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Outline

- Motivation and challenges
- Laser-induced photoacoustic tomography (PAT)
- RF-induced thermoacoustic tomography (TAT)
- Ultrasound-modulated optical tomography (UOT)
- Summary

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Motivation for Optical Imaging

- Safety — Non-ionizing radiation: photon energy is ~2 eV.
- Physics — Related to the molecular conformation of tissue.
- Optics — High intrinsic contrast:
 - Optical absorption: oxyhemoglobin, deoxyhemoglobin, melanin, and exogenous contrast agents.
 - Optical scattering: Size of cell nuclei.
 - Optical polarization: Collagen and muscle fibers.
- Physiology — Functional imaging of physiological parameters:
 - Oxygen saturation of hemoglobin (related to hyper-metabolism)
 - Total hemoglobin concentration (related to angiogenesis)
 - Blood flow (Doppler)
 - Enlargement of cell nuclei
 - Orientation of collagen
 - Denaturation of collagen
- Physiology — Molecular imaging
 - Integrin, VEGF, etc
 - Reporter genes
-

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Challenges in Optical Imaging

1 mm

Soft limit = $\sim \lambda_t$

Hard limit = $\sim 10 \delta = \sim 5 \text{ cm}$

OM, SNOM

CFM, 2PM, SHM, etc.

OCT

DOT, UOT, PAT

OM: Optical microscopy
 SNOM: Scanning near-field optical microscopy
 CFM: Confocal microscopy
 2PM: Two-photon microscopy
 SHM: Second harmonic microscopy
 OCT: Optical coherence tomography
 DOT: Diffuse optical tomography
 UOT: Ultrasound-modulated optical tomography
 PAT: Photoacoustic tomography

Simulation software MCML available from <http://oilab.seas.wustl.edu>

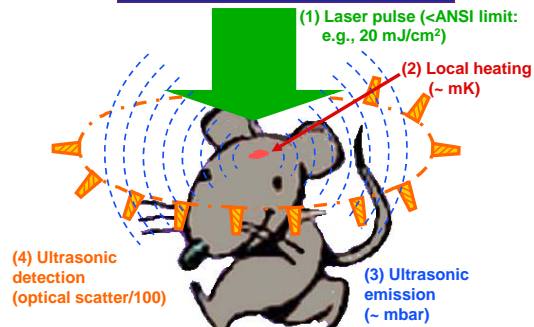
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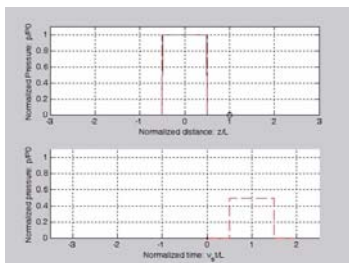
Reconstruction-based (Computed) Photoacoustic Tomography



Physical Review E 71, 016706 (2005).

Phys. Rev. Letters 92, 033902 (2004). <http://oilab.seas.wustl.edu> -- 8

Photoacoustic Forward Solution in an Infinite Medium: Plane Wave



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Spherical Radon Transform and Spherical Back-projection

Physical Review E
71, 016706 (2005).
Physical Review Letters
92, 033902 (2004).

Backprojection for planar, cylindrical, and spherical detection surfaces :

$$p_0(\vec{r}) = \frac{2}{\Omega_0} \int_{\Omega_0} [p(\vec{r}_0, t) - t \partial_t p(\vec{r}_0, t)]_{|\vec{r}-\vec{r}_0|=t} d\Omega_0; \text{ Solid angle : } \Omega_0$$

Beamforming High-frequency contribution

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Transcranial Functional Photoacoustic Imaging of Rat Whisker Stimulation In Vivo: Hemodynamics

Left-whisker stimulation

Right-whisker stimulation

Min Differential absorption Max

Nature Biotech. 21, 803 (2003). <http://oilab.seas.wustl.edu> -- 11

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Functional and Molecular Photoacoustic Imaging: Nude Mouse with a U87 Glioblastoma Xenograft in the Brain

(a) Functional imaging:
Tumor hypoxia

Resolution: 60 μm
Speckle free

(b) Molecular imaging:
Tumor over-expression of integrin

Resolution: 312 μm
Sensitivity: 4 fmol/voxel (40 nM)

Proc. of IEEE (accepted, 2008).
* Contrast agent provided by Chun Li's Group (MD Anderson)

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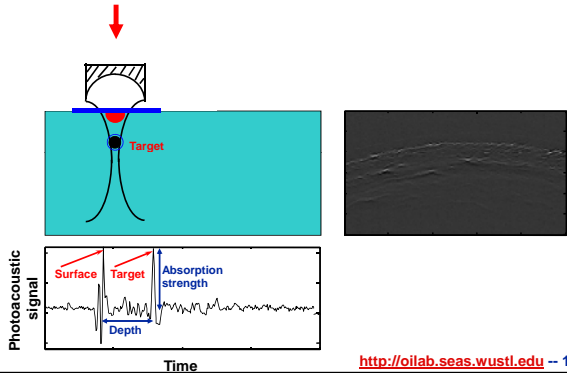
**Real-time Imaging of Nude Mouse Heart Beating:
50 Frames/s at 30 MHz**



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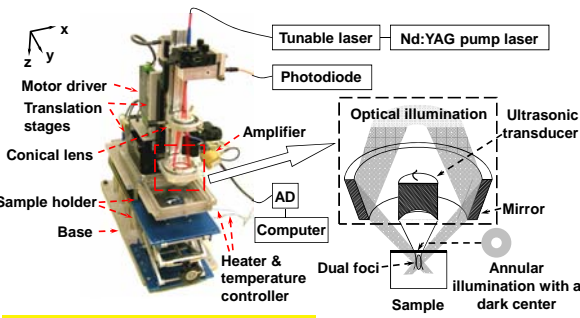
Reflection-mode Photoacoustic Microscopy: Illustration



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Reflection-mode Dark-field Confocal Photoacoustic Microscopy: System



Optics Letters 30, 625 (2005).
Nature Biotech. 24, 848 (2006).

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Photoacoustic Imaging Depth and Resolution: 50 MHz System

B-scan of a black double-stranded cotton thread embedded in rat

- Imaging depth: ~3 mm
- Axial resolution: ~15 microns
- Depth/resolution: ~200 pixels
- Lateral resolution: ~45 microns
- Acquisition time: 2 μs/A-scan
- No signal averaging

Optics Letters 30, 625 (2005).

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Photoacoustic Imaging of Skin Burn in Pigs

Acute thermal (175 °C, 20 s) burn in pig skin *in vivo*.
Postmortem imaging at 584-nm optical wavelength.

Photograph

Photoacoustic image

B-scan image

Histology

J Biomed Optics 11, 054033 (2006).

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Photoacoustic Imaging of Hemodynamics in a Small Animal In Vivo

Total hemoglobin

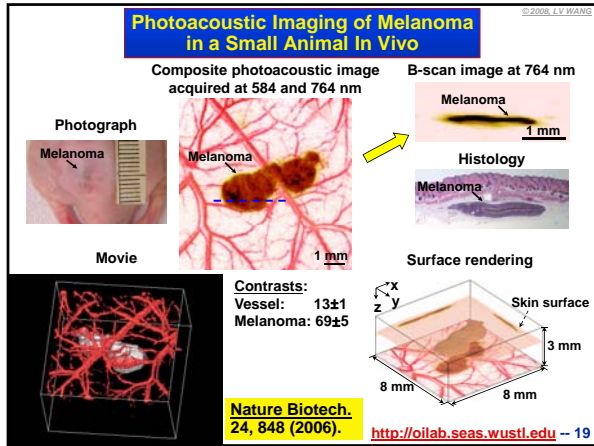
Oxygen saturation

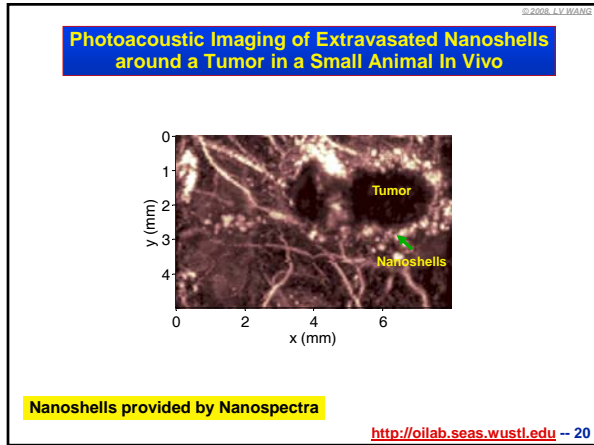
Arteries and veins

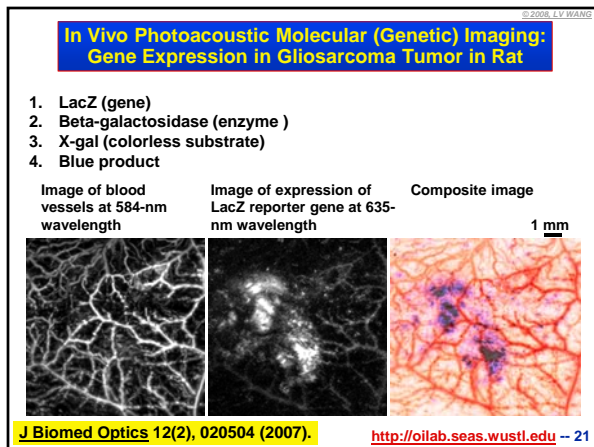
Change in oxygenation

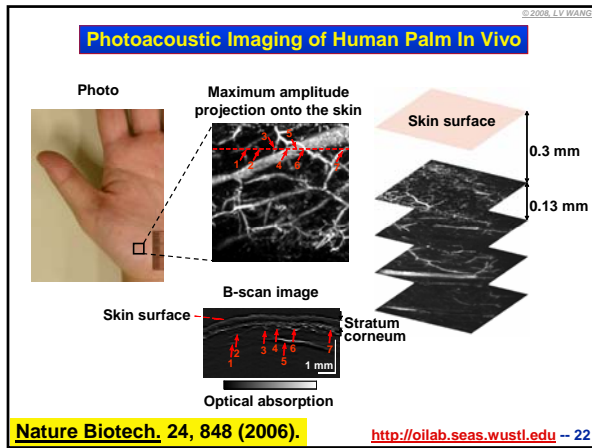
Appl. Phys. Lett. 90, 053901 (2007).

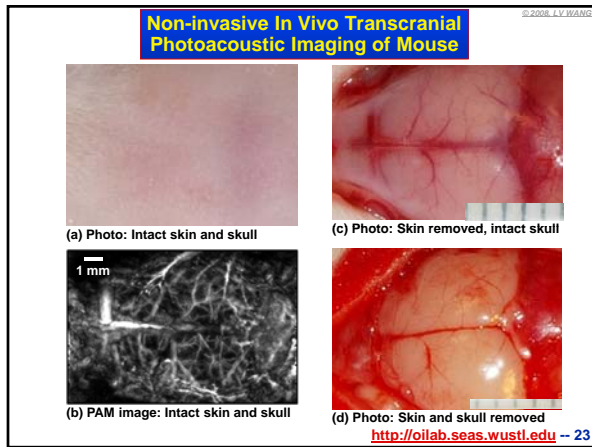
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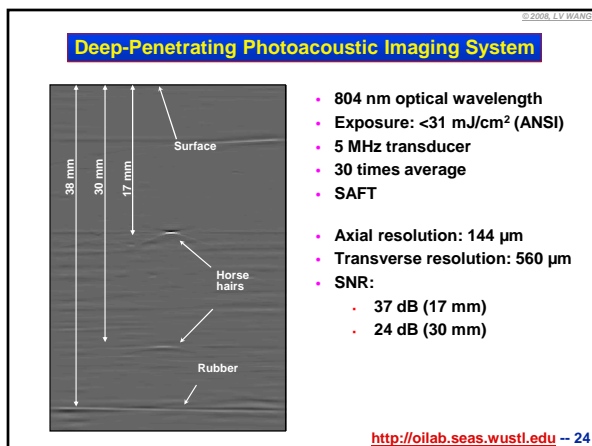


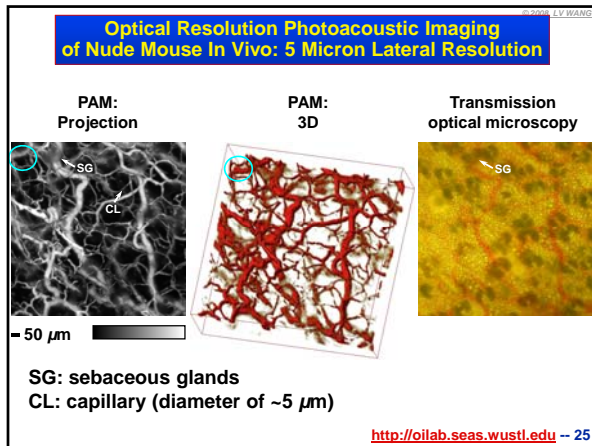


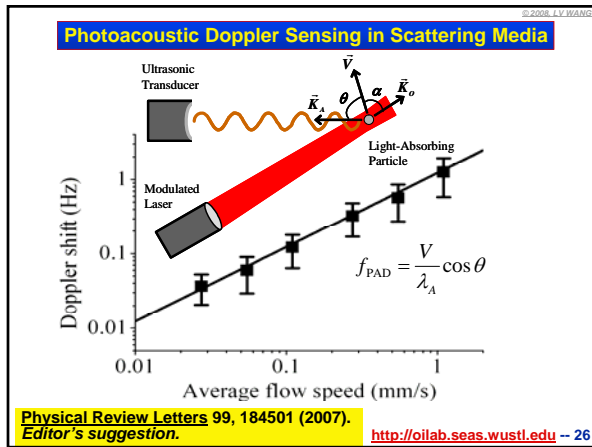












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Modern High-resolution Optical Microscopy (Depth / Resolution > 100)

Modality	Year	Depth	Contrast
Confocal microscopy	1970s	~0.5 mm	Scattering, fluorescence
Two-photon microscopy	1990s	~0.5 mm	Fluorescence
Optical coherence tomography	1990s	~1 mm	Scattering, polarization
Dark-field confocal photoacoustic microscopy	2005*	~3-30 mm, scalable	Absorption

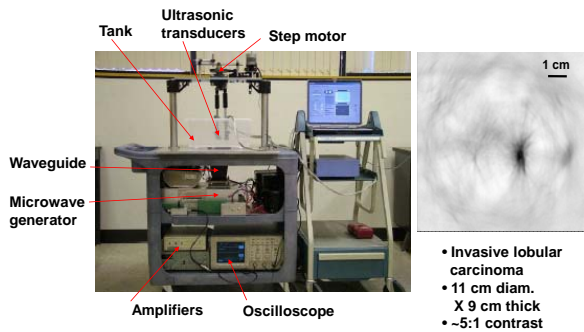
* Optics Letters 30, 625 (2005).
Nature Biotech. 24, 848 (2006).
Nature Protocols 2, 797 (2007). <http://oilab.seas.wustl.edu> -- 27

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Microwave-induced Thermoacoustic Tomography (TAT): Experimental System and Image of Mastectomy Specimen



Tech. in Cancer Res. & Treatment 4, 559 (2005).

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**Ultrasound-modulated Optical Tomography (UOT):
Ultrasonic Frequency Encoding of Diffuse Photons
along Ultrasonic Axis (z)**

(a) Idea (b) Chirp (c) Image

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Summary

- Physically combining ultrasonic and electromagnetic waves (light & RF) provides
 - improved spatial resolution compared with optical/RF imaging,
 - new contrast mechanisms compared with ultrasound imaging.
- Spatial resolution is determined by the ultrasonic parameters.
- Spatial resolution is scalable with the ultrasonic parameters.
- Contrast is provided by the electromagnetic properties.
- Deep (~cm) tissue imaging can be achieved.
- Speckle artifacts do not exist.
- Functional imaging can be accomplished with endogenous contrast.
- Molecular imaging can be accomplished with exogenous contrast agents or reporter genes.
- Non-ionizing radiation is used.
- Costs are comparable with those of ultrasound systems.

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Chapters

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1. Introduction to biomedical optics
2. Single scattering: Rayleigh theory and Mie theory
3. Monte Carlo modeling of photon transport
4. Convolution for broad-beam responses
5. Radiative transfer equation and diffusion theory
6. Hybrid model of Monte Carlo method and diffusion theory
7. Sensing of optical properties and spectroscopy
8. Ballistic imaging and microscopy
9. Optical coherence tomography
10. Mueller optical coherence tomography
11. Diffuse optical tomography
12. Photoacoustic tomography
13. Ultrasound-modulated optical tomography

Homework solutions available to instructors.

Taped presentations available on our web.

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