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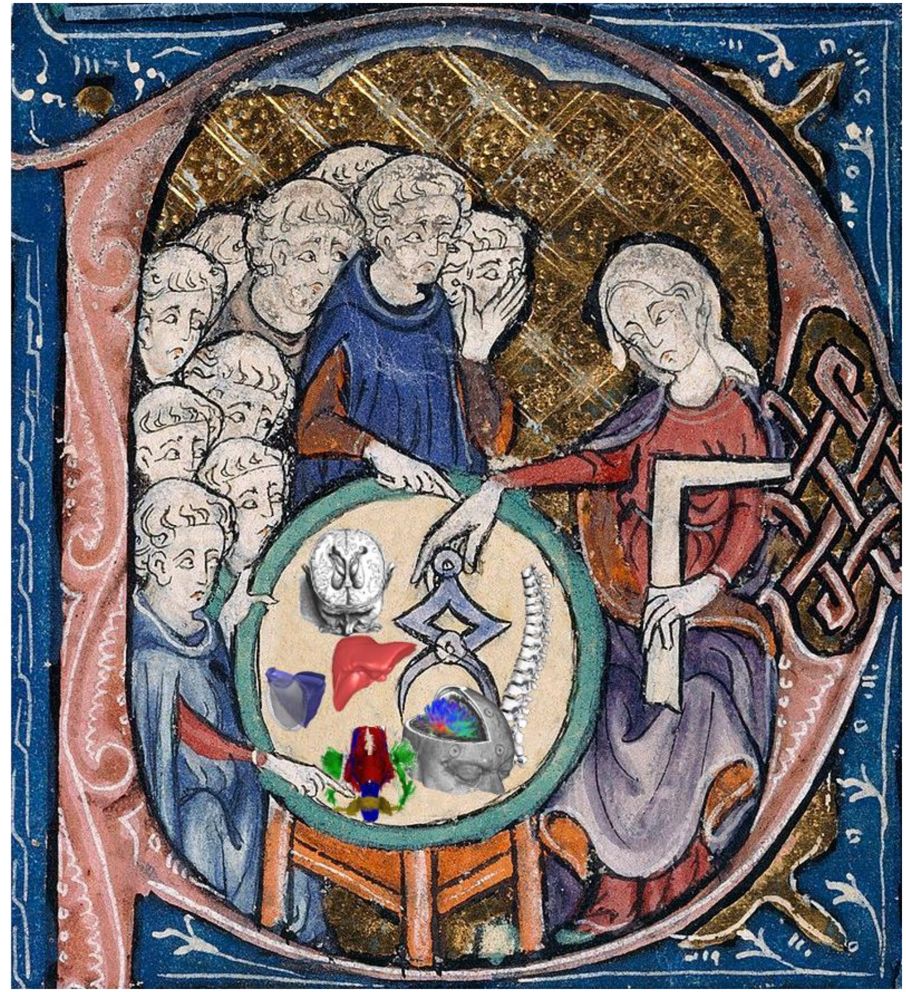
http://www-sop.inria.fr/asclepios/cours/Peyresq_2019/

Geometric Statistics

Mathematical foundations and applications in computational anatomy



Freely adapted from "Women teaching geometry", in Adelard of Bath translation of Euclid's elements, 1310.

4/ Parallel transport to analyze Longitudinal diffeos

Ecole d'été de Peyresq, Jul 1-5 2019

Epione e-patient / e-medicine

UNIVERSITÉ CÔTE D'AZUR

Inria

Geometric Statistics: Mathematical foundations and applications in computational anatomy

Intrinsic Statistics on Riemannian Manifolds

Manifold-Valued Image Processing

Metric and Affine Geometric Settings for Lie Groups

Parallel Transport to Analyze Longitudinal Deformations

Advances Statistics: CLT & PCA

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- Measuring Alzheimer's disease (AD) evolution
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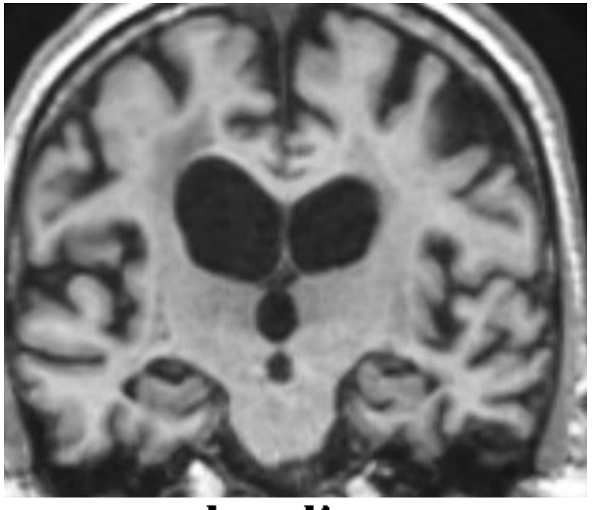
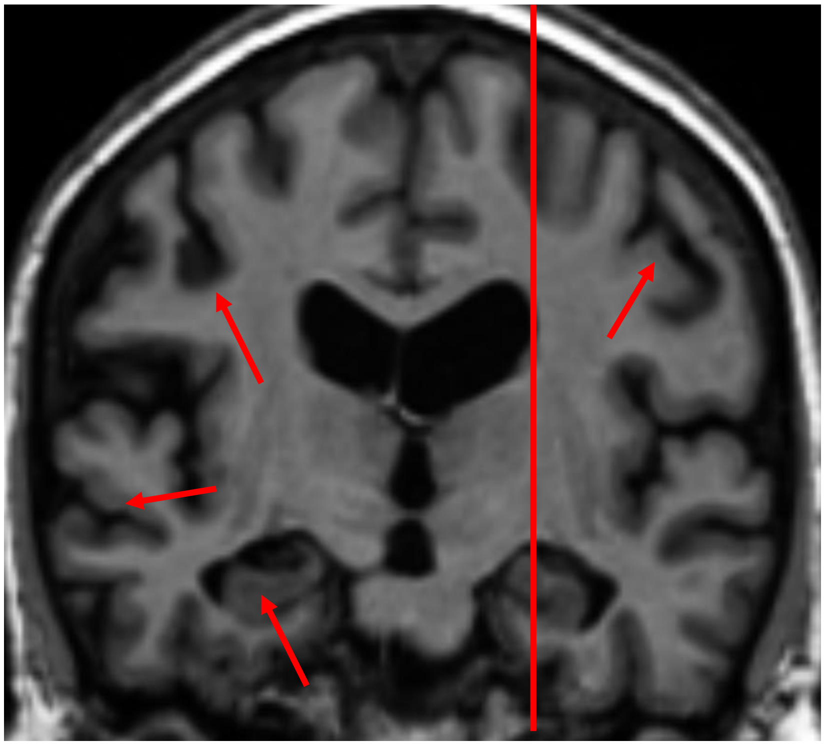
Alzheimer's Disease

- 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

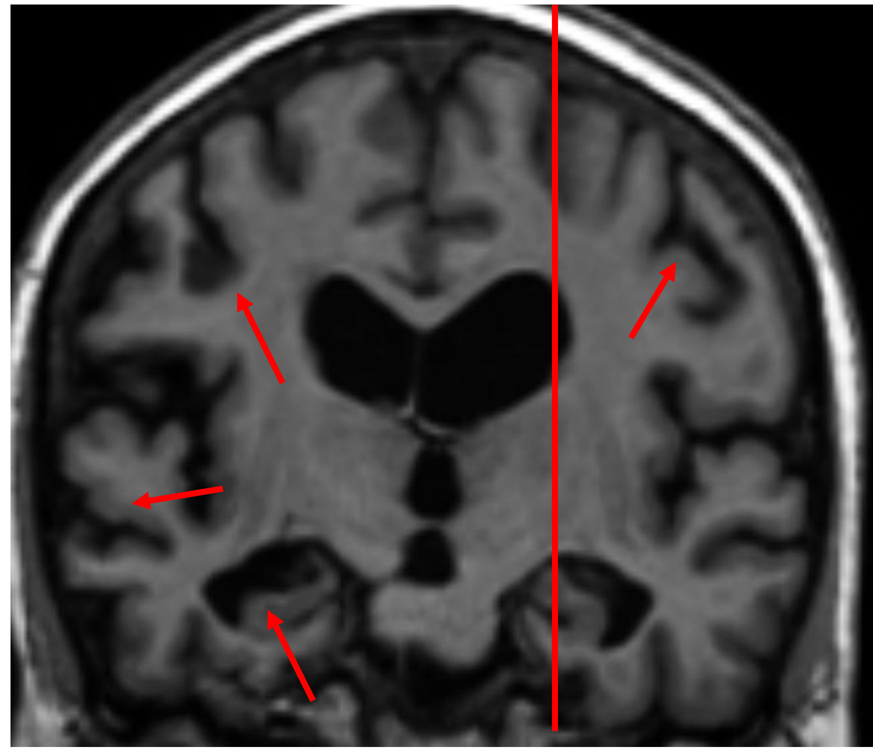


baseline

Longitudinal structural damage in AD



baseline



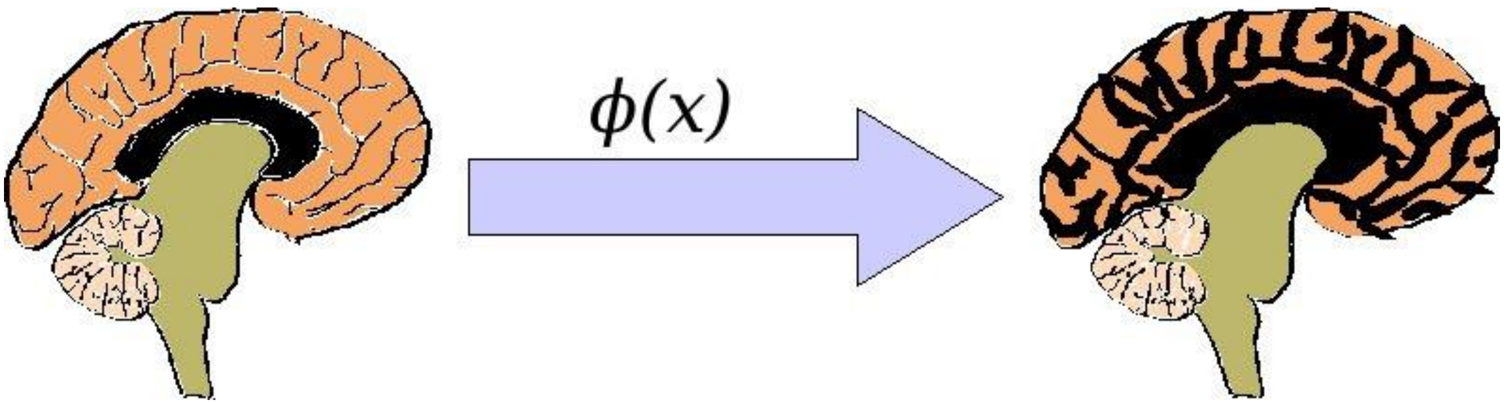
2 years follow-up

Widespread cortical thinning

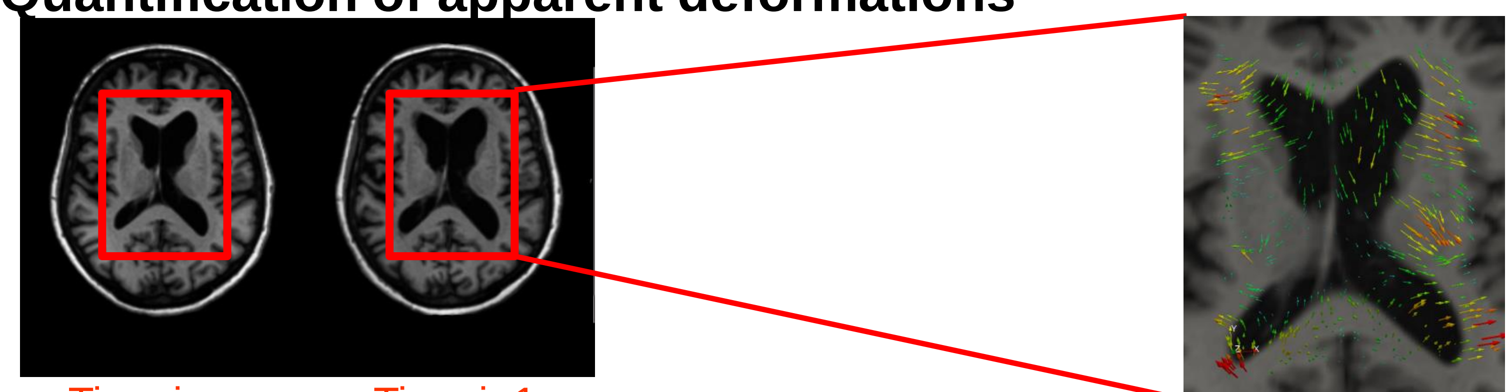
Measuring Temporal Evolution with deformations

Geometry changes (Deformation-based morphometry)

Measure the physical or apparent deformation found by deformable registration



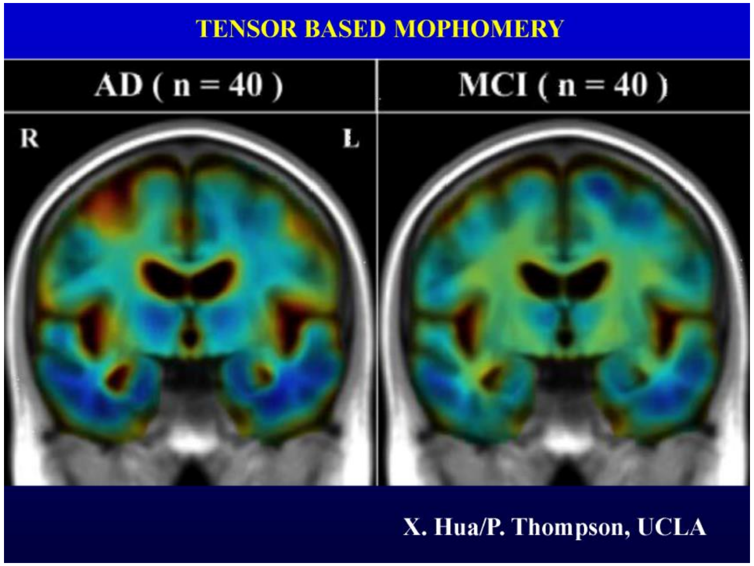
Quantification of apparent deformations

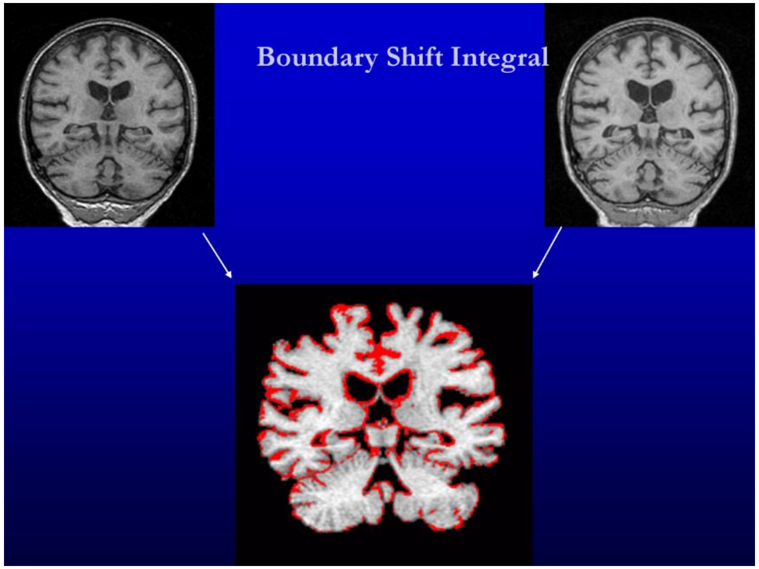


Time i Time i+1

Atrophy estimation for Alzheimer's Disease

Established markers of anatomical changes





Local: TBM (Paul Thompson, UCLA)

Local volume change: Jacobian

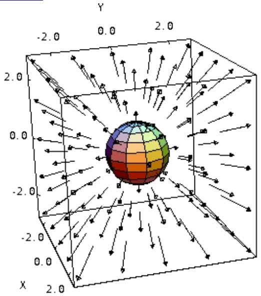
(determinant of spatial derivatives matrix)

Global: BSI / KNBSI (N. Fox, UCL)

Intensity flux through brain surface

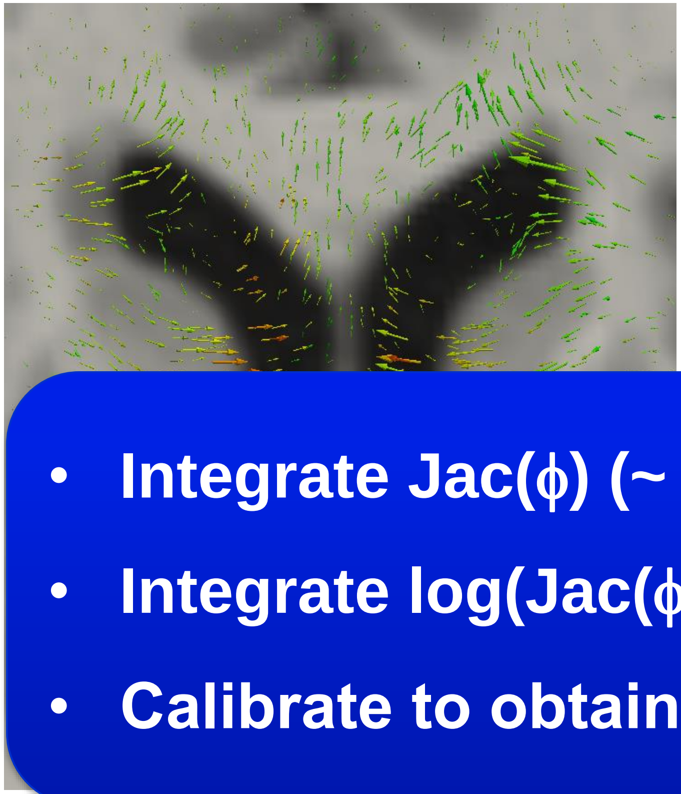
SIENA (S.M. Smith, Oxford)

percentage brain volume change



Atrophy estimation from SVFs

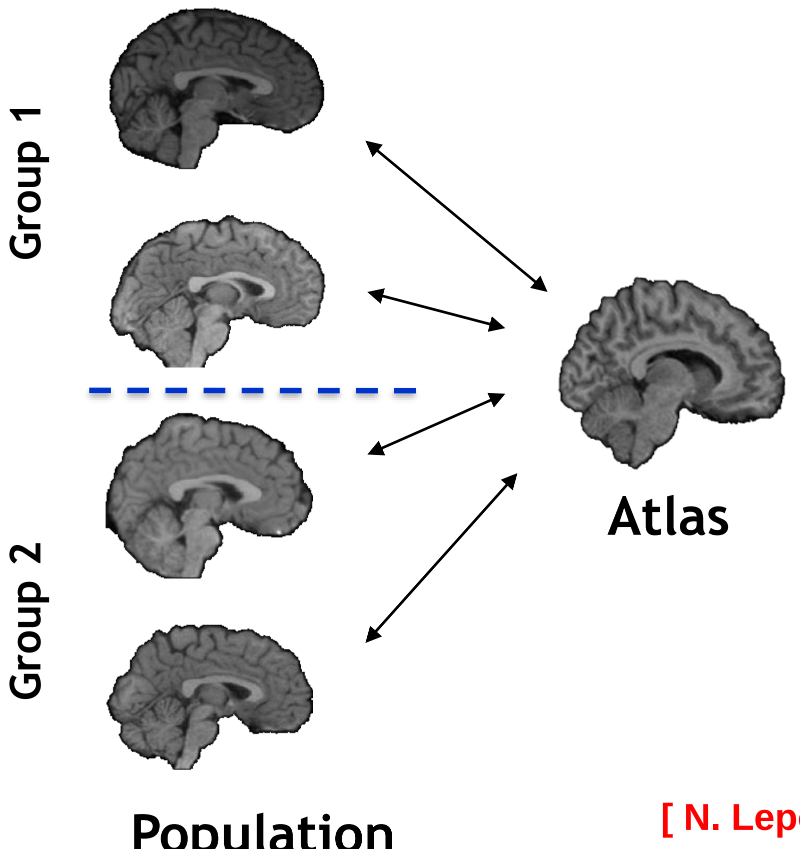
$$\int_0^1 \mathrm{flux}_{\partial\Omega}(\mathbf{v}|_{\phi(x,h)})dh = \iiint_\Omega \log(\det(\nabla\phi(x,1)))d\Omega$$



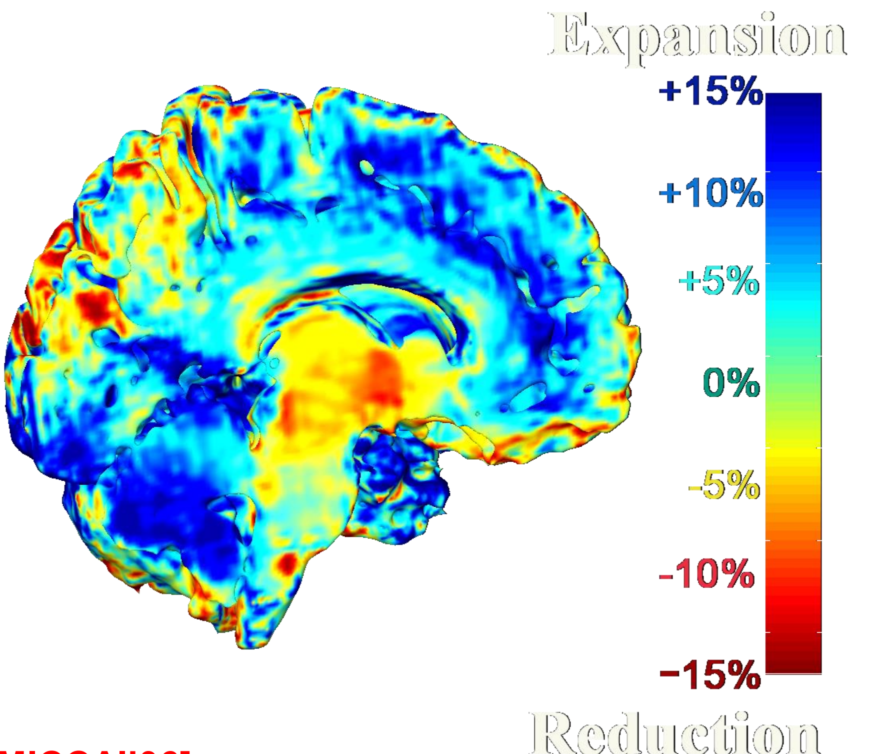
- Integrate Jac(ϕ) (~ TBI) → Volume change
- Integrate log(Jac(ϕ)) → Flux-like (~ BSI)
- Calibrate to obtain “equivalent ”volume changes

Groupwise analysis: deformation-based morphometry

- Register subjects and controls to atlas
- Spatial normalization of Jacobian maps
- Statistical discrimination between groups



$\det(\nabla\Phi(x))$

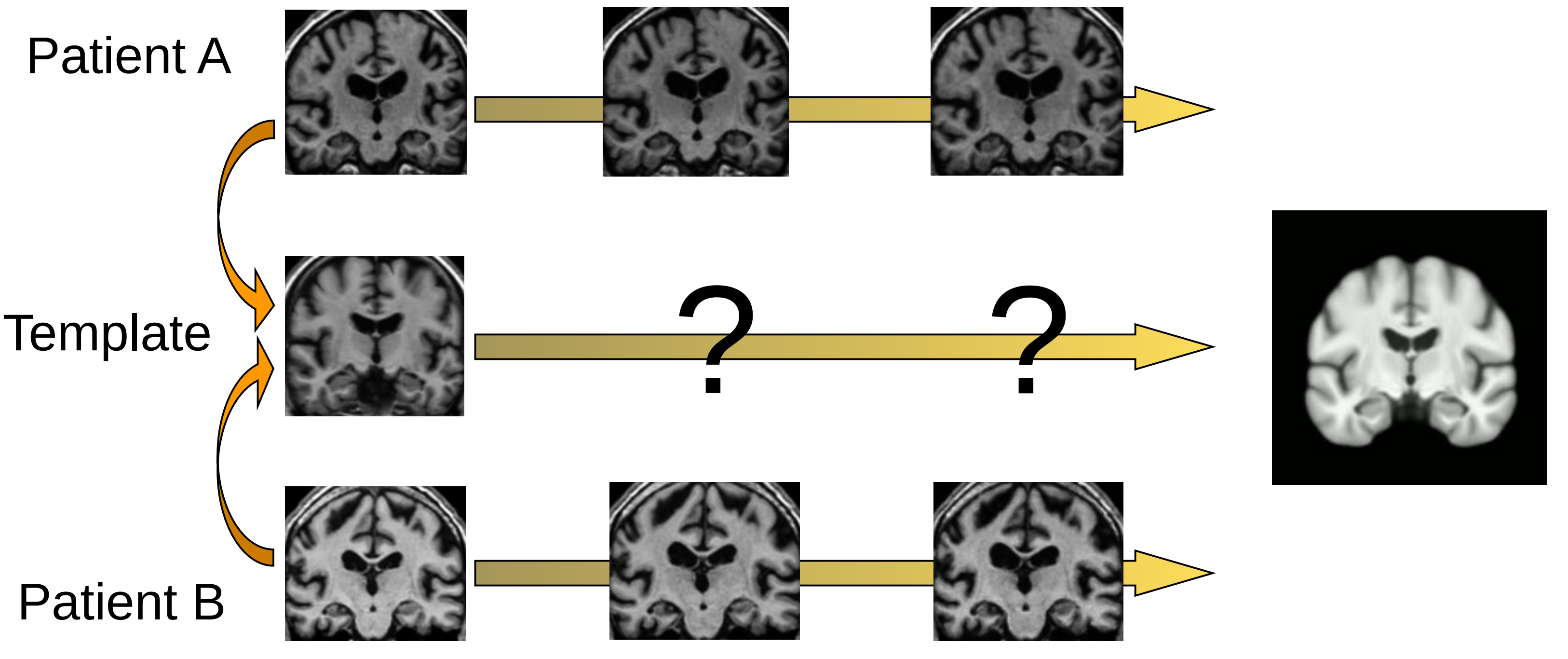


[N. Lepore et al, MICCAI'06]

Longitudinal deformation analysis in AD

From patient specific evolution to population trend:

- Parallel transport of deformation trajectories along inter-subject trajectories
- Consistency of the numerical scheme with geodesics?



[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]

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Advances Statistics: CLT & PCA

Parallel transport of deformation trajectories

Parallel transport

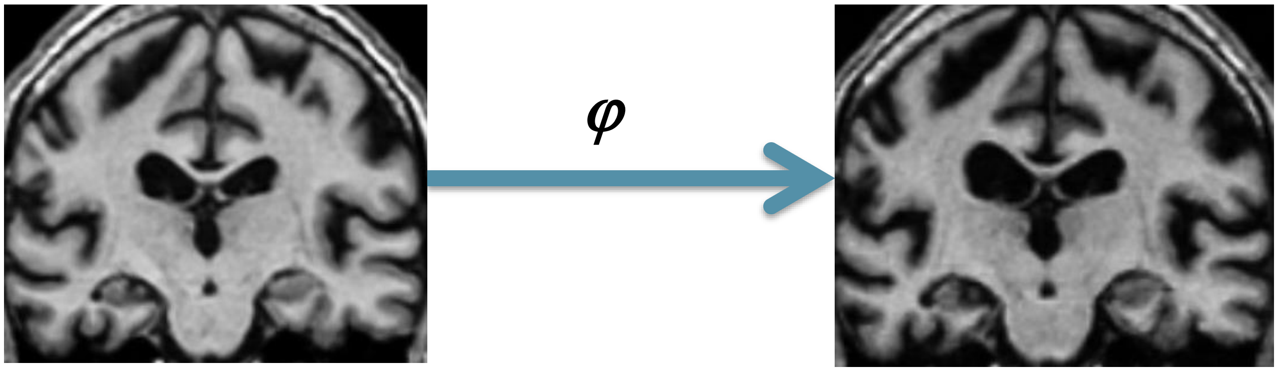
- (small) longitudinal deformation vector
- along the large inter-subject normalization deformation

Existing methods

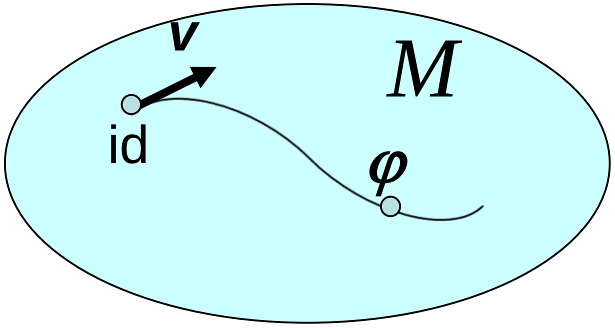
- Resampling scalar summary statistics maps (e.g. jacobian)
- Vector reorientation with Jacobian of inter-subject deformation
- Conjugate action on deformations (Rao et al. 2006)
- LDDMM setting: parallel transport along geodesics via Jacobi fields [Younes et al. 2008]

Intra and inter-subject deformations/metrics are of different nature

Parallel transport 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:

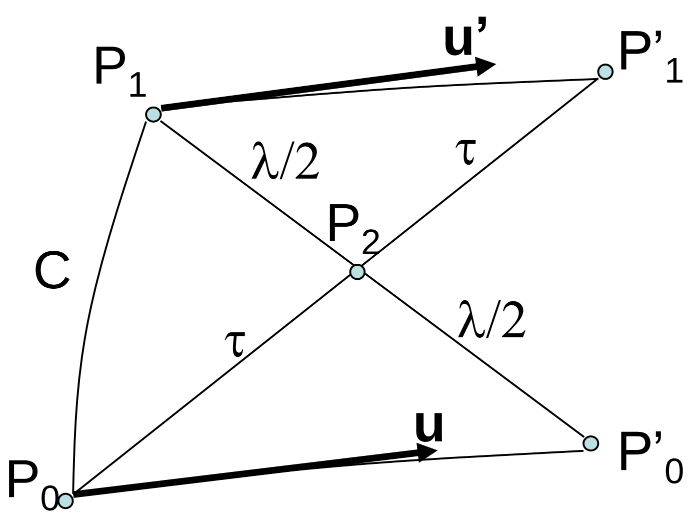
Parallel transport of initial tangent vectors

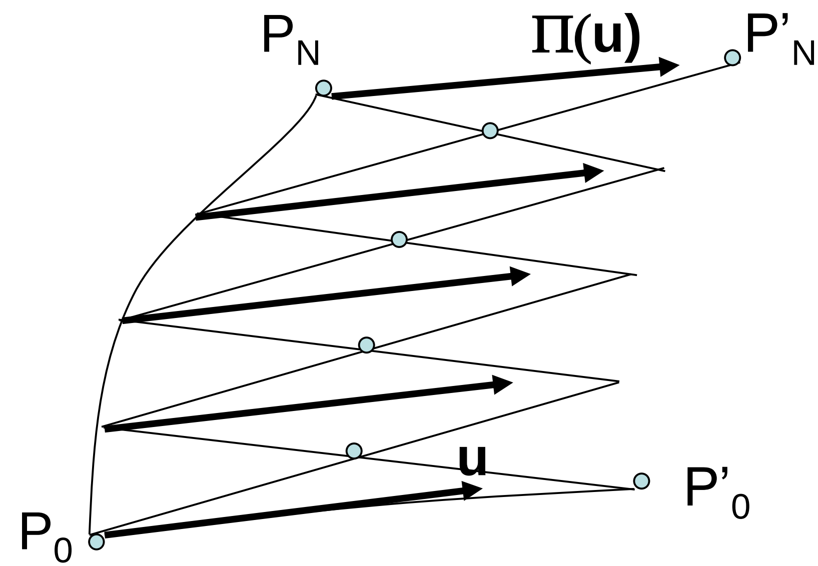
LDDMM: parallel transport along geodesics using Jacobi fields [Younes et al. 2008]

Parallel transport along arbitrary curves

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

- Build geodesic parallelogrammoid
- Iterate along the curve





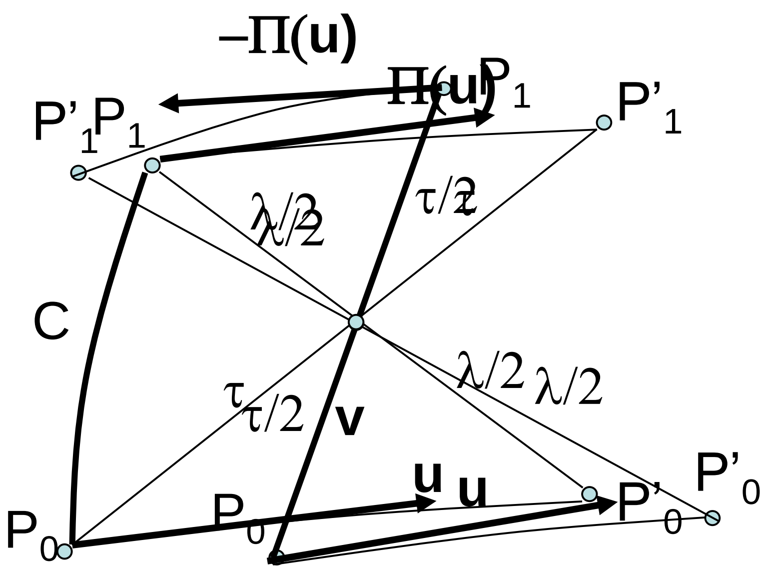
[Lorenzi, Pennec: Efficient Parallel Transport of Deformations in Time Series of Images: from Schild's to pole Ladder, JMIV 50(1-2):5-17, 2013]

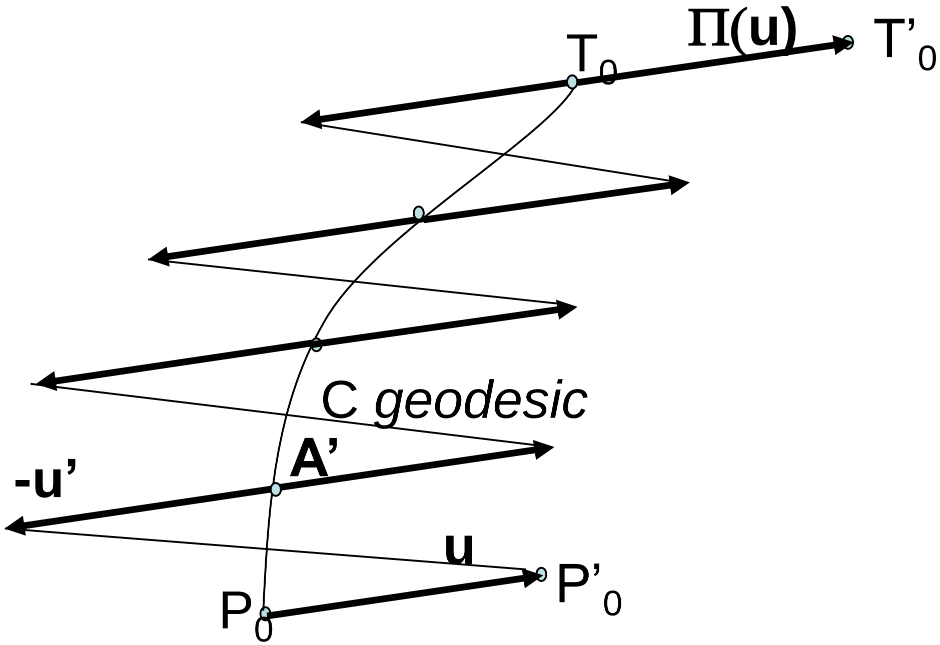
Parallel transport along geodesics

Simpler scheme along geodesics: Pole Ladder

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

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





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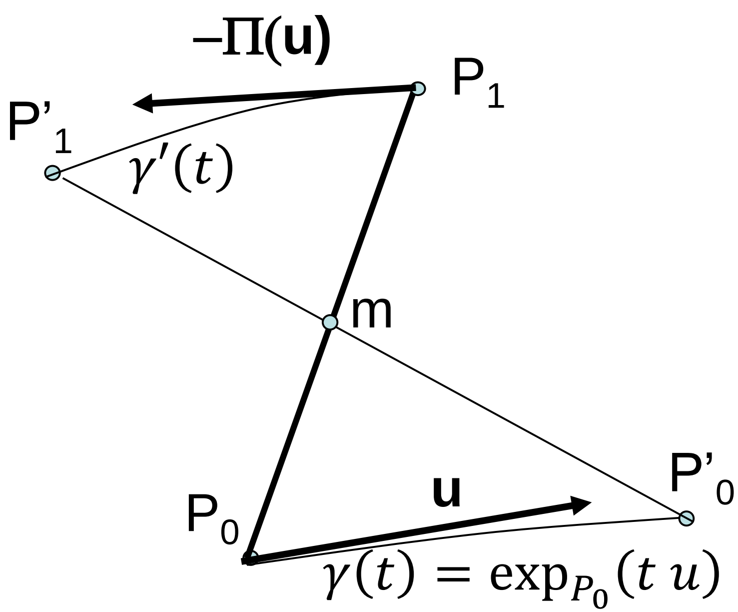


Pole ladder is exact in 1 step in symmetric space

- Symmetry preserves geodesics:
$$S_m(\gamma(t)) = \gamma'(t)$$

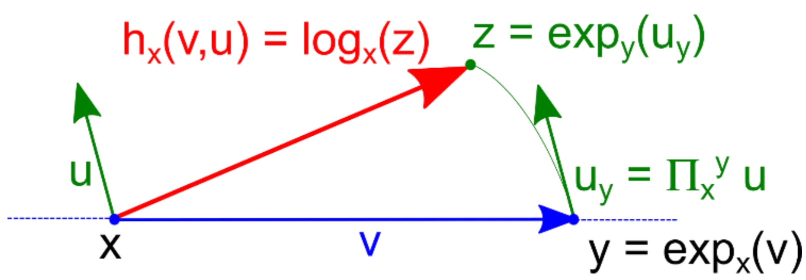
- Parallel transport is differential of symmetry
$$\gamma'(t) = \exp_{P_1}(-\Pi(u))$$

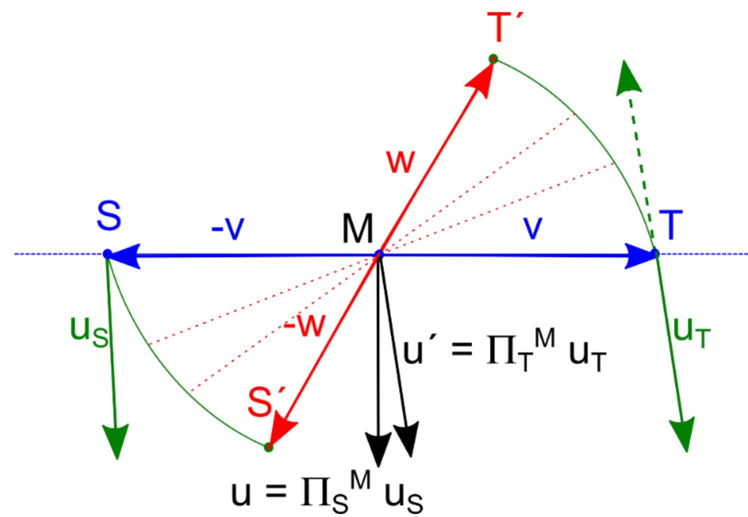
[XP. Parallel Transport with Pole Ladder: a Third Order Scheme in Affine Connection Spaces which is Exact in Affine Symmetric Spaces. Arxiv 1805.11436]

Accuracy of pole ladder

Gavrilov's double exponential series (2006):

$$h_x(v,u) = \log_x(\Pi_x^{\exp_x(v)}\, u)$$
$$= v + u + \frac{1}{6}R(u,v)v + \frac{1}{3}R(u,v)u + \frac{1}{24}\nabla_v R(u,v)(2v+5u) + \frac{1}{24}\nabla_u R(u,v)(v+2u) + O(5)$$





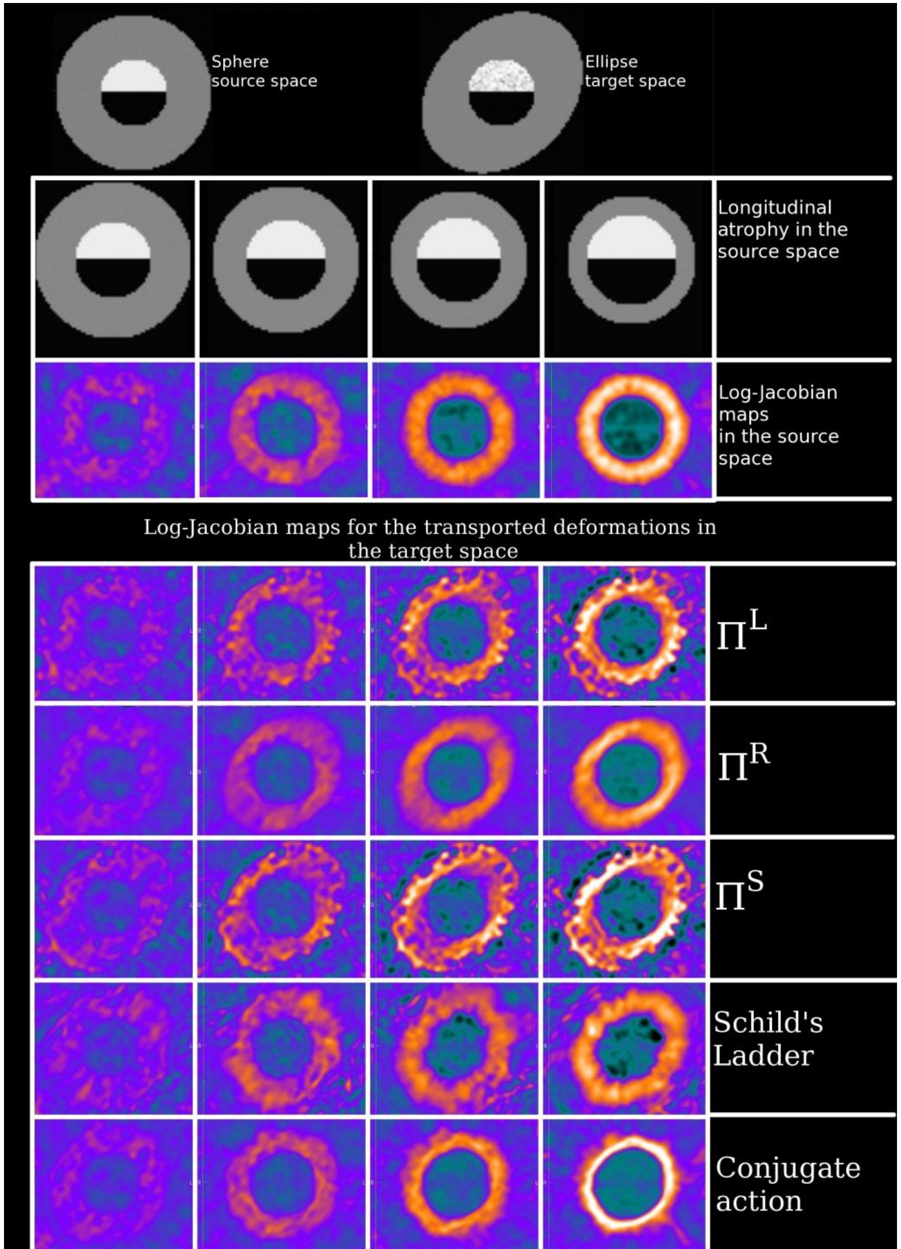
Find u' that satisfies:

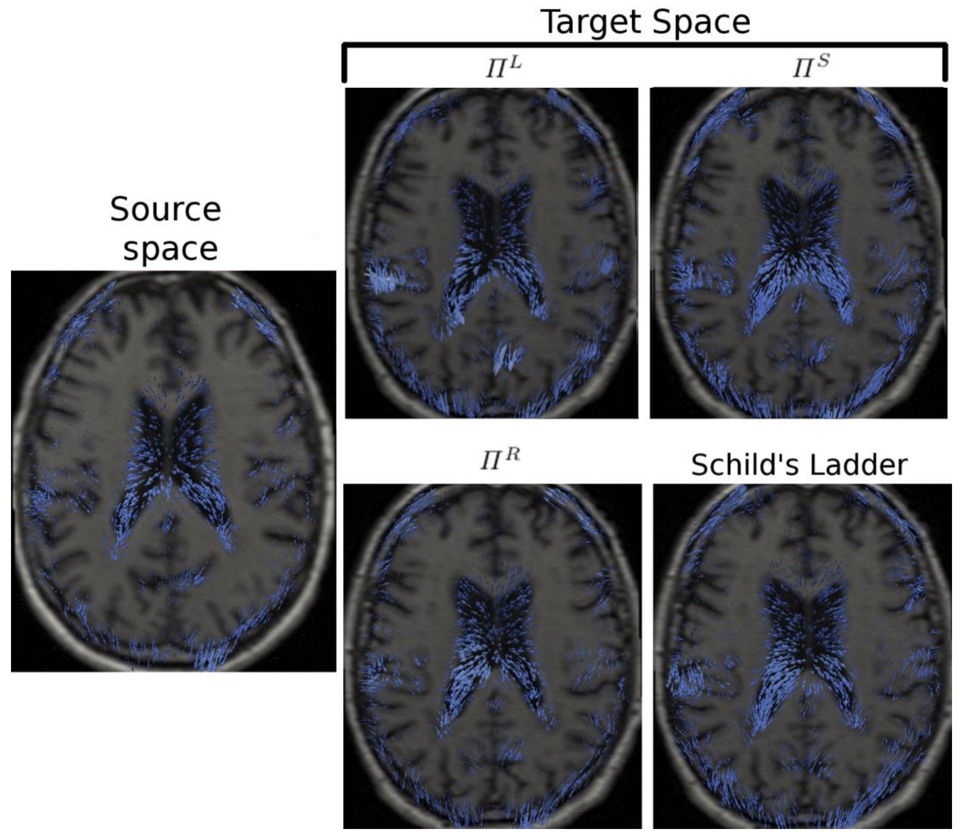
$$h_M(v,-u') + h_M(-v,u) = 0$$
$$u' = u + \frac{1}{12}\nabla_v R(u,v)(5u-2v) + \frac{1}{12}\nabla_u R(u,v)(v-2u) + O(5)$$

- Error term is of order 4 in general affine manifolds
- Error is even zero for symmetric spaces: pole ladder is exact in one 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]

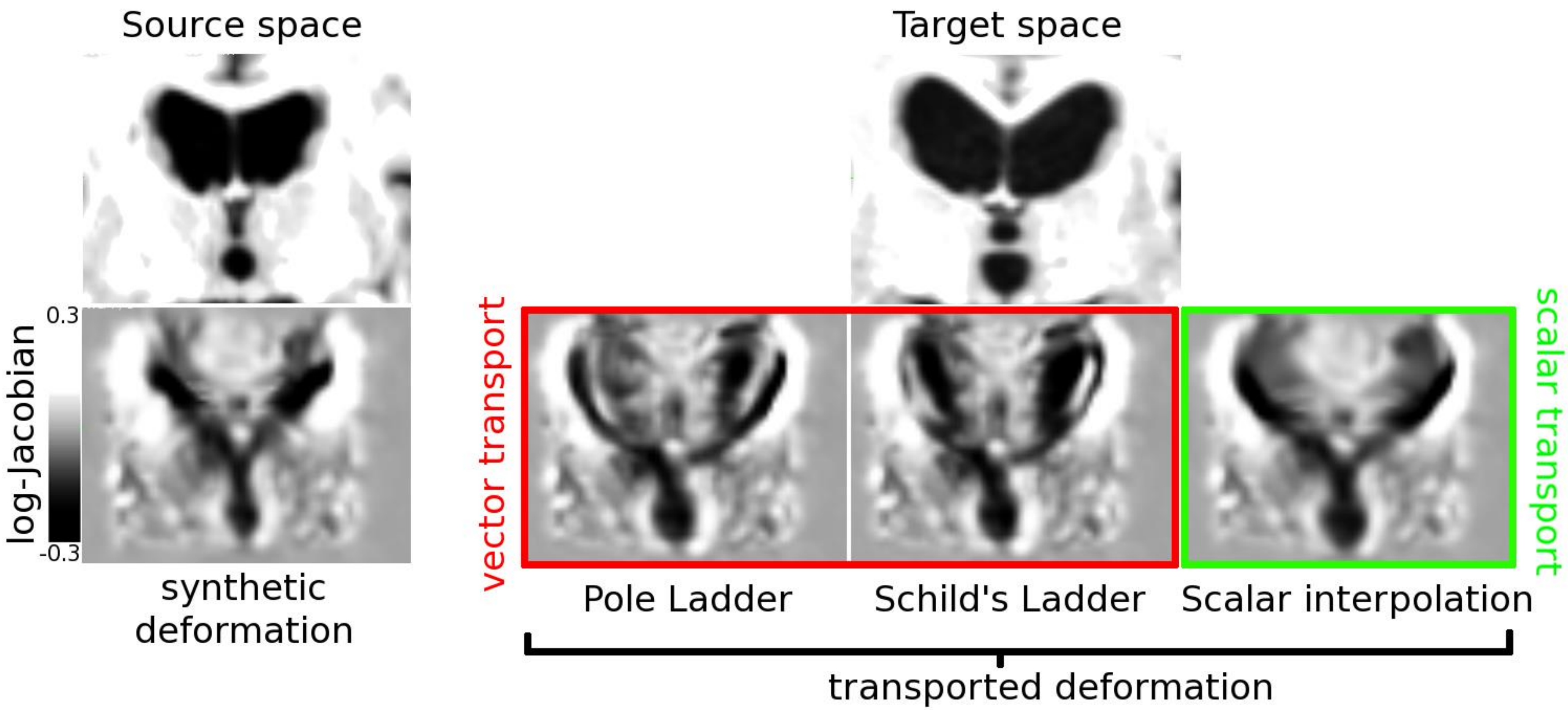
Left, Right and Sym. Parallel Transport along SVFs





Numerical stability of Jacobian computation

Parallel Transport along SVFs



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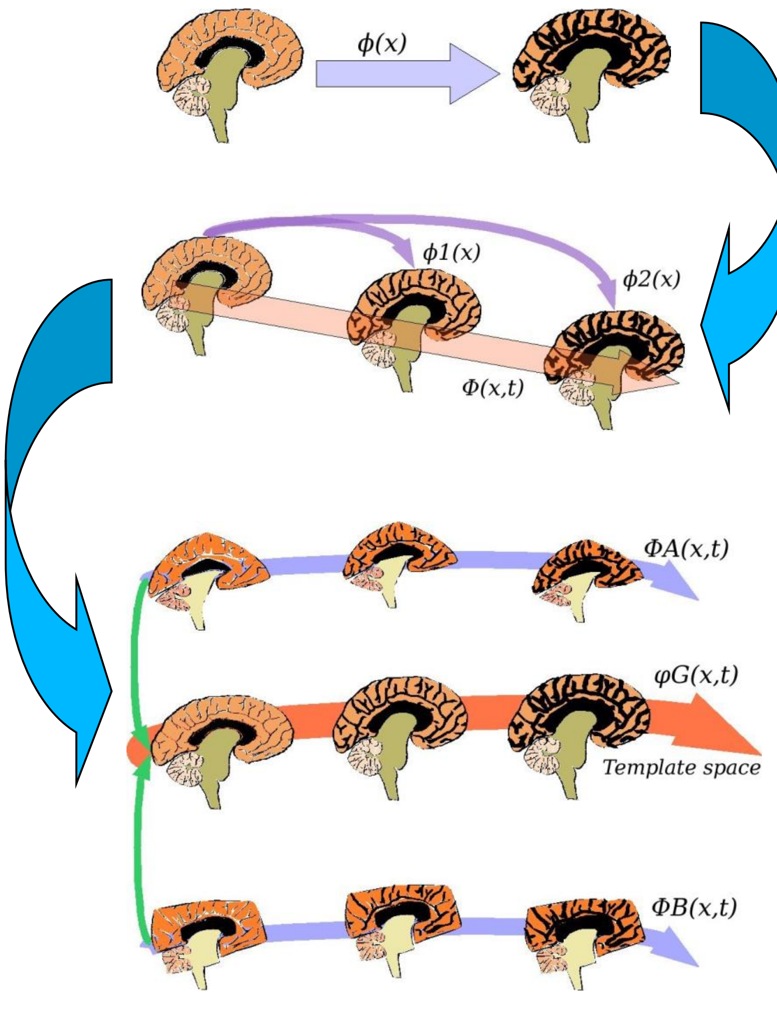
Advances Statistics: CLT & PCA

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

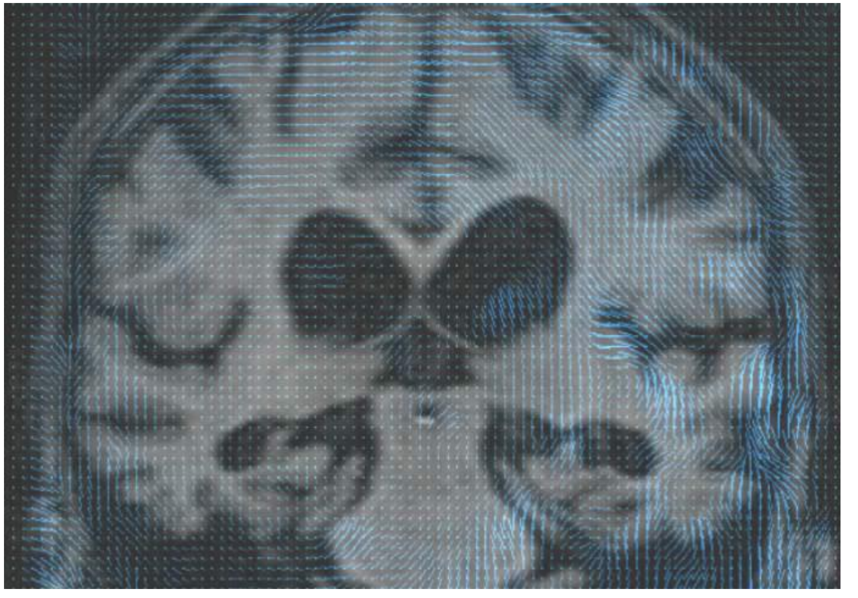
Schild's Ladder

[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



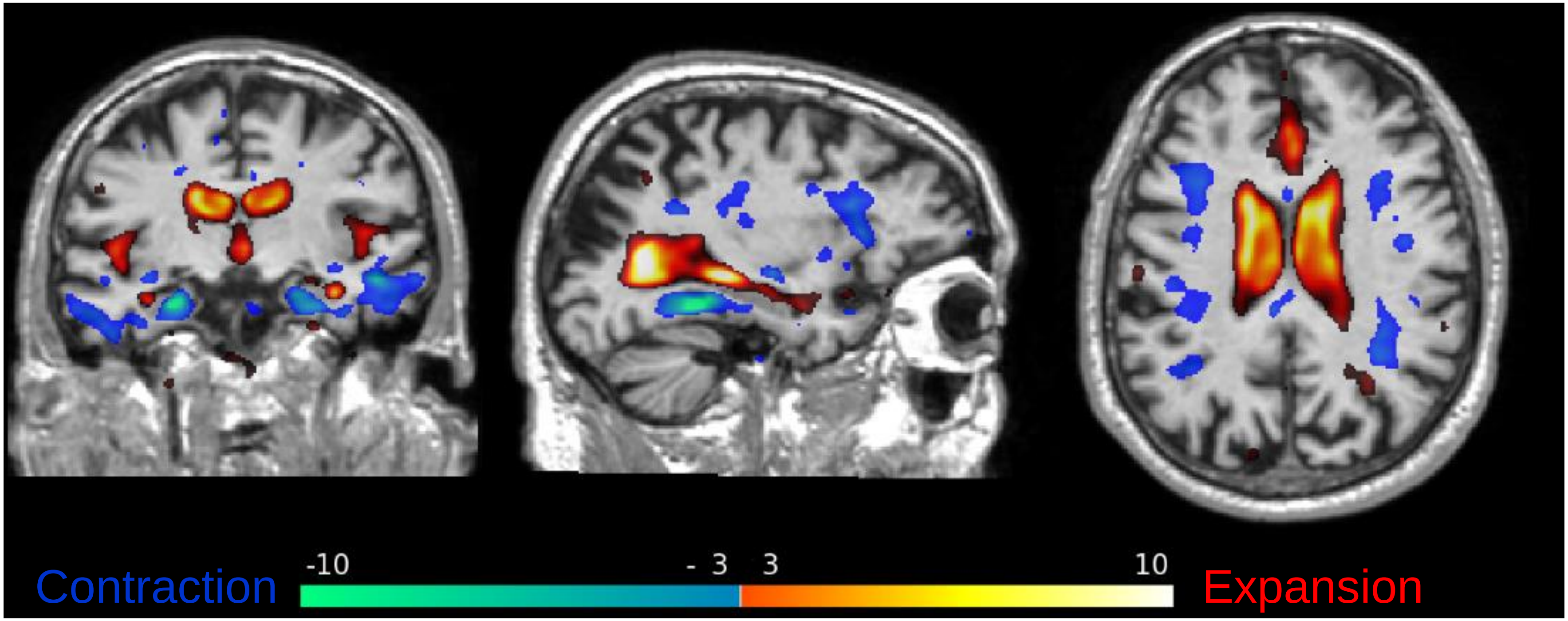
Data collected

- 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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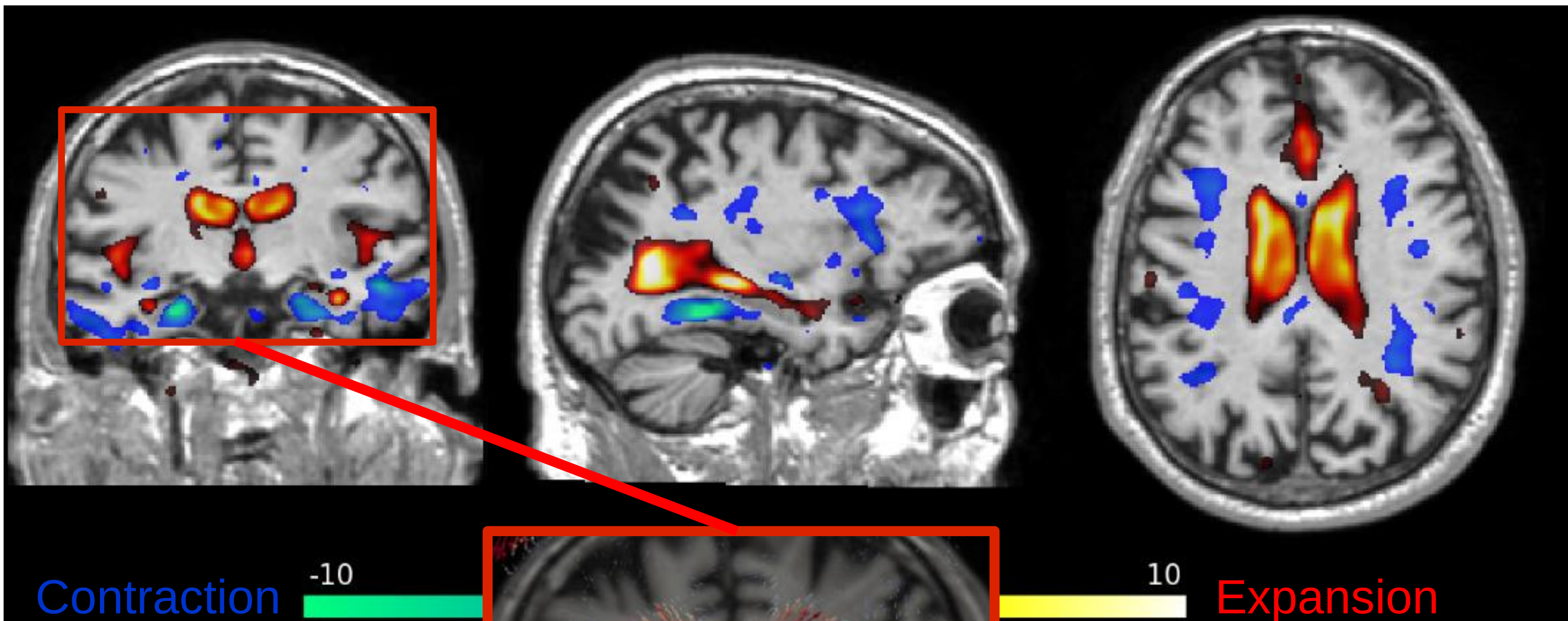

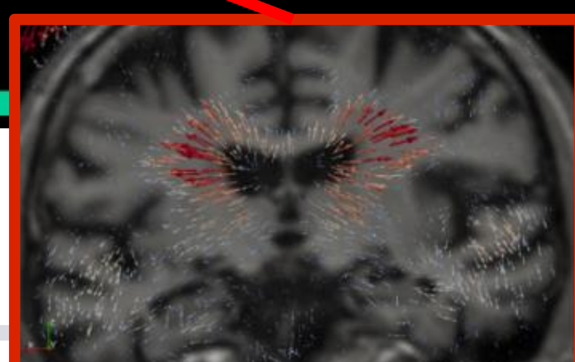

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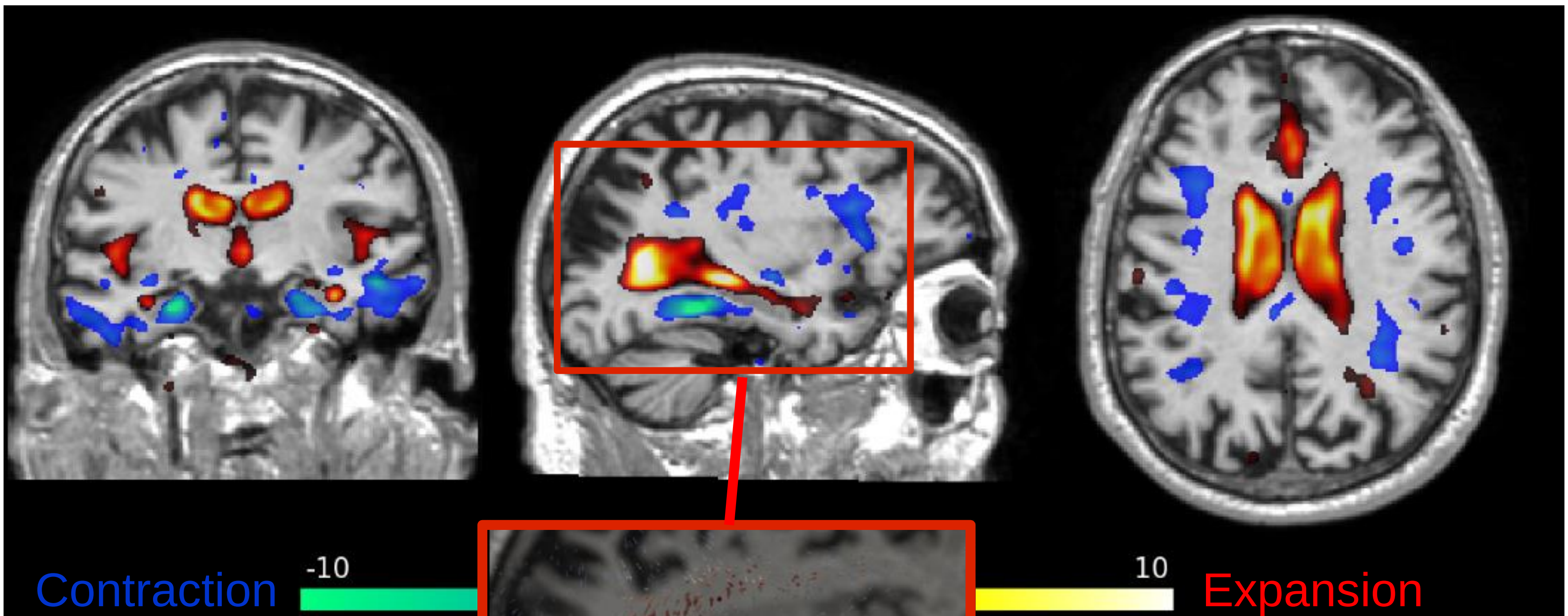

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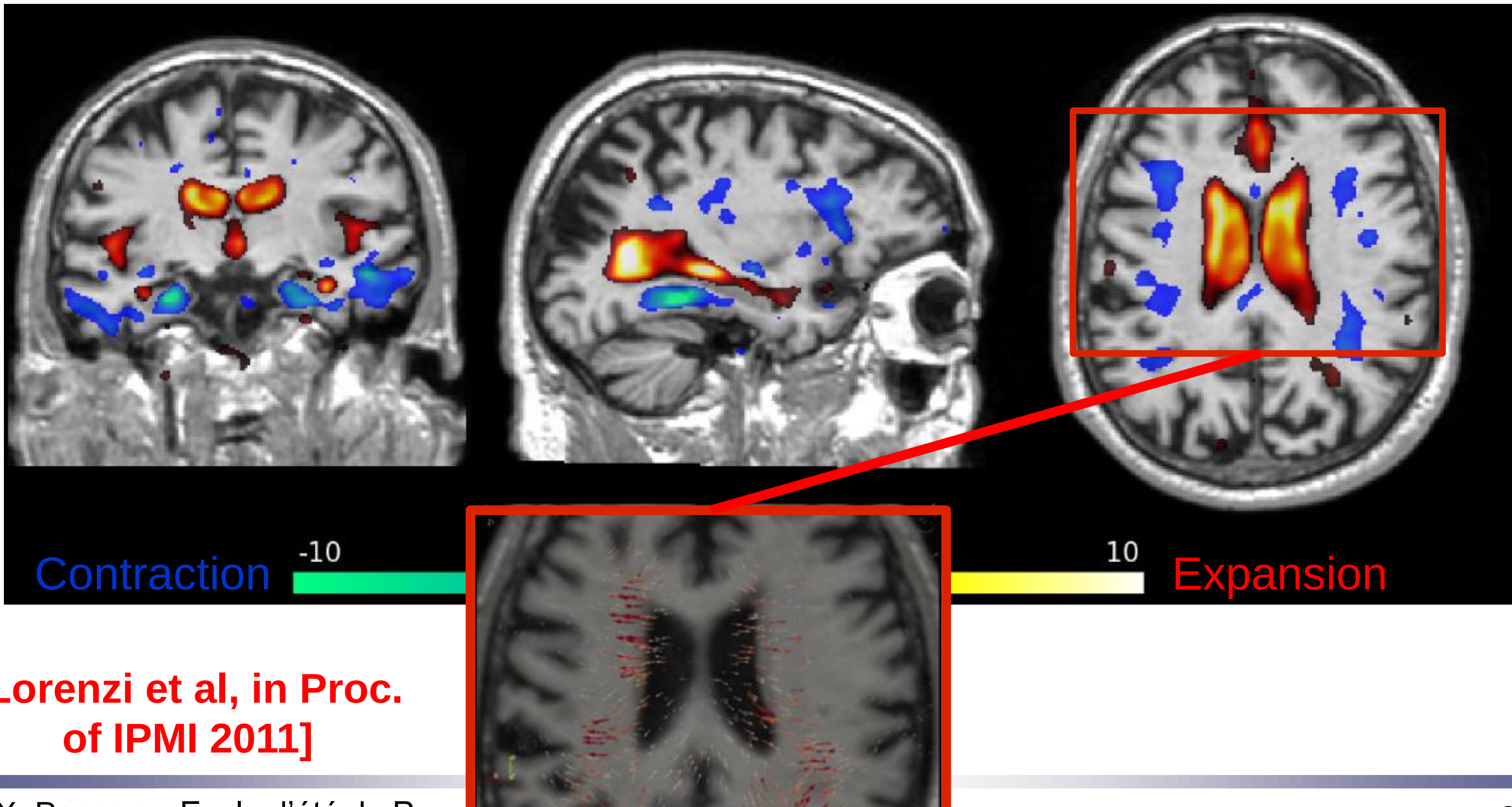
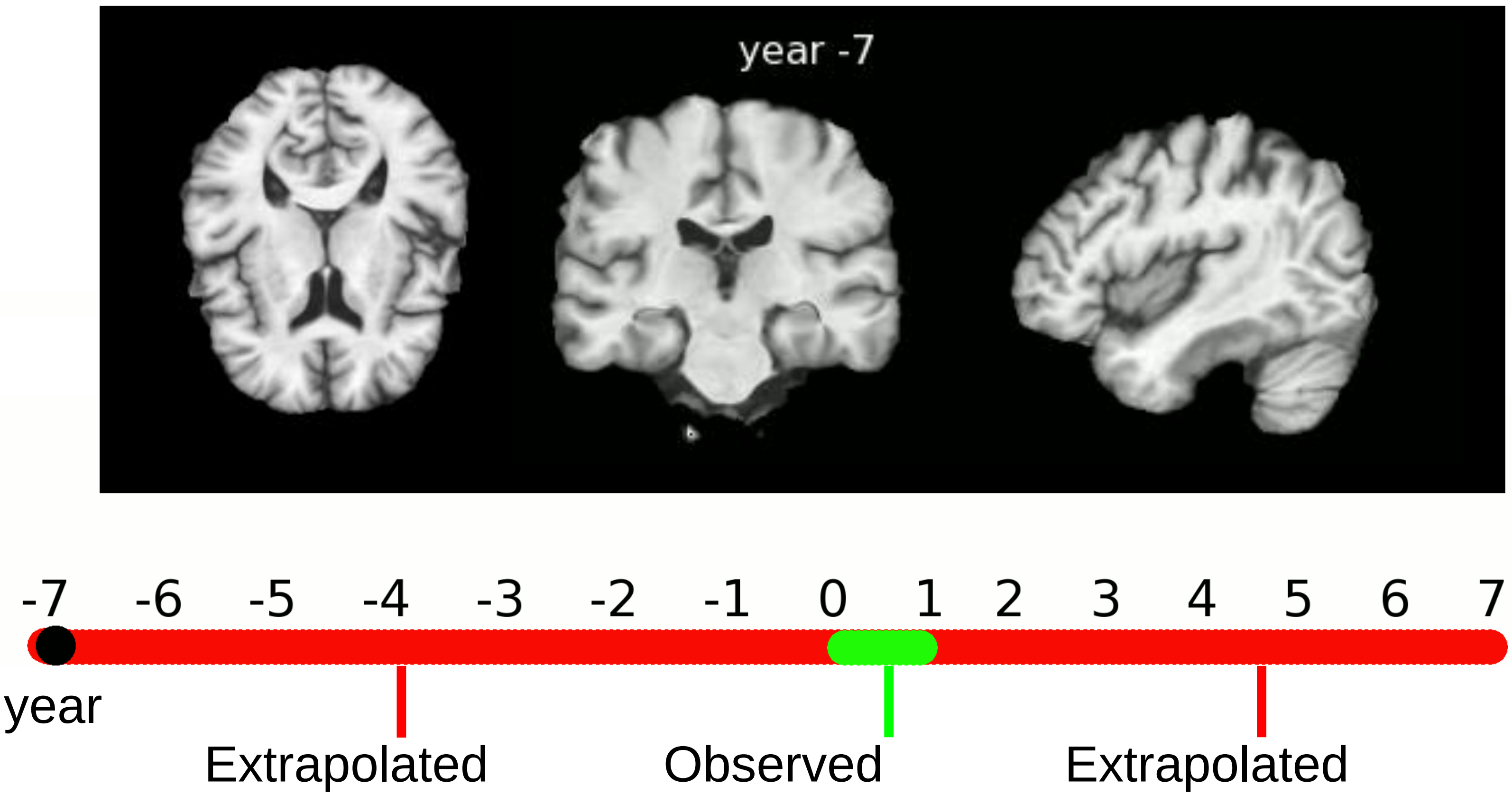


[Lorenzi et al, in Proc. of IPMI 2011]

Longitudinal model for AD

Modeled changes from 70 AD subjects (ADNI data)

Estimated from 1 year changes – Extrapolation to 15 years



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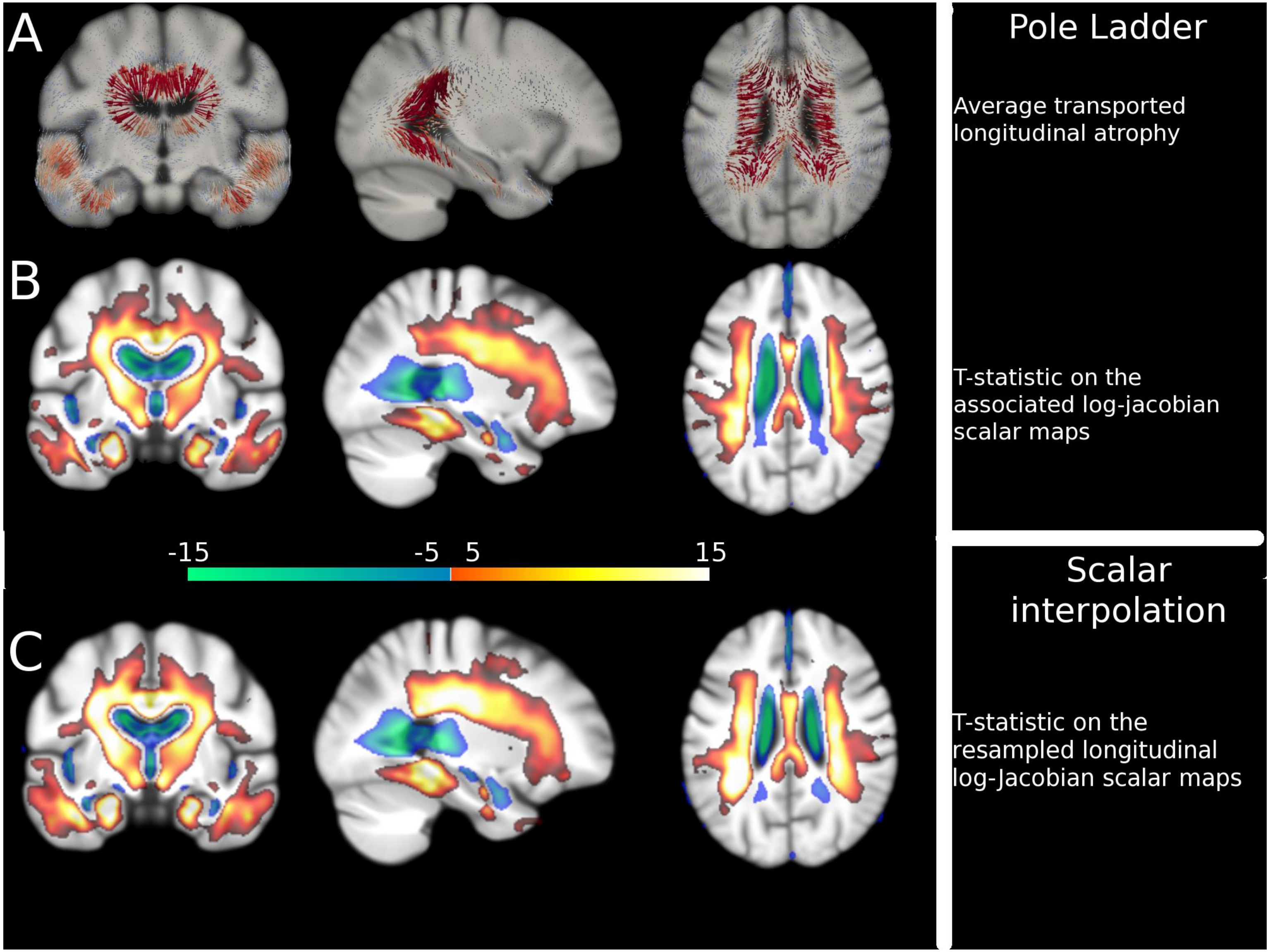
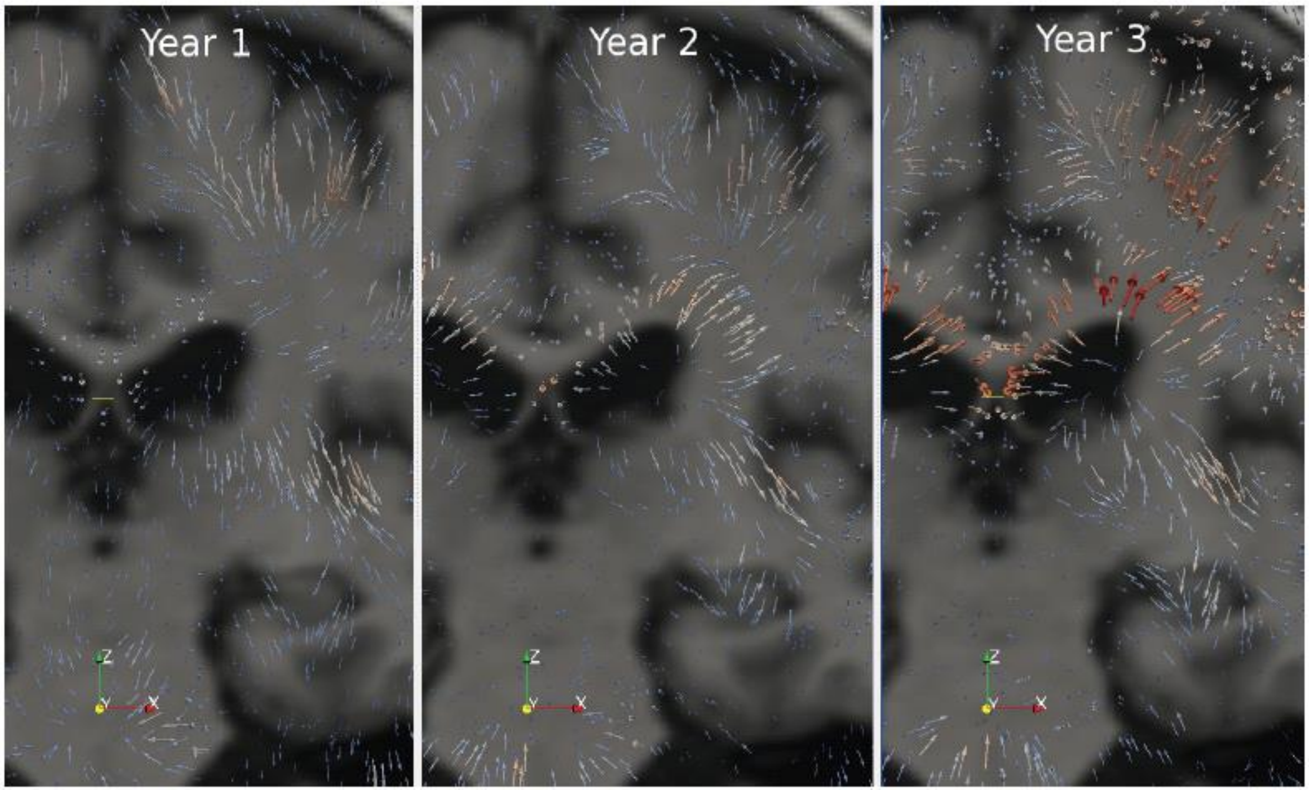


Study of prodromal Alzheimer's disease

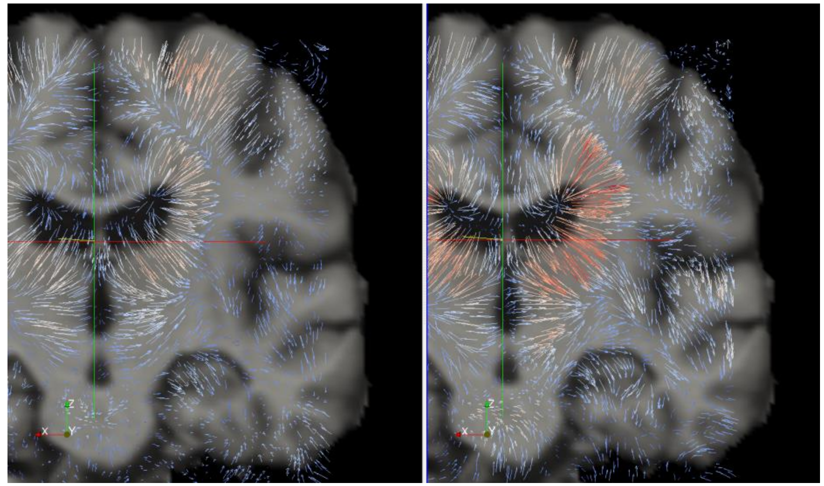
- 98 **healthy subjects**, 5 time points (0 to 36 months).
- 41 subjects Aβ42 positive ("at risk" for Alzheimer's)
- **Q: Different morphological evolution for Aβ+ vs Aβ-?**



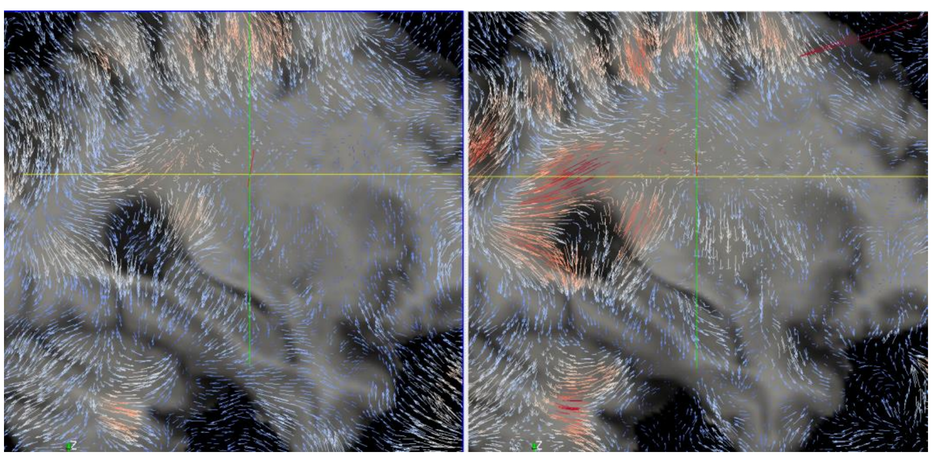
Average SVF for normal evolution (Aβ-)

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

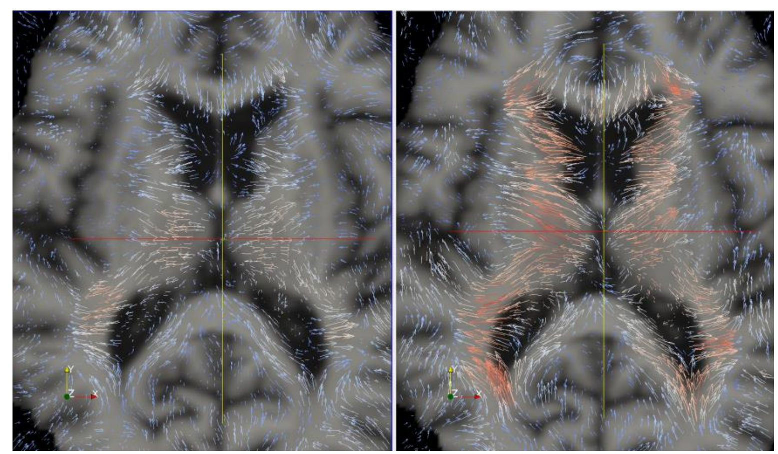
Detail: comparison between average evolutions (SVF)



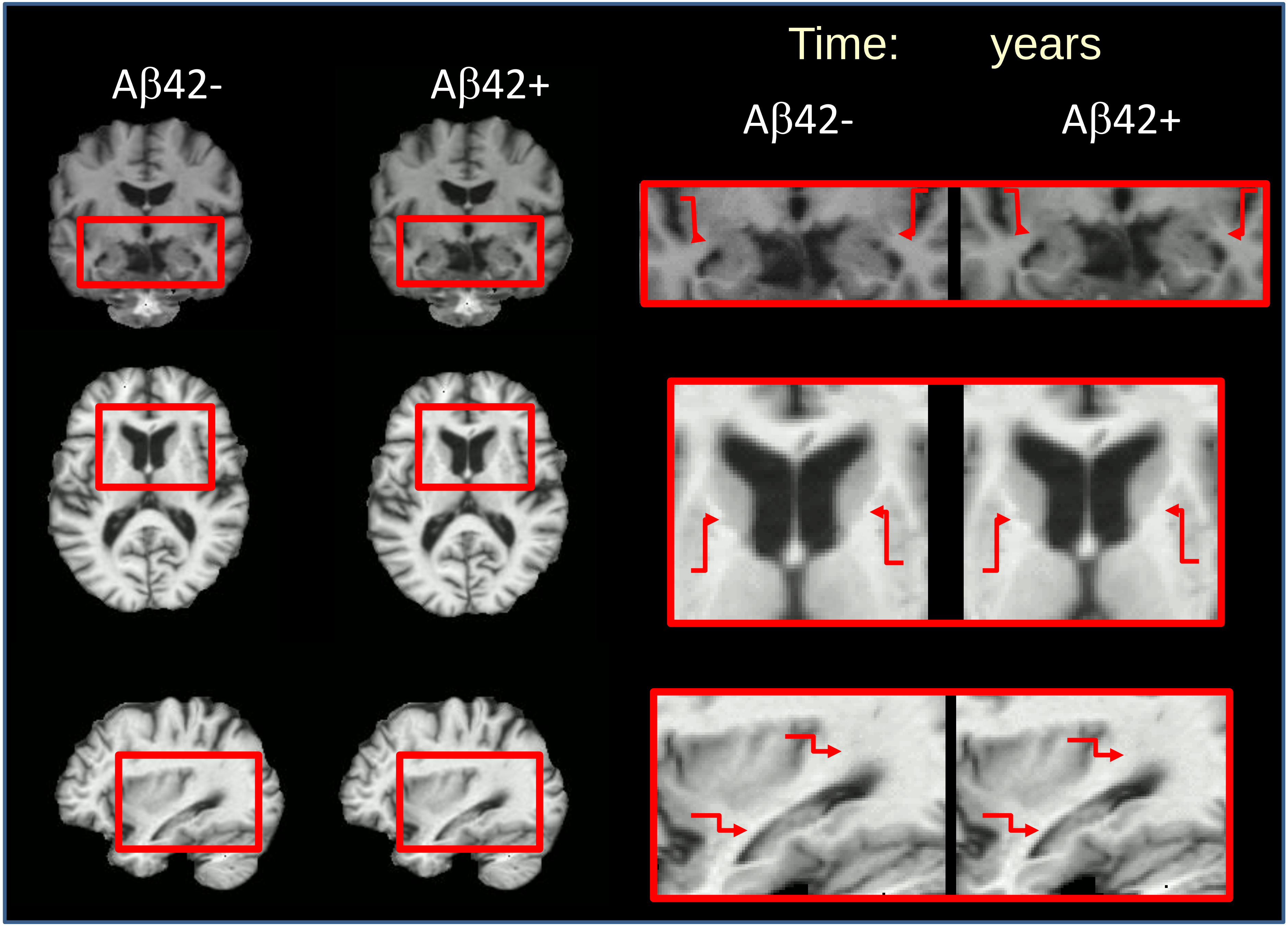
Aβ42- Aβ42+



Aβ42- Aβ42+

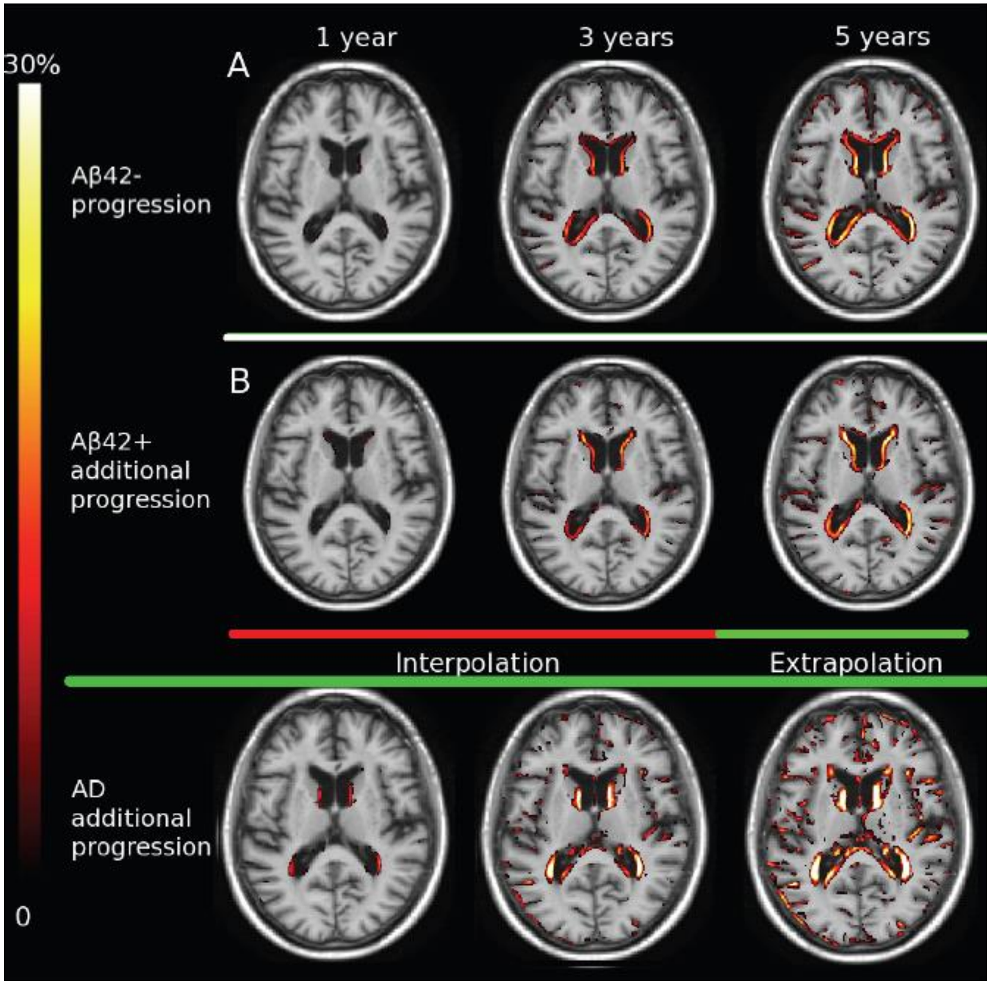


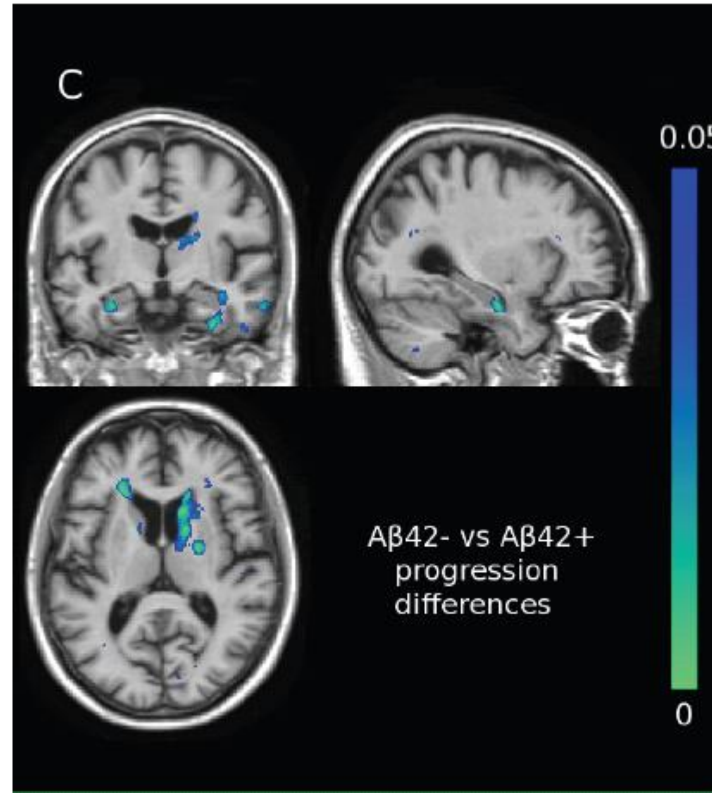
Aβ42- Aβ42+


Time: years
Aβ42-
Aβ42+
Aβ42-
Aβ42+

Study of prodromal Alzheimer's disease

Linear regression of the SVF over time: interpolation + prediction



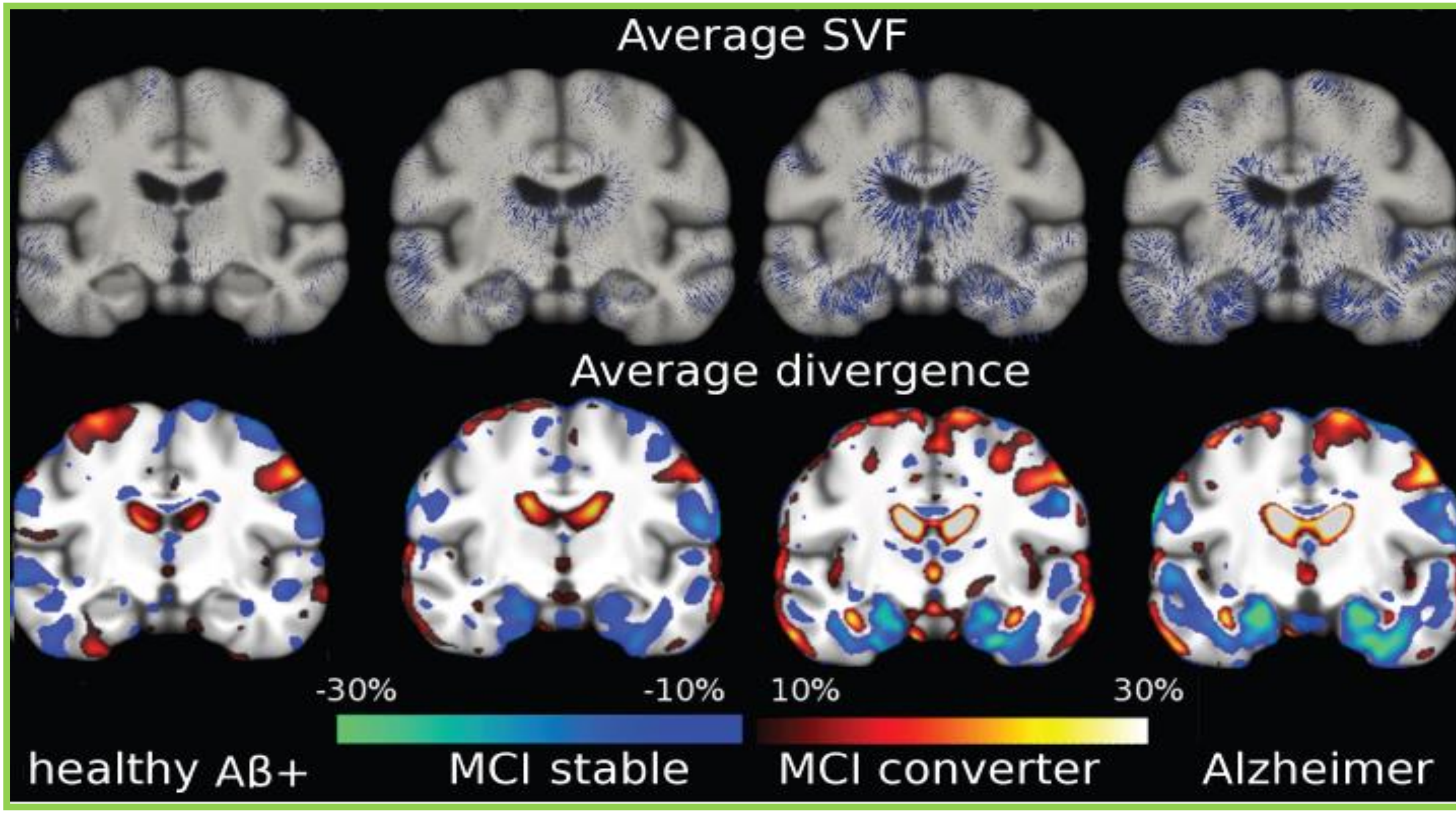


$$T(t) = Exp(\tilde{v}(t)) * T_0$$

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]

Mean deformation / atrophy per group



M Lorenzi, N Ayache, X Pennec G B. Frisoni, for ADNI. Disentangling the normal aging from the pathological Alzheimer's disease progression on structural MR images. 5th Clinical Trials in Alzheimer's Disease (CTAD'12), Monte Carlo, October 2012. (see also MICCAI 2012)

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

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