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The role of onset location and edge resection in epileptic seizure propagation in mice brain: a computational study

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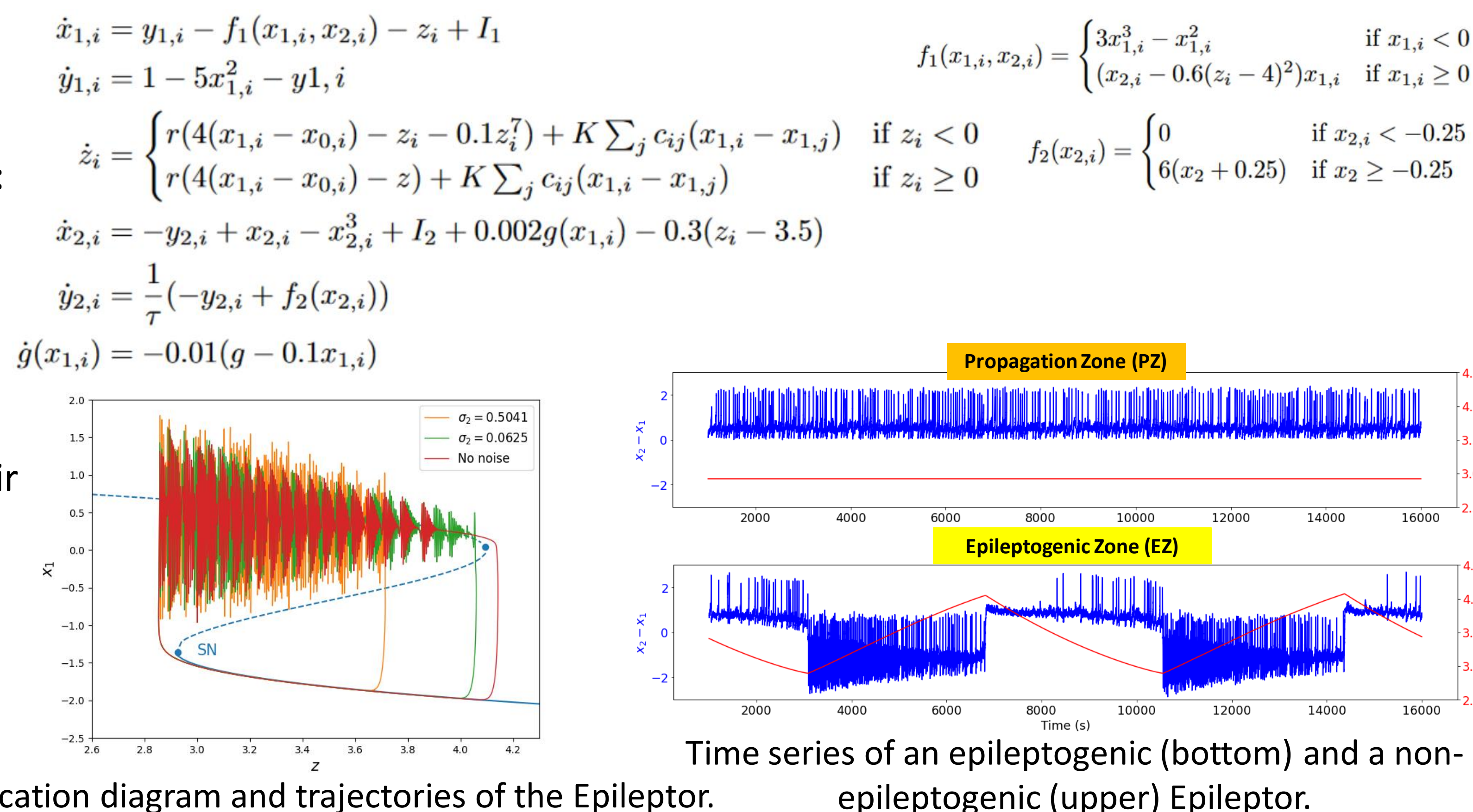
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Introduction

Recent results on seizures' propagation employing dynamical models [1] have reproduced the recruitment order of brain areas in a mouse brain network [2,3]. However, the exact mechanisms of the onset and propagation of a seizure are still not fully understood. We investigate how the location and connectivity of the Epileptogenic Zone affects the spatio-temporal propagation of the seizure in mice brain. Our goal is to identify the underlying properties of critical edges that prevent seizure propagation when being resected.

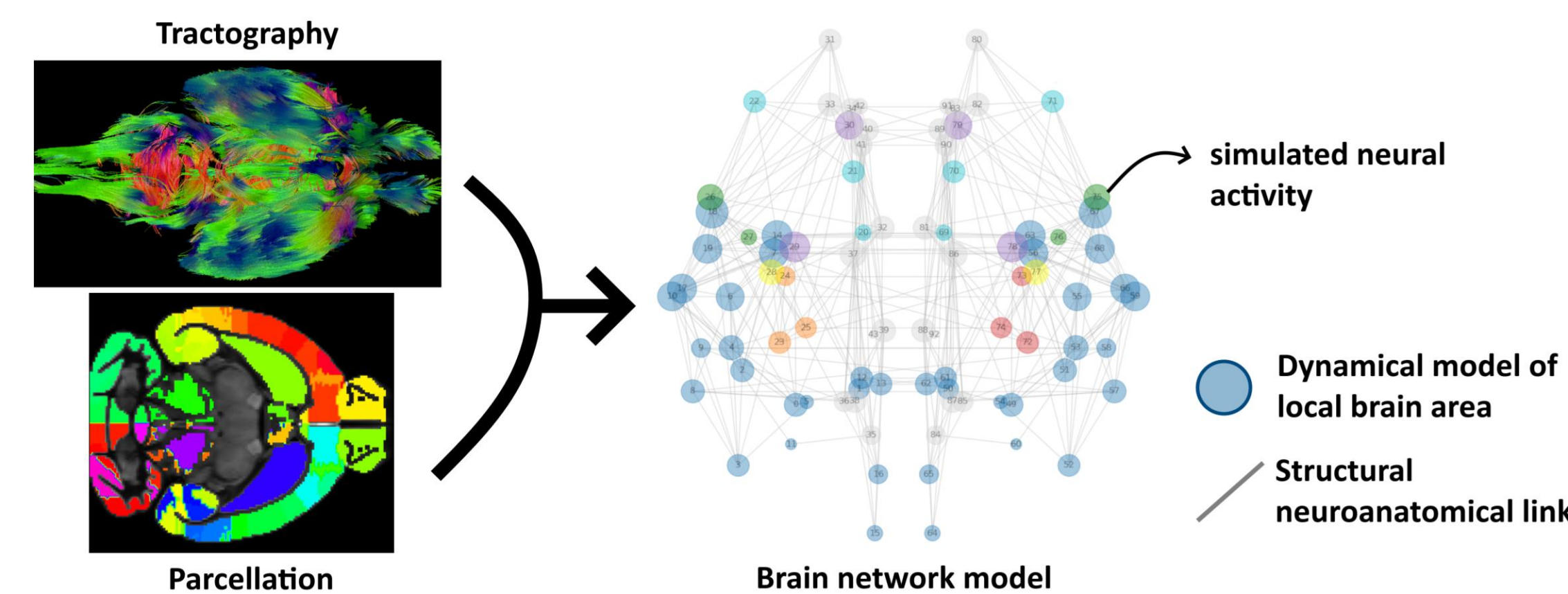
The Epileptor model [1]

- Phenomenological model reproducing the main features of **epileptic seizures**: **slow spiking** (x_1, y_1) [4] and **fast discharges** (x_2, y_2) [5]
- Slow permittivity z acts as a control parameter. **Epileptogenicity** x_0 determines the system's ability to produce spontaneous seizures and their intensity.
- Seizure onset via Saddle-Node bifurcation, offset via Homoclinic bifurcation.
- x_2-x_1 mimics the surface tension.



Seizure propagation in a large brain network

- Network of Epileptors coupled via mouse brain structural connectivity [6], using The Virtual Brain framework
- Definition of an **Epileptogenic Zone** [7] (EZ) and a **Propagation Zone** (PZ). EZ's activity triggers **seizure propagation** in PZ



References

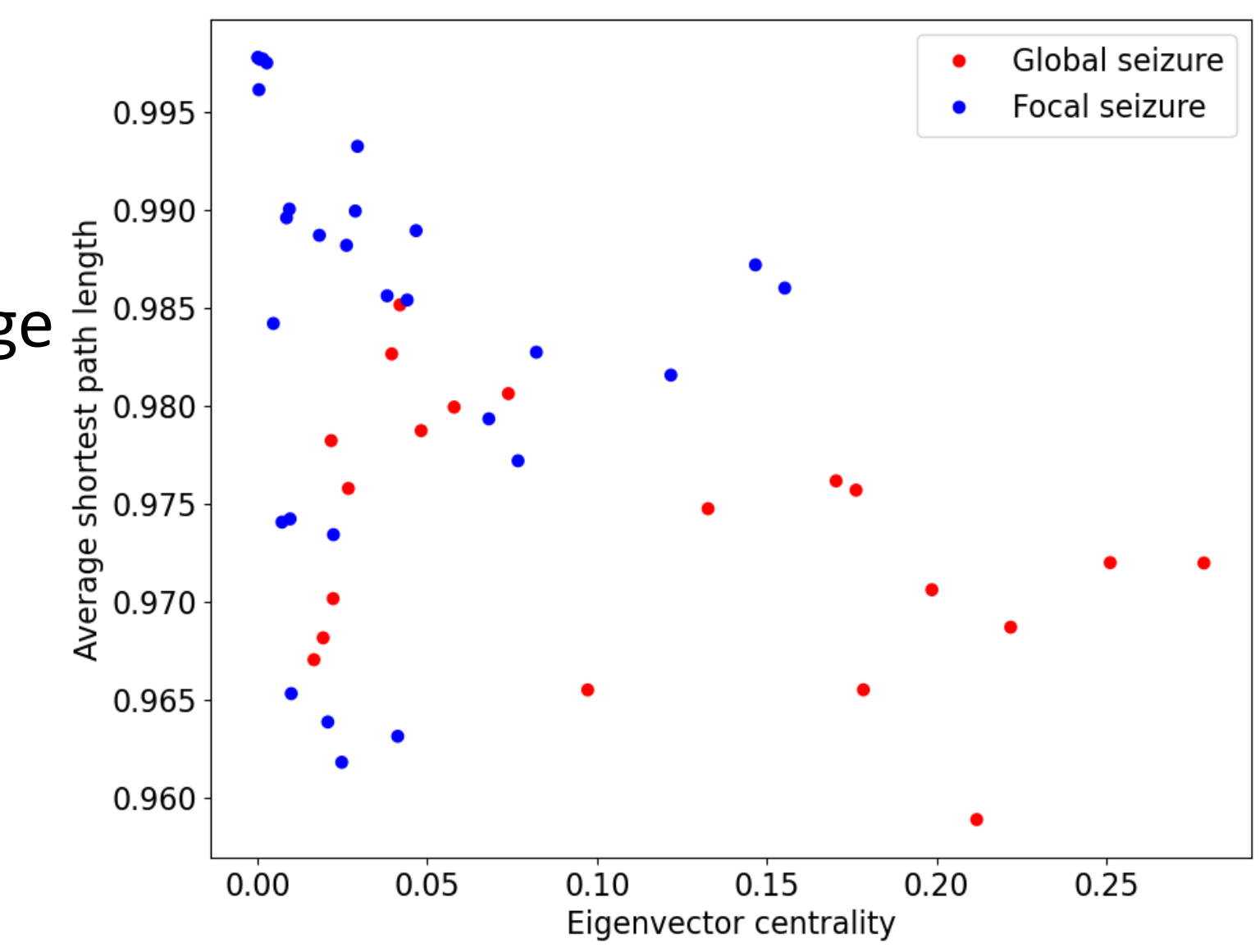
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Results: 1. Effect of the EZ's connectivity on seizure propagation

- To characterize the network's nodes, we use their average shortest path length and their eigenvector centrality

$$x_v = \frac{1}{\lambda} \sum_{t \in V} a_{v,t} x_t$$

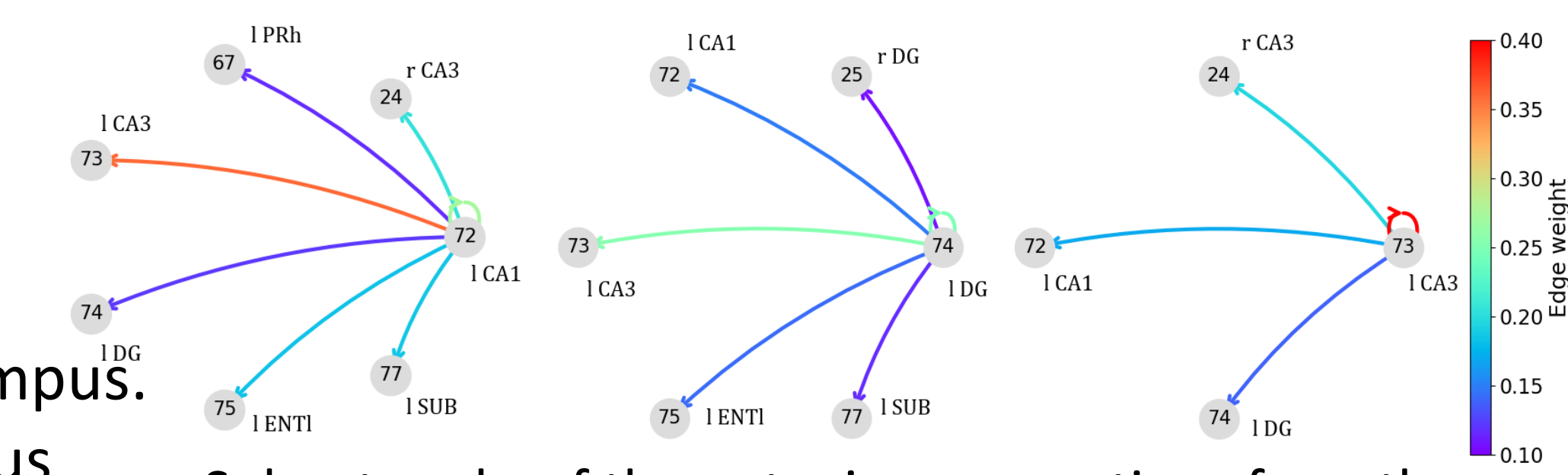
- EZ with high centrality and low shortest path length generate global seizures
- EZ with high shortest path length only generate local seizures
- Hippocampal nodes** have intermediate values. **CA1** and **Dentate Gyrus (DG)** generate global seizures. **CA3** generate local seizures.



Map of the nodes' connectivity properties. Red nodes generate global seizures when being set as the EZ. Seizure initiating at the blue nodes do not spread.

2. Connectivity of the Hippocampal nodes

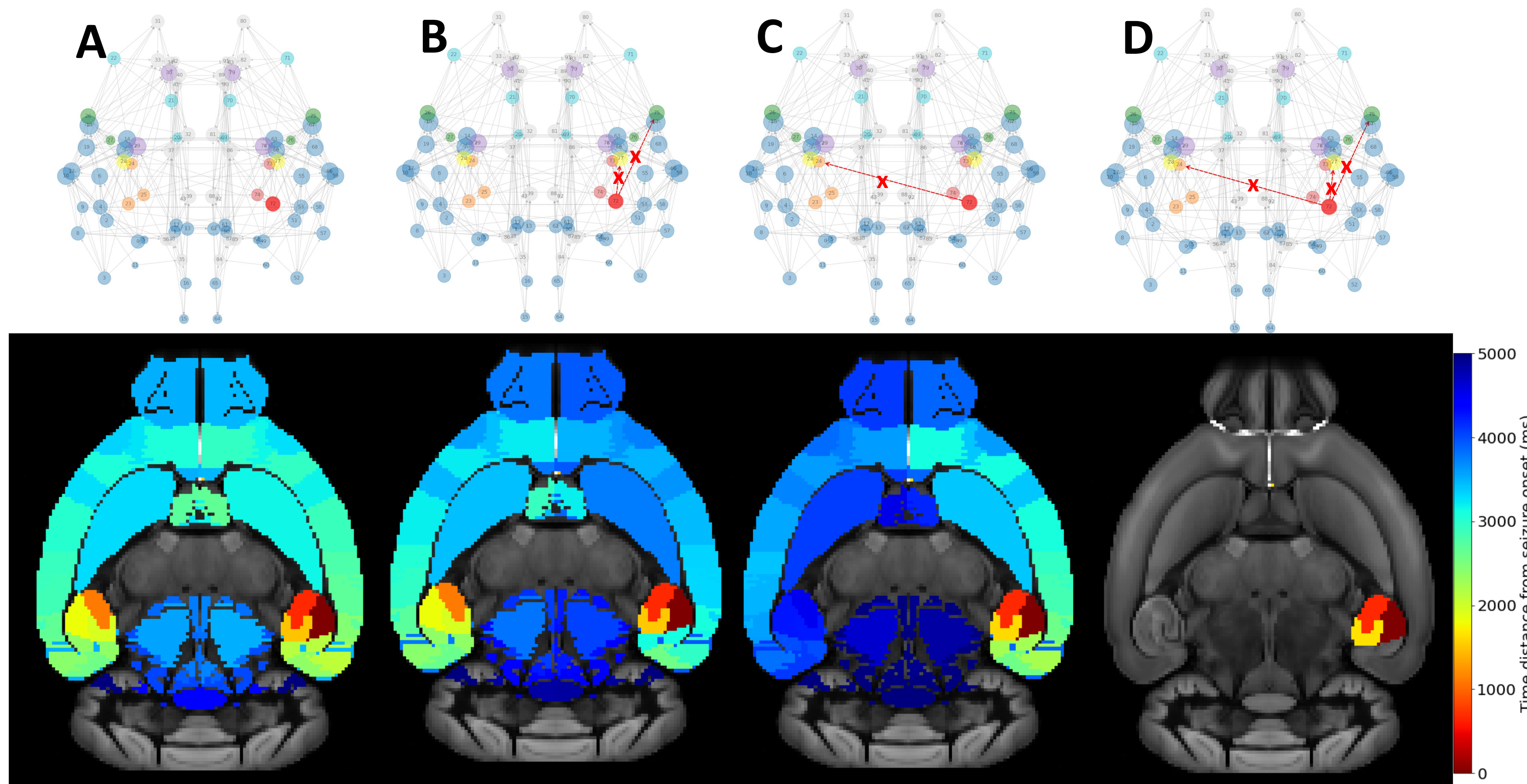
- l CA1, l DG: stronger connections to left **Entorhinal lateral cortex (l ENTl)** and **left Subiculum (l SUB)** areas and right Hippocampus.
- l CA3: mainly connected to the Hippocampus



Subnetworks of the outgoing connections from the three hippocampal nodes, with weights higher than 0.1.

3. Effect of edge removal on seizure propagation

- A: standard seizure** propagation in a mice brain network, when the EZ is left CA1.
- B, C: delayed seizure** propagation. Removing the strongest outgoing connections of l CA1 within the left hemisphere (resp. with the right hemisphere) slows down seizure propagation, mostly in the left (resp. right) hemisphere.
- D: halted seizure** propagation when removing these three connections.



Upper: graph of the brain network. The red node is the EZ, the red edges are removed. Bottom: projection of the time distance from seizure in the brain template.

Conclusions

- Global seizures are produced by the brain network's hubs, but also by some less central areas.
- Both strong connections within the hippocampal loop (Hippocampus, Entorhinal cortex, Subiculum) and between right and left Hippocampus have strong impact in the seizure propagation [8].
- Seizure confinement can be achieved by removing a minimal number of three connections [8] instead of all as presented in [2]