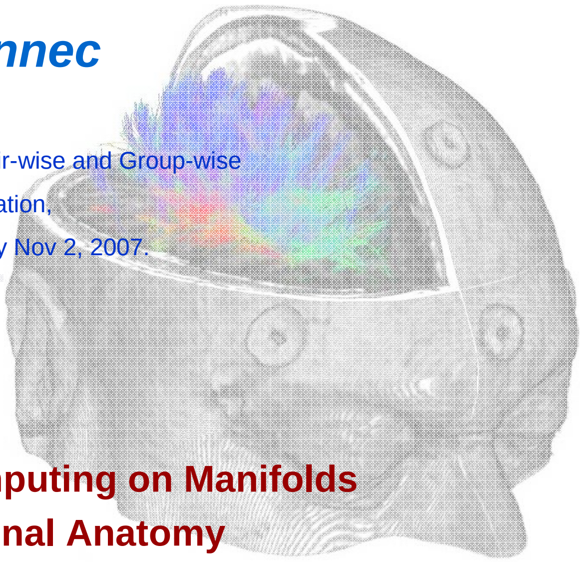
Xavier Pennec

Statistical registration: Pair-wise and Group-wise

Alignment and Atlas formation,

Brisbane, Australia, Friday Nov 2, 2007.

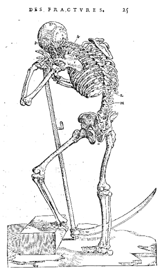


Statistical Computing on Manifolds for Computational Anatomy

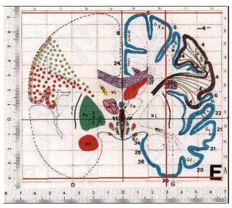
Anatomy

Science that studies the structure and the relationship in space of different organs and tissues in living systems [Hachette Dictionary]

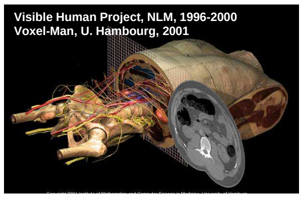
1er cerebral atlas, Vesale, 1543



Paré, 1585



Talairach & Tournoux, 1988



Antiquity
- Animal models
- Philossphical physiology

Renaissance:
- Dissection, surgery
- Descriptive anatomy

17-20e century:
- Anatomo-physiology
- Microscopy, histology

1990-2000:
- Explosion of imaging
- Computer atlases
- Brain decade

Galien (131-201) | **Vésale (1514-1564) Paré (1509-1590)** | **Sylvius (1614-1672) Willis (1621-1675)** | **Gall (1758-1828) : *Phrenologie* Talairach (1911-2007)**

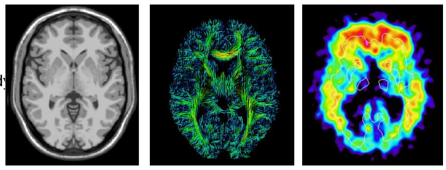
Revolution of observation means (1988-2007) :

- From dissection to in-vivo in-situ imaging

The revolution of medical imaging

In vivo observation of living systems

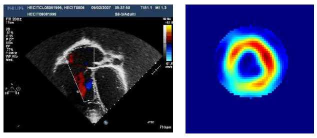
- A large number of modalities to image anatomy and function
  - Growing spatial resolution (molecules to whole body)
  - Multiple temporal scales



brain

Non invasive observations

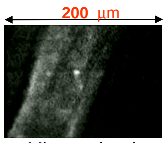
- Emergence of large databases
- From representative individual to population



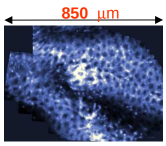
heart

Extract and structure information

- 50 to 150 MB for a clinical MRI
- Computer analysis is necessary
- From descriptive atlases to interactive and generative models (simulation)
  - MNI 305 (1993), ICBM 152 (2001), Brain web (1999)
  - Bone Morphing® (Fleute et al, 2001)

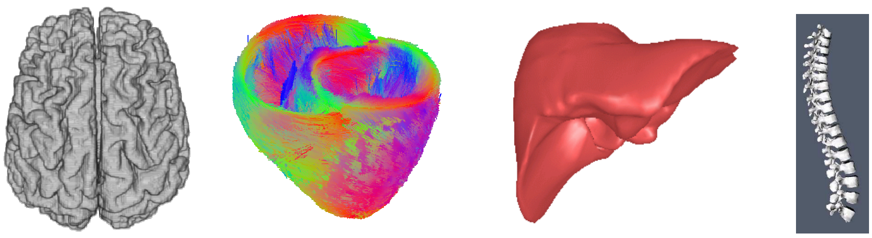


Micro-vaissels



Mouse colon

Computational Anatomy



Algorithms to Model and Analyze the Anatomy

- Estimate representative organ anatomies across species, populations, diseases, aging, ages…
- Model organ development across time
- Establish normal variability

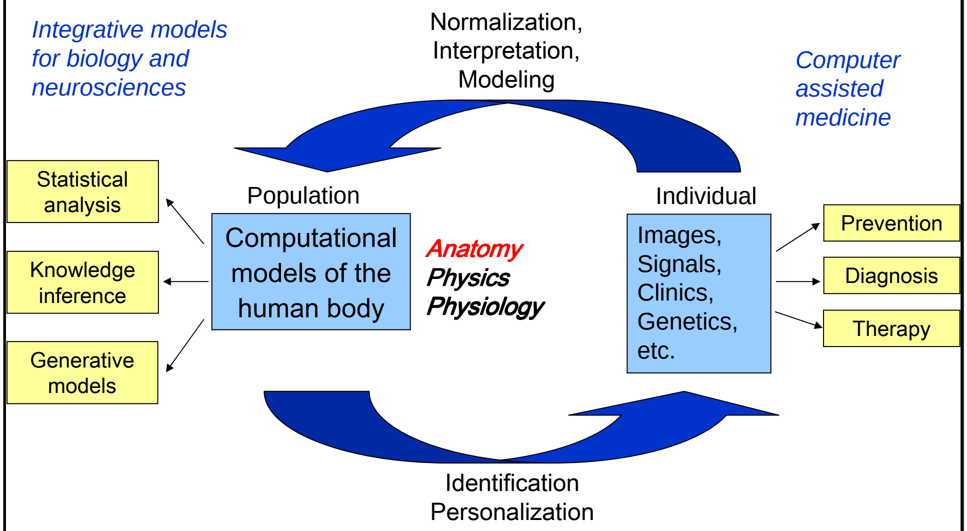
To understand and to model how life is functioning

- Classify pathologies from structural deviations (taxonomy)
- Integrate individual measures at the population level to relate anatomy and function

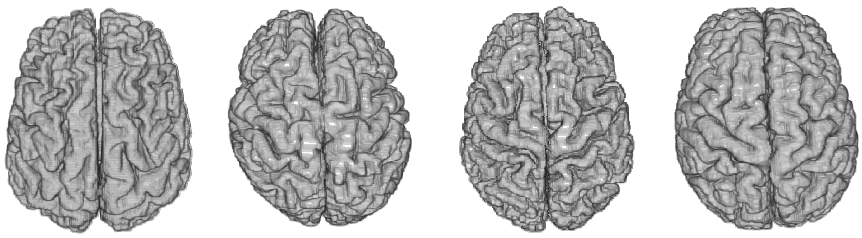
To detect, understand and correct dysfunctions

- From generic (atlas-based) to patients-specific models
- Quantitative and objective measures for diagnosis
- Help therapy planning (before), control (during) and follow-up (after)

Modeling and image analysis: a virtuous loop



Methods of computational anatomy



Structural variability of the cortex

Hierarchy of anatomical manifolds (structural models)

- Landmarks [0D]: AC, PC [Talairach et Tournoux, Bookstein], functional landmarks
- Curves [1D]: crest lines, sulcal lines [Mangin, Barillot, Fillard…]
- Surfaces [2D]: cortex, sulcal ribbons [Thompson, Mangin, Miller…],
- Images [3D functions]: VBM, Diffusion imaging
- Transformations: rigid, multi-affine, local deformations (TBM), diffeomorphisms [Asburner, Arsigny, Miller, Trouve, Younes…]

Groupwise correspondances in the population

Model observations and its structural variability

→ Statistical computing on Riemannian manifolds

Outline

Goals and methods of Computational anatomy

Statistical computing on manifolds

- The geometrical and statistical framework
- Examples with rigid body transformations and tensors

Morphometry of the Brain

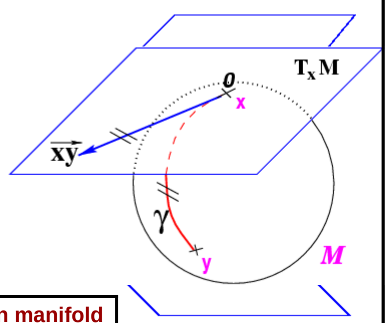
- Statistics on curves to model the cortex variability
- Local statistics on local deformations
- Towards global statistics on (some) diffeomorphisms

Challenges of Computational Anatomy

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 chart (Normal coord. syst.) :

- Development in tangent space along geodesics
- Geodesics = straight lines

Unfolding ($\log_x$), folding ($\exp_x$)

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	$\mathrm{dist}(x, y) = \Vert y - x \Vert$	$\mathrm{dist}(x, y) = \Vert \overrightarrow{xy} \Vert_x$
Gradient descent	$x_{t+\varepsilon} = x_t - \varepsilon \nabla C(x_t)$	$x_{t+\varepsilon} = \exp_{x_t}(-\varepsilon \nabla C(x_t))$

Statistical computing on manifolds

First statistical tools

- Fréchet / Karcher mean: minimize variance
- Covariance Higher order moments in the exponential chart
- Intrinsic vs. extrinsic [Oller & Corcuera 95, Battacharya & Patrangenaru 2002]

Distributions and tests : practical approximations

- Gaussian maximizes entropy knowing mean and covariance

$$N(\mathrm{y}) = k.\exp\left(\left(\overrightarrow{\mathrm{xy}}\right)^{\mathrm{T}}.\boldsymbol{\Gamma}.\left(\overrightarrow{\mathrm{xy}}\right)/2\right) \quad \text{avec} \quad \boldsymbol{\Gamma} = \boldsymbol{\Sigma}^{(-1)} - \tfrac{1}{3}\mathrm{Ric} + O(\sigma) + \varepsilon(\sigma/r)$$

- Mahalanobis distance follows a chi2 law

$$\mu_{\mathbf{x}}^2(\mathbf{x}) = \overrightarrow{\mathrm{\bar{x}}\mathbf{x}}^{t}.\Sigma_{\mathbf{xx}}^{(-1)}.\overrightarrow{\mathrm{\bar{x}}\mathbf{x}} \;\sim\; \chi_n^2 + O(\sigma^3) + \varepsilon(\sigma/r)$$

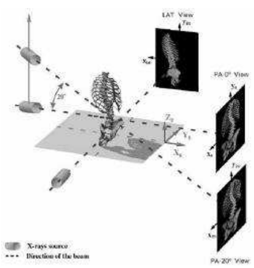
Intrinsic Riemannian computing

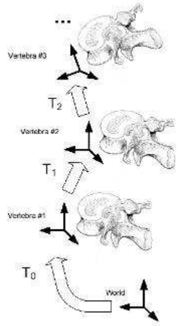
- Interpolation (bi- tri-linear), filtering (e.g. Gaussian): weighted means
- Harmonic / anisotropic regularization: Laplace-Beltrami
  → Trivial numerical scheme in the exponential chart

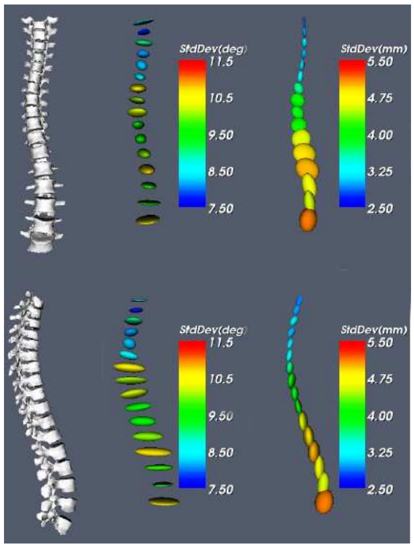
[Pennec, NSIP'99, JMIV 25(1) 2006, Pennec et al, IJCV 66(1) 2006]

Statistical Analysis of the Scoliotic Spine

[J. Boisvert et al., ISBI'06, to appear in IEEE TMI, 2007]







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 rotation var. around anterior-posterior axis

PCA of the Covariance

- 4 first variation modes have clinical meaning

Statistical Analysis of the Scoliotic Spine

[J. Boisvert et al., ISBI'06, to appear in IEEE TMI, 2007]

- 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)

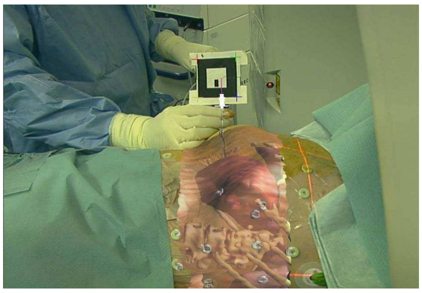
Liver puncture guidance using augmented reality

3D (CT) / 2D (Video) registration

- 2D-3D EM-ICP on fiducial markers
- Certified accuracy in real time

Validation

- Bronze standard (no gold-standard)
- Phantom in the operating room (2 mm)
- 10 Patient (passive mode): < 5mm (apnea)



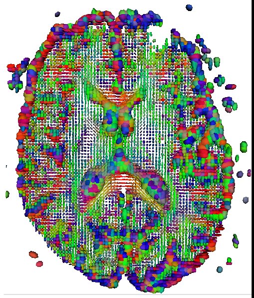
[S. Nicolau, PhD'04 MICCAI05, Comp. Anim. & Virtual World 2005, MICCAI'07]

Metrics for Tensor computing

- Affine invariant metric (curved space – Hadamard)
  - Geodesics $\exp_\Sigma(\overrightarrow{\Sigma\Psi}) = \Sigma^{1/2} \exp(\Sigma^{-1/2}.\overrightarrow{\Sigma\Psi}.\Sigma^{-1/2})\Sigma^{1/2}$
  - Distance $\boxed{\mathrm{dist}(\Sigma,\Psi)^2 = \left\langle \overrightarrow{\Sigma\Psi} \mid \overrightarrow{\Sigma\Psi} \right\rangle_\Sigma = \left\| \log(\Sigma^{-1/2}.\Psi.\Sigma^{-1/2}) \right\|_{L_2}^2}$

[Pennec, Fillard, Ayache: A Riemannian Framework for Tensor Computing, IJCV 66(1), 2006.]

[Fletcher 2004, Moakher SIAM-X 2005, Lenglet, JMIV 2006]

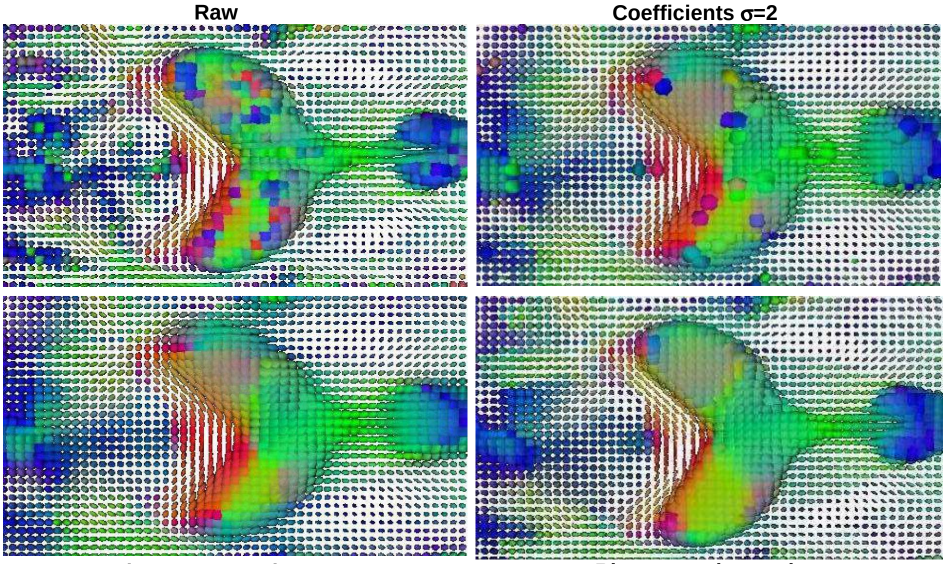


- Log-Euclidean metric (vector space)
  - Geodesics $\exp_\Sigma(\overrightarrow{\Sigma\Psi}) = \exp(\overrightarrow{\Sigma\Psi})$
  - Distance $\boxed{\mathrm{dist}(\Sigma_1,\Sigma_2)^2 \equiv \left\| \log(\Sigma_1) - \log(\Sigma_2) \right\|^2}$

[Arsigny, Pennec, Fillard, Ayache: Fast and Simple Calculus on Tensors in the Log-Euclidean Framework, MICCAI'05, SIMAX 29(1) 2007, MRM 52(6) 2006]

Filtering and anisotropic regularization of DTI

Raw | Coefficients σ=2



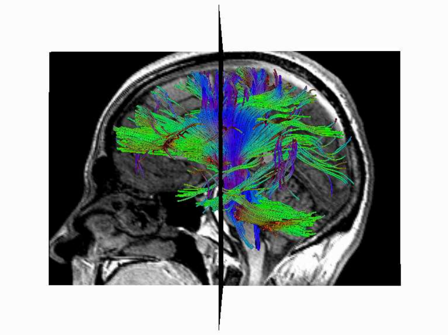
Riemann Gaussian σ=2 | Riemann anisotropic

DTI-based Anatomical models

Diffusion tensor IRM

Covariance of the water Brownian motion

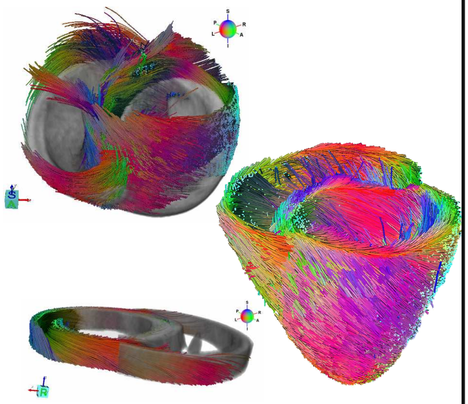
- Estimation, filtering, interpolation
- Fiber extraction: architecture of axons tracts



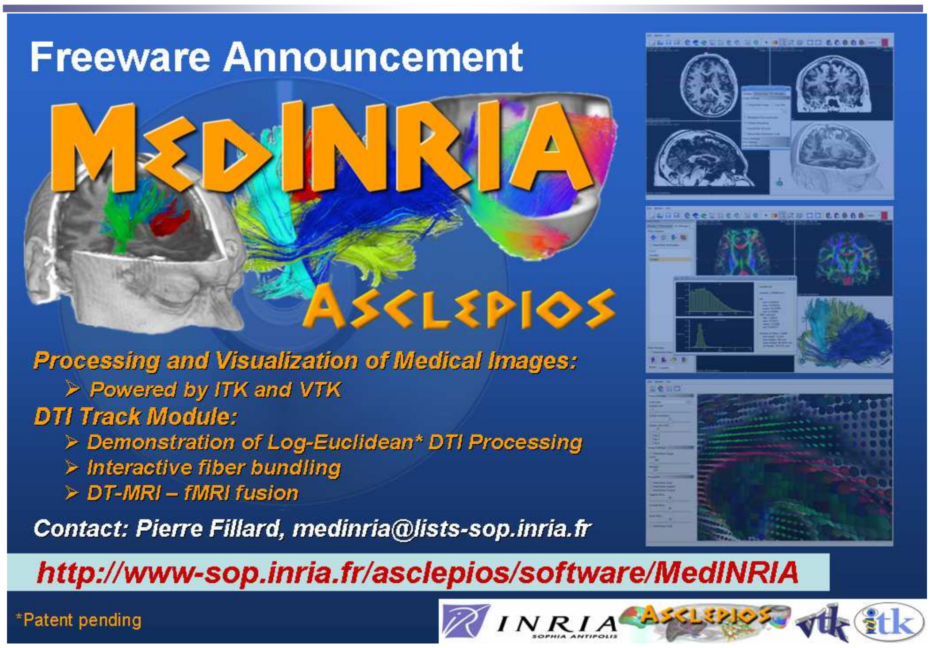
[Pennec et al, IJCV 66(1) 2006,
Fillard et al, ISBI'06 and IEEE TMI, in press]

Atlas of the heart fibers

- 7 DTI of dogs hearts
- Fibers and sheets structure



[J.M. Peyrat et al, MICCAI'06,
To appear in TMI, 2008]



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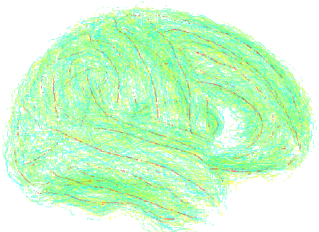
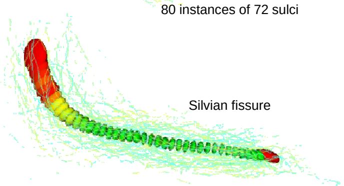
Challenges of Computational Anatomy

Morphometry of the Cortex from Sucal Lines

1/ Mean curve: Alternated minimization of the variance on matches / position



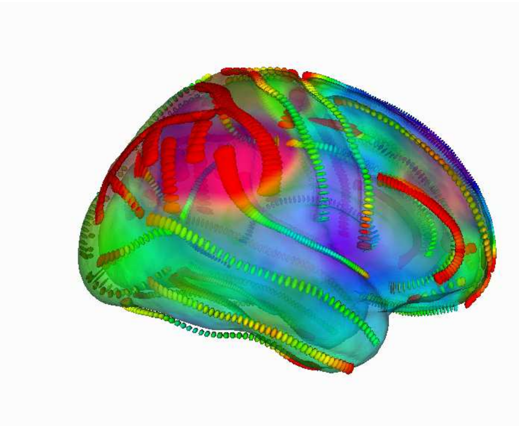
80 instances of 72 sulci



2/ Computation of the covariance tensor at each point of the mean

3/ Extrapolation to the whole volume : harmonic diffusion of tensors

$$C(\Sigma) = \frac{1}{2}\int_{\Omega} \sum_{i=1}^{n} G_{\sigma}(x - x_i)\, dist(\Sigma(x), \Sigma_i)^2\, dx + \frac{\lambda}{2}\int_{\Omega} \|\nabla \Sigma\|^2_{\Sigma(x)}$$



[Fillard et al., IPMI 2005, Neuroimage 34(2), 2007, Extension later today!]

Comparison with a diffeomorphic approach

[S, Durrleman, X. Pennec, A. Trouvé, N. Ayache, MICCAI 2007]

Difference between

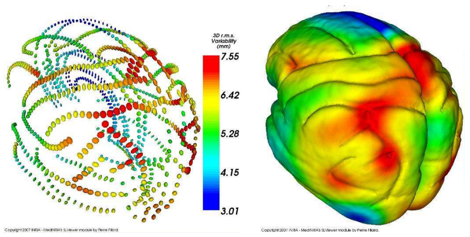
- Matching, then extrapolation [Fillard, NeuroImage 34(2) 2007]
- Extrapolation of speed vectors and trajectory integration

Method

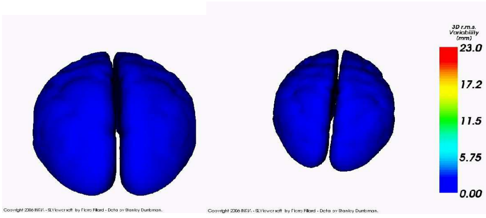
- Global space diffeomorphism parameterized by a finite number of point
- Distance between lines using currents [J. Glaunès, M. Vaillant: IPMI 2005]

Advantages

- Generative model of deformations
- Retrieve the tangential deformation component.



Variability at each point



Global variability (2 PGA modes)

Variability for what?

Several methods with different assumptions:

- Similar results at some locations, different results at other places
- Vary assumptions and discover truth by consensus

Learning / modeling phase (anatomy / neurosciences)

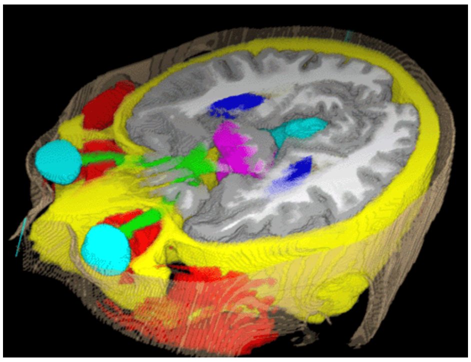
- Goal: analyze and understand the population variability
- Identify anatomical differences between populations
  - Can be computationally intensive,
  - Relies on good quality observations and “mild pathologies”

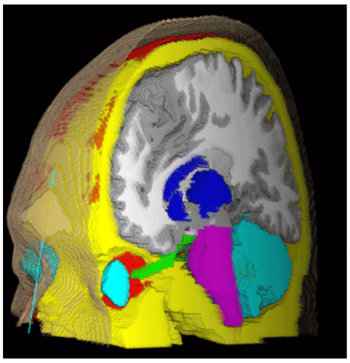
Use in a clinical / medical workflow: Personalization of atlases

- Anatomical prior to compensate for incomplete / noisy / abnormal (pathological) observations.
  - How to use statistics as a regularizer in registration?
  - Need **robust** methods, should be very **fast** (at least efficient)

One example use of variability information: better constrain the atlas to subject registration

- Deform the atlas anatomy (without tumor) towards the patient one
- Segment the structures of interest in the patient image
- Minimize irradiation in areas at risk.



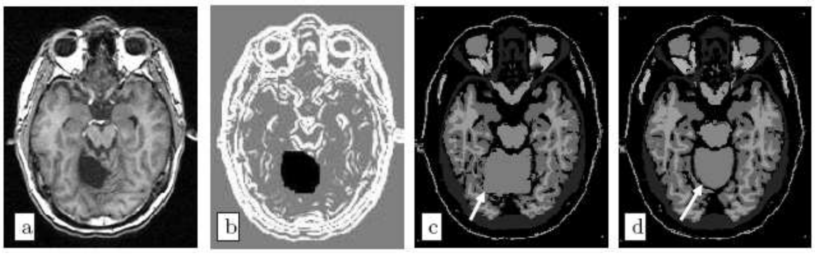


[Commowick, et al, MICCAI 2005]

Introducing local variability and pathologies in non-linear registration

$$E(T) \quad = \quad E_{sim}(I, J(T)) \;+\; \lambda . E_{reg}(T)$$

- Non stationary regularization: anatomical prior on the deformability
- Non stationary image similarity / regularization tradeoff: takes pathologies into account



Patient Stiffness field Atlas to patient With pathology

[Runa. Stefanescu et al, PPL 14(2), 2004 & Med. Image Analysis 8(3), 2003]

Regularization in dense non-linear registration

Physically based regularizations

- Elastic [Bajcsy 89]
- Fluid [Christensen TMI 97]
- Right-invariant distance [LDDMM, Beg IJCV 05]

Efficient regularization methods

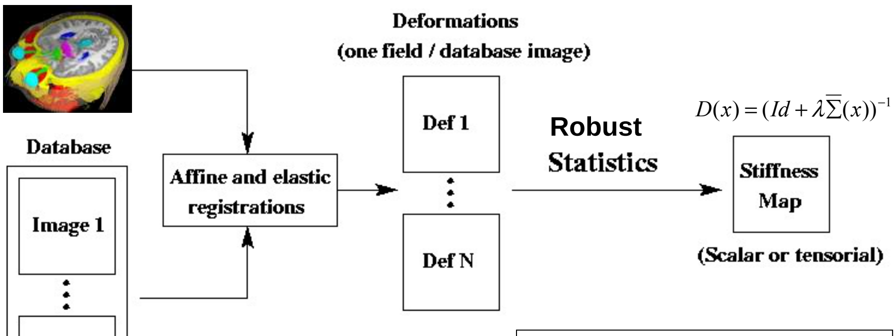
- Gaussian filtering [Thirion Media 98, Modersitzki 2004]
- Isotropic but non stationary [Lester IPMI'99]
- Towards anisotropic non stationary regularization [Stefanescu MedIA 2004]

Observation:

- No regularization model is more justified than others
- Learning statistically the variability from a population
  [Thompson 2000, Rueckert TMI 2003, Fillard IPMI 2005]

Statistics on the deformation field

- Objective: planning of conformal brain radiotherapy (O. Commowick, Dosisoft)
- 30 patients, 2 to 5 time points (P-Y Bondiau, MD, CAL, Nice)



$$D(x) = (Id + \lambda \bar{\Sigma}(x))^{-1}$$

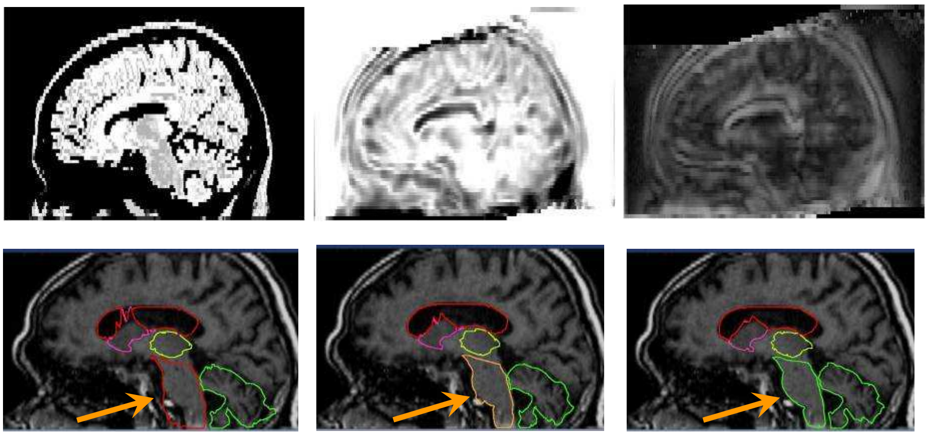
$$\overline{Def}(x) = \tfrac{1}{N} \sum_i \mathrm{abs}(\log(|\nabla \Phi_i(x)|))$$

$$\bar{\Sigma}(x) = \tfrac{1}{N} \sum_i \mathrm{abs}(\log(\Sigma_i(x)))$$

[Commowick, et al, MICCAI 2005, T2, p. 927-931]

Introducing deformation statistics into RUNA

Heuristic RUNA stiffness | Scalar statistical stiffness | Tensor stat. stiffness (FA)



[Commowick, et al, MICCAI 2005, T2, p. 927-931]

Riemannian elasticity : a well posed framework to introduce statistics in non-linear elastic regularization

[Pennec, et al, MICCAI 2005, LNCS 3750:943-950, MFCA'06]

Gradient descent $C(\Phi) = \mathrm{Sim}(\mathrm{Images}, \Phi) + \mathrm{Reg}(\Phi)$

Including statistics in Regularization

- St Venant Kirchoff elastic energy
  - Elasticity is not symmetric
  - Statistics are not easy to include

$$\mathrm{Reg}(\Phi) = \int \mu\, \mathrm{Tr}\big((\Sigma - I)^2\big) + \frac{\lambda}{2}\mathrm{Tr}(\Sigma - I)^2$$

$$\Sigma = \nabla\Phi^t.\nabla\Phi$$

- Idea: Replace the Euclidean by the Log-Euclidean metric

$$\mathrm{Tr}\big((\Sigma - I)^2\big) \;\rightarrow\; \mathrm{dist}_{LE}(\Sigma, I)^2 = \|\log(\Sigma)\|^2$$

- Statistics on strain tensors: Mean, covariance, Mahalanobis computed in Log-space

$$\mathrm{Reg}(\Phi) = \int \mathrm{Vect}\big(\log(\Sigma) - \overline{W}\big)^T.\mathrm{Cov}^{-1}.\mathrm{Vect}\big(\log(\Sigma) - \overline{W}\big)$$

Using Riemannian Elasticity as a metric (TBM)

- The mean provides an unbiased atlas
- Better constraining the deformation should give better results in TBM

[Natsha Lepore + Caroline Brun + Paul Thompson, Equipe Associee Brain Atlas with UCLA]

Statistics on which deformations feature?

Local statistics on local deformation (mechanical properties)

- Gradient of transformation, strain tensor
- [Riemannian elasticity, TBM, N. Lepore + C. Brun]

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

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

- [Vaillant et al., NeuroImage, 04]
- [Durrleman et al, MICCAI'07]
- Based on left-invariant metrics on diffeos [Trouvé, Younes et al.]
- Needs theoretically a finite number of point measures
- Computationally intensive

An alternative: log-Euclidean statistics on diffeomorphisms?

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

Statistics on geometrical objects

A consistent statistical computing framework on Riemannian manifolds with important applications in

- Medical Image Analysis (registration evaluation, DTI)
- Building models of living systems (spine, brain, heart…)

Is the Riemannian metric the minimal structure?

- No bi-invariant metric but bi-invariant means on Lie groups [V. Arsigny] Change the Riemannian metric for the symmetric Cartan connection?

Infinite dimensional manifolds

- Curves and surfaces
- Space of diffeomorphisms

How to chose or estimate the metric?

- Invariance, reacheability of boundaries, learning the metric
- Families of anatomical deformation metrics (models of the Green's function)
- Spatial correlation between neighbors… and distant points

Challenges of Computational Anatomy

Build models from multiple sources

- Curves, surfaces [cortex, sulcal ribbons]
- Volume variability [Voxel/Tensor Based Morphometry, Riemannian elasticity]
- Diffusion tensor imaging [fibers, tracts, atlas]
- Topological changes
- Evolution: growth, pathologies

Compare and combine statistics on anatomical manifolds

- Each method is biased by its assumptions (fewer data than unknowns)
- Validate methods and models by consensus
- Integrative model (transformations ?)

Couple modeling and statistical learning

- Variability estimation / structure inference / model validation and refinement
- Use models as a prior for inter-subject registration / segmentation:
  Validation by better statistics on populations (e.g. functional)
- Need large database and distributed processing/algorithms

Acknowledgements

Associated team Brain Atlas with LONI:

- P. Thompson, N. Lepore, C. Brun

Brain variability:

- P. Fillard, V. Arsigny, S. Durrleman,

Spine shape:

- J. Boisvert, F. Cheriet, Ste Justine Hospital, Montreal.

Inter-subject non-linear registration:

- P. Cathier, R. Stefanescu, O. Commowick

ACI Agir / Grid computing:

- T. Glatard and J. Montagnat, I3S.

N. Ayache and current / former Epidaure / Asclepios team members.