NIRS applications and the role of tissue-like phantoms

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OUTLINE

Absolute NIRS measurements

- Phantom calibration
- Quantitative tests on phantoms

Baseline cerebral concentration and saturation of hemoglobin

- Young vs elderly subjects

Absolute NIRS in two-layered media

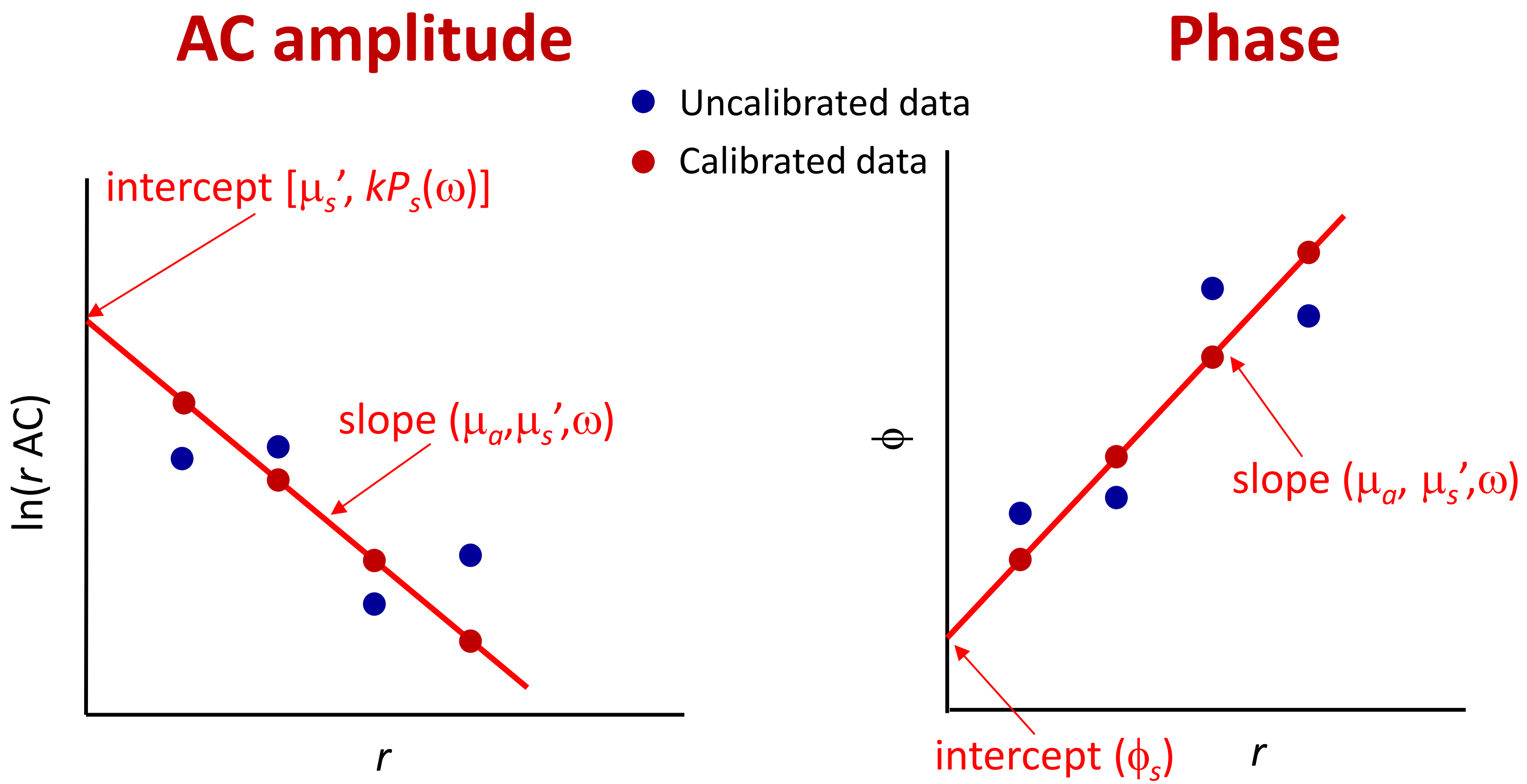
- Phantom tests
- *In vivo* brain measurements in human subjects

Functional brain studies

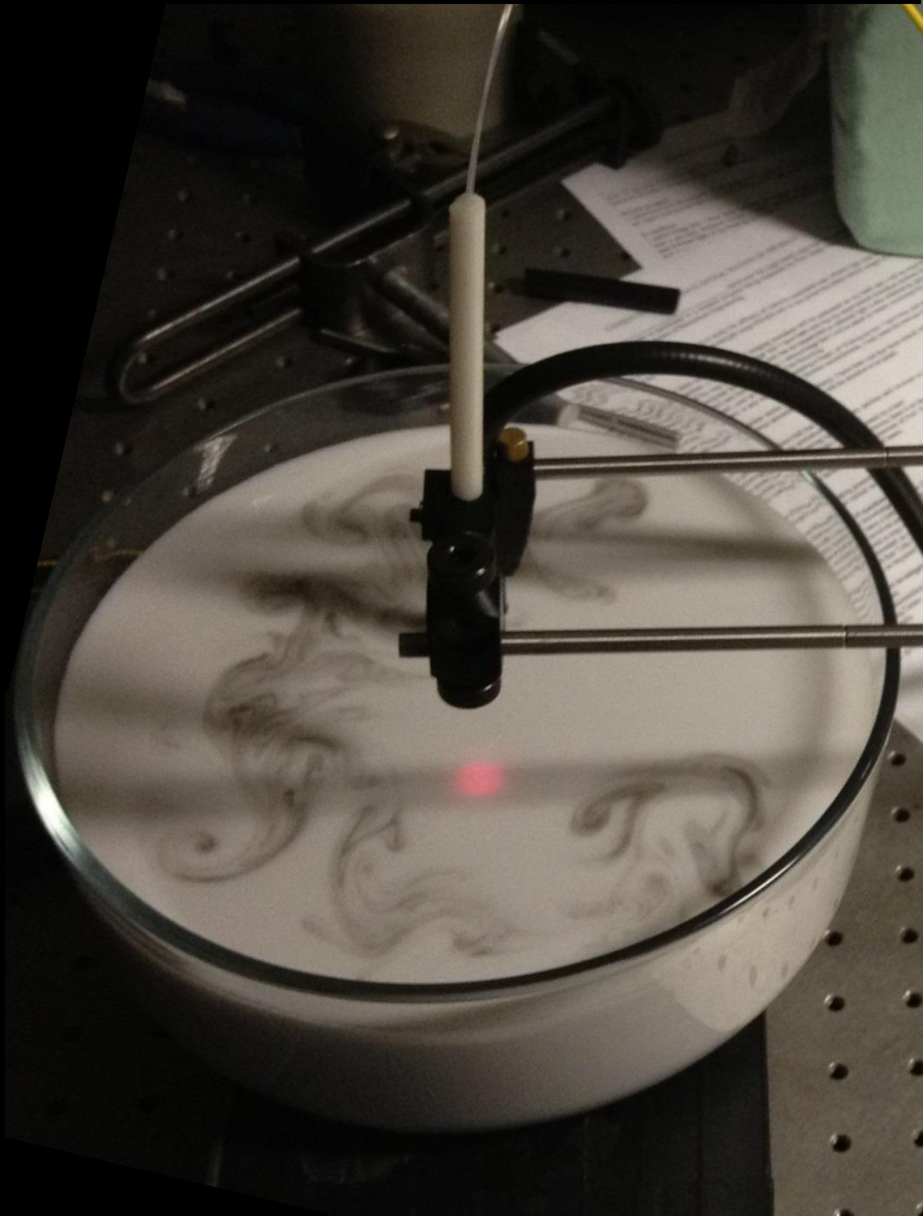
- Translating hemoglobin concentration changes into functional quantities

Absolute NIRS measurements with multi-distance, frequency-domain data

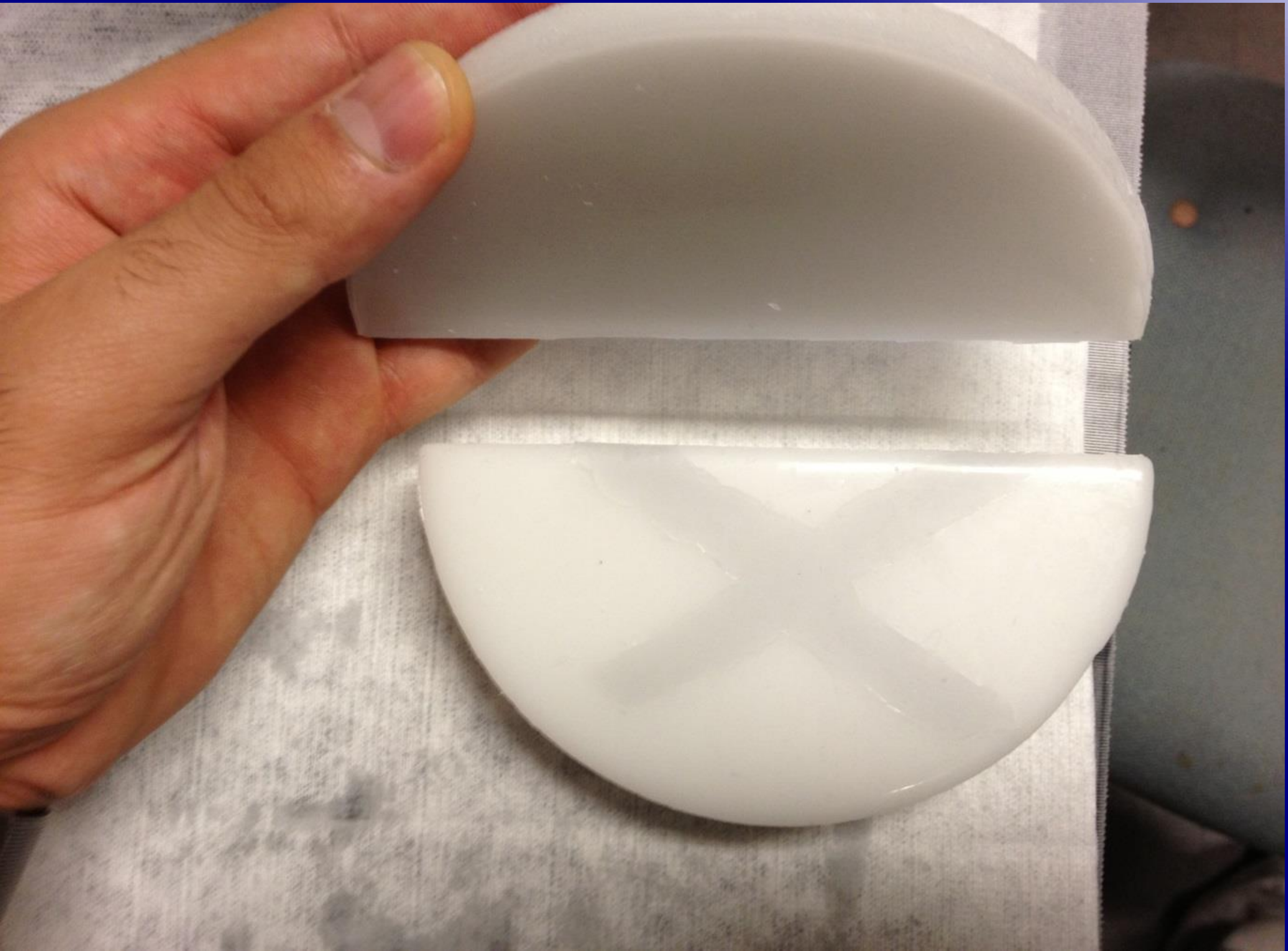
Diffusion theory: Straight lines for amplitude (AC) and phase (ϕ)



Liquid phantoms:
Scattering: Intralipid - Absorption: black India ink



Solid silicone phantoms:
Scattering: TiO_2 - Absorption: black India ink

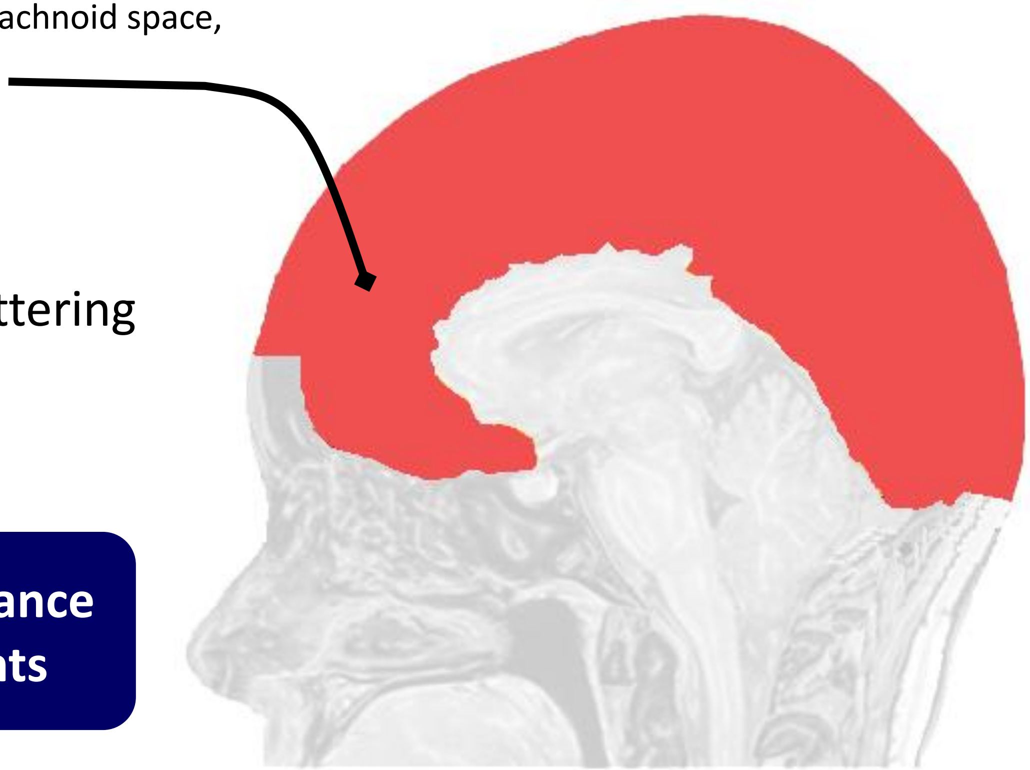


Absolute brain measurements in younger and older subjects

Homogenous Assumption
Human Head NIRS Measurements

Brain Tissue

Scalp, Skull, Dura, subarachnoid space, Brain tissue



Coefficients:

μ_a – absorption

μ_s' – reduced scattering

Diffuse Reflectance Measurements

Elderly and Young Subjects

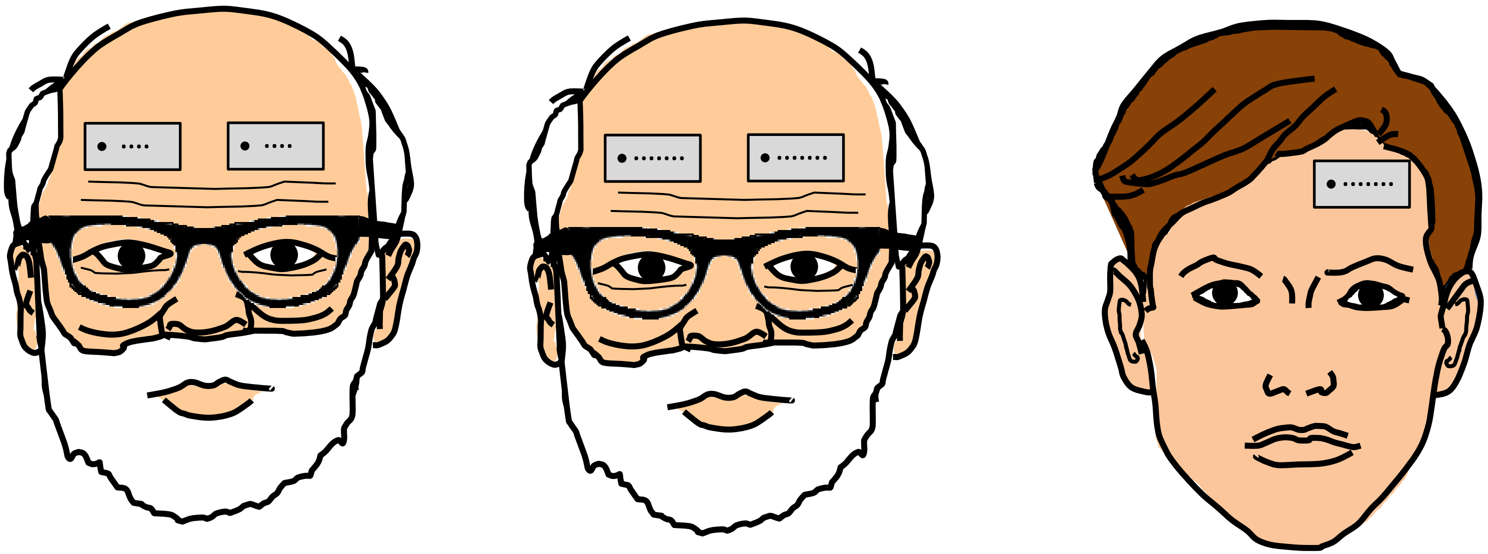
Elderly subjects (age: 70-96)

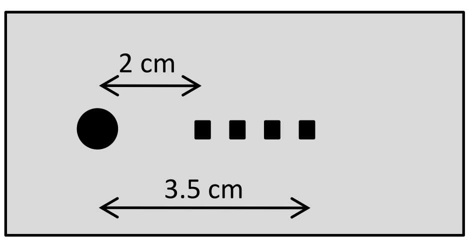
Session 1, May
(*n*=23)

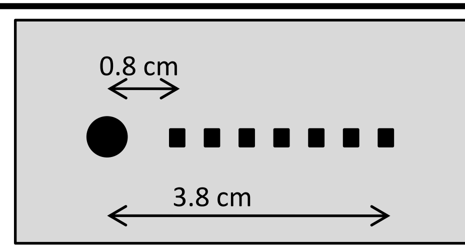
Session 2, October
(*n*=29)

Young subjects (age: 21-34)

Session 3
(*n*=19)

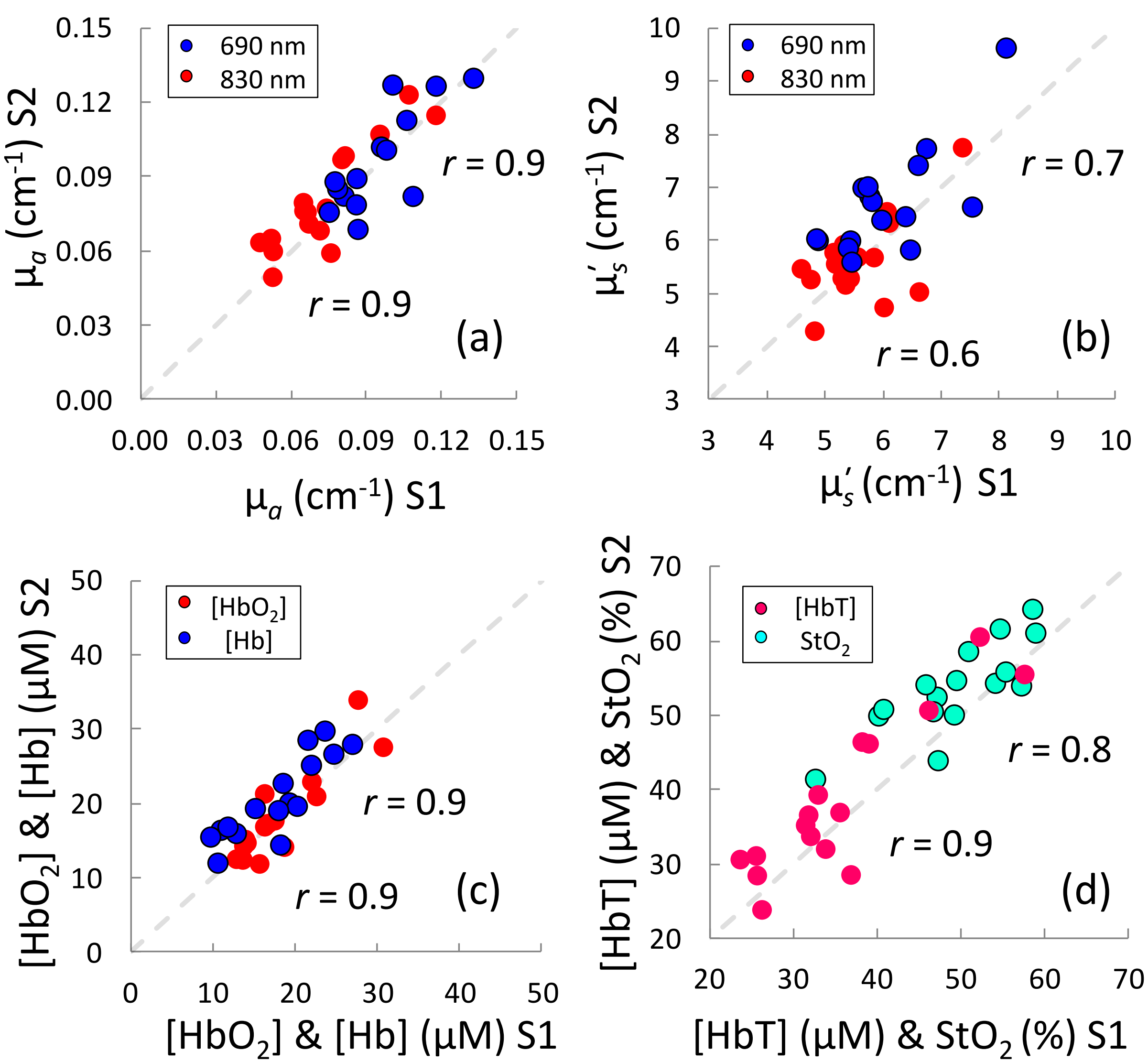






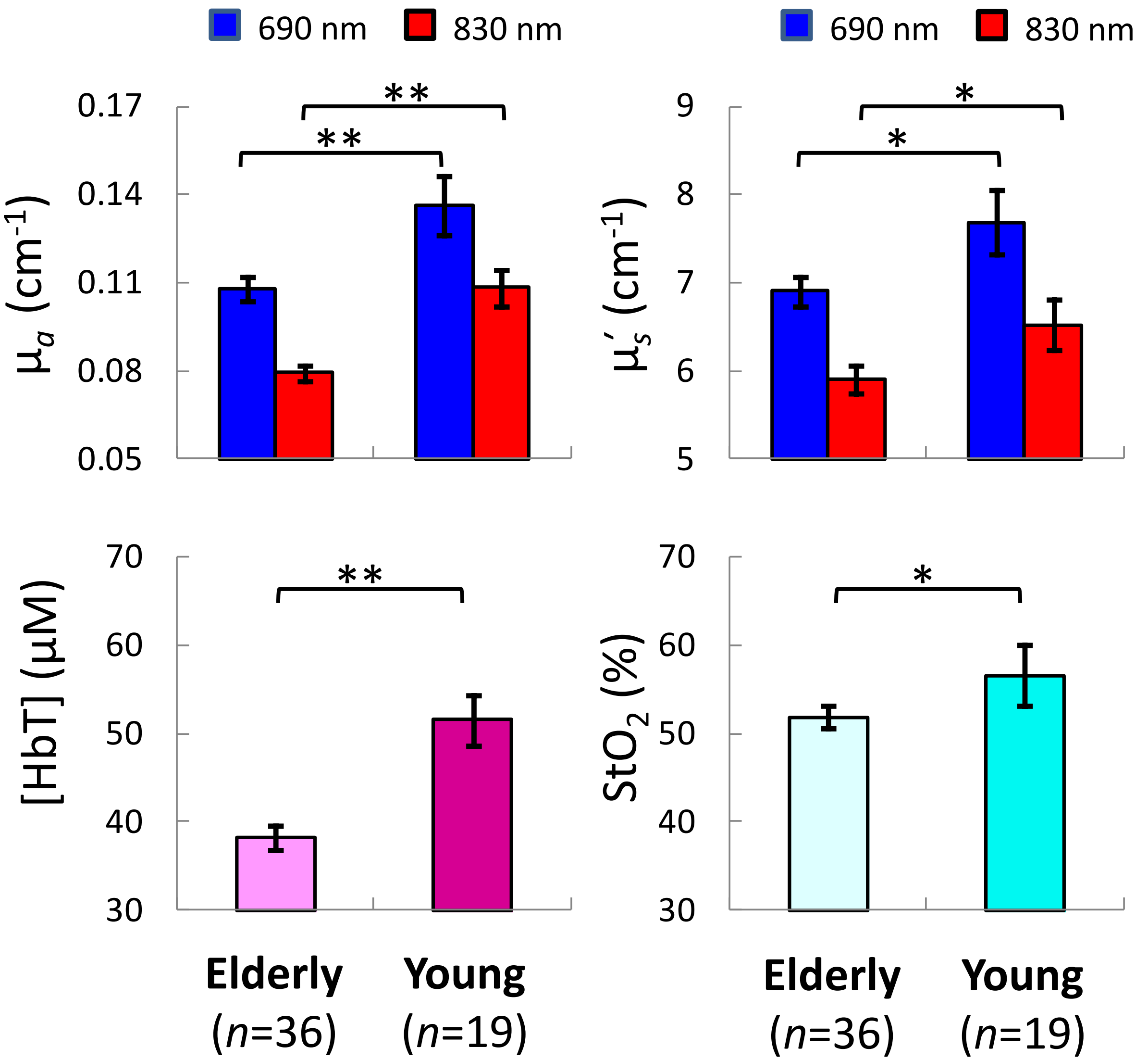
In collaboration with M. Beeri *et al.*, Mount Sinai School of Medicine

Reproducibility (Elderly Subjects)



Session 1 (S1) and Session 2 (S2) were 5 months apart

Significant age-related differences



Hallacoglu *et al.*, J Biomed Opt. **17**, 81406 (2012)

Absolute brain measurements with a two-layer tissue model

Two-layered Analysis
Human Head NIRS Measurements

Extracerebral Layer

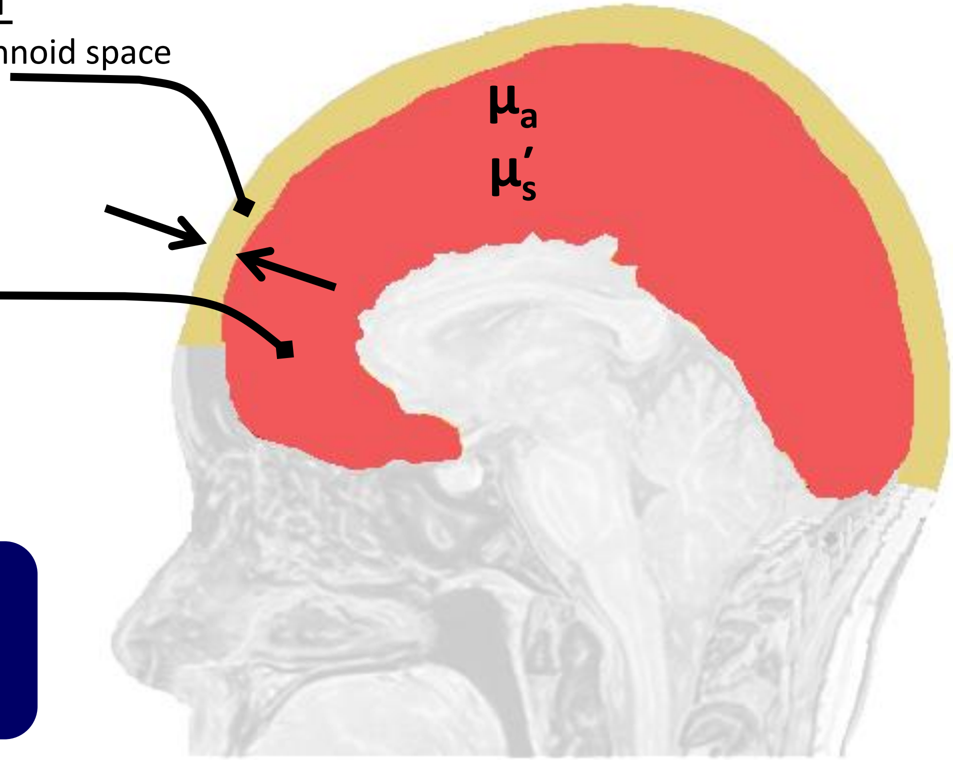
Skull, Scalp, Dura, subarachnoid space

μ_{a1} and μ'_{s1}
Thickness

Cerebral Layer

Cortex

μ_{a2} and μ'_{s2}



Diffuse Reflectance Measurements

Two-layer diffusion model

Frequency-domain solution of DE for a **two-layered cylinder**
Diffusely reflected intensity, I_R; top layer fluence rate, Φ_1

$$I_R(r) = D_1 \frac{\partial}{\partial z} \Phi_1(r,z)\Big|_{z=0}$$, where $D_1 = 1/(3\mu'_{s1})$

Φ_1 from: Liemert and Kienle, J Biomed Opt. **15**, 025002 (2010)

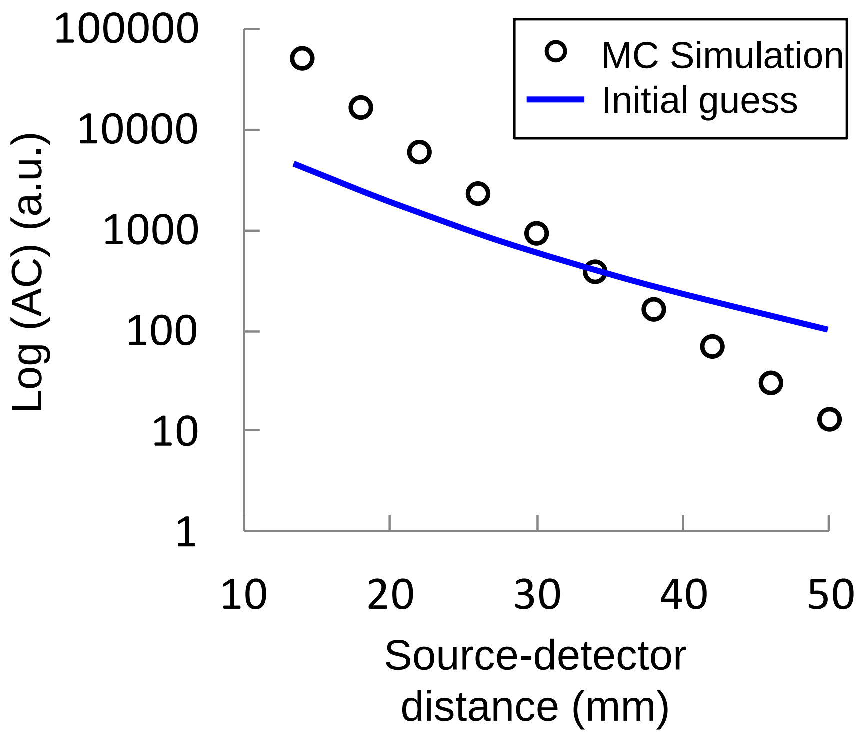
$$\mathrm{AC} = |I_R(r)| \qquad \mathrm{PH} = \arg[I_R(r)]$$

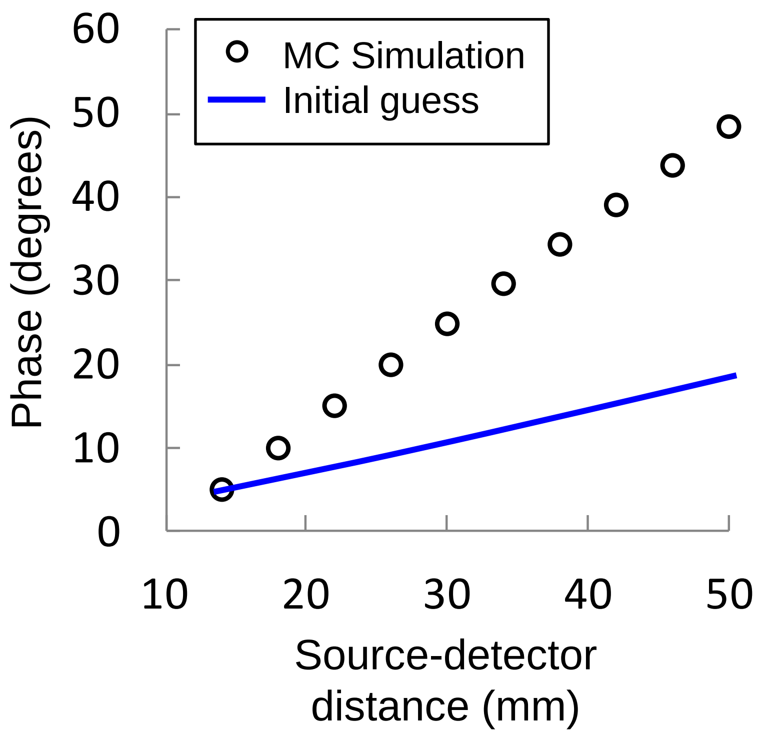
r = source-detector separation

Data collected at multiple source-detector separations: ~1-5 cm

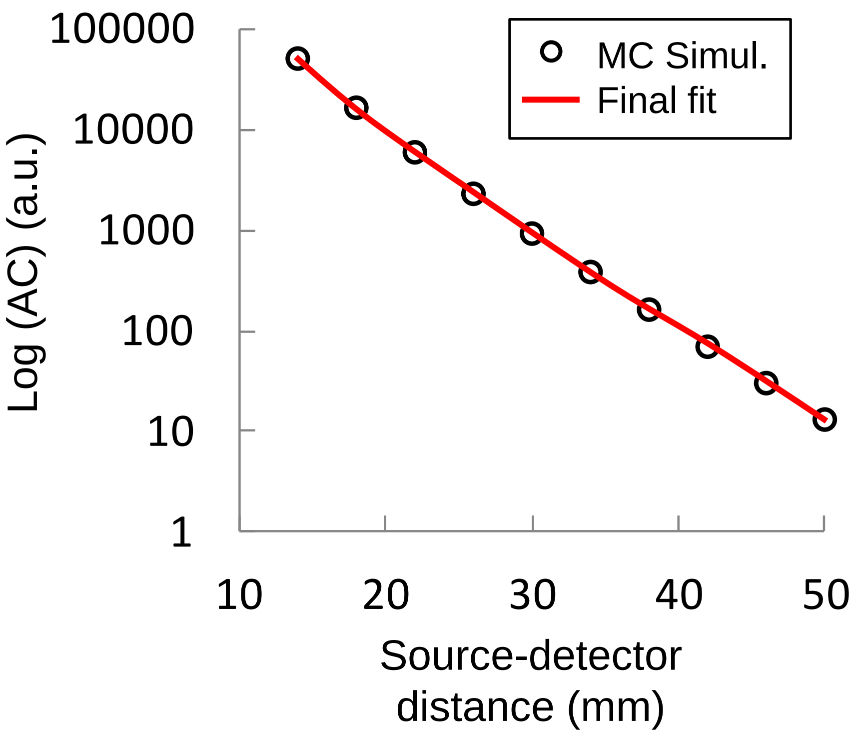
Six fitting parameters: $\mathbf{x} = [\mu_{a1} \;\; \mu'_{s1} \;\; L \;\; \mu_{a2} \;\; \mu'_{s2} \;\; \mathrm{AF}\;]^T$

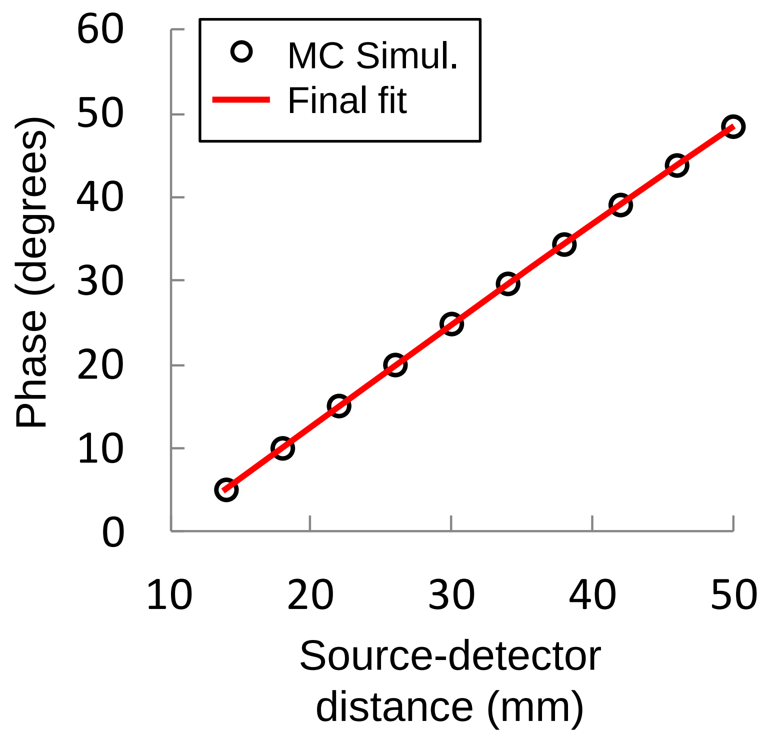
Inversion Procedure





Inversion Procedure





Phantom Experiments

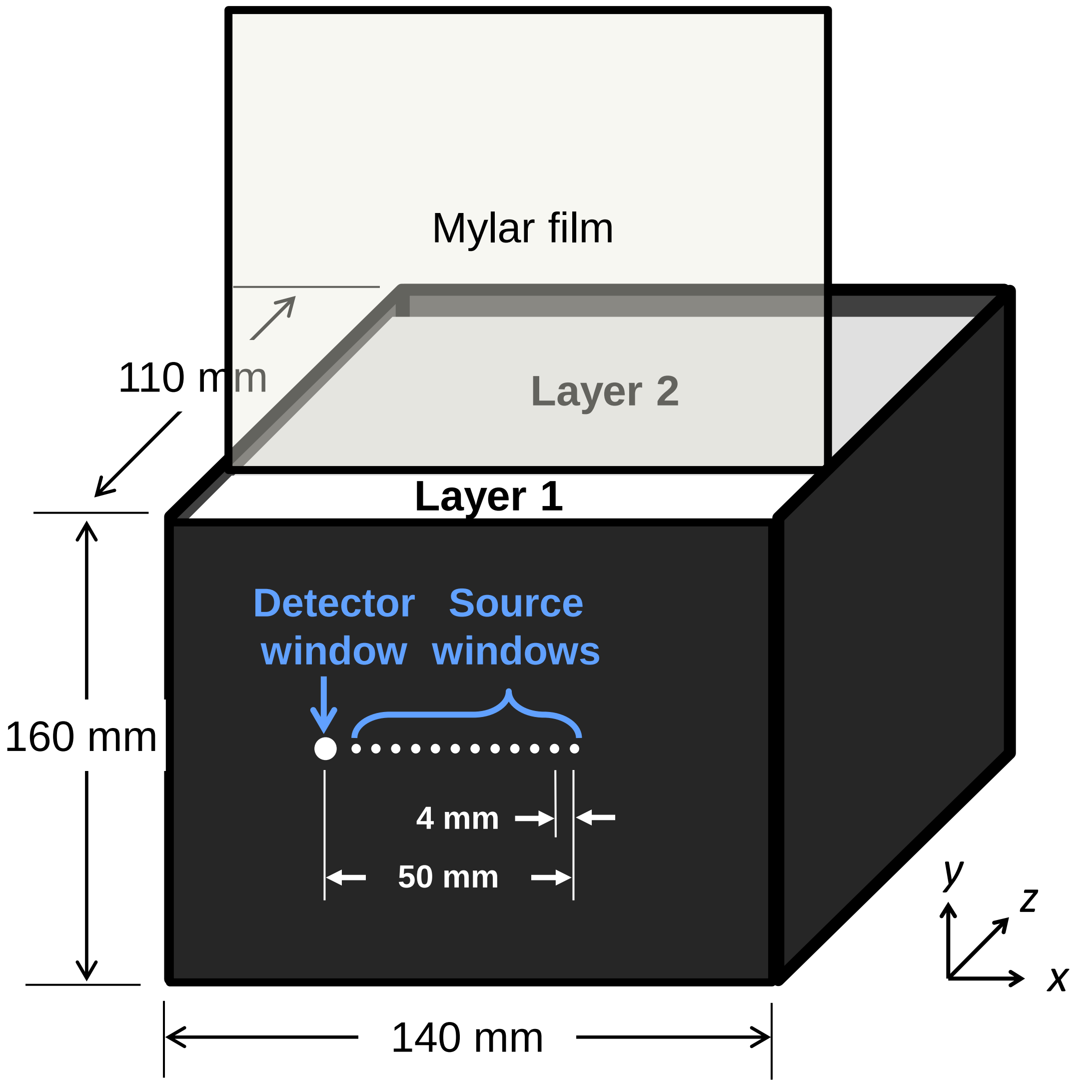
- Two-layered Phantoms
    - 12 Phantoms, Reflectance
- Homogenous Phantoms
    - 8 Phantoms, Infinite Geometry

Two-layered Phantom Experiments

Del Bianco *et al*, Opt Express **12**, 2101 (2004)

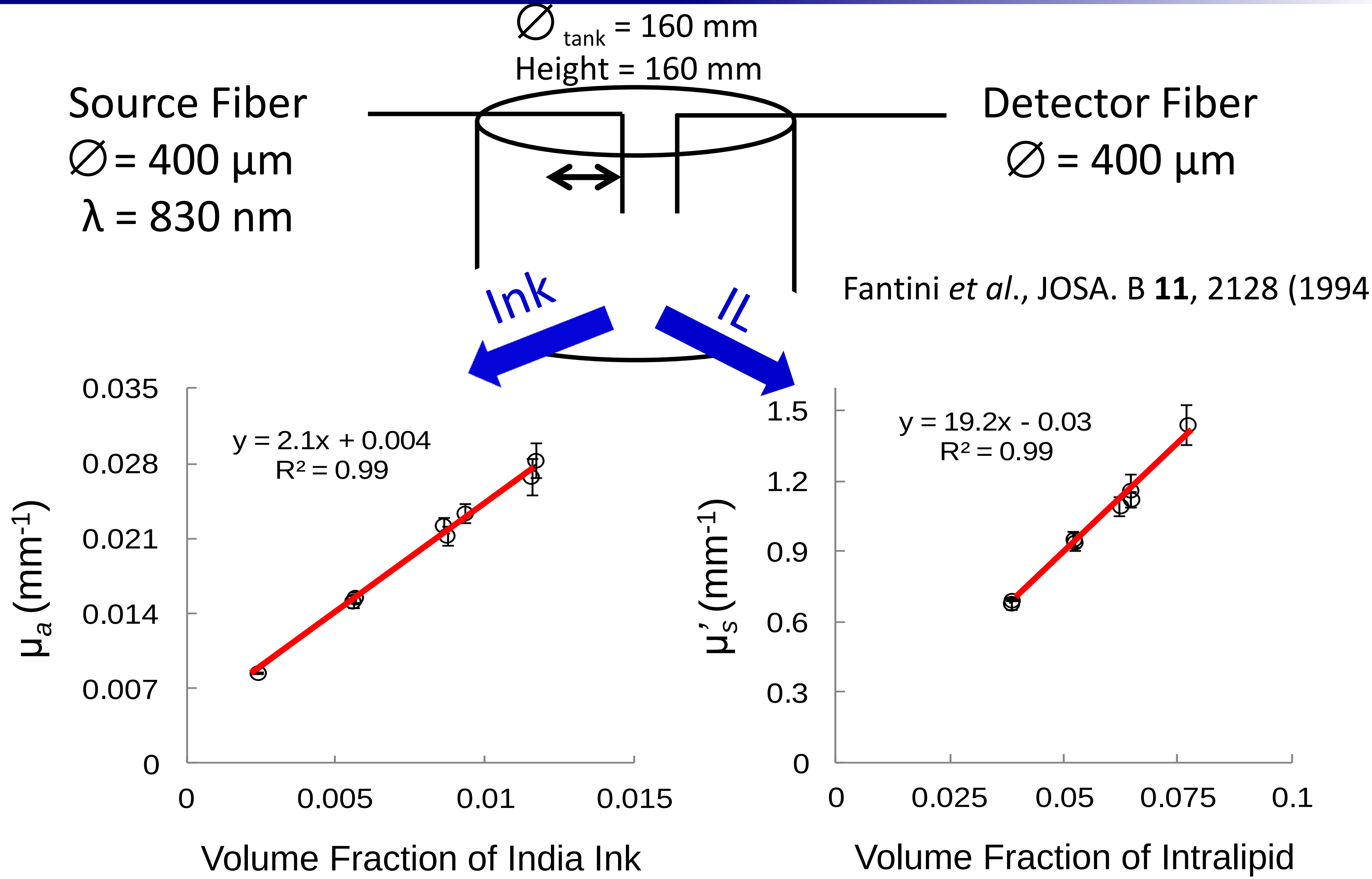
- Black PVC walls (n = 1.56)
  - Totally absorbing boundaries
- Optical windows
  - Detector (x1)
  - Illumination (x12)
  - Range (6–50 mm)
- Mylar Film
  - Small n mismatch
- Suspensions:
  - Intralipid 20% (n = 1.33)
  - India Ink
  - Water

n = Refractive index

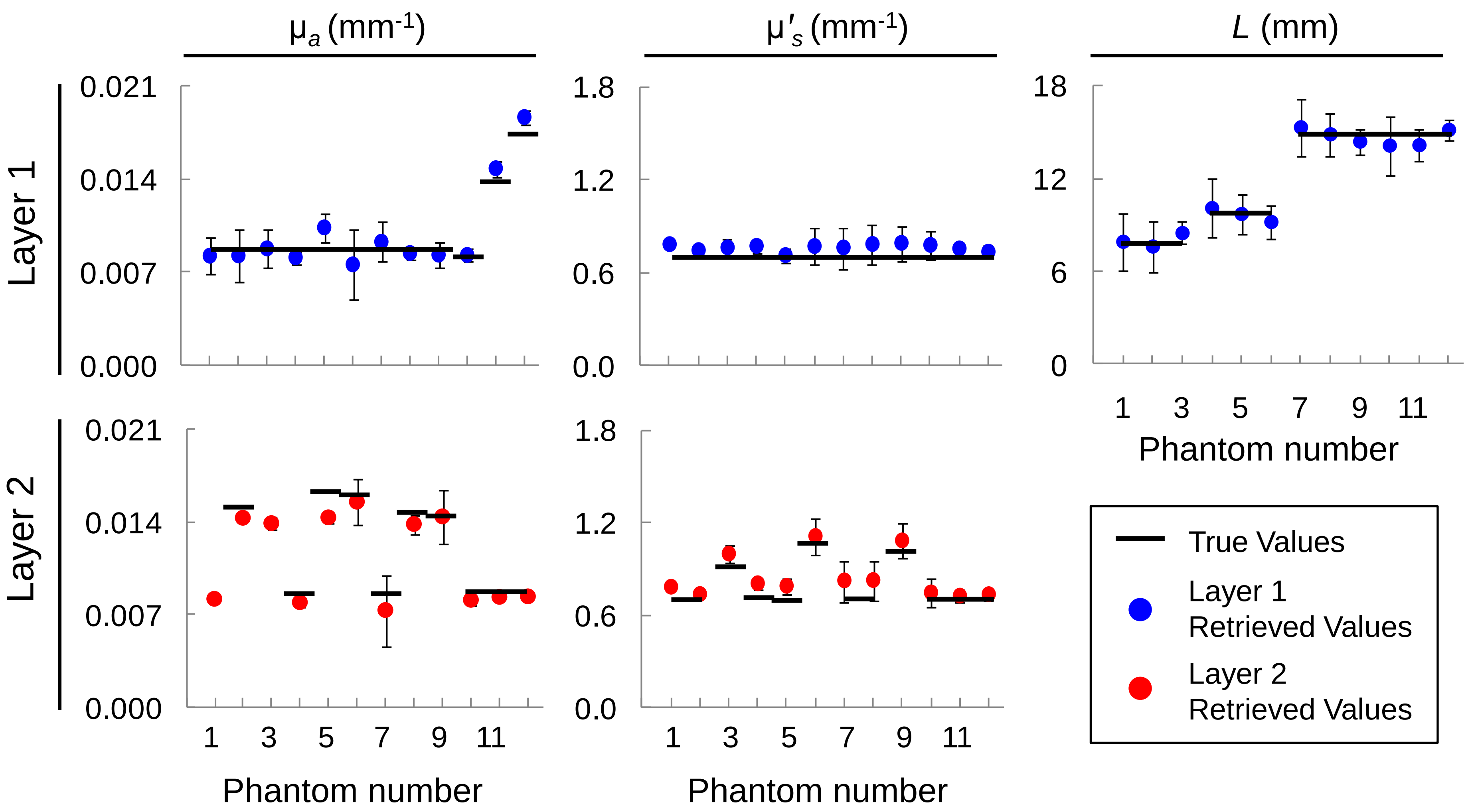


Phantom designed and built in Zaccanti's group (Univ of Florence), courtesy of D. Marcucci

Homogenous Phantom Experiments



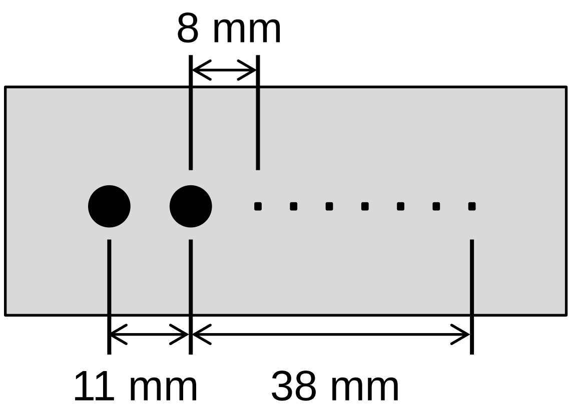
Two-layered Phantom Results

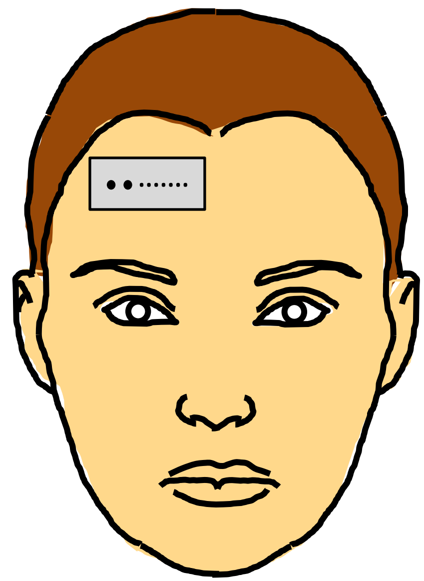


Hallacoglu *et al.*, PLoS ONE **8**, e64095 (2013)

In vivo Experiments

- Optical Detector fibers
- Optical Source fibers



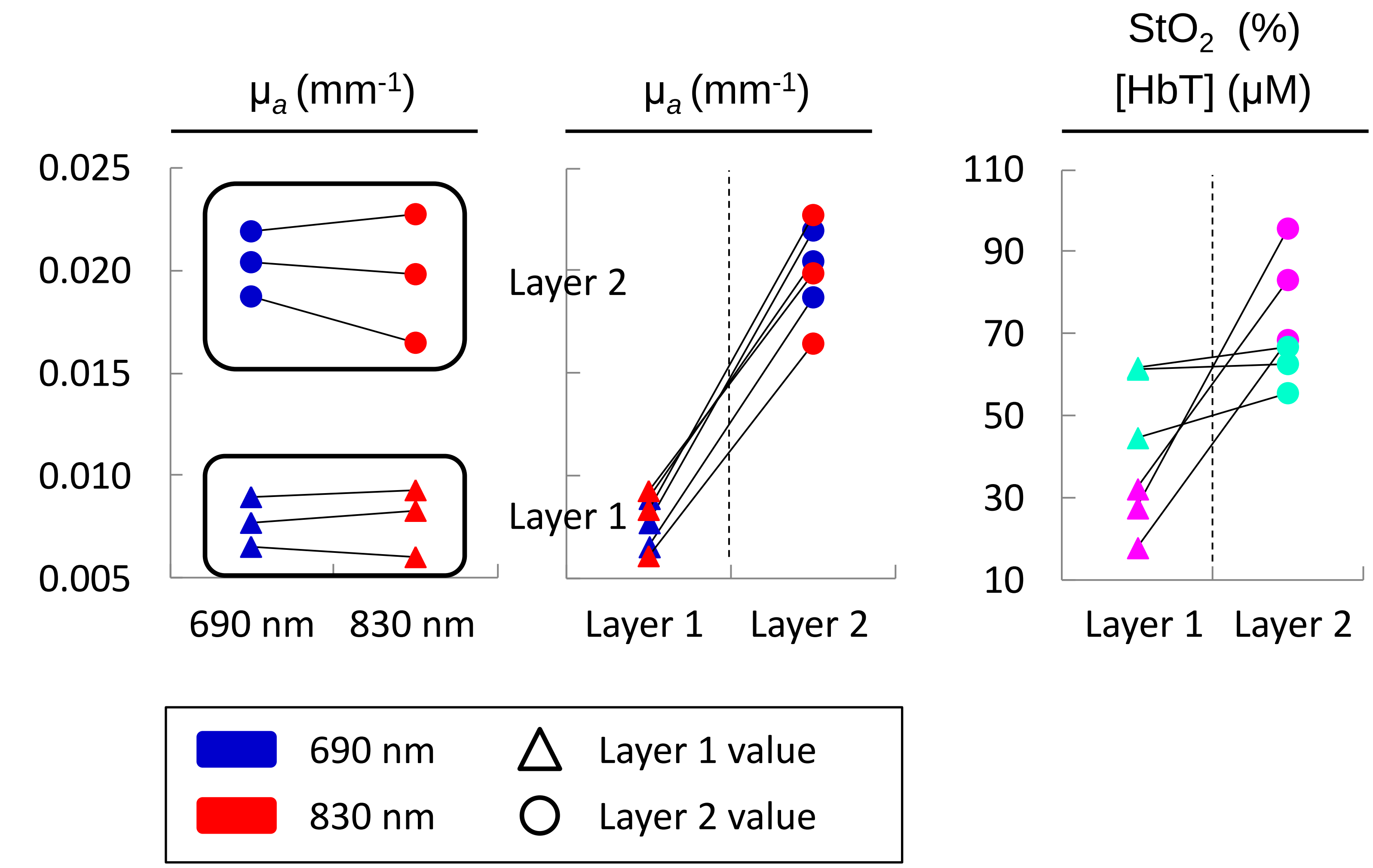


λ_1: 690 nm

λ_2: 830 nm

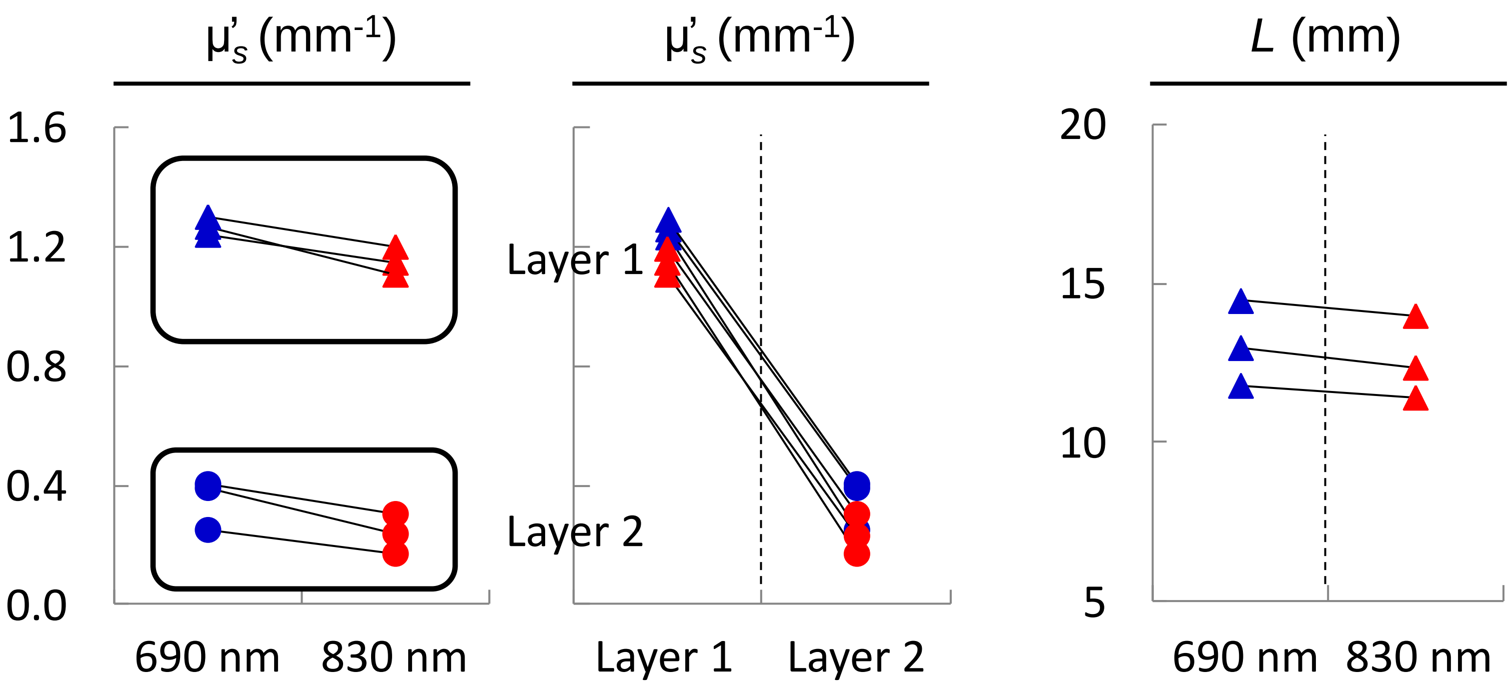
In vivo Results

Absorption Coefficient

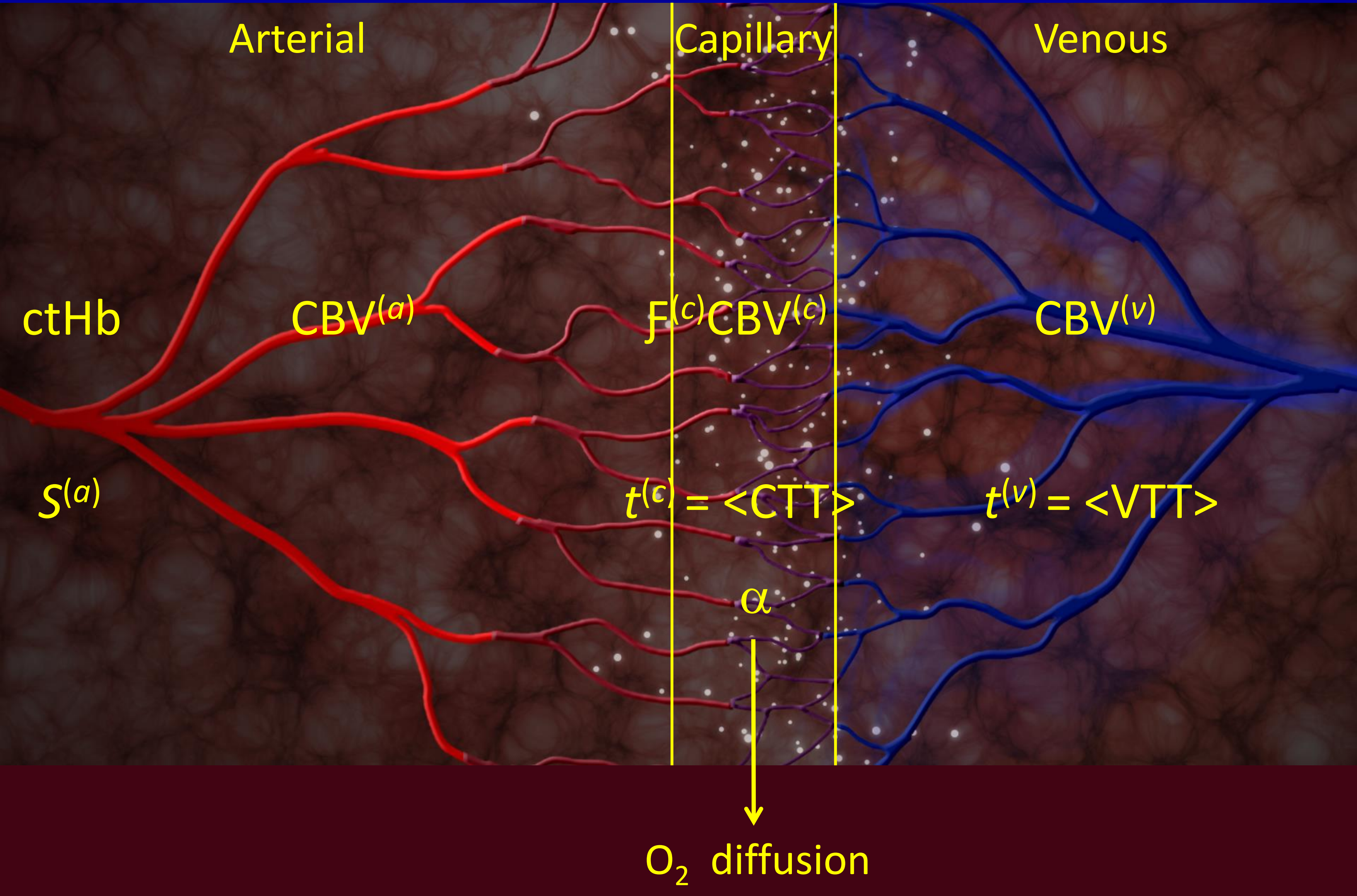


In vivo Results

Scattering coefficient and Layer 1 thickness

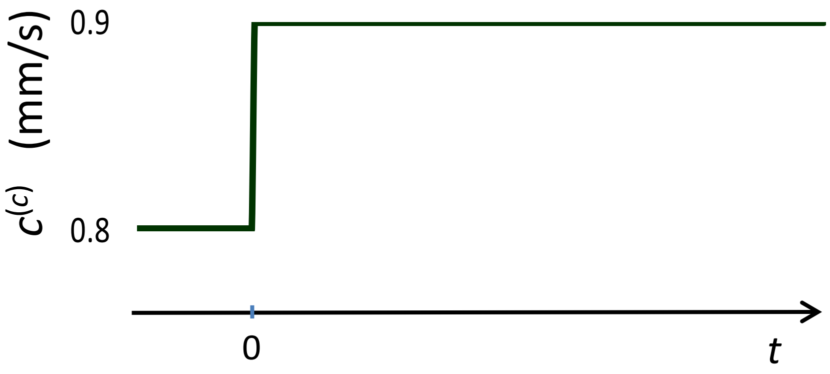


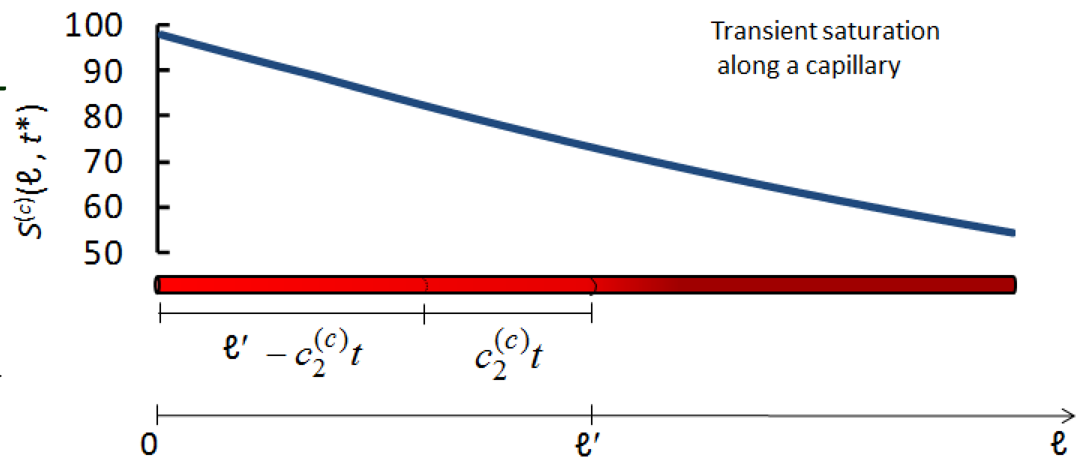
Basic principles of a new hemodynamic model

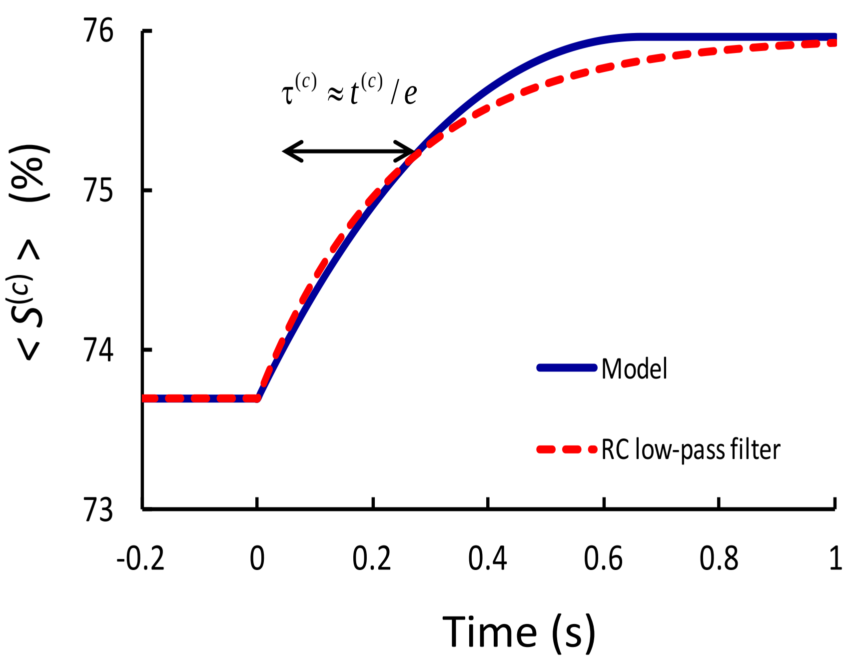


Graphics by Steffan Hacker/Tufts University

Step change in capillary flow velocity: Capillary saturation transient





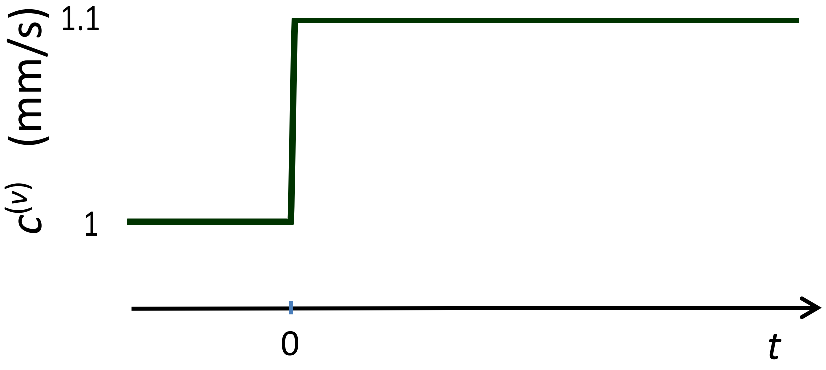


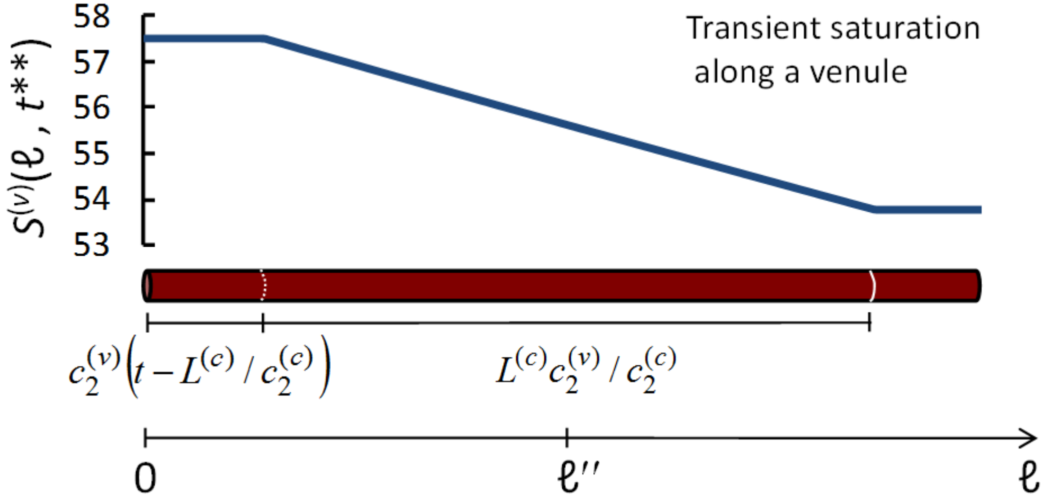
Effect of capillary transit time on the capillary saturation: RC low-pass filter with time constant $\tau^{(c)} = \frac{t^{(c)}}{e}$

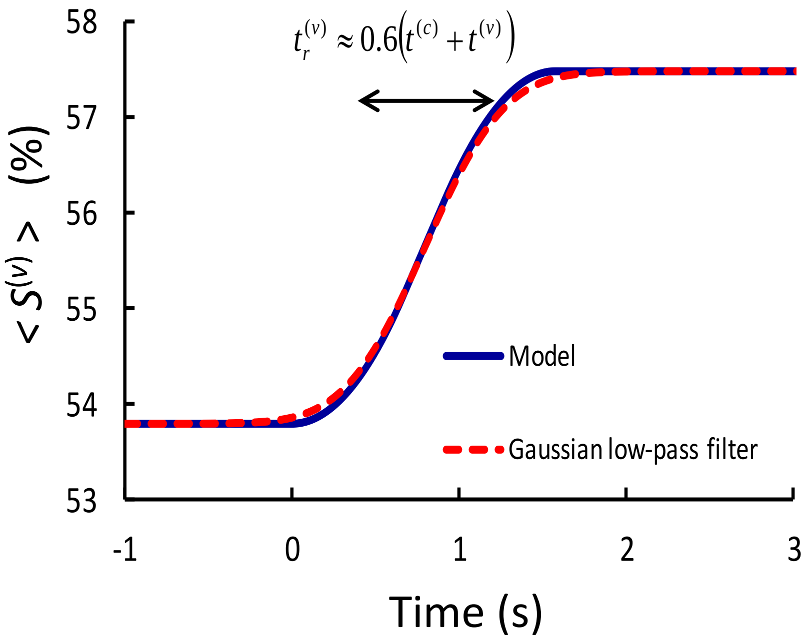
Impulse response: $h_{RC-LP}^{(c)}(t) = \frac{1}{\tau^{(c)}} e^{-t/\tau^{(c)}}$

Transfer function: $\mathcal{H}_{RC-LP}^{(c)}(\omega) = \frac{1}{1+i\omega\tau^{(c)}}$

Step change in flow velocity: Venous saturation transient







Effect of blood transit times on venous saturation: Time-shifted Gaussian low-pass filter with shift time $t_{0.5}^{(v)} = 0.5(t^{(c)} + t^{(v)})$ and rise time $t_r^{(v)} \sim 0.6(t^{(c)} + t^{(v)})$

Impulse response:

$$h_{G-LP}^{(v)}(t) = \frac{1}{t_r^{(v)}} e^{-\pi\left(t - t_{0.5}^{(v)}\right)^2 / \left(t_r^{(v)}\right)^2}$$

Transfer function:

$$\mathcal{H}_{G-LP}^{(v)}(\omega) = e^{-\frac{\ln 2}{2}\left(\frac{\omega t_r^{(v)}}{2\pi\, 0.34}\right)^2} e^{-i\omega t_{0.5}^{(v)}}$$

Hemodynamic model equations

[S. Fantini, NeuroImage **85**, 202-221 (2014)]

[S. Fantini, Physiol. Meas. **35**, N1-N9 (2014)]

Deoxy-hemoglobin concentration:

$$[\mathrm{Hb}](t) = \mathrm{ctHb}\left[\left(1-S^{(a)}\right)\mathrm{CBV}_0^{(a)}\left(1+\mathrm{cbv}^{(a)}(t)\right)+\left(1-\langle S^{(c)}\rangle\right)\mathrm{F}^{(c)}\mathrm{CBV}_0^{(c)}+\left(1-S^{(v)}\right)\mathrm{CBV}_0^{(v)}\left(1+\mathrm{cbv}^{(v)}(t)\right)\right]+$$
$$-\mathrm{ctHb}\left[\frac{\langle S^{(c)}\rangle}{S^{(v)}}\left(\langle S^{(c)}\rangle-S^{(v)}\right)\mathrm{F}^{(c)}\mathrm{CBV}_0^{(c)}h_{RC-LP}^{(c)}(t)+\left(S^{(a)}-S^{(v)}\right)\mathrm{CBV}_0^{(v)}h_{G-LP}^{(v)}(t)\right]*[\mathrm{cbf}(t)-\mathrm{cmro}_2(t)]$$

Oxy-hemoglobin concentration:

$$[\mathrm{HbO}](t) = \mathrm{ctHb}\left[S^{(a)}\mathrm{CBV}_0^{(a)}\left(1+\mathrm{cbv}^{(a)}(t)\right)+\langle S^{(c)}\rangle\mathrm{F}^{(c)}\mathrm{CBV}_0^{(c)}+S^{(v)}\mathrm{CBV}_0^{(v)}\left(1+\mathrm{cbv}^{(v)}(t)\right)\right]+$$
$$+\mathrm{ctHb}\left[\frac{\langle S^{(c)}\rangle}{S^{(v)}}\left(\langle S^{(c)}\rangle-S^{(v)}\right)\mathrm{F}^{(c)}\mathrm{CBV}_0^{(c)}h_{RC-LP}^{(c)}(t)+\left(S^{(a)}-S^{(v)}\right)\mathrm{CBV}_0^{(v)}h_{G-LP}^{(v)}(t)\right]*[\mathrm{cbf}(t)-\mathrm{cmro}_2(t)]$$

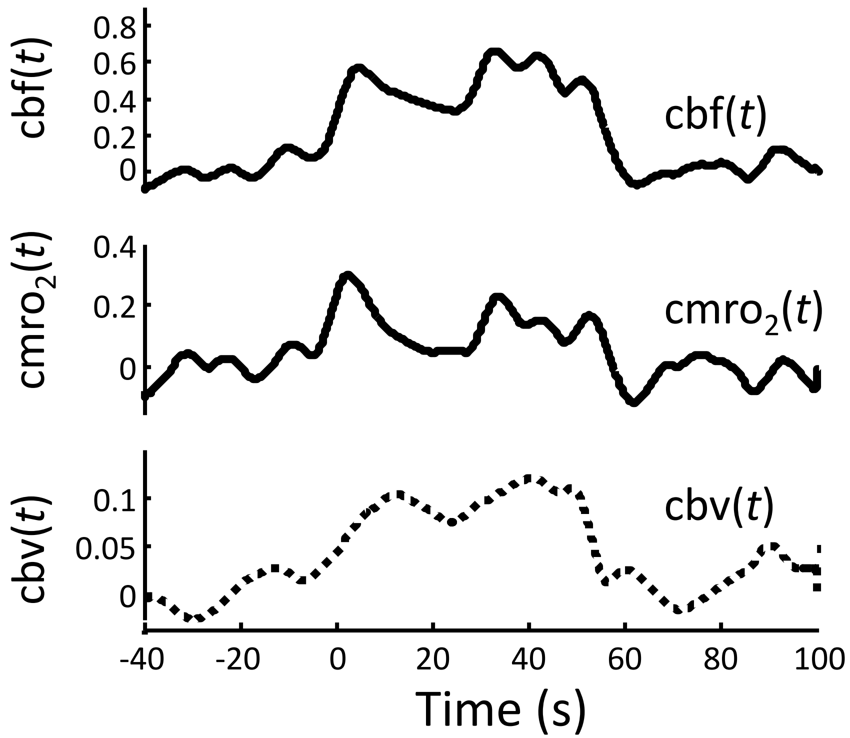
Total hemoglobin concentration:

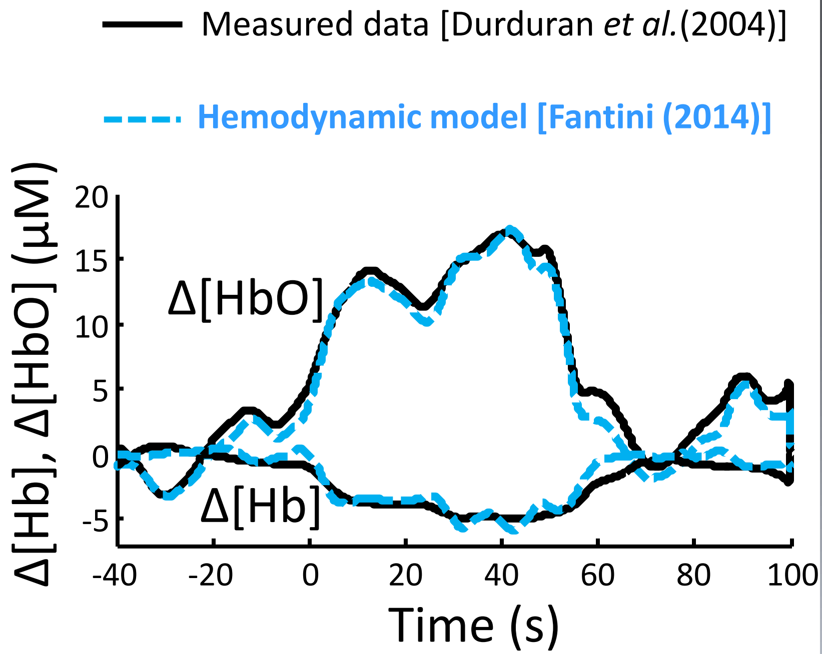
$$[\mathrm{HbT}](t) = [\mathrm{HbT}]_0\,[1+\mathrm{cbv}(t)]$$

Model validation from published fNIRS data: Human brain - finger tapping

cbf(t), cbv(t), and cmro$_2$(t) are inputs to the model

From Durduran *et al.*, Opt. Lett. **29**, 1766 (2004)

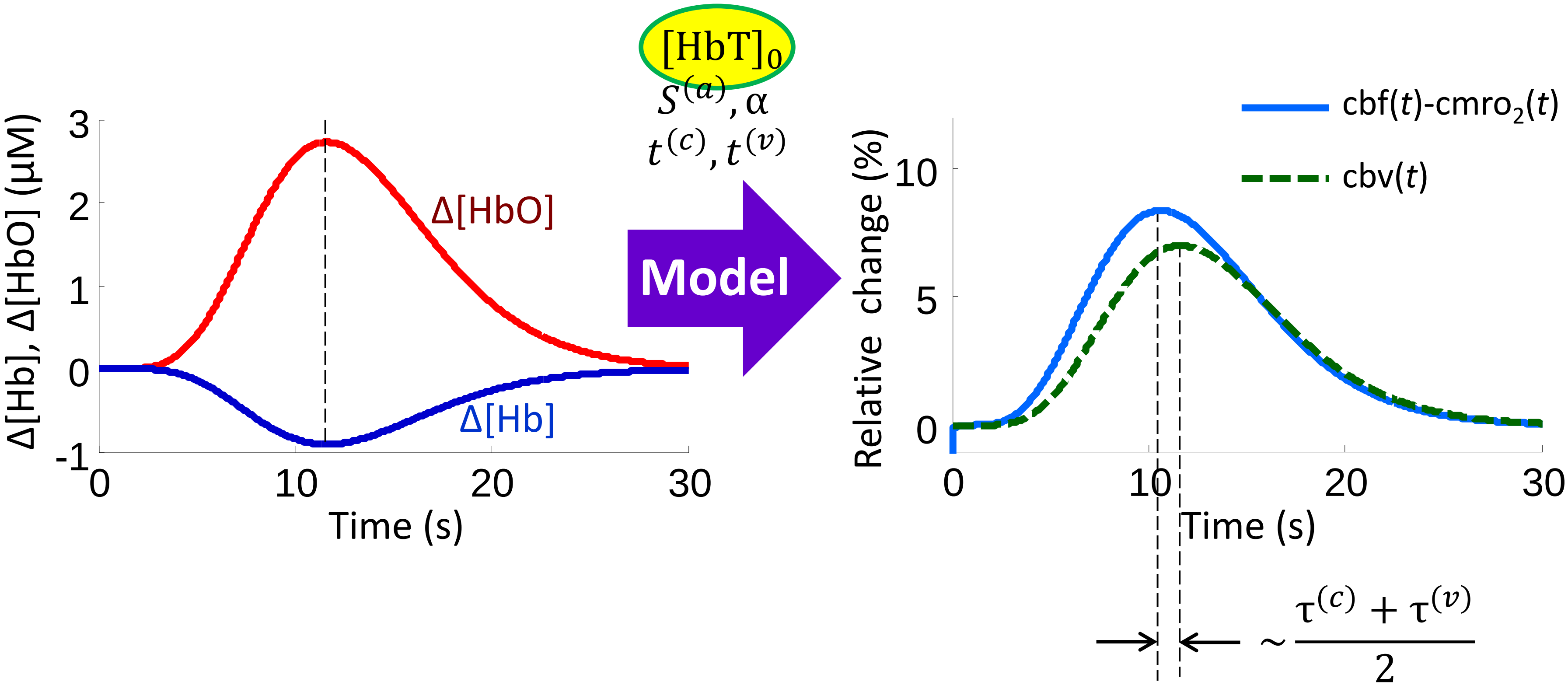




Application of the new hemodynamic model to fNIRS

Measured concentration changes of [HbO] and [Hb]

Relative changes in CBV, CBF, and $CMRO_2$ ($cbv(t)$ and $[cbf(t)-cmro_2(t)]$)



[Kainerstorfer *et al.*, Acad. Rad. **21**, 185 (2014)]

CONCLUSIONS

- The key role of tissue phantoms for calibration and validation of absolute NIRS measurements
- Absolute cerebral concentration and saturation of hemoglobin
- Determination of CBV, CBF, and $CMRO_2$ for functional brain studies

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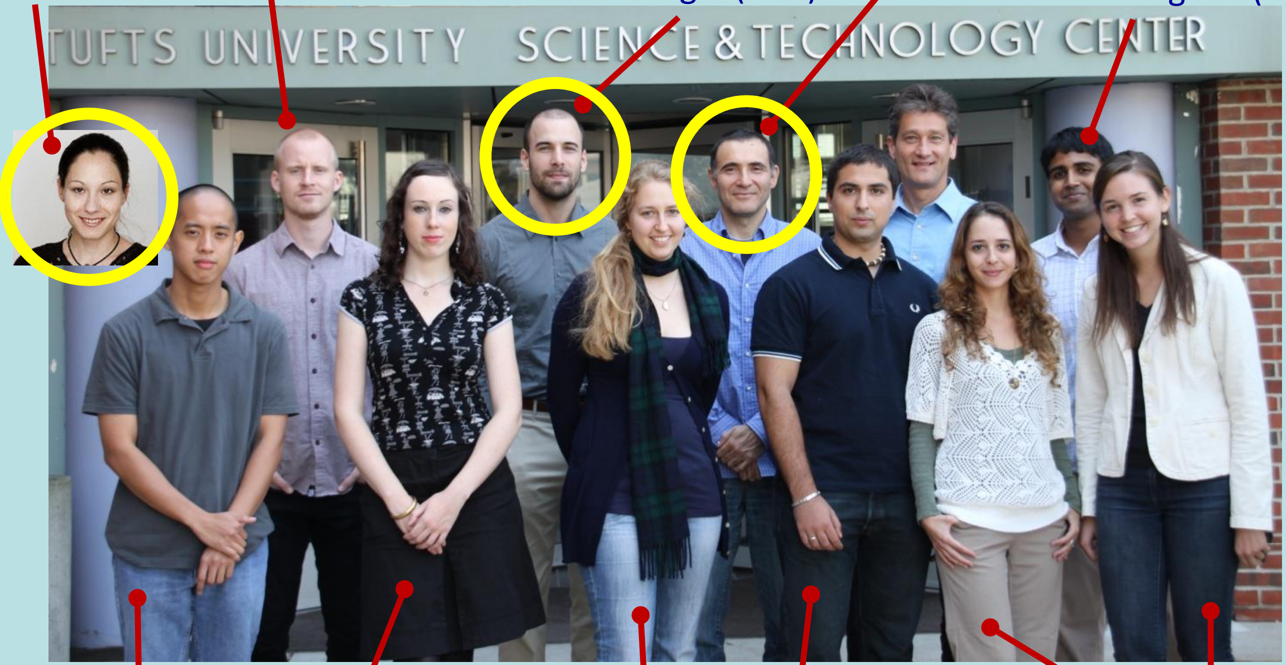

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