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System Bioengineering II: Neurosciences

Essentials of Neural Coding

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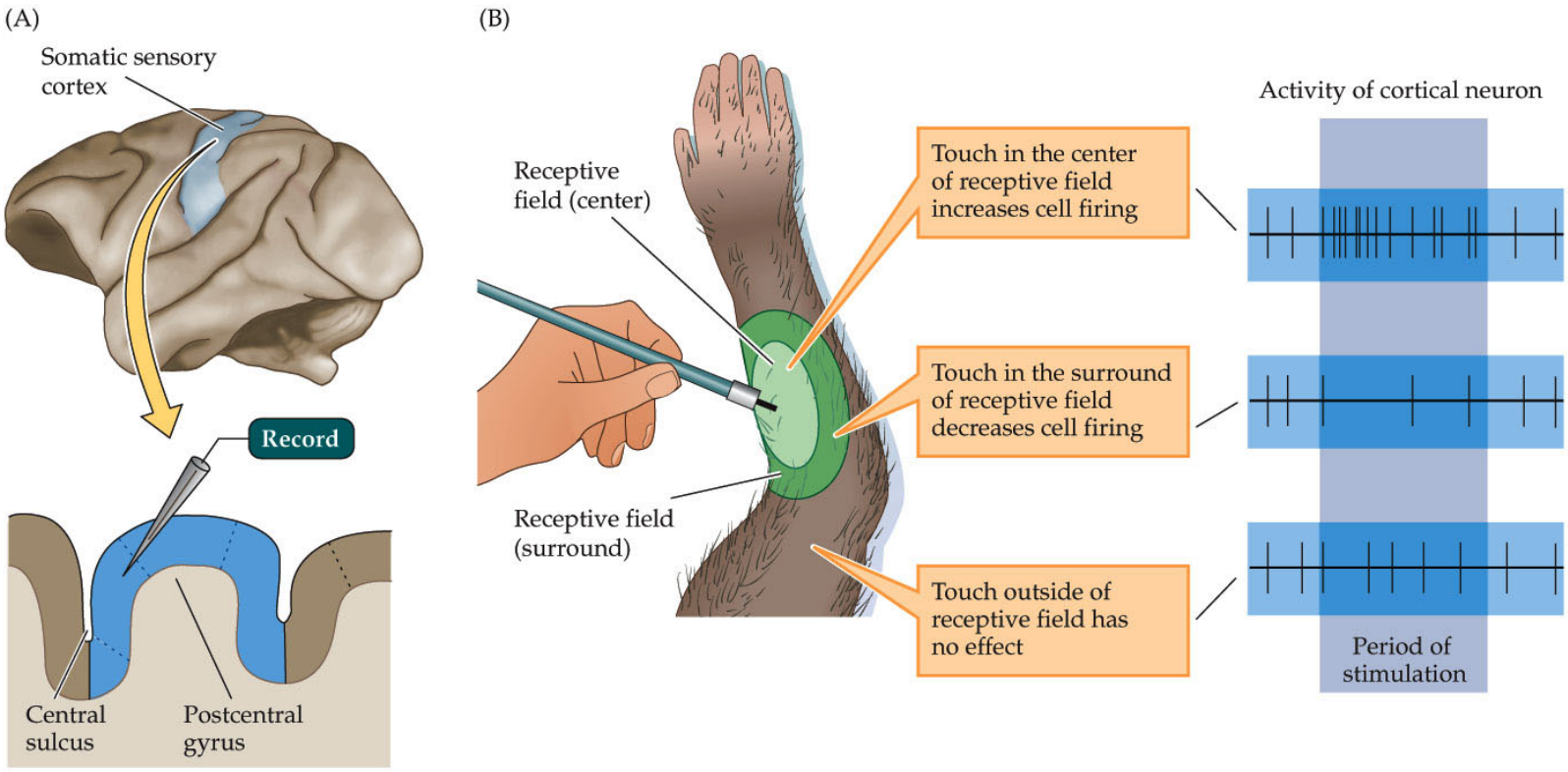
Neural representation of sensory signals and the concept of “receptive field”

Figure 1.13 Single-unit electrophysiological recording from cortical pyramidal neuron

- How to study neural correlates of behaviors?



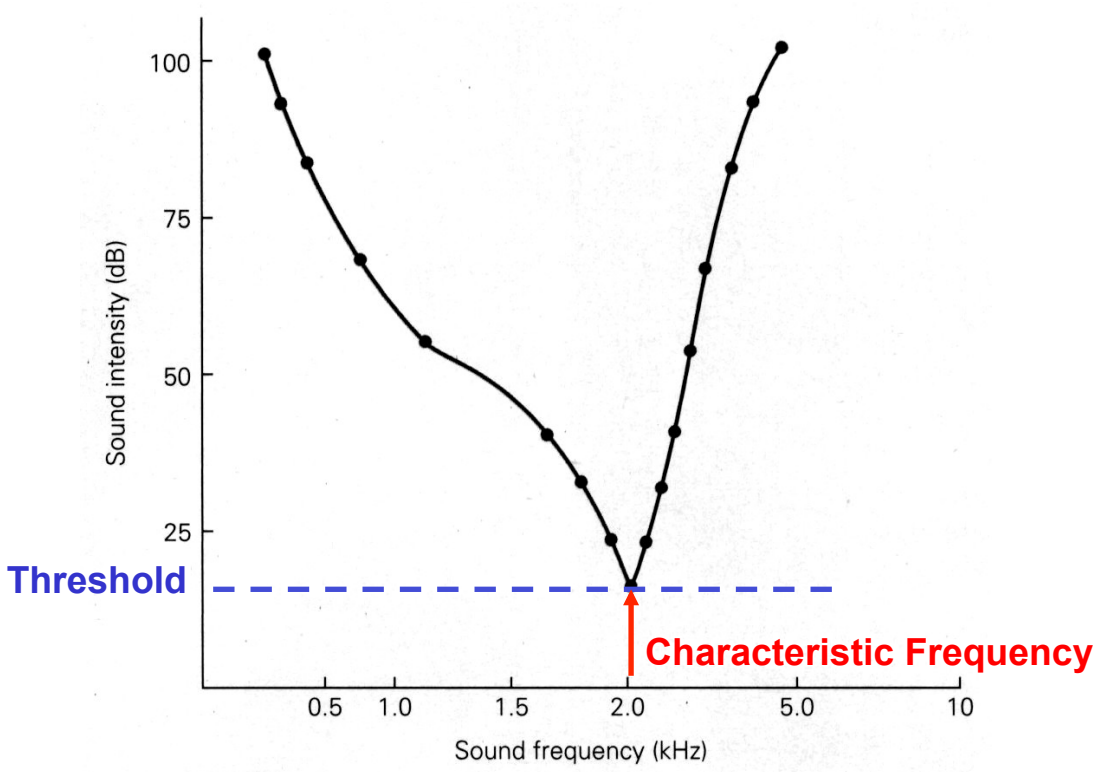
"Receptive field"

***NEUROSCIENCE, Fourth Edition,* Figure 1.13**

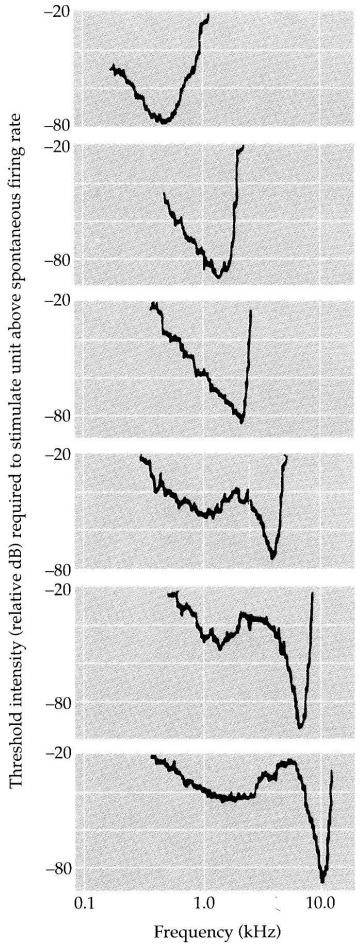
Each receptor responds to a narrow range of stimulus energy

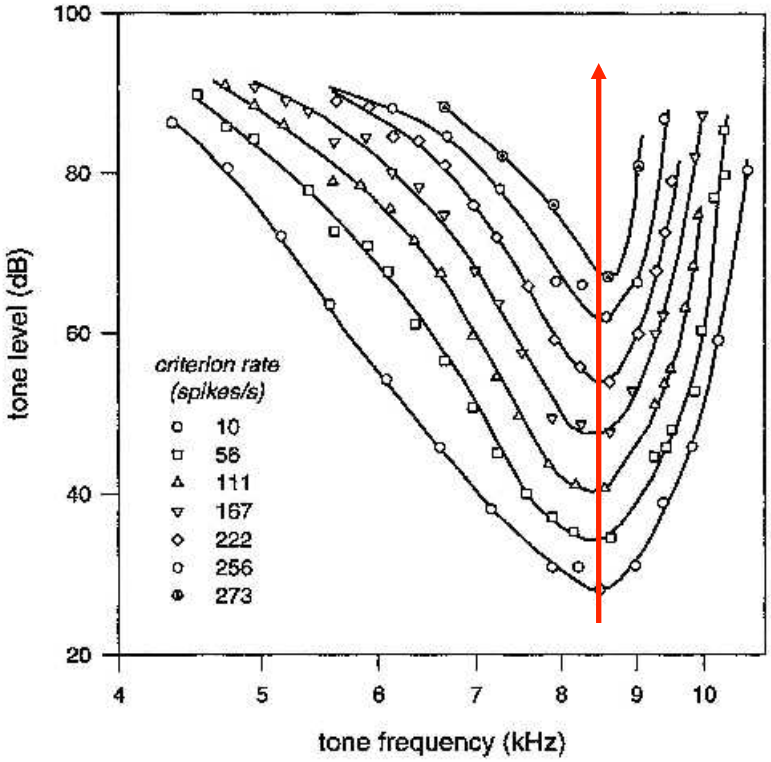
Each receptor responds to a narrow range of stimulus energy. Tuning curves of sensory receptors measure the minimum amplitude of stimulation needed to activate a sensory receptor over a range of stimulus energies. Each sensory receptor responds optimally to a narrow range of intensities of a single type of energy. The tuning curve shown here is for an auditory receptor most sensitive to sound at 2.0 kHz Higher and lower frequencies require stronger amplitude stimuli to evoke a response from the receptor. The tuning curve also illustrates the range of stimulus energies that can excite the receptor when presented at a given intensity In this example, as the loudness of the tone rises, the receptor responds to a greater range of auditory frequencies. However, the receptor provides a stronger response at the preferred frequency than at other frequencies. Graded responses over the energy band- width provide a mechanism for sensory neurons to signal the particular type of stimulus energy that is presented. The auditory system tunes receptors in distinct parts of the sensory epithelium to different frequencies of sound. The relative response amplitude of these receptors to tones signals the sound frequency.

Tuning curve (receptive field) of an auditory neuron



The size of RF depends on the threshold criterion



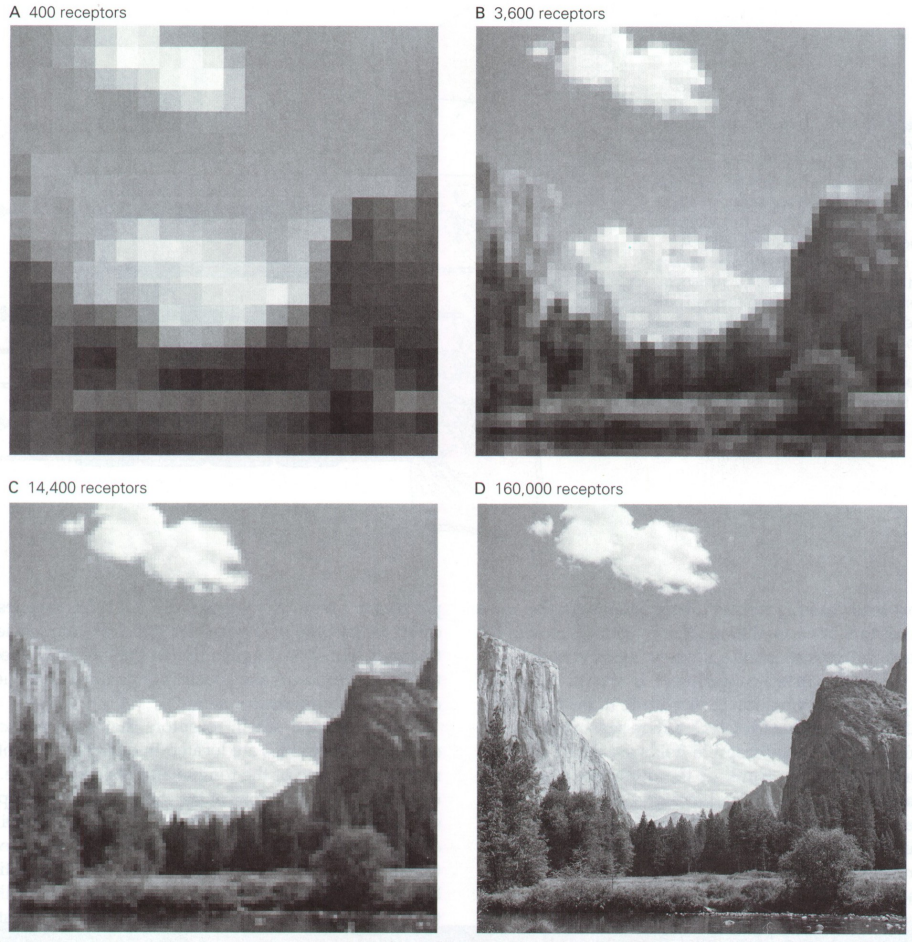


(left) Examples of RF of auditory-nerve fibers tuned to different frequencies. (right) RF of an auditory-nerve fiber defined by different criterion rates. Higher criterion rate results in smaller RF size.

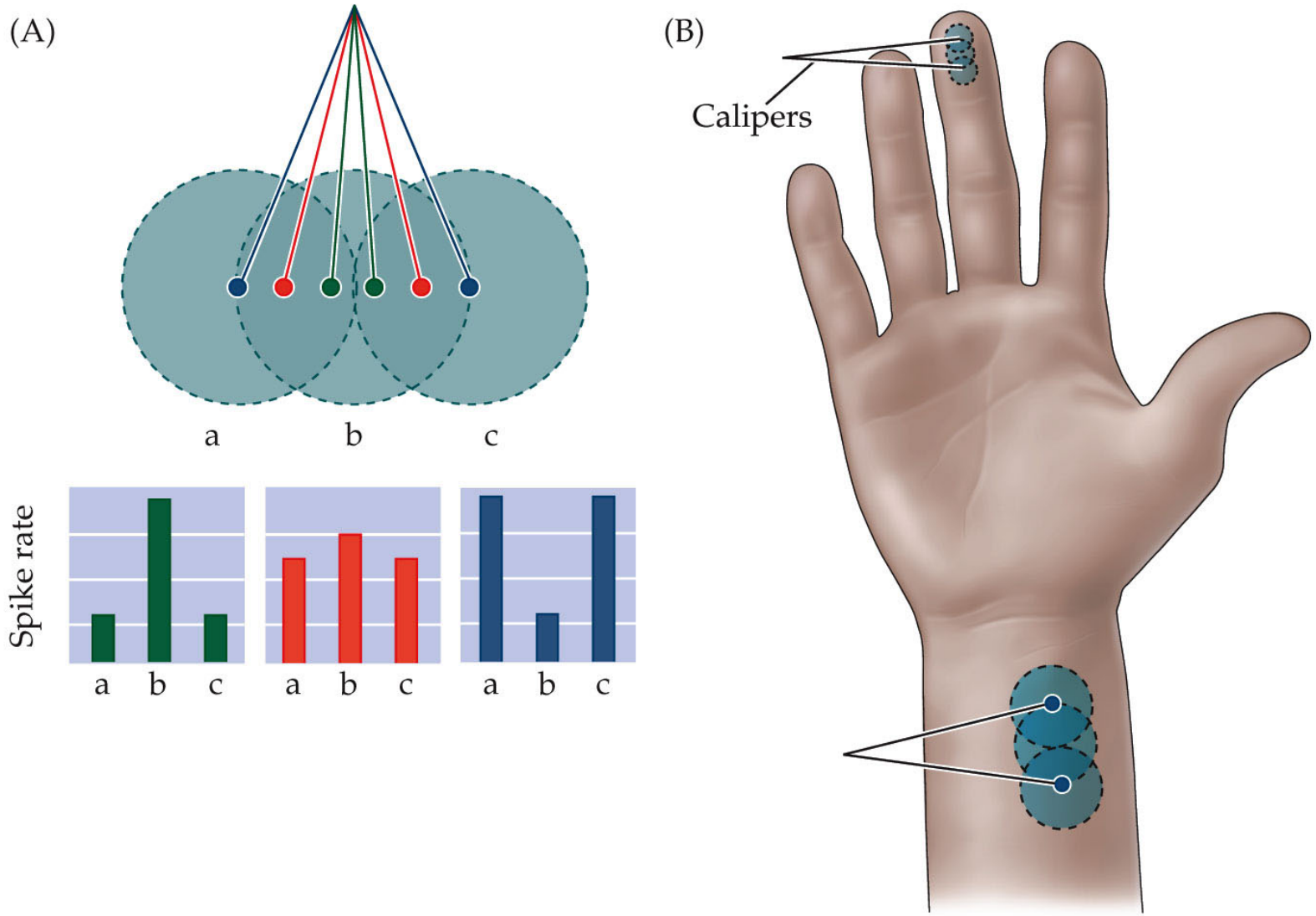
The density of sensory receptors and the size of receptive field determine the resolution of sensory systems

The density of sensory receptors in the retina and the size of the receptive field for each receptor deter- mine the resolution of a visual image. Each square or pixel in these images represents a receptive field. The gray scale is proportional to the average light intensity in that region of the image. White pixels represent receptors with the highest firing rate, while black pixels represent receptors with the lowest firing rate. If there are a small number of receptors and each spans a large area of the scene, the result is a fuzzy, very schematic representation of the scene (**A**). There is no cue from this representation what the picture actually shows. As the density of receptors increases, and the size of the receptive field of each receptor decreases, the spatial detail be- comes clearer (**B-D**). Clouds, mountains, trees, grasslands, and water emerge, until the scenery is identifiable as Yosemite valley. However, the increased resolution comes at the cost of enlarging the total size of the receptor population.

The brain resolves the conflict between information over-load from a huge number of receptors and the need for resolution of spatial detail by having a higher density of receptors in regions of the body where high resolution of detail is behaviorally important and using progressively lower numbers of receptors in surrounding regions. Spatial resolution for vision and touch parallels the density of receptors in the retina and skin. Spatial resolution on the finger-tips approaches that of the image in **D**. Receptor density and tactile sensitivity on the palm is similar to the resolution in **C**. Resolution of spatial detail on the forearm approaches that in image **B**, while on the trunk it is similar to that in image **A**.

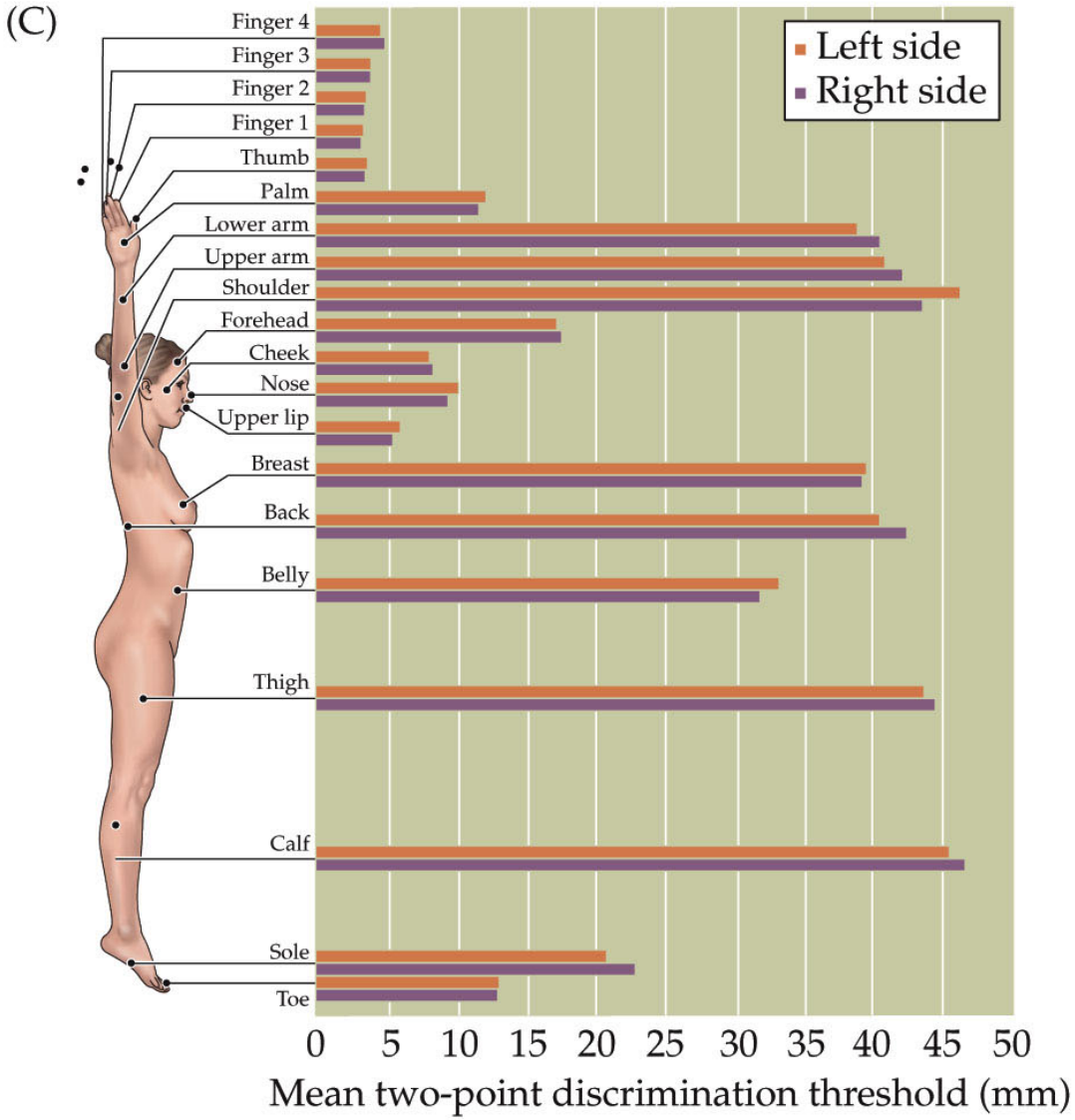


Receptive fields and two-point discrimination threshold (Part 1)



***NEUROSCIENCE, Fourth Edition,* Figure 9.3 (Part 1)**

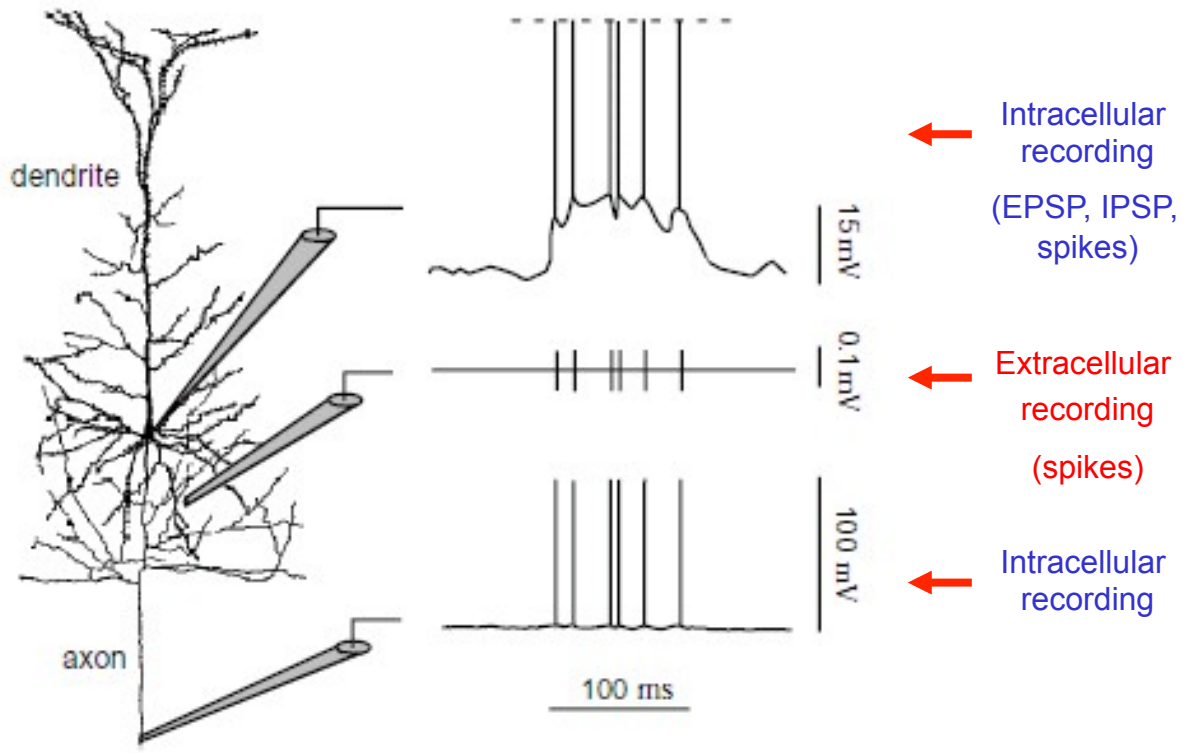
Receptive fields and two-point discrimination threshold (Part 2)



***NEUROSCIENCE, Fourth Edition,* Figure 9.3 (Part 2)**

Neural coding by sequences of action potentials (“spike trains”)

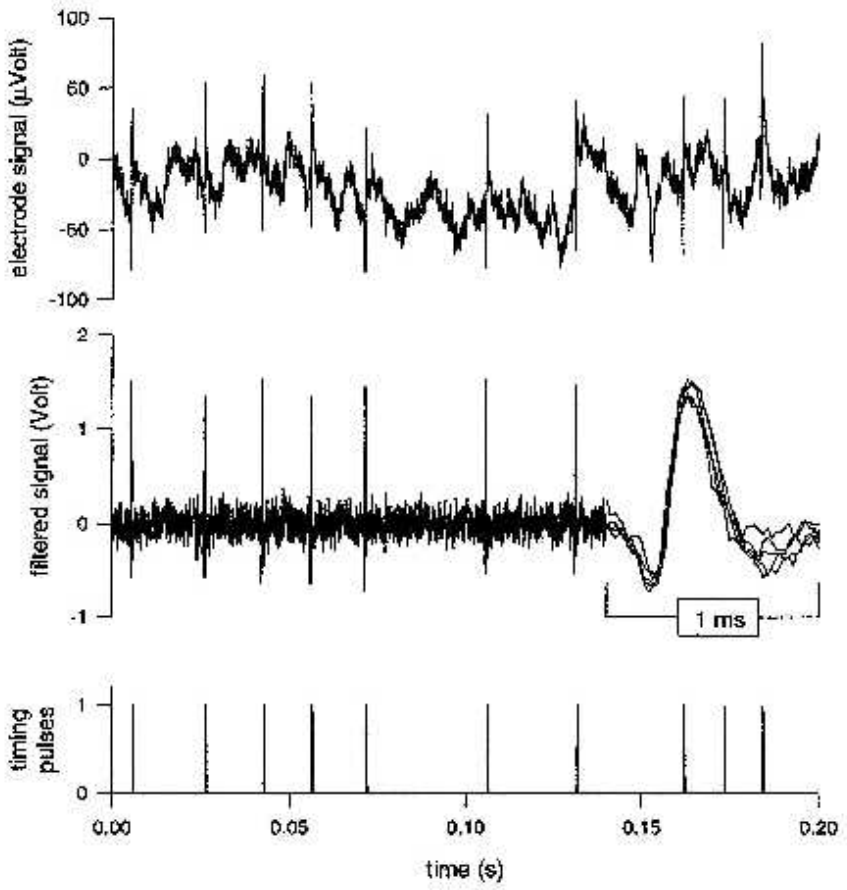
Three simulated recordings from a neuron



In vivo (e.g., intact brain) vs. ***in vitro*** (e.g. brain slice, isolated neurons)

The top trace represents a recording from an intracellular electrode connected to the soma of the neuron. The height or the action potentials has ban clipped to show the subthreshold membrane potential more clearly. The time scale is such that the action potential trajectory cannot be resolved. The bottom trace represents a recording from an intracellular electrode connected to the axon some distance away from the soma. The full height of the action potentials is indicated in the trace. The middle trace is a simulated extracellular recording. Action potentials appear as roughly equal positive and negative potential fluctuations with an amplitude of around 0.1 mV. This is roughly 1000 times smaller than the approximately 0.1 V amplitude of an intracellularly recorded action potential

All-or-none coding by action potentials

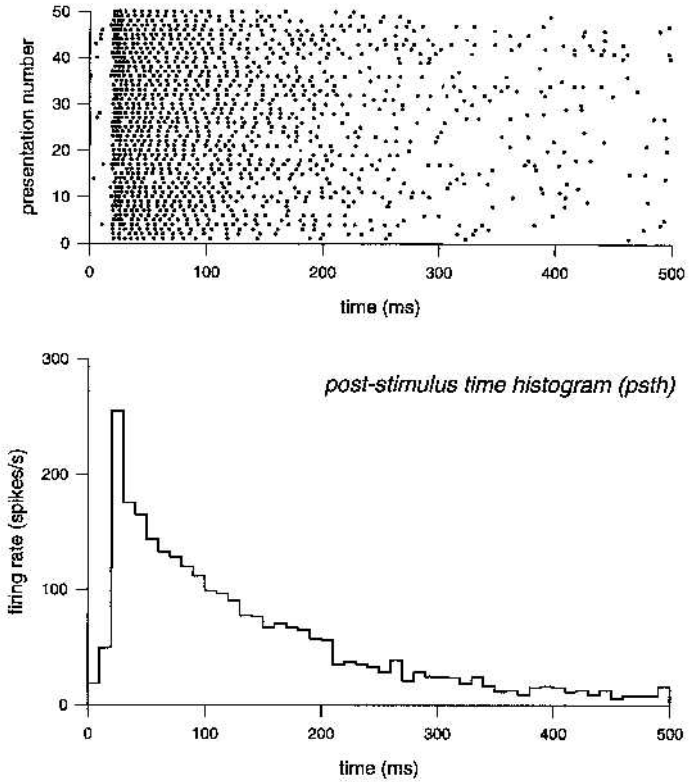


Raw data

Filtered data

Spike train

Each action potential generated by the cell has a similar shape. Thus action potentials are the elementary units of the neural code. The top panel shows the difference between the voltage recorded with a fine tungsten wire placed near a cell in the fly's brain and that recorded with a reference electrode placed in the body fluid. The middle panel shows the same voltage after band-pass filtering to separate the relatively high frequency components in the action potential from low frequency noise; after filtering, the shapes of individual action potentials are quite similar. At the right, five action potentials are shown overlaid on an expanded time scale. This gives an impression of the shape and of the reproducibility of the time course. The bottom panel shows timing pulses generated electronically by a threshold discriminator circuit.



Dot raster

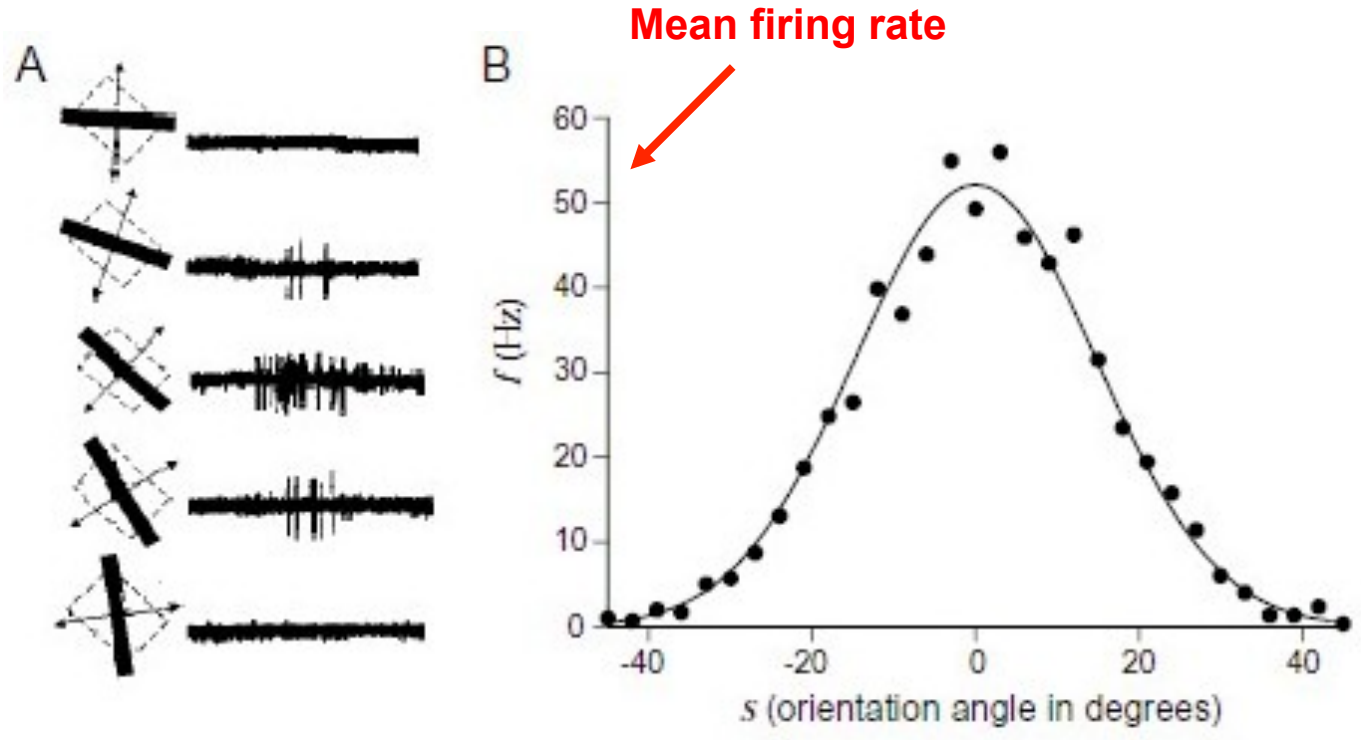
Post-stimulus histogram (PSTH)

Variability of neural responses and construction of the average response. The top panel shows a raster plot of 50 individual spike trains in response to a stimulus at t = 0. Each dot in the raster plot marks the time of occurrence of a single spike. In this case, spikes are recorded extracellularly from the movement sensitive neuron H1 in the fly visual system. The visual pattern seen by the fly makes a step motion at t = 0, creating a brief impulse of nonzero angular velocity. We see that the spike trains in response to repeated presentations of the same stimulus are not identical. A count of the average number of spikes in each bin (10 ms in this case) following stimulus presentation, and normalization to the number of presentations and the bin size, produces the post-stimulus time histogram, or path, shown in the bottom panel. Normalized in this way, the path gives the firing rate-or probability per unit time of firing r(t)- a function of time. The delay before the peak in the firing rate is due to delays in the visual receptors and in the synapses between the receptors and H1.

Response measures of spike trains:

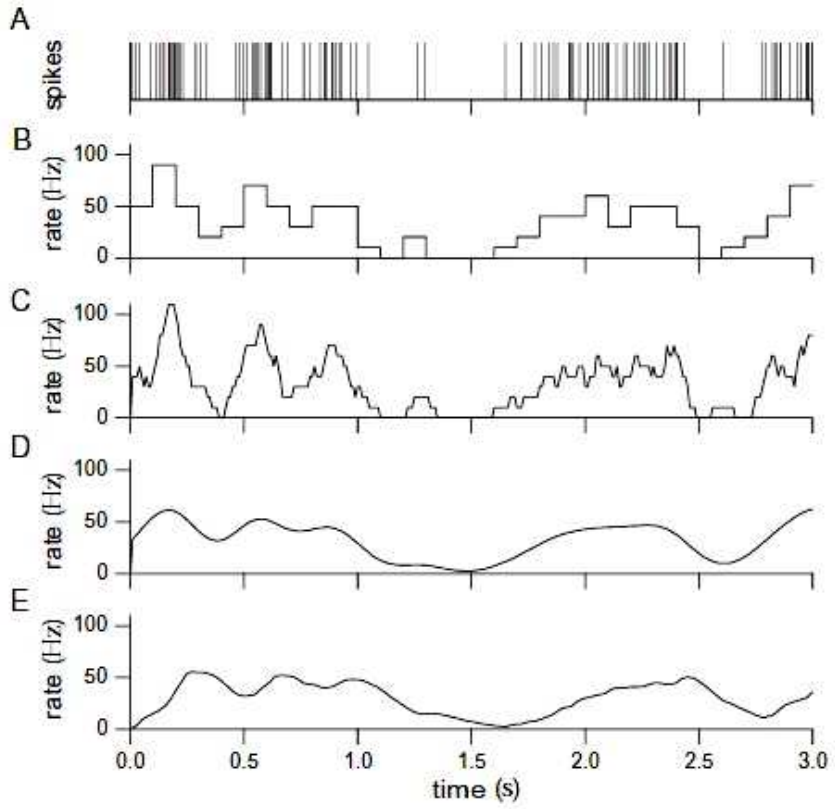
- Mean firing rate
- Post-stimulus histogram (PSTH)
- Period histogram
- Inter-spike interval (ISI) histogram

Firing rate as a measure of a neuron's stimulus selectivity



Firing rate as a measure of a neuron's stimulus selectivity. (A) Recordings from a neuron in the primary visual cortex of a monkey. A bar of light was moved across the receptive field of the cell at different angles. The diagrams to the left of each trace show the receptive field as a dashed square and the light source as a black bar. The bi-directional motion of the light bar is indicated by the arrows. The angle of the bar indicates the orientation of the light bar from the corresponding trace. (**B)** Average firing of a cat V1 neuron plotted as a function of the orientation angle of the light bar stimulus. The curve is a fit of the data.

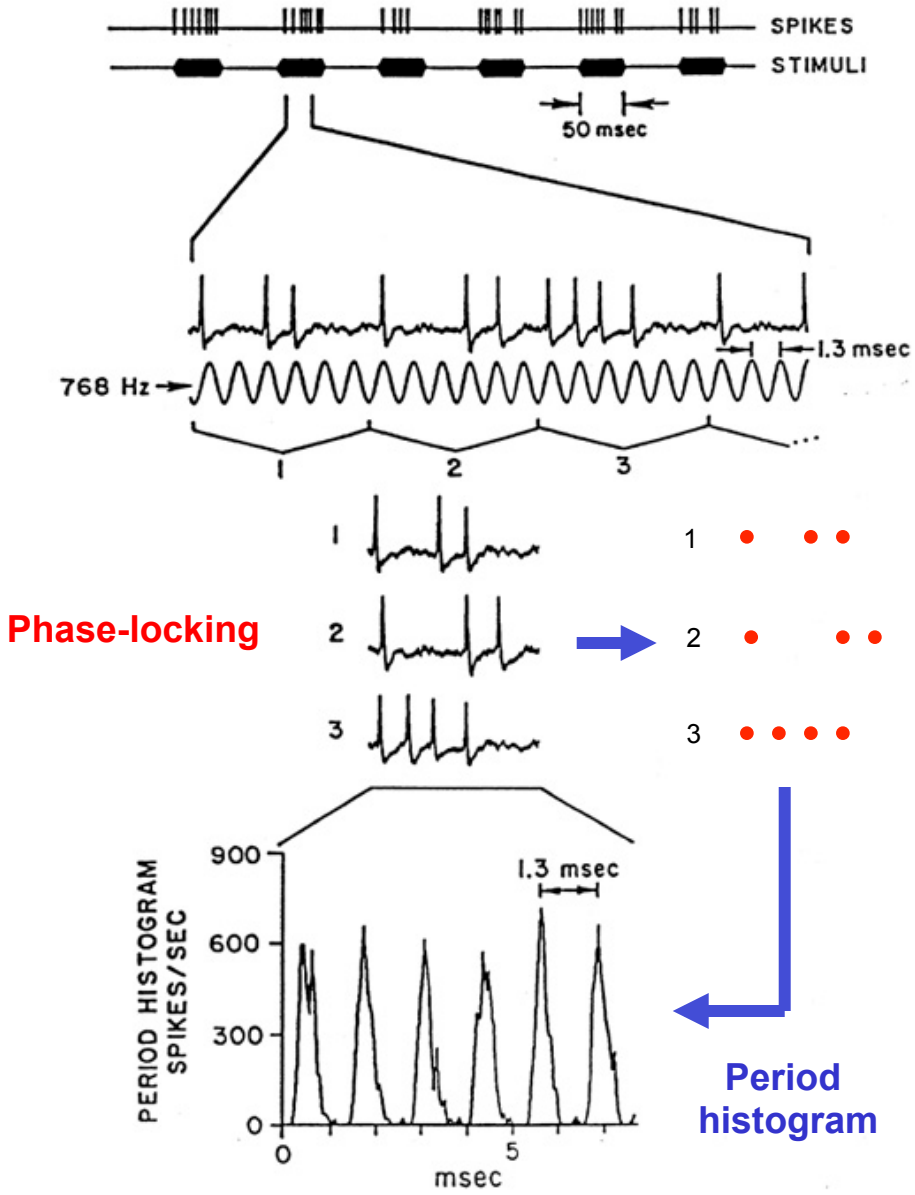
Firing rates approximated by different procedures



A) A spike train from a neuron in the inferior temporal cortex of a monkey recorded while the animal watched a video on a monitor under free viewing conditions. B) Discrete time firing rate obtained by binning time and counting spikes with Δt=100 ms. C) Approximate firing rate determined by sliding a rectangular window function along the spike train with Δt=100 ms. D) Approximate firing rate computed using a Gaussian window function with Δt=100 ms. E) Approximate firing rate for an α window with $1/\alpha$ = 100 ms.

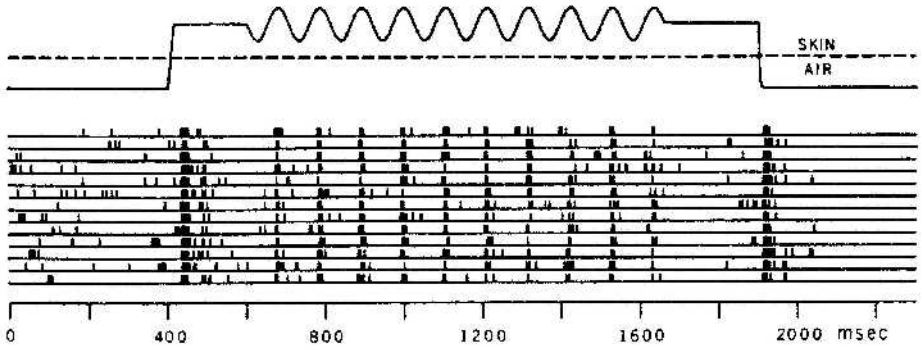
Temporal Structure of Spike Trains

This figures illustrates a phenomenon called "phase-locking" and how to characterize it using the *period histogram*. When burst of tone of a given frequency (represented by the black bars) 50 msec in duration are presented to the ear, auditory-nerve fibers respond with an increase in firing rate of spikes. On an expanded time scale we can see individual cycles of the tone as well as the spikes in more detail. When a spike occurs it always occurs at about the same point (or phase) in the tone cycle. We call this alignment of spikes "phase-locking". We get a quantitative measure of phase-locking as follows: We extract short segment of the spike train (six stimulus cycles long in this case, although the number of cycles used is arbitrary); we line the segments up so tat their starting points coincide. From many such segments (say a total of 5 seconds of spike train record) we construct a histogram of the times when the spikes occur relative to the waveform of the stimulus over a 6-cycle period. This histogram is called a "period histogram" because the response is aligned with the stimulus periods. Phase-locking is shown by the peaks in the period histogram which occur once each stimulus cycle (every 1.3 msec here, corresponding to a frequency of 768 Hz).



Phase-locking in the discharges of somatosensory neurons

Composite showing stimulus pattern, replicas of several individual responses, and examples of the four basis methods of analysis. Stimulus-pattern and spike train replicas share the same time axis (top). The stimulus probe, initially in the air above the skin, is moved to indent the skin 500 um and then after a 200-msec delay set into sinusoidal movement for a period of 1 sec. After a further 300-msec delay the probe is removed from the skin. Typically this procedure is repeated 16 times at a rate of one presentation each 5 sec before the sine-wave frequency and/or amplitude is changed. All other parameters are fixed. Transient discharges at onset and removal of the step stimulus are typical of quickly adapting neurons. For the histogram analyses shown in this figure only data collected during actual sinusoidal stimulation are used. Note that the period of the stimulating sine wave is approximately 105 msec. This defines the rightmost meaningful bin in the period histogram (also referred to as the cycle histogram). The multiple discharges seen in the impulse-train replicas is characteristic of the responses to very low frequency sinusoidal stimulation. It obscures the representation of the period of the stimulating since wave and its subharmonics which are frequently seen in inter-spike interval histograms.



Inter-spike Interval histogram

Period histogram

Phase-locking in a spike train can be quantified by synchronization index or vector strength

Method-1:

$$VS = \frac{1}{n}\sqrt{x^2 + y^2} \quad x = \sum_{i=1}^{n} \cos\,\theta_i \quad y = \sum_{i=1}^{n} \sin\,\theta_i \quad \theta_i = 2\pi\frac{t_i}{T}$$

where n is the total number of spikes, t_i is the time of spike occurrence and T is the period of the stimulus, VS is the vector strength.

Method-2:

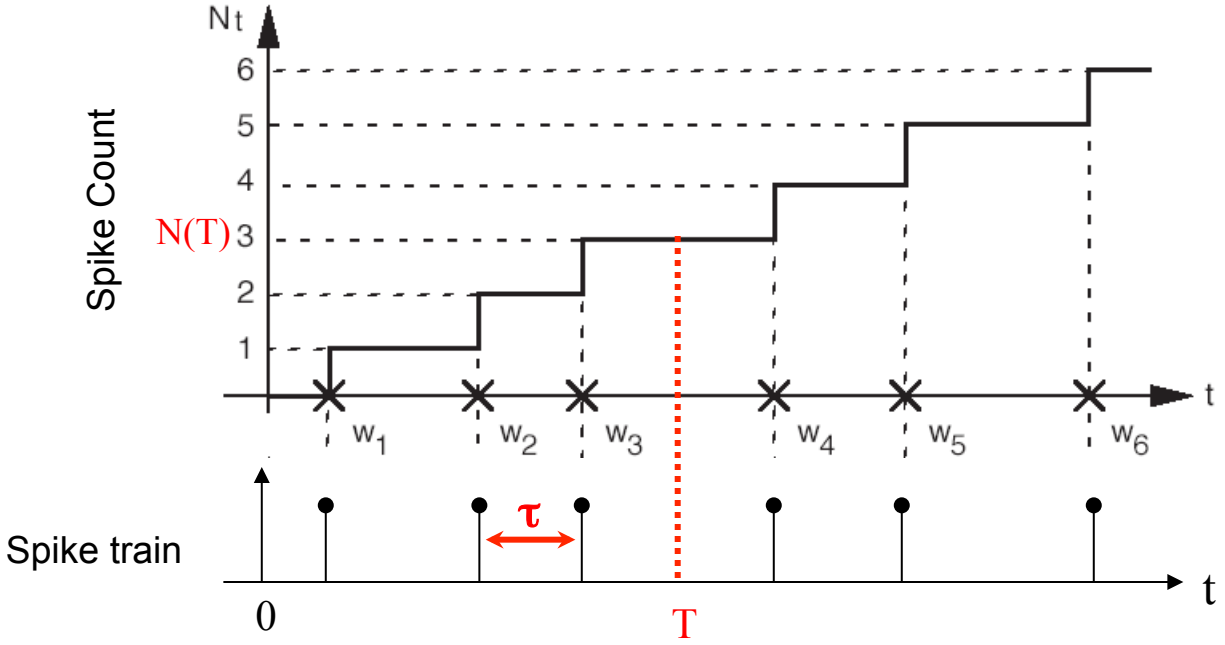
- Find the magnitude of the power spectrum component R(f_0) at stimulus frequency (f_0 =1/T), and then normalize R(f_0) by average discharge rate of the spike train R(0).

Synchronization Index = R(f_0) / R(0)

Spike trains can be modeled as a Poisson process

Spike count: Poisson distribution

$$P(N_T=n) = [(\lambda T)^n/n!] * \exp(-\lambda T)$$



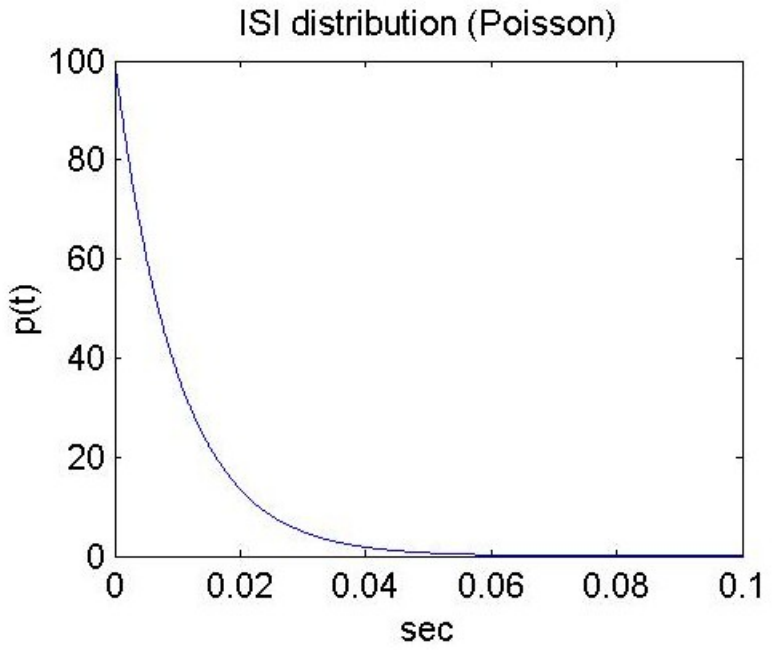
Inter-spike interval (ISI): Exponential distribution

$$p(\tau) = \lambda * \exp(-\lambda\tau)$$

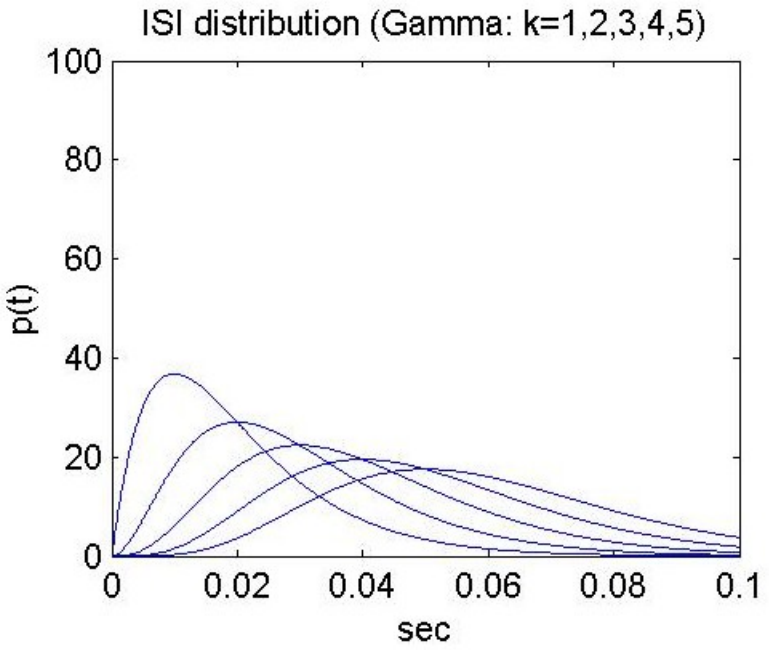
This figure illustrates that a spike train can be modeled as a Poisson processing. There are two equivalent ways to characterize a Poisson process, as a counting process (Poisson distribution) or as an interval process (exponential distribution). The latter is often more convenient for analyzing spike trains.

Refractory periods modify the Poisson process model

$p(\tau) = \lambda \exp(-\lambda\tau)$



$p(\tau) = \lambda(\lambda\tau)^k \exp(-\lambda\tau)/k!$

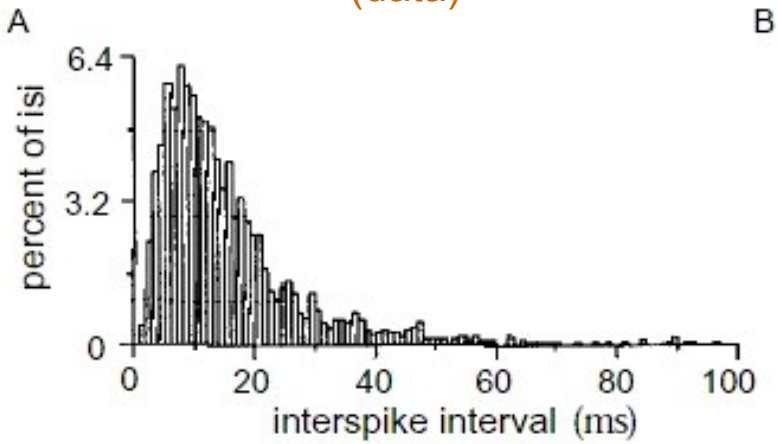


Inter-spike-interval (ISI) distributions for homogeneous Poisson process with exponential function (*left*) and for modified Poisson processes with Gamma functions (*right*).

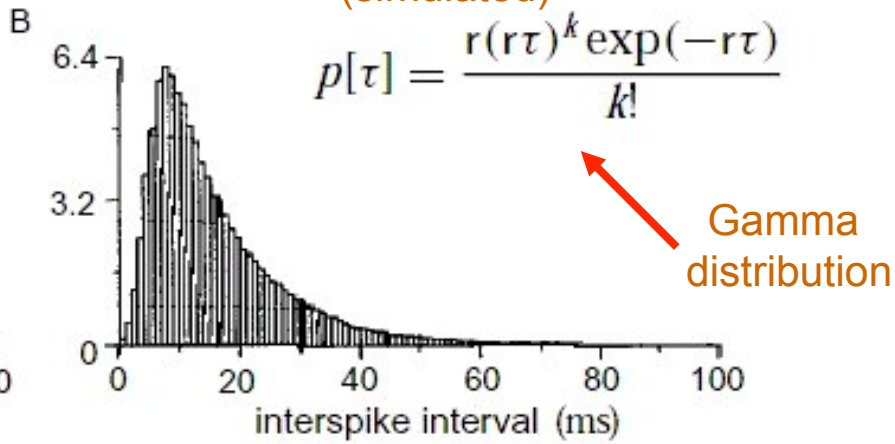
Refractory periods modify the Poisson process model (cont.)

Real world:

ISI histogram
(data)



ISI histogram
(simulated)



$$p[\tau] = \frac{r(r\tau)^k \exp(-r\tau)}{k!}$$

Gamma distribution

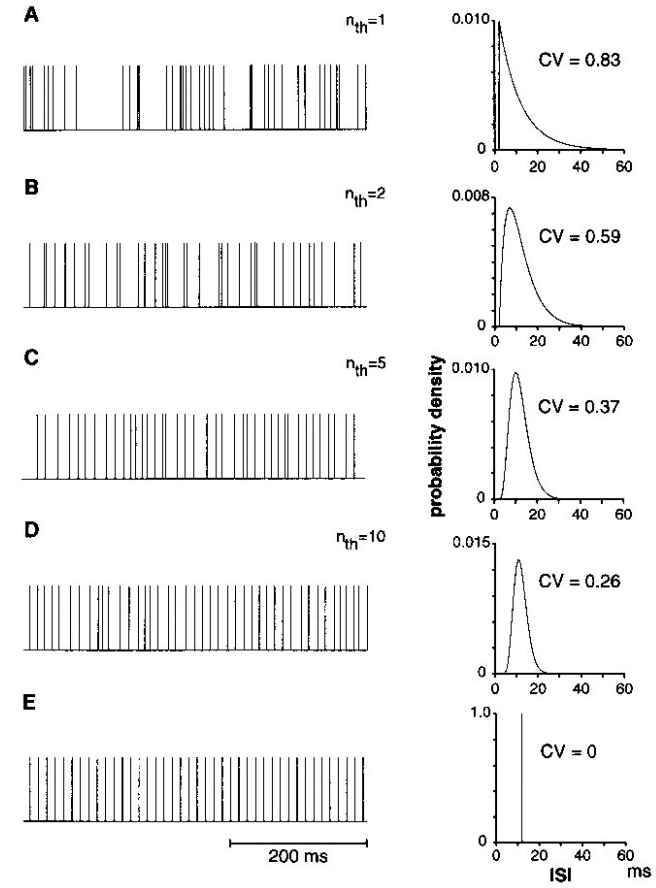
(**A**) Inter-spike interval distribution from a visual neuron responding to a moving random dot image. The probability of inter-spike intervals falling into the different bins, expressed as a percentage, is plotted against inter-spike interval. (**B**) Inter-spike interval histogram generated from a Poisson model with a stochastic refractory period.

The randomness of a spike train can be quantified by Coefficient of Variation (CV) analysis.

$CV = \sigma(\tau) / E(\tau)$

Poisson process:

$E(\tau) = 1/\lambda$
$\sigma^2(\tau) = 1/\lambda^2$
$CV = 1$



Sample spike trains and inter-spike interval (ISl) distributions from various models in response to a constant current input into a perfect integrator model. All models have an absolute refractory period of 2 msec and a mean firing rate of 83 Hz. (A) Poisson-distributed (i.e., exponential) random voltage threshold yields the most irregular spike train and an exponential ISI distribution. In the absence of a refractory period, CV would be 1. (B-D) Gamma-distributed random thresholds of order 2, 5, and 10 yield increasingly regular ISI distributions, which are gamma-distributed of order 2, 5, and 10, respectively. (E) Integrate-and-fire model yields a perfectly regular spike train.

How to simulate a Poisson process?

General Method:

If u is a random variable of uniform distribution [0, 1], and $F(t)$ is the probability distribution function of random variable τ, then

$w=F^{-1}(u)$ is a random variable with probability distribution function $F(t)$.

Poisson process:

$$F(t) = 1 - exp(-\lambda t)$$

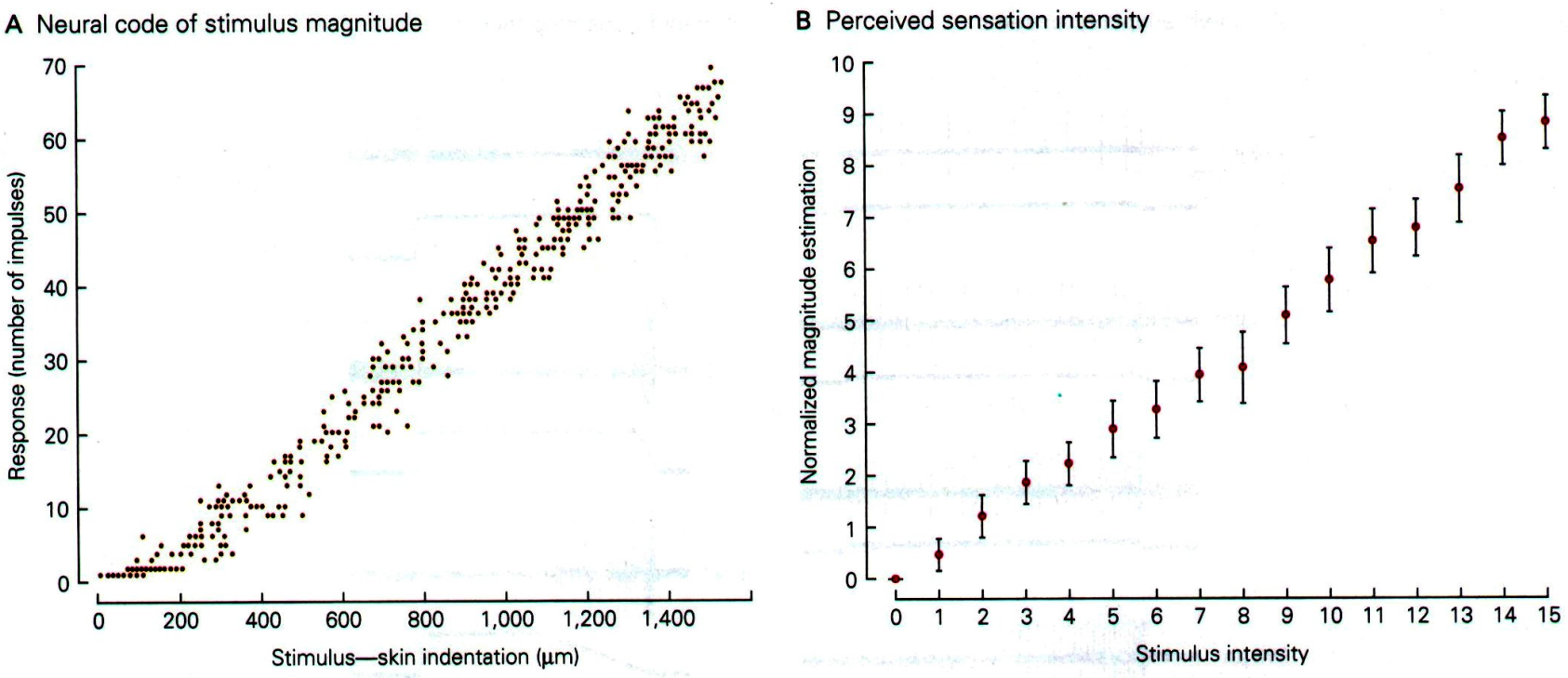
$$w = F^{-1}(u) = -1/\lambda * ln(1-u)$$

Response measures of spike trains:

- Mean firing rate (spikes/second)
- Post-stimulus histogram (PSTH)
- Period histogram
- Inter-spike interval (ISI) histogram

Studying neural basis of behaviors using neurophysiology and psychophysics

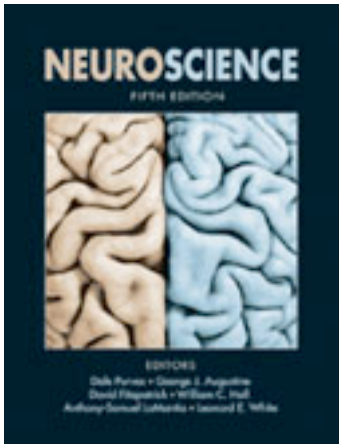
An example



The firing rates of sensory nerves encode the stimulus magnitude.

A. The number of action potentials per second in a slowly adapting mechanoreceptor action the amount of skin indentation. This receptor required a minimum indentation of 80 um to respond. The relationship between increases in frequency of firing and pressure or the skin is linear.

B. Estimates made by a human subject of the magnitude of sensation produced by pressure on the hand increase linearly as a function of skin indentation. The relation between a subject's estimate of the intensity of the stimulus and its strength resembles the relation between the discharge frequency of a sensory neuron and the stimulus strength. These data suggest that the neural coding of stimulus intensity is faithfully transmitted from the peripheral receptors to the cortical centers that mediate sensation.



Suggested readings: Sensory Systems

- Somatic sensory system: touch and proprioception (Chapter 9)
- Visual system (Chapters 11, 12)
- Auditory system (Chapter 13)