The SVF framework for longitudinal statistics on deformations

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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)?
Longitudinal deformation analysis

Dynamic observations

How to transport longitudinal deformation across subjects?
What are the convenient mathematical settings?
Outline

Foundations of statistics on manifolds
- The Riemannian framework
- Lie groups as affine connection spaces
- The SVF framework for diffeomorphisms

Longitudinal analysis of deformations with SFVs
- Parallel transport of deformations germs
- Longitudinal modeling of brain atrophy in AD
- Morphological analysis with Helmoltz decomposition
Bases of Algorithms in Riemannian Manifolds

Riemannian metric:
- Dot product on tangent space
- Speed, length of a curve
- Geodesics are length minimizing curves
- Riemannian Distance

Exponential map (Normal coord. syst.):
- Geodesic shooting: $\text{Exp}_x(v) = \gamma_{(x,v)}(1)$
- Log: find vector to shoot right (geodesic completeness!)

Unfolding ($\text{Log}_x$), folding ($\text{Exp}_x$):
- Vector -> Bipoint (no more equivalent class)

<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>$xy = \text{Log}_x(y)$</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 tools: Moments**

Frechet / Karcher mean minimize the variance

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

Existence and uniqueness : Karcher / Kendall / Le / Afsari

Gauss-Newton Geodesic marching

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

Covariance (PCA) [higher moments]

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

[Oller & Corcuera 95, Battacharya & Patrangenaru 2002, Pennec, JMIV06, NSIP’99]

X. Pennec - STIA - Sep. 18 2014
Limits of the Riemannian Framework

Lie group: Smooth manifold with group structure

- Composition $g \circ h$ and inversion $g^{-1}$ are smooth
- Left and Right translation $L_g(f) = g \circ f$ \hspace{1cm} $R_g(f) = f \circ g$
- Natural Riemannian metric choices
  - Chose a metric at Id: $<x,y>_{Id}$
  - Propagate at each point $g$ using left (or right) translation
    $<x,y>_g = <DL_g^{-1}.x \ , \ DL_g^{-1}.y>_{Id}$

No bi-invariant metric in general

- Incompatibility of the Fréchet mean with the group structure
  - Left of right metric: different Fréchet means
  - The inverse of the mean is not the mean of the inverse
- Examples with simple 2D rigid transformations

- Can we design a mean compatible with the group operations?
- Is there a more convenient structure for statistics on Lie groups?
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Basics of Lie groups

Flow of a left invariant vector field $\tilde{X} = DL.x$ starting from e

- $\gamma_x(t)$ exists for all time
- One parameter subgroup: $\gamma_x(s + t) = \gamma_x(s). \gamma_x(t)$

Lie group exponential

- Definition: $x \in g \rightarrow \text{Exp}(x) = \gamma_x(1) \in G$
- Local chart (not true in general for inf. dim)
- Baker-Campbell Hausdorff (BCH) formula

$$BCH(x, y) = \text{Log}(\text{Exp}(x). \text{Exp}(y)) = x + y + \frac{1}{2} [x, y] + ...$$

3 curves at each point parameterized by the same tangent vector

- Left / Right-invariant geodesics, one-parameter subgroups

Question: Can one-parameter subgroups be geodesics?
Affine connection spaces

**Affine Connection (infinitesimal parallel transport)**

- Acceleration = derivative of the tangent vector along a curve
- Projection of a tangent space on a neighboring tangent space

**Geodesics = straight lines**

- Null acceleration: $\nabla \dot{\gamma} \dot{\gamma} = 0$
- 2nd order differential equation: Normal coordinate system
- Local exp and log maps

Adapted from Lê Nguyên Hoang, science4all.org
Cartan-Schouten Connection on Lie Groups

A unique connection

- Symmetric (no torsion) and bi-invariant
- For which geodesics through $\text{Id}$ are one-parameter subgroups (group exponential)
  - Matrices: $M(t) = A \cdot \exp(t \cdot V)$
  - Diffeos: translations of Stationary Velocity Fields (SVFs)

Levi-Civita connection of a bi-invariant metric (if it exists)

- Continues to exist in the absence of such a metric (e.g. for rigid or affine transformations)

Two flat connections (left and right)

- Absolute parallelism: no curvature but torsion (Cartan / Einstein)
Statistics on an affine connection space

Fréchet mean: exponential barycenters

- $\sum_i \log_{x}(y_i) = 0$ \[\text{[Emery, Mokobodzki 91, Corcuera, Kendall 99]}\]
- Existence & local uniqueness if local convexity \[\text{[Arnaudon & Li, 2005]}\]

For Cartan-Schouten connections \[\text{[Pennec & Arsigny, 2012]}\]

- Locus of points $x$ such that $\sum \log(x^{-1}.y_i) = 0$
- Algorithm: fixed point iteration (local convergence)

$$x_{t+1} = x_t \circ \exp\left(\frac{1}{n} \sum \log(x_t^{-1}.y_i)\right)$$

- Mean stable by left / right composition and inversion
  - If $m$ is a mean of $\{g_i\}$ and $h$ is any group element, then
    - $h \circ m$ is a mean of $\{h \circ g_i\}$
    - $m \circ h$ is a mean of the points $\{g_i \circ h\}$
    - and $m(-1)$ is a mean of $\{g_i^{-1}\}$
Generalization of the Statistical Framework

Covariance matrix & higher order moments

- Defined as tensors in tangent space

\[ \Sigma = \int \text{log}_x(y) \otimes \text{log}_x(y) \mu(dy) \]

- Matrix expression changes according to the basis

Other statistical tools

- Mahalanobis distance well defined and bi-invariant
- Tangent Principal Component Analysis (t-PCA)
- Principal Geodesic Analysis (PGA), provided a data likelihood
- Independent Component Analysis (ICA)
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**Riemannian Metrics on diffeomorphisms**

**Space of deformations**
- Transformation \( y = \phi(x) \)
- Curves in transformation spaces: \( \phi(x, t) \)
- Tangent vector = speed vector field \( v_t(x) = \frac{d\phi(x, t)}{dt} \)

**Right invariant metric**
- Lagrangian formalism
- Sobolev Norm \( H_k \) or \( H_\infty \) (RKHS) in LDDMM \( \rightarrow \) diffeomorphisms
  [Miller, Trouve, Younes, Holm, Dupuis, Beg… 1998 – 2009]
- Geometric Mechanics [Arnold, Smale, Souriau, Marsden, Ratiu, Holmes, Michor…]

**Geodesics determined by optimization of a time-varying vector field**
- Distance
  \[
d^2(\phi_0, \phi_1) = \arg\min_{v_t} \left( \int_0^1 \|v_t\|_{\phi_t}^2 \, dt \right)
\]
- Geodesics characterized by initial velocity / momentum
- Optimization by shooting/adjoint or path-straightening methods
The SVF framework for Diffeomorphisms

Framework of [Arsigny et al., MICCAI 06]
- Use one-parameter subgroups

Exponential of a smooth vector field is a diffeomorphism
- \( u \) is a smooth stationary velocity field
- Exponential: solution at time 1 of ODE \( \frac{\partial x(t)}{\partial t} = u( x(t) ) \)
Efficient numerical methods

- Take advantage of algebraic properties of exp and log.
  - \( \exp(t.V) \) is a one-parameter subgroup.

  → Direct generalization of numerical matrix algorithms.

Efficient parametric diffeomorphisms

- Computing the deformation: Scaling and squaring recursive use of \( \exp(v) = \exp(v/2) \circ \exp(v/2) \)
  [Arsigny MICCAI 2006]

- Updating the deformation parameters:
  BCH formula [Bossa MICCAI 2007]

  \[
  \exp(v) \circ \exp(\epsilon u) = \exp\left( v + \epsilon u + \frac{[v,\epsilon u]}{2} + \frac{[v,[v,\epsilon u]]}{12} + \ldots \right) \]

  * Lie bracket \([v,u](p) = \text{Jac}(v)(p).u(p) - \text{Jac}(u)(p).v(p)\)
Symmetric log-demons [Vercauteren MICCAI 08]


- Parameterize the deformation by SVFs
- Time varying (LDDMM) replaced by stationary vector fields
- Efficient scaling and squaring methods to integrate autonomous ODEs

Log-demons with SVFs

\[
\mathcal{E}(\mathbf{v}, \mathbf{v}_c) = \frac{1}{\sigma^2_i} \left\| F - M \circ \exp(\mathbf{v}_c) \right\|_{L^2}^2 + \frac{1}{\sigma^2_x} \left\| \log(\exp(-\mathbf{v}) \circ \exp(\mathbf{v}_c)) \right\|_{L^2}^2 + \mathcal{R}(\mathbf{v})
\]

- Efficient optimization with BCH formula
- Inverse consistent with symmetric forces
- Open-source ITK implementation
  - Very fast
  - http://hdl.handle.net/10380/3060


Similarity

Measures how much the two images differ

Coupling

Couples the correspondences with the smooth deformation

Regularisation

Ensures deformation smoothness

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Cartan Connections vs Riemannian

What is similar
- Standard differentiable geometric structure [curved space without torsion]
- Normal coordinate system with $\text{Exp}_x$ et $\text{Log}_x$ [finite dimension]

Limitations of the affine framework
- No metric (but no choice of metric to justify)
- The exponential does always not cover the full group
  - Pathological examples close to identity in finite dimension
  - In practice, similar limitations for the discrete Riemannian framework

What we gain
- A globally invariant structure invariant by composition & inversion
- Simple geodesics, efficient computations (stationarity, group exponential)
- The simplest linearization of transformations for statistics?
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Measuring Temporal Evolution with deformations

Fast registration with deformation parameterized by SVF

$$\varphi_t(x) = \exp(t \cdot v(x))$$

[ Lorenzi, Ayache, Frisoni, Pennec, Neuroimage 81, 1 (2013) 470-483 ]

https://team.inria.fr/asclepios/software/lcclogdemons/
Longitudinal deformation analysis in AD

- From patient specific evolution to population trend (parallel transport of deformation trajectories)
- Inter-subject and longitudinal deformations are of different nature and might require different deformation spaces/metrics
Parallel transport of deformations

Encode longitudinal deformation by its initial tangent (co-) vector
  - Momentum (LDDMM) / SVF

Parallel transport
  - (small) longitudinal deformation vector
  - along the large inter-subject normalization deformation

Existing methods
  - Vector reorientation with Jacobian of inter-subject deformation
  - Conjugate action on deformations (Rao et al. 2006)
  - Resampling of scalar maps (Bossa et al, 2010)
  - LDDMM setting: parallel transport along geodesics via Jacobi fields [Younes et al. 2008]

Intra and inter-subject deformations/metrics are of different nature
Parallel transport along arbitrary curves

Infinitesimal parallel transport = connection
\[ \nabla_{\gamma'}(X) : TM \rightarrow TM \]

A numerical scheme to integrate for symmetric connections:
Schild’s Ladder [Elhers et al, 1972]
- Build geodesic parallelogrammoid
- Iterate along the curve

[Lorenzi, Ayache, Pennec: Schild's Ladder for the parallel transport of deformations in time series of images, IPMI 2011]
Parallel transport along geodesics

Along geodesics: Pole Ladder [Lorenzi et al, JMIV 2013]

[ Lorenzi, Pennec: Efficient Parallel Transport of Deformations in Time Series of Images: from Schild's to pole Ladder, JMIV 2014 ]
Efficient Pole and Schild’s Ladder with SVFs

Numerical scheme

- Direct computation
  \[ \Pi_{\text{conj}}(u) = D(\exp(v)) \big|_{\exp(-v) \cdot u \circ \exp(-v)} \]

- Using the BCH:
  \[ \Pi_{\text{BCH}}(u) = u + [v, u] + \frac{1}{2}[v[v, u]] \]

[Lorenzi, Ayache, Pennec: Schild's Ladder for the parallel transport of deformations in time series of images, IPMI 2011]
Runner-up for the IPMI Erbsmann 2011 prize
Analysis of longitudinal datasets  
**Multilevel framework**

**Single-subject, two time points**  
Log-Demons (LCC criteria)

**Single-subject, multiple time points**  
4D registration of time series within the Log-Demons registration.

**Multiple subjects, multiple time points**  
Pole or Schild’s Ladder

[D. Lorenzi et al, in Proc. of MICCAI 2011]
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Mean Longitudinal Model for AD

Estimated from 1 year changes – Extrapolation to 15 years

70 AD subjects (ADNI data)
Longitudinal changes in Alzheimer’s disease

(141 subjects – ADNI data)
Consistency and numerical stability

Vector measure

Scalar summary
(Jacobian det, logJacobian det, ...)

Vector transport

Scalar measure

Scalar transport

Scalar summary
Longitudinal changes in Alzheimer’s disease

(141 subjects – ADNI data)

Comparison with standard TBM

Consistent results

Equivalent statistical power
Study of prodromal Alzheimer’s disease

- **98 healthy subjects**, 5 time points (0 to 36 months).
- **41 subjects** Aβ42 positive (“at risk” for Alzheimer’s)
- **Q**: Different morphological evolution for Aβ+ vs Aβ-?

[Lorenzi, Ayache, Frisoni, Pennec, in Proc. of MICCAI 2011]
Study of prodromal Alzheimer’s disease

Linear regression of the SVF over time: interpolation + prediction

Multivariate group-wise comparison of the transported SVFs shows statistically significant differences (nothing significant on log(det) )

$Lorenzi, Ayache, Frisoni, Pennec, in Proc. of MICCAI 2011$
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Non-rigid registration for longitudinal analysis

Alzheimer’s atrophy trajectory

Baseline MRI → Follow-up MRI

$\varphi = \exp(\nu)$

Atrophy flow encoded by the dense stationary velocity field
Morphological analysis of SVF

\[ \nabla \times A \]

Helmholtz decomposition

Atrophy!!

\[ \nabla \nabla p \]

Volume changes

Structural readjustments
Morphological analysis of SVF

**Discovery**

**Pressure** \( p \)
Defines **sources and sinks**
of the atrophy process

**Quantification**

**Divergence** \( \nabla \cdot \nabla p \)
Defines **flux** across
expanding/contracting regions

---

**Divergence Theorem**

\[
\int_{\partial V} v \cdot n \, dS = \int_V \nabla \cdot v \, dV
\]
Probabilistic definition of the atrophy topography

\[ P(\text{Critical area}) \approx \text{Proximity to critical point} + \text{Surrounding flux} \]

Step 1. Finding local maxima and minima for the pressure field (sources, sinks)
Step 2. Finding surrounding areas of maximal outwards/inwards flux (Expansion and Contraction)

[Lorenzi et al, MICCAI 2012]
Group-wise flux analysis in Alzheimer’s disease: Quantification

From group-wise... ...to subject specific

sample size $\propto \frac{sd}{(\text{mean}_1 - \text{mean}_2)}$

<table>
<thead>
<tr>
<th>Group</th>
<th>Regional flux (all regions)</th>
<th>Hippocampal atrophy [Leung 2010] (Different ADNI subset)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD vs controls</td>
<td>164 [106,209]</td>
<td>121 [77, 206]</td>
</tr>
<tr>
<td>MCI vs controls</td>
<td>277 [166,555]</td>
<td>545 [296, 1331]</td>
</tr>
</tbody>
</table>

Effect size on left hippocampus

<table>
<thead>
<tr>
<th>Group</th>
<th>six months</th>
<th>one year</th>
<th>two years</th>
</tr>
</thead>
<tbody>
<tr>
<td>INRIA - Regional Flux</td>
<td>1.02</td>
<td>1.33</td>
<td>1.47</td>
</tr>
</tbody>
</table>

NIBAD’12 Challenge: Top-ranked on Hippocampal atrophy measures
**Conclusion**

**Cartan connections: a nice setting for transformation groups**
- A connection defines geodesics but no length along them
- Cartan connection: one-parameters subgroups are bi-invariant geodesics
- Fréchet / Karcher means $\rightarrow$ exponential barycenter = bi-invariant mean
  - Fine existence [Pennec & Arsigny 2012] (Uniqueness?)

**Algorithms for SVFs**
- Log-demons: Open-source ITK implementation [http://hdl.handle.net/10380/3060](http://hdl.handle.net/10380/3060)
- Tensor (DTI) Log-demons: [https://gforge.inria.fr/projects/ttk](https://gforge.inria.fr/projects/ttk)
- LCC time-consistent log-demons for AD available soon
- ITK class for SVF diffeos currently under development

**Schildds Ladder for parallel transport**
- Effective instrument for the transport of deformation trajectories
- Key component for multivariate analysis and modeling of longitudinal data
- Stability and sensitivity
The Stationary Velocity Fields (SVF) framework for diffeomorphisms

- SVF framework for diffeomorphisms is algorithmically simple
- Compatible with “inverse-consistency”
- Vector statistics directly generalized to diffeomorphisms
- Efficient parallel transport of deformation trajectories with Schildds/pole ladders

Registration algorithms using log-demons:

- Log-demons: Open-source ITK implementation (Vercauteren MICCAI 2008)
  [MICCAI Young Scientist Impact award 2013]
  http://hdl.handle.net/10380/3060
- Tensor (DTI) Log-demons (Sweet WBIR 2010):
  https://gforge.inria.fr/projects/ttk
- LCC log-demons for AD (Lorenzi, Neuroimage. 2013)
  https://team.inria.fr/asclepios/software/lcclogdemons/
- 3D myocardium strain / incompressible deformations (Mansi MICCAI’10)
- Hierarchichal multiscale polyaffine log-demons (Seiler, Media 2012)
  [MICCAI 2011 Young Scientist award]
Medical image processing and visualization software
Open-source, BSD license
Extensible via plugins
Provides high-level algorithms to end-users
Ergonomic and reactive user interface

Available registration algorithms:
- Diffeomorphic Demons
- Incompressible Log Demons
- LCC Log Demons

http://med.inria.fr

INRIA teams involved: Asclepios, Athena, Parietal, Visages