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Riga Technical University

Dynamics of neural circuits
at different scales

Oxford Applied Topology Seminar

Jānis Lazovskis / November 4, 2022

Slides online at jlazovskis.com/talks

Teamwork

University of Aberdeen, Neuro-Topology group

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EPFL, Blue Brain Project

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Personal history

- 2014 - 2019: University of Illinois at Chicago
- 2019 - 2020: University of Aberdeen
- 2020 - : RTU Riga Business School

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EPFL

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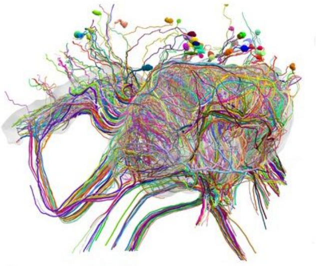
Connectomes

- *White et al 1986 / Watts and Strogatz 1998*
  - C.Elegans (279 neurons, 2.2k connections)
- *Blue Brain Project 2015 (rat-ified mouse)*
  - V5 (31k neurons, 7.8m connections)
  - SSCx (4.2m neurons, 2.5b connections)
- *Janelia 2020*
  - Drosophila (25k neurons, 3.7m connections)
- *Max Planck 2020*
  - Zebrafish (3.6k neurons)
- *Sayre et al 2021*
  - Bumblebee (1.3k neurons)



Blue Brain Project

janelia Research Campus

neuPRINT

mapzebrain max planck zebrafish brain atlas

Blue Brain V5 connectome

Layer structure

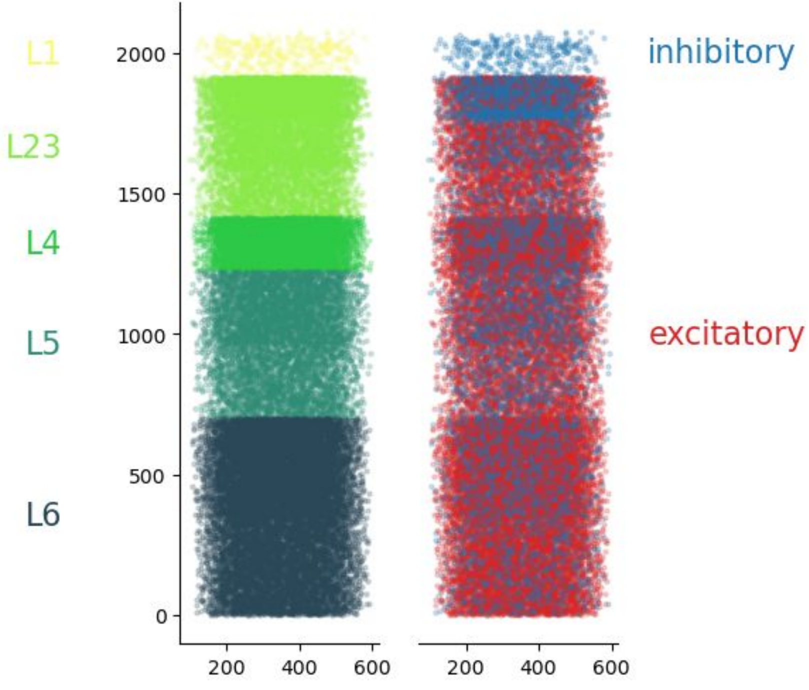
- Higher (L1) = inhibition
- Lower (L6) = information processing

Neuron characteristics

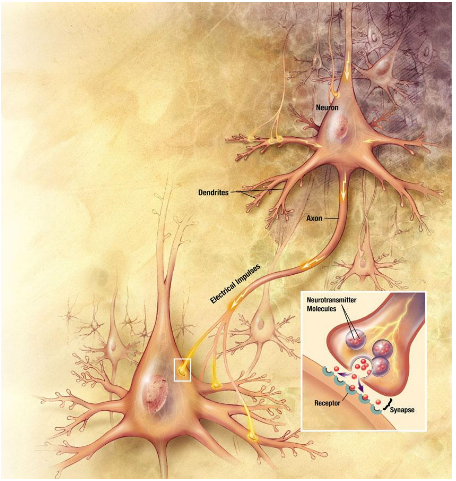
- 31346 in total
- 55 electro-morphological classes

Other facts

- Diameter is 4
- High dimensional simplices are over-represented (*Cliques of neurons, 2017)*
- Reciprocal connections preferentially appear in high-dimensional simplices (*Studying motifs, 2021)*

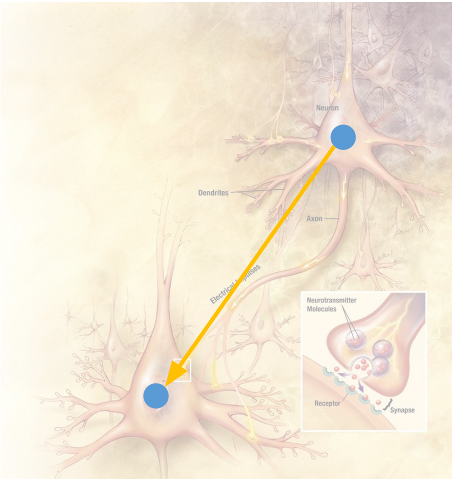


Interpreting neurons

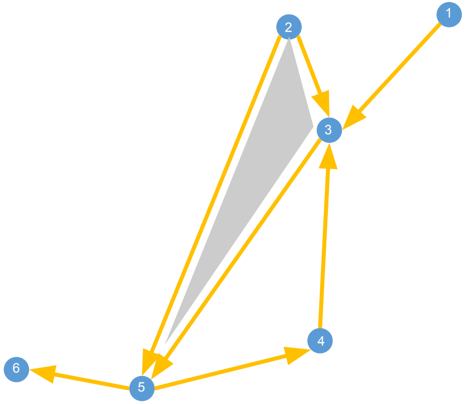


National Institutes of Health, nih.gov

biological data



record connection existence and direction



directed clique complex

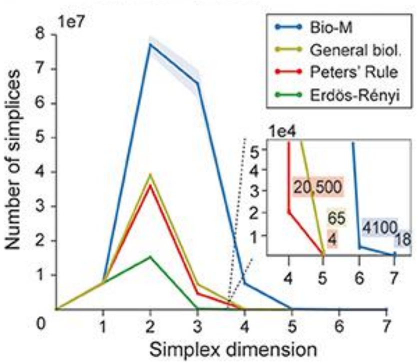
$$\begin{bmatrix} 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

adjacency matrix

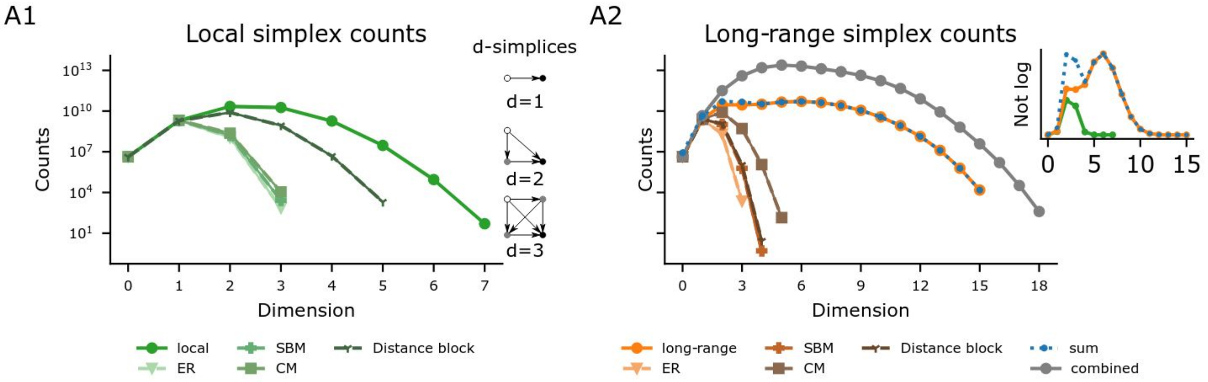
Ignore properties of:

- soma (cell body)
- axons (physical connection)
- dendrites (attachments per axon)
- synapses (types of attachments)

Topological botany



Blue Brain neocortex v5 (2015)



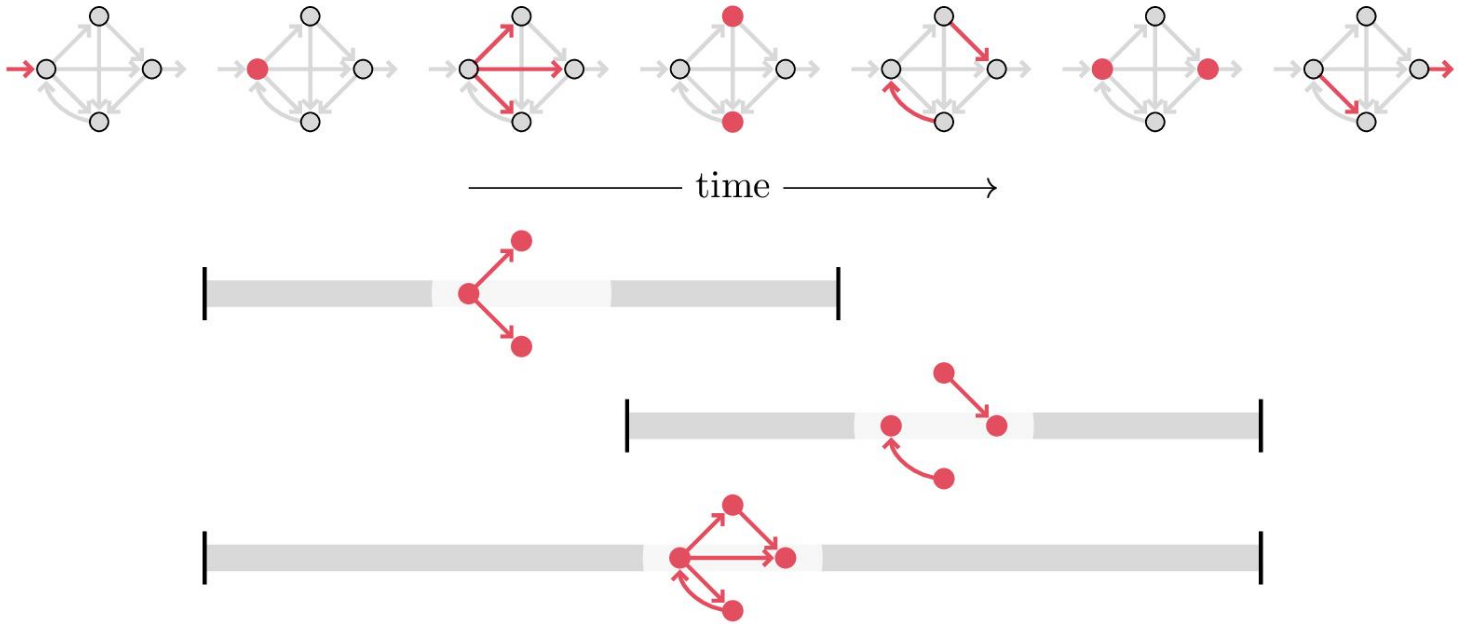
Blue Brain somatosensory cortex (2022)

The Blue Brain circuits are *in-silico reconstructions.*

Extracting graphs from other conectomes is difficult because:

- “Connection” is indirectly given by proximity of synapses
- Synapses do not necessarily pass electricity through the soma →vertex becomes a simplex
- Some cells switch inhibitory and excitatory roles
- Sometimes axons are inhibitory / excitatory, instead of soma

Interpreting neuron dynamics



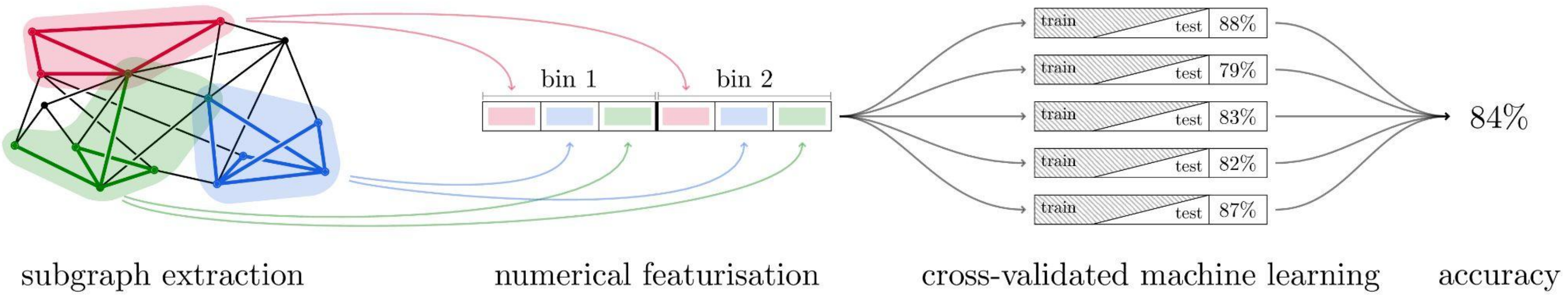
Neurons build up voltage from in-neighbour transmissions

- Once threshold passed, the neuron ***fires***, (probabilistically) transmitting to its out-neighbours

An edge is ***active*** in a given time interval if its tail and head both fire

- The binary dynamics of vertices gives a notion of active subgraphs

Classifying signals: “the pipeline”

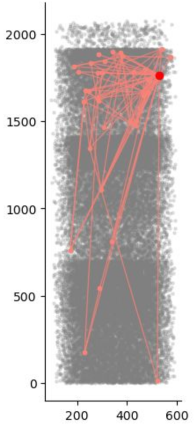


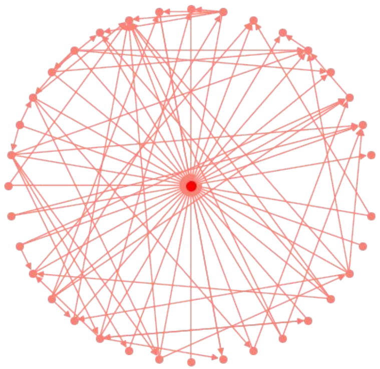
1. **Structure:**
   a. Compute graph / topological parameter for every neighbourhood
   b. Select neighbourhoods with top *N* parameter P_1 values
2. **Function:**
   a. For each selected neighbourhood, identify its active subgraph over *B* time bins
   b. For each active subgraph in each time bin, compute its parameter P_2 value
3. **Classification:**
   a. Construct a feature vector of length $N \cdot B$ for each of *(8 signals)·(557 repetitions)* observations
   b. Classify with support vector machines (SVM) with 60/40 train/test five different ways

Parameters: from graph theory

Let v be a vertex with n neighbours and adjacency matrix $A \in M_{(n+1)\times(n+1)}(\{0,1\})$.

clustering coefficient	transitive clustering coefficient	neighbourhood size	number of reciprocal connections	adjacency spectrum	Laplacian spectrum (Chung)	Laplacian spectrum (Bauer)	transition probability spectrum
Fagiolo (2007) generalizing Watts–Strogatz (1998) to digraphs	ratio of all 3-cliques at v to all possible 3-cliques at v	size of closed neighbourhood	add 1 if $u \to v$ and $v \to u$ both exist	eigenvalues of adjacency matrix	of largest strongly connected component	extension to not necessarily strongly connected graph	eigenvalues of transition probability matrix



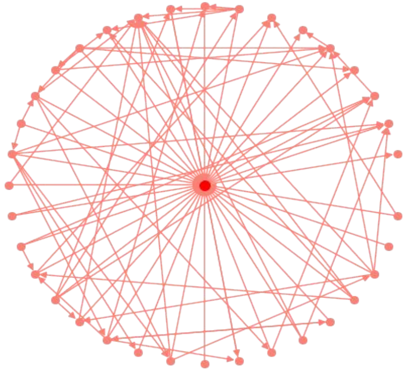


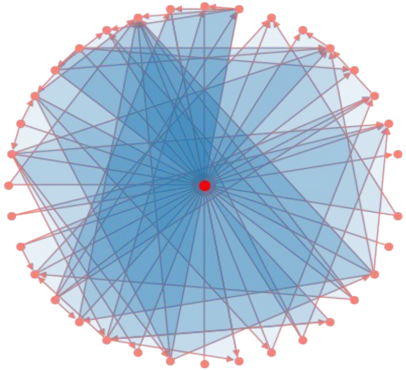
clustering coefficient	0.043
transitive clustering coefficient	0.051
neighbourhood size	36
number of reciprocal connections	1
adjacency spectral gap	1
Chung Laplacian spectral gap	0.5
Bauer Laplacian spectral gap	0.316
transition probability spectral gap	0.707

Parameters: from topology

Topologically significant features indicate neurologically significant activity (*Cliques of neurons*, 2017)

Euler characteristic	normalized Betti coefficient	density coefficient
alternating sum of Betti numbers	weighted sum of Betti numbers, weighted by dimension *d* and number of *d*-simplices	ratio of *(d+1)*-cliques to *d*-cliques, normalised to be 1 on complete graphs

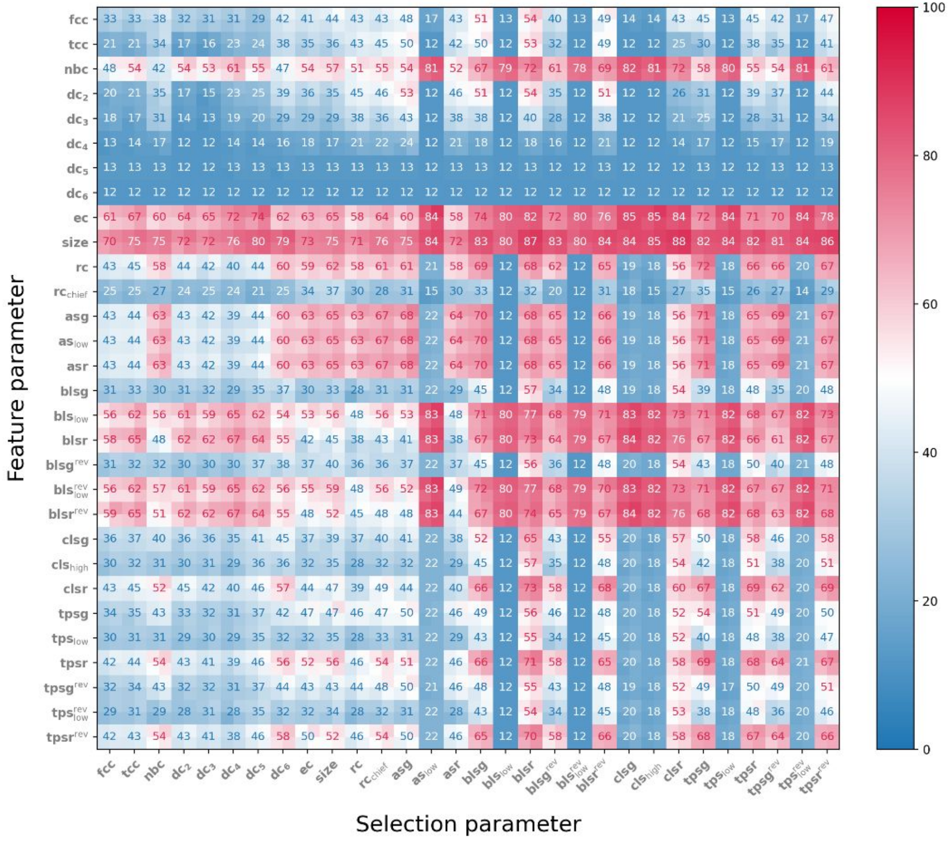




Euler characteristic	1
normalized Betti coefficient	0.027
2nd density coefficient	0.028
3rd density coefficient	0.02
4th density coefficient	0
5th density coefficient	0

Flagser (based on *Ripser*) and its variants *flagser-contain, pyflagser* provide efficient computation

Classifying signals: results



Classification accuracy of ~88% when:

- selecting by a **spectral** parameter
- featurising by neighbourhood **size**

Complications:

- Active neighbourhood size is a measure of firing rate

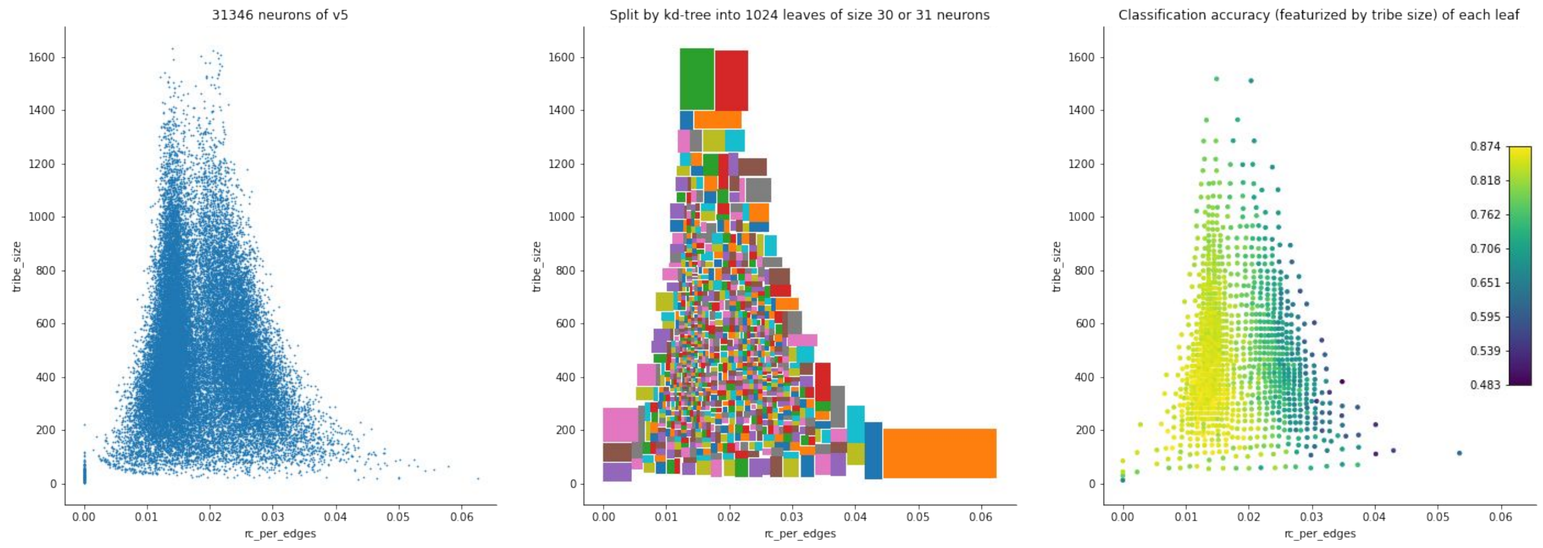
Improving classification

Double selection: Get top 50 neighbourhoods by one parameter, from those select top 25 by another

- *No global improvement:* Lower than or same as previous best results

Double sorting: Split all neurons into groups of ~50 with a *kd*-tree, feed each group into pipeline

- *No global improvement:* Lower than or same as previous best results



Observation: Considering reciprocal connections introduces two classification regimes

RC regimes: Select by P_1 and number of reciprocal connections

Classification accuracy **increases** for all choices of P_1

Classification accuracy **decreases** for all choices of P_1

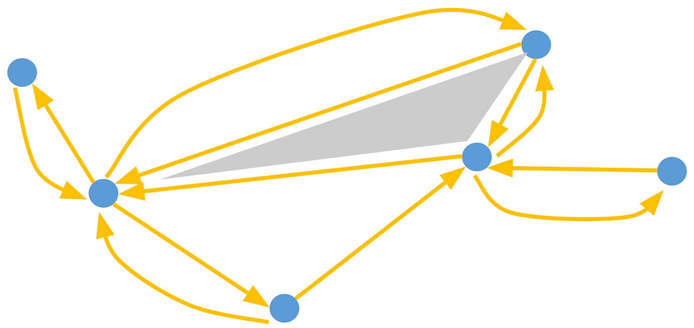
Observation: When accuracy decreases, feature vectors are almost all zero → trivial neighbourhoods

The case for reciprocal connection density

Small neighbourhoods with no RC's ≈ bad for classification

Relatively small neighbourhoods with relatively few RC's ≈ good for classification

Adding backward edges rapidly increases topological structure:



Reciprocal connections in a neighbourhood are:

- bad because: they amplify the effect of firing rate (if active, is very active)
- good because: ensure classification accuracy comes from functional characteristics

→ RC count seems to be a proxy for some notion of density / sparsity ←

Finding a balance

Reliability: Consistent local activity for global input

- High classification accuracy does not imply neighbourhood is reliable
- High classification accuracy + Low reliability suggests non-functional properties affect classification

Measured using *Gaussian kernel reliability*

- Computed among all pairs of experiment repetition spike trains
- Best would be high reliability and high classification accuracy

Further ideas

Consider **maximal** simplices instead

- Far fewer than all simplices
- Highest neurological complexity

Ideas and sources

In neuronal networks:

→ Topologically significant features are also neurologically significant

→ Local activity classifies global signals

→ Reciprocal connections decrease classification accuracy, but increase reliability

Pedro Conceição, Dejan Govc, Jānis Lazovskis, Ran Levi, Henri Riihimäki, Jason P. Smith; ***An application of neighbourhoods in digraphs to the classification of binary dynamics***. Network Neuroscience 2022; 6 (2): 528–551. doi: https://doi.org/10.1162/netn_a_00228

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Thank you!

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