

Noninvasive imaging of the brain with diffusing light pulses

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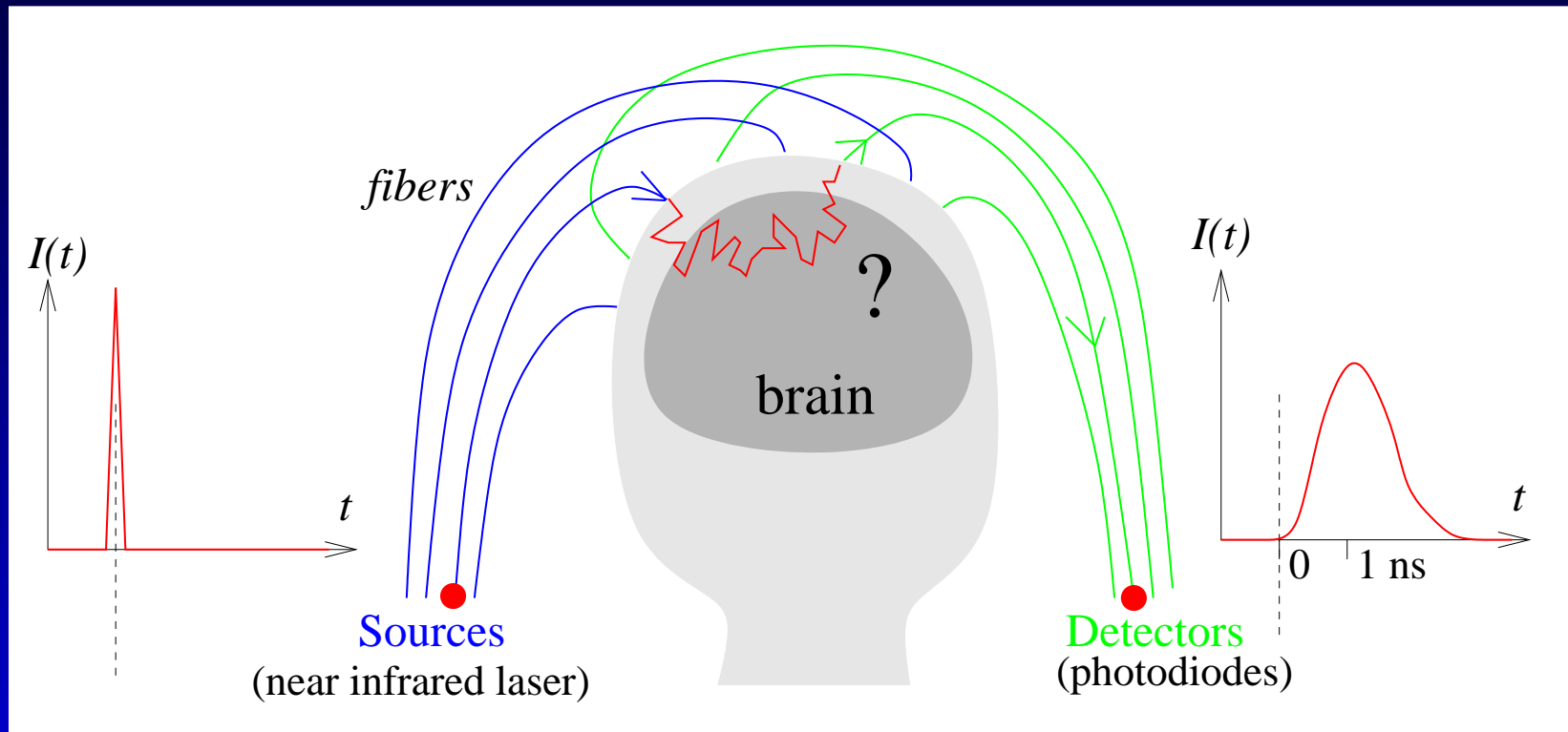
Big picture

What can access optically, from outside the body?

DOT : 'Diffuse Optical Tomography'

Big picture

What can access optically, from outside the body?
DOT : 'Diffuse Optical Tomography'



Tissue is highly scattering (blurring)

Get spatial maps { absorption
scattering } 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
- Imaging stroke (local lack of O₂), hemorrhage

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- Organization of brain:
 - neural response as func of space & time
- functional disorders: seizure, depression

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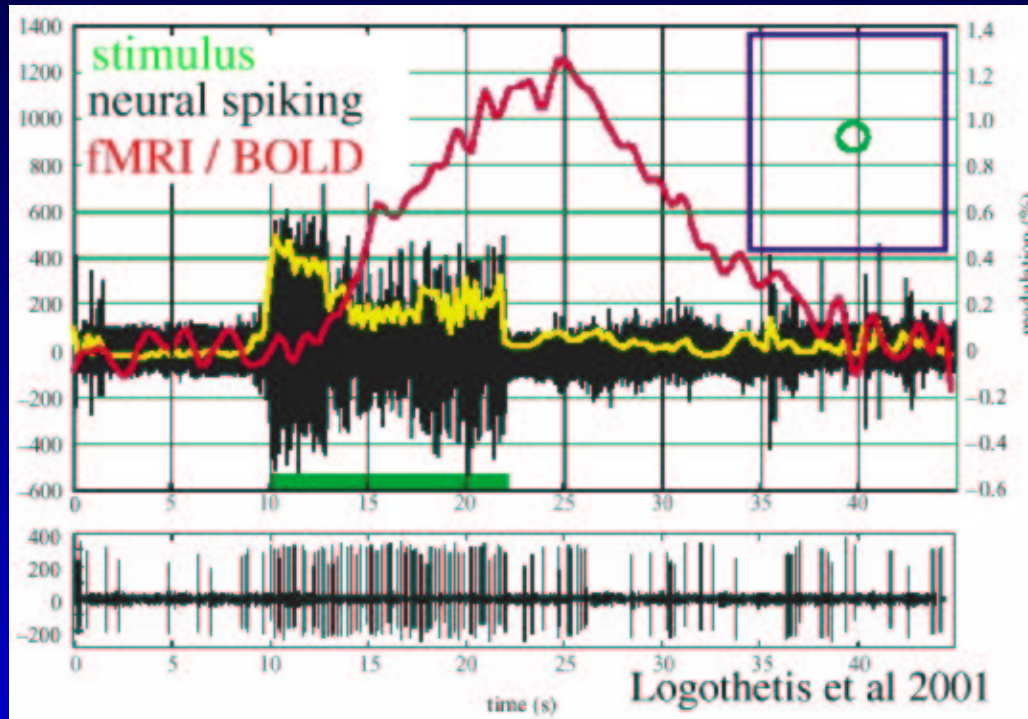
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[also breast tumors, arthritis, muscle oximetry...]

Functional imaging: why blood?

Detect neural firing { microelectrodes — ouch!
MEG — costly, low resolution



‘Hemodynamic
Response
Function’

Neural activation → increased blood flow

1990s: functional MRI revolution (brain mapping)

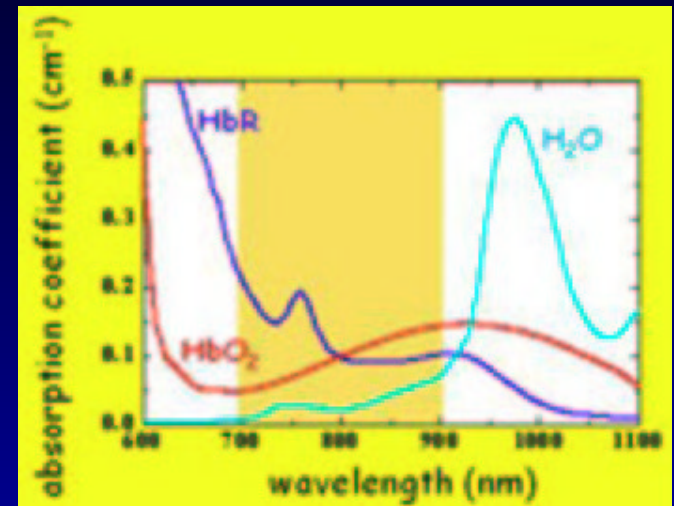
Optical spectroscopy of the body

Near IR 'window' 700-900 nm :

- absorption μ_a low
- hemoglobin dominates μ_a

HbR - deoxy

HbO₂ - oxy



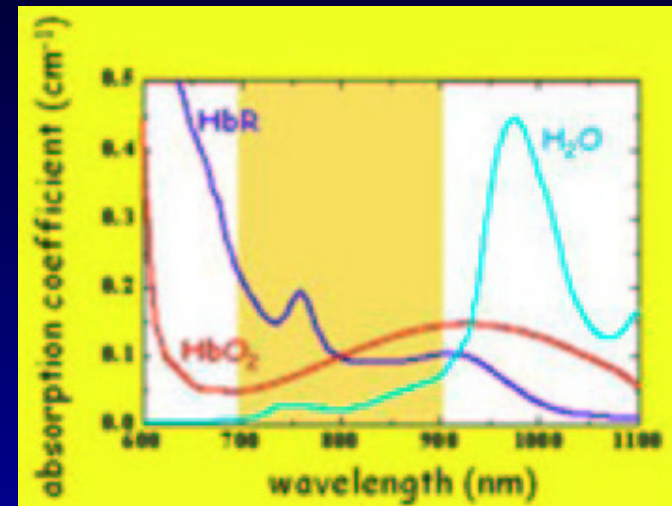
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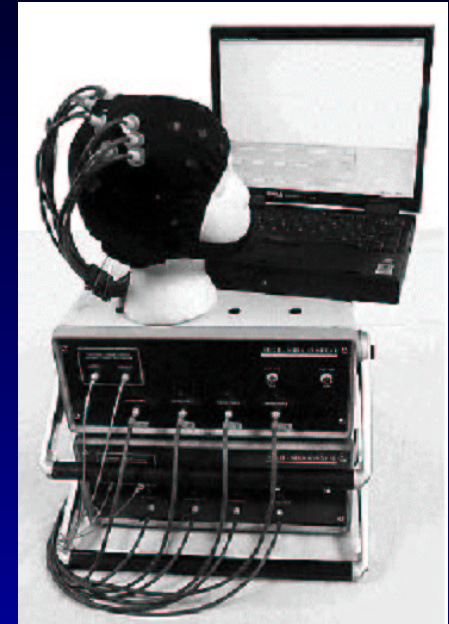
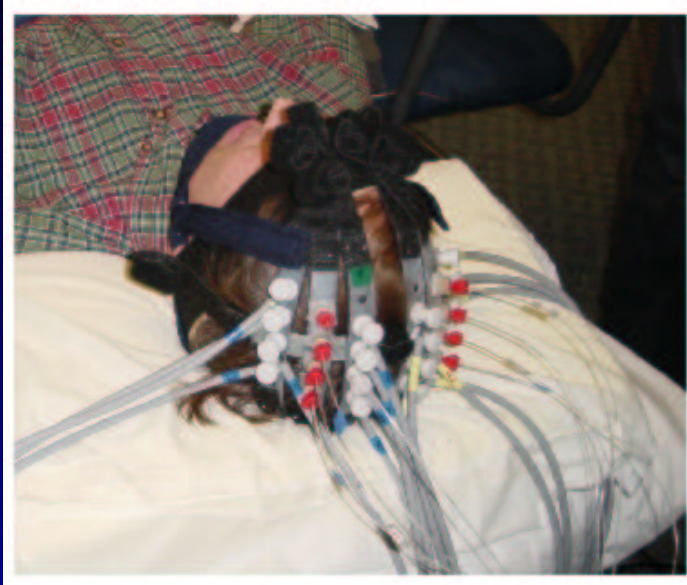
HbR - deoxy

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

Current DOT apparatus



State of the art...

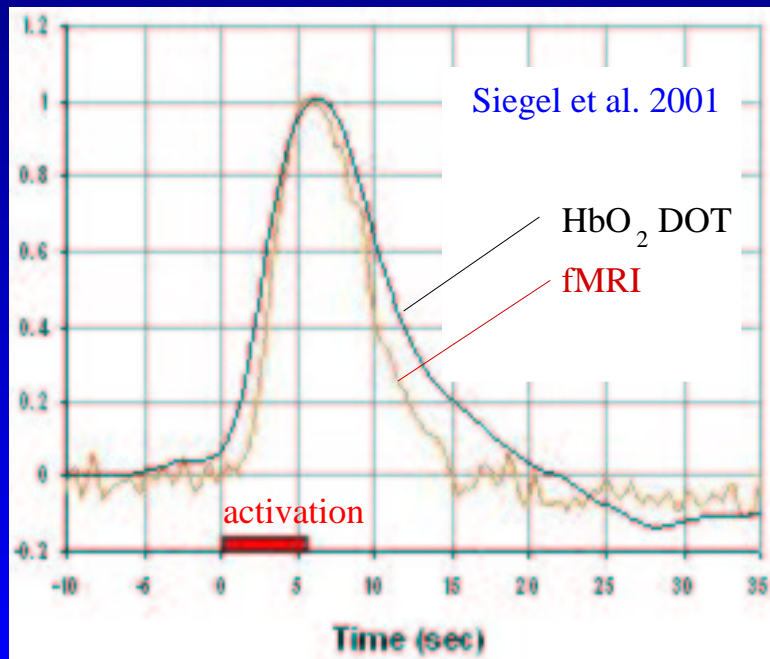
- 32 S by 32 D
- single photon counting
- time-resolution of 100 ps
- several wavelengths

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 \leftrightarrow vascular
- what fMRI measures?

Photon migration

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

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

speed c , absorption μ_a , scattering $\mu_s = \int d\Omega S$

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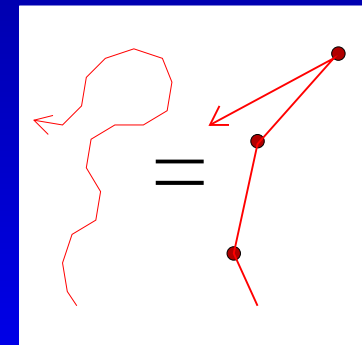
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• Legendre $f(\mathbf{r}, \Omega) = \phi(\mathbf{r}) + \mathbf{j}(\mathbf{r}) \cdot \Omega + \text{ignored} \dots$

\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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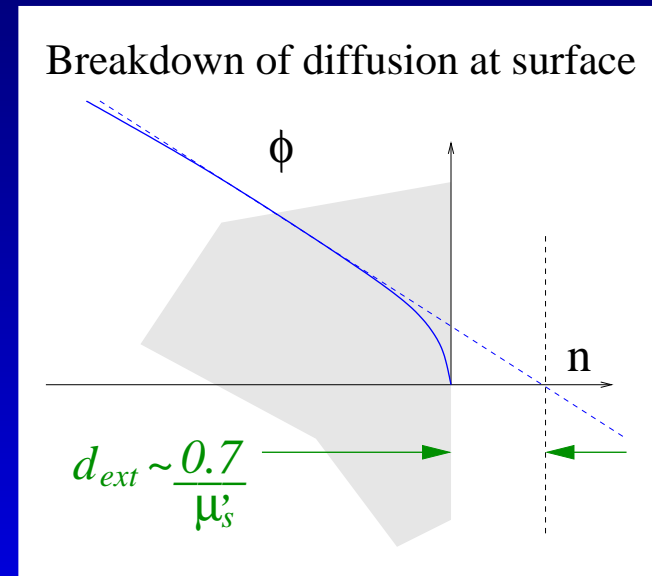
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Robin boundary condition:

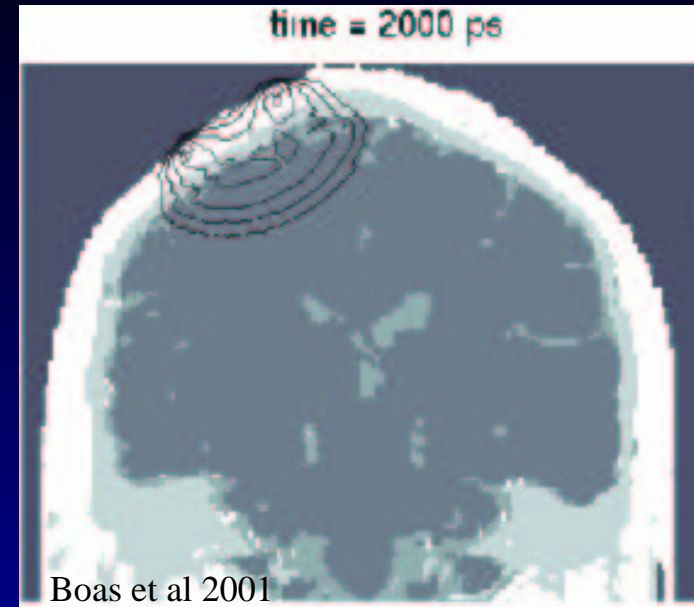
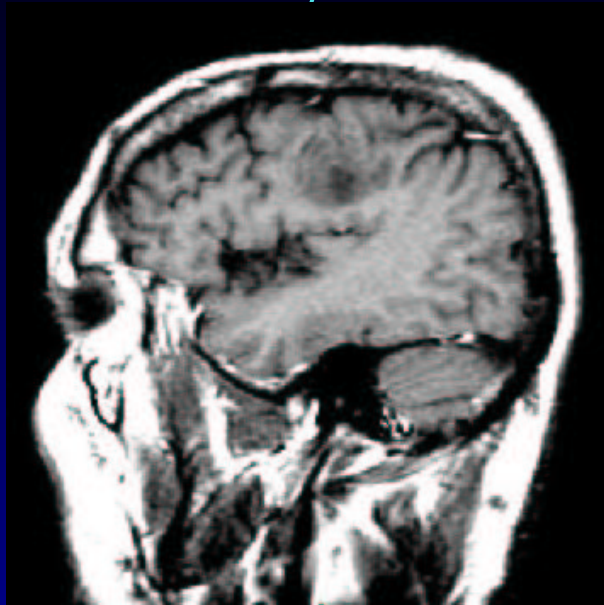
$$\partial\phi/\partial n = -\phi/d_{\text{ext}}$$

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

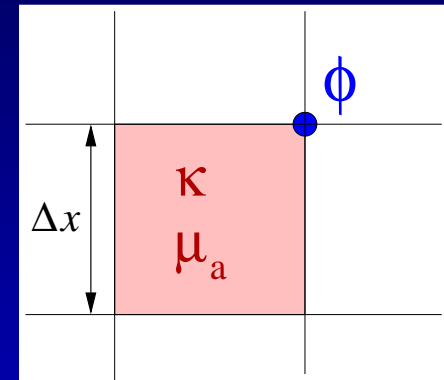


tissue	μ_a (mm ⁻¹)	μ'_s (mm ⁻¹)	shape
scalp	0.015	0.8	7 mm layer
skull	0.01	1.0	7 mm layer
CSF	0.0004	0.01	folded 1–3 mm sheet
brain	0.018	1.3	~ 1 cm folds

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

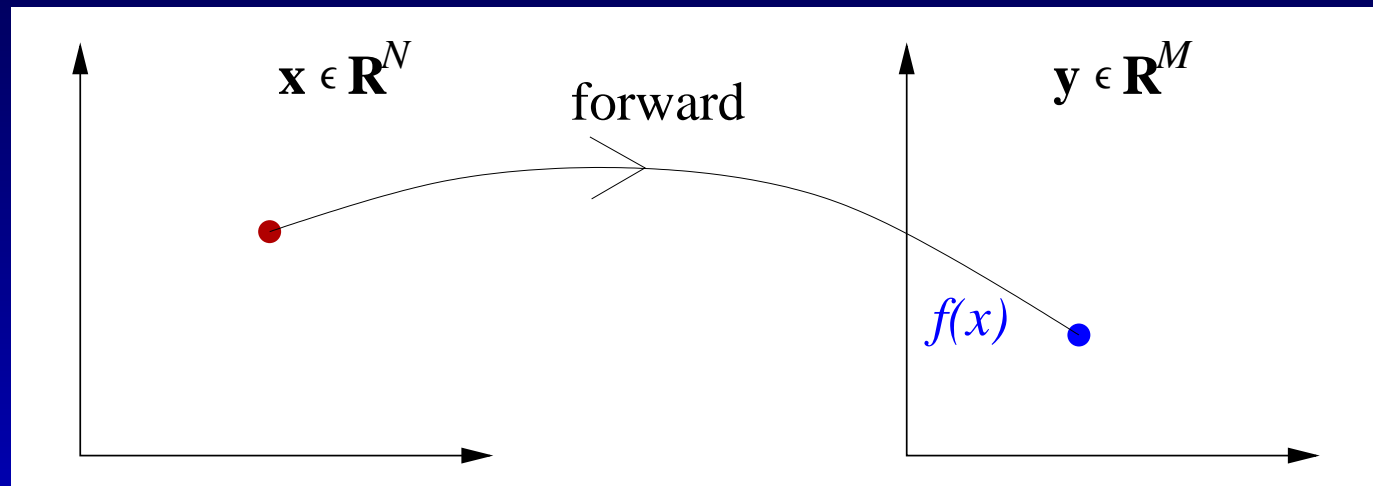
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parameter vector expected signal vector

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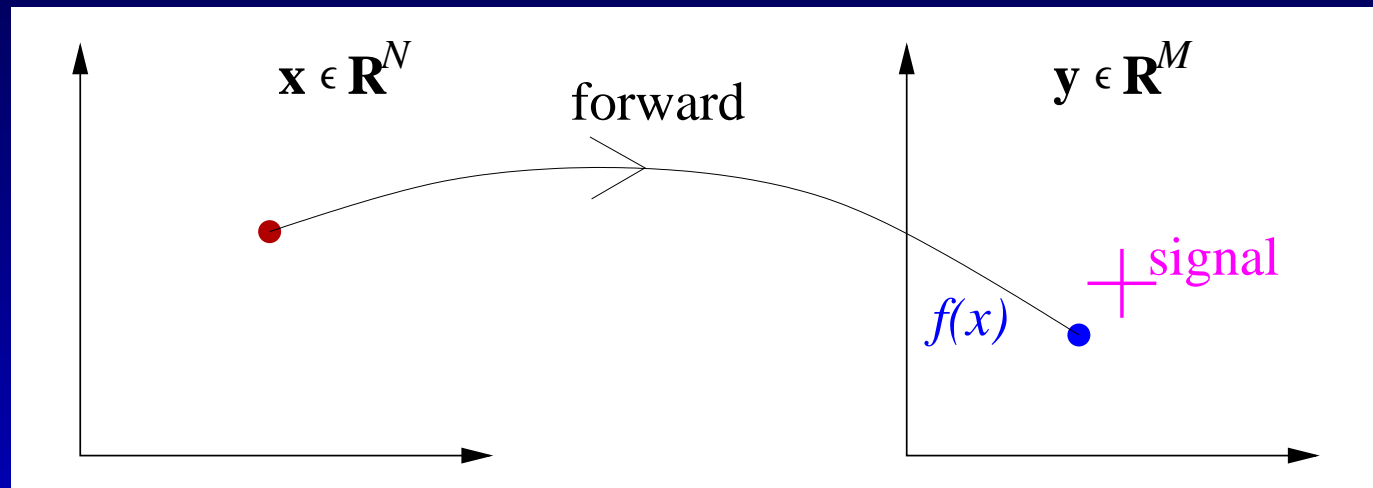
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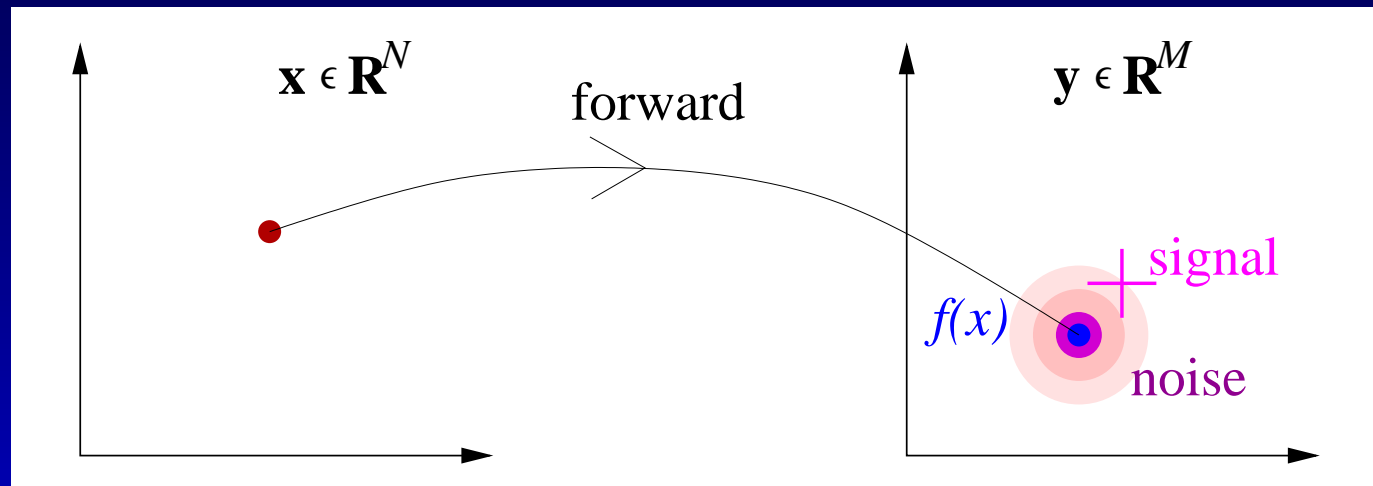
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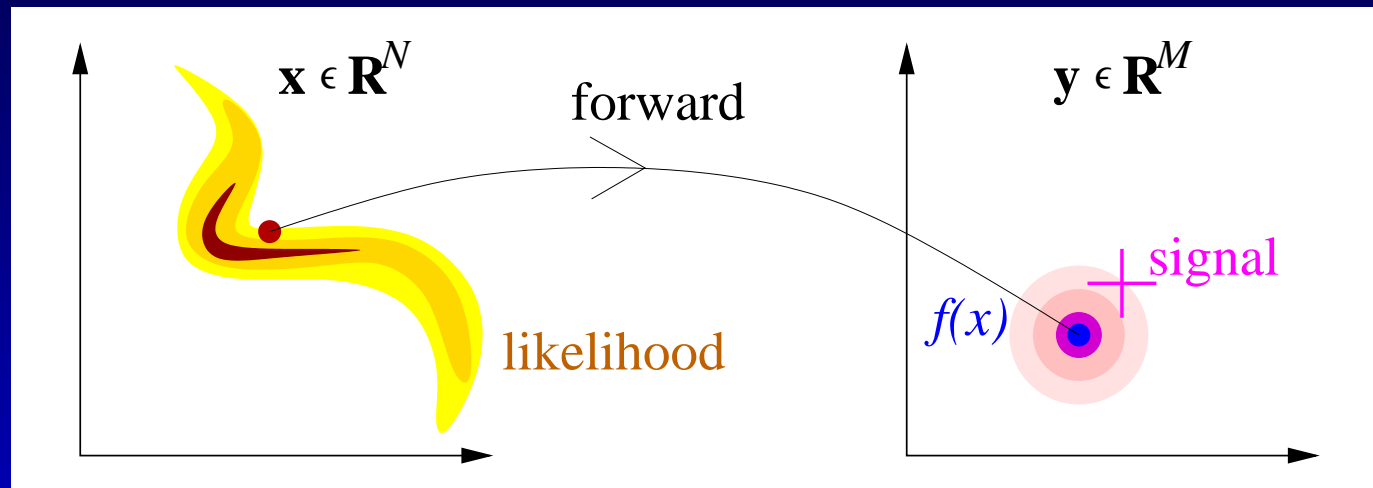
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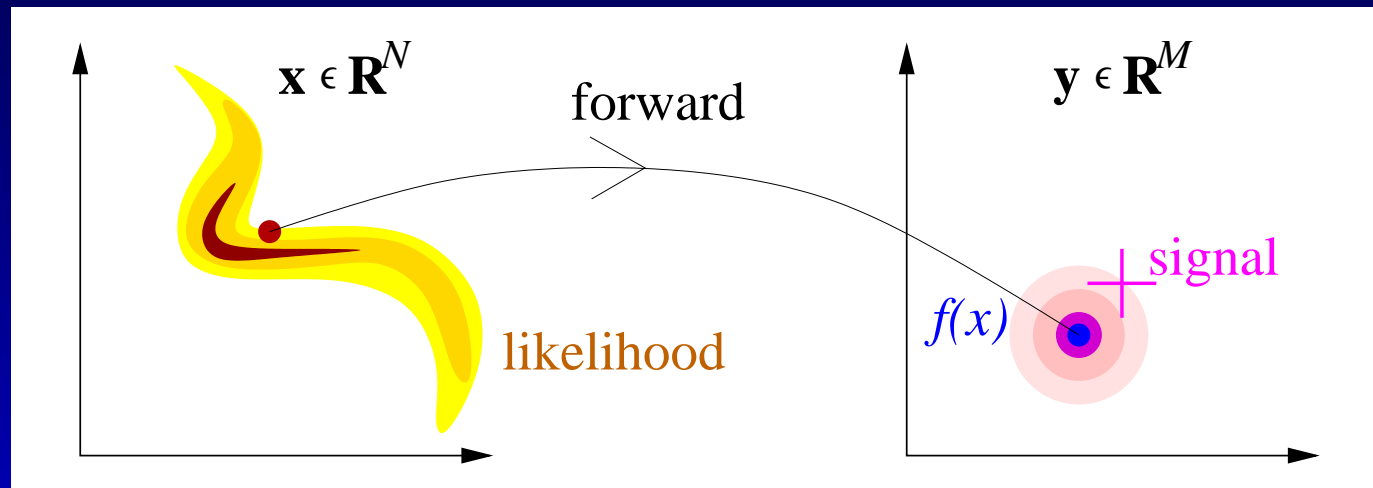
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Nonlinear N -dim optimization problem

$\det\left(\frac{\partial f_m}{\partial x_n}\right) \rightarrow 0$: 'ill-posed' (many \mathbf{x} equally good)

Bayesian statistical method

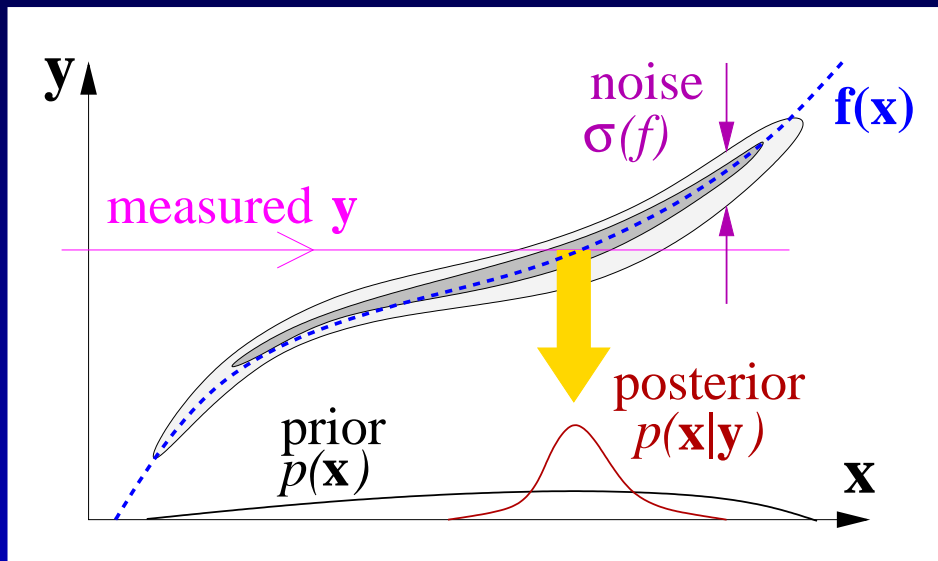
Incomplete info on \mathbf{x} \rightarrow *probability density function*

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

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Bayesian inference

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

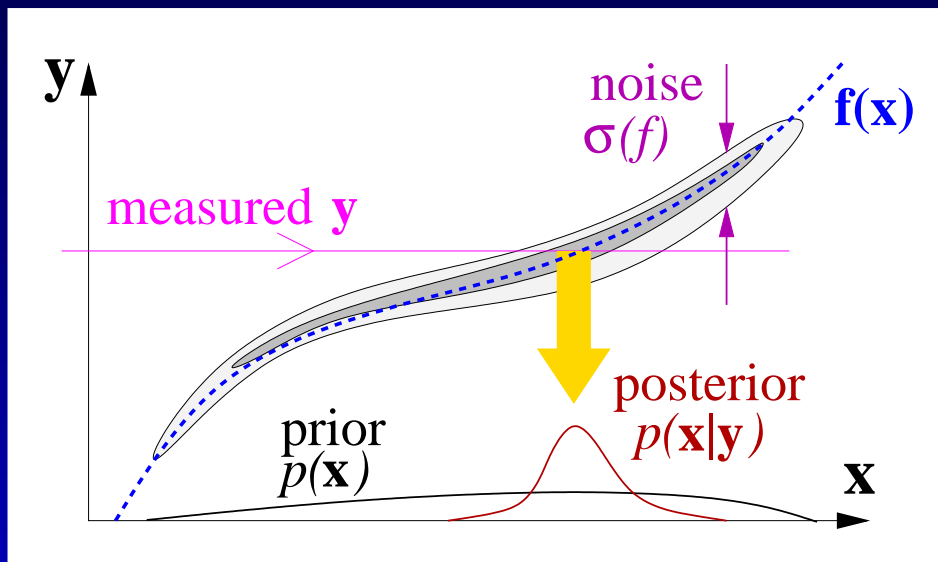
posterior

likelihood prior

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likelihood prior

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

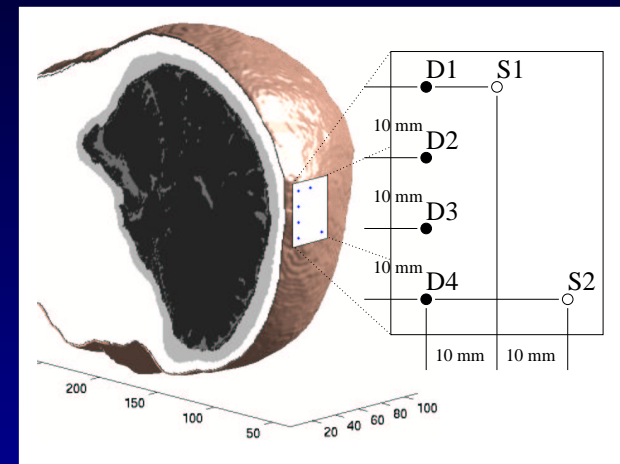
Measure 'baseline' μ_a and μ'_s

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)

- meas *absolute* values is hard
- needed for brain imaging



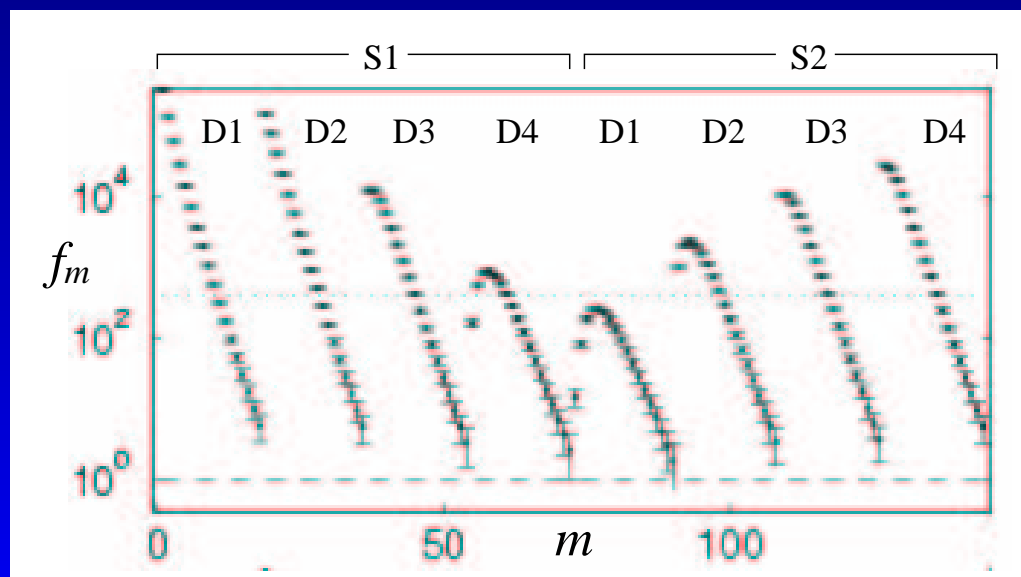
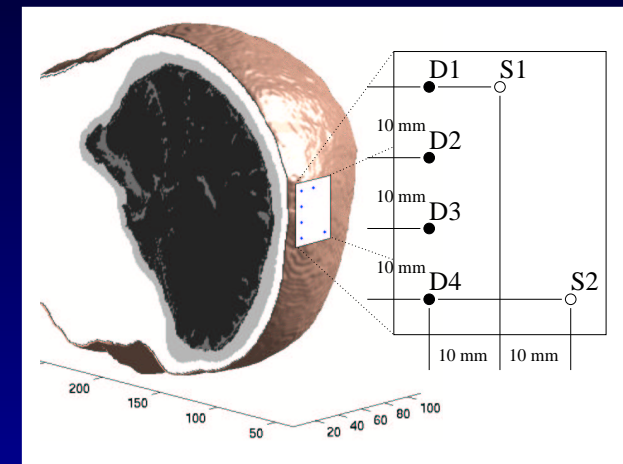
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SIMULATED SIGNALS

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

Realistic noise model

Each signal component $m = 1 \dots M$ 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% !

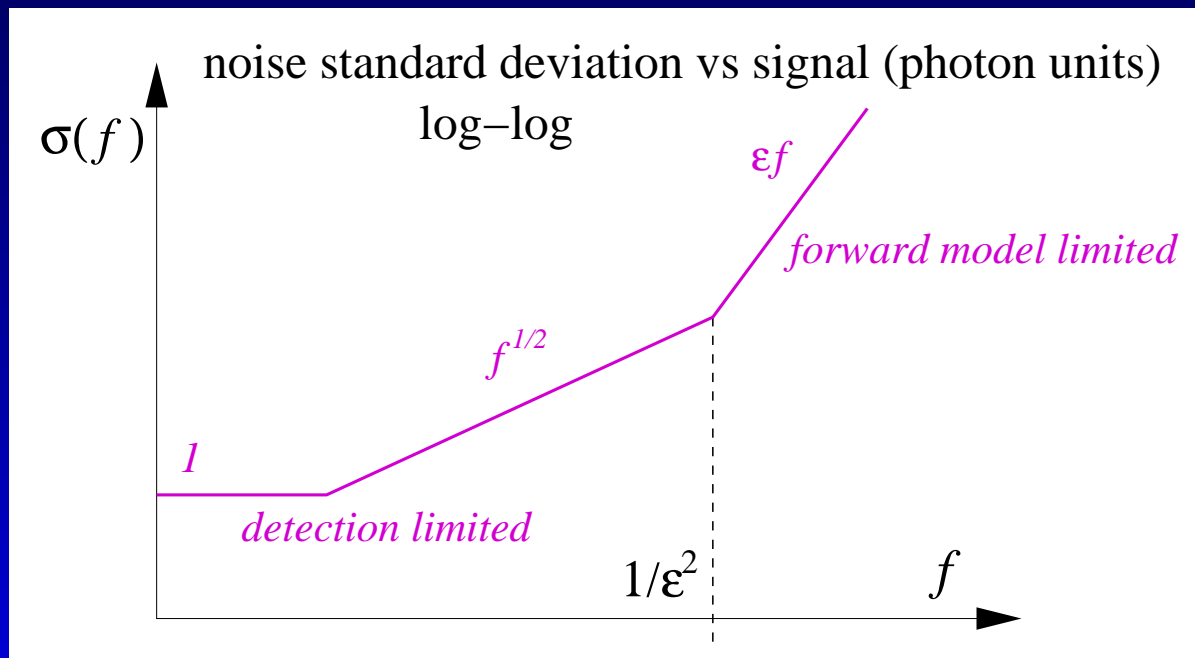
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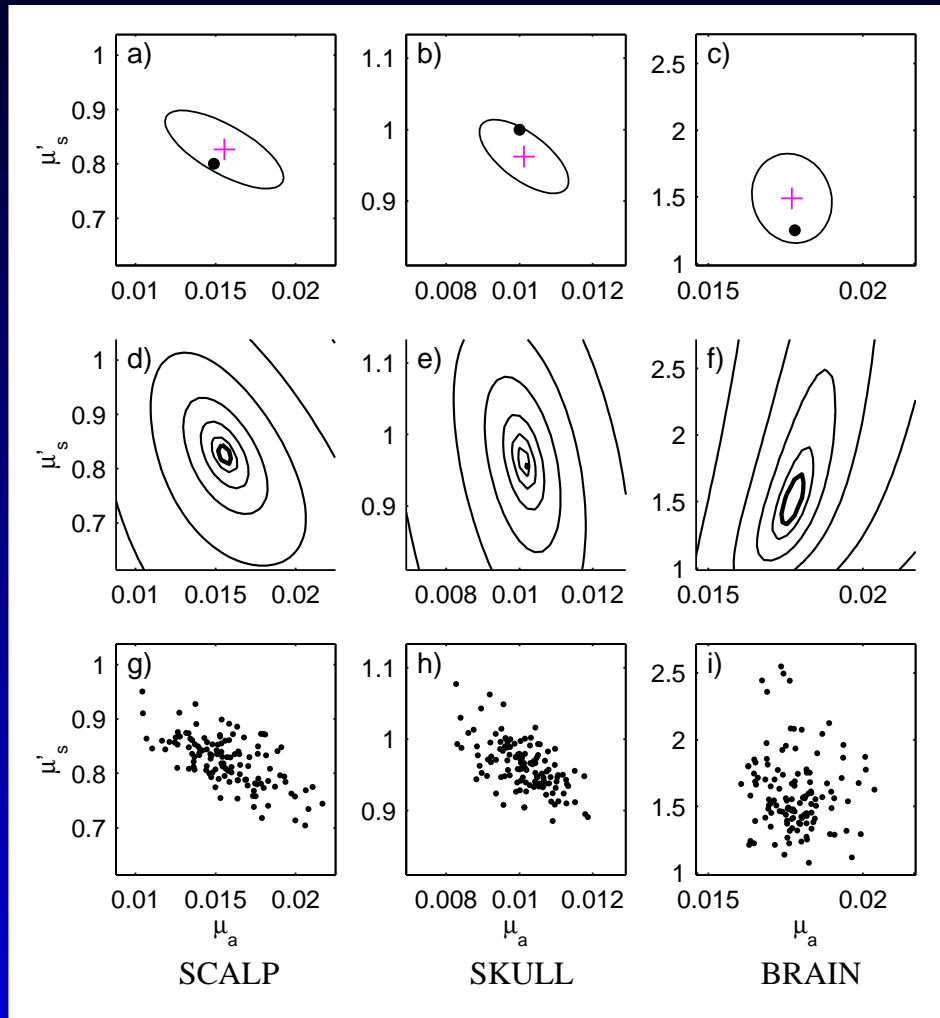
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- ϵ = fractional forward model error *e.g.* 10%
(errors: physics, segmentation, calibration...)

Results: posterior



Marginal distributions

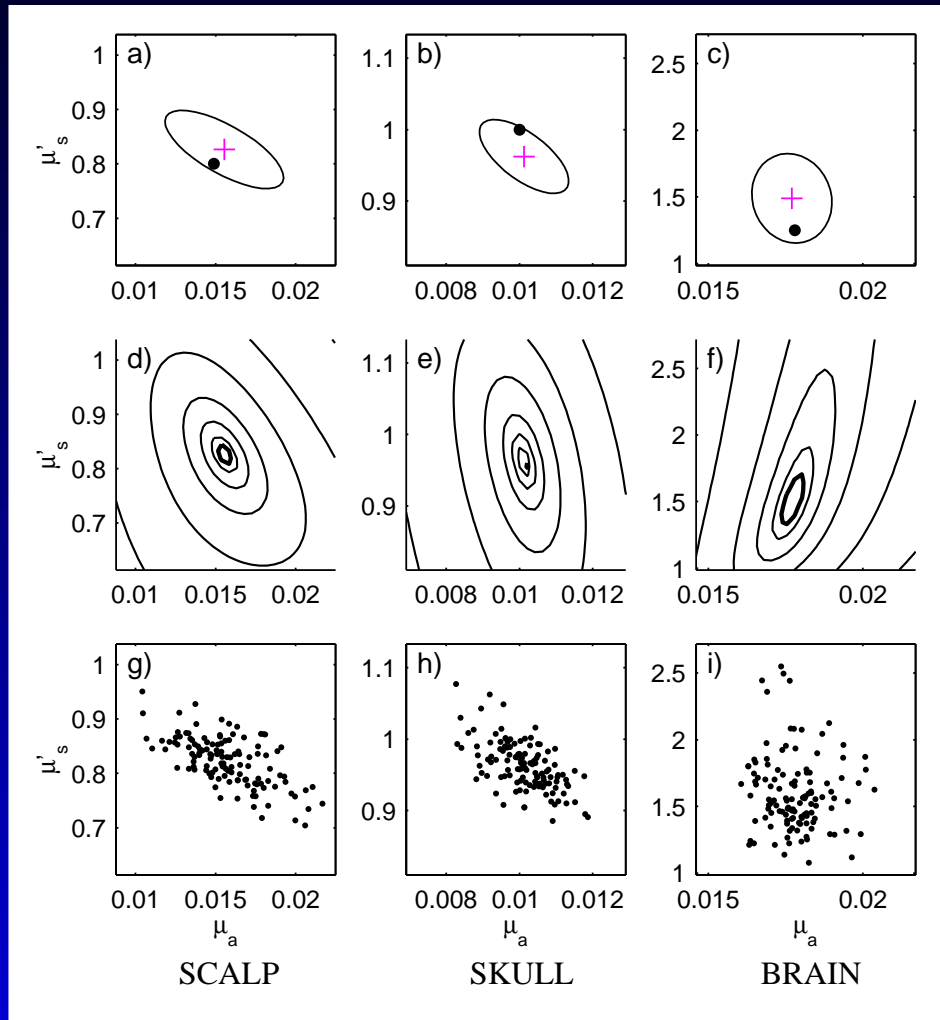
Gaussian approx to PDF

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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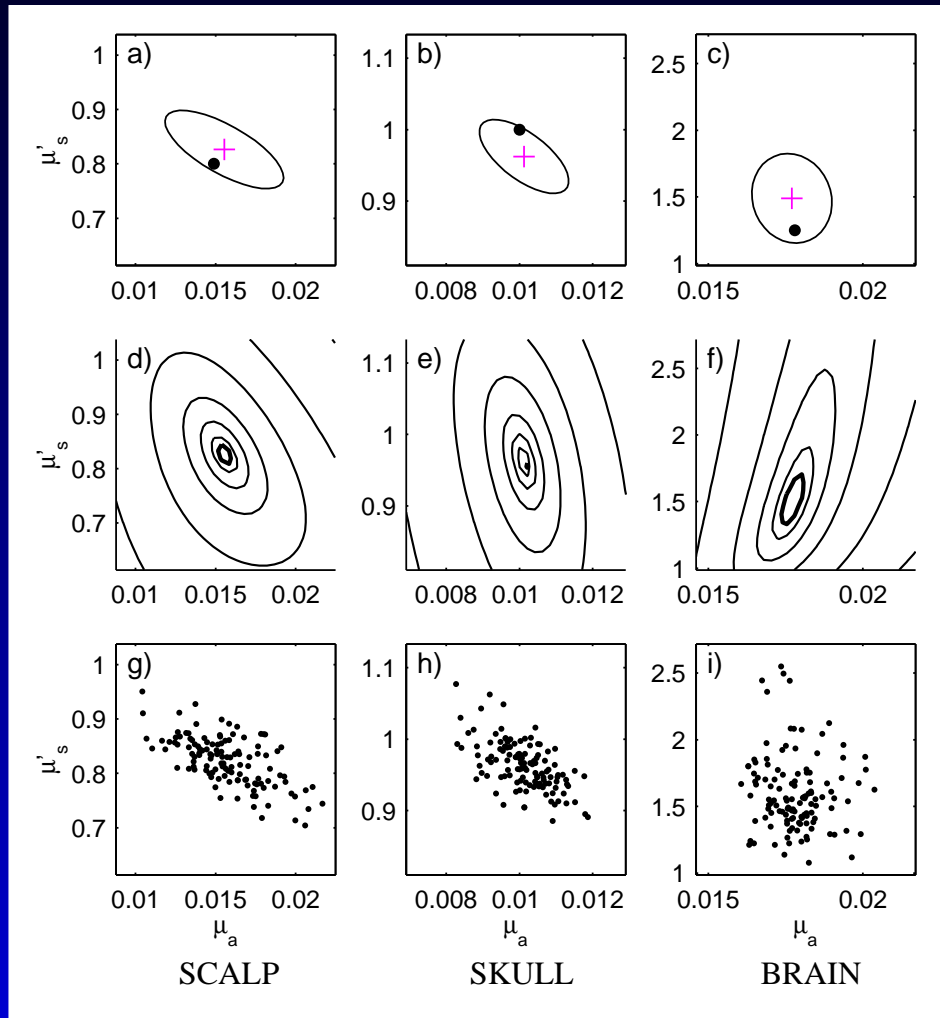
Conditional (slices)

shows nonlinearity

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Sampling exact PDF

Markov chain Monte Carlo

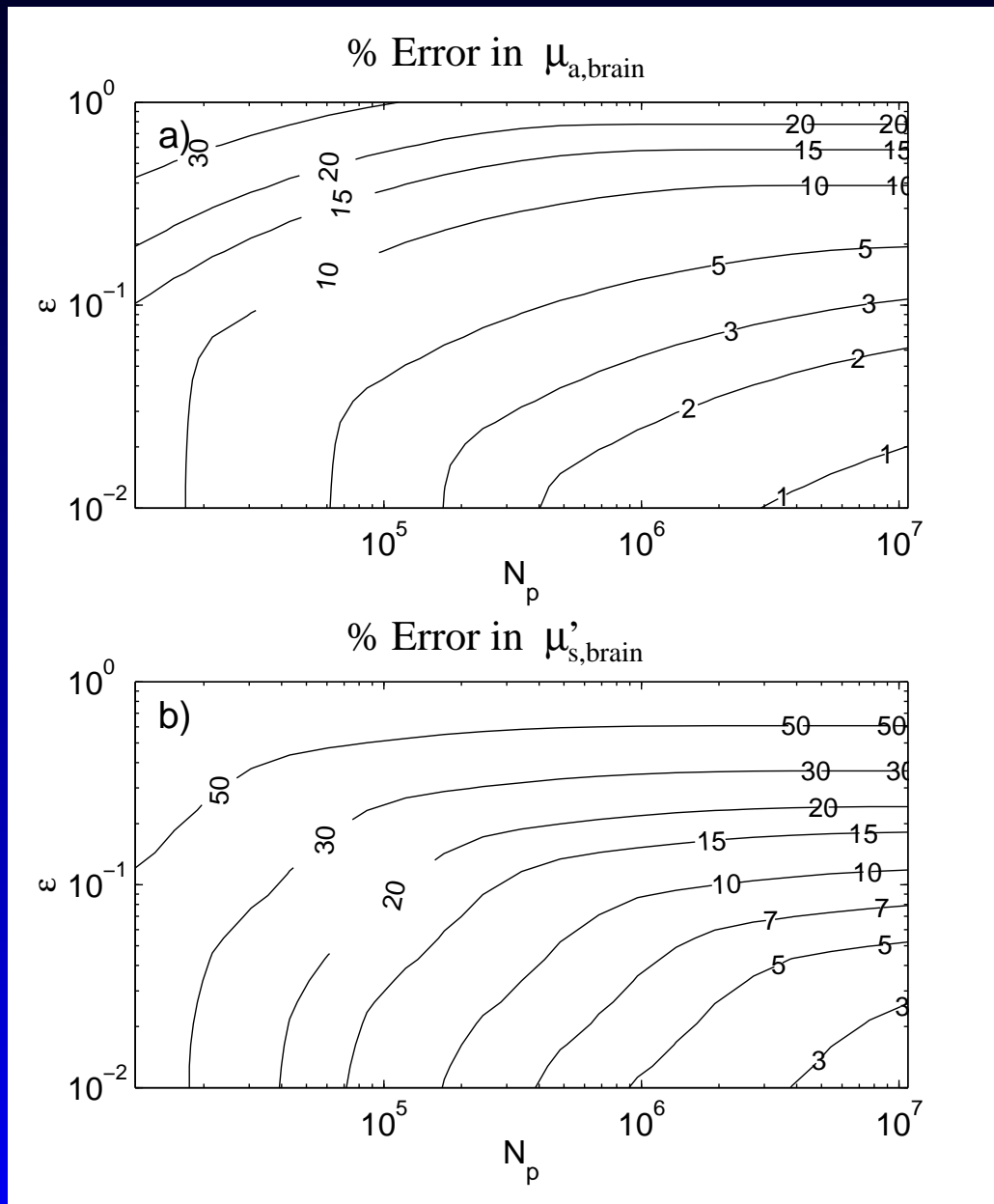
(Metropolis walk)

validates Gaussian approx

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Results: confidence intervals

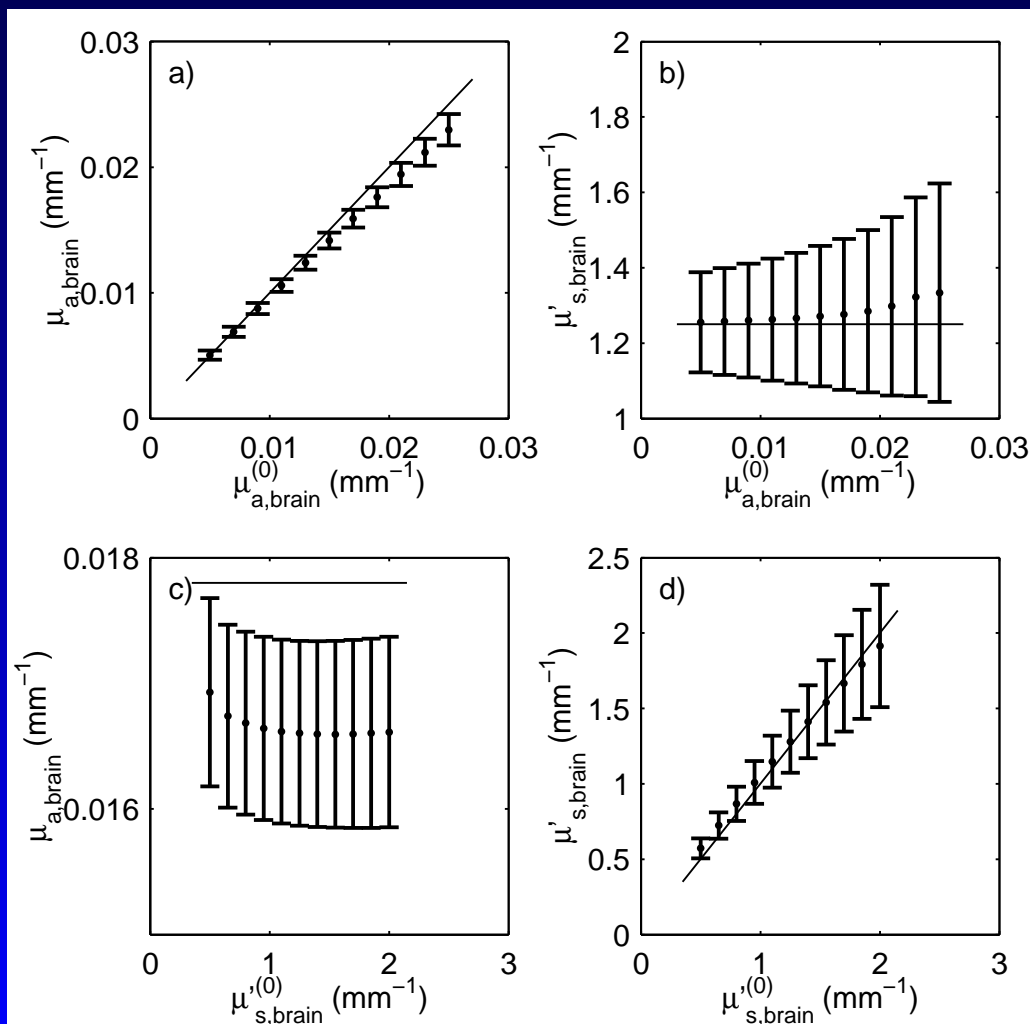


Allows optimal
experimental
design

N_p = total detected
photons

Results: robust to forward error

Simulate signals ($\Delta x = 1$ mm) } up to 50% errors
Inference ($\Delta x = 2$ mm) } (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...