

Resilience of local microcircuitry firing dynamics to selective connectivity degeneration

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Introduction

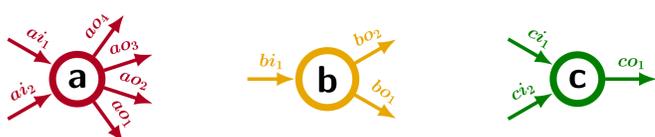
- Local cortical microcircuits shape spiking dynamics which determine the circuit's information bandwidth.
- While traditionally modeled as random (Erdős–Rényi) or structured (small-world, scale-free), real connectomic data reveal dense, non-random clustering.
- Neurodegenerative diseases like Alzheimer's disrupt these networks through neuronal and synaptic loss.

Questions:

- Which local circuit connectivity is the most resilient?
- Can suitable wiring provide a "neuroprotective effect"?

Neurodegenerative models

Figure: Neurons and synapses in a network



Synaptic pruning

- Out-pruning: pick a neuron and prune its axons e.g. out: $bo_1, bo_2, co_1, ao_1, ao_2, ao_3, ao_4, \dots$
- In-pruning: pick a neuron and prune its dendrites e.g. in: $ai_1, ai_2, bi_1, ci_1, ci_2, \dots$
- Random-pruning: pruning synapses at random e.g. $co_1, ai_1, ao_1, ci_1, bi_1, ao_2, ao_3, ai_2, bo_1, \dots$
- ordered-pruning: prune first important synapses
 - Some synapses are more important as they have high precedence of being selected in a *maximum matching set* (link set parsimoniously guaranteeing path integrity) e.g. $ai_1, bi_1, ci_1, ai_2, bo_1, ci_2, ao_1, bo_2, co_1, \dots$
- resilient-pruning: reverse ordered-pruning scheme. e.g. $ao_4, ao_3, ao_2, co_1, bo_2, ao_1, ci_2, bo_1, ai_2, \dots$

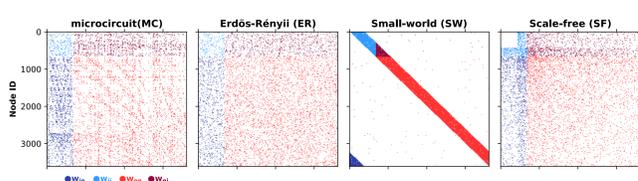
Neuronal death

- increasing-outdegree-based(iout): targeting neurons in increasing order of their out-degree. e.g. c, b, a
- increasing-degree (ideg): targeting neurons in increasing order of their degree. e.g. b, c, a
- random-based(rndn): targeting neurons that are selected at random. e.g. b, a, c
- decreasing-degree-based(ddeg): targeting neurons in decreasing order of their degree. e.g. a, b, c
- decreasing-outdegree-based(dout): targeting neurons in decreasing order of their out-degree. e.g. a, b, c

Local Microcircuit Computational Model

- LIF model and NEST simulator were used.
- $N = 3611, NI = 680, NE = 2931$
- Parameter scaling compliant with empirical data (Landau et al., Neuron 2016):
 $w_{ii}, w_{ie}, w_{ei}, w_{ee} = c(-3, -3, 1.5, 1)$

Figure: A sample of parent network categories



- connection probability $\approx 10\%$

Characterization of neural dynamics

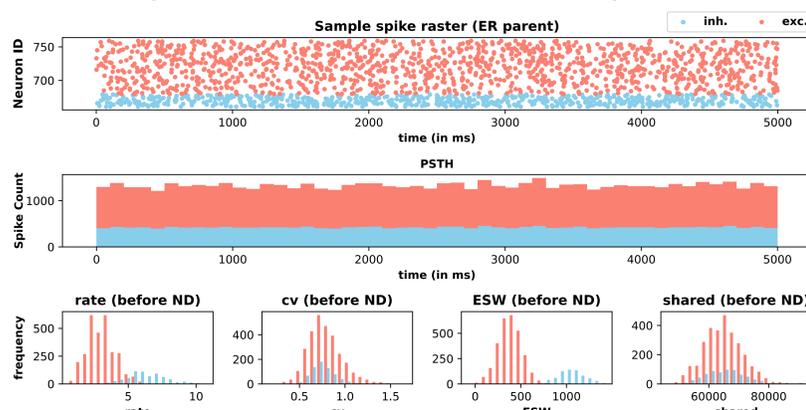
To describe **network activity** and its changes with neurodegeneration, we used some key features:

- firing rate (λ) and its variability in the population (σ_λ)
- synchronization index (SI) of subthreshold membrane potential
- fano-factor (FF) of the PSTH
- coefficient of variation (CV) of the ISIs, as it is a necessary condition for information bandwidth.

We tried then understanding which network or network dynamics more strongly determine activity features. Specifically we focus on:

- effective synaptic weights (esw), i.e. various combinations of total E input conductances and total I conductances, and their variance over nodes

Figure: Distributions at baseline, variation with neurodegeneration



We study the effects on activity features of different neurodegeneration styles on different network ensembles, starting from initial conditions with comparable λ , synch and CV.

Structure, Dynamics and Neurodegeneration

Figure: Evolution of dynamical and effective synaptic features along dendritic neurodegeneration (curve plots below) and all neurodegeneration styles (summary heatmaps)

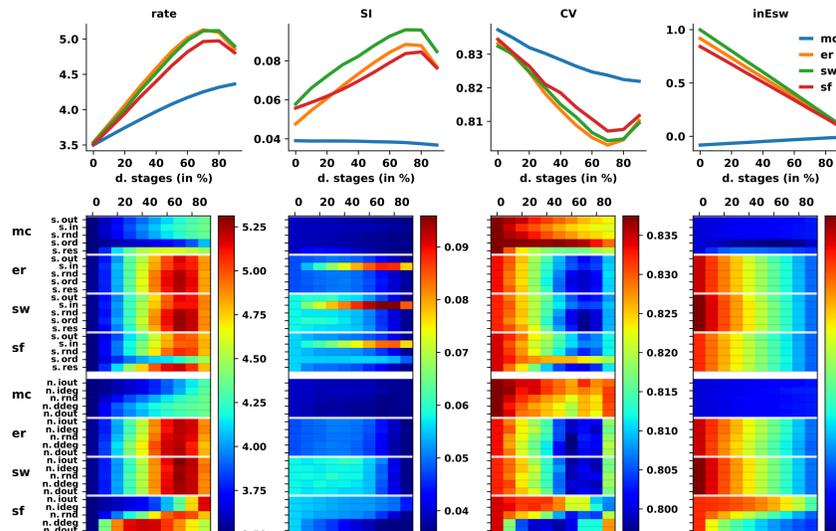
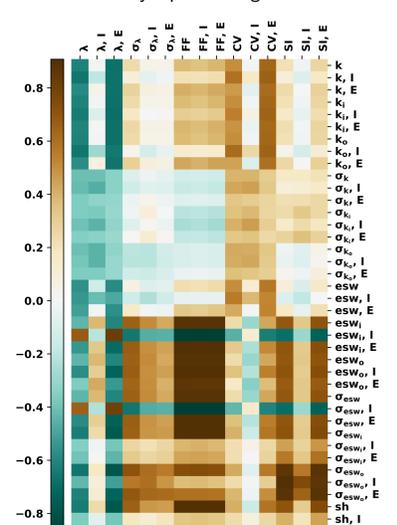
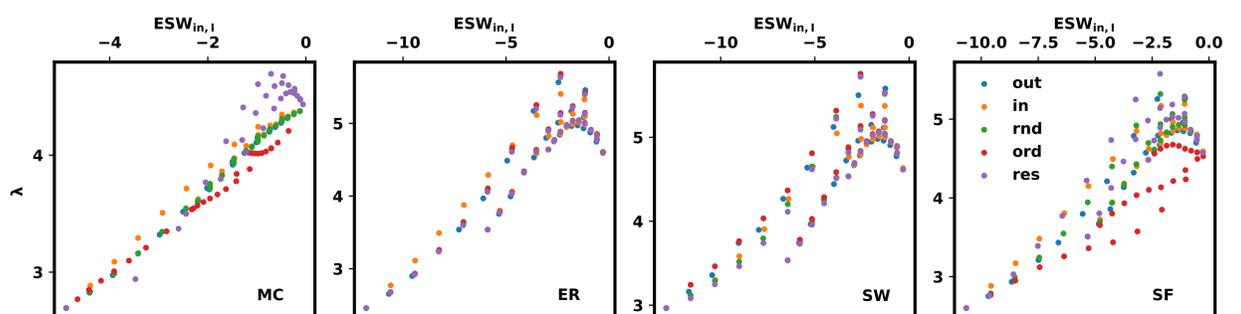


Figure: The network structure features presenting the strongest correlations with activity variations, all ensemble and neurodegeneration styles confounded, are the effective synaptic strengths



- Different random ensembles present similarly large activity variations as an effect of degeneration
- Empirically reconstructed microconnectome display higher resilience of firing rate and CV
- Despite these differences, we can still identify shared principles explaining the different behaviors

Figure: Example correlations: variations of firing rate correlate with average inhibitory in-strength for all the ensembles



- The resilience of the empirical microconnectome could depend on its extreme level of inhibitory stabilization
- Could such a non-random microconnectivity have evolved because of the resilience it confers?