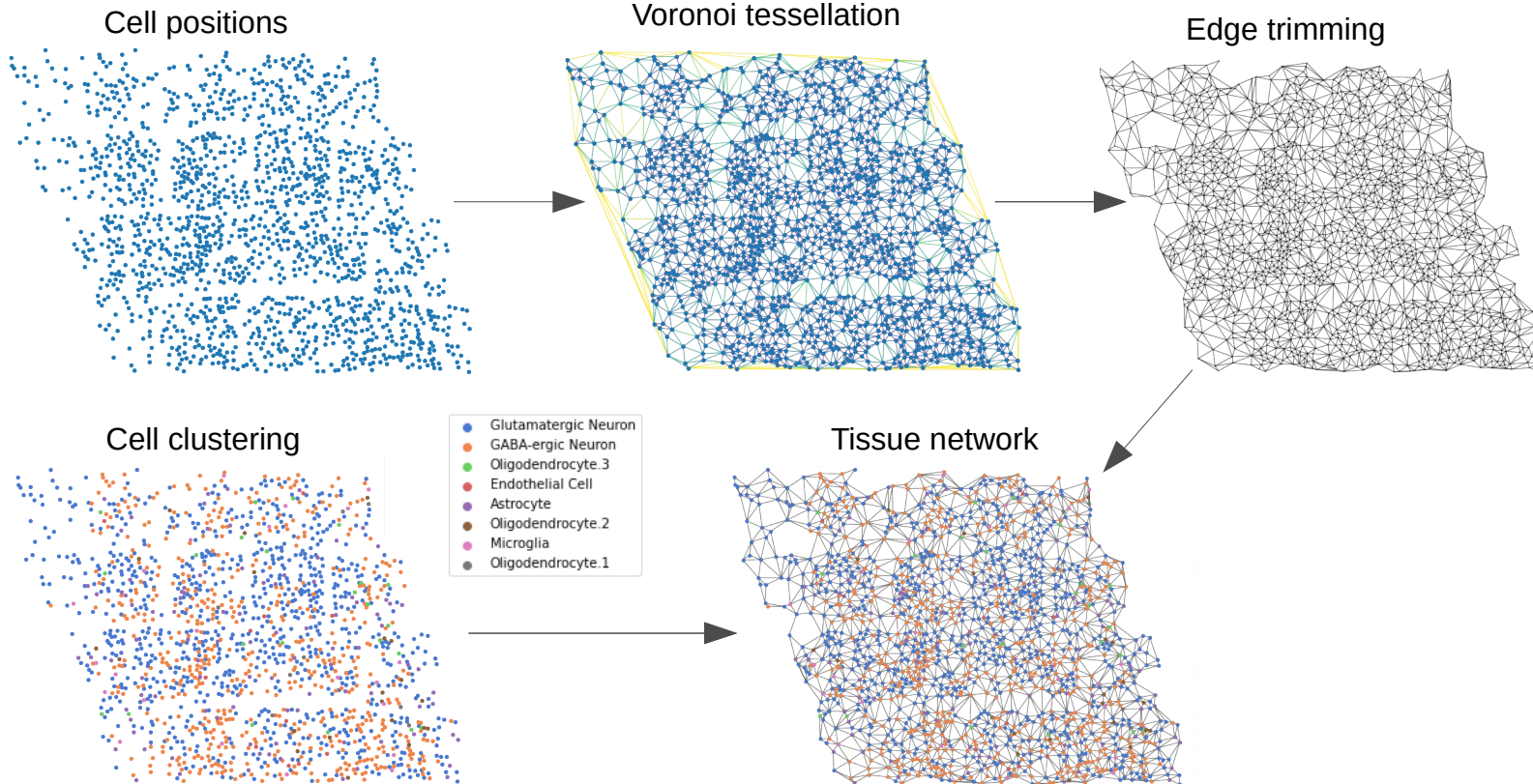# Neighbors Aggregation Statistics for spatial omics data
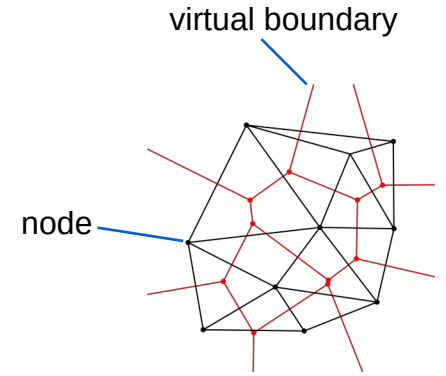
Alexis Coullomb - Vera Pancaldi
CRCT – INSERM – University Toulouse III

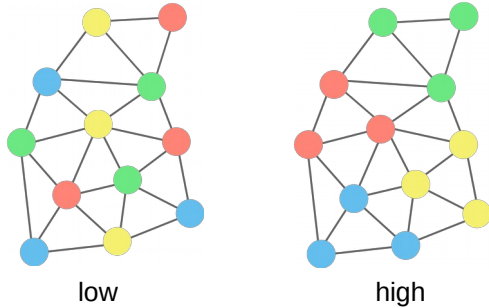## Tysserand : a library for network reconstruction

Cell positions

Voronoi tessellation

Edge trimming

Voronoi tessellation
k-nearest neighbors
neighbors within a given radius
contacting segmented objects
Based on numpy, scipy, scikit-image

virtual boundary

node

Cell clustering

- Glutamatergic Neuron
- GABA-ergic Neuron
- Oligodendrocyte.3
- Endothelial Cell
- Astrocyte
- Oligodendrocyte.2
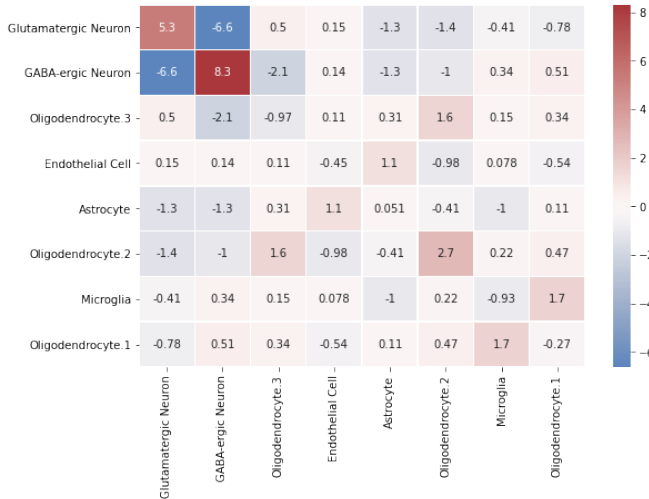- Microglia
- Oligodendrocyte.1

Tissue network

seqFISH spatial transcriptome profiling
Mouse cortex, 113 genes
Zuh *et al.* 2018

Assortativity with *non exclusive* attributes

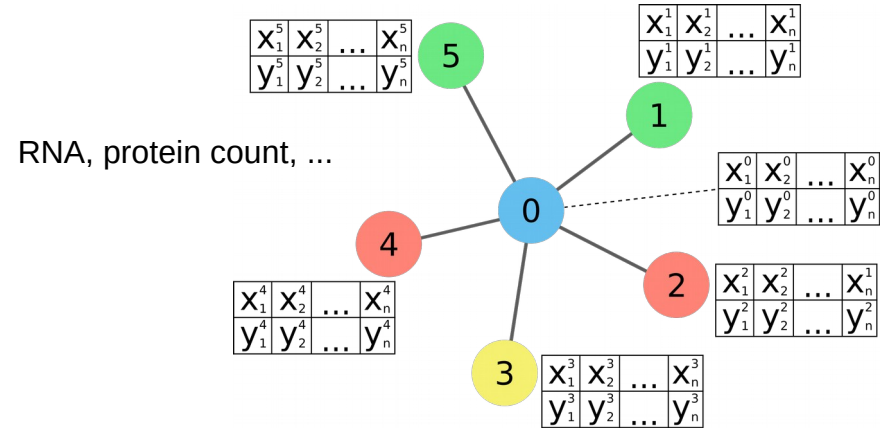Would some cell types interact preferentially with other cell types?

low

high

Z-scored mixing matrix

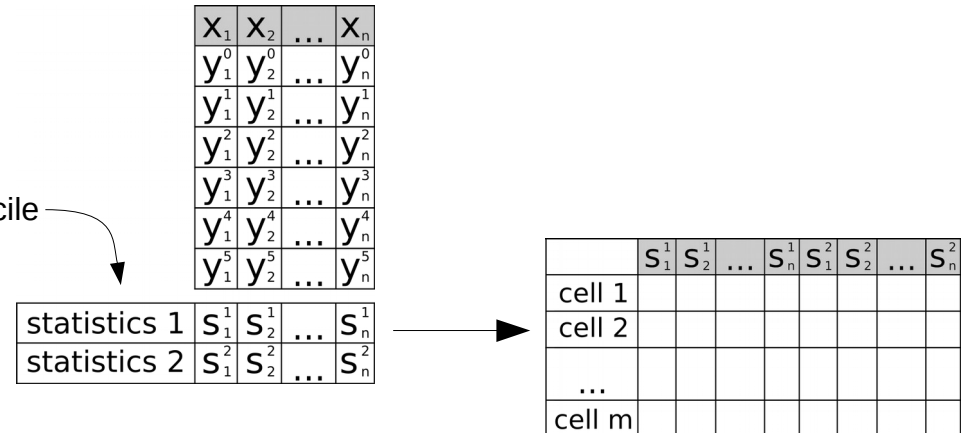|	Glutamatergic Neuron	GABA-ergic Neuron	Oligodendrocyte.3	Endothelial Cell	Astrocyte	Oligodendrocyte.2	Microglia	Oligodendrocyte.1
Glutamatergic Neuron	5.3	-6.6	0.5	0.15	-1.3	-1.4	-0.41	-0.78
GABA-ergic Neuron	-6.6	8.3	-2.1	0.14	-1.3	-1	0.34	0.51
Oligodendrocyte.3	0.5	-2.1	-0.97	0.11	0.31	1.6	0.15	0.34
Endothelial Cell	0.15	0.14	0.11	-0.45	1.1	-0.98	0.078	-0.54
Astrocyte	-1.3	-1.3	0.31	1.1	0.051	-0.41	-1	0.11
Oligodendrocyte.2	-1.4	-1	1.6	-0.98	-0.41	2.7	0.22	0.47
Microglia	-0.41	0.34	0.15	0.078	-1	0.22	-0.93	1.7
Oligodendrocyte.1	-0.78	0.51	0.34	-0.54	0.11	0.47	1.7	-0.27

Newman, 2002 & 2003

pval 0.05 ↔ zscore 1.96

Neighbors Aggregation Statistics

Are there local communities of single or multiple cell types / states ?
How gene expression or protein count is affected by spatial factors ?

RNA, protein count, ...

$\begin{array}{|c|c|c|c|} \hline x_1^5 & x_2^5 & \dots & x_n^5 \\ \hline y_1^5 & y_2^5 & \dots & y_n^5 \\ \hline \end{array}$ 5

$\begin{array}{|c|c|c|c|} \hline x_1^1 & x_2^1 & \dots & x_n^1 \\ \hline y_1^1 & y_2^1 & \dots & y_n^1 \\ \hline \end{array}$ 1

0   $\begin{array}{|c|c|c|c|} \hline x_1^0 & x_2^0 & \dots & x_n^0 \\ \hline y_1^0 & y_2^0 & \dots & y_n^0 \\ \hline \end{array}$

4

$\begin{array}{|c|c|c|c|} \hline x_1^4 & x_2^4 & \dots & x_n^4 \\ \hline y_1^4 & y_2^4 & \dots & y_n^4 \\ \hline \end{array}$

2   $\begin{array}{|c|c|c|c|} \hline x_1^2 & x_2^2 & \dots & x_n^1 \\ \hline y_1^2 & y_2^2 & \dots & y_n^2 \\ \hline \end{array}$

3   $\begin{array}{|c|c|c|c|} \hline x_1^3 & x_2^3 & \dots & x_n^3 \\ \hline y_1^3 & y_2^3 & \dots & y_n^3 \\ \hline \end{array}$

$\begin{array}{|c|c|c|c|} \hline X_1 & X_2 & \dots & X_n \\ \hline y_1^0 & y_2^0 & \dots & y_n^0 \\ \hline y_1^1 & y_2^1 & \dots & y_n^1 \\ \hline y_1^2 & y_2^2 & \dots & y_n^2 \\ \hline y_1^3 & y_2^3 & \dots & y_n^3 \\ \hline y_1^4 & y_2^4 & \dots & y_n^4 \\ \hline y_1^5 & y_2^5 & \dots & y_n^5 \\ \hline \end{array}$

Mean
Std
Median
Interdecile
...

$\begin{array}{|c|c|c|c|c|} \hline \text{statistics 1} & s_1^1 & s_2^1 & \dots & s_n^1 \\ \hline \text{statistics 2} & s_1^2 & s_2^2 & \dots & s_n^2 \\ \hline \end{array}$

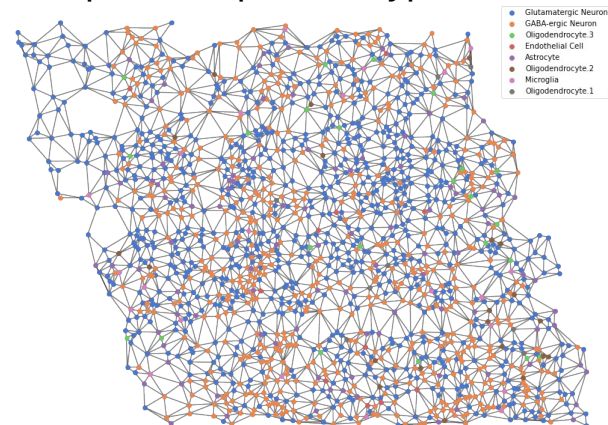|	s_1^1	s_2^1	...	s_n^1	s_1^2	s_2^2	...	s_n^2
cell 1								
cell 2								
...								
cell m								

HDBSCAN clustering of NAS on UMAP projection
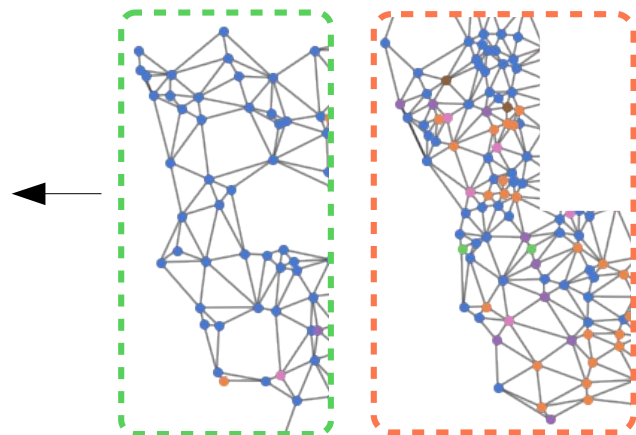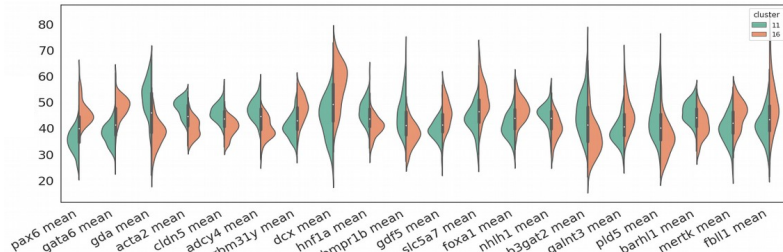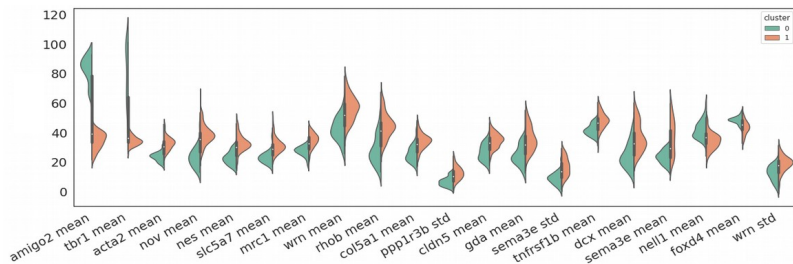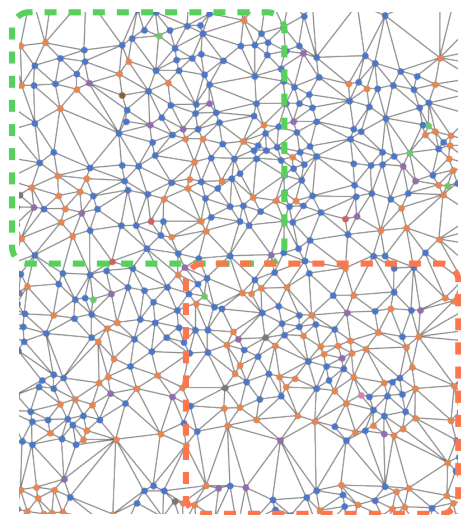
Spatial map of detected areas

Spatial map of cell types

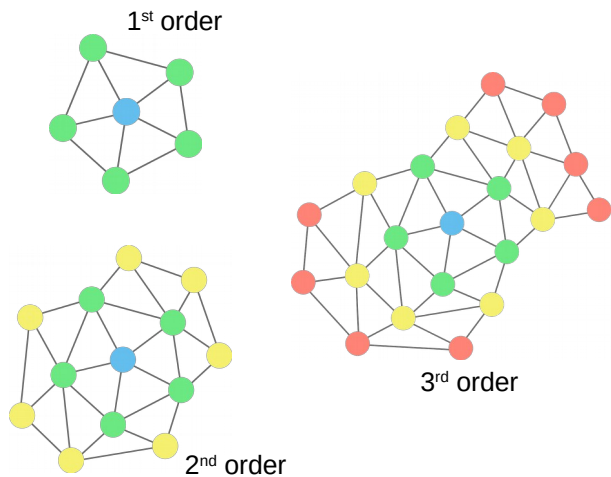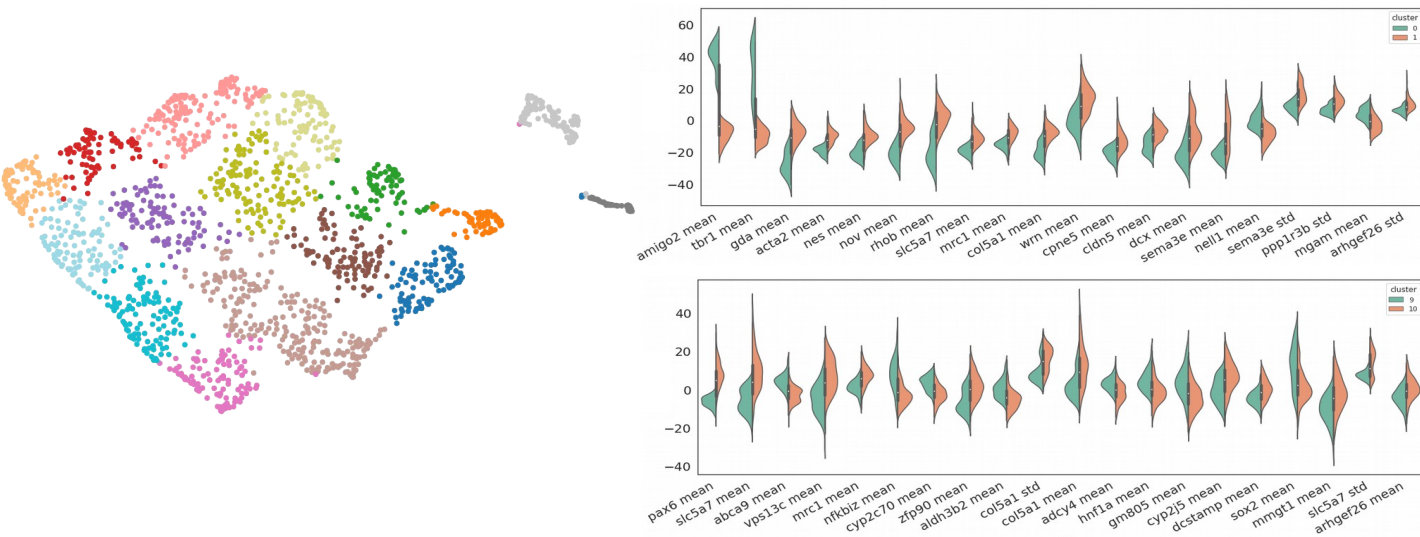
Differential NAS analysis

Higher order neighbors

To detect wider structures

1st order

2nd order

3rd order

UMAP projections of NAS

1st order

2nd order

3rd order

Phenotype susbtraction

Contribution of spatial factors and cellular interactions to omics measurements