Inferring baseline optical properties of the human head

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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 λ
- Motivations:
  - functional imaging requires accurate baseline properties
  - more λ'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 $\mathbf{y}$ tell you about parameters $\mathbf{x}$?

Inference $\rightarrow$ probability distribution functions (PDFs)

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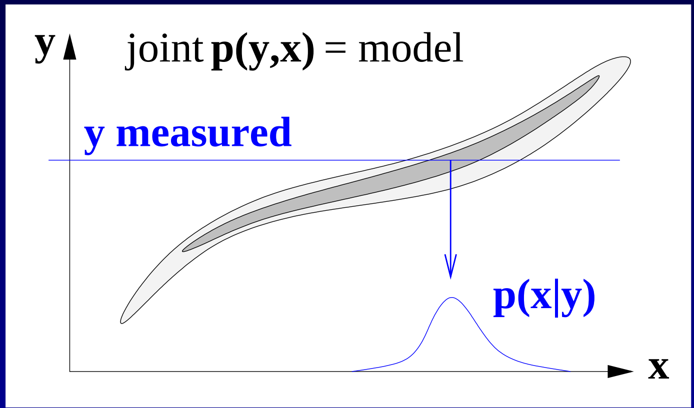

$$
\begin{aligned}
p(\mathbf{x}|\mathbf{y}) &\propto p(\mathbf{y},\mathbf{x}) \\
&= p(\mathbf{y}|\mathbf{x}) \cdot p(\mathbf{x}) \\
\text{posterior} &\propto \text{likelihood} \cdot \text{prior}
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$$

Constant prior $\Rightarrow$ look for peaks in likelihood.

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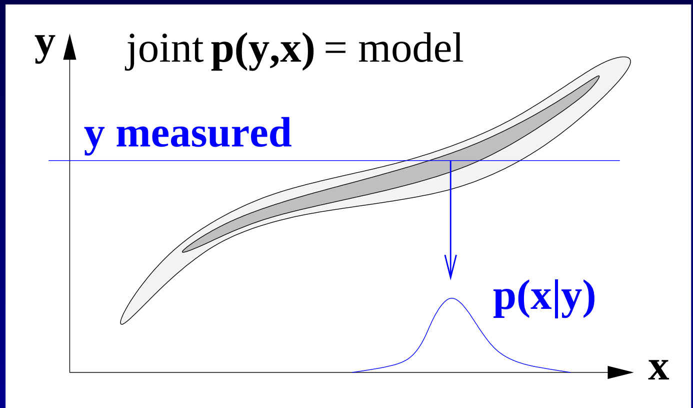

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- Peak widths give all errorbars & correlations

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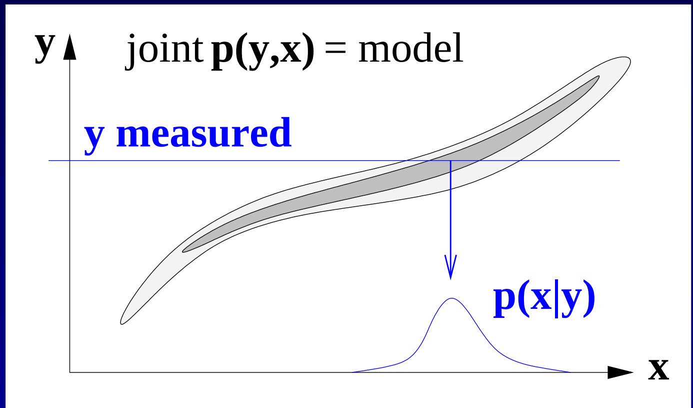

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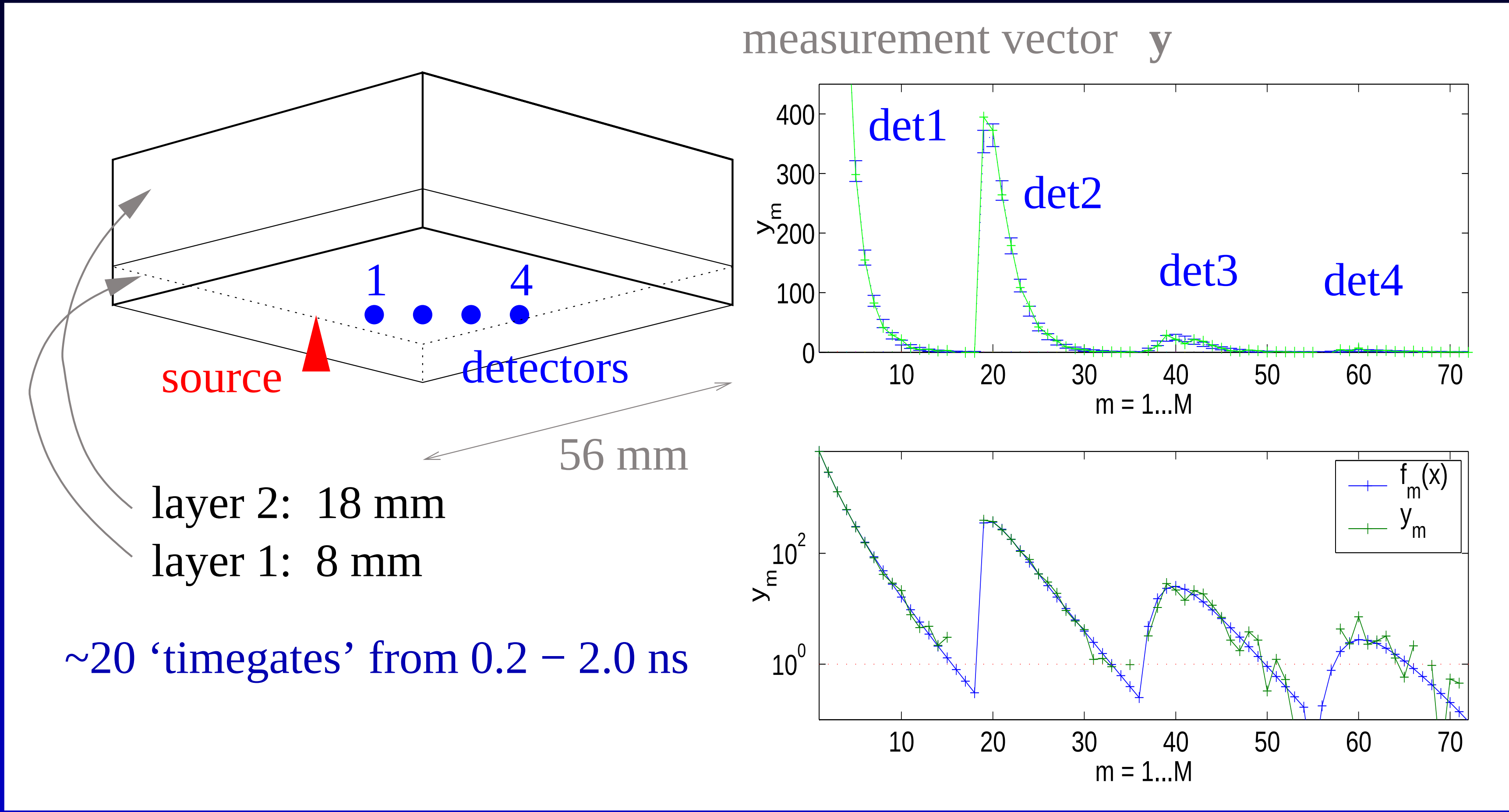
Currently: testing with numerically-generated noisy measurements **y**

Simple 2-layer system

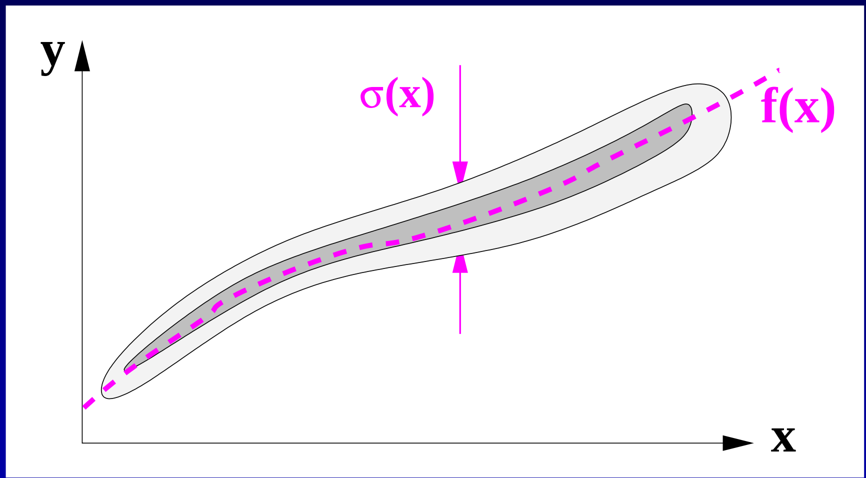


S-D separations of 7, 14, 21, 28 mm

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

Likelihood

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

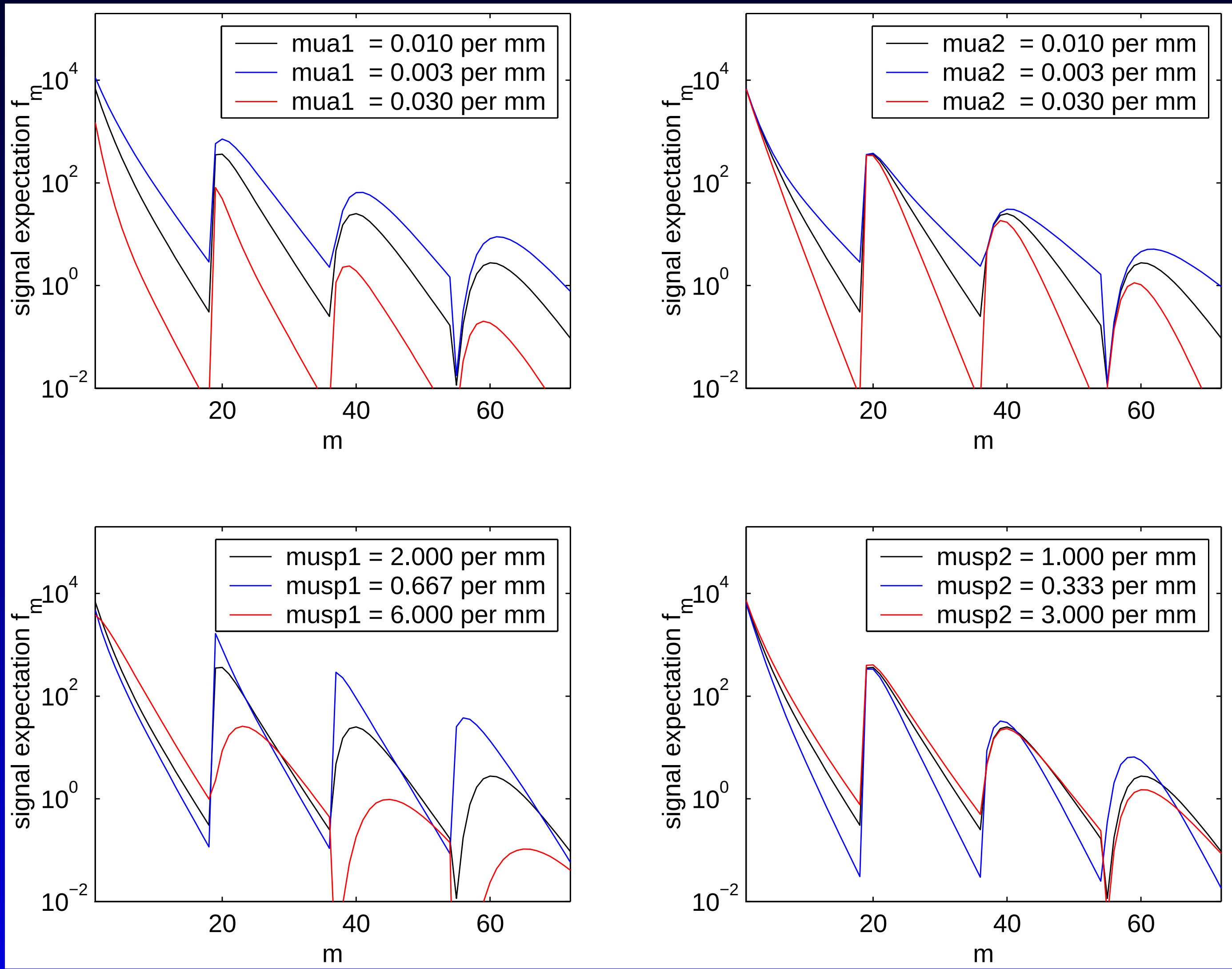


$$p(\mathbf{y}|\mathbf{x}) = p_{\text{noise}}(\mathbf{y} \mid \mathbf{f}(\mathbf{x}))$$

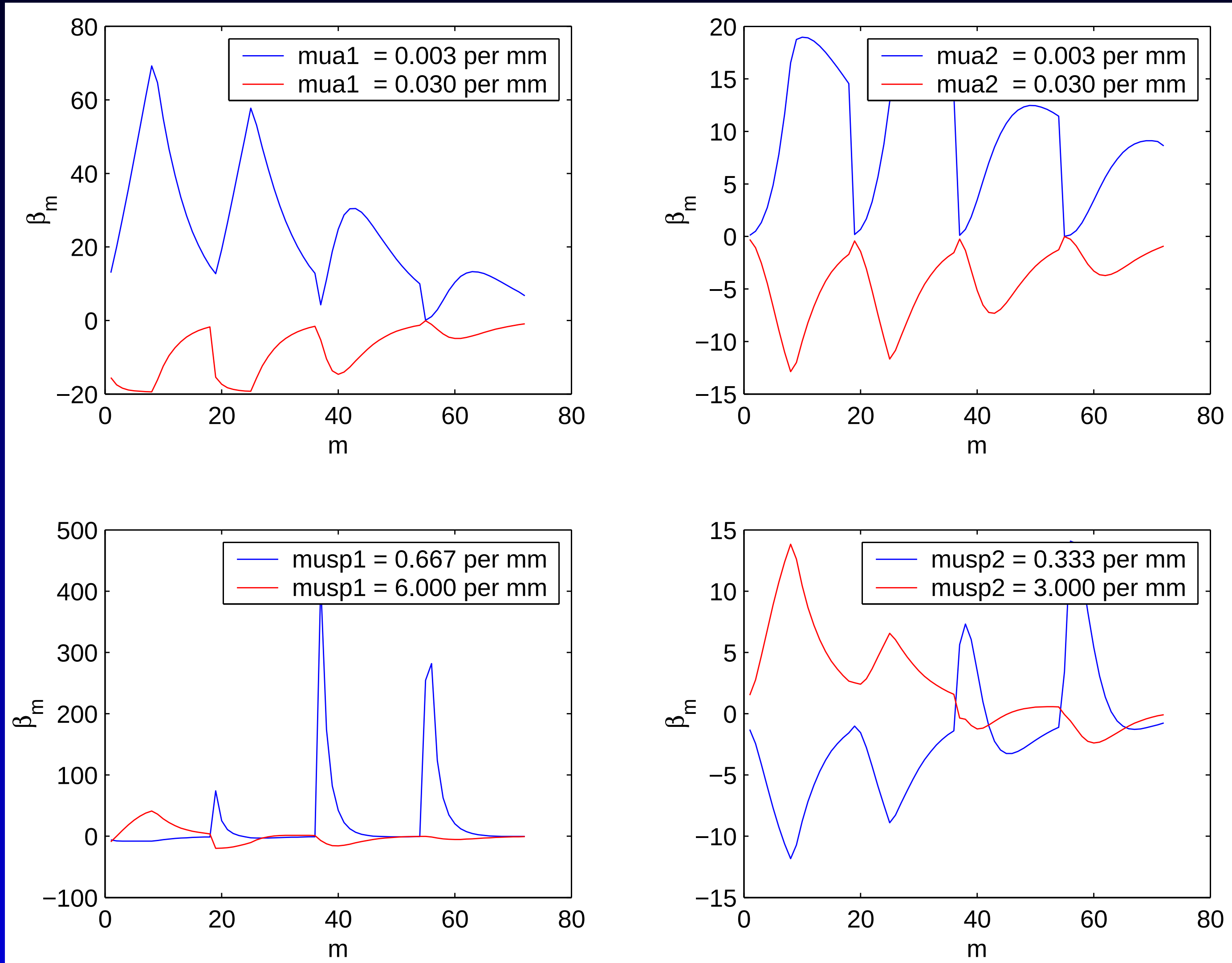
uncorr. gaussian $\longrightarrow \displaystyle\prod_m \frac{1}{\sqrt{2\pi}\sigma_m(\mathbf{x})} e^{-\frac{1}{2}\frac{[y_m - f_m(\mathbf{x})]^2}{\sigma_m^2(\mathbf{x})}}$

σ is some (growing) function of f, giving detection statistics.

Look at sensitivity

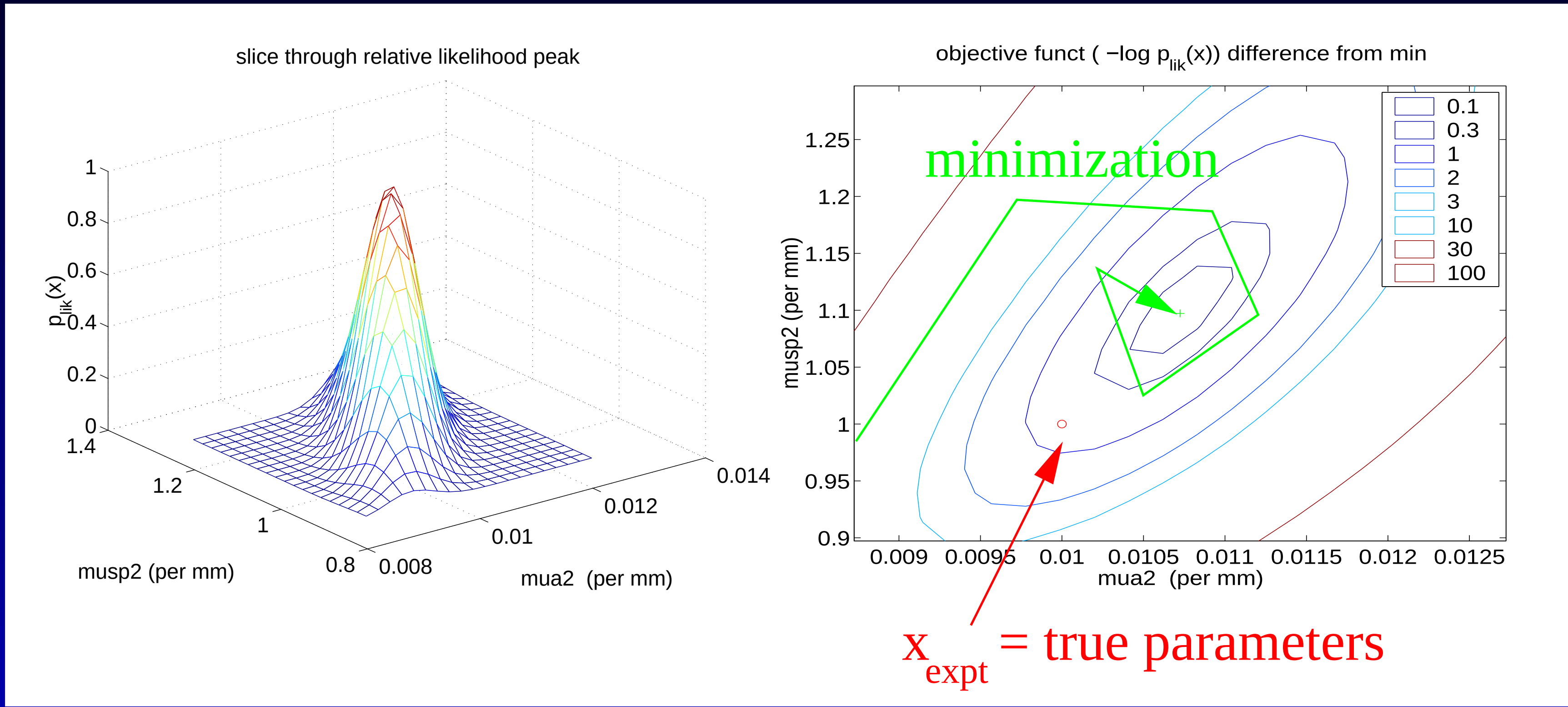


Sensitivity compared to noise



σ-normalized changes : $\beta_m \equiv \Delta f_m / \sigma_m$

Maximizing Likelihood

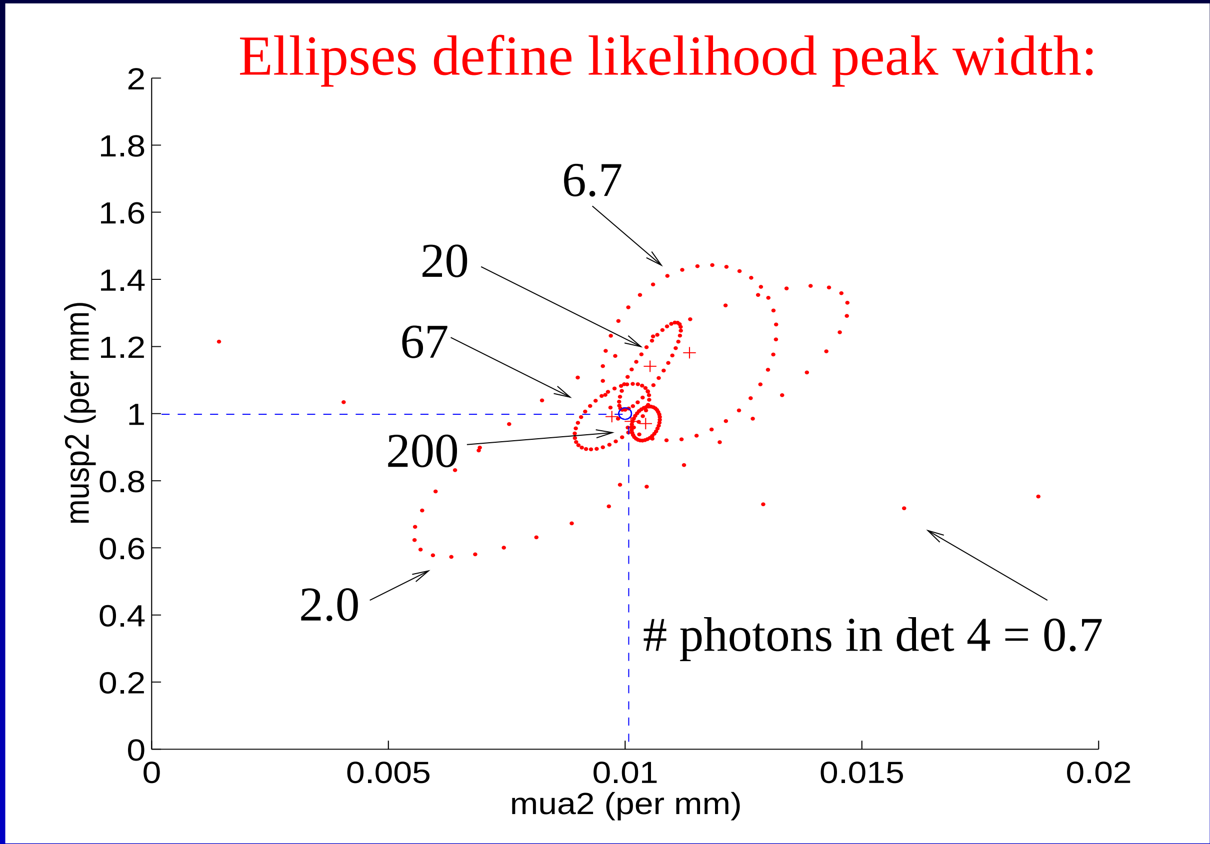


Minimize 'objective function' $\text{NLL} \equiv -\ln p(\mathbf{y}|\mathbf{x})$

- 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

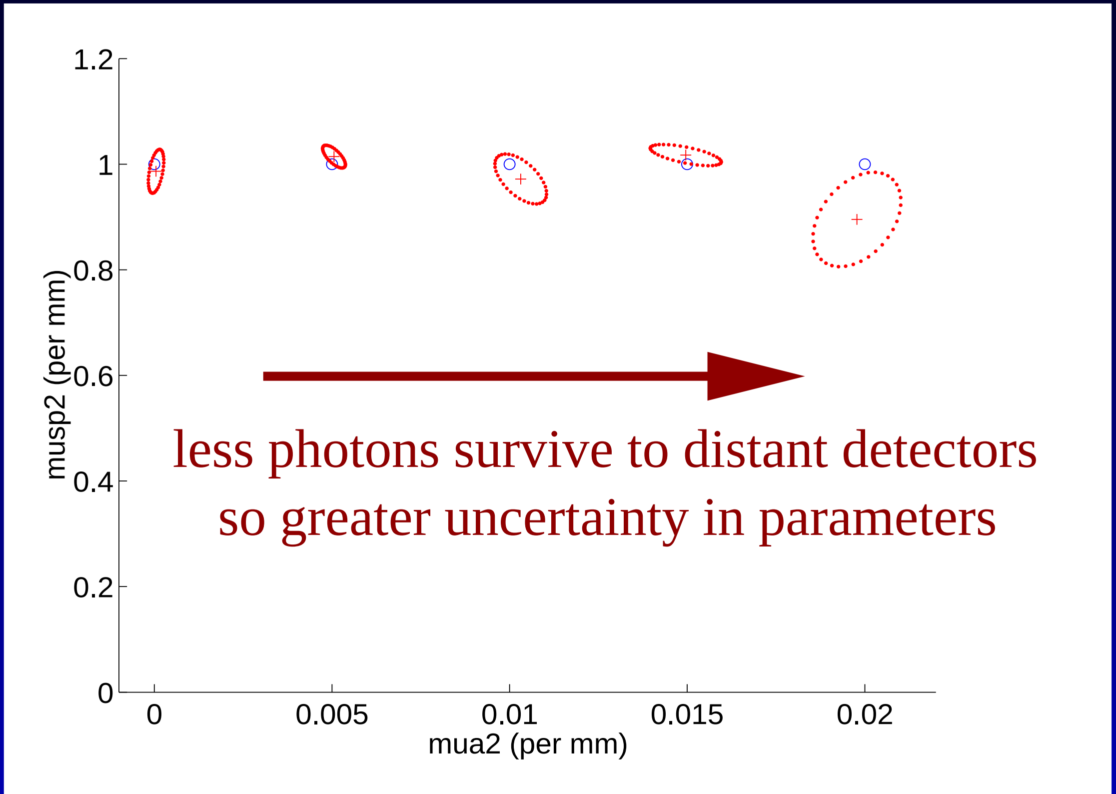
Results : photon number

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



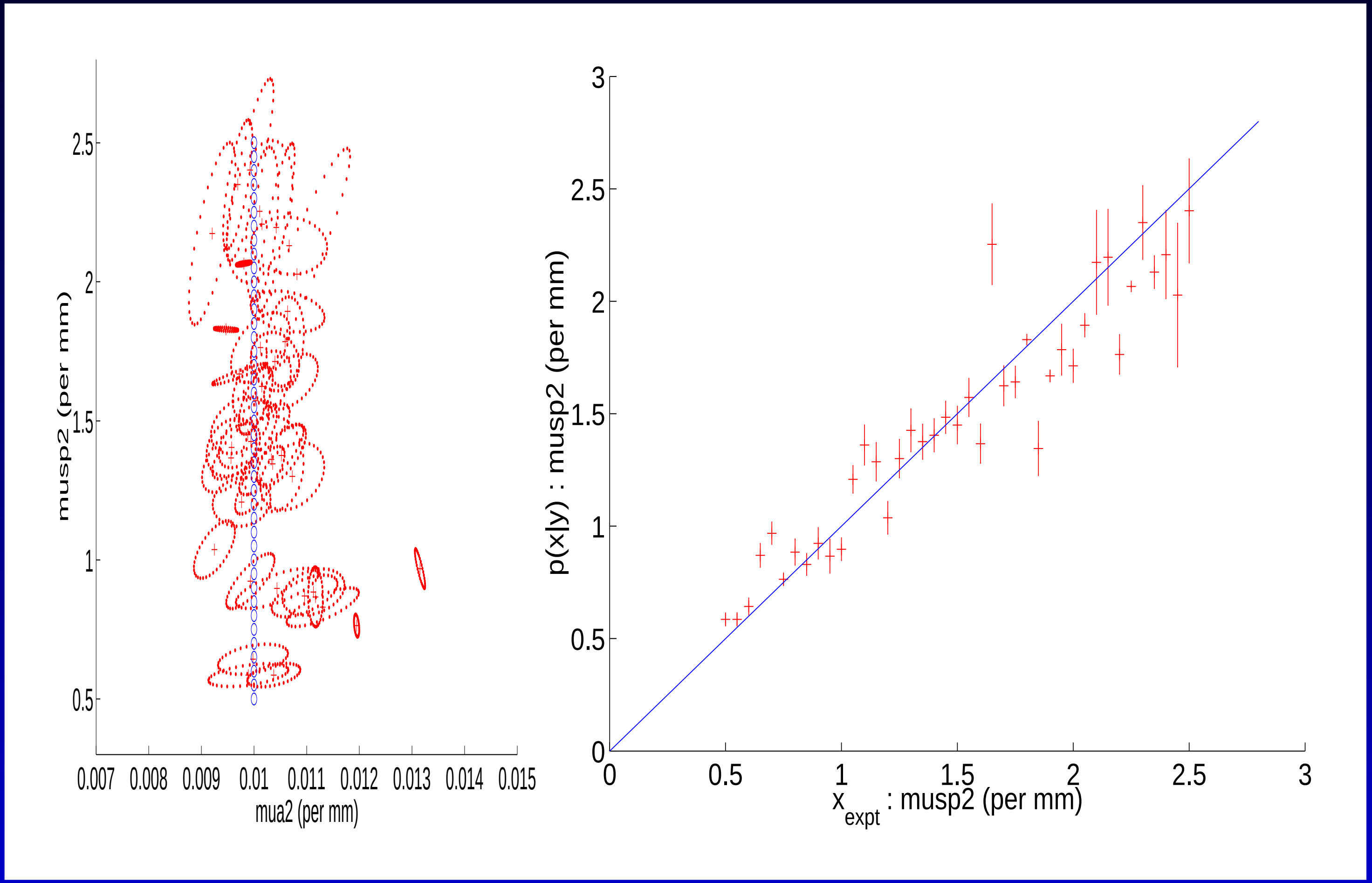
- more photons $\rightarrow$ narrower peak
- true $\mathbf{x}_{\text{expt}}$ rarely outside peak — good!

Results : varying $\mu_a(2)$



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

Results : varying $\mu_s'(2)$



Generally good agreement. Reliability problems. . .

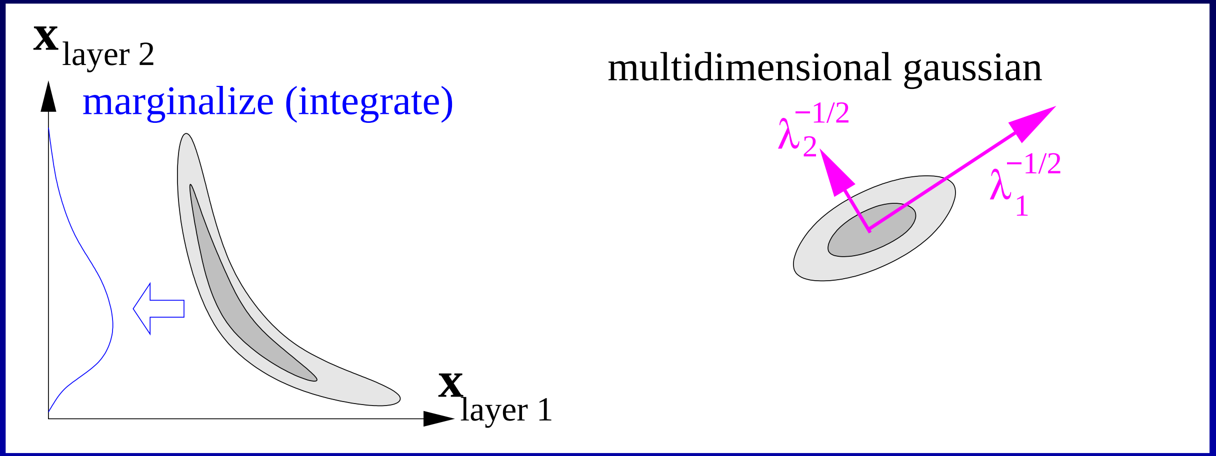
- noise model mismatch ? / optimization getting stuck

Integrating out free parameters

Width in $\mathbf{x}_{\text{layer 1}}$ is *much* less than in $\mathbf{x}_{\text{layer 2}}$.

We only care about $\mathbf{x}_{\text{layer 2}}$ (*e.g.* cortex in head).

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



$$\int d\mathbf{x}\; e^{-\frac{1}{2}\mathbf{x}^{\mathrm{T}} H x} = \frac{(2\pi)^{N/2}}{(\det H)^{1/2}}$$

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)

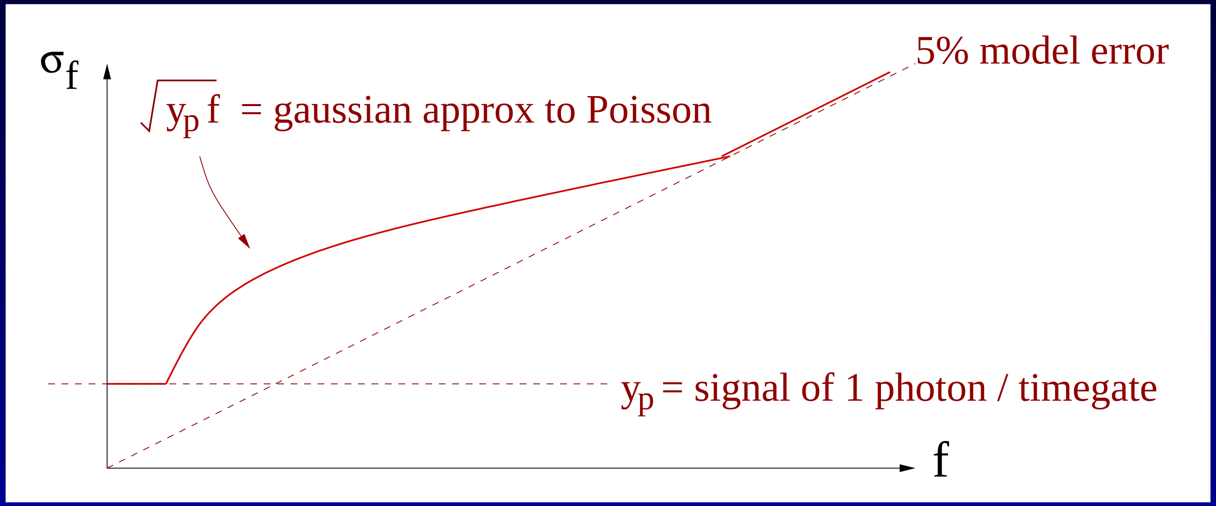
Placement : choose best source/detector locations

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

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

Noise model details

Used uncorrelated gaussian model:

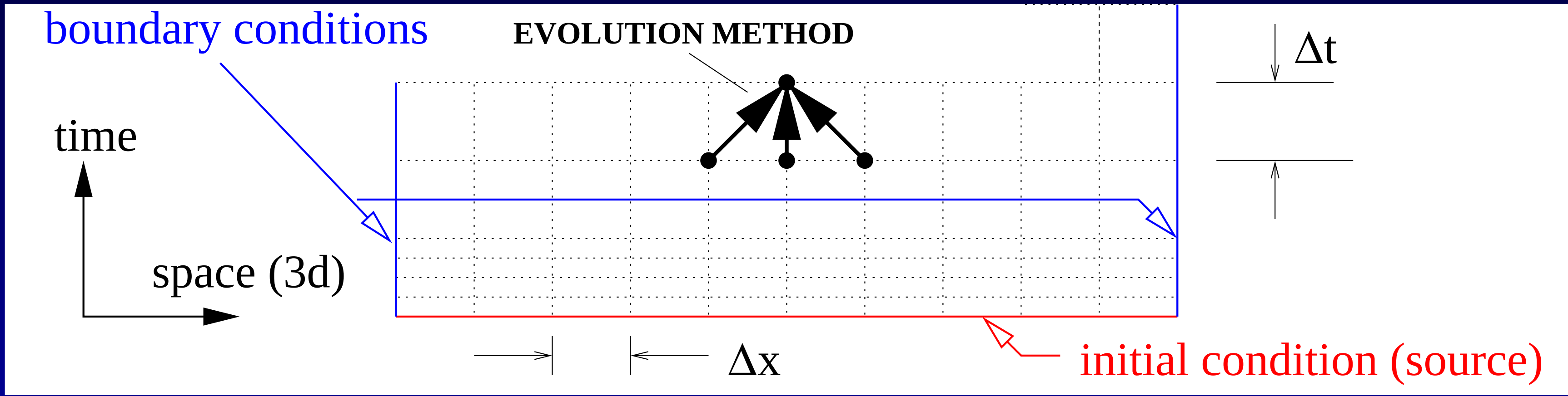


- gaussian approx to poisson, clipped at both ends
- Collect more photons $\Rightarrow$ model error dominates
- Other more *robust* noise models (power law tails, etc) possible, easy to implement in Bayesian formalism.

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 $\times$ 6cm $\times$ 3cm $\times$ 2ns
- Diffusion Approx, validated against Monte Carlo
- Robin BCs, surface normals only $\pm\, xyz$.
- evolution: 'forward-Euler' $O(\Delta t)$, small μ_s' slows it down.

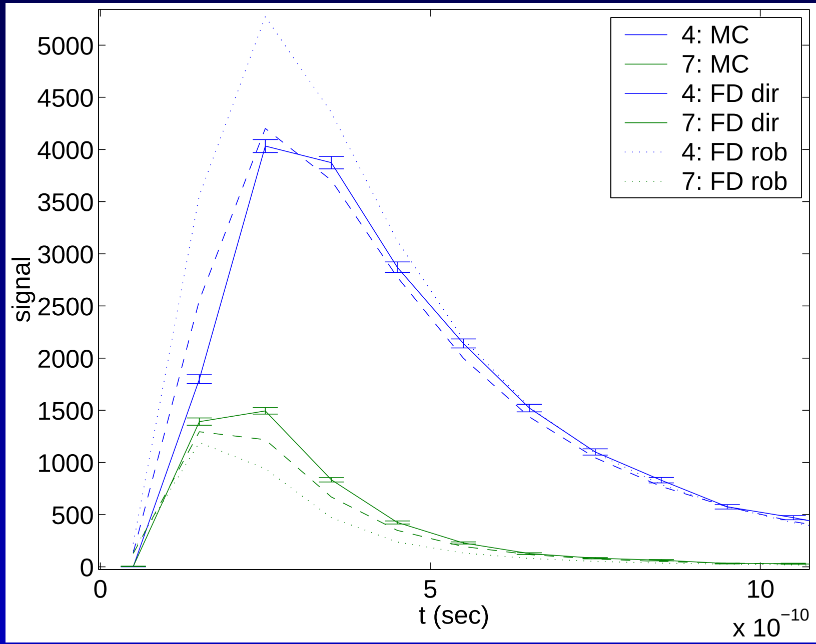
Forward model issues

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 ∞ :

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.

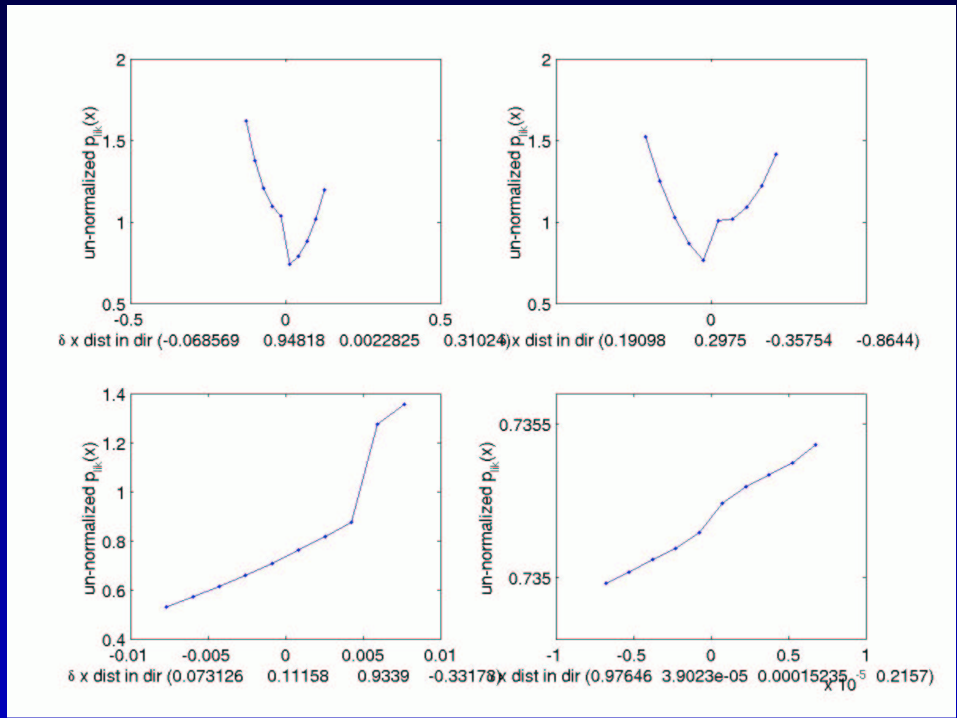
Nonlinear optimization issues

Forward model with discontinuities (jumps) = *bad* :

ridges in $\mathbf{f}(\mathbf{x})$

fake local minima

Had to be removed!



Derivative info *vastly* improves speed/robustness:

- Adjoint ('reverse') differentiation: get $\nabla_{\mathbf{x}}\mathbf{f}$ wrt *all* x_n with little more effort than $\mathbf{f}$ (*e.g.* Hielscher, Klose, Hanson 1999)

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- More sources, experimental phantom verification, heads. . .

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- Developed & validated rapid 3d diffusion forward model
- Bayesian optode calibration and optimal location recipes