Efficient adaptive experimental design

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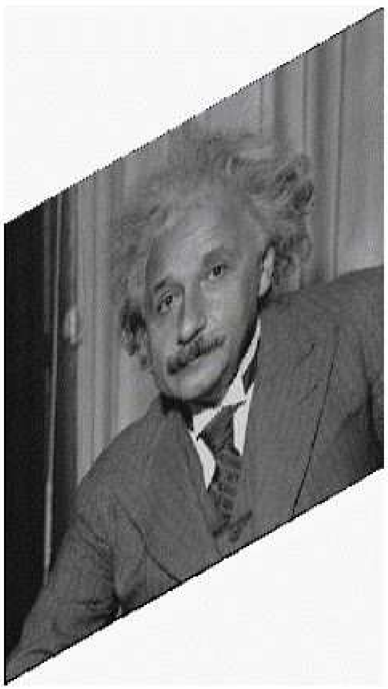
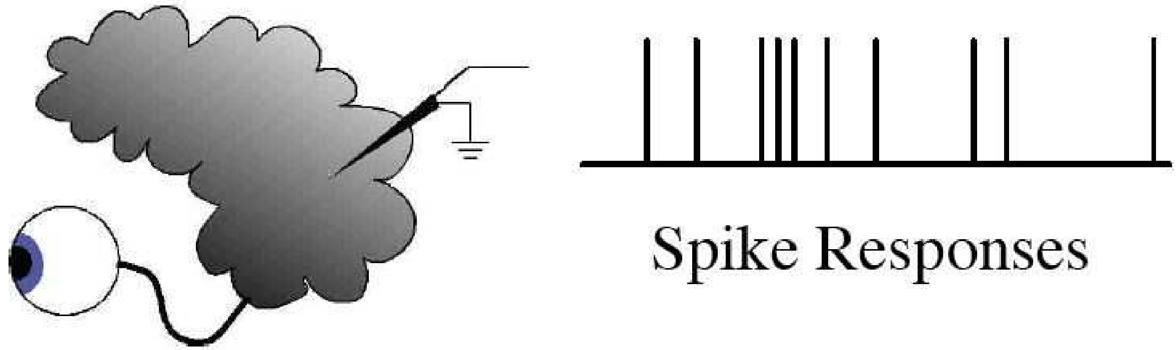
The fundamental question in neuroscience





The **neural code**: what is $P(response \mid stimulus)$?

Main question: how to estimate $P(r|s)$ from (sparse) experimental data?

Curse of dimensionality

Both stimulus and response can be very high-dimensional.

Stimuli:

- images
- sounds
- time-varying behavior

Responses:

- observations from single or multiple simultaneously-recorded point processes

Avoiding the curse of insufficient data

1: Select stimuli more efficiently

— optimal experimental design

2: Estimate some functional $f(p)$ instead of full joint $p(r, s)$

— information-theoretic functionals

3: Improved nonparametric estimators

4: Parametric approaches; connections to biophysical models

Setup

Assume:

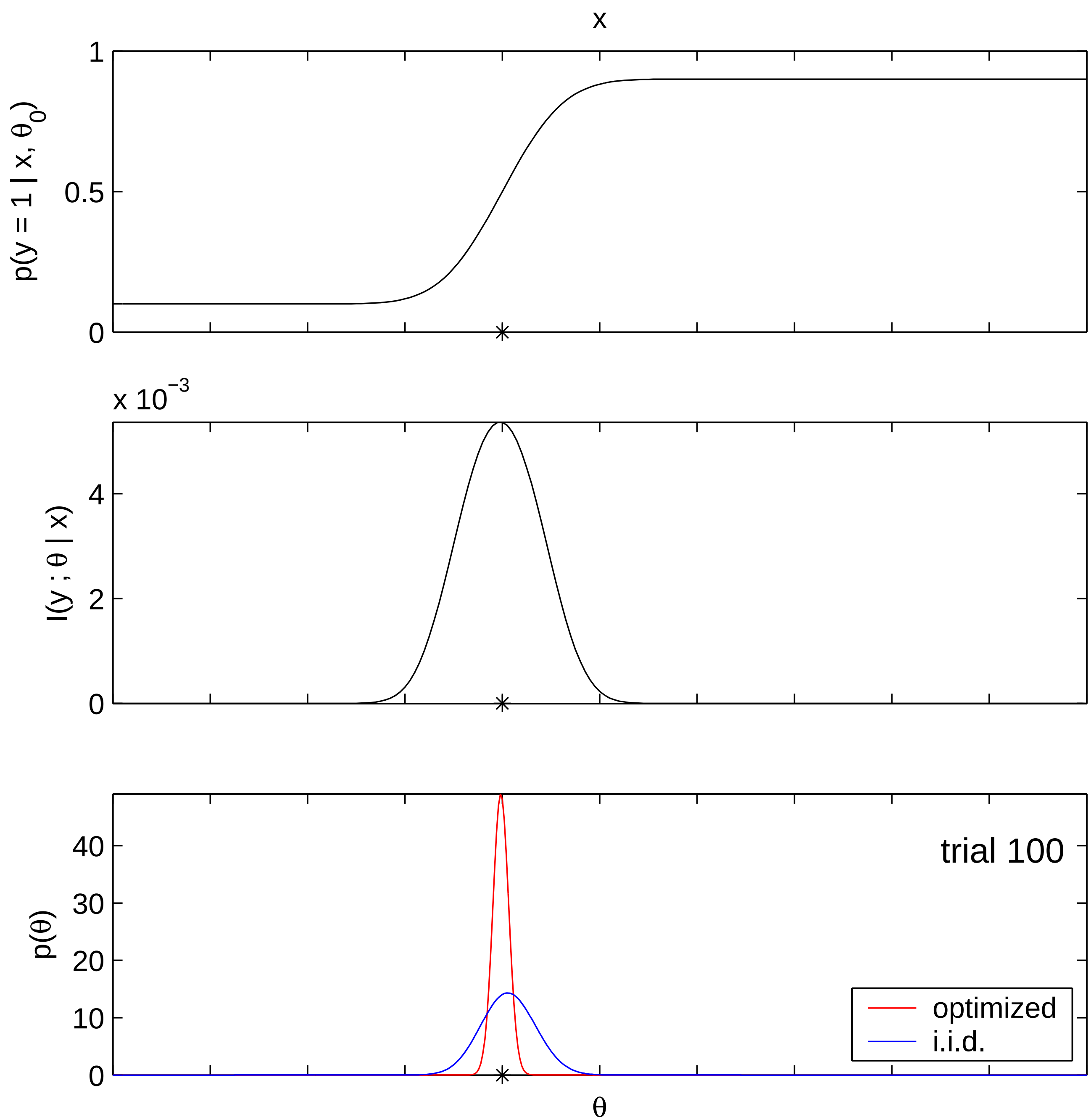
- parametric model $p_\theta(r|\vec{x})$ on responses r given inputs $\vec{x}$
- prior distribution $p(\theta)$ on finite-dimensional model space

Goal: estimate θ from experimental data

Usual approach: draw stimuli i.i.d. from fixed $p(\vec{x})$

Adaptive approach: choose $p(\vec{x})$ on each trial to maximize $I(\theta; r|\vec{x})$ (e.g. "staircase" methods).

Snapshot: one-dimensional simulation



Asymptotic result

Under regularity conditions, a posterior CLT holds (Paninski, 2005):

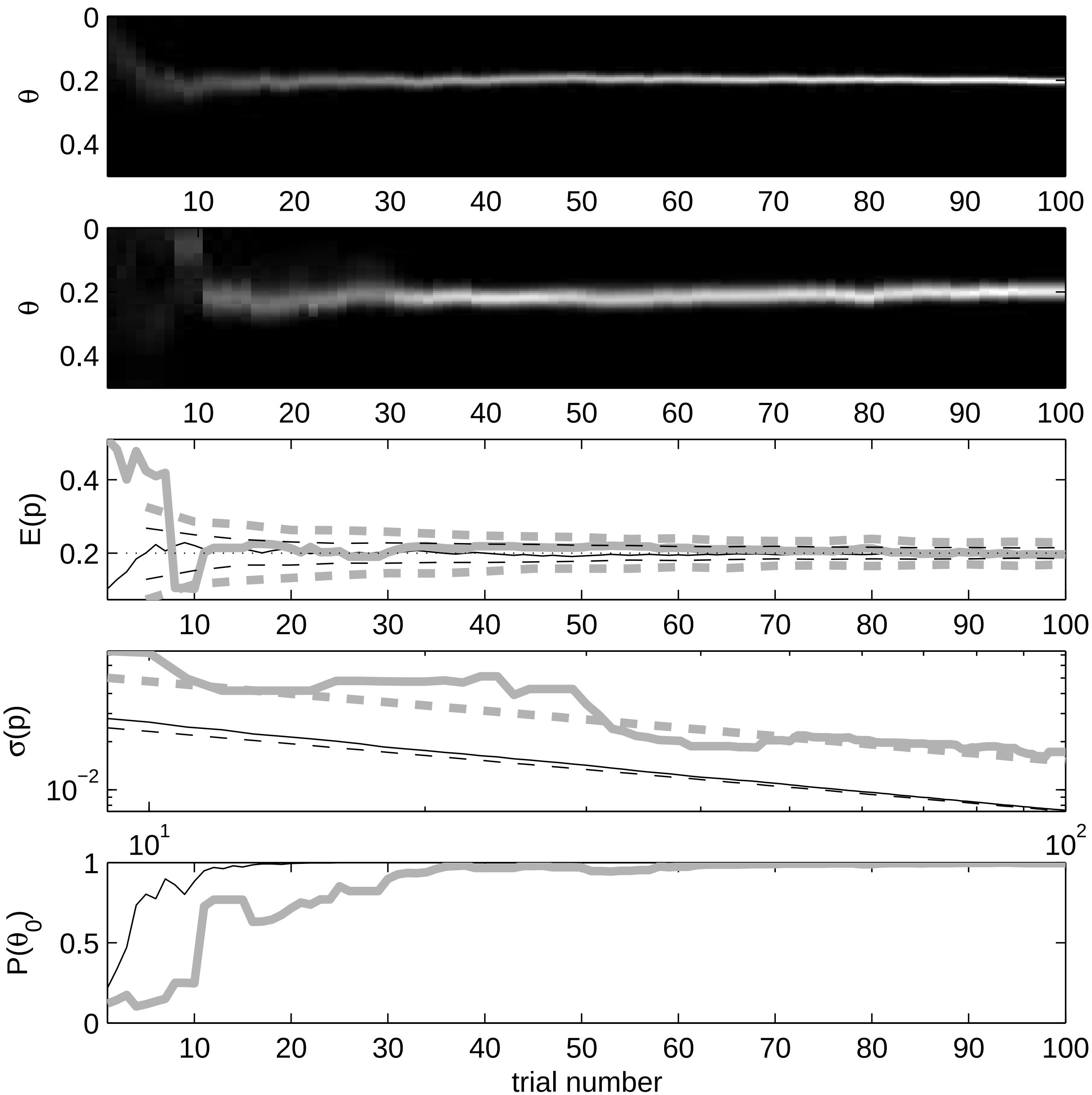
$$p_N\left(\sqrt{N}(\theta - \theta_0)\right) \to \mathcal{N}(\mu_N, \sigma^2); \quad \mu_N \sim \mathcal{N}(0, \sigma^2)$$

- $(\sigma^2_{iid})^{-1} = E_x(I_x(\theta_0))$
- $(\sigma^2_{info})^{-1} = \text{argmax}_{C \in co(I_x(\theta_0))} \log |C|$

$\Longrightarrow \sigma^2_{iid} > \sigma^2_{info}$ unless $I_x(\theta_0)$ is constant in x

$co(I_x(\theta_0))$ = convex closure (over x) of Fisher information matrices $I_x(\theta_0)$. ($\log |C|$ strictly concave: maximum unique.)

Illustration of theorem



Technical details

Stronger regularity conditions than usual to prevent "obsessive" sampling and ensure consistency.

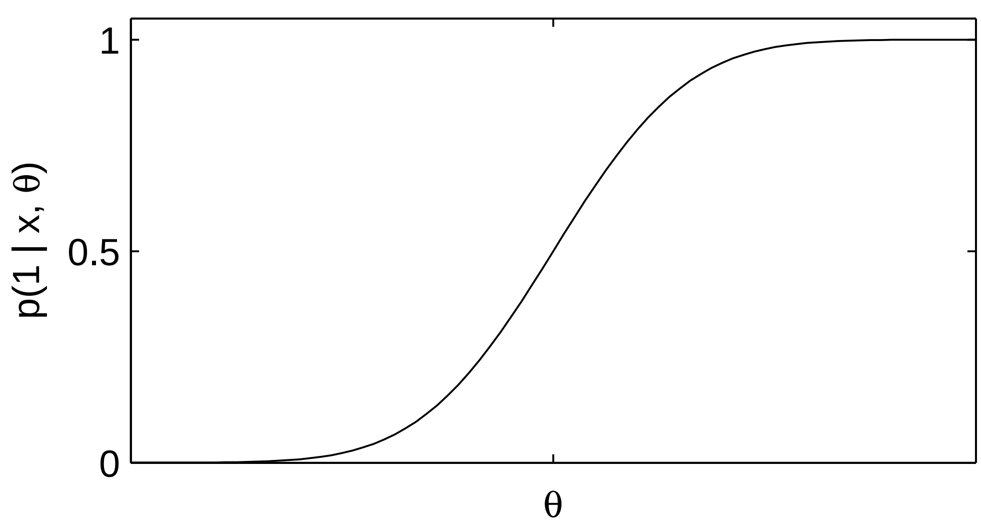
Significant complication: exponential decay of posteriors p_N off of neighborhoods of θ_0 does not necessarily hold.

Psychometric example

- stimuli x one-dimensional: intensity
- responses r binary: detect/no detect

$$p(r = 1|x, \theta) = f((x - \theta)/a)$$

- scale parameter a (assumed known)
- want to learn threshold parameter θ as quickly as possible



Psychometric example: results

- variance-minimizing and info-theoretic methods asymptotically same
- just one unique function f^* for which $\sigma_{iid} = \sigma_{opt}$; for any other f, $\sigma_{iid} > \sigma_{opt}$

$$I_x(\theta) = \frac{(\dot{f}_{a,\theta})^2}{f_{a,\theta}(1 - f_{a,\theta})}$$

- f^* solves

$$\dot{f}_{a,\theta} = c\sqrt{f_{a,\theta}(1 - f_{a,\theta})}$$

$$f^*(t) = \frac{\sin(ct) + 1}{2}$$

- $\sigma^2_{iid}/\sigma^2_{opt} \sim 1/a$ for a small

Part 2: Computing the optimal stimulus

OK, now how do we actually do this in neural case?

- Computing $I(\theta; r|\vec{x})$ requires an integration over θ
  — in general, exponentially hard in $\dim(\theta)$
- Maximizing $I(\theta; r|\vec{x})$ in $\vec{x}$ is doubly hard
  — in general, exponentially hard in $\dim(\vec{x})$

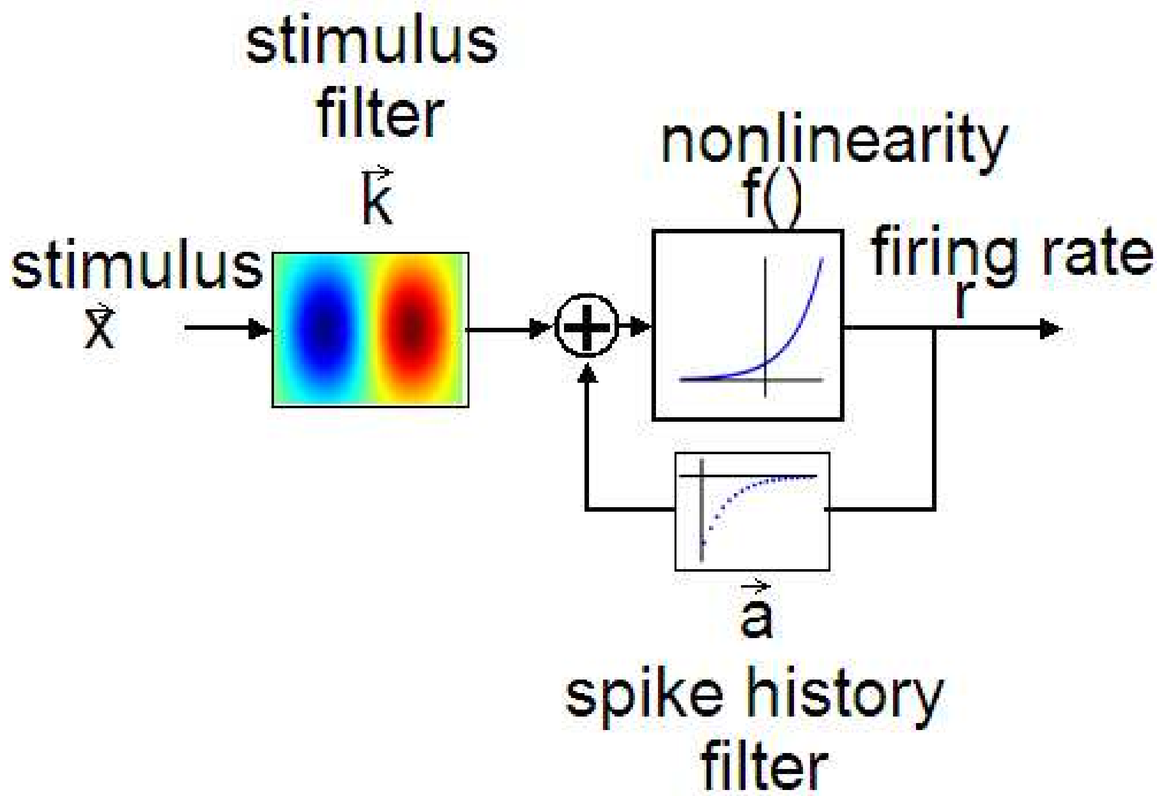
Doing all this in real time ($\sim$ 10 ms - 1 sec) is a major challenge!

Joint work w/ J. Lewi, R. Butera, Georgia Tech. (Lewi et al., 2006)

Three key steps

1. Choose a tractable, flexible model of neural encoding
2. Choose a tractable, accurate approximation of the posterior $p(\vec{\theta}|\{\vec{x}_i, r_i\}_{i\leq N})$
3. Use approximations and some perturbation theory to reduce optimization problem to a simple 1-d linesearch

Step 1: the generalized linear model



$$r_i \sim Poiss(\lambda_i); \qquad \lambda_i | \vec{x}_i, \vec{\theta} = f(\vec{k} \cdot \vec{x}_i + \sum_j a_j r_{i-j})$$

Goal: learn $\vec{\theta} = \{\vec{k}, \vec{a}\}$ in as few trials as possible.

GLM likelihood

$$\lambda_i \sim Poiss(\lambda_i)$$
$$\lambda_i | \vec{x}_i, \vec{\theta} = f(\vec{k} \cdot \vec{x}_i + \sum_j a_j r_{i-j})$$

$$\log p(r_i | \vec{x}_i, \vec{\theta}) = -f(\vec{k} \cdot \vec{x}_i + \sum_j a_j r_{i-j}) + r_i \log f(\vec{k} \cdot \vec{x}_i + \sum_j a_j r_{i-j})$$

Two key points:

- Likelihood is "rank-1" — only depends on $\vec{\theta}$ along $\vec{z} = (\vec{x}, \vec{r})$.
- f convex and log-concave $\implies$ log-likelihood concave in $\vec{\theta}$

Step 2: representing the posterior

Idea: Laplace approximation

$$p(\vec{\theta}|\{\vec{x}_i, r_i\}_{i\leq N}) \approx \mathcal{N}(\mu_N, C_N)$$

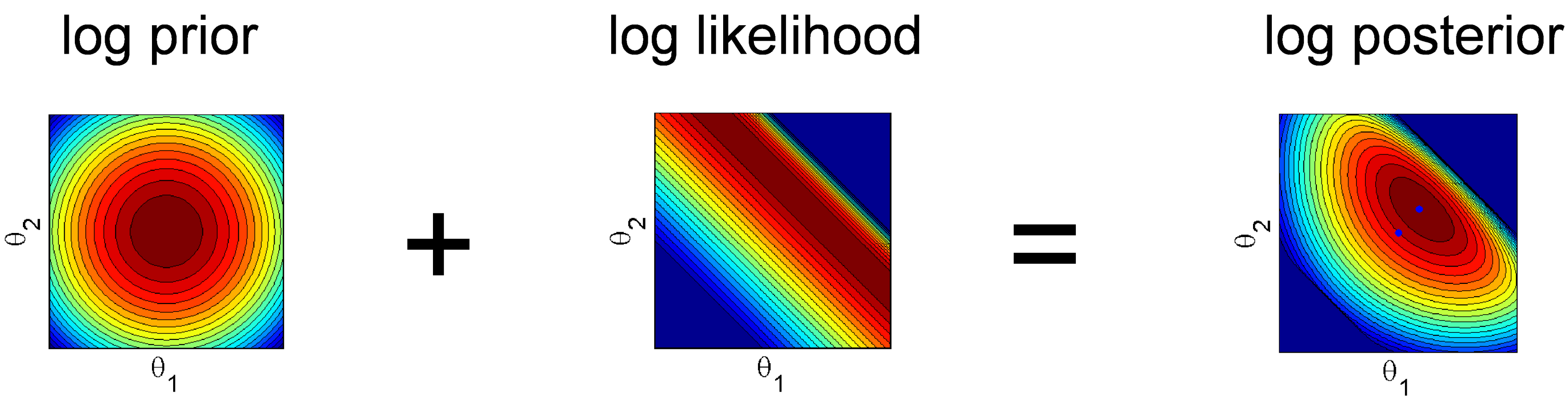
Justification:

- posterior CLT
- likelihood is log-concave, so posterior is also log-concave:

$$\log p(\vec{\theta}|\{\vec{x}_i, r_i\}_{i\leq N}) \sim \log p(\vec{\theta}|\{\vec{x}_i, r_i\}_{i\leq N-1}) + \log p(r_N|x_N, \vec{\theta})$$

— Equivalent to an extended Kalman filter formulation

Efficient updating



Updating μ_N: one-d search

Updating C_N: rank-one update, $C_N = (C_{N-1}^{-1} + b\vec{z}^t\vec{z})^{-1}$ — use Woodbury lemma

Total time for update of posterior: $O(d^2)$

Step 3: Efficient stimulus optimization

Laplace approximation $\implies I(\theta; r|\vec{x}) \sim E_{r|\vec{x}} \log \frac{|C_{N-1}|}{|C_N|}$

— this is nonlinear and difficult, but we can simplify using perturbation theory: $\log |I + A| \approx \text{trace}(A)$.

Now we can take averages over $p(r|\vec{x}) = \int p(r|\theta, \vec{x}) p_N(\theta) d\theta$: standard Fisher info calculation given Poisson assumption on r.

Further assuming $f(.) = \exp(.)$ allows us to compute expectation exactly, using m.g.f. of Gaussian.

...finally, we want to maximize $F(\vec{x}) = g(\mu_N \cdot \vec{x}) h(\vec{x}^t C_N \vec{x})$.

Computing the optimal $\vec{x}$

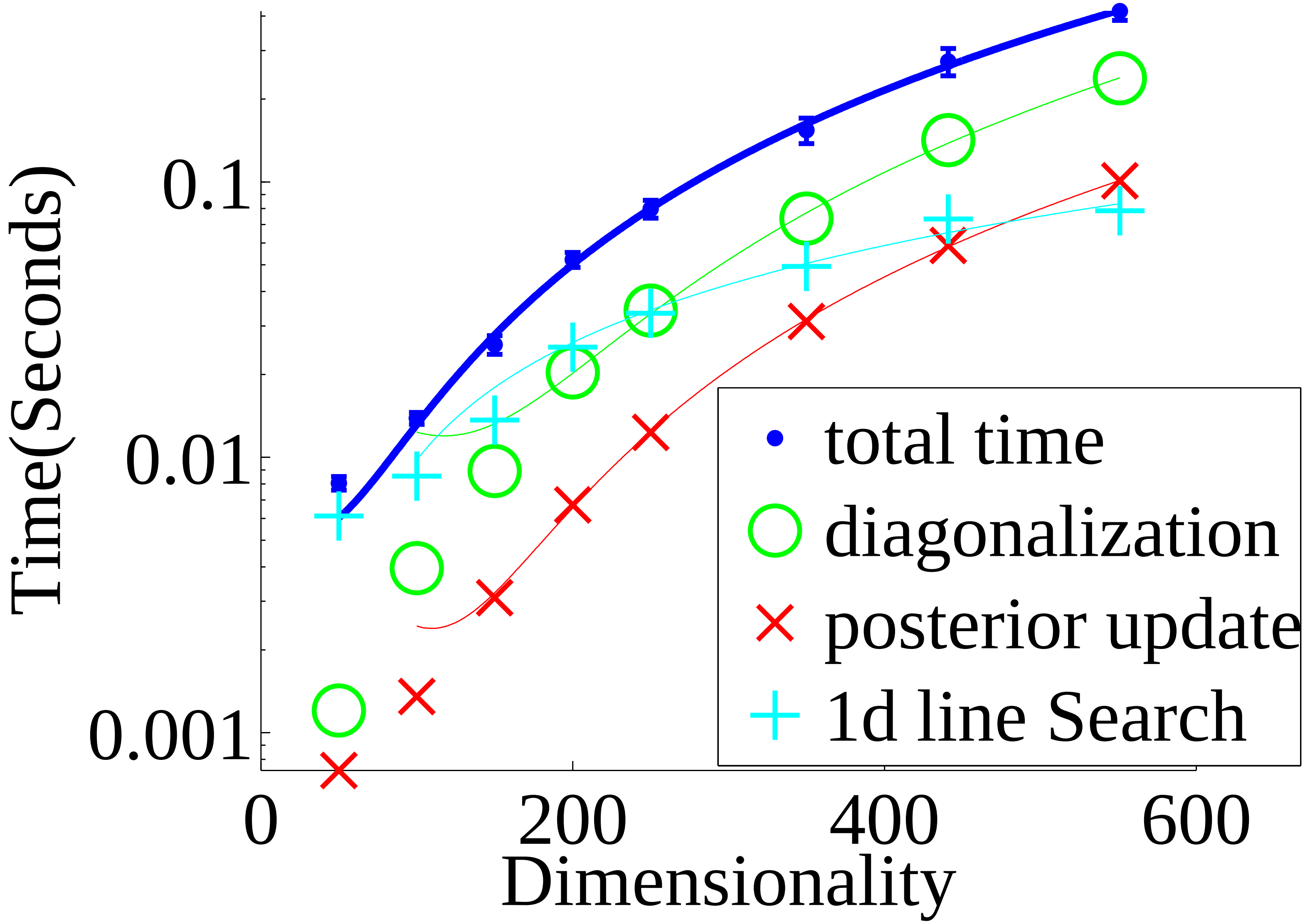
$\max_{\vec{x}} g(\mu_N \cdot \vec{x}) h(\vec{x}^t C_N \vec{x})$ increases with $||\vec{x}||_2$: constraining $||\vec{x}||_2$ reduces problem to nonlinear eigenvalue problem.

Lagrange multiplier approach (Berkes and Wiskott, 2006) reduces problem to 1-d linesearch, once eigendecomposition is computed — much easier than full d-dimensional optimization!

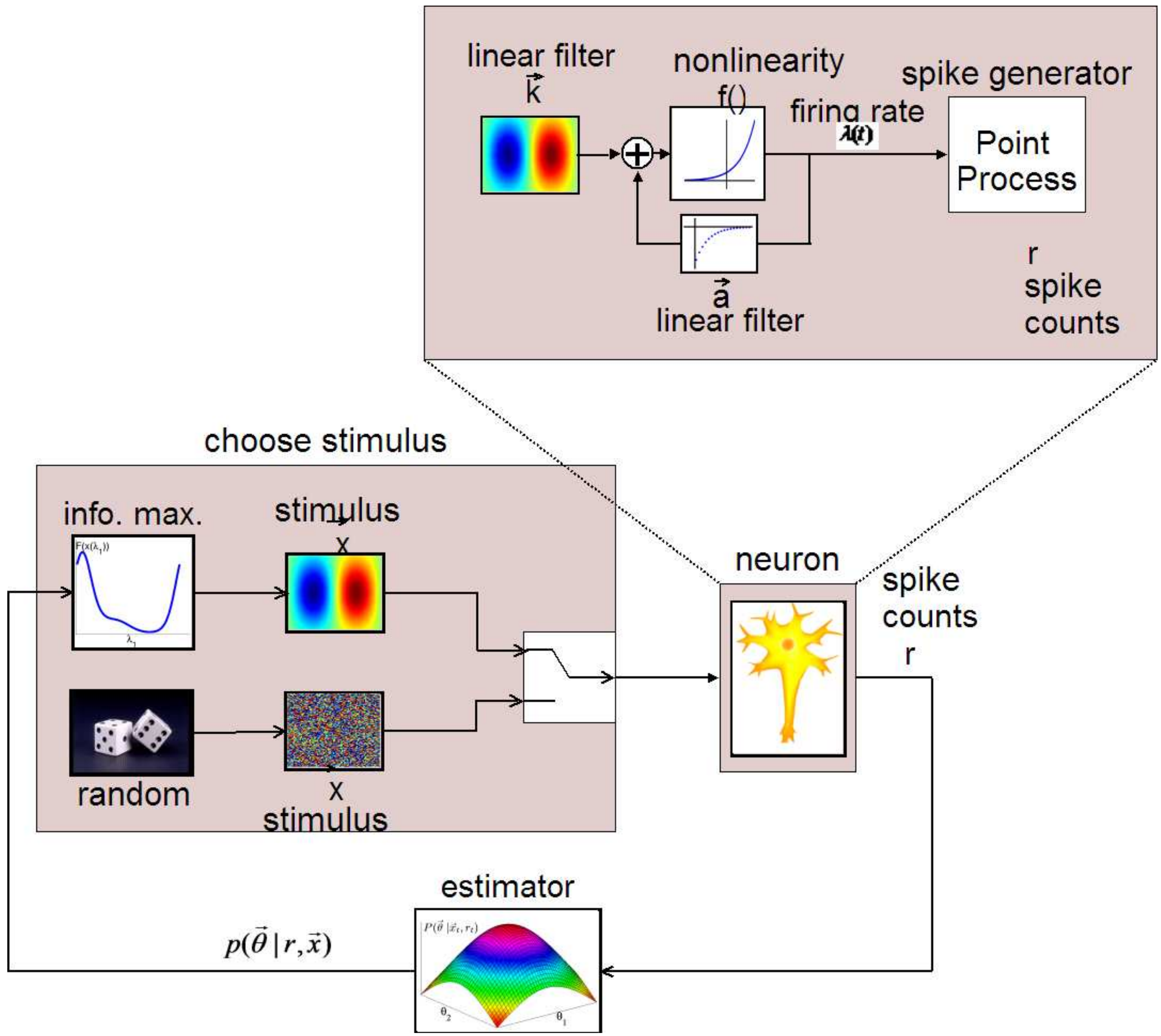
Rank-one update of eigendecomposition may be performed in $O(d^2)$ time (Gu and Eisenstat, 1994).

$\implies$ Computing optimal stimulus takes $O(d^2)$ time.

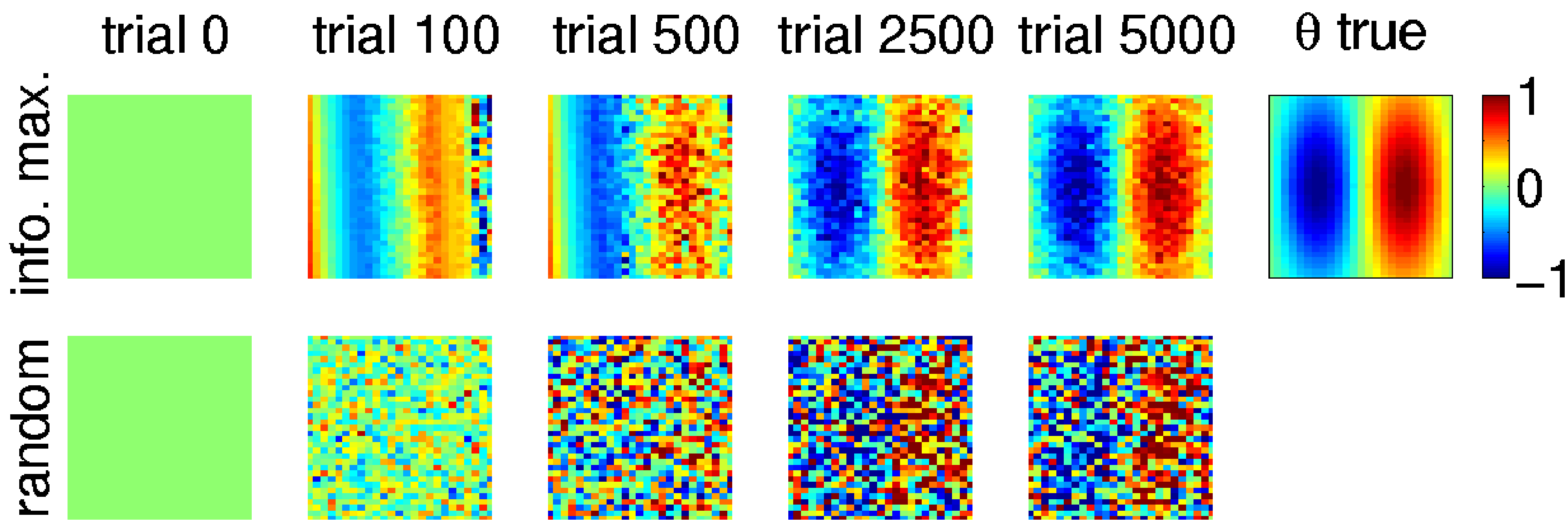
Near real-time adaptive design



Simulation overview



Gabor example



— infomax approach is an order of magnitude more efficient.

Handling nonstationary parameters

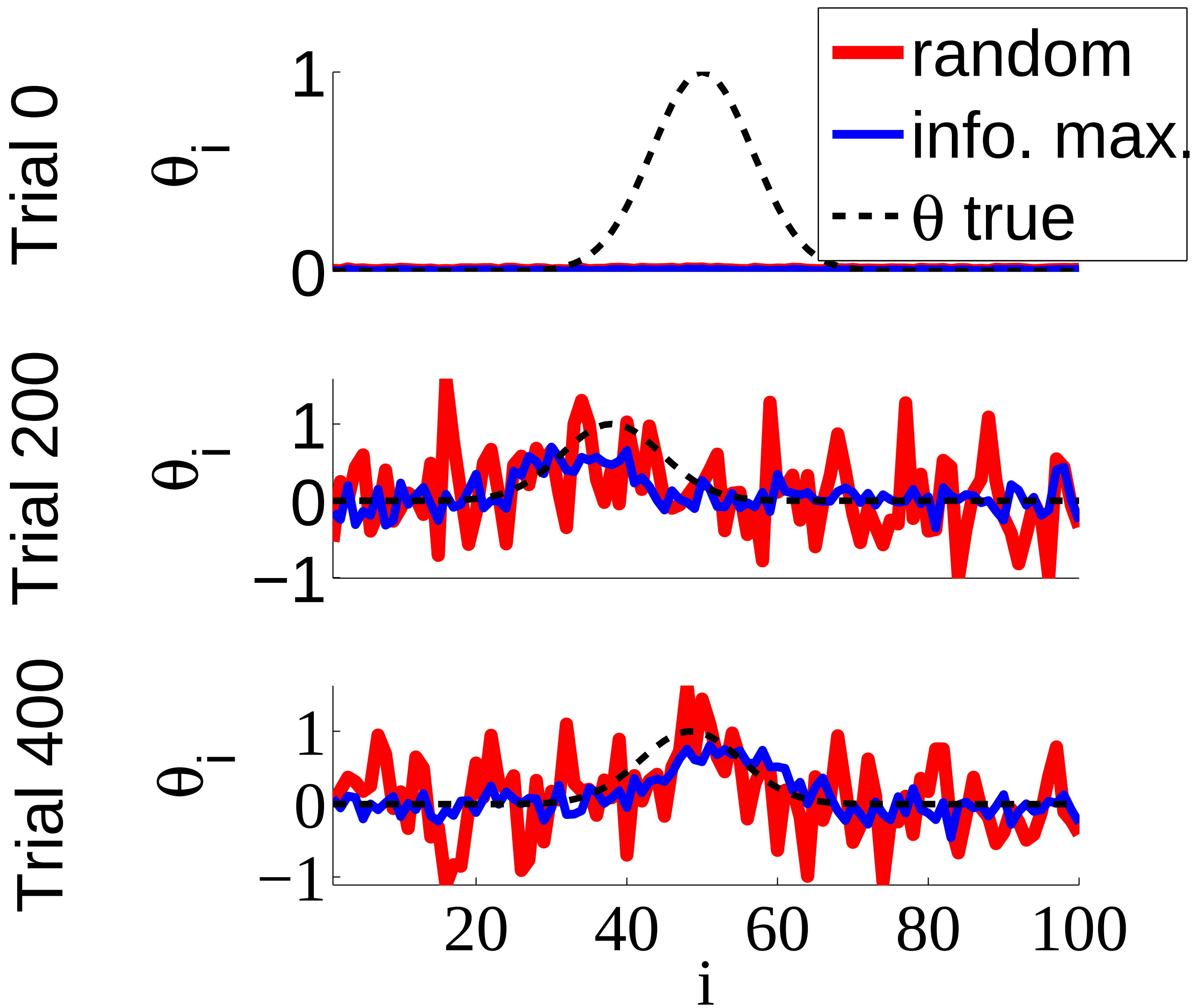
Various sources of nonsystematic nonstationarity:

- Eye position drift
- Changes in arousal / attentive state
- Changes in health / excitability of preparation

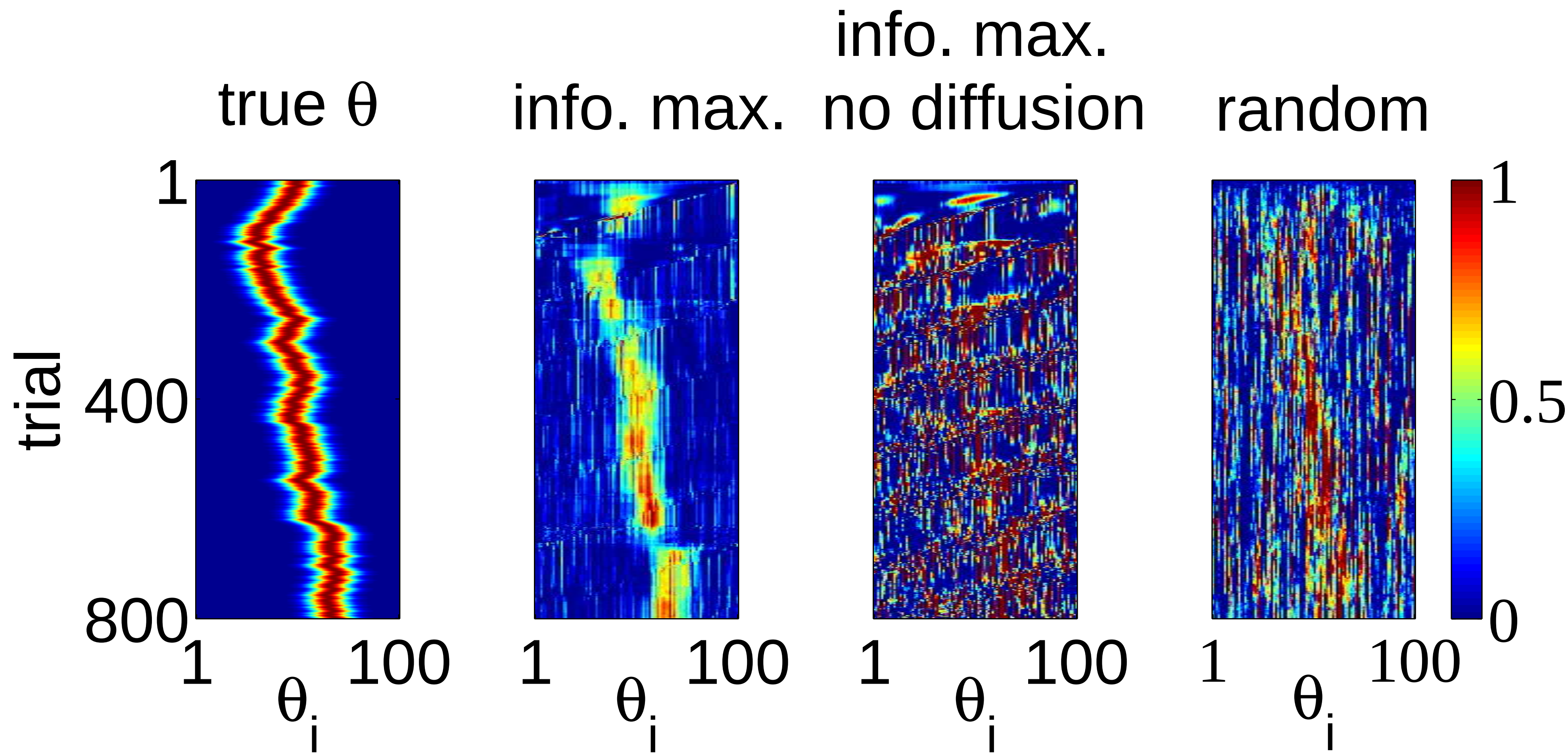
Solution: allow diffusion in extended Kalman filter:

$$\vec{\theta}_{N+1} = \vec{\theta}_N + \epsilon; \quad \epsilon \sim \mathcal{N}(0, Q)$$

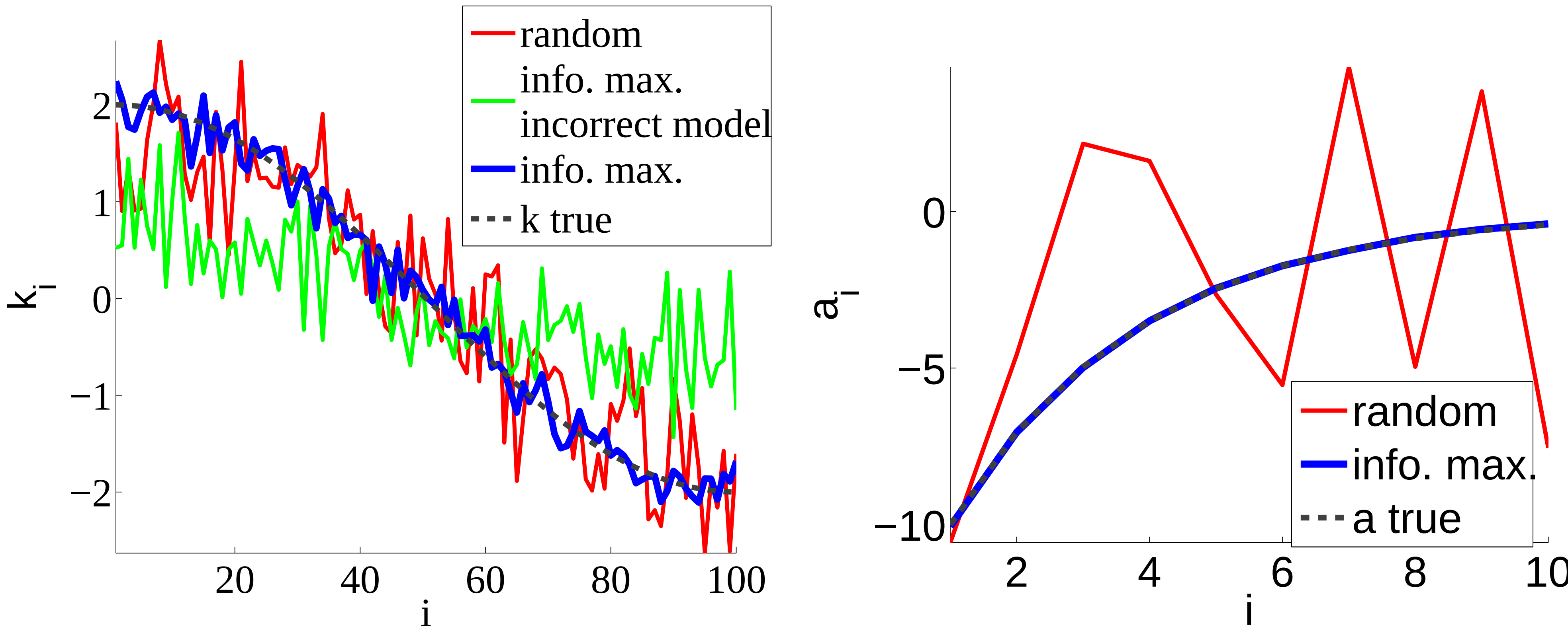
Nonstationary example



Nonstationary example



Spike history example



Conclusions

- Three key assumptions/approximations enable real-time ($O(d^2)$) infomax stimulus design:

  — generalized linear model

  — Laplace approximation

  — first-order approximation of log-determinant

- Able to deal with adaptation through spike history terms and nonstationarity through Kalman formulation

- Extensions: model misspecification; multi-neuron effects; model nonlinearities; application to real data.

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