# Medical Image Processing

# M2 Data Science & AI 2023-2024

https://www-sop.inria.fr/asclepios/cours/MS_DS_2023_2024/

*X. Pennec*

## *Medical image registration*

Epione team
2004, route des Lucioles B.P. 93
06902 Sophia Antipolis Cedex

http://www-sop.inria.fr/epione



## *Medical Image Processing – M2 DSAI 2022-2023*

**Generally Tuesday afternoon 13:30 – 16:30**

**Course notes : https://www-sop.inria.fr/asclepios/cours/MS_DS_2023_2024/**

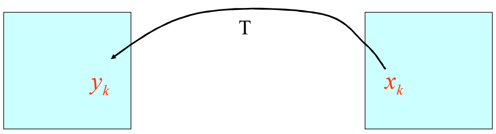
- Tue 09/01, [HD] Introduction to Medical Image Acquisition
- **Tue 16/01: [XP] Medical Image Registration**
- Tue 23/01: [HD] Image filtering, mathematical morphology
- Tue 30/01: [XP] Statistics on Riemannian manifolds and Lie groups
- TBD: [HD] Connexity and Shape Constrained Image segmentation
- Tue 13/02: [XP] Non linear and diffeomorphic Registration
- Tue 20/02: [HD] Shape constraints in Image Segmentation
- TDB: [XP] Computational Anatomy
- Tue 05/03: [XP,HD] EXAM



## *Goals of Registration*

**A dual problem**

- Find the point y of image J which is corresponding (homologous) to each points x of image I.
- Determine the best transformation T that superimposes homologous points

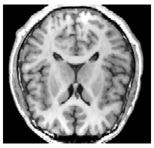


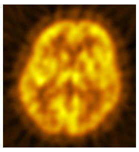
## Principal Applications

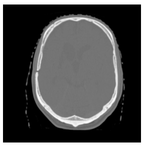
- Fusion of multimodal images
- Temporal evolution of a pathology
- Inter-subject comparisons
- Superposition of an atlas
- Augmented reality



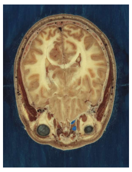
## Fusion of Multimodal Images


MRI


PET


X-scan


US


Histology

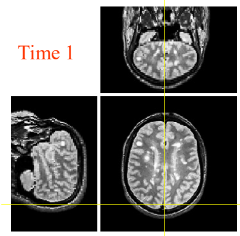
Visible Man



## Temporal Evolution

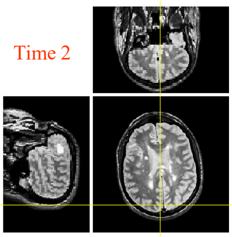
Time 1

coronal

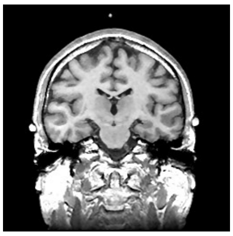

sagittal axial

Time 2

coronal

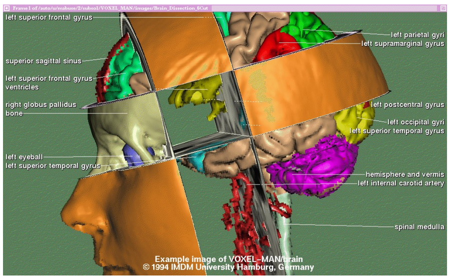

sagittal axial

## Inter-Subject comparison





## Registration to an Atlas




Voxel Man



## Augmented reality

**Brigham & Women 's Hospital**

E. Grimson

## *Classes of problems vs. applications*

| | |
|---|---|
| **Temporal evolution** | **Intra Subject – Monomodal** |
| **Multimodal image fusion** | **Intra Subject - Multimodal** |
| **Inter-subject comparison** | **Inter Subject - Monomodal** |
| **Superposition on an atlas** | **Inter Subject - Multimodal** |

***Intra Subject*: Rigid or deformable**

***Inter Subject*: deformable**



## *Intuitive Example*

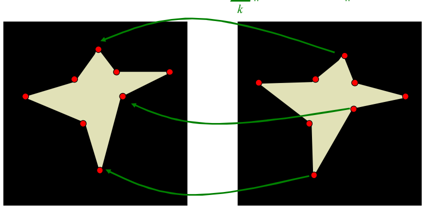
**How to register these two images?**



## *Feature-based/Image-based approach*

Feature detection (here, points of high curvature)

Measure: for instance $S(T) = \sum_k \left\| T(\mathbf{x}_k) - \mathbf{y}_k \right\|^2$



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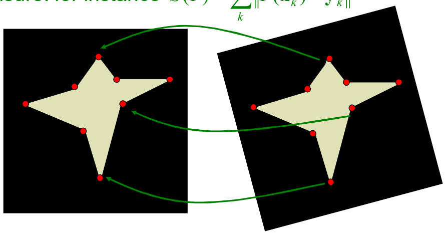


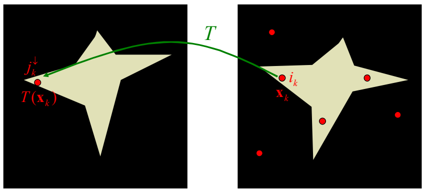


## *Feature-based/Image-based approach*

No segmentation!

Measure: e.g. $S(T)=\sum_k (i_k - j_k^{\downarrow})^2$

Interpolation: $j_k^{\downarrow} \equiv J(T(\mathbf{x}_k))$



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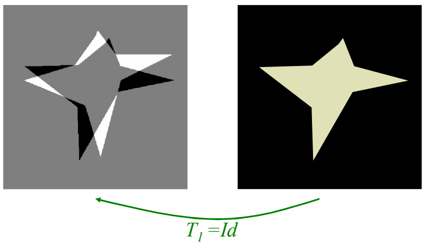

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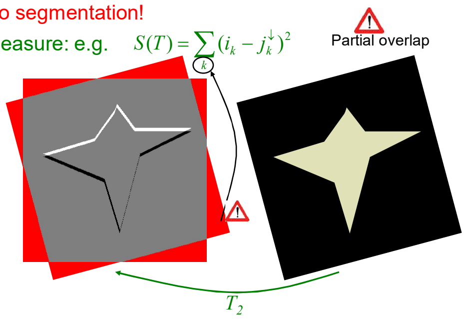


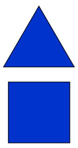



## *Classes of Transformations T*

- Rigid (displacement)
- Similarities
- Affine (projective for 2D / 3D)
- Polynomials
- Splines
- Free-form deformations



## *Classes of Transformations T*

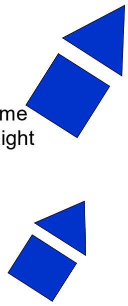


**Rigid:** $T(x) = Rx + t$

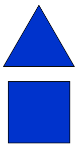
- Rotation and translation
- 6 parameters: (R: 3; t: 3)
- invariants: distances (isometry), frame orientation, curvatures, angles, straight lines

**Similarities:** $T(x) = s.Rx + t$

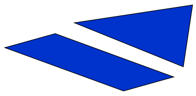
- Add a global scale factor
- 7 parameters
- invariants: ratio of distances, orientation, angles, straight lines



## Classes of Transformations T



**Affine:** $T(x) = Bx + t$



- 3x3 matrix B
- 12 parameters: (B: 9; t: 3)
- invariants: straight lines, parallelism

**Quadratic:** $T(x)^k = a^k_{ij}\, x_i x_j + b^k_i x_i + t^k$

- Add a symmetric 3x3 matrix A per axis
- 30 parameters (A: 18; B: 9; t: 3)
- invariants: do not preserve straight lines **any more**

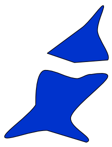


## Classes of Transformations T

**Splines:**

- Local polynomials of degree d, with a global continuity of degree C(d-1).
- number of parameters: depend on the number of control points (knots)
- locally affine: simplified version

**Free form transformations:** $T(x) = x + u(x)$



- a vector $u(x)$ is attached to each point $x$
- parameters: at most 3 times the number of voxels
- regularization: constrain to homeomorphisms (diffeomorphisms)



## Classification of registration problems

**Type of transformation**

- Parametric
  Rigid (displacement), similarity, affine, projective
- Deformables
  Polynomial, spline, free-form deformations

**Type of acquisition**

- Monomodal
- Multimodal

**Homology of observed objects**

- Intra-subject (generally a well posed problem)
- Inter-subject (one-to-one correspondences, regularization ?)

## Mathematical Formulation of registration (Brown, 1992)

- **Registration**: Given two datasets (images) I and J, find the geometric transformation T that « best » aligns the physically homologous points (voxels)

$$\hat{T} = \arg\max_{T \in \mathcal{T}} S(I,J,T)$$

Optimization algorithm

Similarity measure

Transformation space (rigid, affine, elastic,…)



## Course overview

**Feature-based registration**

**Multimodal Intensity-based Registration**



## Geometric methods

**Extract geometric features**
- Invariant by the chosen transformations
  - Points
  - Segments
  - Frames

**Given two sets of features, registration consists in:**
- Feature identification (similarity): Match homologous features
- Localization: Estimate the transformation T

**Algorithms**
- Interpretation trees
- Alignement
- Geometric Hashing
- ICP

## Artificial markers

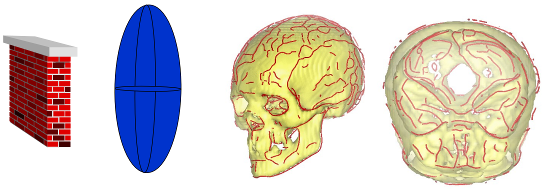
**Stereotactic frame**

- Invasive
- External markers
- Motion
- Short time use



## Anatomical markers

**Find geometric invariants to characterize a small number of singular points on anatomical surfaces**



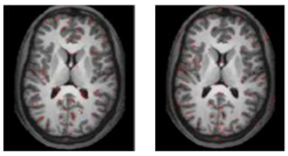
**Generalization of edges and corner points to differentiable surfaces**



## Anatomical markers

**Find geometric invariants to characterize a small number of singular points on anatomical surfaces**

- Multiscale determinant of Hessian function (numerator of Gaussian curvature)
- 3D Harris detector [Rohr 99, Ruiz-Alzola et al 2001] based on the local correlation matrix C= $E(\nabla I \,.\, \nabla I^t)$



Detected salient points in a axial slice of a brain. In a) Beaudet/Thirion curvature based detector, in b) the Harris/Rohr correlation based method is shown. [From Lloyd, Szekely, Kikinis, Warfield 2005]

## Iterative closest point (ICP)

**One global criterion,** $C(A,T) = \sum_i dist(T(P_i), A(P_i))^2$

**alternatively minimized over**

- Step 1: matches $A^* = \underset{A}{\text{Argmin}} \sum_i dist(T(P_i), A(P_i))^2$
- Step 2: transformation $T^* = \underset{T}{\text{Argmin}} \sum_i dist(T(P_i), A(P_i))^2$

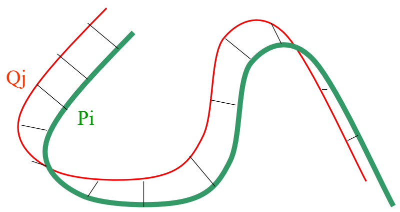
**Positive and decreasing criterion: convergence**

**Robustness w.r.t. outliers: robust distances**

$$dist(x,y)^2 = \Phi(\| x - y \|) \qquad \begin{array}{ll} \Phi(x) = \| x \|^2 & \text{(standard mean)} \\ \Phi(x) = \min\left(\| x \|^2, \chi^2\right) & \text{(saturated mean)} \\ \Phi(x) = \| x \| & \text{(median)} \end{array}$$

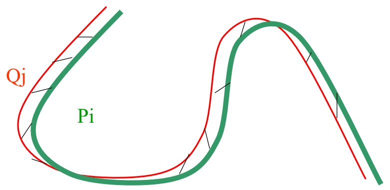


## 1. Optimization for matches

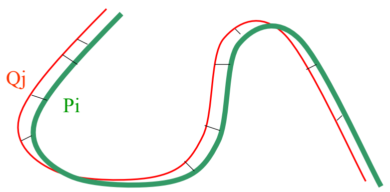





## 2. Optimization for T

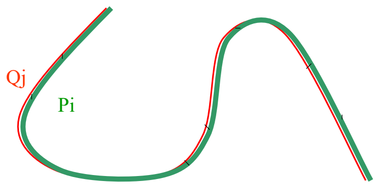


## 1-bis Optimization for matches






## 2-bis Optimization for T

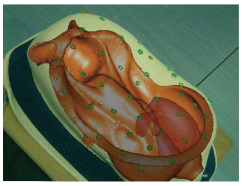





## Augmented reality guided radio-frequency tumor ablation

**Collaboration with IRCAD (Strasbourg, France)**

- Per-operative CT “guidance”
- Respiratory gating
  - Marker based 3D/2D rigid registration



**S. Nicolau, X.Pennec, A. Garcia,L. Soler, N. Ayache** IRCAD

## Increase 3D/2D registration accuracy: A new Extended Projective Point Criterion

**Standard criterion:** $$\sum_{l=1}^{M}\sum_{i=1}^{N}\left\|P^l(T*M_i)-m_i^l\right\|^2$$

- image space minimization (ISPPC)
- noise only on 2D data

**Complete statistical assumptions + ML estimation**

- Gaussian noise on 2D *and* 3D data
- Hidden variables $M_i$ (exact 3D positions)

$$\sum_{l=1}^{M}\sum_{i=1}^{N}\frac{\left\|P^l(T*M_i)-\tilde{m}_i^l\right\|^2}{2\sigma_{2D}^2}+\sum_{i=1}^{N}\frac{\left\|M_i-\tilde{M}_i\right\|^2}{2\sigma_{3D}^2}$$

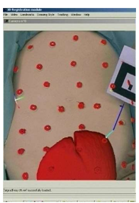


## Registration for Augmented reality

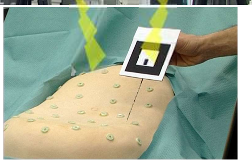


## Whole loop accuracy evaluation

Left monitor with AR & needle tracking



Stereoscopic HD video acquisition

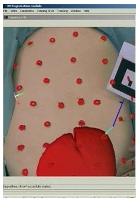


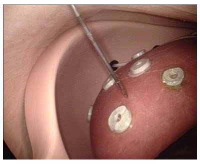
Real scene: phantom + needle

Right monitor with AR & needle tracking

## Whole loop accuracy evaluation

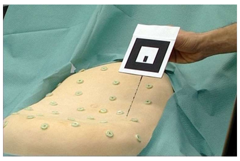
**Left monitor with AR & needle tracking**





Endoscopic control

**Right monitor with AR & needle tracking**



Real scene: phantom + needle

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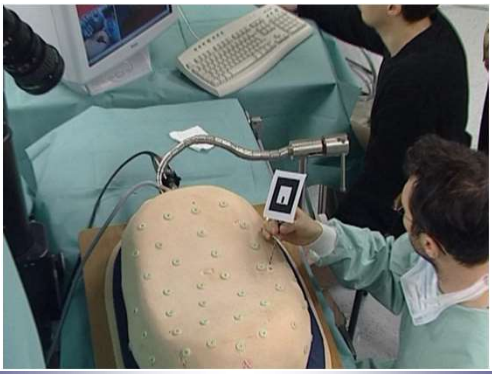
## Whole loop accuracy evaluation



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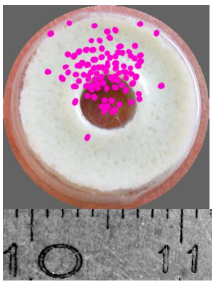
## Whole loop accuracy evaluation

**Experimental setup**

- Two participants (comp. sci. + surgeon)
- 100 needle targeting

**Measures**

- Distribution of hits
  **(endoscopic view, video recording)**
- Average deviation from target
  2.8 mm ± 1.4
- Average targeting time:
  46.6 sec. ± 24.64



[ S. Nicolau, A. Garcia et al., Aug. & Virtual Reality Workshop, Geneva, 2003 ]

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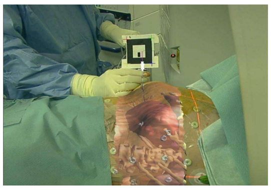
## Liver puncture guidance using augmented reality

**3D (CT) / 2D (Video) registration**
- 2D-3D EM-ICP on fiducial markers
- Certified accuracy in real time

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

[ S. Nicolau, PhD'04 MICCAI05, ECCV04,, IS4TM03, Comp. Anim. & Virtual World 2005 ]



## Course overview

Feature-based registration

**Multimodal Intensity-based Registration**



## Intensity-based methods

**No geometric feature extraction**

**Advantages:**
- Noisy images and/or low resolution
- Multimodal images

**Drawbacks:**
- All voxels must be taken into account

## Compare multi-modal images?

**Which similarity criterion ?**

- Many available criteria:
  - SSD, Correlation, Mutual Information...?
- Variable costs and performances
- Where is the optimum ?

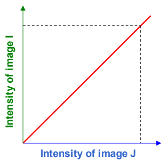
Maintz & Viergever, Survey of Registration Methods, Medical Image Analysis 1997



## Classification of existing measures

**Assumed relationship**

Intensity conservation




**Adapted measures**

Sum of Square Differences
Sum of Absolute value of Differences
Measures of intensity differences (Buzug, 97)

$$S(T) = \sum_k (i_k - j_k^{\downarrow})^2$$

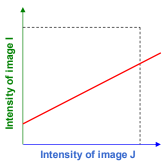
Interpolation: $j_k^{\downarrow} \equiv J(T(\mathbf{x}_k))$



## Classification of existing measures

**Assumed relationship**

Affine




**Adapted measures**

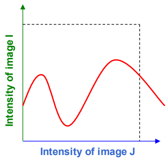
Correlation coefficient

$$\rho_{IJ}(T) = \frac{1}{n\sigma_I \sigma_J} \sum_k (i_k - \bar{I})(j_k^{\downarrow} - \bar{J})$$

## Classification of existing measures

**Assumed relationship**

Functional




**Adapted measures**

Woods' criterion (1993)
Woods' variants (Ardekani, 95; Alpert, 96; Nikou, 97)
Correlation ratio (Roche, 98)

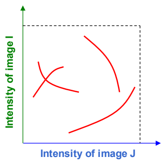
$$\eta^2 = \frac{Var[E(I \mid J(T))]}{Var(I)}$$



## Classification of existing measures

**Assumed relationship**

Statistical




**Adapted measures**

Joint Entropy (Hill, 95; Collignon, 95)
Mutual Information (Collignon, 95; Viola, 95)
Normalized Mutual Information (Studholme, 98)

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



## A general framework

- A. Roche proposed a unifying maximum likelihood framework
- Physical and statistical modeling of the image acquisition process
- Create a hierarchy of criteria

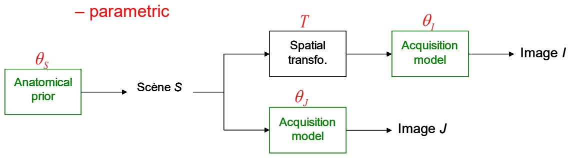
A. Roche, G. Malandain and N.Ayache : *Unifying maximum likelihood approaches in medical image registration.* International Journal of Imaging Systems and Technology : Special Issue on 3D Imaging 11(1), 71-80, 2000.

• Based on pioneer works of (Costa et al, 1993), (Viola, 1995), (Leventon & Grimson, 1998), (Bansal et al, 1998)

## *Principle of the method [A. Roche]*

**Generative model of images**

- probabilistic
- parametric



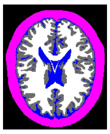

**Maximum likelihood Inference**

$$\max_{T,\theta_I,\theta_J,\theta_S} P(I,J \mid T,\underbrace{\theta_I,\theta_J,\theta_S}_{\text{Auxiliary variables: } q})$$



## *Generic model*

**Scene: discrete random field (segmentation)**



**Assumptions:**

- Spatial independence
- Stationarity

$$\Rightarrow P(S) = \prod_l \pi(s_l)$$



## *Generic model*

**Images: noisy measures of the scene**

$$\begin{cases} i_k &= f(s_k^{\downarrow}) + \varepsilon_k \\ j_l &= g(s_l) + \eta_l \end{cases} \qquad s_k^{\downarrow} \equiv s(T(x_k))$$

**Assumptions on $\varepsilon$ and $\eta$:**

- white (spatial indep.)
- Stationary
- Gaussian
- Additive
- Independent of each other

$$\Rightarrow P(I,J \mid S) = \prod_k G_{\sigma_\varepsilon}(i_k - f(s_k^{\downarrow})) \times \prod_l G_{\sigma_\eta}(j_l - g(s_l))$$

## Likelihood function

**Likelihood = joint law of images**

$$P(I,J)=\int P(I,J\mid S)P(S)dS$$
$$\equiv L(T,\theta)\quad \text{with}\quad \theta\equiv(\pi,f,g,\sigma_\varepsilon,\sigma_\eta)$$

**Log likelihood**

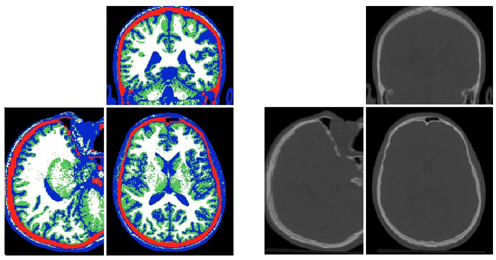
$$\log L(T,\theta)=\underbrace{\sum_{k\in A}\log\frac{P_\theta(i_k,j_k^\downarrow)}{P_\theta(i_k)P_\theta(j_k^\downarrow)}}_{(T,\theta)}+\underbrace{\sum_k \log P_\theta(i_k)+\sum_l \log P_\theta(j_l)}_{(\theta)}$$

$$\text{with}\quad P_\theta(i,j)=\sum_{p=1}^{K}\pi_p G_{\sigma_\varepsilon}(i-f_p)G_{\sigma_\eta}(j-g_p)$$



## Example: X-Scan / MRI rigid registration

The estimation of $\theta$ allows the a posteriori estimation of the scene

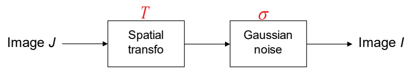




## Particular case 1

**Assumptions**

$$\begin{cases} f=g \\ |\eta|<<|\varepsilon| \end{cases}\Rightarrow i_k\approx j_k^\downarrow+\varepsilon_k$$



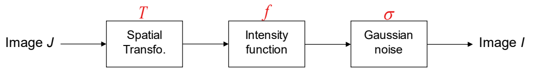

**Maximum Likelihood**

$$\max_\theta L(T,\theta)\propto -n\log\left(\frac{c}{n^2}\underbrace{\sum_k (i_k-j_k^\downarrow)^2}_{\text{SSD}}\right)+E_{\text{cte}}$$

## *Particular case 2*

**Assumptions**

$$\begin{cases} g \text{ injective} \\ |\eta| << |\varepsilon| \end{cases} \Rightarrow i_k \approx f(j_k^\downarrow) + \varepsilon_k, \quad f \text{ constant by part}$$




**Maximum Likelihood**

$$\max_\theta L(T,\theta) \propto -n \log\left(\frac{c}{n} \min_f \sum_k (i_k - f(j_k^\downarrow))^2\right) + E_{cte}$$

Squared fit error



## *Particular case 2*

**Limit case: correlation ratio (CR)**

Squared fit error

$$\eta^2_{I|J}(T) \equiv \frac{\min_f \sum_k (i_k - f(j_k^\downarrow))^2}{n \operatorname{Var}(I)}$$

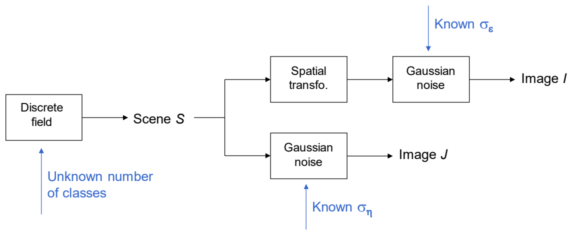
Different normalization of the likelihood criteria

**Equivalence ML / CR**



## *Particular case 3*

**Assumptions**



## Particular case 3

**Maximum Likelihood**

$$\hat{P}(i,j) \approx \frac{1}{n}\sum_k G_{\sigma_\varepsilon}(i-i_k)\,G_{\sigma_\eta}(j-j_k^{\downarrow}) \quad \text{(Parzen)}$$

$$\max_P L(T,P) \propto \sum_k \log \frac{\hat{P}(i_k, j_k^{\downarrow})}{\hat{P}(i_k)\hat{P}(j_k^{\downarrow})} + \text{corrective terms}$$

$n \times$ Mutual Information

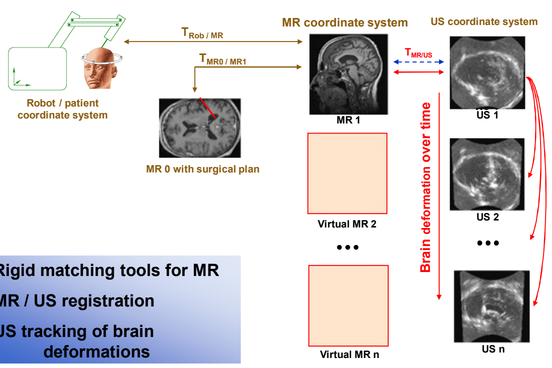


## Choice of a criterion

- Choosing a criterion imposes to deeply understand the physical image acquisition process
- Whenever several models are known, choosing the one with the smallest number of degrees of freedom increase the robustness of the approach.
- Current trend: learn it.
  Pitfall: no idea of #dof and local minima



## Roboscope




- Rigid matching tools for MR
- MR / US registration
- US tracking of brain deformations

## Manipulator

Steady Hand Motion Compensation
Active Motion Constraints

Courtesy B. Davies & S. Starkie

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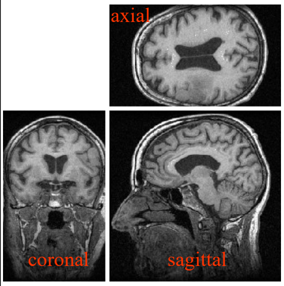
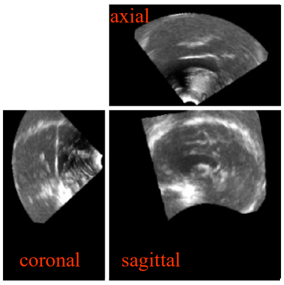
## MR-US Images

Pre - Operative MR Image




Per - Operative US Image




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

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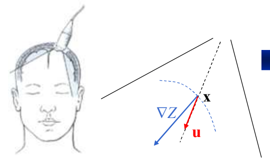
## Ultrasound image / MRI registration

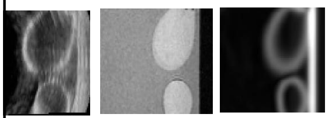
**Elementary principles of US imagery**




$$I_{rf}(\mathbf{x}) = |\nabla Z.\mathbf{u}(\mathbf{x})| \times \xi(\mathbf{x})$$

Logarithmic compression

$$I(\mathbf{x}) \approx A \log|\nabla Z.\mathbf{u}(\mathbf{x})| + B + \varepsilon(\mathbf{x})$$






## Ultrasound image / MRI registration

**Assumption: acoustic impedance is a function of the MR signal (denote by *J*)**

$$Z(\mathbf{x}) = g(J(\mathbf{x})) \quad \Rightarrow \quad \nabla Z(\mathbf{x}) = g'(J(\mathbf{x})) \times \nabla J(\mathbf{x})$$

**Relation between US and MR signals**

$$I(\mathbf{x}) = f\left[J(\mathbf{x}), |\cancel{\nabla J}.\mathbf{u}(\mathbf{x})|\right] + \varepsilon(\mathbf{x})$$

In practice, the influence of orientation is neglected

$$I(\mathbf{x}) \approx f\left[J(\mathbf{x}), \|\nabla J(\mathbf{x})\|\right] + \varepsilon(\mathbf{x})$$



## Bivariate Correlation Ratio

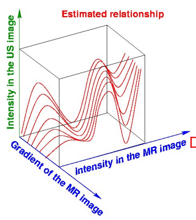
**Intensity = function of 2 variables**

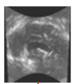
$$I = f(J, |\nabla J|)$$

**2 iterated stages**

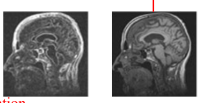
- Robust polynomial approx. of f
- Estimation of T:

$$\boxed{\hat{T} = \arg\min_{T} \sum_k \left( I(x_k) - \hat{f}(J(T(x_k)), |\nabla J(T(x_k))|) \right)^2}$$



Dependency Hypothesis

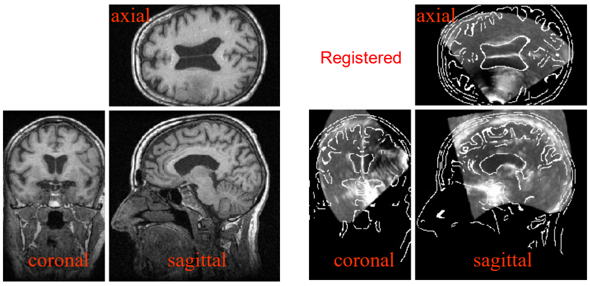


A. Roche, X. Pennec, G. Malandain, and N. Ayache
Rigid Registration of 3D Ultrasound with MR Images:
a New Approach Combining Intensity and Gradient Information.
IEEE Transactions on Medical Imaging, 20(10):1038--1049, October 2001.

## Typical Registration Result with Bivariate Correlation Ratio

Pre - Operative MR Image

Per - Operative US Image




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

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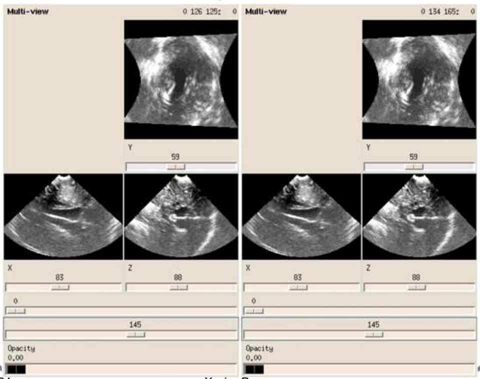
## US Intensity MR Intensity and Gradient

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