Approximate marginalization of absorption and scattering in fluorescence diffuse optical tomography

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Outline:

Part 1: Approximation Error Model

Part 2: Fluorescence Diffuse Optical Tomography

Part 3: Computational Examples
Part 1: Approximation Error Model (AEM)
Introduction

- Consider the inverse problem of estimating $x \in \mathbb{R}^n$ from noisy observation $y \in \mathbb{R}^m$, given the model

$$y = \bar{A}(x, z) + e$$

where
- $x \in \mathbb{R}^n$: primary unknown
- $z \in \mathbb{R}^d$: uninteresting, **auxiliary unknowns**.
- Complete Bayesian solution: Posterior density model

$$\pi(x, z|y)$$

In principle, one should either
- estimate all parameters $(x, z)$ or
- marginalize $\pi(x|y) = \int \int \pi(x, z|y)dz$ (by MCMC)

However, this is often infeasible due to computational time limitations.
• Conventional approximation: treat $z$ as fixed conditioning variables, and estimate $x$ from

$$\pi(x|y, z = z_0)$$

→ large errors if realization $z_0$ is incorrect.

• Figure: 1D-marginal posterior $\pi(x_\ell|y)$:
  • exact marginal $\pi(x_\ell|y)$ (black line)
  • $\pi(x_\ell|y, z = z_0)$ with incorrect $z_0$ (blue)
  • true value of $x_\ell$ (vertical).
• Approximation error approach (Kaipio & Somersalo, 2007); Approximation for the marginalization

\[ \pi(x|y) = \int \int \pi(x, z|y)dz \]

by the following steps:

- Modeling errors caused by inaccurately known \( z \) are modeled as an additive noise process \( \varepsilon(x, z) \) in the measurement model.
- Approximate marginalization over the noise process using a Gaussian approximation for \( \pi(x, \varepsilon) \).

• Remarks:
- Approximation of \( \pi(x, \varepsilon) \) obtained by Monte Carlo integration over samples from prior models of \( (x, z) \). Can be done off-line.
- Allows simultaneous handling of model reduction related errors.
Conventional measurement error model (CEM)

- Consider the conventional measurement model
  \[ y = \bar{A}(x) + e \]  
  (1)

- Joint density
  \[ \pi(y, x, e) = \pi(y\mid x, e)\pi(e\mid x)\pi(x) = \pi(y, e\mid x)\pi(x) \]

- In case of (1), we have
  \[ \pi(y\mid x, e) = \delta(y - \bar{A}(x) - e) \]
  and
  \[ \pi(y\mid x) = \int \pi(y, e\mid x) \, de = \int \delta(y - \bar{A}(x) - e)\pi(e\mid x) \, de = \pi_{e\mid x}(y - \bar{A}(x)\mid x) \]

- In the (usual) case of mutually independent \( x \) and \( e \), we have
  \[ \pi_{e\mid x}(e\mid x) = \pi_e(e) \]
  and
  \[ \pi(y\mid x) = \pi_e(y - \bar{A}(x)) \]
Furthermore, if \( \pi(e) = \mathcal{N}(e_*, \Gamma_e) \) and \( \pi(x) = \mathcal{N}(x_*, \Gamma_x) \), we have

\[
\pi(x \mid y) \propto \exp \left( -\frac{1}{2} \left( \|L_e(y - \bar{A}(x) - e_*)\|^2 + \|L_x(x - x_*)\|^2 \right) \right),
\]

where \( \Gamma_e = L_e^T L_e \) and \( \Gamma_x = L_x^T L_x \).

**MAP estimate with the CEM:**

\[
\min_x \left\{ \|L_e(y - \bar{A}(x) - e_*)\|^2 + \|L_x(x - x_*)\|^2 \right\}
\]
Approximation error model (AEM)

- Accurate measurement model

\[ y = \bar{A}(x, z) + e \]  

(2)

- Instead of using (2) and treating \((x, z)\) as unknowns, we want to fix \(z \leftarrow z_0\) and use a possibly drastically reduced model

\[ x \mapsto A(x, z_0) \]

However, the use of the conventional model

\[ y = A(x, z_0) + e \]

leads to errors in the estimates of \(x\) if i) \(z_0\) is incorrect or/and ii) model reduction errors are not negligible.
In the approximation error approach, we write the measurement model

\[ y = \tilde{A}(x, z) + e \]
\[ = A(x, z_0) + [\tilde{A}(x, z) - A(x, z_0)] + e \]
\[ = A(x, z_0) + \varepsilon(x, z) + e \]  

(3)

where \( \varepsilon(x, z) = \tilde{A}(x, z) - A(x, z_0) \) is the approximation error.

The objective is to formulate posterior model

\[ \pi(x|y) \propto \pi(y|x)\pi(x) \]

using measurement model (3).

We consider \( e \) independent of \((x, z)\).
• Using Bayes formula repeatedly, we get

\[
\pi(y, x, z, e, \varepsilon) = \pi(y | x, z, e, \varepsilon)\pi(x, z, e, \varepsilon) \\
= \delta(y - A(x, z_0) - e - \varepsilon)\pi(e, \varepsilon | x, z)\pi(z | x)\pi(x) \\
= \pi(y, z, e, \varepsilon | x)\pi(x)
\]

• Hence

\[
\pi(y | x) = \int \int \int \int \pi(y, z, e, \varepsilon | x)de d\varepsilon dz \\
= \int \pi_e(y - A(x, z_0) - \varepsilon)\pi_{\varepsilon|x}(\varepsilon | x) d\varepsilon
\]

(note: convolution integral w.r.t. \(\varepsilon\))

• To get a computationally useful and efficient form, \(\pi_e\) and \(\pi_{\varepsilon|x}\) are approximated with Gaussian distributions.
Let the Gaussian approximation of $\pi(\varepsilon, x)$ be

$$\pi(\varepsilon, x) \propto \exp \left\{ -\frac{1}{2} \begin{pmatrix} \varepsilon - \varepsilon_* \\ x - x_* \end{pmatrix}^T \begin{pmatrix} \Gamma_{\varepsilon} & \Gamma_{\varepsilon x} \\ \Gamma_{x \varepsilon} & \Gamma_x \end{pmatrix}^{-1} \begin{pmatrix} \varepsilon - \varepsilon_* \\ x - x_* \end{pmatrix} \right\}$$

Hence $\pi(e) = \mathcal{N}(e_*, \Gamma_e)$, $\pi(\varepsilon | x) = \mathcal{N}(\varepsilon_* | x, \Gamma_{\varepsilon | x})$, where

$$\varepsilon_* | x = \varepsilon_* + \Gamma_{\varepsilon x} \Gamma_x^{-1} (x - x_*), \quad \Gamma_{\varepsilon | x} = \Gamma_{\varepsilon} - \Gamma_{\varepsilon x} \Gamma_x^{-1} \Gamma_{x \varepsilon}$$

Define $\nu | x = e + \varepsilon | x$, $\pi(\nu | x) = \mathcal{N}(\nu_* | x, \Gamma_{\nu | x})$, where

$$\nu_* | x = e_* + \varepsilon_* + \Gamma_{\varepsilon x} \Gamma_x^{-1} (x - x_*), \quad \Gamma_{\nu | x} = \Gamma_e + \Gamma_{\varepsilon} - \Gamma_{\varepsilon x} \Gamma_x^{-1} \Gamma_{x \varepsilon}$$

Approximate likelihood

$$\pi(y | x) = \mathcal{N}(y - A(x, z_0) - \nu_* | x, \Gamma_{\nu | x})$$
• Posterior model

\[ \pi(x \mid y) \propto \pi(y \mid x)\pi(x) \propto \exp \left( -\frac{1}{2} V(x) \right) \]

where \( V(x) \)

\[ V(x) = \| L_{\nu \mid x} (y - A(x, z_0) - \nu_{* \mid x}) \|^2 + \| L_x (x - x_{*}) \|^2 \]

with \( \Gamma^{-1}_{\nu \mid x} = L_{\nu \mid x}^T L_{\nu \mid x} \) and \( \Gamma^{-1}_x = L_x^T L_x \).

• MAP estimate with the AEM:

\[ \min_{x} \{ \| L_{\nu \mid x} (y - A(x, z_0) - \nu_{* \mid x}) \|^2 + \| L_x (x - x_{*}) \|^2 \} \]
Part 2: Fluoresence Diffuse Optical Tomography (fDOT)
Goal: estimate $h(r)$ (concentration of fluorophore markers) by boundary measurements of fluorescence light.

Fluorescence is "excited" by illumination at location $s_j \subset \partial \Omega$, emission of the fluorescent light is measured at detector locations $d_k \subset \partial \Omega$.

Notice: optical properties $(\mu_a(r), \mu_s(r))$ are not known!
Mathematical model:

- Coupled diffusion model:
  \[
  (-\nabla \cdot \kappa(r)\nabla + \mu_a(r)) \Phi^e(r) = 0, \quad r \in \Omega, \quad (4)
  \]
  \[
  \Phi^e(r) + \frac{1}{2\zeta} \kappa(r) \alpha \frac{\partial \Phi^e(r)}{\partial \vartheta} = \begin{cases} 
  \frac{q(r)}{\zeta} & r \in r_s \\
  0 & r \in \partial \Omega \setminus r_s
  \end{cases}, \quad (5)
  \]
  \[
  (-\nabla \cdot \kappa(r)\nabla + \mu_a(r)) \Phi^f(r) = h(r)\Phi^e(r), \quad r \in \Omega, \quad (6)
  \]
  \[
  \Phi^f(r) + \frac{1}{2\zeta} \kappa(r) \alpha \frac{\partial \Phi^f(r)}{\partial \vartheta} = 0, \quad r \in \partial \Omega, \quad (7)
  \]

- Forward mapping (Born normalized):
  \[
  A(\mu_a, \mu_s) h = \frac{\int_{\Omega} \Phi^e(r_s, r)\psi^e(r_d, r) h(r) dr}{\int_{\Omega} \Phi^e(r_s, r) dr}, \quad (8)
  \]

  Discretization by FEM.
Part 3: Computational Examples
Estimates

- **MAP-REF** using correct nominal values \((\mu_a, \mu_s)\)

\[
h_{ref} = \arg \min_{h} \{ \parallel y - A(\mu_a, \mu_s)h \parallel_{\Gamma_e}^2 + \parallel L_h(h - h_*) \parallel^2 \},
\]

- **MAP-CEM** estimate using incorrect \((\mu_{a,*}, \mu_{s,*})\):

\[
h_{cem} = \arg \min_{h} \{ \parallel y - A(\mu_{a,*}, \mu_{s,*})h \parallel_{\Gamma_e}^2 + \parallel L_h(h - h_*) \parallel^2 \},
\]

- **MAP-AEM** estimate using the same incorrect \((\mu_{a,*}, \mu_{s,*})\):

\[
h_{aem} = \arg \min_{h} \{ \parallel y - A(\mu_{a,*}, \mu_{s,*})h - \nu_*h \parallel_{\Gamma_{\nu|h}}^2 + \parallel L_h(h - h_*) \parallel^2 \},
\]
Computation of approximation error statistics

- Approximation error
  \[ \varepsilon = [A(\mu_a, \mu_s) - A(\mu_{a,*}, \mu_{s,*})]h \]

- Draw sets of samples
  \{\mu_a^{(\ell)}\}, \{\mu_s^{(\ell)}\} and \{h^{(\ell)}\} from the prior models \(\pi(\mu_a), \pi(\mu_s)\) and \(\pi(h)\).

- Compute approximation error samples:
  \[ \varepsilon^{(\ell)} = [A(\mu_a^{(\ell)}, \mu_s^{(\ell)}) - A(\mu_{a,*}, \mu_{s,*})]h^{(\ell)} \]

- Estimate \(\varepsilon_{\ast|h}\) and \(\Gamma_{\varepsilon|h}\) as sample averages of \{\(h^{(\ell)}, \varepsilon^{(\ell)}\}\).
**2D Results**

- **Left:** \((\mu_a, \mu_s)\) (columns 1 & 2), \((\mu_{a,*}, \mu_{s,*})\) (columns 3 & 4).
- **Right:** 1) \(h_{\text{true}}\), 2) REF, 3) CEM, 4) AEM
3D example (digimouse)