3D deep tissue imaging technologies for in-vivo diagnostics and digital pathology

Stefan Andersson-Engels

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Acknowledgements

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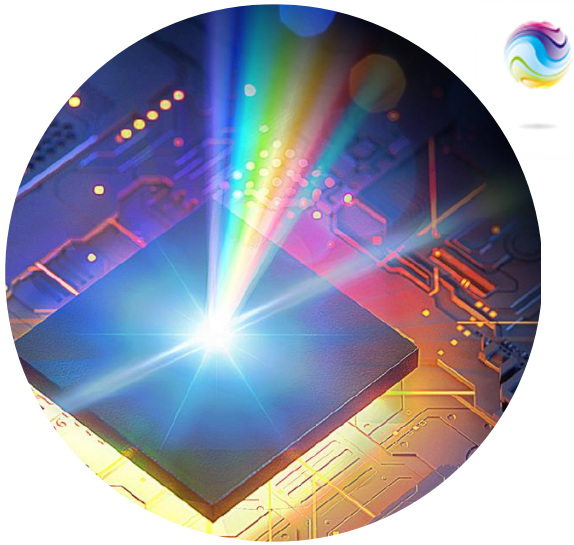
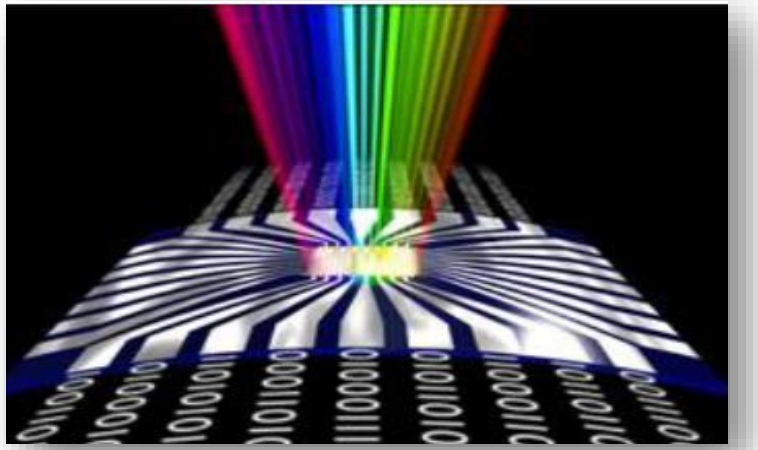
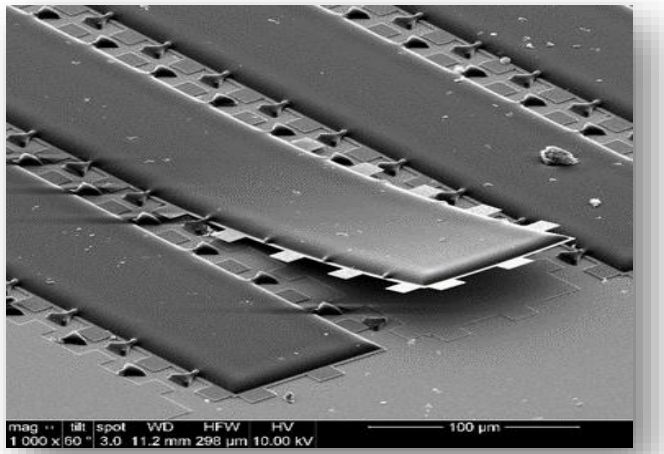
Where am I working?

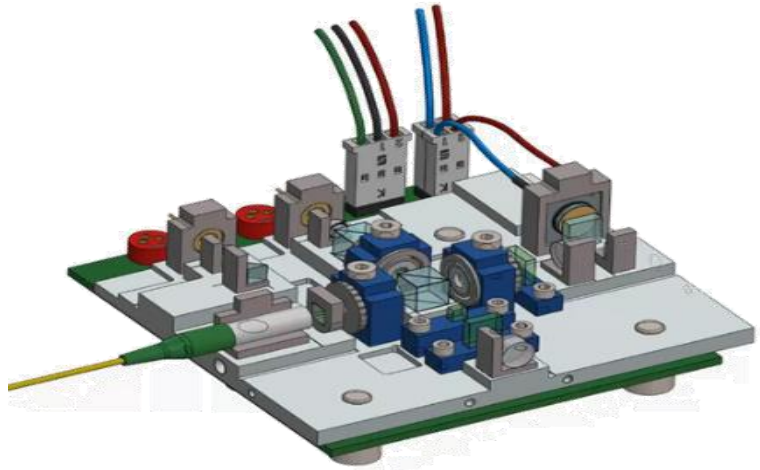


Irish Photonic Integration Centre

- IPIC is Ireland's national photonics research centre
- Focus - Integrated photonic systems (hybrid and heterogeneous integration) for ICT and Medtech







New Centre Research Programme

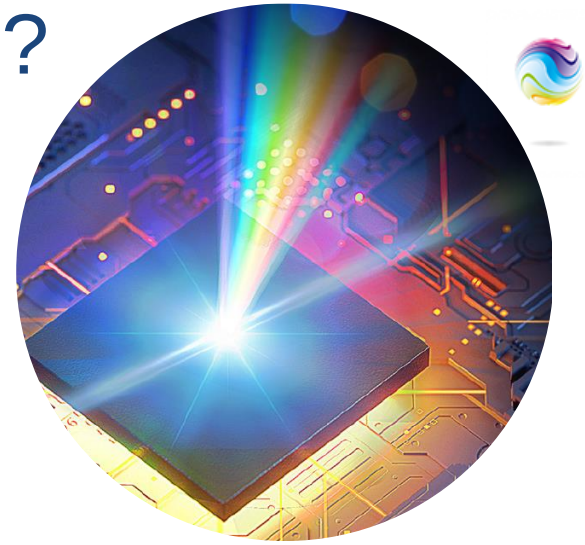
‘World’s smallest integrated imaging system for guided surgery’

‘Coherent everywhere’ – migration of coherent communications to the network edge

‘Breaking the packaging cost barrier’

‘Printed photonics on anything’

Where am I working?



IDA Ireland

KEY FACTS about MedTech in Ireland

15 of the top 20 MedTech companies are in Ireland

250
The number of MedTech companies in Ireland

€7.2bn
The value of annual Irish MedTech exports

25,000
The number of people employed in the industry – the highest number of people working in the industry in any country in Europe, per head of population

33%
The percentage of the world's contact lenses manufactured in Ireland

30m
The number of people with diabetes that rely on an injectable device manufactured in Ireland

The world's
market-leading drug-eluting stent was developed and commercialised in Ireland

>50%
of MedTech companies have a dedicated R&D function

2nd largest
Ireland is the 2nd largest exporter of MedTech products in Europe

8%
Exports of medical devices and diagnostics products now represent 8% of Ireland's total merchandise exports

50%
The percentage of ventilators worldwide in acute hospitals that are Irish made

Just some of the MedTech companies with operations in Ireland

Boston Scientific · Bausch + Lomb · Medtronic (When Life Depends on Medical Technology) · Vistakon (Division of Johnson & Johnson Vision Care, Inc.) · GE Healthcare
Abbott · Baxter · B Braun · Zimmer · Stryker
Siemens · Covidien · Allergan · Johnson & Johnson · BD
Lake Region Medical · Integra · Bard · Hospira

September 2012

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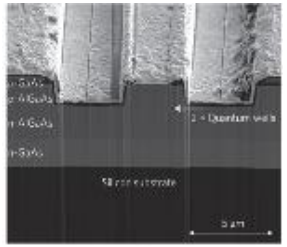
Biophotonics Innovation Chain

Components	Biophotonics System	Pre-Clinical & Clinician	Market Execution



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MCCI Microelectronic Circuits Centre Ireland

ANALOG DEVICES

eblanaphotonics

THORLABS

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UCDAVIS UNIVERSITY OF CALIFORNIA

Caltech

POLITECNICO DI MILANO

ASSERT Enabling Better Safer Healthcare

apc Microbiome Ireland

curam

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SPECTRACURE

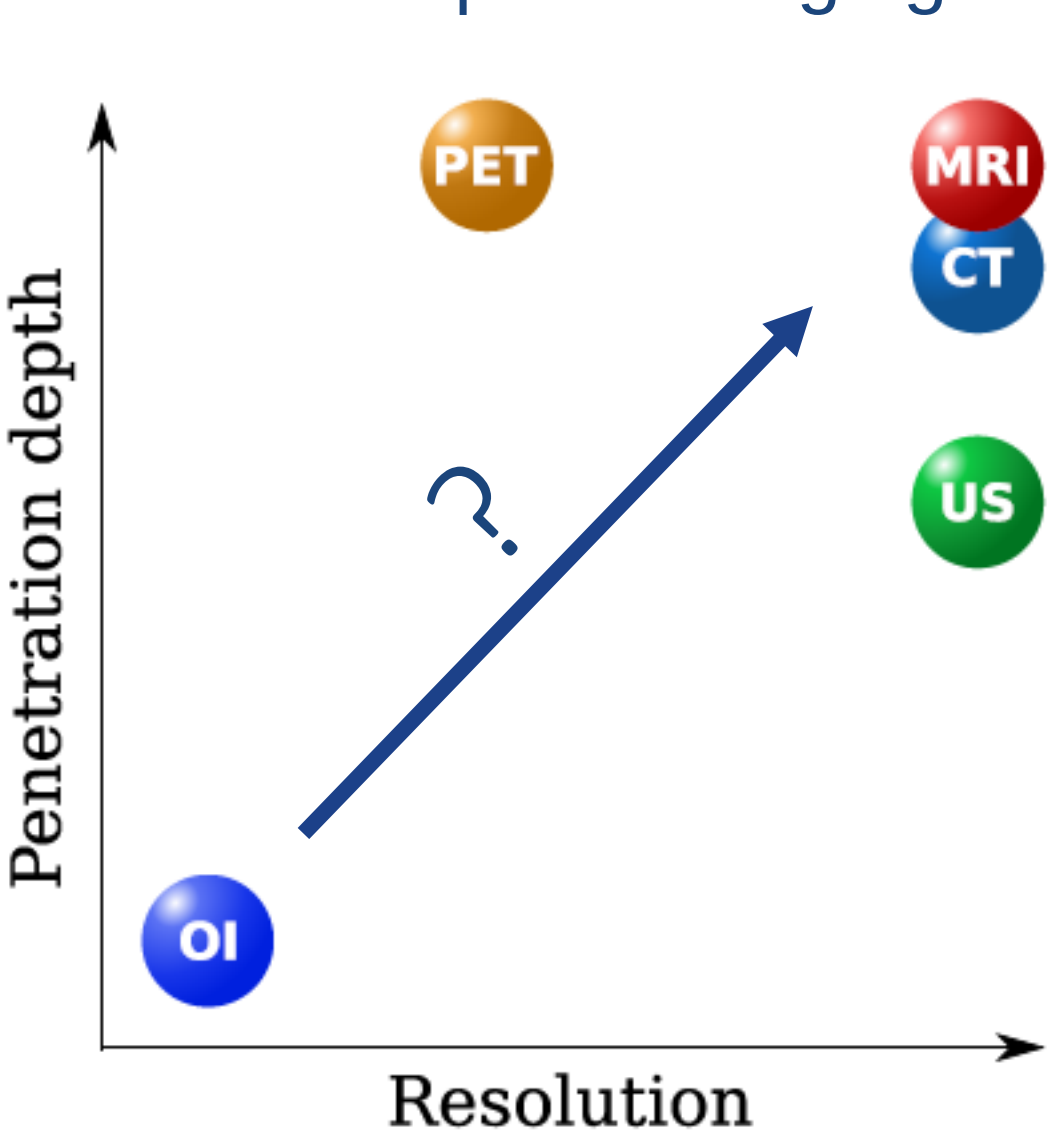
SUNSTAR

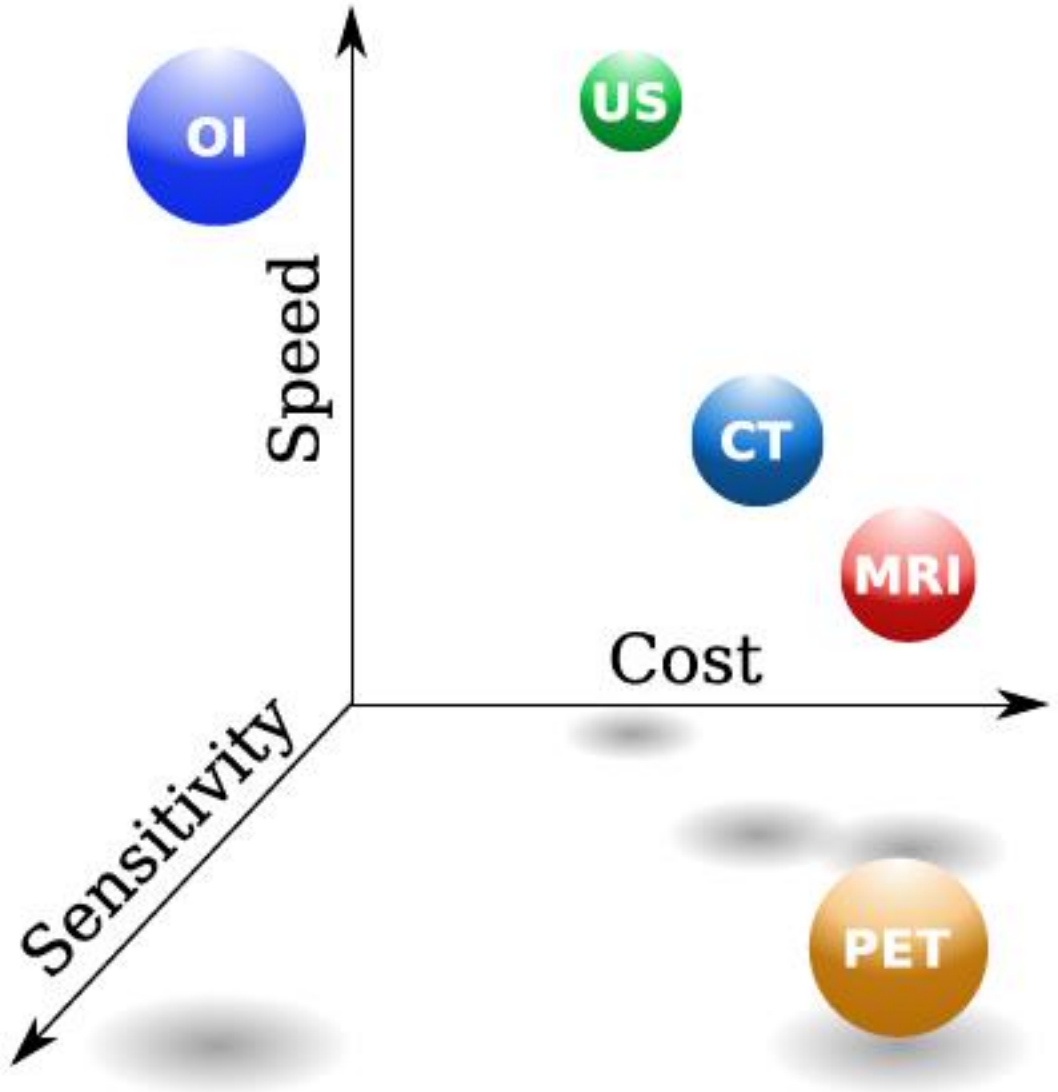
There is a clear need for deep tissue imaging

- Diagnostics
- Treatment guidance

Illustrations by Tualle

Diffuse Optical Imaging





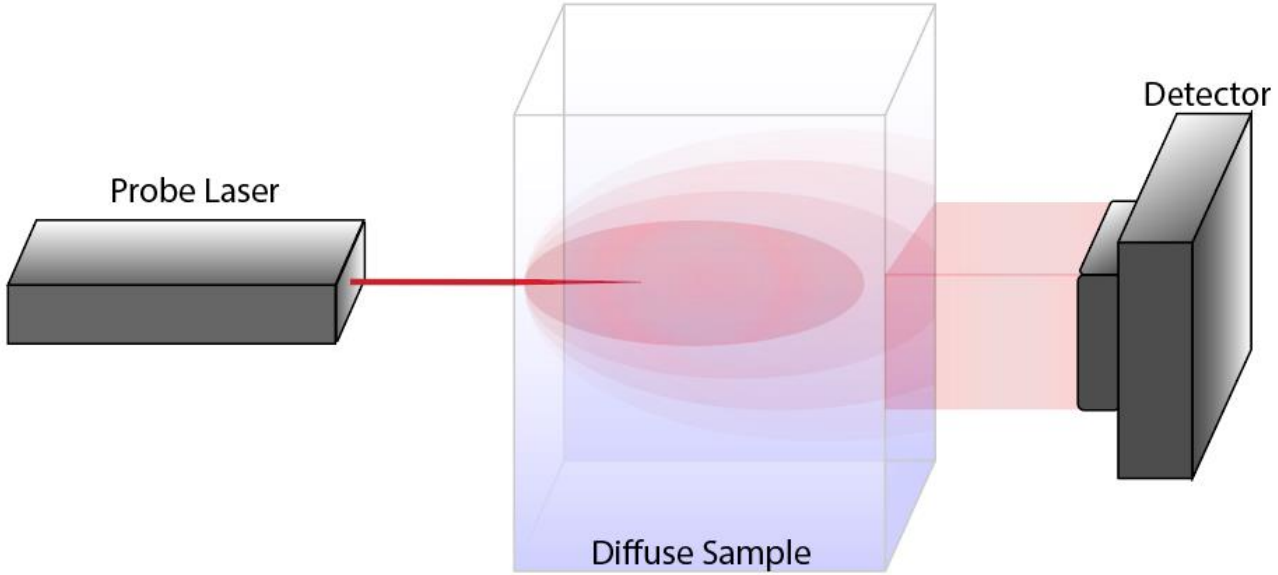
 Xu, Can (2013). *Diffuse optical spectroscopy and imaging of turbid media* (Doctoral dissertation). Lund University, Sweden.

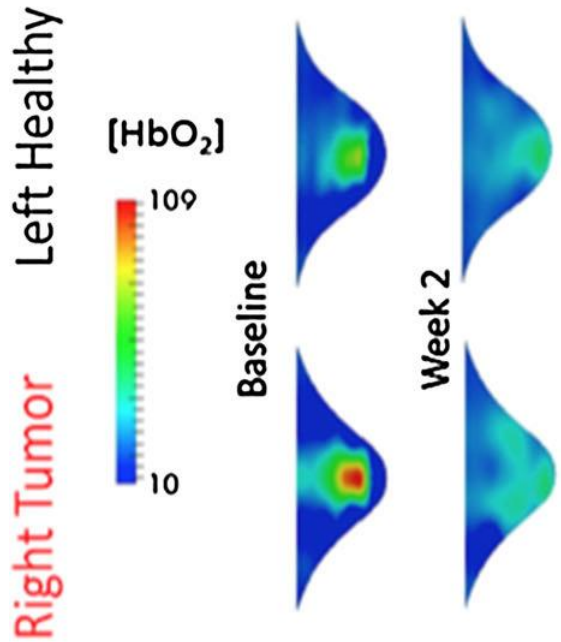
Acoustic Optical Tomography (AOT)

Upconverting Nanoparticles (UCNPs)

Combined Optical and Ultrasound

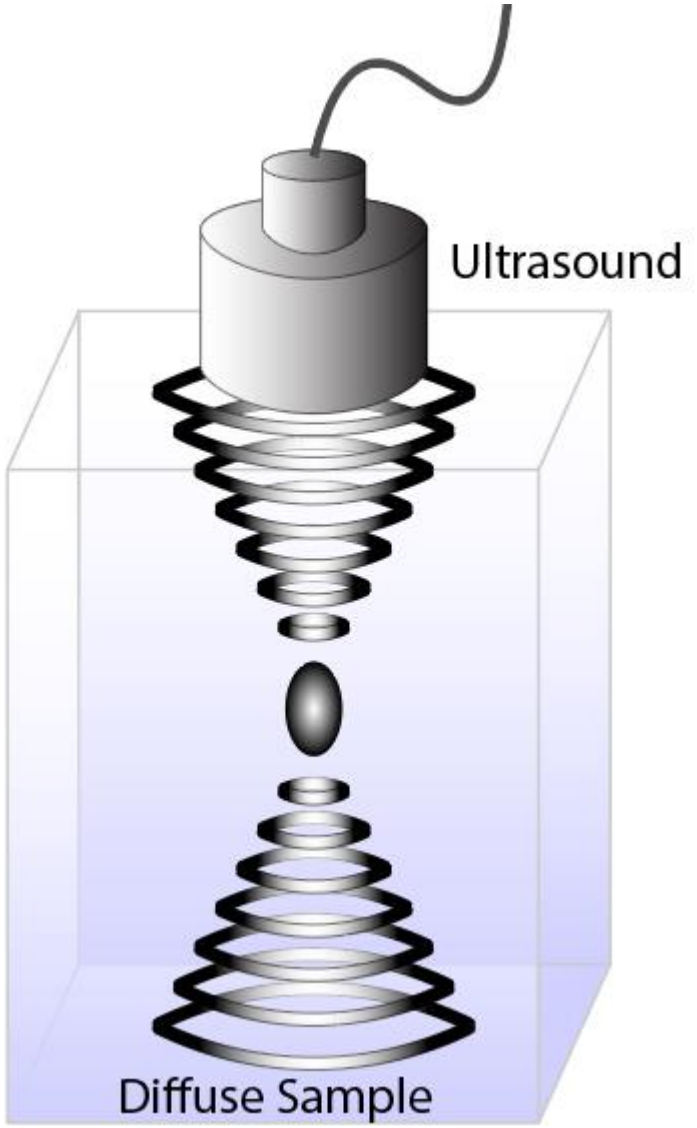
	Contrast	Resolution
Light	☺	☹



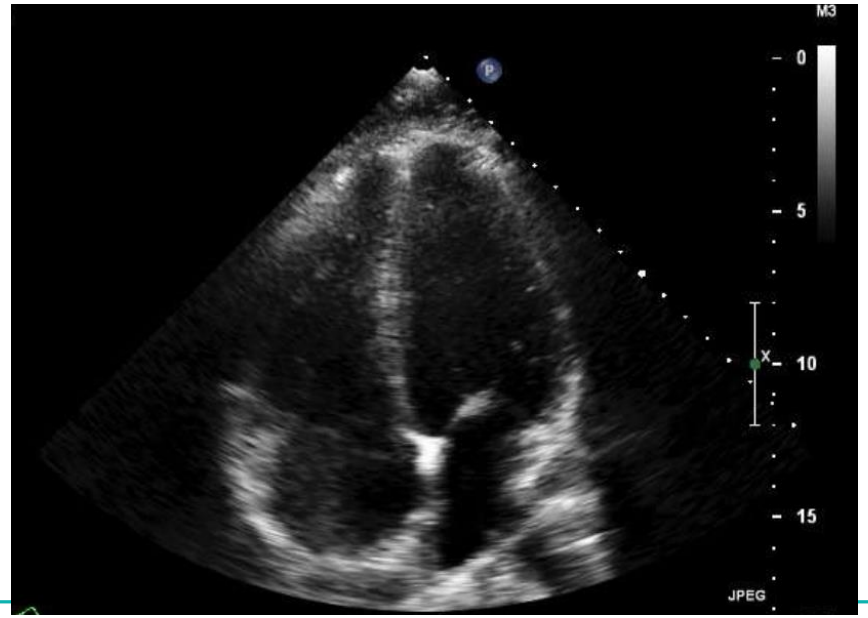


Lim, Emerson A., Gunther, Jacqueline E., et al. "Diffuse optical tomography changes correlate with residual cancer burden after neoadjuvant chemotherapy in breast cancer patients." *Breast cancer research and treatment* 162.3 (2017): 533-540.

Combined Optical and Ultrasound

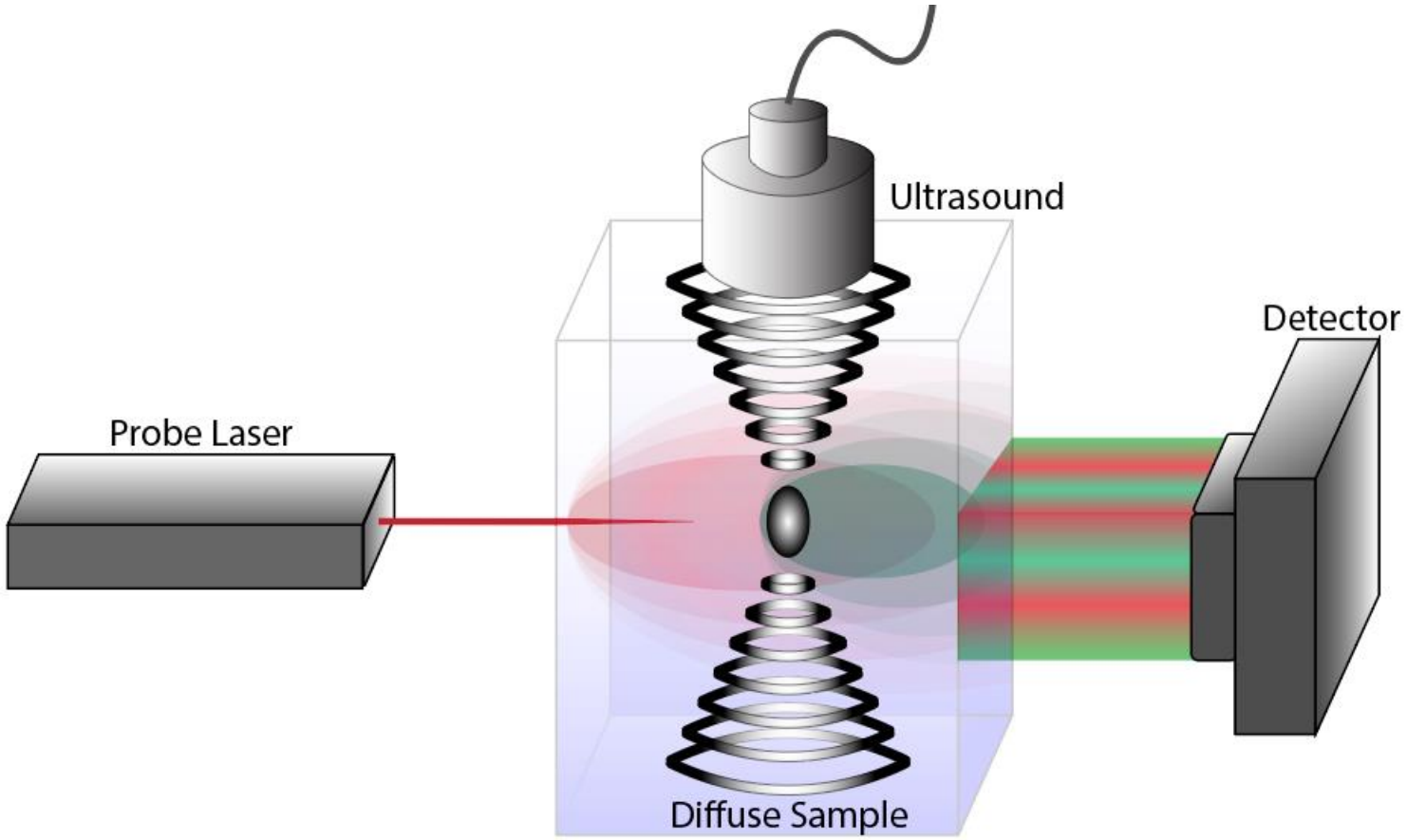


	Contrast	Resolution
Light	☺	☹
Ultrasound	☹	☺

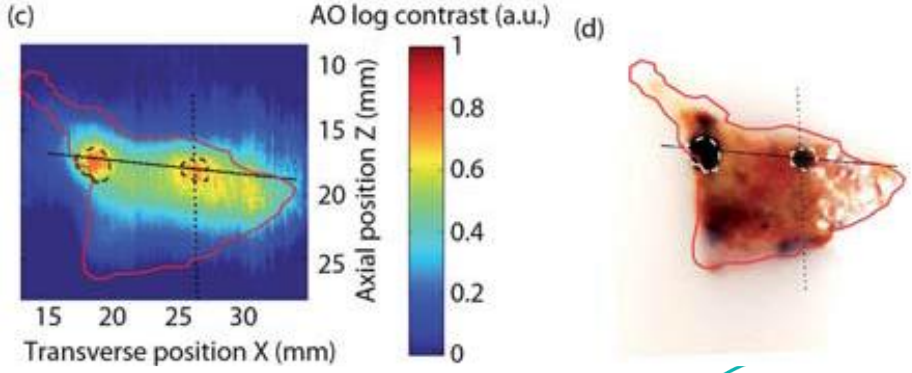


A Wor

Combined Optical and Ultrasound

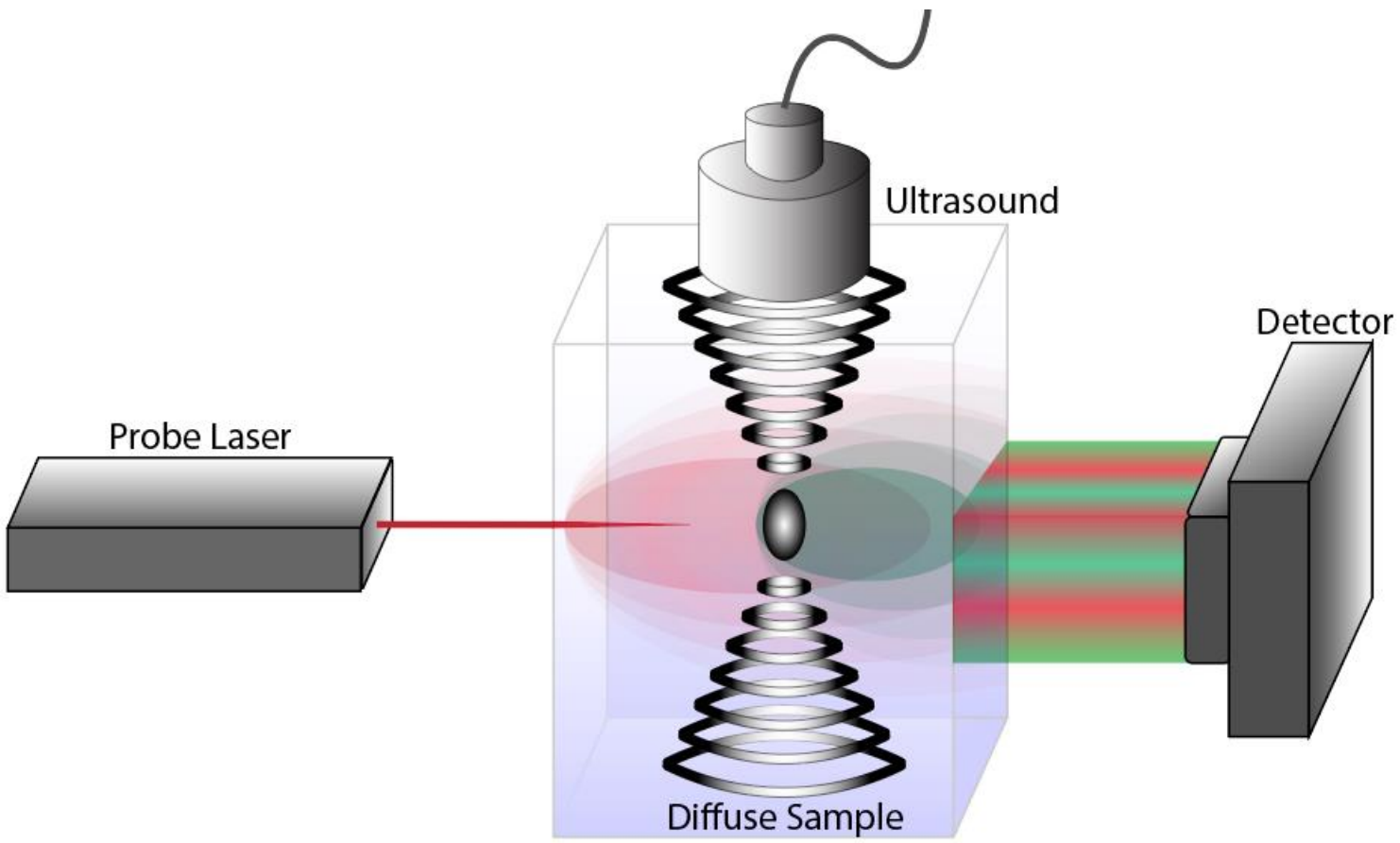


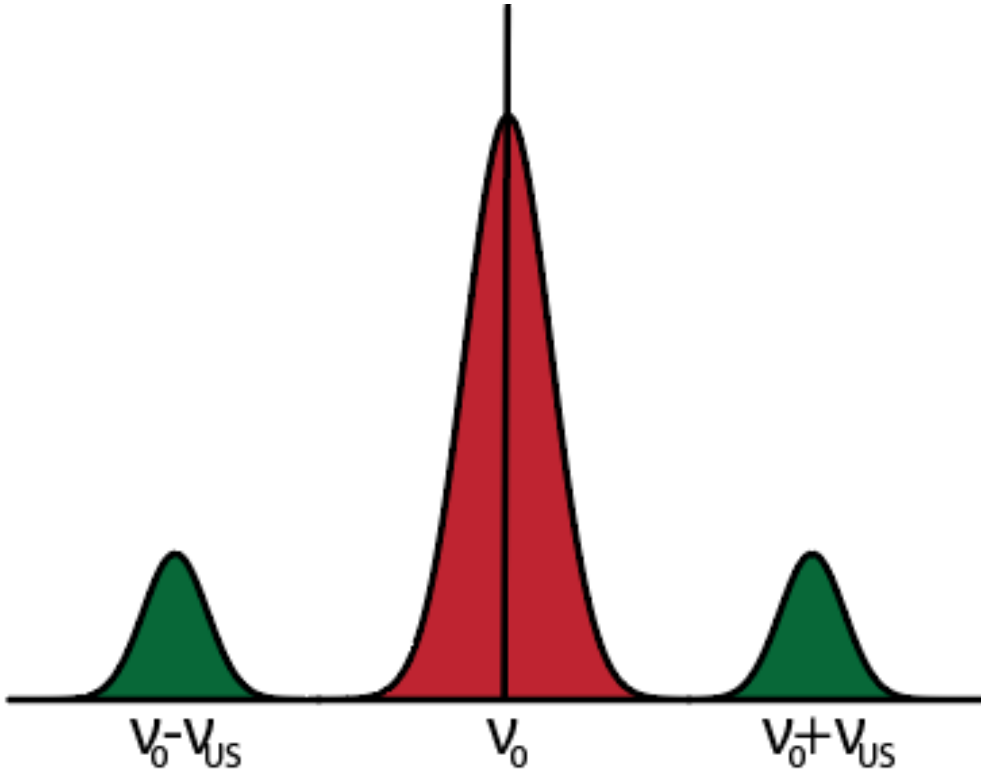
	Contrast	Resolution
Light	☺	☹
Ultrasound	☹	☺
Combined	☺	☺



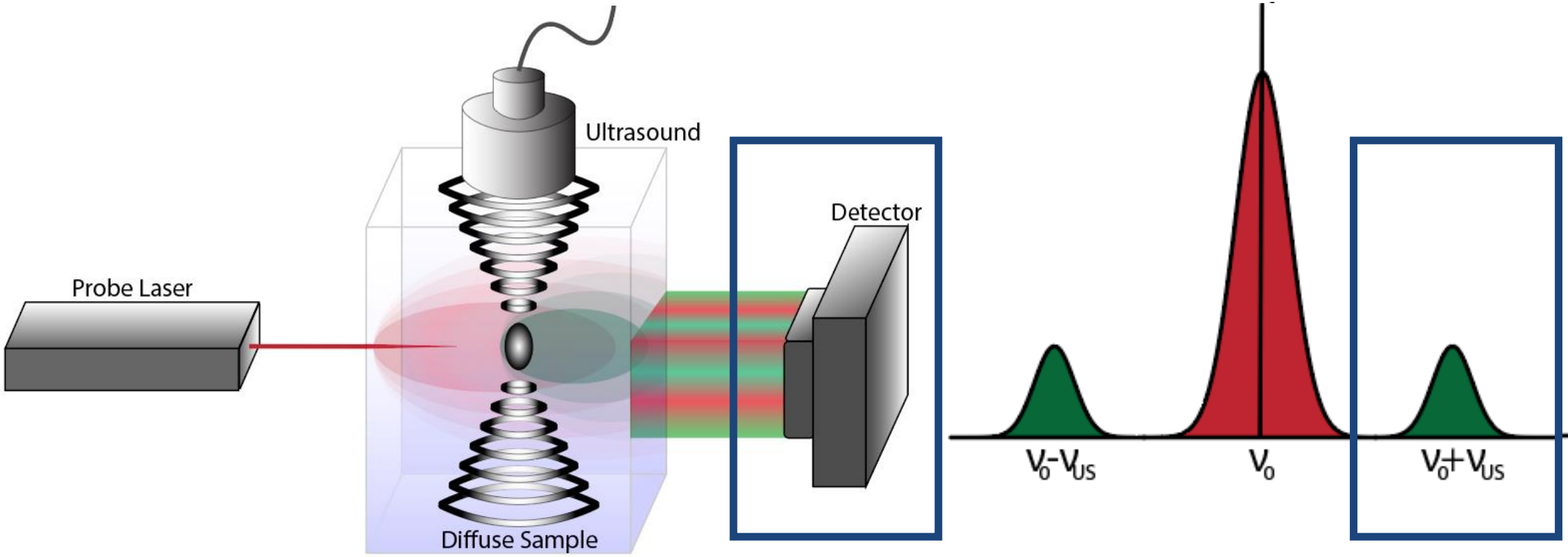
Laudereau J-B, à La Guillaume E B, Servois V, Mariani P, Grabar A A, Tanter M, Gennisson J-L, Ramaz F. Multi-modal acousto-optic/ultrasound imaging of ex vivo liver tumors at 790 nm using a Sn2P2S6 wavefront adaptive holographic setup. Journal of Biophotonics, 2015, 8(5): 429-436

Acousto Optical Tomography – how does it work?

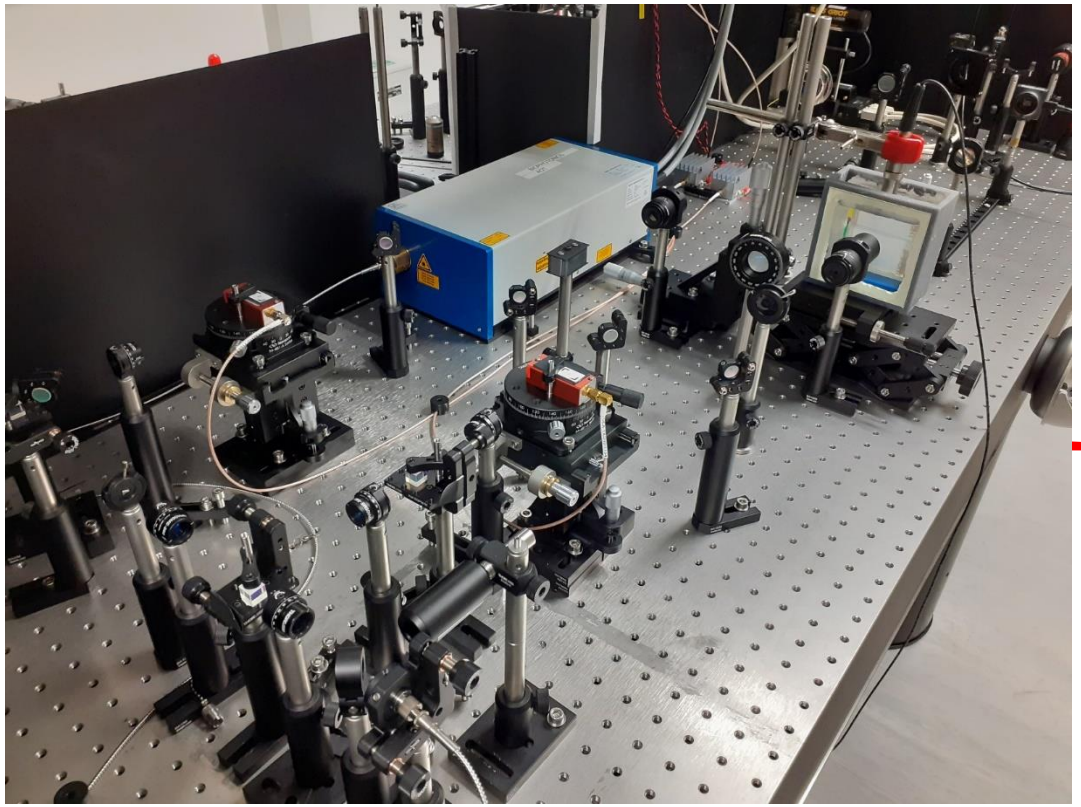




Acousto Optical Tomography – how does it work?

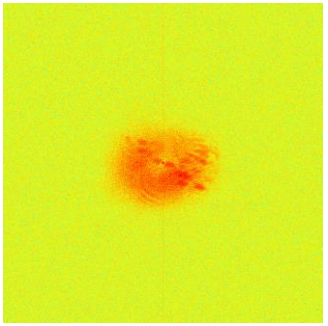


Heterodyne System

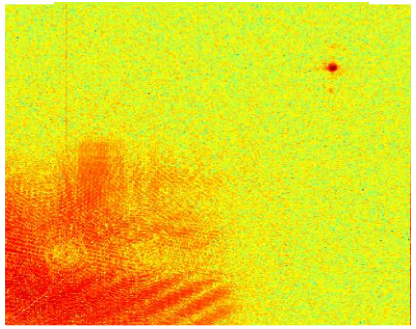


Camera

No Ultrasound

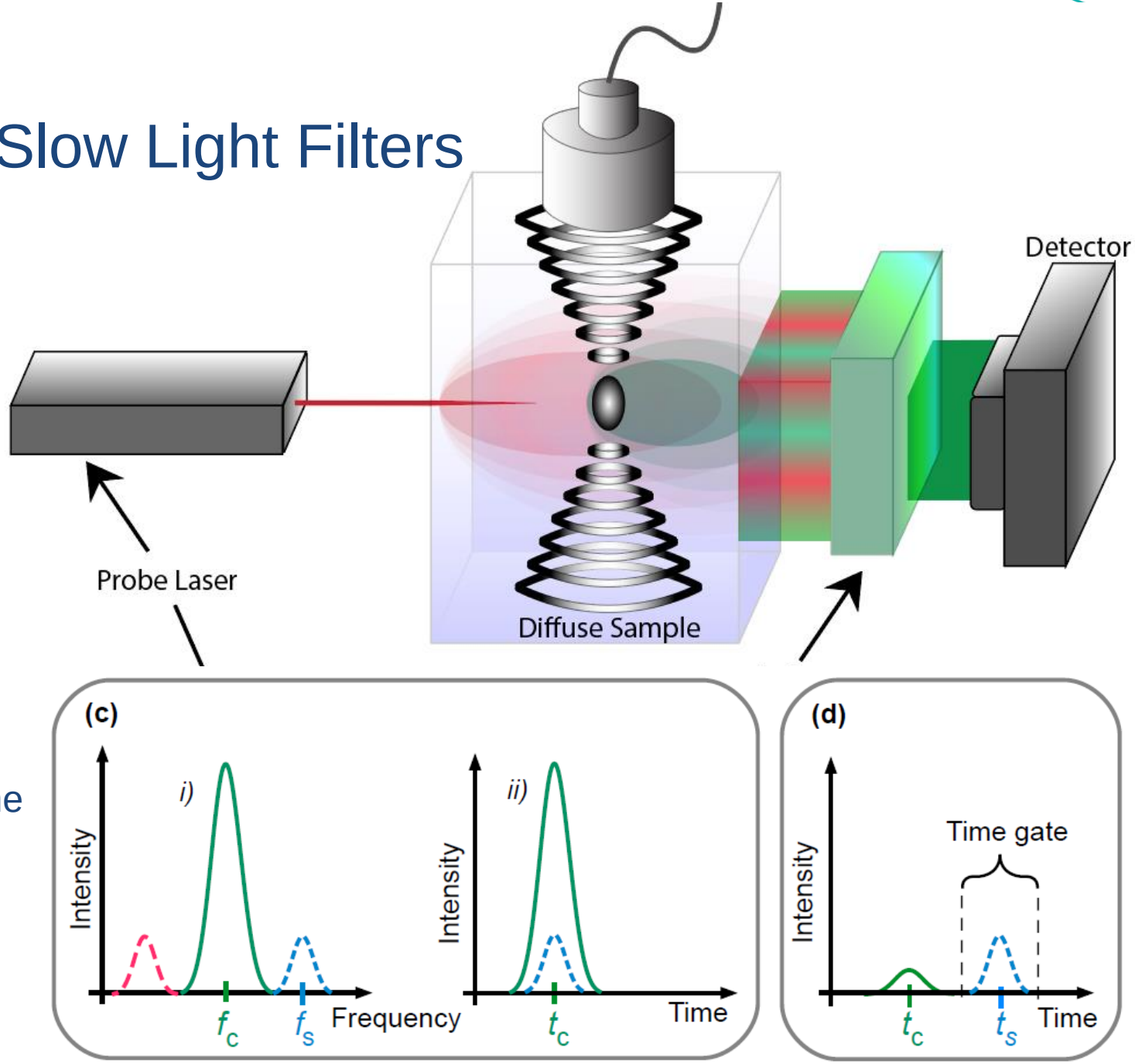


With Ultrasound



Can separate the tagged light by using a simple setup!

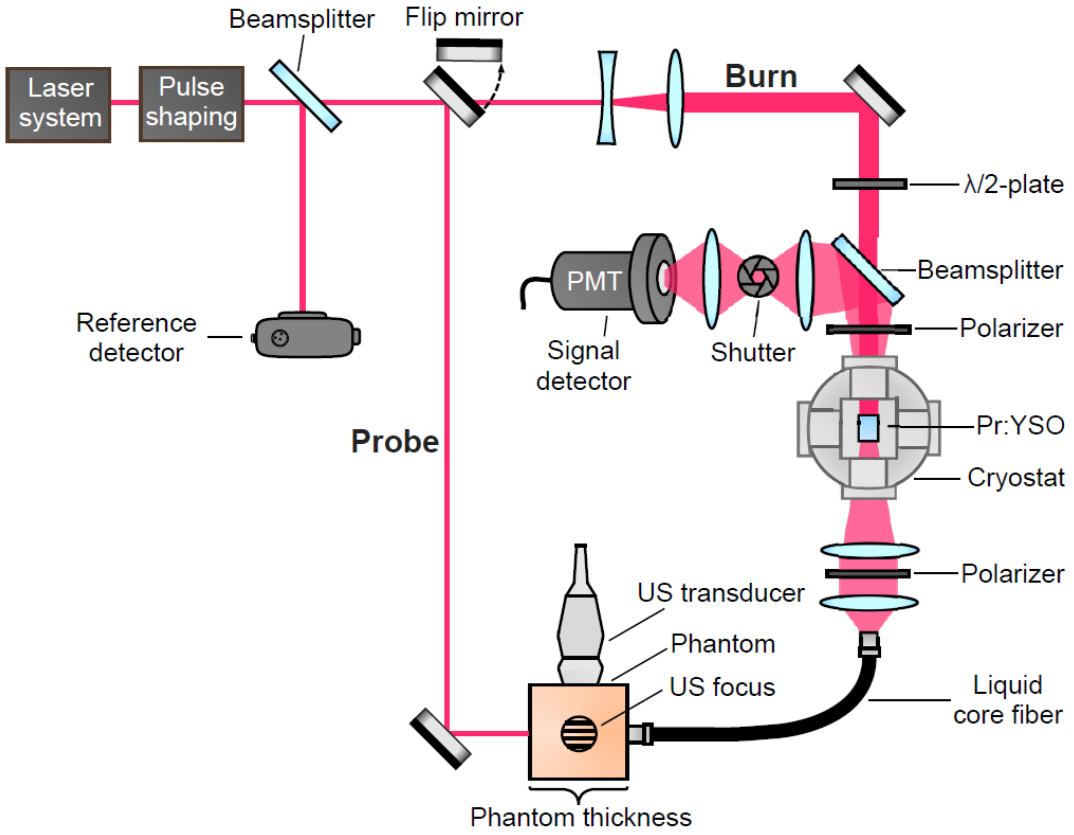
AOT with Slow Light Filters

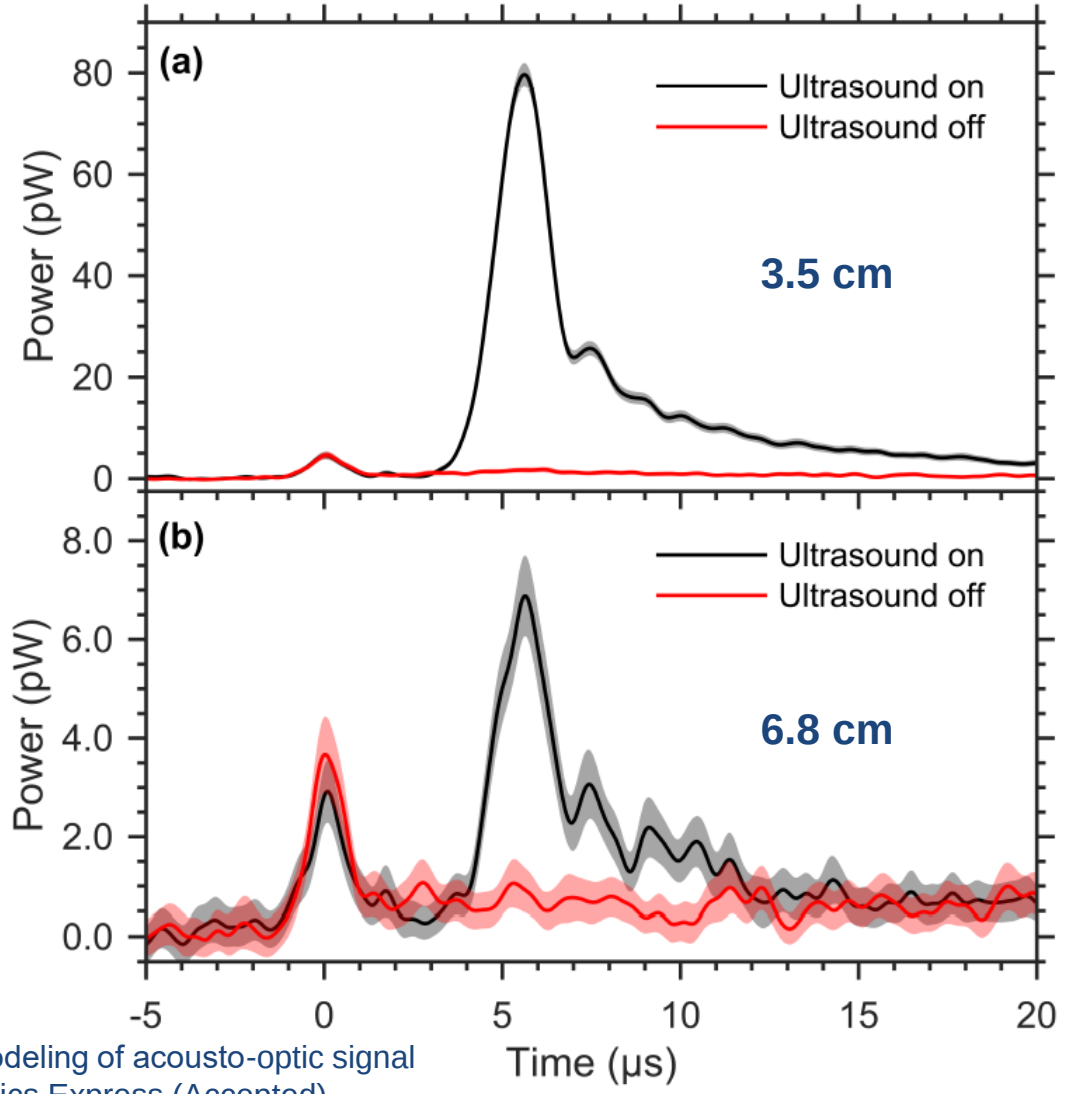


Difference in transit time

$$v_g = \frac{c}{n_g(\omega)} = \frac{c}{n + \omega\frac{dn}{d\omega}}$$

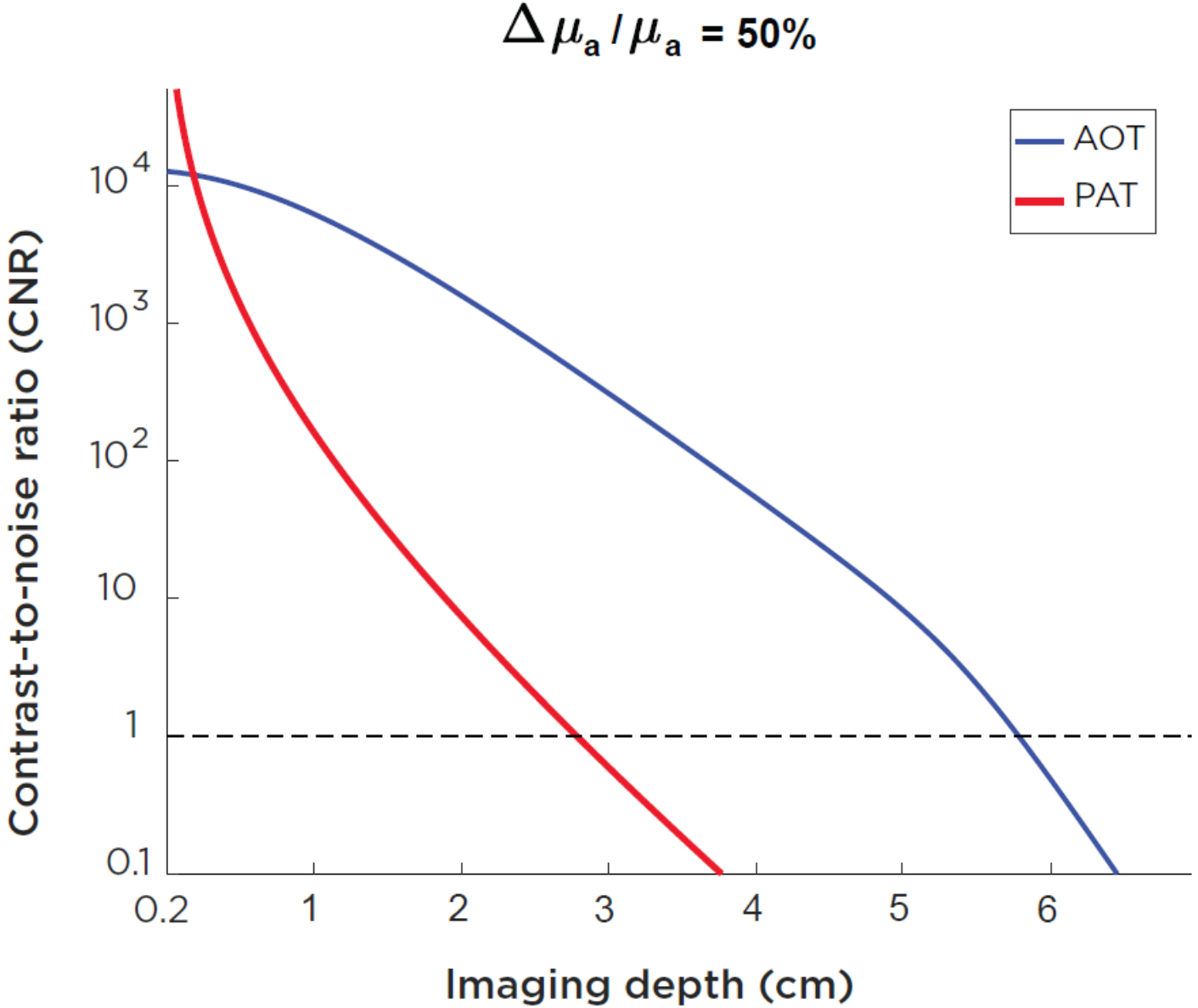
Experimental verification





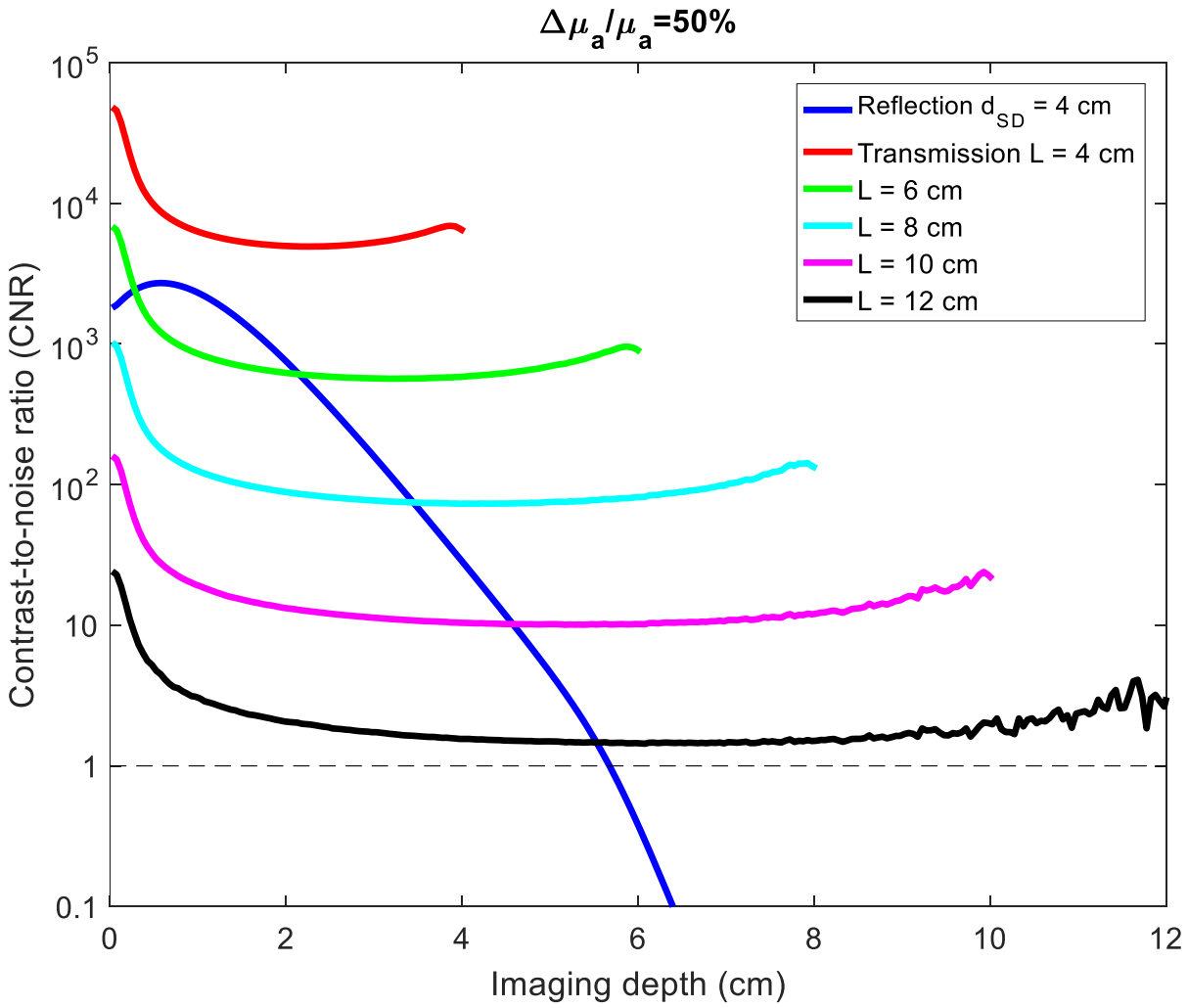
A. Bengtsson, D. Hill, M. Li et al. "Characterization and modeling of acousto-optic signal strengths in highly scattering media. Biomedical Optics Express (Accepted)

Acousto-Optical Tomography versus Photoacoustics



Walther, A., Rippe, L., Wang, LV., Andersson-Engels, S., and Kröll, S. "Analysis of the potential for non-invasive imaging of oxygenation at heart depth, using ultrasound optical tomography (UOT) or photo-acoustic tomography (PAT)." *Biomedical optics express* 8.10 (2017): 4523-4536.

Modelling CNR versus Imaging Depth



Gunther, J., Walther, A., Rippe, L., Kröll, S., and Andersson-Engels, S. Deep tissue imaging with acousto-optical tomography and spectral hole burning with slow light effect: a theoretical study. Journal of Biomedical Optics (2018).

Theoretical possibility to reach centimetres into biological tissue!

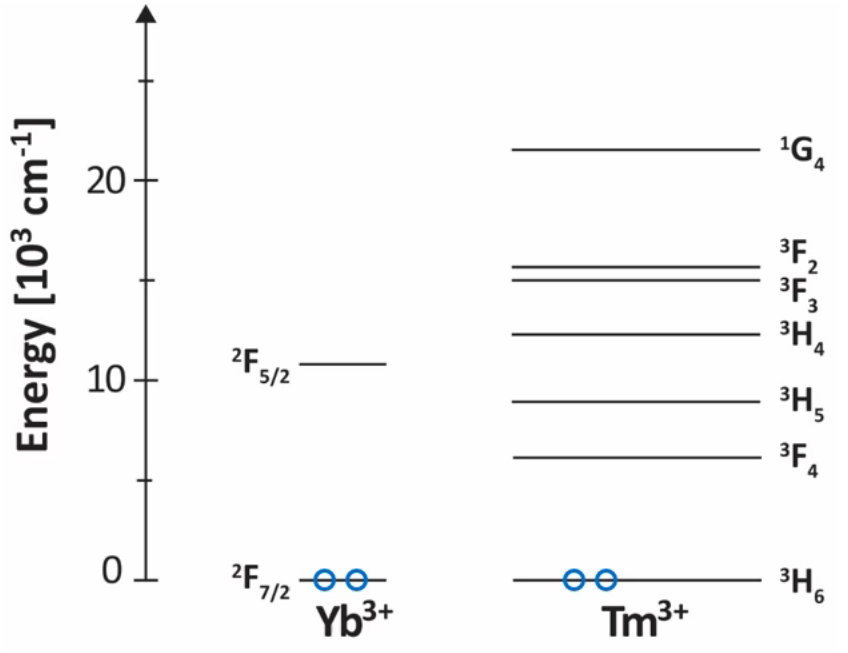
Fundamental research for deep tissue imaging

Acoustic Optical Tomography (AOT)

Upconverting Nanoparticles (UCNPs)

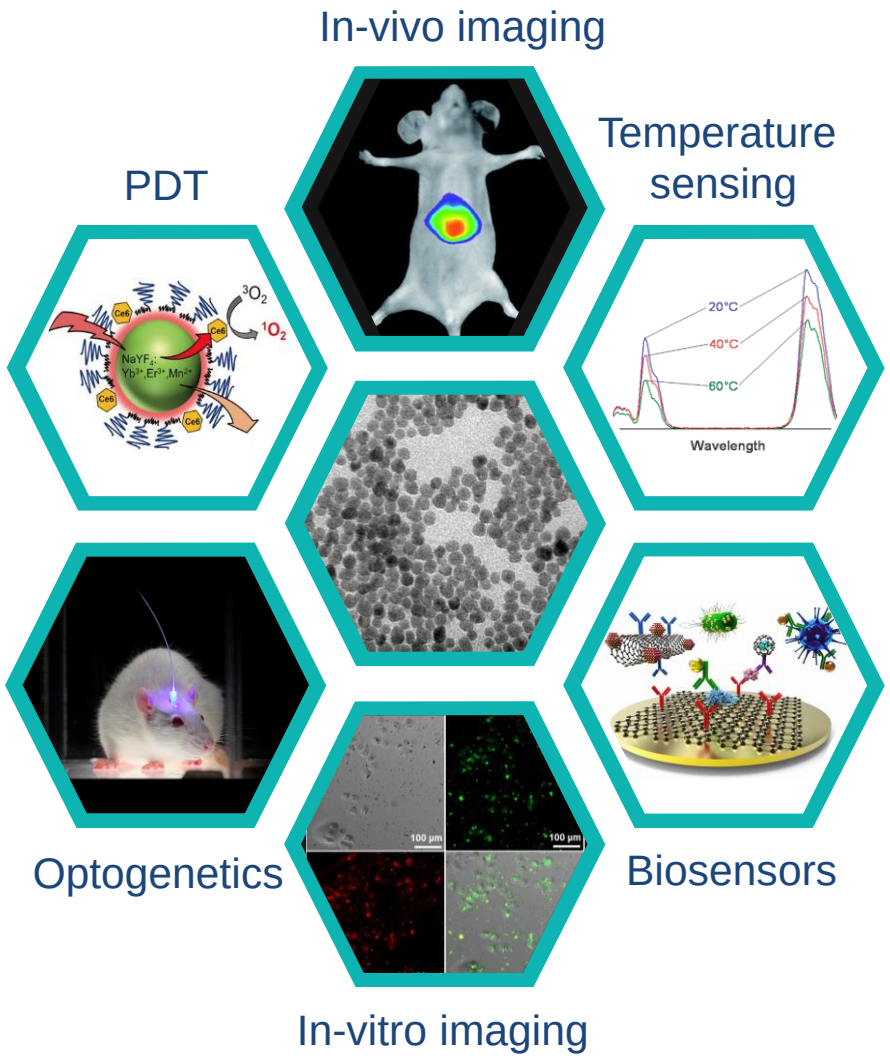
Upconverting nanoparticles

Energy transfer unpconversion (ETU) process



Sensitizer ion

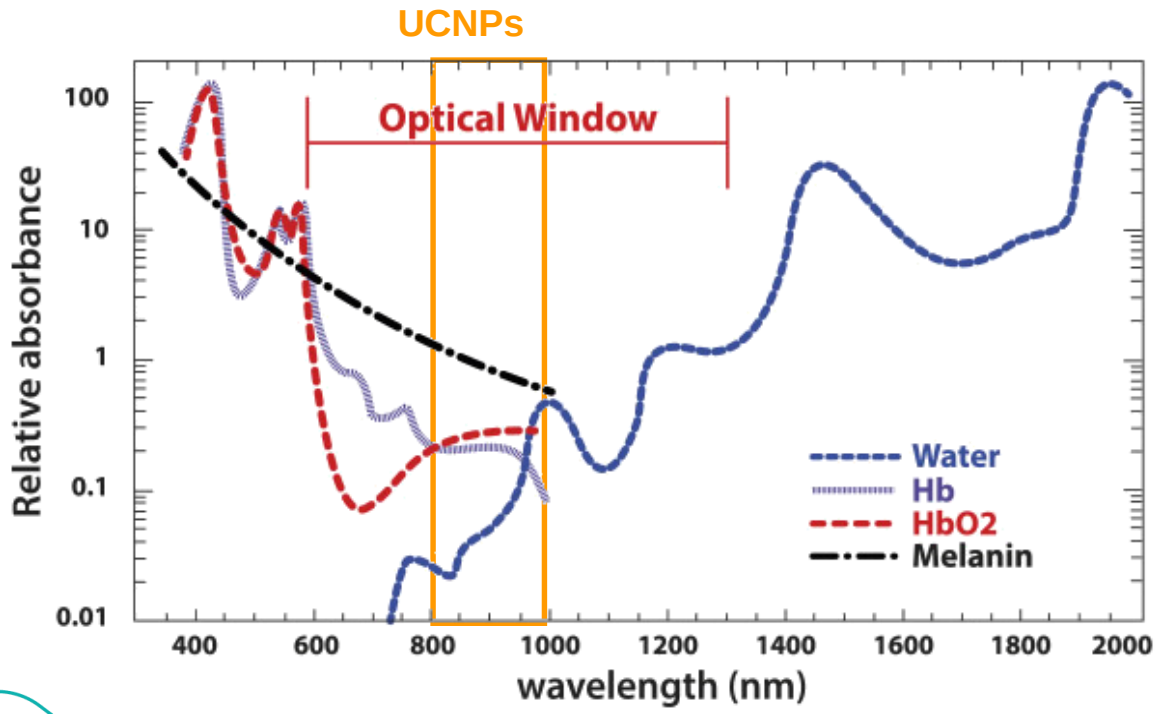
Activator ion



Why UCNPs?

Fluorescence measurements of deep tissue structures are limited by:

- poor light penetration
- superimposed tissue autofluorescence

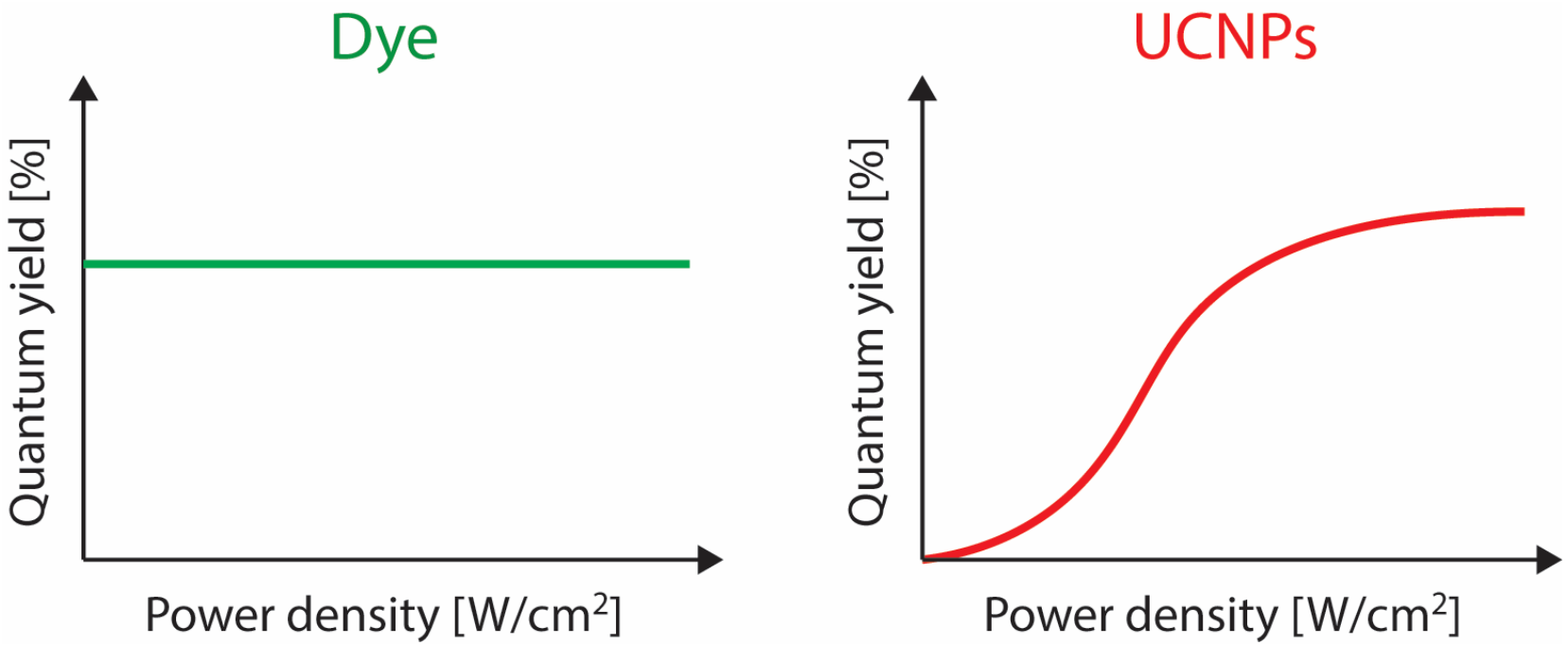


Comparison of fluorescent probes for bioimaging

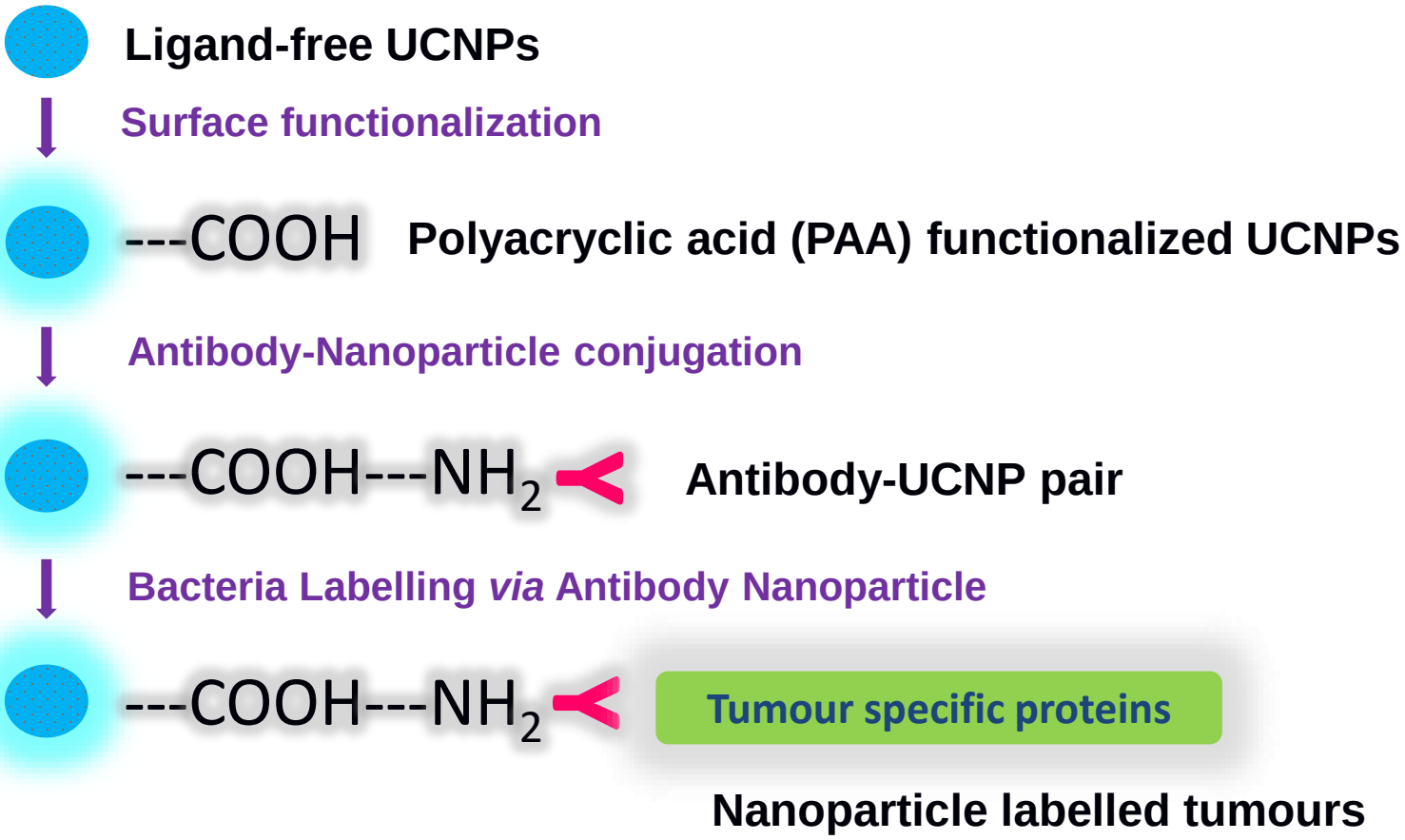
	UCNPs	QDs	Dyes
Non-toxic	✓	✗	✓
No autofluorescence	✓	✗	✗
Penetration depth	✓	✗	✗
Photostability	✓	✓	✗
Chemical stability	✓	✓	✓
Narrow emission line	✓	✗	✗
Functionalisation	✓	✗	✓
Quantum yield	✗	✓	✓

Quantum Yield

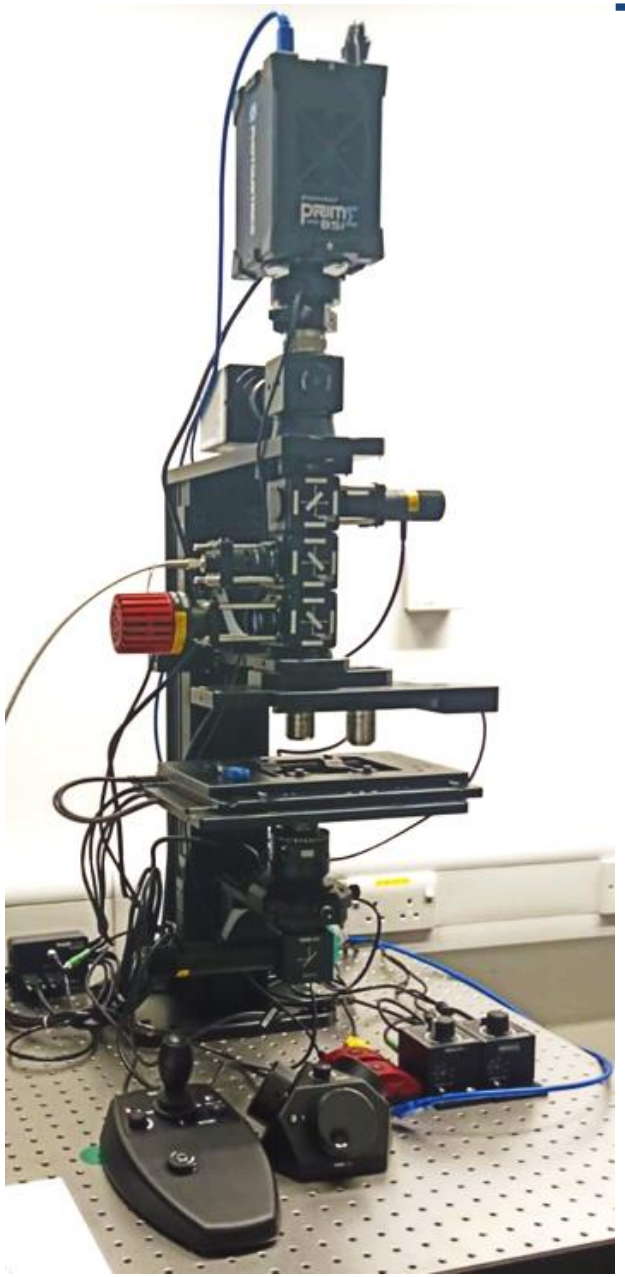
- Need of improving upconversion **efficiency** (~ 2%)
- Multi-photon process yields **power-dependent** QY of UCNPs



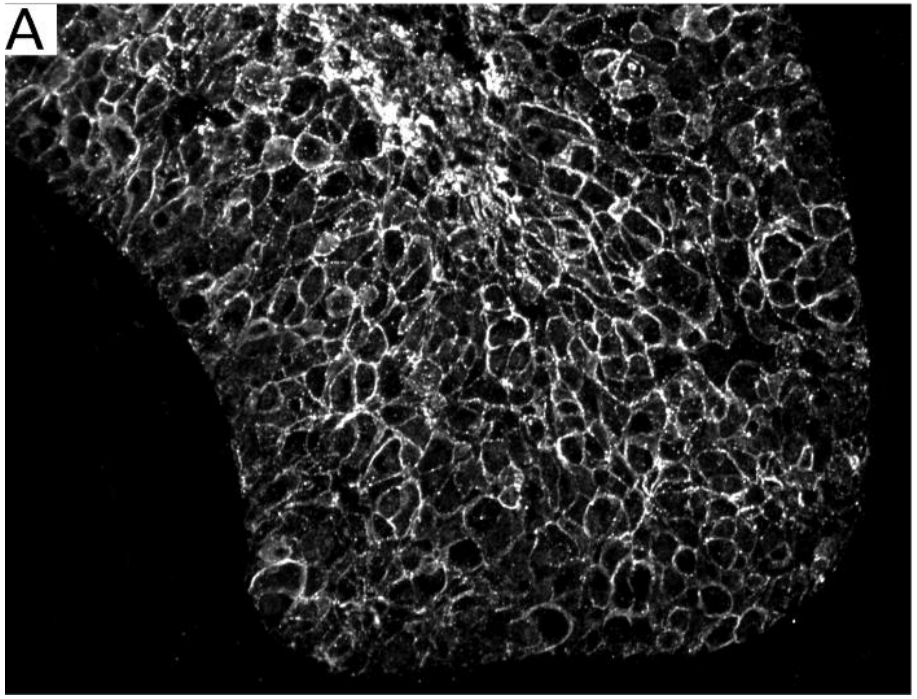
UCNP functionalisation



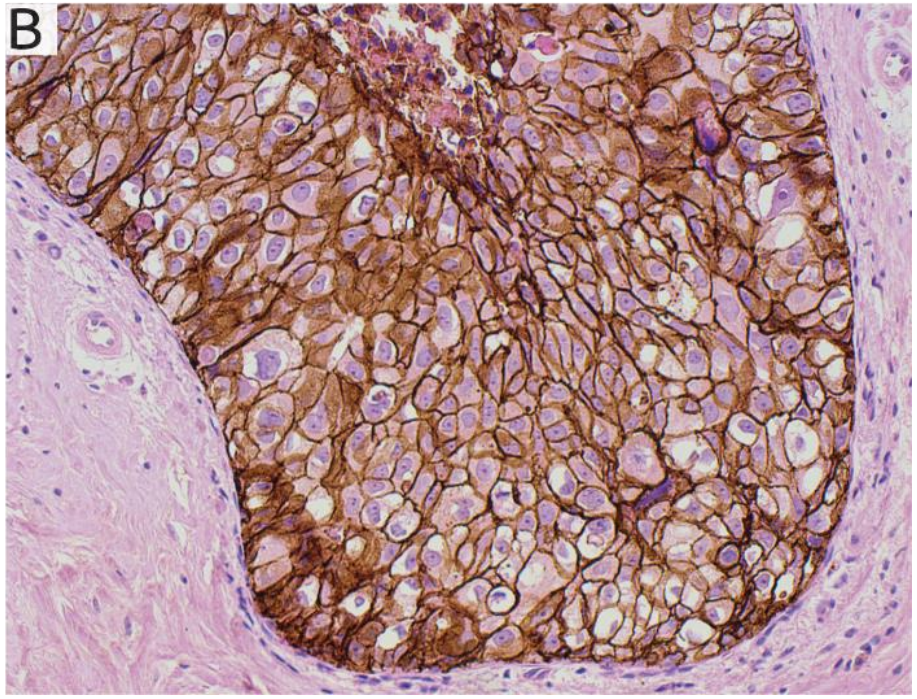
Towards digital pathology



Breast cancer



UCNP stain with HER2 target



H&E

Summary

- IPIC is a strong centre for developing compact biophotonics systems
- Funding mechanisms and proximity of MedTech industry has lead to a strong industry collaboration
- Two novel techniques for deep tissue imaging includes
  - Acousto-Optics
  - Luminescence imaging based on UCNPs
- Also a strong effort towards micro image sensors for imaging “anywhere”

STEFAN ANDERSSON-ENGELS
Sweden

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EPIC Meeting on Photonics for Cancer Diagnostics and Treatment 2019

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