Homological scaffolds of brain functional networks

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Networks and the Brain

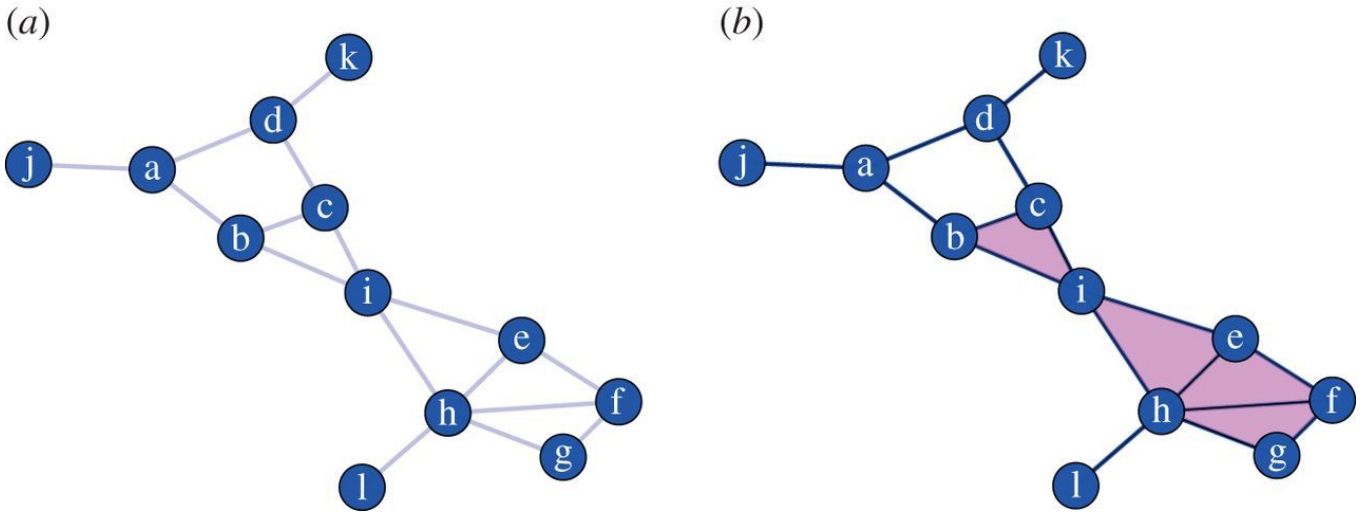
- We have seen a few different ways to model brain organization as a weighted (usually completely connected) functional network.
- Specifically, we would like to study *mesoscopic* phenomena, like "holes" in the connectivity between functional regions.
- However, these models often need to be *thresholded* to ignore weak links, but these weak links may play important roles in some processes.

Question. How can we use persistent homology to analyse brain functional networks while capturing this data?

Cliques as Simplices

Consider a graph $G = (V, E)$ with vertex set V and edge set E.

Recall that the *clique complex* K of G is the simplicial complex we obtain by considering each k-clique as a $(k-1)$-simplex.



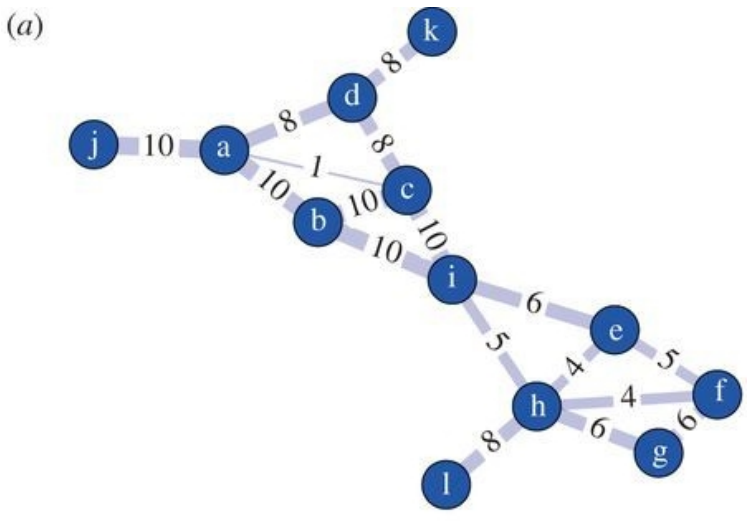
Adding Weights

Now let $\Omega = (V, E, \bar{\omega})$ be a weighted graph with weights $\bar{\omega} : E \to \mathbb{R}$.

Then for $\omega \in \mathbb{R}$ let $E_\omega = \{e \in E \mid \bar{\omega}(e) \leq \omega\}$ and $G_\omega = (V, E_\omega)$.

To each G_ω assign its *clique complex* K_ω, and notice that this forms a filtration since if $\omega \leq \omega'$ then $K_\omega \subseteq K_{\omega'}$.

Then calculate the persistent homology of the filtration $\{K_\omega\}_{\omega \in \mathbb{R}}$.


(a)
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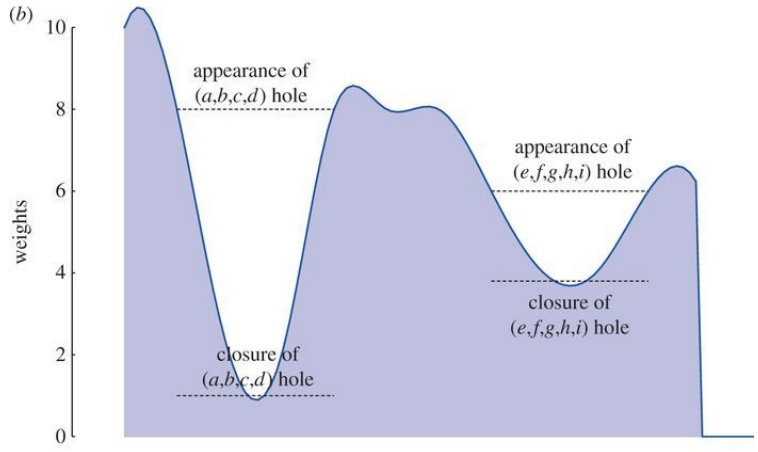
(b)
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(a,b,c,d) hole
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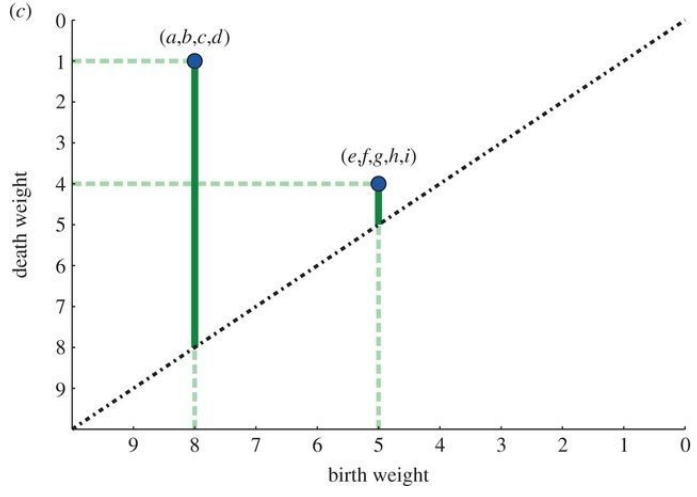
(a,b,c,d) hole


(c)
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3
4
5
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7
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9
death weight
(a,b,c,d)
(e,f,g,h,i)
9
8
7
6
5
4
3
2
1
0
birth weight

Generating Cycles

- Recall that the k-th homology group of a topological space X is given by $Z_k(X)/B_k(X) = \ker \partial / \operatorname{im} \partial$, or *cycles* modulo *boundaries*.
- Intuitively, to count the "holes" in X, we consider as candidates for holes combinations of simplices which have no boundary (cycles), but ignore the ones which bound higher dimensional simplices (boundaries).
- This means that each *homology class* in $H_k(X)$ can be *represented* by cycles in $Z_k(X)$, and (since we usually compute mod 2) we can consider this as a *generator* g for $H_k(X)$.

Persistent Generating Cycles

- Specifically, in [the persistence diagram for $\{K_\omega\}$, each generating cycle g is represented by its birth and death (β_g, δ_g), and has *persistence* $\pi_g = \delta_g - \beta_g$.
- However, each $g \in H_k(K_\omega)$ is an *equivalence class* of cycles, not just one cycle.

Question. How do we pick a cycle to be a representative for g?

Answer. Javaplex returns one!

Some Notation

Let $G = (V, E)$ be a graph.

Suppose $\bar{\omega}$ is a weight function on E and suppose the associated clique complex filtration $\{K_\omega\}$ has persistent homology generators $g_0, g_1, \ldots, g_s$.

We will identify g_i with its representative cycle as returned by Javaplex.

Homological Scaffolds

Definition

The *persistence homological scaffold* of G is $\mathscr{H}_G^p = (V, E, \omega^\pi)$:

$$\omega^\pi(e) = \sum_{g_i \ni e} \pi_{g_i}.$$

Definition

The *frequency homological scaffold* of G is $\mathscr{H}_G^f = (V, E, \omega^f)$:

$$\omega^f(e) = \sum_{g_i} \mathbf{1}_{g_i}(e).$$

Why Homological Scaffolds?

- The homological scaffolds capture the role of edges which are part of long and/or many persistent cycles.
- That is, if an edge has high total persistence, then it is much stronger than other edges in the area.
- Similarly, if an edge has high frequency among homological cycles, then it is important in the filtration.

The Setup

- 15 healthy controls were each scanned twice, with each scan 14 days apart.
- Each scan consisted of a structural MRI image (T1-weighted), followed by a 12 minute eyes-closed resting-state blood oxygen-level-dependent (BOLD) fMRI scan.
- Halfway through one scan, subjects received a placebo (10 ml saline) intravenous injection.
- Halfway through the other scan, subjects received psilocybin (2 mg dissolved in 10 ml saline), again by IV.

The Data

- Structural MRI images were segmented into $n = 194$ cortical and subcortical regions, including white matter cerebrospinal fluid (CSF) compartments.
- fMRI images were corrected for subject motion using a 24-parameter model.
- For each of the 194 regions, alongside the 24 parameter motion model time courses partial correlations were calculated between all couples of time courses (i, j).
- Non-neural time courses (CSF, white matter and motion) were discarded from the resulting functional connectivity matrices, resulting in a 169 region cortical/subcortical functional connectivity corrected for motion and additional non-neural signals (white matter/CSF).

The Data

- The resulting partial correlation matrices $X^\alpha = (X^\alpha_{i,j})$ for each subject can be regarded as a complete weighted graph $\Omega = (V, E, \bar{\omega})$ where $\bar{\omega}(i,j) = X^\alpha_{i,j}$.
- These were analyzed by computing the persistent degree 1 homology of the filtered clique complex, then constructing the persistence and frequency homological scaffolds.
- The results show that cycles in the psilocybin group are less stable than in placebo, but that their edges are more stable.

Probability Densities for Persistent Cycles

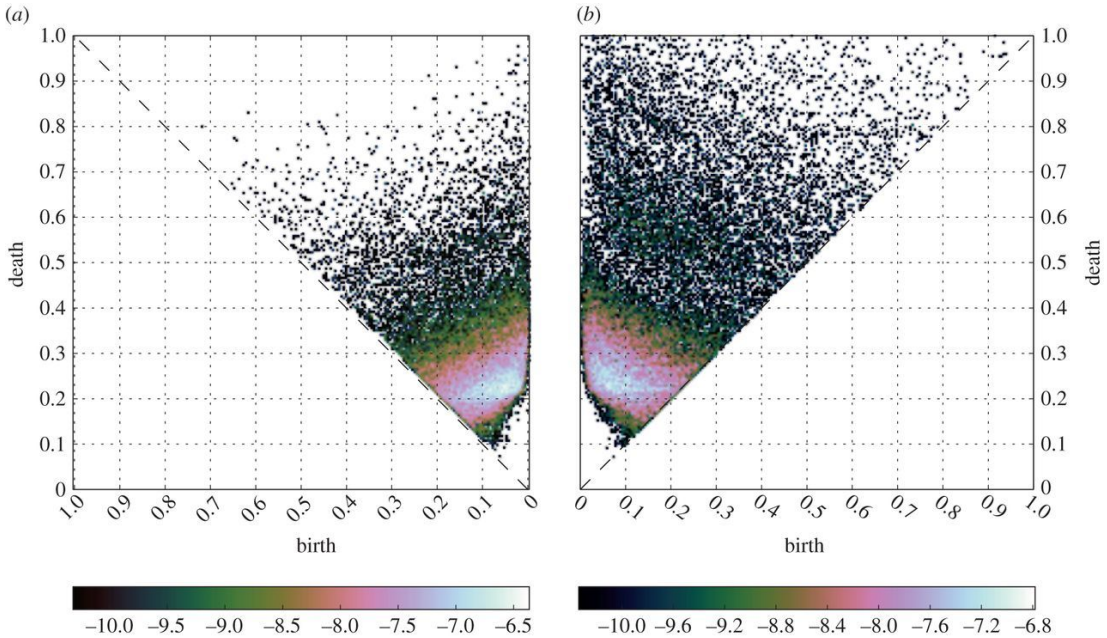

Figure: (Log-)probability densities of combined H_1 persistence diagrams. Panel (a) (left) shows the placebo group while panel (b) (right) shows the psilocybin group.

The two probability densities strongly differ, with a Kolmogorov-Smirnov statistic of 0.22, $p < 10^{-10}$.

Probability Densities for Persistent Cycles

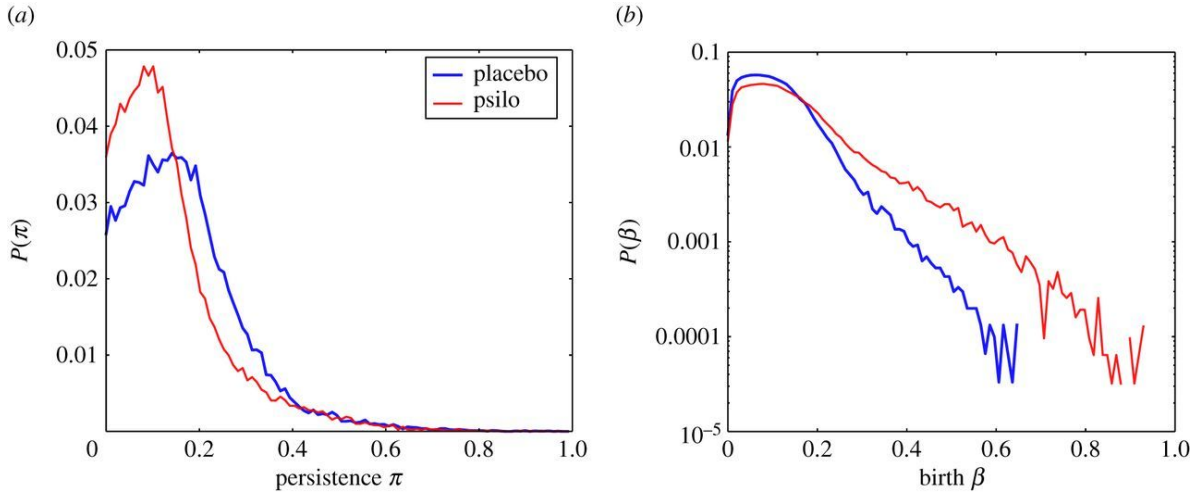

Figure: Persistence (panel (a), left) and birth (panel (b), right) distributions for H_1 generators in placebo group (blue) and psilocybin group (red).

The probability distributions for the persistence and the birth of generators are also significantly different (K-S statistic 0.13, $p < 10^{30}$ for persistence; K-S statistic 0.14, $p < 10^{-35}$ for births).

The Homological Scaffolds

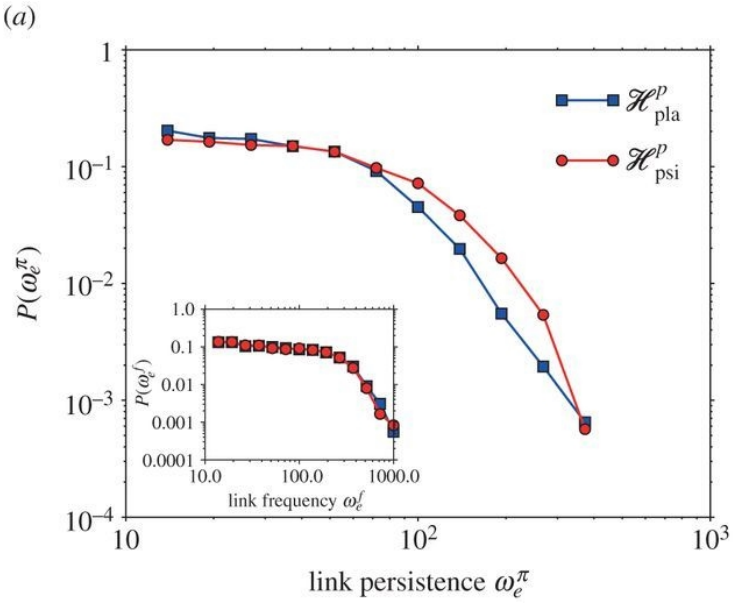

Figure: (Log-binned) probability distributions for edge weights in persistence homological scaffolds (main plot) and the frequency homological scaffolds (inset).

The persistence homological scaffolds and $\mathscr{H}^p_{\text{Pla}}$ for the placebo group and $\mathscr{H}^p_{\text{Psi}}$ for the psilocybin group show a difference in distributions (K-S 0.06, $p < 10^{-20}$) while the frequency scaffolds $\mathscr{H}^f_{\text{Pla}}$ and $\mathscr{H}^f_{\text{Psi}}$ are indistinguishable (K-S 0.008, $p = .72$).

Frequency and Persistence

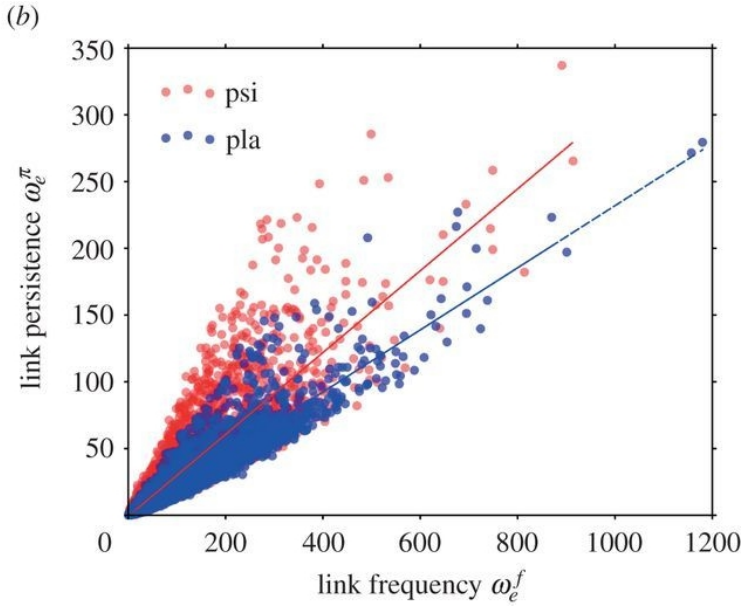

Figure: Scatter plot of the edge frequency versus total persistence.

Both groups have a linear relationship between persistence and frequency ($R^2 = 0.95$, slope=0.23 placbo; $R^2 = 0.9$, slope=0.3 psilocybin) with a larger dispersion in the psilocybin group, as well as significantly greater slope ($p < 10^{-20}$, $n_{\text{Pla}} = 13200$, $n_{\text{Psi}} = 13275$).

Summary

- The psilocybin group displays cycles which have lower average persistence, but the stable cyles are especially persistent.
- The number of connections is comparable in both states, but are stronger in the psilocybin state.

Summary

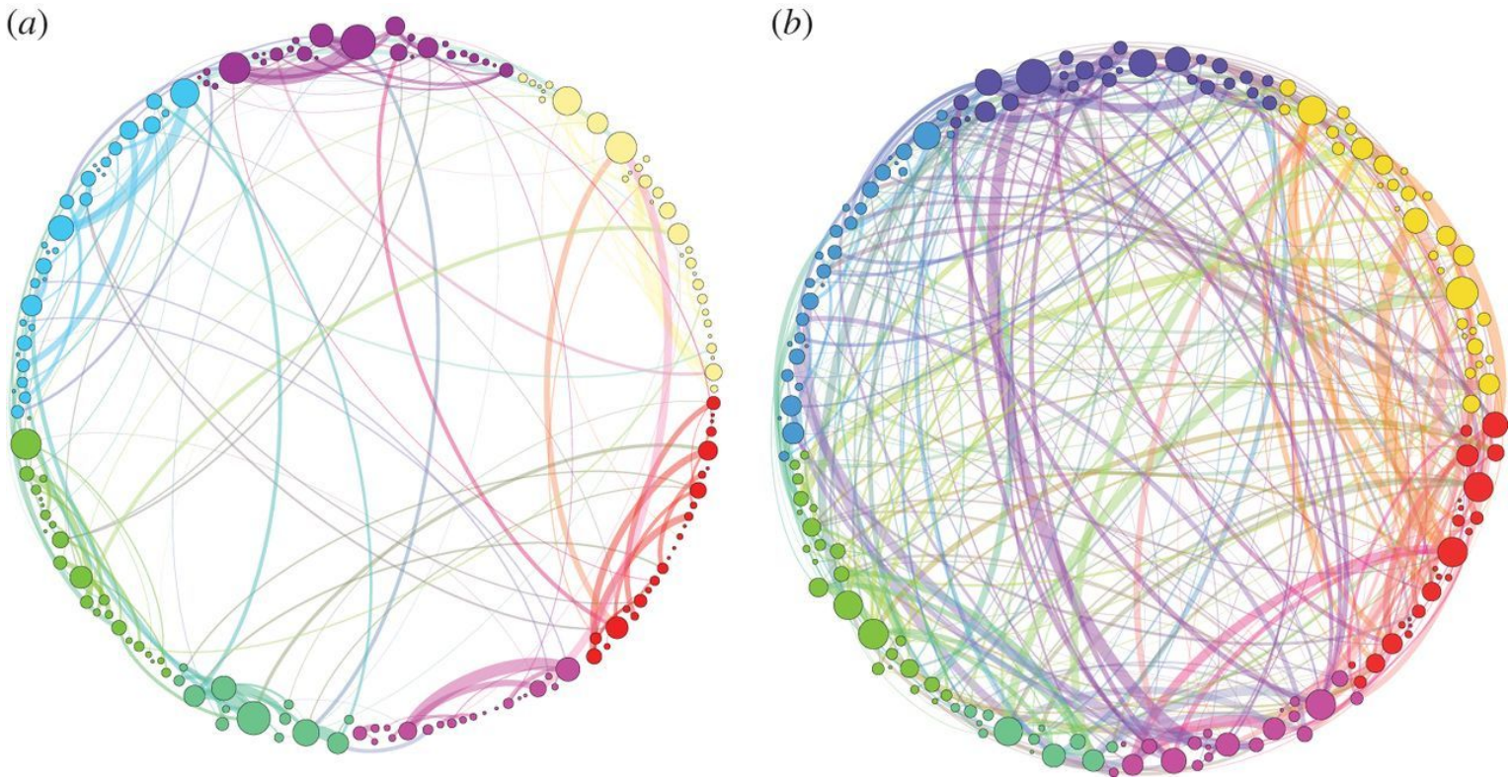

Figure: Visualiztion of edges with total persistence > 80 in $\mathscr{H}^p_{\text{Pla}}$ (a) (left) and $\mathscr{H}^p_{\text{Psi}}$ (b) (right).

Key Insights

- Psilocybin reduces the stability of mesoscopic cycles, but the homological scaffolds reveal more information about organizational features following psilocybin injection.
- The homological scaffolds show a set of connections in the psilocybin group which statistically participate in the same number of cycles as in the placebo group but are more persistent.
- These functional connections support especially stable cycles which are only present in the psilocybin state.

Limitations

- The construction of the homological scaffolds requires a *choice* of generating cycles in the persistent homology, and may differ depending on how that choice is made.
- Guerra, De Gregorio, Fugacci, Petri, and Vaccarino[1] [2] propose using the *minimal* (i.e. shortest) representative cycle as a quasi-canonical basis for the scaffold.
- They also verify that the standard scaffold is statistically a good proxy of the minimal one for sufficiently complex networks.

[1] Petri and Vaccarino are also authors of [1].

References

[1] Petri G. et al. "Homological scaffolds of brain functional networks". In: *J. R. Soc. Interface* 11.101 (2014). DOI: 10.1098/rsif.2014.0873.

[2] Marco Guerra et al. "Homological scaffold via minimal homology bases". In: *Sci Rep* 11.1 (2021). DOI: 10.1038/s41598-021-84486-1.