Inferring baseline optical properties of the human head

Alex Barnett
barnett@nmr.mgh.harvard.edu

MGH/MIT/HMS AAM NMR CBI
Aims

- How well can we measure baseline optical tissue properties? Given...
  - 3d anatomical MRI data
  - optically-uniform segmented tissue types
  - time-resolved measurements
  - single optical $\lambda$
- Motivations:
  - functional imaging requires accurate baseline properties
  - more $\lambda$’s $\rightarrow$ absolute [Hb] and [HbO].
  - sets an upper bound on capability without MRI data.
Outline

1. Bayesian method overview
2. simple layer system
3. likelihood
4. results in layer
5. optode calibration & location
6. preliminary head
7. issues & conclusion
Method overview

What do measurements $y$ tell you about parameters $x$?

Inference $\rightarrow$ probability distribution functions (PDFs)
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\quad p(x|y) & \propto p(y, x) \\
& = p(y|x) \cdot p(x)
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Constant prior $\Rightarrow$ look for peaks in likelihood.
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- Peak widths give all errorbars & correlations
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p(x|y) \propto p(y, x) = \frac{p(y|x) \cdot p(x)}{p(y)}
\]

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Currently: testing with numerically-generated noisy measurements \( y \)
Simple 2-layer system

source

layer 2: 18 mm
layer 1: 8 mm

~20 ‘timegates’ from 0.2 – 2.0 ns

S-D separations of 7, 14, 21, 28 mm

Parameter vector $\mathbf{x} \equiv [\mu_a(1), \mu_a(2),\mu'_s(1), \mu'_s(2)]$
Likelihood

- $f(x) = \textit{forward model}$ (signal expectation)
- $p_{\text{noise}} = \text{noise model}$

$$p(y \mid x) = p_{\text{noise}}(y \mid f(x))$$

uncorr. gaussian $\quad \longrightarrow \quad \prod_{m} \frac{1}{\sqrt{2\pi} \sigma_{m}(x)} e^{-\frac{1}{2} \frac{(y_{m} - f_{m}(x))^{2}}{\sigma_{m}^{2}(x)}}$

$\sigma$ is some (growing) function of $f$, giving detection statistics.
Look at sensitivity
Sensitivity compared to noise

\[ \sigma\text{-normalized changes : } \beta_m = \frac{\Delta f_m}{\sigma_m} \]
Maximizing Likelihood

Minimize ‘objective function’ \( NLL \equiv -\ln p(y|\mathbf{x}) \)

- gaussian noise \( \rightarrow \approx \) ‘weighted least squares’
- peak very narrow in \( \mathbf{x}_{\text{layer 1}} \) \( \rightarrow \) I show only \( \mathbf{x}_{\text{layer 2}} \)
- 1-2 minutes per optimization

Inferring baseline optical properties of the human head – p.9
Results: photon number

typ tissue properties $\mathbf{x}_{\text{expt}} = (0.01, 0.01, 2, 1) \text{ mm}^{-1}$

Ellipses define likelihood peak width:

- more photons $\rightarrow$ narrower peak
- true $\mathbf{x}_{\text{expt}}$ rarely outside peak — good!
Results: varying $\mu_a(2)$

- other 3 parameters held constant
- photon #: 67 photons at det4
- realistic inference of errorbars

less photons survive to distant detectors so greater uncertainty in parameters
Results: varying $\mu'_s(2)$

Generally good agreement. Reliability problems...

- noise model mismatch? / optimization getting stuck
Integrating out free parameters

Width in $x_{\text{layer 1}}$ is \textit{much} less than in $x_{\text{layer 2}}$.

We only care about $x_{\text{layer 2}}$ (e.g. cortex in head).

Once peak found, use gaussian approx: analytic integral over $x_{\text{layer 1}}$:

\[
\int dx \ e^{-\frac{1}{2}x^T H x} = \frac{(2\pi)^{N/2}}{(\det H)^{1/2}}
\]

This illustrates the general Bayesian recipe for free parameters: integrate over them.
Optode calibration & placement

*Optode calibration*: \((N_s + N_d - 1)\) free scale parameters

- As for layer 1, they will be narrow-width
- integrate out with gaussians (fast)

*Placement*: choose best source/detector locations

- use peak volume \((\det H)^{-1/2}\) as objective func.
- fix \(x = x_{\text{expt}}\), and optimize over locations.

For gaussian noise model \(H \approx J^T \cdot \text{diag}(1/\sigma) \cdot J\). with jacobean \(J_{mn}(x) \equiv \partial f_m/\partial x_n\).
Noise model details

Used uncorrelated gaussian model:

- gaussian approx to poisson, clipped at both ends
- Collect more photons $\Rightarrow$ model error dominates
- Other more robust noise models (power law tails, etc) possible, easy to implement in Bayesian formalism.
Forward model details

Time-resolved detector signals \( f \) given params \( x \).

Written finite-difference time-domain (FDTD) code:

- arbitrary 3d tissue geometries
- 0.5s per source, small system 6cm × 6cm × 3cm × 2ns
- Diffusion Approx, validated against Monte Carlo
- Robin BCs, surface normals only ± \( x, y, z \).
- evolution: ‘forward-Euler’ \( O(\Delta t) \), small \( \mu' \) slows it down.
Forward model issues

There are $O(\Delta t^2)$ methods (‘implicit’, e.g. ADI):

- faster (less timesteps), but nonsmooth fluence *bad!*

Boundary Conditions

- *do* matter.
- ‘Stiffness’ tricky for FDTD stability

Avoid large system (head) by matching to $\infty$:
fluence components $\omega \ll c \mu_a$ obey Helmholtz eqn with *fixed* $k \approx i \sqrt{3 \mu_a \mu_s'}$. So, ‘radiative’ BC is just Robin BC.
Nonlinear optimization issues

Forward model with discontinuities (jumps) = \textit{bad}:

- ridges in \( f(x) \)
- fake local minima

Had to be removed!

Derivative info \textit{vastly} improves speed/robustness:
- Adjoint (‘reverse’) differentiation: get \( \nabla_x f \) \textit{wrt} \( all \) \( x_n \) with little more effort than \( f \) \textit{(e.g. Hielscher, Klose, Hanson 1999)}
Future directions

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- More sources, experimental phantom verification, heads.
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- Full posterior (errorbars & correlations) can be handled.
- Developed & validated rapid 3d diffusion forward model.
- Bayesian optode calibration and optimal location recipes.