}.\Sigma_{xx}.\frac{\partial h^T}{\partial \mathbf{x}} \right) \]

Noise model: additive, Gaussian...

Principal component analysis

Statistical distance: Mahalanobis and \( \chi^2 \)
Differentiable manifolds

Définition:
- Locally Euclidean Topological space which can be globally curved
  - Same dimension + differential regularity

Simple Examples
- Sphere
- Saddle (hyperbolic space)
- Surface in 3D space

And less simple ones
- Projective spaces
- Rotations of $\mathbb{R}^3 : SO_3 \sim P_3$
- Rigid, affine Transformation
- Diffeomorphisms
Differentiable manifolds

Computing in a manifold

- **Extrinsic**
  - Embedding in $\mathbb{R}^n$

- **Intrinsic**
  - Coordinates: charts
  - Atlas = consistent set of charts

- **Measuring?**
  - Volumes (surfaces)
  - Lengths
  - Straight lines

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Measuring extrinsic distances

Basic tool: the scalar product

\[ \langle v, w \rangle = v^t w \]

- Norm of a vector
  \[ \|v\| = \sqrt{\langle v, v \rangle} \]

- Angle between vectors
  \[ \langle v, w \rangle = \cos(\alpha) \|v\| \|w\| \]

- Length of a curve
  \[ L(\gamma) = \int \|\dot{\gamma}(t)\|dt \]
Measuring extrinsic distances

Basic tool: the scalar product

$$<v, w> = \mathcal{G}(p)^{t}\, w$$

- Norm of a vector
  $$\|v\|_p = \sqrt{<v, v>_p}$$

- Angle between vectors
  $$<v, w>_p = \cos(\alpha) \|v\|_p \|w\|_p$$

- Length of a curve
  $$L(\gamma) = \int_{\gamma(t)} \|\dot{\gamma}(t)\|_{\gamma(t)} \, dt$$
Riemannian manifolds

Basic tool: the scalar product

\[ \langle v, w \rangle_p = v^t G(p) w \]

- Geodesic between 2 points
  - Shortest path
- Calculus of variations (E.L.):
  2\(^{nd}\) order differential equation
  \[ L(\gamma) = \int_{\gamma(t)} |\gamma'(t)| \, dt \]
  - Specifies acceleration
- Free parameters: initial speed and starting point

Bernhard Riemann
1826-1866

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Bases of Algorithms in Riemannian Manifolds

Exponential map (Normal coordinate system):
- \( \text{Exp}_x \) = geodesic shooting parameterized by the initial tangent
- \( \text{Log}_x \) = unfolding the manifold in the tangent space along geodesics
  - Geodesics = straight lines with Euclidean distance
  - Local \( \rightarrow \) global domain: star-shaped, limited by the cut-locus
  - Covers all the manifold if geodesically complete

Reformulate algorithms with \( \exp_x \) and \( \log_x \)
Vector \( \rightarrow \) Bi-point (no more equivalence classes)

<table>
<thead>
<tr>
<th>Operation</th>
<th>Euclidean space</th>
<th>Riemannian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtraction</td>
<td>( xy = y - x )</td>
<td>( xy = \text{Log}_x(y) )</td>
</tr>
<tr>
<td>Addition</td>
<td>( y = x + xy )</td>
<td>( y = \text{Exp}_x(xy) )</td>
</tr>
<tr>
<td>Distance</td>
<td>( \text{dist}(x, y) = |y - x| )</td>
<td>( \text{dist}(x, y) = |xy|_x )</td>
</tr>
<tr>
<td>Gradient descent</td>
<td>( x_{t+\epsilon} = x_t - \epsilon \nabla C(x_t) )</td>
<td>( x_{t+\epsilon} = \text{Exp}_{x_t}(-\epsilon \nabla C(x_t)) )</td>
</tr>
</tbody>
</table>
**Statistical Computing on Manifolds for Computational Anatomy**

**Simple Statistics on Riemannian Manifolds**
- Introduction to computational anatomy
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**Manifold-Valued Image Processing**
**Metric and Affine Geometric Settings for Lie Groups**
**Analysis of Longitudinal Deformations**
Random variable in a Riemannian Manifold

Intrinsic pdf of $x$

- For every set $H$
  \[
P(x \in H) = \int_H p(y) dM(y)
  \]
- Lebesgue's measure

→ Uniform Riemannian Measure $dM(y) = \sqrt{\det(G(y))} \, dy$

Expectation of an observable in $M$

- $E_x[\phi] = \int_M \phi(y)p(y)dM(y)$
- $\phi = \text{dist}^2$ (variance): $E_x[\text{dist}(.,y)^2] = \int_M \text{dist}(y,z)^2 p(z)dM(z)$
- $\phi = \log(p)$ (information): $E_x[\log(p)] = \int_M p(y)\log(p(y))dM(y)$
- $\phi = x$ (mean): $E_x[x] = \int_M y \, p(y)dM(y)$
Fréchet expectation (1944)

Minimizing the variance

\[ E[x] = \arg\min_{y \in M} \left( E[\text{dist}(y, x)^2] \right) \]

Existence

- Finite variance at one point

Characterization as an exponential barycenter (P(C)=0)

\[ \text{grad} \left( \sigma_x^2(y) \right) = 0 \quad \Rightarrow \quad E[\overrightarrow{xx}] = \int_{M} \overrightarrow{xx}.p_x(z).dM(z) = 0 \]

Uniqueness Karcher 77 / Kendall 90 / Afsari 10 / Le 10

- Unique Karcher mean (thus Fréchet) if distribution has support in a regular geodesic ball with radius \( r < r^* = \frac{1}{2} \min(inj(M), \pi/\sqrt{\kappa}) \) (k upper bound on sectional curvatures on M)
- Empirical mean: a.s. uniqueness [Arnaudon & Miclo 2013]

Other central primitives

\[ E^\alpha[x] = \arg\min_{y \in M} \left( E[\text{dist}(y, x)^\alpha] \right)^{1/\alpha} \]
**Statistical tools: Moments**

Frechet / Karcher mean minimize the variance

\[ E[x] = \arg\min_{y \in M} \left( E[\text{dist}(y, x)^2] \right) \quad \Rightarrow \quad E[\overline{x}x] = \int_{M} \overline{x}x. p_x(z).dM(z) = 0 \quad [P(C) = 0] \]

Gauss-Newton Geodesic marching

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

Covariance (PCA) [higher moments]

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

[Oller & Corcuera 95, Battacharya & Patrangenaru 2002, Pennec, JMIV06, NSIP’99 ]
**Example with 3D rotations**

**Principal chart:** rotation vector: \( r = \theta \cdot n \)

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

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

**Centered chart:**
mean = barycenter

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**Other definitions of the mean**

**Doss [1949] / Herer [1988]:** \( E[x] = \{ y \in M / \text{dist}(y, \bar{x}) \leq E[\text{dist}(y, x)] \} \)

**Convex barycenters (Emery / Arnaudon)**

\[ E[x] = \{ y \in M / \alpha(y) \leq E[\alpha(x)] \text{ for } \alpha \text{ convex on the support of } x \} \]

- Convex functions in compact spaces are constant

**Emery 1991:**

- if the support of \( x \) is included in a strongly convex open set:

  Exponential barycenters \( \subset \) Convex Barycenters

**Picard 1994: Connector (\( \to \)) Connection (\( \to \)) metric**

- Difference between barycenters is \( O(\sigma) \)
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 $p(x,y,t)$ [complex time dependency]
- Wrapped Gaussian [Infinite series difficult to compute]
- **Maximal entropy knowing the mean and the covariance**

\[ \Gamma = \Sigma^{(-1)} - \frac{1}{3} \text{Ric} + O(\sigma) + \varepsilon(\sigma / r) \]
\[ k = (2\pi)^{-n/2} \cdot \text{det}(\Sigma)^{-1/2} \cdot (1 + O(\sigma^3) + \varepsilon(\sigma / r)) \]

Mahalanobis D2 distance / test:
- Any distribution:
  \[ \mathbf{E}[\mu_x^2(x)] = n \]
- Gaussian:
  \[ \mu_x^2(x) \propto \chi_n^2 + O(\sigma^3) + \varepsilon(\sigma / r) \]

[ Pennec, JMIV06, NSIP’99 ]
**Gaussian on the circle**

**Exponential chart:** \( x = r\theta \in ]-\pi r; \pi r[ \)

**Gaussian:** truncated standard Gaussian

\[ \sigma^2 = \frac{\pi^2}{3} \]

\( r \to \infty : \) standard Gaussian (Ricci curvature \( \to 0 \))

\( \gamma \to 0 : \) uniform pdf with \( \sigma^2 = (\pi r)^2 / 3 \) (compact manifolds)

\( \gamma \to \infty : \) Dirac

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**PCA vs PGA**

**PCA**
- Generative model: Gaussian
- Find the subspace that best explains the variance
  → Maximize the squared distance to the mean

**PGA (Fletcher 2004, Sommer 2014)**
- Generative model:
  - Implicit uniform distribution within the subspace
  - Gaussian distribution in the vertical space
- Find a low dimensional subspace (geodesic subspaces?) that minimizes the error
  → Minimize the squared Riemannian distance from the measurements to that sub-manifold (no closed form)

**Different models in curved spaces (no Pythagore thm)**

**Open problem and discussions**
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**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

• 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)

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

[ J. Boisvert et al. ISBI’06, AMDO’06 and IEEE TMI 27(4), 2008 ]
AMDO’06 best paper award, Best French-Quebec joint PhD 2009
Bronze Standard Rigid Registration Validation

Best explanation of the observations (ML):

- LSQ criterion
- Robust Fréchet mean
- Robust initialization and Newton gradient descent

Result

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


Derive tests on transformations for accuracy / consistency
Augmented reality guided radio-frequency tumor ablation

Current operative setup at IRCAD (Strasbourg, France)

- Per-operative CT “guidance”
- Respiratory gating
  ➔ Marker based 3D/2D rigid registration

S. Nicolau, X. Pennec, A. Garcia, L. Soler, N. Ayache
Liver puncture guidance using augmented reality
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)

Results on per-operative patient images

Data (per-operative US)
- 2 pre-op MR (0.9 x 0.9 x 1.1 mm)
- 3 per-op US (0.63 and 0.95 mm)
- 3 loops

Robustness and precision

<table>
<thead>
<tr>
<th></th>
<th>Success</th>
<th>var rot (deg)</th>
<th>var trans (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>29%</td>
<td>0.53</td>
<td>0.25</td>
</tr>
<tr>
<td>CR</td>
<td>90%</td>
<td>0.45</td>
<td>0.17</td>
</tr>
<tr>
<td>BCR</td>
<td>85%</td>
<td>0.39</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Consistency of BCR

<table>
<thead>
<tr>
<th></th>
<th>var rot (deg)</th>
<th>var trans (mm)</th>
<th>var test (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple MR</td>
<td>0.06</td>
<td>0.06</td>
<td>0.10</td>
</tr>
<tr>
<td>Loop</td>
<td>2.22</td>
<td>0.82</td>
<td>2.33</td>
</tr>
<tr>
<td>MR/US</td>
<td>1.57</td>
<td>0.58</td>
<td>1.65</td>
</tr>
</tbody>
</table>

[Roche et al, TMI 20(10), 2001 ]
[Pennec et al, Multi-Sensor Image Fusion, Chap. 4, CRC Press, 2005]

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Mosaicing of Confocal Microscopic in Vivo Video Sequences.

Cellvizio: Fibered confocal fluorescence imaging

[ T. Vercauteren et al., MICCAI 2005, T.1, p.753-760 ]

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Mosaicing of Confocal Microscopic in Vivo Video Sequences.

Common coordinate system

- Multiple rigid registration
- Refine with non rigid

Mosaic image creation

- Interpolation / approximation with irregular sampling

Courtesy of Mike Booth, MGH, Boston, MA

[ T. Vercauteren et al., MICCAI 2005, T.1, p.753-760 ]

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Geometric Sciences of Information - GSI’2013

- Paris, August 28-30 2013
- http://www.gsi2013.org

- Computational Information Geometry
- Hessian/Symplectic Information Geometry
- Optimization on Matrix Manifolds
- Probability on Manifolds
- Optimal Transport Geometry
- Shape Spaces: Geometry and Statistic
- Geometry of Shape Variability
- ..........

- Organizers: S. Bonnabel, J. Angulo, A. Cont, F. Nielsen, F. Barbaresco

Mathematical Foundations of Computational Anatomy Workshop at MICCAI 2013 (MFCA 2013)

- Nagoya, Japan, September 22 or 26, 2013

Proceedings of previous editions:
http://hal.inria.fr/MFCA/
http://www-sop.inria.fr/asclepios/events/MFCA11/
http://www-sop.inria.fr/asclepios/events/MFCA08/
http://www-sop.inria.fr/asclepios/events/MFCA06/
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