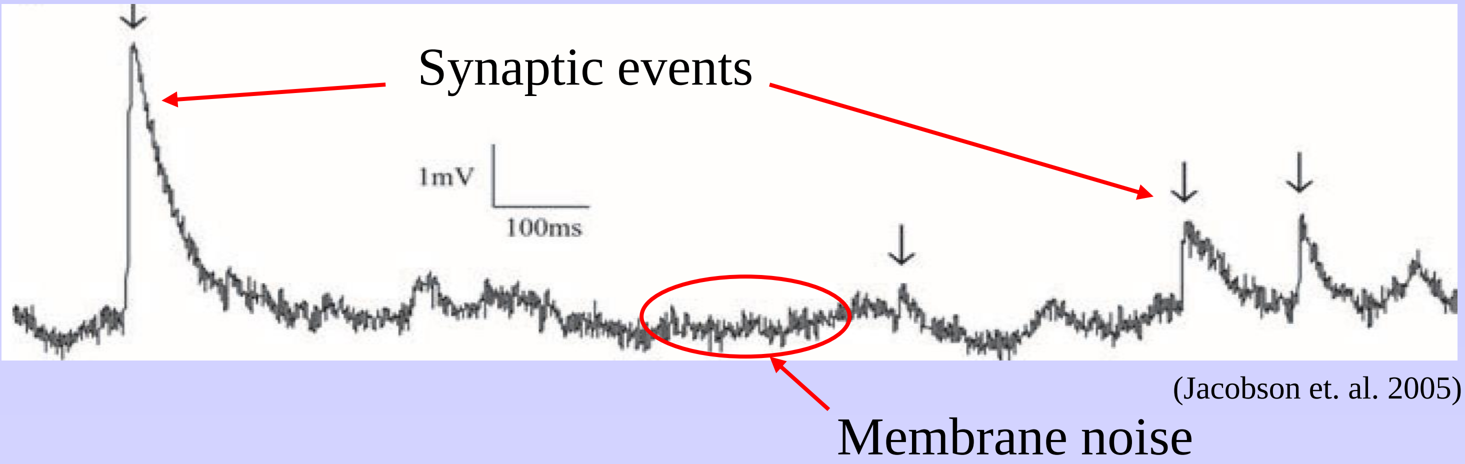
Unit 3

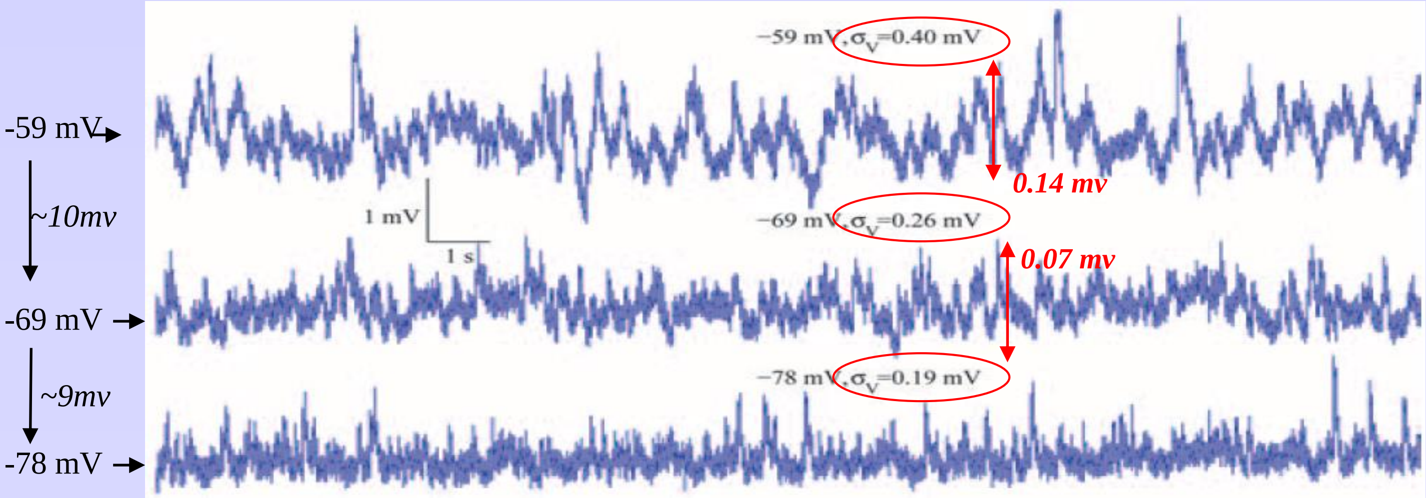
Spontaneous Activity

Spontaneous Activity

- Definition: Spiking activity that is not (temporally) related to a stimulus.
- E.g. Subthreshold ‘noise’:



(Jacobson et. al. 2005)



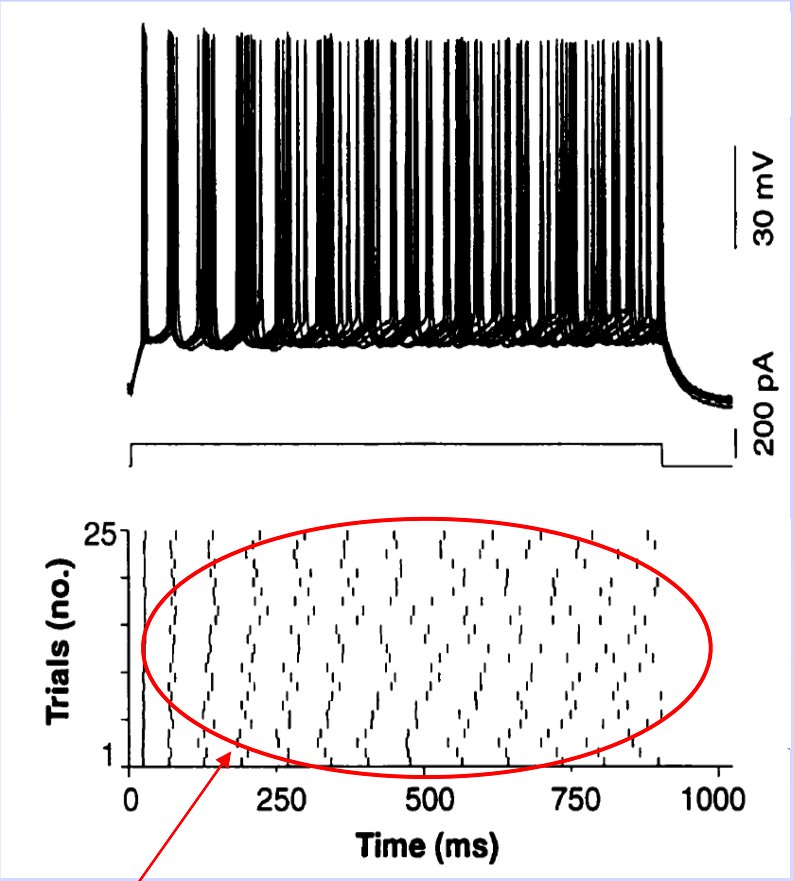
Noise is non-linearly voltage-dependent

(rat cortex, pyramidal cell, in vitro)

(Jacobson et. al. 2005)

- Does membrane noise matter?

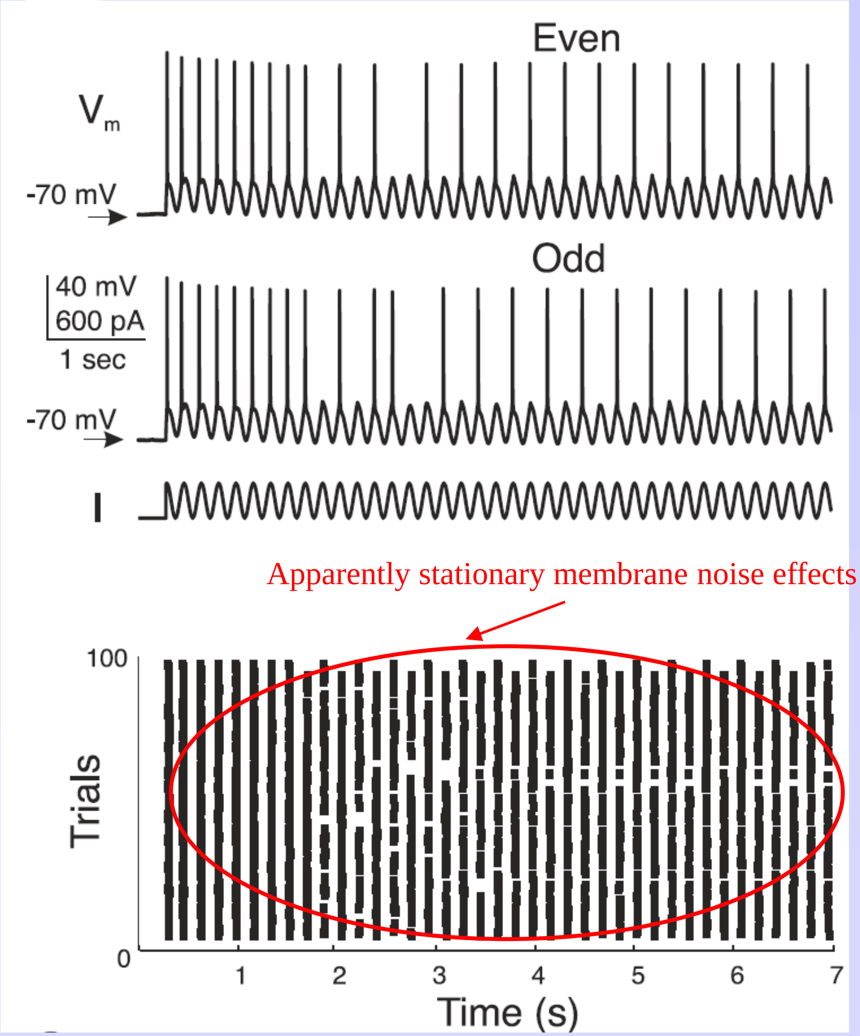
Unstructured inputs



Accumulating effects of membrane noise

(Mainen and Sejnowski, 1995)

Structured inputs



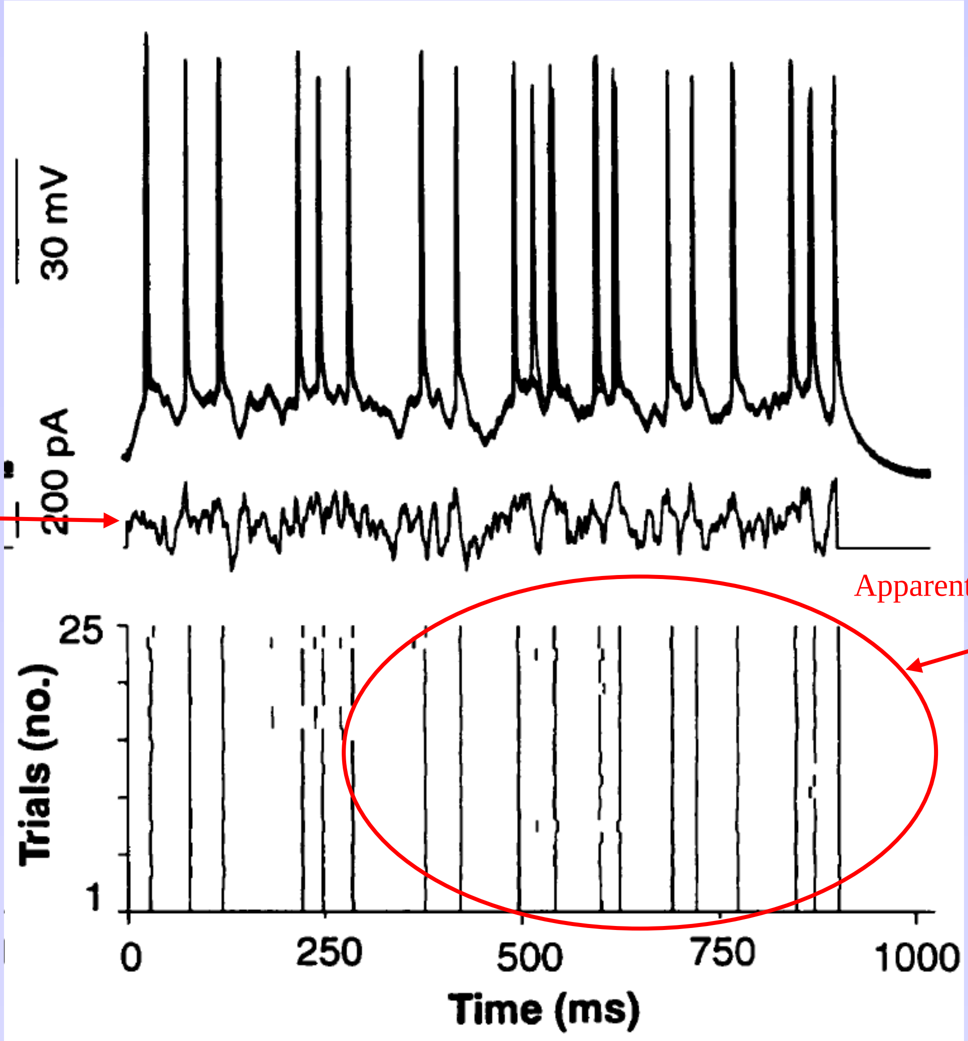
Rat prefrontal cortex pyramidal cells, in vitro, synaptic transmission blocked

(Fellous et. al. 2004)

Spontaneous activity

- But!... What if the inputs are 'synaptic-like'

'Frozen' noise



Apparently NO effect of membrane noise

(Mainen and Sejnowski, 1995)

However…. Two Synaptic inputs are **NEVER** identical…

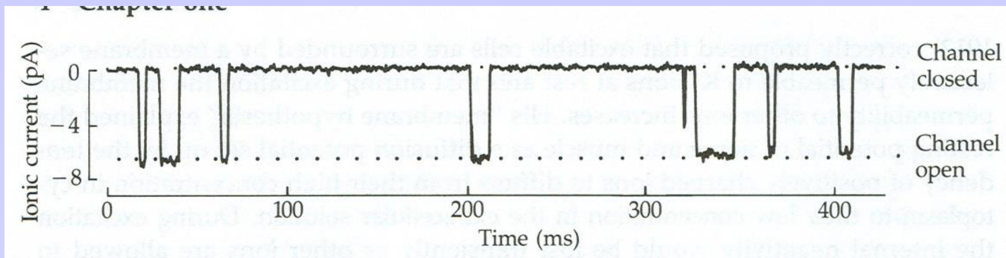
Spontaneous Activity

Sources of noise: Intrinsic? Or Synaptic?

- Thermal noise ('Johnson' noise).

White noise, Gaussian amplitude distribution: ~< 0.5 mV

- Stochastic opening/closing of membrane channels: ~< 0.5 mv

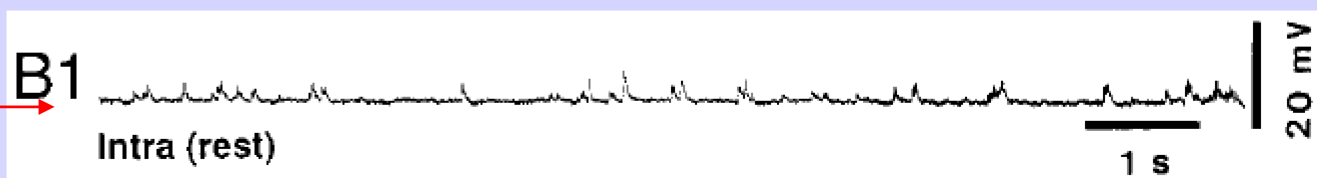


(Temperature dependent)

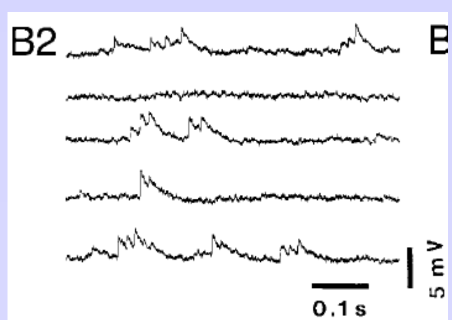
(Hille 2001)

- Synaptic noise: ~2-10 mV

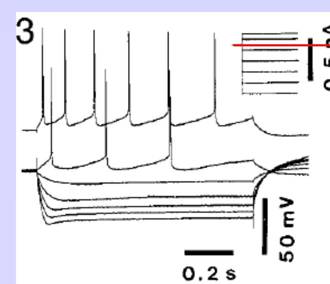
- 76 mV



In *vitro*



(Pare et. al. 1998)



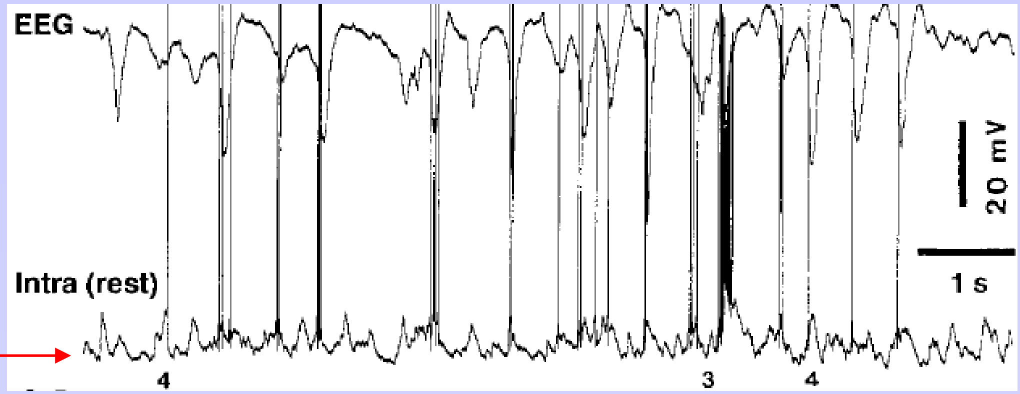
0 nA

Noise Vs APs

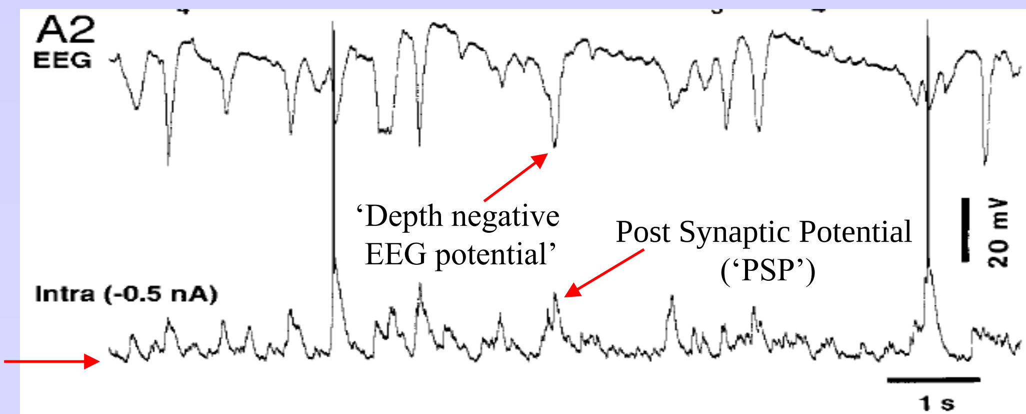
Spontaneous Activity: **Standard deviation** of membrane potential

Quantifying synaptic noise (in *vivo*)

Note: convention:
EEG downward → depolarizing potentials



- 64 mV

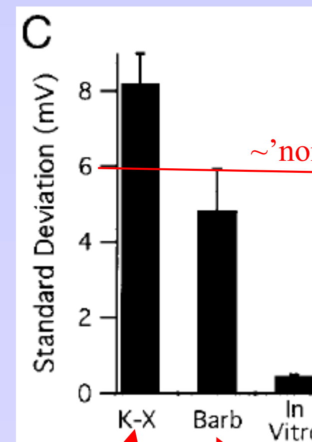


'Depth negative EEG potential'

Post Synaptic Potential ('PSP')

- 82 mV

(Pare et. al. 1998)



~'normal'

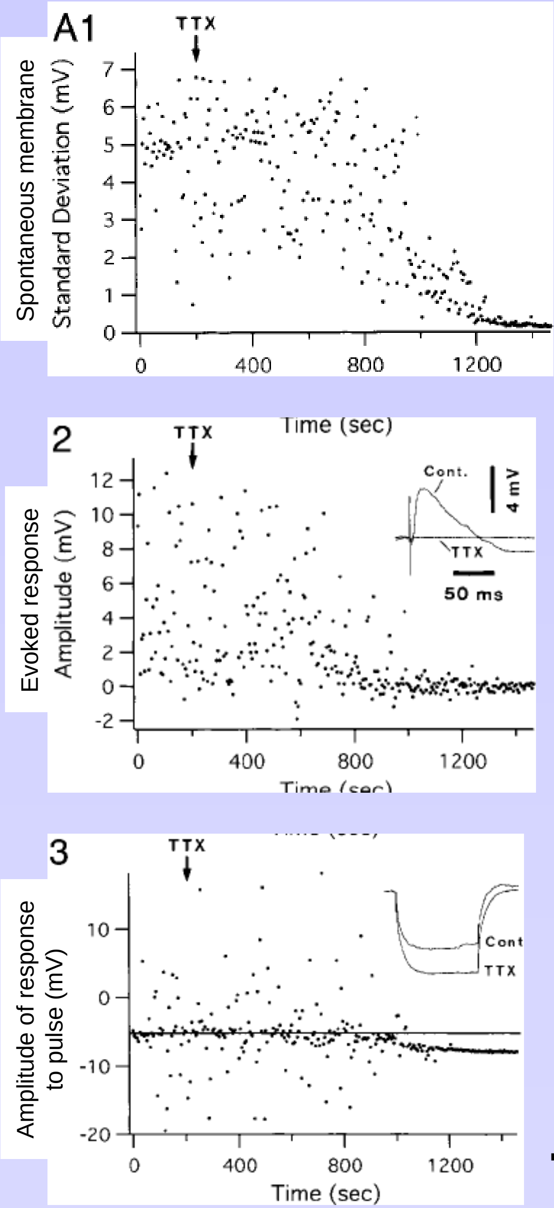
NMDA antagonist

$GABA_A$ agonist

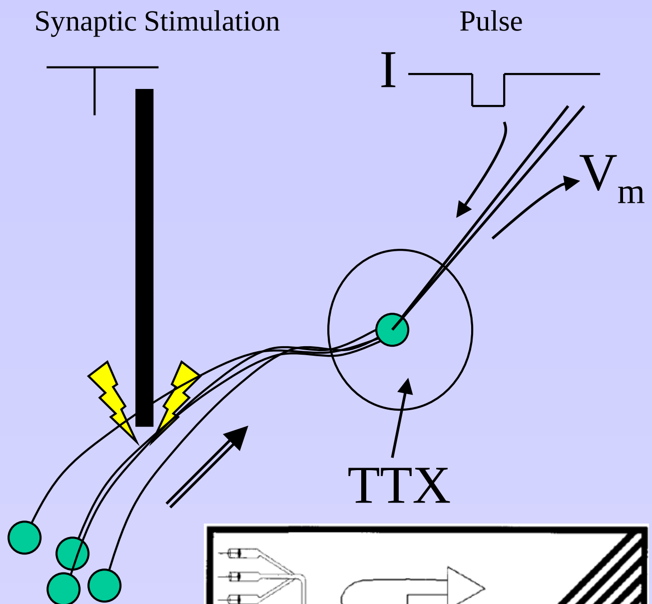
Noise is anesthetics dependent

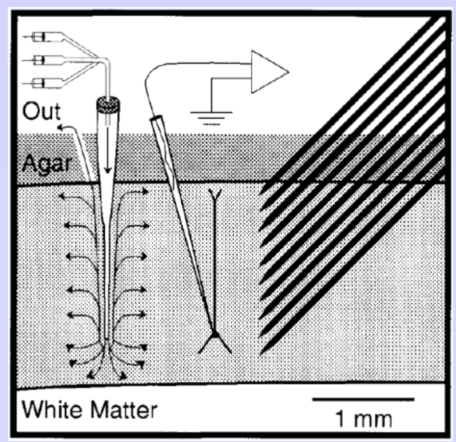
(hyperpolarized to better visualize spontaneous EPSPs)

The subthreshold effects of synaptic activity



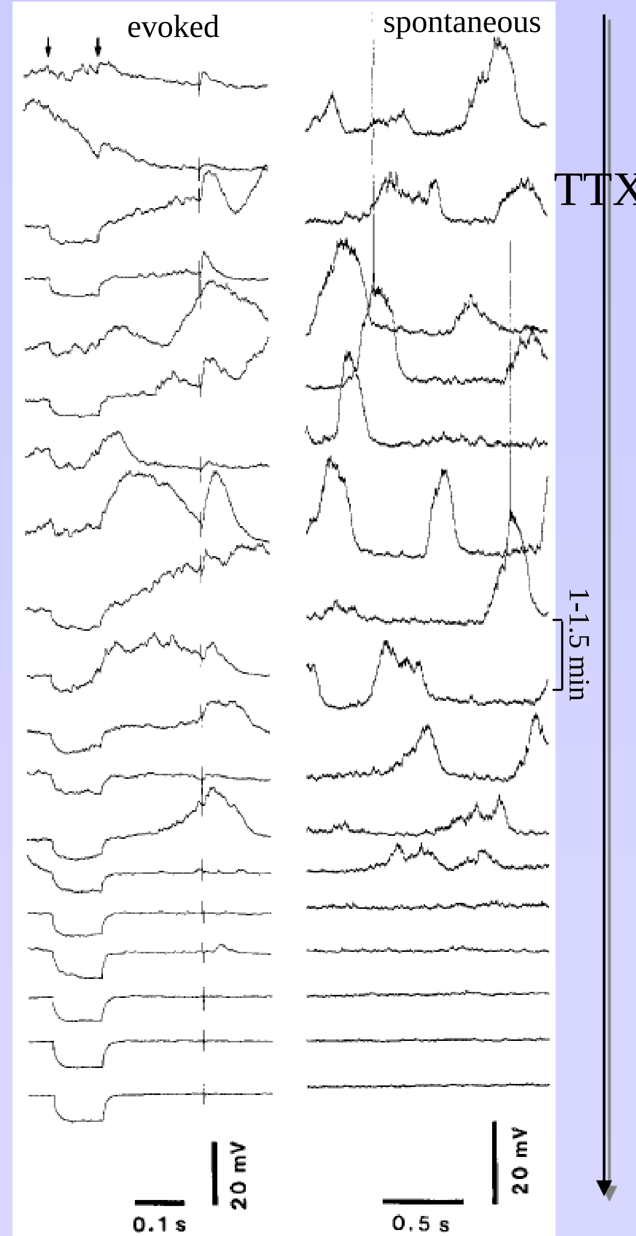
TTX= blocks synaptic transmission





$V_m = R_{in} I$

➔ Synaptic activity decreases Input Resistance



(Pare et. al. 1998)

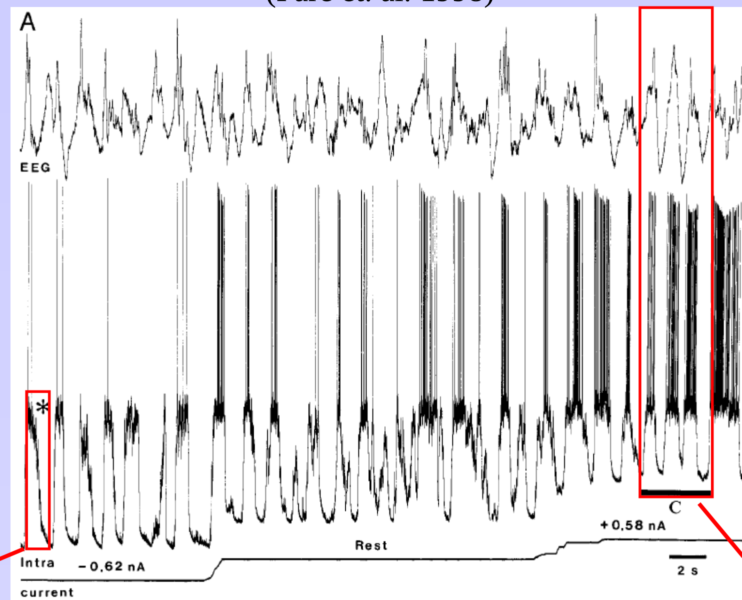
Burst-iness

Burstiness (in mammalian cortex) is (mostly) a network phenomenon: Analyses of simultaneously sampled EEG and spike recordings.

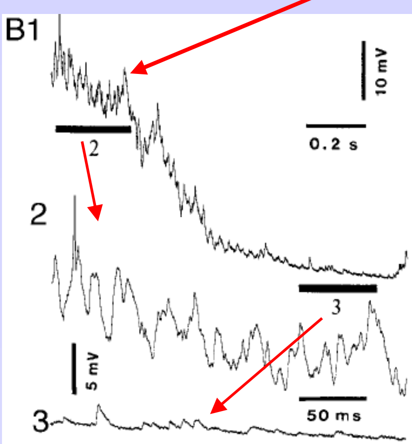
(Pare et. al. 1998)

EEG

Spikes

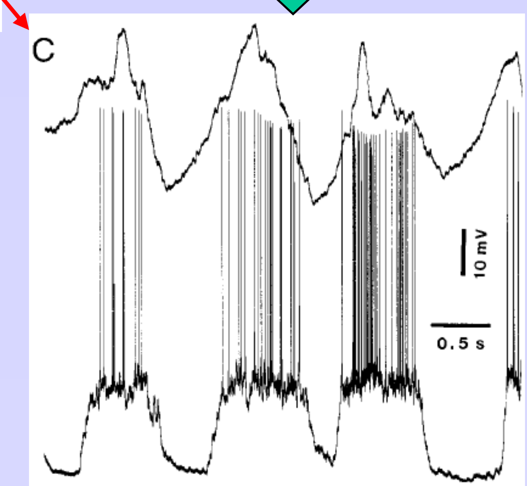


'up'/'down' states
'slow oscillations'



Study of a cell at different holding voltages:

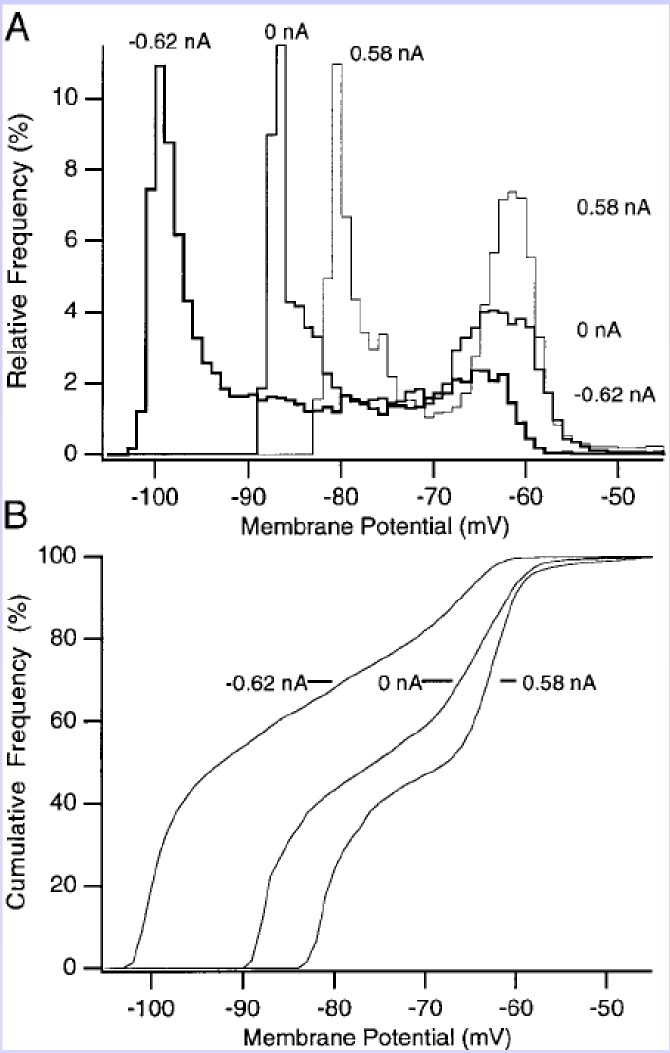
~Lower voltage (less GABA synaptic effects)
~Higher voltage (less AMPA synaptic effects)



Spontaneous Activity: **Histogram** of Membrane Potential

Is the standard deviation the best measure….?

Ketamine-Xylazine



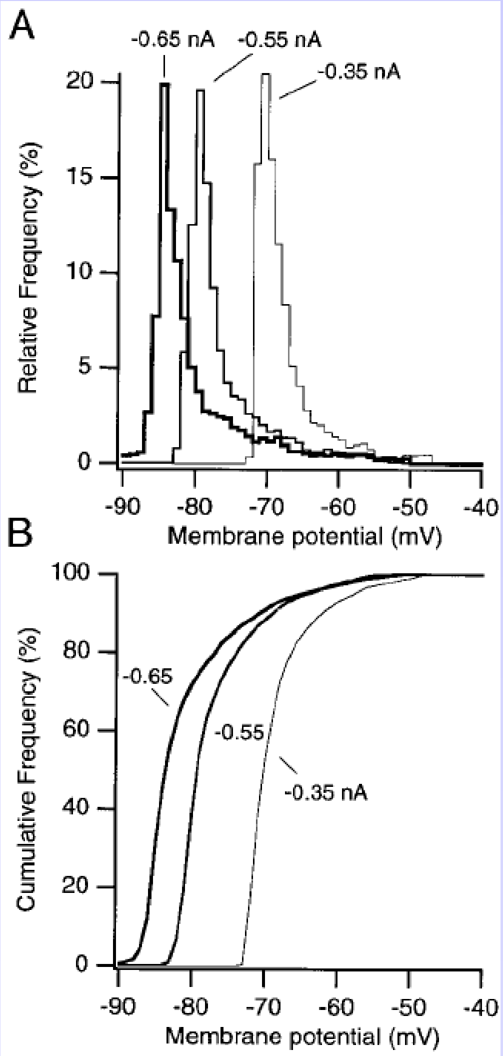
→ 'visualizing' *distribution* shape change

Distributions:

Relative
Vs
Cumulative

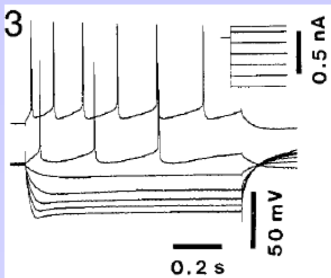
(Pare et. al. 1998)

Barbituate (pentobarbital)



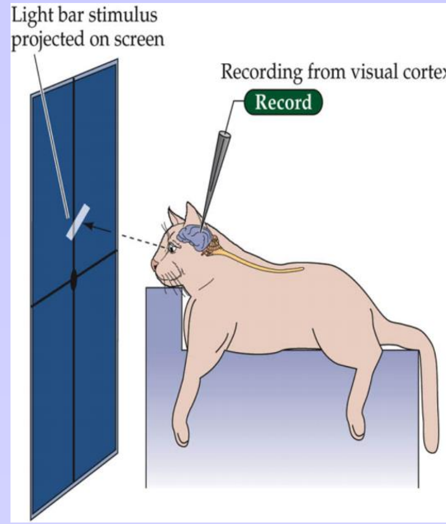
Quantifying Spontaneous **Spiking** Activity

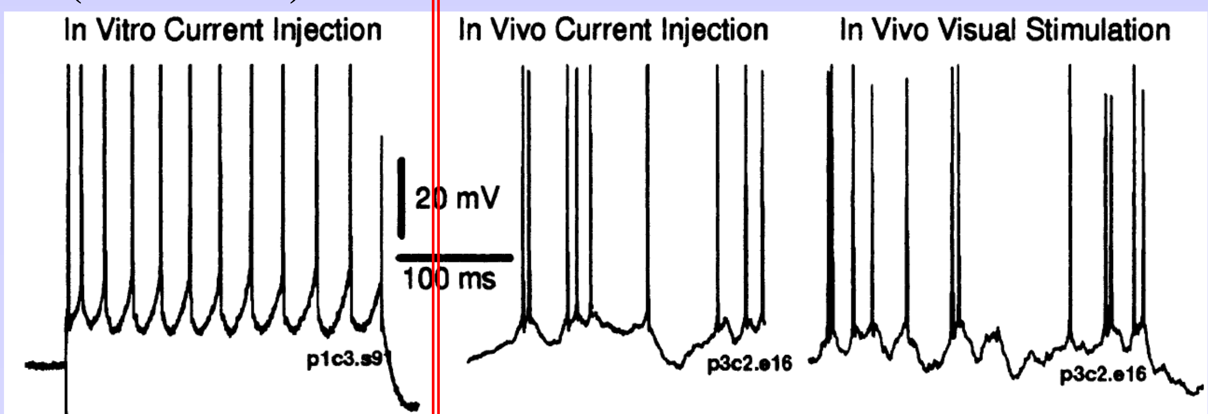
In vitro



(Pare et. al. 1998)

In vivo





(Holt et. al. 1996)

- Is there a number that can indicate whether a cell is firing regularly, randomly (single spikes) or randomly with bursts?

Coefficient of Variation of ISIs

$$CV = C_V = \frac{\sigma_{ISI}}{< ISI >}$$

$$\sigma_{ISI} = \sqrt{\frac{\sum_{i=1}^{N} (ISI_i - < ISI >)^2}{N}}$$

'true mean'

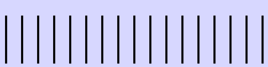
(note: biased Vs. **unbiased estimate of the variance**)

$$\sigma_{ISI} = \sqrt{\frac{\sum_{i=1}^{N} (ISI_i - < ISI >)^2}{N - 1}}$$

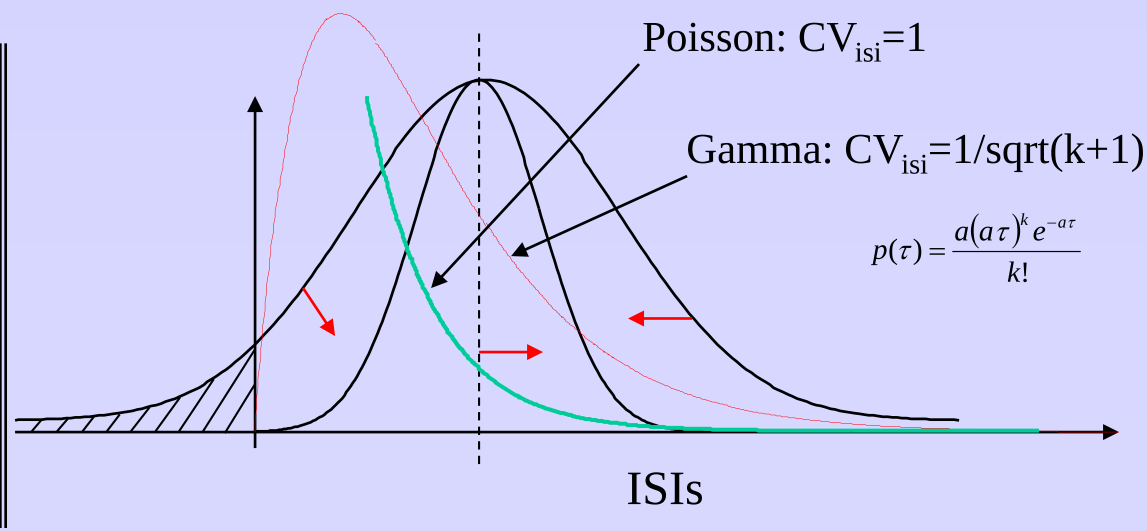
'sample mean'

CV=0

ISI_i=<ISI> →

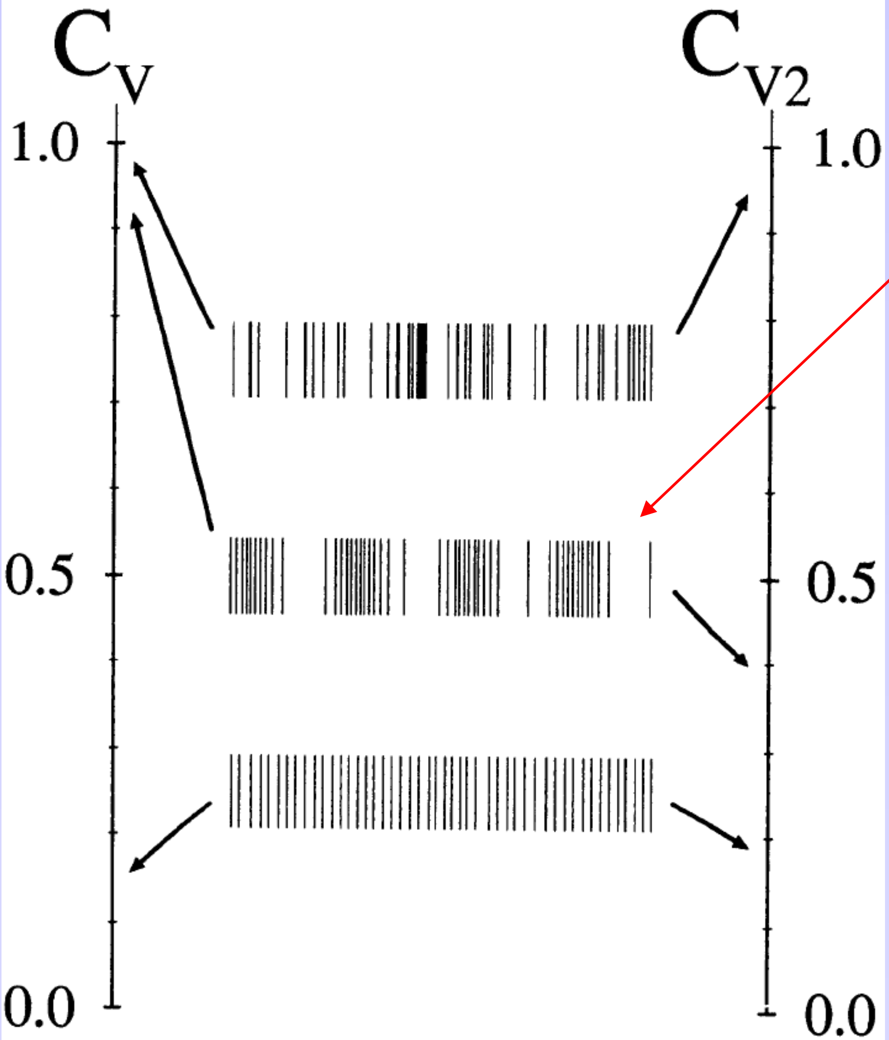


Oscillation



Coefficient of Variation of ISIs

- Is CV the best measure of variability/regularity?



(Holt et. al. 1996)

- The 'significance' of a variation should depend on the mean.
- Slow variations in firing rate should not 'count' as Poisson.

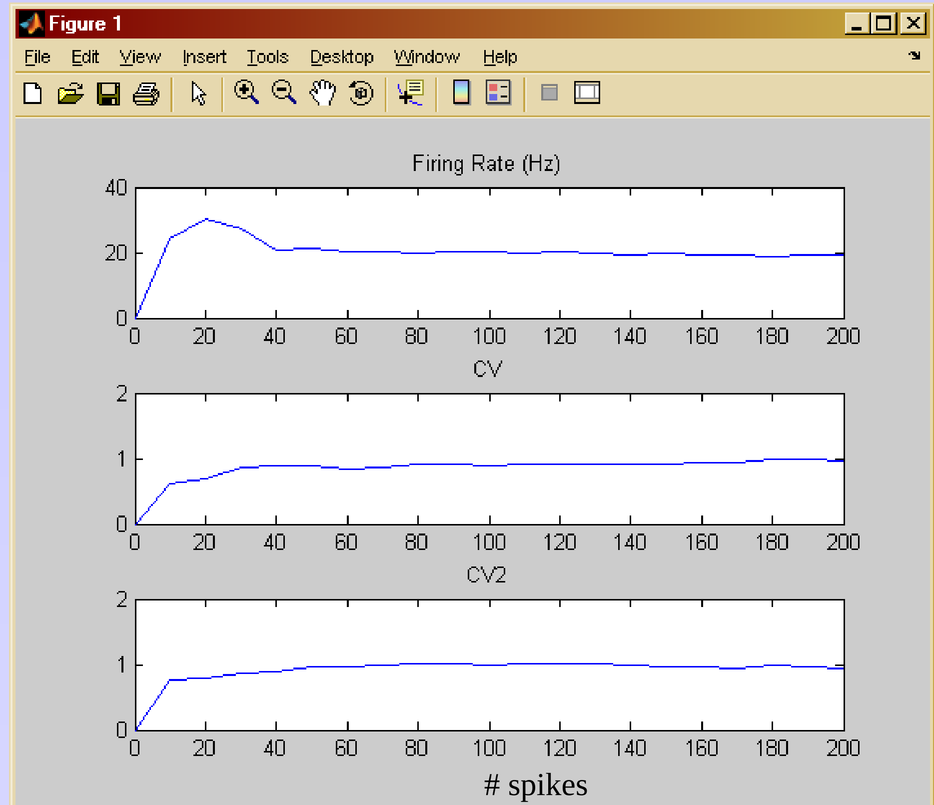
→ One possibility is to 'average' consecutive ISIs.

$$CV_2 = \frac{\sum_{i=1}^{N-1} \frac{2\left|ISI_{i+1} - ISI_i\right|}{ISI_{i+1} + ISI_i}}{N-1}$$

Coefficient of Variation of ISIs

-When do we know we have a meaningful firing rate, CV, CV2? ⬄ When do we know we have **enough data**?

- Cumulative statistics approach:



(example: 200 spikes of a 20Hz Poisson train)

Algorithm…..

```
Take the first n spikes
      compute/plot FR, CV, CV2
            append the next (p) spikes to the list
                  stop if curve is 'stable', otherwise
```

(p=10)

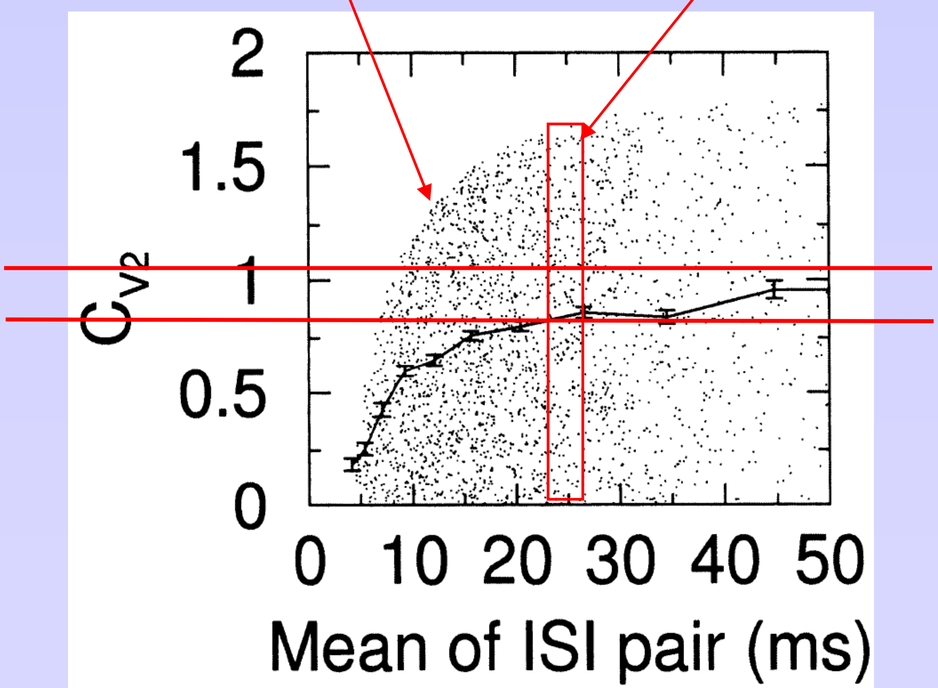
Coefficient of Variation of ISIs

- What is the shortest mean ISI that will be representative of the variability of the whole dataset? What is the time scale of variability?

- Part I: create and study a surrogate dataset

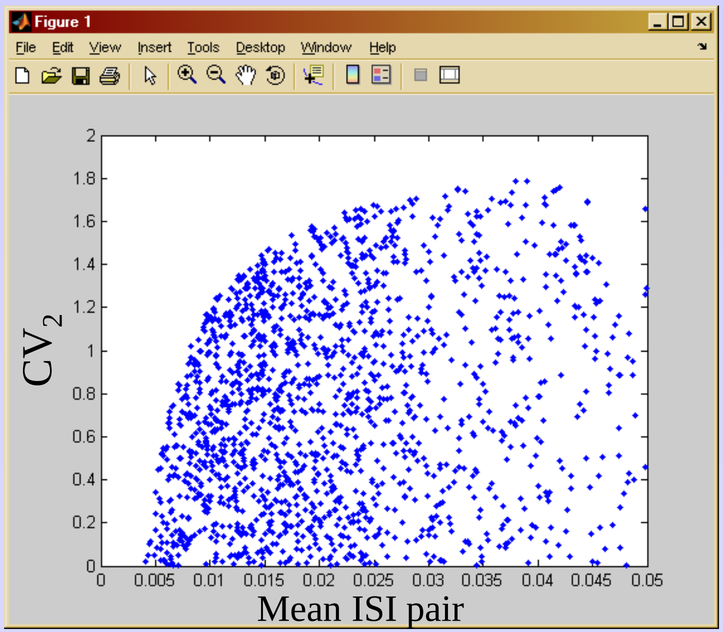
uniform distribution ➔ Poisson

Boundary fit by $2(1-t_r/x)$



(Holt et. al. 1996)

Is the data ‘truly’ random?



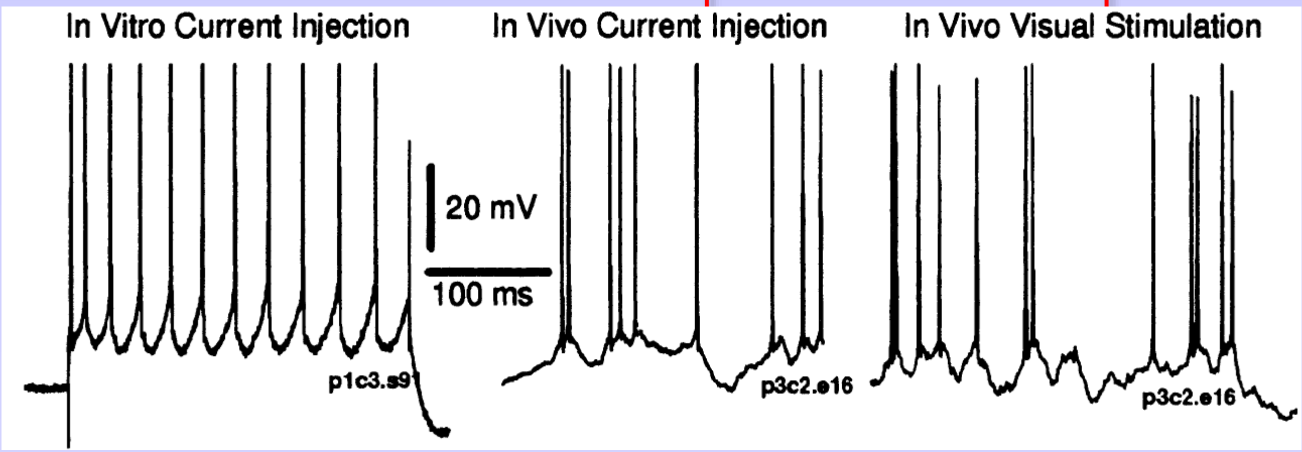
(2000 spikes, 50 Hz Poisson, 4ms refractory period)

t_r = refractory period

Coefficient of Variation of ISIs

- Part II: Compare surrogate set with data

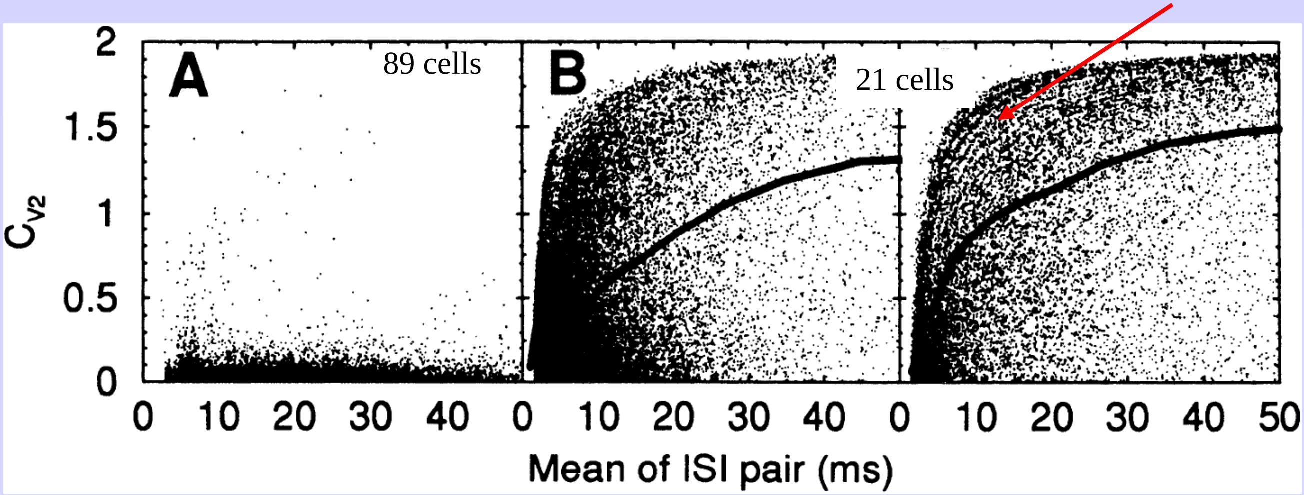
Same cell



(Holt et. al. 1996)

- No *apparent* differences between current injection and visual stimulation? same FR, CV, mean CV_2

Is this significant?

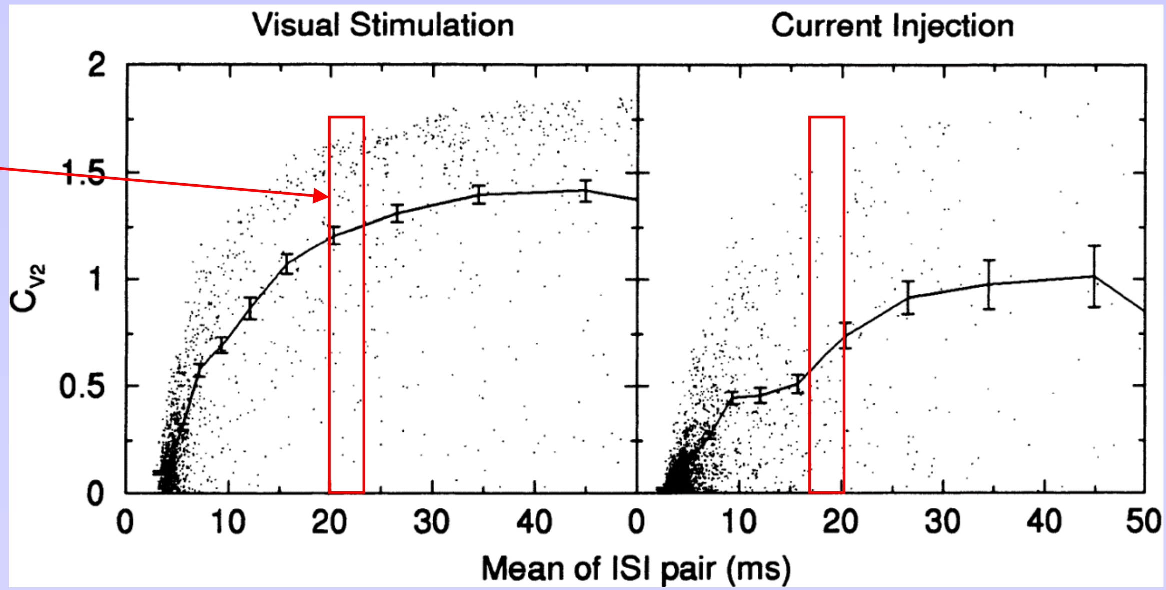


- Subtle (significant?) differences between CV_2 curves

Coefficient of Variation of ISIs

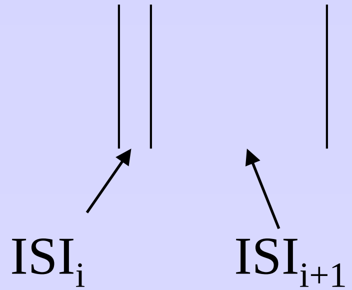
- Part III: Understand individual cases

Not uniform!



(Holt et. al. 1996)

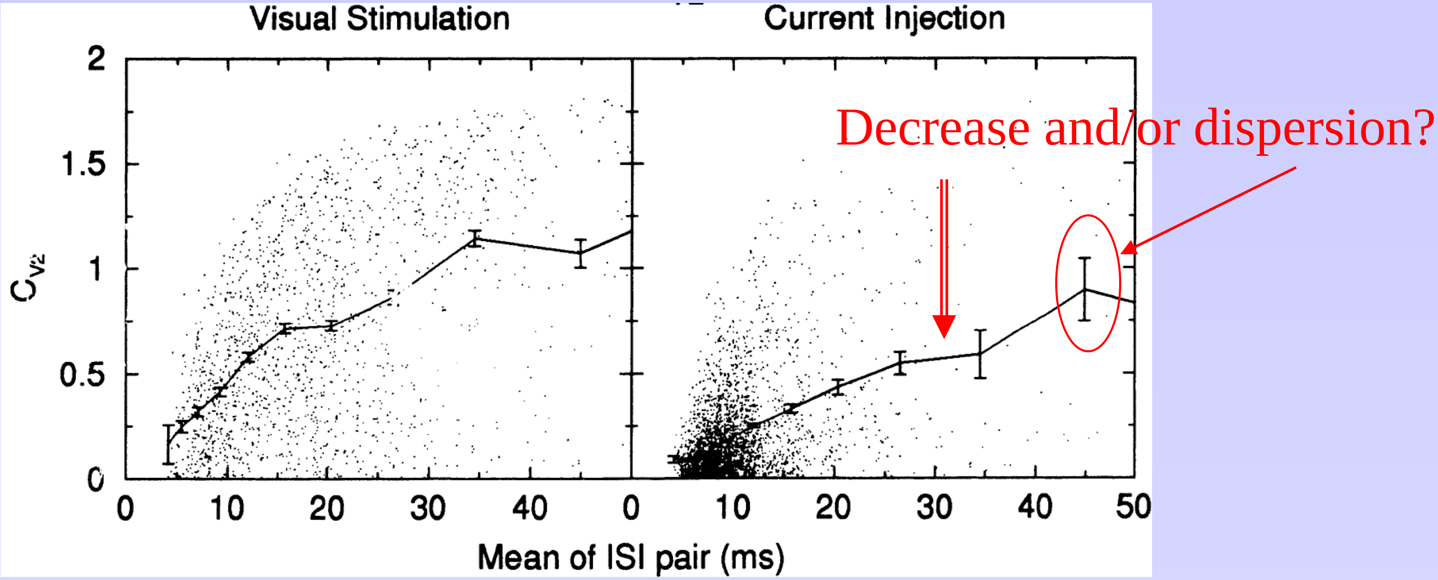
$$CV_2 = \frac{\sum_{i=1}^{N} \frac{2\left|ISI_{i+1} - ISI_i\right|}{ISI_{i+1} + ISI_i}}{N}$$



Bursty cell with visual stimulation, but not with current injection

Coefficient of Variation of ISIs

- Check…. Non bursty cell



(Holt et. al. 1996)

For cells that are not bursty, CV2 decrease during current injections (i.e. cells are more regular at short mean ISIs)

Coefficient of Variation of ISIs

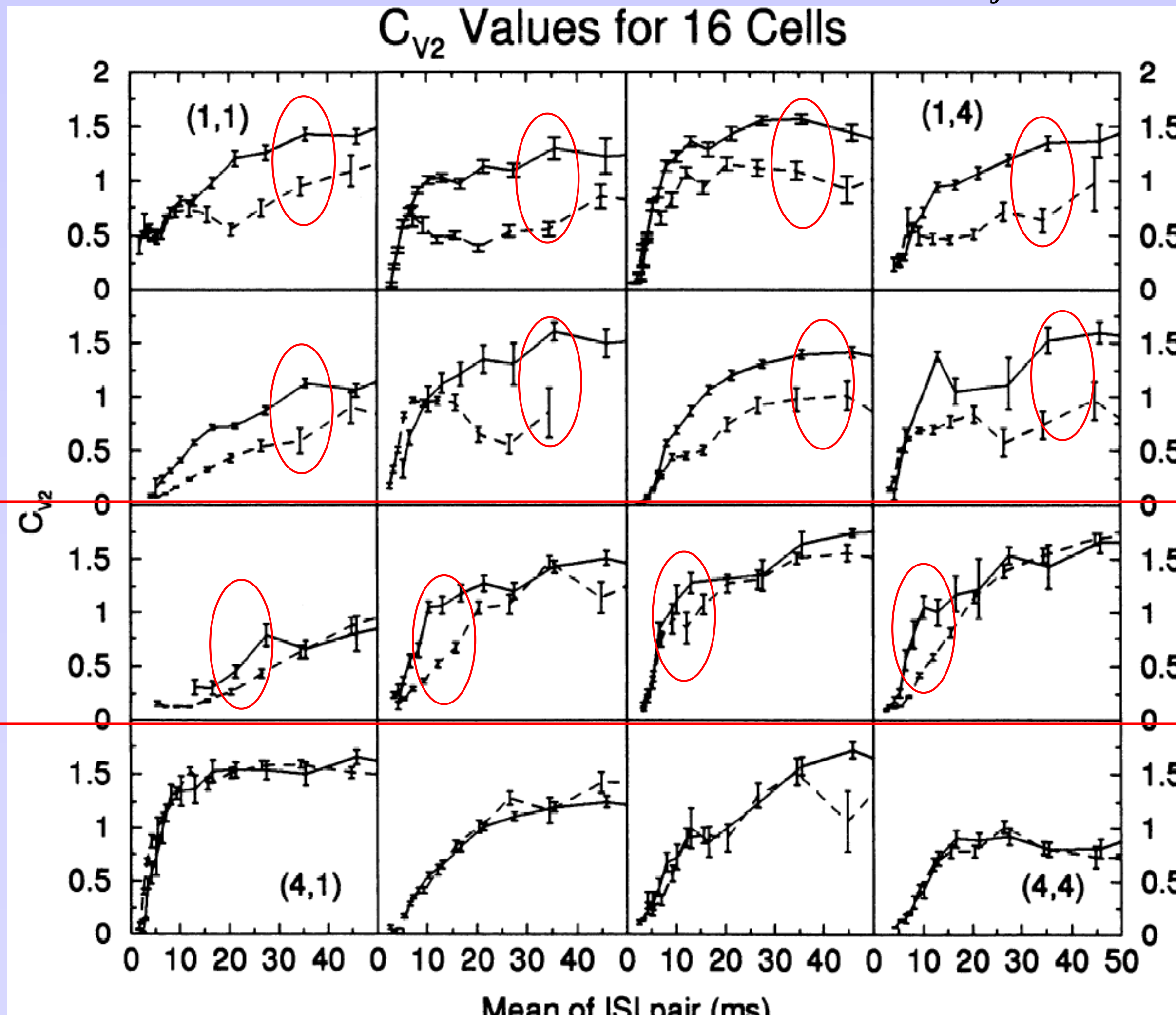
- Population analyses: What do the differences mean?

Visual stimulation ________
Current injection - - - - - - - -

Long ISIs
(more bursty during visual stimulation)

Short ISIs
(relative refractory period differences?)

Same

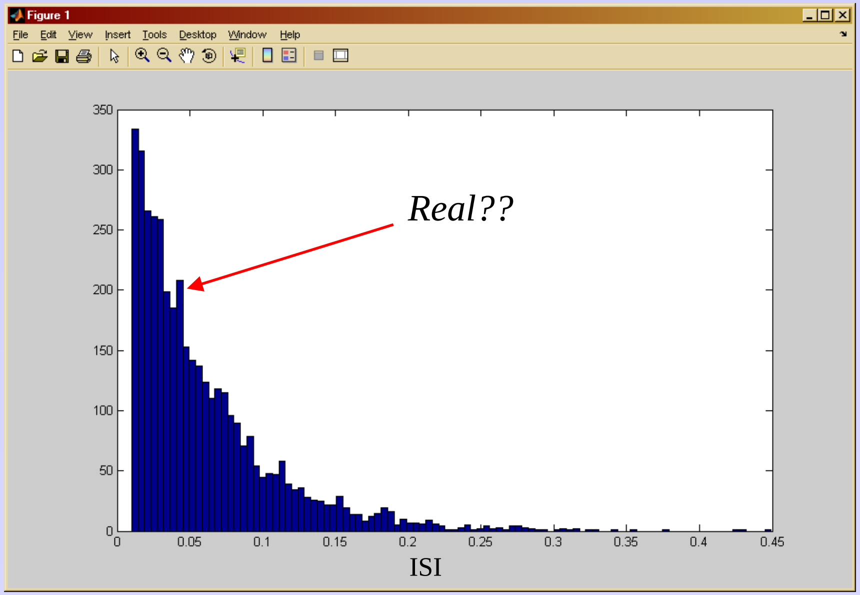


(Holt et. al. 1996)

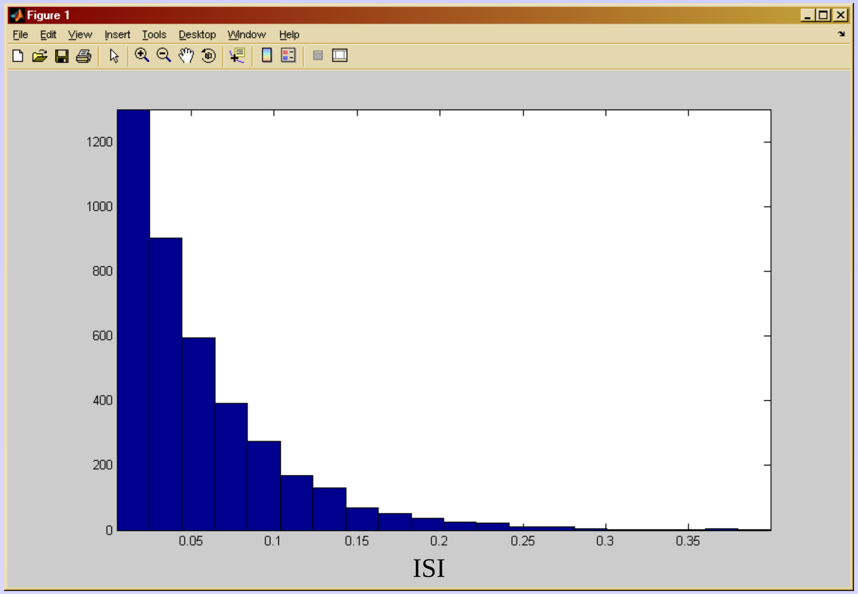
Distribution of ISIs

Side Note: Warning!: Beware of Binning artifacts…

binsize > Refractory_Period



10ms refractory period, 5ms bins



10ms refractory period, 25ms bins

More on this later….

ISI return map

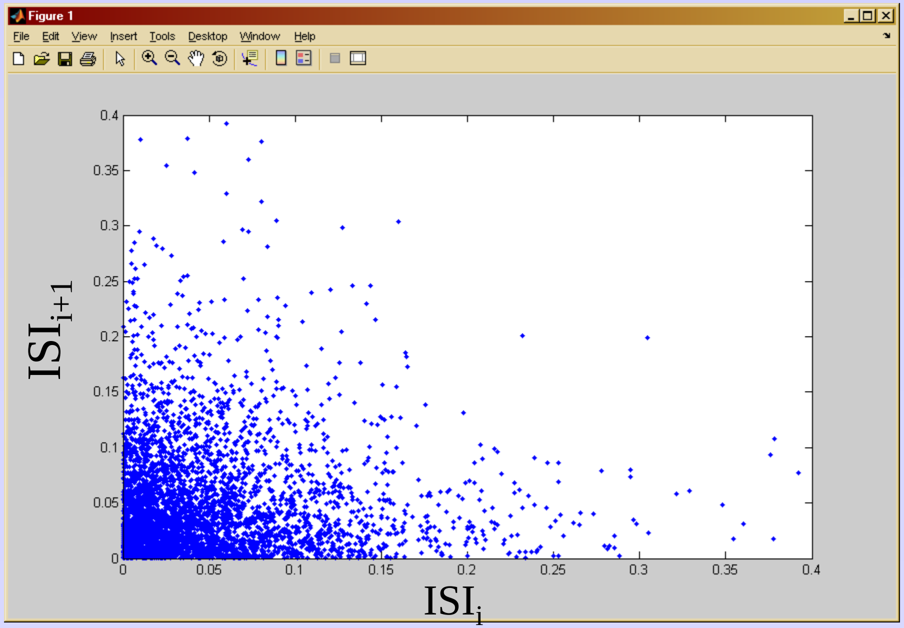
- FR, CV, CV_2 are 'overall' spike train measurements

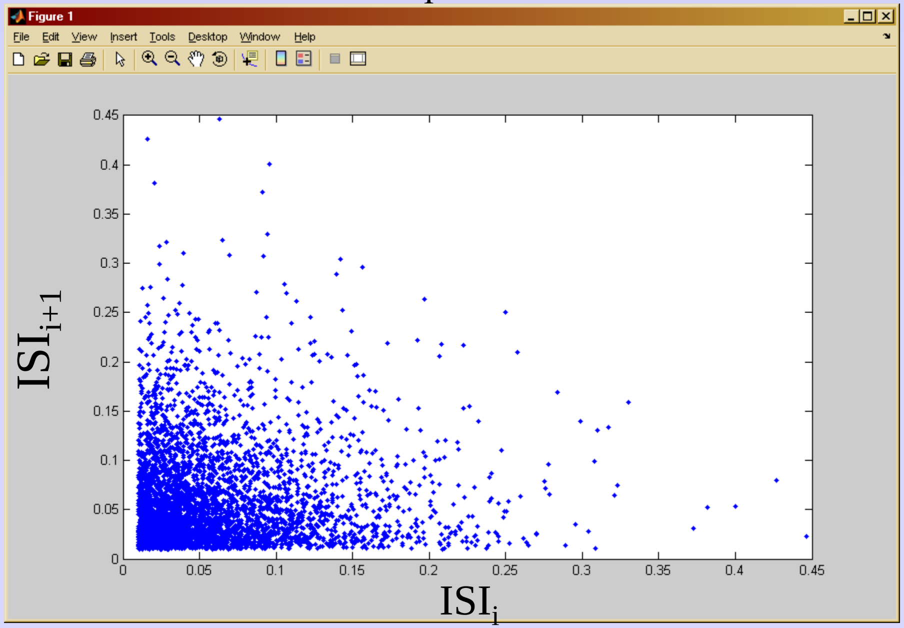
- Goal: Detecting irregular (i.e. not visible 'by eye') temporal structure in spike trains

Henri Poincare
(1854-1912)

➔ **Poincaré map – ISI return map**

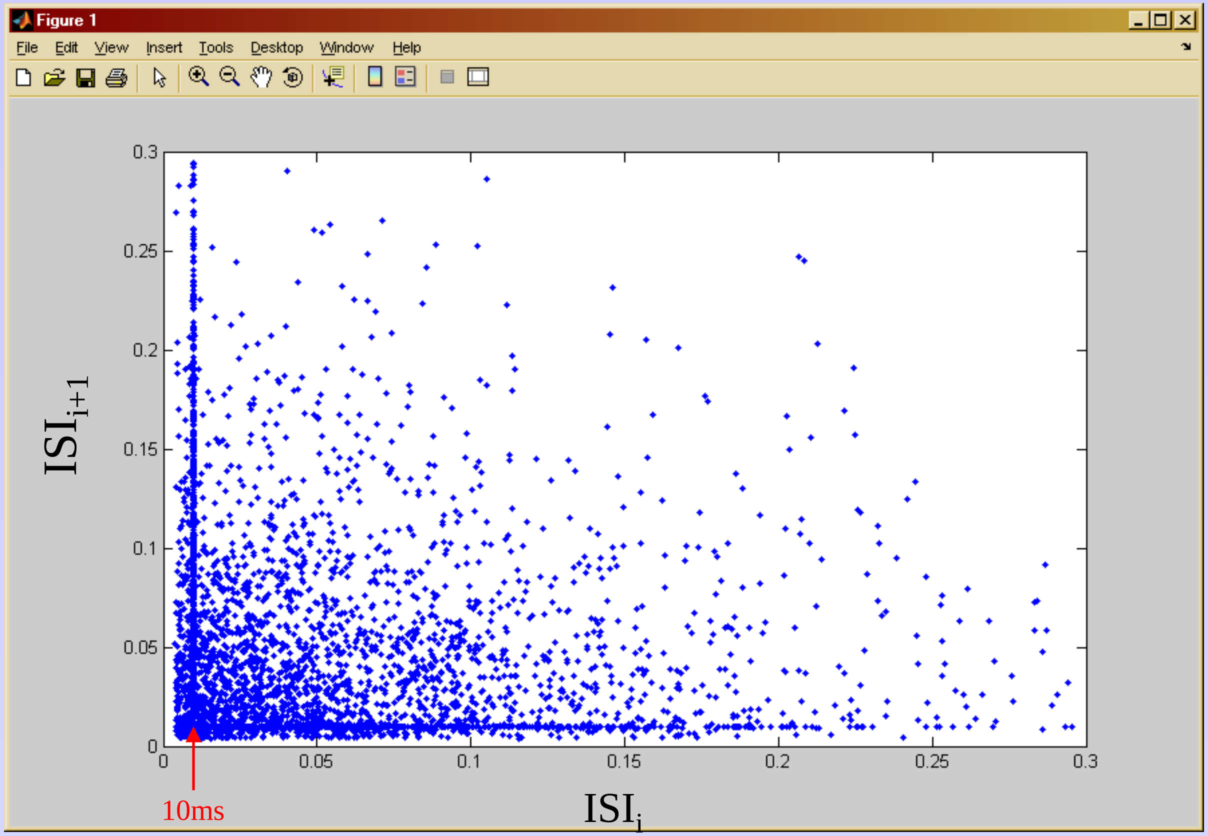
Find and interpret the difference….



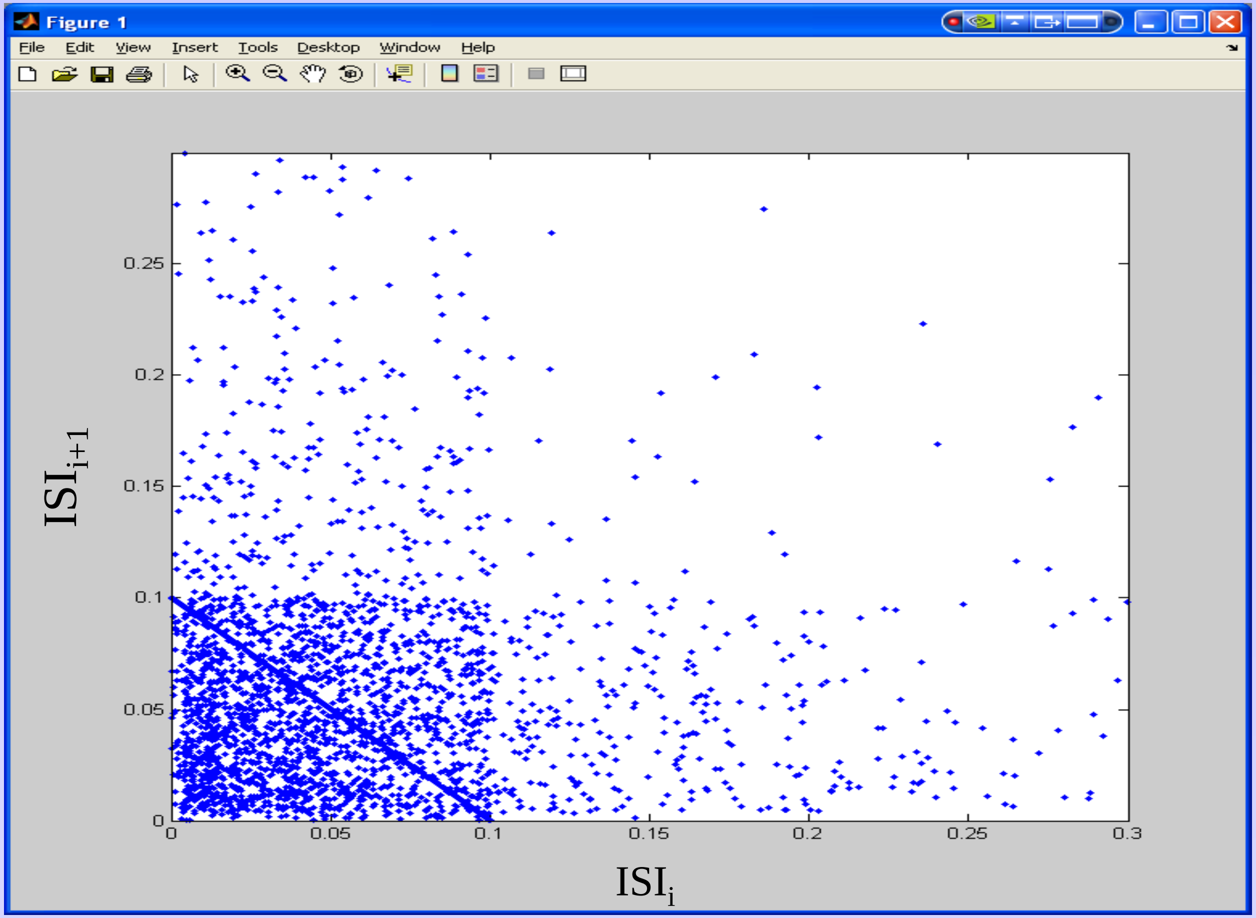


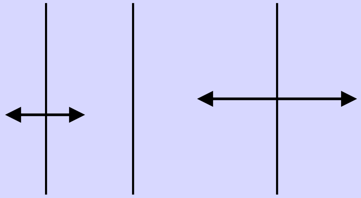
(20 Hz Poisson train)

ISI return map

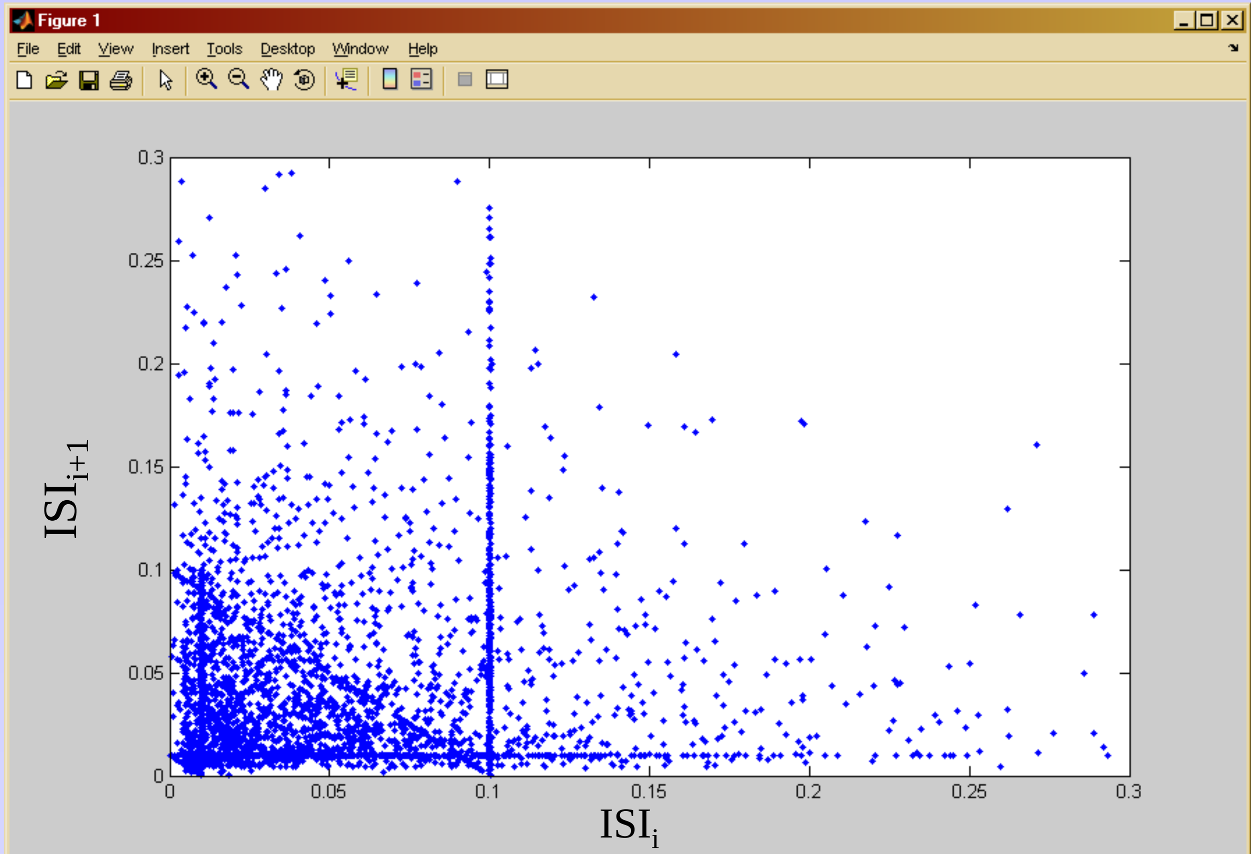


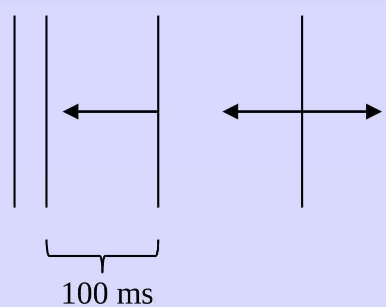
ISI return map





ISI return map

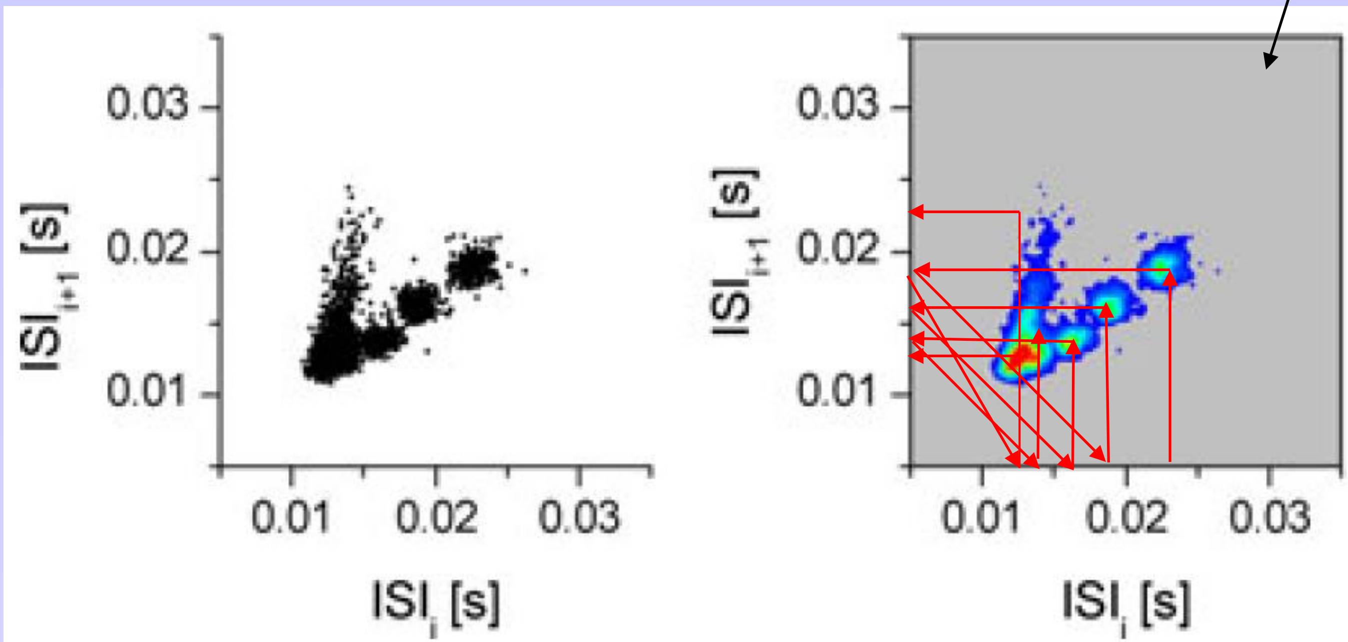




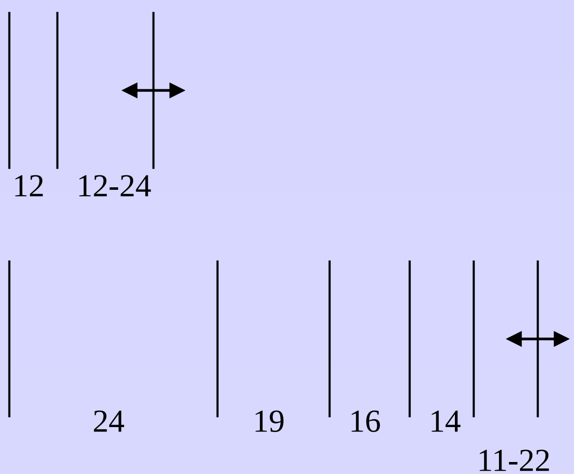
ISI return map… for real

Pyloric neuron lobster STG

Density plot



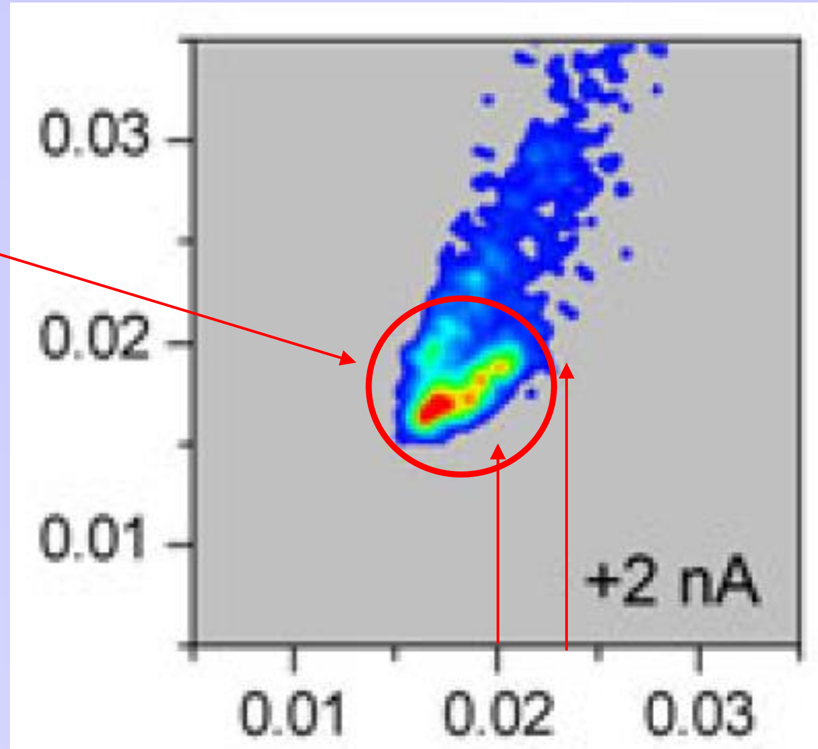
(Szucs et. al. 2005)



Two types of bursts

ISI return map… for real

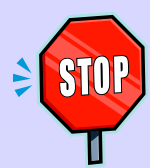
Attractor



(Szucs et. al. 2005)

20 16 16 …?...

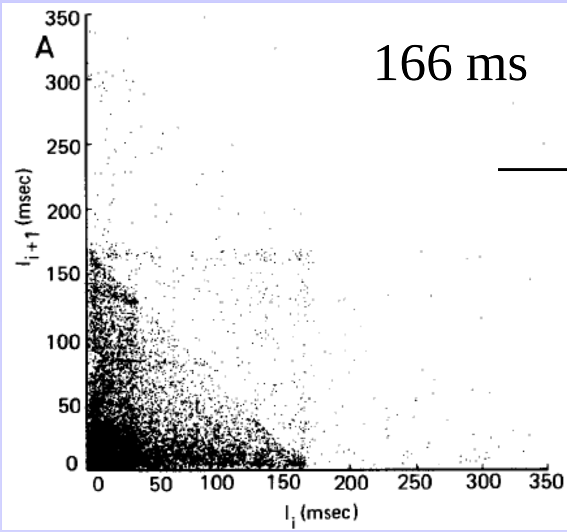
24 25 30

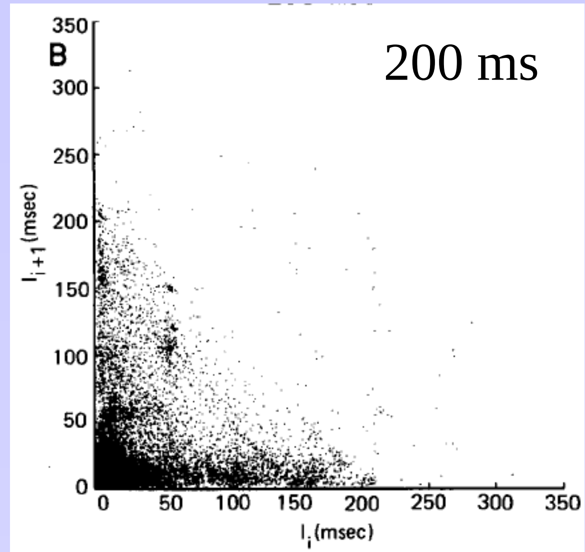


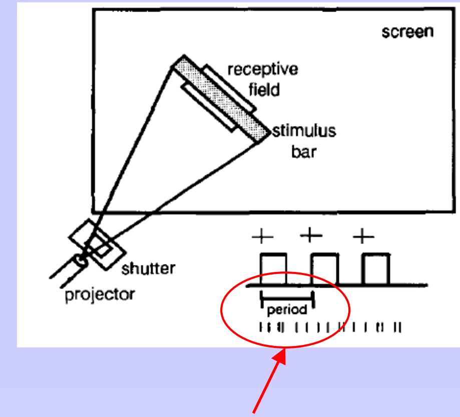
→ Two types of bursts

Other real ISI return maps

Stimulus-triggered Return Map

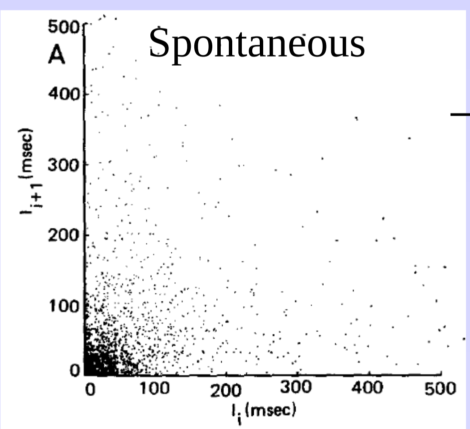


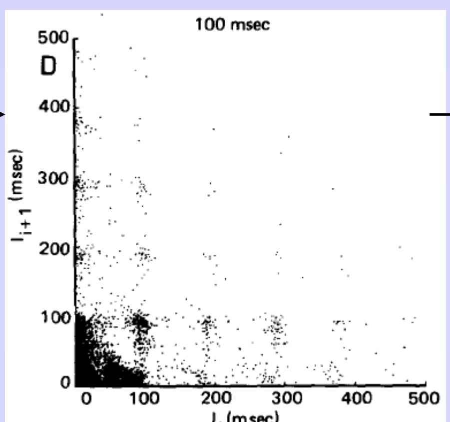


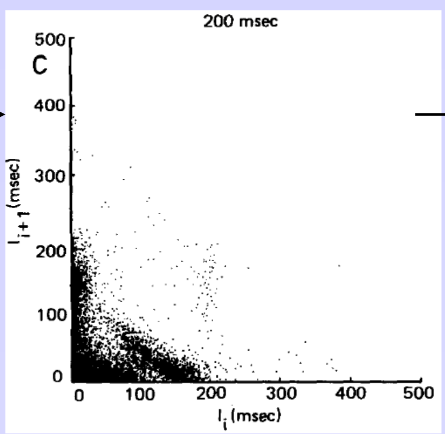


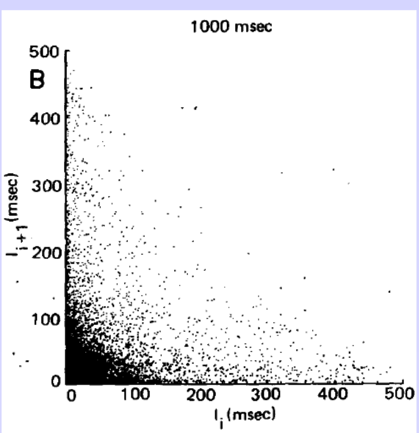
Stimulus period

(Siegel, 1990)









Fano Factor – a.k.a. 'index of dispersion'

Ugo Fano
(1912-2001)

- Measure the presence (and time scale) of intrinsic temporal correlations in a spike train.

- If one measures the distribution of the number of spikes occurring in T seconds (as a result of different experimental conditions for example):

$$FF(T) = \frac{\sigma^2(T)}{\mu(T)}$$

Variance of ISI in T

Mean of ISI in T

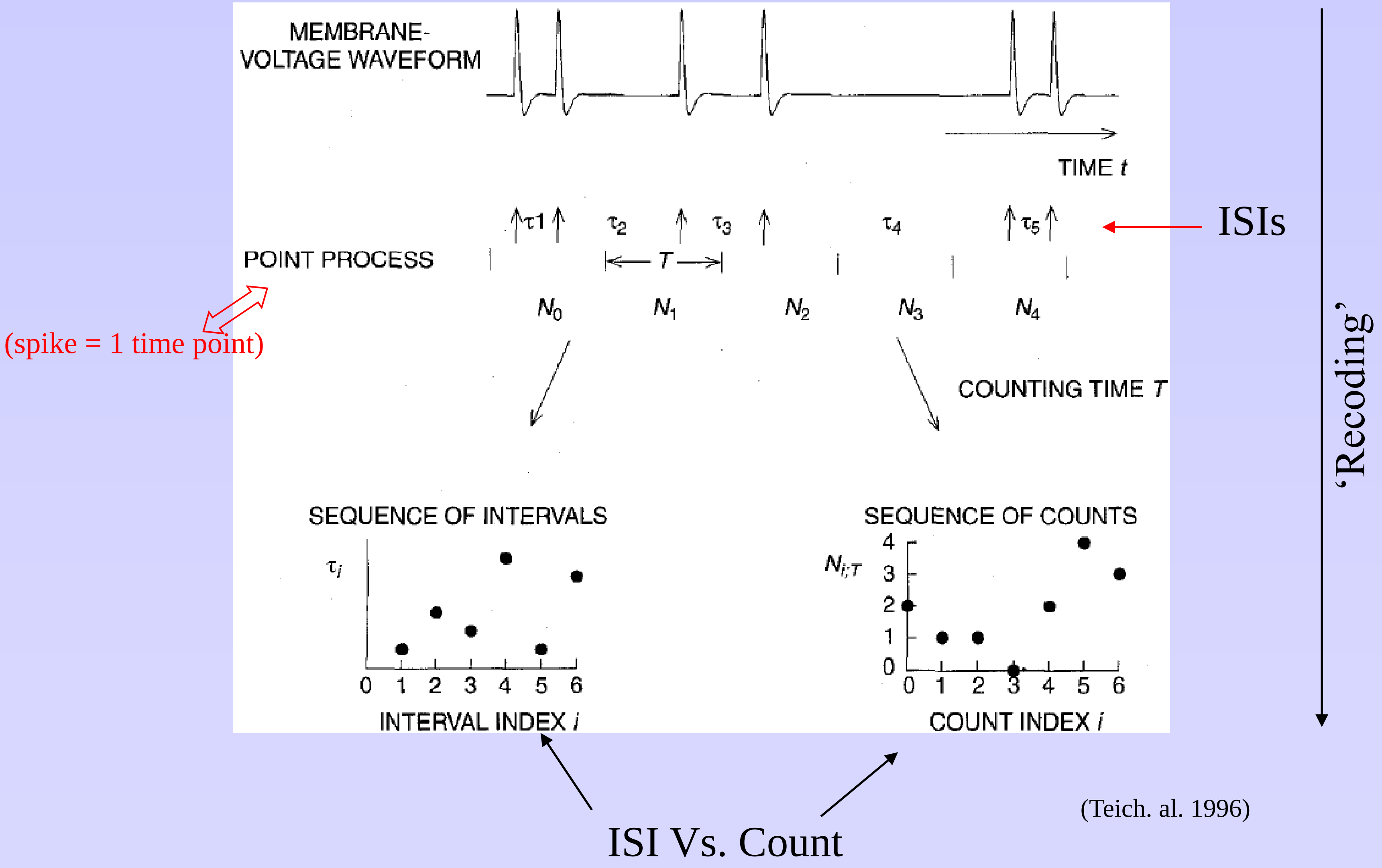
- For a Poisson distribution: FF(T)=1
- For a *renewal* process and large enough T

$$\mu(T) \cong \frac{T}{<ISI>} \qquad \sigma(T) \cong \sqrt{\frac{T\sigma_{ISI}^2}{<ISI>^3}}$$

$$FF(T) = \left(\frac{\sigma_{ISI}}{<ISI>}\right)^2 = CV_{ISI}{}^2$$

Fano Factor

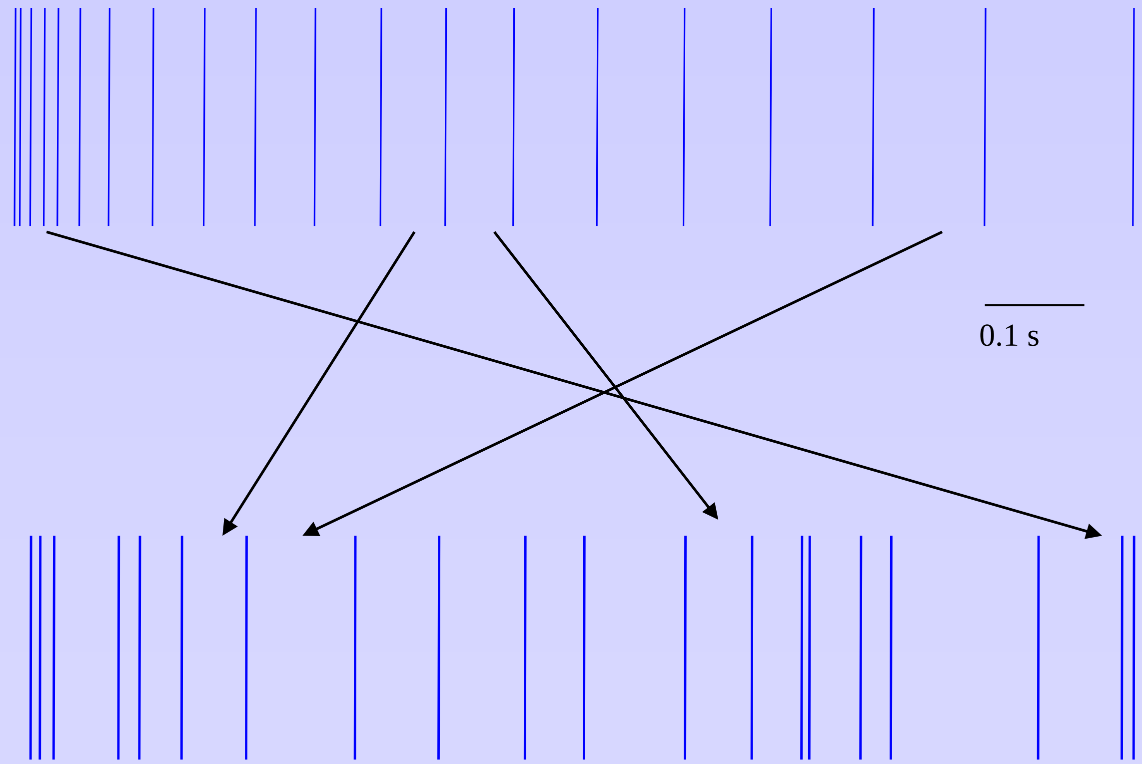
Fano factor uses spike counts, not ISIs



(Teich. al. 1996)

‘Cheap’ Surrogate Dataset: Shuffled ISI

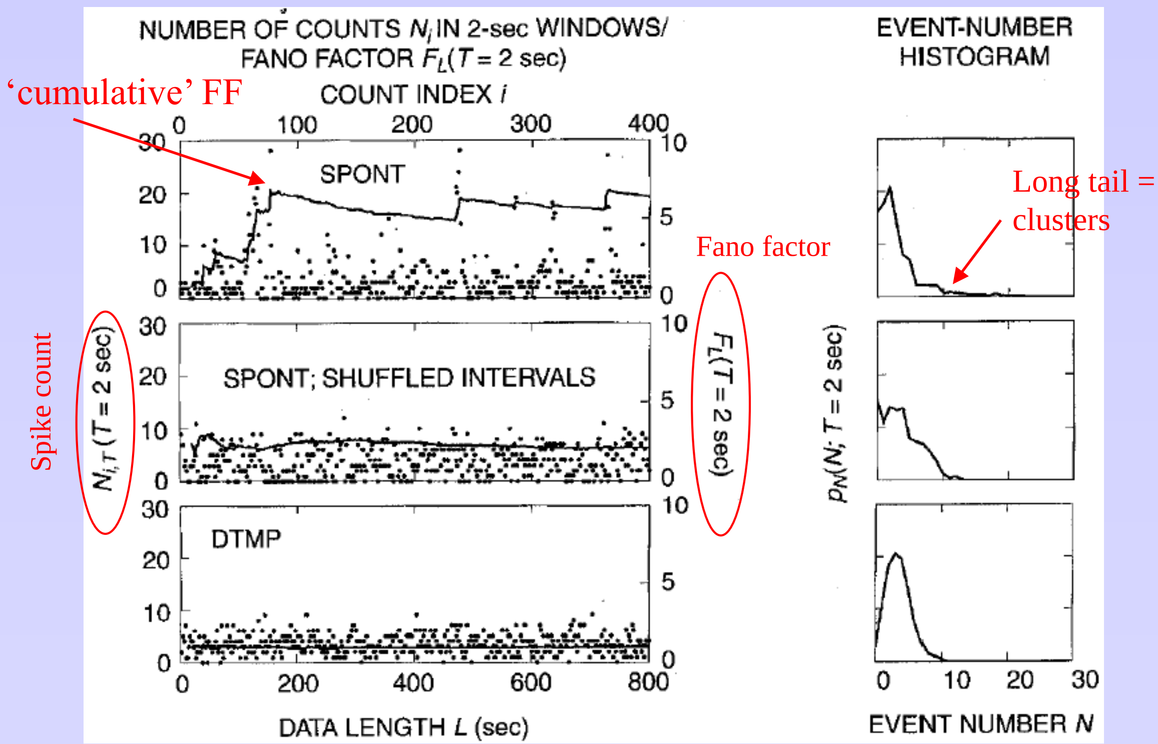
Shuffling does not change ISI distribution (Poisson ➔ Poisson)



Fano Factor

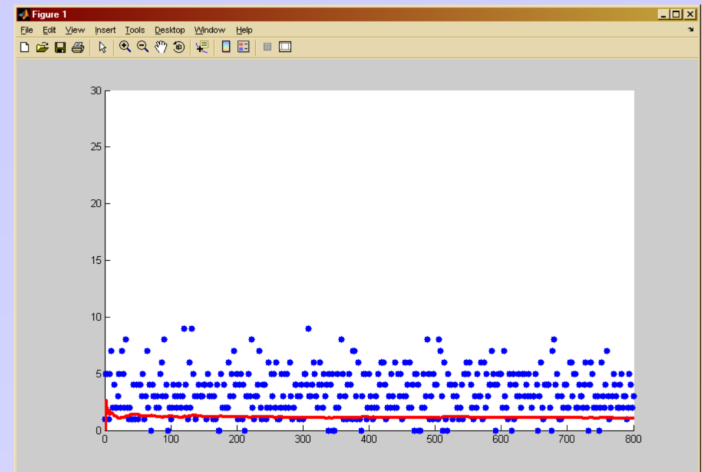
- Data (cat V1) Vs. Shuffled data Vs. Poisson: Testing significance

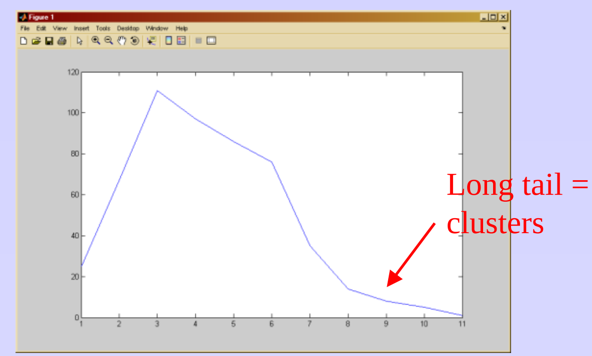
Spontaneous - T=2 sec



(Teich. al. 1996)

Simple (in vivo) Neuron Model



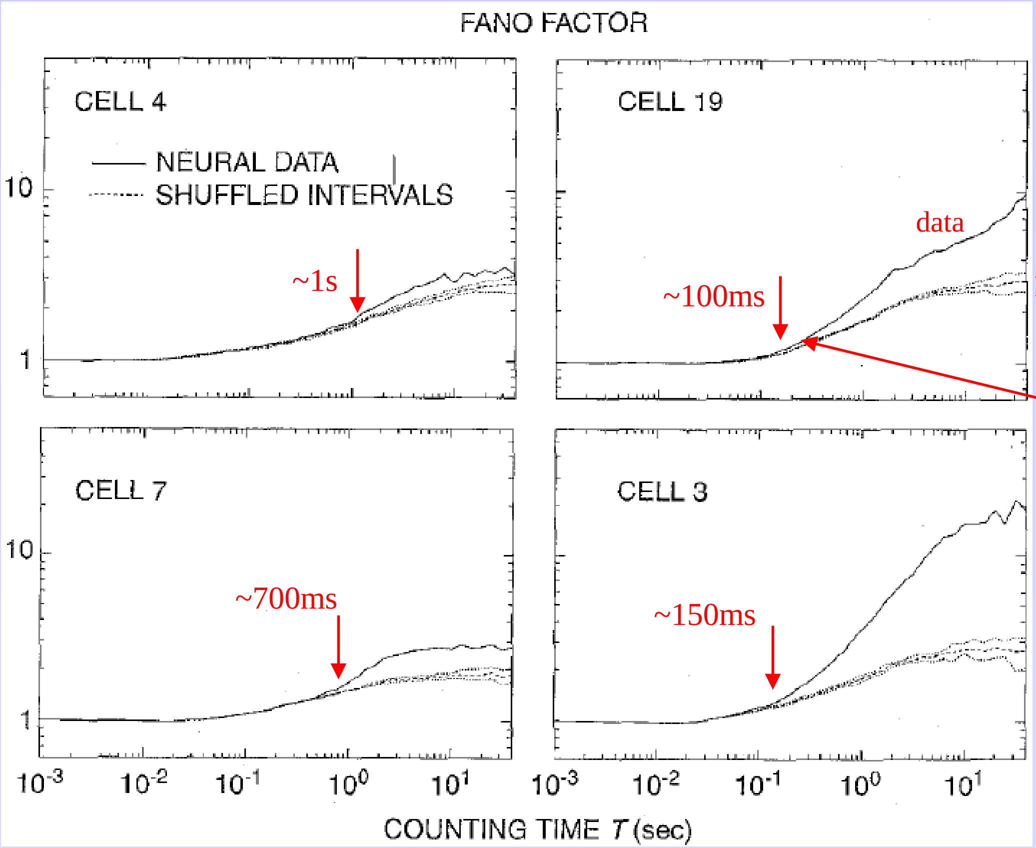


➔ FF jumps when spikes cluster, or when spikes ‘de-cluster’

Fano Factor

- Because FF depends on T, one can study the statistics of the spontaneous activity at *specific* time scales.
- Use of shuffled ISIs as a surrogate dataset.

Spontaneous activity

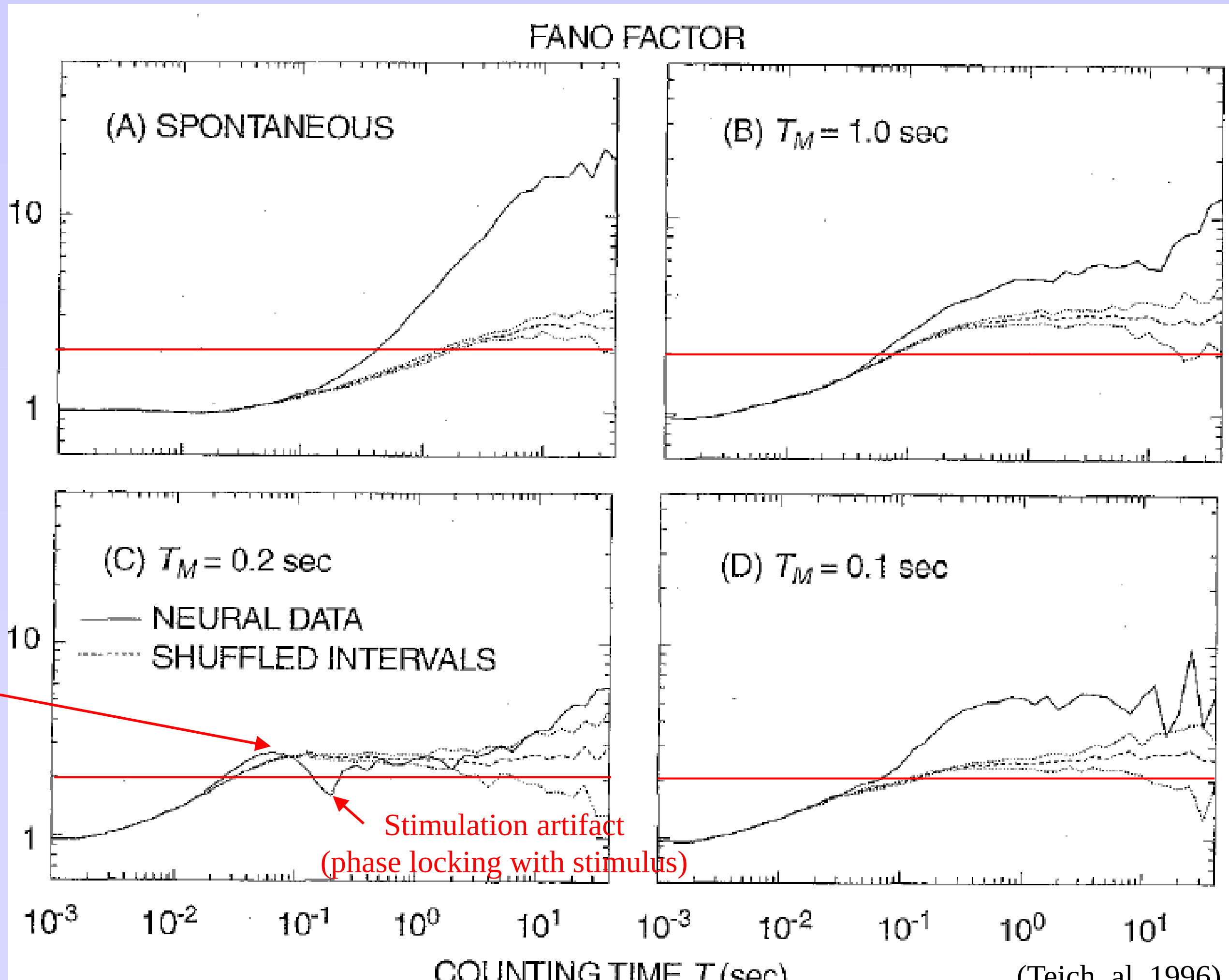


Presence of temporal correlations at this particular time scale

(Teich. al. 1996)

Fano Factor

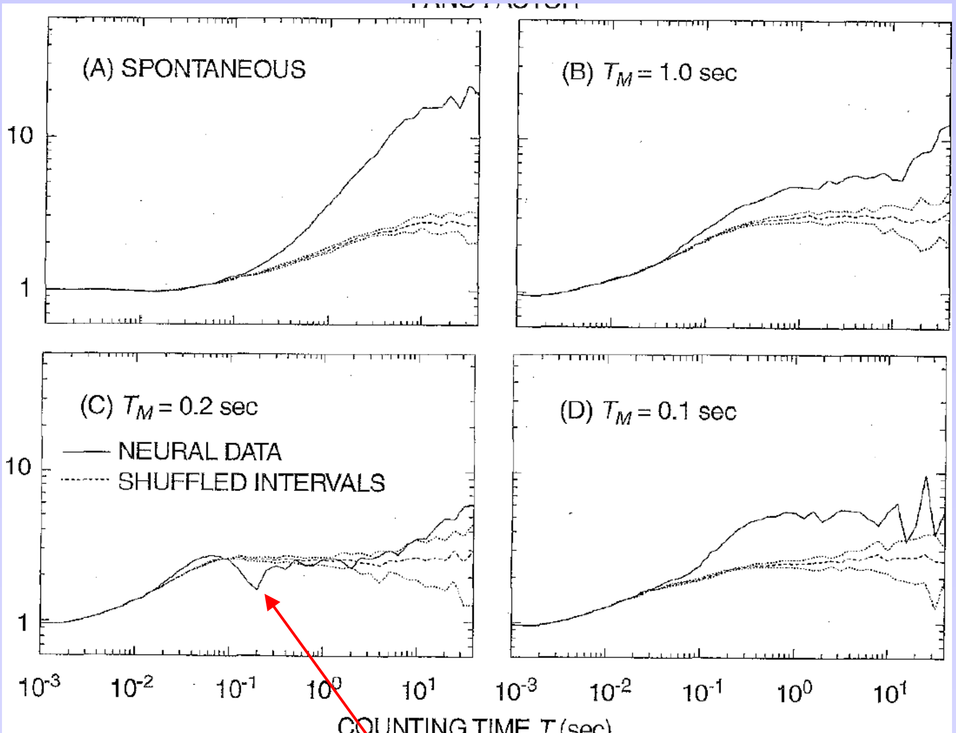
- Fano factor during visual stimulation at 1 Hz, 5 Hz and 10 Hz
- FF > 2 ⬄ CV > 1.4 … Presence of 'clustering' in spike train



Optimum
(~40 Hz)

Fano Factor

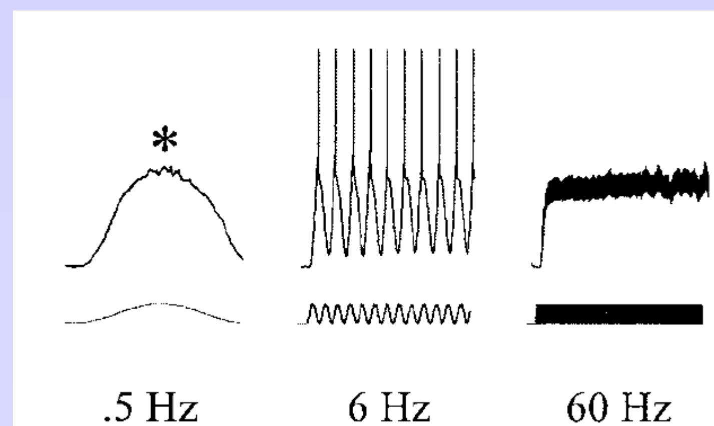
- Allows for the uncovering of frequency/time scale preferences



(Teich et al. 1996)

Entrainment

Resonant frequency

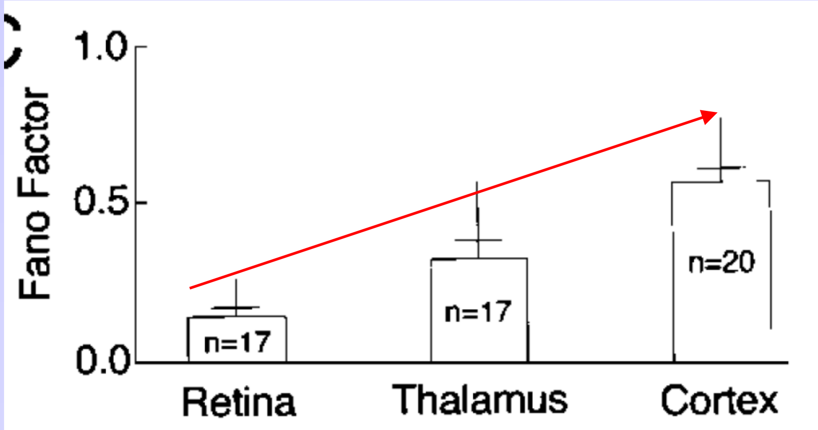


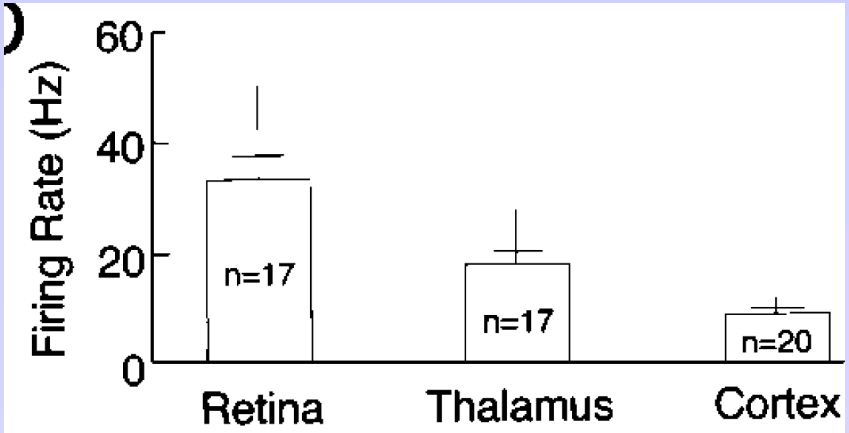
(Fellous et al. 2001)

Fano Factor

- Measuring the variability of neural responses to the same stimuli, **across multiple brain areas**

Simultaneous recordings in anesthetized cat: retina, LGN, V1





(Kara et al. 2000)

➔ Activity is less and less regular from sensation to perception

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Homework 2 – due Next week

- Q1: Using the simpleneuron model: Record the membrane potential (type ‘*RecordMEMPOT(0)*’). Run the model for 10 seconds (spontaneous activity). Use *SaveMEMPOT()* to save the voltage values of the simulation.
> Compute the mean and standard deviation of the membrane potential and compare with (Pare et.al. 1998).

- Q2: Write a routine that takes a spike train and returns the firing rate, the CV and the CV2.

- Q3: Increase the level of noise of the model (in the shell, type ‘*neurs[0].noise.g_e0=0.02*’). Record the action potentials of neuron 0 (type ‘*RecordAP(0)*’).
Run the Neuron model for 150 seconds (spontaneous activity). Use SaveAP() to save the times of the action potentials.
> Compute the cumulative firing rate, CV and CV2. Plot the CV2 Vs mean ISI (see Holt et al. 1996, fig 2). What do you see?

- Q4 (optional):
Generate 2000 spikes Poisson distributed at 20 Hz with a 4 ms absolute refractory period.
> Modify the spike train to produce as ‘**strange**’ of a return map as possible. Plot the return map and a sample of the spike train. Make sure to explain the features of the map, and how they relate to the modifications you introduced.