Fluorescence Ultrasound Modulated Optical Tomography (fUMOT) in the Diffusive Regime

Yang Yang
Computational Math, Science and Engineering (CMSE)
Michigan State University

joint work with:
Wei Li, Louisiana State University
Yimin Zhong, University of California Irvine

Conference on Modern Challenges in Imaging: in the Footsteps of Allan MacLeod Cormack
MS1: Applied Math in Tomography, Tufts University August 5,
Outline

1. Introduction to fUMOT
2. Diffusive Model
3. Results
Optical Tomography

Figure: Credit: Nina Schotland
Fluorescence + Ultrasound Modulation + Optical Tomography (fUMOT)

S: excitation light source, D: detector
solid curve: excitation photon path
dotted curve: emitted fluorescence photon path

Figure: Fluorescence Ultrasound Modulated Optical Tomography (fUMOT). Image from B. Yuan et al, “Mechanisms of the ultrasonic modulation of fluorescence in turbid media”, J. Appl. Phys. 2008; 104: 103102
Incomplete literature

- **Fluorescence Optical Tomography (FOT):** Arridge, Arridge-Schotland, Stefanov-Uhlmann, ...

- **Ultrasound Modulated Optical Tomography (UMOT):** Ammari-Bossy-Garnier-Nguyen-Seppecher, Bal, Bal-Moskow, Bal-Schotland, Chung-Schotland, ...
Outline

1 Introduction to fUMOT
2 Diffusive Model
3 Results
fOT Model

Diffusive regime for fOT (Ren-Zhao 2013):

\[ u(x) \]: excitation photon density, \quad \[ w(x) \]: emission photon density
fOT Model

**Diffusive regime for fOT (Ren-Zhao 2013):**

\[ u(x) \]: excitation photon density, \( w(x) \): emission photon density

- **Excitation process** (subscripted by \( x \)):

\[
\begin{aligned}
- \nabla \cdot D_x \nabla u + (\sigma_{x,a} + \sigma_{x,f}) u &= 0 \quad \text{in } \Omega \\
\quad u &= g \quad \text{on } \partial \Omega.
\end{aligned}
\]

- **Diffusion coefficient** \( D_x(x) \): diffusion coeffi.
- **Boundary illumination** \( g(x) \): boundary illumination
- **Absorption coefficient** of medium \( \sigma_{x,a}(x) \): absorption coeffi. of medium
- **Absorption coefficient** of fluorescence \( \sigma_{x,f}(x) \): absorption coeffi. of fluorescence
fOT Model

**Diffusive regime** for fOT (Ren-Zhao 2013):

\[ u(x): \text{excitation photon density}, \quad w(x): \text{emission photon density} \]

- **excitation process** (subscripted by \( x \)):

\[
\begin{aligned}
- \nabla \cdot D_x \nabla u + (\sigma_{x,a} + \sigma_{x,f}) u &= 0 \quad \text{in } \Omega \\
 u &= g \quad \text{on } \partial \Omega.
\end{aligned}
\]

\( D_x(x) \): diffusion coeffi. \quad \( g(x) \): boundary illumination

\( \sigma_{x,a}(x) \): absorption coeffi. of medium \quad \( \sigma_{x,f}(x) \): absorption coeffi. of fluorephores

- **emission process** (subscripted by \( m \)):

\[
\begin{aligned}
- \nabla \cdot D_m \nabla w + (\sigma_{m,a} + \sigma_{m,f}) w &= \eta \sigma_{x,f} u \quad \text{in } \Omega \\
 w &= 0 \quad \text{on } \partial \Omega.
\end{aligned}
\]

\( D_m(x) \): diffusion coeffi. \quad \( \eta(x) \): quantum efficiency coeffi.

\( \sigma_{m,a}(x) \): absorption coeffi. of medium \quad \( \sigma_{m,f}(x) \): absorption coeffi. of fluorephores
Ultrasound Modulation Model

**Ultrasound modulation** with plane waves:

- weak acoustic field:

\[ p(t, \mathbf{x}) = A \cos(\omega t) \cos(\mathbf{q} \cdot \mathbf{x} + \phi). \]
Ultrasound Modulation Model

Ultrasound modulation with plane waves:

- weak acoustic field:

\[ p(t, \mathbf{x}) = A \cos(\omega t) \cos(\mathbf{q} \cdot \mathbf{x} + \phi). \]

- modulation effect on optical coefficients (Bal-Schotland 2009):

\[
\begin{align*}
D_{x}^{e}(\mathbf{x}) &= (1 + \epsilon \gamma_{x} \cos(\mathbf{q} \cdot \mathbf{x} + \phi))D_{x}(\mathbf{x}), & \gamma_{x} &= (2n_{x} - 1), \\
D_{m}(\mathbf{x}) &= (1 + \epsilon \gamma_{m} \cos(\mathbf{q} \cdot \mathbf{x} + \phi))D_{m}(\mathbf{x}), & \gamma_{m} &= (2n_{m} - 1), \\
\sigma_{x,a}^{e}(\mathbf{x}) &= (1 + \epsilon \beta_{x} \cos(\mathbf{q} \cdot \mathbf{x} + \phi))\sigma_{x,a}(\mathbf{x}), & \beta_{x} &= (2n_{x} + 1), \\
\sigma_{m,a}(\mathbf{x}) &= (1 + \epsilon \beta_{m} \cos(\mathbf{q} \cdot \mathbf{x} + \phi))\sigma_{m,a}(\mathbf{x}), & \beta_{m} &= (2n_{m} + 1), \\
\sigma_{x,f}^{e}(\mathbf{x}) &= (1 + \epsilon \beta_{f} \cos(\mathbf{q} \cdot \mathbf{x} + \phi))\sigma_{x,f}(\mathbf{x}), & \beta_{f} &= (2n_{f} + 1).
\end{align*}
\]
fUMOT Model

For $\epsilon > 0$ small,

- **excitation process** (subscripted by $x$):
  \[
  \begin{cases}
  -\nabla \cdot D_x^\epsilon \nabla u^\epsilon + (\sigma_{x,a}^\epsilon + \sigma_{x,f}^\epsilon) u^\epsilon = 0 & \text{in } \Omega \\
  u^\epsilon = g & \text{on } \partial \Omega.
  \end{cases}
  \]

- **emission process** (subscripted by $m$):
  \[
  \begin{cases}
  -\nabla \cdot D_m^\epsilon \nabla w^\epsilon + (\sigma_{m,a}^\epsilon + \sigma_{m,f}^\epsilon) w^\epsilon = \eta \sigma_{x,f}^\epsilon u^\epsilon & \text{in } \Omega \\
  w^\epsilon = 0 & \text{on } \partial \Omega.
  \end{cases}
  \]

Inverse Problem: recover $(\sigma_x, f, \eta)$. Our strategy: recover $\sigma_x, f$ from the excitation process, then $\eta$ from the emission process.
**fUMOT Model**

For $\epsilon > 0$ small,

- **excitation process** (subscripted by $x$):

  \[
  \begin{cases}
  -\nabla \cdot D^\epsilon_x \nabla u^\epsilon + (\sigma_{x,a}^\epsilon + \sigma_{x,f}^\epsilon) u^\epsilon &= 0 \quad \text{in } \Omega \\
  u^\epsilon &= g \quad \text{on } \partial \Omega.
  \end{cases}
  \]

- **emission process** (subscripted by $m$):

  \[
  \begin{cases}
  -\nabla \cdot D^\epsilon_m \nabla w^\epsilon + (\sigma_{m,a}^\epsilon + \sigma_{m,f}^\epsilon) w^\epsilon &= \eta \sigma_{x,f}^\epsilon u^\epsilon \quad \text{in } \Omega \\
  w^\epsilon &= 0 \quad \text{on } \partial \Omega.
  \end{cases}
  \]

**Measurement**: boundary photon currents \( (D^\epsilon_x \partial_{\nu} u^\epsilon, D^\epsilon_x \partial_{\nu} w^\epsilon) |_{\partial \Omega} \).
**fUMOT Model**

For $\epsilon > 0$ small,

- **excitation process** (subscripted by $x$):

\[
\begin{cases}
-\nabla \cdot D_x^\epsilon \nabla u^\epsilon + (\sigma_{x,a}^\epsilon + \sigma_{x,f}^\epsilon) u^\epsilon &= 0 \quad \text{in } \Omega \\
u^\epsilon &= g \quad \text{on } \partial \Omega.
\end{cases}
\]

- **emission process** (subscripted by $m$):

\[
\begin{cases}
-\nabla \cdot D_m^\epsilon \nabla w^\epsilon + (\sigma_{m,a}^\epsilon + \sigma_{m,f}^\epsilon) w^\epsilon &= \eta \sigma_{x,f}^\epsilon u^\epsilon \quad \text{in } \Omega \\
w^\epsilon &= 0 \quad \text{on } \partial \Omega.
\end{cases}
\]

**Measurement:** boundary photon currents $(D_x^\epsilon \partial_\nu u^\epsilon, D_x^\epsilon \partial_\nu w^\epsilon)|_{\partial \Omega}$.

**Inverse Problem:** recover $(\sigma_{x,f}^\epsilon, \eta)$.
fUMOT Model

For $\epsilon > 0$ small,

- **excitation process** (subscripted by $x$):

$$\begin{cases} -\nabla \cdot D_x^\epsilon \nabla u^\epsilon + (\sigma_{x,a}^\epsilon + \sigma_{x,f}^\epsilon)u^\epsilon &= 0 \quad \text{in } \Omega \\ u^\epsilon &= g \quad \text{on } \partial \Omega. \end{cases}$$

- **emission process** (subscripted by $m$):

$$\begin{cases} -\nabla \cdot D_m^\epsilon \nabla w^\epsilon + (\sigma_{m,a}^\epsilon + \sigma_{m,f}^\epsilon)w^\epsilon &= \eta \sigma_{x,f}^\epsilon u^\epsilon \quad \text{in } \Omega \\ w^\epsilon &= 0 \quad \text{on } \partial \Omega. \end{cases}$$

**Measurement:** boundary photon currents $(D_x^\epsilon \partial_\nu u^\epsilon, D_x^\epsilon \partial_\nu w^\epsilon)|_{\partial \Omega}$.

**Inverse Problem:** recover $(\sigma_{x,f}, \eta)$.

**Our strategy:** recover $\sigma_{x,f}$ from the excitation process, then $\eta$ from the emission process.
Outline

1. Introduction to fUMOT
2. Diffusive Model
3. Results
Derivation of Internal Data: I

For fixed boundary illumination \( g \),

\[
\int_{\Omega} (D_x^\epsilon - D_x^{-\epsilon}) \nabla u^\epsilon \cdot \nabla u^{-\epsilon} + (\sigma_x^\epsilon - \sigma_x^{-\epsilon}) u^\epsilon u^{-\epsilon} \, dx = \int_{\partial\Omega} (D_x^\epsilon \partial_\nu u^\epsilon) u^{-\epsilon} - (D_x^{-\epsilon} \partial_\nu u^{-\epsilon}) u^\epsilon \, ds
\]
For fixed boundary illumination $g$,

$$
\int_{\Omega} \left( (D_x^\epsilon - D_x^{-\epsilon}) \nabla u^\epsilon \cdot \nabla u^{-\epsilon} + (\sigma_x^\epsilon - \sigma_x^{-\epsilon}) u^\epsilon u^{-\epsilon} \right) d\mathbf{x} = \int_{\partial\Omega} (D_x^\epsilon \partial_\nu u^\epsilon) u^{-\epsilon} - (D_x^{-\epsilon} \partial_\nu u^{-\epsilon}) u^\epsilon d\mathbf{s}.
$$

RHS is known. LHS has leading coefficient

$$
J_1(\mathbf{q}, \phi) = \int_{\Omega} \left( \gamma_x D_x |\nabla u|^2 + (\beta_x \sigma_x, a + \beta_f \sigma_x, f) |u|^2 \right) \cos(\mathbf{q} \cdot \mathbf{x} + \phi) d\mathbf{x}.
$$
Derivation of Internal Data: I

For fixed boundary illumination $g$,

$$\int_{\Omega} (D_x^\epsilon - D_x^{-\epsilon}) \nabla u^\epsilon \cdot \nabla u^{-\epsilon} + (\sigma_x^\epsilon - \sigma_x^{-\epsilon}) u^\epsilon u^{-\epsilon} \, dx = \int_{\partial\Omega} (D_x^\epsilon \partial_\nu u^\epsilon) u^{-\epsilon} - (D_x^{-\epsilon} \partial_\nu u^{-\epsilon}) u^\epsilon \, ds.$$

RHS is known. LHS has leading coefficient

$$J_1(q, \phi) = \int_{\Omega} (\gamma_x D_x |\nabla u|^2 + (\beta_x \sigma_x, a + \beta_f \sigma_x, f) |u|^2) \cos(q \cdot x + \phi) \, dx.$$

Varying $q$ and $\phi$ gives the Fourier transform of

$$Q(x) := \gamma_x D_x |\nabla u|^2 + (\beta_x \sigma_x, a + \beta_f \sigma_x, f) |u|^2 \quad \text{in} \ \Omega,$$

where $u$ is the unperturbed solution (i.e., $\epsilon = 0$).
For fixed boundary illumination $g$,

$$\int_{\Omega} (D^\epsilon_x - D_x^- \epsilon) \nabla u^\epsilon \cdot \nabla u^{-\epsilon} + (\sigma^\epsilon_x - \sigma_x^- \epsilon) u^\epsilon u^{-\epsilon} \, dx = \int_{\partial \Omega} (D^\epsilon_x \partial_\nu u^\epsilon) u^{-\epsilon} - (D_x^- \partial_\nu u^{-\epsilon}) u^{-\epsilon} \, ds.$$ 

RHS is known. LHS has leading coefficient

$$J_1(q, \phi) = \int_{\Omega} (\gamma_x D_x |\nabla u|^2 + (\beta_x \sigma_{x,a} + \beta_f \sigma_{x,f}) |u|^2) \cos(q \cdot x + \phi) \, dx.$$ 

Varying $q$ and $\phi$ gives the Fourier transform of

$$Q(x) := \gamma_x D_x |\nabla u|^2 + (\beta_x \sigma_{x,a} + \beta_f \sigma_{x,f}) |u|^2 \quad \text{in } \Omega,$$

where $u$ is the unpertubed solution (i.e., $\epsilon = 0$).

**Observation:** if $u$ can be recovered from $Q$, so can $\sigma_{x,f}$.  

Inverse Problem Recast: recover $u$ from $Q$.

Recall

\[
\begin{aligned}
-\nabla \cdot D_x \nabla u + (\sigma_x a + \sigma_x f)u &= 0 \quad \text{in } \Omega \\
\quad u &= g \quad \text{on } \partial \Omega.
\end{aligned}
\]

and the internal data is

\[
Q(x) := \gamma_x D_x |\nabla u|^2 + (\beta_x \sigma_x a + \beta_f \sigma_x f) |u|^2 \quad \text{in } \Omega.
\]
Inverse Problems Recast: recover $u$ from $Q$.

Recall

\[
\begin{aligned}
-\nabla \cdot D_x \nabla u + (\sigma_{x,a} + \sigma_{x,f})u &= 0 \quad \text{in } \Omega \\
u &= g \quad \text{on } \partial \Omega.
\end{aligned}
\]

and the internal data is

\[
Q(x) := \gamma_x D_x |\nabla u|^2 + (\beta_x \sigma_{x,a} + \beta_f \sigma_{x,f})|u|^2 \quad \text{in } \Omega.
\]

- $\beta_f = 0$: solving a Hamilton-Jacobi equation to find $u$;
- $\beta_f \neq 0$: eliminating $\sigma_{x,f}$ through substitution.
Recovery of $\sigma_{x,f}$: uniqueness

- $\beta_f \neq 0$ (conti.ed):

set $\theta := \frac{\beta_f - \gamma_x}{\beta_f + \gamma_x}$ and $\Psi := u^{\frac{2}{1+\theta}}$

\[
\begin{cases}
\nabla \cdot D_x \nabla \psi &= -\frac{2}{1+\theta} \sigma_{x,a} \left( \frac{\beta_x}{\beta_f} - 1 \right) \psi + \frac{2}{1+\theta} \frac{Q}{\beta_f} |\psi|^{-(1+\theta)} \\
\psi &= g^{\frac{2}{1+\theta}}
\end{cases}
\]

**Theorem (Li-Y.-Zhong, 2018)**

*The semi-linear elliptic BVP has a unique positive weak solution $\Psi \in H^1(\Omega)$ in either of the following cases:

Case (1): $-1 \neq \theta < 0$, $b \geq 0$ and $c \geq 0$;

Case (2): $\theta \geq 0$, $b \geq 0$ and $c \leq 0$.*/
Recovery of $\sigma_{x,f}$: stability and reconstruction

**Theorem (Li-Y.-Zhong, 2018)**

In either Case (1) or Case (2), one has the stability estimate

$$\|\sigma_{x,f} - \tilde{\sigma}_{x,f}\|_{L^1(\Omega)} \leq C \left( \|Q - \tilde{Q}\|_{L^1(\Omega)} + \|Q - \tilde{Q}\|_{L^2(\Omega)}^2 \right)$$

We further give three iterative algorithms with convergence proofs to reconstruct $\sigma_{x,f}$.

**Remark:** uniqueness and stability may fail if $\theta$, $b$, $c$ violate the conditions.
Recovery of $\eta$

Sketch of procedures:

1. derive an integral identity from the emission process;
Recovery of $\eta$

Sketch of procedures:

1. derive an integral identity from the emission process;
2. derive an internal functional $S$ from the leading order term of the identity;
Recovery of $\eta$

Sketch of procedures:

1. derive an integral identity from the emission process;
2. derive an internal functional $S$ from the leading order term of the identity;
3. rewrite the equations for $u$ and $w$ to obtain a Fredholm type equation

$$\mathcal{T}\eta = S;$$
Recovery of $\eta$

Sketch of procedures:

1. derive an integral identity from the emission process;
2. derive an internal functional $S$ from the leading order term of the identity;
3. rewrite the equations for $u$ and $w$ to obtain a Fredholm type equation
   \[ \mathcal{T}\eta = S; \]
4. if 0 is not an eigenvalue of $\mathcal{T}$, then uniqueness, stability and reconstruction are immediate.
Numerical examples

Domain: $[-0.5, 0.5]^2$; excitation source: $g(x, y) = e^{2x} + e^{-2y}$.

The domain is triangulated into 37008 triangles and uses 4-th order Lagrange finite element method to solve the equations.

$$D_x \equiv 0.1, \quad D_m = 0.1 + 0.02 \cos(2x) \cos(2y),$$
$$\sigma_{x,a} \equiv 0.1, \quad \sigma_{m,a} = 0.1 + 0.02 \cos(4x^2 + 4y^2).$$

Figure: Left: The absorption coefficient $\sigma_{x,f}$ of fluorophores. Right: The quantum efficiency coefficient $\eta$. 
Numerical examples- Case I-1

\[ \gamma_x = -2.6, \gamma_m = -2.4, \beta_x = -0.6, \beta_m = -0.4, \beta_f = -0.8 \] and \[ \tau = 3.25, \mu = -0.25 \] and \[ \theta = -\frac{9}{17}. \]

Figure 2: The reconstruction of \( \sigma_{x,f} \) and \( \eta \) in Example I. First row, from left to right, 0%, 1%, 2% random noises are added to the internal data \( Q \) and the relative \( L^1 \) errors of reconstructed \( \sigma_{x,f} \) are 0.000132%, 3.88%, 7.76% respectively. Second row, from left to right, assuming the knowledge of \( \sigma_{x,f} \) from the first row, 0%, 1%, 2% random noises are added to the internal data \( S \). The relative \( L^2 \) errors of reconstructed \( \eta \) are 0.00313%, 5.60%, 11.7% respectively.
Numerical examples- Case I-2

\[ \gamma_x = -1.4, \quad \gamma_m = 0.0, \quad \beta_x = 0.6, \quad \beta_m = 2.0, \quad \beta_f = 0.4 \quad \text{and} \quad \tau = -3.5. \]
\[ \mu = 0.5 \quad \text{and} \quad \theta = -\frac{9}{5}. \]

Figure 3: The reconstruction of \( \sigma_{x,f} \) and \( \eta \) in Example II. First row, from left to right, 0%, 1%, 2% random noises are added to the internal data \( Q \) and the relative \( L^1 \) errors of reconstructed \( \sigma_{x,f} \) are 0.0086%, 2.62%, 5.27% respectively. Second row, from left to right, assuming the knowledge of \( \sigma_{x,f} \) from the first row, 0%, 1%, 2% random noises are added to the internal data \( S \). The relative \( L^2 \) errors of reconstructed \( \eta \) are 0.0150%, 4.23%, 8.89% respectively.
Numerical examples- Case II

\( \gamma_x = 0.2, \gamma_m = 0.6, \beta_x = 2.2, \beta_m = 2.6, \beta_f = -0.3 \) and \( \tau = -\frac{2}{3} \).

\( \mu = -\frac{25}{8} \) and \( \theta = 5 \).

Figure 4: The reconstruction of \( \sigma_{x,f} \) and \( \eta \) in Example III. First row, from left to right, 0%, 1%, 2% random noises are added to the internal data \( Q \) and the relative \( L^1 \) errors of reconstructed \( \sigma_{x,f} \) are 0.00147%, 3.68%, 7.38% respectively. Second row, from left to right, assuming the knowledge of \( \sigma_{x,f} \) from the first row, 0%, 1%, 2% random noises are added to the internal data \( S \). The relative \( L^2 \) errors of reconstructed \( \eta \) are 0.00392%, 4.65%, 9.48% respectively.
Thank you for the attention!

Research partly supported by NSF grant DMS-1715178