Noninvasive imaging of the brain with diffusing light pulses

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Big picture

What can access optically, from outside the body?

DOT : ‘Diffuse Optical Tomography’

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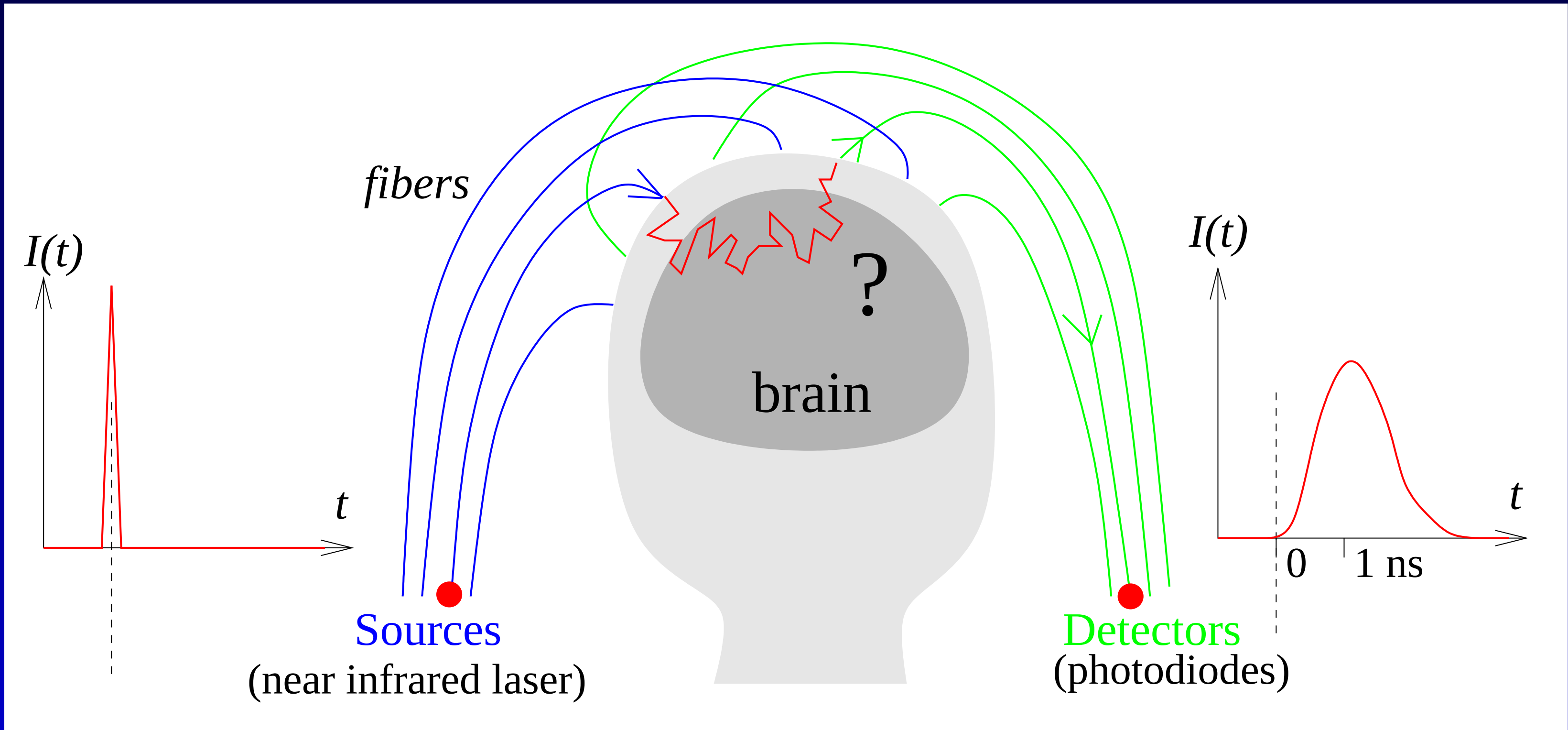

Tissue is highly scattering (blurring)

Get spatial maps $\begin{cases} \text{absorption} \\ \text{scattering} \end{cases}$ at some wavelength(s)?

Outline

- motivation
- background & history
- light in tissue: physics & numerics
- inverse problem
- piecewise homogeneous model
    - anatomy from MRI
    - results inferring 6 params *('baby' problem)*

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Omit. . .

- true 'images', regularization. . .
- details of optimization/sampling

Brain: what interested in?

CLINICAL

- Cerebral oximetry (*e.g.* neonatal):
  ·absolute oximetry hard
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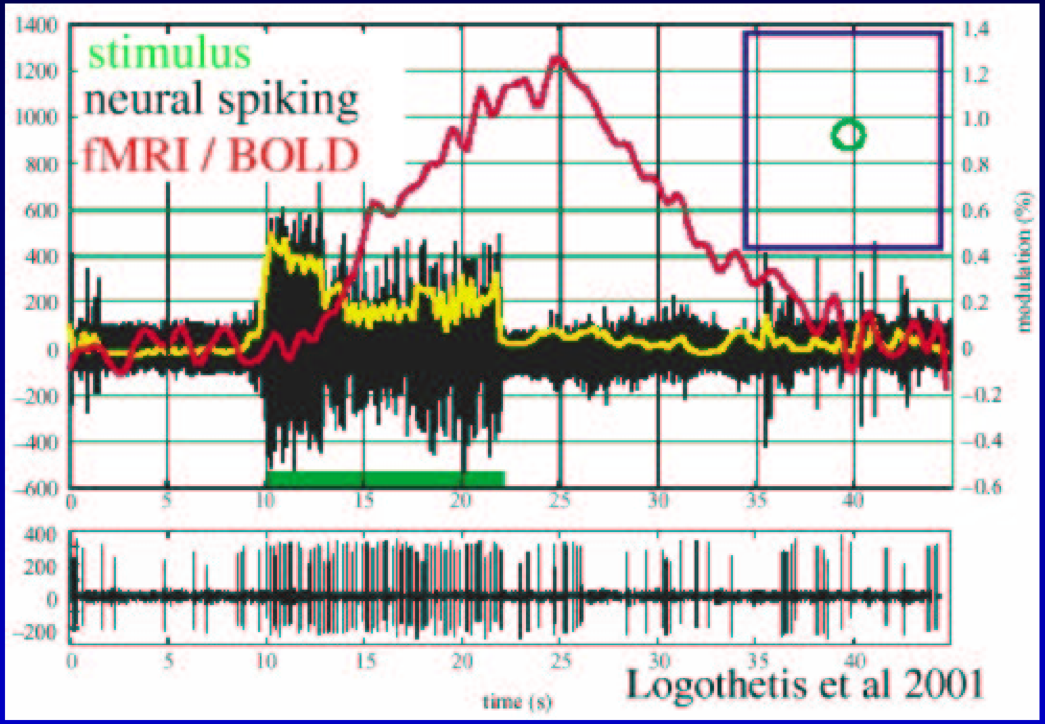
[also breast tumors, arthritis, muscle oximetry. . .]

Functional imaging: why blood?

$$\text{Detect neural firing} \begin{cases} \text{microelectrodes — ouch!} \\ \text{MEG — costly, low resolution} \end{cases}$$



‘Hemodynamic Response Function’

Neural activation → increased blood flow

1990s: functional MRI revolution (brain mapping)

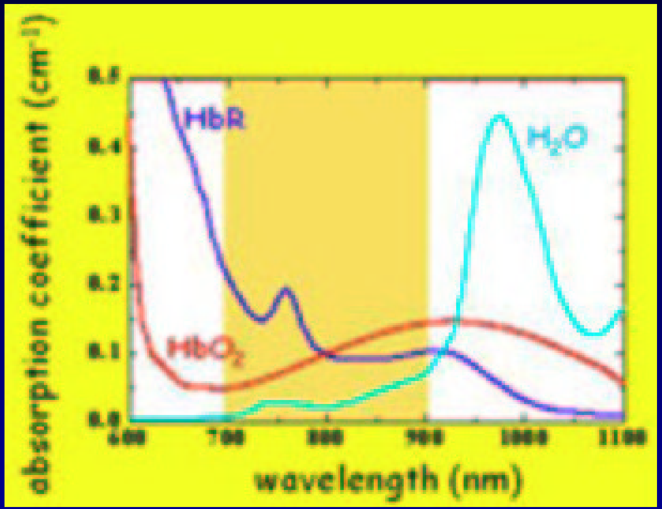
Optical spectroscopy of the body

Near IR 'window' 700-900 nm :

- absorption μ_a low
- hemoglobin dominates μ_a

HbR - deoxy

HbO_2 - oxy



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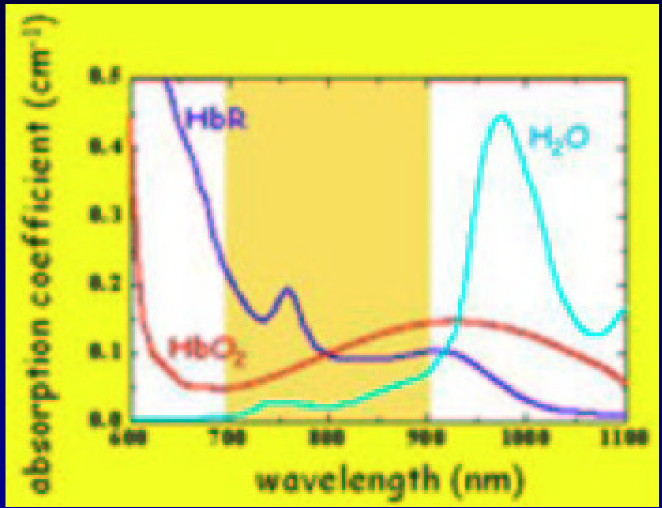

HbR - deoxy
HbO_2 - oxy

von Vierordt 1876:	spectroscope, light through finger
Millikan 1940:	wartime fighter pilot oximeter
Aoyagi 1970s:	pulse oximetry $\rightarrow$ clinical
Jobsis 1980s:	first noninvasive brain activation
1990s:	functional brain mapping

Current DOT apparatus

State of the art. . .

- 32 S by 32 D
- single photon counting
- time-resolution of 100 ps
- several wavelengths

Compare DOT vs fMRI

	fMRI	DOT
space	2–4 mm	1–2 cm, not deep
time	1–2 s	10–100 ms
portable	no	yes
cost	$>\$10^6$	$\leq \$10^5$
sens	HbR only	HbO_2 and HbR

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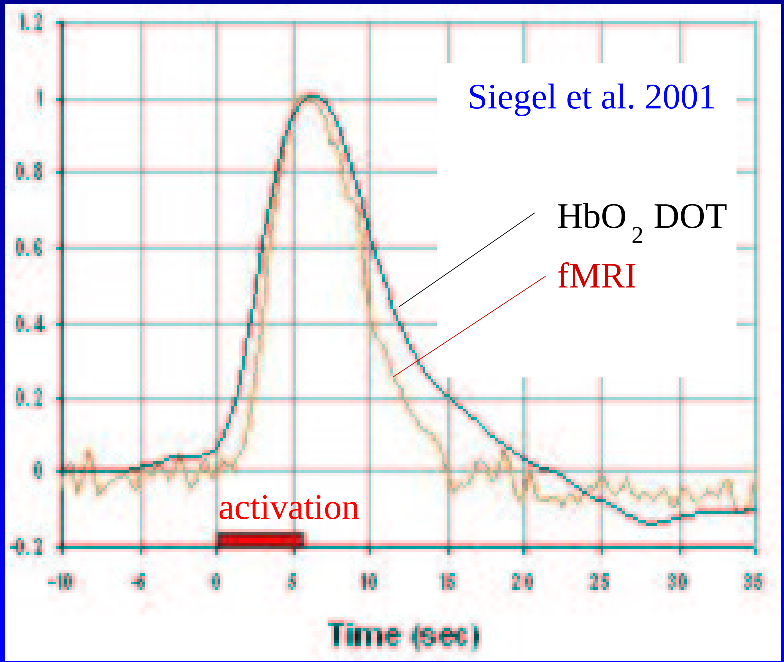

Ongoing:

- validate DOT/fMRI
- neural $\overset{?}{\leftrightarrow}$ vascular
- what fMRI measures?

Photon migration

Incoherent light $\rightarrow$ ballistic transport of $f(\mathbf{r}, \mathbf{\Omega}, t)$:

$$
\begin{aligned}
\frac{1}{c}\dot{f} \quad = \quad & - \mathbf{\Omega} \cdot \nabla f && \text{flow} \\
& - [\mu_a(\mathbf{r}) + \mu_s(\mathbf{r})] f && \text{leaving} \\
& + \int d\mathbf{\Omega}' \, S(\mathbf{r}; \mathbf{\Omega}, \mathbf{\Omega}') \, f(\mathbf{r}, \mathbf{\Omega}') && \text{arriving} \\
& + Q(\mathbf{r}, \mathbf{\Omega}) && \text{source}
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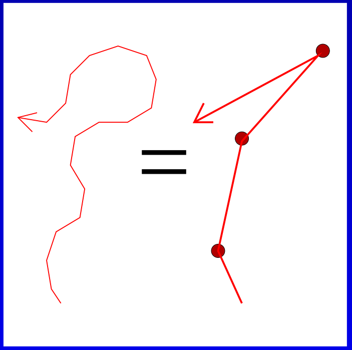
- Legendre $f(\mathbf{r}, \boldsymbol{\Omega}) = \phi(\mathbf{r}) + \mathbf{j}(\mathbf{r}) \cdot \boldsymbol{\Omega} +$ ignored...

$\mathbf{j}$ small, relaxes (fast) to $\propto \nabla \phi$

ϕ diffuses (slow), coeff $\kappa = 1/3\mu_s'$

‘reduced scatt’ $\mu_s' = (1 - \langle \cos\theta \rangle_S)\mu_s$



Diffusion approximation

Needed: $\mu_a \ll \mu_s'$, length scales $\gg \frac{1}{\mu_s'}$

$$\frac{1}{c}\dot{\phi} = \nabla \cdot (\kappa(\mathbf{r})\nabla\phi) - \mu_a(\mathbf{r})\phi + q(\mathbf{r}, t)$$

$\phi =$ fluence

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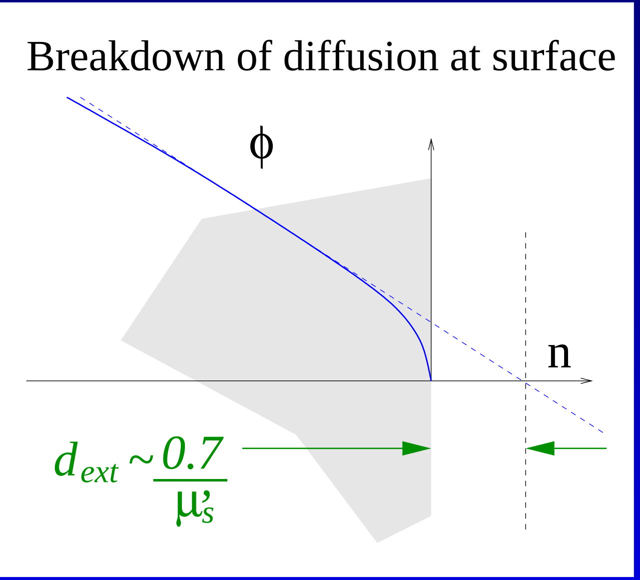
Robin boundary condition:

$$\partial\phi/\partial n \;=\; -\phi/d_{\text{ext}}$$

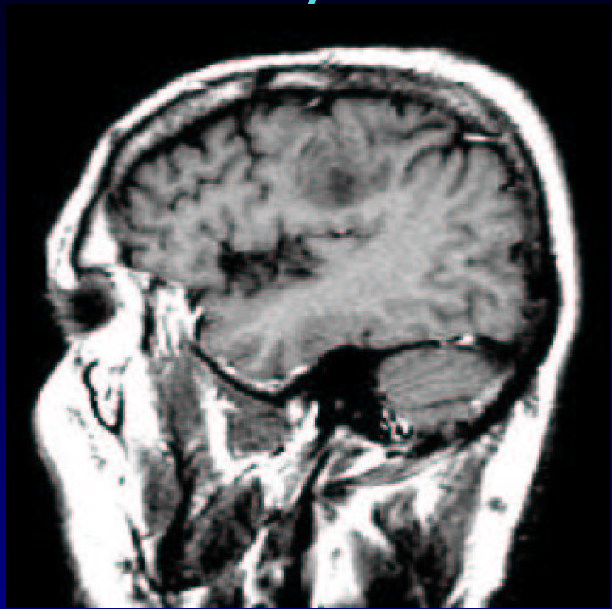


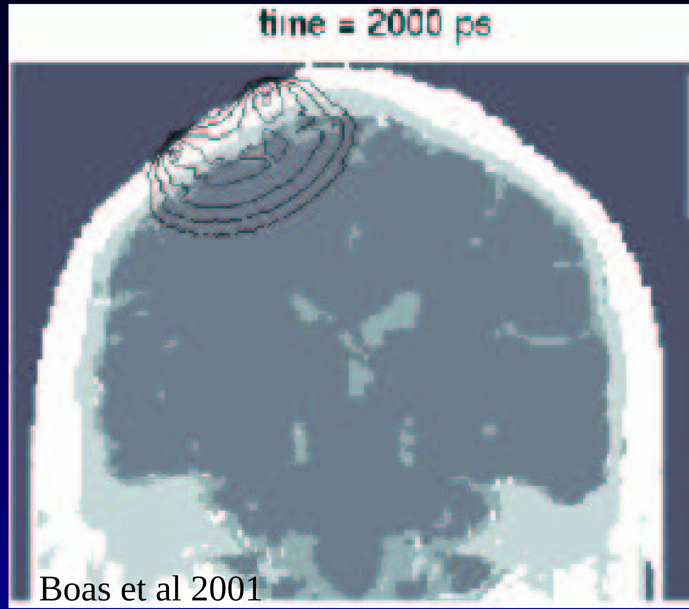
Source: $q(t=0) = \delta(\mathbf{r} - \mathbf{r}_s)$

$\mathbf{r}_s =$ dist $1/\mu_s'$ below surface

Detector: measures $\partial\phi/\partial n$

Geometry





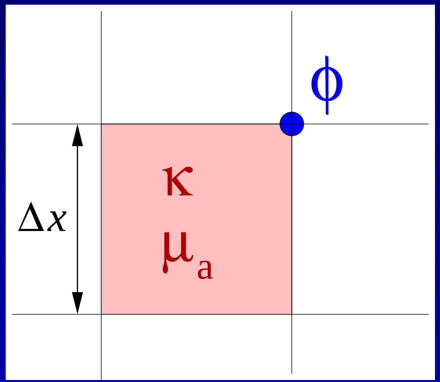
Boas et al 2001

tissue	μ_a (mm^{-1})	μ_s' (mm^{-1})	shape
scalp	0.015	0.8	7 mm layer
skull	0.01	1.0	7 mm layer
CSF	0.0004	0.01	folded 1–3 mm sheet
brain	0.018	1.3	$\sim$ 1 cm folds

Forward model numerics

Diffusion in time = parabolic

- finite difference, Forward Euler
- accuracy $O(\Delta x^2)$, $O(\Delta t)$
- stiff: stability $\Rightarrow$ effort $O(\Delta x^{-5})$
- 3×10^4 nodes, $\Delta x = 2$ mm, $\approx 10^3$ timesteps in 8 s CPU
- Robin BCs with crude normal



Seek better method!

- smooth surface info $\rightarrow$ better BCs, S/D models
- implicit, adaptive timesteps. . .

Crank-Nicholson: not L-stable

Inverse problem

$$\mathbf{x} \equiv \{\mu_a(\mathbf{r}), \mu_s'(\mathbf{r})\} \quad \xrightarrow{\mathbf{f}} \quad \mathbf{y} = \mathbf{f}(\mathbf{x})$$

parameter vector — expected signal vector

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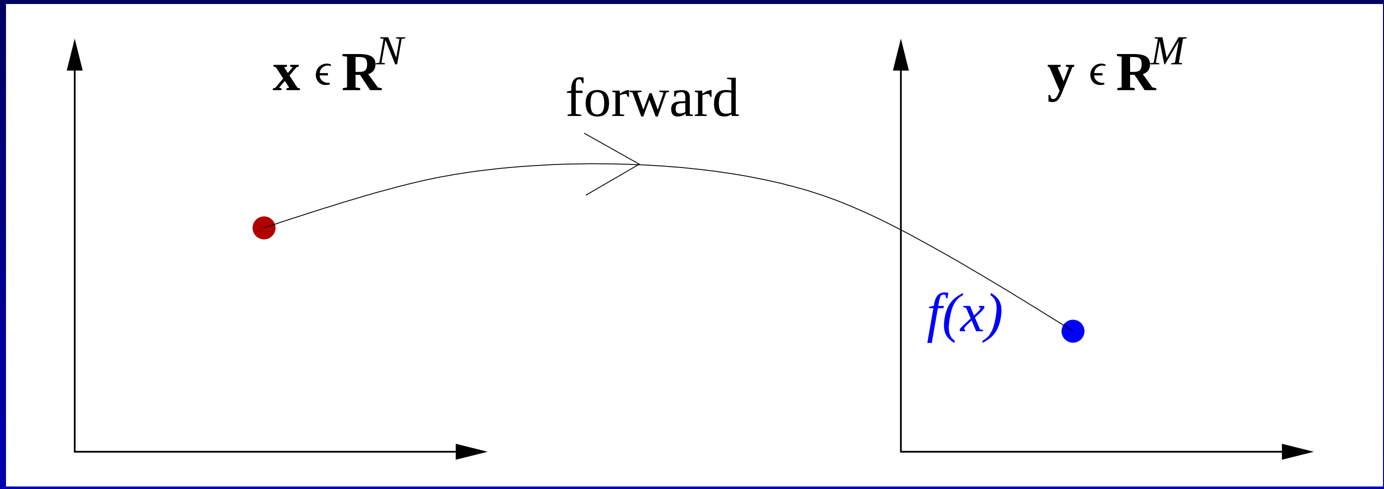

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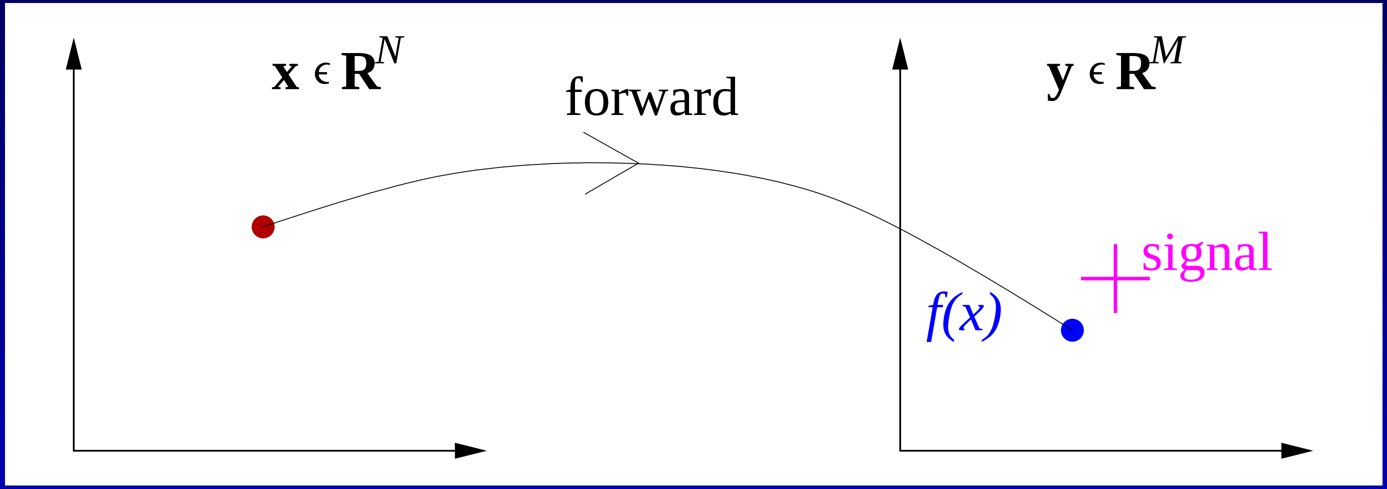

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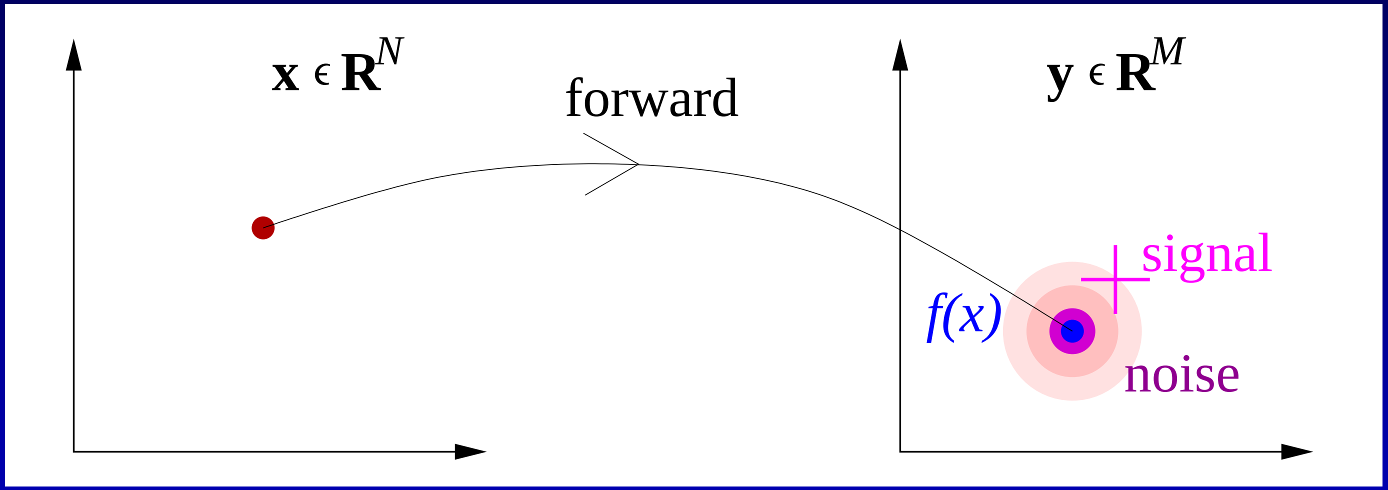

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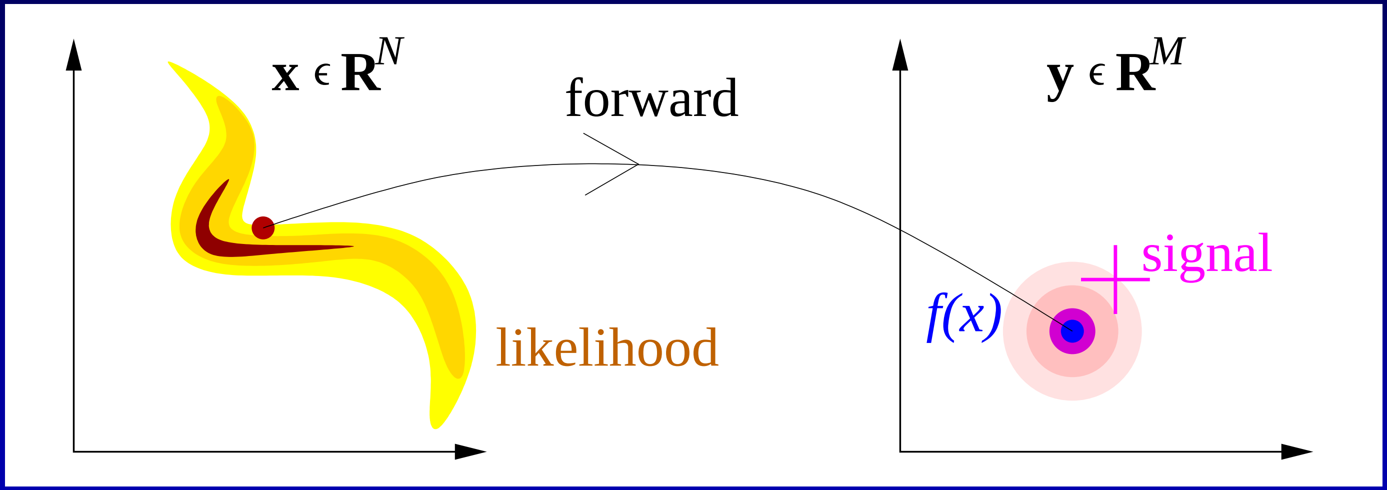

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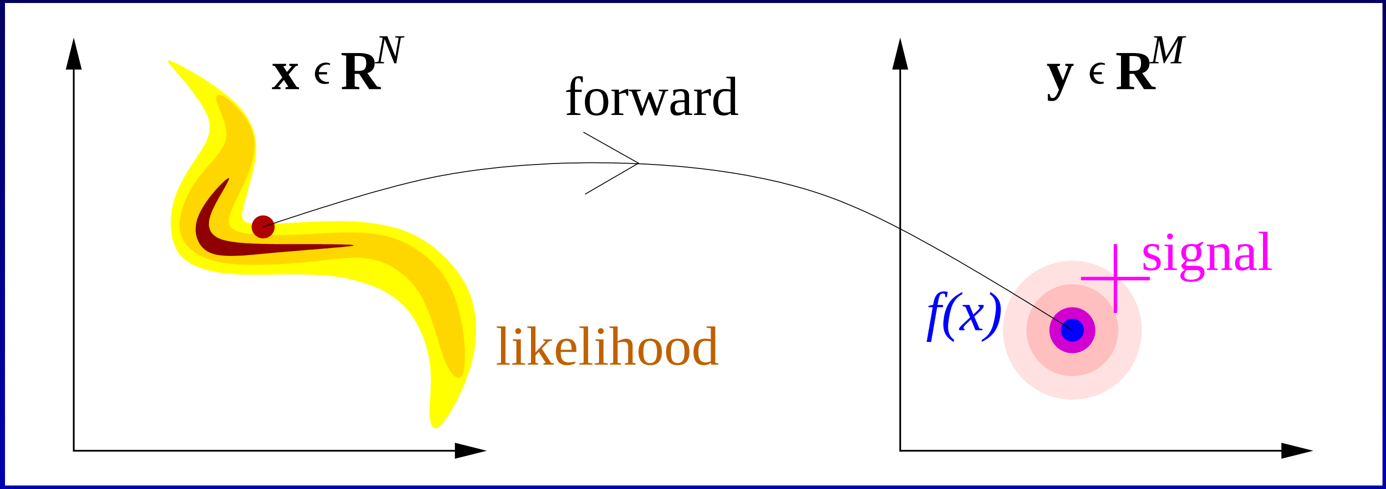

Nonlinear N-dim optimization problem

$\det(\frac{\partial f_m}{\partial x_n}) \to 0$: ‘ill-posed’ (many **x** equally good)

Bayesian statistical method

Incomplete info on $\mathbf{x} \to$ *probability density function*

Entire model = joint PDF $p(\mathbf{x}, \mathbf{y})$

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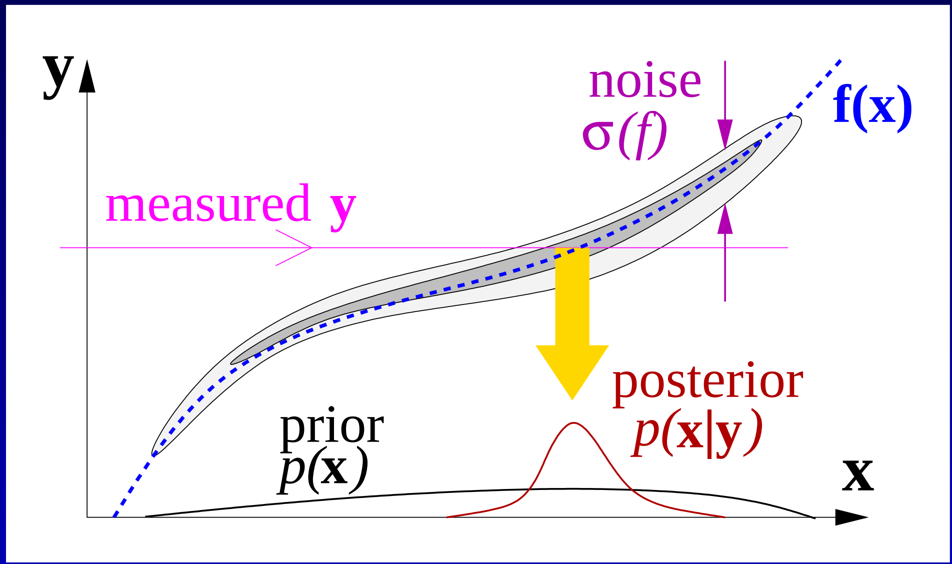

Bayesian inference

$$p(\mathbf{x}|\mathbf{y}) \;\propto\; p(\mathbf{x}, \mathbf{y})$$
$$= p(\mathbf{y}|\mathbf{x}) \cdot p(\mathbf{x})$$

posterior likelihood prior

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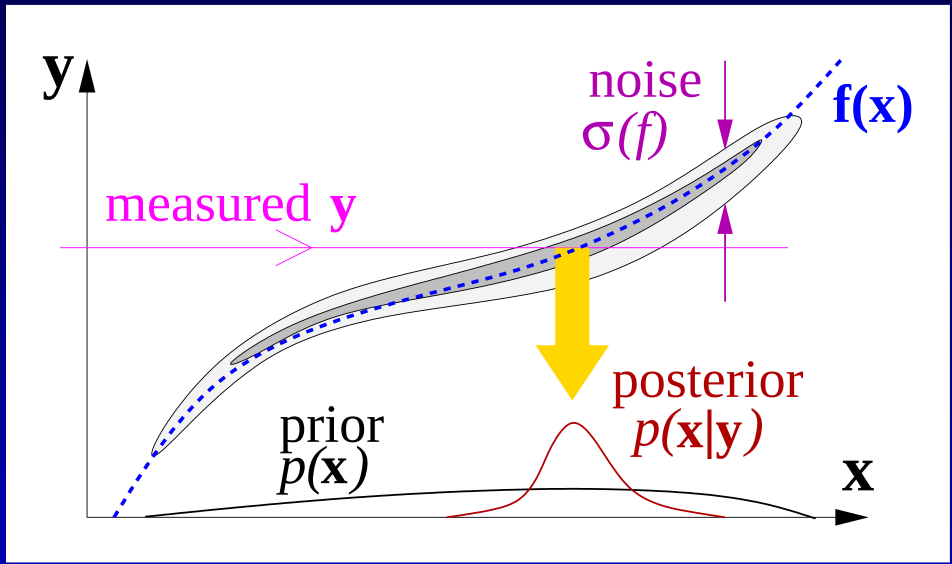

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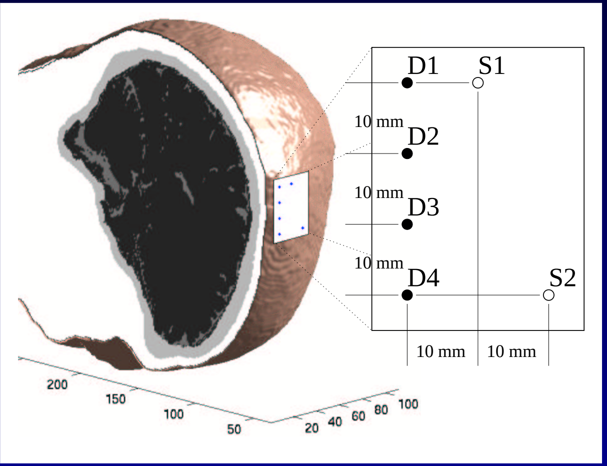
posterior likelihood prior

- embraces ill-posedness
- rigorous, assumptions explicit, no overfitting
- need explore N-dim posterior: many $\mathbf{f}(\mathbf{x})$ evals.

Measure 'baseline' μ_a and μ_s'

Small system (2 S, 4 D). Model: homogeneous tissues $\mathbf{x} \equiv \mu_a, \mu_s'$ for scalp, skull, brain

($N = 6$: grapple with full PDF)



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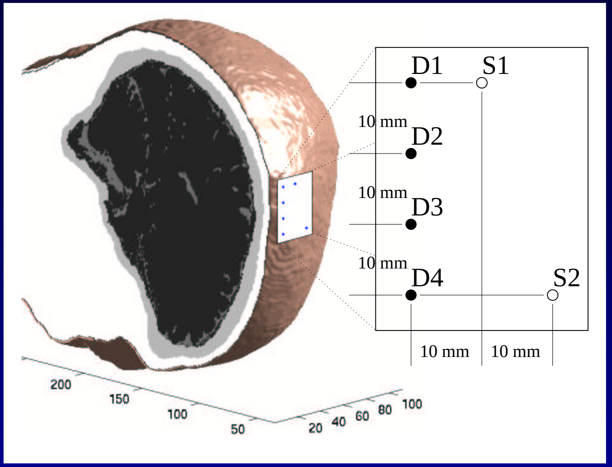

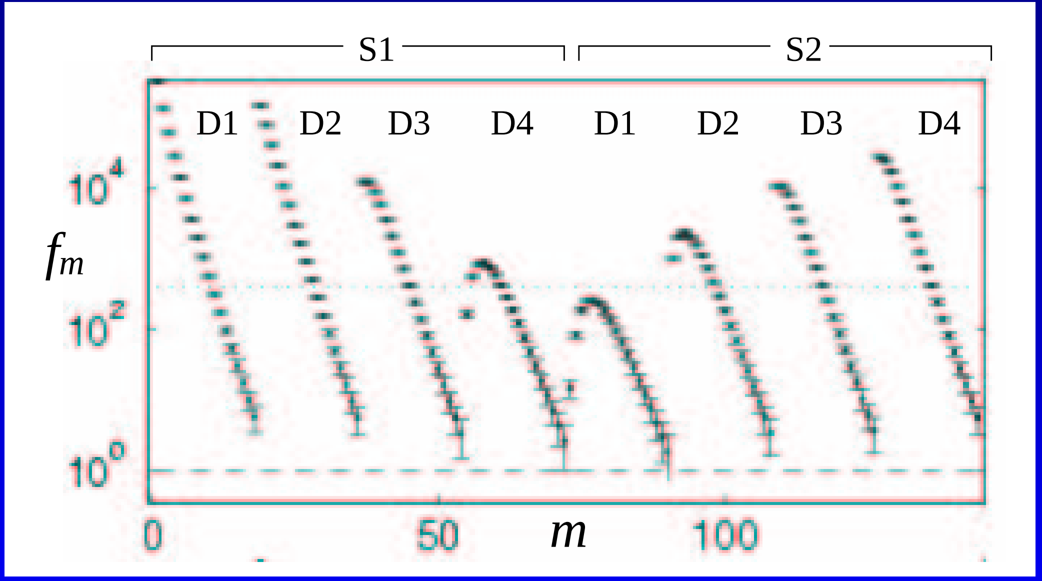

SIMULATED SIGNALS

choose flat prior $p(\mathbf{x})$ (no regularization)

Realistic noise model

Each signal component $m = 1 \cdots M$ independent.

Photons Poissonian: gaussian approx $\sigma(f) = f^{1/2}$

E.g. 10^6 photons = 0.1% frac error

But: we do not trust forward model to 0.1% !

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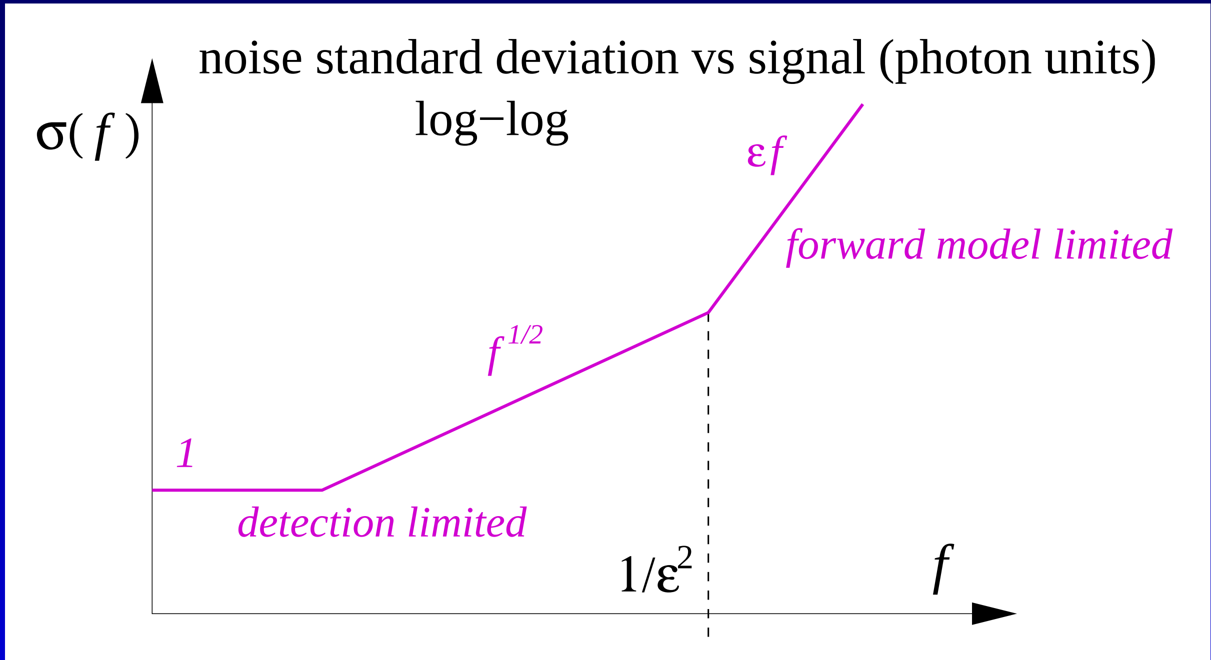
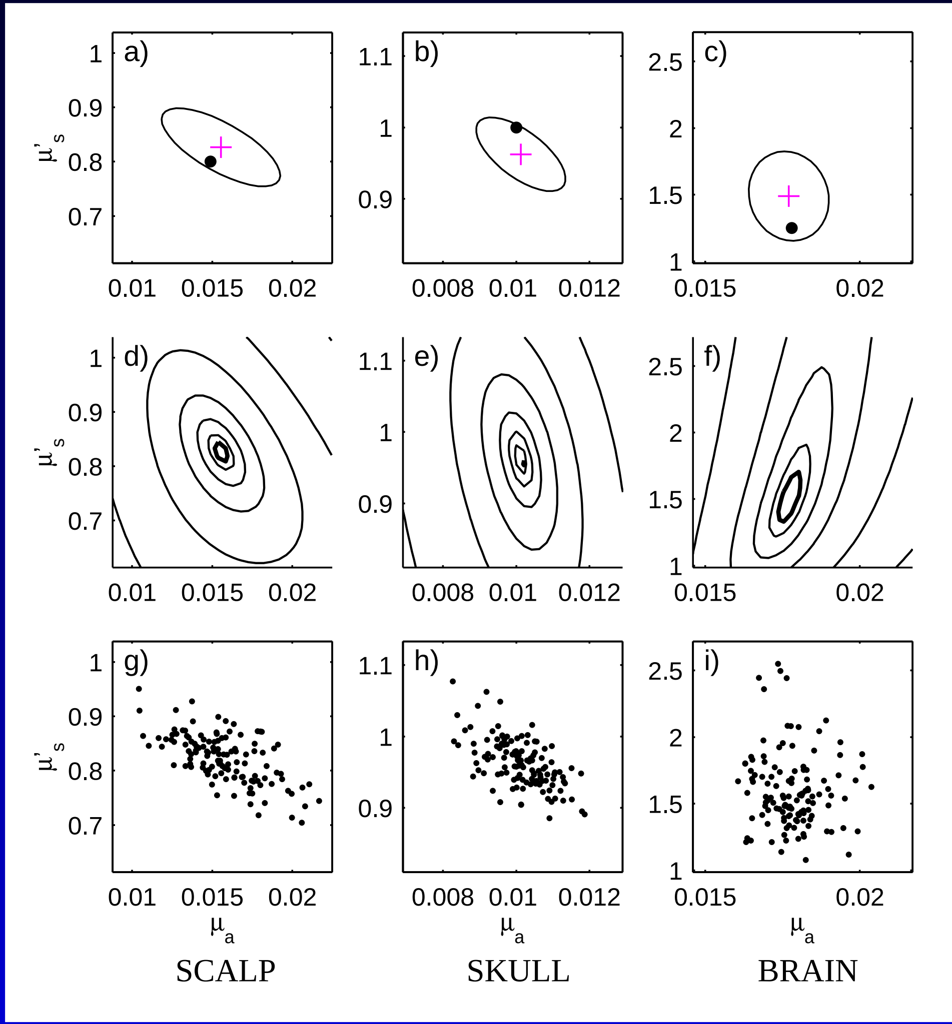


- $\varepsilon =$ fractional forward model error *e.g.* 10% (errors: physics, segmentation, calibration. . .)

Results: posterior



Marginal distributions

Gaussian approx to PDF

pancake: $a_{\max}/a_{\min} = 50$

10^6 detected photons gives 5% in μ_a, 20% in μ_s'

for $\varepsilon = 10\%$

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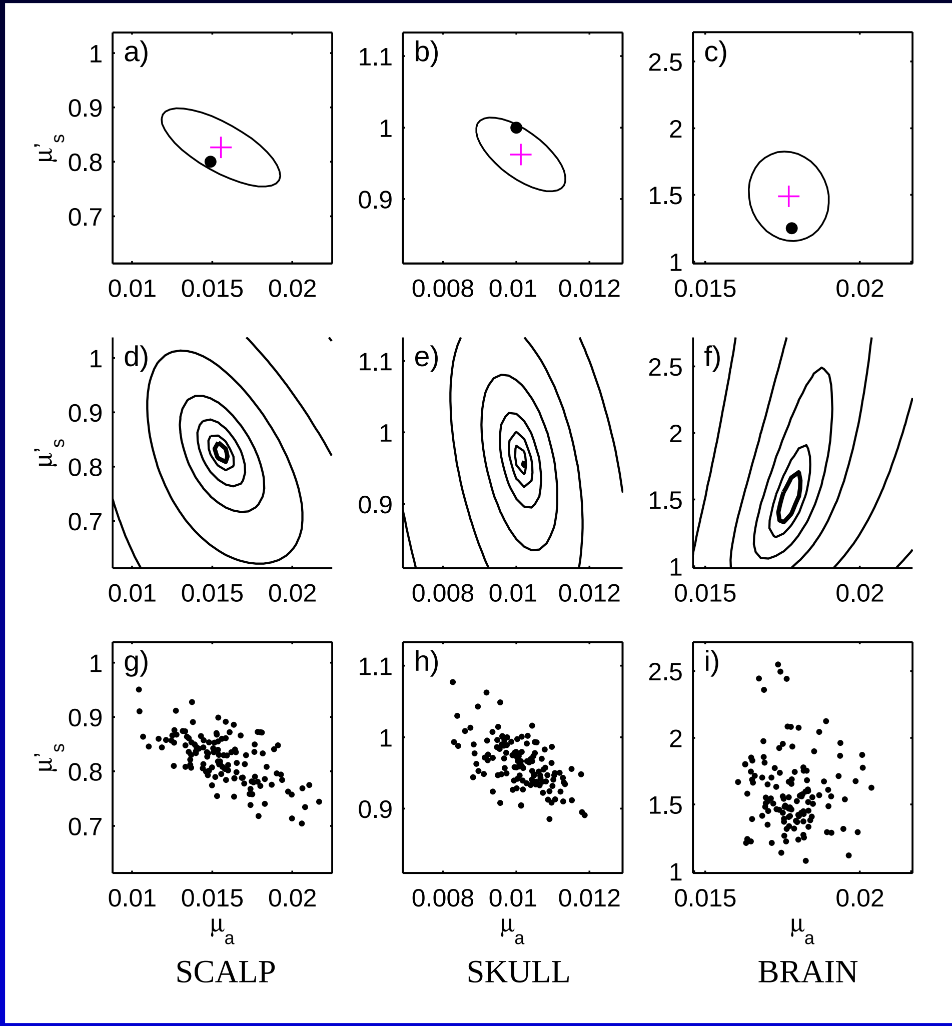

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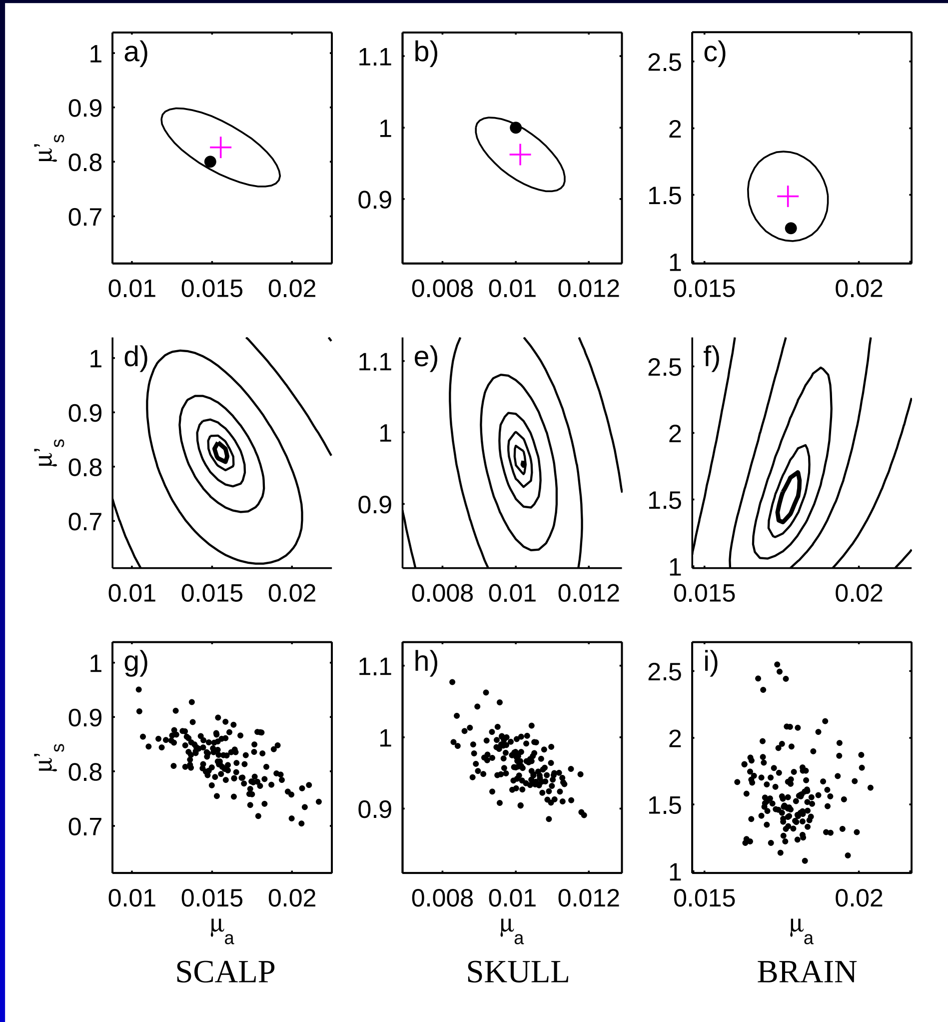

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Sampling exact PDF

Markov chain Monte Carlo

(Metropolis walk)

validates Gaussian approx

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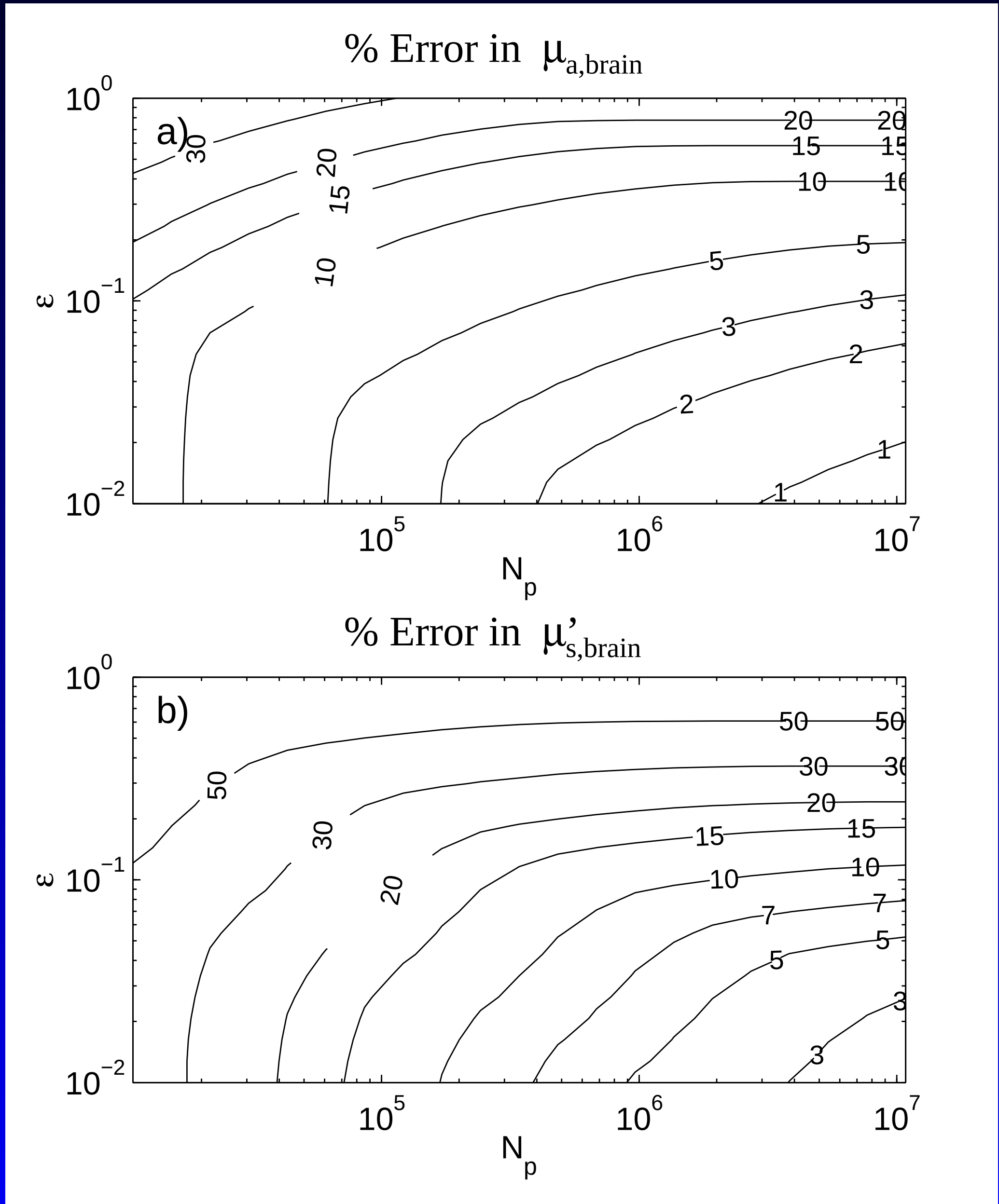
Results: confidence intervals

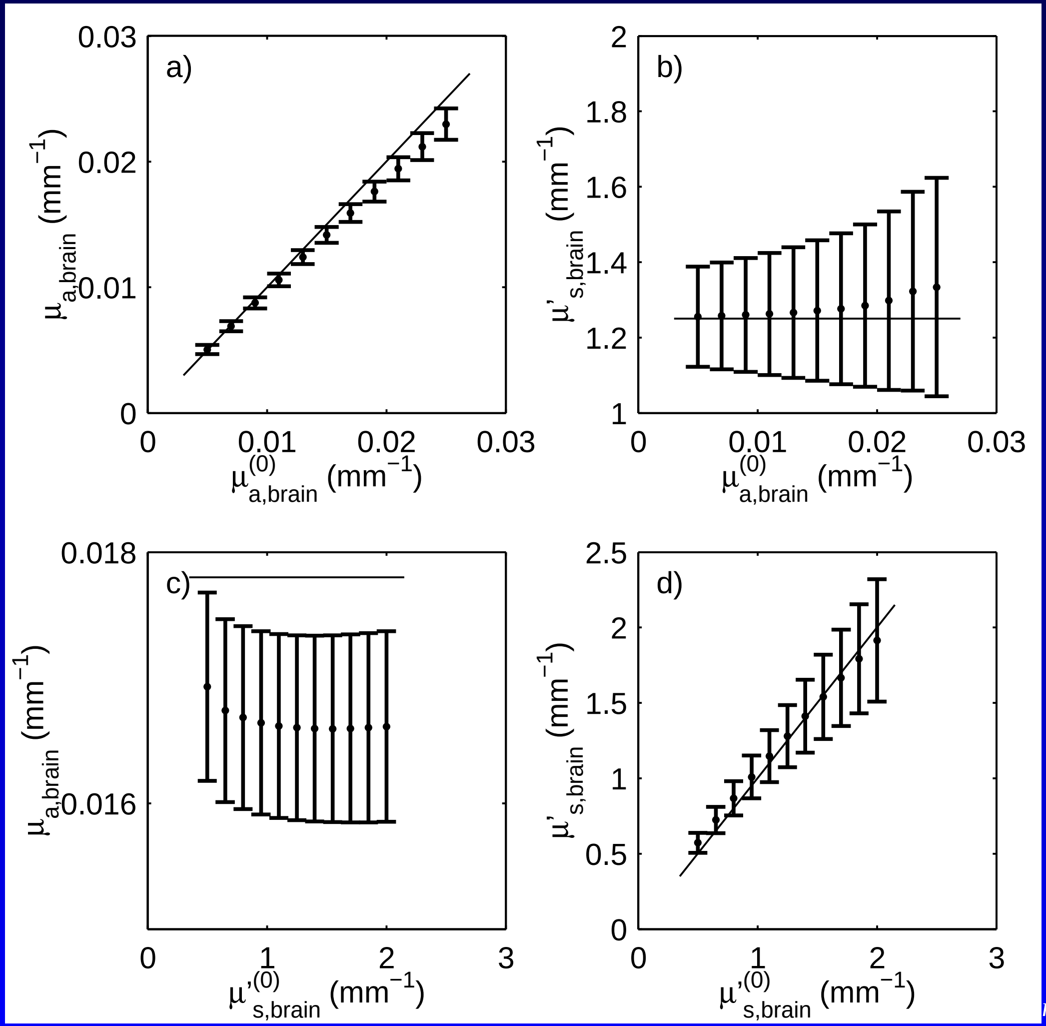


Allows optimal experimental design

N_p = total detected photons

Results: robust to forward error

Simulate signals ($\Delta x = 1$ mm)
Inference ($\Delta x = 2$ mm)
} up to 50% errors (S/D models)



Avoids committing 'inverse crime'

$N_p \approx 10^7$

$\varepsilon = 20\%$ represents typ forward errors

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  best S/D placement, Bayesian calibration...