1: Introduction to the course

- How is the course organized ?
1. What is Bio-imaging ?
2. How can SNR and CNR be optimized ?
3. What is the importance of biomedical imaging ?
4. Examples
- Tour of the Imaging Centre (CIBM)

After this course you
1. know the course organization and coverage of topics;
2. know the contribution of bio-imaging to life science and why it is an interdisciplinary effort.
3. know the main elements required for bio imaging;
4. are able to perform contrast to noise and signal to noise calculations;
5. are familiar with noise error propagation calculations

How is the course organized ?

Course **web site** (moodle, physics, master):
moodle.epfl.ch/course/view.php?id=250
If you are not enrolled yet :
Enrollment key = bioimaging16

Copies of parts of the presentation
Will be provided on moodle (pdf)
Please take notes during lecture !!

Exercises (Fri 15:15 CE 104):
Handed out by assistant on day of lecture
Available on moodle
Solution of selected problems of prior week

If you miss a course …
The course given was filmed and is available on youtube/google+
the link is provided on moodle for each lecture

What is the content of this course ?

Theme	Elements
Introduction (Lectures 1-2)	Definition and importance of bio-imaging Ultrasound imaging Basis of x-ray imaging
X-ray imaging (Lectures 3-7)	Interactions of photons with matter/Radioprotection X-ray imaging (computed tomography) Emission computed tomography Positron emission tomography Tracer dynamics
Magnetic resonance I Basics (Lectures 8-10)	Basis of magnetic resonance effect T_1 and T_2 relaxation Spectroscopy Echo formation
Magnetic resonance II Advanced topics and contrast mechanisms (Lectures 11-13)	Elements of image formation Biophysics of BOLD Contrast agents Diffusion tensor imaging

Links

Life science @ EPFL
- Systems and signals
- Image processing
- Mathematical and computational models in biology

Physics
- Neural networks and biological modeling
- Classical electrodynamics

What supplemental reading/material is recommended ?

I will provide pdf versions of the lecture on moodle

Handouts without your personal notes will not be complete.

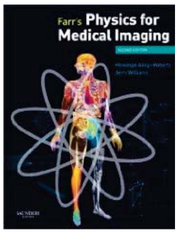
To complete the Handouts

1. personal notes during course
2. incorporate insights gained during exos

For a shorter text: Penelope Allisy-Roberts, Jerry Williams "Farr's Physics for Medical Imaging" (200p., small, ~EUR 50)

USD 30+ on amazon.com

A lot of focus on simple x-ray (not covered in the course)

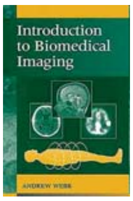


Course text:

Andrew Webb
"Introduction to biomedical imaging"
(250p. ~EUR 110, available as ebook at the library EPFL)

USD 60+ on amazon.com

- Is more complete on MRI
- Excellent reference text for later use



Other Text books

- Zhang-Hee Cho, Joie J. Jones, Manbir Singh "Foundations of Medical Imaging"
- William R. Hendee, E. Russel Ritenour "Medical Imaging Physics"
- Jerrold T. Bushberg, J. Anthony Seibert, Edwin M. Leidholt, John M. Boone "The Essential Physics of Medical Imaging"

1-1. What is Biomedical Imaging ?

Definition of bio-imaging

Localized measurement of a **contrast generating** biophysical effect in body/organ of living system

What is measured (some useful definitions)

Image=nxm matrix of pixels

Pixel = picture element

3D image=kxnxm matrix of voxels

Voxel = volume element

Important:

Contrast between voxels/pixels

In principle n,m,k can be unlimited…

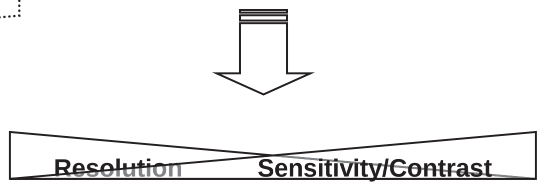
What is Contrast ?

Ability to distinguish tissue features against noise

Contrast = difference in signal between tissues one wishes to distinguish

In reality one needs to deal with Contrast-to-noise

Is there a free lunch for imaging ?



What is the difference between signal-to-noise and contrast-to-noise ratio ?

To obtain good measurements (not only in imaging) we need good signal to noise ratio

Definition

Signal-to-noise ratio (SNR)

S: signal (or measurement variable)

σ: standard deviation of its measurement (either determined experimentally (how?) or estimated quantitatively)

$$SNR = \frac{S}{\sigma}$$

SNR provides a means to estimate the precision with which the signal S is measured

It is possible to have excellent SNR but no CNR (when?)

To discriminate two signals S_1 and S_2 we need more than just good signal to noise ratio. The ability to discriminate the two is assessed using the contrast to noise ratio

Definition

Contrast-to-noise ratio (CNR)

S_1 and S_2 : two signals (or measurement variable) of two different tissues,

σ : standard deviation of their measurement (see left, assumed here to be identical and statistically independent)

$$CNR = \frac{S_1 - S_2}{\sigma}$$

CNR provides a means to estimate the precision with which the signal S_1 can be discriminated from S_2

1-2. How can we optimize SNR ?

It is possible to optimize SNR by performing N repeated measurements S_i.
The precision of the average $<S>=\sum S_i/N$ depends on the **square root law** (4 measurements improve the precision by twofold):

$$S_i=S+\varepsilon_i$$

where $<\varepsilon_i^2>=\sigma^2$, $<\varepsilon_i>=0$.

S is the true signal (unknown)

$$<S>=\sum S_i/N=S+\sum \varepsilon_i/N$$

$$\Delta S \equiv <S>-S=\frac{\sum \varepsilon_i}{N} \quad \Delta S^2=\frac{\left(\sum \varepsilon_i\right)^2}{N^2}$$

$<\varepsilon_i\varepsilon_j>=0,\ i\neq j$

$$\Delta S^2=\frac{\left(\sum \varepsilon_i^2\right)}{N^2}+\frac{\left(\sum_{i\neq j} \varepsilon_i\varepsilon_j\right)}{N^2}$$

$$\left\langle \Delta S^2\right\rangle=\frac{\sum\left\langle \varepsilon_i^2\right\rangle}{N^2}=\frac{N\sigma^2}{N^2}=\frac{\sigma^2}{N}$$

$$\left\langle \Delta S\right\rangle=\frac{\sigma}{\sqrt{N}}$$

This is well-known from statistics (SEM)
⇒ results in increased measurement time

How can we optimize CNR ?

Optimizing contrast = choice of experimental parameters (e.g. protocol) to maximize the difference in two tissue signals S_1 and S_2.

- complex and empirical procedure
- some effects can be predicted/calculated, if the signal behavior can be modeled.

Error propagation calculation
Let the signal S be a function S(k,t)
- k is a tissue property (signal decay rate)
- t an experimental parameter (such as time).

Approach:
1. Determine dS/dk
2. Find t_0 where dS/dk is maximal by taking derivative rel. to t

Example: $S(k,t)=S_0e^{-kt}$

$$\frac{dS(k,t)}{dk}=-S_0te^{-kt}$$

Maximum is where derivative with respect to t is zero

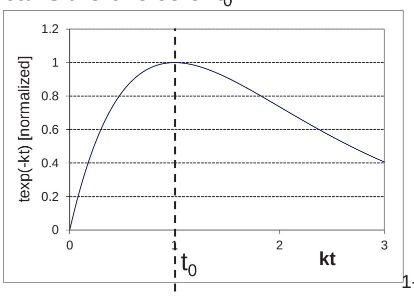
$$\frac{d}{dt}\left(-S_0te^{-kt}\right)=0$$

$$=-S_0e^{-kt}\left(1-kt\right) = 0$$

$t_0=1/k$

For an exponentially decaying signal, the optimal time of measurement is equal to 1/decay rate

How critical is the choice of t_0 ?



1-3. What is the importance of Bio-Imaging ?

Life Sciences are unthinkable without Bio-Imaging

Assessment of biological processes with **minimal** perturbation of the system

Examples:

Humans, animals,
cell/organ preparations

Modalities:

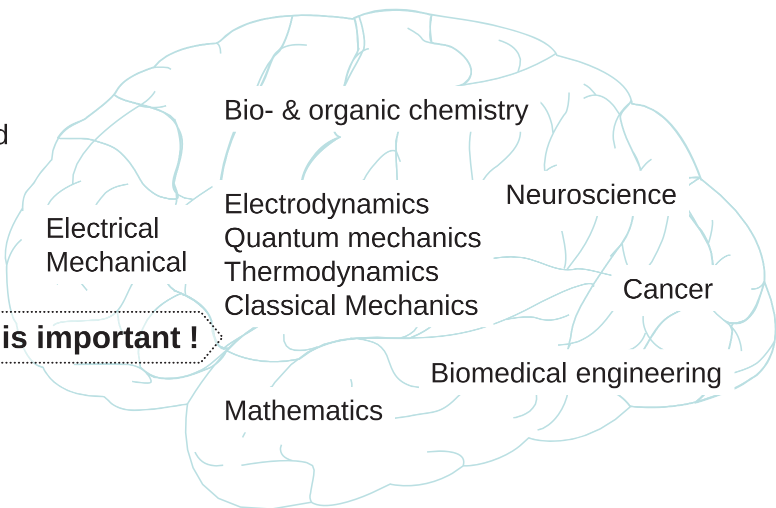
x-ray
computed tomography
positron emission tomography
magnetic resonance
ultrasound
electrical imaging (EEG, MEG)
optical imaging

Development of Bio-Imaging capabilities, modalities and effects

… unthinkable without physics

What are essential ingredients of bio-imaging ?

1. Life Sciences
2. Physics
3. Engineering/Good instrumentation
4. Mathematics
5. Chemistry



Multi-disciplinarity is important !

What is the perfect imaging modality ?

1. Easy to use
2. Portable
3. Highly sensitive/good contrast

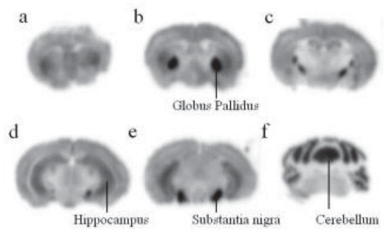
   ⇒ Does this exist ?

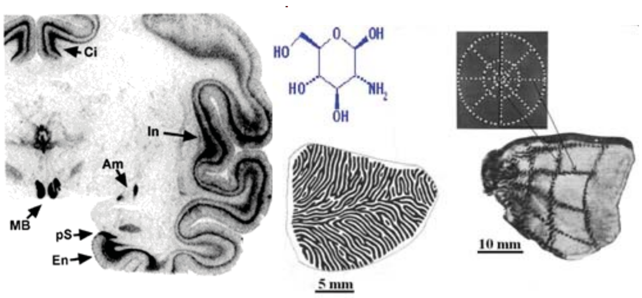
In reality,
every imaging method/modality
has its strengths and limitations

In this course you will learn to appreciate these
and the reasons behind

1-4. Examples
Autoradiography

Autoradiography of a brain slice



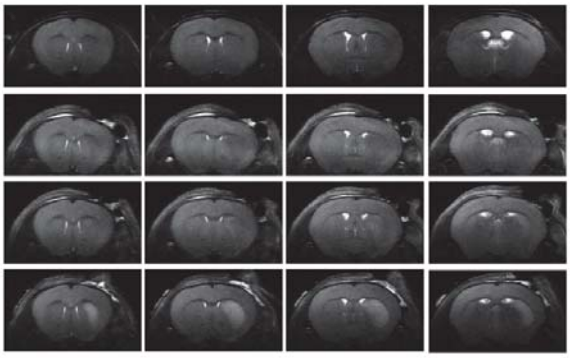


Autoradiography of a monkey brain (visual cortex)

What are the distinct advantages of Bio-imaging compared to tissue analysis ?

Mice subjected to 30 min of stroke

assessed using MRI before and 3-24h after



Histology: Tissue is fixed, cut into slices, then subjected to a dye. The resulting sections are then analyzed.

Imaging advantages

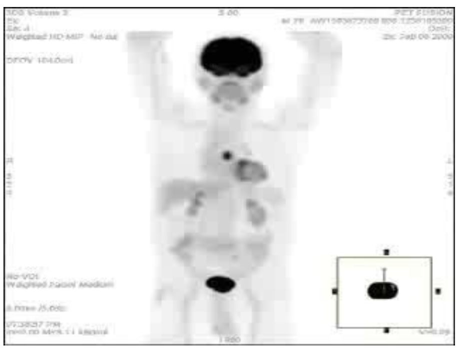
relative to histology or invasive tissue analysis

1. Rapid acquisition of the information
2. Non-destructive, i.e. minimal perturbation
3. In situ or in vivo
4. Repetitive (longitudinal) studies possible

Examples: Biomedical Imaging

http://nobelprize.org/educational_games/physics/imaginglife/narratives.html

3D rendering of tumor for surgical planning (MRI)



Metastasis localization (PET)

fMRI of whole brain activation