



Nanotechnology and Photoacoustic Imaging

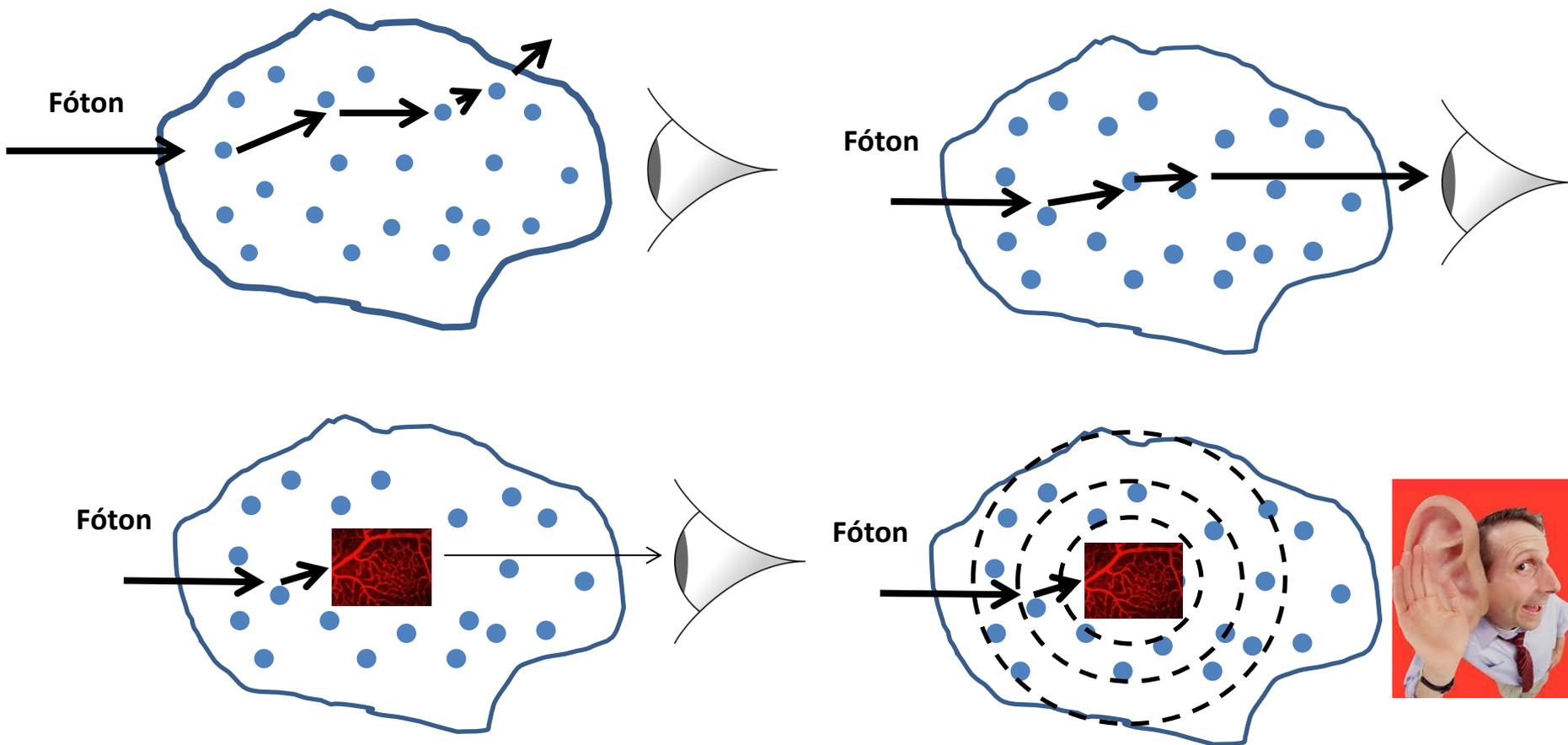
Theo Pavan

Motivação: **Imagem Fotoacústica**

Imagens ópticas:

- Excelente ferramenta na visualização funcional de eventos fisiológicos (concentração de hemoglobina oxigenada, lipídio, etc).
- Fenômenos como difração e espalhamento limitam a profundidade de obtenção de imagens.

Motivação: Imagem Fotoacústica



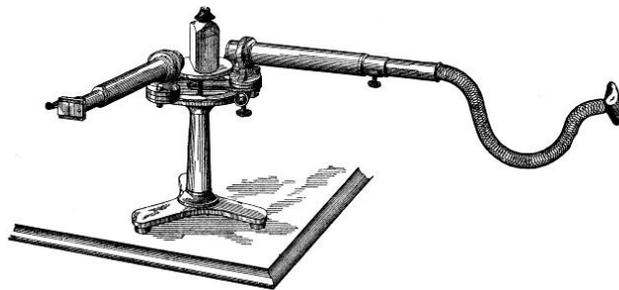
Motivação: Imagem Fotoacústica

➤ Imagem fotoacústica:

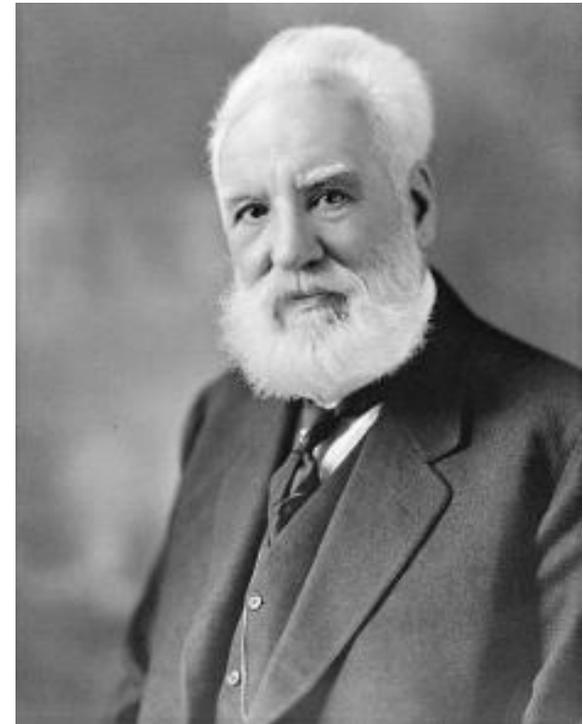
- Gerar imagens baseadas na absorção da luz a partir de detecção de ondas ultrassônicas.
- Maiores profundidades que técnicas puramente ópticas.
- Resolução espacial do ultrassom.

Efeito fotoacústico

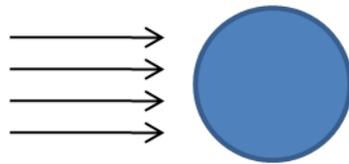
Fotofone



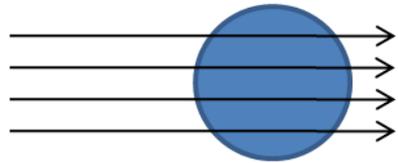
Inventado por Alexander
Graham Bell em 1880



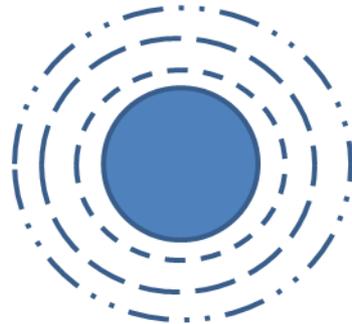
Expansão termoelástica



Tecido é irradiado com pulsos curtos de laser (ns).



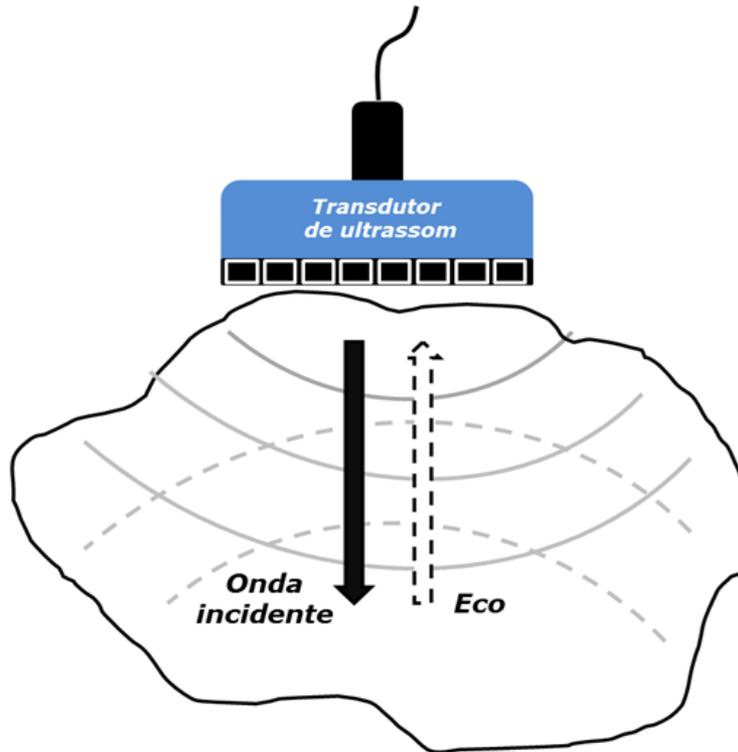
Energia óptica é absorvida e convertida em energia térmica.



Absorção dos curtos pulsos de luz causa rápida expansão térmica gerando transientes de pressão acústica que é usada para formação da imagem.

Imagem fotoacústica

Ultrassom convencional



Fotoacústica

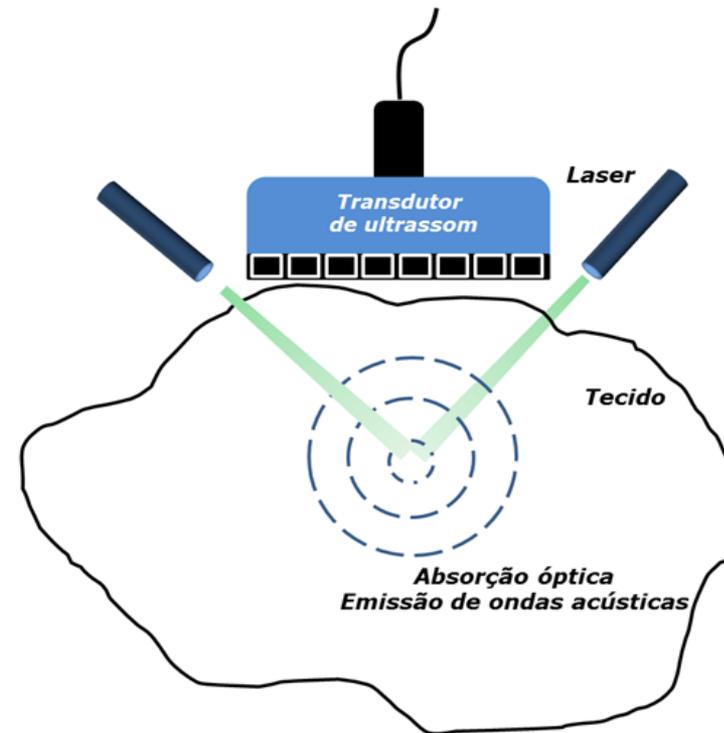
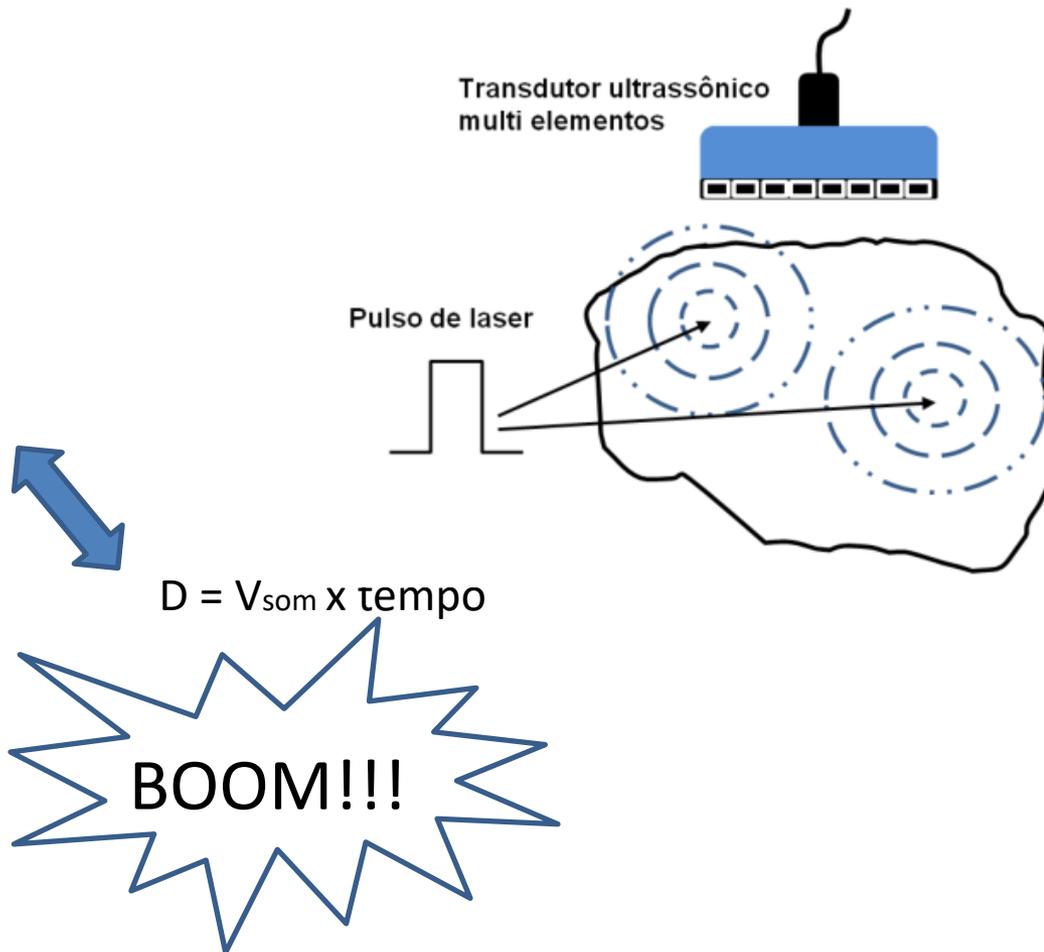
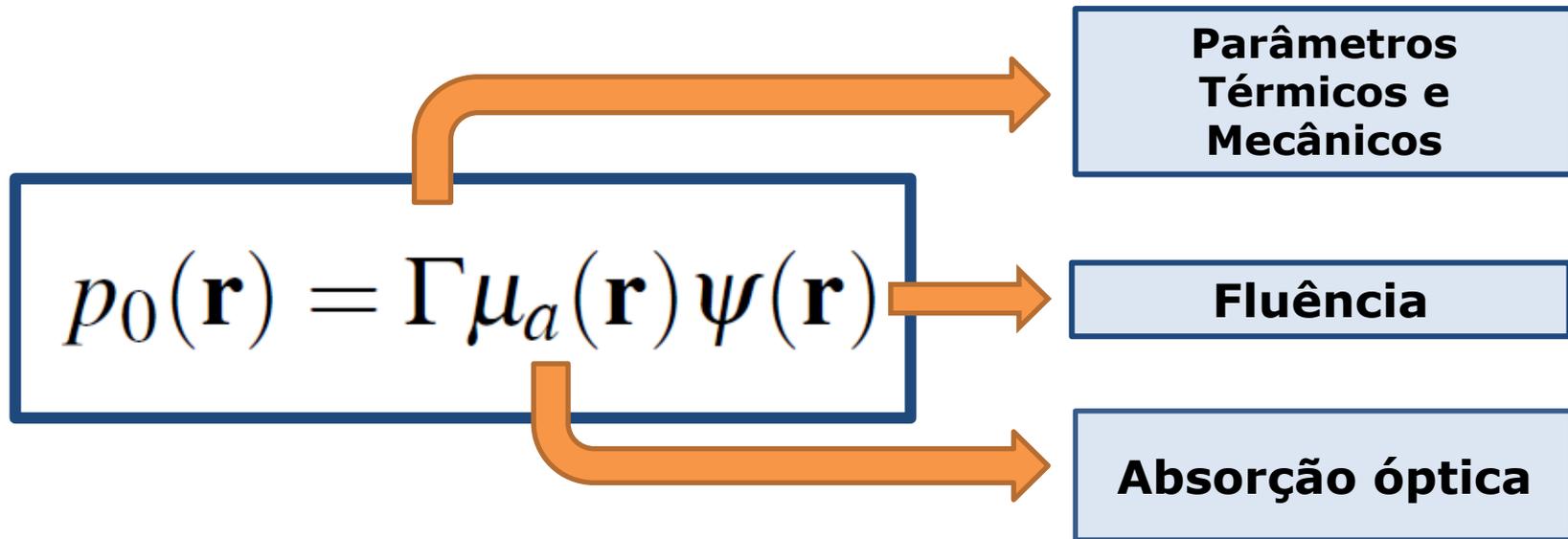


Imagem fotoacústica

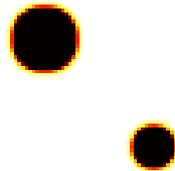


Pressão inicial

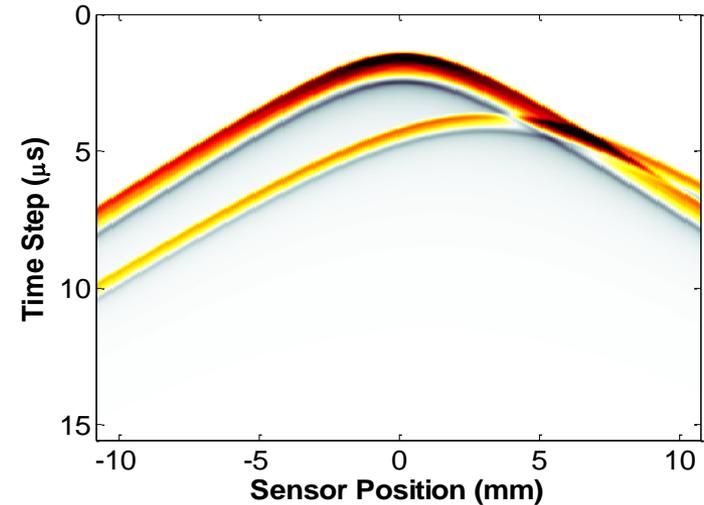
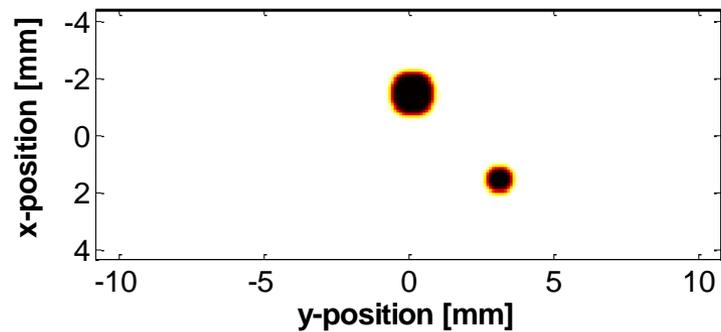


Reconstrução da imagem Array linear

Array de sensores



Distribuição dos absorvedores de luz Pressão inicial



Reconstruída

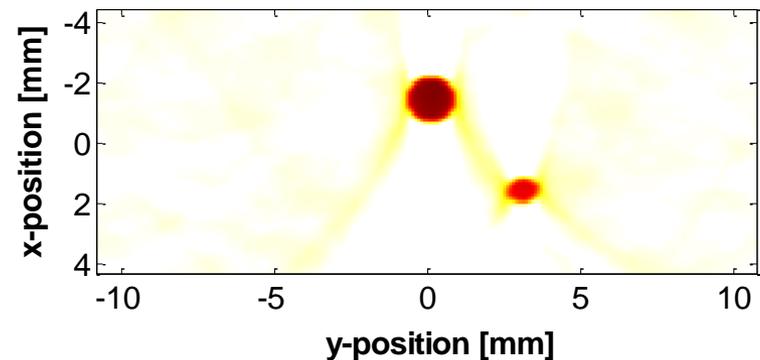
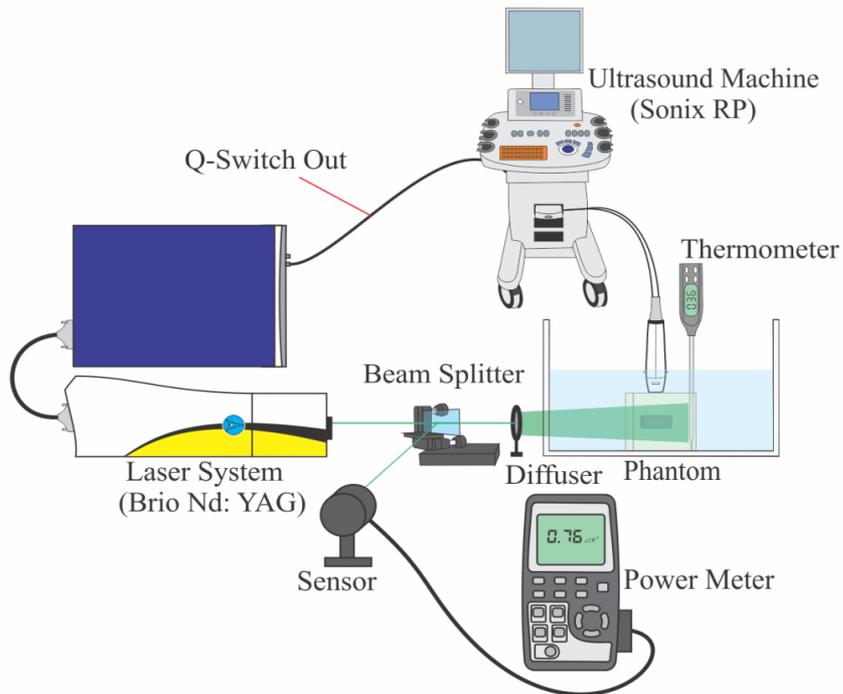
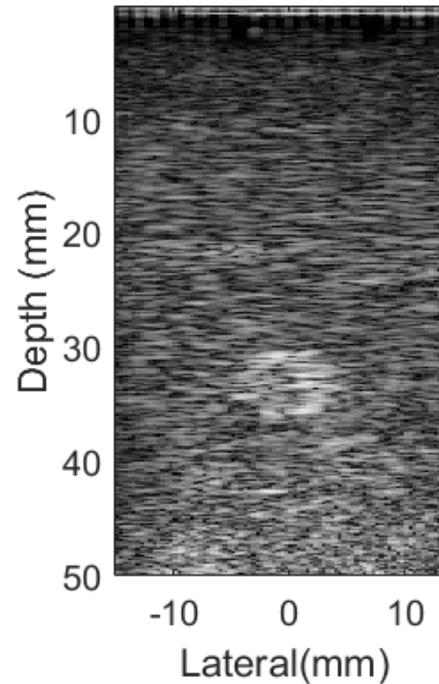


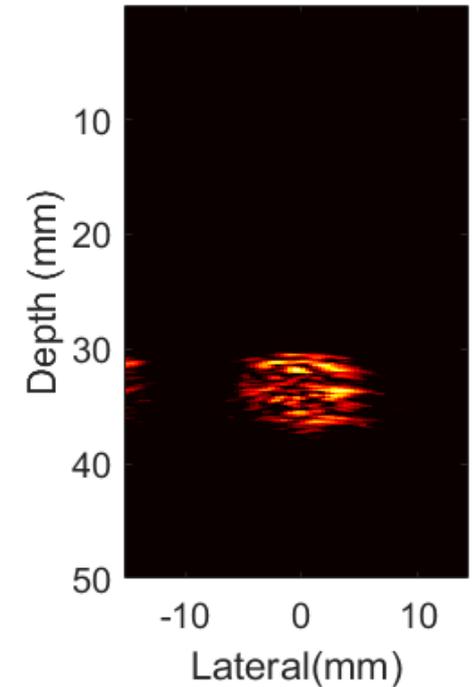
Imagem Phantom



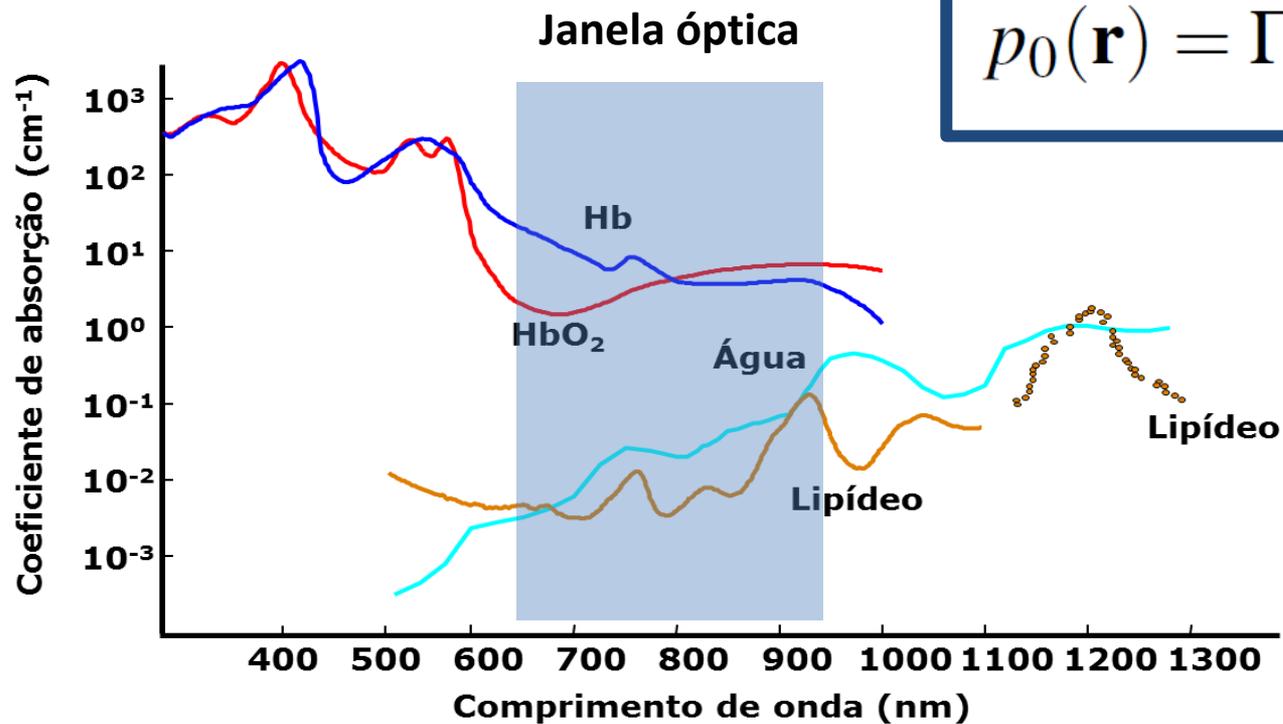
Ultrassom
Modo-B



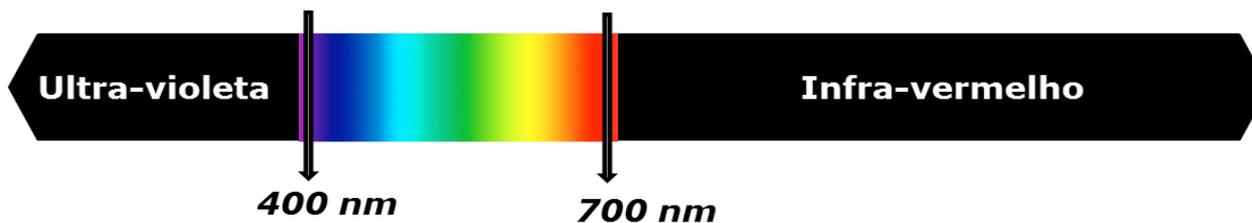
Fotoacústica



Dependência com λ

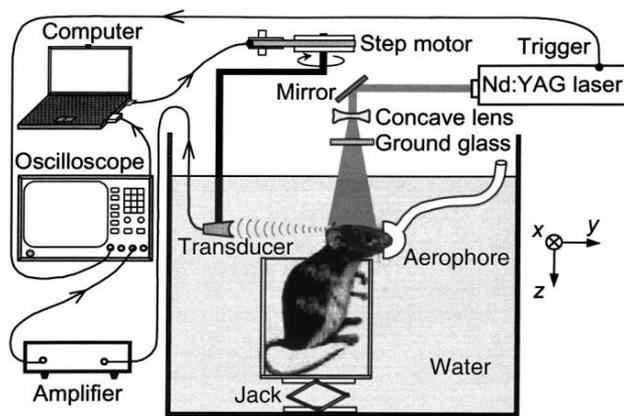


$$p_0(\mathbf{r}) = \Gamma \mu_a(\mathbf{r}) \psi(\mathbf{r})$$

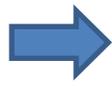


Imagens funcionais do cérebro

Pulsos de Laser → 532 nm

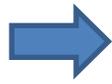


Regiões em
escala de cinza



Rato em repouso e
mostram a anatomia do
cérebro.

Regiões em
mapa de cor



Obtidas enquanto os
bigodes do rato eram
estimulados.

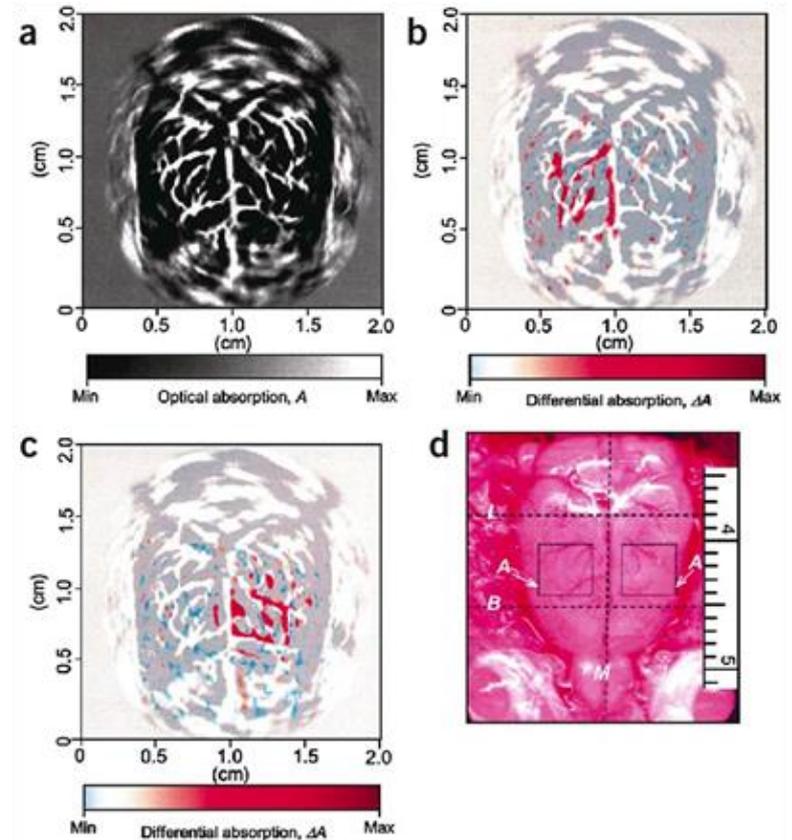


Imagem camundongo

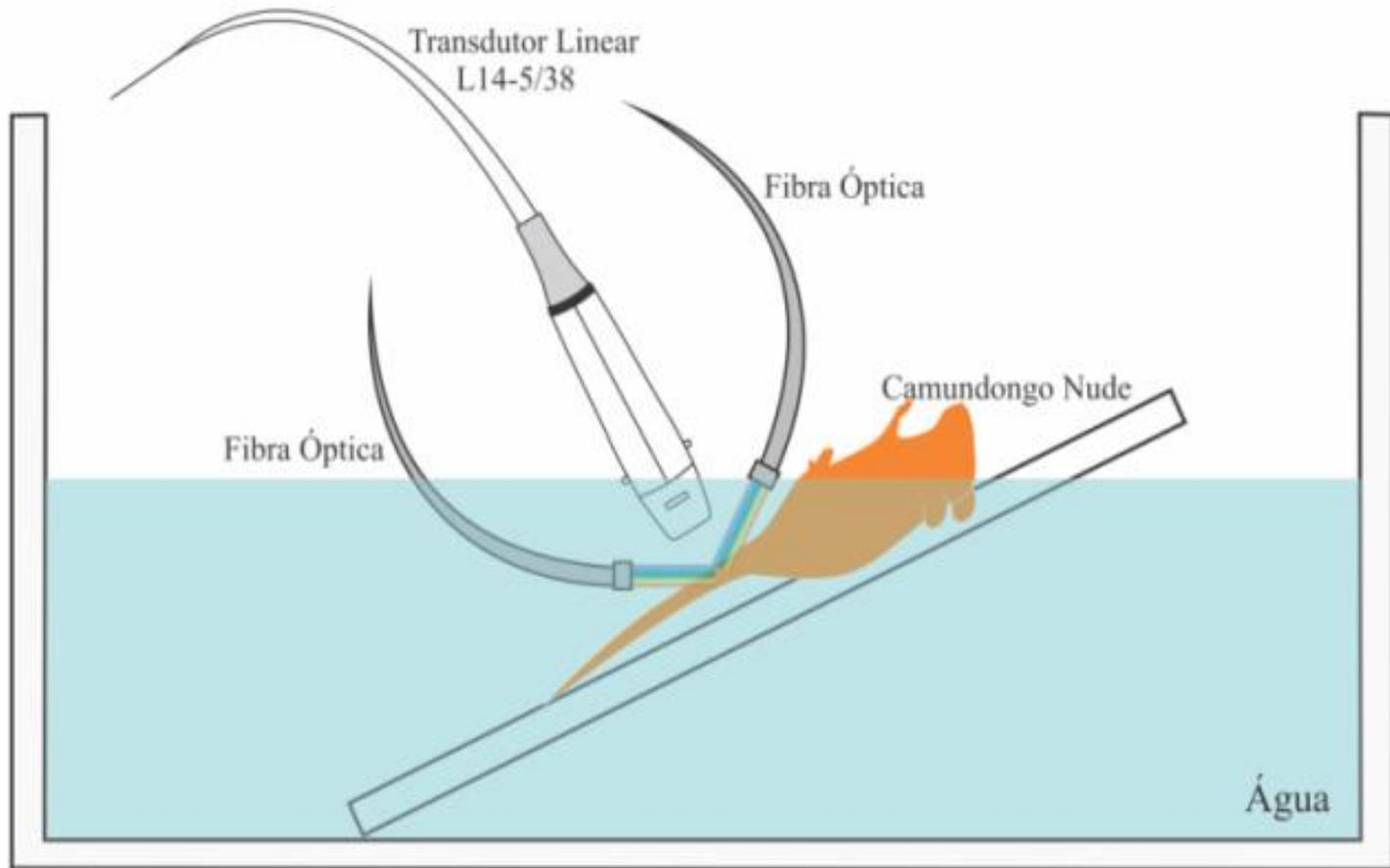
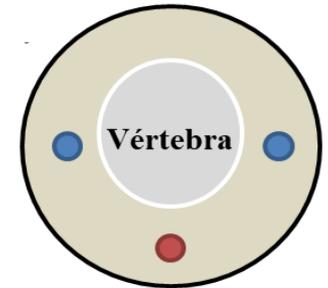
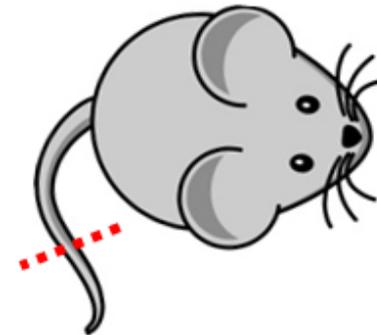
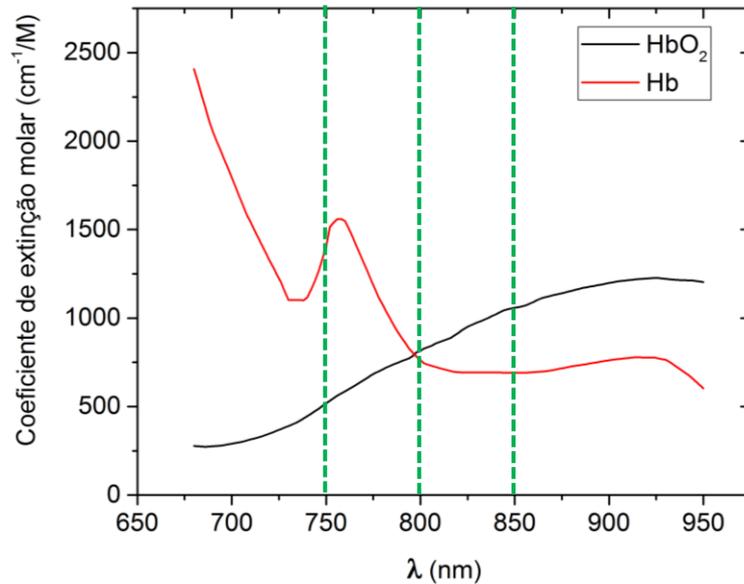
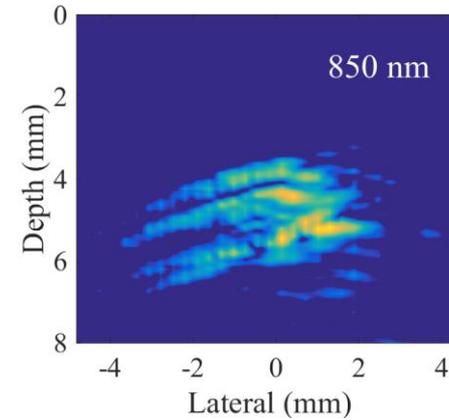
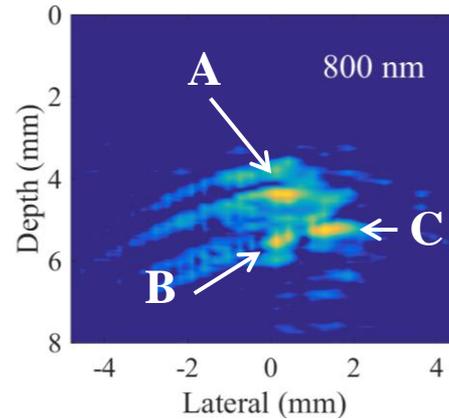
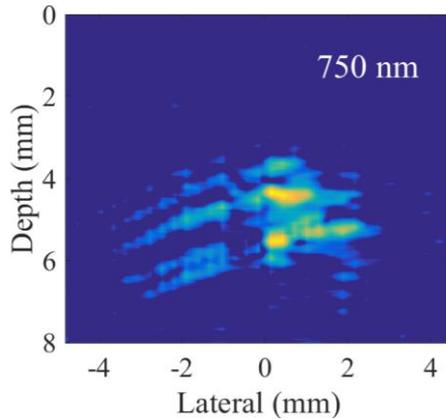


Imagem camundongo



- Veia lateral
- Artéria ventral

A e B → Veias

C → Artéria

Saturação de oxigênio

- É a fração da hemoglobina saturada de oxigênio em relação à hemoglobina total.
- Os níveis normais de oxigênio no sangue em humanos são considerados 95–100 por cento.

$$\mu_a(\lambda_i) = \varepsilon_{Hb}(\lambda_i)[Hb] + \varepsilon_{HbO_2}(\lambda_i)[HbO_2]$$

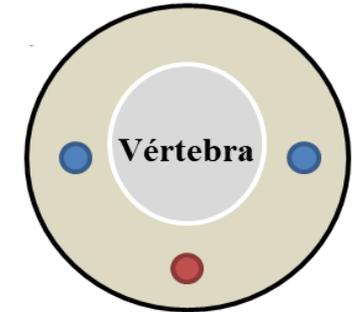
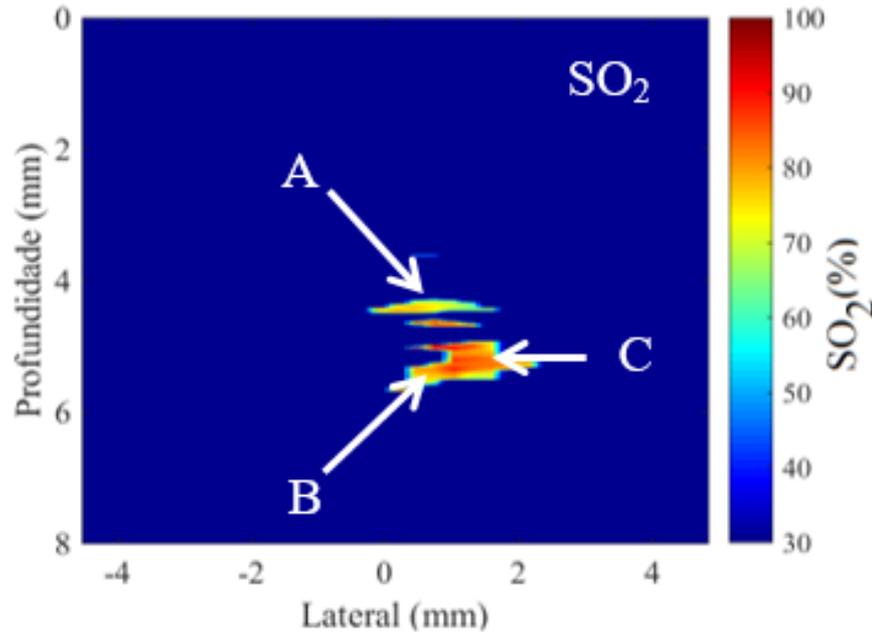
$$SO_2 = \frac{[HbO_2]}{[HbO_2] + [Hb]}$$



Imagem camundongo

$$SO_2 = \frac{[HbO_2]}{[Hbt]}$$

Saturação de oxigênio



- Veia lateral
- Artéria ventral

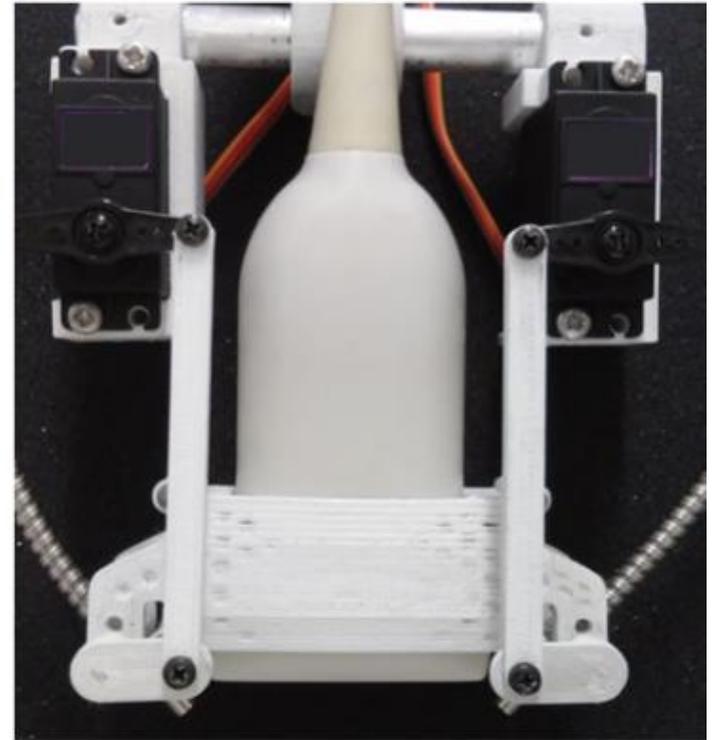
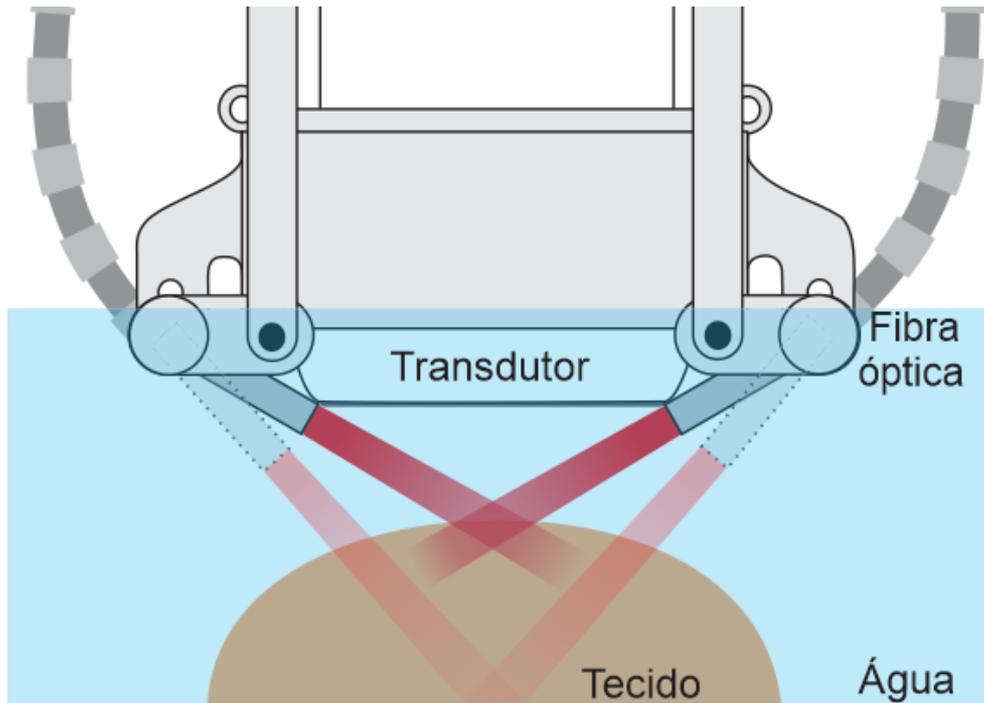
A e B → Veias

SO₂ = 75%

C → Artéria

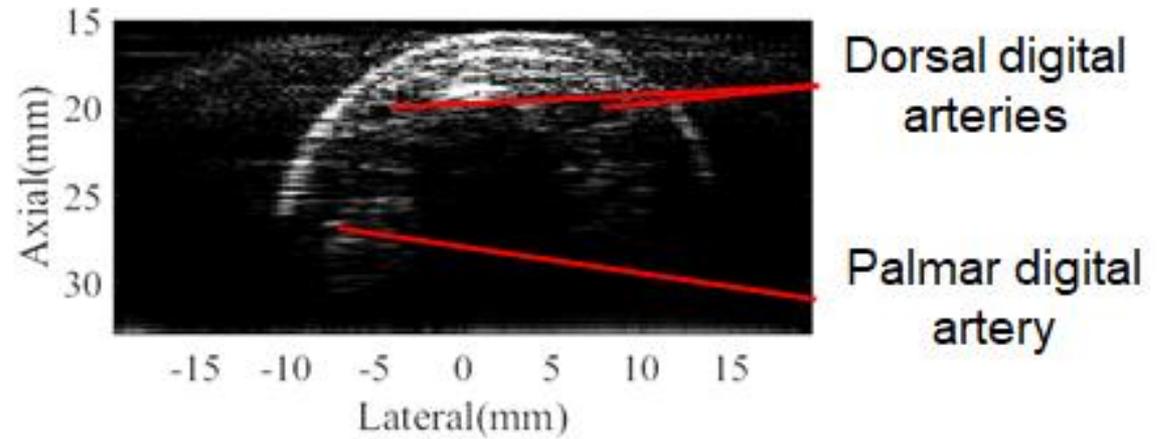
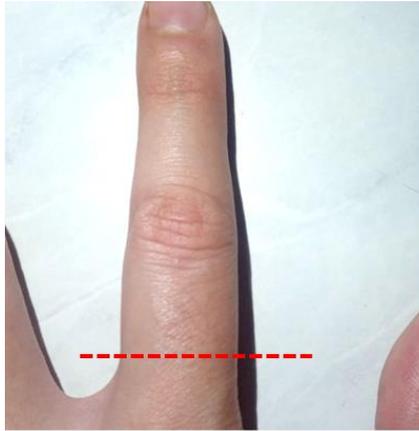
SO₂ = 85%

Imagens em humanos



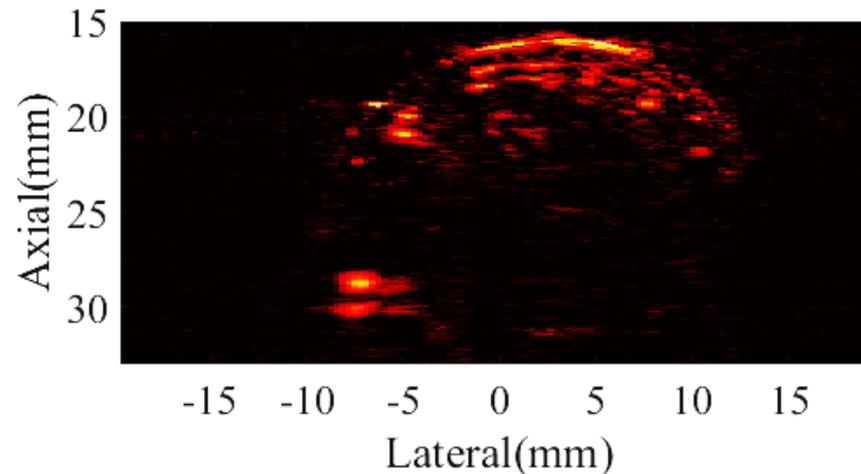
Imagens em humanos

Ultrassom



Uliana et al, Sensors, 2020

Fotoacústica



Contraste exógeno

- Contrastes exógenos desenvolvidos para imagem fotoacústica consistem de corantes biocompatíveis ou nanopartículas altamente absorvedoras.
- Essas substâncias podem estar ligadas a estruturas alvos de biomarcadores na regiões de interesse.
- Exemplo → Azul de metileno, Indiocianina verde.
- Exemplo → Nanopartículas de ouro tem seu pico de absorbância ajustável dependendo da ressonância plasmônica de superfície determinada por sua forma e dimensão.

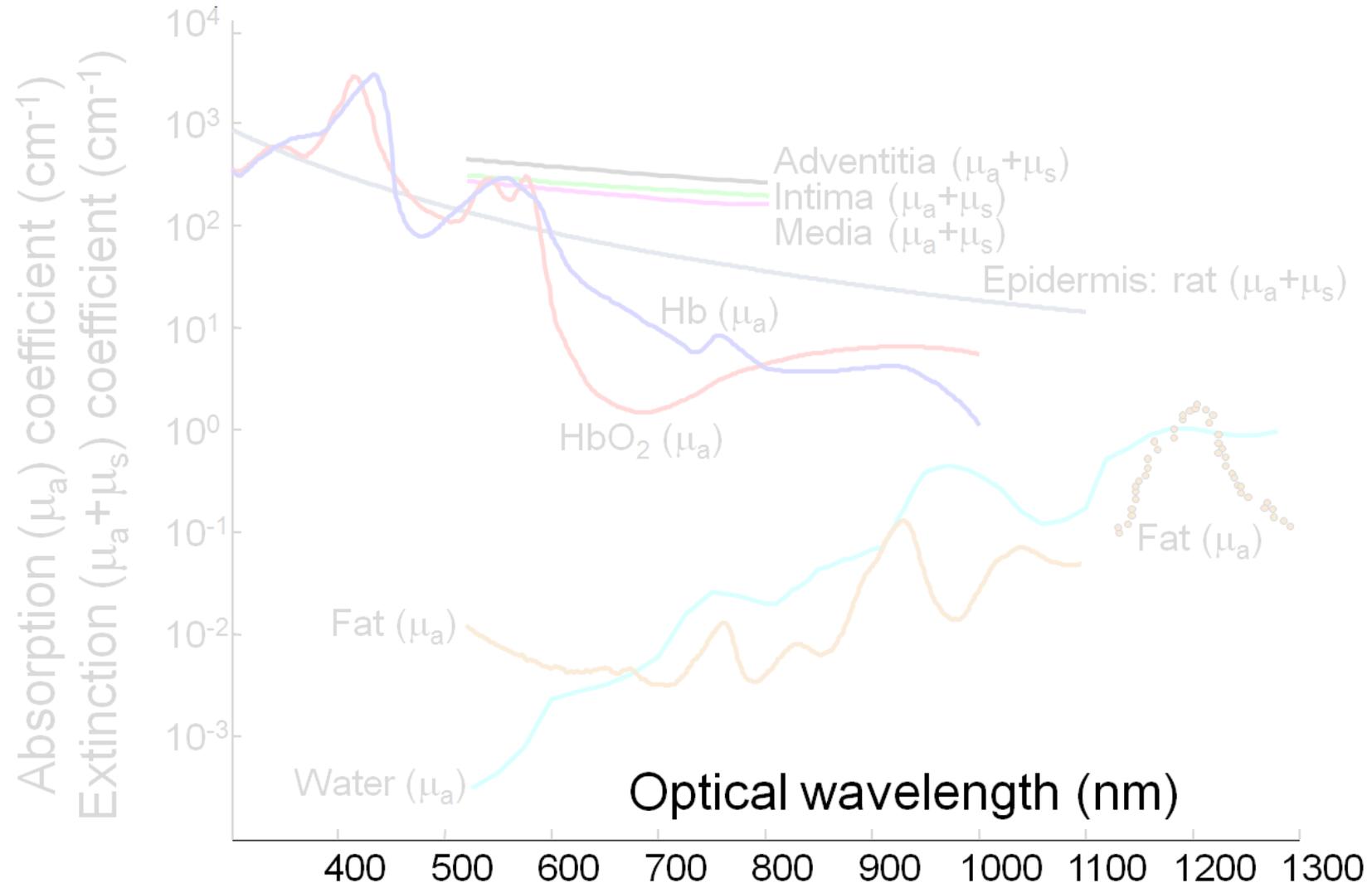


Agradecimento

 A seguir vou apresentar alguns slides gentilmente cedidos pelo Professor **Stas Emelianov do Georgia Tech.**

Molecular Photoacoustic Imaging using Exogenous Contrast: Dyes

Methylene Blue (~680 nm) ●●● Indocyanine Green (~700 nm)



Molecular Photoacoustic Imaging using Exogenous Contrast: Plasmonic Nanoparticles

Nanospheres ●

Aspect Ratio →

Nanorods

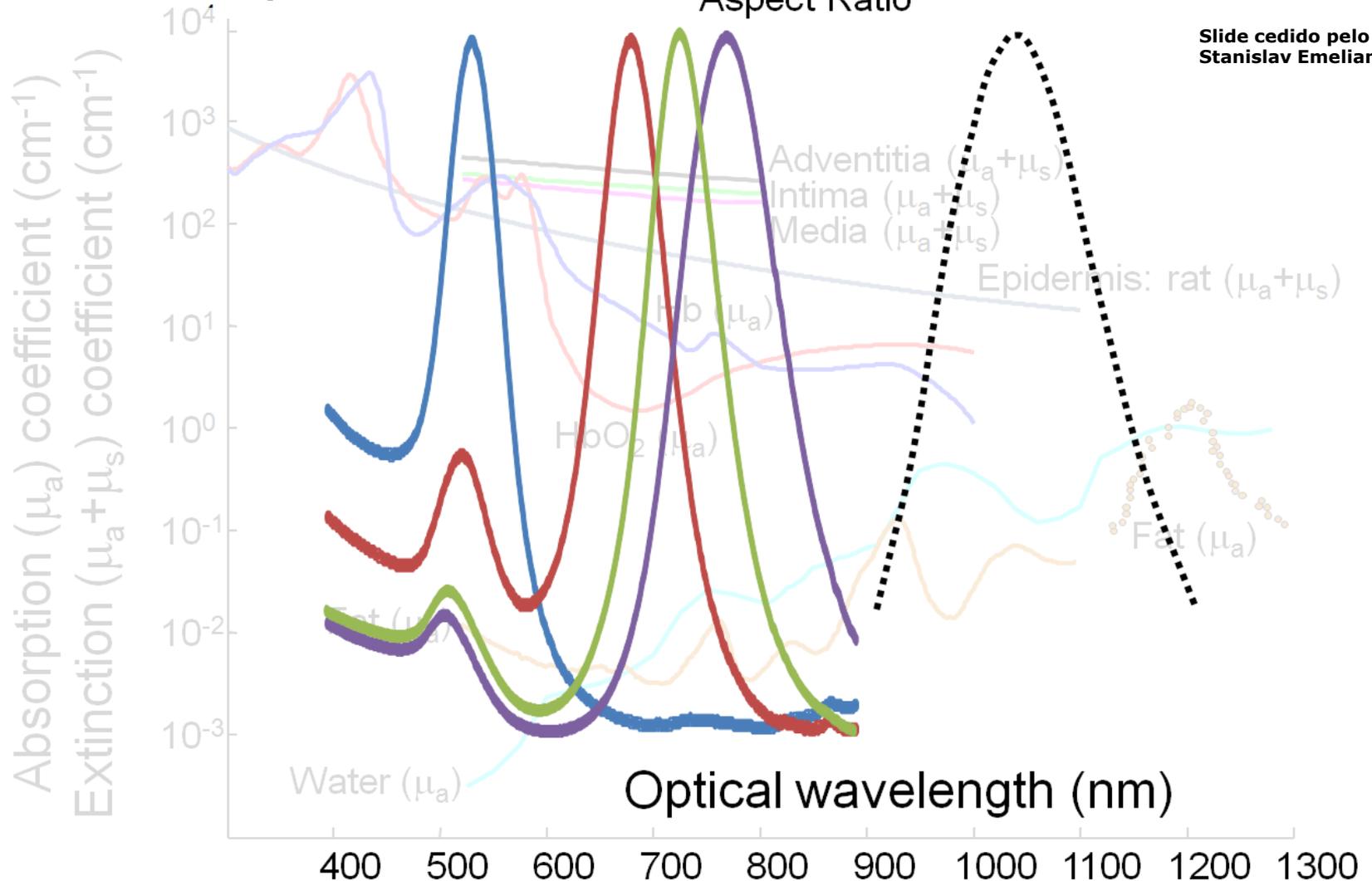
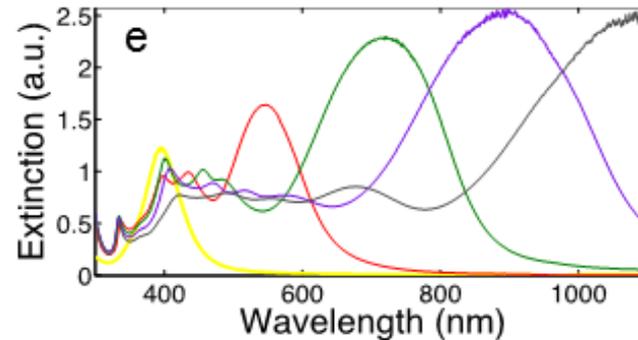
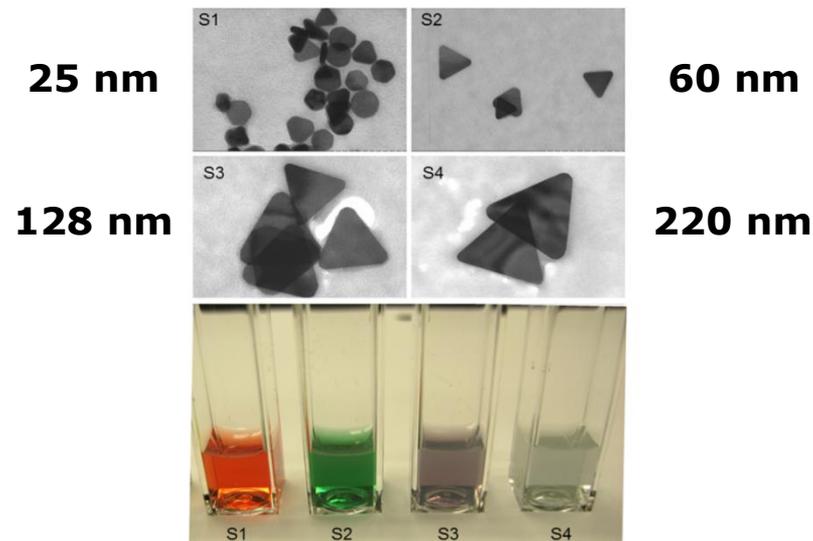
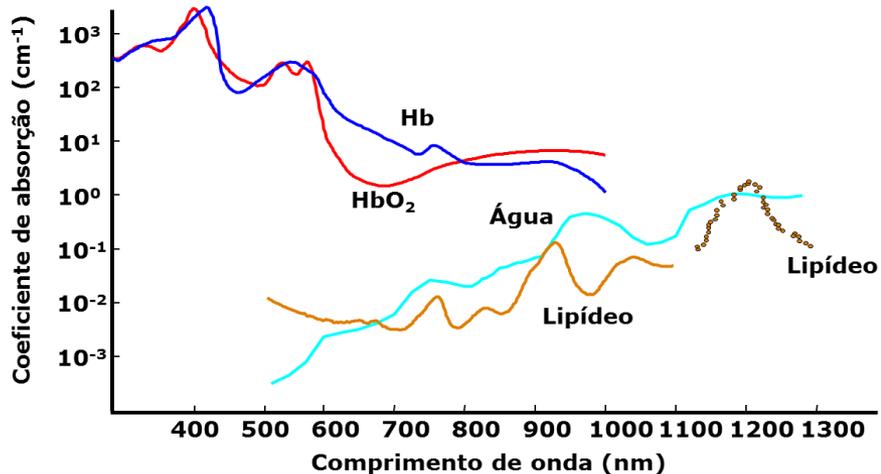


Imagem molecular fotoacústica

Contraste exógeno: nanopartículas

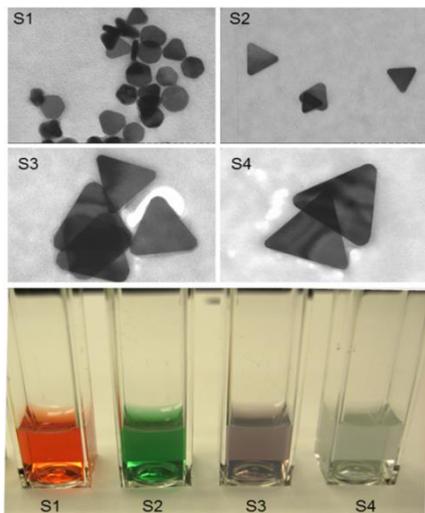


- Imagem fotoacústica espectrocópica foram feitas usando pulsos de laser entre 740 e 900 nm.

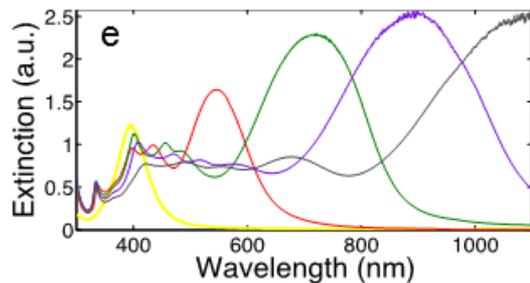
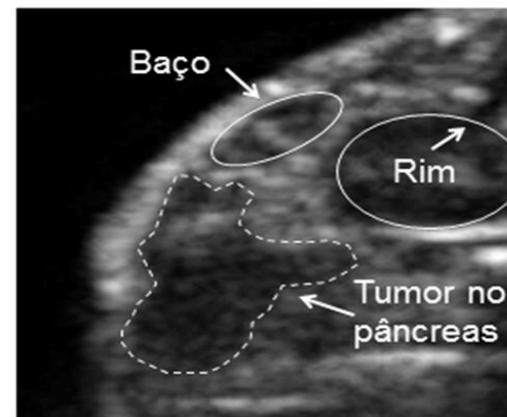
- Nanopartículas com pico de absorção em 800 nm.

Imagem molecular fotoacústica

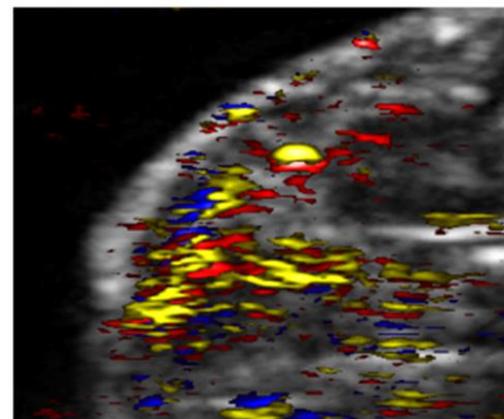
Contraste exógeno: nanopartículas



Modelo animal em rato



α -EGFR, PEG-passivated Ag nanoplates



Agradecimento: Prof. Stanislav Emelianov
Georgia Tech University

Molecular specific optoacoustic imaging with plasmonic nanoparticles

Srivalleesha Mallidi,¹ Timothy Larson,¹ Jesse Aaron,¹
Konstantin Sokolov,^{1,2} Stanislav Emelianov¹

¹*Department of Biomedical Engineering, University of Texas at Austin, Austin, TX 78712 USA*
²*Department of Biomedical Engineering, MD Anderson Cancer Center, Houston, TX 77030 USA*

- ➊ **Three tissue phantoms consisting of human epithelial carcinoma cells (A431 keratinocyte) were used.**
- ➋ (1) the control tissue phantom with no gold nanoparticles;
- ➌ (2) the targeted tissue phantom labeled with EGFR targeted gold nanoparticles.
- ➍ (3) the non-targeted tissue phantom with nanoparticles coated only with a polyethylene glycol-thiol (mPEG-SH) layer which has no molecular specificity.

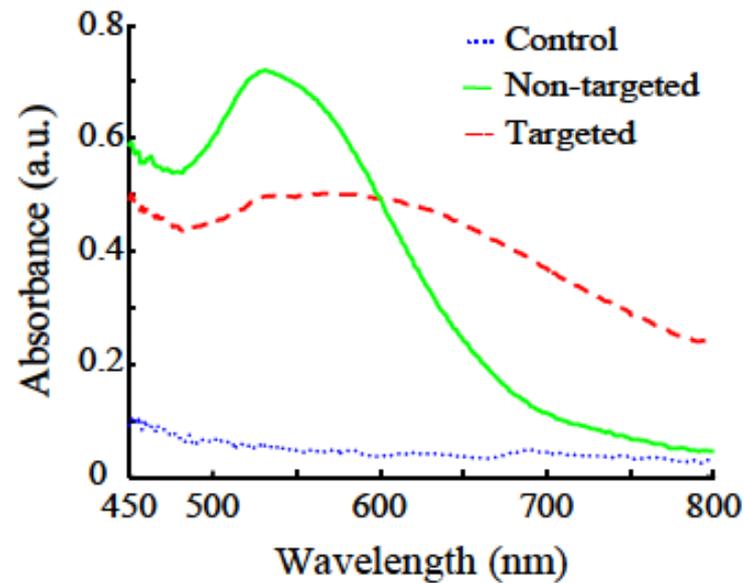


Fig. 2. Absorbance spectra of control, targeted and non-targeted tissue samples normalized to the illumination lamp spectrum.

Molecular specific optoacoustic imaging with plasmonic nanoparticles

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- ➊ Epithelial cancer cells tend to overexpress epithelial growth factor receptor (EGFR), causing the specifically targeted nanoparticles to cluster on the cell surface.
- ➋ This clustering leads to plasmon resonance coupling between nanoparticles and a red shift in the plasmon resonance frequency of the gold nanoparticle assembly.

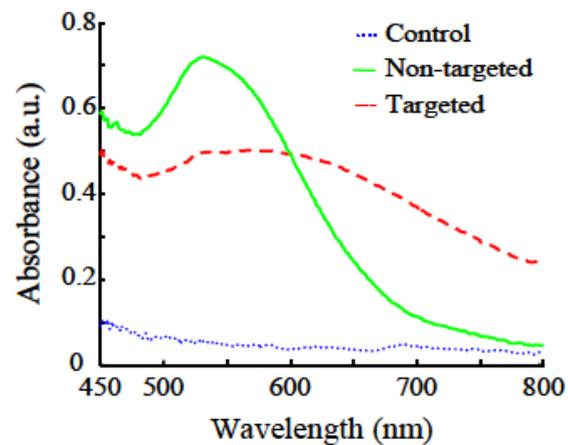
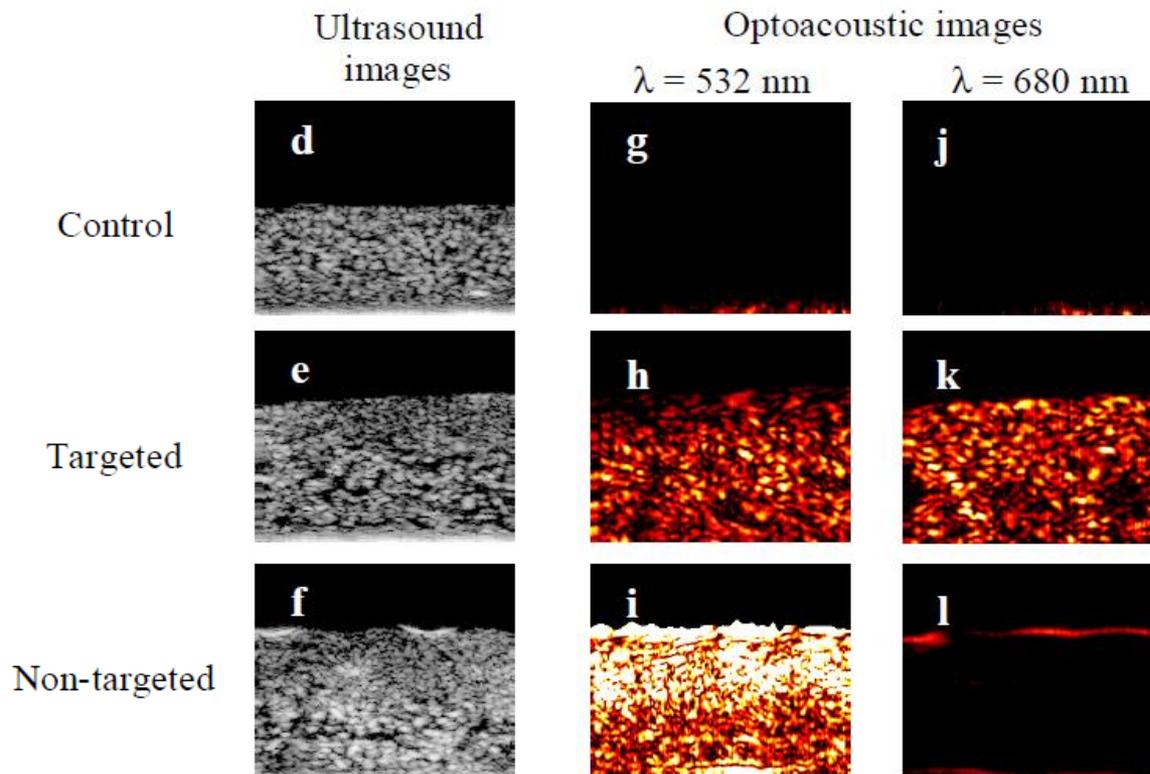


Fig. 2. Absorbance spectra of control, targeted and non-targeted tissue samples normalized to the illumination lamp spectrum.



Nanoflores de ouro

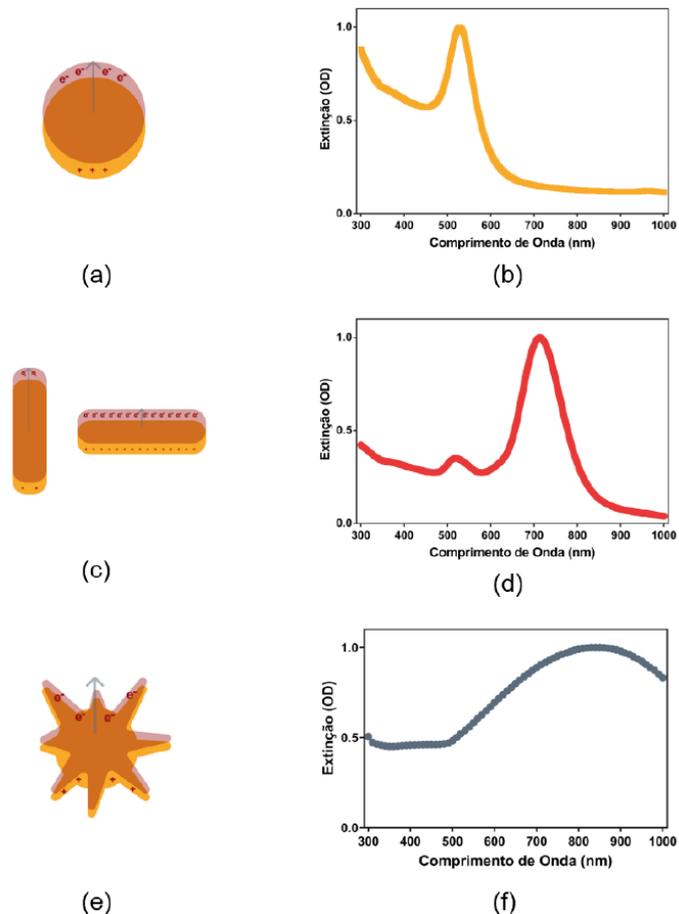


Figura 2 - Influência da geometria no fenômeno de LSPR: (a), (c) e (e) são representações esquemáticas do fenômeno de LSPR de nanopartículas de ouro esféricas, nanobastões e nanoflores, respectivamente. (b), (d) e (f) apresentam os espectros de extinção UV-visível, respectivamente, de nanopartículas de ouro esféricas, nanobastões e nanoflores.

Colaboração Trabalho de mestrado de Olavo Amorin Santos Orientador: Valtencir Zucolotto - IFSC-USP

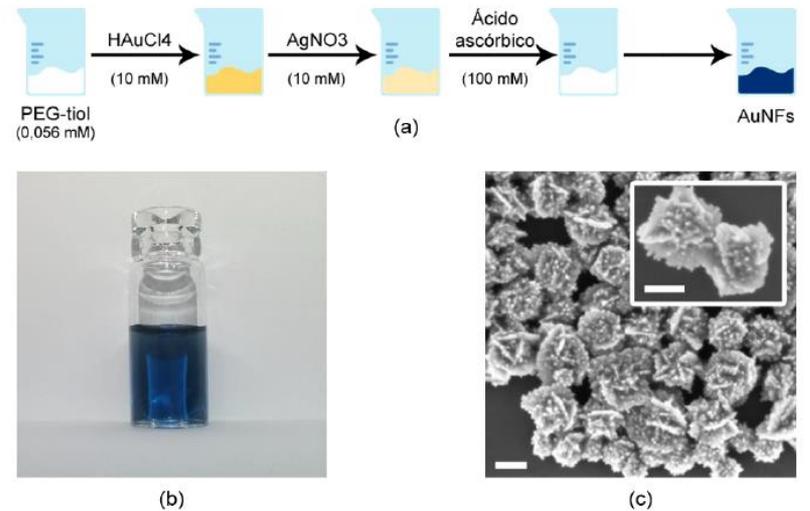
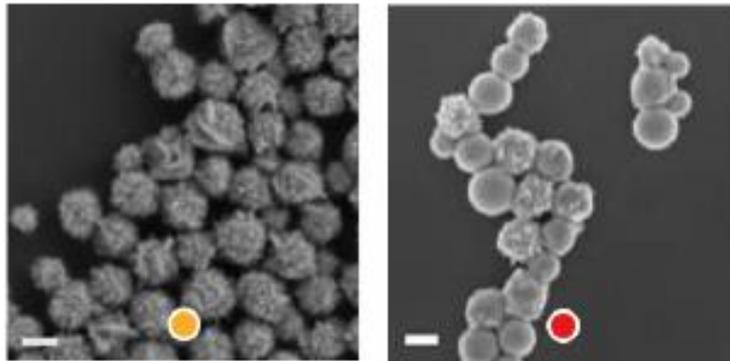


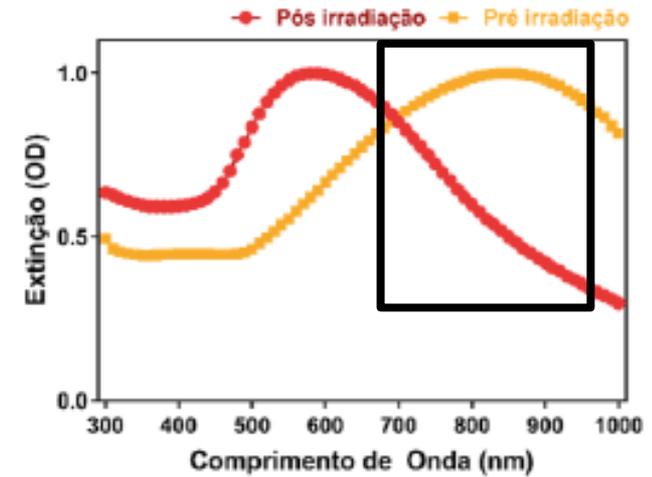
Figura 3 - Síntese das AuNFs: (a) Desenho esquemático do processo de síntese das nanopartículas. (b) Foto da solução final de nanopartículas obtidas pela síntese proposta. (c) Microscopia eletrônica de varredura das nanopartículas obtidas. As barras de escala representam 100 nm.

Estabilidade e imagens fotoacústica



(a)

(b)



(c)

Colaboração

Trabalho de mestrado de Olavo Amorin Santos

Orientador: Valtencir Zucolotto - IFSC-USP

Enhanced thermal stability of silica-coated gold nanorods for photoacoustic imaging and image-guided therapy

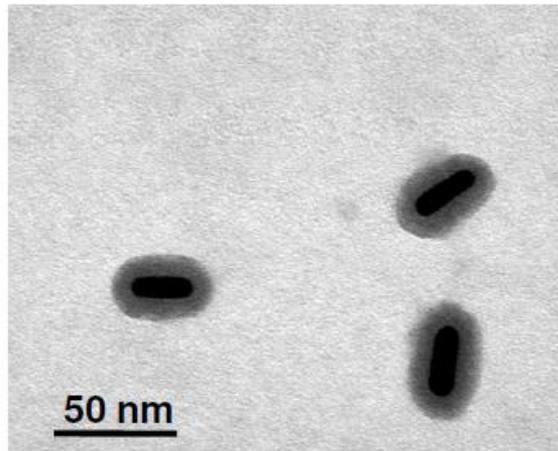
Yun-Sheng Chen,^{1,2} Wolfgang Frey,¹ Seungsoo Kim,¹ Kimberly Homan,¹
Pieter Kruizinga,¹ Konstantin Sokolov,^{1,3} and Stanislav Emelianov^{1,2,3*}

¹Department of Biomedical Engineering, University of Texas at Austin, Austin, TX, 78712, USA

²Department of Electrical and Computer Engineering, University of Texas at Austin, Austin, TX, 78712, USA

³Department of Imaging Physics, University of Texas M.D. Anderson Cancer Center, Houston, Texas 77030, USA

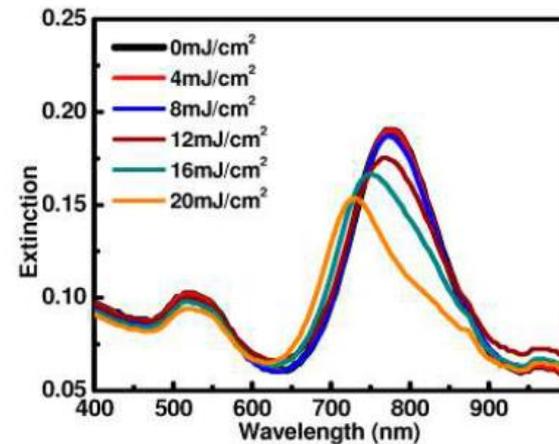
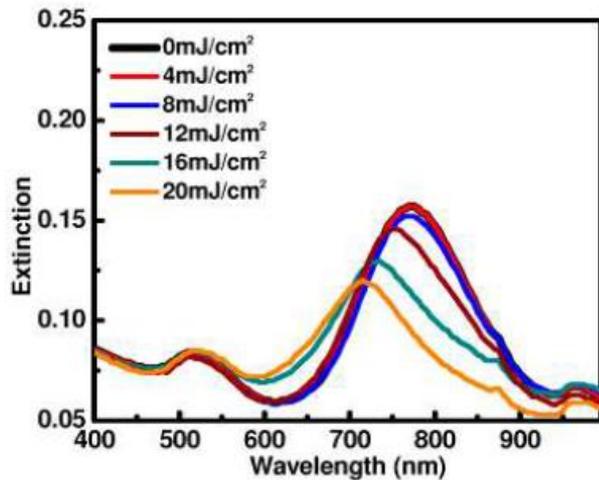
*emelian@mail.utexas.edu



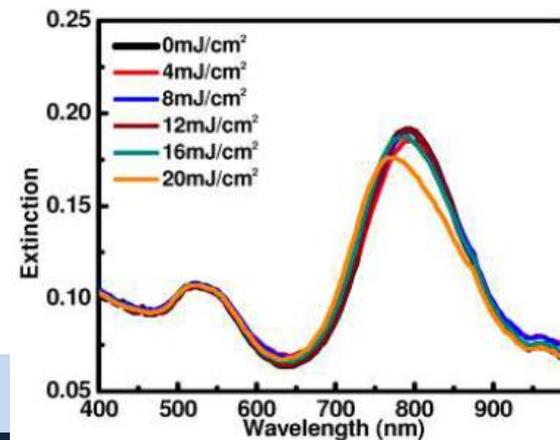
300 laser pulses at various fluences, the longitudinal peak changes shape in all cases above some threshold fluence.

6 nm silica - coated gold nanorods

PEG - coated gold nanorods



20 nm silica - coated gold nanorods



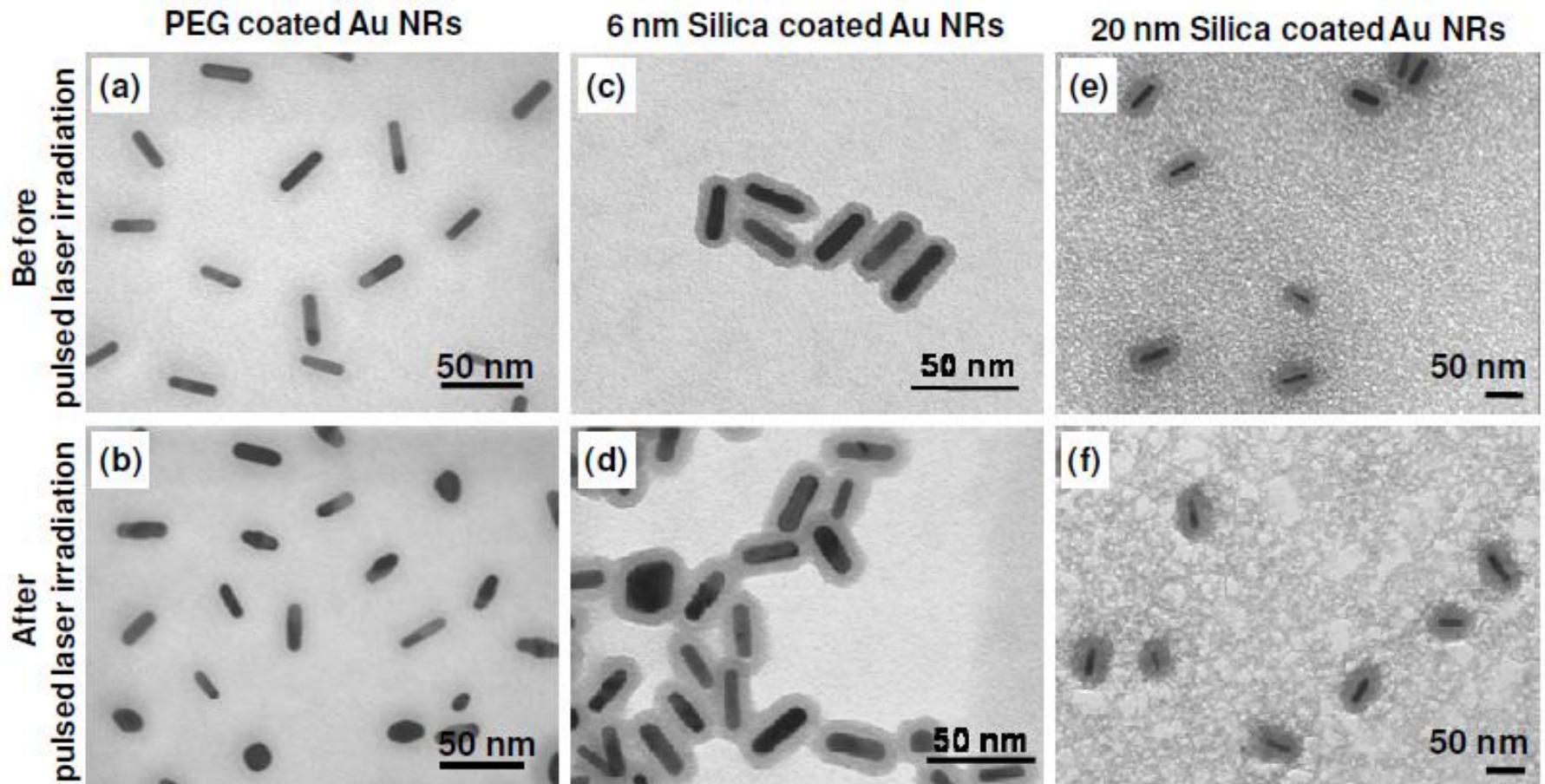


Fig. 4. TEM images show the morphology evolutions of various gold nanorods before and after 300 pulses of $20\text{mJ}/\text{cm}^2$ laser irradiation. (a) and (b): PEG coated gold nanorods; (c) and (d): 6 nm silica-coated gold nanorods; (e) and (f): 20 nm silica-coated gold nanorods.

4 mJ/cm²

18 mJ/cm²

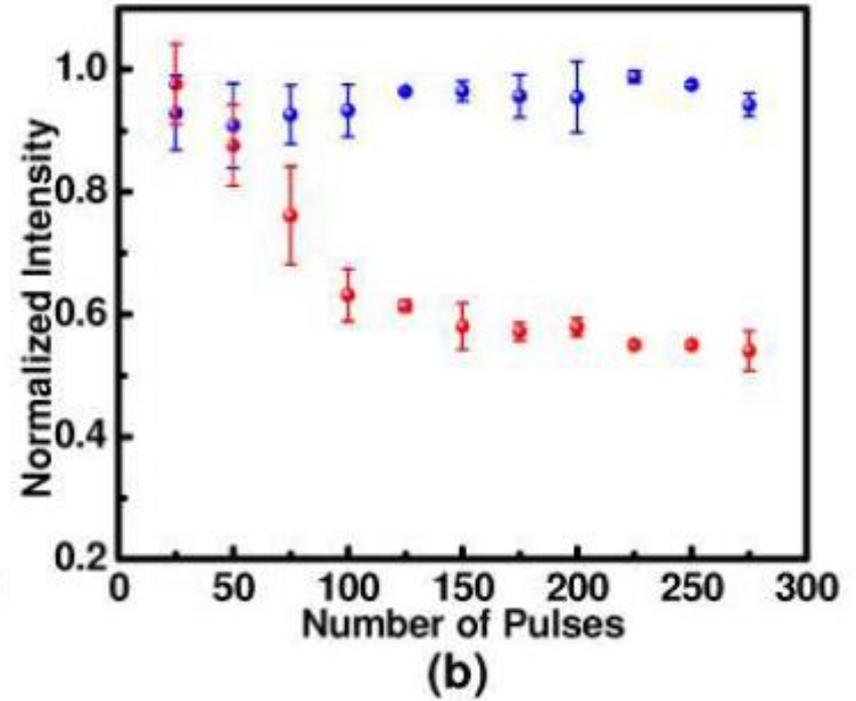
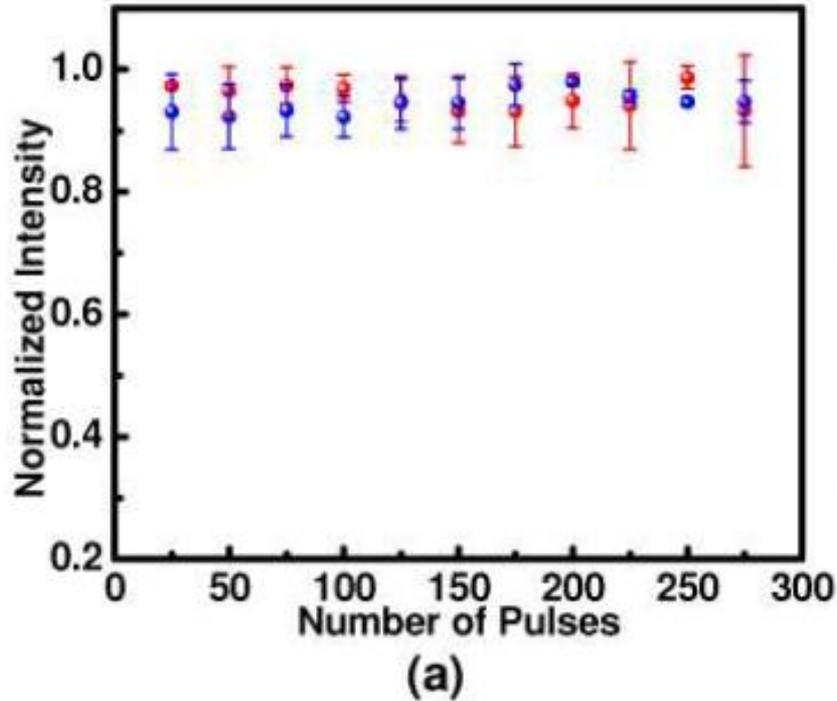


Fig. 7. Photoacoustic signal intensity of PEG-coated gold nanorods (red scatters) and silica-coated gold nanorods (blue scatters) versus number of pulses with fluence (a) 4 mJ/cm² and (b) 18 mJ/cm².

Silica-Coated Gold Nanorods as Photoacoustic Signal Nanoamplifiers

Yun-Sheng Chen,^{†,‡} Wolfgang Frey,[†] Seungsoo Kim,[†] Pieter Kruizinga,[†] Kimberly Homan,[†] and Stanislav Emelianov^{*,†,‡}

[†]Department of Biomedical Engineering and [‡]Department of Electrical and Computer Engineering, University of Texas at Austin, Austin, Texas 78712, United States

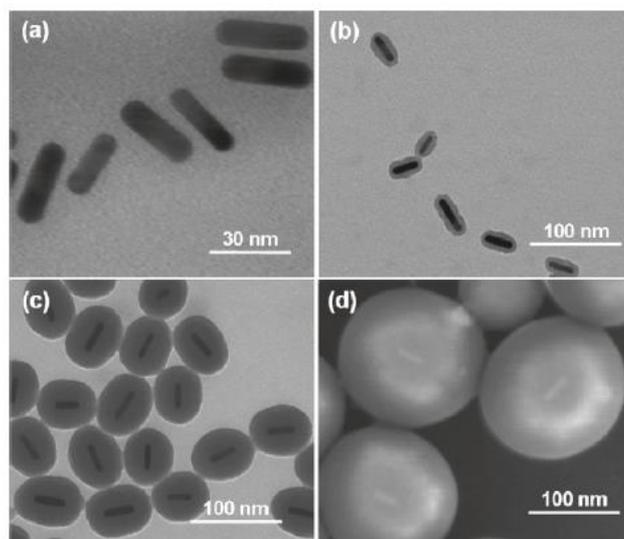
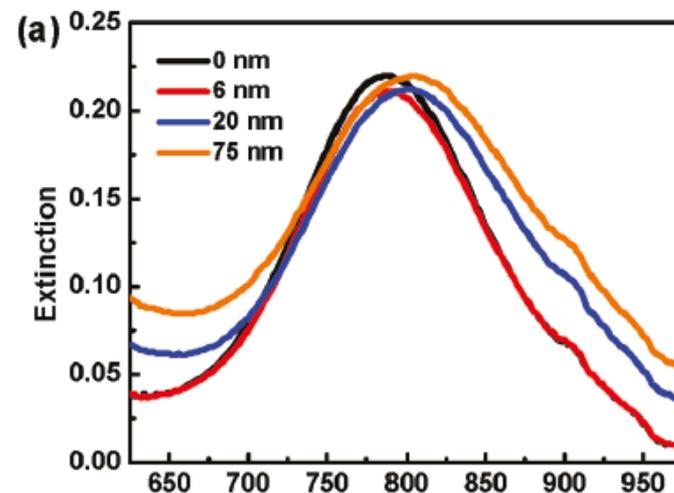
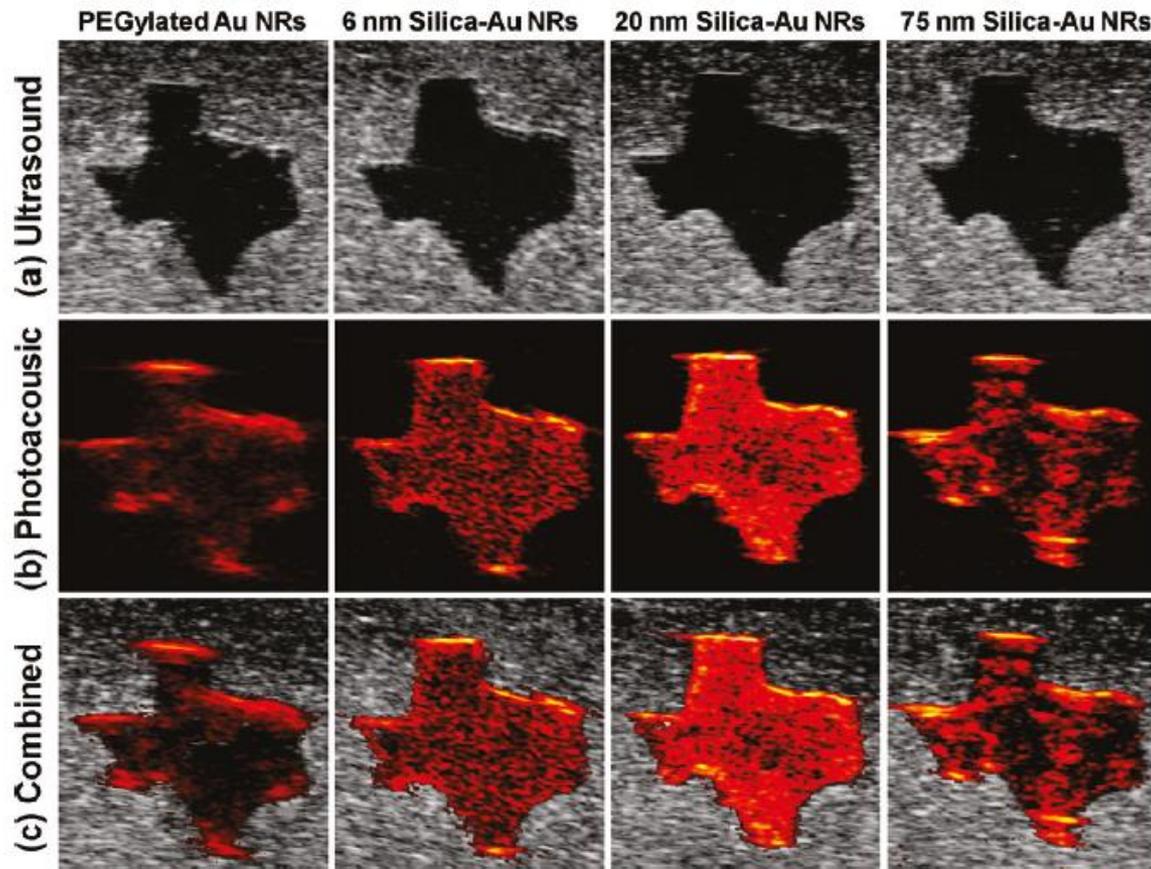


Figure 1. (a) TEM image of PEGylated gold nanorods. TEM images of gold-silica core-shell nanorods with (b) 6 ± 0.5 nm ($N = 100$) and (c) 20 ± 3.6 nm ($N = 100$) thickness of silica coating. (d) SEM image of gold-silica core-shell nanorods with 75 ± 5.0 nm ($N = 100$) thickness of silica coating (the silica shell is too thick for TEM).





The role of the silica shell in amplifying the photoacoustic signal highlights the importance of the heat transfer mechanism from the gold nanoparticle to the ambient signal-generating medium.

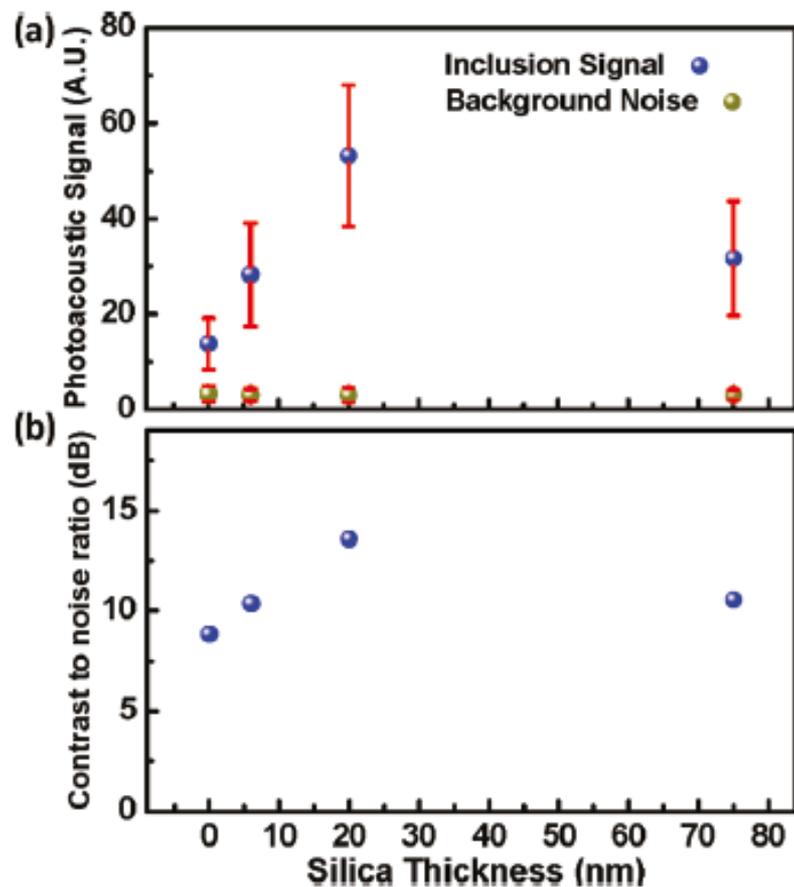


Figure 3. (a) Amplitude of the photoacoustic signal from the background (green dots) and inclusions (blue dots) containing gold nanorods with varying thickness of the silica coating. The error bars show ± 1 standard error. (b) Contrast-to-noise ratios (CNRs) of the photoacoustic images of the inclusions containing gold nanorods with varying thickness of the silica coating.

- PEGylated gold nanorods have a less hydrophilic surface due to the methyl terminal groups than silica.
- When immersed in oil, a higher interfacial thermal conductance could be expected compared to water.
- On the other hand, the hydroxyl groups of the silica surface are able to form hydrogen bonds with water, and have been shown to have a high interfacial thermal conductance.

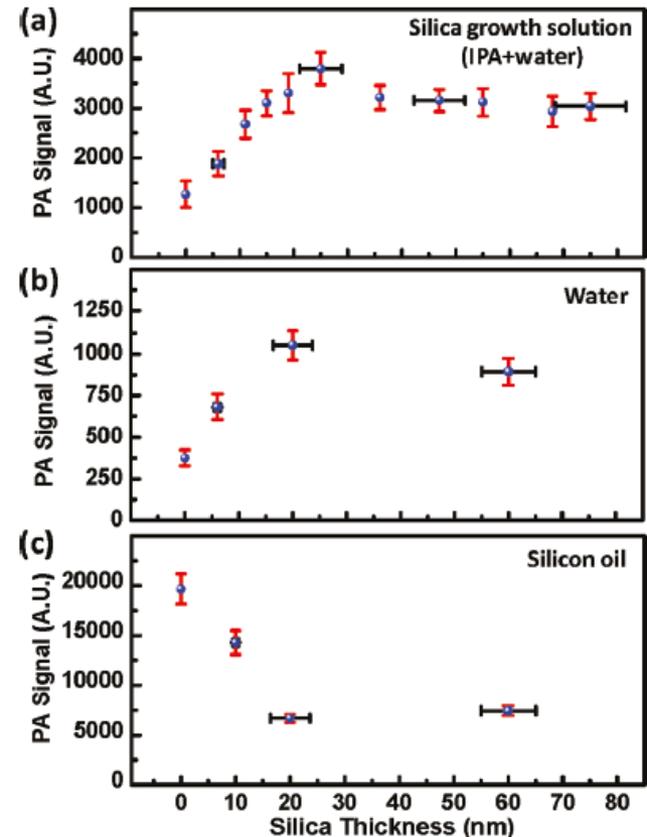


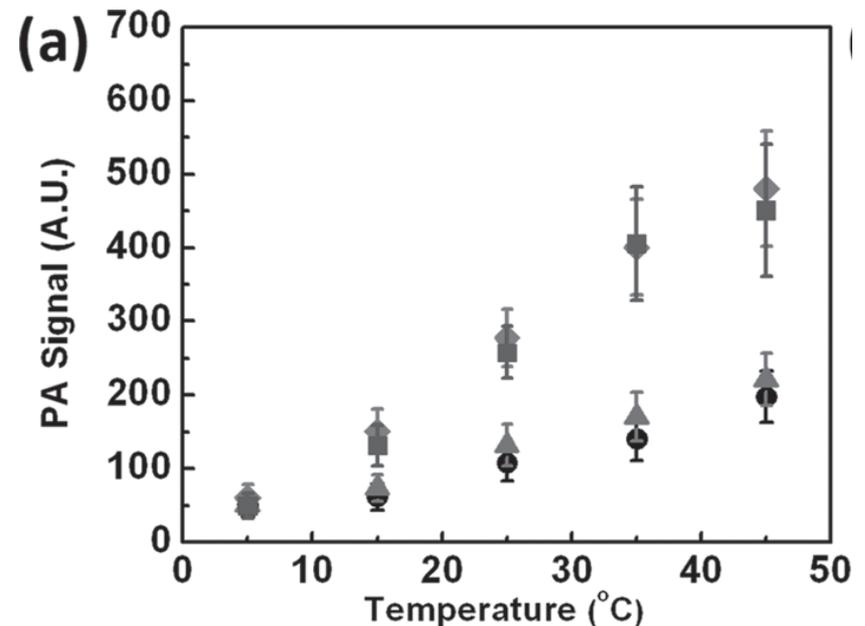
Figure 6. Photoacoustic signal amplitude of gold nanorods with varying thickness of the silica coating in (a) silica growth solution (IPA containing 26 vol % water). (b) water, and (c) silicone oil. In a polar environment the signal is amplified and shows a maximum at ~ 20 nm shell thickness, while in a nonpolar environment the signal monotonically decreases. The vertical error bars represent ± 1 standard deviation of the photoacoustic signal measured using 60 laser pulses of low (4 mJ/cm^2) fluence. The horizontal error bars represent ± 1 standard deviation of the silica thickness measured by TEM.

Environment-Dependent Generation of Photoacoustic Waves from Plasmonic Nanoparticles

*Yun-Sheng Chen, Wolfgang Frey, Salavat Aglyamov, and Stanislav Emelianov**

$$p_0 = \frac{\beta c^2}{C_p} \mu_a F = \Gamma \mu_a F$$

The silica thicknesses are: 0 nm (circle), 6 nm (triangle), 18 nm (square), and 38 nm (rhombus).



The thermal expansion of water at atmospheric pressure vanishes at 3.98 °C