Evaluation of Haemoglobin and Cytochrome responses using a Broadband Time Resolved NIRS system

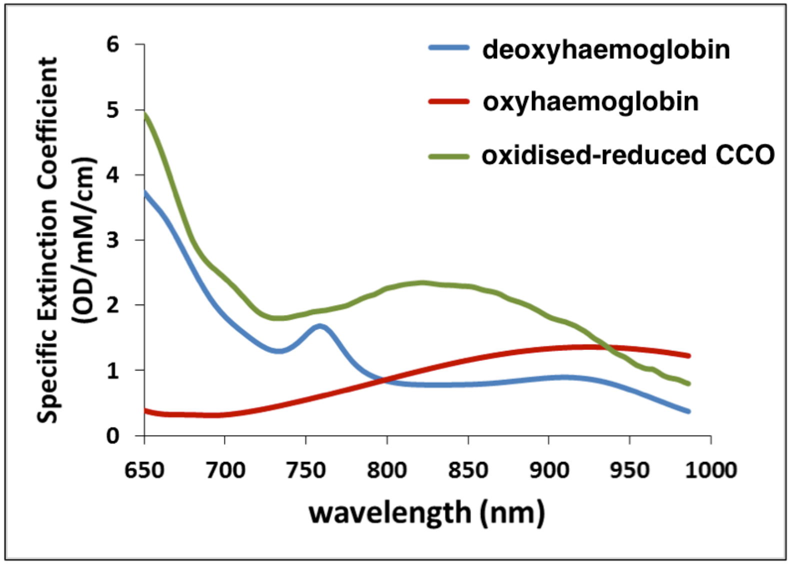
Frédéric Lange[1], Luke Dunne[1], Ilias Tachtsidis[1]

[1]*Department of Medical Physics and Biomedical Engineering, University College London, UK*

Focus of our group [A,B,C]

To develop new instruments and methods in order to retrieve information about cerebral **hemodynamics** and **metabolism**, on healthy subjects or at the patient bedside using NIRS

Metabolism and cytochrome-c-oxidase[1]



- Cytochrome c oxidase (CCO) is the terminal enzyme of mitochrondrial electron transport chain.
- Redox state of CCO is a non-invasive marker of cellular oxygen metabolism
- The broadband NIRS measurement of [oxCCO] is highly associated with MRS marker of metabolism[1]

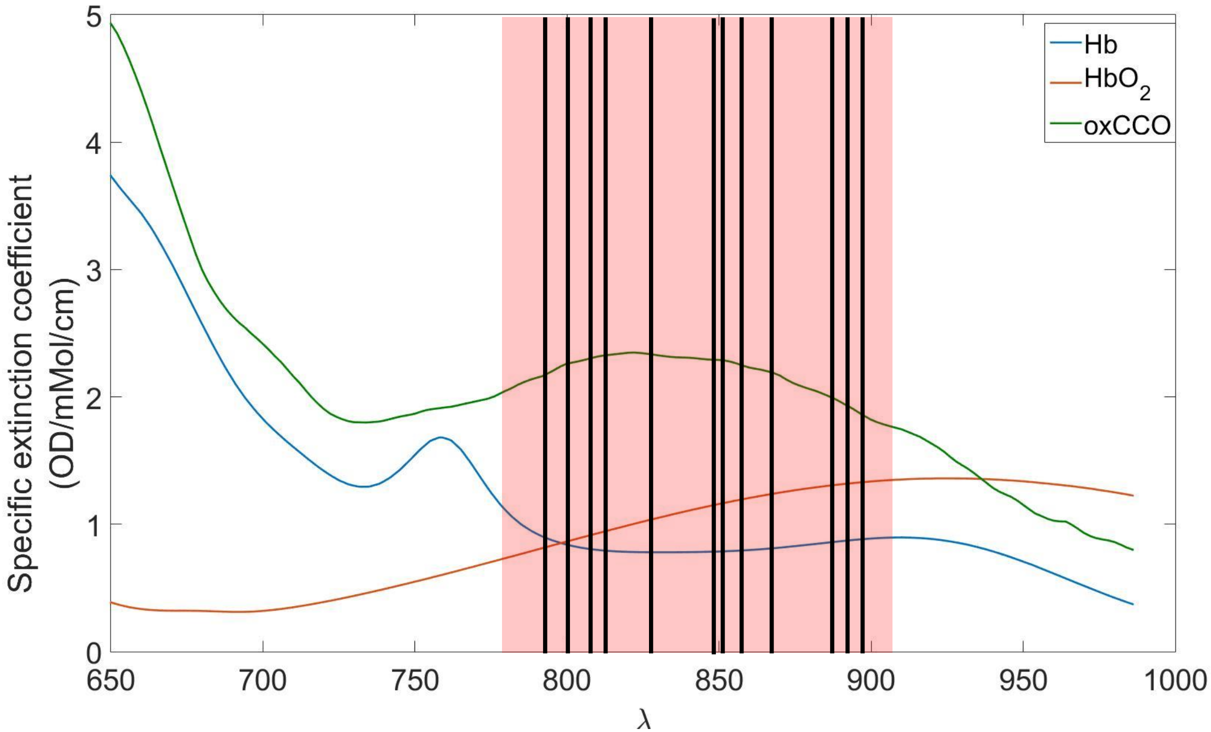
A - Phong Phan's talk, Hardware Session yesterday
B - Isabel de Roever *et al.*, Poster 33
C - Danial Chitnis, (next talk)

[1] Bainbridge *et al.*(2014). *NeuroImage*, *102*(P1), 173–183

Introduction

Measurement Gold standard :

Broadband Continuous Waves (CW) systems [2]



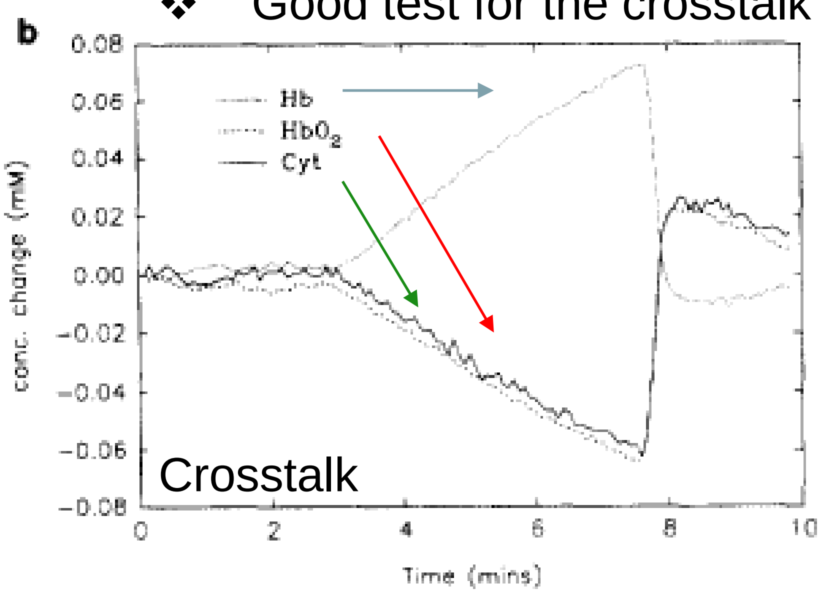
- Multiwavelength will allow the quantification of [Hb] [HbO_2] [oxCCO] [3]
    - 4/5 wavelength : error < 4 %
    - 8 wavelength : error < 2%
- Use time resolved system to improve the accuracy of the quantification

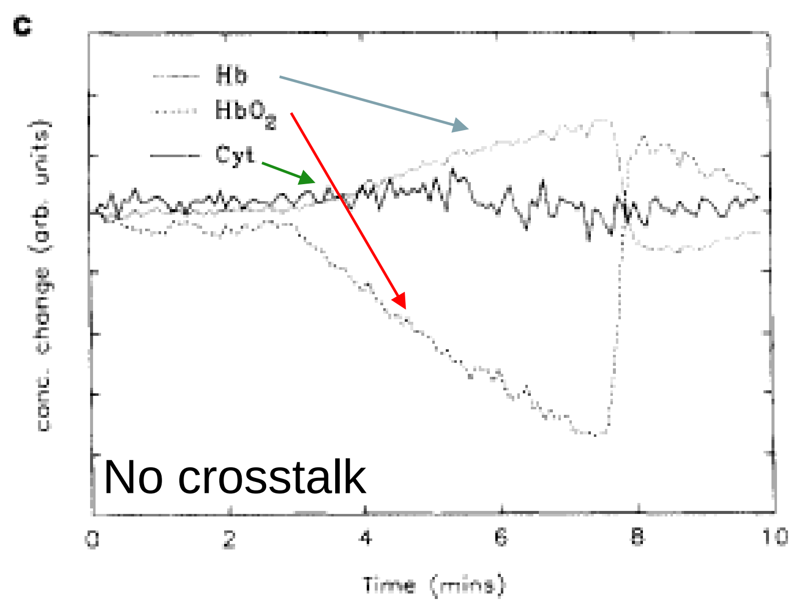
[2] Bale *et al*. (2016) *Journal of Biomedical Optics*, 21(9), 91307.
[3] Arifler *et al.*(2015). *Biomedical Optics Express*, *6*(3), 933.

Introduction

Aims

- ❖ To describe the system
- ❖ First *in-vivo* study to validate the ability of a multi-wavelength Time Resolved NIRS system to monitor both hemodynamic and metabolic responses on a muscular cuff occlusion [4]
  - ➢ Retrieve Δ[Hb] Δ[HbO_2] and Δ [oxCCO] during a large Haemoglobins change
  - ❖ Good test for the crosstalk

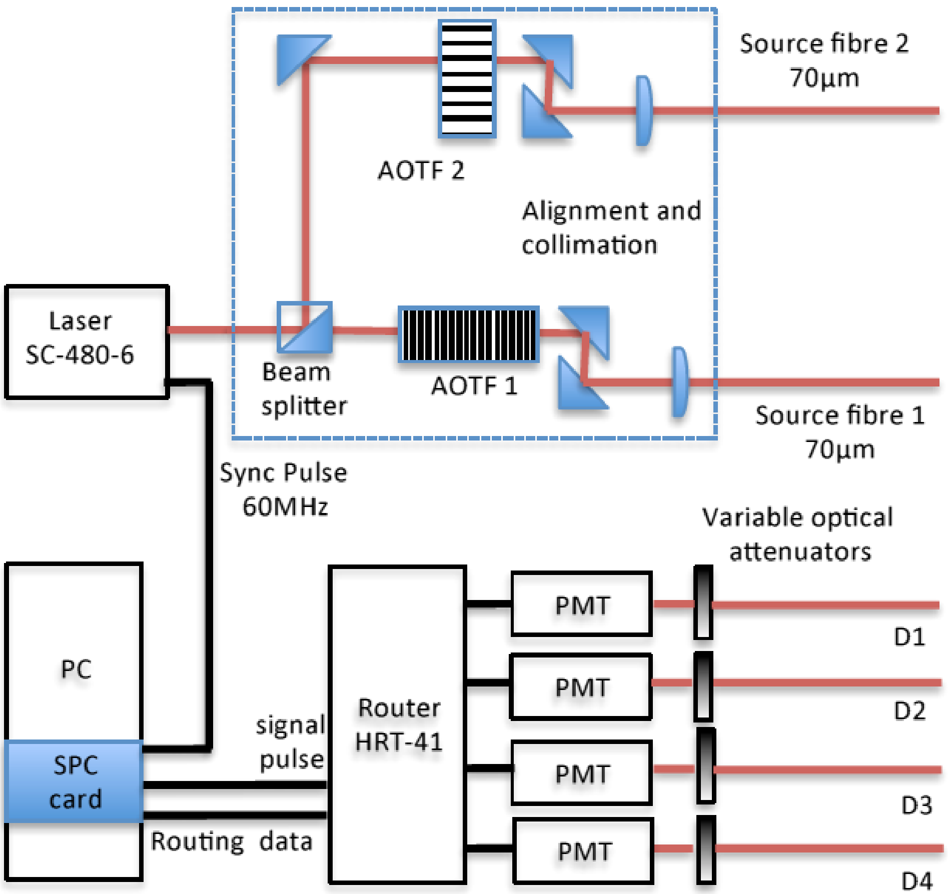




[4] Matcher *et al*.(1995). *Analytical Biochemistry*, 227(1), 54–68

System overview

✓ Time Resolved and Multi-wavelength capabilities[5]



[5] Dunne *et al.* (2014). *Oxygen Transport to Tissue XXXVI*. (Vol. 812).

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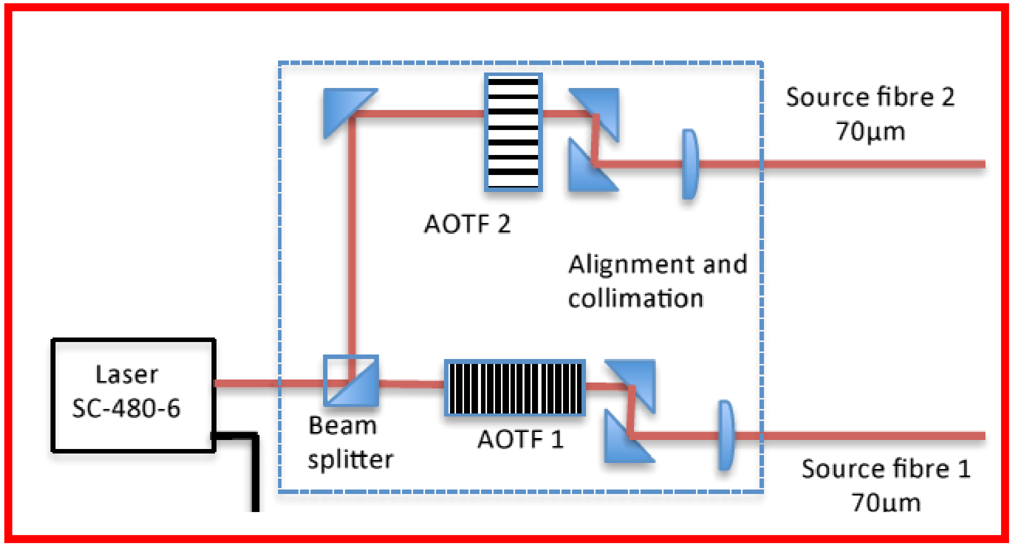
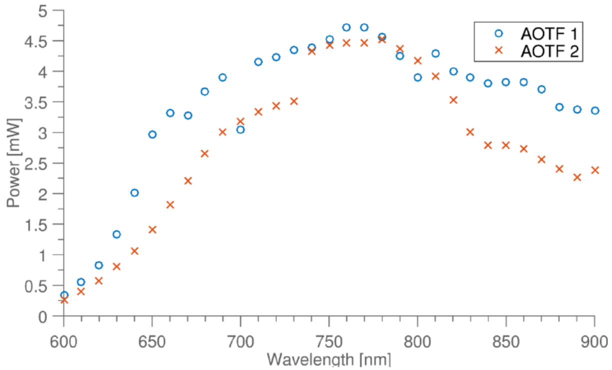
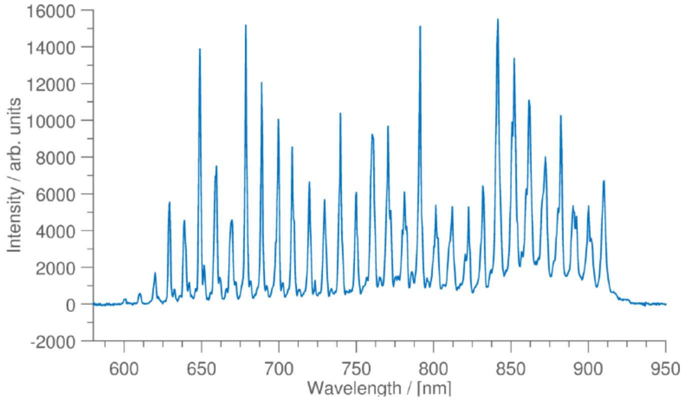




Source part :

- 2 sources
- Discrete number of wavelength (AOTF)
  - ➢ Fast switching mode (100Hz) :16 λ / Source
- Few mW / λ
- FWHM : 2-4 nm



[5] Dunne *et al.* (2014). *Oxygen Transport to Tissue XXXVI*. (Vol. 812).

Methods

System overview

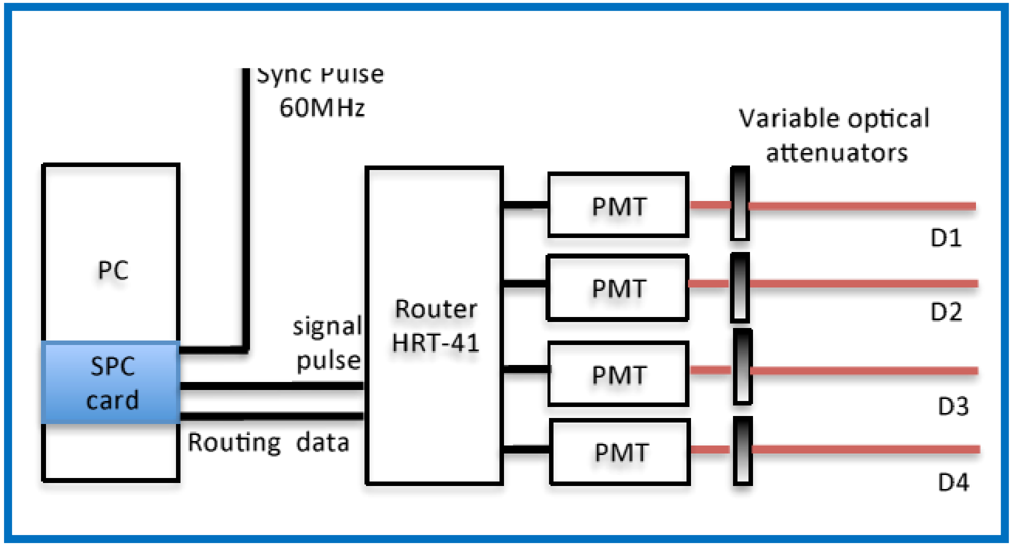
✓ Time Resolved and Multi-wavelength capabilities[5]

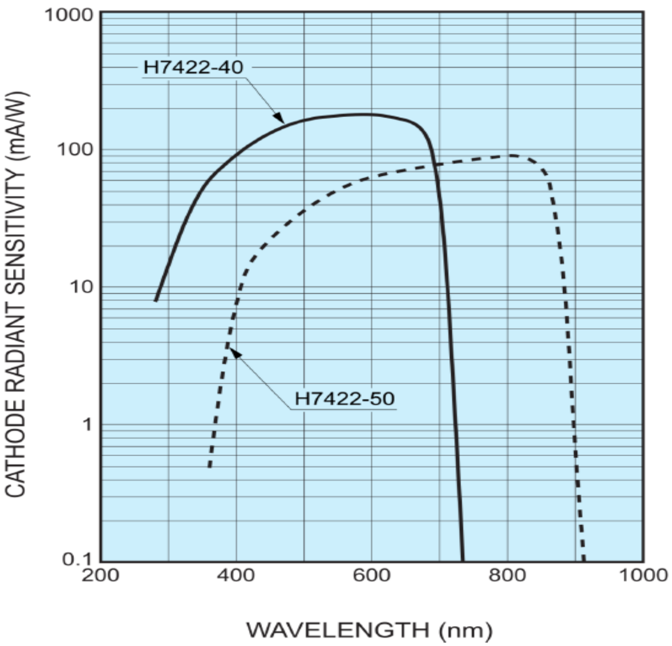
Detection part :

- 4 detectors
  - ➢ 4 Photomultipliers (PMT) + Variable Optical Attenuator
  - ➢ 1 router + 1 acquisition TCSPC card

- Good sensitivity until 870 nm

- Overall spectral bandwidth : 650 / 870 nm





[5] Dunne *et al.* (2014). *Oxygen Transport to Tissue XXXVI*. (Vol. 812).

Methods

- Transportable

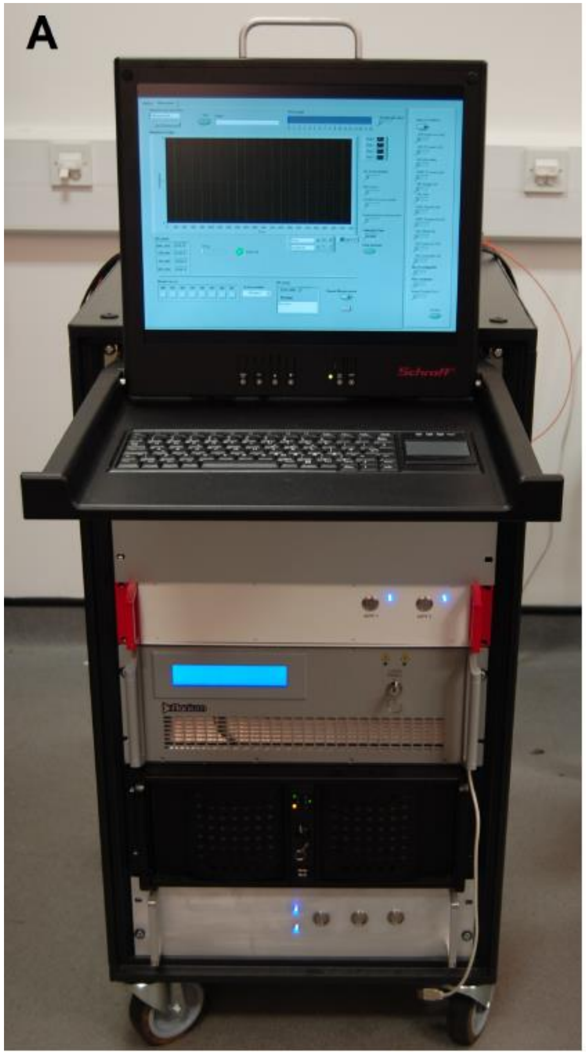
Software

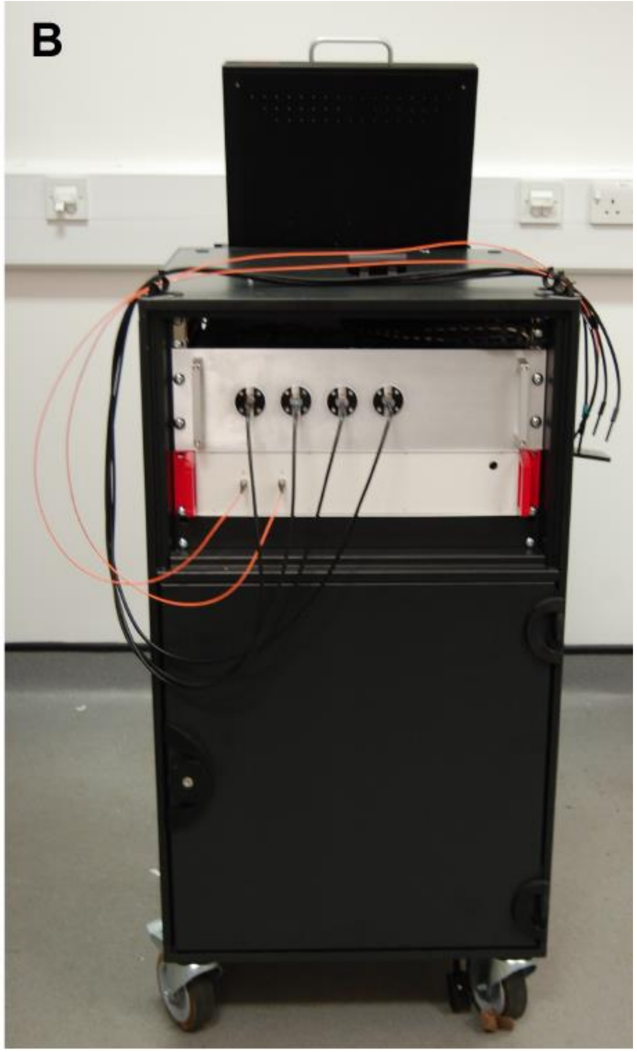
AOTF drivers

Laser

Computer

Power stage





Detection Part

AOTF

A : Front side (Operator) B : Back side (Subject)

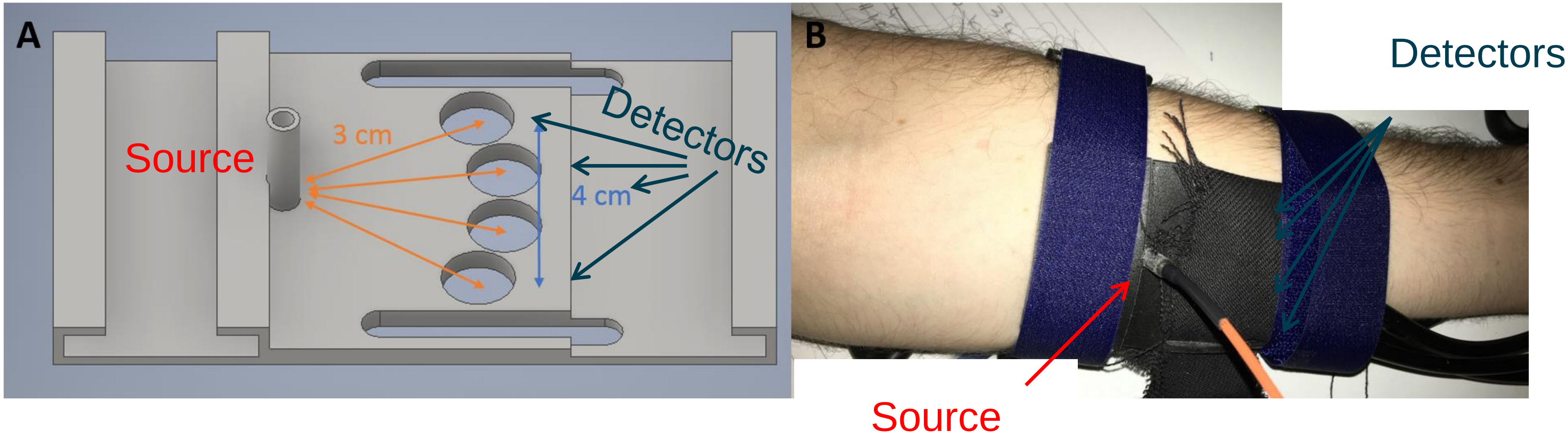
Methods – I Cuff Occlusion

Experiment :

- ❑ Muscular cuff occlusion (arterial) on the left arm
  - 5 min rest
  - 5 min occlusion
  - 5 min recovery
- ❑ 6 subjects (2F / 24-29 years)

Settings :

- ❑ 1 source / 4 detectors (same area)
- ❑ 16 wavelengths
- ❑ (780-870 nm, every 6 nm)
- ❑ IT: 50 ms/λ
- ❑ Acquisition frequency 1Hz



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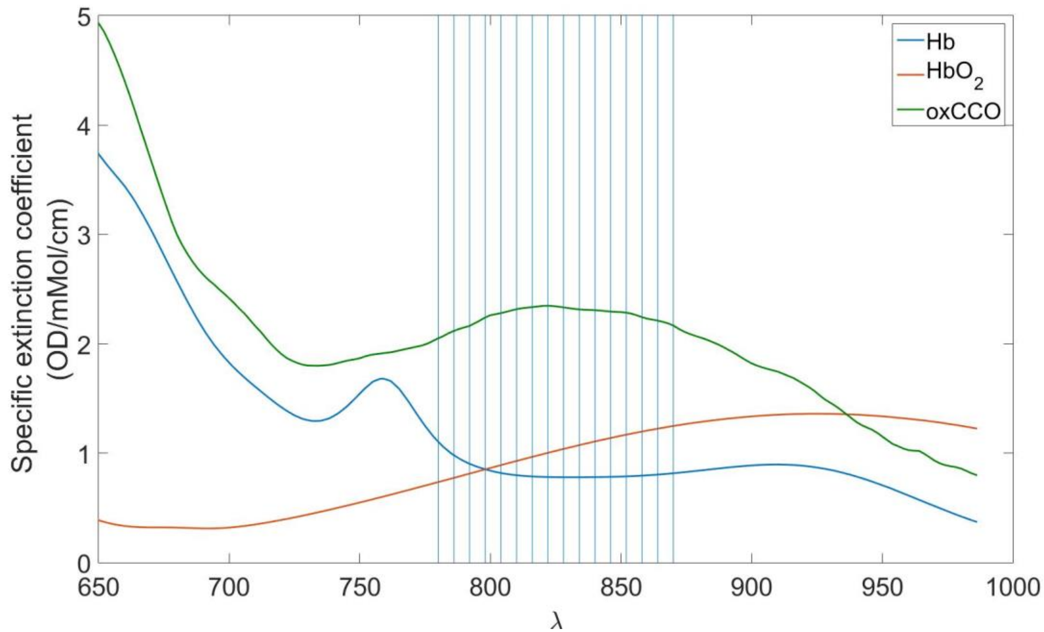


Methods – I Cuff Occlusion

Concentration changes calculation

❖ We used 2 methods to recover the concentration changes

I - Modified Beer Lambert Law (UCLn)

- Classical method with CW systems
- Uses change in attenuation
- Need to provide the pathlength (DPF)

➢ True Pathlength used: Calculated for each subject and each wavelength form the mean time of flight.

❖ Good SNR

II - Change in coefficient of absorption

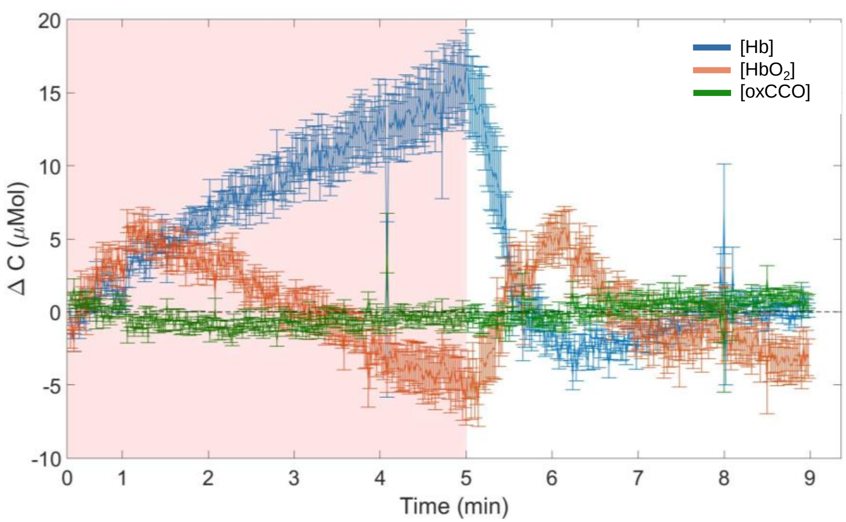
- Fitting procedure to extract absorption and scattering coefficients
- Calculation based on $\Delta\mu_a$

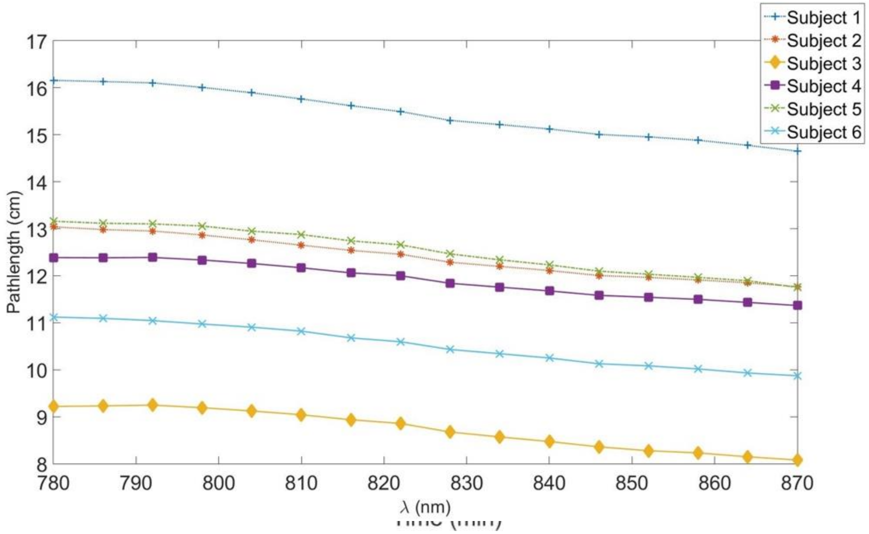
❖ Lower SNR, averaging over 10 time points

Results – I Cuff Occlusion

Grand Average over all subjects and Detectors (n=24)

Method 1 (CW like)





- ✓ Classical hemodynamic response to a cuff occlusion
- ✓ No Crosstalk between haemoglobin and [oxCCO]
  - ✓ Small changes in [oxCCO] compared to haemoglobin
  - ✓ Different time evolution

Results – I Cuff Occlusion

Grand Average over all subjects and Detectors (n=24)

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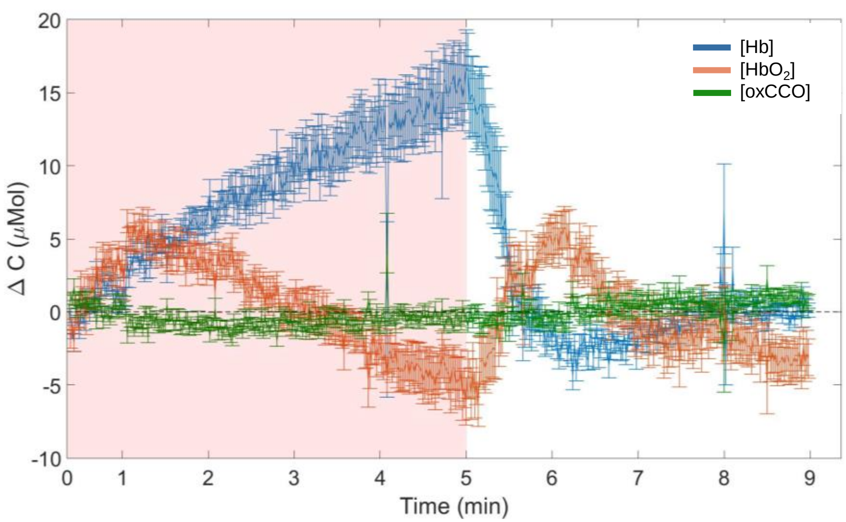
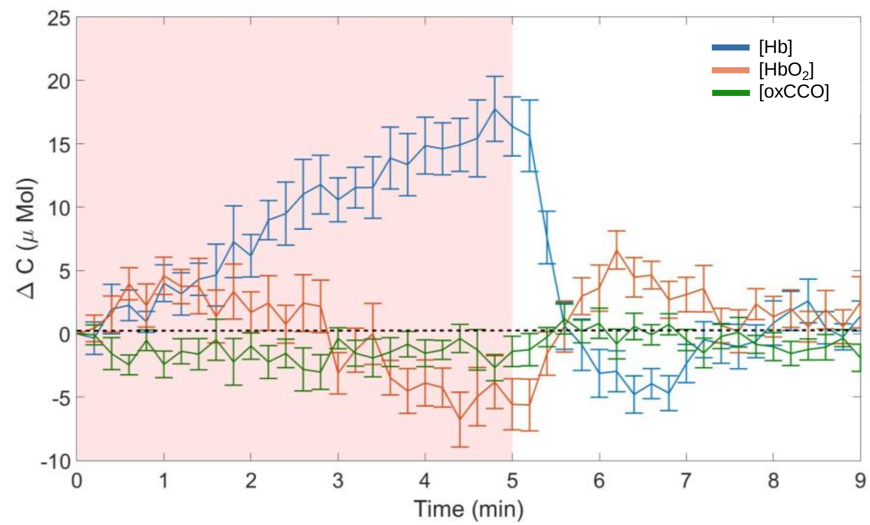


Method 2 (Fitting)



- ✓ Classical hemodynamic response to a cuff occlusion
- ✓ No Crosstalk between haemoglobin and [oxCCO]
  - ✓ Small changes in [oxCCO] compared to haemoglobin
  - ✓ Different time evolution
- ✓ Good agreement between the 2 methods

Conclusions

- We have developed a Multi-wavelength Time Resolved NIRS system :
    - 2 sources
    - 4 detectors
    - Using 16 wavelength from 650 to 870 with a FWHM of 2-4 nm

- We have demonstrated the ability of this system to retrieve the changes in [Hb], [HbO_2] and [oxCCO] during a muscular cuff occlusion

- Our results are in good agreement with the literature

- Both methods are in good agreement
    - ➢ Promising to use the second one in order to investigate scattering effects and retreive absolute concentrations.

- Currently working on functional brain activation detection
    - More challenging : Low changes in concentration and more time constraint
        - ➢ Optimising the SNR of the system

Acknowledgements

UCL

wellcome trust

Thank you for your attention