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2nd Recitation 23.3.22

Tuning Curves, Stochastic processes, Poisson Point Process (CV, FF, neuron simulation)

The recitation notes are based on:

- Drongelen, Signal processing for neuroscience, 2nd edition (2018)
- Lecture notes by dr. Naomi Feldheim, BIU math course: Probability and Stochastic Processes
- Lecture notes by dr. Ohad Feldheim, Stanford university math course: Introduction to Stochastic Processes
- Dayan and Abbott, Theoretical Neuroscience, 1st edition (2005)

Tuning Curves:

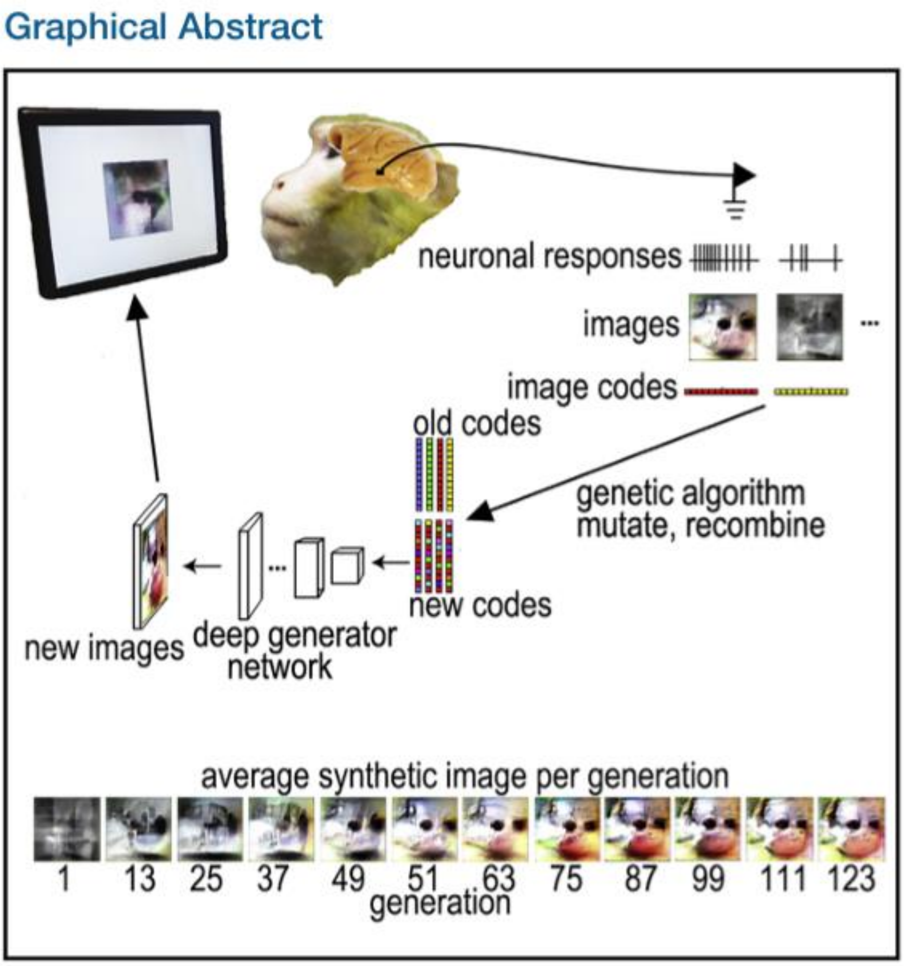
A basic question regarding the behavior of neurons in brains is by what mechanisms information from the outside world is translated to neural representation. Traditionally, tuning curves are a very common method for modeling this translation, mainly in the primary sensory and motor regions in the brain. By stimulating neurons with a range of stimuli (commonly orientation), one can correlate changes in firing rates to the neural representation of the given stimulus. This method must deal with two subsets of major unobvious assumptions:

The philosophical subset:

a. There's a preferred stimulus for a neuron (commonly we mistakenly refer to that stimulus as the only stimulus this neuron reacts to).
b. There's an injective function which relates one type of stimulus to only one reaction and vice versa. This is very similar to a stationary or ergodic assumption, but not the same.
c. Neurons discretize a range of stimuli to a countable set of behaviors. For example a neuron sensitive to triangles will react with the same firing rate to an isosceles and equilateral triangles but with different firing rate to a right triangle.

The methodic subset:

a. There's a good justification for the type of stimuli chosen for the experiments (There's a growing field in neuroscience, commonly using deep learning methods, which indicate this assumption is wrong, for example the revolutionary study of Ponce et al., 2019)



b. The appropriate firing rate computation method (wide average, bins, convolution). Commonly we explain why we chose a certain method.

c. The appropriate change in firing rate computation. We'll discuss some basic ideas regarding this computation:

   I. The naive attitude: The change in firing rate is transient between baseline phase and stimulated one, and there's a point in time in which firing rate changes (for example stimulus onset, or some known delayed time after it).

   II. The dynamic attitude: The change in firing rate is gradual between the baseline phase and the stimulated one, and even each one of the phases might dynamically change.

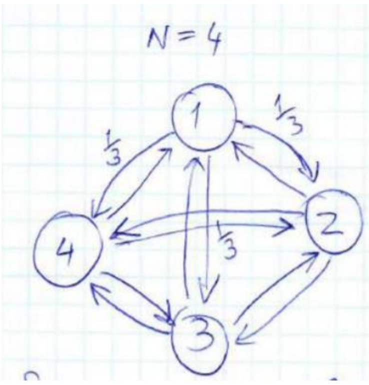
   III. The normalization attitude: Changes in firing rates must always be normalized to the given baseline in each trial and should be computed as a relative change (percentages, probabilities) and not as one value of firing rate.

There are more attitudes towards the question of tuning curve. Anyway, we should justify the method we chose, at least by presenting the distribution of results and its average and variance when creating a tuning curve based on the changes in firing rates averaged across trials. As a thumb rule, the smaller the variance across trials, the better justification we have for the method.

Short explanation about the paper in project 01: Butts and Goldman 2006

Stochastic Processes:

Mathematically, stochastic matrix is a transition matrix describing the probabilities of transitions between different states of a system. Example: the probability of a frog jumping between the leaves:



The stochastic matrix:

$$\mathbb{P} = \begin{pmatrix} 0 & \frac{1}{3} & \frac{1}{3} & \frac{1}{3} \\ \frac{1}{3} & 0 & \frac{1}{3} & \frac{1}{3} \\ \frac{1}{3} & \frac{1}{3} & 0 & \frac{1}{3} \\ \frac{1}{3} & \frac{1}{3} & \frac{1}{3} & 0 \end{pmatrix}$$

This matrix must define a Markov chain which has a Markov property of memoryless process. In neurons, we refer to this memoryless property regarding the assumption that in the short term of few hours, the probability for a neuron creating new spike does not depend on how many spikes the neuron ever produced and how many stimuli it was presented with. For this reason, we use the term "stochastic process" to refer to the neuron as a random system, non-deterministic.

How do we check stochasticity of a process? If it can be written with a deterministic equation, it is not stochastic (proof by contradiction). Practically in neuroscience, we want to check if a stochastic process is one of the following:

Stationary process	Weak stationary process	Ergodic process
Same distribution all along the process	Expectation and Covariance over time are constant	Expectation and Covariance over time and over trials are constant

Class Exercise: Define the following processes

Write three examples for processes or distributions- one stationary and ergodic, another one stochastic and not stationary and another stationary but not ergodic.

3 examples:

- Rolling a dice (Stationary and ergodic)
- Birds on a tree every day (Stochastic, not stationary)
- Average time of sport for every man (Stationary, not ergodic)

Poisson point processes:

So far, we can point at two basic behaviors that a brain computational unit must fulfill two demands regarding the encoding of stimuli:

- Response to a range of stimuli with a specific pattern (for example tuning curve)
- Responds in a stochastically manner

Therefore, tools from the mathematical Markov theory for stochastic processes fit our description for neuron using a mathematical model of Poisson Point Process. Stochastic processes can be divided to two kinds:

a. Discrete processes, in which there is a countable set of states that the transition between them is probable. Based on these tools, the Boltzmann model for neurons arises, modeling only two states of the neurons- firing or not (1,0). Boltzmann model does not treat the question of time to transition between the two states, only the probability to move between them.

b. Continuous processes, in which the states are taken from a continuous group, meaning any partial group is considered as a state and the transition between them is given by a known PDF. Given that time is continuous, the tools from this field allow to model spiking activity changes within time. In this paradigm we will treat the number of spikes for each interval $(\Delta \mathrm{t})$ as a state:

Neuron state in interval Δt = $Num\ of\ spikes$

To simplify the stochastic continuous process, we will base our model on two assumptions:

- Renewal process: the probability for a certain number of spikes (n) in each interval (Δt) is independent of the preceding intervals. If it is constant, we refer to it as homogenous process and if not- non-homogenous process.
- Firing rate as probability: The probability for a neuron to generate a spike is constant given that a neuron didn't generate one yet. This assumption will be later used for creating a simulation of poisson neuron and for understanding its survival function.

During the lectures, you have learnt the mathematical proof that the two assumptions model a neuron with firing probabilities corresponding to poisson and exponential distributions. Now we can understand the mathematical definition of poisson point process:

Consider $\{\mathrm{E}_i\}_{i\in\mathbb{N}}$, a sequence of independent random variables [for example: number of spikes in a given interval], exponentially distributed with parameter λ [or r in our field]. Define a sequence of points $S_i = \sum_{j=1}^{i} E_i$. A Poisson Point Process on $[0,\infty)$ with intensity λ [r] is $X_t = \begin{cases} 1 & t \in \{\mathrm{S}_i\}_{i\in\mathbb{N}} \\ 0 & otherwise \end{cases}$.

(Adapted from Ohad Feldheim lecture notes).

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Class Exercise: Calculations with numbers

If we have a sample rate of 1000 Hz with a firing rate of $r = 20\frac{spikes}{second}$, what is the probability of 4 spikes within 12 ms? Use the following illustration:

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

………etc

(Adapted from Drongelen)

Solution:

Using the binomial distribution:

$$p = \binom{M}{n}(r\Delta t)^n(1 - r\Delta t)^{M-n} = \binom{12}{4}\left(20 \cdot \frac{12}{1000}\right)^4\left(1 - 20 \cdot \frac{12}{1000}\right)^{12-4}$$

Some important notes:

- As proved in lectures when $\Delta t \to 0$, the spiking activity acts as a Poisson distribution, so using a binomial distribution could be a good approximation for a Poisson neuron simulation for bins with one spike at most.
- Why not use the PDF as defined in exponential distribution? The probability is given by $p = \lambda e^{-\lambda x}$ when $\lambda = rT$ and T is a given time in the recording and x can't be translated.
- Commonly students tend to be confused between the number of spikes within a certain time duration and the probability of them. Given a firing rate function, we don't know how many spikes were at each second, but only the probability for a certain number of spikes within each second.
- Note that a Poisson distribution is given by $p(n) = \frac{\lambda^n}{n!}e^{-\lambda}$ when $\lambda = rT$ and represents the probability for a certain number of spikes by the time T.
- Importantly, note that in Poisson distribution the expectation λ and the most probable value are the same, but in exponential distribution not:

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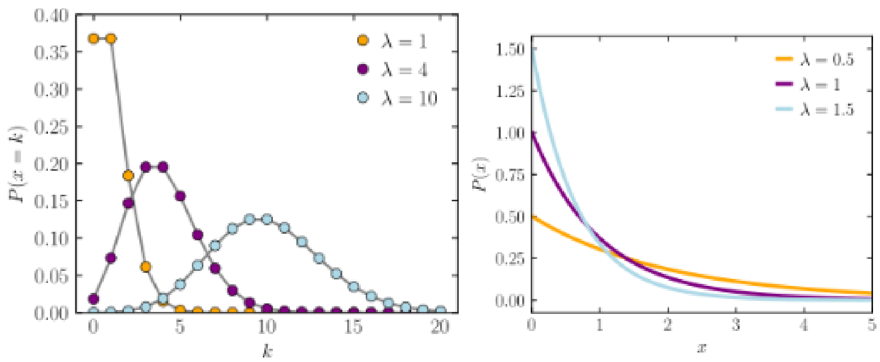
Poisson distribution and exponential distribution from Wikipedia:



Poisson neuron simulation

There are two attitudes for simulating a Poisson neuron:

- By definition: After each spike choosing randomly the interval to the next spike from an exponential distribution with $\lambda = rT$ when T is the current time of the spike.
- Preferably: Based on the binomial approximation, for each small bin Δt_i choosing randomly a number x_i from a given uniform distribution (the simple rand function). Only if $r_i \Delta t > x_i$ the simulated neuron generates a spike (assigned as 1; otherwise assigned as 0). This method must assume for a relevant approximation that the possible change in $r(t) \gg \text{bin size}$, and that for each bin, number of spikes is 1 at most.

Expansion: How Poisson model for neuron is used in real research

Studying the olfactory system, Van Drongelen et al. (1978) used the Poisson model for receptor cells in the olfactory system. In the olfactory system, around 1000 peripheral sensory neurons project to a single mitral cell in olfactory bulb in the brain. Using different levels of stimulation, the authors demonstrated how the neurons show different patterns of probabilistic firing rates. Thus, the particular neuron's threshold can be defined by the stimulus level that evokes response in 50% of the presentation of that stimulus. Mitral cells receive input from very large number of neurons at the same time, and this might predict a lower threshold for concentrations of odorant as compared with peripheral threshold (called convergence effect). Given the probability of a single peripheral neuron to spike for odorant at time T is e^{-pT}, the probability that none of the neurons fired is $1 - (e^{-pT})^{1000}$. This represent the threshold differences between peripheral neurons and the mitral cells, which were indeed experimentally confirmed.

Basic Terms and Measurements regarding Poisson model:

- **ISI:** Inter-spike Interval. In regular process it will be a constant number and in Poisson process it is stochastic and in homogenous Poisson process it is approximated by the binomial distribution:

$$P(ISI = \ k \ intervals) = (1-p)^{k-1} \cdot p \quad when \, p = rT$$

If for example we want to calculate the probability for ISI of 5 bins, we assume that for 4 bins there was no spike and in the 5th one there was. If the given firing rate is $r = 20 \frac{spikes}{sec}$ and each bin is 1 ms, then:

$$P = (1 - 20 \cdot 0.001)^4 \cdot 20 \cdot 0.001$$

For a continuous homogenous poisson process, we assume homogenicity for a short time dt when the spike occurred during τ and than:

$$P(N(t, t+\tau) = k) = \frac{e^{-\lambda\tau}(\lambda\tau)^k}{k!}$$

$$P(ISI = \tau) = P(N(0, \tau - dt) = 0) \cdot P(N(\tau - dt, \tau) = 1)$$

- **CV:** coefficient of variance, used for ISI only. Since for exponential distribution standard deviation and expectation are the same, for Poisson neuron model $CV \approx 1$ and for regular neuron $CV \approx 0$:

$$C_V = \frac{std(ISI)}{E(ISI)}$$

- **Fano Factor:** used for spike counts only (number of spikes in each bin). Since for Poisson distribution variance deviation and expectation are the same, for Poisson neuron model $FF \approx 1$ using small bins and for regular neuron FF will change more dramatically as a function of the bin size. Using big bins for a Poisson neuron, for example few seconds, might lead to $FF > 1$.

$$FF = \frac{Var(spike\ count\ over\ T)}{E(spike\ count\ over\ T)}$$

Fano Factor and CV are dispersion measurements of distribution, indicating the level of density:

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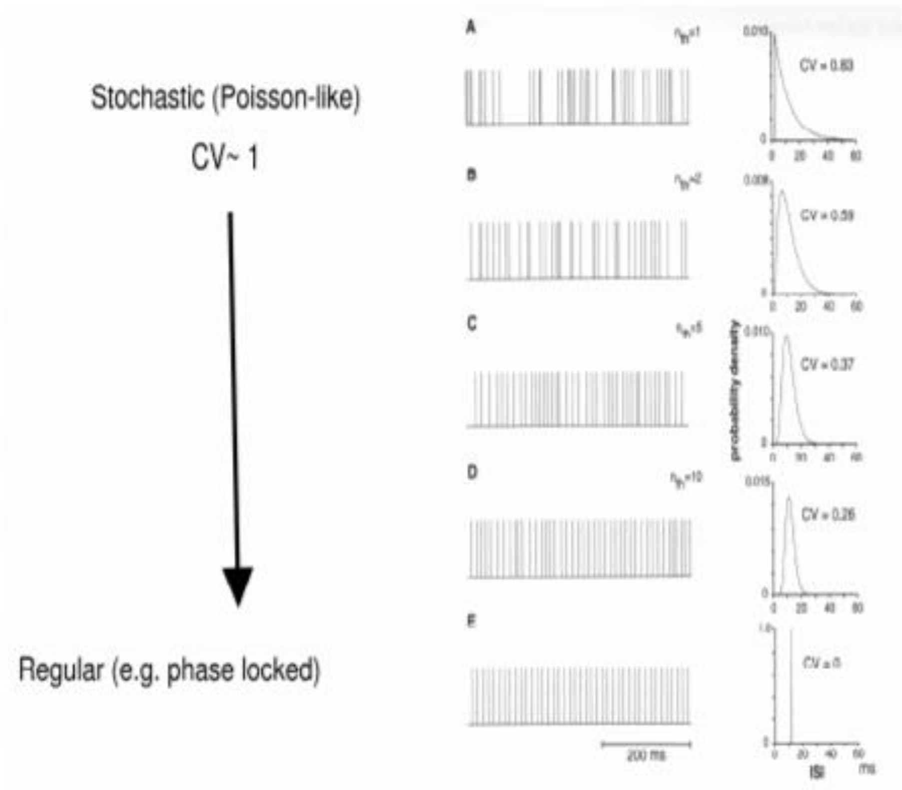
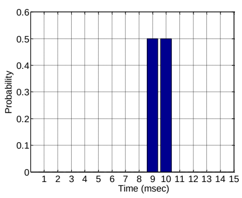


Question for discussion: If $FF = CV \approx 1$ can we assume we have a Poisson neuron? Not necessarily, it might be also a kind of a burster neuron with stochastically changing number of bursts.

Examples from past exams:

2007 exam: The ISI histogram of a neuron in the Quasis Regularlis ganglion is plotted below:



1. Calculate the CV, compare to Poisson.
2. Estimate the Fano factor (100msec window for rate calculation), compare to Poisson.

Solution:

1. The CV can be calculated directly from the histogram:

$E(ISI) = 0.5 \cdot 9 + 0.5 \cdot 10 = 9.5 \quad var(ISI) = 0.5 \cdot (9 - 9.5)^2 + 0.5 \cdot (10 - 9.5)^2 = 0.5^2$

$$C_V = \frac{\sqrt{var(ISI)}}{E(ISI)} = \frac{\sqrt{0.5^2}}{9.5} \ll 1$$

This is much smaller than 1, and therefore this neuron is much closer to a regular neuron.

2. Using the expectation of the interval, we can estimate the expectation of the spike count:

$$E(spike\ over\ T) = \frac{T}{E(ISI)} = \frac{100}{9.5} \sim 10.5$$

To calculate the variance, we look what is the difference between min spike count and max spike count, and this is the maximum std:

$$min(spike\ over\ T) = \frac{100}{10} = 10, max(spike\ over\ T) = \frac{100}{9} \sim 11$$

$$var(spike\ over\ T) \leq 0.5^2$$

$$FF \leq \frac{var(spike\ over\ T)}{E(spike\ over\ T)} \approx \frac{0.5^2}{10.5} \ll 1$$

Also based on Fano factor, the given neuron isn't Poisson neuron.

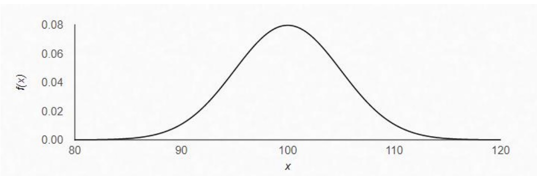
2005 exam: A pacemaker neuron fires 10 spikes/s in a fairlyregular manner ISI=N(100ms,5ms) draw the ISI distribution and estimate the Fano factor and calculate the coefficient of variation. (Normal distribution is given by $f_X(x) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\left(\frac{x-\mu}{\sqrt{2}\sigma}\right)^2}$)

Solution:

Calculating the CV is by definition:

$$C_V = \frac{std(ISI)}{E(ISI)} = \frac{5}{100}$$

For FF calculation we can use an illustration:



1 std stands for 68% of the graph, two thirds of the ISI are between 90 and 110, so we can evaluate that the std of spike counts over T are given by:

$$min(spike\ over\ T) = \frac{T}{110} \quad max(spike\ over\ T) = \frac{T}{90}$$

To evaluate the expectation, we can choose an interval of $T = 100ms$ which is also the median of the ISI distribution, meaning that for half of bins of 100 there is no spike and for the other only one:

$$p(0\ spikes\ ver\ 100\ ms) = p(1\ spike\ ver\ 100\ ms) = 0.5$$

$$E(spikes\ over\ 100\ ms) = 0 \cdot 0.5 + 1 \cdot 0.5 = 0.5$$

$$min(spikes\ over\ 100\ ms) = \frac{100}{110} \approx 0 \quad max(spikes\ over\ 100\ ms) = \frac{100}{90} \approx 1$$

Therefore:

$$var(spike\ over\ 100\ ms) = 0.5 \cdot (0 - 0.5)^2 + 0.5 \cdot (1 - 0.5)^2 = 0.5^2$$

$$var(spike\ over\ T) \leq 0.5^2$$

$$FF \approx \frac{0.5^2}{0.5} = 0.5$$