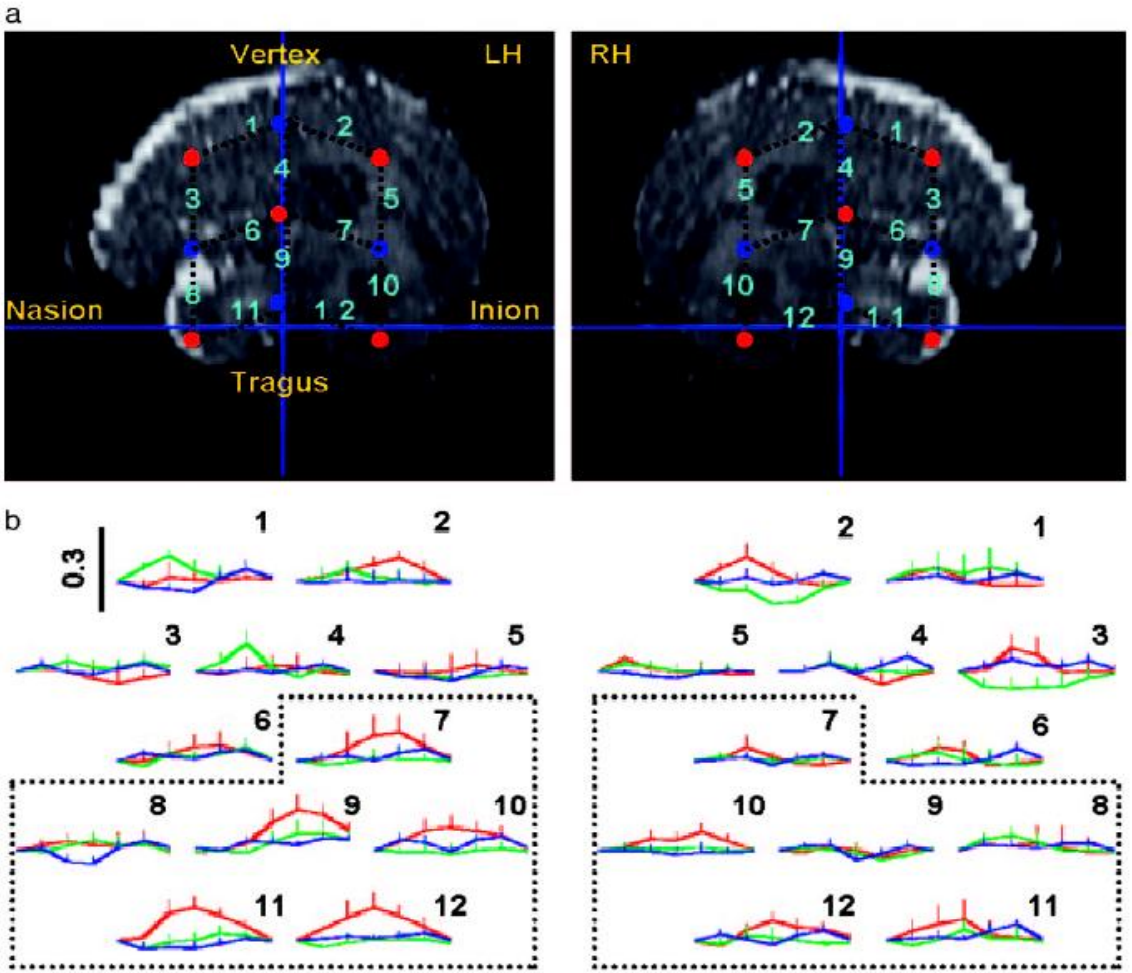
The determination of brain function is relevant to study language acquisition. Very recently it has been shown, that this can be done via optical methods.

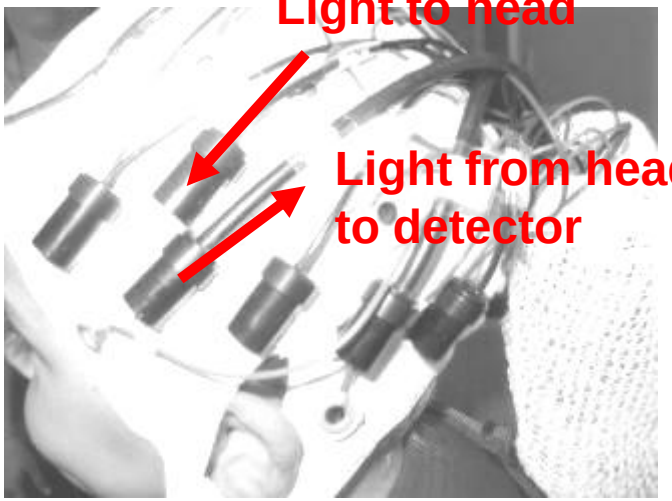
Application



M. Pena, … , J. Mehler 2003, PNAS

Technology wise the method is based on determining ‚transflected' intensity changes.

Technology

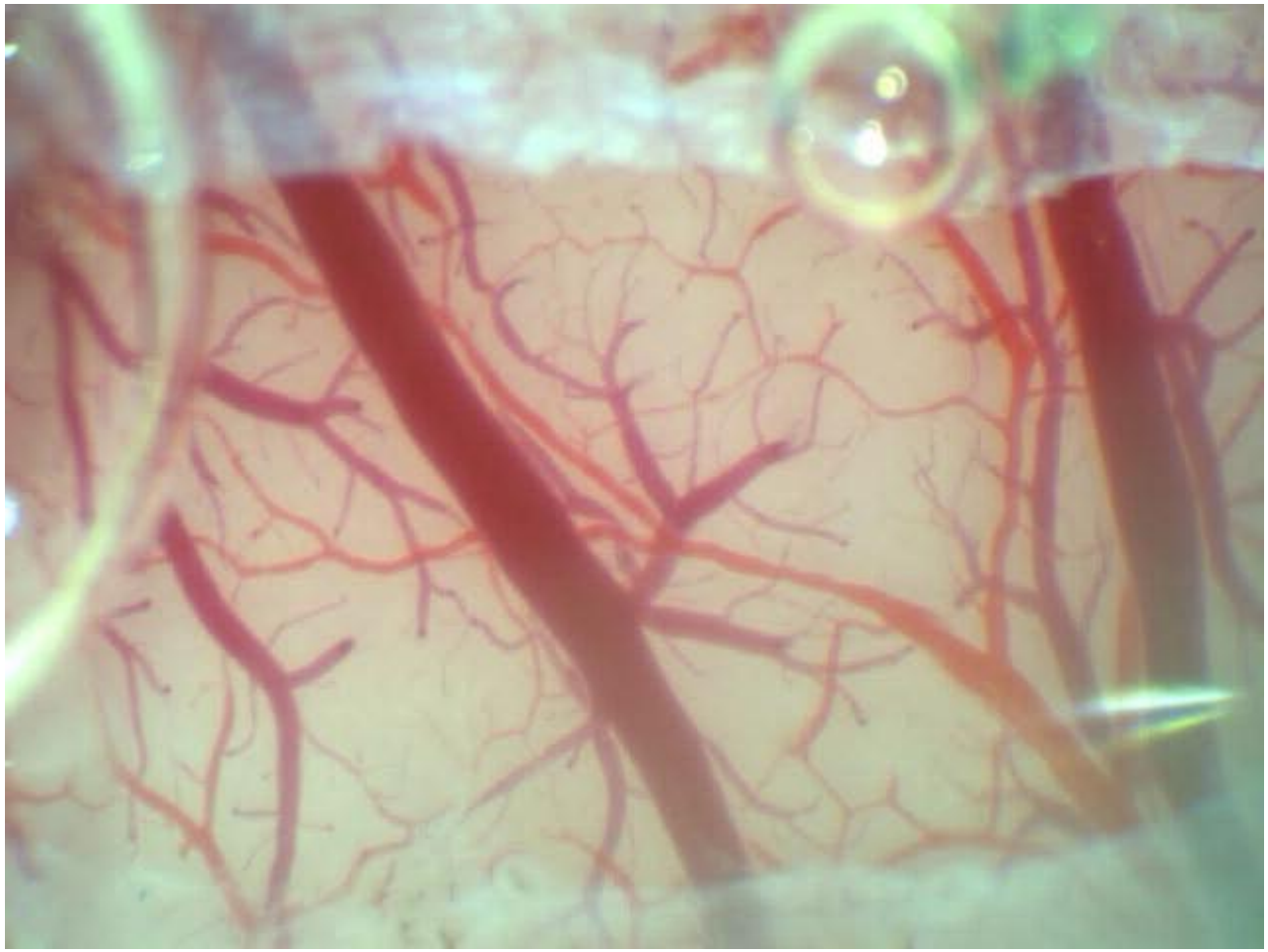


NIRS-probe arragement

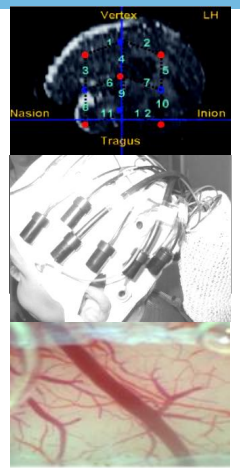
Wartenburger, … ,Obrig, Neuroimage. 2007

The contrast is based on a change in the hemoglobin concentrations.

Physiology



BNIC/Charité



When the Brain Turns Red or Pale: Introduction to Non-Invasive Optical Brain Imaging

Jens Steinbrink, Berlin NeuroImaging Center

BIOMED, 2008

Many names have been used to describe the method, each having certain advantages. In this talk I will use the term ‚Optical Topography‘

Names

Near Infrared Spectroscopy (NIRS)

Diffuse Optical Imaging (DOI)

Diffuse Optical Topography (DOT)

Optical Imaging (OI, mostly invasive)

Optical Topography (OT)

Agenda

Non-invasive Optical Imaging – Intro & History
- Invasive Imaging
- Equations
- Applications

Novel Technological Improvement
- Hyper-resolution
- Depth Resolution
- Portability

Other Contrasts
- Cytochrome Oxidase
- Scattering Changes
- Dynamic Scattering Changes
- Fluorescence (endogenous)
- Fluorescence (exogenous)

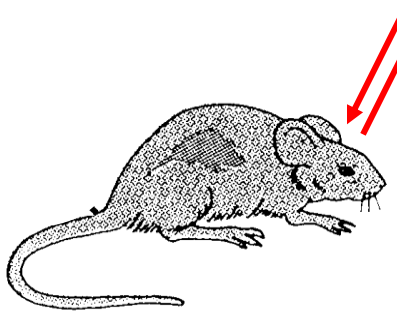
Clinical Applications

Brain Computer Interface

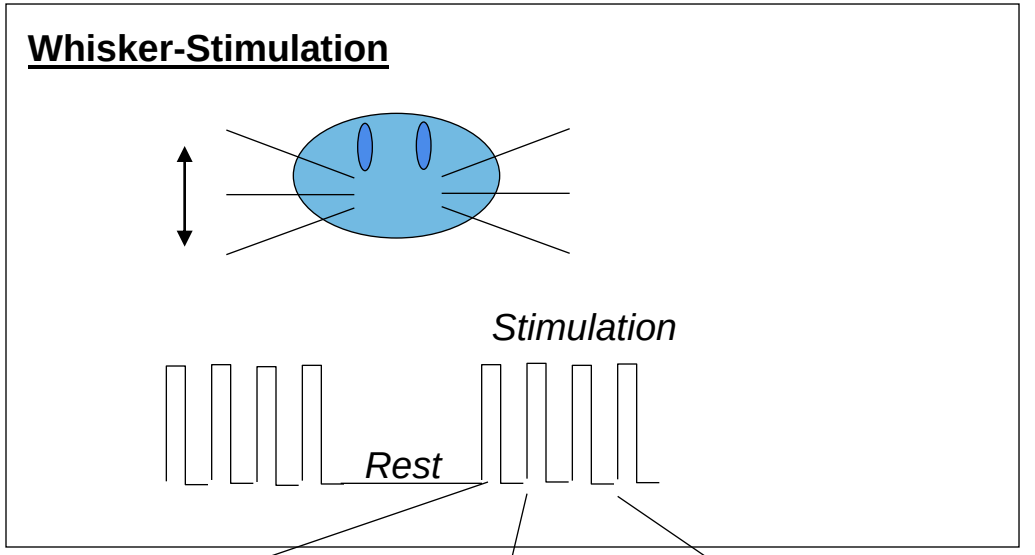
Small changes in color during a functional activation.

Invasive optical Imaging -- Principle

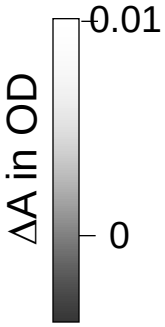
Set-up



Whisker-Stimulation



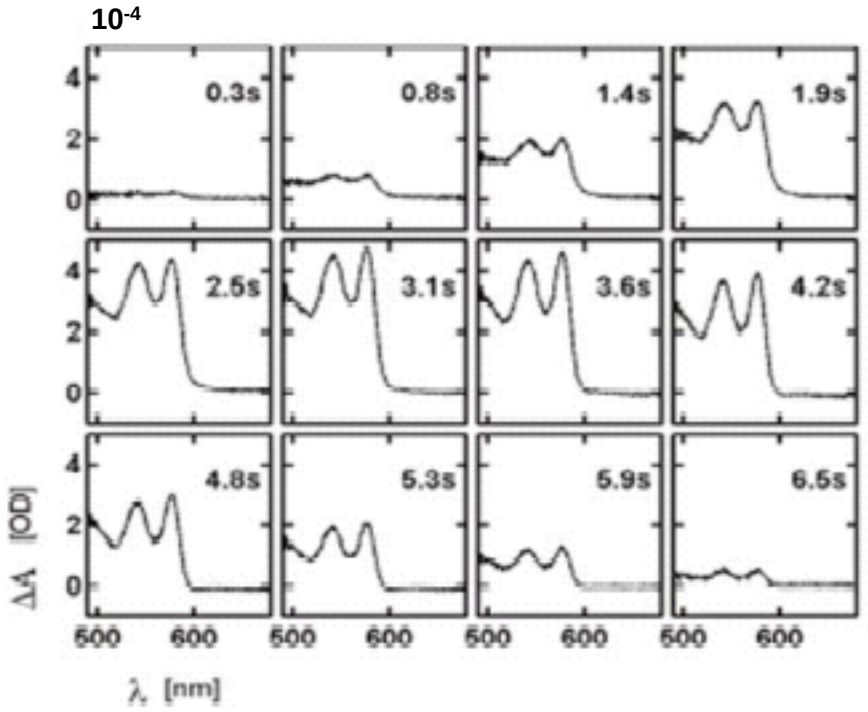
Intensity Change



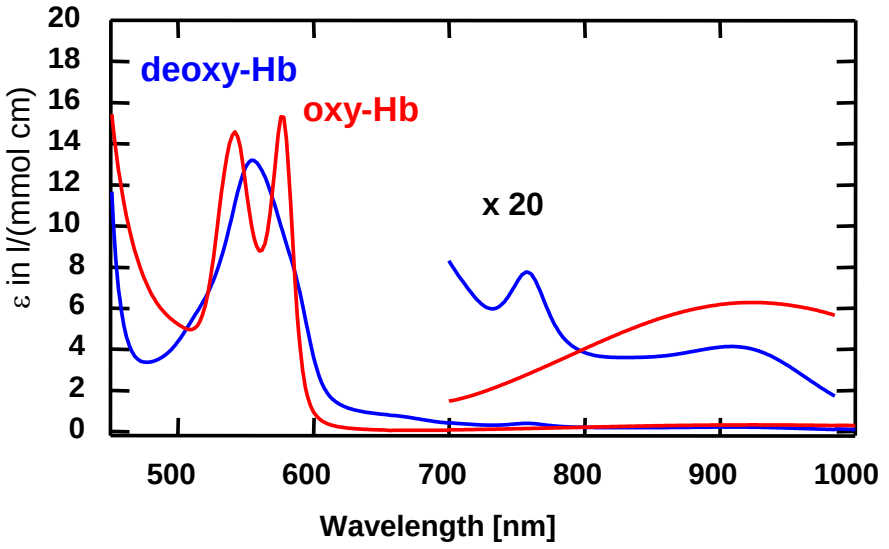
The changes in the reflections spectrum are similar to the extinction-coefficient of oxy-hemoglobin and deoxy-hemoglobin.

Invasive optical imaging -- spectroscopy

Spectral Absorption Change



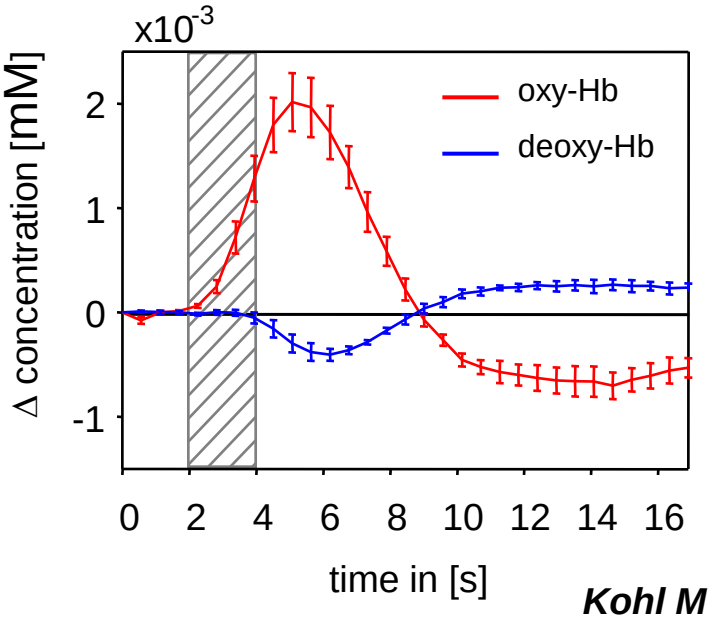
Extinction-Coefficients



One can find an increase in oxy- and a decrease in deoxy-hemoglobin.

Invasive optical imaging (Result)

*Wavelength-**dependent** pathlength:*



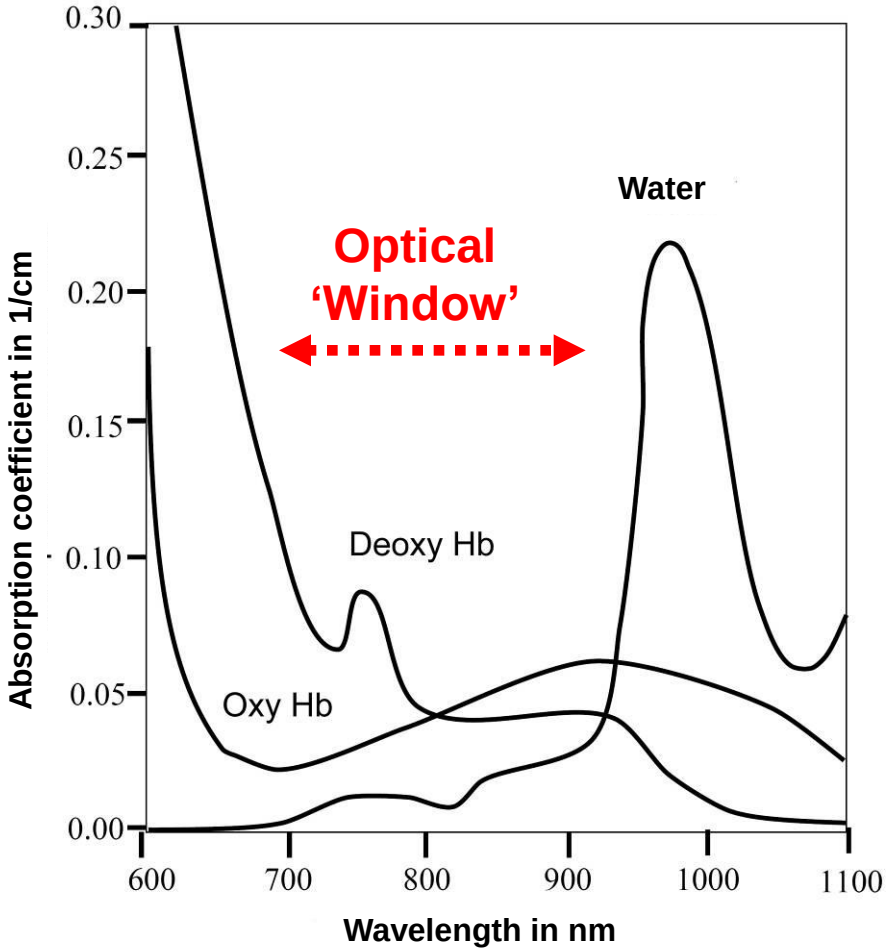
Increase in Oxyhemoglobin
and wash-out of deoxy-hemoglobin
caused by increase in blood flow.

Kohl M ,.. , Dirnagl U. Phys. Med. Bio. 2000

See also: BME2/Monday, 4:45 p.m. - 5:15 p.m.—*Multidimensional Functional Optical Imaging of the Brain* --Elizabeth M. Hillman1, et. al.

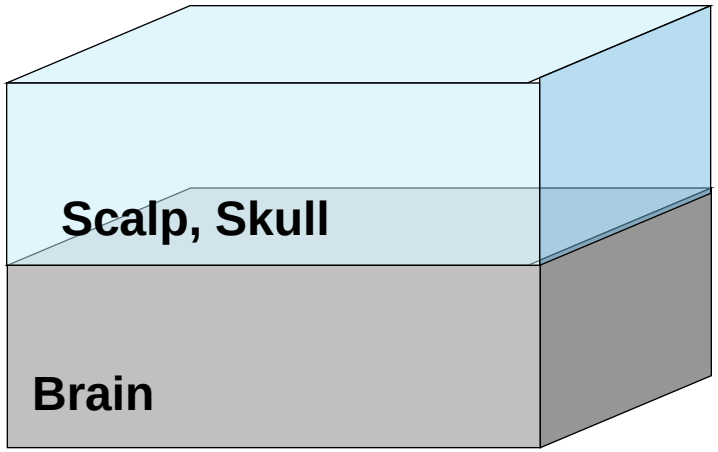
The absorption by tissue is low in the near infrared thus allowing to look onto the brain through the skull and scalp.

Definition of the optical ‘window’

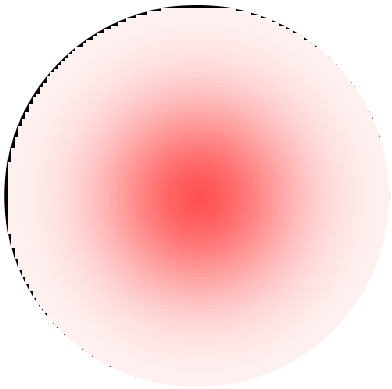


However the spatial resolution is limited due to large light scattering.

‚Blurring' by scattering



Milkglas (ca. 10mm)



Agenda

Non-invasive Optical Imaging – Intro & History

- Invasive Imaging
- Equations
- Applications

Novel Technological Improvement

- Hyper-resolution
- Depth Resolution
- Portability

Other Contrasts

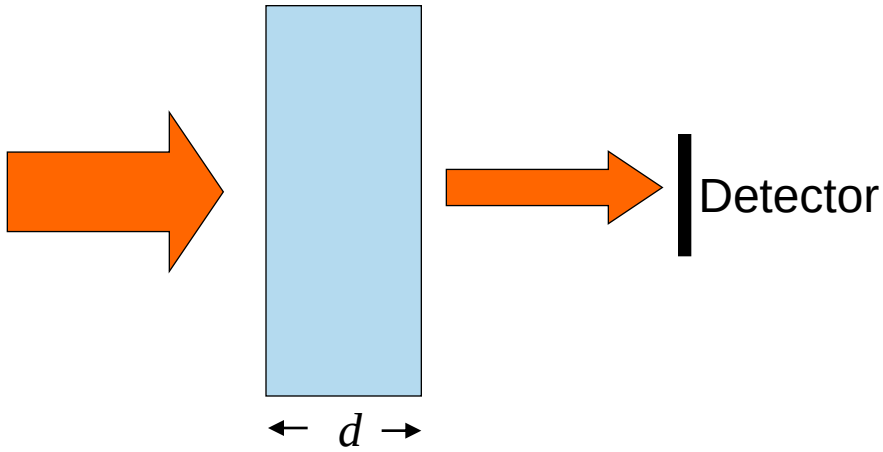
- Cytochrome Oxidase
- Scattering Changes
- Dynamic Scattering Changes
- Fluorescence (endogenous)
- Fluorescence (exogenous)

Clinical Applications

The Lambert-Law (originally formulated by Bouguer) and the Beer-Law layed the basis for in-vivo transmission imaging (Modified Beer-Lambert law)

Lambert-Beer-Law

Cuvette



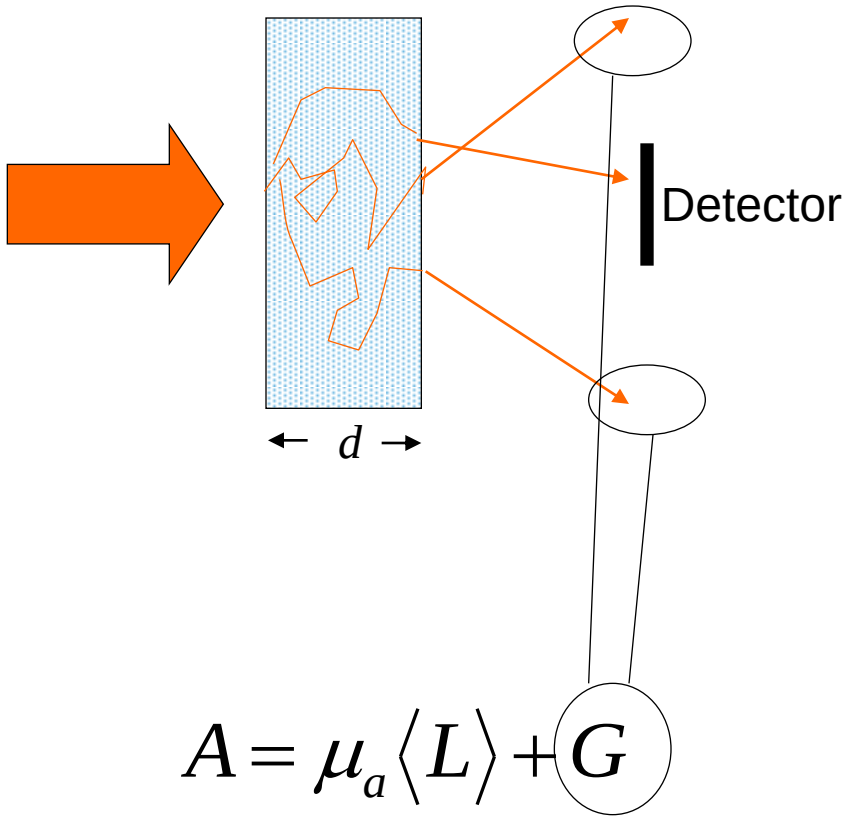
$$A = -\ln\left(\frac{I}{I_0}\right) = \mu_a d$$

Bouguer (1729)

$$\mu_a(\lambda) = \sum_i \varepsilon_i(\lambda) c_i$$

Beer (1852)

Cuvette with scattering media

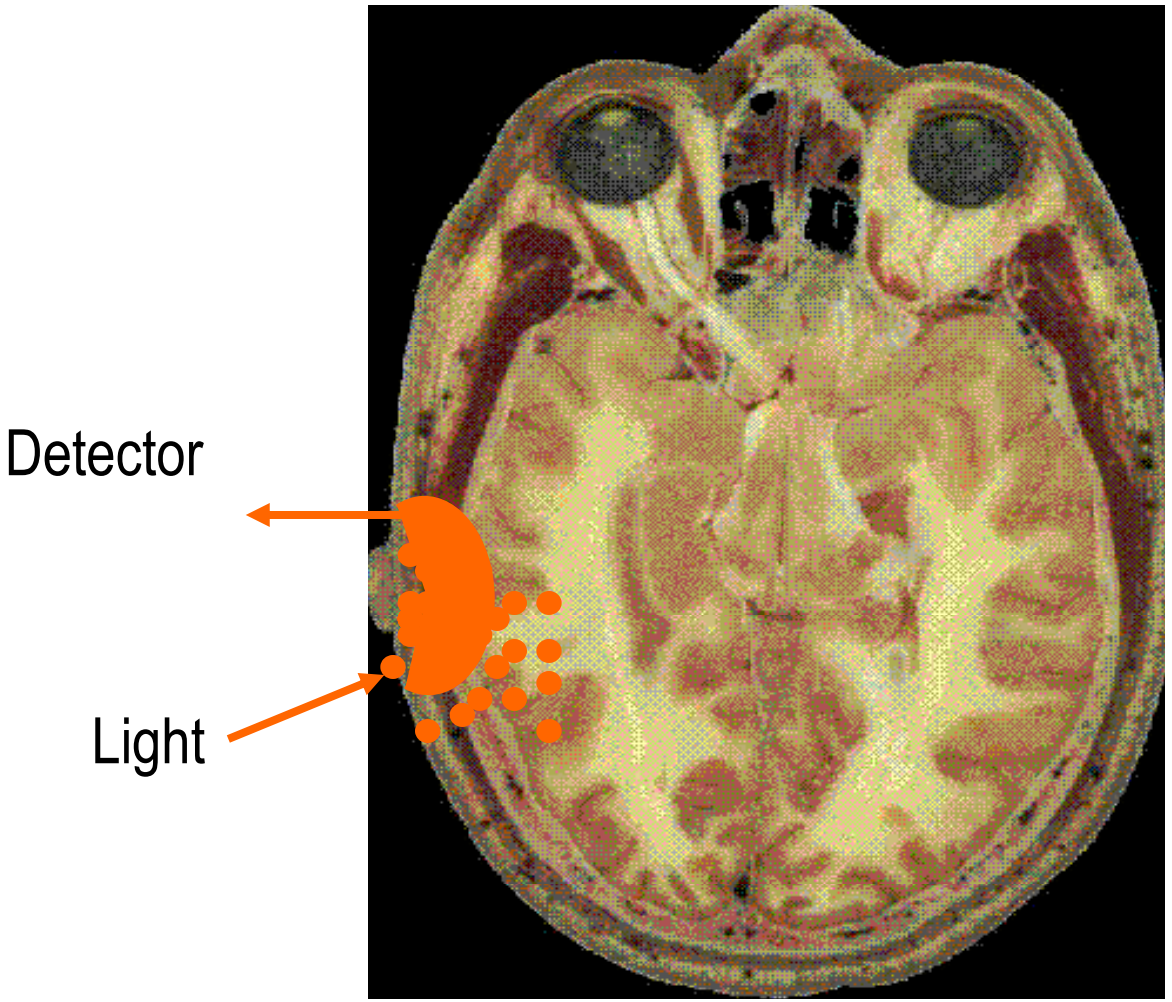


$$A = \mu_a \langle L \rangle + G$$

Delpy et. al (1988)

For the human head the same equations can be applied

Lambert-Beer-Law & Human Head



$$A = \mu_a \langle L \rangle + G$$

In case of

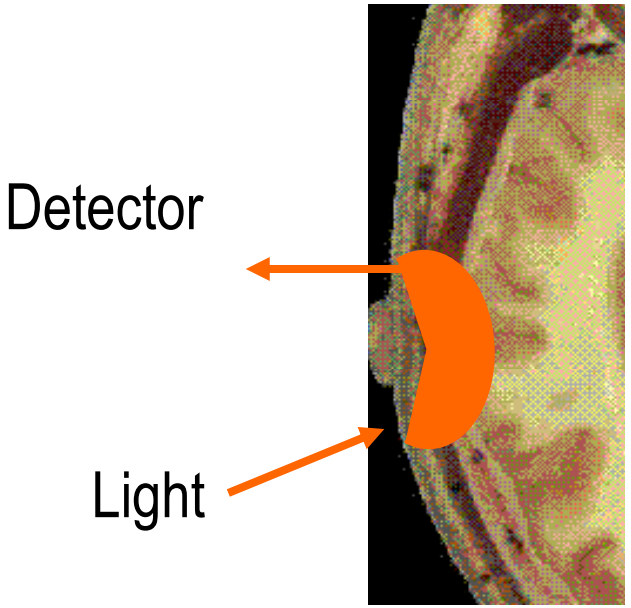
- Homogenous Change
- Small Change
- No Scattering Change

→

$$\Delta A = \Delta \mu_a \langle L \rangle$$

The success of non-invasive optical brain imaging comes from that the fact that function is determined rather than structure.

What is it, that makes brain imaging so easy ??????



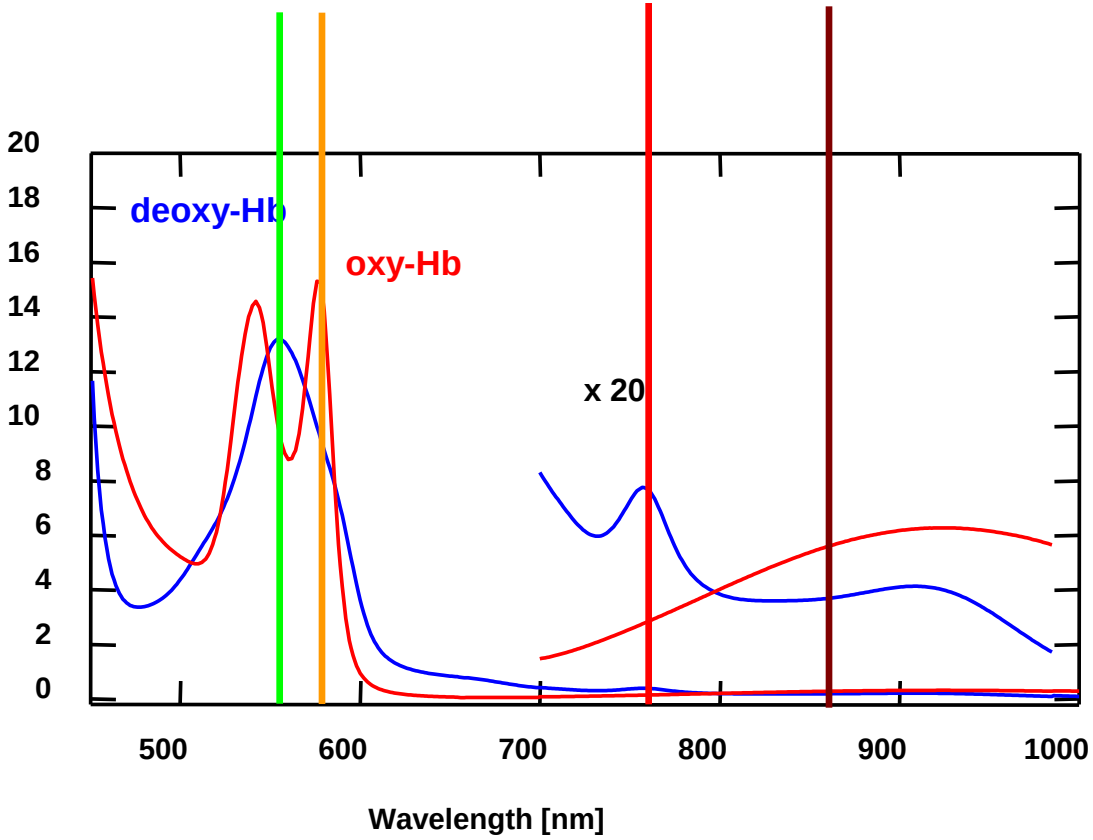
$$\Delta A = \log(I / I_0) = \Delta \mu_a \langle L \rangle$$

Resting State provides Reference

See also: BSuB7/Sunday, 9:30 a.m. - 9:45 a.m.--**Dynamic Functional and Mechanical Response of Breast Tissue to Compression**--Stefan Carp, et. al.

To determine changes in Oxy- and Deoxyhaemoglobin 2-wavelength-combinations are sufficient.

Wavelength combinations for functional optical imaging



$$\mu_a(\lambda) = \sum_i \varepsilon_i(\lambda) c_i$$

Beer (1852)

In his ground breaking work Jöbsis proposed to use optical transmission detection in humans.

Jöbsis, Science, 1977

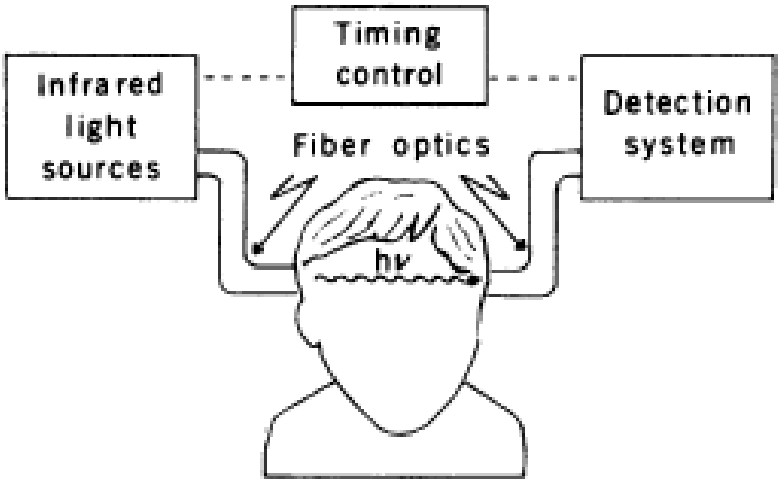
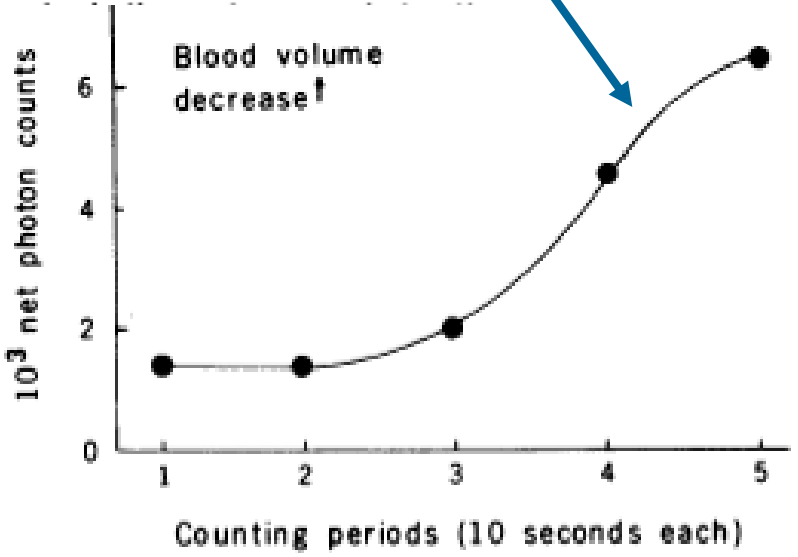


Fig. 4. Infrared monitoring of cerebral circulation and oxygen sufficiency.

This decrease was correlated with statements by the subject who reported increasing degrees of dizziness starting in the third counting period. After the fifth period the subject felt too dizzy to continue and hyperventilation was terminated. Thus, partial cerebral ischemia was monitored.



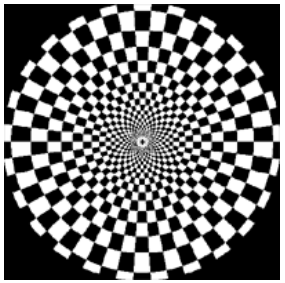
The first reports on optical imaging of brain activations in humans was triggered by the invention of functional magnetic resonance imaging (fMRI).

The first four papers on functional optical imaging in 1993

Trigger: The first two papers reporting fMRI

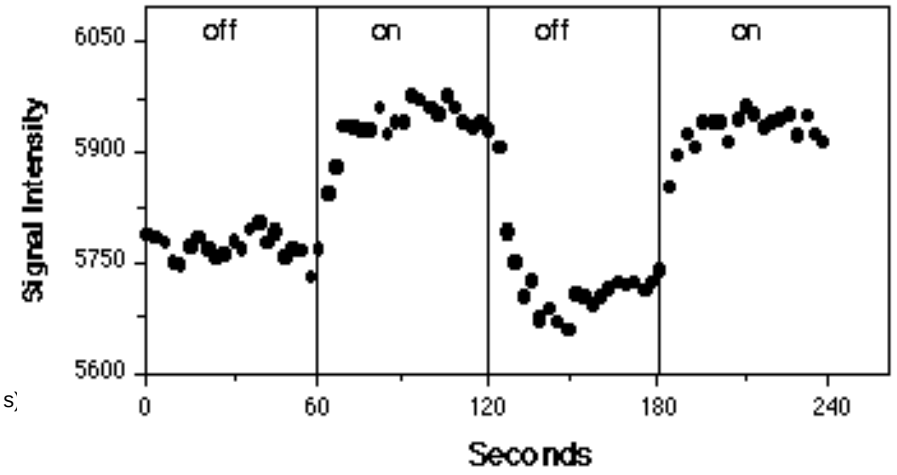
Seiji Ogawa 1992

Kenneth Kwong 1992



Flickering Checkerboard

OFF (60 s) - ON (60 s) -OFF (60 s) - ON (60 s) - OFF (60 s)



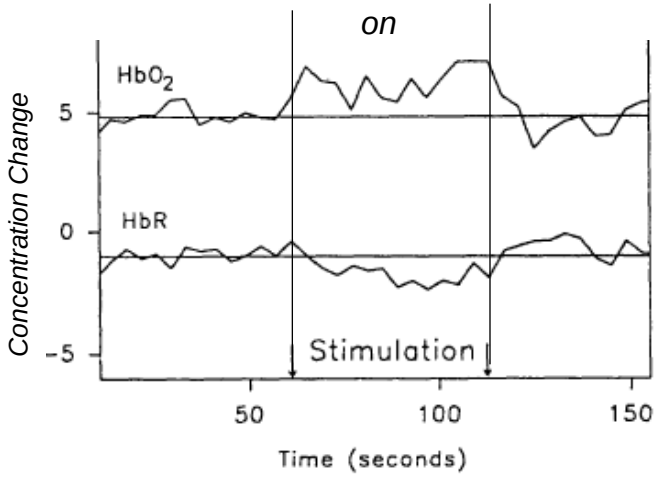
The first four papers reporting fOT

A. Villringer, … , U. Dirnagl, *Neurosci. Lett.* 1993.

Y. Hoshi, M. Tamura, *J. Appl. Physiol.* 1993.

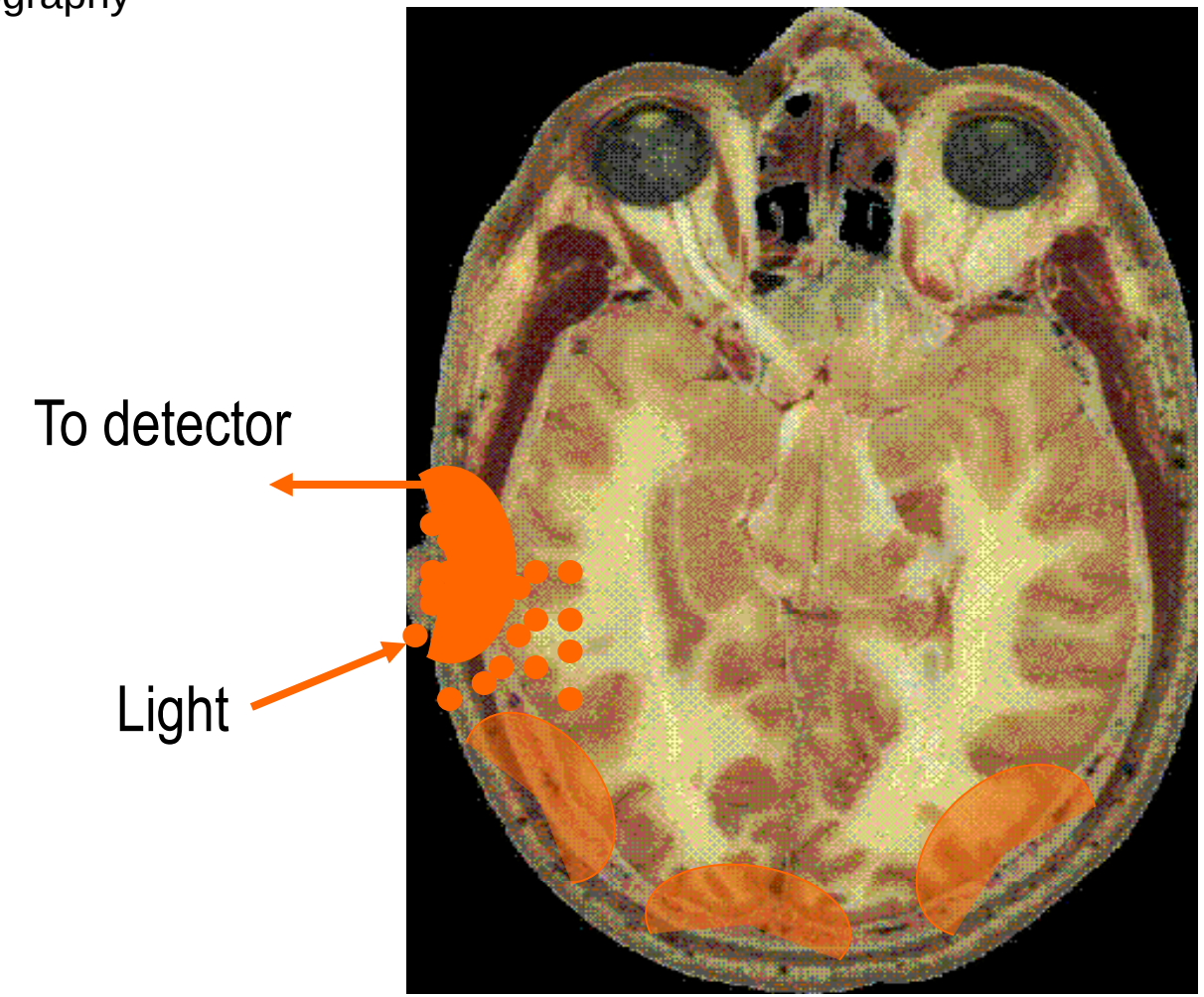
Y. Hoshi, M. Tamura, *Neurosci. Lett.* 1993.

T. Kato, .. ,T. Ozaki, *J. Cereb. Blood Flow Metab.* 1993.



Brain tissue can be probed by near infrared light in a topgraphic manner.

Prinzipal of the optical topography



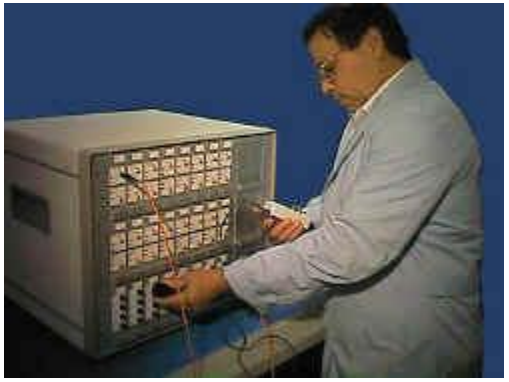
Problems:
Low penetration depth

Today there are various systems on the market.

NIRX: Dynot

ISS: Imagent

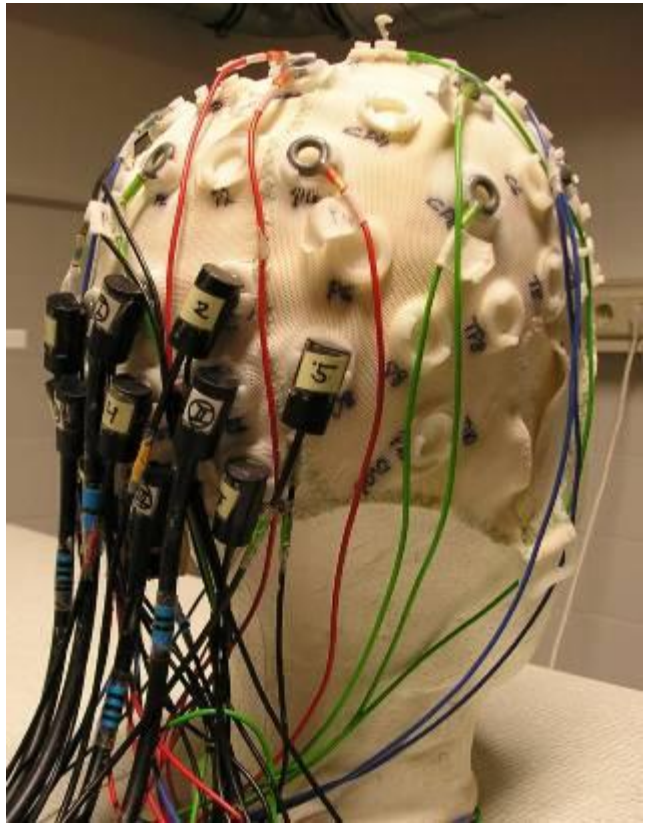
Hitachi: ETG



Techen: CW4/5

Charité Home Build Sytem.

NIRS-imager

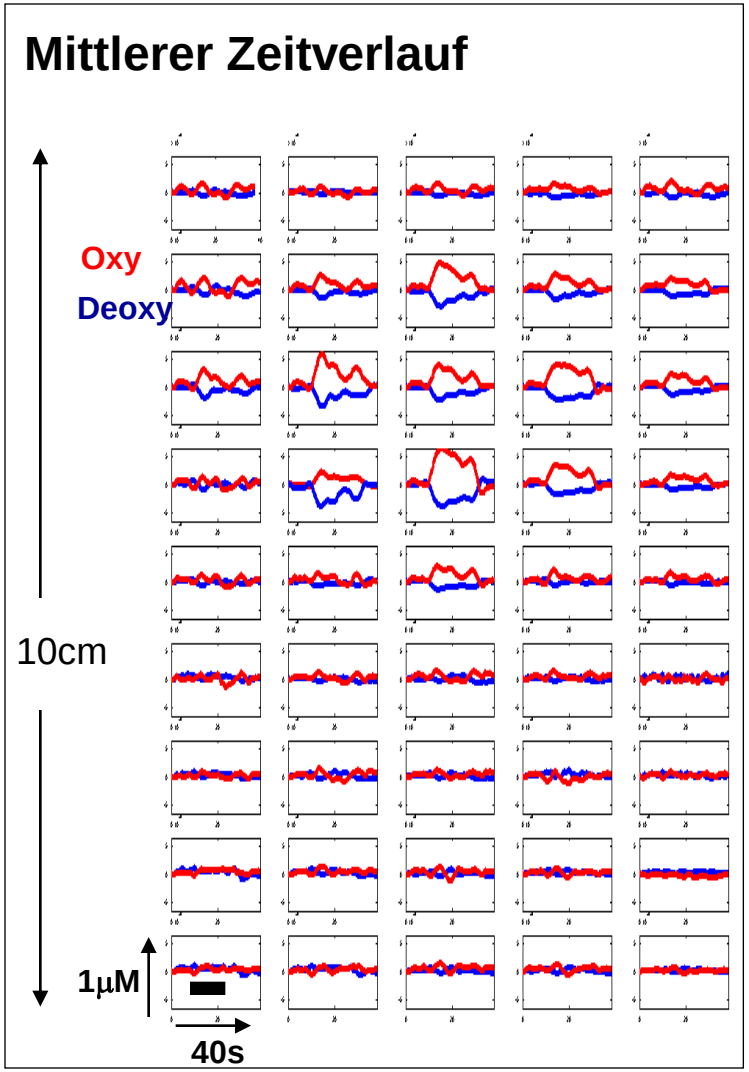


8 avalanche photo diode

8x 760 and 830nm diode-laser

Mit M. Kohl-Bareis, Remagen

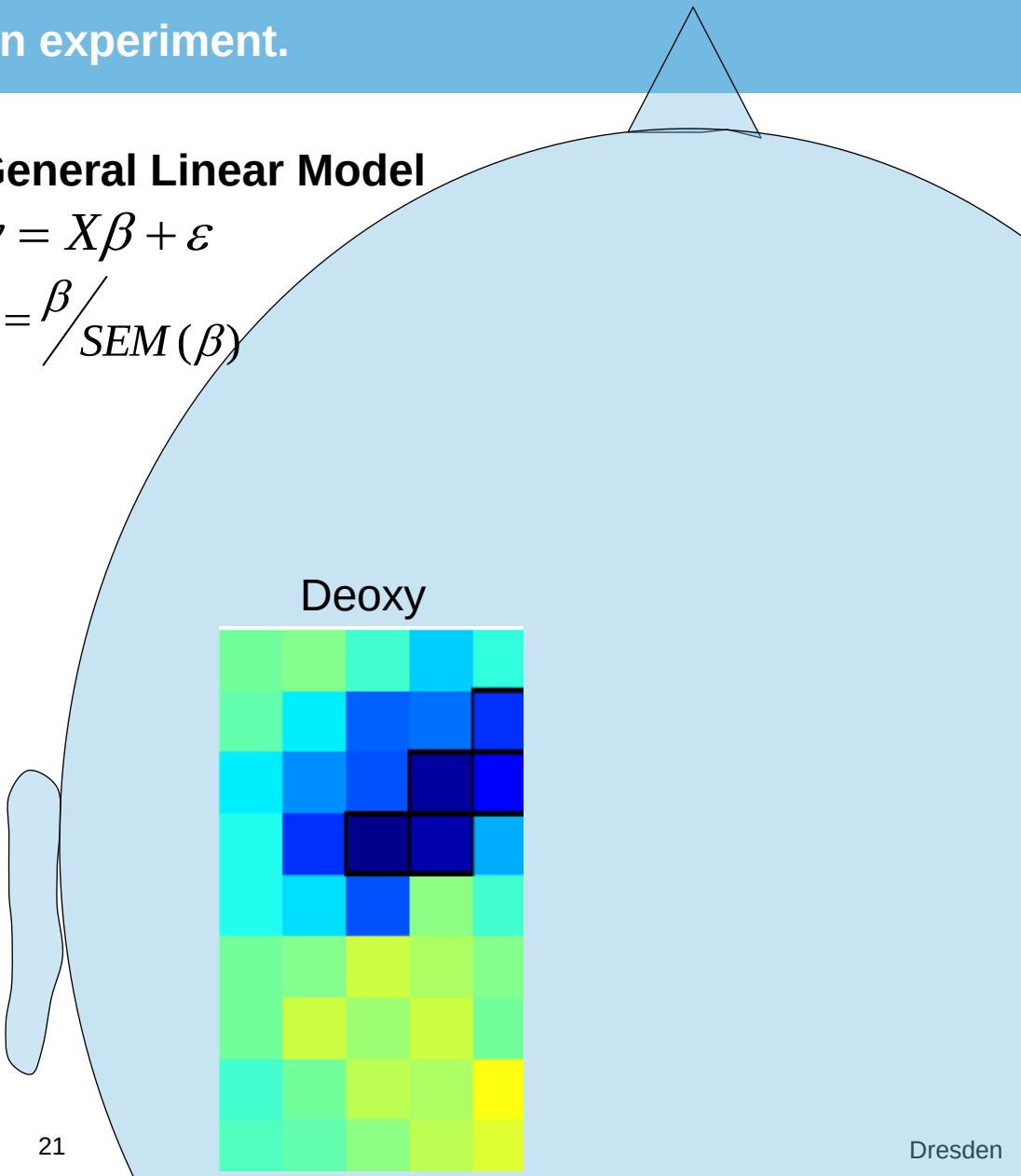
Typical result of a functional stimulation experiment.



General Linear Model

$$y = X\beta + \varepsilon$$

$$t = \beta / SEM(\beta)$$



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- Scattering Changes
- Dynamic Scattering Changes
- Fluorescence (endogenous)
- Fluorescence (exogenous)

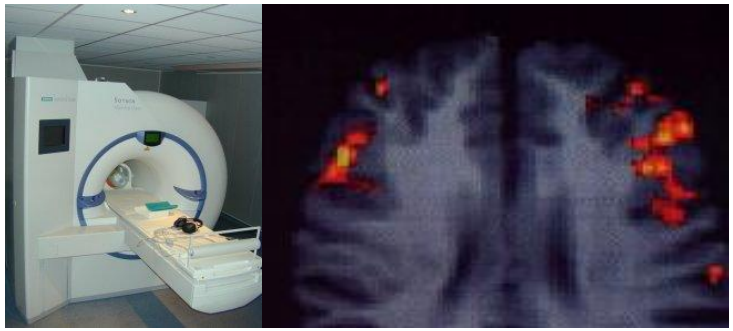
Clinical Applications

The power of OT is portability and sensitivity to changes in physiological parameter.

Pros	Cons
Portability	**Penetration Depth around 1.5cm**
Determination of Oxy- und Deoxyhemoglobin	Lateral Resolution around 1cm
Low Price (50-250tEuro)	**Sensitive to extracerebral Absorption changes (blood pressure)**

However other methods are more powerful and thus, niche applications have to be defined.

fMRI (Standard)



+ Spatial Resolution (1mm)
+ Whole Head
- Not bedside applicable

fNIRS → 'Niche Functional Imaging'

1. Study the basis of functional imaging

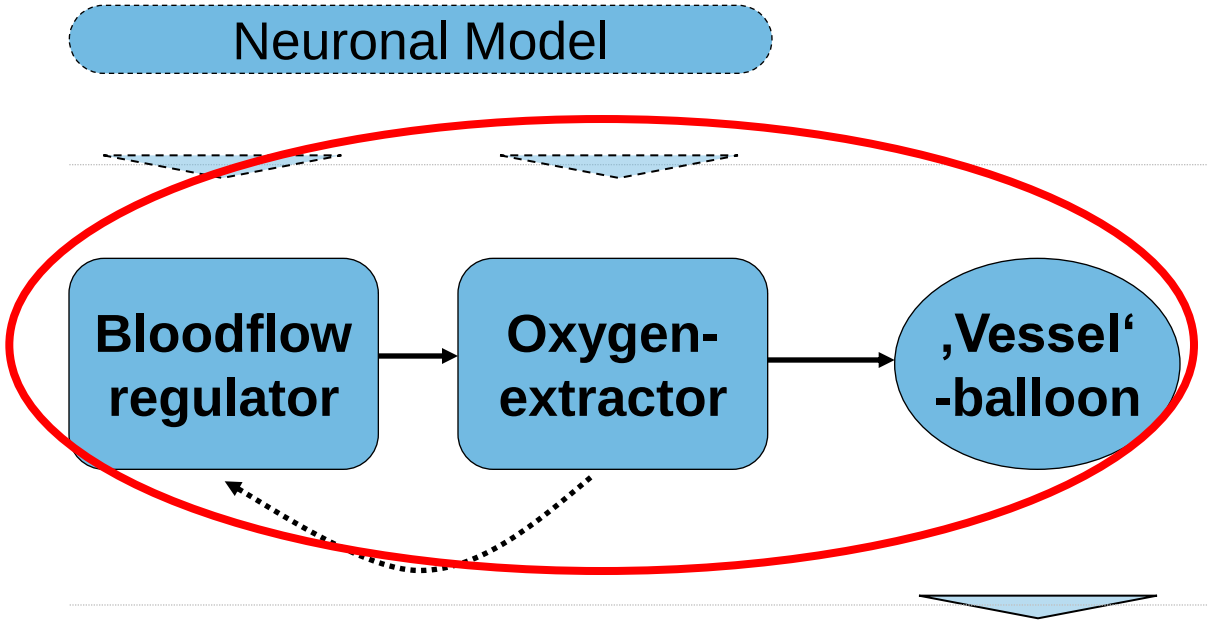
2. New borns and children

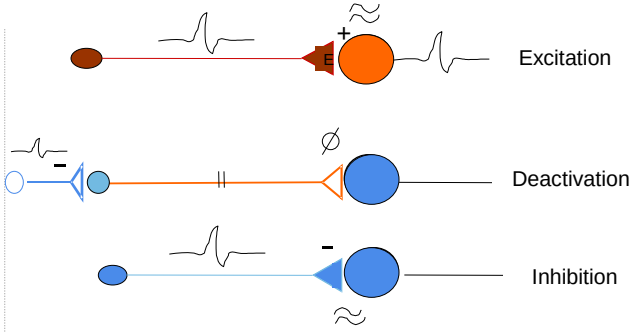
3. 'Freely behaving' adults

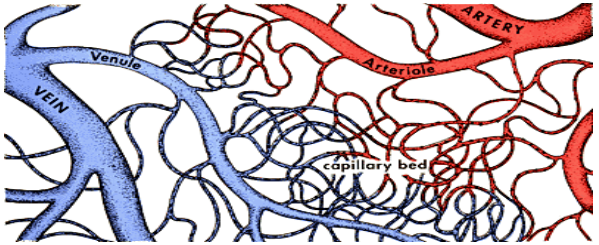
4. Bedside Imaging

OT is well suited to study neurovascular coupling, since it allows determined well defined physiological parameters.

Model System

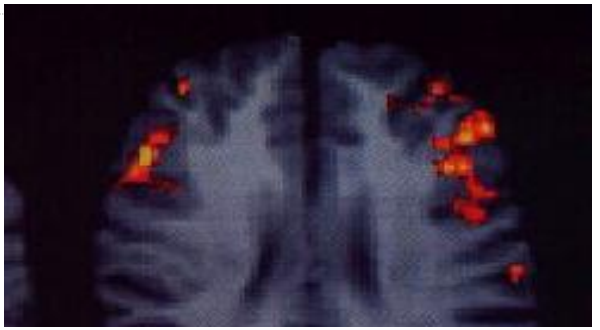






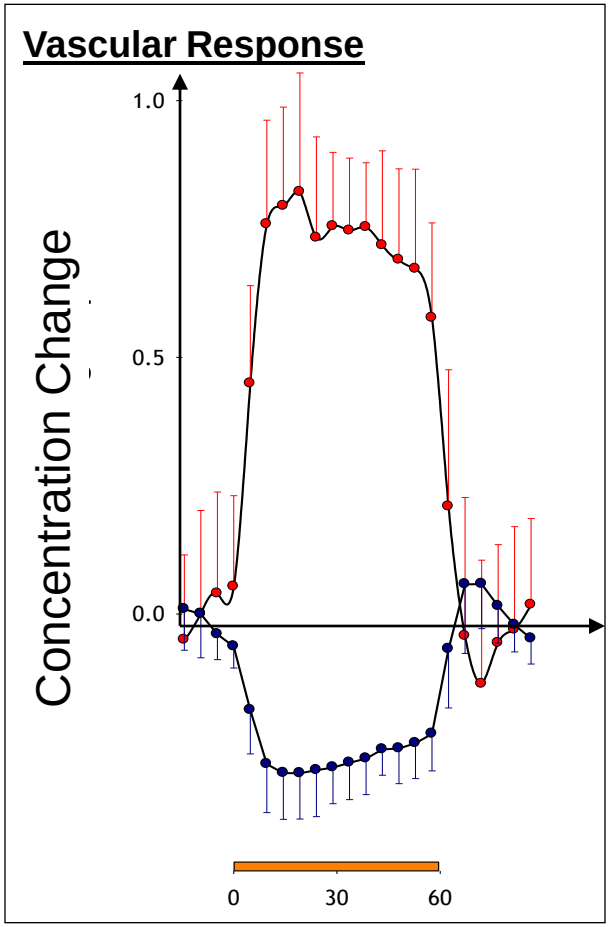
Steinbrink J, Boden S, Haux D, Villringer A, Obrig H. **MRI 2006**

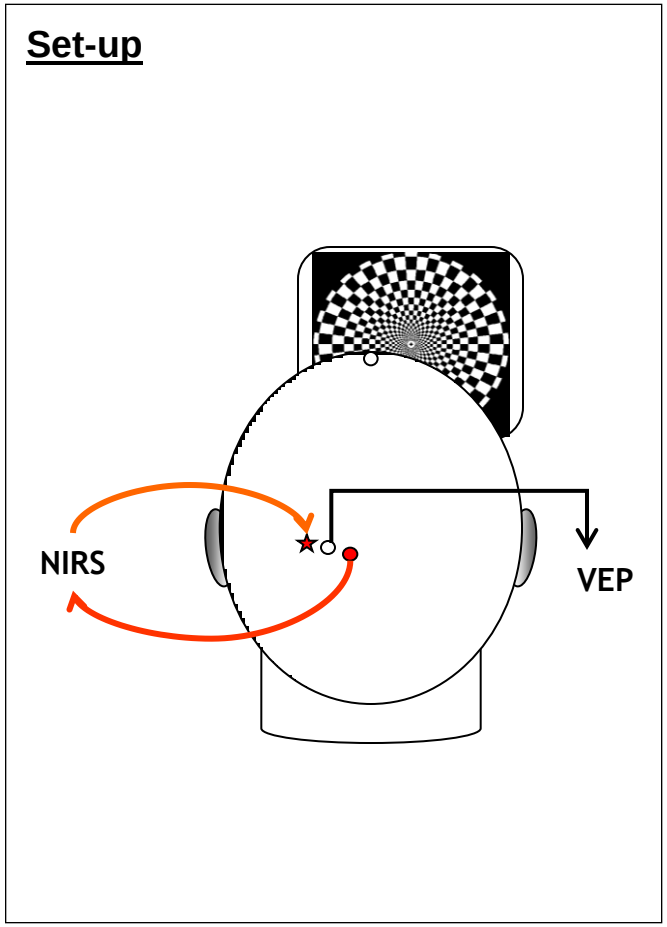
fMRI Signal

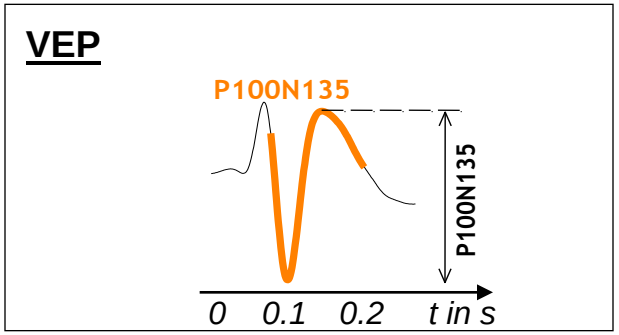


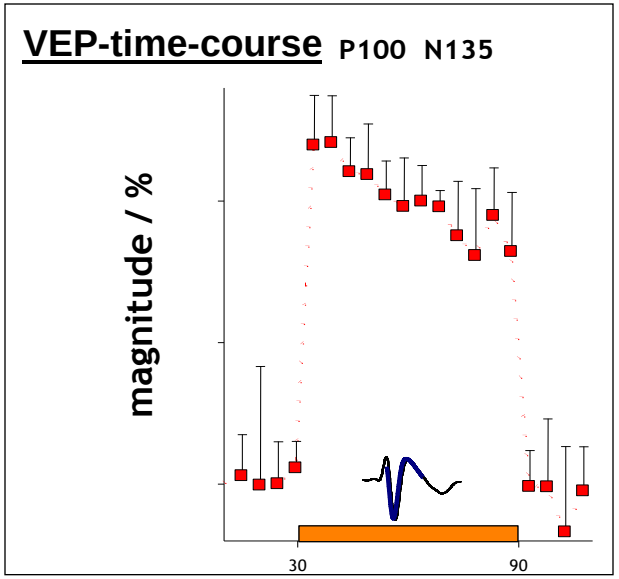
Neurovascular coupling is studied by comparing electrophysiological measures with vascular changes. Here an amplitude of the visual evoked potential is compared to changes in oxy- and deoxy-hemoglobin.

Application 1: Habituation Study









See also: BWC5/Wednesday, 11:30 a.m. - 11:45 a.m.--**Study of Neurovascular Coupling via Simultaneous MEG DOI Acquisition**--Wanmei Ou1 et. al..

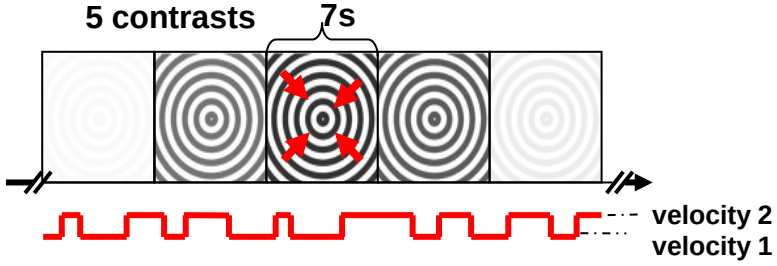
***Obrig**,2000, NIMG*

Non-invasive studies at the cat could show the correlation between gamma activity and blood flow response.

Blutfluß und Gamma (Niessing Science 2005)

Stimulus:

Grating with different contrast

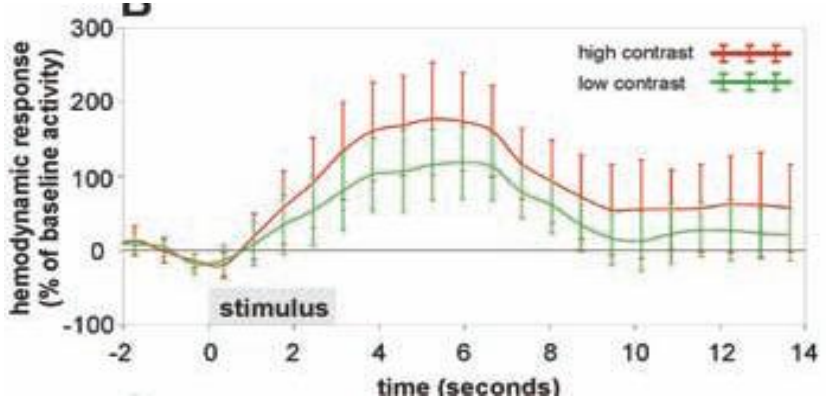


Modell:

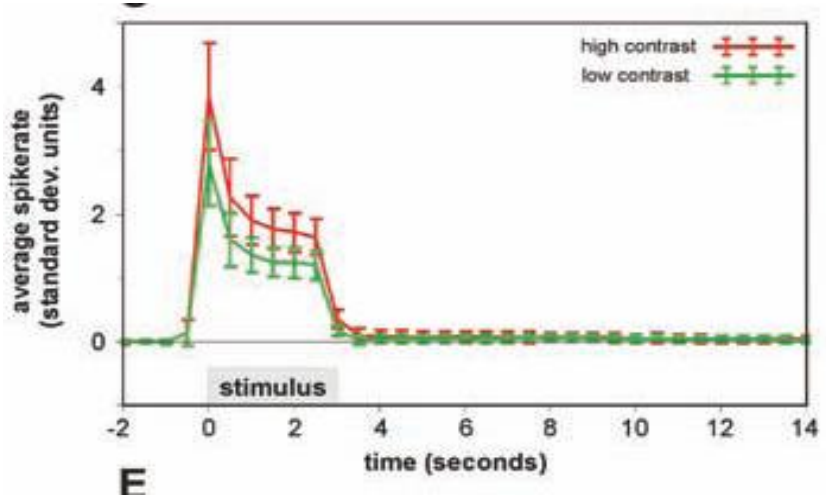
Cat,
Optical Glas Window,
Multi-Unit-Activity (MUA)

1. Result:

High Contrast = High Blood Flow Respons



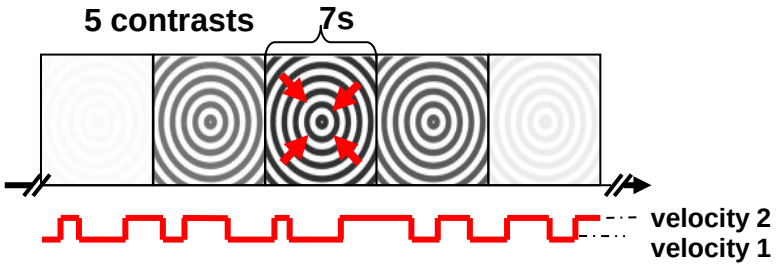
High Contrast = High MUA



Non-invasive studies at the cat could show the correlation between gamma activity and blood flow response.

Blutflow and Gamma (Niessing Science 2005)

Stimulus:
Grating with different contrasts

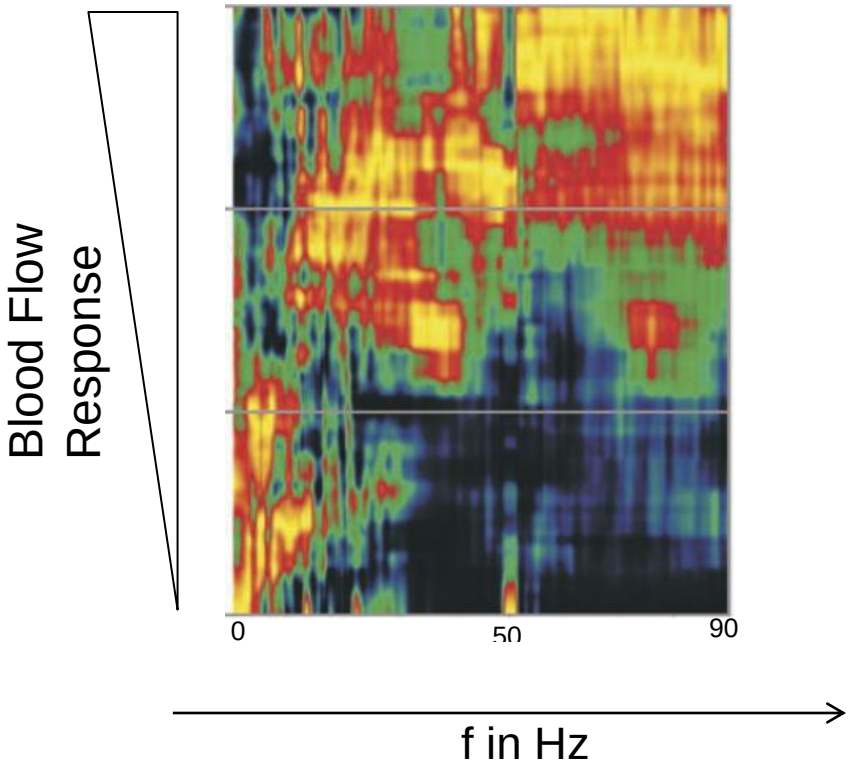


Modell:

Cat,
Optical Glas Window,
Multi-Unit-Activity (MUA)

2. Result:

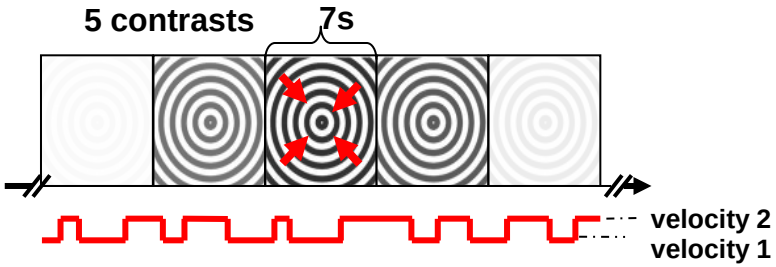
Blood Flow Response
correlates with Gamma Activity:



Its also feasible in humans.

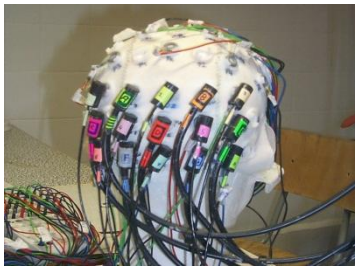
Bloodflow and Gamma (Koch, J. NeuroSci 2005)

Stimulus:
Grating with different contrasts



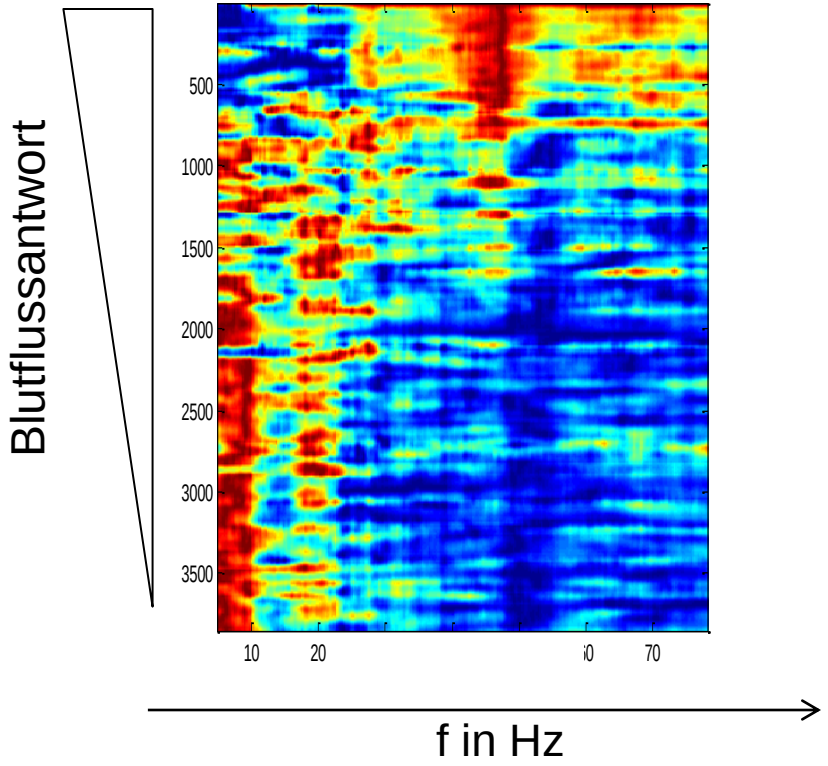
Modell:

HUMAN
NIRS
EEG



2. Result:

Blood Flow Response
correlates with Gamma Activity:



First reports on studies in ‘freely behaving’ adults have been provided.

Appl. 2: Imaging of freely behaving adults

Sustained decrease in oxygenated hemoglobin **during video games** in the dorsal prefrontal cortex: A NIRS study of children

Matsuda, et. al. NIMG, 2006

Miyai, et. al. NIMG, 2001

Miyai, et. al. NIMG, 2001

See also: BWG2/Wednesday, 4:15 p.m. - 4:30 p.m.--**A New Wireless Multichannel Near Infrared Imaging System**--Thomas L. Muehlemann, et. al

Agenda

Non-invasive Optical Imaging – Intro & History

- Invasive Imaging
- Equations
- Applications

Novel Technological Improvement

- Hyper-resolution
- Depth Resolution
- Portability

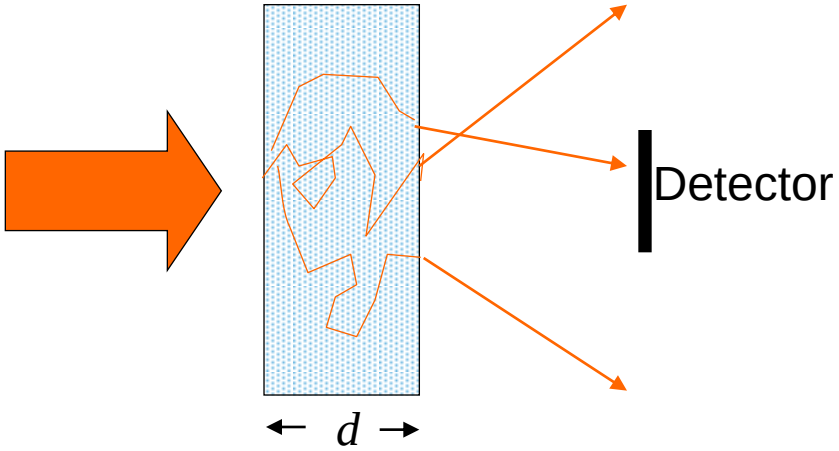
Other Contrasts

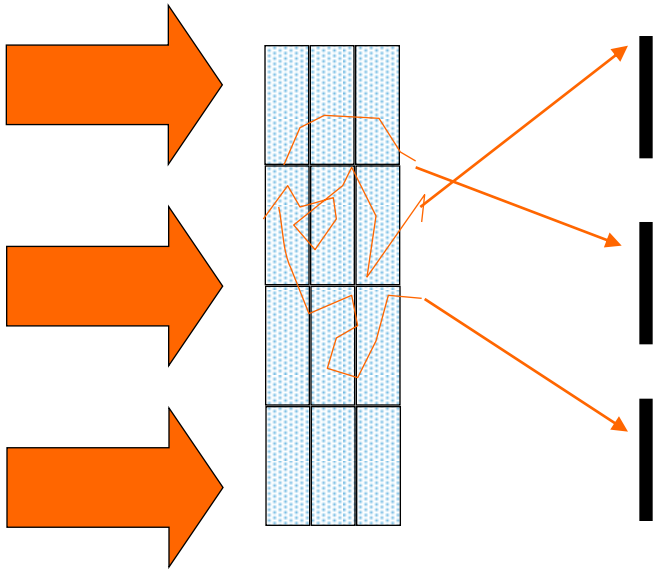
- Cytochrome Oxidase
- Scattering Changes
- Dynamic Scattering Changes
- Fluorescence (endogenous)
- Fluorescence (exogenous)

Clinical Applications

For a hyper-resolution imaging ‚reconstruction' techniques are needed.

Principles of reconstruction techniques (linear appox.)





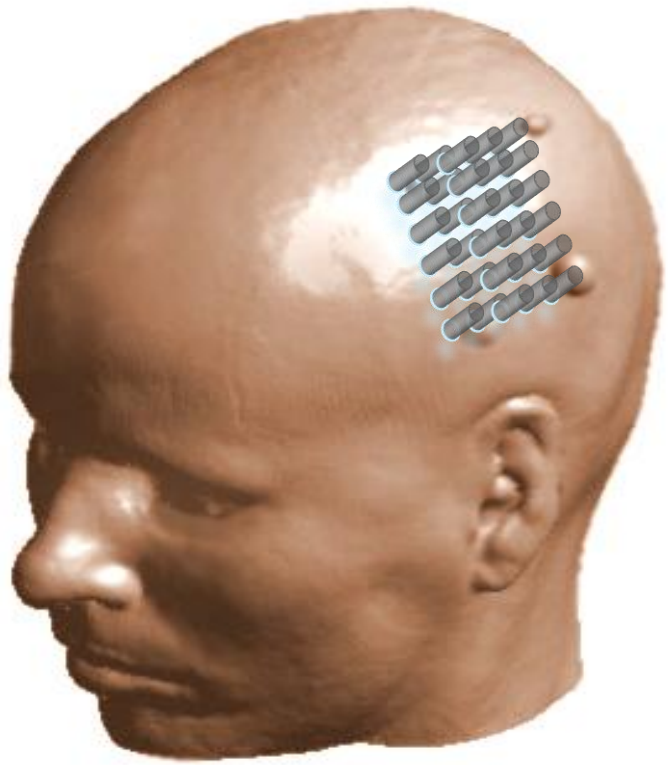
$$\Delta A = \Delta \mu_a \langle L \rangle$$

$$\Delta A^k = \sum_{j=1}^{N_{Voxel}} \Delta \mu_a^j \langle L \rangle_k$$

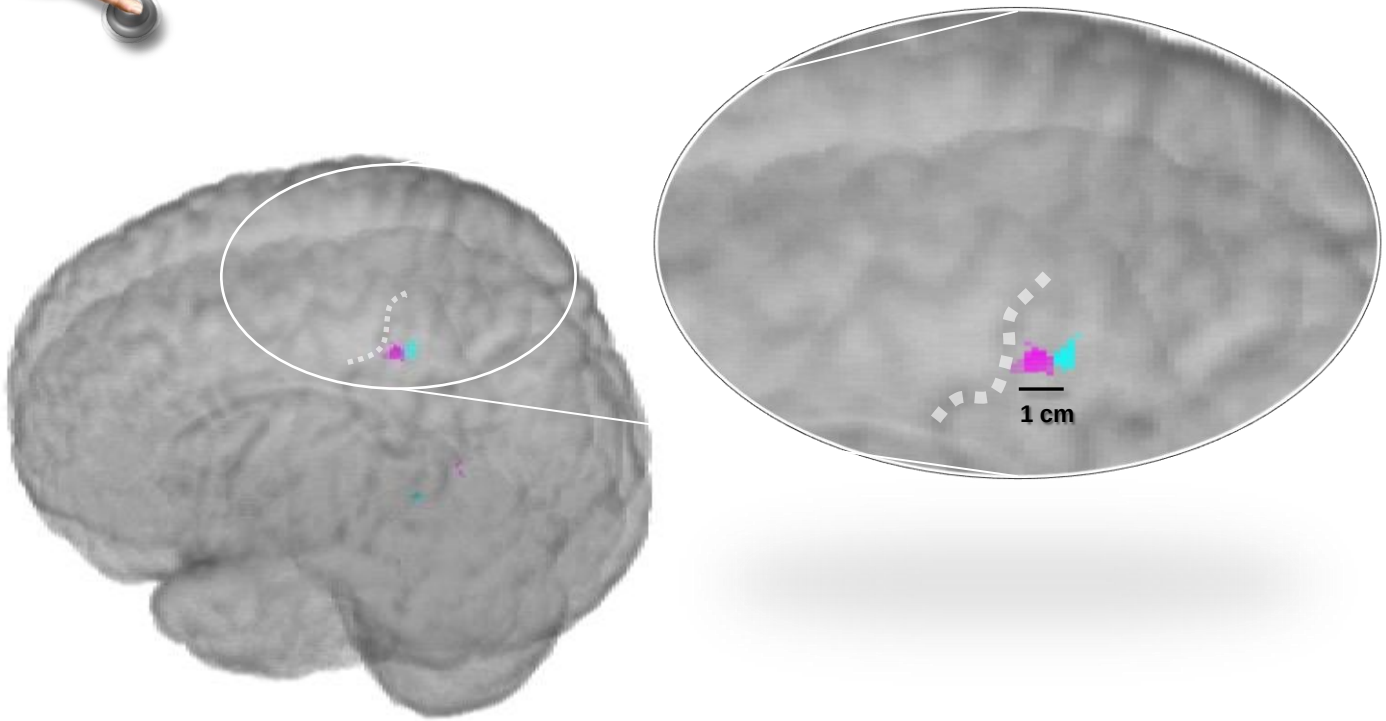
k is index for source detector combination

Also a ‚hyperdense' distribution of source and detectors is needed.

Hyperdense Mapping



Tomography strongly increases the spatial resolution!!!



1st finger

5th finger

superior

anterior

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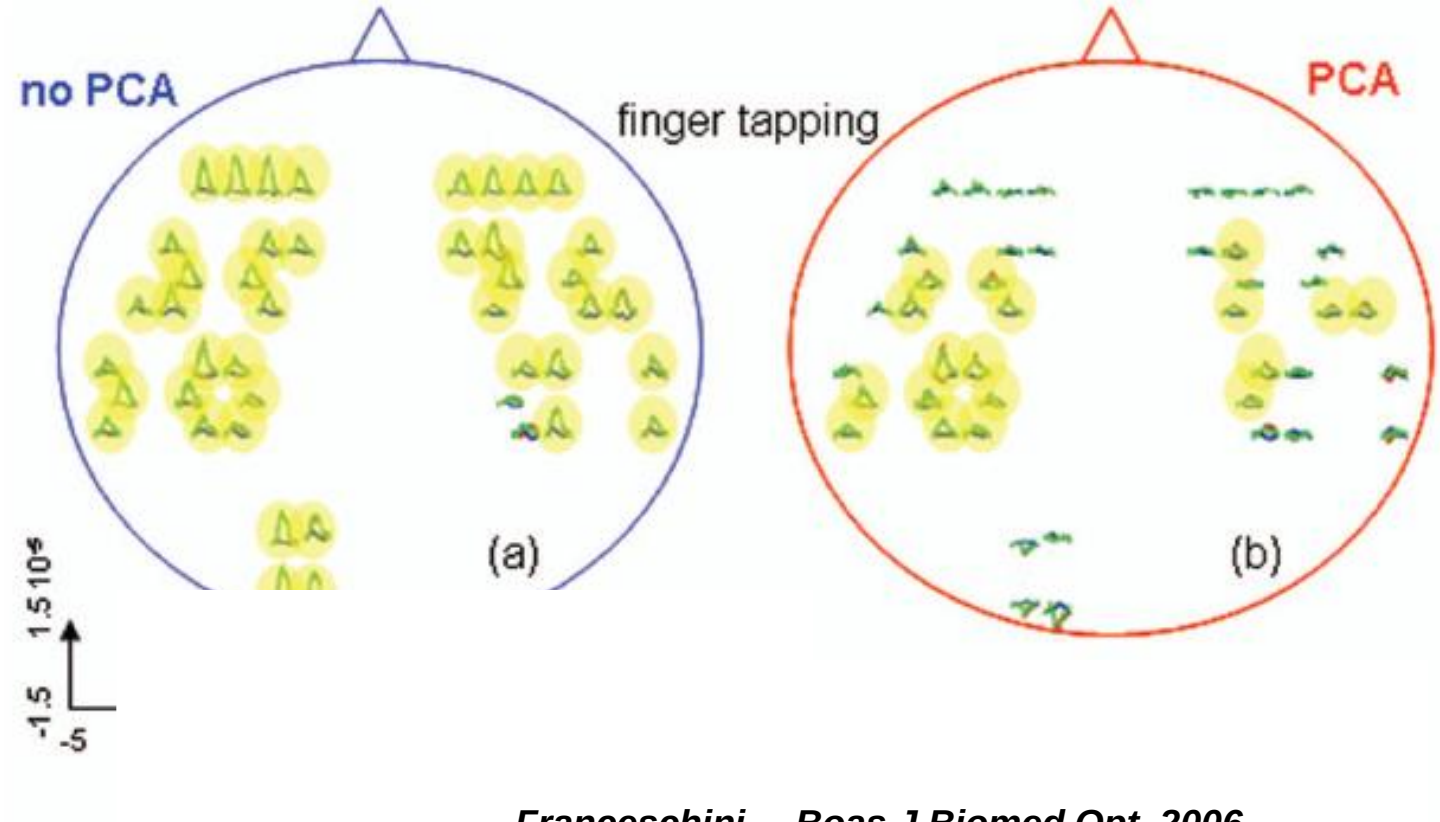
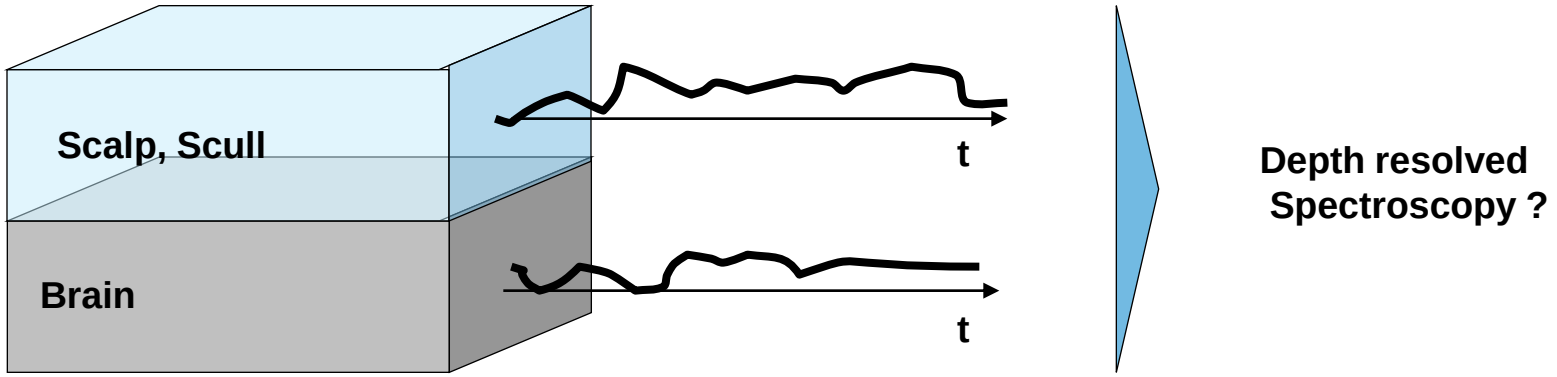
Clinical Applications

A challenge of OT is the sensitivity to ‘global’ changes in blood pressure.



Franceschini,.., Boas J Biomed Opt. 2006

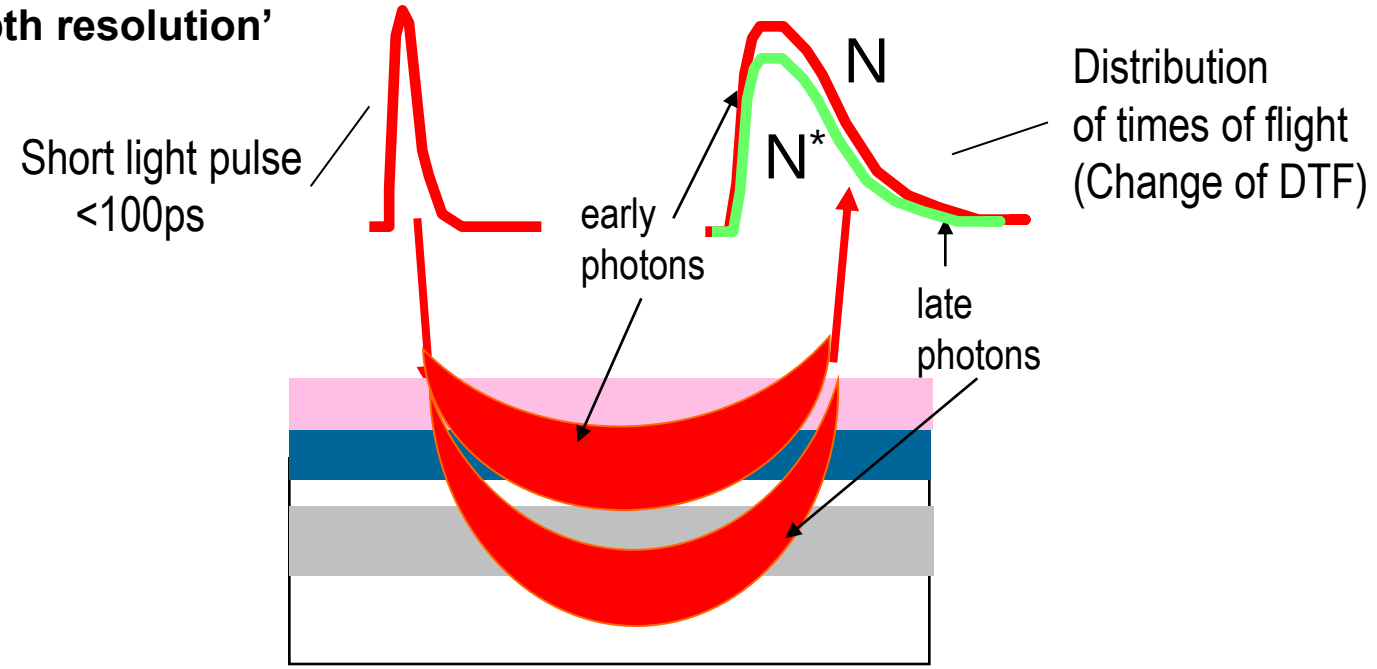
Detected ‚systemic‘ artefact can have an extra-cerebral component.



An approach with pico-second time resolution allows for the determination of depth resolved absorption changes and thus discriminate extra-cerebral changes.

Principle of 'depth resolution'

Idea



Theory: $$\Delta A(t) = -\log\left(N^*(t)/N(t)\right) = \sum_j \left\langle l_j \right\rangle (t)\Delta\mu_{a,j}$$

Change in DTF

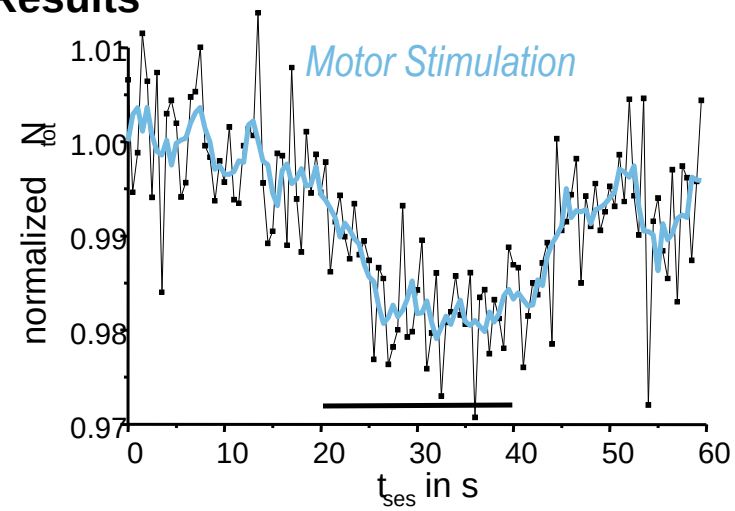
Mean partial path length (time dependent)

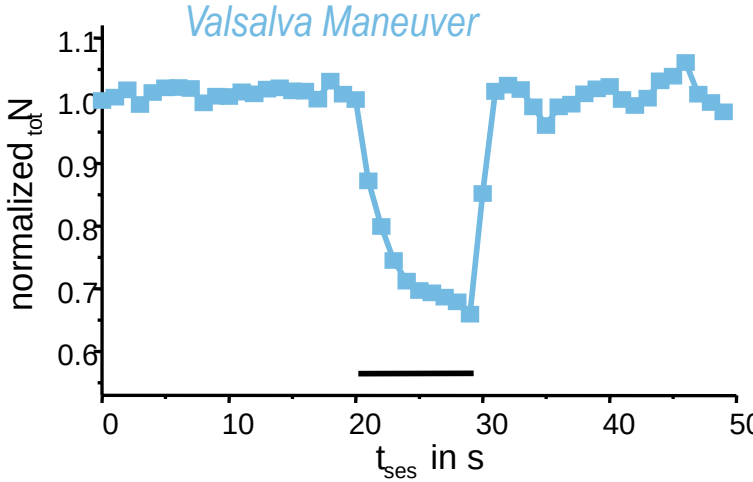
Change in absorption in depth z_j

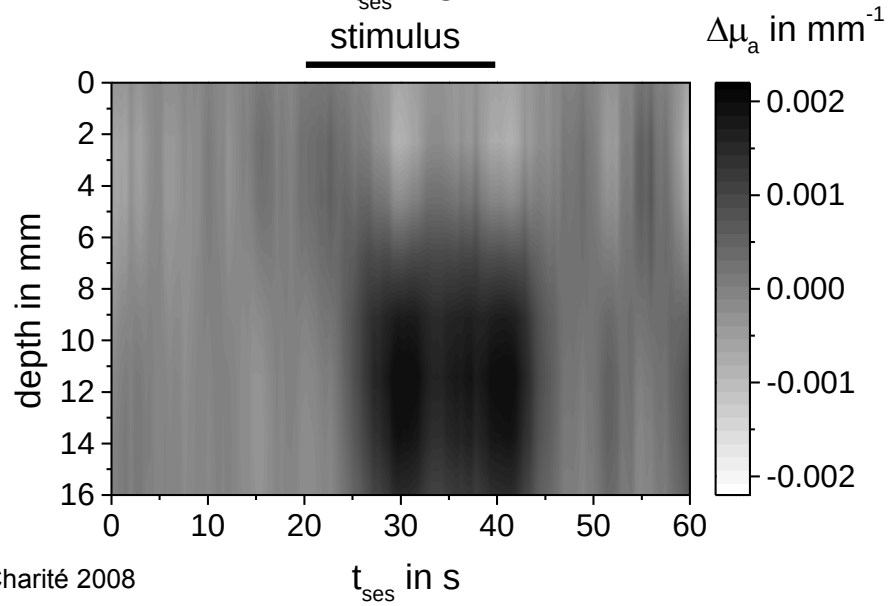
Steinbrink et al, PMB. 2000

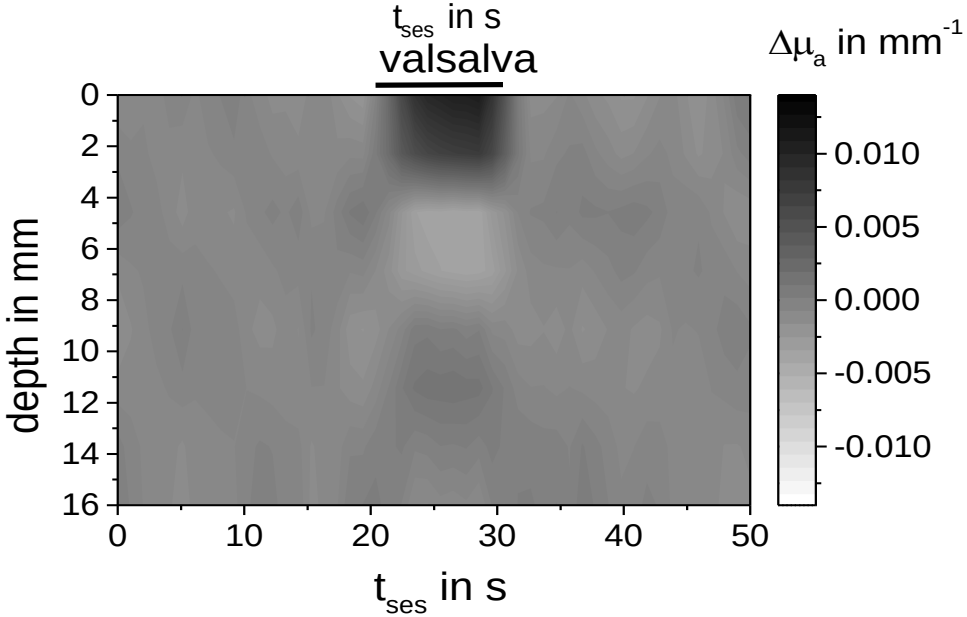
Depth resolution works!

Results









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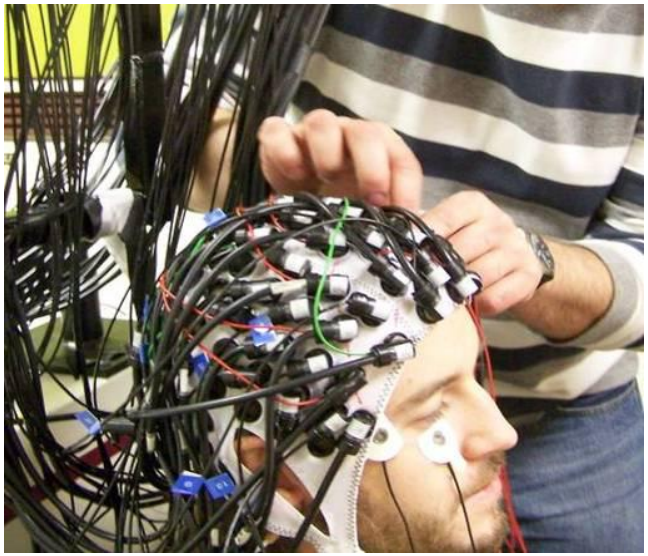
Clinical Applications

How to integrate NIRS?

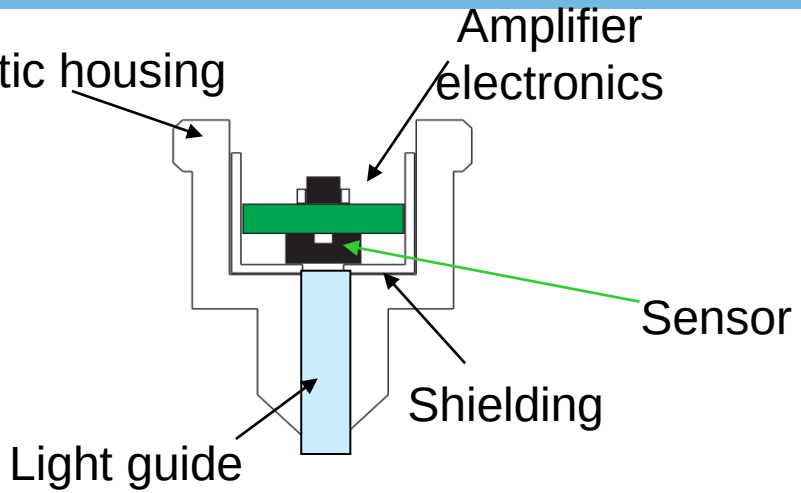


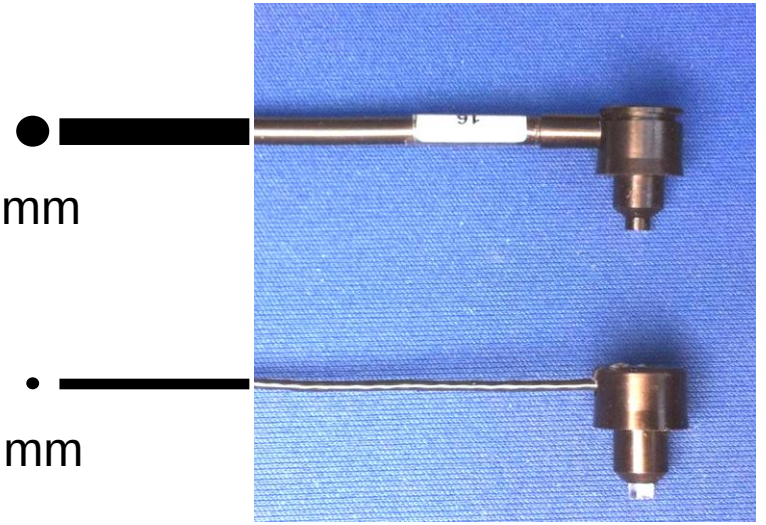
?

Active Detection Concept

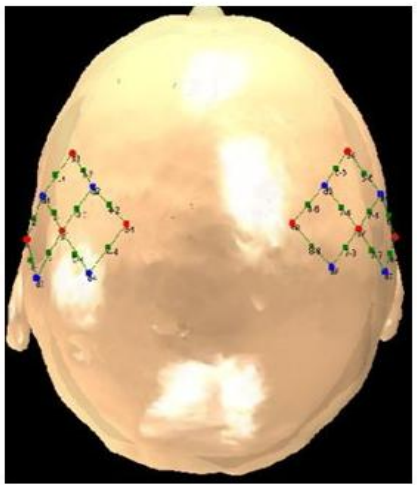
Illumination, currently

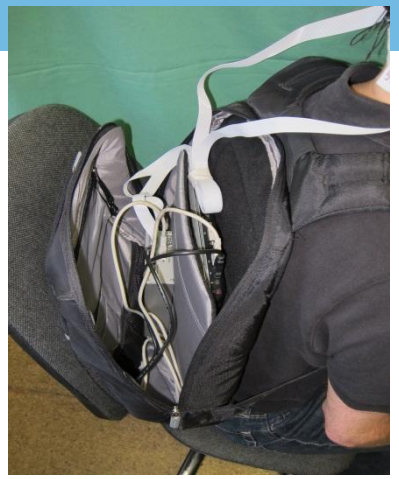
Similar form factor for receiver

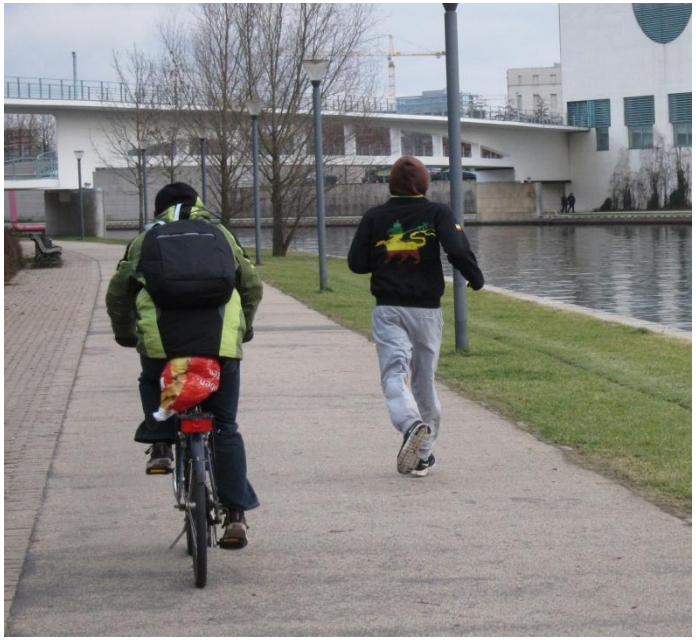




Bicycle Experiment

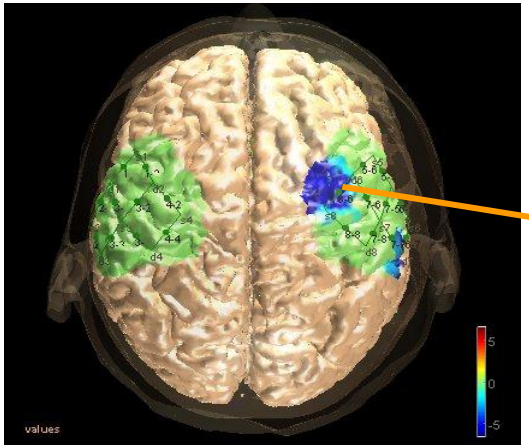


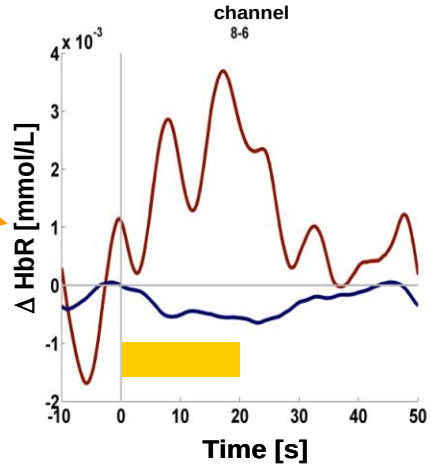


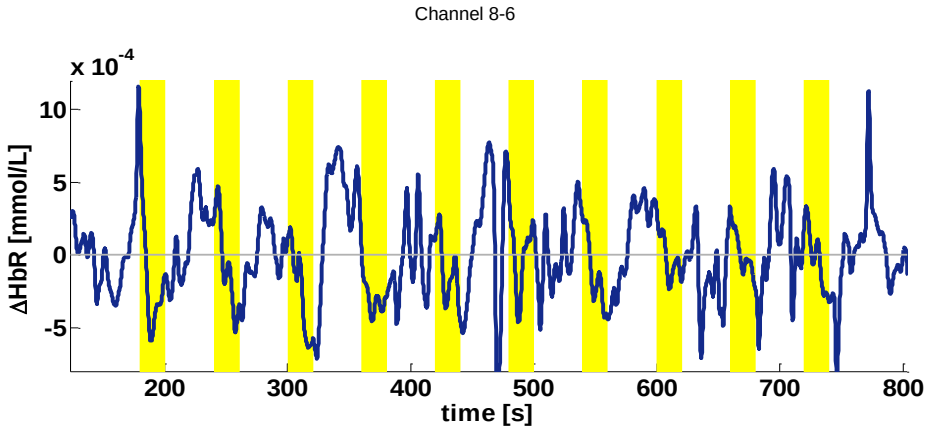


- Left-hand clenching (~1..2 Hz)
- 20 sec activation / 40 sec pause / 10 trials
- Biking outside vs. training bike vs. no pedaling
- N = 4 subjects
- Artifact removal (1-2 trials/subject)

Single-Subject during Biking







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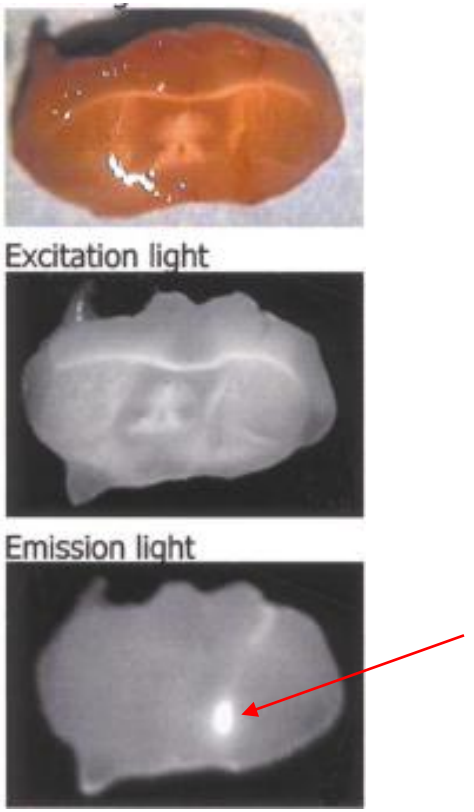
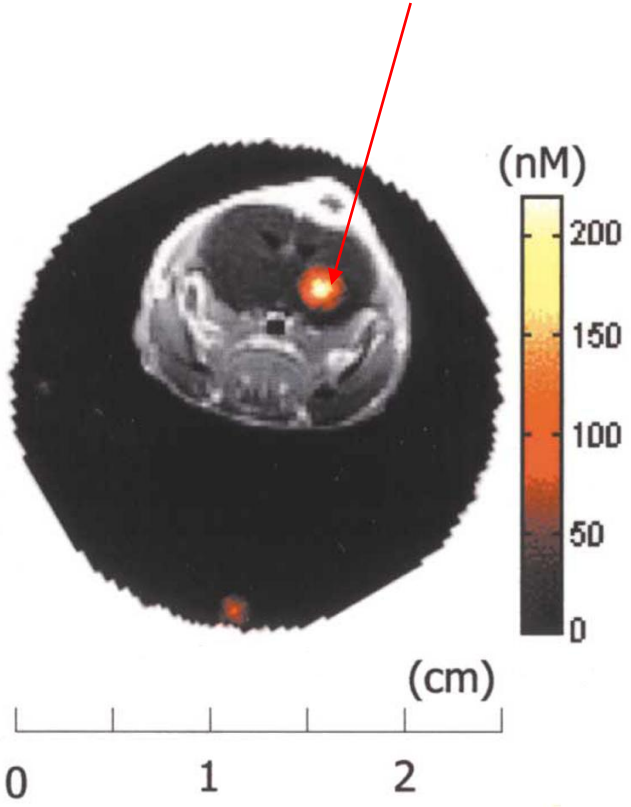
Clinical Applications

In a breathtaking paper Ntziachristos et al. Proposed the usage of non-invasive optical fluorescence tomography for the brain.

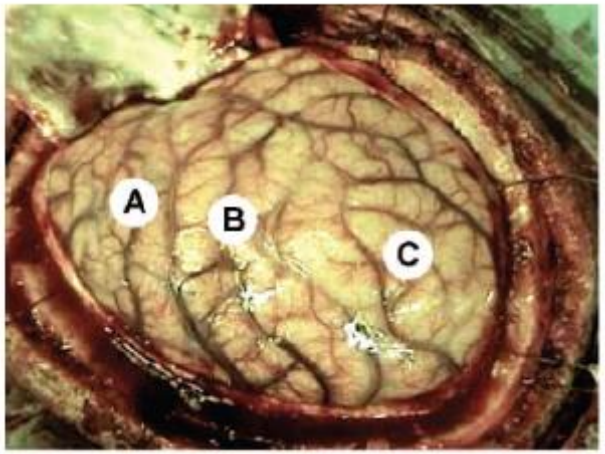


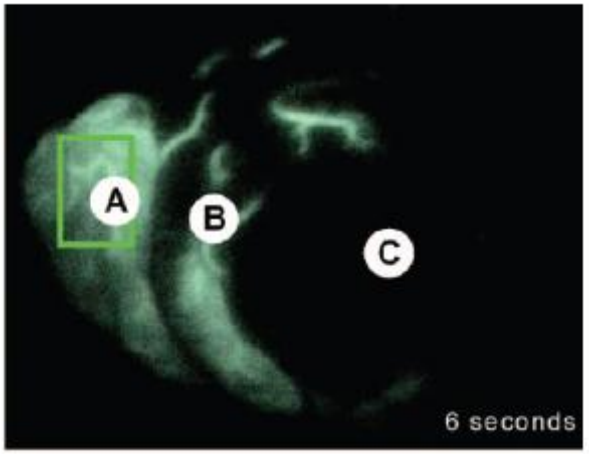


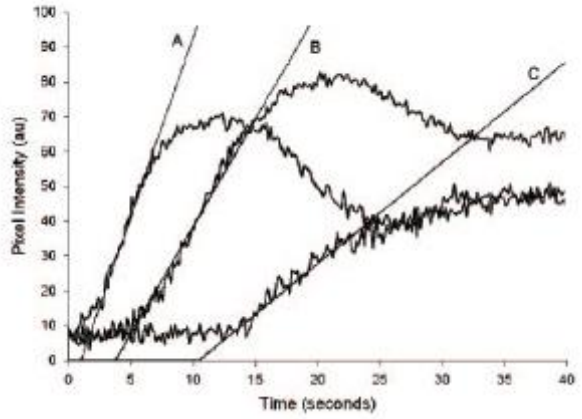
Ntziachristos, .. , Weissleder Nature Medicine (2002)

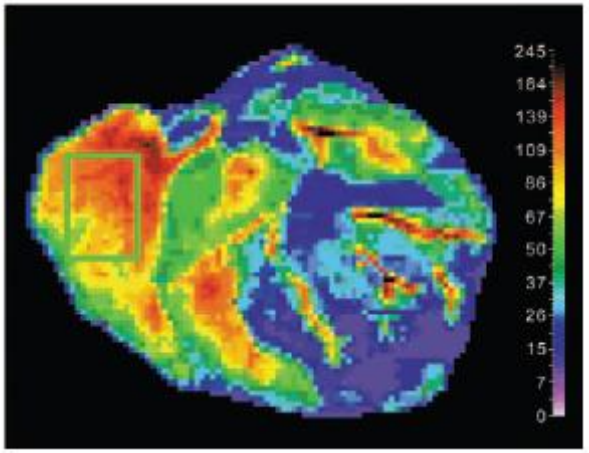
In the exposed cortex fluorescence Imaging of an ICG Bolus allows to determine perfusion deficits. Is a non-invasive application in sight?

Perfusion imaging via ICG detection









C Thomé J Woitzik, PG Peña-Tapia, U. Schneider, P. Vajkoczy, Stroke 2006

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Clinical Applications

Clinicians are interested in the TiO2. OT has been proposed to determine two parameters influencing TiO2: a) CBF and b) oxygen saturation.

- TiO2: *O2 conc. in tissue*
- CMRO2: *Cerebral Metabolic Rate of Oxygen*

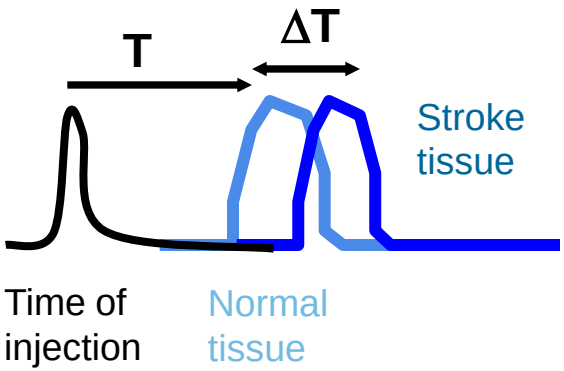
CBF: Flow
- *Arterial*
- *Venous*
- *Mixed*

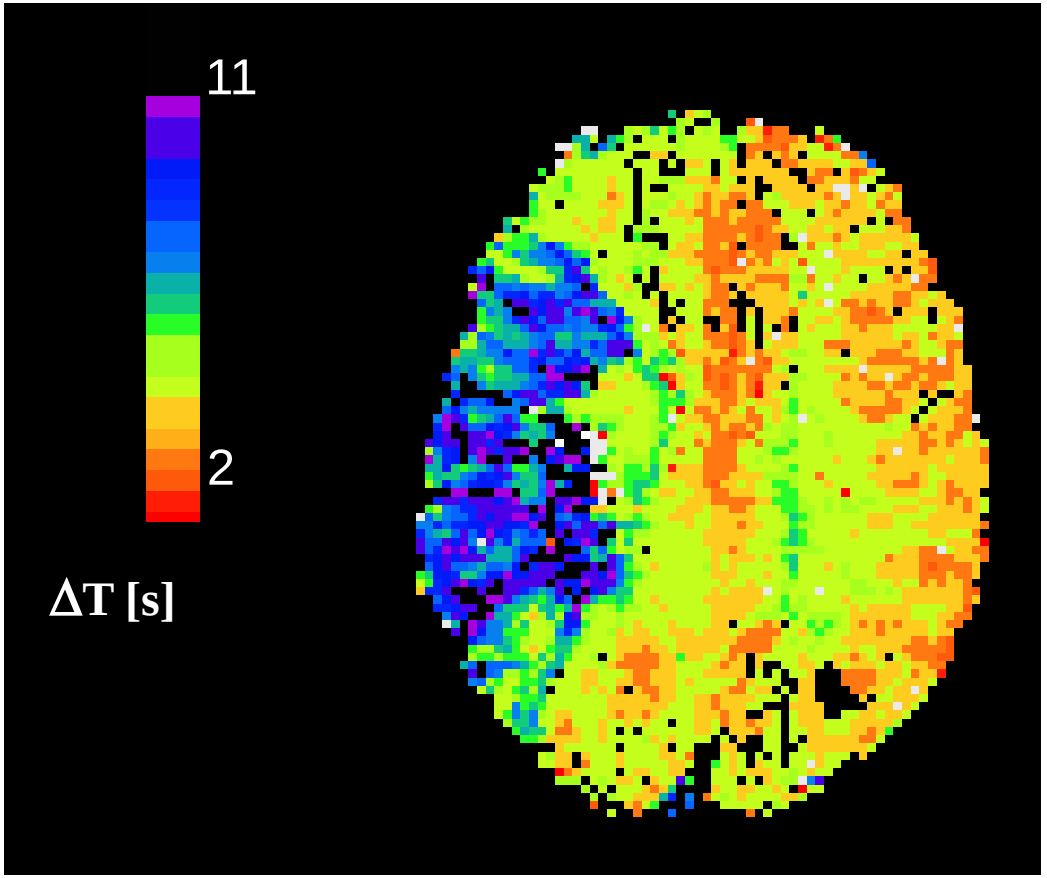
Y: Oxygen saturation:
- *Arterial*
- *Venous*
- *Mixed*

On the other hand OT has been proposed to use a contrast agent based blood flow imaging, similar to CT or MRI.

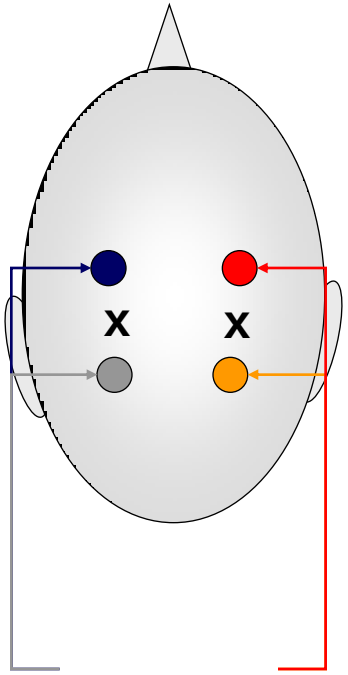
Principle of perfusion weighted imaging

Concept





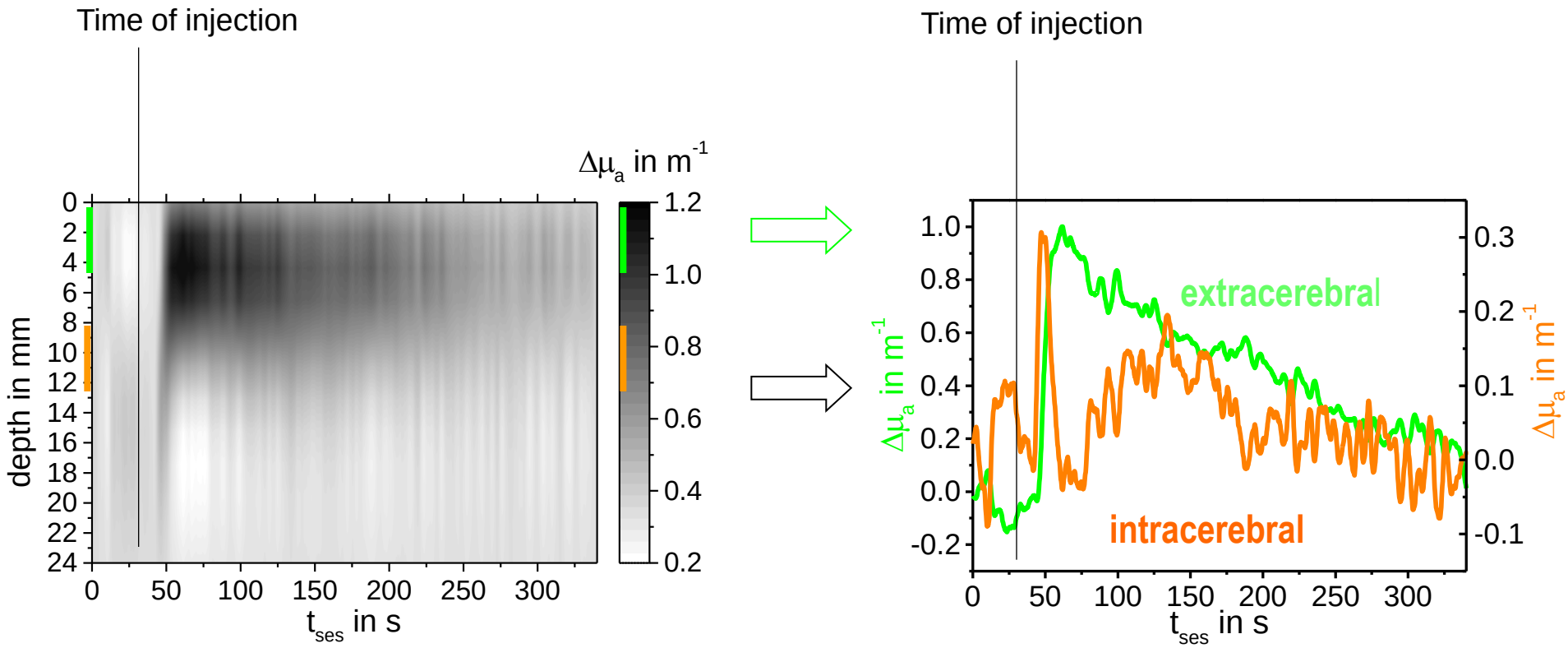
For the patient study a hand-held-probe was designed to increase the speed of the measurement, which were performed at a specialized stroke-ICU.



2 sources
4 detectors

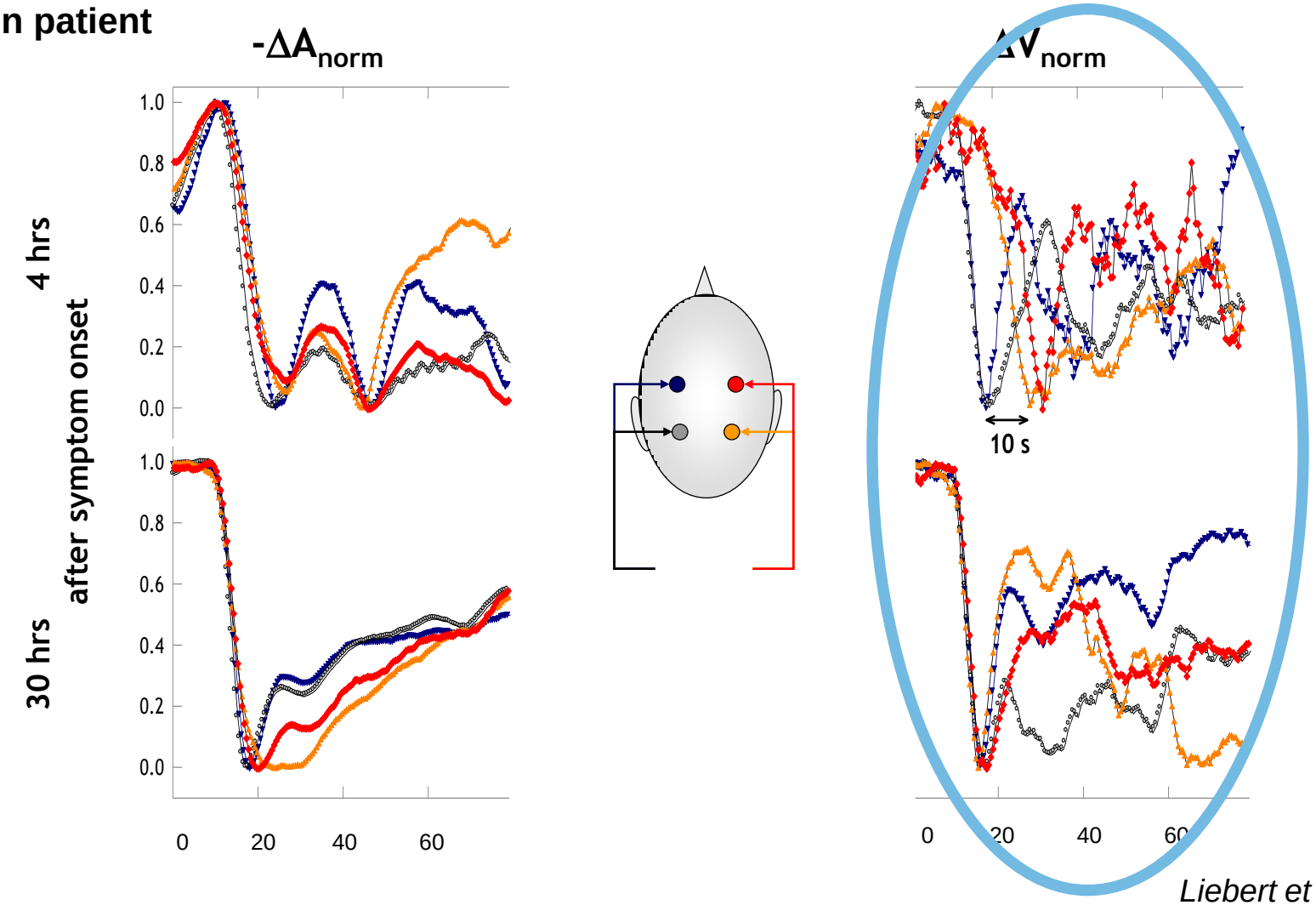
Depth resolution is relevant to differentiate the intra- and the extracerebral compartment for the determination of CBF.

Study with ICG



A patient monitored 4 hours after stroke showed a delay on the effected side, which normalized after 30h .

Result on patient



Liebert et al, NIMG2004

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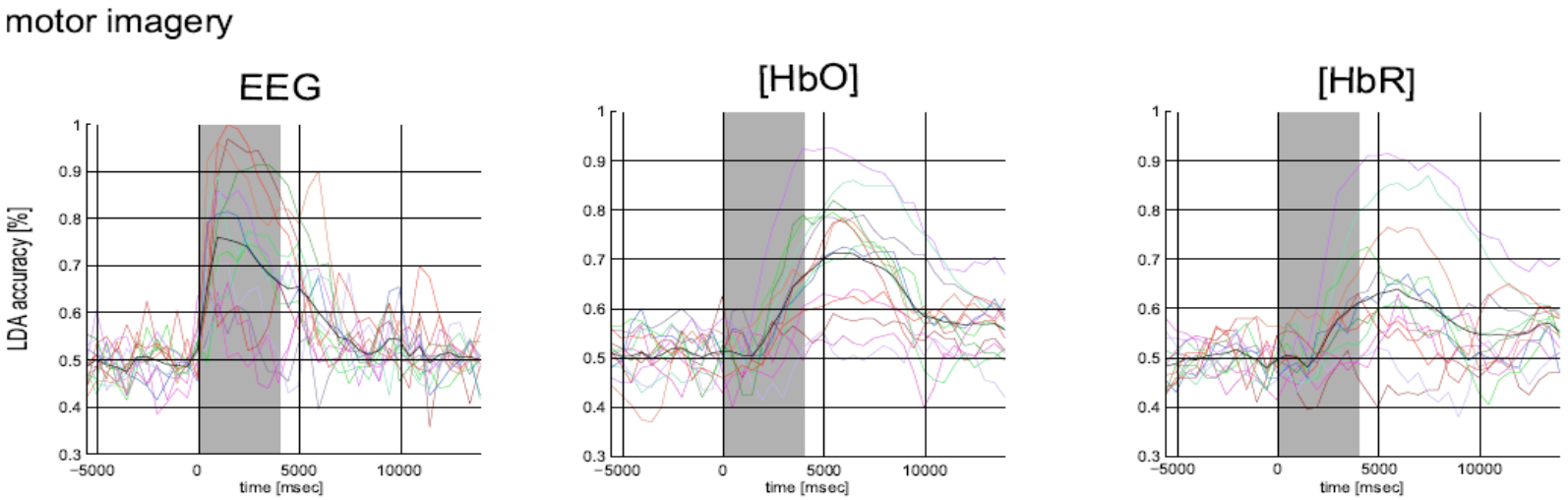
Clinical Applications

Brain Computer Interface

Temporal Reliability of Classification in Motor Imagery



- EEG peaks earlier as compared to HbO and HbR
- Physiological reliability: HRF shaped classification accuracies over time
- Classification accuracy higher for EEG
- Classification accuracy lower than in executed movements

Fazli et al. 2012