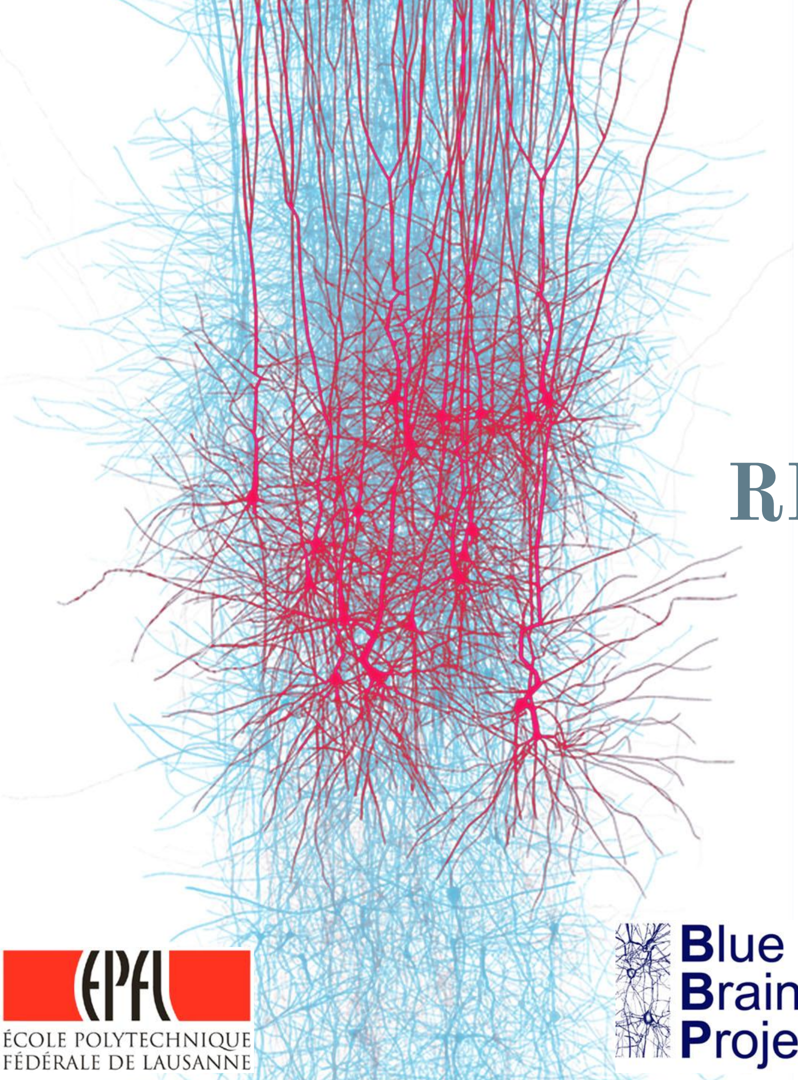

GSP ON THE DIGITAL RECONSTRUCTION OF THE BRAIN

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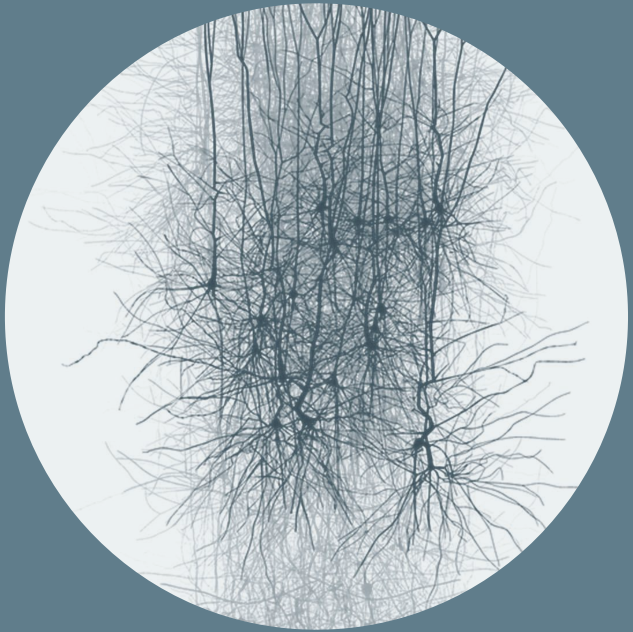
NTDS Project 2017/18

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Blue Brain Project

- **Data Exploration**
- **Network Analysis**
- **Clusters**
- **Layers Prediction**



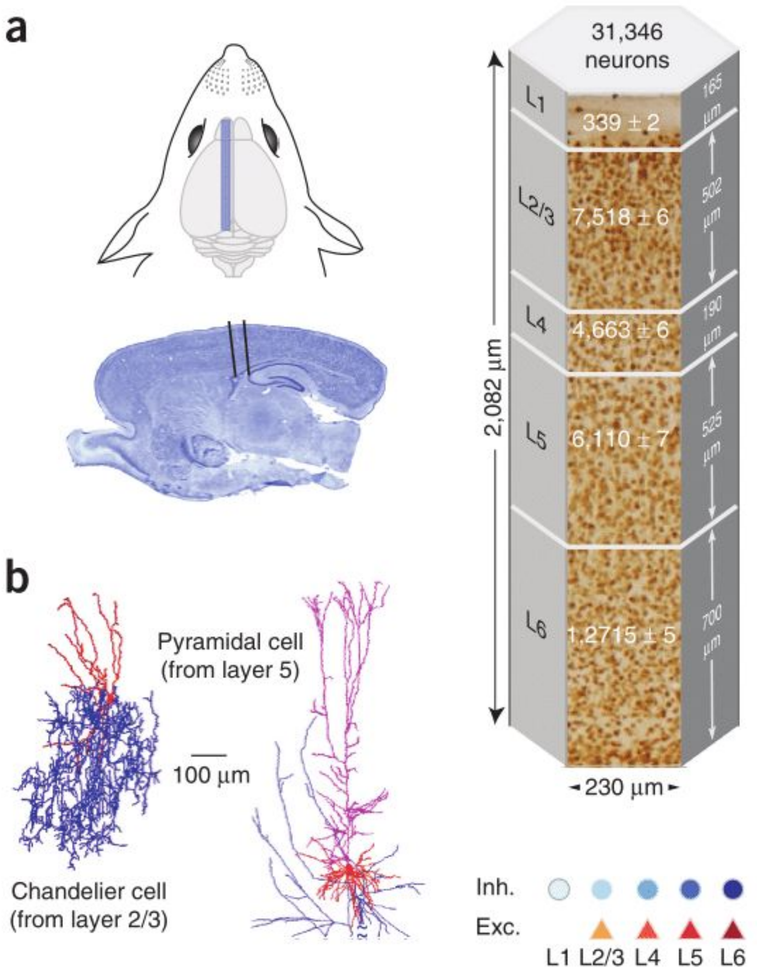
Blue Brain Project

Digital Reconstruction of Neocortical Microcircuitry:

- ➢ Biologically consistent
- ➢ Reproduce anatomy and physiology

Modeled subunits/microcolumns:

- ➢ ~31000 neurons
- ➢ ~7.8 million connections
- ➢ 6 layers



Data available for each Neuron:

(The Neocortical Microcircuit Collaboration Portal)

Inner-connections

Connection Failure Mean

3D Locations

Connectivity Matrix: 31346 nodes, p=0.015%
&
Weights

55 Morpho-Type

Layer 1-6

Connections outside the volume

Inhibitory Excitatory

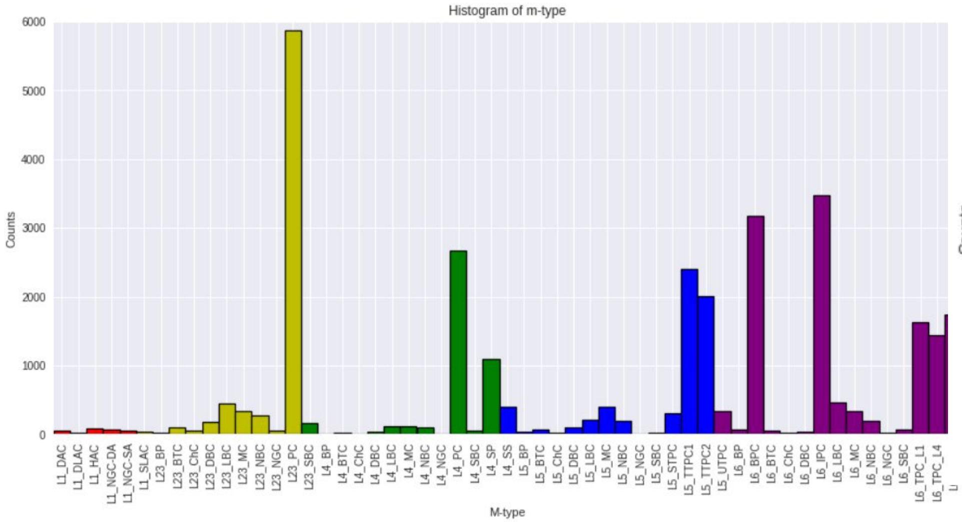
Number In-Out Synapses

Statistical Analysis
&
Labels

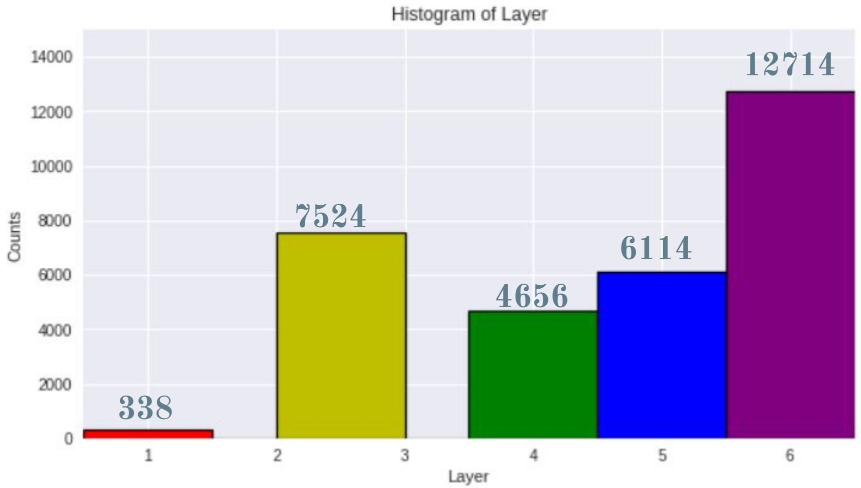
Network properties

➢ Original graph is directed

Histogram of the 55 morphological types:



Histogram of the 6 layers:

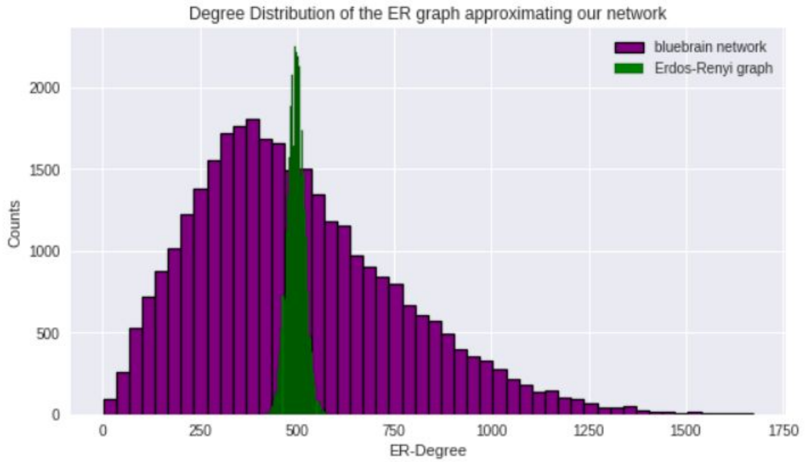


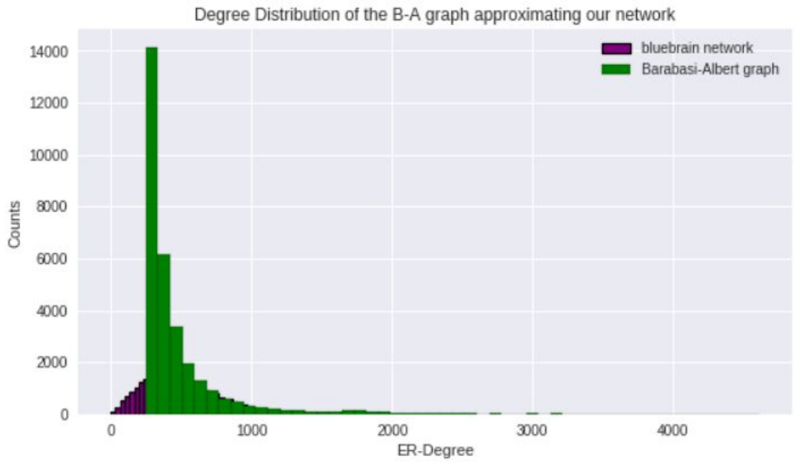
Hubs: different m-types are typically hubs for the out-degree (L4_PC) and the in-degree (L5_TTCP)

Network models

Can our network be approximated by an Erdős–Rényi or a Barabasi-Albert network?

→ Create networks with same amount of nodes and connection probability





Degree distribution of our network is widely distributed but not by a power law
→ Degree distribution can not be modeled by either of the networks

Network models properties

Network	**Average path length**	**Diameter**	**Clustering Coefficient**
BlueBrain network directed	2.48	-	-
BlueBrain network undirected	2.33	5	0.057
Erdós-Rényi-Graph	1.98	3	0.016
Barabàsi-Albert-Graph	1.99	3	0.048

- ➢ small world property ✓
- ➢ Clustering coefficient ✗

Spectral Clustering

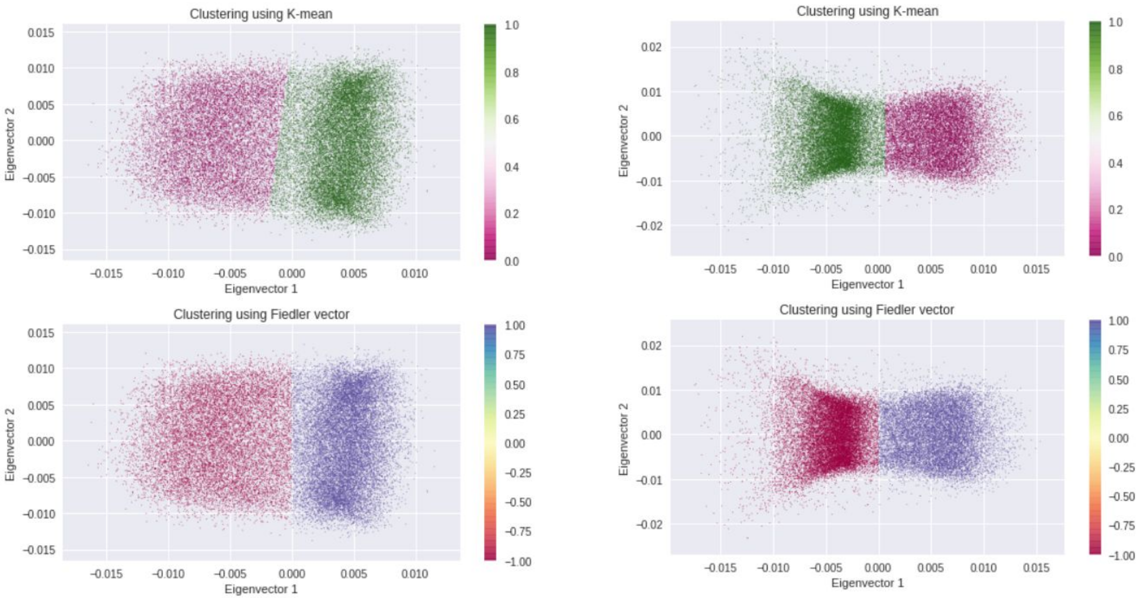
- **Goal:** can spectral clustering classify neurons by biological or structural properties?
- **Matrices:** unweighted connectivity matrix and weighted connectivity matrix (failure rates)

Embedding using Laplacian eigenmaps of the Unweighted and Weighted Normalized Laplacian

unweighted | weighted

k-mean (k = 2)

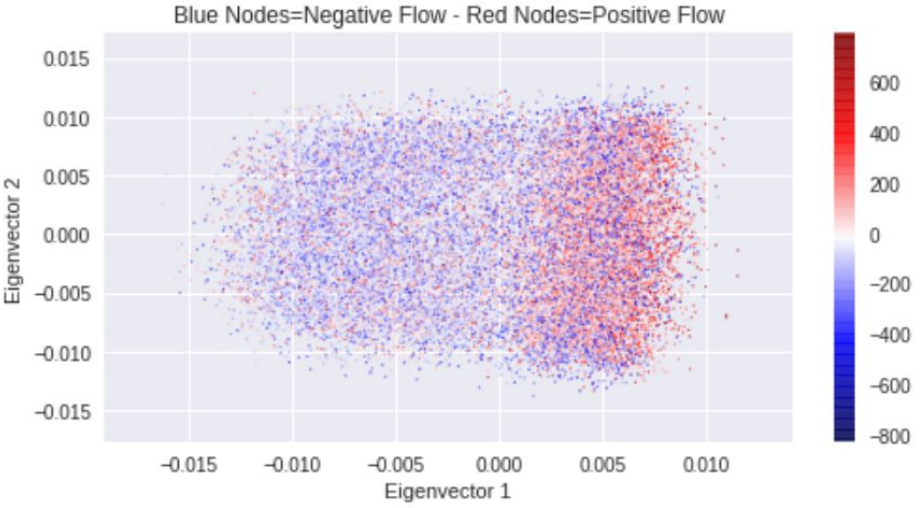
sign Fiedler vector



Signal-flow based Clustering

- ➢ Goal: how strongly the signal flows through every node (processing depth) is correlated with the 1st or 2nd eigenvector?
- ➢ Inspiration: embedding of the C. elegans network [1] using Laplacian eigenmaps
- ➢ Labels: Total Flow = Out-Degree - In-Degree
- ➢ Classifier: sign of the Fiedler vector

Embedding using Laplacian eigenmaps of the Unweighted Normalized Laplacian



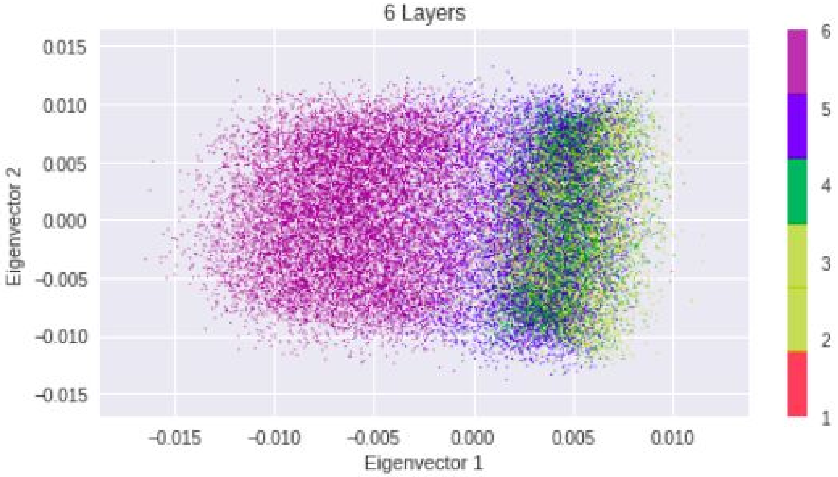
- ➢ Obtained accuracy when predicting the sign of the Total Flow: 68.44%

Layers-based clustering

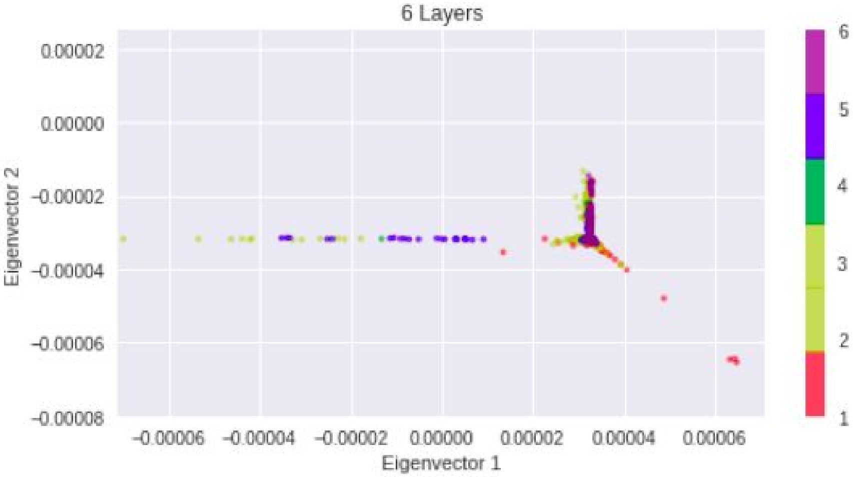
- Goal: are the 1st or 2nd eigenvectors related to the position of the neurons layers 1-6?
- Labels: Layer 1-5 and Layer 6
- Classifier: sign of the Fiedler vector

Embedding using Laplacian eigenmaps of the :

Unweighted Normalized Laplacian



Unweighted Combinatorial Laplacian

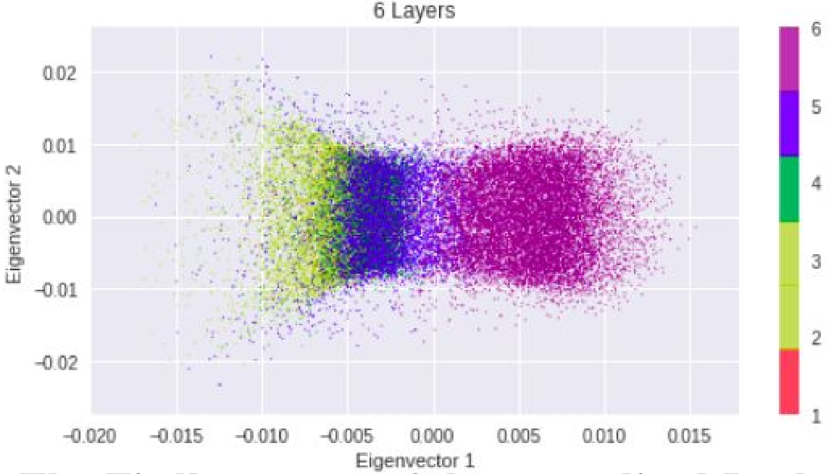


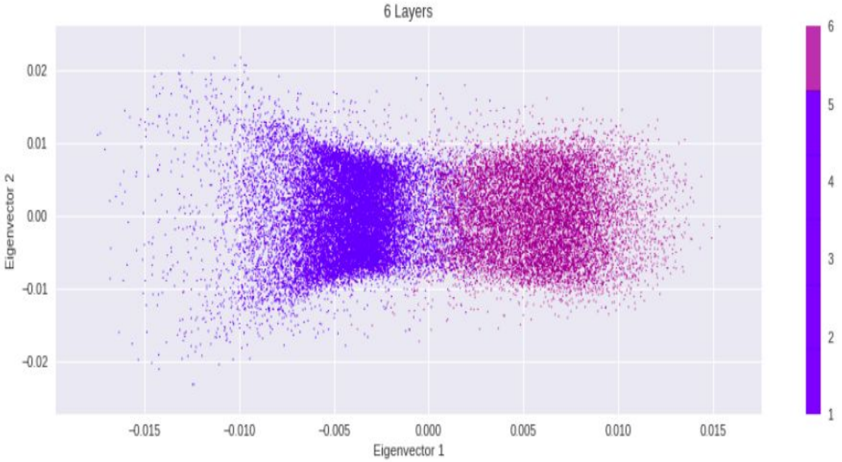
- Sign of the Fiedler vector of the normalized laplacian separates layer 6 from all other layers!
- It separates layer 6 from all other layer with an accuracy of 94.76%

Layers-based clustering: weighted connectivity matrix

- ➢ Weights: failure mean
- ➢ Labels: Layer 1-5 and Layer 6
- ➢ Classifier: sign of the Fiedler vector

Embedding using Laplacian eigenmaps of the Weighted Normalized Laplacian



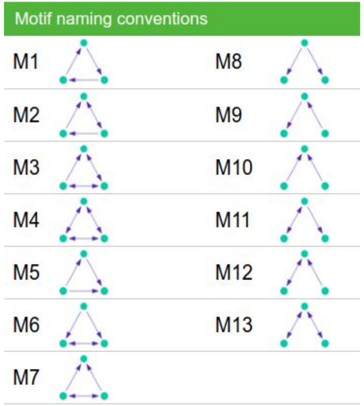


- ➢ The Fiedler vector of the normalized Laplacian is a spatial separator: it distinguish 3 layers!
- ➢ The sign of the Fiedler vector separates layer 6 from all other layer with an accuracy of 96.58%

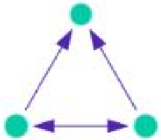
Motif-based clustering

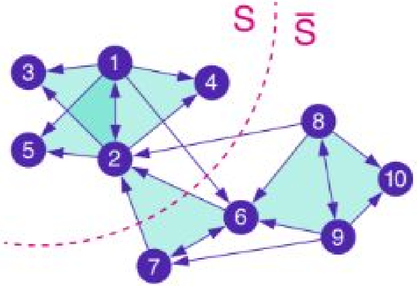
Motivation: taking into account the direction of signal flow

1.Choose motif

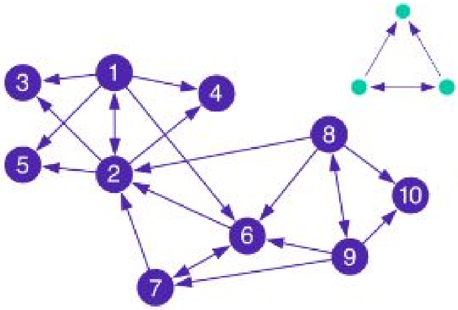


Idea:
minimize motifs cut



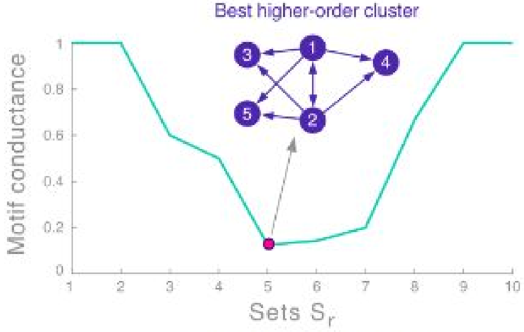


$$\phi_M(S) = \frac{\text{motifs cut}}{\min(8, 10)} = \frac{1}{8}$$



Nodes

Nodes	1	2	3	4	5	6	7	8	9	10
1	0	**3**	1	1	1	0	0	0	0	0
2	**3**	0	1	1	1	1	1	0	0	0
3	1	1	0	0	0	0	0	0	0	0
4	1	1	0	0	0	0	0	0	0	0
5	1	1	0	0	0	0	0	0	0	0
6	0	1	0	0	0	0	1	1	1	0
7	0	1	0	0	0	1	0	0	0	0
8	0	0	0	0	0	1	0	0	**2**	1
9	0	0	0	0	0	1	0	**2**	0	1
10	0	0	0	0	0	0	0	1	1	0

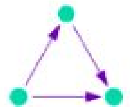


σ = (4,5,1,3,2,7,6,9,8,10)

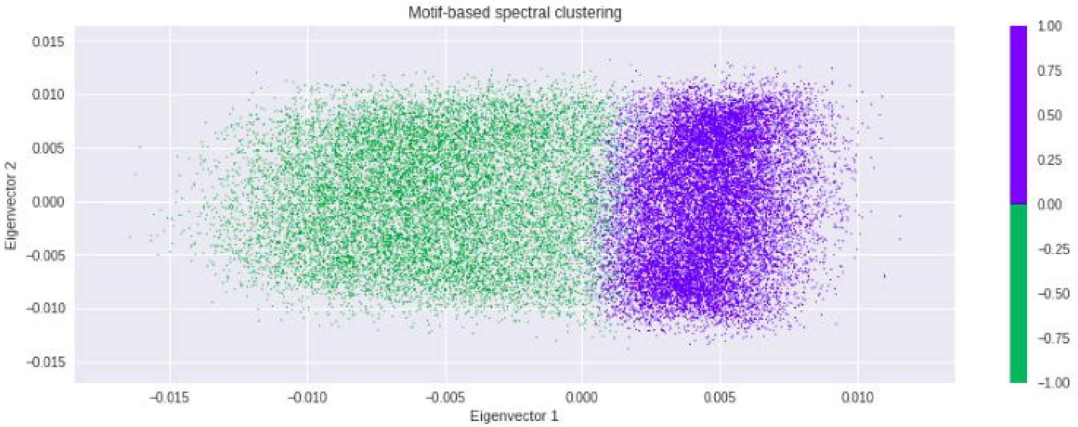
Motif-based clustering on the connectivity matrix

1. Choose the most recurrent motif in the microcircuit network:

M5



2. Compute the 2 cluster given by the motif-based spectral clustering algorithm.



- ➢ Accuracy in distinguish neurons in layer 6: 94.06%
- ➢ Similar clustering as the sign of the Fiedler vector

Prediction of layers

- Goal: Predict if a neuron is in layer 6 just knowing the connectivity matrix.
- How: revisited linear regression with ‘smoothness of signal’ on the graph

$$\mathbf{x}^* = \underset{\mathbf{x}\in\mathbb{R}^N}{\arg\min} \|\mathbf{y} - \mathbf{M}\mathbf{x}\|_2^2 + \alpha\mathbf{x}^\intercal\mathbf{L}\mathbf{x}$$

$$\left(\mathbf{M}^2 + \alpha\mathbf{L}\right)\mathbf{x}^* = \mathbf{M}\mathbf{y}$$

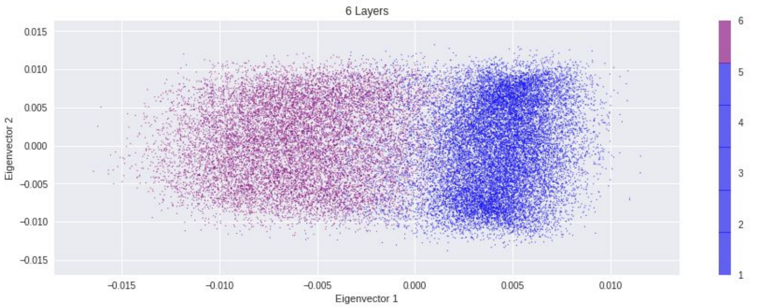
- α is an hyper-parameter which controls the trade-off between the data fidelity term and the smoothness prior

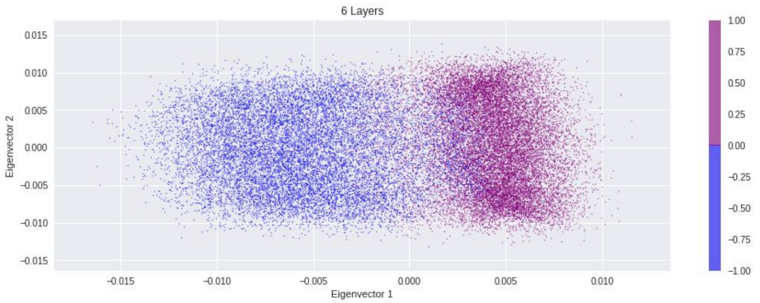
Prediction : visualization

Original data

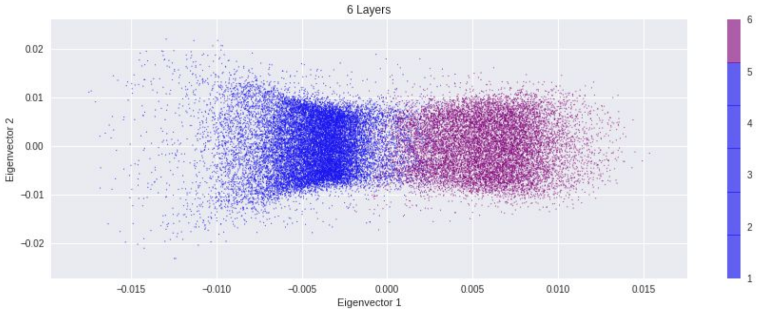
Predicted data

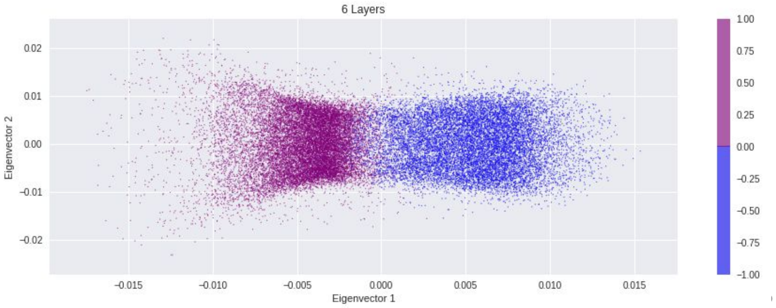
Unweighted





Weighted

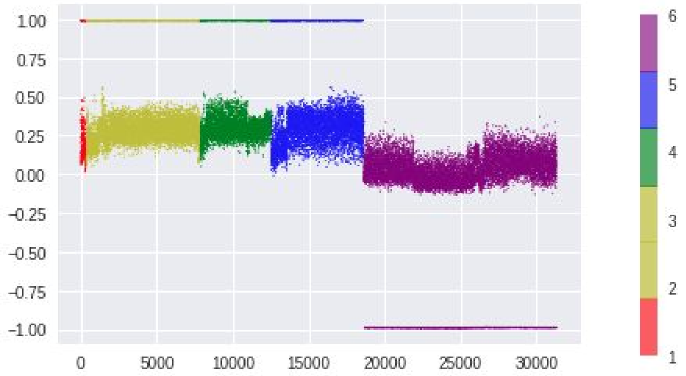




Prediction : performances

- $\alpha = 0.01$
- Keeping **10%** of the original data

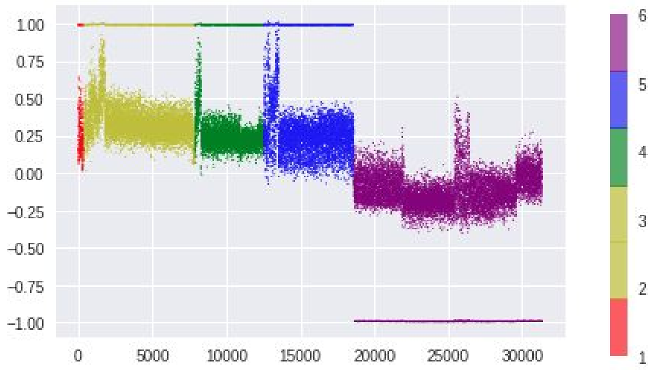
Unweighted



Unweighted : We can predict if a neuron is in the 6th layer, or not, with an error equal to : **7.55%**

Weighted : **4.72%** of errors

Weighted



- **Failure rate** is a **reasonable weight** to be used when distinguishing 6th layer from the other ones

Prediction : influence of the parameters

Unweighted connectivy matrix | **Weighted** connectivy matrix

p	α = 0.01	α = 0.1	α = 1
0.05	15.6 | 8.05	16.7 | 8.60	25.7 | 14.6
0.1	7.55 | 4.72	8.04 | 4.86	12.7 | 6.41
0.2	4.93 | 3.68	7.55 | 3.69	6.95 | 4.24
0.5	2.59 | 2.31	2.62 | 2.29	2.89 | 2.24

Error rates

- α decreases -----> error **decreases**
- p decreases -----> error **increases**

Conclusion

1. **Caveats: It is hard to interpret very complex biological data**
2. **Results: It is possible to distinguish layer 6 from all the others only by knowing the connectivity matrix**
3. **Future directions: excitatory-inhibitory predictions by changing the matrix weights, using as a signal the voltage coming from simulations.**

Thank you for your attention!

References

[1] http://www.wormatlas.org/neuronalwiring.html#CelegansNeuralNetwork

[2] Motif-based spectral clustering SNAP, Stanford.

[3] Reconstruction and Simulation of Neocortical Microcircuitry (Markram et al., Cell)