How fast transients shape whole-brain dynamics: theoretical perspectives and clinical implications

Pierpaolo Sorrentino

SIPF – Siena, 11 Novembre 2023

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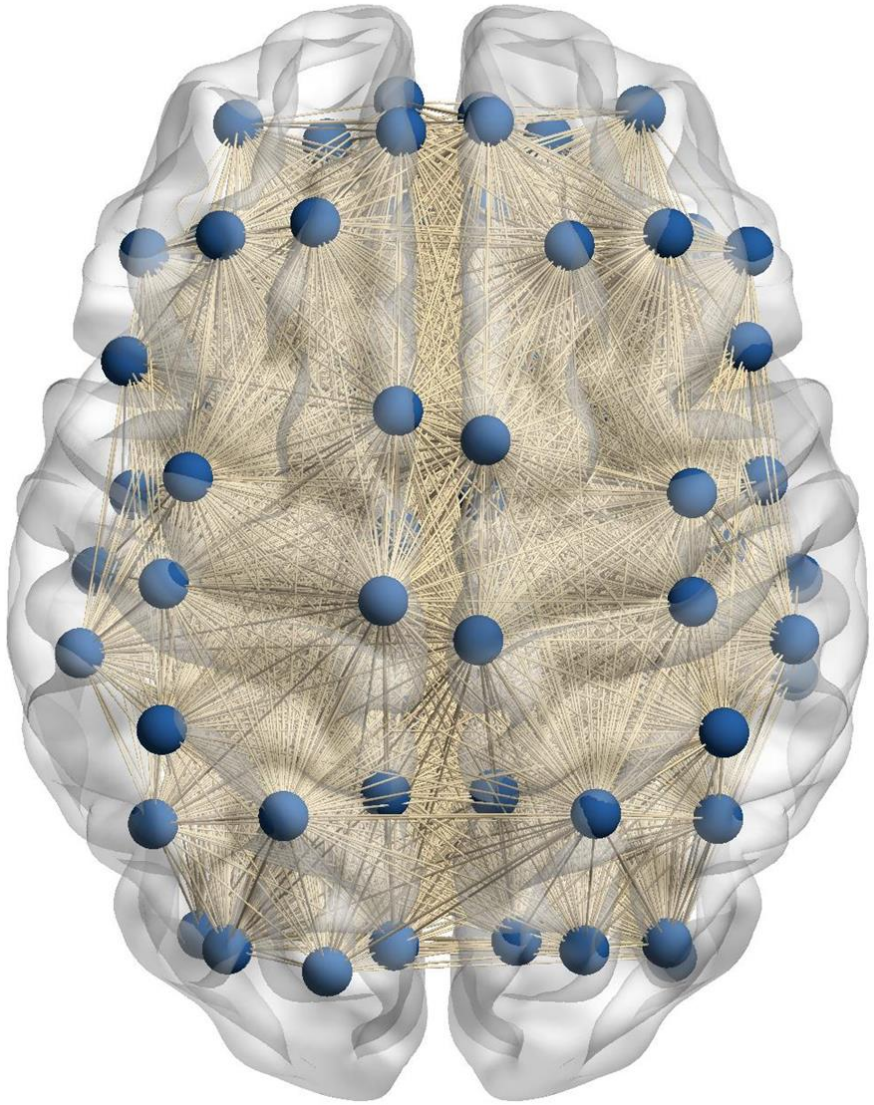
@PierpaSorre

Consiglio Nazionale delle Ricerche

INS

WHAT MAKES THE BRAIN “HEALTHY” ?



1. **EFFICIENT COMMUNICATION AMONG AREAS**

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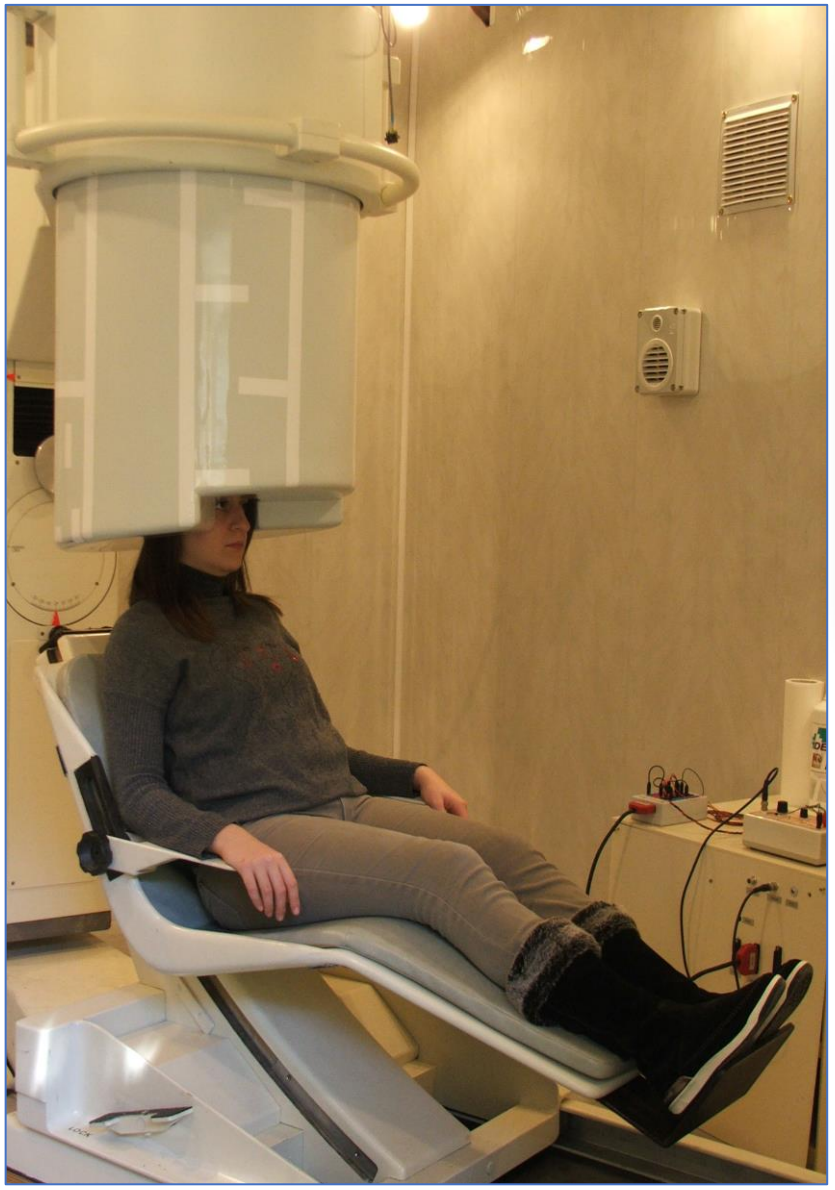
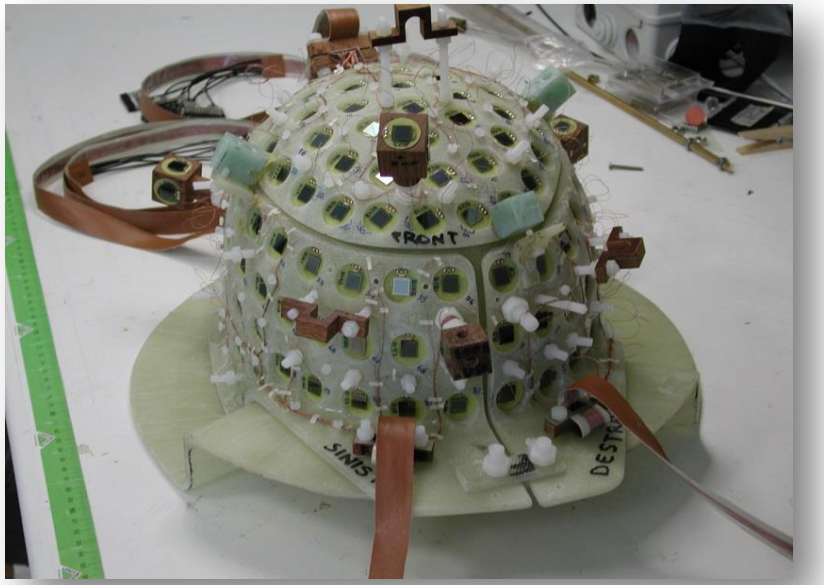
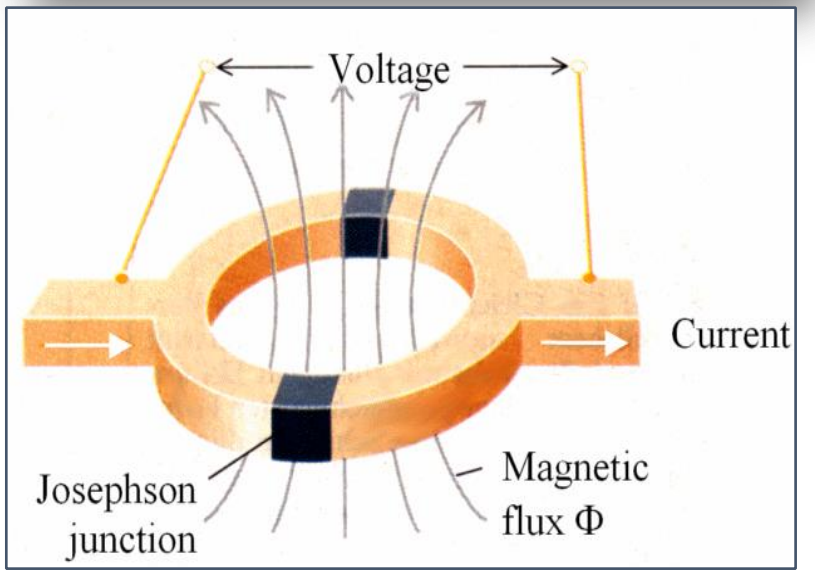
2. **EFFICIENT RECONFIGURATION OF ACTIVATION**

THE BRAIN CAN “ADAPT” TO A VARIETY OF STIMULI

MAGNETOENCEPHALOGRAPHY IN NAPLES





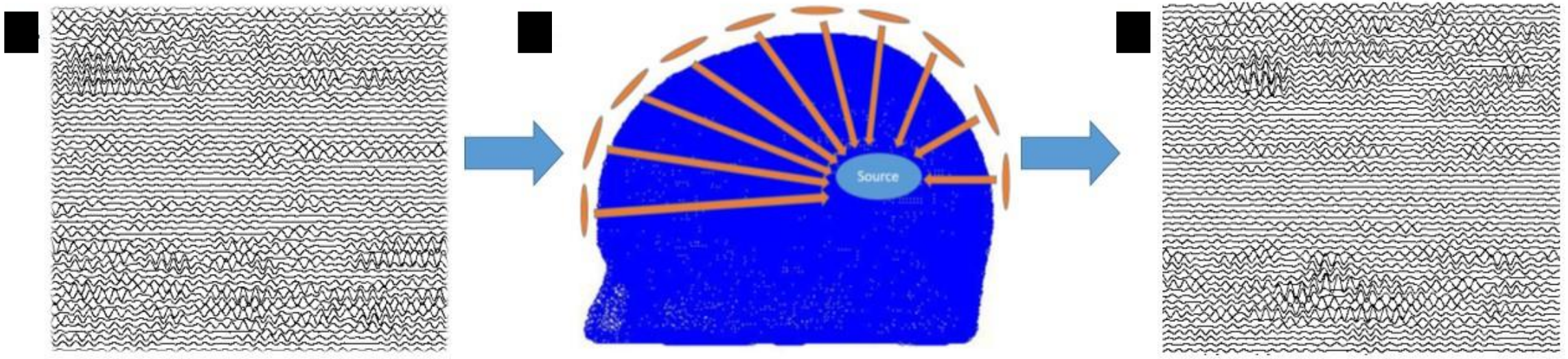


SOURCE RECONSTRUCTION

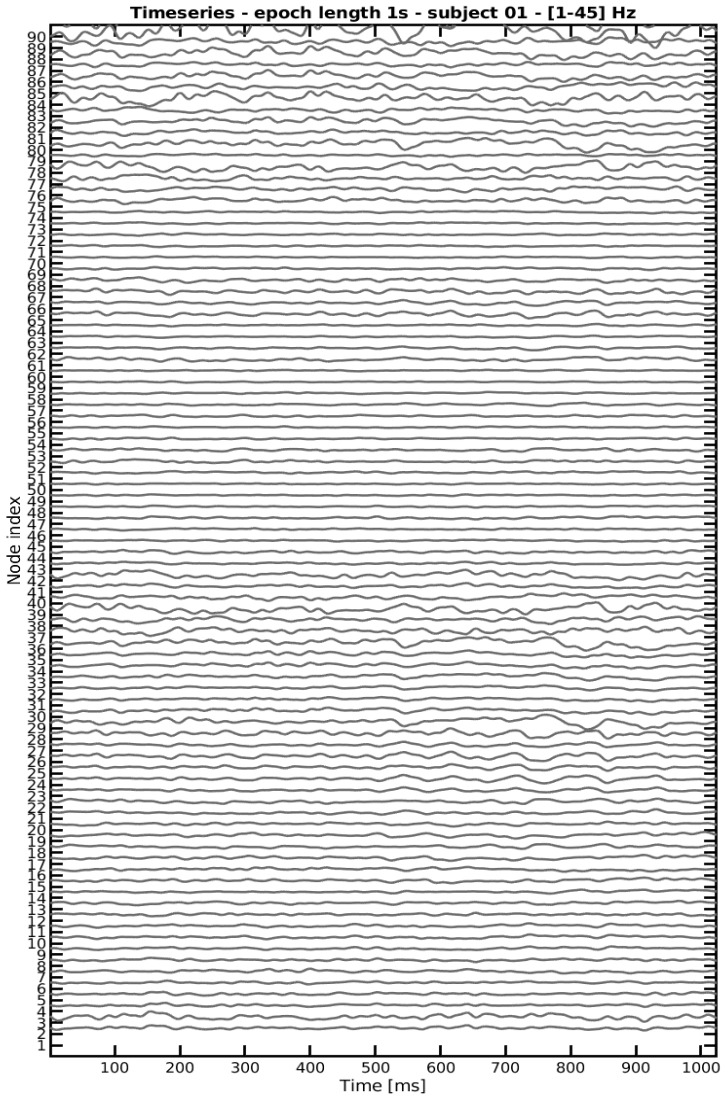
SENSOR LEVEL

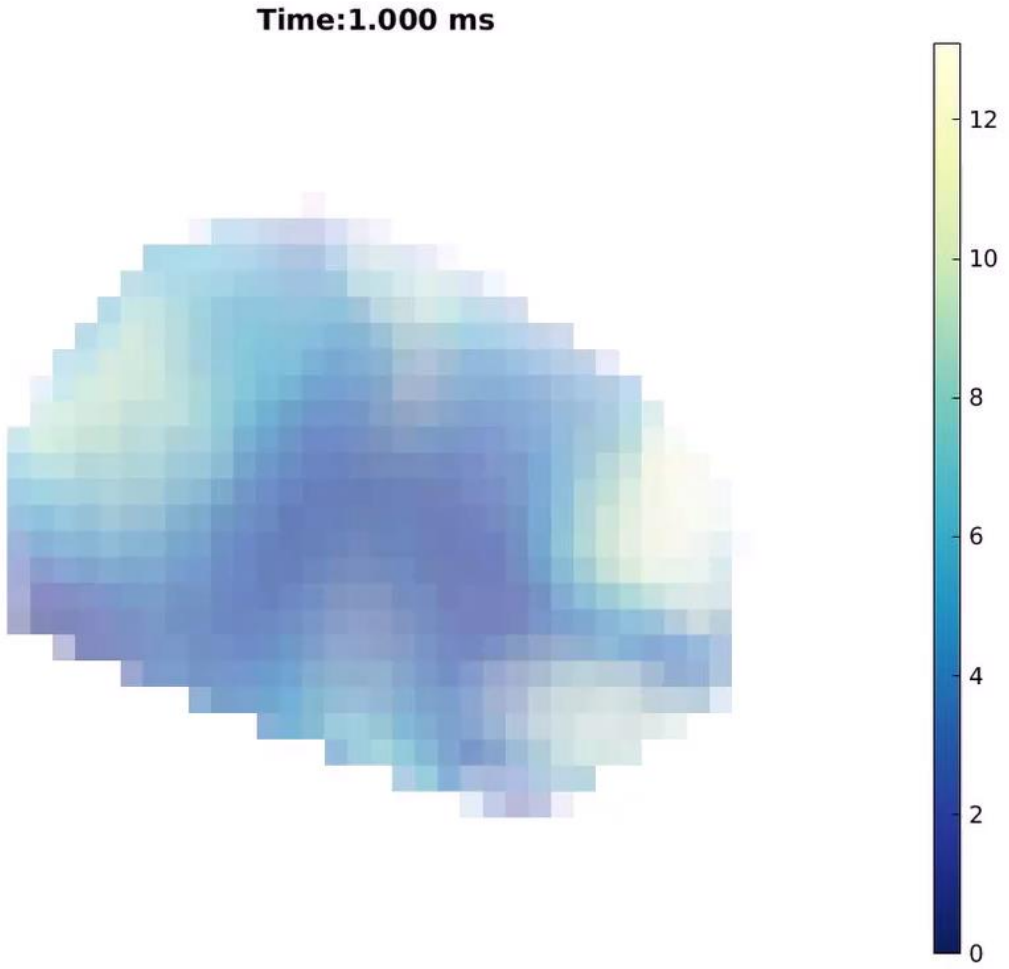
BEAMFORMER

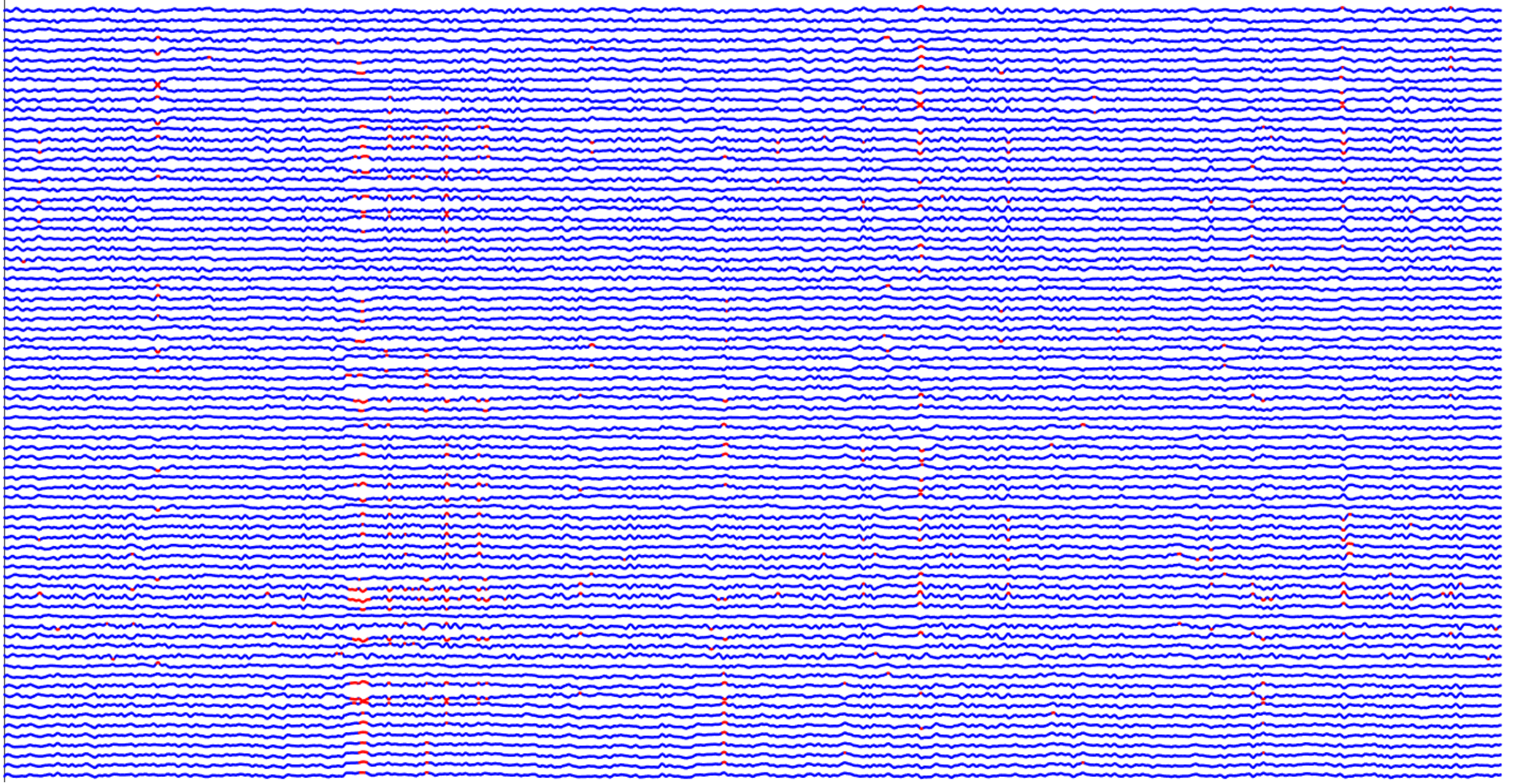
SOURCE LEVEL (AAL)



WHOLE BRAIN PROPAGATION OF ACTIVITY

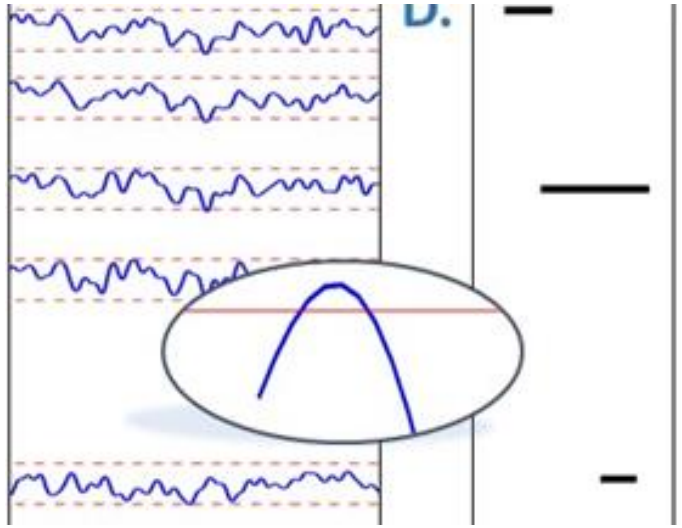






AVALANCHE

- **Spatio-temporal fluctuations of the activity**

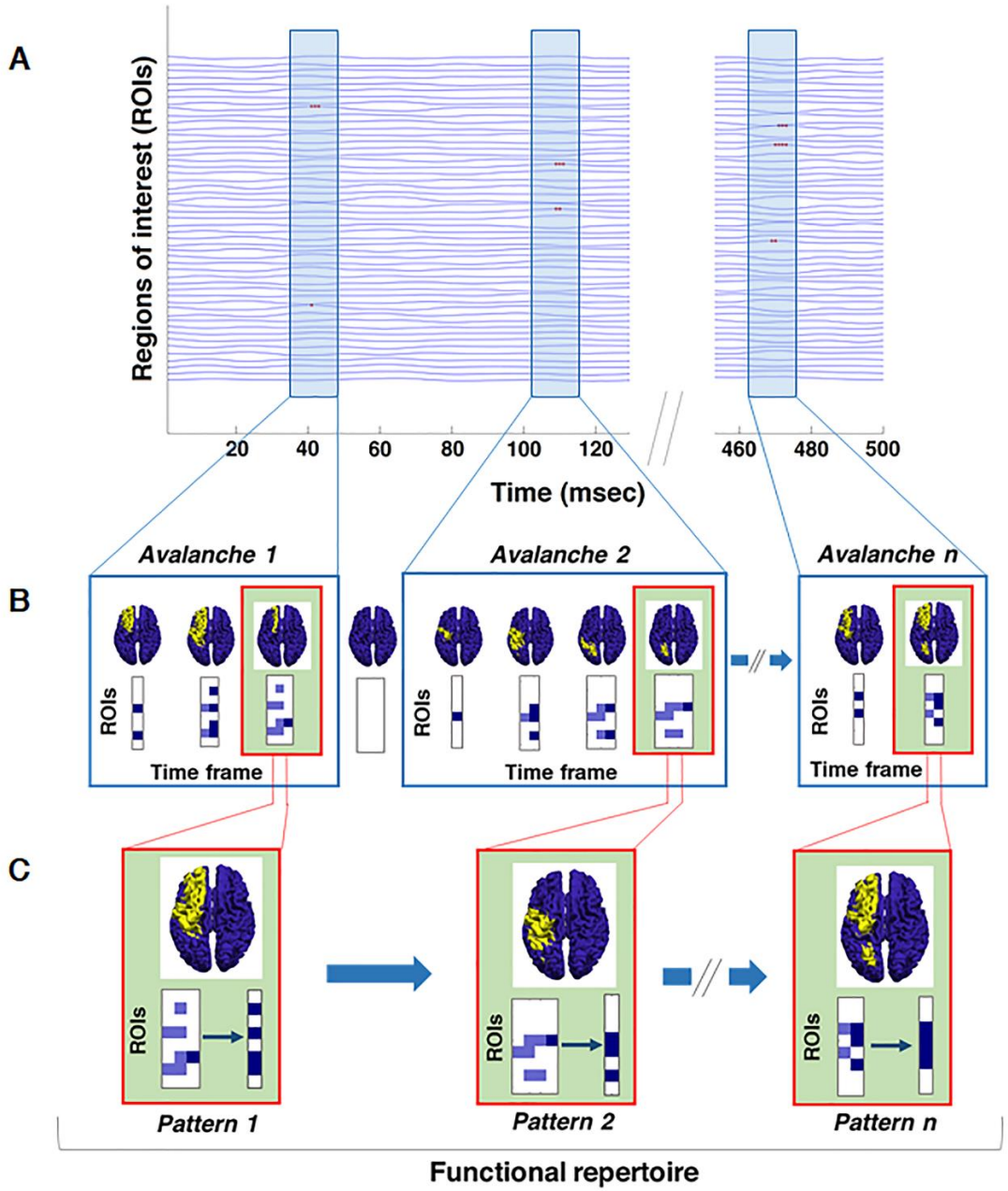


- **Starts:** when any area is active
- **Stops:** when no area is active

- How do we define active (‘an event’)?

  <u>if</u> the absolute value of **<u>the z-score</u>** of the intensity of the magnetic field, computed over all the intensities values of a channel throughout the whole acquisition, **<u>is > 3</u>**

Functional repertoire



Healthy dynamics

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Flexible Dynamics

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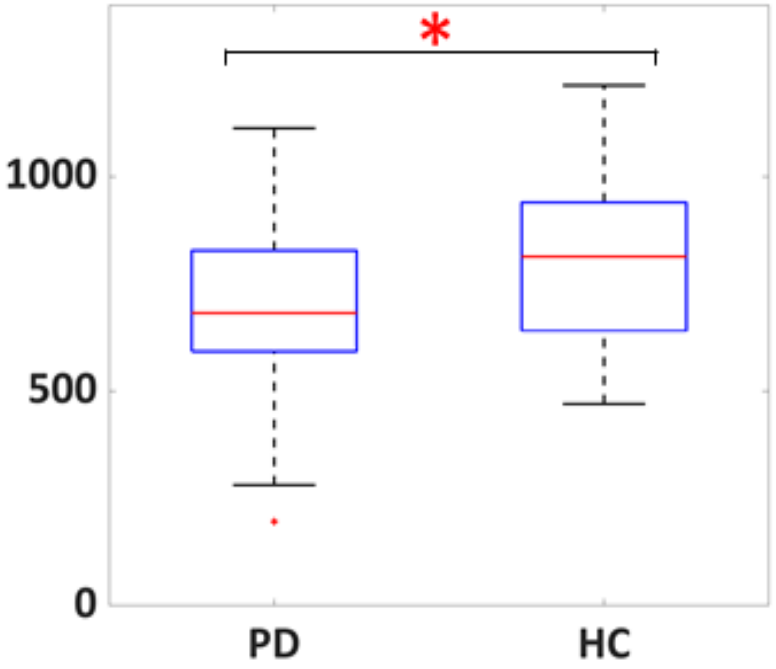
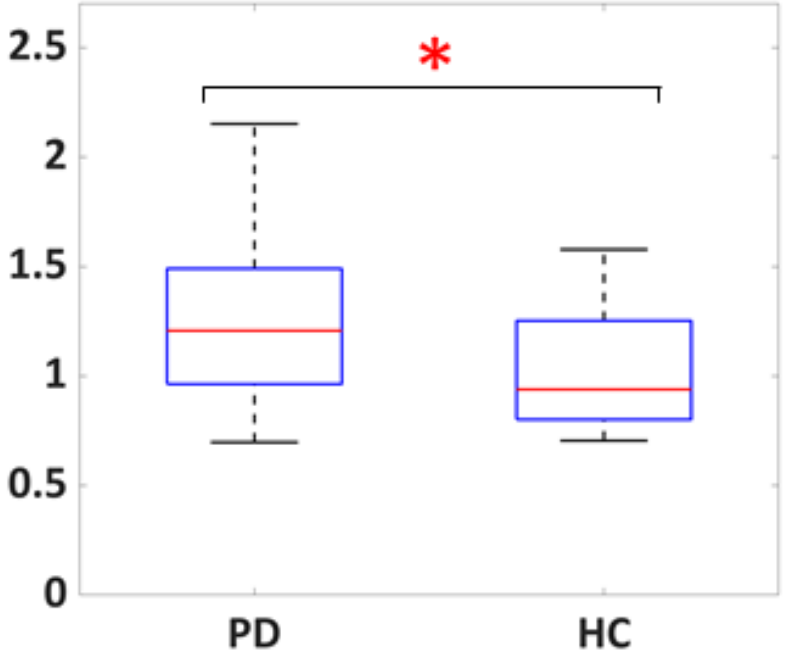
Large “functional repertoire”

Functional repertoire in Parkinson's disease

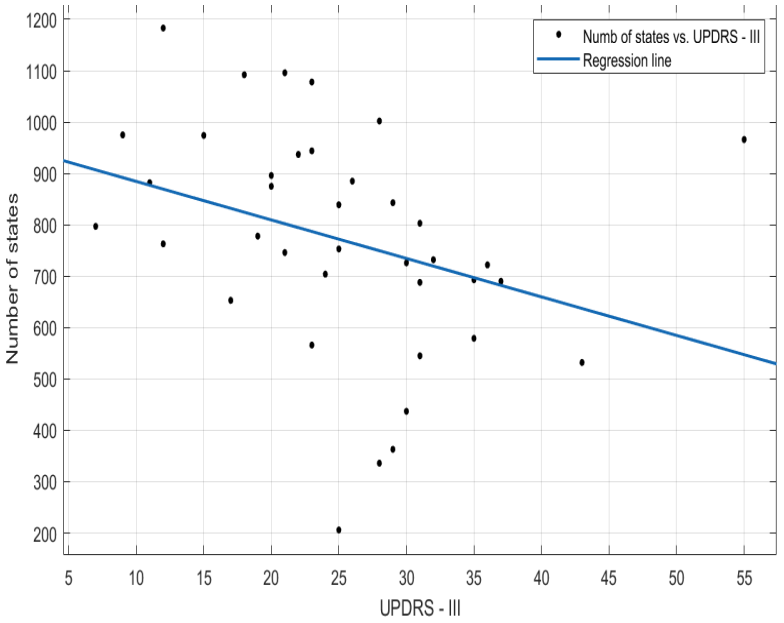
SIZE OF FUNCTIONAL REPERTOIRE



«SWITCH RATE»

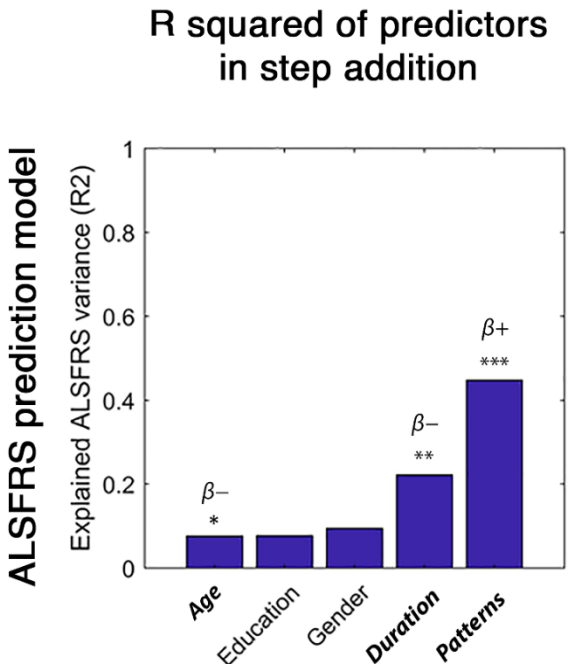


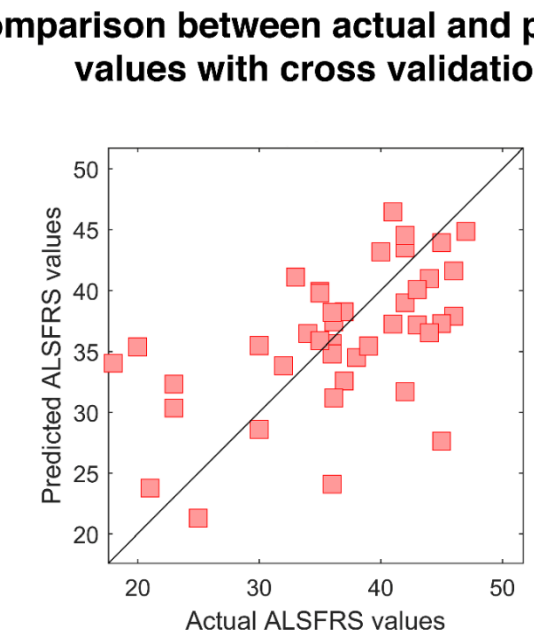
CLINICAL CORRELATION

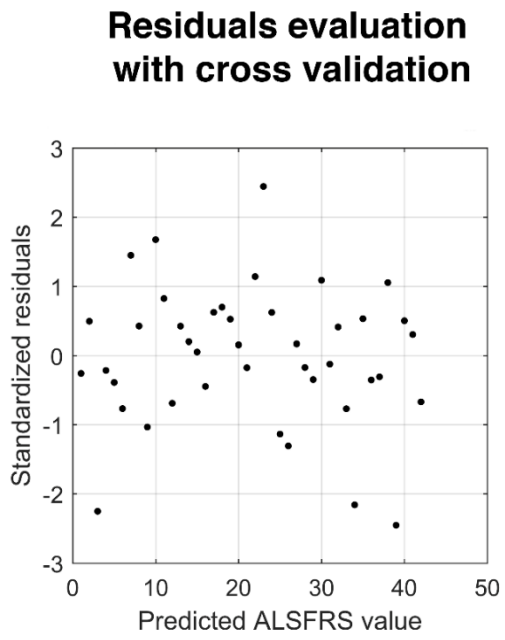


Sorrentino et al., Sci Rep, 2021

Functional repertoire in Amyotrophic lateral sclerosis

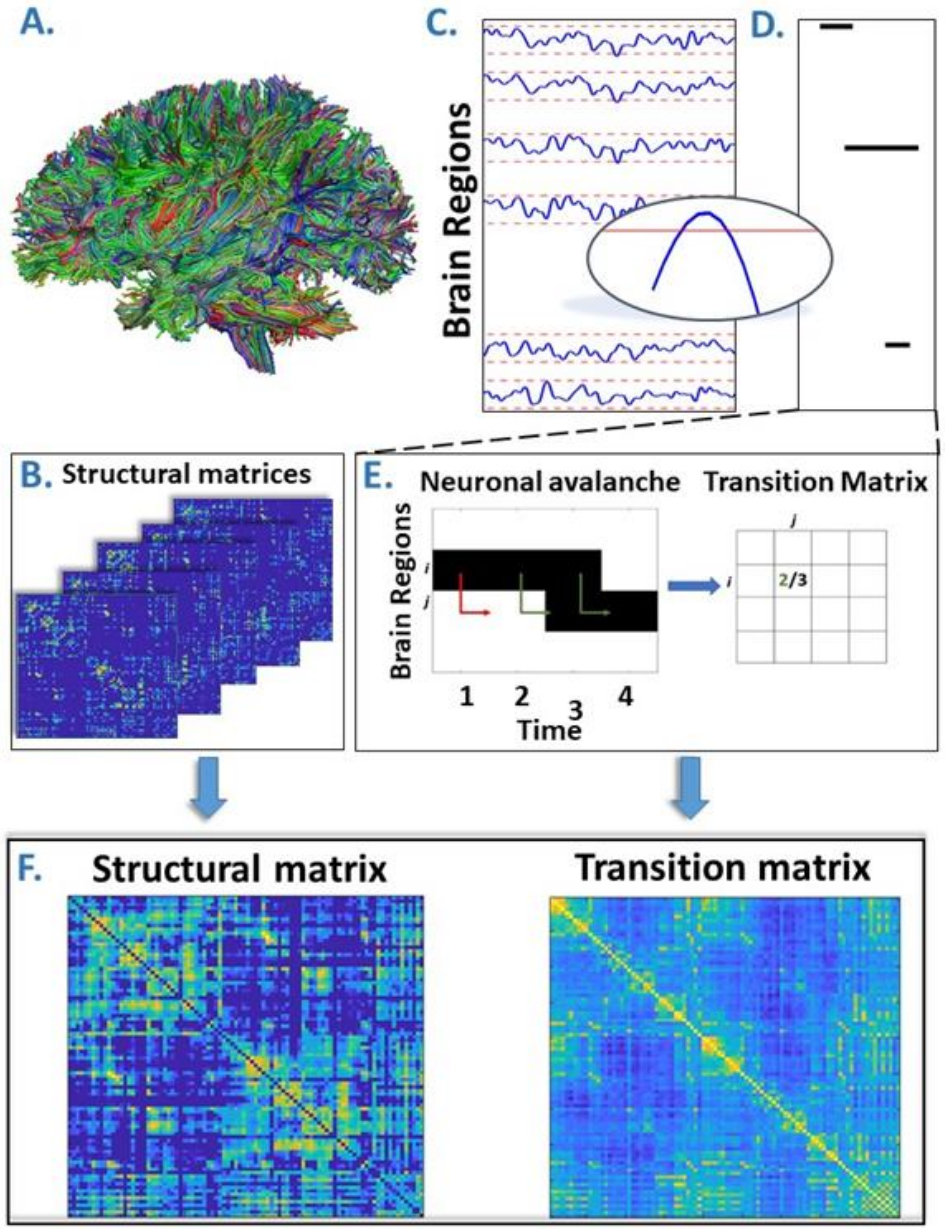






Polverino et al., Neurology, 2022

HOW DO THE STRUCTURAL CONNECTOME INFLUENCES THE SPREADING OF AVALANCHES



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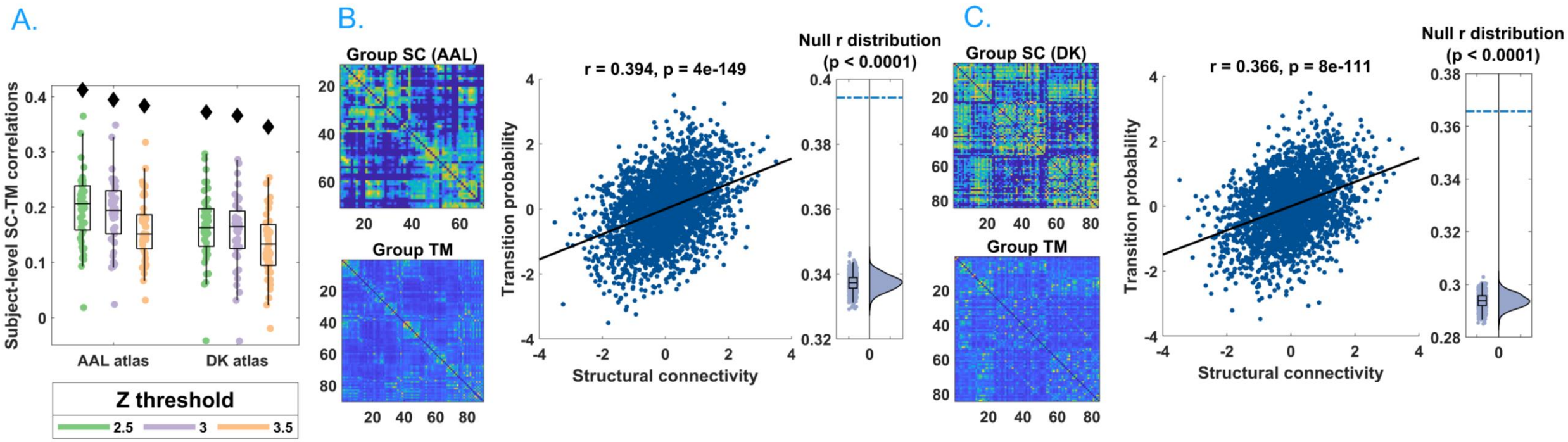
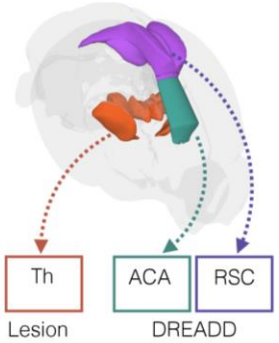
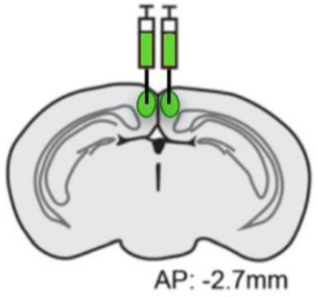


Sorrentino et al. ELife

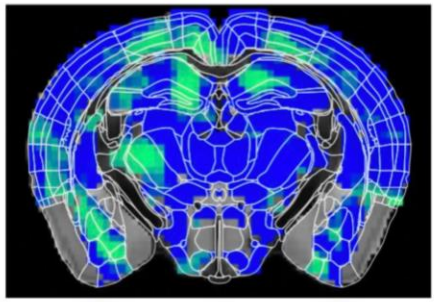
Probing the effect of local changes on large-scale bursts spreading



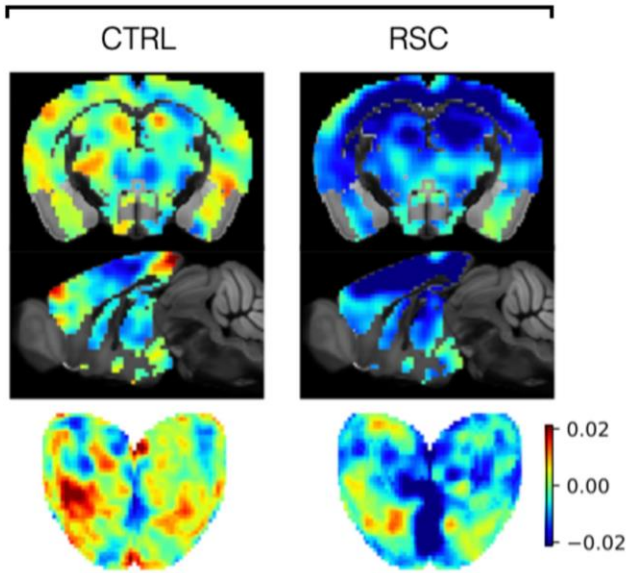
Focal silencing

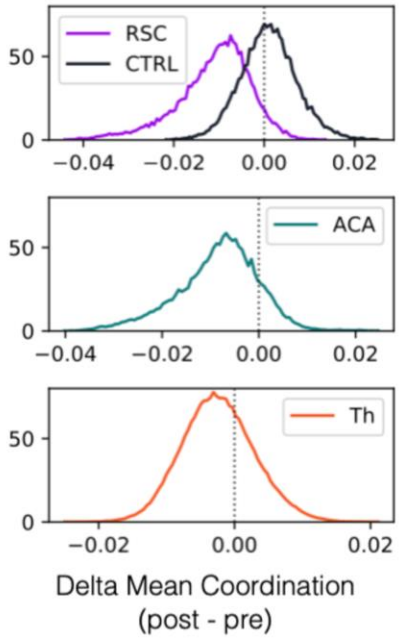


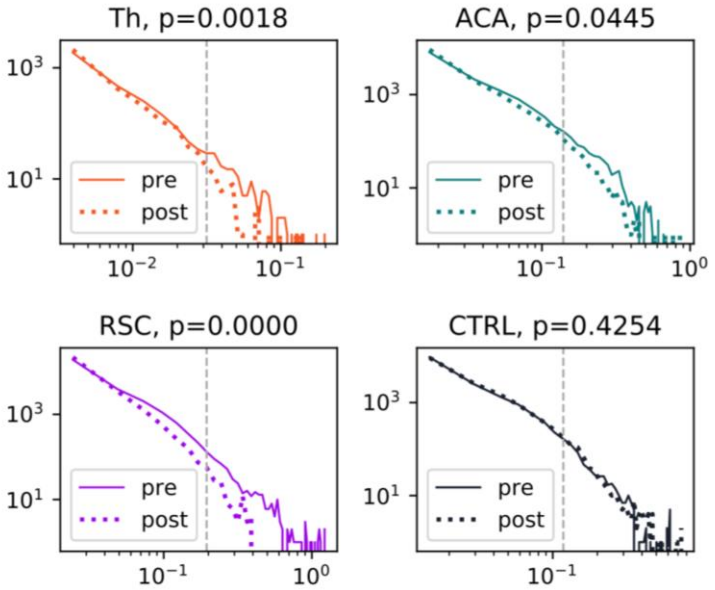
Global effects



FC degree (post-pre)

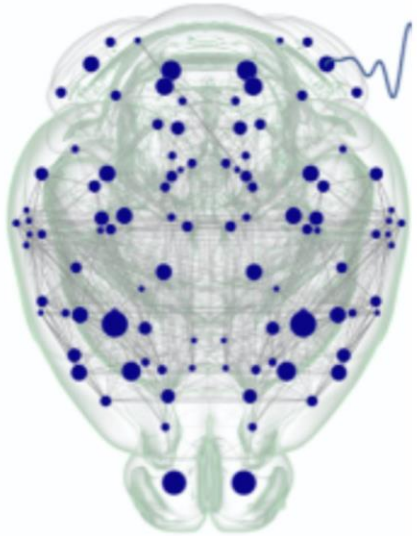






Probing the effect of local changes on large-scale bursts spreading

The Virtual Mouse Brain



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Neural Mass Model

$$\dot{X} = f(X)$$

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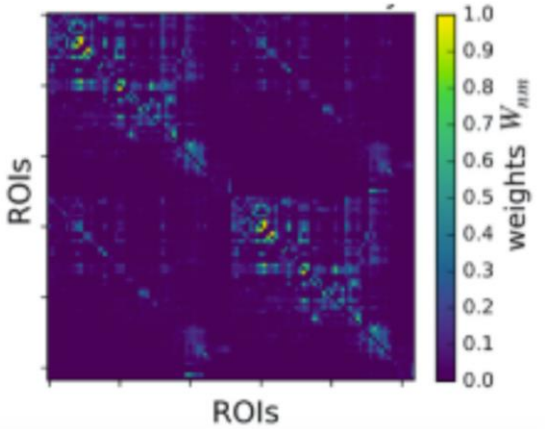
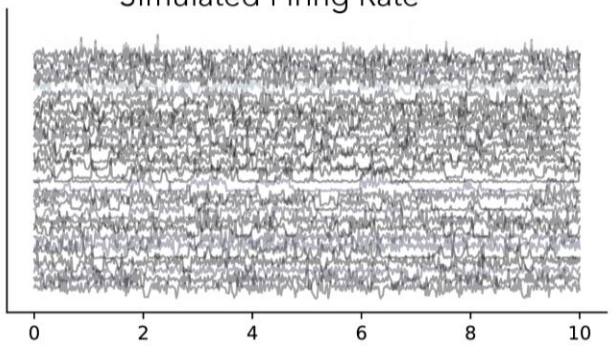
Allen Mouse Connectome

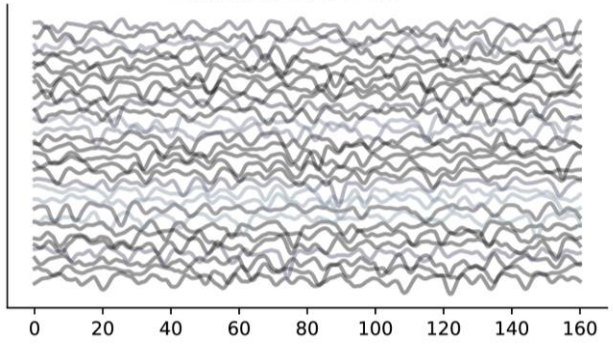


Simulated Firing Rate



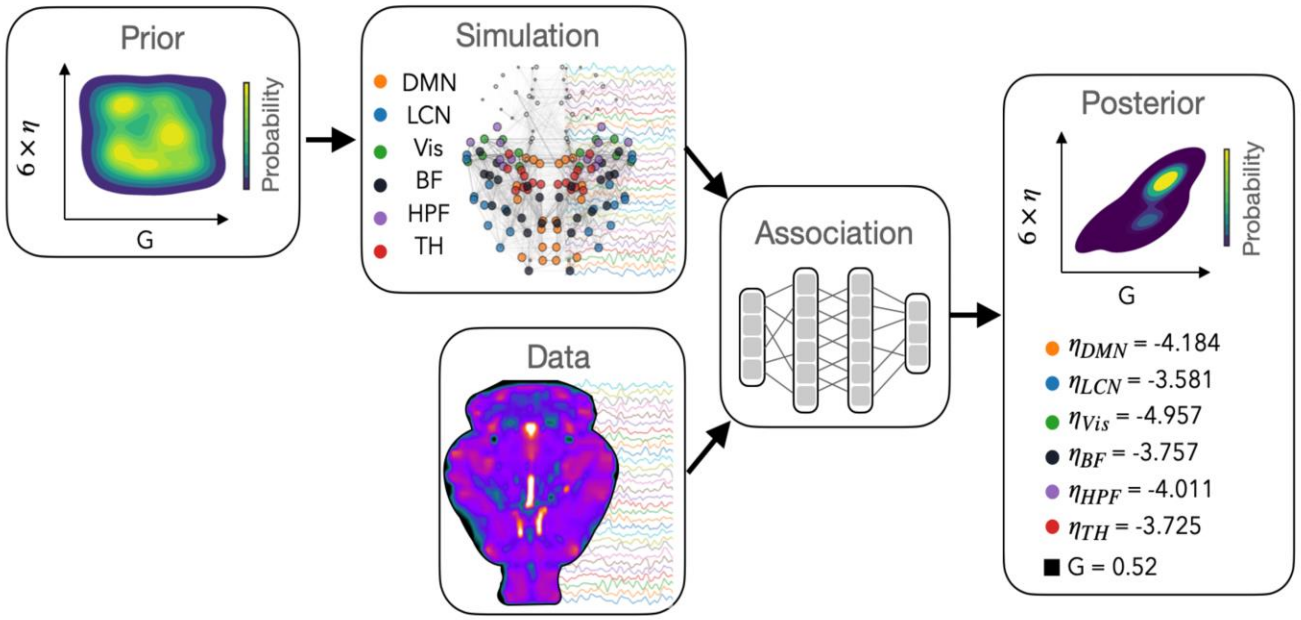
Balloon model

Simulated BOLD



Probing the effect of local changes on large-scale bursts spreading

Virtualized mouse pre-DREADD



Abolfazl Ziaee Mehr

Meysam Hashemi

- TVMB + Simulation-based inference (SBI)

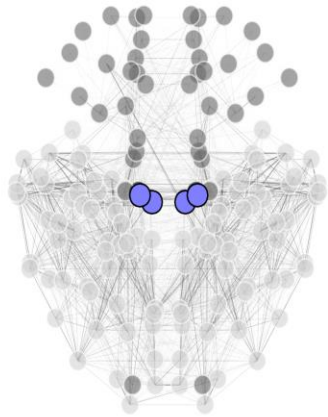
infer optimal parameter configuration where simulations match the experimental data

Cranmer et al. *PNAS* 2020

Hashemi, et al. *MedrXiv* 2022

Effects of decreasing local excitability

- 100 baseline simulations VS 100 simulations with decreased RSC excitability:

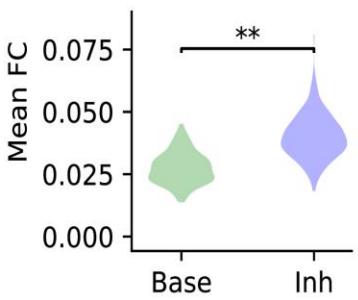


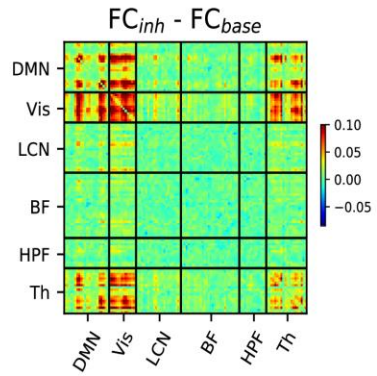
$$\eta_{RSC,Base} = -4.184$$

$$\eta_{RSC,Inh} = -4.6$$

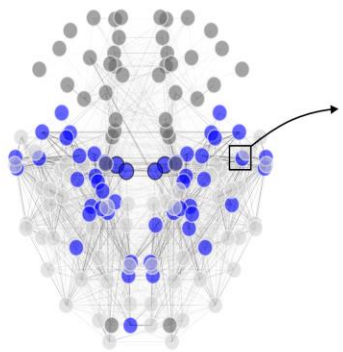
- Results:

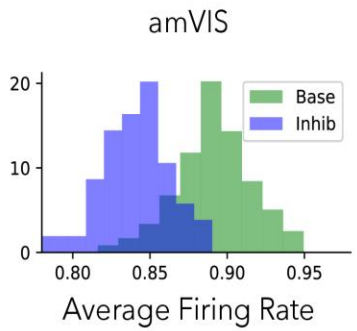
1.BOLD over-connectivity



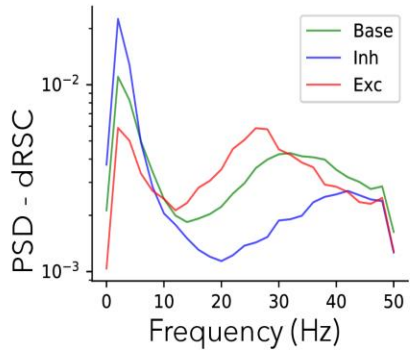


2.Firing rate decrease in subnetwork



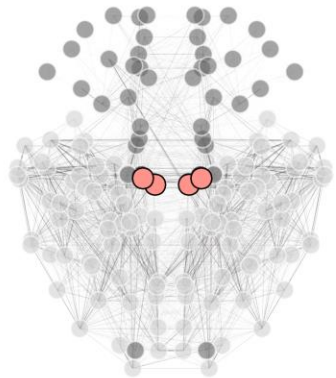


3.Increased slow frequencies



Effects of decreasing local excitability

- 100 baseline simulations VS 100 simulations with increased RSC excitability:

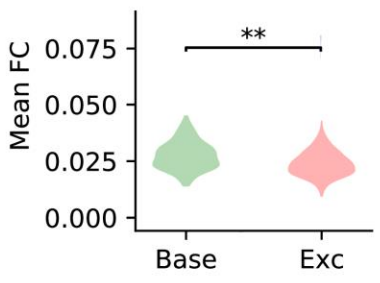


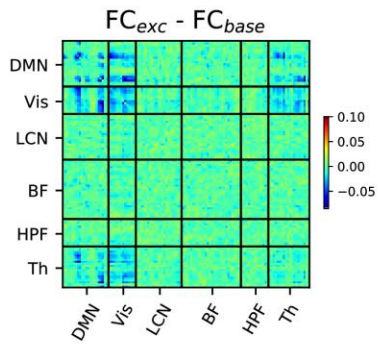
$\eta_{RSC,Inh} = -3.8$

$\eta_{RSC,Base} = -4.184$

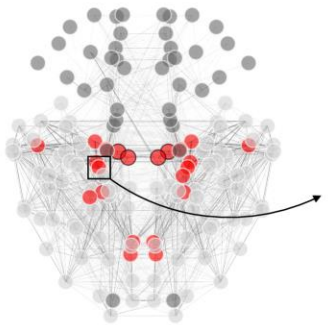
- Results:

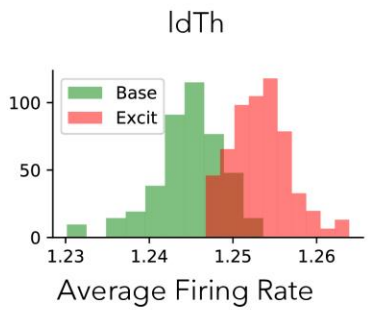
1.fMRI hypo-connectivity



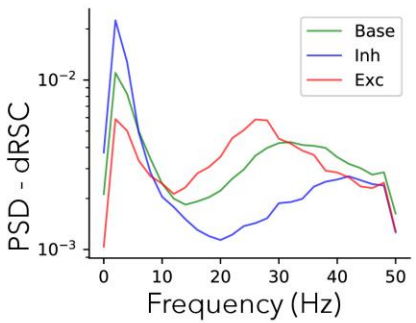


2.Firing rate increase in subnetwork





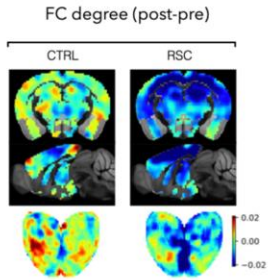
3.Decreased slow frequencies



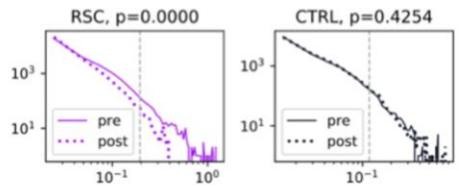
- Increased local excitability explains our observations! ⇒ Lesion and DREADD increased overall excitability

Take home

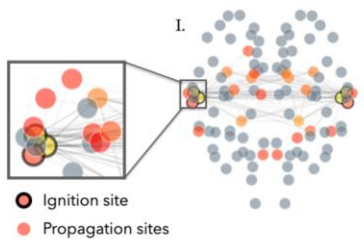
- Focal silencing (Lesion and DREADD) caused drop of global FC



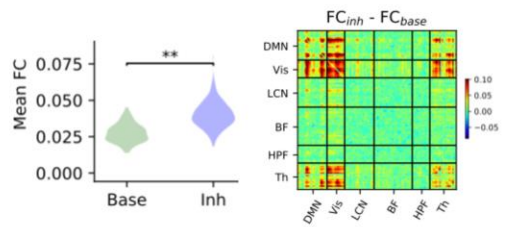
- The FC drop was due to an impaired capability of bursting



- Bursts are building blocks of FC and depend on local activity



- Virtual brain models confirm previous results, allow to interpret new data, and make predictions



Thank you for your attention ☺

The Naples MEGLab

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Michael Breakspear

Viktor Jirsa

Andrew Zaleski

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