MetaboLight Workshop

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59th LIYSF
July, 28th 2017

Who we are…

METABO LIGHT

Engineering light to monitor brain metabolism in babies

Supported by wellcome trust UCL

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- Email: info@metabolight.org
  Twitter: @metabolight
  Facebook: metabolight
- www.ucl.ac.uk/medphys/research/borl/nirs/mms

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UCL Biomedical Optics Research Laboratory

What we do…

We are a team of engineers, scientists and doctors at UCL who works on developing new light-based technologies to help diagnose and monitor brain injuries in human, especially new-born babies.

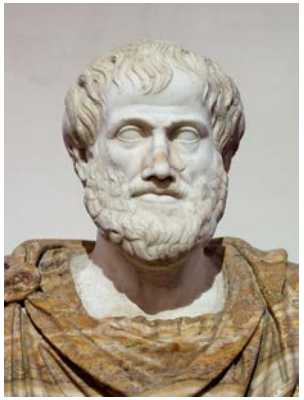
We also work on techniques to study and research human brain and its functions using non-invasive imaging modalities based on **Near-Infrared Light (NIR)**

Today schedule

1. The Brain
2. Light Transport
   - Light and its constituents
   - Light interaction with tissue
3. Medical Application
4. Brain Monitoring with Light
   - NIRO
5. Our Research
6. Summary
7. Q&A

The Brain : An important part?

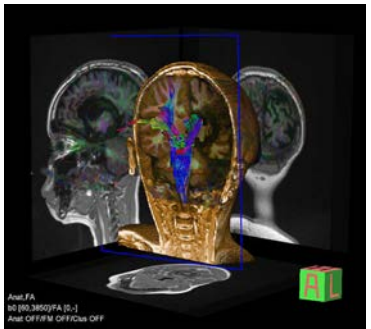
From the heart
(Aristotle, 384 BC-322 BC),



"mind-body dualism" (Descartes, 1596-1650),

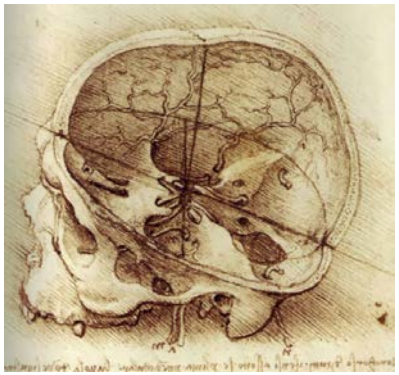
and Phrenology
(Joseph ,1848-1916),

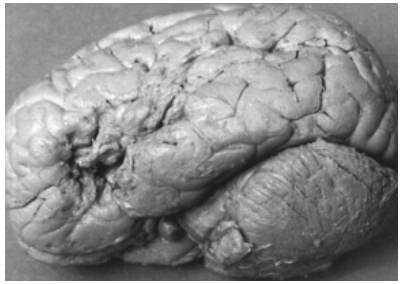
to neuroscience (XXs)



What made the comprehension of the role of the brain possible?

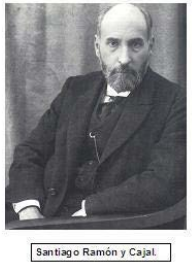
- Dissections
  - First anatomical knowledge

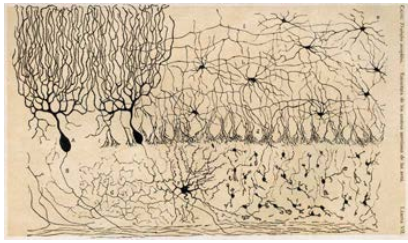




- Anatomo-clinical
  - Like computers you know how it works when it breaks)

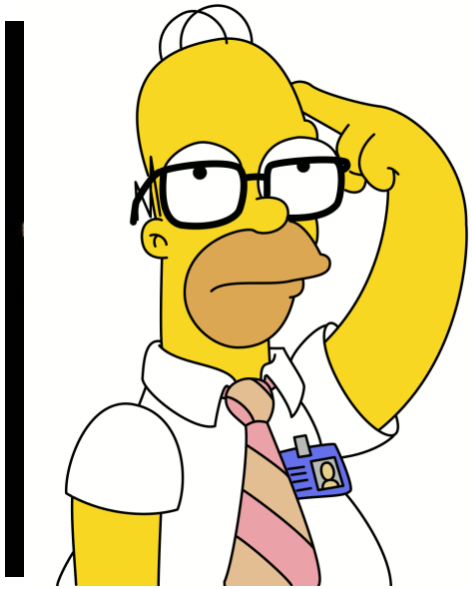
- Technology development
  - First microscopy: Neuron identification
  - Recent: Imaging techniques (MRI, etc)

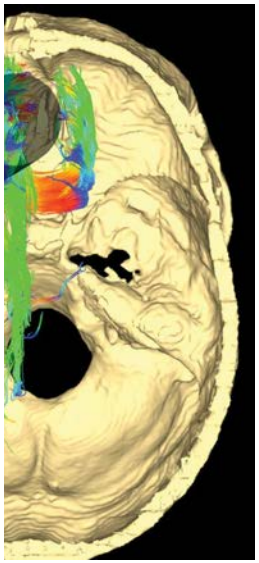




Phineas Gage

- **Phineas P. Gage** (1823–1860) was an American railroad construction foreman remembered for his improbable survival of an accident in which a large iron rod was driven completely through his head, destroying much of his brain's left frontal lobe, and for that injury's reported effects on his personality and behaviour over the remaining twelve years of his life—effects sufficiently profound (for a time at least) that friends saw him as "no longer Gage."

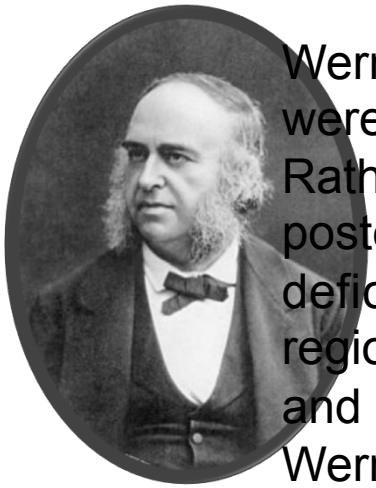




The Brain

Paul Broca (1824-1880)

Carl Wernicke (1848-1905)



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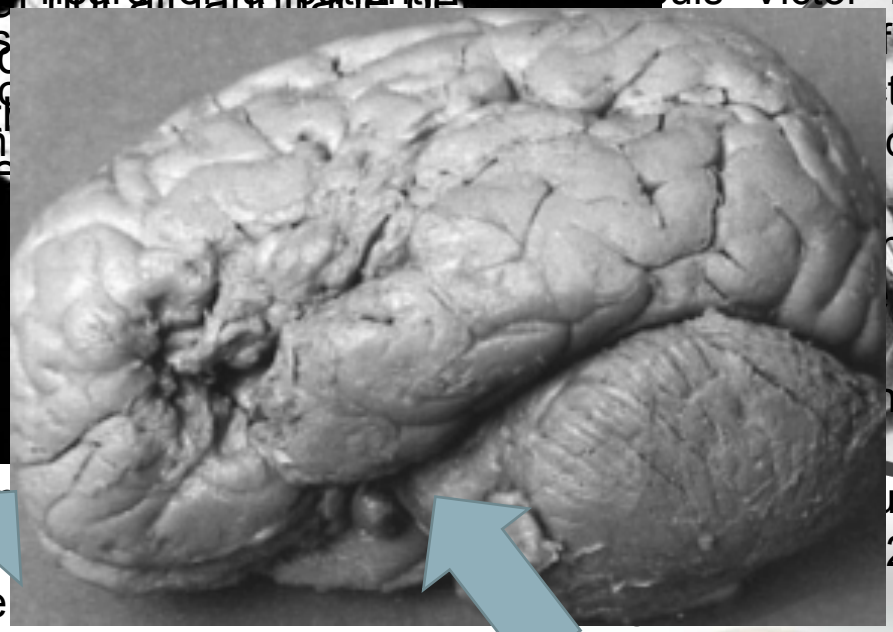
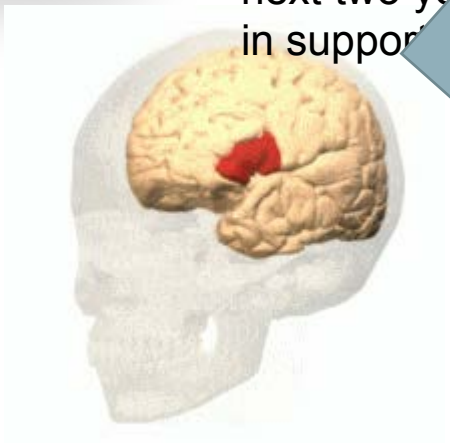
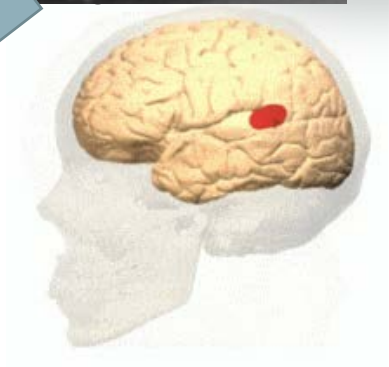




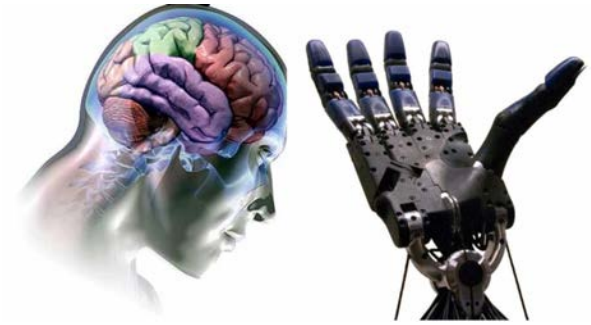


Why is it important to understand how the brain works?

Neuroscience: comprehension of how the brain works

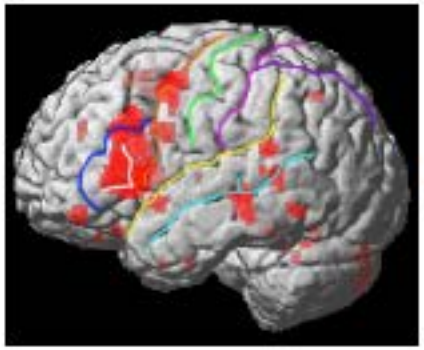
Clinic: brain injury / stroke / Alzheimer …

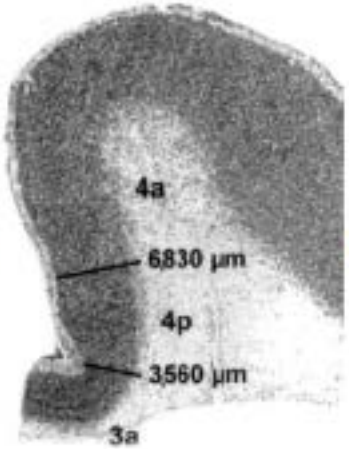
BCI: Brain Computer Interface

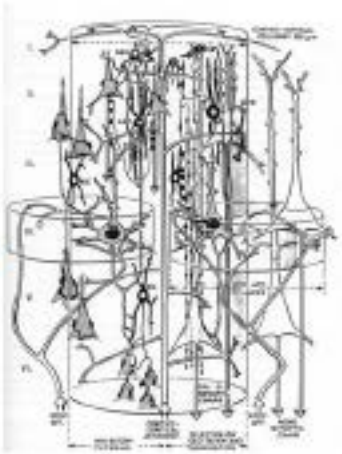


Structure of the brain

multiscale:







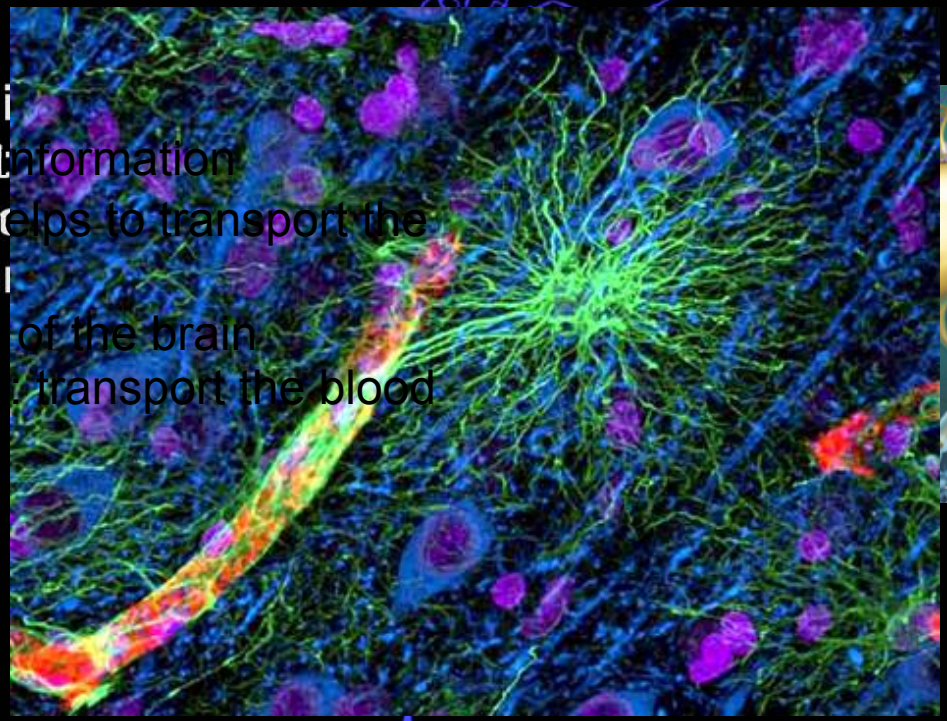
Microscopic structure

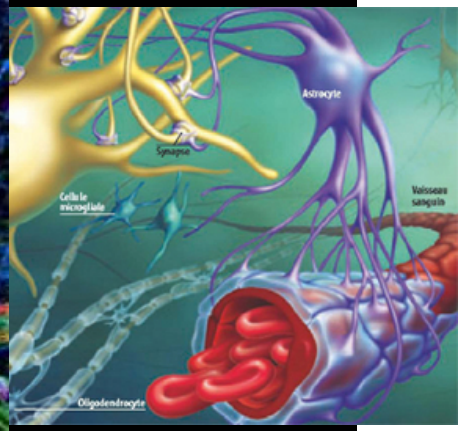
The Crystalli

- Network of t information
- Cortex as the elps to transport the

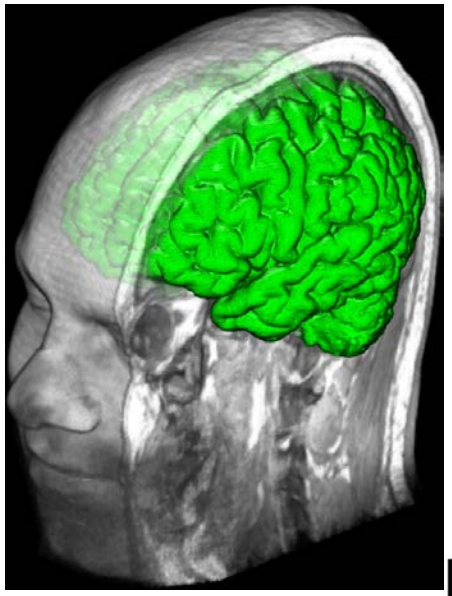
Unit of the Ner

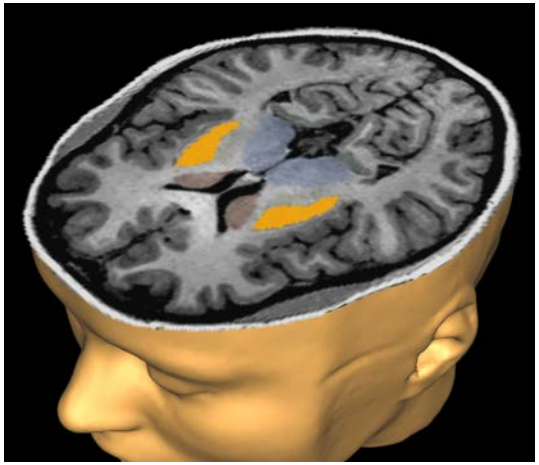
- of the brain
- transport the blood

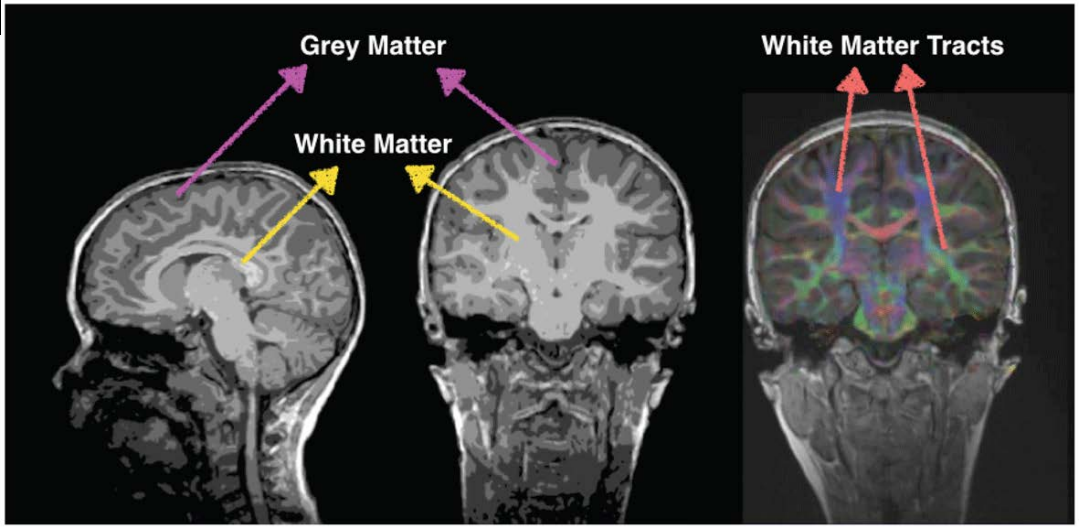


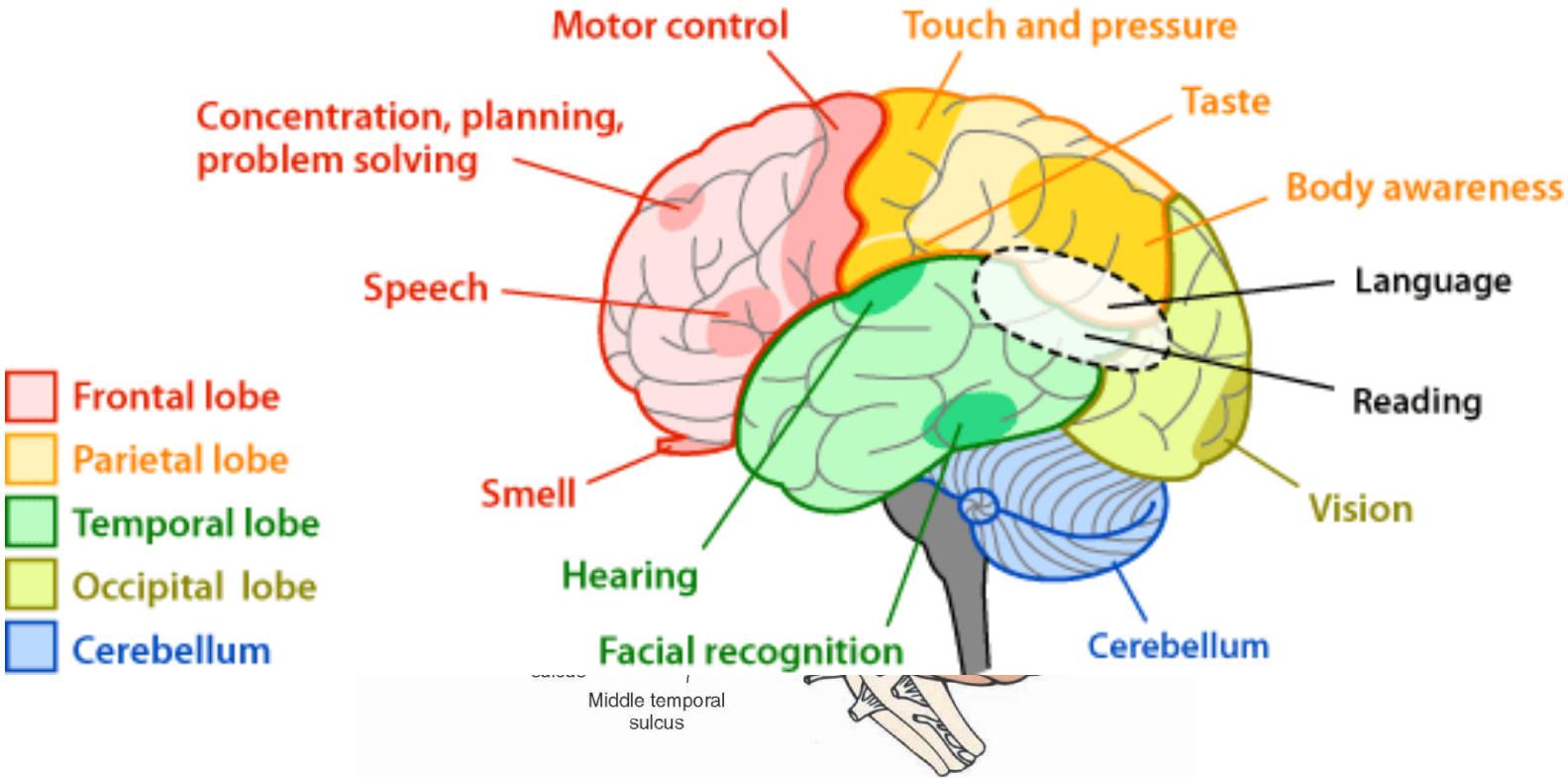


Macroscopic structure





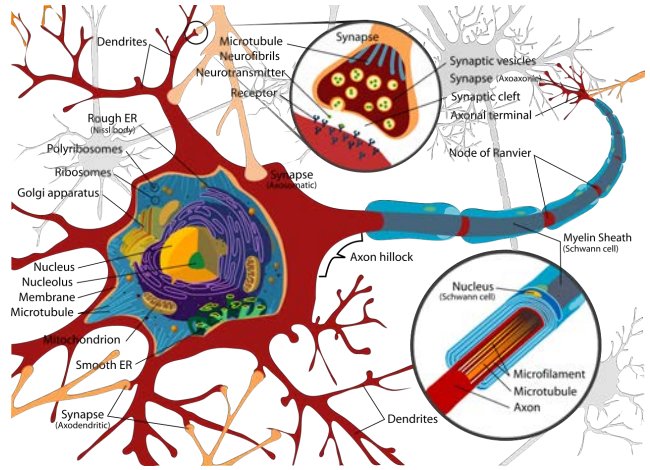


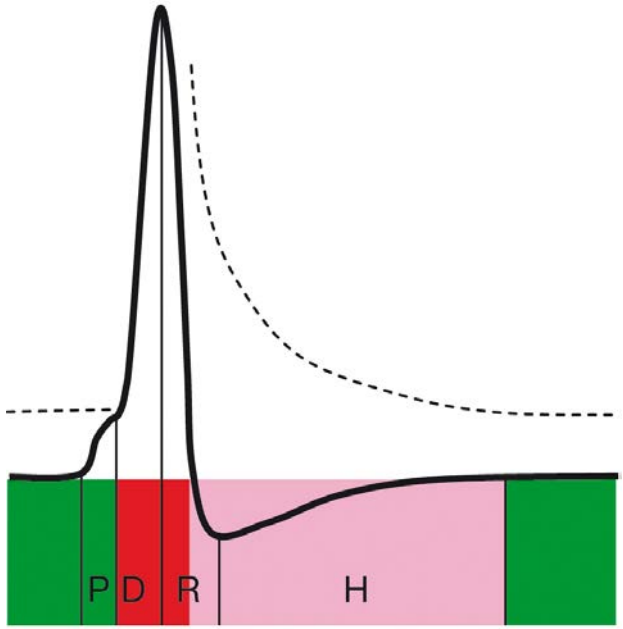

Motor control
Touch and pressure
Concentration, planning, problem solving
Taste
Body awareness
Speech
Language
Reading
Frontal lobe
Parietal lobe
Temporal lobe
Occipital lobe
Cerebellum
Smell
Vision
Hearing
Facial recognition
Cerebellum
Middle temporal sulcus

Physiology Basics: How does it work ?

Neurons: Brain activity via electricity

Propagation via Action Potential (AP)
Quick: few milliseconds





Need more energy !!

Physiology Basics: How does it work ?

Neurons need more energy to propagate the AP

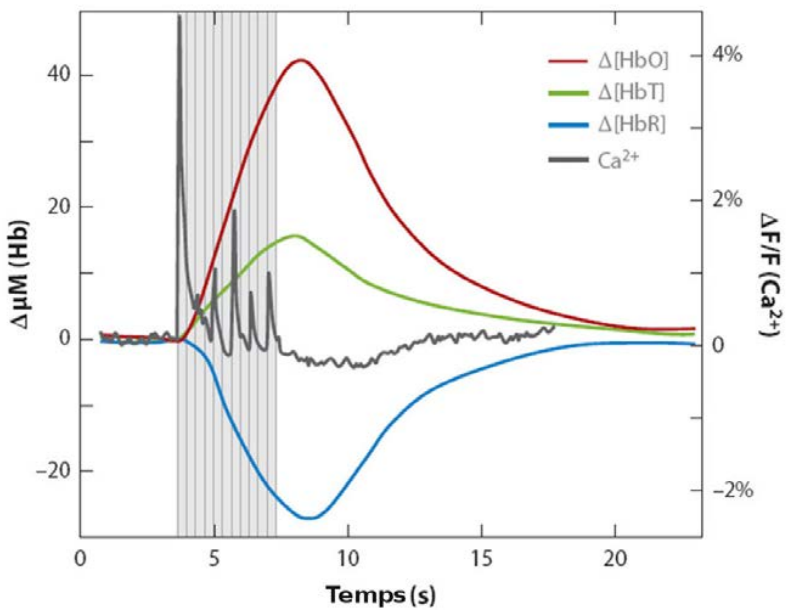
Glucose + O_2 → ATP (Energy)

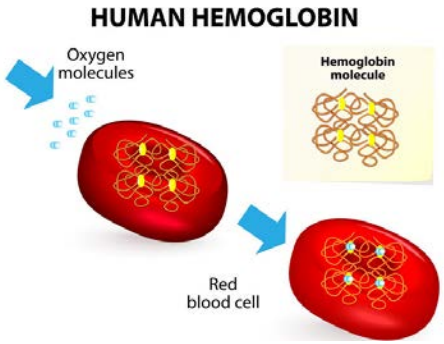
Transported by the blood

Brain is a massive energy consumer:
Although the human brain represents only 2% of the body weight, it receives 15% of the cardiac output, 20% of total body oxygen consumption, and 25% of total body glucose utilization.

Physiology Basics: How does it work ?

Oxygen carried in the blood by hemoglobin





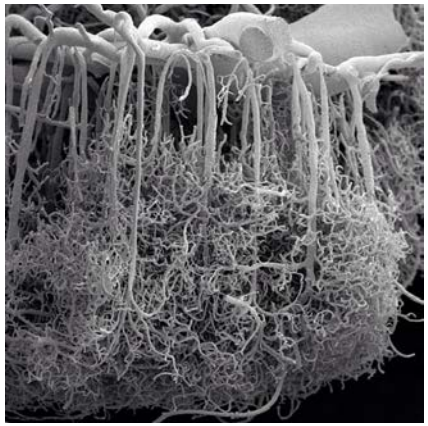
Oxyhemoglobin (HbO_2)
With O_2

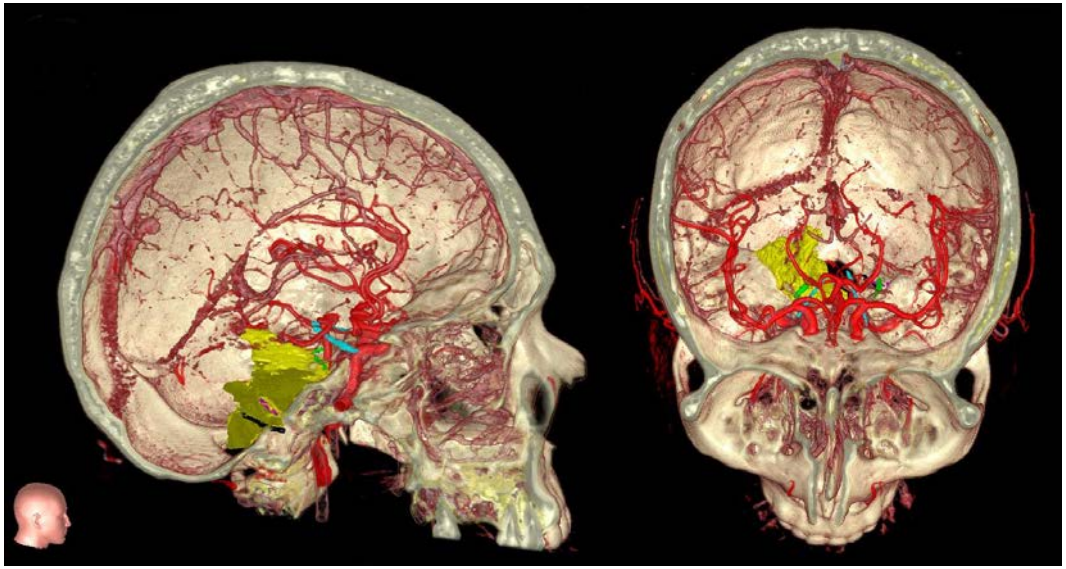
Deoxyhemoglobin (HHb)
Without O_2

Oxygen response slower than neuron response: few seconds

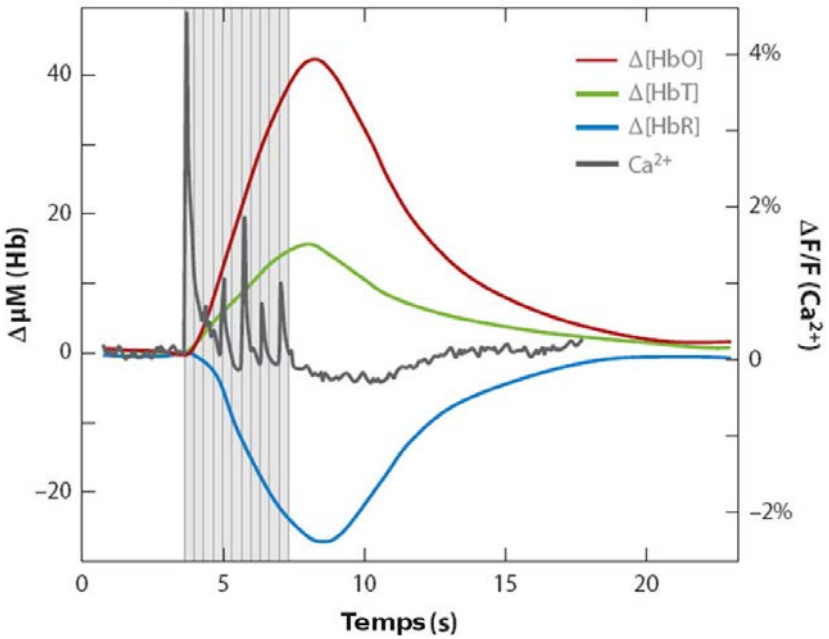
Neurovascular coupling

refers to the relationship between local neural activity and subsequent changes in cerebral blood flow





Neurovascular coupling



http://www.martinos.org/martinos/research/MultimediaGallery/DOT_materials/dot.html

Imaging:
A non invasive way to reveal brain's structure and function

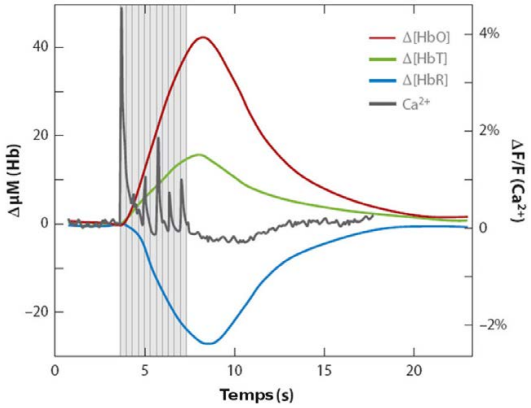
1 - Magnetic Resonance Imaging (MRI) for the structure

- Different tissue have different magnetic properties

And function:

- HbO_2 and HHb have different magnetic properties

- Vascular response

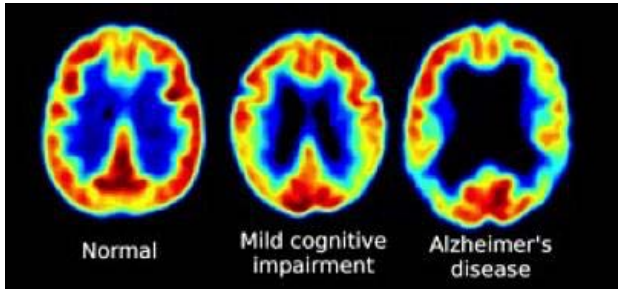


Imaging:
A non invasive way to reveal brain structure and function

❖ For function:

➢ Positron emission tomography (PET)

- Uses a radioactive element to asses metabolism and blood flow



➢ Used for clinical application
➢ One of the first imaging technique to assess brain function with a good resolution (90's)

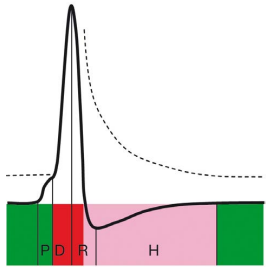
➢ Vascular response and cells response

! radioactive

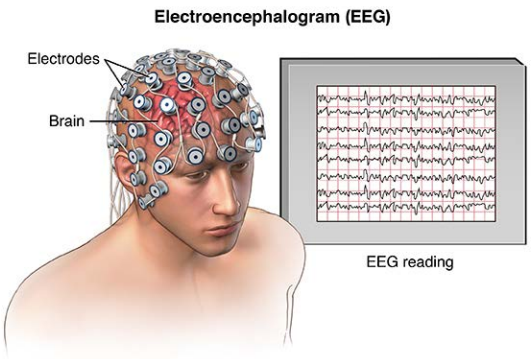
Imaging:
A non invasive way to reveal brain structure and function

❖ For function:

To asses the neuron directly by detecting the electricity



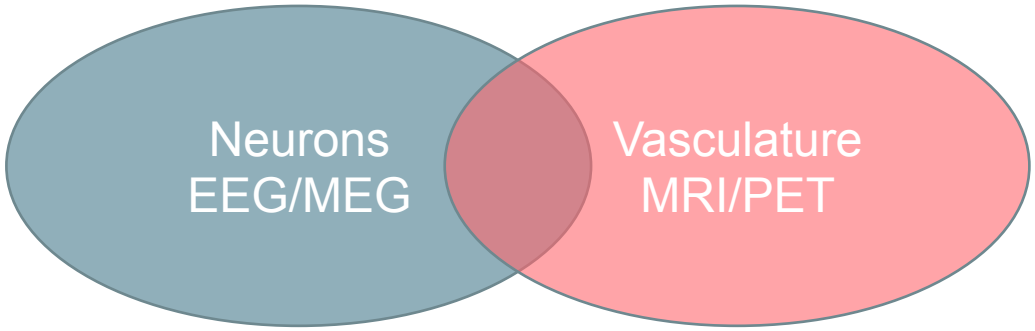
➢ Electroencephalography (EEG)



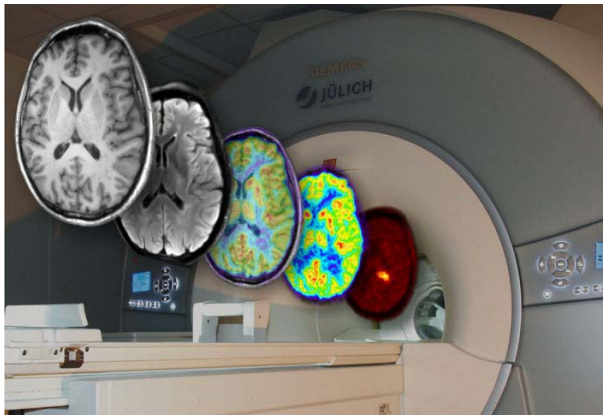
➢Magnetoencephalography (MEG)

Imaging:
A non invasive way to reveal brain structure and function

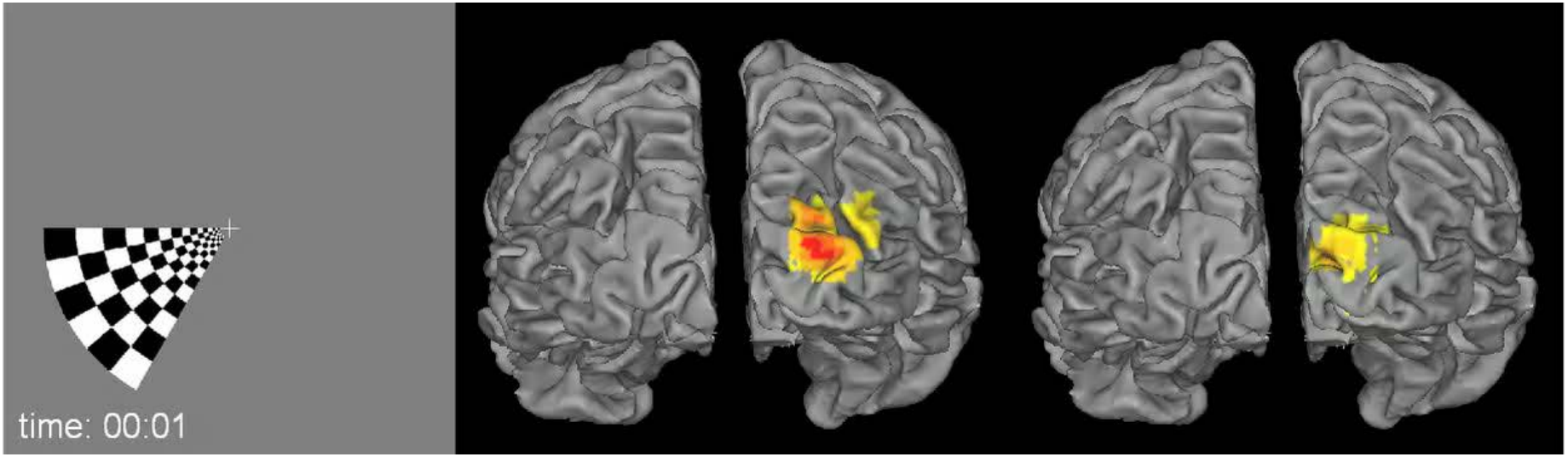
- Different technic to asses the different components of the neurovascular coupling



- Combine them to offer a better understanding of the brain function



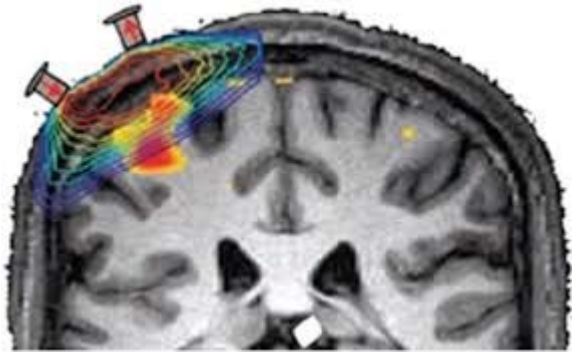
The Brain



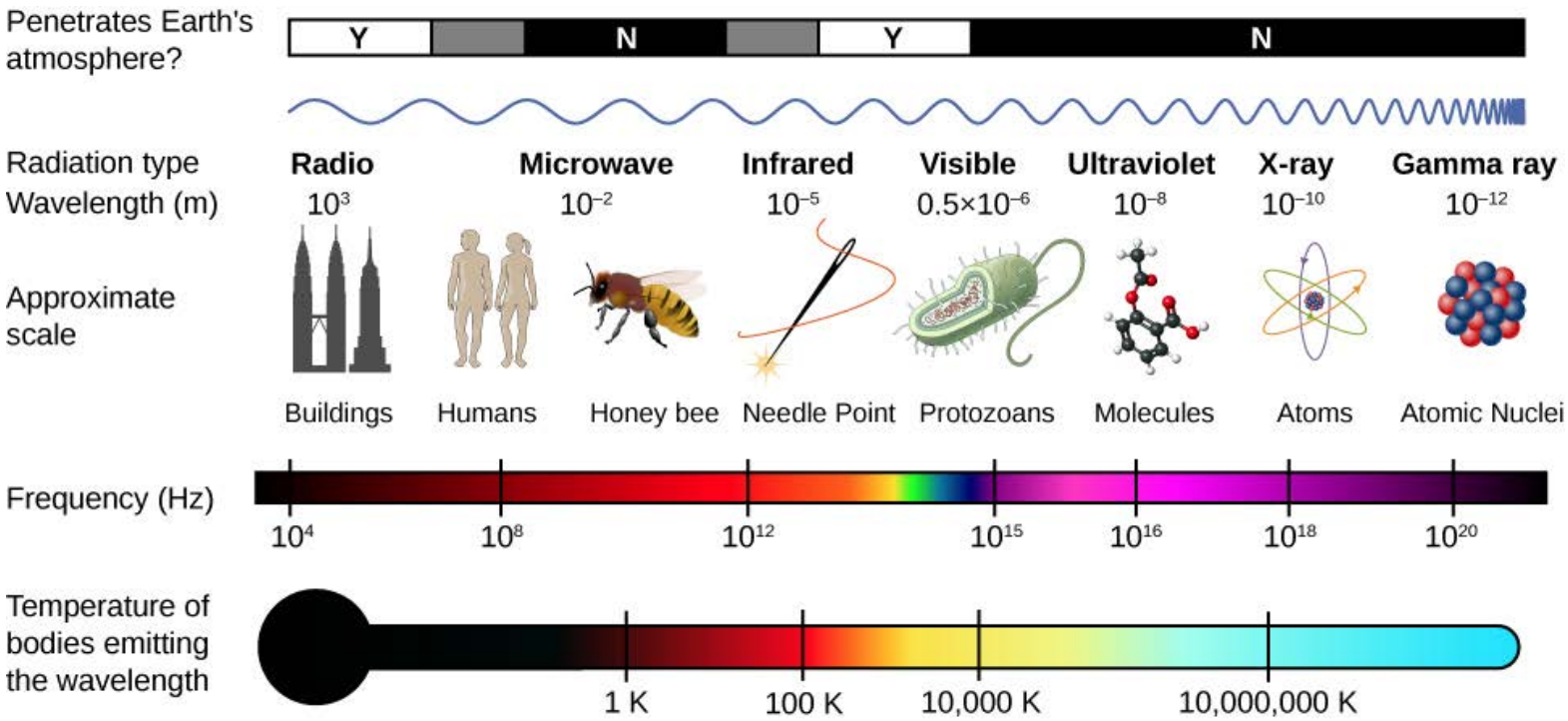
DOI: 10.1016/j.neuroimage.2012.01.124

Towards Near InfraRed Spectroscopy (NIRS)

Uses Light…



Light and its constituents

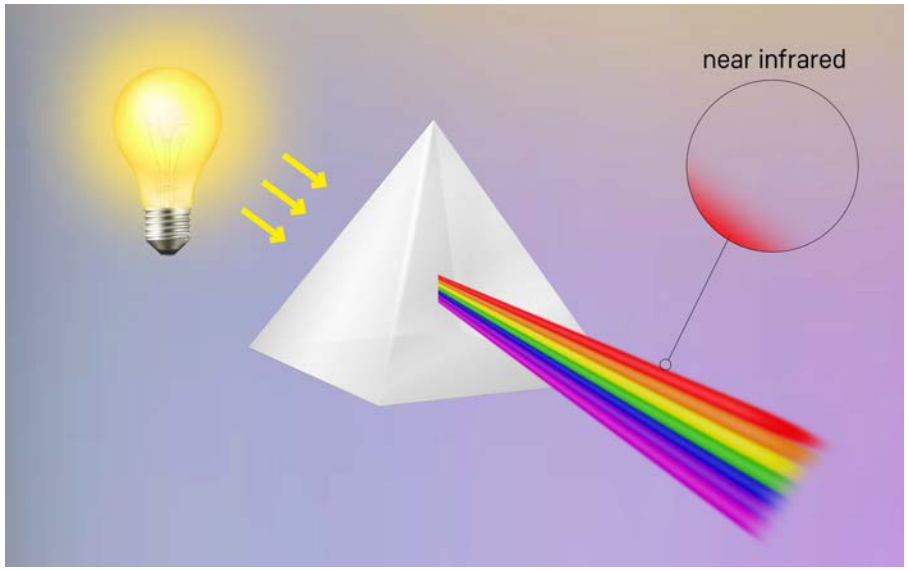


White light is composed of a multitude of wavelengths that covers the **visible (colours)** and non-visible **(UV and NIR)** spectrum.

Splitting light in its constituents wavelength can be easily achieved using specific dispersive devices such as:

- **Prisms**
- **Diffraction gratings**

Light and its constituents



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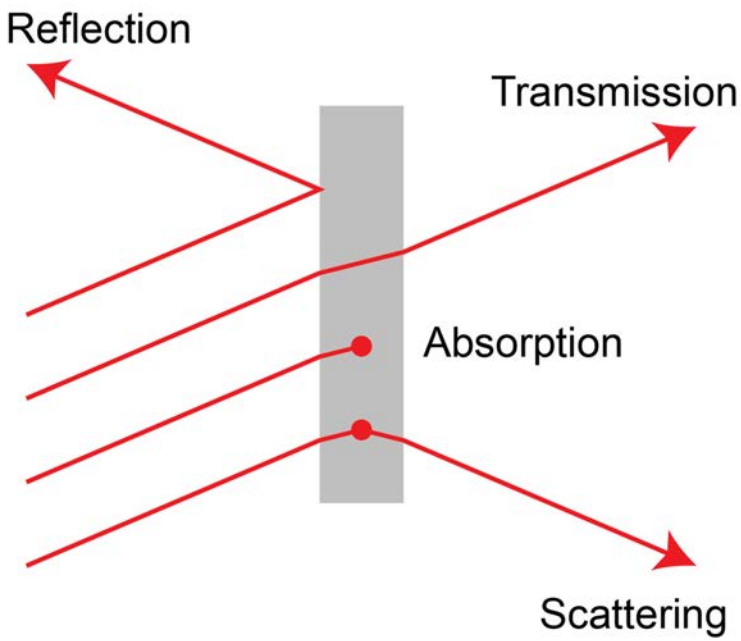
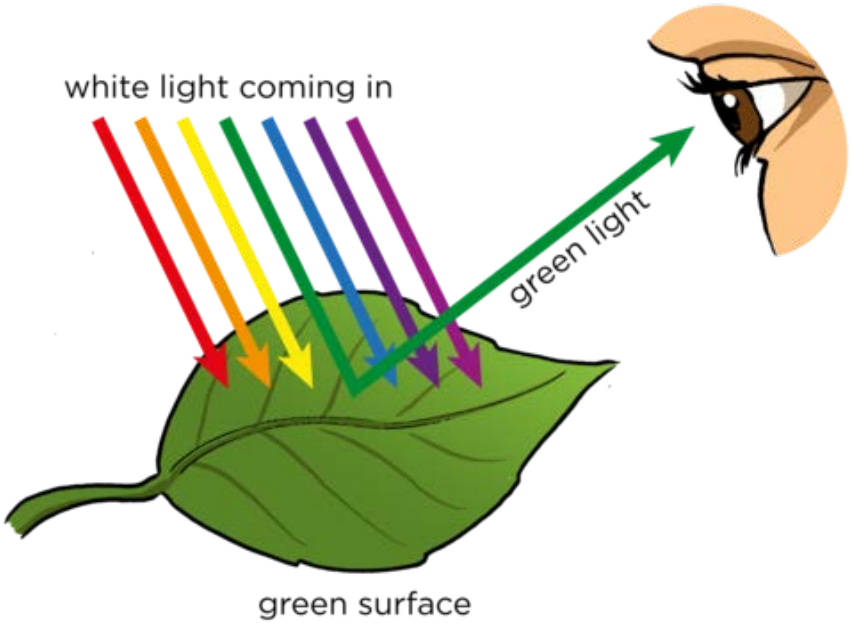
Light interacting with tissues

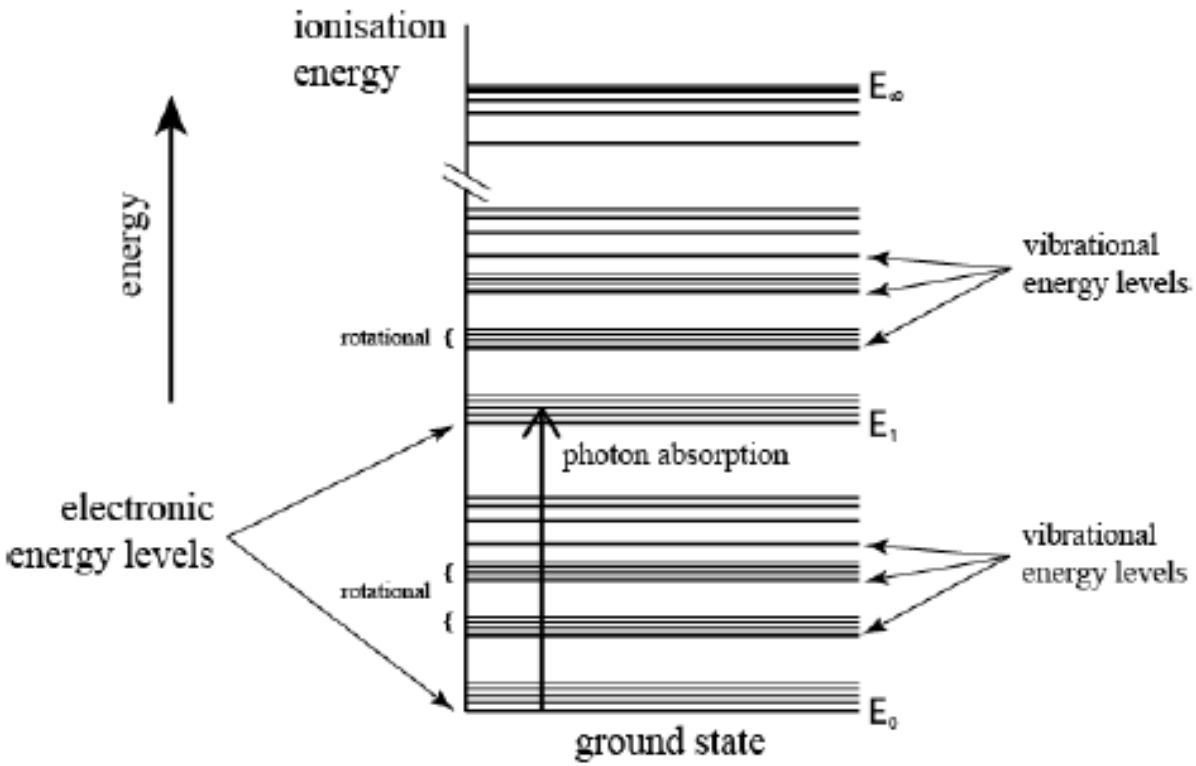




Light can interact with tissue in different ways. In particular, the most important interactions it can have in biological matter are:

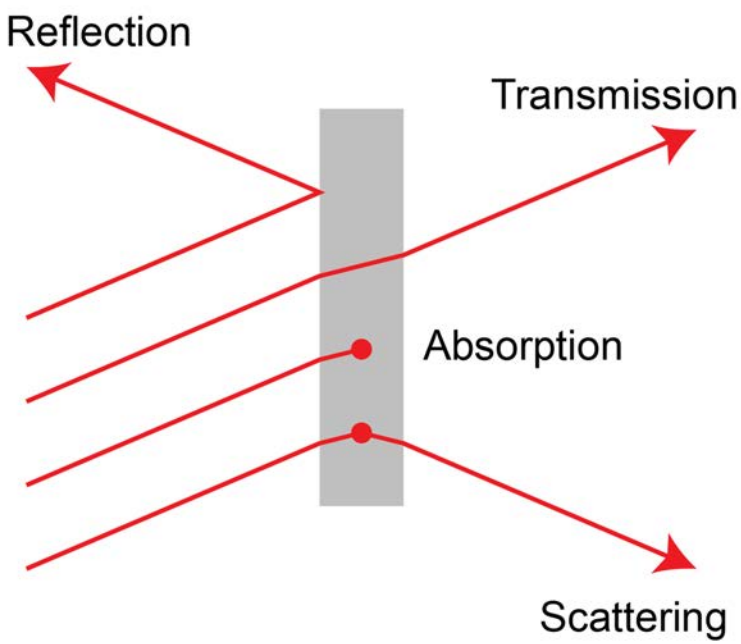
- **<u>Absorption</u>**
- **Scattering**

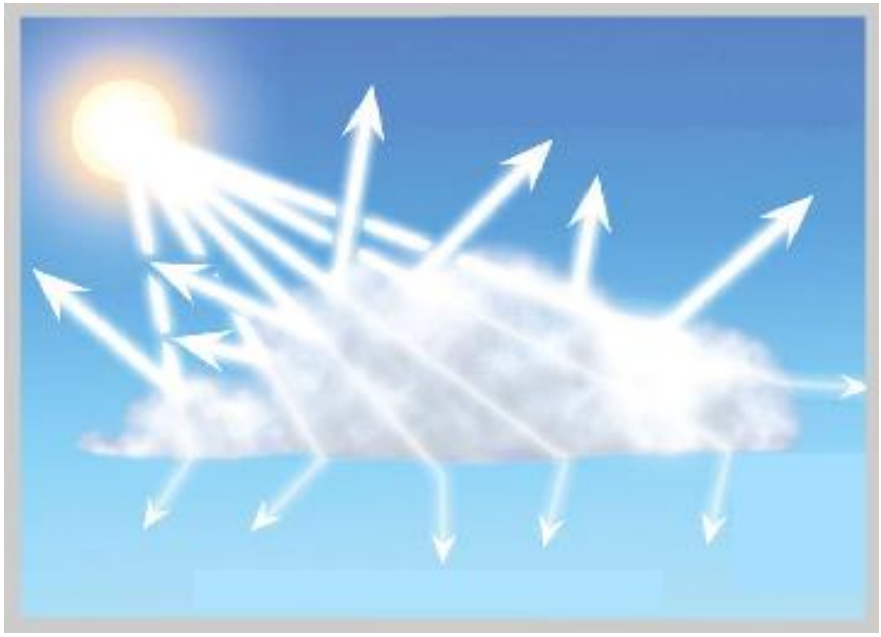
Light interacting with tissues



For the energy of a light particle (photon) to be absorbed by a certain molecule, **the photon frequency must match a natural frequency of the molecule**. Because this is a quantum effect, it is equivalent to saying that absorption is highly likely when **the photon energy equals the energy difference between the current state** (the current energy level) **and an excited state**.

Light interacting with tissues





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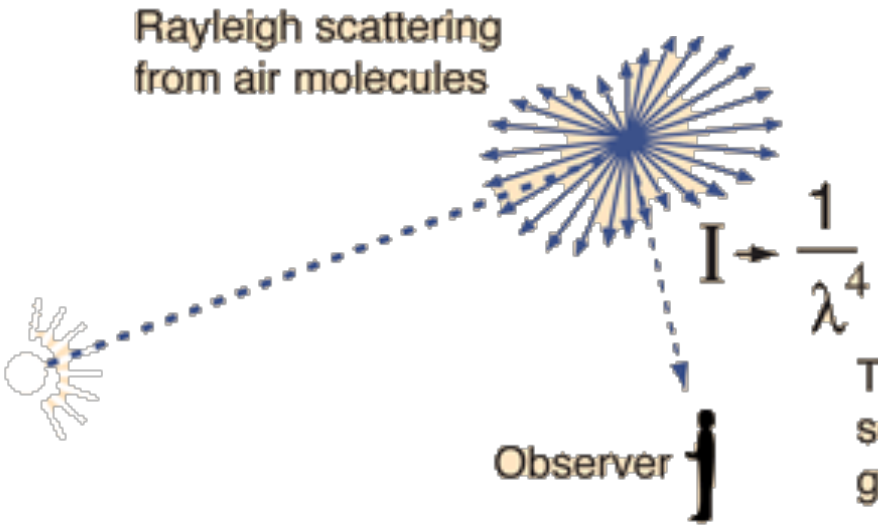
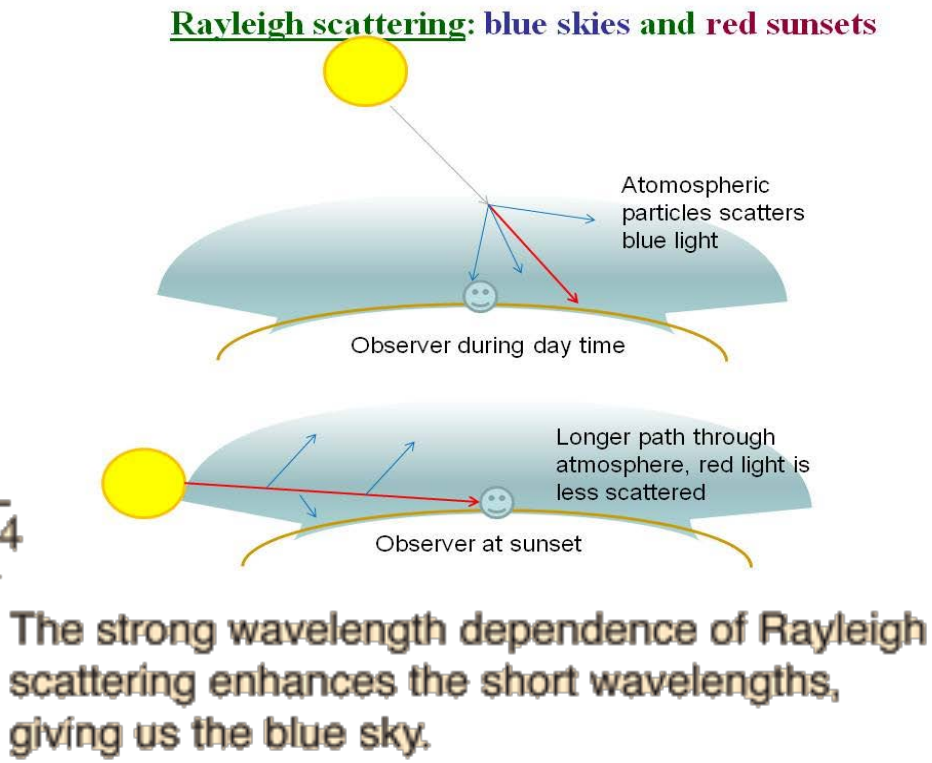




When the wavelength of light is very much larger than the scatterer's dimensions, as in the case of molecular scattering, the scattering is often known as **Rayleigh scattering**. For a particle of characteristic dimension d, the criteria for Rayleigh scattering is:

$$\boxed{\lambda \gg \pi d}$$

Light interacting with tissues

Biological tissues are relatively transparent to **NIR light** (optical window) and such type of light can be used to penetrate deep in the head and provide information about the **haemodynamic and metabolic states of the brain** based on how much it is diffused and absorbed.

Medical NIRS

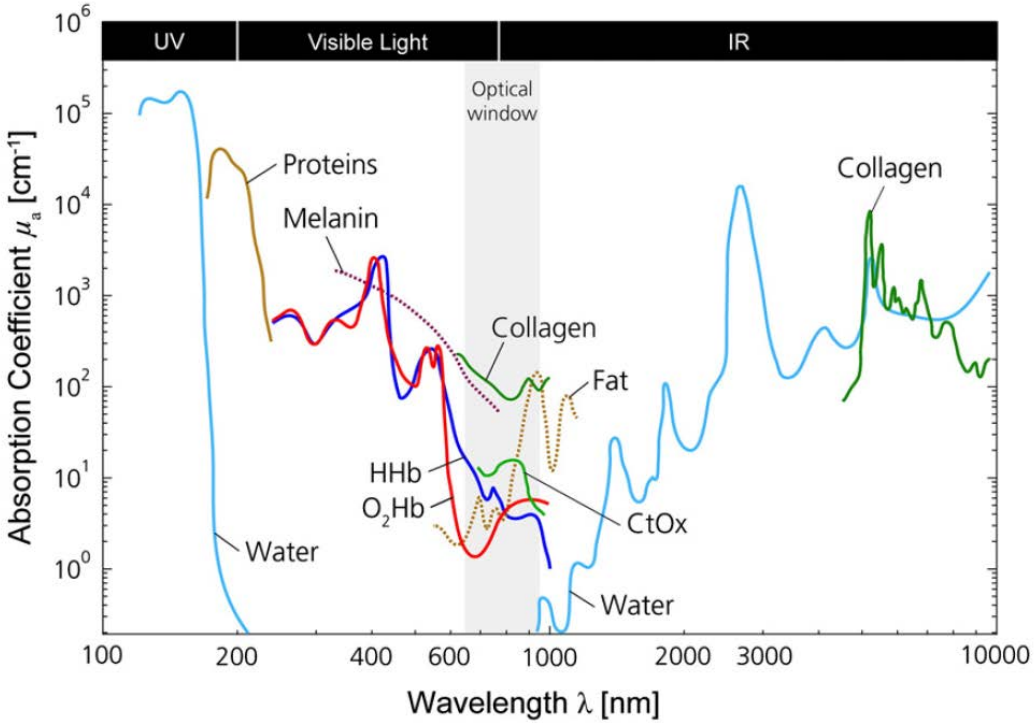
Light travels through tissue and interacts with it via scattering and absorption.

Chromophores = light absorbing molecules.

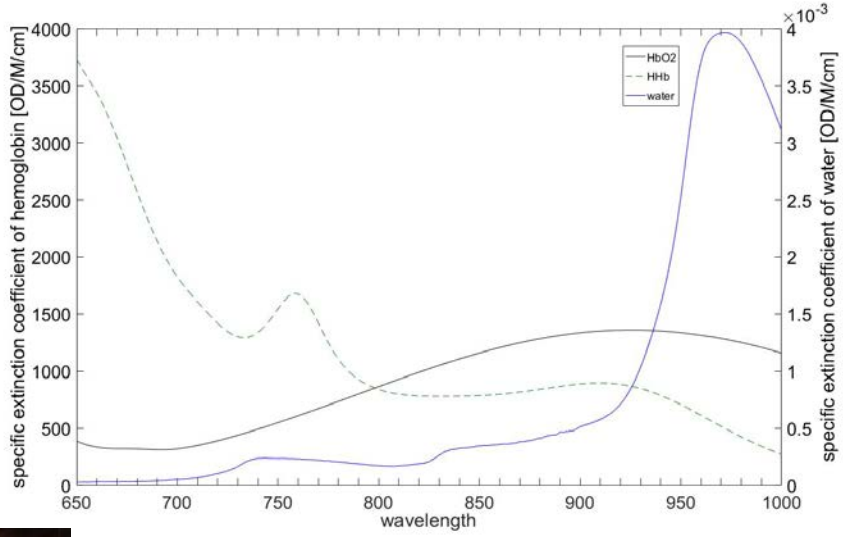
Important chromophores in tissue: water, lipids, melanin, **haemoglobin...**.

NIR range: haemoglobin the main chromophore.

The interaction of chromophores with light depends on the **absorption spectra of the chromophores.**



Haemoglobin absorption spectra



Which one is oxygenated and which one is deoxygenated blood?

Oxygenated Blood

Deoxygenated Blood

Near-infrared Spectroscopy

Please update your notes

NIRS is based on quantifying this difference between the two oxygenation states of haemoglobin – it is an indicator of the oxygen content in the volume of interest.

The absorption of light in tissue changes with time depending on the amount of oxygenated and deoxygenated haemoglobin in the volume of interest → shine light into the tissue and measure what travels through it.

The amount of light absorbed in the medium at each time point informs on the haemoglobin changes.

Measuring concentration changes

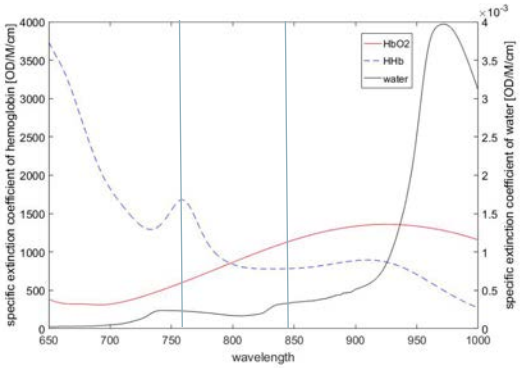
$$\Delta A = l \times absorption \times \Delta c$$

Change of light attenuation between time point 1 and 2.

Pathlength of photons, experimentally measured consta

Haemoglobin absorption properties at selected wavelengths – different for HHb and HbO2

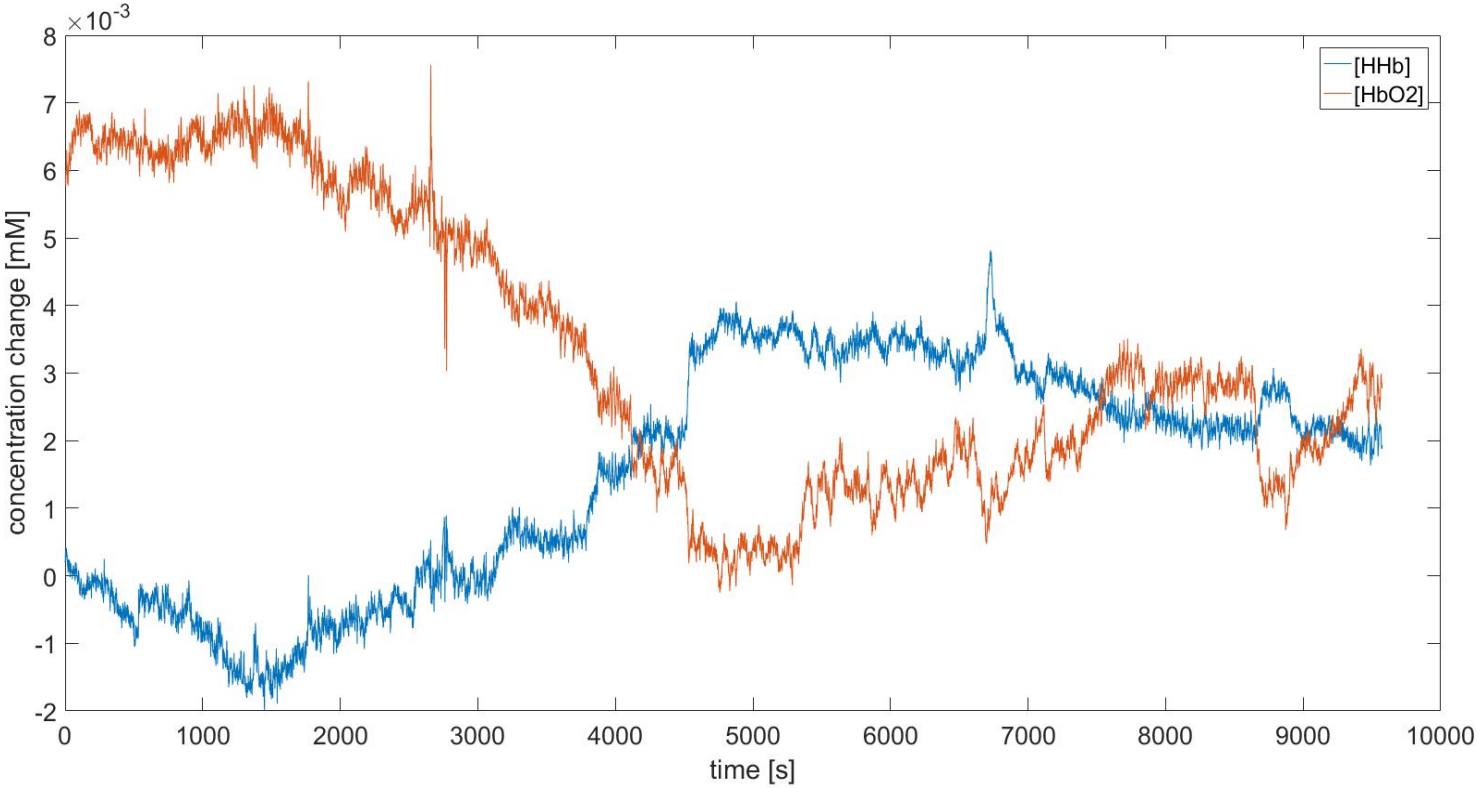
Change of HHb and HbO2 concentrations



At least two wavelengths are used to see the difference in the absorption properties

Medical NIRS

Now we can non-invasively monitor concentration changes of haemoglobin real-time



Medical NIRS

We now have a simple real-time indicator of regional haemodynamics, which can be used for both:

Functional activation in the region of interest

- Functional activation of a brain region increases oxygen consumption
- We can track these changes and relate them to stimuli

Pathology occurring in the region of interest

- Mostly cerebral monitoring, can be also placed on muscle or liver region
- Cardiovascular surgeries, brain injury, neonatology

How can we build our own machine to measure brain activity?

- What have we learnt so far?

How can we build our own machine to measure brain activity?

- What have we learnt so far?
  - When light interacts with something, it is attenuated due to scattering and absorption (i.e. there is light loss)
  - We know that materials have colour because they absorb certain parts of the spectrum and reflect other parts back to the eye
  - We can assume that scattering properties of the head remain the same (so we can ignore attenuation due to scattering)
  - HbO_2 and HHb have different colours (look at the different absorption spectra)
  - We can shine a light through something to learn about the colours within it
  - Light (at the red and infrared end of the spectrum) can travel through tissue

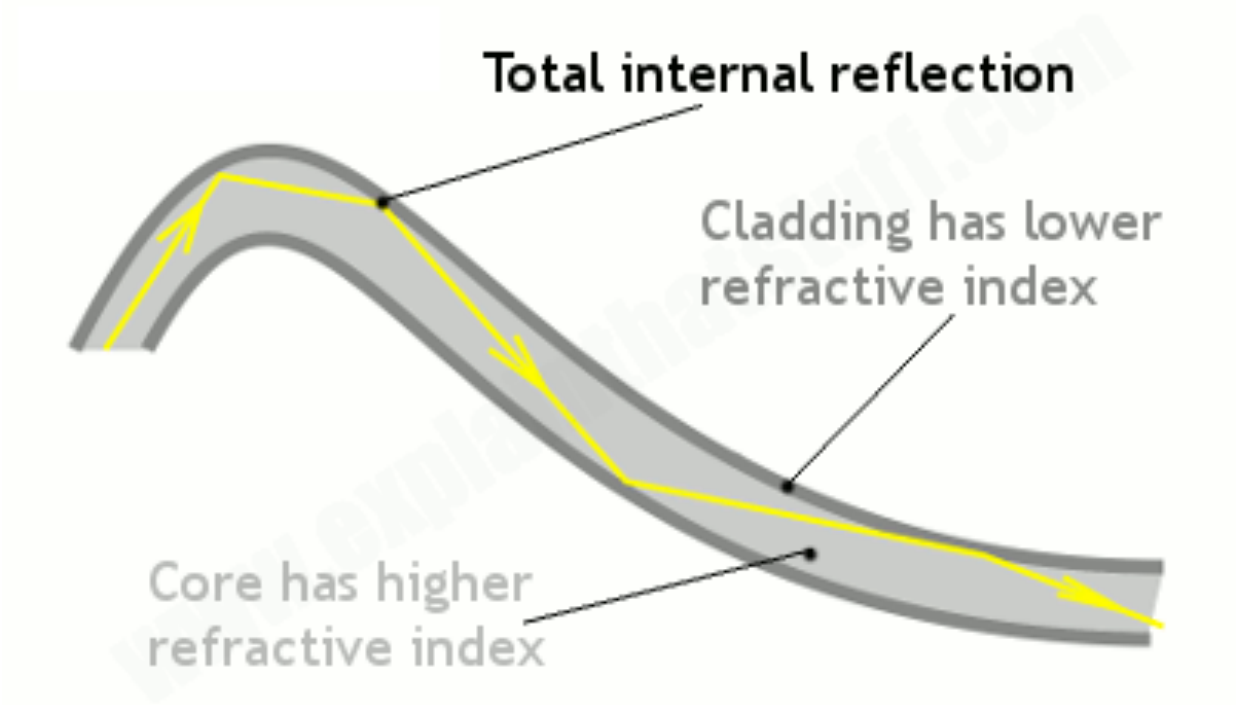
Light source

LEDs

Laser

Light bulb

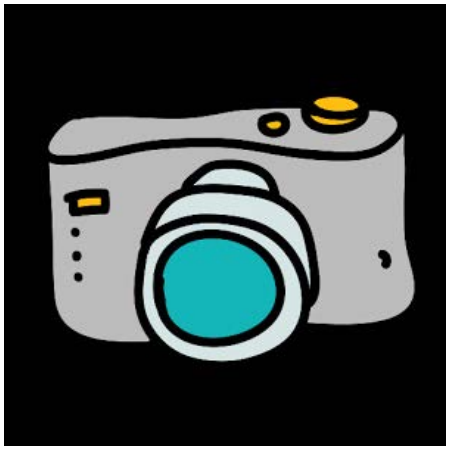
Optical fibres



Detector

- Photodiode → converts light to an electrical current via the photoelectric effect

- Charge-coupled-device (CCD) → formed of 2D array of pixels. Light is converted to electrons via the photoelectric effect at each pixel, hence we can detect a broadband light source if the light is separated into individual wavelengths

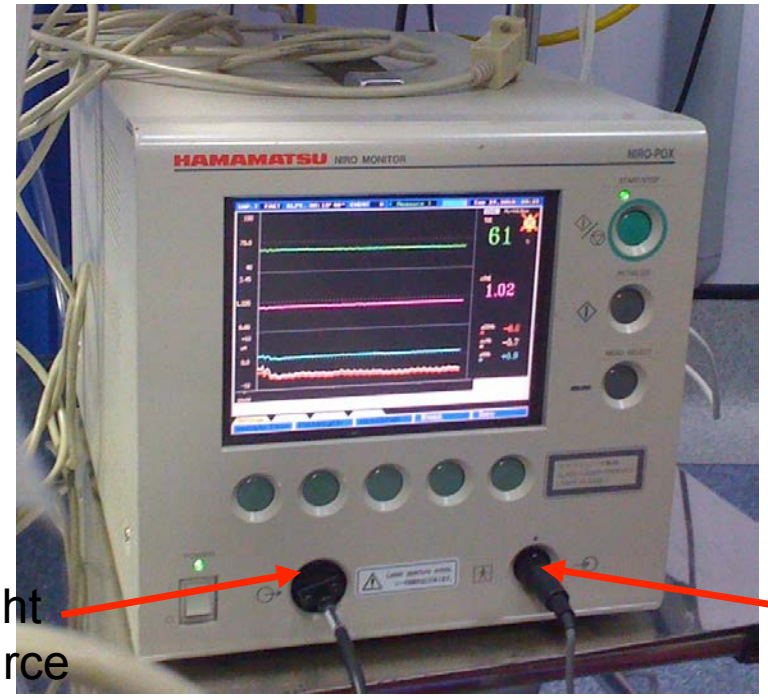


Software

- Computer can be used to process the data – i.e. take the raw intensity of light after it has travelled through the head and calculate the concentration changes using the modified Beer-Lambert law

$$\Delta A = l \times absorption \times \Delta c$$

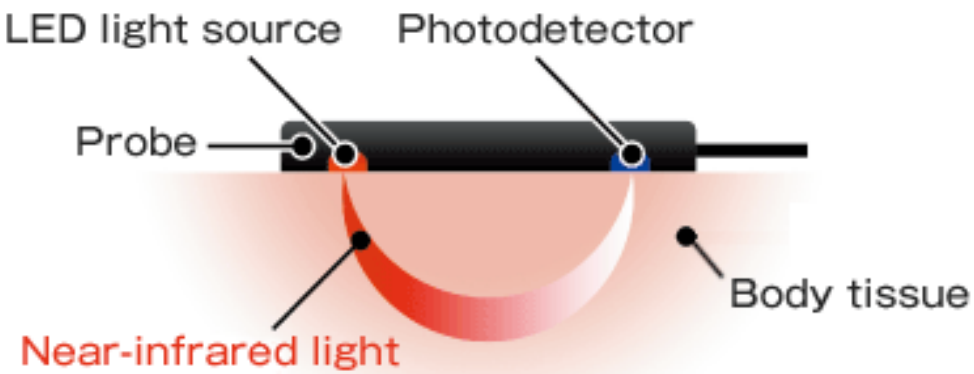
Building a brain monitor



light source

detector

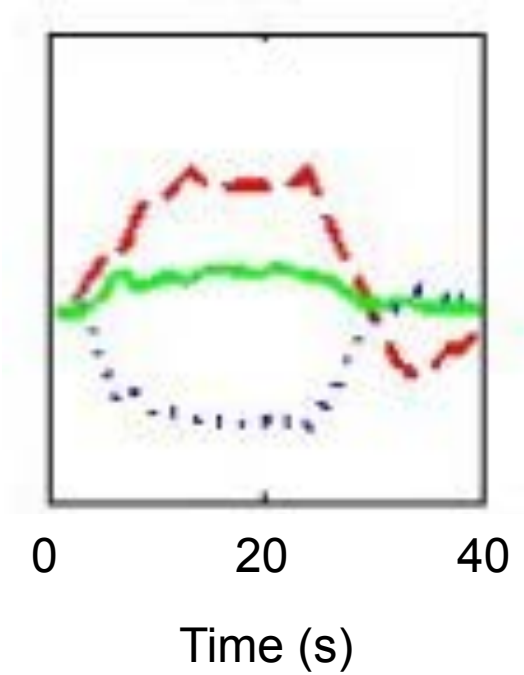
Hamamatsu NIRO system



Demonstration – functional activation experiment

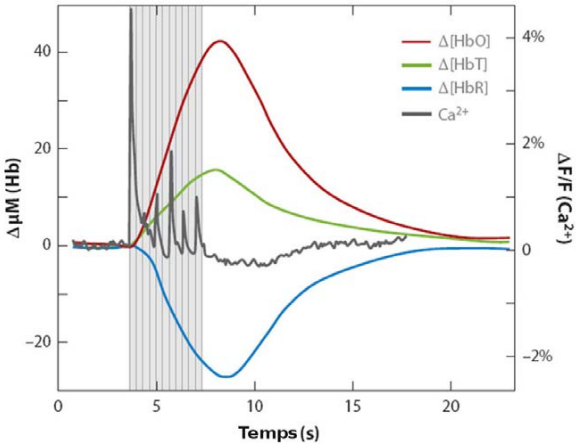
- Can we measure your brain activity using light?

Demonstration – functional activation experiment
What do we expect to see?



oxygenated

deoxygenated



*Data from our lab (Phan (2016))

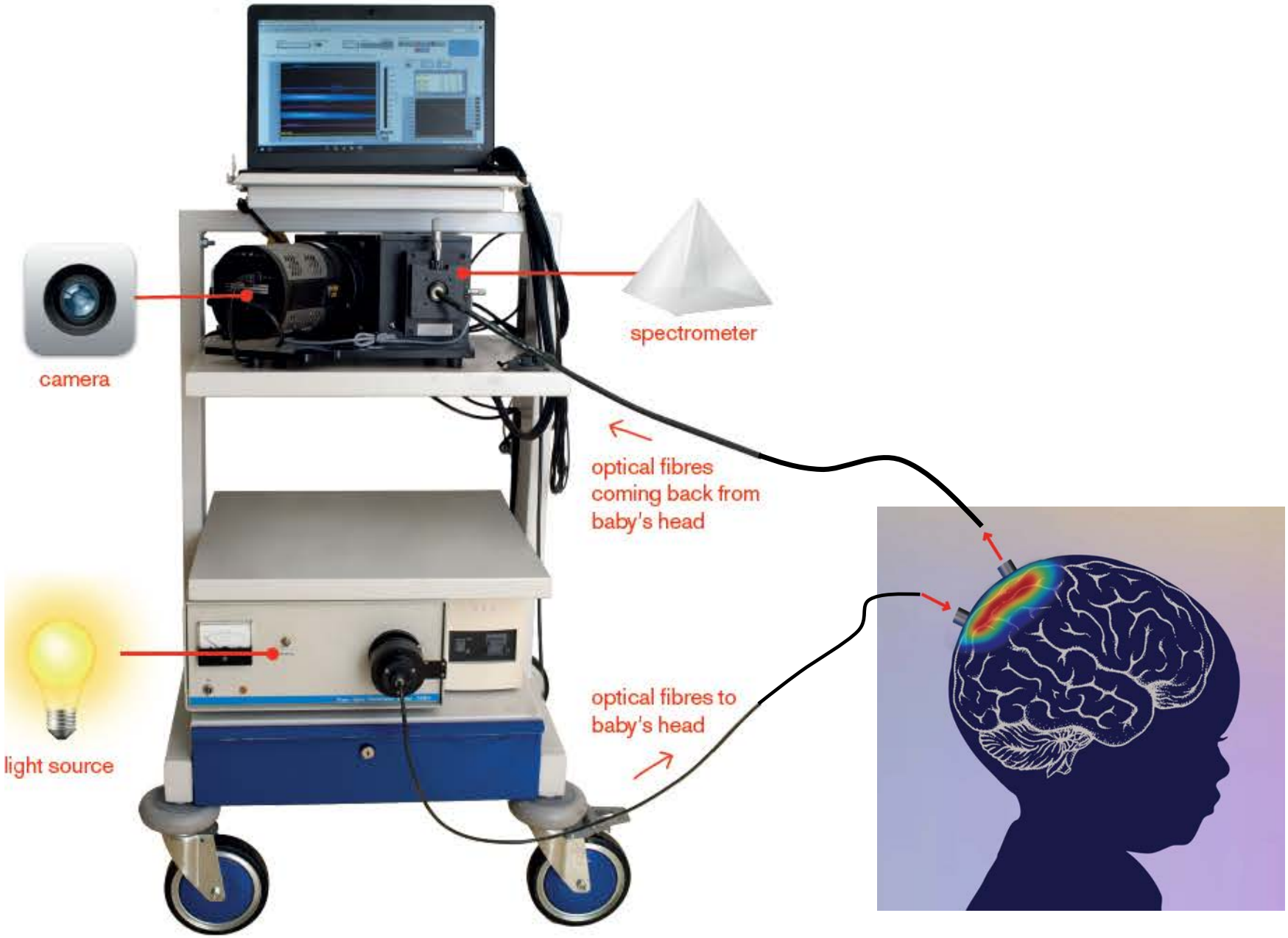
Baby brain injury

- Our group is interested in monitoring changes in brain physiology of newborn babies who are at risk of brain injury
- The doctors need a monitor of brain health to treat these babies
- We might be able to use NIRS to help...

Example of a birth-asphyxiated newborn who is being treated at UCL Hospital

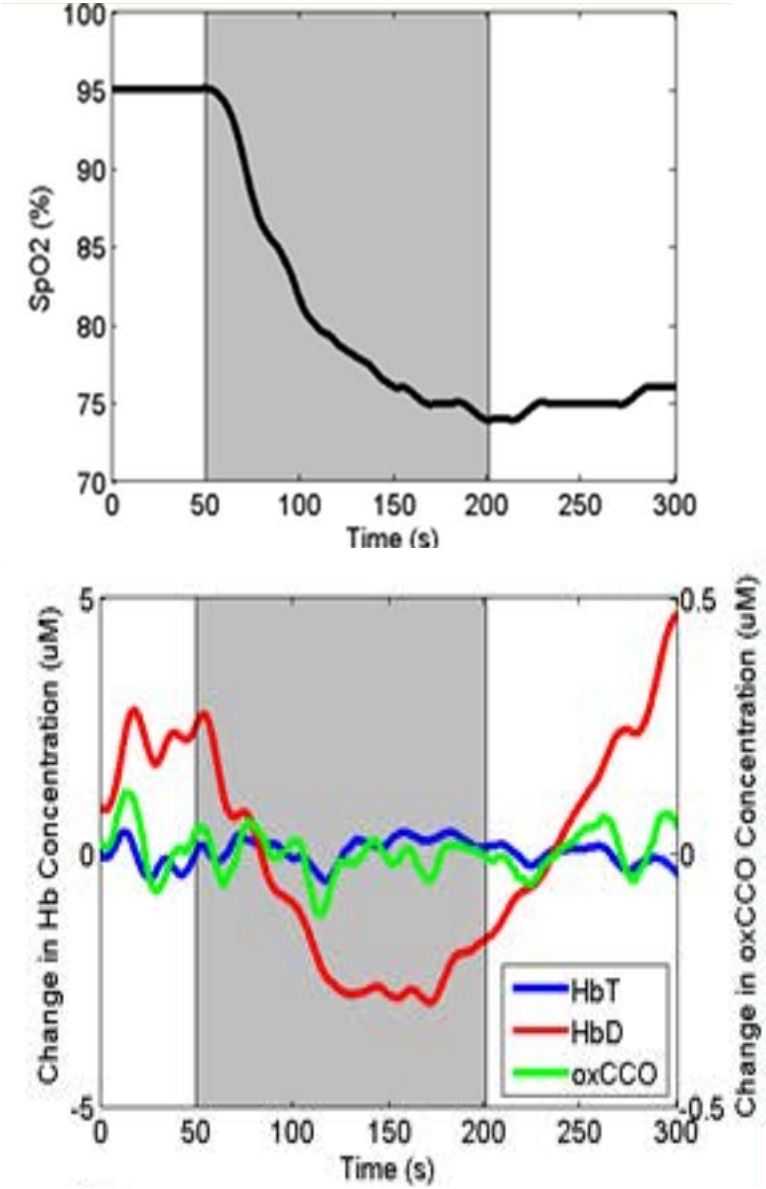
Our research

Our research

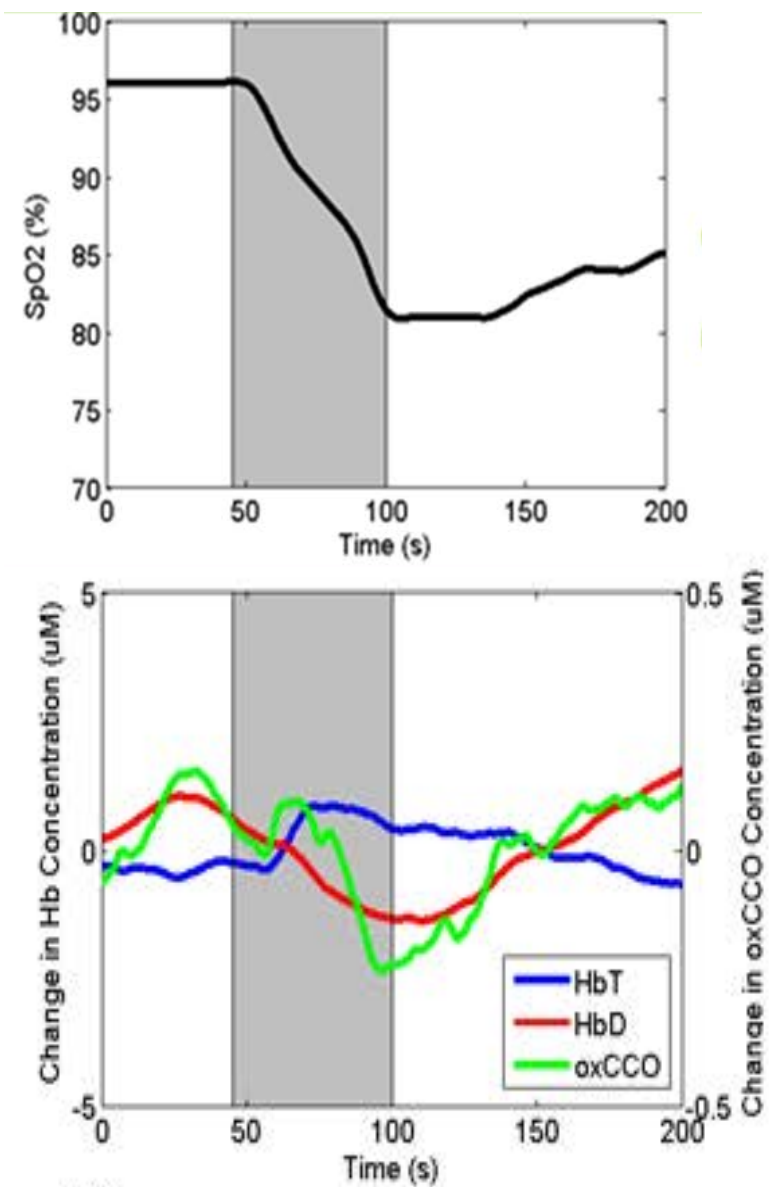


Our research

Baby with a good outcome



Baby with a poor outcome



Summary and conclusion

- We have demonstrated
  - White light is made of many different wavelengths;
  - Some of those wavelengths can travel through biological tissue;
  - Colour changes in the body can relate to physiological changes;
  - We can engineer light to monitor those changes.

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Thank you!