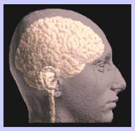
Digital Processing of Medical Images



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First Medical Image

Roentgen, 1895

Development of Computed Tomography

History

1895
Röntgen
Discovery of X-rays

1917
Radon
Mathematical foundations

1963
Cormack
X-ray tomography idea

1972
Hounsfield
First CT scanning system

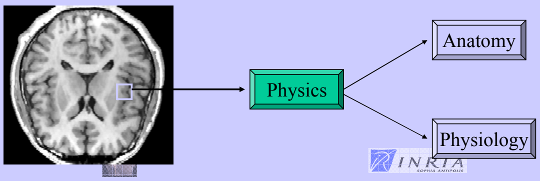
1989
Kalender
Introduction of helical CT

1998
First multi-line CT system

2004
Cone beam CT systems

Characteristics of medical images (1)

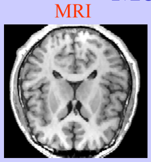
Intensity values are related to physical tissue characteristics which in turn may relate to a physiological phenomenon



Main Imaging Modalities

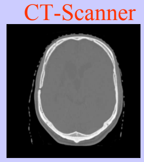
MRI

Density and structure of Protons



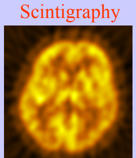
CT-Scanner

Density of X-Ray absorption



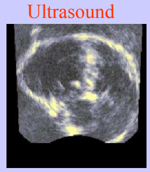
Scintigraphy

Density of injected isotopes



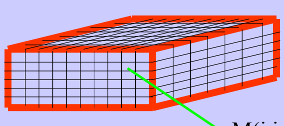
Ultrasound

Variations of Acoustic Impedance



Common Structure of 3-D Images

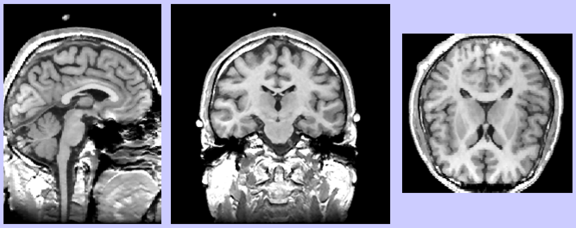
- Voxel Representation



M(i,j,k) = I (x,y,z)

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

Magnetic Resonance Imagery (MRI)

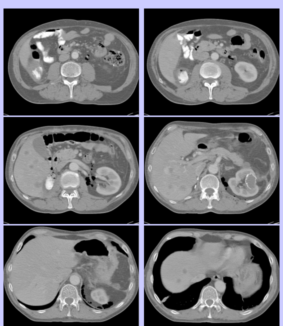


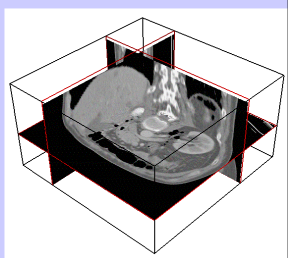
Sagittal Coronal Axial

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)

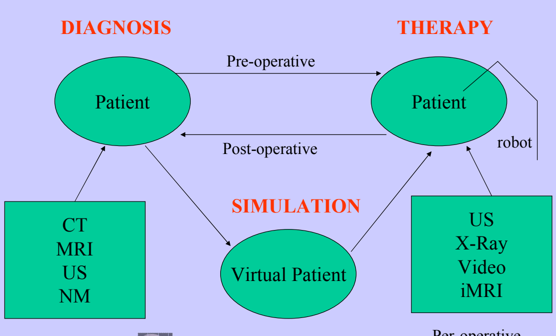
Visual Examination

- 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

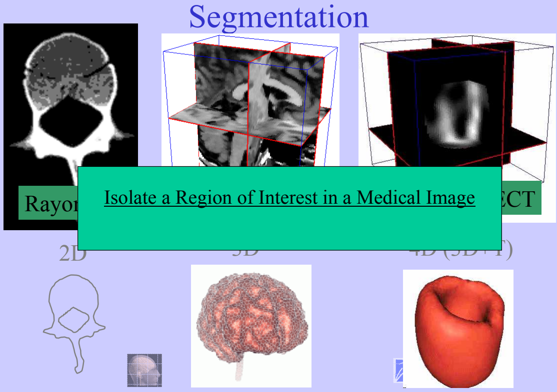
1. Enhancement
2. Visualization
3. Segmentation
4. Compression
5. Registration
6. Statistics
7. Morphometry
8. Motion
9. Simulation
10. Robotics,

...

Segmentation

1. Introduction

Image Segmentation



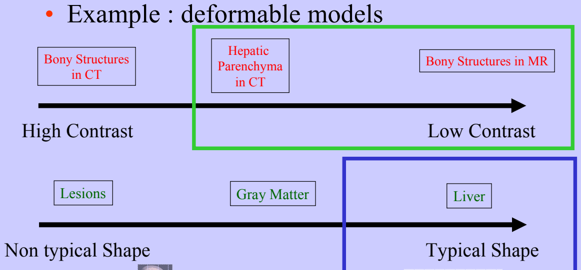
Isolate a Region of Interest in a Medical Image

Segmentation Task

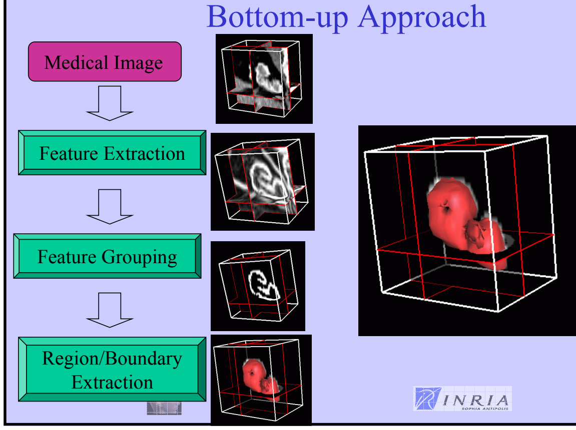
- Large number of available algorithms
- Possible classifications :
  - Generic vs task-oriented
  - Bottom-up vs Top-down approaches
  - Boundary vs Region approaches
  - Explicit vs Implicit A priori knowledge
- Validation

No Universal Segmentation Algorithm

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



Bottom-up Approach



Region vs Boundary Methods

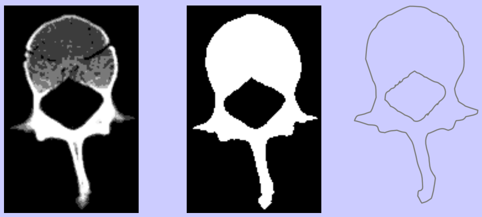


Image | Region-based segmentation | Boundary-based segmentation

Computational vs Explicit A priori knowledge

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

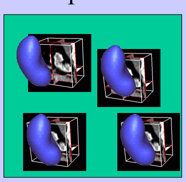


Image + structure Database

Statistical classifier

Neural Networks

Principal Component Analysis

…..

Training

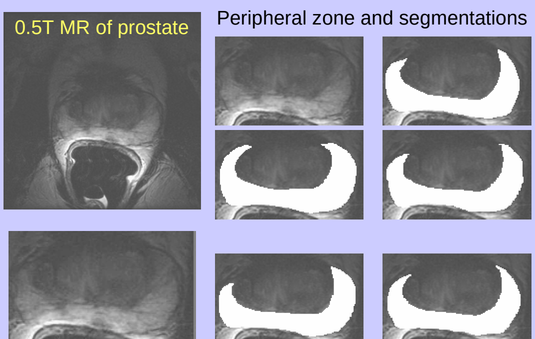
Explicit knowledge

- 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?



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

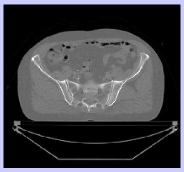
- Basic idea :

  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)



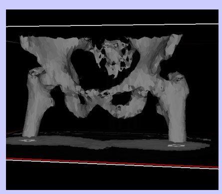
Interactive thresholding

Abdominal CT scan Image

Thresholded Image

Thresholding Example (2)

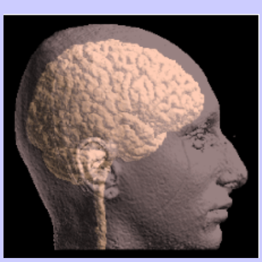
Isosurface



After mathematical morphology operations

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)

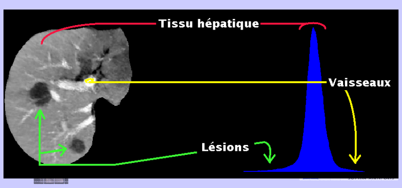
→ Use of classification methods

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 $\boldsymbol{x}$ has a probability $p_k(\boldsymbol{x})$ of belonging to a tissue class k $(1 \leq k \leq K)$

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

CT scan image of the Liver with 3 tissue classes

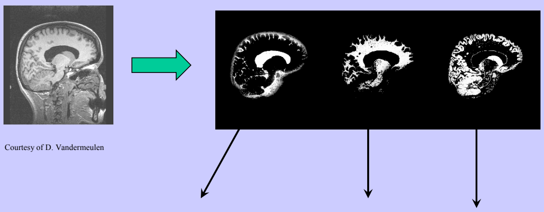


Classification Method (2)

- 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

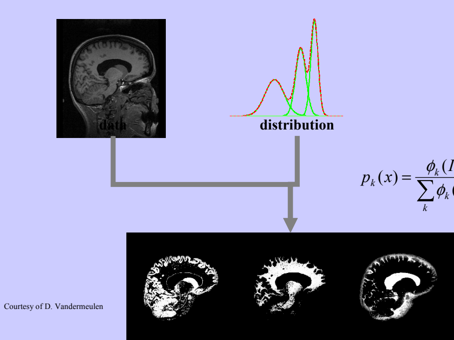


Optimisation (3)

- Use the EM algorithm [Dempster77,Wells94] :

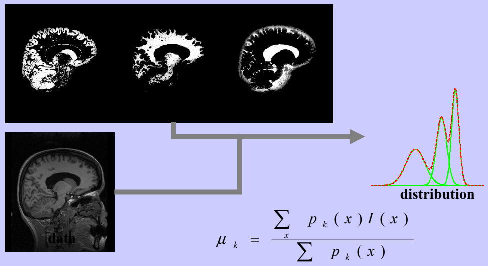
Expectation-Maximisation

Stage 1: classification



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

Stage 2: Distribution Estimation



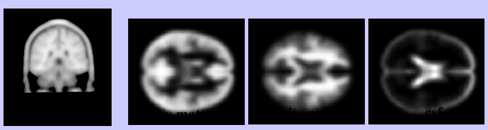
$$\mu_k = \frac{\sum_x p_k(x) I(x)}{\sum_x p_k(x)}$$

$$\sigma_k^2 = \frac{\sum_x p_k(x)\left(I(x) - \mu_k\right)^2}{\sum_x p_k(x)}$$

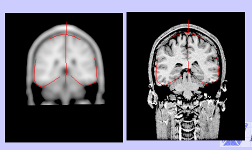
Courtesy of D. Vandermeulen

Initialisation issue

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

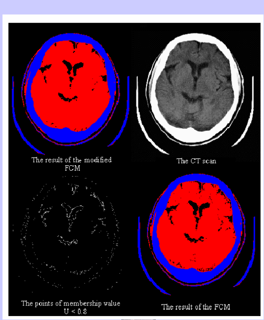


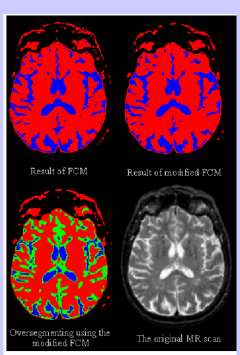
Affine registration between the image and atlas to initialize $p_k(x)$



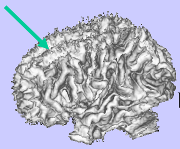
Courtesy of D. Vandermeulen

Fuzzy C-means (Exemple)

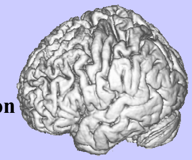


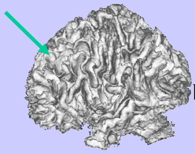


Results

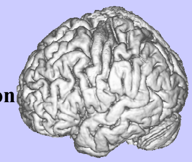


without
bias correction





with
bias correction



white matter surface

Courtesy of D. Vandermeulen

gray matter surface

Segmentation

3. Deformable Models

Deformable model

- Snake / active contours
  - Minimisation of a two/three terms energy:

$$E(v(s)) = \int_0^1 \underbrace{E_{in}(v(s))} + \underbrace{E_{im}(v(s))} + \underbrace{E_{con}(v(s))} ds$$

E_{in} : internal energy (regularisation)

$$E_{in}(v(s)) = \alpha(s)|v_s(s)|^2 + \beta(s)|v_{ss}(s)|^2$$

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

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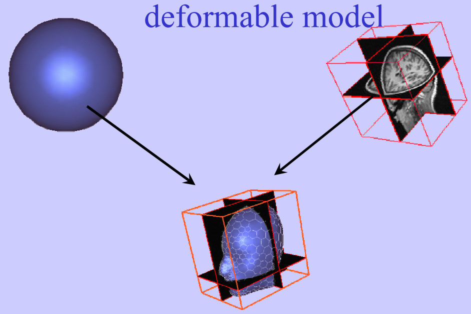
Weak prior deformable model



•Valid for highly contrasted structrures

•May require user interaction

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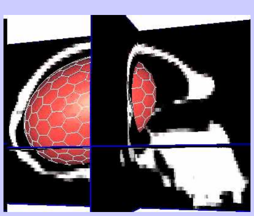
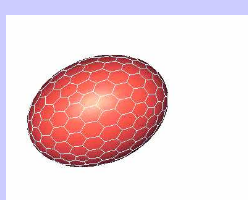
Segmentation: endocranium

CT scan image, Bony structures



Time of convergence : 13,8 s



model: 1169 cm^3
mold: 1150 cm^3

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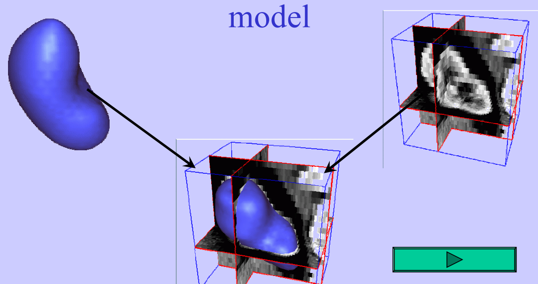
Strong prior deformable model

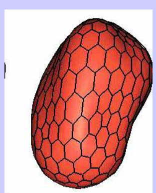


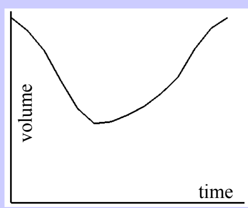
•Valid a given structure and a given image modality

•More robust except with abnormal shapes

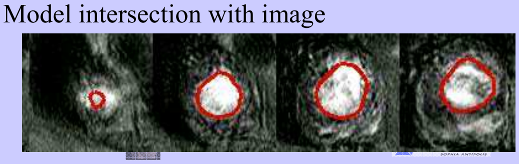
Segmentation: MRI

Deformed 4D model

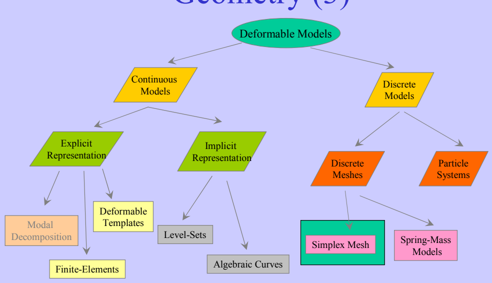




Model intersection with image



Deformable Model Geometry (3)

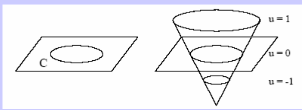


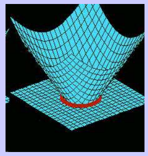
[Montagnat2001]

Deformable models

- Level-sets
  - Curve/Surface C (in $\Re^2/\Re^3$) that corresponds to an iso-level of a surface/hypersurface (in $\Re^3/\Re^4$)

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





  - 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 in 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

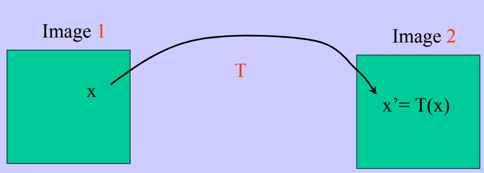
Registration

- 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

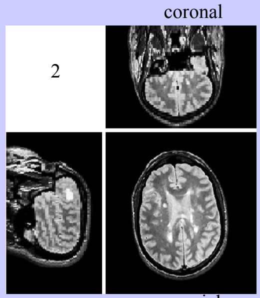


Main Applications

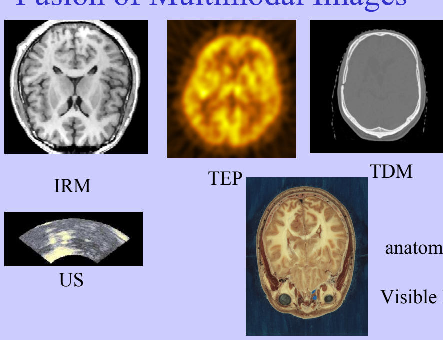
- Temporal Evolution
- Fusion of multimodal images
- Inter-patients comparaison
- Atlas Superposition

Temporal Evolution

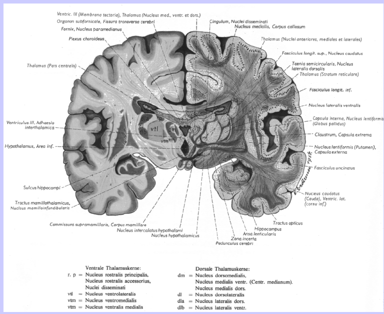
- Precise comparison of images of a given patient, taken at different times.
- One must suppress the apparent motion of the patient.



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

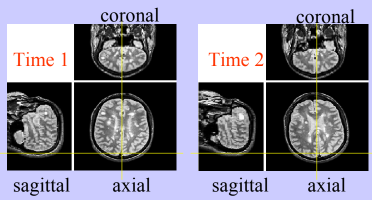
2. Geometric Approaches

Principle of Geometric (Feature-Based) Approaches

- Extract geometric landmarks
- Find correspondences and best transformation T

Temporal Evolution (To Start!)

- Rigid, Mono-patient, Monomodal



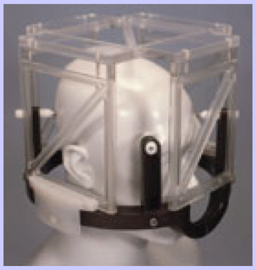
Choosing a Class of Transformations

- 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

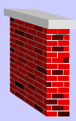
Artificial Landmarks



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

Anatomical Landmarks

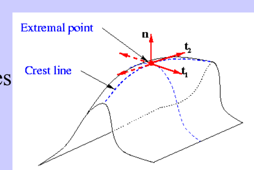
- Search for geometric invariants to characterize a limited number of singular points and lines on anatomical surfaces



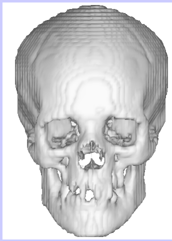
- Generalization of edges and vertices on differentiable surfaces (Monga-Ayache-Sander, Thirion)

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



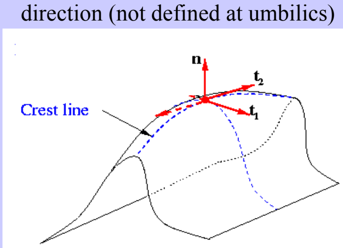
$$f(x, y, z) = I$$

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

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

Stage 2: Crest Lines

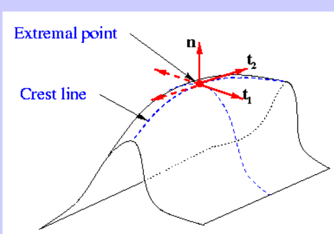
- Maximum principal curvature (in absolute value) must be extremal in the associated principal direction (not defined at umbilics)



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

Stage 3: Extremal Points

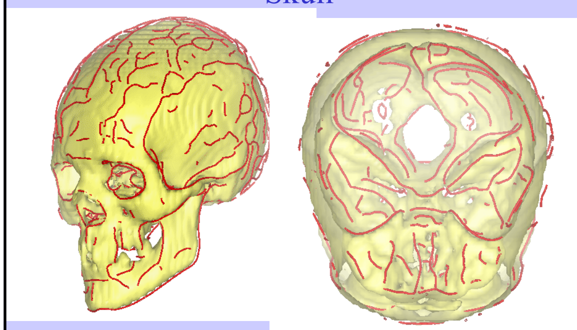
- Second principal curvature is also extremal in the second principal direction.



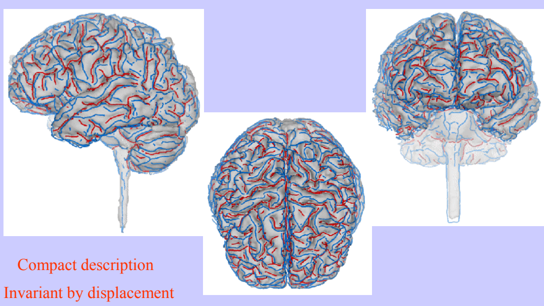
$$e_1 = \nabla k_1 . t_1 = 0$$

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

Skull



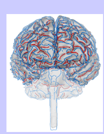
Crest Lines on Cortex (IRM)



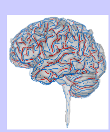
Compact description

Invariant by displacement

Rigid Registration



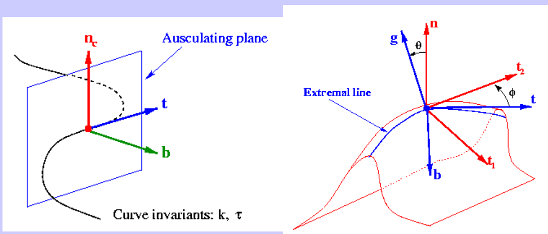
- Geometric Hashing algorithms establish correspondences between homologous points and the best rigid transformation between the 2 images (Rigoutsos-Wolfson, Guéziec-Pennec-Ayache-IEEE Trans. Computers)



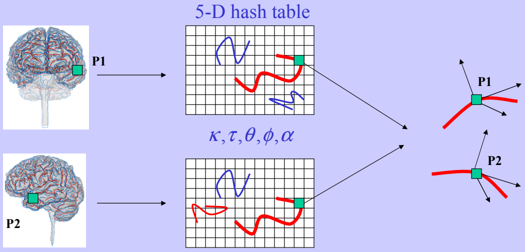
- These algorithms use additional invariants computed along crest lines and on the underlying anatomical surface

Geometric Invariants on Crest Lines

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

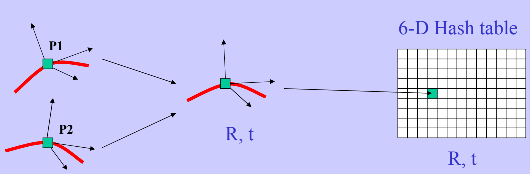


Registration by Geometric Hashing



Guéziec-Ayache

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

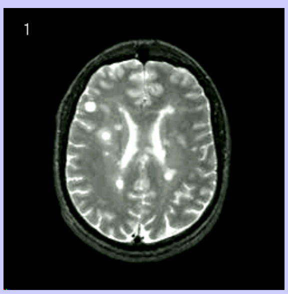
24 3-D images before registration

- Same patient followed during one year

Brigham & Women's Hospital
Harvard Medical School

After Rigid Registration (24 times)

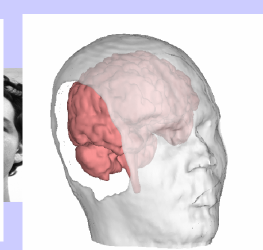
24 3-D images after rigid registration



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

J.P. Thirion
IJCV'98

Geometric Registration of Surfaces



Collaboration Epidaure-Robotvis

Feldmar-Devernay

Augmented Reality (Fiction)

Feldmar-Devernay

Augmented Reality (Real)

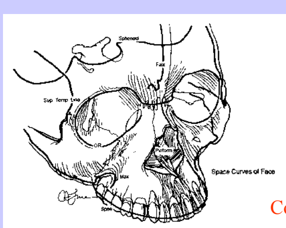
- Active Stereovision

Brigham & Women's Hospital- MIT

E. Grimson et al.

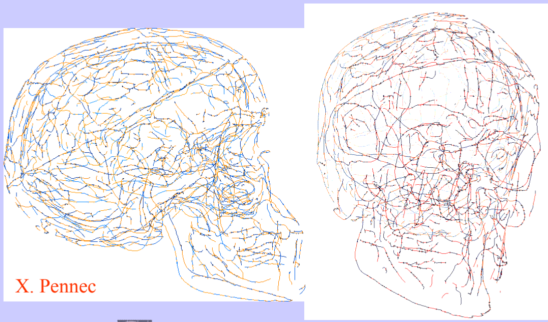
Non Rigid Geometric Registration

- Some crest lines are anatomical invariants



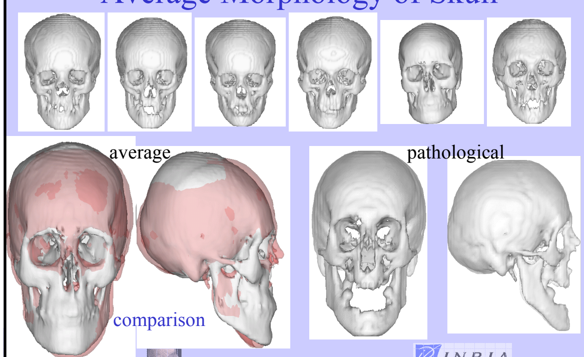
Court Cutting et al.

Skull (Scanner)



Average Morphology of Skull

G. Subsol

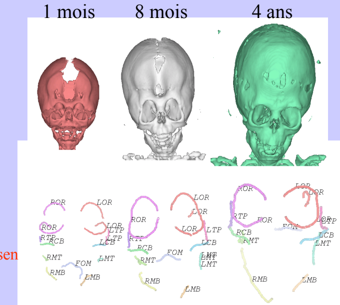


Skull Growth trough Aging

1 mois 8 mois 4 ans

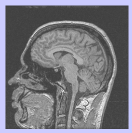
G. Subsol

Andresen & Nielsen



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....

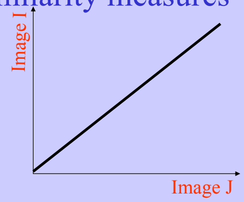
Minimization Algorithms

- 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



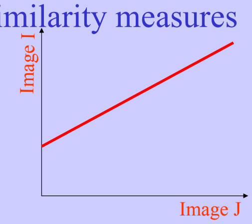
- Adapted measures

  Sum of Squared Differences $SSD(I,J) = \sum_k (I_k - J_k)^2$
  Sum of Absolute Differences
  Measures based on image difference (Buzug et al, 1997)

Classification of similarity measures

- Assumed relationship

  Affine



- Adapted measures

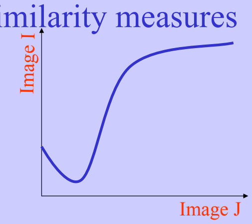
  Correlation Coefficient

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

Classification of similarity measures

- Assumed relationship

  Functional



- Adapted measures

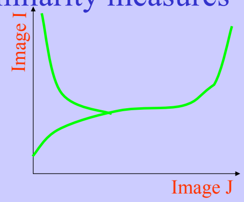
  Woods criterion (Woods et al, 1993)
  Robust Woods criterion (Nikou et al, 1997)
  Correlation Ratio (Roche et al, 1998)

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

Classification of similarity measures

- Assumed relationship

  Statistical



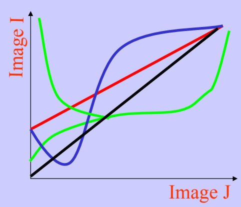
- Adapted measures

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



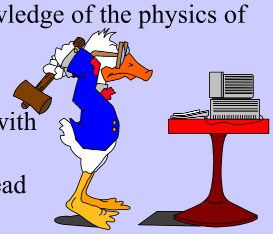
A common framework ?

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

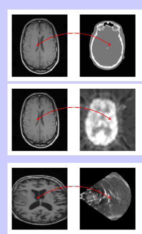
Correlation Ratio vs. Mutual information

(-) simplistic model | (+) more realistic model

(+) few parameters | (-) many parameters

- Accuracy study
  CT / MR rigid registration

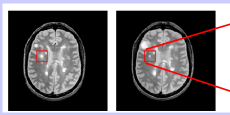
  PET / MR rigid registration
- Robustness study
  Ultrasound / MR rigid registration



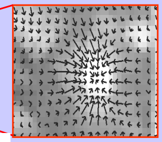
Some Applications of Iconic Registration

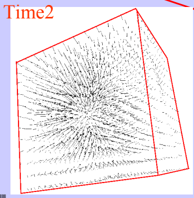
- 1. Detection and Measure of Lesions
- 2. Inter-patient comparisons
- 3. Superposition of an Atlas
- 4. Measure of Asymmetry
- 5. Superposition MRI-Ultrasounds
- 6. Stress-Rest Comparisons

1. Detection and Measure of Multiple Sclerosis Lesions



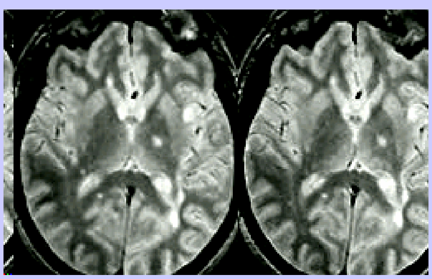
Time 1 Time2





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

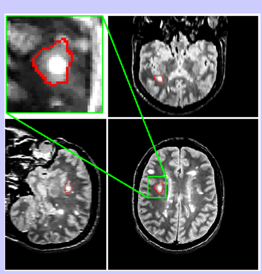
Deformation Field



Time 1 Time 2

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

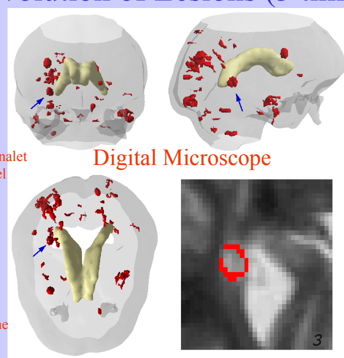


D. Rey, G. Subsol, H. Delingette,N.Ayache
IPMI'99

Evolution of Lesions (3 times)

Frontal

Sagittal



Rey-Le Brun-Chanalet
-Ayache-Chatel
2000

Digital Microscope

Time 1
Time 2
Time 3

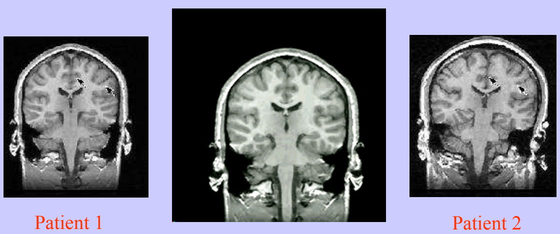
Axial

Rey-Subsol-
Delingette-Ayache
IPMI'99

European project
Biomorph

INRIA

2. Application to inter-patient comparison



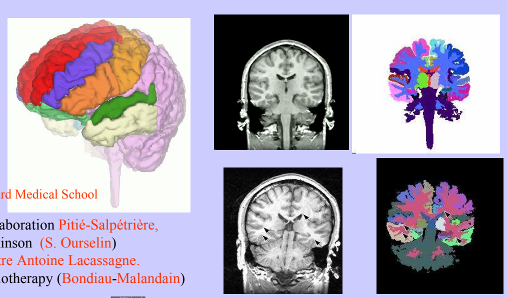
Patient 1 Patient 2

Morphometry: average subjects/patients, variations around average
Would Require BOTH Geometric and Iconic Methods

J.P. Thirion, X. Pennec, G. Subsol, A.Guimond,...

INRIA

3. Application to the Superposition of a Brain Atlas



Harvard Medical School

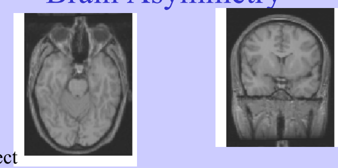
Collaboration Pitié-Salpêtrière,
Parkinson (S. Ourselin)
Centre Antoine Lacassagne.
Radiotherapy (Bondiau-Malandain)

INRIA

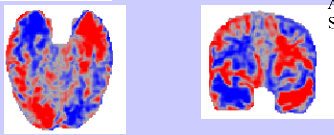
4. Quantitative Measure of Brain Asymmetry

European Project
Biomorph

Prima-Subsol-
Thirion-Roberts
Miccai '98



Application to
Schizophrenia

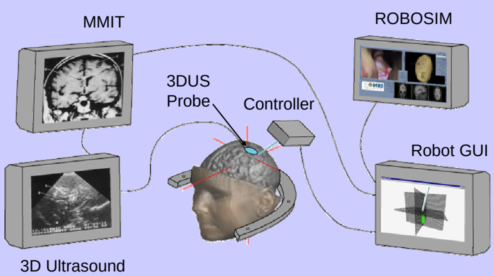


Blue: larger than on opposite side

Red: smaller than on opposite side

Roboscope

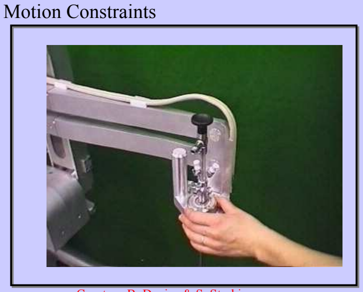
Image-Guided Manipulator-Assisted Neuro-Endoscopy



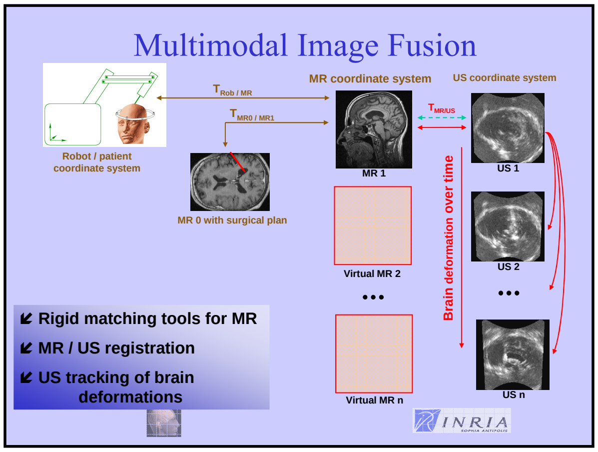
Courtesy Brian Davies

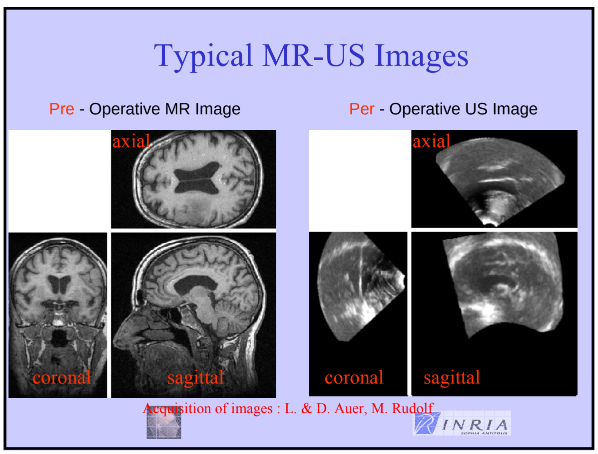
Manipulator

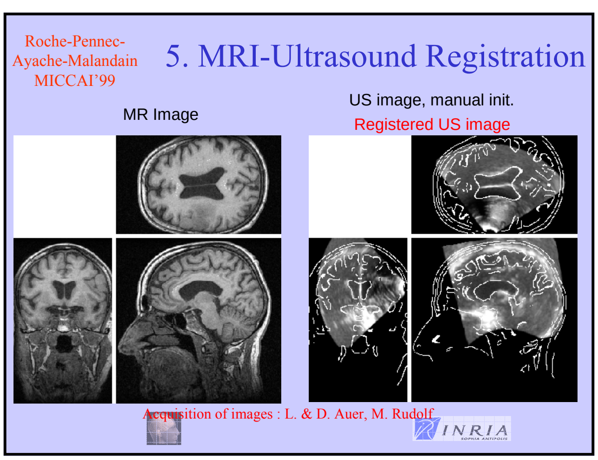
Steady Hand Motion Compensation
Active Motion Constraints



Courtesy B. Davies & S. Starkie

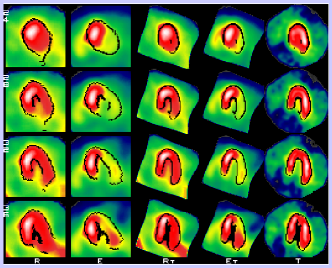

Multimodal Image Fusion
MR coordinate system
US coordinate system
$T_{Rob / MR}$
$T_{MR0 / MR1}$
$T_{MR/US}$
Robot / patient coordinate system
MR 0 with surgical plan
MR 1
US 1
Virtual MR 2
US 2
Virtual MR n
US n
Brain deformation over time
Rigid matching tools for MR
MR / US registration
US tracking of brain deformations
INRIA


Typical MR-US Images
Pre - Operative MR Image
Per - Operative US Image
axial
coronal
sagittal
axial
coronal
sagittal
Acquisition of images : L. & D. Auer, M. Rudolf
INRIA


Roche-Pennec-Ayache-Malandain MICCAI'99
5. MRI-Ultrasound Registration
MR Image
US image, manual init.
Registered US image
Acquisition of images : L. & D. Auer, M. Rudolf
INRIA

6. Application to 3-D Stress-Rest comparison (Gated Spect)

Rest Stress Rest Stress Model



- Perfusion of cardiac muscle
- lateral ischemia
- CardioMatch (Focus Imaging)
- Declerck-Feldmar

Conclusion

- Medical Imaging is nearing maturity
- New image modalities across scale and function
- Validation of algorithms sometimes impossible always difficult
- Growing availability of large image databases