MATHEMATICAL AND NUMERICAL CHALLENGES IN DIFFUSE OPTICAL TOMOGRAPHY (DOT) FOR BREAST SCREENING

P. Causin (in collaboration with G. Naldi, M.Lupieri, R.Weishaeupl)

University of Milano

Introduction

Scope of the work:

$$\left.\begin{array}{l}\bullet \text{ Accurate numerical solutions}\\[1em] \bullet \text{ Short computational times}\end{array}\right\} \rightarrow \text{cornerstones for marketable DOT devices}$$

Introduction

Scope of the work:

$$\left.\begin{array}{l}\bullet \text{ Accurate numerical solutions}\\[1em] \bullet \text{ Short computational times}\end{array}\right\} \rightarrow \text{cornerstones for marketable DOT devices}$$

DOT employs **near-infrared** (NIR, $600-900$ *nm*) light to illuminate the biological tissue *in vivo*.

DOT Inverse problem: Infer the optical parameter (biomarkers of pathogenic processes) "inverting" a mathematical model for light propagation in tissue based on experimental measurements of the light fluence.

Introduction

Scope of the work:

$$\left.\begin{array}{l}\bullet\ \text{Accurate numerical solutions}\\[1em] \bullet\ \text{Short computational times}\end{array}\right\} \rightarrow \text{cornerstones for marketable DOT devices}$$

DOT employs **near-infrared** (NIR, $600 - 900$ *nm*) light to illuminate the biological tissue *in vivo*.

DOT Inverse problem: Infer the optical parameter (biomarkers of pathogenic processes) "inverting" a mathematical model for light propagation in tissue based on experimental measurements of the light fluence.

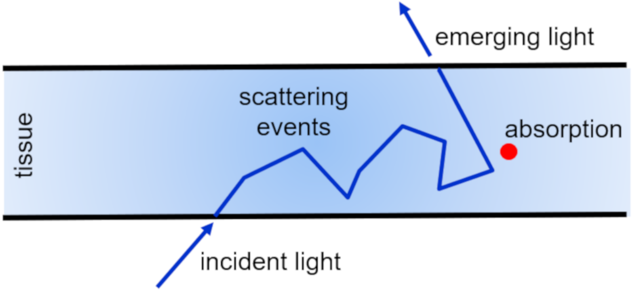
- Non-invasive
- Non-ionizing radiation

Optical Properties of Biological Tissue

The propagation of light through biological tissues is affected by **absorption** and **scattering** characterized by the absorption coefficient (μ_a $[cm^{-1}]$) and the scattering coefficient (μ_s $[cm^{-1}]$), respectively.

Optical Properties of Biological Tissue

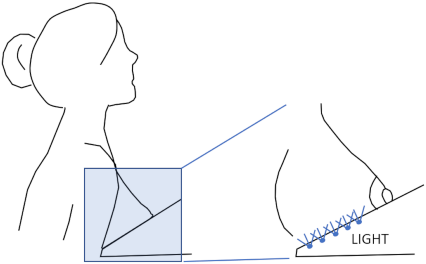
The propagation of light through biological tissues is affected by **absorption** and **scattering** characterized by the absorption coefficient (μ_a $[cm^{-1}]$) and the scattering coefficient (μ_s $[cm^{-1}]$), respectively.



In the NIR spectral window the scattering effect can be **100x** larger than absorption. Due to the strong scattering light photons travel in tortuous paths.

Methodology

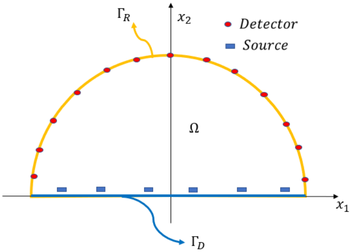
We address the application of DOT to female **breast screening** to detect possible **cancerous lesions**.



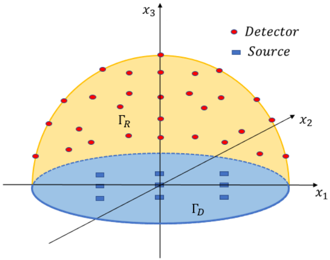
Methodology

We address the application of DOT to female **breast screening** to detect possible **cancerous lesions**.

- **Geometry and source-detector arrangement**
  Female breast supported on a solid plate.
  Γ_D: tissue-plate interface $\rightarrow$ light sources,
  Γ_R: tissue-air interface $\rightarrow$ detectors.



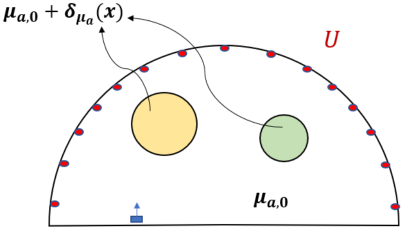
2D



3D

Methodology

We address the application of DOT to female **breast screening** to detect possible **cancerous lesions**.



- **Light source**
  LED modeled as Dirac delta source terms $S(x) = \delta(x - x_s)$, x_s source position.
- **Data**
  For each source, light fluence U at the detectors.
- **Optical parameter to infer**
  Absorption coefficient $\mu_a(x) = \mu_{a,0} + \delta_{\mu_a}(x)$ (constant scattering coefficient).

Model for light propagation in tissue

Radiative transport equation (RTE) for the **light radiance**

$$\Big\Downarrow \begin{array}{c} \text{if } \mu_s \gg \mu_a \\ P_1 \text{ approximation } + \text{ stationary case} \end{array}$$

Diffusion Equation (DE)

$$-D\triangle U(x) + \mu_a(x)U(x) = S(x)$$

where $U(x)$ is the **photon fluence rate**, D is the **diffusion coefficient**.

Model for light propagation in tissue

Radiative transport equation (RTE) for the **light radiance**

$$\Big\Downarrow \begin{array}{c} \text{if } \mu_s \gg \mu_a \\ P_1 \text{ approximation } + \text{ stationary case} \end{array}$$

Diffusion Equation (DE)

$$-D\triangle U(x) + \mu_a(x)U(x) = S(x)$$

where $U(x)$ is the **photon fluence rate**, D is the **diffusion coefficient**.

Boundary Conditions for the fluence rate

Γ_D	tissue-plate interface	totally opaque plate	$U = 0$	Dirichlet BC
Γ_R	tissue-air interface	Fresnel reflection	$\frac{\partial U}{\partial \hat{n}} + \frac{1}{2AD}U = 0$	Robin BC

Rytov Approximation

Rytov approximation: $U(x) = \mathrm{e}^{\psi(x)}$ where $\psi(x) = \sum_{i=0}^{N} \psi_i(x)$.

Rytov Approximation

Rytov approximation: $U(x) = \mathrm{e}^{\psi(x)}$ where $\psi(x) = \sum_{i=0}^{N} \psi_i(x)$.

From the DE, under the 1*st* order Rytov approximation, defining the **Modified Helmholtz operator** $\mathcal{L} = \triangle - \frac{\mu_{a,0}}{D} \Rightarrow$

Problem for $U_0 = \mathrm{e}^{\psi_0}$ *background fluence*

$$\begin{cases} \mathcal{L} U_0(x) = -\frac{1}{D}\delta(x - x_s) & x \in \Omega \\ U_0(x) = 0 & x \in \Gamma_D \\ \frac{\partial U_0}{\partial \hat{n}}(x) + \frac{1}{2AD} U_0(x) = 0 & x \in \Gamma_R \end{cases}$$

Problem for $U_0\psi_1$, $\psi_1(x) = \log \frac{U(x)}{U_0(x)}$ *logarithmic amplitude fluctuation of the light fluence*

$$\begin{cases} \mathcal{L}\left(U_0\psi_1\right)(x) = U_0(x)\frac{\delta_{\mu_a}(x)}{D} & x \in \Omega \\ \left(U_0\psi_1\right)(x) = 0 & x \in \Gamma_D \\ \frac{\partial (U_0\psi_1)}{\partial \hat{n}}(x) + \frac{1}{2AD}\left(U_0\psi_1\right)(x) = 0 & x \in \Gamma_R \end{cases}$$

Green's Function method

$$\left.\begin{cases} \mathcal{L}G(x,x') = \delta(x-x') & x \in \Omega \\ G(x,x') = 0 & x \in \Gamma_D \end{cases}\right\} \rightarrow \text{ Green Dipole } (G_D)$$

$$\frac{\partial G}{\partial \hat{n}}(x,x') + \frac{1}{2AD} G(x,x') = 0 \quad x \in \Gamma_R \longrightarrow \boxed{\text{Numerical approach}}$$

Green's Function method

$$\left\{\begin{array}{ll}\mathcal{L}G(x,x') = \delta(x-x') & x \in \Omega \\ G(x,x') = 0 & x \in \Gamma_D \\ \dfrac{\partial G}{\partial \hat{n}}(x,x') + \frac{1}{2AD}G(x,x') = 0 & x \in \Gamma_R \end{array}\right.$$

$\left.\begin{array}{l}\mathcal{L}G(x,x') = \delta(x-x'),\ x \in \Omega \\ G(x,x') = 0,\ x \in \Gamma_D\end{array}\right\} \rightarrow$ Green Dipole (G_D)

$x \in \Gamma_R \longrightarrow$ $\boxed{\text{Numerical approach}}$

Problem for $U_0\psi_1 \Rightarrow$

Linearized problem:
Fredholm integral equation of the first kind for δ_{μ_a}

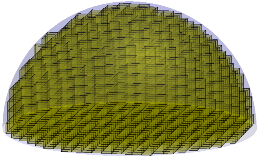
$$(U_0\psi_1)(x) = \int_\Omega G(x,x')\frac{\delta_{\mu_a}(x')}{D}U_0(x')dx'$$

Discrete Inverse Problem 1/2

Starting from the Fredholm integral equation of the first kind

(1.) **evaluation** at the detector positions, $x = x_{d,\nu}$ for $\nu = 1, \ldots, N_{Det}$ for each source position $x_{s,l}$ for $l = 1, \ldots, N_{Src}$,

(2.) domain discretization through a **voxel-based mesh** composed of N_v elements of centroids $\{x_j\}_{j=1}^{N_v}$ and volumes $\{\Delta V_j\}_{j=1}^{N_v}$,



(3.) **midpoint quadrature rule** to discretize the integral,

(4.) use of the **dataset of measurements**:
$U^m(x_{d\nu}, x_{sl})$ and $U_0^m(x_{d\nu}, x_{sl})$ for $l = 1, \ldots, N_{Src}$ and $\nu = 1, \ldots, N_{Det}$.

Discrete Inverse Problem 2/2

From steps **(1.)** – **(4.)**

$$\underbrace{log\left(\frac{\boxed{U^m(x_{d,v},x_{s,l})}}{\boxed{U_0^m(x_{d,v},x_{s,l})}}\right)}_{y_i} \approx \sum_{j=1}^{N_v} \delta_{\mu_a}(x_j)\, \underbrace{\frac{\Delta V_j}{D\,\boxed{U_0\,(x_{d,v},x_{s,l})}}\,\boxed{U_0\,(x_j,x_{s,l})}\,\boxed{G(x_{d,v},x_j)}}_{J_{i,j}}$$

$$i \to \{l, v\}$$

—	Calculate
—	Known from measurements or simulate

$$i = 1, \dots, M$$
$$M = N_{Src} \times N_{Det}$$

$\boxed{J\delta_{\mu_a} \approx y}$ where J is called **sensitivity matrix**

Discrete Inverse Problem

$$\delta_{\mu_a}^{LS} = \arg\min_x \mathcal{F}(x), \text{ where } \mathcal{F}(x) = ||Jx - y||_2^2$$

Method of Fundamental Solutions

Goal: Find a numerical method to enforce the Robin BC that preserves high speed

Method of fundamental solutions (MFS) vs Boundary element method (BEM)

$\rightarrow$ **MFS** is faster and provides more accurate results

Method of Fundamental Solutions

Goal: Find a numerical method to enforce the Robin BC that preserves high speed

Method of fundamental solutions (MFS) vs Boundary element method (BEM)

$\rightarrow$ **MFS** is faster and provides more accurate results

Method of Fundamental Solutions

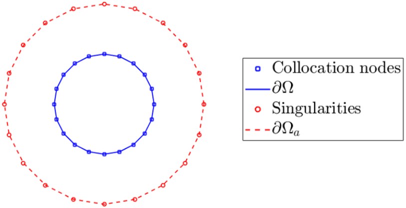
Goal: Find a numerical method to enforce the Robin BC that preserves high speed

Method of fundamental solutions (MFS) vs Boundary element method (BEM)

$\rightarrow$ **MFS** is faster and provides more accurate results

Single-layer potential representation on an auxiliary boundary Ω_a *s.t.* $\overline{\Omega} \subset \Omega_a$

$$u(x) = \int_{\partial\Omega_a} \sigma(\xi) G(x,\xi) dS_\xi$$



Discretization $\Rightarrow u_{MFS}(x) = \sum_{j=1}^{N} a_j G(x, \xi_j)$

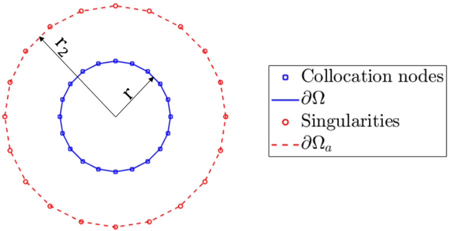
- ***Singularities***: $\{\xi_j\}_{j=1}^{N} \in \partial\Omega_a$
- ***Collocation nodes***: $\{x_i\}_{i=1}^{M} \in \partial\Omega$
- **Unknowns**: $\{a_j\}_{j=1}^{N}$, determined imposing the BCs at the collocation nodes

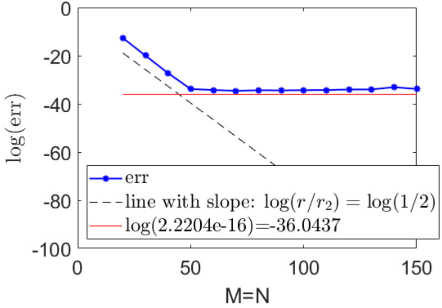
$M \geq N \Rightarrow M \times N$ linear system for the unknowns a_j.

$$\left\| u - u_{MFS} \right\|_{L^2(\Omega)} = O\left(\left(\frac{r}{r_2} \right)^M \right)$$

$M = \#collocation\ nodes$
$N = \#singularities$

Test case in two-dimensions $\left[\triangle - k^2\right] u(x) = 0$ with $k = \sqrt{2}$.
Exact solution: $u(x) = \mathrm{e}^{x_1 + x_2}$



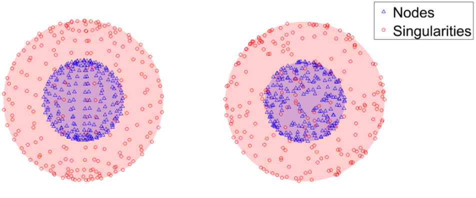


MFS convergence

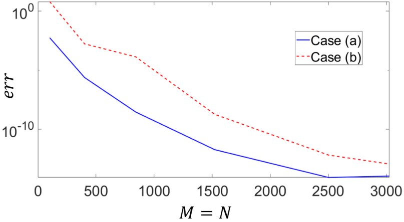
$$\|u - u_{MFS}\|_{L^2(\Omega)} = O\left(\left(\frac{r}{r_2}\right)^M\right)$$

$M = \#collocation\ nodes$
$N = \#singularities$

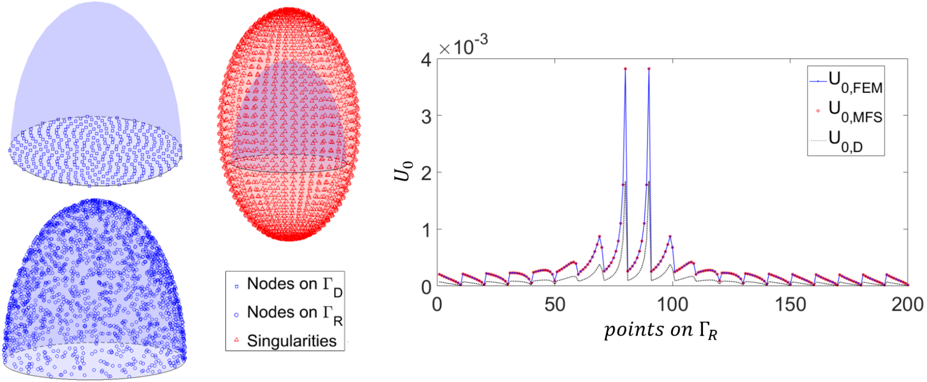
Test case in three-dimensions $\left[\triangle - k^2\right] u(x) = 0$ with $k = \sqrt{3}$.
Exact solution: $u(x) = \mathrm{e}^{x_1+x_2+x_3}$



(a) (b)



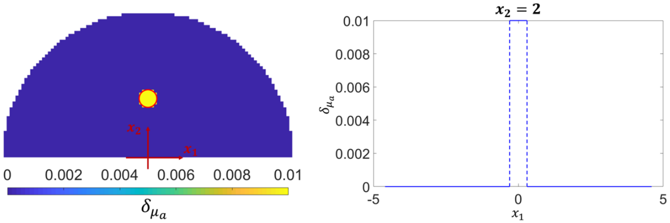
MFS for DOT


Nodes on Γ_D
Nodes on Γ_R
Singularities
$\times 10^{-3}$
U_0
$U_{0,FEM}$
$U_{0,MFS}$
$U_{0,D}$
0
1
2
3
4
0
50
100
150
200
$points\ on\ \Gamma_R$

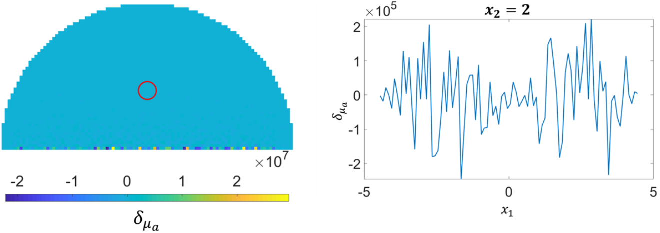
Necessity of Regularization

$$\delta_{\mu_a}^{LS} = \underset{x \in \mathbb{R}^{N_v}}{\arg\min}\, \mathcal{F}(x), \text{ where } \mathcal{F}(x) = \|Jx - y\|_2^2$$

Exact



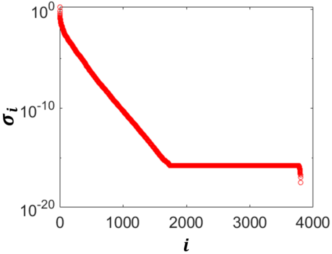
LS



Necessity of Regularization

$$\delta_{\mu_a}^{LS} = \underset{x\in\mathbb{R}^{N_v}}{\arg\min}\,\mathcal{F}(x), \text{ where } \mathcal{F}(x) = \|Jx - y\|_2^2$$

Singular values of the sensitivity matrix



Necessity of Regularization

$$\delta_{\mu_a}^{LS} = \underset{x \in \mathbb{R}^{N_v}}{\arg\min}\, \mathcal{F}(x), \text{ where } \mathcal{F}(x) = \|Jx - y\|_2^2$$

Regularization

$$\min_x \mathcal{F}(x) \text{ s.t. } ||x||_p^p \leq \delta \Leftrightarrow \min_x \mathcal{F}_{\lambda,p}(x), \text{ where } \mathcal{F}_{\lambda,p}(x) = \mathcal{F}(x) + \lambda ||x||_p^p$$

Necessity of Regularization

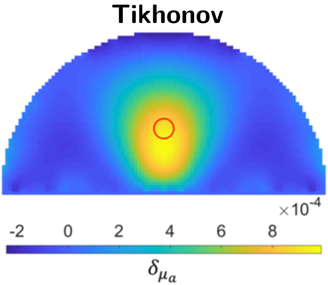
$$\delta_{\mu_a}^{LS} = \arg\min_{x \in \mathbb{R}^{N_v}} \mathcal{F}(x), \text{ where } \mathcal{F}(x) = \|Jx - y\|_2^2$$

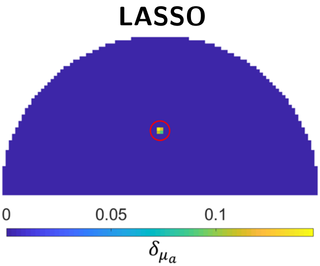
Regularization

$$\min_x \mathcal{F}(x) \text{ s.t. } ||x||_p^p \leq \delta \Leftrightarrow \min_x \mathcal{F}_{\lambda,p}(x), \text{ where } \mathcal{F}_{\lambda,p}(x) = \mathcal{F}(x) + \lambda ||x||_p^p$$

- **Tikhonov**: $p = 2$
- **LASSO**: $p = 1$

Regularization for DOT





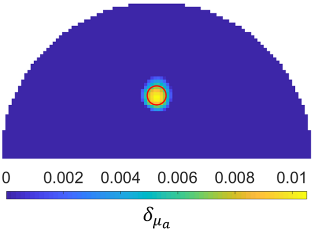
	DOFS	$\|\|\delta_{\mu_a}\|\|_\infty$
Exact	32	0.01
Tikhonov	$N_v = 3822$	$8 \cdot 10^{-4}$
LASSO	4	0.15

Regularization for DOT

Elastic net: $\min_x \mathcal{F}_{\lambda,\alpha}(x)$, where $\mathcal{F}_{\lambda,\alpha}(x) = \mathcal{F}(x) + \lambda\{\alpha\|x\|_1 + (1-\alpha)\|x\|_2^2\}$,

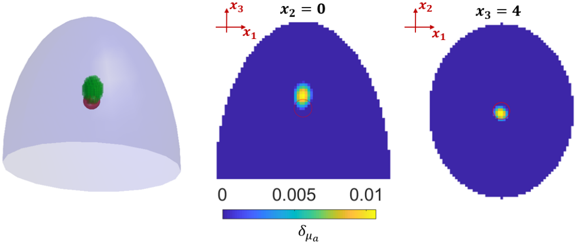
$$\alpha \in [0, 1]$$

Elastic net $\boldsymbol{\alpha = 0.3}$

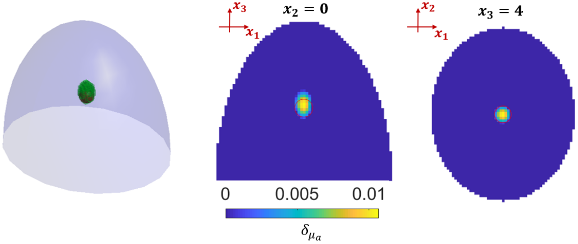


α	**DOFS**	$\|\|\delta_{\mu_a}\|\|_\infty$
Exact	32	0.01
0	N_v	$8 \cdot 10^{-4}$
0.1	178	$5 \cdot 10^{-3}$
0.2	119	$8 \cdot 10^{-3}$
0.3	93	0.01
0.4	74	0.013
0.5	63	0.016
0.6	51	0.02
0.7	37	0.025
0.8	24	0.03
0.9	17	0.06
1	4	0.15

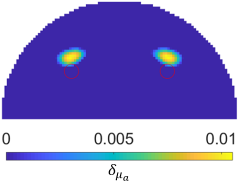
Dipole Approximation



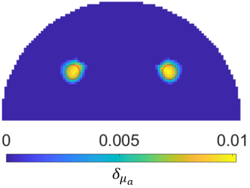
Robin BC (MFS)

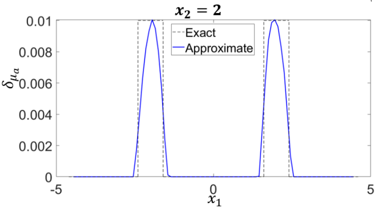


Dipole Approximation



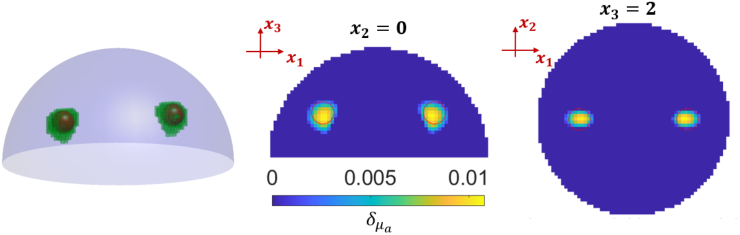
Robin BC (MFS)





Numerical Results

Robin BC (MFS) 3D

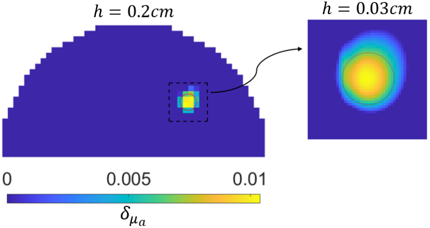


Computational Time

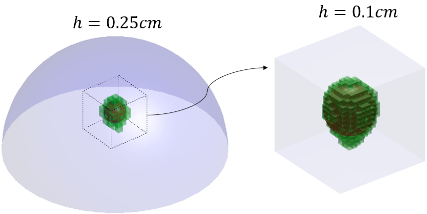
Computational Time in 3D		
$N_v = 72407$	Dipole Approximation	113 s
	Robin BC	160 s

Computational Time

Computational Time in 3D		
$N_v = 72407$	Dipole Approximation	113 s
	Robin BC	160 s



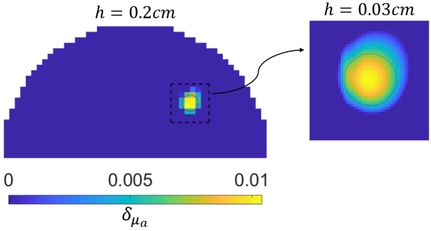
2D



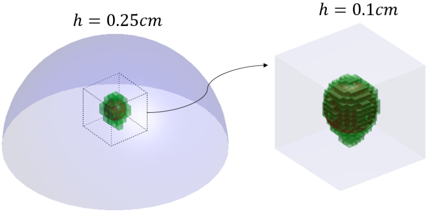
3D

Computational Time

Computational Time in 3D		
$N_v = 72407$	Dipole Approximation	113 s
	Robin BC	160 s



2D



3D

3D	$\boldsymbol{N_v}$	**Computational Time**
$h = 0.1$ cm (whole domain)	72407	160 s
$h = 0.25$ cm (whole domain)	14876	30 s
$h = 0.1$ cm (cube of size 2 cm)	8000	17 s

$\}< 1\text{min}$

Conclusions

The approach proposed accurately detects the inclusion/inclusions

- Size and intensity $\rightarrow$ **elastic net**
- Location $\rightarrow$ **enforcement of the Robin BC**.

The times of execution are short thanks to

- the choice of the framework: linearization under Rytov approximation adopting the DE as model equation
- the fast numerical method **MFS**
- a general **optimization**, in terms of computational costs, of the code.