Medical Image Analysis based on generative, geometric and biophysical models

MVA 2024-2025

www-sop.inria.fr/teams/asclepios/cours/MVA/

X. Pennec

Introduction to medical image acquisition and image registration

Epione team
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Course teachers

Hervé Delingette 

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Inria Research Centers

Epione Research Team

1. Biomedical Image/Data Analysis, Machine Learning
2. Imaging & Phenomics, Biostatistics
3. **Computational Anatomy, Geometric Statistics**
4. Computational Physiology & Image-Guided Therapy
5. Computational Cardiology & Image-Based Interventions

Medical Image Analysis – MVA 2024-2025

Wednesday / Friday afternoon

Course notes : http://www-sop.inria.fr/teams/asclepios/cours/MVA/

- Tue. Oct 1 2024, 14:00 ENS 1Z25 [XP] Introduction to Medical Image Acquisition & Image Registration
- Tue. Oct 8 2024, 14:00 ENS 1Z25 [XP] Riemanian Geometry and Statistics
- Tue. Oct 15 2024, 14:00 ENS 1Z25 [HD] Image Filtering & Segmentation
- Tue. Oct 22 2024: 14:00 ENS 1Z25 [HD] Image Segmentation based on Clustering and Markov Random Fields
- Tue. Nov 5 2024: 14:00 ENS 1Z25 [XP] Analysis in the space of Covariance Matrices
- Tue. Nov 12 2024: 14:00 ENS 1Z25 [HD] Shape constrained image segmentation
- Tue. Nov 19 2024: 14:00 ENS 1Z25 [XP] Diffeomorphic Registration and Computational Anatomy
- Tue. Nov 26 2024: 14:00 ENS 1Z25 [HD] Biophysical Modeling
- Tue. Dec 3, 2024, 14:00 (Visio) [XP & HD] Exam

Medical Image Processing – MVA 2024

Exam: 4 components :

- Scientific Article Study :
  - [1] 10 min oral presentation
  - [2] 10 min Questions & Answers
  - [3] 5-6 page report presenting the paper and putting it in perspective.
  - Implementation (optional)
  - May be performed in pairs or triplets depending on class size
- [4] Multiple choice Quizz : 10-15 questions

Course overview

The data of Computational Anatomy & Physiology

Image acquisition

Medical Image Registration

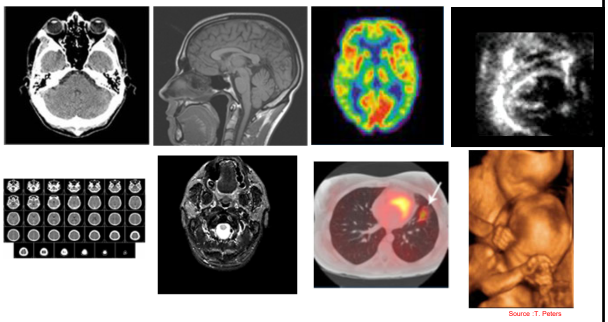
1895: invention of X-ray imaging

Roentgen

First Nobel prize
in Physics in 1901

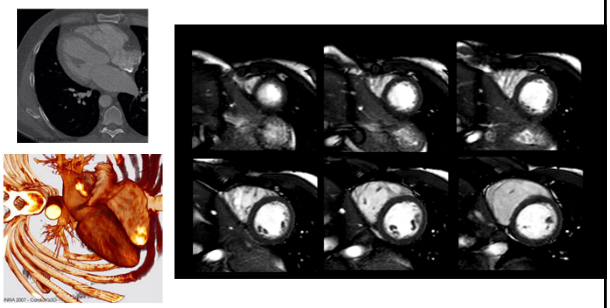
Todays's Medical Imaging modalities

CT Scan — MRI — PET — Ultrasound



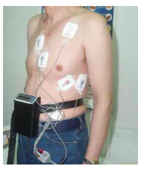
Dynamic Images (4-D)

CT Scan — MRI



Bio-signals

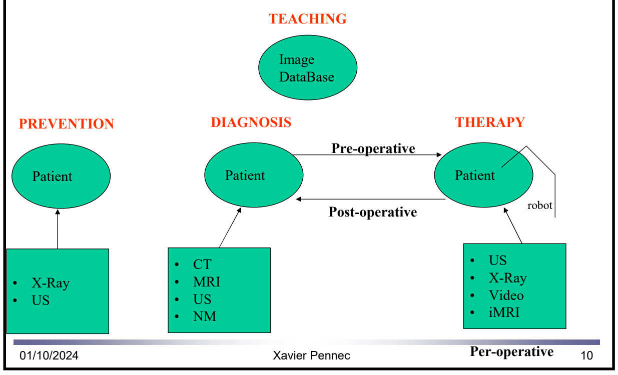
ECG



Pressure Sensor

Temperature

Medical Imaging in clinical practice



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Course overview

The data of Computational Anatomy & Physiology

Image acquisition
- Introduction
- Tomography
- MRI
- Nuclear medicine

Medical Image Registration

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Different imaging modalities

- X-ray
- Magnetic resonance imaging
  - anatomic, functional, angiographic, diffusion, spectroscopic, tagged
- Transmission Tomography (X Scan)
- Nuclear Medicine :
  - Positron emission tomography (PET)
  - Single photon emission tomography (SPECT)
- Ultrasonography
- Histological Imaging, confocal in-vivo microscopy, molecular imaging,…

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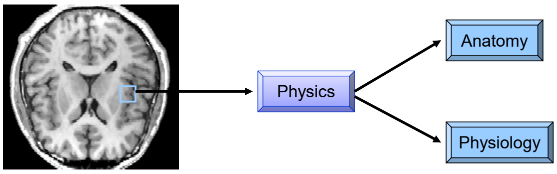
Characteristics of medical images

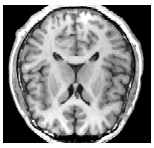
Intensity values are related to physical tissue characteristics which in turn may relate to a physiological phenomenon



Characteristics of Medical images

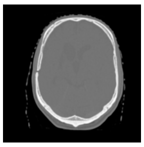
MRI

Density and structure of protons



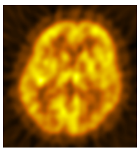
X-Scan

X-ray absorption density



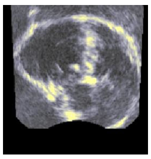
PET / SPECT

Density of Radioactive isotopes



Ultrasounds

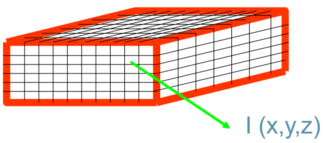
Variations of acoustic impedance



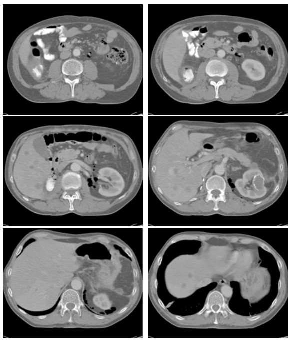
Volumetric medical images

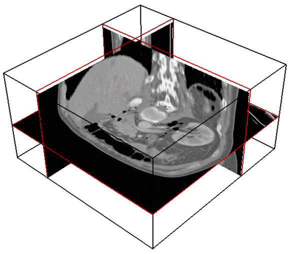
Very often medical images are volumetric

→ **Voxel Representation**



Example of volumetric images : CT-scan (Scanner)

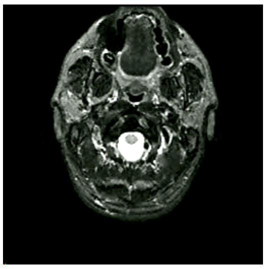




Size: 512 x 512 x 128

Resolution: 0.5 x 0.5 x 1 mm

Volumetric images



T2 MRI

Course overview

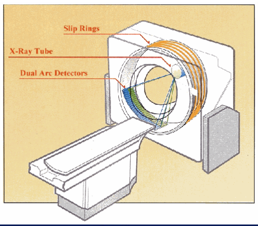
The data of Computational Anatomy & Physiology

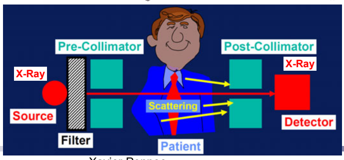
Image acquisition

- Introduction
- Tomography
- Nuclear medicine
- MRI

Medical Image Analysis processing

Principle of CT Imaging (1)

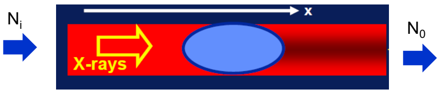




Principle of CT Imaging (2)

Input X-Ray intensity : N_i

Measured Output X-Ray intensity : N_o



Exponential attenuation :

$$N_o = N_i e^{-\int_{-\infty}^{+\infty} \mu(x)dx}$$

Objective :

- measure $\mu(x)$ = absorption coefficient of X-ray

Computed Tomography

Principle :

- Reconstruct n dimensional function (image) from projected data of (n–1) dimension

Radon Transform (1917)

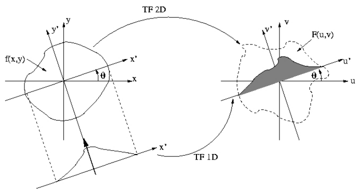
- “Two dimension and three dimension object can be reconstructed from the infinite set of projection data”.

Fourier Slice Theorem

1D Fourier Transform of Projected slice of 2D field μ(x,y)

is equal to

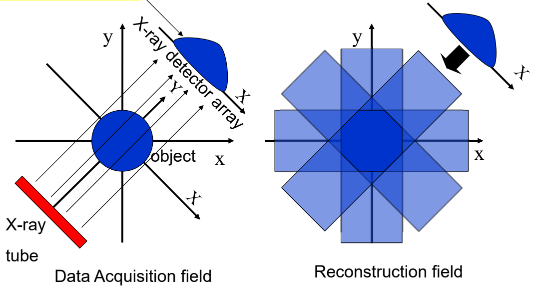
1D slice in the same direction of the 2D Fourier Transform of μ(x,y)



Basic principle of CT

-Reconstruction of 2 dimensional image-

Projection Data curvilinear integral of absorption coefficient regarding Y



Simple Backprojection

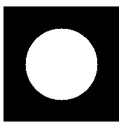
Reconstruction Principle

Backprojection based on inverse Radon Transform

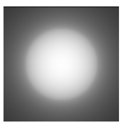
$$\widetilde{\mu(x)} = \frac{1}{2\pi}\int_{\alpha=0}^{2\pi} R\mu(\alpha, n_\alpha . x)\, d\alpha$$

$$n_\alpha = (\cos\alpha, \sin\alpha)$$

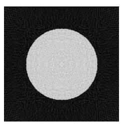
In practice use filtered back-projection to remove blur



Model Image



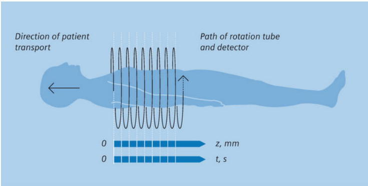
Simple Backprojection



Filtered Backprojection

Spiral (3D) CT

X-ray tube and detectors rotate 360 deg
Patient table is continuously moving
Produce an helix of image projections
3D reconstruction



CT Scan Imaging

Measure absorption coefficient of X-ray related to density of tissue

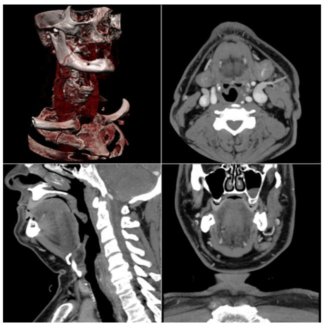
Invasive image modality (ionizing rays)

Absolute Hounsfield Unit

$$HU(\mu) = 1024 \frac{\mu - \mu_{water}}{\mu_{water}}$$

- HU(water)=0, HU(air)= -1024, HU(Bone)=175 to 3000
- Coded on signed 12 bits

Tomotensitometrie (Scanner X)

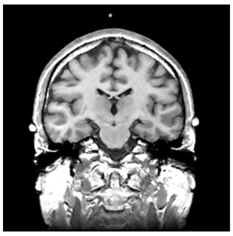


Magnetic resonance imaging

Density and structure of protons

Magnetic resonance imaging

Sagittal



Coronal or Frontal

Axial or Transverse

dimension: 256 x 256 x 128 **résolution: 1x1x1.5 mm**

MRI: a few dates

- 1946: MR phenomenon - Bloch et Purcell
- 1952: Nobel prize - Bloch et Purcell
- 1950-1970: development but no imaging
- 1980: MRI feasibility
- 1986 - …: real development

MRI: One modality with multiple sequences

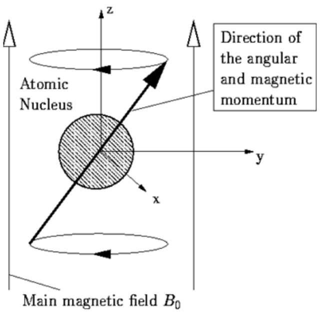
- Anatomic MRI: T1, T2, DP weighted images
- Angiographic MR
- Functional MR: cognitive studies
- Diffusion MR: brain connectivity
- MR Spectroscopy

No absolute quantification

Magnetism at the molecular level

Electric charges in motion

- magnetic momentum
- Precession motion in a magnetic field



Bloch's Equations

- **Link between spin and magnetic momentum**

$$\mu = \gamma S$$

μ Nuclear magnetic momentum
γ Gyromagnetic ratio

- **Fundamental motion equation**

$$\frac{dS}{dt} = m$$

S: Angular speed (spin)
m: Momentum (mechanic)

- **In a magnetic field** $m = \mu \wedge B$

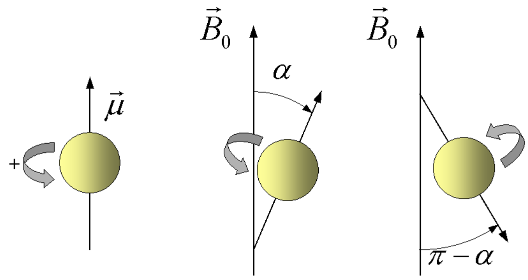
Bloch's Equations

Thus $\frac{d\mu}{dt} = \gamma(\mu \wedge B)$

$$B_0 = \begin{pmatrix} 0 \\ 0 \\ B_0 \end{pmatrix} \Rightarrow \mu = \begin{pmatrix} \mu_t \cos(\omega_L t + \varphi) \\ -\mu_t \sin(\omega_L t + \varphi) \\ \mu_{z_0} \end{pmatrix}$$

Larmor's frequency $\omega_L = \gamma\, B_0$

Magnetism at the macroscopic level



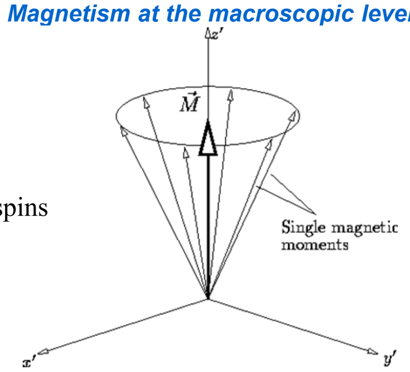
$P_{+1/2}$=0.5000049

B_0=1.5 T

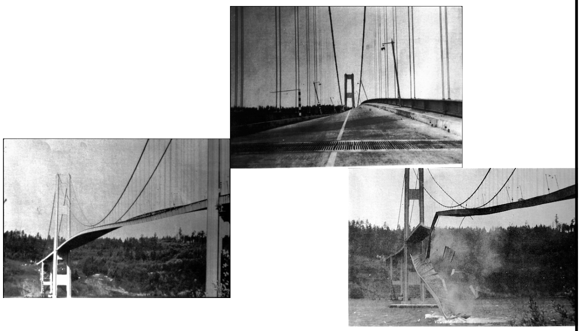
$P_{-1/2}$=0.4999951

Magnetism at the macroscopic level

10^{23} spins



Resonance



Magnetic Resonance / excitation

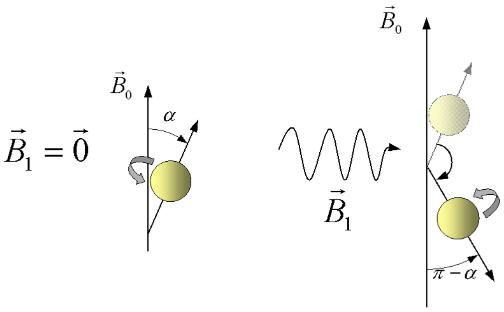
- Electro-magnetic field at Larmor's frequency

$$\omega_L = \gamma\, B_0$$

- Hydrogen protons enter into resonance

Flip of the macroscopic momentum M

Magnetic Resonance / excitation



Magnetic Resonance / relaxation

- Return to equilibrium / B_0: time constant T_1

$$\frac{dM_z}{dt} = \gamma(M \times B)_z - \frac{M_z}{T_1}$$

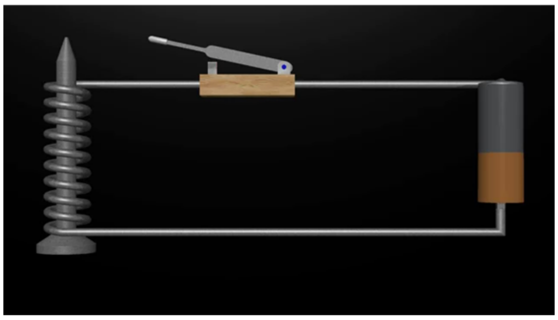
- Spin dephasing: Time constant T_2

$$\frac{dM_{x,y}}{dt} = \gamma(M \times B)_{x,y} - \frac{M_{x,y}}{T_2}$$

Magnetic Resonance / relaxation

TISSUE	T1 (ms)		T2(ms)
	0.5 T	1.5 T	
Muscle	550	870	45
Heart	580	865	55
Liver	325	490	50
Kidney	495	650	60
Spleen	495	650	58
Fat	215	262	85
Brain, grey matter	655	920	100
Brain, white matter	540	785	90

MRI basics in video

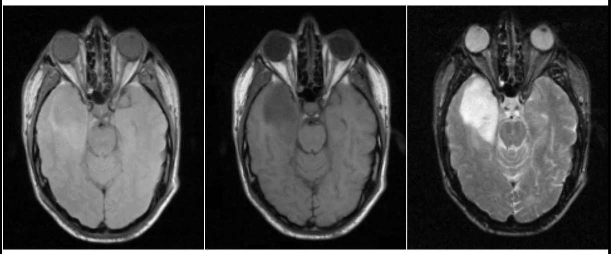


https://www.youtube.com/watch?v=djAxjtN_7VE

MRI / frequency selection

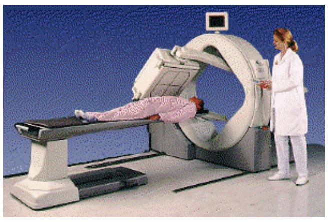
- X encoding by frequency
- Y encoding by phase
- Several measures are necessary

Anatomical MRI



Proton density T_1 T_2

Nuclear Medicine



Density of radioactive tracers

Principle of nuclear imaging

- Introduction into the patient body of a couple
  (radio-isotope / vector molecule)

Vector Molecule ⇒ Targets organ (drug, protein, blood cells…)
Radio-isotope ⇒ Detection of the molecule

- **Emission imaging : the targeted organ emits radioactivity**

⇒ Reflect the metabolic function of the organ
⇒ *Metabolic* or *functional imaging*
→ Local relative concentration (relative)
→ Concentration evolution during time

Nuclear Medicine / radioactivity

- **Nucleus (Rutherford)**

A= nucleon number	Isobars	A = constant
Z = proton number	**Isotopes**	Z = constant
N = neutron number	Isotones	N = constant

- **Radioactivity (Curie)**

Alpha:	Helium nucleus
Beta:	1/ electron β-
	2/ positron β+ → 2 photons γ (511 kev)
Gamma:	Photon

Single photon gamma imaging

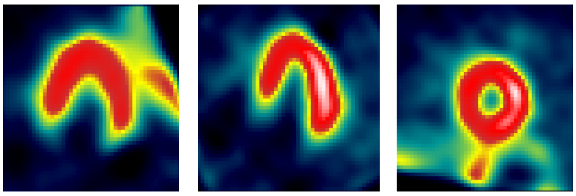
- **Radio-isotopes**

Single photon emitters

Technetium Tc 99m	6 h	140 kev	Portative generator
Iodine I 131	8 j	360 kev	Reacteur (fission)
Iodine I 123	13 h	159 kev	Cyclotron (industry)
Thallium Tl 201	73 h	80 kev	Cyclotron (industry)

Krypton (Kr 81 m), Gallium (Ga 67), Indium (In 111), **Xenon (Xe 133, gaz)**

Single photon gamma imaging



Heart (myocardium perfusion)

- Stress/rest exam

perfusion	/ perfusion	⇒ Healthy area
perfusion	/ (hypo/non-)perfusion	⇒ Zone at risk (ischemia)
(hypo/non-)perfusion	/ (hypo/non-)perfusion	⇒ Infarcted Area

Positron emission tomography (PET)

- **Radio-isotopes**

Emission : positron (β+) → Annihilation
→ 2 photons of 511 kev at 180º

Positron emitters

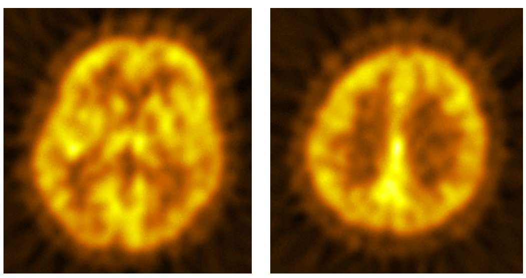
Carbon ^{11}C	20 mn	cyclotron (medical)
Nitrogen ^{13}N	10 mn	cyclotron (medical)
Oxygen ^{15}O	2 mn	cyclotron (medical)
Fluor ^{18}F	112 mn	cyclotron (medical)

- **Physiological molecules**

water → H_2O^{15}

glucose → fluoro-deoxyglucose ($F^{18}DG$)

Positron emission tomography (PET)



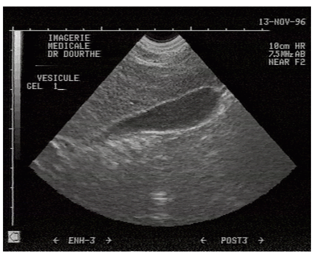
PET Scan

https://www.youtube.com/watch?v=GHLBcCv4rqk

Echography

Local variation of acoustic impedance

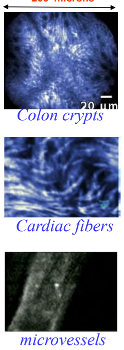
Echography



Gall Blader

New images

- Optical Coherent Tomography (OCT)
- Elastometry (MRI, US, etc.)
- Spectroscopic Imaging
- Terahertz Imaging
- Fibered Confocal Imagery *in vivo*
- etc.



Source : Mauna Kea Technologies

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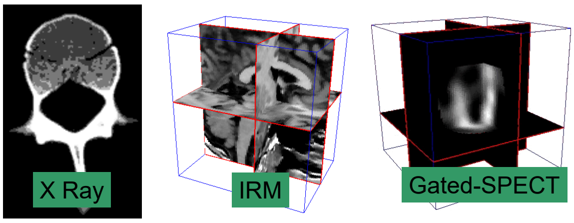
Medical Imaging Classification (1)

Dimensionality



2D 3D 4D (3D+T)

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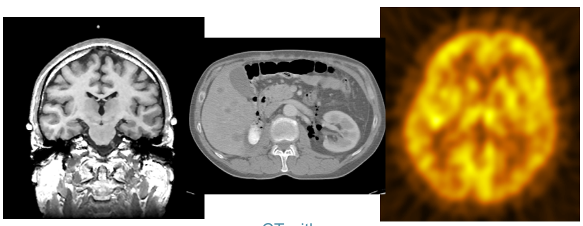
Medical Imaging Classification (2)

Anatomical vs functional Imagery



MRI | CT with contrast agent | PET scan

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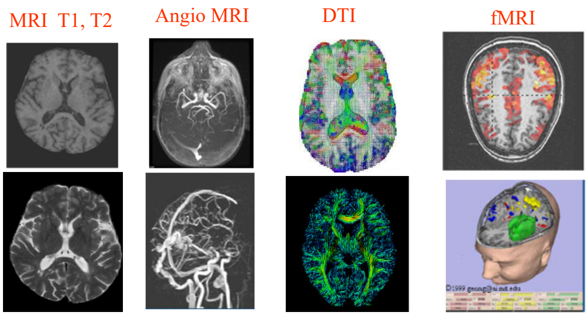
Multiparametric Images



Course overview

The data of Computational Anatomy & Physiology

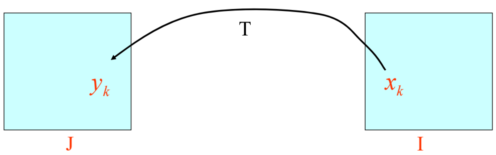
Image acquisition

Medical Image Registration

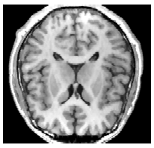
Medical Image Registration

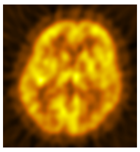
A dual problem

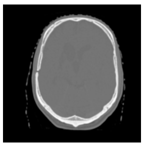
- Find the point y of image J which is corresponding (homologous) to each points x of image I.
- Determine the best transformation T that superimposes homologous points



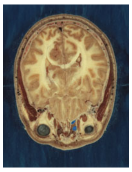
Fusion of Multimodal Images


MRI


PET


X-scan


US


Histology

Visible Man

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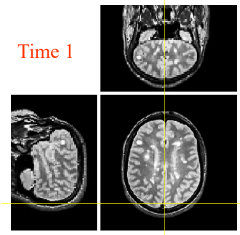
Temporal Evolution

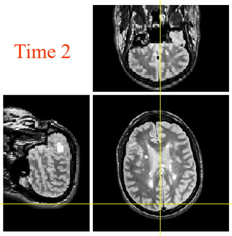
Time 1

coronal


sagittal axial

Time 2

coronal


sagittal axial

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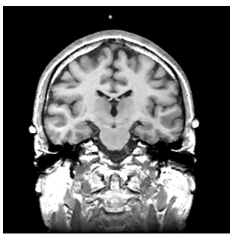
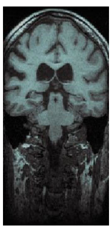
Inter-Subject comparison





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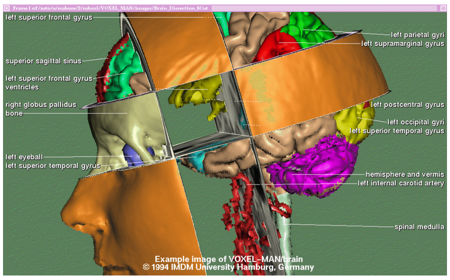
Registration to an Atlas



Voxel Man

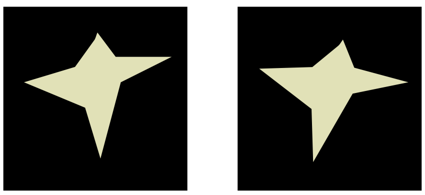
Augmented reality

Brigham & Women 's Hospital

E. Grimson

Intuitive Example

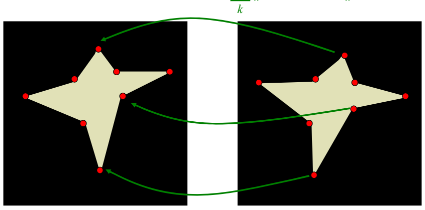
How to register these two images?



Feature-based/Image-based approach

Feature detection (here, points of high curvature)

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



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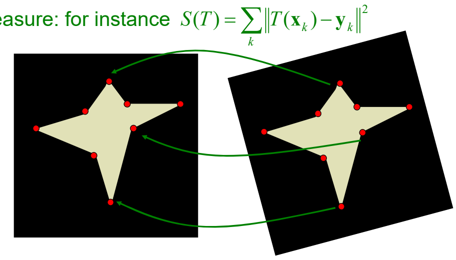
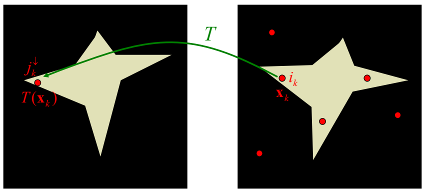


Feature-based/Image-based approach

No segmentation!

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

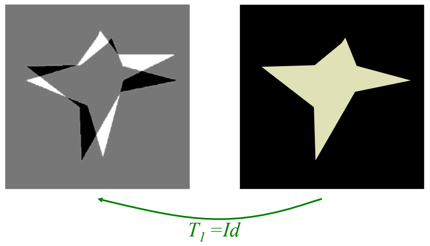
Interpolation: $j_k^{\downarrow} \equiv J(T(\mathbf{x}_k))$



Feature-based/Image-based approach

No segmentation!

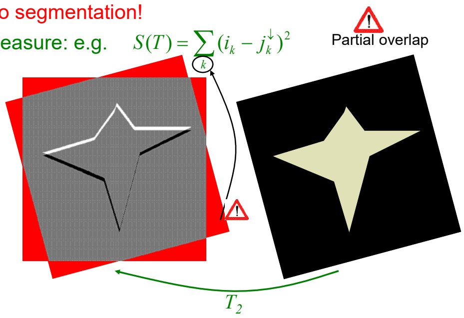
Measure: e.g. $S(T) = \sum_k (i_k - j_k^{\downarrow})^2$



Feature-based/Image-based approach

No segmentation!

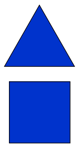
Measure: e.g. $S(T) = \sum_k (i_k - j_k^{\downarrow})^2$



Classes of Transformations T

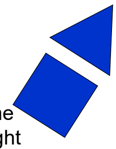
- Rigid (displacement)
- Similarities
- Affine (projective for 2D / 3D)
- Polynomials
- Splines
- Free-form deformations

Classes of Transformations T



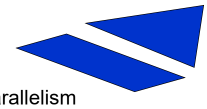
Rigid: $T(x) = Rx + t$

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



Affine: $T(x) = B.x + t$

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



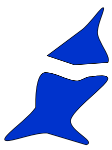
Classes of Transformations T

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,…)

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

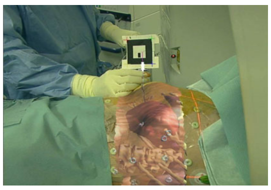
Liver puncture guidance using augmented reality

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]

Intensity-based methods

No geometric feature extraction

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

Drawbacks:
- All voxels must be taken into account

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

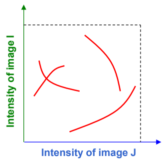
Woods' criterion (1993)
Woods' variants (Ardekani, 95; Alpert, 96; Nikou, 97)
Correlation ratio (Roche, 98)

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

Classification of existing measures

Assumed relationship

Statistical

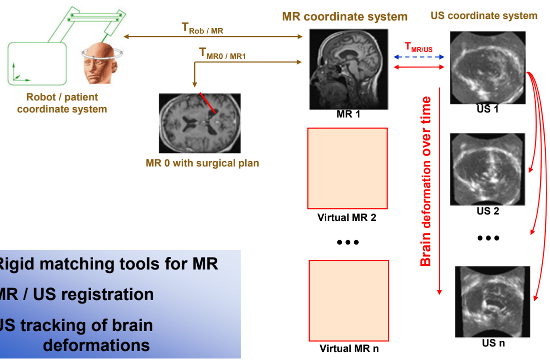


Adapted measures

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

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

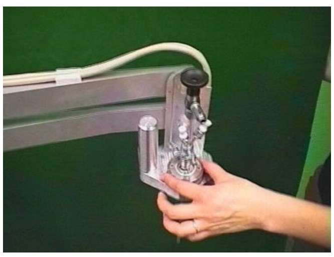
Roboscope



- 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

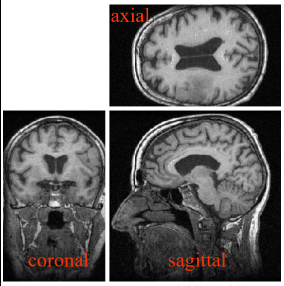
Manipulator

Steady Hand Motion Compensation
Active Motion Constraints

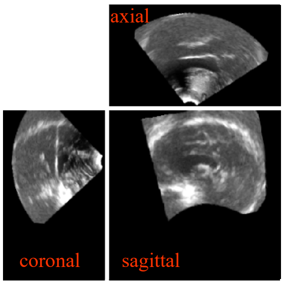
Courtesy B. Davies & S. Starkie

MR-US Images

Pre - Operative MR Image



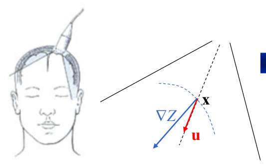
Per - Operative US Image



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

Ultrasound image / MRI registration

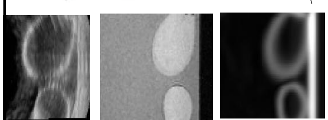
Elementary principles of US imagery



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

Logarithmic compression

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



US MRI Grad MRI

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

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

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

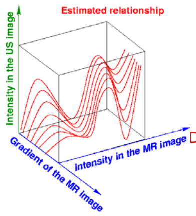
I function of 2 variables

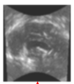
$$I = f(J, |\nabla J|)$$

2 iterated stages

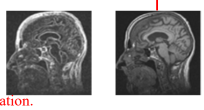
- Robust polynomial approx. of f
- Estimation of T:

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





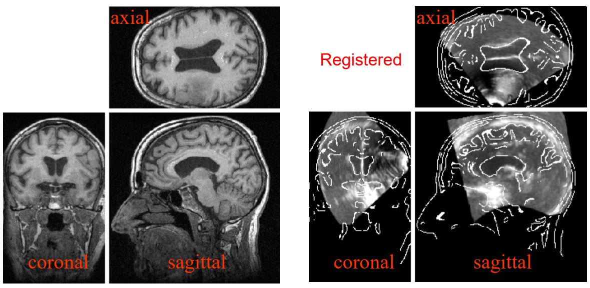
Dependency Hypothesis



A. Roche, X. Pennec, G. Malandain, and N. A.
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.

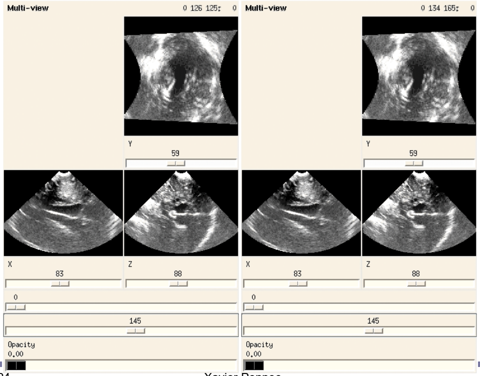
Typical Registration Result with Bivariate Correlation Ratio

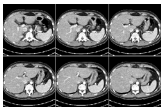
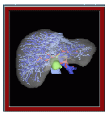
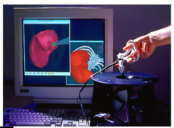
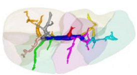
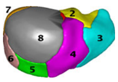
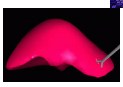
Pre - Operative MR Image Per - Operative US Image



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

US Intensity
MR Intensity and Gradient



On line references and reports
http://www-sop.inria.fr/epione/