Zero-lag and anticipated synchronization in neuronal circuits: an interdisciplinary approach

Claudio R. Mirasso

Instituto de Física Interdisciplinar y Sistemas Complejos

Universitat de les Illes Balears - CSIC

Palma de Mallorca

*IFISC

CSIC

UIB Universitat de les Illes Balears

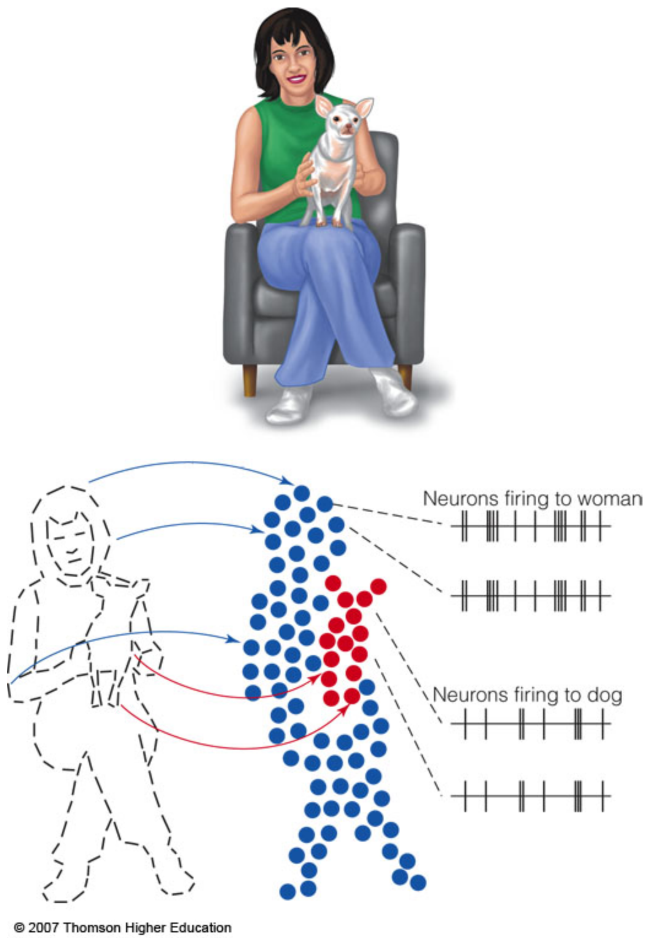
Outline Part I: Zero-lag Synchronization

- *Introduction and Motivation*
- *Interacting neurons with delay*
- *Neuron populations*
- *Physiological Plausibility*
- *Thalamo-Cortical Circuit*
- *Hippocampal Dynamical Relying*
- *Summary & Conclusions*

*IFISC

CSIC UIB

The Feature Binding Problem



Separate neurons respond to color (green, blue, white), contours (orientations), textures, so on.

Synchrony hypothesis:

When the features come from the same object (i.e., the woman), these neurons fire at the same time in the same manner.

When the neurons fire at the same time and in the same manner, we perceive "binding" of features.

Singer, W. 2007. Binding by synchrony. Scholarpedia 2:1657.

Zero-Lag Long-Range Synchronization in the Brain

Neurophysiological experiments: even in the presence of substantial coupling delays different cortical areas exhibit isochronous synchronization at zero lag

Visuomotor integration is associated with zero time-lag synchronization among cortical areas

Pieter R. Roelfsema*†, Andreas K. Engel*, Peter König‡ & Wolf Singer*

NATURE · VOL 385 · 9 JANUARY 1997

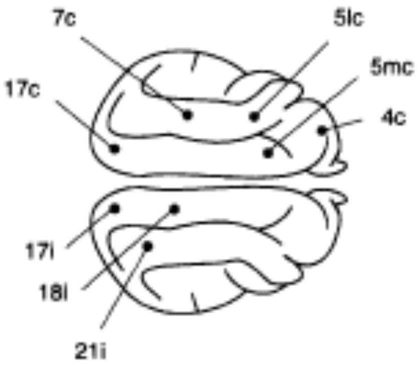
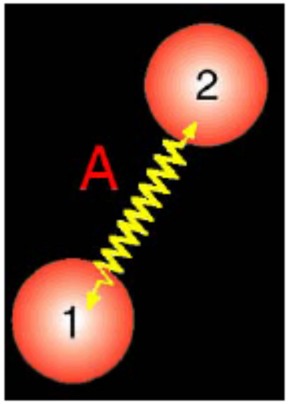


TABLE 1 Strength of zero-time-lag synchronization between cortical areas

Areas	Correlation coefficient (%)	Range	N	Areas	Correlation coefficient (%)	Range	N
17c–7c	9 ± 4	4–14	4	5lc–4c	2 ± 3	0–5	2
17c–5lc	0		2	5lc–17i	0		2
17c–5mc	0		3	5lc–18i	4 ± 5	0–8	2
17c–4c	0		2	5lc–21i	4 ± 4	0–8	3
17c–17i	22 ± 7	12–28	4	5mc–4c	10 ± 1	9–11	2
17c–18i	12 ± 3	7–14	4	5mc–17i	0		3
17c–21i	8 ± 2	7–10	3	5mc–18i	0		3

How can two distant neural assemblies synchronize their firings at zero-lag even in the presence of non-negligible delays in the transfer of information between them?



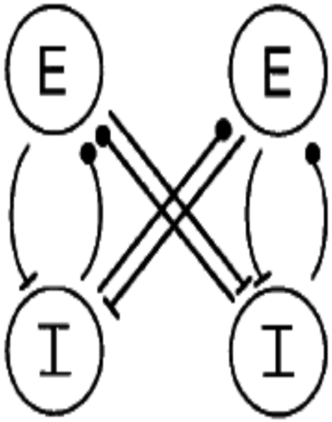
Which is the physical and anatomical substrate for this dynamical and precise synchrony?

- Direct cortico-cortical connections
- Inhibitory connections
- Gap junctions
- Complex Networks

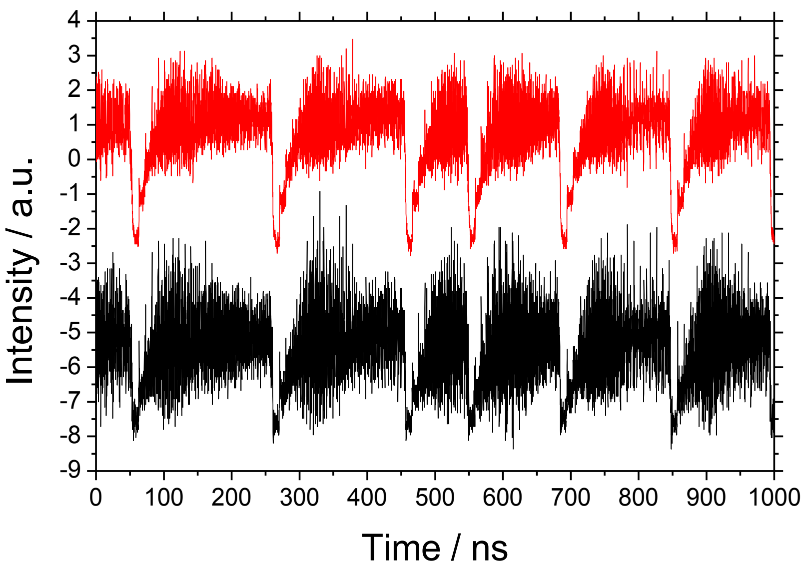
(Inhibitory connections and Gap junctions:) Enhance synchronization

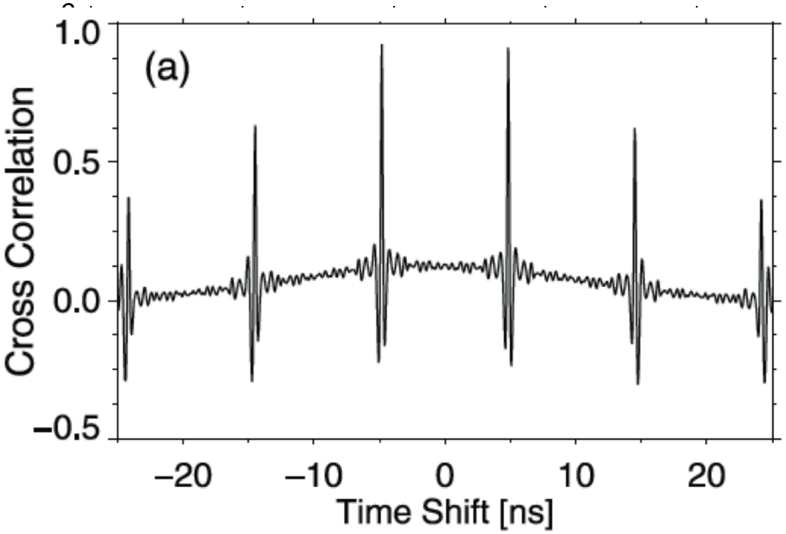
R. Traub et al., Nature **383**, p. 621, 1996;
G. B. Ermentrout & N. Kopell, *Proc. Natl. Acad. Sci. USA* **95**, p. 1259, 1998;

- Excitatory-Inhibitory networks favor γ-frequency rhythms
- Inhibitory cells produce spike doublets
- Connections between such networks favor zero-lag synchronization.



2 Coupled Semiconductor Lasers

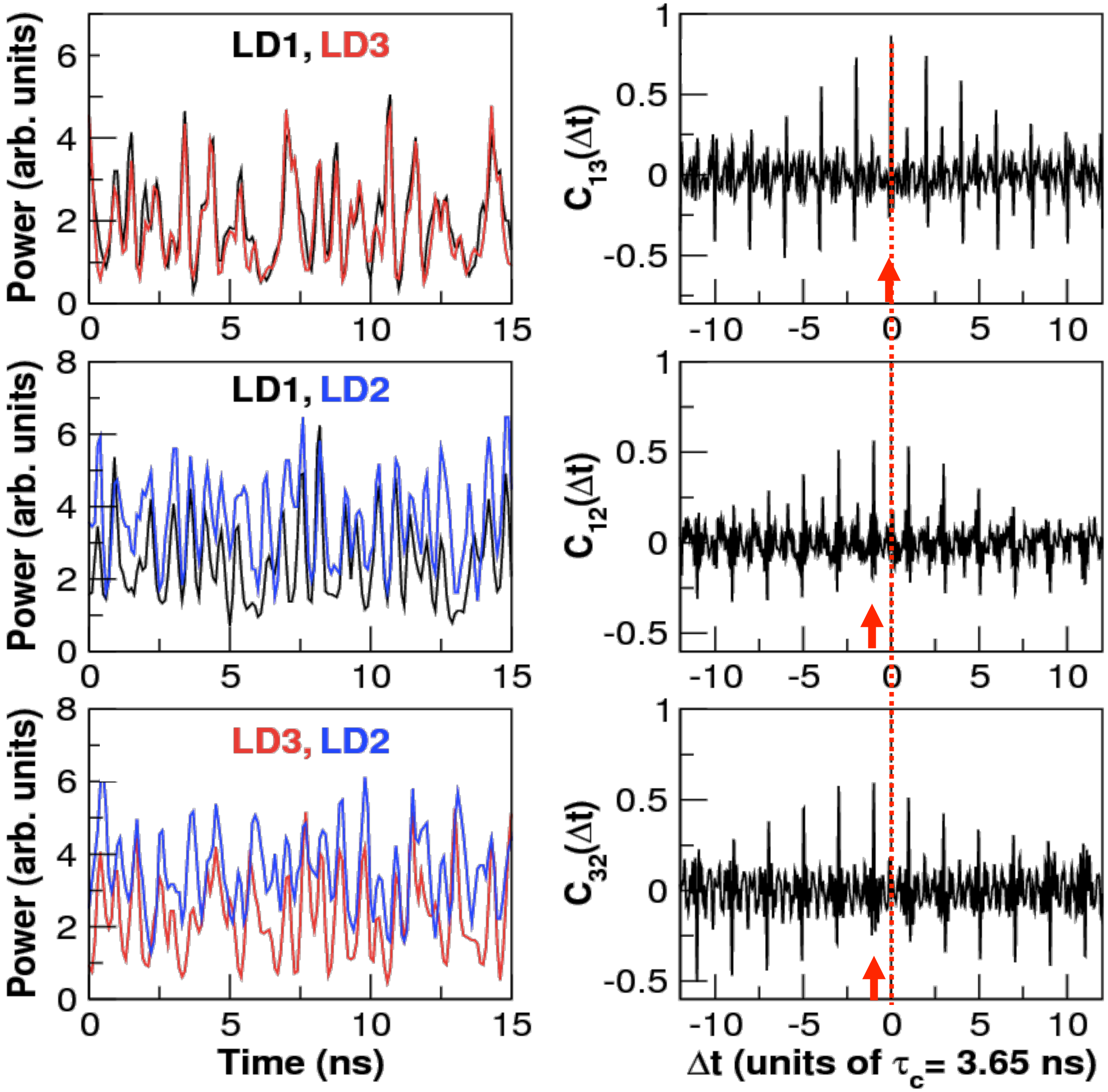




- onset of coupling-induced intensity pulsations
- synchronization among the two lasers
- synchronization of ns and sub-ns pulsations
- however:
- one time series temporally shifted by τ_{cp}
- leader & laggard (achronal synchronized solution)
  - CC_{max} at +/- n* τ

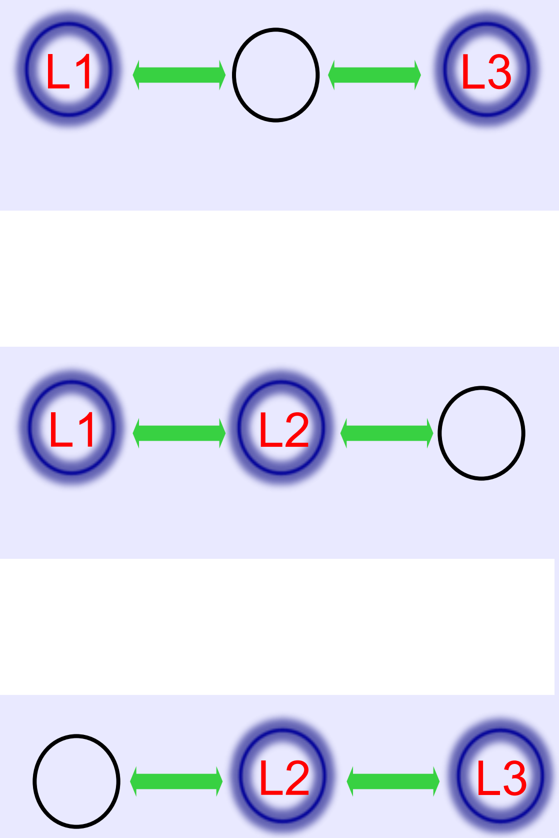
T.Heil, I.Fischer, W.Elsäßer, J.Mulet, C.R.Mirasso, Phys.Rev.Lett. 86, 795 (2001)

Chain of 3 Lasers



I.Fischer et al., Phys.Rev.Lett. 97, 123902 (2006)

- L1 and L3 identically synchronise with zero lag

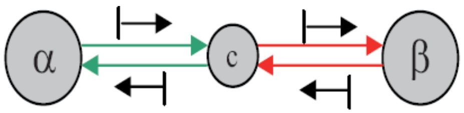


Center laser (L2) lags behind the outer lasers (L1,L3), **no master!**

Can the zero-lag sync mechanism observed in lasers be generalized to models of neuronal systems?

Neuron are excitable systems

They couple via chemical synapses (pulse coupling)

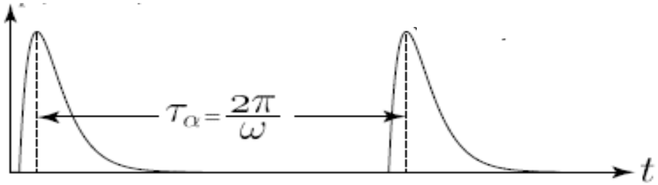


Model at the level of Hodgkin-Huxley:

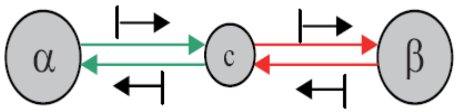
$$C\frac{dV}{dt} = -g_{Na}m^3h(V-E_{Na}) - g_K n^4(V-E_k) - g_L(V-E_L) + I_{ext} + I_{syn}$$

$$I_{syn}(t) = -g_{max}\sum_{\tau_l}\sum_{spikes}\alpha\left(t - t_{spike} - \tau_l\right)\left(V(t) - E_{syn}\right)$$

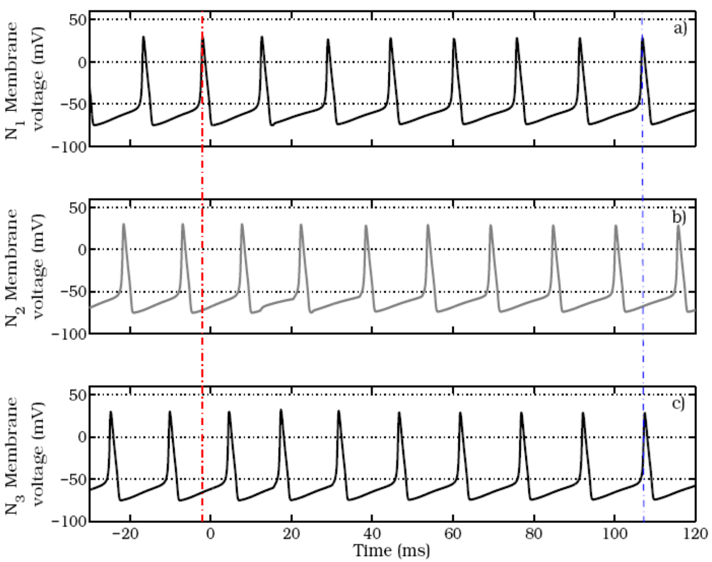
$$\alpha(t) = \frac{1}{\tau_d - \tau_r}\left(\exp\left(-t/\tau_d\right) - \exp\left(-t/\tau_r\right)\right)$$



Simulating conditions:



- periodic firing regime (T = 14.7 ms, f = 68.02 Hz)
- each neuron with a random initial phase
- different synaptic rise and decay times
- excitatory and inhibitory synapses

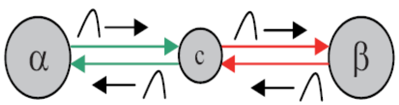


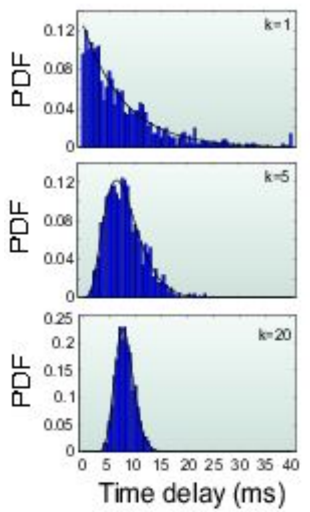
$$g_{max} = 0.5$$
$$E_{syn} = 0 \text{ mV}$$
$$\tau_l = 8 \text{ ms}$$
$$\tau_r = 0.1 \text{ ms}$$
$$\tau_d = 3 \text{ ms}$$

- self-organization toward the synchronization of outer neuron spikes
- zero-phase sync due to relay and redistribution of EPSP / IPSP

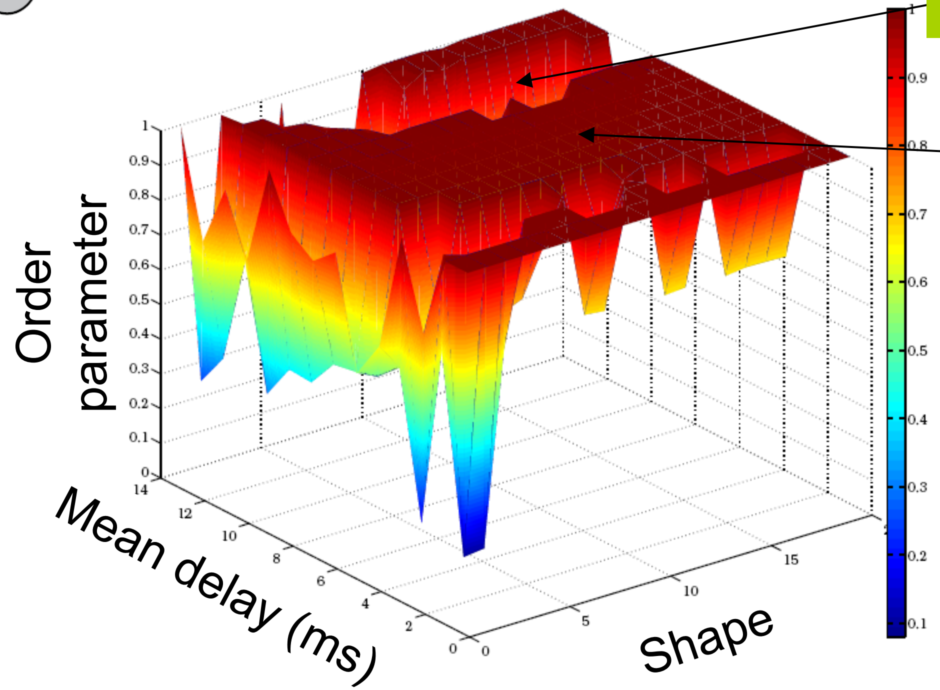
True for E-E or I-I couplings and different α-functions

A crucial point to check is whether the observed synchronized state is particular to single latency synapsis or is maintained for broad distribution of synaptic delays.





Delta Function: cracterized by a mean value and a shape factor



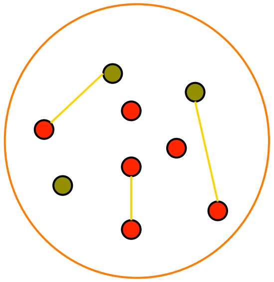
Non-locking frequency area (irregular firing)

Large plateau where the oscillations are isochronous (2-9 ms)

$$g_{max} = 0.2$$
$$E_{syn} = 0 \text{ mV}$$
$$\tau_r = 0.1 \text{ ms}$$
$$\tau_d = 3 \text{ ms}$$

Populations?

Populations of neurons with the same reciprocal connectivity subjected to independent Poissonian input trains of spikes.



~4000 IAF neurons

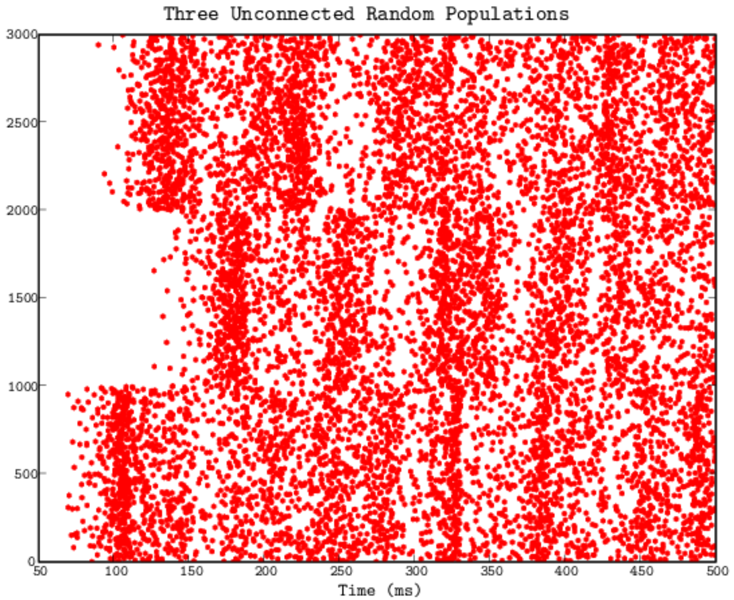
80 % excitatory
internal random connectivity,
10% connectivity

V threshold : 20 mV
V reset : 10 mV
refractory time: 2 ms
time constant : 20 ms

$$\tau \dot{V}_i(t) = -V_i(t) + RI_i(t)$$

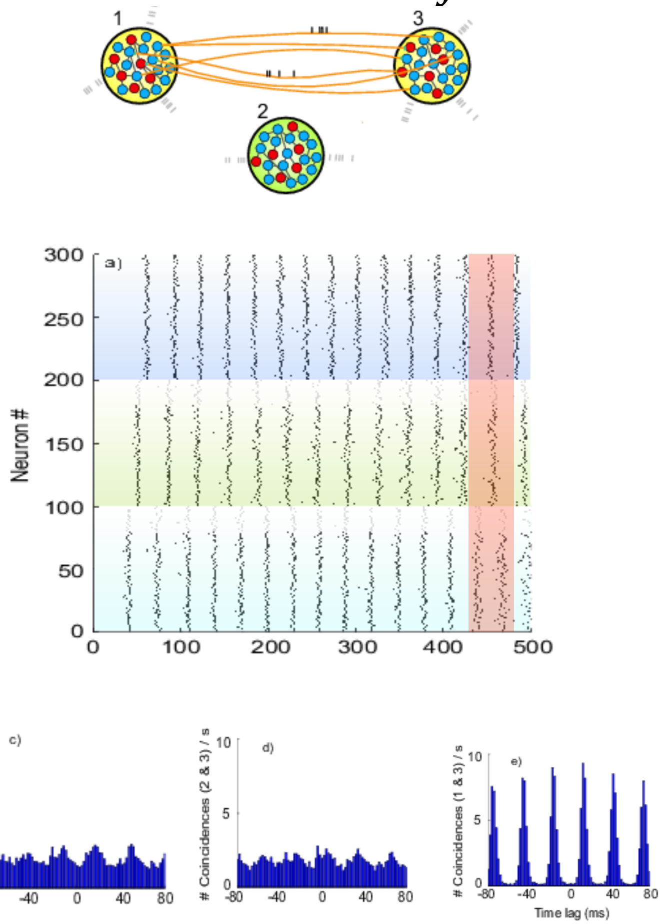
$$RI_i(t) = \tau \sum_j J_{ij} \sum_k \delta\left(t - t_j^k - D\right)$$

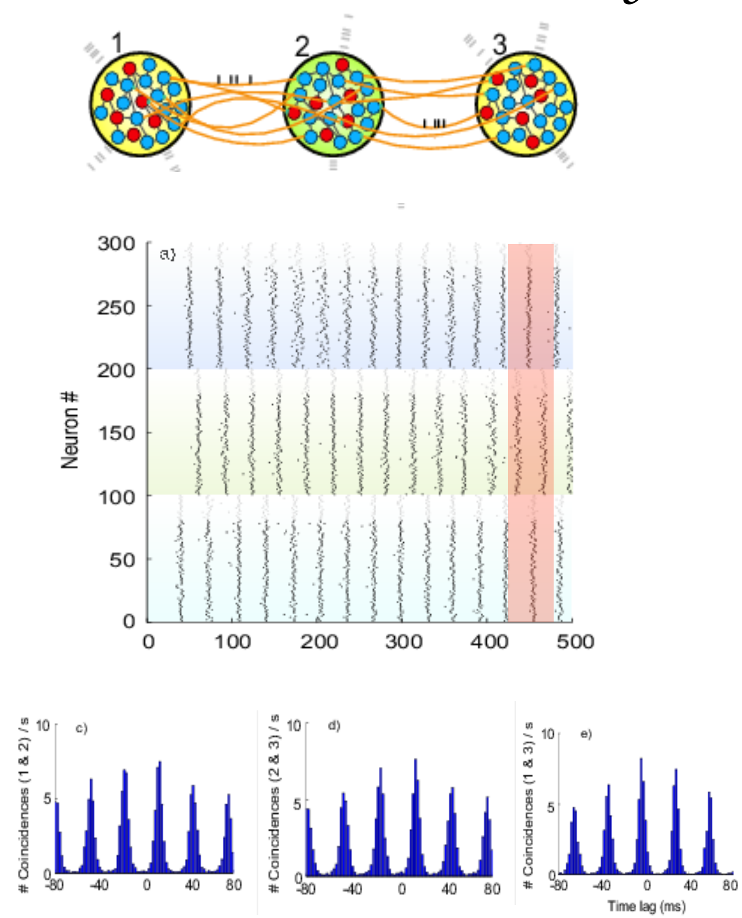
N. Brunel, J. Comp. Neurosc. **8**, 183, 2000.



3 coupled neuron populations

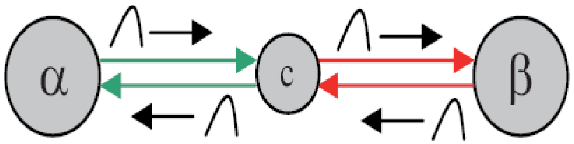
Each neuron connects excitatory and randomly to 0.25% of the neurons of the other population with 15 ms delay





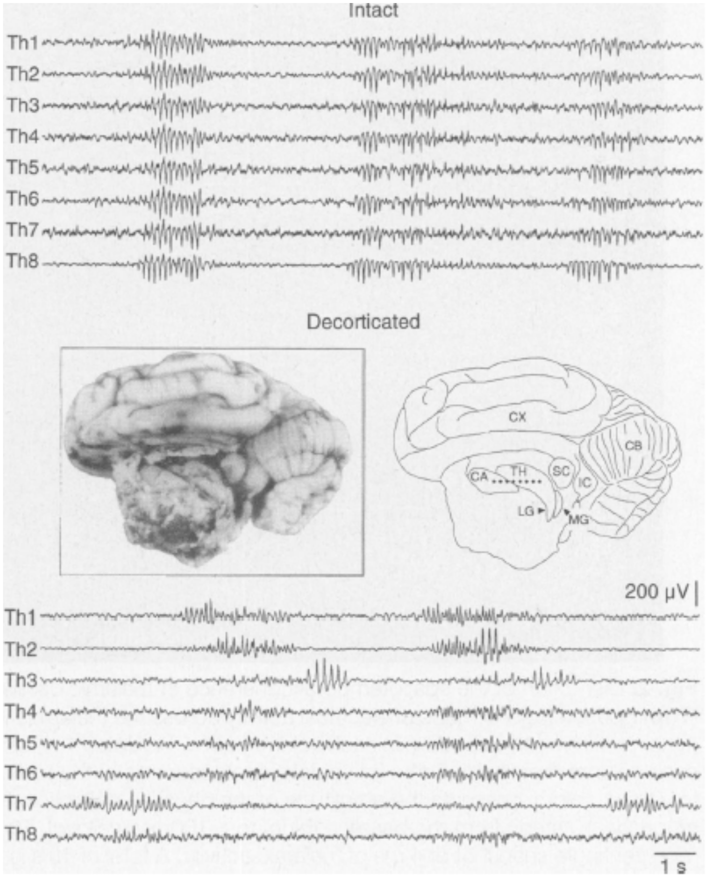
“Dynamical relaying can yield zero time lag neuronal synchrony despite long conduction delays”, R. Vicente, L. L. Gollo, C. R. Mirasso, I. Fischer and G. Pipa, PNAS **105**, 17157 (2008).

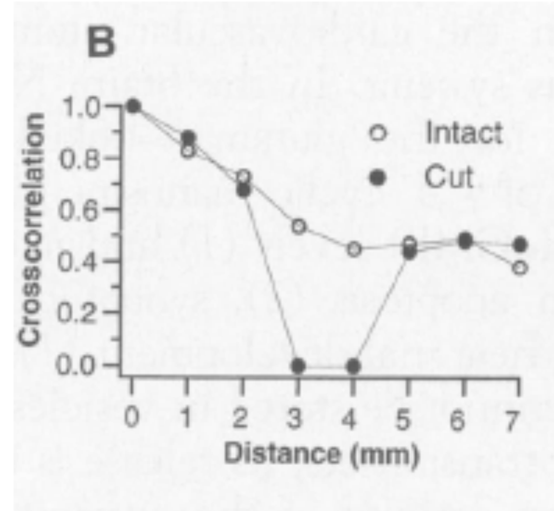
Physiological plausibility.

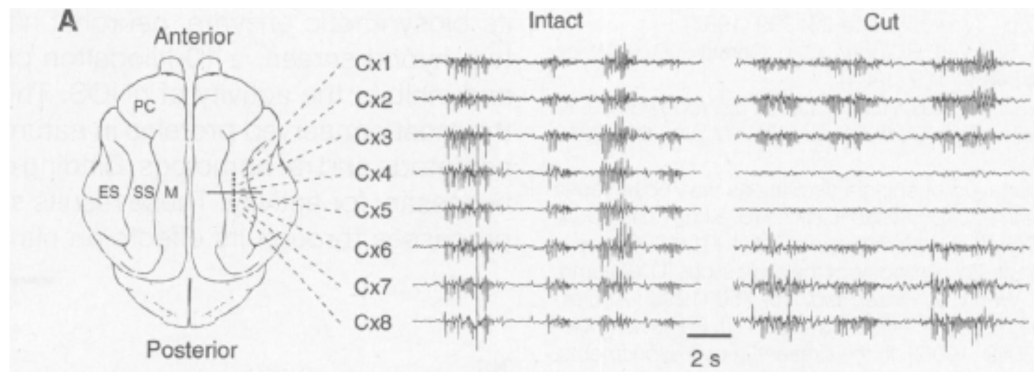


Thalamus is the main relay unit of sensory information to the cortex with bidirectional connections

Physiological Plausibility





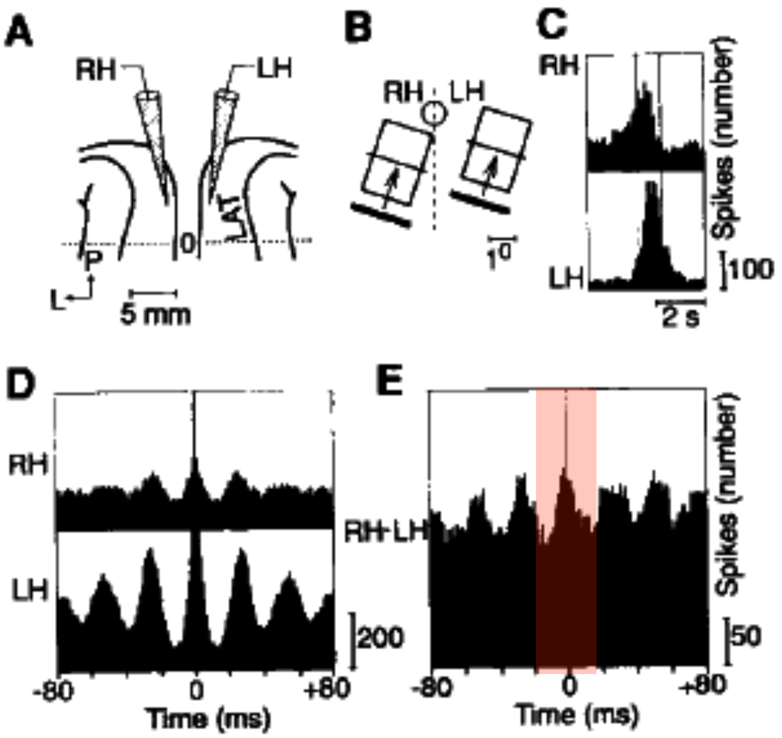


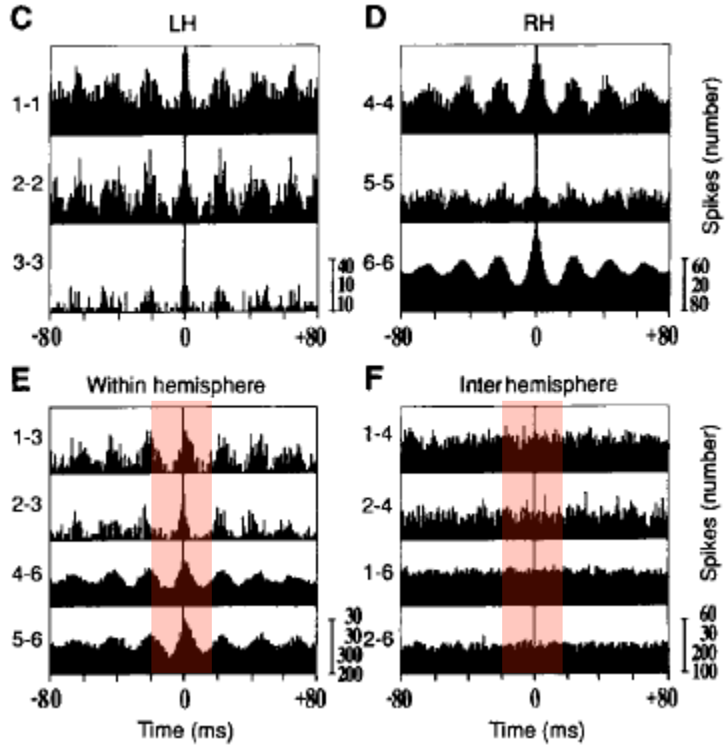
9-10 Hz oscillation in the thalamus. Intact and with a cortex lesion.

Synchrony of oscillations is not determined by intra-cortical connectivity

Control of Spatiotemporal Coherence of a Thalamic Oscillation by Corticothalamic Feedback, D. Contreras, A. Destexhe, T. J. Sejnowski, M. Steriade, Science 274, 771 (1996).

Interhemispheric Synchronization





Interhemispheric Synchronization of Oscillatory Neuronal Responses in Cat Vis... ***A.*** *Engel, et al. Science 252, 5009 1991.*

Interhemisferic synchronization is absent when the corpus callosum is sectioned

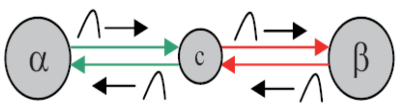
CPC circuits mimic direct CC pathways but with more overlap ➡ *facilitation of transarea sync.*
*S. Shipp, Philos Trans R Soc Lond B Biol Sci, **358**, 1605, (2003).*

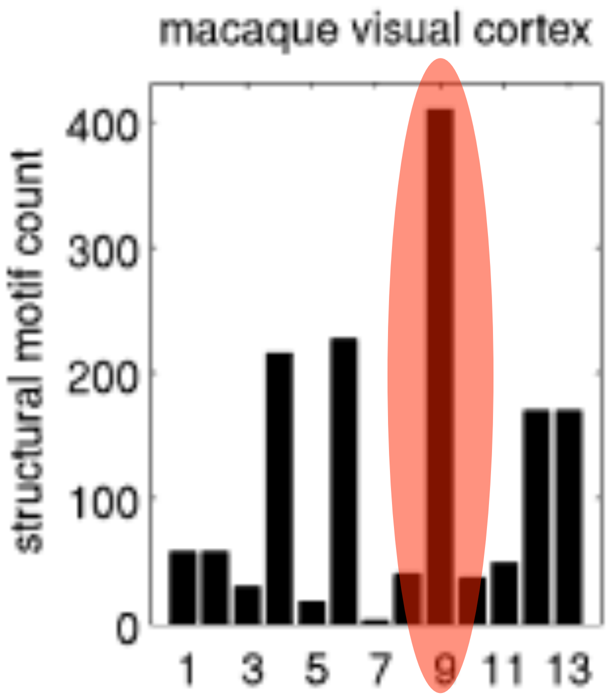
"The driving projections to thalamus would thus provide a significant alternative path for inter-areal communication".
*Douglas and Martin, Annu. Rev. Neurosci. **27**, 419, 2004*

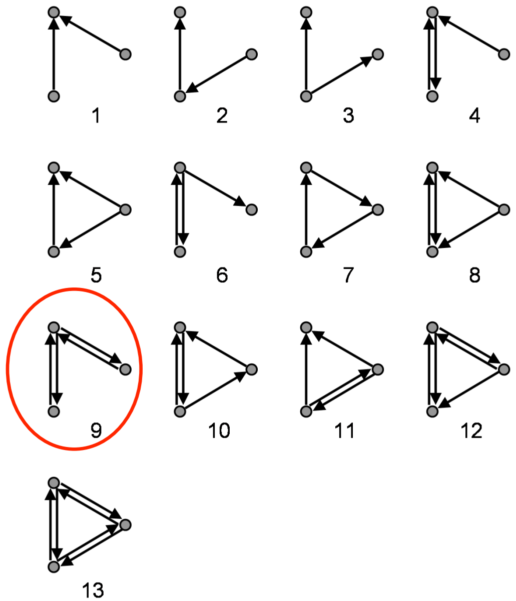
Recent studies have shown the constant latency between the thalamus and almost any area in the rat cortex.
"Change of conduction velocity by regional myelination yields constant latency irrespective of distance between thalamus and cortex."
*Salami et al., PNAS, **100**, 6174, (2003).*

Stronger TC connections than expected.
"Cortex Is Driven by Weak but Synchronously Active Thalamocortical Synapses"
*Bruno and Sakmann, Science, **312**, 1622, (2006).*

Also.......the proposed motif is a building block of the mammalian cortex. But has the proposed motif a specific role in the brain network?



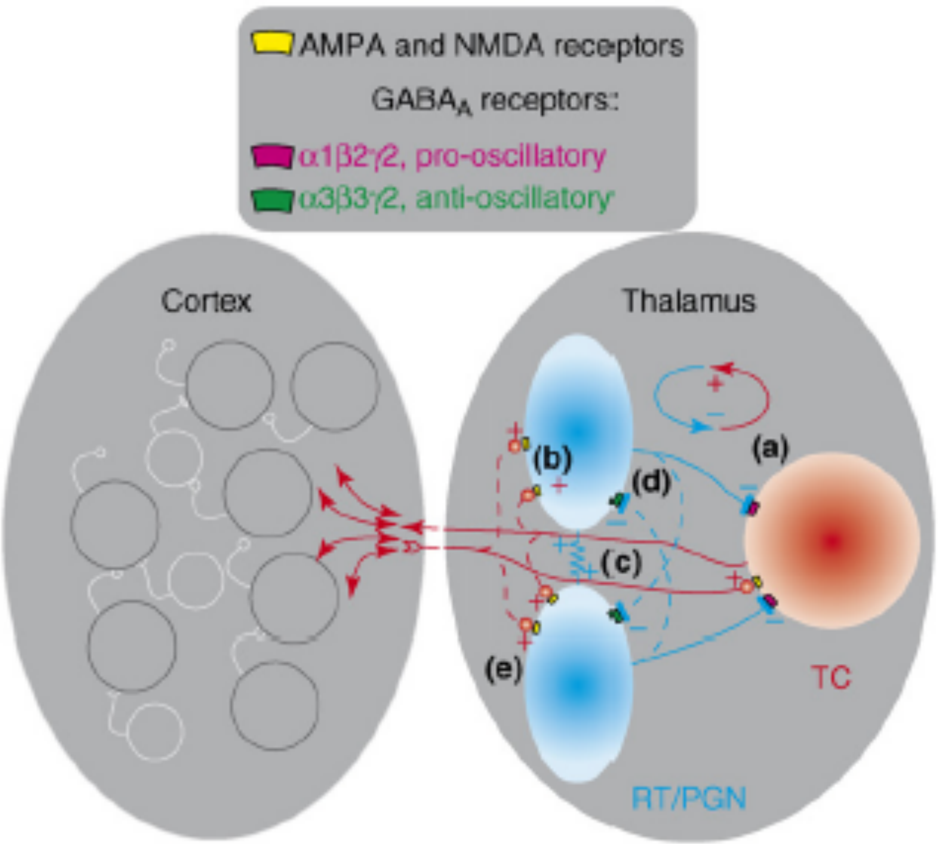




Sporns & Kötter

PLoS Biology, **2**, *1910, (2004).*

Thalamo-Cortical Interaction.

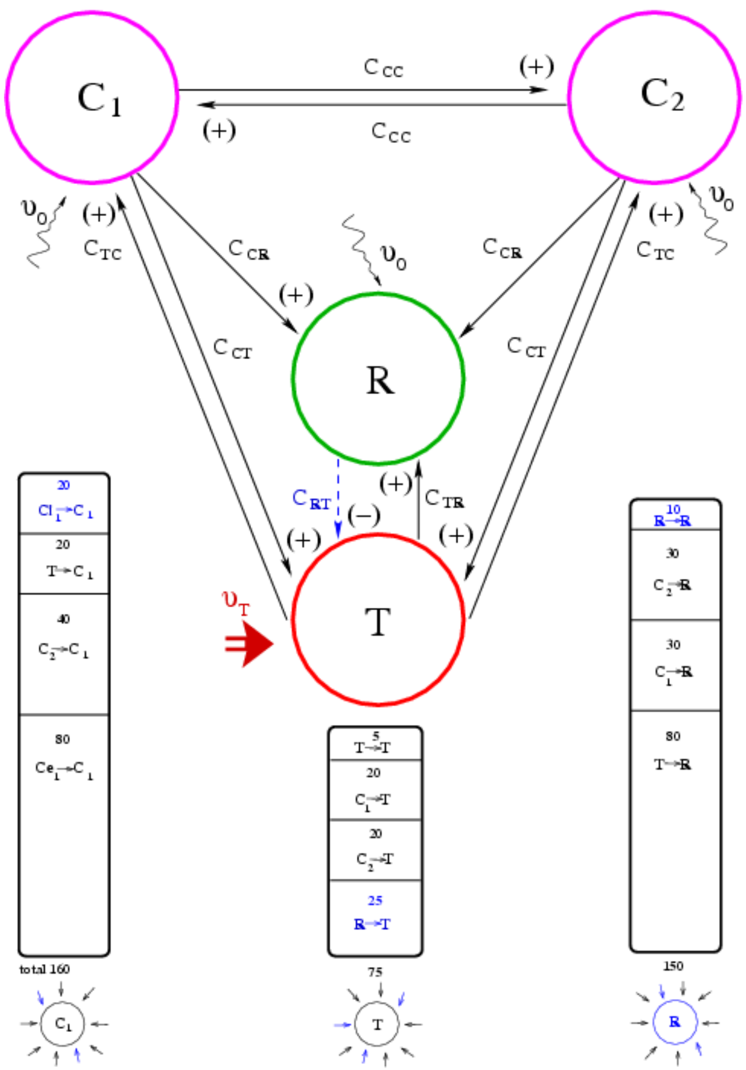


TC: Thalamo-Cortical Network

RT: Reticular Nuclei

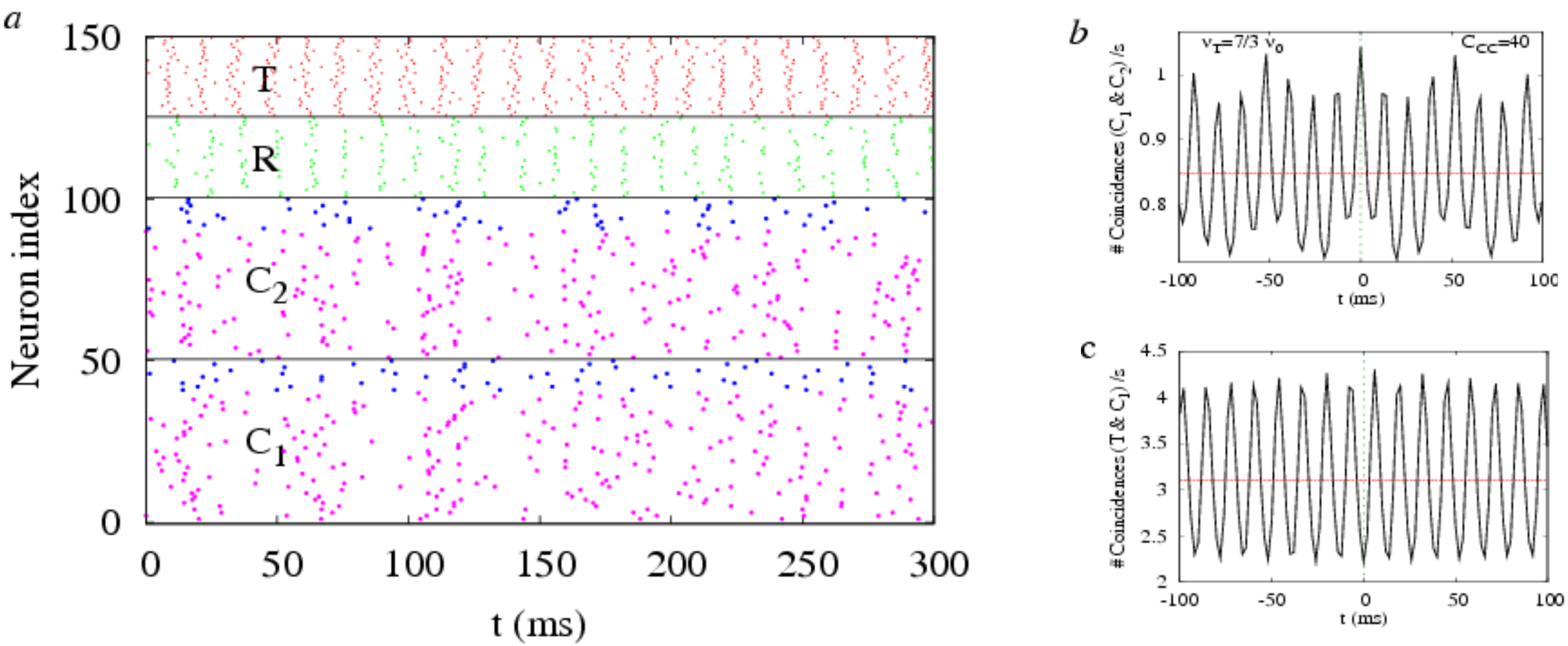
PGN: Perigeniculate Nuclei

Thalamo-Cortical Interaction.

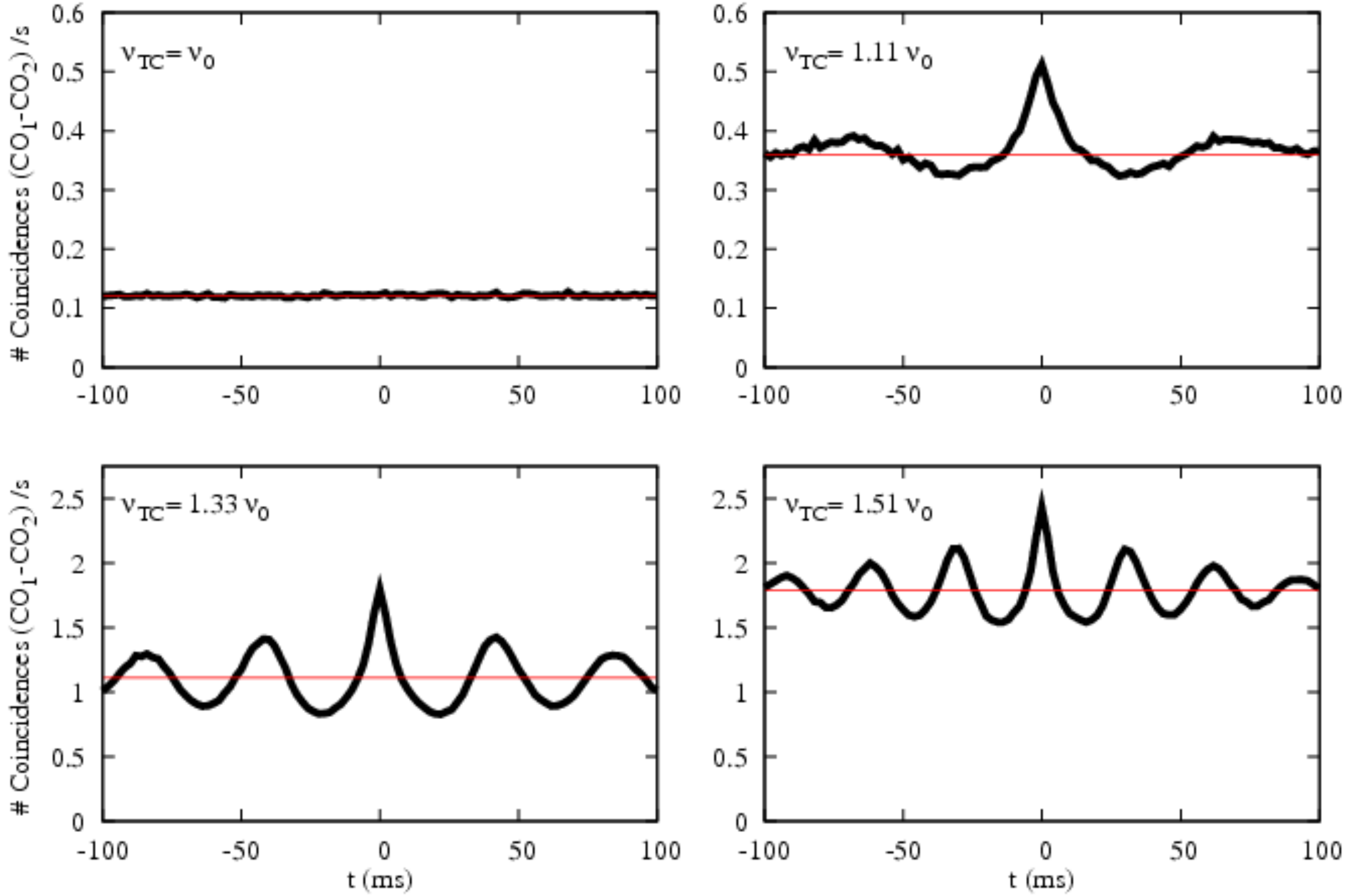


Each neuron is subject to an independent Poisson noise P(t)=κ $e^{\nu_0 t}$

Thalamic neurons are subject to a Poisson noise P(t)=κ $e^{\nu_T t}$

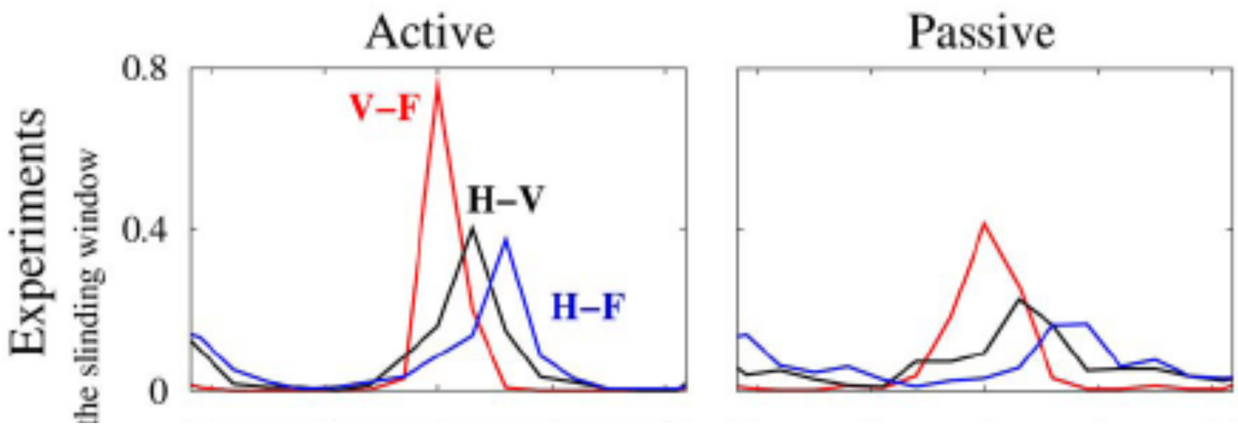


300 pairs of neurons averaged over 100 different noise realizations

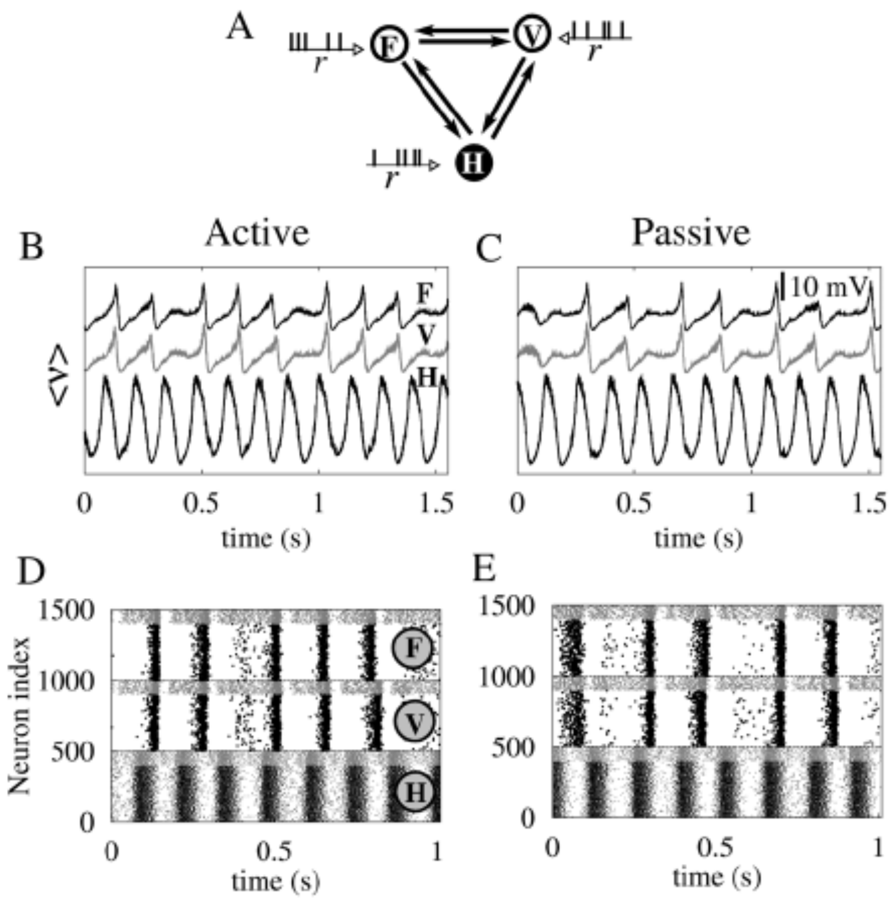


Hippocampal Dynamical Relaying

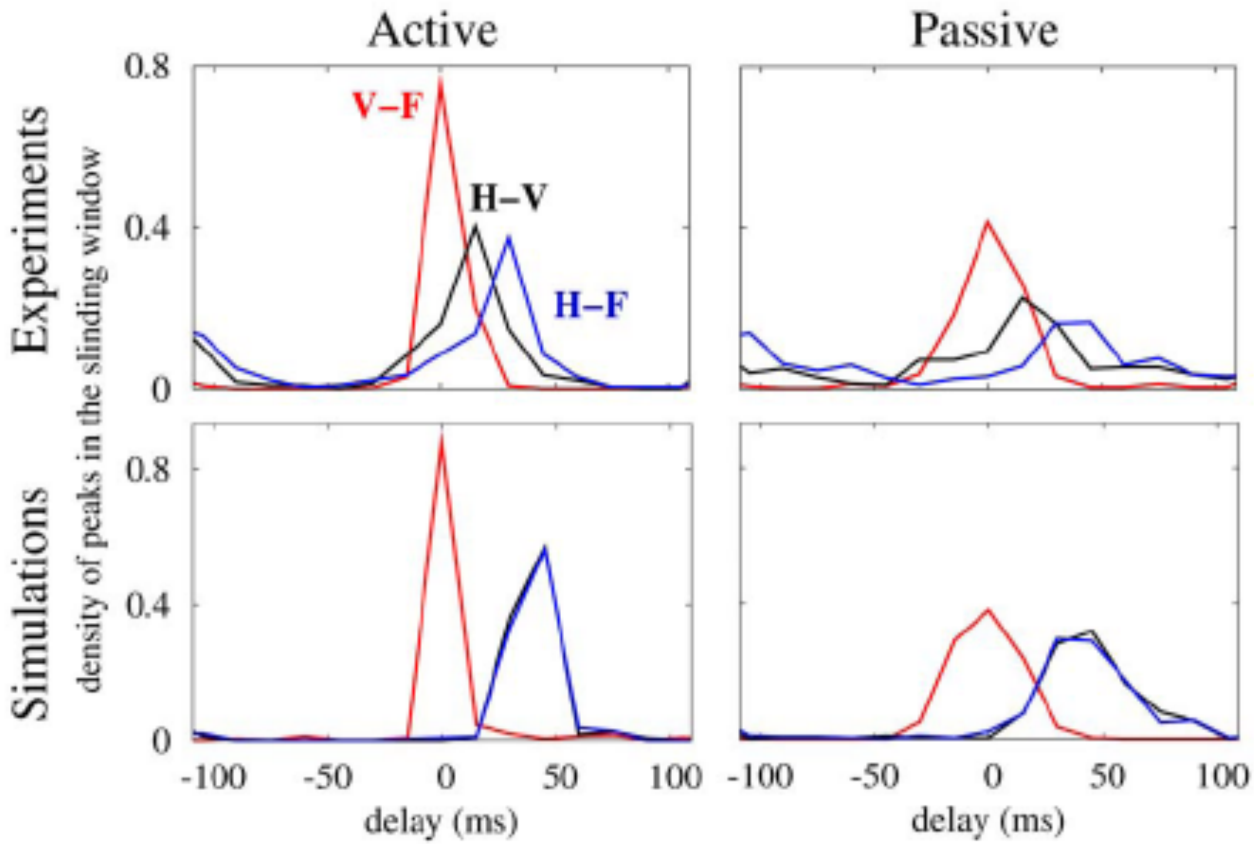
In mice, zero-lag long-range synchronizatio between the anterior (frontal) and posterior (occipital) cortical regions was experimentally observed when the amplitude of the theta oscillations was prominent in the hippocampus.



Connected activity



"Theta band zero-lag long-range cortical synchronization via hippocampal dynamical relaying", L. L. Gollo, C. R. Mirasso, M. Atienza, M. Crespo-Garcia and J. L. Cantero, PLoS One **6**, e17756 (2011).



"Theta band zero-lag long-range cortical synchronization via hippocampal dynamical relaying", L. L. Gollo, C. R. Mirasso, M. Atienza, M. Crespo-Garcia and J. L. Cantero, PLoS One **6**, e17756 (2011).

Part I: Summary & Conclusion

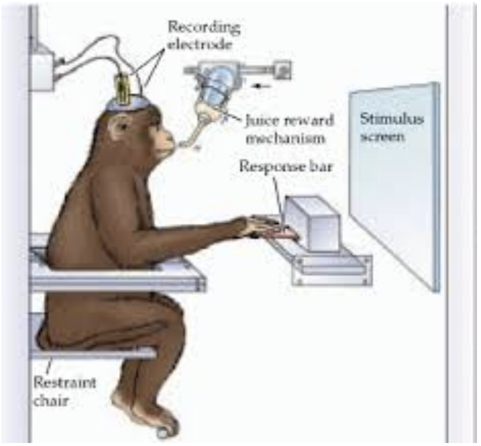
- We have proposed an alternative mechanism that gives rise to zero (or almost zero)-lag (or phase) long-range synchronization in neuronal models.
- A relay element must mediate the dynamics between two neurons or neuron populations.
- It might be possible that the thalamus acts as a relay element, although cortico-cortical interaction without thalamus mediation are also possible.
- In active and passive mice, the synchronize activity observed between frontal and visual cortex might be mediated by the hippocampus.

Outline Part II: Anticipated Synchronization

- *Introduction and Motivation*
- *Anticipated synchronization*
- *Simple motif*
- *Populations*
- *Experimental Evidence*
- *Summary & Conclusions*

Motivation

Different techniques can be used to readout neuronal activity



EPRs provide cleaner data, with better S/N, high temporal resolution and precise location. Array of electrodes are being used.

Mainly applied to animals, correlation, MI, transfer entropy, etc. are routinely computed. The technique permits the computation of functional, effective and even anatomical connectivity.

Other non-invasive techniques include EEG, MEG, fMRI, etc.

PNAS

Beta oscillations in a large-scale sensorimotor cortical network: Directional influences revealed by Granger causality

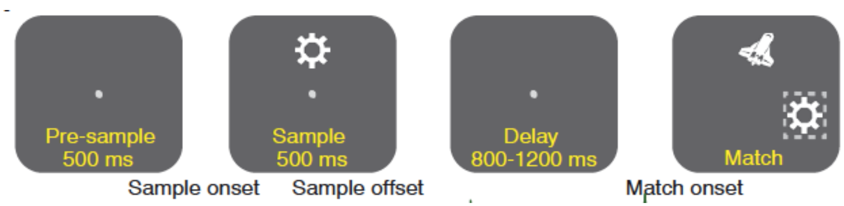
Andrea Brovelli*, Mingzhou Ding*, Anders Ledberg*, Yonghong Chen*, Richard Nakamura†, and Steven L. Bressler*‡

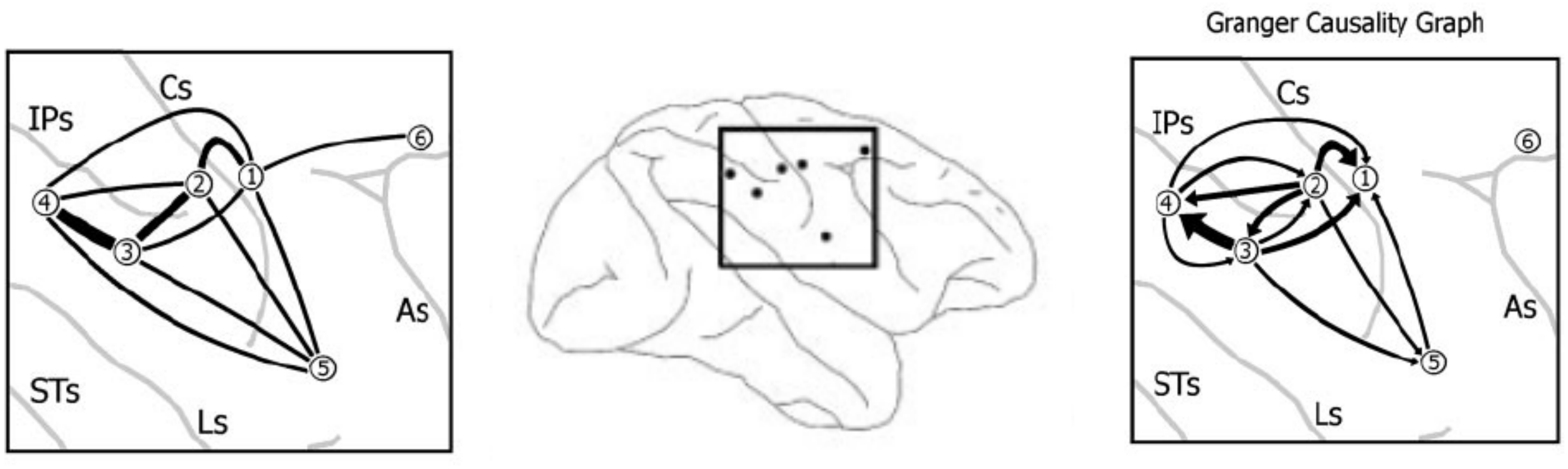
PNAS | June 29, 2004 | vol. 101 | no. 26 | 9849–9854

GO/NO GO visual discrimination task. Monkeys pressed a hand lever during waiting period and if they released it in less than 500 ms after stimulus appeared, they got water reward

Content-Specific Fronto-Parietal Synchronization During Visual Working Memory

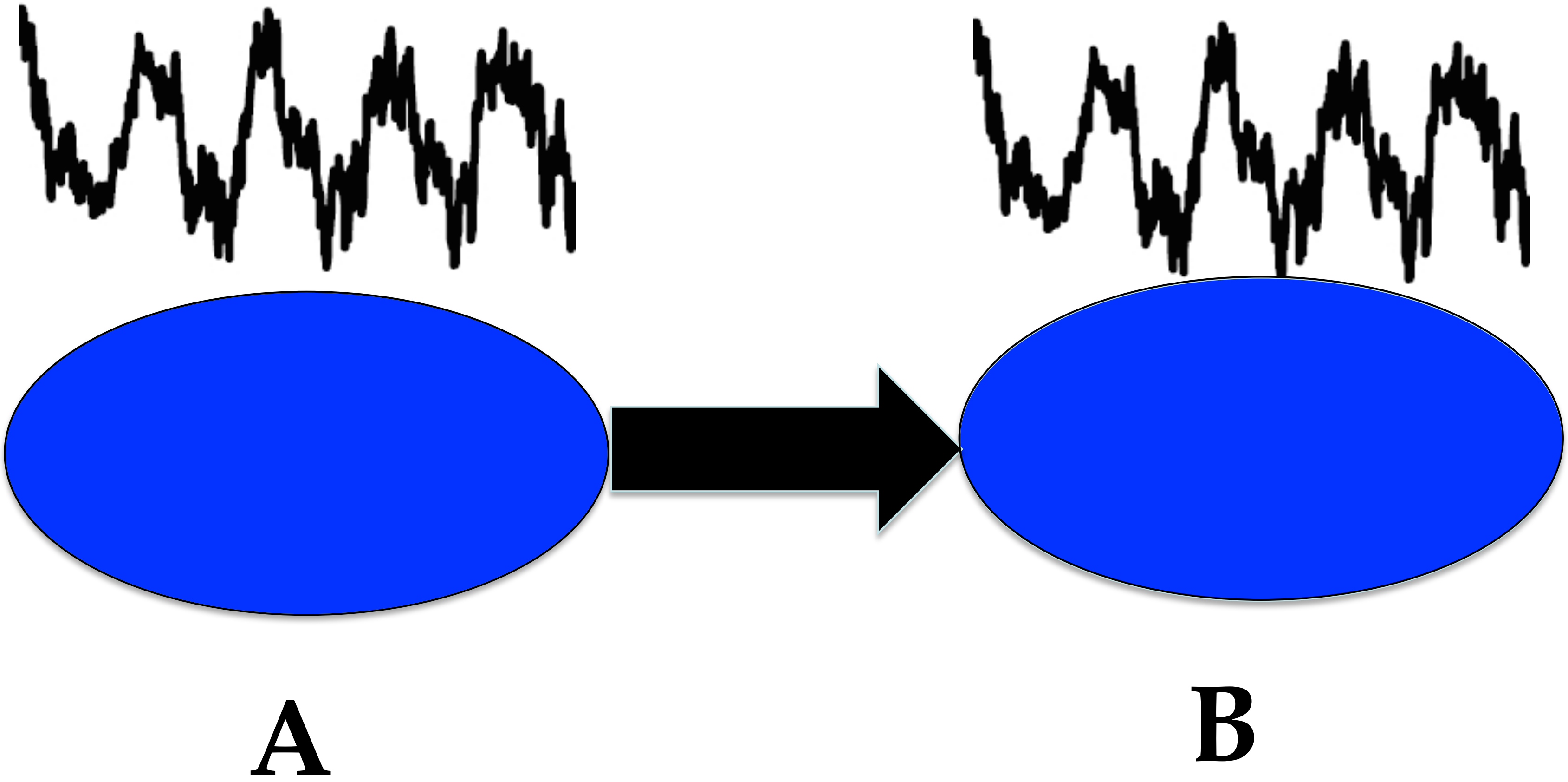
R. F. Salazar,[1] N. M. Dotson,[1] S. L. Bressler,[2] C. M. Gray[1]* SCIENCE VOL 338 23 NOVEMBER 2012

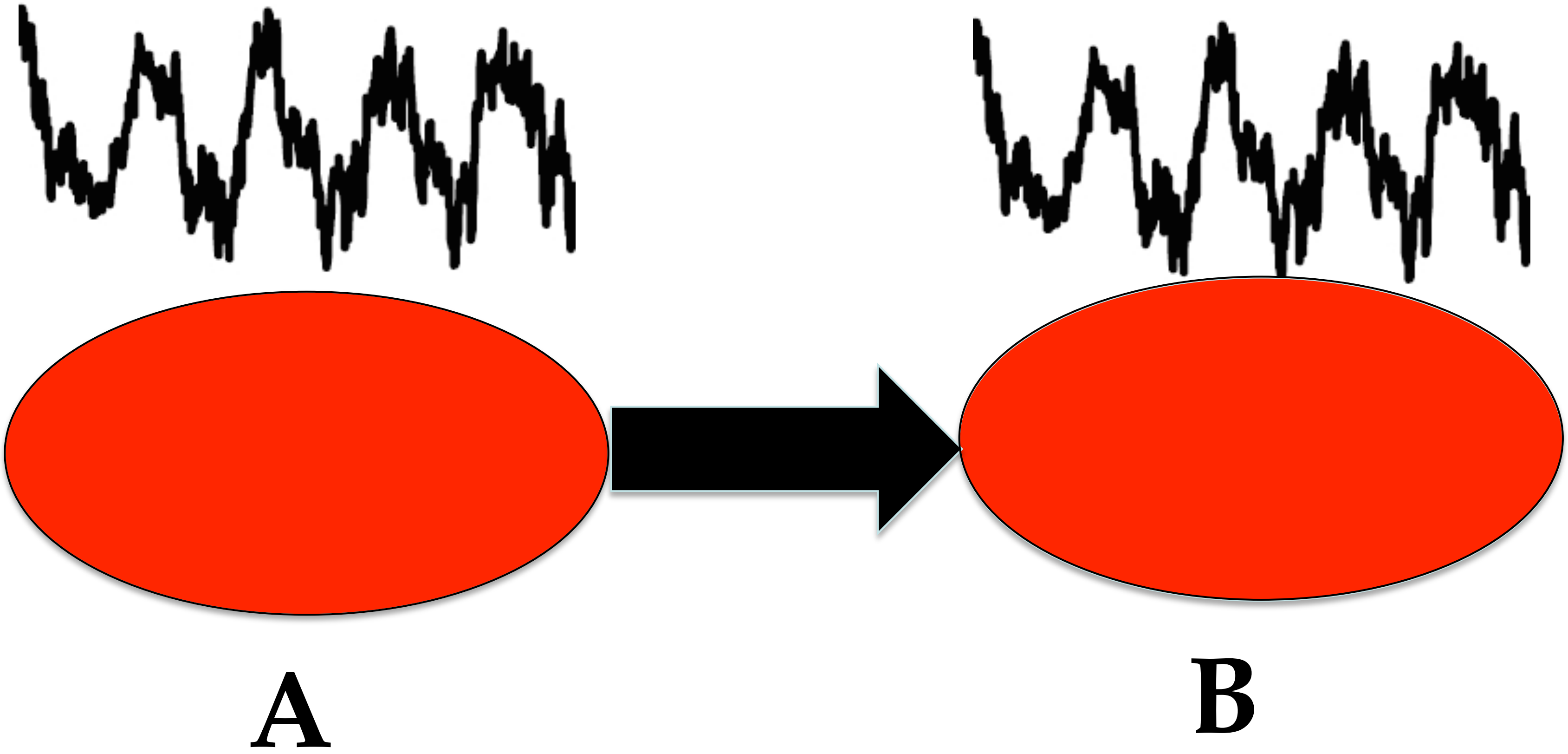




Strong causal influences *observed from primary somatosensory cortex to both motor cortex and inferior posterior parietal cortex.*

Causality relations were generally **inconsistent** with time delay values: the sign of the time delay did not predict the direction of causality: **"relative phase is not a reliable index of neural influence"**


A
B



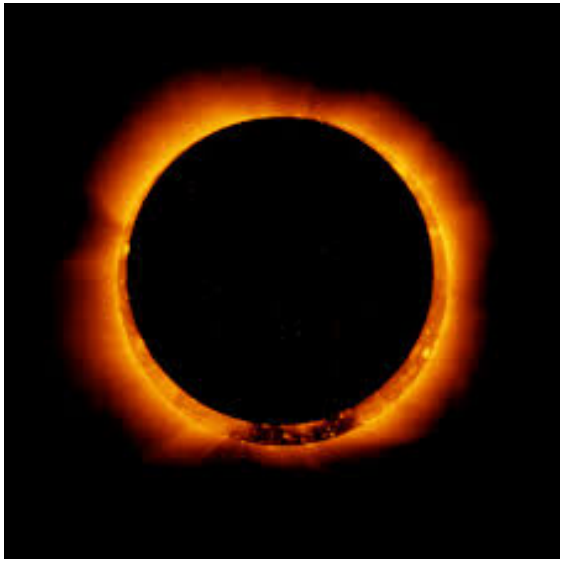
The receiving population is predicting what the emitting population is going to do in the future

Can we predict or anticipate the future?

If you give me the equation of motion and the initial conditions

$$\frac{dx}{dt} = F(x,t), \quad x(0) = x_0$$

YES!



There will be a total solar eclipse on April 20th 2023

Will be visible in South/East Asia, North/west Australia, Pacific, Indian Ocean, Artic & Antartic

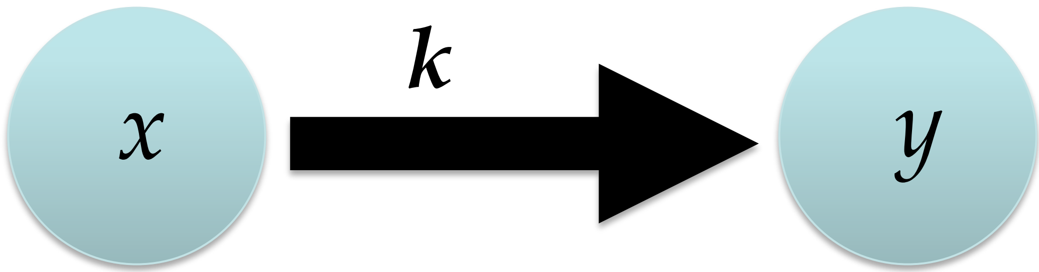
But many times we have to deal with fast varying (even chaotic) dynamical systems for which initial conditions are not known with enough precision…..

Henning Voss

Proposed a novel method to predict the response of a dynamical system based on the use of an auxiliary system.

The prediction is done by anticipating the evolution of the system of interest.

Synchronization of coupled systems



$$\left.\begin{aligned} \dot{x} &= f(x(t)) \\ \dot{y} &= f(y(t)) + k\,[x(t) - y(t)] \end{aligned}\right\} \Rightarrow x(t) = y(t)$$

$\Delta(t) = x(t) - y(t) = 0$ is a fixed point of the dynamics

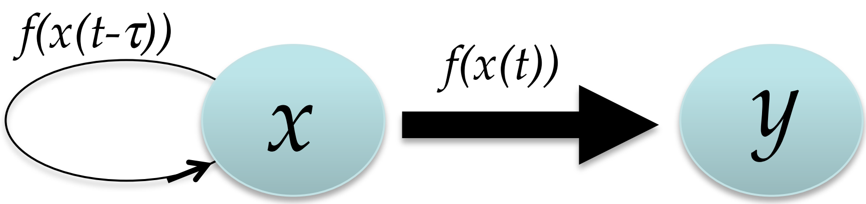
$\dot{\Delta}(t) = [f'(t) - k]\,\Delta(t)$ can be stable for large enough k

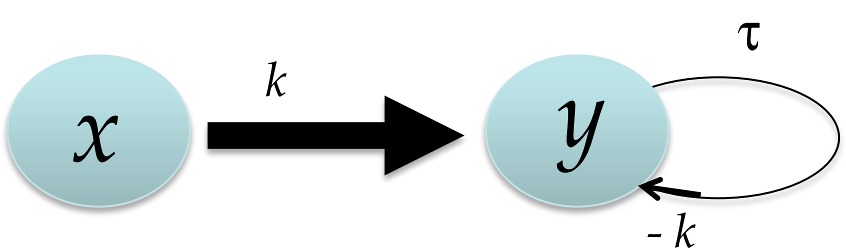
This is true even for chaotic systems

Anticipated Synchronization

Voss discovered a new synchronization scheme, the ***"Anticipated Synchronization"*** ***where the*** *slave system predicts the dynamics of the master system*. H. U. Voss, P.RE **61**, 5115 (2000)

Two coupling schemes were proposed:





Complete Replacement

$$\dot{x}(t) = -a\,x(t) + f(x(t-\tau))$$

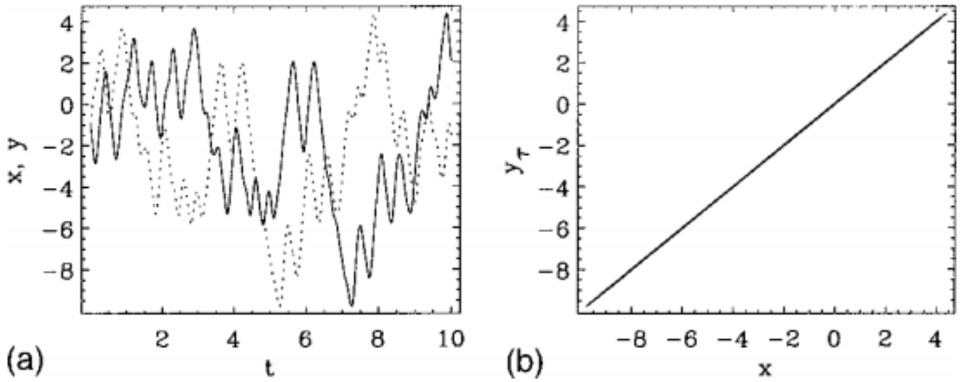
$$\dot{y}(t) = -a\,y(t) + f(x(t))$$

Delayed Coupling

$$\dot{x}(t) = f(x(t))$$

$$\dot{y}(t) = f(y(t)) + k\,[x(t)-y(t-\tau)]$$

- ✓ *f (x) is a function which defines the autonomous dynamical system under consideration.*
- ✓ *In both schemes the manifold $y(t) = x(t+\tau)$ is a solution of the equations and Voss showed that it can be structurally stable.*
- ✓ *This is more remarkable when the dynamics of the emitter system x is "intrinsically unpredictable" as in the case of chaotic systems.*
- ✓ *In the complete replacement scheme τ can be arbitrarily large while in the delay coupling scheme there are some constrains on* τ and κ

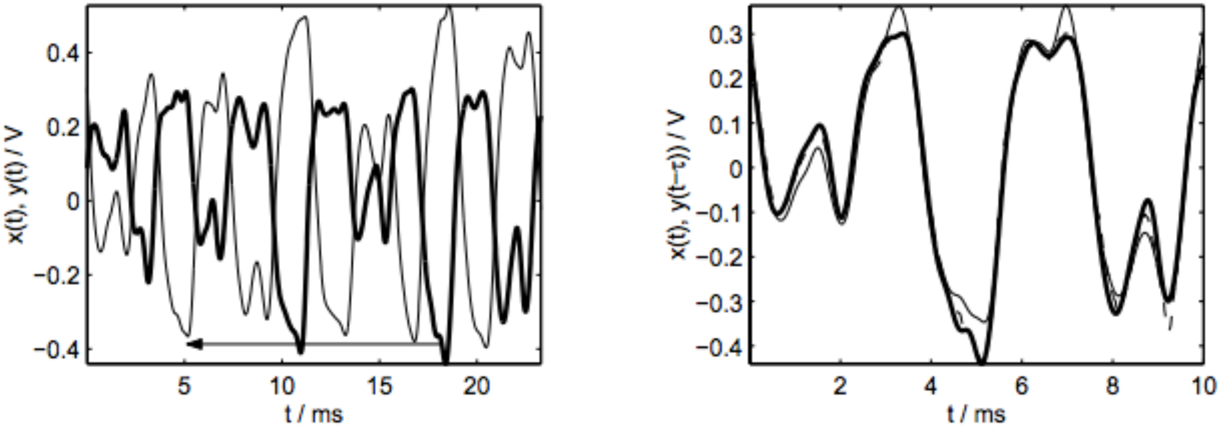


Ikeda Equations

$$\dot{x} = -a\,x - b\,\sin(x(t-\tau))$$

$$\dot{y} = -a\,y - b\,\sin(x)$$

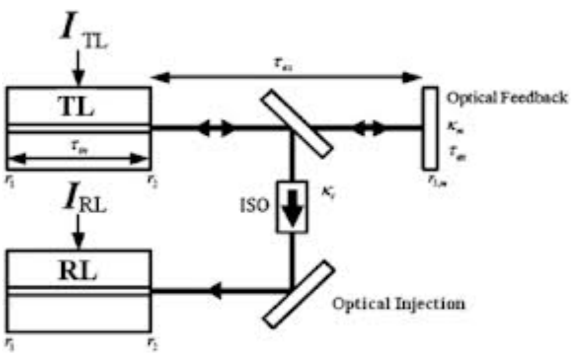
H.Voss, Phys. Rev. E 61, 5115 (2000)

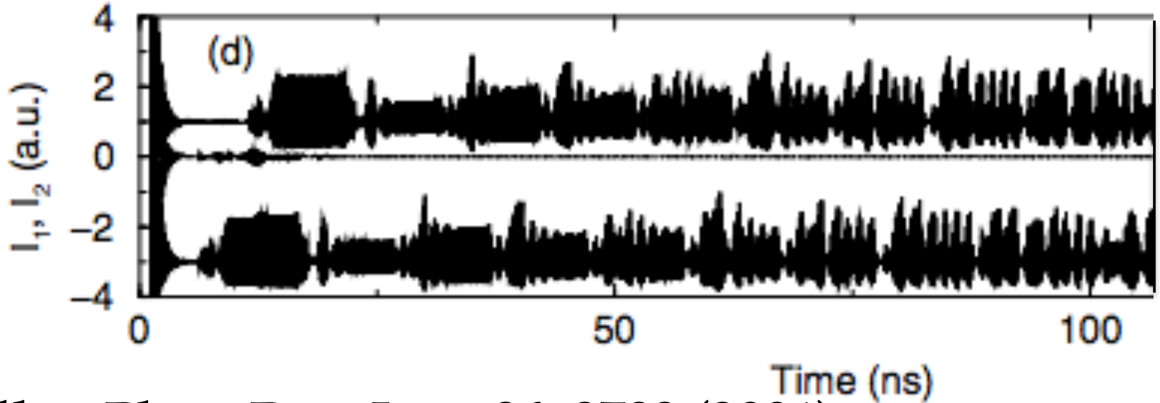


Electronic circuit with a strong non-linearity

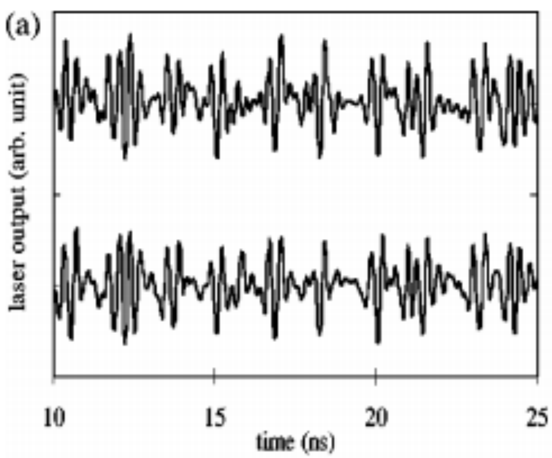
H.Voss, Int. J. Bifurc. Chaos 12, 1619 (2002)

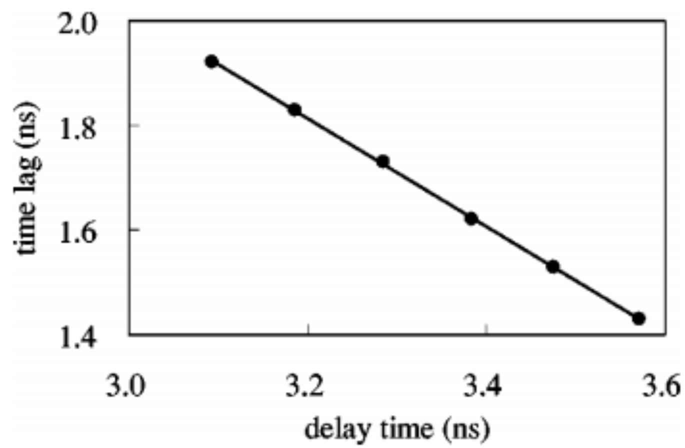
Complete replacement scheme in laser systems





C. Masoller, Phys. Rev. Lett. 86, 2782 (2001)



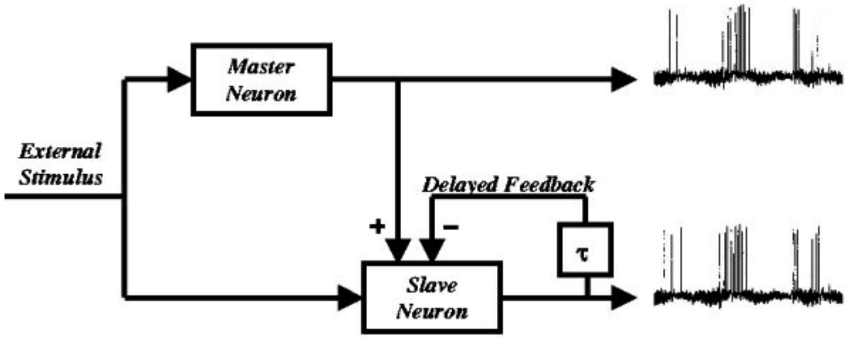


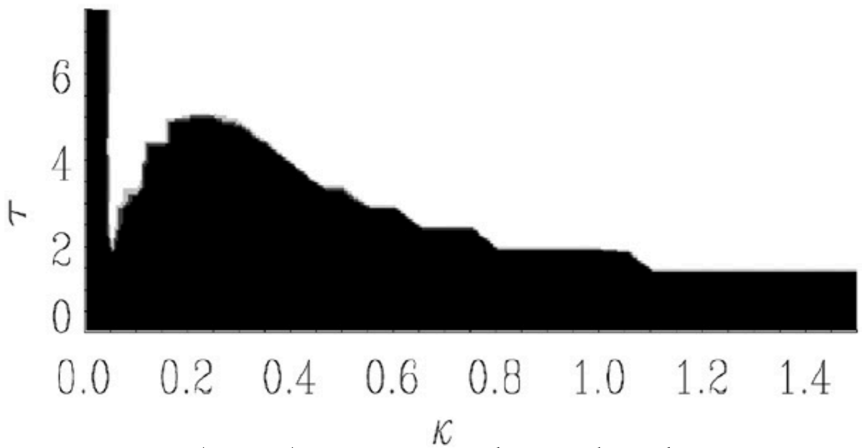
Y. Liu et al., Appl. Phys Lett. 80, 4306 (2002)

Coupled Fitzhugh-Nagumo Systems

$$\dot{x}_1 = -x_1(x_1 - a)(x_1 - 1) - x_2 + I(t)$$
$$\dot{x}_2 = \epsilon(x_1 - bx_2)$$

$$\dot{y}_1 = -y_1(y_1 - a)(y_1 - 1) - y_2 + I(t) + K[x_1(t) - y_1(t - \tau)]$$
$$\dot{y}_2 = \epsilon(y_1 - by_2)$$

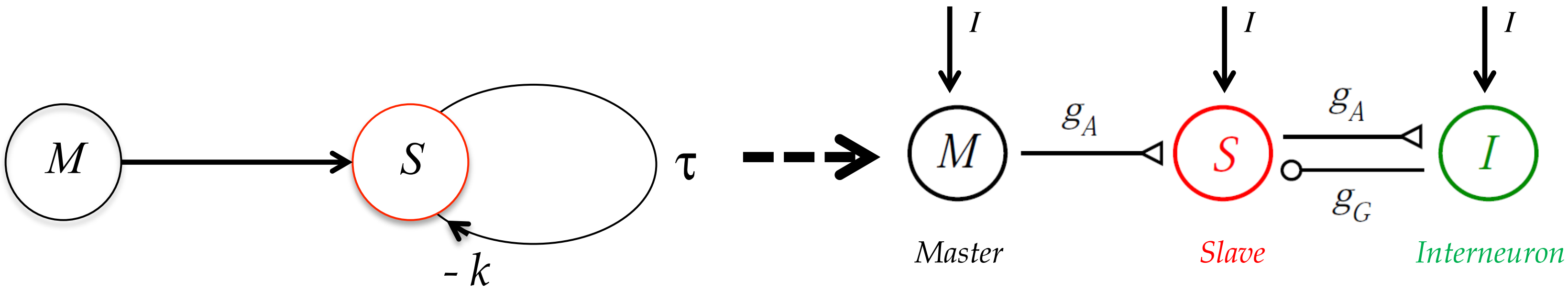




R. Toral et al., Physica A **325**, 192 (2003), M. Ciszak et al., Phys. Rev. Lett. **90**, 204102 (2003)

IFISC

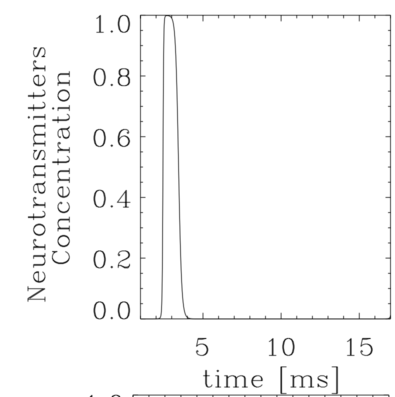
How do we extend Voss ideas to neuronal circuits?



Hodgkin-Huxley Model

Membrane potential

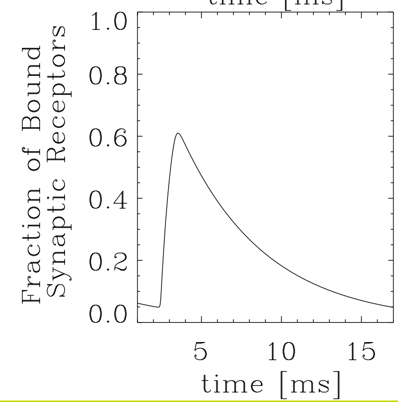
$$C_m \frac{dV}{dt} = \overline{G}_{Na} m^3 h (E_{Na} - V) + \overline{G}_K n^4 (E_K - V) + G_m (V_{rest} - V) + I + \sum I_{syn}$$



Synapsis dynamics

$$I^{(i)} = -g_i r^{(i)} (V - E_i)$$

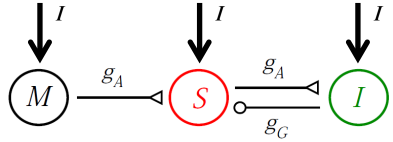
$$\frac{dr^{(i)}}{dt} = \alpha_i [T](1 - r^{(i)}) - \beta_i r^{(i)},$$



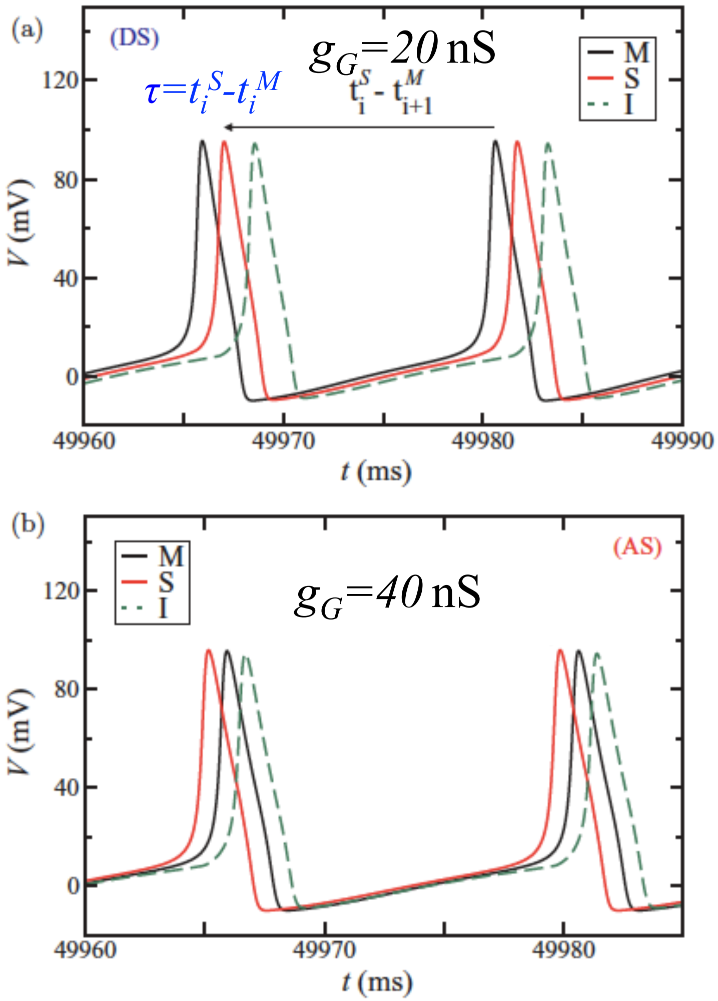
r: fraction of bound synaptic receptors

T: neurotransmitter concentration in the synaptic cleft

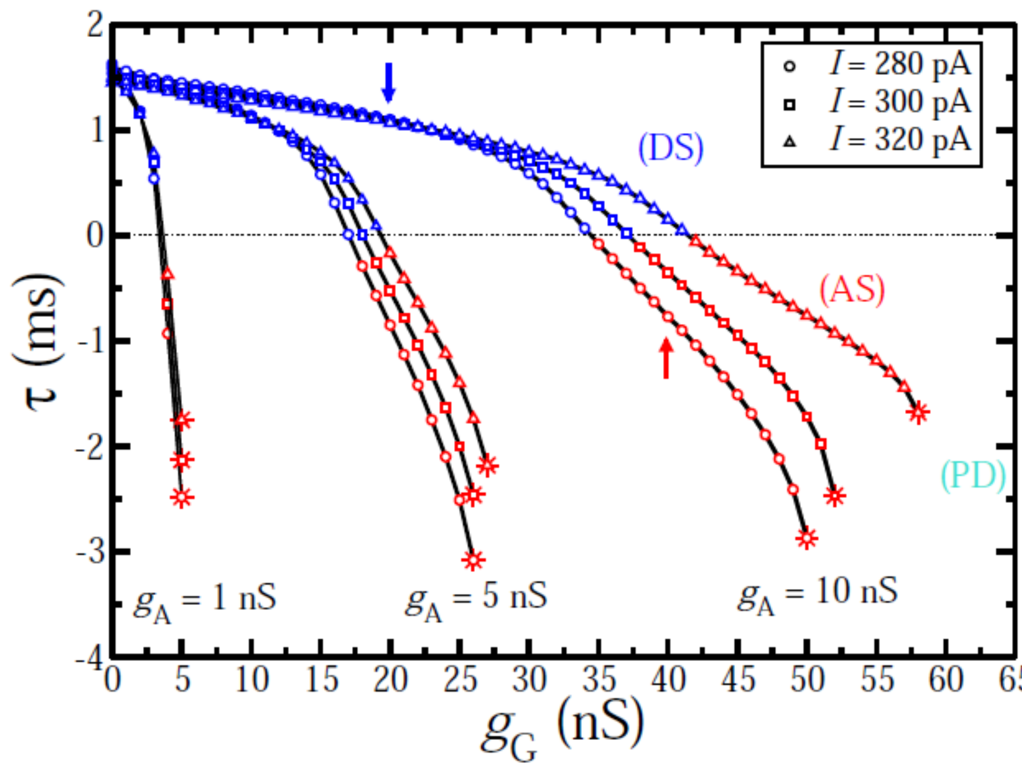
3 coupled neurons



$g_A=10$ nS, $I=280$ pA



Activation time (τ): $\tau \equiv t_i^S - t_i^M$

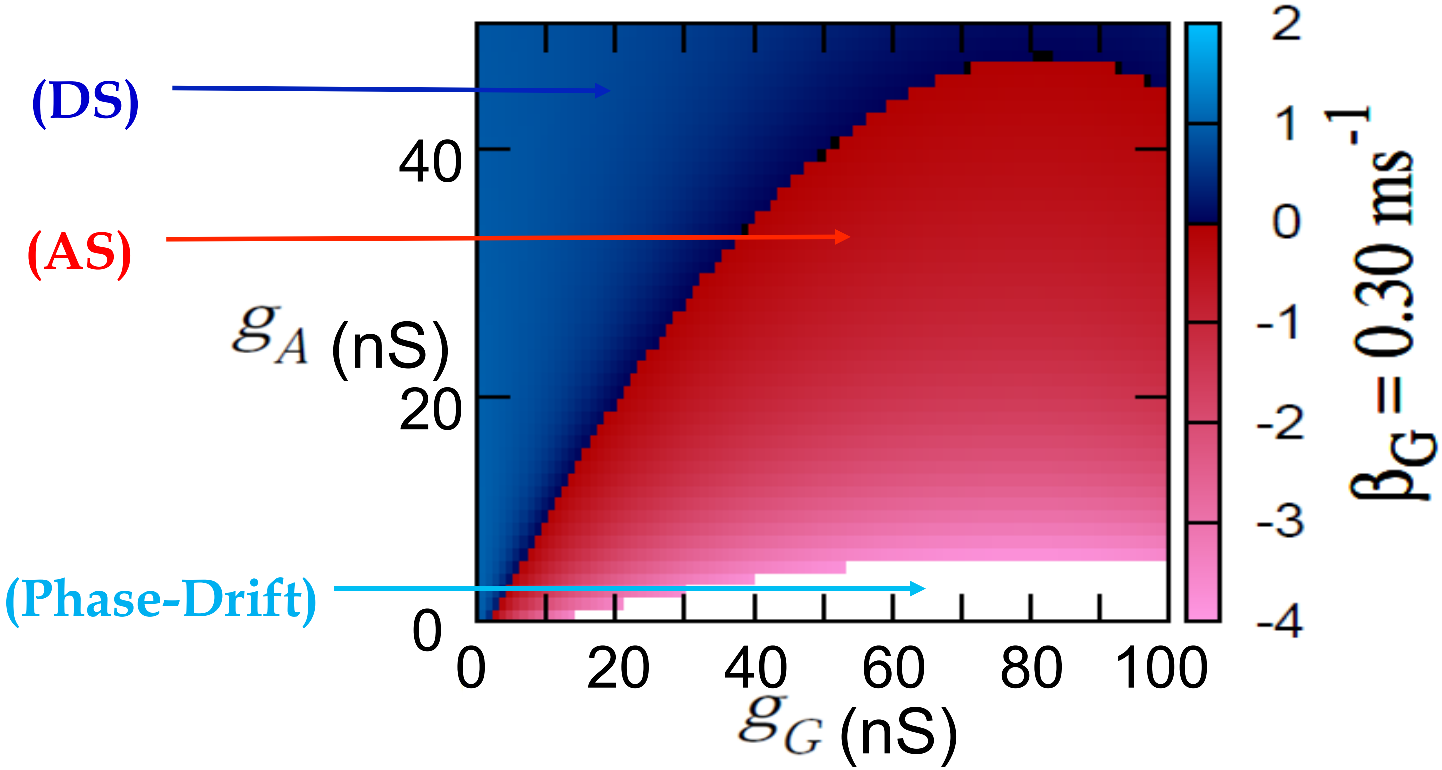


F. S. Matias, et al., Phys. Rev. E **84**, 021922 (2011)

Activation time in the g_A vs. g_G plane

Large regions of AS and DS in the parameter space

Independent of initial conditions and stable to perturbations



F. S. Matias, et al., Phys. Rev. E **84**, 021922 (2011)

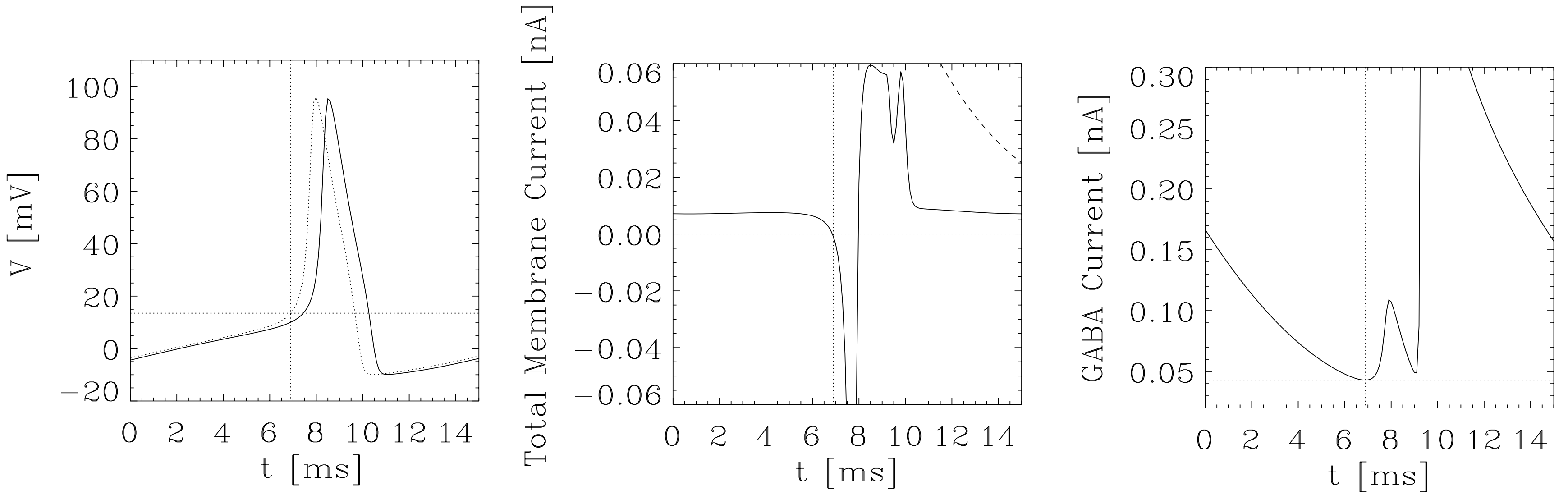
Robust against:

-External current

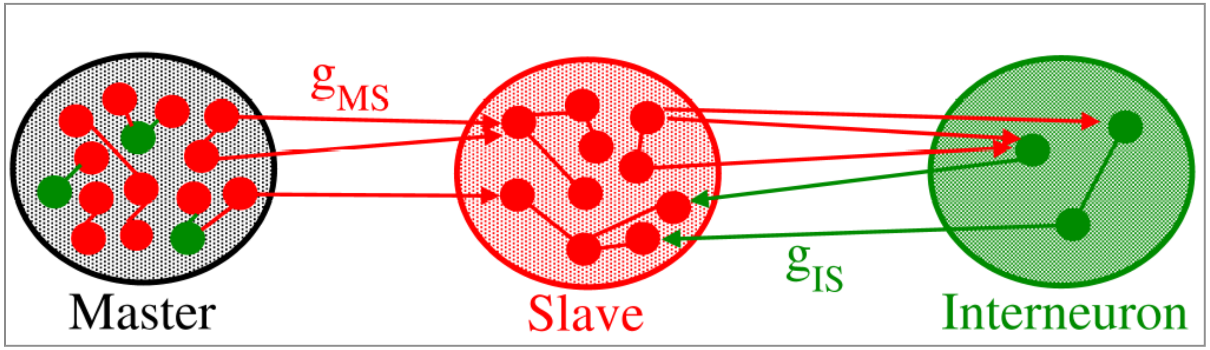
-Decay constants of the synapse

-Driver neuron

In neuronal systems preliminary results suggest that the system self-organizes to a situation in which at the time the membrane currents cross the zero (depolarizing the membrane), inhibitory synapsis reaches its minimum value, facilitating a pulse in the slave to be fired.



AS in neuronal populations?



Izhikevich Neuron Model

$$\frac{dv}{dt} = 0.04v^2 + 5v + 140 - u + \sum I_x$$

$$\frac{du}{dt} = a(bv - u) \quad v \geq 30\text{mV} \quad \begin{matrix} v \longrightarrow c \\ u \longrightarrow u+d \end{matrix}$$

Synapses mediated by AMPA and $GABA_A$

Short-range interactions: excitatory and inhibitory

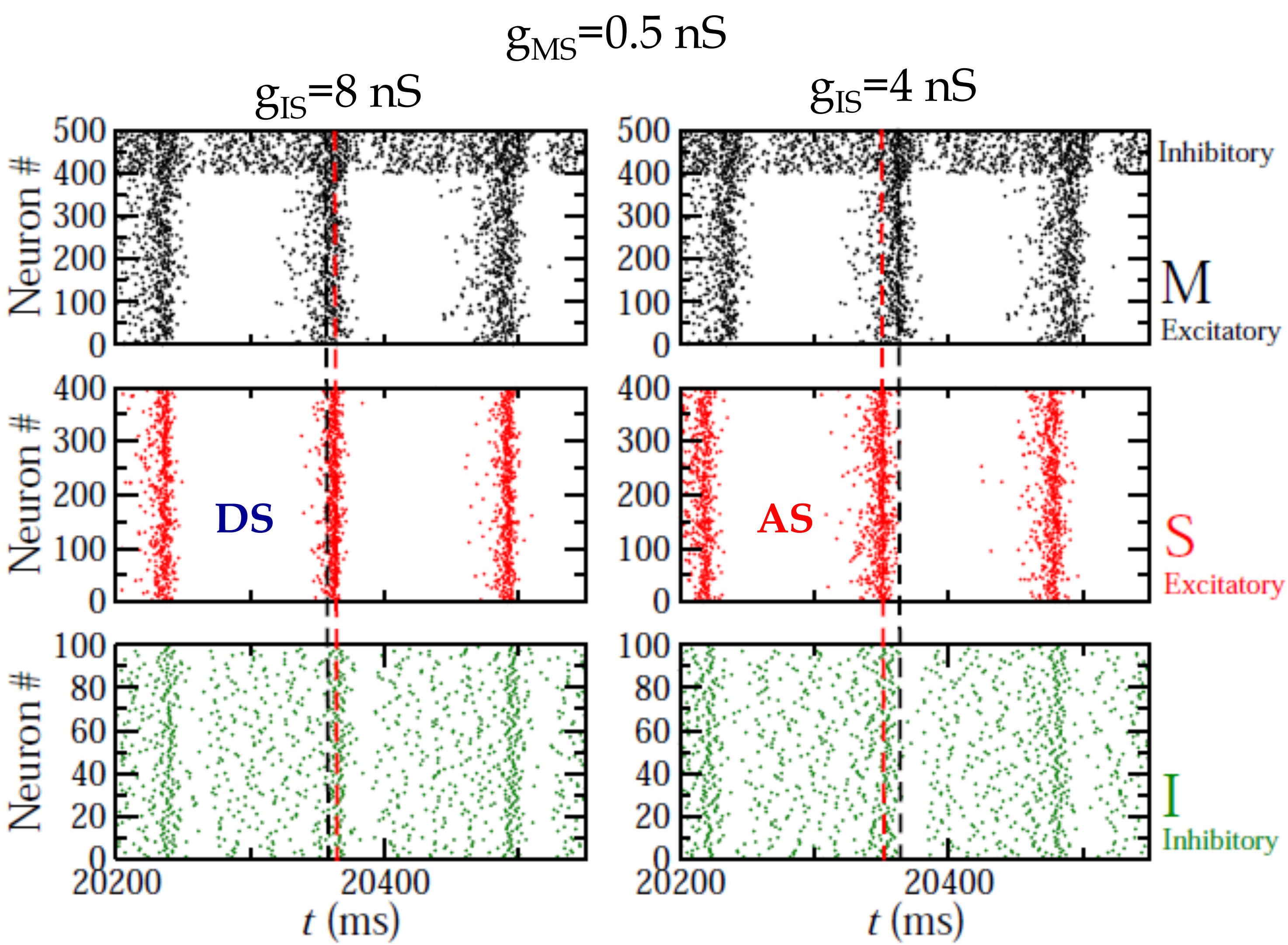
Long-range interactions: excitatory

Include neuronal diversity

Sparse connectivity

Each neuron receives an independent Poisson input

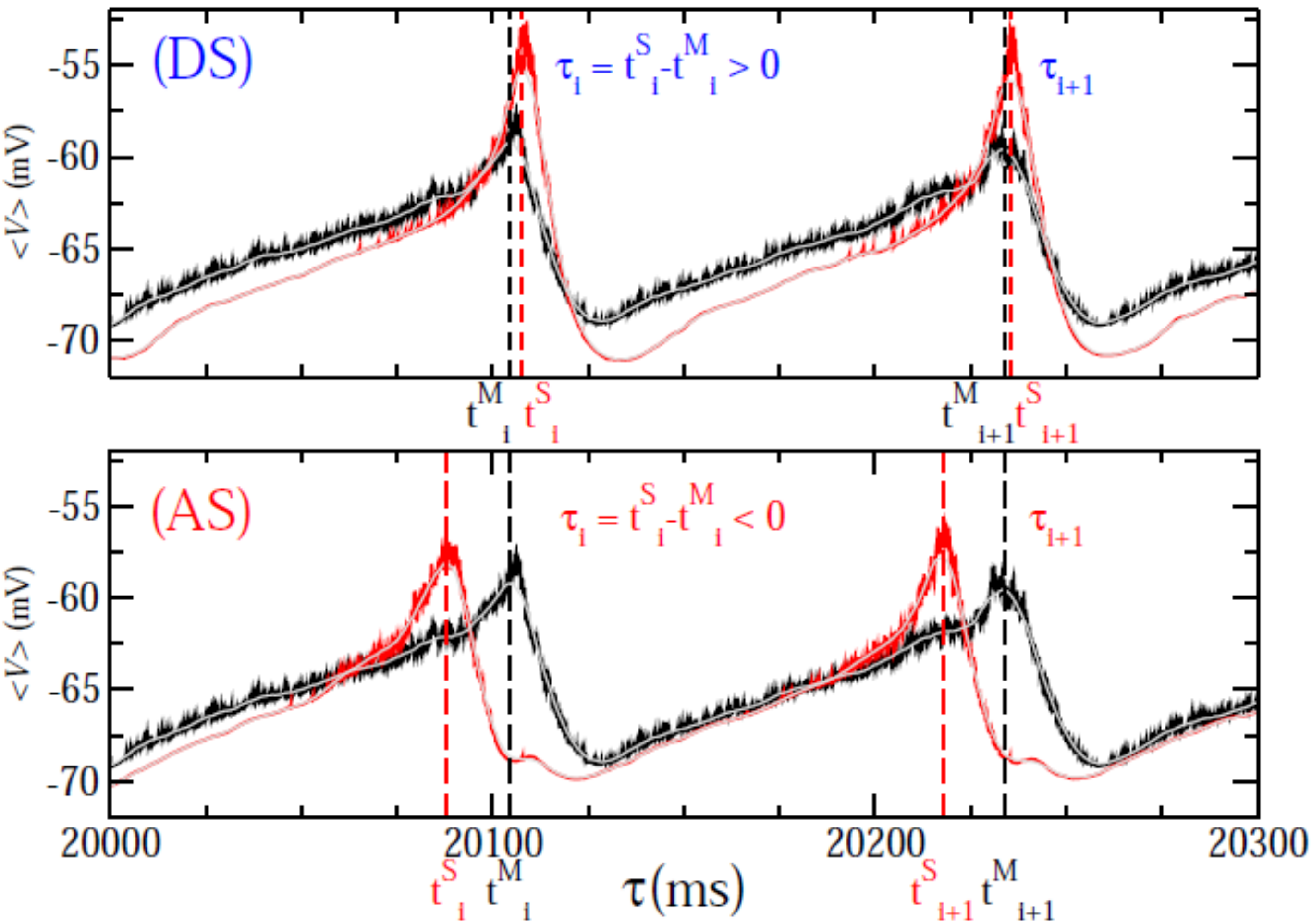
Raster plots



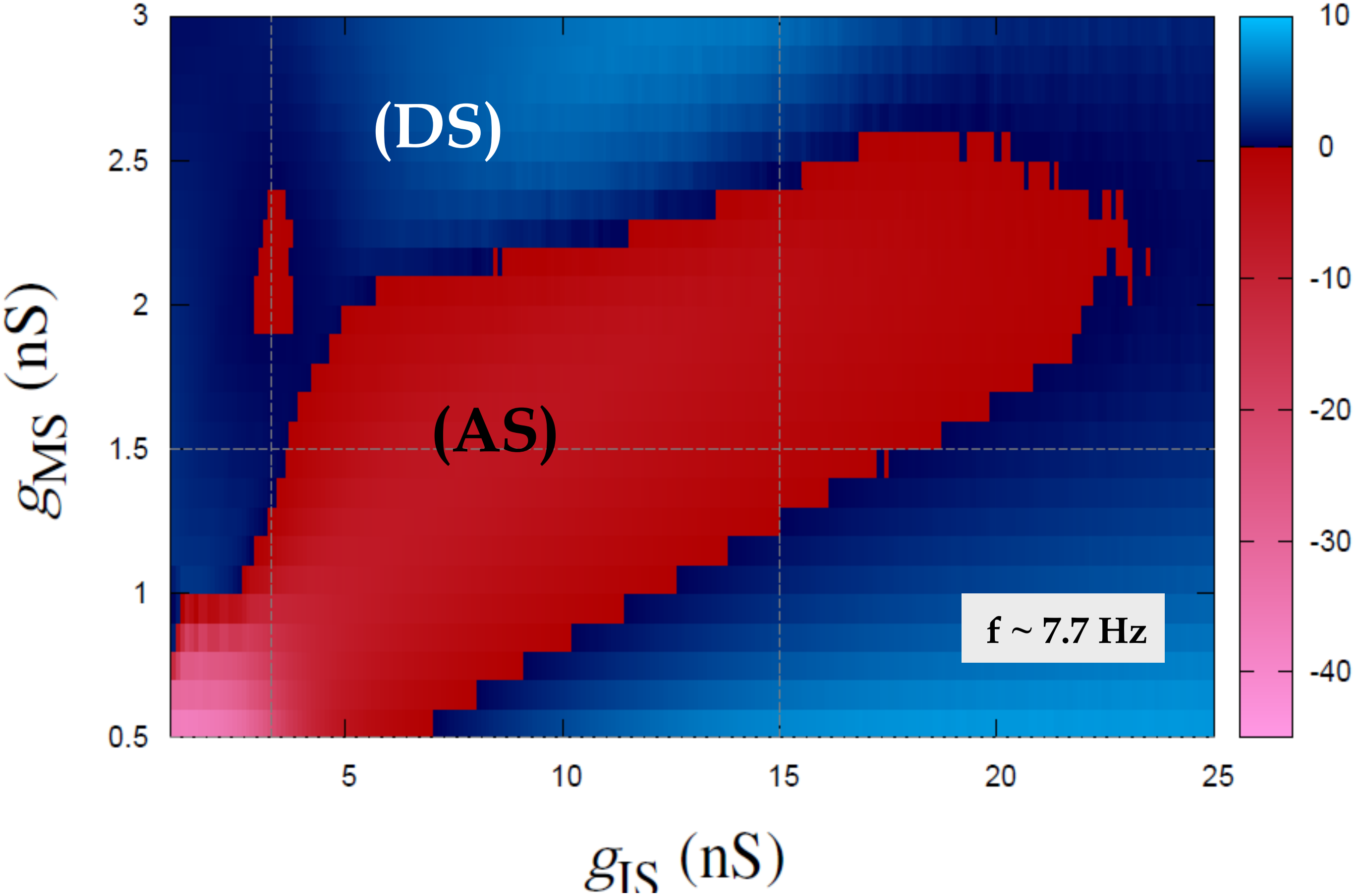
Mean Membrane Potential (LFP)

$$T_i^x \equiv t_{i+1}^x - t_i^x$$

$$\tau_i \equiv t_i^S - t_i^M$$



Mean Period *T = 130* ms (*f = 7.7* Hz)


(DS)
(AS)
f ~ 7.7 Hz
3
2.5
2
1.5
1
0.5
5
10
15
20
25
10
0
-10
-20
-30
-40
g_{MS} (nS)
g_{IS} (nS)

Experimental Evidence?

Beta oscillations in a large-scale sensorimotor cortical network: Directional influences revealed by Granger causality

Andrea Brovelli*, Mingzhou Ding*, Anders Ledberg*, Yonghong Chen*, Richard Nakamura†, and Steven L. Bressler*‡

PNAS | June 29, 2004 | vol. 101 | no. 26 | 9849–9854

Content-Specific Fronto-Parietal Synchronization During Visual Working Memory

R. F. Salazar,[1] N. M. Dotson,[1] S. L. Bressler,[2] C. M. Gray[1]*

SCIENCE VOL 338 23 NOVEMBER 2012 1097

Experimental Results: Coherence (and Activation time) & Granger Causality

Coherence: The coherence function gives the linear correlation between two signals as a function of the frequency.

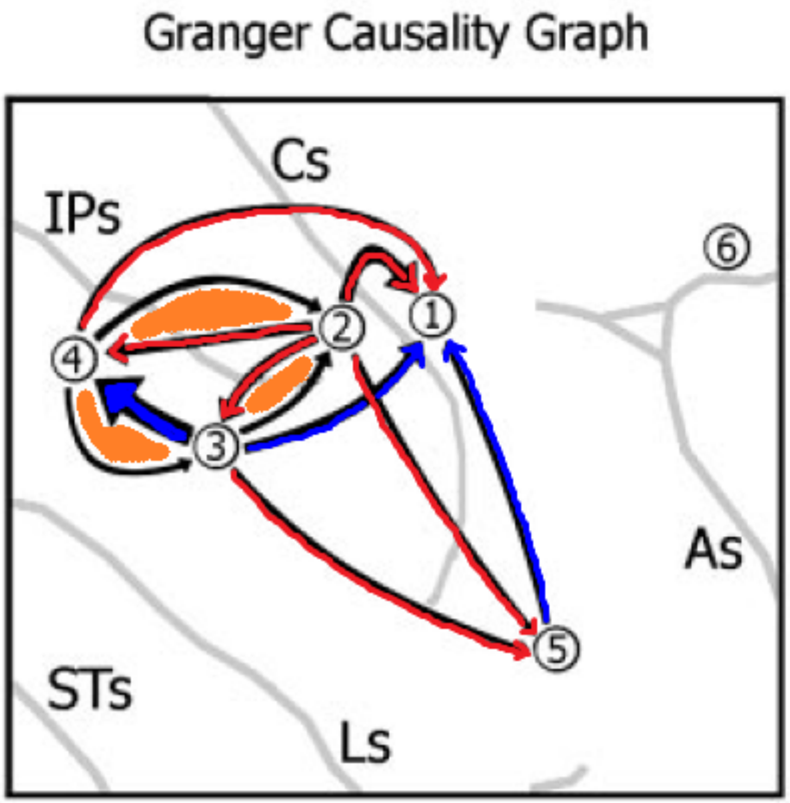
Activation time: it is estimated from the coherence spectrum as:

$$\tau_{lk} = \phi_{lk}(f_{peak})/(2\pi f_{peak})$$

$$\phi_{lk}(f) = \tan^{-1}[\mathrm{Im}(S_{lk})/\mathrm{Re}(S_{lk})]$$

Granger Causality: if a signal X is influencing Y, then adding past values of the first variable to the regression of the second one will improve its prediction performance.

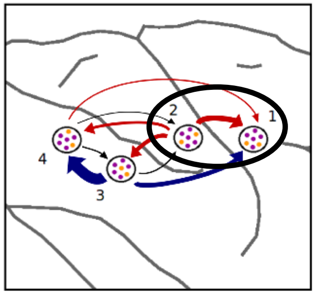
Experimental Results:
Coherence (and Activation Time) & Granger Causality

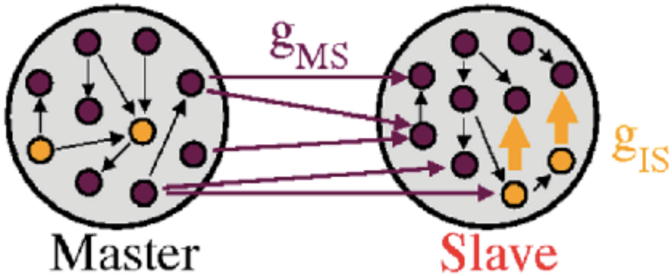


Granger causality and phase difference have different directions **(AS)**

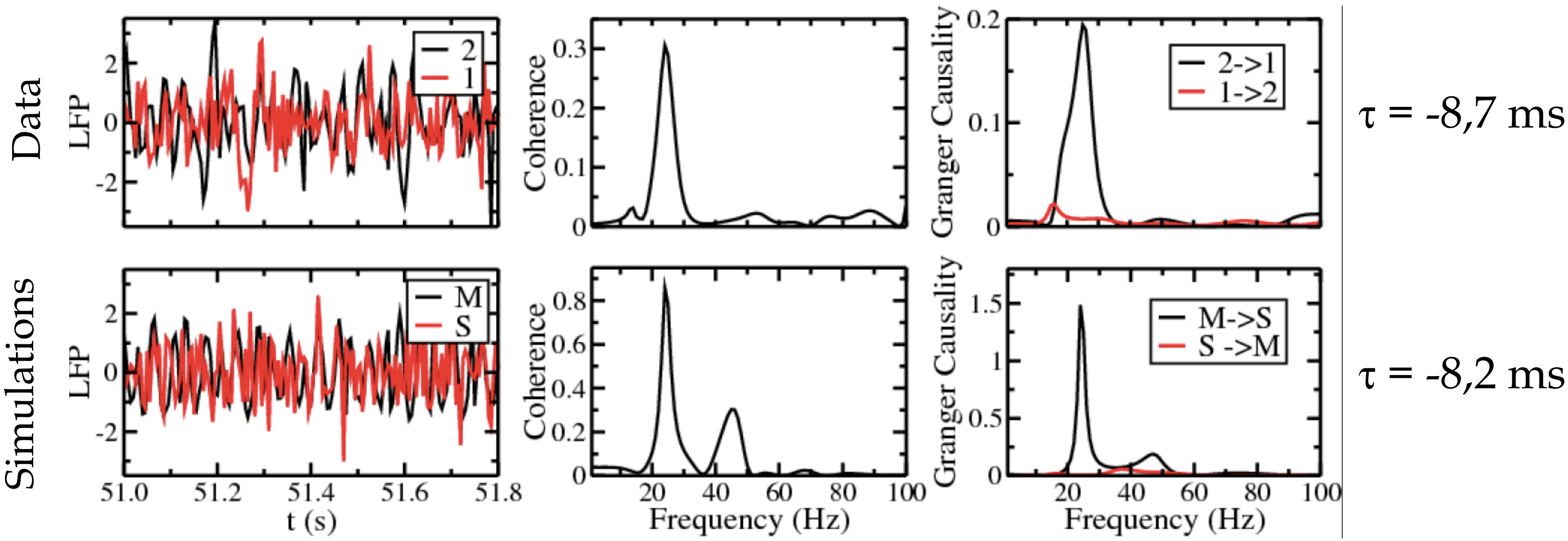
Granger causality and phase difference have the same direction **(DS)**

Granger causality is bidirectional but stronger in one direction

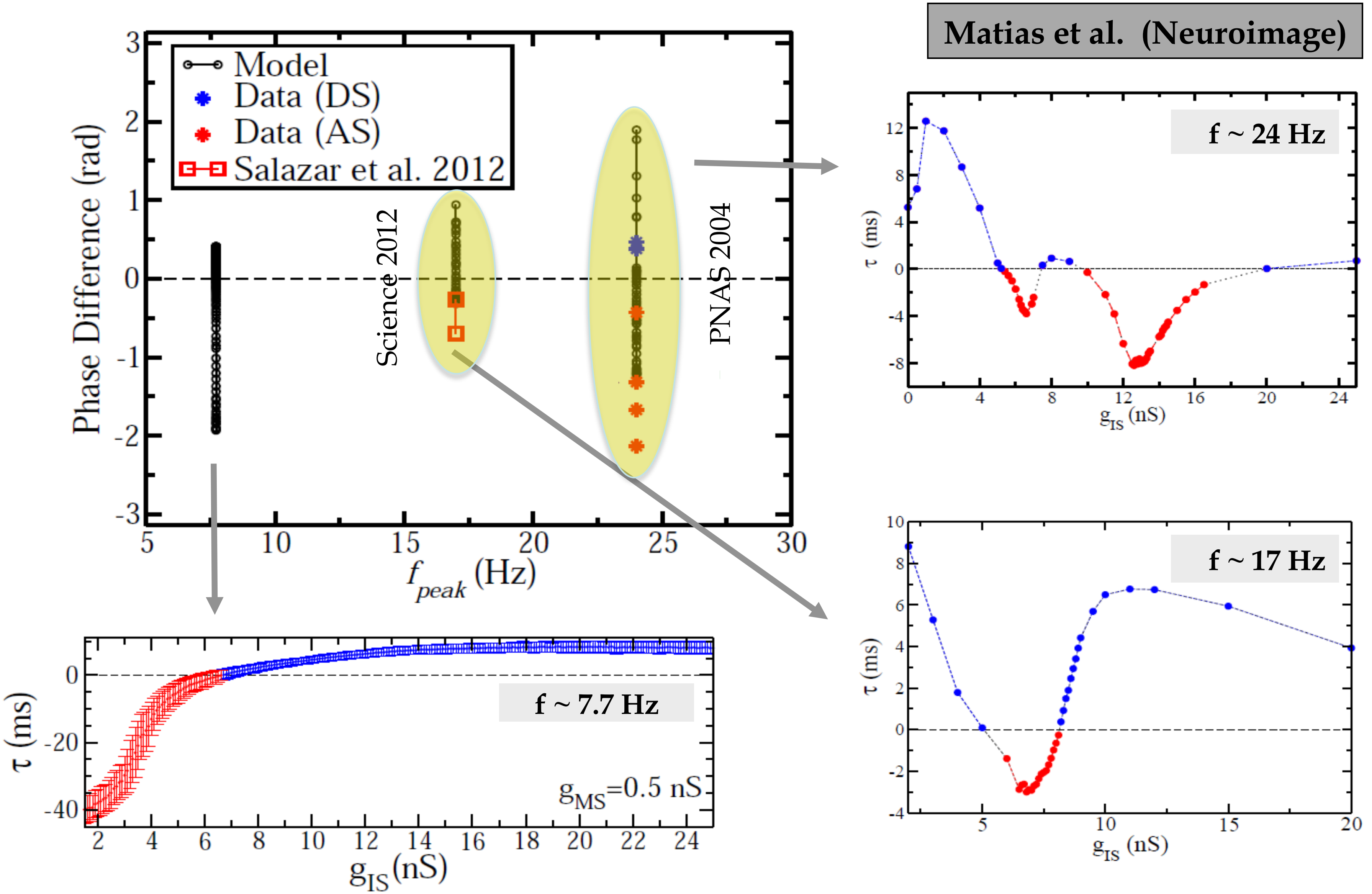




Site 2 Granger causes site 1



Matias et al., NeuroImage **99**, 411 (2014)


Matias et al. (Neuroimage)
Model
Data (DS)
Data (AS)
Salazar et al. 2012
Science 2012
PNAS 2004
Phase Difference (rad)
f peak (Hz)
f ~ 24 Hz
τ (ms)
g_IS (nS)
f ~ 17 Hz
τ (ms)
g_IS (nS)
f ~ 7.7 Hz
g_MS=0.5 nS
τ (ms)
g_IS (nS)

Summary & Conclusions

- ✓ A neuronal circuits of excitatory and inhibitory neurons gives rise to anticipated synchronization, even in the absence of an explicit delay loop.
- ✓ the interplay between excitation and inhibition regulates the transition between DS and AS.
- ✓ Experimental observations of negative delay with "positive" Granger causality has been experimentally observed in monkeys and reproduced with the model.
- ✓ Besides the reduction of information transmission time, any other functional role of AS is not clear yet.

Part I

Raûl Vicente: University of Tartu, Estonia

Leonardo Lyra: Queensland Institute of Medical Research, Brisbane, Australia

Gordon Pipa: University of Osnabrück, Germany

Ingo Fischer, IFSIC, Mallorca, Spain

Jordi García-Ojalvo: University Pompeu Fabra, Barcelona, Spain

Javier Buldú: Center for Biomedical Technology, Madrid, Spain

Carme Torrens: Polytechnic University of Catalunya, Spain

José Luis Cantero: University Pablo Olavide, Sevilla, Spain

Alessandro Villa: Université de Lausanne, Switzerland

Part II

Fernanda Matias: Universidade Federal de Alagoas, Maceió, Alagoas, Brazil

Mauro Copelli: Universidad Federal de Pernambuco, Brazil

Pedro Carelli: Universidad Federal de Pernambuco, Brazil

Leonardo Lyra: Queensland Institute of Medical Research, Brisbane, Australia

Steve Bressler: Center for Complex Systems & Brain Sciences, Boca Raton, USA.

Osvado Rosso: Universidade Federal de Alagoas, Maceió, Alagoas, Brazil

Fernando Montani: Instituto de Física de Líquidos y Sistemas Biológicos La Plata, Argentina

All papers available at

ifisc.uib-csic.es/publications/

Thanks for your attention