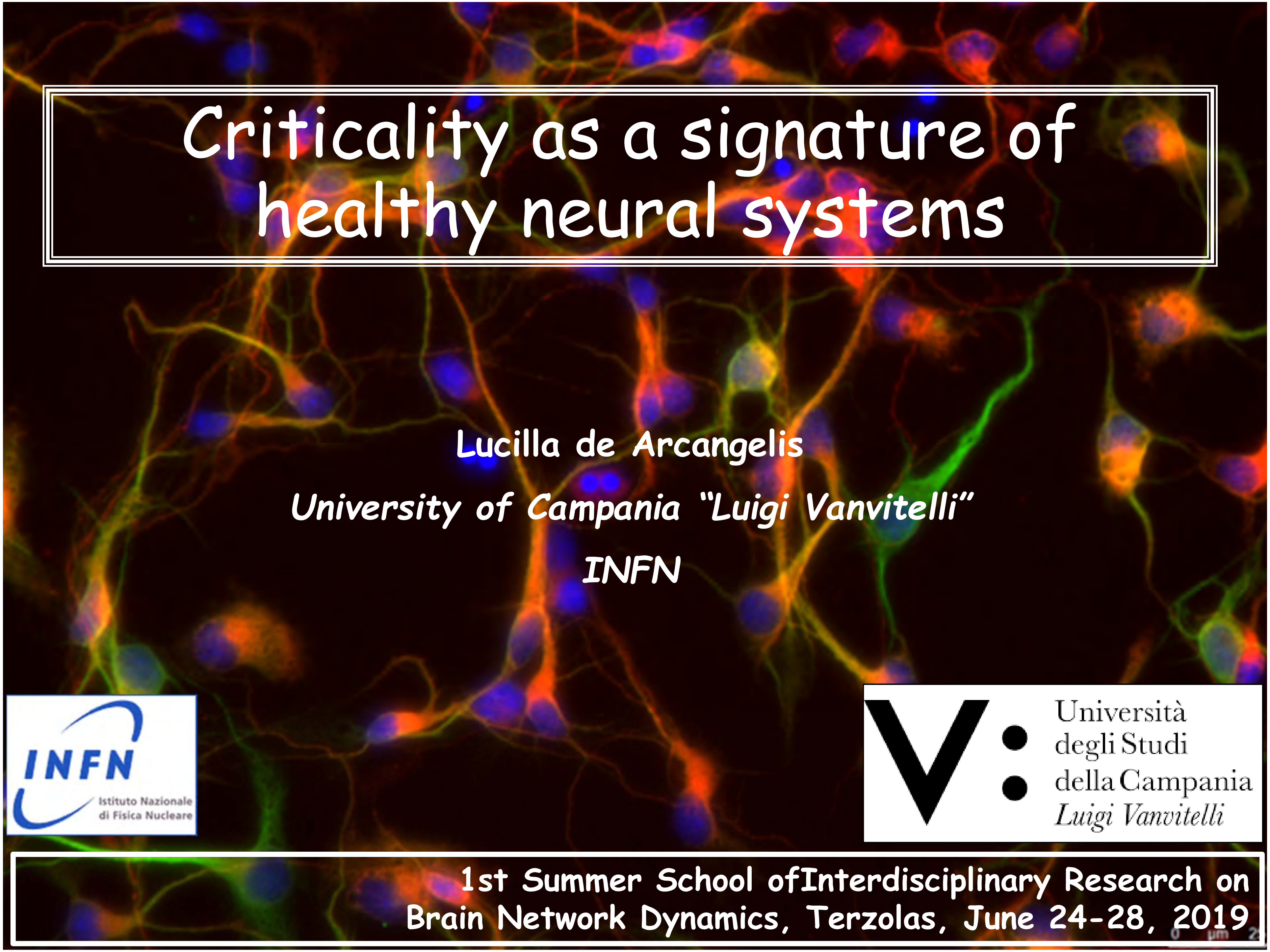

Criticality as a signature of healthy neural systems

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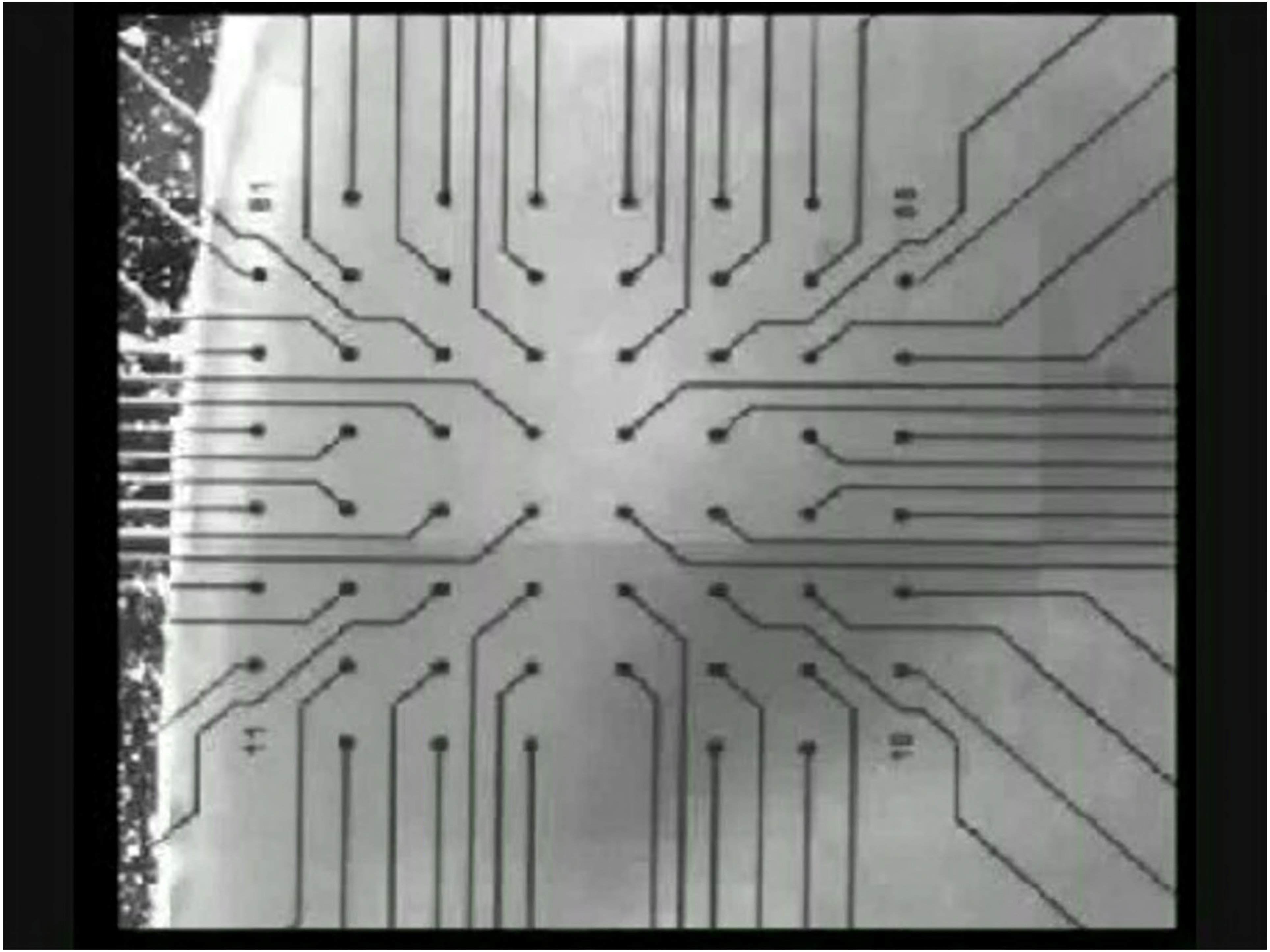
Università degli Studi della Campania *Luigi Vanvitelli*

1st Summer School ofInterdisciplinary Research on Brain Network Dynamics, Terzolas, June 24-28, 2019

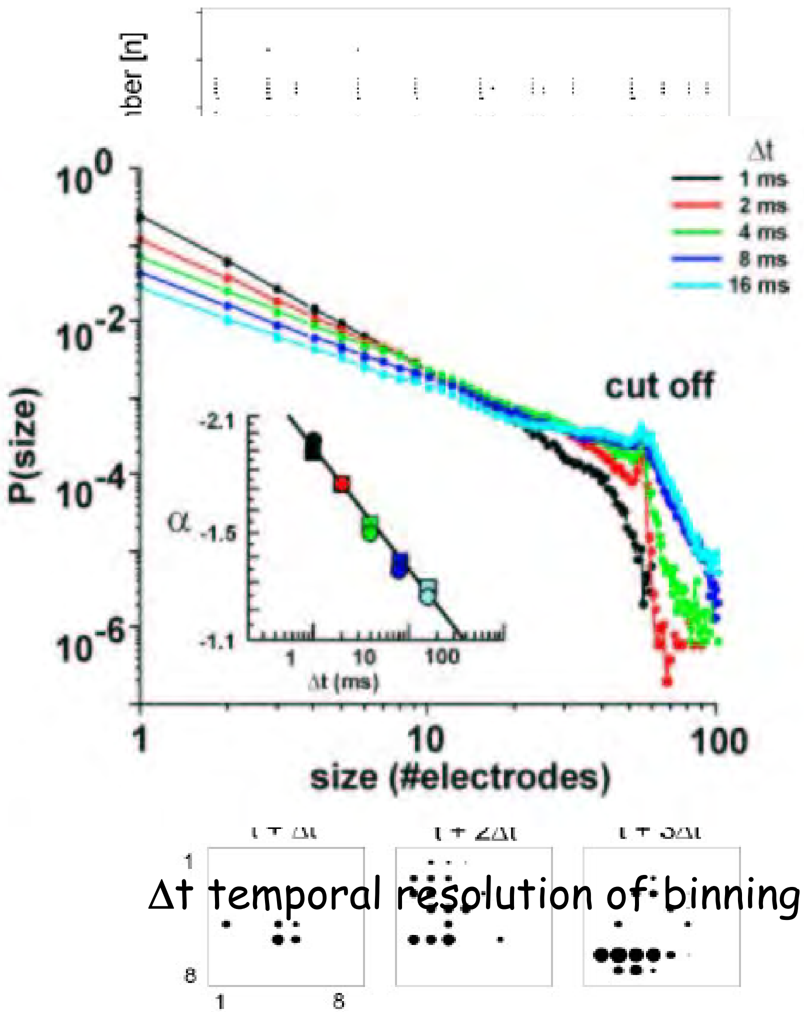


Neuronal avalanches

Beggs & Plenz (J. Neuroscience 2003) have measured spontaneous local field potentials continuously using a 60 channel multielectrode array in mature organotypic cultures of rat cortex

They have shown that spontaneous activity has an avalanche mode:

- Several avalanches (active electrodes) of all size per hour
- Activity initiated at one electrode may spread later to other electrodes in a not necessarily contiguous manner
- Avalanche size distribution is a power law with an exponent close to -3/2
- Avalanche duration distribution is a power law with an exponent close to -2.0



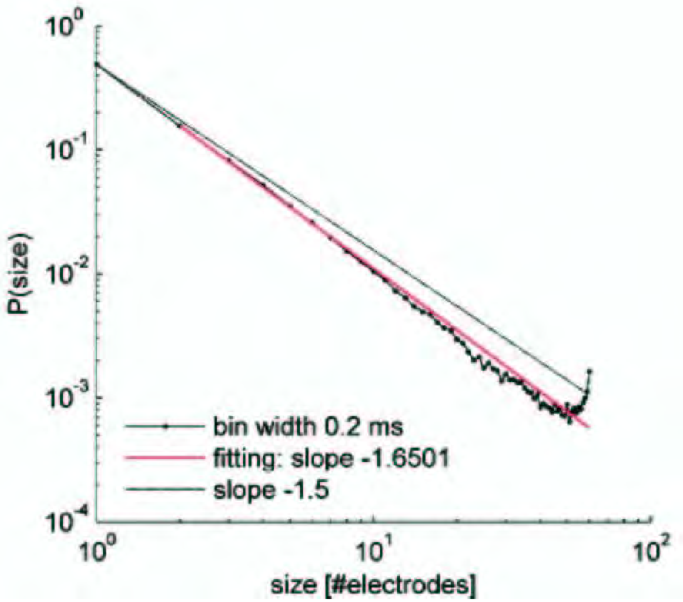
Δt temporal resolution of binning

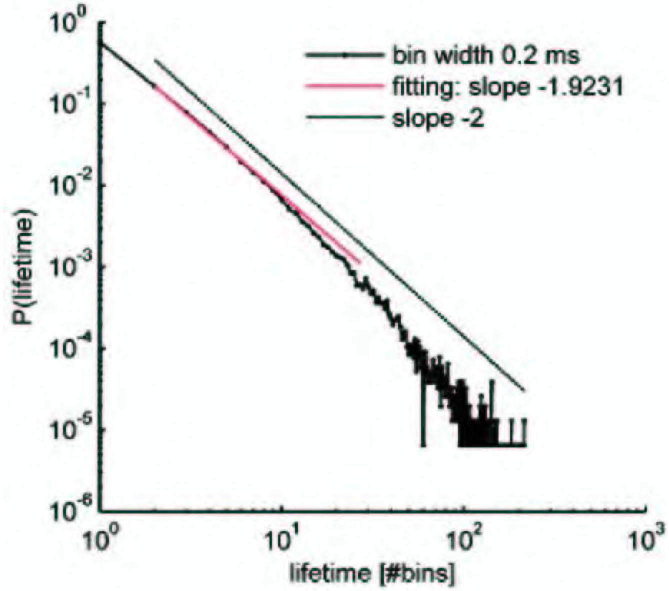
➡ Universality class
Mean field branching model

Avalanche activity found also in dissociated rat cortical neurons

(V. Pasquale et al, Neuroscience 2008)

- Neuronal avalanche behavior depends on time scale of observation
- Neuronal cultures developing in vitro organize differently and exhibit different dynamic state (critical, subcritical, supercritical)
- Critical behaviour depends on the interplay between spiking and bursting activity

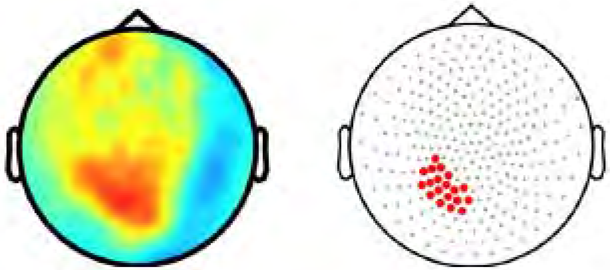


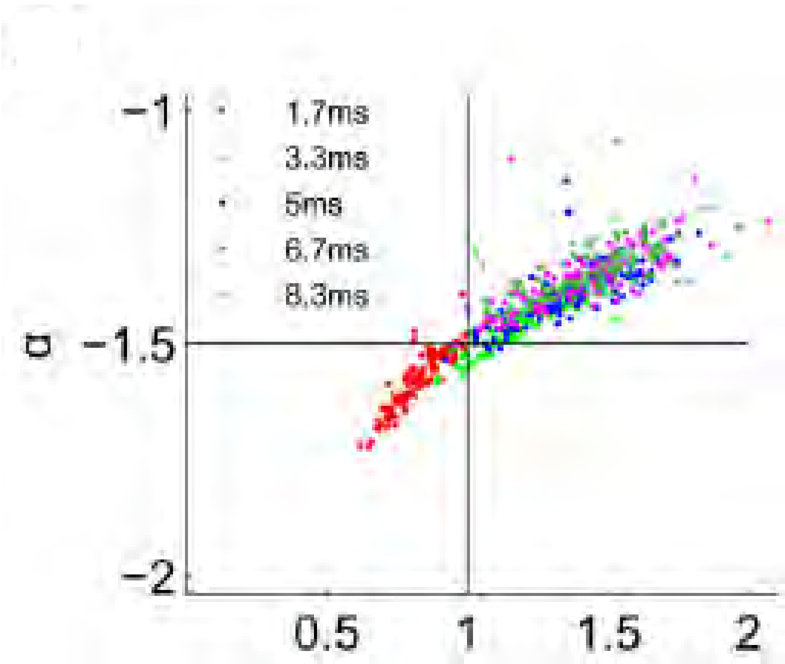


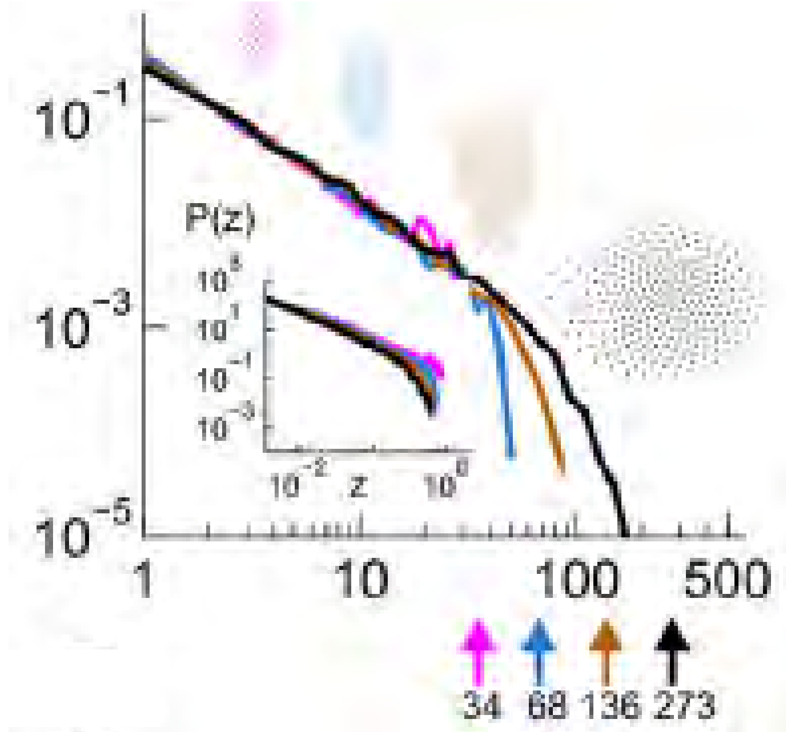
- Similar scaling behavior found for dissociated rat hippocampal neurons and leech ganglia (A. Mazzoni et al PLoS ONE 2007)

Behaviour at large scale

MEG measurements on humans
(124 patients)







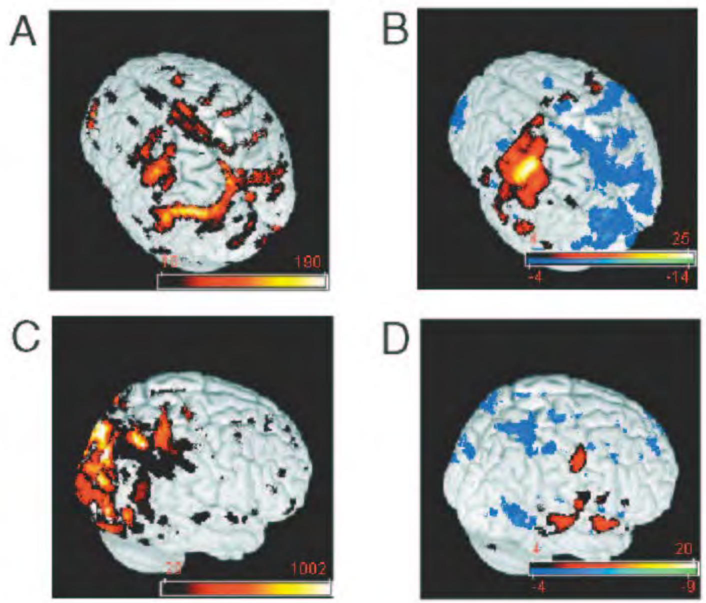
Shriki et al (J. Neurosci. 2013)
Size distribution of activity
Cascades scales with exponent -1.5
for a critical branching process

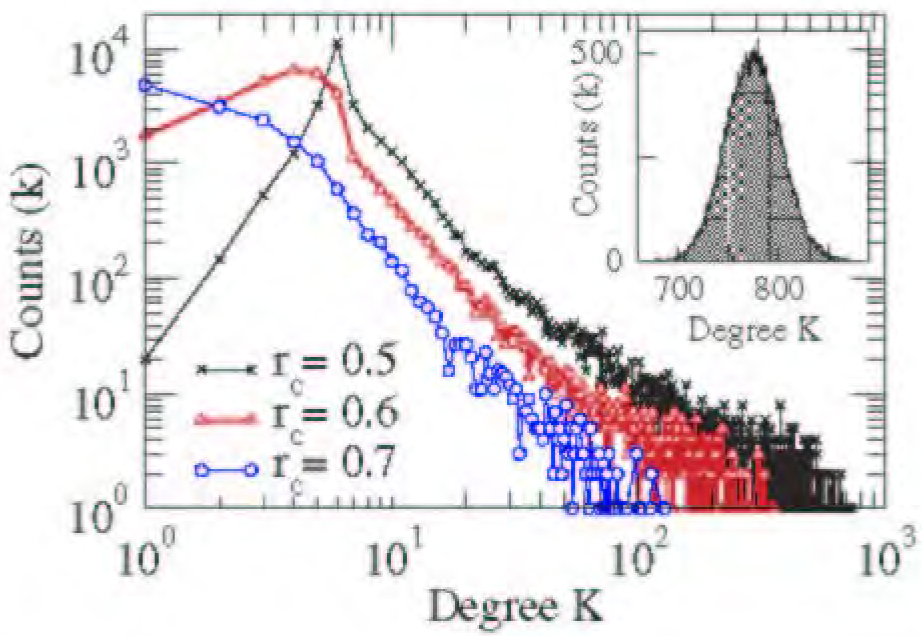
Scale-free Brain Functional Network

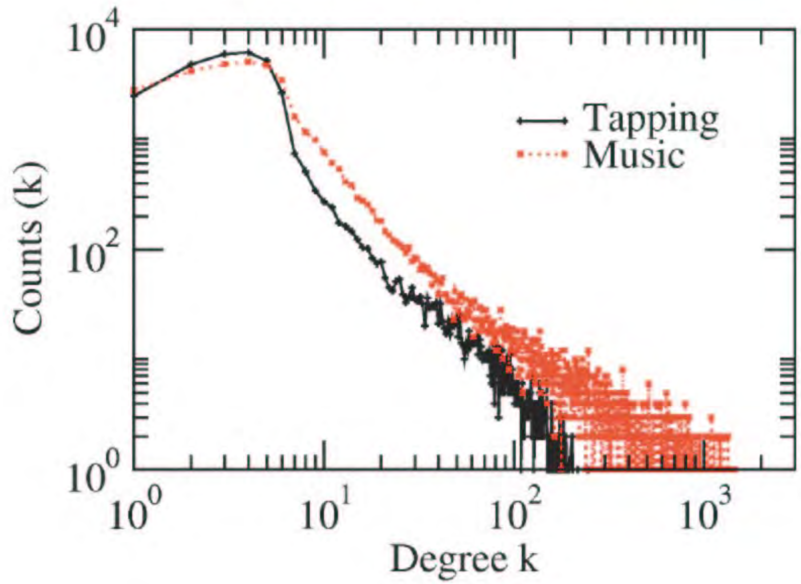
Eguiluz, Chialvo, Cecchi, Baliki, and Apkarian (PRL 2005) measured by MRI the functionality network in humans performing different tasks

- Correlation coefficient between magnetic resonance activity in any pair of voxels, $r(x_1, x_2)$ averaged over time
- Two voxels are functionally correlated if

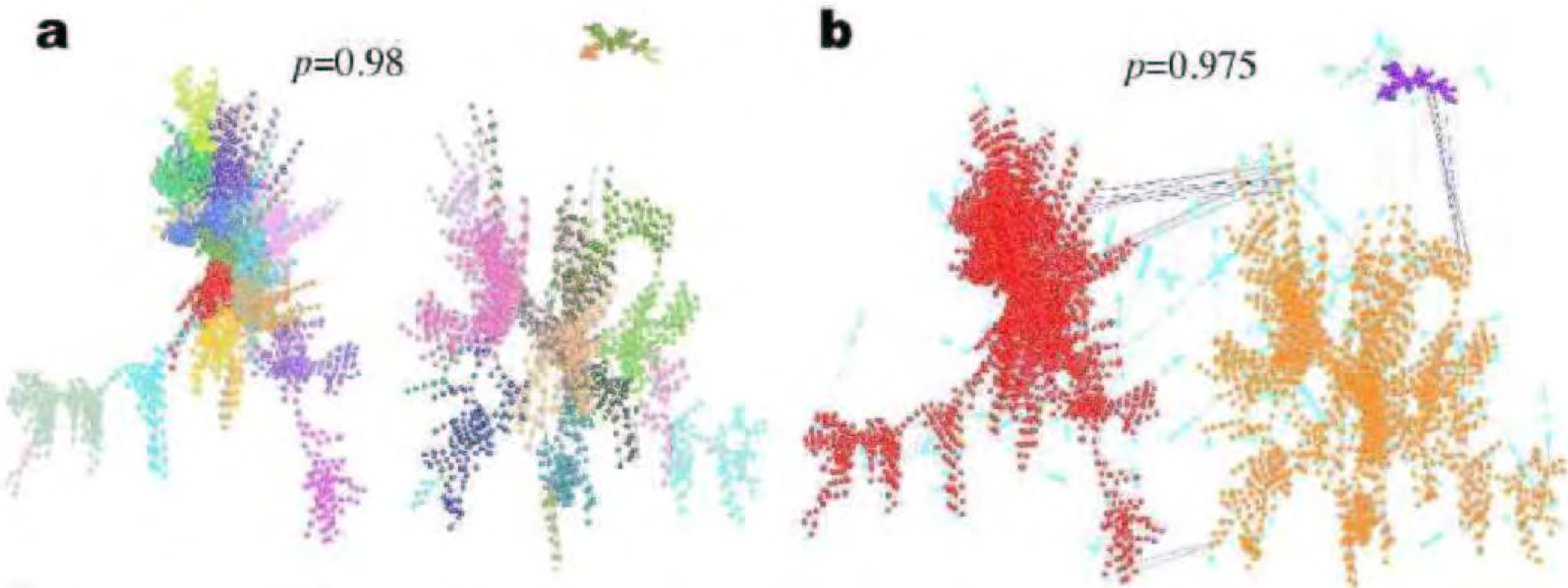
$$r(x_1, x_2) > r_c$$







Functional brain network in humans is highly modular (Gallos etal PNAS 2012)



- Self-similar modules of strong links & Weaker links make it small world
- Modules with *scale free* connections $P(k) \sim k^{-\gamma}$ $\gamma = 2.1 \pm 0.1$
- 8% synaptic connections between modules
- Strength of intra-module synapses > Strength of inter-module synapses
- Inter-module synaptic connections are established between low connectivity neurons $P(k_1, k_2) \sim k_1^{-\gamma+1} k_2^{-\epsilon}$ $\epsilon = 2.1 \pm 0.1$

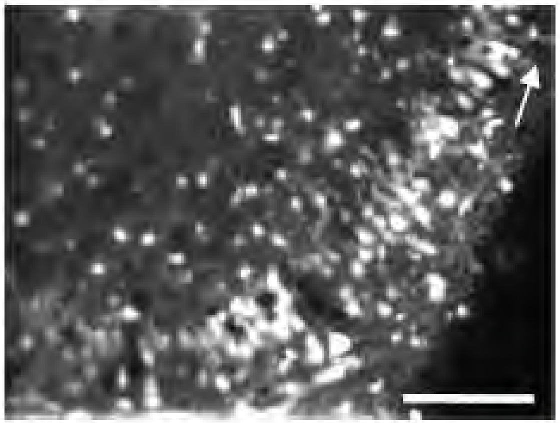
Role of Inhibitory Synapses

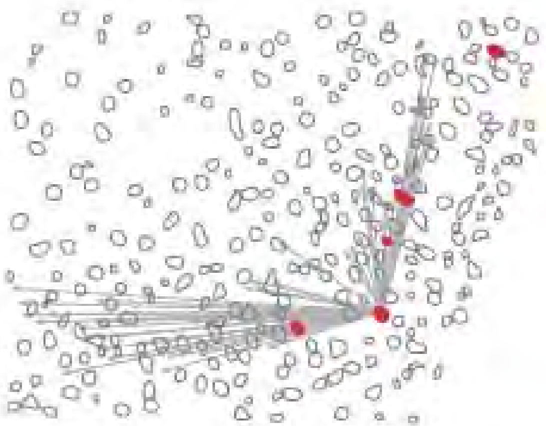
About 20-30% inhibitory synapses in mammals (GABA-immunostaining measurements in rat hippocampus (Gulyàs AI et al. J. Neurosci. 1999)

(Bonifazi P. et al. Science 2009)

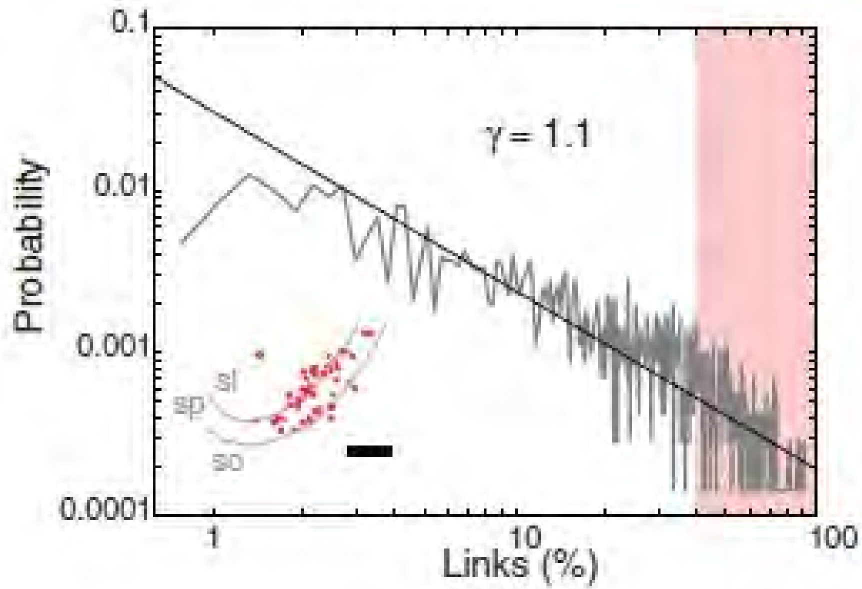
Are hubs present in neuronal assemblies?

- Measurements of temporal correlations of calcium activity in hippocampal slices of knockin rats and mice ➡ functional hubs exist





- Perturbation of a single hub triggers the entire network dynamics
- By GFP measurements functional hubs are GABAergic interneurons

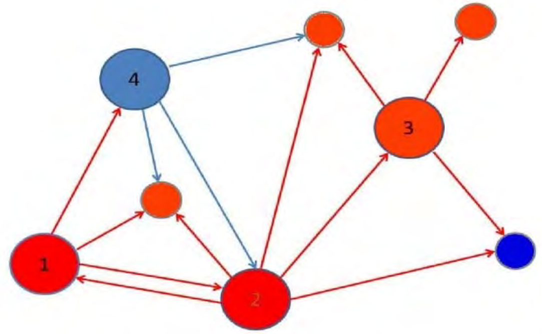


ACTIVITY DEPENDENT MODEL

LdA,CPC, HJH, PRL 2006, PRE 2007

We introduce the main ingredients of neural activity:

Threshold firing, Neuron refractory period, Activity dependent synaptic plasticity



- We assign to each neuron a potential v_i

  and to each synapse a strength g_{ij}

$$\boxed{g_{ij} \neq g_{ji}}$$

- A neuron fires when the potential is at or above threshold v_{max} (-55mV)
- Neurons can be excitatory or inhibitory

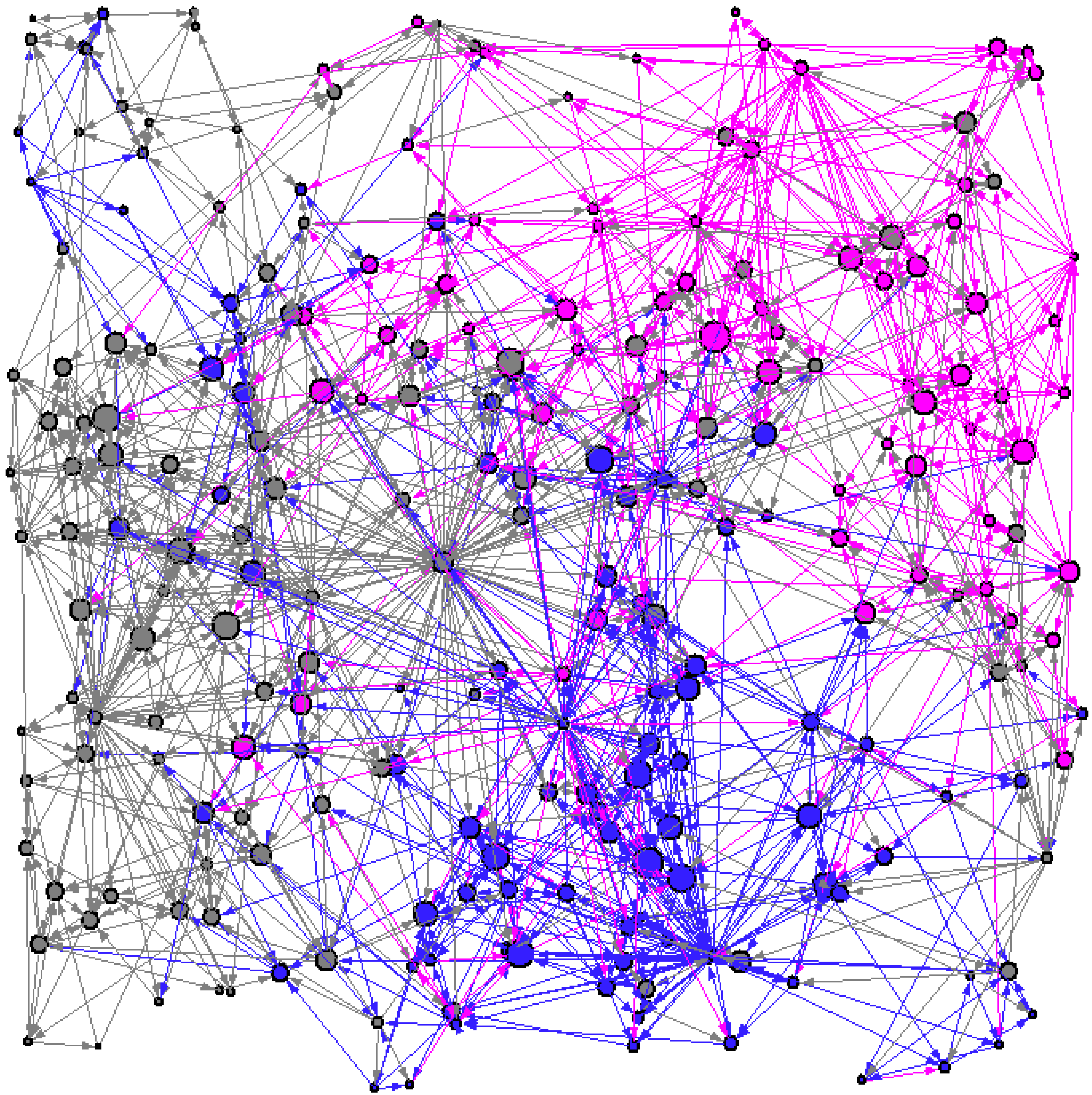
$$v_j(t+1) = v_j(t) \pm \frac{k^i_{out}}{k^j_{in}} v_i \frac{g_{ij}(t)}{\sum_k g_{ik}(t)}$$

- After firing a neuron is set to zero resting potential (-70mV) and remains quiescent for one time step (refractory period)
- Activity dependent long-term (Hebbian) plasticity and pruning

$$g_{ij}(t+1) = g_{ij}(t) + \alpha\left(v_j(t+1) - v_j(t)\right)/v_{\max}$$

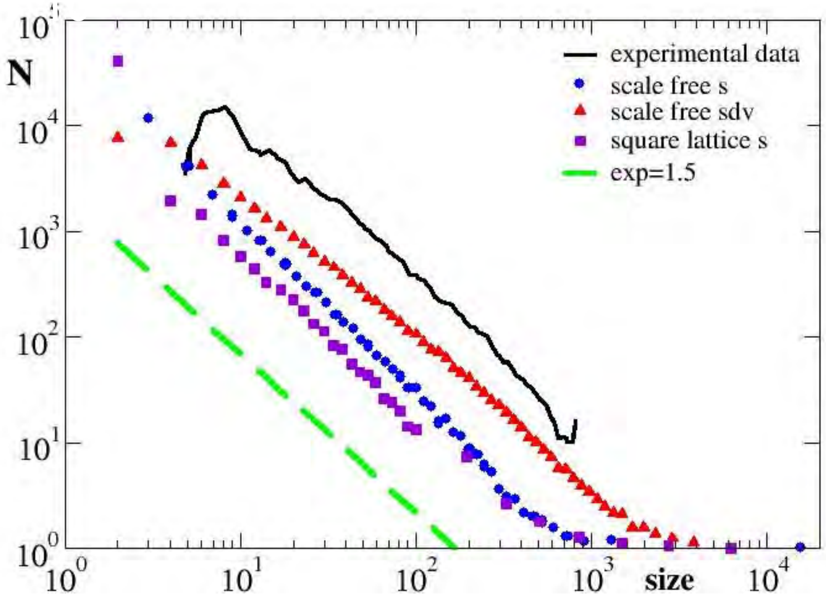
$$g_{ij}(t+1) = g_{ij}(t) - \langle \delta g_+ \rangle$$

- Activity is triggered by random stimulation of a single neuron



AVALANCHE DISTRIBUTIONS

After training the network by plastic adaptation, we apply a sequence of stimuli at random to trigger avalanche activity

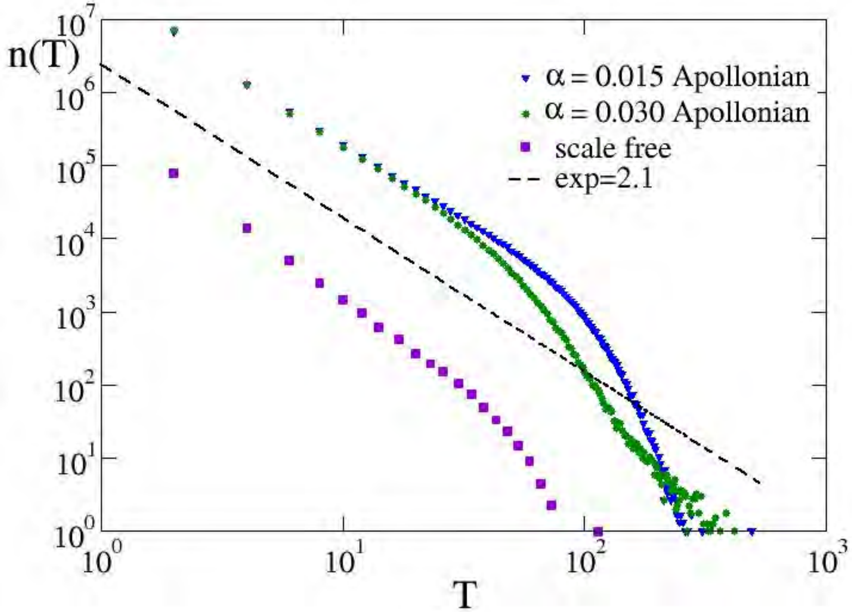


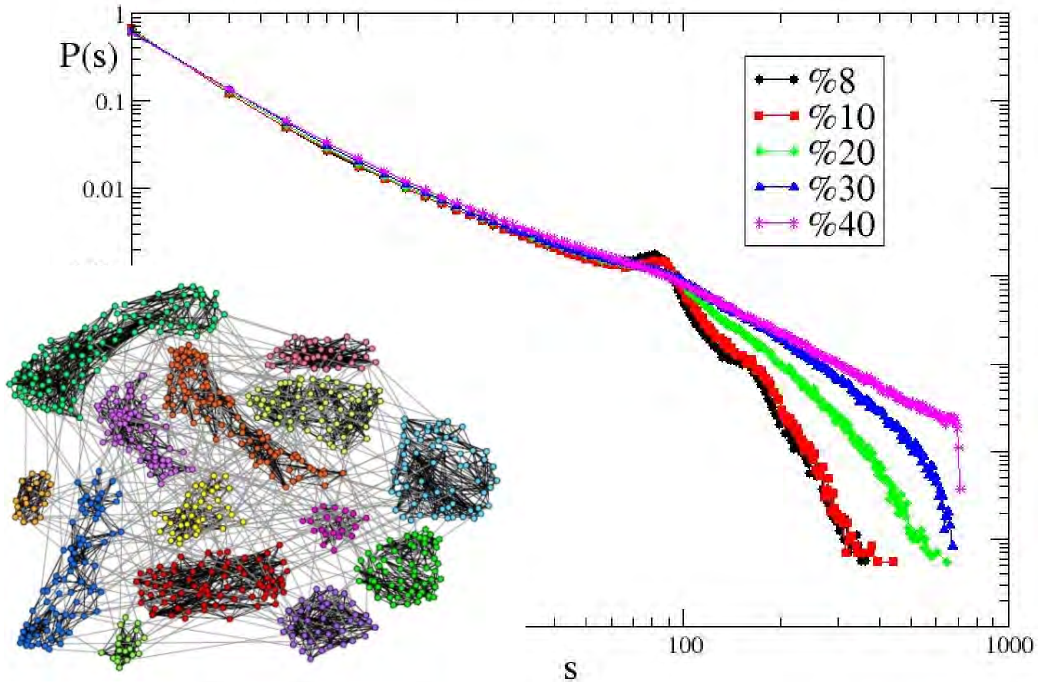
- different α
- regular, small world, scale-free networks
- excitatory and inhibitory synapses

1.5±0.1 & 2.1±0.1 for avalanche size & duration

Levina, M. Herrmann, T. Geisel, Nat Phys 2007

Millmann, Mihalas, Kirkwood, Niebur, Nat Phys 2010





Russo et al Nat. Sci. Rep. 2013

ORIGIN OF THE SCALING BEHAVIOR

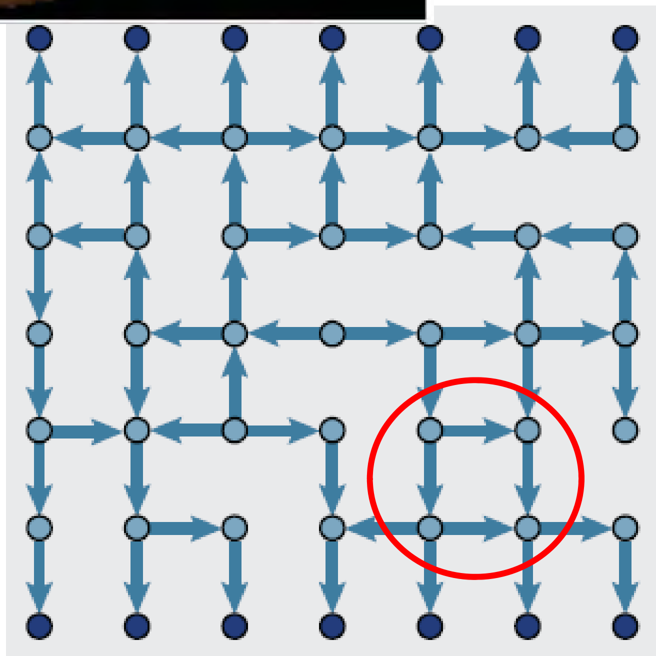
L. Michiels van Kessenich et al
Nat. Sci. Rep. 2016

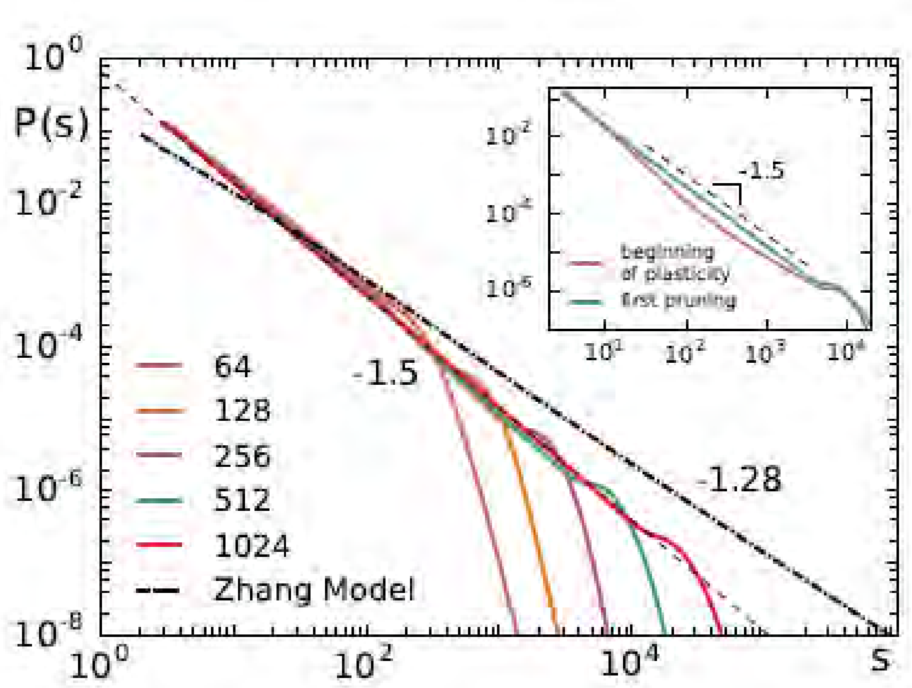
Critical scaling $(\sigma = 1)$ 1.28 (Zhang model) for no plasticity
no refractory time

(Katifori e al PRL 2010; Corson PRL 2010)

with plasticity and refractory time

$\boxed{1.5 \pm 0.1}$



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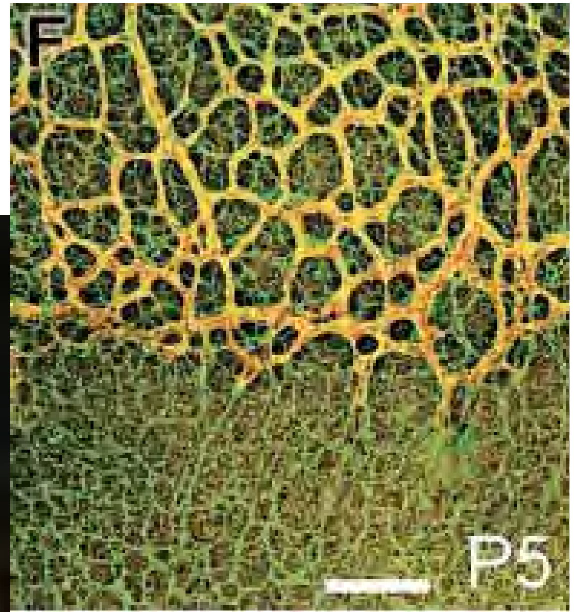
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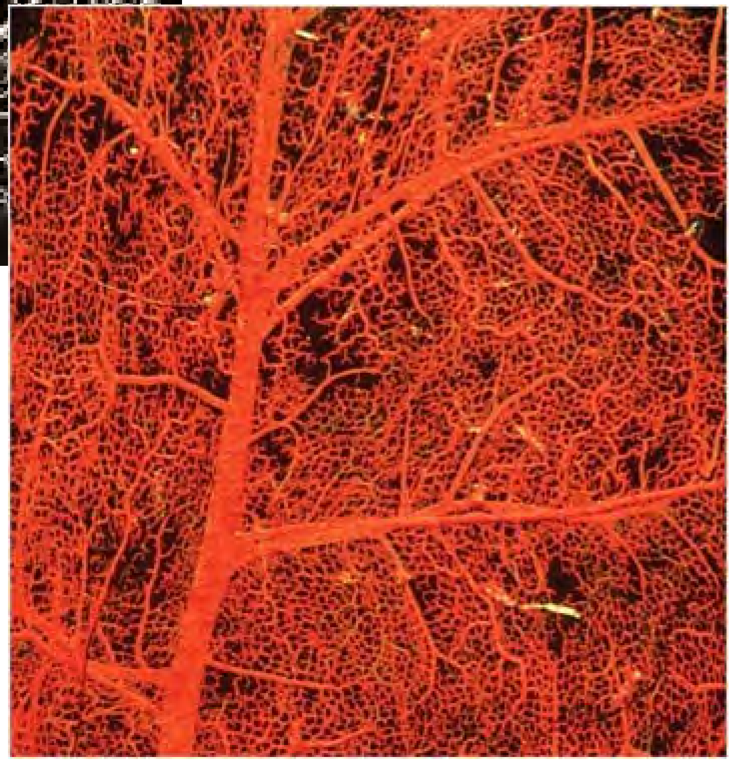
Resilience to damage

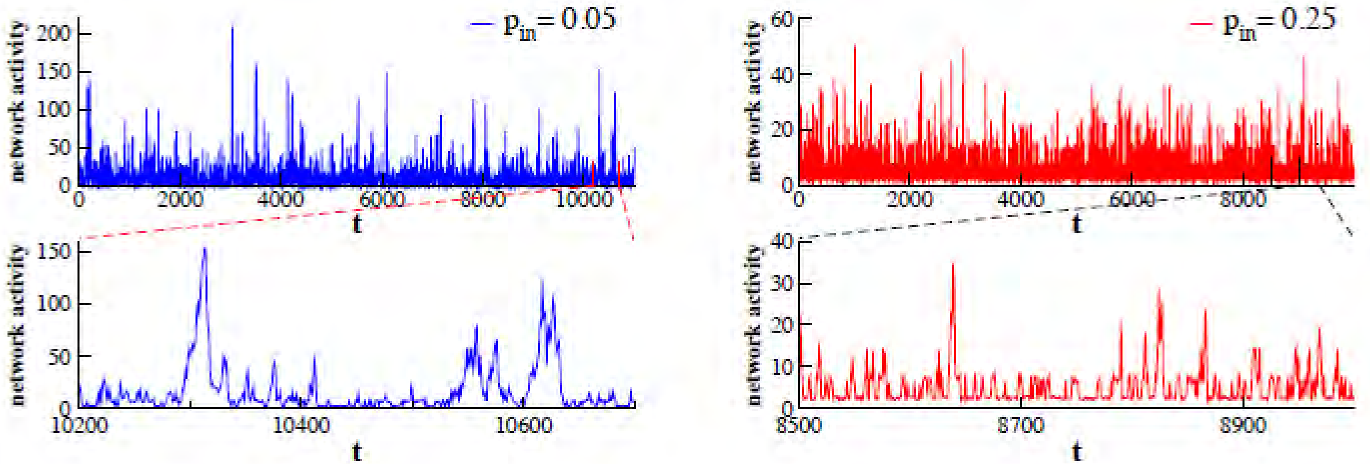


Power spectra of spontaneous neuronal activity

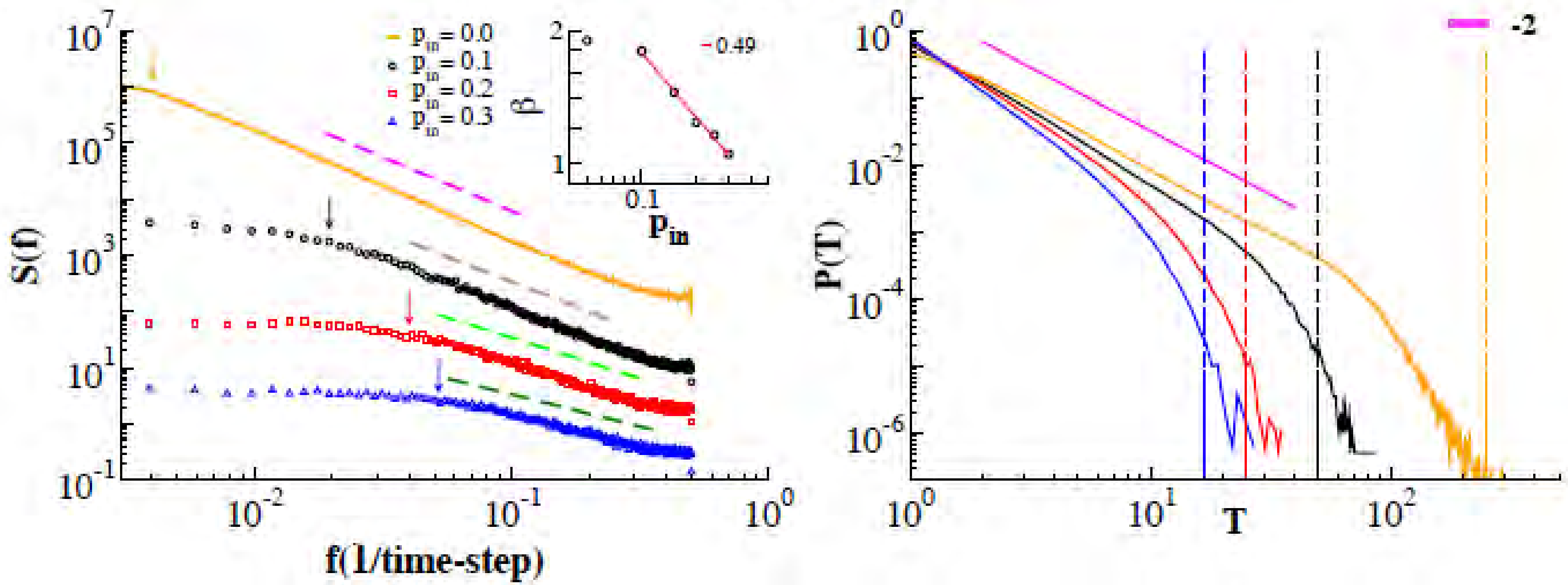
$S(f) \propto 1/f^{\beta}$ — Lombardi et al, Chaos 2017

- EEG exponent varies $\beta \in [0.9, 1.3]$ with frequency range, exp. condition, brain regions (Pritchard 1992, Freeman et al 2000)
- EEG-MEG in temporal and frontal areas $\beta \approx 2$
  whereas in midline channels 1/f (Dehghani et al 2010)
- Spectrum $1/f^{\beta}$ for α oscillations in EEG and MEG data with smaller exponent (Linkenkaer-Hansen et al 2001)
- 1/f spectrum of fMRI signal (He et al 2014), $\beta \approx 2$ for epileptic patients

→ Numerically the EEG signal from a neuronal network is the sum of potential variations occurring at all neurons at each time step



Scale free



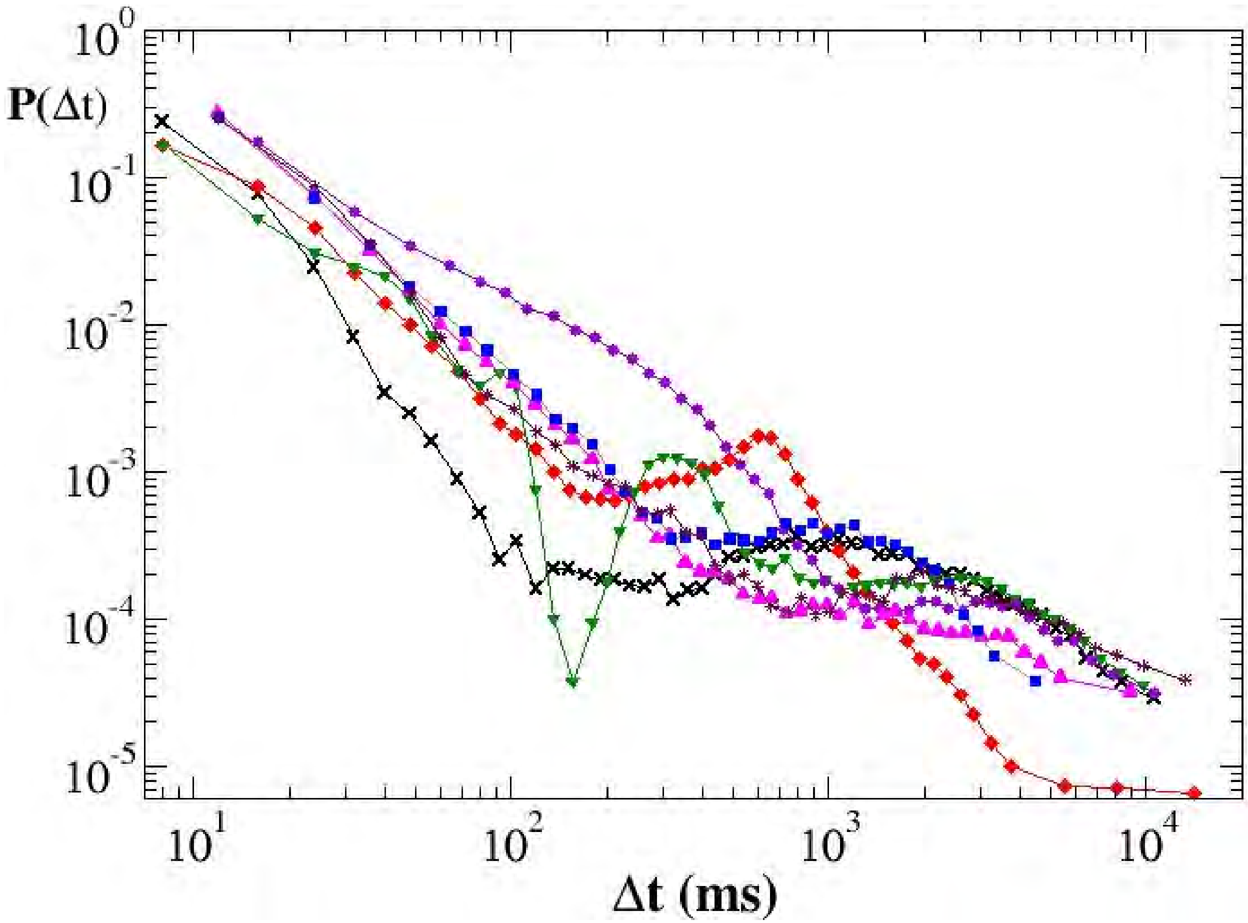
- Power law regime in a frequency range 1-100Hz
- Low frequency cutoff towards white noise ⟹ avalanche durations T in the exponential cutoff of P(T)
- Exponent $\beta \approx 2$ (brown noise) for purely excitatory networks

$$\boxed{\beta \rightarrow 1 \quad \text{for} \quad p_{in} \rightarrow 30\%}$$

⟹ Balance of excitation and inhibition controls long-range temporal correlations

Experimental avalanche inter-time distribution

Experiments by D. Plenz on coronal slices from rat dorsolateral cortex
(Lombardi et al PRL 2012)



- Initial power law regime with exponent

$$2.15 \pm 0.32$$

- Minimum at about

$$\Delta t \approx 200 ms$$

- Maximum at about

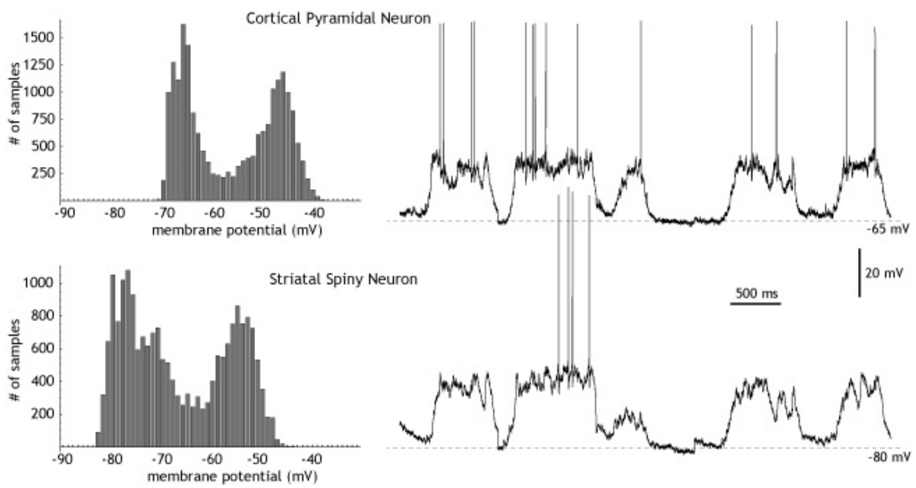
$$\Delta t \approx 1 - 2 s$$

Up-states and down-states

- Spontaneous neuronal activity can exhibit slow oscillations between bursty periods, or up-states, and quiet periods, called down-states.
- Down-states due to a decrease in the neurotransmitter release (exhaustion of available synaptic vesicles or increase of a factor inhibiting the release, as nucleoside adenosine), the blockade of receptor channels by the presence of external magnesium, spike adaptation…
  "Down-state of the network is a state of mutually-enforced quiet"
- Network properties explain the up-state: Any input may trigger some mutual excitation and the network will re-excite itself to the up-state
- Avalanches are critical in the up-state and subcritical in the down-state (Millman et al Nat Phys 2010)
- The alternation between US and DS is expression of the balance between excitation and inhibition

Wilson, Scolarpedia

Neuron state:
Neurons toggle between two preferred membrane potentials: a hyper-polarized one in the down state, and a more positive, depolarized one, in the up-state.



Implementation of up and down states

- Down-state ⟶ After an avalanche with $\boxed{s \geq s_{\min}}$

all neurons active in the last avalanche become hyperpolarized depending on their own activity

$$\boxed{v_i = v_i - h\delta v_i}$$

$h > 0$ is a hyper-polarization constant

short term memory at neuron level

System is stimulated by a small constant random drive

- Up-state ⟶ After an avalanche with $\boxed{s < s_{\min}}$

all neurons active in the last avalanche become depolarized depending on the last avalanche size

$$\boxed{v_i = v_{\max}(1 - s/s_{\min})}$$

the smaller the last avalanche
the closer the potential to the firing threshold

Memory at the network level

System is stimulated by a random drive
(network effect which sustains the up-state) $\boxed{\in]0, s_{\min}/s[}$

Spontaneous neuronal activity exhibits
slow oscillations between
up-states, and down-states

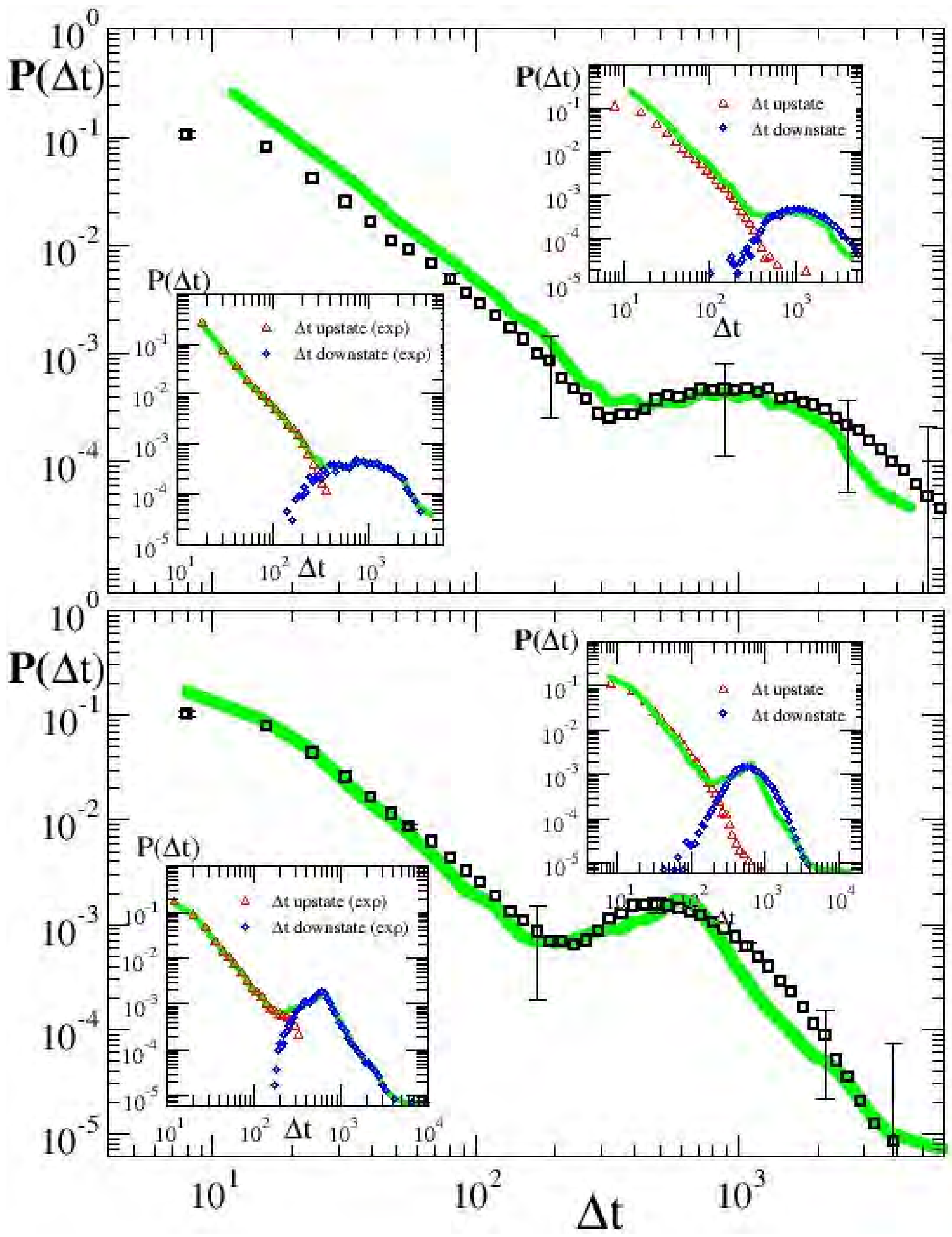
Small correlated avalanches,
neurons depolarized after firing

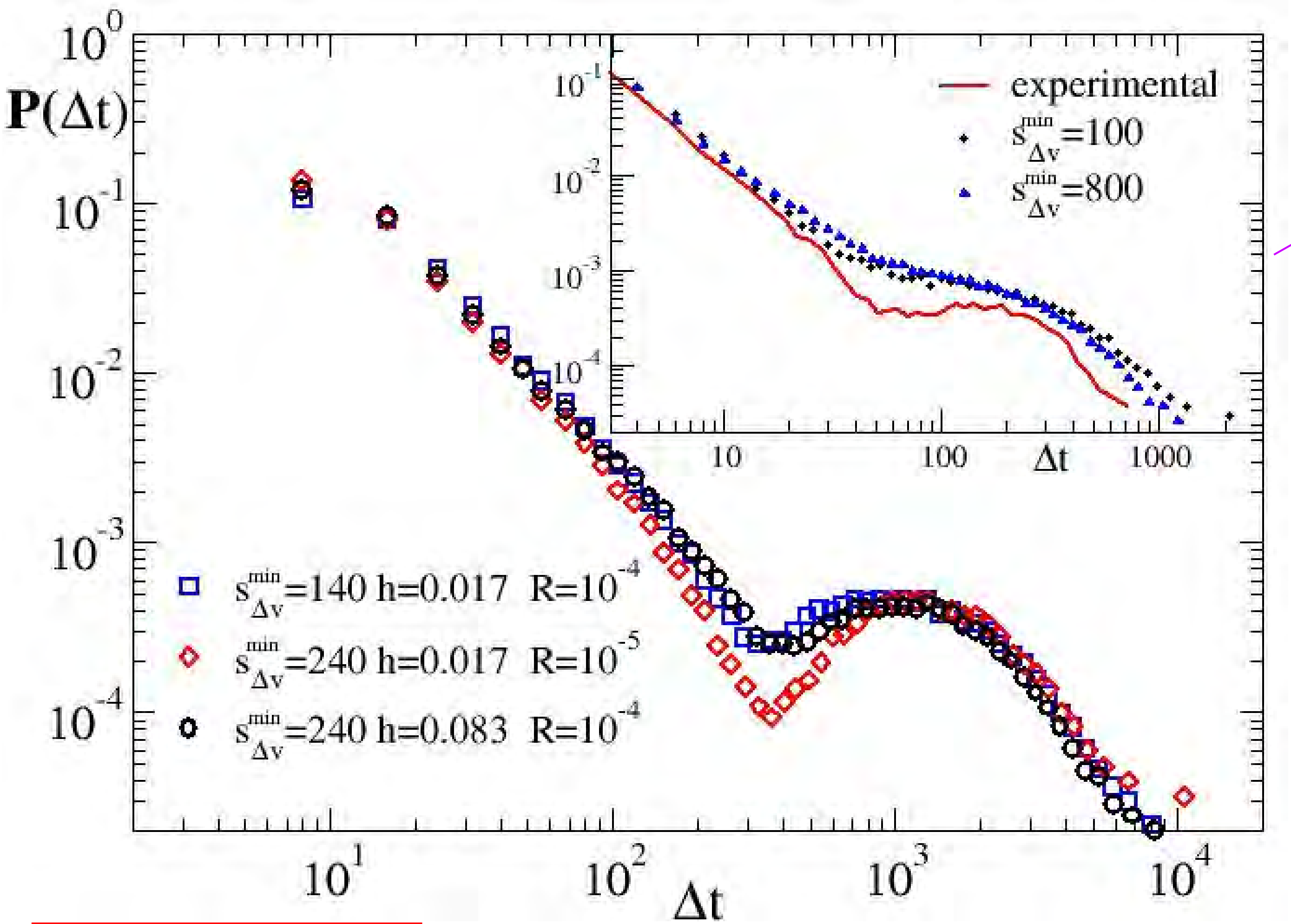
Disfacilitation period after large avalanches
Neurons hyperpolarized after firing

Balance between excitation and inhibition

↓

Homeostatic regulatory mechanism





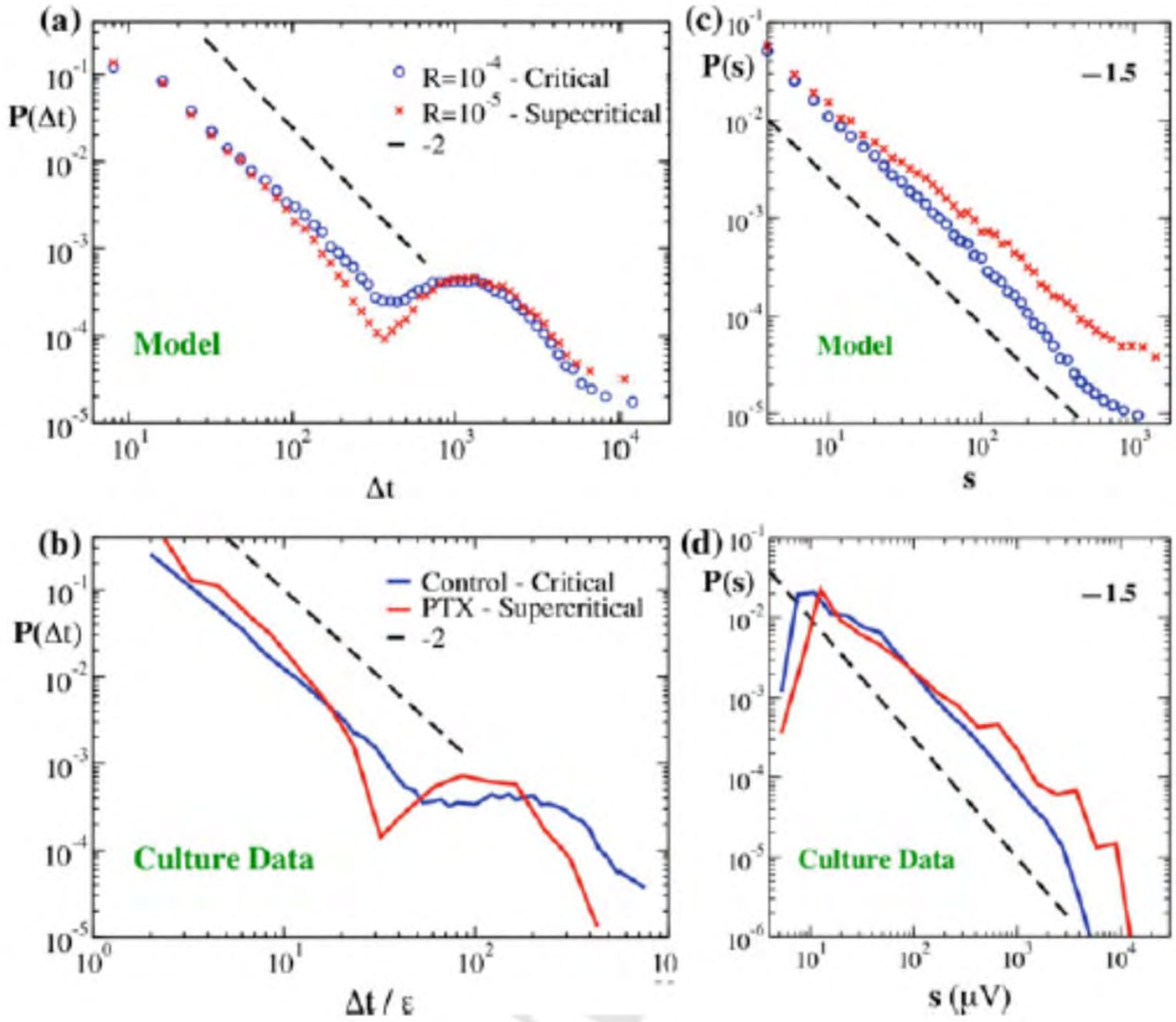
simple dual drive does not work!

$$\boxed{R = h / s_{\min}}$$

espressing the balance between excitation and inhibition
is the unique parameter controlling the distribution

→ Homeostatic regulatory mechanism

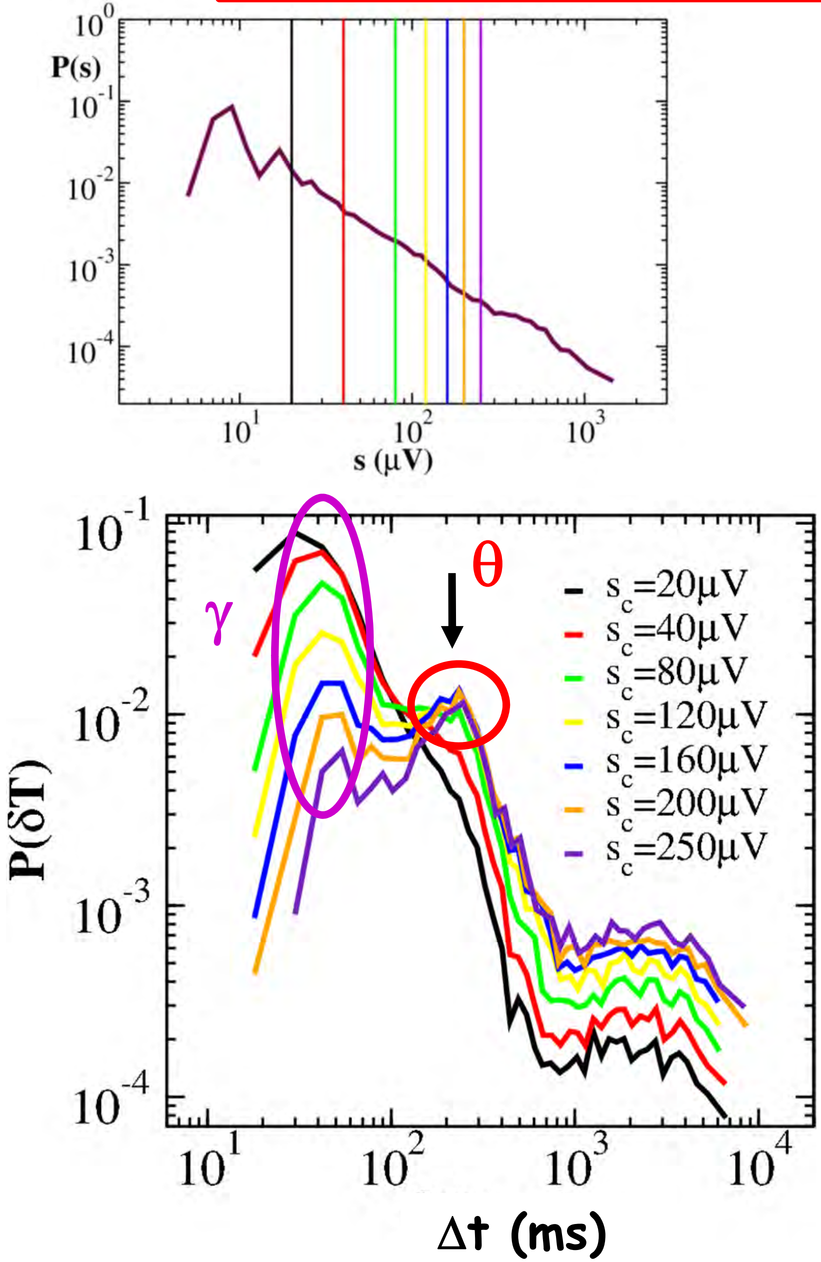
Critical vs. supercritical systems



Brainwaves, Frequencies and Functions

Unconscious		Conscious		
Delta	**Theta**	**Alpha**	**Beta**	**Gamma**
0,5 – 4 Hz	4 – 8 Hz	8 – 13 Hz	13 – 30 Hz	30-42 Hz
Instinct	**Emotion**	**Consciousness**	**Thought**	**Will**
Survival Deep sleep Coma	Drives Feelings Trance Dreams	Awareness of the body Integration of feelings	Perception Concentration Mental activity	Extreme focus Energy Ecstasy

$P(\Delta t, s_c)$ for avalanches with $s > s_c$

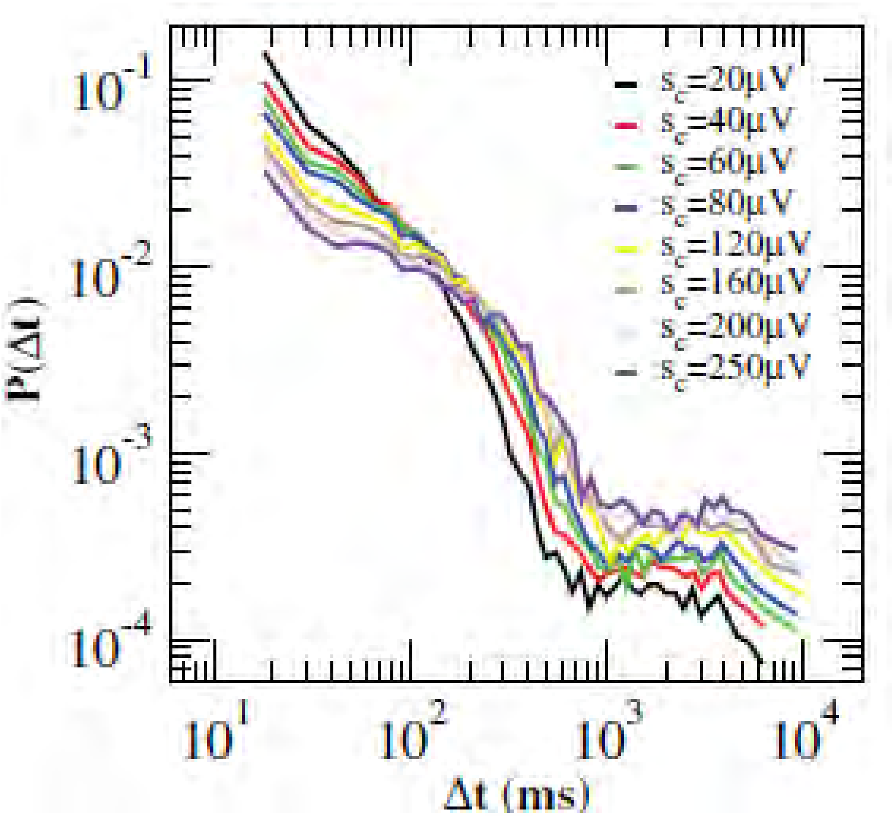


- Remove avalanches smaller than a given **threshold s_c**
- Evaluate new **$P(\Delta t,\ s_c)$**
- Peaks develop

  at θ band (4-15 Hz)

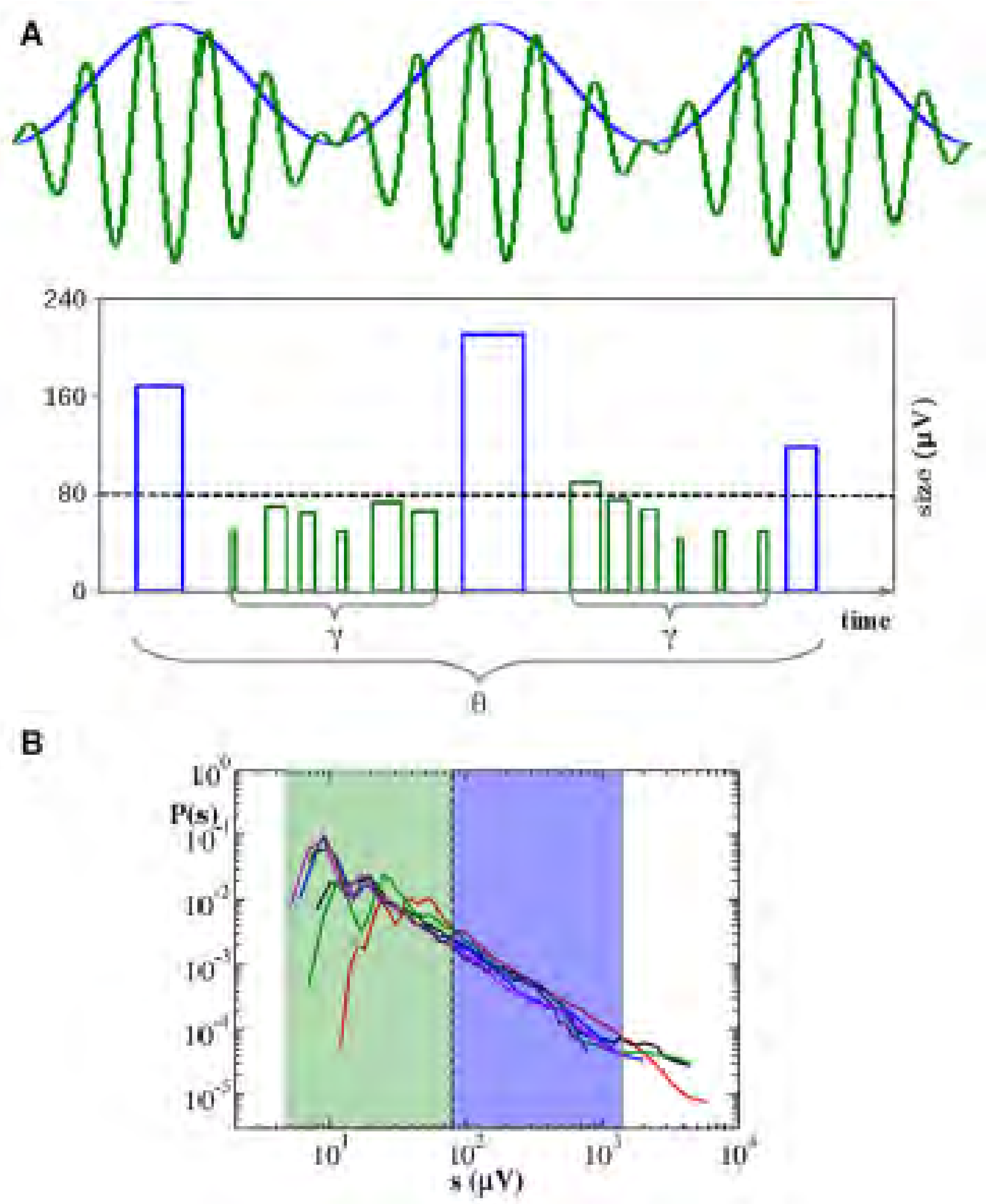
  at γ band (30-100 Hz)

Correlations exist between size and quiet times



No peaks emerge
for reshuffled time series

Avalanches and oscillations



- Hierarchical structure corresponding to nested θ-γ oscillations
- **Large avalanches** occur with **θ (4-15 Hz)** frequency and trigger **smaller ones** corresponding to faster **γ (30-100 Hz)** oscillations
- Sizes related to **θ** cycles fall within the **blue region of P(s)**
- Sizes related to **γ** cycles fall within the **green region of P(s)**
- The relationship between avalanches and **oscillations** does **not** imply a **characteristic size**

Lombardi F, Herrmann HJ, Plenz D, de Arcangelis L. *Front. Syst. Neurosci.* 8:204 (2014)

Collaborations

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