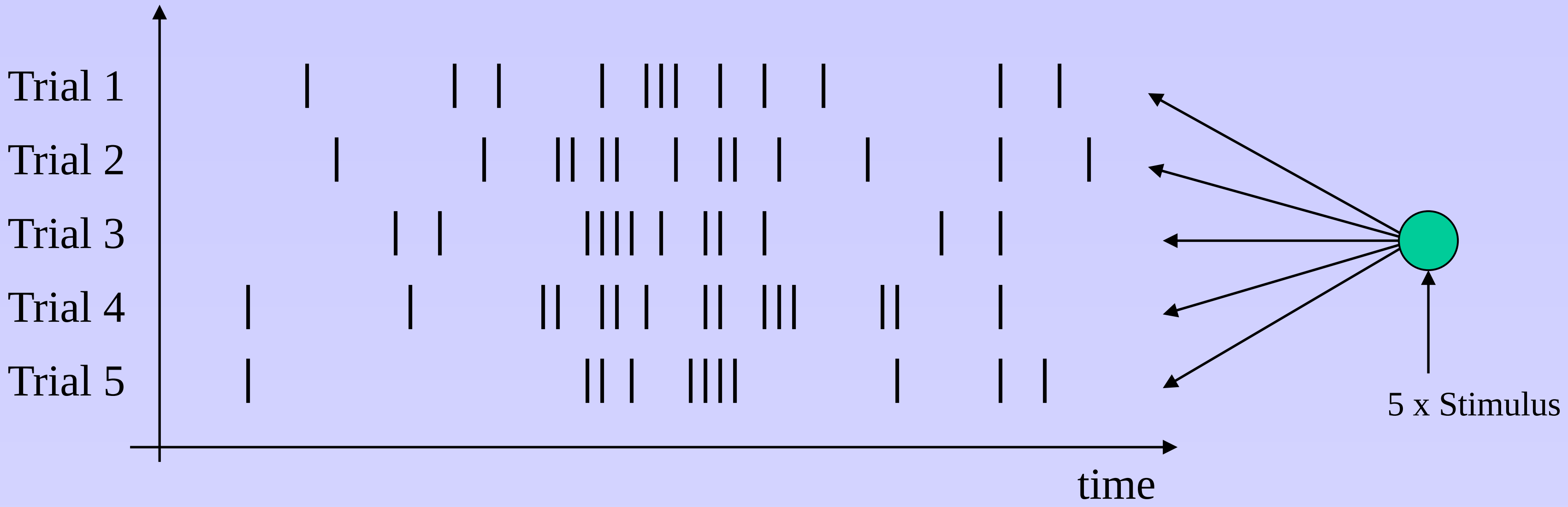
Unit 7

Spike Timing
Spike Patterns

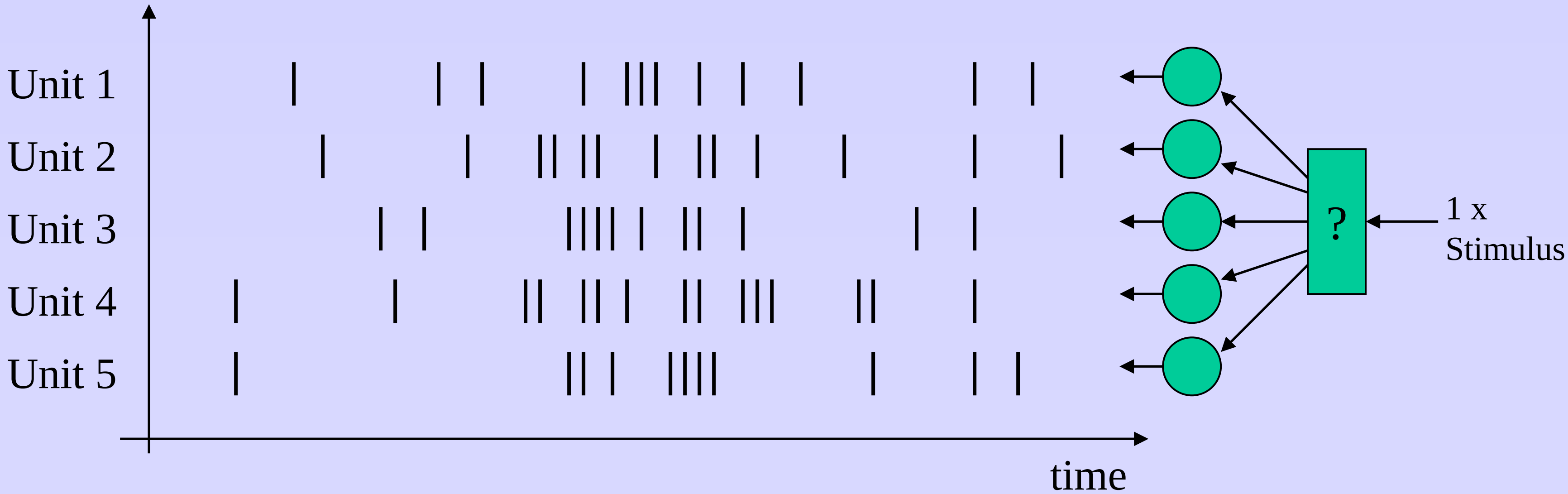
Midterm next week. Take Home (at least in part).

Spike timing

- What is the 'neural code' ?

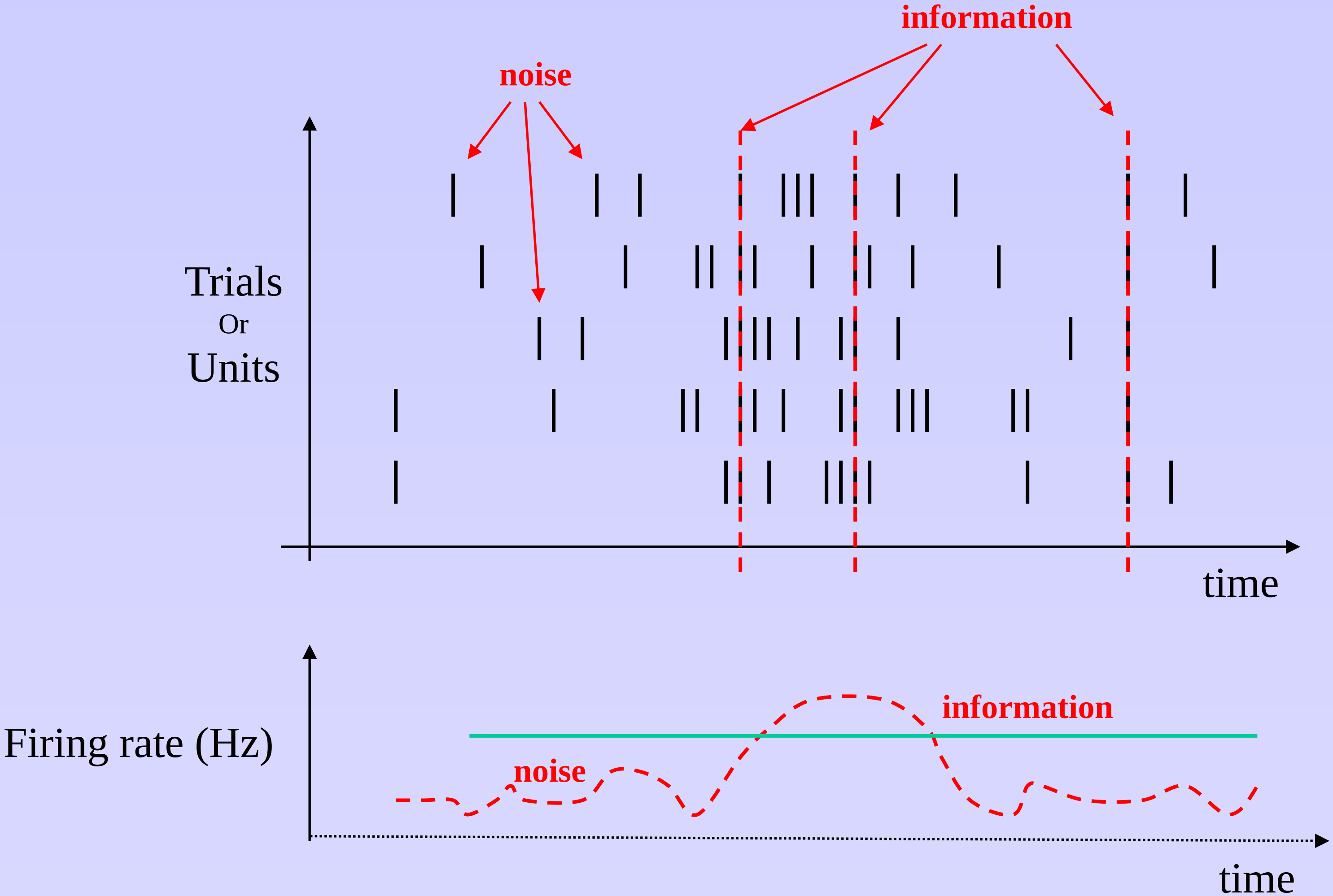


OR



Spike timing

- Two ‘competing’ theories: Rate Vs. Temporal code



(Kumar et al, 2010; Ainsworth et al, 2012)

Spike timing

- Why would one need precise spike timing ?... Elicit a spike

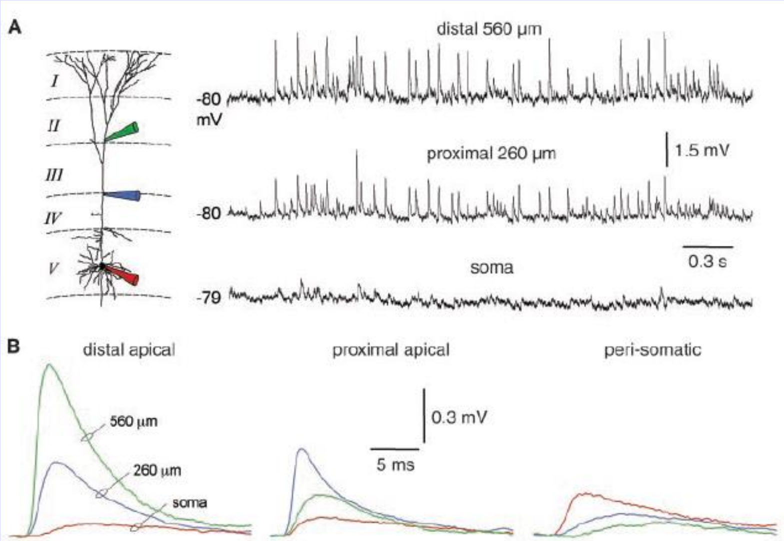
Presynaptic strength is small.

● Paired recordings: 1 EPSP ~1-3 mv → need 3-5 *almost simultaneous* presynaptic synaptic releases to trigger a spike in a postsynaptic cell (cortex).

● Synapses fail ~3 out of 4 times → need 12 to 20 *almost simultaneous* neurons to trigger a postsynaptic cell (hippocampus).

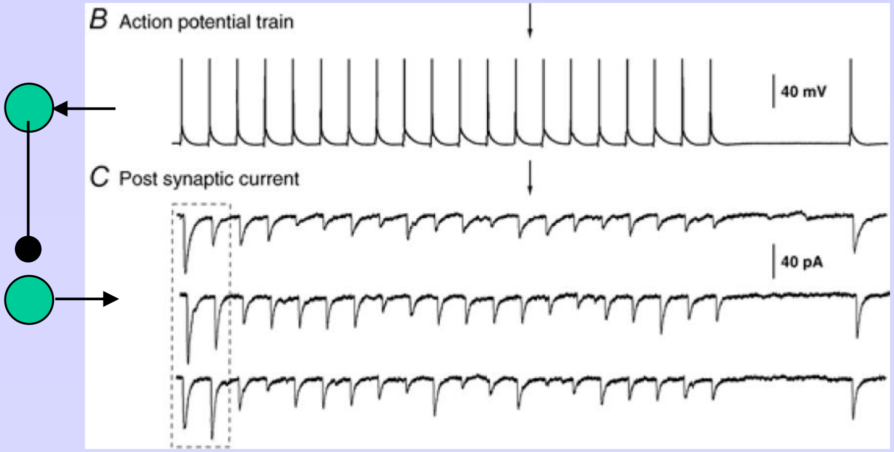
● In *vivo*, synchrony occurs with ~3-20 ms jitter → realistically need ~50-100 *synchronous* presynaptic neurons to trigger a postsynaptic cell.

● Not accounting for synaptic dynamics (depression, facilitation) or dendritic synaptic location.



Dendritic attenuation

(Williams and Stuart 2002)



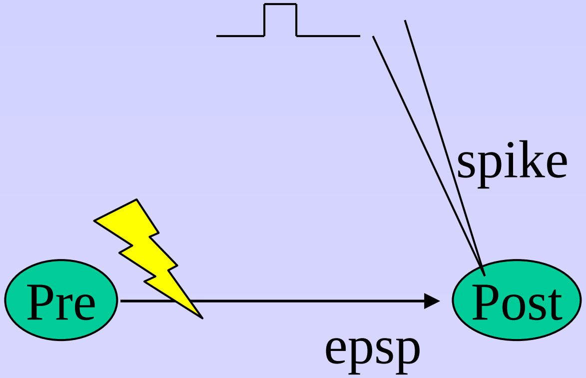
Facilitation and depression

(Furhman et. al. 2004)

Spike timing

- Why would one need spike timing: … Synaptic plasticity
  Spike-Timing-Dependent-Plasticity (STDP)

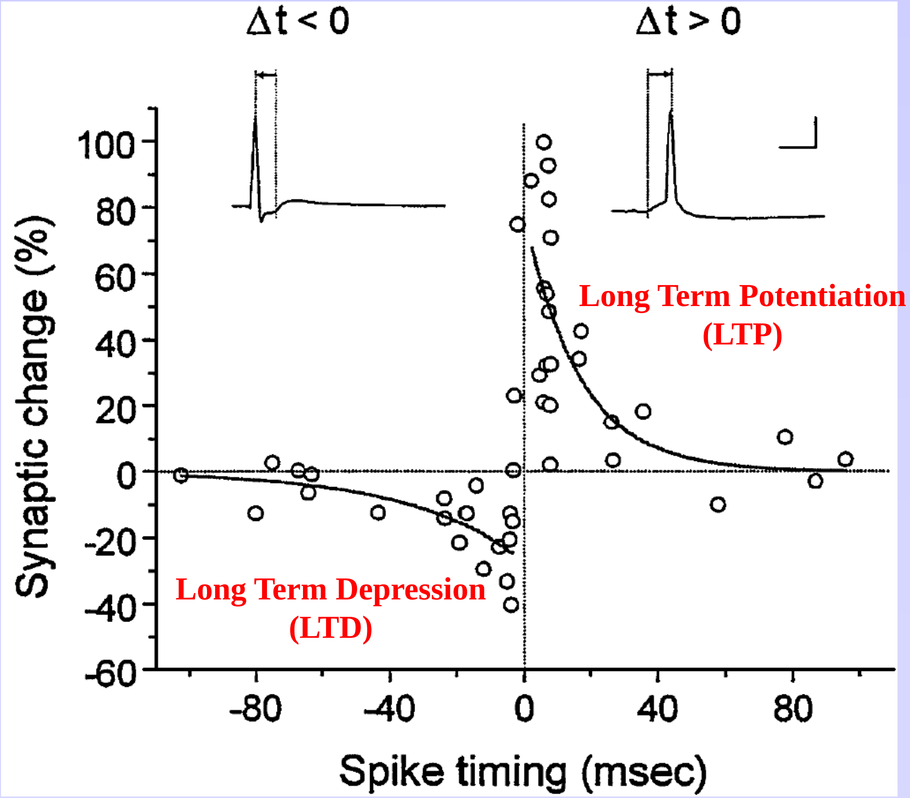
Repeated pairings: spike/epsp



$\Delta t = Post_{spike} - Pre_{epsp}$

Post → Pre

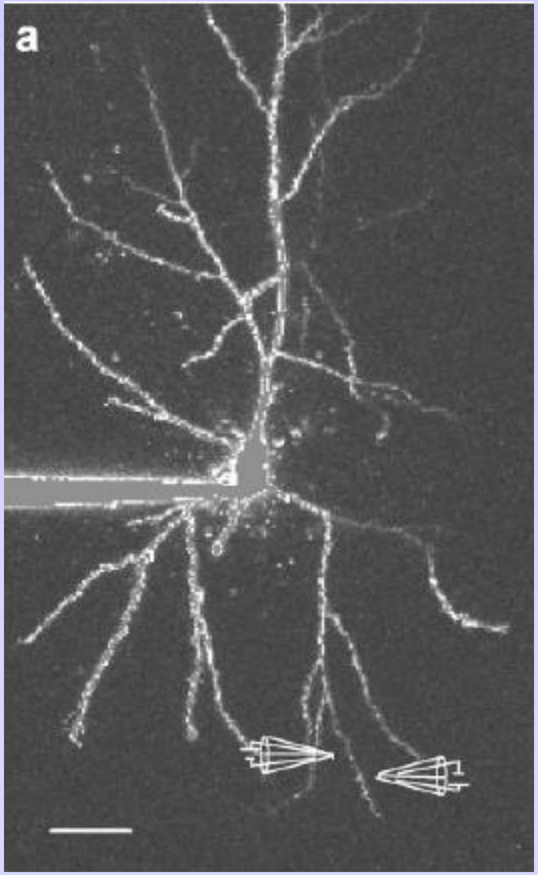
Pre → Post



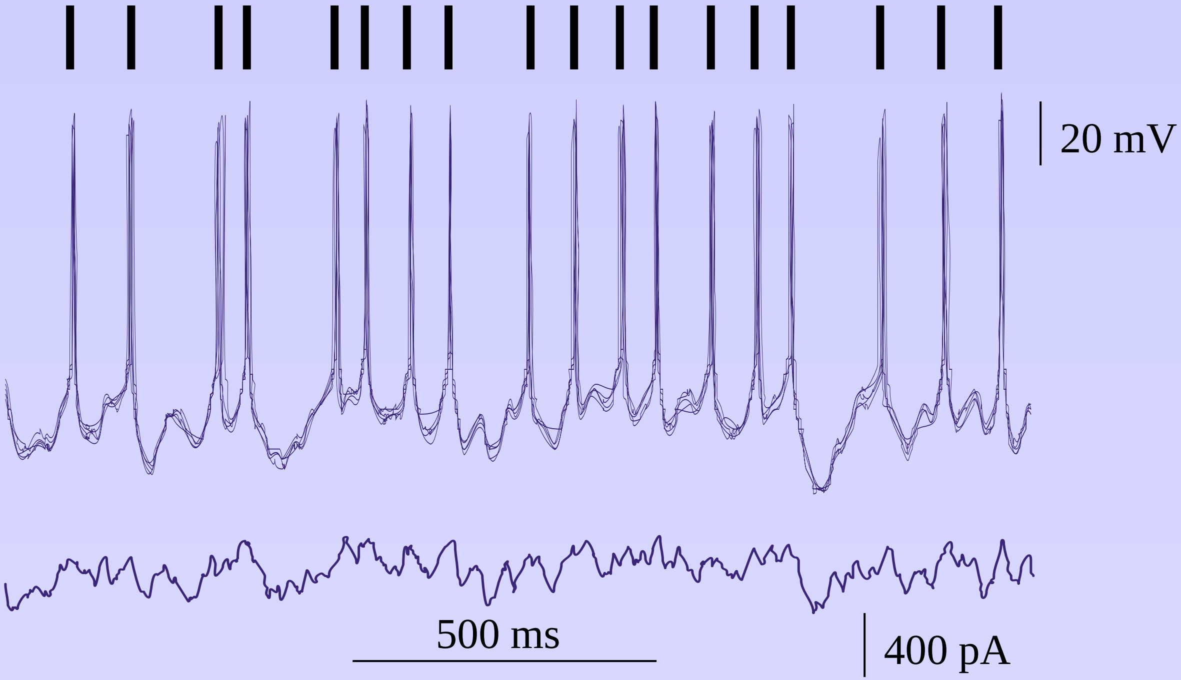
(Bi & Poo, 2001)

Spike timing

- What is the experimental evidence that spike timing may carry information: Reliable spiking *in vitro*



(Ariav et al. 2003)

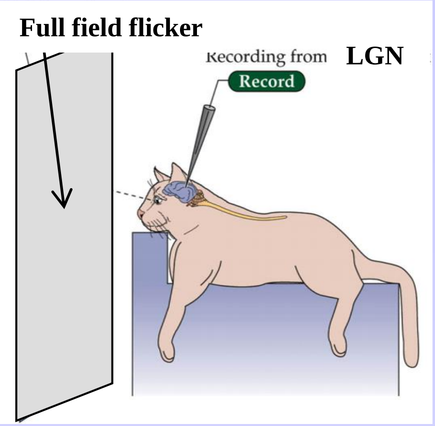


(Mainen & Sejnowski, 1995)

Determinism: Same stimulus → Same spike times

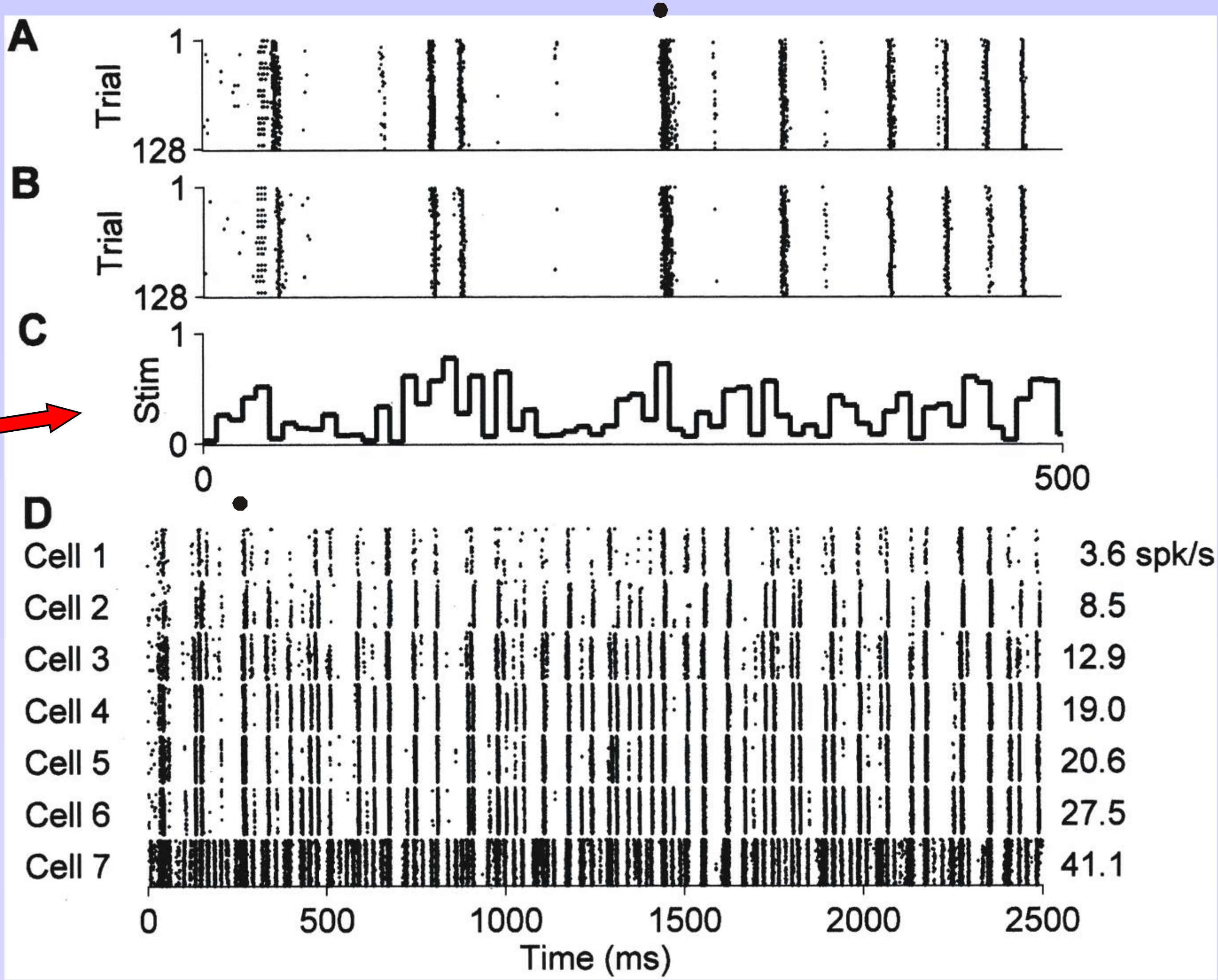
Spike timing

- What is the experimental evidence for spike timing: Reliable spiking *in vivo*



Visual Stimulation (grey levels)

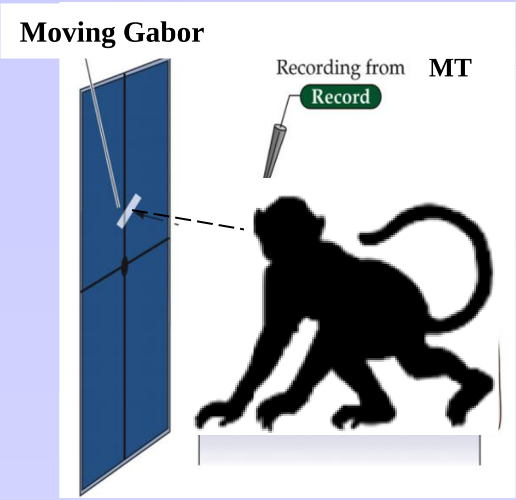
Different animals!



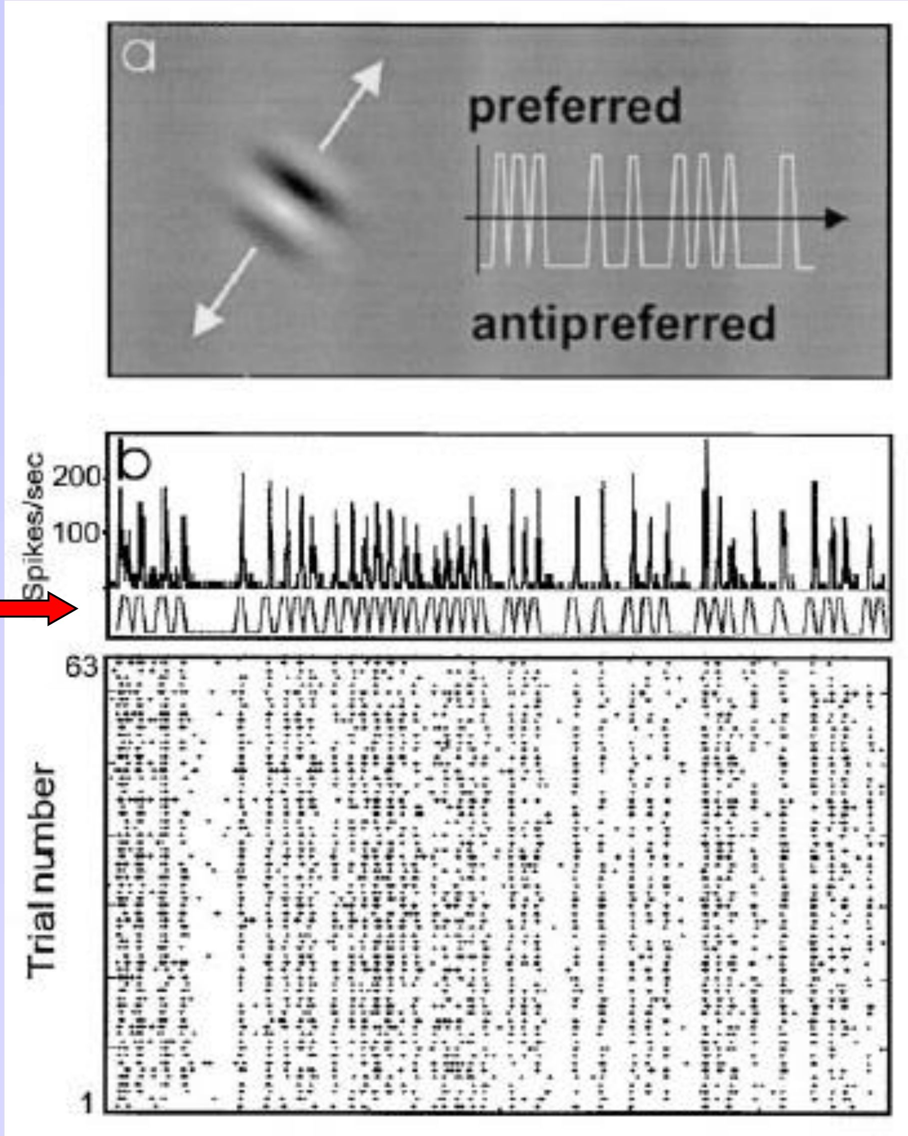
(Reinagel & Reid 2002)

Spike timing

- What is the experimental evidence for spike timing: Reliable spiking *in vivo*



Visual Stimulation



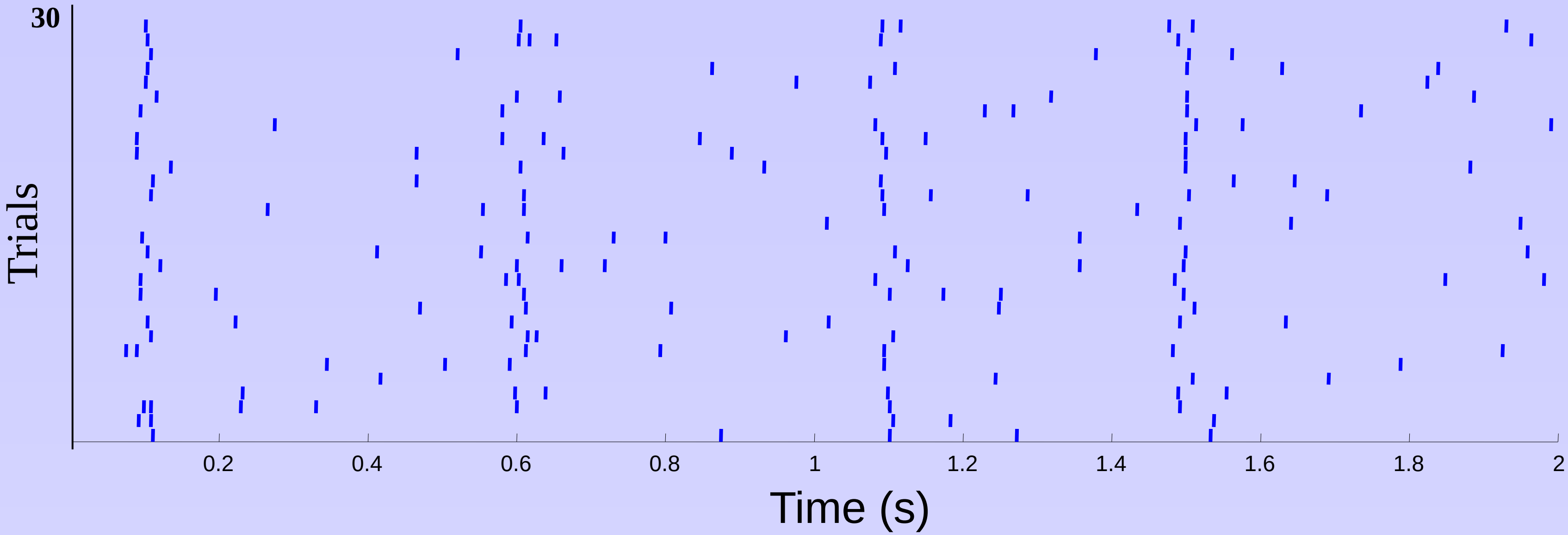
>12 synapses from the stimulus !

Stimulus → Eye →LGN →V1 →V2 → V4 →MT

(Buracas, Zador, DeWeese, Albright, 1998)

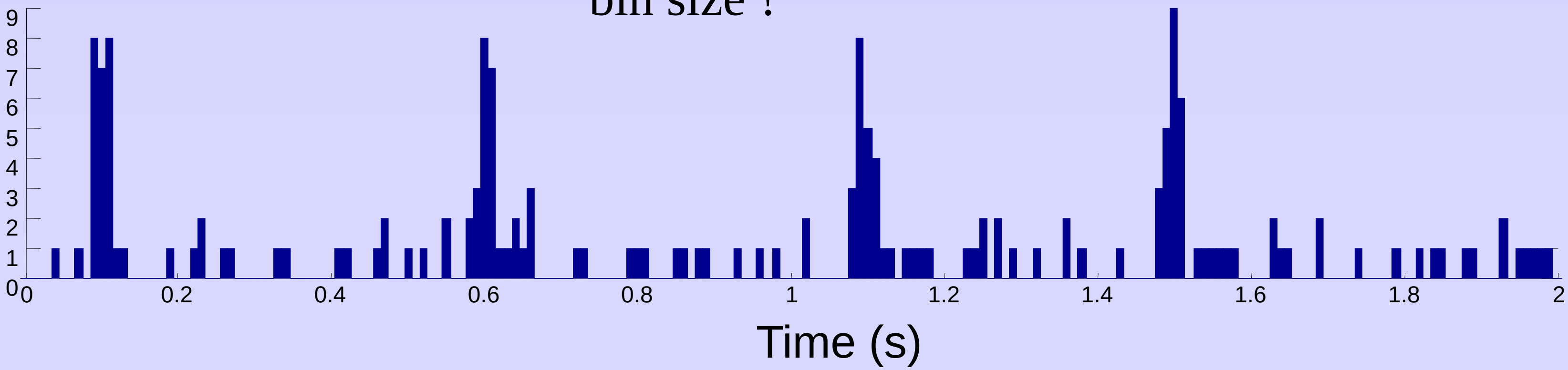
Spike timing

- Analyzing spike timing: **Reliability** (‘repeatability’) and **precision** (‘tightness’)



- **Step 1**: histogram

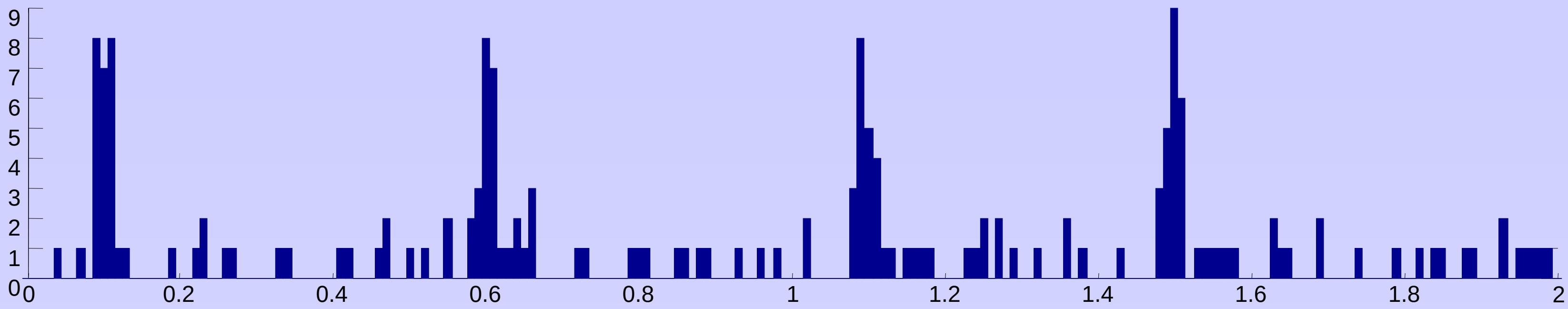
bin size ?

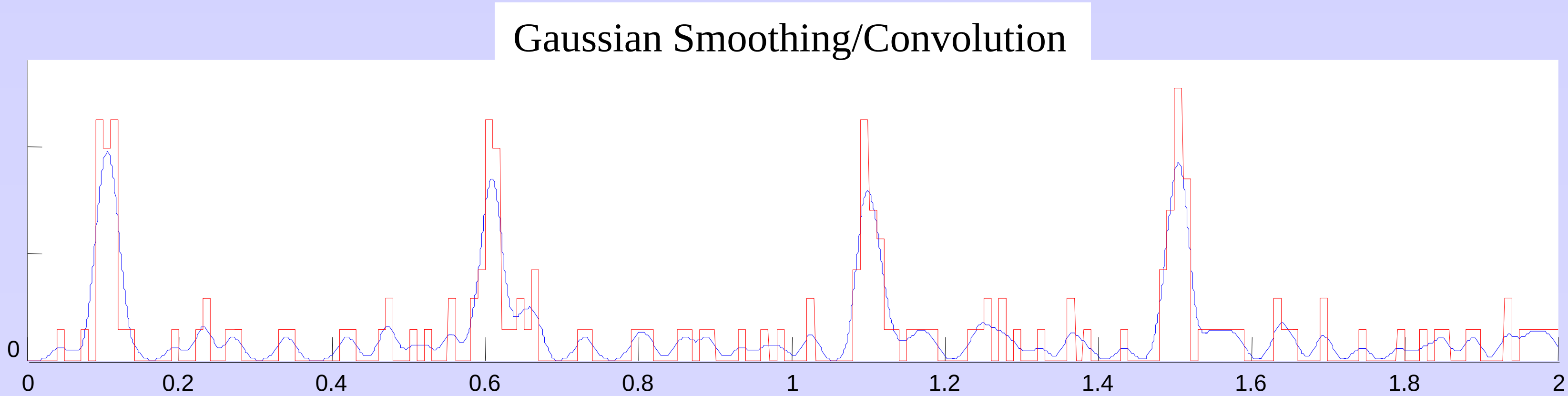


Spike timing

- Analyzing spike timing: Reliability and Precision

- **Step 2**: smoothing the histogram





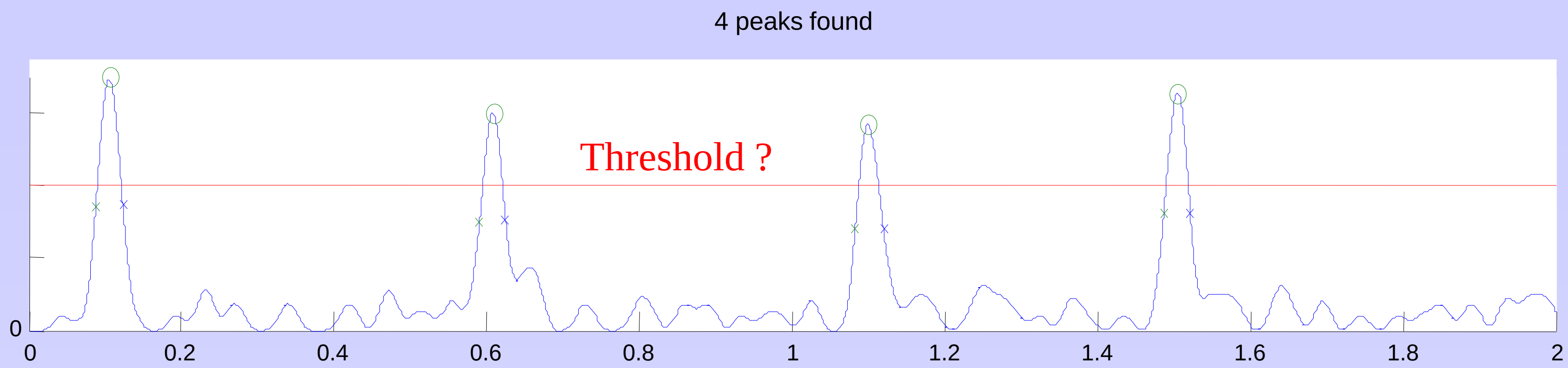
Rule of thumb…Smoothing window= ~1x/2x bin size

Also see *smooth()* in Matlab for a simple 'moving average' smoothing method

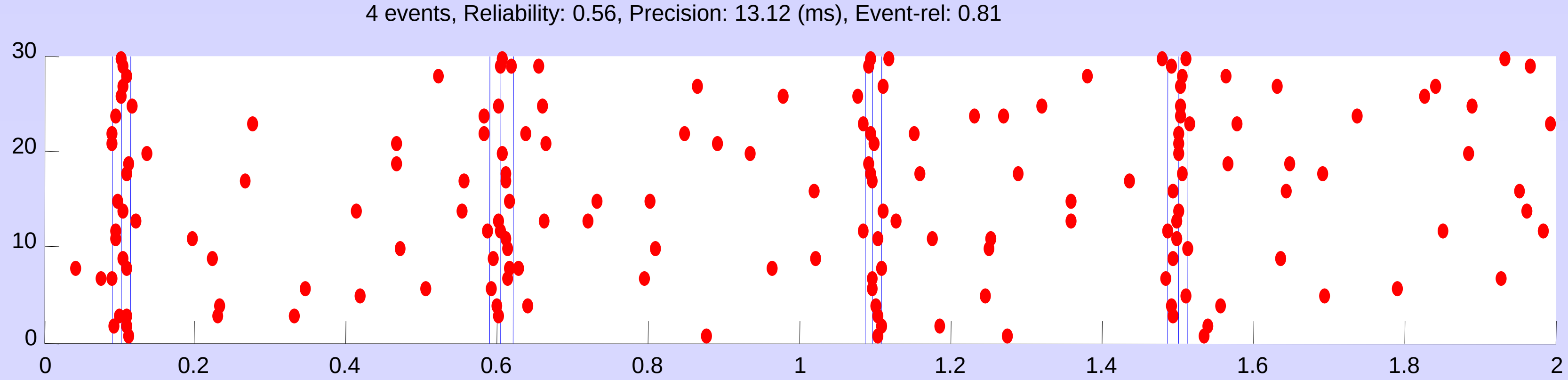
Spike timing

- Analyzing spike timing: Reliability and Precision

- **Step 3**: Finding 'events'



- **Step 4**: Computing (average) Reliability and Precision



Spike timing: Reliability and Precision

- Analyzing spike timing: Reliability and Precision

- Precision

$$P = \left(\frac{\sum_e \sigma_e}{e} \right)^{-1}$$

(average) jitter

- Reliability

$$R = \frac{\sum_e N_e}{N}$$

With N_e = number of spikes within event e
N= total number of spikes

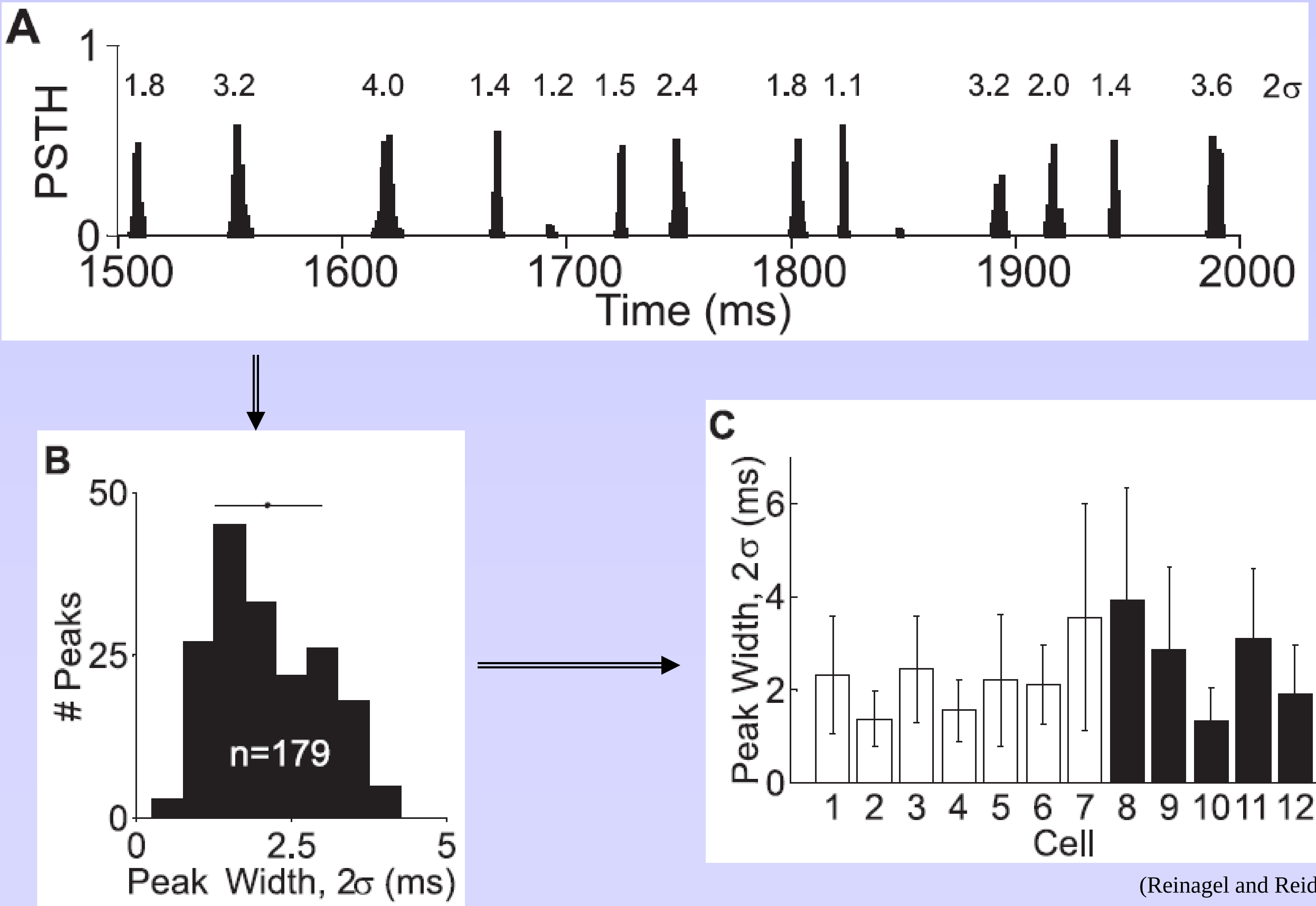
- Average event-reliability

$$r = \frac{1}{e} \sum_e \frac{N_e}{N_t}$$

With N_t = number of trials/units

Spike timing

- Computing Reliability and Precision *in vivo*

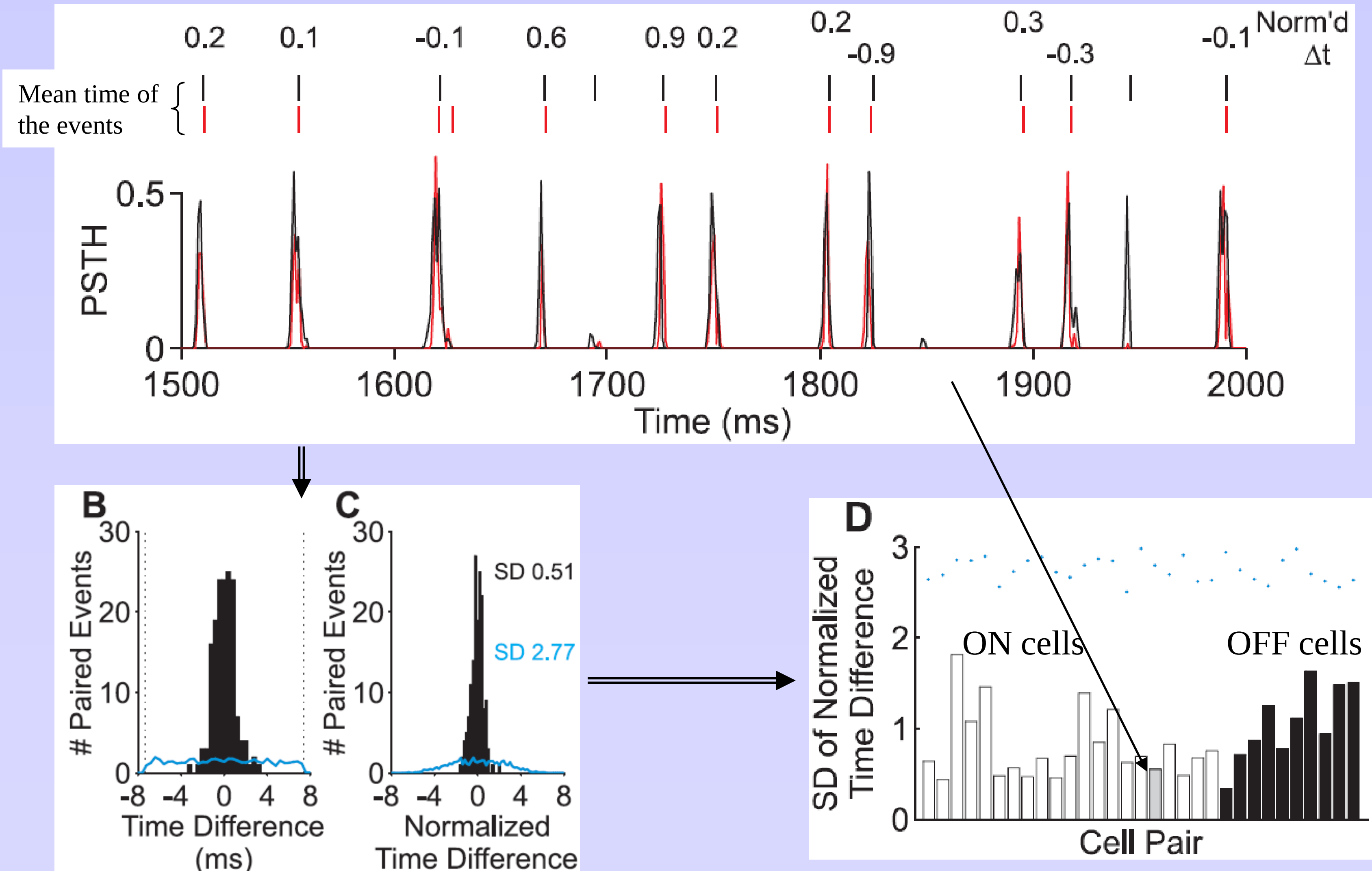


(Reinagel and Reid 2002)

Spike timing

- Comparing the firing of two cells

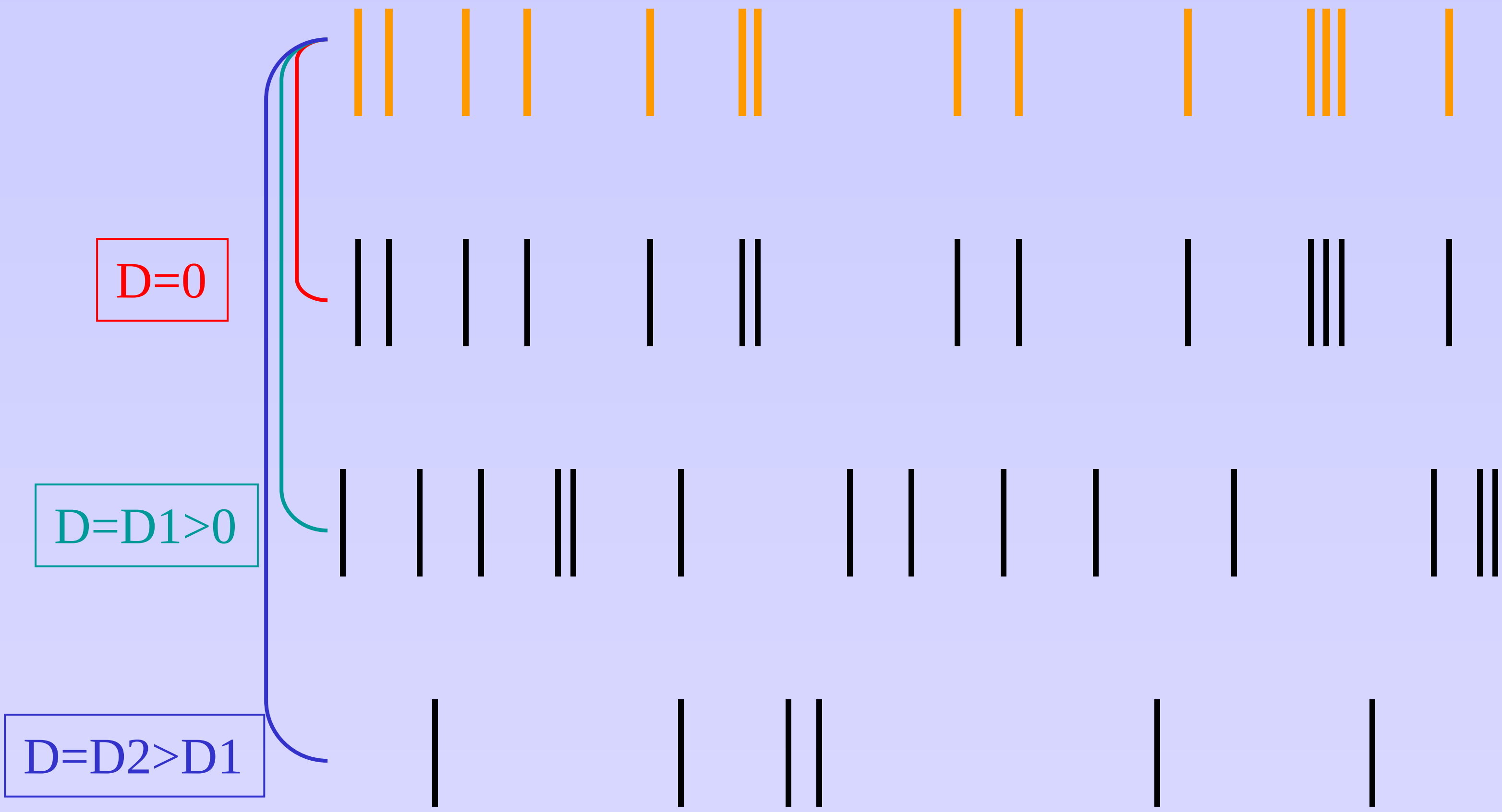
$$\Delta t = \frac{\mu_1 - \mu_2}{<\sigma>}$$



(Reinagel and Reid 2002)

Spike timing

- Analyzing spike timing: Spike train distances



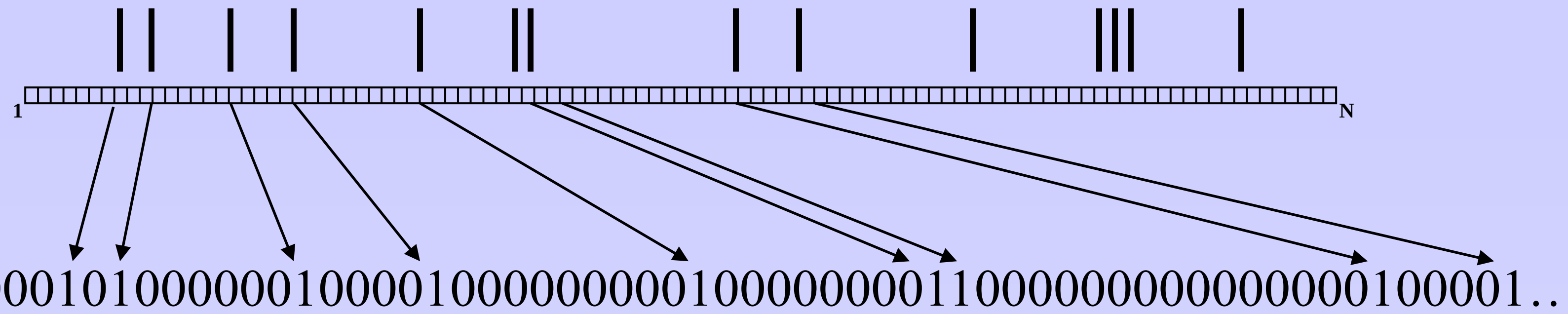
What is D? (metric)

Side bar: Distance Vs Metric

Spike timing

- Distances: Vectorial approach

• Binning



N-dimensional vectorial space

• Use Euclidian Distance in N-Dimensional space (a.k.a L2 norm)

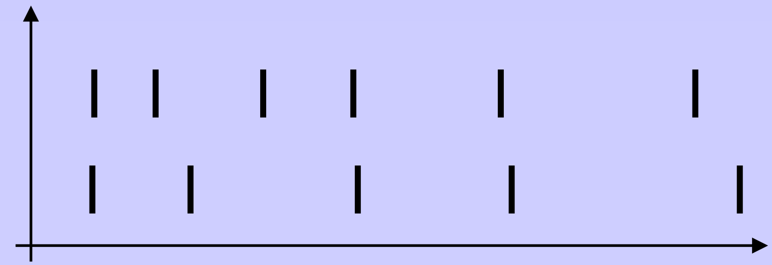
2 spike trains *v* and *w*:

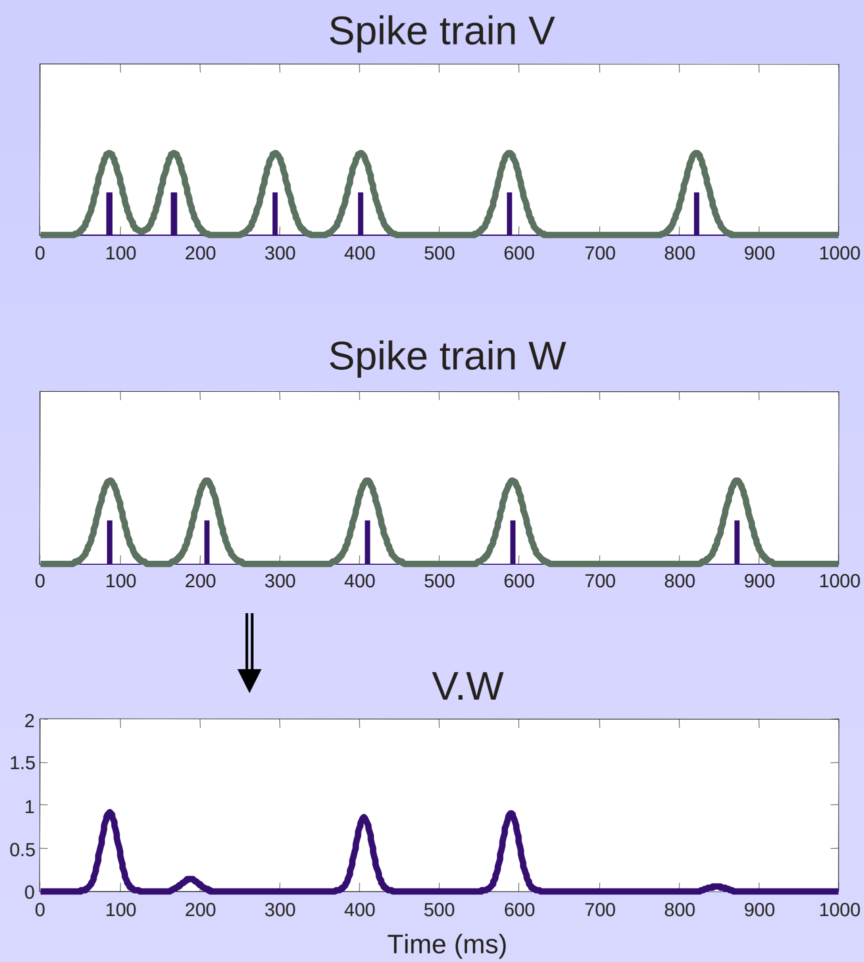
$$D(v, w) = \sqrt{\sum_{i=1}^{N} (v_i - w_i)^2}$$

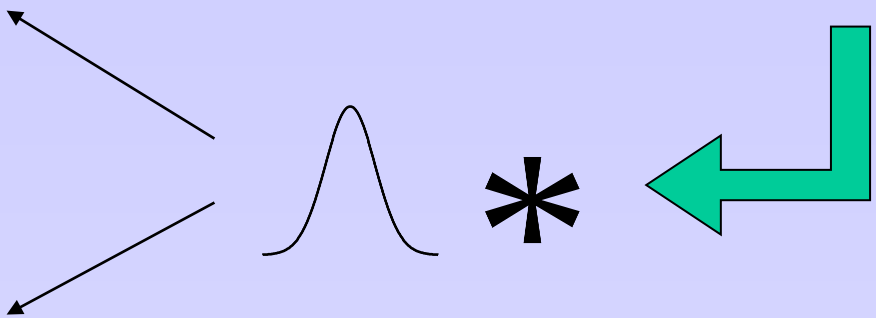
• Problem: High dimensional space (computationally expensive)
small spike jitter ➔ discrete shifts in new dimensions

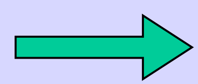
Spike Timing

- Metric: Bin-less approach





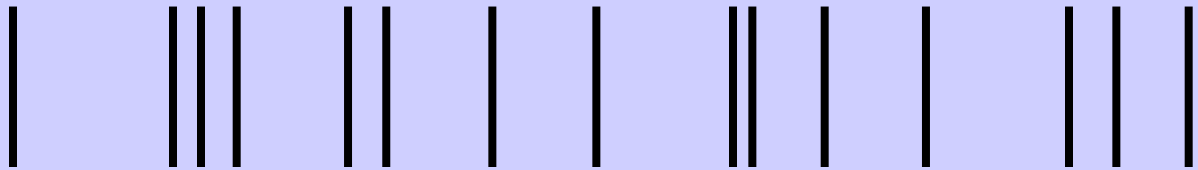




$$D(V,W) = 1 - \frac{\sum_{i=1}^{N} V_i . W_i}{\|V\| . \|W\|}$$

(Kruskal et al, 2007; Lyttle and Fellous, 2011)

Spike patterns



How is information represented in the brain?

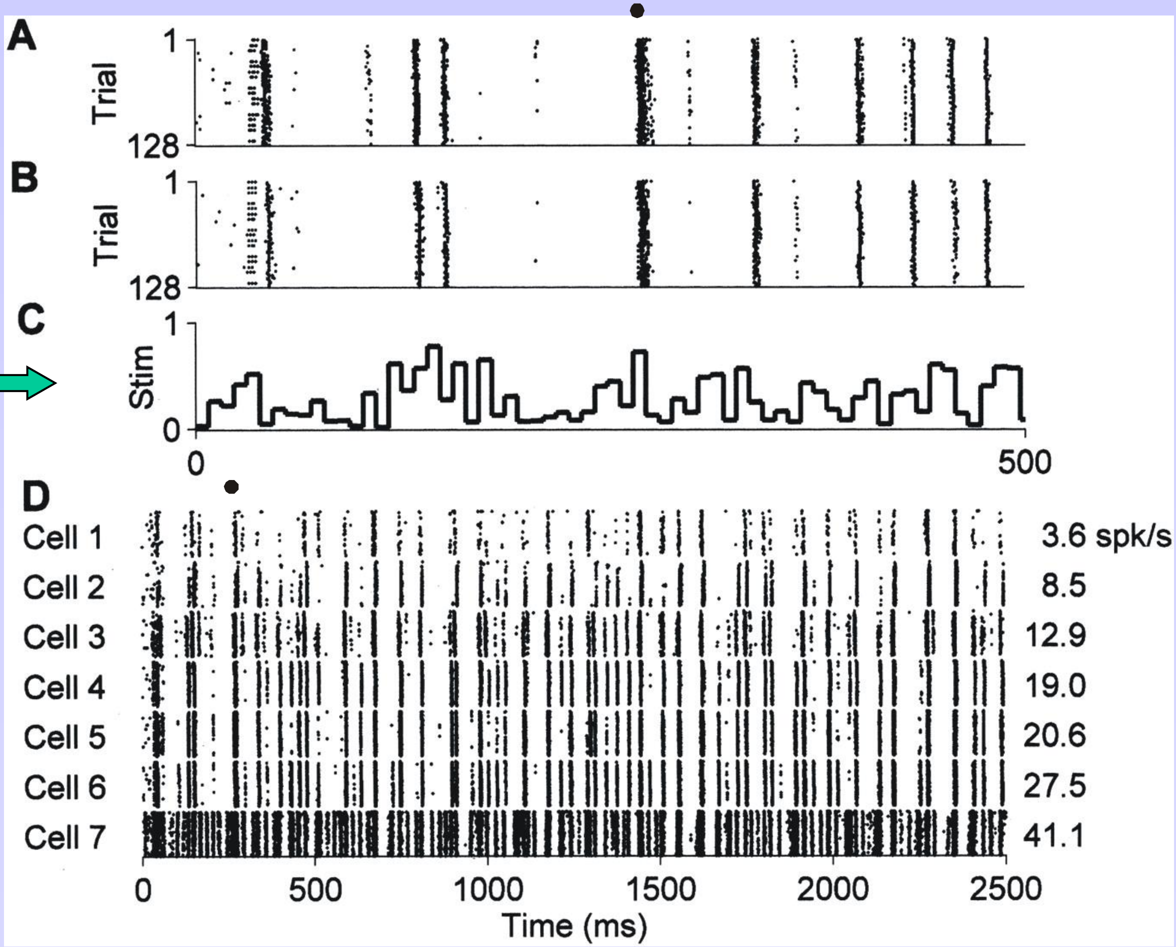
- Spike Count
- Firing Rate
- Spike Timing
-…?...

Reliability In Vivo: Cat LGN

- Stimulus-dependent sensory information (e.g. Vision) is represented by precise and reliable firing events. Recall:

Visual Stimulation

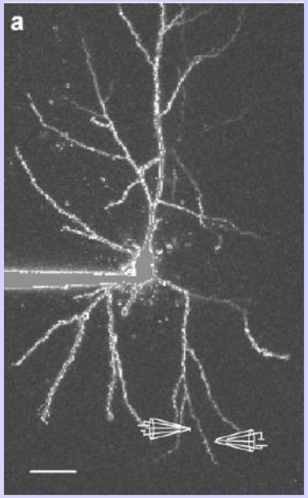
Different animals!



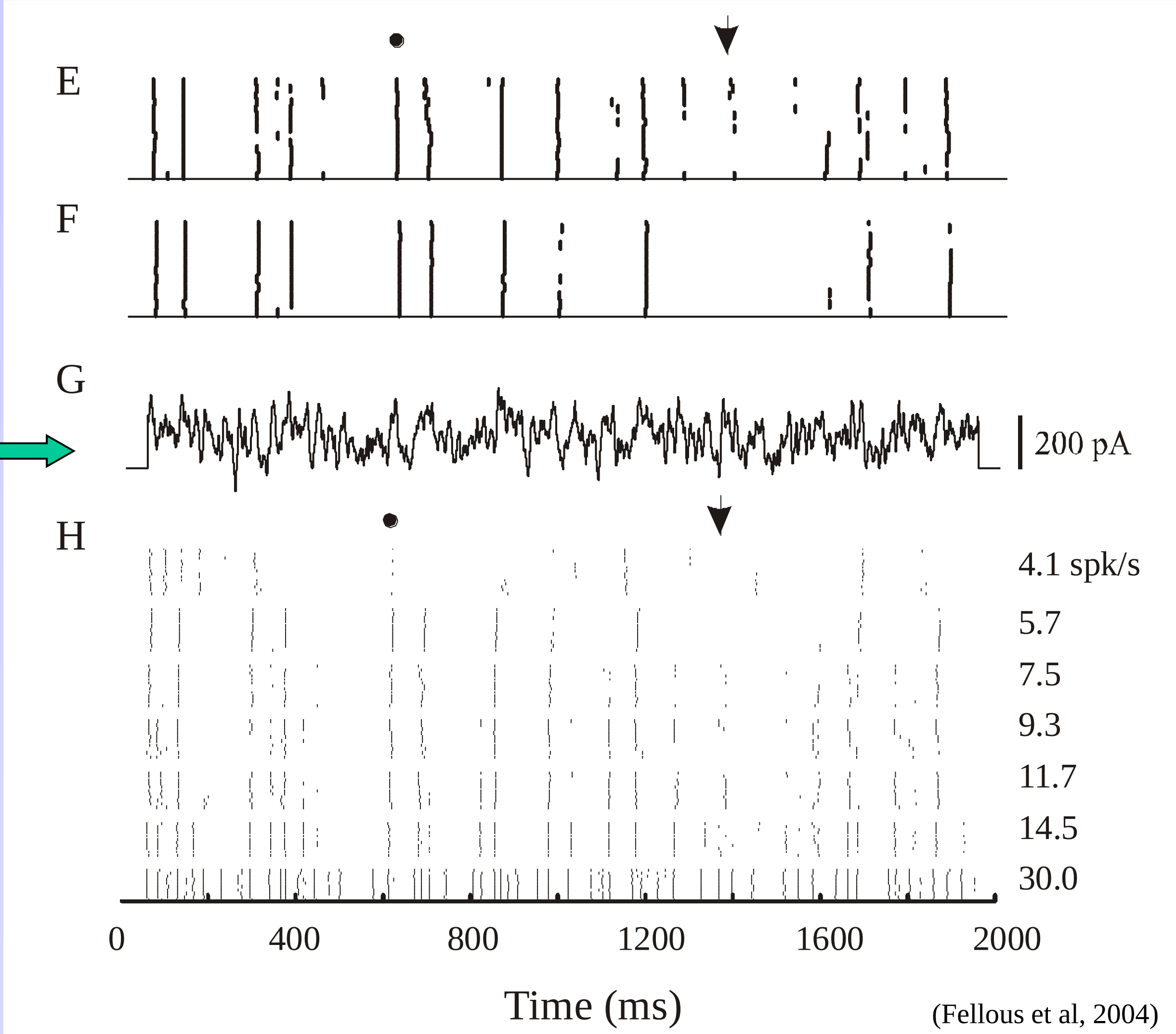
(Reinagel & Reid 2002)

Reliability in Vitro

- Same *in vitro* (i.e. no synaptic activity)



Somatic Injection



(Fellous et al, 2004)

Reliability in the Face of Unreliability

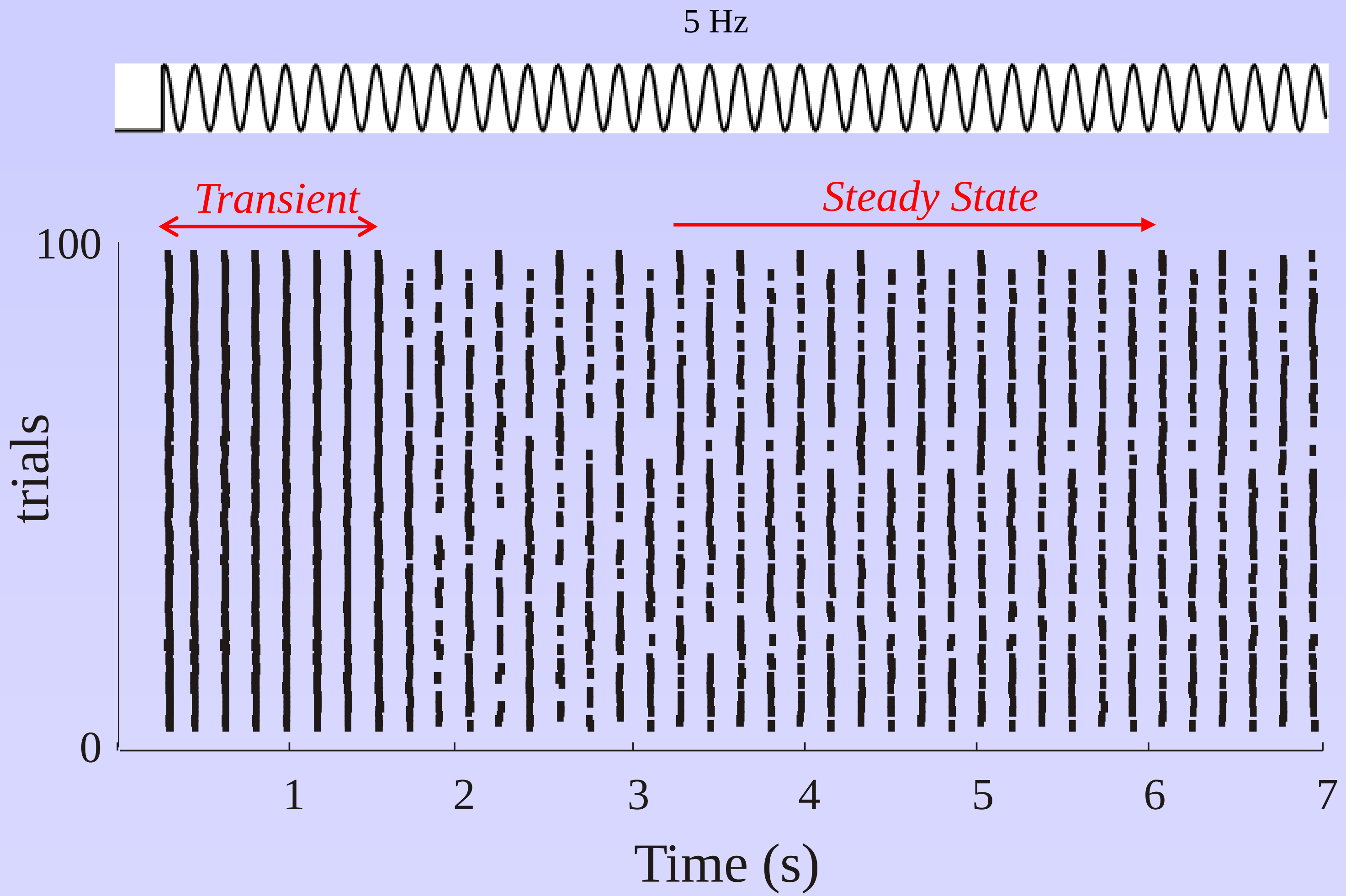
- Neurons receives thousands of background (noise) synaptic inputs.
- Synaptic transmission is unreliable (p ~= 0.2-0.3).
- Network configurations are different from animal to animal.

How can a neuron *in vivo*, several synapses away from a stimulus, fire reliably with millisecond precision?

What are some of the characteristics of *in vivo* reliable and precise firing?

In Vitro: Reliabilities

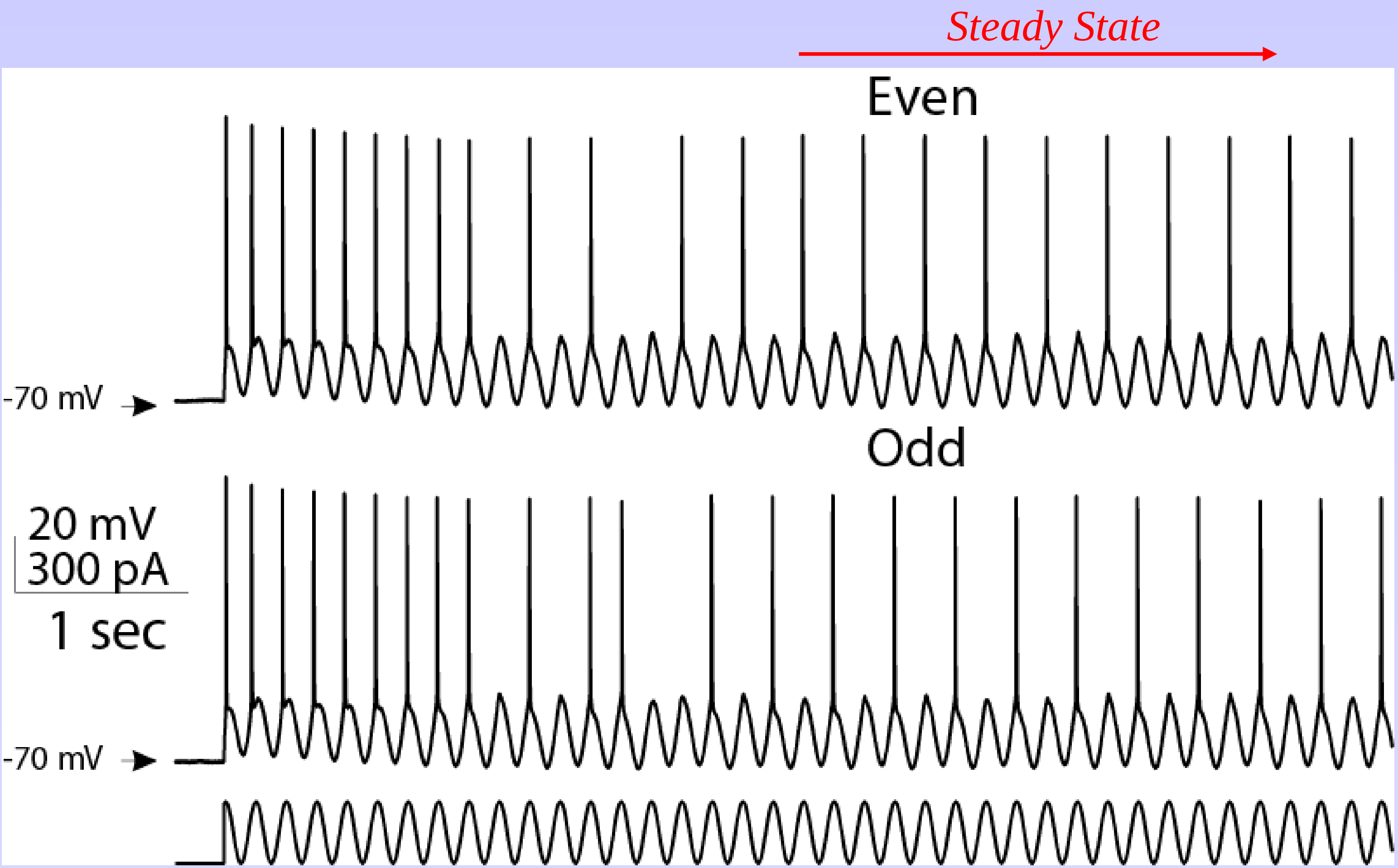
- Response to a stimulus is non-stationary and (in at least some cases) non deterministic



(Fellous et al, 2004)

In Vitro: Reliabilities

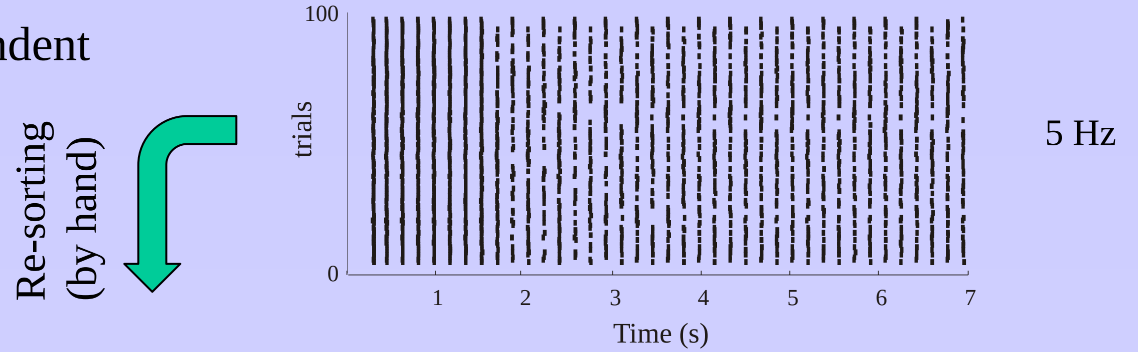
- Limited non-determinism: Cycle skipping

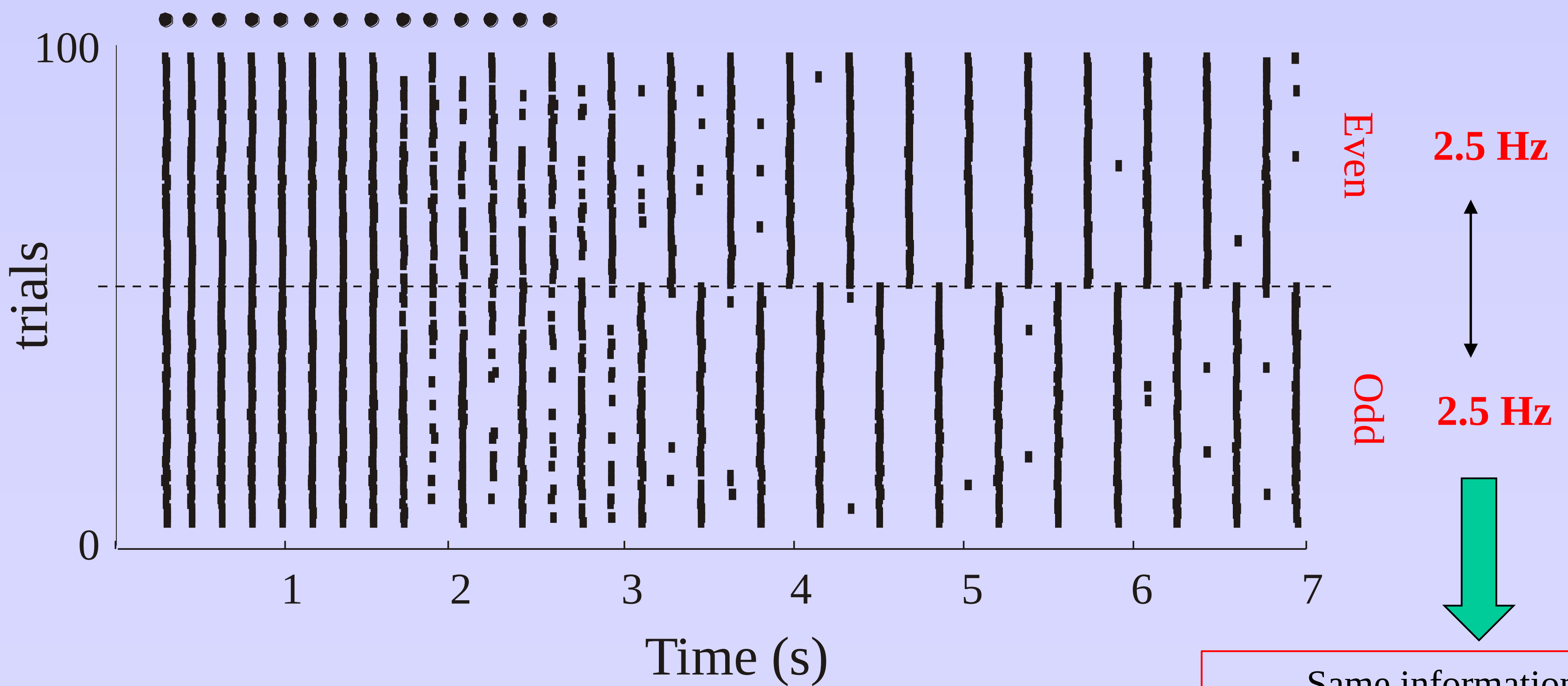


(Fellous et al, 2004)

In Vitro: Reliabilities

Assumption: trials are independent



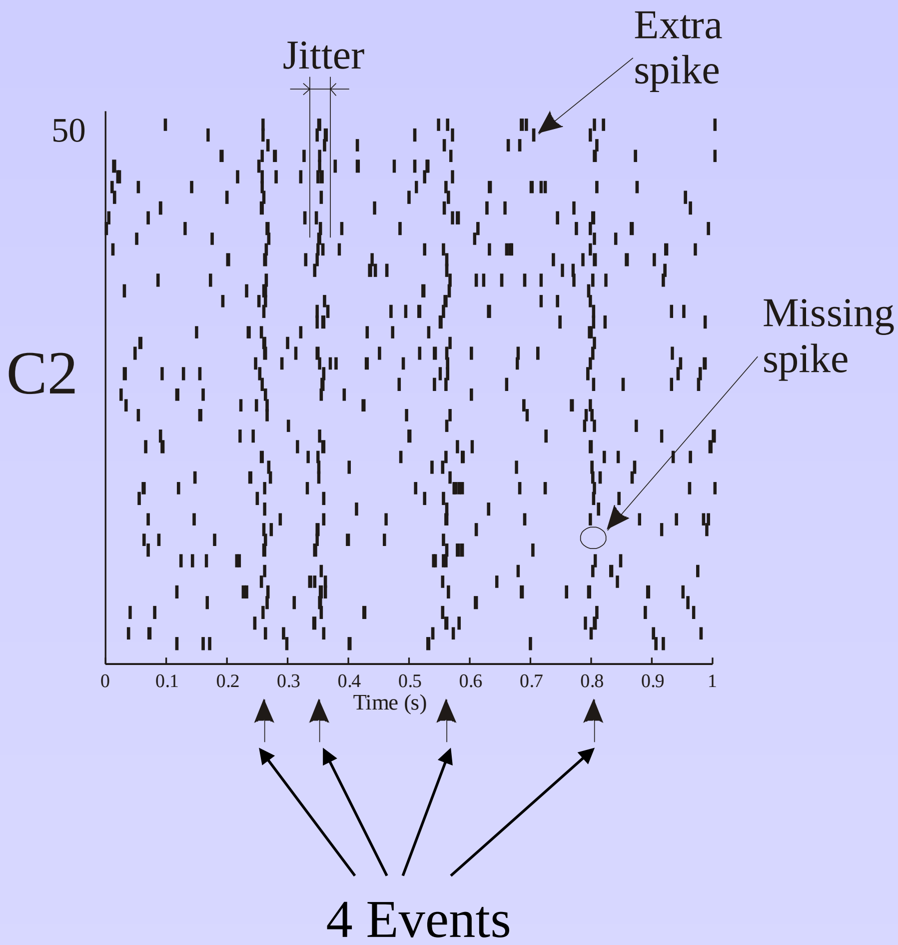


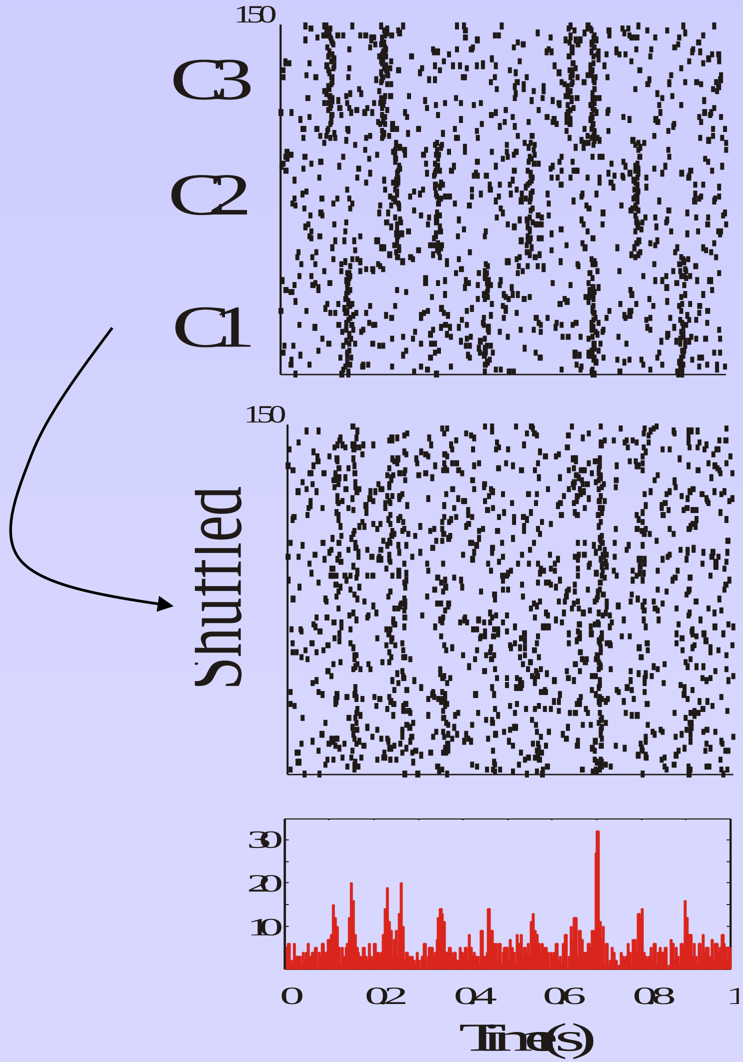
Same information
Two different **spike patterns**

(Fellous et al, 2004)

Surrogate dataset

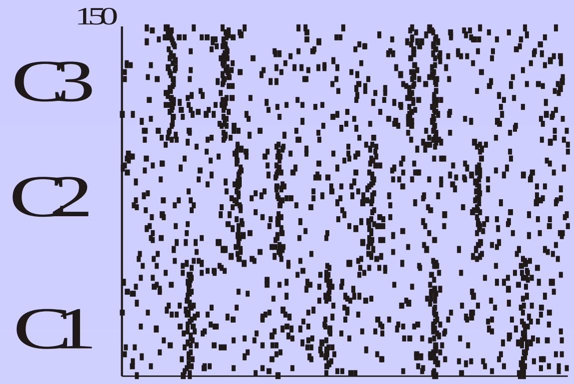
- Can one hide/find different spike patterns?
- Surrogate set: Jitter, Noisy-spikes, missing spikes

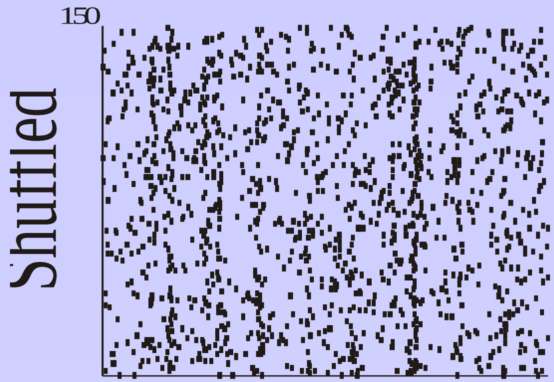




(Fellous et al, 2004)

Clustering

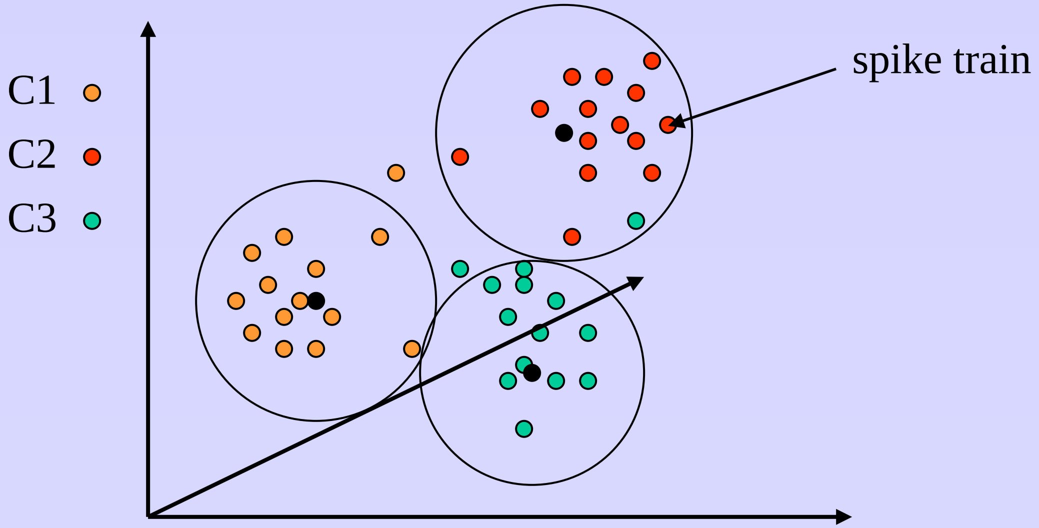




Find spike patterns

⇕

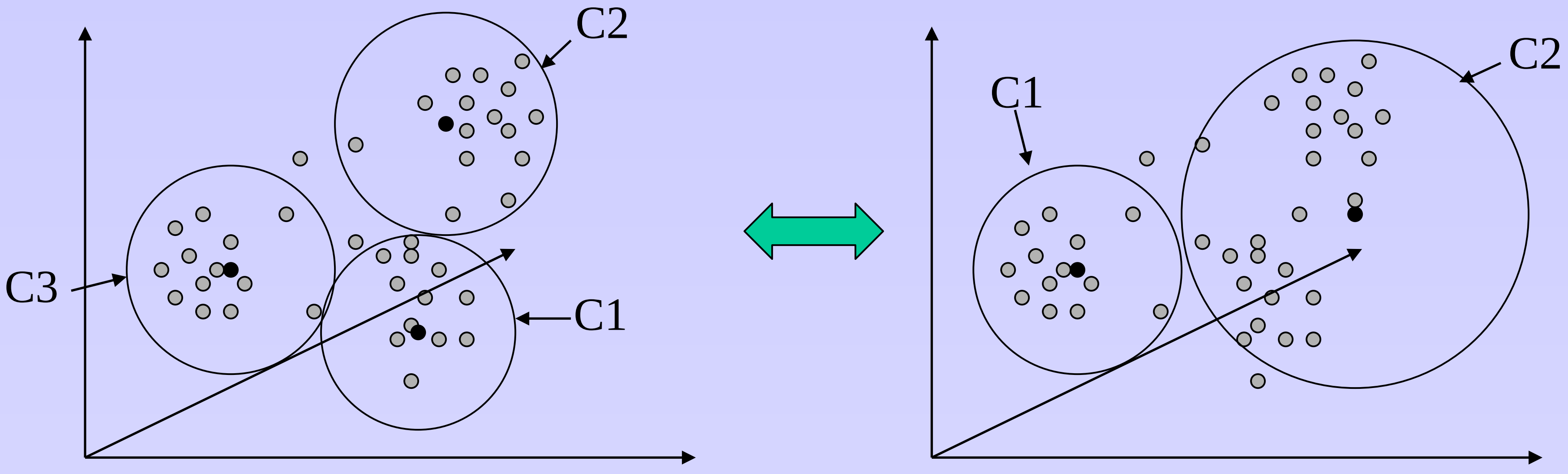
Find cluster centers, and cluster radii to maximize correct classification



Spike patterns

- Real Data: No knowledge of the cluster structure – ‘unsupervised learning’

- Find cluster centers, and cluster radii to *minimize* the number of outliers



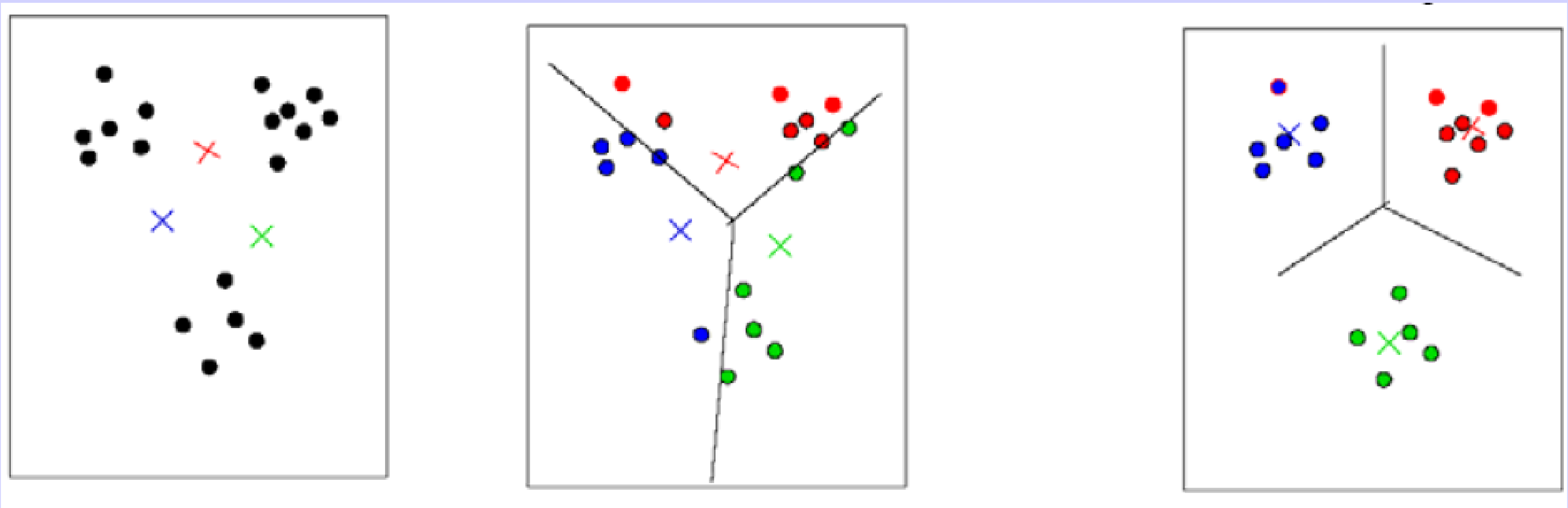
- Find cluster centers {C}, and radii {R} to *maximize* an ‘objective function’

$$O(C,R) = \frac{D_{between\_clusters}}{D_{within\_clusters}}$$

Spike patterns - Clustering

- K-means clustering

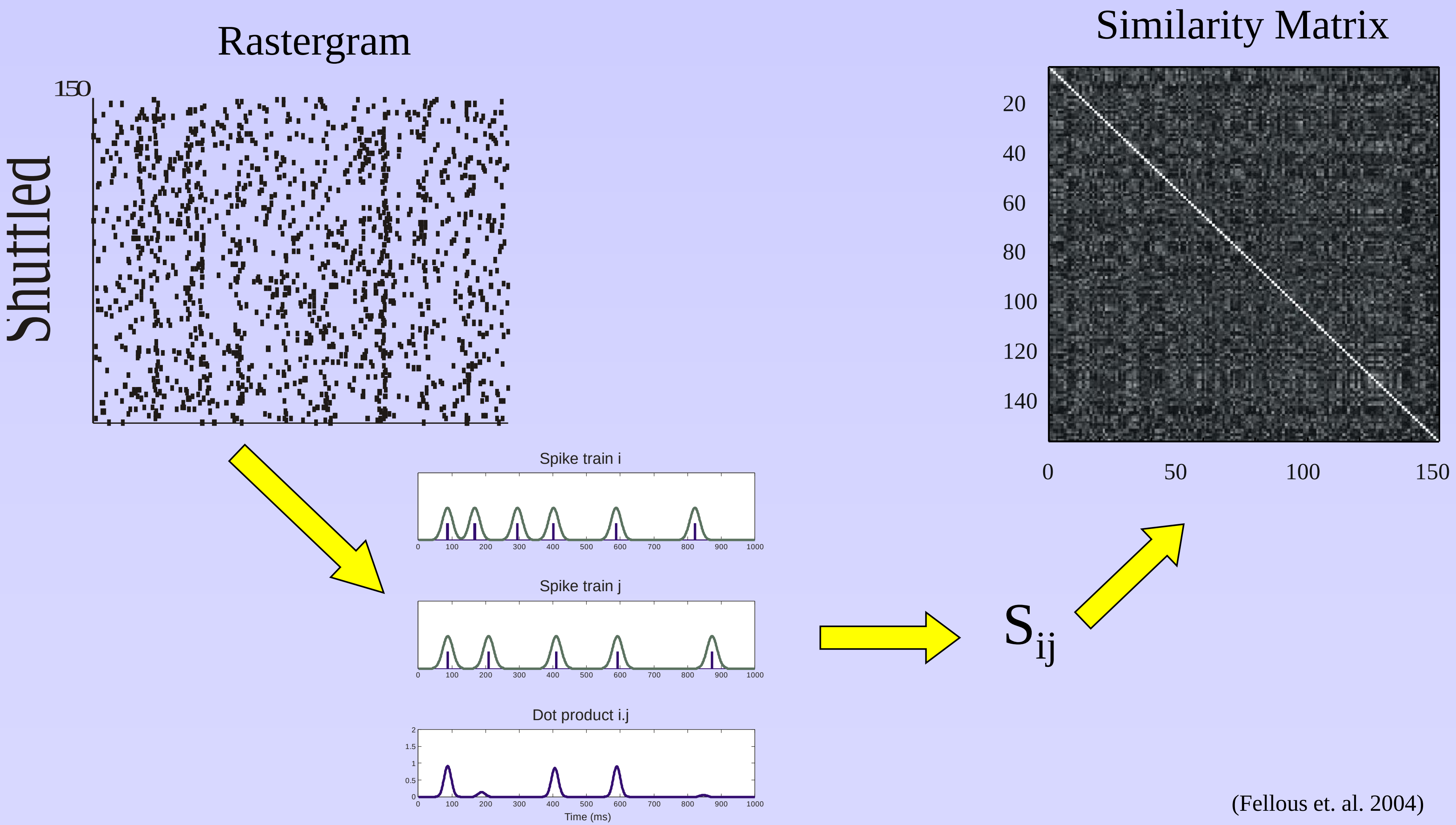
  - 1: Start with random guess: K cluster centers.
  - 2: Assign each data point to the nearest cluster (also called ‘Centroidal Voronoi tesselation’). If no new assignments: STOP
  - 3: Move each cluster center to the mean of the data assigned to it.
  - 4: Go to 2.



- Other algorithms: Mixture of Gaussian (EM-algorithm), Fuzzy K-Means …

Recoding: ‘Everything is Relative’

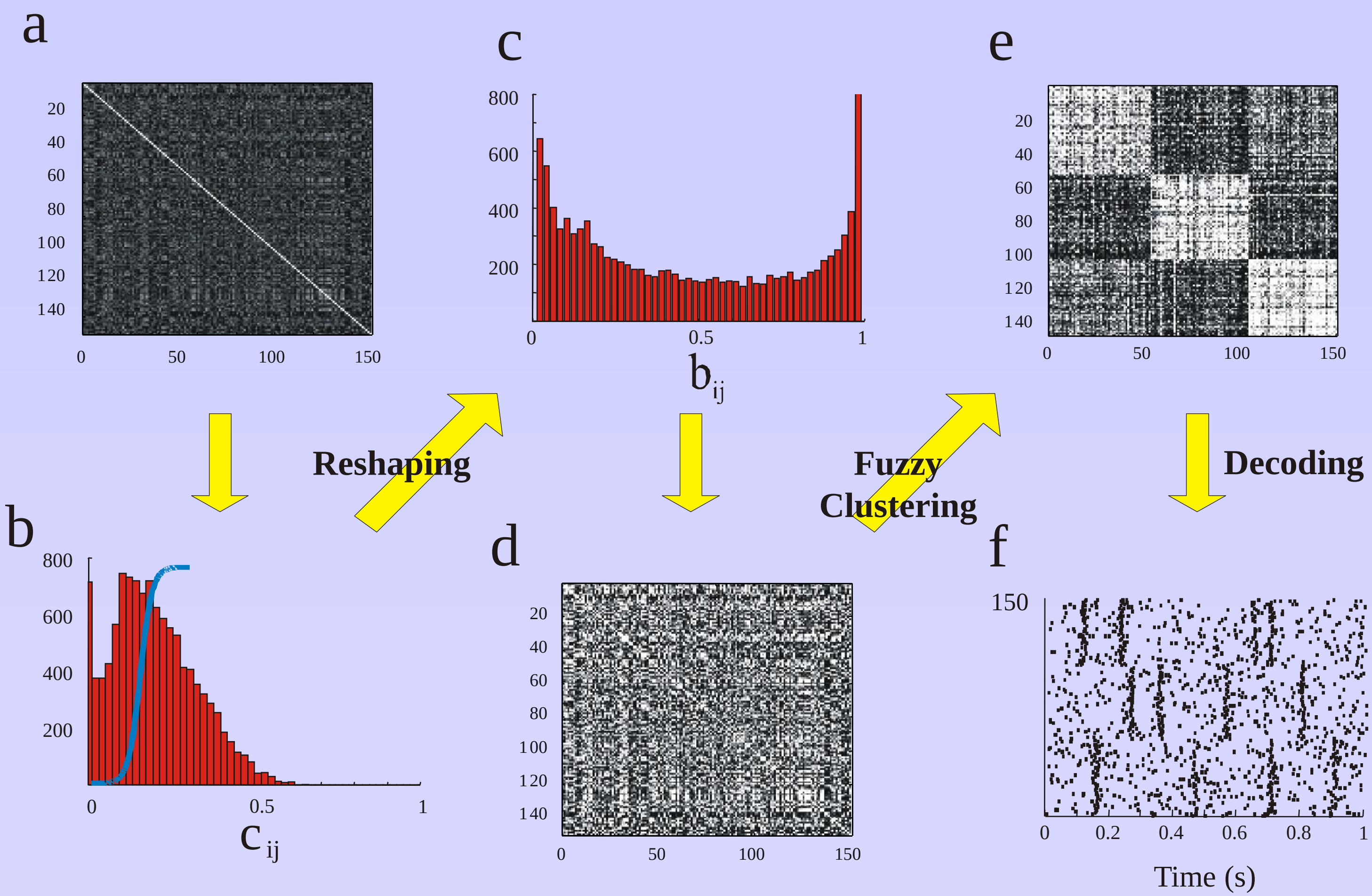
- Problem: Space of spike trains is large and infinite.
- → Recode in a smaller, finite space.



(Fellous et. al. 2004)

Clustering Method: Clustering

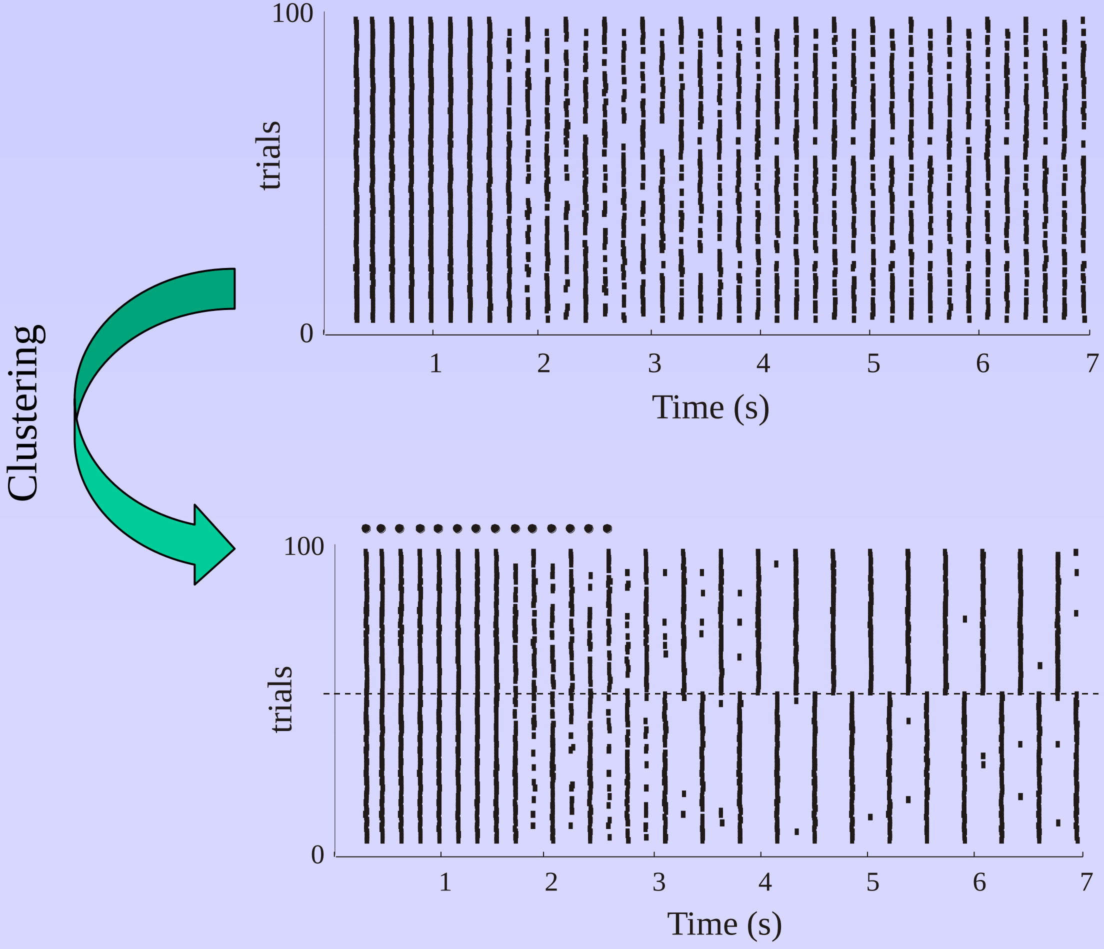
- Maximize Spike train space occupancy



(Fellous et. al. 2004)

Spike Patterns In Vitro

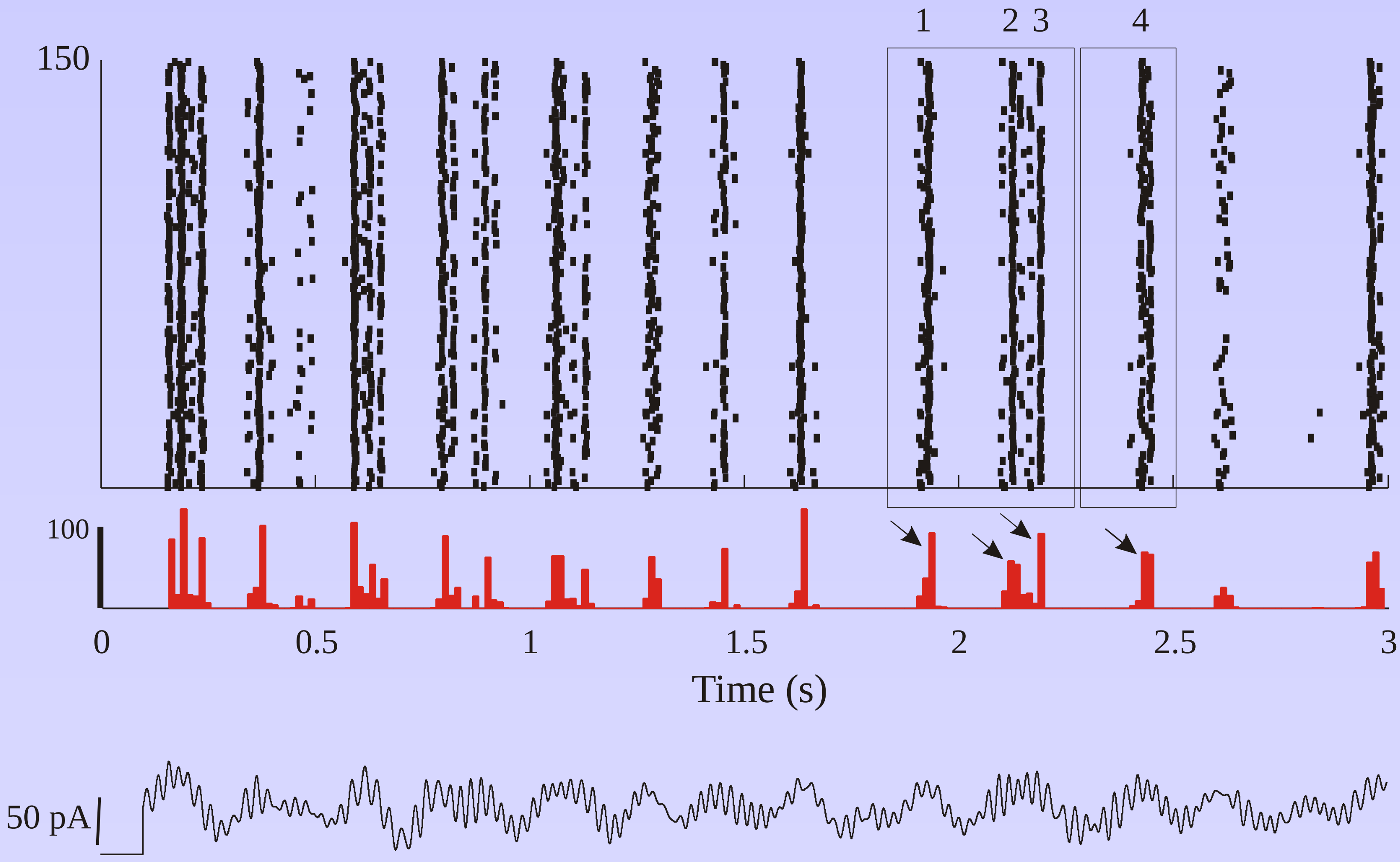
- → Surrogate sets: As expected…
- In *vitro* data: As expected …



(Fellous et. al. 2004)

Complex Inputs

- Complex inputs *in vitro* (prefrontal cortex, rat)

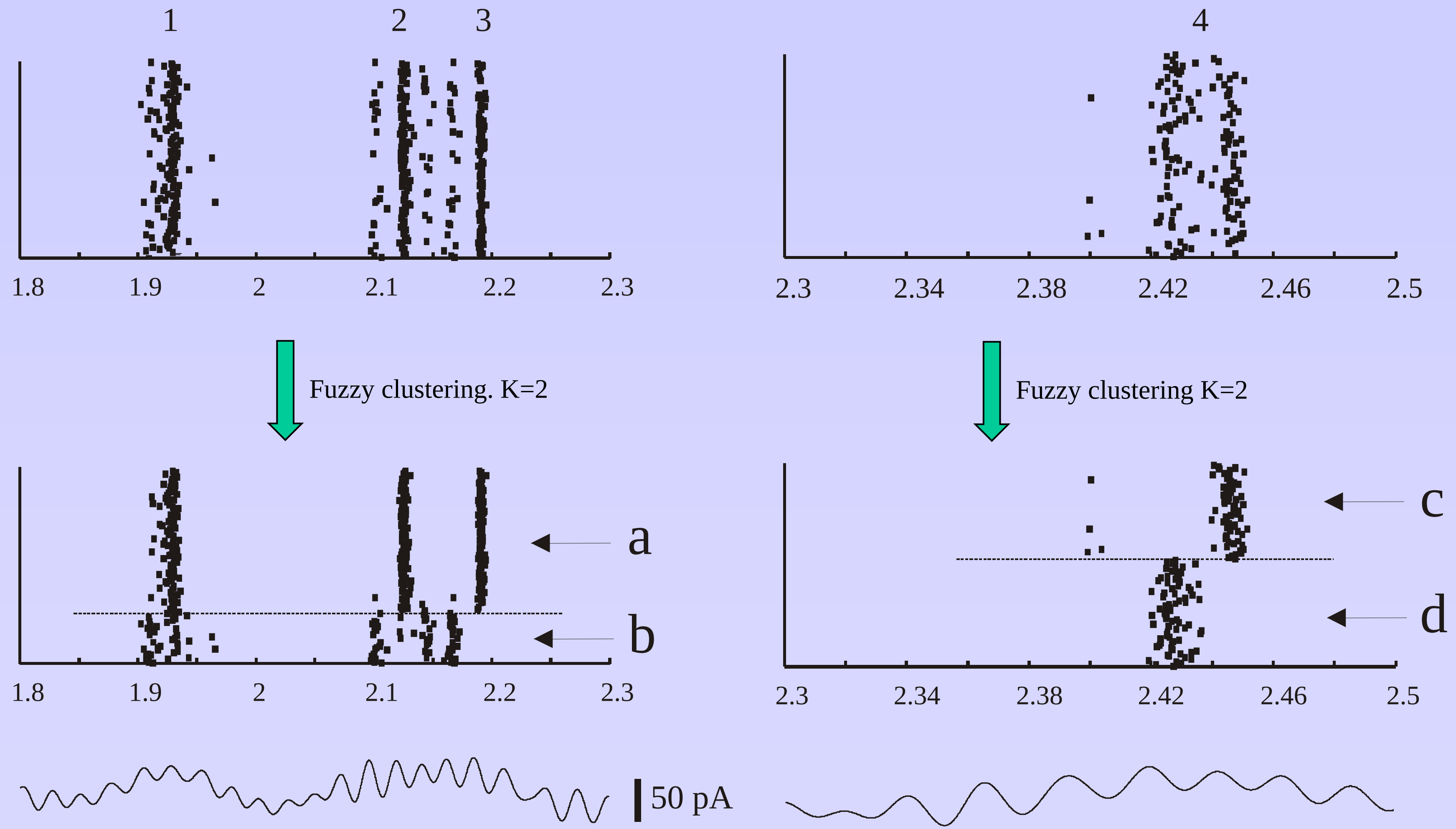


(Fellous et. al. 2004)

Complex Inputs

- Complex inputs in vitro (prefrontal cortex, rat)

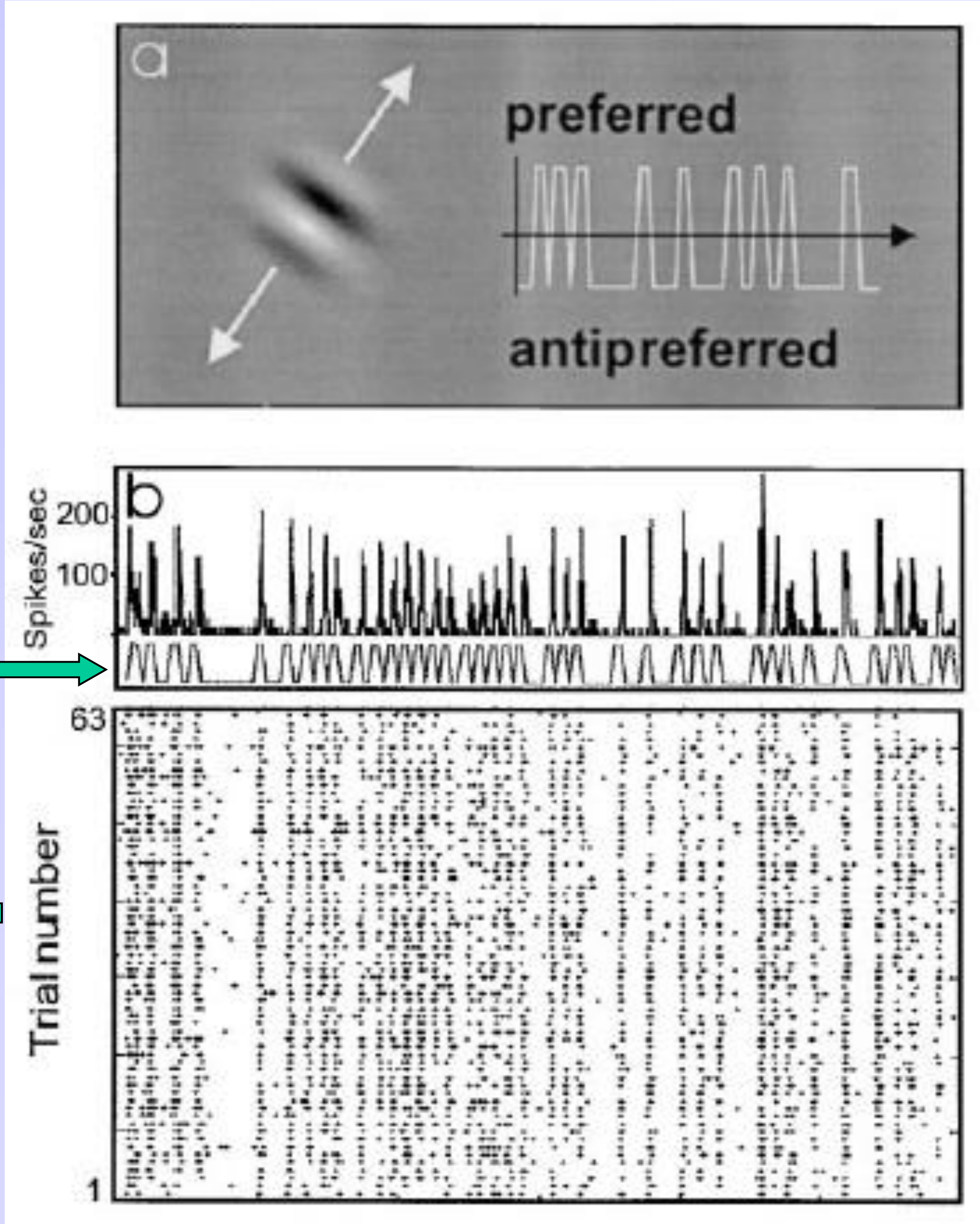
→ Discrete clusters in response to the same stimuli



(Fellous et. al. 2004)

Spike Patterns in Vivo

- Behaving monkey, Area MT
- Visual stimulation, moving Gabor patches



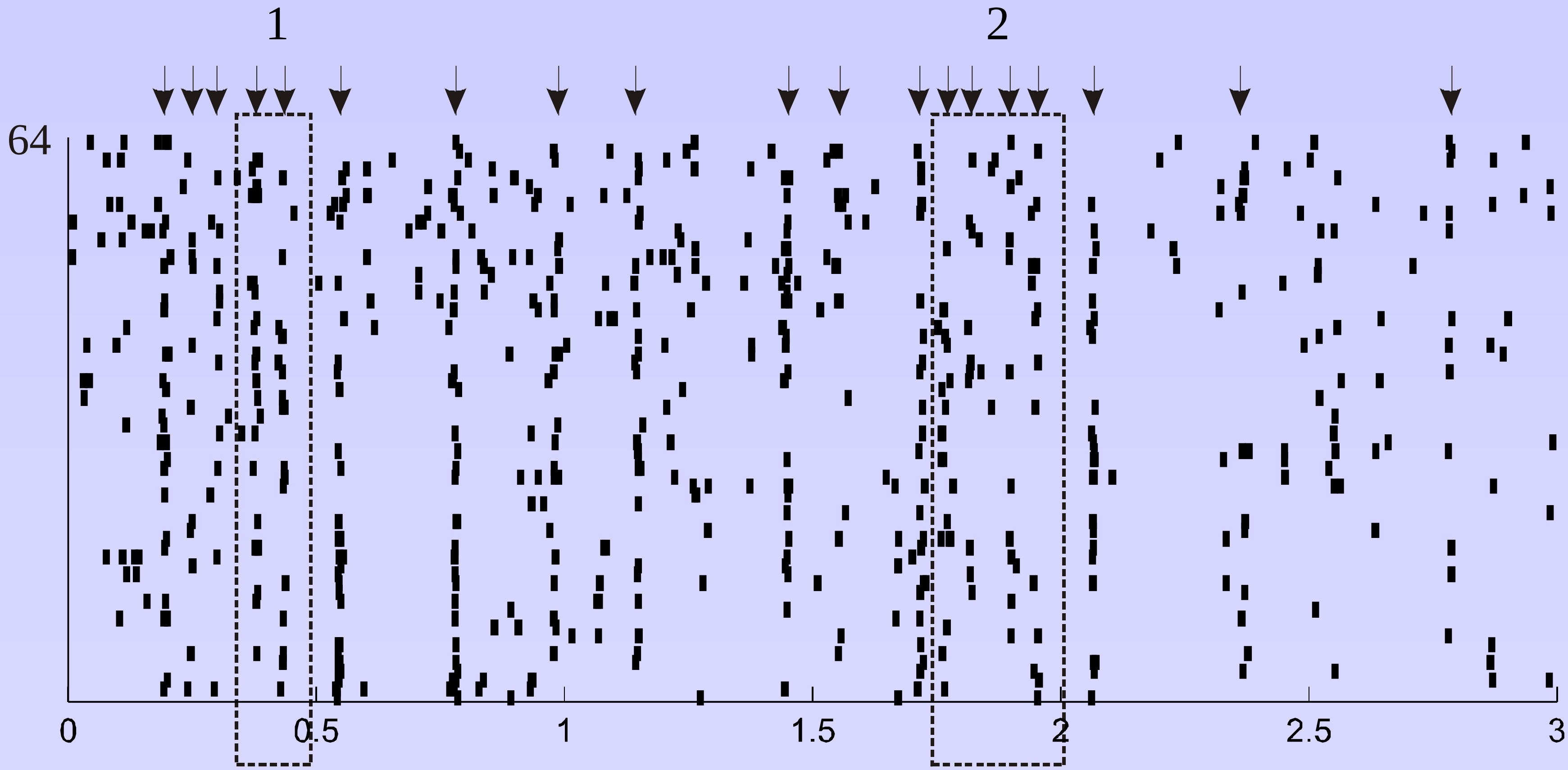
Visual Stimulation

Is there more to ‘global alignments’?

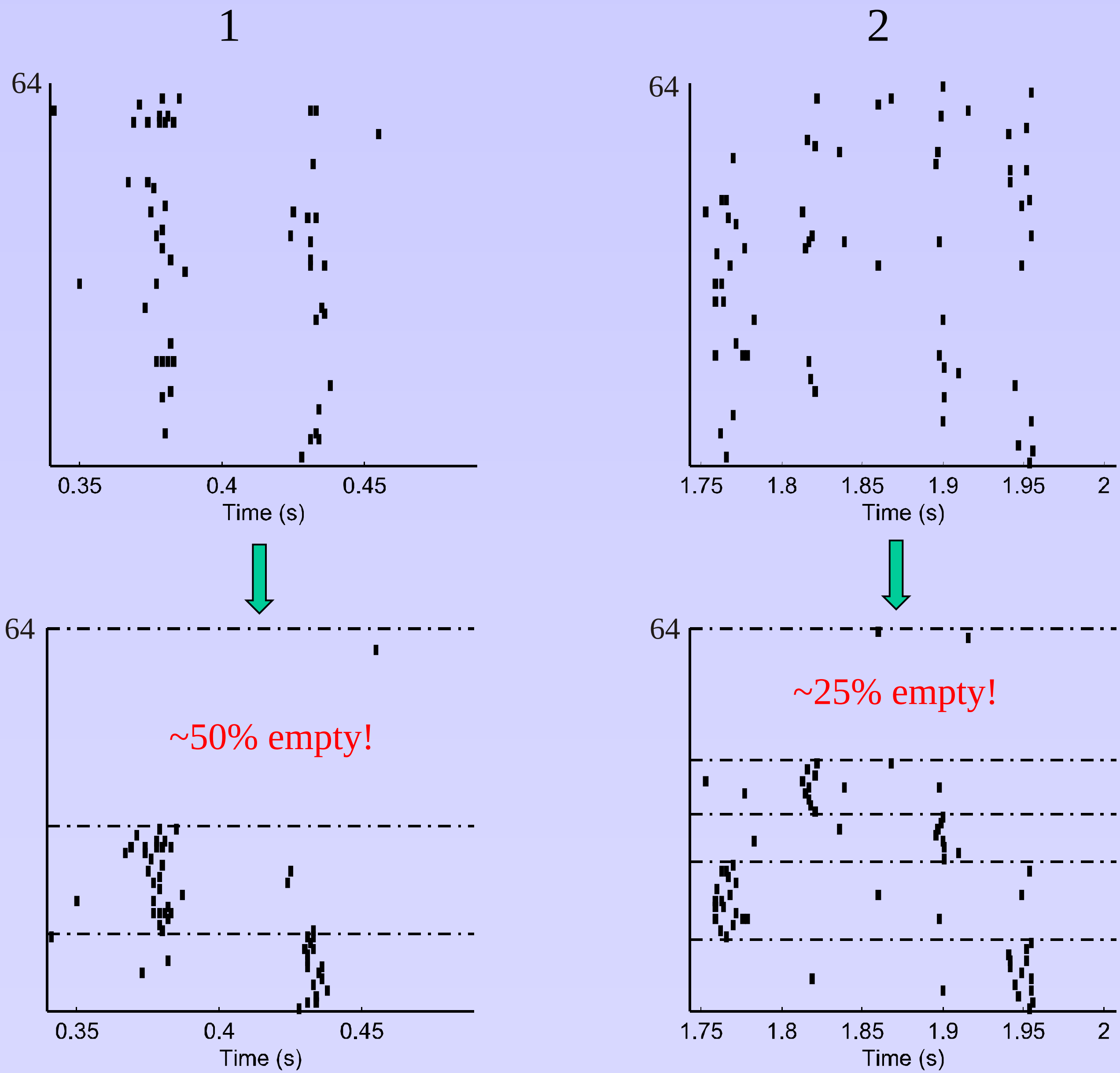
(Buracas, Zador, DeWeese, Albright, 1998)

Spike Patterns in Vivo

- Is there more to ‘global alignments’?



In Vivo: Behaving Monkey, MT



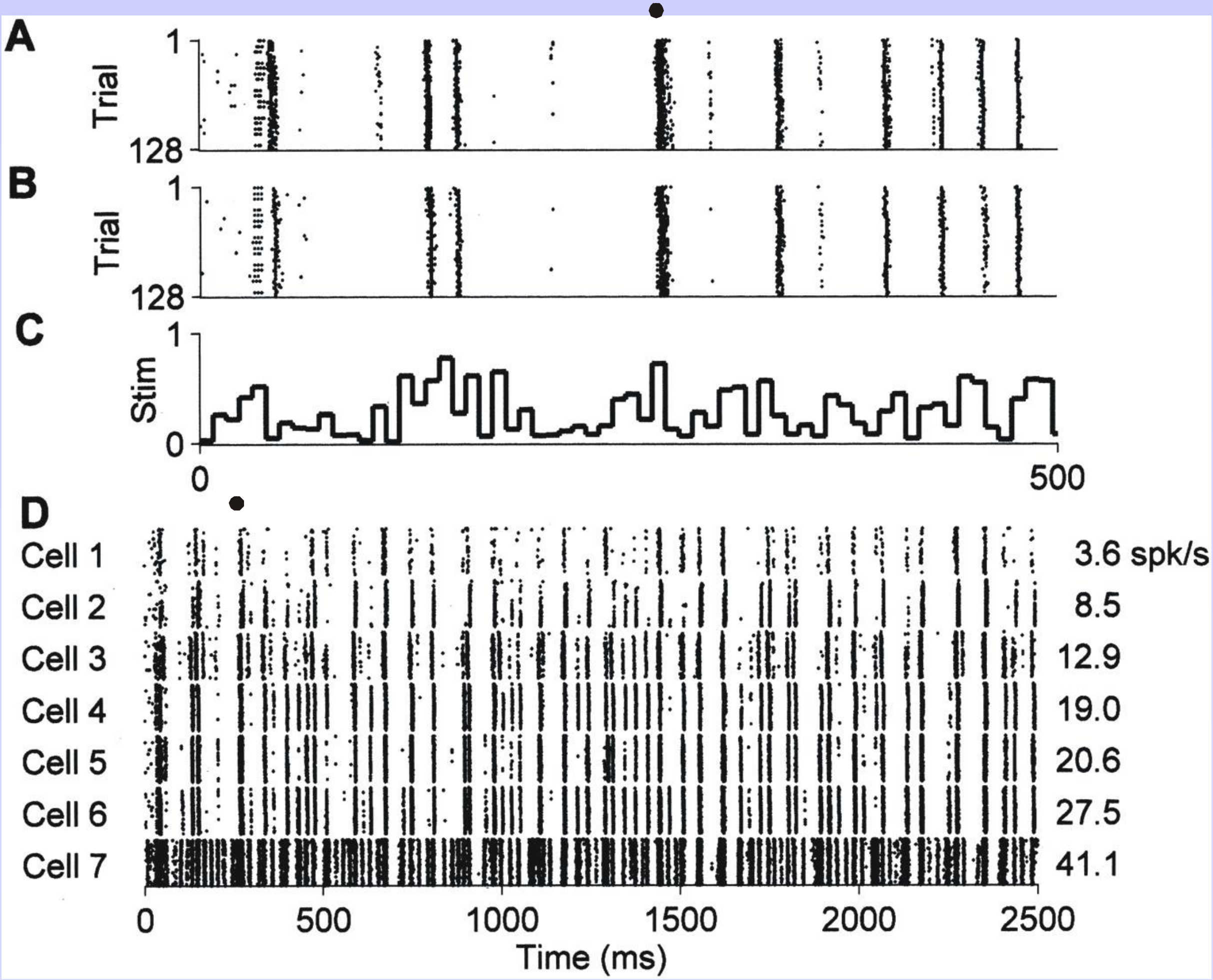
3 clusters

5 clusters

Spike Patterns in Vivo

- Is there more to 'global alignments'?

Within cells
Vs
Across cells

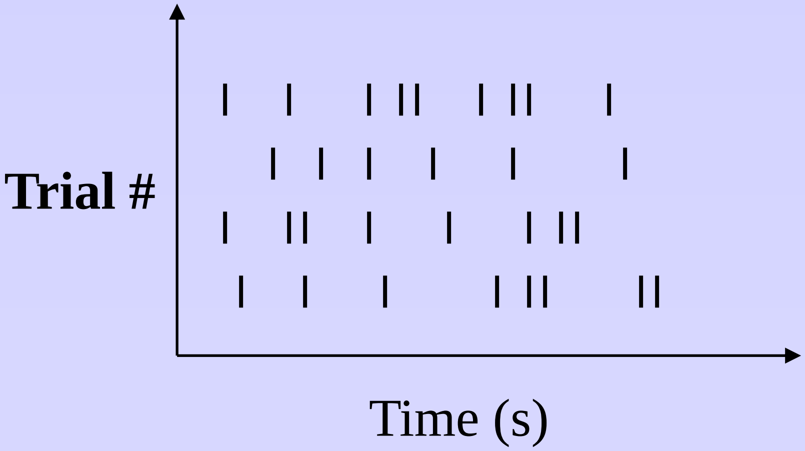


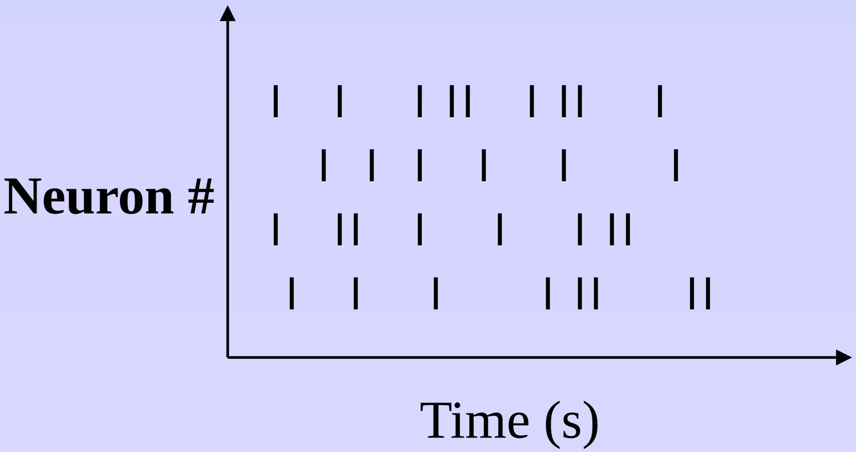
In Vivo: Anesthetized Cat, LGN

- 2 Clusters
- Long-term determinism

Multi-unit spike patterns

From Multiple Trials
to
Multiple Neurons





Spike Patterns *in vitro*?

- Population dynamics in vitro: Are there spatio-temporal patterns of spiking?

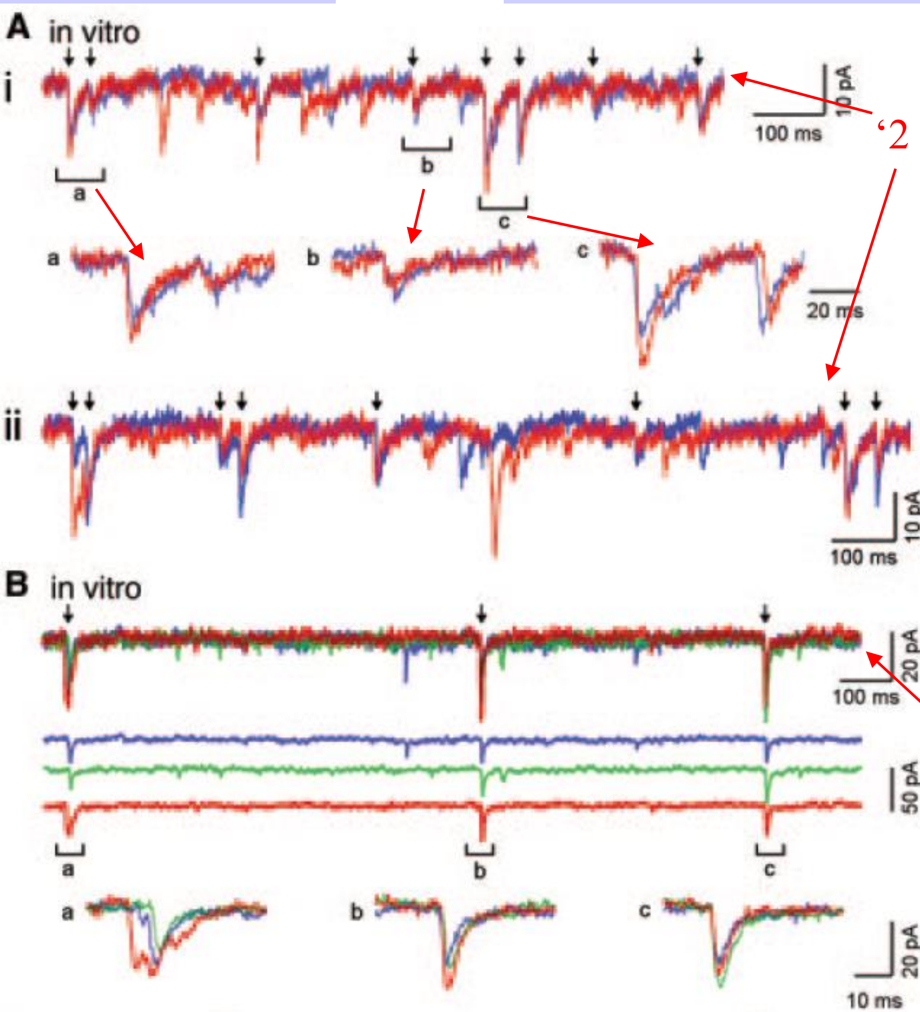
Mice visual cortical slices, Fura2-AM, 2-photon imaging:

(Ikegaya, Aaron, Cossart, Aronov, Lampl, Ferster, Yuste 2004)

Spike Patterns *in vitro/ in vivo*?

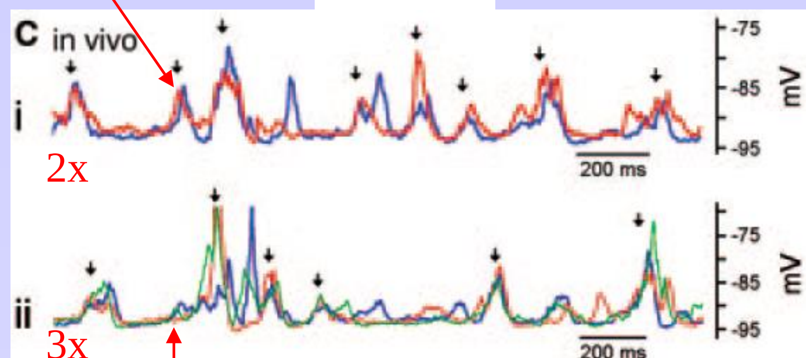
- Record spontaneous post-synaptic events
  → Single cell receives repeating patterns of (near identical) synaptic inputs

E/IPSC



'2 Motifs/Patterns'

E/IPSPs



2x

3x

(Ikegaya, et al 2004)

'3 Motifs/Patterns'

(Ctx, Layer 5, mice)

Spike Patterns *in vitro*?

Repeating pattern of synaptic inputs

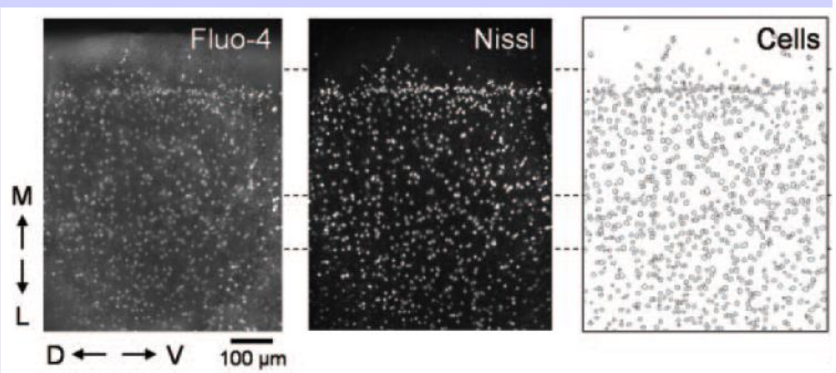
⟺ Repeating pattern of (presynaptic) firing

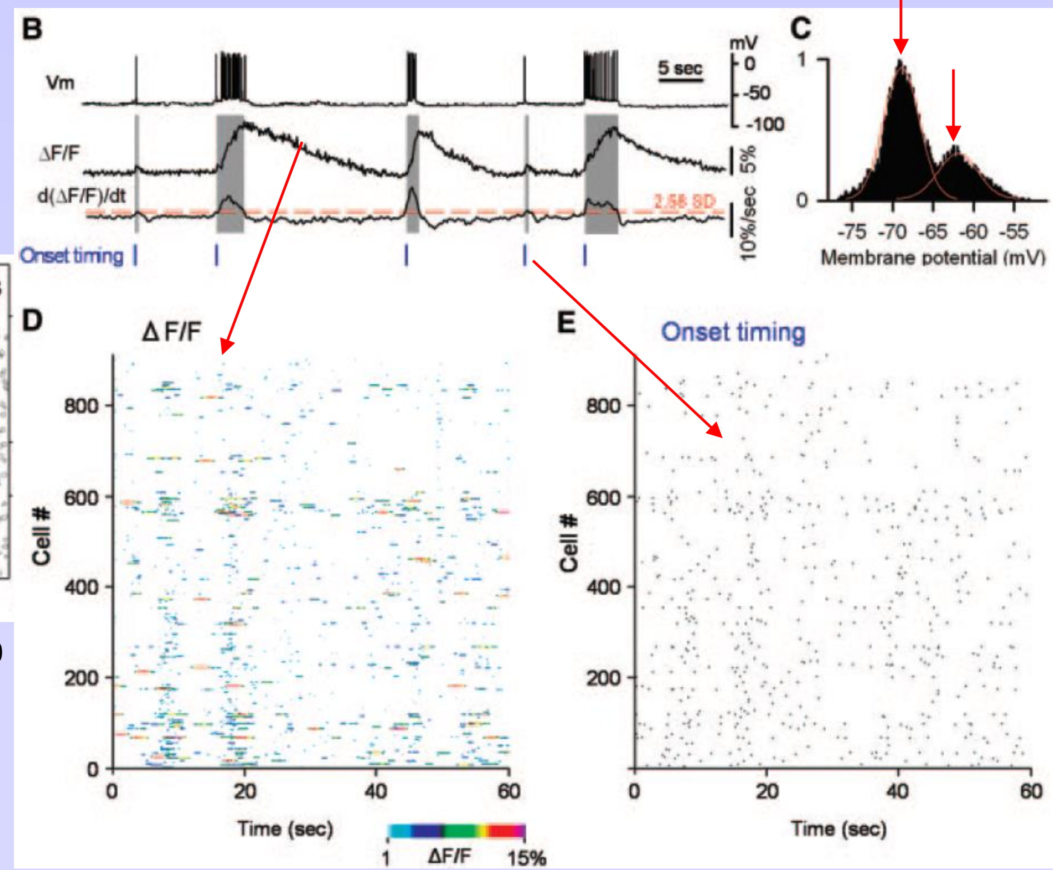
Problem: Need to record from neurons!

Recording from >800 neurons simultaneously.

→ Use calcium imaging

→ 'Bursts' detection

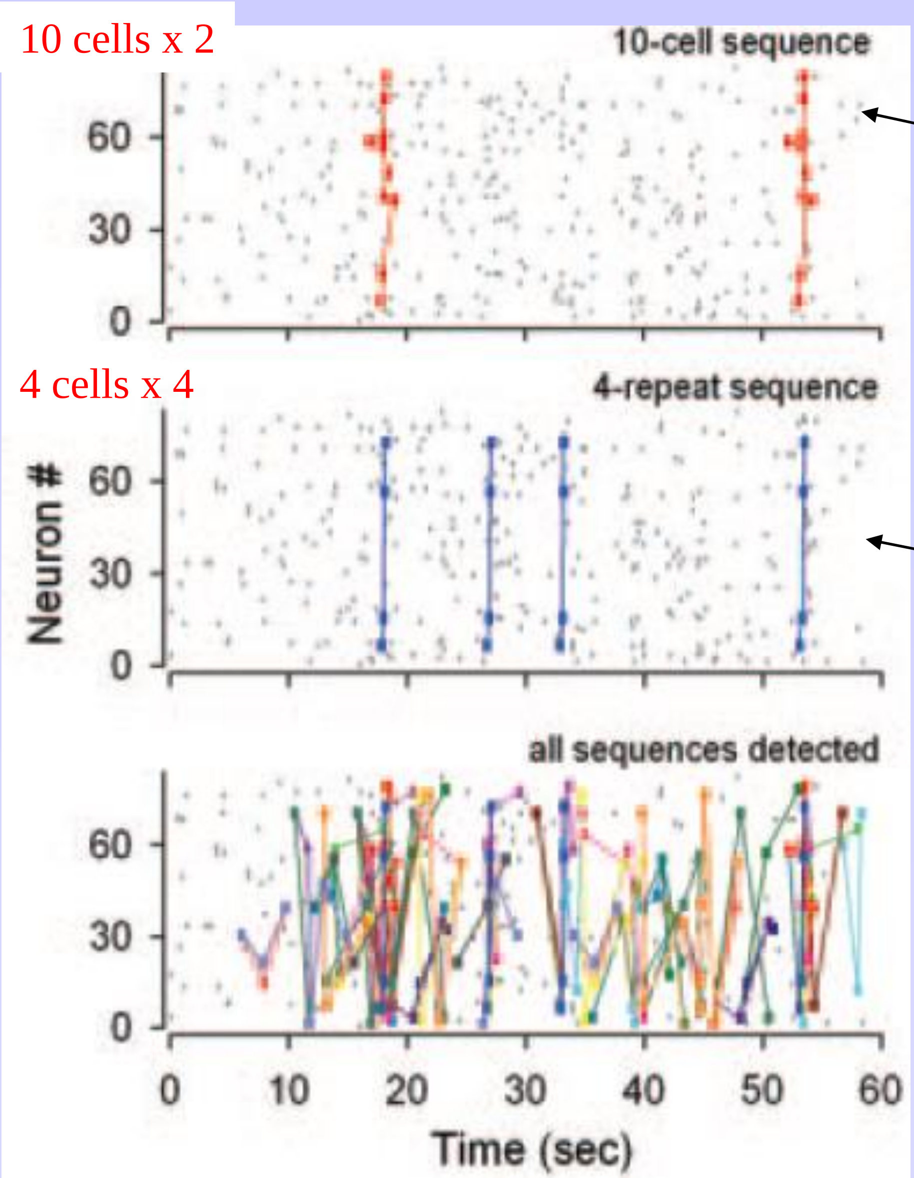


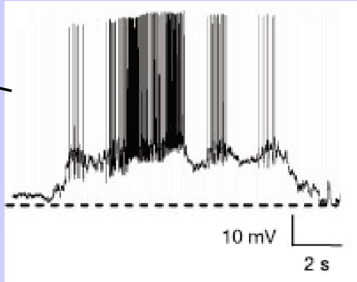


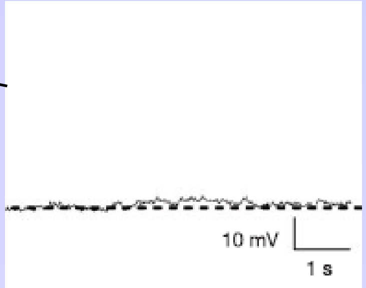
(Ikegaya, et al 2004)

Spike Patterns *in vitro*?

- Repeated Motifs across cell populations





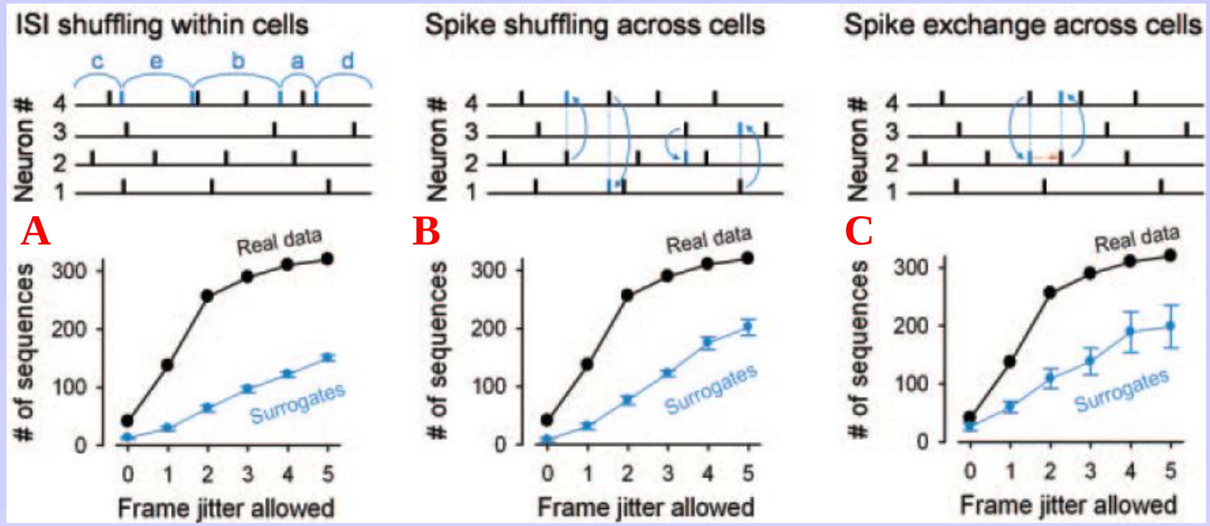


Warning: bursts… not spikes!

Significance and Surrogate Datasets

- Motifs by chance?

Surrogate datasets for controls



'Frame jitter' = 'temporal jitter' in terms of image frames

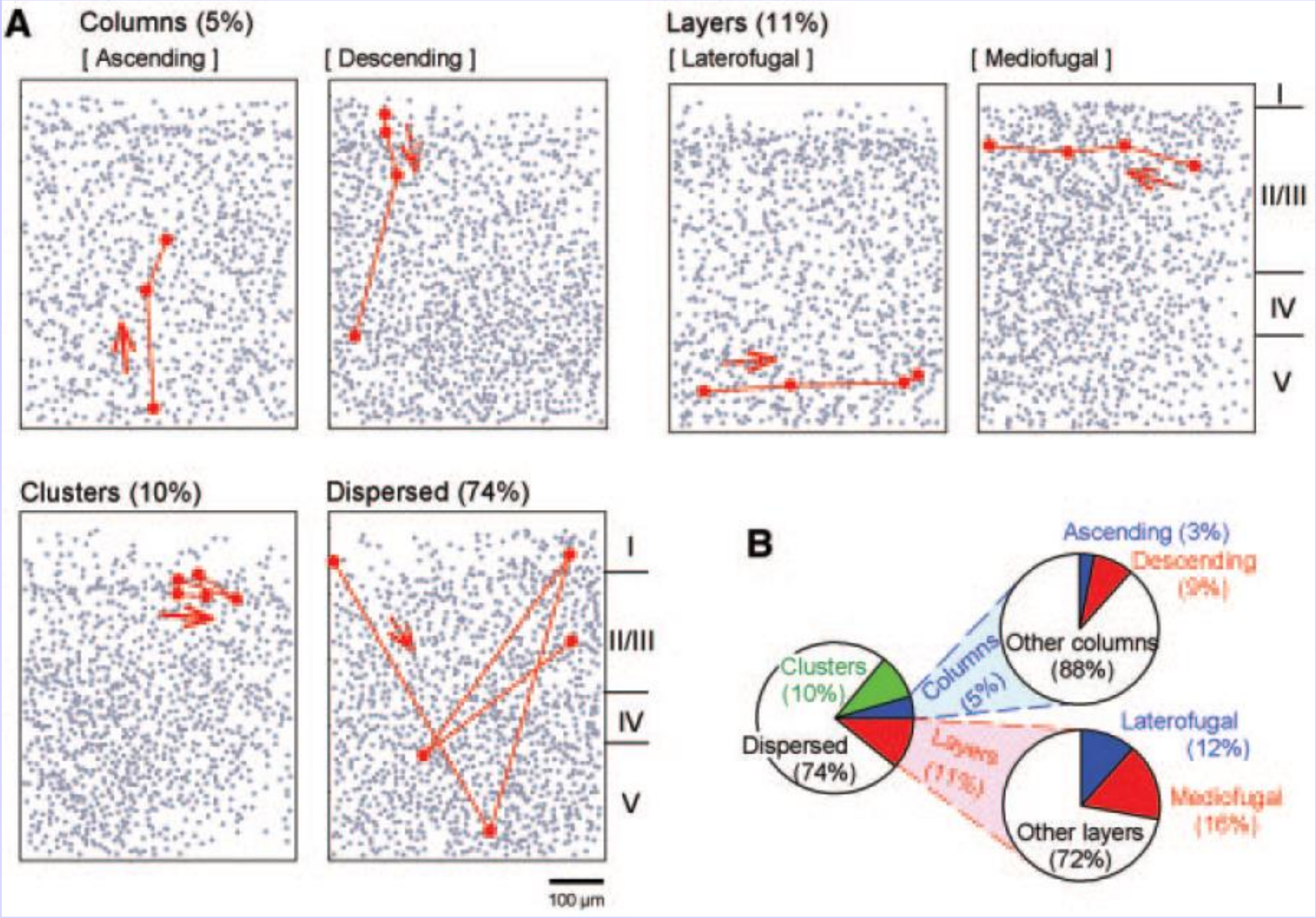
A: Destroys temporal correlations within cells (e.g. oscillations) – Preserves firing rate.
B: Destroys motif cell composition - Preserves partial synchronization.
C: Destroys spike orders within motif - Preserves number of spikes per cell, and population firing modulations.

For more on the debate: → (Mokeichev et al, 2007) → (Ikegaya et al 2008)

Spike Patterns *in vitro*?

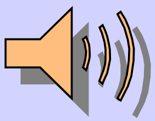
- Is there topographic (spatial) organization for each Motif?

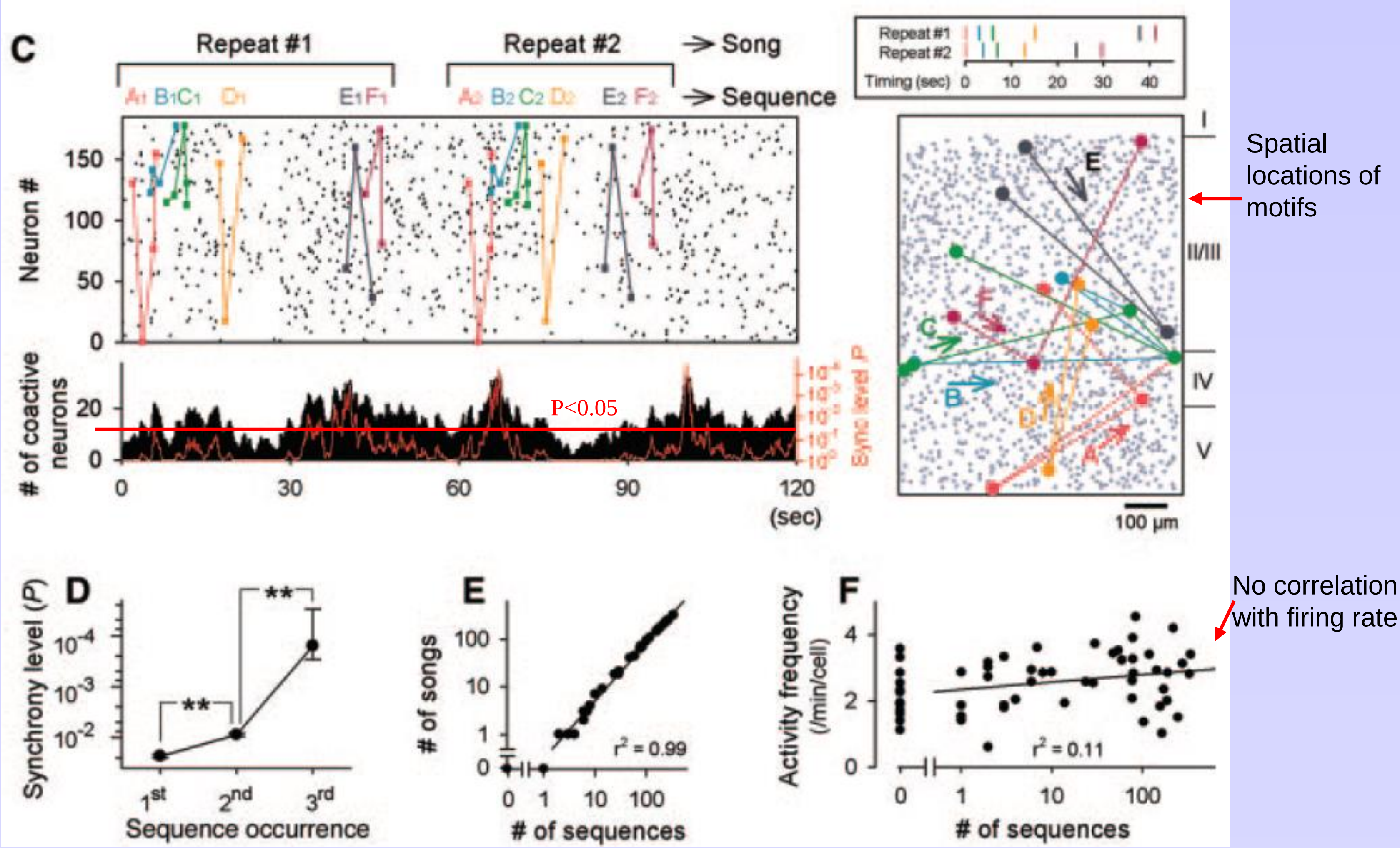
→ classification problem (no theory… yet)



Spike Patterns *in vitro*?

- Motifs of Motifs….Cortical songs



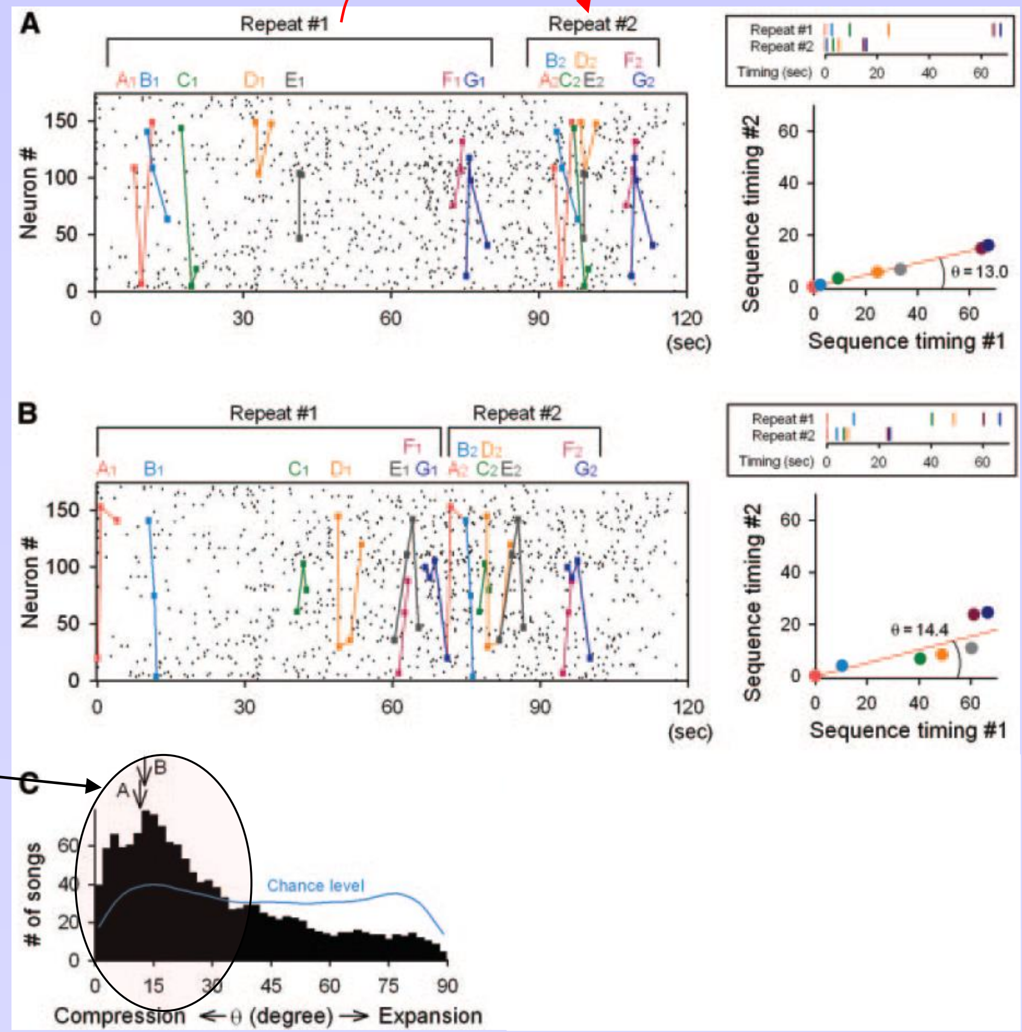


➔ 2 major issues: detecting songs, and assessing their (statistical) significance

Spike Patterns *in vitro*?

- Is there temporal compression?

compression



Most motifs compress in time