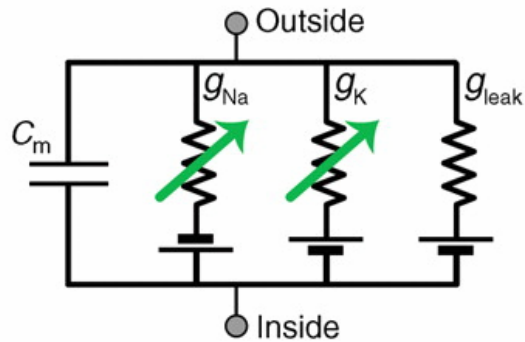


BME 665/565

Cascade models and Spike Trains:
Probabilistic Firing and Noise

Levels of Modeling: Biophysical Models

Level I: Single-compartment models



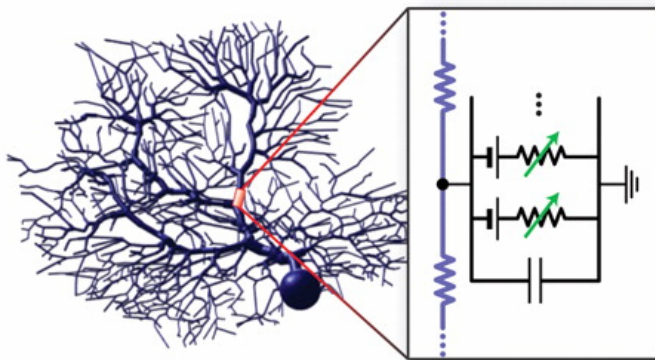
Hodgkin-Huxley model

$$C \frac{dV}{dt} = I - \bar{g}_{Na} m^3 h (V - V_{Na}) - \bar{g}_K n^4 (V - V_K) - g_L (V - V_L)$$

$$\frac{dm}{dt} = \alpha_m(V)(1-m) - \beta_m(V)m \quad \frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)h$$

$$\frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n$$

Level II: Detailed compartmental models



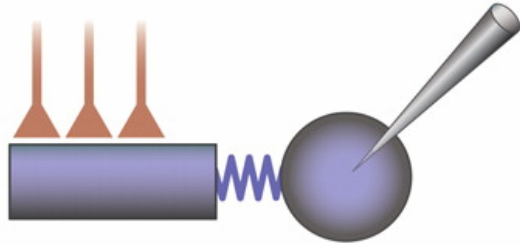
Two-dimensional models

$$\lambda^2 \frac{\partial^2 V}{\partial x^2} - \tau \frac{\partial V}{\partial t} - V = 0$$

$$\tau = r_m c_m, \quad \lambda = \sqrt{\frac{r_m}{r_a}}$$

Levels of modeling: Information coding

Level III: Reduced compartmental models



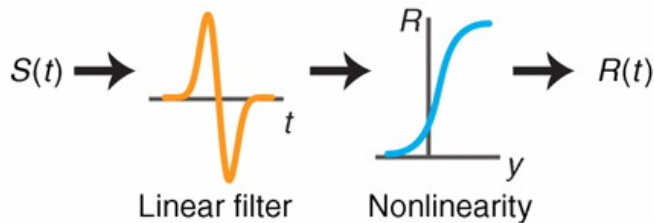
Integrate-and-fire models

$$\tau_m \frac{dV}{dt} = E_L - V + R_m I_e \quad \text{If } V > V_{th}, \text{ then } V = V_{reset}$$

Spike Response Models

$$V(t) = \eta(t - \hat{t}) + \int_0^\infty \kappa(t - \hat{t}, s) I(t - s) ds$$

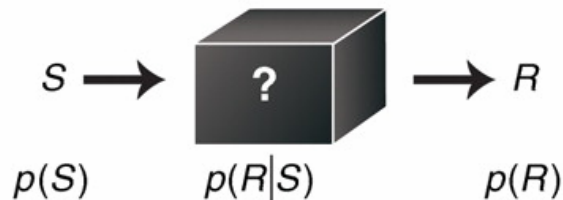
Level IV: Cascade models



Rate and timing codes

$$r = \frac{n}{T} = \frac{1}{T} \int_0^T d\tau \rho(\tau) \quad r_{est}(t) = r_0 + \int_0^\infty D(\tau) s(t - \tau) d\tau$$

Level V: Black-box models



Population equations and decoding

$$P[r | s] = \prod_{a=1}^n \frac{(f_a(s)T)^{r_a T}}{(r_a T)!} e^{-f_a(s)T} \quad s_{ML} = \frac{\sum r_a s_a / \sigma_a^2}{\sum r_a / \sigma_a^2}$$

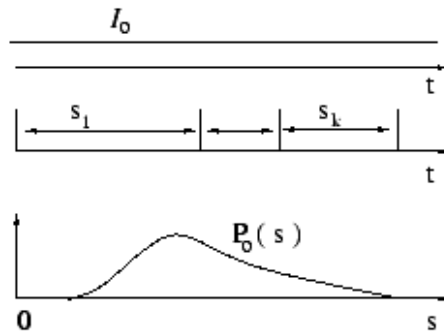
Application of information coding approaches

Biological Goal	Computation	Biophysical Mechanism	Level	Experimental systems
Motion anticipation	Linear filtering with negative feedback	Adaptation of neuronal gain	4	Salamander and rabbit retinal ganglion cells
Motion detection	Logical AND or AND-NOT comparisons of temporal shifted info	Coincidence detection of one lagged and on nonlagged spike	4	Peripheral neurons in the fly visual system
Intensity-invariant recognition of patterns	Separation of pattern identity and intensity; compare to stored template	Transformation of local stimulus to spike time; coincidence detection	1,4	Insect and vertebrate olfactory neurons
Redundancy reduction	Subtraction of local signal minus background signal	Dendritic summation	4	Center-surround receptive fields in the visual system
Efficient coding in variable environment	Modification of turning curve to track time-varying stimulus ensemble	Adaptation of single-cell input-output function	3,4,5	Motion-sensitive H1 neuron in the fly visual system

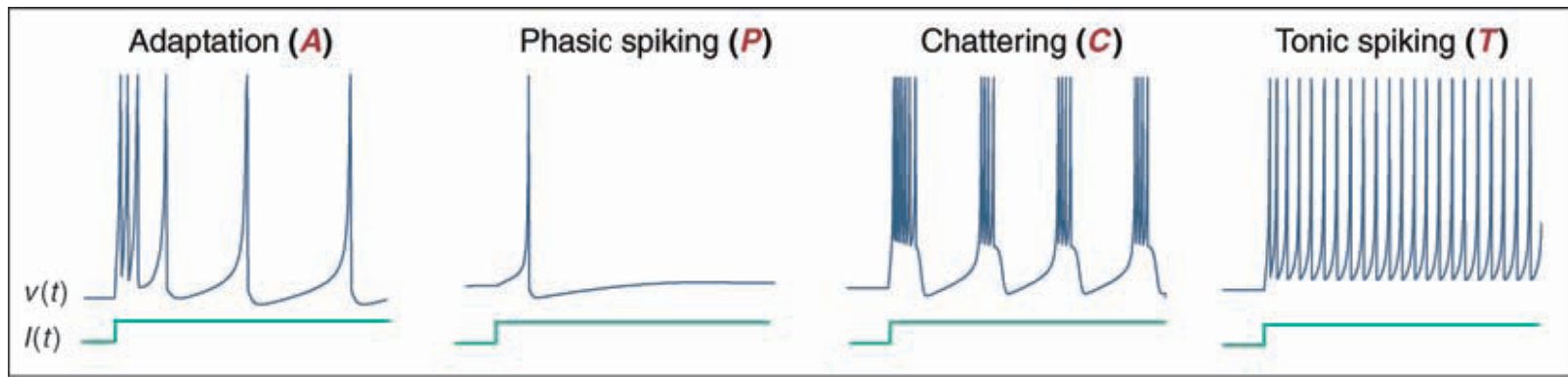
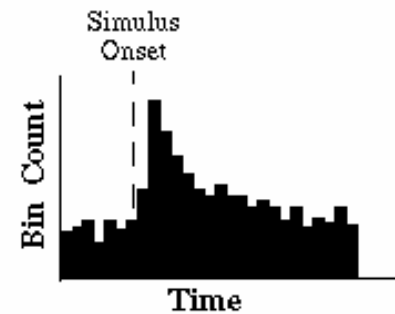
Adapted from Herz et al., *Science*. 2006 Oct 6;314(5796):80-5.

Variability in neuronal firing

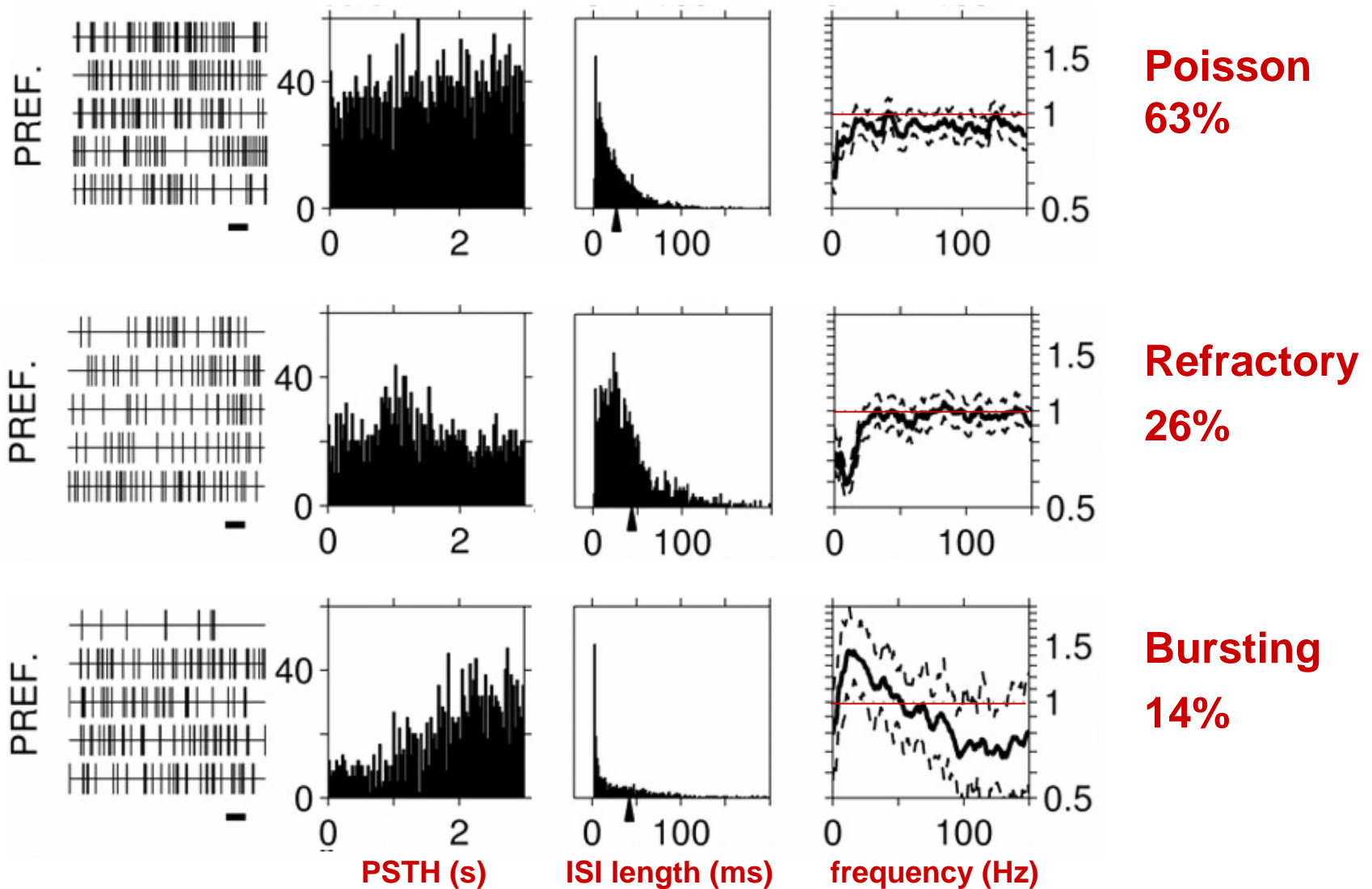
Inter-Spike Interval (ISI)



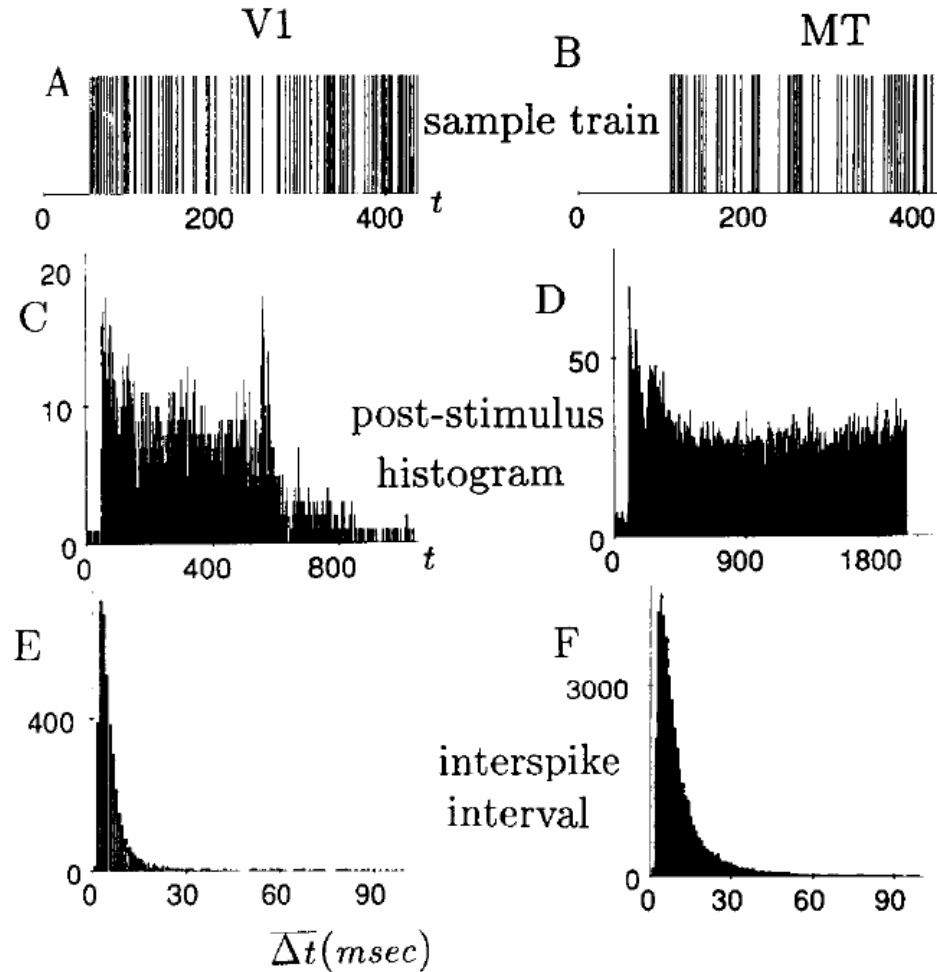
Post-Stimulus Time Histogram (PSTH)



Neuronal firing patterns (primate PFC)

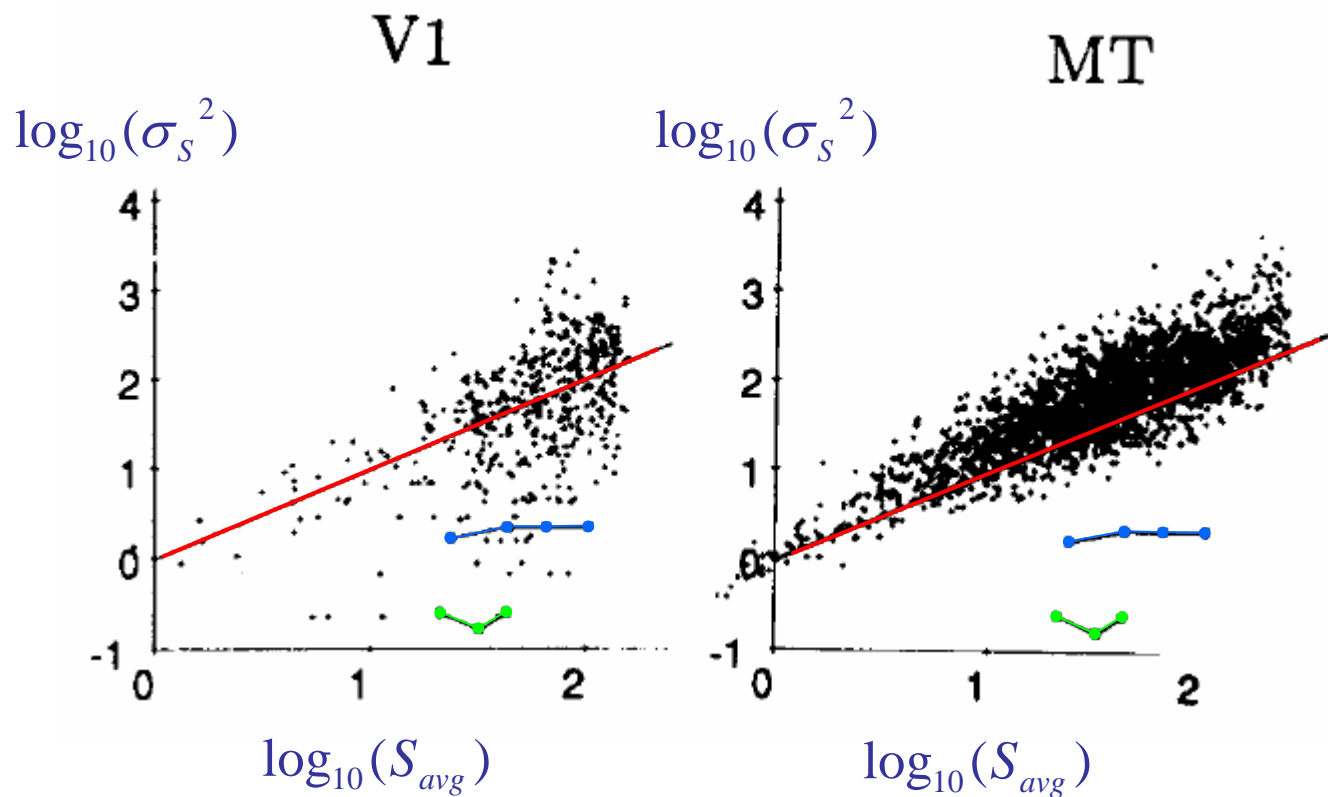


Modeling variability in firing patterns



Compartmental models of variability to not match experimental results

- Poisson firing rate
- Compartmental model with realistic parameters
- Compartmental model with “Barely Plausible” parameters
(all synapses on apical dendrite 60pm from soma, fast and strong EPSP)



Homogeneous Poisson process

- Simple random process with no memory: every event is independent of any previous event
- Assume an average cell firing rate r
 - The firing rate r is the probability of firing a spike in an interval Δt around t , as $\Delta t \rightarrow 0$
 - So, the probability of a single spike occurring in that interval is $r\Delta t$
- Since all spikes are independent of each other, we can express the probability density solely as a function of the number of spikes during an interval
- Take an interval T and divide it into M bins of size Δt :

$$\Delta t = T/M$$

- Choose Δt so that we never get 2 spikes in a single bin

Homogeneous Poisson process (cont.)

- How do we determine $P_T(n)$ = Probability of exactly n spikes occurring during the interval T ?
- $P_T(n)$ is the product of:
 - The probability of generating n spikes within M bins
 - The probability of not generating spikes in the remaining bins
 - The number of ways in which n spikes can occur in M bins

Determining $P_T(n)$

- $P_T(n)$ is the product of:
 - The probability of generating n spikes within M bins
 - The probability of not generating spikes in the remaining bins
 - The number of ways in which n spikes can occur in M bins
-
- Since we chose Δt to ensure at most one spike per bin, the probability of generating n spikes is equivalent to the probability that n of the M bins contain a spike
 - Spikes are independent
 - Probability of spike in 1 bin is $r\Delta t$
 - So, probability of generating a spike in each of n bins is $(r\Delta t)^n$

Determining $P_T(n)$ (cont.)

- $P_T(n)$ is the product of:
 - The probability of generating n spikes within M bins
 - The probability of not generating spikes in the remaining bins
 - The number of ways in which n spikes can occur in M bins
-

- The probability of not having a spike in a given bin is

$$1 - r\Delta t$$

- The probability of having the remaining $M-n$ bins without any spikes in them is:

$$(1 - r\Delta t)^{M-n}$$

Determining $P_T(n)$ (cont.)

- $P_T(n)$ is the product of:
 - The probability of generating n spikes within M bins
 - The probability of not generating spikes in the remaining bins
 - The number of ways in which n spikes can occur in M bins
-

- The number of ways of putting n spikes into M bins is given by the binomial coefficient:

$$\frac{M!}{(M - n)!n!}$$

Determining $P_T(n)$ (cont.)

- Hence, the probability of n spikes in time T is:

$$P_T(n) = \lim_{\Delta t \rightarrow 0} \frac{M!}{(M-n)!n!} (r\Delta t)^n (1-r\Delta t)^{M-n}$$

- For large M and small n (i.e. Low firing rates), approximate:

$$(M-n) \approx M = T/\Delta t \quad \text{and} \quad \frac{M!}{(M-n)!} \approx M^n = (T/\Delta t)^n$$

- So,

$$\lim_{\Delta t \rightarrow 0} (1-r\Delta t)^{M-n} = \lim_{\Delta t \rightarrow 0} (1-r\Delta t)^M = \lim_{\Delta t \rightarrow 0} (1-r\Delta t)^{\frac{T}{\Delta t}} = \lim_{\Delta t \rightarrow 0} (1-r\Delta t)^{\frac{-rT}{-r\Delta t}}$$

Determining $P_T(n)$ (cont.)

- Let: $\varepsilon = -r\Delta t$

and note that by definition $\lim_{\varepsilon \rightarrow 0} \left((1 + \varepsilon)^{\frac{1}{\varepsilon}} \right) = e$

- So: $\lim_{\Delta t \rightarrow 0} (1 - r\Delta t)^{M-n} = \lim_{\Delta t \rightarrow 0} (1 - r\Delta t)^{\frac{-rT}{-r\Delta t}} = \lim_{\varepsilon \rightarrow 0} \left((1 + \varepsilon)^{\frac{1}{\varepsilon}} \right)^{-rT} = e^{-rT}$

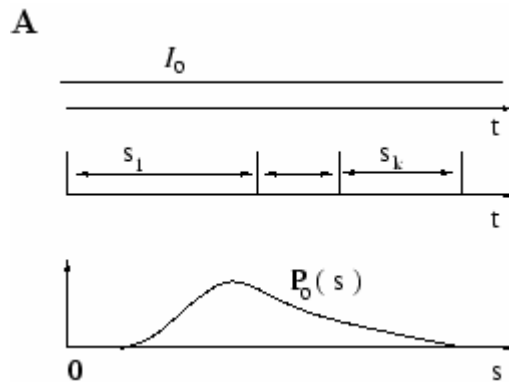
- Substitute into:

$$\begin{aligned}
 P_T(n) &= \lim_{\Delta t \rightarrow 0} \frac{M!}{(M-n)!n!} (r\Delta t)^n (1 - r\Delta t)^{M-n} \\
 &= \lim_{\Delta t \rightarrow 0} \left(\frac{T}{\Delta t} \right)^n \frac{1}{n!} (r\Delta t)^n e^{-rT} \\
 &= \lim_{\Delta t \rightarrow 0} \frac{(rT)^n}{n!} e^{-rT}
 \end{aligned}$$

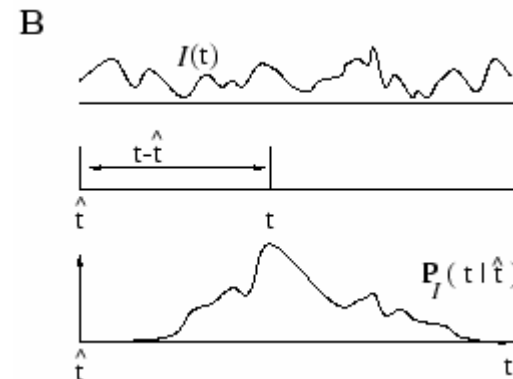
Determining $P_T(n)$ (cont.)

- The result is the Poisson distribution:
$$P_T(n) = \frac{(rT)^n}{n!} e^{-rT}$$

Applying this to Interspike Intervals



Constant input, stationary interval distribution: $P_0(t)$ represented by the interspike histogram



Time-varying input, input-dependent interval distribution: $P_I(t|\hat{t})$ represents probability density that next spike occurs after an interval $t-\hat{t}$

Survivor function

- The probability that a spike occurs between time t_1 and t_2 is just the integration of the probability density, given by:

$$\int_{t_1}^{t_2} P_I(t | \hat{t}) dt$$

- The survivor function is the probability that a spike doesn't occur in that interval
 - For a spike at time \hat{t} the survivor function is defined as:

$$S_I(t | \hat{t}) = 1 - \int_{\hat{t}}^t P_I(t' | \hat{t}) dt'$$

Hazard function

- The hazard function is the probability of firing at point t , given we haven't fired yet
- Defined as the rate of decay of the survivor function:

$$\rho_I(t | \hat{t}) = \frac{-\frac{d}{dt} S_I(t | \hat{t})}{S_I(t | \hat{t})}$$

Probability of firing at point t , given we haven't fired yet

$$\frac{\rho_I(t | \hat{t}) S_I(t | \hat{t})}{dt} = -\frac{d}{dt} S_I(t | \hat{t})$$

Probability of not firing up until point t

Probability density

Hazard function

- How do we interpret this?
 - The hazard is a measure of the likelihood of firing given no spike occurred up to time t
 - Example: reduced hazard at times close to the previous firing is characteristics of a refractory period
 - Example: increasing hazard implies that the likelihood of firing increases the longer it has been since the last spike

Hazard function for a Poisson Process

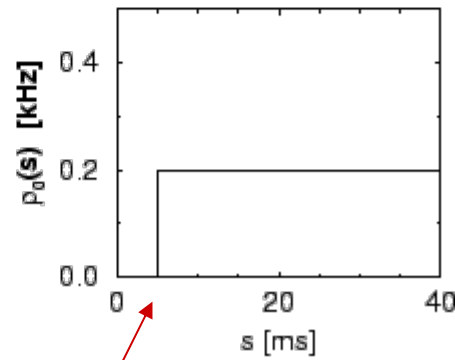
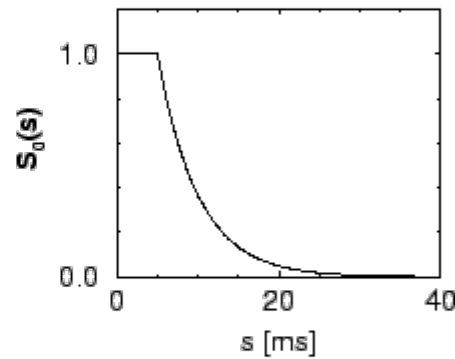
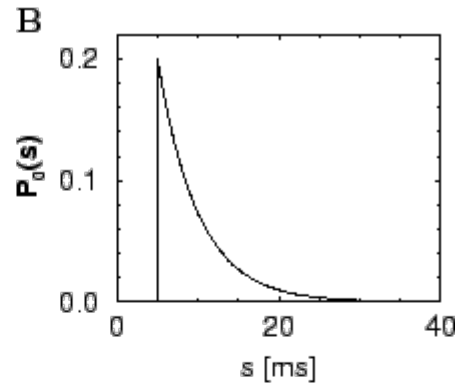
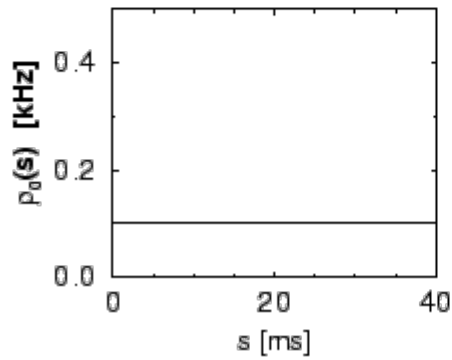
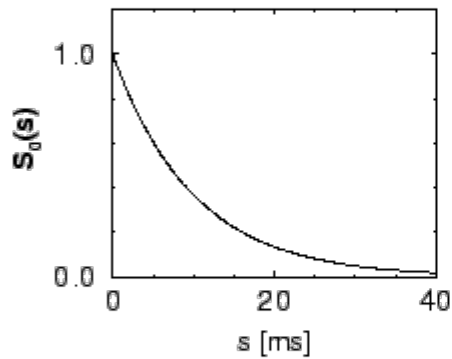
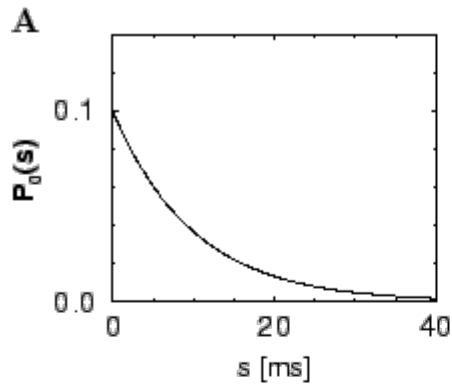
For the Poisson distribution:

$$P_T(n) = \frac{(rT)^n}{n!} e^{-rT}$$

The probability of not firing a spike ($n=0$) for a period t is e^{-rt} , which is the survivor function

So the hazard function for the Poisson process is simply the (constant) firing rate:

$$\rho_I(t|\hat{t}) = \frac{-\frac{d}{dt} S_I(t|\hat{t})}{S_I(t|\hat{t})} = r$$



Example: Poisson firing rate, with and without a refractory period

$$\rho_I(t | \hat{t}) = r \cdot \Theta(t - \Delta_{abs})$$

Δ_{abs}

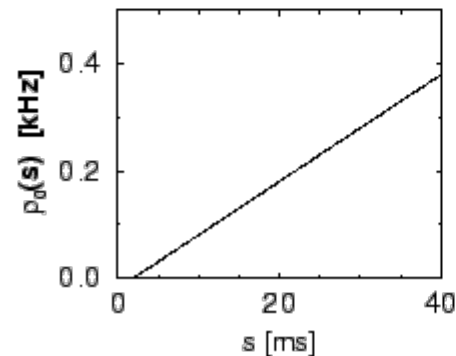
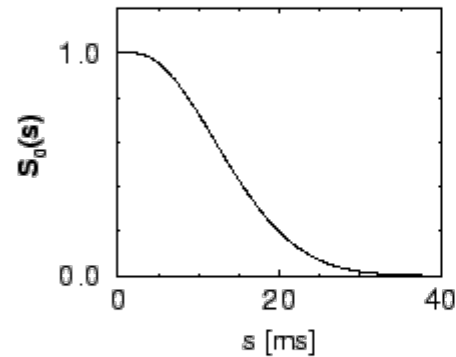
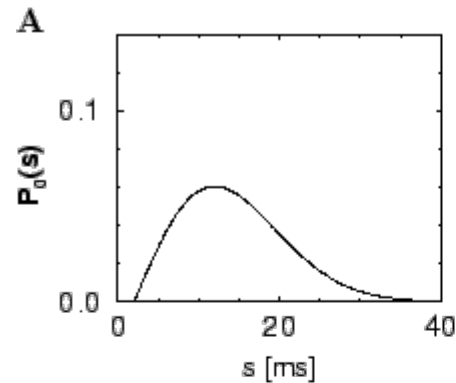
Note that this formalization allows us to derive all of these functions if one can be acquired empirically

$$S_I(t | \hat{t}) = 1 - \int_{\hat{t}}^t P_I(t' | \hat{t}) dt'$$

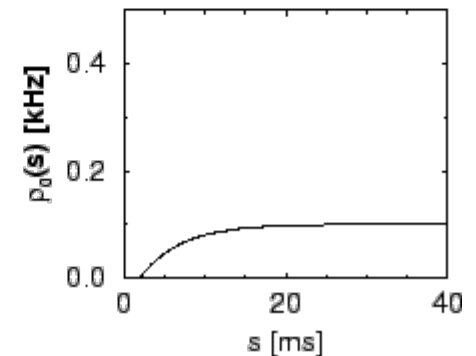
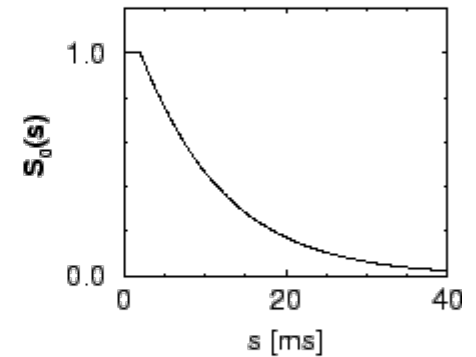
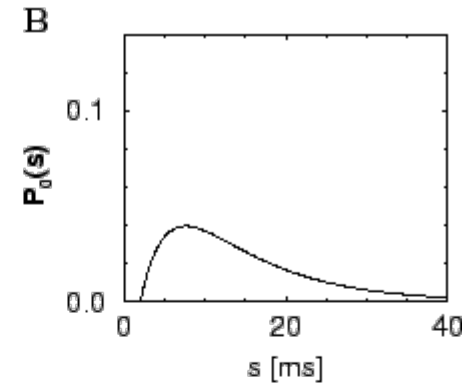
$$\Rightarrow P_I(t | \hat{t}) = -\frac{d}{dt} S_I(t | \hat{t})$$

$$\rho_I(t | \hat{t}) S_I(t | \hat{t}) = -\frac{d}{dt} S_I(t | \hat{t})$$

$$\Rightarrow S_I(t | \hat{t}) = \exp\left(-\int_{\hat{t}}^t \rho_I(t' | \hat{t}) dt'\right)$$

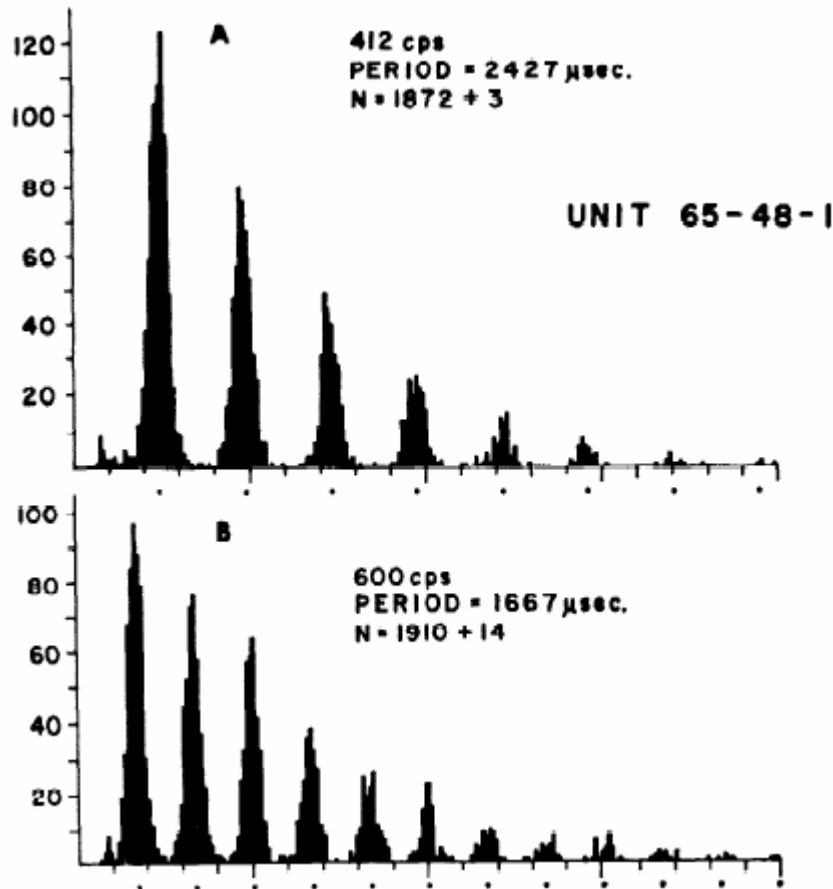


$$\rho = a_0(t - \Delta_{abs})$$



$$\rho = r(1 - \exp(-\lambda(t - \Delta_{abs})))$$

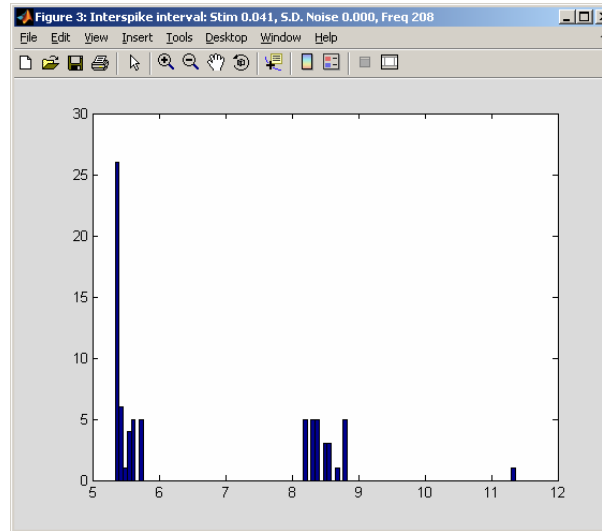
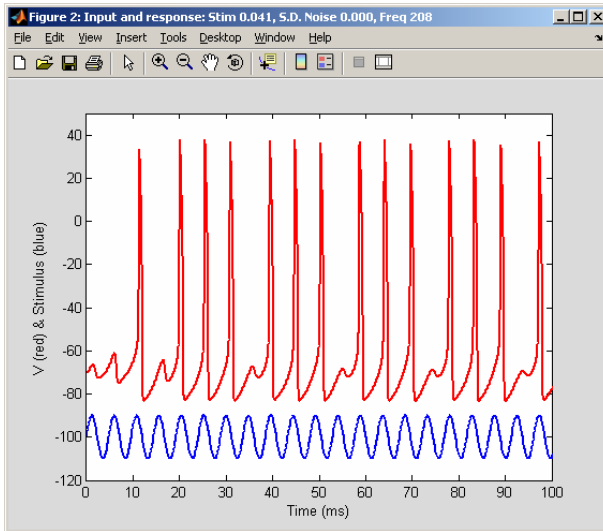
Functional relevance of noisy firing rates



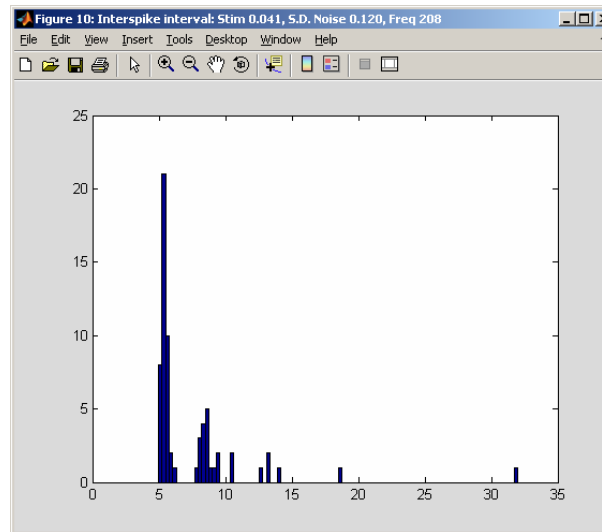
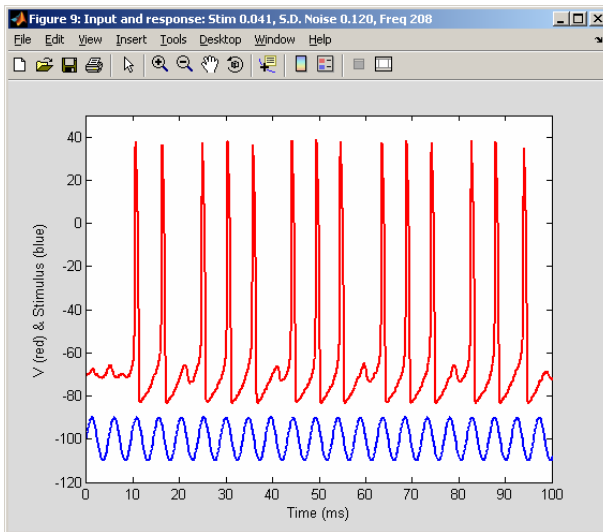
Auditory nerve response to pure tone stimulation, in squirrel monkey

ISI shows that neurons do not fire during every period of the stimulus, but miss periods (with an exponentially decreasing likelihood)

Noisy firing rates improve auditory thresholds



Threshold to produce a spike train without noise is about 0.041.



With a small amount of noise (s.d.=0.12) the threshold to spike is reduced to about 0.025

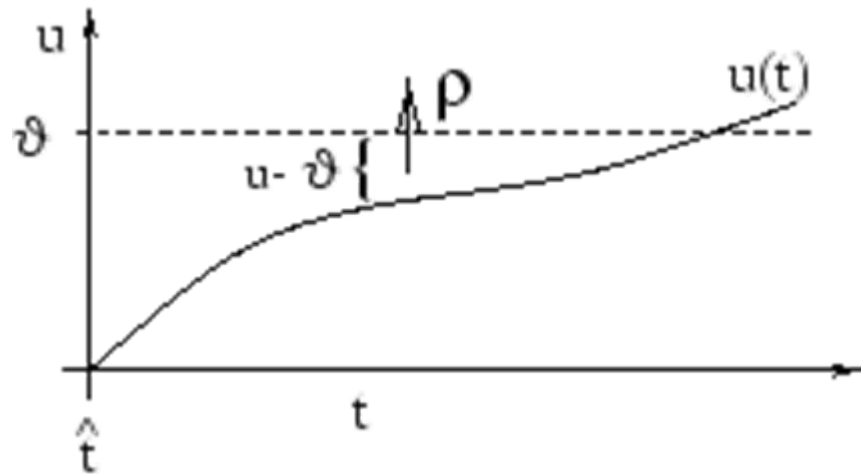
Noise and firing rates

- If the probability density is a function of noise, the distribution of inter-spike intervals will change

Noisy threshold: define our hazard as a function of the distance from threshold

$$\rho(t | \hat{t}) = f[u(t | \hat{t}) - v]$$

The function f defines the “escape rate” that causes “jitter” in the firing threshold



Noisy thresholds

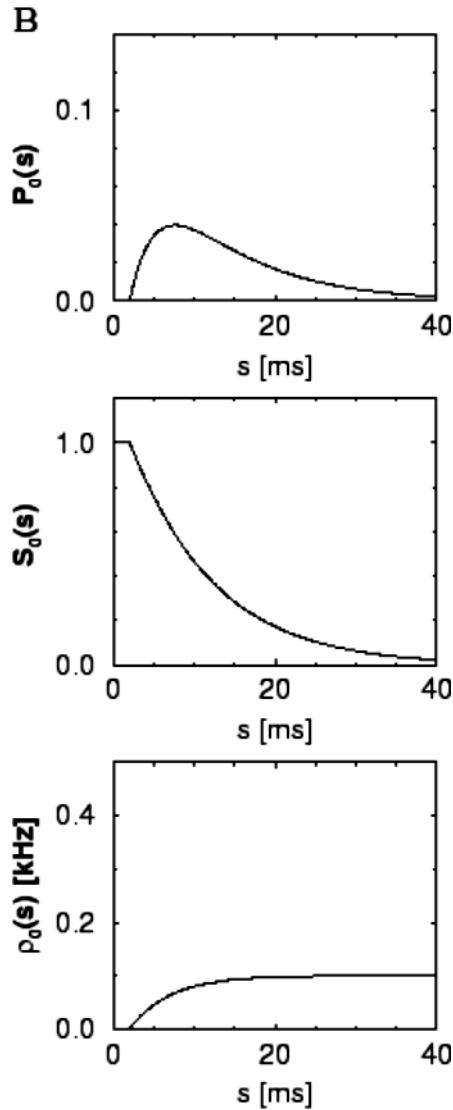
- Consider our leaky integrate-and-fire neuron:

$$I(t) = C \frac{dV(t)}{dt} + \frac{V(t)}{R} \quad \longrightarrow \quad V(t | \hat{t}) = RI_0 \left[1 - \exp\left(-\frac{t - \hat{t}}{\tau_m}\right) \right]$$

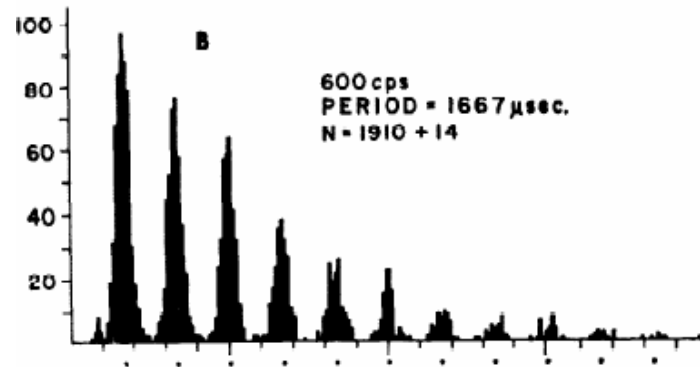
- Assuming a linear escape rate: $\rho(t | \hat{t}) = \beta[u(t | \hat{t}) - v]$

If we let $r = \beta RI_0$ and $\lambda = \tau_m^{-1}$ then for $v = 0$

$$\rho(t - \hat{t}) = r \left[1 - \exp(-\lambda(t - \hat{t})) \right]$$

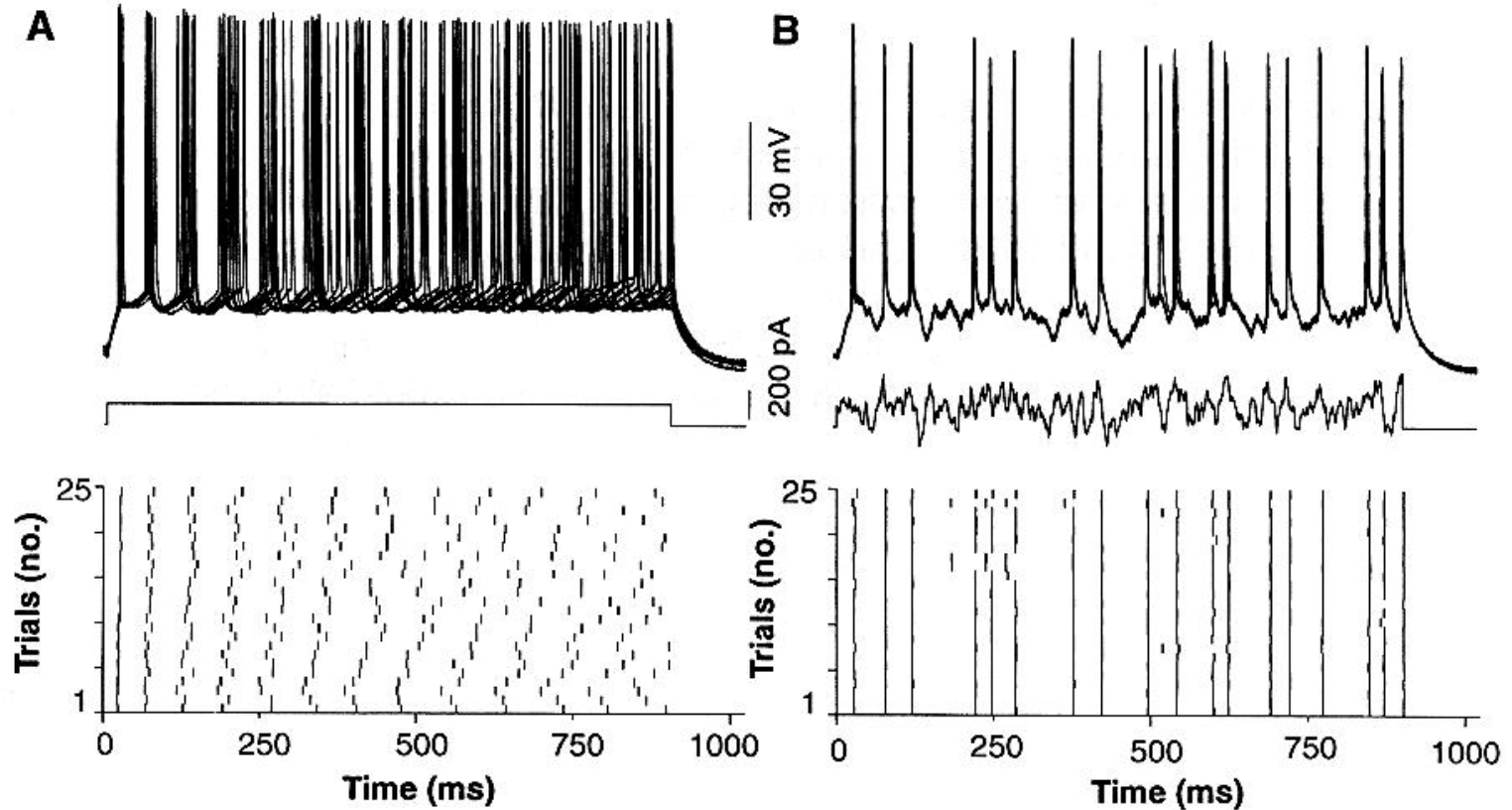


In mammalian auditory neurons, the hazard function increases, after a refractory period, to a constant level



$$\rho(t - \hat{t}) = r \left[1 - \exp(-\lambda(t - \hat{t})) \right]$$

Highly reproducible firing patterns with noisy input

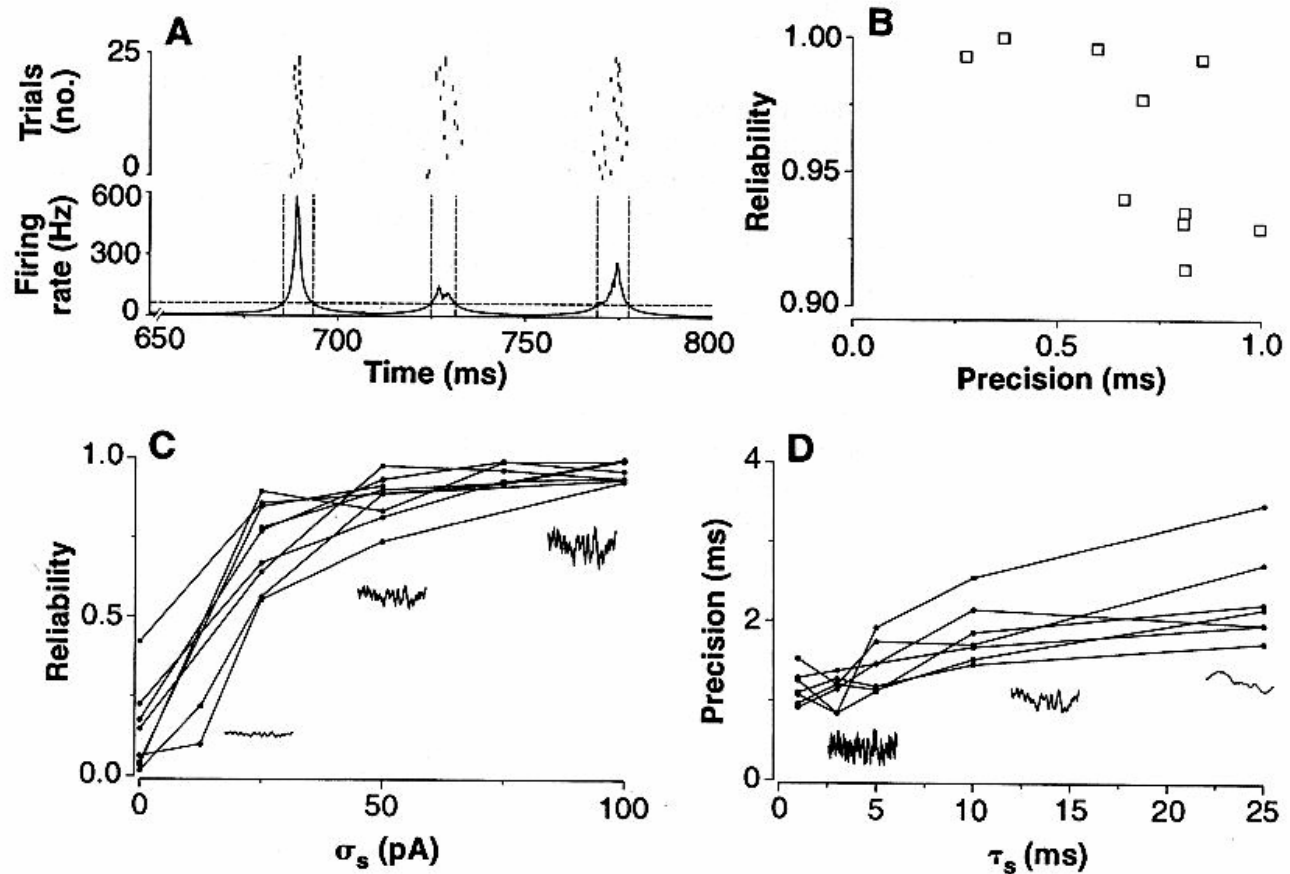


(rat neocortex)

Noisy inputs leads to increased reliability and precision

Reliability: Fraction of spikes occurring in the peri-stimulus region

Precision: S.D. of spike times within the event



Gaussian response of IIF neuron

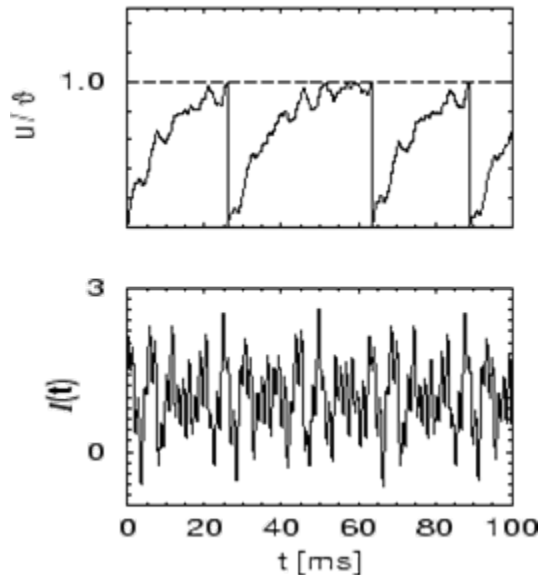
$$C \frac{dV(t)}{dt} = -\frac{V(t)}{R} + I_0 + \xi(t)$$

Langevin equation

Consider a Gaussian additive noise source ξ with probability density

$$P(V | t) = \frac{1}{\sqrt{2\pi\sigma^2 t}} \exp\left(-\frac{V^2}{2\sigma^2 t}\right)$$

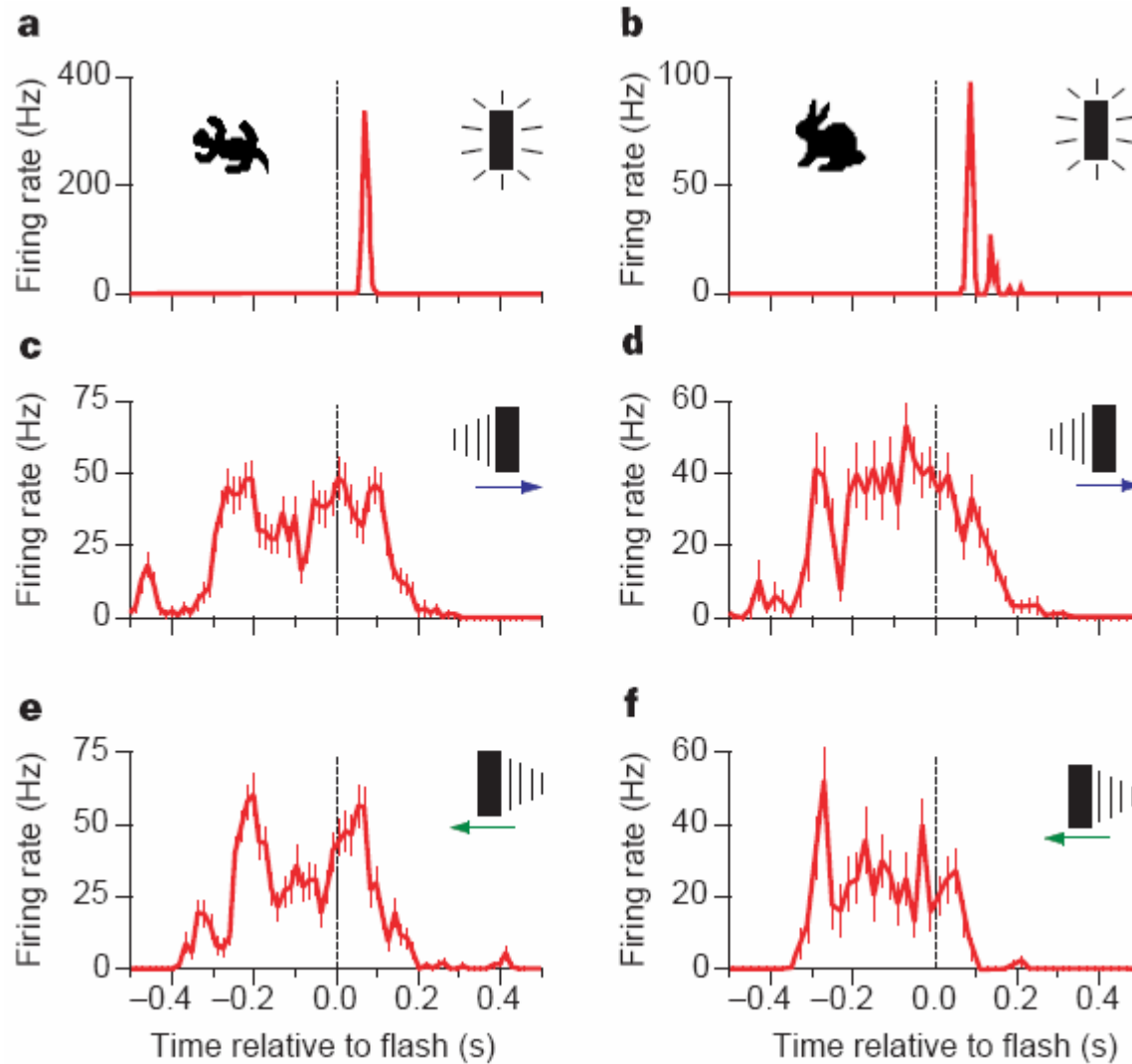
$$\langle \xi(t) \rangle = 0$$



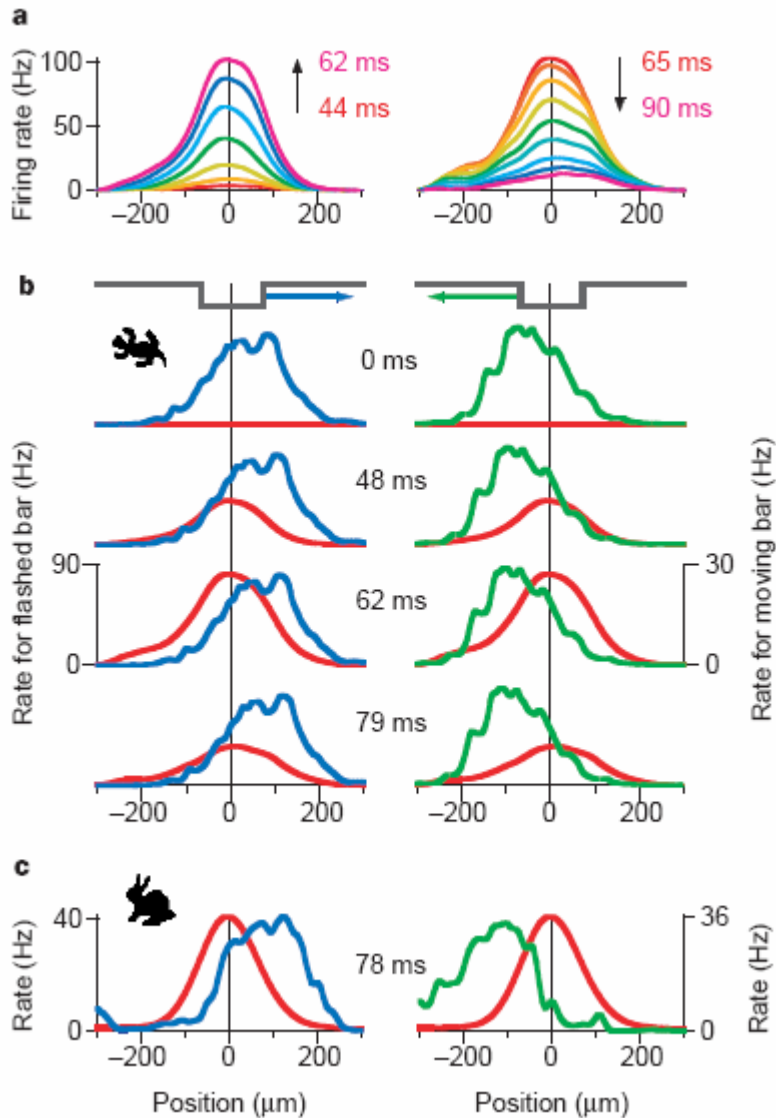
Understanding neuronal responses to stimuli

- We'd like to be able to characterize the properties of the neuronal firing patterns using well-understood statistical methods
 - Allows us to examine how different stimuli change the behavior
 - Allows us to predict a response to new stimuli
- In order to do this, we must
 - Pick an encoding (e.g. firing rate, interval distribution, etc.)
 - Characterize it appropriately to derive characteristic properties

Motion Anticipation: Single neuron response to stimulus



Population 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 100 μm .