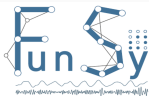


Structural Control of Spiking Neuronal Network Degeneration

Inhibitory gain, architecture and resilience

Simachew Mengiste

May 25, 2026



PROGRAMME
DE RECHERCHE
SANTÉ
NUMÉRIQUE

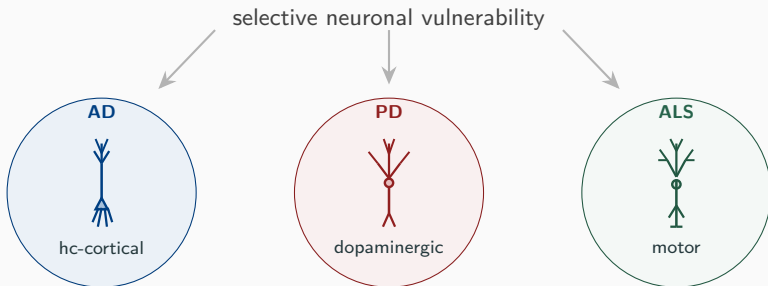


BrainNet 2026

Neurodegeneration Is Structured Circuit Damage

- Dementia affected **57 million** people worldwide in 2021
 - Alzheimer disease accounts for **60–70%** of cases.
- Parkinson disease affected **over 8.5 million** people globally in 2019.
- 2022 estimates of ALS in the US: roughly **33,000**.

Across diseases, structural change and functional change can dissociate, raising the question when/how circuits remain resilient or compensation breaks down.



Questions

- How can structural loss reshape the activity of cortical circuit?
firing rate (λ), synchrony (**FF**, **SI**), irregularity (**CV**), ...
- Which architectures keep degeneration near the baseline activity state?
- Which structural features correlate most strongly with the resulting activity changes?
- To what extent can those structure–activity relations be turned into prediction?

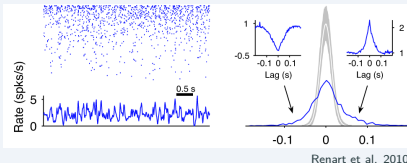
Which circuits are more likely to preserve health-like population activity as synapses or neurons are progressively lost?

Computational Ingredients for Circuit Degeneration

Healthy cortical microcircuits are generally expected to operate in an **asynchronous-irregular** spiking regime with moderate rate (1–10 Hz).

Healthy baseline activity

- Softky & Koch 1993
- van Vreeswijk & Sompolinsky 1996, 1998
- Shadlen & Newsome 1998
- Brunel 2000
- Renart et al. 2010
- Ecker et al. 2011, 2014
- ...



Neuron model

leaky integrate-and-fire (LIF) excitatory and inhibitory spiking neurons

Network architectures

empirical microcircuit and matched synthetic controls

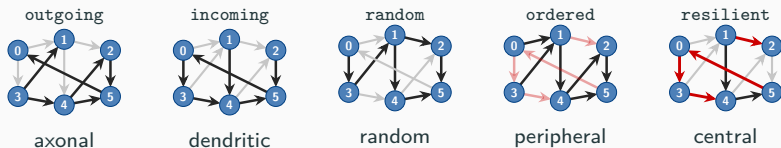
Degeneration rules

synaptic and neuronal loss across staged pruning strategies

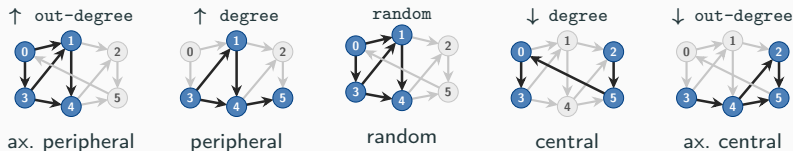
We Compare Synaptic Loss and Neuronal Loss

- We have 9 stages. At each stage, 10% of elements are gone.
- experimentally: *dendritic degeneration*, *diffuse synapse loss*, *selective loss of strong broadcasters*, and *hub-targeted disruption*.

Synaptic pruning rules (eg. trimming 4 links)

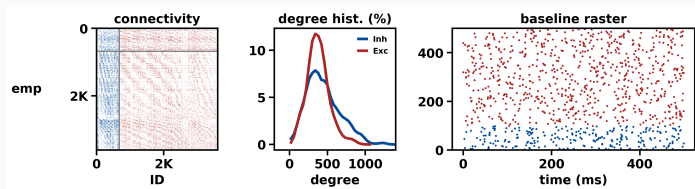


Neuronal pruning rules (eg. trimming 2 nodes)



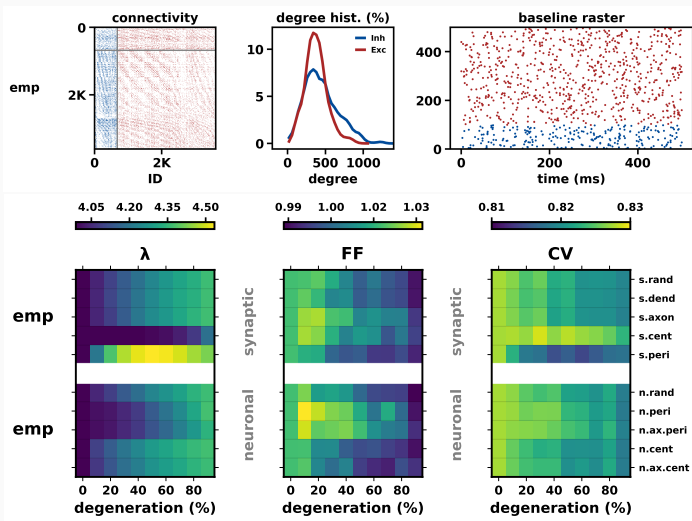
The Empirical Microcircuit Has Structured E/I Connectivity

- Landau et al., 2016: $w = \alpha(1.0, -3, 1.5, -3) \mid p = (9, 18, 12, 15)$



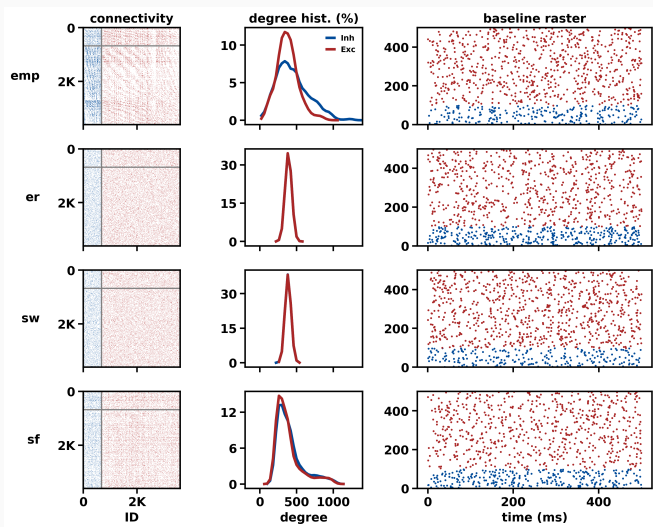
The Empirical Microcircuit Has Structured E/I Connectivity

- Landau et al., 2016: $w = \alpha(1.0, -3, 1.5, -3) \mid p = (9, 18, 12, 15)$



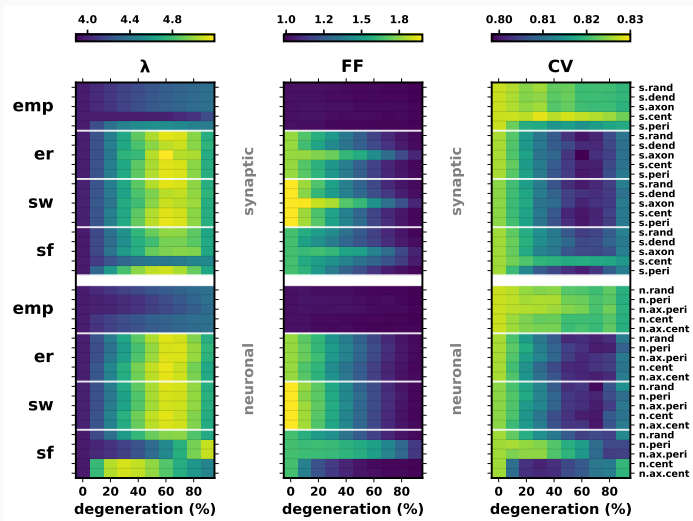
Canonical Networks Match Size but Not E/I Organization

- Synthetic: Erdős-Rényi (er), small-world (sw) and scale-free(sf).



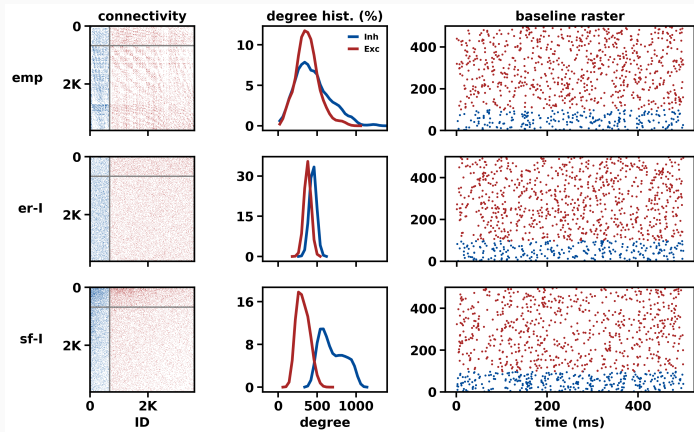
Canonical Architectures Drift Differently Under Degeneration

- It appears that the cortical microcircuit maintains higher resilience.



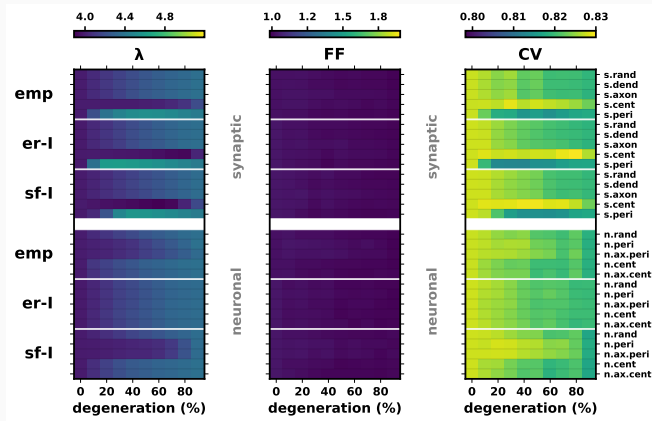
Two Synthetic Controls Enrich Inhibitory Organization

- er-l: preserving subpopulation resolved connection density.
- sf-l: sf that assigns hubs as inhibitory neurons.



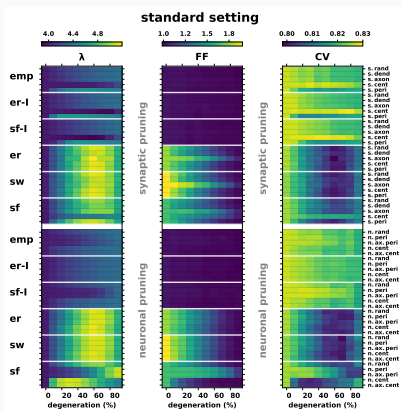
Inhibitory Organization Restores Resilience

- Inhibitory promoting architectures also maintain comparable resilience to that of the microcircuit architecture.
- The way inhibition is embedded in a network is an important factor of network resilience to degeneration.



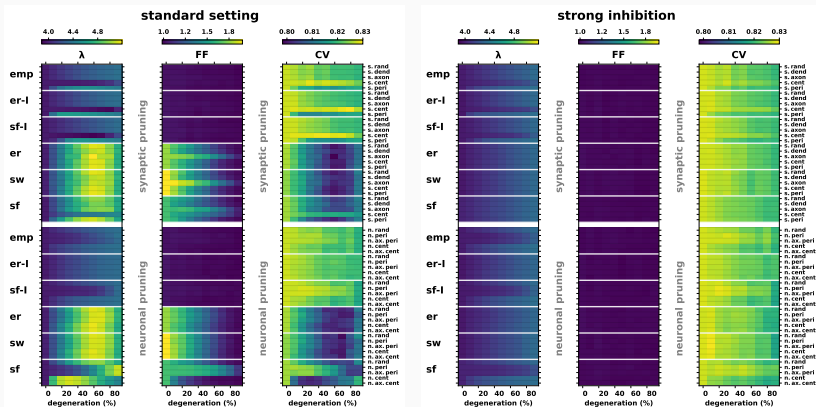
Resilience Depends on Architecture and Inhibitory Gain

- **emp**, **er-l**, and **sf-l**, networks with inhibition promoting architectures, needed moderate inhibition for stabilization.
- **er**, **sw**, and **sf** need extra inhibitory reinforcement to avoid larger shifts.



Resilience Depends on Architecture and Inhibitory Gain

- **emp**, **er-l**, and **sf-l**, networks with inhibition promoting architectures, needed moderate inhibition for stabilization.
- **er**, **sw**, and **sf** need extra inhibitory reinforcement to avoid larger shifts.



- **Resilience**

Across network ensembles, resilience can be recovered when inhibition is sufficiently strong or structurally well placed.

- **Prediction?**

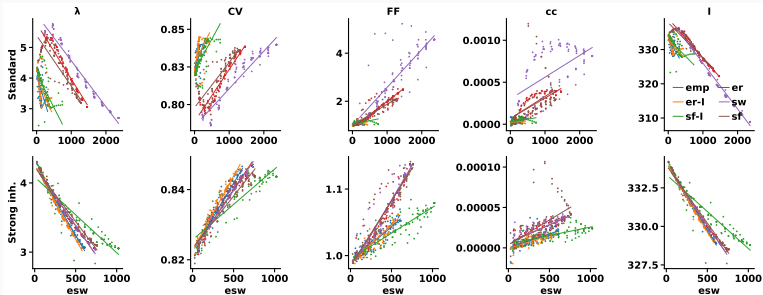
If inhibition provides a shared control axis, can we use it to predict degeneration effects across otherwise diverse circuits and pruning rules?

Global Coupling Organizes Degeneration Within Classes

- **ESW**, the *effective synaptic weight* of a neuron, is its net presynaptic strength.
- Within each network class, **ESW** gives a clear activity axis.
- Across all network classes, not so much.

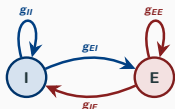
Data summary

- tuned/untuned (2)
 - networks (6)
 - realizations (10)
 - schemes (2)
 - degeneration (2)
 - pruning (5)
 - stages (10)
 - weights (10)
- baselines: 1,200
- degenerates per baseline: 90
- tuned/untuned: 109,200 **total: 218,400**



Weight-Aware Features Track Activity Better Than Topology

- Weight-aware descriptors correlate much more strongly with activity than weight-unaware structural summaries.
- The three local weight-aware blocks, mean drives g , fluctuation scales σ , and interaction motifs, all show strong correlations with many observables.



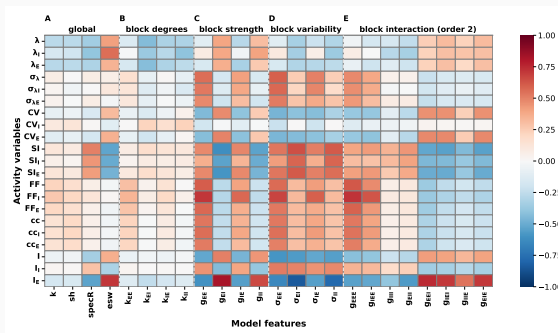
$$X \rightarrow Y \rightarrow Z$$

- $k_{YX} := p_{YX} N_X$

- $g_{YX} := k_{YX} w_{YX}$

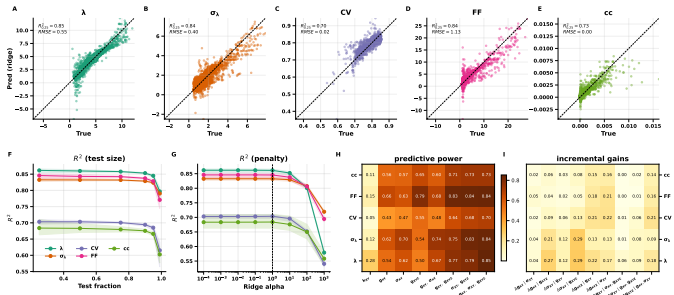
- $\sigma_{YX} := \sqrt{k_{YX} w_{YX}^2}$

- $g_{ZYX} = g_{ZY} g_{YX}$



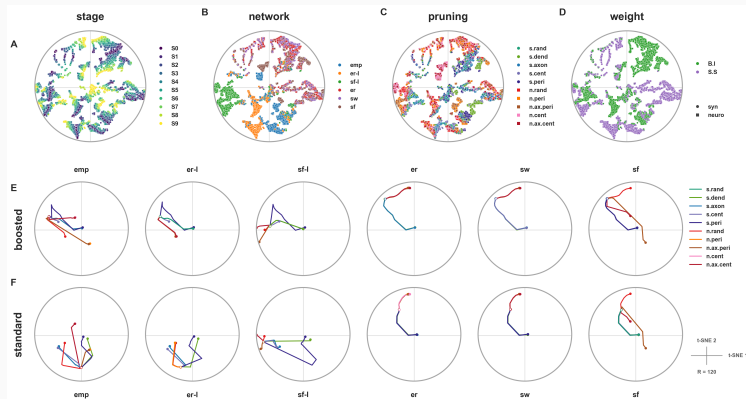
A Compact Weight-Aware Model Predicts Activity

- A 16-dimensional, **weight-aware, subpopulation-resolved** representation predicts activity much better than degree-only structure or global strength.
- Each weight-aware group (g_{YX} , σ_{YX} or g_{ZYX}) is strongly predictive on its own, with g and σ behaving almost like duplicates of one another.
- This suggests that biologically relevant degeneration is better summarized by who drives inhibition than by connection counts alone.



Degeneration Follows Structured Activity Trajectories

- Degeneration stage produces the clearest local progression through the embedding.
- Network class and weighting scheme define the large-scale geometry; pruning mostly modulates trajectories within that space.



Summary

- Degeneration responses are governed jointly by architecture and inhibitory gain.
- ESW is an important global structural control axis, but it does not collapse all architecture-dependent variation.
- Weight-aware, subpopulation-resolved descriptors provide the clearest predictive account of degeneration dynamics.
- Degeneration trajectories remain structured on a shared activity manifold rather than collapsing diffusely.
- For experimental interpretation, preserving where inhibition sits in the circuit may matter as much as preserving how much connectivity remains.

Possible biological implications

- **Inhibitory vulnerability:** if inhibition is a shared control axis, even modest inhibitory damage can have disproportionate effects on circuit activity.
- **Sprouting:** compensatory growth may restore connection number, but semi-random new links can blur the fine architectural embedding of inhibition.
- **Therapeutic direction:** boosting inhibition, or improving its recruitment, may stabilize circuit dynamics even under ongoing degeneration.
- **Next tests:** vary inhibitory gain, cell-type vulnerability, sprouting rules, lesion tempo, baseline state, and network heterogeneity.

Thanks!



Thank you for listening!
(Questions and Discussion ...)



Collaborators



Arvind Kumar



Demian Battaglia



Ad Aertsen

Colleagues @ FunSy - Unistra

Demian Battaglia
Romain Goutagny
Jyotika Bahuguna
Yaroslav Sych

Karin Herbeaux
Anagh Pathak
Flora Thellier
Zoé Weiblé

Thomas Blondel
Swarag Thaikkandi
Caroline Mursch
Samy Castro

Coline Porter
Matthieu Aguilera
Vandana Prasad
Jungyoung Kim

Laura Lopez Galdo
Ludovic Spaeth
Chen-Hwa Chen
Vinicius Lima