

Stochastic neuronal discharge models and their inference

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LASCON, January 24 2018, Lecture 4

Outline

What are we going to discuss?

In defense of a modeling approach with a strong stochastic element

Descriptive stats, stationary discharge 1 neuron

Descriptive stats, stationary discharge 2 neurons

Descriptive stats, stimulus response 1 neuron

Some stochastic models of neuronal discharges

Working with the intensity of the process

Model and inference

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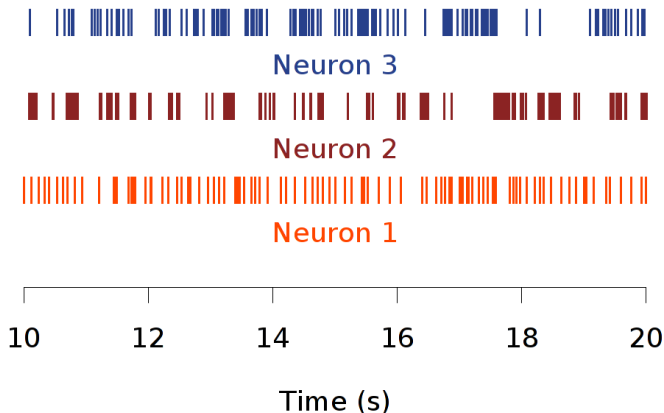
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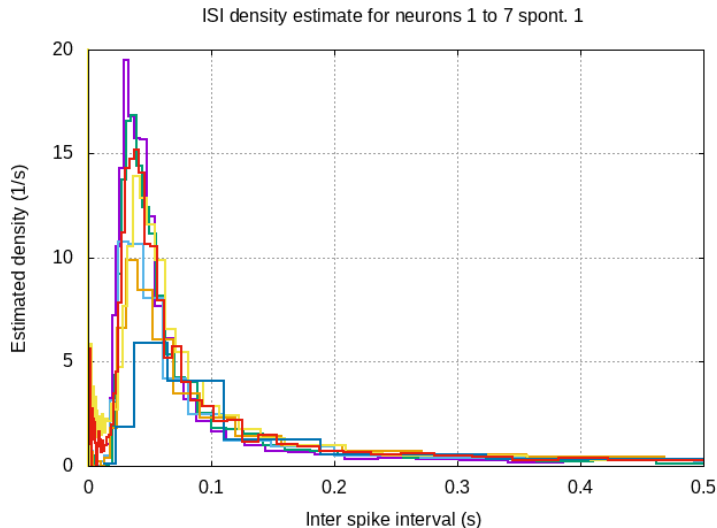
Model and inference

Spike trains

After a "rather heavy" pre-processing stage called **spike sorting**, the **raster plot** representing the spike trains can be built:

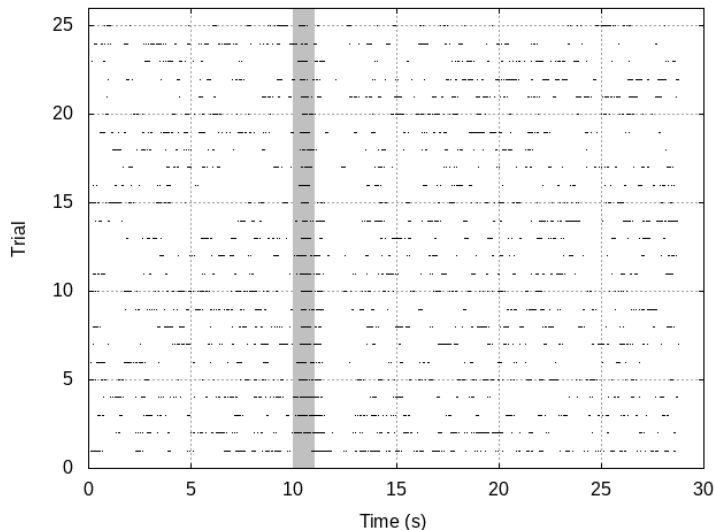


Inter Spike Intervals (ISI)

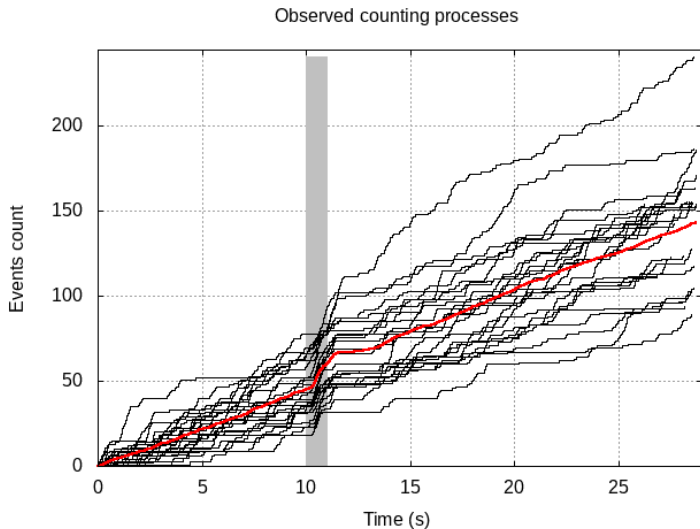


Estimated ISI densities of 7 neurons recorded simultaneously from the locust antennal lobe.

Responses to stimulation



Raster plots from one of the neurons showing the responses to 25 presentations (gray background) of cis-3-hexen-1-ol.



The observed counting processes associated with the 25 observed point processes just shown. In red the empirical mean of the 25.

Modeling spike trains: Why and How?

- ▶ A key working hypothesis in Neurosciences states that the spikes' occurrence times, as opposed to their waveform are the only information carriers between brain region (Adrian and Zotterman, 1926).
- ▶ This hypothesis encourages the development of models whose goal is to predict the probability of occurrence of a spike at a given time, without necessarily considering the biophysical spike generation mechanisms.

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Membrane noise can lead to output fluctuations

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PROCEEDINGS OF THE IEEE, VOL. 56, NO. 6, JUNE 1968

Fluctuation Phenomena in Nerve Membrane

A. A. VERVEEN AND H. E. DERKSEN

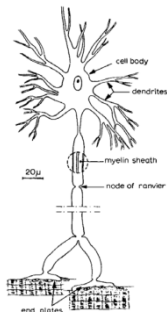


Fig. 1. Schematic representation of neuron

ulus per two seconds. Both the mean of the distribution function (defined as the threshold) and the standard deviation show an approximately hyperbolic relation to stimulus duration. The coefficient of variation (the normalized standard deviation) is constant for a given fiber. The latency distributions exhibit a rather complex dependence on duration and amplitude of the stimulus (Pecher,^[8] Horvath *et al.*,^[9] ten Hoopen and Verveen^[10]).

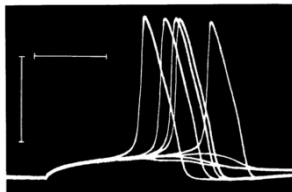


Fig. 2. Response of a Ranvier node to repeated stimulation at threshold intensity. Stimulus duration: 5 ms. Interval between successive stimuli: 2 seconds. Superposition of eight successive sweeps.

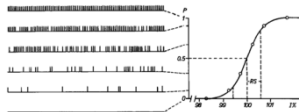
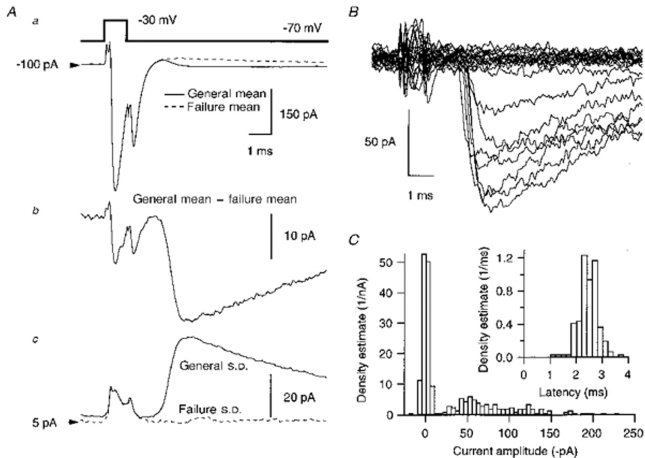


Fig. 3. Relation between stimulus intensity and probability of response. Frequency of stimulation: 0.5 Hz. (From Verveen^[6].)

Synaptic noise is ubiquitous



(Pouzat & Marty, 1998)

Action potential propagation failures can occur

J. Physiol. (1980), **301**, pp. 243-259

With 8 text-figures

Printed in Great Britain

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MECHANISMS OF ACTION POTENTIAL PROPAGATION FAILURE AT SITES OF AXON BRANCHING IN THE CRAYFISH

By DEAN O. SMITH

From the Department of Physiology, University of Wisconsin, 470 North Charter Street, Madison, Wisconsin 53706 U.S.A.

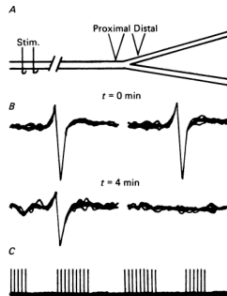


Fig. 1. Action potential propagation failure at branch points. *A*; action potentials are recorded extracellularly with microelectrodes located within distances less than 100 μm proximal and distal to a region of axon bifurcation. The nerve is stimulated by a suction electrode located more centrally. *B*, at the onset of stimulation at 50 impulses/sec, action potentials were recorded from both sites; after 4 min of repetitive stimulation, the action potential failed to propagate to the distal recording site. *C*, intermittent periods of action potential conduction alternate with failure. Records in *B* and *C* have been retouched for clarity.

A Summary of noise sources

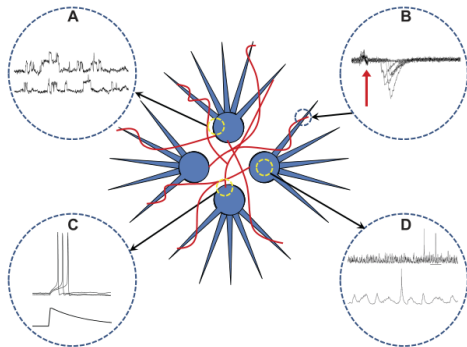


FIGURE 1 Origin of voltage noise in neurons. Schematic representation of a network of four neurons interconnected by reciprocal synapses (axons in red, dendrites in blue). *A*: channel noise illustrated by patch-clamp recording at -20 mV from cerebellar Purkinje cell. The noisy nature of channel activity is expressed by the random step-like changes in current flow. *B*: synaptic noise illustrated by fluctuations in synaptic current in loose patch recording from frog neuromuscular junction. The synaptic responses were evoked by stimulating the motor nerve. Arrow marks arrival of action potential at the synaptic site. Note the variable amplitude and onset of synaptic responses. (Records kindly provided by H. Parnas and I. Parnas.) *C*: uncertain spike timing: jittery spike initiation. Three superimposed responses to simulated synaptic current injected in the cell body of an interneuron from the cerebellar cortex. [From Mann-Metzer and Yarom (71).] *D*: background synaptic activity recorded from cortical neuron in anesthetized rat. The bottom trace is an enlargement of the marked line in the upper trace. (From Yarom-Jakoubovitch et al., unpublished data.)

Fig. 1 of Yarom and Hounsgaard (2011).

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Single neuron spike trains

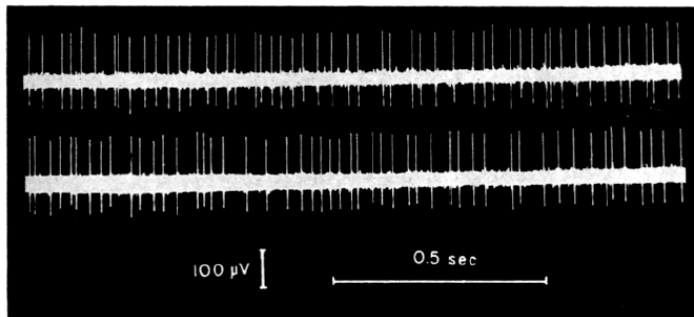


FIG. 6. Maintained discharge in a single off-center ganglion cell, showing fluctuations in the durations of successive intervals. Retouched photographic records.

A recording from a cat (retinal) ganglion cell by Kuffler, Fitzhugh and Barlow (1957).

ISI histograms

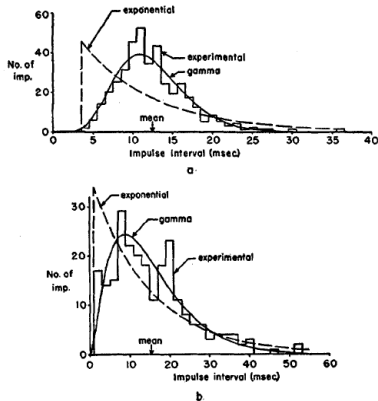
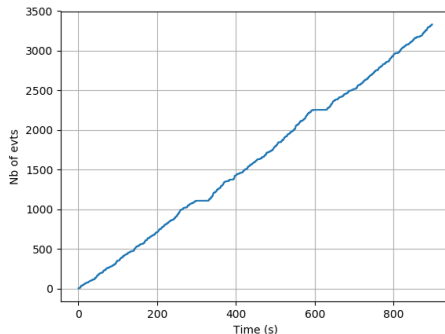


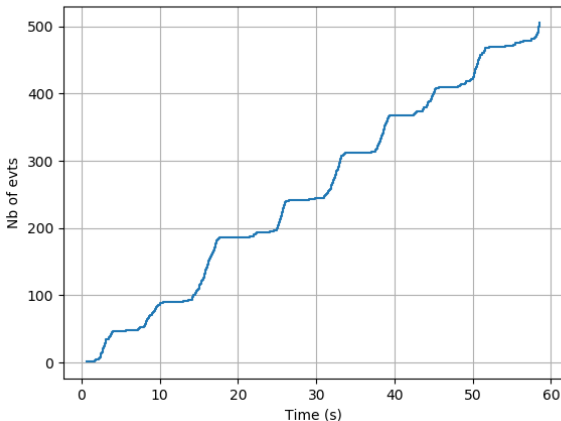
FIG. 7. Two distributions of impulse intervals from different ganglion cells. (a) shows unit 3 (see Table I), and (b), unit 4. Two theoretical curves, the exponential and the gamma distributions, are shown. Only the gamma gives a satisfactory fit.

They got good fits with a gamma distribution.

An alternative display: the observed counting process

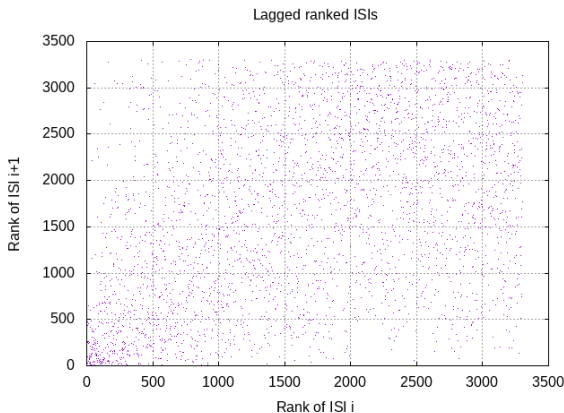


In their **first figure**, Cox & Lewis (*The Statistical Analysis of Series of Events*, 1966) use this kind of display, showing the *observed counting process* (what Guilherme wrote $N(t)$ yesterday). Here applied to spontaneous data recorded from a well isolated neuron in the locust antennal lobe.



Another example from a neuron recorded and sorted from the cockroach *Periplaneta americana* by Antoine Chaffiol.

Check the potential correlations between successive ISI



Here the locust data. The *rank* of ISI_{k+1} is shown against the rank of ISI_k .

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Recurrence times

ANALYSIS OF DISCHARGES RECORDED SIMULTANEOUSLY FROM PAIRS OF AUDITORY NERVE FIBERS

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From the Eaton-Peabody Laboratory of Auditory Physiology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts 02114, and Research Laboratory of Electronics, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139. Dr. Johnson's present address is Lincoln Laboratory, Lexington, Massachusetts 02173.

ABSTRACT Spike trains were recorded simultaneously from pairs of auditory nerve fibers in anesthetized cats. Tests for correlation between spike trains were developed for spontaneous activity and for discharge patterns resulting from single-tone stimuli. The application of these tests to the recordings indicates that the responses of auditory nerve fibers to a tone and to silence can be described as statistically independent point processes. This result implies that the initiation of spikes in these fibers is governed by localized processes specific for each fiber.

Johnson & Kiang (1976) *J Neurophysiol.*

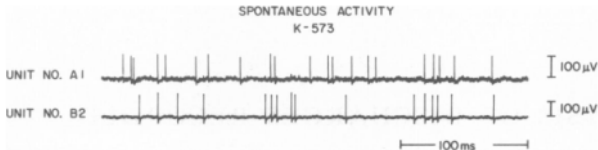


FIGURE 1 Simultaneously recorded spike trains from two auditory nerve fibers. The characteristic frequency of unit A1 is 2.58 kHz and that of B2 is 2.41 kHz. Their spontaneous discharge rates are 44.2 spikes/s and 40.7 spikes/s, respectively. An upward deflection of each trace corresponds to positivity of the recording microelectrode relative to the headholder.

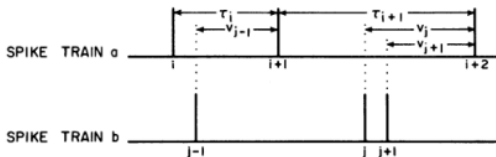
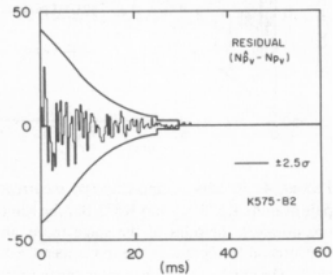
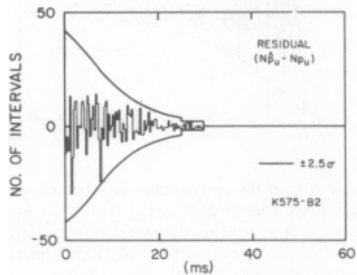
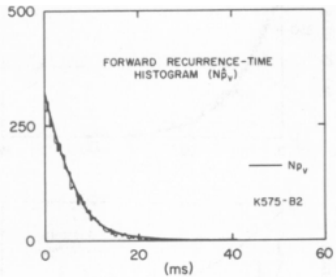
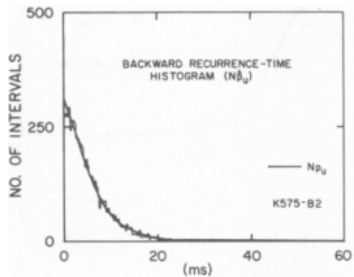


FIGURE 2 Definitions of the quantities used in the recurrence-time test. The quantity τ is a random variable denoting the interval between successive spikes in spike train a . τ_i is the measured interval between the i^{th} and $(i+1)^{\text{th}}$ spike. The random variable v_j denotes the forward recurrence time measured with respect to the j^{th} spike in spike train b .



Cross-correlation histograms

Biol. Cybernetics 22, 213—228 (1976)
© by Springer-Verlag 1976

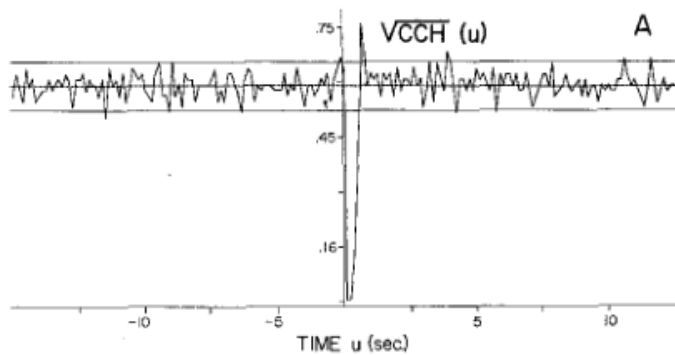
Identification of Synaptic Interactions★

David R. Brillinger

Department of Statistics, University of California, Berkeley, California

Hugh L. Bryant, Jr., and José P. Segundo

Department of Anatomy and the Brain Research Institute, University of California, Los Angeles, California USA



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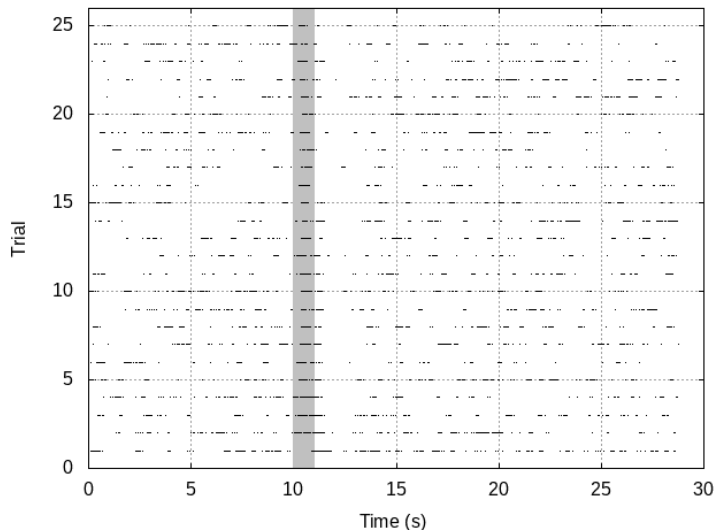
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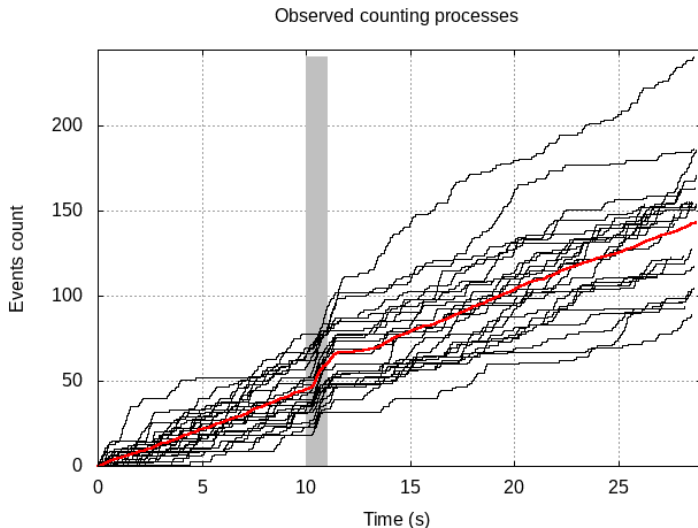
Model and inference

The classical *raster plot*



Raster plots from one of the neurons showing the responses to 25 presentations (gray background) of cis-3-hexen-1-ol.

The more informative observed counting processes



The observed counting processes associated with the 25 observed point processes just shown. In red the empirical mean of the 25.

The Peri-Stimulus Time Histogram

For details on PSTHs, don't miss my Saturday morning talk!

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A random walk with a drift

RANDOM WALK MODELS FOR THE SPIKE ACTIVITY OF A SINGLE NEURON

GEORGE L. GERSTEIN *and* BENOIT MANDELBROT

From the Center for Communication Sciences, Research Laboratory of Electronics, Massachusetts Institute of Technology, Cambridge, Massachusetts; Harvard University, Cambridge, Massachusetts; and I. B. M. Thomas J. Watson Research Center, Yorktown Heights, New York

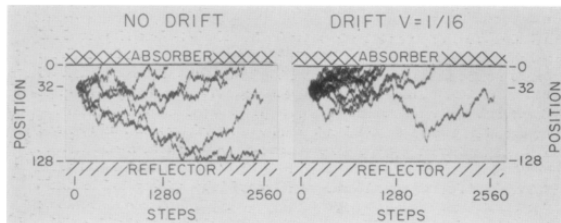


FIGURE 3 Typical random walks in one dimension in a computer simulation of the model.

(Biophysical Journal, 1964)

Maximum Likelihood Identification of Neural Point Process Systems

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¹ Department of Biomedical Engineering, The Johns Hopkins School of Medicine, Baltimore, MD 21205, USA

² Department of Mathematical Sciences, G.W.C. Whiting School of Engineering, The Johns Hopkins University, Baltimore, MD 21218, USA

Assume that the SI of the i th component can be written $j = 1, \dots, J$. With F_t^N as defined in the previous section, as a sum of integrals (having time-invariant kernels) the likelihood function corresponding to observations with respect to the system counting process paths: over $[0, t]$ (see Karr 1986) is

$$\lambda_i(t) = h_i^0 + \sum_{j=1}^J \int_0^t h_{ij}(t-u) N_j(du). \quad (1) \quad \exp \left[\sum_{j=1}^J \int_0^t [1 - \lambda_j(u)] du + \sum_{j=1}^J \int_0^t \log[\lambda_j(u)] dN_j(u) \right], \quad (2)$$

but, without further restrictions on the kernels $h_{ij}(\cdot)$, the likelihood value is unbounded except in degenerate cases. This difficulty will be avoided here by turning to a parametric model. Assume, for each i and j , that $h_{ij}(\cdot)$ is of finite duration (i.e., the system has finite memory) and is piecewise constant:

A generalized linear model (GLM)

Biol. Cybern. 59, 189–200 (1988)

Biological
Cybernetics
© Springer-Verlag 1988

Maximum Likelihood Analysis of Spike Trains of Interacting Nerve Cells*

D. R. Brillinger

Statistics Department, University of California, Berkeley, CA 94720, USA

computational purposes. Specifically, in the case of a neuron B influencing a neuron C , the unknown parameters are estimated by maximizing the expression

$$\prod_i p_i^{C_i} (1 - p_i)^{1 - C_i},$$

where, if B_t and C_t are 0–1 time series corresponding to the spike trains and if γ_t is the time elapsed since neuron C last fired

$$p_t = \Phi \left(\sum_{u=0}^{\gamma_t-1} b_u B_{t-u} + \theta_1 \gamma_t + \theta_2 \gamma_t^2 + \theta_3 \gamma_t^3 - \theta \right) \quad (1.1)$$

for $\Phi(x)$ the normal cumulative function. It is an approximation to the probability that neuron C fires at time t given the past behaviours.

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Few definitions

Counting Process: For points $\{t_j\}$ randomly scattered along a line, the counting process $N(t)$ gives the number of points observed in the interval $(0, t]$:

$$N(t) = \#\{t_j \text{ with } 0 < t_j \leq t\}$$

where $\#$ stands for the number of elements of a set.

History: The history, \mathcal{H}_t , consists of the variates determined up to and including time t that are necessary to describe the evolution of the counting process. \mathcal{H}_t can include all or part of the neuron's discharge up to t but also the discharge sequences of other neurons recorded simultaneously, the elapsed time since the onset of a stimulus, the nature of the stimulus, etc. One of the major problems facing the neuroscientist analysing spike trains is the determination of what constitutes \mathcal{H}_t for the data at hand. A pre-requisite for practical applications of the approach described here is that \mathcal{H}_t involves only a finite (but possibly random) time period prior to t .

Conditional Intensity: For the process N and history \mathcal{H}_t , the conditional intensity at time t is defined by:

$$\lambda(t \mid \mathcal{H}_t) = \lim_{\delta \downarrow 0} \frac{\mathbb{P}\{N(t, t + \delta) - N(t) = 1 \mid \mathcal{H}_t\}}{\delta}$$

Probability of an ISI based on the intensity

We will find the probability density of the interval between two successive events, $I_j = t_{j+1} - t_j$.

Defining $\delta = \frac{t_{j+1} - t_j}{K}$, where $K \in \mathbb{N}^*$, we write the probability of the interval as the following product:

$$\begin{aligned}\mathbb{P}\{I_j\} &= \mathbb{P}\{N(t_j + \delta) - N(t_j) = 0 \mid \mathcal{H}_{t_j}\} \cdot \\ &\quad \cdot \mathbb{P}\{N(t_j + 2\delta) - N(t_j + \delta) = 0 \mid \mathcal{H}_{t_j + \delta}\} \cdots \\ &\quad \cdots \mathbb{P}\{N(t_j + K\delta) - N(t_j + (K-1)\delta) = 0 \mid \mathcal{H}_{t_j + (K-1)\delta}\} \cdot \\ &\quad \cdot \mathbb{P}\{N(t_j + (K+1)\delta) - N(t_j + K\delta) = 1 \mid \mathcal{H}_{t_j + K\delta}\}\end{aligned}$$

If we interpret our definition of the conditional intensity as meaning:

$$\mathbb{P}\{N(t, t + \delta) - N(t) = 0 \mid \mathcal{H}_t\} = 1 - \lambda(t \mid \mathcal{H}_t) \delta + o(\delta)$$

$$\mathbb{P}\{N(t, t + \delta) - N(t) = 1 \mid \mathcal{H}_t\} = \lambda(t \mid \mathcal{H}_t) \delta + o(\delta)$$

$$\mathbb{P}\{N(t, t + \delta) - N(t) > 1 \mid \mathcal{H}_t\} = o(\delta)$$

where $o(\delta)$ is such that $\lim_{\delta \rightarrow 0} \frac{o(\delta)}{\delta} = 0$.

The interval's probability becomes the outcome of a sequence of Bernoulli trials, each with an inhomogeneous success probability given by $\lambda_i \delta + o(\delta)$, where, $\lambda_i = \lambda(t_j + i \delta \mid \mathcal{H}_{t_j + i \delta})$ and we get:

$$\mathbb{P}\{I_j = t_{j+1} - t_j\} = \left(\prod_{k=1}^K (1 - \lambda_k \delta + o(\delta)) \right) (\lambda_{K+1} \delta + o(\delta))$$

We can rewrite the first term on the right hand side as:

$$\begin{aligned}\prod_{k=1}^K (1 - \lambda_k \delta + o(\delta)) &= \exp \log \prod_{k=1}^K (1 - \lambda_k \delta + o(\delta)) \\&= \exp \sum_{k=1}^K \log(1 - \lambda_k \delta + o(\delta)) \\&= \exp \sum_{k=1}^K (-\lambda_k \delta + o(\delta)) \\&= \exp\left(-\sum_{k=1}^K \lambda_k \delta\right) \cdot \exp(K o(\delta))\end{aligned}$$

Using the continuity of the exponential function, the definition of the Riemann's integral, the definition of δ and the property of the $o()$ function we can take the limit when K goes to ∞ on both sides of our last equation to get:

$$\lim_{K \rightarrow \infty} \prod_{k=1}^K (1 - \lambda_k \delta + o(\delta)) = \exp - \int_{t_j}^{t_{j+1}} \lambda(t \mid \mathcal{H}_t) dt$$

And the probability density of the interval becomes:

$$\lim_{K \rightarrow \infty} \frac{\mathbb{P}\{I_j = t_{j+1} - t_j\}}{\frac{t_{j+1} - t_j}{K}} = \lambda(t_{j+1} \mid \mathcal{H}_{t_{j+1}}) \exp - \int_{t_j}^{t_{j+1}} \lambda(t \mid \mathcal{H}_t) dt$$

If we now define the *integrated conditional intensity* by:

$$\Lambda(t) = \int_{u=0}^t \lambda(u \mid \mathcal{H}_u) du$$

We see that Λ is increasing since by definition $\lambda \geq 0$. We see then that the mapping:

$$t \in \mathcal{T} \subseteq \mathbb{R}^{+*} \rightarrow \Lambda(t) \in \mathbb{R}^{+*} \tag{1}$$

is one to one and we can transform our $\{t_1, \dots, t_n\}$ into $\{\Lambda_1 = \Lambda(t_1), \dots, \Lambda_n = \Lambda(t_n)\}$.

If we now consider the probability density of the intervals $t_{j+1} - t_j$ and $\Lambda_{j+1} - \Lambda_j$ we get:

$$\begin{aligned} p(t_{j+1} - t_j) dt_{j+1} &= \lambda(t_{j+1} | \mathcal{H}_{t_{j+1}}) \exp \left(- \int_{t_j}^{t_{j+1}} \lambda(t | \mathcal{H}_t) dt \right) dt_{j+1} \\ &= \frac{d\Lambda(t_{j+1})}{dt} dt_{j+1} \exp - (\Lambda(t_{j+1}) - \Lambda(t_j)) \\ &= d\Lambda_{j+1} \exp - (\Lambda_{j+1} - \Lambda_j) \end{aligned}$$

That is, **the mapped intervals, $\Lambda_{j+1} - \Lambda_j$ follow an exponential distribution with rate 1.** This is the substance of the *time transformation* of Ogata (1988) and of the *time rescaling theorem* of Brown Et Al (2002). This has been repetitively derived in the neuroscience literature: Hagiwara (1954), Brillinger (1988), Chornoboy et al (1988), Johnson (1996),...

Consequences

1. The conditional intensity, with its dependence on the past through \mathcal{H}_t , describes a process "making a decision" to spike or not to spike at each time step that can include *time dependent* effects of synaptic coupling and stimulation.
2. The conditional intensity allows us to compute the *likelihood* of an observed spike train.
3. The time transformation:
 $\{t_1, \dots, t_n\} \rightarrow \{\Lambda_1 = \Lambda(t_1), \dots, \Lambda_n = \Lambda(t_n)\}$, leads to goodness of fit tests *since the mapped intervals should be the realization of a Poisson process with rate 1*.
4. This time transformation can also be used for simulations.

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Model considered

We are going to write our $\lambda(t \mid \mathcal{H}_t)$ as a transformation of a "more basic" quantity, the *membrane potential process* (MPP), $u(t \mid \mathcal{H}_t)$:

$$\lambda(t \mid \mathcal{H}_t) \equiv \lambda_{\max} (1 + \exp -u(t \mid \mathcal{H}_t))^{-1} ,$$

where $\lambda_{\max} > 0$ is a parameter allowing us to have the proper rate (in Hz).

We are going to write $u(t \mid \mathcal{H}_t)$ as:

$$u(t \mid \mathcal{H}_t) \equiv s(t - t_l) + \sum_{j \in \mathbb{P}} \sum_{x \in T_j, x > t_l} g_j(t - x) , \quad \text{for } t > t_l ,$$

where t_l stands for the time of the last spike of the neuron of interest, \mathbb{P} is the index set of the neurons of the network that are presynaptic to the neuron of interest, T_j stands for the set of spike times of neuron j , $g_j(t - x)$ is the effect of a spike in neuron j at time x , $s(t - t_l)$ stand for the "self" or more appropriately "unobserved" effect.

On the "self" or "unobserved" effect

In an actual setting, only a tiny fraction of the neurons of a network are observed, but we know from the biophysics of these neurons and from the anatomy and function of the first olfactory relay that 3 "factors" will contribute in making a neuron spike:

- ▶ The so called "intrinsic properties" of the neuron, that is, the set of voltage dependent conductances present in the neuron's membrane, as well as their localization (not to mention the actual geometry of the neuron. . .).
- ▶ The continuous asynchronous and "random" input the neuron gets from the olfactory receptors in the "spontaneous" regime. We know that this factor is a key contributor to the spontaneous activity in the first olfactory relay since this activity essentially disappear if we cut the antennal nerve (that is, the bunch of olfactory receptor axons entering into the first olfactory relay).
- ▶ The synaptic inputs from the other neurons of the network.

"Pragmatic" choices

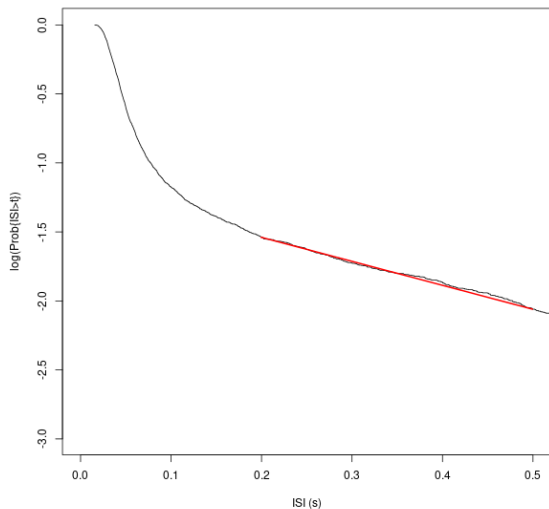
Since the likelihood computation implies the evaluation of many terms like:

$$\lim_{K \rightarrow \infty} \frac{\Pr\{I_j = t_{j+1} - t_j\}}{\frac{t_{j+1} - t_j}{K}} = \lambda(t_{j+1} \mid \mathcal{H}_{t_{j+1}}) \exp - \int_{t_j}^{t_{j+1}} \lambda(t \mid \mathcal{H}_t) dt$$

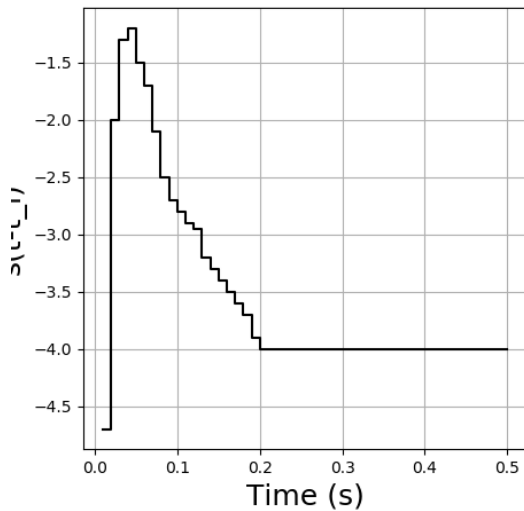
we will model our "self" and synaptic coupling effects as piecewise constant functions. Our MPP and $\lambda(t_{j+1} \mid \mathcal{H}_{t_{j+1}})$ will therefore be piecewise constant functions and the integrated intensity $\Lambda(t)$ will be piecewise linear.

The "self" effect will be $-\infty$ on the left of a *refractory period* and *constant* on the right of a cutoff time. The synaptic effects will have a bounded support.

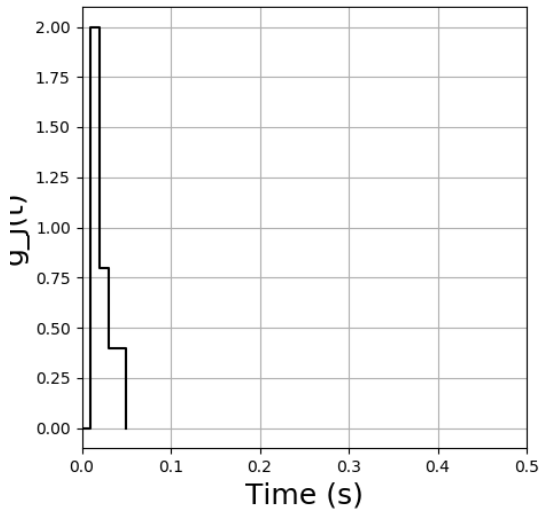
Justification of the constant rate after a cutoff



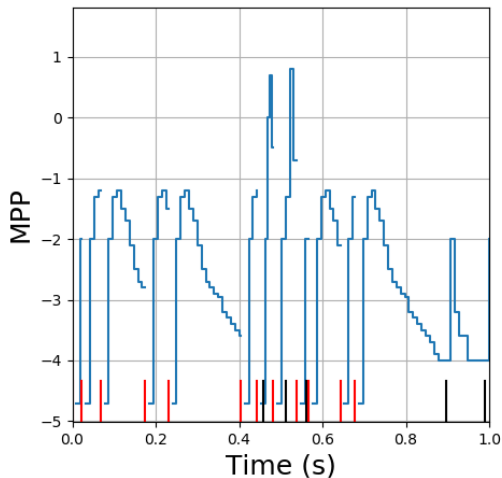
Example of "self" effect



Example of synaptic coupling

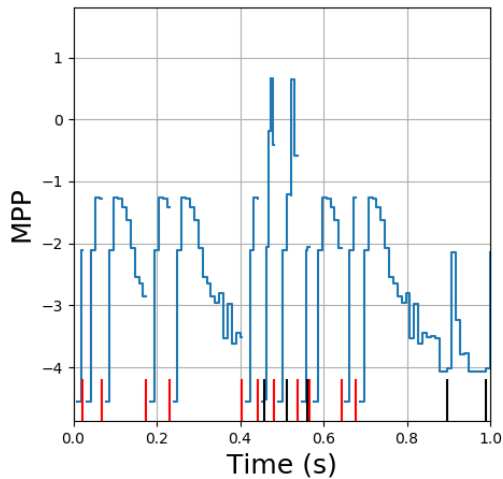


Example of MPP realization



The presynaptic neuron (black ticks) spikes independently as a renewal process.

Example of fitted MPP



Thanks

That's all for today folks. Thanks for listening!