CHRIST UNIVERSITY
BANGALORE, INDIA
Declared as Deemed to be University under Section 3 of UGC Act 1956

Comparative Study and 3D Modelling of Breast Cancer Using NIR-fDOT in Comsol

SOORYA PETER
IVEN JOSE
CHRIST UNIVERSITY FACULTY OF ENGINEERING

COMSOL CONFERENCE 2014 BANGALORE
Excerpt from the Proceedings of the 2014 COMSOL Conference in Bangalore

Introduction:

- **Cancer is one of the most dreaded diseases of the modern world.**
- ***Breast cancer* is the second leading cause (after lung cancer) of morbidity and mortality in women.**
- **The International Agency for Research on Cancer (IARC), the specialized cancer agency of the WHO, releases data on cancer incidence, mortality, and prevalence worldwide.**
- **The statistics point out a sharp increase in the incidence of breast cancer**
- **In 2012, 1.7 million women were diagnosed with breast cancer**

- **6.3 million women had been diagnosed with breast cancer in the previous five years(from 2012).**

- **Since the 2008 estimates, breast cancer incidence has increased by more than 20%, while mortality has increased by 14%.**

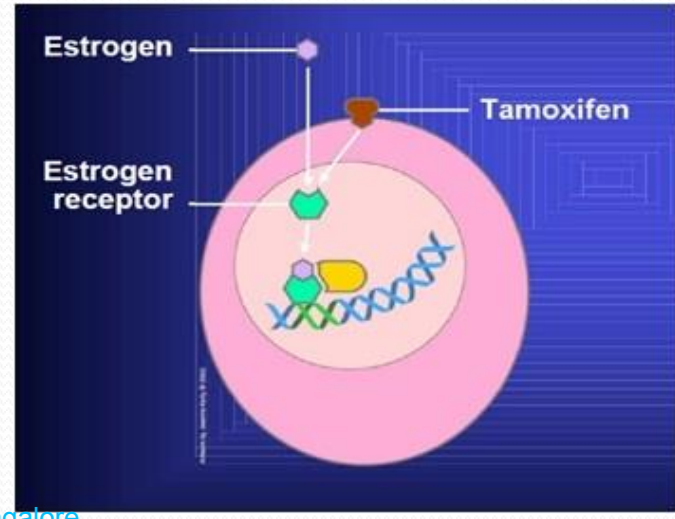
- **It is the most frequently diagnosed cancer among women in 140 of 184 countries worldwide.**

- **Diagnosis of small pre- malignant lesions and early stage primary tumors, is crucial for the success of cancer therapy and can hence increase survival rates.**

- **optical imaging technique, can detect lesions as small as 200 microns.**

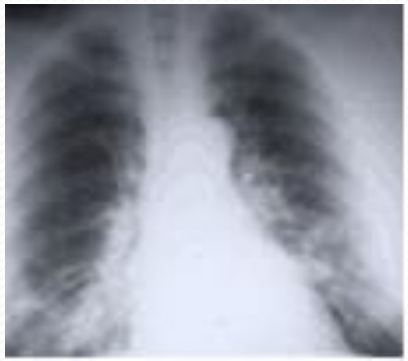
Importance of determination of estrogen receptor status in diagnosis of cancer

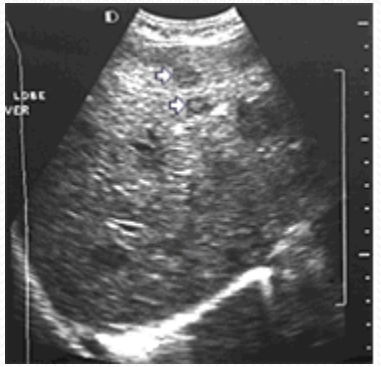
- **Prominent types of breast cancer - Ductal carcinoma in situ, Invasive (or infiltrating) ductal carcinoma, Invasive (or infiltrating) lobular carcinoma.**
- **Estrogen induced proliferation of mutant cells is one of the major risk determining factor in the development of breast cancer.**
- **Hence determination of the Estrogen Receptor[ER] status is of paramount importance if cancer pathogenesis is to be detected and rectified at an early stage.**
- **In fDOT we use an exogenous target (estrogen) specific dye.**



Types of imaging techniques :-

- Digital Mammography
- CT-Computed Tomography.
- X-Ray.
- MRI – Magnetic Resonance Imaging.
- Ultrasound.
- DOT-Diffuse optical tomography.





WHY DIFFUSE OPTICAL TOMOGRAPFY(DOT)..?

- **Low power hence non-ionizing**
- **non-invasive**
- **good penetration**
- **spectral contrast**
- **inexpensive**

Why fDOT??

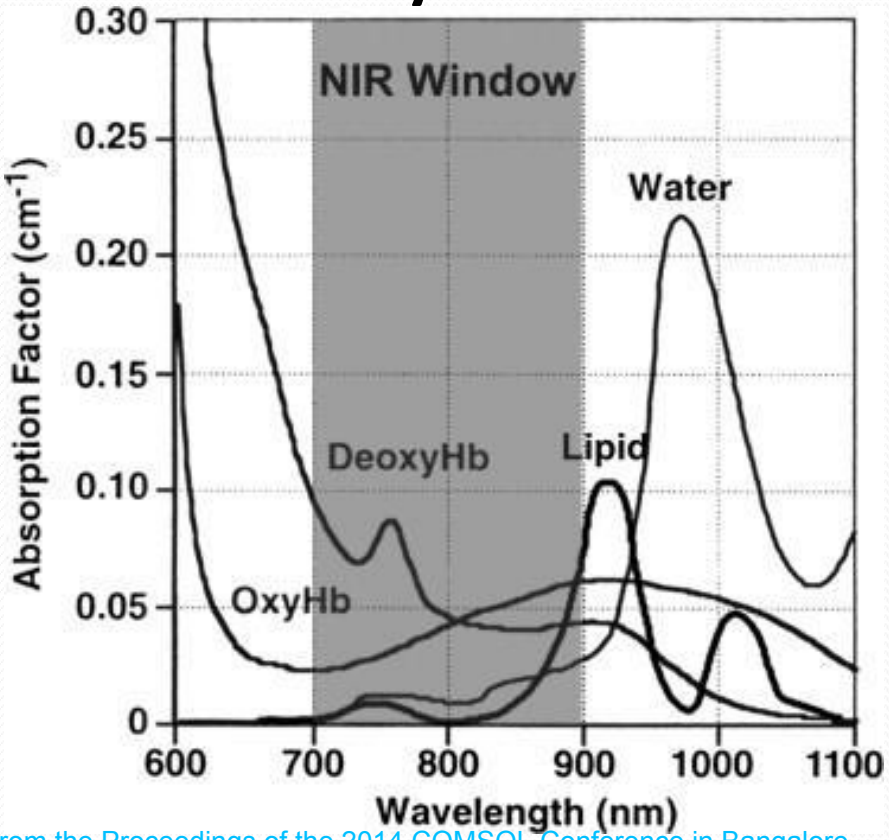
- **Fluorescence diffuse optical tomography (f-DOT) is an attractive component of optical tissue tomography.**

- **Fluorescence tomography methods aim at reconstructing the concentration of fluorophores within the imaged object.**

- **Exogenous fluorophores furnish the desperately needed sensitivity and specificity that is lacking in NIR optical tomography.**

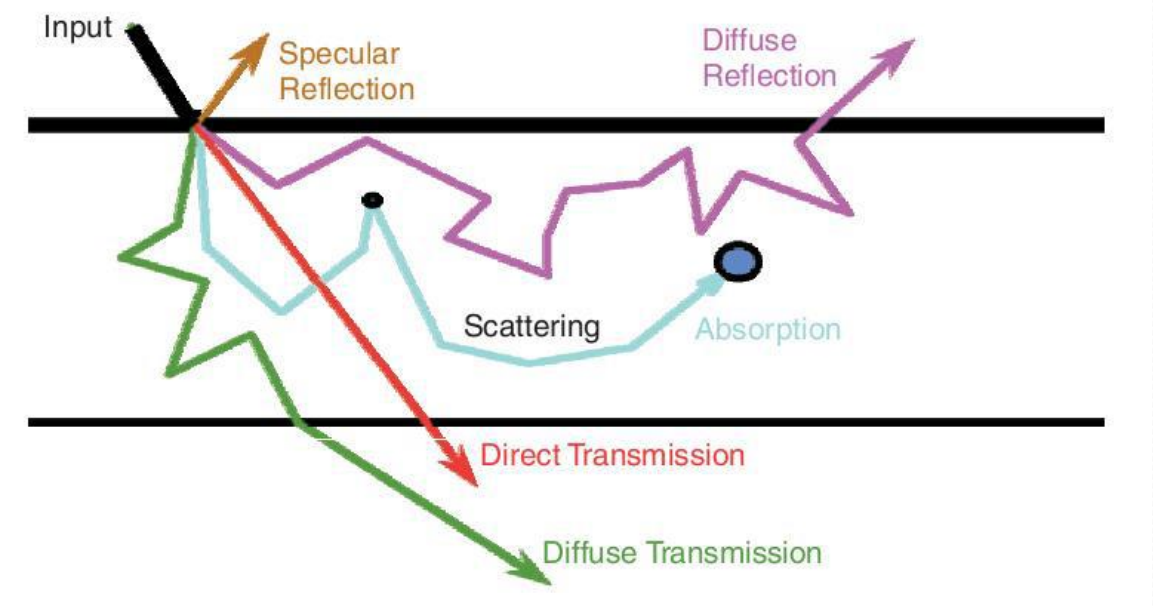
WHY NIR??

- **Existence of spectral region where the absorption of light by tissue is relatively low.**



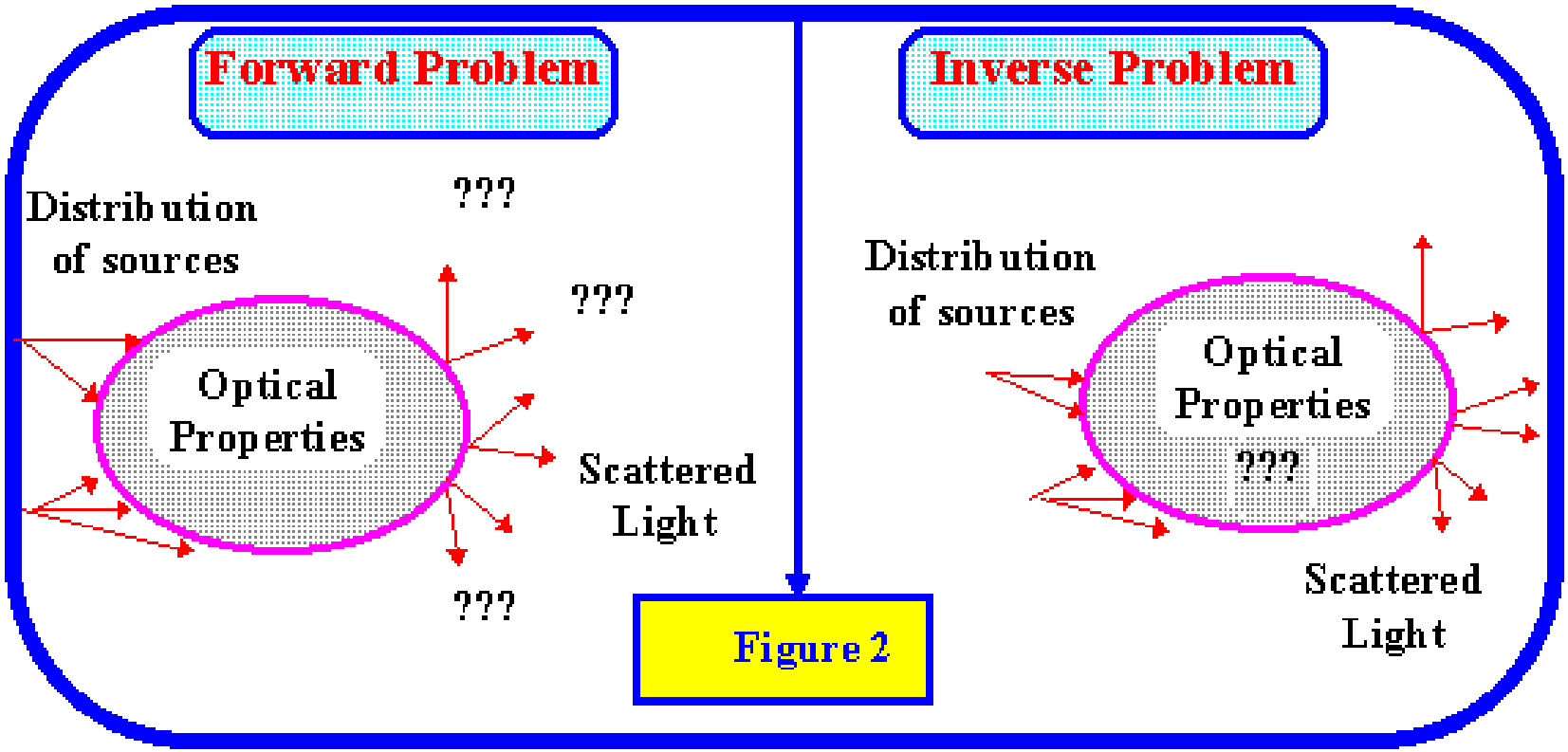
DIFFUSE OPTICAL TOMOGRAPHY

- **Light propogation in tissues:**



- **Major optical properties considered: scattering , absorption**

FORWARD MODEL AND INVERSE MODEL IN OPTICAL TOMOGRAPHY



Main equations in DOT:

- **RTE - Radiative transport equation - equation for the radiant intensity**

$$\frac{1}{v}\frac{\partial L(\mathrm{r},\hat{\Omega},t)}{\partial t}+\nabla\cdot L(\mathrm{r},\hat{\Omega},t)\hat{\Omega}+\mu_t L(\mathrm{r},\hat{\Omega},t)$$
$$=\mu_s\int_{4\pi} f(\hat{\Omega},\hat{\Omega}')L(\mathrm{r},\hat{\Omega}',t)\,d\hat{\Omega}'+Q(\mathrm{r},\hat{\Omega},t),$$

- **Diffusion approximation:**

$$-\nabla.\mathrm{k}(\mathrm{r})\nabla\Phi(\mathrm{r},\omega)+(\mu_a(\mathrm{r})+\frac{i\omega}{c_m(\mathrm{r})})\Phi(\mathrm{r},\omega)=\mathrm{q}_0(\mathrm{r},\omega)$$

- **Reconstruction:**

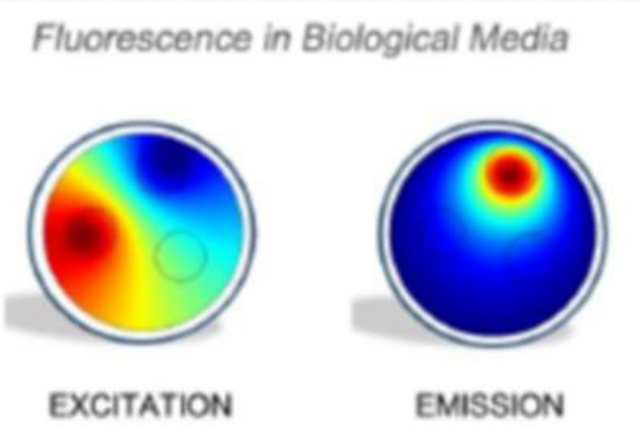
$$\Delta\mu=[\mathrm{J}^T\mathrm{J}+\lambda\,\mathrm{I}]^{-1}J^T(\Phi^c-\Phi^M)$$

- **Fluorophores are illuminated at a particular wavelength and the emission occurs at a different wavelength.**

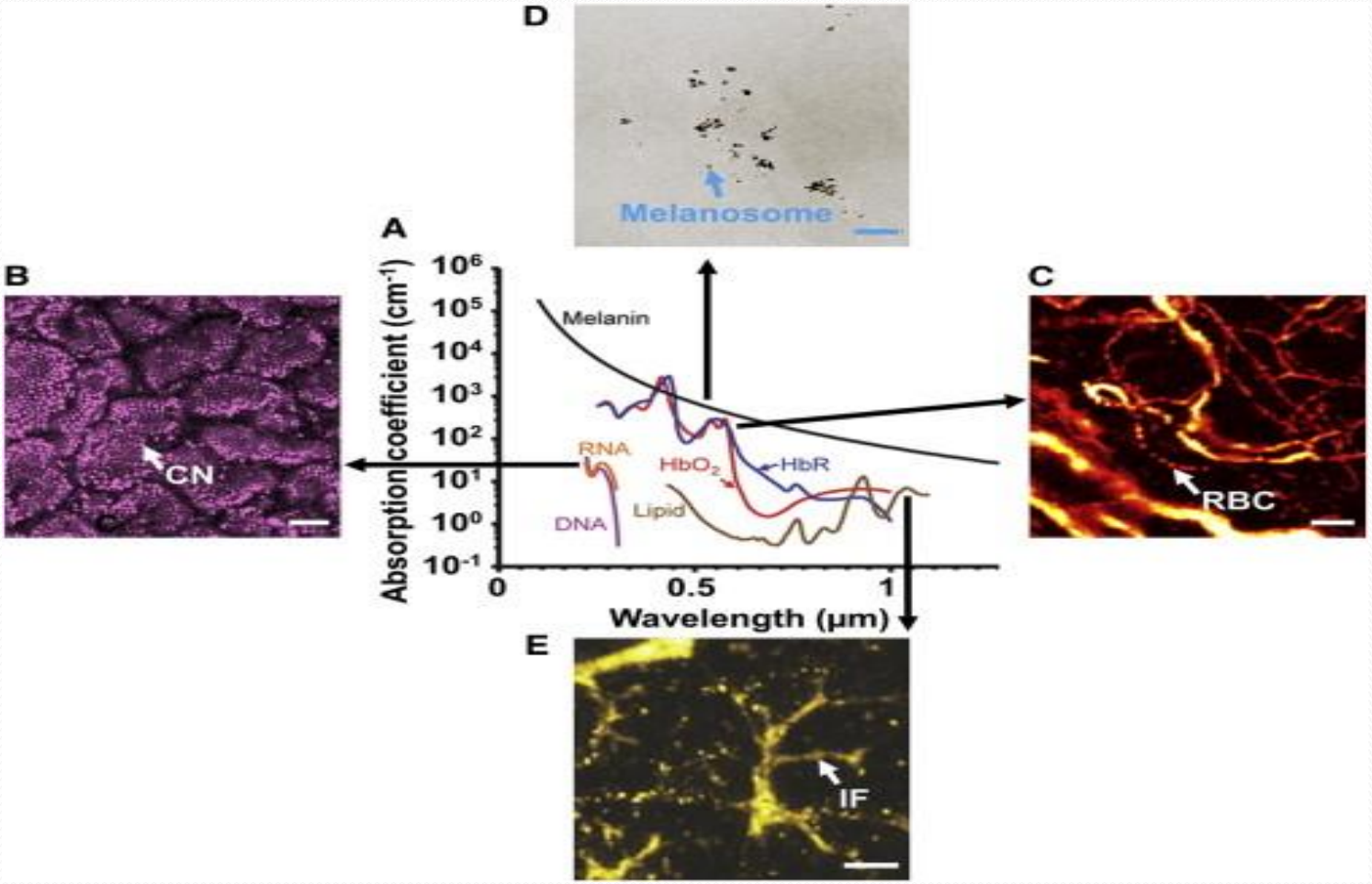
- **Equations for fDOT:**

$$(-\nabla D_x \nabla + \mu_{ax}(\mathrm{r}) + \varepsilon_x \, \mathrm{c}(\mathrm{r}))\Phi_x(\mathrm{r}) = \Theta_s \partial_0 (r - r_s)$$

$$(-\nabla \, \mathrm{D}_m \, \nabla + \mu_{am}(\mathrm{r}))\Phi_f(\mathrm{r}) = \gamma_m \varepsilon_x c(\mathrm{r})\Phi_x(\mathrm{r})$$

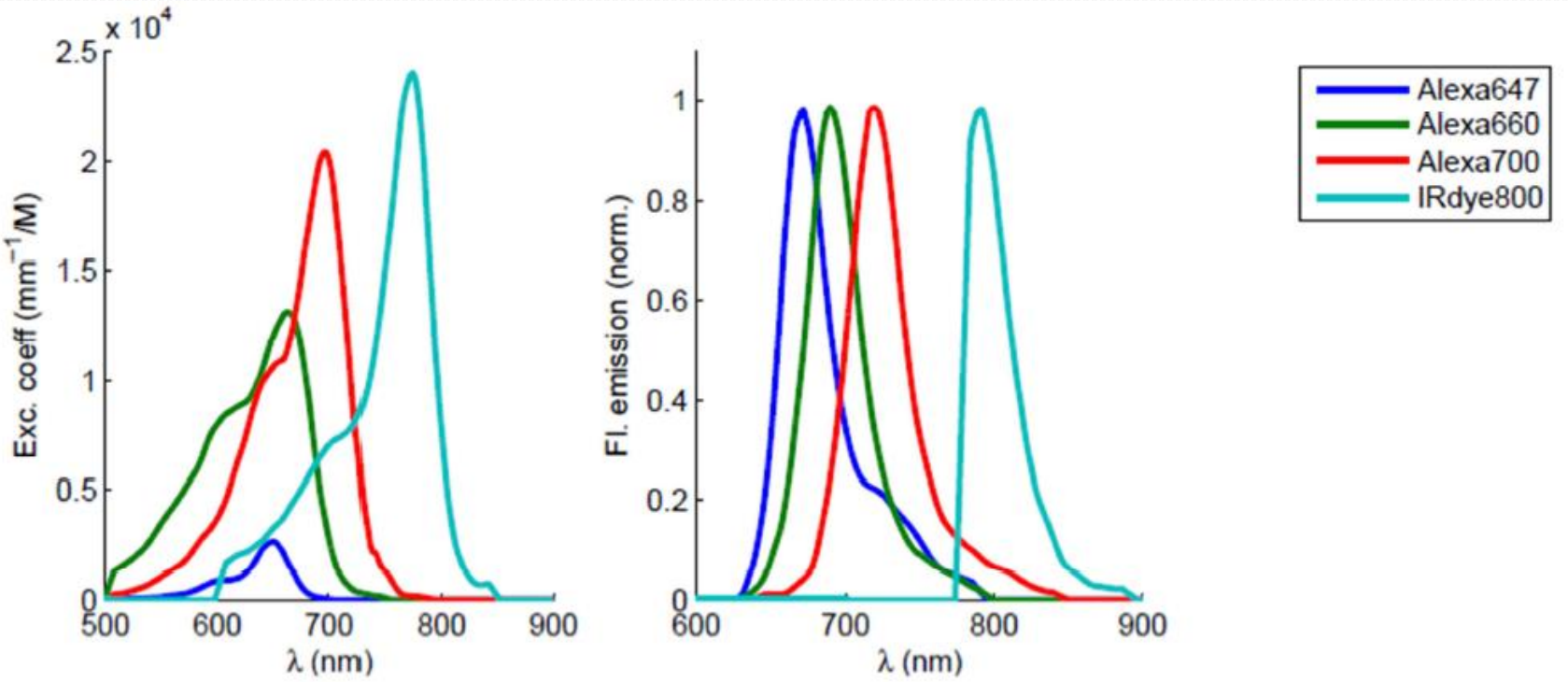


Endogenous fluorophores :-



Excerpt from the Proceedings of the 2014 COMSOL Conference in Bangalore

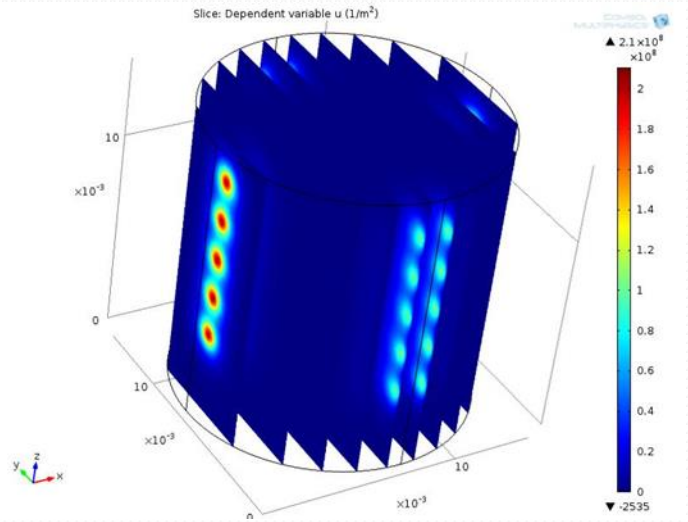
Exogenous fluorophores:

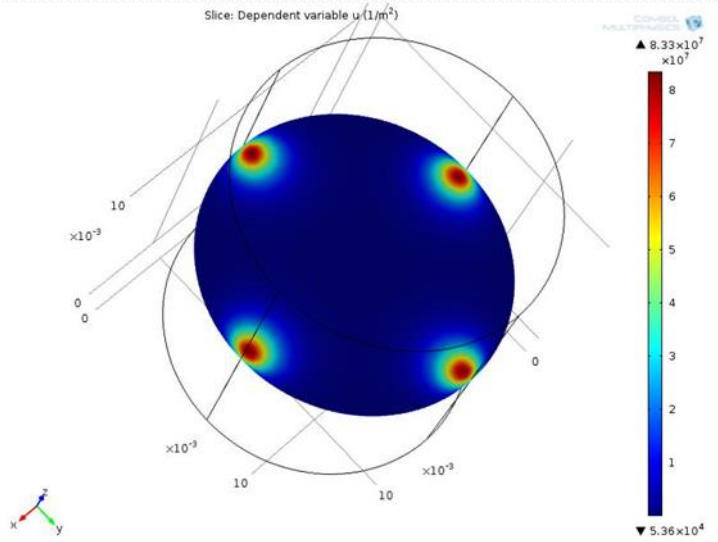


Extinction and emission properties of some selected fluorophores

Simulations

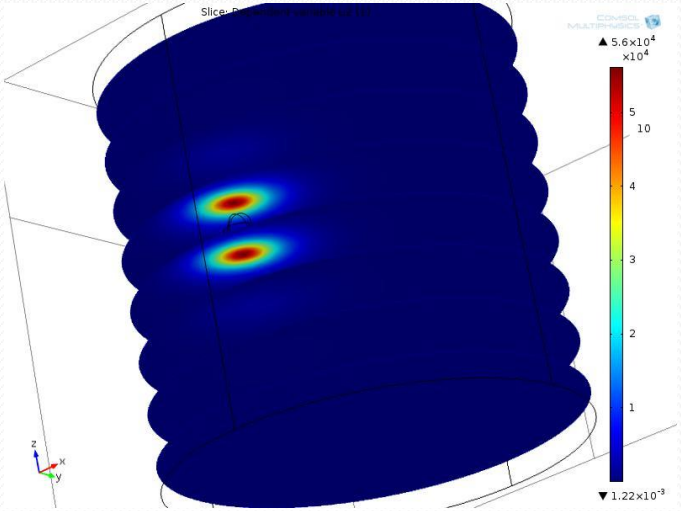
- **Figs show a simulated model of a phantom with its optical properties similar to human tissue.**
- **Irradiated at 750nm.**

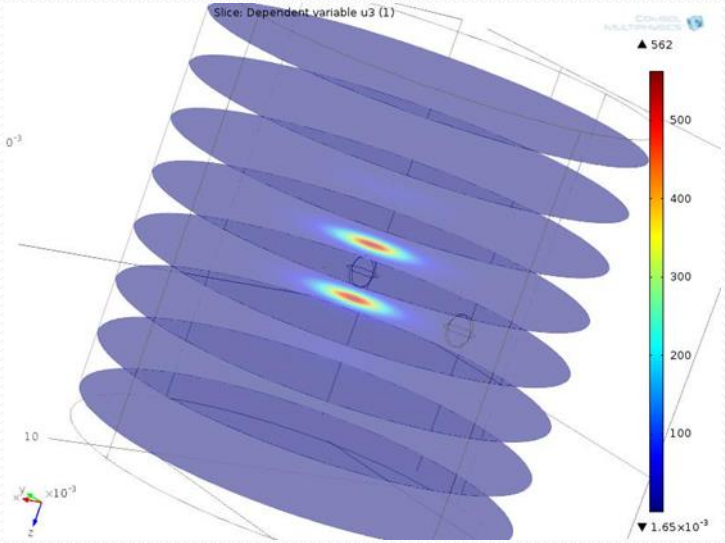




Simulations:

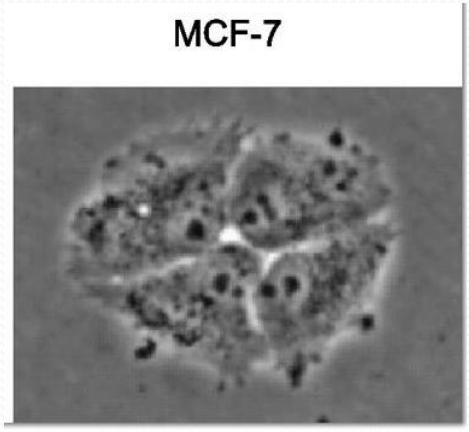
- The fluorescence occurs at a wavelength (λ_{em}) at 783 nm
- The following figures shows the reconstructed fluorescence optical parameters (λ_{em}) at 783 nm

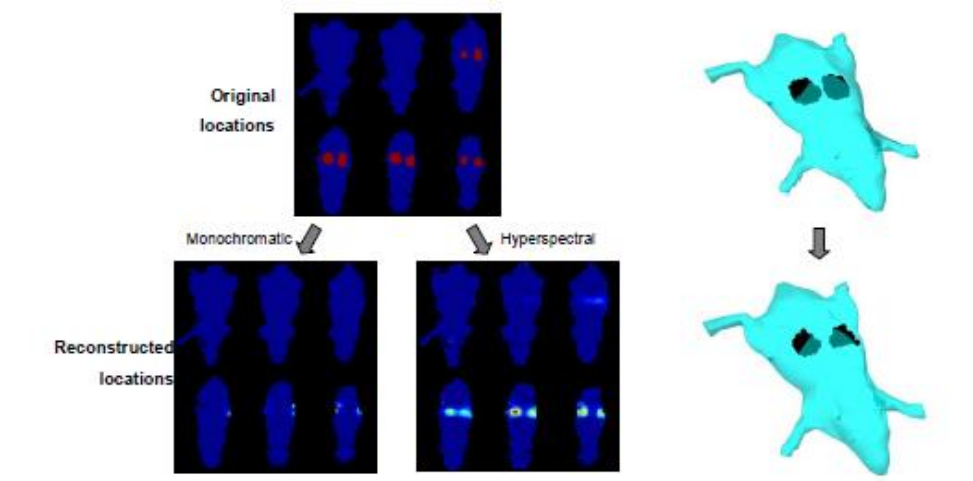




- It shows the dye accumulation in the inhomogeneity ,which fluoresce.

in-vivo and in-vitro studies





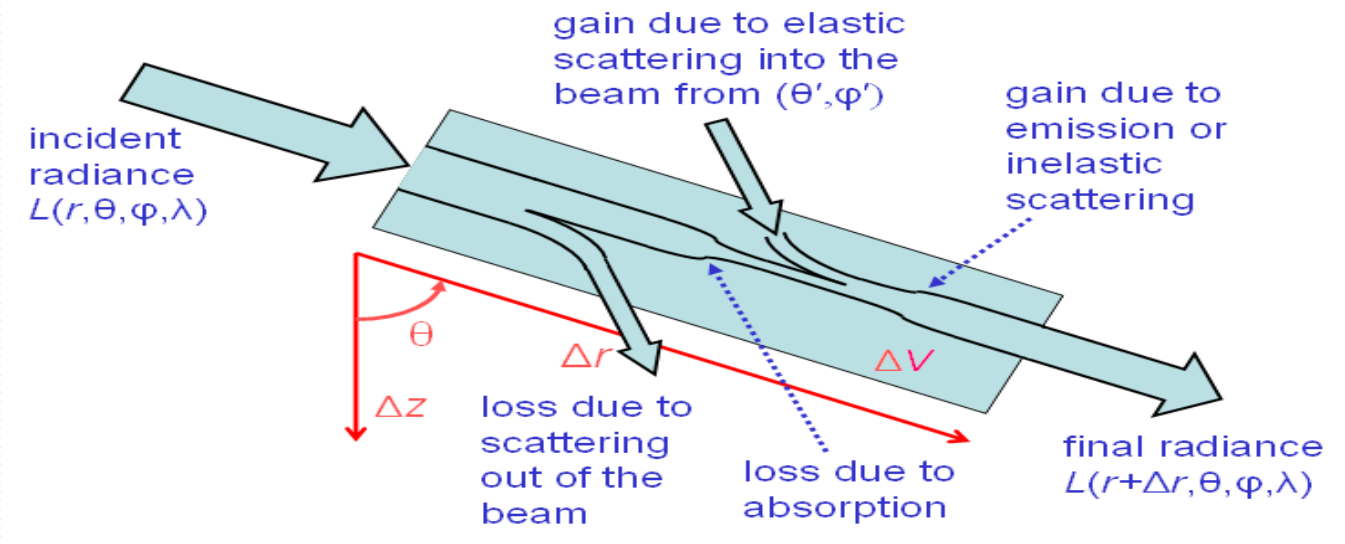
Excerpt from the Proceedings of the 2014 COMSOL Conference in Bangalore

THANK YOU FOR YOUR ATTENTION!

ANY QUESTIONS?

FORWARD PROBLEM

- Radiative transport equation - equation for the radiant intensity
- obtained by balancing the absorption and scatter mechanisms by which the photons can be gained or lost from arbitrary volume considered



- Diffusion approximation to RTE
- If the magnitude of the isotropic fluence within tissue is significantly larger than the directional flux magnitude ,i.e, the light field is 'diffuse'.
- The diffusion approximation in the frequency domain is given by

$$-\nabla.\mathrm{k(r)}\nabla\Phi(\mathrm{r},\omega)+(\mu_a(\mathrm{r})+\frac{i\omega}{c_m(\mathrm{r})})\Phi(\mathrm{r},\omega)=\mathrm{q}_0(\mathrm{r},\omega)$$

$$k=1/3(\mu_a+\mu_s^{/})$$

- The air tissue boundary is represented by an index-mismatched type III condition (also known as Robin or mixed boundary condition)

- The flux leaving the external boundary is equal to the fluence rate at the boundary weighted by a factor that accounts for the internal reflection of light back into the tissue

$$\Phi(\xi,\omega)+2A\hat{n}.k(\xi)\nabla\Phi(\xi,\omega)=0$$

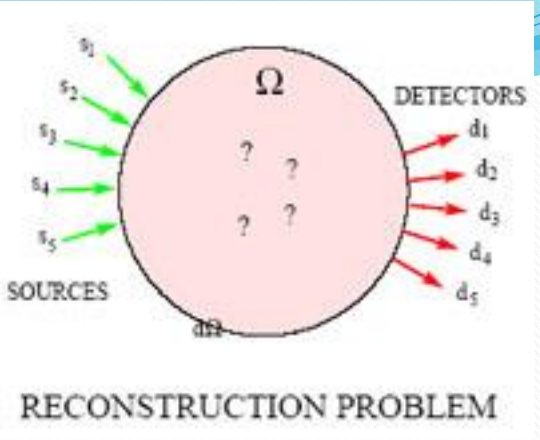
FINITE ELEMENT IMLEMENTATION

- volume, Ω, subdivided D elements joined at V vertex nodes.
- the fluence at a given point, Φ(r) is approximated by the piecewise continuous polynomial function

$$\Phi^h(\mathrm{r})=\sum_1^V \Phi_i u_i(r)\Omega^h$$

- Solution for ϕ(r) becomes a sparse matrix inversion -bi-conjugate gradient stabilized iterative solver .

INVERSE PROBLEM



- recovery of optical properties μ at each FEM node within the domain using measurements of light fluence from the tissue surface.

- inversion can be achieved using a modified-Tikhonov minimization.

$$X^2 = \min_{\mu} \left\{ \sum_{i=1}^{NM} (\Phi_i^M - \Phi_i^C)^2 + \lambda \sum_{j=1}^{NN} \left(\mu_j - \mu_0 \right)^2 \right\}$$

- It has been found that if the initial estimate, μ_0 , is not too far from the actual parameter distribution, second term can be ignored.

- Minimized function given by:

$$X^2 = \left\{ \sum_{i=1}^{NM} (\Phi_i^M - \Phi_i^C)^2 \right\}$$

- the equation for the optical property update is given by

$$\Delta\mu = [\mathrm{J}^T \mathrm{J} + \lambda \mathrm{I}]^{-1} J^T (\Phi^c - \Phi^M)$$

- Where $\left(\frac{\partial \Phi^c}{\partial \mu} \right)$ the Jacobian matrix J.

- λ is the regularisation parameter

- Jacobian, sometimes referred to as the sensitivity or weight matrix, defines the relationship between changes in boundary data, and small changes in optical properties.

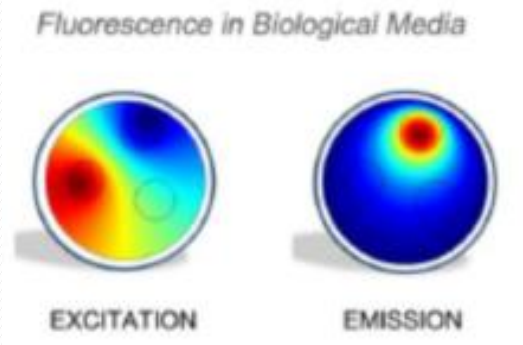
- Uses both amplitude and phase data

$$J = \begin{bmatrix} \frac{\delta \ln I_1}{\delta D_1} & \frac{\delta \ln I_1}{\delta D_2} & \cdots & \frac{\delta \ln I_1}{\delta D_{NN}}; & \frac{\delta \ln I_1}{\delta \mu_{a1}} & \frac{\delta \ln I_1}{\delta \mu_{a2}} & \cdots & \frac{\delta \ln I_1}{\delta \mu_{aNN}} \\ \frac{\delta \theta_1}{\delta D_1} & \frac{\delta \theta_1}{\delta D_2} & \cdots & \frac{\delta \theta_1}{\delta D_{NN}}; & \frac{\delta \theta_1}{\delta \mu_{a1}} & \frac{\delta \theta_1}{\delta \mu_{a2}} & \cdots & \frac{\delta \theta_1}{\delta \mu_{aNN}} \\ \frac{\delta \ln I_2}{\delta D_1} & \frac{\delta \ln I_2}{\delta D_2} & \cdots & \frac{\delta \ln I_2}{\delta D_{NN}}; & \frac{\delta \ln I_2}{\delta \mu_{a1}} & \frac{\delta \ln I_2}{\delta \mu_{a2}} & \cdots & \frac{\delta \ln I_2}{\delta \mu_{aNN}} \\ \frac{\delta \theta_2}{\delta D_1} & \frac{\delta \theta_2}{\delta D_2} & \cdots & \frac{\delta \theta_2}{\delta D_{NN}}; & \frac{\delta \theta_2}{\delta \mu_{a1}} & \frac{\delta \theta_2}{\delta \mu_{a2}} & \cdots & \frac{\delta \theta_2}{\delta \mu_{aNN}} \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ \frac{\delta \ln I_{NM}}{\delta D_1} & \frac{\delta \ln I_{NM}}{\delta D_2} & \cdots & \frac{\delta \ln I_{NM}}{\delta D_{NN}}; & \frac{\delta \ln I_{NM}}{\delta \mu_{a1}} & \frac{\delta \ln I_{NM}}{\delta \mu_{a2}} & \cdots & \frac{\delta \ln I_{NM}}{\delta \mu_{aNN}} \\ \frac{\delta \theta_{NM}}{\delta D_1} & \frac{\delta \theta_{NM}}{\delta D_2} & \cdots & \frac{\delta \theta_{NM}}{\delta D_{NN}}; & \frac{\delta \theta_{NM}}{\delta \mu_{a1}} & \frac{\delta \theta_{NM}}{\delta \mu_{a2}} & \cdots & \frac{\delta \theta_{NM}}{\delta \mu_{aNN}} \end{bmatrix}$$

FLUORESCENCE DIFFUSE OPTICAL TOMOGRAPHY

- Fluorescence diffuse optical tomography (f-DOT) is an attractive component of optical tissue tomography.
- Exogenous fluorophores furnish the desperately needed sensitivity and specificity that is lacking in NIR optical tomography
- Fluorescence tomography methods aim at reconstructing the concentration of fluorophores within the imaged object.
- provide a measure for receptor concentration, gene expression or enzymatic activity

- Fluorophores are illuminated at a particular wavelength and the emission occurs at a different wavelength.

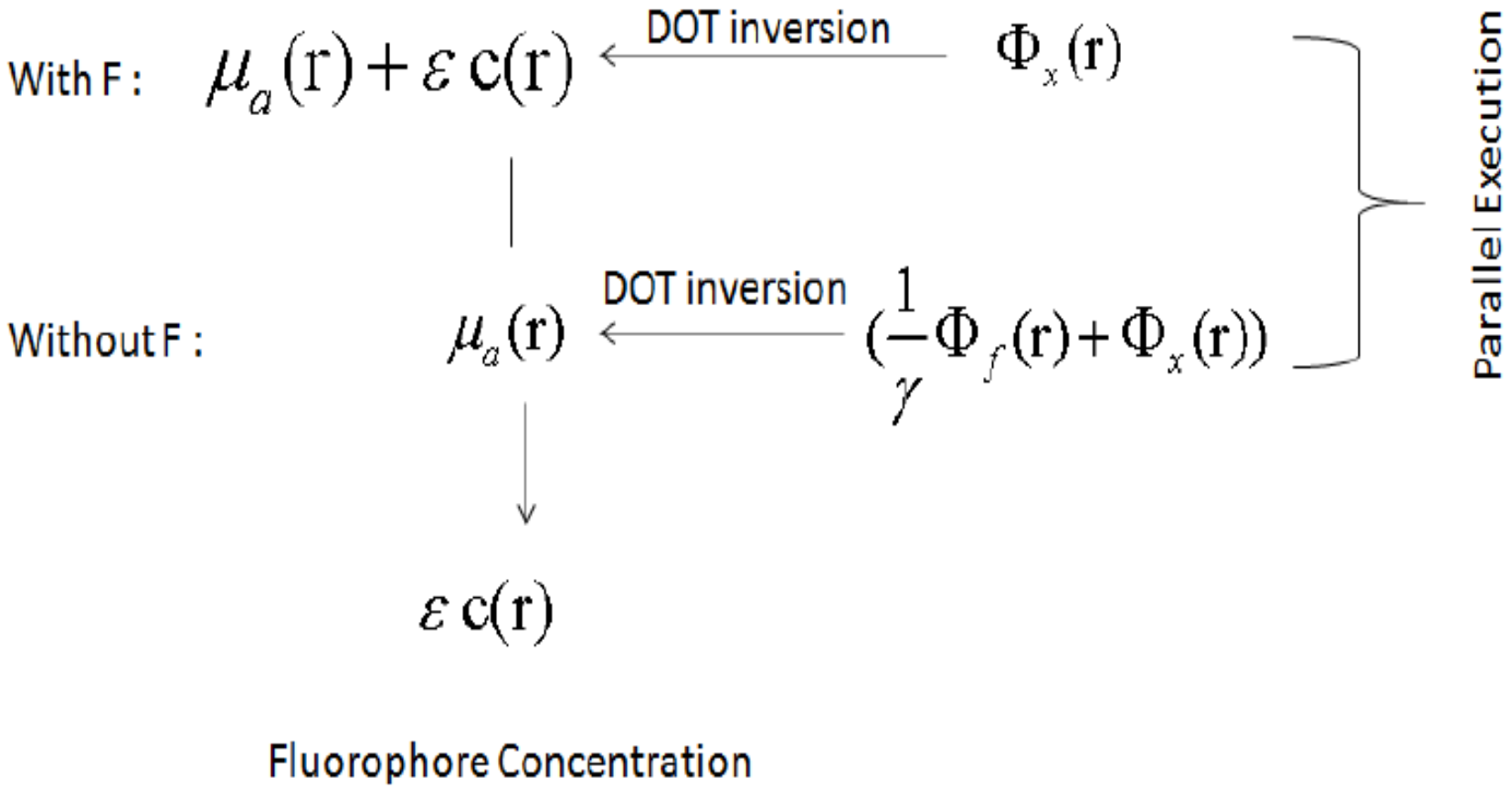


- **INDEPENDENT FORMULATION OF EXCITATION AND EMISSION**
- Fluorochrome within domain Ω increases the absorption at λ by $\varepsilon c(r)$
- excitation wavelength λ x and emission wavelength λm

$$(-\nabla D_x \nabla + \mu_{ax}(\mathrm{r}) + \varepsilon_x\, \mathrm{c}(\mathrm{r}))\Phi_x(\mathrm{r}) = \Theta_s \partial_0 (r - r_s)$$

$$(-\nabla\, \mathrm{D}_m\, \nabla + \mu_{am}(\mathrm{r}))\Phi_f(\mathrm{r}) = \gamma_m \varepsilon_x c(\mathrm{r})\Phi_x(\mathrm{r})$$

PARALLEL INVERSION SCHEME



$$(-\nabla D_x \nabla + \mu_{ax}(\mathrm{r}) + \varepsilon_x\, \mathrm{c}(\mathrm{r}))\Phi_x(\mathrm{r}) = \Theta_s \partial_0 (r - r_s)$$

$$(-\nabla D \nabla + \mu_a(\mathrm{r}))(\frac{1}{\gamma}\Phi_f(\mathrm{r}) + \Phi_x(\mathrm{r})) = \Theta_s \delta_0(\mathrm{r} - \mathrm{r}_s)$$