Biomedical Signal Processing

- Spike Train Analysis (1) -

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Introduction

- Spike train – a crucial role in communication btw cells in the nervous system
- Time series of action potentials (APs)
  - Intracellular measurement: all aspects of the membrane potential fluctuations
  - Extracellular spike train: the timing of the occurrence of an AP
- AP in a nerve fiber → generator for extracellular current
  - Current – measured by a biological amplifier
  - Vertical or horizontal current
    - Depending on the positions of the recording electrodes relative to the nerve fiber
  - Tri- or biphasic wave (spike) for each action potential
- Different wave morphology in spike trains
  - d/t differences in relative position and impedance btw electrodes and different neurons
  - Different cells → spike with differences in amplitude and waveform

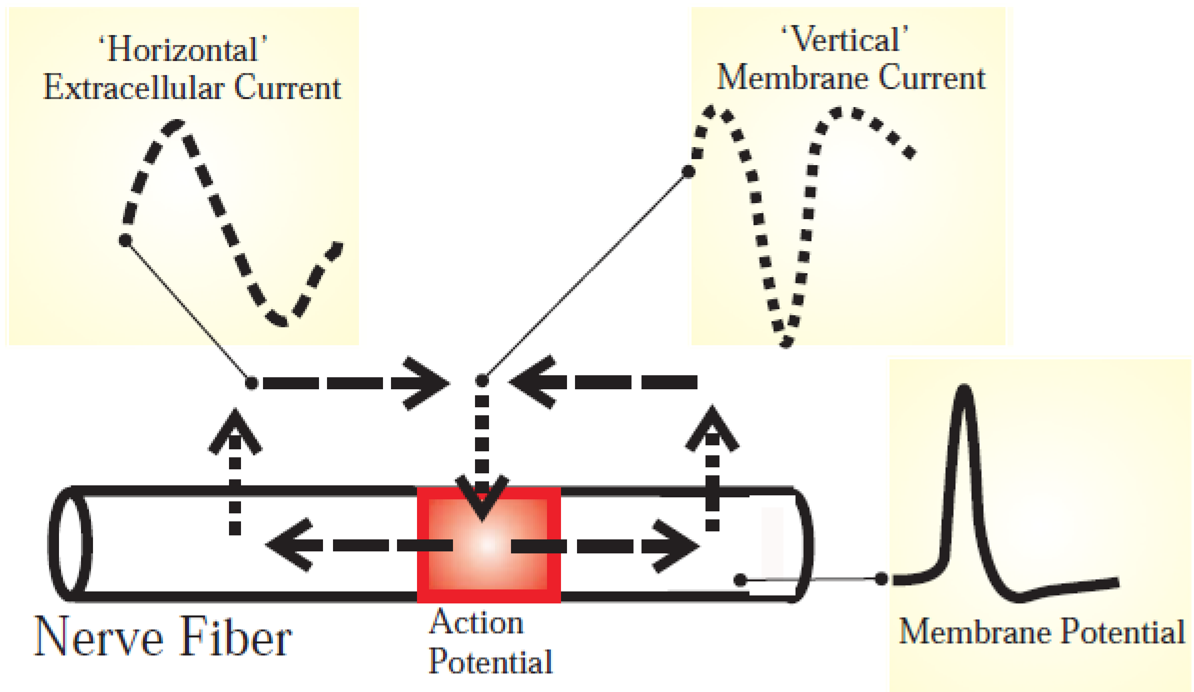

Figure 14.1 Schematic representation of intracellular, membrane, and extracellular currents associated with an action potential.

Introduction

- Deterministic versus Probabilistic Approach
  - Spike train – considered as a list of the times t_i where spikes have occurred
  - Hodgkin and Huxley equations
    - Generation of a spike train $\{t_i\}$ – fundamentally <u>deterministic process</u>
    - The response to a given stimulus – reproducible and fully determined by the underlying equations
  - <u>Probabilistic approach</u> to the analysis of spike train data
    - Neural responses to the same stimuli s in repeated trials – seldom completely identical
    - $P(\{t_i\} | s)$: the probabilistic of observing spike train $\{t_i\}$ given that stimulus s occurred
    - Not only consider the response but also the stimulus to be drawn from a probability density function
    - Analogous to what brain must do to interpret incoming spike trains and link these to external stimuli
    - Bayes' rule
      - Link the probability $P(\{t_i\} | s)$ of observing a response $\{t_i\}$ to a given stimulus s with the probability that stimulus s occurred when response $\{t_i\}$ is observed, $P(s | \{t_i\})$

Example of the latter approach: attempt to determine the stimulus based on a recorded spike train

Assumption: the external stimulus evoking the spike is masked by a random (noise) component that can be reduced by averaging

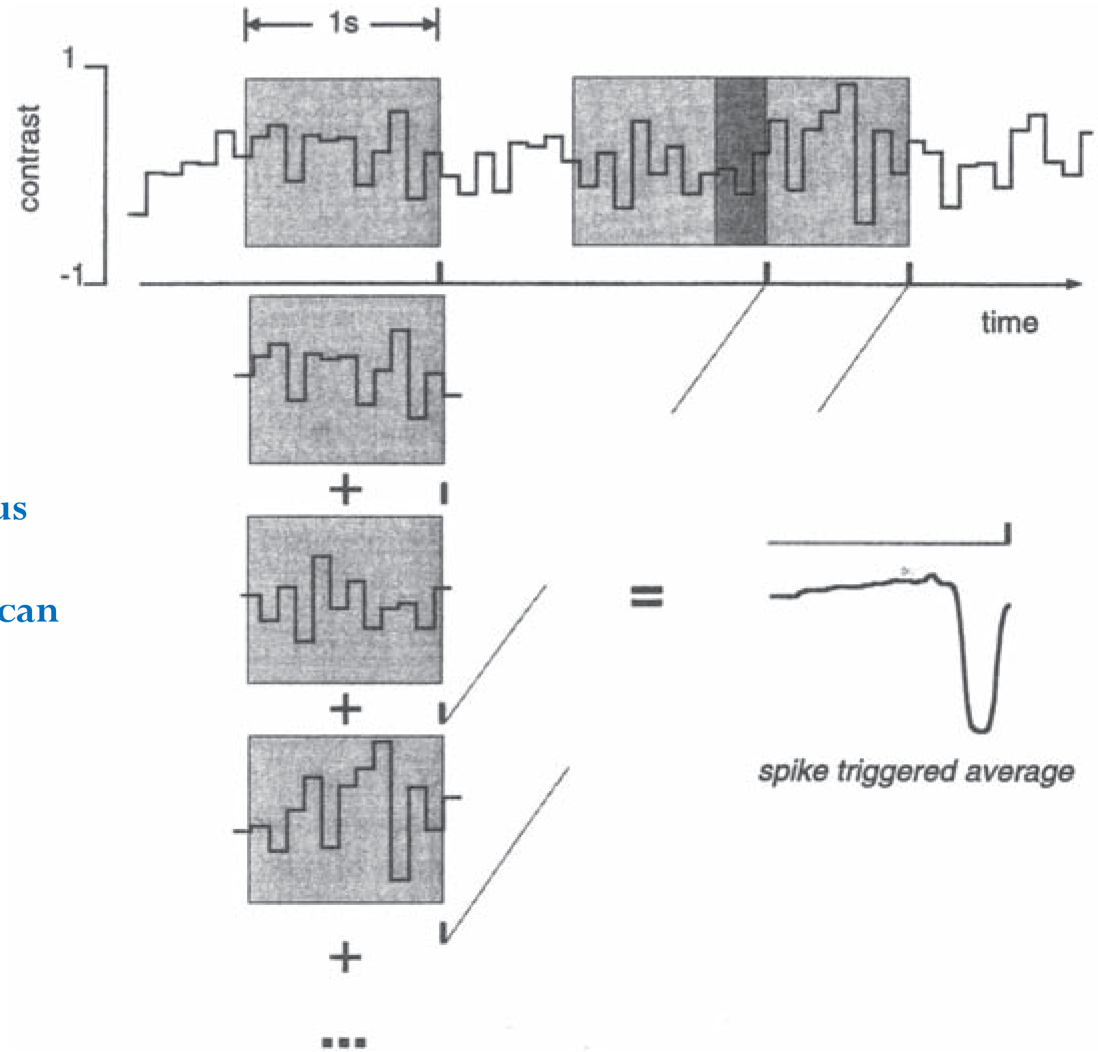

Figure 14.2 Interpretation of a spike train by averaging a prespike window of the stimulus. Top: trace stimulus; second trace shows a spike train with three spikes. The gray boxes represent the prespike windows that can be averaged to estimate a spike-triggered average. (From Rieke et al., 1999.)

Introduction

- The δ function
  - A spike in a spike train – thought as an all-or-nothing process
  - A train of APs = a series of events occurring in time
    - At any given time, an event is either absent (off) or present (on)
  - Raster plots (Fig. 14.3)
    - A time axis with each spike represented by a dot (or a short vertical line) on this axis
    - AP – reduced to an event on a time line, with an event duration of zero (the dot/line)
    - Used to derive a formal representation of a spike train

More conventional approach – determines spike activity evoked by a given stimulus

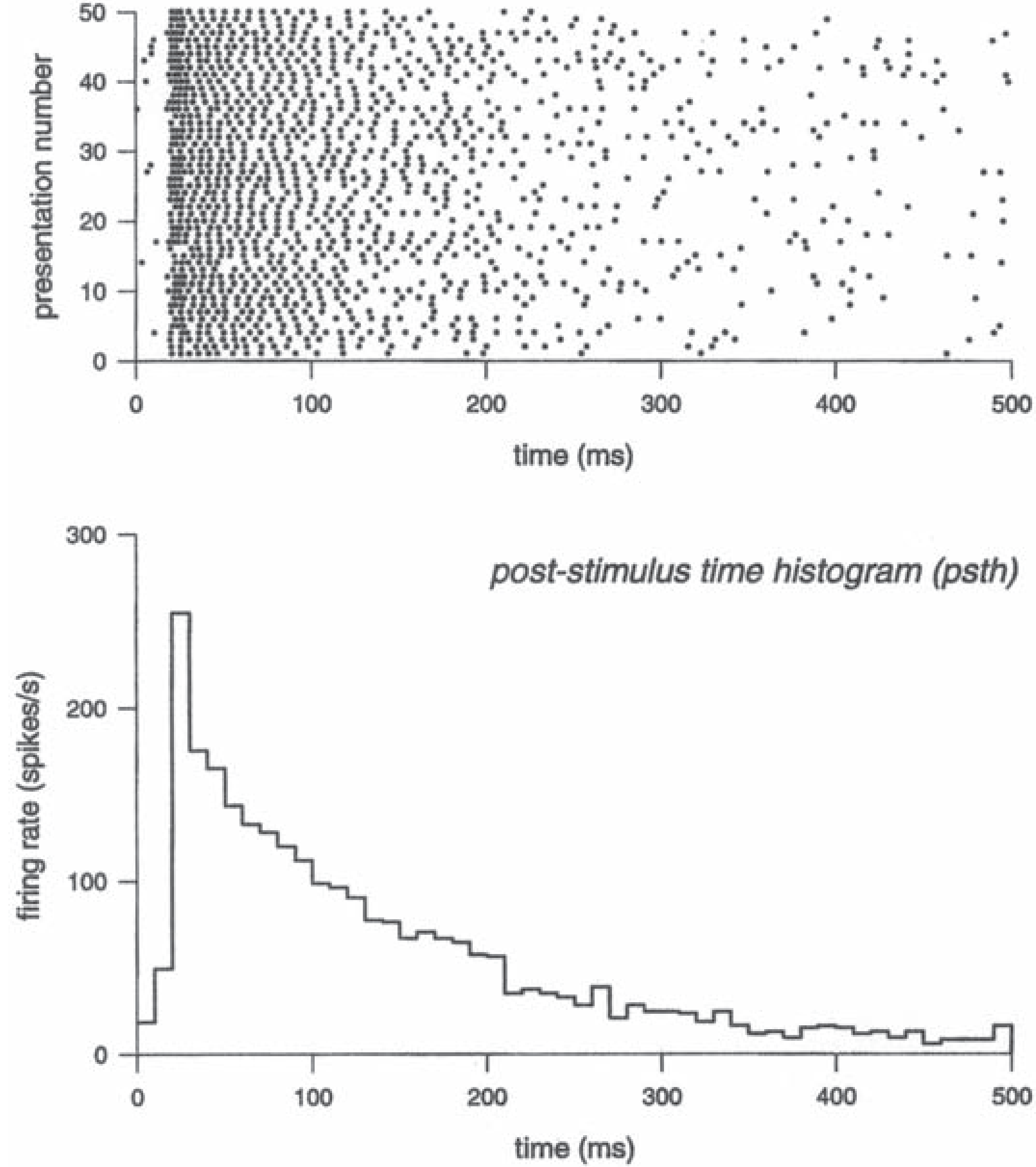

Figure 14.3 Top: Raster plots showing spikes in subsequent responses to the same stimulus. Each row is a single response plotted against time. Bottom: The raster plot data are used to plot the average spike count ⟨N⟩ in 10-ms bins. This is the so-called poststimulus time histogram. (From Rieke et al., 1999.)

Introduction

- The δ function
  - Spike count function f_s for an epoch
    - An epoch on the time line with an interval of size 1 and located btw -1/2 and 1/2
    - $$\begin{cases} f_s[\tau] = 1 & if \quad -\frac{1}{2} \le \tau \le \frac{1}{2} \\ f_s[\tau] = 0 & otherwise \end{cases}$$
      - Used to evaluate an epoch Δ around a particular time by evaluating $f_s[(t-t_i)/\Delta]$
    - If there is a spike at t_i, the function generates a 1 → Evaluating the sum of this function for a spike train including all times where a spike is found – increment by 1 for each spike and obtain a spike count N:

      $$N = \sum_i f_s[(t - t_i)/\Delta]$$
    - In real spike train
      - The neural response – typically variable and usually characterized by the average of a series of responses to an identical stimulus

Introduction

- The δ function
  - Instantaneous rate r(t)
    - Spike rate in each bin – calculated as <N>/Δ (<N>: the average count over the trials)
    - $$r(t) = \lim_{\Delta \to 0} \frac{\langle N \rangle}{\Delta} = \left\langle \lim_{\Delta \to 0} \frac{1}{\Delta} \sum_i f_s[(t - t_i)/\Delta] \right\rangle = \left\langle \sum_i \delta(t - t_i) \right\rangle$$
      - <.>: the (vertical) average over each bin in the subsequent trials
    - Limiting case as $\Delta \to 0$: instantaneous rate – expressed as the average of the Dirac delta functions that sift out the spike timing in the responses

Introduction

- The δ function

  < Note >

  1. Division of f_s (amplitude of 1) by a factor Δ (dimension of time) → r(t) – the dimension s^{-1}
     - δ function – does not have the s^{-1} dimension (∵ a dimensionless 1/τ amplitude factor – included in the definition of Dirac function (Ch. 2))
  2. Spikes – actually a finite duration → derivation of the Dirac by letting ($\Delta \rightarrow 0$) – not strictly appropriate for this application
     - One tries to determine Δ so that (for a single trace) the bin contains either one or no spikes
     - Notwithstanding, δ function - often used to formally represent a spike in a spike train (∵ it allows development of mathematical expressions for spike train analysis such as convolution, correlation, and so forth)

Poisson Processes and Poisson Distributions

- Introduction to the Poisson process
  - An important statistical model for understanding spike trains
  - Explored most fruitfully in the context of a branch of statistics ("renewal theory")
    - The major challenge in renewal theory: to understand component failure and its associated statistics
    - A similarity btw the component failure events and the occurrences of spikes in a spike train
    - Simplest model of the occurrence of an event → to assume <u>a constant probability ρ of a component failing, given that it has not failed yet</u>
      - Ex: lightbulbs in a building where all lights are always on (broken bulbs – replaced immediately)
        - ρ = the probability that a functional bulb will fail

Poisson Processes and Poisson Distributions

- The process leading to a spike event of a single unit
  - Compared to observing a new bulb failing in a single light fixture
  - The process of resetting the membrane potential after the spike – analogous to replacing a bulb that has failed
  - Conditional probability (age-specific failure rate) described by PDF f(t)
    - Interpreted as the product of ρ and the survival function $\mathscr{F}(t) = 1 - F(t)$ (∵ a bulb cannot fail twice – a broken bulb stays broken)
      - $f(t) = \rho \times \mathscr{F}(t)$
    - F(t): the cumulative distribution function

Poisson Processes and Poisson Distributions

- The process leading to a spike event of a single unit
  - PDF for the time of occurrence of a failure given by

$$f(t) = \rho e^{-\rho t} \text{ (with f(t) = 0 for t < 0)}$$

    - Satisfies the previous condition:

$$\text{Survival } \mathcal{F}(t) = 1 - F(t) = \int_t^\infty f(x)\,dx = [-e^{-\rho t}]_t^\infty = 0 - [-e^{-\rho t}] = e^{-\rho t}$$

$$d\mathcal{F}(t)/dt = \frac{de^{-\rho t}}{dt} = -\rho e^{-\rho t}$$

$$d\mathcal{F}(t)/dt = d[1 - F(t)]/dt = -dF(t)/dt = -f(t)$$

$\rightarrow$ $f(t) = \rho e^{-\rho t}$ and $\mathcal{F}(t) = e^{-\rho t}$

(consistent with the initial assumption in that this PDF embodies a constant failure (event) probability for a component that has not previously failed)

Poisson Processes and Poisson Distributions

- Poisson process
  - Process satisfying $f(t) = \rho e^{-\rho t}$
  - Memory-less
    - $\because$ this process does not have a specific aging component (i.e., given the absence of previous failure, there is a constant probability that a failure will occur)
  - An important statistical feature of the PDF of Poisson process
    - Equal mean and standard deviation ($= 1/\rho$) (Appendix 14.2)
    - In spike trains
      - This property – evaluated by calculating mean and standard deviation of the inter-spike intervals

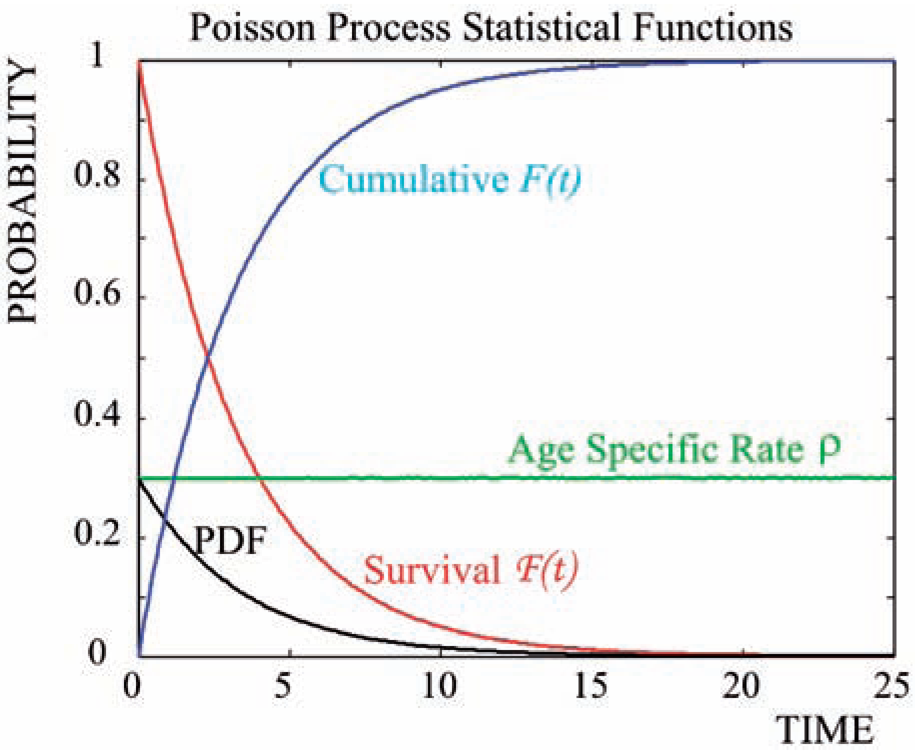

Figure 14.4 Overview of statistical functions associated with the Poisson process.

Poisson Processes and Poisson Distributions

- The spike train in discrete time
  - A set of events in a binned trace
    - Some of the bins will contain spikes; others will be empty
  - An epoch of stationary spike activity in n bins of duration Δt
    - Bins – about <u>the duration of a single action potential</u>
  - Sequence example: 0 0 1 0 1 1 0 0 0 1 0 0
    - 4 spikes & 8 empty bins
    - Described by the binomial distribution
      - The probability of a hit (event) occurring = p
      - The probability of a failure q = 1-p
    - $p = \rho\Delta t + O(\Delta t)$
      - $\rho\Delta t$: the probability that one event occurs in Δt
      - $O(\Delta t)$: the probability that more than one event occurs in Δt
      - A suitably small value for Δt → we can ignore $O(\Delta t)$ ($\because$ there will not be more than one spike per interval)
        - A bit tricky ($\because$ Δt cannot approach 0 either because of the finite duration of a spike)

Poisson Processes and Poisson Distributions

- The spike train in discrete time
  - Sequence example: 0 0 1 0 1 1 0 0 0 1 0 0
    - Independence assumption for the occurrence of hits and failures → the probability of counting 4 spikes in 12 bins = p^4q^8
  - Probability for encountering i hits in n trials
    - Correction needed for all the other arrangements of a total count of 4 spikes such as:

$$\begin{array}{cccccccccccc}
1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 \\
\ldots & \text{and so on} & & & & & & & & & &
\end{array}$$

    - $\binom{n}{i} = \frac{n!}{(n-i)!i!} = \frac{12!}{8!4!} = 12 \times 11 \times 10 \times 9 / 4 \times 3 \times 2 \times 1 = 495$ different ways over the 12 bins (n=12 trials, i=4 hits and n-i=8 failures)
    - Derivation of the binomial distribution
      - $P(i) = \frac{n!}{(n-i)!i!} p^i (1-p)^{n-1}$
      - Links the probability p of a single hit occurring in one trial to the probability P(i) of encountering i hits in n trials

Poisson Processes and Poisson Distributions

- Real spike trains
  - The intervals – considered very small (a few ms) compared to the complete time series length (usually 1 to several seconds)
    - With typical spike rates → most intervals do not contain spikes
  - Preceding probability function for very large n and small values of p
    - Average number of hits in n observations = λ (assumption) → p= λ/n
    - $$P(i) = \frac{n!}{(n-i)!\,i!}\left(\frac{\lambda}{n}\right)^{i}\left(1-\frac{\lambda}{n}\right)^{n-i}$$

$$= \frac{n(n-1)(n-2)\ldots(n-i+1)}{i!}\left(\frac{\lambda}{n}\right)^{i}\left(1-\frac{\lambda}{n}\right)^{n-i}$$

$$= \frac{n(n-1)(n-2)\ldots(n-i+1)}{\left(1-\frac{\lambda}{n}\right)^{i} i!}\left(\frac{\lambda}{n}\right)^{i}\left(1-\frac{\lambda}{n}\right)^{n}$$

$$= \frac{n(n-1)(n-2)\ldots(n-i+1)}{n^{i}\left(1-\frac{\lambda}{n}\right)^{i} i!}\lambda^{i}\left(1-\frac{\lambda}{n}\right)^{n}$$

$$= \frac{1(1-1/n)(1-2/n)\ldots(1-(i-1)/n)}{\left(1-\frac{\lambda}{n}\right)^{i} i!}\lambda^{i}\left(1-\frac{\lambda}{n}\right)^{n}$$

Poisson Processes and Poisson Distributions

- Real spike trains
  - For large n
    - All terms in the first part containing a division by n → 0:

$$\frac{1(1-1/n)(1-2/n)\ldots(1-(i-1)/n)}{\left(1-\frac{\lambda}{n}\right)^{i} i!}\lambda^{i} \to \frac{\lambda^{i}}{i!}$$

    - Second term → a power series: $\left(1-\frac{\lambda}{n}\right)^{n} \to e^{-\lambda}$
  - Combining above results → equation for the Poisson distribution:

$\boxed{P(i)=\frac{\lambda^{i}}{i!}e^{-\lambda}}$ or $\boxed{P(i)=\frac{(\rho t)^{i}}{i!}e^{-\rho t}}$ (Second version: $\lambda = n\Delta t\rho = t\rho$) (p=λ/n & p=ρΔt)

    - PDF in which the sum of probabilities of all possible outcomes $\sum_{i=0}^{\infty}\frac{\lambda^{i}}{i!}e^{-\lambda} = 1$
      - Seen by substituting the series $\sum_{i=0}^{\infty}\frac{\lambda^{i}}{i!}$ by exponential e^{λ} :

$$e^{\lambda} = 1+\lambda+\frac{\lambda^{2}}{2!}+\frac{\lambda^{3}}{3!}+\ldots$$

Poisson Processes and Poisson Distributions

- Real spike trains
  - Comparing the Poisson distribution with the Poisson process $f(t) = \rho e^{-\rho t}$
    - The number of events in a fixed interval (e.g., spike counts in a ½ s epoch) → satisfy a Poisson distribution
  - Mean and variance of the Poisson distribution – both equal to λ
    - Mean value:

$$E\{i\} = \sum_{i=0}^{\infty} i \frac{\lambda^i}{i!} e^{-\lambda} = e^{-\lambda} \sum_{i=0}^{\infty} \frac{1}{i!} \lambda \frac{\partial}{\partial \lambda} \lambda^i = e^{-\lambda} \lambda \frac{\partial}{\partial \lambda} \sum_{i=0}^{\infty} \frac{1}{i!} \lambda^i = e^{-\lambda} \boldsymbol{\lambda} \frac{\partial}{\partial \lambda} e^{\lambda} = e^{-\lambda} \lambda e^{\lambda} = \lambda$$

      - Using $i\lambda^i = \lambda \frac{\partial}{\partial \lambda} \lambda^i$, $\partial e^{\lambda} / \partial \lambda = e^{\lambda}$, and $\sum_{i=1}^{\infty} \frac{\lambda^i}{i!} e^{-\lambda} = 1$
    - Variance: $E\{i^2\} - E\{i\}^2 = \lambda$ (= mean)
      - Using the second derivative: $i(i-1)\lambda^i = \lambda^2 \frac{\partial^2 \lambda^i}{\partial \lambda^2}$
  - Fano factor
    - The ratio btw variance/mean (= 1 for Poisson distribution)
    - ~1 for short spike trains (order of second(s))
    - Usually >1 for larger epochs

Poisson Processes and Poisson Distributions

- Study for sensitivity effects of convergence of receptor cells in the olfactory system using Poisson process (van Drogelen et al., 1978)
  - ~1000 peripheral sensory neurons – project onto a single mitral cell in the olfactory bulb
  - At threshold levels of stimulation
    - Sensory neurons – show probabilistic firing patterns
    - A particular unit's threshold – arbitrarily defined as the stimulus level that evokes a response in 50% of the presentations of that stimulus
  - Mitral cells – receive input from a thousand neurons at the same time
    - Prediction: threshold levels – occur at significantly lower concentrations of odorant compared to the peripheral threshold (i.e., the signal is amplified by the convergence of sensory neurons)
  - Amplification effect – estimated using a simplified model
    - Assumption: absence of spontaneous activity & a sensory cell's firing probability upon stimulation equal to ρ
    - The probability that a stimulated sensory neuron fires at least once in observation interval T:

$$1 - (\text{probability that the sensory neuron does } \textit{not} \text{ fire}) = 1 - e^{-\rho T}$$

Poisson Processes and Poisson Distributions

- Study for sensitivity effects of convergence of receptor cells in the olfactory system using Poisson process (van Drogelen et al., 1978)
  - Single mitral cell observing 1000 of these sensory cells
    - Further assumption: the mitral cells – rather sensitive → it spikes upon a spike in any of its connected sensory cell population
    - The probability that the mitral cell fires in the same interval T:

      1 – (probability that *none* of the 1000 sensory neurons fires)
    - Considering the activity of the sensory neurons independent
      - Not a bad assumption at low levels of odorant diffusing in the olfactory mucosa
      - The probability that none of the 1000 sensors fires = the product of the individual probabilities (= $(e^{-\rho T})^{1000}$)
    - Prediction
      - The probability that the mitral cell fires = $1 - (e^{-\rho T})^{1000}$
        - Much higher than the probability that a single sensory cell fires ($1 - e^{-\rho T}$)
      - Experimentally confirmed (Duchamp-Viret et al., 1989)