Xavier Pennec

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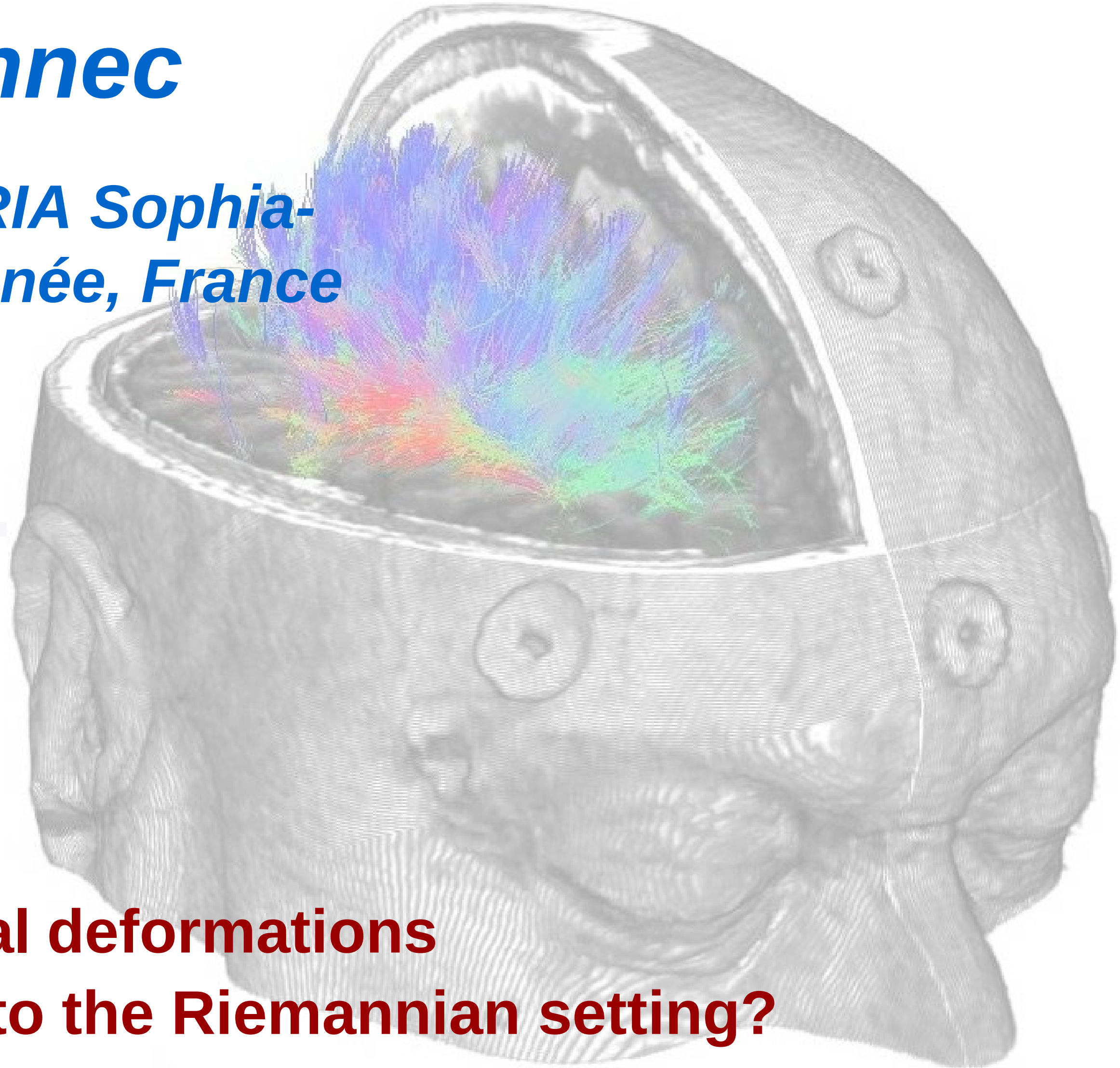


Joint work with M. Lorenzi, based on ideas developed with V. Arsigny

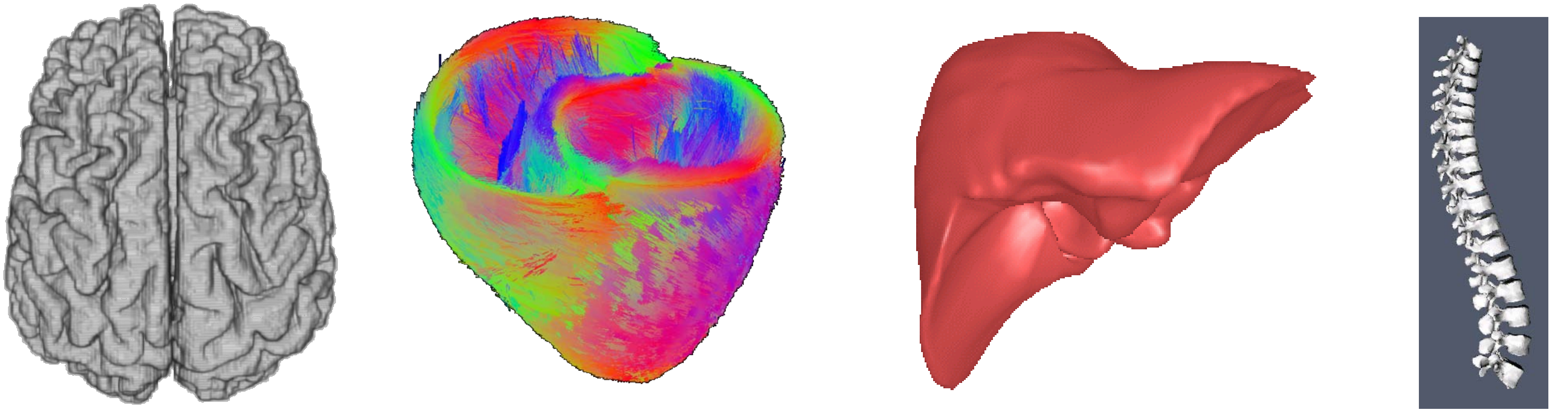
Analysis of longitudinal deformations
Is there an alternative to the Riemannian setting?

ASCLEPIOS

Banff, August 29, 2011

INRIA SOPHIA ANTIPOLIS

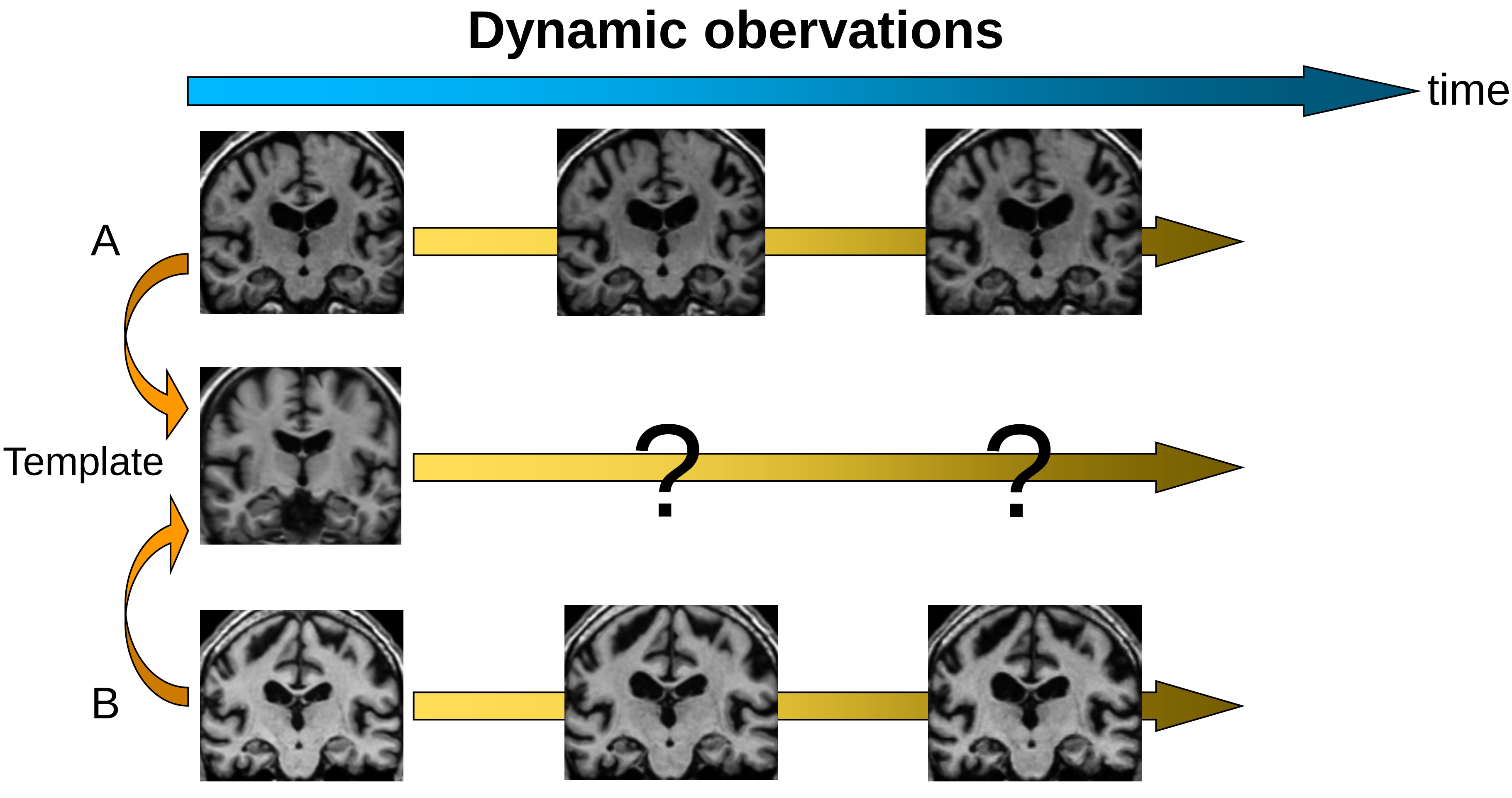
Computational Anatomy



Design Mathematical Methods and Algorithms to Model and Analyze the Anatomy

- Statistics of organ shapes across subjects in species, populations, diseases…
  - Mean shape
  - Shape variability (Covariance)
- Model organ development across time (heart-beat, growth, ageing, ages…)
  - Predictive (vs descriptive) models of evolution
  - Correlation with clinical variables

Longitudinal deformation analysis in AD



How to transport longitudinal deformation across subjects?

What are the convenient mathematical settings?

Roadmap

Statistics on shapes: the Riemannian setting

The Stationary Velocity Fields (SVF) framework

Modeling longitudinal evolution in AD

Conclusion and challenges

Riemannian geometry is a powerful structure to build consistent statistical computing algorithms

Shape spaces & directional statistics

- [Kendall StatSci 89, Small 96, Dryden & Mardia 98]

Numerical integration, dynamical systems & optimization

- [Helmke & Moore 1994, Hairer et al 2002]
- Matrix Lie groups [Owren BIT 2000, Mahony JGO 2002]
- Optimization on Matrix Manifolds [Absil, Mahony, Sepulchre, 2008]

Information geometry (statistical manifolds)

- [Amari 1990 & 2000, Kass & Vos 1997]
- [Oller & Corcuera Ann. Stat. 1995, Battacharya & Patrangenaru, Ann. Stat. 2003 & 2005]

Statistics for image analysis

- Rigid body transformations [Pennec PhD96]
- General Riemannian manifolds [Pennec JMIV98, NSIP99, JMIV06]
- PGA for M-Reps [Fletcher IPMI03, TMI04]
- Planar curves [Klassen & Srivastava PAMI 2003]

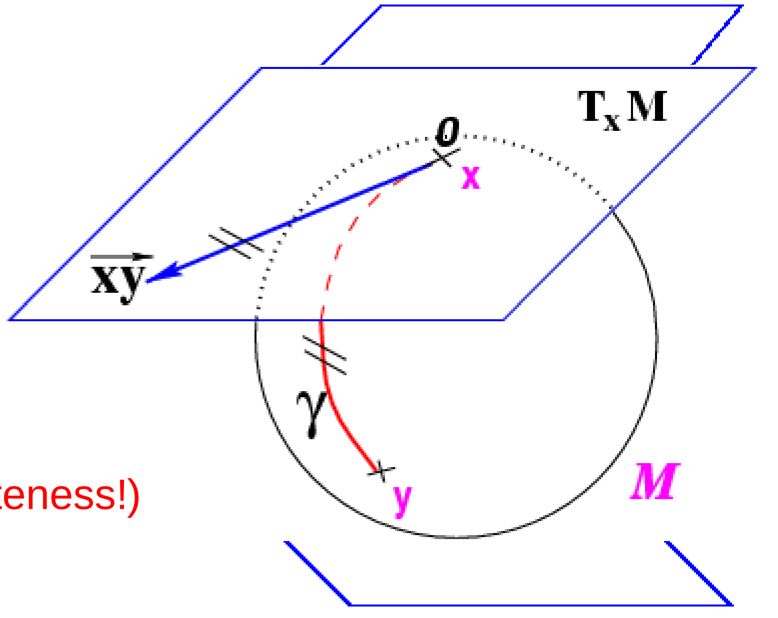
Geometric computing

- Subdivision scheme [Rahman,…Donoho, Schroder SIAM MMS 2005]

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 (geodesic completeness!)

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	$x_{t+\varepsilon} = x_t - \varepsilon \nabla C(x_t)$	$x_{t+\varepsilon} = Exp_{x_t}(-\varepsilon \nabla C(x_t))$

First statistical tools: moments

Probability measures

- Metric -> Volume form *dM(x)*
- Intrinsic probability density functions *dP(z) = p(z).dM(z)*

Expectation of a function from M into R

- Variance : $\sigma_{\mathbf{x}}^2(y) = \mathrm{E}\left[\mathrm{dist}(y,\mathbf{x})^2\right] = \int_{\mathrm{M}} \mathrm{dist}(y,z)^2 .dP(z)$
- Information : $\mathrm{I}[\mathbf{x}] = \mathrm{E}\left[\log(p(\mathbf{x}))\right]$

Fréchet / Karcher mean: minimize the variance

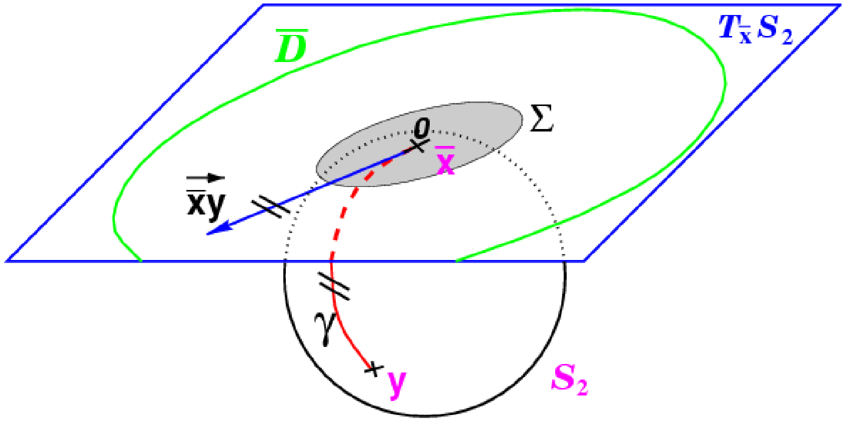
$$\mathrm{E}^{\alpha}[\mathbf{x}] = \underset{y\in \mathrm{M}}{\mathrm{argmin}} \left(\mathrm{E}\left[\mathrm{dist}(y,\mathbf{x})^{\alpha}\right]\right)^{1/\alpha}$$

- Optimum: exponential barycenter $\mathrm{E}\left[\overrightarrow{\bar{\mathrm{x}}\mathbf{x}}\right] = \int_{\mathrm{M}} \overrightarrow{\bar{\mathrm{x}}\mathbf{x}}.dP(z) = 0 \quad [P(C)=0]$
- Gauss-Newton Geodesic marching

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

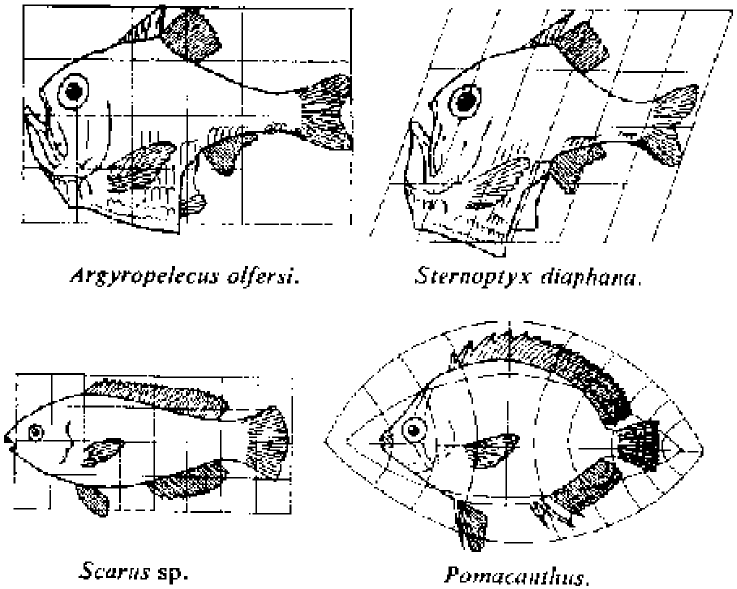
Covariance (tPCA) and higher orders

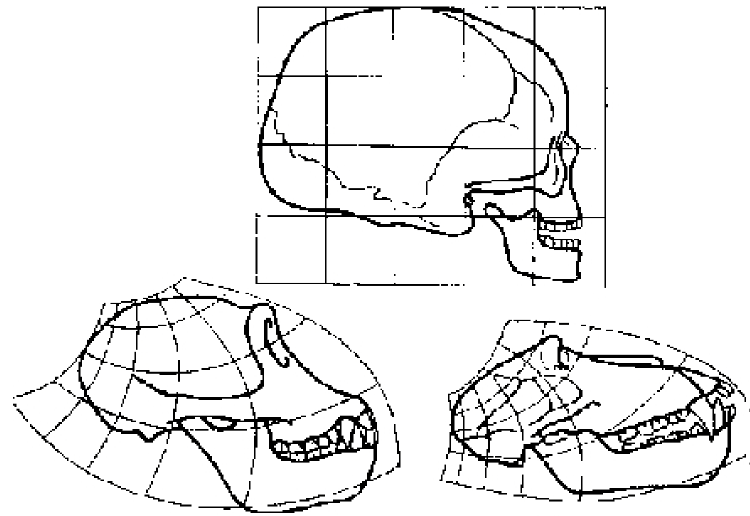
$$\Sigma_{\mathbf{xx}} = \mathrm{E}\left[\left(\overrightarrow{\bar{\mathrm{x}}\mathbf{x}}\right)\left(\overrightarrow{\bar{\mathrm{x}}\mathbf{x}}\right)^{\mathrm{T}}\right] = \int_{\mathrm{M}} \left(\overrightarrow{\bar{\mathrm{x}}z}\right)\left(\overrightarrow{\bar{\mathrm{x}}z}\right)^{\mathrm{T}}.dP(z)$$



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

Shapes: forms & deformations





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

Riemannian Shape space setting

- Forms live in a shape space with a Riemannian metric
- Use Frechet/Karcher mean, covariance, Tangent PCA

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]

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

- Eulerian scheme

$$\left\| v_t \right\|_{\phi_t} = \left\| v_t \circ \phi_t^{-1} \right\|_{Id}$$

- 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

$$d^2(\phi_0, \phi_1) = \arg\min_{v_t} \left(\int_0^1 \left\| v_t \right\|_{\phi_t}^2 .dt \right)$$

- 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]

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?

- [Arsigny, MICCAI’07]
- [Bossa, MICCAI’07, Vercauteren MICCAI’07, Ashburner NeuroImage 2007]
- Mathematical problems but efficient numerical methods!

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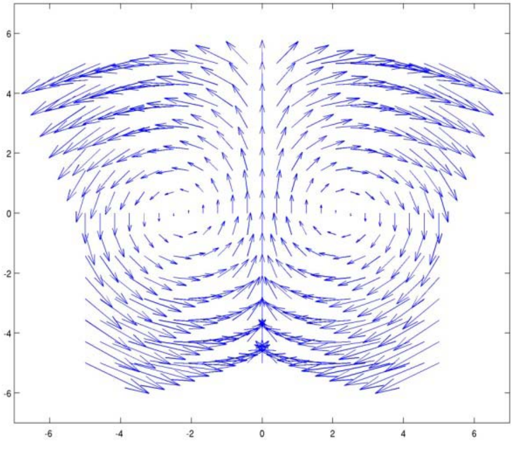
The SVF framework for Diffeomorphisms

Framework of [Arsigny et al., MICCAI 06]

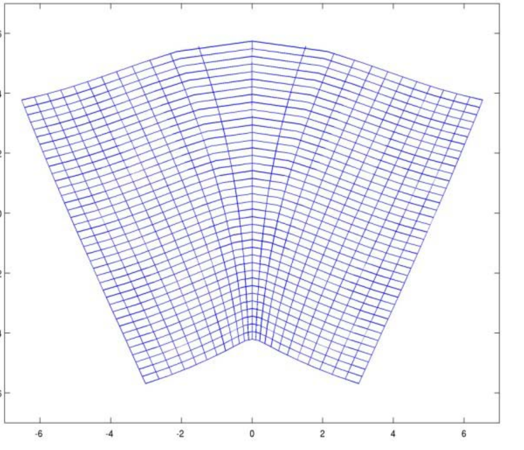
- Use one-parameter subgroups

Exponential of a smooth vector field is a diffeomorphism

- $\boldsymbol{u}$ 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

Efficient numerical methods

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

$\longrightarrow$ Direct generalization of numerical matrix algorithms.

Efficient parametric diffeomorphisms

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

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

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

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

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

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

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 $\frac{D\dot{\gamma}}{dt} = \nabla_{\dot{\gamma}}\dot{\gamma} = 0$
- Canonical symmetric Cartan Connection: unique symmetric left AND right invariant linear connection on a Lie group $\nabla_{\tilde{X}}\tilde{Y} = \frac{1}{2}[\tilde{X}, \tilde{Y}]$
- Null torsion, Curvature $R(\tilde{X}, \tilde{Y})\tilde{Z} = -\frac{1}{4}[[\tilde{X}, \tilde{Y}], \tilde{Z}]$

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

Generalizing the statistical setting to affine connection spaces?

Intuition: from Euclidean to affine spaces (but with curvature)

Mean value

- Fréchet / Karcher means not usable (no distance)
- Can be defined through exponential barycenters
- Existence? Uniqueness? OK for convex affine manifolds with semi-local convex geometry [Arnaudon & Li, Ann. Prob. 33-4, 2005]
- Algorithm to compute the mean: fixed point iteration (stability?)
- Cannonical symmetric Cartan connection:
  Bi-invariant mean on Lie groups [Arsigny Preprint 2006 + PhD 2006]

Covariance matrix & higher order moments

- Cannot be defined as $\Sigma_{ij} = E(<x|e_i><x|e_j>)$ (no dot product)
- $\Sigma_{ij} = E(x_i.x_j)$ can be defined in any specific basis (but depends on it)
- PCA has no meaning: change it to ICA?
- Anyway, the distribution is more important than the distance [Anuj yesterday]

Roadmap

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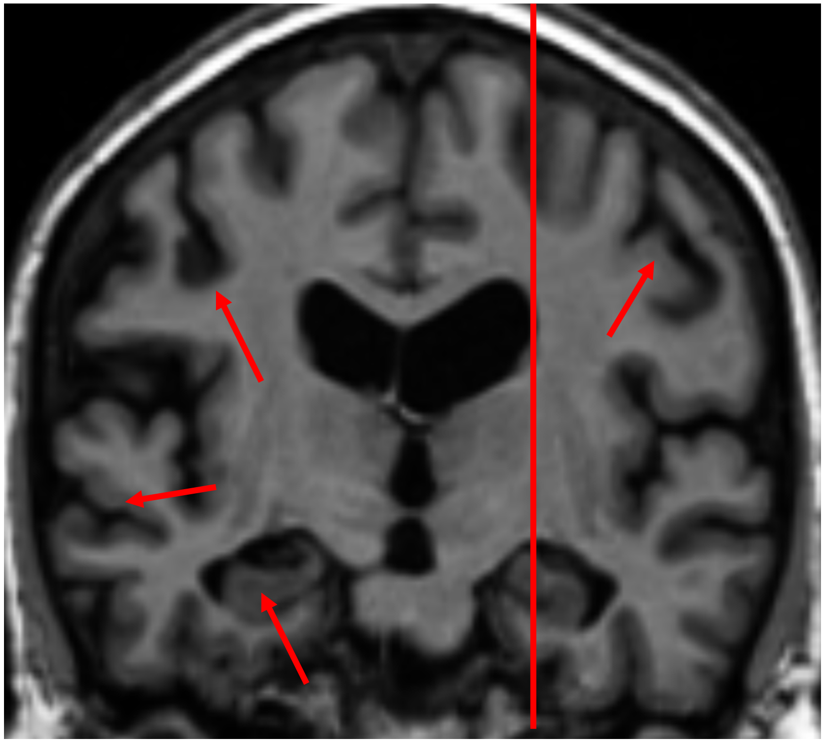
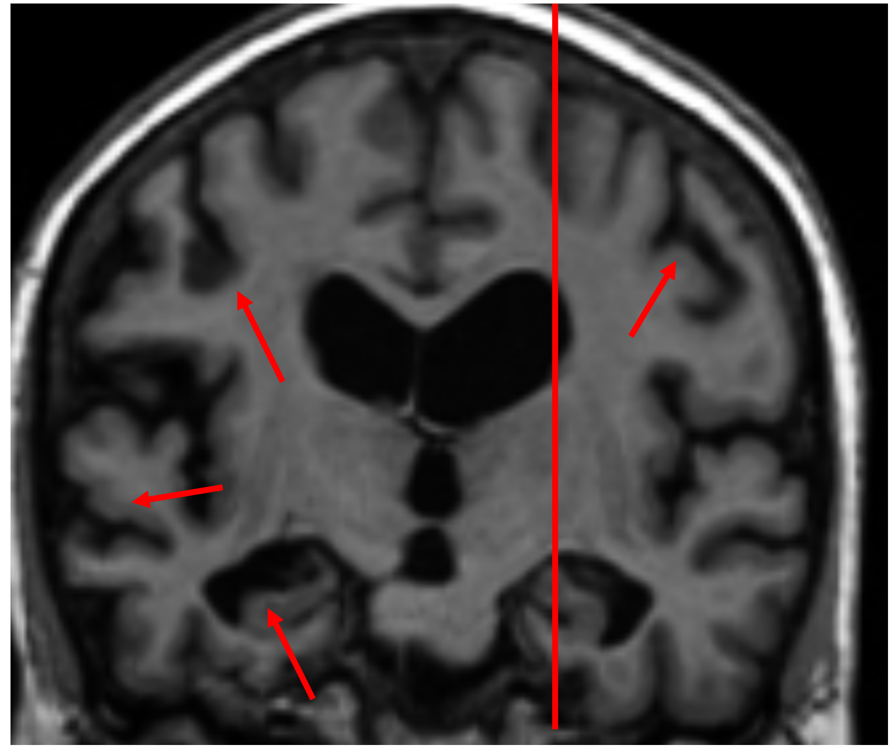
Conclusion and challenges

Longitudinal structural damage in AD



baseline

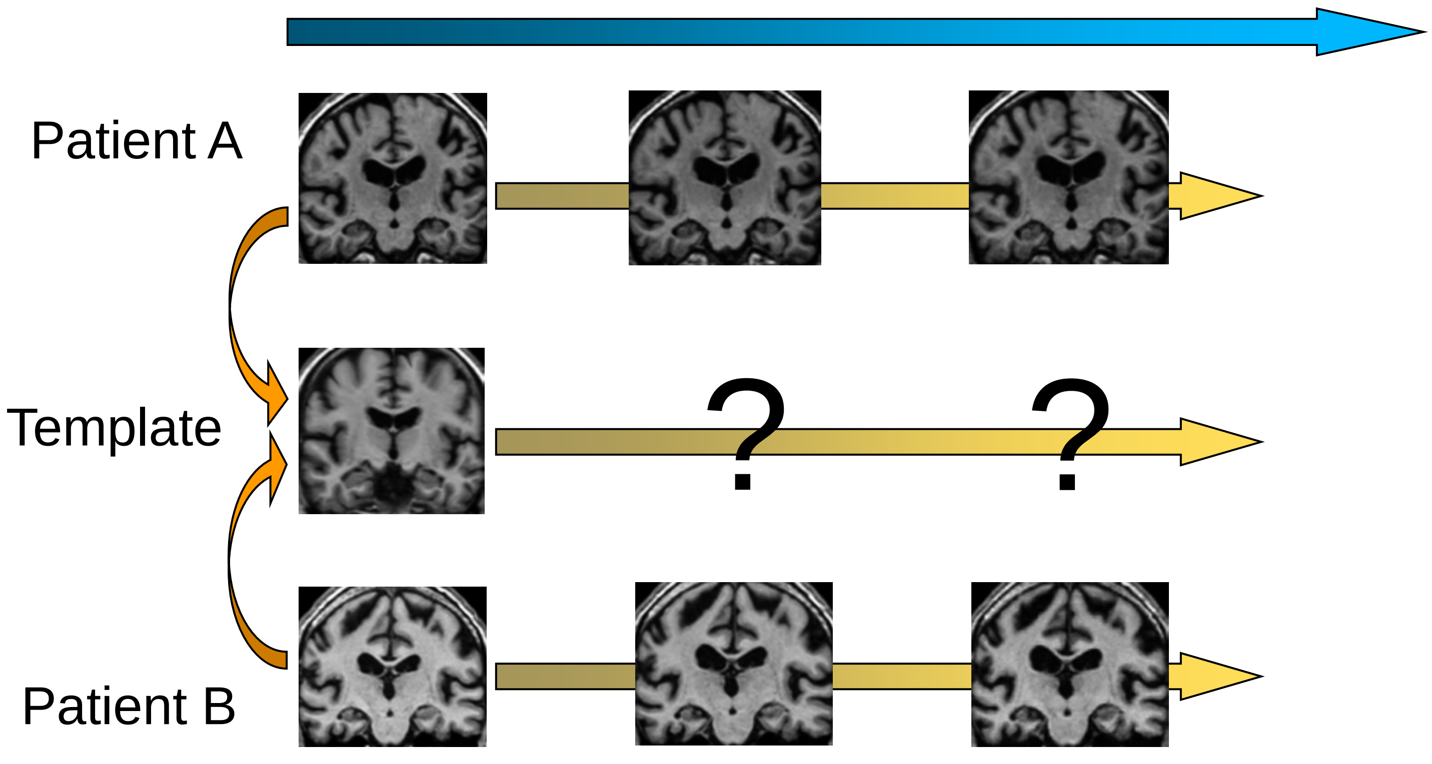


2 years follow-up

Widespread cortical thinning

Modeling longitudinal atrophy in AD from images

- 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 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

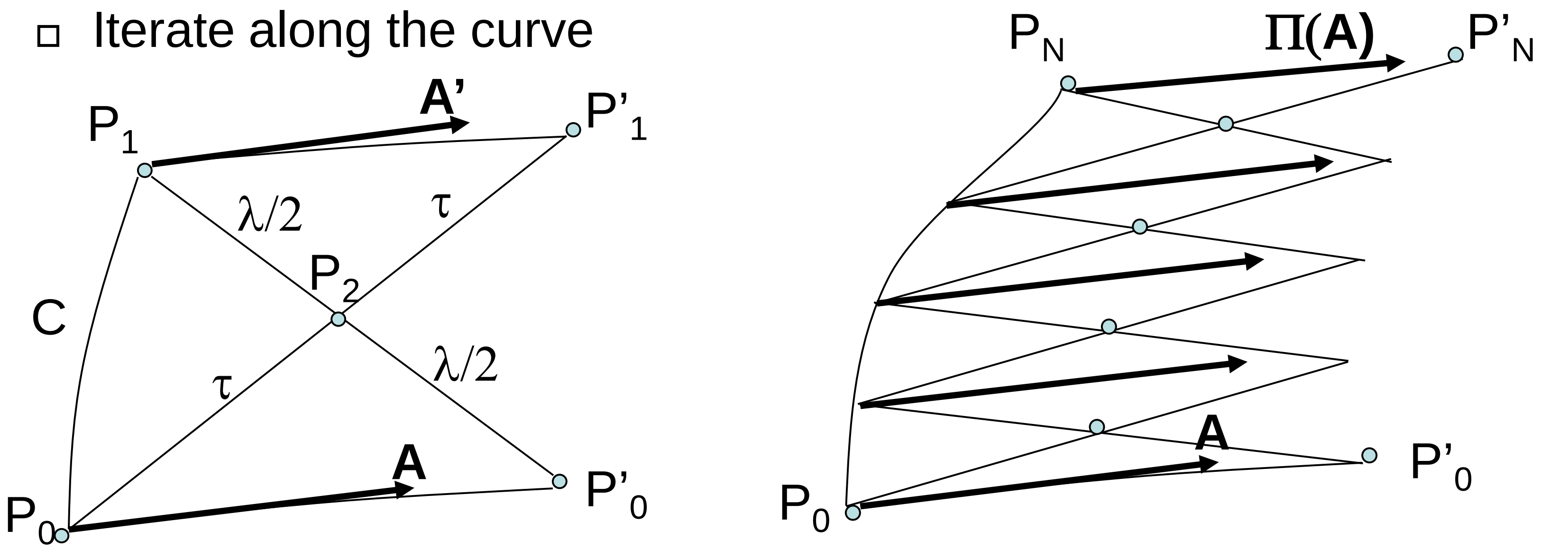
Parallel transport along arbitrary curves

Infinitesimal parallel transport = connection

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

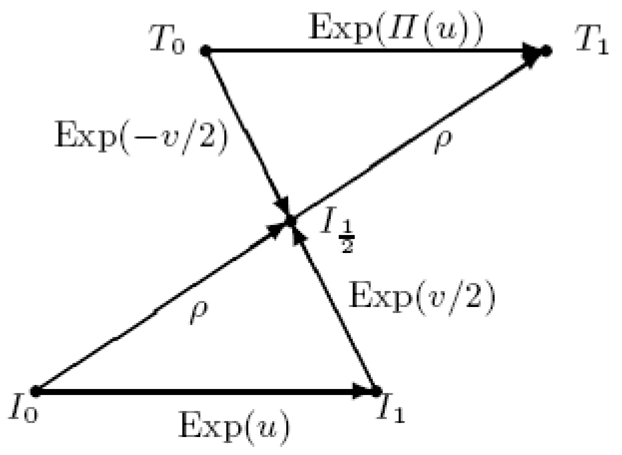
A numerical scheme to integrate for symmetric connections: Schild's Ladder [Elhers et al, 1972]

- 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]

Efficient Schild's Ladder with SVFs



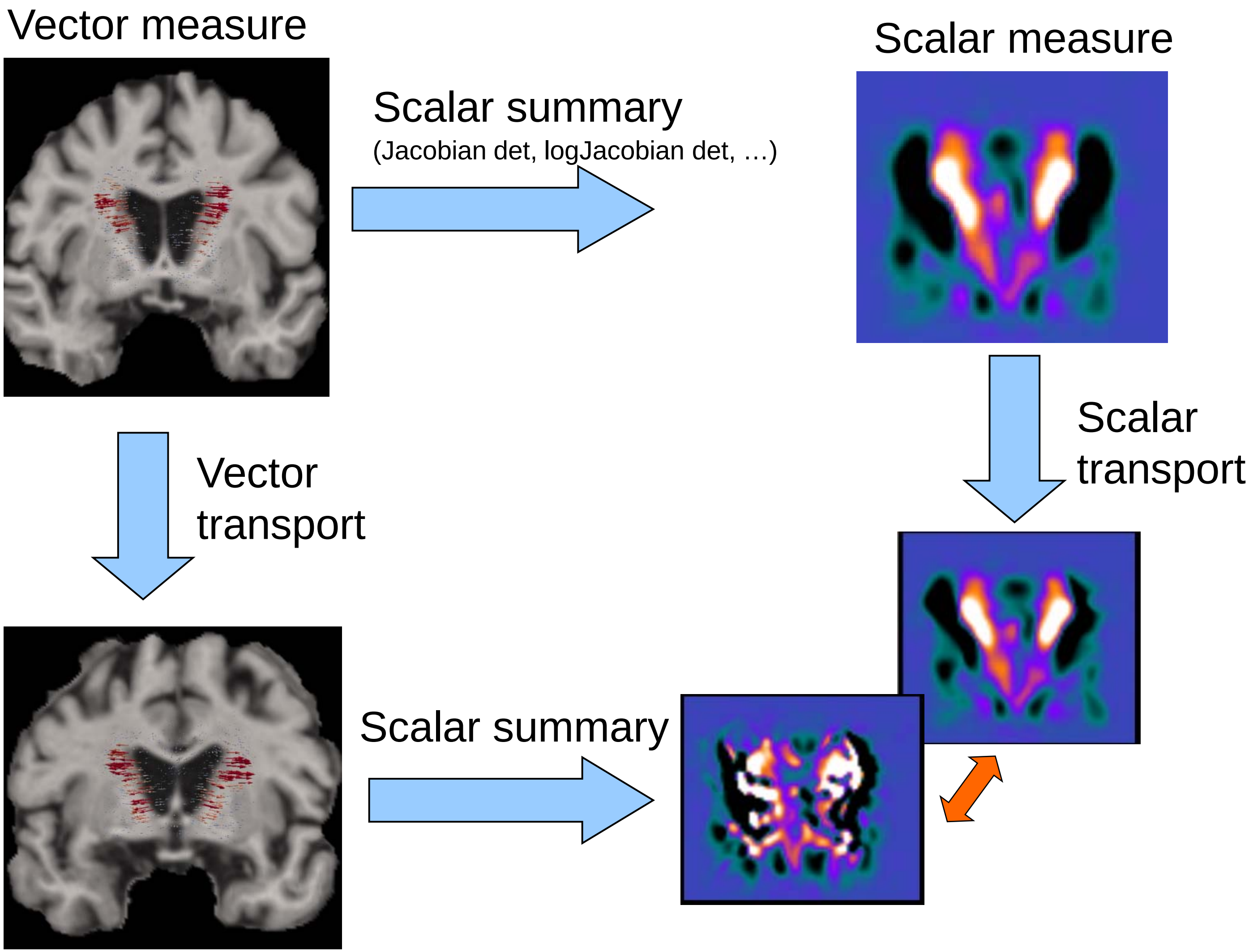
$$\mathrm{Exp}(\Pi(u)) = \mathrm{Exp}(v/2) \circ \mathrm{Exp}(u) \circ \mathrm{Exp}(-v/2)$$

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

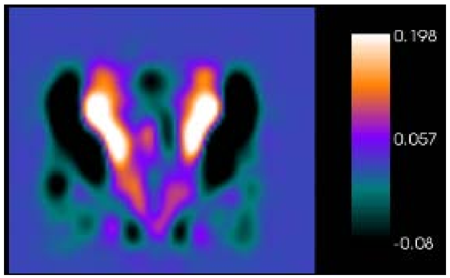
[Lorenzi, Ayache, Pennec: Schild's Ladder for the parallel transport of deformations in time series of images, IPMI 2011]

Synthetic experiments (Consistency)

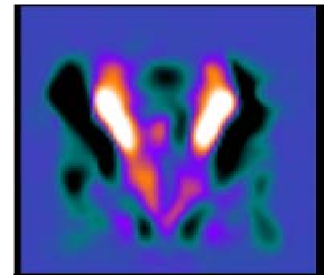


Synthetic experiments (Consistency)

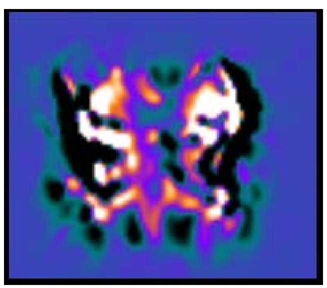
Original longitudinal Log-Jacobian map



Scalar transport

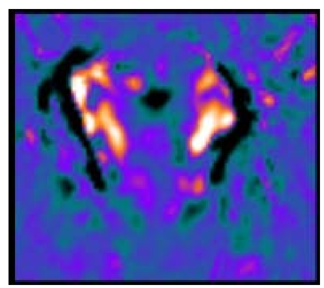


Vector transport:



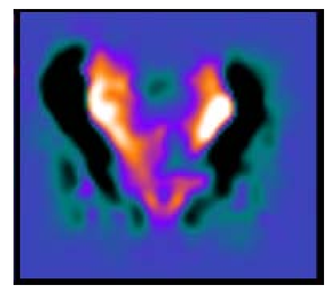
Conjugation
(deformation field)

$$Ad_{\psi_T}(\varphi_i) = \psi_T^{-1} \circ \varphi_i \circ \psi_T$$



Reorientation
(velocity field)

$$J_{\psi_T} v_i$$

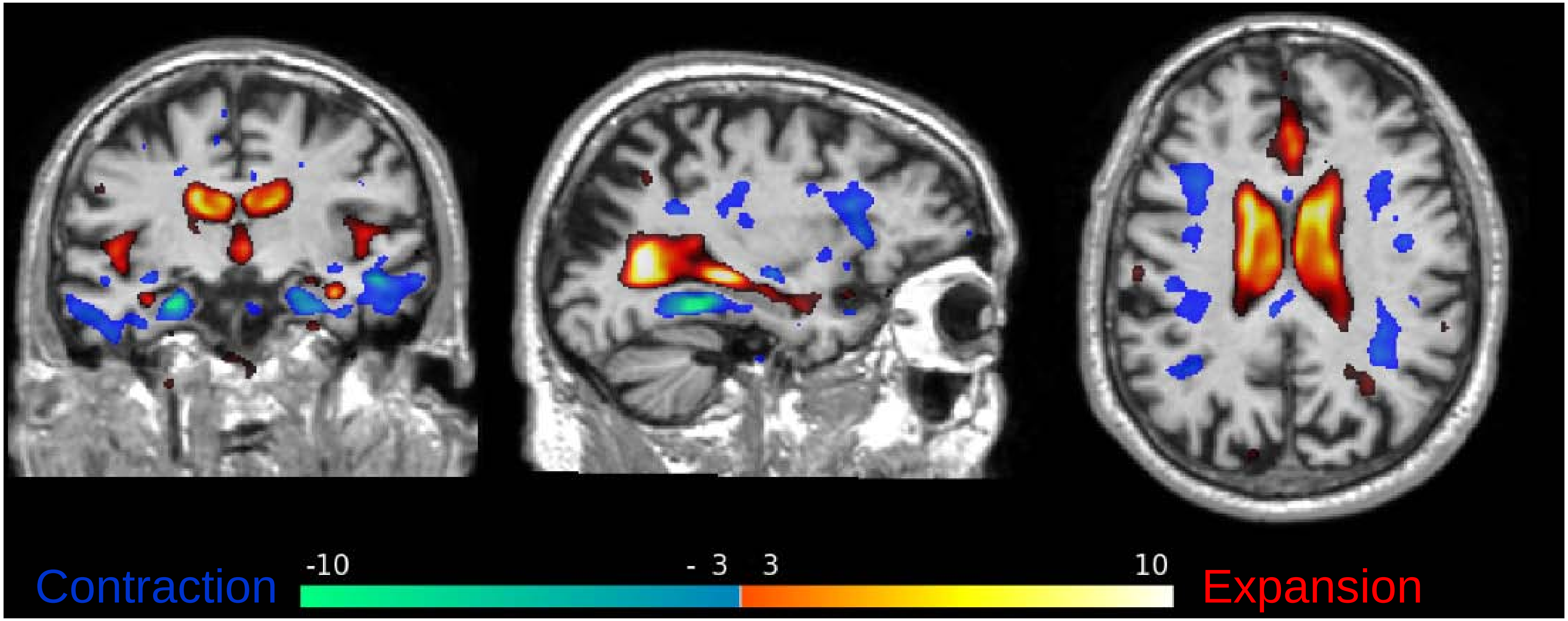


Schild's Ladder
(velocity field)

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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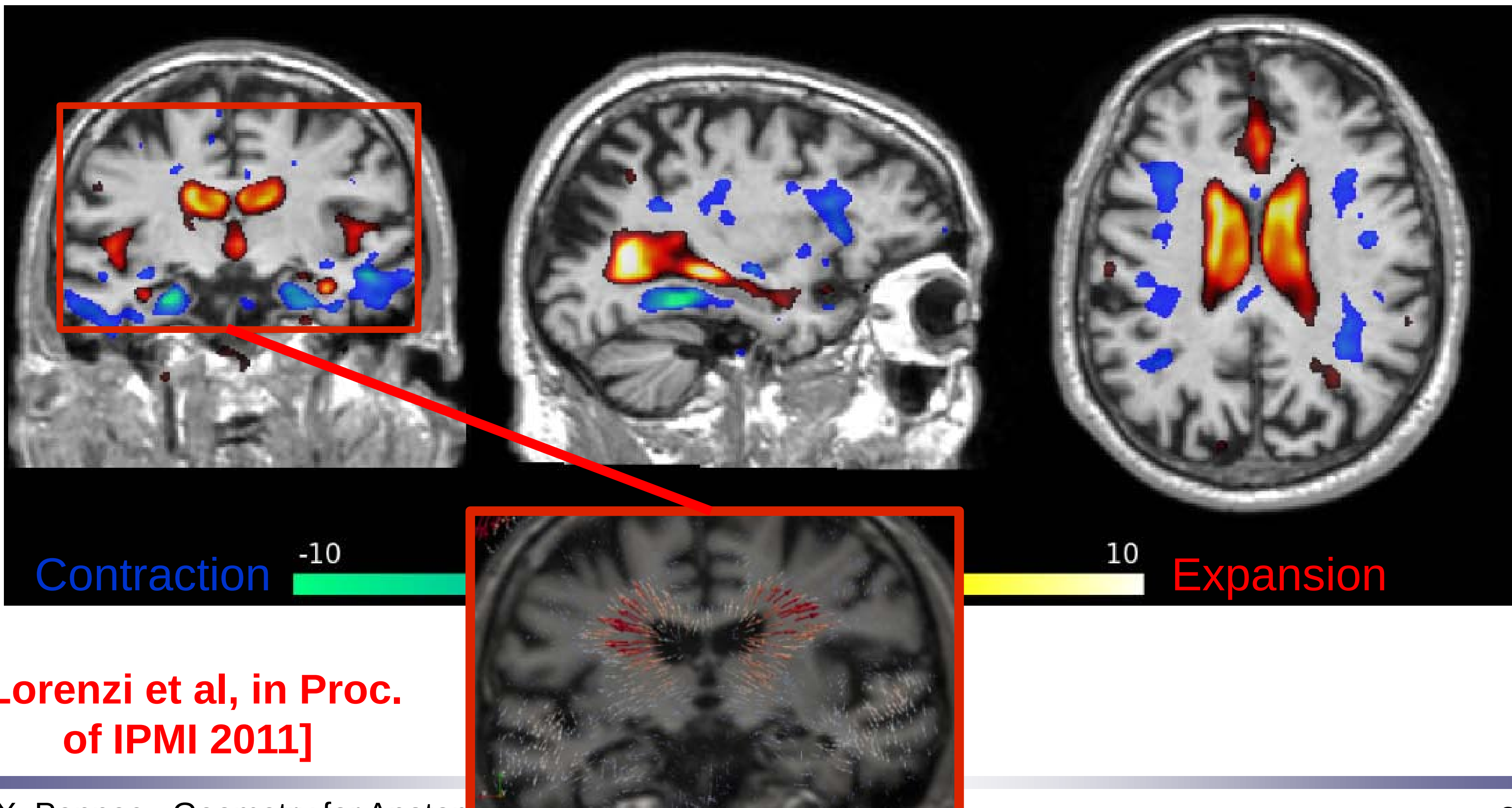

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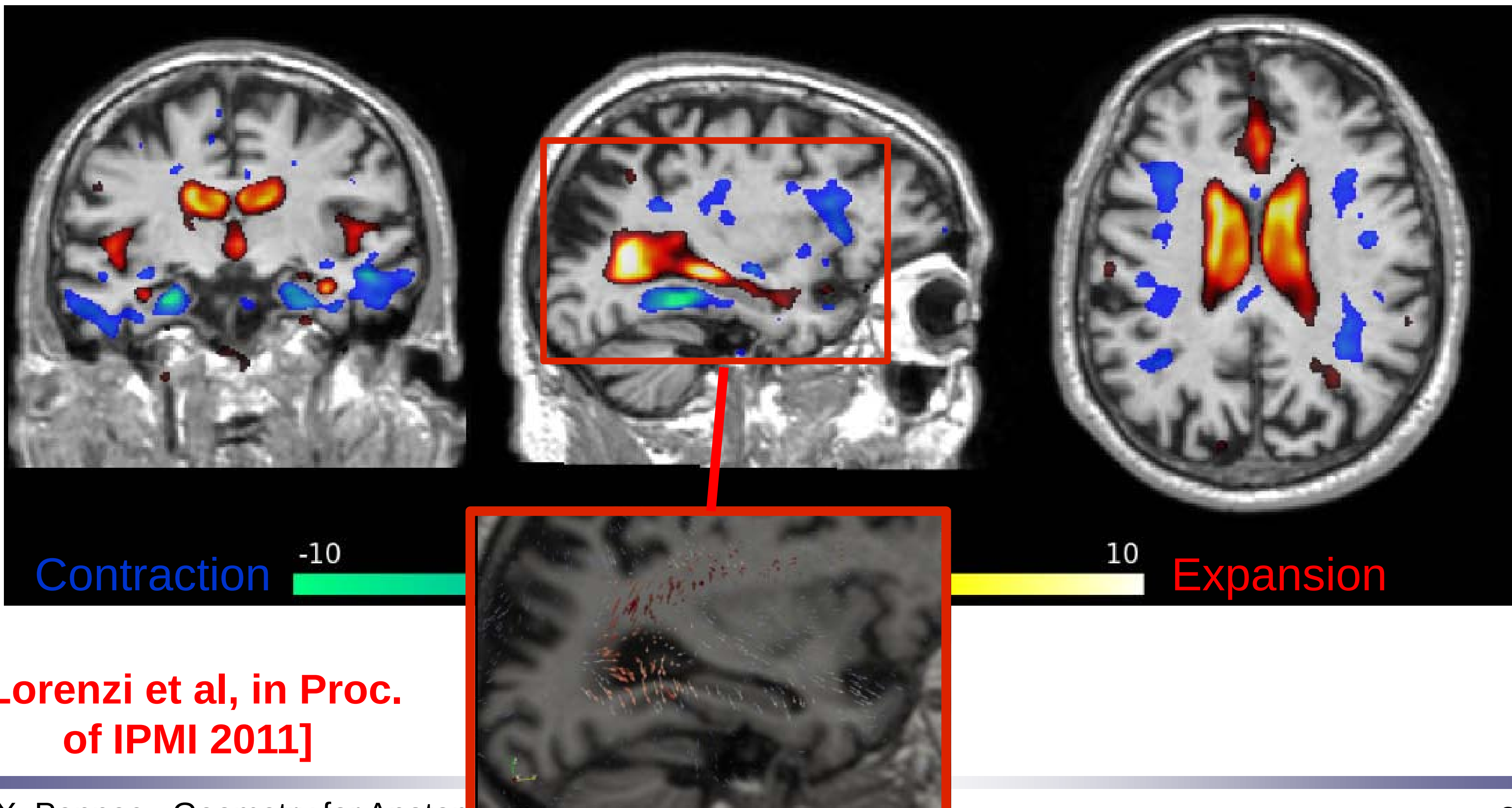

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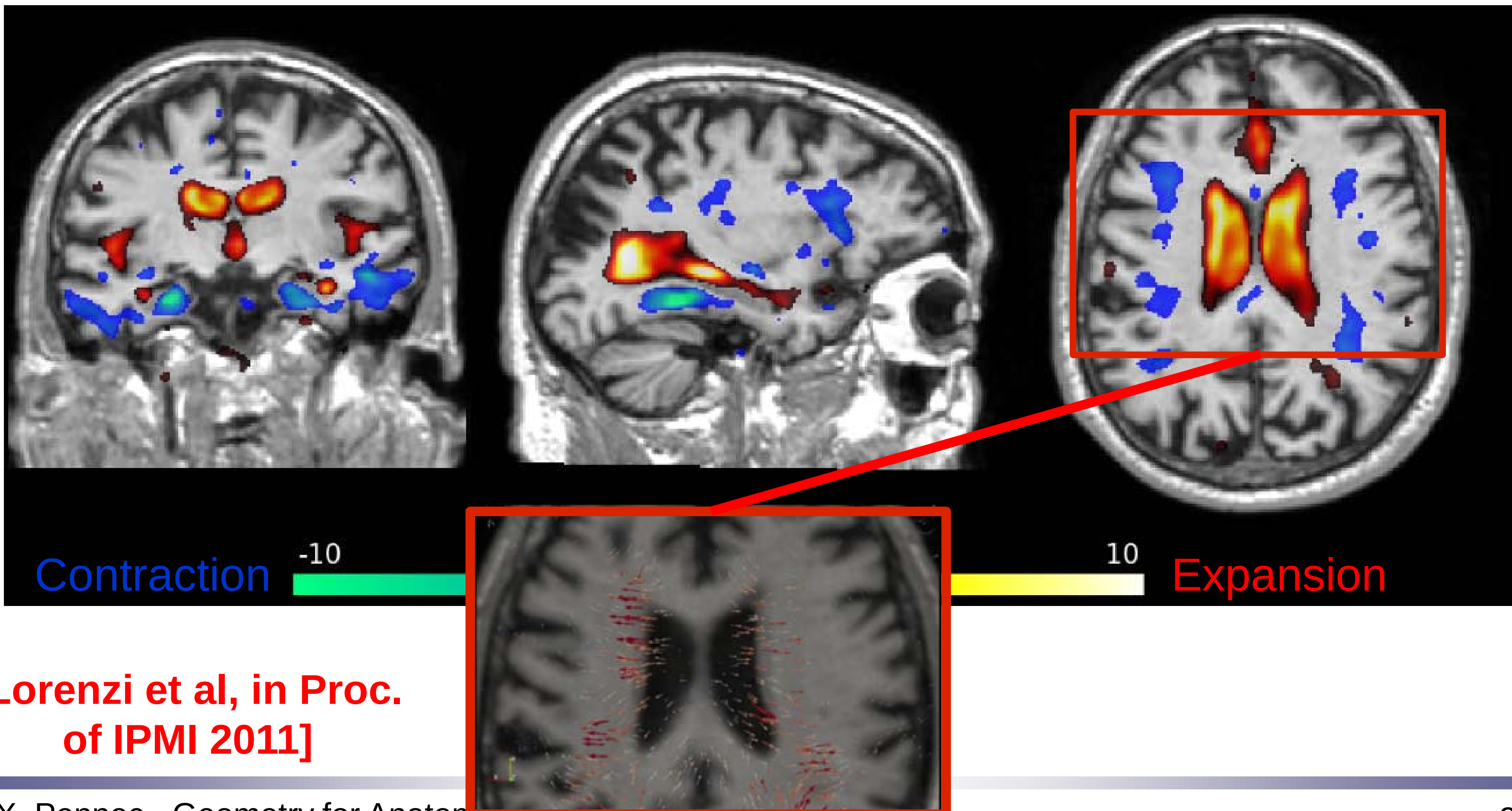
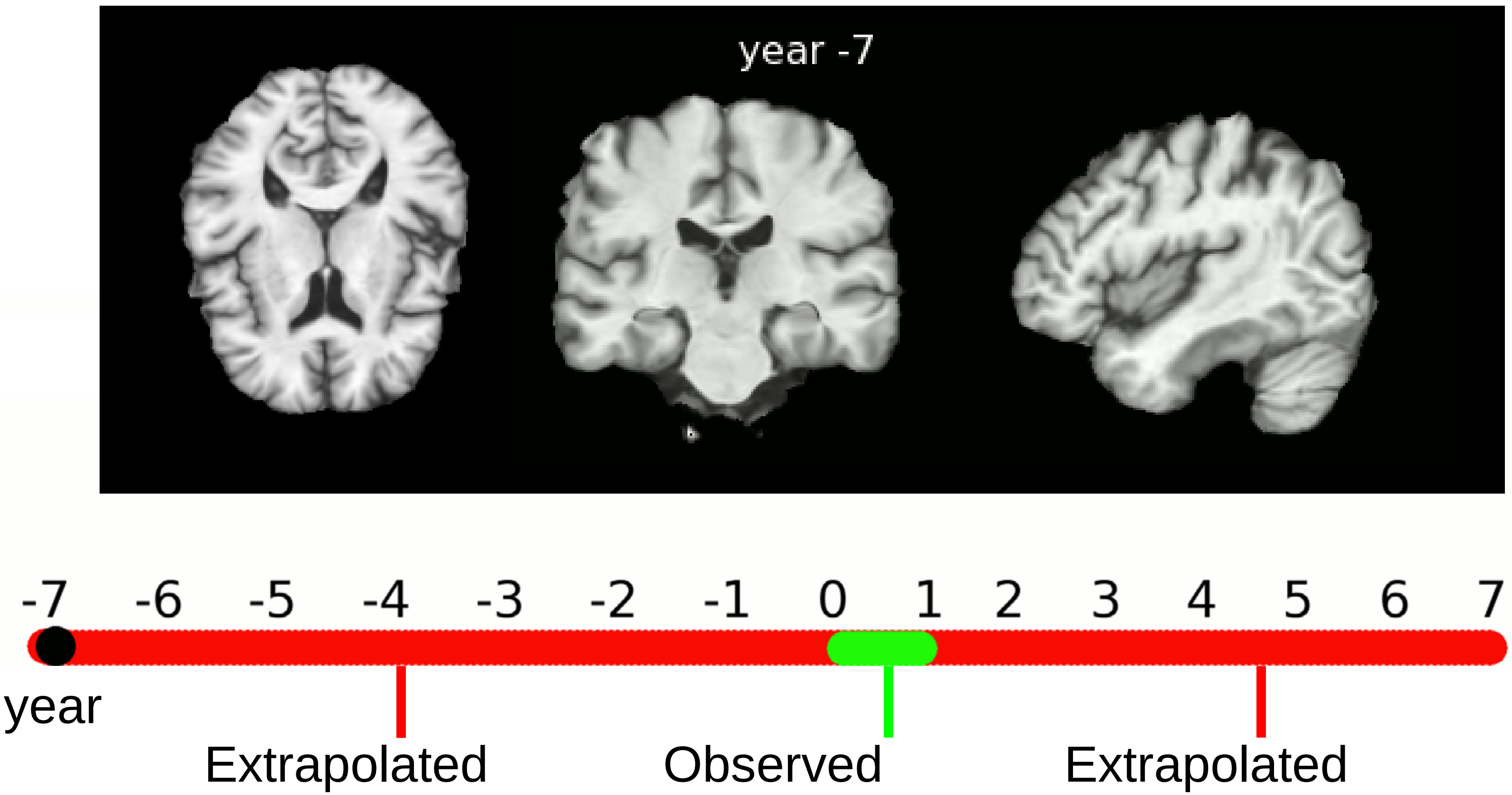


[Lorenzi et al, in Proc. of IPMI 2011]

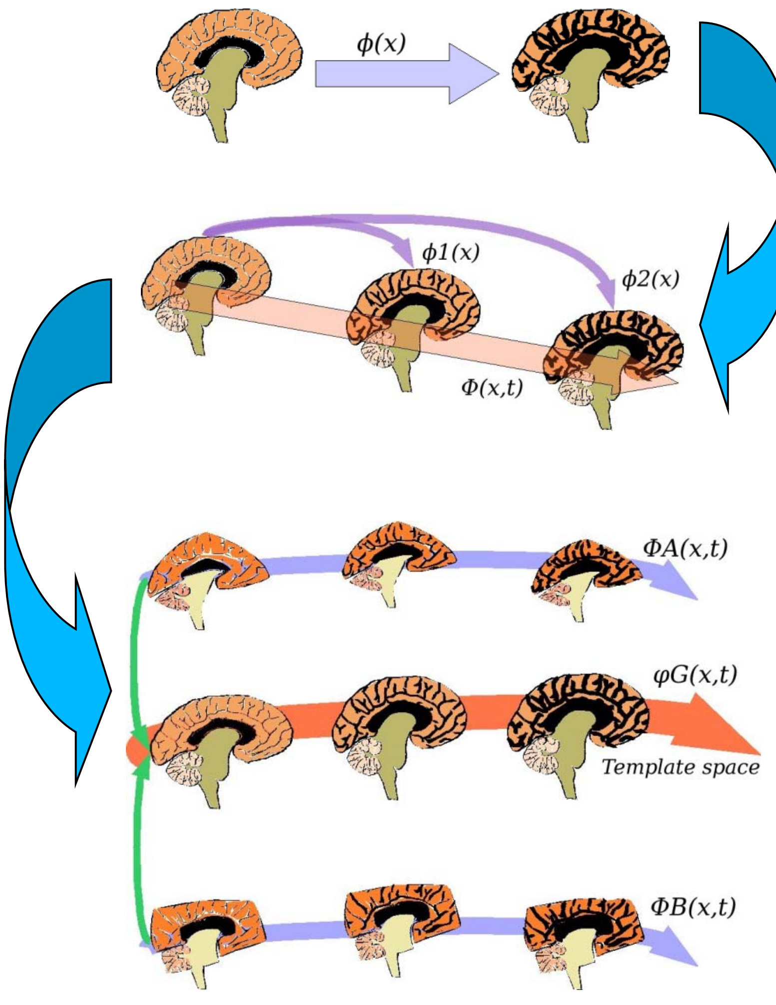
Longitudinal model for AD

Modeled changes from 70 AD subjects (ADNI data)

Extrapolation



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.

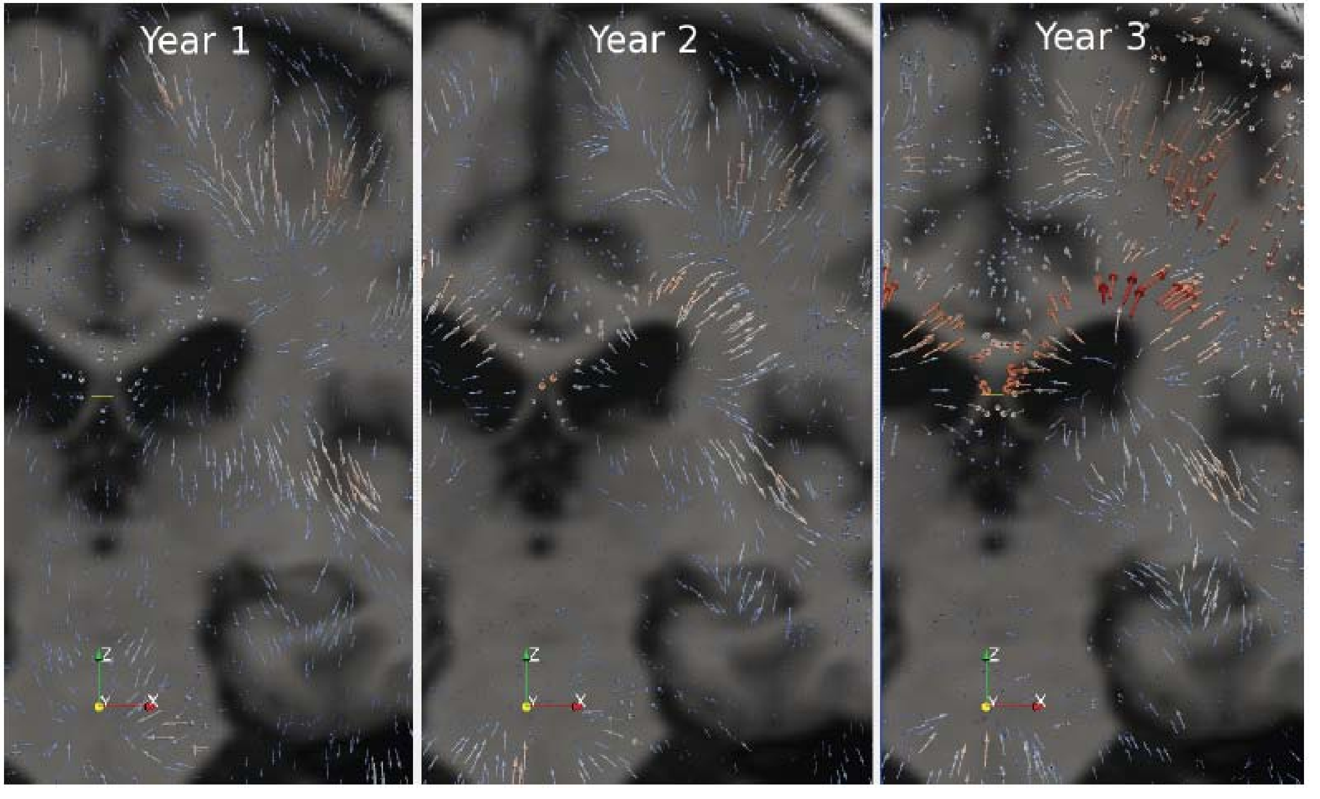
Multiple subjects, multiple time points

Schild's Ladder

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

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-?**

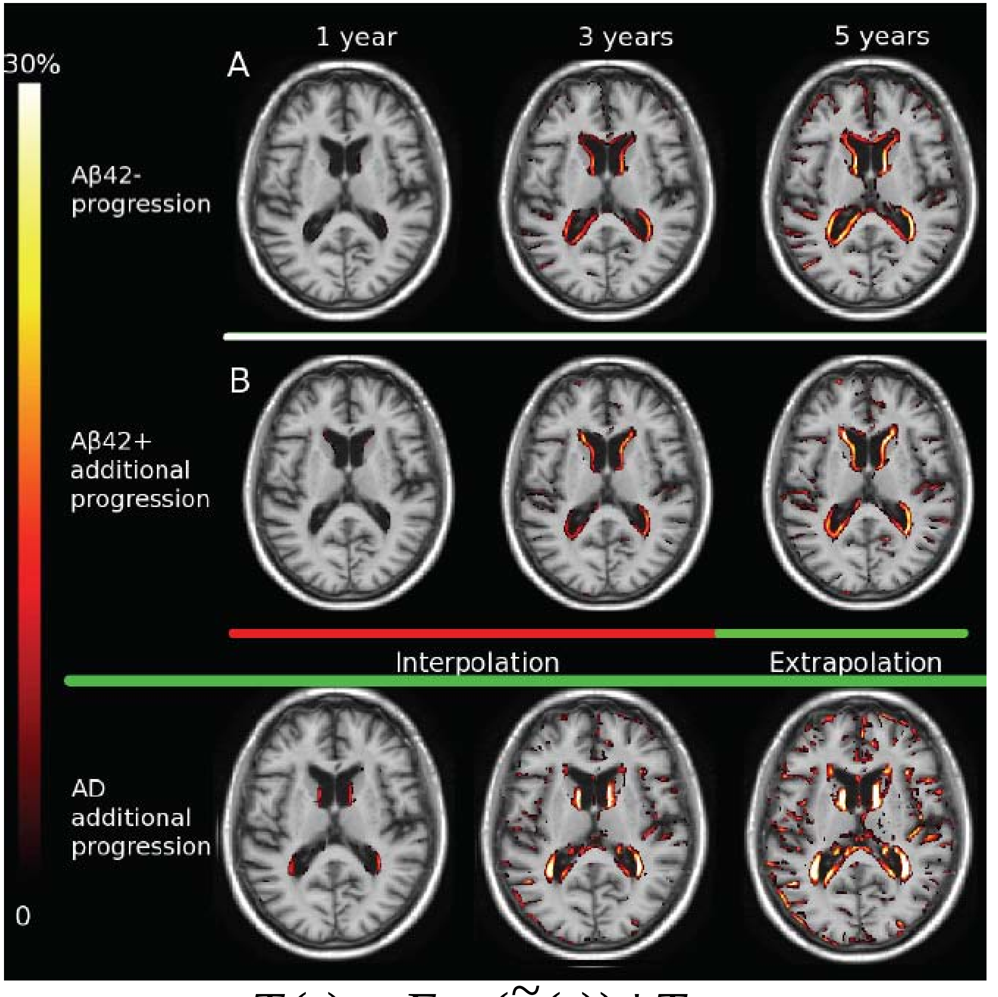


Average SVF for normal evolution (Aβ-)

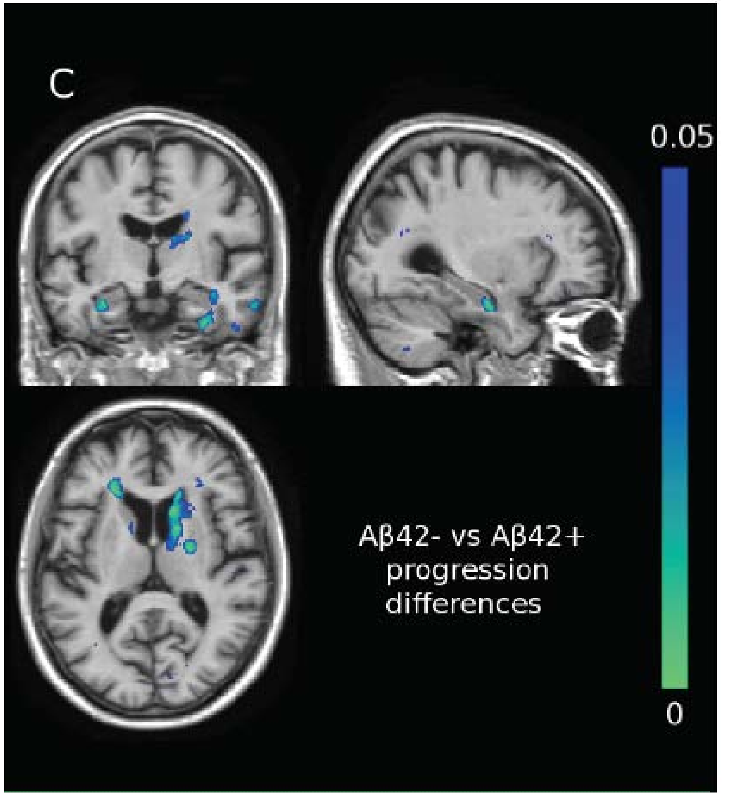
[Lorenzi, Ayache, Frisoni, Pennec, in Proc. of MICCAI 2011]

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

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Conclusion

Algorithms for SVFs

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

Schilds 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

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)

Conclusion

Affine connection instead of Riemannian spaces?

- A symmetric connection defines geodesics but no length along them
- Not always a geodesic joining two points
- Covariance matrix makes sense in a basis but no canonical basis
- PCA -> ICA?

An apparently nice setting for transformation groups

- Canonical Cartan connection on Lie groups: one-parameters subgroups
- Bi-invariant mean on Lie groups [Arsigny Preprint + PhD 2006]
- Parallel transport is easy using Schilds Ladder

Left/right invariant metrics (LDDMM) and symmetric Cartan connection

- Quantify differences between geodesics
- Evaluate the practical impact on statistics

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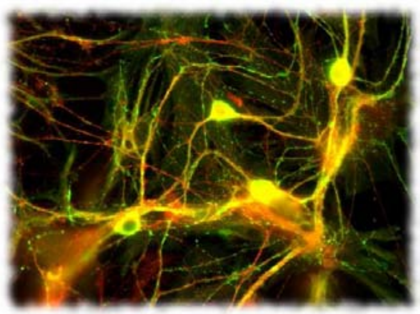
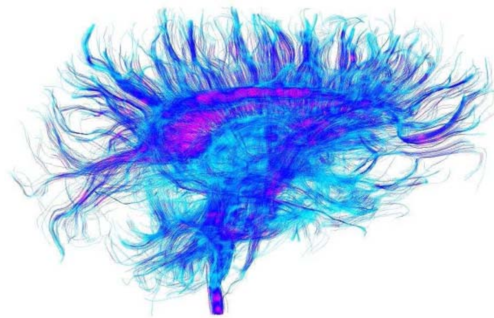
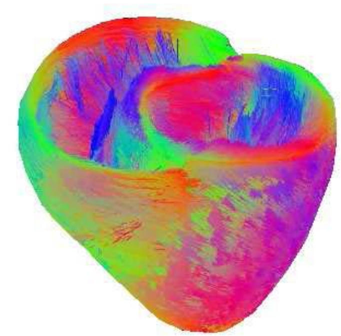
Master of Science in Computational Biology at Nice-Sophia Antipolis University

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

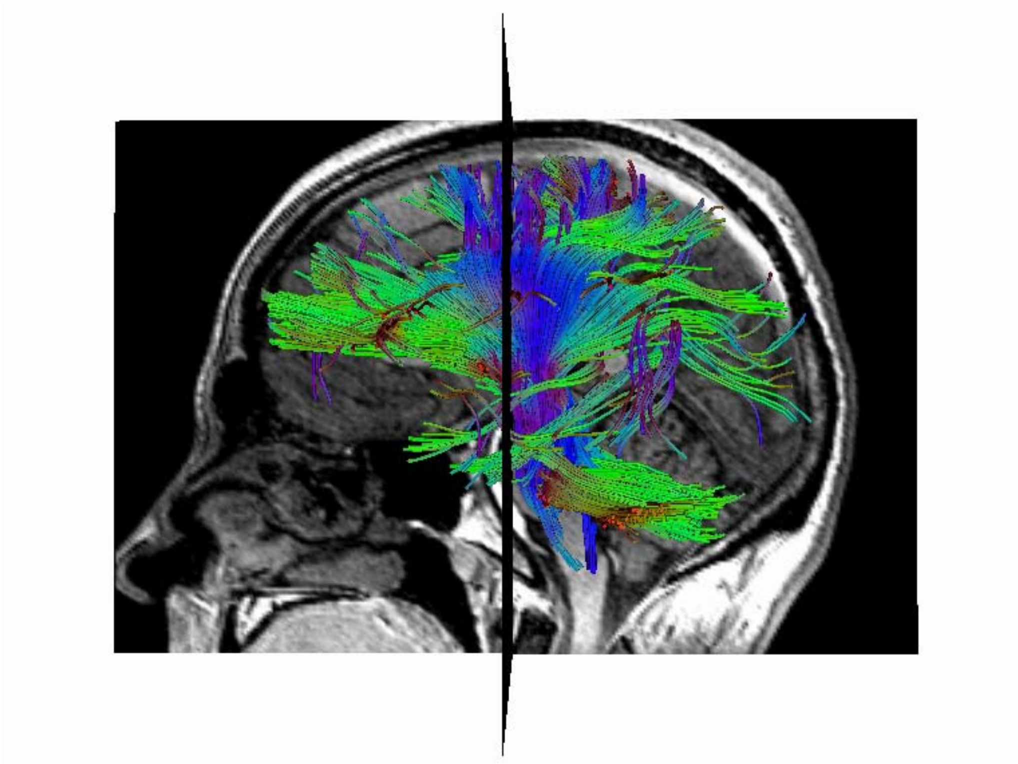





Workshop Mathematical Foundations of Computational Anatomy at MICCAI 2011

- Toronto, September 18 or 22, 2011
  - http://www-sop.inria.fr/asclepios/events/MFCA08/
  - http://www-sop.inria.fr/asclepios/events/MFCA06/

Thank You!



Publications: http://www.inria.fr/sophia/asclepios/biblio

Software: http://www.inria.fr/sophia/asclepios/software/MedINRIA.

Special thanks to Pierre Fillard for many illustrations!