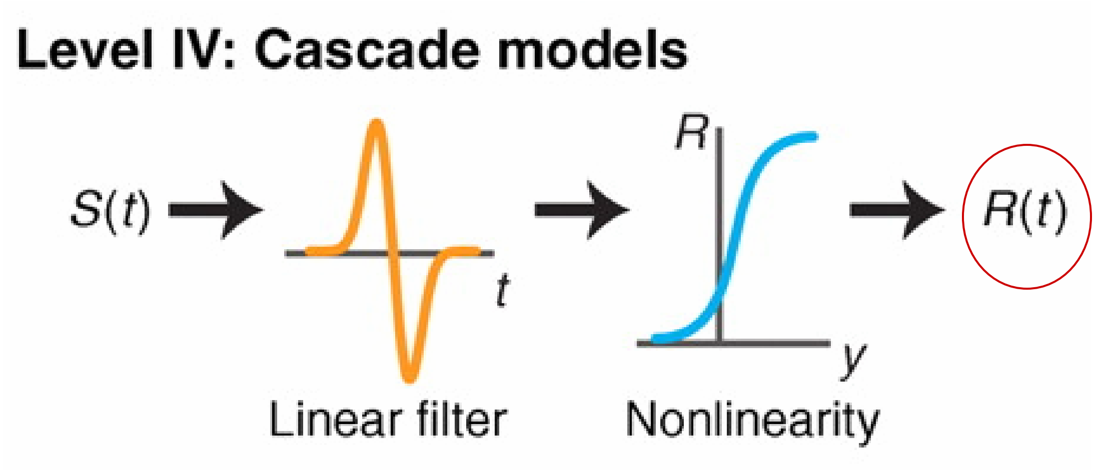
BME 665/565

Rate Codes and Cascade models

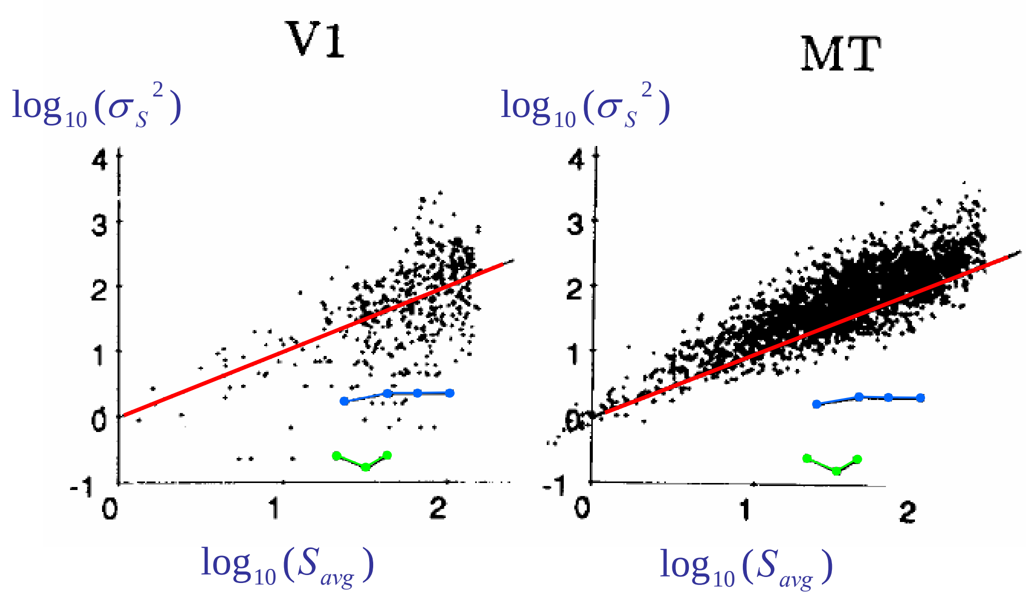
Cascade Models: Understanding the response to stimuli



Firing rates of neurons

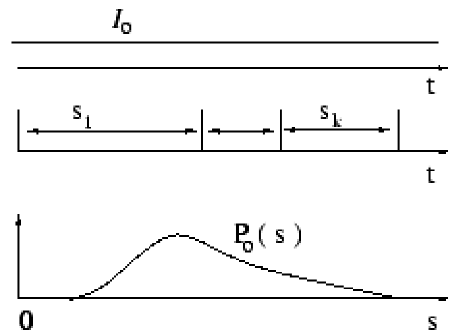
- Last time we considered the firing rate as a Poisson process
  - Clearly, not all neurons exhibit such firing behavior, nor do they exhibit such behavior all the time
  - In fact, many neurons show variability greater than than predicted by a Poisson model

Can we characterize the firing rate of specific neurons based on empirical data?



Spike-count rates

- Again, treat action potentials as a series of n spikes occurring at times t_i *:*



- Then the spike sequence can be considered a series of Dirac functions:

$$\rho(t) = \sum_{i=1}^{n} \delta(t - t_i) \qquad \text{note:} \qquad \int d\tau \rho(\tau) = n$$

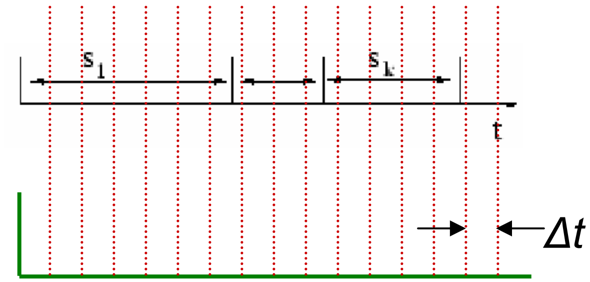
- So, the spike-count rate r for an interval T is given by:

$$r = \frac{n}{T} = \frac{1}{T} \int_0^T d\tau \rho(\tau)$$

Note: this is not time-dependent

Time-dependent firing rate

- If the rate changes over time, we can estimate it by looking at shorter intervals *Δt*

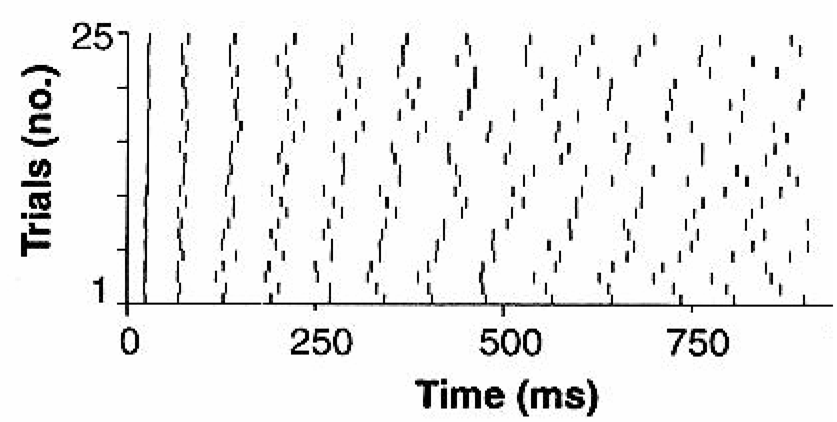


$$r(t) = \frac{1}{\Delta t} \int_{t}^{t+\Delta t} d\tau \, \rho(\tau)$$

- However, for sufficiently short *Δt*, there will likely be only 1 or 0 spikes – i.e. only 2 possible firing rates

Time-dependent firing rate

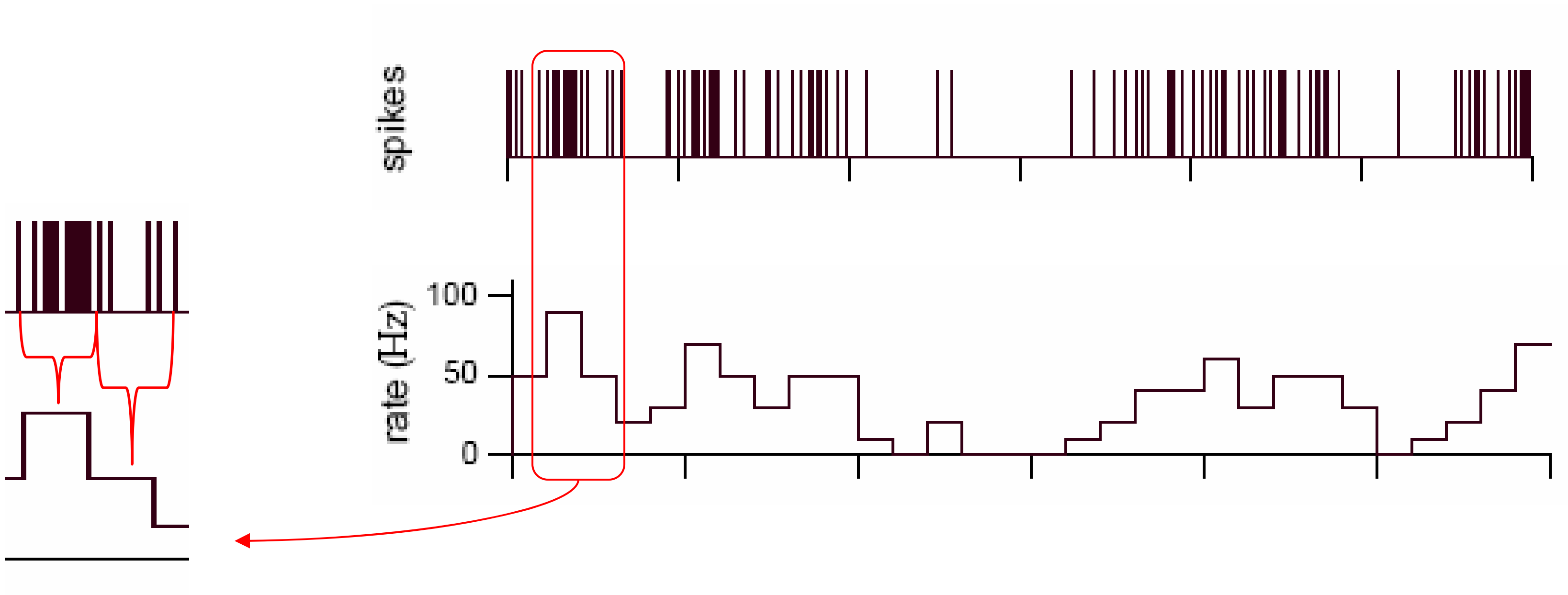
- Alternative: determine the time-dependent firing rate by averaging over trials



$$r(t) = \frac{1}{\Delta t} \int_{t}^{t+\Delta t} d\tau \langle \rho(\tau) \rangle$$

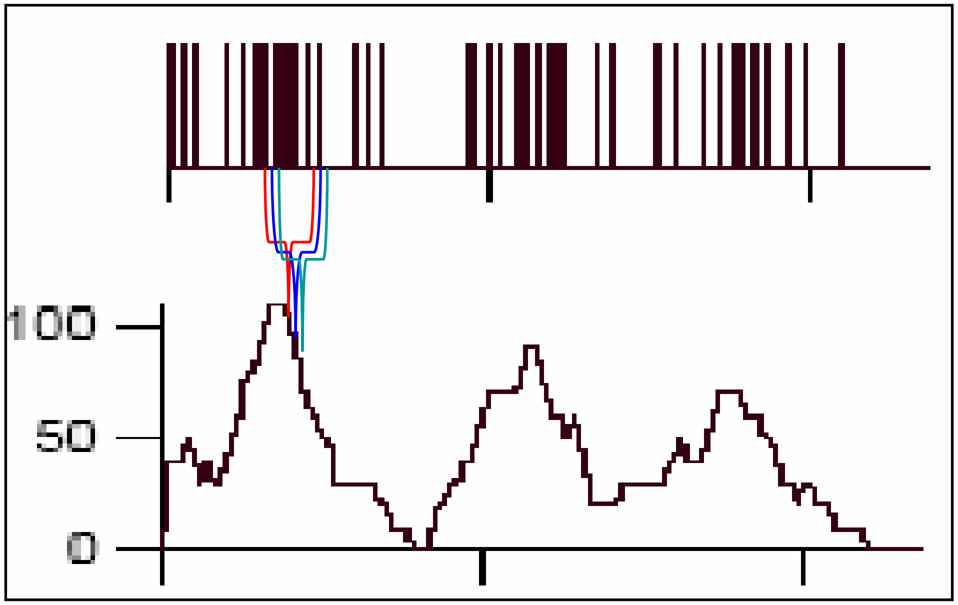
- If we have only a few trials (or only one), it is still possible to estimate the time-dependent firing rate

Approximating firing rates from a single trial



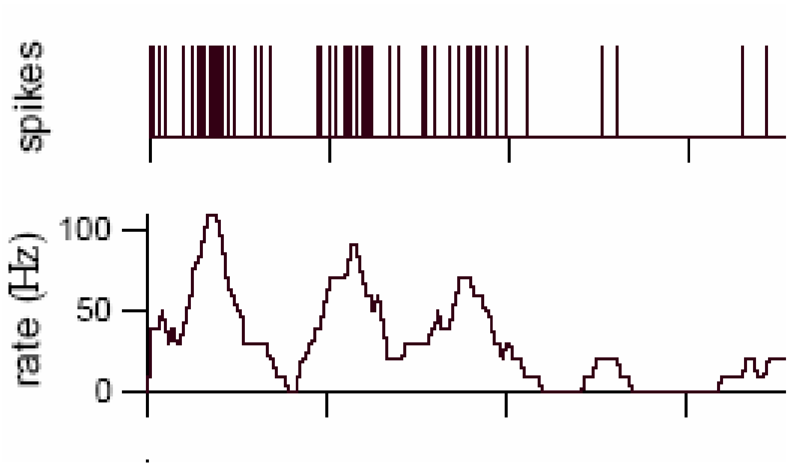
- Simple histogram: divide timeline into intervals of time *Δt*, count spikes, and divide by *Δt*
- Problem: affected by both the size and location of the time bins

Approximating firing rates from a single trial (cont.)



- Moving window: using an interval of Δt, count spikes in a moving window as it slides along the spike train

Approximating firing rates (cont.)



$$r(t) = \sum_{i=1}^{n} w(t - t_i)$$

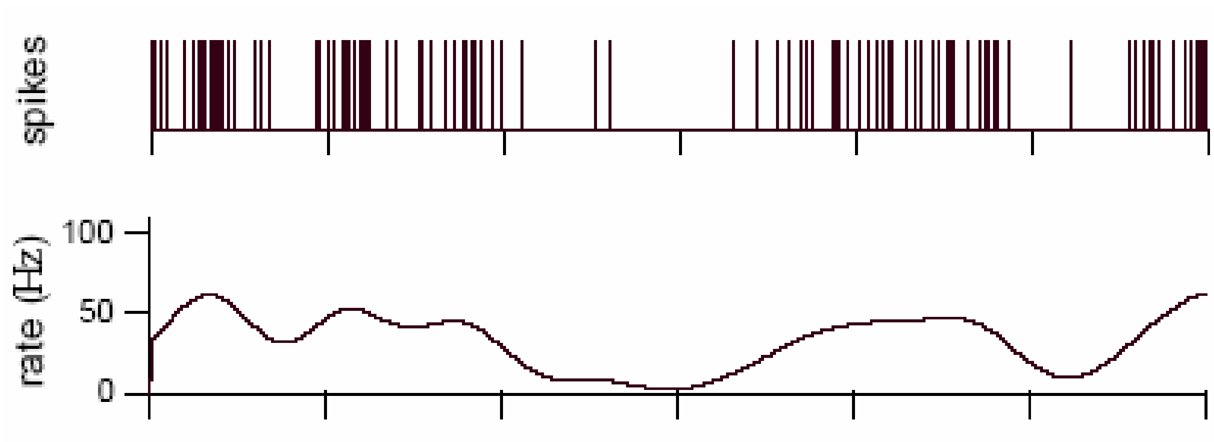
$$w(t) = \begin{cases} 1/\Delta t & \text{if} \quad -\frac{\Delta t}{2} \leq t < \frac{\Delta t}{2} \\ 0 & \text{otherwise} \end{cases}$$

- This rate can also be written as a linear filter:

$$r(t) = \int_0^\infty \underbrace{w(\tau)}_{\text{Filter kernel}} \rho(t-\tau)\, d\tau$$

Filter kernel

Approximating firing rates (cont.)



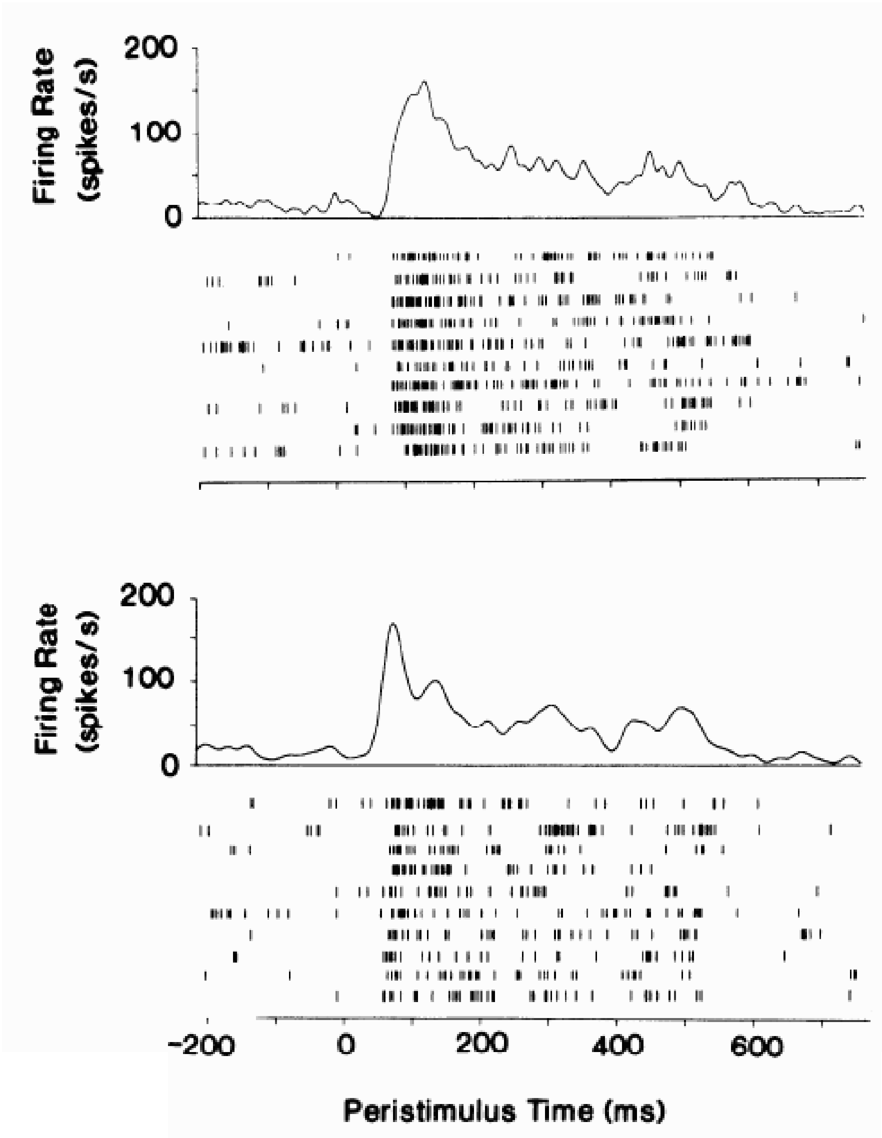
- Selection of an appropriate kernel (windowing function) *w(t)* determines the smoothness of the curve

If *w(t)* is a Gaussian: $$w(t) = \frac{1}{\sqrt{2\pi\sigma_w}} \exp\left(-\frac{t^2}{2\sigma_w^2}\right)$$

Then *r(t)* is a smooth function of time

Clearly, one could do both (average over trials, using a kernel)

Example:



Study of the information encoding of primate inferior temporal cortex (response to faces)

Single neuron response on multiple trials

Gaussian kernel, σ=*5ms*

Of particular use because the stimulus was very complex.

Tovey et al., ***J Neurophysiol*** 70: 640-654, 1993

Alternative: identify the stimulus-specific response

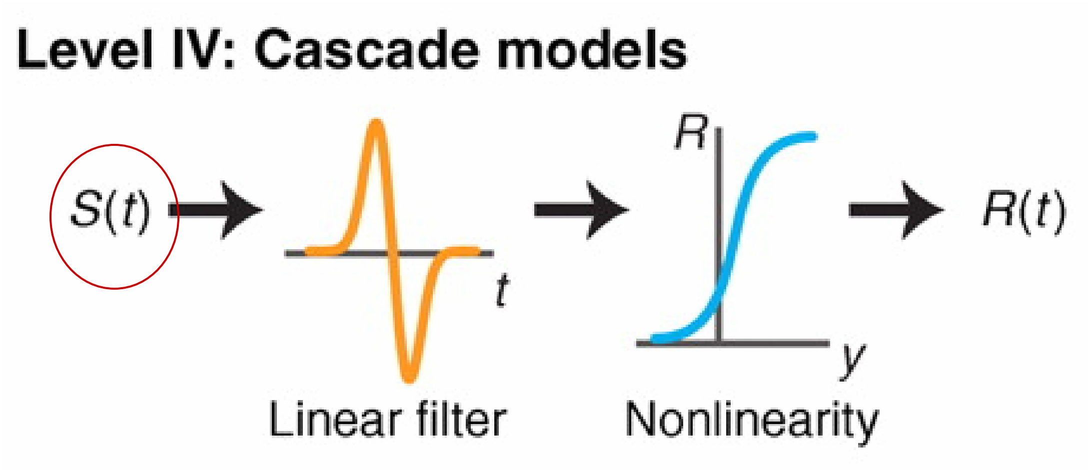
- If the stimulus is known, a better understanding of the time-dependent response to that stimulus can be obtained by looking at the time-dependent change in the stimulus leading to a spike

- Many systems adapt to the average level of stimulus intensity, so that the just-noticeable difference Δs between two stimuli is a function of stimulus intensity s

- We can study the response of the system to fluctuations in the average stimulus: i.e. define $s(t)$ so that

$$\frac{1}{T}\int_0^T s(t)dt = 0$$

Cascade Models: Understanding the response to stimuli



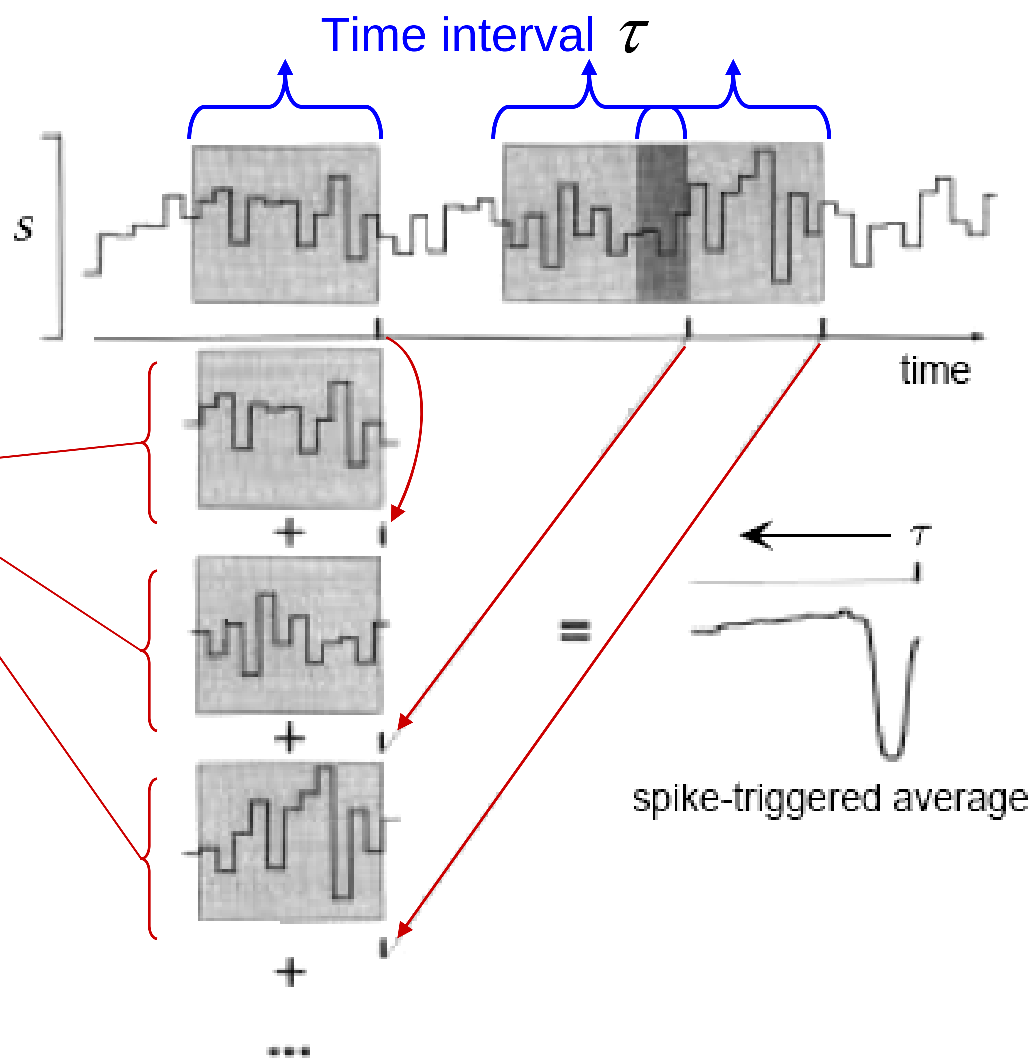
Representing the Stimulus: Spike-triggered average

Average over all
n spikes in a trial

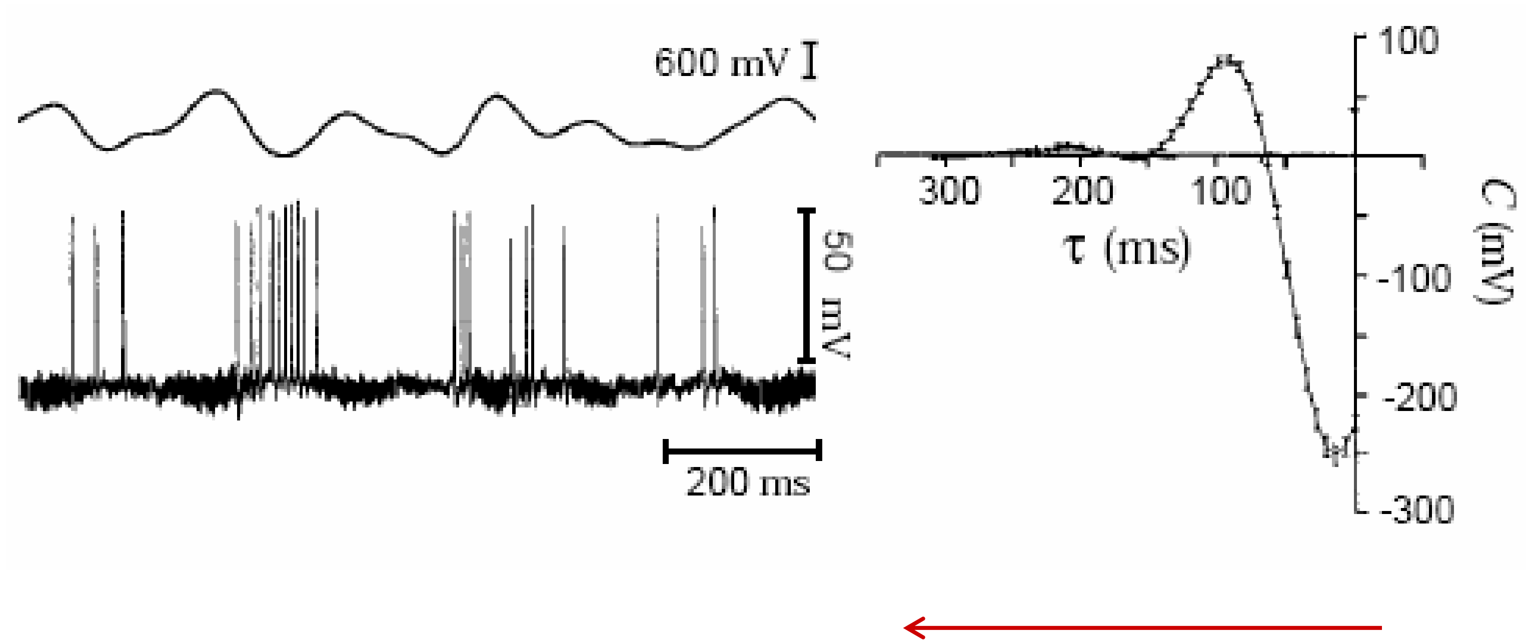
$$\frac{1}{n}\sum_{i=1}^{n} s(t_i - \tau)$$

Then, average over trials:

$$C(\tau) = \left\langle \frac{1}{n}\sum_{i=1}^{n} s(t_i - \tau) \right\rangle$$



Spike-triggered average



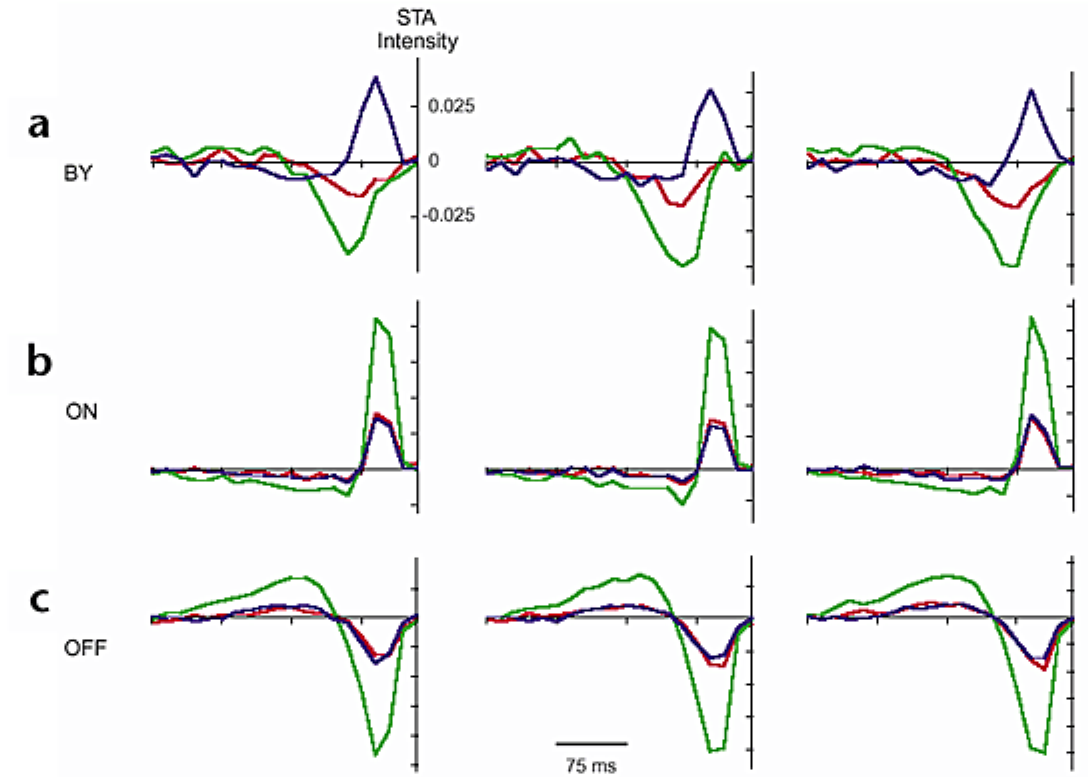
Note direction of the time access,
reflecting the average over past stimuli

Spike-triggered average: example

BY cells

Non-opponent
ON cells

Non-opponent
OFF cells



Macaque ganglion cells, response to red, green, and blue stimuli

Chichilnisky et al., ***Nature Neuroscience*** 2, 889 - 893 (1999)

Spike-triggered average (cont.)

- The spike-triggered average can be expressed as an integral:

$$C(\tau) = \left\langle \frac{1}{n} \sum_{i=1}^{n} s(t_i - \tau) \right\rangle$$

$$\rightarrow \quad C(\tau) = \frac{1}{\langle n \rangle} \int_0^T r(t)\, s(t_i - \tau)\, d\tau$$

Why do we include the rate term?

Spike triggered average stimulus = Reverse correlation function

- The spike-triggered average is related to the correlation of the firing rate and the stimulus:

$$Q_{rs}(\tau) = \frac{1}{T}\int_0^T r(t)s(t+\tau)\,dt$$

- If the average firing rate over all trials is $\langle r \rangle = \frac{\langle n \rangle}{T}$

Then

$$C(\tau) = \frac{1}{\langle r \rangle} Q_{rs}(-\tau)$$

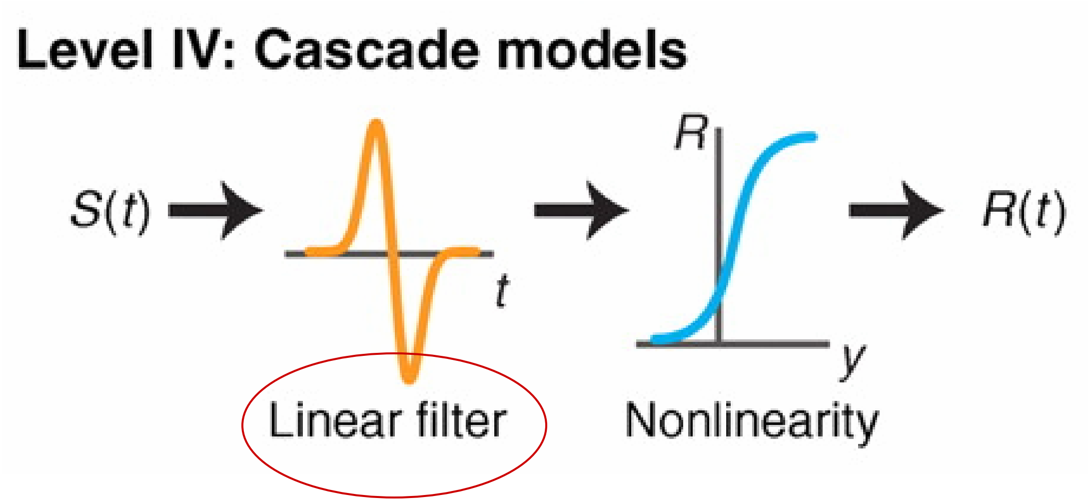
Reverse correlation function

Why negative??

Improving the approximation

- These examples have all estimated the firing rate as an instantaneous function
- Neurons respond to inputs over a period of time (a few hundred msec)
  - How can we estimate a firing rate that responds to these inputs?

Cascade Models: Understanding the response to stimuli



Linear estimation of firing rate

- Given a firing rate *r(t)* evoked by a stimulus *s(t)*, the (linear) estimated firing rate is:

$$r_{est}(t) = r_0 + \int_0^{\infty} D(\tau)s(t-\tau)d\tau$$

- *D(ti)* is known as the linear kernel and weights the stimuli at times *(t – ti)*
- We want to choose a kernel D to minimize the squared difference between the estimated and actual response:

$$E = \frac{1}{T}\int_0^T (r_{est}(t) - r(t))^2 dt \;=\; \frac{1}{T}\int_0^T \left(r_0 + \int D(\tau)s(t-\tau)d\tau - r(t) \right)^2 dt$$

average over the
duration of the trial

Estimation of firing rate (cont.)

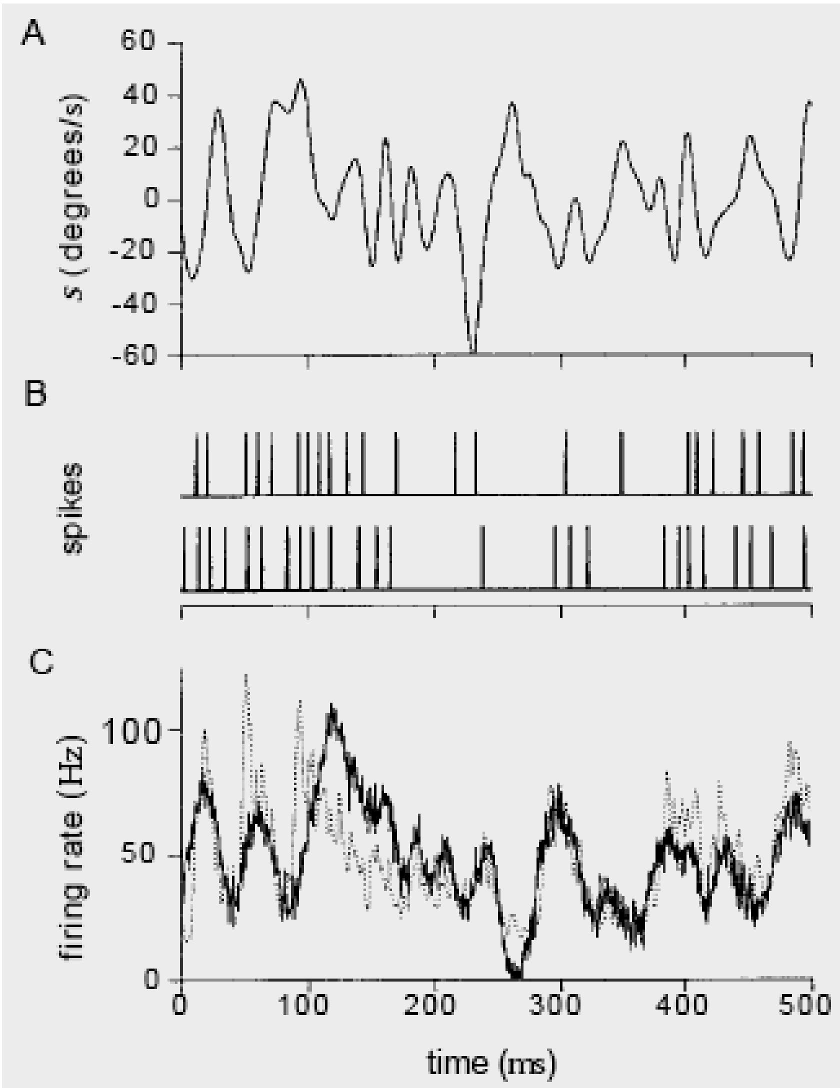
- This function is minimized by setting the derivative with respect to D to 0
- Solution is a function of
  - the stimulus correlation function $Q_{rs}(\tau) = \frac{1}{T}\int_0^T r(t)s(t+\tau)\,dt$
  - the stimulus autocorrelation function

$$Q_{ss}(\tau) = \frac{1}{T}\int_0^T s(t)s(t+\tau)\,dt$$

So, the optimal kernel is given by the solution of:

$$\int_0^\infty Q_{ss}(\tau-\tau')D(\tau')d\tau' = Q_{rs}(-\tau)$$

How good is our "optimal" kernel?



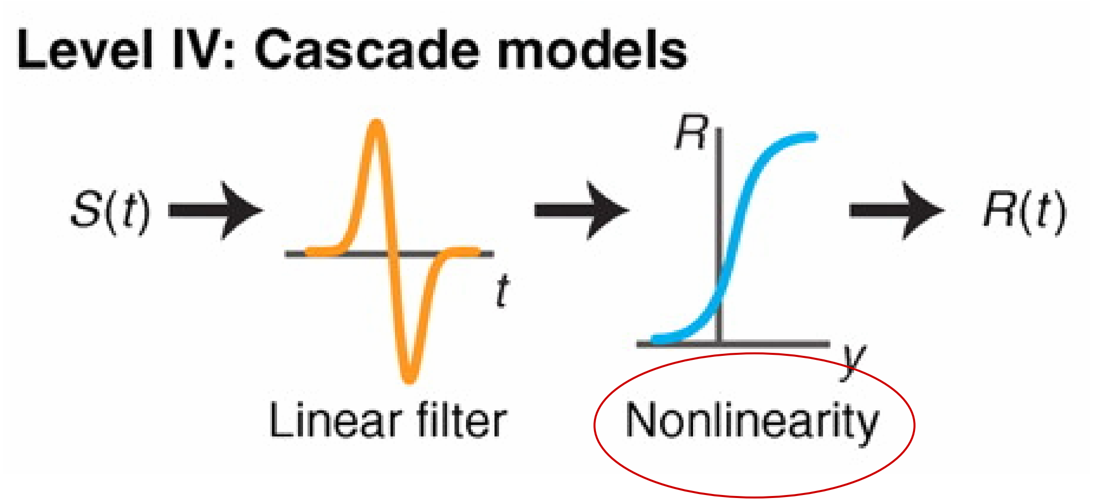
Velocity coding in the fly visual system:

Stimulus velocity modeled by white noise

Dashed line: measured time-dependent firing rate

Solid line: estimated time-dependent firing rate

Cascade Models: Understanding the response to stimuli



How can we improve our estimate?

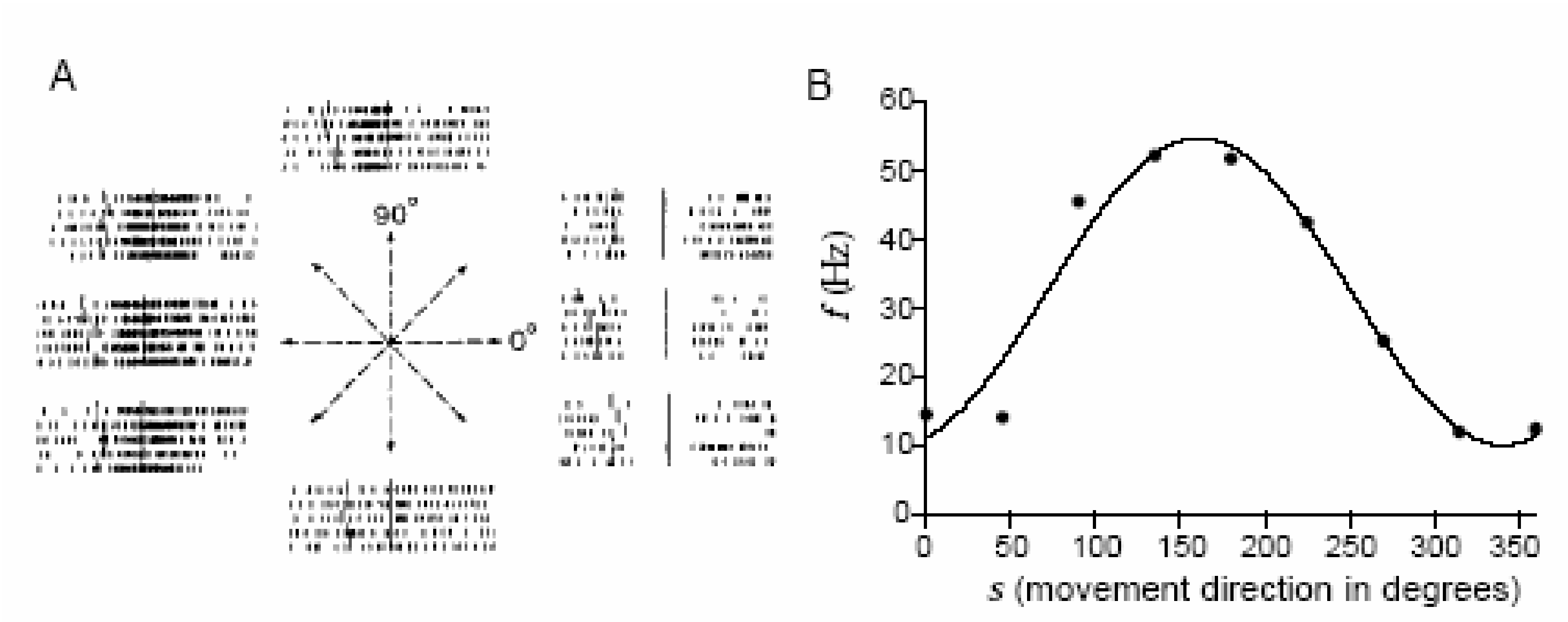
- Incorporate static nonlinearities:
  - Our current (linear) response is $L(t) = \int_0^\infty D(\tau) s(t-\tau) d\tau$
  - Replace the linear prediction with a nonlinear function of the linear filter value
  - Allows us to bound the firing rate appropriately, and perhaps model nonlinearities of our particular system
  - This is often referred to as the *gain function* or the *generator signal* of the neuronal response

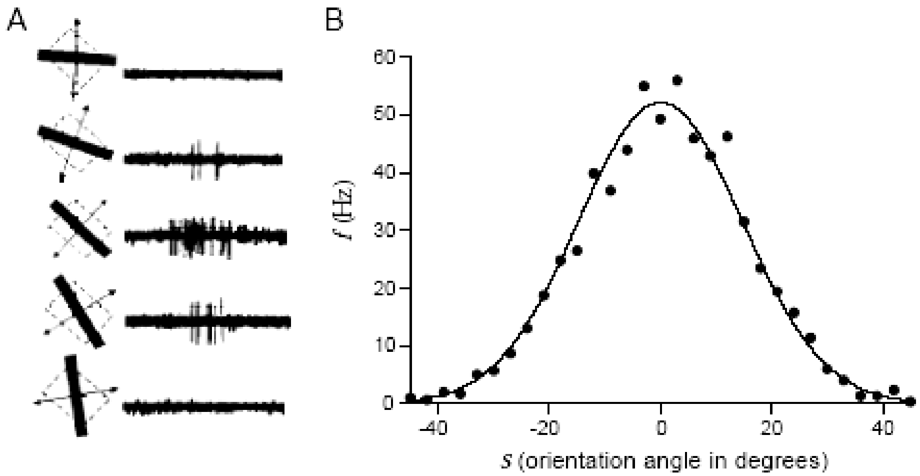
$$r_{est}(t) = r_0 + F(L(t))$$

Directional sensitivity

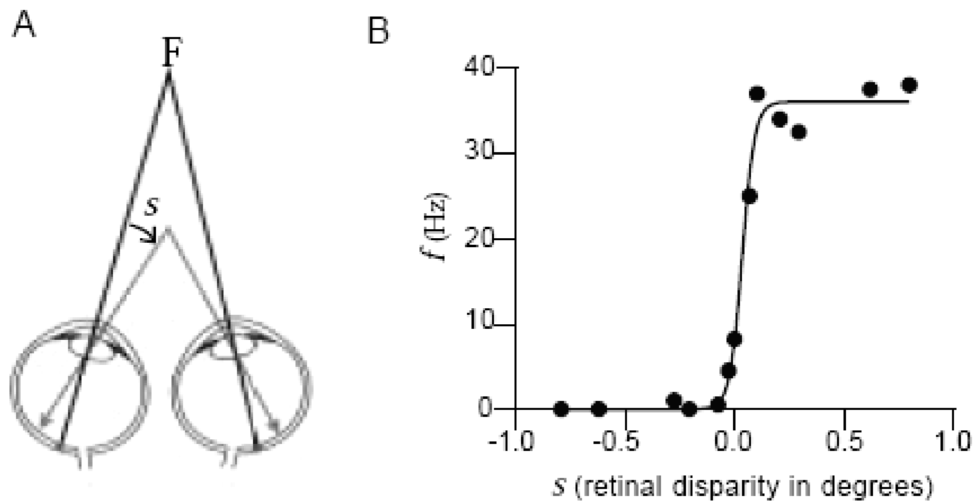
- Directional tuning in motor cortex of primates
  - Data show a tuning curve of

$$f(s) = r_0 + (r_{max} - r_0)\cos(s - s_{max})$$



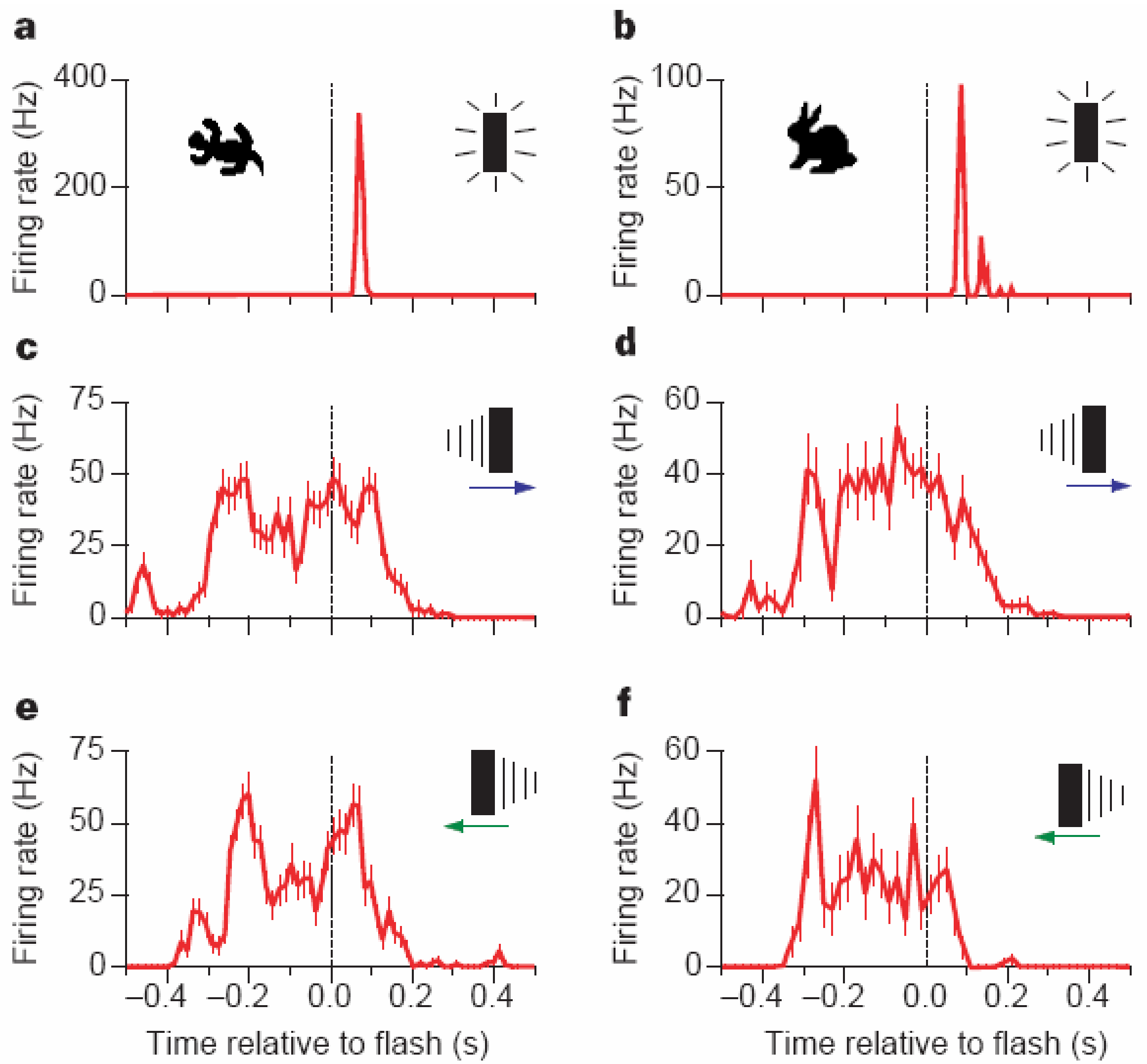


$$F(L) = r_{\max} \exp\left(-\frac{1}{2}\left(\frac{L - L_{\max}}{\sigma_f} \right)^2 \right)$$



$$F(L) = \frac{r_{\max}}{1 + \exp\left(g_1 (L_{1/2} - L) \right)}$$

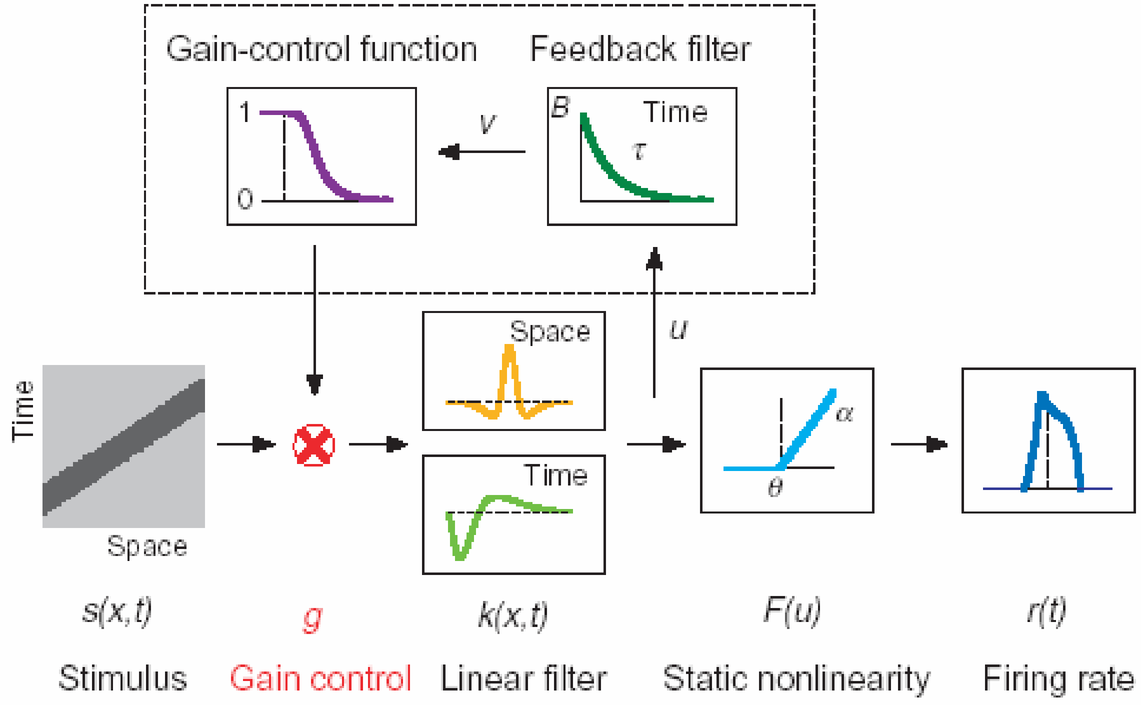
Example: Motion Anticipation



Single neuron response to stimulus

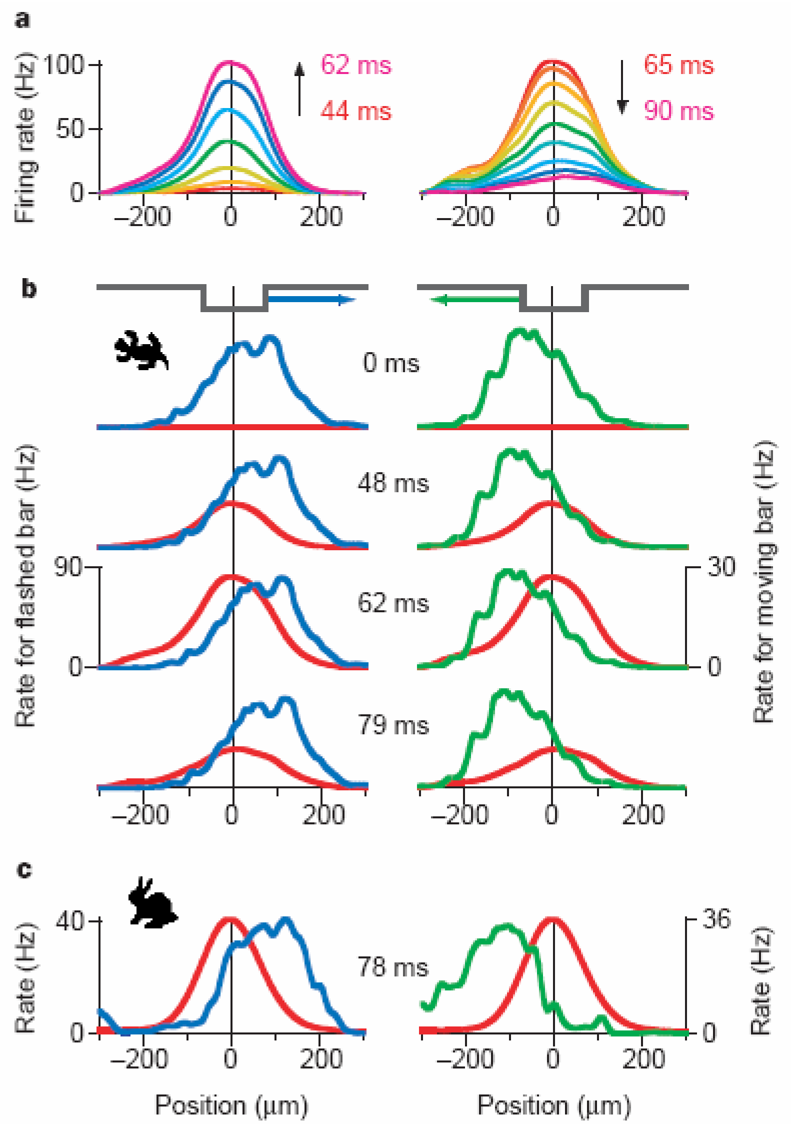
Berry et al., ***Nature***, 3/25/99, Vol. 398 Issue 6725, p334

Example: Motion Anticipation



Berry et al., ***Nature***, 3/25/99, Vol. 398 Issue 6725, p334

Spatial response to flashing and moving bars



After a latency of 40ms, neural activity increases to a peak at 60ms. Profile is centered on location of the flashing bar, and has a width at half-maximum that is ~the size of the receptive field for these neurons

For a moving bar, the neural activity leads the center of the bar by about 100µm.

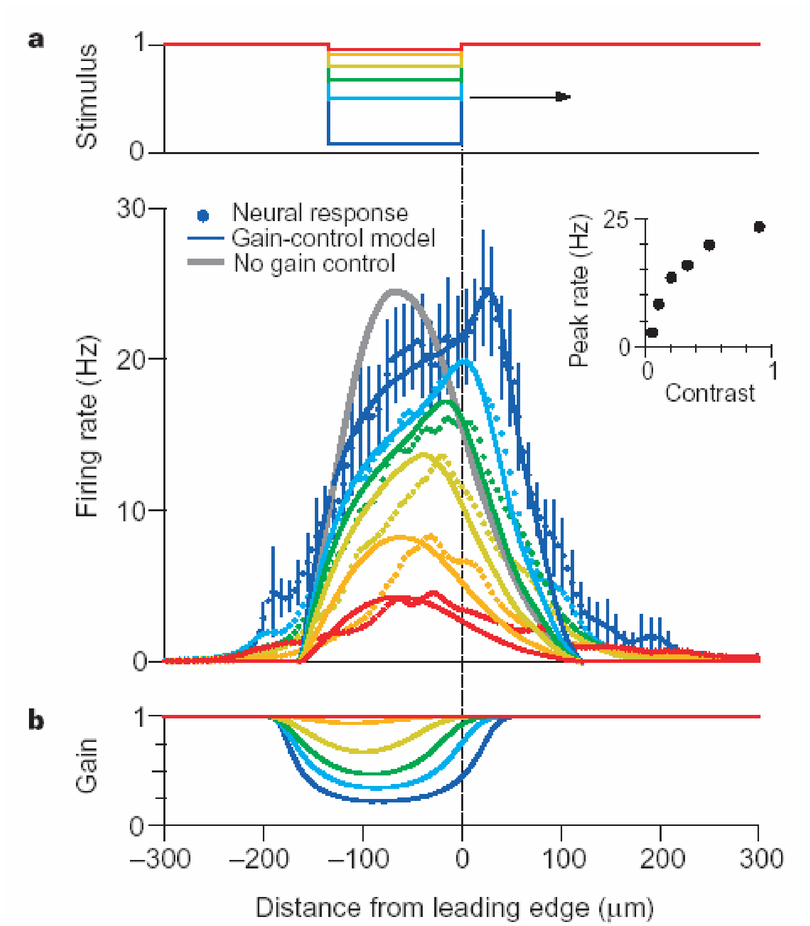
For a moving bar, the neural activity leads the center of the bar by about 100µm.

From these data, can derive the linear kernel *k(s,t)* which defines the response rate to our stimulus:

$$u(t) = g(v)\int_{-\infty}^{\infty} dx \int_{-\infty}^{t} dt'\; s(x,t')k(x,t-t')$$

Berry et al., ***Nature***, 3/25/99, Vol. 398 Issue 6725, p334

Contrast sensitivity: "gain" control



Response is exponentially filtered in time (has the effect of averaging it):

$$v(t) = \int_{-\infty}^{t} dt'\; u(t')B \exp\left(-\frac{t-t'}{\tau}\right)$$

High-contrast stimulus desensitizes the response → model incorporated a negative feedback loop known as "gain control":

$$g(v) = \begin{cases} 1 & v < 0 \\ 1/(1+v^4) & v > 0 \end{cases}$$

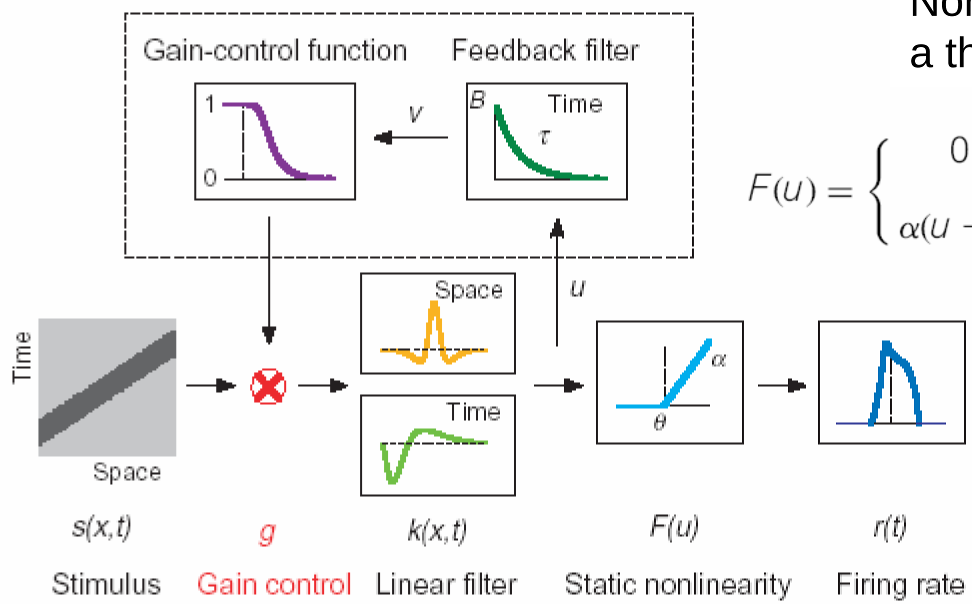
Berry et al., ***Nature***, 3/25/99, Vol. 398 Issue 6725, p334

Example: Motion Anticipation

$$v(t) = \int_{-\infty}^{t} dt'\, u(t') B \exp\left(-\frac{t-t'}{\tau}\right)$$

Non-linear filter provides a threshold for firing

$$F(u) = \begin{cases} 0 & u < \theta \\ \alpha(u-\theta) & u > \theta \end{cases}$$

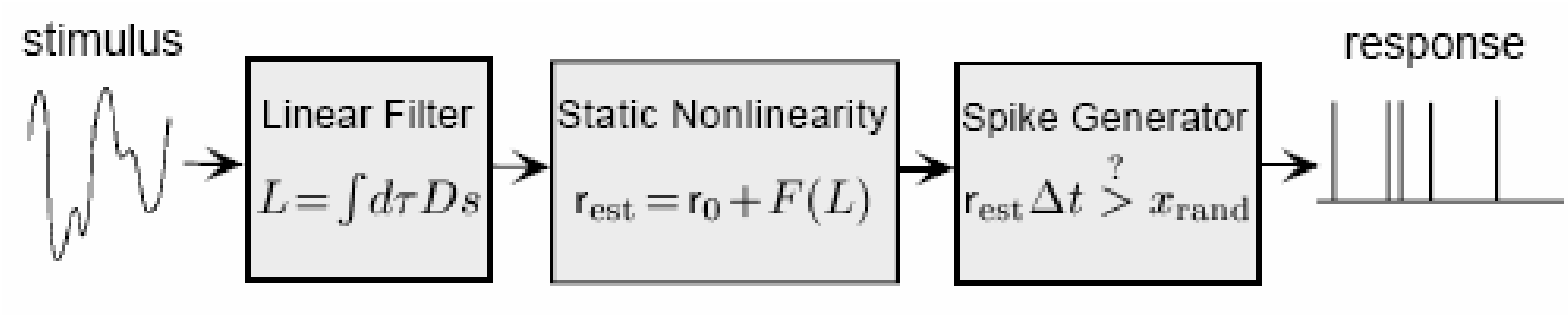


$$g(v) = \begin{cases} 1 & v < 0 \\ 1/(1+v^4) & v > 0 \end{cases}$$

$$u(t) = g(v) \int_{-\infty}^{\infty} dx \int_{-\infty}^{t} dt'\, s(x,t') k(x,t-t')$$

Berry et al., ***Nature***, 3/25/99, Vol. 398 Issue 6725, p334

White noise analysis



- Choose randomly selected stimuli
- Compute the spike-triggered average (or other estimate of rate) → estimate the linear filter
- Fit the mean spike rate as a function of the generator signal → estimate the nonlinearity
- Compare with actual response data to evaluate the model

White noise as stimuli

- Clearly, the response depends upon the nature of the stimulus

- A very common technique used for analyzing neuronal response patterns is to use a white noise stimulus

- By definition: $Q_{ss}(\tau) = \sigma_s^2 \delta(\tau)$ for a Gaussian (white noise)

  (i.e. inputs uncorrelated)

White noise analysis (cont.)

- So, for white noise stimuli, we can determine our optimal linear kernel:

$$\int_0^\infty Q_{ss}(\tau - t)D(t)dt = \sigma_s^2 \int_0^\infty \delta(t-\tau)D(\tau)d\tau = \sigma_s^2 D(\tau)$$

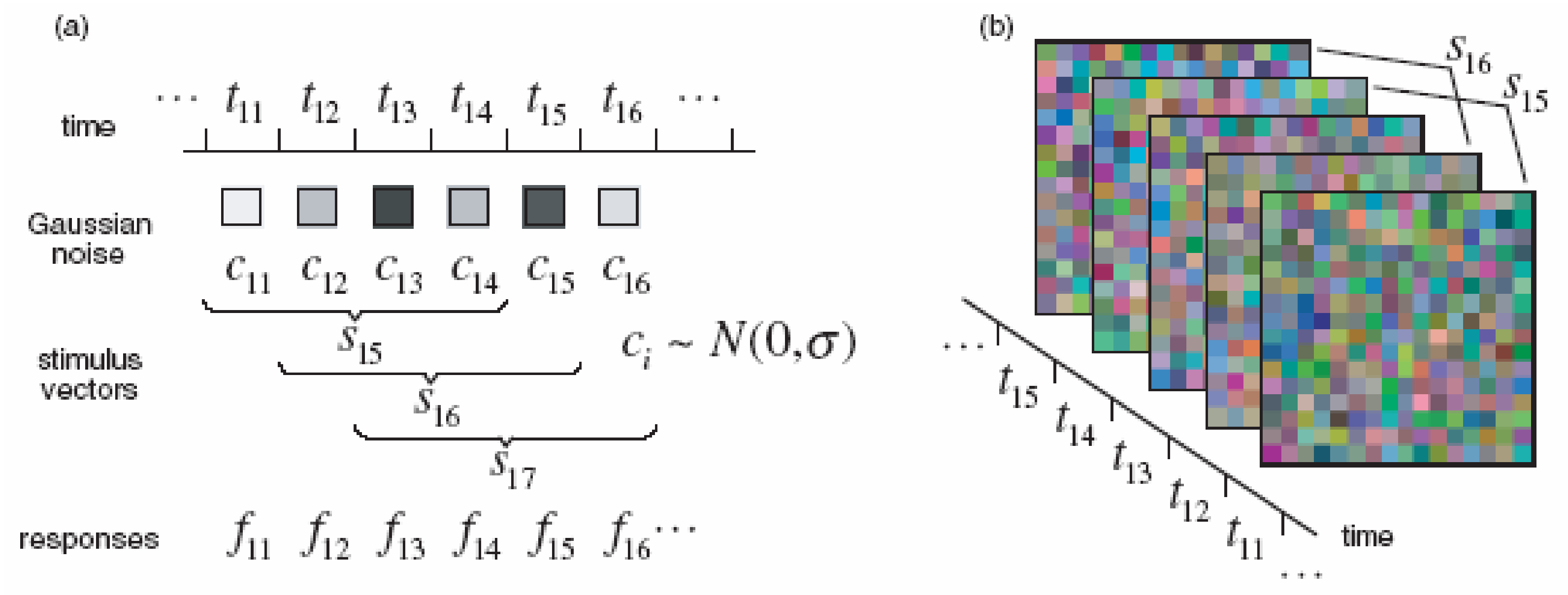
Since $\int_0^\infty Q_{ss}(\tau-\tau')D(\tau')d\tau' = Q_{rs}(-\tau)$

the optimal kernel for a white noise stimulus is:

$$D(\tau) = \frac{Q_{rs}(-\tau)}{\sigma_s^2} = \frac{\langle r \rangle C(\tau)}{\sigma_s^2}$$

Example: White noise analysis of retinal ON- and OFF-center cells

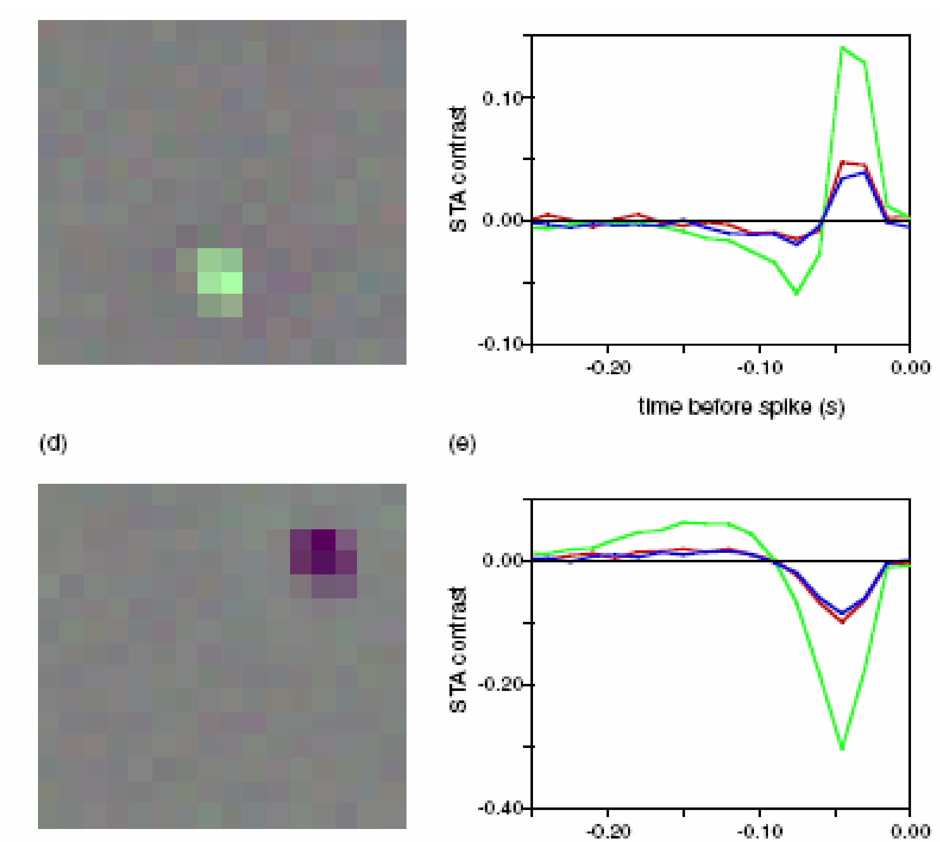
- Stimuli:



Chichilnisky, ***Network: Comput. Neural Syst***. 12 (2001) 199–213

White noise analysis (cont.)

- Calculate the spike-triggered average:



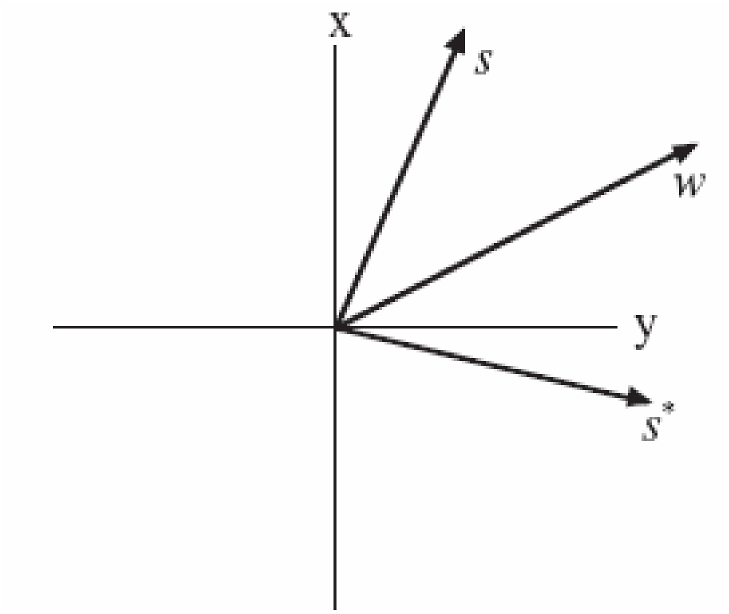
$$a = \frac{\sum_{t=1}^{T} s_t f_t}{\sum_{t=1}^{T} f_t}$$

Chichilnisky, ***Network: Comput. Neural Syst***. 12 (2001) 199–213

White noise analysis (cont.)

- Estimate the linear filter
  - w is the neuron's stimulus selectivity
  - s is the stimulus
  - Response of the neuron is estimated as the dot product of the selectivity vector w and the stimulus s:

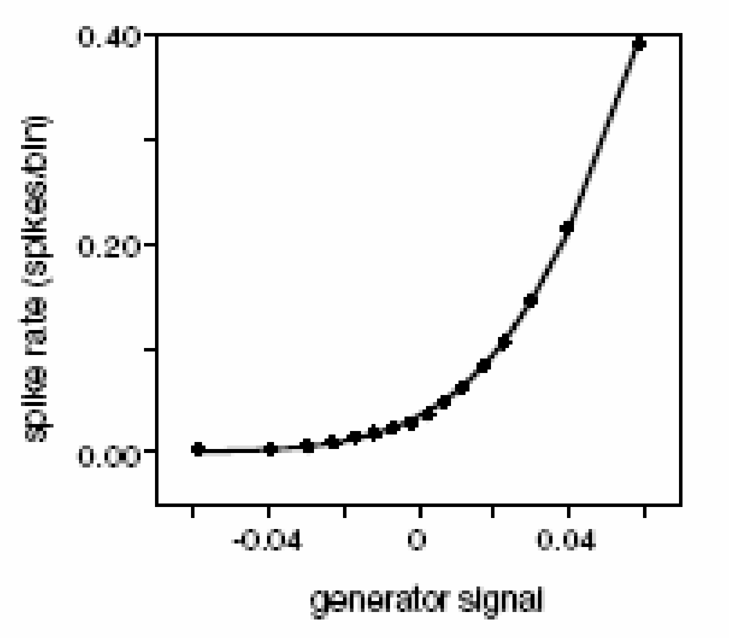
$$L = w \cdot s = w \cdot s^*$$



Chichilnisky, ***Network: Comput. Neural Syst***. 12 (2001) 199–213

White noise analysis (cont.)

- Estimate the non-linear function: plot the spike-triggered average as a function of L
- Fit an appropriate non-linear function (generator signal/gain)

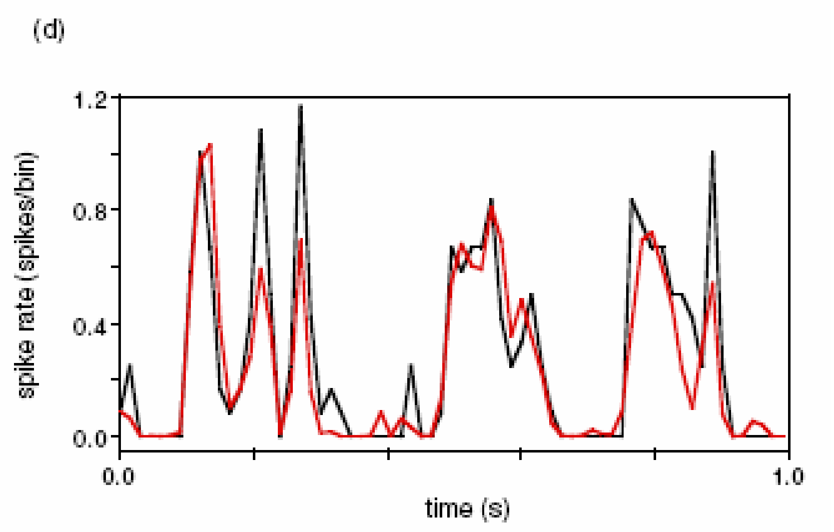


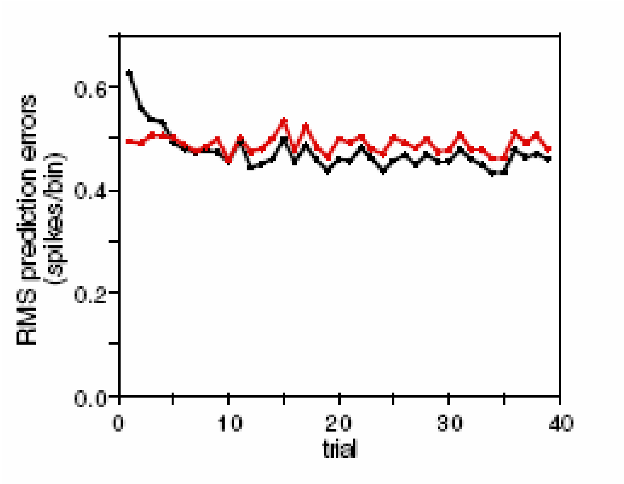
$$F(L) \approx r_{\max} C(\beta L + r_0) \qquad C = cumulative\ \ normal\ \ distribution$$

Chichilnisky, ***Network: Comput. Neural Syst***. 12 (2001) 199–213

White noise analysis (cont.)

- Evaluate the fit





Chichilnisky, ***Network: Comput. Neural Syst***. 12 (2001) 199–213