# Signal & Data Analysis in Neuroscience 2020
## Part 2: Stochastic processes

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## Overview

- Stochastic processes
- Point processes
- Appendix: extracellular recording

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## Modeling our measurements

- Repetition of the same experiment will not lead to the exact same response.
- Example: The spike train of a neuron in response to stimuli is different…
- Typically we would like to know:
  - When is something unexpected?
  - What are the "normal" values?
- Thus, analyzing a sequence of measurements requires modeling of the underlying process.

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## Stochastic process
### Definition

- **Stochastic** – (1) Involving chance or probability (2) Random (3) Non-deterministic (Merriam-Webster & Wikipedia).
- **Stochastic process** - an indexed collection of random variables $\{X_i\}$, where the index $i$ ranges through an index set $I$, defined on the probability space $(\Omega, P)$. The index set may be discrete or continuous (Wikipedia).

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## Stochastic process
### Special cases

- A stochastic process defined over the time interval domain is called a **time series**.
  - Example of *a* continuous time series: temperature in BIU throughout the day.
  - Example of a discrete time series: amount of rain in BIU on a specific day on of the year.
  - Example of a quantized discrete time series: did rain fall in BIU on a specific day of the year?
  - Example of discrete non-time series: height of people entering Gonda building each day
- A stochastic process defined over the space interval domain is called a **random field**.

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## Stationary processes
### Strict / Strong

- A stochastic process whose unconditional joint probability distribution does not change when shifted in its index (typically time).

$$F_X(x_{t_1+\tau},\ldots,x_{t_n+\tau}) = F_X(x_{t_1},\ldots,x_{t_n}) \quad \text{for all } \tau, t_1,\ldots,t_n \in \mathbb{R} \text{ and for all } n \in \mathbb{N}$$

- Probability density function (PDF) – p(x) describes the distribution of a continuous random variable, x.

$$\int_{-\infty}^{\infty} p(x)dx = 1$$

- Cumulative function: $F(x) = \int_{-\infty}^{x} p(y)dy$
- Survival function : $1 - F(x) = \int_{x}^{\infty} p(y)dy$
- $N^{th}$ order stationary process is defined for all n={1, … N}

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## Stationary processes
### Wide-sense / Weak

- A weak or wide-sense stationary (WSS) process only is a second degree stationary process.
- Equal mean value

$$E(X(t)) = \mu_x(t) = \mu_x(t+\tau) \qquad \forall \tau \in \mathbb{R}$$

- Covairance dependent only on index difference

$$E(X(t_1) - \mu_x(t_1) \cdot (X(t_2) - \mu_x(t_2))) = Cov(X(t_1), X(t_2))$$

$$= Cov(X(t_1 + \tau), X(t_2 + \tau)) = Cov(X(t_1 - t_2), 0)$$

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## Stationary processes - examples

- Stationary example: Sequence of L/R button presses. Each press has a 90% probability of being in the same direction as its predecessor.
  - Stationary despite strong temporal covariance.
- Non-stationary example: Amount of rainfall for each day of the year.
  - In many cases long term changes may be removed using **de-trending** techniques.

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## Ergodicity

- If averaging over time and space are equal the process is **ergodic**.
- Ergodicity is usually described in terms of properties of an ensemble of objects.
- Example: Finding out how people spend their spare time. Sampling one person over 1000 days would yield the same result as sampling 1000 people once in an ergodic system.

**Reading material:**
http://news.softpedia.com/news/What-is-ergodicity-15686.shtml

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## Ergodic & stationary processes

- In an ergodic process, the following are equal
  - Averaging across repeated trials
  - Averaging across time for a single trial
- An ergodic process is always stationary, the reverse may not be true
- A stationary process is ergodic if samples that are far enough in time are independent (asymptotic independence).

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## Overview

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- Appendix: extracellular recording

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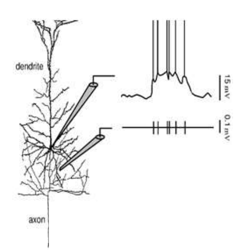
## Intracellular vs. Extracellular neuronal potentials

- Intracellular soma
- Extracellular

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## Extracellular spike trains

- Transformation from a continuous recording to a series of discrete **timestamps**.
- Is all the information contained in the **timing** of the spikes?
- What are we losing?
  - Spike shapes
  - Non spiking activity
  - Sub-threshold activity

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## Time series & Point processes

- Continuous time series
  - Electroencephalogram (EEG)
  - Electromyogram (EMG)
  - Intracellular potential
  - …

(Note: “Continuous” is the common term but is misleading since it applies to both discrete and continuous in time)

- Stochastic point processes
  - Neural action potentials
  - Heart beats
  - Behavioral events
  - …

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## Delta functions (reminder)

- Dirac’s delta function

$$\delta(x-\tau) = 0 \quad x \neq \tau$$

$$\int_{-\infty}^{\infty} \delta(x-\tau)dx = 1$$

- Kronecker’s delta function

$$\delta(n-k) = \begin{cases} 1 & n = k \\ 0 & n \neq k \end{cases} \qquad \sum_{n=-\infty}^{\infty} \delta(n) = 1$$

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## Point process

- The spike train is represented by the sum of Dirac's delta functions at its firing times ($t_i$)

$$\rho(t) = \sum_{i=1}^{n} \delta(t - t_i)$$

- Point processes are unitary events in time. The actual values in time are meaningless.

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## Properties of a single spike train

- Firing rate
- Response to events
- Firing pattern
- Exact timing
- Entropy
- …

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## The neural transformation

$x(t)$ → Sensors → $r(t)$ → Spike Generator → $\rho(t)$

$x(t)$ = external signal

$r(t)$ = spike rate

$\rho(t)$ = actual spikes

We observe $\rho(t)$, and we need to estimate $r(t)$

(eventually we will use this to estimate $x(t)$)

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## Firing rate definition

- There are different definitions to firing rate
  - r – rate over the whole period T also called *spike count rate*
  - <r> - rate averaged over all the trials, also called *average firing rate*
  - *r(t)* – trial average rate over a short period ($\Delta t \rightarrow 0$)

and they are constantly mixed…

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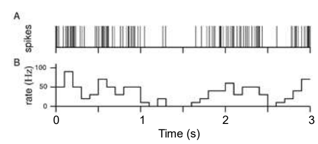
## Firing rates – number of spikes

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

Δt = 100 ms




From: Theoretical neuroscience / Dayan & Abbott

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## Convolution

- Convolution is an **operator** which takes two functions *f* and *g* and produces a third function that represents the overlap between *f* and a reversed version of *g*.
- Continuous: $(f * g)(t) = \int f(\tau)g(t-\tau)\,d\tau$
- Discrete: $(f * g)(m) = \sum_n f(n)g(m-n)$

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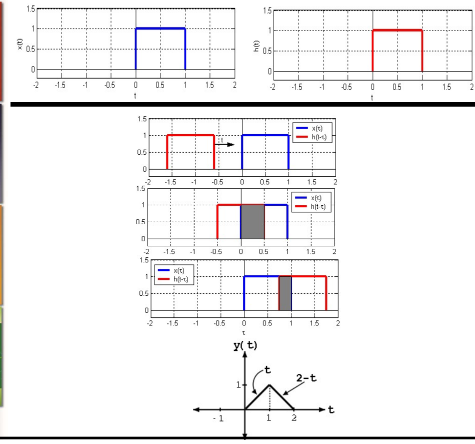


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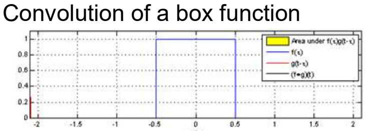
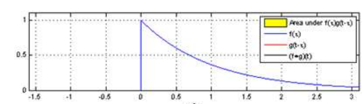
## Convolution examples

- Convolution of a box function



- Convolution of a spiky function



(From: www.wikipedia.org, Brian Amberg)

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## Convolution & Moving average

- A convolution is a general **moving average** when the averaging function integral is 1.
- In that case it functions as a **smoothing** function.
- When the averaging function is square it will function as regular mean using **overlapping bins**.
- Non-square functions enable **emphasis** of parts of the window.

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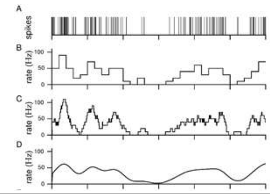
## Firing rates – sliding windows

Other definitions of firing rate use a sliding window: $r(t) = \int_{-\infty}^{\infty} d\tau\, w(\tau)\rho(t-\tau)$, with

$$w(t) = \frac{1}{\Delta t}, \quad -\Delta t/2 \le t \le \Delta t/2$$

$$w(t) = \frac{1}{\sqrt{2\pi}\sigma_w} \exp\left(-\frac{t^2}{2\sigma_w^2}\right)$$




Sliding rectangular window
Δt = 100 ms

Sliding Gaussian window
$\sigma_t$ = 100 ms

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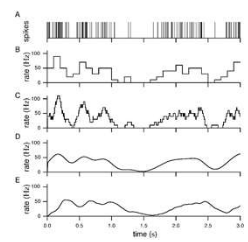
## Firing rates - causal windows

Temporal averaging with windows is non-causal. A causal alternative is $w(t)=[\alpha^2\, t\, e^{-\alpha t}]_+$




Sliding causal window
1/α = 100 ms

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## Smoothing & Convolution

- Smoothing and convolution pitfalls
  - Introduces spurious correlations over time
  - Hidden assumption about smoothness of the external sensory or motor data
  - Edge effects: what happens at the start and end of the data?
  - Phase lag: peaks of smoothed data may occur later than the peaks in the original data. True for non-symmetric kernels and all causal filters

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## Tuning curves

- r() can be a function of something other than time. e.g. r(angle) if the rate varies with direction of hand movement
- r(x) will still be time-varying if the argument x changes with time as x(t). It can also change dependence on x, if r = r(x,t).
- Describes the "tuning" of the neuron. x can be a scalar, vector, or function (pattern)
- A tuning curve is a model for the neuron's behavior, and is always an approximation since neurons are likely to have multiple inputs and respond to multiple internal and external variables.

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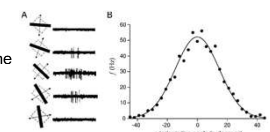
## Sensory tuning curves

- For sensory neurons, the firing rate depends on the stimulus s
- Extra cellular recording V1 monkey
- Response depends on angle of moving light bar
- Average over trials is fitted with a Gaussian




$$r(s) = r - \frac{(s - s2_{\max}}{2 \cdot \sigma^2}_{\max}$$

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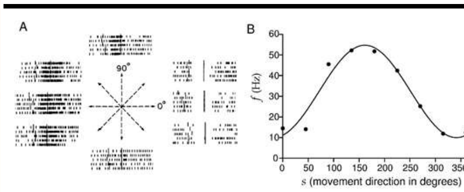
## Motor tuning curves




Extra cellular recording of monkey primary motor cortex M1 in arm-reaching task. Average firing rate is fitted with $r(s) = r_0 + (r0 \cos(_{\max_{\max}}$

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## Spike count variability

- Tuning curves model average behavior.
- Deviations of individual trials are given by a noise model.
  - Additive noise is independent of stimulus
    $r(s) = f(s) + \xi$
  - Multiplicative noise is proportional to stimulus
    $r(s) = f(s) + g(s) \cdot \xi$

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## Signal to noise ration

- **Power** of the signal (**m**ean **s**quare)

$Discrete\ \frac{1}{N}\sum_{i=1}^{N} {x_i}^2\ \ Contiuous\ \frac{1}{T}\int_0^T {x_i}^2$

- **Amplitude** of the signal (**r**oot **m**ean **s**quare)

$Discrete\ \sqrt{\frac{1}{N}\sum_{i=1}^{N} {x_i}^2}\ Contiuous\ \sqrt{\frac{1}{T}\int_0^T {x_i}^2}$

- The signal to noise ratio (SNR) may be calculated

  directly: $\frac{ms(signal)}{ms(signal)}\ \ or\ \ (\frac{rms(signal)}{rms(signal)})^2$

- However, typically a decibel (dB) scale is used…

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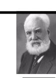
## Decibel (dB)



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- The **decibel** (**dB**) is a logarithmic measure of the ratio between two quantities:

$SNR_{dB} = 10log_{10}\frac{ms(signal)}{ms(signal)}\ \ or\ 20log_{10}\frac{rms(signal)}{rms(signal)}$

- SNR of 3 dB is roughly double the power while 10 dB is ten times the power.
- SNR of 6 dB is roughly double the amplitude while 20 dB is ten times the power.

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## Overview

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**Recommended reading:**
R. Lemon, Methods for neuronal recording in conscious animals, 1984, Chapter 2

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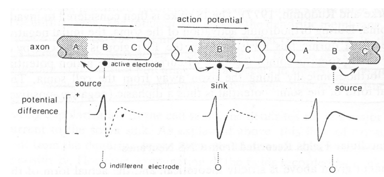
## Formation of extracellular potential I

- Different membrane potentials of the neuron lead to flow of current within the neuron which is matched by an **extracellular return current**.




**Sink** – Active area, current flows into the neuron
**Source** – Inactive region, current flow out of the neuron.

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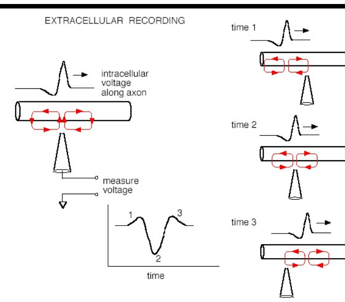
## Formation of extracellular potential II




Axon – Triphasic shape (+/-/+)

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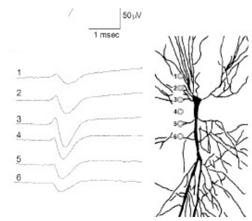
## Somatic extracellular spike shape

- Soma – Biphasic shape (-/+),
  - Negative due to flow from the initial segment
  - Positive due to flow to dendrite.
- Magnitude is proportional to surface area divided by the distance.

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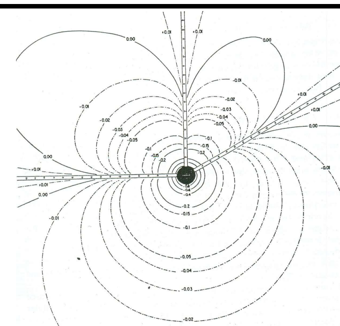
## Decay of extracellular signal



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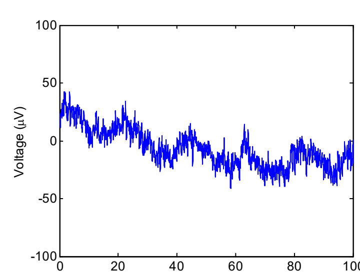
## Extracellular recording I

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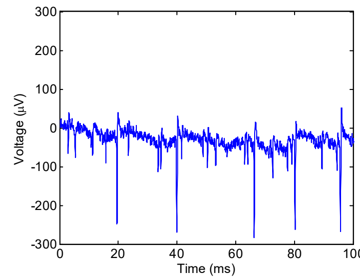
## Extracellular recording II

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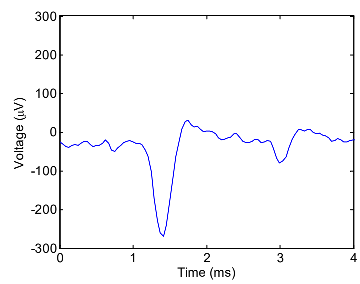
## Extracellular recording III

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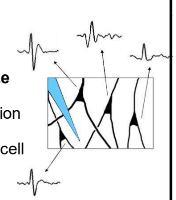
## Multiple units

- The electrode detects multiple neurons (also called **units**) which are close to its tip.
- The signals differ in:
  - **Amplitude** -dependent on cell **size** and **distance**.
  - **Phase shape** - depends on direction to soma, axon & dendrites.
  - **Temporal shape** - dependent on cell type.



- Spikes from the same neuron also vary significantly due to noise, bursts, drift of electrode, etc..

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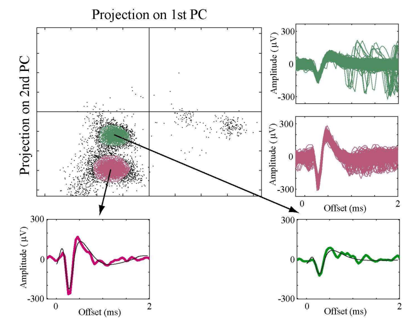
## Sorting multiple units

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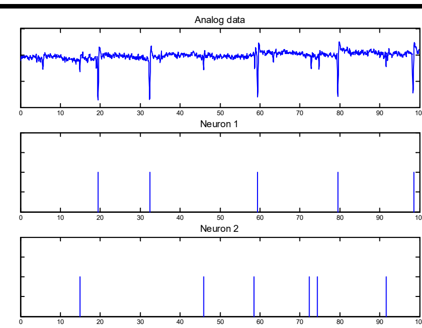
## Continuous signal → multiple spike trains (single units)

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## Multiple units

- Multiple single units
- Multi-unit activity
- Local field potential

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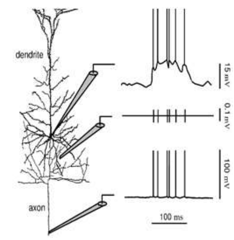
## Intracellular vs. Extracellular neuronal potentials

- Intracellular soma
- Extracellular
- Intracellular axon

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## Spike trains

- Transformation from a continuous recording to a series of discrete **timestamps**.
- Is all the information contained in the **timing** of the spikes?
- What are we losing?
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  - Non spiking activity
  - Sub-threshold activity

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