Mathematical Tools
for Neural and Cognitive Science

Fall semester, 2023

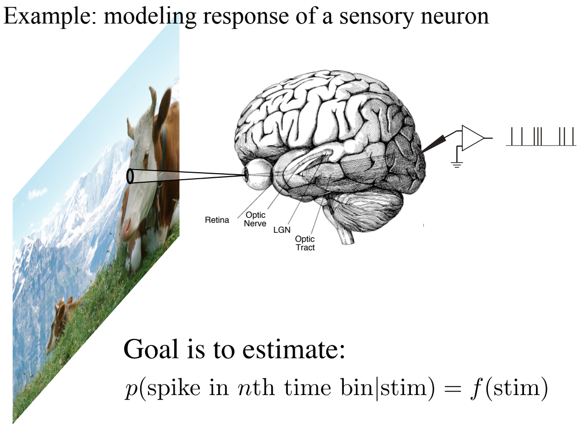
Section 6a:

Fitting simple neural models

## 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

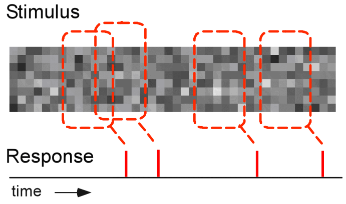



Goal is to estimate:

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

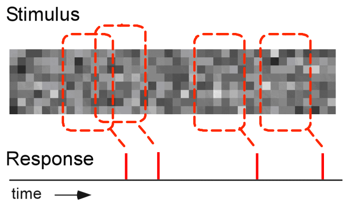
# Geometric view

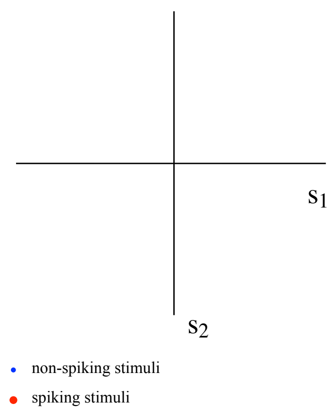
1D stimulus over time
(e.g., flickering bars)



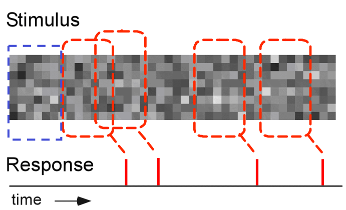

• 8 x 6 stimulus block
= 48-dimensional vector

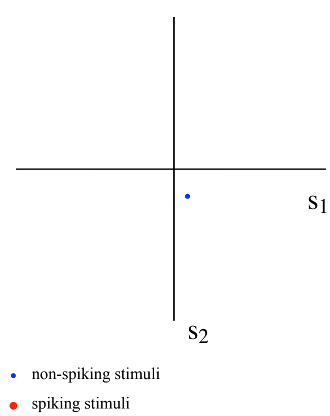
# Geometric picture

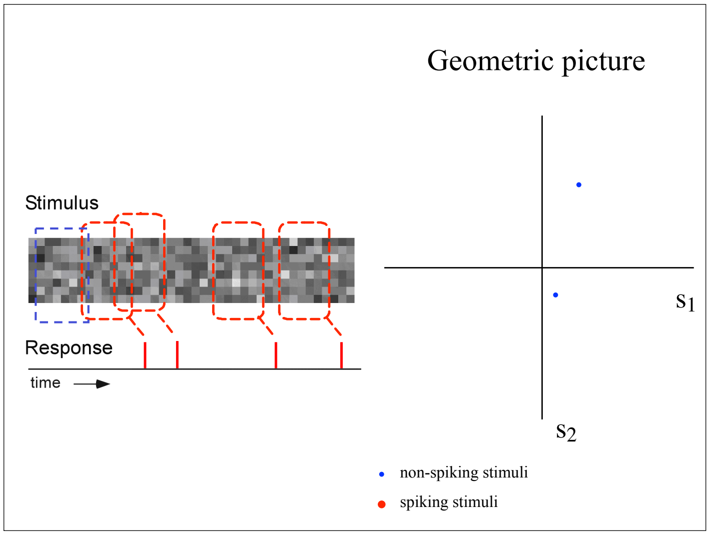


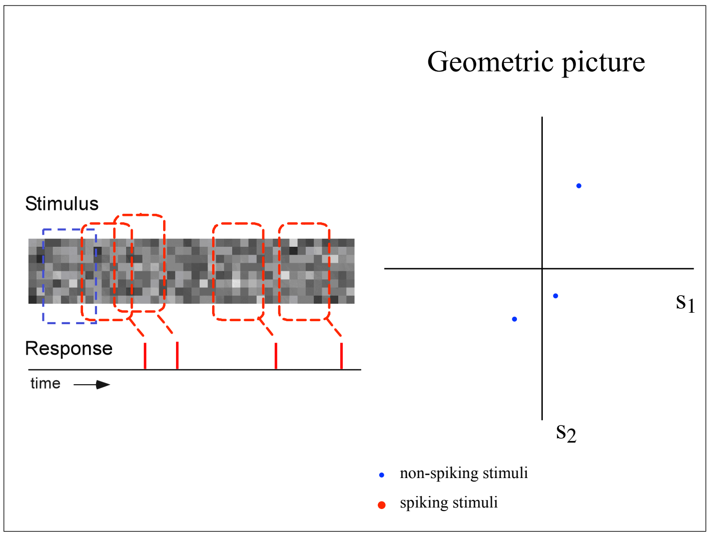




# Geometric picture




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


Geometric picture
Stimulus
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$s_1$
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non-spiking stimuli
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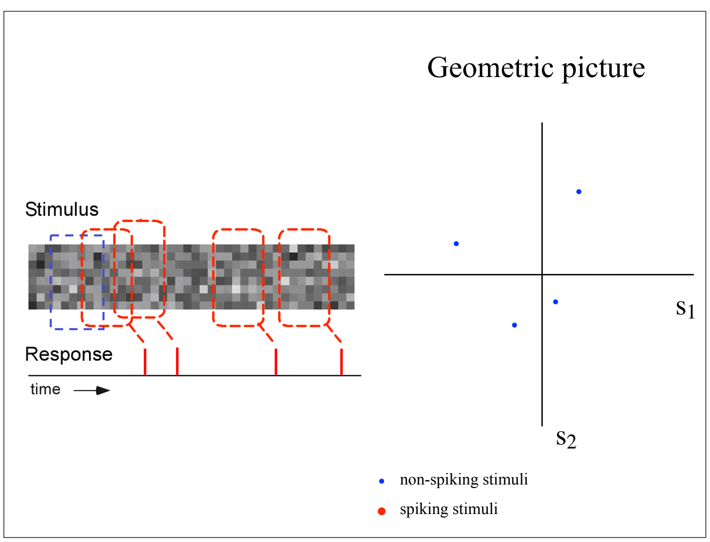
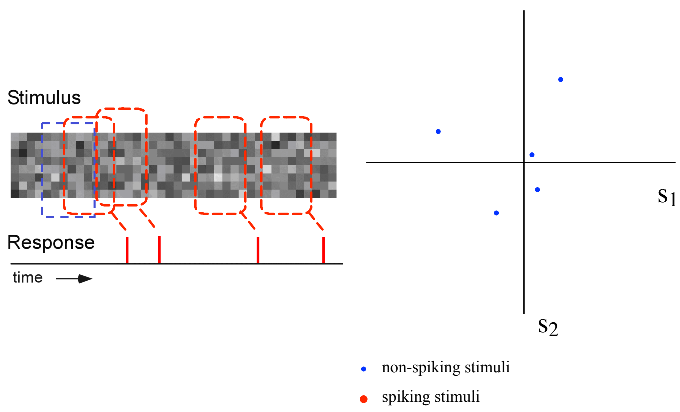
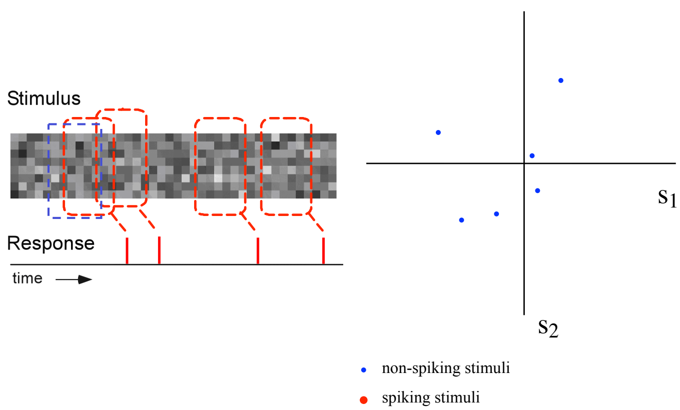

Geometric picture
Stimulus
Response
time
$s_1$
$s_2$
non-spiking stimuli
spiking stimuli

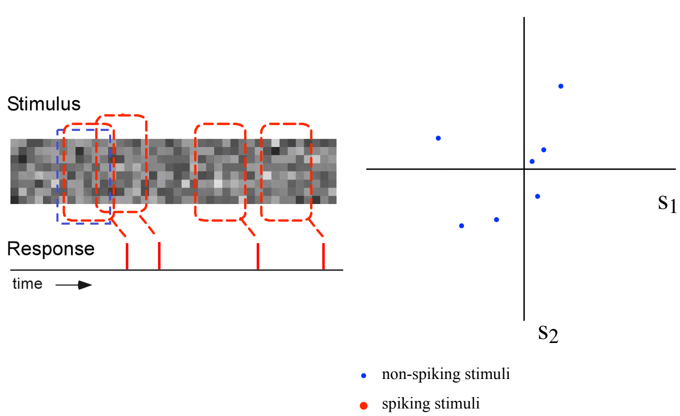
## Geometric picture



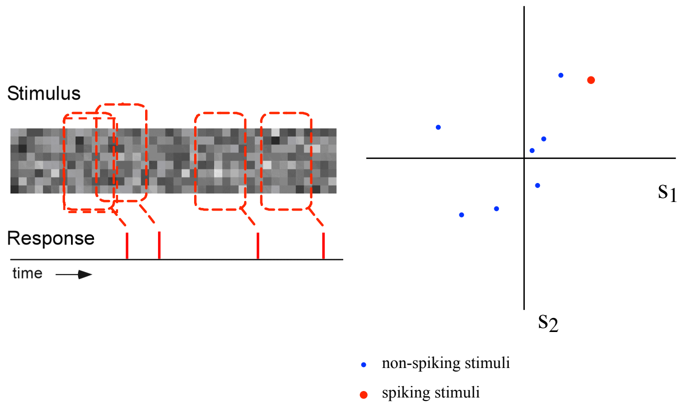

## Geometric picture



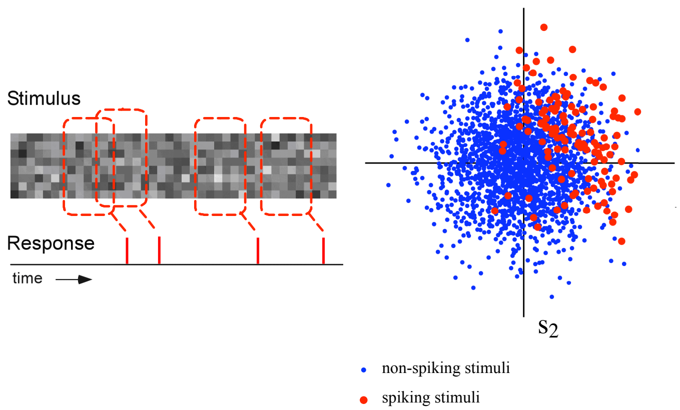

## Geometric picture



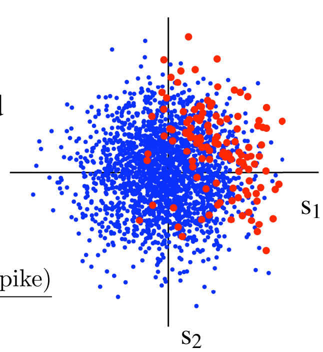
## Geometric picture




## 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:



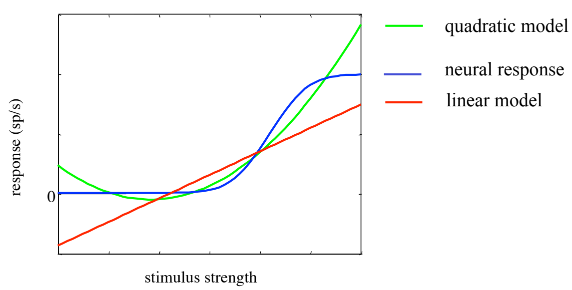

$$P(\text{spike}|\vec{s}) = \frac{P(\vec{s}\ |\text{spike})P(\text{spike})}{P(\vec{s})}$$

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

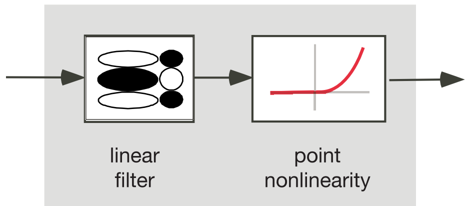
## Some tractable model options

- 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

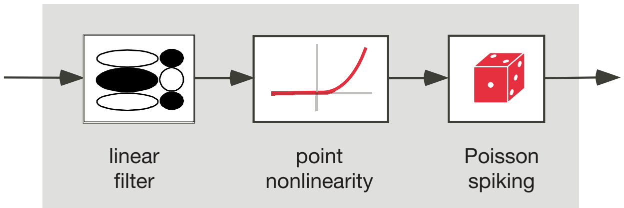



## Example: LN cascade model




- 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



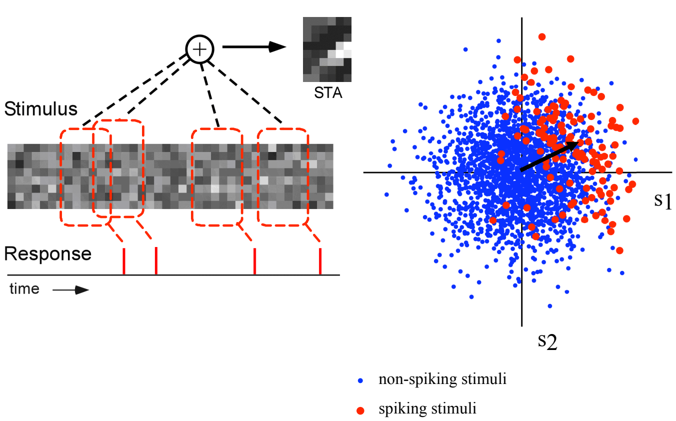

- Simplest descriptive spiking model
- Easily fit to (extracellular) data
- Descriptive, and interpretable (although *not* mechanistic)

# Simple LNP fitting

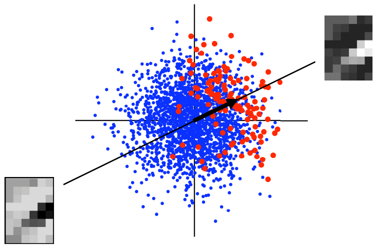
- Assuming:
  - stochastic stimuli, spherically distributed
  - average of spike-triggered ensemble (STA) is shifted from that of raw ensemble
- The STA (i.e., linear regression!) gives an **unbiased** estimate of w (for any f). *[on board]*
- For exponential f, this is the ML estimate! *[on board]*

[Bussgang 52; de Boer & Kuyper 68]

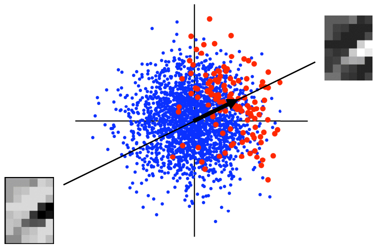
## Computing the STA



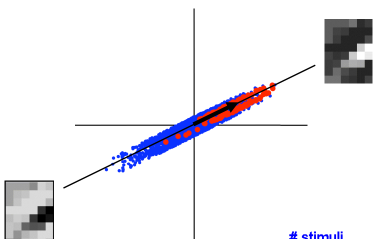
## STA corresponds to a “direction” in stimulus space



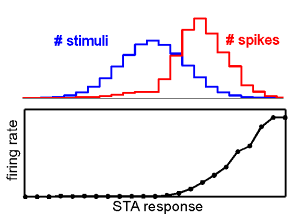
## Projecting onto the STA



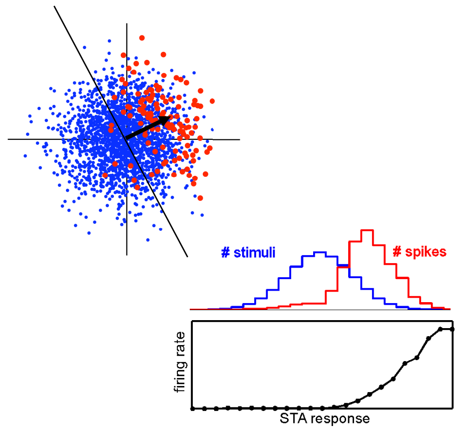
## Solving for nonparametric nonlinearity



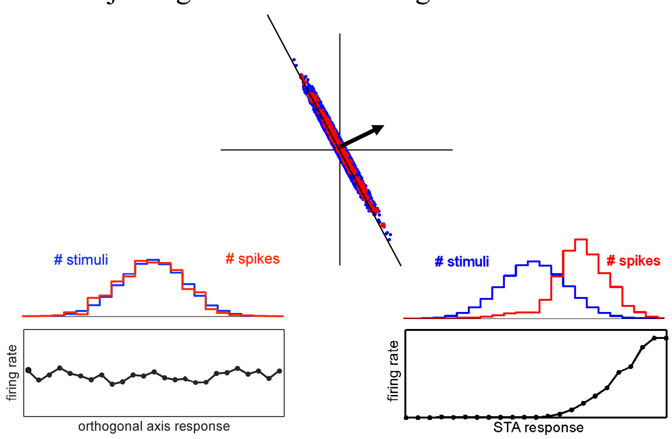
$$P(\text{spike}|\vec{s}) = \frac{P(\vec{s}\ |\text{spike})P(\text{spike})}{P(\vec{s})}$$



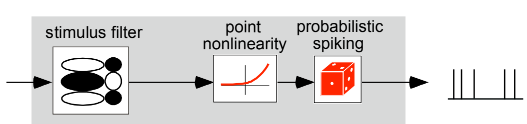
## Projecting onto an axis orthogonal to the STA

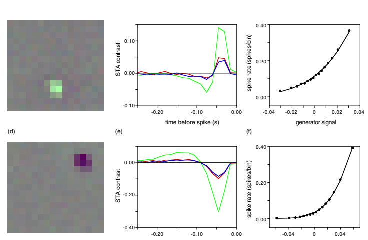



## Projecting onto an axis orthogonal to the STA

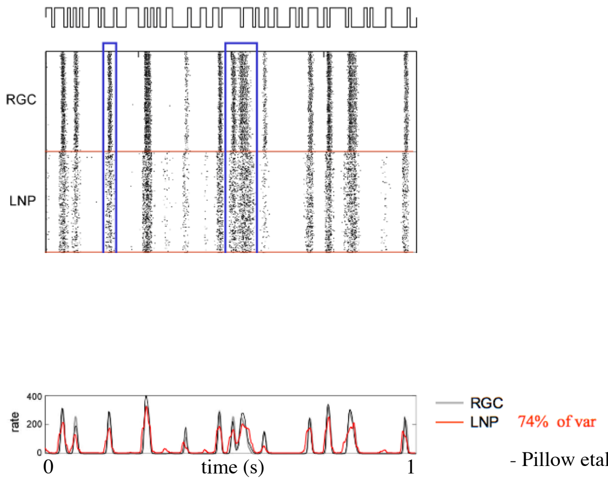



## LNP model, fit to retinal ganglion cells



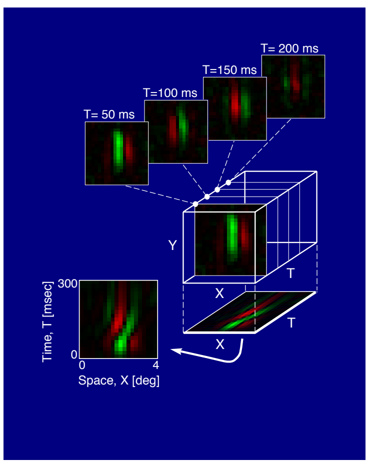




[Chichilnisky & Kalmer, 2002]

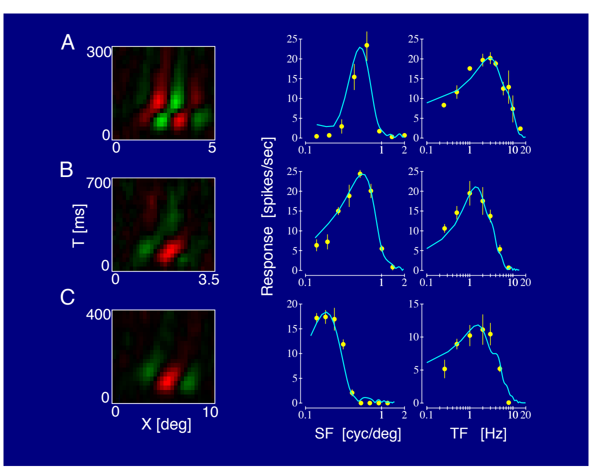



- Pillow etal, 2004

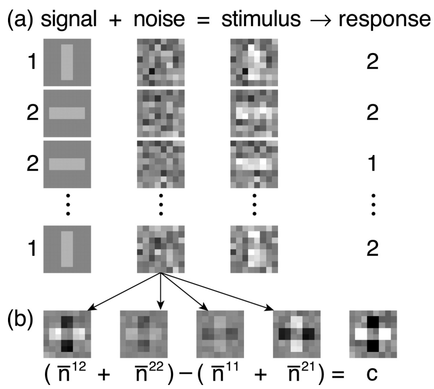
V1
simple
cell




- Ozhawa, etal

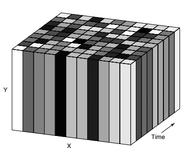


Psychophysical “Classification Image”

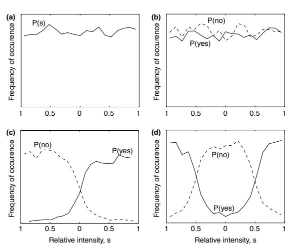


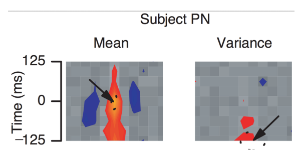

Murray R F J Vis 2011;11:2

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

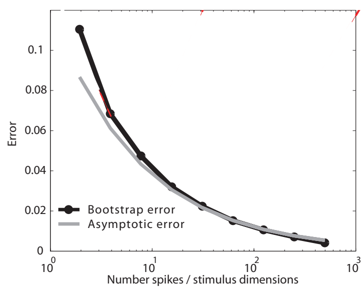
$(\vec{k} \cdot \vec{x}(t))^\alpha, \quad 1 < \alpha < 2$

[Paninski, ’04]

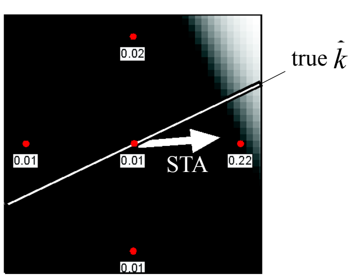
# Sources of STA estimation error

- Finite data (convergence goes as 1/N)
- Non-spherical stimuli (estimator can be biased)
- Model failures

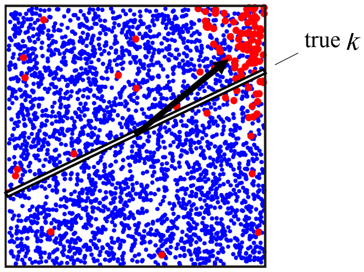
# Variance behavior of STA




Example 1:
"sparse" noise



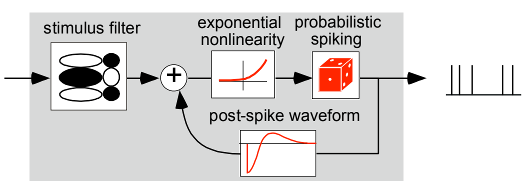
Example 2:
uniform noise




## LNP model failures (& solutions)

- 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

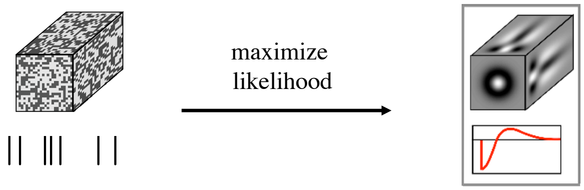



[Truccolo et al '05; Pillow et al '05]

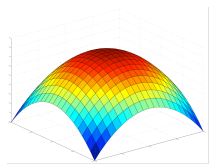
stimulus & spike train

maximize likelihood

model parameters

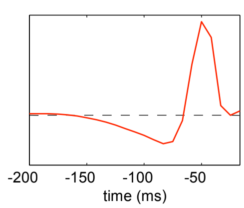


Critical: Likelihood function has no local maxima [Paninski 04]

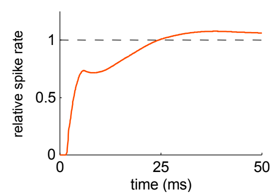


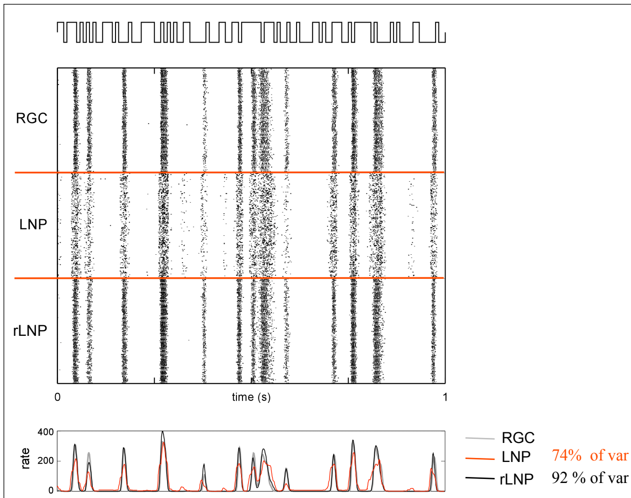
# Example ON cell

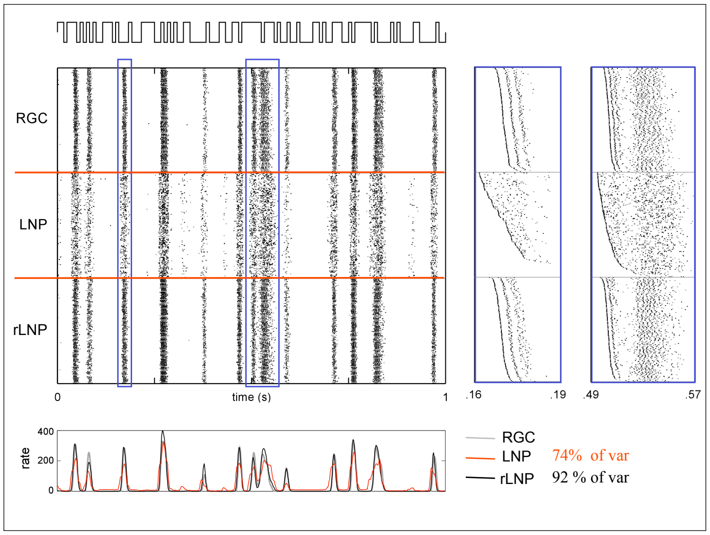
temporal filter

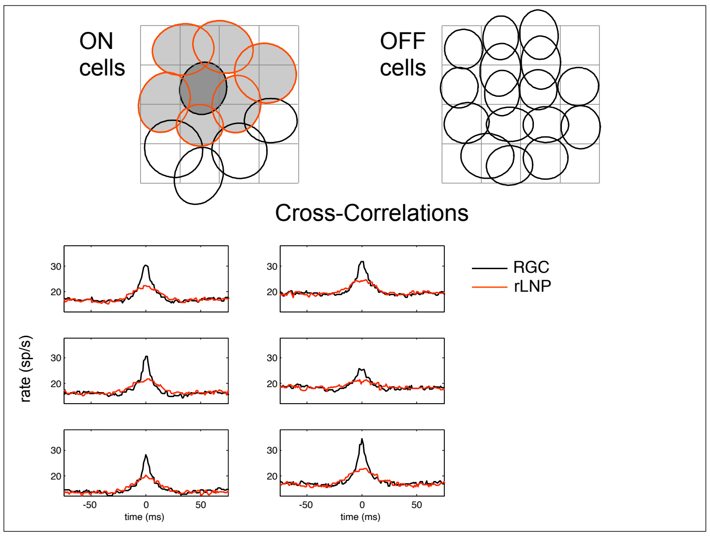


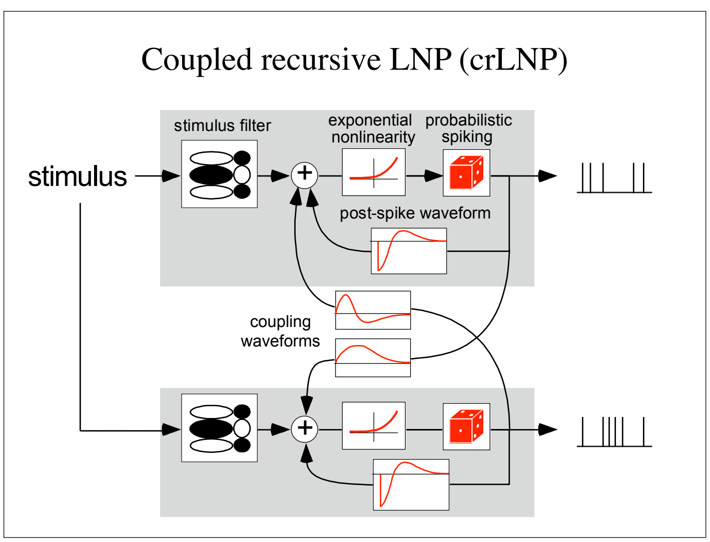

post-spike waveform

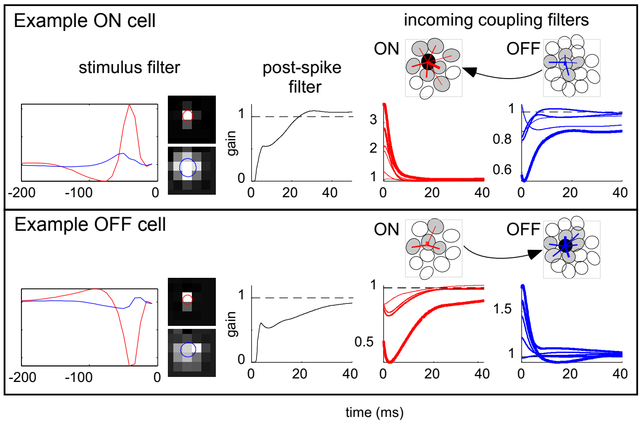


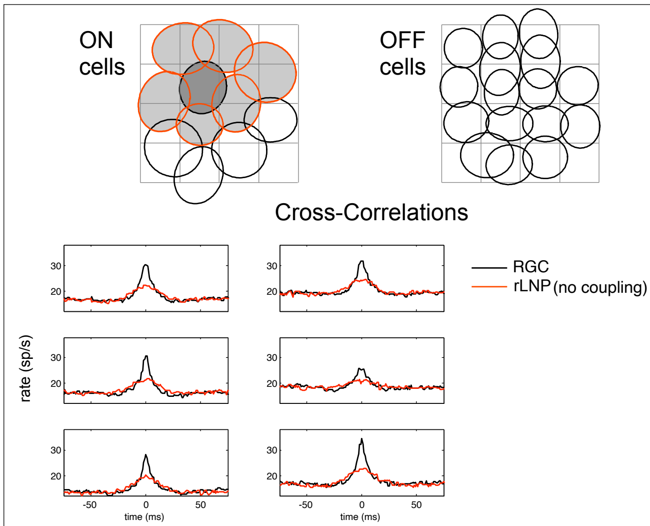

RGC
LNP
rLNP
0
time (s)
1
.16
.19
.49
.57
rate
400
200
0
RGC
LNP
rLNP
74% of var
92 % of var

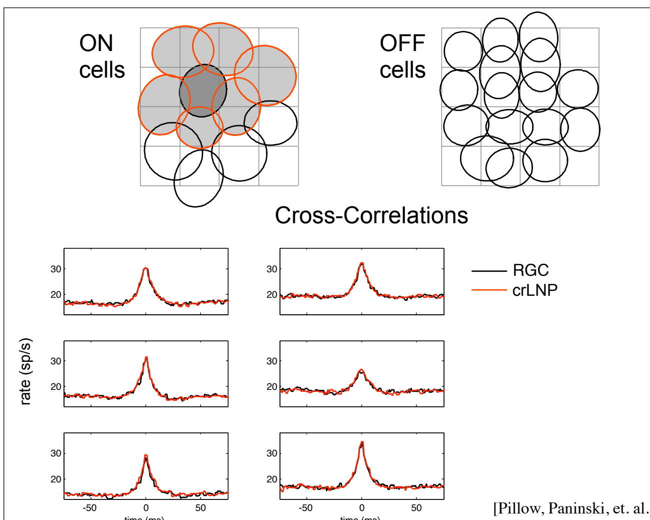

ON cells
OFF cells
Cross-Correlations
RGC
rLNP
rate (sp/s)
30
20
-50
0
50
time (ms)


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



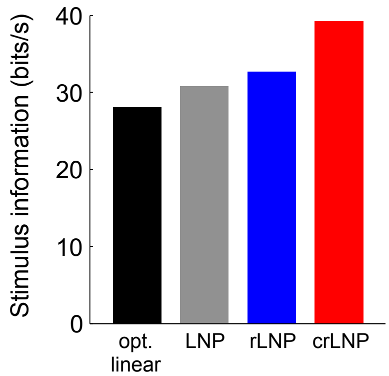

[Pillow, Paninski, et. al., 08]



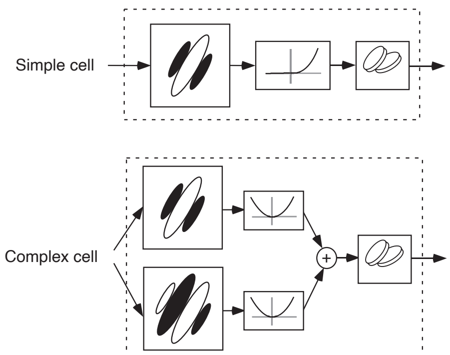

[Pillow, Paninski, et. al., 08]

## Decoding



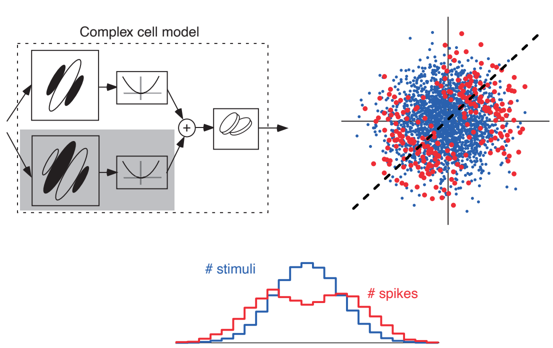

[Pillow, Paninski, et. al., 08]

## Classic V1 models

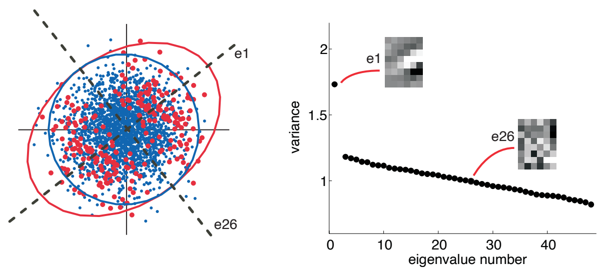



"Energy model" (Adelson/Bergen, 1985)

## STA failure on complex cell

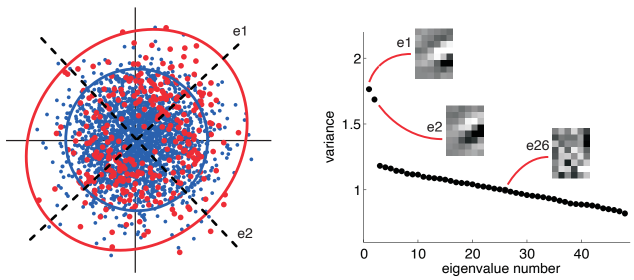


## Spike-triggered covariance (STC)



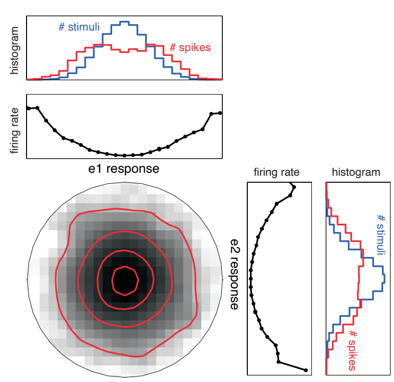

[Bialek ‘88; Brenner etal ‘00; Schwartz etal ‘01; Touryan and Dan ‘02; ...]

## STC on complex cell (simulation)

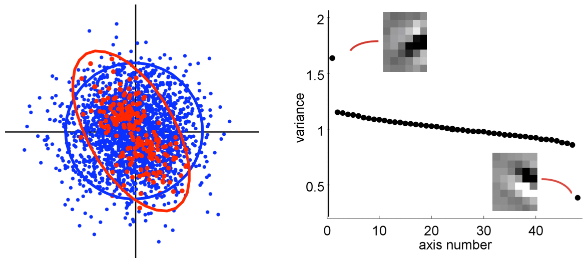



Use STC to find subspace that modulates response

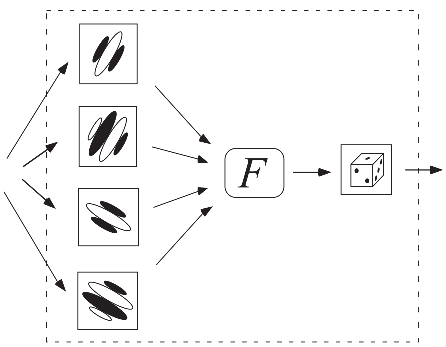
## STC on complex cell (simulation)



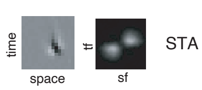
## STC: suppressive filters




## Subspace LNP model

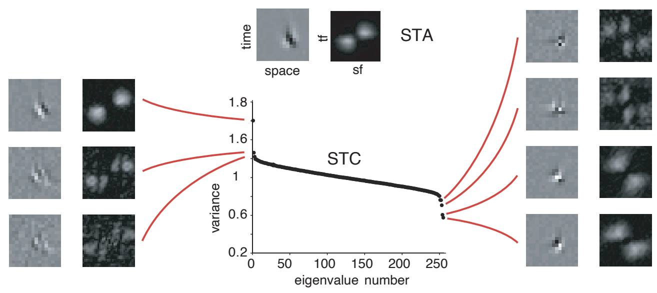



## V1 simple cell



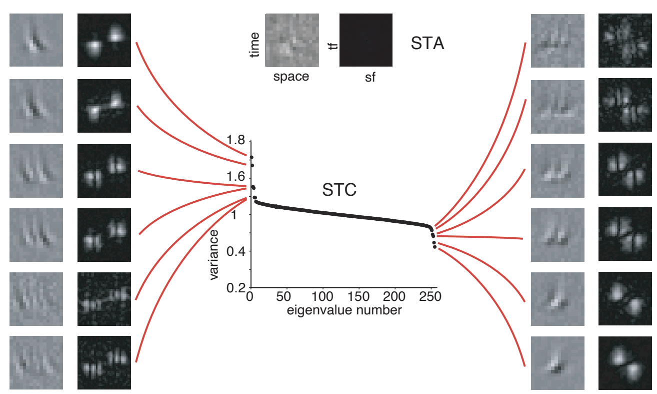

[Rust, Schwartz, et. al., 2005]

# V1 simple cell

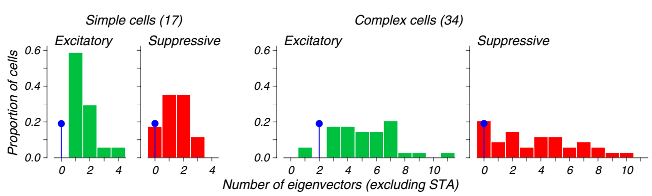



[Rust, Schwartz, et. al., 2005]

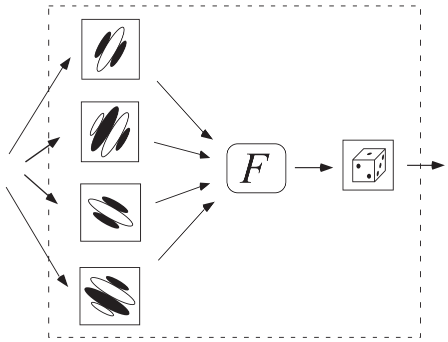
# V1 complex cell

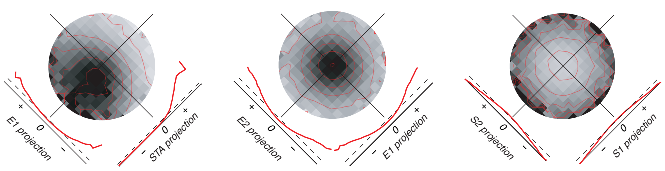



[Rust, Schwartz, et. al., 2005]

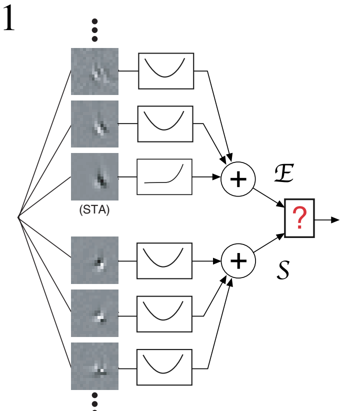



[Rust, Schwartz, et. al., 2005]



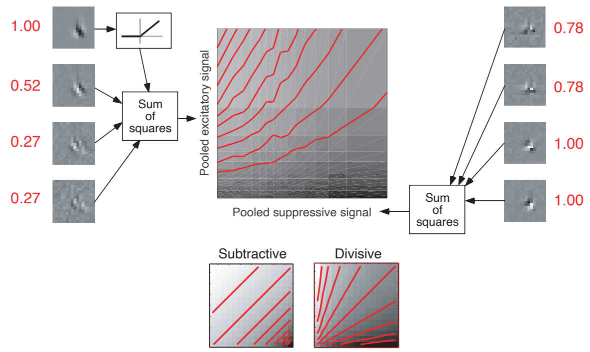




# Generic V1 model



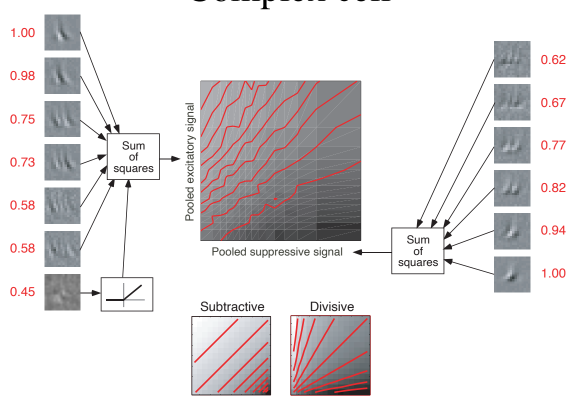

[Rust, Schwartz, et. al., 2005]

# Simple cell

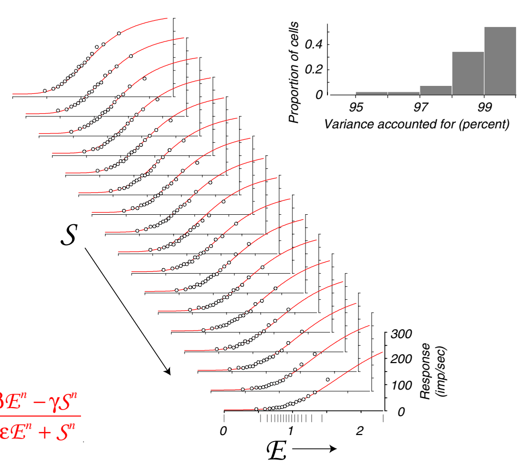



[Rust, Schwartz, et. al., 2005]

# Complex cell



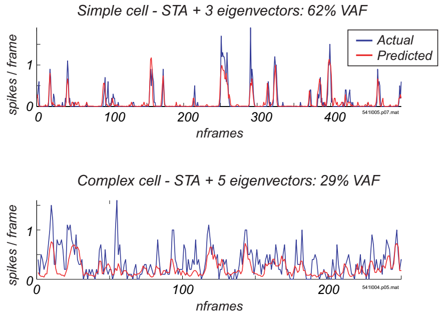

[Rust, Schwartz, et. al., 2005]




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

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

# PSTH validation

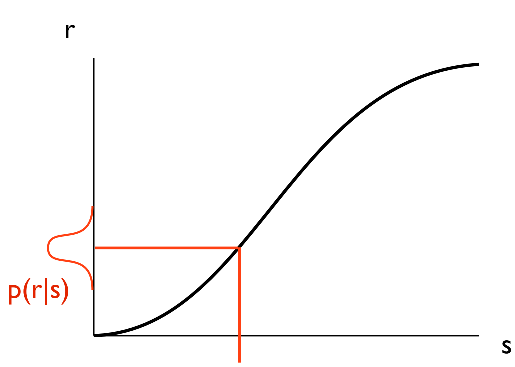



Failure of Poisson spiking assumption

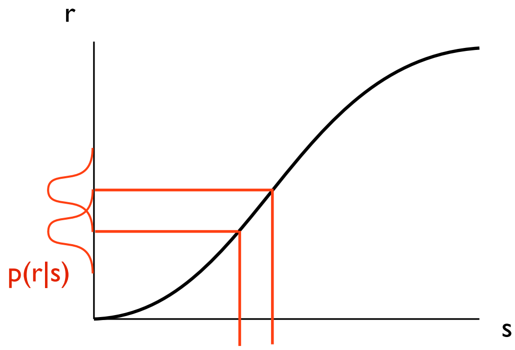
# "Decoding" neural populations?

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

# Encoding determines discriminability

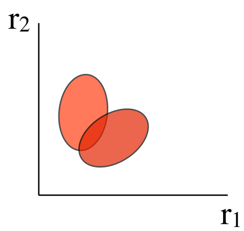


## Probabilistic encoding model determines discriminability




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]

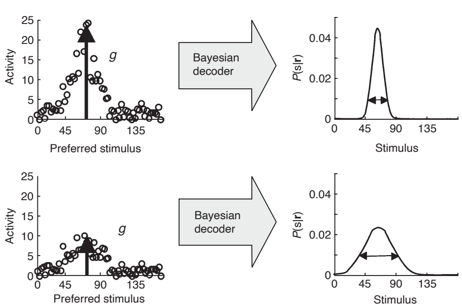
$$p(\vec{r}|s) = \prod_{n=1}^{N} \frac{h_n(s)^{r_n} \; e^{-h_n(s)}}{r_n!}$$

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

If $\sum_{n=1}^{N} h_n(s)$ is constant (i.e., tuning curves "tile"), just minimize the response-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 $h_n(s) = \exp\left(\kappa \cos(s - s_n)\right)$

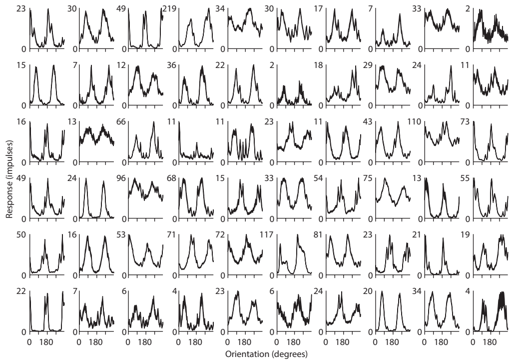



$$\hat{s}(\vec{r}) = \frac{\sum_n r_n s_n}{\sum_n r_n} \qquad \hat{\sigma}(\vec{r}) = \frac{\sum_n r_n}{\sigma}$$

[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):

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

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

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

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

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

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

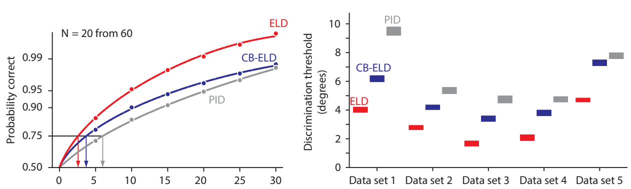
[Graf, Kohn, Jazayeri & Movshon, 11]

# Comparing population decoders

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

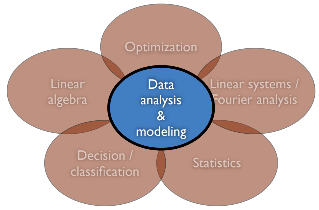
$$y(\theta_1, \theta_2) = \sum_{i=1}^{N} w_i(\theta_1, \theta_2)r_i + b(\theta_1, \theta_2)$$

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]

## Where we've been…




- Linear algebra / linear systems
  - Ex: Trichromacy
- Least squares
  - regression / PCA
- Linear shift-invariant systems
  - convolution / Fourier transforms
  - Ex: Auditory filtering
- Summary statistics - dispersion, central tendency
- Statistical inference
  - estimation, bias, variance, convergence
  - maximum likelihood estimator (MLE), MAP, Bayes
  - Ex: signal detection theory
  - Classification, clustering
- Model fitting
  - model comparison, overfitting, regularization, cross-validation
  - Ex: fitting an LNP model
  - Ex: population decoding