Quantitative Photoacoustic Tomography with Two-photon Absorption

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Presentation Outline

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Photoacoustic Tomography (PAT)

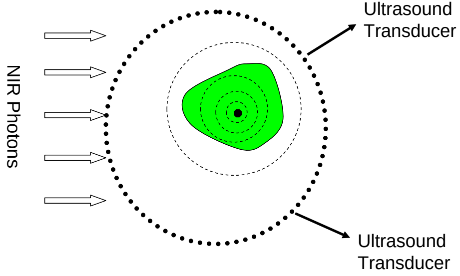

Figure 1: Photoacoustic Tomography (PAT) combines diffuse optical tomography with ultrasound imaging using the photoacoustic effect. The object to be probed is illuminated by a short pulse of NIR light and absorbs energy which is converted into an ultrasound pressure field. The waves propagate outwards and are detected by ultrasonic devices.

PAT: Diffusion of Photons as in OT

- The density of photons $u(\mathbf{x})$ solves the diffusion equation:

$$\begin{aligned} -\nabla\cdot\gamma(\mathbf{x})\nabla u(\mathbf{x})+\sigma(\mathbf{x})u(\mathbf{x}) &= 0 \quad \text{in } \Omega \\ u &= g(\mathbf{x}) \quad \text{on } \partial\Omega \end{aligned}$$

- The initial pressure field generated though photoacoustic effect at $\mathbf{x}\in\Omega$ is given by:

$$H(\mathbf{x})=\Gamma(\mathbf{x})\sigma(\mathbf{x})u(\mathbf{x})$$

- The Grüneisen coefficient Γ measures the efficiency of the photoacoustic effect in the medium.

PAT: Acoustic Field

- The acoustic wave equation for the pressure field:

$$\begin{aligned} \frac{1}{c^2(\mathbf{x})}\frac{\partial^2 p}{\partial t^2} - \Delta p &= 0, && \text{in } \mathbb{R}_+ \times \mathbb{R}^d \\ p(0,\mathbf{x}) &= H \equiv \Gamma(\mathbf{x})\sigma(\mathbf{x})u(\mathbf{x}), && \text{in } \mathbb{R}^d \\ \frac{\partial p}{\partial t}(0,\mathbf{x}) &= 0, && \text{in } \mathbb{R}^d \end{aligned}$$

- It turns out that change of optical properties has very small impact on ultrasound wave speed $c(\mathbf{x})$. Thus the coupling between the diffusion and acoustic process is only through the initial pressure field.
- The ultrasound wave speed field $c(\mathbf{x})$ is usually assumed *known*.

PAT: Data and Reconstruction

- Measured data: We measure $p(t, \mathbf{x})_{|(0,t_{\max})\times\Sigma}$ for $t_{\max}$ large and $\Sigma \subset \partial\Omega$.
- Objective: To reconstruct Γ, $\sigma(\mathbf{x})$ and $\gamma(\mathbf{x})$ from measured data.

- Two-step Reconstruction:
  - Step I: to reconstruct the initial pressure field H from measured acoustic data by solving an inverse source problem to the acoustic wave equation (by for instance time reversal); This is a relatively "stable" process.

  - Step II: to reconstruct Γ, σ and γ from the *internal* data H by solving the inverse coefficient problem to the diffusion equation. This is also a "stable" process.

Photoacoustic Tomography (PAT)

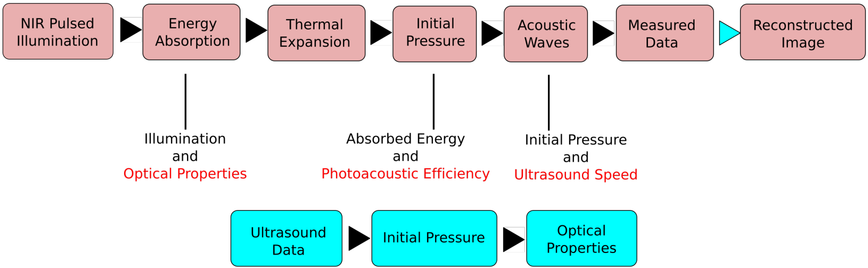

Figure 2: Two physical process in PAT: diffusion of NIR radiation and propagation of ultrasound. Time scale separation between the two processes due to the fact that photons travel much faster than ultrasound signals.

PAT: Acoustic Reconstructions

- The case $c = 1$ has been studied by many authors: Agranovsky, Ambartsoumian, Ammari, Anastasio, Arridge, Finch, Haltmeier, Kuchment, Kunyansky, Nguyen, Patch, Quinto, Rakesh, Scherzer, Wang, and many more.
- The case of $c = c(\mathbf{x})$ is much more complicated, and has been studied in: Acosta-Montalto IP 15, Hristova-Kuchment-Nguyen IP 08, Hristova IP 09, Qian-Stefanov-Uhlmann-Zhao SIAM 11, Stefanov-Uhlmann IP 09, Stefanov-Uhlmann TAMS 12, Stefanov-Yang IP 15, Tittelfitz IP12 (elastic media), and more.
- Acoustic attenuation effects can also be considered: Ammari-Bretin-Jugnon-Wahab-LNM11, Haltmeier etal SPIE07, Kowar-Scherzer-LNM12, La Riviére-Zhang-Anastasio OL06, Patch-Greenleaf 06, Treeby-Zhang-Cox IP10.

PAT: Optical Reconstructions

- There were many computational results on optical reconstructions in PAT in the earlier years: Cox-Arridge-Köstli-Beard AO 06, Laufer-Cox-Zhang-Beard AO 10, Zemp AO 10, etc.

- The first systematic mathematical analysis of optical reconstruction in PAT was done by in Bal-Uhlmann IP 10 where $\Gamma = 1$ is assumed. There have been many subsequent studies: Alessandrini *et al* arXiv 15, Ammari-Bossy-Jugnon-Kang, SIAM Rev 10, Bal-Uhlmann CPAM 13, Bal-R. CM 11, Gao-Osher-Zhao LNM12, R.-Gao-Zhao SIIMS 13, Naetar-Scherzer SIIMS 15, Pulkkinen-Cox-Arridge-Kaipio-Tarvainen IP 14, R.-Zhao SIIMS 13, Shao-Cox-Zemp AO 11, Triki IP 10, etc.

PAT: Optical Reconstructions

- It was shown in Bal-R. IP 11 that only two of the three coefficients (Γ, σ, γ) can be reconstructed uniquely when data from only a single optical wavelength are used. Multi-wavelength data indeed allow the reconstruction of (Γ, σ, γ) in simplified settings as shown in Bal-R. IP 12.
- The same inverse problem in the transport regime has been studied in Bal-Jollivet-Jugnon IP 10, Cox-Tarvainen-Arridge CM 11, Mamonov-R. CMS 14, R.-Zhang-Zhong IP15, Saratoon-Tarvainen-Cox-Arridge, IP 13 etc.

PAT with Two-photon Absorption

- The principle of two-photon PAT (TP-PAT) is the same as that of the regular PAT, except that the photoacoustic signals in TP-PAT are induced via two-photon absorption in addition to the usual single-photon absorption.

- Here by two-photon absorption we mean the phenomenon that an electron transfers to an excited state after simultaneously absorbing two photons whose total energy exceed the electronic energy band gap.

PAT with Two-photon Absorption

- The main motivation for developing two-photon PAT is that the two-photon optical absorption can often be tuned to be associated with specific molecular signatures, such as in stimulated Raman PAM, to achieve label-free molecular imaging. Therefore, TP-PAT is molecular imaging modality that aims at visualizing particular cellular functions and molecular processes inside biological tissues.

- Several groups have experimentally studied TP-PAT: Y.-H. Lai *et al* OE 14, G. Langer *et al* OE 13, V. Ntziachristos *et al* OL 14, B. Urban *et al* JBO 14, P. Winter *et al* Optica 14, Y. Yamaoka *et al* OE 11, Yelleswarapu-Kothapalli OE 10. Reconstructions are so far limited in the acoustic step.

PAT with Two-photon Absorption

- The density of NIR inside the medium, say Ω, solves the following nonlinear diffusion equation:

$$\begin{array}{rcll} -\nabla \cdot \gamma(\mathbf{x})\nabla u(\mathbf{x}) + \sigma(\mathbf{x})u(\mathbf{x}) + \mu(\mathbf{x})|u|u(\mathbf{x}) & = & 0, & \text{in } \Omega \\ u(\mathbf{x}) & = & g(\mathbf{x}), & \text{on } \partial\Omega \end{array}$$

  where the coefficients $\sigma(\mathbf{x})$ and $\mu(\mathbf{x})$ denote the single-photon and the two-photon absorption coefficients respectively, and $\gamma(\mathbf{x})$ is diffusion coefficient, and g is the incoming photon source.
- The initial pressure field that is generated in TP-PAT is given by

$$H(\mathbf{x}) = \Gamma(\mathbf{x})\Big[\sigma(\mathbf{x})u(\mathbf{x}) + \mu(\mathbf{x})u^2(\mathbf{x})\Big], \qquad \mathbf{x} \in \Omega.$$

Presentation Outline

The Forward Model

- Recall that the semilinear diffusion model for TP-PAT

$$\begin{aligned} -\nabla\cdot\gamma(\mathbf{x})\nabla u(\mathbf{x}) + \sigma(\mathbf{x})u(\mathbf{x}) + \mu(\mathbf{x})|u|u(\mathbf{x}) &= 0, \quad \text{in } \Omega \\ u(\mathbf{x}) &= g(\mathbf{x}), \quad \text{on } \partial\Omega \end{aligned}$$

- To establish simiar uniqueness and stability results as in the regular PAT case, we want the solution to this diffusion equation to: i) be bounded; ii) be positive for positive g; and iii) have (strong) comparison principle.

- If we have i) - iii), we can show that $g \geq \varepsilon > 0 \implies u \geq \varepsilon' > 0$. This is a critical result.

The Forward Model

To simplify the notations, let:

$$\mathcal{L}u = \nabla \cdot (\gamma \nabla u),$$
$$\mathcal{Q}u = \nabla \cdot (\gamma \nabla u) - \sigma u - \mu |u| u.$$

We assume:

- The domain Ω is smooth enough and satisfies exterior cone condition;
- The boundary source $g \in C^0(\partial\Omega)$ or better when needed;
- The coefficients:

$$0 < \theta \le \Gamma, \gamma, \sigma, \mu \le \Theta < \infty.$$

It is clear that the linear differential operator $-\mathcal{L}$ is uniformly elliptic.

The Forward Model

Let $\mathcal{A} = \{w \in W^{1,2}(\Omega) | w = g \text{ on } \partial\Omega\}$, we define the following Lagrangian for any $w \in \mathcal{A}$,

$$I[w] = \int_\Omega L(Dw, w, \mathbf{x}) d\mathbf{x} = \int_\Omega \frac{1}{2}\gamma|\nabla w|^2 + \frac{1}{2}\sigma w^2 + \frac{1}{3}\mu|w|w^2 d\mathbf{x},$$
$$w = g \quad \text{on } \partial\Omega.$$

It is straightforward to verify that $I[w]$ is strictly convex and the following growing conditions,

$$\begin{aligned} |L(p, z, \mathbf{x})| &\leq C(|p|^2 + |z|^3 + 1), \\ |D_p L(p, z, \mathbf{x})| &\leq C(|p| + 1), \\ |D_z L(p, z, \mathbf{x})| &\leq C(|z|^2 + 1), \end{aligned}$$

for all $p \in \mathbb{R}^n$, $z \in \mathbb{R}$, $\mathbf{x} \in \Omega$.

The Forward Model

Define the weak solution $u \in W^{1,2}(\Omega)$ to the diffusion equation in the sense:

$$\int_\Omega \gamma \nabla u \cdot \nabla v + \sigma uv + \mu |u| uv d\mathbf{x} = 0, \quad \forall v \in W_0^{1,2}(\Omega), .$$

There exist a unique $u \in \mathcal{A}$ satisfies

$$I[u] = \min_{w \in \mathcal{A}} I[w],$$

and u is the unique weak solution to the semilinear diffusion equation. By Sobolev embedding, when $n = 2, 3$, there exists $q > n$, such that $u \in L^q(\Omega)$.

The Forward Model

We note that u can also be viewed as a solution to the equation

$$-\nabla \cdot (\gamma \nabla u) = f(u, \mathbf{x}) \quad \text{in } \Omega,$$
$$u = g \quad \text{on } \partial\Omega,$$

where $f(u, \mathbf{x}) = -\sigma(\mathbf{x})u - \mu(\mathbf{x})|u|u$. By our assumption on the coefficients, $f \in L^{q/2}$, thus we conclude $u \in C^{\alpha}(\Omega)$ for some $0 < \alpha < 1$, where $\alpha = \alpha(n, \Theta/\theta)$. Moreover, if $g \in C^0(\partial\Omega)$, then $u \in C^0(\bar{\Omega})$. If we imposed further that the coefficients of (16) are in $C^{\alpha}(\Omega)$, then we may conclude $u \in C^{2,\alpha}(\Omega)$.

The Forward Model

Proposition

Assume that the coefficients of the diffusion equation satisfy the assumptions we have. Then there exists a unique weak solution such that $u \in C^{\alpha}(\Omega) \cap C^{0}(\bar{\Omega})$. *If we require further that the coefficients are* $C^{\alpha}(\Omega)$, *then* $u \in C^{2,\alpha}(\Omega) \cap C^{0}(\bar{\Omega})$.

The Forward Model

We need the following comparison principle to get positivity of solutions.

Proposition

Let $\mathcal{L}$ be defined as before, and $f(z, \mathbf{x})$ be continuously differentiable with respect to z variable in $\mathbb{R} \times \bar{\Omega}$ such that $0 \leq f_z(z, \mathbf{x}) \leq h(|z|)$ for some h non-decreasing function on $\mathbb{R}^+ \to \mathbb{R}^+$. Let $\mathcal{Q}u = (\mathcal{L} - f)u$. If $u, v \in W^{1,2}(\Omega) \cap C^0(\bar{\Omega})$ satisfy $\mathcal{Q}u \geq 0$ in Ω, $\mathcal{Q}v \leq 0$ in Ω and $u \leq v$ on $\partial\Omega$, then $u \leq v$ in Ω.

The Forward Model

We can then easily show:

Corollary

If $u \in \mathrm{W}^{1,2}(\cdot) \cap \mathrm{C}^0(\bar{\Omega})$ is a solution to the diffusion equation with boundary condition $u = g \geq 0$ on $\partial\Omega$, then $u \geq 0$ in Ω.

In fact, the following strong comparison principle can be established:

Proposition

Let $\mathcal{L}$ be defined as before, and $f(z, \mathbf{x})$ be continuously differentiable with respect to z variable in $\mathbb{R} \times \bar{\Omega}$ such that $0 \leq f_z(z, \mathbf{x}) \leq h(|z|)$ for some h non-decreasing function on $\mathbb{R}^+ \to \mathbb{R}^+$. Let $\mathcal{Q}u = (\mathcal{L} - f)u$. If $u, v \in W^{1,2}(\Omega) \cap C^0(\bar{\Omega})$ satisfy $\mathcal{Q}u \geq 0$ in Ω, $\mathcal{Q}v \leq 0$ in Ω and $u \leq v$ on $\partial\Omega$, then either $u \equiv v$ or $u < v$ in Ω.

The Forward Model

It is straight forward to get the following result on the separation of solutions.

Lemma

Let u_1 and u_2 be solutions with boundary conditions g_1 and g_2. Then $g_1 > g_2$ implies $u_1 > u_2$ in Ω.

We also have the following boundedness of solutions.

Proposition

We have $\sup_{\bar{\Omega}} u \leq \sup_{\partial\Omega} g$.

Presentation Outline

The Case of a Single Coefficient

It is trivial to see that we can uniquely and stably reconstruct either σ or μ (assuming all other coefficients are known) with one (well-selected) data set.

Theorem

Let H and $\tilde{H}$ be data with coefficient μ and $\tilde{\mu}$ respectively with boundary condition $g > 0$ satisfying certain requirements. Then

$$H = \tilde{H} \implies \mu = \tilde{\mu}.$$

Moreover,

$$\|\tilde{\mu} - \mu\|_{L^\infty(\Omega)} \le C \left\| \tilde{H} - H \right\|_{L^\infty(\Omega)}.$$

for some constant C depending on g and other coefficients.

The Case of a Single Coefficient

A trivial proof.

It is easy to verify

$$-\nabla \cdot (\gamma \nabla u) = -\frac{H}{\Gamma} \quad \text{in}\, \Omega,$$
$$u = g \quad \text{on}\, \partial\Omega.$$

This gives us u. We then reconstruct μ as

$$\mu = \frac{H}{\Gamma u|u|} - \frac{\sigma}{|u|}.$$

□

We see here why we need all the properties on u that we have discussed.

The Case of a Single Coefficient

A trivial proof (continued).

The stability result follows from the fact that $w = \tilde{u} - u$ solves

$$-\nabla \cdot \gamma \nabla w = -\frac{1}{\Gamma}(\tilde{H} - H) \quad \text{in}\, \Omega,$$
$$w = 0 \quad \text{on}\, \partial\Omega.$$

This implies

$$\sup_{\Omega} |\tilde{u} - u| \leq C \left\| \tilde{H} - H \right\|_{L^\infty(\Omega)},$$

which can then be combined with

$$|\tilde{\mu} - \mu| = |(\frac{\tilde{H}}{\Gamma \tilde{u}|\tilde{u}|} - \frac{\sigma}{|\tilde{u}|}) - (\frac{H}{\Gamma u|u|} - \frac{\sigma}{|u|})|$$

to get the stability estimate.

The Case of Two Coefficients

In fact, we can generalize the previous idea to have the following result on reconstructing (σ, μ) with two data sets.

Theorem

Let (H_1, H_2) *and* $(\tilde{H}_1, \tilde{H}_2)$ *be data corresponding to* (σ, μ) *and* $(\tilde{\sigma}, \tilde{\mu})$ *respectively, with boundary sources* (g_1, g_2) *satisfying certain requirements. Then*

$$(\tilde{H}_1, \tilde{H}_2) = (H_1, H_2) \implies (\tilde{\sigma}, \tilde{\mu}) = (\sigma, \mu).$$

Moreover, we have

$$\|\tilde{\sigma} - \sigma\|_{L^\infty(\Omega)} + \|\tilde{\mu} - \mu\|_{L^\infty(\Omega)} \leq C\left(\left\|\tilde{H}_1 - H_1\right\|_{L^\infty(\Omega)} + \left\|\tilde{H}_2 - H_2\right\|_{L^\infty(\Omega)}\right)$$

The Case of Three Coefficients (γ, σ, μ)

- It turns out that the idea of vector field introduced in Bal-Uhlmann IP 10 and Bal-R. IP 11 can NOT be used here to deal with the case of reconstructing more than the two absorption coefficients due to the nonlinearity of the diffusion equation here.
- The only tool we know so far is the Douglis-Nirenberg theory for elliptic systems that were introduced for the analysis of hybrid inverse problems in Bal CM 13; see also Widlak-Scherzer IP 15 for an application in elastography.
- The main idea is use redundant data to construct an elliptic system (in the sense of Douglis-Nirenberg) for the unknown coefficients as well as the solution to the PDEs.
- It turns out that the machinary works for our nonlinear diffusion model.

The Case of Three Coefficients (γ, σ, μ)

Let us assume that we have J set of data $\{H_j\}_{j=1}^J$. We linearize that data and the diffusion equation to have, $1 \le j \le J$:

$$
\begin{aligned}
-\nabla\cdot(\delta\gamma\nabla u_j) - \nabla\cdot(\gamma\nabla\delta u_j) &= -\delta H_j \quad \text{in}\,\Omega,\\
\delta\sigma u_j + \sigma\delta u_j + \delta\mu|u_j|u_j + 2\mu|u_j|\delta u_j &= \delta H_j \quad \text{in}\,\Omega.
\end{aligned}
$$

Let $v = (\delta\gamma, \delta\sigma, \delta\mu, \delta u_1, \ldots, \delta u_J)$, and $\mathcal{S} = (-\delta H_1, \delta H_1, \ldots, -\delta H_J, \delta H_J)$. Then we can write the above system as

$$
\mathcal{A}(x, D)v = \mathcal{S},
$$

where $\mathcal{A}(x, D)$ is a matrix differential operator.

The Case of Three Coefficients (γ, σ, μ)

Let $\mathcal{A}_0(x, D)$ be the principal part of $\mathcal{A}(x, D)$, then for $\xi \in \mathbb{S}^{n-1}$,

$$\mathcal{A}_0(x, \mathrm{i}\xi) = \begin{pmatrix} -\mathrm{i}F_1 \cdot \xi & 0 & 0 & \gamma|\xi|^2 & \dots & 0 \\ 0 & u_1 & |u_1|u_1 & \sigma + 2\mu|u_1| & \dots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ -\mathrm{i}F_J \cdot \xi & 0 & 0 & 0 & \dots & D|\xi|^2 \\ 0 & u_J & |u_J|u_J & 0 & \dots & \sigma + 2\mu|u_J| \end{pmatrix}$$

where $F_j = \nabla u_j$. The associated Douglis-Nirenberg numbers are $(s_i)_{i=1}^{2J} = (1, -1, \dots, 1, -1)$ and $(t_j)_{j=1}^{J+3} = (0, 1, 1, 1, \dots, 1)$. When $\mathcal{A}_0(x, \mathrm{i}\xi)$ is of full-rank for all $\xi \in \mathbb{S}^{n-1}$ and $x \in \bar{\Omega}$, we say that $\mathcal{A}$ is elliptic. Since $\gamma > 0$, the requirement can be reduced to that for all $x \in \bar{\Omega}$, $u_j \neq 0$ and $|u_i| \neq |u_j|$ if $i \neq j$.

The Case of Three Coefficients (γ, σ, μ)

Let us augment the system with boundary conditions to have

$$\mathcal{A}v = \mathcal{S} \quad \text{in}\,\Omega,$$
$$\mathcal{B}v = \phi \quad \text{on}\,\partial\Omega,$$

where $\mathcal{B}(x, D)$ is a matrix differential operator. Let $\mathcal{B}_0(x, D)$ be the principal part of $\mathcal{B}$.

The Case of Three Coefficients (γ, σ, μ)

Fix $\mathbf{y} \in \partial\Omega$, and let ν be the inward unit normal vector at $\mathbf{y}$. Let ζ be any non-zero tangential vector to Ω at $\mathbf{y}$. We consider on the half line $\mathbf{y} + z\nu, z > 0$ the system of ordinary equations

$$\mathcal{A}_0(\mathbf{y}, \mathrm{i}\zeta + \nu\frac{d}{dz})\tilde{u}(z) = 0 \quad z > 0,$$
$$\mathcal{B}_0(\mathbf{y}, \mathrm{i}\zeta + \nu\frac{d}{dz})\tilde{u}(z) = 0 \quad z = 0.$$

If for any $\mathbf{y} \in \partial\Omega$, the only solution to the above system such that $\tilde{u}(z) \to 0$ as $z \to \infty$ is $u \equiv 0$, then $(\mathcal{A}, \mathcal{B})$ satisfies the Lopatinskii criterion.

A redundant elliptic system of equations can be solved up to possibly a finite dimensional subspace when it satisfies the Lopatinskii criterion.

The Case of Three Coefficients (γ, σ, μ)

Indeed, we can show that the boundary condition

$$(\delta\gamma, \delta\sigma, \delta\mu) = (\phi_1, \phi_2, \phi_3) \quad \text{on } \partial\Omega$$

satisfies the Lopatinskii criterion for a set of well chosen u_j (which we control by adjusting g_j).

The Case of Three Coefficients (γ, σ, μ)

If we impose that $(\mathcal{S}, \phi)$ is in the space

$$\mathcal{R}(l) = H^{l-s_1}(\Omega) \times \ldots \times H^{l-s_{2J}}(\Omega) \times H^{l-\sigma_1-\frac{1}{2}}(\partial\Omega) \times \ldots H^{l-\sigma_3-\frac{1}{2}}(\partial\Omega),$$

for some $l > n + \frac{1}{2}$, we can have the following regularity result.

Theorem

Given $J = n$, there exists $\{g_j\}_{j=1}^{n}$ such that the system for $v = (\delta\gamma, \delta\sigma, \delta\mu, \delta u_1, \ldots, \delta u_J)$ augmented with Dirichlet BC is elliptic. Moreover, we have the following estimate

$$\sum_{j=1}^{J+3} \|v_j\|_{H^{l+t_j}(\Omega)} \leq C\Big(\sum_{j=1}^{2J} \|\mathcal{S}_j\|_{H^{l-s_j}(\Omega)} + \sum_{j=1}^{3} \|\phi_j\|_{H^{l-\sigma_j-\frac{1}{2}}(\partial\Omega)}\Big) + C_2 \sum_{t_j>0} \|v_j\|_{L^2(\Omega)}$$

for all $l > n + \frac{1}{2}$, provided that $(\gamma, \sigma, \mu, \{u_j\})$ are sufficiently smooth.

The Case of Three Coefficients (Γ, σ, μ)

- The same result can be proved for the reconstruction of (Γ, σ, μ).
- However, we can NOT prove the same result for the case of reconstructing all four coefficients $(\Gamma, \sigma, \mu, \gamma)$.

Numerical Reconstructions with Synthetic Data

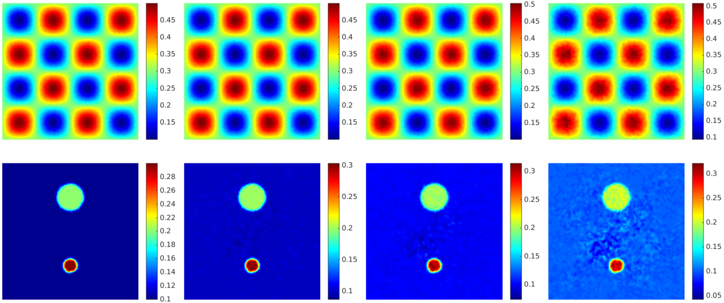

Figure 3: Simultaneously recovered (σ, μ) using direct algorithm, from left to right are using synthetic data with $\eta = 0, 1, 2, 5$.

Numerical Reconstructions with Synthetic Data

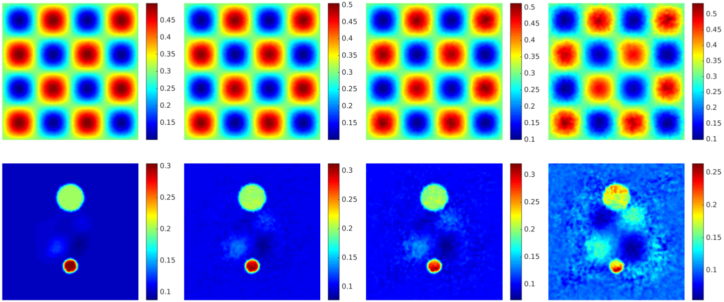

Figure 4: Simultaneously recovered (σ, μ) using optimization algorithm, from left to right are using synthetic data with $\eta = 0, 1, 2, 5$.