# Biomedical Signal Processing

## - Spike Train Analysis (2) -

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# Entropy and Information

- Information
  - Daily life → a familiar concept because information exchange (sending and receiving messages) is important
  - Nervous system → need a formal definition and preferably a metric quantifying information content
- Shannon's communication system
  - A framework for analyzing the transmission of a message from a source to a destination
  - A set of messages → using <u>entropy</u> of this set to quantify its potential information content
  - Entropy measure
    - Different from the everyday sense of information content
    - Does not capture the information in a single message but merely quantifies the potential information of the ensemble of messages → somewhat strange

# Entropy and Information

- Example
  - Continuously transmitting the same message
    - No need for information to be transmitted or
    - (from a data transmission standpoint) no information sent at all
  - Received message – always the same
    - No reason to receive the message ( ∵ no information)
- Shannon's entropy concept
  - The context of the message in its ensemble and variability → critical for quantifying information content
  - In the analysis of spike trains
    - Commonly consider both the stimulus and the neural response to be drawn from a PDF → making it possible that variability is associated with information

# Entropy and Information

- Entropy measure (1)
  - X: a message consisting of two statistically independent random variables $X_1$ and $X_2$
  - The probability of observing $X_1$ and $X_2$ = the product of the individual probabilities ($p[X_1] \times p[X_2]$)
    - The uncertainty of X or the information conveyed by revealing that message has taken on the values $X_1$ and $X_2$ – dependent on the PDF of $X_1$ and $X_2$
  - Functional S
    - To denote the entropy associated with the observation $X_1$ and $X_2$
    - Information gained from observation $X_1$ – $S\{p[X_1]\}$
    - Information associated with observation $X_2$ – $S\{p[X_2]\}$
    - Information associated with both $X_1$ and $X_2$:

$$S\{p[X]\} = S\{p[X_1, X_2]\} = S\{p[X_1]\} + S\{p[X_2]\}$$

      - The product $p[X_1] \times p[X_2]$ – converted into a sum of entropies
      - Entropy behaves as a logarithm of the distribution

# Entropy and Information

- Entropy measure (2)
  - Intuitive notion
    - Entropy of a system – proportional with the logarithm of the number of its possible states
  - Discrete variable X
    - A spike train response to a stimulus – taking a finite number of possible values $x_1$, $x_2$, …, $x_N$
    - Assumption1: each state – equally likely to occur (i.e., p=1/N)
      - Entropy – proportional to log(N) or –log(1/N)
    - Assumption2: states – not equally probable but occurring with probabilities $p_1$, $p_2$, …, $p_N$ (such that $\sum_{i=1}^{N} p_i = 1$ )
      - Entropy – proportional to $-\sum_{i=1}^{N} p_i \log p_i$
      - Entropy expressed in bits – a base 2 logarithm used: $S = -\sum_{i=1}^{N} p_i \log_2 p_i$ bits
  - Entropy-information quantification approach
    - Information content – established only if the PDF associated with a message is known

# Entropy and Information

- Open interpretation for Shannon's approach when applied to spike trains
  - A reflection of ignorance of neural coding
  - Example: recording of a particular response with $N_1$ spikes
    - Questions:
      - The number $N_1$ – a number drawn from a PDF or not?
      - What PDF assumed ?
      - Is the timing of each spike important ?, or is it just the number $N_1$ that captures the essence of the message?
    - Difficult to answer without knowing how the nervous system processes this particular message
    - The answers to these questions – directly determine the assumed PDF from which our observation is drawn and therefore determines the entropy

# Entropy and Information

- Several possible approaches – $N_1$ spikes in a trace with N bins
  - Example 1 (Fig. 14.5B)
    - N bins → support N+1 spike counts (3 bins → 0, 1, 2, 3 – possible observations)
    - Assumption that each response to be equally likely → entropy (S) = $\log_2(N+1)$ bits
    - Somewhat silly concept because → **$S=\log_2(4)=2$ bits**
      - The result depends on 'the number of bins' which was set arbitrarily
      - It is unlikely that all responses (0~N spikes) are equal
    - Certain choice of interval → **'the number of spike'** – the important message
  - Example 2 (Fig. 14.5C)
    - $N_1$ spikes & assuming that timing is important
      - $N!/(N_1!\ N_0!)$ possible arrangements over the N bins ($N_0 = N-N_1$)
    - Assumption that each arrangement is equally likely → entropy = $\log_2[N!/(N_1!\ N_0!)]$
    - A little less silly concept
      - It still does not account for the fact that the observation of $N_1$ spikes varies
        - The observation of $N_1$ spikes – considered as deterministic
    - Different distributions allowed over the available bins within the given number of spikes → **'the effect of timing'** considered
    - Ex: two spikes in a trace with three bins ($N_1=2$)
      - $3!/(2!1!) = 3$ possibilities
      - Assuming these all equally likely → total entropy = $3 \times 1/3 \times \log_2(3) \approx 1.6$

# Entropy and Information

- Several possible approaches – $N_1$ spikes in a trace with N bins
  - Example 3 (Fig. 14.5A)
    - Observed spike train – drawn from a PDF such as a Poisson or a binomial distribution
    - The number of spikes – not fixed
      - Ex: 0, 1, 2, 3 allowed instead of 2 over 3 bins
    - **The number of spikes** & **their timing** – both important
    - Ex – assuming a binomial distribution (1 or 0 in each bin – equally likely → p=0.5)

$$\text{Count} = 0 \quad \rightarrow \quad \frac{3!}{3!0!}\left(\frac{1}{2}\right)^0\left(\frac{1}{2}\right)^3 = \frac{1}{8} \quad \text{one out of eight cases}$$

$$\text{Count} = 1 \quad \rightarrow \quad \frac{3!}{2!1!}\left(\frac{1}{2}\right)^1\left(\frac{1}{2}\right)^2 = \frac{3}{8} \quad \text{three out of eight cases}$$

$$\text{Count} = 2 \quad \rightarrow \quad \frac{3!}{1!2!}\left(\frac{1}{2}\right)^2\left(\frac{1}{2}\right)^1 = \frac{3}{8} \quad \text{three out of eight cases}$$

$$\text{Count} = 3 \quad \rightarrow \quad \frac{3!}{0!3!}\left(\frac{1}{2}\right)^3\left(\frac{1}{2}\right)^0 = \frac{1}{8} \quad \text{one out of eight cases} \qquad (0! \equiv 1)$$

      - Eight arrangements – equally likely → total entropy:

$$S = -\sum_{i=1}^{8} p_i \log_2 p_i = -8 \times \frac{1}{8}\log_2\frac{1}{8} = \log_2 8 = 3 \text{ bits}$$

      - A single, particular sequence → (total number of bits × the probability of that single scenario) information: 3 × 1/8 bits of information

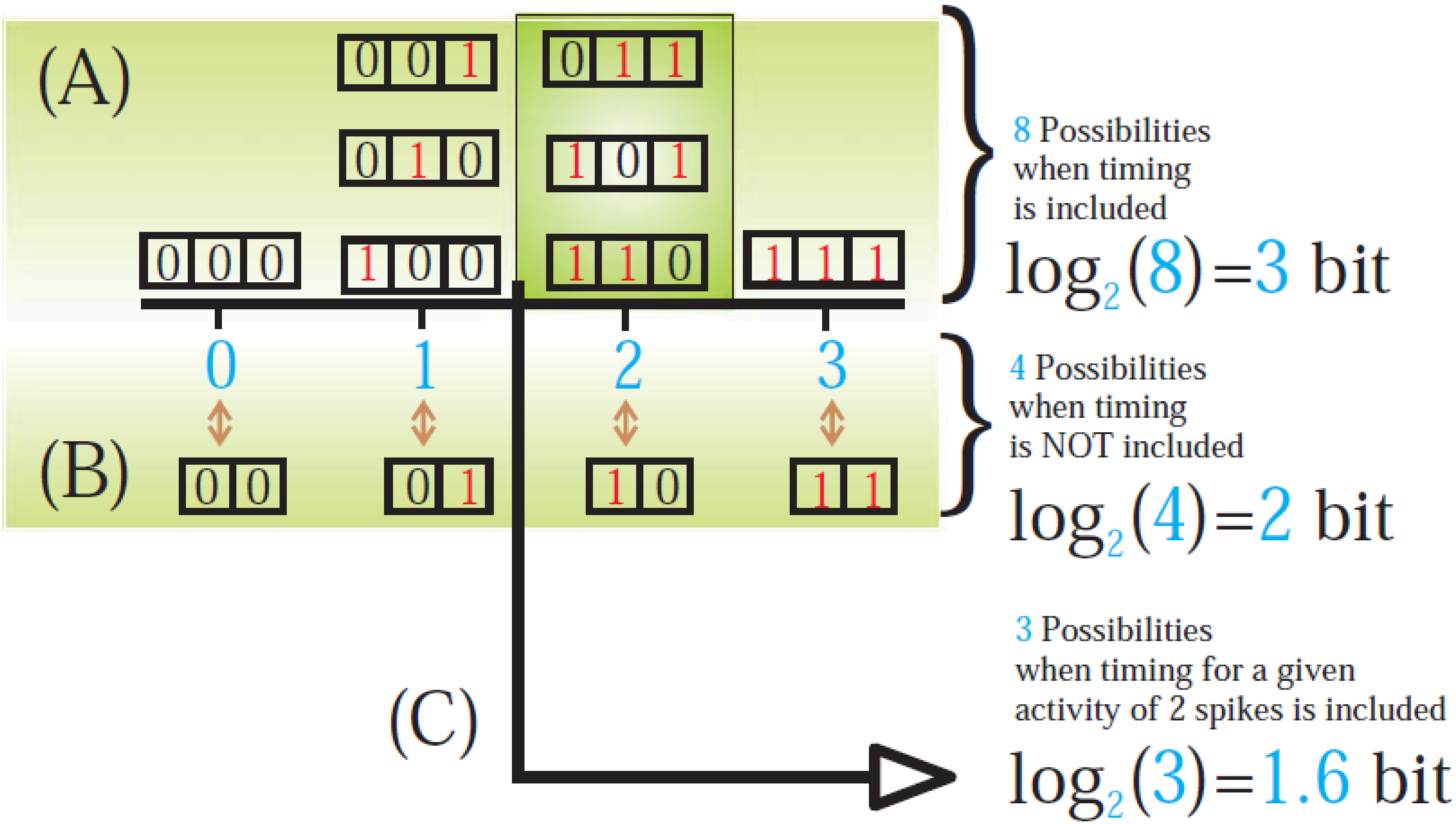


**Figure 14.5** Simplified example of a spike train of three bins. The bin size is selected such that it can either contain one or no spikes. All eight possibilities having zero, one, two, or three spikes in the set of three bins are shown in (A). This results in an entropy value of 3 bits. This comes as no surprise since we have three bins that could contain zero or one. (B) If we consider the number of spikes, without paying attention to the timing, there are only four possibilities resulting in a 2-bit value for the entropy. Decimal values are shown in blue; binary values are black (0) or red (1). When taking the activity level as a given, for instance, two spikes in a three bin observation span, the timing of those spikes determines the entropy. In example (C) we have three possible arrangements, leading to a value of 1.6 bits.

# Entropy and Information

- Several possible approaches – $N_1$ spikes in a trace with N bins
  - Bin size – affects the outcome of the entropy measure
    - Approach to obtain an objective and reasonable bin size for the particular problem at hand – needed
    - Commonly used approach
      - To find a distribution or bin size that maximizes the entropy
        - at minimum: a bin = the duration of a spike plus the absolute refractory period
        - determines the upper bound of the information of a measured spike train

- In studies of spike trains
  - Probability of spike occurrence – often estimated from the recorded time series
  - Bin size – usually selected to generate a maximum entropy value
  - The spike activity of single cortical neurons – associated with bursting activity of the surrounding cortical network
  - The network burst – used to align the spike trains (a similar procedure as a stimulus is used as the trigger)
  - The aligned spike trains – binned to allow estimation of each spike train's entropy

# Entropy and Information

- An illustration of the application of entropy calculation (Fig. 14.6)
  - 4 spike train trials – triggered (aligned) by a population burst
  - Each trial – divided into 9 bins → a total of 4×9=36 bins
  - In all of 36 bins:

    14 bins with 0 spikes ($p_0 = 14/36$), 16 bins with 1 spikes ($p_1 = 16/36$)
    5 bins with 2 spikes ($p_2 = 5/36$), 1 bin with 3 spikes ($p_3 = 1/36$)
    → total entropy $H_t$: $-(14/36) \times \log_2(14/36) - (16/36) \times \log_2(16/36) - (5/36) \times \log_2(5/36) - (1/36) \times \log_2(1/36) \approx 1.6$ bits

    (normally correction of the estimate for bias – needed → omitted to keep example simple)
  - If the spike activity was only d/t the population activity
    - The number of spikes across the vertical bins – should be identical
    - The variability across the vertical bins – represents activity that is not associated with the burst (the trigger event) → considered as noise
      - First column: $-(1/2)\times\log_2(1/2) - (1/2)\times\log_2(1/2)$
      - Second column: $-(3/4)\times\log_2(3/4) - (1/4)\times\log_2(1/4)$

        …
  - Average noise entropy for all nine columns = mean($H_n$)
  - Information that is associated with the burst $H_{burst}$: $H_{burst} = H_t - \mathrm{mean}(H_n)$

(total entropy in all traces – average noise entropy for all nine columns)

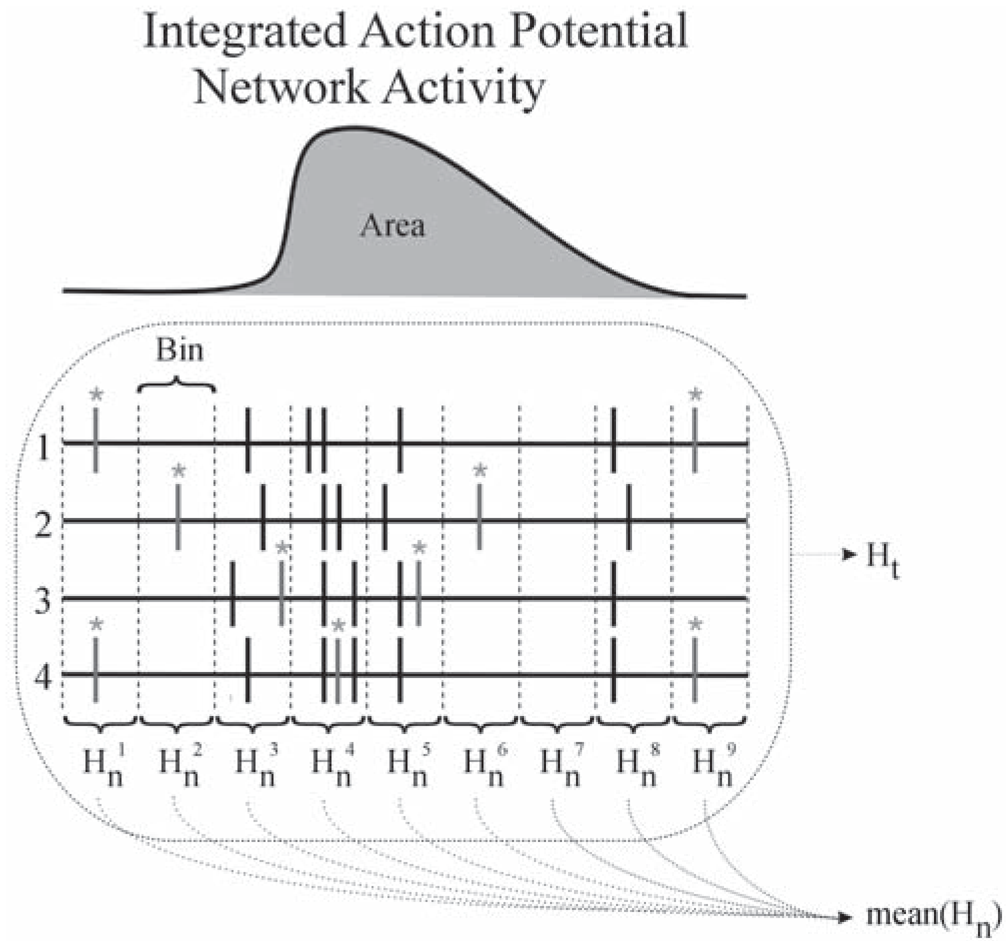


**Figure 14.6** Integrated network activity-triggered average of a single neuron's spike train. In this theoretical example, the spikes marked with * are not burst related. This is only for the sake of the example; in a real measurement, the origin of the spikes is, of course, not known. Modifi ed from van Drongelen et al., 2003.

# The Autocorrelation Function

- Specific properties of the spike train → applications of signal processing techniques such as correlation – differ somewhat from the conventional approaches
- Autocorrelation
  - Spike train → no continuous signal, but instantaneous rate function r(t) as a proxy
  - Definition of autocorrelation $R_{rr}(t_1,t_2)$ of $r$:

    $$R_{rr}(t_1, t_2) = E\{r(t_1)r(t_2)\}$$

    - Using a time average (denoted by <.>):

    $$R_{rr}(t_1, t_2) = E\{r(t_1)r(t_2)\} = \langle r(t_1)r(t_2)\rangle$$

# The Autocorrelation Function

- Rate function
  - Definition: the spike average over a large number of epochs
    - Practical ( ∵ the average can be easily determined directly from experimental observations)
  - More theoretical aspect
    - Rate – related to the probability of the occurrence of a spike at a given time (which follows from the definition of the rate)
    - Two extremes for average
      (1)There is always a spike in the observed epochs, or
      (2)We never observe any action potential in these epochs
      ➔ resulting average for the rate (in terms of spiking probability) = 1 or 0
    - In all other cases
      - Average value representing the instantaneous rate – between 0 and 1
  - Estimate <u>spike probability (btw 0 and 1)</u> instead of obtaining <u>values using dividing by the bin width Δ (in spikes/s)</u>
  - Alternative interpretation of the instantaneous rate: the probability of the occurrence of an action potential (not weighed by Δ)

# The Autocorrelation Function

- Autocorrelation of a single spike train $R_{rr}(t_1,t_2)$
  - Proportional with the probability of observing spikes at $t_1$ and $t_2$:
  - $$P(\text{spike at } t_1 \,\&\, \text{spike at } t_2) = \underbrace{P(\text{spike at } t_1 \mid \text{spike at } t_2)}_{\text{conditional rate}} \times \underbrace{P(\text{spike at } t_2)}_{-r(t_2)}$$
    - Conditional rate (the first term) – usually called the autocorrelation of the spike train
    - The probability of a spike at $t_1$ – estimated using a time average of traces where spike occurrence is used to align the traces
      - Similar fashion to determining the probability of spiking after a stimulus using a time average
    - Example (Fig. 14.7)
      - Correlation function of the spike train – obtained from shifts that bring each subsequent occurrence of a spike to time 0 (instead of shifting the time series by a small regular interval $dt$) → $P(\text{spike at } t_2) = 1$
      - This process – repeated several times & then the average of the binned traces – used as an estimate of the autocorrelation function
      - Dividing the outcome by the bin width → obtain a value in spikes/s
      - Each spike in the train – used in the average
        - The process – assumed to be stationary → the autocorrelation only depends on the difference $\tau = t_2 - t_1$

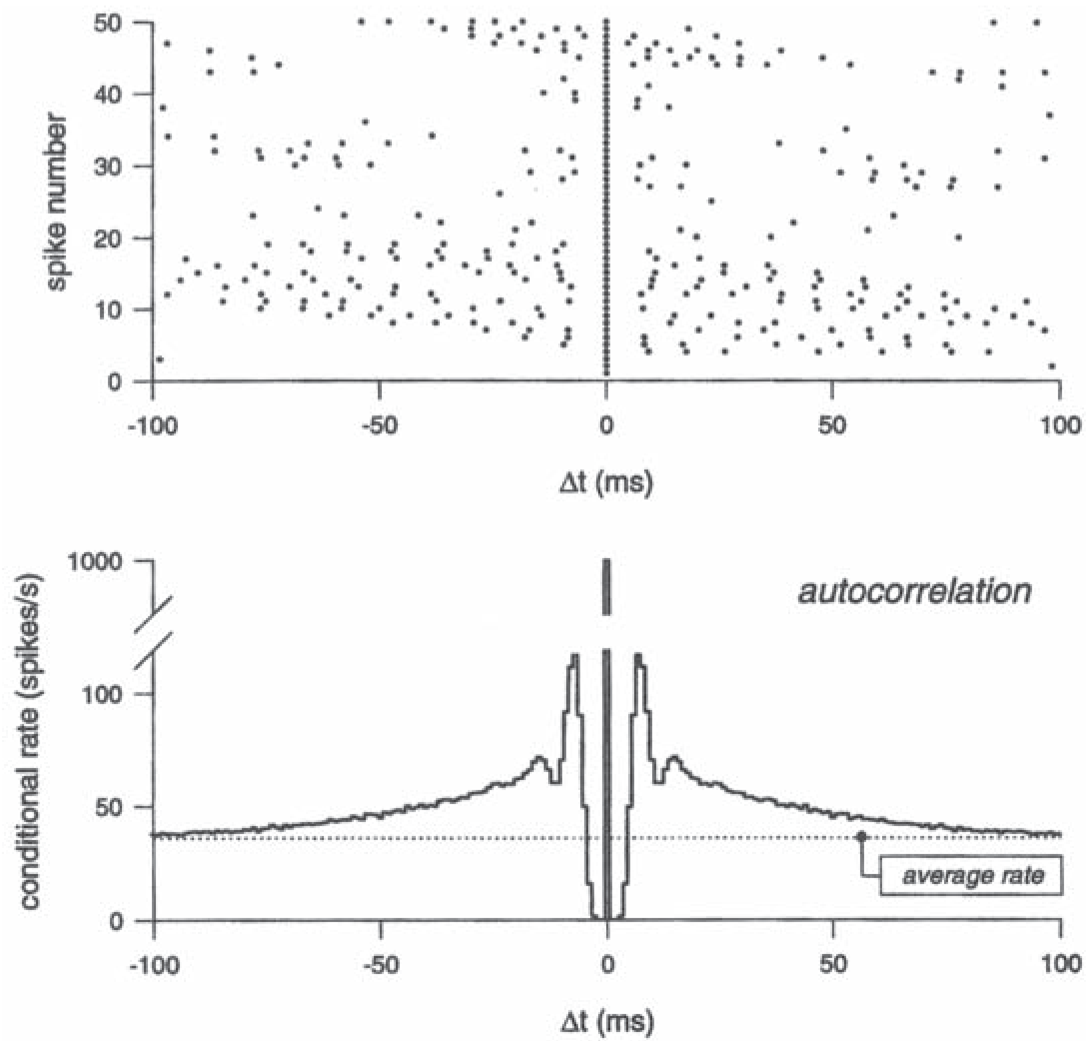


**Figure 14.7** Autocorrelation of a spike train. Top: Raster plot of spike activity; each row is a plot of spike occurrence that is aligned with the middle spike in the top row. Bottom: The average of the spikes in each bin as a function of delay. (From Rieke et al., 1999.)

# The Autocorrelation Function

- An alternative procedure used for calculating the autocorrelation
  - Following from the definition of autocorrelation in chapter 8 & the representation of the spike train as a series of unit impulses
  - if spike train – a <u>stationary process</u> → underlying distributions – invariant & only the difference $\tau = t_2 - t_1$ – relevant: $R_{rr}(\tau) = E\{r(t)r(t+\tau)\}$
  - Assuming <u>ergodicity</u> → time average used: $R_{rr}(\tau) = \lim_{T\to\infty} \frac{1}{T}\int_0^T r(t)r(t+\tau)\,dt$
  - T → very large ( ∞ ): $R_{rr}(\tau) = \int_{-\infty}^{\infty} r(t)r(t+\tau)\,dt$
    - Definition of autocorrelation function (chapter 8)
    - For each value of τ, the spike train is correlated with itself
  - A single instantiation of a spike train – represented by <u>a series of Diracs</u> $\sum_{j=1}^{N}\delta(t-t_j)$ → for each, this series of Diracs may be correlated with itself:

$$R_{rr}(\tau) = \int_{-\infty}^{\infty} \sum_{i=1}^{N}\delta(t-t_i)\sum_{j=1}^{N}\delta(t-t_j+\tau)\,dt$$

  - Assuming that we may interchange the integration and summation:

$$\boxed{R_{rr}(\tau) = \sum_{i=1}^{N}\sum_{j=1}^{N}\int_{-\infty}^{\infty} \delta(t-t_i)\delta(t-t_j+\tau)\,dt}$$

    - which can be simplified by using the sifting property of the δ function

# The Autocorrelation Function

- Simple example
  - A spike train with 3 spikes at $t_1=0$, $t_2=1$, and $t_3=4$ & no other spike activity
  - For the first spike:

$i = 1$ and $j = 1$: $$\boxed{\int_{-\infty}^{\infty} \delta(t-t_1)\delta(t-t_1+\tau)dt = \delta(t_1-t_1+\tau) = \delta(\tau)}$$

or $$\int_{-\infty}^{\infty} \delta(t-t_1)\delta(t-t_1+\tau)dt = \delta(t_1-\tau-t_1) = \delta(-\tau)$$

$i = 1$ and $j = 2$: $$\boxed{\int_{-\infty}^{\infty} \delta(t-t_1)\delta(t-t_2+\tau)dt = \delta(t_1-t_2+\tau) = \delta(\tau-1)}$$

or $$\int_{-\infty}^{\infty} \delta(t-t_1)\delta(t-t_2+\tau)dt = \delta(t_2-\tau-t_1) = \delta(-\tau+1)$$

$i = 1$ and $j = 3$: $$\boxed{\int_{-\infty}^{\infty} \delta(t-t_1)\delta(t-t_3+\tau)dt = \delta(t_1-t_3+\tau) = \delta(\tau-4)}$$

or $$\int_{-\infty}^{\infty} \delta(t-t_1)\delta(t-t_3+\tau)dt = \delta(t_3-\tau-t_1) = \delta(-\tau+4)$$

- The results for sifting one delta with the other (and vice versa) → a pair of mirror shifts
  - $\tau$ and $-\tau$; $\tau-1$ and $-\tau+1$; $\tau-4$ and $-\tau+4$
  - Autocorrelation – an even function (e.g., $R_{rr}(\tau)=R_{rr}(-\tau)$) → only consider shifting in one direction

# The Autocorrelation Function

- Simple example
  - For the second spike:

$i = 2$ and $j = 1$: $\boxed{\int_{-\infty}^{\infty} \delta(t - t_2)\delta(t - t_1 + \tau)dt = \delta(t_2 - t_1 + \tau) = \delta(\tau + 1)}$

$i = 2$ and $j = 2$: $\boxed{\int_{-\infty}^{\infty} \delta(t - t_2)\delta(t - t_2 + \tau)dt = \delta(t_2 - t_2 + \tau) = \delta(\tau)}$

$i = 2$ and $j = 3$: $\boxed{\int_{-\infty}^{\infty} \delta(t - t_2)\delta(t - t_3 + \tau)dt = \delta(t_2 - t_3 + \tau) = \delta(\tau - 3)}$

  - For the third spike:

$i = 3$ and $j = 1$: $\boxed{\int_{-\infty}^{\infty} \delta(t - t_3)\delta(t - t_1 + \tau)dt = \delta(t_3 - t_1 + \tau) = \delta(\tau + 4)}$

$i = 3$ and $j = 2$: $\boxed{\int_{-\infty}^{\infty} \delta(t - t_3)\delta(t - t_2 + \tau)dt = \delta(t_3 - t_2 + \tau) = \delta(\tau + 3)}$

$i = 3$ and $j = 3$: $\boxed{\int_{-\infty}^{\infty} \delta(t - t_3)\delta(t - t_3 + \tau)dt = \delta(t_3 - t_3 + \tau) = \delta(\tau)}$

# The Autocorrelation Function

- Simple example
  - Summing the results for i and j from 1 to 3:

$$R_{rr}(\tau) = \sum_{i=1}^{3}\sum_{j=1}^{3}\int_{-\infty}^{\infty}\delta(t-t_i)\delta(t-t_j+\tau)dt = \sum_{i=1}^{3}\sum_{j=1}^{3}\delta(t_i-t_j+\tau)$$

$$= [\delta(\tau+4)+\delta(\tau+3)+\delta(\tau+1)+3\times\delta(\tau)+\delta(\tau-1)+\delta(\tau-3)+\delta(\tau-4)]$$

  - Figure 14.8
    - Panel A
      - Shifting the spike train for each spike relative to one of the spikes → summation
      - Black (spike at $t_1=0$), red (spike at $t_2=1$), and blue (spike at $t_3=4$)
    - Panel B
      - Summation underlying the result in above equation
    - Identical results
    - Normalization
      - Autocorrelation function at $\tau=0$ – always contain the summation of N=3 spikes → a scaled correlation equal to 1 at $\tau=0$ by dividing the summed result by N

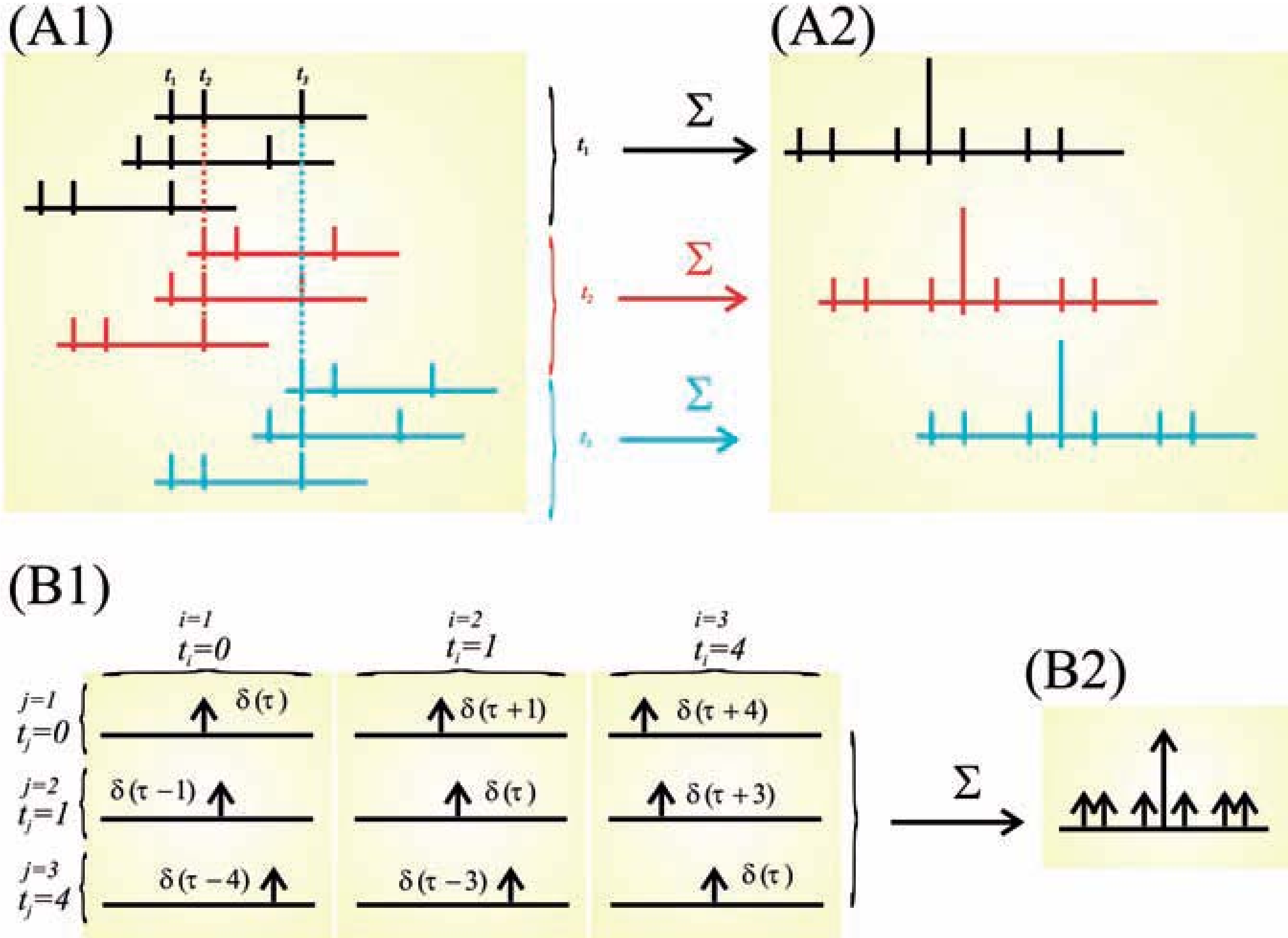


**Figure 14.8** Example of a series of three spikes (A1) and the autocorrelation function (A2) based on the first spike (black), the second spike (red), and the third one (blue). The Σ symbol indicates the summation of the three traces of the associated color. In this example, there are few spikes so that each event can be indicated individually. In real spike trains, the traces are binned and the number of spikes per bin is determined because there can be many closely spaced spikes (see Fig. 14.7). In addition, it is customary to scale the ordinate to represent spikes/s or the correlation coefficient. Panels (B1) and (B2) show the correlation function based on Equations (14.19) and (14.20). Comparing the autocorrelation in (A2) and (B2), note that the different approaches generate the same result.

# Cross-Correlation

- Cross-correlation btw two spike trains
  - Similar procedure to that for autocorrelation
  - Two spike trains – shifted relative to each other & the spike-triggered average – represents an estimate of the cross-correlation
- Another interesting application of cross-correlation
  - Between a spike and a continuous signal such as the stimulus s(t) evoking the spike train $\{t_i\}$
  - Example (Fig. 14.9)
    - A cross-correlation btw a stimulus signal s(t) and a train with a single spike at time $t_i$ over an interval T:

$$R(\tau)_{s(t),\{t_i\}} = \int_T s(t)\underbrace{\delta(t-t_i+\tau)}_{\delta(t-(t_i-\tau))}dt = s(t_i-\tau)$$

    - Cross-correlation of two signals – usually not an even function
      - $\tau<0$: the correlation of the signal at $s(t_i-\tau)$ → the spike predicts the stimulus – a fairly unrealistic assumption ($\because$ it violates causality)
      - Only consider $\tau>0$ in $s(t_i-\tau)$ → we are looking from the spike time $t_i$ backward (reverse-correlation function)

# Cross-Correlation

- For a spike train with N spikes over interval T & signal s(t)
  - The reverse-correlation function:

$$R(\tau)_{s(t),\{t_i\}} = \int_T s(t)\left[\sum_{i=1}^{N} \delta(t - t_i + \tau)\right] dt$$

  - Interchanging the integration and summation:

$$R(\tau)_{s(t),\{t_i\}} = \sum_{i=1}^{N} \int_T s(t)\delta(t - t_i + \tau)\, dt = \sum_{i=1}^{N} s(t_i - \tau)$$

    - The cross-correlation – estimated by the sum of the signal epochs preceding each evoked spike
  - Common normalization
    - Dividing by N → $\frac{1}{N}\sum_{i=1}^{N} s(t_i - \tau)$ (a spike-triggered signal average of the stimulus preceding each evoked spike)
- Use of reverse correlation – directly related to the facts
  - that we are considering the stimulus signal &
  - that the spiking neuron obeys causality

  → this reasoning would reverse if the signal s(t) – a movement & the spike train – from a motoneuron steering this movement

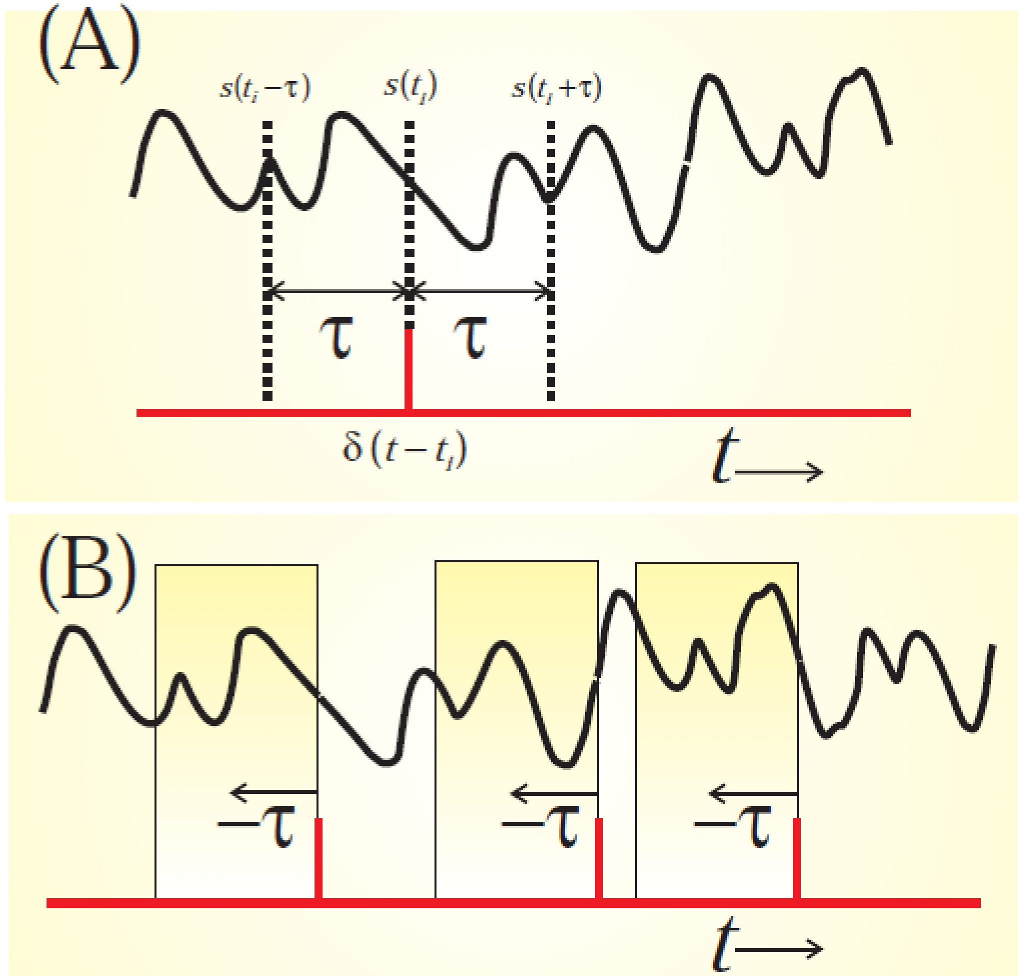


**Figure 14.9** Cross-correlation between a spike train (red) and a continuous signal (black) representing the stimulus evoking the train. (A) shows the relationship between a single spike and its correlation. Because of the causal relationship between stimulus and spike, we are only interested in $s(t)$ preceding the spike, the so-called reverse-correlation function. (B) shows a spike train with three spikes and the associated preceding correlation windows. When the signal in these windows is averaged, we obtain the spike-triggered average (i.e., the estimated reverse correlation), as in the example shown in Figure 14.2.