

Medical Image Analysis



Hervé Delingette

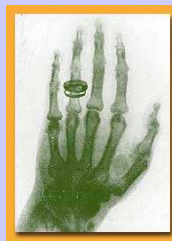
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<http://www.inria.fr/epidaure/personnel/Delingette/>



First Medical Image



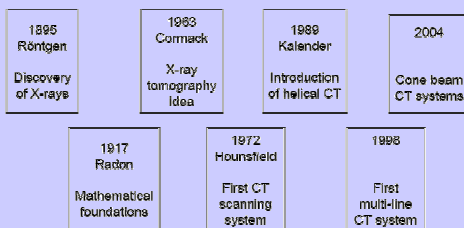
Roentgen, 1895



Development of Computed Tomography

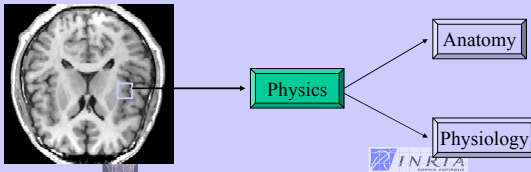


History →

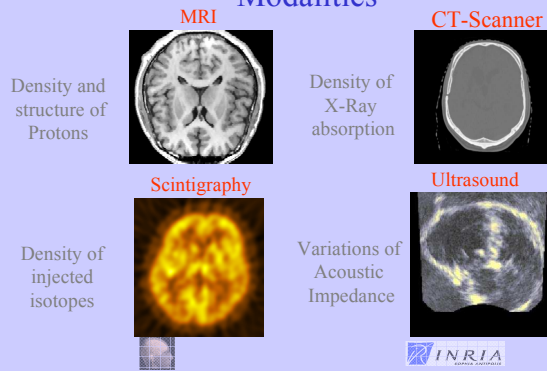


Characteristics of medical images (1)

Intensity values are related to physical tissue characteristics which in turn may relate to a physiological phenomenon

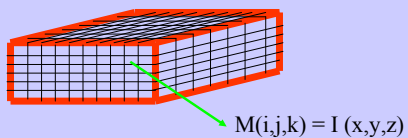


Main Imaging Modalities



Common Structure of 3-D Images

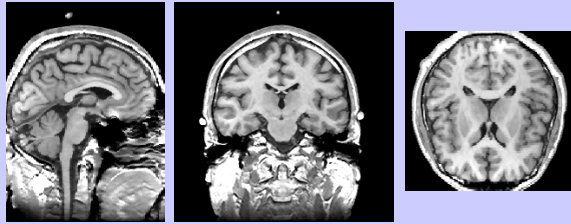
- Voxel Representation



- $I(x,y,z)$ measures physical properties of a volume element centered around (x,y,z) .



Magnetic Resonance Imagery (MRI)



Sagittal

Coronal

Axial

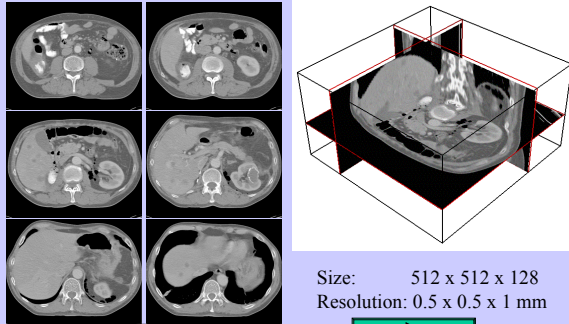
$I(x,y,z)$ measures a function of the density and structure of protons

Millimeter Resolution

16 millions of points



CT-scan (Scanner)



Size: 512 x 512 x 128
Resolution: 0.5 x 0.5 x 1 mm



Other 3-D Modalities

- Functional MRI (fMRI), DT MRI
- Interventional MRI (iMRI)
- MR Angiographies (MRA)
- Spectroscopic MRI
- US Angiographies, Perfusion US,
- Magneto-EncephaloGraphies (MEG)
- Electro-EncephaloGraphies (EEG)



Visual Examination

- Difficult task, mainly qualitative

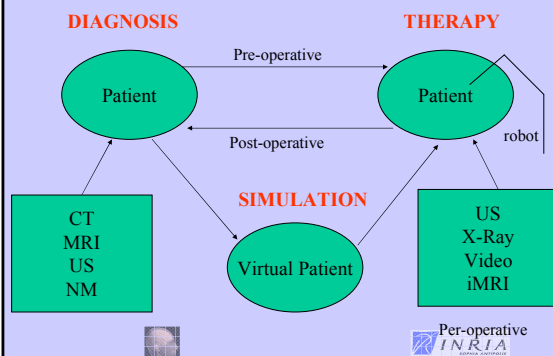


Digital Image Analysis

- To improve diagnosis
 - quantitative and objective measurements
 - Fusion and comparison of images, patients
- To improve therapy
 - planning before
 - control during
 - evaluation after



Intensive Use of Medical Imaging



Digital Image Analysis : Classes of *Generic* Problems

1. Enhancement
2. Visualization
3. Segmentation
4. Compression
5. Registration
6. Statistics
7. Morphometry
8. Motion
9. Simulation
10. Robotics,

...

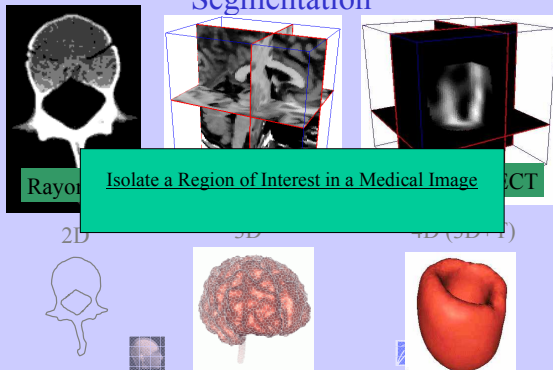


Segmentation

1. Introduction



Image Segmentation



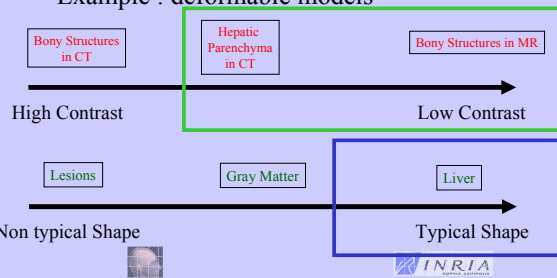
Segmentation Task

- Large number of available algorithms
- Possible classifications :
 - Generic vs task-oriented
 - Bottom-up vs Top-down approaches
 - Boundary vs Region approaches
 - Explicit vs Implicit A priori knowledge
- Validation

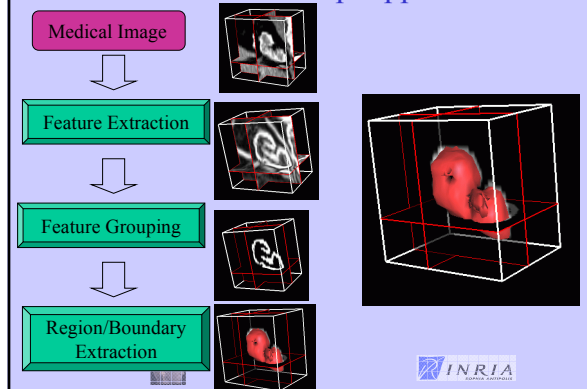


No Universal Segmentation Algorithm

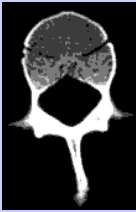
- A segmentation algorithm has a limited range of application
- Example : deformable models




Bottom-up Approach



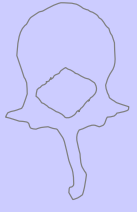
Region vs Boundary Methods





Image



Region-based segmentation



Boundary-based segmentation

Computational vs Explicit A priori knowledge

- A priori knowledge about the structure to segment is the key to enhance robustness
- Computational knowledge : statistical analysis

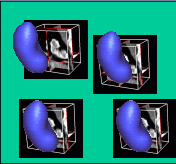


Image + structure Database

➔



Statistical classifier

Neural Networks

Principal Component Analysis


.....

Training

Explicit knowledge

- Explicit knowledge : expert system
 - Define rules of delineation from expert
 - Translate predicate into high/low level image processing
 - Combine rules in a probabilistic framework




Validation of Segmentation Algorithm

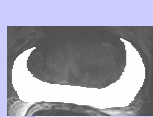
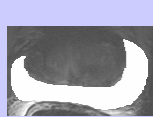
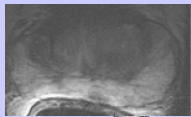
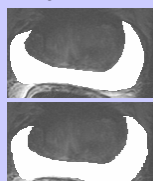
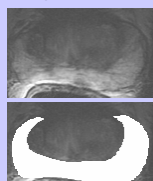
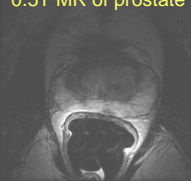
- **Intrinsic Validation** : comparison against
 - Observation of Physical Phantoms
 - Difficult and expensive to build
 - May not be representative of real data
 - Simulated images (MNI Brain Atlas,...)
 - Difficult to simulate artefacts
 - Segmentation of experts
 - Large inter and intra variability of segmentation across experts
 - May not be representation of population variability



How to judge segmentations of the peripheral zone?

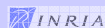
0.5T MR of prostate

Peripheral zone and segmentations



Validation of Segmentation Algorithm (2)

- **Extrinsic Validation** : comparison against other segmentation algorithms
 - Only possibility when no ground truth exists (Inter-patient registration of images) or when it not available
 - Estimate consistency, repeatability and size of convergence basin



Two Segmentation Methods

Focus on 2 segmentation methods :

- **Bottom-up** : Thresholding /Classification
- **Top-down** : 3D and 4D deformable models

	Thresholding/Classification	Deformable Models	Markov Random Field
Shape Information	None	Important	local
Intensity Information	Essential	Important	Important
Boundary/ Region	Region	Boundary	Region



Segmentation

2. Thresholding and Classification

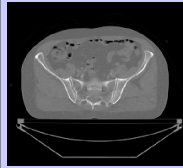


Thresholding and classification

- Basic idea :
a structure is uniquely characterized by its intensity values in the image
- ➡ Valid for highly contrasted structures
- Basic thresholding algorithm :
 - Thresholding between two grey-levels (windowing)
 - Mathematical morphology operations [Serra82]
 - Erosion and Dilation
 - Closure and Opening
 - Connected components extraction



Thresholding Example (1)



Abdominal CT scan Image

Interactive thresholding



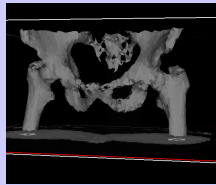
Thresholded Image

Thresholding Example (2)



After mathematical
morphology operations

Isosurface



Isosurfacing (Marching Cube)
+ decimation algorithm



Thresholding + mathematical morphology + connected components



Limitation of thresholding

Thresholding :

- Choice of threshold can be computed from grey-level histogram
- Does not assume any spatial correlation of voxel intensity
- Does not take into account the effect of **partial volume effect (PVE)**



Use of classification methods

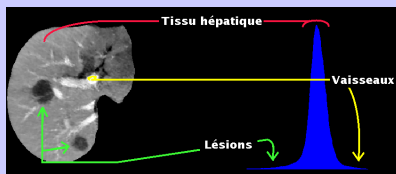


Classification Method

- It is often not valid to consider that a voxel belongs to a single tissue type.
- It is therefore reasonable to estimate that each voxel \mathbf{x} has a probability $p_k(\mathbf{x})$ of belonging to a tissue class k ($1 \leq k \leq K$)

$$\sum_{k=1}^K p_k(\mathbf{x}) = 1$$

CT scan image of the Liver with 3 tissue classes



Classification Method (2)

- Various classification methods :
 - Fuzzy c-means
 - General classification approach
 - Non parametric
 - EM Algorithm
 - Parametric approach (mixture of Gaussians)
 - Can take into account bias field
 - Curve fitting
 - Use a hierarchical approach
 - Non-linear optimization



Brain Tissue Classification

- Typical application : use MR cerebral image

Cerebro-spinal fluid Grey matter White matter

Courtesy of D. Vandermeulen

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Optimisation (3)

- Use the EM algorithm [Dempster77,Wells94] :

Expectation-Maximisation

classification $p_k(x)$

distribution estimation

Courtesy of D. Vandermeulen

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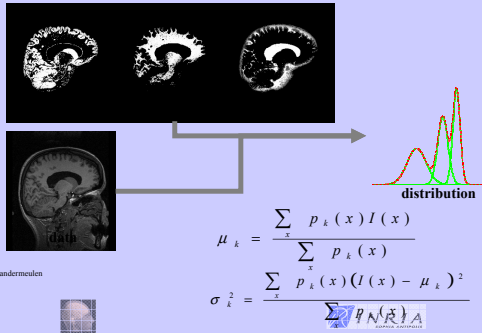
Stage 1: classification

$$p_k(x) = \frac{\phi_k(I(x))}{\sum_k \phi_k(I(x))}$$

Courtesy of D. Vandermeulen

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Stage 2: Distribution Estimation

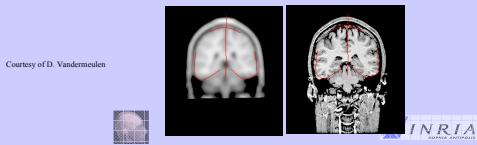


Initialisation issue

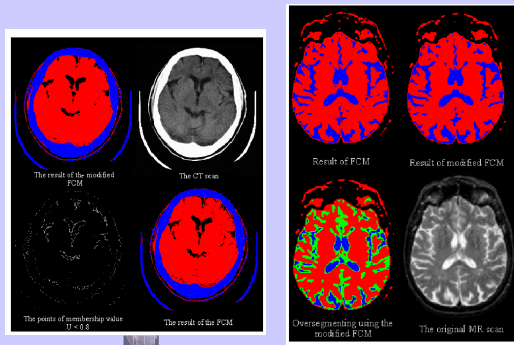
Use a computed digital atlas with $p_k(x)$

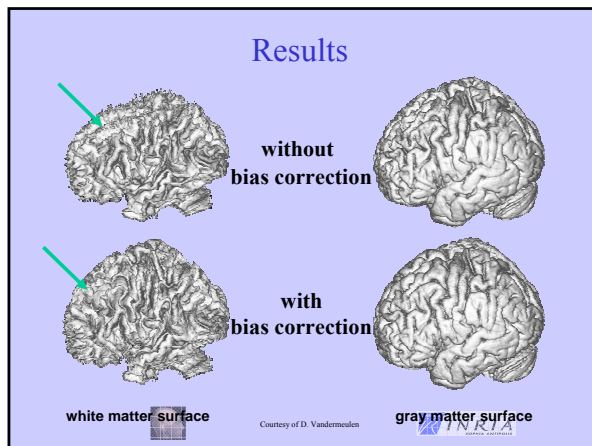


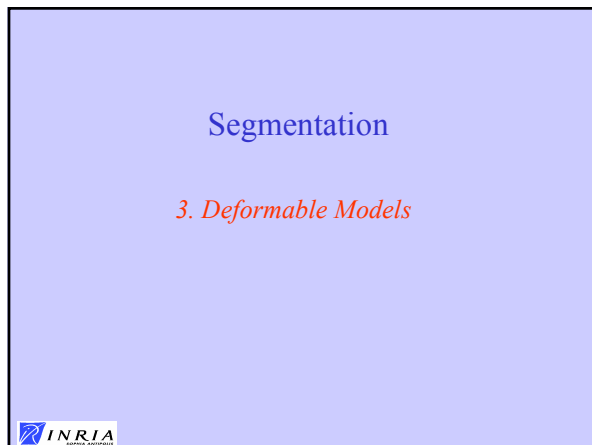
Affine registration between the image and atlas to initialize $p_k(x)$

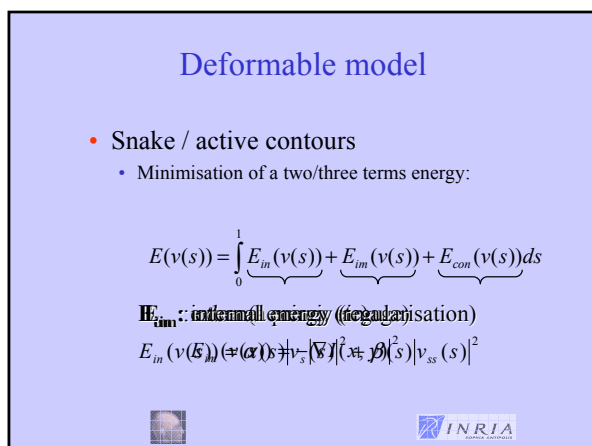


Fuzzy C-means (Exemple)









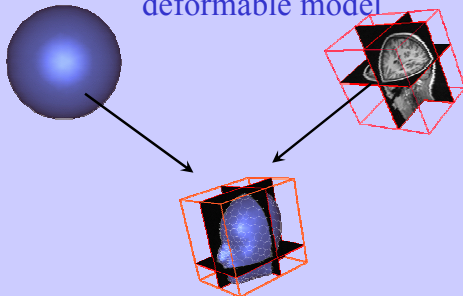
Deformable Model Segmentation

- A deformable model is a container of prior knowledge about the **Shape** and **Appearance** of anatomical structures in medical images
- Two levels of prior knowledge :

	Weak Prior	StrongPrior
Shape	C1 or C2 continuity constraint Initialize with generic shape (sphere, ...)	Shape continuity constraint Initialize with mean shape
Appearance	Use gradient, edge or region information	Use intensity profile or block matching information



Weak prior deformable model



- Valid for highly contrasted structures

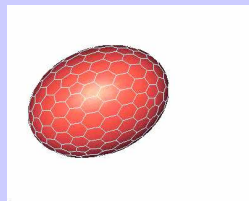
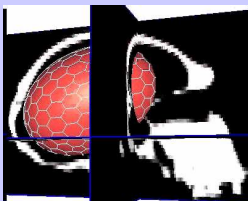


- May require user interaction



Segmentation: endocranium

CT scan image, Bony structures



Time of convergence : 13,8 s

model: 1169 cm³
mold: 1150 cm³



Strong prior deformable model

- Valid a given structure and a given image modality
- More robust except with abnormal shapes

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Segmentation: MRI

Deformed 4D model

Model intersection with image

Deformable Model Geometry (3)

```

graph TD
    DM([Deformable Models]) --> CM[/Continuous Models/]
    DM --> DisM[/Discrete Models/]
    CM --> ER[/Explicit Representation/]
    CM --> IR[/Implicit Representation/]
    ER --> MD[Modal Decomposition]
    ER --> DT[Deformable Templates]
    MD --> FE[Finite-Elements]
    IR --> LS[Level-Sets]
    LS --> AC[Algebraic Curves]
    DisM --> DMesh[/Discrete Meshes/]
    DisM --> PS[/Particle Systems/]
    DMesh --> SM[Simplex Mesh]
    PS --> SMM[Spring-Mass Models]
  
```

[Montagnat2001]

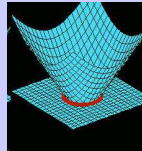
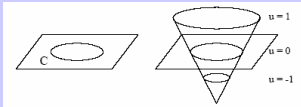
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Deformable models

- Level-sets

- Curve/Surface C (in $\mathbb{R}^2/\mathbb{R}^3$) that corresponds to an iso-level of a surface/hypersurface (in $\mathbb{R}^3/\mathbb{R}^4$)

$$C(t) = \{(x, y) \mid u(x, y, t) = 0\} \quad u_t + F |\nabla u| = 0$$



- Implicit representation



Main difficulties in segmentation algorithms

- Ill-posed problem
 - Boundaries between structures may not be seen on images
 - Strong variability between experts for validation
- Most algorithms are dependent on the acquisition protocole and image modality
- Robustness required in the presence of pathologies



Use of Image Segmentation Software

- Segmentation software is not widely available in current medical practice :
 - Diagnosis (low demand):
 - Currently almost no quantitative analysis is performed even in oncology
 - Therapy planning (high demand)
 - Bottleneck stage in radiotherapy or surgery planning



Perspectives (1)

- Current trends in medical imaging
 - Number of image modalities is exploding
 - Image resolution is increasing
 - Image quality is improving
 - IT is invading hospitals (PACS)
 - More patients less doctors



Perspectives (2)

- Applications of segmentation :
 - Diagnosis
 - demand for very fast and automated algorithms with degree of confidence
 - Planning - Prediction -Prevention
 - demand for accurate but potentially not fully automated algorithms combined with high quality meshing
 - Clinical Research
 - demand for automated and accurate algorithm for use with large database (grid computing)



Perspectives (3)

- Segmentation techniques is more and more split between :
 - Registration techniques :
 - registration with a anatomical/physical/physiological model
 - registration with a set of images (data fusion)
 - Low-level techniques :
 - anisotropic filtering, watershed, mathematical morphology



Need to define a unifying framework

Registration

1. Introduction



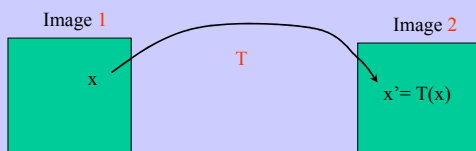
Registration

- A central problem
- Survey by Maintz and Viergever in *Medical Image Analysis journal (MedIA)* (300 references)
[vol 2, No 1, pages 1-36, 1998]



Objective of Registration

- Find the best geometric transformation T which superimposes homologous points between two 3-D images



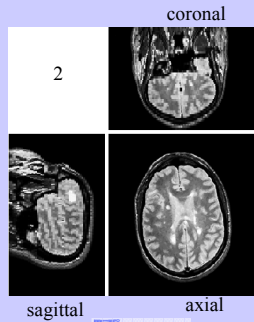
Main Applications

- Temporal Evolution
- Fusion of multimodal images
- Inter-patients comparaison
- Atlas Superposition

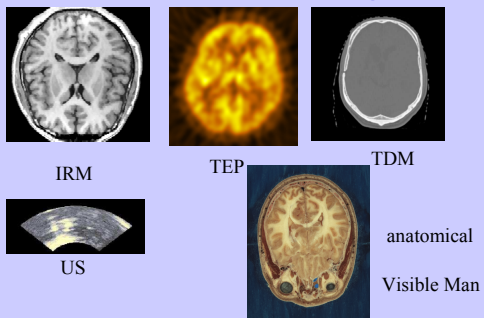


Temporal Evolution

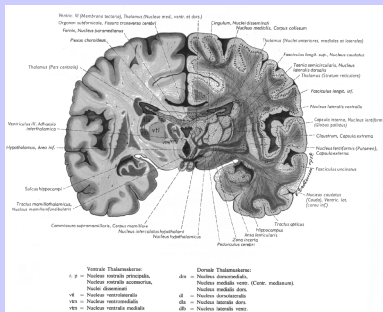
- Precise comparison of images of a given patient, taken at different times.
- One must suppress the apparent motion of the patient.



Fusion of Multimodal Images



Atlas Superposition



Classes of Problems

- Mono- or multimodal images
- Intra- or Inter-patients
- Rigid or Deformable





Classes of Problems vs. Applications

- Temporal Evolution
- Fusion multimodal images
- Inter-patients comparaison
- Atlas Superposition
- Intra Patient - Monomodal
- Intra Patient - Multimodal
- Inter Patients - Monomodal
- Inter Patients - Multimodal
- Intra Patient : Rigid or Non-Rigid
- Inter Patients : Non-Rigid



Classes of Solutions

- Geometric Registration (or feature-based)
- Iconic Registration (or intensity-based)





Registration

2. Geometric Approaches



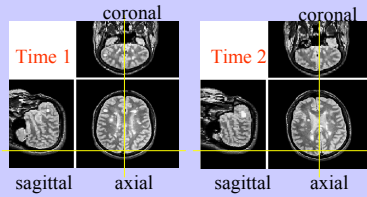
Principle of Geometric
(Feature-Based) Approaches

- Extract geometric landmarks
- Find correspondences and best transformation T



Temporal Evolution (To Start!)

- Rigid, Mono-patient, Monomodal



Choosing a Class of Transformations

- In the case of brain images of the same patient, one can restrict the geometric transformation to the group of **rigid** transformations (3-D displacements)
- Combination of Rotation and Translation (6 parameters)

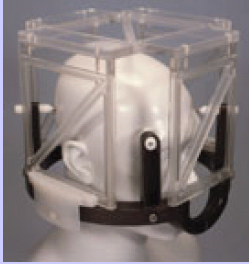


Issues

- Not a one to one mapping between images (occlusions)
- For an accurate solution, one must find explicitly correspondences (matches) between images
- High computational complexity



Artificial Landmarks



- Stereotactic Frame
 - Invasive
 - External markers
 - Brain motion
 - Limited period



Anatomical Landmarks

- Search for **geometric invariants** to characterize a limited number of singular points and lines **on anatomical surfaces**

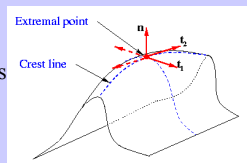


- Generalization of edges and vertices on differentiable surfaces (Monga-Ayache-Sander, Thirion)

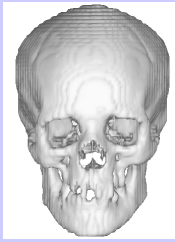


Crest Lines and Extremal Points

- Defined from differential properties of the anatomical surfaces;
- Correspond to extremal values of one or two principal curvatures



Stage 1: Anatomical Surfaces



$$f(x, y, z) = I$$

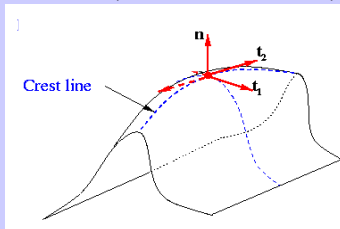
$$\nabla^2 f(x, y, z) = 0$$

- Iso-surfaces defined by an implicit equation
- Zero-crossings of the Laplacian of the intensity



Stage 2: Crest Lines

- Maximum principal curvature (in absolute value) must be extremal in the associated principal direction (not defined at umbilics)

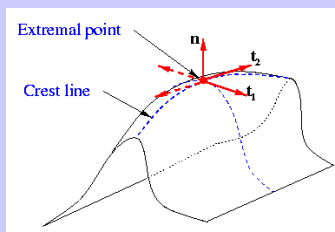


$$e_1 = \nabla k_1, t_1 = 0$$



Stage 3: Extremal Points

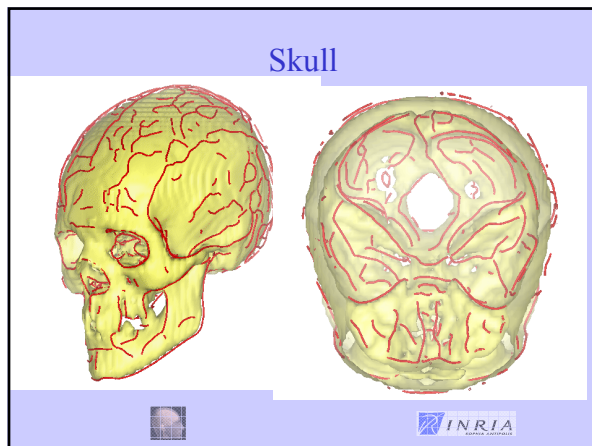
- Second principal curvature is also extremal in the second principal direction.

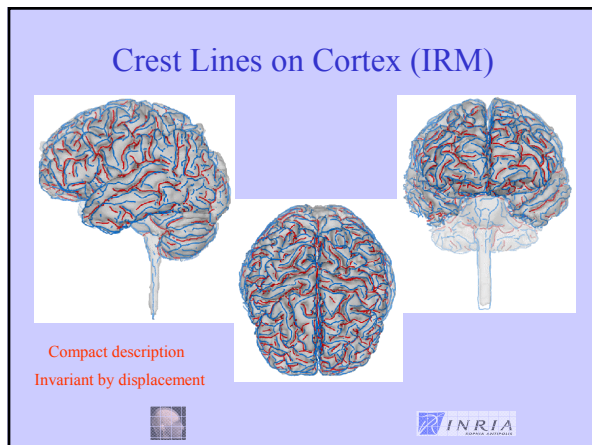


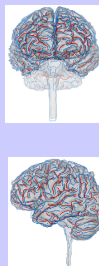
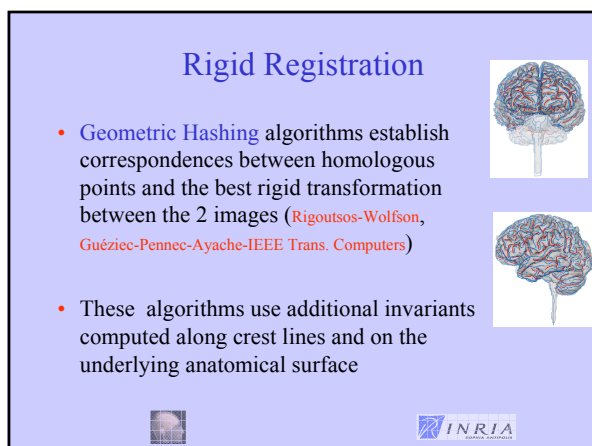
$$e_1 = \nabla k_1, t_1 = 0$$

$$e_2 = \nabla k_2, t_2 = 0$$



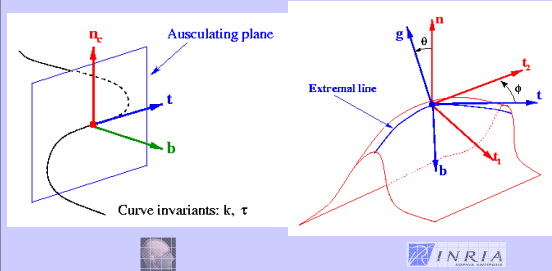




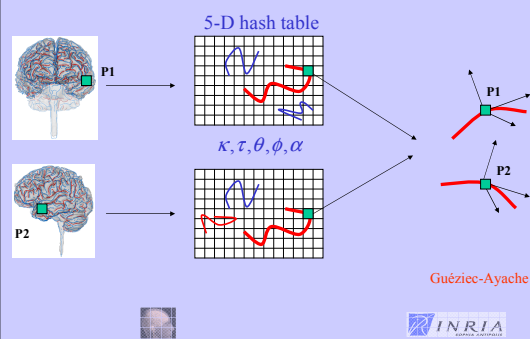


Geometric Invariants on Crest Lines

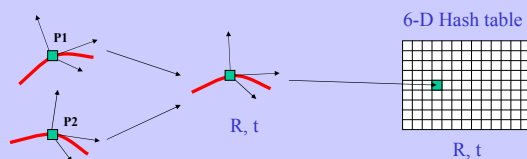
- Curvature, Torsion, and angles between Frénet frame and local surface frame



Registration by Geometric Hashing



Geometric Hashing (2)

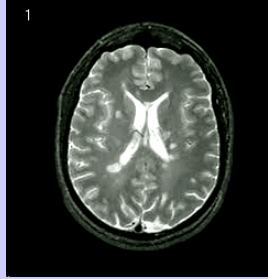


- The sought transformation is the most represented one
- Robust to occlusions and small local deformations
- Fully automatic, low computational complexity, high accuracy

Application of Rigid Registration to Multiple Sclerosis Evolution

24 3-D images before registration

- Same patient followed during one year

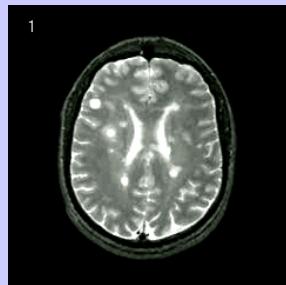


Brigham & Women's
Hospital
Harvard Medical
School



After Rigid Registration (24 times)

24 3-D images after rigid registration

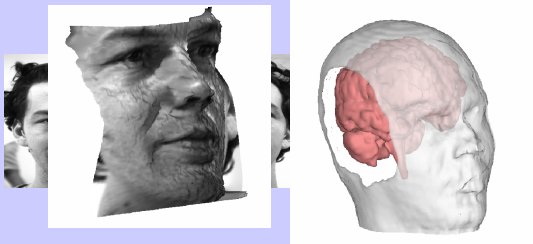


J.P. Thirion
IJCV'98

Thanks to rigid
registration, one
can follow the
temporal
evolution in any
arbitrary 2-D
plane



Geometric Registration of Surfaces



Collaboration Epidaure-Robotvis

Feldmar-Devernay



Augmented Reality (Fiction)



Feldmar-Devernay



Augmented Reality (Real)

- Active Stereovision



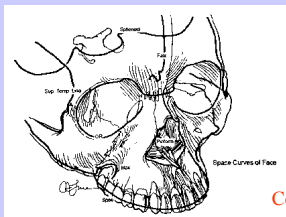
Brigham & Women's Hospital- MIT

E. Grimson et al.



Non Rigid Geometric Registration

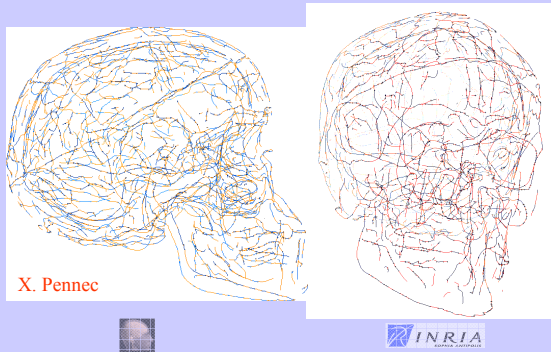
- Some crest lines are anatomical invariants



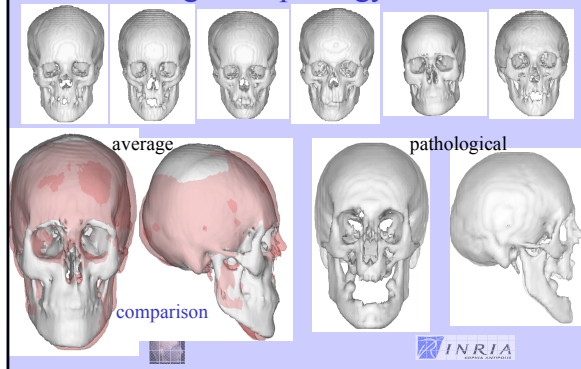
Court Cutting et al.



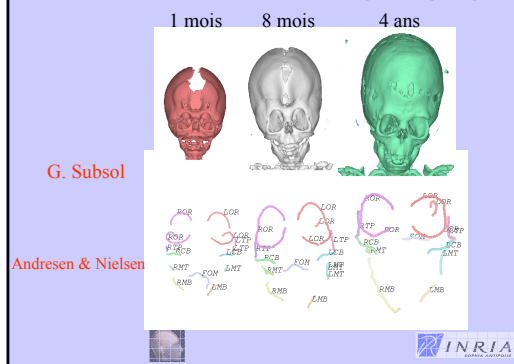
Skull (Scanner)



Average Morphology of Skull G. Subsol

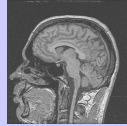


Skull Growth trough Aging



Geometric Registration

- Can be applied to surface registration in augmented reality problems
- Fuse **per-operative** images with **pre-operative** images



Limitations of Geometric Registration

- Previous geometric invariants not valid in general to compare **multimodal** images, or arbitrary homologous structures between **different patients** (e.g. brain)
- Problems with **low-resolution** or **noisy** images.
- Distribution of geometric invariants might be too sparse to handle **local deformations**



Registration

3. Iconic Approaches



Principle of **Iconic** (Intensity-Based) Registration

- Use all voxels and their **intensity** to guide the registration process
- Energy minimization between registered images



Energy Minimization

- Energy with **two** components:

$$W(T) = \iiint f(I, J \circ T)^2 dx dy dz + W_d(T)$$

- f : Measure of intensity **similarity** between homologous points;
- W_d : Measure of **deformation** to insure a regular solution (Tikhonov, linear elasticity, viscous fluid, etc.). **Bajcsy, Christensen, Bro-Nielsen, Thirion, Pennec, Cachier, Ourselin....**



Minimization Algorithms

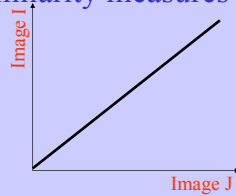
- Non Convex Energy
- Convergence towards a Local Minimum
- Important Stages:
 - Good initialization (rigid registration)
 - Multi-scale analysis
 - Hierarchy of deformations
 - similitude, affine, polynomial, free-form, etc.



Classification of similarity measures

- Assumed relationship

Identity



- Adapted measures

Sum of Squared Differences $SSD(I, J) = \sum_i (I_i - J_i)^2$

Sum of Absolute Differences

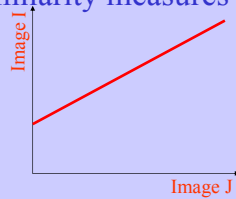
Measures based on image difference (Buzug et al, 1997)



Classification of similarity measures

- Assumed relationship

Affine



- Adapted measures

Correlation Coefficient

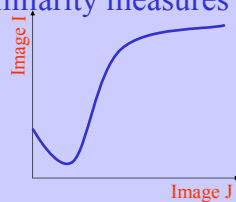
$$\rho(I, J) = \frac{\text{cov}(I, J)}{\sqrt{\text{var}(I) \text{var}(J)}}$$



Classification of similarity measures

- Assumed relationship

Functional



- Adapted measures

Woods criterion (Woods et al, 1993)

Robust Woods criterion (Nikou et al, 1997)

Correlation Ratio (Roche et al, 1998)

$$\eta^2(I, J) = 1 - \frac{\text{var}(I - \hat{\phi}(J))}{\text{var}(I)}$$



Classification of similarity measures

- Assumed relationship

Statistical

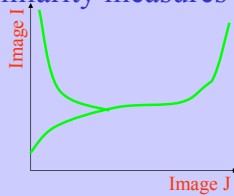
- Adapted measures

Joint Entropy (Hill et al., 94)

Mutual Information (Viola & Wells, 1997; Maes et al, 1997)

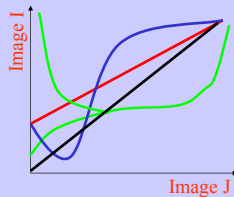
Normalised Mutual Information (Studholme, 1998)

$$MI(I, J) = H(I) - H(I / J) = \sum_i \sum_j p(i, j) \log \frac{p(i, j)}{p(i)p(j)}$$



Measure of Intensity Similarity

- sum of squared differences
- correlation coefficient
- correlation ratio
- mutual information



A common framework ?



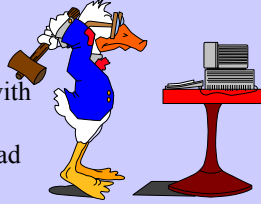
A General Framework

- [Roche-Malandain-Ayache-Prima, MICCAI '99, pp.555-566]
- A Dependence Model between images and a Maximum Likelihood approach
- Following the pioneering work of (Costa et al, 1993), (Viola, 1995), (Leventon & Grimson, 1998), (Bansal et al, 1998)



Choosing the right similarity measure

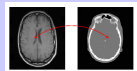
- Requires a good knowledge of the physics of image formation
- Choosing the model with the lowest number of parameters tends to lead to higher robustness



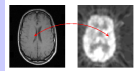
Experimental Comparison

Correlation Ratio vs. Mutual information
(-) simplistic model (+) more realistic model
(+) few parameters (-) many parameters

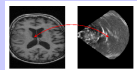
- Accuracy study
CT / MR rigid registration



PET / MR rigid registration



- Robustness study
Ultrasound / MR rigid registration



Some Applications of Iconic Registration

1. Detection and Measure of Lesions
2. Inter-patient comparisons
3. Superposition of an Atlas
4. Measure of Asymmetry
5. Superposition MRI-Ultrasounds
6. Stress-Rest Comparisons



1. Detection and Measure of Multiple Sclerosis Lesions

Time 1 Time 2

J.P Thirion
Medical Image Analysis
2:3, 1998

INRIA

Deformation Field

Time 1 Time 2

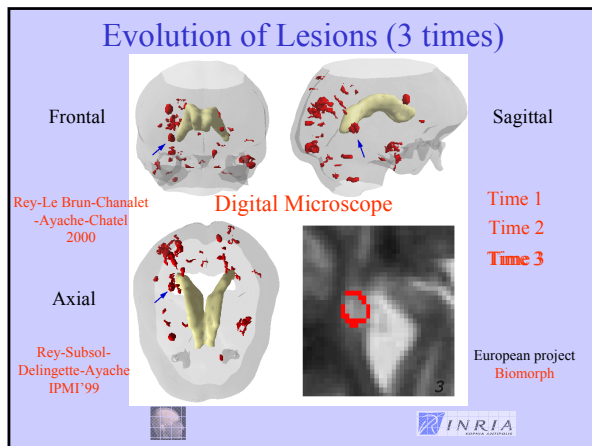
INRIA

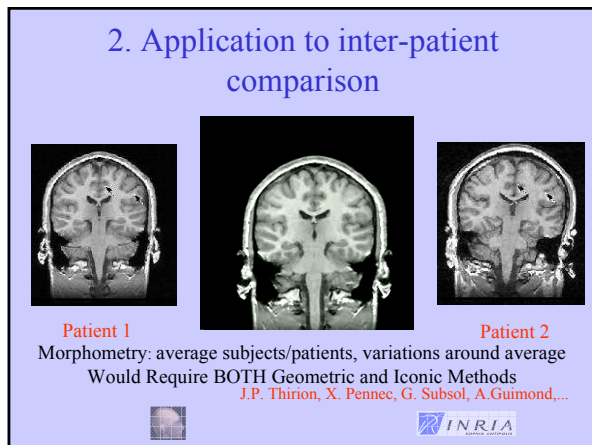
Analysis of deformations

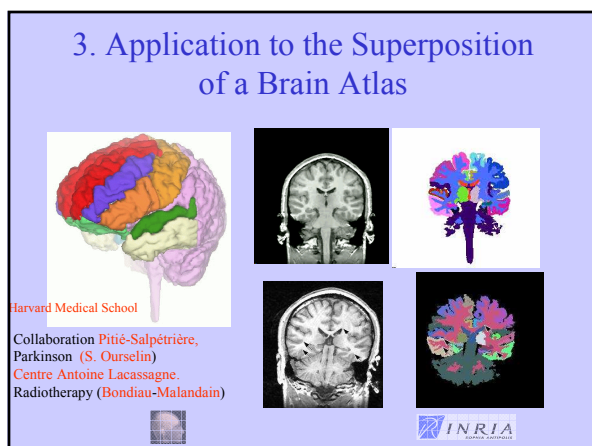
- Automatic extraction of regions with an **apparent variation of volume**. (Jacobian operator)
- Segmentation of evolving lesions
- Robust to small errors of rigid registration

D. Rey, G. Subsol, H. Delingette, N. Ayache
IPMI'99

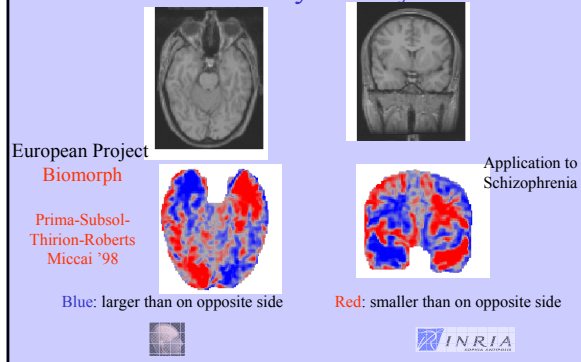
INRIA

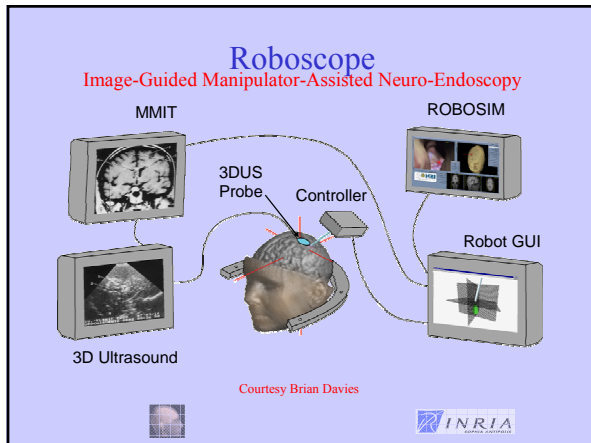




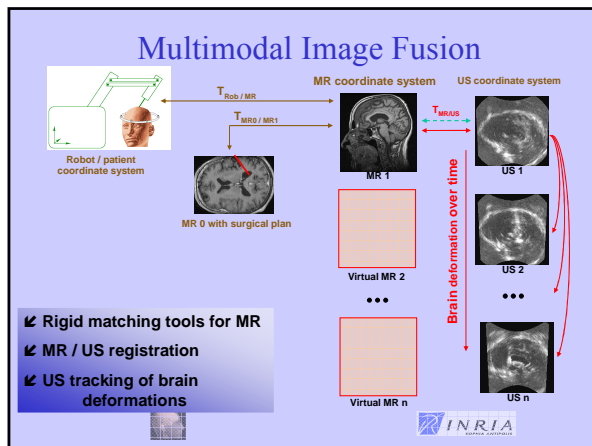


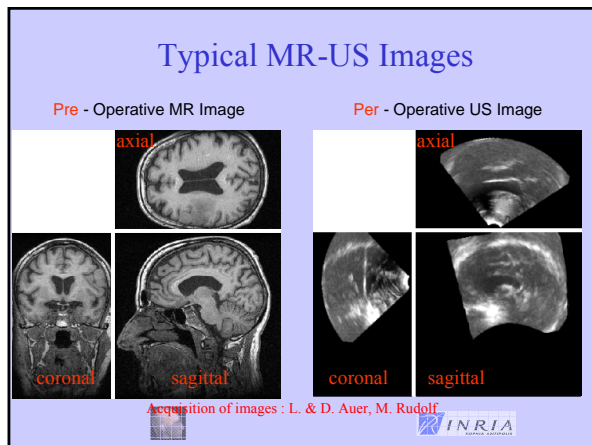
4. Quantitative Measure of Brain Asymmetry

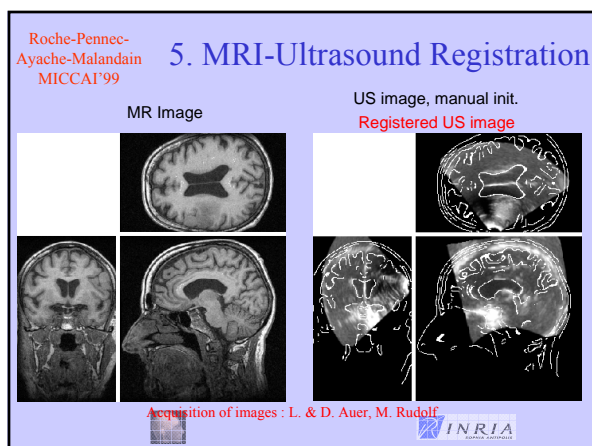




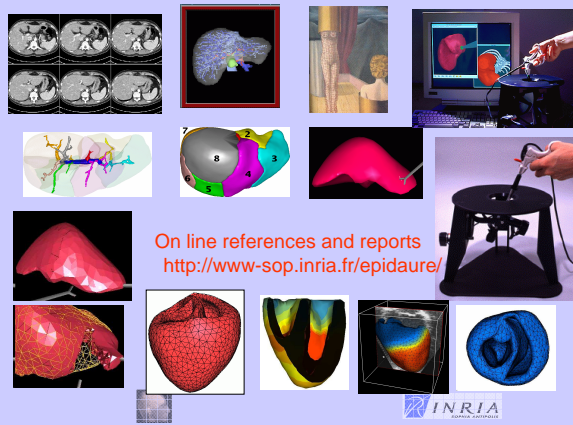








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In Vivo Microscopic Confocal Imaging

Source: Mauna Kea Technologies

Reflectance imaging

Fluorescence imaging

160 microns

- Confocal flexible microscope
- High resolution optical sections of tissues

The endoscopy "pill"

Source: Given Imaging

INRIA

Images obtained when passing through the bowel (Given Imaging System)

Credits

- **Members and Collaborators of the Epidaure group:** J. Bertot, S. Cotin, P. Cachier, J. Declercq, H. Delingette, J. Feldmar, A. Guimond, K. Krissian, J.C. Lombardo, G. Malandain, J. Montagnat, S. Ourselin, F. Pez , G. Picinbono, S. Prima, X. Pennec, D. Rey, A. Roche, G. Subsol, L. Soler, J.P. Thirion,...
- **Medical and Academic Partners**
- **Gilles Kahn**



Conclusion

- Digital Image Processing increases potential use of medical images in medicine, as **microscope** in 17th century.
- Several connected application domains:
Pharmacy, biology, neuroscience, paleontology, anthropology, geology, non destructive control, etc.