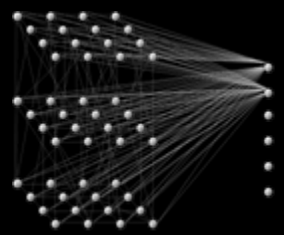
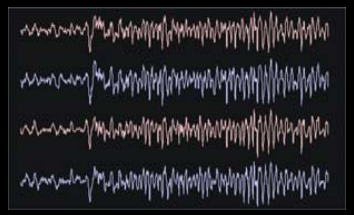
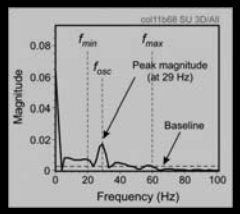
Looking into the brain: where modeling, experiment and analysis meet







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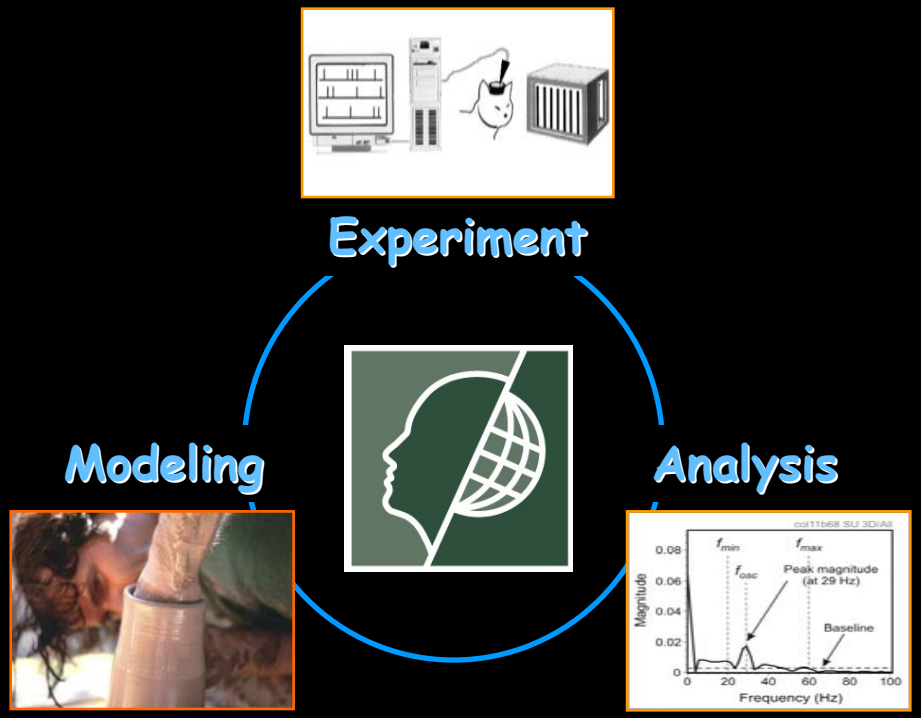
A multiple perspectives approach



- One of the most complex systems known in the universe
- Neuroscience: highly interdisciplinary
- No single approach alone can shed full light on brain function

- **Why modeling?**
  - The brain is very large / inaccessible / fragile
  - To understand and reproduce some fundamental principles

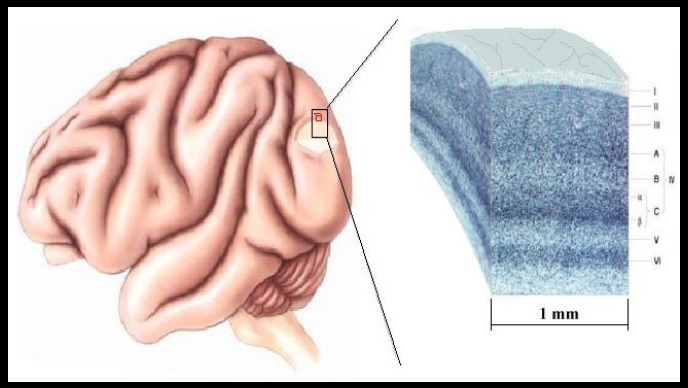
- **Why experiment?**
  - To measure the real system
  - To discover basic phenomena
  - To test hypotheses

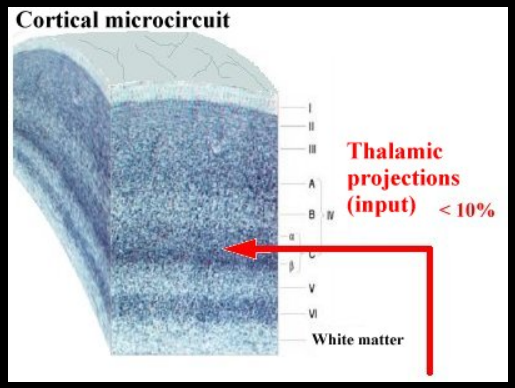
- **Why analysis?**
  - The more data, the more difficult it is to make sense of it
  - Frequently, classical methods fail to reveal complex, nonlinear dynamics

I. Theory and modeling

Neuronal microcircuits

- Microcircuits – building blocks of neocortex
- Canonical structure (Henry Markram, Sten Grillner)





?
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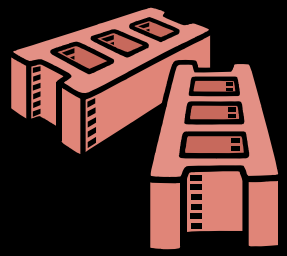
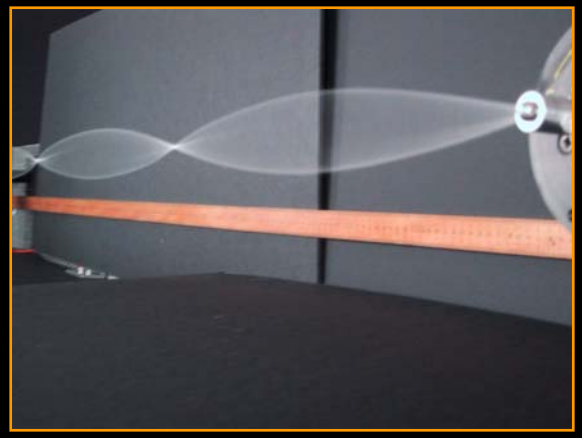


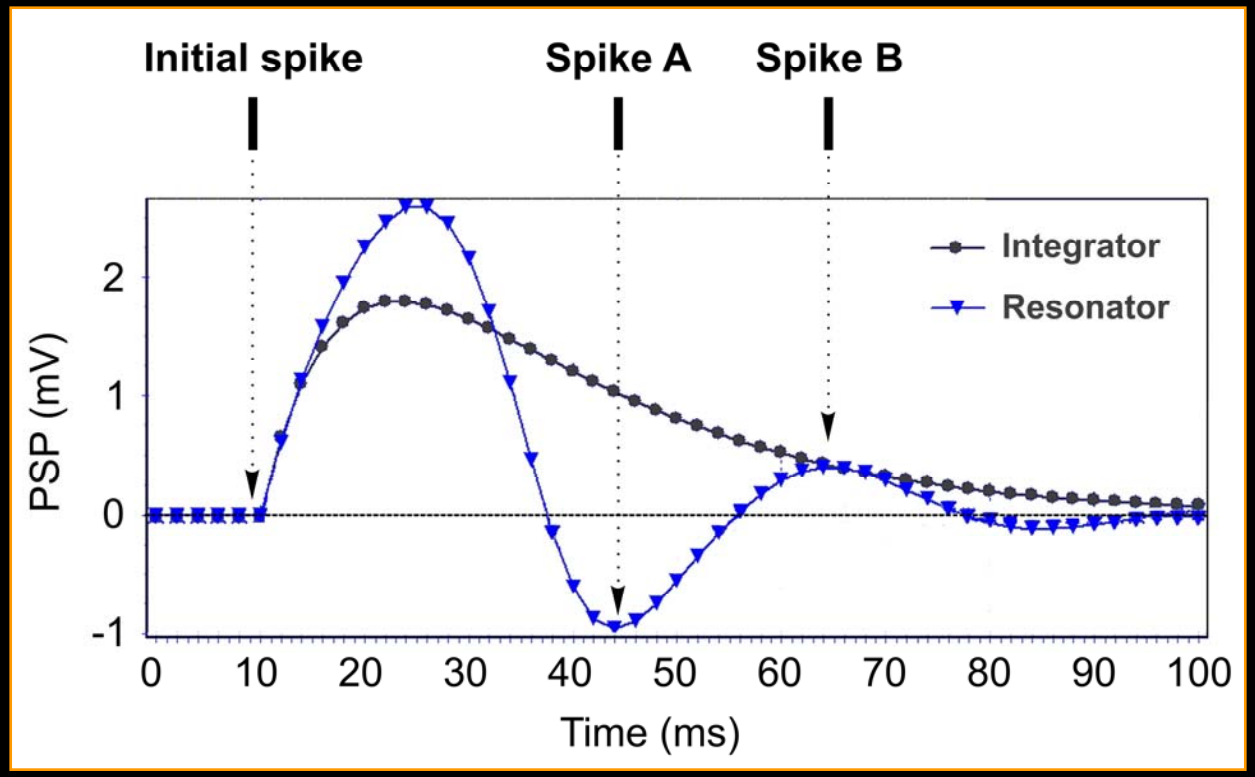
- Focus: *dynamics of microcircuits*
- How do membrane properties influence
  - Stability and excitability

Is there a right time for neurons?

- The concept of *membrane resonance*



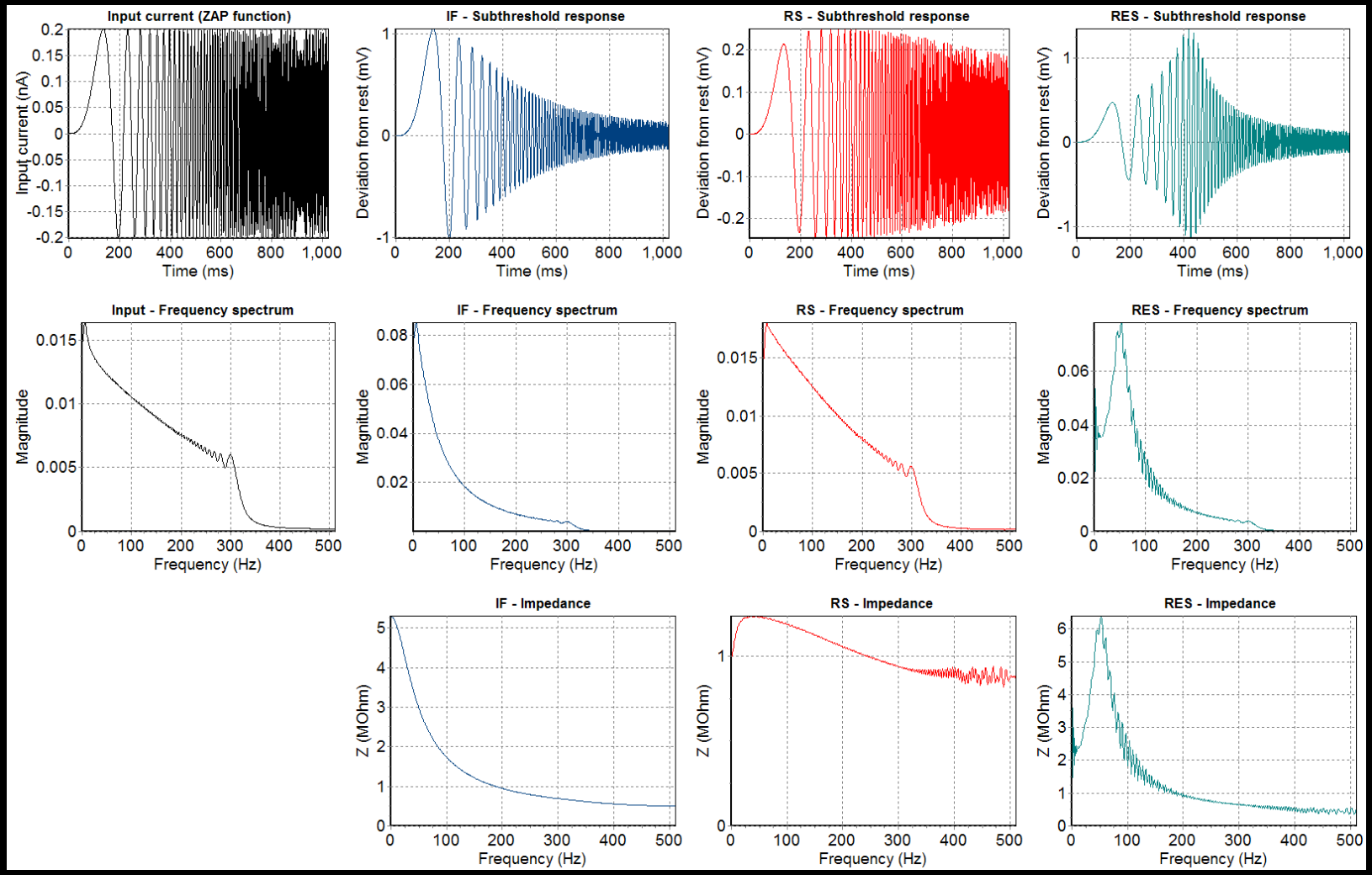
- Low volt. act. Ca^{2+} curr. (I_T)
- Hyperpol. act. cation curr (I_H)
- Interplay of I_{Na} and I_K



- ✓ **Somatosensory cortex** (Hutcheon et al. 1996; Ulrich 2002), **Prefrontal cortex** (Fellous et al. 2001), **Entorhinal cortex** (Erchova et al. 2004; Schreiber et al. 2004), **Thalamus** (Puil et al. 1994), **Hippocampus** (Leung and Yu 1998), **Interneurons** (Pike et al. 2000)

Integration versus Resonance

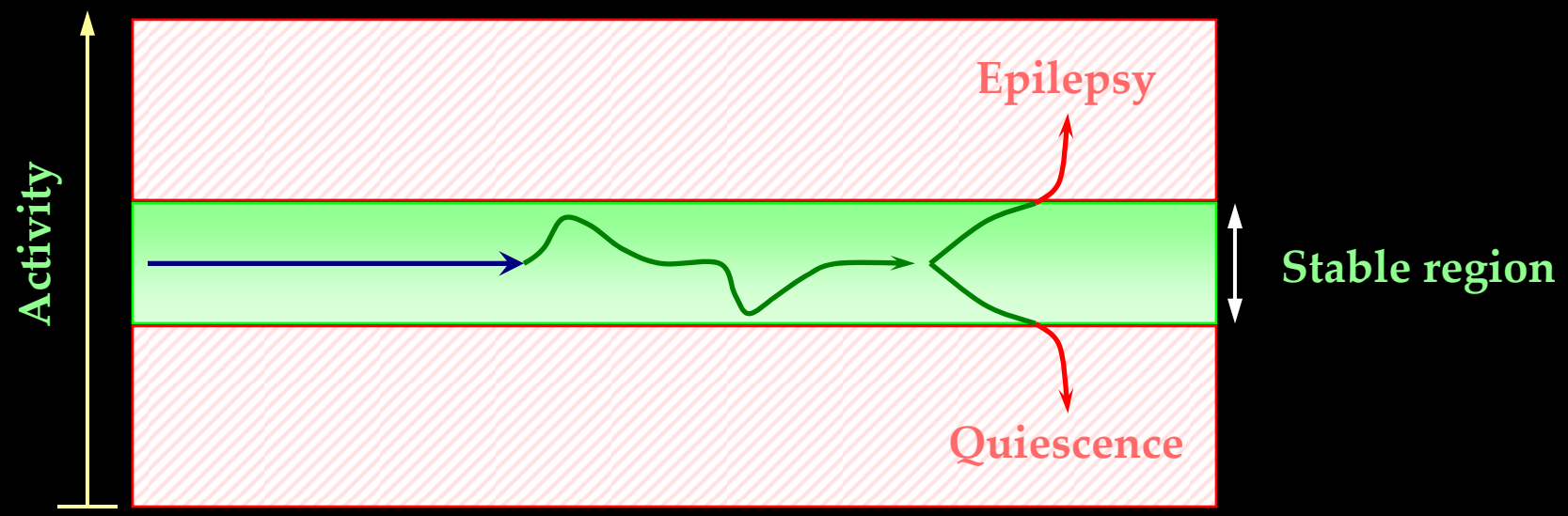
- ZAP input current (Puil et al., 1986 *J Neurophysiol*)



Muresan & Savin (2007), *J Neurophysiol* 97:1911-1930.

The stability / excitability dilemma

- *Sustained activity* requires *stability* (energy efficiency)



- Excitability and stability are quite incompatible

Very Stable => usually NOT Excitable

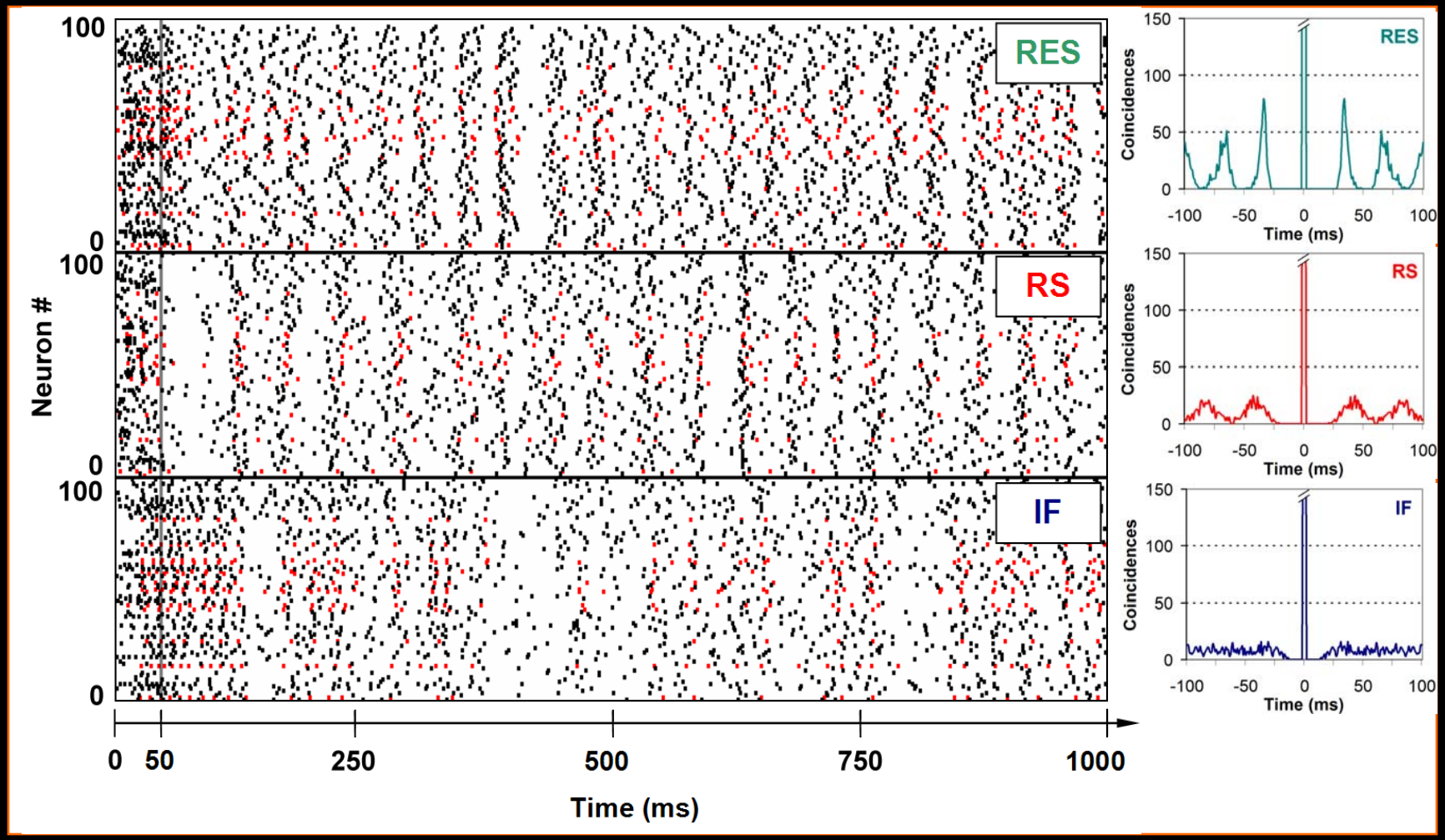
Very Excitable => usually NOT Stable

(especially in systems with positive feedback)

Networks with integration or resonance?

- Large recurrent networks (computer simulation)

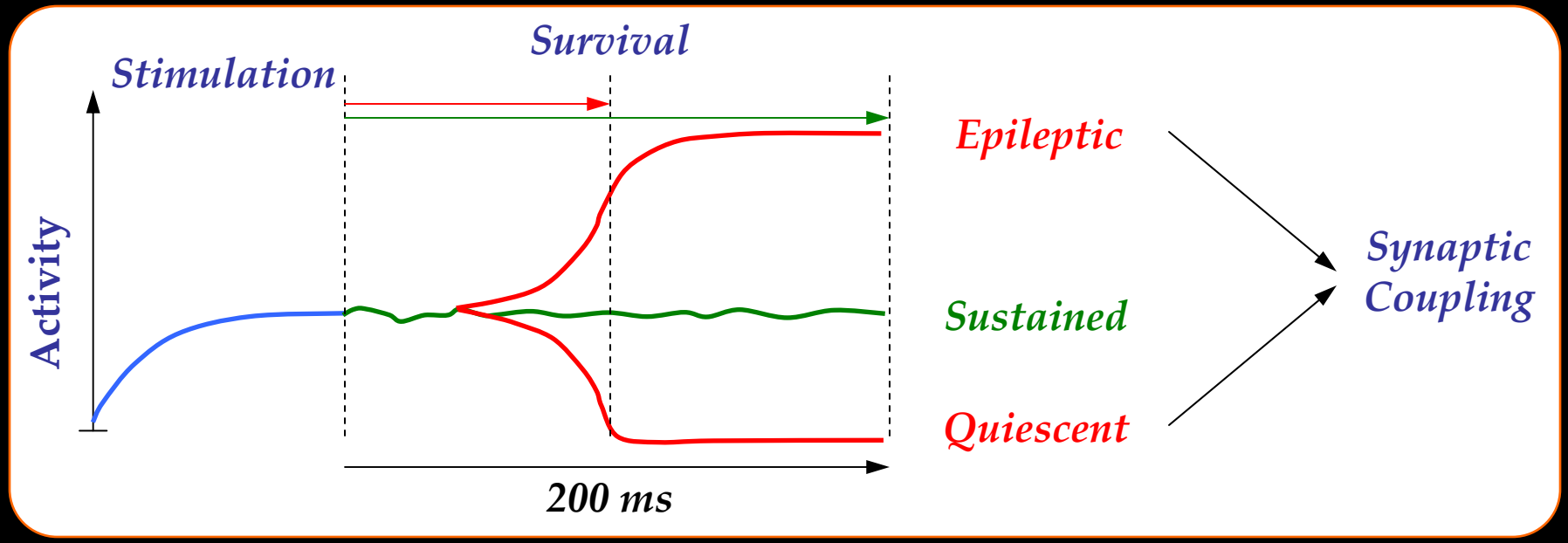
IF = Integrate&Fire; RS = Regular-Spiking; RES = Resonance



Muresan & Savin (2007), *J Neurophysiol* 97:1911-1930.

Stability test I.

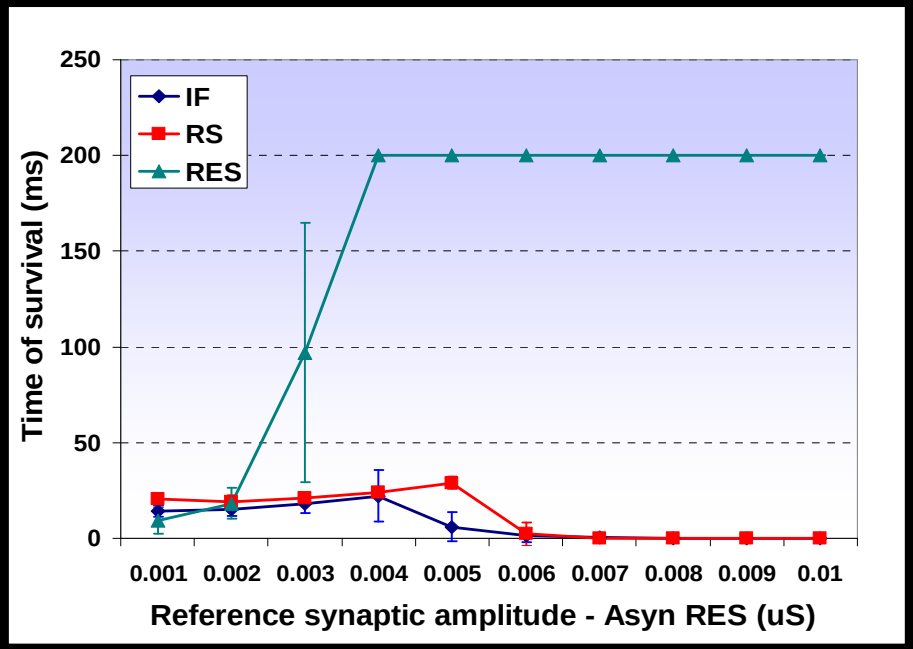
- Test setup

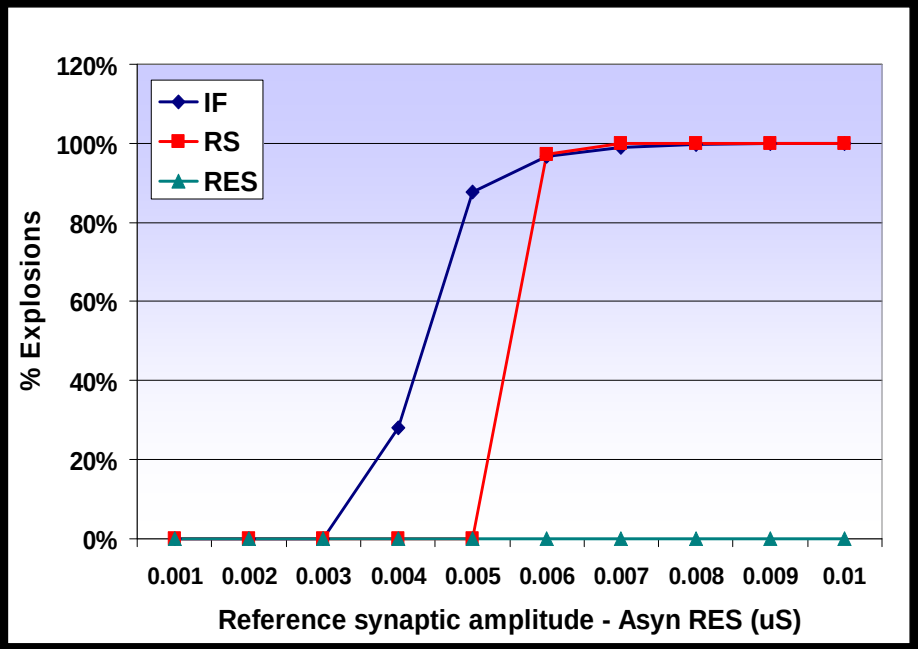


- Relevant parameter: *synaptic coupling*
- 3 *identical networks* (IF, RS, RES)

Stability test II.

- Time of survival + %Epileptic nets



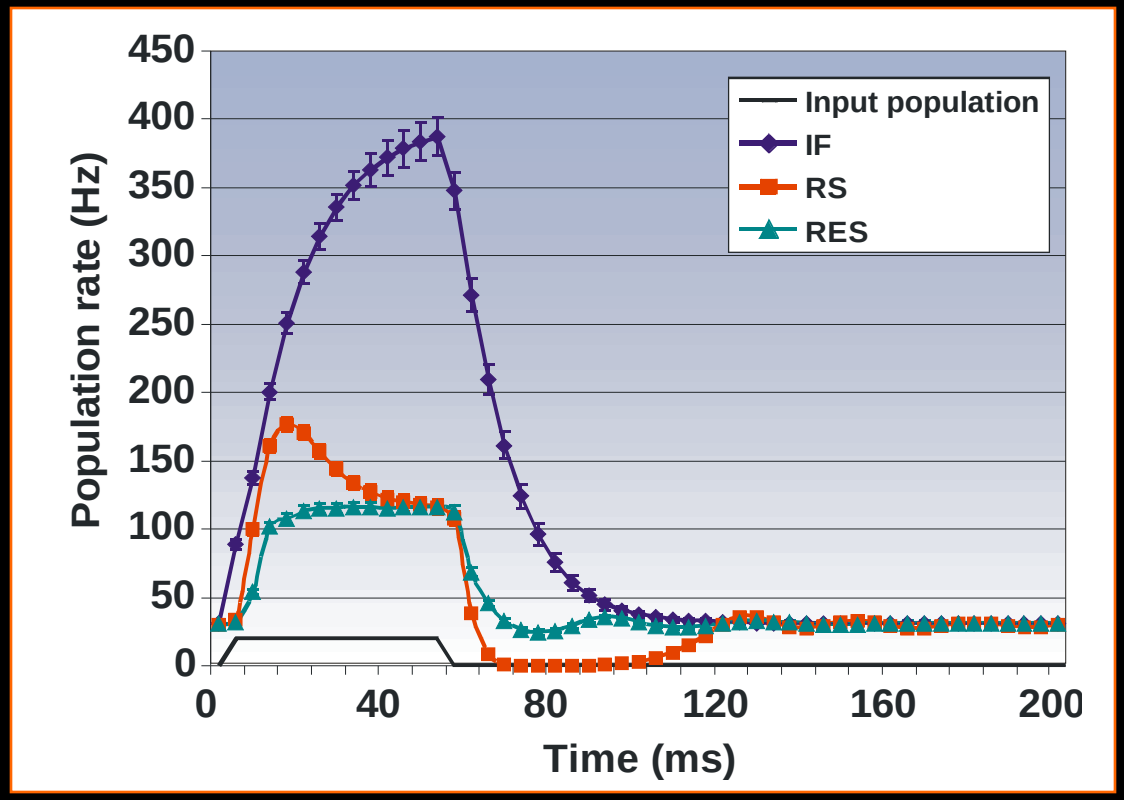


Syn. Coupling:	*Weak*	*Medium*	*Strong*
IF:	↘	↗	↗
RS:	↘	↘	↗
RES:	↘	—	—

Muresan & Savin (2007), *J Neurophysiol* 97:1911-1930.

Excitability test

- Stimulation of 3 sustained networks

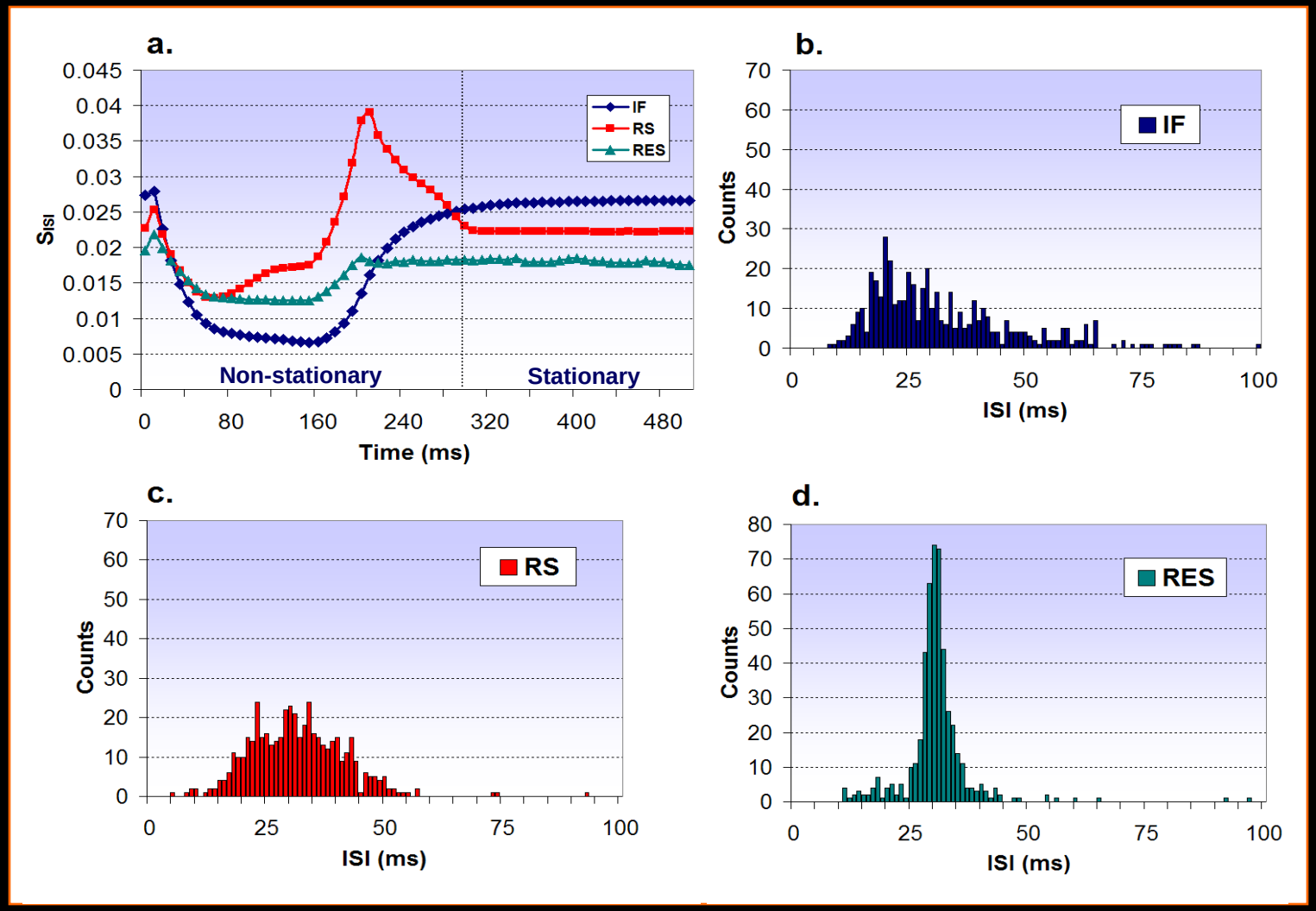


- IF: *very responsive*
- RS: *mild response*
- RES: *reluctant to input*

Muresan & Savin (2007), *J Neurophysiol* 97:1911-1930.

Temporal patterns

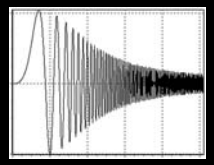
- Population ISI randomness (S_{ISI}: Muresan and Savin, 2007)



Muresan & Savin (2007), *J Neurophysiol* 97:1911-1930.

Integration + Resonance = Rate + Time ?

Integration



Unstable networks

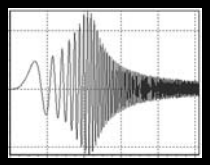
Hardly oscillating

Many degrees of freedom

Very responsive

<u>Rate</u>

Resonance



Stable networks

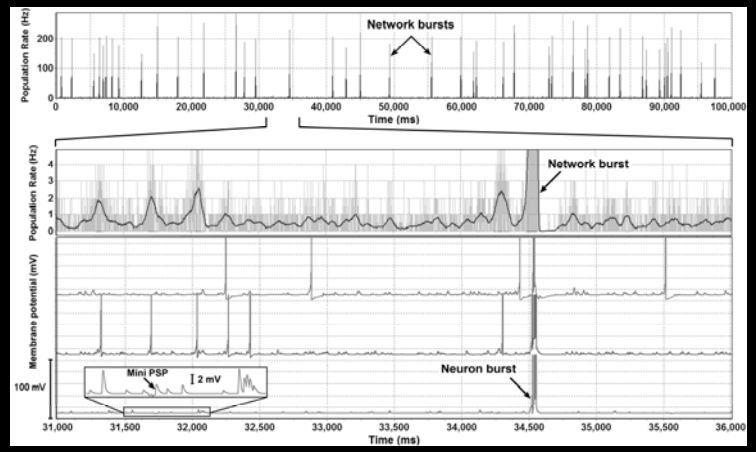
Oscillations are intrinsic

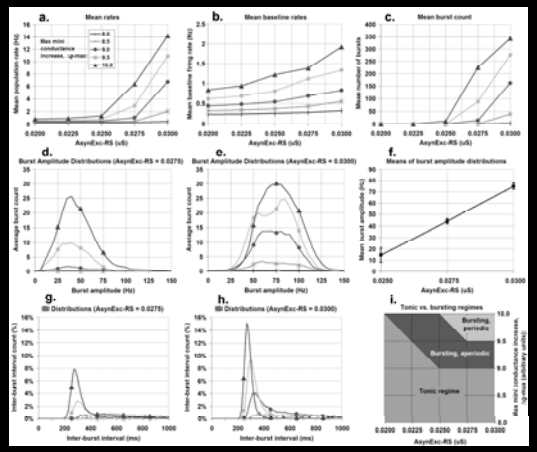
Order

Reluctant to input

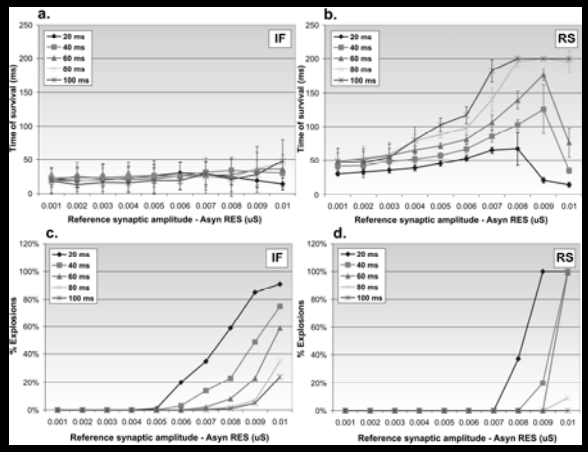
<u>Time</u>

More details





Spontaneous activity and minis in cortical slabs (Timofeev et al 2000) and *in vivo (Paré et al. 1997; 1998)*



Synaptic delays and stability

Muresan & Savin (2007), *J Neurophysiol* 97:1911-1930.

Conclusion

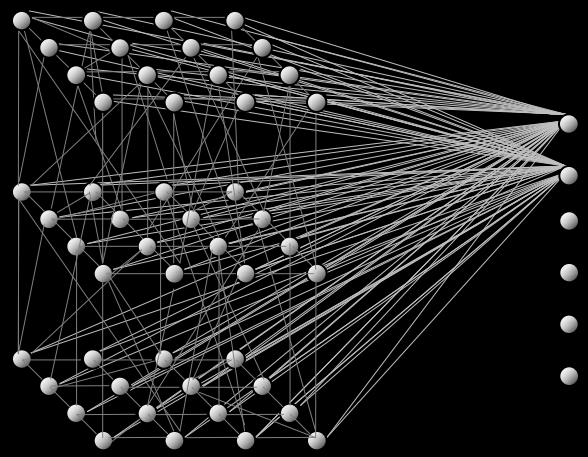
- Modeling can help us understand fundamental phenomena

II. Modeling & Experiment

Decoding brain circuits: neurons read neurons

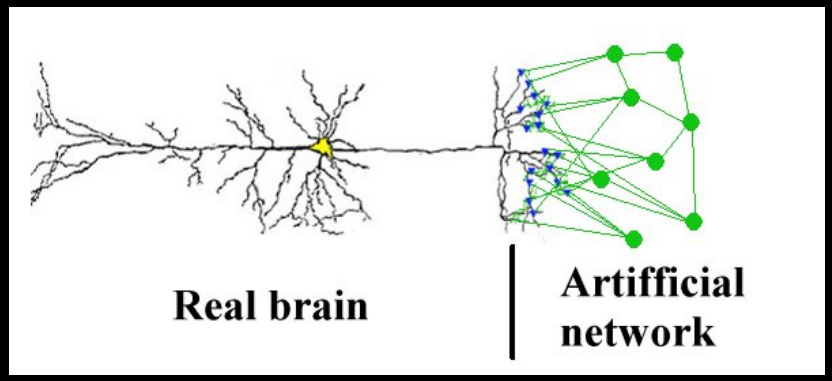
- Inspired from microcircuit model studies

Microcircuit

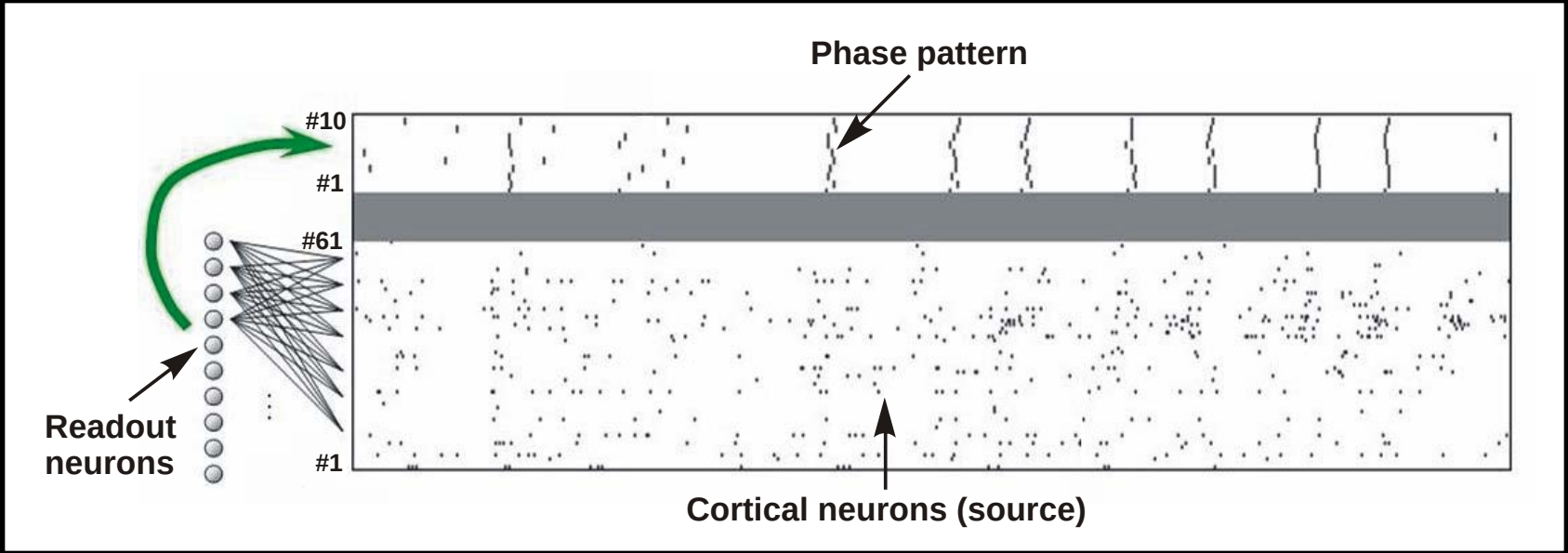


Analysis population

- Neurons read neurons !



Searching temporal patterns in the data

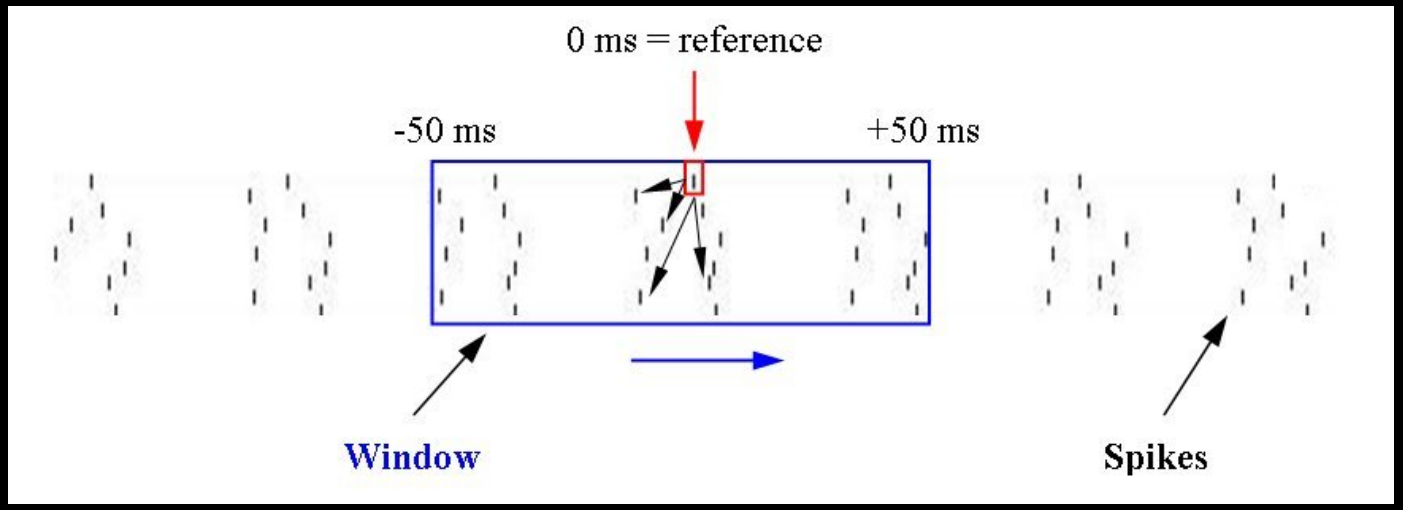


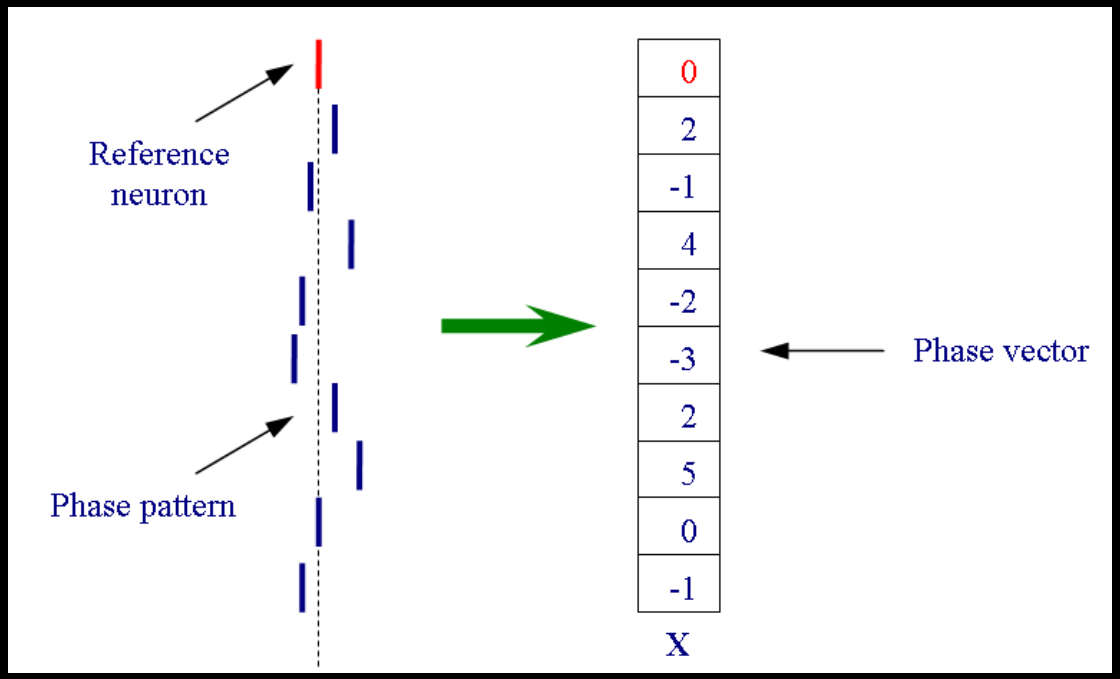
Cortex space → **Artificial neurons space**

- Reduce dimensions
- Preserve temporal information
- Reduce the influence of firing rate

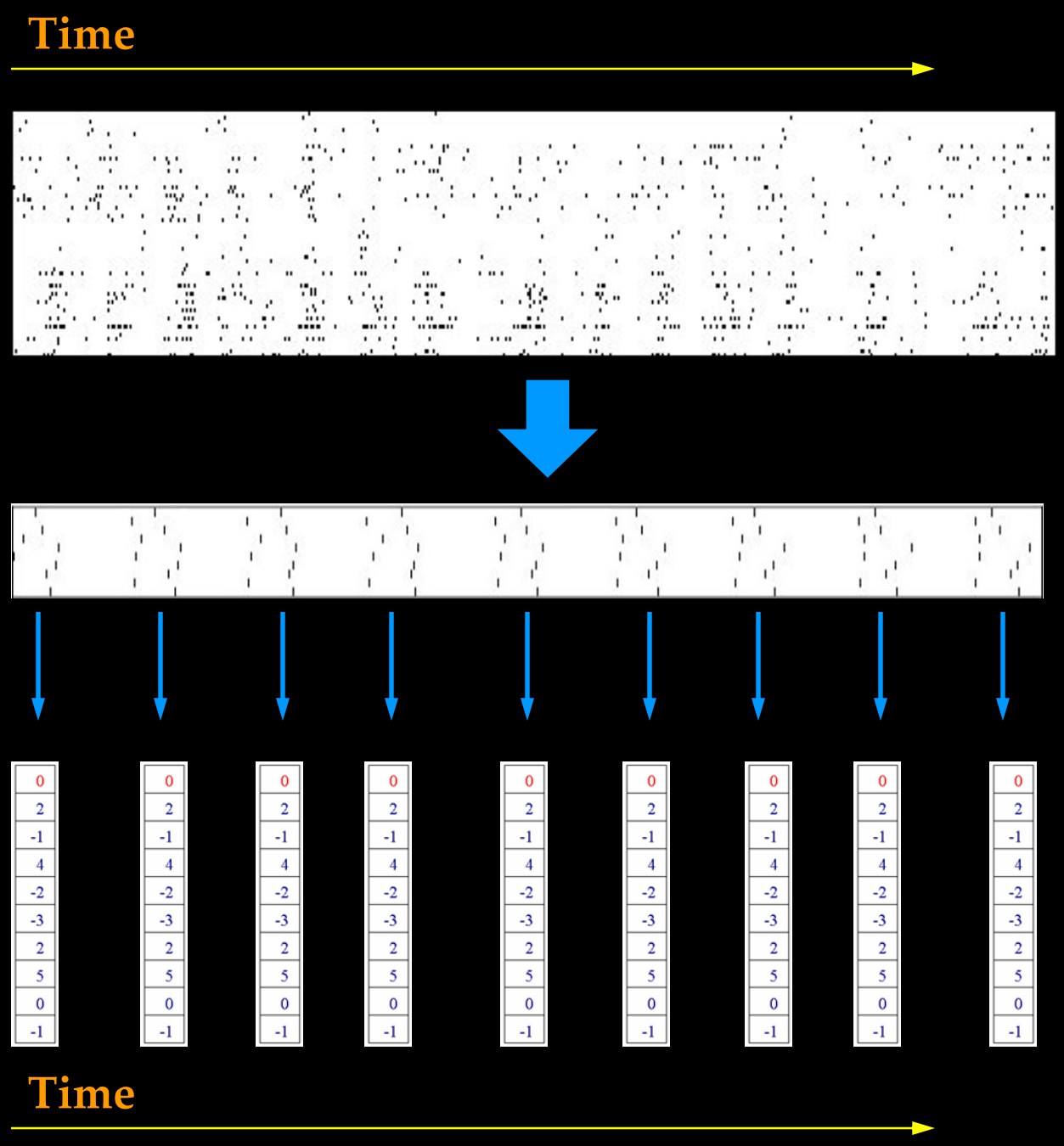
Muresan et al. (2008), *LNCS Springer* 5164, 498-507.

Phase patterns in the artificial neurons space



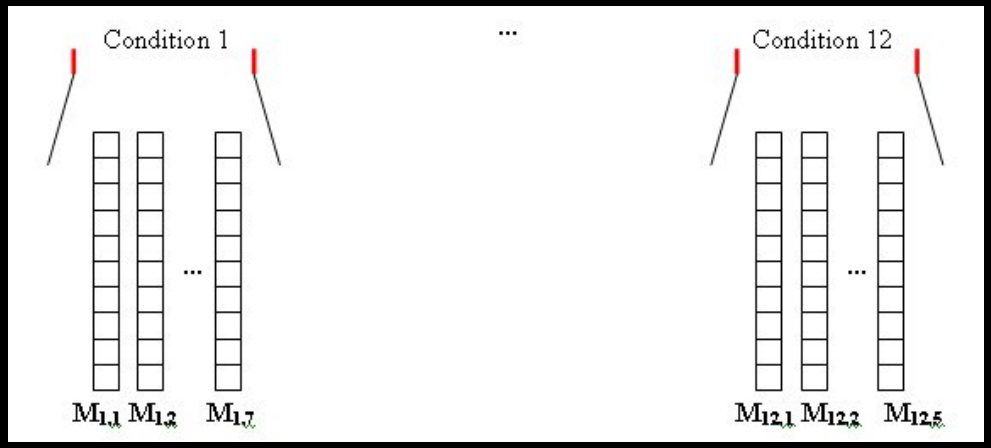


Muresan et al. (2008), *LNCS Springer* 5164, 498-507.


Time
Data space
Pattern space
Phase vector space
0 2 -1 4 -2 -3 2 5 0 -1
Time

- Do phase vectors contain information about stimulus?

- Build the "InfoPhase" classifier



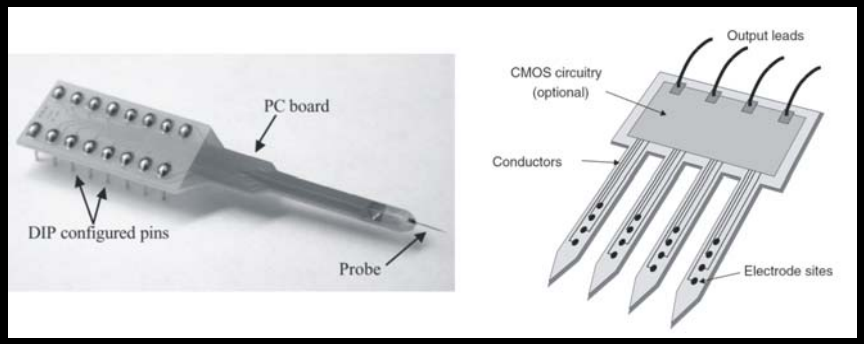
Compute a set of model vectors for each class

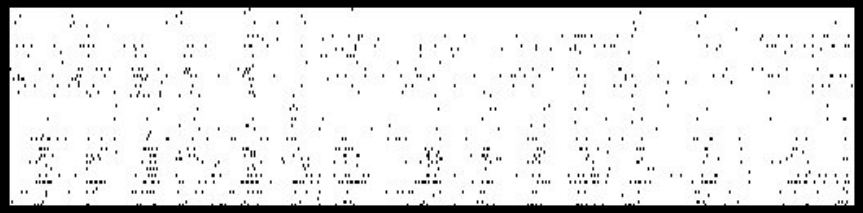
(class = experimental condition)

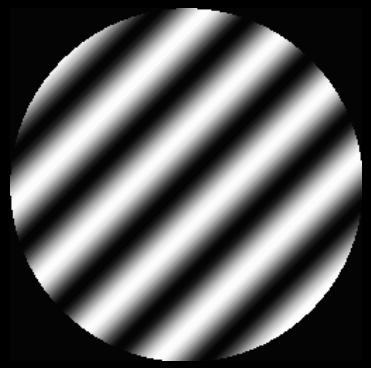
- Identify the class of a new trial based on the models

Analysis of experimental data

- Data from cat experiments in Max Planck, Frankfurt







- Anesthetized cat preparation – Area 17
- 32 channels recorded (2 probes), 64 SUs after sorting
- 12 stimuli (different drifting direction of grating)
- half trials used for training and half for testing the system

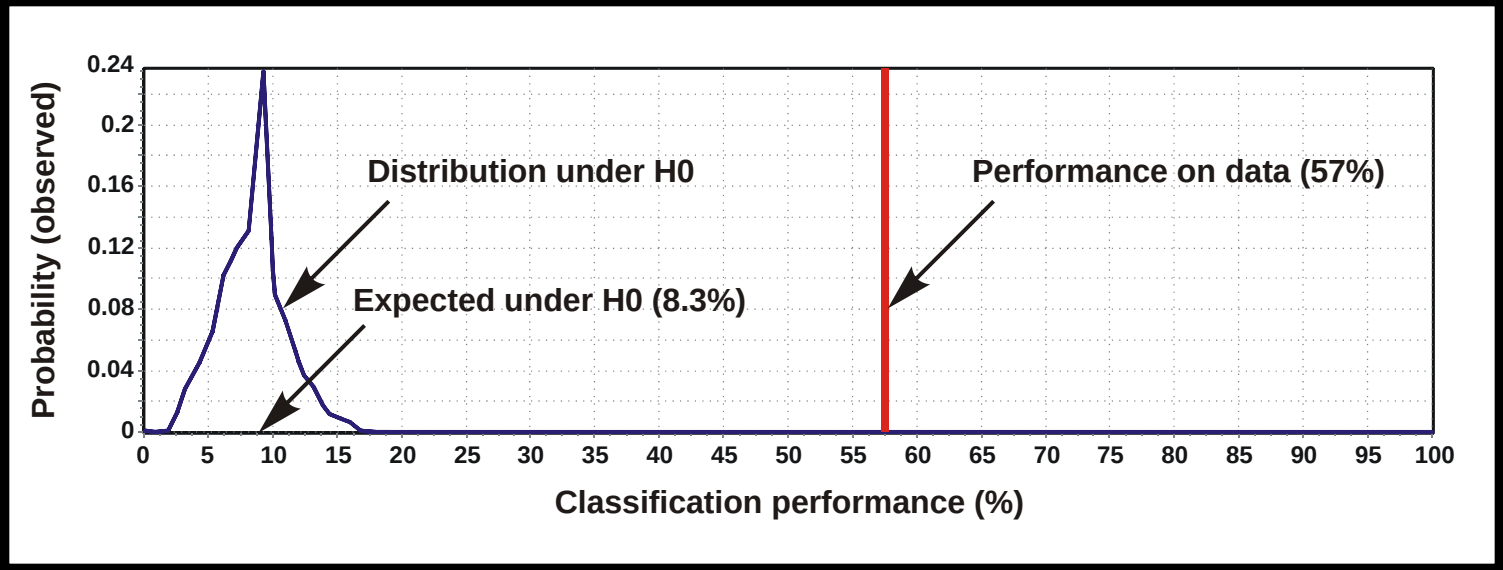
Classification performance:

- Identify what the cat was looking at from the recorded spikes

57% correct classification

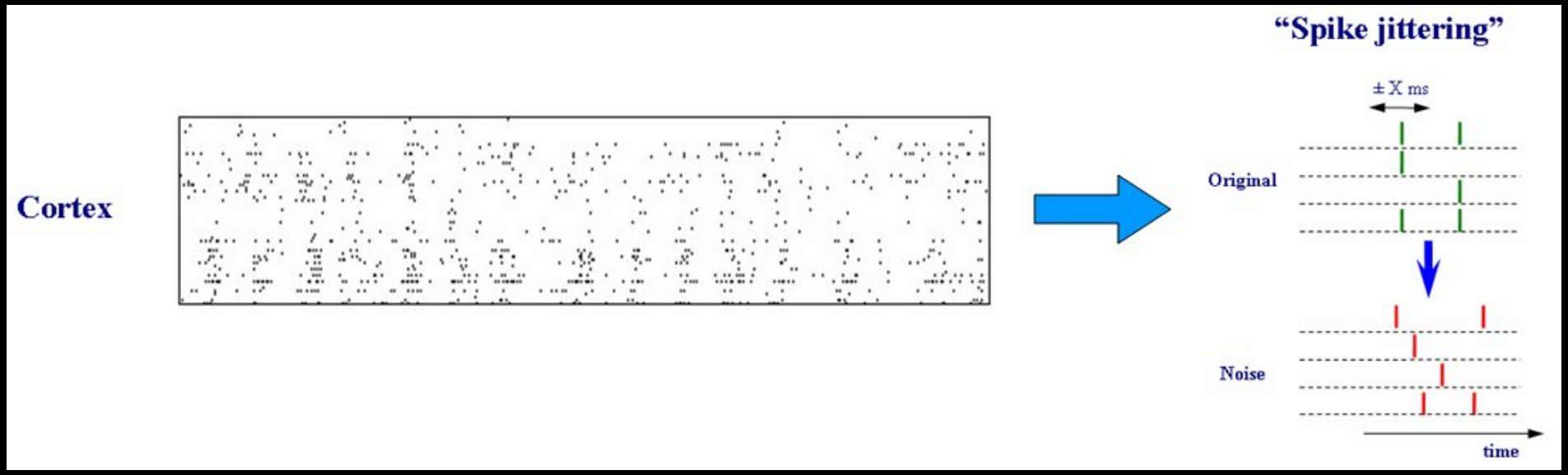
(chance: 8.3%)

Statistical significance (H_0 chance): $p << .001$



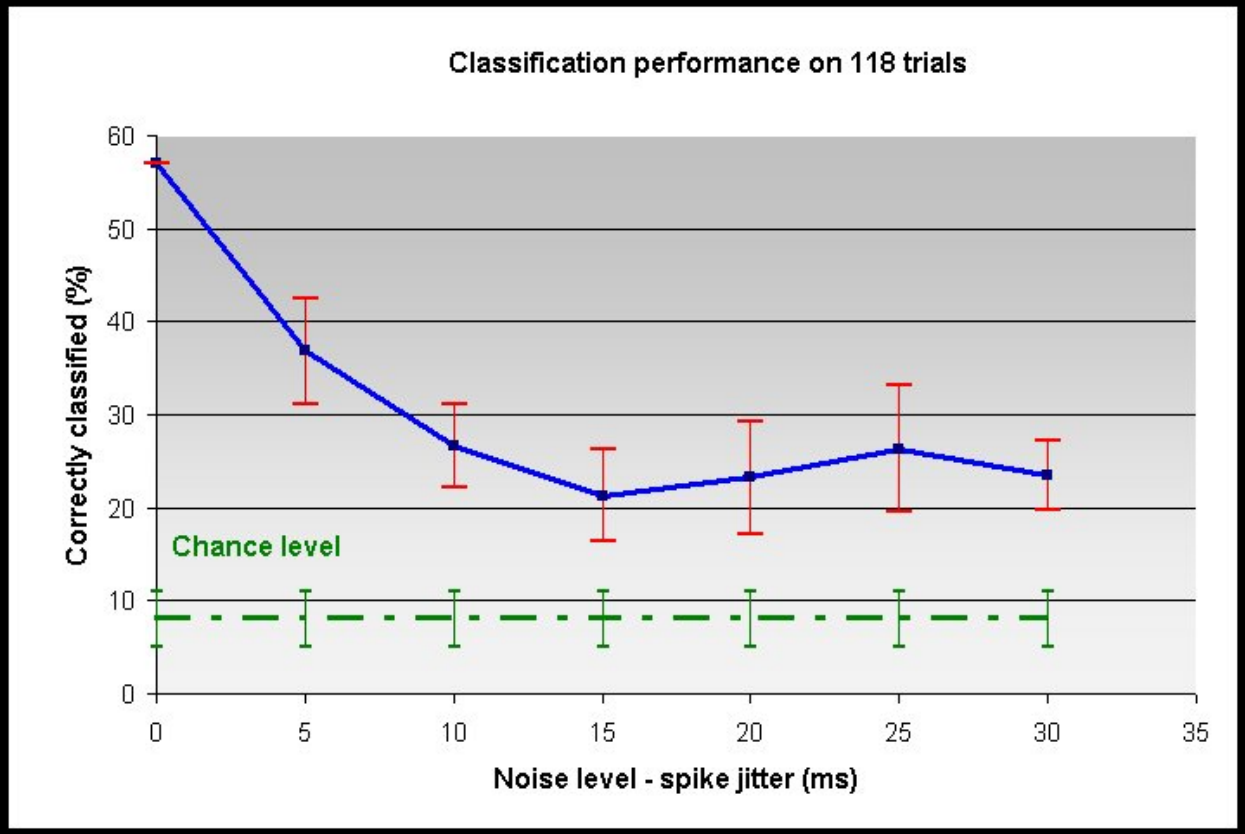
Muresan et al. (2008), *LNCS Springer* 5164, 498-507.

- Phase patterns – contain stimulus related information
- What kind of information is extracted from data?
- Temporal coding?



Temporal jitter of recorded spikes (jitter the data)

- Mean firing rate is not affected.
- Fine temporal code => classification performance should drop!



Muresan et al. (2008), *LNCS Springer* 5164, 498-507.

- Artificial neurons extract information encoded in the timing of spikes from primary visual cortex

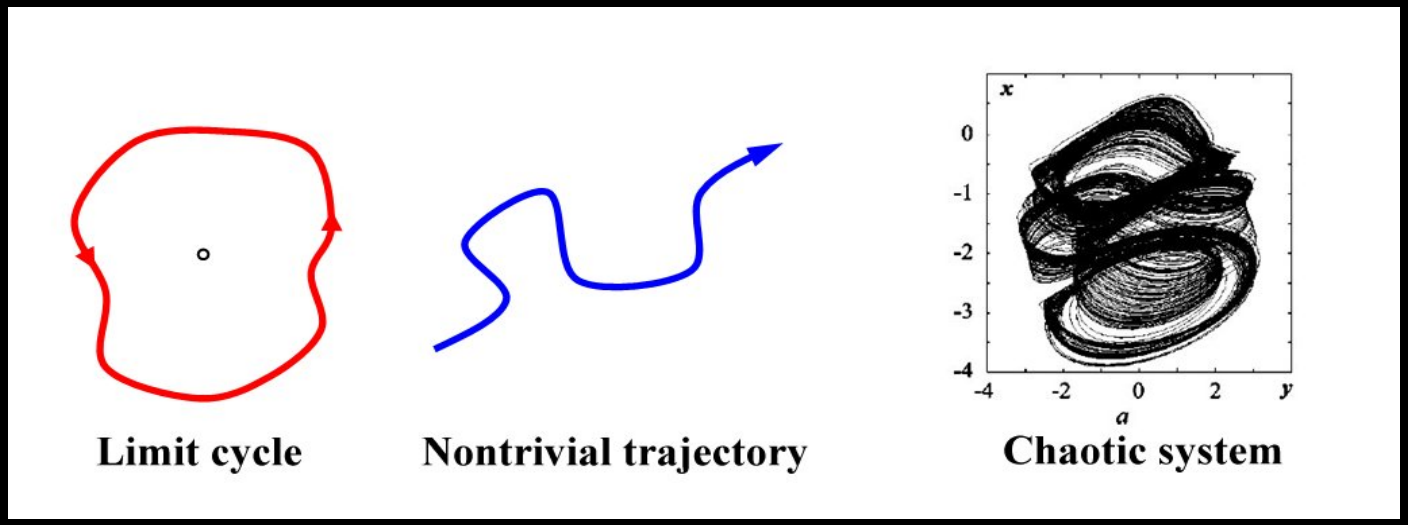
Conclusion

- Experimental data and modeling can be fruitfully combined

III. Experiment & Analysis

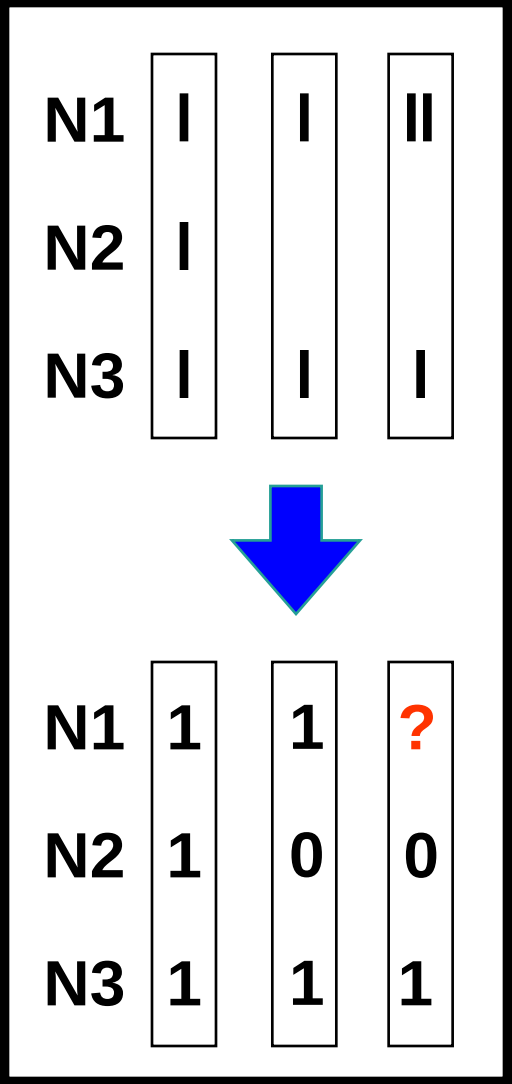
How can we visualize high-dimensional data?

- Brain activity is **multidimensional** (billions of neurons) and **dynamic** (continuously changing input)
- Dynamical systems approach: **trajectory => succession of states** => visualize these states **in an intuitive way!**



- Problem: **how do we define the states** for spiking signals?

Solution 1: binning and binarization



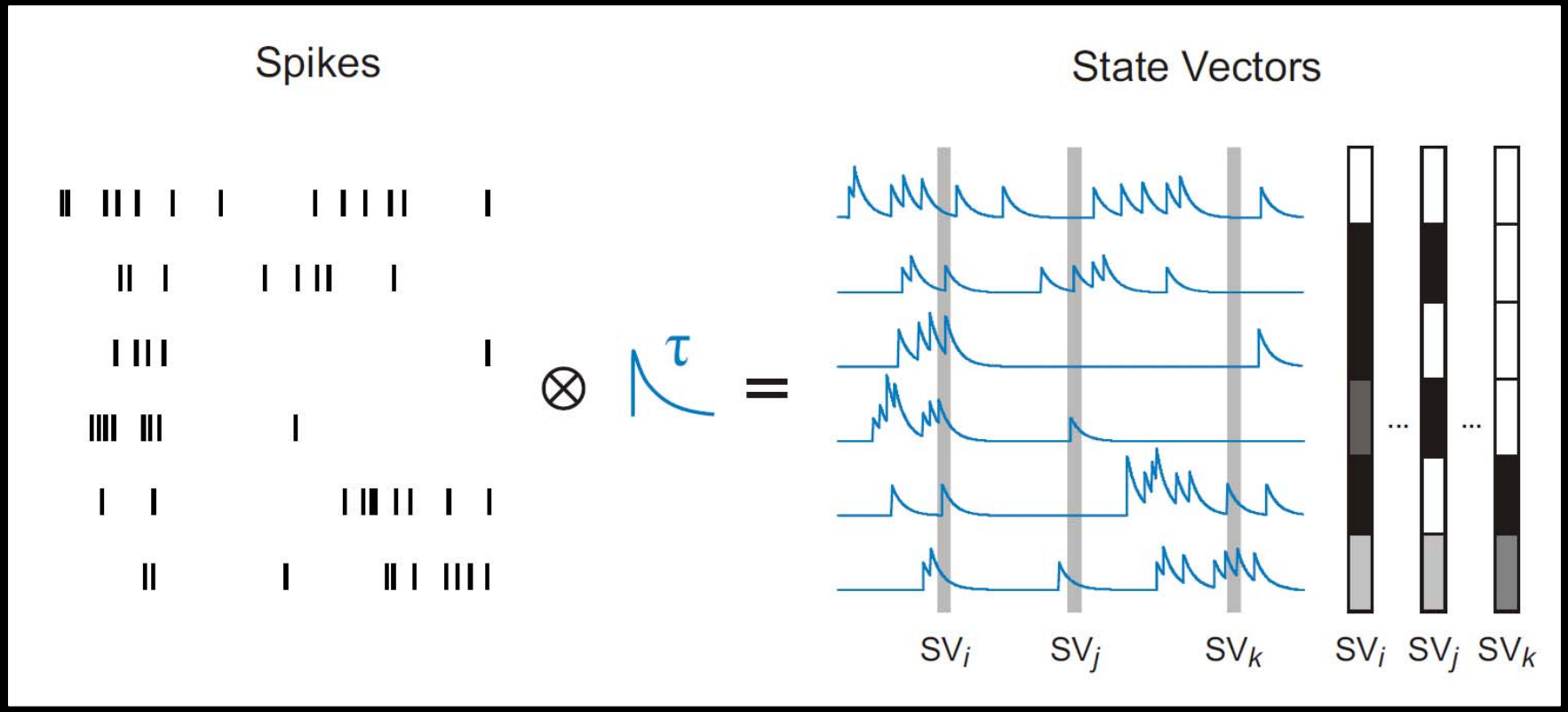
- Very popular method:

  Grün et al., 2002
  Pipa et al. 2008
  Schneidman et al., 2006

- Advantage: fixed number of clearly defined states: 2^N

- Problem: limited to joint-spike-events => cannot handle multiple timescales!

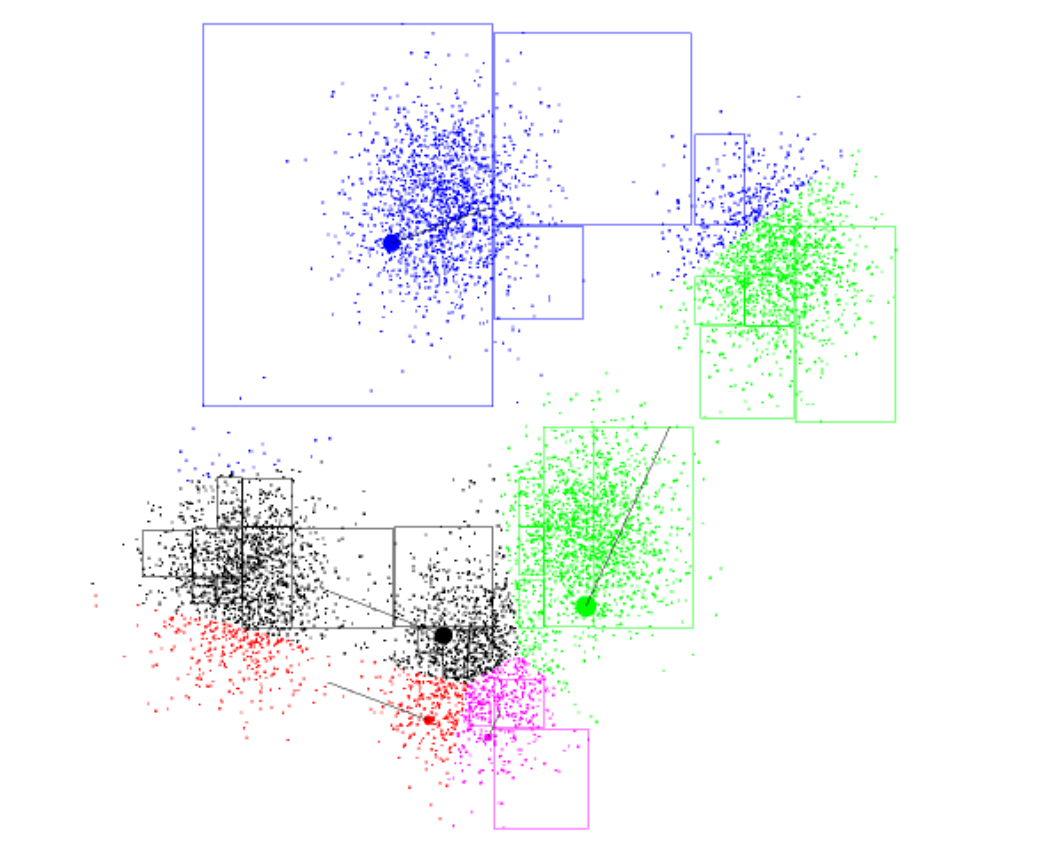
Solution 2: convolution with exponential kernels



- Has been used before (Gerstein; Maass; Nikolić)
- Advantage: flexible timescale; realistic (synaptic currents)
- Problem: an infinity of possible patterns!

Identification of stereotypical patterns

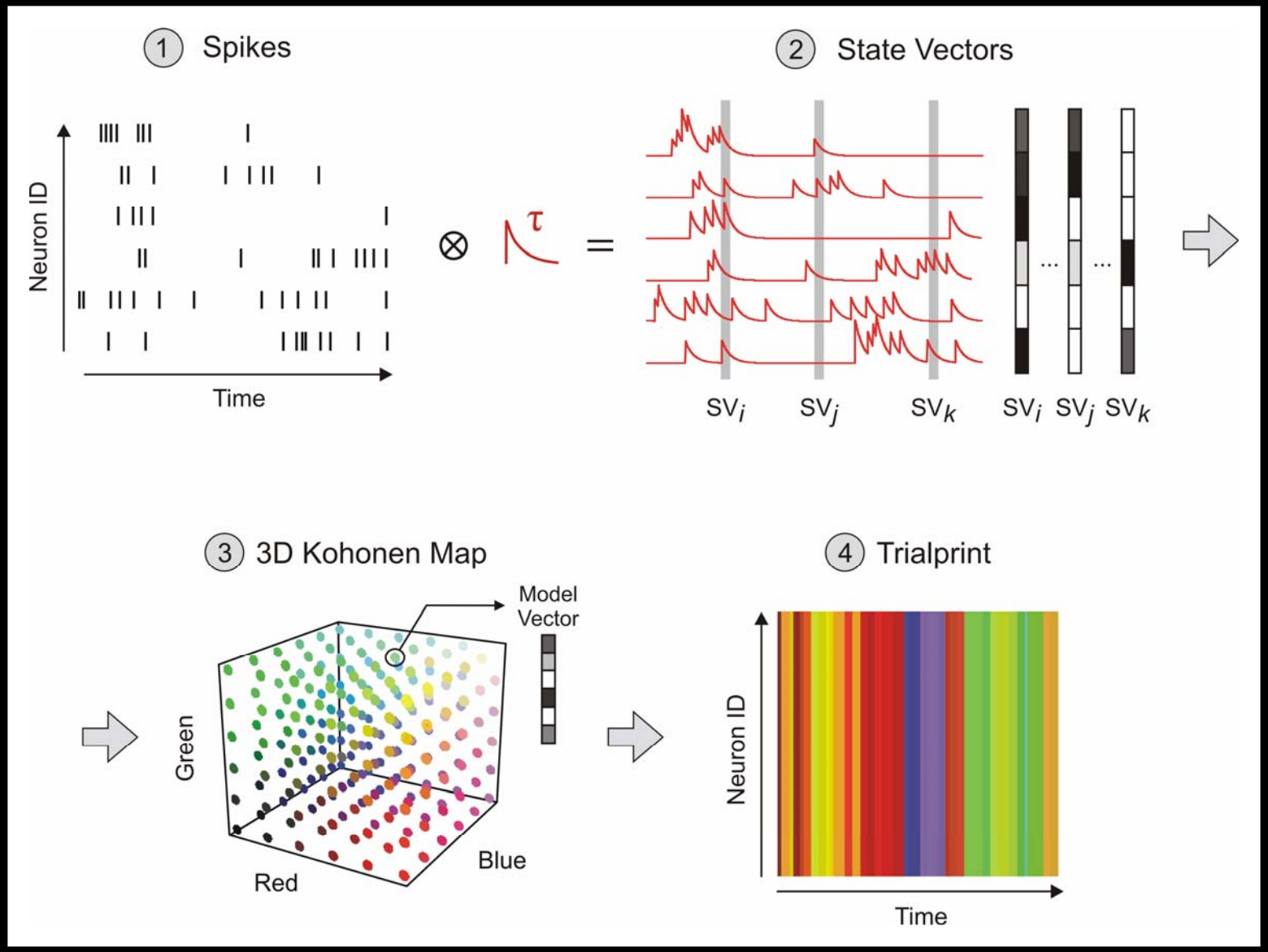
N1	0.5	?	0.51
N2	0	=	0
N3	1.1		1.1



Solution:

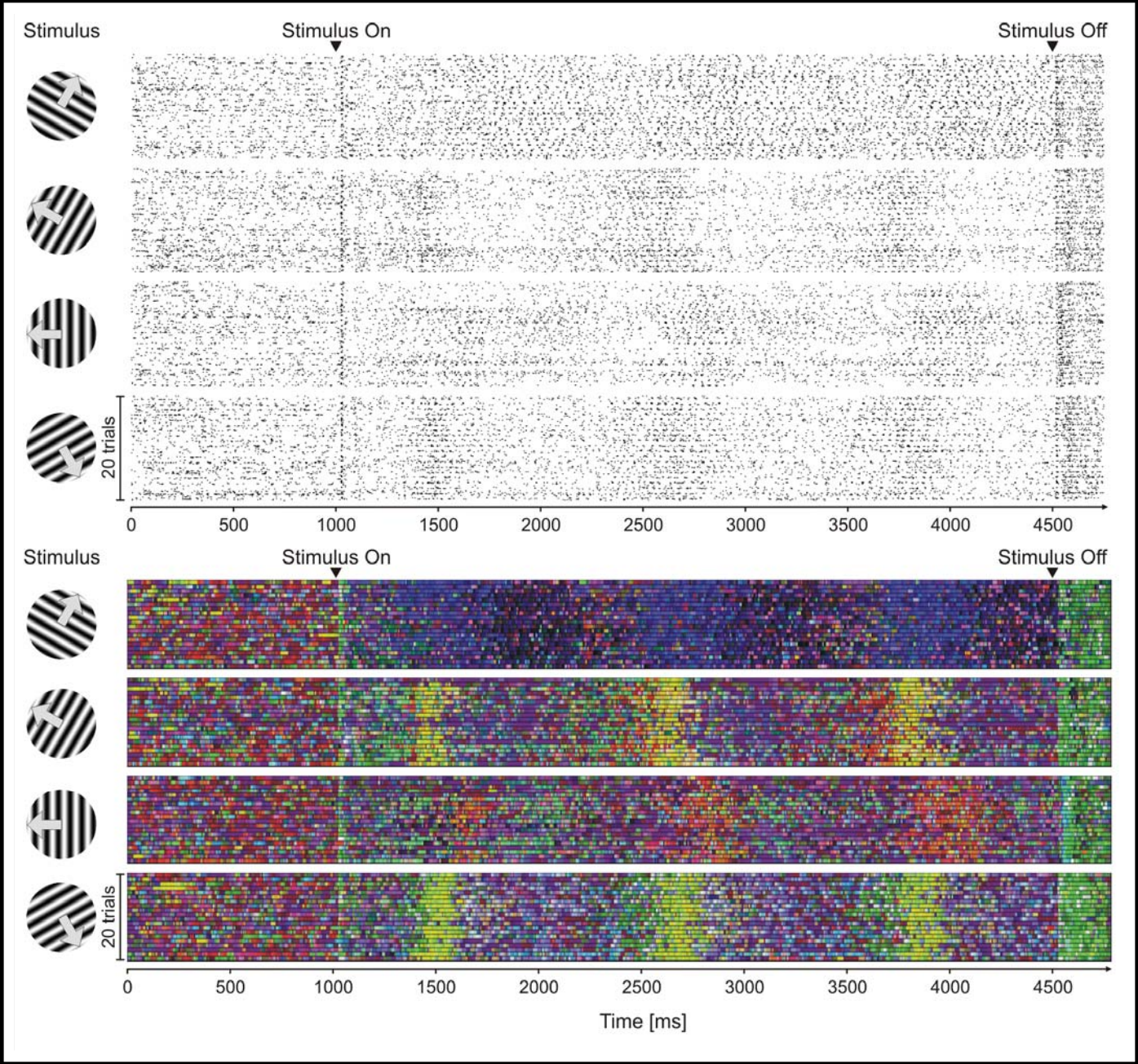
Clustering

Convolution + Clustering + Visualization



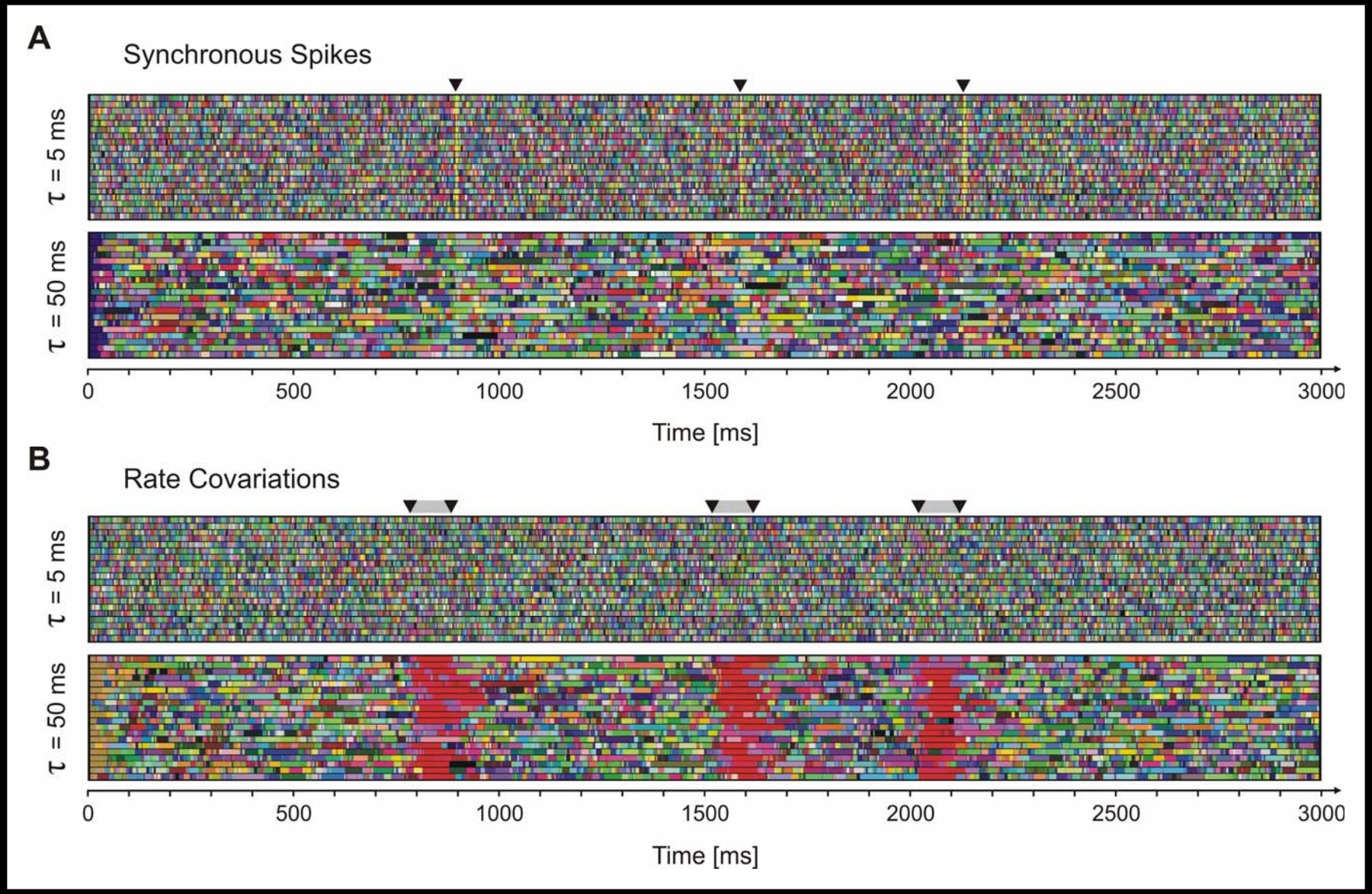
Jurjut et al. (2009), *J Neurophysiology* 102: 3766-3778

Trialprints (color sequences)



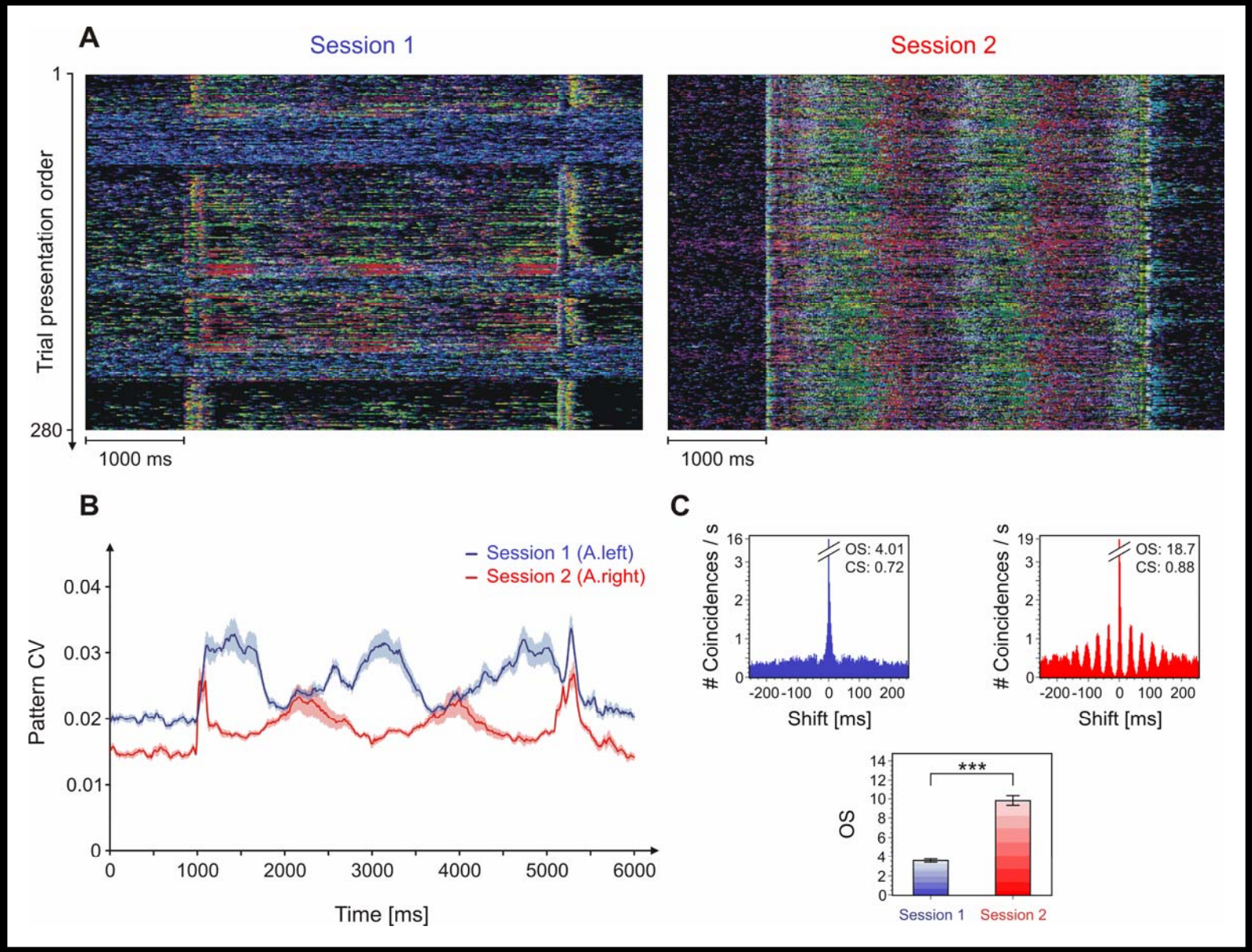
Jurjut et al. (2009), *J Neurophysiology* 102: 3766-3778

Investigation of multiple timescales



Jurjut et al. (2009), *J Neurophysiology* 102: 3766-3778

Investigation of cortical state changes

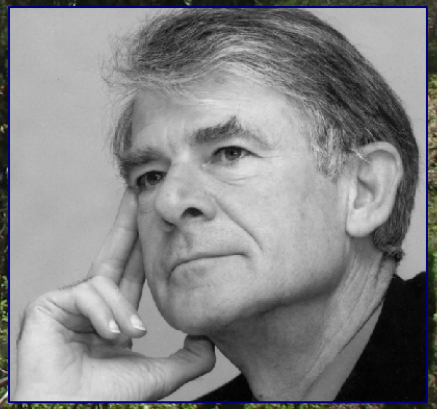


Jurjut et al. (2009), *J Neurophysiology* 102: 3766-3778

Conclusions

- We need to advance modeling, experiment and analysis in order to understand the brain
- Combined approaches can be fruitful and worth pursuing
- Multiple perspectives enable one to investigate a given phenomenon more thoroughly and to explore different possible interpretations / explanations

Collaborators



Thank you!