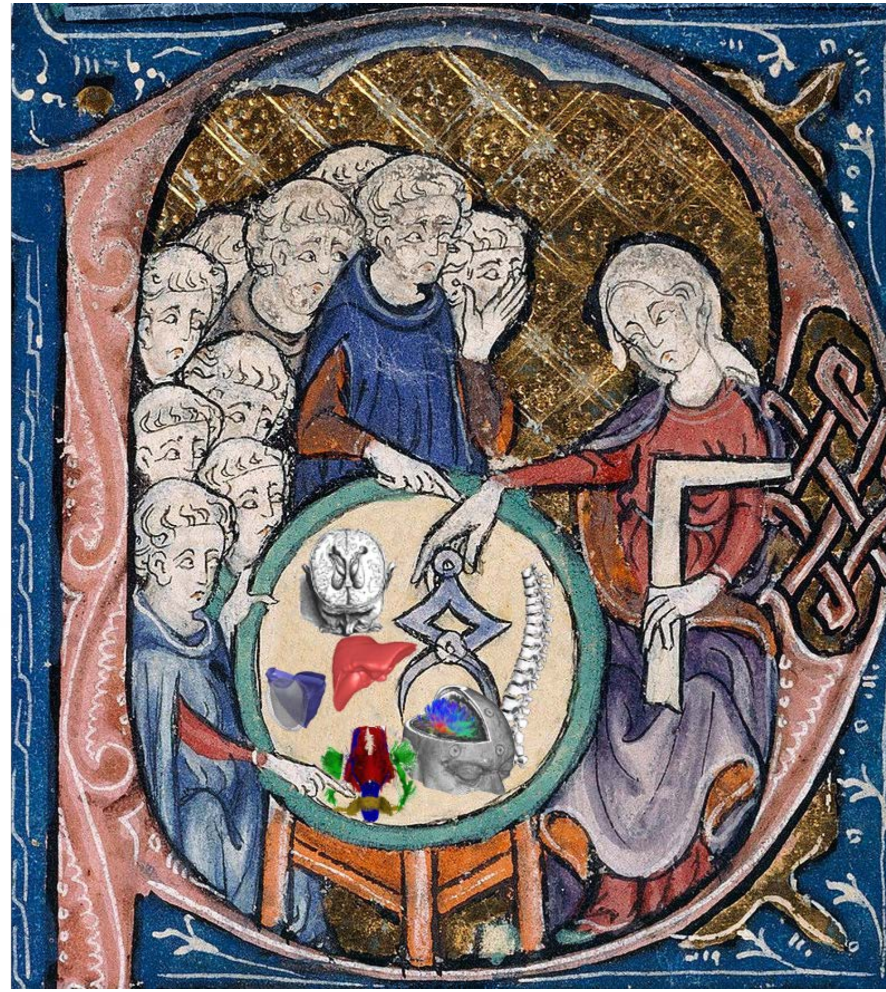
Xavier Pennec

Univ. Côte d'Azur and Inria, France

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.

1/ Intrinsic Statistics on Riemannian Manifolds

Geometric Statistics workshop 09/2019

Collaborators

Researchers from Epione/Adclepios/Epidaure team

- Maxime Sermesant
- Nicholas Ayache

Former PhD students

- Jonathan Boisvert
- Pierre Fillard
- Vincent Arsigny
- Kristin McLeod
- Nina Miolane
- Loic Devillier
- Marc-Michel Rohé
- Tom Vercauteren
- Stanley Durrleman
- Marco Loreni
- Christof Seiler
- …..

Current PhD students

- Yan Thanwerdas
- Nicolas Guigui
- Shuma Jia

Geometric Statistics

PhDs and Post-docs available

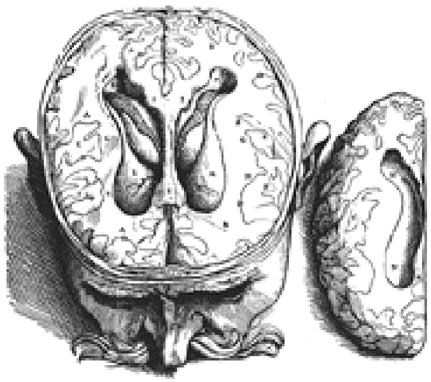
Epione e-patient / e-medicine

UNIVERSITÉ CÔTE D'AZUR

Inria

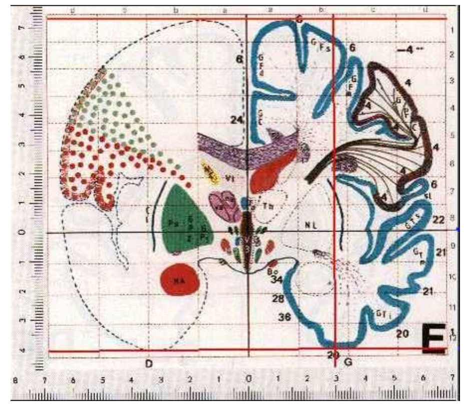
Anatomy

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

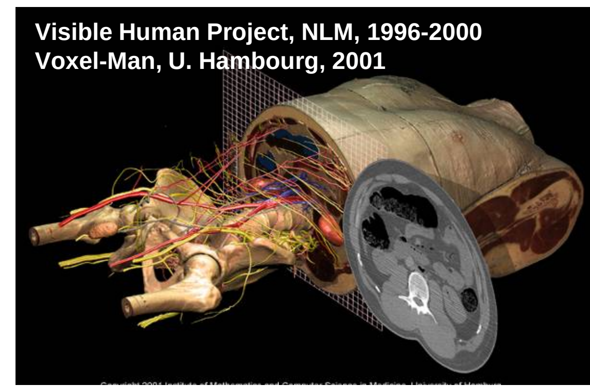


1er cerebral atlas, Vesale, 1543

Paré, 1585



Talairach & Tournoux, 1988

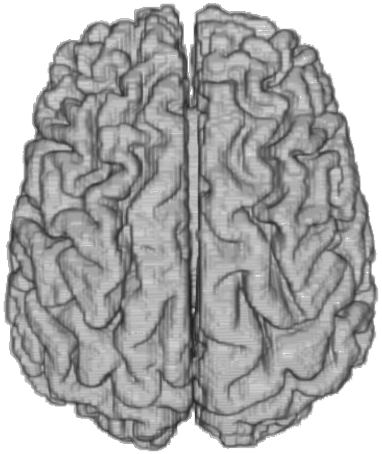
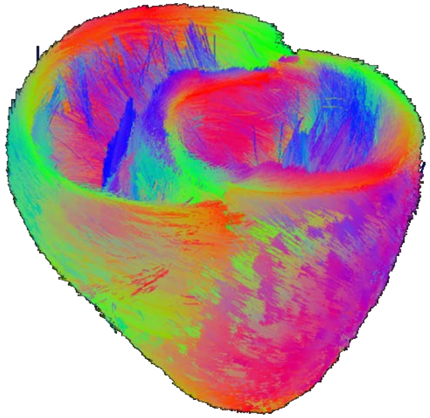
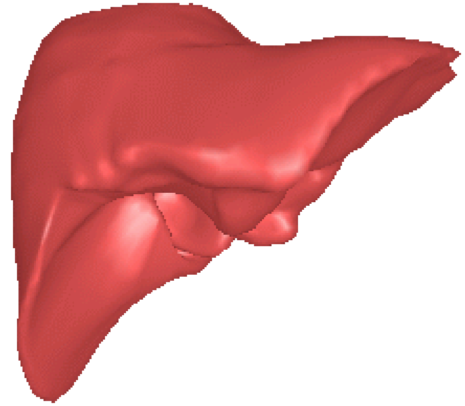


Galien (131-201) → **Vésale (1514-1564)** **Paré (1509-1590)** → **Sylvius (1614-1672)** **Willis (1621-1675)** → **Gall (1758-1828) :** ***Phrenology*** **Talairach (1911-2007)**

Revolution of observation means (~1990):

- From dissection to in-vivo in-situ imaging
- From the description of one representative individual to generative statistical models of the population

Computational Anatomy


Statistics of organ shapes across subjects in species, populations, diseases…

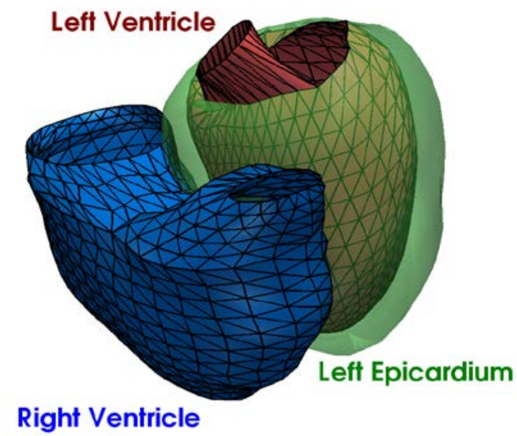
- Mean shape (atlas), subspace of normal vs pathologic shapes
- Shape variability (Covariance)
- Model development across time (growth, ageing, ages…)

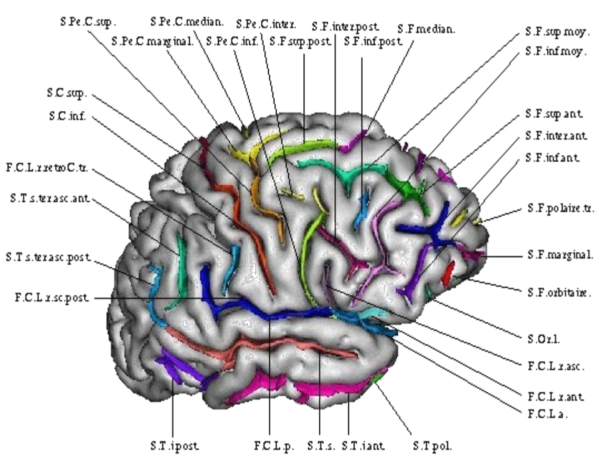
Use for personalized medicine (diagnostic, follow-up, etc)

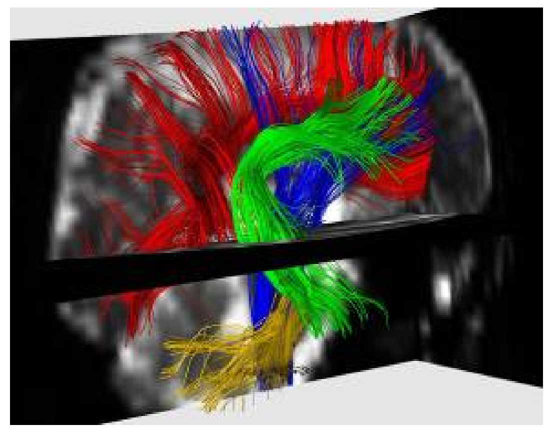
Geometric features in Computational Anatomy

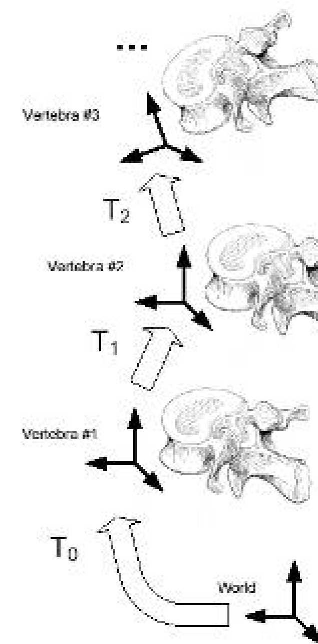
Noisy geometric features

- Curves, sets of curves (fiber tracts)
- Surfaces, SPD matrices
- Transformations









Statistical modeling at the population level

- **Simple Statistics on non-linear manifolds?**
  - Mean, covariance of its estimation, PCA, PLS, ICA
- **GS**: Statistics on manifolds vs **IG**: manifolds of statistical models

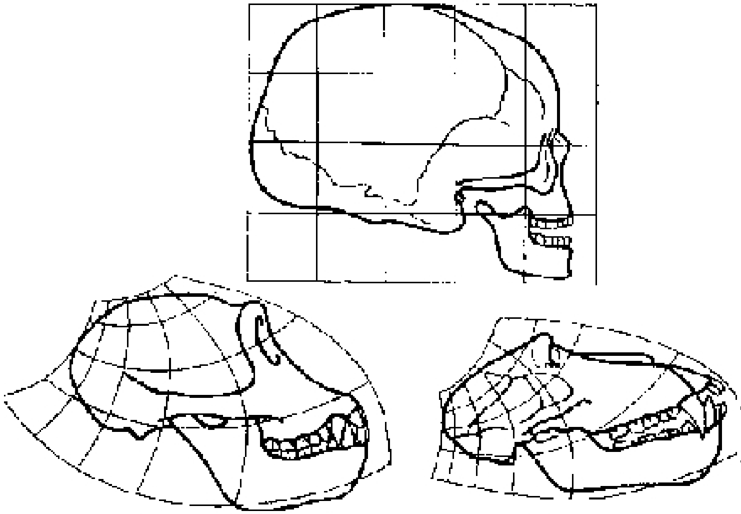
Methods of computational anatomy

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

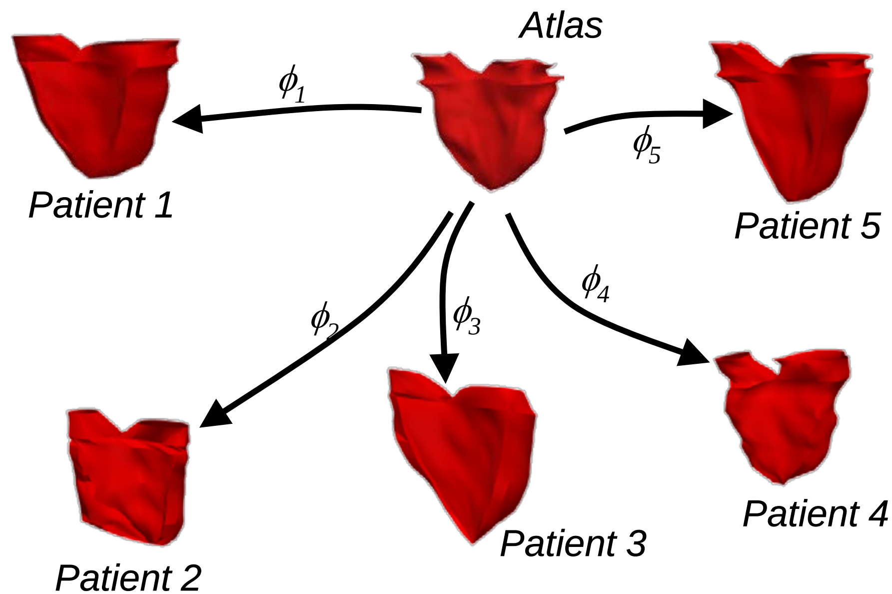
- Mean shape
- Shape variability
- Correlation with clinical variables
- Predicting remodeling effect

Shape of RV in 18 patients

Morphometry through Deformations



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



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

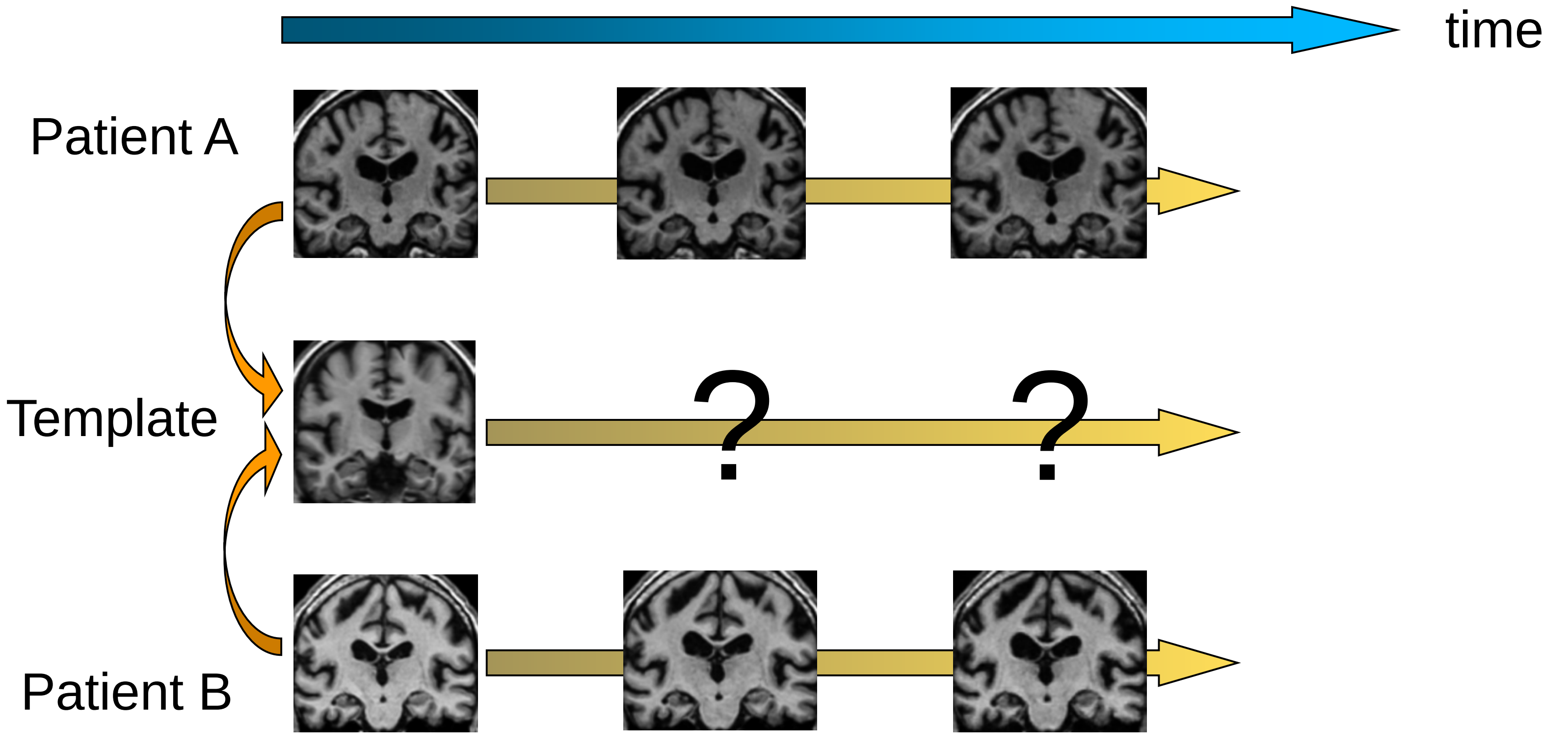
- Observation = "random" deformation of a reference template
- Reference template = Mean (atlas)
- Shape variability encoded by the deformations

Statistics on groups of transformations (Lie groups, diffeomorphism)?

Consistency with group operations (non commutative)?

Longitudinal deformation analysis

Dynamic obervations



How to transport longitudinal deformation across subjects?

What are the convenient mathematical settings?

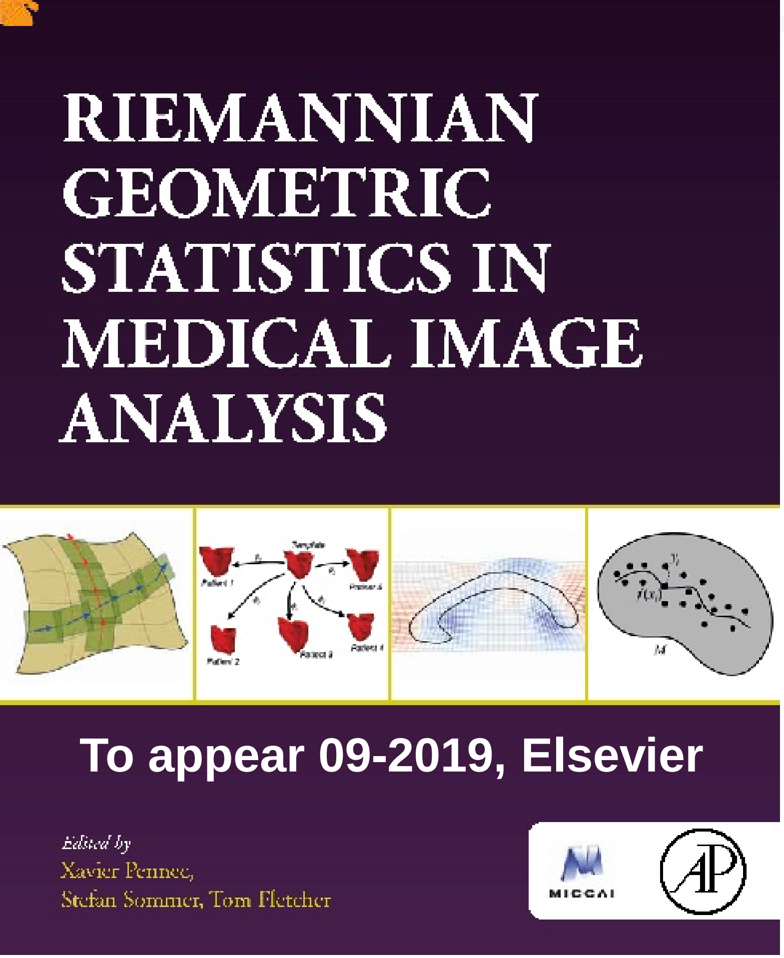
Geometric Statistics: Mathematical foundations and applications in computational anatomy

Intrinsic Statistics on Riemannian Manifolds

Metric and Affine Geometric Settings for Lie Groups

Parallel Transport to Analyze Longitudinal Deformations

Advances Statistics: CLT & PCA



Part 1: Foundations

- 1: Riemannian geometry [Sommer, Fetcher, Pennec]
- 2: Statistics on manifolds [Fletcher]
- 3: Manifold-valued image processing with SPD matrices [Pennec]
- 4: Riemannian Geometry on Shapes and Diffeomorphisms [Marsland, Sommer]
- 5: Beyond Riemannian: the affine connection setting for transformation groups [Pennec, Lorenzi]

Part 2: Statistics on Manifolds and Shape Spaces

- 6: Object Shape Representation via Skeletal Models (s-reps) and Statistical Analysis [Pizer, Maron]
- 7: Inductive Fréchet Mean Computation on S(n) and SO(n) with Applications [Chakraborty, Vemuri]
- 8: Statistics in stratified spaces [Ferage, Nye]
- 9: Bias in quotient space and its correction [Miolane, Devilier,Pennec]
- 10: Probabilistic Approaches to Statistics on Manifolds: Stochastic Processes, Transition Distributions, and Fiber Bundle Geometry [Sommer]
- 11: Elastic Shape Analysis, Square-Root Representations and Their Inverses [Zhang, Klassen, Srivastava]

Part 3: Deformations, Diffeomorphisms and their Applications

- 13: Geometric RKHS models for handling curves and surfaces in Computational Anatomy : currents, varifolds, f-shapes, normal cycles [Charlie, Charon, Glaunes, Gori, Roussillon]
- 14: A Discretize-Optimize Approach for LDDMM Registration [Polzin, Niethammer, Vialad, Modezitski]
- 15: Spatially varying metrics in the LDDMM framework [Vialard, Risser]
- 16: Low-dimensional Shape Analysis In the Space of Diffeomorphisms [Zhang, Fleche, Wells, Golland]
- 17: Diffeomorphic density matching, Bauer, Modin, Joshi]

Supports for the course

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

- 1/ Intrinsic Statistics on Riemannian Manifolds
  - Introduction to differential and Riemannian geometry. **Chapter 1**, RGSMIA. Elsevier, 2019.
  - Intrinsic Statistics on Riemannian Manifolds: Basic Tools for Geometric Measurements. JMIV 2006.
- 2/ SPD matrices and manifold-valued image processing
  - Manifold-valued image processing with SPD matrices. **Chapter 3** RGSMIA. Elsevier, 2019.
  - Historical reference: A Riemannian Framework for Tensor Computing. IJCV 2006.
- 3/ Metric and affine geometric settings for Lie groups
  - Beyond Riemannian Geometry The affine connection setting for transformation groups Chapter 5, RGSMIA. Elsevier, 2019.
- 4/ Parallel transport to analyze longitudinal deformations
  - Geodesics, Parallel Transport and One-parameter Subgroups for Diffeomorphic Image Registration. IJCV 105(2), November 2013.
  - Parallel Transport with Pole Ladder: a Third Order Scheme…[arXiv:1805.11436]
- 5/ Advanced statistics: central limit theorem and extension of PCA
  - Curvature effects on the empirical mean in Riemannian and affine Manifolds [arXiv:1906.07418]
  - Barycentric Subspace Analysis on Manifolds. Annals of Statistics. 46(6A):2711-2746, 2018. [arXiv:1607.02833]

Geometric Statistics: Mathematical foundations and applications in computational anatomy

Intrinsic Statistics on Riemannian Manifolds

- Introduction to computational anatomy
- The Riemannian manifold computational structure
- Simple statistics on Riemannian manifolds
- Applications to the spine shape and registration accuracy

Metric and Affine Geometric Settings for Lie Groups

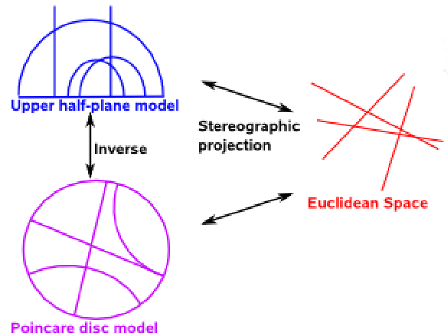
Parallel Transport to Analyze Longitudinal Deformations

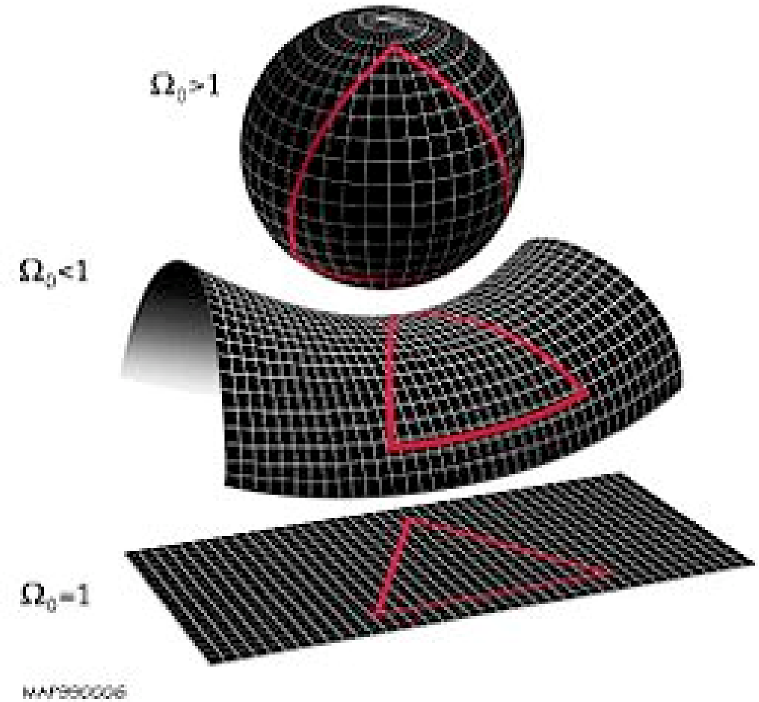
Advances Statistics: CLT & PCA

Which non-linear space?

Constant curvatures spaces

- Sphere,
- Euclidean,
- Hyperbolic





Homogeneous spaces, Lie groups and symmetric spaces

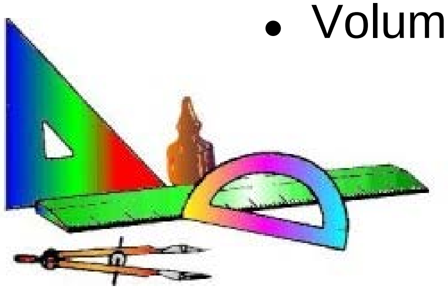
Riemannian or affine connection spaces

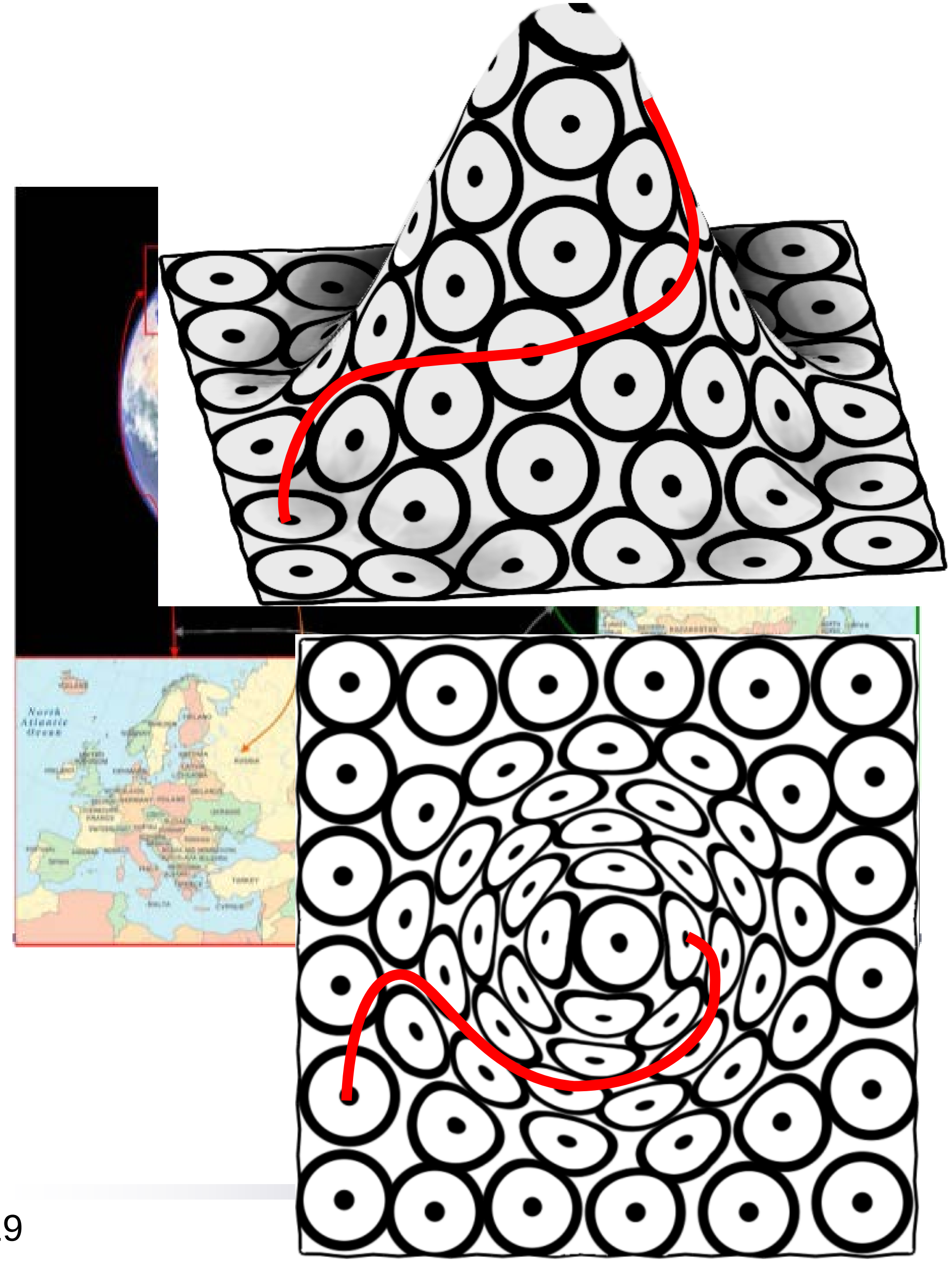
Towards non-smooth quotient and stratified spaces

Differentiable manifolds

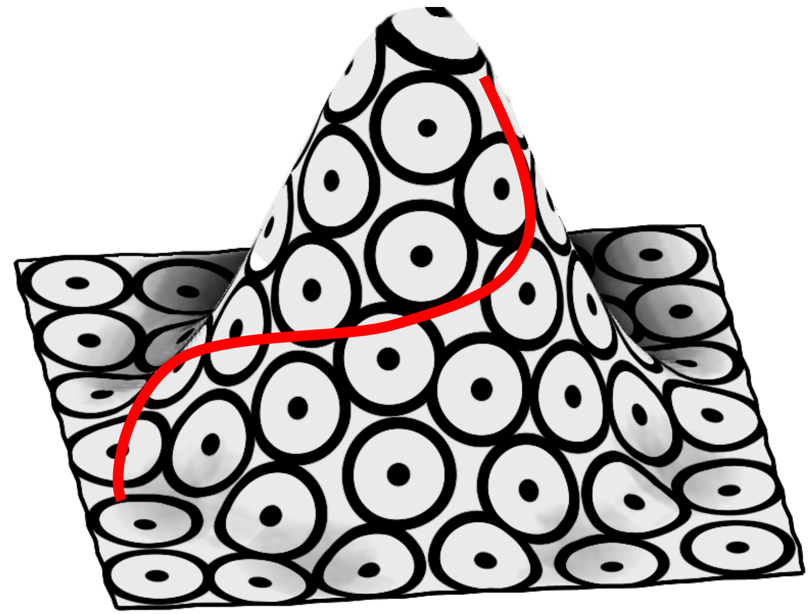
Computing on a manifold

- Extrinsic
  - Embedding in $\mathbb{R}^n$
- Intrinsic
  - Coordinates : charts
- Measuring?
  - Lengths
  - Straight lines
  - Volumes





Measuring extrinsic distances

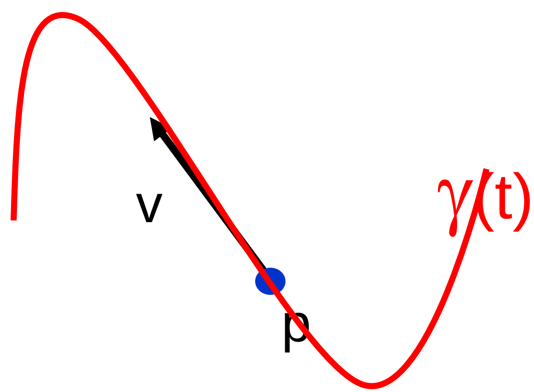


Basic tool: the scalar product

$$< v, w >= v^t w$$

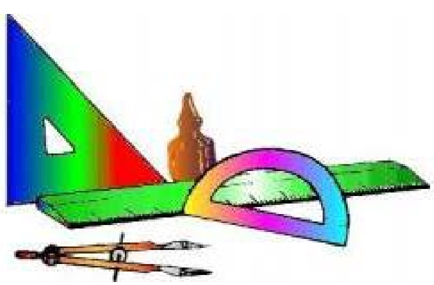
- Norm of a vector

$$\|v\| = \sqrt{< v, v >}$$



- Length of a curve

$$L(\gamma) = \int \|\dot{\gamma}(t)\| \, dt$$



Measuring extrinsic distances

Basic tool: the scalar product

Bernhard Riemann
1826-1866

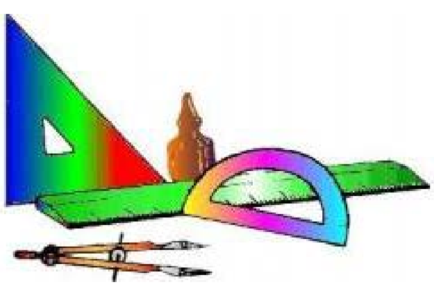
$$<\mathbf{v},\mathbf{w}>_p = v^t\, G(p)\, w$$

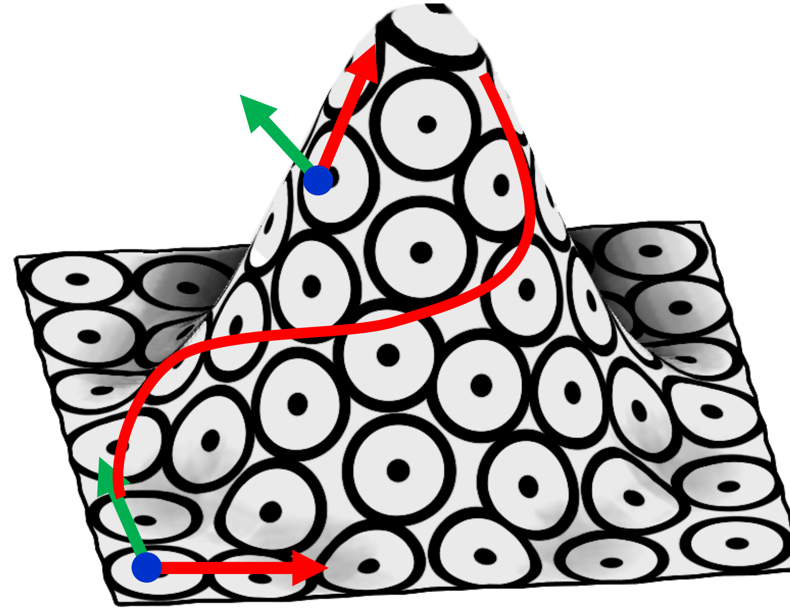
- Norm of a vector

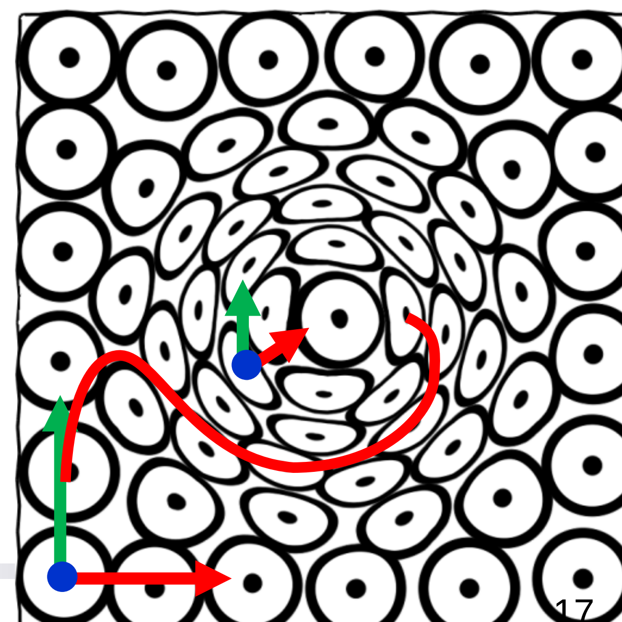
$$\|v\|_p = \sqrt{<v,v>_p}$$

- Length of a curve

$$L(\gamma) = \int \|\dot{\gamma}(t)\|\, dt$$





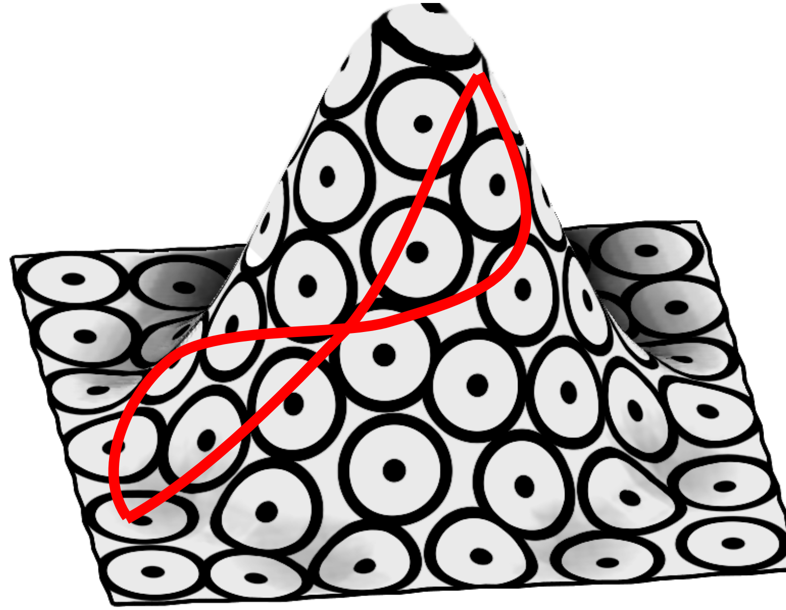


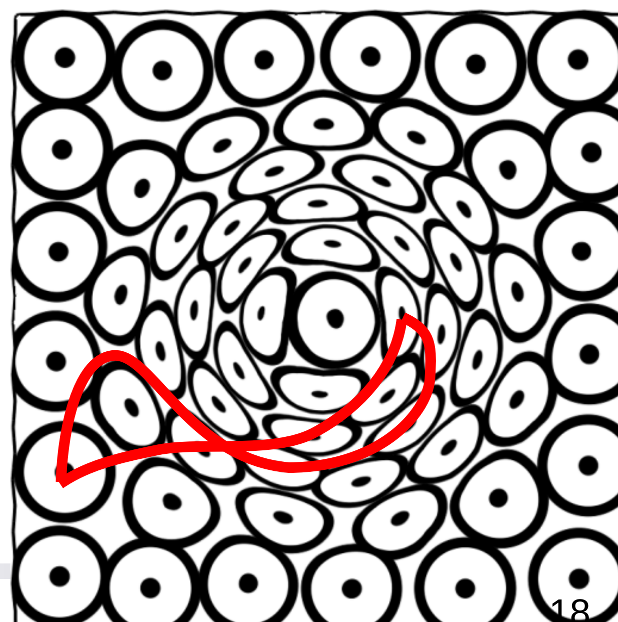
Riemannian manifolds

Basic tool: the scalar product

$$< v, w >_p = v^t G(p) w$$

Bernhard Riemann
1826-1866

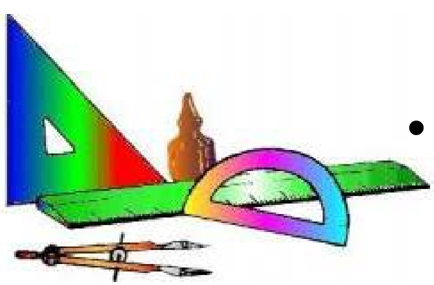




- Geodesics
  - Shortest path between 2 points
  - Calculus of variations (E.L.) : 2[nd] order differential equation (specifies acceleration)
  - Free parameters: initial speed and starting point

- Length of a curve

$$L(\gamma) = \int \|\dot{\gamma}(t)\| \, dt$$



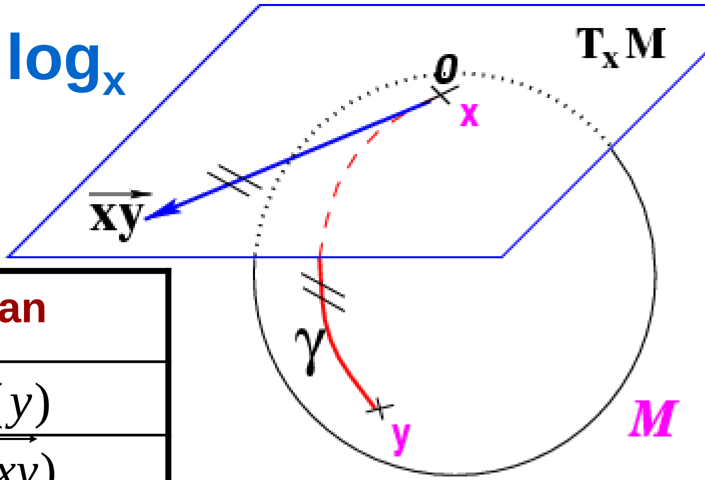
Bases of Algorithms in Riemannian Manifolds

Exponential map (Normal coordinate system):

- **Exp_x** = geodesic shooting parameterized by the initial tangent
- **Log_x** = unfolding the manifold in the tangent space along geodesics
  - Geodesics = straight lines with Euclidean distance
  - Geodesic completeness: covers M \ Cut(x)

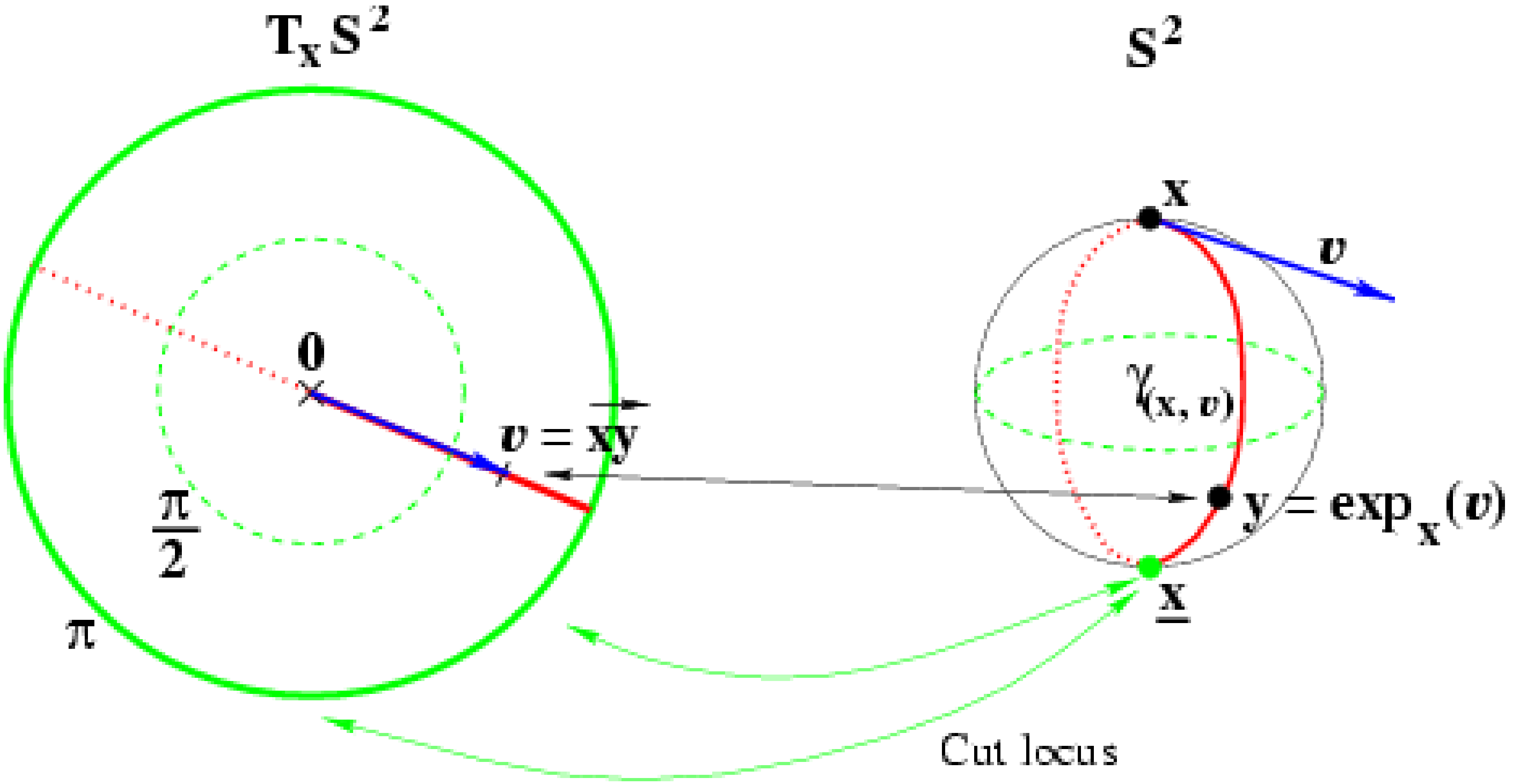
Reformulate algorithms with exp_x and log_x

Vector -> Bi-point (no more equivalence classes)



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

Cut locus



$T_x S^2$
S^2
x
v
0
$\gamma_{(x,v)}$
$v = \overrightarrow{xy}$
$y = \exp_x(v)$
$\frac{\pi}{2}$
$\underline{x}$
π
Cut locus

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Basic probabilities and statistics

Measure: random vector x of pdf $p_{\mathbf{x}}(z)$

Approximation: $\mathbf{x} \sim (\overline{\mathrm{x}}, \boldsymbol{\Sigma}_{\mathbf{xx}})$

- Mean: $\overline{\mathrm{x}} = \mathrm{E}(\,\mathbf{x}\,) = \int z.p_{\mathbf{x}}(z).dz$
- Covariance: $\Sigma_{\mathbf{xx}} = \mathrm{E}\left[(\mathbf{x} - \overline{\mathrm{x}}).(\mathbf{x} - \overline{\mathrm{x}})^T\right]$

Propagation:

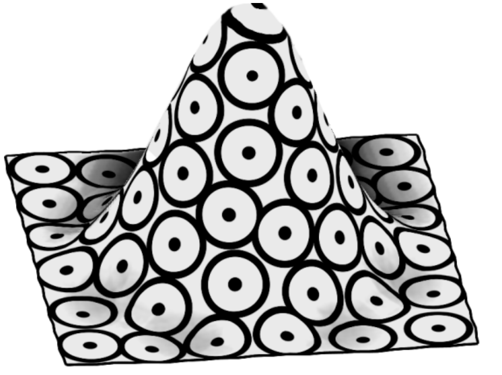
$$\mathbf{y} = h(\mathbf{x}) \sim \left(h(\overline{\mathrm{x}}),\ \frac{\partial h}{\partial \mathrm{x}}.\boldsymbol{\Sigma}_{\mathbf{xx}}.\frac{\partial h}{\partial \mathrm{x}}^{\mathrm{T}} \right)$$

Noise model: additive, Gaussian...

Principal component analysis

Statistical distance: Mahalanobis and χ^2

Random variable in a Riemannian Manifold



Intrinsic pdf of x

- For every set H

$$P(\mathbf{x} \in H) = \int_H p(y)dM(y)$$

- ~~Lebesgue's measure~~

→ Uniform Riemannian Mesure $dM(y) = \sqrt{\det\big(G(y)\big)}\, dy$

Expectation of an observable in M

- $\boldsymbol{E}_{\mathbf{x}}[\phi] = \int_M \phi(y)p(y)dM(y)$
- $\phi = dist^2$ (variance) : $\boldsymbol{E}_{\mathbf{x}}[dist(.,y)^2] = \int_M dist(y,z)^2 p(z)dM(z)$
- $\phi = \log(p)$ (information) : $\boldsymbol{E}_{\mathbf{x}}[\log(p)] = \int_M p(y)\log(p(y))dM(y)$
- ~~$\phi = x$ (mean) : $\boldsymbol{E}_{\mathbf{x}}[\mathbf{x}] = \int_M y\, p(y)dM(y)$~~

First statistical tools

Moments of a random variable: tensor fields

- $\mathfrak{M}_1(x) = \int_M \overrightarrow{xz}\, P(dz)$ Tangent mean: (0,1) tensor field
- $\mathfrak{M}_2(x) = \int_M \overrightarrow{xz} \otimes \overrightarrow{xz}\, P(dz)$ Covariance: (0,2) tensor field
- $\mathfrak{M}_k(x) = \int_M \overrightarrow{xz} \otimes \overrightarrow{xz} \otimes \cdots \otimes \overrightarrow{xz}\, P(dz)$ k-contravariant tensor field

Fréchet mean set

- Integral only valid in Hilbert/Wiener spaces [Fréchet 44]
- $\sigma^2(x) = Tr_g\left(\mathfrak{M}_2(x)\right) = \int_M dist^2(x,z)\, P(dz)$
- **Fréchet mean** [1948] = global minima
- **Exponential barycenters** [Emery & Mokobodzki 1991]

  $\mathfrak{M}_1(\bar{x}) = \int_M \overrightarrow{\bar{x}z}\, P(dz) = 0$ [critical points if P(C) =0]

Maurice Fréchet
(1878-1973)

Fréchet expectation (1944)

Minimizing the variance

$$\mathrm{E}[\mathbf{x}] = \underset{y \in \mathrm{M}}{\operatorname{argmin}} \left(\mathrm{E}\left[\operatorname{dist}(y, \mathbf{x})^2 \right] \right)$$

Existence

- Finite variance at one point

Characterization as an exponential barycenter (P(C)=0)

$$\operatorname{grad}\left(\sigma_{\mathbf{x}}^2(y)\right) = 0 \quad \Rightarrow \quad \mathrm{E}\left[\overrightarrow{\mathrm{x}\mathbf{x}}\right] = \int_{\mathrm{M}} \overrightarrow{\mathrm{x}\mathbf{x}}.p_{\mathbf{x}}(z).d\mathrm{M}(z) = 0$$

Uniqueness **Karcher 77 / Kendall 90 / Afsari 10 / Le 10**

- Unique Karcher mean (thus Fréchet) if distribution has support in a regular geodesic ball with radius $r < r^* = \frac{1}{2}\min(inj(M), \pi/\sqrt{\kappa})$ (k upper bound on sectional curvatures on M)
- Empirical mean: a.s. uniqueness [Arnaudon & Miclo 2013]

Other central primitives

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

A gradient descent (Gauss-Newton) algorithm

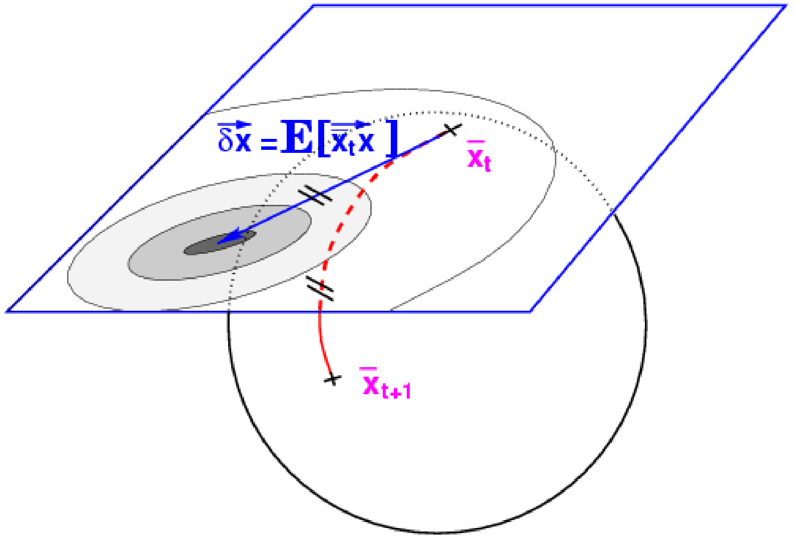
Vector space

$$f(x+v) = f(x) + \nabla f^{T}.v + \frac{1}{2} v^{T}.H_f.v$$

$$x_{t+1} = x_t + v \quad \text{with} \quad v = -H_f^{(-1)}.\nabla f$$

Manifold

$$f(\exp_x(v)) = f(x) + \nabla f(v) + \frac{1}{2} H_f(v,v)$$



$$\nabla\left(\sigma_{\mathbf{x}}^2(\mathrm{y})\right) = -2\,\mathrm{E}\left[\overrightarrow{\mathrm{y}\mathbf{x}}\right] = \frac{-2}{n}\sum_i \overrightarrow{\mathrm{y}\mathrm{x}_i}$$

$$H_{\sigma_{\mathbf{x}}^2} \approx 2Id$$

Geodesic marching

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

Example on 3D rotations

Space of rotations SO(3):

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

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

- Left / right invariant / induced by ambient space $\langle X, Y \rangle = Tr(X^T Y)$

Group exponential

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

$$Log_R(U) = R \log(R^T U) \qquad Exp_R(X) = R \exp(R^T X)$$

Bi-invariant Riemannian distance

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

Example with 3D rotations

Principal chart: rotation vector : $r = \theta.n$

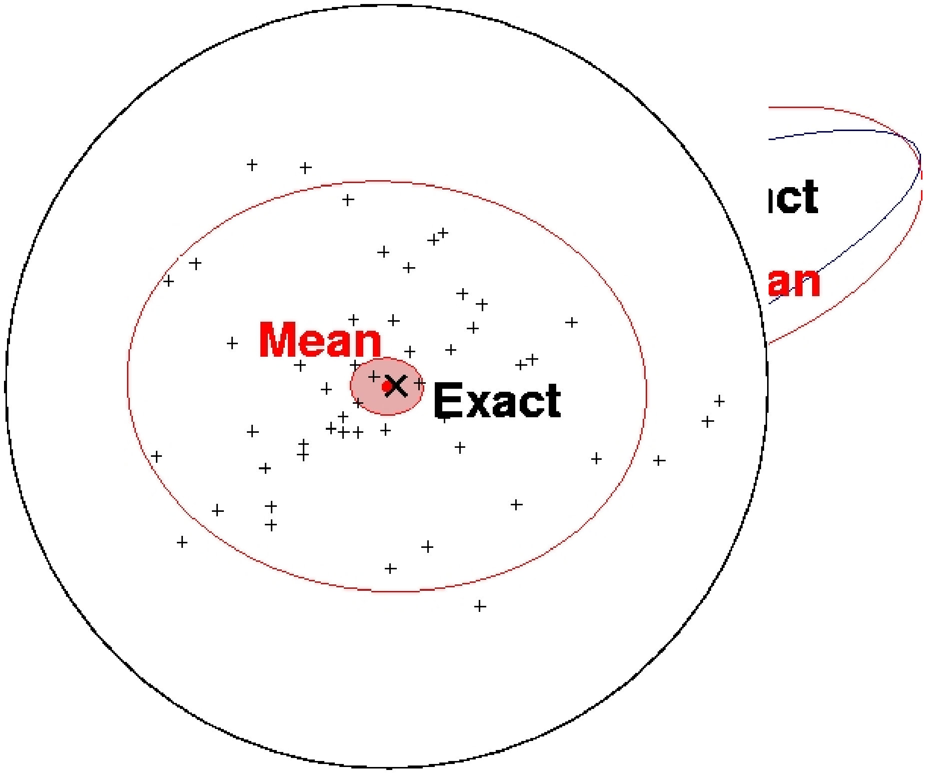
Distance: $\text{dist}(R_1, R_2) = \left\| r_1^{(-1)} \circ r_2 \right\|$

Frechet mean:

$$\overline{R} = \arg\min_{R \in SO_3} \left(\sum_{\text{i}} \text{dist}(R, R_i) \right)$$

Centered chart:

mean = barycenter



Distributions for parametric tests

Uniform density:

- maximal entropy knowing X

$$p_{\mathbf{x}}(z) = \mathrm{Ind}_X(z) / \mathrm{Vol}(X)$$

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:

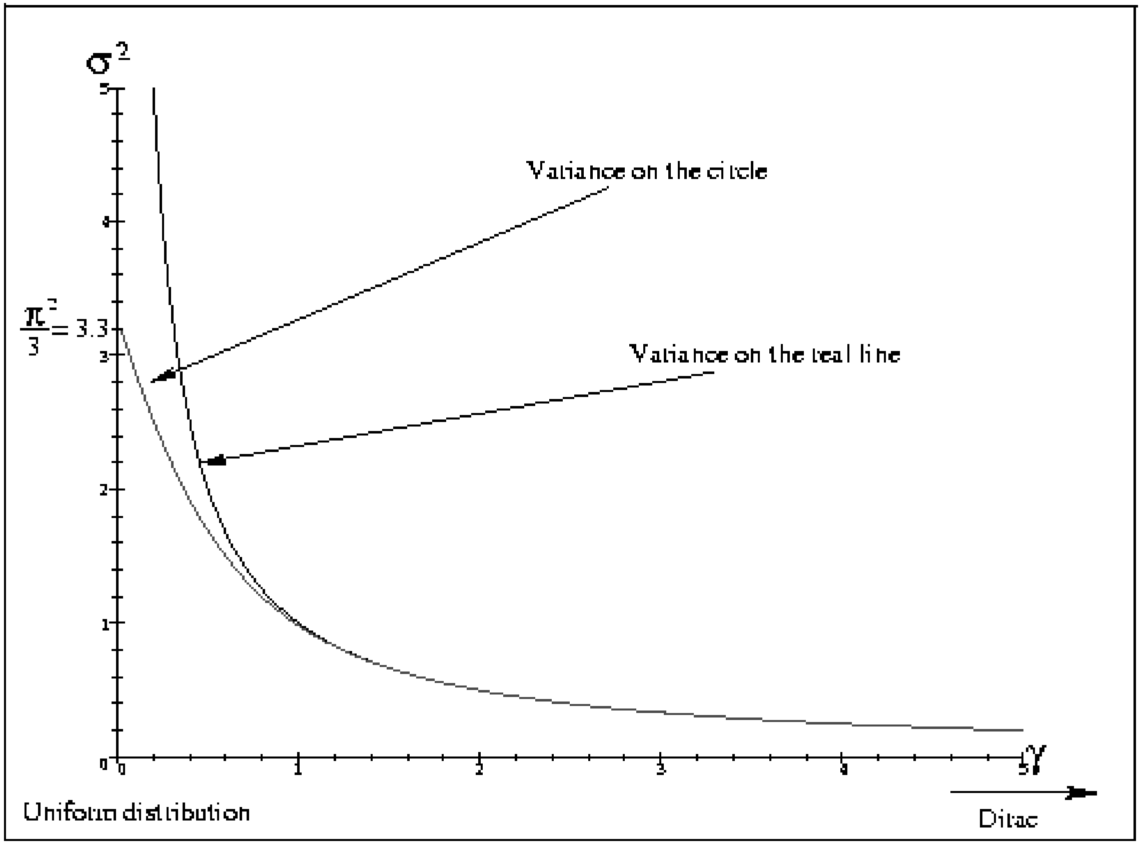
$$\mu_{\mathbf{x}}^2(\mathbf{x}) \propto \chi_n^2 + O(\sigma^3) + \varepsilon(\sigma/r)$$

[Pennec, JMIV06, NSIP'99]

Gaussian on the circle

Exponential chart: $x = r\theta \in \left]-\pi.r \,;\, \pi.r\right[$

Gaussian: truncated standard Gaussian



$r \to \infty$: standard Gaussian (Ricci curvature → 0)

$\gamma \to 0$: uniform pdf with

$$\sigma^2 = (\pi.r)^2 / 3$$

(compact manifolds)

$\gamma \to \infty$: Dirac

tPCA vs PGA

tPCA

- Generative model: Gaussian
- Find the subspace that best explains the variance

  → Maximize the squared distance to the mean

PGA (Fletcher 2004, Sommer 2014)

- Generative model:
  - Implicit uniform distribution within the subspace
  - Gaussian distribution in the vertical space
- Find a low dimensional subspace (geodesic subspaces?) that minimizes the error

  → Minimize the squared Riemannian distance from the measurements to that sub-manifold (no closed form)

Different models in curved spaces (no Pythagore thm)

Extension to BSA tomorrow

Geometric Statistics: Mathematical foundations and applications in computational anatomy

Intrinsic Statistics on Riemannian Manifolds

- Introduction to computational anatomy
- The Riemannian manifold computational structure
- Simple statistics on Riemannian manifolds
- Applications to the spine shape and registration accuracy

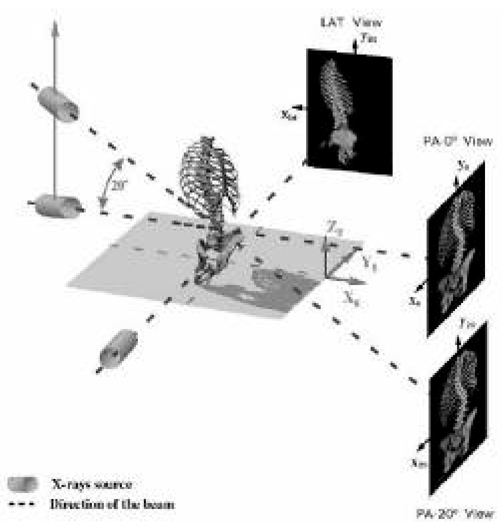
Metric and Affine Geometric Settings for Lie Groups

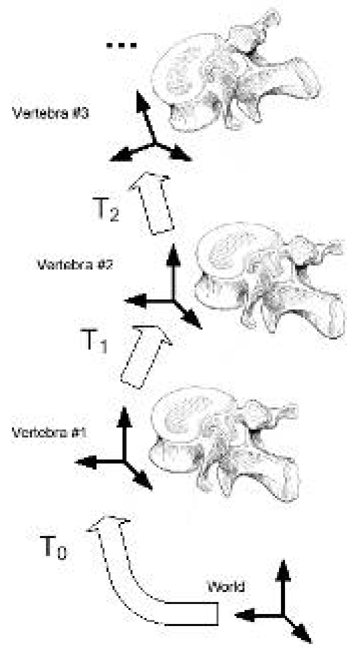
Parallel Transport to Analyze Longitudinal Deformations

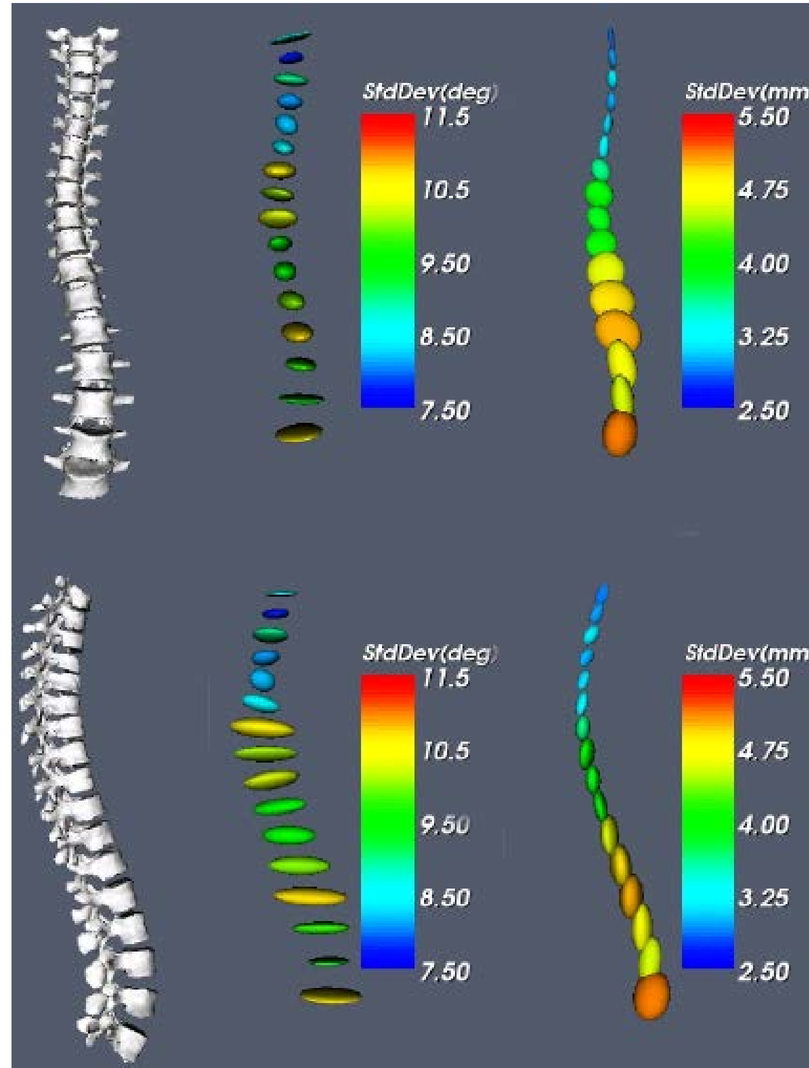
Advances Statistics: CLT & PCA

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

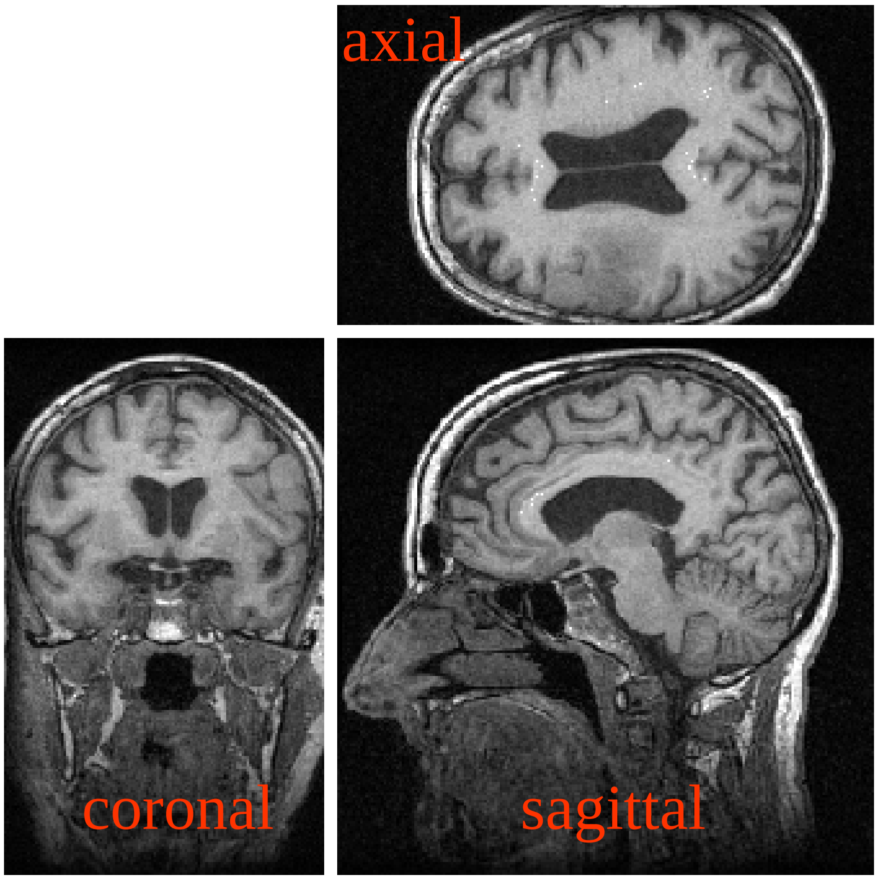
[J. Boisvert et al. ISBI'06, AMDO'06 and IEEE TMI 27(4), 2008]
AMDO'06 best paper award, Best French-Quebec joint PhD 2009

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)

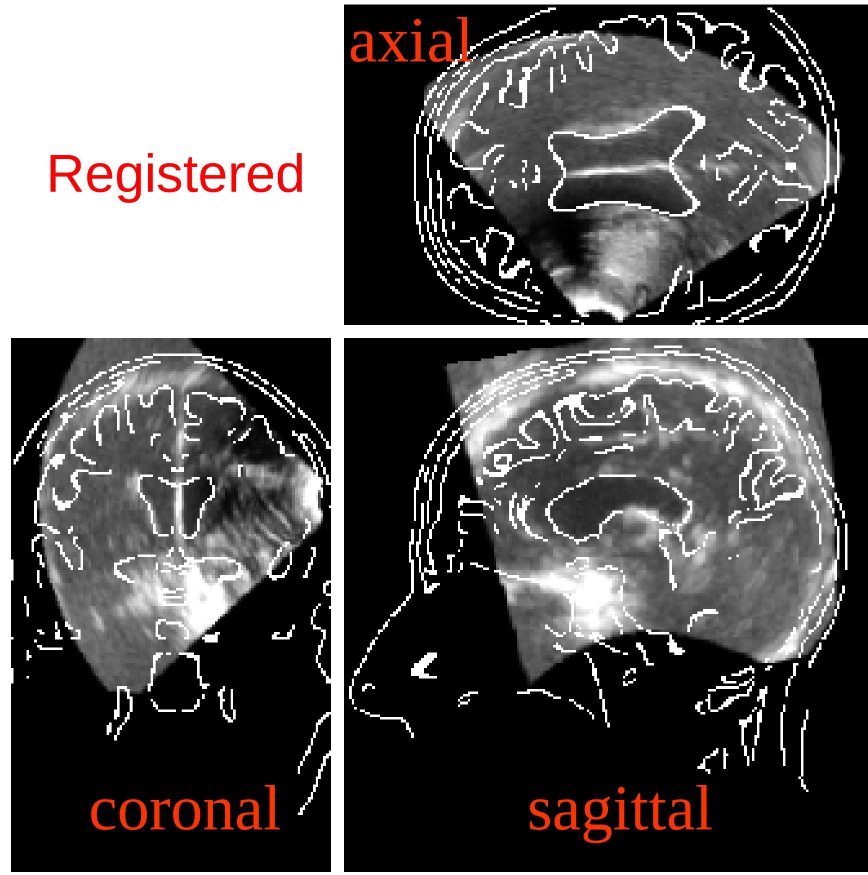
Typical Registration Result with Bivariate Correlation Ratio

Pre - Operative MR Image



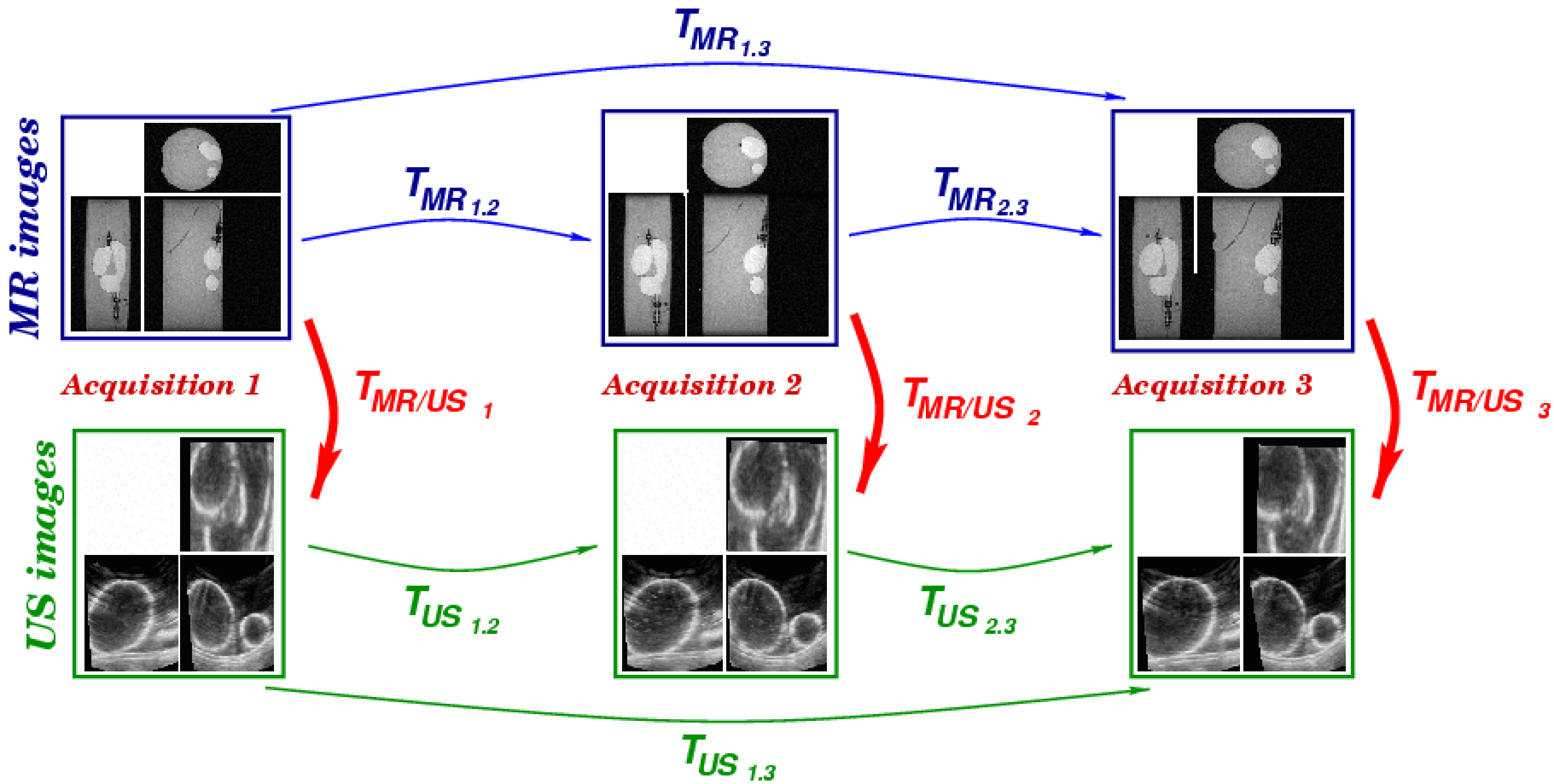
Per - Operative US Image

Registered



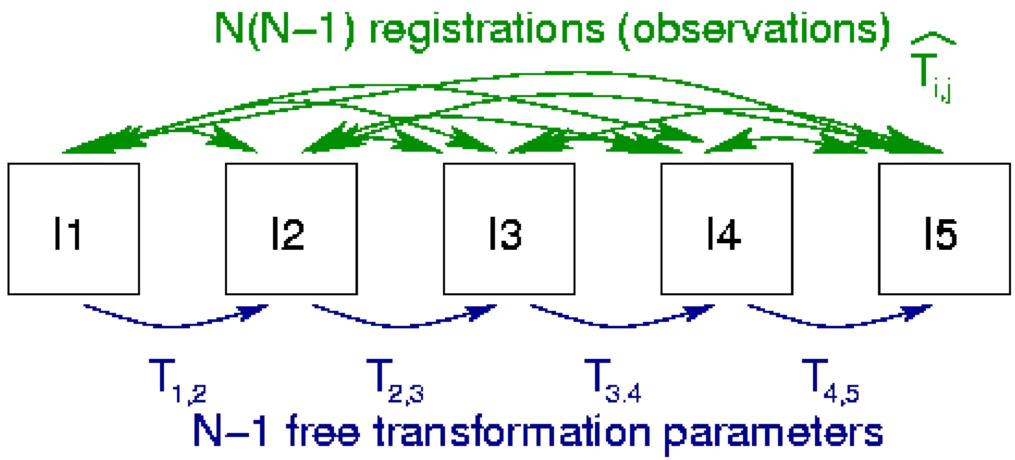
Acquisition of images : L. & D. Auer, M. Rudolf

Accuracy Evaluation (Consistency)



$$\sigma^2_{loop} = 2\sigma^2_{MR/US} + \sigma^2_{MR} + \sigma^2_{US}$$

Bronze Standard Rigid Registration Validation



Best explanation of the observations (ML) : $C = \sum_{ij} d^2(T_{ij}, \hat{T}_{ij})$

- LSQ criterion
- Robust Fréchet mean $d^2(T_1, T_2) = \min\left(\mu^2(T_1, T_2), \chi^2\right)$
- Robust initialization and Newton gradient descent

Result $\boxed{T_{i,j}, \sigma_{rot}, \sigma_{trans}}$

[T. Glatard & al, MICCAI 2006,

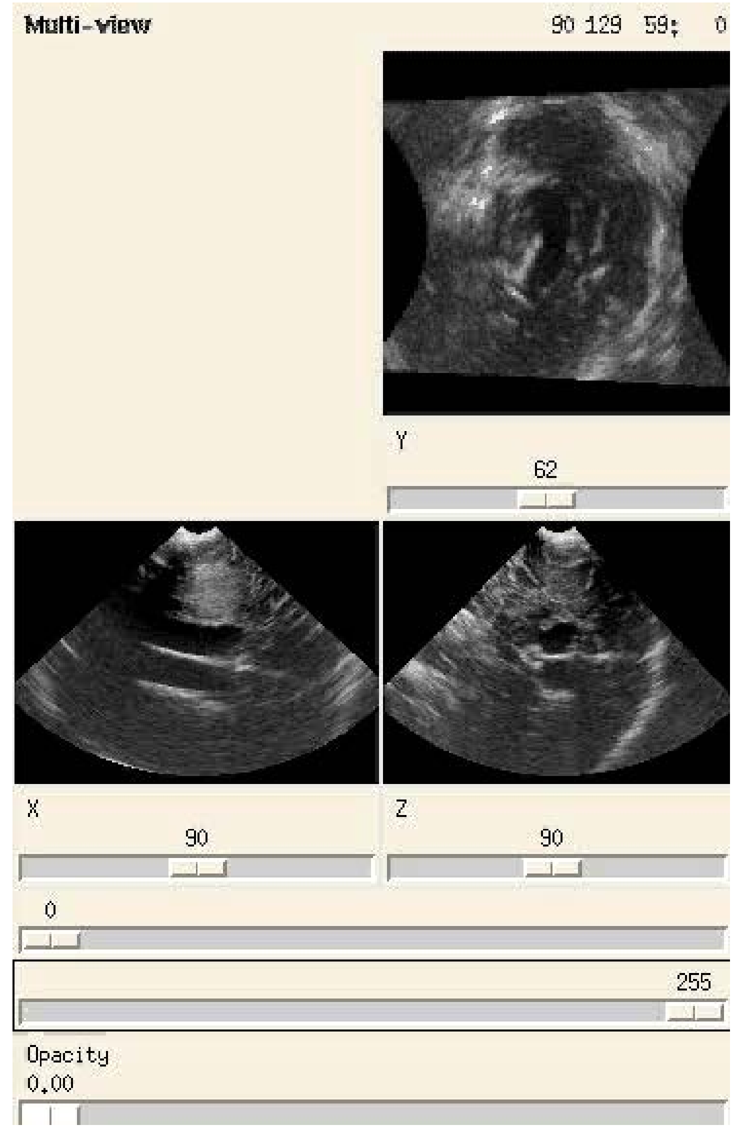
Int. Journal of HPC Apps, 2006]

Derive tests on transformations for accuracy / consistency

Results on per-operative patient images

Data (per-operative US)

- 2 pre-op MR (0.9 x 0.9 x 1.1 mm)
- 3 per-op US (0.63 and 0.95 mm)
- 3 loops



Robustness and precision

	Success	var rot (deg)	var trans (mm)
MI	29%	0.53	0.25
CR	90%	0.45	0.17
BCR	**85%**	**0.39**	**0.11**

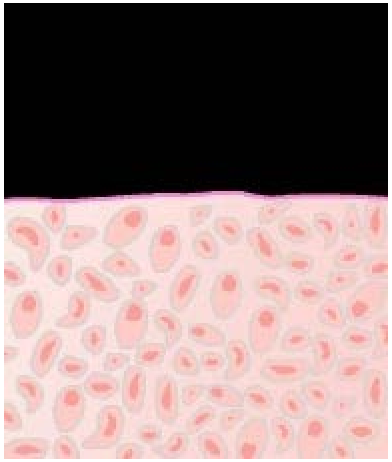
Consistency of BCR

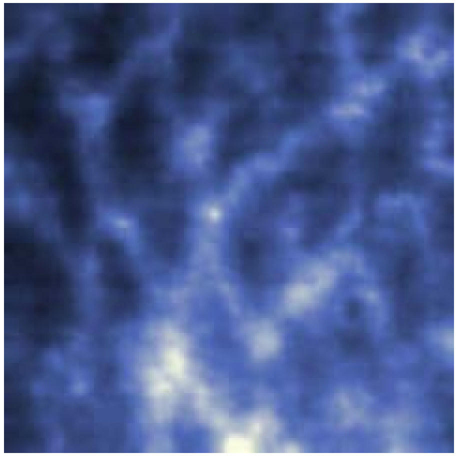
	var rot (deg)	var trans (mm)	var test (mm)
Multiple MR	0.06	0.06	0.10
Loop	2.22	0.82	2.33
MR/US	**1.57**	**0.58**	**1.65**

[Roche et al, TMI 20(10), 2001]
[Pennec et al, Multi-Sensor Image Fusion, Chap. 4, CRC Press, 2005]

Mosaicing of Confocal Microscopic in Vivo Video Sequences.

Cellvizio: Fibered confocal fluorescence imaging





FOV 200x200 µm

Courtesy of Mike Booth, MGH, Boston, MA

FOV 2747x638 µm

[T. Vercauteren et al., MICCAI 2005, T.1, p.753-760]

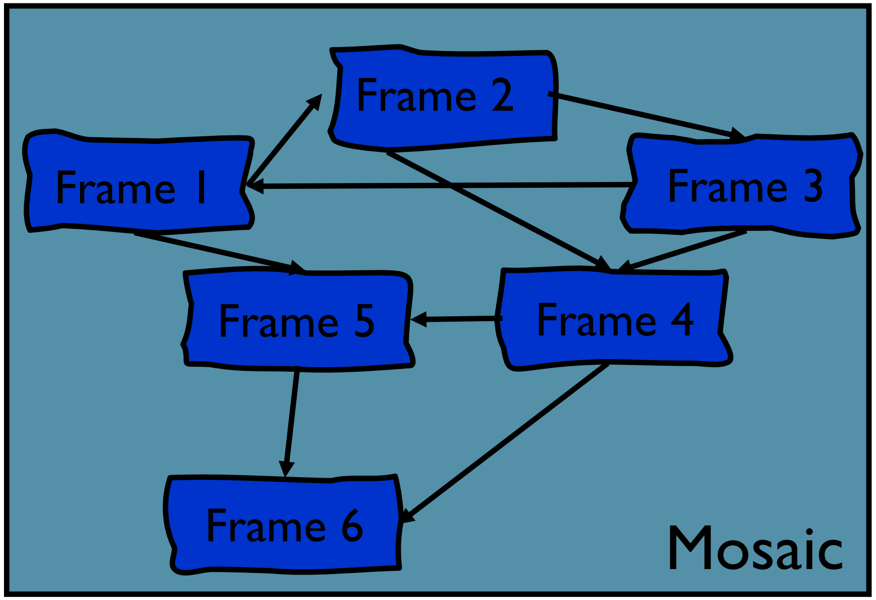
Mosaicing of Confocal Microscopic in Vivo Video Sequences.

Common coordinate system

- **Multiple rigid** registration
- Refine with **non rigid**

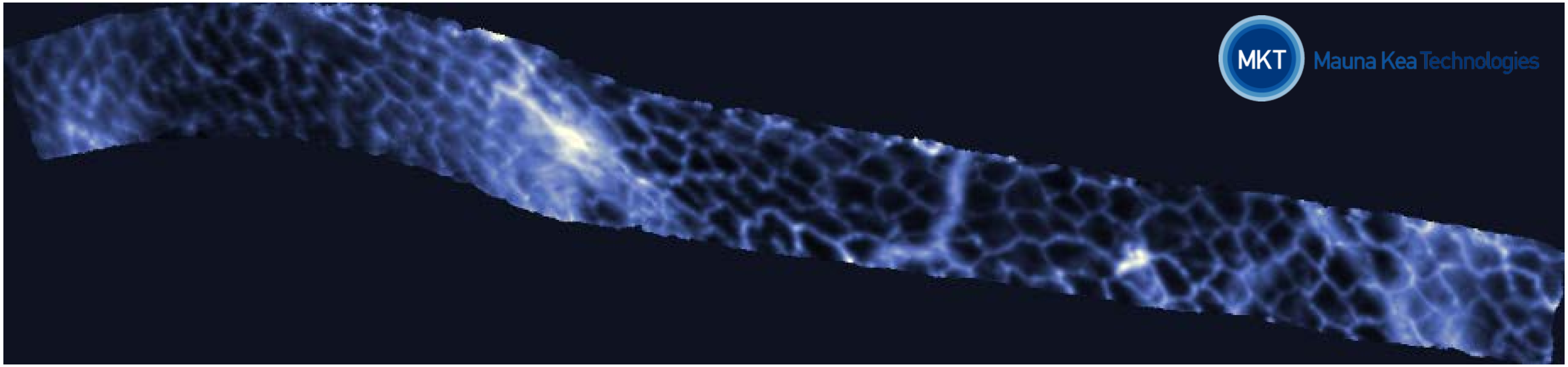
Mosaic image creation

- Interpolation / approximation with **irregular sampling**



Courtesy of Mike Booth, MGH, Boston, MA

FOV 2747x638 μm



[T. Vercauteren et al., MICCAI 2005, T.1, p.753-760]