Computational Anatomy & Physiology

M2 BioComp 2013-2014

http://www-sop.inria.fr/teams/asclepios/cours/M2-CompBio-2013-2014/

X. Pennec

Introduction to medical image acquisition & treatment

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

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Computational Anatomy & Physiology
M2 BioComp

- Tue. Oct. 1 (9-12 AM): Introduction to Medical Image Analysis [XP]
- Tue. Oct 8 (9-12 AM): Medical Image Registration [XP]
- Tue. Oct 29 (9-12 AM): Biomechanics [HD]
- Tue. Nov 5 (9-12 AM): Statistics on Riemannian manifolds and Lie groups [XP]
- Tue. Nov 12 (9-12 AM): Manifold valued image processing: the tensor example [XP]
- Tue. Nov 19 (9-12 AM): Non-linear registration and statistics on deformations [XP]
- Tue. Nov 26(9-12 AM): Cardiac & Tumor Growth Modelling [HD]
- Tue. Dec 3(9-12 AM): Exam [Xavier Pennec & Herve Delingette]

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Course overview

- → **Introduction**
- **Image acquisition**
  - Tomography
  - Nuclear medicine
  - MRI
- **Image processing**

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1632…

Rembrandt: The anatomy lesson of Dr. Tulp

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1895

Roentgen

First Nobel prize
in Physics in 1901

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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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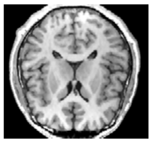
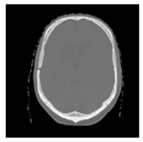
Today

MRI



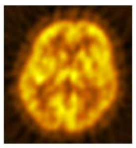
Density and structure of protons

X-Scan



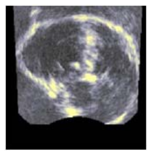
X-ray absorption density

PET / SPECT



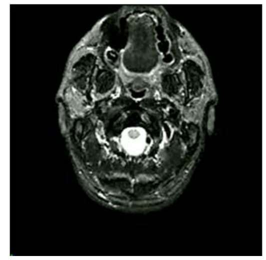
Density of Radioactive isotopes

Ultrasounds



Variations of acoustic impedance

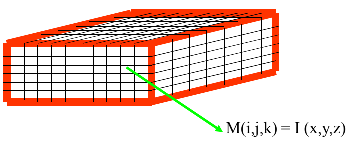
Volumetric images



T2 MRI

Volumetric images

Discrete representation of part of a body described by a 3 dimensional matrix of voxels



I(x,y,z) measures some physical, chemical properties of the human body in one volume element

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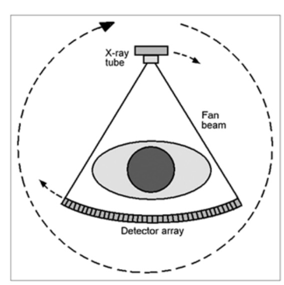
- **Image processing**

Tomography

Reconstruction from projections

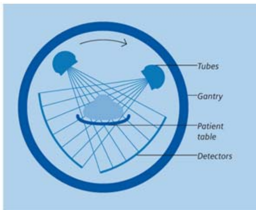
- **X-Scan (tomodensitometry)**
- **Nuclear medicine**
- **MRI (historical)**

Tomography



Sequential CT

X-ray tube and detectors rotate 360 deg
Patient table is stationary
Produce one cross-sectional image
Move table and acquire next slice



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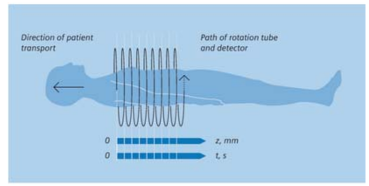
Spiral (3D) CT

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



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1D Fourier Transform

- Direct

$$f(x) \xrightarrow{TF_{1D}} F(X) = \int_{-\infty}^{+\infty} f(x) e^{-i2\pi xX} dx$$

- Inverse

$$F(X) \xrightarrow{TF_{1D}^{-1}} f(x) = \int_{-\infty}^{+\infty} F(X) e^{i2\pi xX} dX$$

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Fourier for tomography

The 1D Fourier transform of a 1D projection of the original 2D image is equal to the 1D slice in the same direction of the 2D Fourier transform of the original image.

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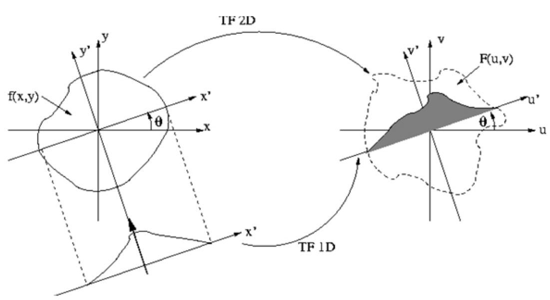
Fourier for tomography



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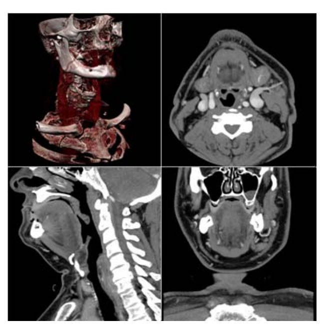
Tomotensitometrie (Scanner X)



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Course overview

- **Introduction**
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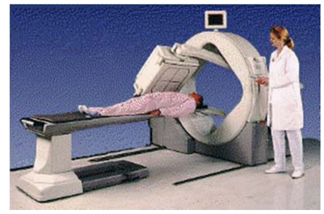
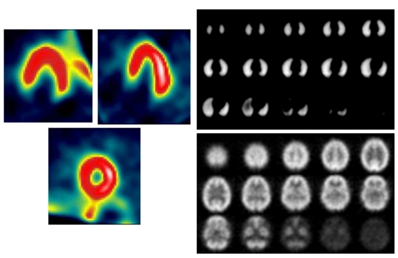
  - Tomography
  - Nuclear medicine
  - MRI
- **Image processing**

Nuclear Medicine

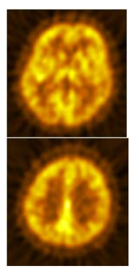


Density of radioactive tracers

Nuclear Medicine



SPECT: (gamma camera) Single photon emission tomography



PET: Positron emission tomography

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

Nuclear Medicine / radioactivity

- **Radioactive Decay Law**

- $N(t)$: number of radioactive nuclei
- N_0 : number of nuclei at $t=0$
- λ : radioactive constant (probability of disintegration)

$$N(t) = N_0 e^{-\lambda t}$$

- T : half-life period $\lambda T = \ln(2)$

Principle of gamma imaging

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

Vector Molecule	⇒	Targets organ
Radio-isotope	⇒	Detection of the molecule

- **Emission imaging : the targeted organ emits the γ**
- **Artefacts :**
  - Diffusion into the body
  - Auto-attenuation by the organ
  - distortion dues to the detector (γ-camera)

Principle of gamma imaging

- **Information given by the image**

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

- **Vector molecules :**

  drug, protein, blood cells, ...

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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)**

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Single photon gamma imaging

- **Detection**

  γ-camera: scintillation crystals (NaI), photomultiplicators
  Collimators: to measure the γ rays arriving in a known direction (tomography assumptions)

- ***Single Photon Emitting Computed Tomography (SPECT)***

- **Images = projection of the volume on a plane**

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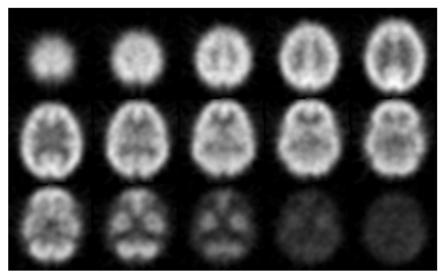
Single photon gamma imaging



Brain
Necrosis: hypo fixation **Tumor:** hyper fixation

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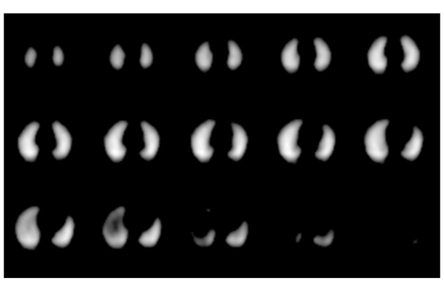
Single photon gamma imaging

Lungs



- **Bronchopneumopathy:** change of texture
- **Pulmonary embolism:** change of morphology

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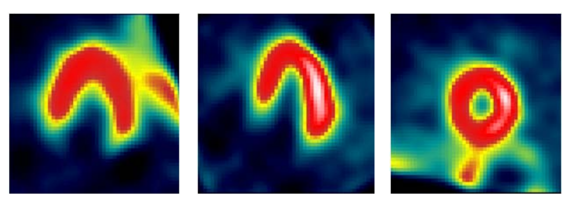
Single photon gamma imaging



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

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Positron emission tomography (PET)

- **Radio-isotopes**

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

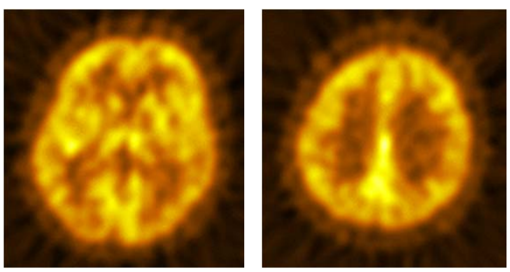
Positron emitters

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)

Positron emission tomography (PET)

- **Physiological molecules**
  - water → H_2O^{15}
  - glucose → fluoro-deoxyglucose ($F^{18}DG$)
- **Detection**
  Positron camera: scintillation crystals (NaI) and photomultiplicators *diametrically opposed* .
  Detection of coinciding of annihilation photons
- **Image(s) = projection of the radioactive volume on a plane**

Positron emission tomography (PET)



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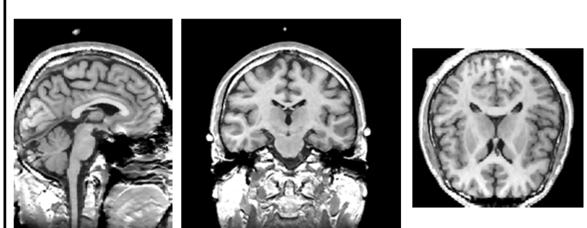
  - MRI
- **Image processing**

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

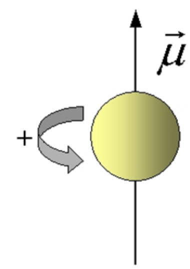
Plan du Cours

- **Introduction**
- **Tomography**
- ➔ **MRI**
  - Magnetic resonance
    - The molecular level
    - The macroscopic level
    - resonance
- **Nuclear medicine**

Magnetism at the molecular level

Electric charges in motion:

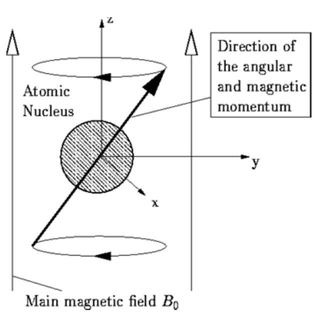
- magnetic momentum



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**

$$\vec{\mu} = \gamma \, \vec{S}$$

$\vec{\mu}$ Nuclear magnetic momentum

γ Gyromagnetic ratio

- **Fundamental motion equation**

$$\frac{d\vec{S}}{dt} = \vec{m}$$

$\vec{S}$ Angular speed (spin)

$\vec{m}$ Momentum (mechanic)

- **In a magnetic field** $\vec{m} = \vec{\mu} \times \vec{B}$

Bloch's Equations

Thus $\frac{d\vec{\mu}}{dt} = \gamma\left(\vec{\mu} \times \vec{B}\right)$

$$\vec{B}_0 = \begin{pmatrix} 0 \\ 0 \\ B_0 \end{pmatrix} \Rightarrow \vec{\mu} = \begin{pmatrix} \mu_t \cos(\omega_L t + \varphi) \\ -\mu_t \sin(\omega_L t + \varphi) \\ \mu_{z_0} \end{pmatrix}$$

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

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Magnetism at the molecular level

Nucleus	%	γ (MHz/T)
^{1}H	99.985	42.575
^{2}H	0.015	6.53
^{13}C	1.108	10.71
^{14}N	99.63	3.078
^{15}N	0.37	4.32
^{17}O	0.037	5.77
^{19}F	100	40.08
^{23}Na	100	11.27
^{31}P	100	17.25

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Magnetism at the macroscopic level

Macroscopic magnetic momentum

$$\vec{M} = \sum_{i=0}^{N} \vec{\mu}_i \qquad \frac{d\vec{M}}{dt} = \gamma\left(\vec{M} \times \vec{B}\right)$$

Component is negligible orthogonally to B_0

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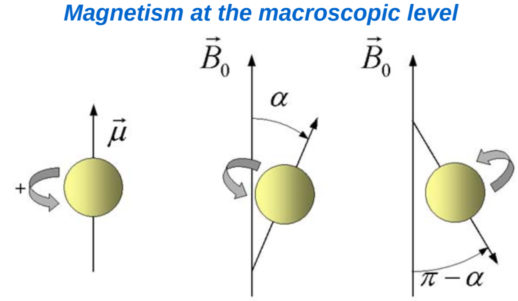
Magnetism at the macroscopic level



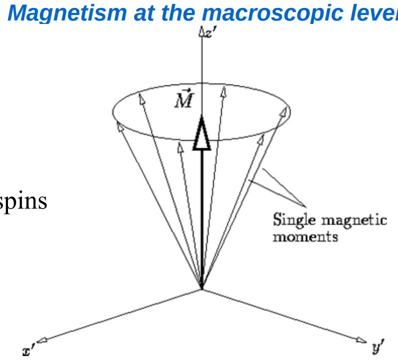
$P_{+1/2}$=0.5000049

B_0=1.5 T

$P_{-1/2}$=0.4999951

Magnetism at the macroscopic level

10^{23} spins



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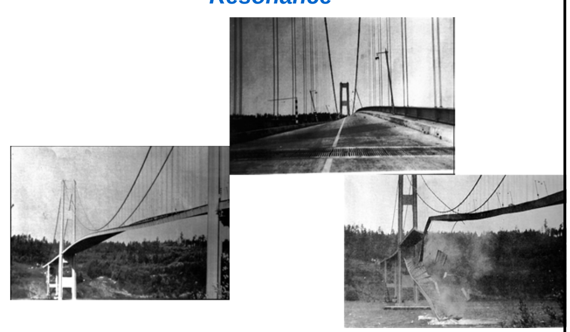
Resonance



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Magnetic Resonance / excitation

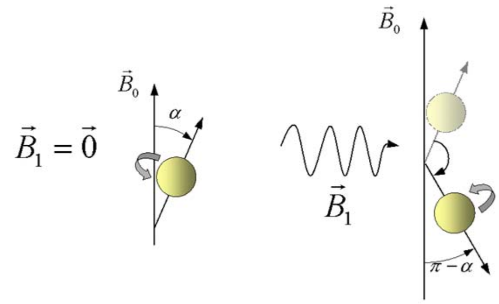
- Electro-magnetic field at Larmor's frequency

$\omega_L = \gamma B_0$

- Hydrogen protons enter into resonance

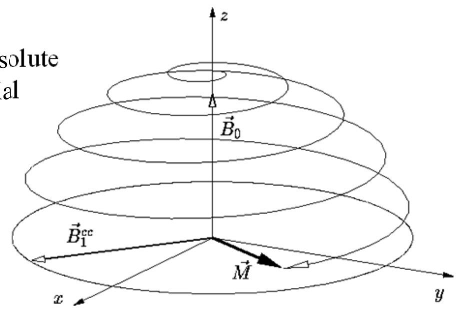
Flip of the macroscopic momentum M

Magnetic Resonance / excitation



Magnetic Resonance / excitation

In an absolute referential



Magnetic Resonance / relaxation

- Return to equilibrium / B_0: time constant T_1

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

- Spin dephasing: Time constant T_2

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

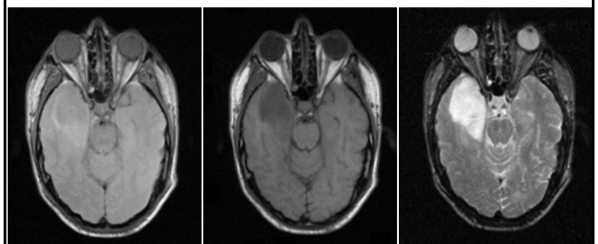
Magnetic Resonance / relaxation

TISSUE	T1 (ms) 0.5 T	T1 (ms) 1.5 T	T2(ms)
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 / frequency selection

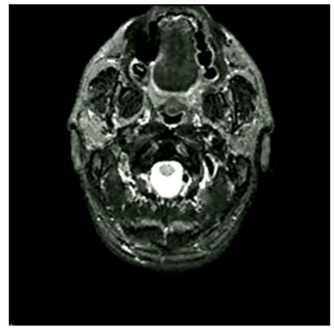
- **X encoding by frequency**
- **Y encoding by phase**
- **Several measures are necessary**

Anatomical MRI



Proton density | T_1 | T_2

Anatomical MRI

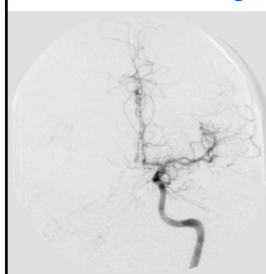


Angiographic MRI

- INFLOW
- Phases

Maximum intensity projection (MIP)

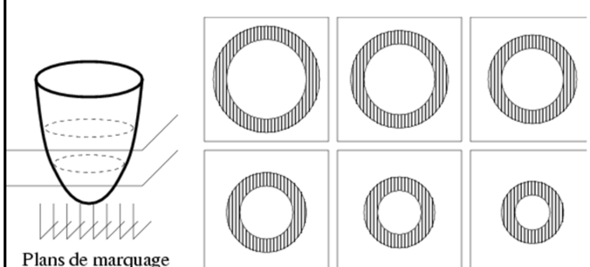
Angiographic MRI



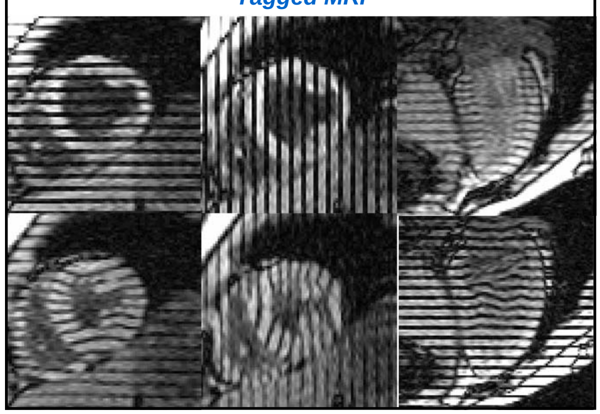
X-Scan / radiology

Selective injection of a contrast agent in one artery

Tagged MRI



Tagged MRI



Functional MRI

- BOLD : blood oxygen level dependent
  - (oxy)-hemoglobin: diamagnetic
  - deoxy-hemoglobin: paramagnetic

Neuronal activation
- Local oxygen consumption
- Change the ratio of concentration
- Variation of the measured signal

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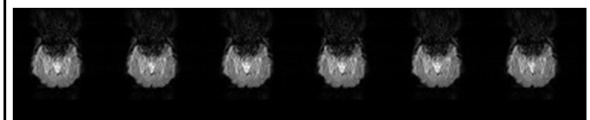
Functional MRI

- Variation of 1-5% for B0= 1.5 T (~ noise)
- Variation of 5-20% for B0= 4.0 T



- Statistical analysis on large series
- Motion and intensity biases correction…

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More information

http://en.wikipedia.org/wiki/Magnetic_resonance_imaging

http://en.wikibooks.org/wiki/Basic_Physics_of_Nuclear_Medicine

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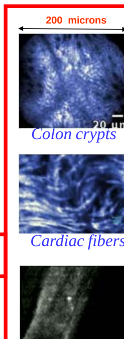
New images

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



Colon crypts
Cardiac fibers
microvessels

Source : Mauna Kea Technologies

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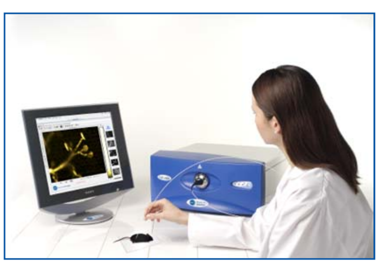
In Vivo *Cellular & Molecular Imaging*



In vivo, in situ fibered confocal microscopy

CellVizio, Mauna Kea Technologies, Paris

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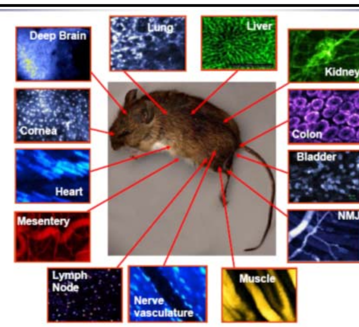

Figure 19.6: Different types of images from Leica FCM1000 microscope (Cellvizio® technology for small animal distributed by Leica microsystems).

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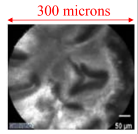
In vivo *Clinical Microscopic Imagery*



gastro-esophagus Mucosa

Pr A. Meining, Munich

Cellvizio®, Mauna Kea Technologies (MKT) , Paris

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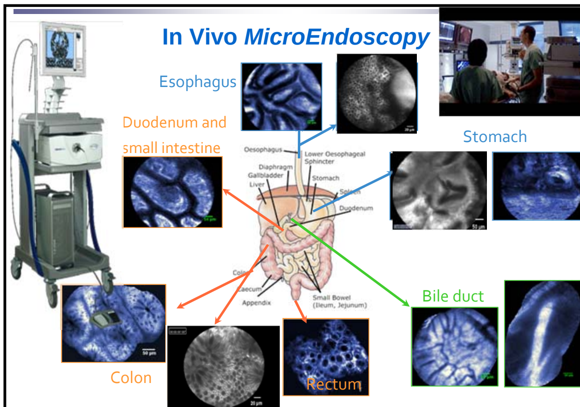
In Vivo *MicroEndoscopy*



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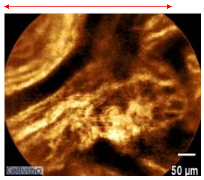
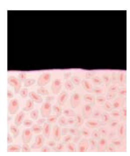
Advanced Image Processing

240 microns





Small bowel

Precision and field of view?

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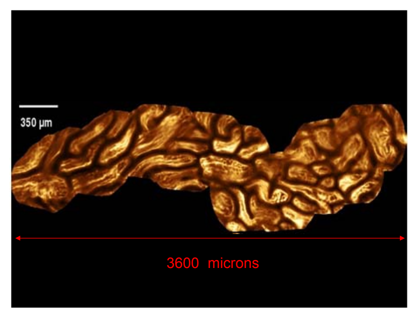
Automatic Mosaicing

Elsevier-MedIA PRIZE 2006
ITK freeware available

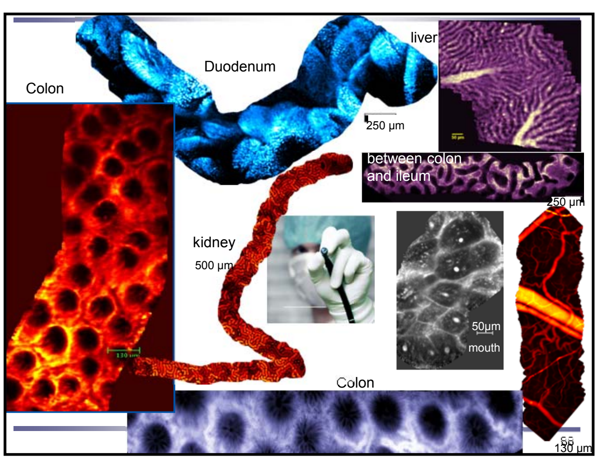
240 microns

Small bowel



T. Vercauteren, A. Perchant, X. Pennec, G. Malandain, N. Ayache, *Robust Mosaicing with Correction of Motion Distortions and Tissue Deformation for In Vivo Fibered Microscopy.* Medical Image Analysis, October 2006.

87



Course overview

- **Introduction**
- **Image acquisition**
  - Tomography
  - Nuclear medicine
  - MRI
- → **Image processing**

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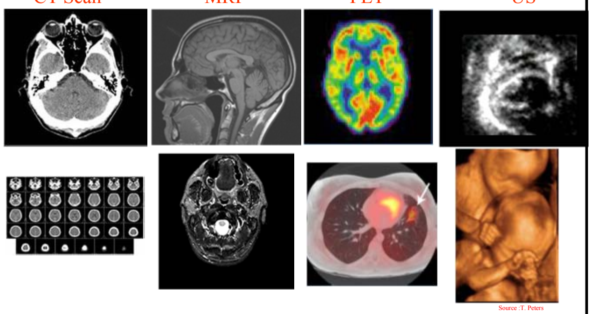
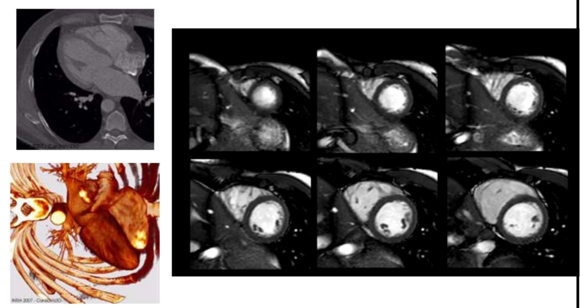
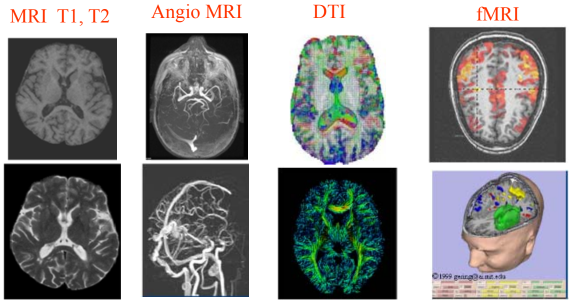
3D image modalities



4-D Images



Multiparametric Images



Medical Imaging Today

Large Choice of *in vivo* modalities
High temporal and spatial resolution
Large parameter space
Large Databases
Image-guided Therapy

Da Vinci Surgical Robot

Quantity of information too high : cannot be processed without the help of computer science

Computational Medical Image Analysis (1980 - Today)

Assist Diagnosis

- Objective quantitative measurements
- fusion of multimodal, multidimensional, multiparameter images

Assist Therapy

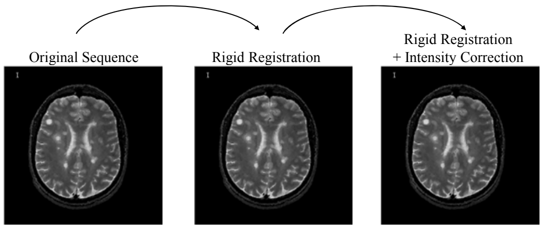
- Plan, simulate *(before)*
- Control *(during),* follow-up *(after)*

J. Duncan & N. A, *Medical Image Analysis, Progress over two decades and the challenges ahead,* IEEE – Pami, 2000.

Classification of 3D image processing problems

- Segmentation (organs, lesions, activations,…)
- Registration (comparison, fusions)
- Motion analysis (cardiac imaging)
- Deformable models (Surgery simulation)
- Medical Robotics (image guided surgery, telesurgery…)

Spatio-Temporal Cartography of Multiple Sclerosis Lesions 1/3

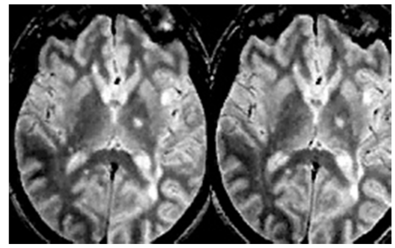


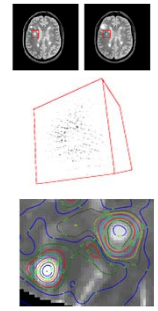
Patient Followed during 18 months (24 acquisitions)

Collaboration INRIA with Ron Kikinis, SPL

X Pennec, N A and JP Thirion. Landmark-based registration using features identified through differential geometry. In Handbook of Medical Imaging, 2000.

Spatio-Temporal Cartography of Multiple Sclerosis Lesions 2/3





Residual apparent deformations

J.-P. Thirion and G. Calmon. Deformation Analysis to Detect and Quantify Active Lesions in Three-Dimensional Medical Image Sequences. IEEE Transactions on Medical Imaging, 18(5):429-441, 1999.

Spatio-Temporal Cartography of Multiple Sclerosis Lesions

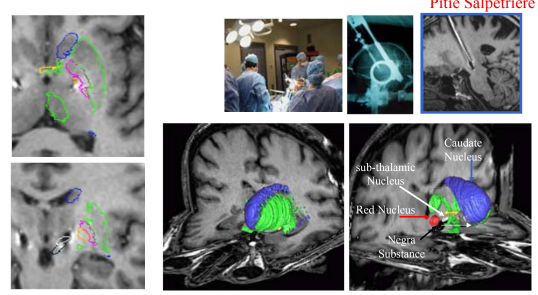
Collaboration with Ron Kikinis, SPL

D. Rey, G. Subsol, H. Delingette, N.A : *Automatic Detection and Segmentation of Evolving Processes in 3D Medical Images: Application to Multiple Sclerosis.* Medical Image Analysis, 6(2):163-179, June 2002.

Image-Guided Neurosurgery

Electrostimulation of Parkinson Patients

INRIA
Pitié Salpêtrière



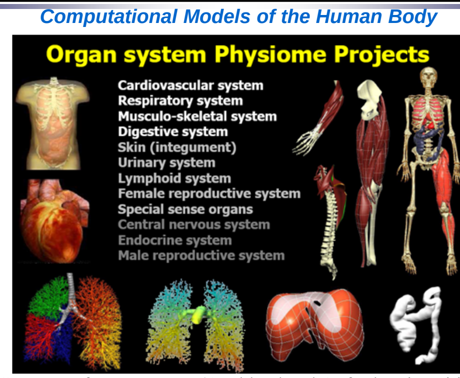
J Yelnik, E Bardinet, D Dormont, G Malandain, S Ourselin, D Tande, C Karachi, N Ayache, P Cornu, Y Agid. *A three-dimensional, histological and deformable atlas of the human basal ganglia. I. Atlas construction based on immunohistochemical and MRI data.* Neuroimage, 2007

Medical robotics

Da Vinci

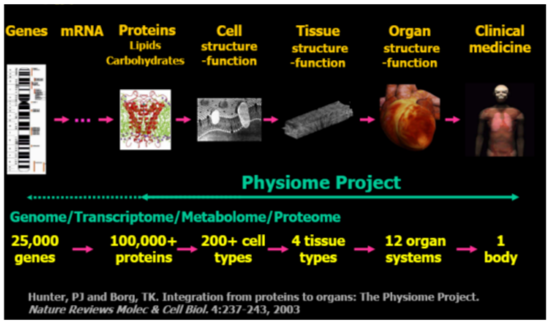
Zeus

Computational Models of the Human Body

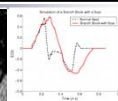


Courtesy of Peter Hunter (Auckland and Oxford Universities)

Computational Models of the Human Body

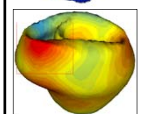


Courtesy of Peter Hunter (Auckland and Oxford Universities)

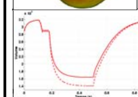



Normal/abnormal ECG

Ischemia



Pathological depolarization pattern



Reduced ejection fraction

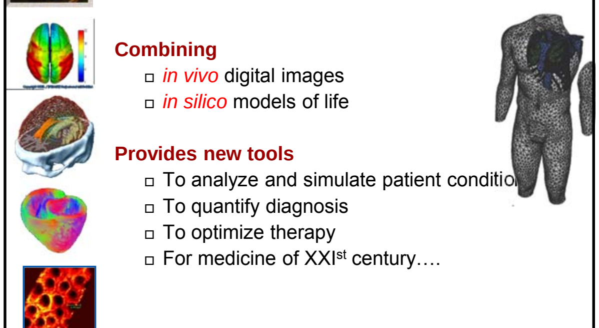
Grand Challenge : *Link Models to Images*

Build *patient-specific* computational models from biomedical signals and images
(Image Analysis, Data Assimilation)

Towards a more personalized and predictive medicine

- explain observations
- detect pathologies before symptoms
- predict evolutions *(in silico models)*
- simulate therapies and evaluate

Virtual Physiological *Patient*



Combining

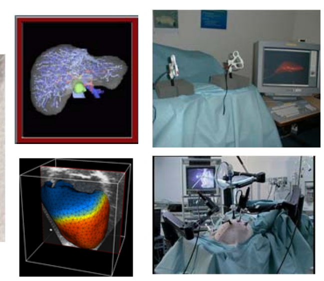
- *in vivo* digital images
- *in silico* models of life

Provides new tools

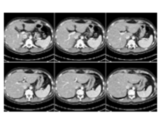
- To analyze and simulate patient conditio
- To quantify diagnosis
- To optimize therapy
- For medicine of XXIst century….

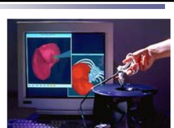
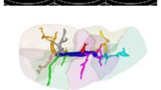
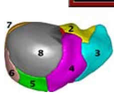
Conclusion

Cut before Seeing
(courtesy of Rembrandt)

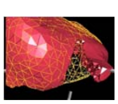
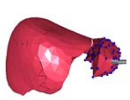
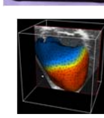


See, Measure and Simulate before (Minimal) Cutting




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

Computational Anatomy & Physiology
M2 BioComp

Tue. Oct. 1 (9-12 AM): Introduction to Medical Image Analysis [XP]

Tue. Oct 8 (9-12 AM): Medical Image Registration [XP]

Tue. Oct 29 (9-12 AM): Biomechanics [HD]

Tue. Nov 5 (9-12 AM): Statistics on Riemannian manifolds and Lie groups [XP]

Tue. Nov 12 (9-12 AM): Manifold valued image processing: the tensor example [XP]

Tue. Nov 19 (9-12 AM): Non-linear registration and statistics on deformations [XP]

Tue. Nov 26(9-12 AM): Cardiac & Tumor Growth Modelling [HD]

Tue. Dec 3(9-12 AM): Exam [Xavier Pennec & Herve Delingette]