Using Topology in the Study of Brain Structure and Function

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Some images by Blue Brain Project Visualisation Team

How can we study complex networks with the tools of topology?

Combinatorial topology

Graph constructions

Category theoretic ideas

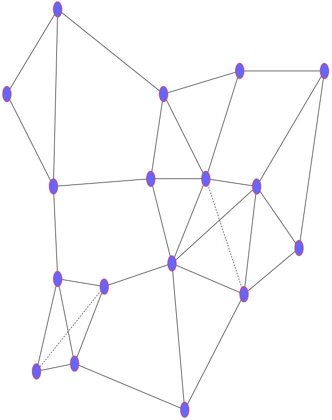
Next time :-)

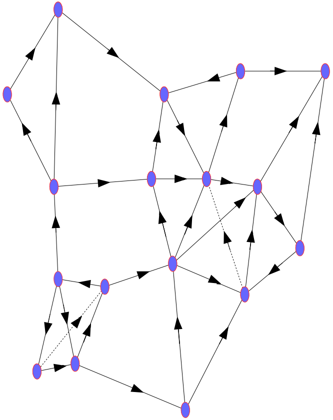
- A biologically accurate digital reconstruction of the neocortical column of a 14 days old rat.
- Each microcircuit $\sim 3 \cdot 10^4$ neurons, $\sim 8 \cdot 10^6$ connections.
- Data obtained from 5 rats, each used to create 7 instantiations, + 7 more based on averaged data.
- Current reconstruction: the entire somatosensory cortex: $1.7 \cdot 10^6$ neurons and $1.1 \cdot 10^9$ connections.
- Functional plasticity.

Data arising from the Blue Brain Project reconstruction

- The reconstruction allows recovering an abundance of information. For example:
  - The full adjacency matrix: Every modeled neuron is identified by a unique number (GID). One gets a matrix $A = (a_{i,j})$, with $a_{i,j} = 1$ if the axon of neuron i is connected to the dendrite of neuron j.
  - The strength of each connection: How many synapses and "weight" of each.
  - The type and spatial position of each individual neuron, soma and synapses.
  - Full spiking data for each neuron under varying electrical and chemical conditions.
- This gives rise to directed graphs (potentially weighted, and time dependent).
- Graphs give rise to topological objects. This project and several that follow are based on studying these topological objects.

The Flag Complex and directed flag complex





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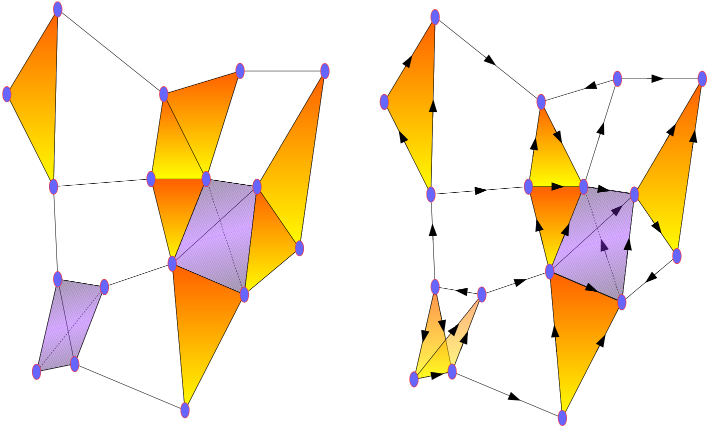


Flagser

A package written by Daniel Lütgehetmann:

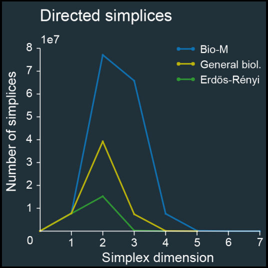
- Flagser constructs the directed flag complex of a directed graph in a parallelisable way.
- Flagser allows associating a predesigned weighting system with the flag complex.
- Flagser computes persistent homology of the resulting directed flag complex, based on Uli Bauer's *Ripser* algorithm, but:
- Flagser allows computation of homology within a range of accuracy that can be controlled.

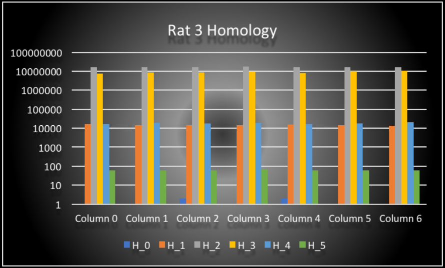
Example

Flagser computes the directed flag complex of the Blue Brain graph (31,000 vertices, 8 million edges) in 11 seconds on 8 cores (Macbook Pro, 16GB RAM). It computes H_2 of this complex ($\beta_2 \sim 1.5 \cdot 10^7$) with 1.5% accuracy within an hour.

Structural analysis of the Blue Brain Project Reconstruction

We constructed the directed flag complex for each reconstruction, and computed homology. We also compared to certain null models

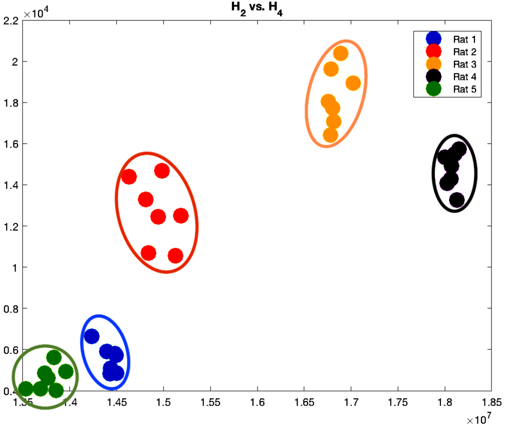




The higher degree of topological complexity of the reconstruction compared to any of the null models presumingly depends on the morphological detail of neurons.

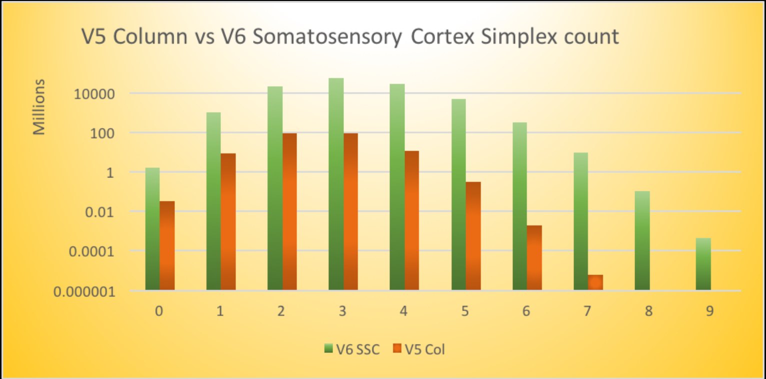
Structural analysis of the Blue Brain Project Reconstruction

Topological metrics reflecting relationships among the cliques revealed biological differences in the connectivity of reconstructed microcircuits.



The Somatosensory Cortex

Recent development: A reconstruction of the full somatosensory cortex with 1.7 million neurons and 1.1 billion connections.

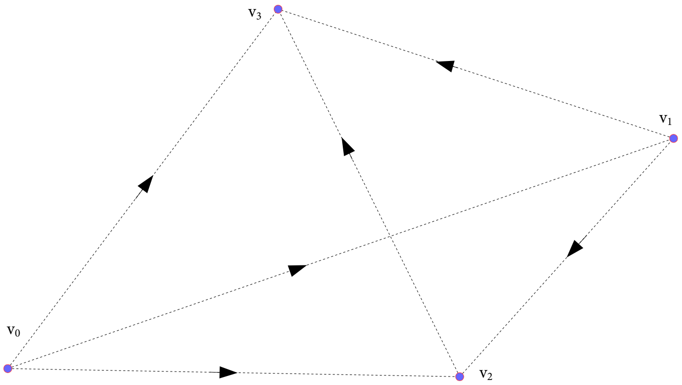


Activity: The Transmission-Response method

- The microcircuit is stimulated in time intervals of 50ms for a whole second. The reaction is recorded in time bins $t = 0 \dots 199$ of 5 ms each (size optimised by experimentation).
- Let A denote the structural connectivity matrix for the given microcircuit.
- In each time bin k consider the "successful transmission" connectivity matrix A^k where $A^k_{i,j} = 1$ if and only if the following three conditions are satisfied:
  - $A_{i,j} = 1$, i.e., there is a structural connection from neuron i to neuron j,
  - neuron i fired in time bin k, and
  - neuron j fired within 10ms after neuron i did (optimised by experimentation).

Activity: The Transmission-Response method

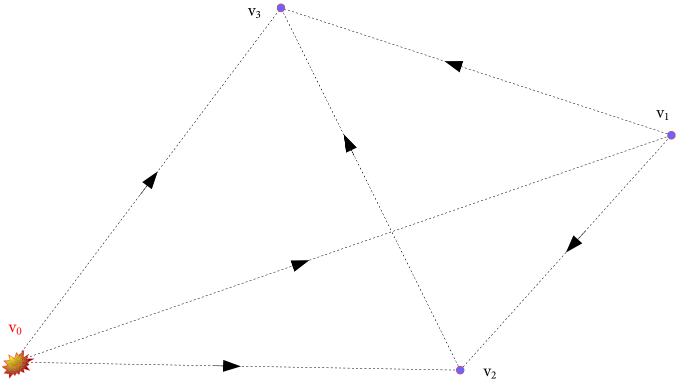
Example: What has to happen for a 3-simplex to be formed in a TR graph within a given time bin.



0) There is an underlying structural 3-simplex $[v_0, v_1, v_2, v_3]$.

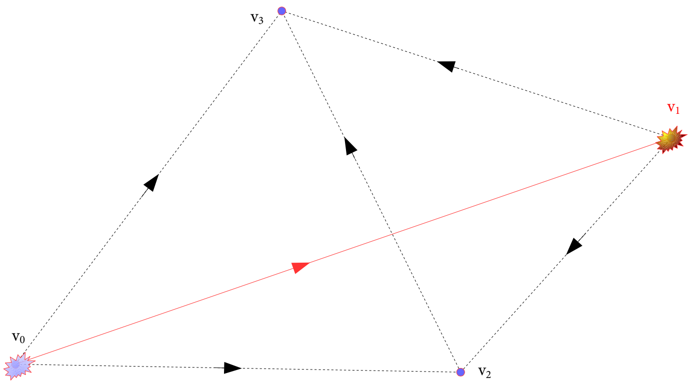
Activity: The Transmission-Response method

1) v_0 fires within the given 5ms time bin.



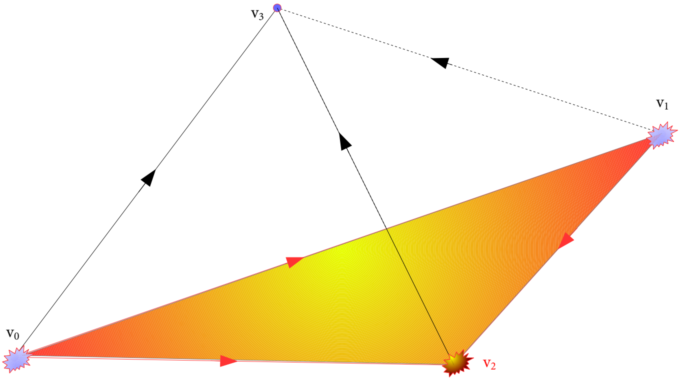
Activity: The Transmission-Response method

2) v_1 fires within 10ms after v_0.



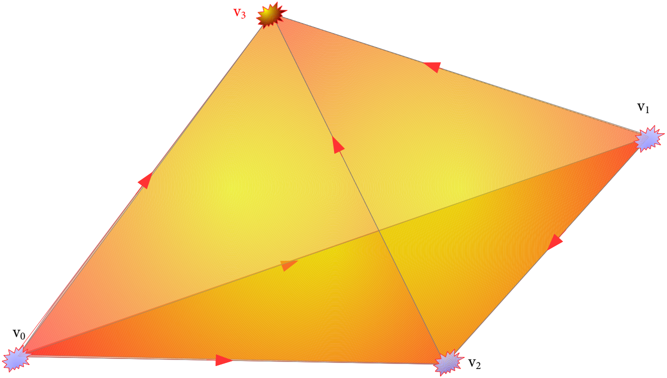
Activity: The Transmission-Response method

3) v_2 fires within 10ms after v_0 (and v_1).



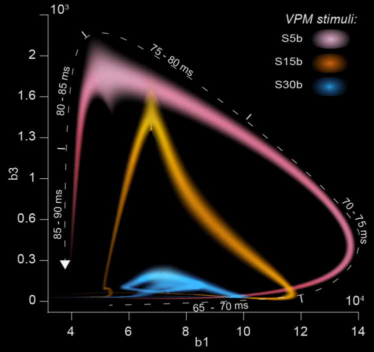
Activity: The Transmission-Response method

4) v_3 fires within 10ms after v_0, (and v_1, v_2).



All four have to fire in quick succession within 10ms from the point v_0 fired.

Stimulation experiments



Trace of time series of β_1 against β_3: β_1 grows to a peak, then starts declining as β_3 starts growing, to its peak and then the reaction disintegrates.

Weighted graphs

An increasing weighting system on a simplicial complex K (ordered or not) is a function $\omega\colon \bigcup_{n\geq 0} K_n \to \mathbb{R}$, and a family of functions $\{g_m\colon \mathbb{R}^{m+1} \to \mathbb{R} \mid m \geq 1\}$, such that for each $\sigma \in K_m$, the following conditions are satisfied:

i) $\omega(\sigma) = g_m(\omega(\sigma_0), \omega(\sigma_1), \ldots, \omega(\sigma_m))$, where $\sigma_i = \partial_i \sigma$, the i-th face of σ, and $m \geq 1$.

ii) $\omega(\sigma) \geq \omega(\tau)$ for any face τ of σ.

For example ω on a vertex is given, and
$g_n = \frac{1}{n}(\omega(\sigma_0) + \cdots \omega(\sigma_n))$.
An increasing weighting system on a complex K induces an increasing filtration on the complex, by taking sub-level sets
$\omega^{-1}(-\infty, a]$
By analogy one can define what it means to be a decreasing weighting system.

Weighted graphs

Example

Examples for weights on neural graphs:

- Firing rate of neurons (vertices).
- Synaptic weights (edges).
- Activity correlation weights (edges).
- Graph properties - e.g., degree, in-degree, out-degree, signed degree, minimal graph distance from hubs,.......

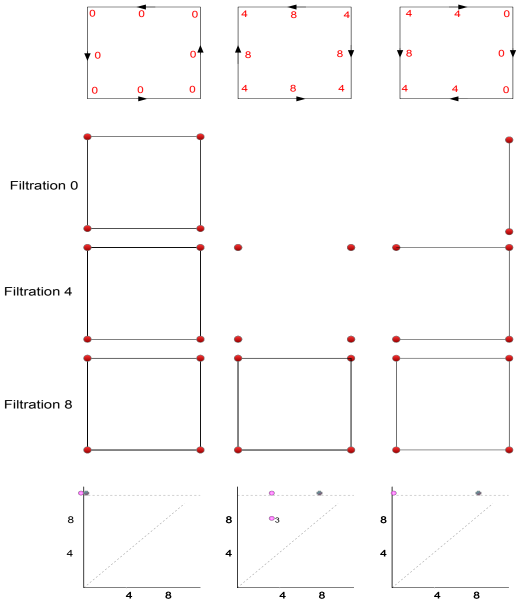
Other graph constructions

Given a directed graph, we can consider all cliques in it in any orientation of edges.
Not only $\{1, 2, 3\}$ is not the same as $\{3, 2, 1\}$, but also the cycle $1 \longrightarrow 2$, $2 \longrightarrow 3$ and $3 \longrightarrow 1$ will define a 2-simplex.
The complex may be bigger, but could contain more topological information about the graph.

Example

Assign to each vertex v the weight $(\mathrm{indeg}(v) - \mathrm{outdeg}(v))^2$ and to each simplex some nice function of the values on vertices (e.g., sum). Persistence homology of the resulting filtered complex separates directed graphs better than ordinary homology of the flag complex.

Other graph constructions



Persistence Movies

- Instead of fixed weights on the simplices of a complex, we can consider the weights being functions of a parameter, still satisfying the requirements of a weighting system.
- For instance, in a real brain synaptic weight (roughly speaking, the “quality of a connection”) changes with time, and the change represents learning. This is called Synaptic Functional Plasticity.
- In that case by computing persistence diagrams in small intervals along the parameter, we obtain a ”persistence movie”.
- By presenting a variety of “not at all random weights” on the edges of an ER random directed graph, create several funny looking persistence diagrams and interpolate (just for demonstration)

Examples of persistence movies

Examples of persistence movies


THANK YOU