

Spike Train Analysis II: correlation analysis and surrogate methods

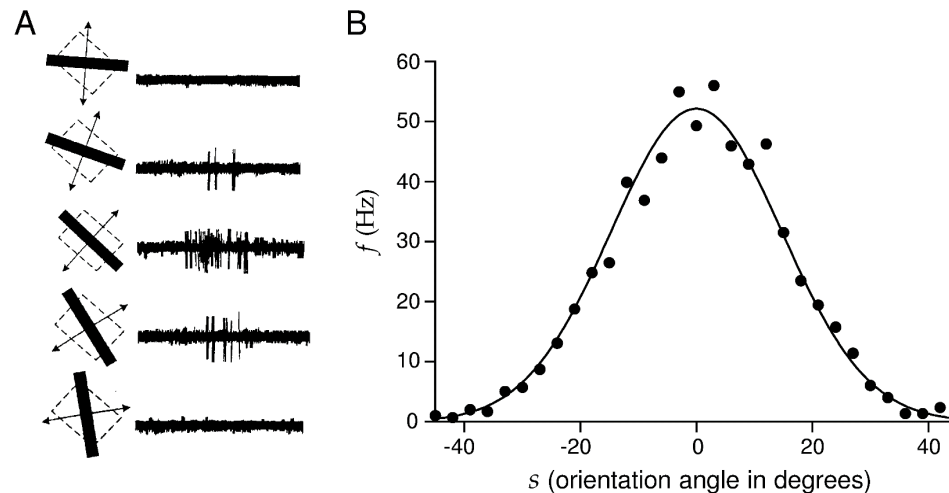
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9th Latin American School on Computational Neuroscience (LASCON 2024)
NeuroMat, University of Sao Paulo, Sao Paulo, Brazil | January 20, 2024

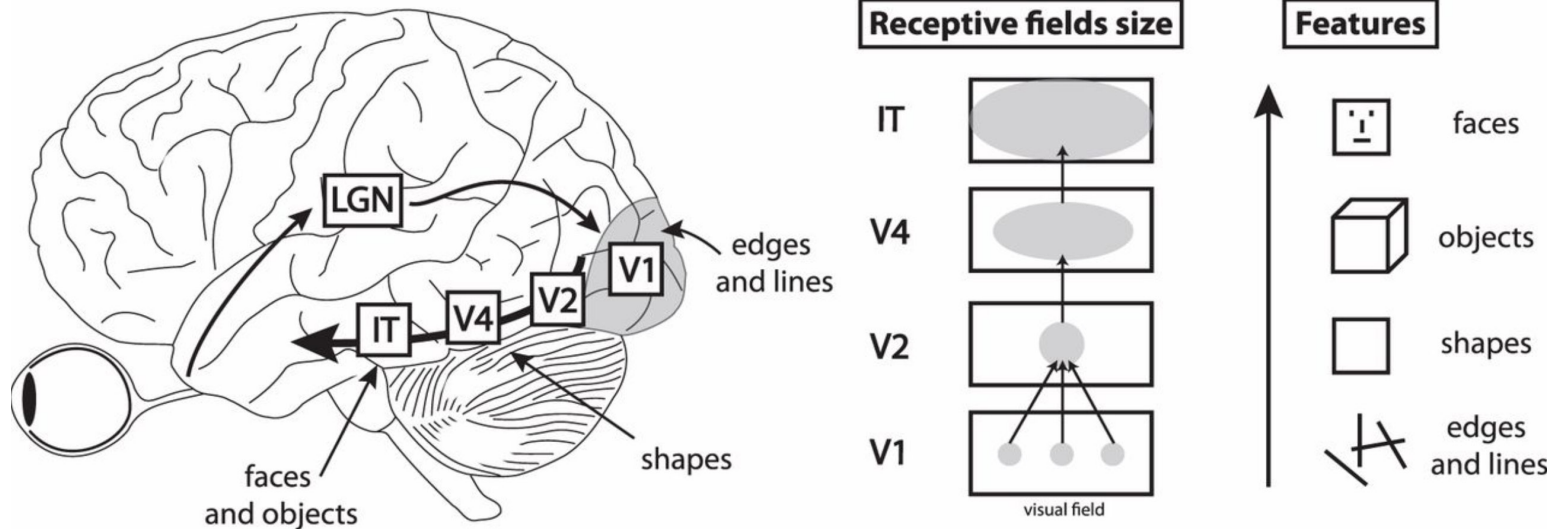
Recap | response to visual stimulus

- Neurons in the primary visual cortex have...
 - **Receptive field**: a particular region of the visual field in which a stimulus triggers the firing of that neuron.
 - **Orientation preference**: a particular orientation of stimulus to which that neuron respond strongly



From: Dayan and Abbott (2008)

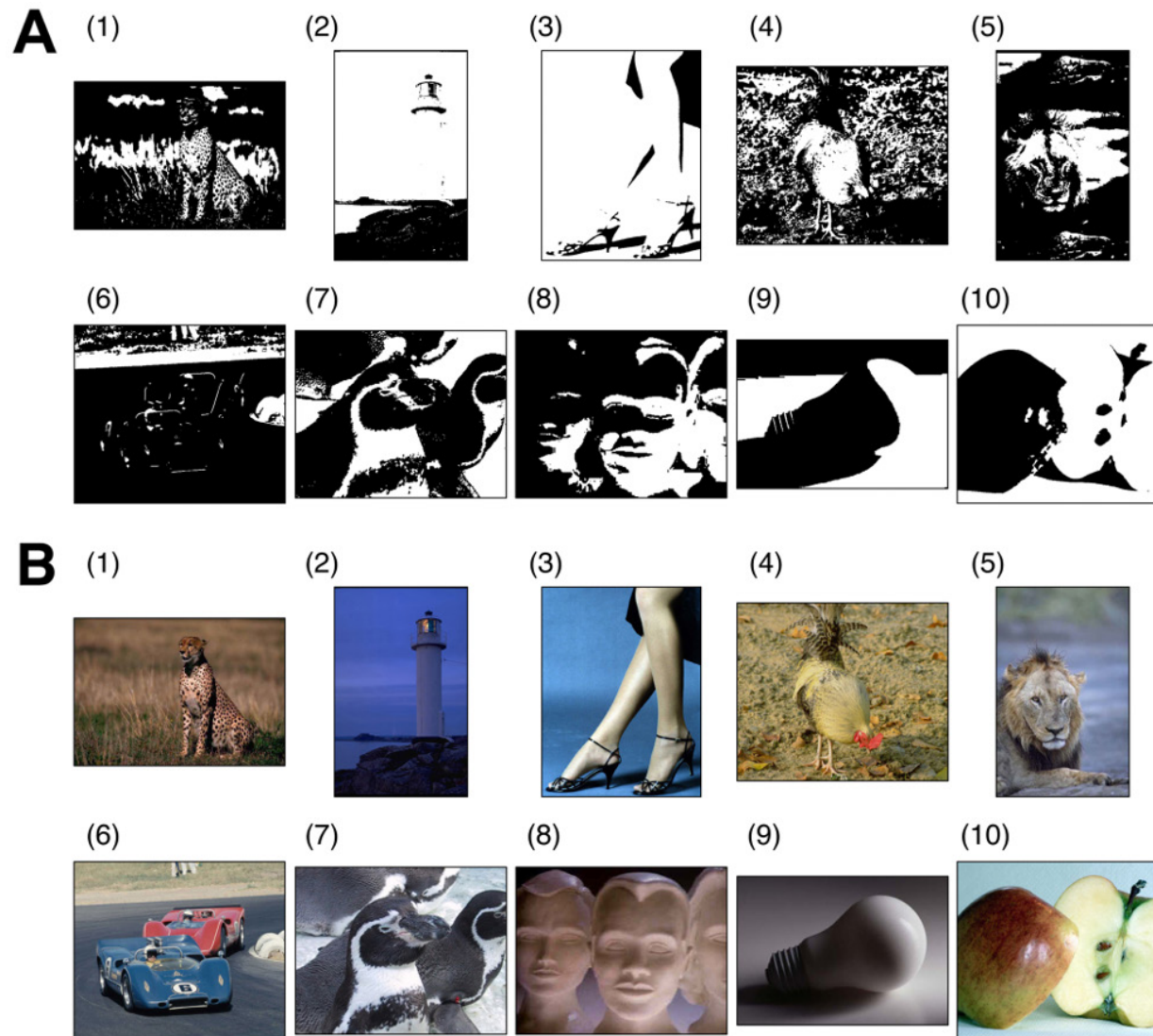
Introduction | hierarchical visual processing



From: Mannasi et al. (2005) J Vis 13:1-10

- As processing proceeds through the hierarchy...
 - Receptive field size gets larger
 - Represented feature gets more complex

Demo



From: Murata et al. (2014) PLoS ONE 9:e115658

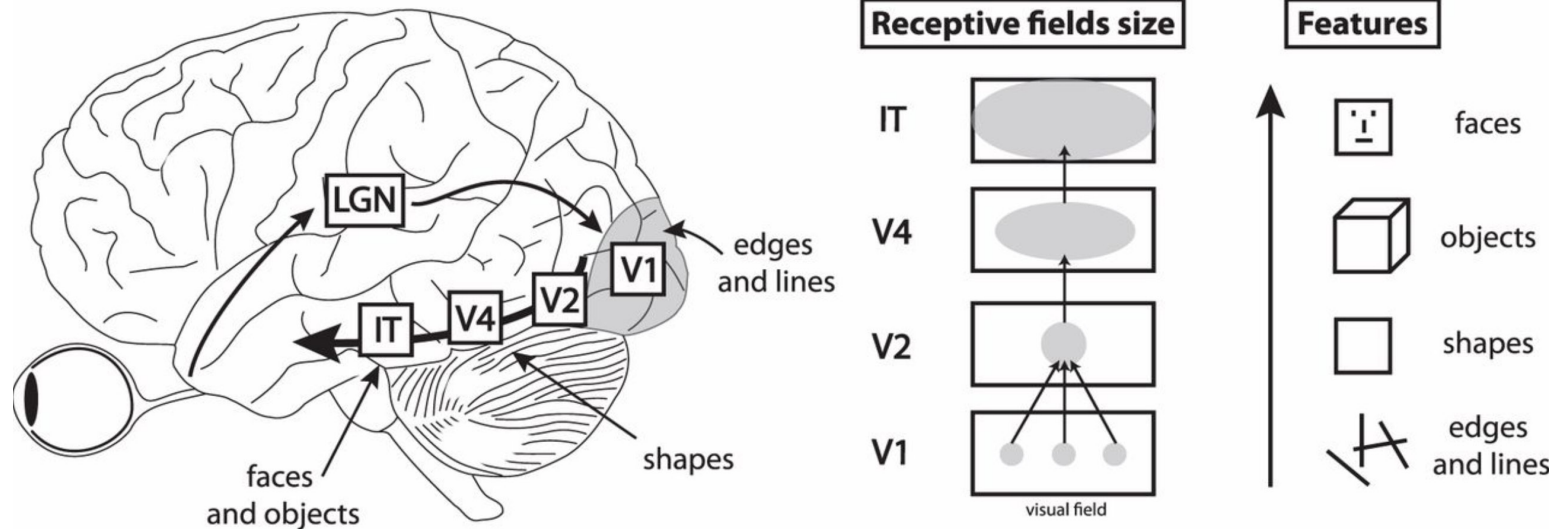
Demo



Demo



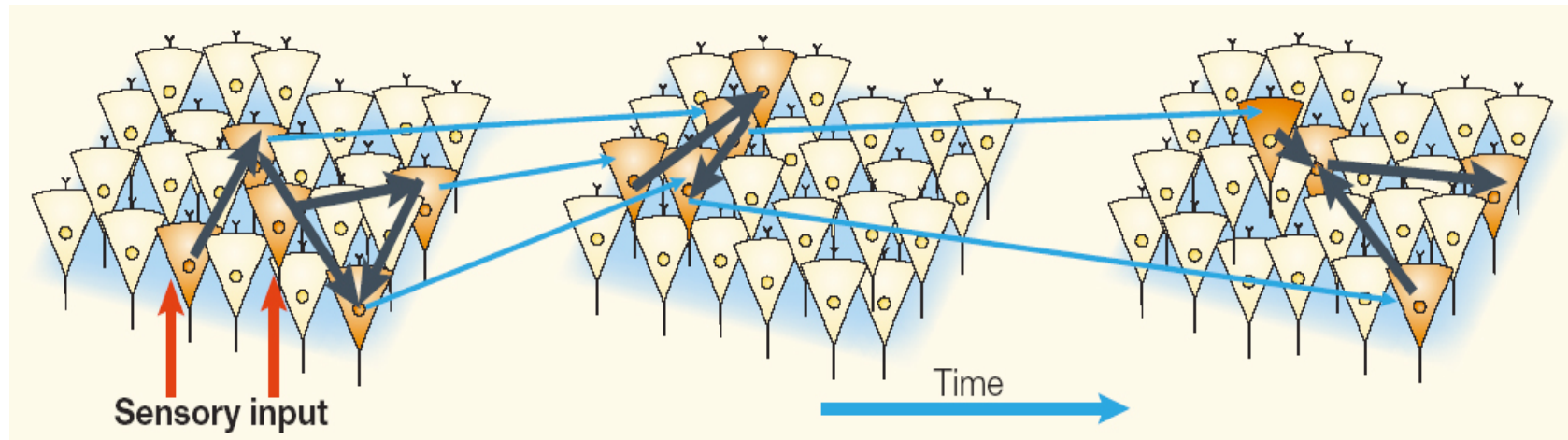
Motivation | question



From: Mannasi et al. (2005) J Vis 13:1-10

- In the demo, you saw **exactly the same image** before and after you were aware of the dog.
- **What difference in the brain activity makes you aware or not aware of the dog?**

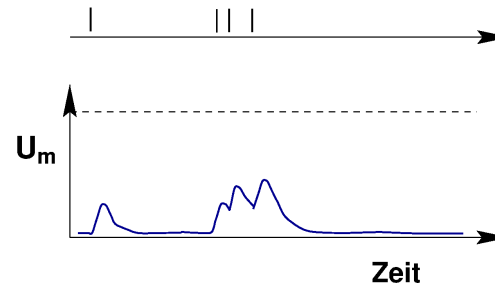
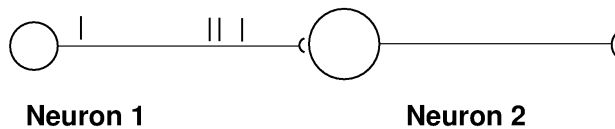
Motivation | underlying neuronal activity



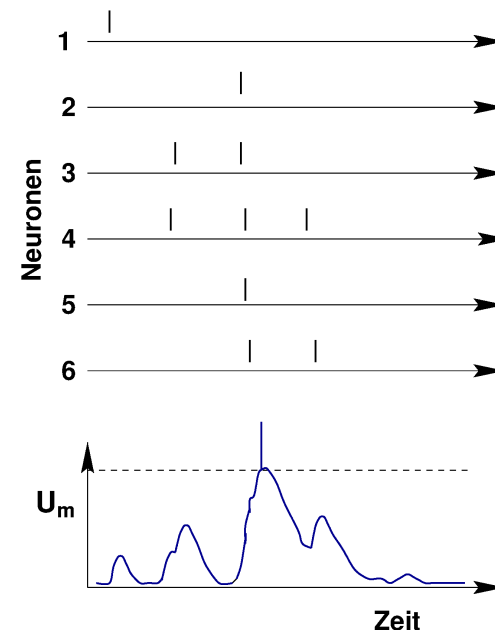
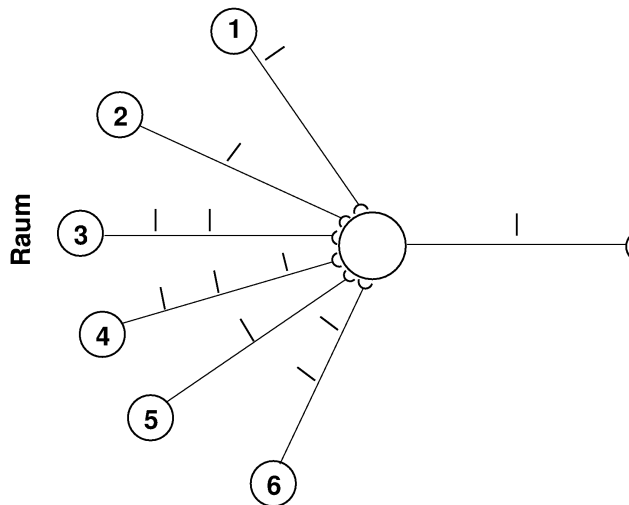
From: Harris (2005) Nat Rev Neurosci 6:399-407

- Processing by interaction of neurons
- Activity propagates across processing stages

Motivation | what makes a neuron fire?



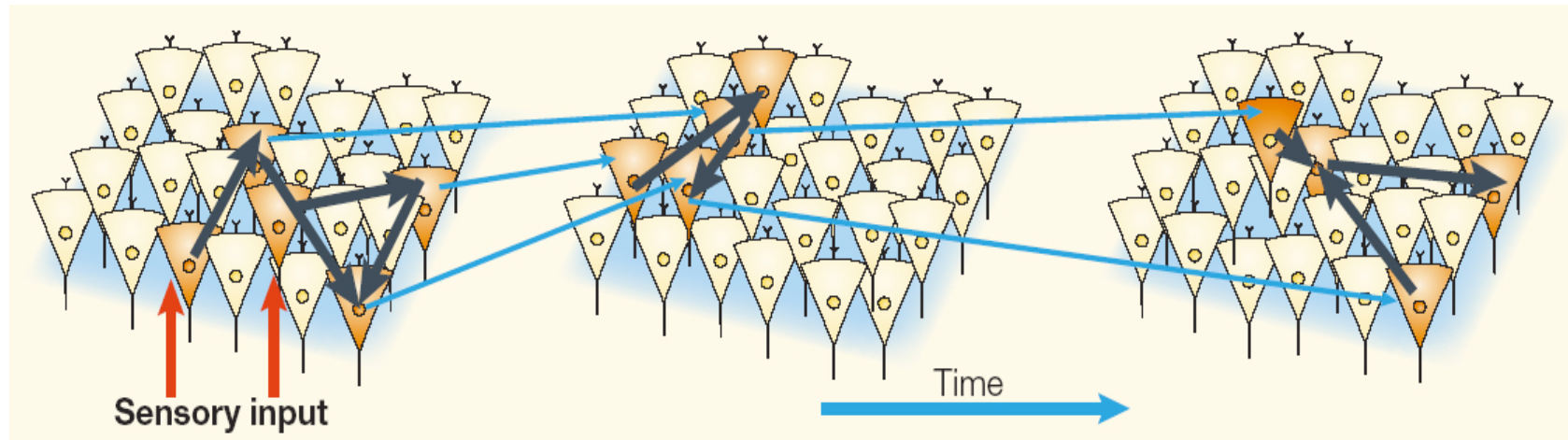
- Cortical neuron: single EPSP far from threshold



- Synchronous input effective in generating output spikes

Abeles (1982) *Isr J Med Sci* 18: 83--92; Abeles (1991) *Corticonics*, Cambridge Univ Press; Koenig et al (1996) *TINS* 19: 130--137; Salinas & Sejnowski (2000) *JNS* 20:6193-6209; etc.

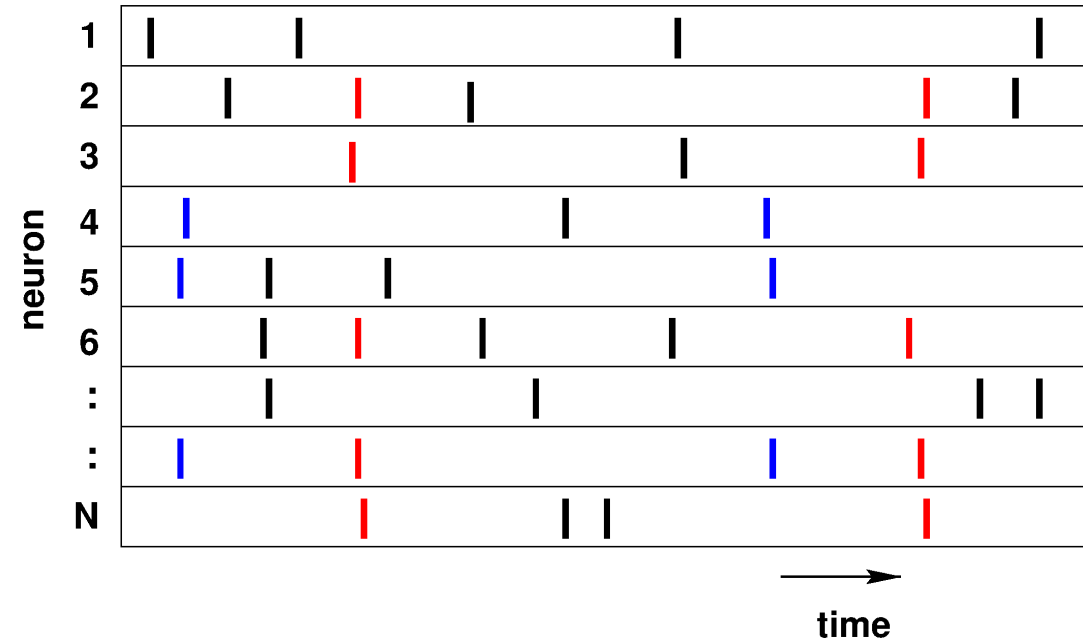
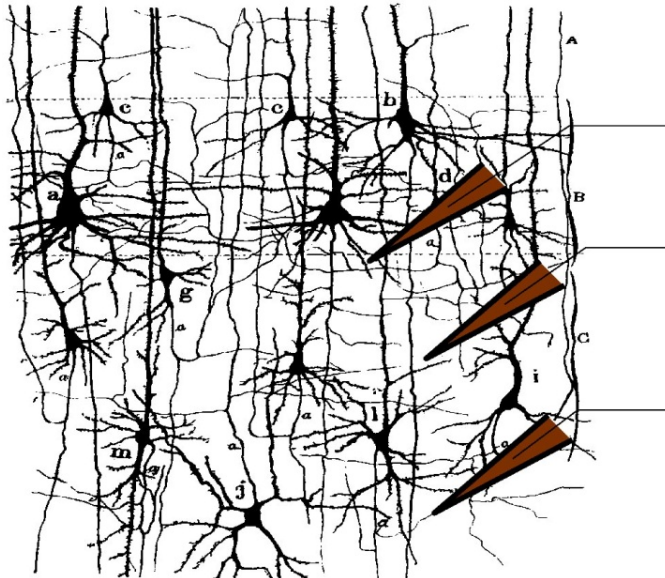
Motivation | binding-by-synchrony hypothesis



From: Harris (2005) Nat Rev Neurosci 6:399-407

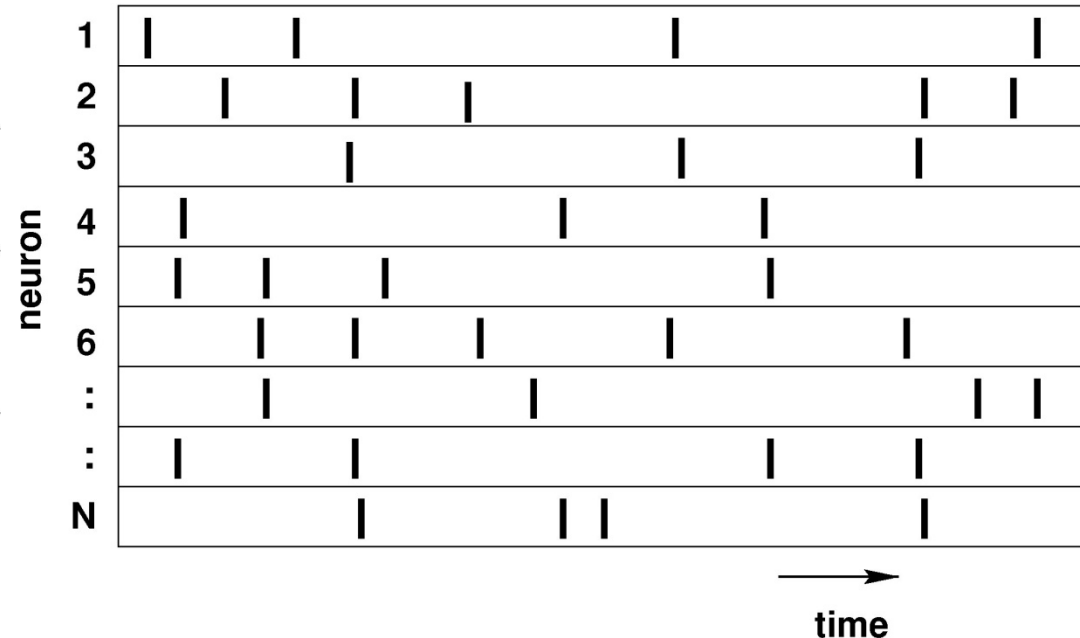
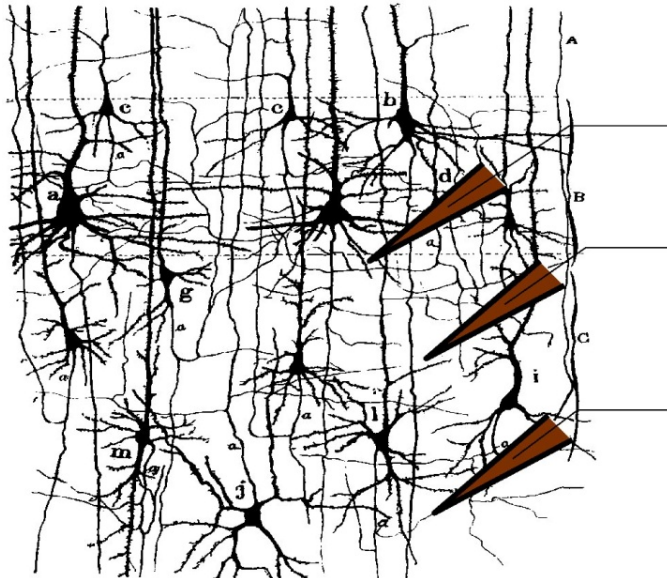
- Cell assemblies act as building blocks for information processing, by **firing spikes synchronously**, in order to propagate their activity stably across processing stages

Motivation | binding-by-synchrony hypothesis



- Cell assemblies act as building blocks for information processing, by **firing spikes synchronously**, in order to propagate their activity stably across processing stages
- Assembly membership is expressed by **coordinated spiking activity**

Motivation | goal



- Identify coordinated spiking activity in spike trains of multiple neurons
→ **cross-correlation analysis**

Outline

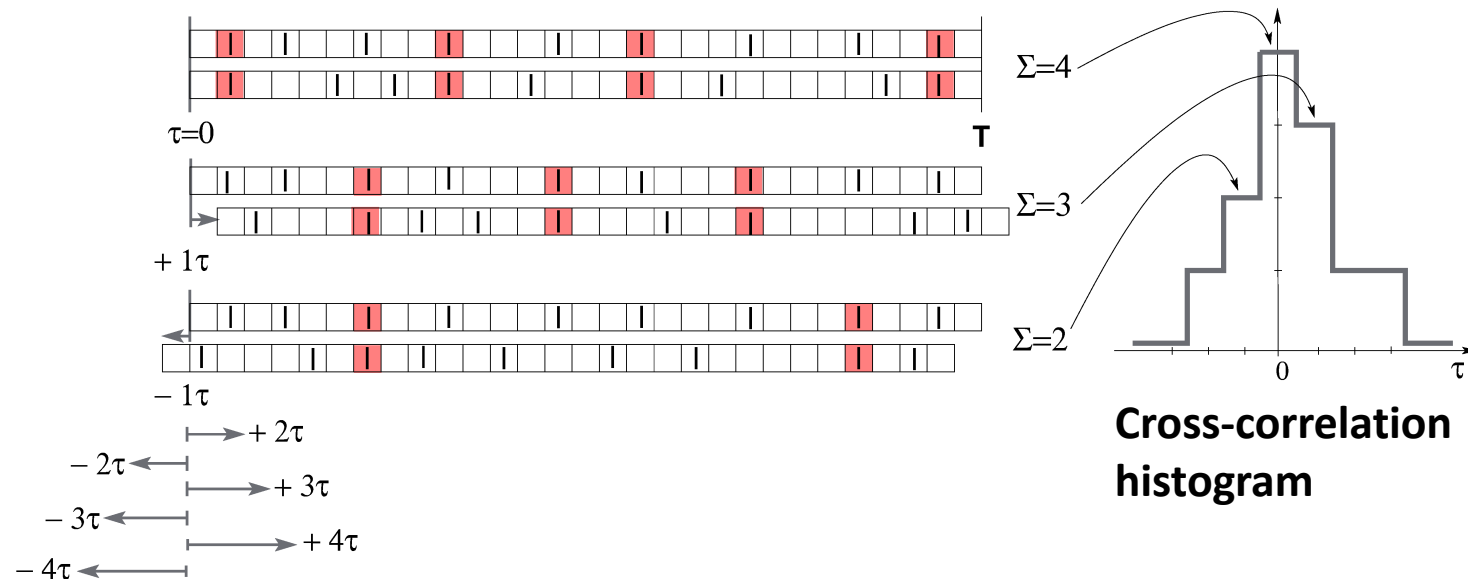
- **Methods**
 - Cross-correlation analysis
 - Significance test
- **Applications**
 - Relation to gestalt perception
 - Cat V1 data (response to visual edges)
 - Monkey MT data (response to visual movement)
 - Relation to network architecture
 - Rat somatosensory cortex (anesthesia)
 - Human neocortex (during sleep)

Methods | cross-correlation histogram

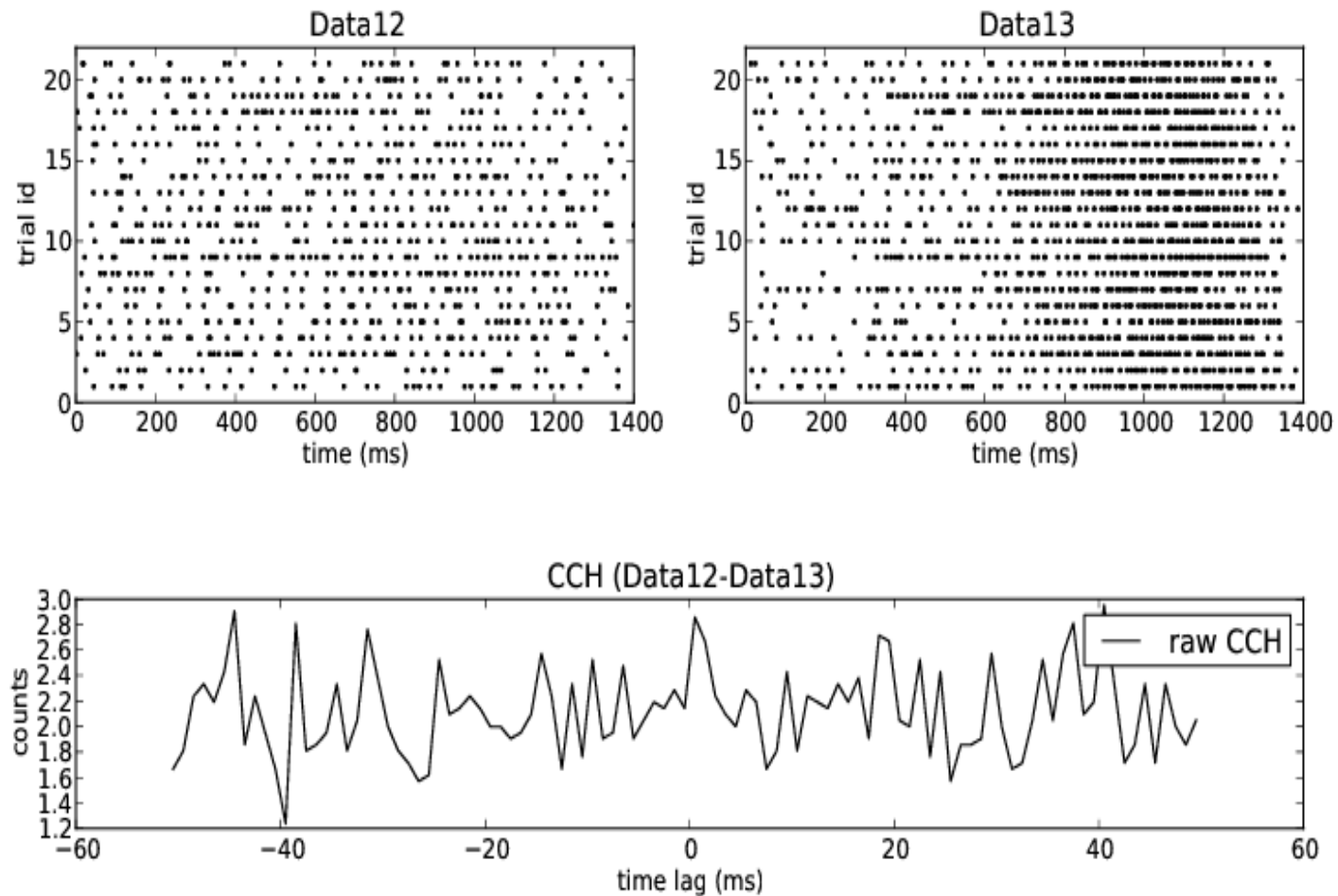
- The **cross-correlation function** is a measure of similarity between two time series $s_1(t)$ and $s_2(t)$ defined as:

$$\rho_{12}(\tau) = \int s_1(t) \cdot s_2(t - \tau) dt$$

- In the case of spike trains, computation is performed directly on binned spike trains as **cross-correlation histogram (CCH)**



Methods | CCH example



Methods | beyond chance?

- Trivially, the higher the rates, the more coincidences (just by chance!)
- Coherent changes in firing rates may induce a peak in a CCH
- How many chance coincidences are expected given the firing rates and their modulations?
 - Solution: compare to CCHs expected from uncorrelated data (**‘predictor’**)

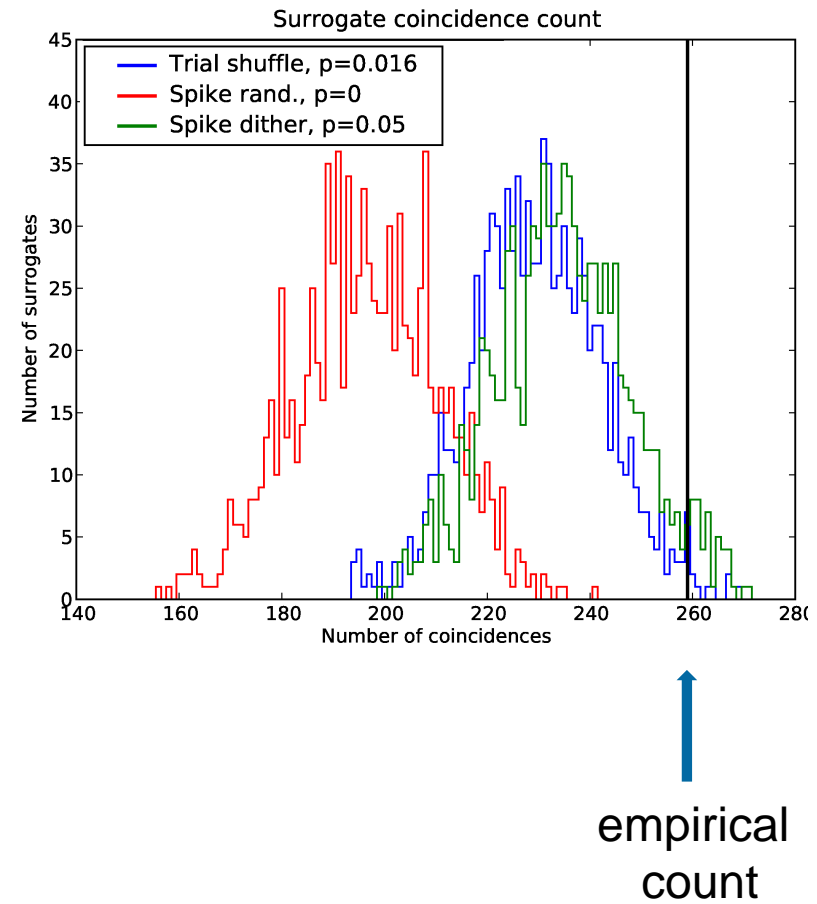
Why and When Surrogates

- Goal: test if *an empirical measure deviates from its predictor*
 - Requires knowledge of probability distribution of the predictor: **null distribution**
 - When unknown, **parametric** or **nonparametric** statistical methods may be used
 - Parametric tests: require model of the data and parameter estimates → often difficult to obtain
- Non-parametric surrogate statistical tests
 - Empirically estimate the null distribution by use of **surrogate data**, i.e., modified samples of the original data
 - Surrogate methods include bootstrap resampling, **randomization** approaches, and so on
 - In our case of correlation analysis: **destroy potentially existing correlations but keep (ideally all) other statistical features intact**

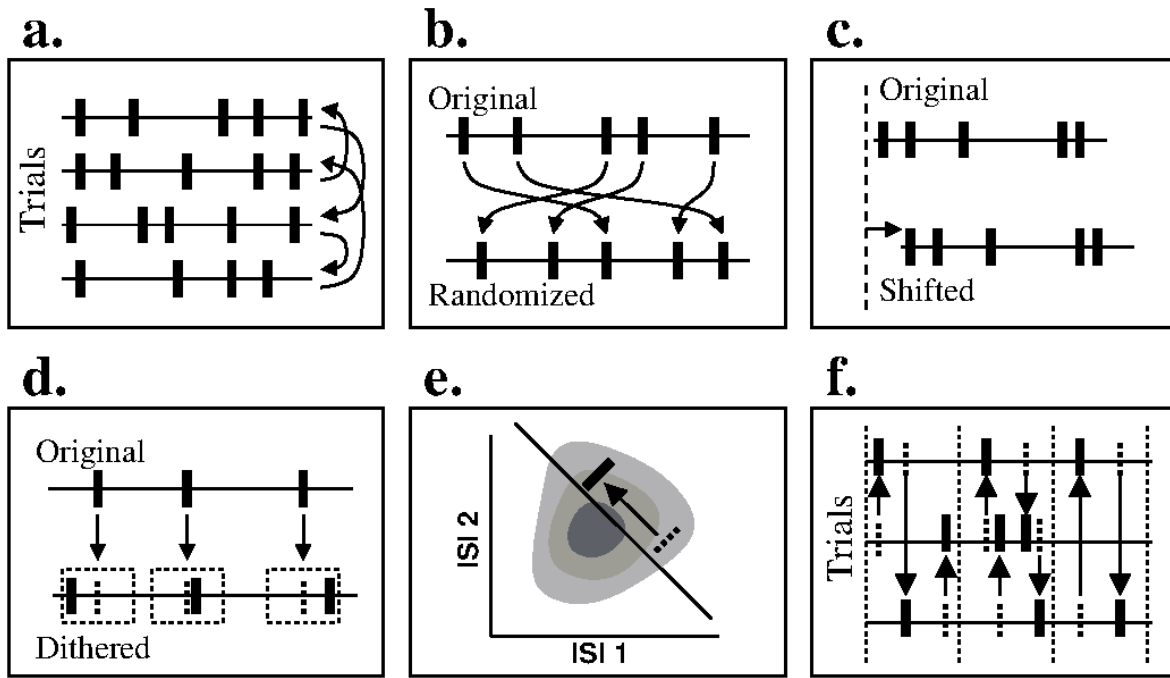
(In parts from: http://sccn.ucsd.edu/wiki/Chapter_5.2._Nonparametric_surrogate_statistics)

Practical procedure

1. **Generate a surrogate** by manipulating the original data to destroy potential fine temporal correlation
2. **Compute the same measure** as from the original data
3. **Repeat steps 1 and 2** many times
4. **Derive the distribution** of the measure extracted from the surrogates
5. **Compare the empirical measure** to the surrogate distribution
6. **Derive significance** (p-value, surprise, etc.)



Surrogates for significance estimation



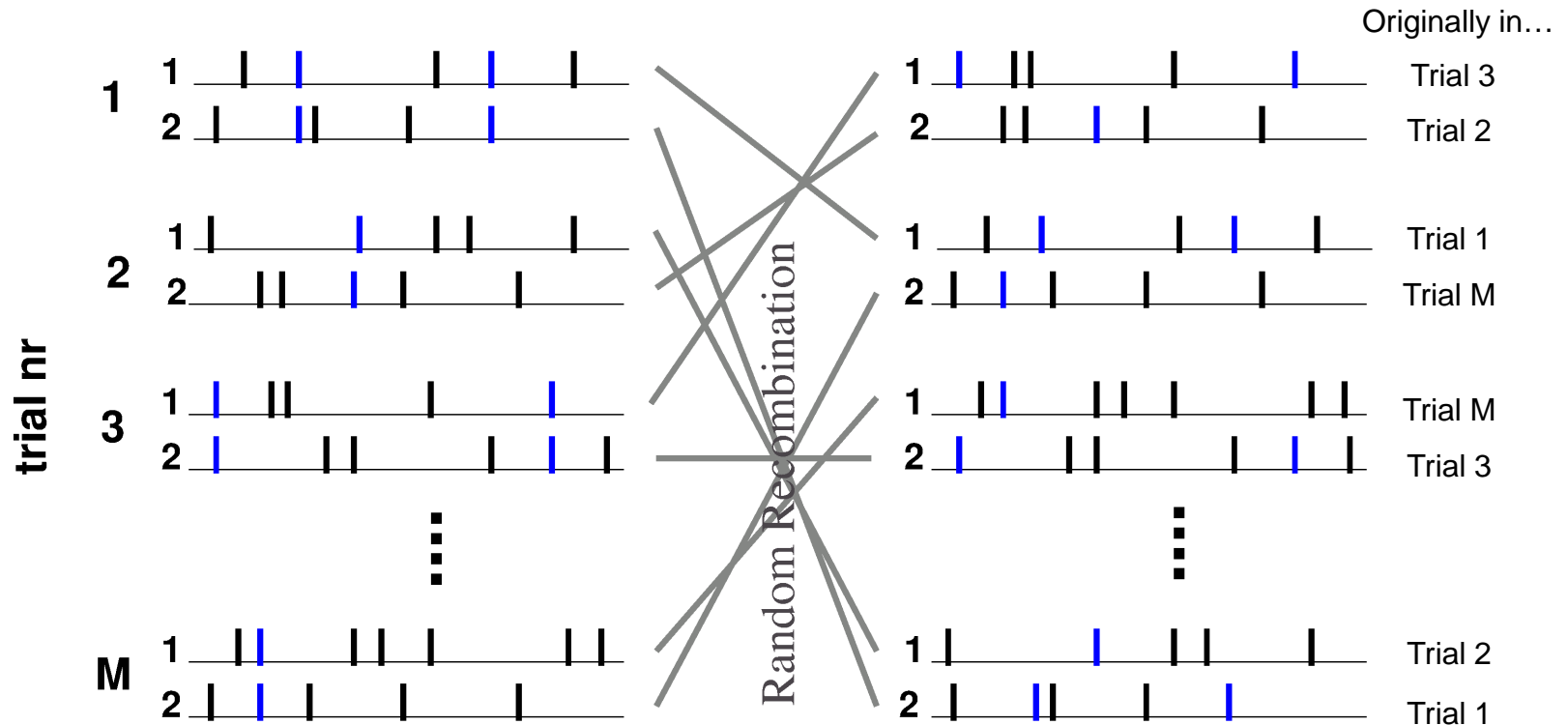
- More surrogates available / to be invented
- Concern: keep the changes in other statistical features of spike trains as little as possible

Grün (2009) *J Neurophysiol* (review)

Louis et al. (2010) *Front Comput Neuroscience*

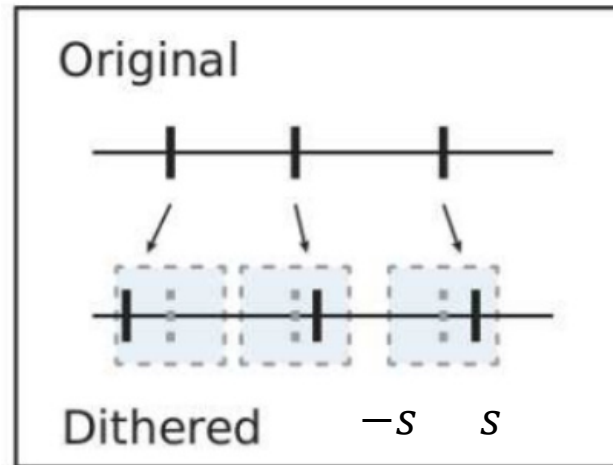
Louis et al. (2010) in *Analysis of Parallel Spike Trains* (2010) Eds: Grün & Rotter, Springer

Trial shuffling



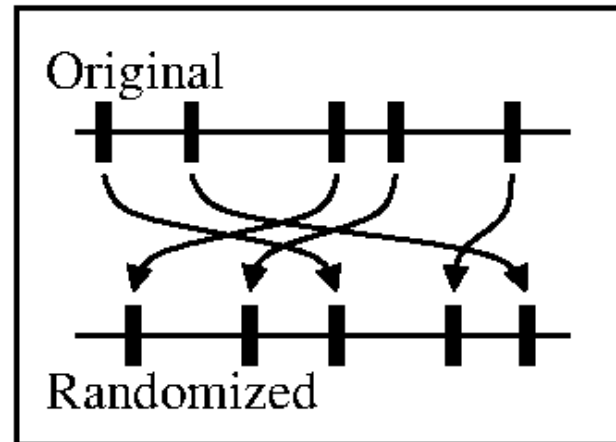
- Random recombination of trials
- **Effect:** spike trains are not changed, only their trial combination
- **Assumption:** stationarity across trials
 - For short-term stationarity: shift predictor = recombination with shifted trial IDs

Spike time dithering



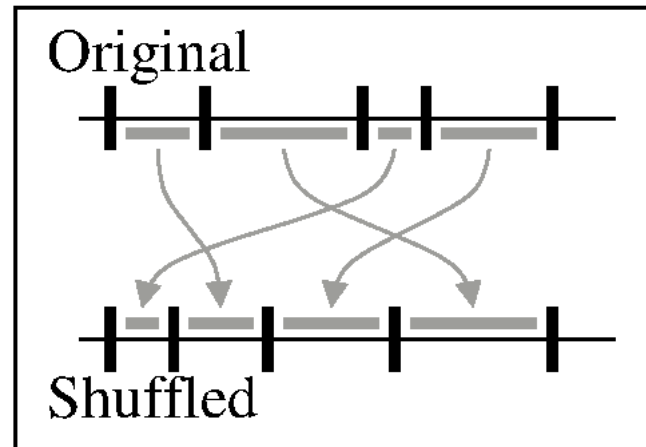
- Apply to each spike a small random shift with weighted probability within $[-s, s]$
 - Choice of s : larger than temporal jitter of correlation, small enough not to alter the firing rate modulations on a larger time scale
- **Effect:** ISIs modified, firing rate modulations smoothed
- **Assumptions:** stationarity on the time scale of the dither width

Spike time randomization



- Randomize times of spike occurrences
- **Effects:**
 - destroys ISIs (makes spike train become Poisson)
 - flattens the firing rate modulations
- **Assumption:** Poisson, stationarity

ISI randomization



- Randomize ISIs
- **Effects:**
 - keeps the distribution of ISIs
 - flattens the firing rate modulations
- **Assumption:** renewalty (more general than Poisson), stationarity

Pros-and-cons of different surrogate methods

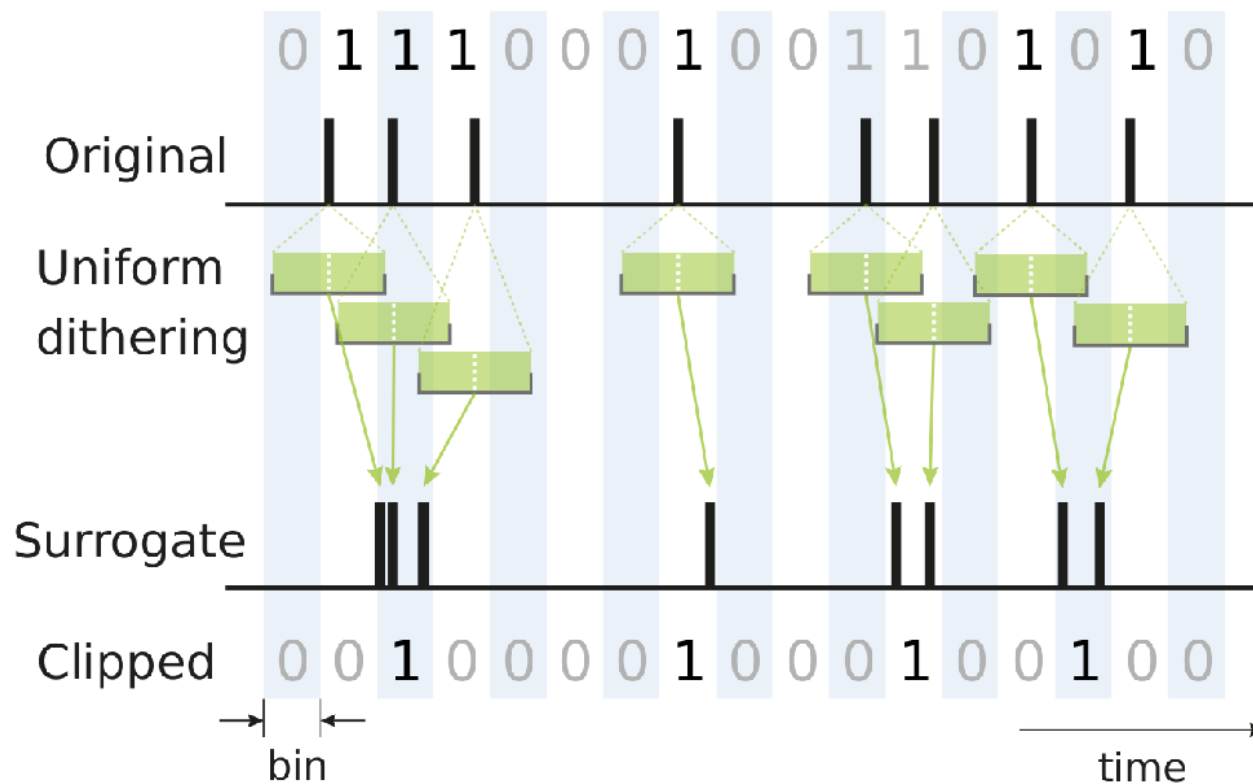
TABLE 1. *Methods for implementing the null-hypothesis, divided into model based and data based*

	Method				Problems accounted for			Assumptions	Conserves		Destroys	
					Non-Stat Rate in Time	Cross-Trial Non-Stat	Non-Poisson		Single Neuron	Parallel Neurons	Single Neuron	Parallel Neurons
Model based	A	Homogeneous Poisson process	Parameter estimation from trial average	Parameter estimation in single trials			(X)	• Poisson • stat	• average rate	• average rates of all neurons	• ISI • PSTH	• POPH
	B	Homogeneous model process					(X)	• Model process • stat	• average rate	• average rates of all neurons	• PSTH	• POPH
	C	Inhomogeneous Poisson process			(X)		(X)	• Poisson • Non-stat	• PSTH	• Co-var rate	• ISI	• POPH
	D	Inhomogeneous model process			(X)		(X)	• Model process • Non-stat	• PSTH • ISI	• Co-var rate		• POPH
Data-based surrogates	E	Spike time randomization (within single trials)				X		• Poisson • stat	• SpC	• SpC co-var	• ISI • PSTH • Sp-tr struc	• POPH
	F	ISI shuffling (within single trials)				X	X	• Renewal • stat rate • stat proc param	• SpC	• SpC co-var	• PSTH • Sp tr struc	• POPH
	G	ISI shuffling (across trials)					X	• Renewal • stat rate • cr-tr stat	• tot SpC • tot ISI	• tot SpC per neuron	• PSTH • ISI • Sp-tr struc	• POPH
	H	Trial shuffling			X			• cr-tr stat	• PSTH • ISI • Sp-tr struc	• tot POPH	• Trial ids	• POPH • SpC
	I	Shift predictor			X	(X)		• Short-term cr-tr stat	• PSTH • sp tr struc • ISI	• tot POPH	• Trial ids	• POPH • SpC co-var
	J	Spike shuffling across neurons (within trials)						• cr-tr stat • SpC co-var • Poisson			• PSTH • ISI • SpC • sp-tr struc	
	K	Spike exchange across neurons (within trials)						• stat rate • Poisson	• SpC	• POPH	• PSTH • ISI • sp-tr struc	
	L	Dithering			(X)	X	(X)		• sp-tr struc (approx) • SpC • ISI (smoothed) • PSTH (smoothed)	• POPH (smoothed)		
	M	Soft dithering (according to ISI distribution)			(X)	X	X		• sp-tr struc (approx) • SpC • ISI • PSTH (smoothed)	• POPH (smoothed)		
	N	Shifting spike trains of neurons against each other			(X)	X	X		• Sp-tr struc • SpC (approx) • PSTH (smoothed)	• POPH (smoothed)		

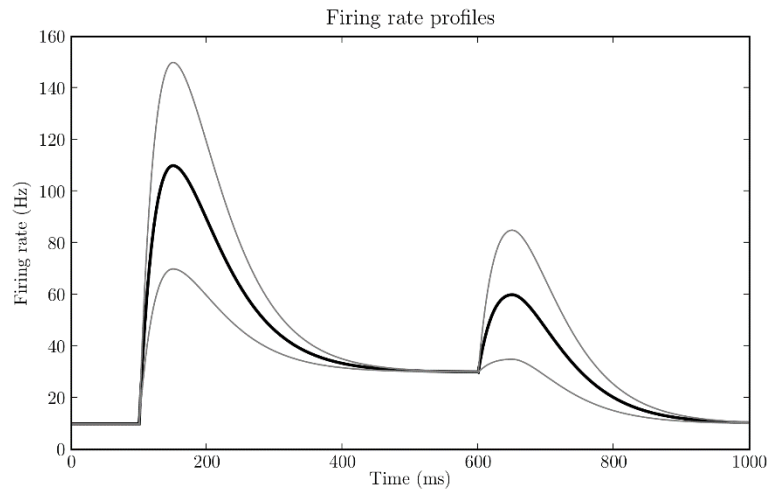
Spike timing across neurons

Pros-and-cons of different surrogate methods

- Example drawback: applying **spike time dithering** on data to be discretized can lead to spike count reduction



Surrogate performance | test data



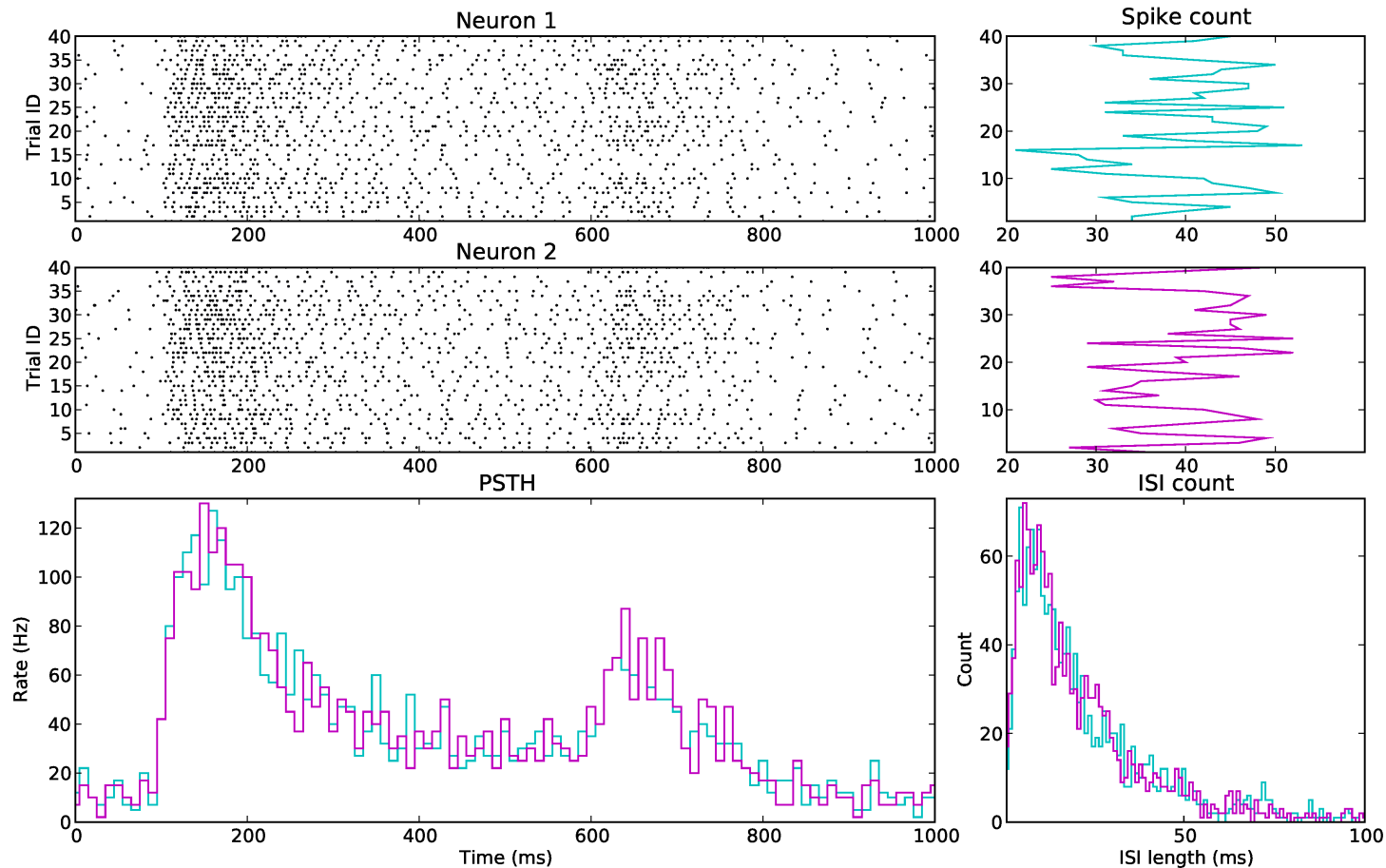
Type	Process	Nonstat. in time	Cross-trial nonstat.	γ	Δ
1	Poisson	no	no	1	0
2	Poisson	yes	no	1	0
3	Poisson	no	yes	1	0.235
4	Poisson	yes	yes	1	0.5
5	Gamma	yes	yes	3	0.5

- To evaluate the performance of different surrogate methods, a test data set is generated
 - Non-stationary firing rates according to a profile
 - Cross-trial variations by random selections (per trial) of rate modulation depth Δ
 - Different regularities of the ISIs by gamma processes of different shape factors γ
- Correlations are introduced by inserting coincident spikes in a pair of spike trains at a given rate

Louis et al. in *Analysis of Parallel Spike Trains* (2010)
Eds: Grün & Rotter, Springer

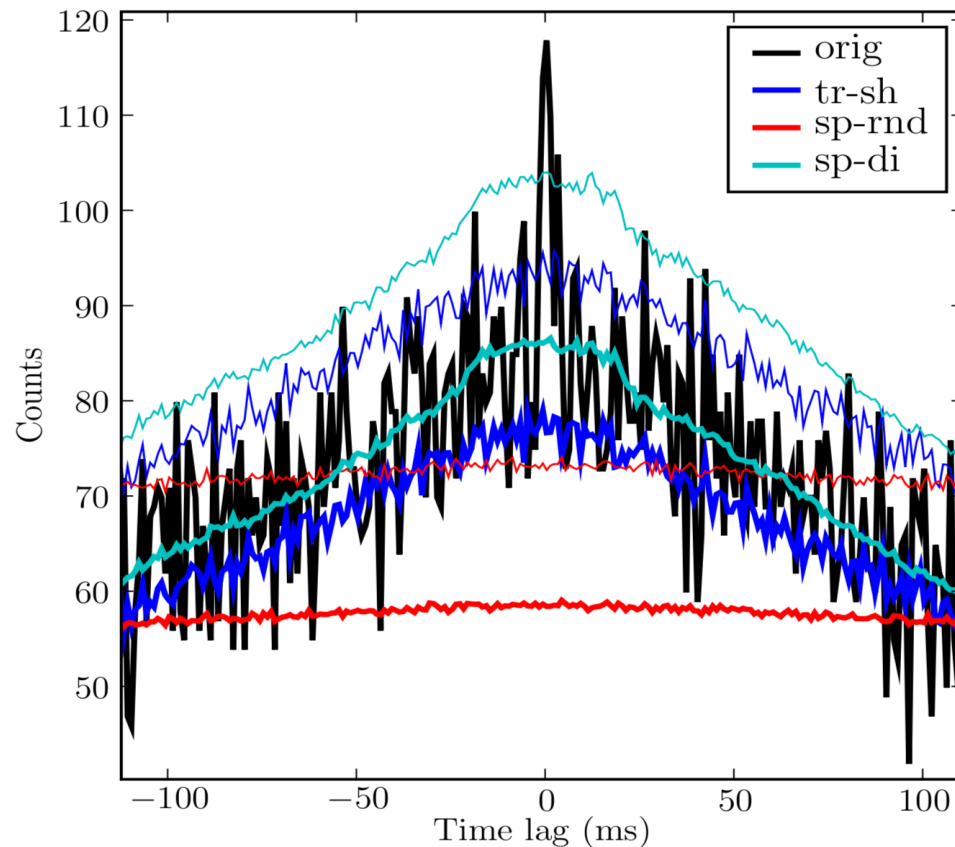
Surrogate performance | test data

An example of type 5 data



Louis et al. in *Analysis of Parallel Spike Trains* (2010) Eds: Grün & Rotter, Springer

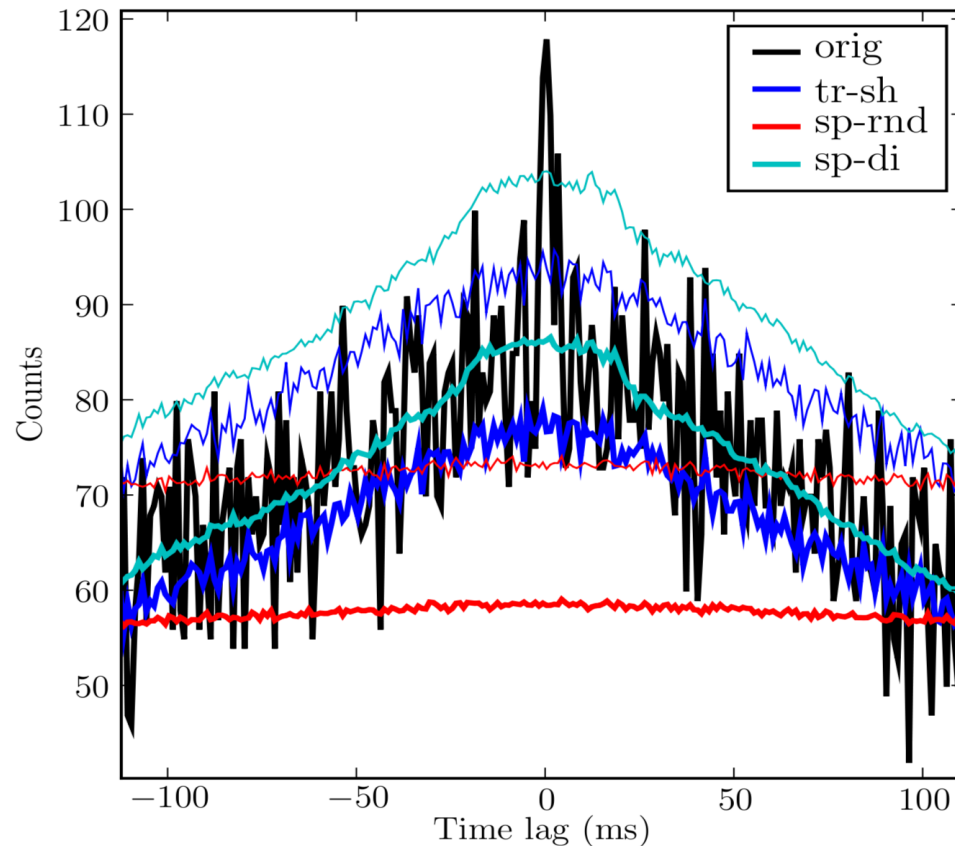
Surrogate performance | CCH



- Two temporally different components in the original data
 - Broad peak: due to the non-stationarity of the firing rate
 - Narrow peak at zero-lag: fine temporal correlation

Louis et al. in *Analysis of Parallel Spike Trains* (2010)
Eds: Grün & Rotter, Springer

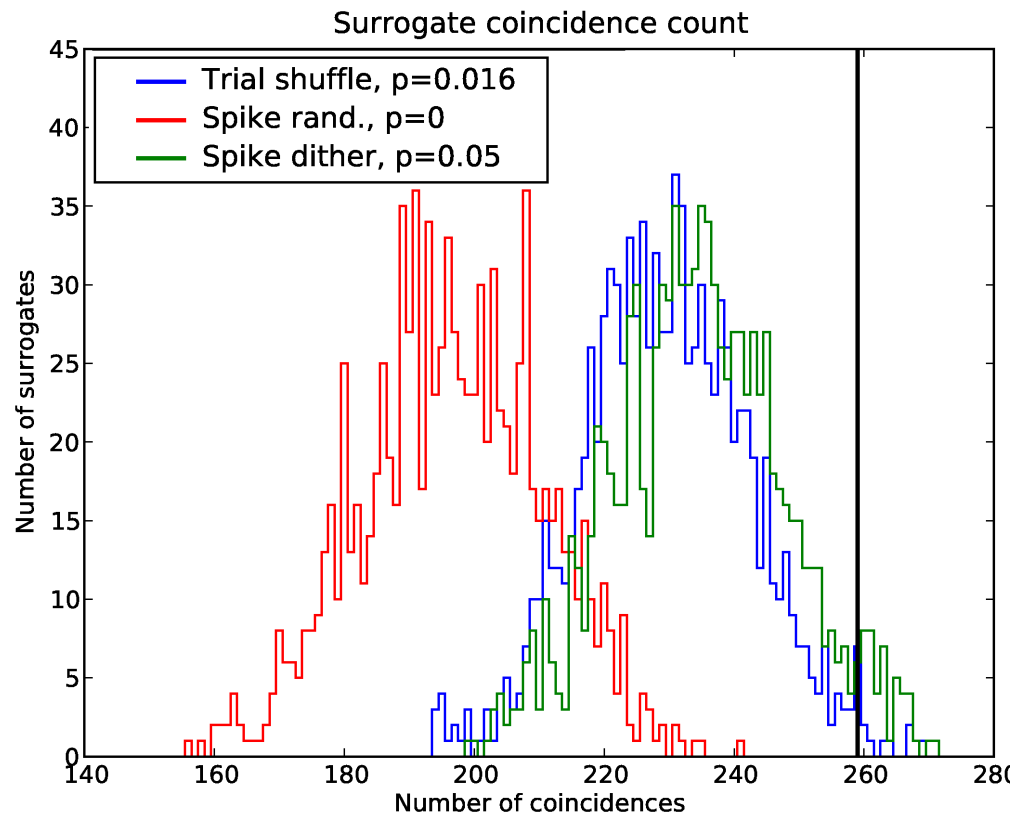
Surrogate performance | CCH



- **Spike time randomization**
 - Flat CCH – due to destruction of firing rate changes
- **Trial shuffling**
 - Under-estimation of the amplitude of the rate peak due to the variability across trials
- **Spike time dithering**
 - Reproduces the broad peak

Louis et al. in *Analysis of Parallel Spike Trains* (2010)
Eds: Grün & Rotter, Springer

Surrogate performance | zero-lag synchrony



- Empirical coincidence count at 258
 - Its percentile score in each surrogate distribution is shown in the legend
- With a 5% significance threshold, the empirical count is significantly large in comparison to all types of surrogates
- But mostly due to wrong reasons** – all but **spike time dithering** tend to lead to false positives!

Louis et al. in *Analysis of Parallel Spike Trains* (2010)
Eds: Grün & Rotter, Springer

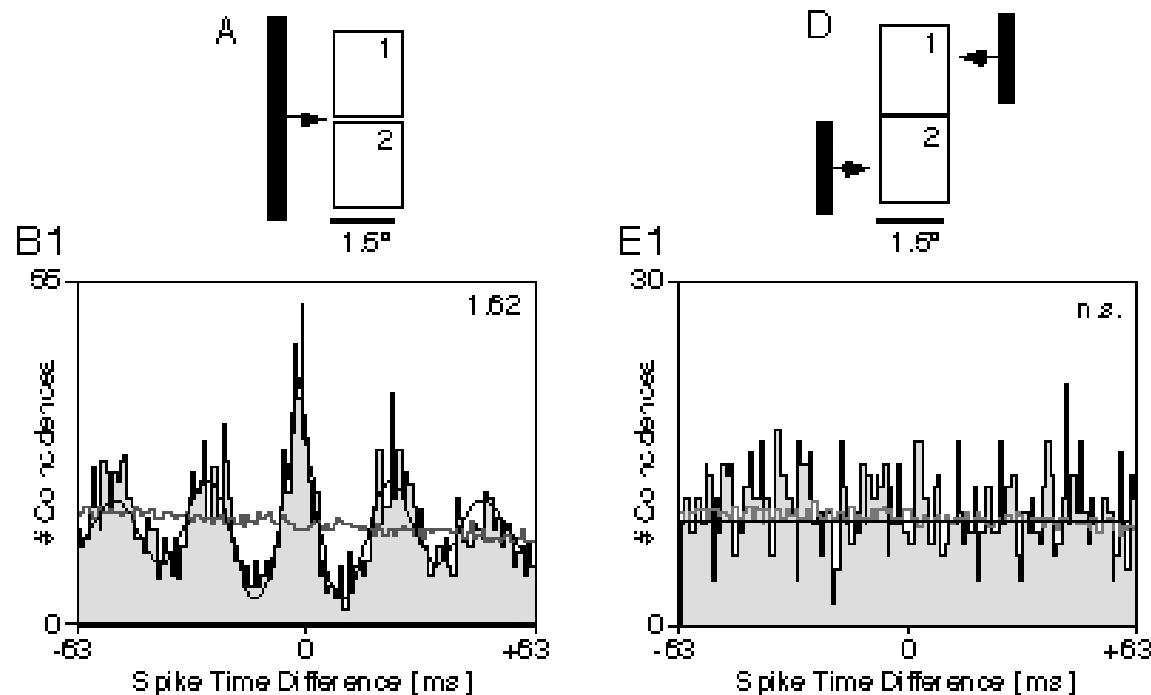
Methods | summary

- **Cross-correlation histogram (CCH)** is a standard tool for examining synchronized or delayed spike correlation.
- Comparison to **surrogate data** allows to differentiate excess correlation from chance correlation, which occurs just by chance.
 - Choosing an appropriate surrogate method is crucial for drawing proper conclusions

Outline

- **Methods**
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 - Significance test
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 - Relation to network architecture
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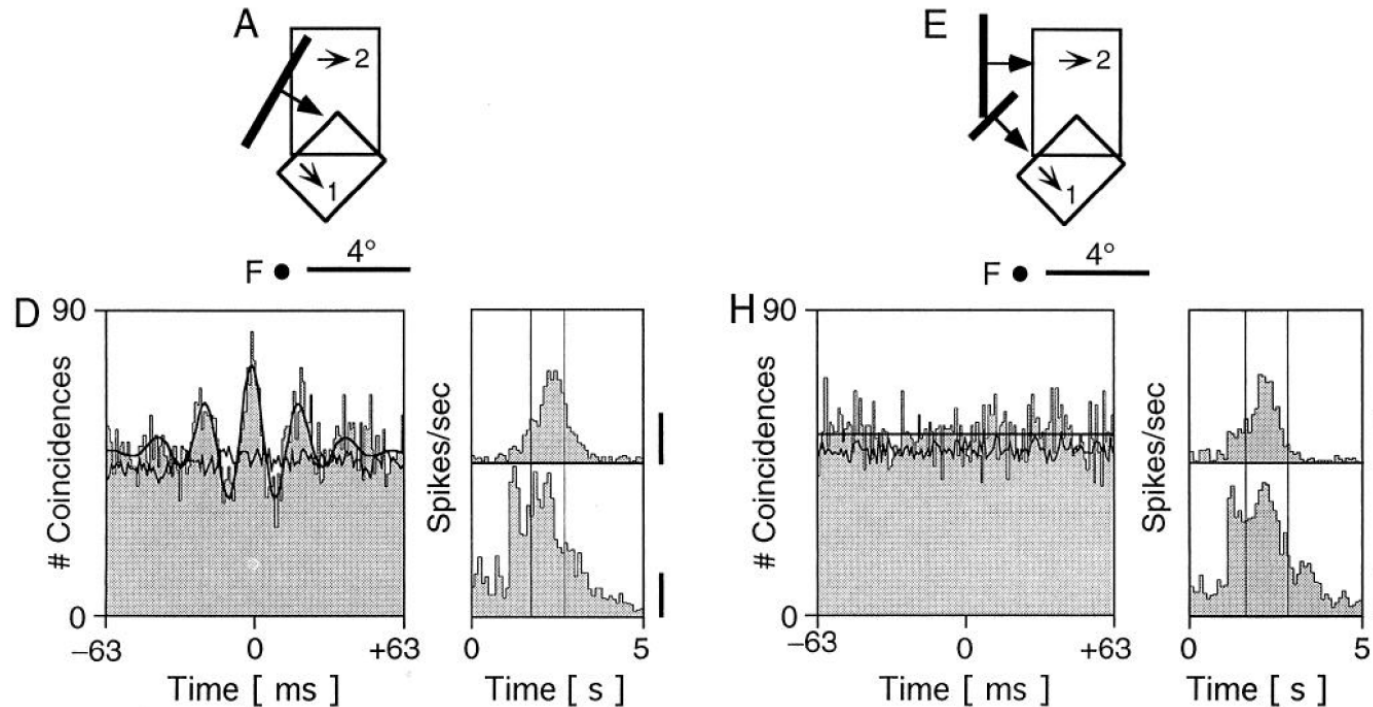
Application | relation to gestalt perception



Freiwald et al. (1995) NeuroReport 6: 2348--2352

- Simultaneous recording from pairs of single units in the primary visual cortex (A17) of cats
- Long bar condition: **synchronized spike response**
- Dual bar condition: absence of synchronization

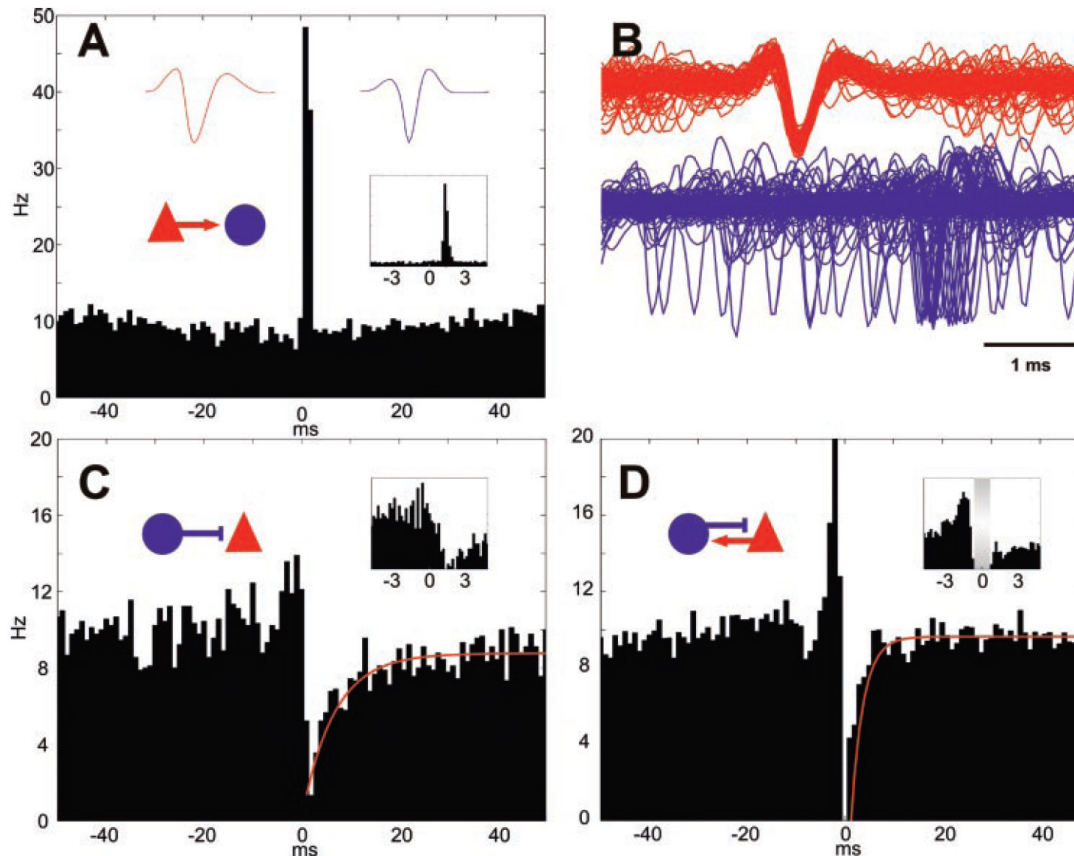
Application | relation to gestalt perception



Kraiter and Singer (1996) J Neurosci 16:2381-2396

- Simultaneous recording from pairs of single units in area MT of monkeys
- Long bar condition: **synchronized spike response**
- Dual bar condition: absence of synchronization

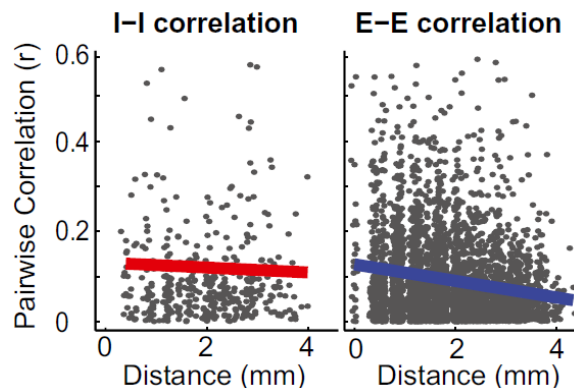
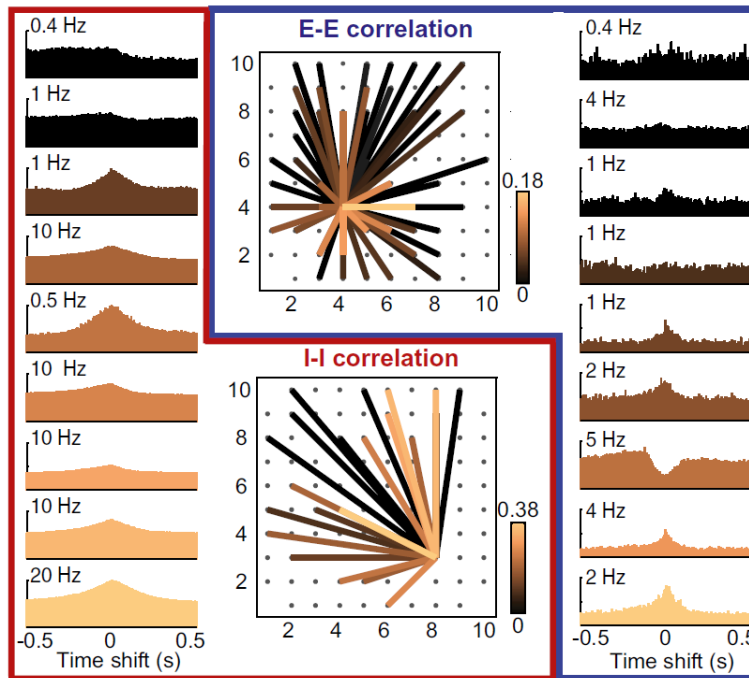
Application | relation to network architecture



Bartho et al. (2004) J Neurophysiol 92:600-608

- Simultaneous recording from multiple single units in rat somatosensory cortex using a 64-ch electrode array
- ~0.25% of the recorded cell pairs showed short-latency peak and/or trough in their CCHs
- **Short-latency peak**
→ **excitatory** connection
- **Short-latency trough**
→ **inhibitory** connection

Application | relation to network architecture



- Simultaneous recording from multiple single units in the middle temporal gyrus of epilepsy patients using a 10x10 grid of electrodes
- Correlation between **inhibitory** neurons
→ **constant over distance**
- Correlation between **excitatory** neurons
→ **decay with distance**

Peyrache et al. (2012) PNAS 109:1731-1736

Summary

- **Cross-correlation histogram (CCH)** is a standard tool for examining synchronized or delayed spike correlation.
- Comparison to **surrogate data** allows to differentiate excess correlation from chance correlation, which occurs just by chance.
- Converging evidence suggests that gestalt perception requires binding of single unit activities via spike synchrony.
- The type and direction of synaptic connections between neurons can be inferred from the shape of CCH.