Higher-Order Correlations in Large Neuronal Populations

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What are “higher-order correlations” (HOCs)?

The effect of HOCs on single-neuron dynamics

CuBIC: Cumulant-based inference of HOCs

Non-stationary spike trains

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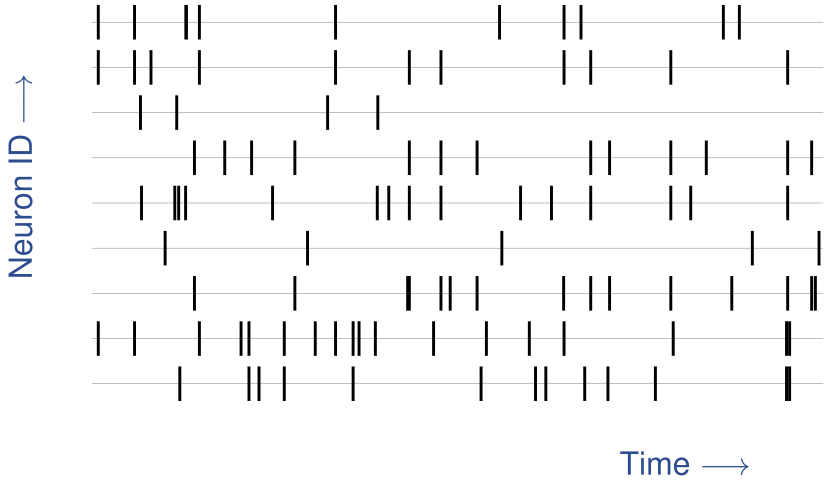
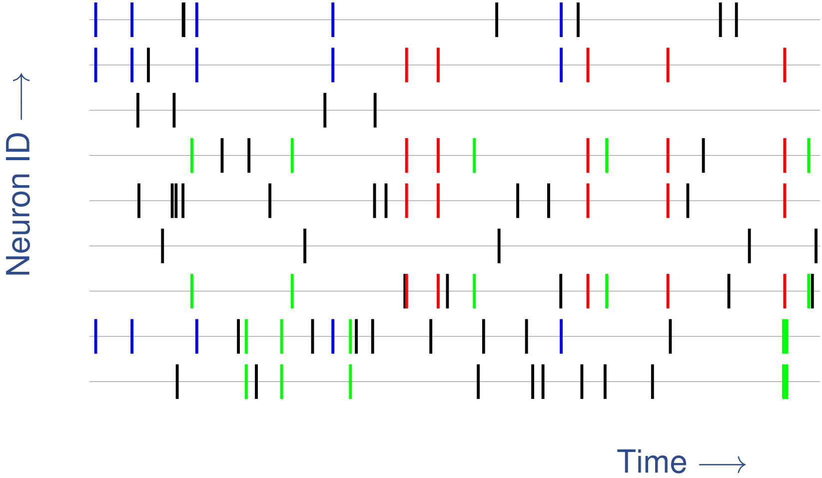
Co-activated neuronal groups



Question:
Are there any neuronal groups that systematically fire together?

Co-activated neuronal groups



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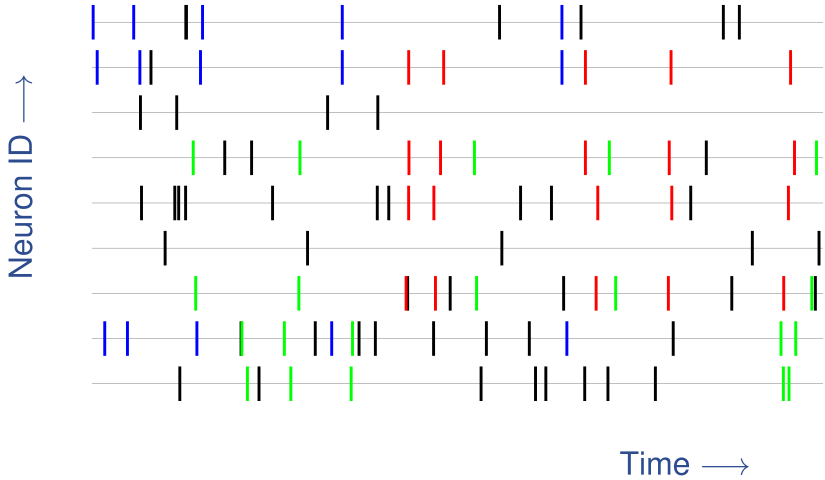


Question:

Are there any neuronal groups that systematically fire together?

Higher-order correlations?

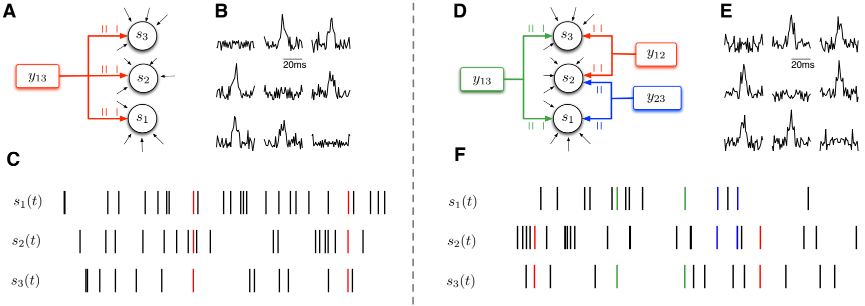
spike train
= spiking of one particular neuron
= activity of patterns this neuron is a member of

pairwise correlation
= joint spiking of two neurons
= activity of patterns that comprise both neurons

triplet correlation
= joint spiking in three neurons
= activity of patterns that comprise all three neurons

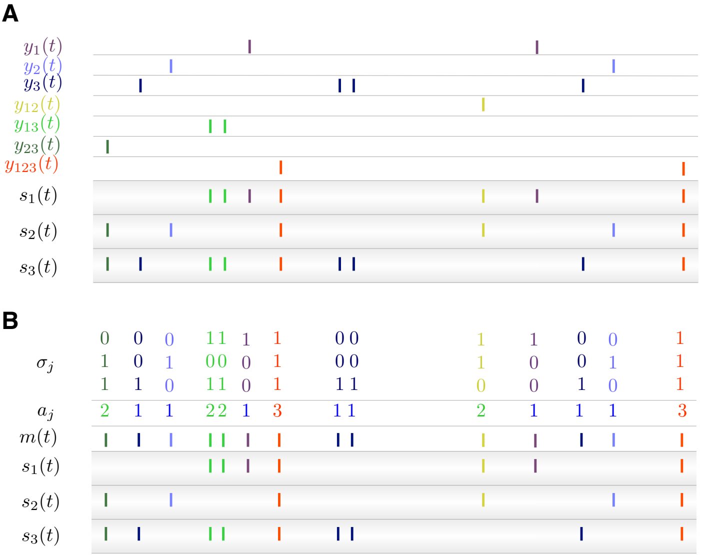
and so on.

Additive common components



Staude, Grün, Rotter, 2010

Correlated Poisson processes



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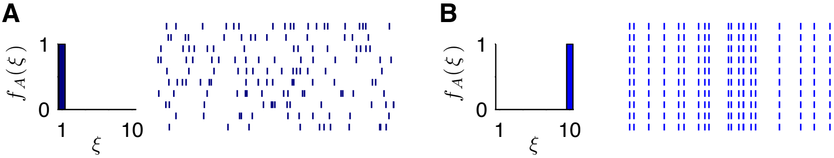
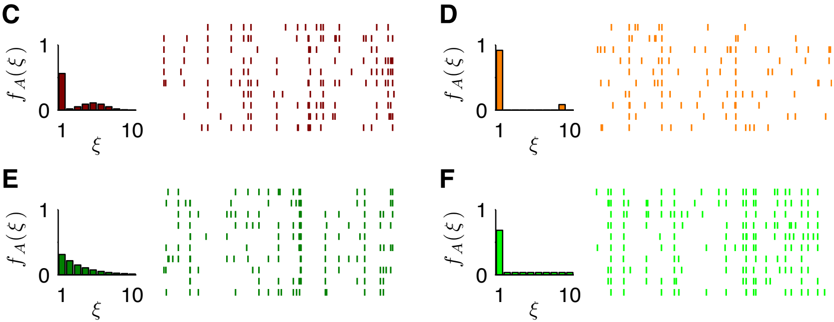


fully independent

fully correlated

Correlated Poisson processes



pairwise correlation coefficient $c = 0.4$

Problems and issues of HOC inference

Combinatorial explosion: A population of N neurons could in principle form 2^N different groups/assemblies:

N	10	100	273
2^N	10^3	10^{30}	1.5×10^{82}

Very large samples: Statistical estimation of very many parameters calls for very, very long stationary recordings.

Spike sorting: Single-units must be reliably isolated from extracellular spike train recordings.

Uneasy mathematics: There seems to be no “natural” parametrization of HOCs, and the results of modeling and data analysis are strongly model-dependent.

Are HOCs relevant at all?

Argument 1: Natural stimulation of sensor arrays (e.g. in vision or touch) carries gestalt information, i.e. HOCs.

Argument 2: Certain brain theories imply and/or make use of HOCs (Hebb's neuronal assemblies, Abeles' synfire chains).

Argument 3: Nonlinear synaptic input integration (e.g. via thresholding) turns neurons into sensible HOC detectors.

What are “higher-order correlations” (HOCs)?

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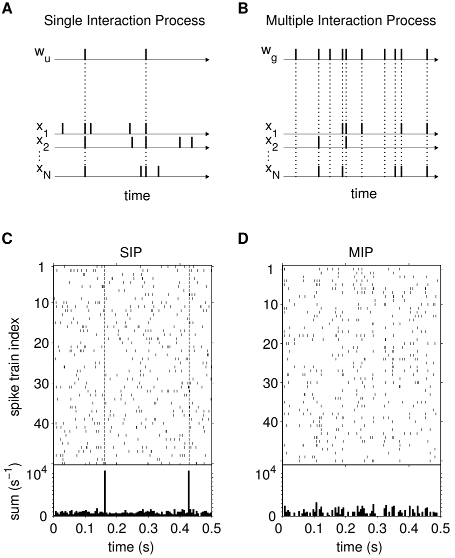
Non-stationary spike trains

Comparing two different input ensembles

- identical rates and pairwise correlations
- different higher-order correlations

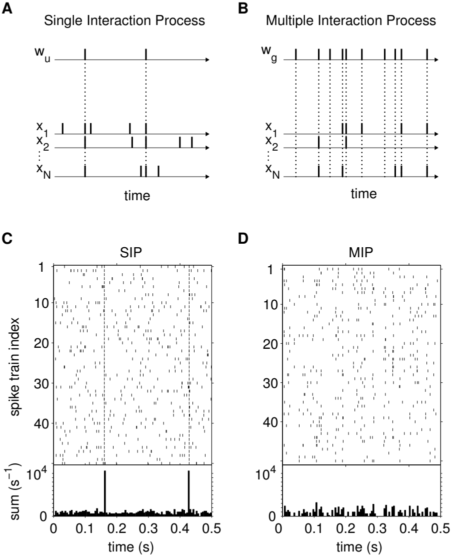


Kuhn, Aertsen, Rotter, 2002/2003

Comparing two different input ensembles

- identical rates and pairwise correlations
- different higher-order correlations

SIP	
single rate	$r = \alpha + \beta$
correlation	$c = \beta/(\alpha + \beta)$
cluster rate	$\beta = r\, c$
MIP	
single rate	$r = \alpha\, \beta$
correlation	$c = \beta$
cluster rate	$\alpha = r/c$



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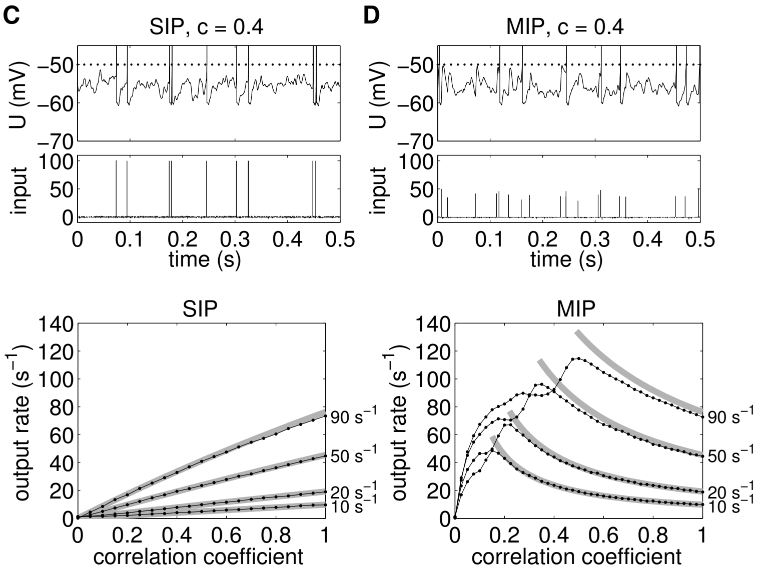
Higher-order correlations do matter!



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The compound Poisson process (CPP)

$$z(t) = \sum_l \delta(t - t_l)$$

Carrier rate ν

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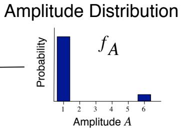
$$z(t) = \sum_l \delta(t - t_l) \cdot a_l$$

Carrier rate ν



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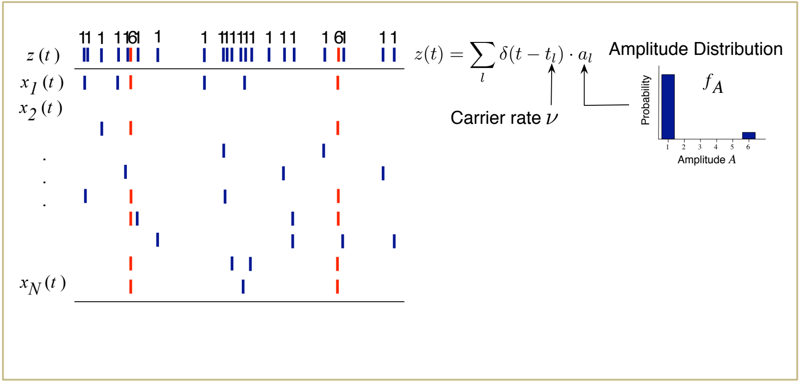

- Spike trains are continuous-time Poisson processes.
- "Injecting" simultaneous spikes into ξ spike trains yields correlations of all orders up to ξ.
- carrier rate $\nu \to$ neuronal firing rates
  amplitude distribution $f_A \to$ correlation structure.

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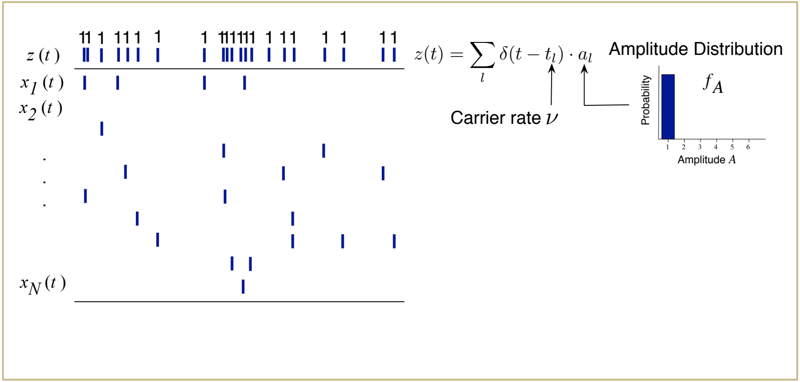

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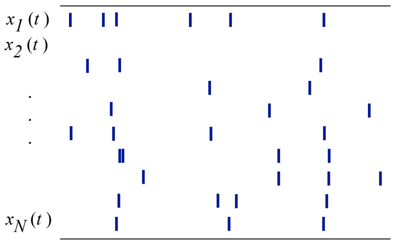

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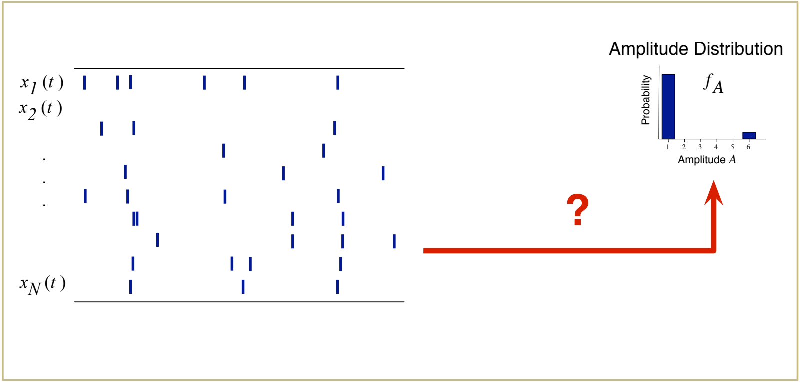


Task: Infer amplitude distribution f_A from measured spike trains

HOCs in population spike trains

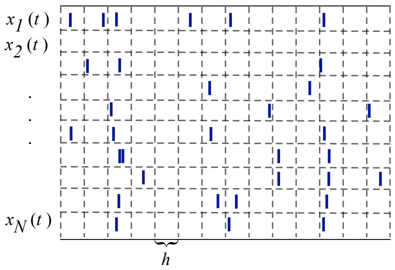
Instead of tackling the difficult problem

Which exact neuronal groups carry HOCs?

try to answer a less specific question

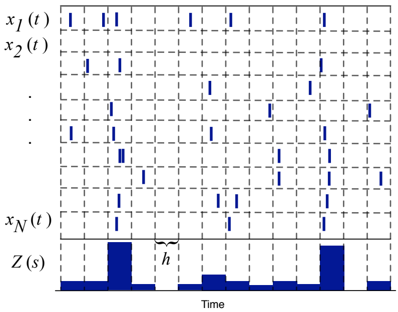
Are there any HOCs in a given population of neurons?

Measurement



- Segment spike trains into bins of width h, the resulting counting variables X_i for each neuron are not binary.

Measurement



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- Count spikes across the population, yielding the population spike count $Z = \sum_{i=1}^{N} X_i$ with distribution f_Z.

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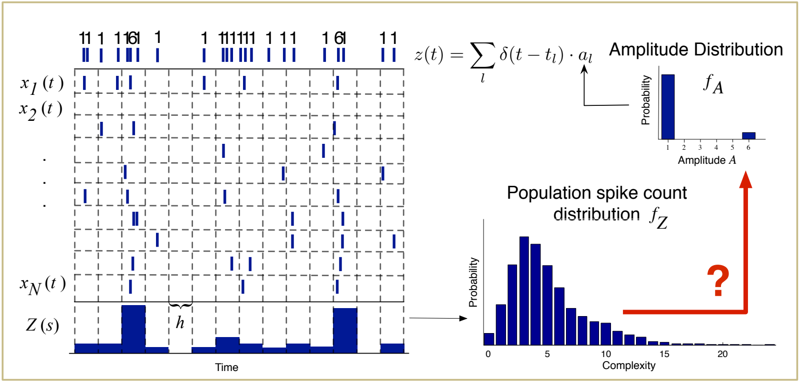
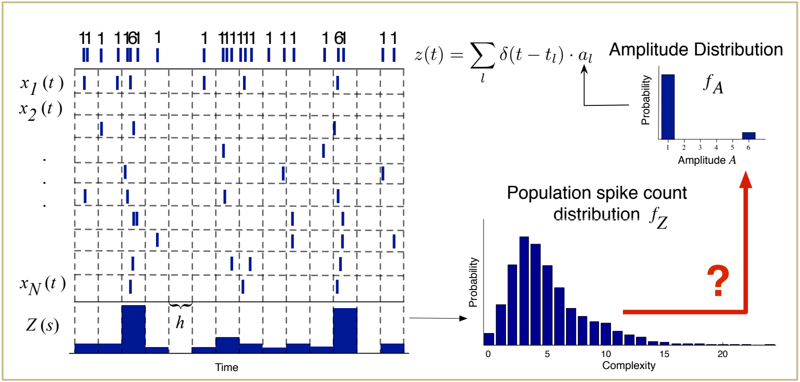


- Segment spike trains into bins of width h, the resulting counting variables X_i for each neuron are not binary.
- Count spikes across the population, yielding the population spike count $Z = \sum_{i=1}^{N} X_i$ with distribution f_Z.
- Infer amplitudes f_A from observed population activity f_Z.

Cumulants and correlations



- CPPs satisfy: $\kappa_m[Z] = \mathrm{E}[A^m]\nu h \quad (m = 1, 2, \ldots, N)$

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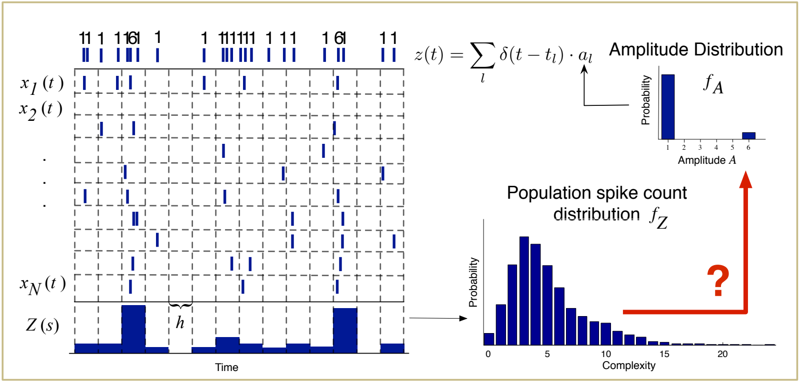

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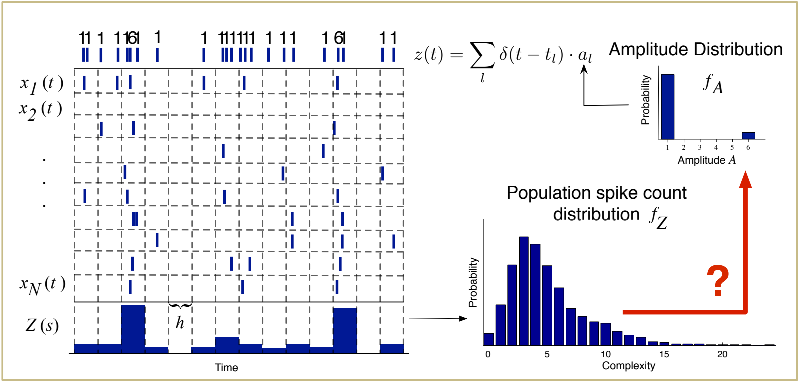

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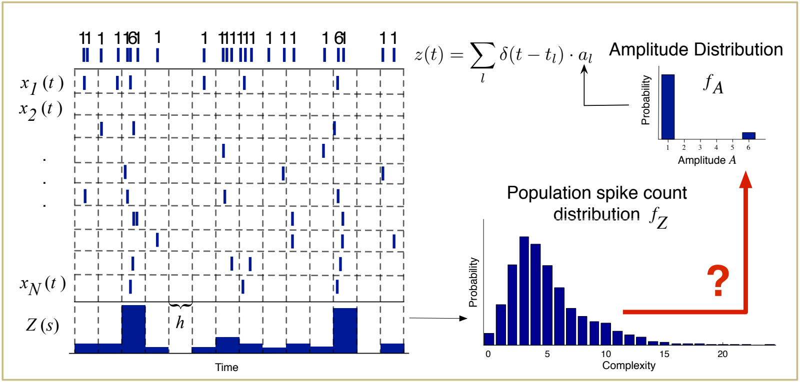

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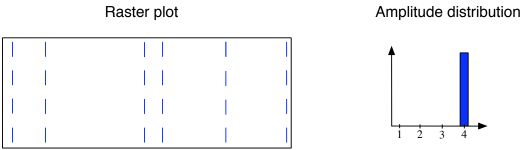
- $\kappa_m[Z] = \sum m^{\text{th}}$ order correlations

CuBIC

Pairwise correlations imply higher-order correlations!



m neurons with identical spike trains
$\Leftrightarrow$ all pairwise correlation coefficients 1

$\Rightarrow$ correlations of order m

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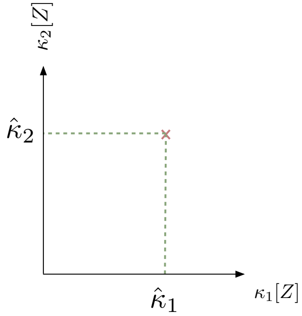

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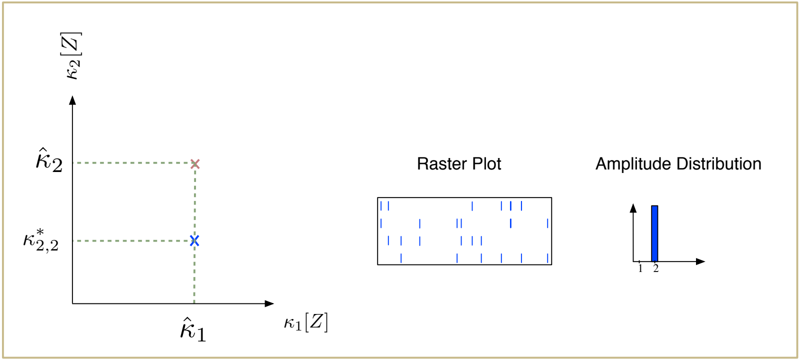

- $\kappa^*_{2,2} = \max\{\kappa_2[Z] \mid f_A(i) = 0$ for $i > 2$ and $\kappa_1[Z] = \hat{\kappa}_1\}$

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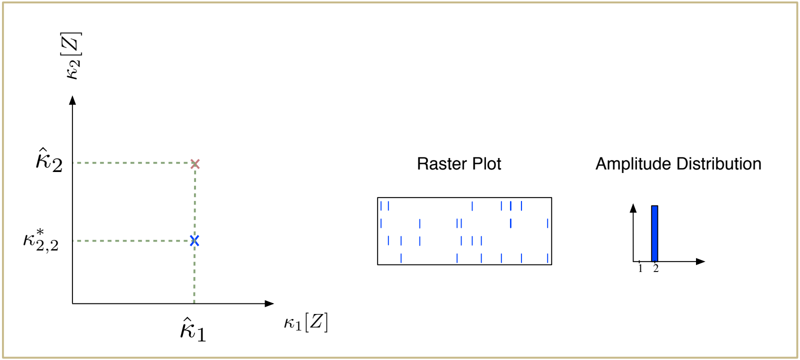

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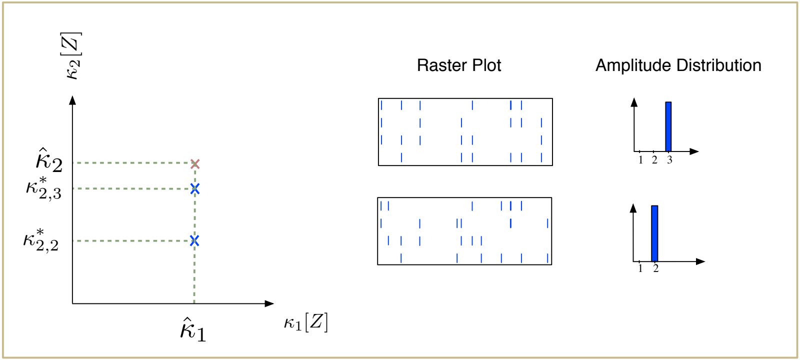

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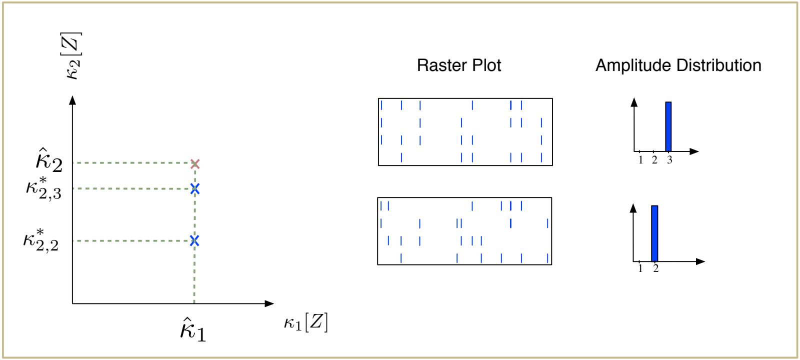
- $\hat{\kappa}_2 > \kappa^*_{2,3}$: pairwise correlations imply correlations of order > 3

CuBIC



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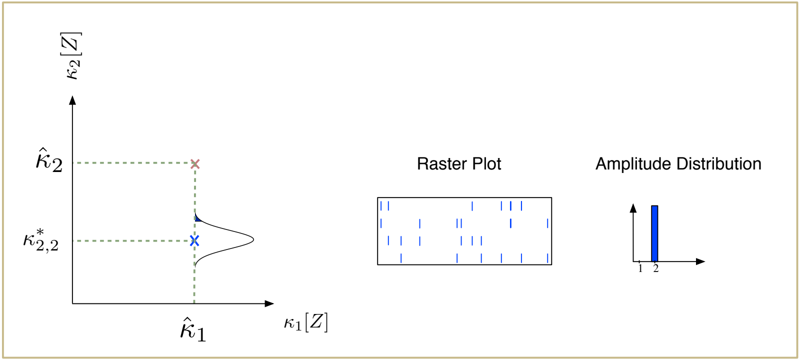
- $\hat{\kappa}_3 > \kappa^*_{3,15}$: triplet correlations imply correlations of order > 15

CuBIC

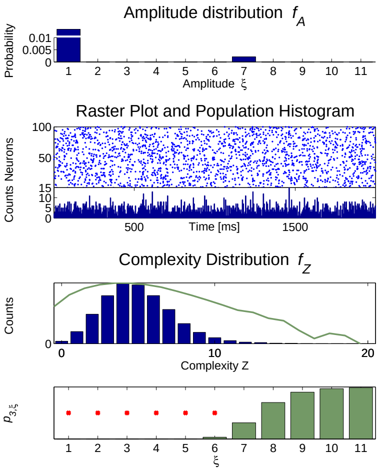


Hypothesis testing

$H_0^{m,\xi}$	observed cumulants $\hat{\kappa}_1[Z], \ldots, \hat{\kappa}_m[Z]$ are statistically compatible with correlations bounded by ξ
$p_{m,\xi} < \alpha$	observed cumulants imply correlations of order strictly larger than ξ

CuBIC: illustration

- 100 simulated spike trains
  $100\,\mathrm{s}$, $10\,\mathrm{Hz}$, bin size $5\,\mathrm{ms}$
- 70 independent and 30 correlated neurons
- independent background plus patterns of order 7
- pairwise correlation $c = 0.01$ in correlated subgroup
- only low-order cumulants are measured: $\hat{\kappa}_1[Z]$, $\hat{\kappa}_2[Z]$, $\hat{\kappa}_3[Z]$



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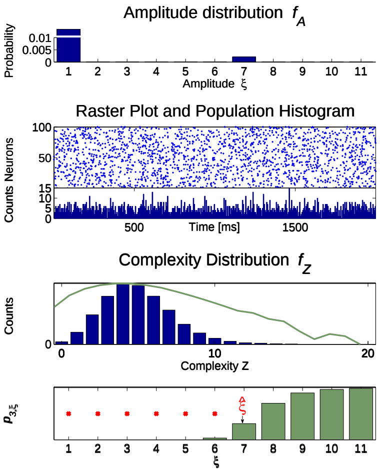

$\hat{\xi} =$ lower bound on the order of correlation

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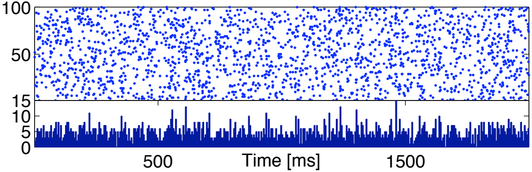
Non-stationary spike trains

Non-stationary firing rates



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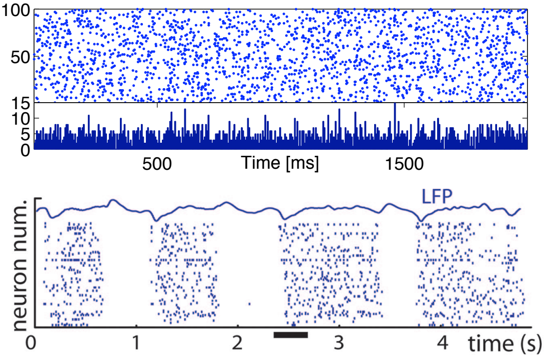

Luczak et al 2007, rat somatosensory cortex, up/down states

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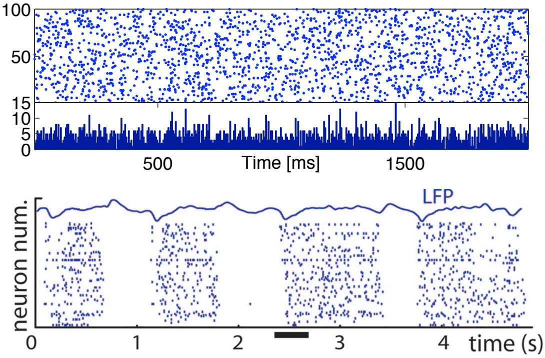
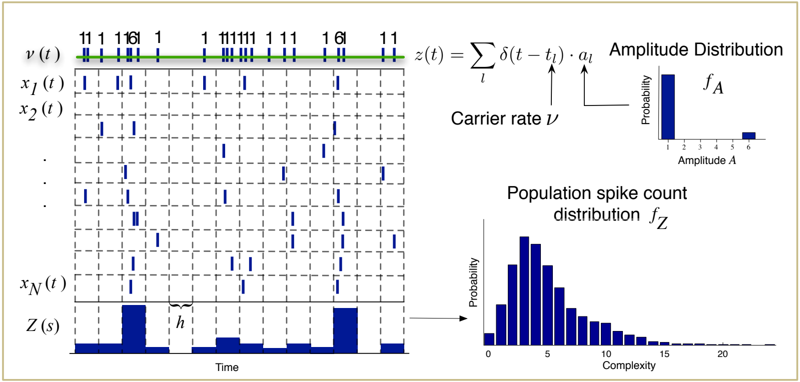
Non-stationary firing rates



Luczak et al 2007, rat somatosensory cortex, up/down states

- CuBIC assumes spike trains with stationary firing rates
- Spike trains observed in experiments often exhibit spontaneous and stimulus/behavior induced non-stationarities
- Co-varying firing rates induce correlations, which may lead CuBIC to overestimate the correlation order

Non-stationary CPP



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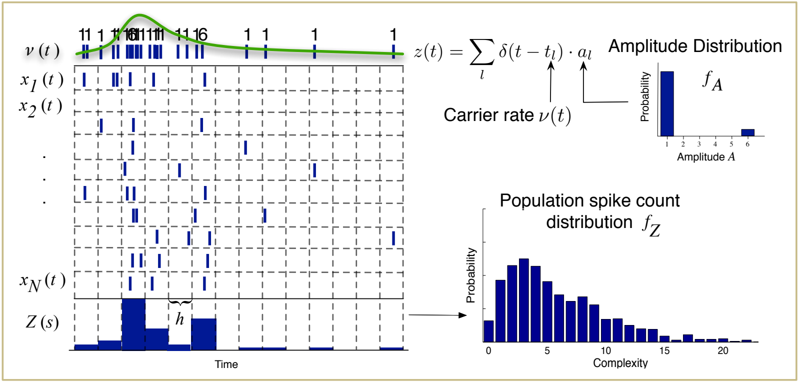

- Time-varying carrier rate $\nu(t)$, constant correlation structure f_A

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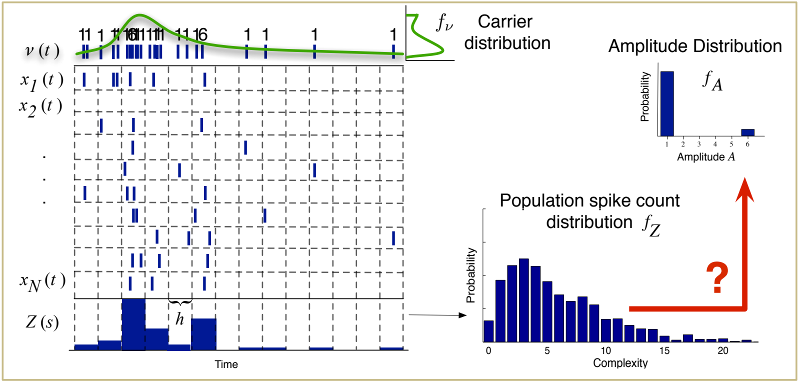

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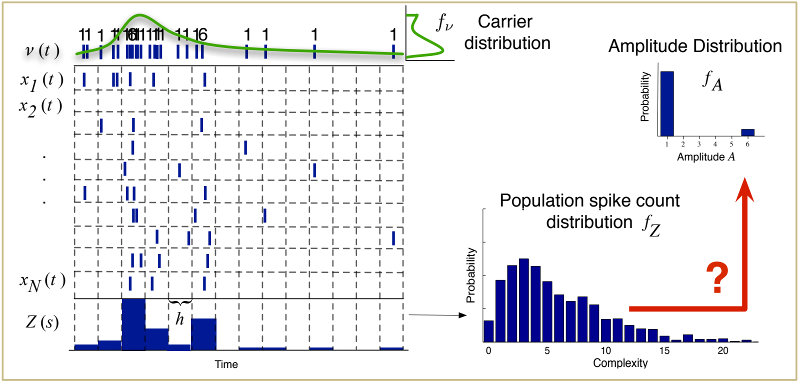

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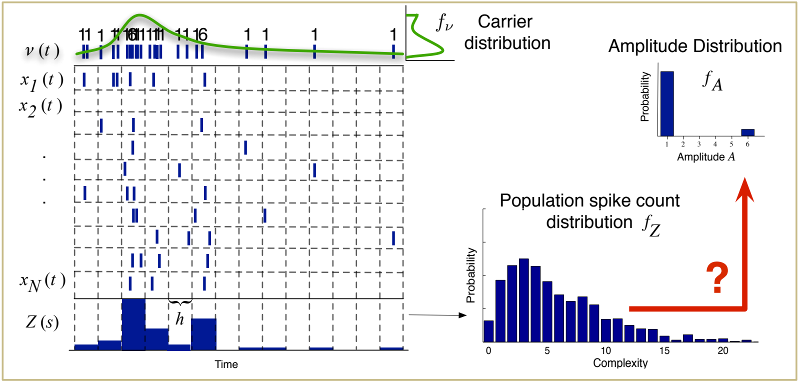

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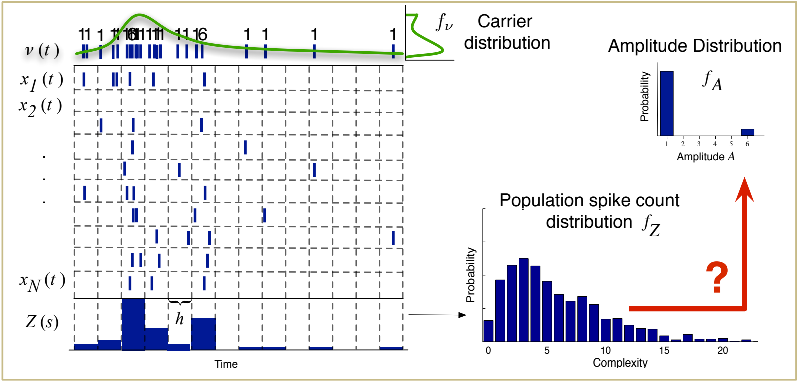
Non-stationary CPP



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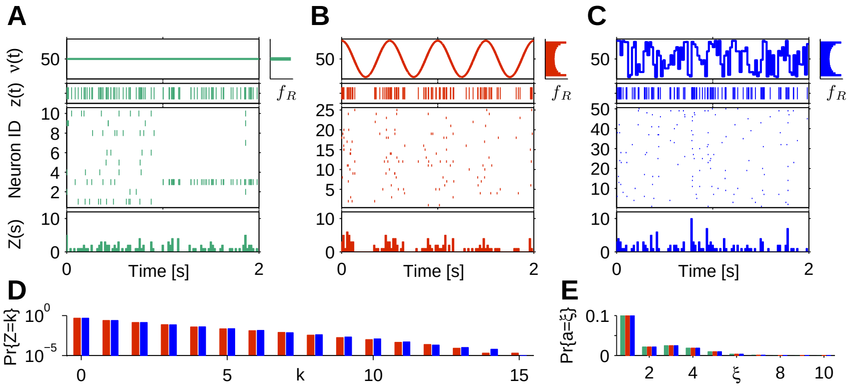
- $\kappa_3[Z] = \mathrm{E}[A^3]\kappa_1[\nu]h + 3\,\mathrm{E}[A]\,\mathrm{E}[A^2]\kappa_2[\nu]h^2 + \mathrm{E}[A]^3\kappa_3[\nu]h^3$

Non-stationary CuBIC

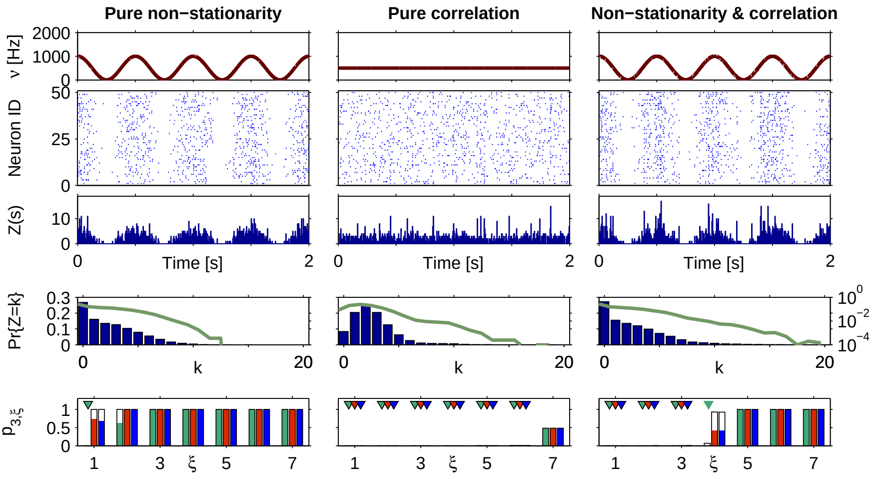


relevant: carrier rate distribution f_R (resp. f_ν)

irrelevant: assignment of spikes to individual neurons

Staude, Grün, Rotter, 2010

“Stimulus-driven” non-stationarities

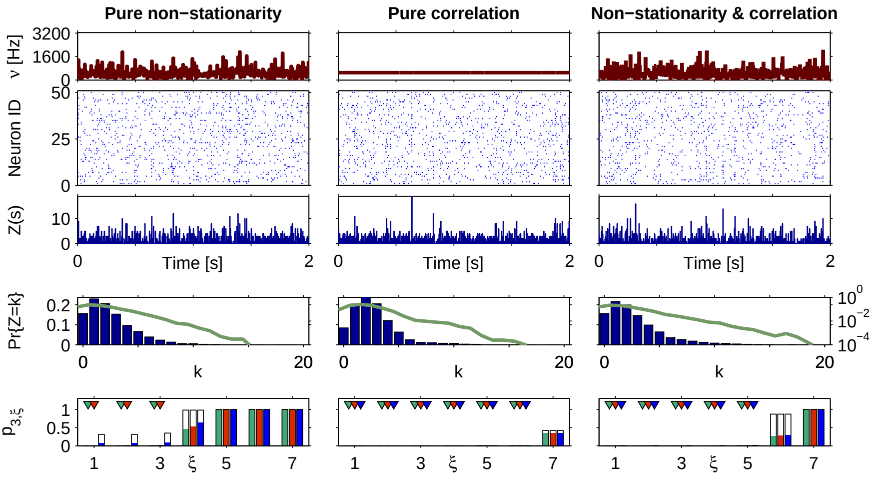


cosine-like modulation of carrier rate

Staude, Grün, Rotter, 2010

assuming stationary rates, cosine modulation, or two rate levels

"Internally generated" non-stationarities



gamma-distributed modulation of carrier rate

Staude, Grün, Rotter, 2010

assuming stationary rates, uniform modulation, or gamma modulation

Conclusions

- Higher-order correlations in the presynaptic population strongly influence single-neuron spike trains, in particular firing rates.
- For the point process models in continuous time considered here, additive spike patterns and cumulants are tightly related. Therefore, cumulants provide intuitive measures of correlation.
- Cumulants and log-linear parameters establish quite different views on higher-order correlations. In particular, zero log-linear interactions do NOT imply the absence of synchronous patterns.
- CuBIC can infer the presence of high-order patterns from measured low-order cumulants of population spike counts. The necessary sample sizes are fully compatible with state-of-the-art *in vivo* multi-neuron spike train recordings.
- Non-stationary rates are smoothly integrated into hypothesis testing, with reliable performance. Non-Poissonian spiking as found in real neurons can be tolerated to some degree.

Benjamin	Staude
Imke	Reimer
Sonja	Grün
Clemens	Boucsein
Werner	Ehm
Robert	Gütig
Alexandre	Kuhn
Ad	Aertsen

Thanks!

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SPRINGER SERIES IN
COMPUTATIONAL NEUROSCIENCE

Analysis of Parallel Spike Trains

Action potentials, or spikes, are the most salient expression of neuronal processing in the active brain, and they are likely an important key to understanding the neuronal mechanisms of behavior. However, it is the group dynamics of large networks of neurons that are likely to underlie brain function, and this can only be appreciated if the action potentials from multiple individual nerve cells are observed simultaneously. Techniques that employ multielectrodes for parallel spike train recordings have been available for many decades, and their use has gained wide popularity among neuroscientists. To reliably interpret the results of such electrophysiological experiments, solid and comprehensible data analysis is crucial. The development of data analysis methods, however, has not really kept pace with the advances in recording technology. Neither general concepts, nor statistical methodology seem adequate for the new experimental possibilities. Promising approaches are scattered across journal publications, and the relevant mathematical background literature is buried deep in journals of different fields and compiling a useful reader for students or collaborators is both laborious and frustrating. This situation led us to gather state-of-the-art methodologies for analyzing parallel spike trains into a single book, analysis which will serve vantage point for current techniques and a launching point for future development.

Sonja Grün, born 1960, received her MSc (University of Tübingen and Max-Planck Institute for Biological Cybernetics) and PhD (University of Bochum, Weizmann Institute of Science in Rehovot) in physics (theoretical neuroscience), and her Habilitation (University of Freiburg) in neurobiology and biophysics. During her postdoc at the Hebrew University in Jerusalem, she performed multiple single-neuron recordings in behaving monkeys. Equipped with this experience she returned back to computational neuroscience to further develop analysis tools for multi-electrode recordings, first at the Max-Planck Institute for Brain Research in Frankfurt/Main and then as an assistant professor at the Freie Universität in Berlin associated with the local Bernstein Center for Computational Neuroscience. Since 2006 she has been unit leader for statistical neuroscience at the RIKEN Brain Science Institute in Wako-Shi, Japan. Her scientific work focuses on cooperative network dynamics relevant for brain function and behavior.

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Sonja Grün
Stefan Rotter
Editors

Springer

Publications on higher-order correlations

Staude B, Grün S, Rotter S
Higher-order correlations
In: Grün S, Rotter S (eds) Analysis of Parallel Spike Trains
Springer Series in Computational Neuroscience, Vol. 7, 2010

Staude B, Grün S, Rotter S
Higher-order correlations in non-stationary parallel spike trains: statistical modeling and inference
Frontiers in Computational Neuroscience 4: 16, 2010

Staude B, Rotter S, Grün S
CuBIC: cumulant based inference of higher-order correlations in massively parallel spike trains
Journal of Computational Neuroscience, epub ahead of print, 2009

Ehm W, Staude B, Rotter S
Decomposition of neuronal assembly activity via empirical de-Poissonization
Electronic Journal of Statistics 1: 473-495, 2007

Gütig R, Aertsen A, Rotter S
Analysis of higher-order neuronal interactions based on conditional inference
Biological Cybernetics 88(5): 352-359, 2003

Kuhn A, Aertsen A, Rotter S
Higher-order statistics of input ensembles and the response of simple model neurons
Neural Computation 15(1): 67-101, 2003

Kuhn A, Rotter S, Aertsen A
Correlated input spike trains and their effects on the response of the leaky integrate-and-fire neuron
Neurocomputing 44-46: 121-126, 2002

Correlated Poisson processes

Consider N neurons with spike trains $s_1(t), s_2(t), \dots, s_N(t)$.

- For every non-empty group $G \subseteq \{1, 2, \dots, N\}$ of neurons ("pattern"), the joint spiking (some jitter allowed) of all its group members is described by a Poisson process $y_G(t)$.
- The spike train $s_i(t)$ of neuron i is comprised of all spikes of all groups neuron i is a member of

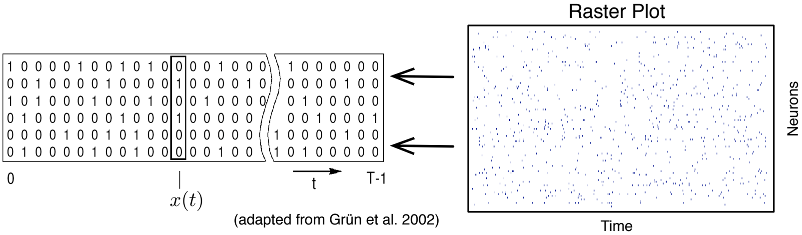
$$s_i(t) = \sum_{G \ni i} y_G(t).$$

- Alternatively, one may consider the carrier process comprising all spikes

$$y(t) = \sum_{G} y_G(t)$$

and assign a mark to each of its events, namely the pattern produced at that point in time.

Correlated Bernoulli variables



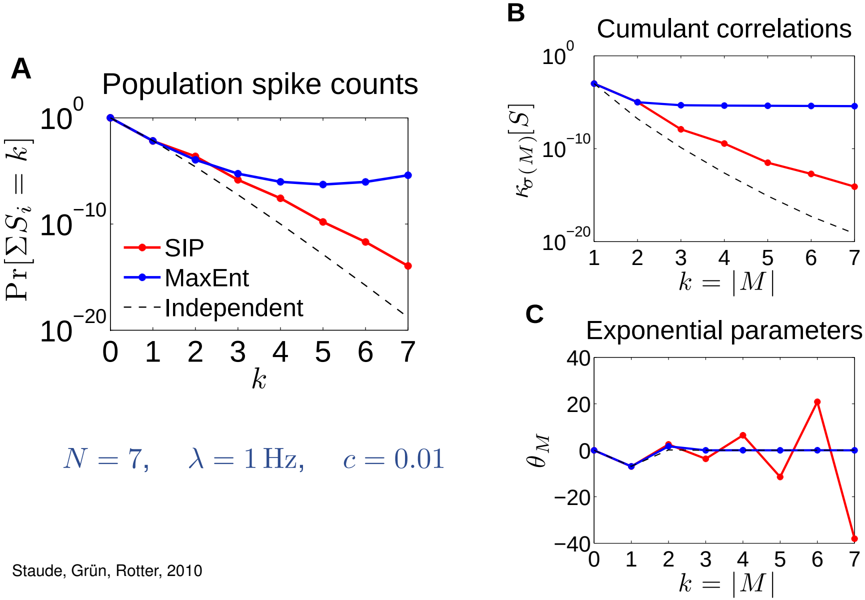
(adapted from Grün et al. 2002)

$$P(x) = \exp\left[\theta + \sum_i \theta_i x_i + \sum_{i<j} \theta_{ij} x_i x_j + \sum_{i<j<k} \theta_{ijk} x_i x_j x_k + \dots\right].$$

The θ_{ij} represent pairwise, the θ_{ijk} triplet correlations, ...

Martingnon et al 1995, 2000; Nakahara & Amari 2002; Shlens et al 2006; Schneidman 2006; Roudi et al 2009 and many others

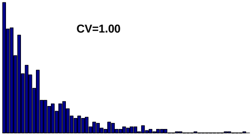
Cumulants vs. log-linear parameters



$$N = 7, \quad \lambda = 1\,\mathrm{Hz}, \quad c = 0.01$$

Staude, Grün, Rotter, 2010

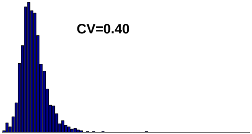
Non-Poissonian spike trains

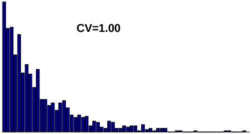


Poisson

coefficient of variation $\mathrm{CV} = \frac{\sqrt{\mathrm{Var}[\mathrm{ISI}]}}{\mathrm{E}[\mathrm{ISI}]}$

Non-Poissonian spike trains

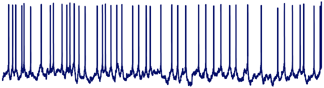




$\mathrm{CV} < 1$

regular

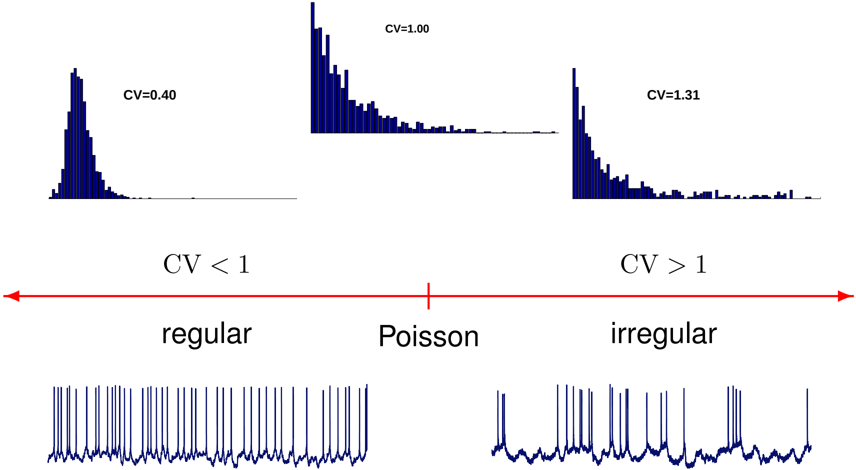
Poisson



rat somatosensory cortex

(Boucsein et al.)

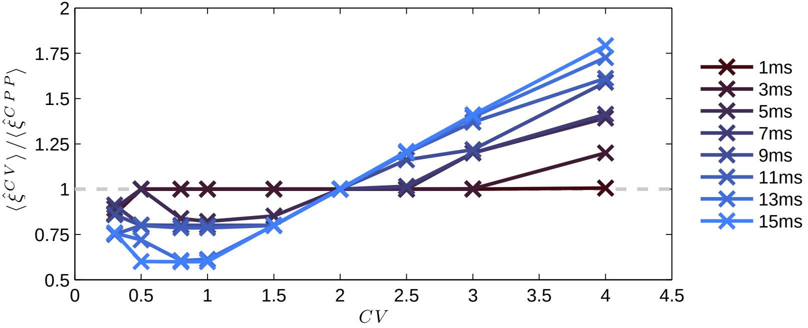
Non-Poissonian spike trains



rat somatosensory cortex
(Boucsein et al.)

rat visual cortex
(Boucsein et al.)

Robustness of CuBIC



Correlated log-normal processes generated via thinning:

$N = 50,\ \lambda = 10\,\mathrm{Hz},\ c = 0.05,\ T = 500\,\mathrm{s},\ \langle\hat{\xi}\rangle =$ mean over 100 simulations