Medical Imaging

MVA 2023-2024

http://www-sop.inria.fr/teams/asclepios/cours/MVA/

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Diffeomorphic deformations and computational anatomy

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Medical Image Processing – MVA 2023-2024

Tuesday afternoon

Course notes : http://www-sop.inria.fr/teams/asclepios/cours/MVA/

- Tue Oct 3, ENSPS 2E30, Introduction to Medical Image Acquisition and Image Filtering, [HD]
- Tue Oct 10, ENSPS 3E34, Medical Image Registration [XP]
- Tue Oct 17, ENSPS 2E30, Riemanian Geometry & Statistics [XP]
- Tue Oct 24, ENSPS 1B18, Basis of Image Segmentation [HD]
- Tue Nov 7, ENSPS 2E30, Image Segmentation based on Clustering and Markov Random Fields [HD]
- Tue Nov 14, ENSPS 3E34, Shape constrained image segmentation and Biophysical Modeling [HD]
- Tue Nov 21, ENSPS 2E30, Analysis in the space of Covariance Matrices [XP]
- **Tue Nov 28, ENSPS 1B18, Diffeomorphic Registration end computational anatomy [XP]**
- Tu Dec 5, VISI Exam [HD, XP]

Statistical Computing on Manifolds for Computational Anatomy

Metric and Affine Geometric Settings for Lie Groups

- Deformable image registration
- Riemannian frameworks on Lie groups
- Lie groups as affine connection spaces
- Extending statistics without a metric
- The SVF framework for diffeomorphisms

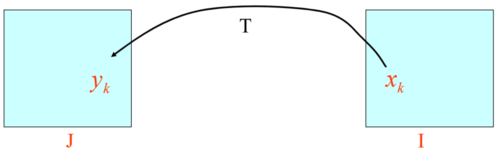
Modeling longitudinal deformations in AD

- Parallel transport of deformation trajectories
- From velocity fields to AD models

Goals of Registration

A dual problem

- Find the point y of image J which is corresponding (homologous) to each points x of image I.
- Determine the best transformation T that superimposes homologous points



Mathematical Formulation of registration (Brown, 1992)

■ **Registration**: Given two datasets (images) I and J, find the geometric transformation T that « best » aligns the physically homologous points (voxels)

$$\hat{T} = \arg\max_{T \in \Gamma} S(I, J, T)$$

Optimization algorithm

Similarity measure

Transformation space (rigid, affine, elastic,…)

The deformable registration landscape in 1995

Transformation encoded by a displacement field: $T(x) = x + u(x)$

Optical flow $F(x,u) = -(I(x) - J(x+u))\nabla J(x+u)$

- Horn and Schunck, Artif. Intell. 17, 1981;
- Aggarwal and Nandhakumar, Proc. IEEE 76, 1988;
- Barron *et al., 1994.*

$$\frac{\partial u}{dt} \propto F(x,u)$$

Linear elastic deformation $\mu \nabla^2 u + (\mu + \lambda)\nabla(div(u)) = F$

- Broit, PhD 1981.
- Bajcsy and Kovacic CVGIP 46, 1989
- Gee, Reivich, Bajcsy, *J. Comp. Assis.Tom. 17,* 1993.

Fluid (images & surface) $\mu \nabla^2 v + (\mu + \lambda)\nabla(div(v)) = F$

- Christensen, Rabbitt, Miller, *Phys. Med. Biol. 39,* 1994.
- Christensen, Rabbitt, Miller. IEEE TIP. 5(10), 1996.
- Thompson and Toga, IEEE TMI 15(4), 1996.

$$\frac{\partial u}{\partial t} = v - (\nabla u)\, v$$

Differential equations were costly to solve: > 1 day on mass-parallel machine

Demons' algorithm (MRCAS 95, CVPR96, Media98)

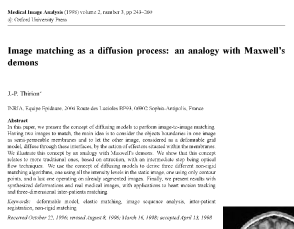

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Image matching as a diffusion process: an analogy with Maxwell's demons

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Abstract
In this paper, we present the concept of diffusing models to perform image-to-image matching. Having two images to match, the main idea is to consider the objects boundaries in one image as semi-permeable membranes and to let the other image, considered as a deformable grid model, diffuse through these interfaces, by the action of effectors situated within the membranes. We illustrate this concept by an analogy with Maxwell's demons. We show that this concept relates to more traditional ones, based on attraction, with an intermediate step being optical flow techniques. We use the concept of diffusing models to derive three different non-rigid matching algorithms, one using all the intensity levels in the static image, one using only contour points, and a last one operating on already segmented images. Finally, we present results with synthesized deformations and real medical images, with applications to heart motion tracking and three-dimensional inter-patients matching.

Keywords: deformable model, elastic matching, image sequence analysis, inter-patient registration, non-rigid matching

Received October 22, 1996; revised August 8, 1996; March 16, 1998; accepted April 13, 1998

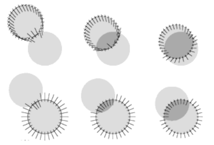
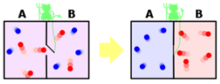
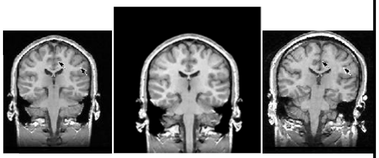


Figure 5. Three iterations of a model based on attraction (top row) and a rigid diffusing model (bottom row). These examples are produced by actual implementations.





Patient 1 Patient 2

Demons' algorithm (MRCAS 95, CVPR96, Media98)

- T_0= Identity
- Update field $$U_{n+1} = \frac{I - J \circ T_n}{\|\nabla I\|^2 + (I - J \circ T_n)^2} \nabla I$$
- Regularization by Gaussian filtering

Elastic

$$\hat{T}_{n+1} = T_n \circ U_{n+1}$$
$$T_{n+1} = G_\sigma * \hat{T}_{n+1}$$

Fluid

$$\tilde{U}_{n+1} = G_\sigma * U_{n+1}$$
$$T_{n+1} = T_n \circ \tilde{U}_{n+1}$$

Why does that work? Convergence? Change the similarity metric?

Interpretation of demons

$$E(C,T) = SSD(I,J,C) + \sigma \| C - T \|^2 + \sigma\lambda.\mathrm{Reg}(T)$$

- *SSD* : measures the similarity of intensities
- *Reg* : regularization energy (quadratic)
- λ , σ : smoothing and noise parameters
- *C* : correspondences between points (vectors field)
- *T* : transformation (regularized vector field)

- Introduce correspondences (matches) as an auxiliary variable to decouple into a local non-convex

P. Cachier E. Bardinet, D. Dormont, X. Pennec and N. A.: *Iconic Feature Based Nonrigid Registration: the PASHA Algorithm*, Comp. Vision and Image Understanding (CVIU), Special Issue on Non Rigid Registration, 89 (2-3), 272-298, 2003.

PASHA Algorithm (2/2)

$$E(C,T) = SSD(I,J,C) + \sigma \| C - T \|^2 + \sigma\lambda.\mathrm{Reg}(T)$$

Alternated minimization

- Minimization with respect to C :
  - Find matches between points by optimizing E_S + **in the neighborhood of** T
  - Gradient descent (1st, 2bd order, e.g. Gauss-Newton)
- Minimization with respect to T :
  - Find a smooth transformation that approximates C
  - Quadratic energy $\Rightarrow$ convolution
- **Interest**: fast computation

Newton optimization of the correspondence energy

$$E(C) = \int (I(x) - J(C(x))^2.dx + \frac{\sigma_i^2}{\sigma_x^2}\int \left\| C(x) - T(x) \right\|^2.dx$$

Exact solution of the quadratic approximation of the SSD

- Solve $\left[(\nabla J \circ T).(\nabla J \circ T)^t + \frac{\sigma_i^2}{\sigma_x^2} Id \right].u = (J \circ T - I).(\nabla J \circ T)$
- By inversion lemma: $u = \dfrac{(J \circ T - I).(\nabla J \circ T)}{\left\| \nabla J \circ T \right\|^2 + \sigma_i^2 / \sigma_x^2}$
- Local estimation of intensity variance: $\sigma_i^2 = (J \circ T - I)^2$
- Assuming isotropic voxel size: $\sigma_x^2 \approx 1$

$$u = \frac{I - J \circ T}{\left\| \nabla I \right\|^2 + (I - J \circ T)^2} \nabla I$$

Efficient Regularization

Quadratic regularizer $\mathrm{Reg}(T) = \int \sum_{k=1}^{\infty} \dfrac{\sum_{i_1 \ldots i_k} \left\| \partial_{i_1} \ldots \partial_{i_k} (T - Id) \right\|^2}{\sigma_d^{2k}.k!}$

Euler Lagrange optimization of $\mathrm{E(T)} = \int \left\| \mathrm{C} - \mathrm{T} \right\|^2 + \mathrm{Reg}(T)$

$$C - T + \sum_{k=1}^{\infty} \frac{(-1)^k \Delta^k (T - Id)}{\sigma_d^{2k}.k!} = 0$$

Solution: Gaussian smooting $\mathrm{T_{opt}} = G_\sigma * C$ with $\sigma = 1/\sigma_d$

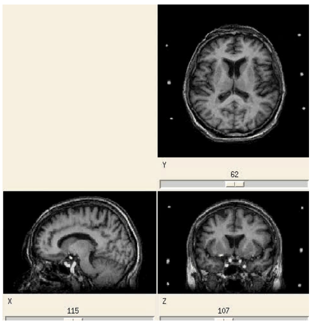
Pennec, Cachier, Ayache. Understanding the ``Demon's Algorithm'': 3D Non-Rigid registration by Gradient Descent. MICCAI 1999.

Extension to a family of quadratic filters

$$G_{\sigma,\kappa}(\mathbf{u}) = \frac{1}{(\sigma\sqrt{2\pi})^3(1+\kappa)} \left(\mathrm{Id} + \frac{\kappa}{\sigma^2}\mathbf{u}\mathbf{u}^T \right) \exp\left(\frac{\mathbf{u}^T\mathbf{u}}{2\sigma^2} \right)$$

P. Cachier and N. Ayache. Isotropic energies, filters and splines for vectorial regularization. J. of Math. Imaging and Vision, 20(3):251-265, May 2004.

Inter-subject registration
Affine transformation



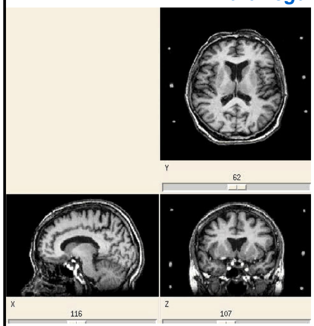
MR T1 Images

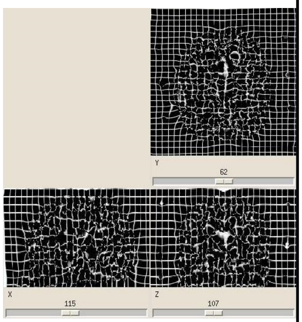
256x256x120 voxels

Atlas to patient registration
for radiotherapy planning

Correct size and position but high remaining variability in cortex and deep structures

Inter-subject registration
Fluid regularization

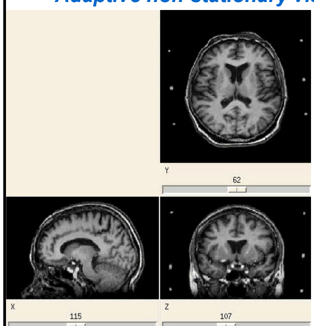


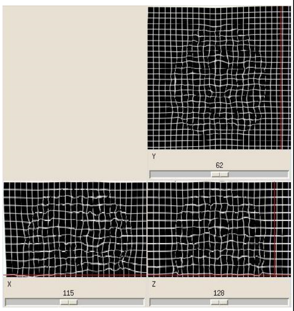


Very good image correspondence

But anatomically meaningless deformation
Jacobian [1/50;50]

Inter-subject registration
Adaptive non-stationary visco-elastic regularization





Registration in 5 min on 15 PCs

Anatomically more meaningful deformation
Jacobian [1/5;5]

Statistical Computing on Manifolds for Computational Anatomy

Metric and Affine Geometric Settings for Lie Groups

- Reminder on deformable image registration
- Riemannian frameworks on Lie groups
- Lie groups as affine connection spaces
- Extending statistics without a metric
- The SVF framework for diffeomorphisms

Modeling longitudinal deformations in AD

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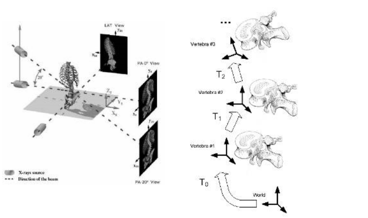
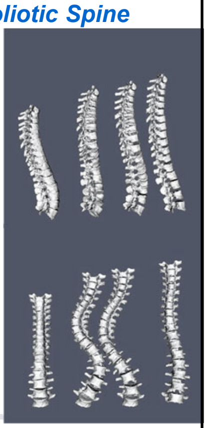
Statistical Analysis of the Scoliotic Spine





Data

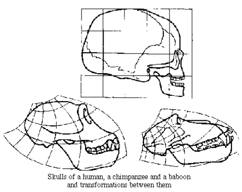
- 307 Scoliotic patients from the Montreal's St-Justine Hosp
- 3D Geometry from multi-planar X-rays
- Articulated model:17 relative pose of successive vertebras

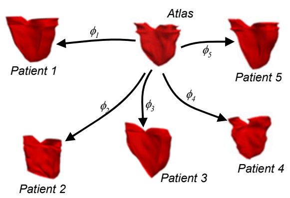
Statistics

- Main translation variability is axial (growth?)
- Main rot. var. around anterior-posterior axis
- **4 first variation modes related to King's classes**

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

Morphometry through Deformations

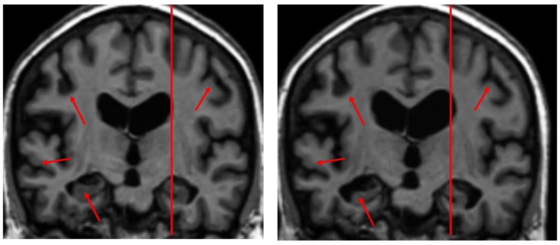




Measure of deformation [D'Arcy Thompson 1917, Grenander & Miller]

- Observation = "random" deformation of a reference template
- Deterministic template = anatomical invariants [Atlas ~ mean]
- Random deformations = geometrical variability [Covariance matrix]

Longitudinal structural damage in Alzheimer's Disease

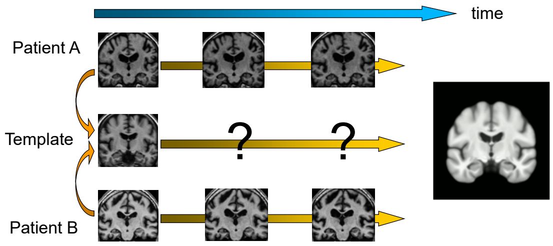


baseline — 2 years follow-up

Widespread cortical thinning

Longitudinal deformation analysis

Deformation trajectories in different reference spaces



Mean longitudinal deformation across subjects?
Convenient mathematical settings for transformations?

Statistics on deformations

Statistics on displacement field/transformation parameters

- Splines [Rueckert et al., TMI, 03],
- PCA of Statistical shape models
- Simple vector statistics, but inconsistency with group properties

The Riemannian approach (LDDMM)

- Right-invariant metric on diffeos [Joshi, Miller, Trouvé, Younes…]
- Parameterize diffeomorphisms by time-varying velocity fields
- Good mathematical bases for statistics on non-linear spaces

No bi-invariant metric in general

- Left/right Fréchet mean incompatible with group structure
- The inverse of the mean is not the mean of the inverse
- Examples with simple 2D rigid transformations

Natural Riemannian Metrics on Transformations

Transformations are Lie groups: Smooth manifold G compatible with group structure

- Composition g o h and inversion g^{-1} are smooth
- Left and Right translation $L_g(f) = g \circ f$ $R_g(f) = f \circ g$
- Conjugation $Conj_g(f) = g \circ f \circ g^{-1}$

Natural Riemannian metric choices

- Chose a metric at Id: $<x,y>_{Id}$
- Propagate at each point g using left (or right) translation $<x,y>_g = < DL_{g^{(-1)}}.x \, , DL_{g^{(-1)}}.y >_{Id}$

Implementation

- Practical computations using left (or right) translations

$$\mathrm{Exp}_f(x) = f \circ \mathrm{Exp}_{Id}(DL_{f^{(-1)}}.x) \qquad \overrightarrow{fg} = \mathrm{Log}_f(g) = DL_f.\mathrm{Log}_{Id}(f^{(-1)} \circ g)$$

Example on 3D rotations

Space of rotations SO(3):

- Manifold: $R^T.R=Id$ and $\det(R)=+1$
- Lie group (R_1 o R_2 = $R_1.R_2$ & Inversion: $R^{(-1)} = R^T$)

Metrics on SO(3): compact space, there exists a bi-invariant metric

- Left / right invariant / induced by ambient space $<X, Y> = Tr(X^T Y)$

Group exponential

- One parameter subgroups = bi-invariant Geodesic starting at Id
  - Matrix exponential and Rodrigue's formula: R=exp(X) and X = log(R)
- Geodesic everywhere by left (or right) translation

$$\mathrm{Log}_R(U) = R \log(R^T U) \qquad \mathrm{Exp}_R(X) = R \exp(R^T X)$$

Bi-invariant Riemannian distance

- $d(R,U) = \|\log(R^T U)\| = \theta(R^T U)$

General Non-Compact and Non-Commutative case

No Bi-invariant Mean for 2D Rigid Body Transformations

- Metric at Identity: $dist(Id, (\theta; t_1; t_2))^2 = \theta^2 + t_1^2 + t_2^2$
- $T_1 = \left(\frac{\pi}{4}; -\frac{\sqrt{2}}{2}; \frac{\sqrt{2}}{2}\right)$ $T_2 = \left(0;\ \sqrt{2}; 0\right)$ $T_3 = \left(-\frac{\pi}{4}; -\frac{\sqrt{2}}{2}; -\frac{\sqrt{2}}{2}\right)$
- Left-invariant Fréchet mean: $(0; 0; 0)$
- Right-invariant Fréchet mean: $\left(0; \frac{\sqrt{2}}{3}; 0\right) \simeq (0; 0.4714; 0)$

Questions for this talk:

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

Statistical Computing on Manifolds for Computational Anatomy

Metric and Affine Geometric Settings for Lie Groups

- A short introduction to deformable image registration
- Riemannian frameworks on Lie groups
- Lie groups as affine connection spaces
- Extending statistics without a metric
- The SVF framework for diffeomorphisms

Modeling longitudinal deformations in AD

- Parallel transport of deformation trajectories
- From velocity fields to AD models

MVA 2023-2024 25

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 (ATTN: different from Riemannian Exp)

- Definition: $x \in \mathfrak{g} \rightarrow Exp(x) = \gamma_x(1) \epsilon\, G$
- Diffeomorphism from a a neighborhood of 0 in $\mathfrak{g}$ to a neighborhood of e in G (not true in general for inf. dim)
- Baker-Campbell Hausdorff (BCH) formula

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

3 curves at each point parameterized by the same tangent vector

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

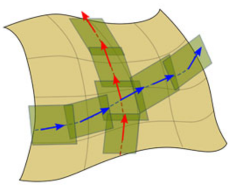
Question: Can one-parameter subgroups be geodesics?

MVA 2023-2024 27

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: $\nabla_{\dot{\gamma}}\dot{\gamma} = 0$
- 2[nd] order differential equation: Normal coordinate system
- Local exp and log maps (Strong form of Whitehead theorem: *In an affine connection space, each point has a normal convex neighborhood (unique geodesic between any two points included in the NCN)*

MVA 2023-2024 28

Canonical Connections on Lie Groups

A unique Cartan-Schouten connection

- Symmetric (no torsion) and bi-invariant
- For which geodesics through Id are one-parameter subgroups (group exponential)
  - Matrices: M(t) = A.exp(t.V)
  - Diffeos: left/right translations of Stationary Velocity Fields (SVFs)

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

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

Symmetric space with central symmetry $S_\psi(\phi) = \psi\phi^{-1}\psi$

- Matrix geodesic symmetry: $S_A(M(t)) = A\exp(-tV)A^{-1}A = M(-t)$

[Lorenzi, Pennec. Geodesics, Parallel Transport & One-parameter Subgroups for Diffeomorphic Image Registration. Int. J. of Computer Vision, 105(2):111-127, 2013.]

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Mean value on an affine connection space

Fréchet / Karcher means not usable (no distance) but:

$$E[\mathbf{x}] = \underset{y \in M}{\operatorname{argmin}} \left(E\left[\operatorname{dist}(y, \mathbf{x})^2 \right] \right) \Rightarrow E\left[\overrightarrow{\bar{x}\mathbf{x}}\right] = \int_M \overrightarrow{\bar{x}\mathbf{x}}.p_{\mathbf{x}}(z).dM(z) = 0 \quad [P(C) = 0]$$

Exponential barycenters

- [Emery & Mokobodzki 91, Corcuera & Kendall 99]

$$\int Log_x(y)\,\mu(dy) = 0 \quad \text{or} \quad \sum_i Log_x(y_i) = 0$$

- Existence? Uniqueness?
- OK for convex affine manifolds with semi-local convex geometry [Arnaudon & Li, Ann. Prob. 33-4, 2005]
  - Use a separating function (convex function separating points) instead of a distance
- Algorithm to compute the mean: fixed point iteration (stability?)

Bi-invariant Mean on Lie Groups

Exponential barycenter of the symmetric Cartan connection

- Locus of points where $\sum Log(m^{-1}.g_i) = 0$ (whenever defined)
- Iterative algorithm: $m_{t+1} = m_t \circ Exp\left(\frac{1}{n}\sum Log(m_t^{-1}.g_i)\right)$
- First step corresponds to the Log-Euclidean mean
- Corresponds to the first definition of bi-invariant mean of [V. Arsigny, X. Pennec, and N. Ayache. Research Report RR-5885, INRIA, April 2006.]

Mean is 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 $\{g_i^{(-1)}\}$

[Pennec & Arsigny, Ch.7 p.123-166 , Matrix Information Geometry, Springer, 2012]

Special matrix groups

Heisenberg Group (resp. Scaled Upper Unitriangular Matrix Group)

- No bi-invariant metric
- Group geodesics defined globally, all points are reachable
- **Existence and uniqueness of bi-invariant mean** (closed form resp. solvable)

Rigid-body transformations

- Logarithm well defined iff log of rotation part is well defined, i.e. if the Givens rotation have angles $|\theta_i| < \pi$
- **Existence and uniqueness with same criterion as for rotation parts (same as Riemannian)**

SU(n) and GL(n)

- Logarithm does not always exists (need 2 exp to cover the group)
  - If it exists, it is unique if no complex eigenvalue on the negative real line
- **Generalization of geometric mean**

Example mean of 2D rigid-body transformation

$$T_1 = \left(\frac{\pi}{4}; -\frac{\sqrt{2}}{2}; \frac{\sqrt{2}}{2}\right) \quad T_2 = (0; \sqrt{2}; 0) \quad T_3 = \left(-\frac{\pi}{4}; -\frac{\sqrt{2}}{2}; -\frac{\sqrt{2}}{2}\right)$$

- Metric at Identity: $dist(Id,(\theta;t_1;t_2))^2 = \theta^2 + t_1^2 + t_2^2$
- Left-invariant Fréchet mean: $(0;0;0)$
- Log-Euclidean mean: $\left(0; \frac{\sqrt{2}-\pi/4}{3}; 0\right) \simeq (0; 0.2096; 0)$
- Bi-invariant mean: $\left(0; \frac{\sqrt{2}-\pi/4}{1+\pi/4(\sqrt{2}+1)}; 0\right) \simeq (0; 0.2171; 0)$
- Right-invariant Fréchet mean: $\left(0; \frac{\sqrt{2}}{3}; 0\right) \simeq (0; 0.4714; 0)$

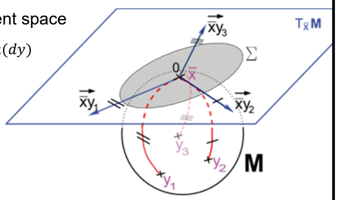
Generalization of the Statistical Framework

Covariance matrix & higher order moments

- Defined as tensors in tangent space

$$\Sigma = \int Log_x(y) \otimes Log_x(y)\, \mu(dy)$$

- Matrix expression changes according to the basis



Other statistical tools

- Mahalanobis distance well defined and bi-invariant

$$\mu_{(m,\Sigma)}(g) = \int [Log_m(g)]^i \Sigma_{ij}^{(-1)} [Log_m(g)]^j \mu(dy)$$

- ~~Tangent Principal Component Analysis (t-PCA)~~
- Principal Geodesic Analysis (PGA), provided a data likelihood
- Independent Component Analysis (ICA)

Cartan Connections vs Riemannian

What is similar

- Standard differentiable geometric structure [curved space without torsion]
- Normal coordinate system with Exp_x et 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
- Global existence and uniqueness of bi-invariant mean?
  Use a bi-invariant pseudo-Riemannian metric? [Miolane MaxEnt 2014]

What we gain

- A globally invariant (composition & inversion) symmetric space structure
- Simple geodesics, efficient computations (stationarity, group exponential)
- The simplest linearization of transformations for statistics?

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- The SVF framework for diffeomorphisms

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Riemannian Metrics on diffeomorphisms

Space of deformations

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

Right invariant metric $\|v_t\|_{\phi_t} = \|v_t \circ \phi_t^{-1}\|_{Id}$

- Eulerian scheme
- Sobolev Norm H_k or H_∞ (RKHS) in LDDMM → diffeomorphisms [Miller, Trouve, Younes, Holm, Dupuis, Beg… 1998 – 2009]

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 for images is quite tricky (and lenghty)

Log-Euclidean Framework

Log-Euclidean processing of tensors

[Arsigny et al, MRM'06, SIAM'6]

- Idea: one-to-one correspondence of tensors with symmetric matrices, via the matrix logarithm.
- Simple processing of tensors via their logarithm (vector space)!
- Consistency with group structure (e.g., inversion-invariance)

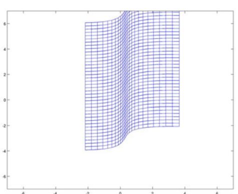
Log-Euclidean processing of linear transformations

[Arsigny et al, WBIR'06, Commowick, ISBI'06, Alexa et al, SIGGRAPH'02]

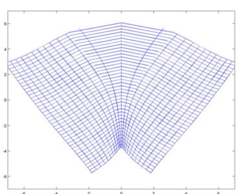
- Idea: linearize geometrical transformations close enough to identity via matrix logarithm [restriction to data whose logarithm is well-defined]
- Simply process transformations via their logarithm (vector space)!
- E.g., fuse local linear transformations into global invertible deformations.

Use the group exp/log to map the group to its Lie Algebra

Examples: Polyaffine Transformations



Fusing two translations



Fusing two rotations

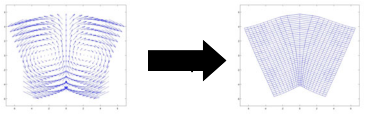
[Arsigny, Pennec, Ayache, Medical Image Analysis, 9(6):507-523, Dec. 2005]

[Arsigny et al WBIR'06]

The SVF framework for Diffeomorphisms

Idea: **[Arsigny MICCAI 2006, Bossa MICCAI 2007, Ashburner Neuroimage 2007]**

- Exponential of a smooth vector field is a diffeomorphism
- **Parameterize deformation by ~~time-varying~~ Stationary Velocity Fields**



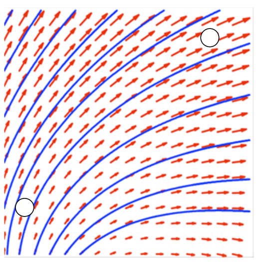
Stationary velocity field — Diffeomorphism

Direct generalization of numerical matrix algorithms

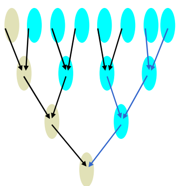
- Computing the deformation: **Scaling and squaring** **[Arsigny MICCAI 2006]**
  recursive use of exp($\boldsymbol{v}$)=exp($\boldsymbol{v}$/2) o exp($\boldsymbol{v}$/2)
- Updating the deformation parameters: **BCH formula** **[Bossa MICCAI 2007]**
  exp($\boldsymbol{v}$) ○ exp($\varepsilon\boldsymbol{u}$) = exp($\boldsymbol{v} + \varepsilon\boldsymbol{u}$ + [$\boldsymbol{v}$,$\varepsilon\boldsymbol{u}$]/2 + [$\boldsymbol{v}$,[$\boldsymbol{v}$,$\varepsilon\boldsymbol{u}$]]/12 + …)
  - Lie bracket [$\boldsymbol{v}$,$\boldsymbol{u}$](p) = Jac($\boldsymbol{v}$)(p).$\boldsymbol{u}$(p) - Jac($\boldsymbol{u}$)(p).$\boldsymbol{v}$(p)

Computing the exponential

exp($\boldsymbol{u}$) = exp($\boldsymbol{u}/N$) ^{N}



$$\frac{\partial x}{\partial t} = v(x)$$
$$x(0) = x_0$$
$$x(1) = \int_0^1 v(x(t))dt$$
$$\triangleq \exp(v)$$



exp($\boldsymbol{v}$/8) ≈ Id + $\boldsymbol{v}$/8

exp($\boldsymbol{v}$/4) = exp($\boldsymbol{v}$/8)²

exp($\boldsymbol{v}$/2) = exp($\boldsymbol{v}$/4)²

exp($\boldsymbol{v}$)

[V. Arsigny, O. Commowick, X. Pennec, N. Ayache. A Log-Euclidean Framework for Statistics on Diffeomorphisms. In Proc. of MICCAI'06, LNCS 4190, pages 924-931, 2-4 October 2006.]

Symmetric log-demons [Vercauteren MICCAI 08]

Idea: **[Arsigny MICCAI 2006, Bossa MICCAI 2007, Ashburner Neuroimage 2007]**

- 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

$$\mathcal{E}(\mathbf{v},\mathbf{v}_c) = \underbrace{\frac{1}{\sigma_i^2}\|F - M \circ \exp(\mathbf{v}_c)\|^2_{L_2}}_{\text{Similarity}} + \underbrace{\frac{1}{\sigma_x^2}\|\log(\exp(-\mathbf{v}) \circ \exp(\mathbf{v}_c))\|^2_{L_2}}_{\text{Coupling}} + \underbrace{\mathcal{R}(\mathbf{v})}_{\text{Regularisation}}$$

Similarity — *Measures how much the two images differ*

Coupling — *Couples the correspondences with the smooth deformation*

Regularisation — *Ensures deformation smoothness*

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

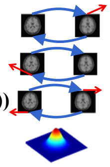
[T Vercauteren, et al.. *Symmetric Log-Domain Diffeomorphic Registration: A Demons-based Approach*, MICCAI 2008]

Symmetric Log-Domain Demons

Use easy inverse: $T^{-1} = \exp(-v)$

Iteration

- Given images I_0, I_1 and current transformation $T=\exp(v)$
- Forward demons forces u^{forw}
- Backward demons forces u^{back}
- Update $v_c \leftarrow ½ \,(\,BCH(v,u^{forw}) - BCH(-v,u^{back}))$
- Regularize (Gaussian): $v \leftarrow K_{diff} * v_c$



Open-source ITK implementation

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[T Vercauteren, et al.. *Symmetric Log-Domain Diffeomorphic Registration: A Demons-based Approach*, MICCAI 2008]

MVA 2023-2024 47

Statistical Computing on Manifolds for Computational Anatomy

Metric and Affine Geometric Settings for Lie Groups

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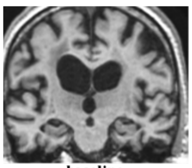
MVA 2023-2024 48

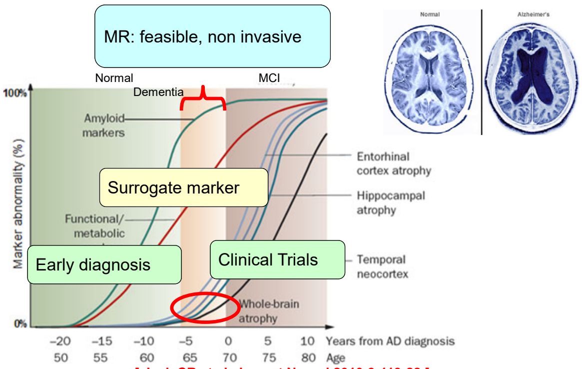
Alzheimer's Disease

- Most common form of dementia
- 18 Million people worldwide
- Prevalence in advanced countries
  - 65-70: 2%
  - 70-80: 4%
  - 80 - : 20%
- If onset was delayed by 5 years, number of cases worldwide would be halved


baseline

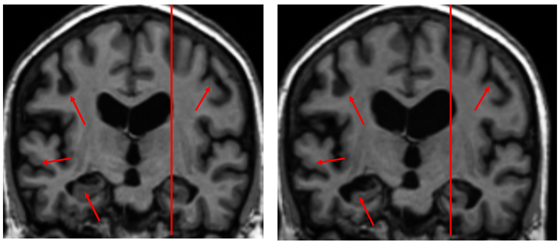
MVA 2023-2024 49

Natural progression of Alzheimer's disease



[Jack CR et al., Lancet Neurol 2010;9:119-28]

Longitudinal structural damage in AD



baseline 2 years follow-up

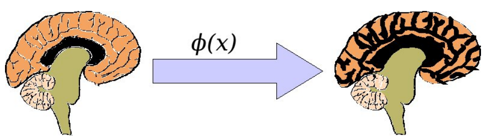
Widespread cortical thinning

PhD Marco Lorenzi - Collaboration With G. Frisoni (IRCCS FateBenefratelli, Brescia)

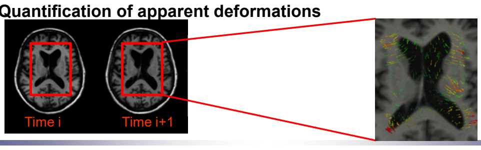
Individual Measure of Temporal Evolution

Geometry changes (Deformation-based morphometry)

- Measure the physical or apparent deformation through registration



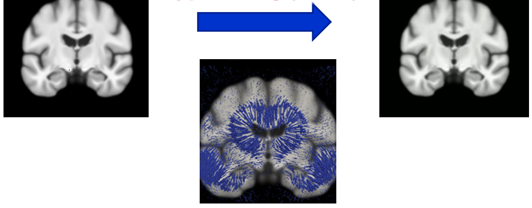
Quantification of apparent deformations



Measuring Temporal Evolution with deformations: Deformation-based morphometry

Fast registration with deformation parameterized by SVF

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

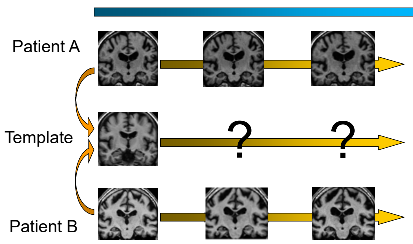


https://team.inria.fr/asclepios/software/lcclogdemons/

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

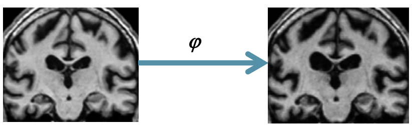
Longitudinal deformation analysis in AD

- 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

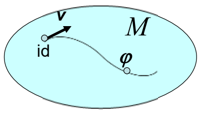


PhD Marco Lorenzi - Collaboration With G. Frisoni (IRCCS FateBenefratelli, Brescia)

Parallel transport of deformation trajectories



SVF setting
- ***v stationary*** *velocity field*
- *Lie group Exp(v) non-metric geodesic wrt Cartan connections*



LDDMM setting
- ***v time-varying*** *velocity field*
- *Riemannian $exp_{id}(v)$ metric geodesic wrt Levi-Civita connection*
- *Defined by* ***intial momentum***

Transporting trajectories:

Parallel transport of initial tangent vectors

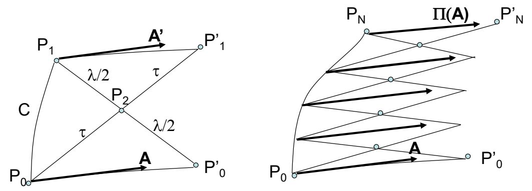
LDDMM: parallel transport along geodesics using Jacobi fields [Younes et al. 2008]

From gravitation to computational anatomy: Parallel transport along arbitrary curves

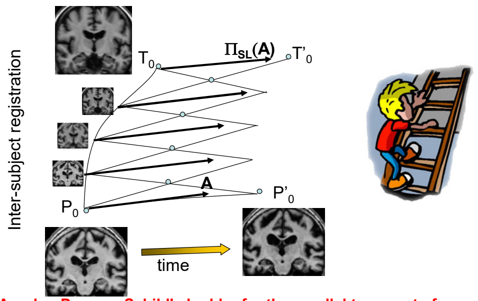
Infinitesimal parallel transport = connection $\nabla_\gamma(X) : TM \rightarrow TM$

A numerical scheme to integrate symmetric connections: Schild's Ladder [Elhers et al, 1972]

- Build geodesic parallelogrammoid
- Iterate along the curve



Schild's Ladder
Intuitive application to images



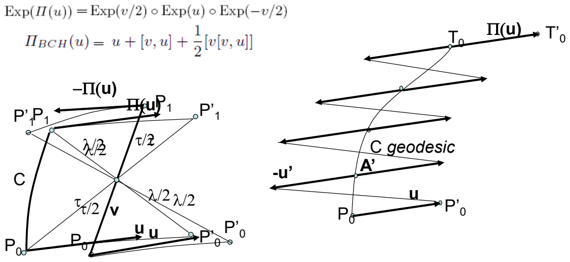
[Lorenzi, Ayache, Pennec: Schild's Ladder for the parallel transport of deformations in time series of images, IPMI 2011]

Parallel transport along geodesics

Simpler scheme along geodesics: Pole Ladder

$$\mathrm{Exp}(\Pi(u)) = \mathrm{Exp}(v/2) \circ \mathrm{Exp}(u) \circ \mathrm{Exp}(-v/2)$$

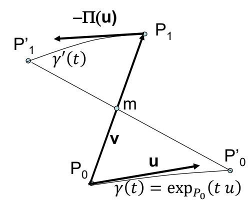
$$\Pi_{BCH}(u) = u + [v, u] + \frac{1}{2}[v[v, u]]$$



[Lorenzi, Pennec: Efficient Parallel Transport of Deformations in Time Series of Images: from Schild's to pole Ladder, JMIV 50(1-2):5-17, 2013]

Parallel transport along geodesics

Simpler scheme along geodesics: Pole Ladder



Numerical accuracy of pole ladder

- Order 4 in general affine manifolds

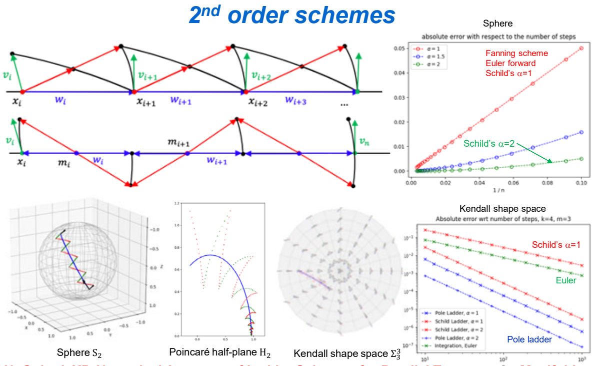
$$\text{pole}(u) = \Pi(u) + \frac{1}{12}\nabla_v R(u,v)(5u - 2v) + \frac{1}{12}\nabla_u R(u,v)(v - 2u) + O(5)$$

- Error vanishes in symmetric spaces:

Pole ladder is exact in 1 step!

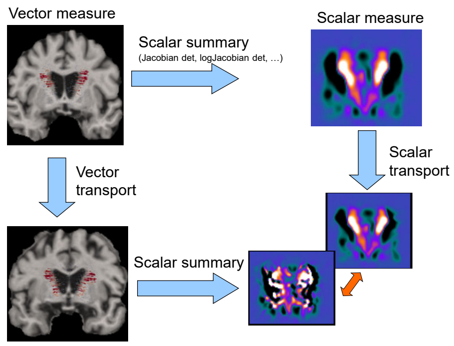
[XP. Parallel Transport with Pole Ladder: a Third Order Scheme in Affine Connection Spaces which is Exact in Affine Symmetric Spaces. Arxiv 1805.11436]

Discrete ladders with approximate geodesics: 2nd order schemes

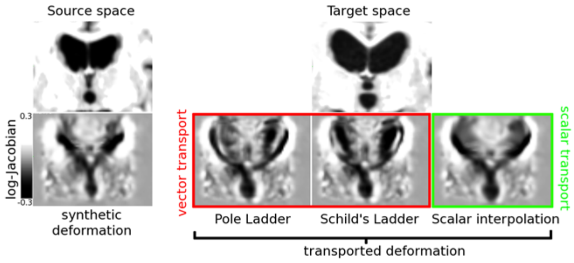


[N. Guigui, XP, Numerical Accuracy of Ladder Schemes for Parallel Transport on Manifolds. Arxiv 2007.07585. To appear in Foundations of Computational Mathematics, 2021]

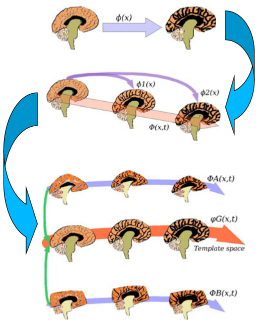
Synthetic experiments (Consistency)



Parallel Transport along SVFs



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

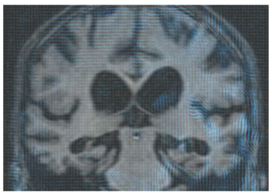
Schild's Ladder

[Lorenzi et al, in Proc. of MICCAI 2011]

Atrophy estimation for Alzheimer

Alzheimer's Disease Neuroimaging Initiative (ADNI)

- 200 NORMAL 3 years
- 400 MCI 3 years
- 200 AD 2 years
- Visits every 6 month
- 57 sites



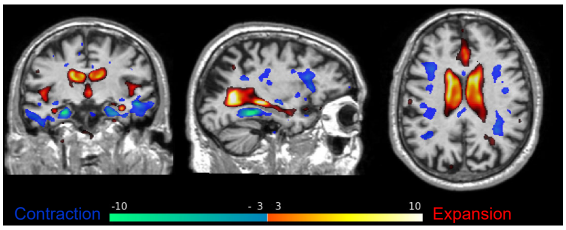
Data collected

- Clinical, blood, LP
- Cognitive Tests
- **Anatomical images:1.5T MRI** (25% 3T)
- Functional images: FDG-PET (50%), PiB-PET (approx 100)

Modeling longitudinal atrophy in AD from images

One year structural changes for 70 Alzheimer's patients

- Median evolution model and significant atrophy (FdR corrected)



[Lorenzi et al, in Proc. of IPMI 2011]

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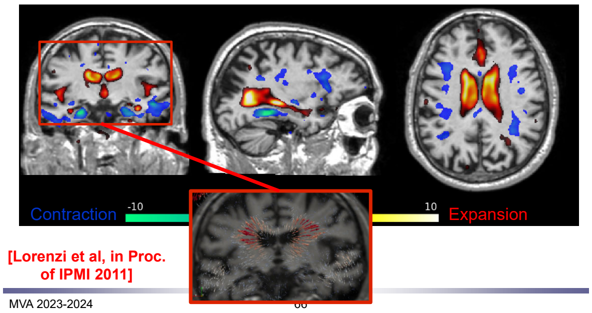

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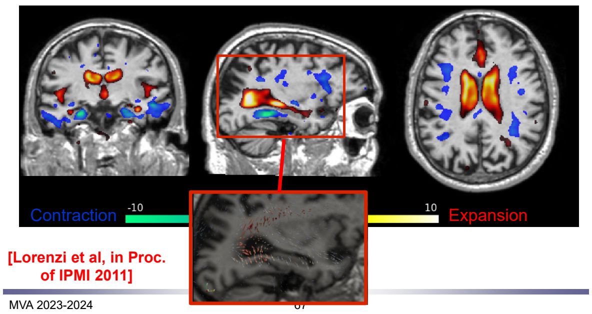

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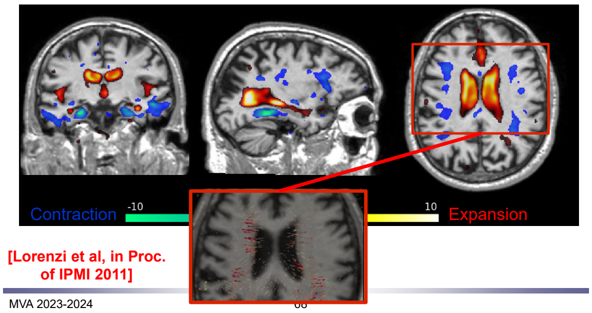
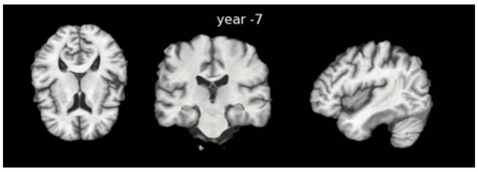
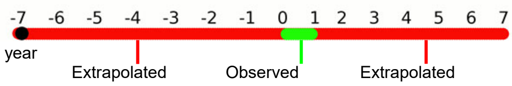


[Lorenzi et al, in Proc. of IPMI 2011]

Longitudinal model for AD

Estimated from 1 year changes – Extrapolation to 15 years
70 AD subjects (ADNI data)





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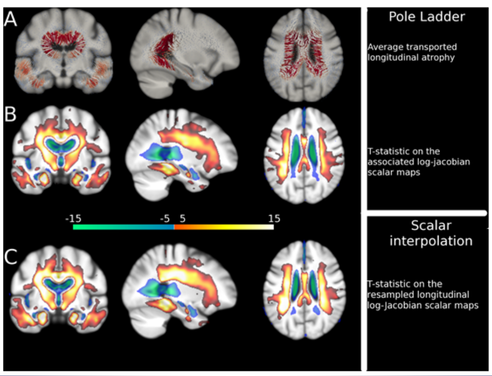
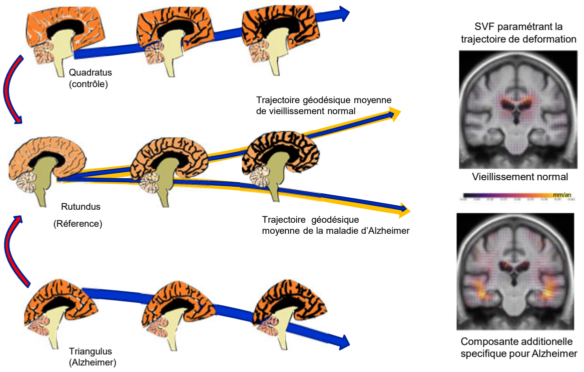
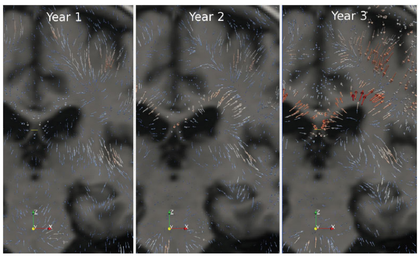


Modeling Normal and AD progression



Study of prodromal Alzheimer's disease

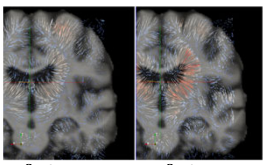
- 98 **healthy subjects**, 5 time points (0 to 36 months).
- 41 subjects Aβ42 positive ("at risk" for Alzheimer's)
- **Q: Different morphological evolution for Aβ+ vs Aβ-?**



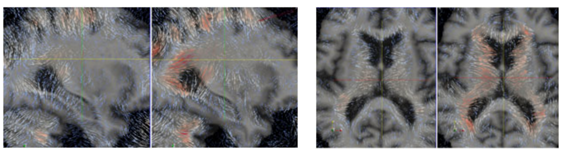
Average SVF for normal evolution (Aβ-)

[Lorenzi, Ayache, Frisoni, Pennec, in Proc. of MICCAI 2011]

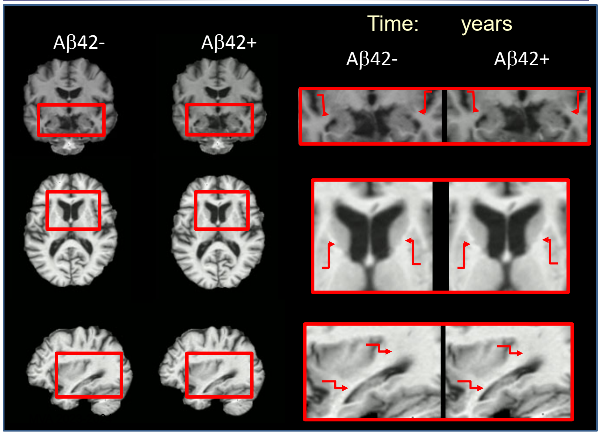
Detail: comparison between average evolutions (SVF)



Aβ42- Aβ42+

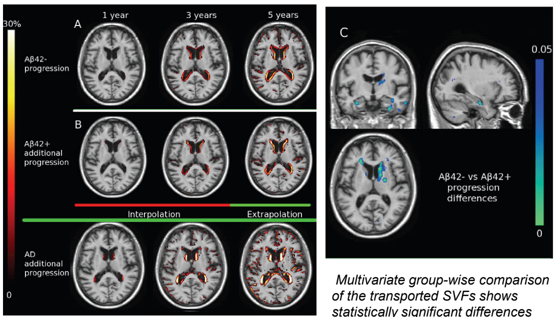


Aβ42- Aβ42+ Aβ42- Aβ42+



Study of prodromal Alzheimer's disease

Linear regression of the SVF over time: interpolation + prediction



$T(t) = Exp(\tilde{v}(t)) * T_0$

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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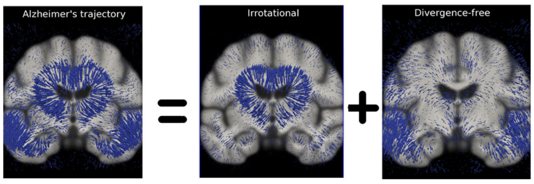
Morphological analysis of SVF



v = Volun ∇p anges $+$ $\nabla \times A$

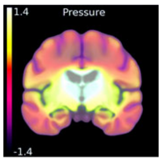
Helmholtz decomposition

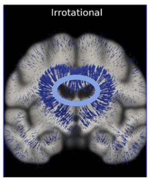
Atrophy!! Structural readjustments

Morphological analysis of SVF

Discovery

Pressure p
Defines **sources and sinks** of the atrophy process

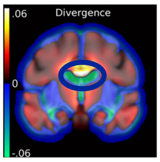




∇p

Quantification

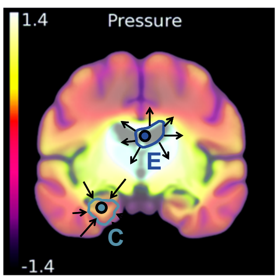
Divergence $\nabla \cdot \nabla p$
Defines **flux** across expanding/contracting regions

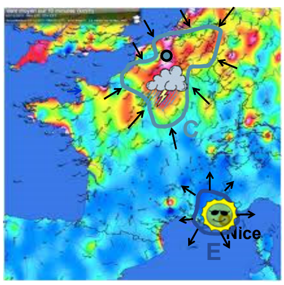


Divergence Theorem

$$\oint_{\partial V} v \cdot \boldsymbol{n}\, dS = \int_V \nabla \cdot v\, dV$$

Probabilistic definition of the atrophy topography





P(Critical area) $\approx$ Proximity to critical point + Surrounding flux

Step1. Finding local maxima and minima for the pressure field (sources,sinks)
Step2. Finding surrounding areas of maximal outwards/inwards flux (Expansion and Contraction)

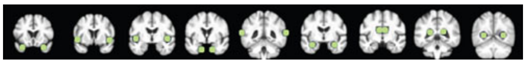
Statistics on the topology of pressure maps

Critical areas optimizing the expected flux population-wise

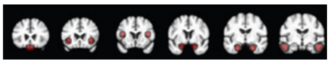
- Detect minima and maxima of mean symmetrized pressure maps
- Extend probabilistic regions to zero crossings (pressure=probability)

Critical regions for the 1-year atrophy on 20 AD patients

Expansion



Contraction

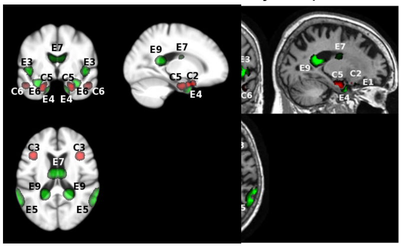


Biologically meaningful areas

- Statistics on a multiscale Morse-Smale complex?

Group-wise flux analysis in Alzheimer's
Quantification

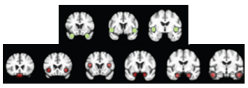
From group-wise… …to subject specific



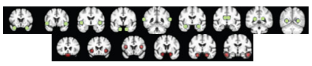
From ~10^6 voxels to 15 regions

From discovery to quantification

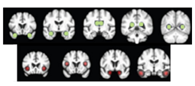
AD vs controls



MCI vs controls

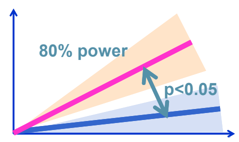


Controls Aβ42+ vs controls Aβ42-



Sample size analysis

[Fox 2000]



sample size ∝ sd/($mean_1$-$mean_2$)

	Regional flux (all regions)	Hippocampal atrophy [Leung 2010] *(Different ADNI subset)*
AD vs controls	164 [106,209]	121 [77, 206]
MCI vs controls	277 [166,555]	545 [296, 1331]

Hippocampal atrophy measures

NIBAD'12
MICCAI 2012 WORKSHOP ON NOVEL IMAGING BIOMARKERS FOR ALZHEIMER'S DISEASE AND RELATED DISORDERS

MICCAI NICE 2012

46 patients, 23 controls, blinded diagnosis
0,2,6,12,26,38 and 52 weeks scans, only baseline information
Test on intra-subject pairwise atrophy rates

Effect size on left hippocampus

Group	six months	one year	two years
INRIA - Regional Flux	1.02	1.33	1.47

Top-ranked on Hippocampal atrophy measures

Among competitors:
Freesurfer (Harvard, USA)
Montreal Neurological Institute, Canada
Mayo Clinic, USA
University College of London, UK
University of Pennsylvania, USA

Statistical Computing on Manifolds for Computational Anatomy

Metric and Affine Geometric Settings for Lie Groups
- Riemannian / affine connection frameworks on Lie groups
- Extending statistics without a metric
- The SVF framework for diffeomorphisms

Modeling longitudinal deformations in AD
- Parallel transport of deformation trajectories
- From velocity fields to AD models

Perspectives on statistics on deformation

The Stationnary Velocity Fields (SVF) framework for diffeomorphisms

- SVF framework for diffeomorphisms is algorithmically simple
- Compatible with “inverse-consistency”
- Vector statistics directly generalized to diffeomorphisms.

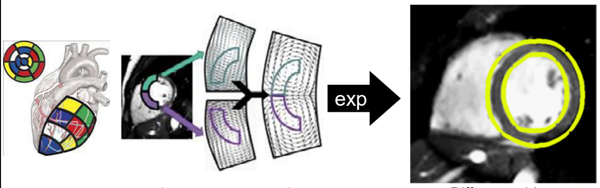
Registration algorithms using log-demons:
- Log-demons: Open-source ITK implementation (Vercauteren MICCAI 2008)
  http://hdl.handle.net/10380/3060
  [MICCAI Young Scientist Impact award 2013]
- Tensor (DTI) Log-demons (Sweet WBIR 2010):
  https://gforge.inria.fr/projects/ttk
- LCC log-demons for AD (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)
  http://www.stanford.edu/~cseiler/software.html
  [MICCAI 2011 Young Scientist award]

A powerful framework for statistics

Parametric diffeomorphisms [Arsigny et al., MICCAI 06, JMIV 09]

- One affine transformation per region (polyaffines transformations)
- Cardiac motion tracking for **each subject** [McLeod, Miccai 2013]

Log demons projected but with 204 parameters instead of a few millions



A powerful framework for statistics

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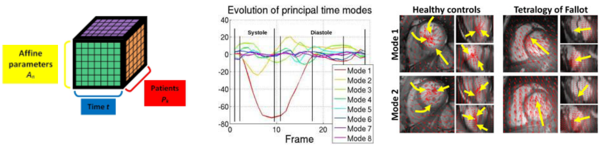
Log demons projected but with 204 parameters instead of a few millions

- **Group analysis** using tensor reduction : reduced model

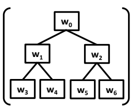
8 temporal modes x 3 spatial modes = 24 parameters (instead of 204)



Hierarchical Deformation model

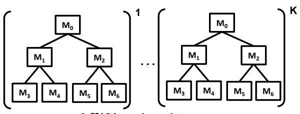
Population level:

Spatial structure of the anatomy common to all subjects

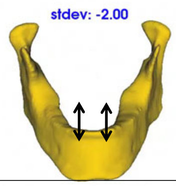


Subject level:

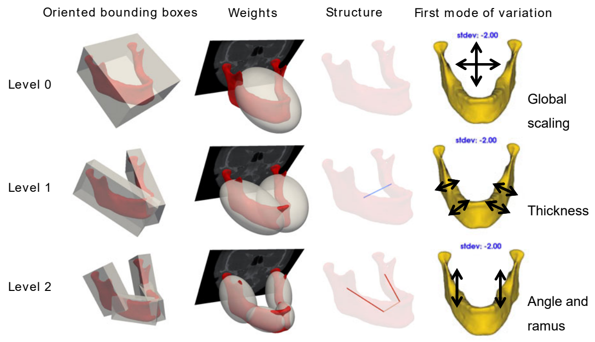
Varying deformation atoms for each subject



Aff(3) valued trees

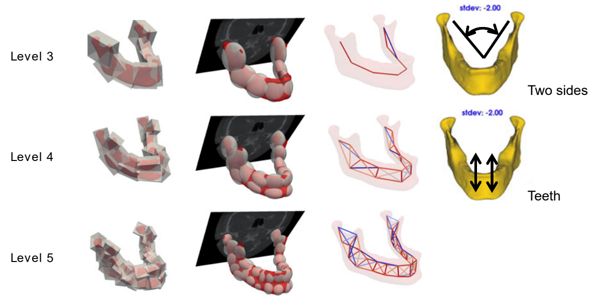


Hierarchical Estimation of the Variability



47 subjects [Seiler, Pennec, Reyes, Medical Image Analysis 16(7):1371-1384, 2012]

Hierarchical Estimation of the Variability

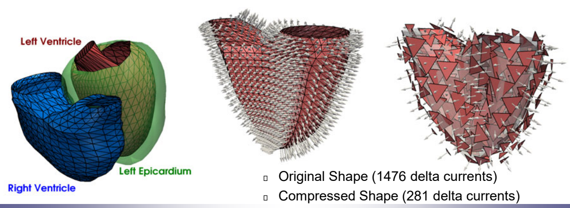


47 subjects [Seiler, Pennec, Reyes, Medical Image Analysis 16(7):1371-1384, 2012]

Towards more complex geometries?

Statistics on surfaces seen as currents / varifolds

- Characterize curves or surfaces by the flux (along or through them) of all smooth vector fields (in a RKHS)
- Extrinsinc statistical analysis in space of currents (mean, PCA) [Durrleman et al, MFCA 2008] (**mean current is not a surface**)
- Need for sub-Riemannian geometry



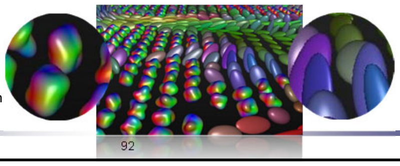
- Original Shape (1476 delta currents)
- Compressed Shape (281 delta currents)

Towards more complex geometries?

Non quadratic metric: Statistics on Finsler spaces?

[Image from Sepasian, Thije Boonkkamp, Florack, Ter Haar Romeny, Vilanova Riemann-Finsler Multi-valued Geodesic Tractography for HARDI]

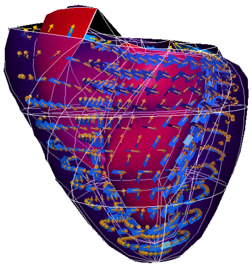
Finsler manifold-valued image processing?

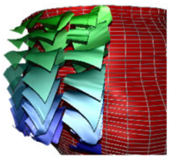


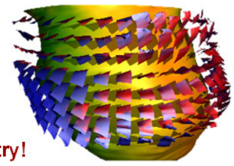
[Image shamelessly stolen from Luc Florac's talk]

Towards more complex geometries?

Laminar sheets in the myocardium:







→ Torsion: Non-integrable geometry!

Geometric Statistics for anatomical shapes

Study geometric structures
- Riemannian, Finsler, affine, bundles, Lie groups

Generalize statistics
- Real data have noise
- Approximate invariance, factor analysis…

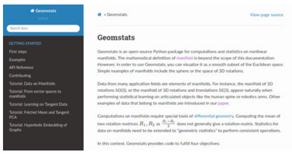
Design algorithm
- Dimension reduction, Image processing…

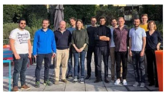
With important medical applications
- Heart, brain diseases

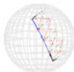
http://geomstats.ai : a python library to implement generic algorithms on many Riemannian manifolds

pypi package 2.2.0 | build passing | codecov 92%

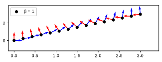
- Mean, PCA, clustering, **parallel transport**…
- 15 manifolds / Lie groups already implemented (SPD, H(n), SE(n), etc)
- **Generic manifolds with geodesics by integration / optimization**
- scikit-learn API (hide geometry, compatible with GPU & learning tools).
- 10 introductory tutorials
- ~ 35000 lines of code
- ~30 academic developers
- 7 hackathons organized in 2020-2022
- Last one: **17-21 October 2022 IHP, Paris**



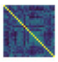




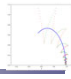
Schild's/pole Ladders



Rotations-Translations



SPD



**[Miolane et al, JMLR 2020, Scipy 2020
Guigui et al, FnT in Mach. Learning 2023]**

Pushing the frontiers of Geometric Statistics

Beyond the Riemannian / metric structure
- Riemannian manifolds, Non-Positively Curved (NPC) metric spaces
- **Affine connection, Quotient, Stratified spaces (trees, graphs)**

Beyond the mean and unimodal concentrated laws
- **Nested sequences (flags) of subspace in manifolds**
- A continuum from PCA to Principal Cluster Analysis?

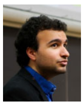
Geometrization of statistics
- Geometry of the space of samples
  - Smooth manifolds with rough boundaries
- Explore **influence of curvature, singularities** (borders, corners, stratifications) on non-asymptotic estimation theory

erc Geometric Statistics

Make G-Statistics an effective discipline for life sciences

The G-Statistics groups

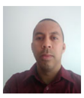
erc Geometric Statistics



Yann Thanwerdas

Nicolas Guigui

Morten Pedersen



Dimbihery Rabenoro

Anna Calissano

James Benn

Elodie Maignant

Luis G. Pereira

Tom Szwagier

Internship + PhD positions available