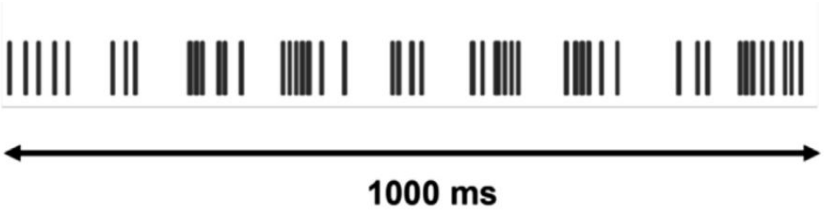
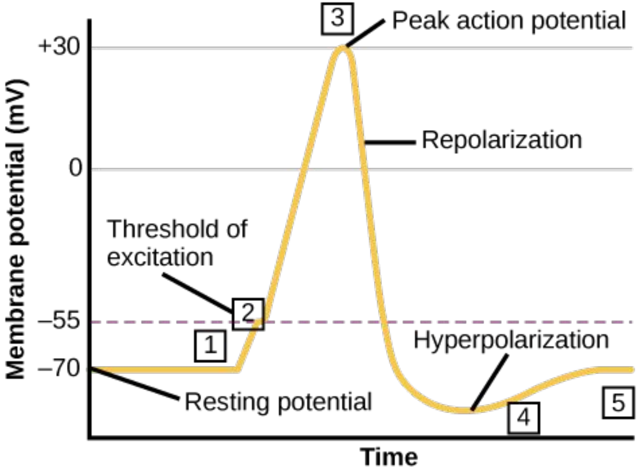
Lecture 4

Spike Stimulus Analysis

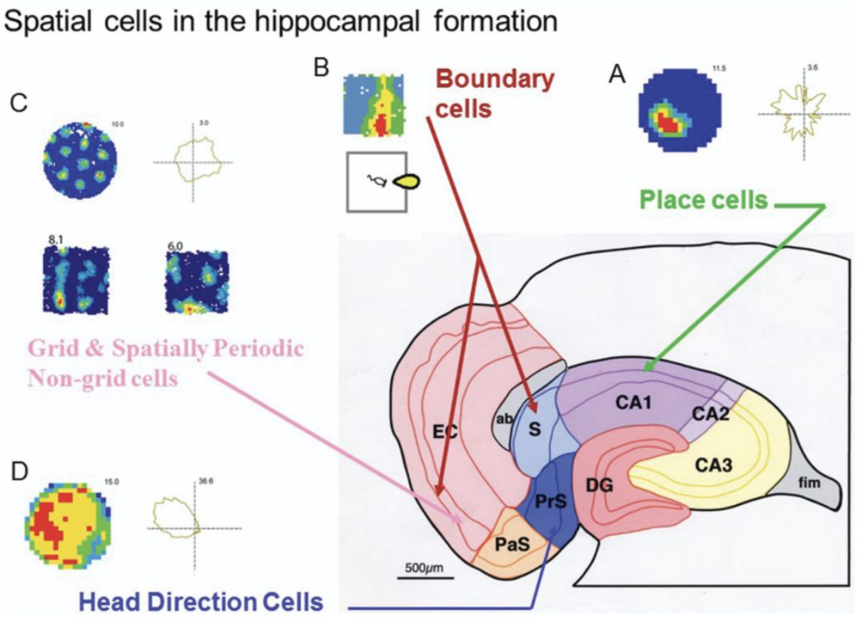
Last time: Action potentials from a neuron can be represented as a sequence of times (spike train)



{0.003, 0.030, 0.34, …}

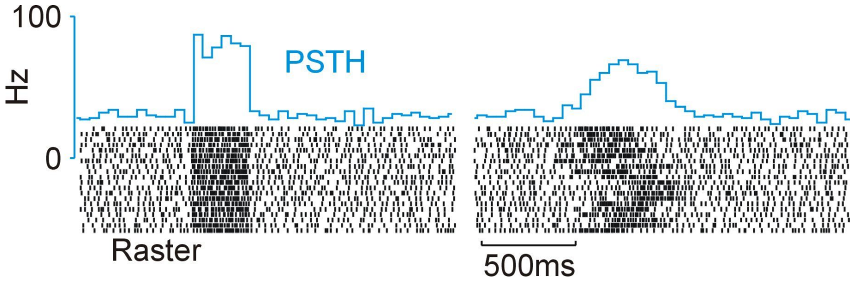


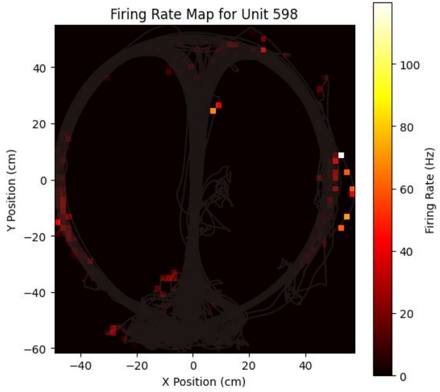
Spike times can vary based on internal dynamics (refractory period, bursting) or external stimuli

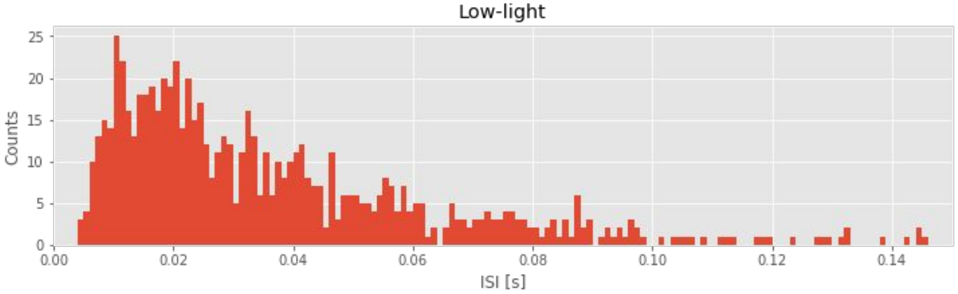


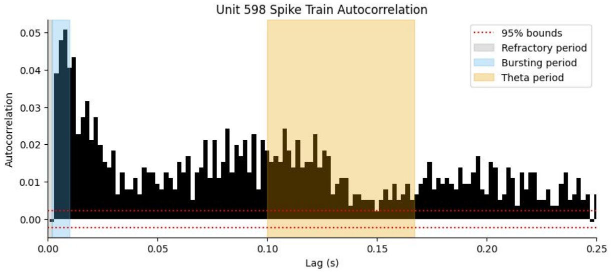
Our goal in systems neuroscience is to understand this variation in spiking.

We talked about some basic visualizations and calculations to understand variation in spiking









Agenda: more explicit statistical models for describing spiking of neurons

Temporal point processes as a model for spiking

Homogeneous Poisson point processes

Inhomogeneous Poisson point processes

Non-Poisson Point Processes

Conditional Intensity Function - Generalized Poisson rate function

Poisson regression to fit conditional intensity functions

Evaluating fit of models

Why do we need more explicit statistical models?

Measure how well the data is described by a particular model (how valid is the model?)

Compare models and test hypotheses (does one model fit the data better?)

Calculate confidence intervals (model uncertainty, a PETH/rate map only describes what happens on average)

Control for more than one effect (what are the contributions of position and speed? what is the contribution of bursting?)

Making assumptions explicit

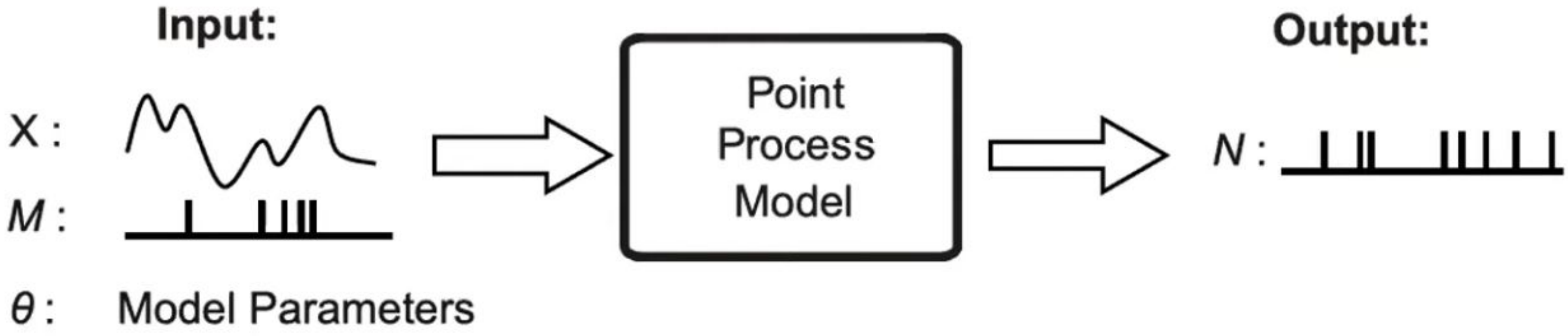
To understand variation in spiking, we can characterize the spike times as the result of a temporal point process

A point process is a stochastic process that generates discrete events occurring at random times (e.g. spike times, earthquakes, subway arrival times, volcanic eruptions, births, receiving emails)

A stochastic process specifies a probability law for how a system evolves over time, including how values at different times depend on one another.

A temporal point process is one that evolves just in time (a point process can be more general and evolve in spatial dimensions or some abstract space).

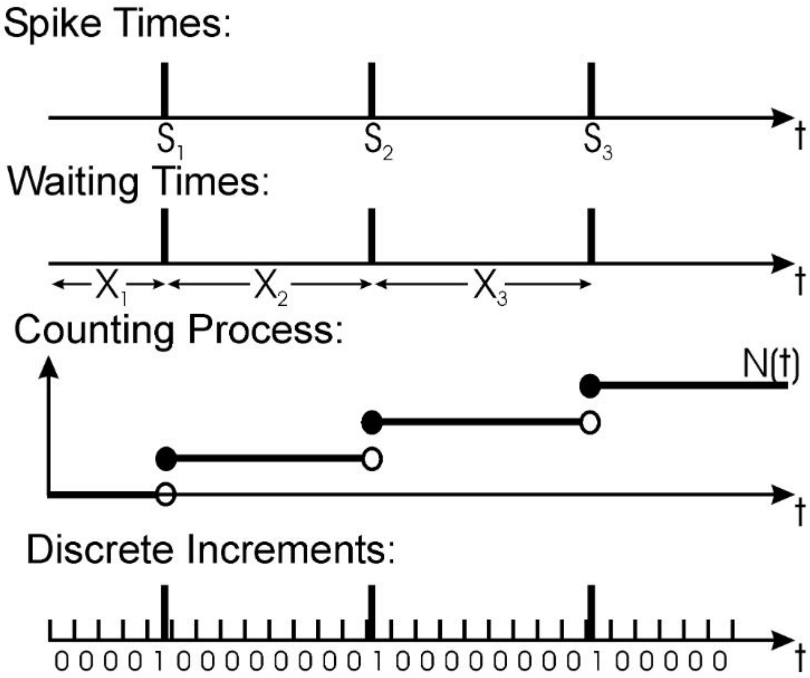
To understand variation in spiking, we can characterize the spike times as the result of a temporal point process



You can think of a probabilistic generator that determines, at each moment in time, how likely the neuron is to spike based on stimuli, internal dynamics, and past spikes.

The goal of statistical modeling is to estimate the rules governing that generator.

A temporal point process may be specified in terms of spike times, inter-spike intervals, or spike counts.



You can choose to model point processes in terms of these different characterizations.

Kass, Eden, Brown 2014

Simple temporal point process: Homogeneous Poisson

Poisson processes are point processes for which **spiking probabilities do not depend on occurrence or timing of past spikes.** The number of spikes for a given interval is Poisson distributed.

A homogeneous Poisson process has a **constant spiking rate over time**.

This lacks many features of neuronal spiking, but is an important building block for understanding how to characterize neural point processes.

$$P(k) = \frac{\lambda^k e^{-\lambda}}{k!}$$

lambda = rate (expected number of events)

P(k) = probability of k spikes

Homogeneous Poisson

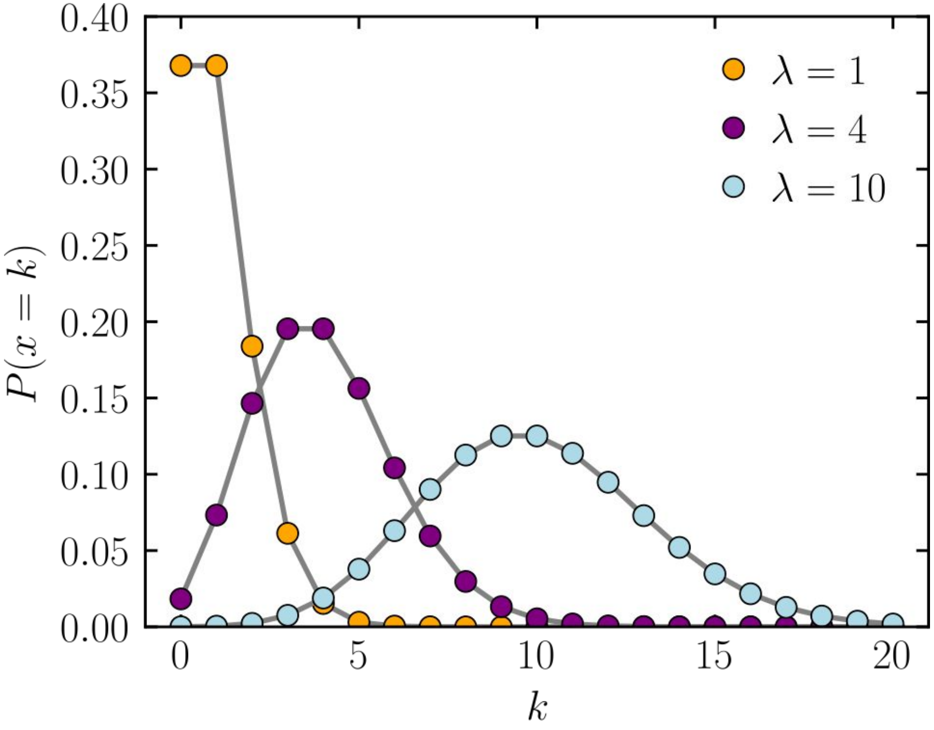
$$P(k) = \frac{\lambda^k e^{-\lambda}}{k!}$$

Low rate (lambda = 1): most probable one spike

Medium rate (lambda = 4):

most probable 4 spikes but long tail

High rate (lambda = 10): Gaussian-like



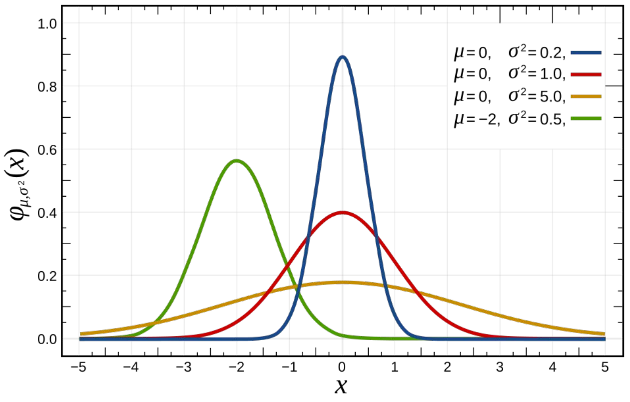
Number of spikes

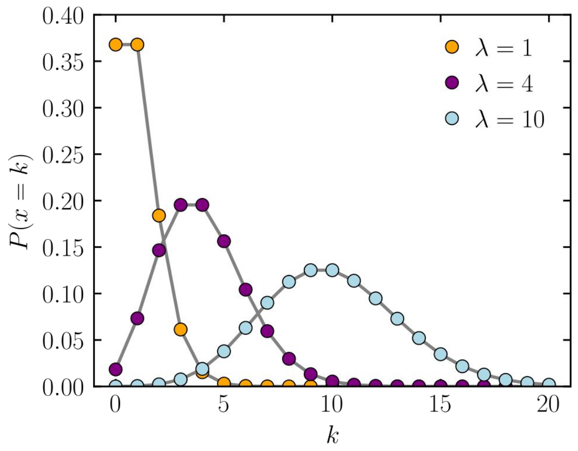
Why this is better than using a Gaussian

Modeling discrete integer counts, not continuous values

With a Gaussian, you can go below zero but spike rate is non-negative

With a Poisson, mean and variance are linked: higher rate → higher variability. Poisson captures this with one parameter; Gaussian can't.





Important properties of homogeneous Poisson processes

Stationary increments: distribution of spike counts depends only on the length of the interval, not on where the interval occurs in time.

Spike counts from non-overlapping intervals are independent: the distribution of the number of events in any interval does not depend on any of the spiking activity outside that interval.

Knowing the number (or times) of one or more events tells us nothing about other possible events.

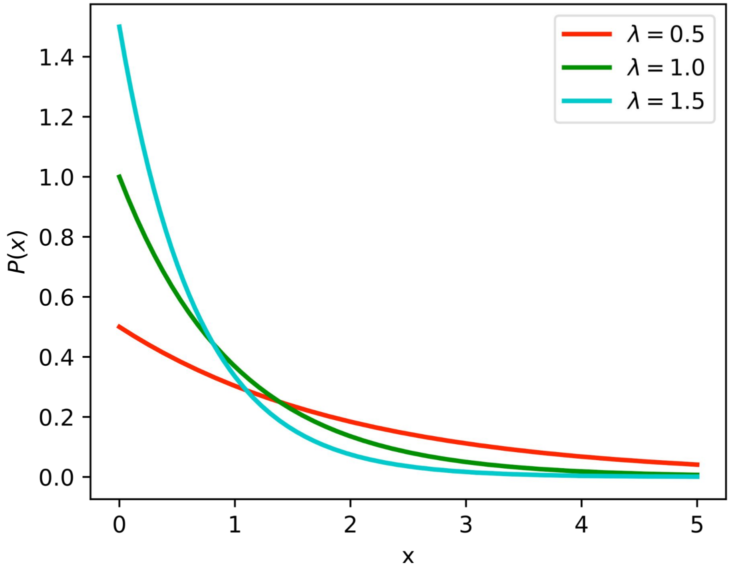
Memorylessness: the probability of the next spike does not depend on how long since the last spike.

Homogeneous Poisson Point Processes have exponential waiting time distributions

Mostly short ISIs with some long ISIs. As you increase the rate, the number of short waiting times increases.

Given that no spike has occurred for some time, the distribution of the remaining waiting time is the same as it was at the start.

Make sure you understand the difference between the waiting times (exponentially distributed) and the counts (poisson distributed)

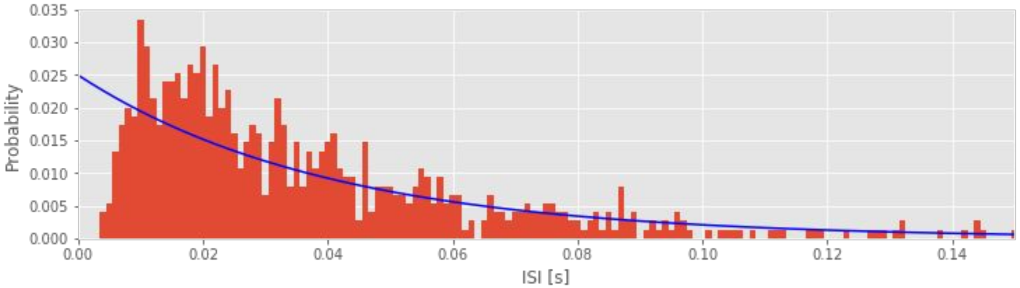


$$f(x) = \lambda \exp(-\lambda x)$$

Why didn't our simple Poisson model fit well?

Simple homogeneous Poisson model assumes:

- Constant rate over time
- No spike-history dependence (memoryless)



But real neurons:

- Rate depends on covariates (position, direction, stimulus, behavior)
- Exhibit refractory periods and bursting (history dependence)
- Are modulated by rhythms (e.g., theta phase)

Extension: Inhomogeneous Poisson

Allow firing rate to change over time (probability of firing a spike in a small interval varies in time)

$$\lambda(t)$$ **Poisson rate function**

$$P(\text{spike}) \approx \lambda(t_i)\Delta t$$

Imagine subdividing time into time bins

Before we assumed these all had the same constant rate

$$\lambda(t) = \lim_{\Delta t \to 0} \frac{\Pr\left(\Delta N_{(t,t+\Delta t]} = 1\right)}{\Delta t}.$$

Now we assume each can have its own rate that depends on time.

As the bin width goes to zero, the expected spike count in an interval becomes:

$$\sum_i \lambda(t_i)\Delta t \;\to\; \int_a^b \lambda(u)\, du$$

Extension: Inhomogeneous Poisson

If the rate varies with time $\lambda(t)$, then for an interval $[a, b]$:

$$\mu = \int_a^b \lambda(u)\, du$$

and:

$$P(N(b) - N(a) = k) = \frac{\left(\int_a^b \lambda(u)\, du\right)^k e^{-\int_a^b \lambda(u)\, du}}{k!}$$

just substitute the integral into the Poisson

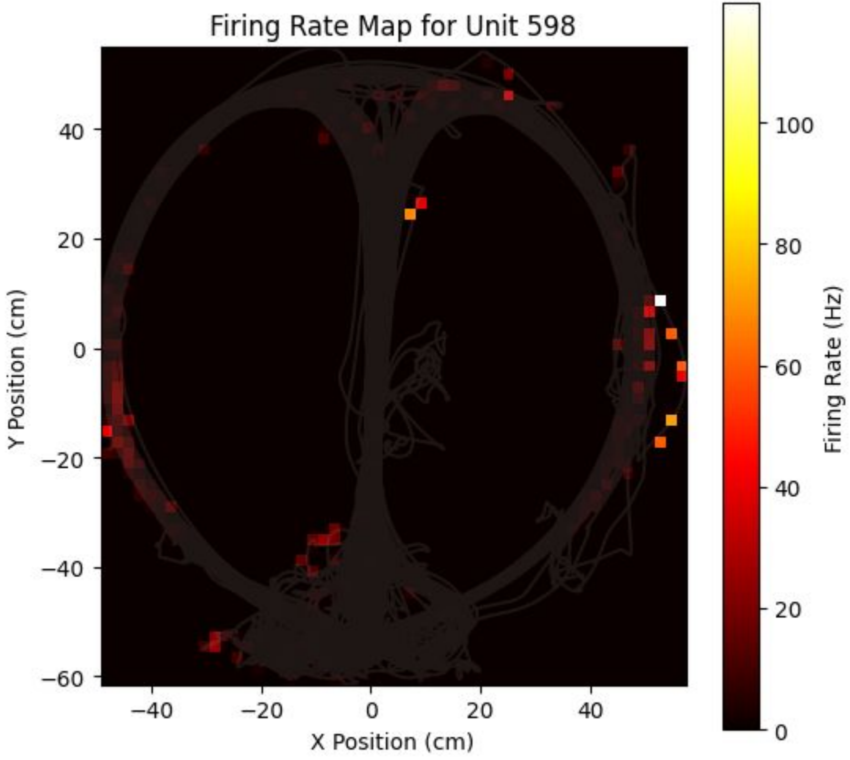
Allowing the rate to change over time is powerful

We actually can describe a change in firing rate in terms of not just time but any covariate like position.

$$\lambda(t) = f(X(t))$$

The notion of a place field is that firing rate changes over position, that it is greater at certain positions.

Counts in intervals are still Poisson distributed.



Likelihood of a spike train: probability of spikes given the model

$$L(\lambda) = \left[\prod_{i=1}^{n} \lambda(t_i)\right] \exp\left(-\int_0^T \lambda(t)\,dt\right)$$

$$\log L = \sum_{i=1}^{n} \log \lambda(t_i) - \int_0^T \lambda(t)\,dt$$

Also possible to define Inhomogeneous Poisson in terms of its ISI distribution

$$\boxed{f_{S_i}\left(s_i \mid S_{i-1} = s_{i-1}\right) = \lambda(s_i)\exp\left\{-\int_{s_{i-1}}^{s_i} \lambda(t)\,dt\right\}}$$

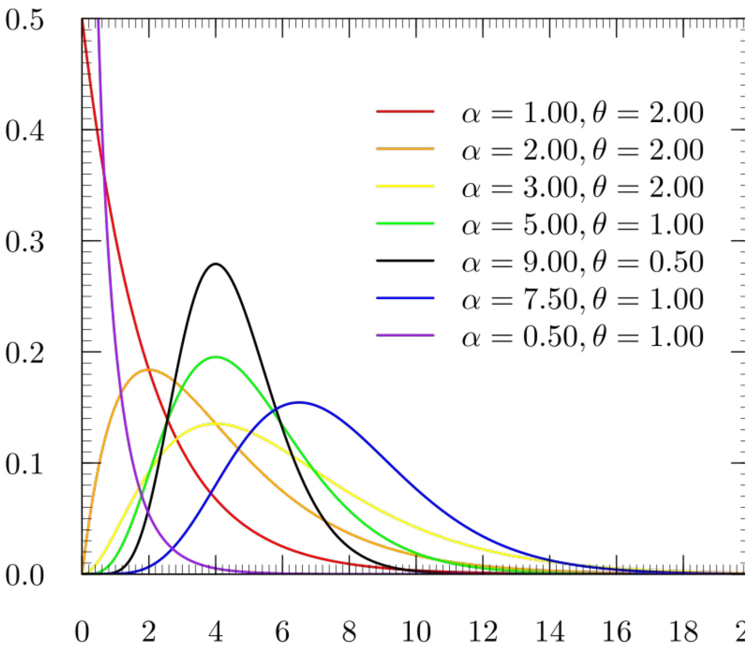
The inhomogeneous Poisson process can also be described through its waiting-time distribution, which depends on the integral of the rate function over time.

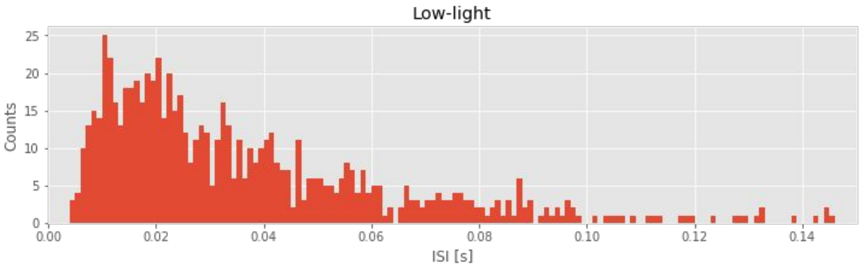
We still haven’t dealt with history dependence in spiking: refractory periods, bursting

A r**enewal process** is a simple point process for which the probability of firing a spike at any point in time can depend on the occurrence time of the last spike, but not on any spikes before then.

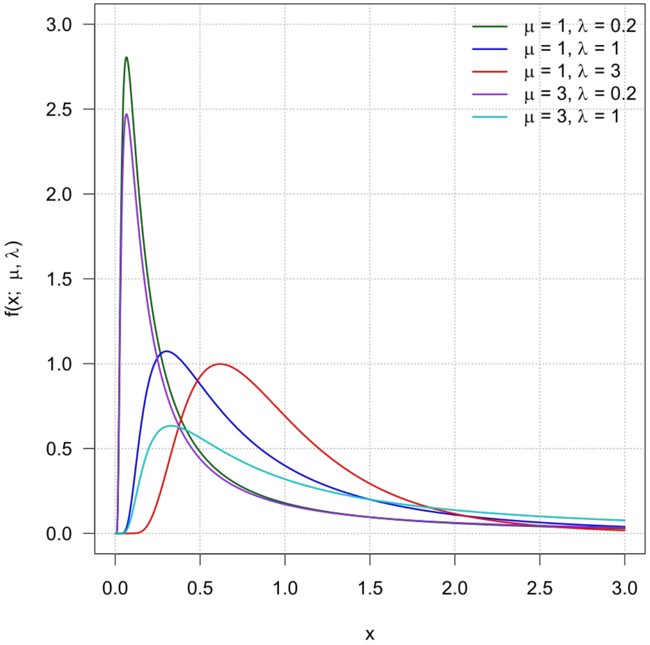
We specify a renewal process by writing down a distribution of the interspike interval. We can technically use any distribution, but there are common ones like **Gamma and Inverse Gaussian**

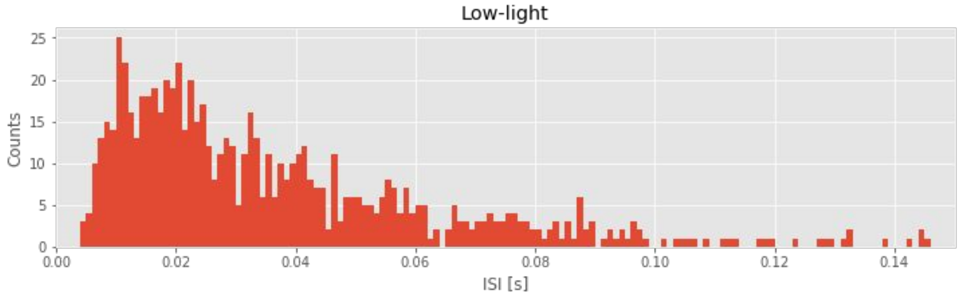
Gamma distribution is a flexible two parameter distribution that has exponential as a special case





Inverse Gaussian distribution is another flexible two parameter probability distribution (useful for modeling refractory period)





Renewal Process Limitations

Break memorylessness

But still assume only one-step memory

Cannot model dependence on multiple past spikes

Cannot naturally incorporate covariates

So far we've seen these point processes:

Poisson → no memory

Inhomogeneous Poisson → time-varying rate

Renewal → depends only on time since last spike

How do we write down a model that allows dependence on all of these?

Conditional Intensity Function

Generalizes the Poisson rate function by allowing dependence on all the past spikes

Poisson Rate Function

$$\lambda(t) = \lim_{\Delta t \to 0} \frac{\Pr\left(\Delta N_{(t,t+\Delta t]} = 1\right)}{\Delta t}.$$

Conditional Intensity Function

$$\lambda(t \mid H_t) = \lim_{\Delta t \to 0} \frac{\Pr(\Delta N_{(t,t+\Delta t]} = 1 \mid H_t)}{\Delta t}$$

Generalizes the homogeneous and inhomogenous Poisson

$$\lambda(t \mid H_t) = \lambda_0 .$$ Homogeneous Poisson

$$\lambda(t \mid H_t) = \lambda(t) .$$ Inhomogeneous Poisson

Conditional Intensity Function

We no longer assume independent increments.

The probability of spiking depends on previous spikes.

The process is no longer determined solely by clock time.

If λ depends on history deterministically → not Poisson.

If λ is stochastic (e.g. depends on stochastic spike history) → doubly stochastic.

But counts in infinitesimal bins are still conditionally Poisson.

Conditional Intensity Function $\lambda(t \mid \mathcal{H}_t, X(t))$

In principle, this can be an arbitrary function of history and covariates.

But we cannot estimate an arbitrary function.

We need:

- A parameterized family
- Something flexible but learnable
- Something with a tractable likelihood

Linear predictor

A simple idea is to assume the log firing rate depends linearly on covariates.

$$\lambda(t) = \exp(\eta(t))$$

where

$$\eta(t) = \beta^\top X(t)$$

Then:

$$\lambda(t) = \exp(\beta^\top X(t))$$

This guarantees:

- $\lambda(t) > 0$
- Convex log-likelihood
- Tractable optimization

How do we learn the mapping from covariates (like position) to rate?

Our goal is to estimate the parameters (beta) such that the Poisson likelihood is maximized

$$\lambda(t) = e^{\beta_0 + \beta_1 x_1(t)}$$

Maximize the log likelihood of the data given the parameters

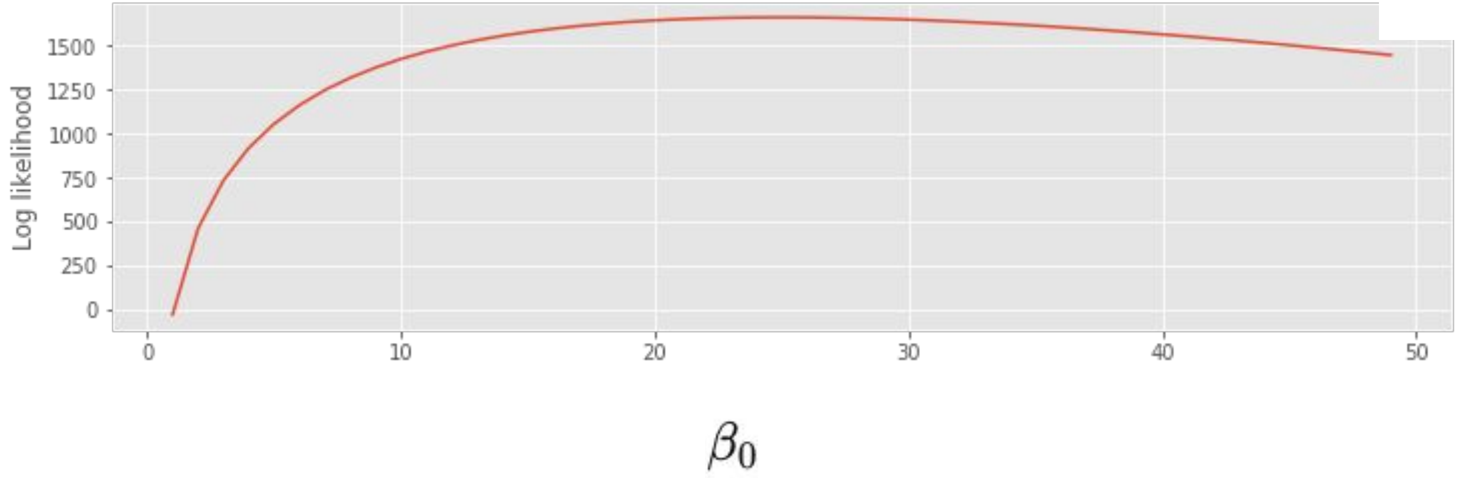
$$\log P(\mathbf{y} \mid \mathbf{X}, \theta) = \sum_t \log P(y_t \mid \mathbf{x_t}, \theta),$$

where

$$P(y_t \mid \mathbf{x_t}, \theta) = \frac{\lambda_t^{y_t} \exp(-\lambda_t)}{y_t!}, \text{ with rate } \lambda_t = \exp(\mathbf{x_t}^\top \theta).$$

Maximize the log likelihood of the spikes given the parameters

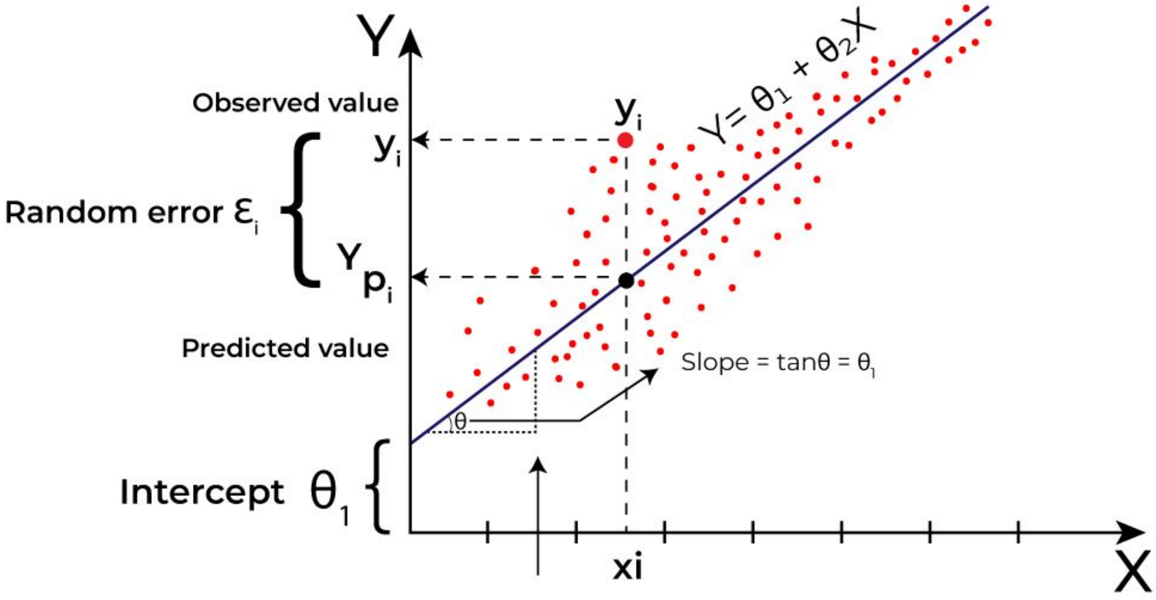
$$P(k) = \frac{\lambda^k e^{-\lambda}}{k!}$$



$$\lambda(t) = e^{\beta_0 -}$$

Peak gives you your most likely parameters, curvature gives you uncertainty

This also happens in linear regression



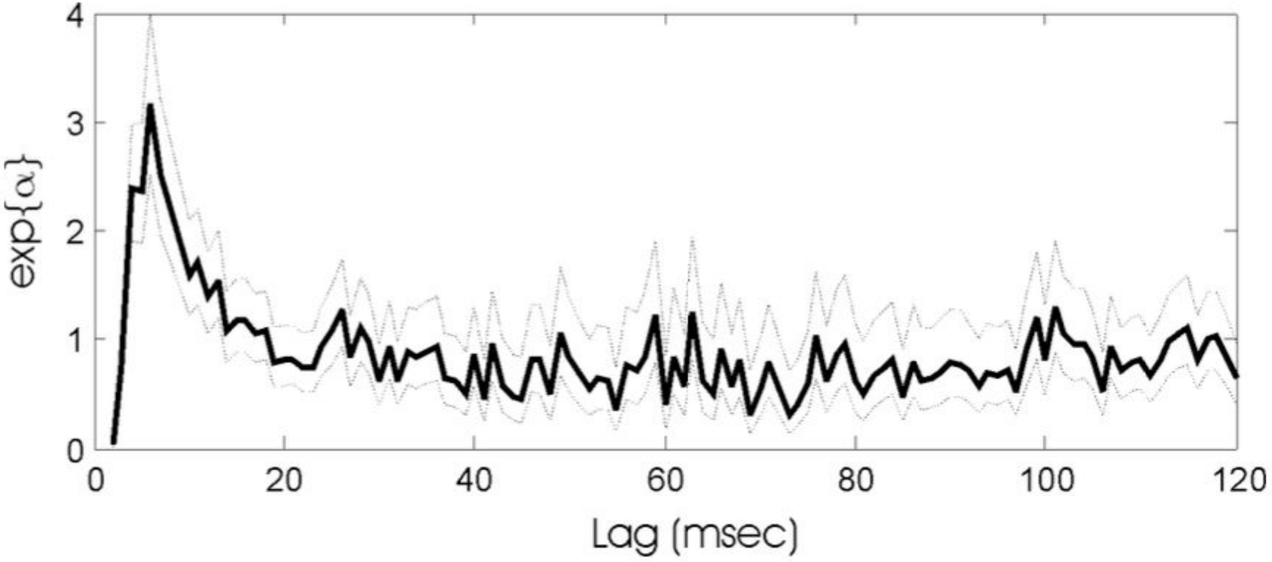
Example of fitting discrete covariates

Interpreting coefficients

Example of fitting a PETH: adding indicators

Example of adding history Dependence

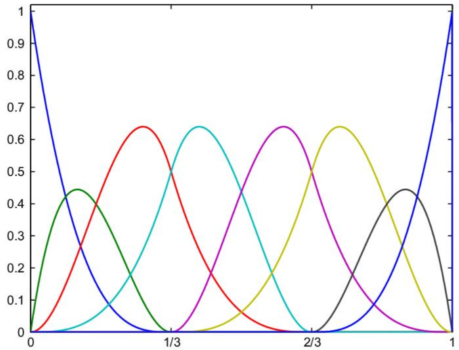
Example of history dependence

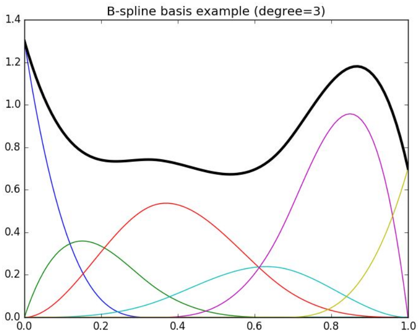


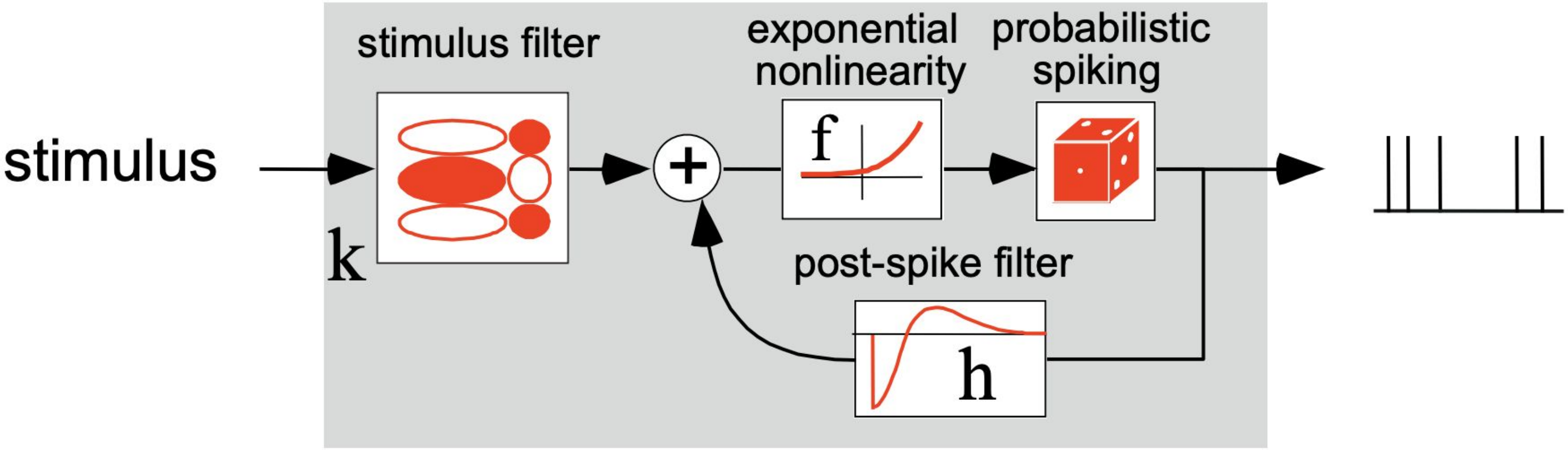
Spline models

Indicator functions are like histograms. They have a lot of parameters and don’t enforce smoothness between adjacent bins.

Splines are piecewise polynomials that enforce smoothness at the joins. Their height is controlled by the parameter corresponding to that polynomial.






stimulus
stimulus filter
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