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Model Reduction and Modelling of Uncertainties in Quantitative Photoacoustic Tomography

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Inverse Problems on Large Scales

RICAM, Linz, November 28 – December 2, 2022

Finnish Centre of Excellence in Inverse Modelling and Imaging 2018-2025

This is joint work with

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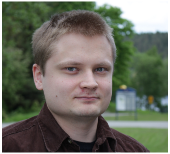
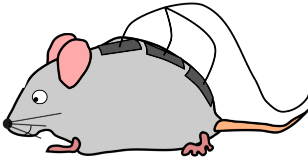
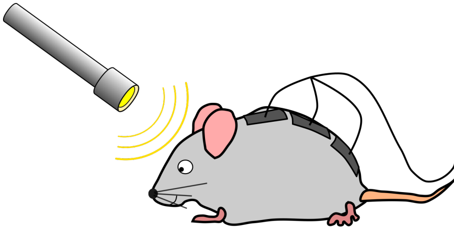
  

Photoacoustic tomography (PAT)



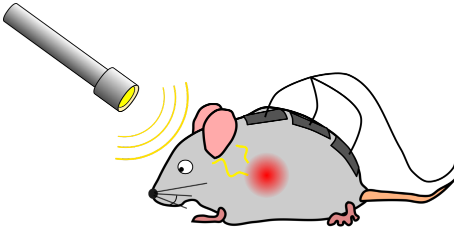
Photoacoustic tomography (PAT)

- Tissue is illuminated with a short pulse of light



Photoacoustic tomography (PAT)

- Tissue is illuminated with a short pulse of light
- As light propagates within the tissue, it is absorbed by chromophores
- The absorbed energy causes pressure rise



Photoacoustic tomography (PAT)

- Tissue is illuminated with a short pulse of light
- As light propagates within the tissue, it is absorbed by chromophores
- The absorbed energy causes pressure rise
- This pressure increase propagates through the tissue as an acoustic wave and can be measured on the boundary of the tissue using ultrasound sensors

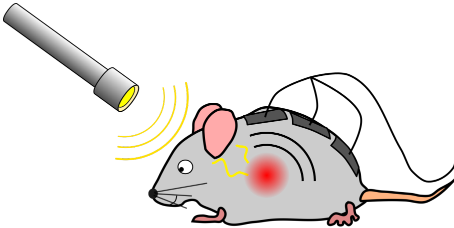
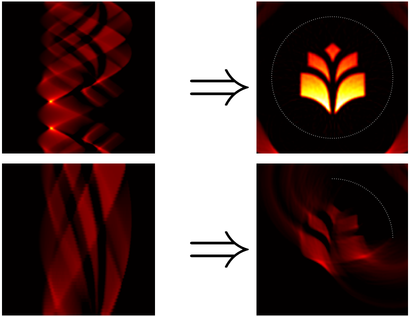
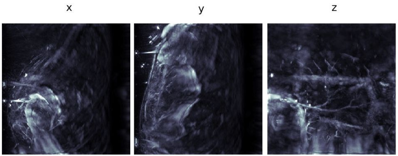


Image reconstruction

- Reconstruct the initial pressure (or absorbed optical energy density) from the photoacoustic signal measured on the boundary of the tissue



- Photoacoustic tomography combines benefits of optical and acoustic methods
- Contrast through optical absorption
  - Tissue chromophores: oxygenated and deoxygenated haemoglobin, water, lipids, melanin
  - Contrast agents
- Resolution by ultrasound
  - Low scattering in soft biological tissue
- Applications in imaging of tissue vasculature, tumours, small animal imaging, etc.



J. Tick et al, Three dimensional photoacoustic tomography in Bayesian framework, *J Acoust Soc Am* 144:2061-2071, 2018

Quantitative photoacoustic tomography (QPAT)

- Aims is to estimate the concentrations of light absorbing molecules
- Two inverse problems:
  - Acoustic inverse problem: estimation of initial pressure from photoacoustic measurements
  - Optical inverse problem: estimation of optical parameters from the initial pressure
- Modelling of light propagation, photoacoustic efficiency and ultrasound propagation are needed

- In this work, the optical inverse problem of QPAT is approached in the framework of Bayesian inverse problems
- We aim at accurate estimates and reliable error limits of these estimates
- We study how errors and uncertainties in modelling affect to the solution of the inverse problem
- Modelling of these errors utilising Bayesian approximation error modelling is investigated

Optical forward problem of QPAT

- Modelling light transport
  - Radiative transfer equation (RTE)

$$\hat{s} \cdot \nabla\phi(r, \hat{s}) + (\mu_s + \mu_a)\phi(r, \hat{s}) = \mu_s \int_{S^{n-1}} \Theta(\hat{s} \cdot \hat{s}')\phi(r, \hat{s}')\mathrm{d}\hat{s}', \quad r \in \Omega$$

$$\phi(r, \hat{s}) = \begin{cases} \phi_0(r, \hat{s}), & r \in \epsilon_j, \quad \hat{s} \cdot \hat{n} < 0 \\ 0, & r \in \partial\Omega \backslash \epsilon_j, \quad \hat{s} \cdot \hat{n} < 0 \end{cases}$$

    where $\phi(r, \hat{s})$ is radiance, μ_a is absorption, μ_s is scattering, $\Theta(\hat{s} \cdot \hat{s}')$ is scattering phase function and $\phi_0(r, \hat{s})$ is light source in position r and direction $\hat{s}$
  - Monte Carlo method for light transport
    - Based on random sampling of photon paths as they propagate in scattering medium
  - Monte Carlo and RTE simulate light propagation accurately in scattering medium
  - They are computationally challenging

- Diffusion approximation (DA)

$$
\begin{aligned}
-\nabla \cdot \kappa(r)\nabla\Phi(r) + \mu_a(r)\Phi(r) &= 0 \qquad r \in \Omega \\
\Phi(r) + \frac{1}{2\gamma_n}\kappa(r)A\frac{\partial\Phi(r)}{\partial\hat{n}} &= \begin{cases} \frac{I_s}{\gamma_n}, & r \in \epsilon_i \\ 0, & r \in \partial\Omega \setminus \epsilon_i \end{cases}
\end{aligned}
$$

  where $\Phi(r) = \int_{S^{n-1}} \phi(r, \hat{s})\mathrm{d}\hat{s}$ is photon fluence and $\kappa = (d(\mu_a + \mu_s(1-g)))^{-1}$ is diffusion coefficient
- The DA is a special case of the first order approximation of the spherical harmonics extension of the RTE
- The approximation is valid in a highly scattering medium relatively far from the light source

- Absorbed optical energy density

$$H(r) = \mu_a(r)\Phi(r)$$

- Initial acoustic pressure

$$p_0(r) = p(r, t = 0) = G(r)H(r) = \frac{\beta c^2}{C_p}H(r)$$

where $G(r)$ is the Grüneisen parameter describing photoacoustic efficiency

Bayesian approach to the optical inverse problem

- Optical inverse problem: estimate distribution of optical parameters from absorbed optical energy density (or initial pressure)
- In this work, estimation of absorption and scattering is studied
- Bayesian approach to the inverse problem is taken

- A discrete observation model for QPAT in the presence of additive noise model is

$$y = A(x) + e$$

where $y \in \mathbb{R}^m$is the data, $x \in \mathbb{R}^n$ are the unknown optical parameters, $A \in \mathbb{R}^{m \times n}$ is the discretised forward model that is assumed to be exact within measurement precision, $e \in \mathbb{R}^m$ denotes the noise

- Let us consider all parameters as random variables
- The solution of the inverse problem given by the Bayes' formula (posterior probability distribution)

$$\pi(x|y) \propto \pi(y|x)\pi(x)$$

  where $\pi(y|x)$ is the likelihood and $\pi(x)$ is the prior
- If we assume that the noise e and and the unknown x are mutually independent, observation model leads to likelihood

$$\pi(y|x) = \pi_e(y - A(x))$$

  where π_e is the probability distribution of the noise e

- The unknown x and noise are modelled as Gaussian random variables

$$x \sim \mathcal{N}(\eta_x, \Gamma_x), \quad e \sim \mathcal{N}(\eta_e, \Gamma_e)$$

where $\eta_x \in \mathbb{R}^n$ and $\eta_e \in \mathbb{R}^m$ are the means and $\Gamma_x \in \mathbb{R}^{n\times n}$ and $\Gamma_e \in \mathbb{R}^{m\times m}$ are the covariance matrices

- In this case, the posterior distribution becomes

$$\pi(x|y) \propto \exp\left\{-\frac{1}{2}\|L_e(y - A(x) - \eta_e)\|^2 - \frac{1}{2}\|L_x(x - \eta_x)\|^2\right\}$$

where $\Gamma_e^{-1} = L_e^T L_e$ and $\Gamma_x^{-1} = L_x^T L_x$

- The practical solution for the inverse problem is obtained by calculating point estimates from the posterior distribution
- We consider here the maximum a posteriori (MAP) estimate

$$x_{\mathrm{MAP}} = \arg\min_x \left\{ \frac{1}{2}\|L_e(y - A(x) - \eta_e)\|^2 + \frac{1}{2}\|L_x(x - \eta_x)\|^2 \right\}$$

- To evaluate the credibility of the MAP estimate, we approximate the forward model using the first order Taylor series

$$A(x) \approx A(\hat{x}) + J(\hat{x})(x - \hat{x}),$$

and form a local Gaussian approximation

$$(x|y) \propto \mathcal{N}(\hat{\eta}, \hat{\Gamma})$$

where $\hat{\eta} = \hat{x}$ is the MAP estimate and

$$\hat{\Gamma} = (J(\hat{x})^{\mathrm{T}} \Gamma_e^{-1} J(\hat{x}) + \Gamma_x^{-1})^{-1}$$

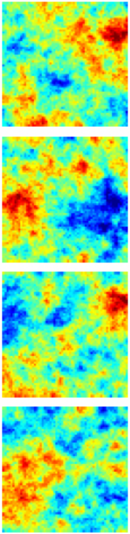
where $J(\hat{x})$ is the Jacobian

- Credible intervals $[\hat{x} - 3\sigma_{\hat{x}} \, , \, \hat{x} + 3\sigma_{\hat{x}}]$ where $\sigma_{\hat{x}_j} = \sqrt{\hat{\Gamma}(j,j)}$

- In this work, we use Gaussian Ornstein-Uhlenbeck prior distribution
  - Ornstein-Uhlenbeck covariance

$$\Gamma_{x,ij} = \sigma^2 \exp\left\{-\frac{\|r_i - r_j\|}{\zeta}\right\}$$

  - The mean was chosen as the midpoint between expected minimum and maximum absorption and scattering parameter values
  - The standard deviation was chosen such that the expected maximum is within one standard deviation from the mean (68 % lie within an interval between maximum and minimum values)
  - The characteristic length scale ζ (controls spatial correlation) was chosen based on expected size of target structures



Inverse problem in the presence of modelling errors

- If an approximate (i.e. reduced or inexact) forward model $\tilde{A}$ is utilised, the discrepancy between the exact and reduced models can be described as

$$\varepsilon = A(x) - \tilde{A}(x)$$

and observation model can be written utilising Bayesian approximation error modelling[1] in the form

$$\begin{aligned} y &= A(x) + \tilde{A}(x) - \tilde{A}(x) + e \\ &= \tilde{A}(x) + \varepsilon + e \\ &= \tilde{A}(x) + n \end{aligned}$$

- Thus, if $\tilde{A} = A$, forward model is exact and $\varepsilon = 0$

[1] J. Kaipio and E. Somersalo: *Statistical and Computational Inverse Problems*, Springer, 2005

- Let us assume that x and e are mutually independent and Gaussian distributed

$$x \sim \mathcal{N}(\eta_x, \Gamma_x), \quad e \sim \mathcal{N}(\eta_e, \Gamma_e)$$

- Approximate the modelling error ε and the total error $n = \varepsilon + e$ as Gaussian

$$\varepsilon \sim \mathcal{N}(\eta_\varepsilon, \Gamma_\varepsilon), \quad n \sim \mathcal{N}(\eta_n, \Gamma_n)$$

- Let us ignore the mutual dependence of x and modelling error ε (so called enhanced error model)

- Following a similar derivation as in the case of the exact forward model, the posterior distribution can be derived

$$\pi(x|y) \propto \exp\left\{-\frac{1}{2}\|L_n(y - \tilde{A}(x) - \eta_n)\|^2 - \frac{1}{2}\|L_x(x - \eta_x)\|^2\right\}$$

where η_n and η_x are the means and L_n and L_x are the Cholesky decompositions of the inverse covariance matrices of the noise and prior $L_n^{\mathrm{T}} L_n = \Gamma_n^{-1}$ and $L_x^{\mathrm{T}} L_x = \Gamma_x^{-1}$, and $\eta_n = \eta_\varepsilon + \eta_e$ and $\Gamma_n = \Gamma_\varepsilon + \Gamma_e$

- MAP estimate

$$x_{\mathrm{MAP}} = \arg\min_x \left\{ \frac{1}{2} \| L_n(y - \tilde{A}(x) - \eta_n) \|^2 + \frac{1}{2} \| L_x(x - \eta_x) \|^2 \right\}$$

- Credible intervals $[\hat{x} - 3\sigma_{\hat{x}}\,,\ \hat{x} + 3\sigma_{\hat{x}}]$ where $\sigma_{\hat{x}_j} = \sqrt{\hat{\Gamma}(j,j)}$ where $(x|y) \propto \mathcal{N}(\hat{\eta}, \hat{\Gamma})$ where $\hat{\eta} = \hat{x}$ is the MAP estimate and $\hat{\Gamma} = (J(\hat{x})^{\mathrm{T}} \Gamma_n^{-1} J(\hat{x}) + \Gamma_x^{-1})^{-1}$ where $J(\hat{x})$ is the Jacobian

- The modelling error ε can be, for example, approximated by sampling
  - Drawing samples from the training distribution of x
  - Calculating samples of the modelling error using exact and approximate forward models

$$\varepsilon^\ell = A(x)^\ell - \tilde{A}(x)^\ell$$

  - Estimating the mean and covariance of the modelling error as

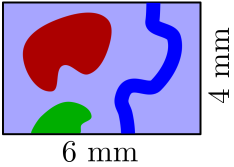
$$\eta_\varepsilon = \frac{1}{L} \sum_{\ell=1}^{L} \varepsilon^\ell$$

$$\Gamma_\varepsilon = \frac{1}{L-1} \sum_{\ell=1}^{L} (\varepsilon^\ell - \eta_\varepsilon)(\varepsilon^\ell - \eta_\varepsilon)^T$$

Simulations

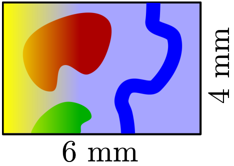
- In this work, we study modelling of errors due to using the DA as a light transport model in the inverse problem of QPAT when the exact model is Monte Carlo
- Modelling of errors
  1. Inverse problem using a reduced forward model $\tilde{A}(x)$ with a Gaussian approximation for the modelling errors $\varepsilon \sim \mathcal{N}(\eta_\varepsilon, \Gamma_\varepsilon)$
  2. Inverse problem using a reduced forward model $\tilde{A}(x)$ and ignoring the modelling errors ($\varepsilon = 0$)
- We investigate
  - Different ranges of scattering parameters (i.e. validity of the DA)
  - Different noise levels

Data simulation

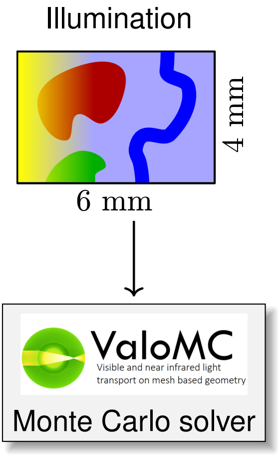


Data simulation

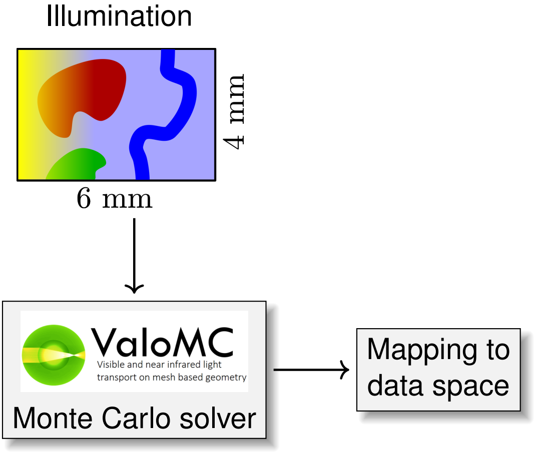
Illumination



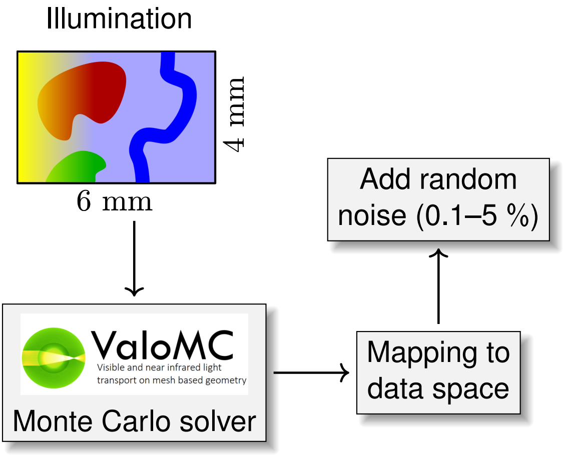
Data simulation



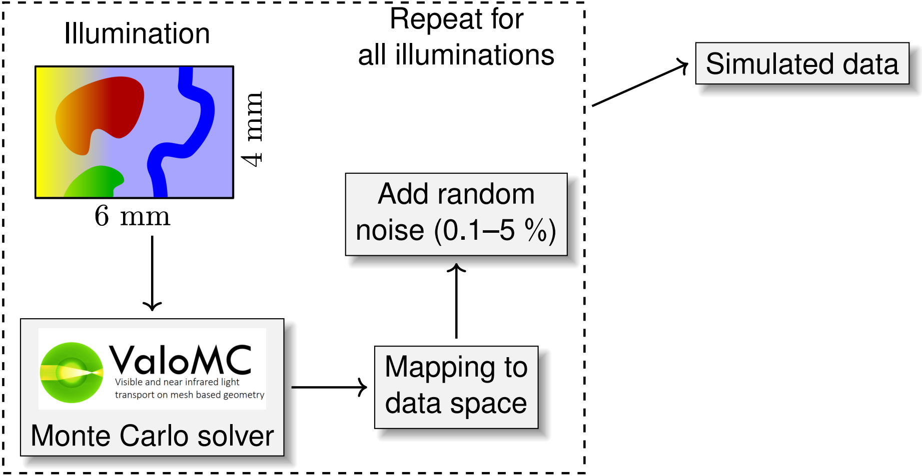
Data simulation



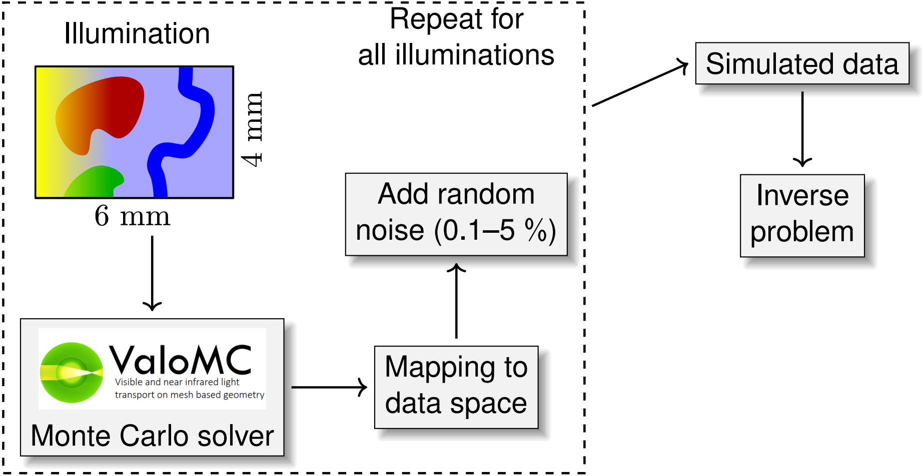
Data simulation



Data simulation



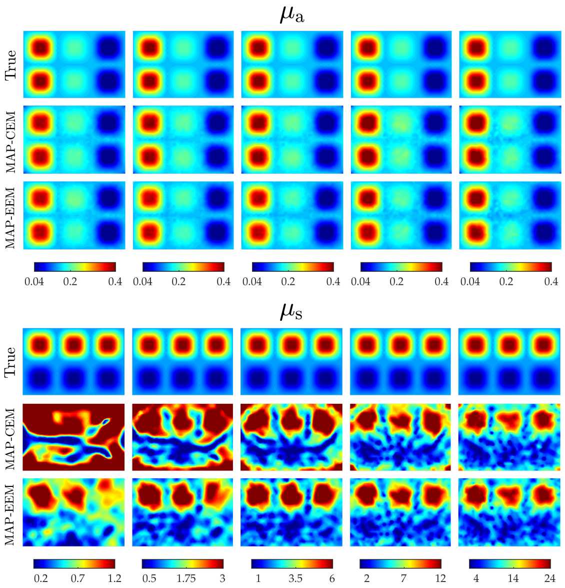
Data simulation

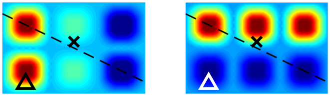


Inverse problem

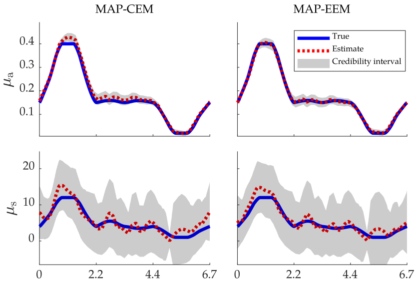
Computed MAP estimate using the DA as the forward model (reduced forward model $\tilde{A}(x)$) with two approaches

- Gaussian approximation for the modelling errors $\varepsilon \sim \mathcal{N}(\eta_\varepsilon, \Gamma_\varepsilon)$ (MAP-EEM)
- Ignoring the modelling errors ($\varepsilon = 0$) (MAP-CEM)

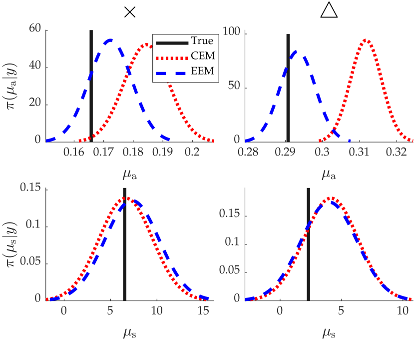

μ_a
True
MAP-CEM
MAP-EEM
0.04 0.2 0.4
0.04 0.2 0.4
0.04 0.2 0.4
0.04 0.2 0.4
0.04 0.2 0.4
μ_s
True
MAP-CEM
MAP-EEM
0.2 0.7 1.2
0.5 1.75 3
1 3.5 6
2 7 12
4 14 24



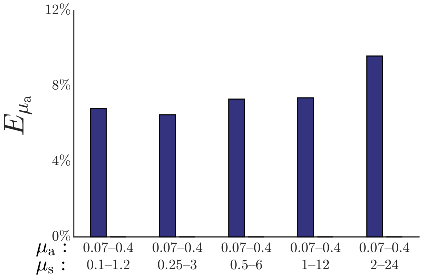
MAP ± 3 sd on a cross section

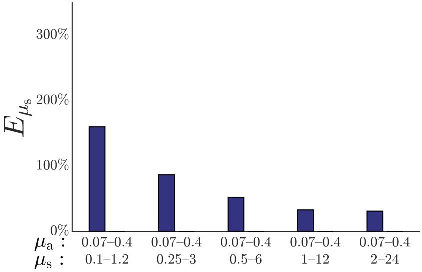


Marginal densities

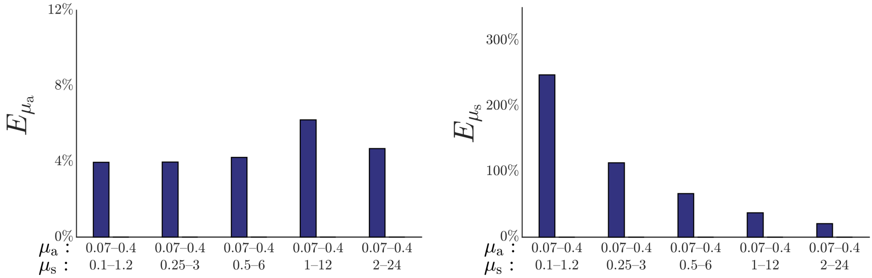


Relative errors of the estimates at different scattering value regimes (5% noise)
Modelling errors neglected (dark blue)

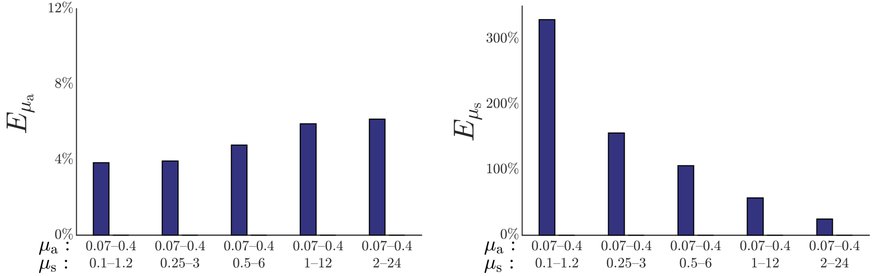




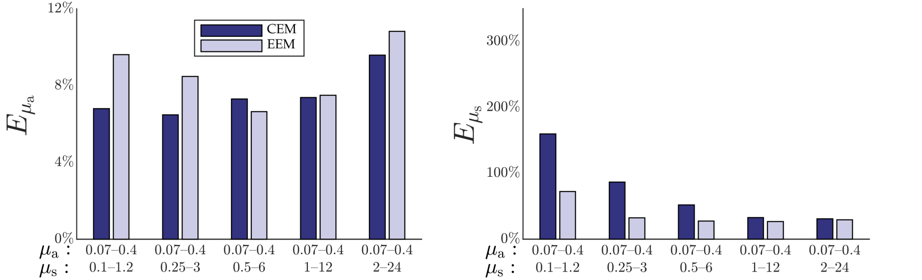
Relative errors of the estimates at different scattering value regimes (1% noise)
Modelling errors neglected (dark blue)



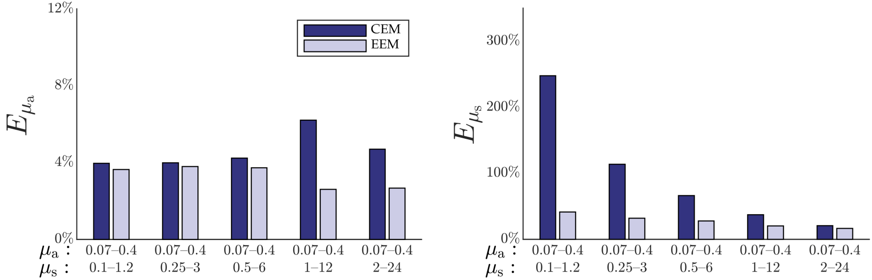
Relative errors of the estimates at different scattering value regimes (0.1% noise)
Modelling errors neglected (dark blue)



Relative errors of the estimates at different scattering value regimes (5% noise)
Modelling errors neglected (dark blue)
Modelling errors taken into account (light blue)



Relative errors of the estimates at different scattering value regimes (1% noise)
Modelling errors neglected (dark blue)
Modelling errors taken into account (light blue)



Relative errors of the estimates at different scattering value regimes (0.1% noise)
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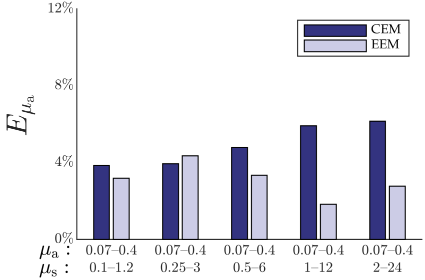
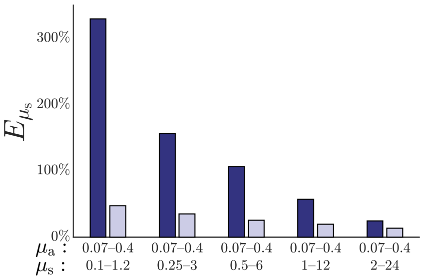
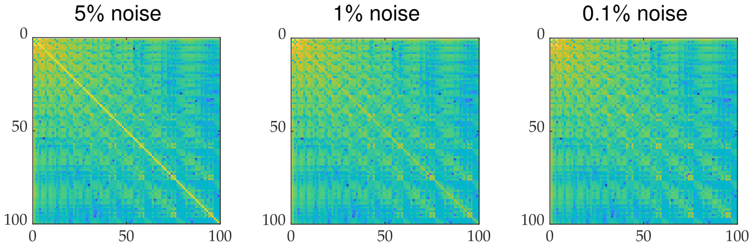




Logarithm of the total error (noise and modelling error) covariance corresponding to first 100 data points with different noise levels



Summary

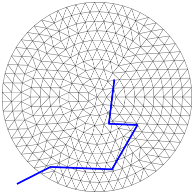
- Optical inverse problem of QPAT was approached in a Bayesian framework
- MAP estimates were computed and their reliability was evaluated
- More research is required to study the safety of the reliability estimates
- The results show that modelling errors can result into inexact (quantitative) estimates, although qualitatively the reconstructions may look ’quite nice’
- The Bayesian approximation error modelling can be utilised in modelling of errors (to some extent)

Inverse problem utilising optical Monte Carlo

- We are interested in using an optical Monte Carlo model – a stochastic forward model – in the inverse problem of QPAT
- We utilise a perturbation Monte Carlo approach to form Jacobians for the forward model

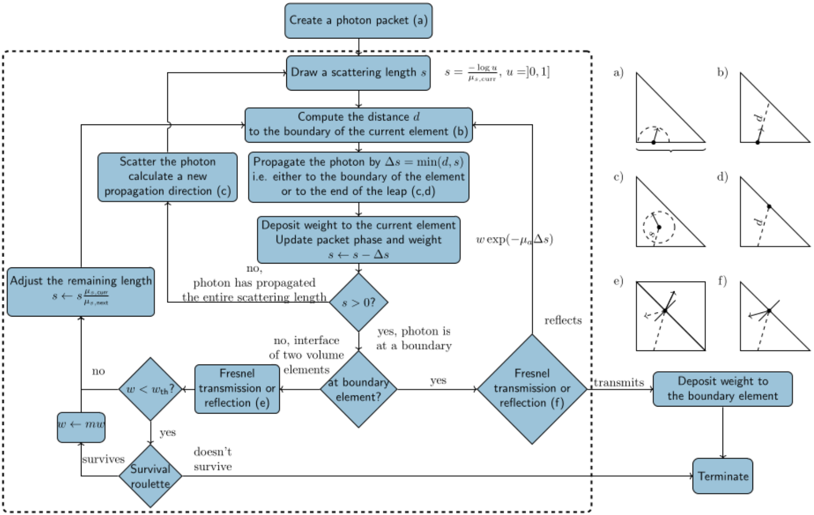
Monte Carlo simulation of light transport

- The probability for photon absorption in a small length $\mathrm{d}s$ in a propagation direction is $\mu_\mathrm{a}\mathrm{d}s$, and the probability for photon scattering is $\mu_\mathrm{s}\mathrm{d}s$
- Scattering length follows an exponential probability distribution function $f(l) = \mu_\mathrm{s}(l)\exp\left[-\int_0^l \mu_\mathrm{s}(s)\mathrm{d}s\right]$
- Scattering angle follows a probability distribution (Henyey-Greenstein phase function)
- Photon packet method: weight of a photon packet along trajectory is reduced due to absorption $w(S) = \exp\left[-\int_S \mu_\mathrm{a}(s)\mathrm{d}s\right]$
- In this work, a Monte Carlo software ValoMC is used (https://inverselight.github.io/ValoMC/)



ValoMC
Visible and near infrared light transport on mesh based geometry

A.A. Leino, A. Pulkkinen, T. Tarvainen, ValoMC: a Monte Carlo software and MATLAB toolbox for simulating light transport in biological tissue, *OSA Continuum* 2:957–972, 2019



Create a photon packet (a)
Draw a scattering length s
$s = \frac{-\log u}{\mu_{s,\mathrm{curr}}}$, $u =]0,1]$
Compute the distance d
to the boundary of the current element (b)
Scatter the photon
calculate a new
propagation direction (c)
Propagate the photon by $\Delta s = \min(d, s)$
i.e. either to the boundary of the element
or to the end of the leap (c,d)
Deposit weight to the current element
Update packet phase and weight
$s \leftarrow s - \Delta s$
$w\exp(-\mu_a \Delta s)$
Adjust the remaining length
$s \leftarrow s\frac{\mu_{s,\mathrm{curr}}}{\mu_{s,\mathrm{next}}}$
no,
photon has propagated
the entire scattering length
$s > 0$?
yes, photon is
at a boundary
reflects
no, interface
of two volume
elements
no
$w < w_{\mathrm{th}}$?
Fresnel
transmission or
reflection (e)
at boundary
element?
yes
Fresnel
transmission or
reflection (f)
transmits
Deposit weight to
the boundary element
$w \leftarrow mw$
yes
survives
Survival
roulette
doesn't
survive
Terminate
a)
b)
c)
d)
e)
f)

Perturbation Monte Carlo

- The effect of a small change in the optical parameters (perturbation) to the simulation results is evaluated efficiently by re-using the trajectories from an unperturbed simulation
- Considering the ratio between probability density functions between scattering lengths in perturbed and unperturbed regions, the weight of a photon packet in a perturbed simulation can be derived

$$\tilde{w} = w \left(\frac{\tilde{\mu}_s}{\mu_s} \right)^k \exp\left[-(\tilde{\mu}_s - \mu_s) L_{tot} \right]$$

  where $\tilde{w}$ is the perturbed weight, w is the unperturbed weight, $\tilde{\mu}_s$ is the perturbed scattering coefficient, L_{tot} is the total distance travelled by the photon packet inside the perturbed region, and k the number of scattering events in the perturbed region

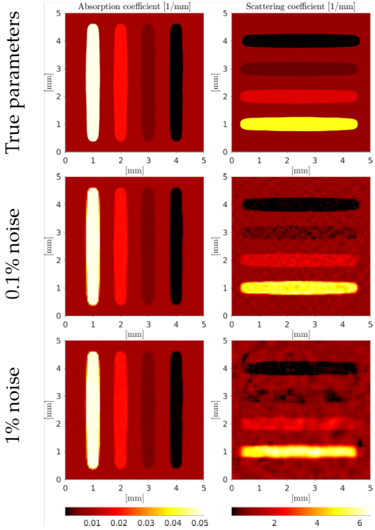
Inverse problem

- Inverse problem is approached in a Bayesian framework
- MAP estimates solved using the Gauss-Newton method
- Perturbation Monte Carlo is utilised in computing Jacobians for scattering

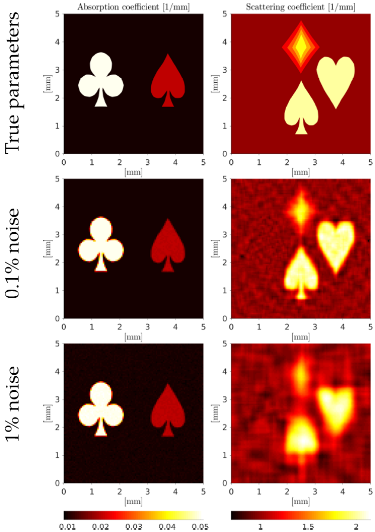
  Simulations

  - $5 \times 5\,\mathrm{mm}$ square computation domain
  - μ_a in scale $[0.0001\,,\,0.05]\,\mathrm{mm}^{-1}$ and μ_s in scale $[0.01\,,\,5]\,\mathrm{mm}^{-1}$
  - Henyey-Greenstein scattering anisotropy parameter $g = 0.9$
  - Four illuminations with light coming from each of the sides in turn
  - Two noise levels at 0.1 % and 1 %

- Relative errors of the estimates
  $E_{\mu_a} = 0.3\%$ and $E_{\mu_s} = 11\%$
  $E_{\mu_a} = 2.2\%$ and $E_{\mu_s} = 20\%$



- Relative errors of the estimates
  $E_{\mu_a} = 0.2\%$ and $E_{\mu_s} = 6.1\%$
  $E_{\mu_a} = 1.9\%$ and $E_{\mu_s} = 11\%$



Summary

- Monte Carlo method for light transport can be utilised in the inverse problem of QPAT
- More research is required for example to study the number of photon packets required for forward solution and Jacobian, and evaluating the reliability of the estimates

Thank you for your attention!

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