24/03/2021

QLS Exam

Dynamical signatures of structural connectivity damage to a model of the brain posed at criticality

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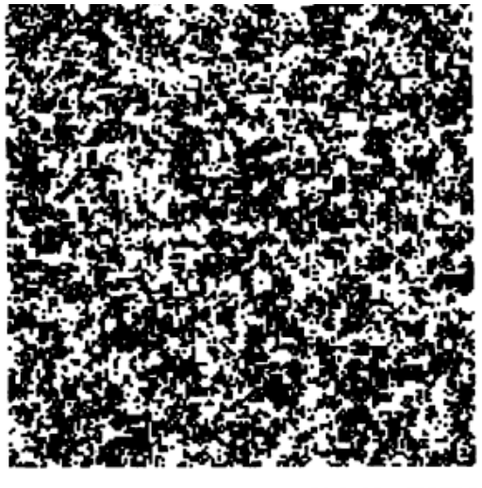
Introduction: criticality

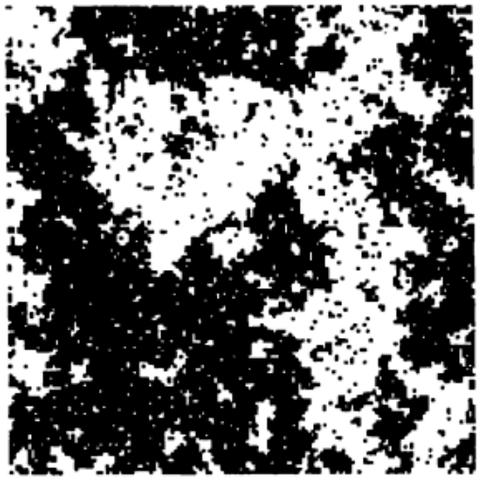
- Critical point → separation between two phases;

- Characteristic from both phases, in Ising model an ordered and a disordered one;

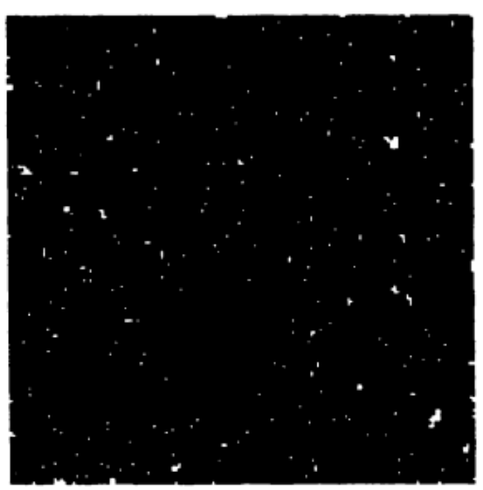
- Infinite correlation length.



$T > T_c$



$T \sim T_c$



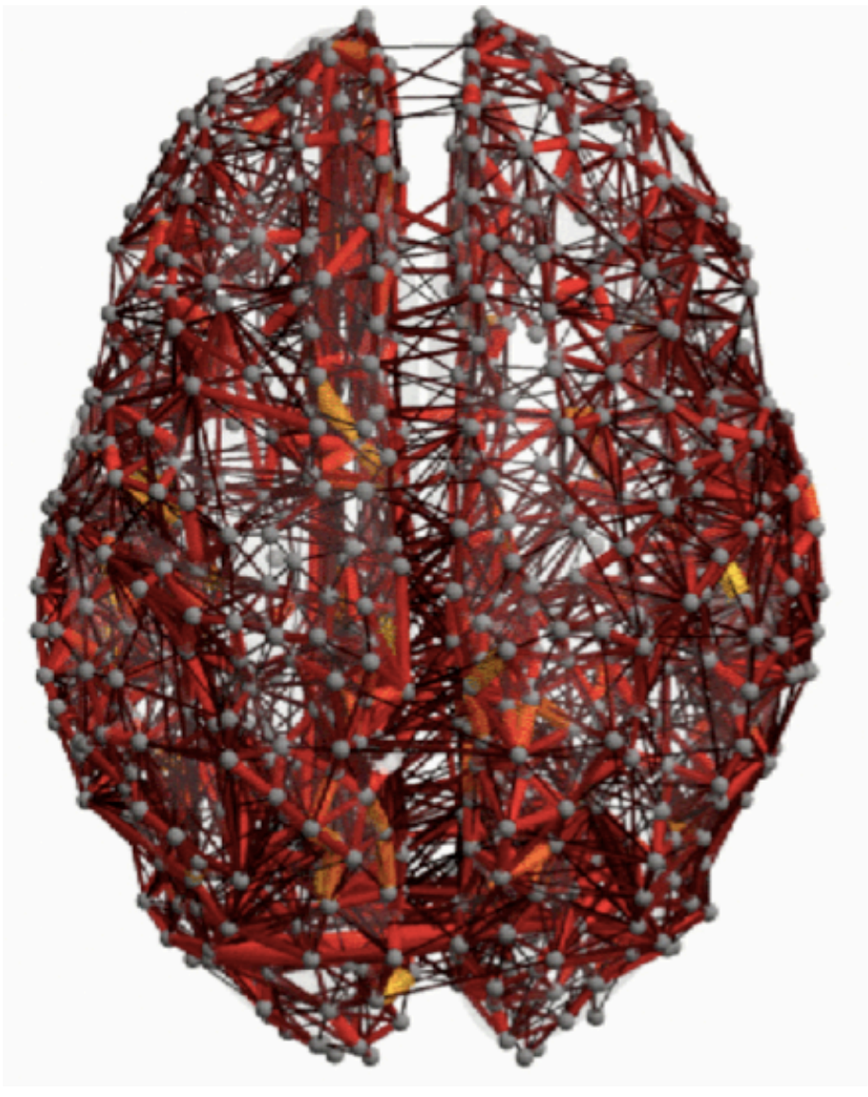
$T < T_c$

Introduction: brain criticality

- **The Brain is never at rest:** it presents complex spatio-temporal patterns of coordinated activity;

- **Extremely sensitive to small perturbation:** infinite correlation length;

- **Not random:** ordered patterns emerge to support human cognition.



Introduction: brain criticality

Long-range coordinated activity fluctuations (Fraiman and Chialvo, 2012)

Maximal sensitivity to external perturbations (Tagliazucchi et al, 2013)

Optimal exploration of transient states (Werner, 2007)

Scale-free distribution of avalanches (Beggs and Plenz, 2003)

Critical!

Underlies the flexible and adaptive information processing capabilities (Chialvo, 2010)

Introduction: question

Can we model brain injuries as a displacement from the critical point?

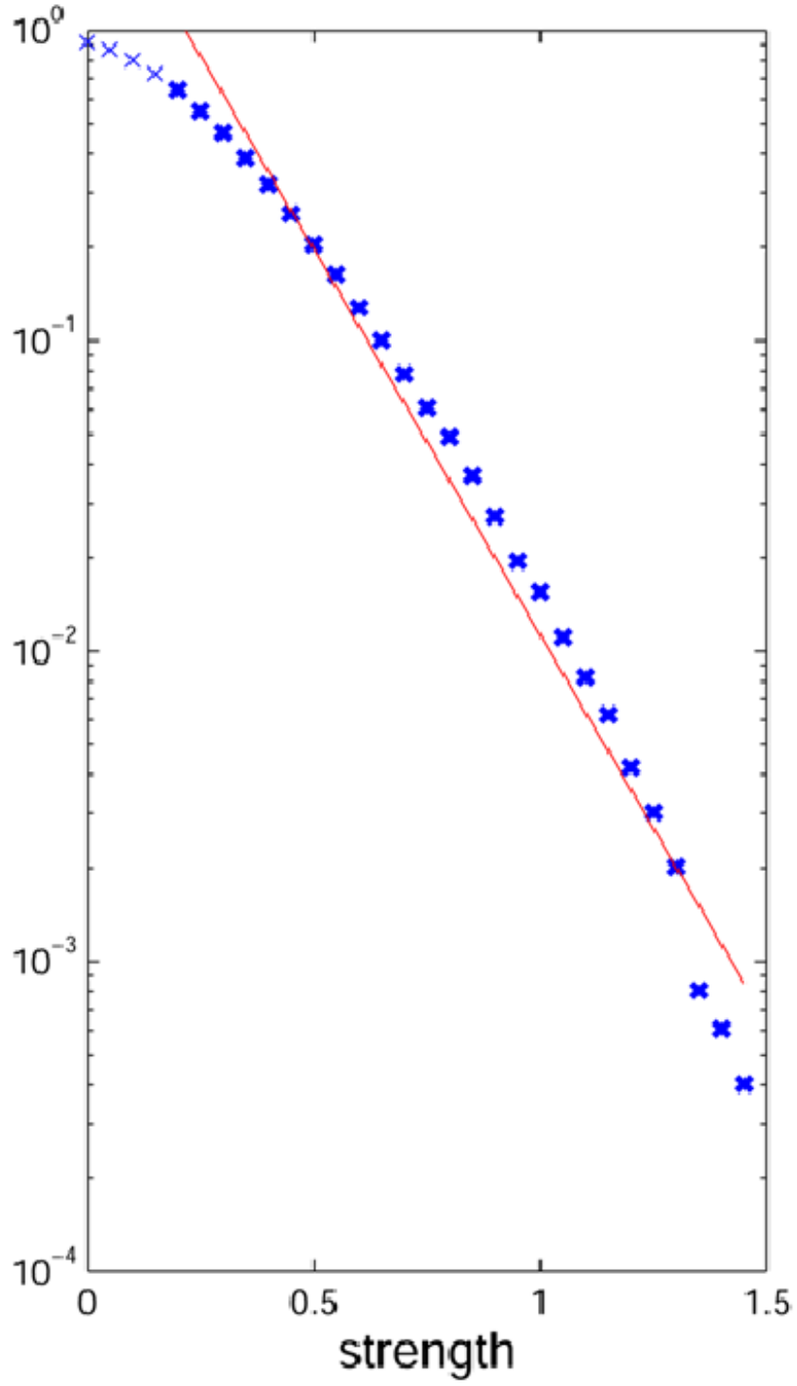
Using as connectivity matrix the realistic brain connectome (Done in paper)

Using as connectivity matrix appropriate random matrices (Additional work)

Simulate functional connectome

Introduction: random adj matrix

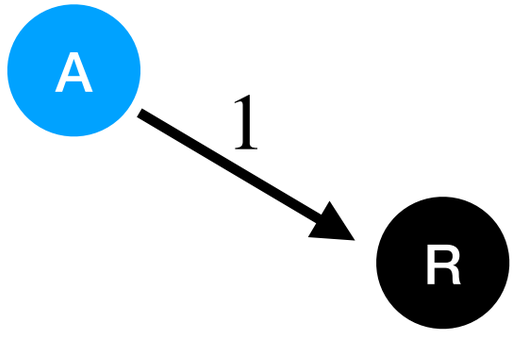
- Create a scale-free adjacency matrix;
- Sample its weight from the weight distribution;
- Use this weighted adjacency matrix as connectivity matrix of the experiment.



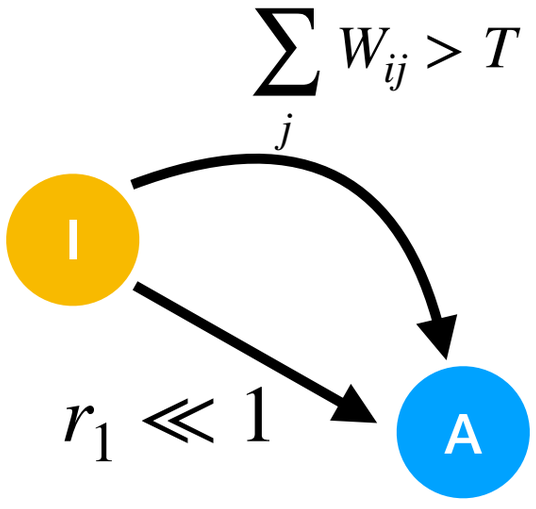
Computational model (CM)

Active: A **Inactive:** I **Refractory:** R

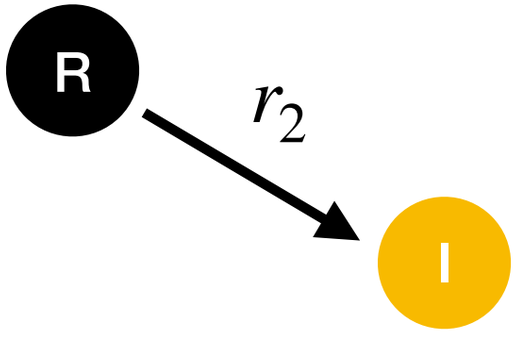
DEACTIVATION



ACTIVATION



RELAXATION

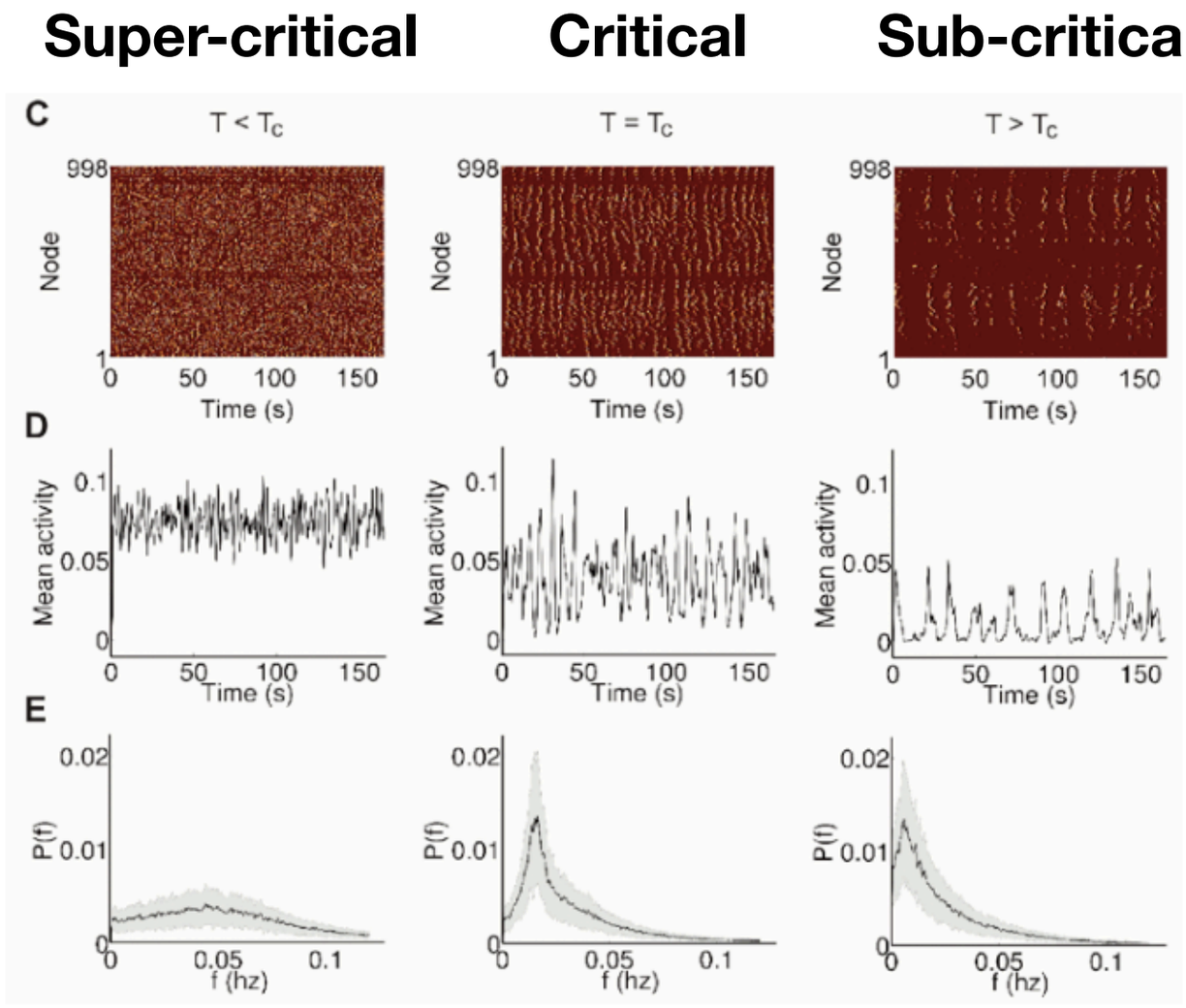


CM: Parameter description

- r_1: **self-activation rate**;
  - Very small, fixed at 10^{-3} ;

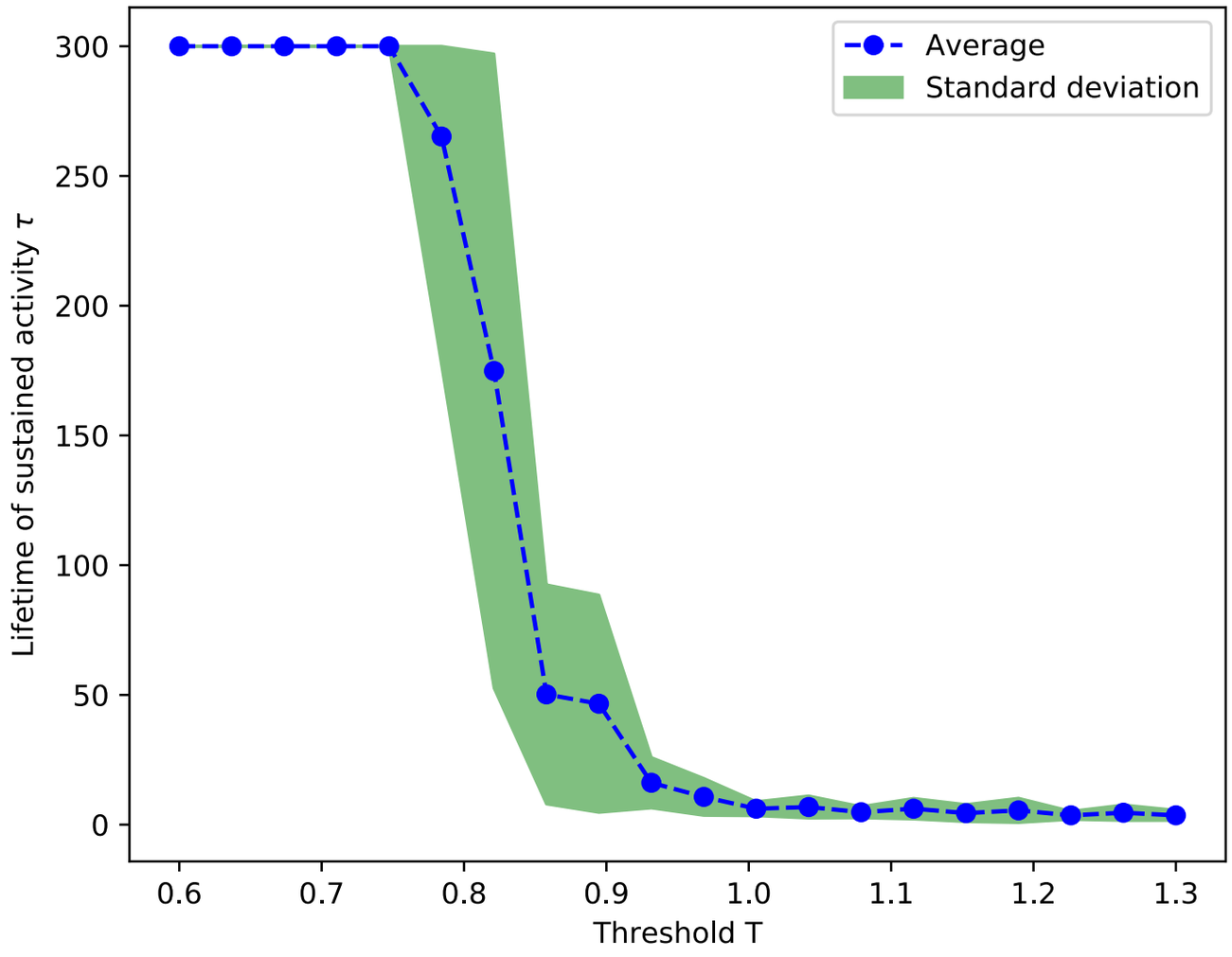
- r_2: **relaxation rate**;
  - Introduces a delay between the state R and I;
  - It will take time between two consecutive activations;

- T: **activation threshold**;
  - $T < T_c$ super-critical phase, sustained but not coherent activity;
  - $T > T_c$ sub-critical phase, alternating activation and quiescence;



Metrics: lifetime

- Lifetime τ: number of iteration after which the activity stops;
- If the activity continues for the full simulation time (300 iterations) then we assign $\tau = 300$.
- It is the classical control parameter for the GH model;

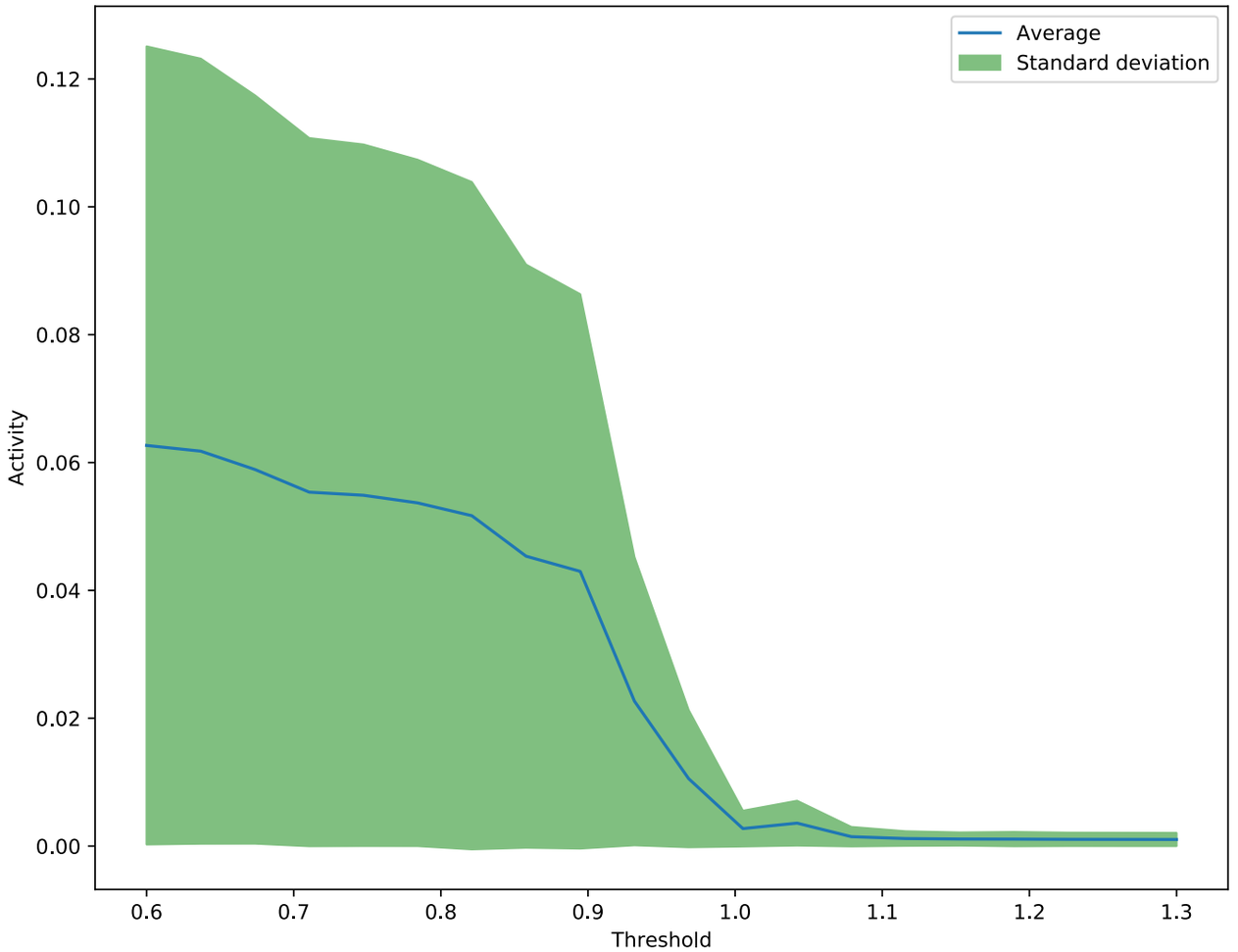


Metrics: Activity

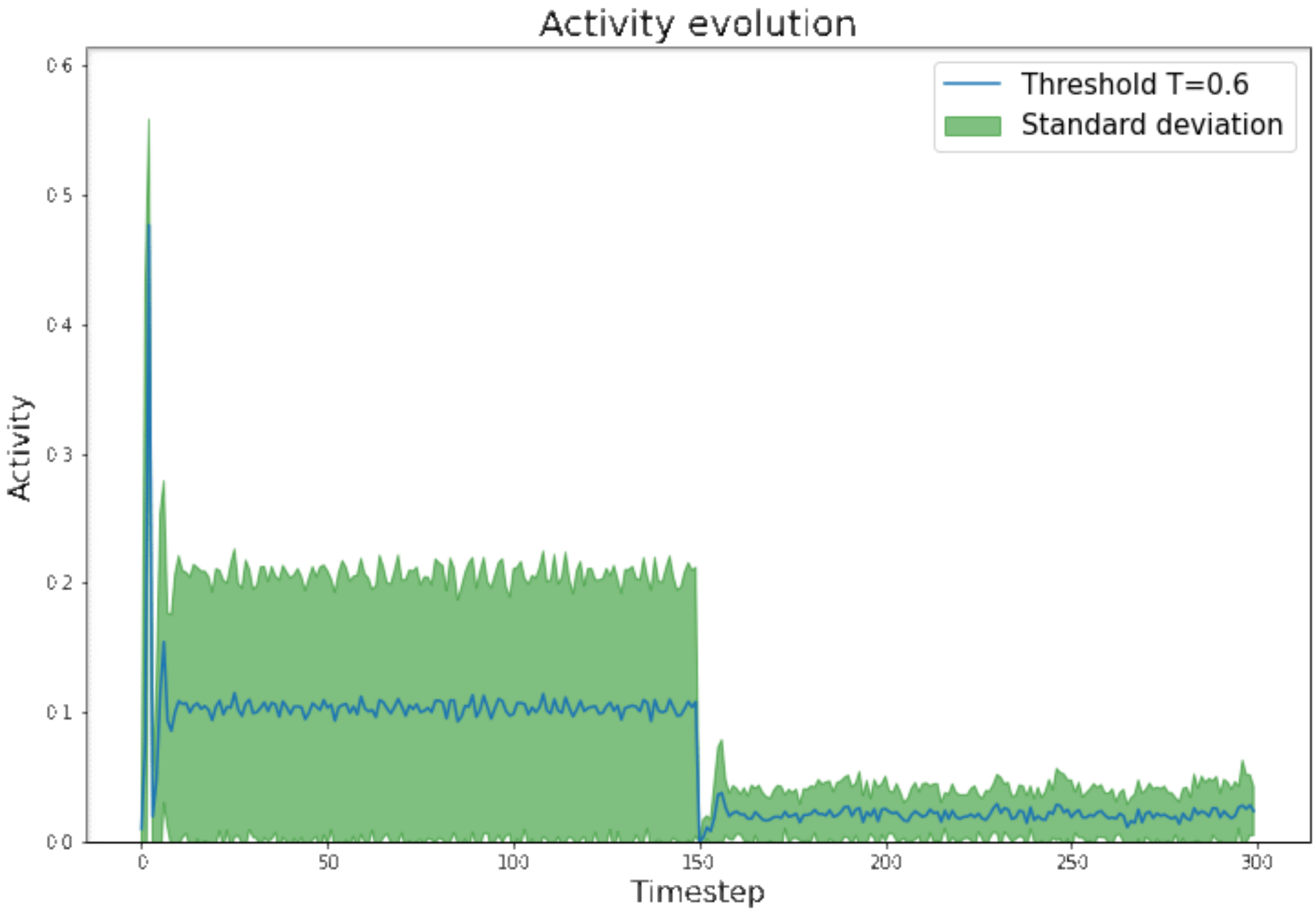
- Captures the fraction of active neurons

- Shows whether global brain dynamics present temporal variability or is stable;

- Absence of variability have been linked to brain pathology and ageing;

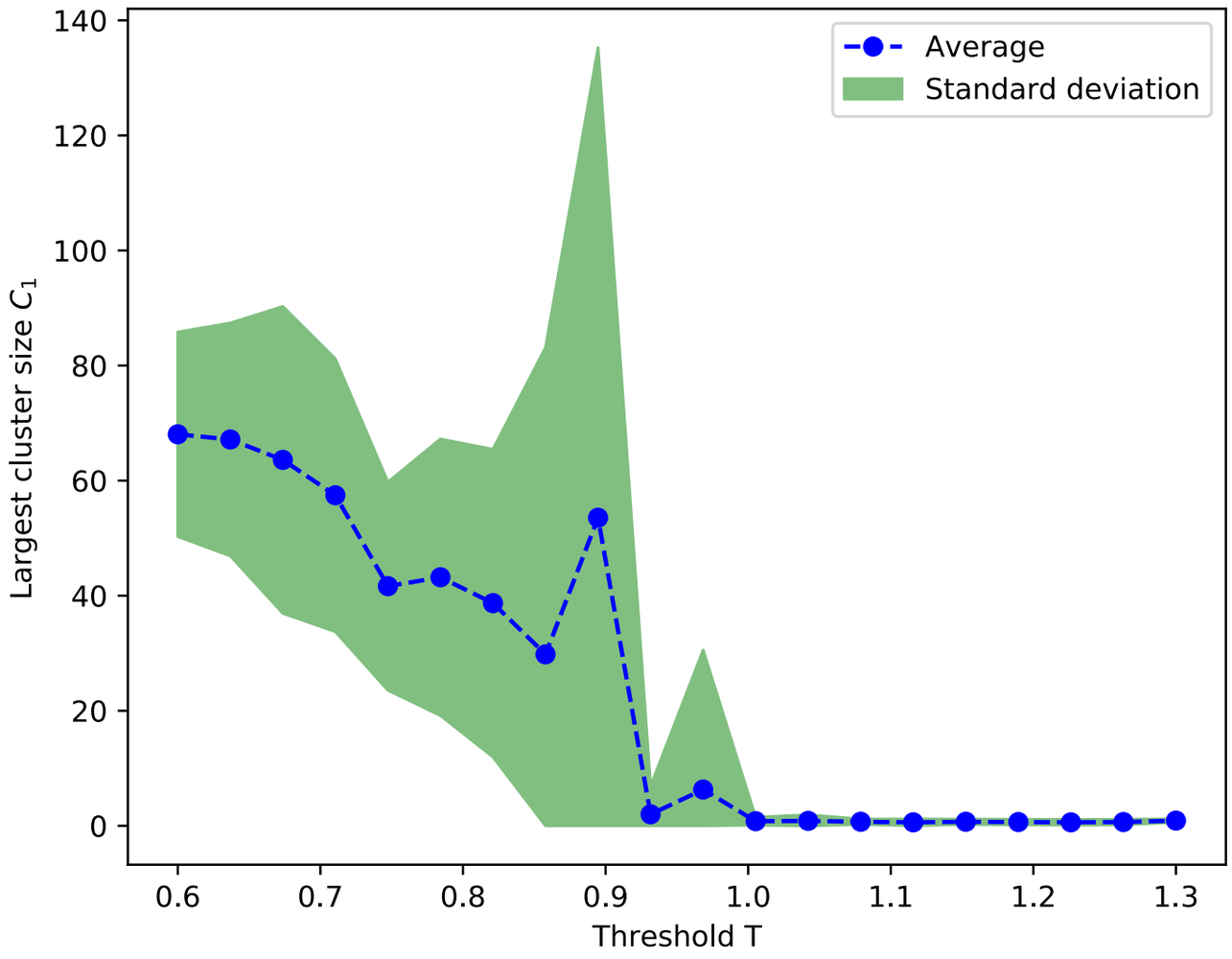


Metrics: Activity



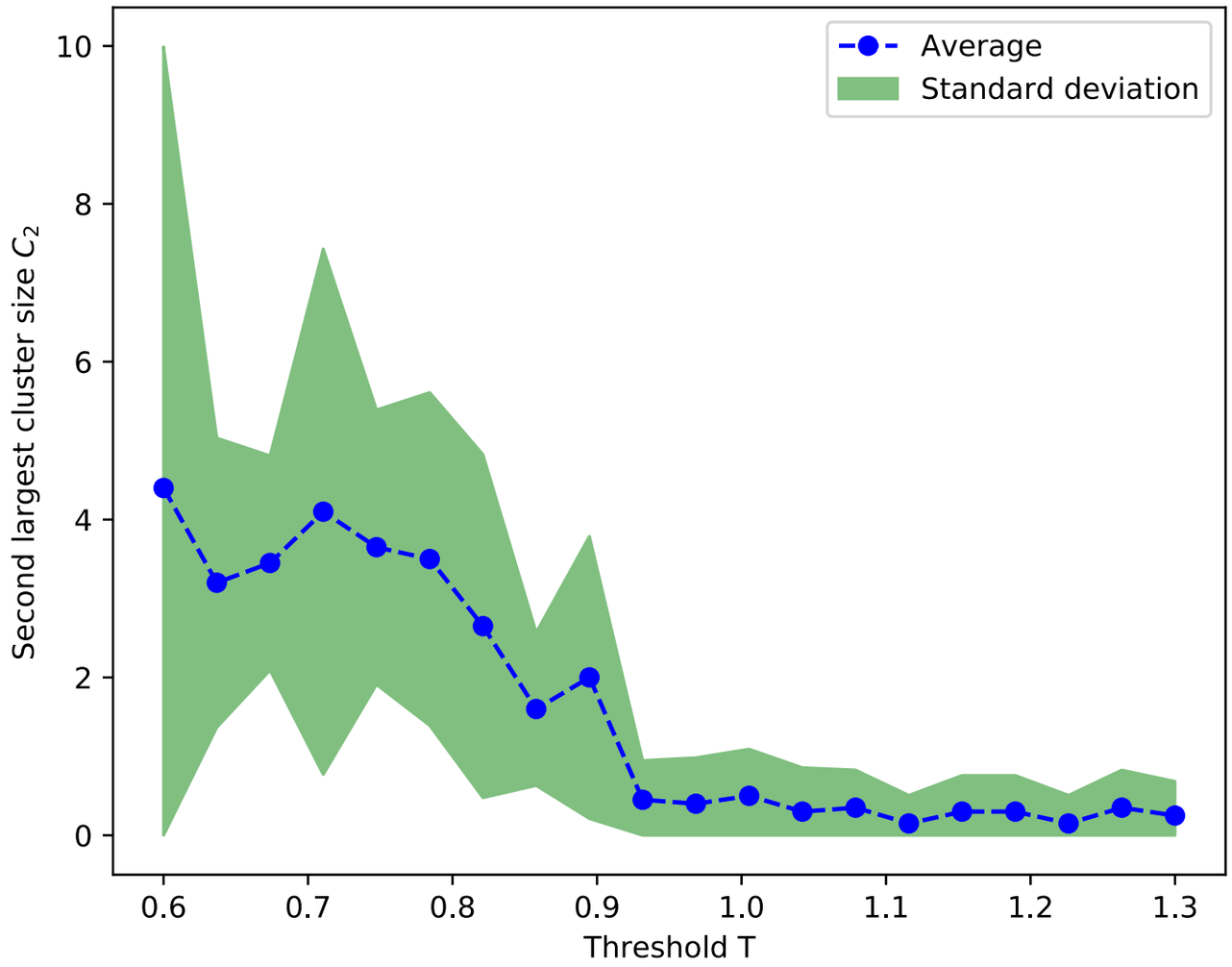
Metrics: C_1

- Size of the largest cluster of active neurons;
- It is also used as order parameter for the GH model.



Metrics: C_2

- Size of the second largest cluster of active neurons;
- Peaks right before coalescing into a giant connected component;
- Captures how close the brain is to a massive co-activation, similar to neural avalanches.

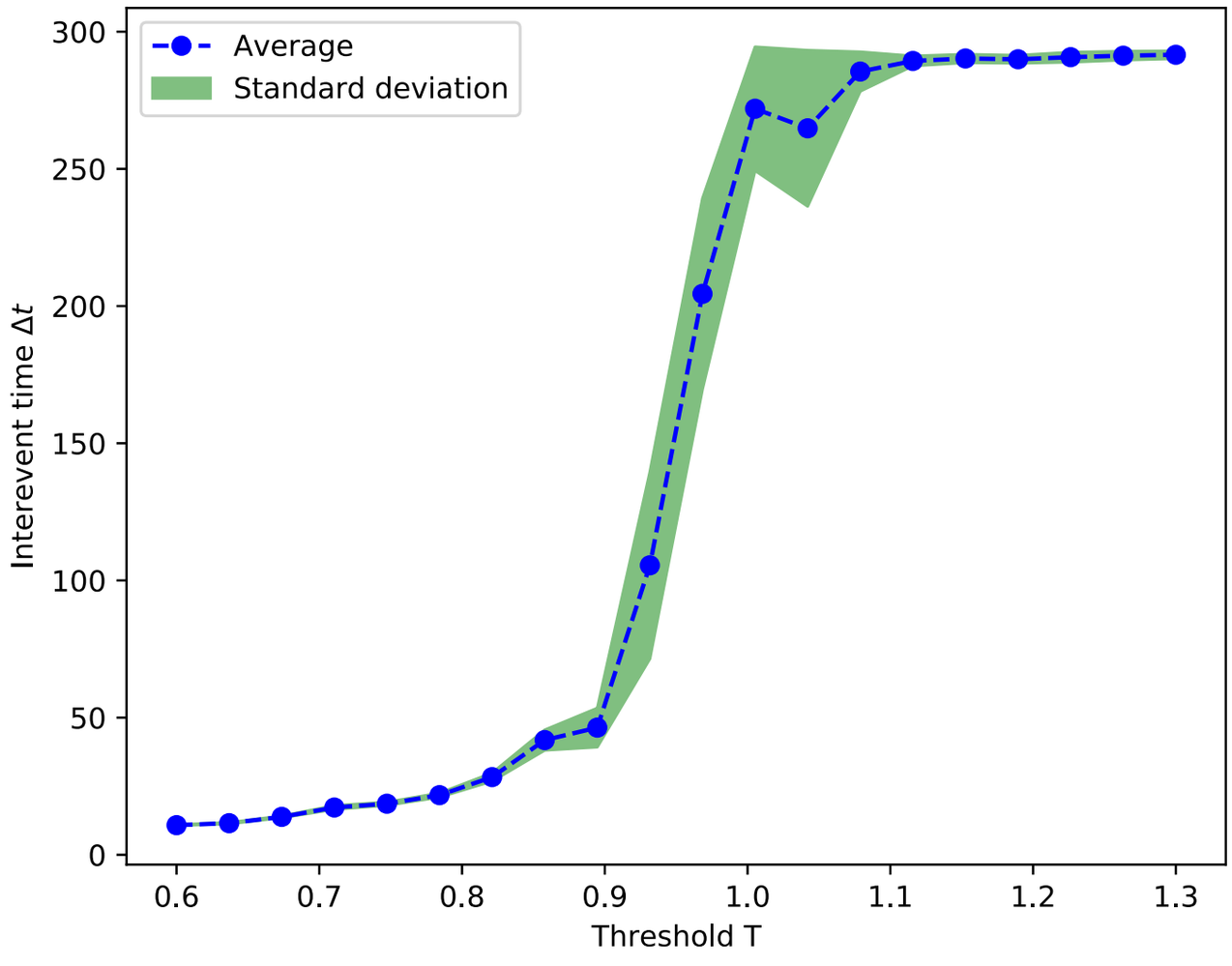


Metrics: inter-event time Δt

- It is defined as the mean number of time steps between two consecutive activations;

- Local measure of frequency of activation;

- Relevant for structural lesion simulation, since brain injuries slow down activation frequency in EEG.



Hemodynamic function

- Needed to pass from discrete activation to continuous signal, by convolving it activation pattern;

$$h(t) = \frac{1}{k\tau_h(k-1)!}\left(\frac{t}{\tau_h}\right)^k e^{t/\tau_k}$$

- Used to pass from structural to functional connectivity, reproducing blood flow;

$$s_i(t) = A(t) * h(t)$$

- Gamma-variate function;

Metrics: Pairwise correlation

- It is defined as:

$$C_{ij} = \frac{< (s_i(t)\mu_i)(s_j(t)\mu_j >}{\sigma_i \sigma_j} \qquad \mu_i = < s_i(t) >$$

$$\sigma_i = \sqrt{Var(s_i(t))}$$

- We will also investigate its mean and standard deviation.

- It captures the global functional connectivity and its variability

- Notice that functional connectivity is used to denote statistical covariance between model time series and not between empirical fMRI time series.

Metrics: struct-func correlation

- Correlation between functional and structural network in two different ways;

- Using the weighted version of the matrices

$$C(F,S)_w = \frac{2}{N(N-1)} \frac{1}{\sigma(W)\sigma(C)} \sum_{i \neq j} (W_{ij} - < W >)(C_{ij} - < C >)$$

- Using a thresholded version

$$C(F,S)_b = \frac{2}{N(N-1)} \frac{1}{\sigma(Adj)\sigma(B)} \sum_{i \neq j} (Adj_{ij} - < Adj >)(B_{ij} - < B >)$$

Metrics: susceptibility

- The system was perturbed activating $60\,\%$ of the nodes at time $t = 0$;
- Each node's time series was convolved with the Hemodynamic response function;
- The variance of the mean response was computed in sliding windows of 20 time steps;
- The susceptibility χ was identified with the time elapsed until the variance decayed beyond a threshold of 10^{-3}.
- The capability of generating widespread and persistent activity has been postulated as a fundamental feature of conscious information access.

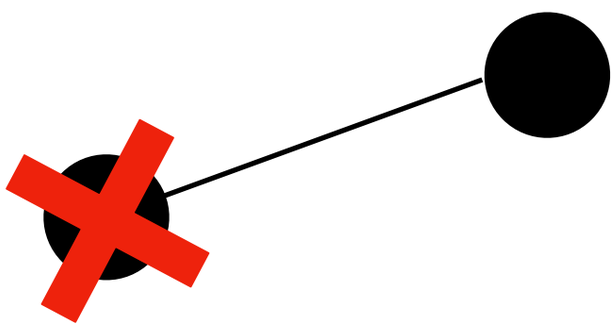
Types of lesions

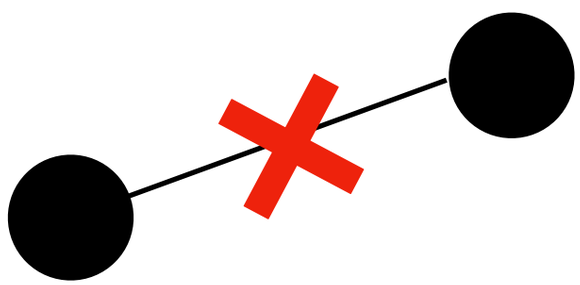
Nodes:

- with largest degree;
- with largest connectivity strength;
- with largest betweenness centrality;
- with largest eigenvector centrality;
- with largest participation coefficient;
- randomly.

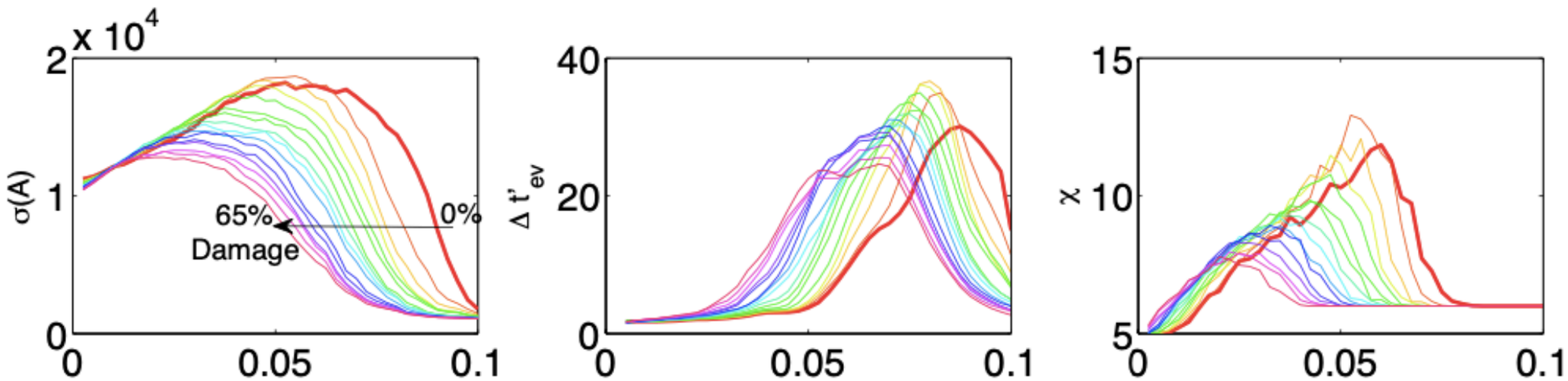
Links:

- with largest betweenness centrality;
- with the heaviest weights
- Randomly

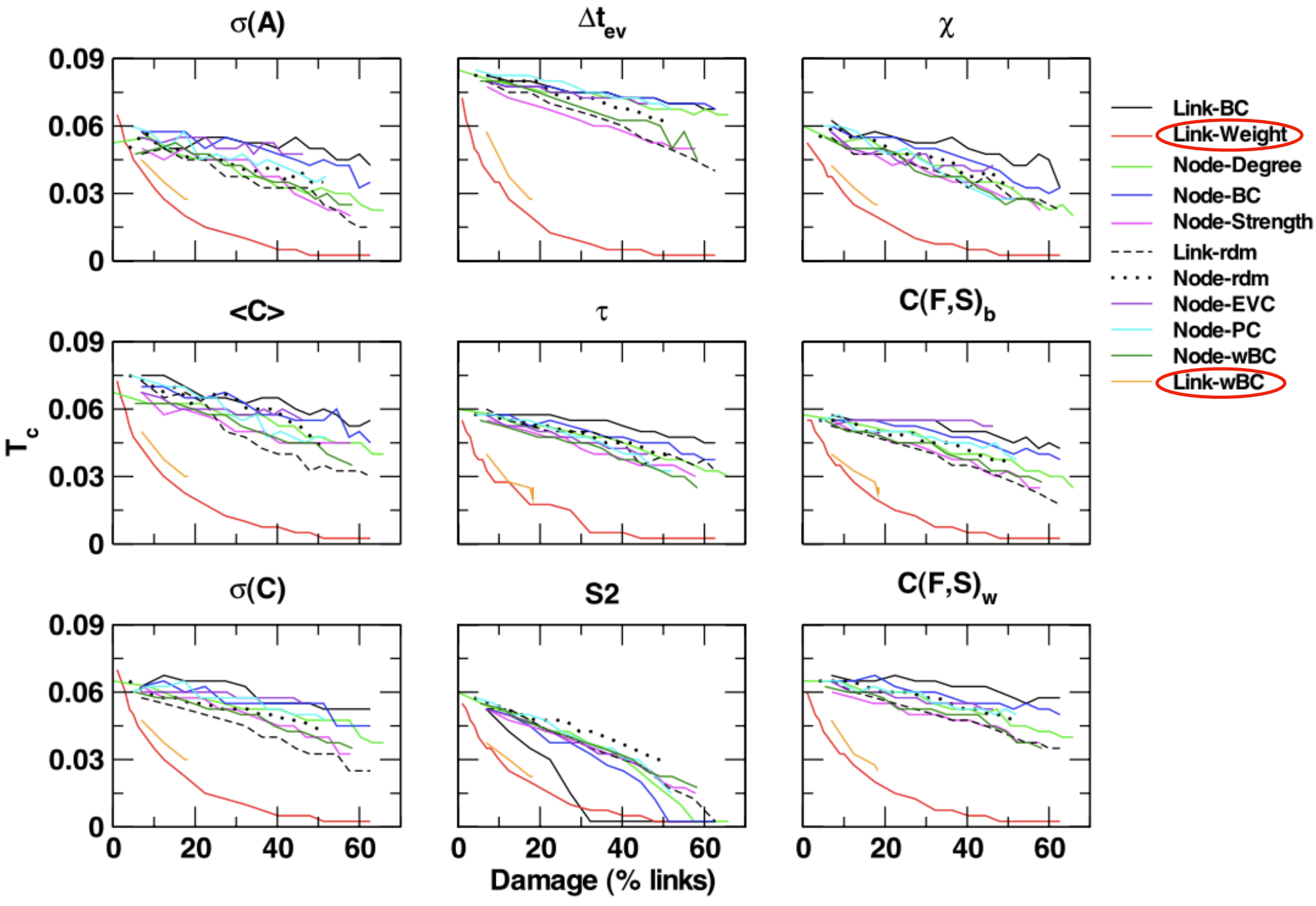




Lesions at 998 neurons



Critical point displacement



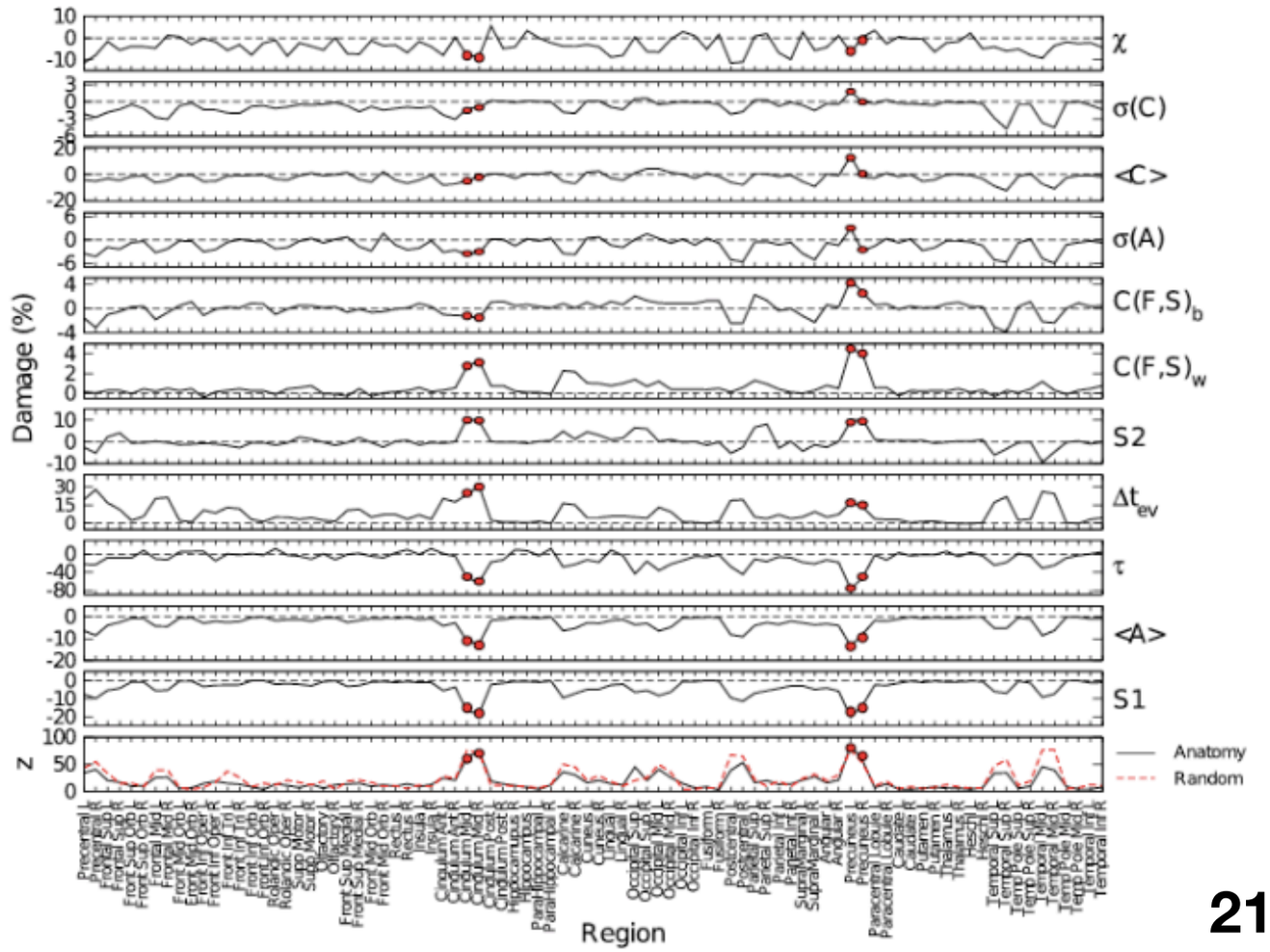
Lesions at coarser regions

- It is difficult to investigate damage to functional roles at 998 nodes;
- We so simulate the network on 998 and then project it on 90 cortical regions.
- Lesions removed all connection with at least one end attached to any node within the region
- Relative deviation:

$$\Delta O = \frac{O - O_0}{O_0} \cdot 100$$

- Damage index:

$$Z = \sqrt{\sum_0 (\Delta O)^2}$$



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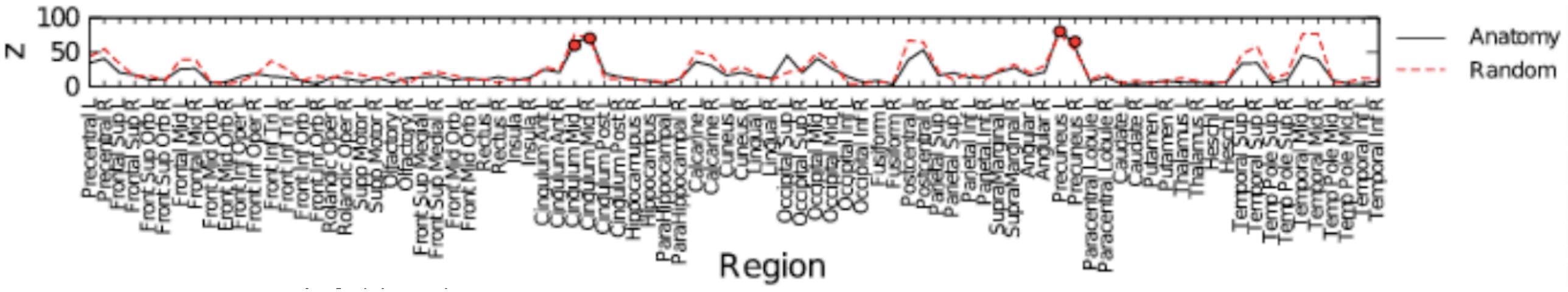
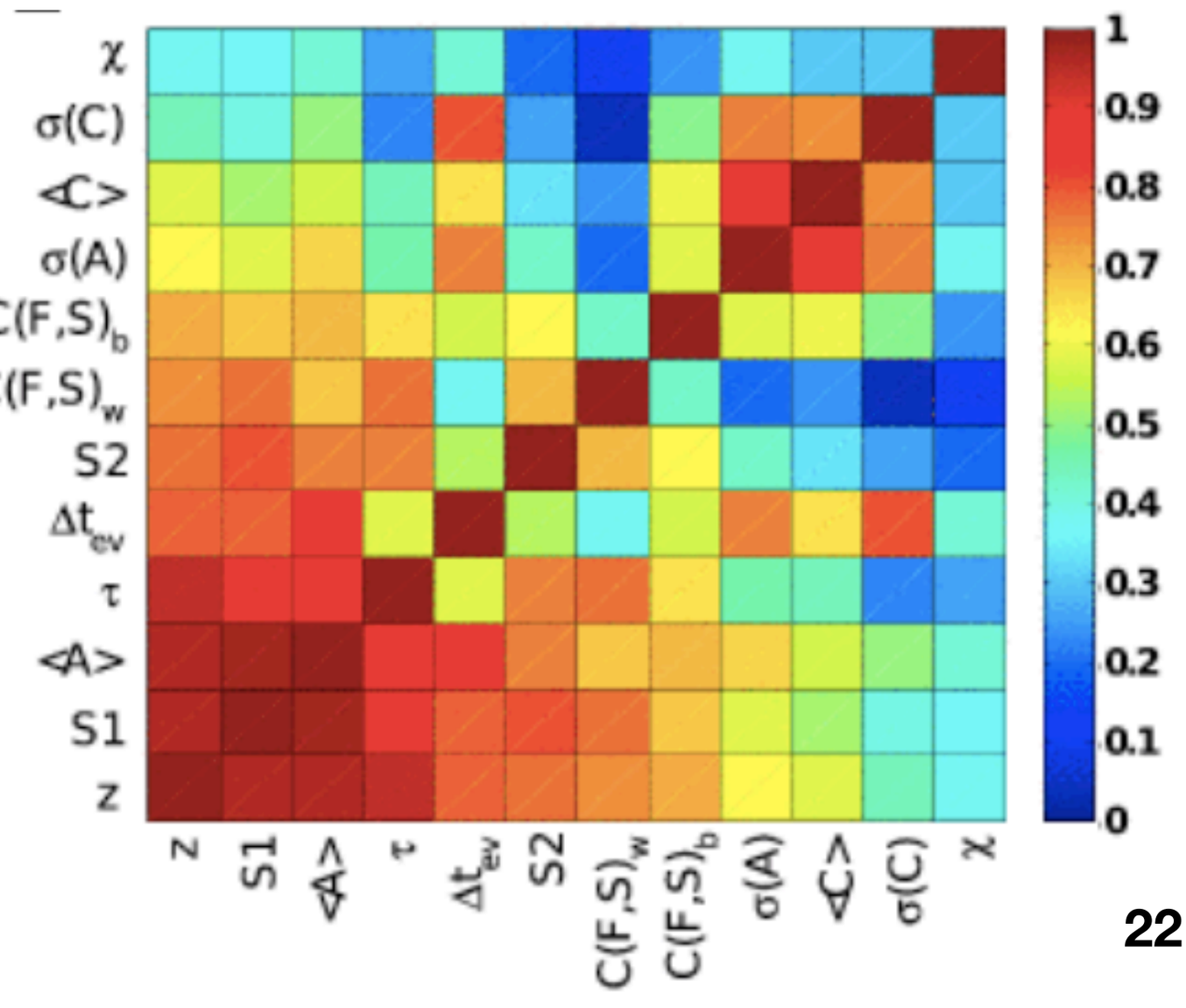


Correlation

- We want to investigate similarity between results with different metrics;
- Correlation between pairs of the previous plots, in absolute value

High Correlation ⇒ **Similar Behaviour**

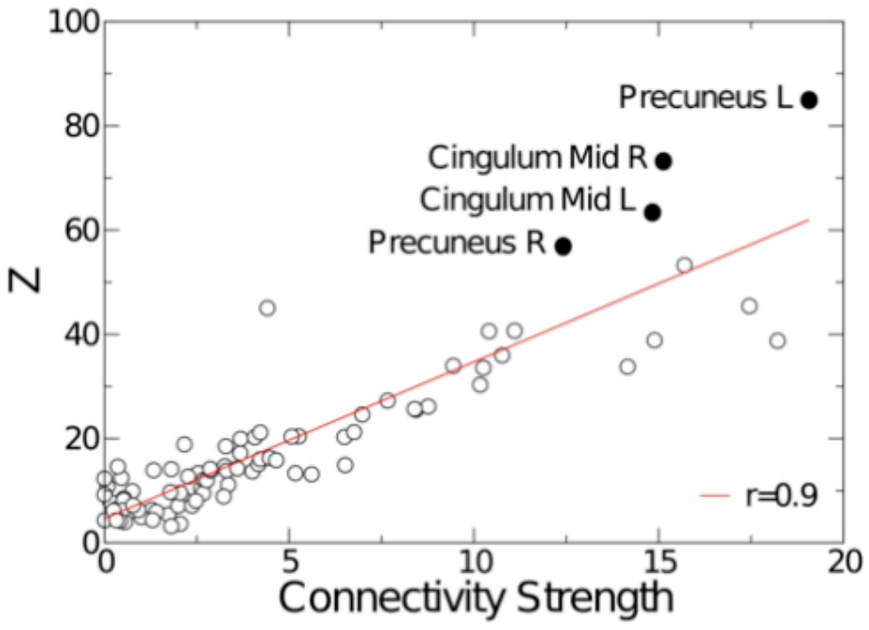
Low Correlation ⇏ **Different aspect of network damage**

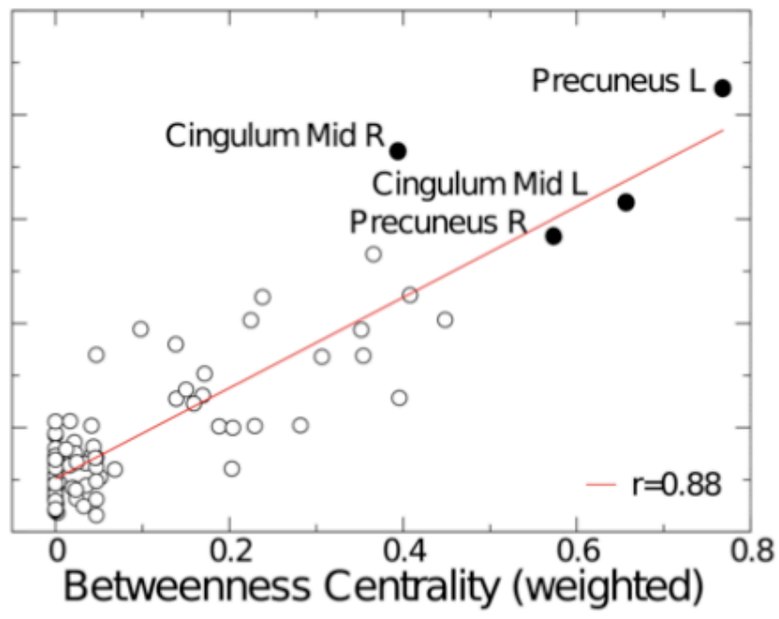


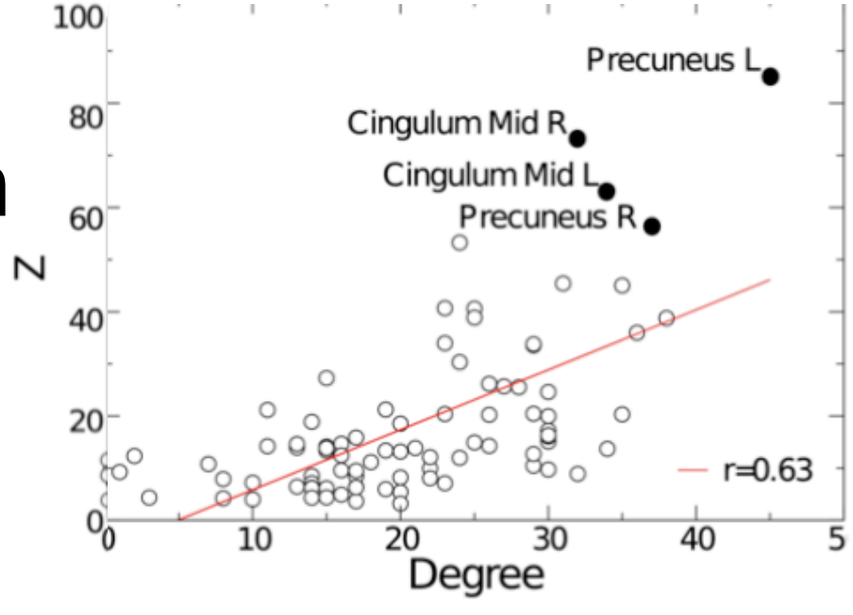
Damage index and topology

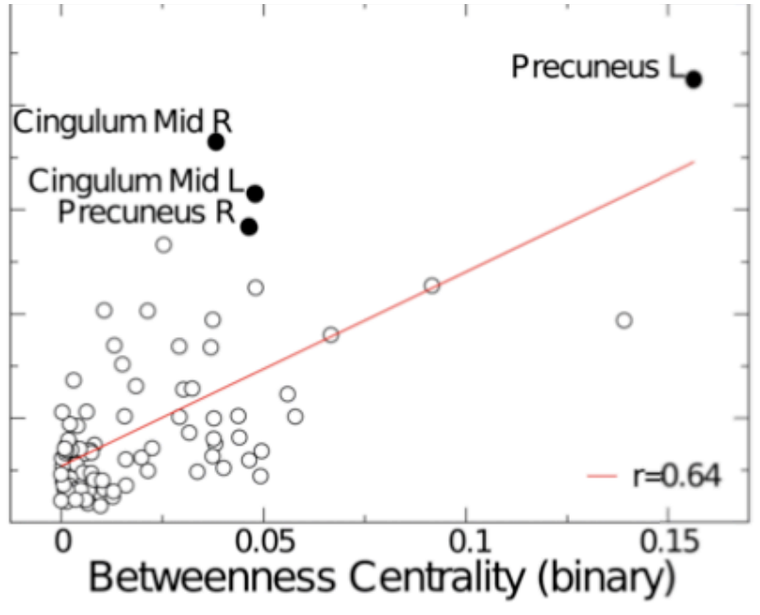
Network feature using weights

Higher correlation with Z



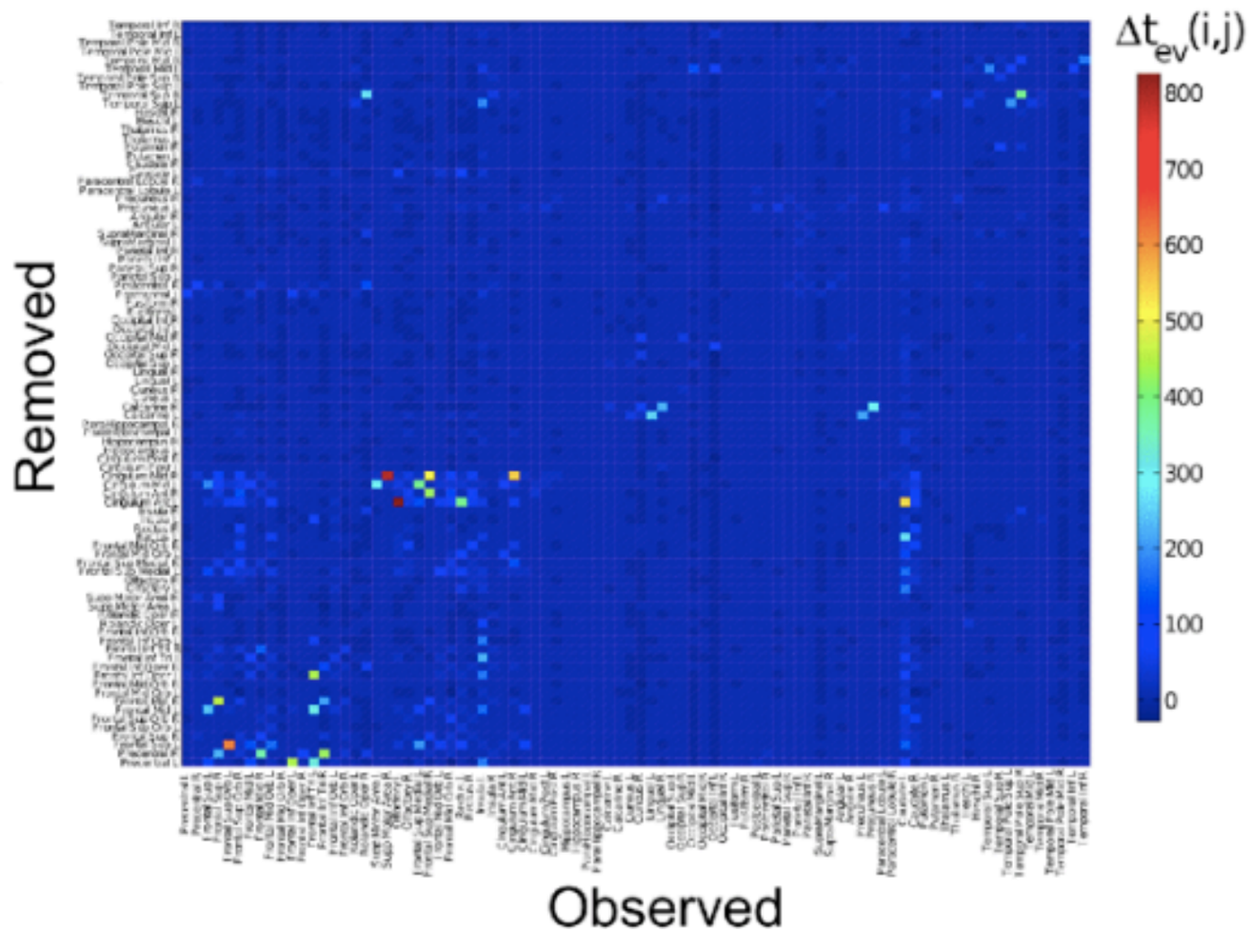


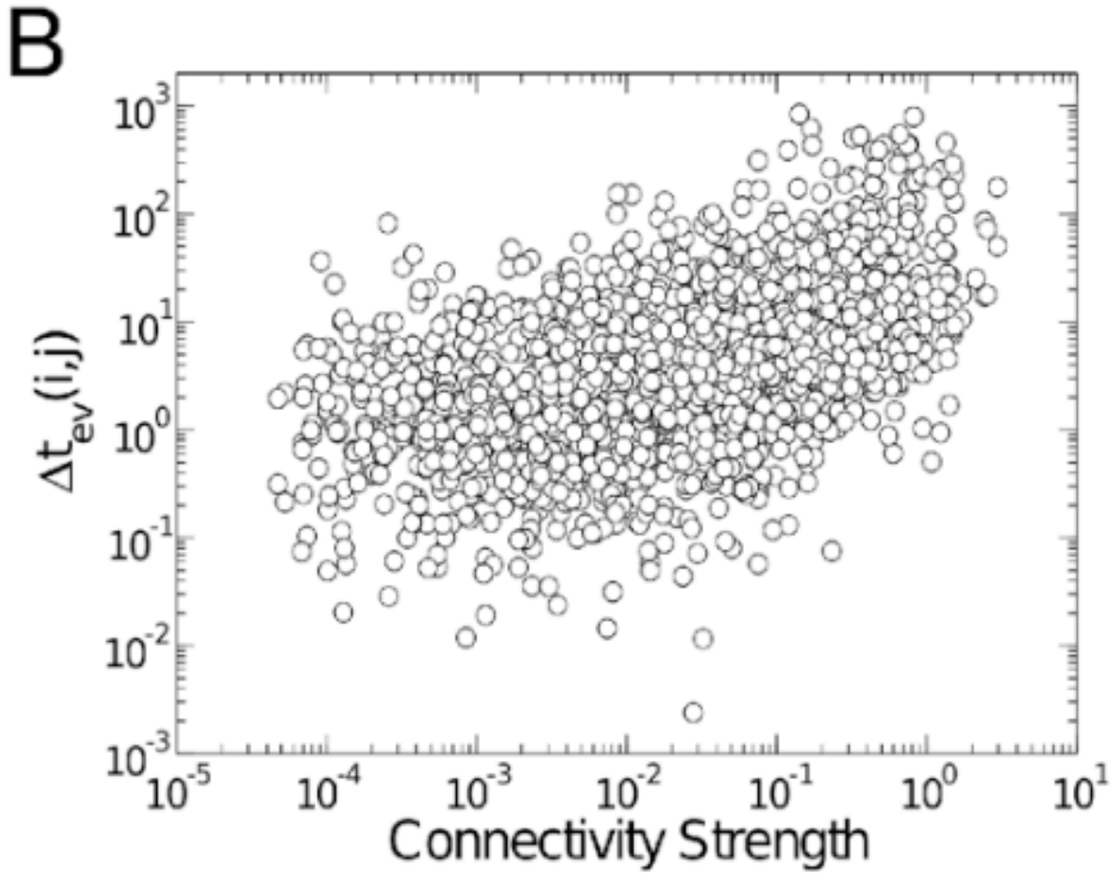




Consequences on local dynamics

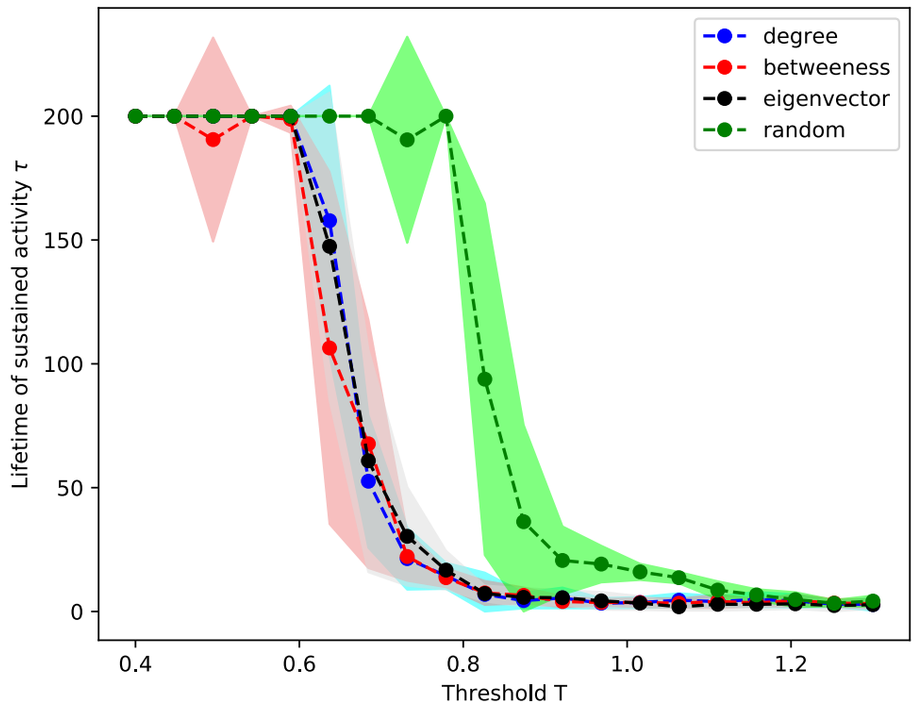
- Specific effect of damaging each brain region on interevent time
- Most affected if close to the damaged area
- Correlation between weight and Δt_{ev}

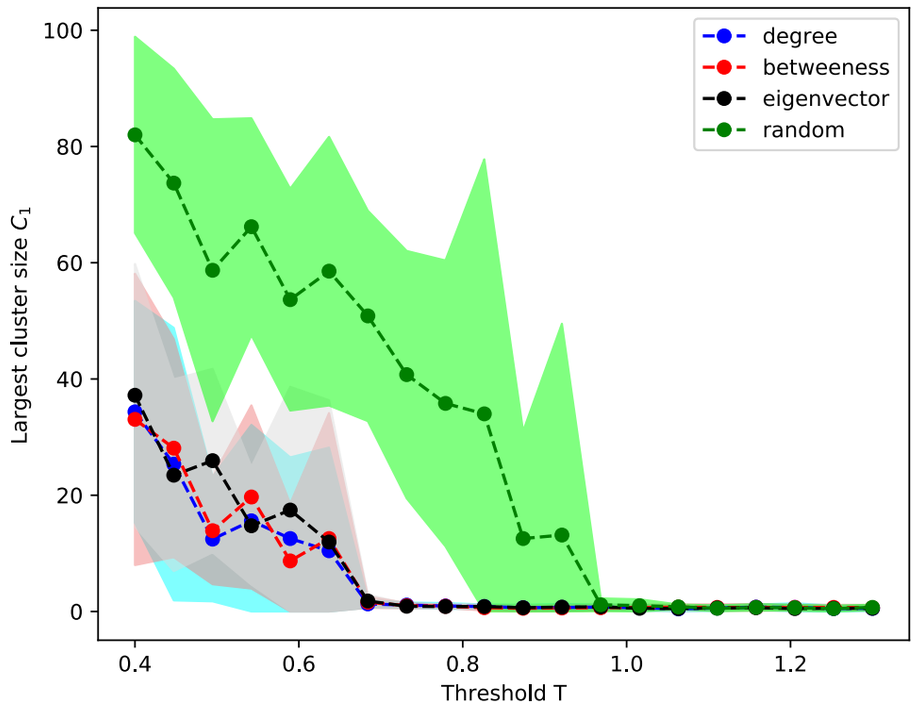


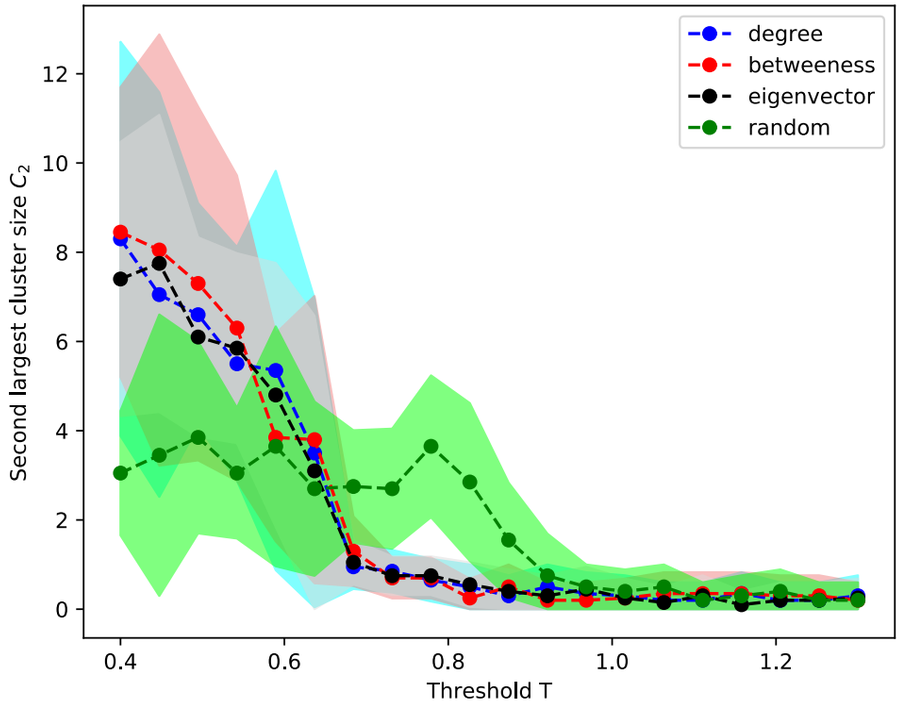


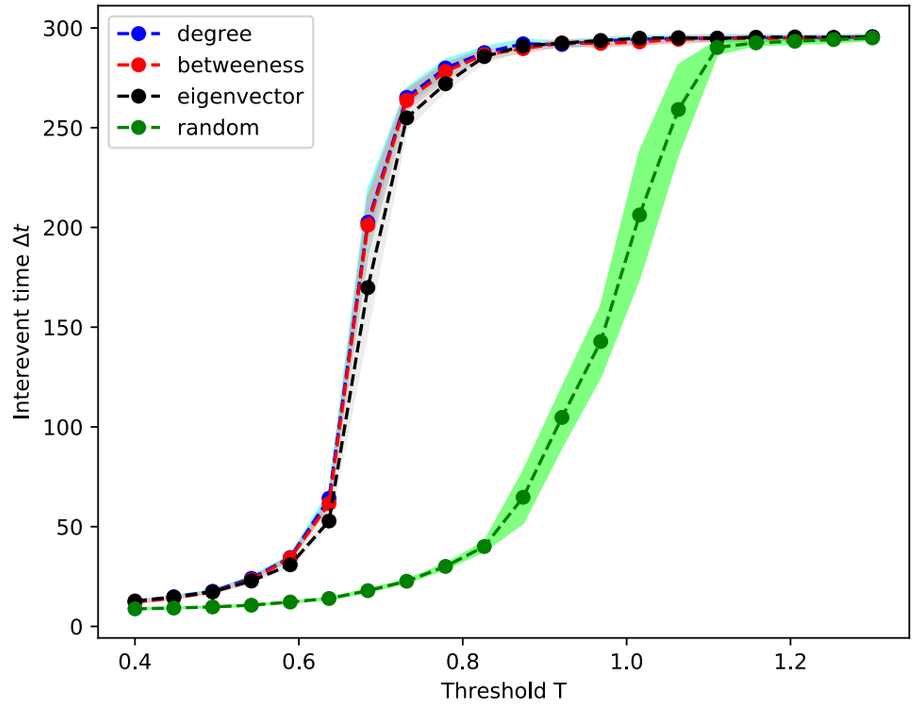
Lesions at random matrices

Damage:
50 neurons
5% of network









Discussion

Healthy brain

Attacks at high-weights connections

Sub-critical phase

Effects on healthy brain metrics

- Diminished reactivity to external perturbations
- Slowing down of fluctuations
- Loss of functional connectivity and its variability
- Decrease in activity levels

Role of criticality

Role of criticality

Criticality

Applies to the brain

?

Useful approximation

Epilepsy
(Meisel, 2012)

Anesthesia
(Scott, 2014)

Slow waves sleep
(Priesemann, 2013)

Selection of statistically relevant description of data
(Marsili, 2013)

Bias of inference methods
(Mastromatteo and Marsili, 2011)

Role of criticality

Really critical? Or slightly sub-critical? (Priesemann, 2014)

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Role of criticality

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Criticality

Applies to the brain

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Useful approximation

What are the dynamical consequences of structural damage to a model of the brain dynamics posed at criticality?

Comparison with previous studies

Damage to human and macaque
Midline and parietal zone→hubs
(Honey and Spoons, 2012)

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Damage to hubs →
increased metastability. Were they at criticality or super-critical?
(Vasa, 2015)

Comparison with previous studies

Damage to human and macaque Midline and parietal zone→hubs (Honey and Spoons, 2012)

Damage to hubs → increased metastability. Were they at criticality or super-critical? (Vasa, 2015)

Metabolism slowing down due to less energy demand (Vagnozzi, 2010)

Reduced reactivity, less efficient percolation of sensory informations (Stuss, 1989)

Brain injuries

Reduced long-range functional communication in the brain (Mayer, 2011)

Low degree of differentiation, loss of conscious contents/awareness (Tononi, 2004)

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Reduced reactivity, less efficient percolation of sensory informations (Stuss, 1989) Δt_{ev}

Brain injuries

Reduced long-range functional communication in the brain (Mayer, 2011) χ

Low degree of differentiation, loss of conscious contents/awareness (Tononi, 2004) $\sigma(A)$

Slow wave sleep, anesthesia→Decoupling of brain structure/ function (Tagliazucchi, 2015) $C(F, S)$

Are hubs specials?

Hubs have special topological role

We can induce the same effect lesioning a larger number of smaller-degree nodes

Are hubs specials?

Hubs have special topological role

We can induce the same effect lesioning a larger number of smaller-degree nodes

Brain pathologies arise due to widespread damage amounting to a certain weights of structural connections

Why don't we see them in experiments?

Inter-individual variability will obscure differences that are not located at hubs

Limitations

- Diffusion spectrum imaging is an imperfect technique for determining the brain structural connectivity;

- The model lacks plasticity, cannot reorganise the connections to account for damage;

- The displacement towards the subcritical regime could be predicted from the absence of inhibitory connections;

- The model is simple and non-realistic, but this should not be a problem given the universality of critical dynamics.

Conclusions

- The authors have combined empirical networks with the hypothesis of a critical dynamics;

- We also understood that there are differences between the structural connectome and a random adjacency matrix, with weights sampled from same distribution;

- The hypothesis of criticality is an interesting tool to study not only the health state, but also to take into account anatomical damage.

Thank you

for your attention

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