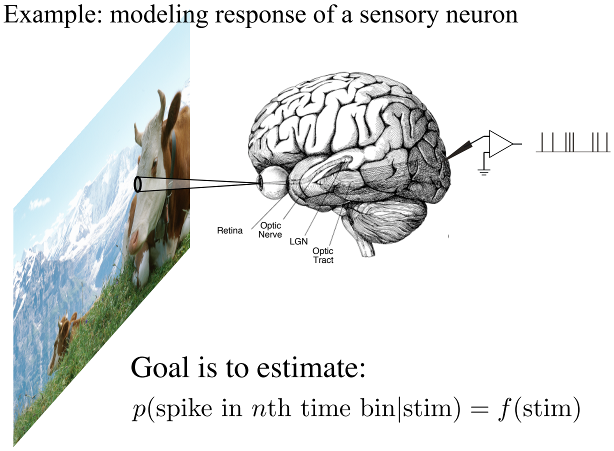
Fitting models to data

- How do we estimate parameters?
  - formulate model + objective function (common choice: ML)
  - optimize (closed form, gradient descent, etc)
- How good are parameter estimates?
- How well does model fit ?
  - likelihood or posterior comparisons
  - model failures

Example: modeling response of a sensory neuron

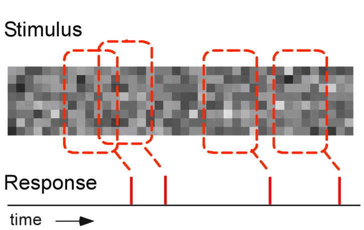


Goal is to estimate:

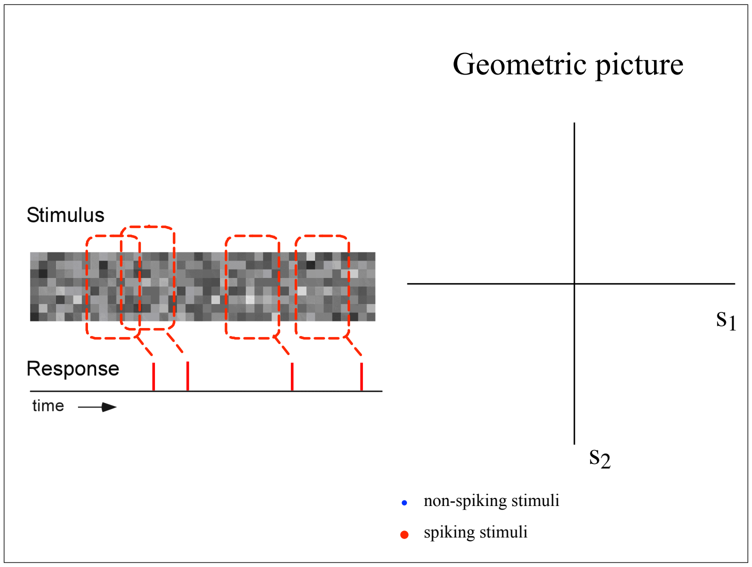
$p(\text{spike in } n\text{th time bin}|\text{stim}) = f(\text{stim})$

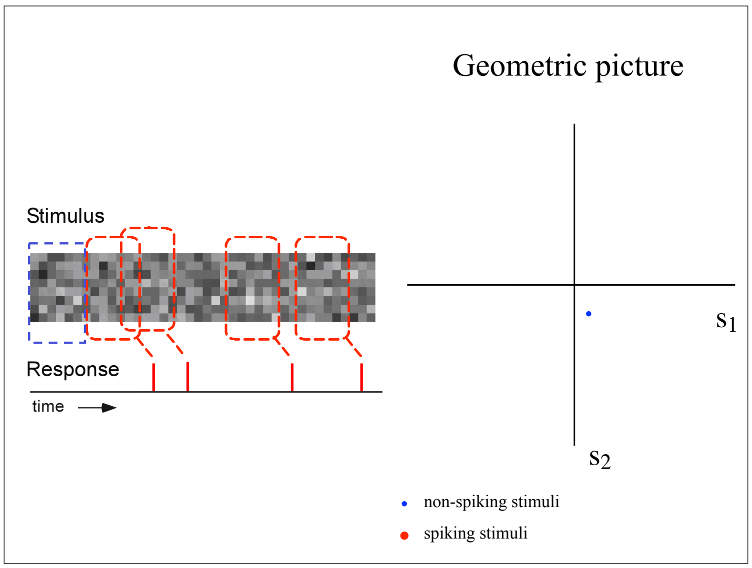
Geometric view

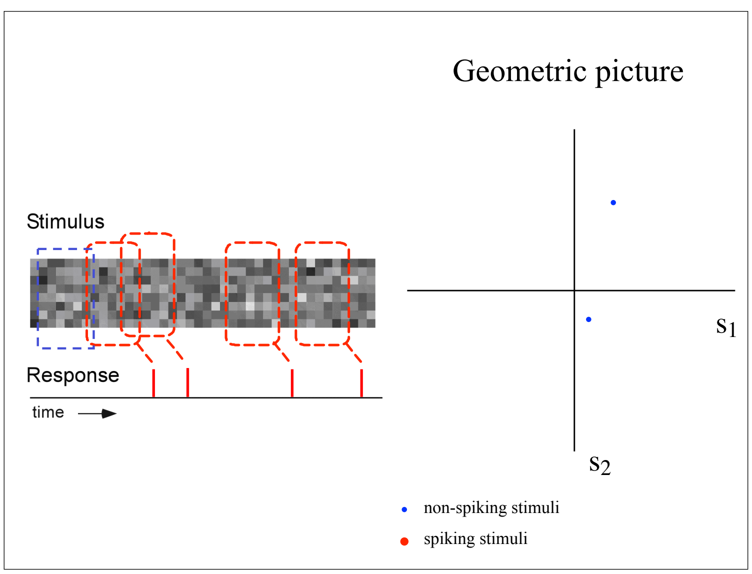
1D stimulus over time
(e.g., flickering bars)



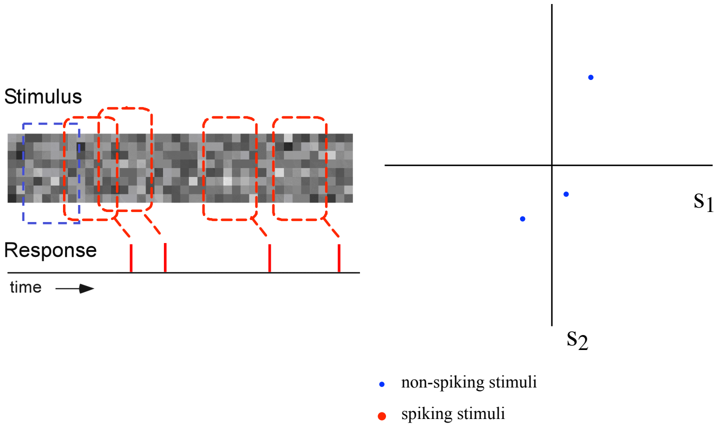
- 8 x 6 stimulus block
  = 48-dimensional vector


Geometric picture
Stimulus
Response
time
s_1
s_2
non-spiking stimuli
spiking stimuli

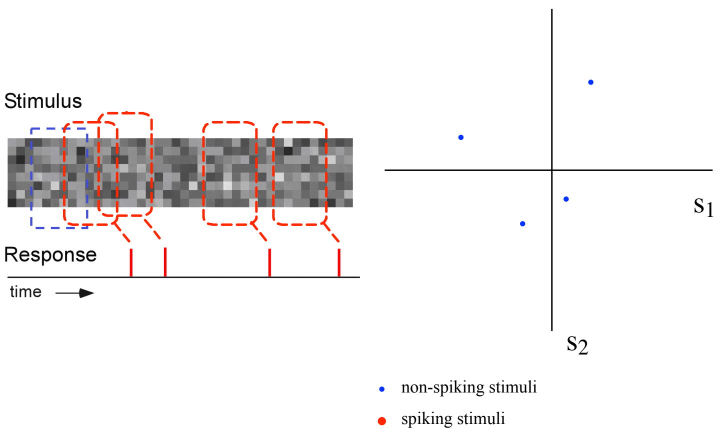

Geometric picture
Stimulus
Response
time
s_1
s_2
non-spiking stimuli
spiking stimuli


Geometric picture
Stimulus
Response
time
s_1
s_2
non-spiking stimuli
spiking stimuli

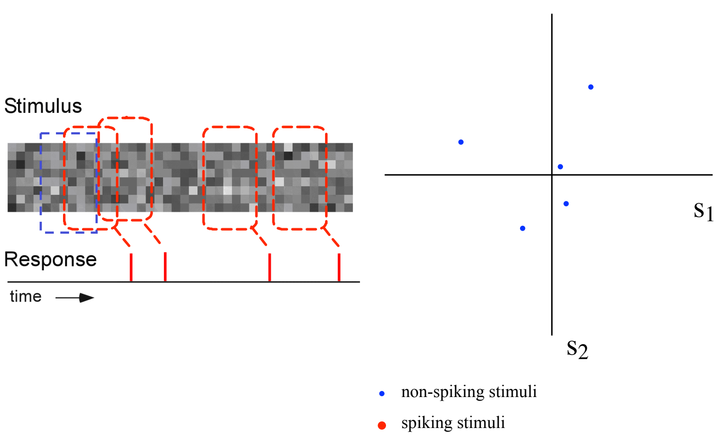
Geometric picture



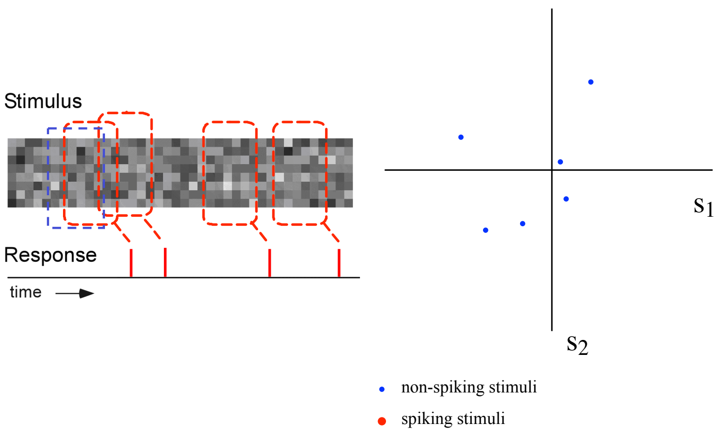
Geometric picture



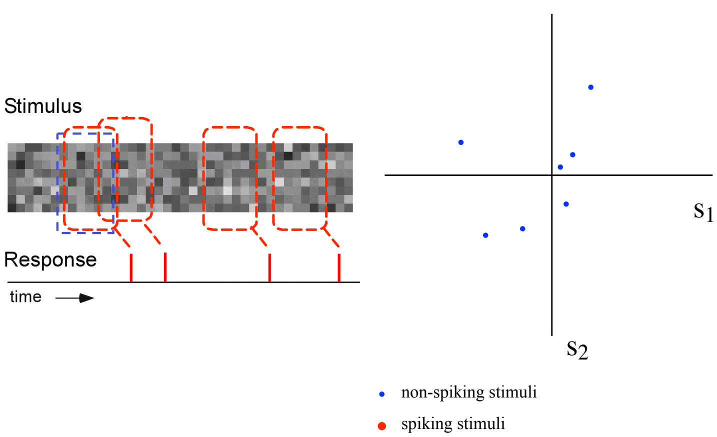
Geometric picture



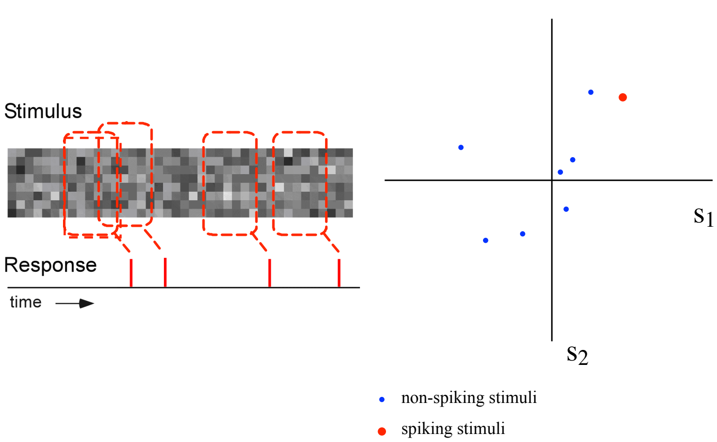
Geometric picture



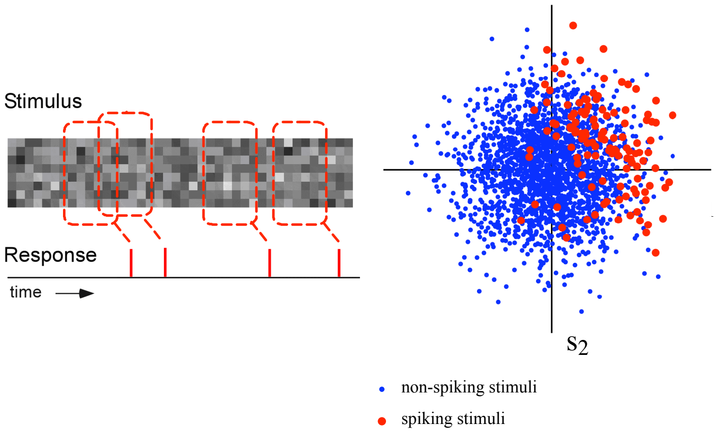
Geometric picture



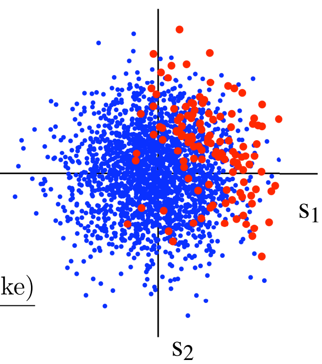
Geometric picture



Geometric picture



Response is captured by relationship between the distribution of red points (spiking stim) and blue+red points (all stim), expressed in terms of Bayes' rule:



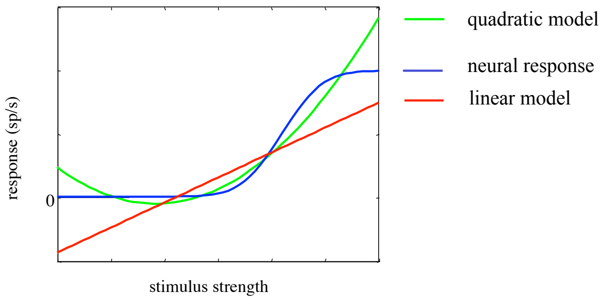
$$P(\text{spike}|\vec{s}) = \frac{P(\vec{s}\ |\text{spike})P(\text{spike})}{P(\vec{s})}$$

Cannot estimate directly ("curse of dimensionality"). We need a **model**

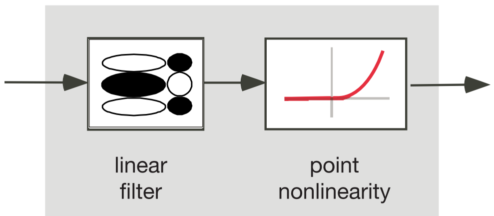
Some tractable model options

- Low-order polynomial [Volterra '13; Wiener '58; DeBoer and Kuyper '68; ...]
- Low-dimensional subspace [Bialek '88; Brenner etal '00; Schwartz etal '01; Touryan and Dan '02; ...]
- Recursive linear with exponential nonlinearity [Truccolo etal '05; Pillow etal '05]

Low-order polynomial model

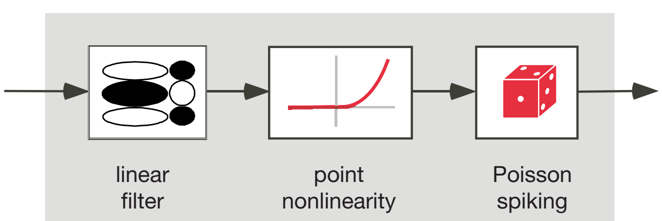


Example: LN cascade model



- Threshold-like nonlinearity => linear classifier
- Classic model for Artificial Neural Networks
  - McCullough & Pitts (1943), Rosenblatt (1957), etc
- No spikes (output is firing rate)

LNP cascade model



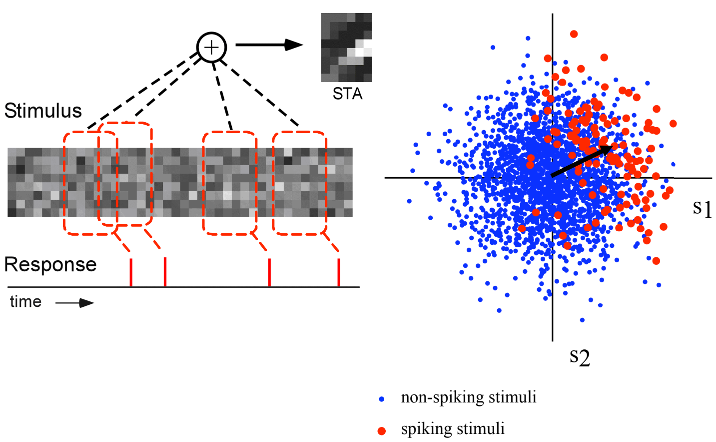
- Simplest descriptive spiking model
- Easily fit to (extracellular) data
- Descriptive, and interpretable (although *not* mechanistic)

Simple LNP fitting

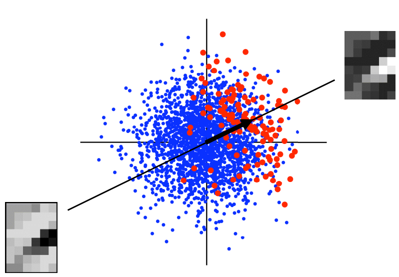
- Assuming:
  - stochastic stimuli, spherically distributed
  - average of spike-triggered ensemble (STA) is shifted from that of raw ensemble
- The STA (i.e., linear regression!) gives an **unbiased** estimate of w (for any f). *[on board]*
- For exponential f, this is the ML estimate! *[on board]*

[Bussgang 52; de Boer & Kuyper 68]

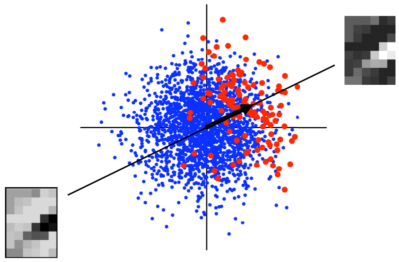
Computing the STA



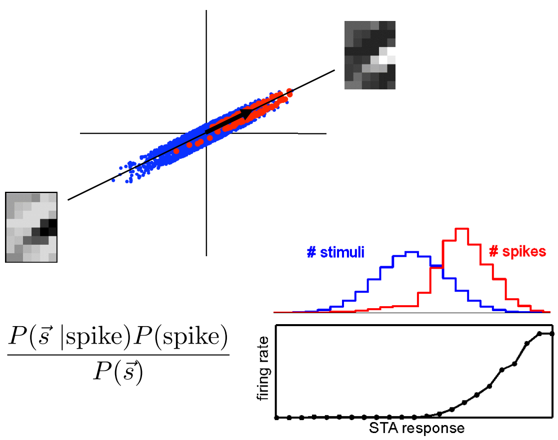
STA corresponds to a “direction” in stimulus space



Projecting onto the STA

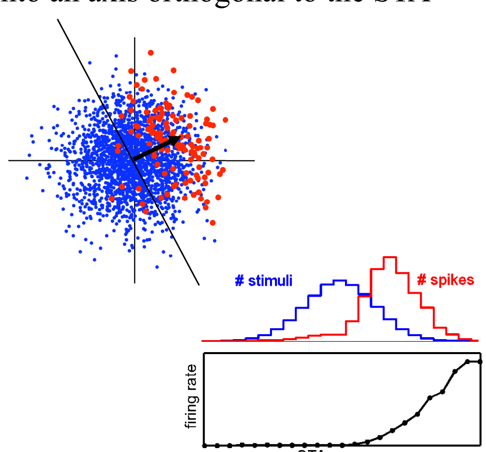


Solving for nonparametric nonlinearity

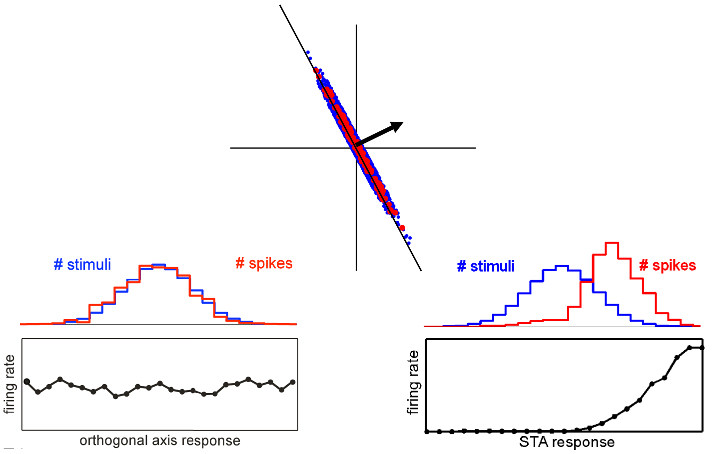


$$P(\text{spike}|\vec{s}) = \frac{P(\vec{s}\ |\text{spike})P(\text{spike})}{P(\vec{s})}$$

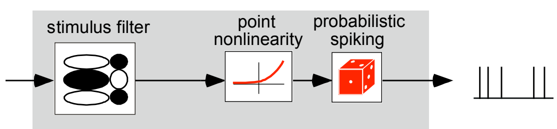
Projecting onto an axis orthogonal to the STA

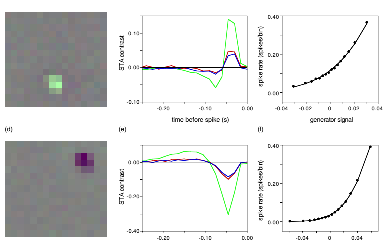


Projecting onto an axis orthogonal to the STA

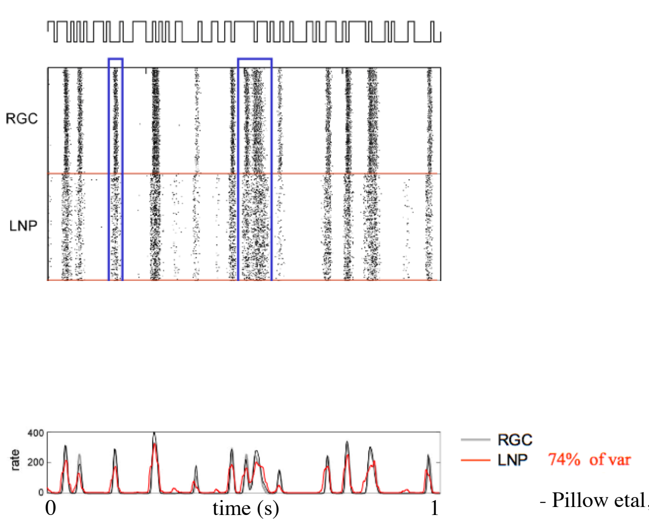


LNP model, fit to retinal ganglion cells



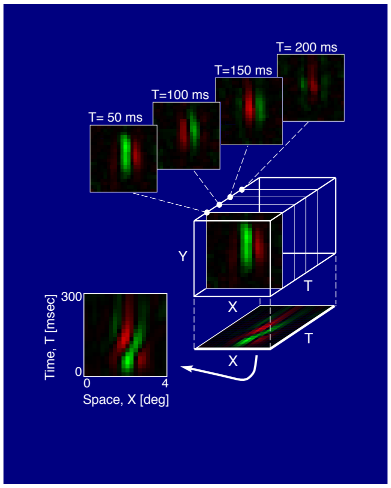


[Chichilnisky & Kalmer, 2002]

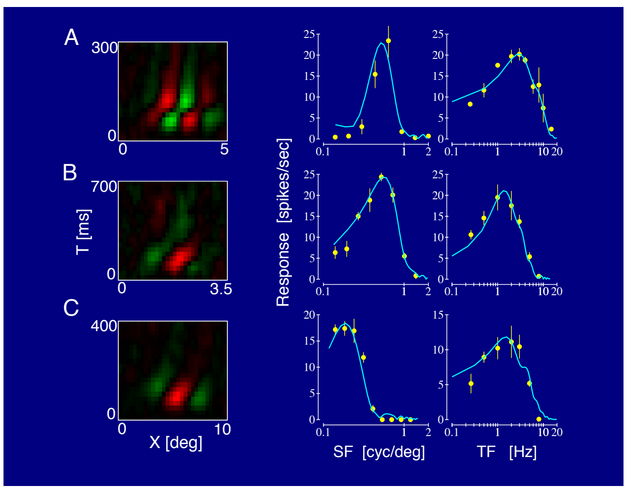


- Pillow etal, 2004

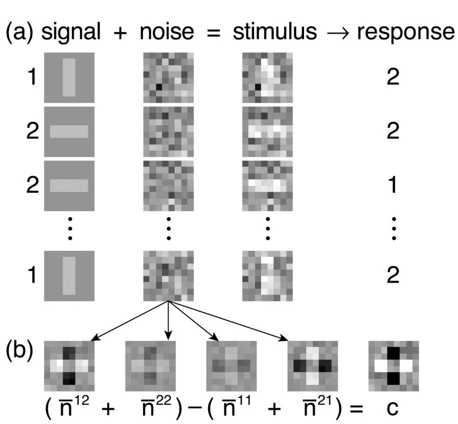
V1
simple
cell



- Ozhawa, etal

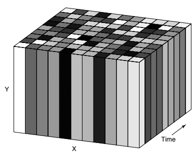


Psychophysical “Classification Image”

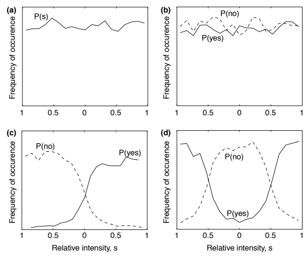


Murray R F J Vis 2011;11:2

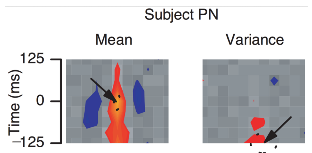
Stimuli: 11x9 movie of bars, uniform random intensities



Task:
Is center bar of middle frame brighter or darker than the mean?



Simulation:
a) raw stimulus distribution
b) cond. dist. for irrelevant bar
c) cond. dist. for linear response model
d) cond. dist. for quadratic (contrast) response



[Neri & Heeger, 2002]

ML estimation of LNP

If $f_\theta(\vec{k}\cdot\vec{x})$ is convex (in argument and theta),
and $log\, f_\theta(\vec{k}\cdot\vec{x})$ is concave,
the likelihood of the LNP model is convex
(for all data, $\{n(t), \vec{x}(t)\}$)

Examples: $e^{(\vec{k}\cdot\vec{x}(t))}$

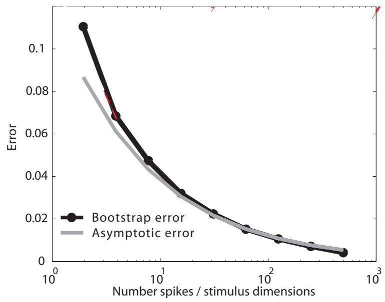
$(\vec{k}\cdot\vec{x}(t))^\alpha, \quad 1 < \alpha < 2$

[Paninski, '04]

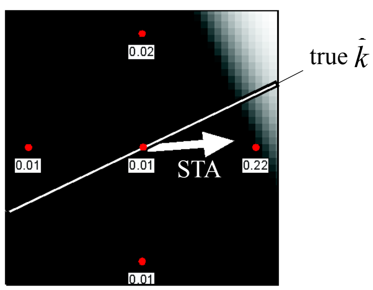
Sources of STA estimation error

- Finite data (convergence goes as 1/N)
- Non-spherical stimuli (estimator can be biased)
- Model failures. Examples:
  - symmetric nonlinearity (causes no change in STE mean)
  - response not captured by 1D linear projection
  - spike history dependence (non-Poisson)

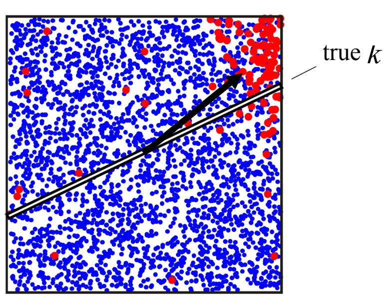
Variance behavior of STA



Example 1:
"sparse" noise



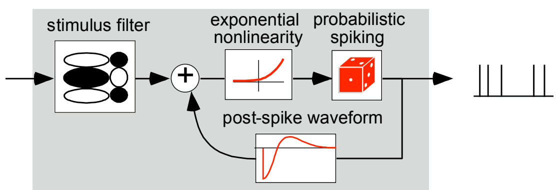
Example 2:
uniform noise



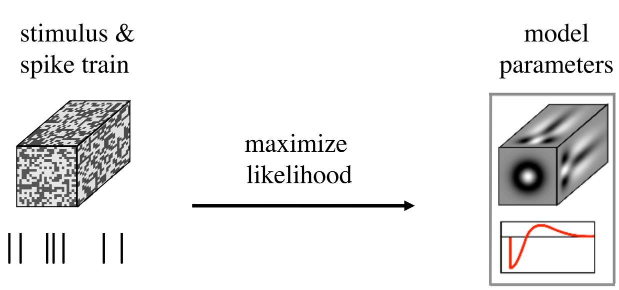
LNP model limitations

- Neural response depends on spike history
  => introduce spike history feedback
- Symmetric nonlinearities and/or multi-dimensional front-end (e.g., V1 complex cells)
  => spike-triggered covariance, subspace analyses
- White noise doesn't drive mid- to late-stage neurons well
  => cascade LNP on top of an "afferent" model

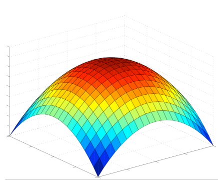
Recursive LNP

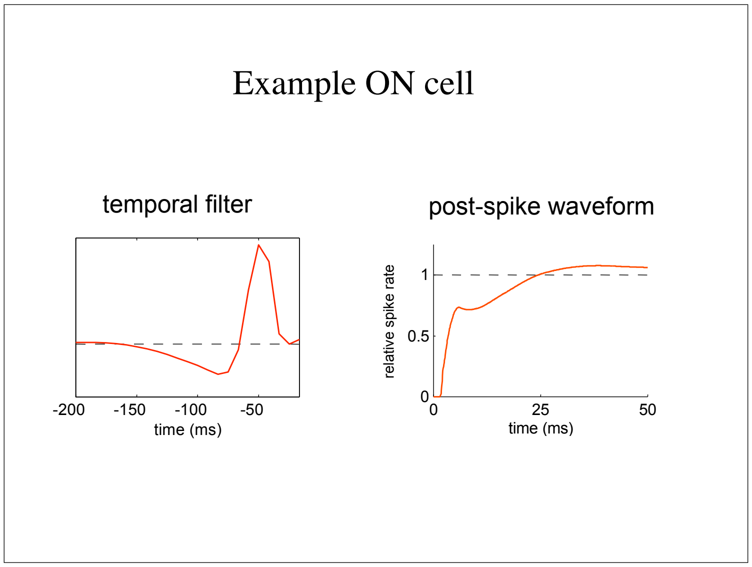


[Truccolo et al '05; Pillow et al '05]

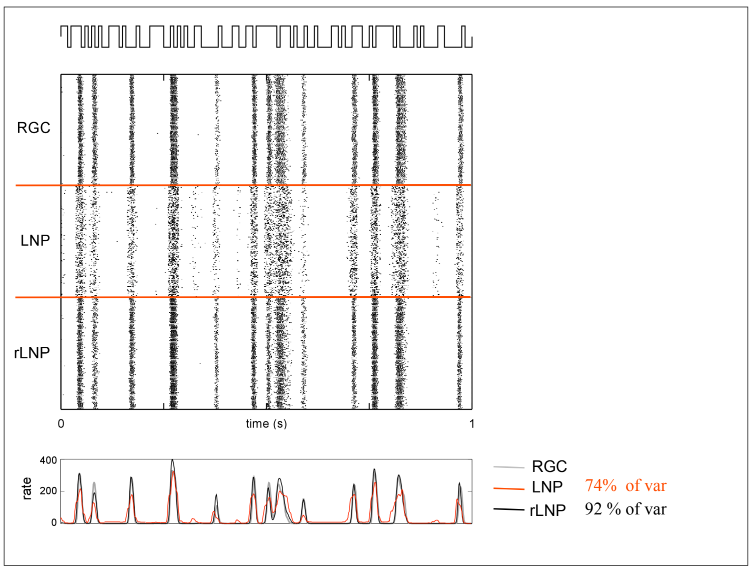


Critical: Likelihood function has no local maxima [Paninski 04]

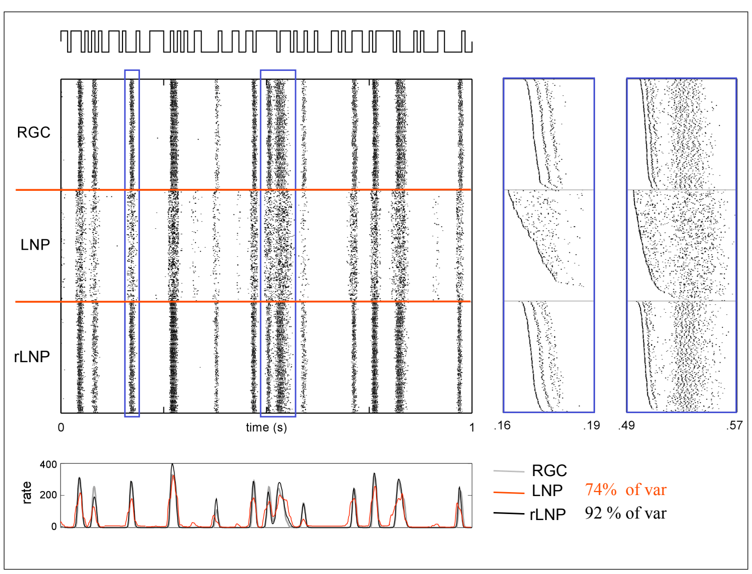




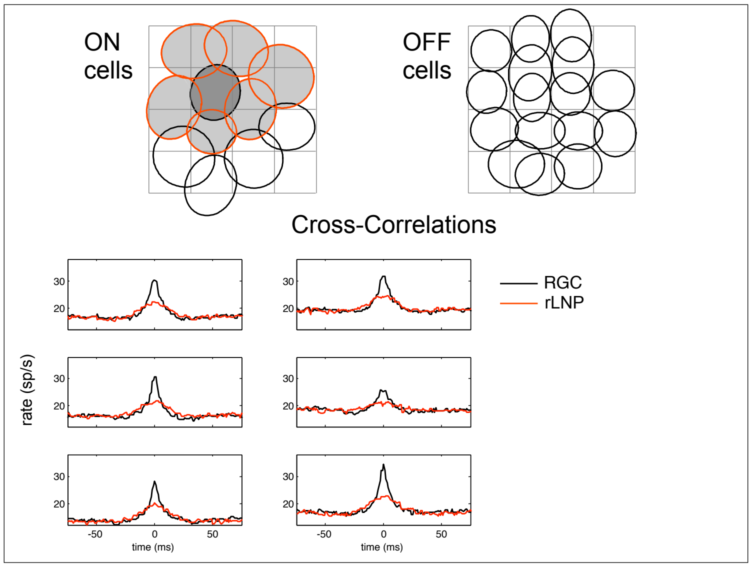
Example ON cell
temporal filter
-200
-150
-100
-50
time (ms)
post-spike waveform
relative spike rate
1
0.5
0
0
25
50
time (ms)

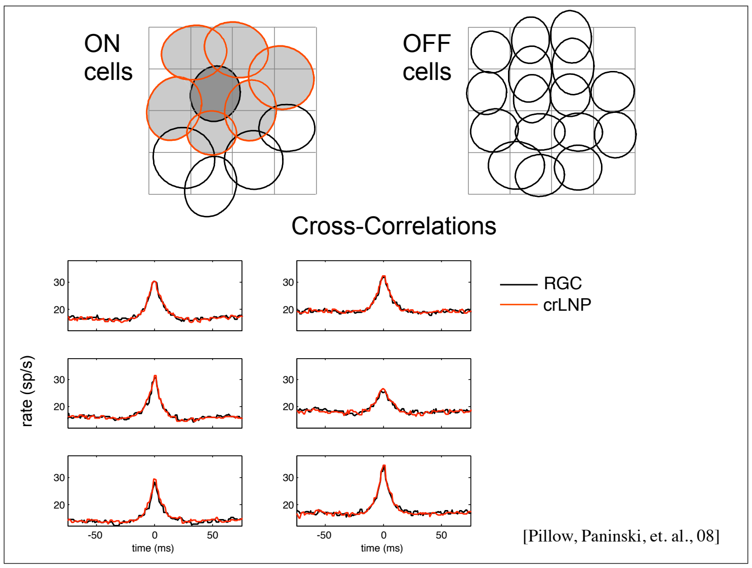


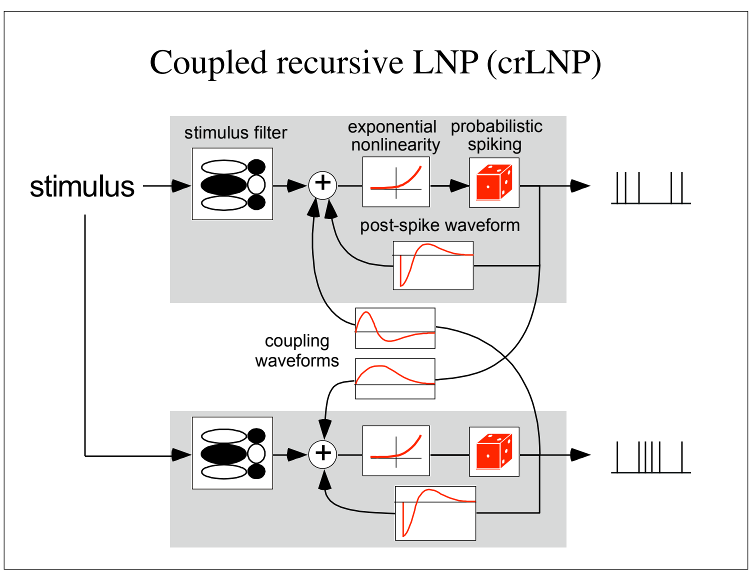
RGC
LNP
rLNP
0
time (s)
1
rate
400
200
0
RGC
LNP
rLNP
74% of var
92 % of var

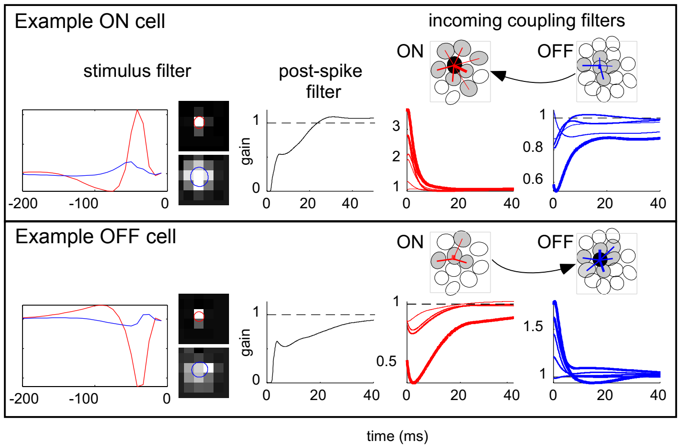


RGC
LNP
rLNP
0
time (s)
1
.16
.19
.49
.57
rate
400
200
0
RGC
LNP
rLNP
74% of var
92 % of var

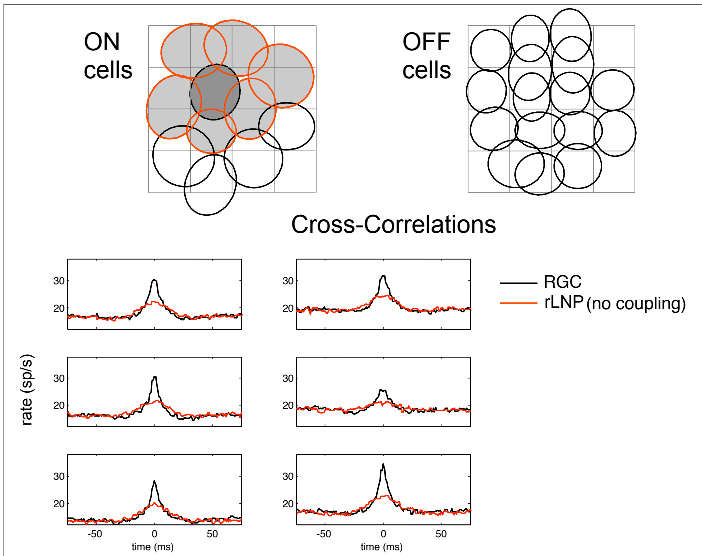

ON cells
OFF cells
Cross-Correlations
RGC
rLNP
rate (sp/s)
time (ms)


ON cells
OFF cells
Cross-Correlations
RGC
crLNP
rate (sp/s)
time (ms)
[Pillow, Paninski, et. al., 08]

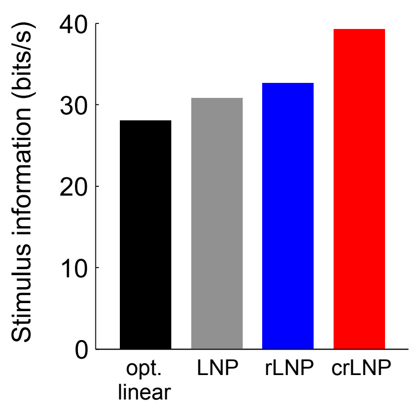

Coupled recursive LNP (crLNP)
stimulus
stimulus filter
exponential nonlinearity
probabilistic spiking
post-spike waveform
coupling waveforms



[Pillow, Paninski, et. al., 08]

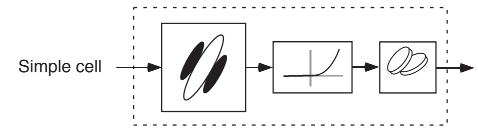


Decoding

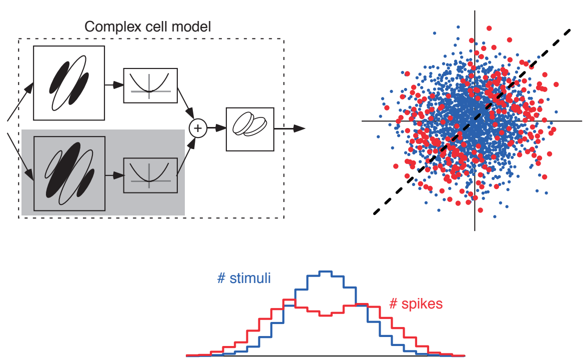


[Pillow, Paninski, et. al., 08]

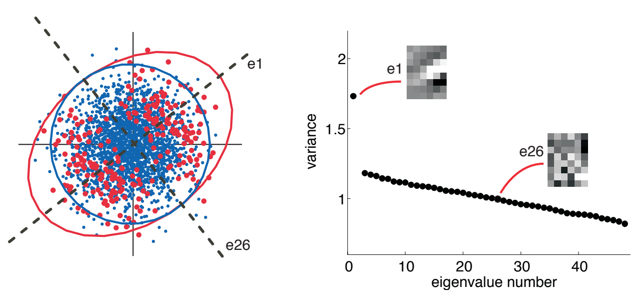
Classic V1 models



STA failure on complex cell

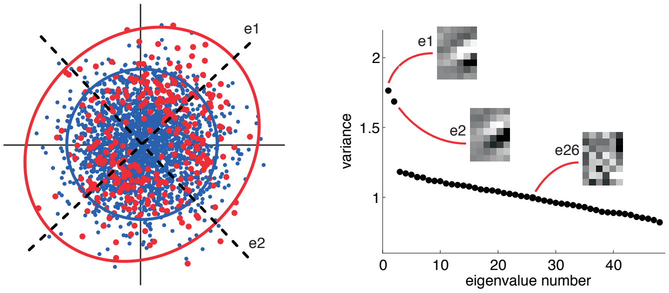


Spike-triggered covariance (STC)



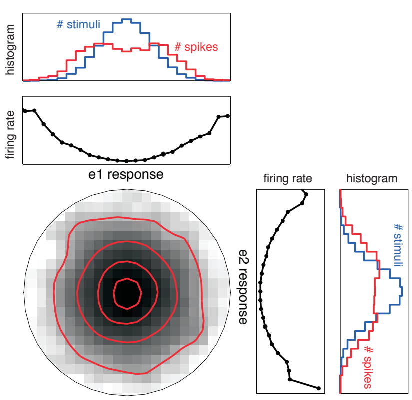
[Bialek '88; Brenner etal '00; Schwartz etal '01; Touryan and Dan '02; ...]

STC on complex cell (simulation)

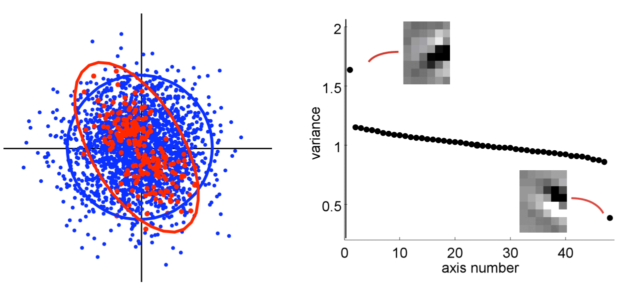


Use STC to find subspace that modulates response

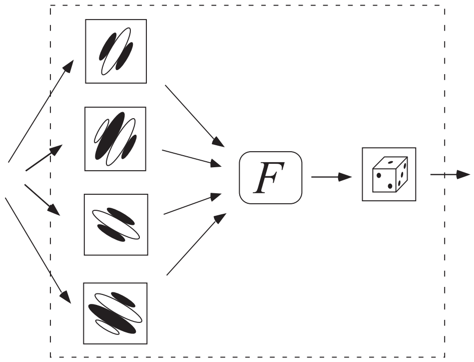
STC on complex cell (simulation)



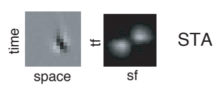
STC: suppressive filters



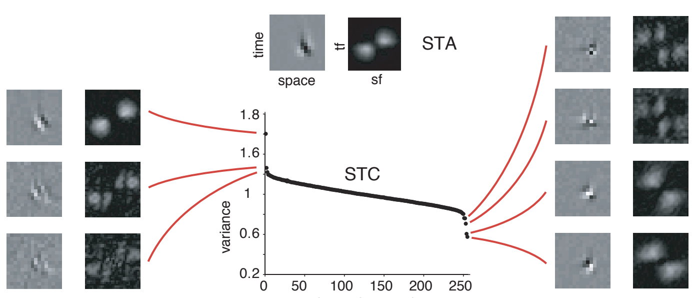
Subspace LNP model



V1 simple cell

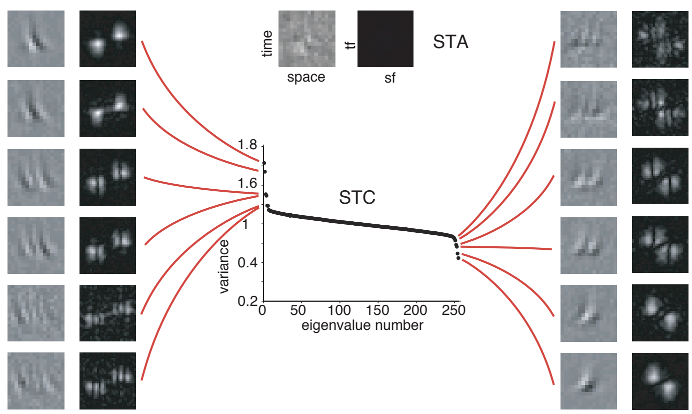


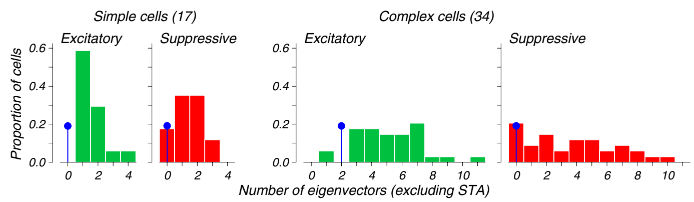
V1 simple cell

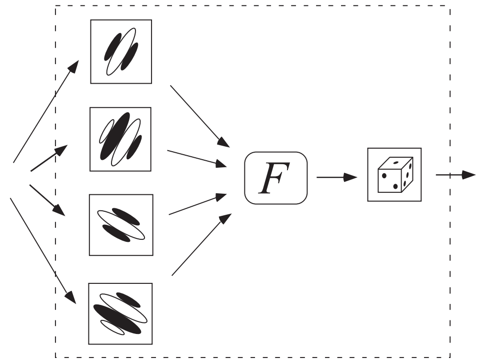


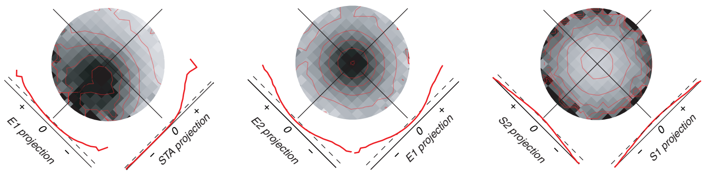
[Rust, Schwartz, et. al., 2005]

V1 complex cell

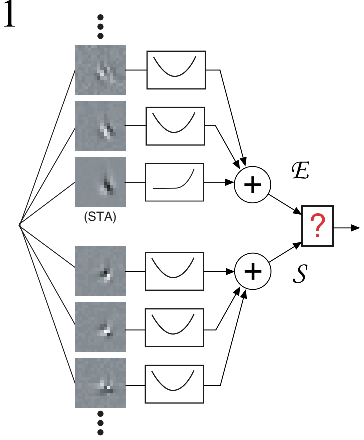






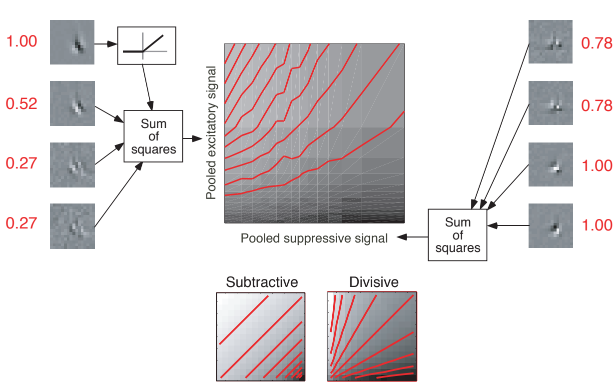


Generic V1 model

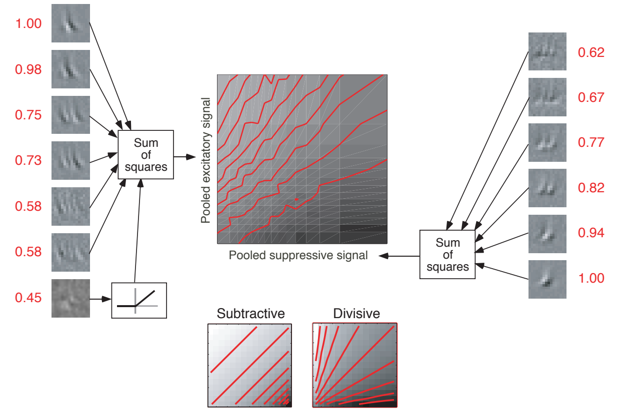


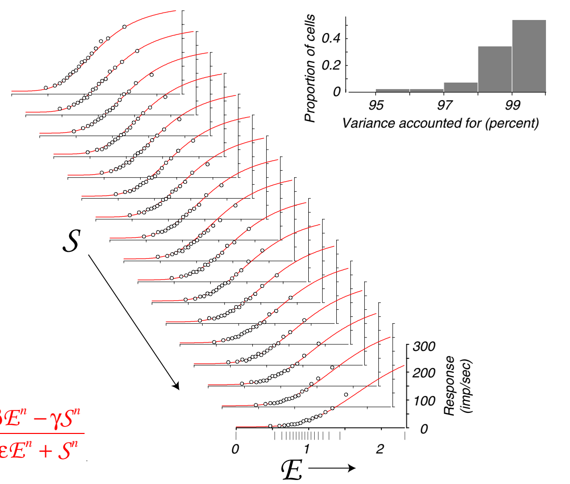
[Rust, Schwartz, et. al., 2005]

Simple cell



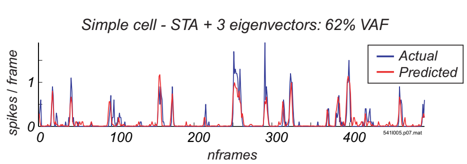
Complex cell

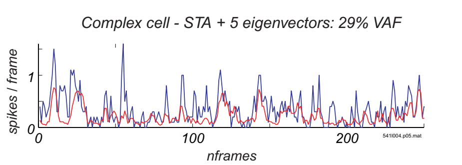




$$\frac{\alpha + \beta \mathcal{E}^n - \gamma \mathcal{S}^n}{\delta^n + \varepsilon \mathcal{E}^n + \mathcal{S}^n}$$

PSTH validation



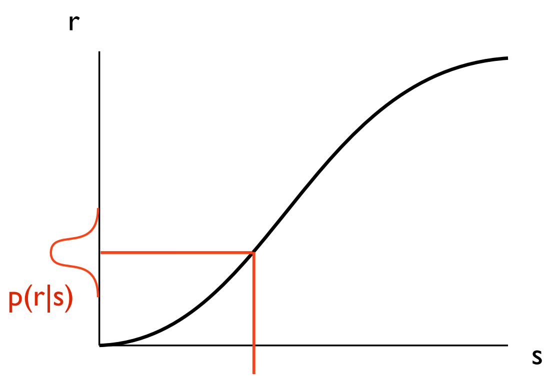


Failure of Poisson spiking assumption

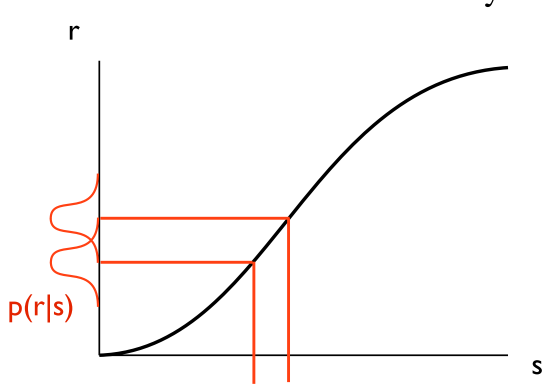
“Decoding” neural populations?

- Connecting neural response to behavior
- Engineering: Brain-Computer Interfaces
- Test/compare encoding models

Encoding determines discriminability

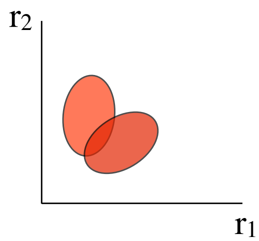


Probabilistic encoding model determines discriminability



Discriminability (d’) is (approximately) slope/stdev

Two neurons



Same fundamental issues as 1D case:

- Probabilistic encoding determines discriminability
- Intuitively, overlap is distance/spread
- For linear decoding: project onto discrimination axis

I. Simple/intuitive population decoding

- Linear? $\hat{s}(\vec{r}) = \sum_n r_n s_n$

  (simple, but usually doesn't work well)

- Winner-take-all $\hat{s}(\vec{r}) = s_m, \qquad m = \arg\max_n \{r_n\}$

  (simple, but discontinuous and noise-susceptible)

- Population vector [Georgopoulos et.al., 1986] $\hat{s}(\vec{r}) = \frac{\sum_n r_n s_n}{\sum_n r_n}$

  (also simple, more robust)

II. Statistically optimal decoding

- Maximum likelihood (ML) $\hat{s}(\vec{r}) = \arg\max_s p(\vec{r}|s)$

- Maximum a posteriori (MAP) $\hat{s}(\vec{r}) = \arg\max_s \; p(\vec{r}|s) \cdot p(s)$

- Minimum Mean Squared Error (MMSE), a.k.a. Bayes Least Squares (BLS) $\hat{s}(\vec{r}) = \mathbf{E}(s|\vec{r})$

ML decoding for a Poisson-spiking neural population

[Ma, Beck, Latham, Pouget, 2006; Jazayeri & Movshon, 2006]

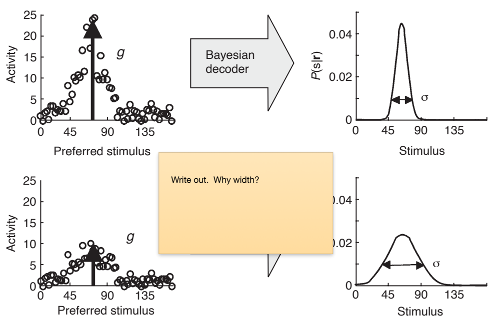
$$p(\vec{r}|s) = \prod_{n=1}^{N} \frac{h_n(s)^{r_n} \; e^{-h_n(s)}}{r_n!}$$

$$\log\left(p(\vec{r}|s)\right) = \sum_{n=1}^{N} r_n \log(h_n(s)) - h_n(s) - \log(r_n!)$$

If we assume $\sum_{n=1}^{N} h_n(s)$ is constant (i.e., tuning curves "tile" the space), this is a weighted sum of log tuning curves.

Special cases allow closed-form solutions:

- Gaussian tuning curves $h_n(s) = \exp\left(-(s-s_n)^2/2\sigma^2\right)$
- von Mises tuning curves $h_n(s) = \exp\left(\kappa \cos(s-s_n)\right)$



$$p(\theta\,|\,\vec{r}) \propto p(\vec{r}\,|\,\theta)p(\theta)$$

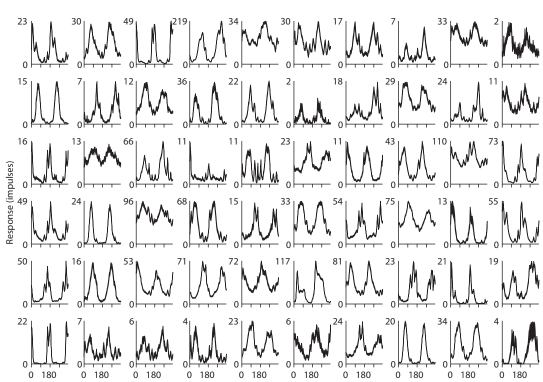
For independent Poisson firing rates: $p(\theta\,|\,\vec{r}) \propto \prod_i \frac{e^{-f_i(\theta)} f_i(\theta)^{r_i}}{r_i!} p(\theta)$

Integration by summing spikes!

[Ma, Beck, Latham & Pouget, 06]

Population Decoding

The data: tuning curves f_i



[Graf, Kohn, Jazayeri & Movshon, 11]

Comparing population decoders

1) The ML decoder, assuming independent Poisson responses (the PID):

$$\log L(\theta) = \log\left(\prod_{i=1}^{N} p(r_i \mid \theta)\right) = \sum_{i=1}^{N} \log\left(\frac{f_i(\theta)^{r_i}}{r_i!}\exp(-f_i(\theta))\right)$$

$$= \sum_{i=1}^{N} \log(f_i(\theta))r_i - \sum_{i=1}^{N} f_i(\theta) - \sum_{i=1}^{N} \log(r_i!) = \sum_{i=1}^{N} W_i(\theta)r_i + B(\theta)$$

For discrimination between two values, likelihood ratio is *linear* function of responses:

$$\log LR(\theta_1, \theta_2) = \log\left(\frac{L(\theta_1)}{L(\theta_2)}\right) = \log L(\theta_1) - \log L(\theta_2)$$

$$= \sum_{i=1}^{N} [W_i(\theta_1) - W_i(\theta_2)]r_i + [B(\theta_1) - B(\theta_2)]$$

$$= \sum_{i=1}^{N} w_i(\theta_1, \theta_2)r_i + b(\theta_1, \theta_2)$$

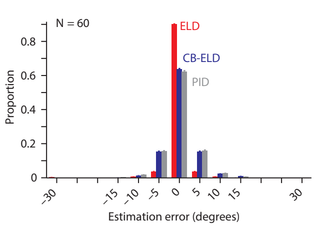
[Graf, Kohn, Jazayeri & Movshon, 11]

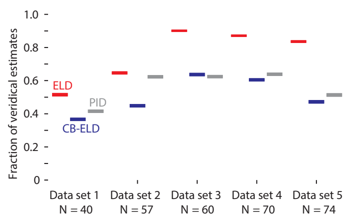
Comparing population decoders

2) Alternatively, compute an SVM on the measured response vectors for each orientation, the empirical linear decoder (ELD):

$$y(\theta_1, \theta_2) = \sum_{i=1}^{N} w_i(\theta_1, \theta_2)r_i + b(\theta_1, \theta_2) \equiv \log LR(\theta_1, \theta_2)$$

3) For each neuron and orientation, shuffle the responses across trials and train a new SVM, the correlation-blind empirical linear decoder (CB-ELD).





[Graf, Kohn, Jazayeri & Movshon, 11]

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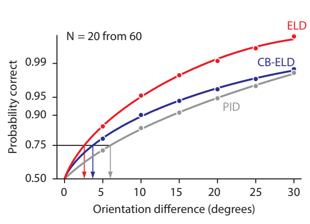
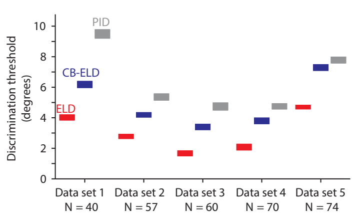
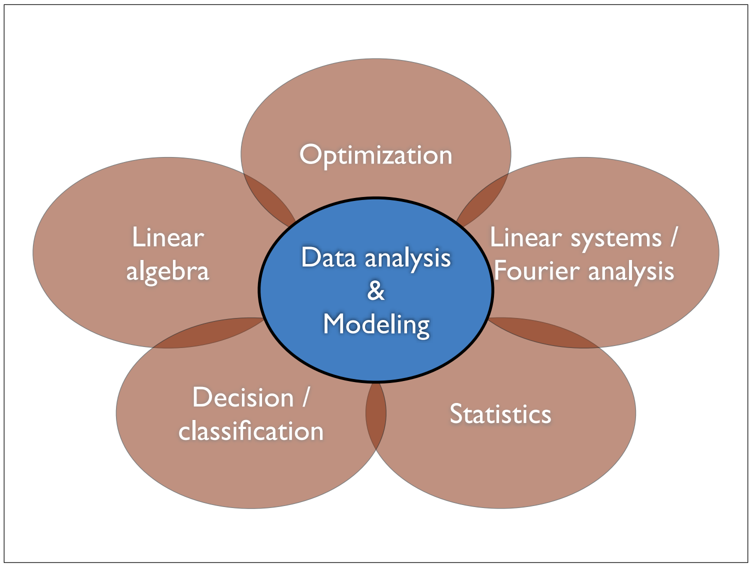
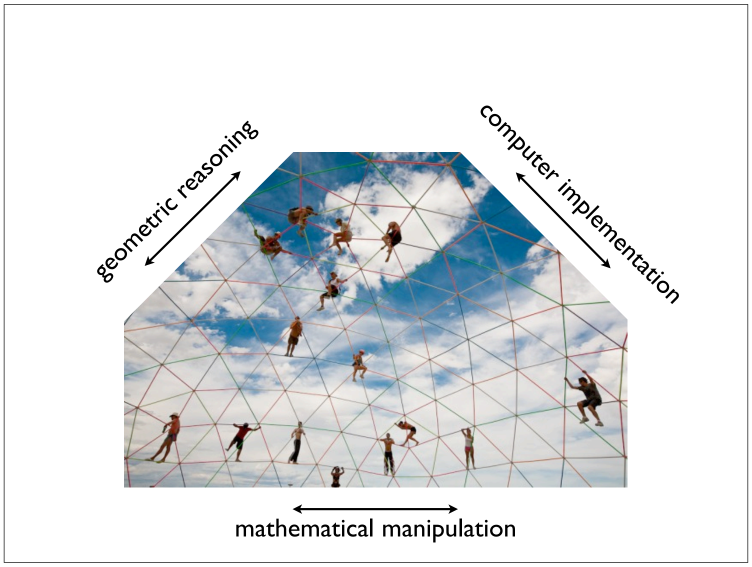




[Graf, Kohn, Jazayeri & Movshon, 11]



Optimization
Linear algebra
Data analysis & Modeling
Linear systems / Fourier analysis
Decision / classification
Statistics



geometric reasoning
computer implementation
mathematical manipulation