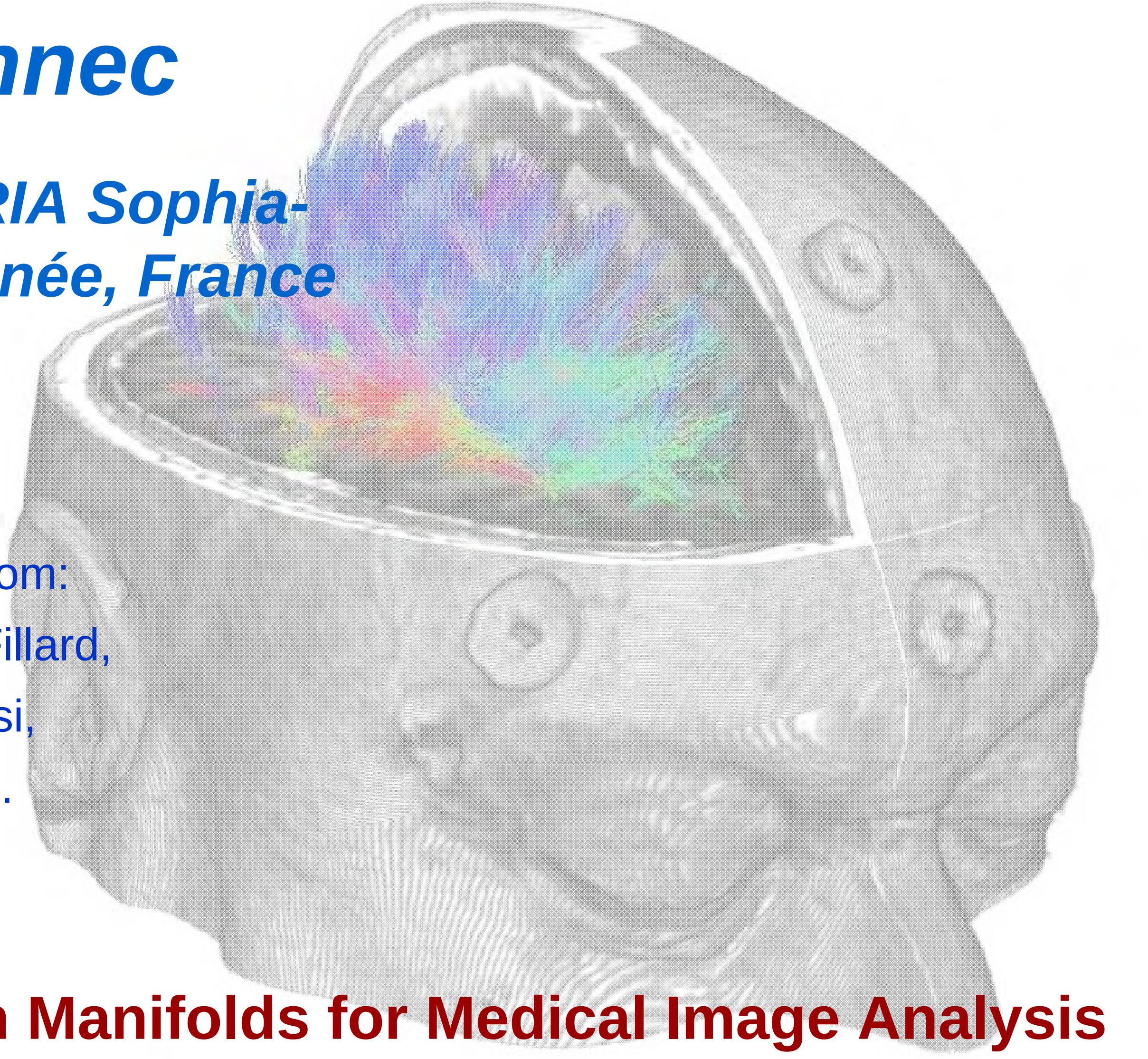
Xavier Pennec

Asclepios team, INRIA Sophia-Antipolis – Mediterranée, France



With indebting contributions from:

S. Durrleman, M. Lorenzi, P. Fillard,

V. Arsigny, J. Boisvert, T. Mansi,

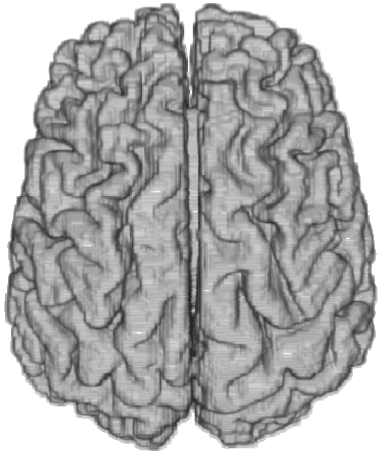
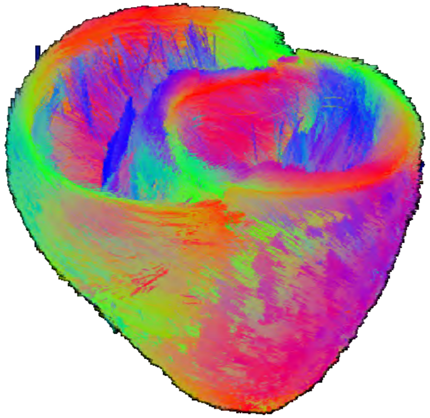
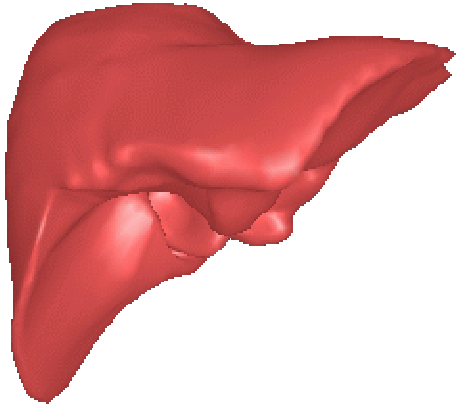
Nicholas Ayache, and others…

Statistical Analysis on Manifolds for Medical Image Analysis

Fields-MITACS Conf. on Mathematics of Medical Imaging– June 22, 2011

INRIA SOPHIA ANTIPOLIS

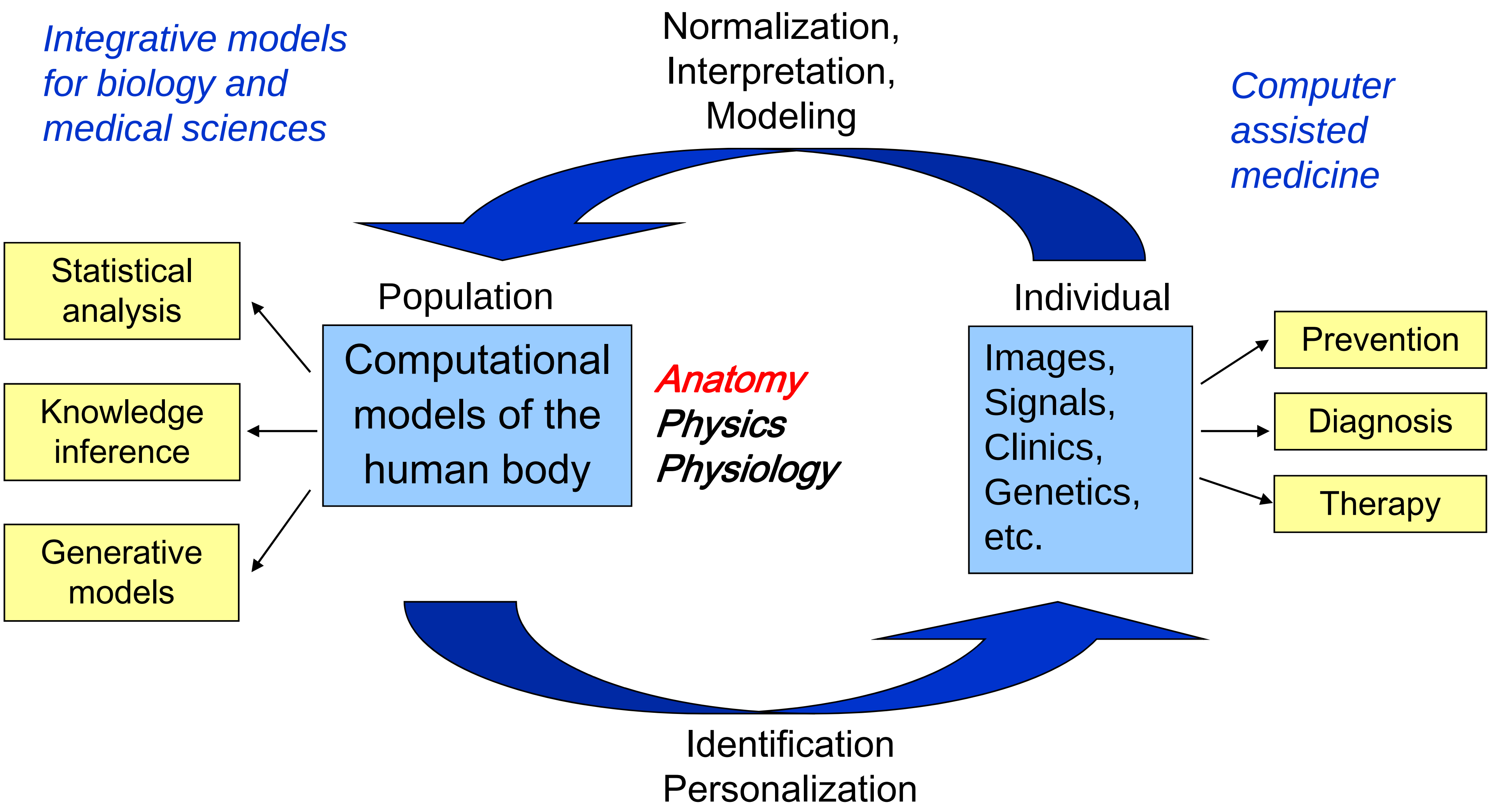
Computational Anatomy

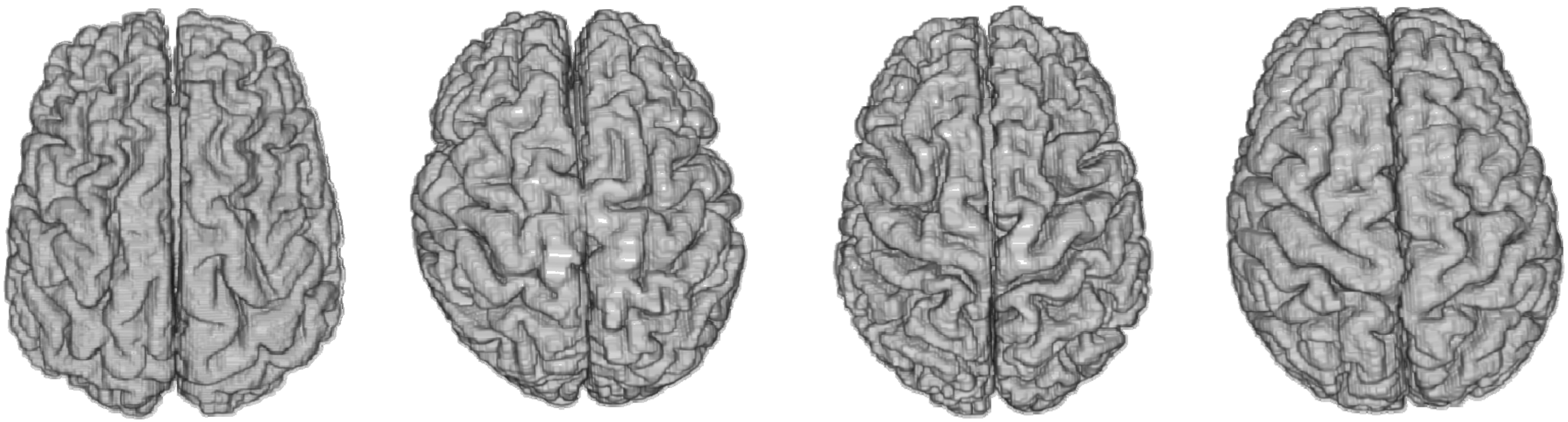
Design Mathematical Methods and Algorithms to Model and Analyze the Anatomy

- Statistics of organ shapes across species, populations, diseases…
- Model organ development across time (heart-beat, growth, ageing, ages…)
- To understand and to model the substrate of life
  - 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
  - UCLA summer school 04 & 08, MFCA06, 08 & 11 workshops

Statistical analysis, modeling and applications

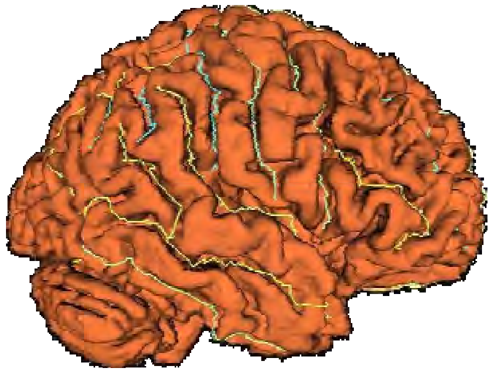


Methods of computational anatomy

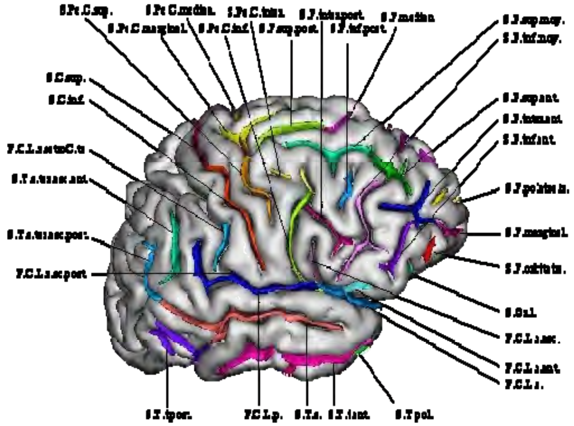


Structural variability of the cortex

- Hierarchy of anatomical features (structural models)
- Group-wise correspondences in the population
- Model observations and its structural variability

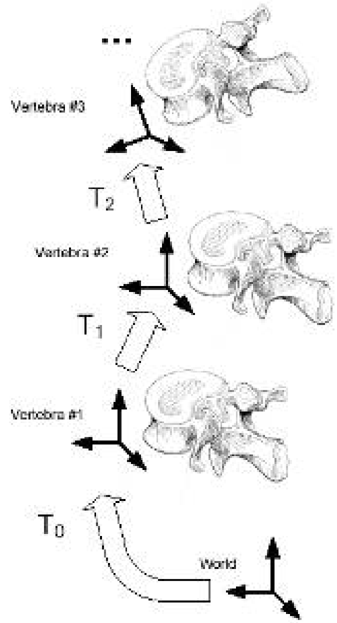


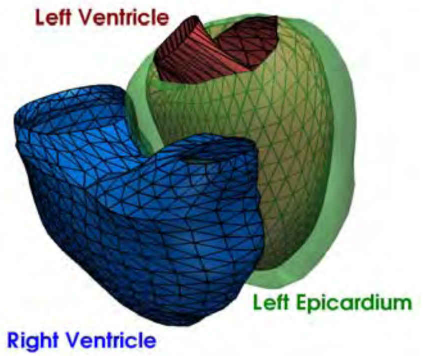
Statistical Analysis of Geometric Features

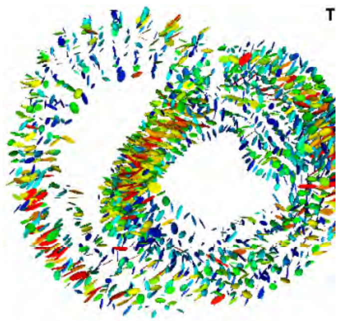


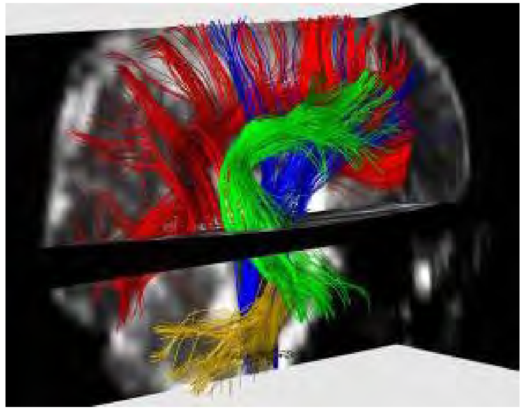
Geometric features belong to manifolds

- Curves, tracts
- Surfaces
- Tensors, covariance matrices
- Transformations / deformations









Algorithms for statistics on geometric manifolds

- Definition of mean / covariance / PCA / distributions of geometric features?
- Mathematical structure = algorithmic bases

Roadmap

Goals and methods of Computational anatomy

Statistical computing on manifolds

- The mathematical framework
  - Simple statistics on Riemannian manifolds
  - Extension to manifold-values images

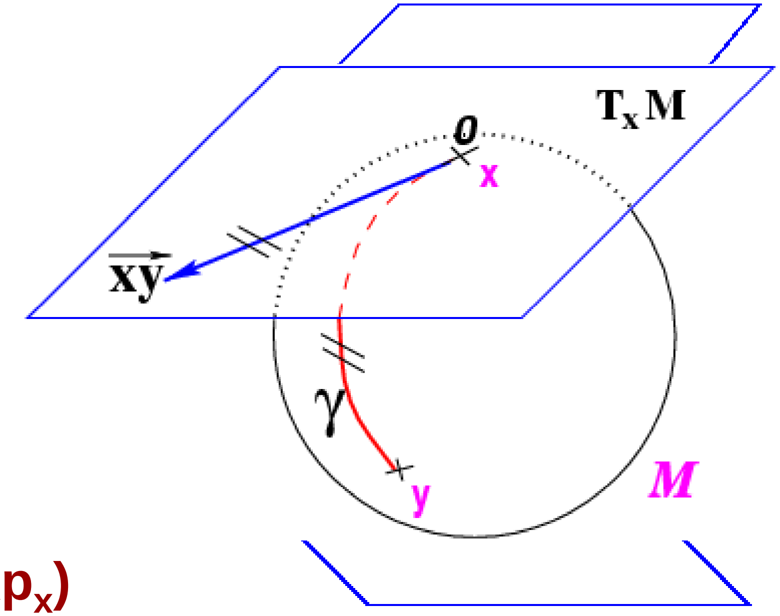
Statistics on shapes through deformations

Conclusion and challenges

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 map (Normal coord. syst.) :

- Geodesic shooting: $Exp_x(v) = \gamma_{(x,v)}(1)$
- Log: find vector to shoot right

Basic tools: Unfolding (Log_x), folding (Exp_x)

- Vector -> Bipoint (no more equivalent class)

Operator	Euclidean space	Riemannian manifold
Subtraction	$\overrightarrow{xy} = y - x$	$\overrightarrow{xy} = Log_x(y)$
Addition	$y = x + \overrightarrow{xy}$	$y = Exp_x(\overrightarrow{xy})$
Distance	$\text{dist}(x, y) = \lVert y - x \rVert$	$\text{dist}(x, y) = \lVert \overrightarrow{xy} \rVert_x$
Gradient descent	$x_{t+\varepsilon} = x_t - \varepsilon \nabla C(x_t)$	$x_{t+\varepsilon} = Exp_{x_t}(-\varepsilon \nabla C(x_t))$

Statistical tools: Moments

Definition: Frechet / Karcher mean minimize the variance

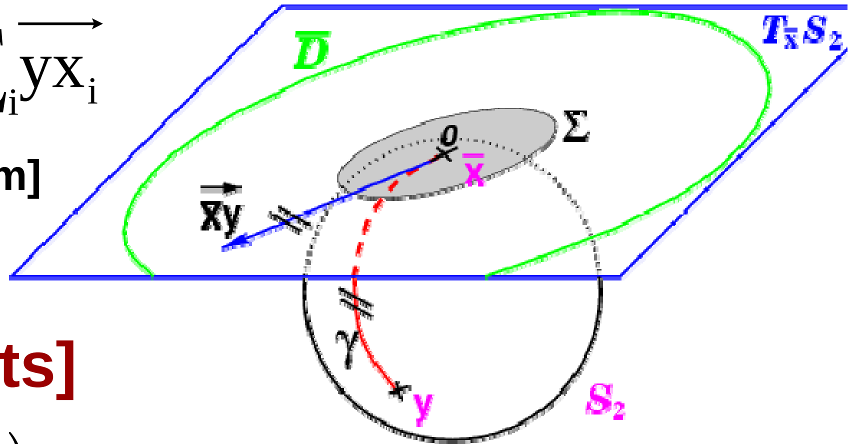
$$\mathrm{E}[\mathbf{x}] = \underset{y \in \mathcal{M}}{\operatorname{argmin}} \left(\mathrm{E}\left[\operatorname{dist}(y, \mathbf{x})^2 \right] \right) \quad \Rightarrow \quad \mathrm{E}\left[\overrightarrow{\bar{\mathrm{x}}\mathbf{x}} \right] = \int_{\mathcal{M}} \overrightarrow{\bar{\mathrm{x}}\mathbf{x}}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

Existence and uniqueness : Karcher and Kendall

Algorithm: Gauss-Newton Geodesic marching

$$\bar{\mathrm{x}}_{t+1} = \exp_{\bar{\mathrm{x}}_t}(v) \quad \text{with} \quad v = \mathrm{E}\left[\overrightarrow{\mathrm{y}\mathbf{x}} \right] = \frac{1}{n} \sum_{\mathrm{i}} \overrightarrow{\mathrm{y}\mathrm{x}_{\mathrm{i}}}$$

[Fletcher: Median / Arnaudon: stochastic algortithm]



Covariance (PCA) [higher moments]

$$\Sigma_{\mathbf{xx}} = \mathrm{E}\left[\left(\overrightarrow{\bar{\mathrm{x}}\mathbf{x}} \right) . \left(\overrightarrow{\bar{\mathrm{x}}\mathbf{x}} \right)^{\mathrm{T}} \right] = \frac{1}{n} \sum_i \left(\overrightarrow{\bar{\mathrm{x}}\mathrm{x}_{\mathrm{i}}} \right) . \left(\overrightarrow{\bar{\mathrm{x}}\mathrm{x}_{\mathrm{i}}} \right)^{\mathrm{T}}$$

[Oller & Corcuera 95, Battacharya & Patrangenaru 02, Pennec 96, NSIP'99, JMIV06]

Distributions for parametric tests

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

$$N(y) = k.\exp\left(\left(\overrightarrow{\bar{\mathrm{x}}\mathbf{x}}\right)^{\mathrm{T}}.\mathbf{\Gamma}.\left(\overrightarrow{\bar{\mathrm{x}}\mathbf{x}}\right)/2\right)$$

$$\mathbf{\Gamma} = \mathbf{\Sigma}^{(-1)} - \tfrac{1}{3}\mathrm{Ric} + O(\sigma) + \varepsilon(\sigma / r)$$

$$k = (2\pi)^{-n/2}.\det(\mathbf{\Sigma})^{-1/2}.\left(1 + O(\sigma^3) + \varepsilon(\sigma / r)\right)$$

Mahalanobis D2 distance / test:

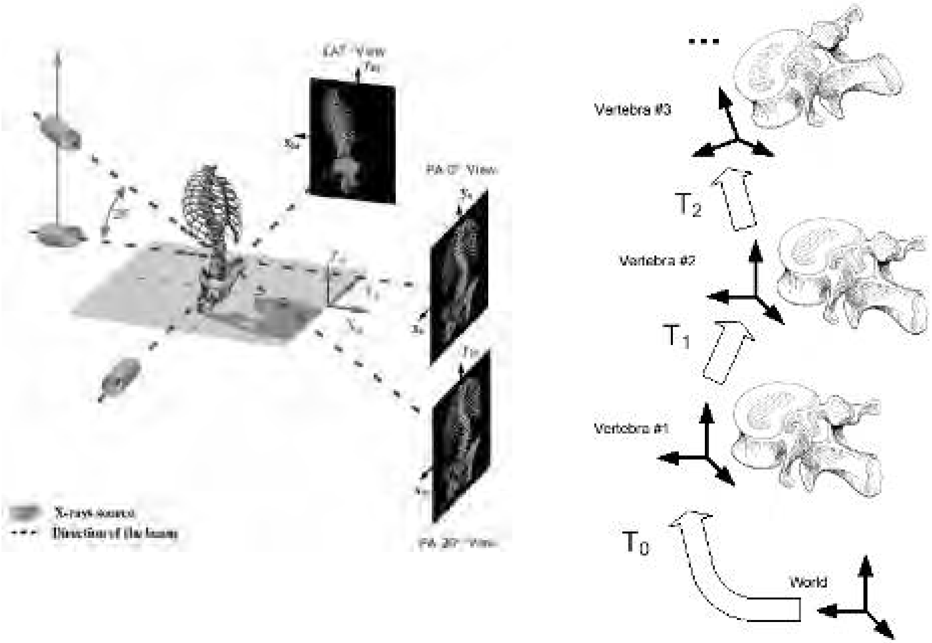
$$\mu_{\mathbf{x}}^2(\mathrm{y}) = \overrightarrow{\bar{\mathrm{x}}\mathrm{y}}^t.\Sigma_{\mathbf{xx}}^{(-1)}.\overrightarrow{\bar{\mathrm{x}}\mathrm{y}}$$

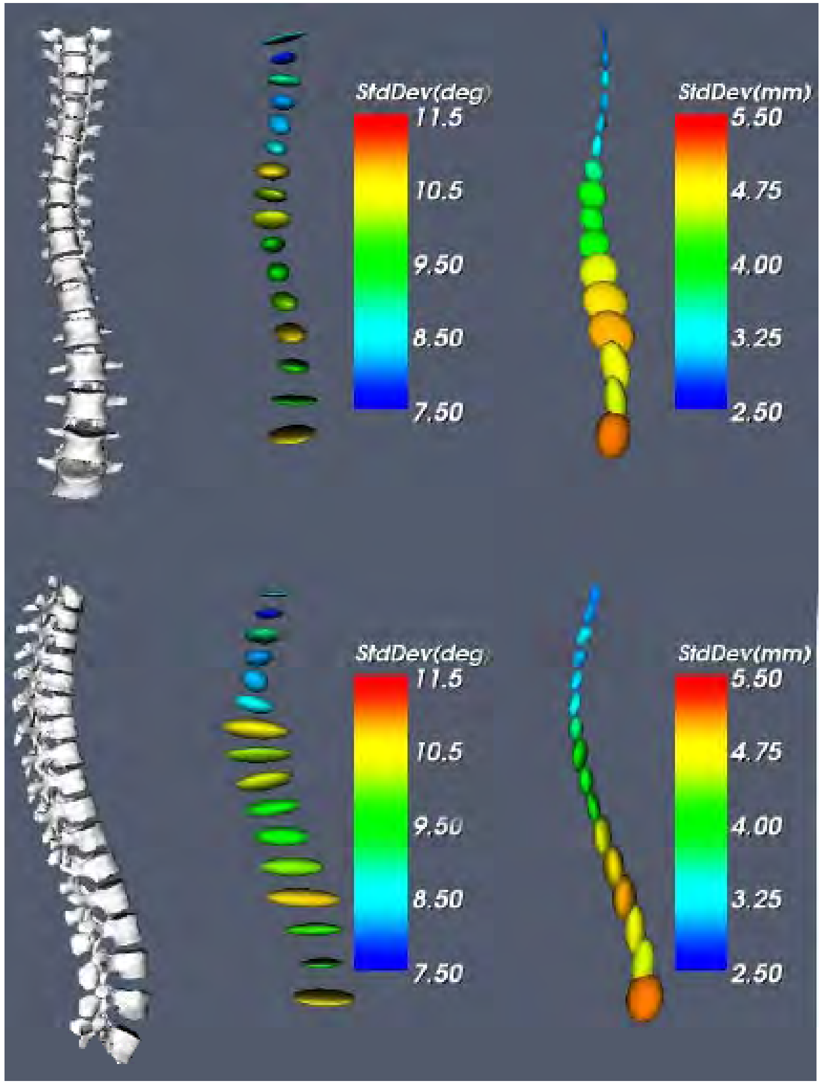
- Any distribution: $\mathrm{E}\left[\mu_{\mathbf{x}}^2(\mathbf{x})\right] = n$
- Gaussian: $\mu_{\mathbf{x}}^2(\mathbf{x}) \propto \chi_n^2 + O(\sigma^3) + \varepsilon(\sigma / r)$

[Pennec, RR-5093 1999, NSIP'99 JMIV06]

Statistical Analysis of the Scoliotic Spine

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





Database

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

Mean

- Main translation variability is axial (growth?)
- Main rot. var. around anterior-posterior axis

Statistical Analysis of the Scoliotic Spine

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

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

- Mode 1: King's class I or III
- Mode 2: King's class I, II, III
- Mode 3: King's class IV + V
- Mode 4: King's class V (+II)

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Conclusion and challenges

Diffusion Tensor Imaging

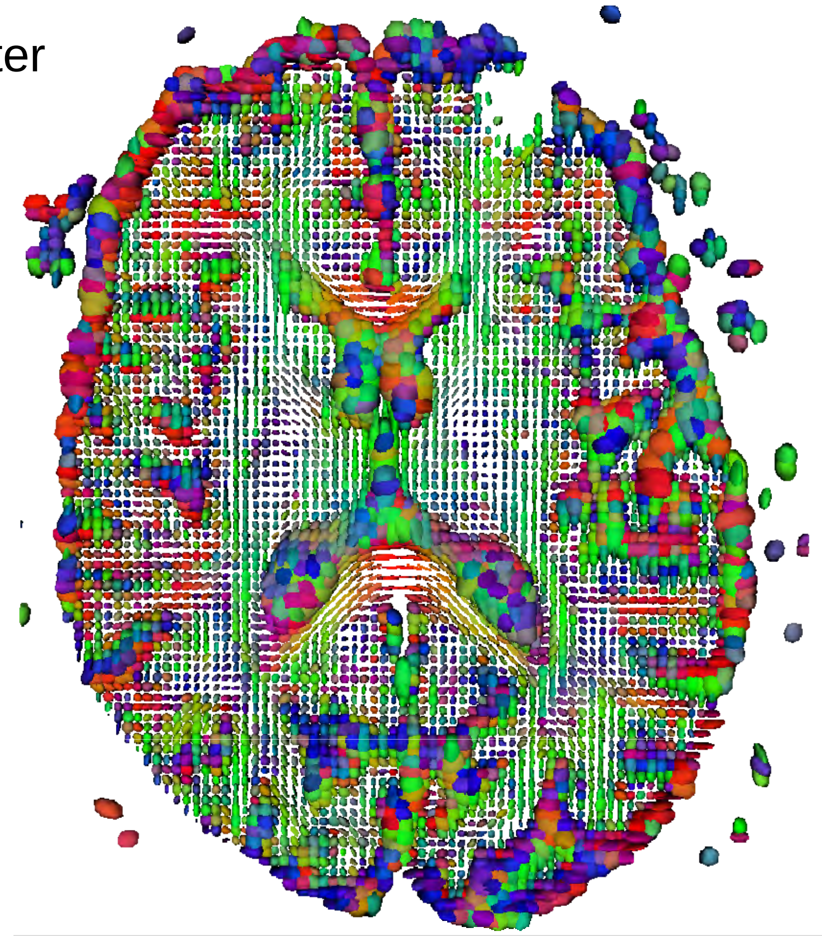
Covariance of the Brownian motion of water
-> Architecture of axonal fibers

Very noisy data

- Tensor image processing
  - Robust estimation
  - Filtering, regularization
  - Interpolation / extrapolation
- Information extraction (fibers)

Symmetric positive definite matrices

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



Diffusion Tensor Filed
(slice of a 3D volume)

Intrinsic computing on Manifold-valued images?

Riemannian Frameworks on tensors

Affine-invariant Metric (homogeneous manifold – Hadamard space)

- Dot product $\langle V \mid W \rangle_\Sigma = \langle AVA^T \mid AWA^T \rangle_{A\Sigma A^T} = \langle \Sigma^{-1/2} V \Sigma^{-1/2} \mid \Sigma^{-1/2} W \Sigma^{-1/2} \rangle_{Id}$
- Geodesics $Exp_\Sigma(\overrightarrow{\Sigma\Psi}) = \Sigma^{1/2} \exp(\Sigma^{-1/2}.\overrightarrow{\Sigma\Psi}.\Sigma^{-1/2})\Sigma^{1/2}$
- Distance $\mathrm{dist}(\Sigma, \Psi)^2 = \langle \overrightarrow{\Sigma\Psi} \mid \overrightarrow{\Sigma\Psi} \rangle_\Sigma = \left\| \log(\Sigma^{-1/2}.\Psi.\Sigma^{-1/2}) \right\|_{L_2}^2$

[Pennec, Fillard, Ayache, IJCV 66(1), 2006, Lenglet JMIV'06, etc]

Log-Euclidean similarity invariant metric (vector space)

- Transport Euclidean structure through matrix exponential
- Dot product $\langle V \mid W \rangle_\Sigma = \langle \partial_V \log(\Sigma) \mid \partial_W \log(\Sigma) \rangle_{Id}$
- Geodesics $Exp_\Sigma(\overrightarrow{\Sigma\Psi}) = \exp(\log(\Sigma) + \partial_{\overrightarrow{\Sigma\Psi}} \log(\Sigma))$
- Distance $\mathrm{dist}(\Sigma_1, \Sigma_2)^2 \equiv \left\| \log(\Sigma_1) - \log(\Sigma_2) \right\|^2$

[Arsigny, Pennec, Fillard, Ayache, SIAM'06, MRM'06]

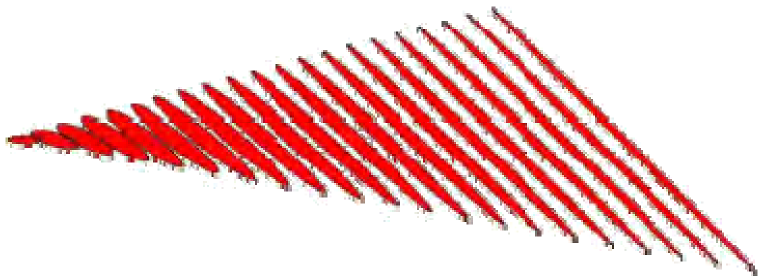
Intrinsic Riemannian Image Processing

Intrinsic formulations with weighted means

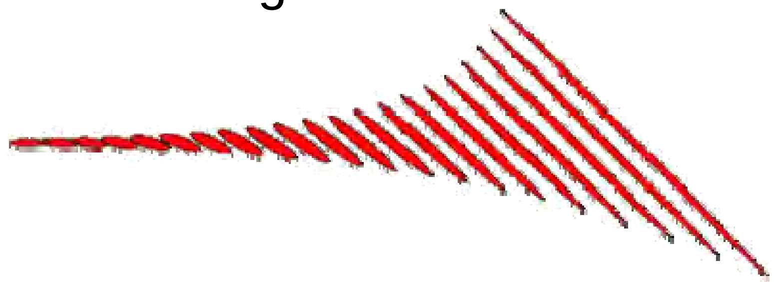
- Interpolation
  - Linear between 2 elements: interpolation geodesic

$$x(t) = \exp_{x_1}(t\, \overrightarrow{x_1 x_2})$$

Euclidean interpolation (coefficients)



Interpolation along the Affine-invariant geodesic:



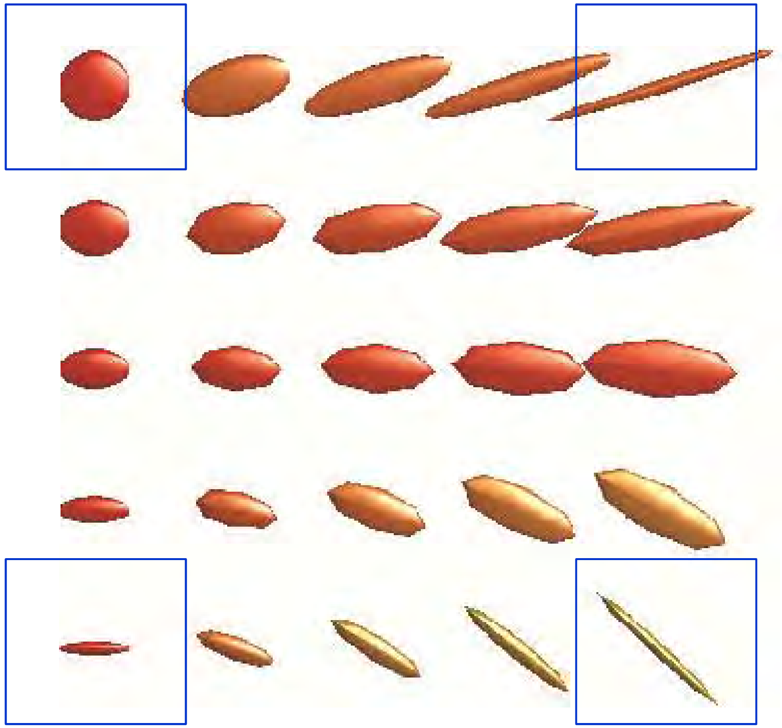
[Pennec, Fillard, Ayache, IJCV 66(1), 2006]

Intrinsic Riemannian Image Processing

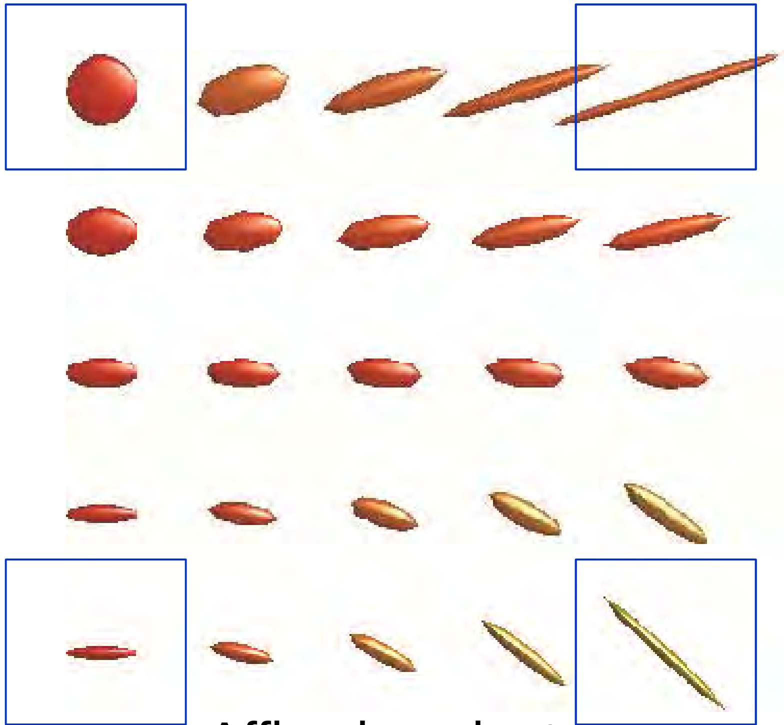
Intrinsic formulations with weighted means

- Interpolation
  - Linear between 2 elements: interpolation geodesic
  - Bi- or tri-linear in images: weighted means

$$x(t) = \exp_{x_1}(t\,\overrightarrow{x_1 x_2})$$



Euclidean



Affine invariant

[Pennec, Fillard, Ayache, IJCV 66(1), 2006]

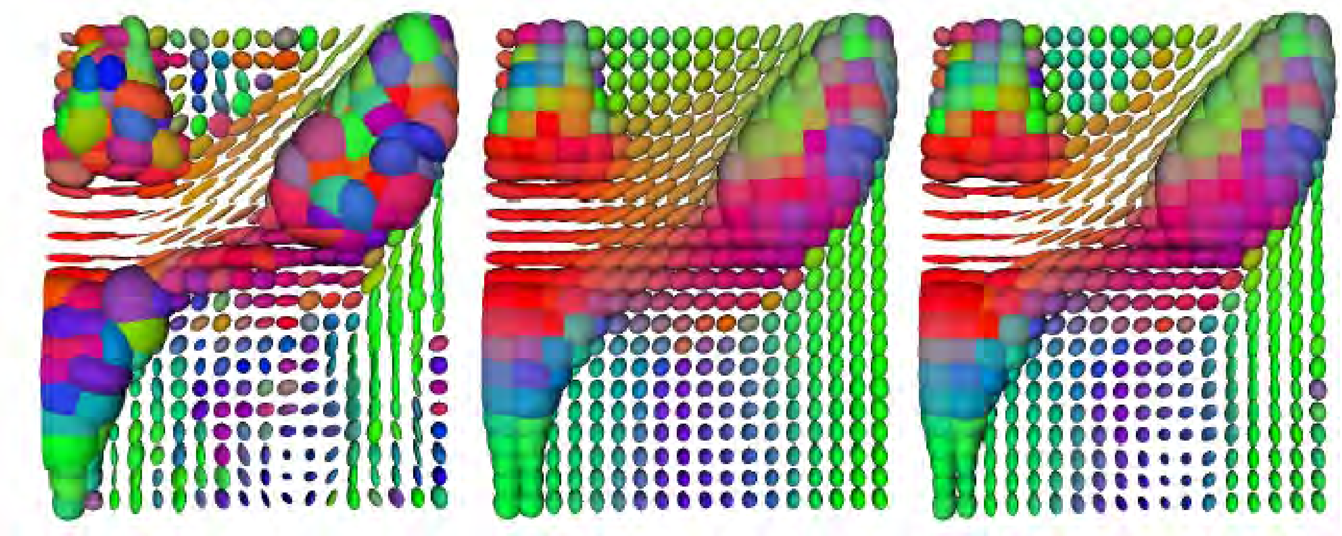
Intrinsic Riemannian Image Processing

Regularization / anisotropic filtering

- Harmonic: Laplace Beltrami $\mathrm{Reg}(\Sigma) = \int \|\nabla\Sigma(x)\|^2_{\Sigma(x)}\, dx$
- Anisotropic
  - Perona-Malik 90 / Gerig 92
  - Robust functions

$$\Delta_w \Sigma(x) = \sum_u w\left(\|\partial_u \Sigma(x)\|_{\Sigma(x)}\right) \Delta_u \Sigma(x)$$
$$\mathrm{Reg}(\Sigma) = \int \Phi\left(\|\nabla\Sigma(x)\|^2_{\Sigma(x)}\right) dx$$

- Trivial intrinsic numerical schemes thanks the exponential maps!



[Arsigny, Fillard, Pennec, Ayache, MICCAI 2005, MRM'06]

A Statistical Atlas of the Cardiac Fiber Structure

[J.M. Peyrat, et al., MICCAI'06, TMI 26(11), 2007]

Database

- 7 canine hearts from JHU
- Anatomical MRI and DTI

Method

- Normalization based on aMRIs
- Log-Euclidean statistics of Tensors: analysis more powerful than dyadic

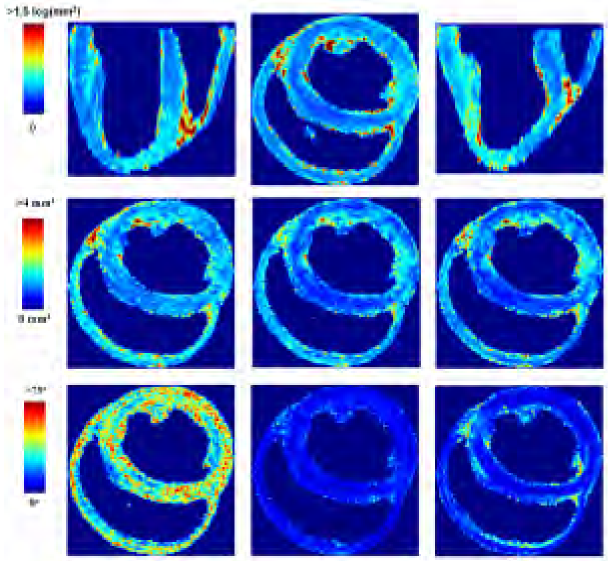
•*Average cardiac structure*

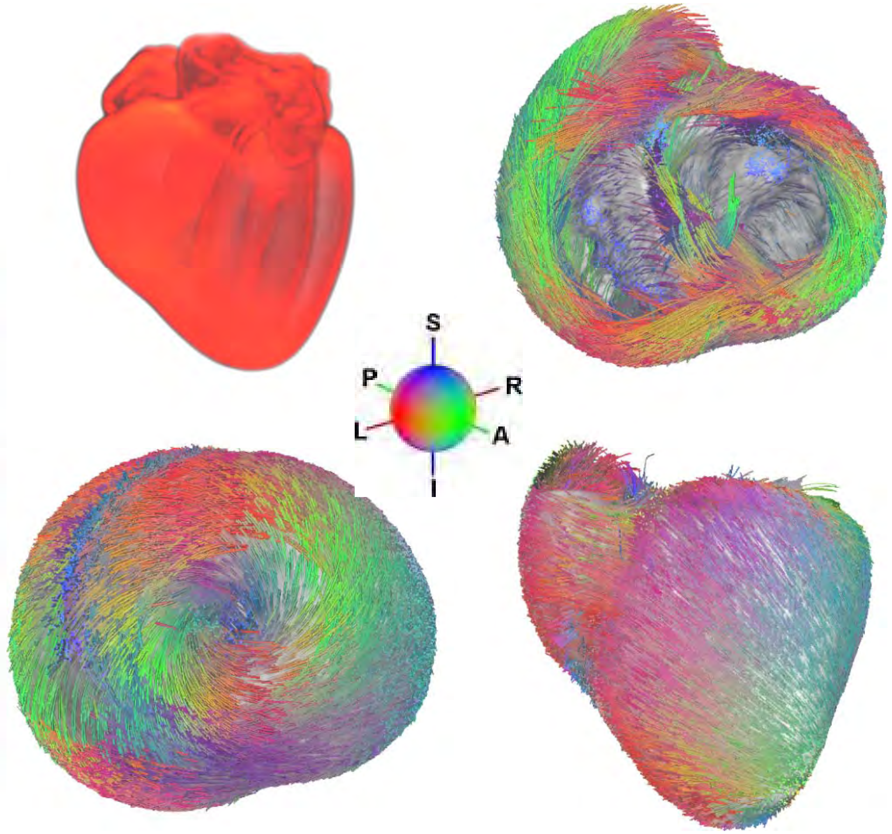
•Variability of fibers, sheets

Norm covariance

Eigenvalues covariance (1^{st}, 2^{nd}, 3^{rd})

Eigenvectors orientation covariance (around 1st, 2nd, 3rd)



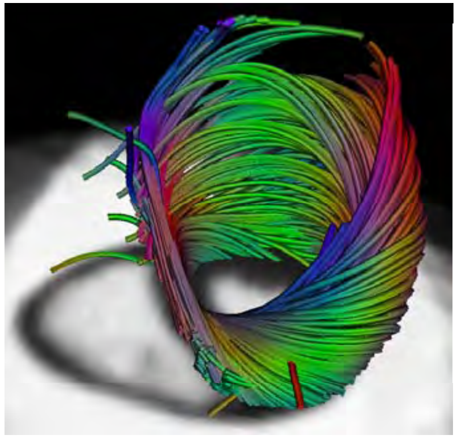


Freely available at **http://www-sop.inria.fr/asclepios/data/heart**

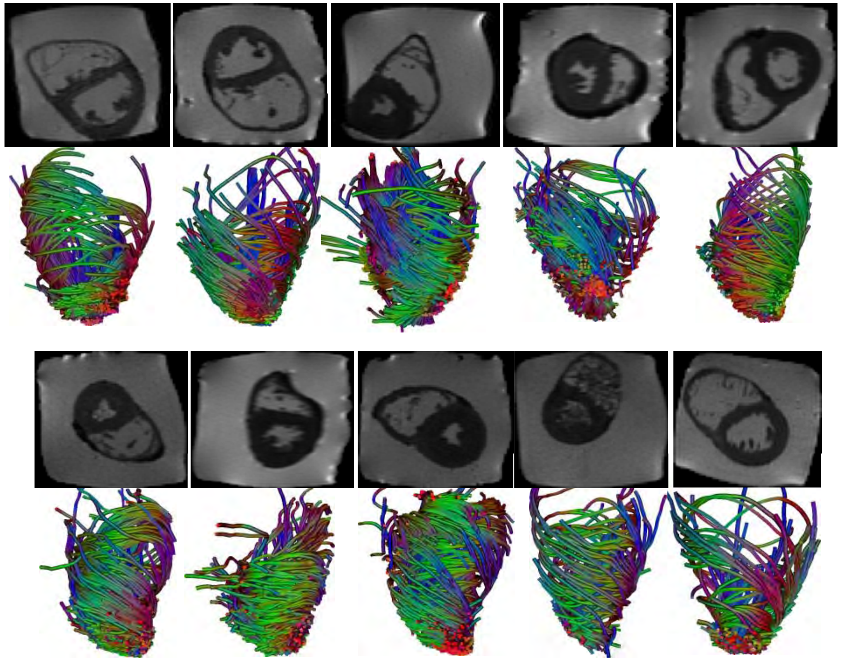
Diffusion model of the human heart

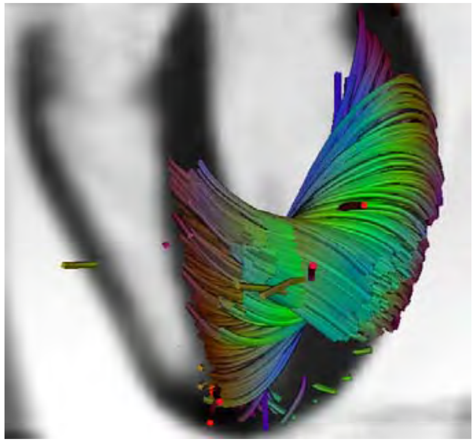
10 human ex vivo hearts (CREATIS-LRMN, Lyon, France)

- Classified as healthy (controlling weight, septal thickness, pathology examination)
- Acquired on 1.5T MR Avento Siemens
  - bipolar echo planar imaging, 4 repetitions, 12 gradients
- Volume size: 128×128×52, 2 mm resolution



Fiber tractography in the left ventricle





Helix angle highly correlated to the transmural distance

[H. Lombaert Statistical Analysis of the Human Cardiac Fiber Architecture from DT-MRI, ISMRM 2011, FIMH 2011]

Roadmap

Goals and methods of Computational anatomy

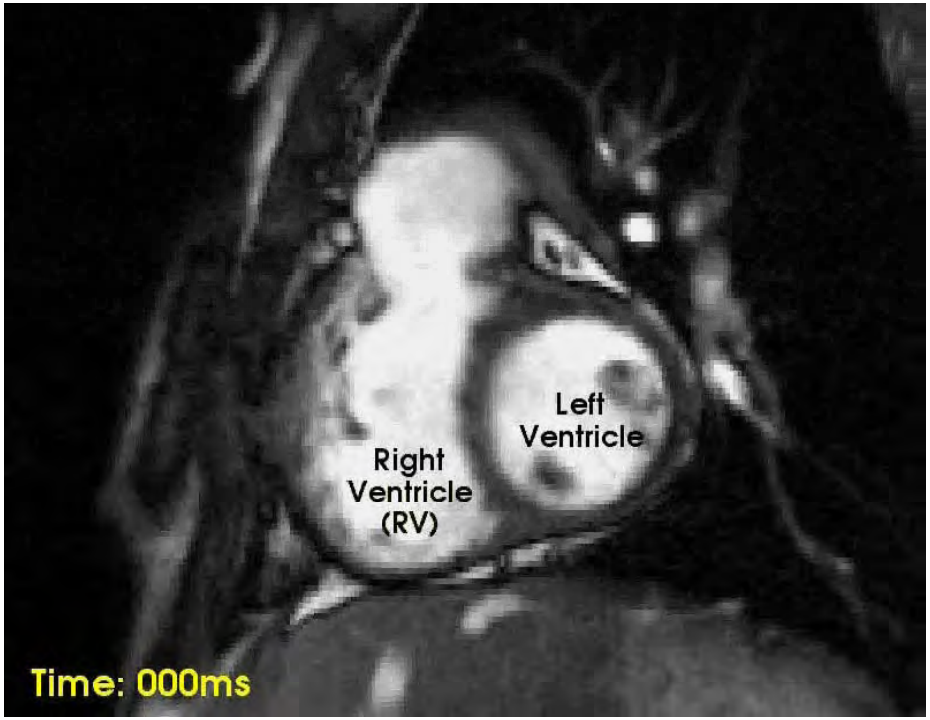
Statistical computing on manifolds

Statistics on shapes through deformations

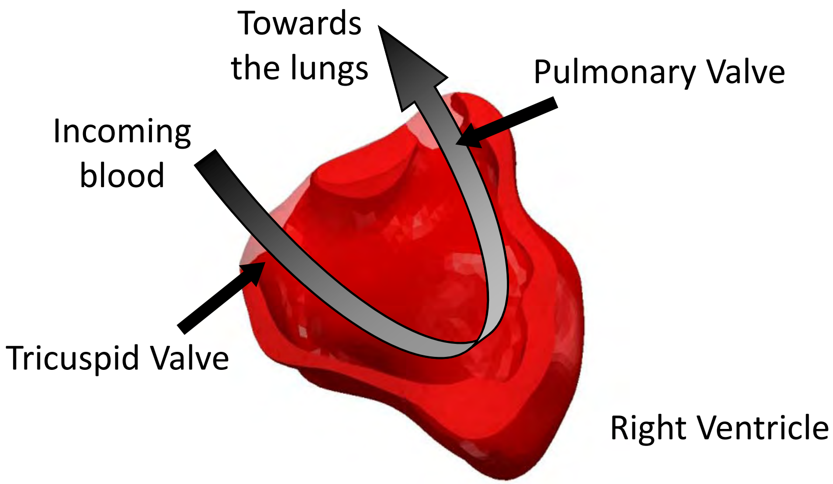
- Growth model of the right ventricle surface
- Statistics on image-based deformations
- Modeling longitudinal evolution in AD

Conclusion and challenges

Repaired Tetralogy of Fallot



- *Severe Congenital Heart Disease*
- *Occurs 1 of 2500 (Hoffman, JACC 02)*
- *Surgical repair in infancy*
- *After repair: chronic pulmonary valve regurgitations and extremely dilated right ventricle (RV).*



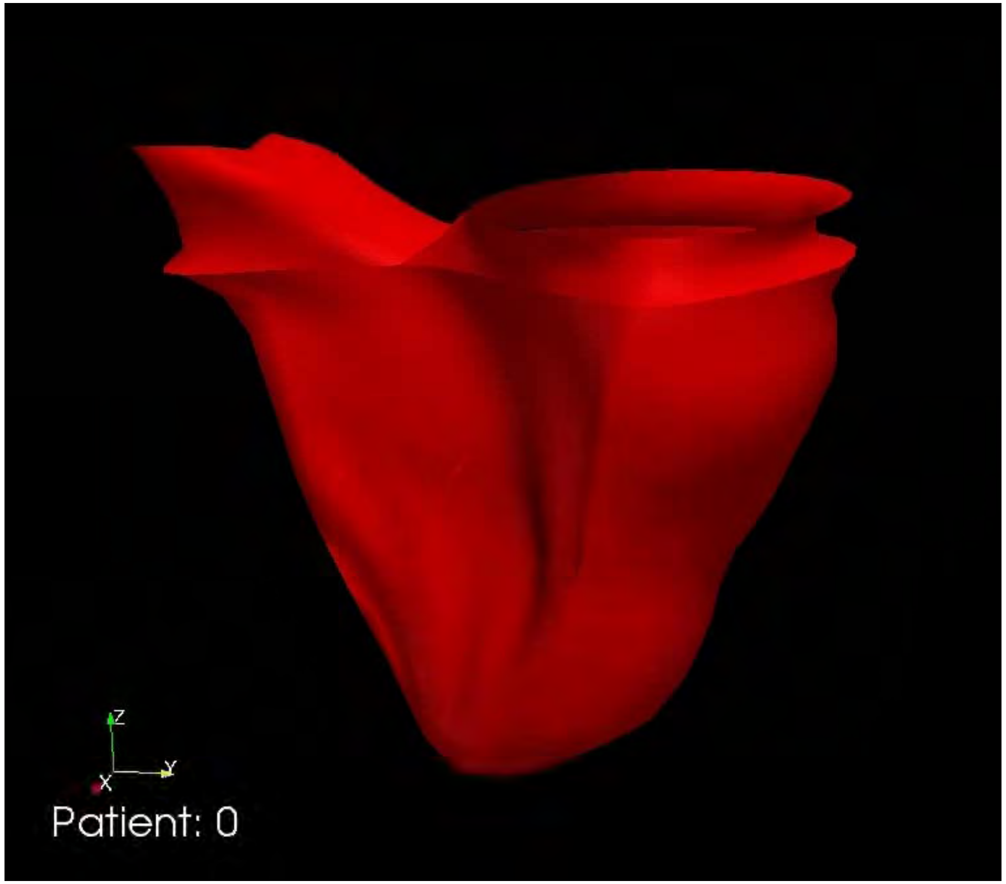
Best time for valve replacement: understand / quantify the remodeling

http://www-sop.inria.fr/asclepios/projects/Health-e-Child/ShapeAnalysis/index.php

Repaired Tetralogy of Fallot

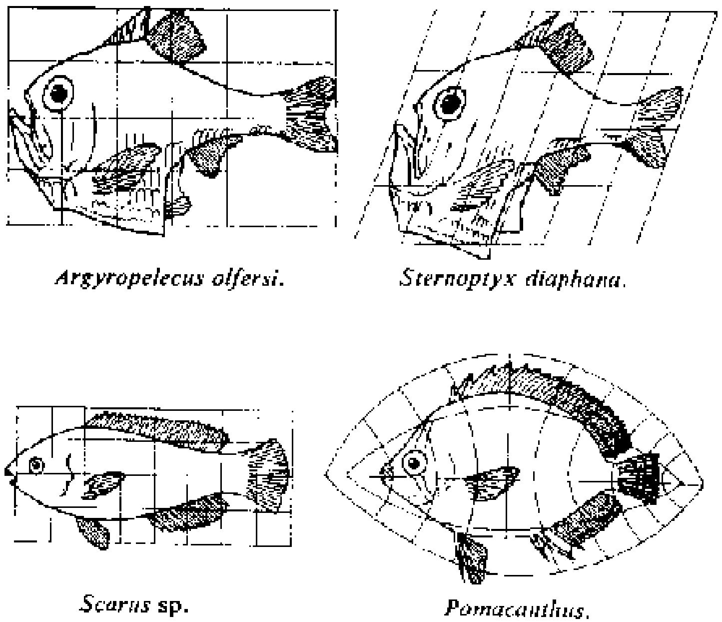
Remodeling of the right ventricle of the heart in tetralogy of Fallot

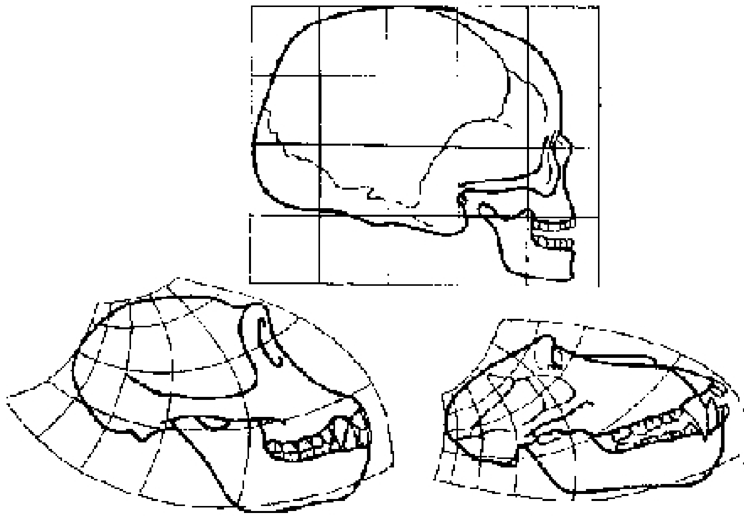
- Mean shape
- Shape variability
- Correlation with clinical variables
- Predicting remodeling effect



Shape of RV in 18 patients

Shapes: forms & deformations





Skulls of a human, a chimpanzee and a baboon
and transformations between them

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

- Deterministic template (atlas) = anatomical invariants
- Random deformations = geometrical variability
- Observations = "**random**" deformations of an **unknow** template

Riemannian metrics on diffeomorphisms

Space of deformations

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

Right invariant metric

- Eulerian scheme $\|v_t\|_{\phi_t} = \|v_t \circ \phi_t^{-1}\|_{Id}$
- Sobolev Norm H_k or H_∞ (RKHS) in LDDMM → diffeomorphisms **[Miller, Trouve, Younes, Dupuis 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 momentum
- Point supported objects (Currents, e.g. curves, surface): finite dimensional parameterization with Dirac currents **[Glaunes PhD'06]**
- Images: more difficult implementation [Beg IJCV 2005, Niethammer 09]

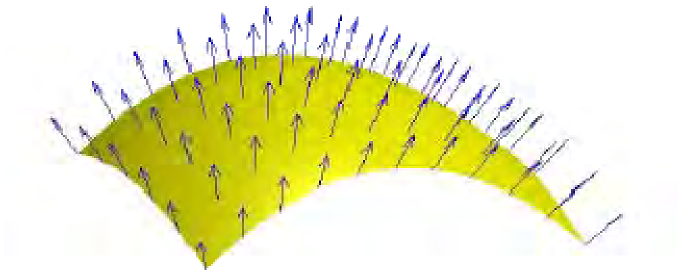
Currents for lines and surfaces

Generalization of distributions (e.g. Dirac) to vectors

- *[Vaillant and Glaunes IPMI'05; Glaunes PhD'06]*
- Distributions are known through their action on smooth test functions
- Currents integrate smooth vector fields (e.g. $W=K\otimes L_2$ with $K=G_\sigma.Id$): they measure the flux along lines or through surface
- Closed form distance for RKHS

$$\langle L, L' \rangle_{W^*} \approx \sum_{i,j} t_i^T . K(x_i - x'_j).t'_j$$

  - (+) No point correspondences needed
  - (+) No conditions on the sampling required
  - (-) "soft" distance: curvature not accounted for
  - (-) Arbitrary choice of the kernel (shape & size)



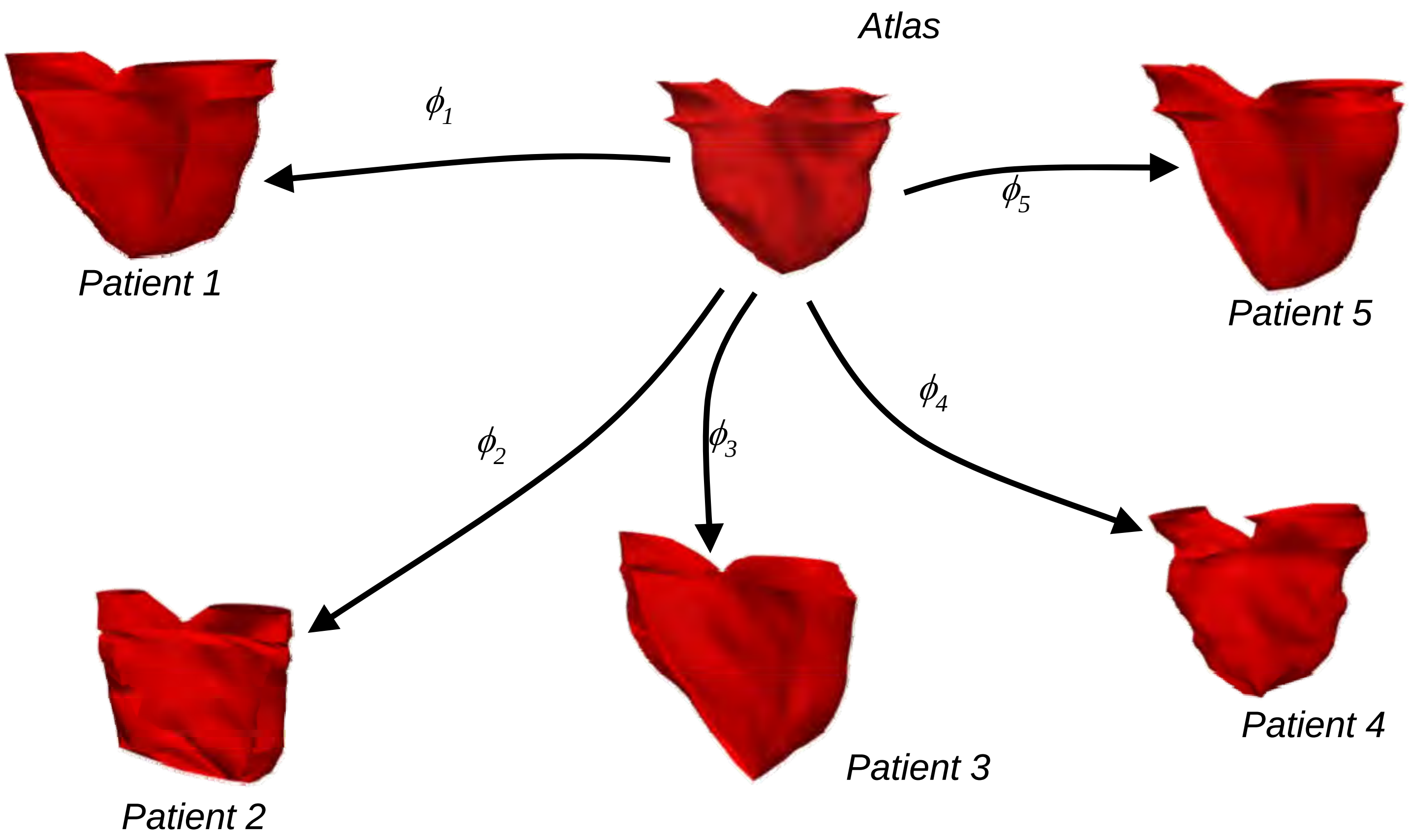
$$S(\omega) = \int_S \langle \omega(x), n_x \rangle \, d\sigma(x)$$

Algorithms on currents

- Statistical analysis (mean, PCA) **[Durrleman et al, Media 13(5) 2009]**
- Fast and stable computations thanks to controlled approximations (matching pursuit) **[Durrleman, MICCAI08 : Young investigator award]**

Atlas and Deformations Joint Estimation

Estimate mean and modes of the end-diastolic RV shape

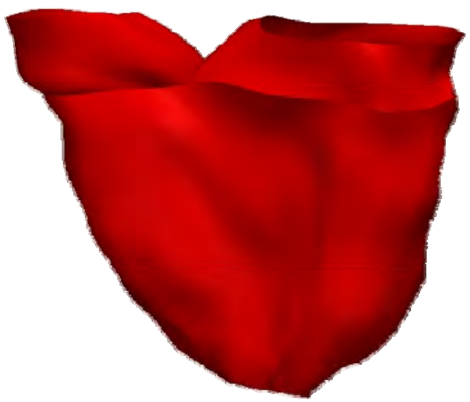


[Mansi et al, MICCAI 2009, TMI 2011 (to appear)]

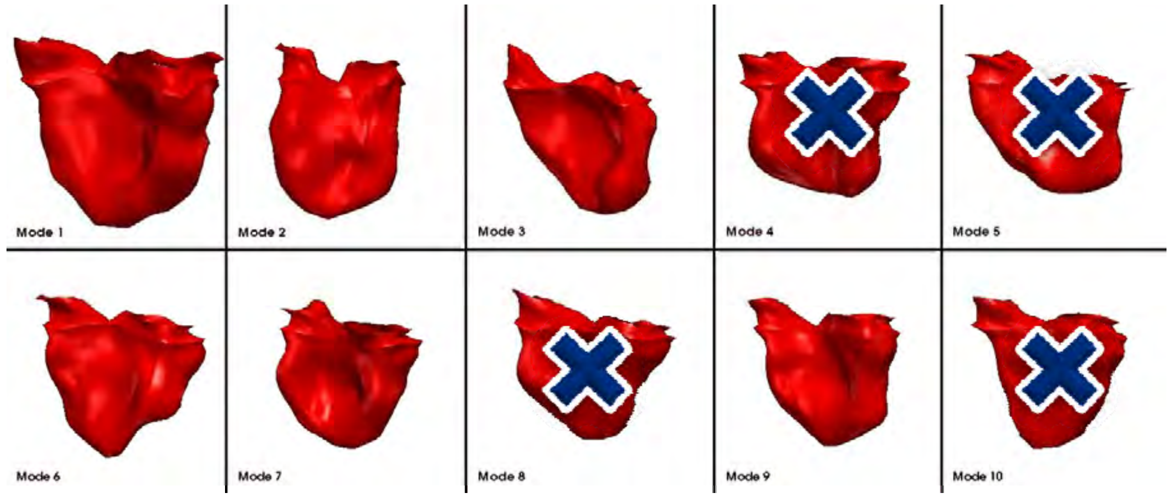
Atlas and Deformations Joint Estimation

Method: PLS (better than PCA + CCA) to

- Find modes that are significantly correlated to clinical variables (body surface area, tricuspid and pulmonary valve regurgitations).
- Create a generative model by regressing shape vs BSA



Average RV anatomy of 18 ToF patients



10 Deformation Modes = 90% of spectral energy
6 modes significantly related to BSA

[Mansi et al, MICCAI 2009, TMI 2011 (to appear)]

Statistical Remodeling of RV in Tetralogy of Fallot

[Mansi et al, MICCAI 2009, TMI 2011 (to appear)]

Predicted remodeling effect … has a clinical interpretation

Volume increases → Valve annuli deform → Pulmonary stenosis reduces → RV pressure decreases → Septum pushed inwards → RV free-wall outwards

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Statistics on which deformations feature?

Space of "initial momentum" [Quantity of motion instead of speed]

- [Vaillant et al., NeuroImage, 04, Durrleman et al, MICCAI'07]
- Based on right-invariant metrics on diffeos [Trouvé, Younes et al.]
- No more finite dimensional parameterization with images
- Computationally intensive for images

Global statistics on displacement field or B-spline parameters

- [Rueckert et al., TMI, 03], [Charpiat et al., ICCV'05],[P. Fillard, stats on sulcal lines]
- Simple vector statistics, but inconsistency with group properties

Local statistics on local deformation (mechanical properties)

- Gradient of transformation, strain tensor
- Riemannian elasticity [Pennec, MICCAI'05, MFCA'06]
- TBM [N. Lepore & C. Brun, MICCAI'06 & 07, ISBI'08, Neuroimage09]

An alternative: "log-Euclidean" statistics on diffeomorphisms?

- Stationary velocity fields [Arsigny, MICCAI'06]
- [Bossa, MICCAI'07, Vercauteren MICCAI'07, MICCAI 08, Ashburner NeuroImage 2007]
- Efficient numerical methods!

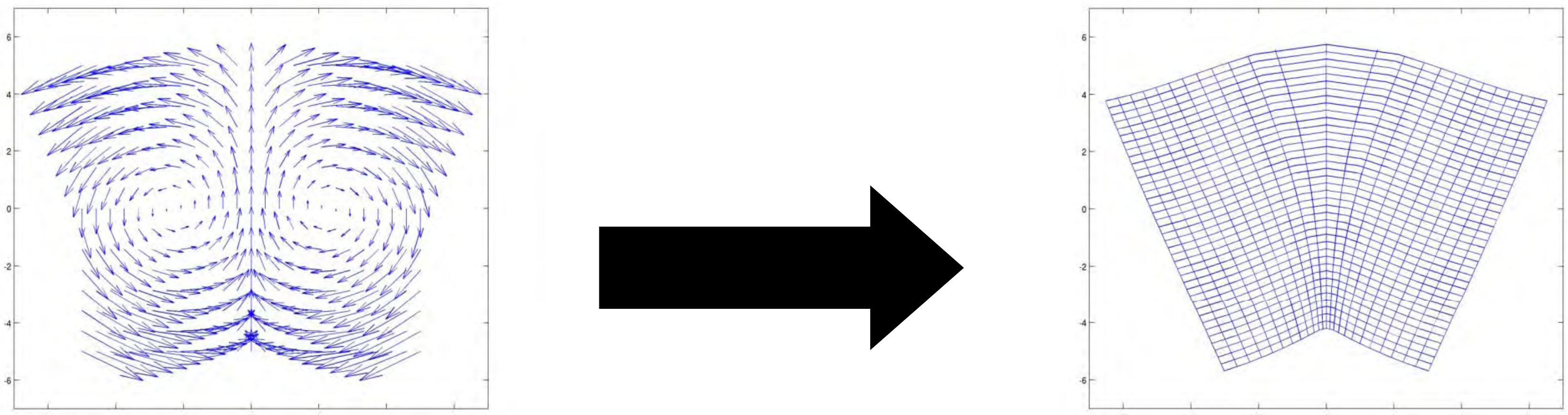
The SVF framework for Diffeomorphisms

Stationary velocity fields [Arsigny et al., MICCAI 06]

- Group exponential (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 $\partial x(t) / \partial t = \boldsymbol{u}(x(t))$



Stationary velocity field → Diffeomorphism

The SVF framework for Diffeomorphisms

Numerical methods

- Take advantage of algebraic properties of exp and log.

$\longrightarrow$ Direct generalization of numerical matrix algorithms.

Efficient parametric diffeomorphisms

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

Compatible with group structure

- Inversion: $T^{-1} = \exp(-v)$
- Composition: BCH formula **[Bossa MICCAI 2007]**

  $\log(\exp(\boldsymbol{v}) \circ \exp(\varepsilon \boldsymbol{u})) = \boldsymbol{v} + \varepsilon \boldsymbol{u} + [\boldsymbol{v},\varepsilon \boldsymbol{u}]/2 + [\boldsymbol{v},[\boldsymbol{v},\varepsilon \boldsymbol{u}]]/12 + \ldots$

  - Lie bracket $[\boldsymbol{v},\boldsymbol{u}](p) = Jac(\boldsymbol{v})(p).\boldsymbol{u}(p) - Jac(\boldsymbol{u})(p).\boldsymbol{v}(p)$

Symmetric log-demons [Vercauteren MICCAI 08]

Demons framework [Thirion, MRCAS 95, CVPR96, Media98]

- Pragmatic alternated optical flow and Gaussian smoothing
- Rigorously justified by adding correspondences (matches) as an auxiliary variable [Cachier, CVIU:89(2-3), 2003]

Log-demons with SVFs

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

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]

The SVF framework for Diffeomorphisms

Can we justify that? [Pennec & Lorenzi, MFCA11]

- Drop the metric, use connection to define geodesics
- Canonical symmetric Cartan Connection: unique symmetric left AND right invariant linear connection on a Lie group.

What we gain

- Geodesics are left (and right) translations of one-parameter subgroups
- Invariance by left and right translations + inversion
- Efficiency (PDEs -> ODEs)

What we loose

- No compatible metric for non compact non abelian groups
- Geodesic completeness but no Hopf-Rinow theorem
  - There is not always a smooth geodesic joining two points (e.g. SL_2, no pb for GL_n)
- Infinite dimensions: exponential might not be locally diffeomorphic
  - Known examples on Diff(S^1) but with $\|\phi\|_{H^k} \xrightarrow{k \to +\infty} \infty$

In practice

- Reachable diffeos seem to be sufficient to describe anatomical deformations

Roadmap

Goals and methods of Computational anatomy

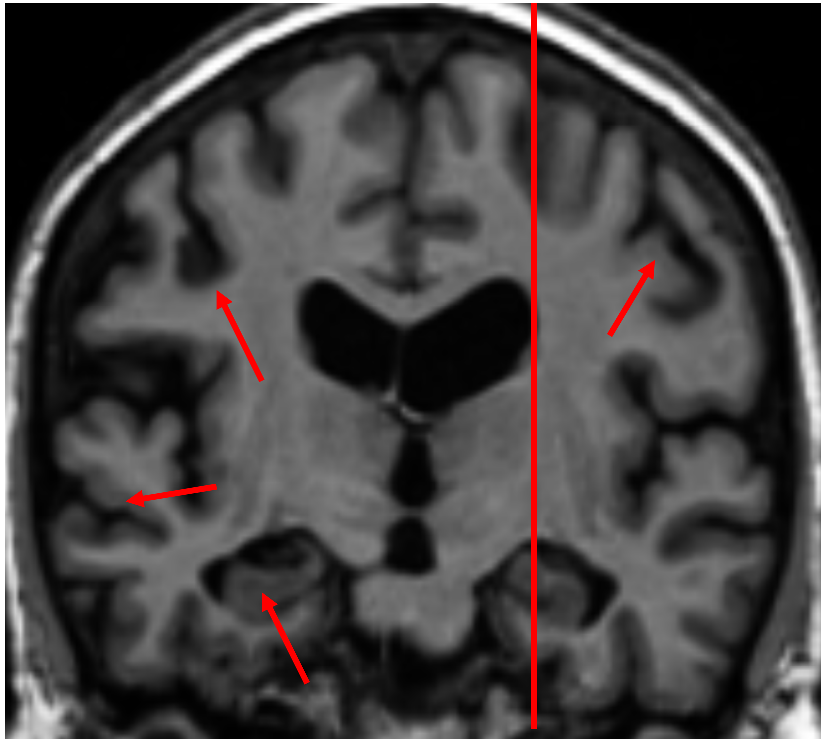
Statistical computing on manifolds

Statistics on shapes through deformations

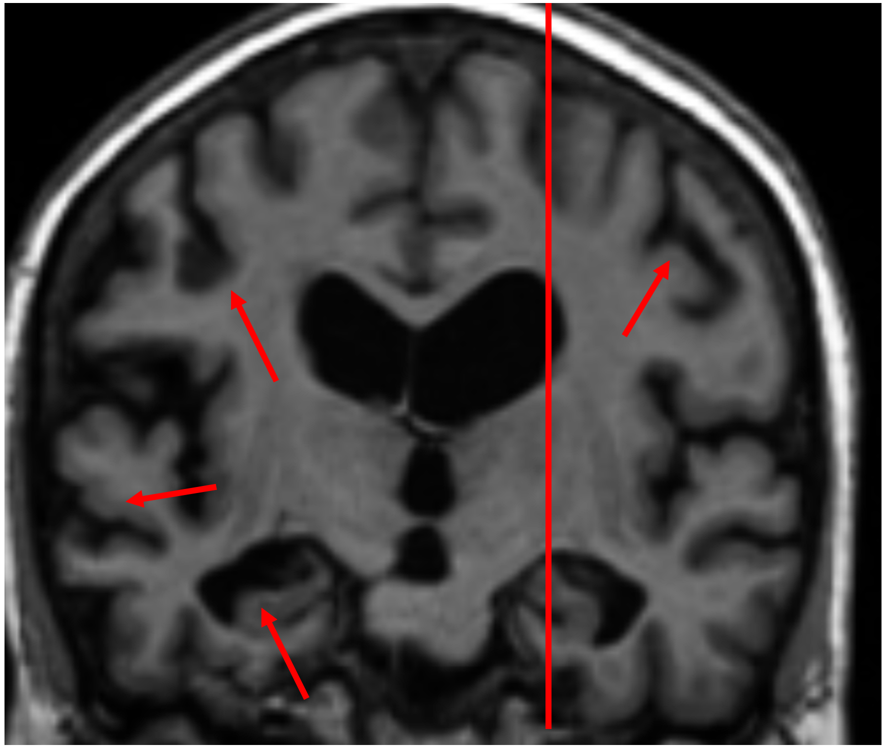
- Growth model of the right ventricle surface
- Statistics on image-based deformations
- Modeling longitudinal evolution in AD

Conclusion and challenges

Longitudinal structural damage in AD



baseline



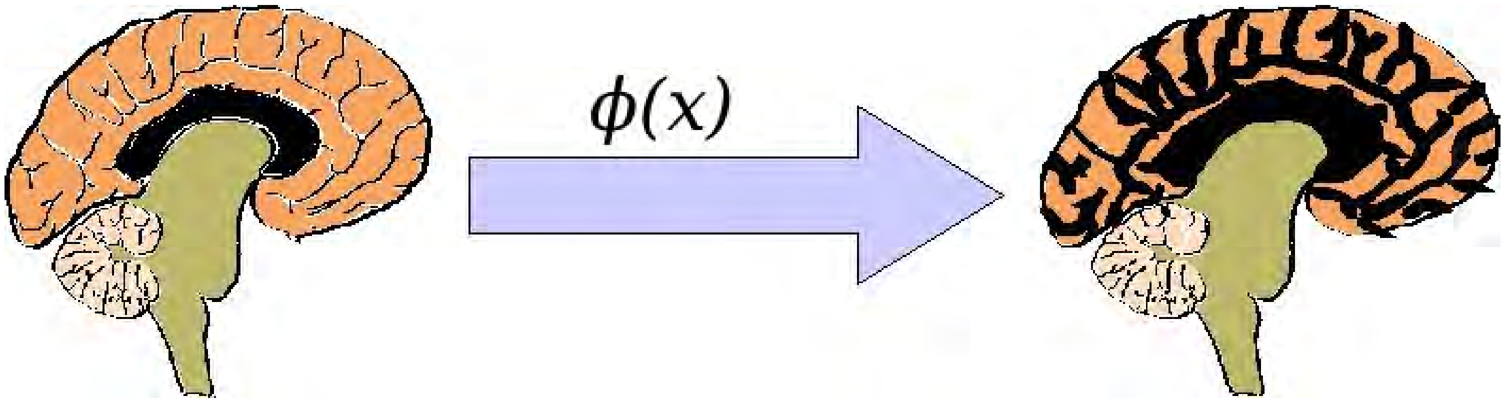
2 years follow-up

Widespread cortical thinning

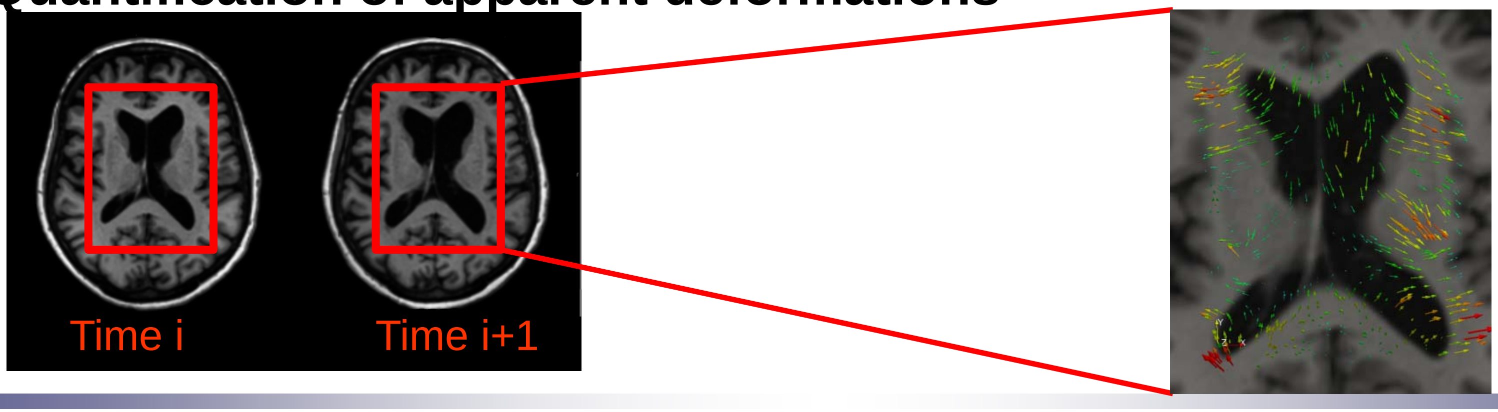
Individual Measure of Temporal Evolution

Geometry changes (Deformation-based morphometry)

- Measure the physical or apparent deformation through registration

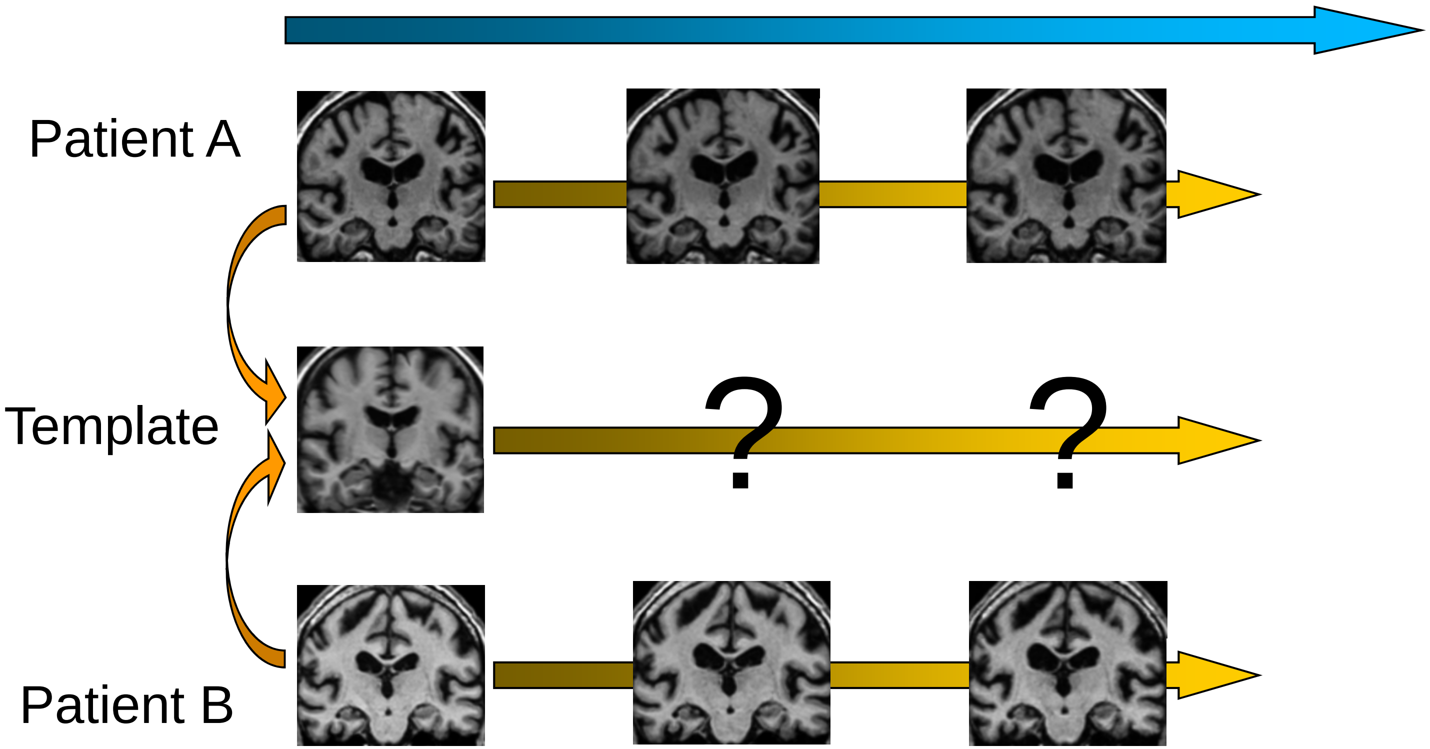


Quantification of apparent deformations



Modeling longitudinal atrophy in AD from images

- Log-demons: consistent deformation along subject-specific trajectories
- **From patient specific evolution to population trend**



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

Parallel transport of deformations

Encode longitudinal deformation by its initial tangent vector

- Momentum (LDDMM) / SVF

Parallel transport

- The (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

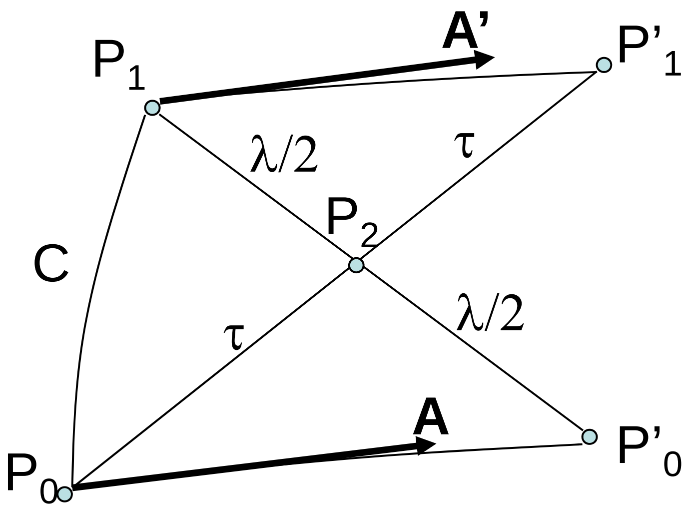
Parallel transport along arbitrary curves

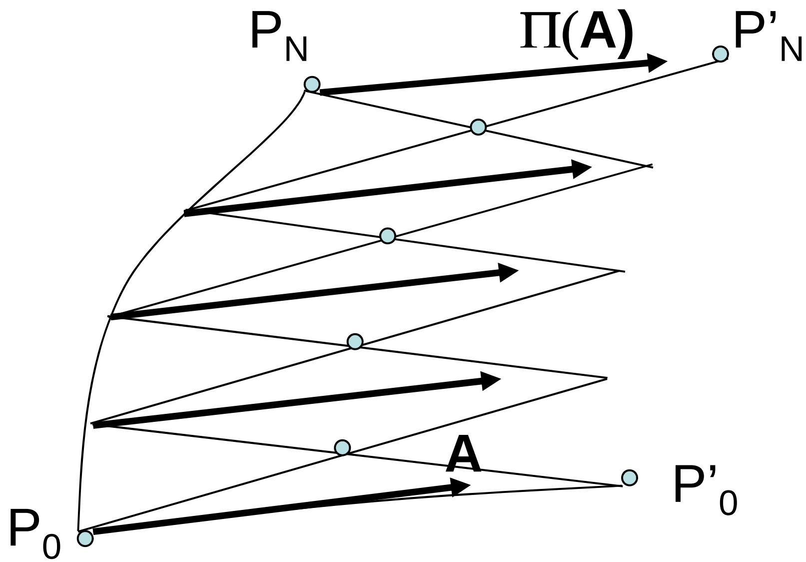
Infinitesimal parallel transport = connection

$\nabla_{\gamma'}(X) : TM \rightarrow TM$

A numerical scheme for symmetric connections: Schild's Ladder

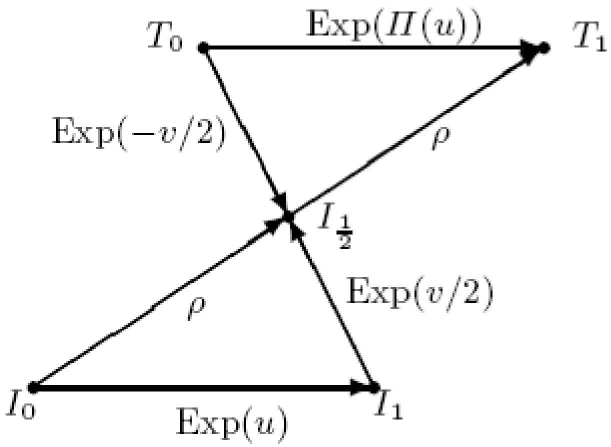
- Recover connection using only exp and log
- Build geodesic parallelogrammoid
- Iterate along the curve





[Elhers et al, 1972]

Efficient Schild's Ladder with SVFs



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

Numerical scheme

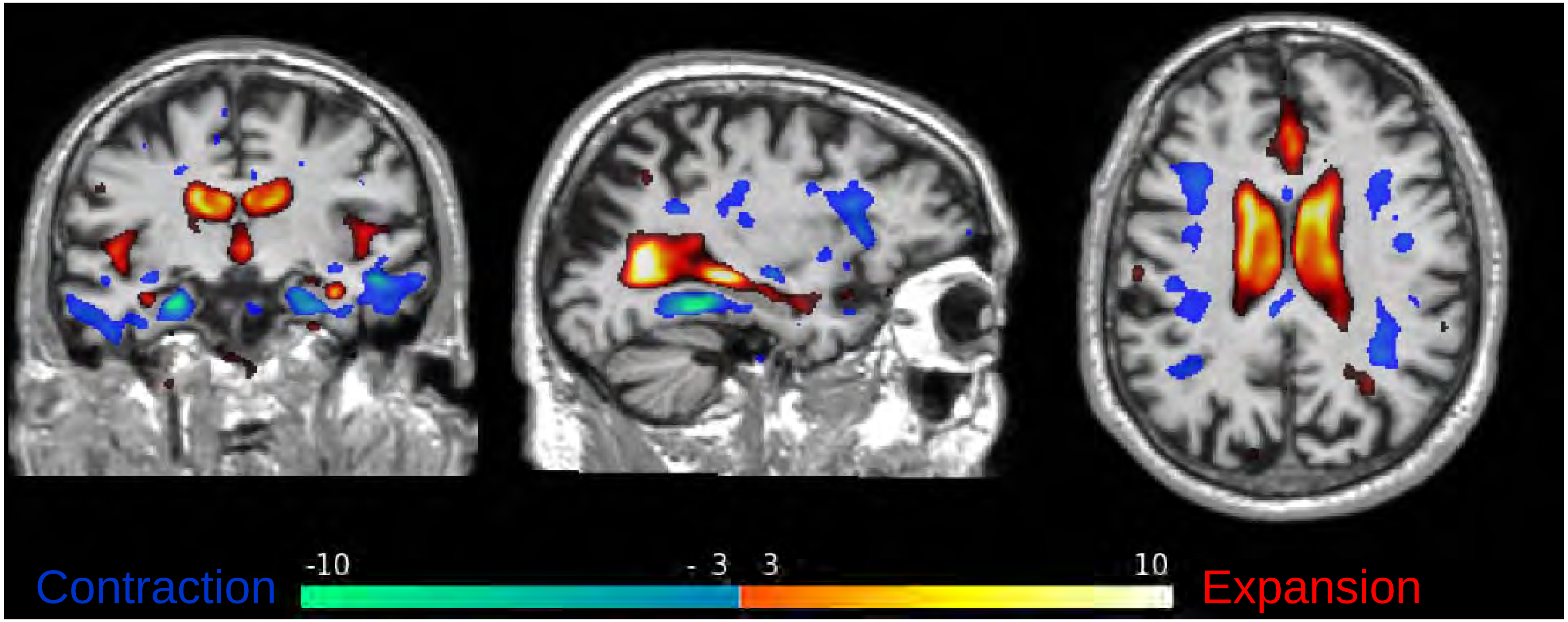
- Direct computation $\Pi_{conj}(u) = \mathrm{D}\left(\mathrm{Exp}(v)\right)|_{\mathrm{Exp}(-v)} \cdot u \circ \mathrm{Exp}(-v)$
- Using the BCH: $\Pi_{BCH}(u) = u + [v, u] + \frac{1}{2}[v[v, u]]$

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

Modeling longitudinal atrophy in AD from images

One year structural changes for 70 Alzheimer's patients

- Median evolution model and significant atrohpy (FdR corrected)



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

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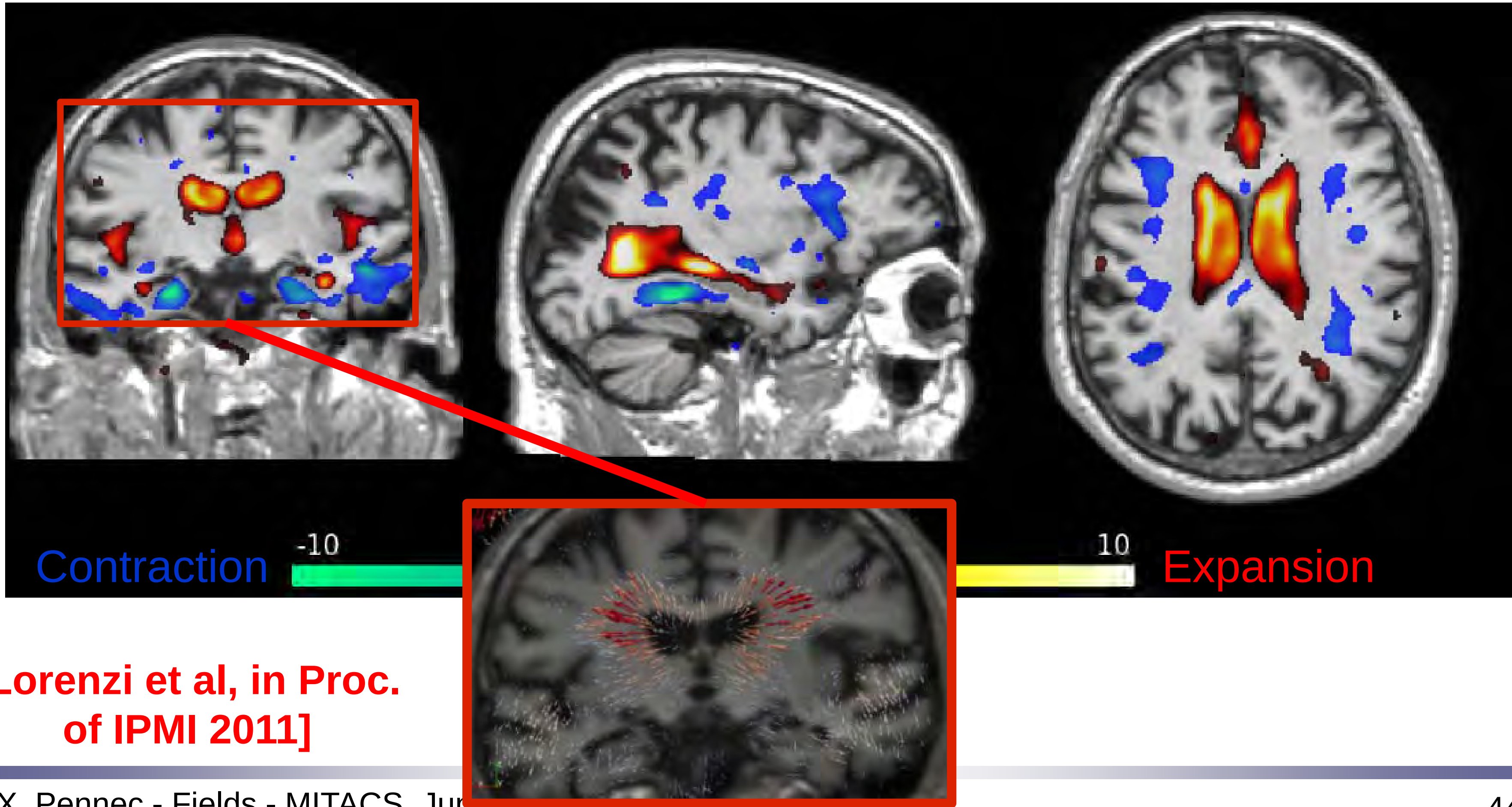

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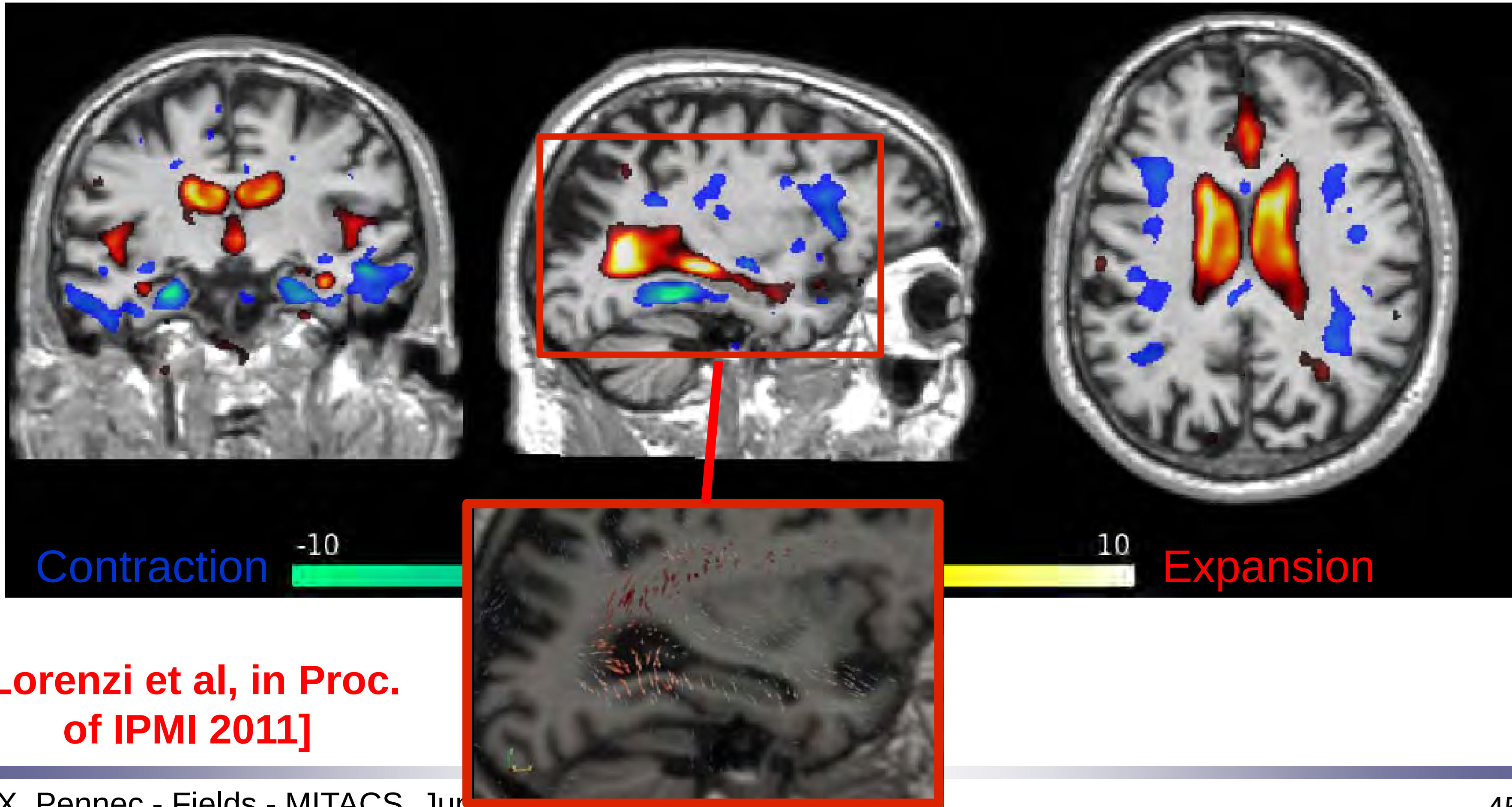

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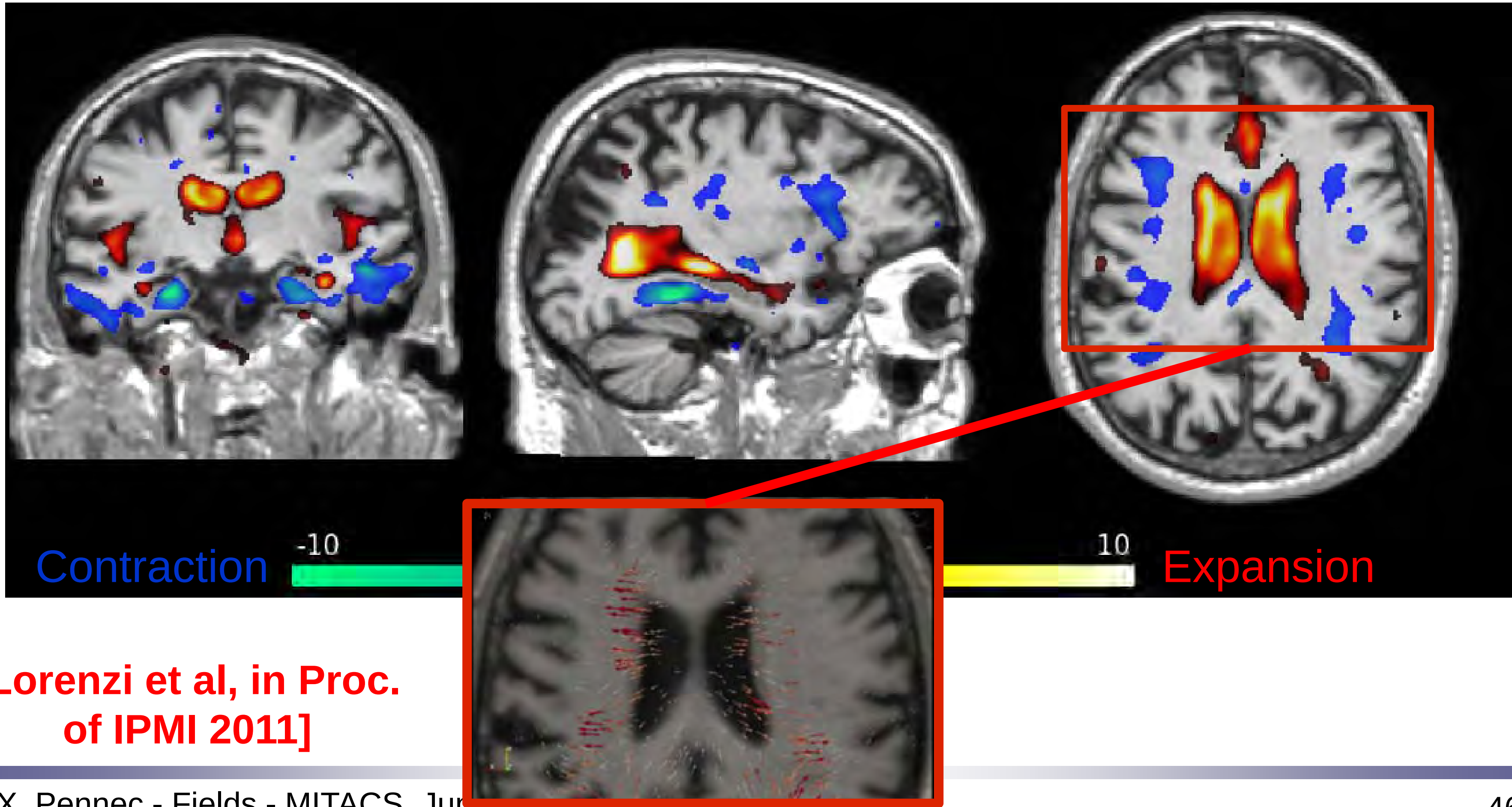
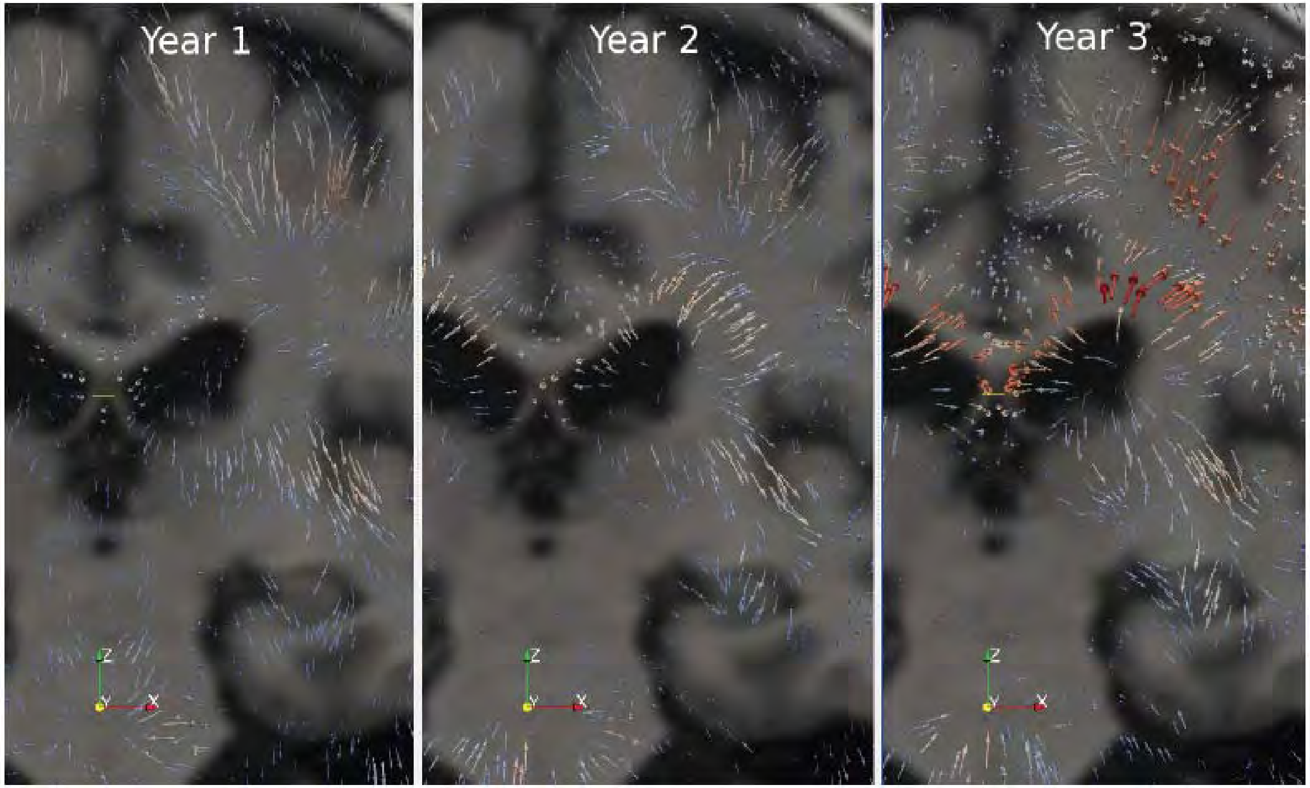


[Lorenzi et al, in Proc. of IPMI 2011]

Study of prodromal Alzheimer's disease

Different morphological evolution for the Aβ+ vs Aβ-?

- 98 healthy subjects, 5 time points (0 to 36 months).
- 41 subjects Aβ42 positive ("at risk" for Alzheimer's)

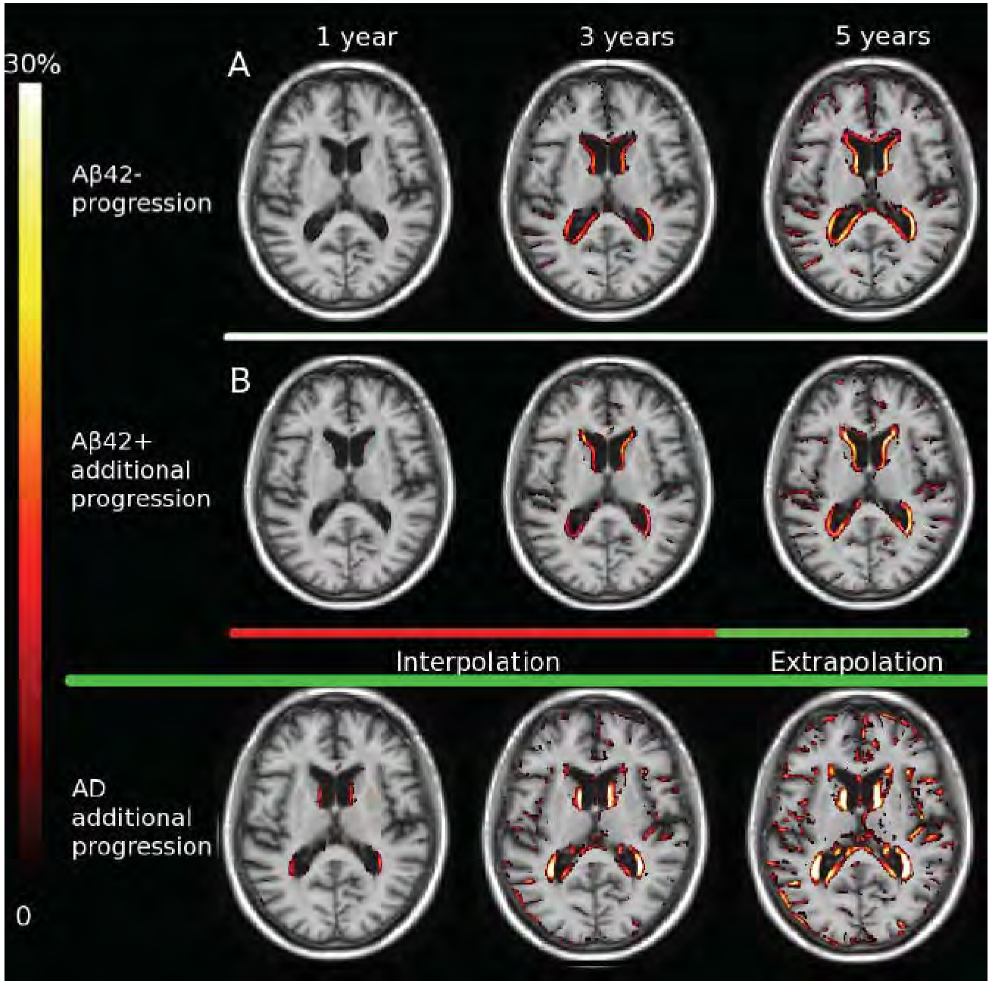


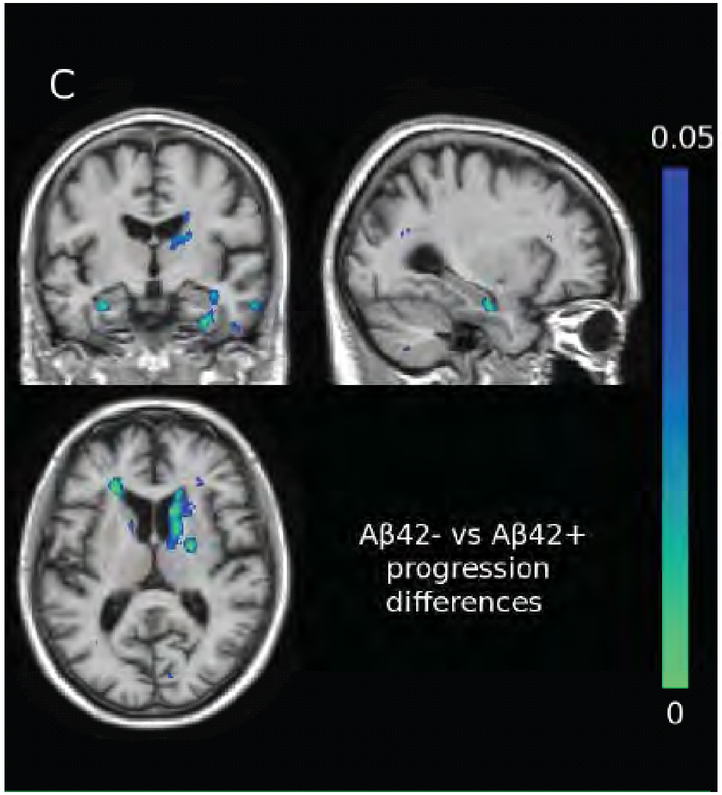
Average SVF for normal evolution (Aβ-)

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

Study of prodromal Alzheimer's disease

Linear regression of the SVF over time: interpolation + prediction





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

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]

Roadmap

Goals and methods of Computational anatomy

Statistical computing on manifolds

Statistics on shapes through deformations

Conclusion and challenges

Statistics on geometrical objects

How to chose or estimate the metric for Riemannian manifolds?

- Invariance principles, learning the metric?
- Anatomical deformation metrics?

Can we generalize the statistical setting to affine connection spaces?

- Bi-invariant mean on Lie groups [Arsigny Preprint + PhD 2006]
- Covariance matrices? ICA instead of PCA?

What about geodesically non complete manifolds?

- E.g. Power metrics for tensors
- Accumulation at boundaries for diffusion?

Numerical issues: from continuous to discrete algorithms

- Discrete atlas might not converge to continuous model [Allassonniere: Bernouilli 16(3):641-678, 2010].
- Guaranty the quality of approximations?
- Efficient methods?

Computational anatomy

Mathematics & Computer science

- Anatomy is geometry: population studies imply statistics on manifolds
- Large data sets require efficient algorithms to process them

Applications in medicine

- Morphometry:
  - Shape relationship with clinical indices
- Support for the physiology:
  - Statistics on geometric physiological parameters
- From group models to subject-specific measures
  - Faithful measure at individual level: diagnosis / follow-up
  - Model at group level: statistical prediction (extrapolation)
  - Personalized model: prediction (prognosis)

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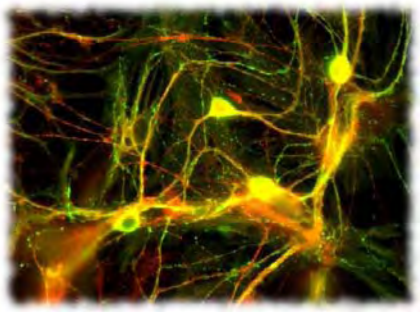
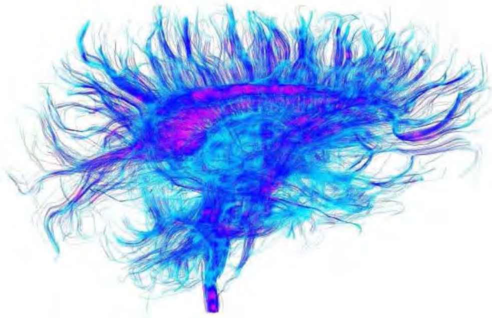
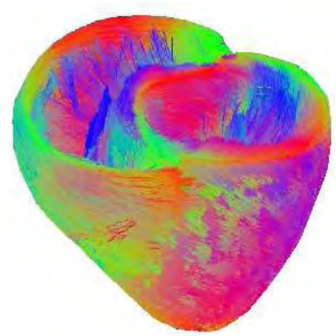
Master of Science in Computational Biology

at Nice-Sophia Antipolis University

- **http://www.computationalbiology.eu**

Workshop Mathematical Foundations of Computational Anatomy at MICCAI 2011

- Toronto, September 18 or 22, 2011
  - http://www-sop.inria.fr/asclepios/events/MFCA11/

Acknowledgements

People and Projects

- Collaboration with Montreal Polytechnique School (2006-2008)
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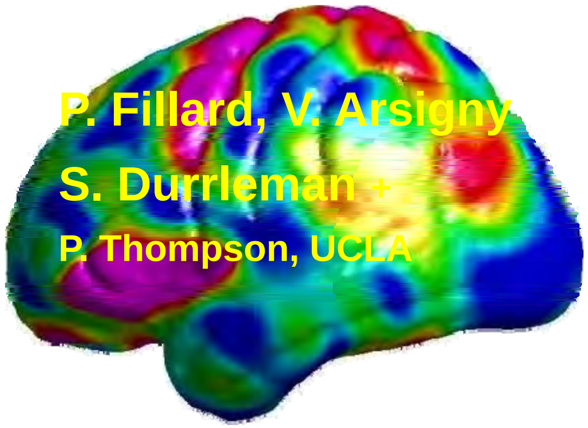
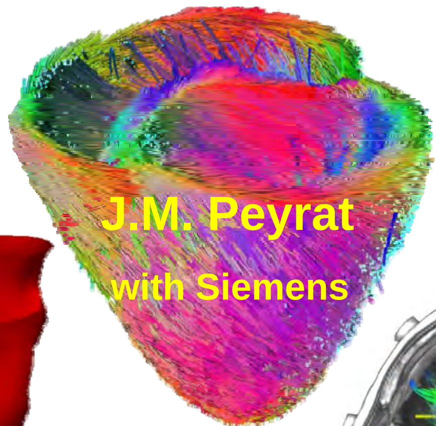
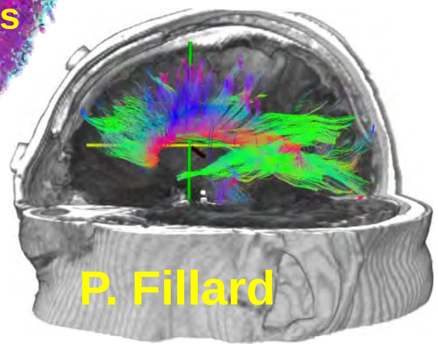
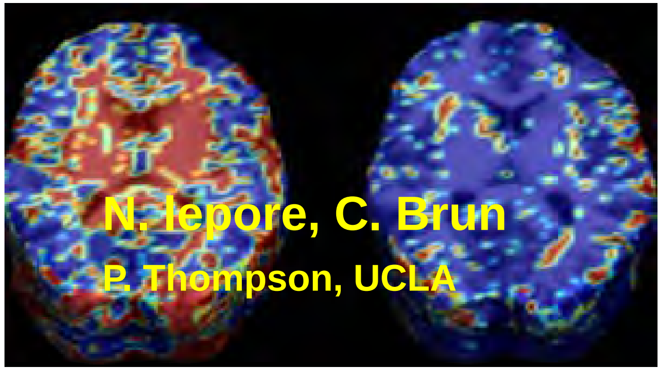
- ANR Karametria (2008-2012)









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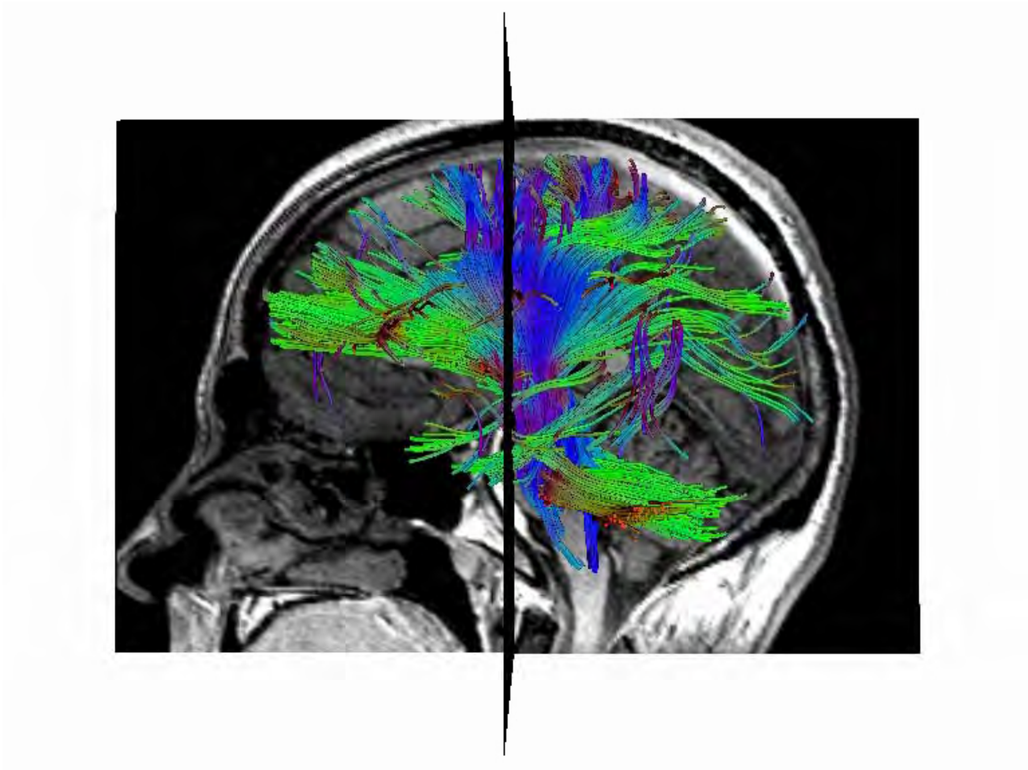

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