Graph representations and niche reconstruction

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ELIXIR Spatial Omics Data Analysis

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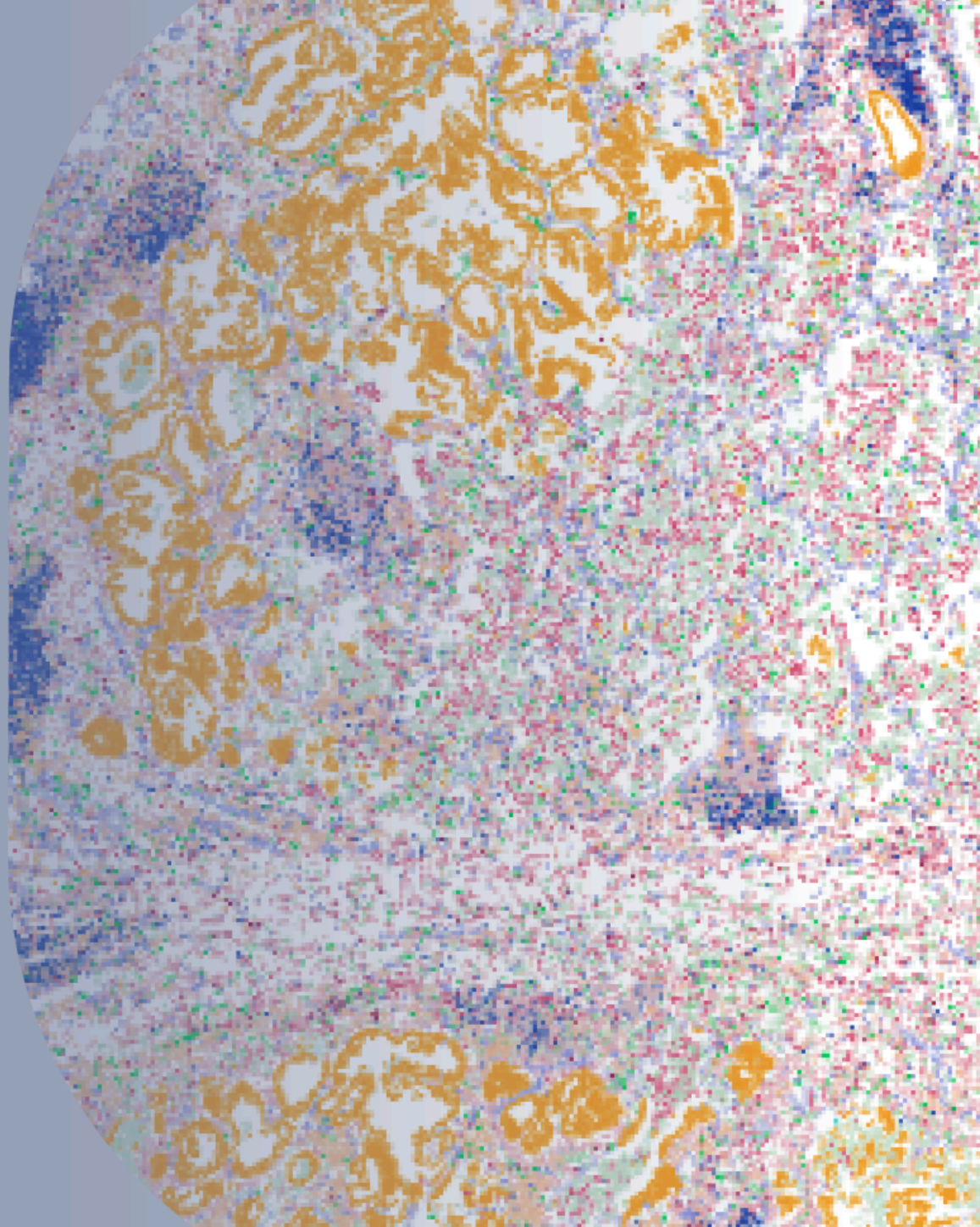

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What are graphs and niches?

Dictionary

Definitions from Oxford Languages · Learn more

graph[1]

/grɑːf/

noun

a diagram showing the relation between variable quantities, typically of two variables, each measured along one of a pair of axes at right angles.

Similar: chart | diagram | grid | histogram | bar chart | pie chart

verb

plot or trace on a graph.

Similar: plot | trace | draw up | delineate

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niche

/niːʃ,nɪtʃ/

noun

1. a comfortable or suitable position in life or employment.
   "he is now a partner at a leading law firm and feels he has found his niche"

   Similar: ideal position | calling | vocation | métier | place | function | job
2. a specialized segment of the market for a particular kind of product or service.
   "he believes he has found a niche in the market"

adjective

denoting products, services, or interests that appeal to a small, specialized section of the population.
"other companies in this space had to adapt to being niche players"

verb

place (something) in a niche or recess.
"these elements were niched within the shadowy reaches"

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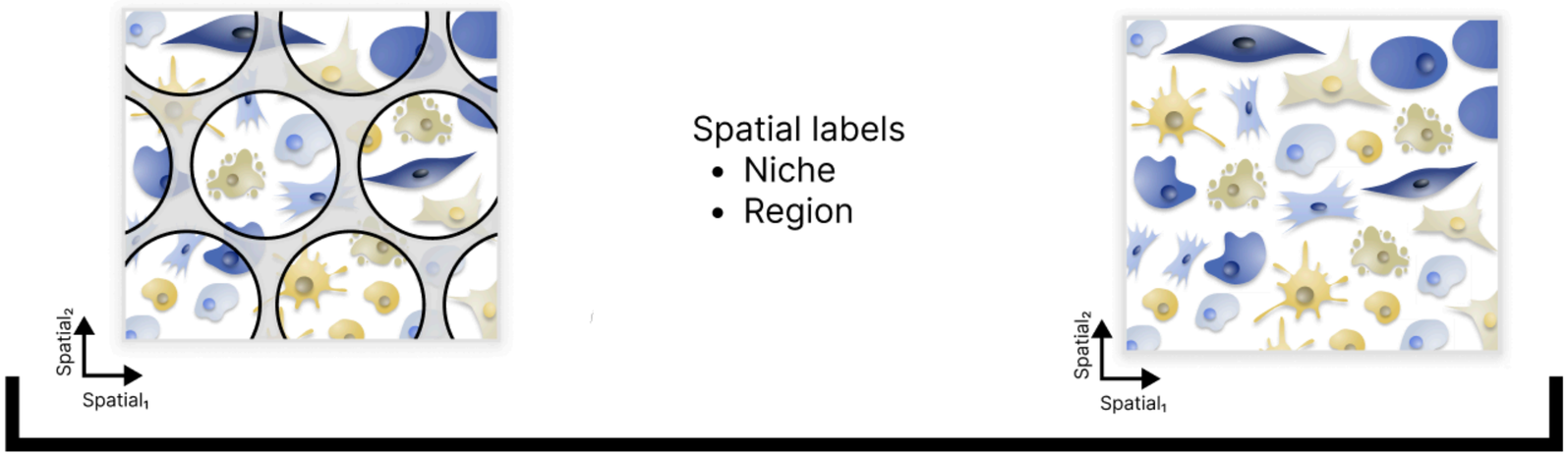

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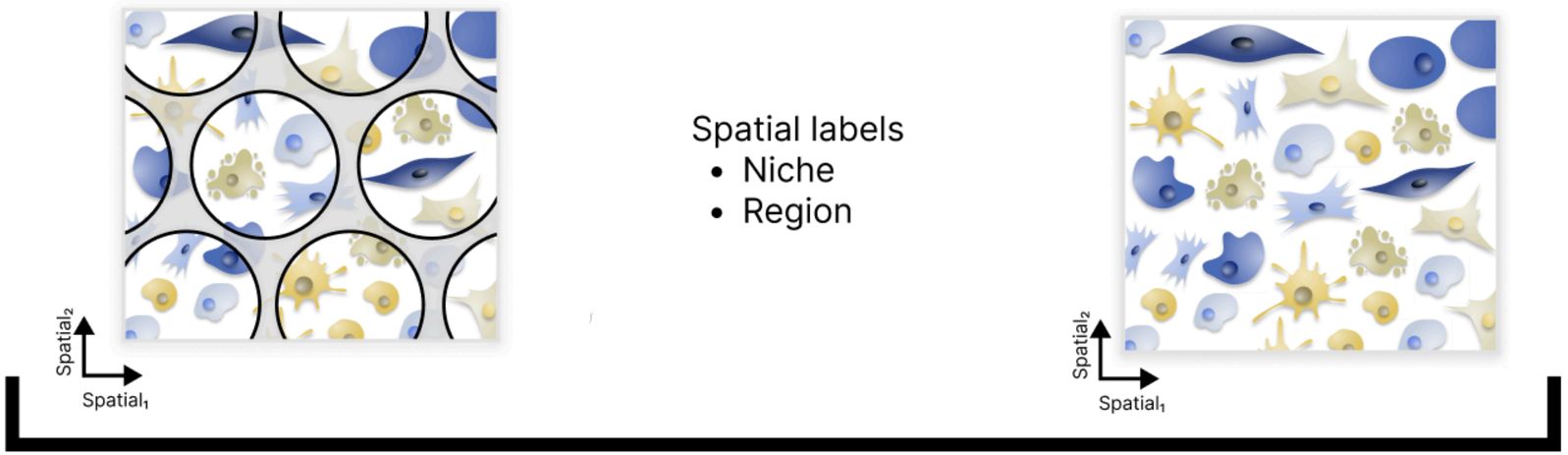

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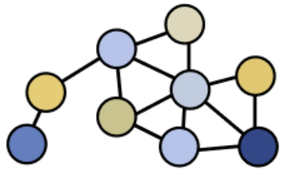

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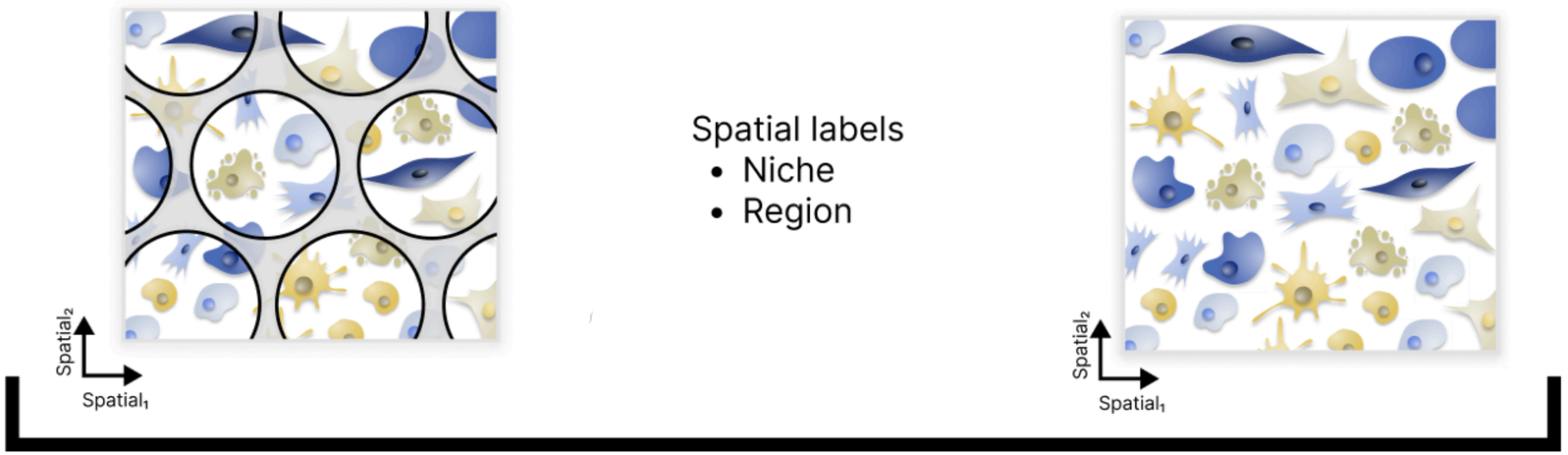

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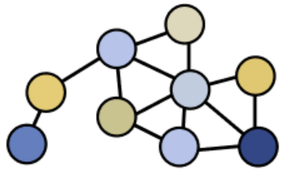

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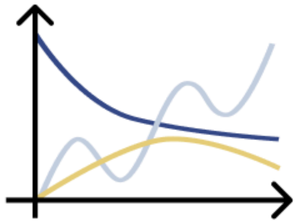
Spatial metrics



- GEX changes
- Spatially variable genes

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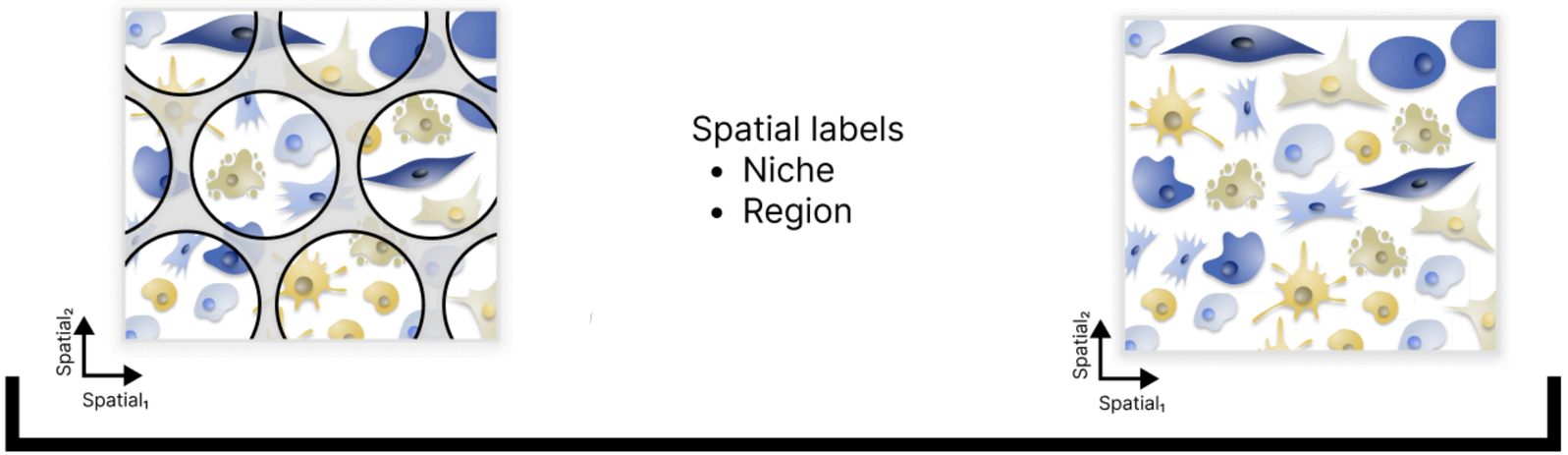
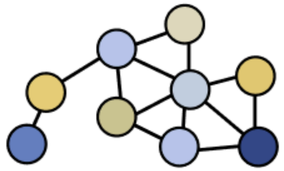
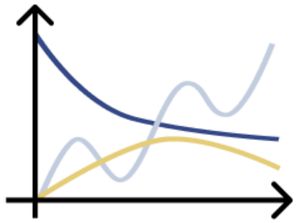


Spatial graph



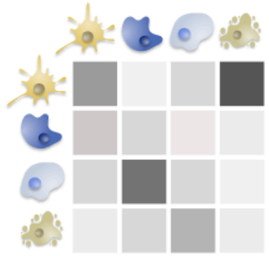
- Graph structure based on physical distances

Spatial metrics



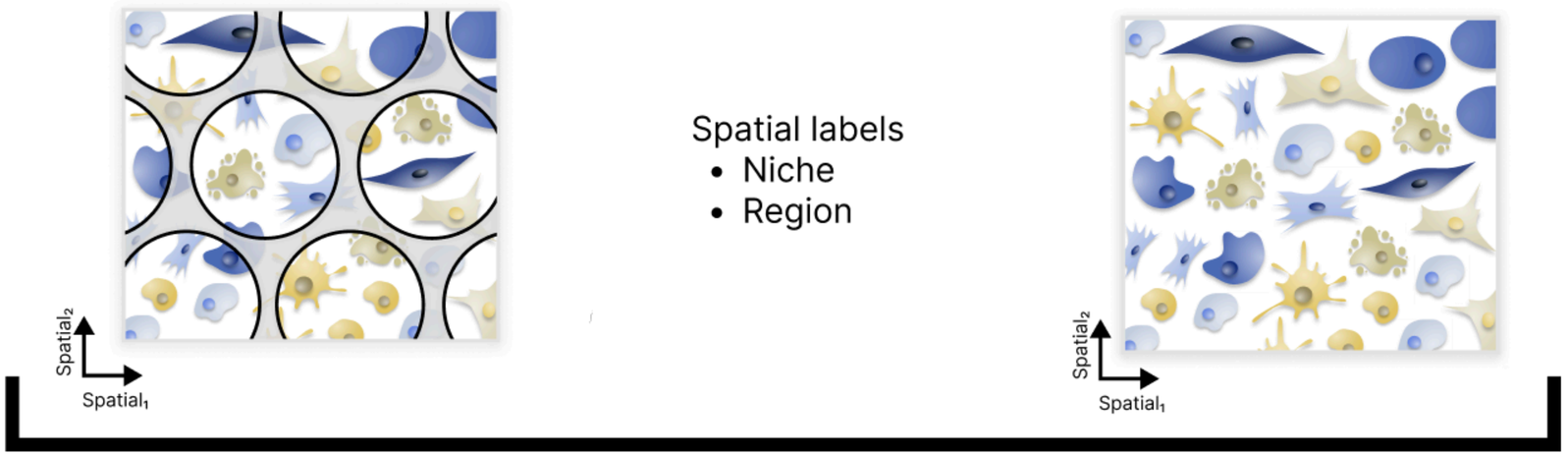
- GEX changes
- Spatially variable genes

Spatial composition

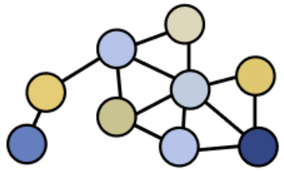


- Neighbourhood analysis
- Tumor mirco-environments

What are graphs and niches in the context of spatial omics?



Spatial graph



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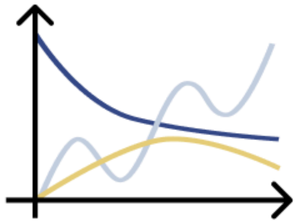

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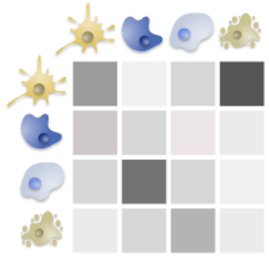
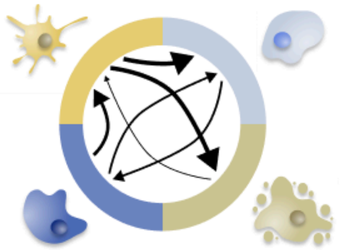


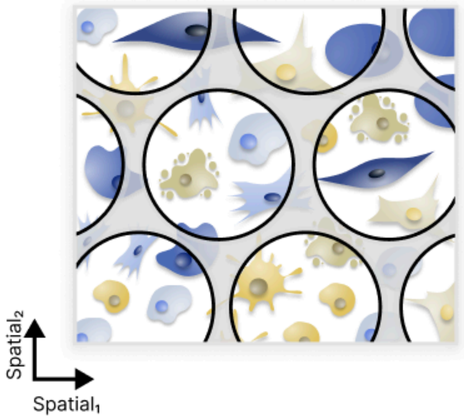
- Neighbourhood analysis
- Tumor mirco-environments

Cell-cell communication

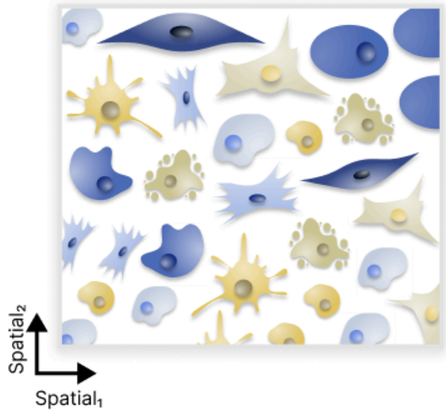


- Constraint cell-cell communication

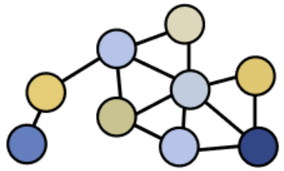
What are graphs and niches in the context of spatial omics?



Spatial labels
- Niche
- Region



Spatial graph



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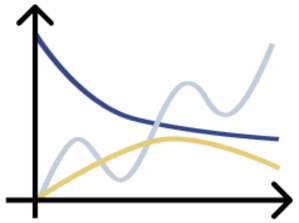

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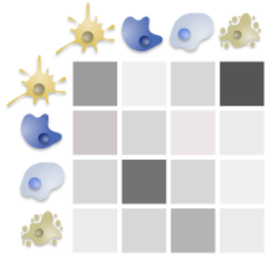

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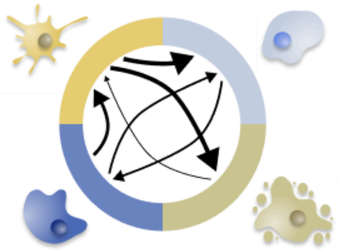
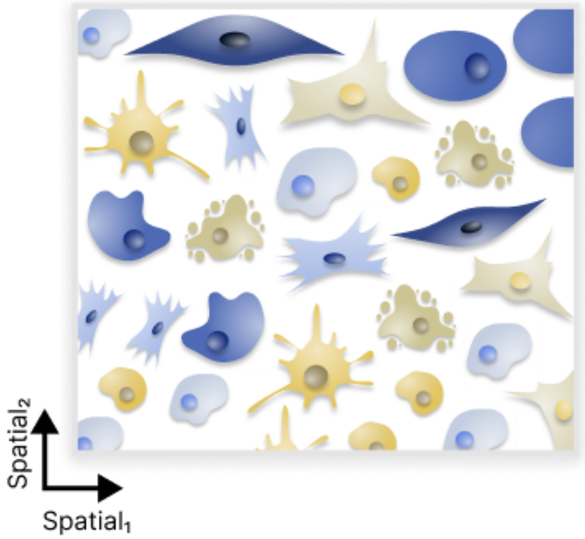


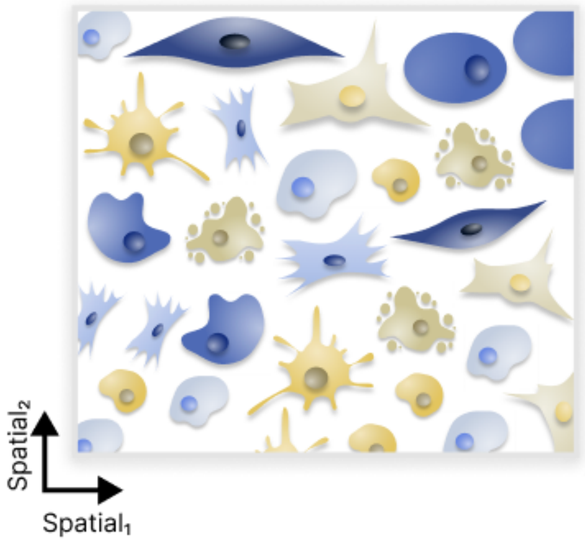
- Constraint cell-cell communication

Defining spatial graphs of cells based on spatial proximity

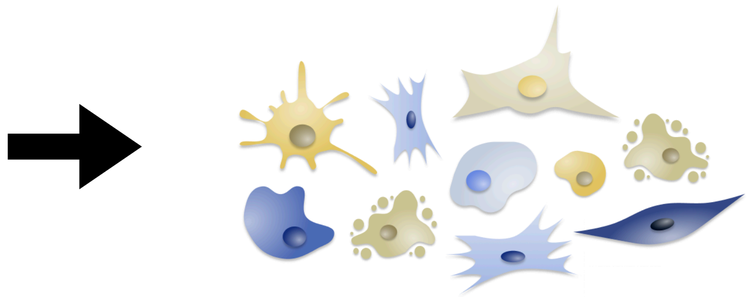


Segmented targeted spatial omics

Defining spatial graphs of cells based on spatial proximity



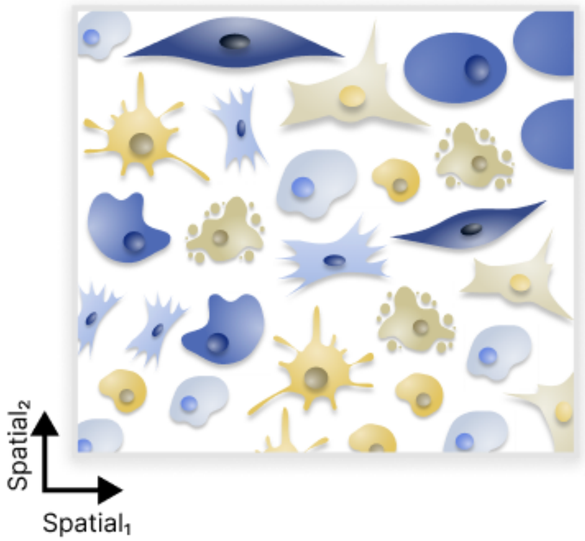
Segmented targeted spatial omics



Cells resolved at their physical location

- Coordinates
- Gene expression vector
- Cell type annotations

Defining spatial graphs of cells based on spatial proximity



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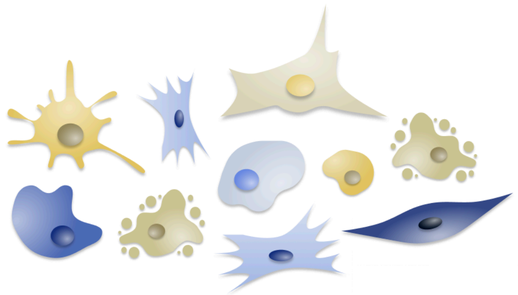

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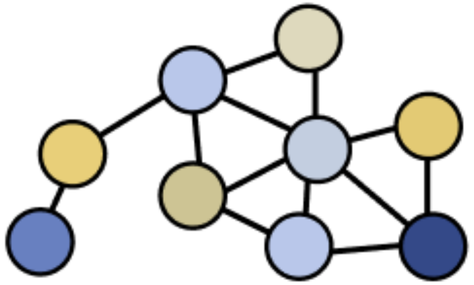
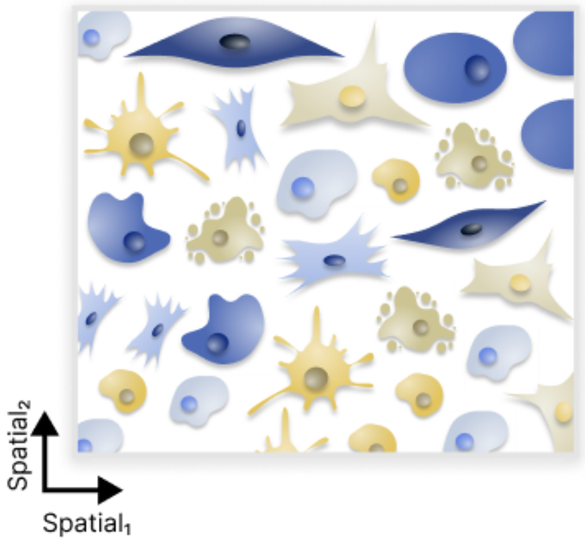


Spatial graph of cells

Defining spatial graphs of cells based on spatial proximity



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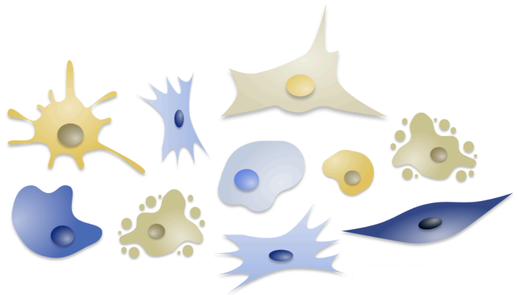

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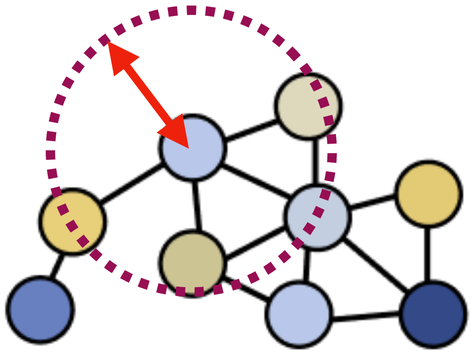
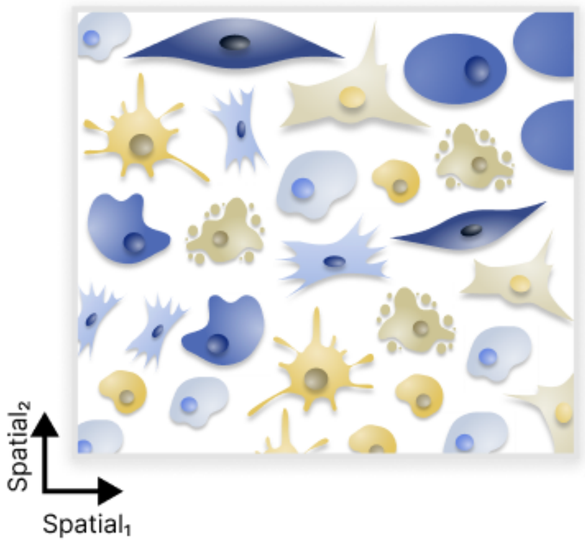
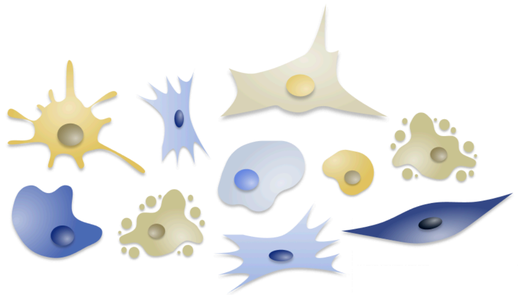


Spatial graph of cells

Defining spatial graphs of cells based on spatial proximity



Segmented targeted spatial omics



Cells resolved at their physical location

- Coordinates
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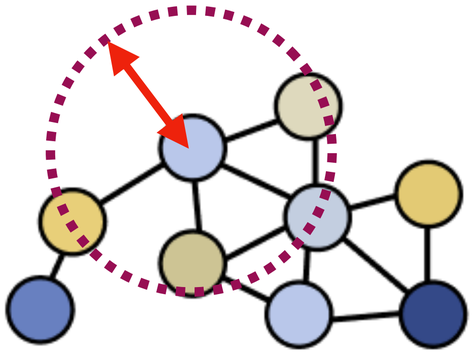
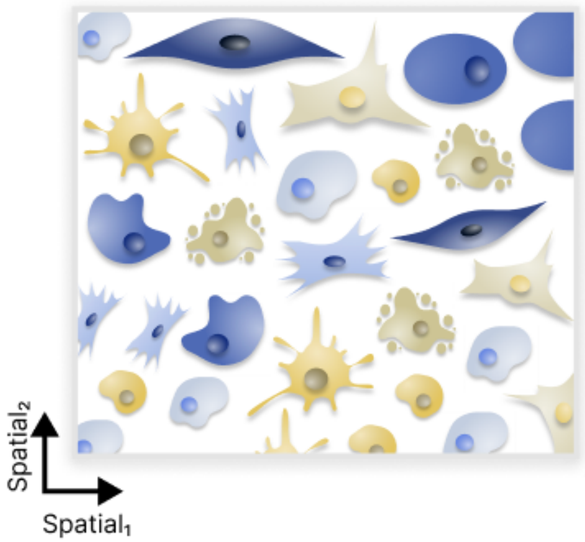
- Cell type annotations

Resolution/ radius



Spatial graph of cells

Defining spatial graphs of cells based on spatial proximity



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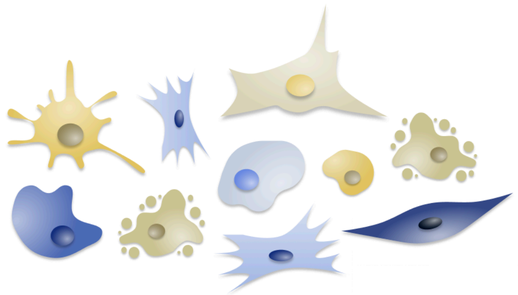

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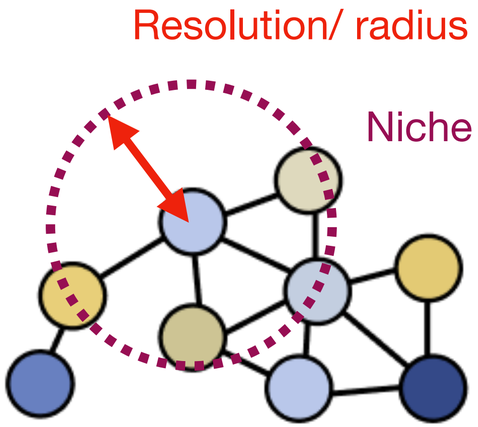
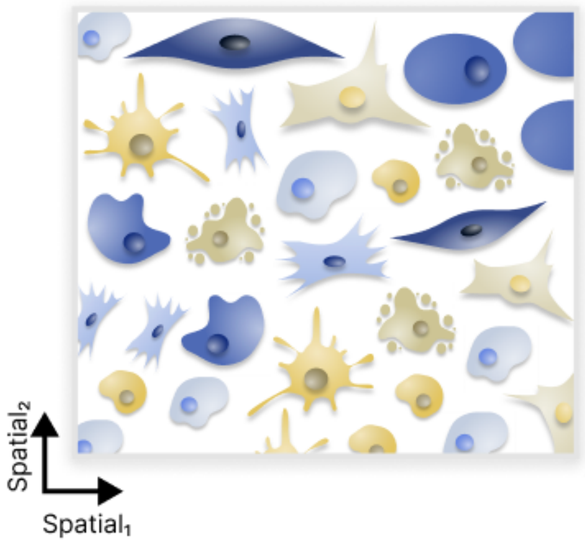


Spatial graph of cells

Defining spatial graphs of cells based on spatial proximity



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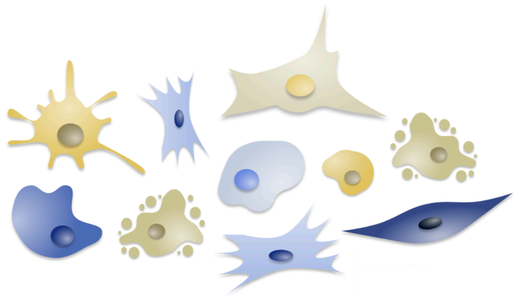

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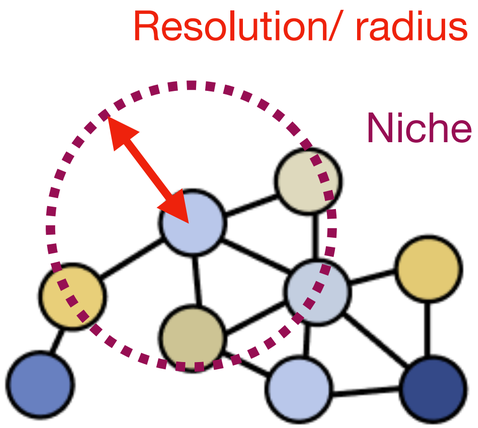
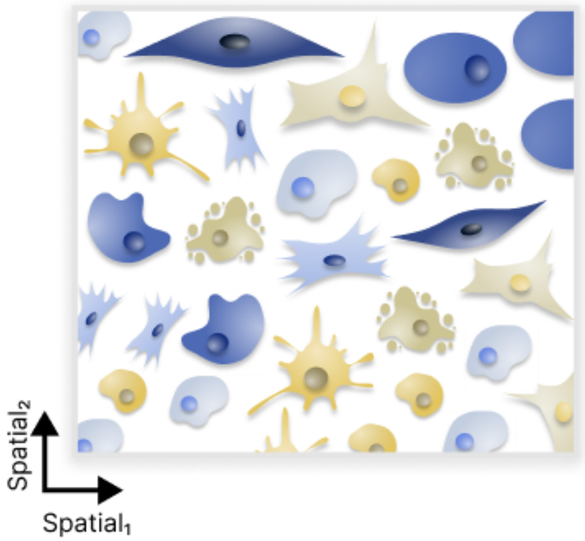


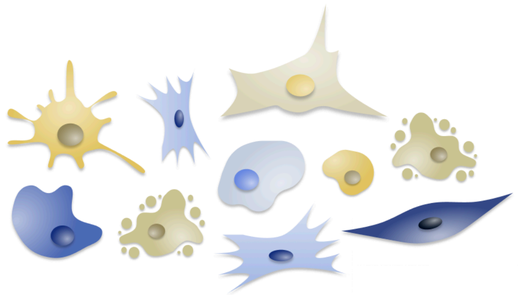
Spatial graph of cells

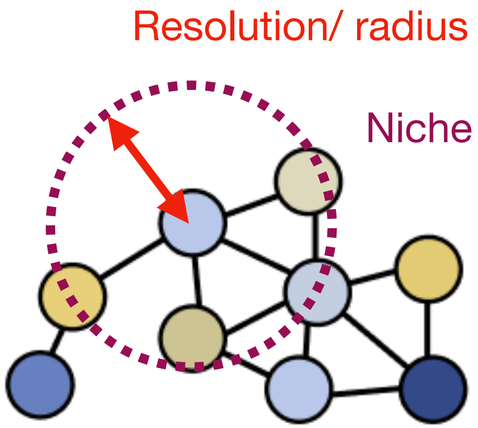
$A \in \{0;1\}^{\{c \times c\}}$ adjacency matrix

with $a_{ij} = 1$ if $d(x_i,x_j) \leq r$ with d being the euclidean distance between two cells in the slide

Defining spatial graphs of cells based on spatial proximity







Segmented targeted spatial omics

Cells resolved at their physical location

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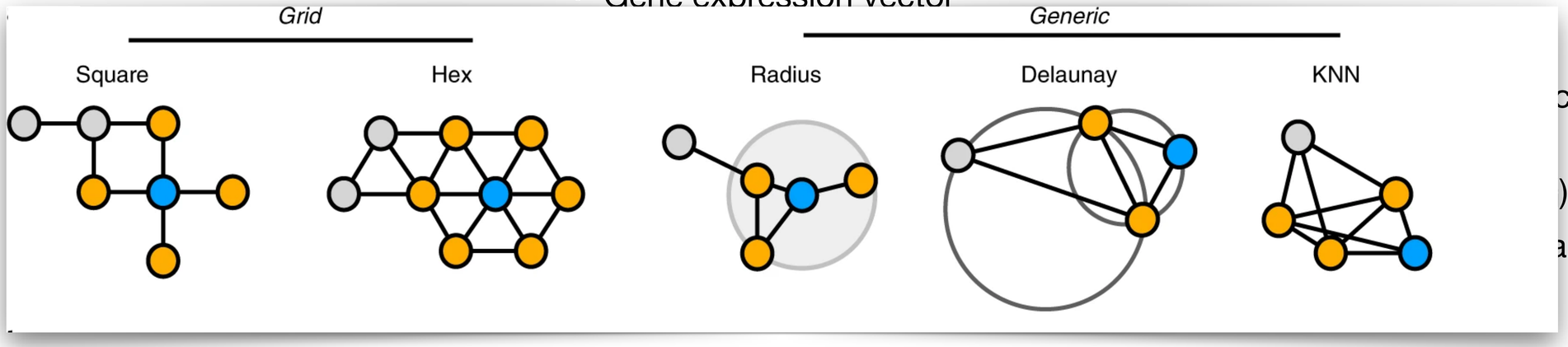
Spatial graph of cells



cency matrix

) ≤ r with d being

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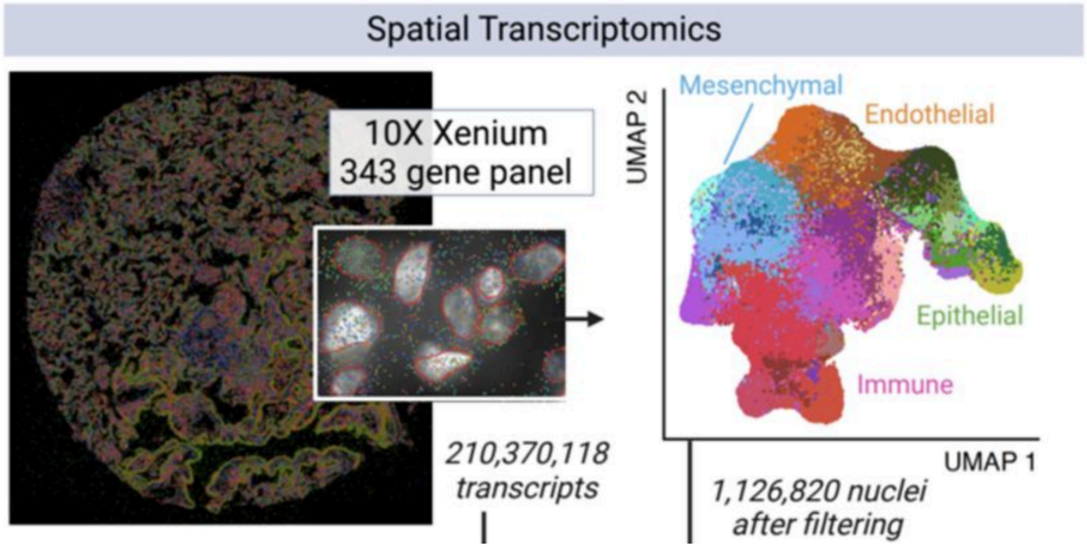
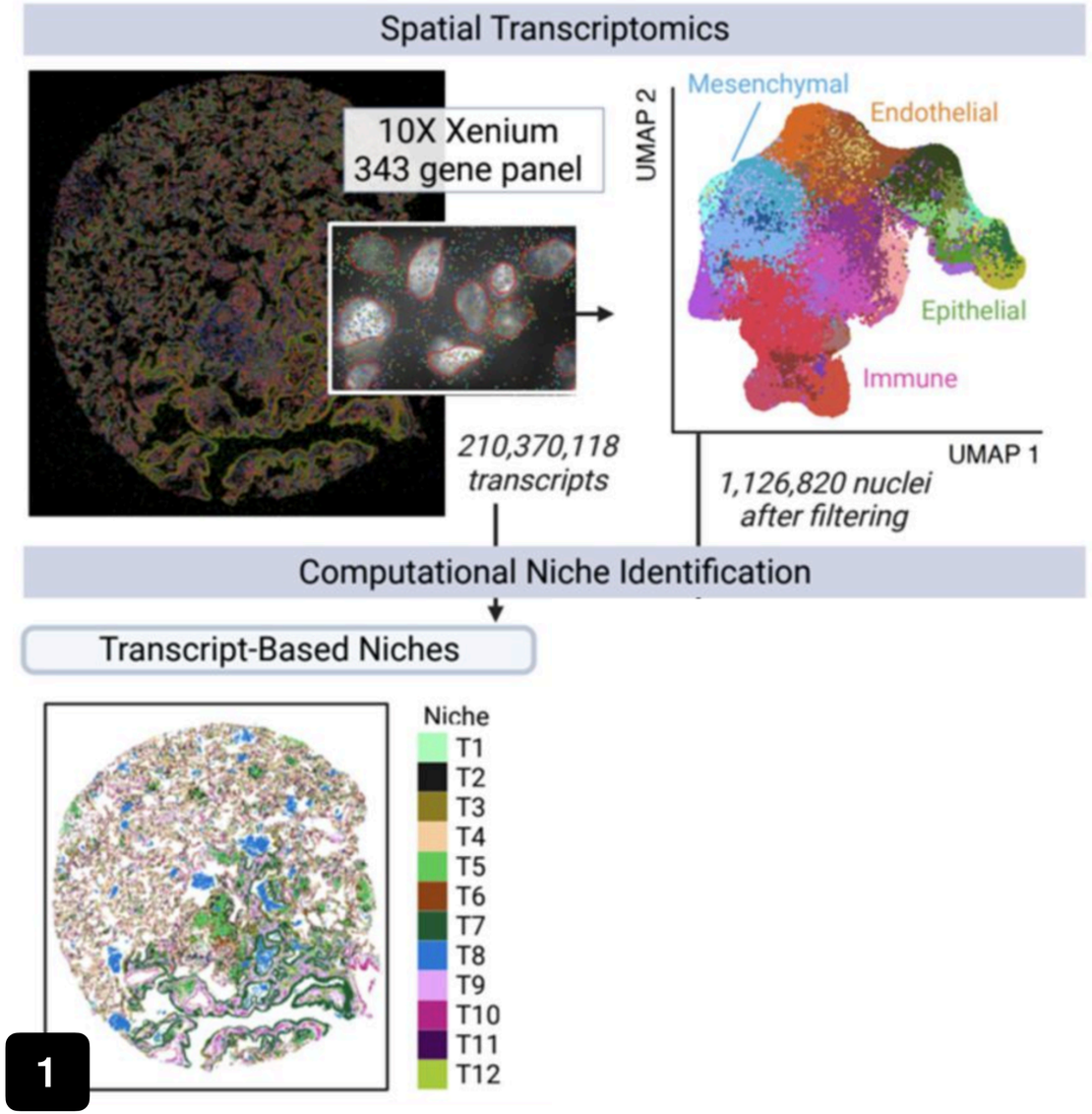
Palla, G., Spitzer, H., Klein, M. *et al.* Squidpy: a scalable framework for spatial omics analysis. *Nat Methods* **19**, 171–178 (2022). https://doi.org/10.1038/s41592-021-01358-2

How to define niche labels in practice?



Vannan, A., *et al.* Image-based spatial transcriptomics identifies molecular niche dysregulation associated with distal lung remodeling in pulmonary fibrosis. b*ioRix*, (2023).

How to define niche labels in practice?



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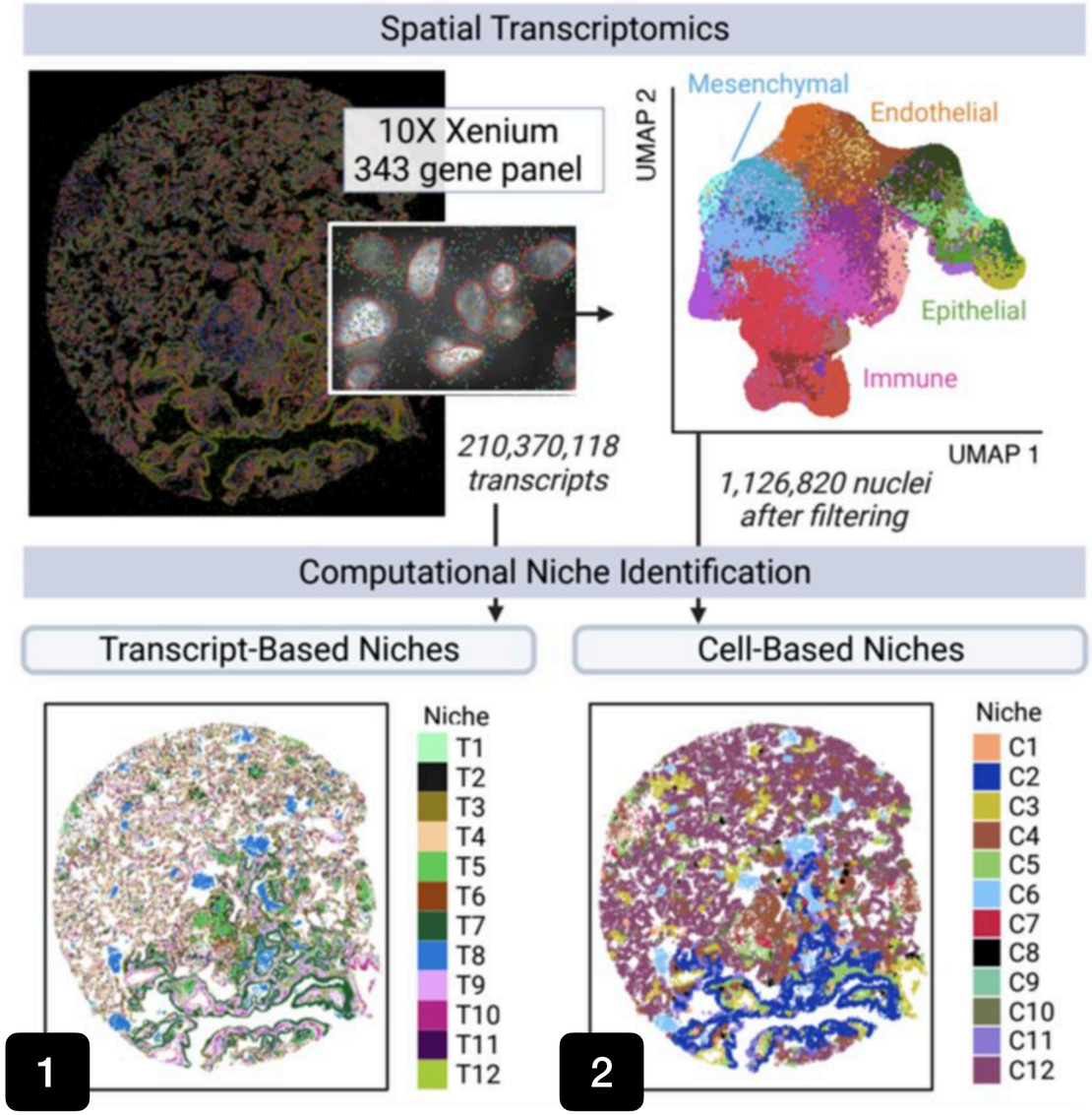

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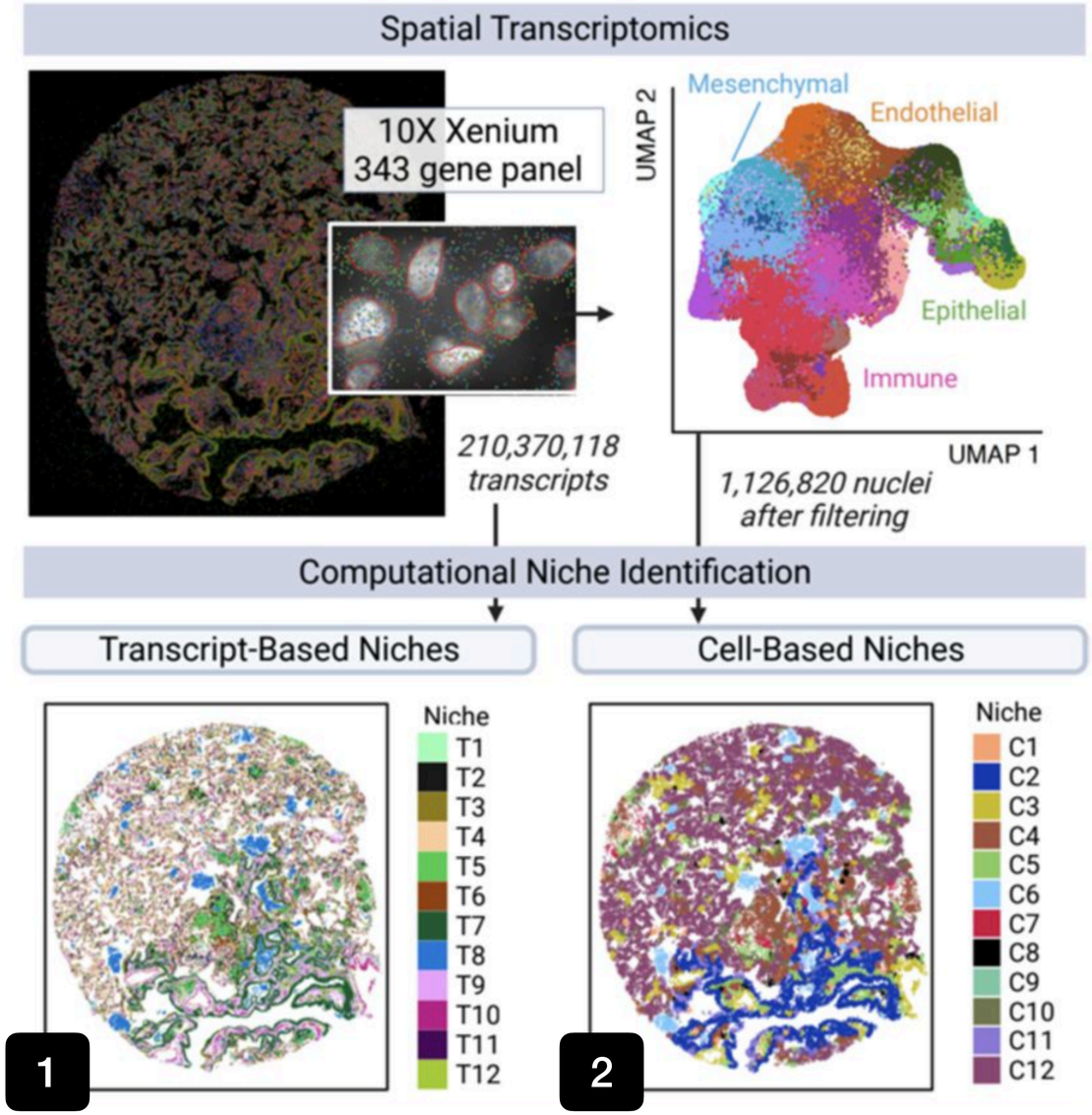

Communication-based Niches

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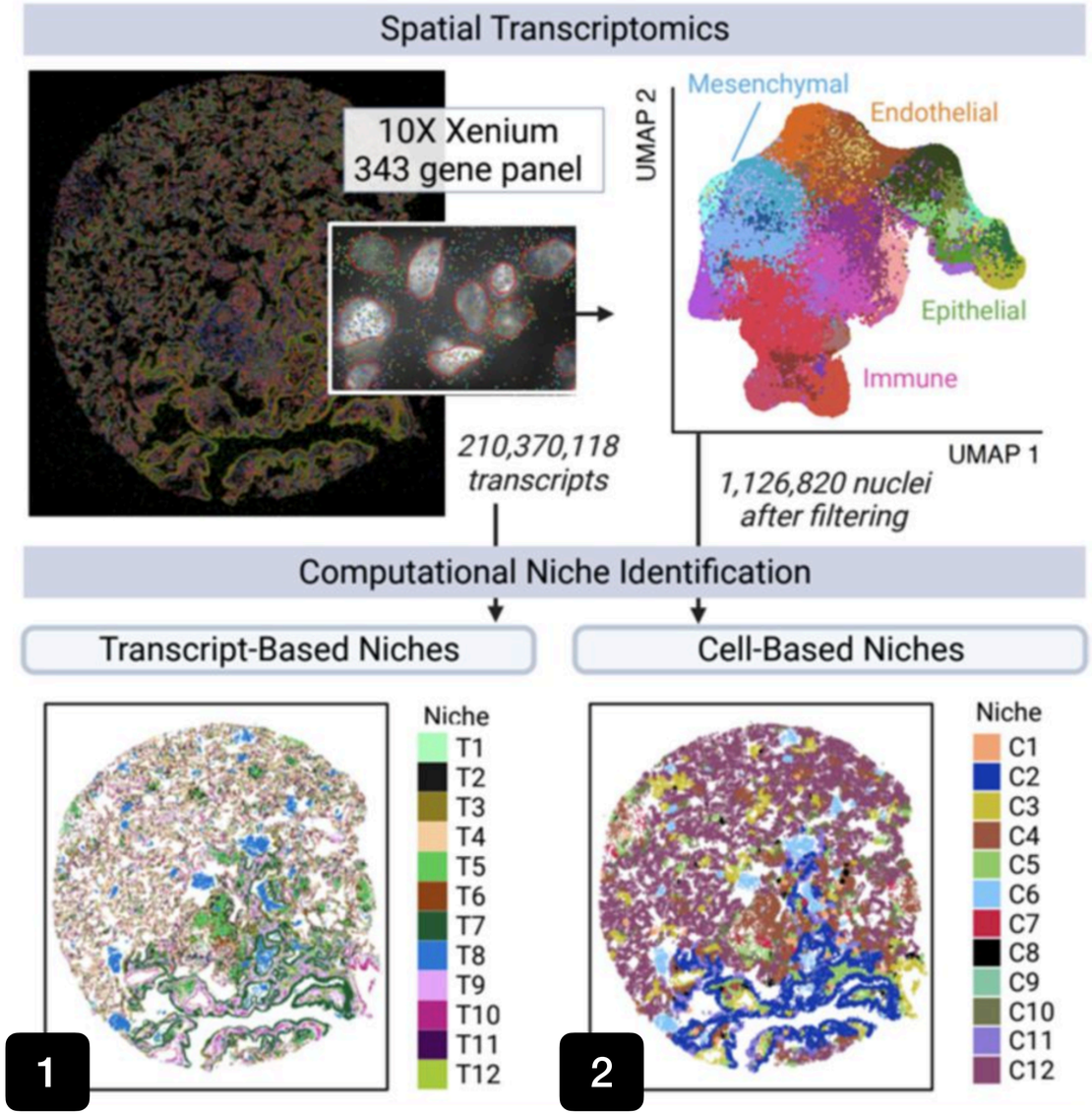


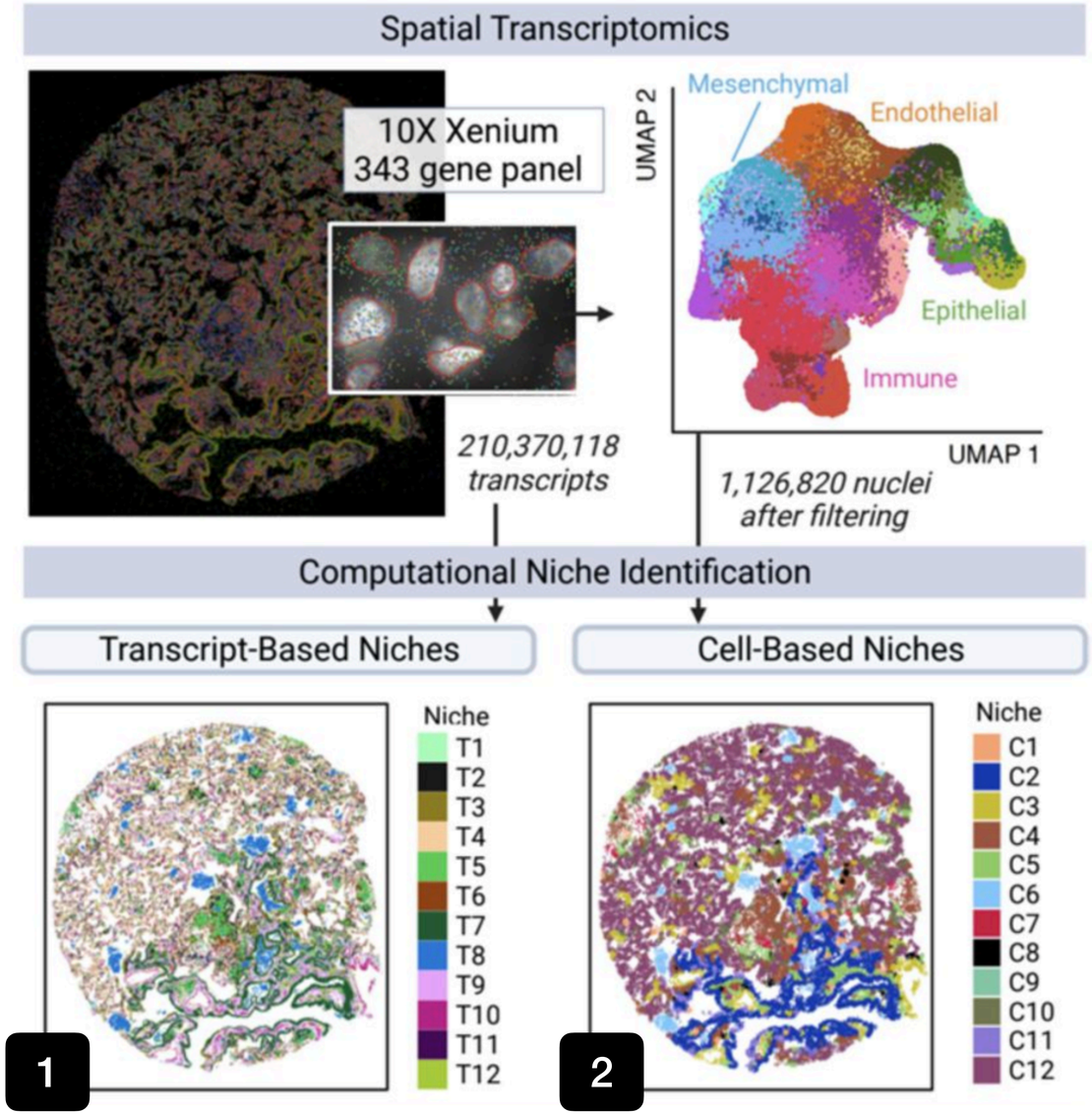
Note:

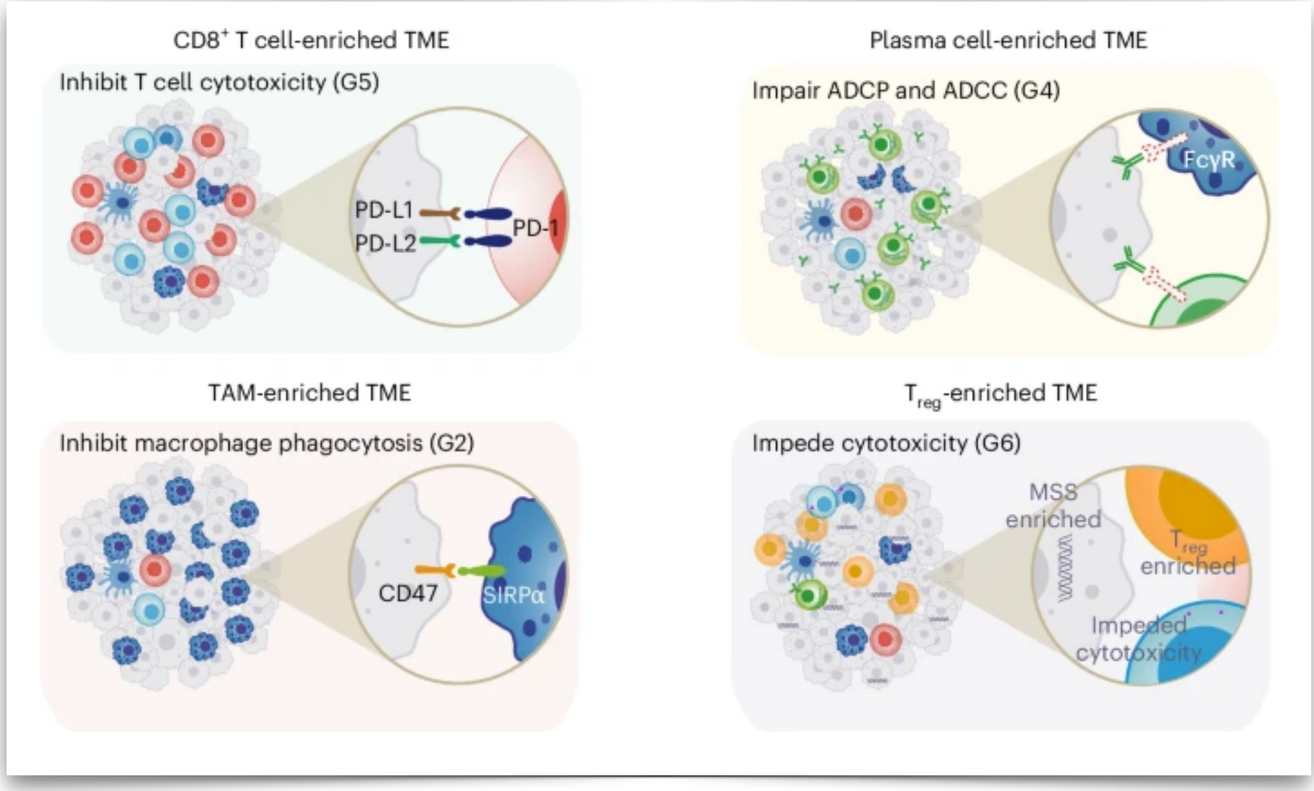
- Niche labels can be very tissue dependent
- Niche labels strongly depend on the specific use-case you are interested in
- Batch-effects might not be only technical variability, but biological differences

Communication-based Niches

Vannan, A., *et al.* Image-based spatial transcriptomics identifies molecular niche dysregulation associated with distal lung remodeling in pulmonary fibrosis. b*ioRix*, (2023).

How to define niche labels in practice?





Chu, X., *et al.* Integrative single-cell analysis of human colorectal cancer reveals patient stratification with distinct immune evasion mechanisms. *Nat Cancer* **5**, (2024).

Communication-based Niches

3

Vannan, A., *et al.* b*ioRix*, (2023).

Transcription-based niches

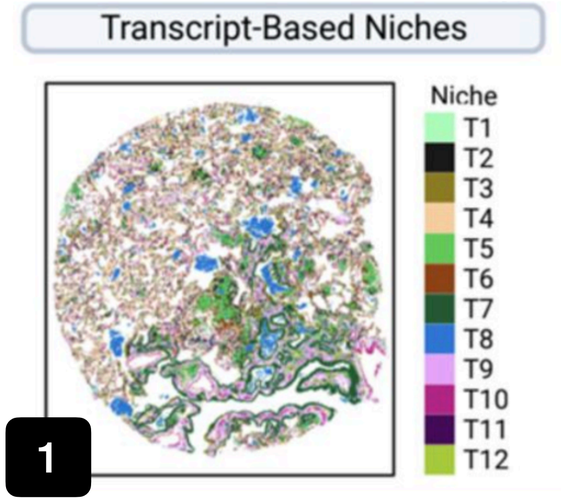
i.e. define a niche based on the expression profile of its surrounding neighbours

$A \in \{0;1\}^{\{c \times c\}}$ adjacency matrix

$Y \in \mathbb{R}^{+,\{c \times g\}}$ gene expression matrix

with c number of cells,

g number of genes



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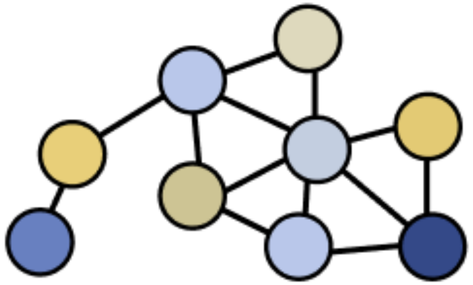
Spatial graph of cells



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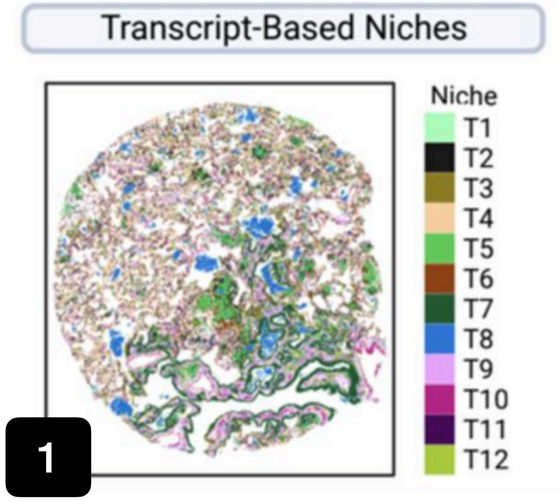

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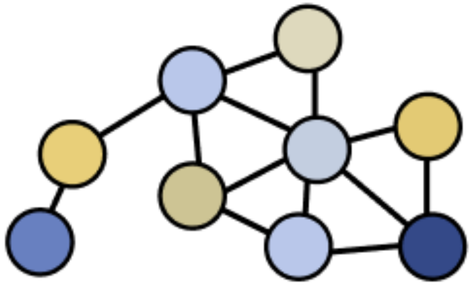

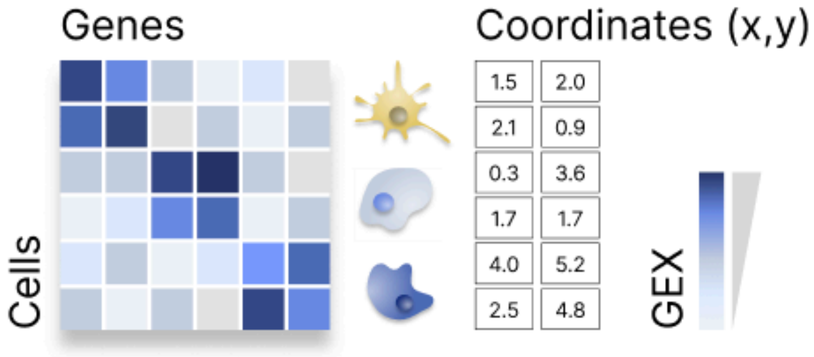

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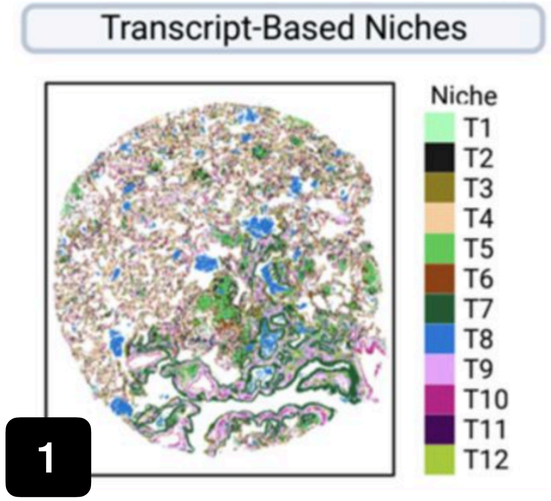

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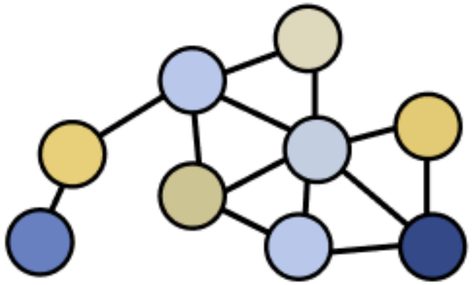

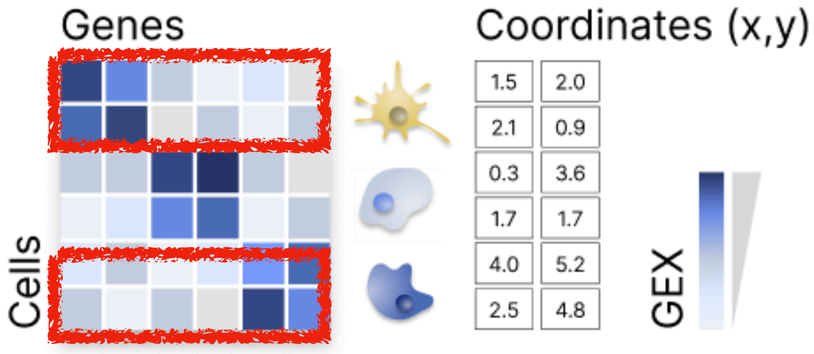

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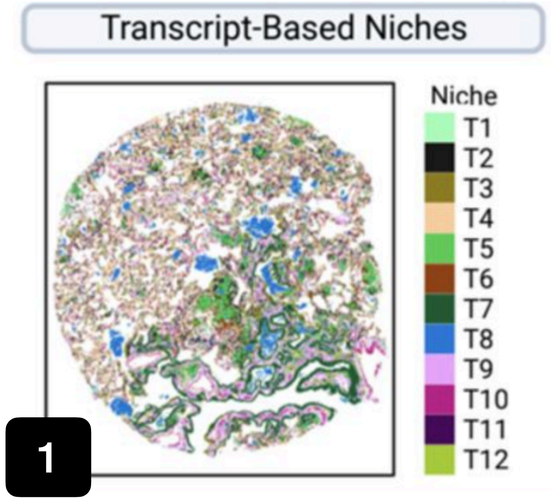
with c number of cells,

g number of genes



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Transcription-based niches

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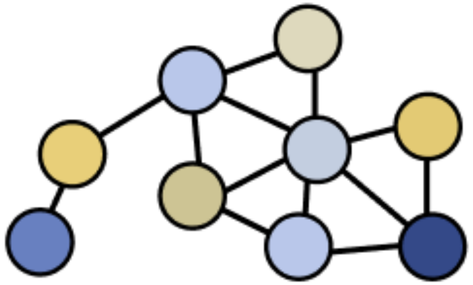

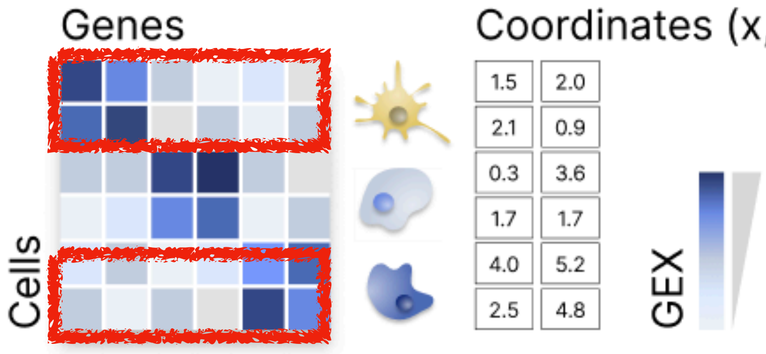

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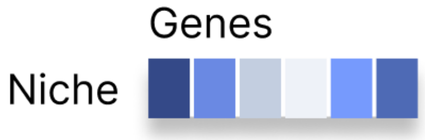

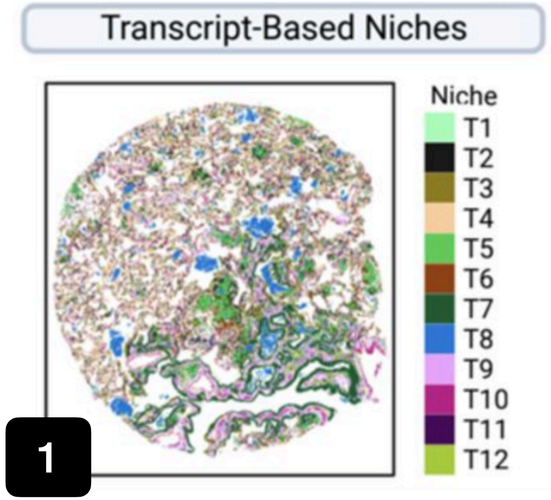

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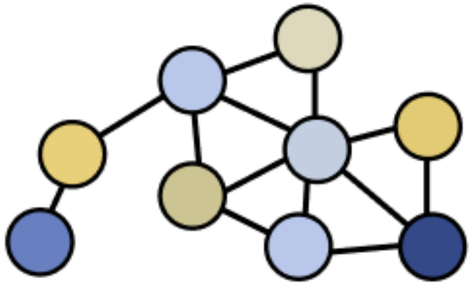

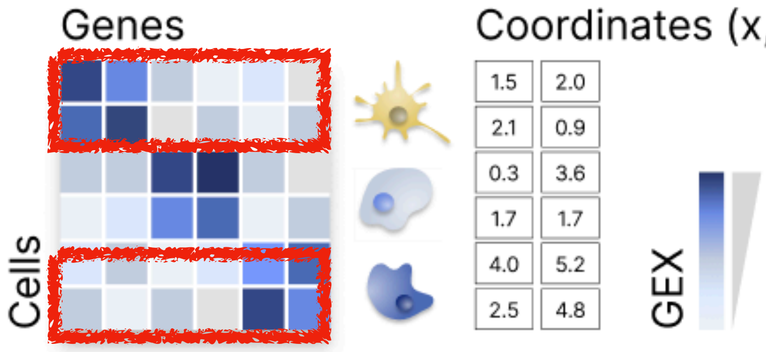

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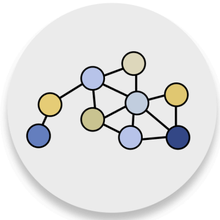
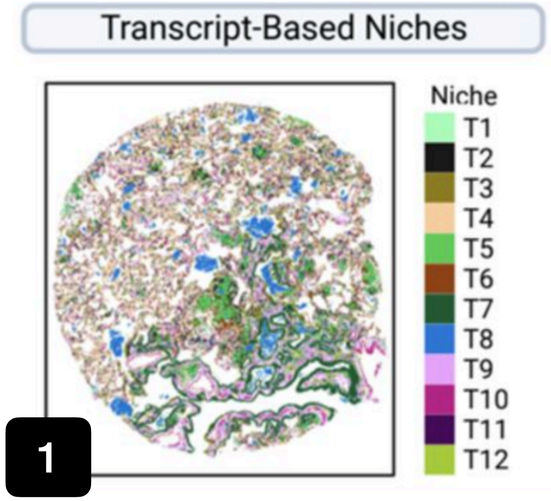


Trivial example: pseudo Visium spots

$\sum Y \cdot A$



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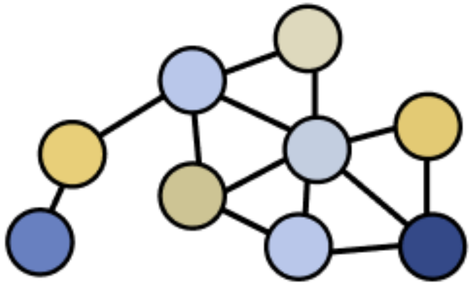


Coordinates (x,y)

1.5 2.0

$A \in \{0;1\}^{\{c \times c\}}$ adjacency matrix

sion matrix

es

Article | Open access | Published: 27 February 2024

BANKSY unifies cell typing and tissue domain segmentation for scalable spatial omics data analysis

Vipul Singhal, Nigel Chou, Joseph Lee, Yifei Yue, Jinyue Liu, Wan Kee Chock, Li Lin, Yun-Ching Chang, Erica Mei Ling Teo, Jonathan Aow, Hwee Kuan Lee, Kok Hao Chen & Shyam Prabhakar

Nature Genetics **56**, 431–441 (2024) | Cite this article

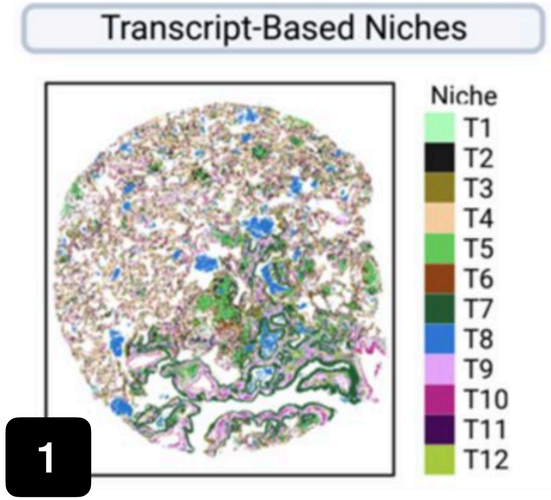
Aggreg

For each gene q, we computed the mean expression in the neighborhood of cell $u \in \mathcal{U}$ as:

$$M_u^{(q)} = \sum_{v \in \eta_{k_{\text{geom}}}^u} g_v^{(q)} \Gamma_{uv}^{k_{\text{geom}}}$$

where $g_v^{(q)}$ is the expression of the qth gene in neighboring cell v and the term $\Gamma_{uv}^{k_{\text{geom}}}$ is a Gaussian weighting envelope defined as:

$$\Gamma_{uv}^{k_{\text{geom}}} = \frac{\exp \frac{-r_{uv}^2}{r_{u\bar{v}}^2}}{\sum_{w \in \eta_{k_{\text{geom}}}^u} \left(\exp \frac{-r_{uw}^2}{r_{u\bar{v}}^2} \right)}$$



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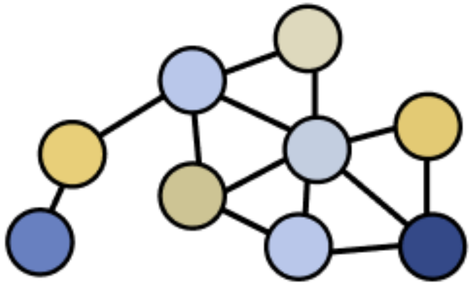

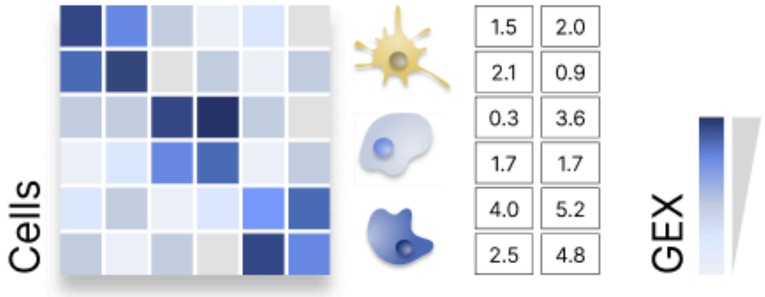

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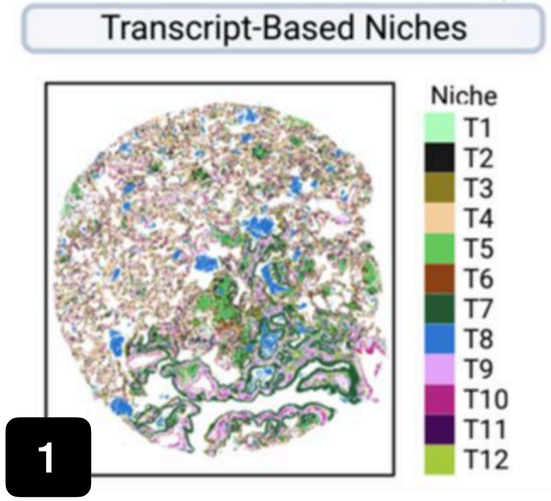

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Cell-based niches

i.e. define a niche based on the composition of neighbouring cell types

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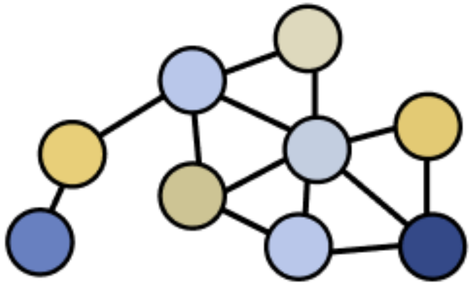

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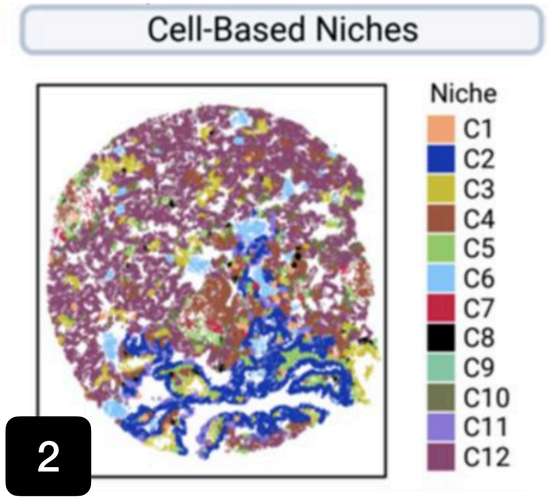

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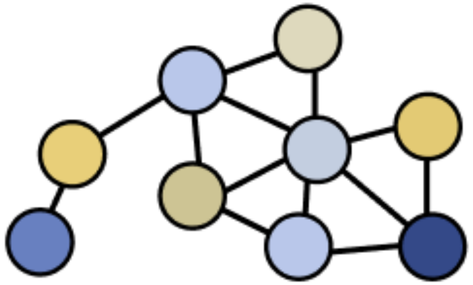

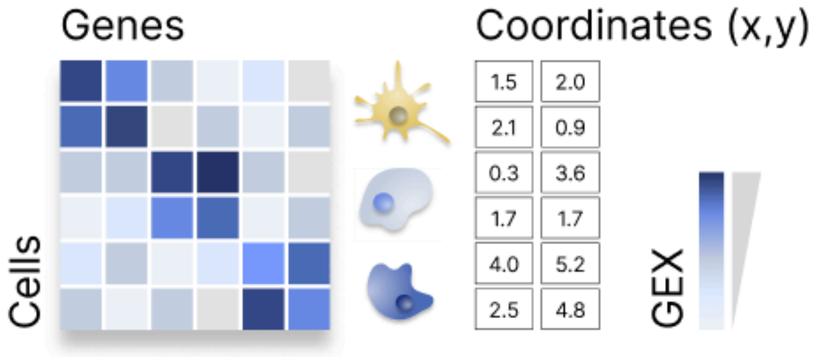

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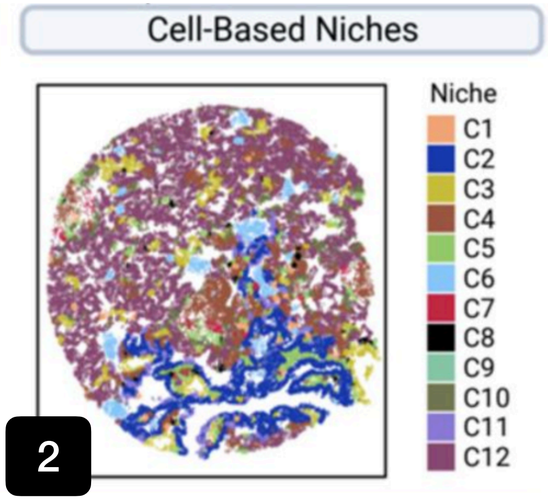

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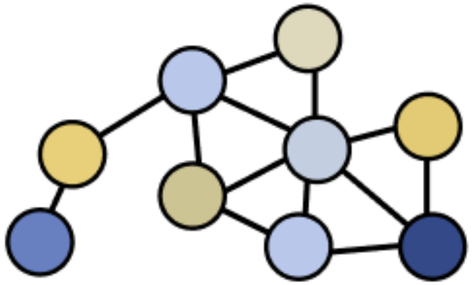

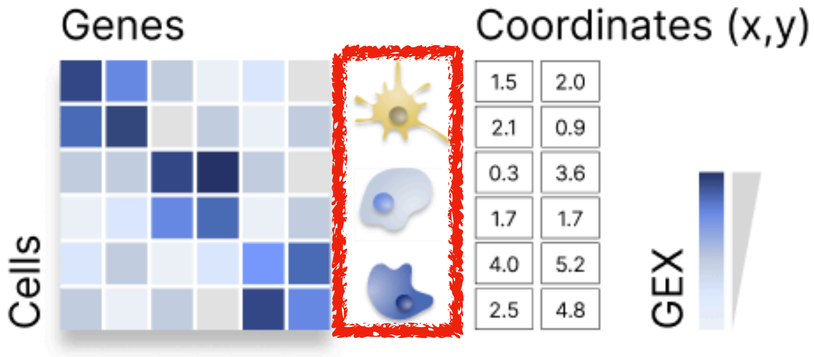

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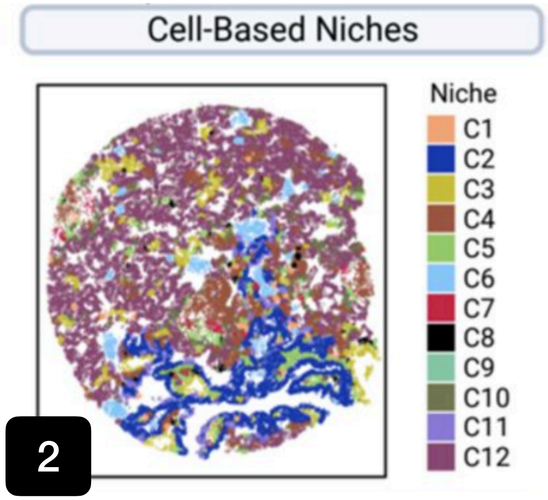

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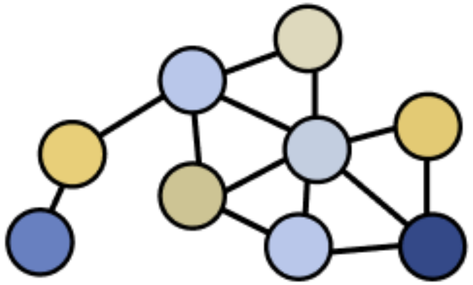

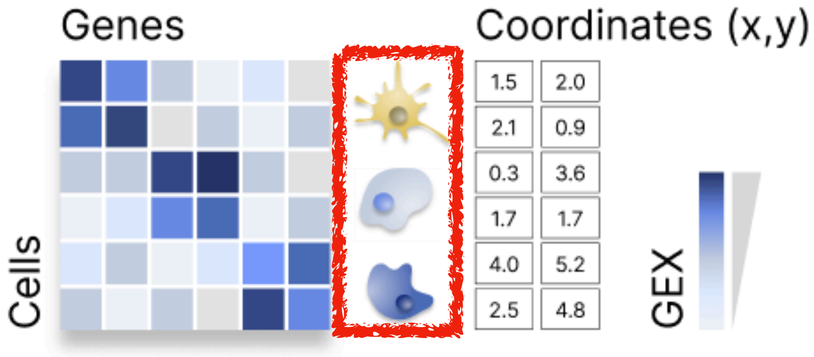

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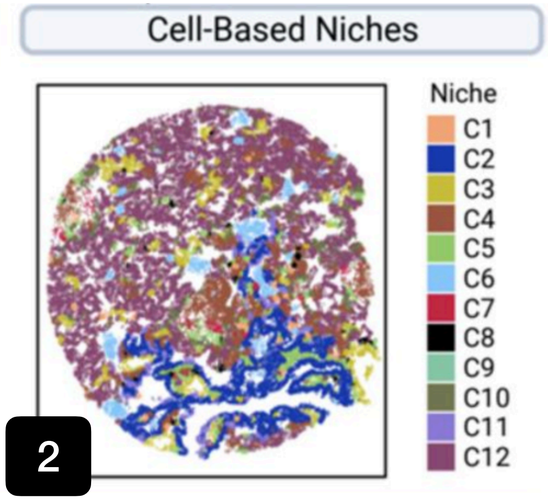

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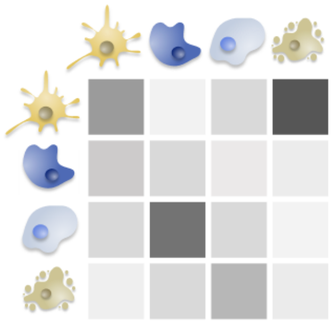

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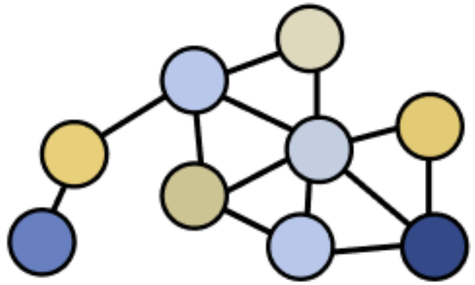

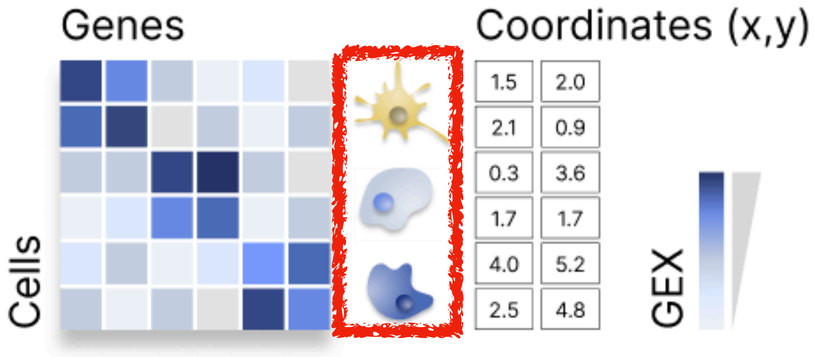

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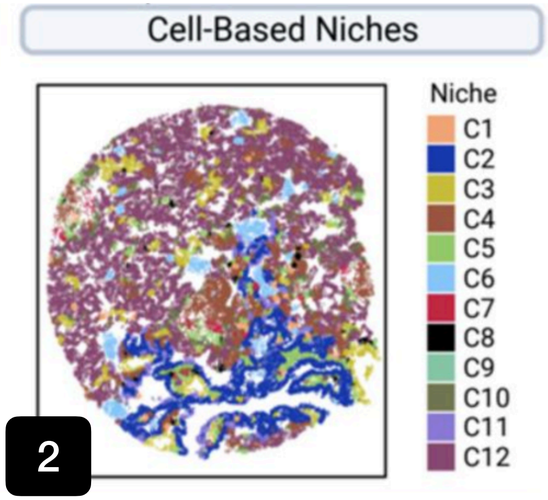

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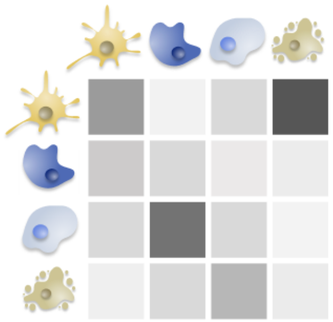

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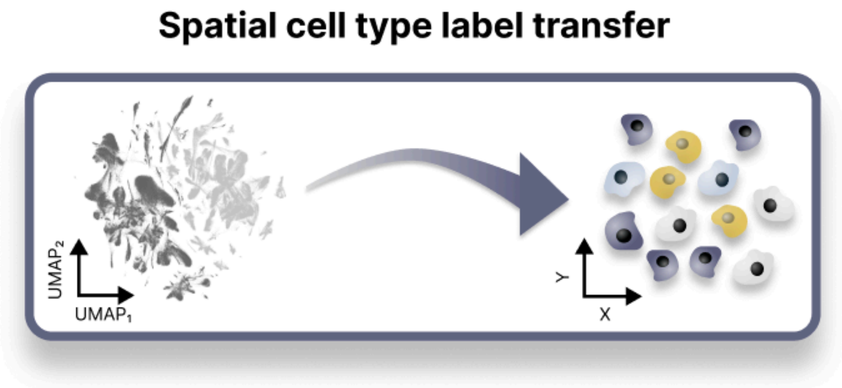
Can we transfer niche labels to dissociated single-cell data?



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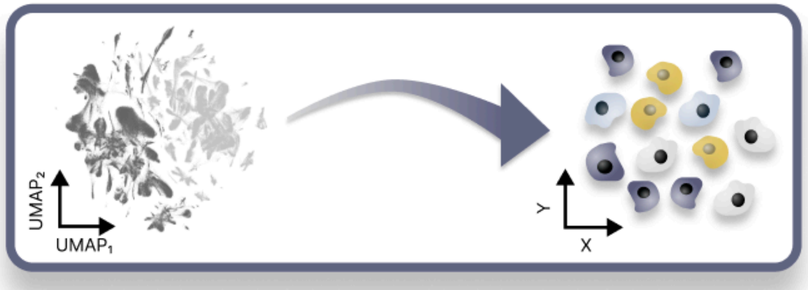
Spatial cell type label transfer



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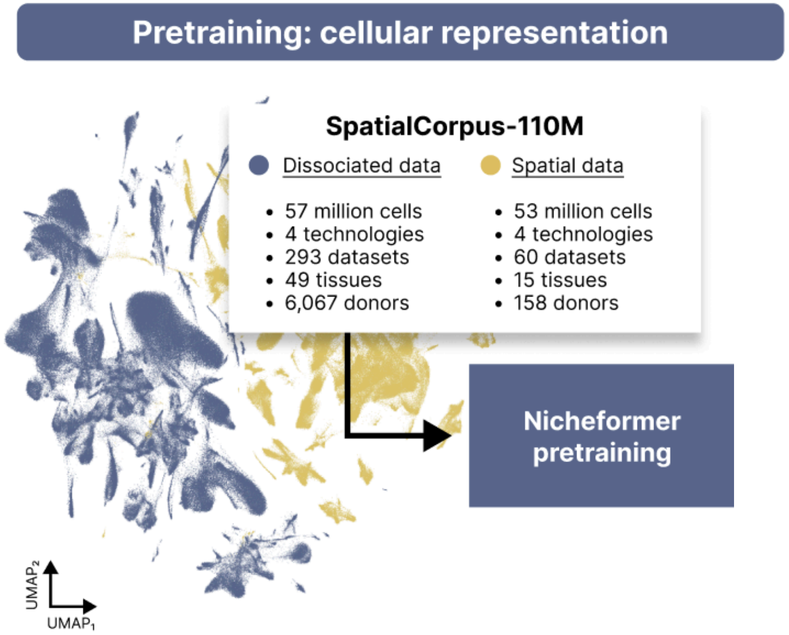

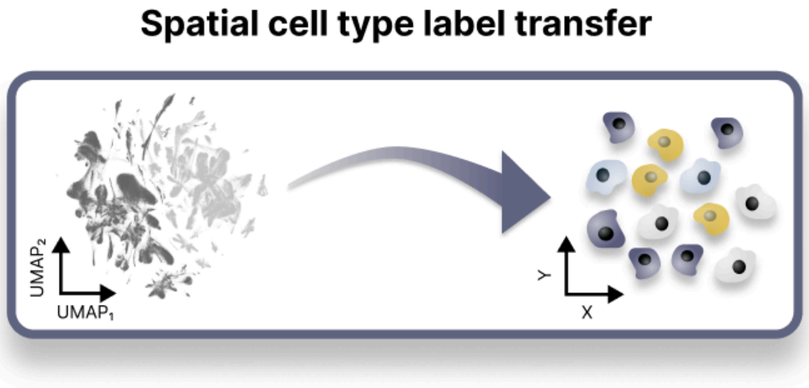

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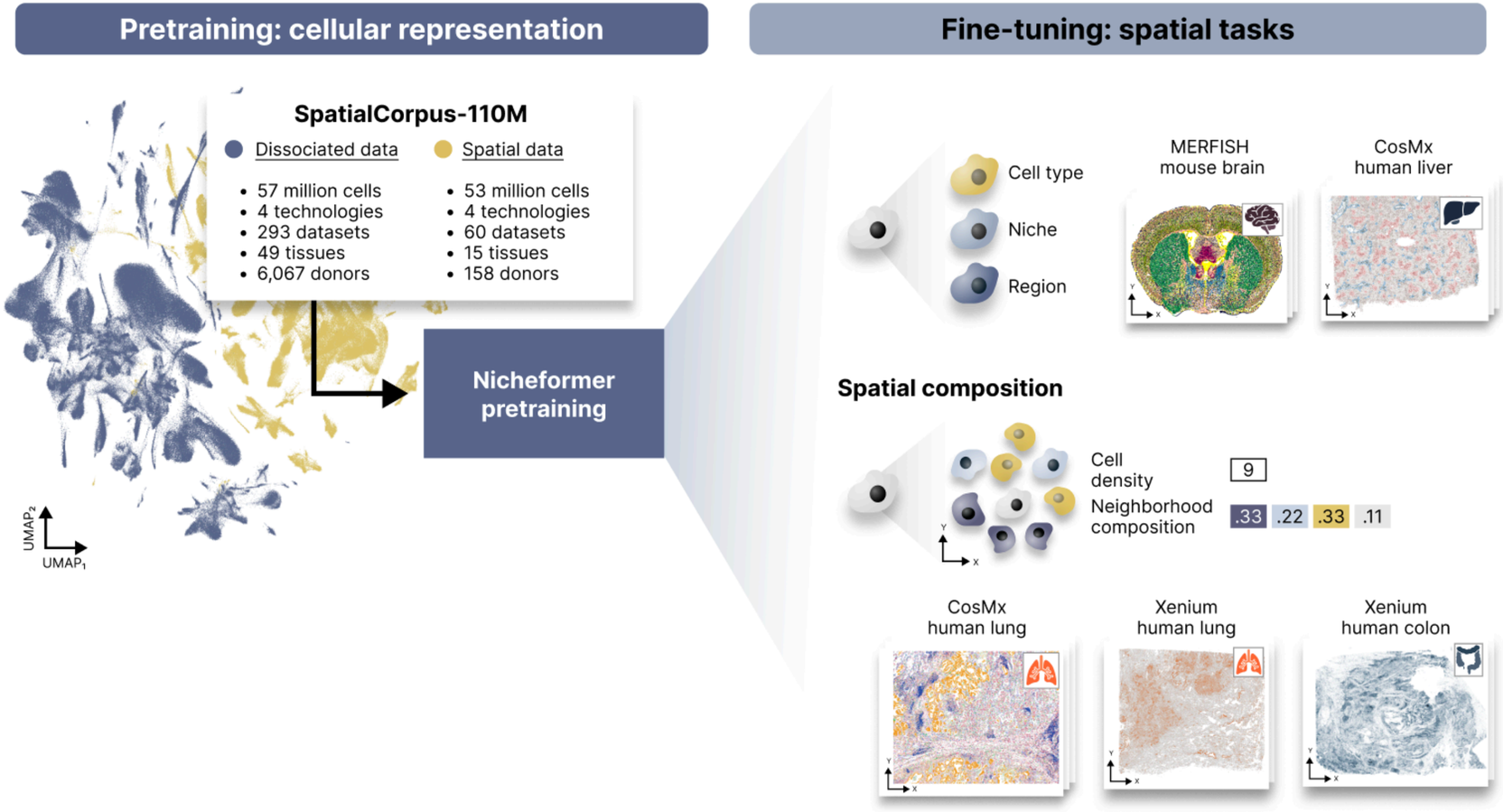

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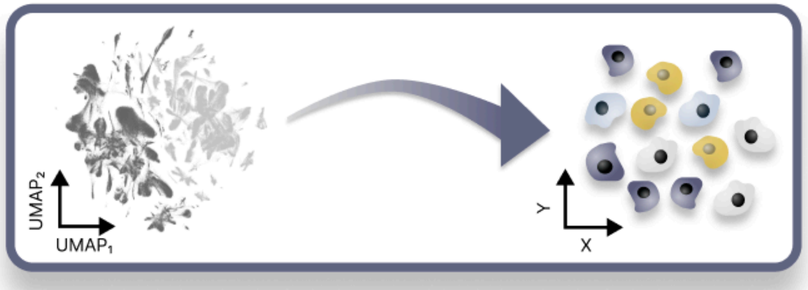

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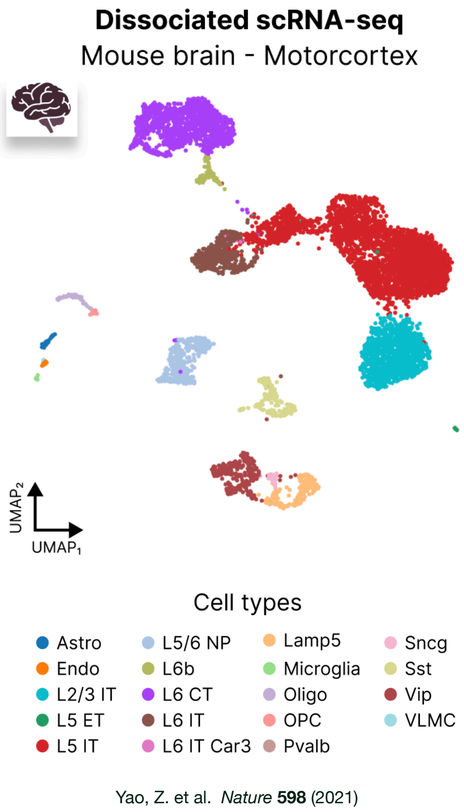

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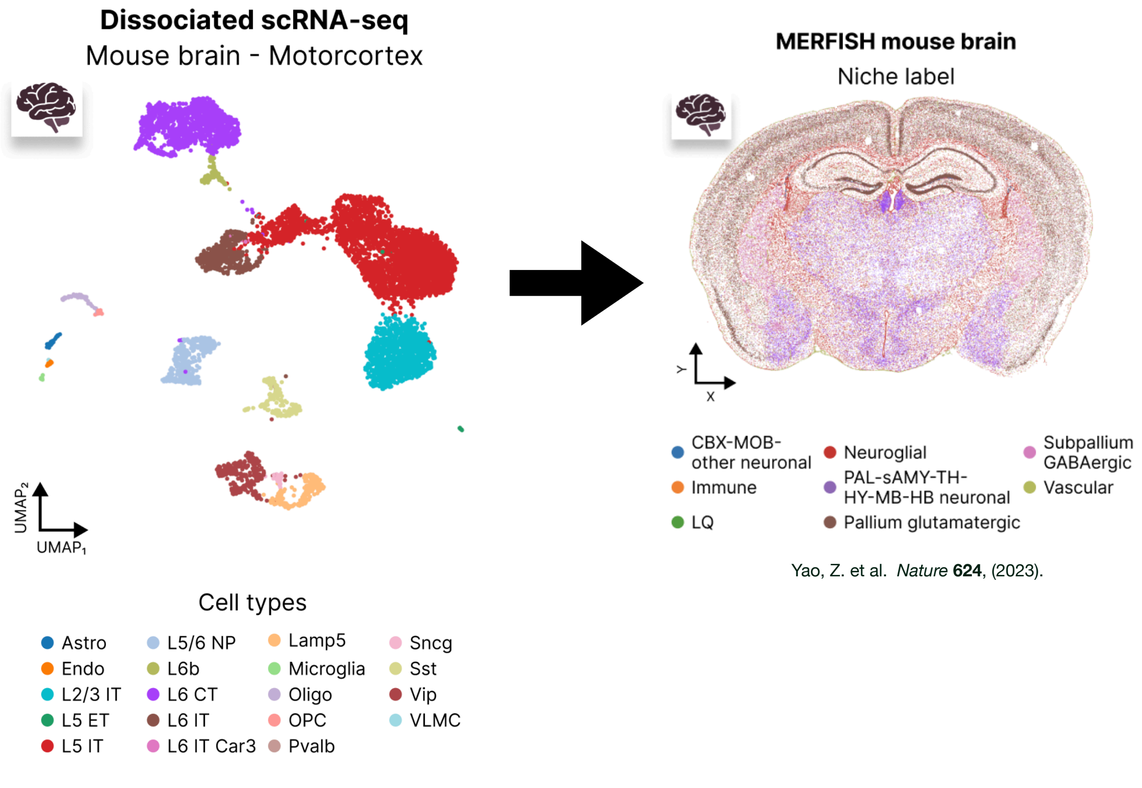

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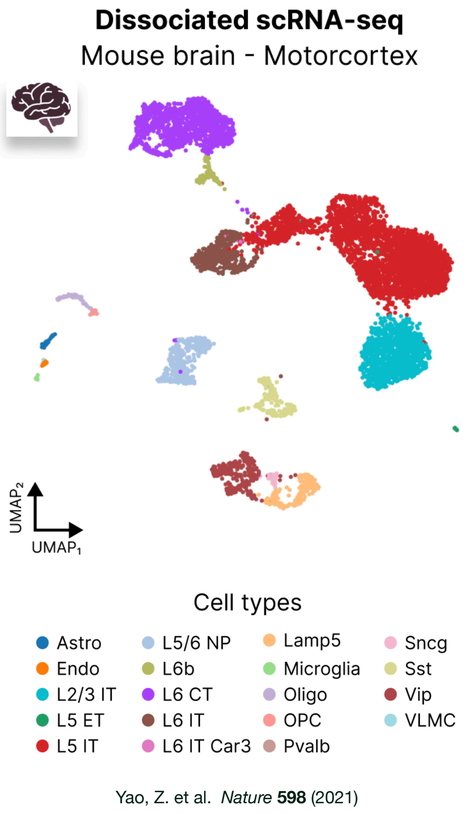

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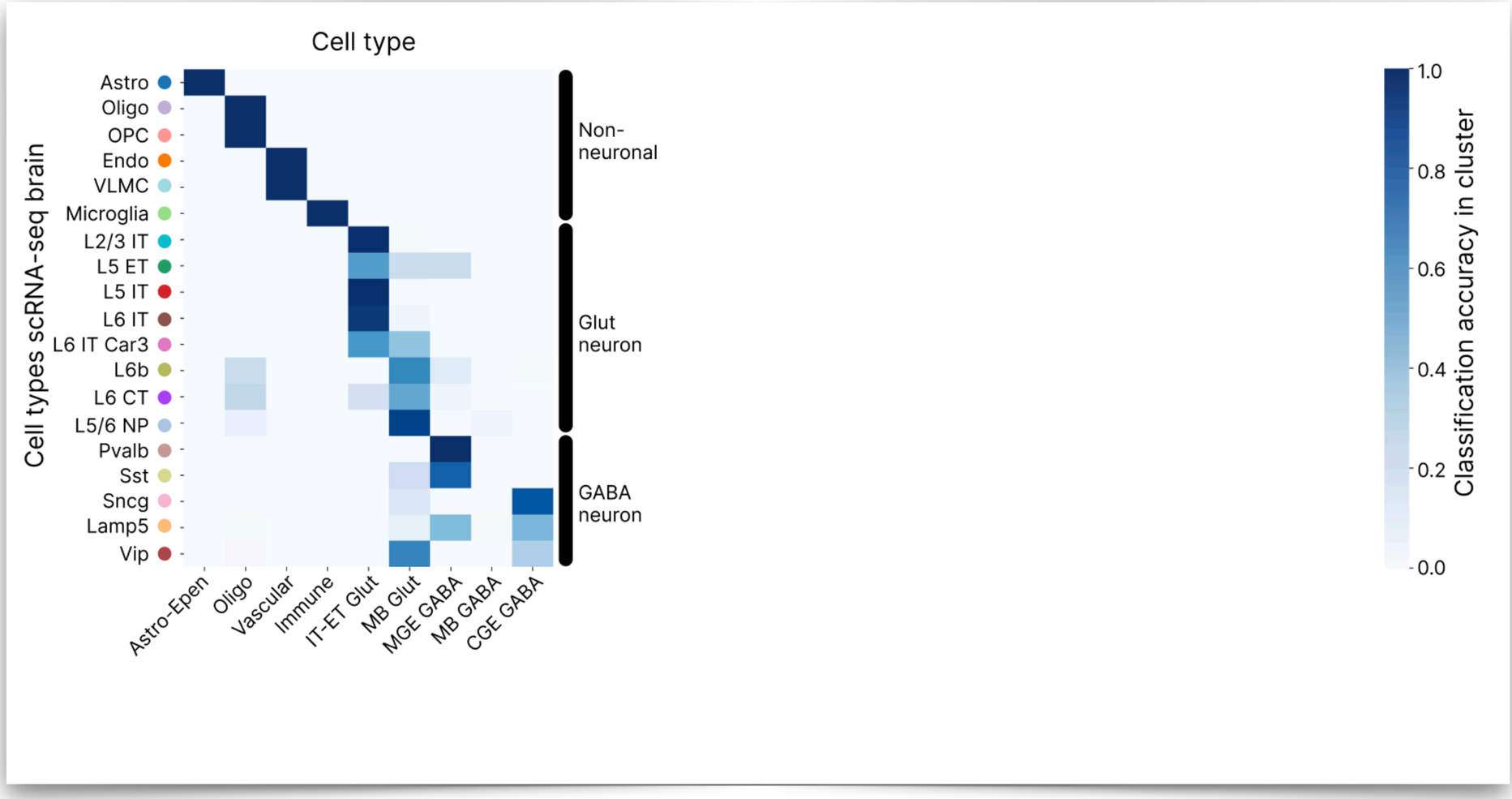
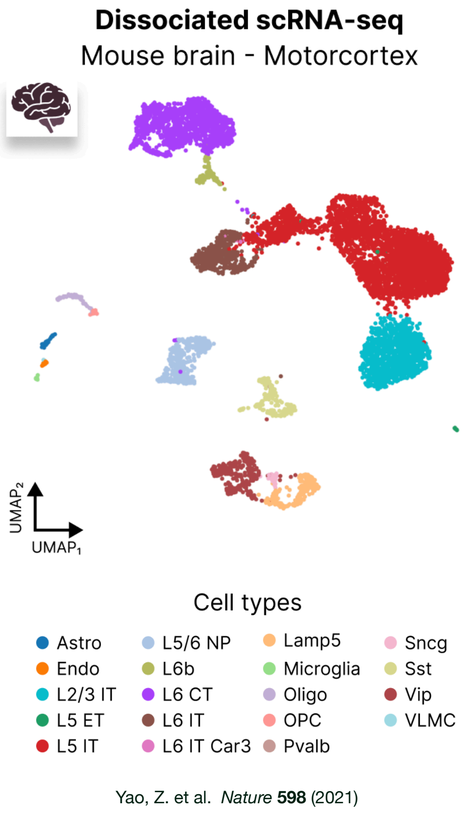
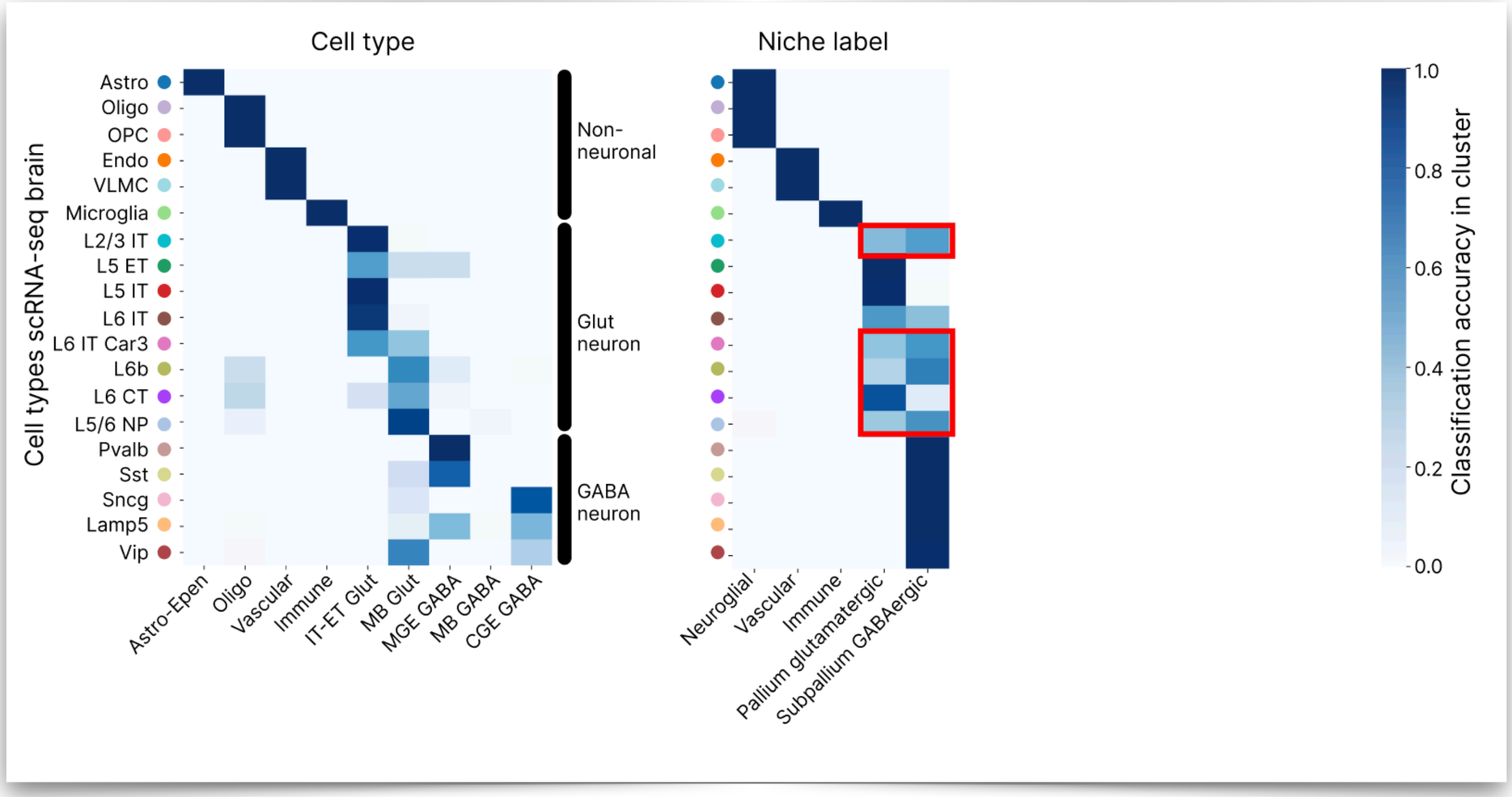


Nicheformer spatial label transfer



Yao, Z. et al. *Nature* **598** (2021)



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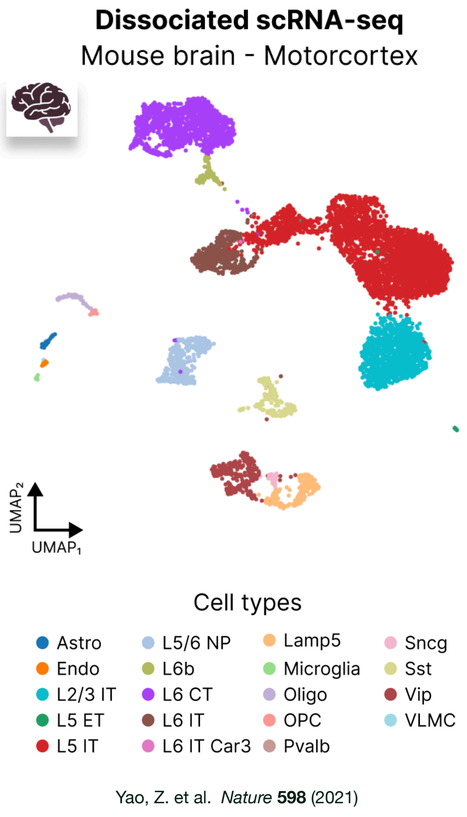

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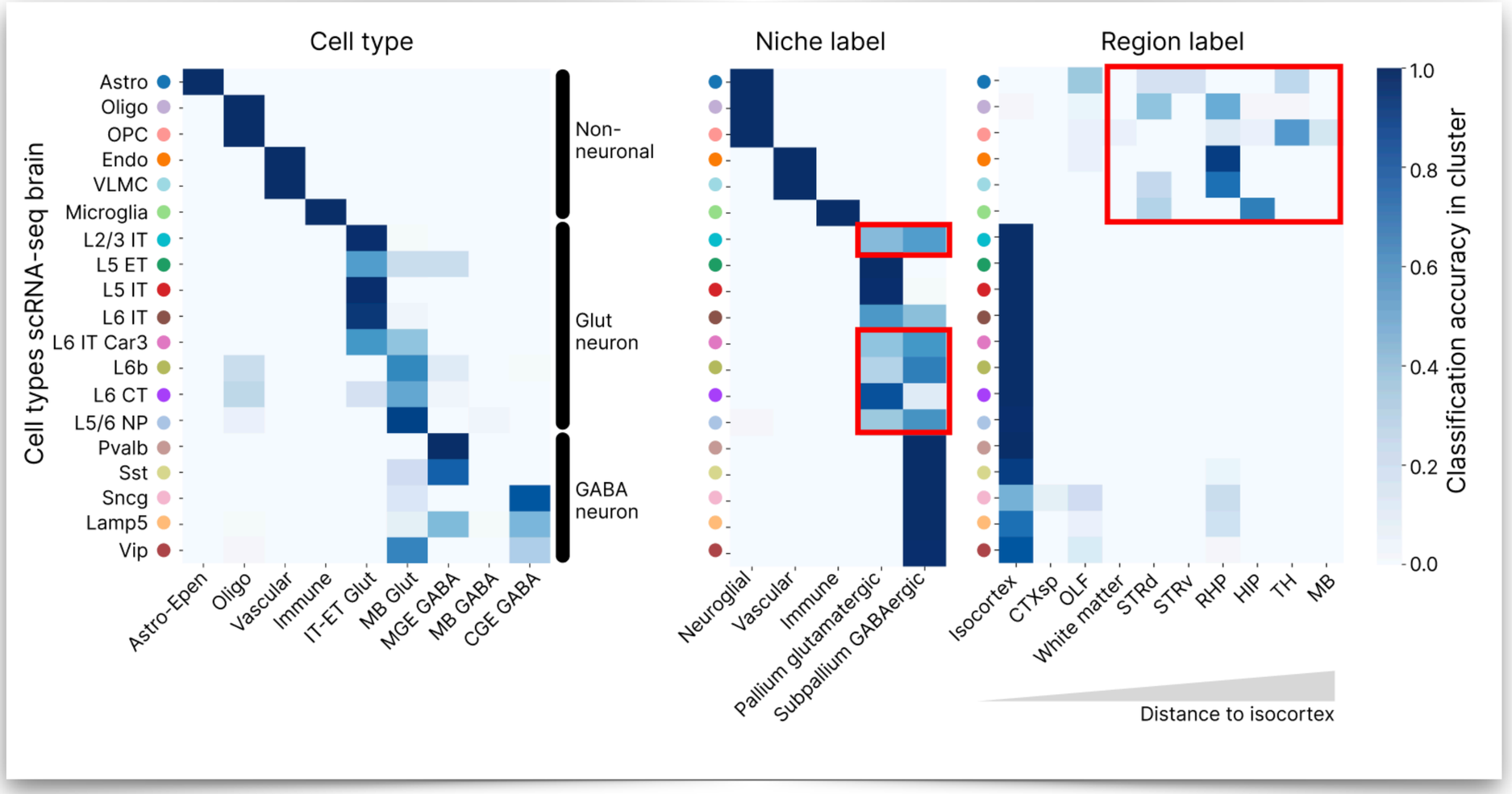

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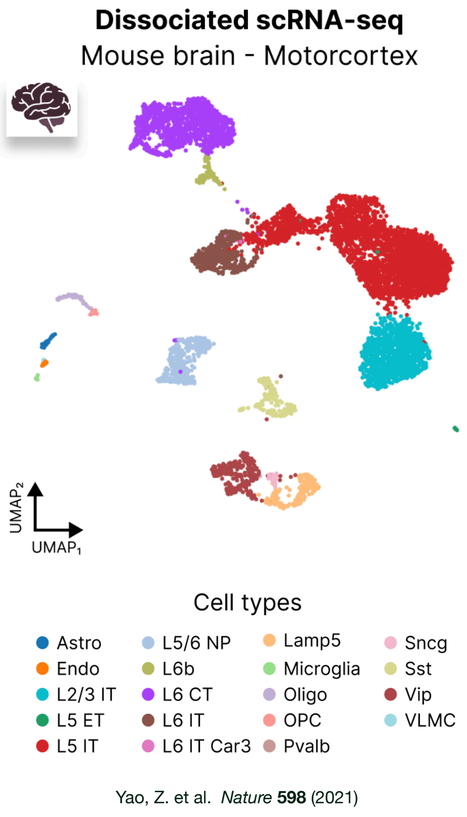

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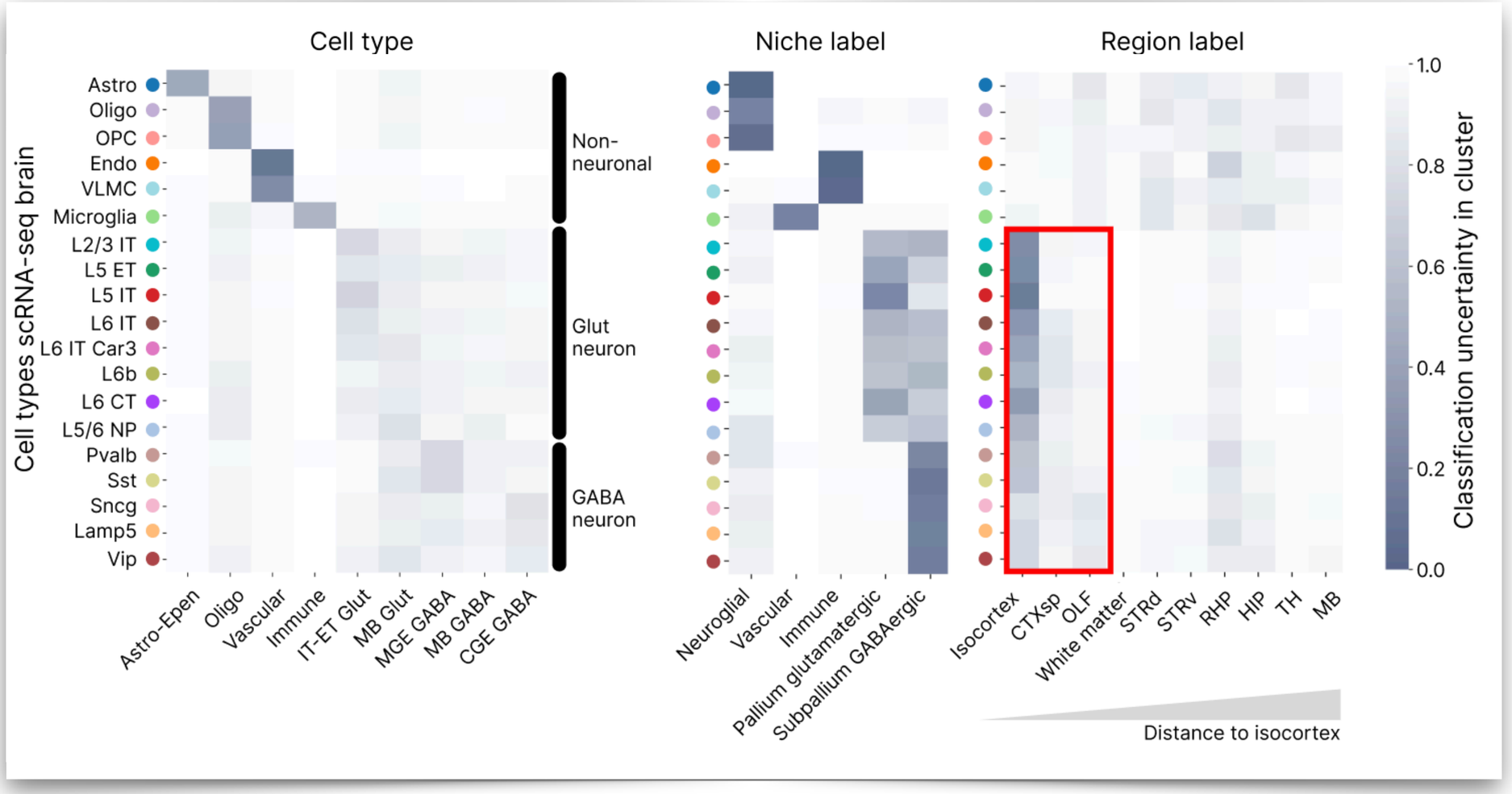

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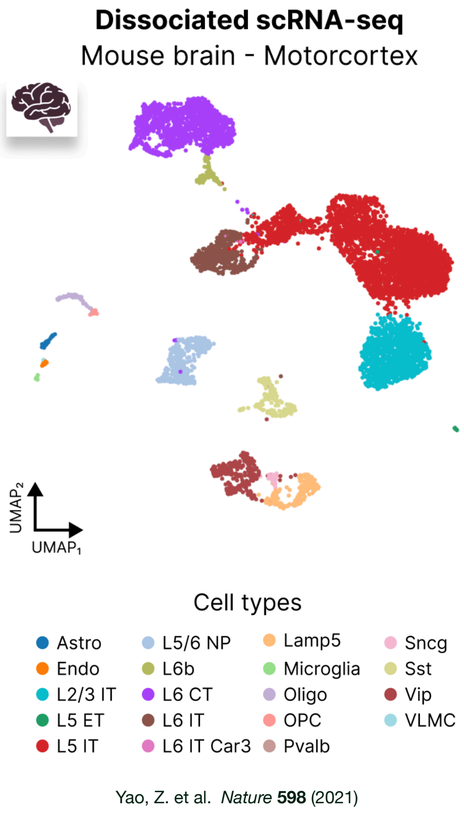

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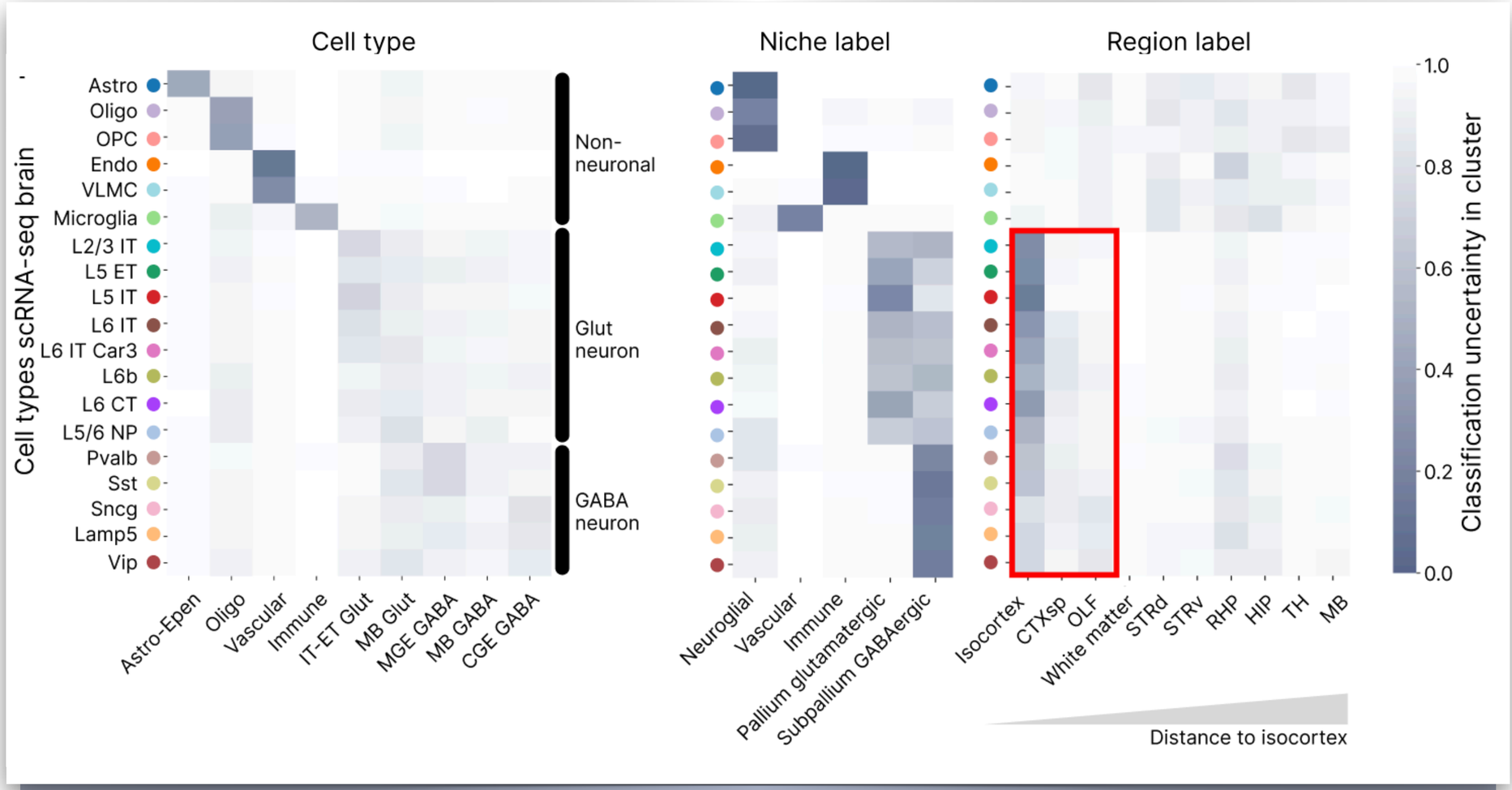

Outlook: Spatial omics will soon **outgrow** dissociated single-cell data when it comes to number of cells. However, we still lack extensive spatial transcriptomics atlases with **diverse panels capturing various disease states**, this will enable us to start **transferring** knowledge generated with the spatial context onto ‘traditional’ single-cell data.

COVET for niche identification and reconstruction

Article | Open access | Published: 02 April 2024

The covariance environment defines cellular niches for spatial inference

Doron Haviv, Ján Remšík, Mohamed Gatie, Catherine Snopkowski, Meril Takizawa, Nathan Pereira, John Bashkin, Stevan Jovanovich, Tal Nawy, Ronan Chaligne, Adrienne Boire, Anna-Katerina Hadjantonakis & Dana Pe'er

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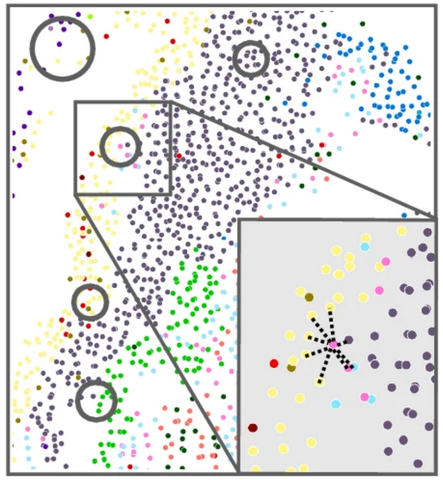
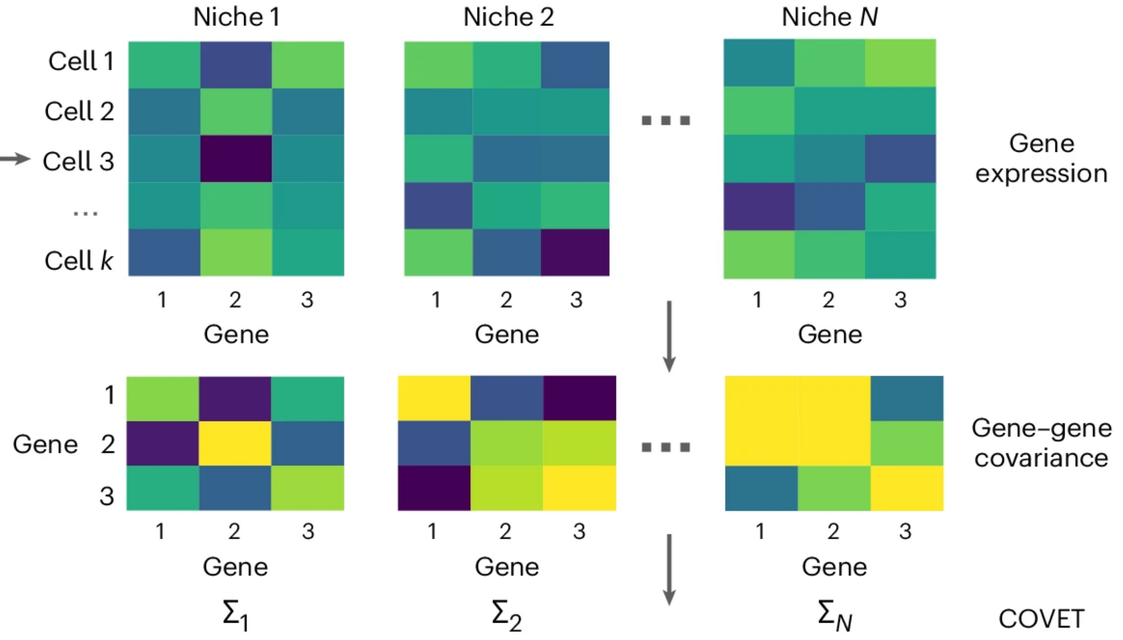
COVET: defines niches based on k spatial nearest neighbours and identifies niche similarities based on OT computed on gene-gene covariances (covariance environment)



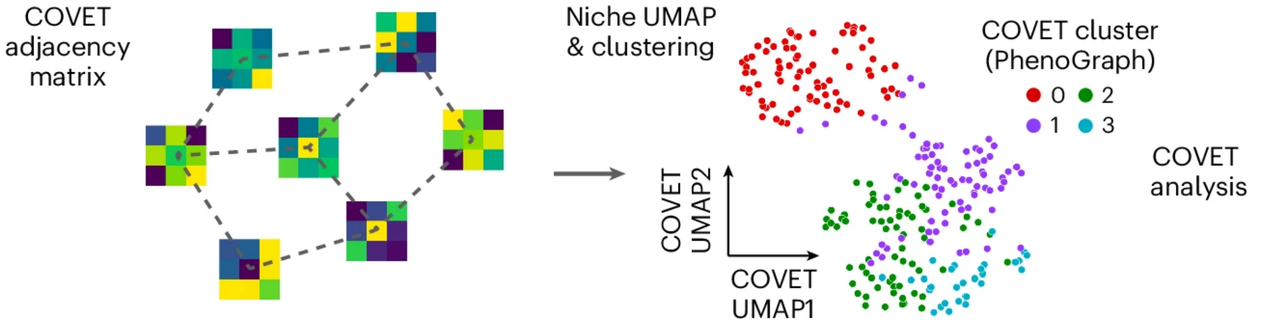
Define cellular niches
(*k* spatial nearest neighbors)



Fast approximation of optimal transport (AOT)

$$\Delta(\Sigma_i,\Sigma_j) = OT(\Sigma_i,\Sigma_j) \approx L_2^2(\sqrt{\Sigma_i},\sqrt{\Sigma_j})$$

Distance between niches



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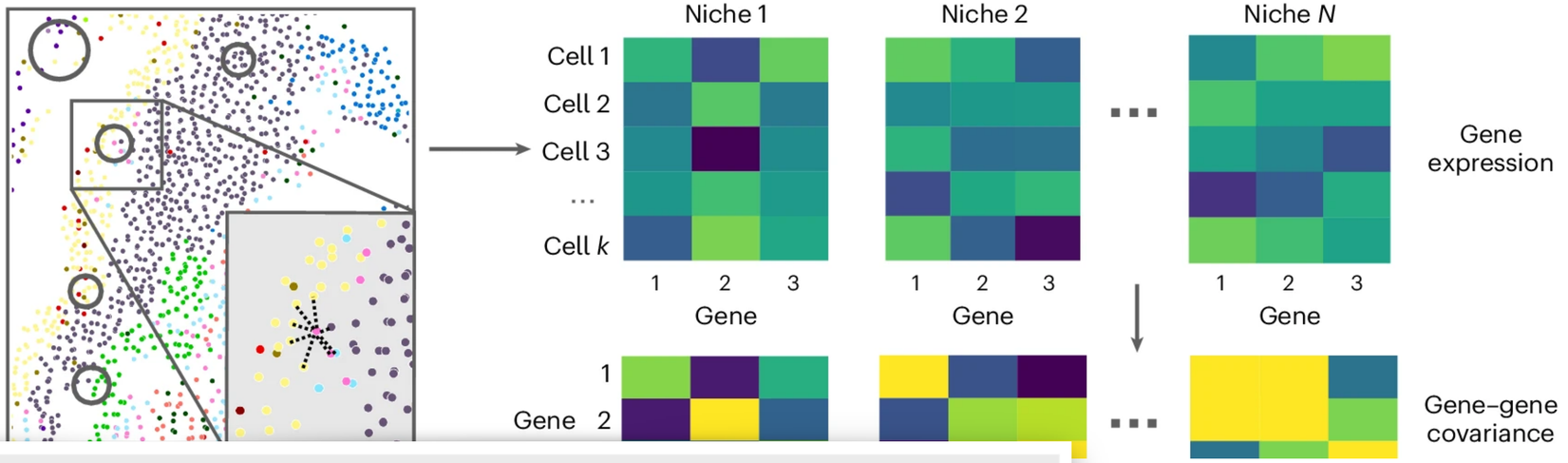
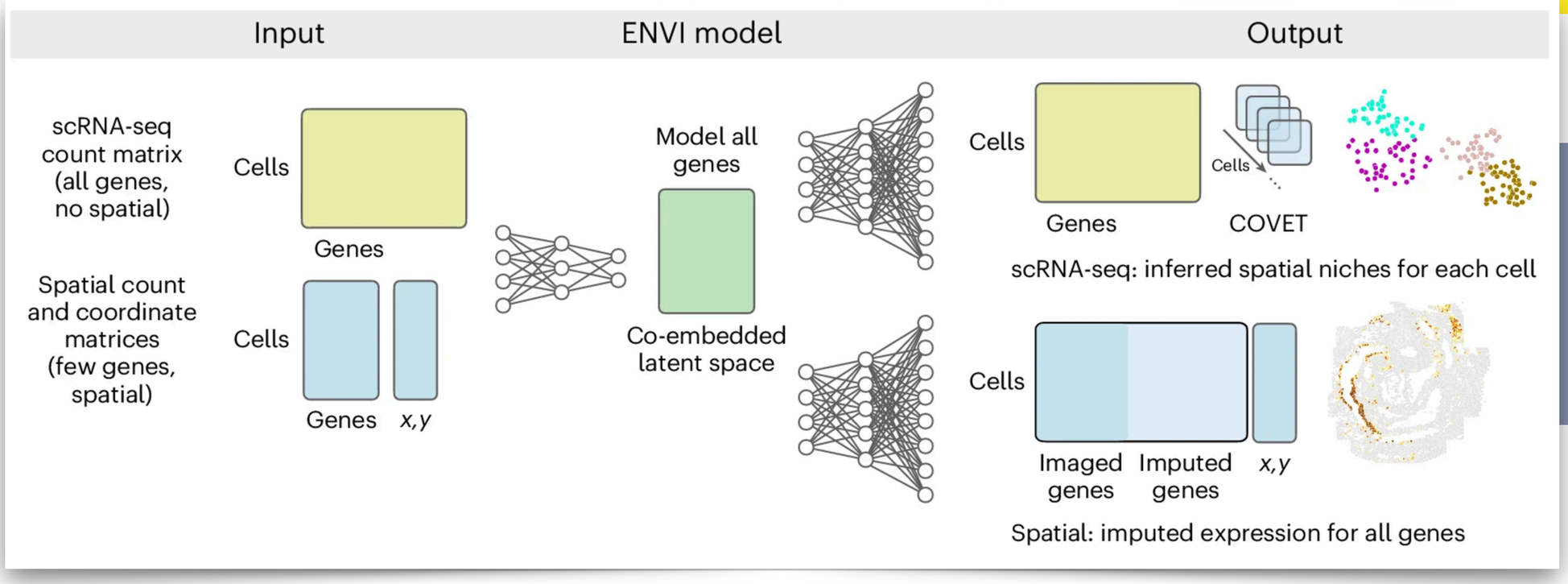
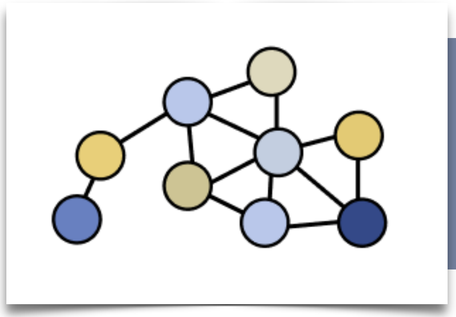




ENVI: paired with a conditional autoencoder that simultaneously embeds scRNA-seq and multiplexed spatial transcriptomic data into a unified latent embedding one can transfer niches onto scRNA-seq data

Summary: What are graphs and niches in spatial comics?



Graph: Often defined based on spatial proximity in µm or pixels

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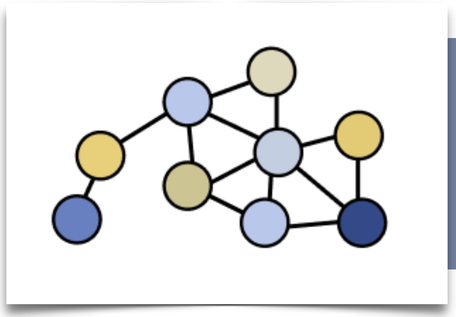

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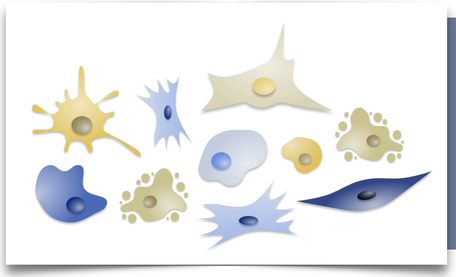

Niche: Cellular microenvironment often defined on a close to intermediate length scale

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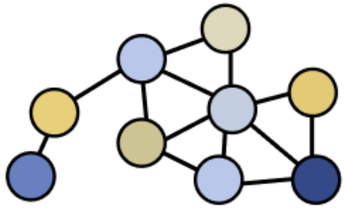

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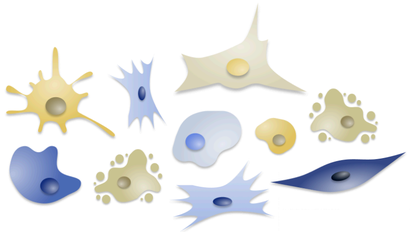

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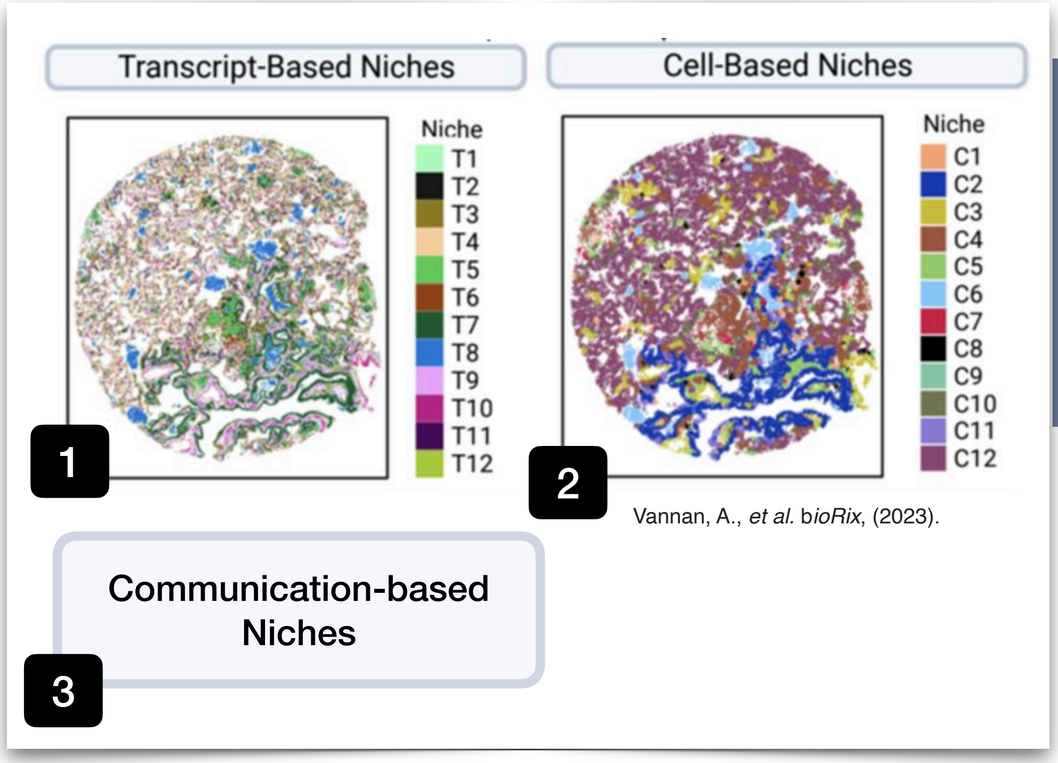

Vannan, A., *et al.* b*ioRix*, (2023).

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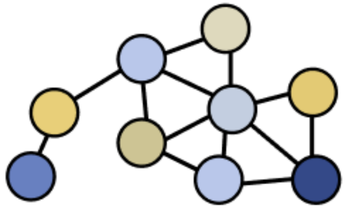

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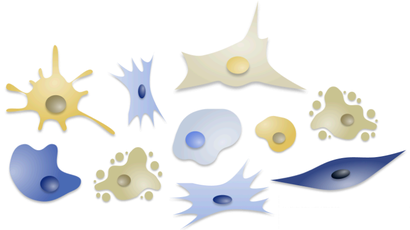

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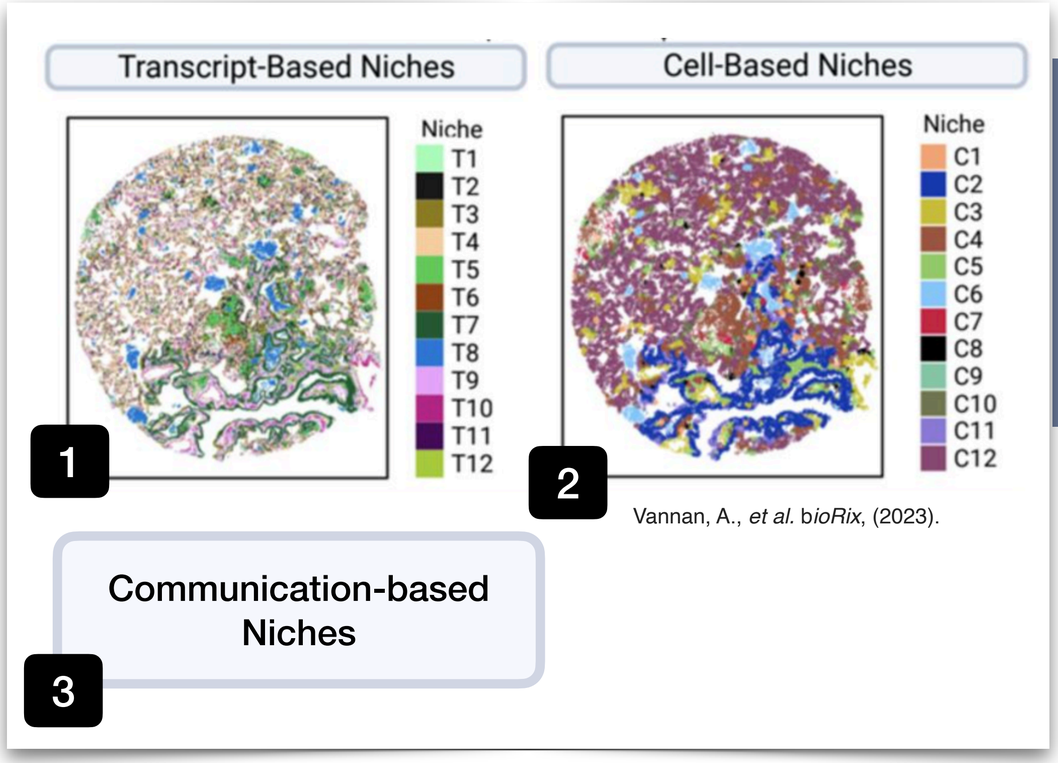

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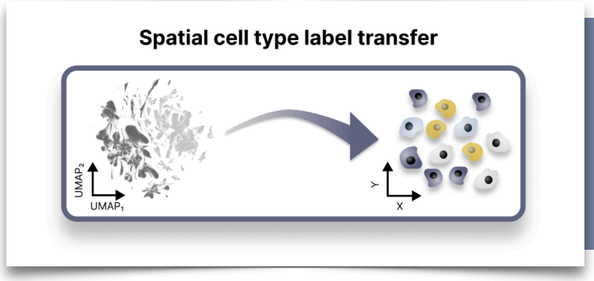

Niche transfer: Recent methods aim to enrich dissociated data with knowledge obtained through spatial mics

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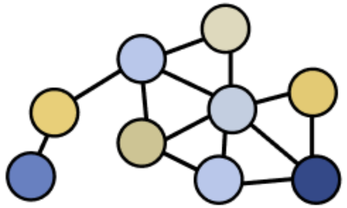

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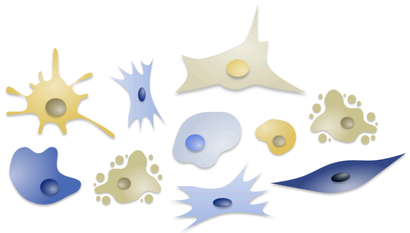

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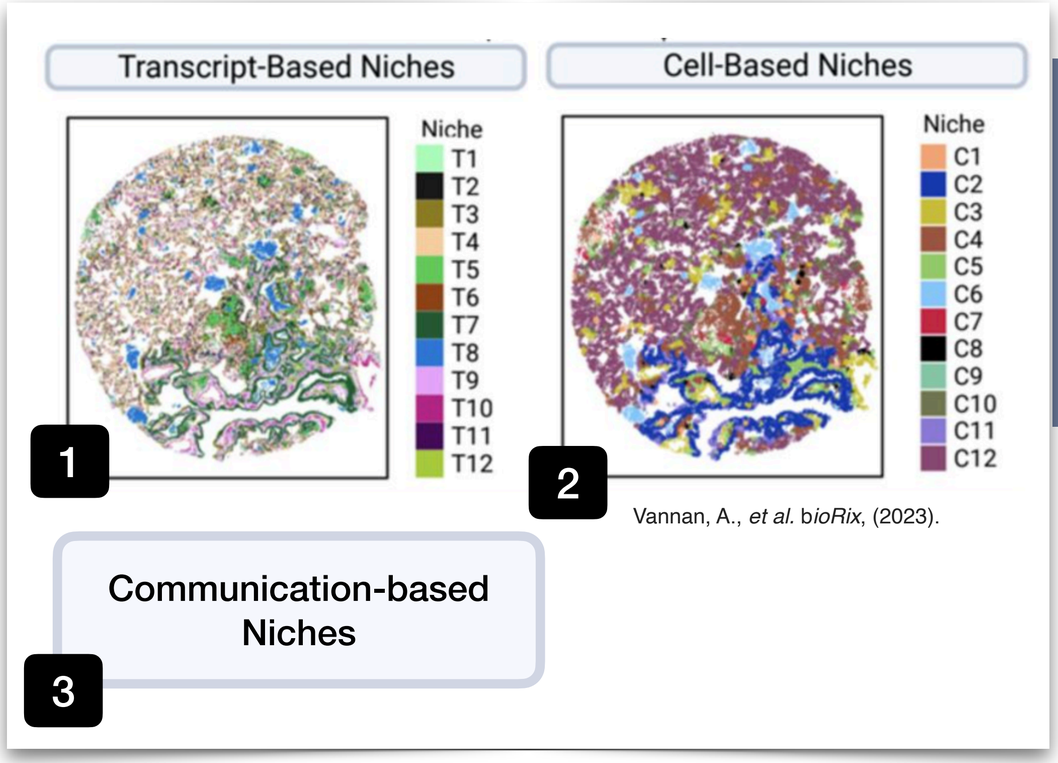

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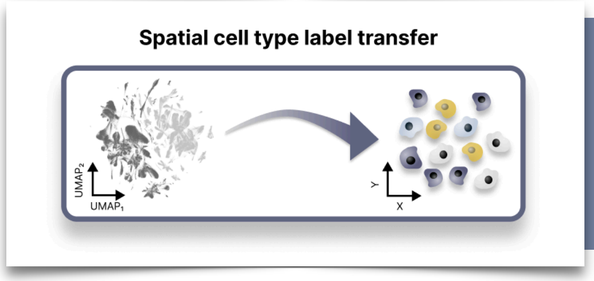

Niche transfer: Recent methods aim to enrich dissociated data with knowledge obtained through spatial mics

Clinical relevance: Differences in spatial niches in disease cohorts can be liked to patient sub stratification and is useful for overall survival analysis.

Acknowledgements

Fabian J. Theis

Alejandro Tejada-Lapuerta

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BIOPTIMUS

HELMHOLTZ MUNICH

scverse

Technical University of Munich

mcml Munich Center for Machine Learning

ForInter Bayerischer Forschungsverbund Interaktion von humanen Gehirnzellen

Thank you!

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