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COMSOL CONFERENCE INDIA 2012

Non-invasive Breast Cancer Imaging Using Novel Estrogen Conjugates NIR Fluorescent Dye

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Diffuse Optical Tomography(DOT) in cancer detection

- Diffuse Optical Tomography ? NIR?
- Why not MIR, PET, CT, x ray mammogram?
- Add on existing modalities.
- Non-invasive,Inexpensive,Low power,Portable,Resolution
- Tracking cancer spread.

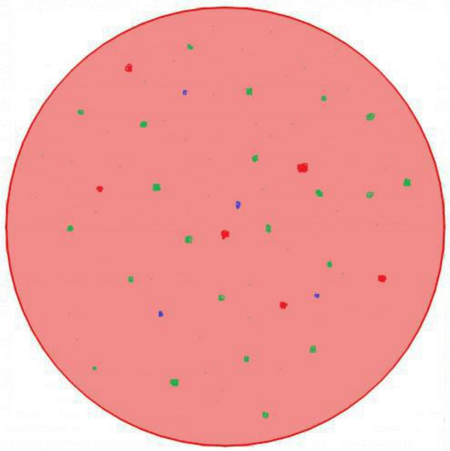
Tissue interrogation using laser

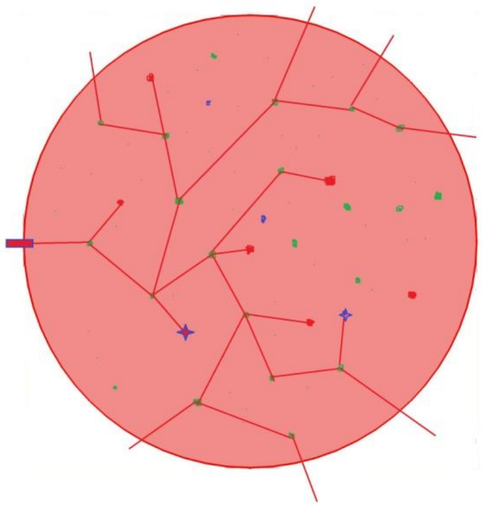
- P1 Approximation of Radiative Transport Equation

$$-\nabla.(D_x \nabla \phi_x(r)) + \left[\mu_{axi} + \mu_{axf} + \frac{i\omega}{c} \right] \phi_x(r) = -\Theta_s \delta(r - r_s) \qquad D_x = \frac{1}{3(\mu_{axi} + \mu_{axf} + \mu'_{sx})}$$

- Robin Boundary condition

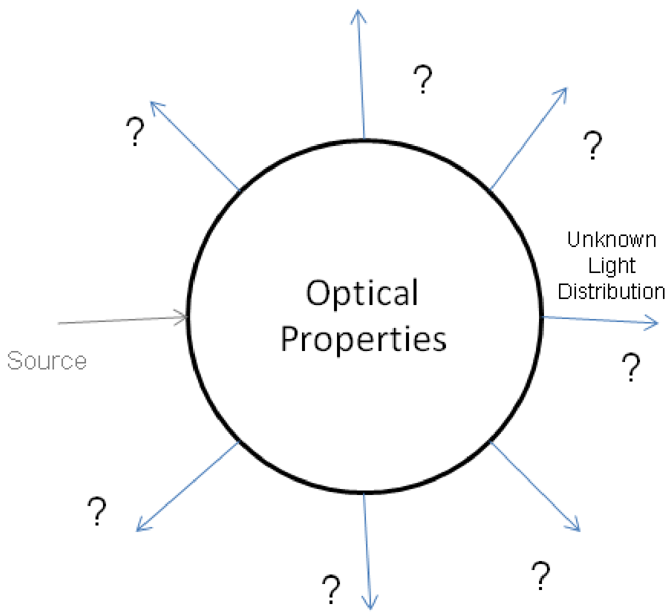
$$\mathbf{n}.[2A_x D_x \nabla \phi_x(r)] + \phi_x(r) = 0 \quad \forall r \in \partial\Omega$$



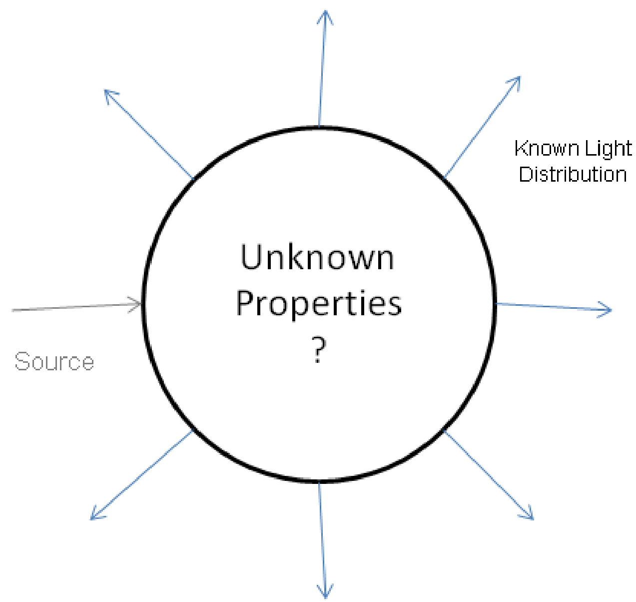


Problems in DOT

Forward problem



Inverse problem



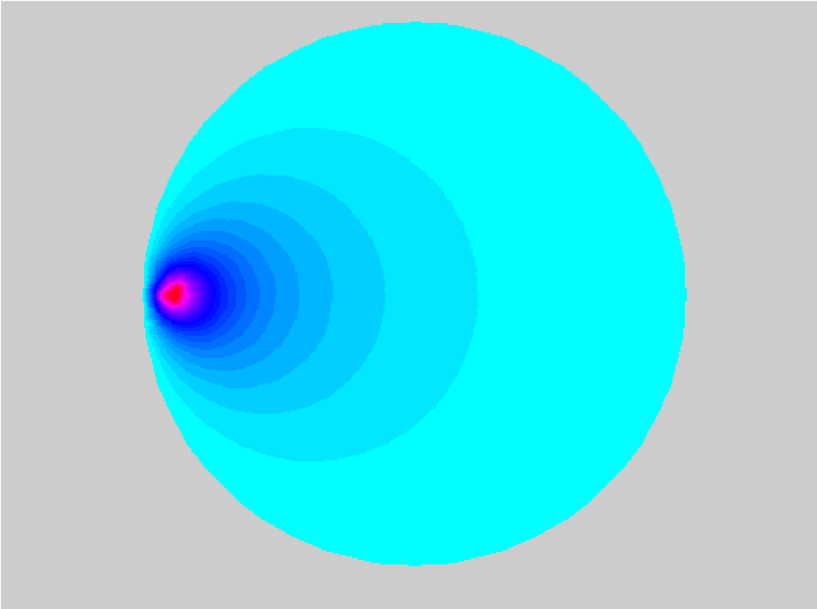
Normal tissue μ_a 0.005 to 0.02 mm-1

$\mu_s^{'}$ 2 to 15 mm

Inverse problem in DOT

- Start with uniform optical properties
- Jacobian – using adjoint method

$$\frac{\partial \phi^{C}}{\partial \mu}$$



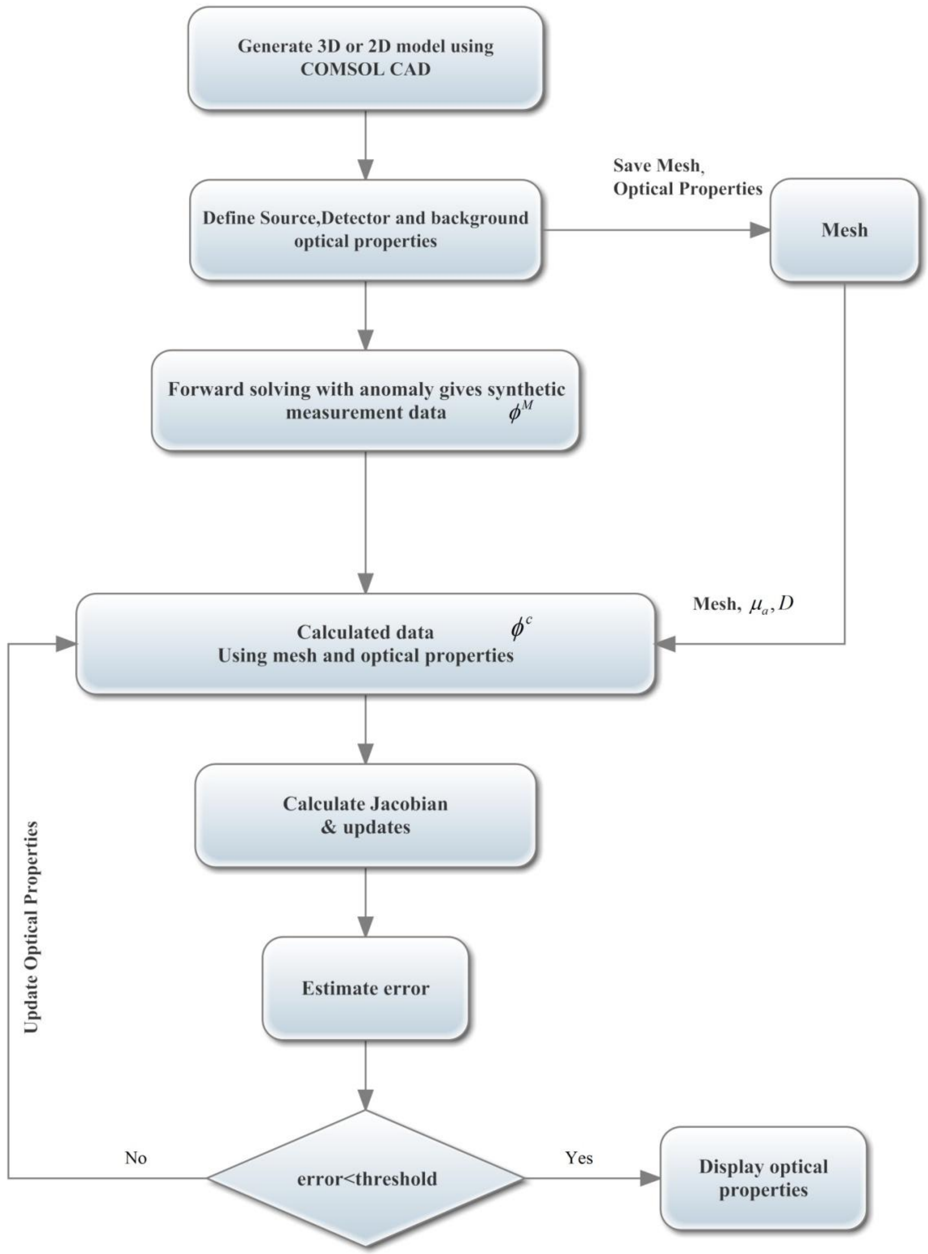
- Optical Property update

Levenberg-Marquardt

$$\partial \mu = (J^{T} J + \bar{\lambda} I)^{-1} J^{T} \partial \phi$$

- Tikhonov minimization of error

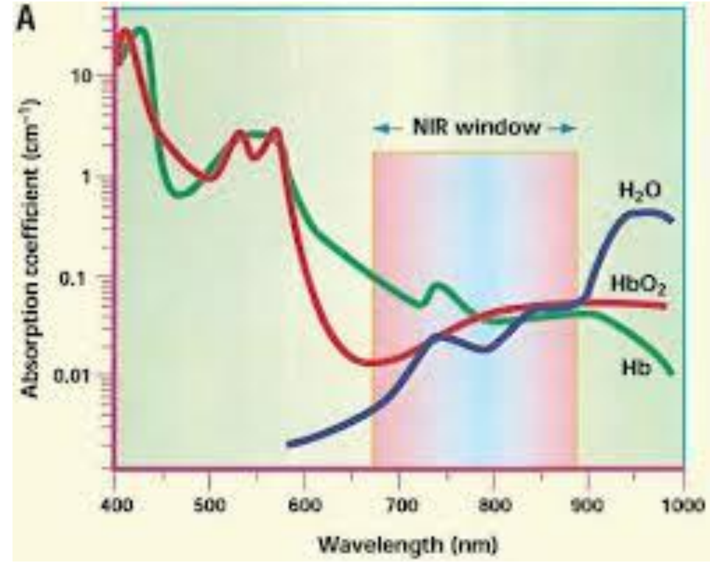
$$\chi^{2} = \min_{\mu} \left\{ \sum_{i=1}^{M} (\phi_i^{M} - \phi_i^{C})^{2} \right\}$$

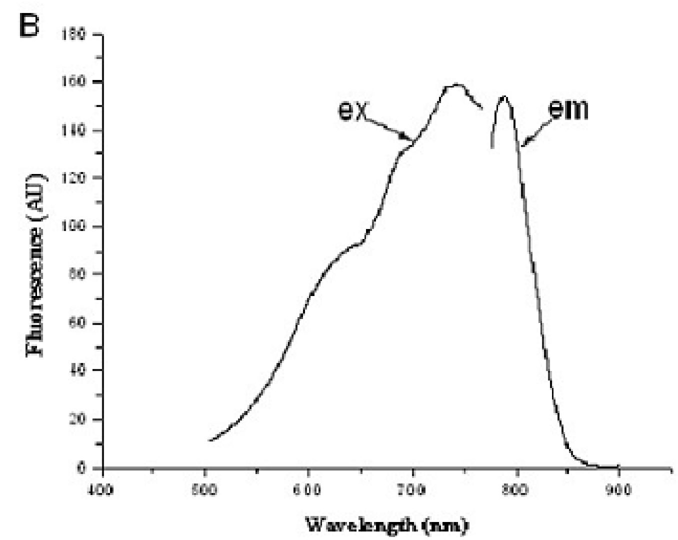


Generate 3D or 2D model using COMSOL CAD
Define Source,Detector and background optical properties
Save Mesh, Optical Properties
Mesh
Forward solving with anomaly gives synthetic measurement data ϕ^M
Mesh, μ_a, D
Calculated data ϕ^c
Using mesh and optical properties
Calculate Jacobian & updates
Estimate error
Update Optical Properties
No
error<threshold
Yes
Display optical properties

Target specific fluorescent dye

- Contrast agents –ICG
- Estrogen receptor
- $\lambda_{ex} = 754nm \,\&\, \lambda_{em} = 787nm$
- Early cancer detection & tracking





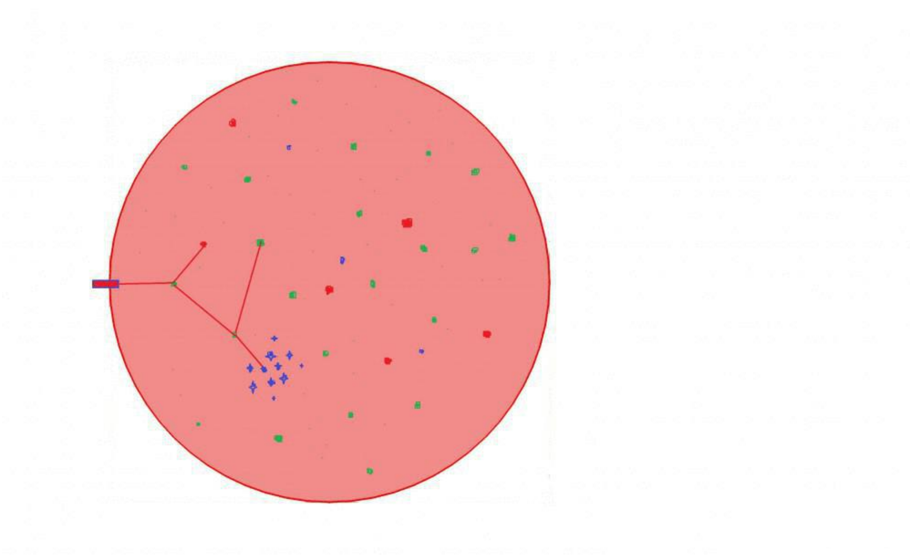


Image courtesy :National Cancer Institute

Modeling fluorescent dye

- Forward solving

>>Excitation

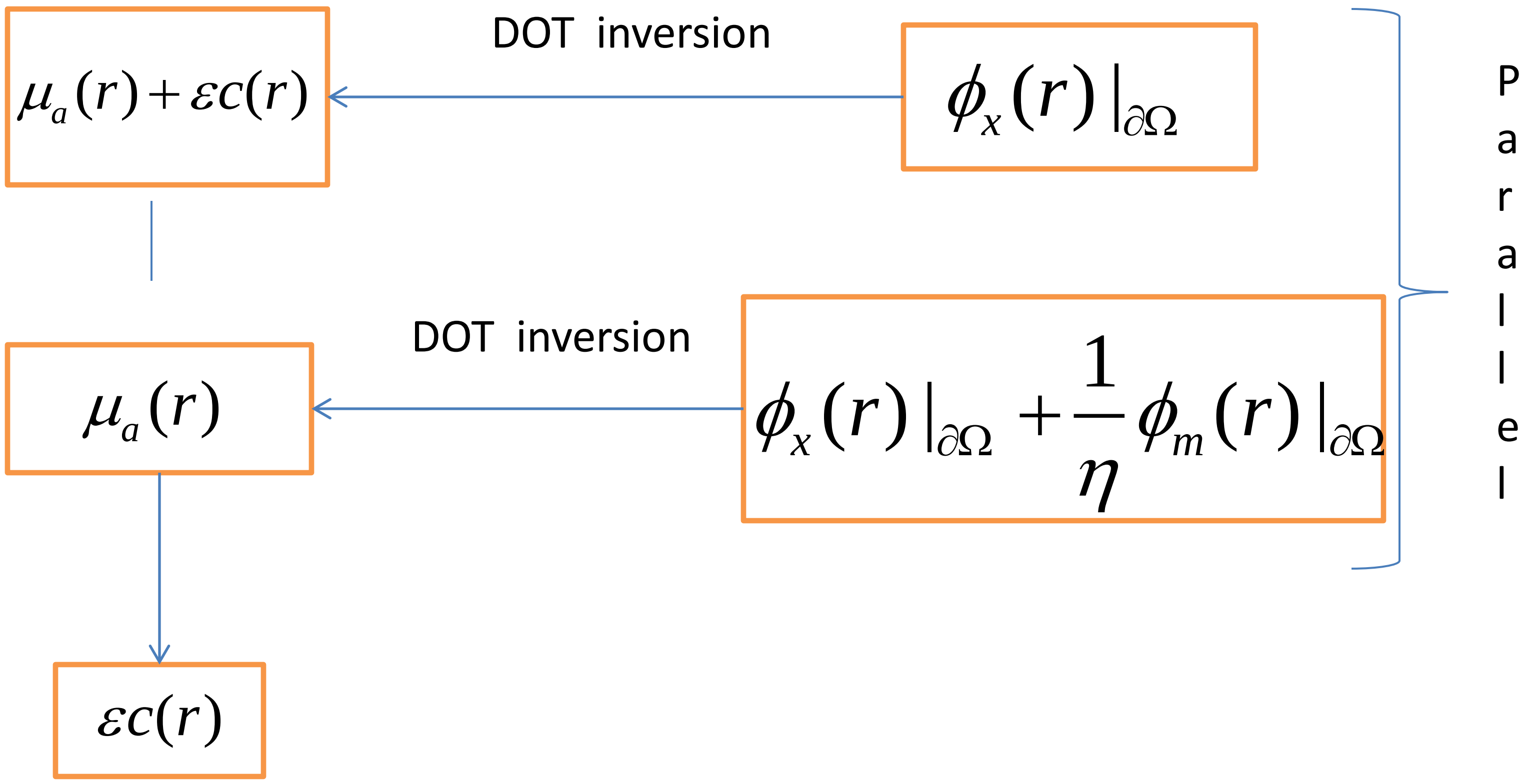
$$-\nabla.(D_x \nabla \phi_x(r)) + \left[\mu_{axi} + \mu_{axf} + \frac{i\omega}{c} \right] \phi_x(r) = -\Theta_s \delta(r - r_s)$$

>>Emission

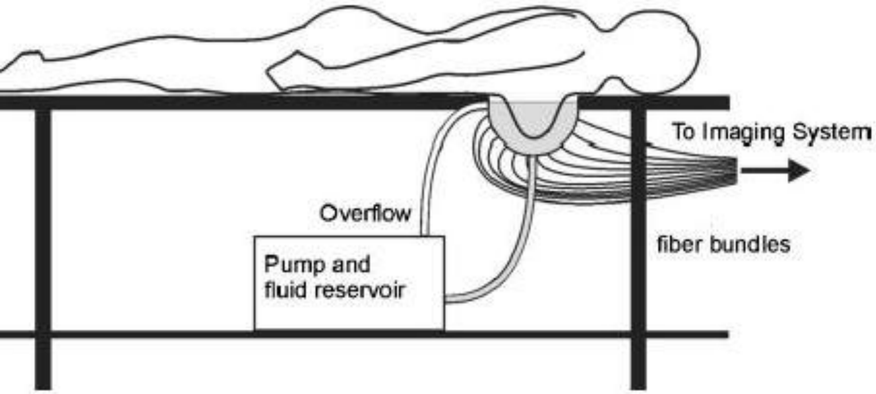
$$-\nabla.(D_m \nabla \phi_m(r)) + \left[\mu_{ami} + \frac{i\omega}{c} \right] \phi_m(r) = -\frac{\phi_x(r)\eta\mu_{axf}}{1 - i\omega\tau}$$

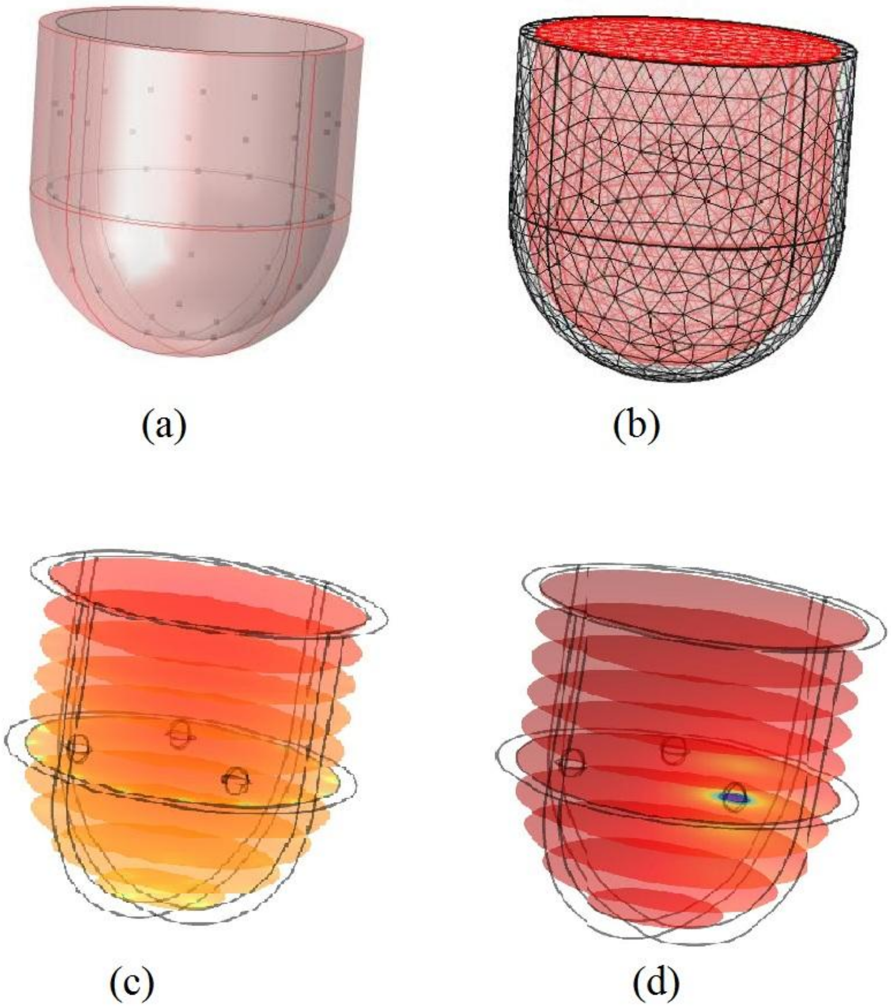
- Robin boundary condition
- Separating coupled equations

Fluorescent reconstruction

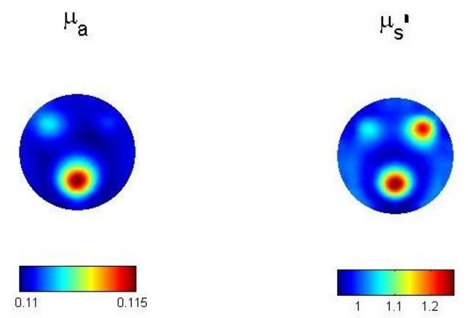


Results

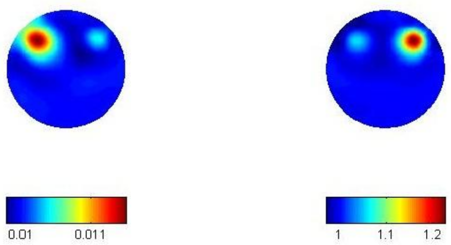

To Imaging System
Overflow
fiber bundles
Pump and
fluid reservoir


(a)
(b)
(c)
(d)

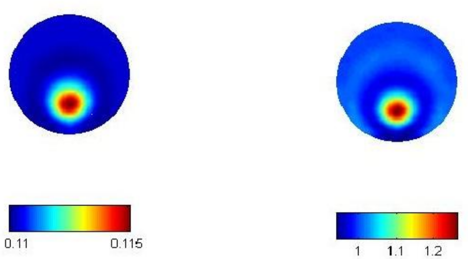
Results



(a) Optical properties at excitation wavelength



(b) Optical properties at emission wavelength



(c) Reconstructed optical properties of fluorecent dye

Domain	μ_a (mm-1)	μ'_s (mm-1)
Background	0.01	1
Absorber	0.02	1
Scatterer	0.01	2
Dye	0.115	2

$$E = \frac{1}{N} \| F(x) - y \|^2$$

Parameter	Error Function (E)
Amplitude	9.3705e-07
Phase	2.4401e-03

Parameter	MSE
μ_a	0.0024
μ'_s	0.0010

Reference

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8. Tara D, S R. Arridge, Time-resolved optical mammography using a liquid coupled interface, Journal of Biomedical Optics , Vol 10,p054011-1- 10(2005)
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Thank You!

More details…

Inverse solving

Tikhonov Minimization $$\chi^2 = \min_{\mu} \left\{ \sum_{i=1}^{M} (\phi_i^M - \phi_i^C)^2 \right\}$$

$$\frac{\partial \chi^2}{\partial \mu} = 0$$

$$\left(\frac{\partial \phi^C}{\partial \mu} \right)^2 (\phi^M - \phi^C) = 0$$

Jacobian $\frac{\partial \phi^C}{\partial \mu}$

LM iterative equation $\partial \mu = (J^T J + \overline{\lambda} I)^{-1} J^T \partial \phi$

More details...

$$
J = \begin{bmatrix}
\frac{\delta \ln I_1}{\delta \kappa_1} & \frac{\delta \ln I_1}{\delta \kappa_2} & \cdots & \frac{\delta \ln I_1}{\delta \kappa_{\mathrm{NN}}}; & \frac{\delta \ln I_1}{\delta \mu_{\mathrm{a}1}} & \frac{\delta \ln I_1}{\delta \mu_{\mathrm{a}2}} & \cdots & \frac{\delta \ln I_1}{\delta \mu_{\mathrm{aNN}}} \\
\frac{\delta \theta_1}{\delta \kappa_1} & \frac{\delta \theta_1}{\delta \kappa_2} & \cdots & \frac{\delta \theta_1}{\delta \kappa_{\mathrm{NN}}}; & \frac{\delta \theta_1}{\delta \mu_{\mathrm{a}1}} & \frac{\delta \theta_1}{\delta \mu_{\mathrm{a}2}} & \cdots & \frac{\delta \theta_1}{\delta \mu_{\mathrm{aNN}}} \\
\frac{\delta \ln I_2}{\delta \kappa_1} & \frac{\delta \ln I_2}{\delta \kappa_2} & \cdots & \frac{\delta \ln I_2}{\delta \kappa_{\mathrm{NN}};} & \frac{\delta \ln I_2}{\delta \mu_{\mathrm{a}1}} & \frac{\delta \ln I_2}{\delta \mu_{\mathrm{a}2}} & \cdots & \frac{\delta \ln I_2}{\delta \mu_{\mathrm{aNN}}} \\
\frac{\delta \theta_2}{\delta \kappa_1} & \frac{\delta \theta_2}{\delta \kappa_2} & \cdots & \frac{\delta \theta_2}{\delta \kappa_{\mathrm{NN}};} & \frac{\delta \theta_2}{\delta \mu_{\mathrm{a}1}} & \frac{\delta \theta_2}{\delta \mu_{\mathrm{a}2}} & \cdots & \frac{\delta \theta_2}{\delta \mu_{\mathrm{aNN}}} \\
\vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\
\frac{\delta \ln I_{\mathrm{NM}}}{\delta \kappa_1} & \frac{\delta \ln I_{\mathrm{NM}}}{\delta \kappa_2} & \cdots & \frac{\delta \ln I_{\mathrm{NM}}}{\delta \kappa_{\mathrm{NN}}}; & \frac{\delta \ln I_{\mathrm{NM}}}{\delta \mu_{\mathrm{a}1}} & \frac{\delta \ln I_{\mathrm{NM}}}{\delta \mu_{\mathrm{a}2}} & \cdots & \frac{\delta \ln I_{\mathrm{NM}}}{\delta \mu_{\mathrm{aNN}}} \\
\frac{\delta \theta_{\mathrm{NM}}}{\delta \kappa_1} & \frac{\delta \theta_{\mathrm{NM}}}{\delta \kappa_2} & \cdots & \frac{\delta \theta_{\mathrm{NM}}}{\delta \kappa_{\mathrm{NN}}}; & \frac{\delta \theta_{\mathrm{NM}}}{\delta \mu_{\mathrm{a}1}} & \frac{\delta \theta_{\mathrm{NM}}}{\delta \mu_{\mathrm{a}2}} & \cdots & \frac{\delta \theta_{\mathrm{NM}}}{\delta \mu_{\mathrm{aNN}}}
\end{bmatrix}
$$

More Details…

FEM formulation

$$\left(K(\kappa) + C\left(\mu_a + \frac{i\omega}{c_m}\right) + \frac{1}{2A} F \right) \Phi = q_0$$

where the matrices $K(\kappa)$, $C((\mu_a + i\omega/c_m))$ and F have entries given by

$$K_{ij} = \int_\Omega \kappa(r) \nabla u_i(r) \cdot \nabla u_j(r) \, d^n r$$

$$C_{ij} = \int_\Omega \left(\mu_a(r) + \frac{i\omega}{c_m(r)} \right) u_i(r) u_j(r) \, d^n r$$

$$F_{ij} = \oint_{\partial\Omega} u_i(r) u_j(r) \, d^{n-1} r$$

and the source vector q_0 has terms

$$q_{0_i} = \int_\Omega u_i(r) q_0(r) \, d^n r$$

More detail…

$$-\nabla\cdot\kappa(r)\nabla\Phi(r,\omega)+\left(\mu_{\mathrm{a}}(r)+\frac{\mathrm{i}\omega}{c_{\mathrm{m}}(r)}\right)\Phi(r,\omega)=q_0(r,\omega)$$

$$\kappa=1/3(\mu_{\mathrm{a}}+\mu_{\mathrm{s}}')$$

$$\Phi(\xi,\omega)+2A\hat{\mathbf{n}}\cdot\kappa(\xi)\nabla\Phi(\xi,\omega)=0$$

$$A=\frac{2/(1-R_0)-1+|\cos\theta_c|^3}{1-|\cos\theta_c|^2}$$

$$\vartheta_c=\arcsin(n_{\mathrm{AIR}}/n_1)$$

$$R_0=(n_1/n_{\mathrm{AIR}}-1)^2/(n_1/n_{\mathrm{AIR}}+1)^2$$

More Detail

$$-\nabla.(D_x \nabla \phi_x(r)) + \left[\mu_{axi} + \mu_{axf} + \frac{i\omega}{c}\right]\phi_x(r) = -\Theta_s \delta(r - r_s) \qquad (1a)$$

$$-\nabla.(D_m \nabla \phi_m(r)) + \left[\mu_{ami} + \frac{i\omega}{c}\right]\phi_m(r) = -\frac{\phi_x(r)\eta\mu_{axf}}{1 - i\omega\tau} \qquad (1b)$$

$$D_x = \frac{1}{3(\mu_{axi} + \mu_{axf} + \mu'_{sx})}$$

$$D_m = \frac{1}{3(\mu_{ami} + \mu'_{sm})}$$

$$\mathbf{n}.[2A_x D_x \nabla \phi_x(r)] + \phi_x(r) = 0 \qquad \forall r \in \partial\Omega \qquad (2a)$$

$$\mathbf{n}.[2A_m D_m \nabla \phi_m(r)] + \phi_m(r) = 0 \qquad \forall r \in \partial\Omega \qquad (2b)$$

More Details…

$$A = \frac{2/(1-R_0)-1+|\cos(\theta_c)|^3}{1+|\cos(\theta_c)|^2}$$

$$D_x = D_m = D \qquad \mu_{ax} = \mu_{am} = \mu_a$$

$$-\nabla.(D_x \nabla \phi_x(r)) + \left[\mu_a + \varepsilon_x c(r) + \frac{i\omega}{c}\right]\phi_x(r) = -\Theta_s \delta(r - r_s) \qquad (3a)$$

$$-\nabla.(D_m \nabla \phi_m(r)) + \left[\mu_a + \frac{i\omega}{c}\right]\phi_m(r) = -\frac{\phi_x(r)\eta\varepsilon_x c(r)}{1-i\omega\tau} \qquad (3b)$$

$$\varepsilon_x c(r)\phi_x(r) = \Theta_s \delta(r - r_s) - \left(-\nabla D \nabla + \mu_a(r) + \frac{i\omega}{c}\right)\phi_x(r) \qquad (4)$$

More Details…

$$\left[-\nabla D\nabla + \mu_a(r) + \frac{i\omega}{c}\right]\left(\frac{1-i\omega\tau}{\eta}\phi_m(r) + \phi_x(r)\right) = \Theta_s\delta(r-r_s) \qquad (5)$$

Let $\frac{1-i\omega\tau}{\eta}\phi_m(r) + \phi_x(r) = \phi_t(r)$

$$\left[-\nabla D\nabla + \mu_a + \varepsilon_x c(r) + \frac{i\omega}{c}\right]\phi_x(r) = -\Theta_s\delta(r-r_s) \qquad (6a)$$

$$\left[-\nabla D\nabla + \mu_a(r) + \frac{i\omega}{c}\right]\phi_t(r) = \Theta_s\delta(r-r_s) \qquad (6b)$$