Inverse transport problems in quantitative PAT for molecular imaging

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Presentation Outline

Photoacoustic Tomography(PAT)

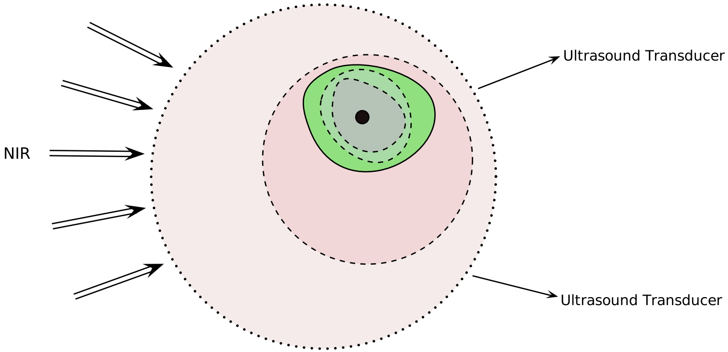

Figure : Photoacoustic Tomography: To recover scattering, absorption and photoacoustic efficiency properties of tissues from boundary measurement of acoustic signal generated with the photoacoustic effect. Two processes: propagation of NIR radiation and propagation of ultrasound. There is a (time) scale separation between the two processes.

Regular PAT workflow

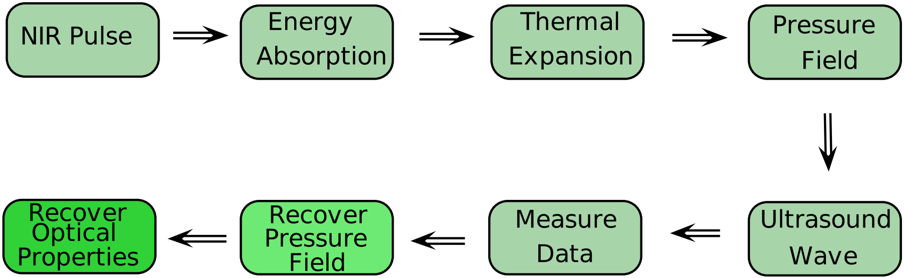

Figure : Workflow chart of both physical process during PAT and regular inversion process

Photon Transport Process

Let $\Omega \subset \mathbb{R}^d$ be the domain of medium, and denote $\mathbb{S}^{d-1}$ as unit sphere in $\mathbb{R}^d$. Then the time-integrated(accumulative) equation of photon density $\psi(\mathbf{v}, \mathbf{x})$ along unit direction $\mathbf{v}$ satisfies

$$\mathbf{v} \cdot \nabla \psi(\mathbf{v}, \mathbf{x}) + \sigma_t(\mathbf{x})\psi(\mathbf{v}, \mathbf{x}) = \sigma_s(\mathbf{x}) K_\Theta(\psi)(\mathbf{v}, \mathbf{x}) \tag{1}$$

with incoming boundary condition

$$\psi|_{\Gamma_-} = g(\mathbf{v}, \mathbf{x}) \tag{2}$$

where $\Gamma_- = \{(\mathbf{v}, \mathbf{x}) \in \mathbb{S}^{d-1} \times \partial\Omega, (\mathbf{n}, \mathbf{v}) < 0\}$ and σ_a, σ_s are absorption and scattering coefficients resp.

Remark

Sometimes, we can use diffusion equation to approximate the process when scattering coefficient dominates absorption.

Photon Transport Process

The scattering operator K_Θ is formulated as

$$K_\Theta(\psi)(\mathbf{v}, \mathbf{x}) = \int_{\mathbb{S}^{d-1}} \Theta(\mathbf{v}', \mathbf{v})\psi(\mathbf{v}', \mathbf{x})d\mathbf{v}' \tag{3}$$

where the probability kernel $\Theta(\mathbf{v}', \mathbf{v})$ is symmetric and normalized that

$$\int_{\mathbb{S}^{d-1}} \Theta(\mathbf{v}', \mathbf{v})d\mathbf{v}' = 1 \tag{4}$$

Photoacoustic Effect

1. The medium absorbs part of the energy of NIR photons, generate initial pressure field $H(\mathbf{x})$ through photoacoustic effect.

$$H(x) = \gamma(\mathbf{x})\sigma_a(\mathbf{x}) \int_{\mathbb{S}^{d-1}} \psi(\mathbf{v}, \mathbf{x}) d\mathbf{v} = \gamma(\mathbf{x})\sigma_a(\mathbf{x}) K_I(\psi) \tag{5}$$

2. $\gamma(x)$ is Grüneisen coefficient, measures the efficiency of photoacoustic effect(energy $\rightarrow$ pressure).

Acoustic Wave Propagation

The initial pressure field generates acoustic wave(ultrasound),

$$\frac{1}{c^2(\mathbf{x})} p_{tt} - \Delta p = 0 \tag{6}$$

$$p(0, \mathbf{x}) = H(x) = \gamma(\mathbf{x})\sigma_a(\mathbf{x})K_I(\psi) \tag{7}$$

$$p_t(0, \mathbf{x}) = 0 \tag{8}$$

during the photoacoustic process, wave speed $c(\mathbf{x})$ is assumed to be unchanged.

Measurement of PAT and Inversion

1. We measure the pressure field(ultrasound signal) on the surface $\Sigma = \partial\Omega$ of domain for sufficient long time T

$$m(t, \mathbf{x}) = p(t, \mathbf{x})|_{[0,T]\times\Sigma} \tag{9}$$

2. The objective of PAT is to recover information of $\gamma(\mathbf{x})$, $\sigma_a(\mathbf{x})$ and $\sigma_s(\mathbf{x})$.
3. The regular reconstruction process is illustrated as following

$$m(t, \mathbf{x}) \to H(\mathbf{x}) \to (\gamma, \sigma_a, \sigma_s) \tag{10}$$

Reconstruction of $H(\mathbf{x})$

The inversion process from $m(t, \mathbf{x}) \to H(\mathbf{x})$, there are plenty of literatures on this topic.

1. case $c \equiv 1$, for some geometry(e.g. sphere, plane), there is explicit formula to reconstruct, we can use time reversal to reconstruct.
2. case $c = c(\mathbf{x})$ variable speed, time reversal can provide an approximation of H, assuming all waves are gone when T sufficiently large. Ulhmann and Stefanov showed that error operator of time reversal is actually a contraction and provides a Neumann series approach.

Reconstruction of $(\gamma, \sigma_a, \sigma_s)$

The quantitative PAT(qPAT) step is to reconstruct one or more coefficients of $(\gamma, \sigma_a, \sigma_s)$ using internal data.

$$\mathbf{v} \cdot \nabla u(v, x) + (\sigma_a + \sigma_s) u(v, x) \; = \; \sigma_s K_\Theta(u)(v, x) \tag{11}$$

with incoming boundary condition on Γ_-

$$u(v, x) \; = \; g(v, x) \tag{12}$$

internal data is

$$H(x) = \gamma(x) \sigma_a(x) K_I(u) \tag{13}$$

Reconstruction of $(\gamma, \sigma_a, \sigma_s)$

Theorem (Bal-Jollivet-Jugnon, 10)

If γ is known, then the following map

$$\Lambda : g(v, x) \rightarrow H(x)$$

uniquely determines (σ_a, σ_s).

Theorem (Mamonov-Ren, 14)

We can reconstruct any two of the $(\gamma, \sigma_a, \sigma_s)$ if the third is known and Λ is provided(similar result in diffusion regime, when σ_a is small and σ_s is large w.r.t domain size).

Presentation Outline

Introduction to fPAT

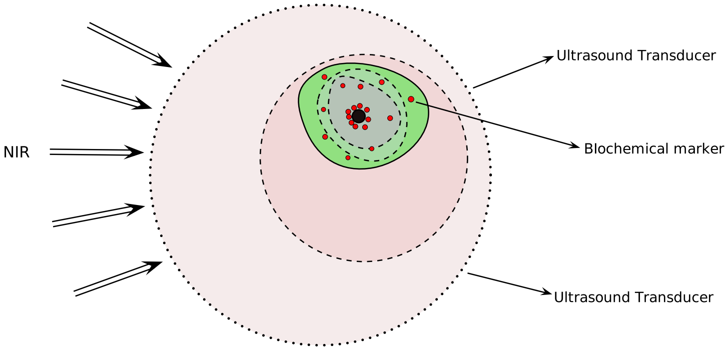

Figure : Fluorescence Generation: fluorescent biochemical markers are injected into medium(e.g. tissue), and the markers(probes) will travel inside the medium and accumulate on target(e.g. cancer tissue).

Introduction to fPAT

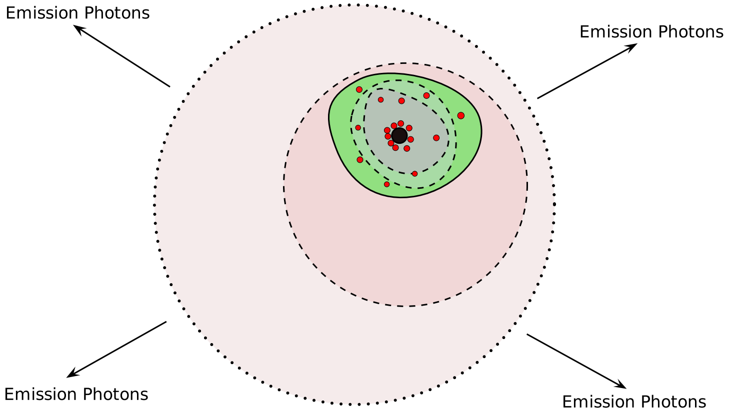

Figure : we send NIR photons with specific wavelength λ_x into the medium to excite the markers, fluorescent markers will emit NIR photons with a different wavelength λ_m, the energy will come from both excitation and emission photons.

Photon Transport Process for fPAT

Let $u_x(x, v)$ and $u_m(x, v)$ be density of photons at excitation and emission wavelengths at $x \in \Omega$, traveling along $v \in \mathbb{S}^{d-1}$.

$$\begin{aligned} v \cdot \nabla u_x(x, v) + (\sigma_{a,x} + \sigma_{s,x}) u_x(x, v) &= \sigma_{s,x} K_\Theta(u_x) \\ v \cdot \nabla u_m(x, v) + (\sigma_{a,m} + \sigma_{s,m}) u_m(x, v) &= \sigma_{s,m} K_\Theta(u_m) + \eta \sigma_{a,xf}(x) K_I(u_x) \\ u_x(x, v) = g_x(x, v), \qquad u_m(x, v) &= 0, \text{ on } \Gamma_- \end{aligned}$$

x and m denotes the associated variable with excitation and emission wavelengths respectively. $\sigma_{a,x}$ and $\sigma_{s,x}$(resp. $\sigma_{a,m}$ and $\sigma_{s,m}$) are absorption and scattering coefficients at wavelength λ_x(resp. λ_m).

Photon Transport Process for fPAT

1. The scattering operator K_Θ and K_I are defined as

$$K_\Theta u_x(x,v) = \int_{\mathbb{S}^{d-1}} \Theta(v,v')u_x(x,v')dv' \quad (14)$$

$$K_I u_x(x,v) = \int_{\mathbb{S}^{d-1}} u_x(x,v')dv' \quad (15)$$

2. The total absorption coefficient $\sigma_{a,x}$ consists of two parts: $\sigma_{a,xi}$ from intrinsic tissue chromophores and $\sigma_{a,xf}$ from fluorophores of markers.

$$\sigma_{a,x} = \sigma_{a,xi} + \sigma_{a,xf}$$

$\eta(x)$ is quantum efficiency of the fluorophores.

The coefficients η and $\sigma_{a,xf}$ are the main quantities associated with the biochemical markers.

Photon Transport Process for fPAT

The energy absorbed by the medium and markers comes from two parts : $\sigma_{a,x} K_I(u_x)$ from excitation photons and $\sigma_{a,m} K_I(u_m)$ from emission photons. The pressure field generated by the photoacoustic effect is

$$
\begin{aligned}
H(x) &= \Xi(x)\left[(\sigma_{a,x} - \eta\sigma_{a,xf})K_I(u_x) + \sigma_{a,m}K_I(u_m)\right] \\
&= \Xi(x)\left[\sigma^{\eta}_{a,x}K_I(u_x) + \sigma_{a,m}K_I(u_m)\right]
\end{aligned}
$$

where $\Xi(x)$ is Grüneisen coefficient that measures the photoacoustic efficiency.

Inversion for fPAT

Our goal is to reconstruct fluorescent marker related properties $\eta, \sigma_{a,xf}$ from measured boundary data $p|_{\partial\Omega\times[0,T]}$.

From regular PAT reconstruction process, we assume $H(x)$ is recovered from the boundary data.

Also, we assume

1. Grüneisen coefficient Ξ,
2. medium absorption and scattering coefficients at λ_x, i.e. $\sigma_{a,xi}$, $\sigma_{s,x}$,
3. medium absorption and scattering coefficients at λ_m, i.e. $\sigma_{a,m}$, $\sigma_{s,m}$

and are recovered from other imaging techniques.

Presentation Outline

Reconstruction of single coefficient η

Assuming $\sigma_{a,xf}$ is known. It is a linear inverse source problem. Only one measurement is needed. We conclude uniqueness and stability argument as following

Theorem (Uniqueness and Stability)

Assuming $g_x \in L^p(\Gamma_-)$ guarantee the solution u_x such that $K_I(u_x) \geqslant \hat{c} > 0$ for any admissible pair of $(\eta, \sigma_{a,xf})$. Let $H, \tilde{H}$ be two data sets associated with coefficients $(\eta, \sigma_{a,xf})$ and $(\tilde{\eta}, \sigma_{a,xf})$ resp. Then $H = \tilde{H}$ implies $\eta = \tilde{\eta}$, moreover,

$$c\|H - \tilde{H}\|_{L^p(\Omega)} \leqslant \|(\eta - \tilde{\eta})\sigma_{a,xf} K_I(u_x)\| \leqslant C\|H - \tilde{H}\|_{L^p(\Omega)}$$

Reconstruction of single coefficient η

Numerically, we reconstruct η by

1. using known $\sigma_{a,xf}$ to solve u_x from the first transport equation.
2. evaluate source $q(x) = \sigma_{a,x} K_I(u_x) - \frac{H}{\Xi}$
3. solve transport equation for u_m

$$v \cdot \nabla u_m + (\sigma_{a,m} + \sigma_{s,m}) u_m = (\sigma_{a,m} + \sigma_{s,m}) K_{\tilde{\Theta}}(u_m) + q(x)$$

4. reconstruct $\eta = -\left(\frac{H}{\Xi} - \sigma_{a,x} K_I(u_x) - \sigma_{a,m} K_I(u_m)\right) / (\sigma_{a,xf} K_I(u_x))$

here $\tilde{\Theta}$ is a linear interpolation of I and Θ,

$$\tilde{\Theta} = \frac{\sigma_{a,m}}{\sigma_{t,m}} + \frac{\sigma_{s,m}}{\sigma_{t,m}} \Theta$$

Reconstruction of single coefficient $\sigma_{a,xf}$

Now assume η is known.It is nonlinear problem about $\sigma_{a,xf}$. We still can show that

Theorem (Uniqueness and Stability)

Let g_x be the boundary such that $K_I(u_x) = u_x \geqslant \hat{c} > 0$ for some $\hat{c}$ for any admissible pair $(\eta, \sigma_{a,xf})$. Let H and $\tilde{H}$ are two data sets associated with coefficients pairs $(\eta, \sigma_{a,xf})$ and $(\eta, \tilde{\sigma}_{a,xf})$ resp. Then $H = \tilde{H}$ implies $\sigma_{a,xf} = \tilde{\sigma}_{a,xf}$. Moreover,

$$c\|H - \tilde{H}\|_{L^p(\Omega)} \leqslant \|(\sigma_{a,xf} - \tilde{\sigma}_{a,xf})K_I(u_x)\|_{L^p(\Omega)} \leqslant C\|H - \tilde{H}\|_{L^p(\Omega)}$$

Reconstruction of single coefficient $\sigma_{a,xf}$: linearized case

We can derive the following modified transport system

$$v \cdot \nabla v_x + \sigma_{t,x} v_x + \sigma'_{s,xm} K_I(v_m) = \sigma_{s,x} K_\Theta(v_x) + \sigma'_{s,x} K_I(v_x) - \frac{u_x H'_\sigma}{(1-\eta)\Xi K_I(u_x)}$$

$$v \cdot \nabla v_m + \sigma_{t,m} v_m + \sigma'_{s,m} K_I(v_m) = \sigma_{s,m} K_\Theta(v_m) + \sigma'_{s,mx} K_I(v_x) + \frac{\eta H'_\sigma}{(1-\eta)\Xi}$$

where we have performed transform $v_x \to -v_x$ in the first equation. And $\sigma'_{s,x} = \frac{\sigma^\eta_{a,x} u_x}{(1-\eta) K_I(u_x)}$, $\sigma'_{s,xm} = \frac{\sigma_{a,m} u_x}{(1-\eta) K_I(u_x)}$, $\sigma'_{s,m} = \frac{\eta \sigma_{a,m}}{1-\eta}$, $\sigma'_{s,mx} = \frac{\eta \sigma_{a,xi}}{1-\eta}$ are known for background solution.

Reconstruction of single coefficient $\sigma_{a,xf}$: linearized case

Numerically, we can reconstruct $\sigma_{a,xf}$ through

1. solve u_x with background $\sigma_{a,xf}$ and evaluate $K_I(u_x)$ and H'_σ,
2. evaluate coefficients $\sigma'_{s,x}$, $\sigma'_{s,xm}$, $\sigma'_{s,m}$, $\sigma'_{s,mx}$.
3. solve the modified transport system for (v_x, v_m) and perform transform $v_x \to -v_x$.
4. reconstruct perturbation $\delta\sigma_{a,xf} = [\frac{H'_\sigma}{\Xi} - \sigma^{\eta}_{a,x} K_I(v_x) - \sigma_{s,m} K_I(v_m)]/[(1-\eta)K_I(u_x)]$

Presentation Outline

Reconstruction of both η and $\sigma_{a,xf}$

The first special case is the linearized case for small coefficients perturbed around $(0,0)$. We can observe that background solution $v_m = 0$ because of vanished source.

$$\frac{1}{\Xi} H'[0,0](\delta\eta, \delta\sigma_{a,xf}) = \delta\sigma_{a,xf} K_I(u_x) + \sigma_{a,xi} K_I(v_x)$$

where v_x satisfies

$$v \cdot \nabla v_x + \sigma_{t,x} v_x = \sigma_{s,x} K_\Theta(v_x) - \delta\sigma_{a,xf} u_x$$

we can see that perturbation of $\delta\eta$ does not show up, thus η is not possible to be recovered.

Reconstruction of both η and $\sigma_{a,xf}$

Moreover, regarding $\sigma_{a,xf}$, we have

Theorem (Uniqueness and Stability)

Let $H'[0,0]$ and $\tilde{H}'[0,0]$ be perturbed data sets as above. Then we have uniqueness and stability argument,

$$c\|H'[0,0]-\tilde{H}'[0,0]\| \leqslant \|(\delta\sigma_{a,xf}-\widetilde{\delta\sigma_{a,xf}})K_I(u_x)\| \leqslant C\|H'[0,0]-\tilde{H}'[0,0]\|$$

under $L^p(\Omega)$ norm.

Reconstruction of both η and $\sigma_{a,xf}$: Linearized Model

Now we look at linearized case with general background($\eta \neq 0$, $\sigma_{a,xf} \neq 0$). We have multiple data sets, $H_1, \dots, H_J$, $J \geqslant 2$, $1 \leqslant j \leqslant J$,

$$\frac{H_j'[\eta, \sigma_{a,xf}](\delta\eta, \delta\sigma_{a,xf})}{\Xi K_I(u_x^j)} =$$

$$(-\delta\eta\sigma_{a,xf} + (1-\eta)\delta\sigma_{a,xf}) + \frac{\sigma_{a,x}^{\eta}}{K_I(u_x^j)} K_I(v_x^j) + \frac{\sigma_{a,m}}{K_I(u_x^j)} K_I(v_m^j)$$

taking variables $\zeta = \delta(\eta\sigma_{a,xf})$ and $\xi = \delta\sigma_{a,xf}$, we have following system.

$$\Pi \begin{pmatrix} \xi \\ \zeta \end{pmatrix} = z = \begin{pmatrix} \frac{H_1'(\delta\eta, \delta\sigma_{a,xf})}{\Xi K_I(u_x^1)} \\ \cdots \\ \frac{H_J'(\delta\eta, \delta\sigma_{a,xf})}{\Xi K_I(u_x^J)} \end{pmatrix}$$

where element of Π satisfy $\Pi_{j,1} = -Id + \Pi_\zeta^j$, $\Pi_{j,2} = -Id + \Pi_\xi^j$, Π_ζ^j and Π_ξ^j are compact operators on $L^2(\Omega)$.

Reconstruction of both η and $\sigma_{a,xf}$: Partially linearized Model

In fluorescence optical tomography, it is popular to approximate $\sigma_{a,x}$ by $\sigma_{a,xi}$, since $\sigma_{a,xf}$ is small compared to $\sigma_{a,xi}$.

$$\begin{aligned} v \cdot \nabla u_x^j(x,v) + (\sigma_{a,xi} + \sigma_{s,x}) u_x^j(x,v) &= \sigma_{s,x} K_\Theta(u_x^j) \\ v \cdot \nabla u_m^j(x,v) + (\sigma_{a,m} + \sigma_{s,m}) u_m^j(x,v) &= \sigma_{s,m} K_\Theta(u_m^j) + \eta\sigma_{a,xf}(x) K_I(u_x^j) \\ u_x^j(x,v) = g_x^j(x,v), \qquad & u_m^j(x,v) = 0, \text{ on } \Gamma_- \end{aligned}$$

this permits us to compute u_x^j directly from first equation and data can be simplified as $\widehat{H}_j = \frac{H_j}{\Xi K_I(u_x^j)} - \sigma_{a,xi} = (1-\eta)\sigma_{a,xf} + \frac{\sigma_{a,m}}{K_I(u_x^j)} K_I(u_m^j)$. Taking new variables $\zeta = (1-\eta)\sigma_{a,xf}$ and $\xi = \sigma_{a,xf}$, we have similar result:

$$\Pi = \begin{pmatrix} Id - \Pi_\zeta^1 & \Pi_\xi^1 \\ \cdots & \cdots \\ Id - \Pi_\zeta^J & \Pi_\xi^J \end{pmatrix}, z = \begin{pmatrix} \widehat{H}_1 \\ \cdots \\ \widehat{H}_J \end{pmatrix}$$

Regularized inversion with two data sets

when $J = 2$, we regularize the matrix operator Π by

$$\Pi_\alpha = \Pi + \begin{pmatrix} 0 & 0 \\ 0 & \alpha I \end{pmatrix}$$

where $\alpha > 0$.

Theorem

Let z and $\tilde{z}$ be two perturbed data sets associated with Π(either linearized model or partial linearized model).Let (ζ, ξ) and $(\tilde{\zeta}, \tilde{\xi})$ be solutions to $\Pi_\alpha(\zeta, \xi)^t = z$ and $\Pi_\alpha(\tilde{\zeta}, \tilde{\xi})^t = \tilde{z}$ resp. for some α, then

$$c\|z - \tilde{z}\| \leqslant \|(\zeta - \tilde{\zeta}, \xi - \tilde{\xi})\|_{L^2(\Omega)\times L^2(\Omega)/\mathcal{N}(\Pi_\alpha)} \leqslant C\|z - \tilde{z}\|$$

where $\mathcal{N}(\Pi_\alpha)$ is null space of Π_α.

Reconstruction of both coefficients

For linearized cases, we can adopt Landweber iteration method by

$$\begin{pmatrix} \zeta_{k+1} \\ \xi_{k+1} \end{pmatrix} = (I - \tau \Pi^* \Pi) \begin{pmatrix} \zeta_k \\ \xi_k \end{pmatrix} + \tau \Pi^* z$$

For non-linearized case, we use L^2 optimization, minimizing following objective functional,

$$\Phi(\eta, \sigma_{a,xf}) = \frac{1}{2} \sum_{j=1}^{J} \int_\Omega \{\Xi[\sigma_{a,x}^{\eta} K_I(u_x^j) + \sigma_{a,m} K_I(u_m^j)] - H_j\}^2 dx + \beta R(\eta, \sigma_{a,xf})$$

where $R(\eta, \sigma_{a,xf}) = \frac{1}{2}\left(\|\nabla \eta\|^2 + \|\nabla \sigma_{a,xf}\|^2\right)$.

We solve this optimization problem by using gradient-based optimization method, such as quasi-Newton(BFGS) and applying adjoint state technique.

Numerical results

Reconstruct single coefficient η with known $\sigma_{a,xf}$.

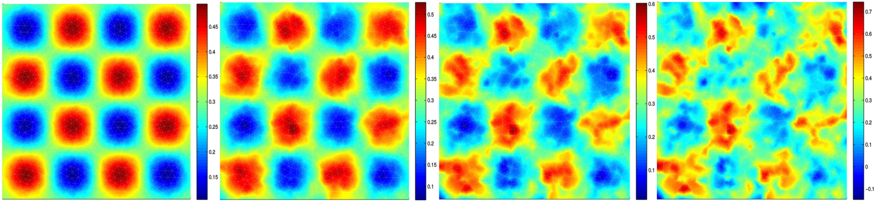

Figure : The quantum efficiency η reconstructed with different types of data. The noise levels in the data used for the reconstructions, from left to right are $\gamma = 0, 2, 5$ and 10 respectively. The base scattering strength is $\sigma_s^b = 1.0$. The relative L^2 errors in the four reconstructions are 0.01%, 6.42%,16.06% and 32.12% respectively.

Numerical results

Reconstruct single coefficient $\sigma_{a,xf}$ with η known.

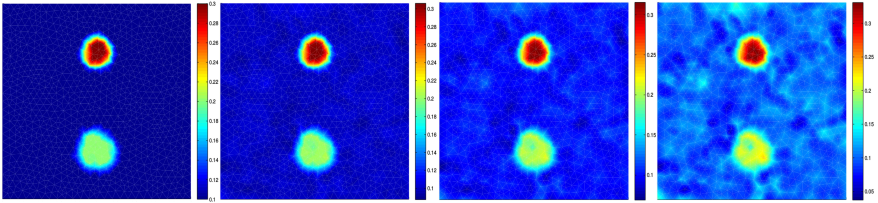

Figure : The fluorescence absorption coefficient $\sigma_{a,xf}$ reconstructed with different types of data. The noise level in the data used for the reconstructions, from left to right are: $\gamma = 0$ (noise-free), $\gamma = 2$, $\gamma = 5$, and $\gamma = 10$. The base scattering strength is $\sigma_s^b = 1.0$. The relative L^2 errors are 0.02%,6.70%,16.74% and 33.42%, respectively.

Numerical results

Reconstruction of both coefficients in non-linear setting.

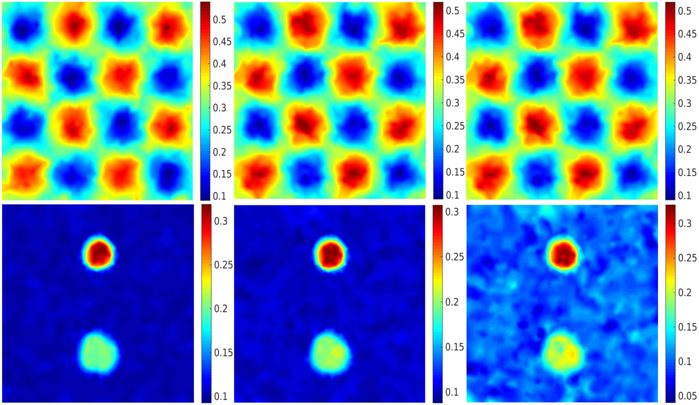

Figure : Simultaneous reconstruction of the coefficient pair $(\eta, \sigma_{a,xf})$ in the nonlinear setting with different types of data. The noise level in the data used for the reconstructions, from left to right, are respectively $\gamma = 0$, 1 and 2.

Questions ?

Questions?