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Résolution de l'ETR par une méthode de volumes finis modifiés – application à la détection de tumeurs cancéreuses

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- Introduction
- □ The Modified Finite Volume Method
- □ The reconstruction algorithm and results
 - with diffuse light
 - with fluorescence light
- □ Conclusions, future works

Motivation





also membranes (lipids) and collagene fibers



Skin has a complex structure



How a cancer tumor can be detected?

- The cancer leads to physiological changes that affect the optical properties (scattering, absorption, asymmetry factor,...) of biological tissues
- A tumor is highly vascularized: change in absorption coefficients
- Change in size of nucleus of cancer cells: change in scattering coefficients

	Healthy liver	Metastatic liver
Absorption coefficient μ_a (mm ⁻¹)	0.1	0.06
Scattering coefficient μ_s (mm ⁻¹)	20.4	10.8
Asymmetry factor g	0.955	0.902
Optical penetration depth (mm)	1.8	2.3

Germer et al., Laser Sureg Med, 1998



very fast, simple cases)

" false scattering " (spatial discretization) "ray-effect " (angular discretization)

Angular discretization

- Discrete direction $\mathbf{\Omega}^{\mathbf{k}}$ with an azimutal angle $\theta \in [0, 2\pi]$ and a polar angle $\varphi \in [0, \pi]$
- Constant step



Applying the angular discretization to the RTE

$$\frac{n_{\lambda}(s)}{c} \frac{\partial \psi_{\lambda}(s, \mathbf{\Omega}^{\mathbf{k}}, t)}{\partial t} + \mathbf{\Omega}^{\mathbf{k}} \cdot \nabla \psi_{\lambda}(s, \mathbf{\Omega}^{\mathbf{k}}, t) = -\mu_{t\lambda}(s) \psi_{\lambda}(s, \mathbf{\Omega}^{\mathbf{k}}, t) + \mu_{s\lambda}(s) \sum_{k'=1}^{N} p_{\lambda}(\mathbf{\Omega}^{\mathbf{k'}}, \mathbf{\Omega}^{\mathbf{k}}) \psi_{\lambda}(s, \mathbf{\Omega}^{\mathbf{k'}}, t) \omega^{k'} + S_{\lambda}(s, \mathbf{\Omega}^{\mathbf{k}}, t)$$

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$$+ \mu_{s\lambda}(s) \sum_{k=1}^{N} p_{\lambda}(\mathbf{\Omega}^{\mathbf{k}'}, \mathbf{\Omega}^{\mathbf{k}}) \psi_{\lambda}(s, \mathbf{\Omega}^{\mathbf{k}'}, t) \omega^{k'} + S_{\lambda}(s, \mathbf{\Omega}^{\mathbf{k}}, t)$$

• First, the simplified equation (steady-state, wavelength indepedent properties, non-scattering) has to be solved:

$$\mathbf{\Omega}^{\mathbf{k}} \cdot \nabla \psi(s, \mathbf{\Omega}^{\mathbf{k}}) = -\mu_a(s)\psi(s, \mathbf{\Omega}^{\mathbf{k}}) + S(s, \mathbf{\Omega}^{\mathbf{k}})$$

• The sum with scattering and BC are taken into account by iterations

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- The sum with scattering and BC are taken into account by iterations
- The normalization technique is applied to the H-G phase function:

$$\widetilde{p}^{m \to n} = \frac{\int \int \Omega^{m} \int \Omega^{n} p(\mathbf{\Omega}' \cdot \mathbf{\Omega}) d\Omega' d\Omega}{\Delta \Omega^{m} \Delta \Omega^{n}} \quad p(\mathbf{\Omega}' \cdot \mathbf{\Omega}) = \frac{1}{4\pi} \frac{1 - g^{2}}{(1 + g^{2} - 2g \mathbf{\Omega}' \cdot \mathbf{\Omega})^{3/2}}$$
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2D control volume with a cell-vertex formulation

• The RTE has to be solved at each node of the mesh



Applying Gauss divergence theorem:

$$\int_{\Gamma_{P}} \int_{\Delta\Omega^{k}} \psi(s, \mathbf{\Omega}) \left(\mathbf{\Omega} \cdot \mathbf{n}_{out}\right) d\Omega \, dS = \int_{V_{P}} \int_{\Delta\Omega^{k}} -\mu_{a}(s) \psi(s, \mathbf{\Omega}) + S(s, \mathbf{\Omega}) \, d\Omega \, dV$$

$$panel \int_{\Gamma_{P}} \vec{n}_{f}$$

- If one considers:
- an average value ψ^k_P in V_P
- an average value $\psi_{i_f}^k$ on a panel f

N

 A_f is the length of the panel f

$$\Delta_f^k = \int_{\Delta\Omega^k} \left(\mathbf{\Omega} \cdot \mathbf{n}_f \right) \, d\Omega$$

• The FVM gives:

$$\sum_{f=1}^{N_f} \psi_{i_f}^k A_f \Delta_f^k = \left[-\mu_{a,P} \psi_P^k + S_P^k\right] \Delta \Omega^k V_P$$

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Conservation of energy

*l*11

l₁₀

10

h

Applying Gauss divergence theorem:

$$\int_{\Gamma_{p}} \int_{\Delta\Omega^{k}} \psi(s, \mathbf{\Omega}) (\mathbf{\Omega} \cdot \mathbf{n}_{out}) d\Omega dS = \int_{V_{p}} \int_{\Delta\Omega^{k}} -\mu_{a}(s) \psi(s, \mathbf{\Omega}) + S(s, \mathbf{\Omega}) d\Omega dV$$
• If one considers:
- an average value ψ_{p}^{k} in V_{p}
- an average value $\psi_{i_{f}}^{k}$ on a panel f
 A_{f} is the length of the panel f
 $\Delta_{f}^{k} = \int_{\Delta\Omega^{k}} (\mathbf{\Omega} \cdot \mathbf{n}_{f}) d\Omega$
• The FVM gives:
$$\sum_{f=1}^{N_{f}} \psi_{i_{f}}^{k} A_{f} \Delta_{f}^{k} = \left[-\mu_{a,p} \psi_{p}^{k} + S_{p}^{k}\right] \Delta\Omega^{k} V_{p}$$

Exponential scheme for the closure relations

• Integral form of the RTE

$$\psi_{i_f}^k = \psi_{u_f}^k \exp\left(-\int_{u_f}^{i_f} \mu_a(s) \, ds\right) + \int_{u_f}^{i_f} S^k(s) \exp\left(-\int_{s}^{i_f} \mu_a(u) \, du\right) \, ds$$



• $\psi_{u_f}^k$ has to be determined according to the radiances given at the nodes of the mesh

2D projections and interpolations

• for a reference triangle



Solution for the radiative intensity



Explicit solution: $I_P^k = f(I_{P_a}^k, I_{P_b}^k, I_{P_c}^k)$

Marching order map



Boundary

Boundary

Initial mesh

Renumbered mesh according to the given direction

3D control volume



3D projections and interpolations



Validation of the 2D/3D MFVM

• **Relative differences < 1%** on the reflectances or transmittances with a suitable mesh (**comparison with MC or "analytical solutions**")

Conditions: homogeneous and two layered media, semi-transparent boundaries (with Fresnel reflections at the interface), steady-state and time domains

Asllanaj et al. (2014), J Biomedical Optics

Asllanaj et al. *Fluorescence* and diffuse light propagation in biological tissue based on the 3D radiative transport equation. Part I: computational method Asllanaj et al. *Part II: simulations*

Asllanaj and Fumeron (**2012**), **J Biomedical Optics** Asllanaj et al. (**2015**), *JQSRT*

The RTE in the frequency domain



The RTE in the frequency domain



Reconstruction of the optical properties

- PhD thesis of Ahmad Addoum (2014 2017)
- From boundary data (reflectance)

$$J(\theta) = \frac{1}{2} \left\| R(\theta) - d_{obs} \right\|^2$$

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• The reconstruction algorithm is based on an iterative solution of the RTE (forward model) and his adjoint state (solved also with the MVFM)

$$\frac{\partial i\omega}{c/n}\phi(\boldsymbol{r},\boldsymbol{\Omega},\omega) - \boldsymbol{\Omega} \cdot \nabla \phi(\boldsymbol{r},\boldsymbol{\Omega},\omega) = -(\mu_{s}(\boldsymbol{r}) + \mu_{a}(\boldsymbol{r}))\phi(\boldsymbol{r},\boldsymbol{\Omega},\omega) + \mu_{s}(\boldsymbol{r}) \int_{\Omega'=4\pi} p(\boldsymbol{\Omega'},\boldsymbol{\Omega})\phi(\boldsymbol{r},\boldsymbol{\Omega'},\omega) d\Omega' + H(\boldsymbol{r},\boldsymbol{\Omega},\omega)$$

Adjoint source term

- Update reconstructed parameters with Lm-BFGS using an efficient calculation of $\nabla J(\theta)$

2D reconstruction of the optical properties

4 illuminated boundaries, 10 frequencies on [100 MHz; 1 GHz]

0.95

0.9

0.85

25

2

0.95



Reconstruction of µs for skin



Addoum et al. (2018), JQSRT

3D reconstruction



100 000 nodes (spatial mesh), 64 directions (simulated boundary data obtained with this mesh)

Reconstruction of µs

600 MHz



5 frequencies in [100 MHz, 1 GHz]



Reconstruction of µs



Simultaneously reconstruction of 2 coefficients



Challenge

- EXPLOR project, Nancy
- To test the reconstruction with a large amount of data: 1,5 million of nodes (for the spatial mesh)
- Parallel computing (in frequency and direction) with MPI and Open MP, running on a set of multi-core machines (collab with LORIA Nancy)

- 256 directions

- 8 frequencies in [500 MHz, 1 GHz] (allows to be rich in information

and to raise the under-determined character of the inverse problem)

- calculation during 1 week (21/11 – 27/11) on a cluster of 2048 cores

Diagnosis with Fluorescence

Collab with

- Pr Kienle (Germany)
- Institut de Cancérologie de Lorraine



Diagnosis with Fluorescence



Fluorescence light model

• Excitation at λ^x

$$\left(\mathbf{\Omega}\cdot\nabla+\frac{i\omega_m}{v^x}+\mu_t^x(\mathbf{\Gamma})+\mu_a^{x\to m}(\mathbf{\Gamma})\right)\psi^x(\mathbf{\Gamma},\mathbf{\Omega},\omega_m)=\mu_s^x(\mathbf{\Gamma})\int_{\Omega'=4\pi}p^x(\mathbf{\Omega'},\mathbf{\Omega})\psi^x(\mathbf{\Gamma},\mathbf{\Omega'},\omega_m)\,d\Omega'$$

• Emission at λ^m

$$\left(\boldsymbol{\Omega}\cdot\boldsymbol{\nabla} + \frac{i\omega_m}{v^m} + \mu_t^m(\boldsymbol{r})\right)\psi^m(\boldsymbol{r},\boldsymbol{\Omega},\omega_m) = \mu_s^m(\boldsymbol{r})\int_{\boldsymbol{\Omega}'=4\pi}p^m(\boldsymbol{\Omega}',\boldsymbol{\Omega})\psi^m(\boldsymbol{r},\boldsymbol{\Omega}',\omega_m)\,d\boldsymbol{\Omega}' + \frac{\eta(\boldsymbol{r})\ \mu_a^{x\to m}(\boldsymbol{r})}{1+i\ \omega_m\ \tau(\boldsymbol{r})}\int_{\boldsymbol{\Omega}=4\pi}\psi^x(\boldsymbol{r},\boldsymbol{\Omega},\omega_m)\,d\boldsymbol{\Omega}$$

Fluorescence light model

- Excitation at $\lambda^{x} = \varepsilon C$ (= concentration) $\left(\mathbf{\Omega} \cdot \nabla + \frac{i\omega_{m}}{v^{x}} + \mu_{t}^{x}(\mathbf{r}) + (\mu_{a}^{x \to m}(\mathbf{r}))\right) \psi^{x}(\mathbf{r}, \mathbf{\Omega}, \omega_{m}) = \mu_{s}^{x}(\mathbf{r}) \int_{\Omega'=4\pi} p^{x}(\mathbf{\Omega'}, \mathbf{\Omega}) \psi^{x}(\mathbf{r}, \mathbf{\Omega'}, \omega_{m}) d\Omega'$
- Emission at λ^m absorption coefficient of fluorophores

$$\left(\mathbf{\Omega} \cdot \nabla + \frac{i\omega_m}{v^m} + \mu_t^m(\mathbf{r}) \right) \psi^m(\mathbf{r}, \mathbf{\Omega}, \omega_m) = \mu_s^m(\mathbf{r}) \int_{\Omega'=4\pi} p^m(\mathbf{\Omega'}, \mathbf{\Omega}) \psi^m(\mathbf{r}, \mathbf{\Omega'}, \omega_m) d\Omega' + \frac{\eta(\mathbf{r}) \left(\mu_a^{x \to m}(\mathbf{r}) \right)}{1 + i \omega_m \tau(\mathbf{r})} \int_{\Omega=4\pi} \psi^x(\mathbf{r}, \mathbf{\Omega}, \omega_m) d\Omega$$

Fluorescence light model

- Excitation at $\lambda^{x} = \varepsilon C$ (= concentration) $\left(\Omega \cdot \nabla + \frac{i\omega_{m}}{v^{x}} + \mu_{t}^{x}(\mathbf{r}) + (\mu_{a}^{x \to m}(\mathbf{r}))\psi^{x}(\mathbf{r}, \Omega, \omega_{m}) = \mu_{s}^{x}(\mathbf{r})\int_{\Omega'=4\pi} p^{x}(\Omega', \Omega)\psi^{x}(\mathbf{r}, \Omega', \omega_{m}) d\Omega'$ • Emission at λ^{m} absorption coefficient of fluorophores $\left(\Omega \cdot \nabla + \frac{i\omega_{m}}{v^{m}} + \mu_{t}^{m}(\mathbf{r})\right)\psi^{m}(\mathbf{r}, \Omega, \omega_{m}) = \mu_{s}^{m}(\mathbf{r})\int_{\Omega'=4\pi} p^{m}(\Omega', \Omega)\psi^{m}(\mathbf{r}, \Omega', \omega_{m}) d\Omega'$ $+ \frac{\eta(\mathbf{r})(\mu_{a}^{x \to m}(\mathbf{r}))}{1+i\omega_{m}\tau(\mathbf{r})}\int_{\Omega=4\pi} \psi^{x}(\mathbf{r}, \Omega, \omega_{m}) d\Omega$
- Adjoint in fluorescence (collab with a mathematician of Nancy) Emission $\left(\mathbf{\Omega} \cdot \nabla - \frac{i\omega_m}{v^m} + \mu_t^m(\mathbf{r}) \right) \phi^m(\mathbf{r}, -\mathbf{\Omega}, \omega_m) = \mu_s^m(\mathbf{r}) \int_{\Omega'=4\pi} p^m(\mathbf{\Omega}', -\mathbf{\Omega}) \phi^m(\mathbf{r}, \mathbf{\Omega}', \omega_m) d\Omega'$ Diffuse excitation, $\phi_s^x(\mathbf{r}, -\mathbf{\Omega}, \omega_m)$ depending on ϕ^m Collimated excitation, $\phi_c^x(\mathbf{r}, \omega_m)$ depending on ϕ^m and ϕ_s^x + adjoint BC

Analytical expression of $\nabla J(\mu_a^{x \to m})$ 36

2D reconstruction of the absorption of fluorophore



 η = 0.012; τ = 0.52 ns (Indocyanine Green)



Asllanaj et al. (2017, submitted), Inverse Problems

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Conclusions on the MFVM

Advantages

- Suitable for predicting fluorescence and diffuse light propagation in absorbing and highly forward-scattering media subjected to a collimated laser beam
- Good level of accuracy; a relative difference < 1% can be obtained when compared to MC or analytical solutions
- Explicit solution of the radiance (without solving a linear system)
- Use of unstructured meshes

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- Explicit solution of the radiance (without solving a linear system)
- Use of unstructured meshes
- (Actual) disadvantage: time consuming

256 (or more) RTEs have to be solved (in the multiple scattering regime). Several iterations (100 - 1000) are needed to compute the different orders of scattering 39

Conclusions on the optical tomography software

- Based on an accurate deterministic forward model
- Can reconstruct (in 2D/3D):
 - $\mu_a(\mathbf{r}), \mu_s(\mathbf{r}), g(\mathbf{r})$

Actually, 2 coefficients can be reconstructed simultaneously but not 3 - $\mu_a^{x \to m}(\mathbf{r})$

- The 3D computational times are actually too high for a (pre)clinical application
- Probably, we can optimize the MVFM and the inverse algorithm..., couple MVFM and MC,

Future works

- Optical imaging
- Applications:
 - Validation on (epoxy resin) phantoms (with Pr Kienle, Germany)
 - **Project** with the **Institut de Cancérologie de Lorraine** on the study of fluorophore diffusion (used in **Photodynamic Therapy**) in a preclinical model (multicellular tumor spheroid model)

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- Photoacoustic imaging (take advantage of optic and acoustic for a high spatial resolution and a deeper penetration)
- Coupled heat transfers in biological tissues: study of the tissue denaturation mechanism

Thank you for your attention!

Collaborations

Pr Contassot-Vivier

Pr Kienle Institut for Laser Technology in Medicine and Metrology

Angewandte Photonik (stay of 10 months)

ulm university universität

Pr J. R. Roche Institute of Mathematics, Lorraine



Pr L. Bolotine S. Marchal, CR

Institut de Cancérologie de Lorraine Alexis Vautrin Ensemble, construisons l'avenir

Semitransparent boundaries

Specular reflection

$$\psi(s, \boldsymbol{\Omega}, t) = (1 - \rho(\Theta)) \Upsilon(s, \boldsymbol{\Omega}, t) + \rho(\Theta) \psi(s, \boldsymbol{\Omega_{inc}}, t) \quad \text{for} \quad \boldsymbol{\Omega} \cdot \boldsymbol{n} > 0,$$

where $\boldsymbol{\Omega}$ is the specular reflection of $\boldsymbol{\Omega}_{inc}$: $\boldsymbol{\Omega}_{inc} = \boldsymbol{\Omega} - 2 (\boldsymbol{\Omega} \cdot \boldsymbol{n}) \boldsymbol{n}$. The angle Θ satisfies $\cos \Theta = \boldsymbol{\Omega}_{inc} \cdot \boldsymbol{n}_{out} > 0$ where

 n_{out} is local unit outward normal vector. The directional reflection $\rho(\Theta)$ is given by Snell-Descartes laws. Considering that $n^2 \ll k^2$ (n, k being the real and imaginary parts of the complex refractive index, respectively):

$$\rho(\Theta) = \begin{cases} \frac{1}{2} \left(\frac{\cos \Theta - n_r R(\Theta)}{\cos \Theta + n_r R(\Theta)} \right)^2 + \frac{1}{2} \left(\frac{n_r \cos \Theta - R(\Theta)}{n_r \cos \Theta + R(\Theta)} \right)^2 & \text{if } \Theta < \Theta_{crit} \\ 1 & \text{otherwise,} \end{cases}$$

with $R(\Theta) = \sqrt{1 - n_r^2 \sin^2 \Theta}$ and $n_r = \frac{n}{n_{out}}$ is the relative refractive index between the two media. The critical angle satisfies Snell's law: $\sin \Theta_{crit} = n_r^{-1}$. In our application, $n_{out} = 1$, $n_r = n = 1.4$ and $\Theta_{crit} = 45.58^{\circ}$.

Diffuse reflection

Change
$$\rho(\Theta)\psi(s, \mathbf{\Omega}_{inc}, t)$$
 by $\frac{1}{\pi}Q_{out}(s, t)$

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Biomedical diagnosis



 An important issue in Optical Tomography is to have an efficient **forward solver** (accurate, fast, suitable for irregular geometries) combined with an efficient inverse method for reconstructing the mesoscopic optical properties

Different methods for solving the RTE

Diffusion Equation

• Approximate model (deduced from the RTE) yet widely used

• 3 assumptions:

(1) low absorption, $\mu_a \ll \mu_s$

(2) large spatial and time scales, $l_{tr} << L$ and $\frac{l_{tr}}{c} << T$ $l_{tr} = 1/\mu_s^*$: transport length with $\mu_s^* = \mu_s (1-g)$

= path taken by a collimated beam before it becomes isotropic *T*: observation time. *L*: characteristic length of the medium
(3) does not correctly model the BC with a collimated (laser) beam

Reconstruction of µs

600 MHz



3D



Semi-transparent boundaries

Elastically scattered light



The spatial mesh (in the plane (Oyz)) was refined around the strong variation of the Gaussian function

1st case



2nd case



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3rd case

