Neurotopology: The Topology of Neural Systems

Applications of combinatorial algebraic topology to neuroscience

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Topological Data Analysis

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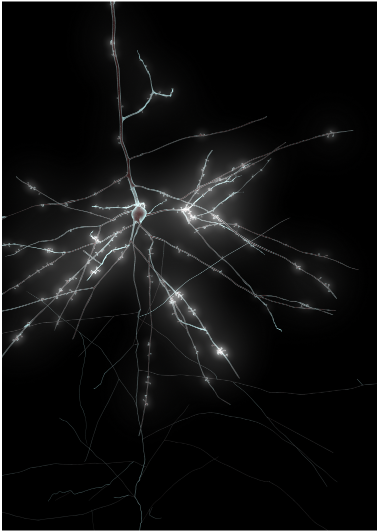
The Blue Brain Project

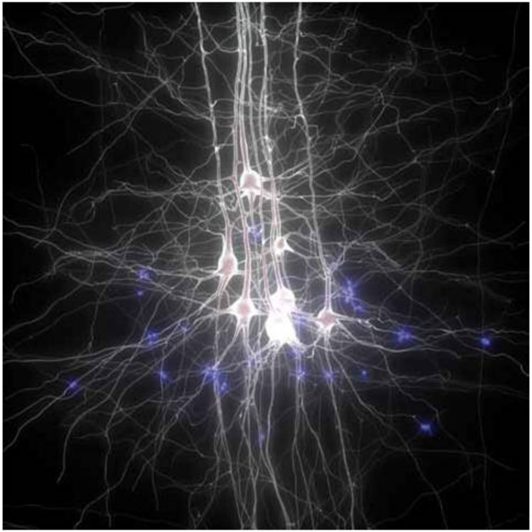
- Digital reconstruction of the microcircuitry of the hind-limb somatosensory cortex of a 14 days old rat, based on detailed experimental data from five live rat brains.
- "The column": $\sim 31,000$ simulated neurons of 55 morphological types in 6 layers, $\sim 8.2 \times 10^6$ connections, and $\sim 36.7 \times 10^6$ synapses. Simulating a cortex region 0.5mm in diameter and 2mm high.
- Data at our disposal: 42 such columns, 7 for each rat and 7 based on averaged data from all of them.
- Validated against experimental data sets not used in the reconstruction.
- Key application: Study emergent properties of the microcircuit through simulated structure and activity.

A single Neuron

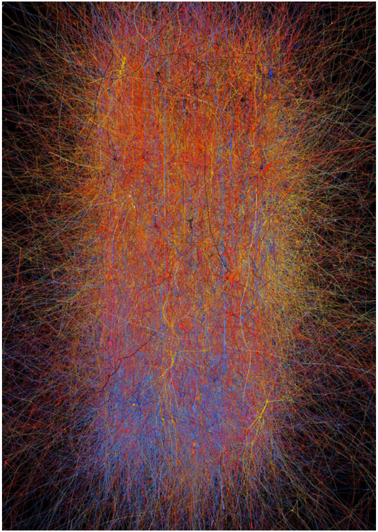


Current estimates claim that the human brain contains approximately 86 billion neurons.

A 7-neuron Microcircuit Model

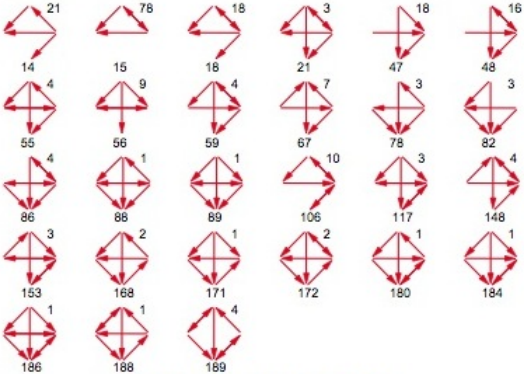


A neocortical column (31,000 neurons)



Connectivity patterns in rat brains

Overexpressed three-neuron connectivity patterns



Overexpressed four-neuron connectivity patterns

The Connectome

Describe the brain network of neurons as a graph. This can be done on several levels:

- Neurons connected to each other via synapses.
- Functional clusters within a microcircuit connected to each other via multiple synaptic connections.
- Microcircuits (mini columns) connected to each other.
- Brain regions connected to each other.
- Hierarchically modular graphs - several levels of connections simultaneously.

Example:

- Connections among brain regions can be successfully mapped using fMRI.
- Various psychiatric and neurological conditions are detected and sometimes distinguished by deviation from standard graph theoretic invariants of the relevant connectome.

Functional connectivity

Microcircuits examined in vitro can only be mapped on a very small scale.
The Blue Brain in silico models are fully functional.

- Individual columns can be connected to each other to create larger regions of the cortex.
- Columns can be stimulated and their reaction measured and recorded in great detail.
- Various electro-chemical conditions in which the brain normally functions can be simulated.
- The full connectivity matrix of a column or any cluster of columns can be extracted, including information on morphological types, strength of connection, more.
- An active column gives rise to a time series of connectivity matrices by recording the activity in time bins.

The directed flag complex

- A directed graph $\mathcal{G}$ is a pair (V, E) where V is the set of vertices and $E \subseteq V \times V$ is the set of directed edges.
- With $\mathcal{G}$ we associate its geometric realisation: a vertex for every $v \in V$, and a directed edge from v to w for every $(v, w) \in E$.
- The directed flag complex of a directed graph $\mathcal{G}$ is the abstract simplicial complex $K(\mathcal{G})$, whose n-simplices are $(n+1)$-tuples of vertices

$$\{(v_0, v_1, \ldots, v_n) \mid (v_i, v_j) \in E, \ \forall 0 \leq i < j \leq n\}$$

- The basic data object: An adjacency matrix - an $n \times n$ binary matrix $A = (a_{i,j})$ with $a_{i,j} = 1$ if there is connection from neuron i to neuron j. (In Blue Brain every neuron has a numerical name or a GID.)

Topological Invariants

The topological invariants and metrics we discuss can obviously be associated to any (oriented simplicial complex).

- Betti numbers (in our computations mod-2) but only for computational convenience.
- Euler characteristic.

Question: The column construction algorithm is based on semi stochastic processes. How do we know that its connectivity structure is not random?

Dim	Random	BB
0	31146	31146
1	7764739	7648079
2	15492757	73036616
3	247176	59945205
4	36	6599529
5	0	133115
6	0	529

Number of simplices by dimension in an Erdös Renyi random graph vs. typical Blue Brain graph.

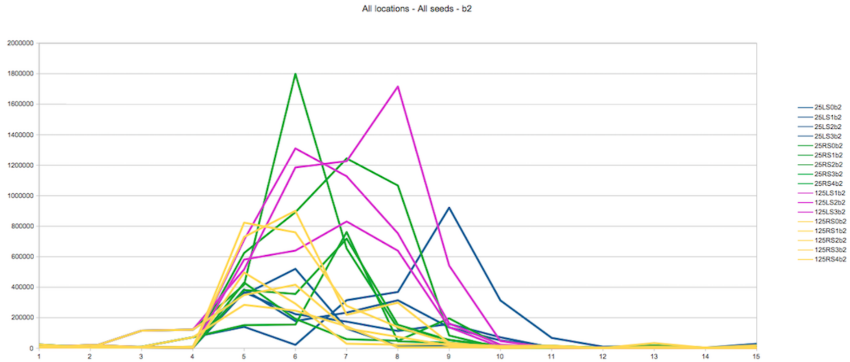
Betti numbers

- Work of Matthew Kahle puts strong restrictions on Betti numbers of (non-directed) flag complexes of random graphs with a given number of vertices and connection probability.
- Kahle's theorem implies that the flag complex X of a random graph with our parameters (31000 vertices and $p = 0.008$) satisfies w.h.p $H_2(X, \mathbb{Z}) \neq 0$, and that w.h.p $H_i(X, \mathbb{Z}) = 0$ for $i > 2$.
- Explicitly computing homology for a complex this size is beyond the capacity of a computer with 0.5TB RAM.
- We considered the 5-coskeleta of our directed flag complexes. This allowed us to compute $H_i(-, \mathbb{F}_2)$ for all 42 columns for $i \geq 0$. In all cases $H_6 = 0$, but $H_5 \neq 0$.
- Next task: Construct a connectivity matrix which emulates only the probabilility of connections between different types of neurons depending on their relative distance. Compute complex and homology.

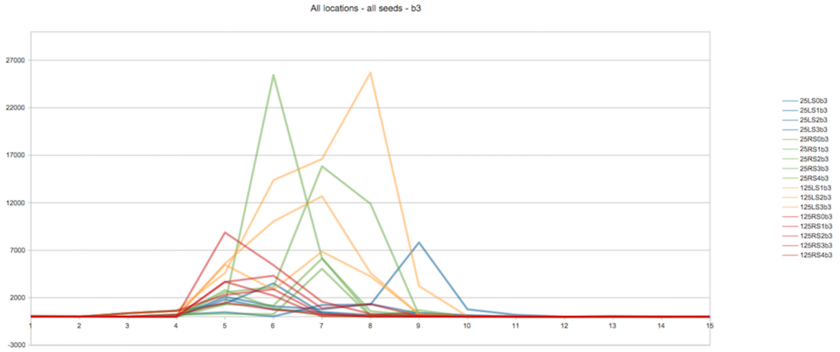
Activity - a homological approach

- As the column is stimulated, the reaction is recorded in time bins of 5, 10 or 25 ms.
- In each bin consider the connectivity matrix where columns representing neurons not active in a time bin are set to be 0. (or rows + columns , or a more sophisticated version, taking into account "successful transmission")
- The result is a sequence of matrices which are the adjacency matrices for subcomplexes of the flag complex for the column.
- We compute the homology of each such subcomplex and obtain sequences of betti numbers, creating a pattern of evolution of the activity complexes.

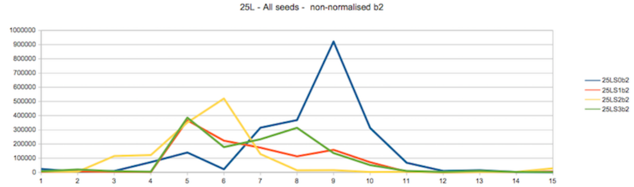
Activity - a homological approach

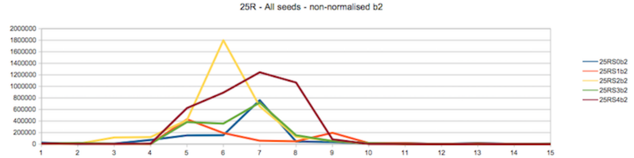


Activity - a homological approach

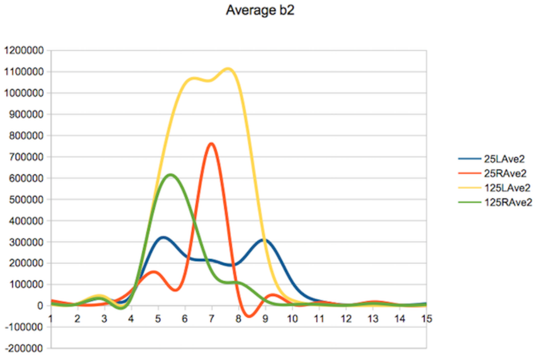


Activity - a homological approach

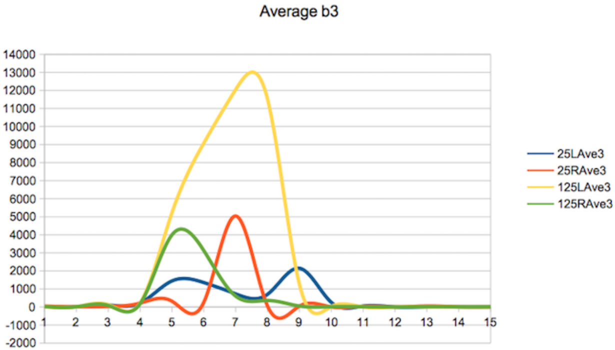




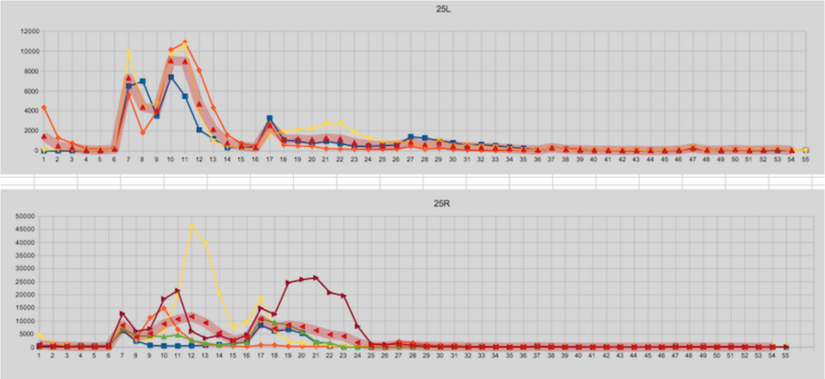
Activity - a homological approach



Activity - a homological approach

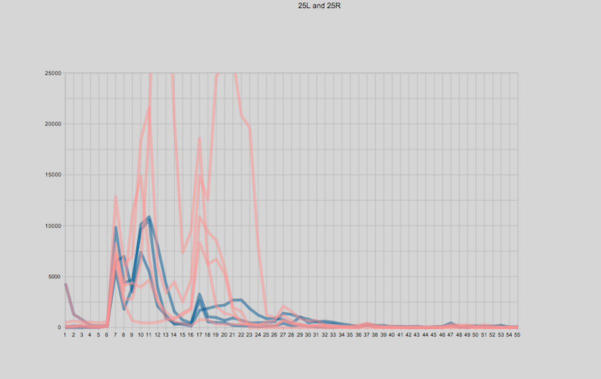


Activity - a homological approach



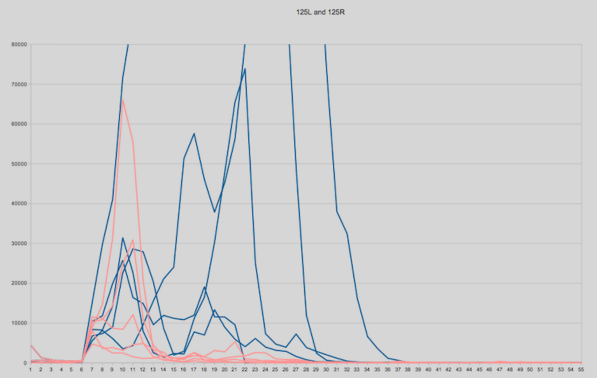
5ms bins, 25 Left and 25 Right, all computed seeds, thick red is average.

Activity - a homological approach



A comparison of all 25 left and 25 right seeds.

Activity - a homological approach



A comparison of all 125 left and 125 right seeds.

Segregation and Integration - Graph theoretic approach

Based on a survey paper by Rubinov and Sporns: There are many graph theoretic invariants which proved useful in neuroscience. We restrict to a few such invariants.

- The degree k_i of a node i: the number of nodes connected to i.
- A basic measure of segregation at a node i: The number t_i of triangles with i as a vertex.
- The clustering coefficient of a node i: $C_i = \frac{2t_i}{k_i(k_i-1)}$ = the number of triangles divided by the number of possible triangles. The clustering coefficient of the network: $C = \frac{1}{n}\sum_i C_i$.
- Measure of integration: $L = \frac{1}{n}\sum_i L_i$, where L_i is the average path length from i to any other node.
- Small worldness: Higher than random segregation, close to random integration.

Topological metrics - Clustering and Segragation

Let X be a simplicial complex.

- For $v \in X_0$, let $M_k^{\text{out}}(v)$ denote the outgoing k-valence of v - the number of simplices $\sigma \in X_k$, such that v is an initial vertices in σ. Similarly, define $M_k^{\text{in}}(v)$ - the incoming k-valence of v.
- Define the outgoing clustering polynomial of $v \in X_0$ by

$$S_v^{\text{out}}(t) = \sum_{k \geq 0} M_k^{\text{out}}(v) t^k,$$

  and similarly define $S_v^{\text{in}}(t)$.
- Define the outgoing segregation polynomial of X to be

$$S_X^{\text{out}}(t) = \frac{1}{|X_0|} \sum_{v \in X_0} S_v^{\text{out}}(t),$$

  and similarly define $S_X^{\text{in}}(t)$.

Clustering and Segregation

- $S_X^{\text{out}}(t) = S_X^{\text{in}}(t)$ for any oriented simplicial complex X.
- There is an obvious analog of these polynomials which doesn't take orientation into account.
- $S_X^{\text{out}}(-1) = \frac{\chi(X)}{|X_0|}$.
- Example: if X is the standard n-simplex $(v_0, \ldots v_n)$, then

$$S_X^{\text{out}}(t) = \frac{1}{n+1}\left(a_0 + a_1 t + \cdots + a^{n-1}t^{n-1} + t^n\right),$$

where

$$a_i = \binom{n-i+1}{i} + \binom{n-i}{i} + \cdots \binom{i+1}{i} + 1.$$

Highways and Flow

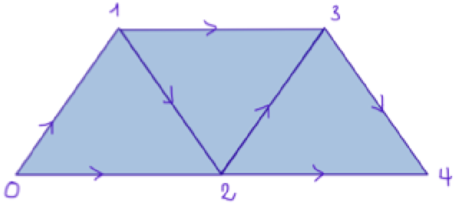
- Let X be an oriented simplicial complex, and let $x, y \in X_0$ be any two vertices.
- A d-dimensional highway from x to y is either a d-simplex $(x, x_1, \ldots x_{d-1}, y)$ in X_d or a sequence of simplices

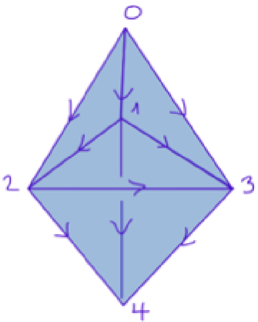
  $$\sigma_0, \ldots, \sigma_m$$

  of simplices in X such that $\sigma_i \cap \sigma_{i+1}$ is a back face of σ_i and a front face of σ_{i+1} of dimension $d+1$, for all $i \geq 0$, and such that x is an initial vertex in σ_0 and y is a final vertex in σ_m.
- The highway dimension between two distinct vertices x and y is the highest dimension $h(x, y)$ of a highway from x to y.

Highways and Flow

a 1-dimensional and a 2-dimensional highway from 0 to 4:





Highways and Flow

- If the edges of a simplicial complex are weighted, then one can assign a weight, or a flow capacity to each highway.
- For each pair of vertices, x, y, let $f_d(x, y)$ denote the maximum flow capacity on a d-dimensional highway.
- The flow polynomial of a (weighted) oriented simplicial complex X is defined by

$$F_X(t) = \frac{1}{|X_0|(|X_0 - 1|)} \cdot \sum_{(x,y) \in X_0 \times X_0} \sum_{d \geq 0} f_d(x, y) t^d.$$

We propose the segregation polynomial and the flow polynomial as multidimensional replacement for the segregation and integration coefficients.

Thank you.