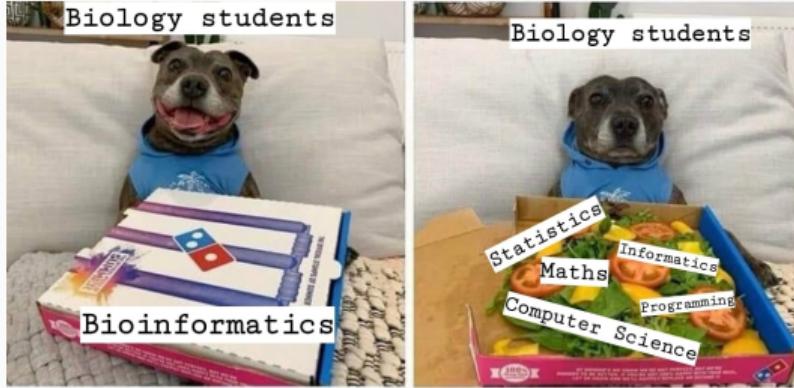


SPATIAL TRANSCRIPTOMICS

Harshavardhan BV

June 11, 2025



¹Credits: u/isinaltinkaya

CELL-CELL COMMUNICATION

LIGAND-RECEPTOR INTERACTIONS

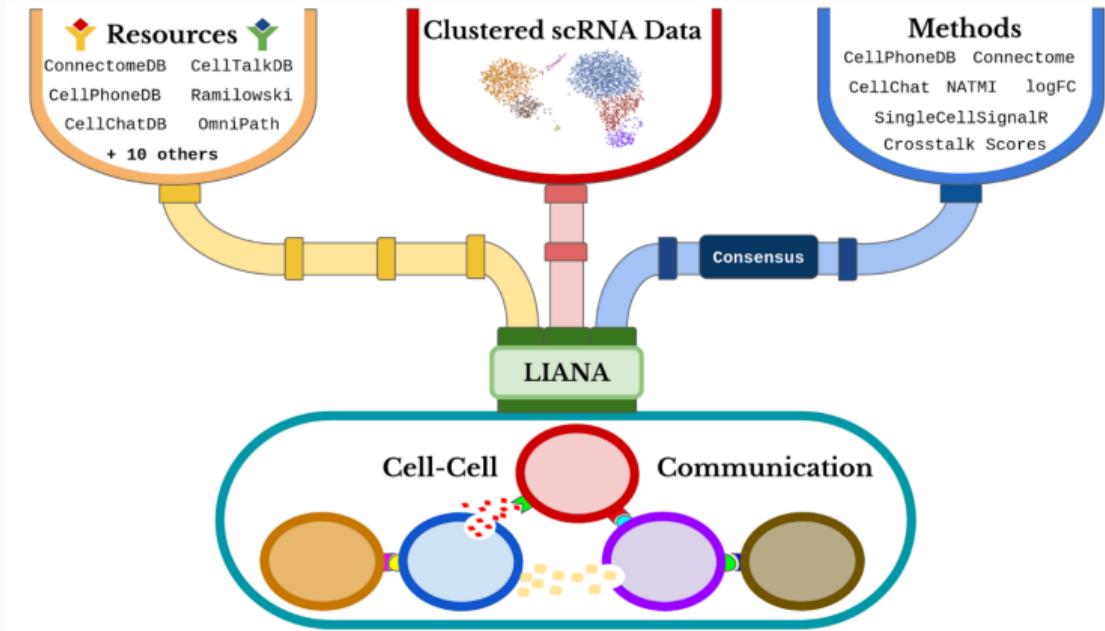


Figure: LIANA Pipeline ¹

¹Dimitrov et al., *Nat Commun*, 2022; Dimitrov et al., *Nat Cell Biol*, 2024

LIANA RESULTS

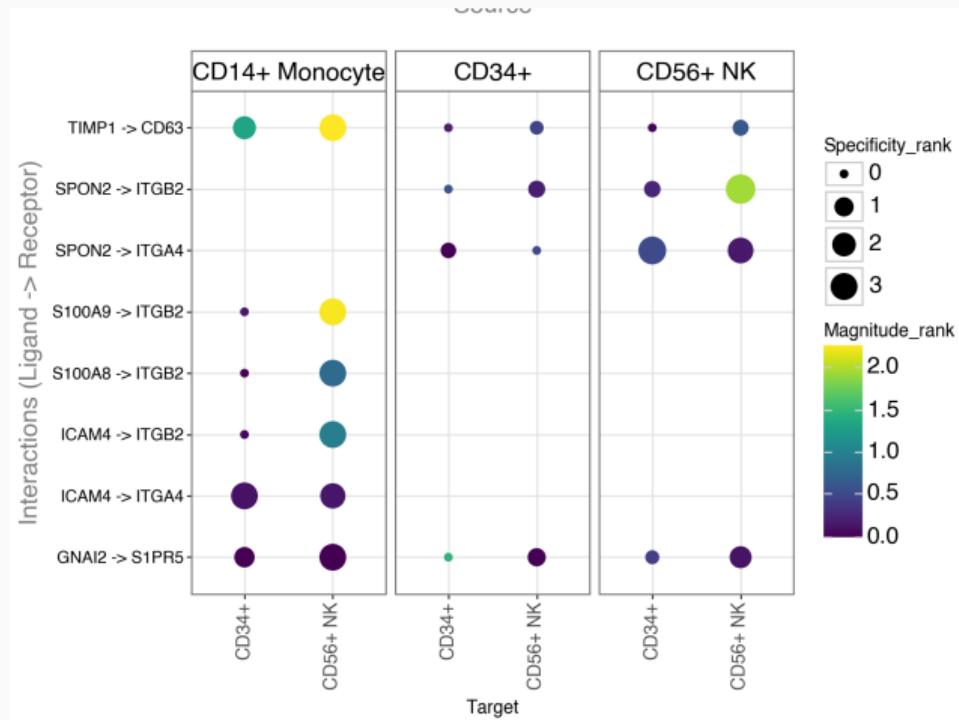
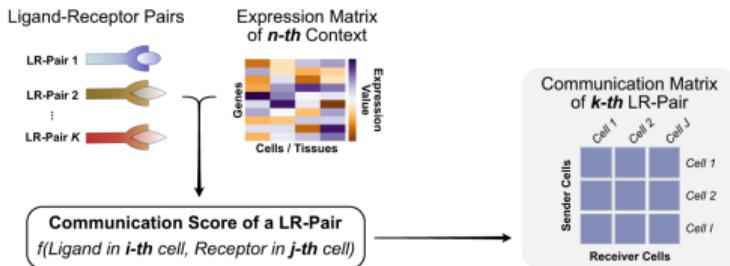


Figure: LIANA Dotplot¹

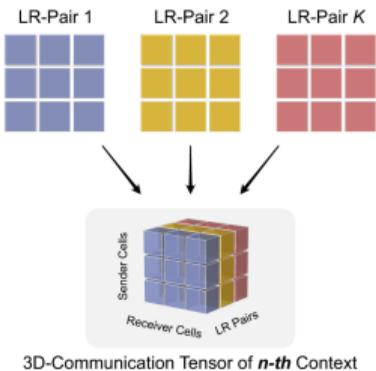
¹https://liana-py.readthedocs.io/en/latest/notebooks/basic_usage.html

CONTEXT DEPENDENT INTERACTIONS

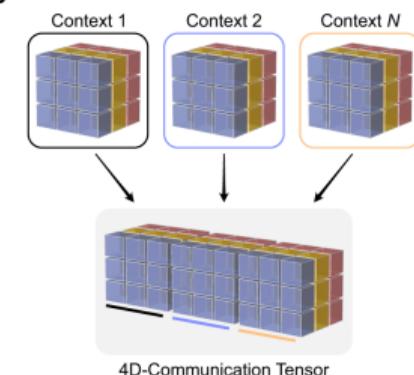
a



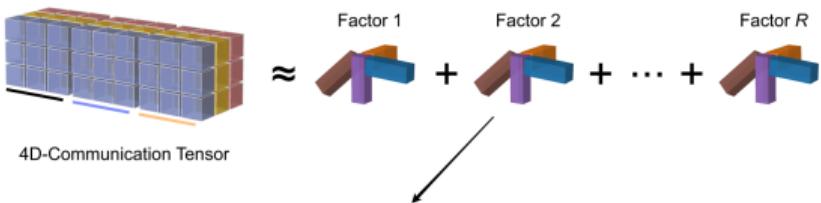
b



c



d



e

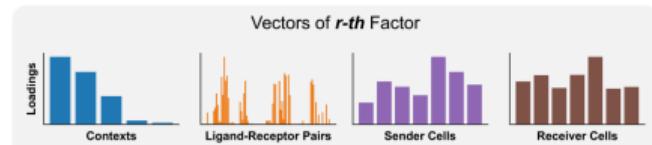
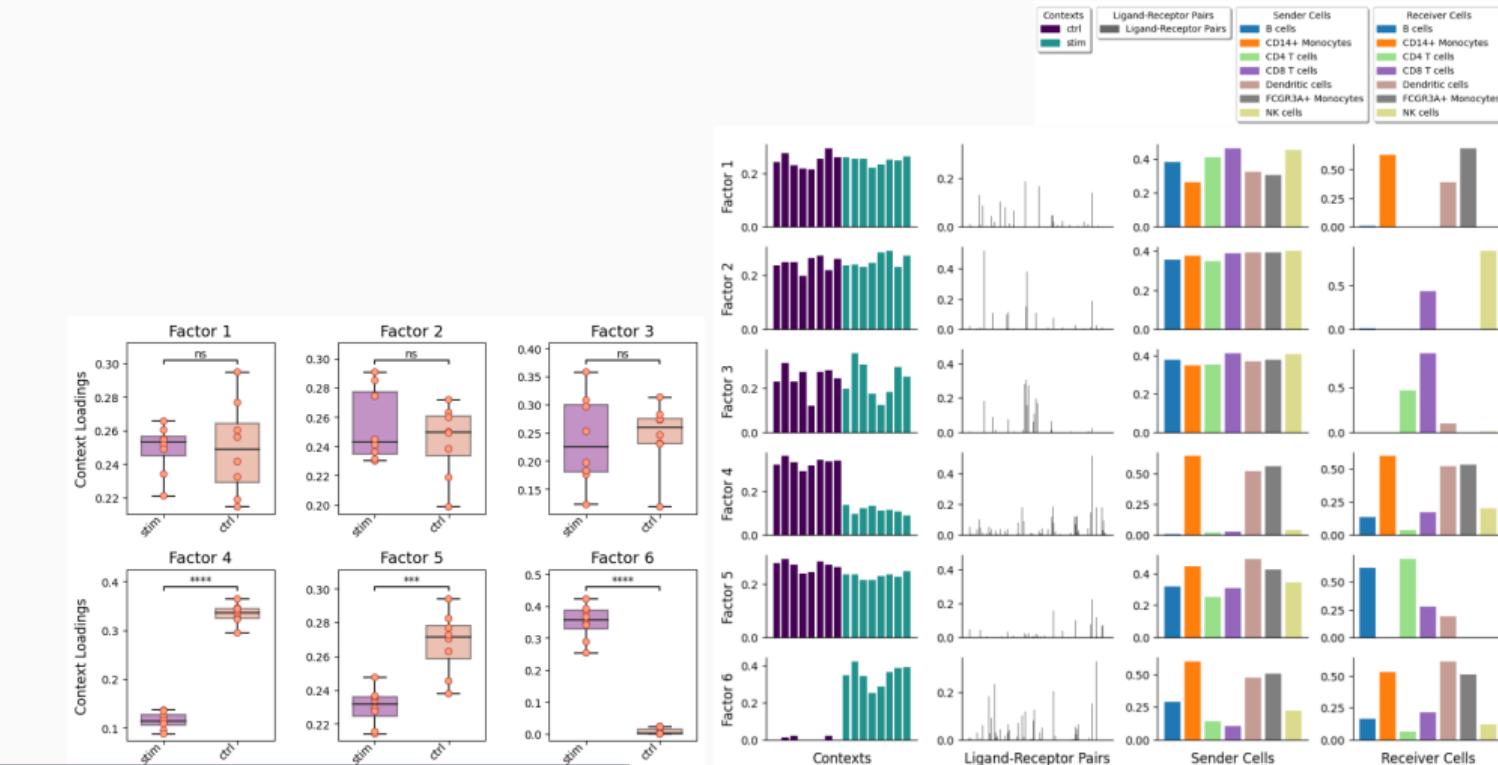


Figure: Tensor-cell2cell decomposition¹

¹Armingol et al., Nat Commun, 2022

TENSOR C2C RESULTS



¹https://liana-py.readthedocs.io/en/latest/notebooks/liana_c2c.html

WHAT IS SPATIAL TRANSCRIPTOMICS?

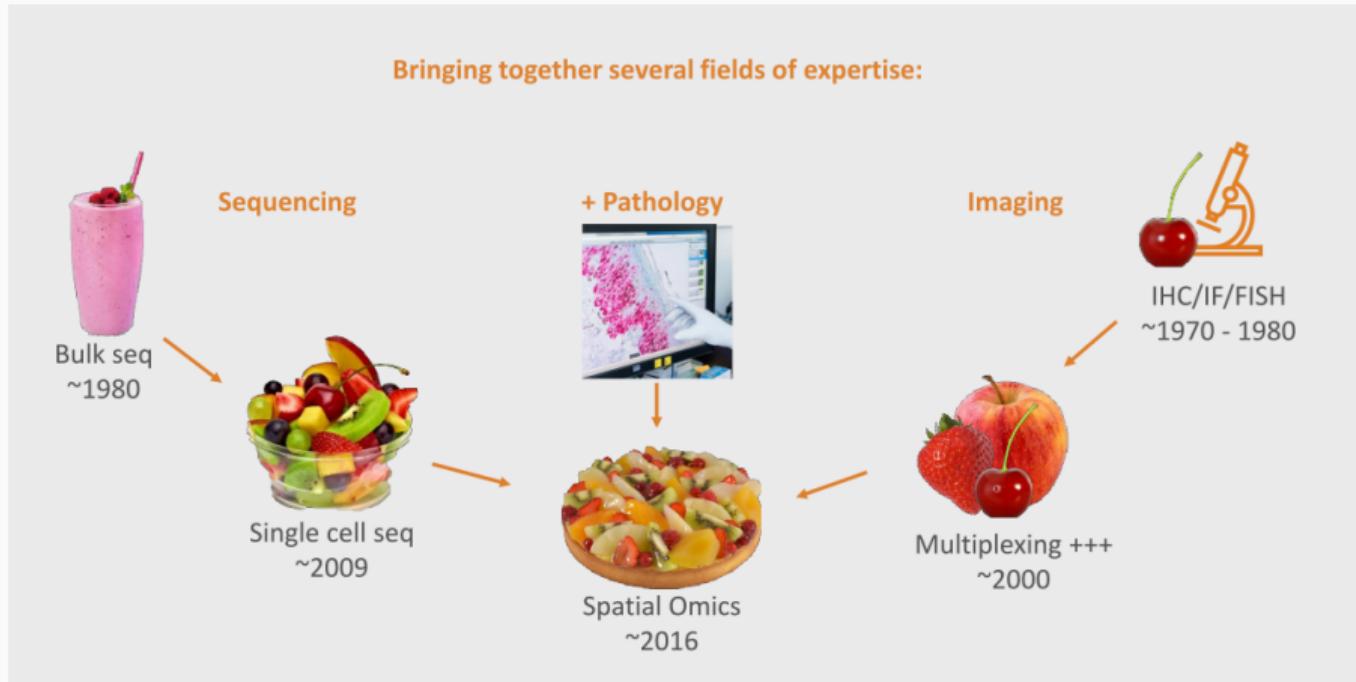


Figure: Schematic of Spatial transcriptomics (ST)¹

¹Figures by Leanne de Koning, Nicolas Servant (Institut Curie)

How?

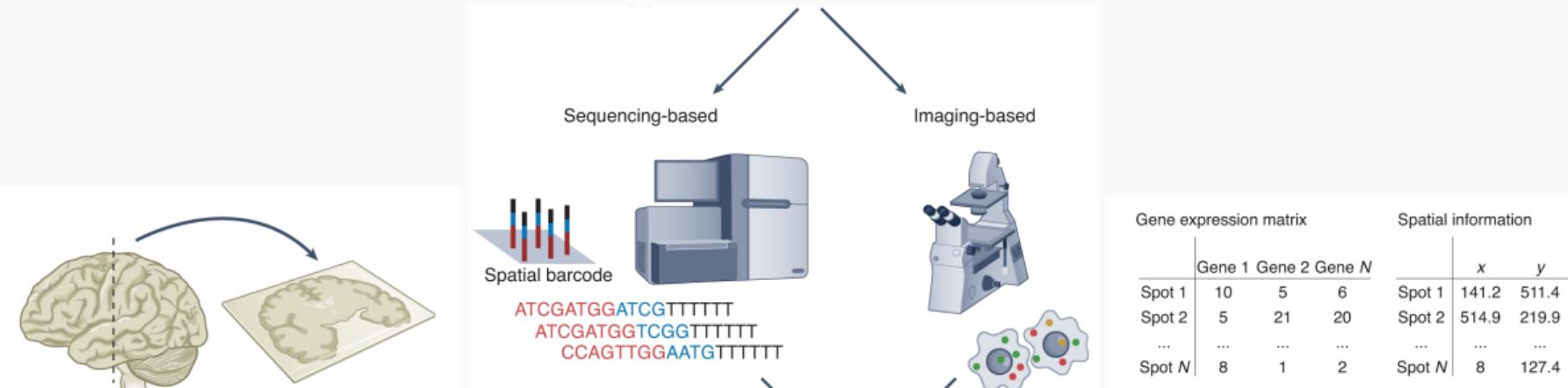
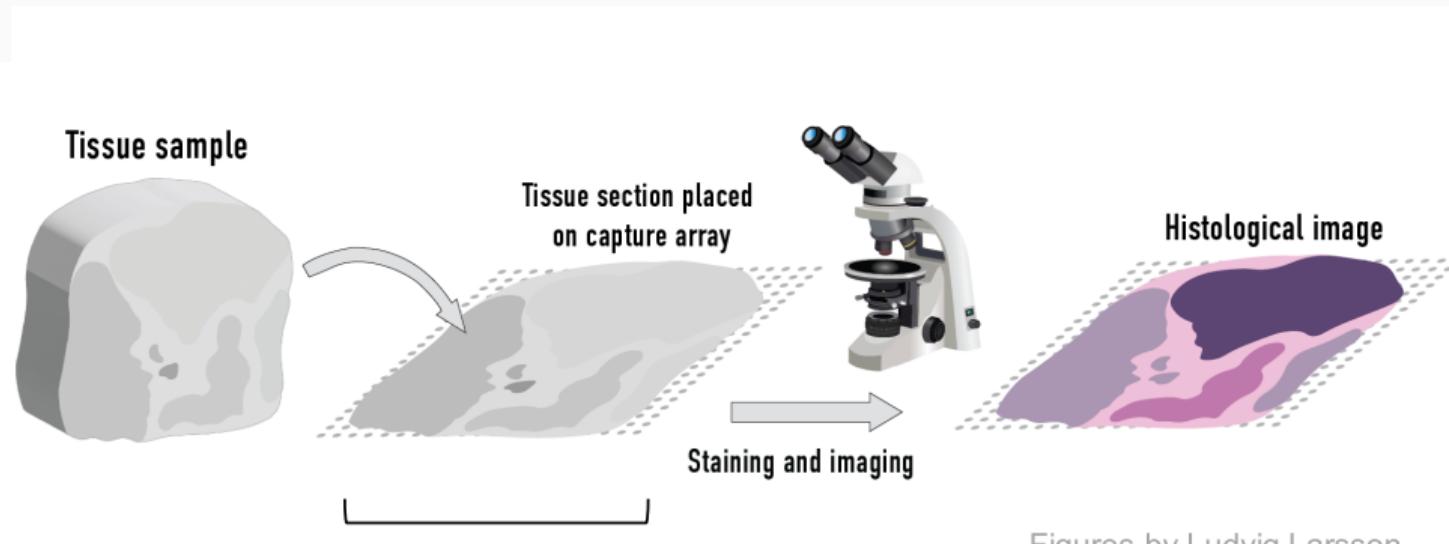
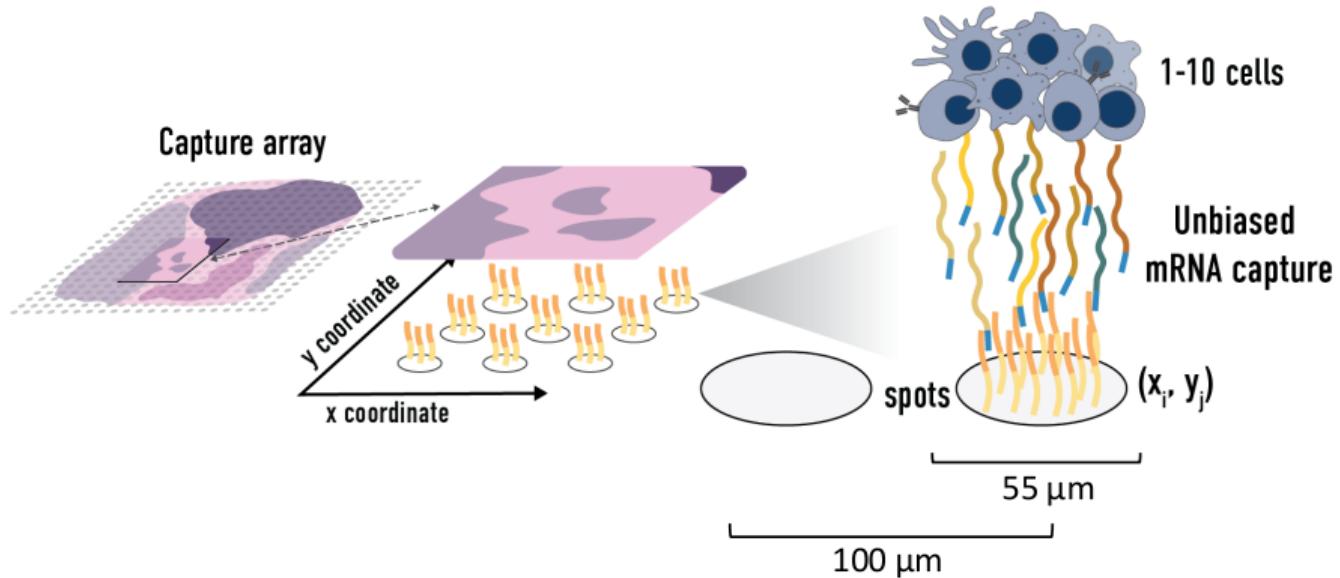


Figure: Classes of ST technologies ¹

¹Tian et al., *Nat Biotechnol*, 2023



Figures by Ludvig Larsson



Figures by Ludvig Larsson

TRADE-OFFS

Better gene level resolution



Worse spatial resolution



CAN WE DO BETTER?



DECONVOLUTION

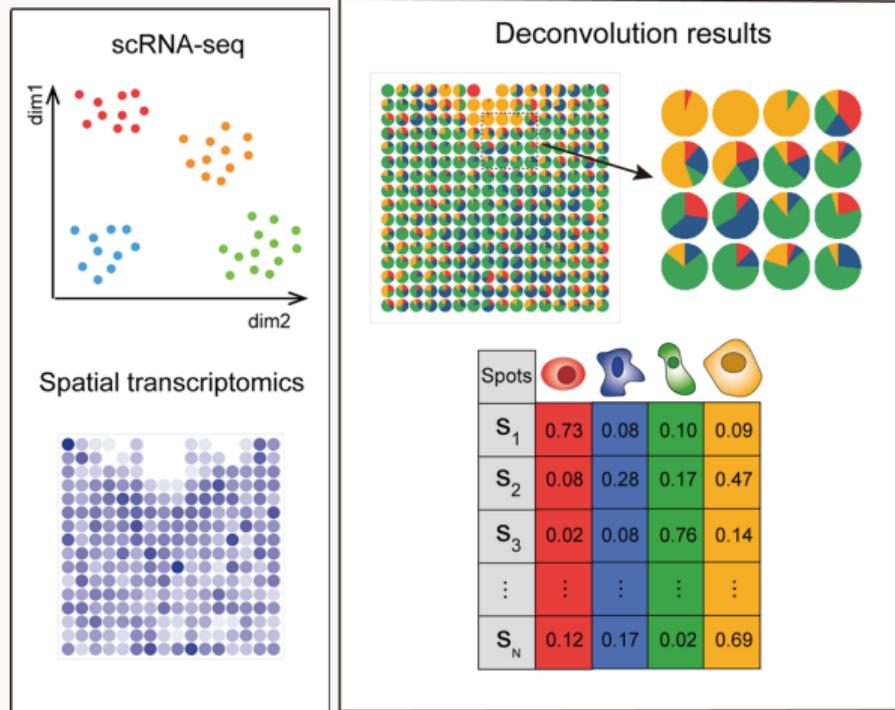
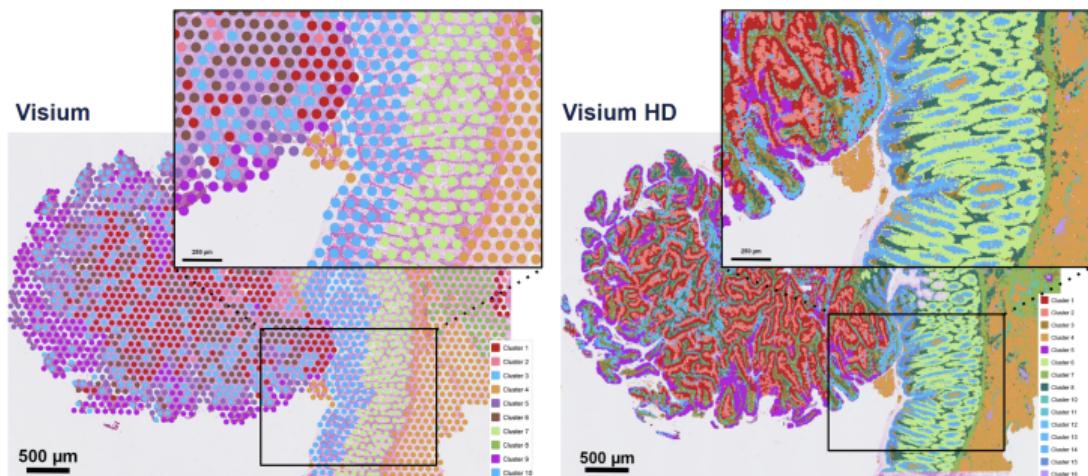
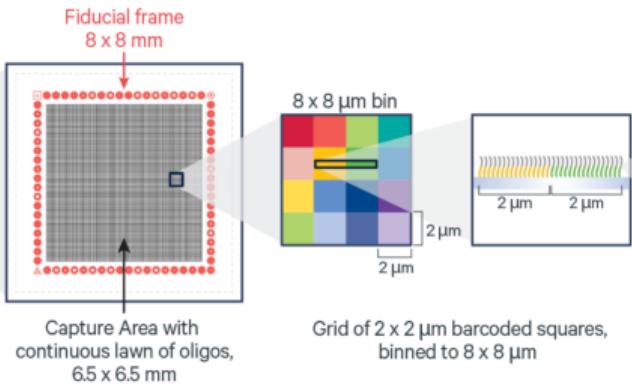


Figure: Deconvolution ¹

¹Li et al., *Nature Communications*, 2023



¹Figures from <https://www.10xgenomics.com/blog/your-introduction-to-visium-hd-spatial-biology-in-high-definition>

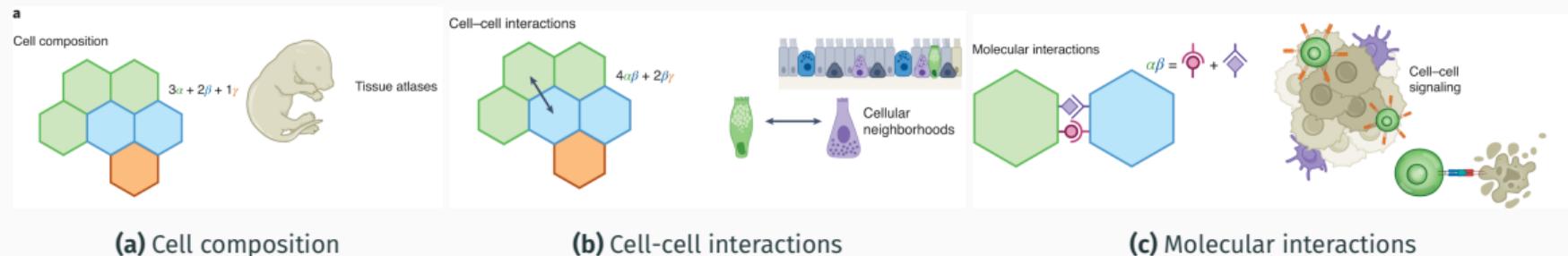
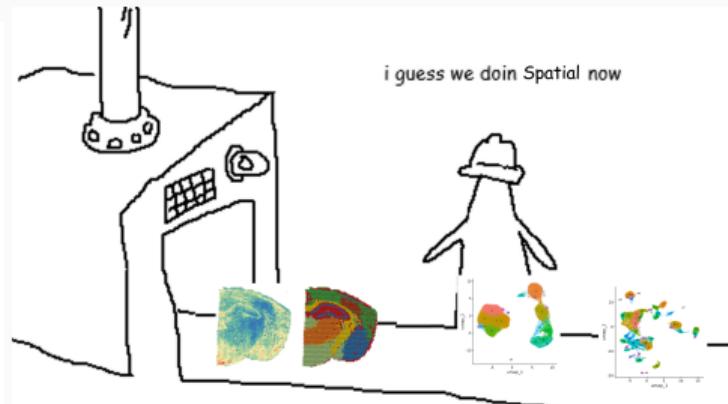
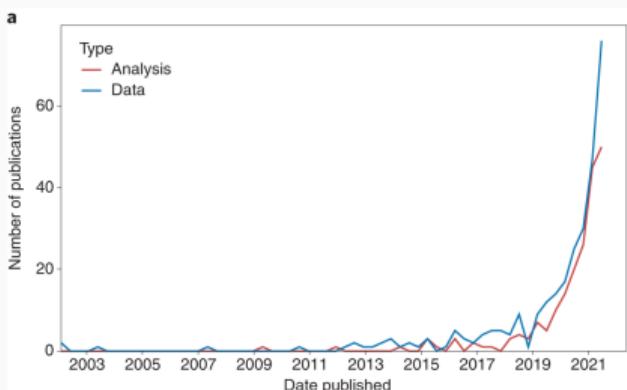
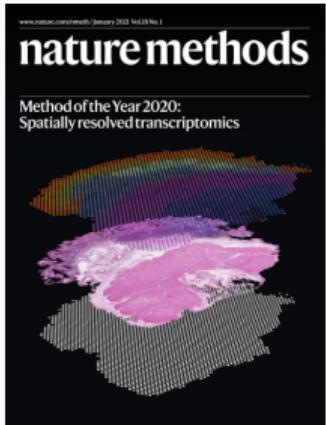


Figure: Classes of biological questions addressed by ST¹

¹Tian et al., *Nat Biotechnol*, 2023

WHY?



¹Marx, *Nat Methods*, 2021; Moses and Pachter, *Nat Methods*, 2022

SQUIDPY PIPELINE

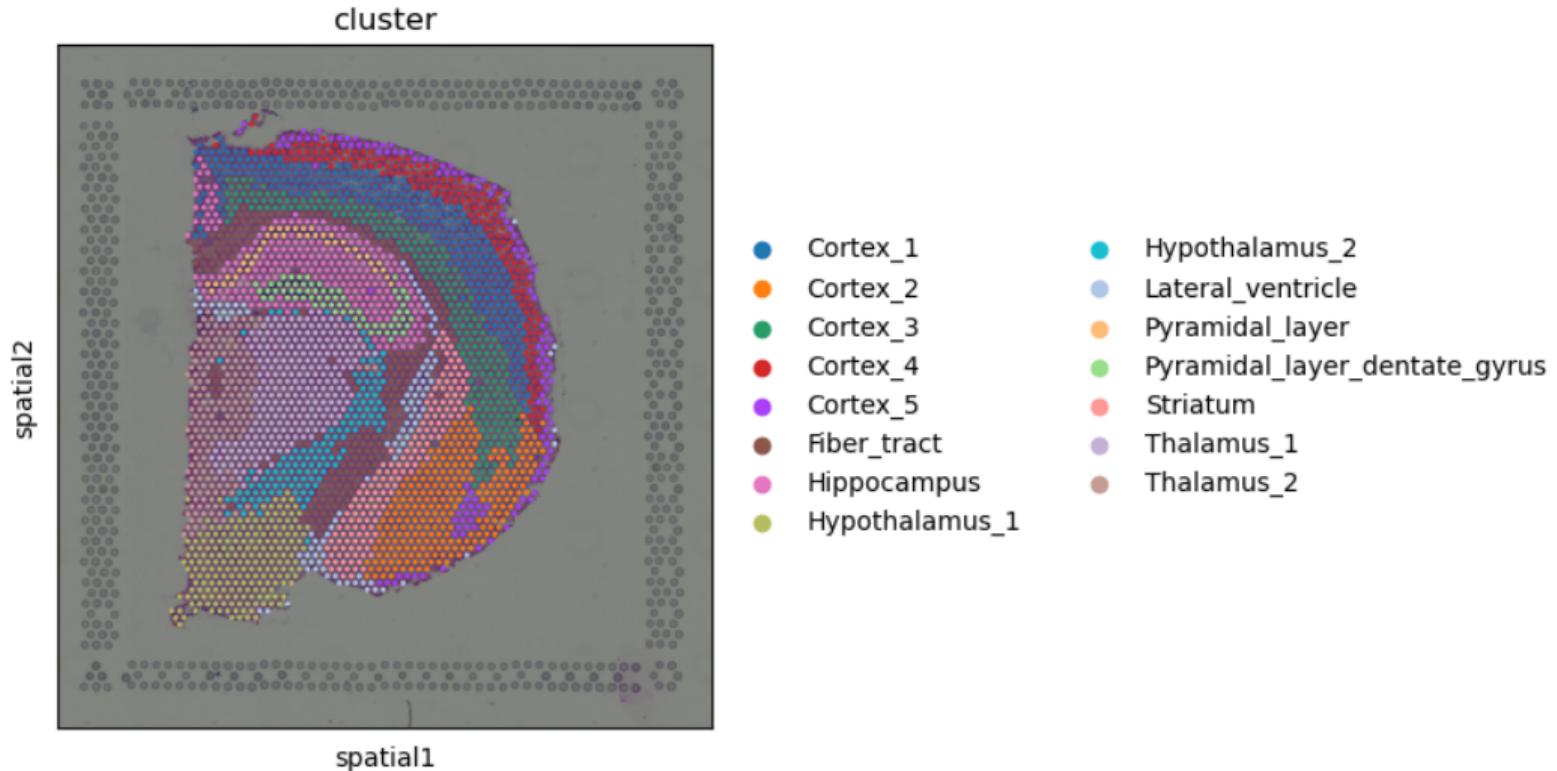


Figure: Spatial Scatter

¹https://squidpy.readthedocs.io/en/stable/notebooks/tutorials/tutorial_visium_hne.html

SPATIAL STATISTICS



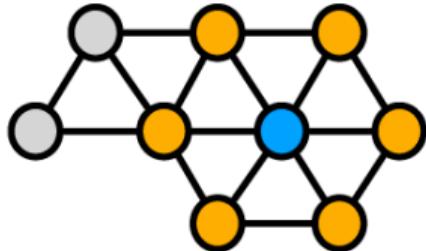


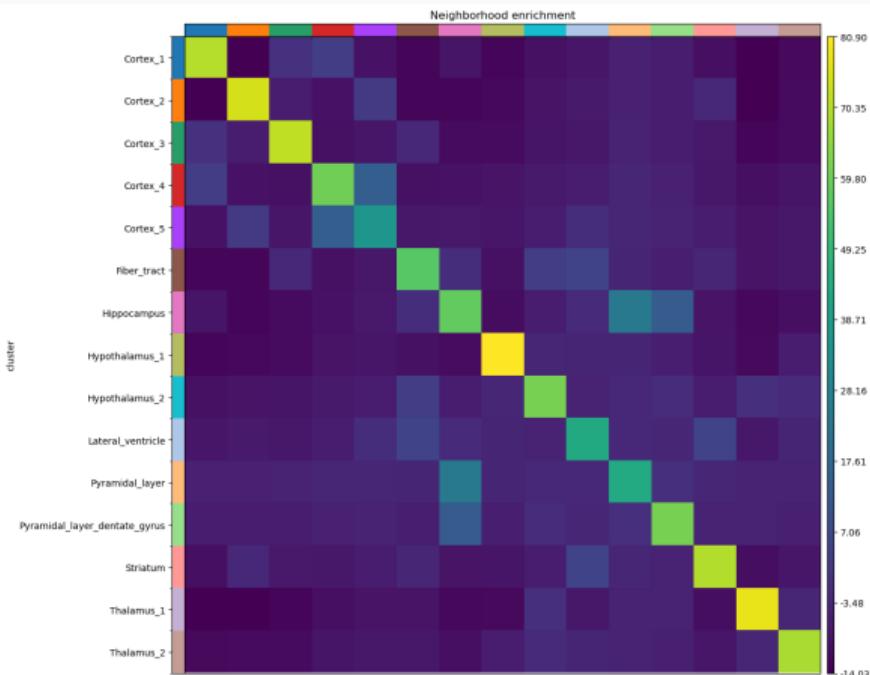
Figure: Neighbourhood graph

- Enrichment score based on proximity on the connectivity graph of cell clusters
- The number of observed events is compared against permutations and a z-score is computed

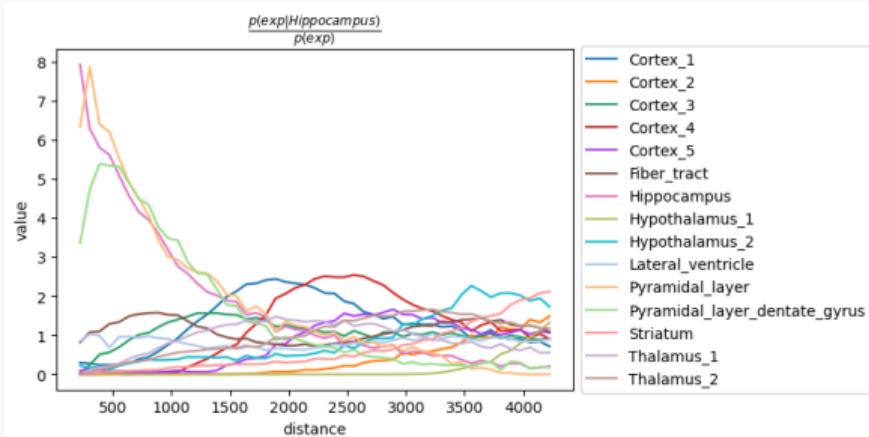
$$\text{Co-occurrence Score} = \frac{p(\text{exp}|\text{cond})}{p(\text{exp})}$$

- $p(\text{exp}|\text{cond})$ = conditional probability of observing a cluster exp conditioned on the presence of a cluster cond
- $p(\text{exp})$ = probability of observing exp in the radius size of interest
- computed across increasing radii size around each cell in the tissue

NEIGHBOURHOOD STATISTICS



(a) Neighbourhood enrichment¹



(b) Co-occurrence¹

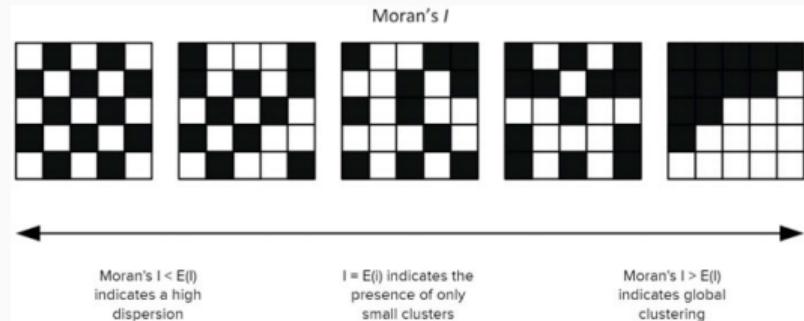
¹https://squidpy.readthedocs.io/en/stable/notebooks/tutorials/tutorial_visium_hne.html

$$I(x) = \frac{N}{W} \frac{\sum_{i=1}^N \sum_{j=1}^N w_{ij}(x_i - \bar{x})(x_j - \bar{x})}{\sum_{i=1}^N (x_i - \bar{x})^2}$$

$$W = \sum_{i=1}^N \sum_{j=1}^N w_{ij}$$

- w_{ij} = Spatial weights b/w spots i, j
- x_i = Observation x at spot i
- \bar{x} = Mean value of x

Autocorrelation: Similar/dissimilar at different locations



MORAN'S I RESULTS

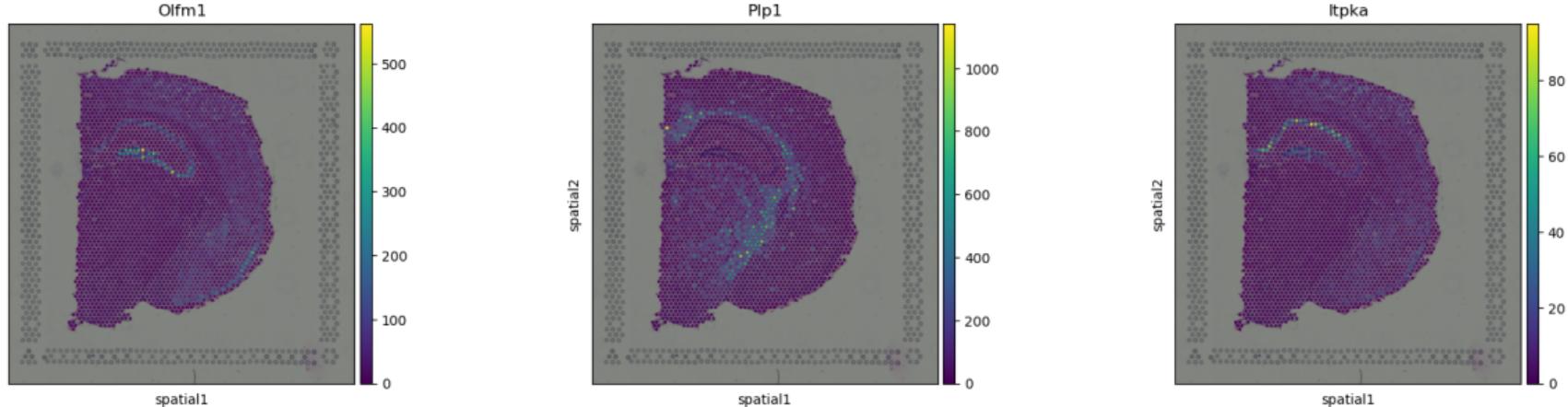
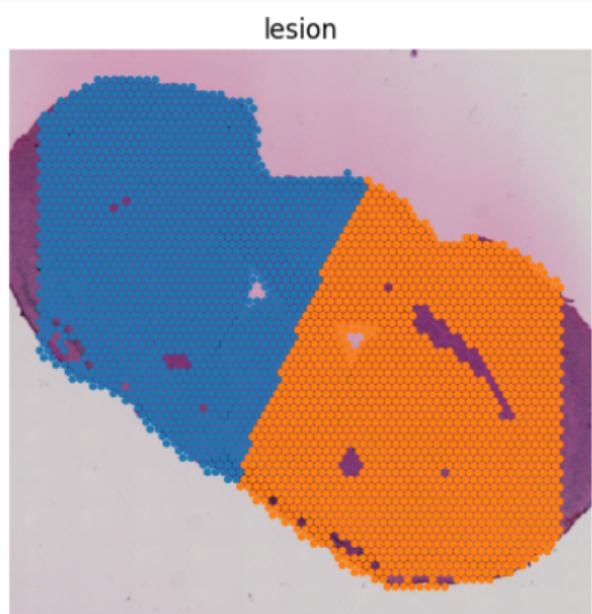


Figure: Spatially varying genes ¹

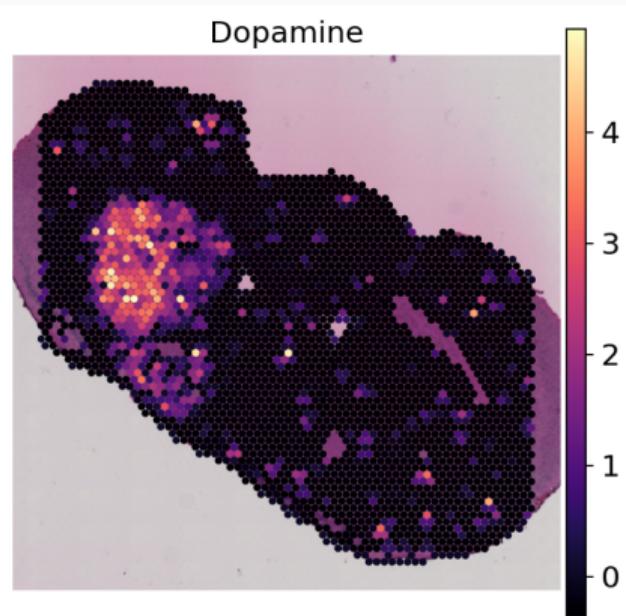
¹https://squidpy.readthedocs.io/en/stable/notebooks/tutorials/tutorial_visium_hne.html

SPATIAL CELL-CELL COMMUNICATION

DOPAMINE RESPONSE TO LESION



(a) Lesion



(b) Dopamine ¹

¹<https://liana-py.readthedocs.io/en/latest/notebooks/sma.html>

LIGAND RECEPTOR RESULTS

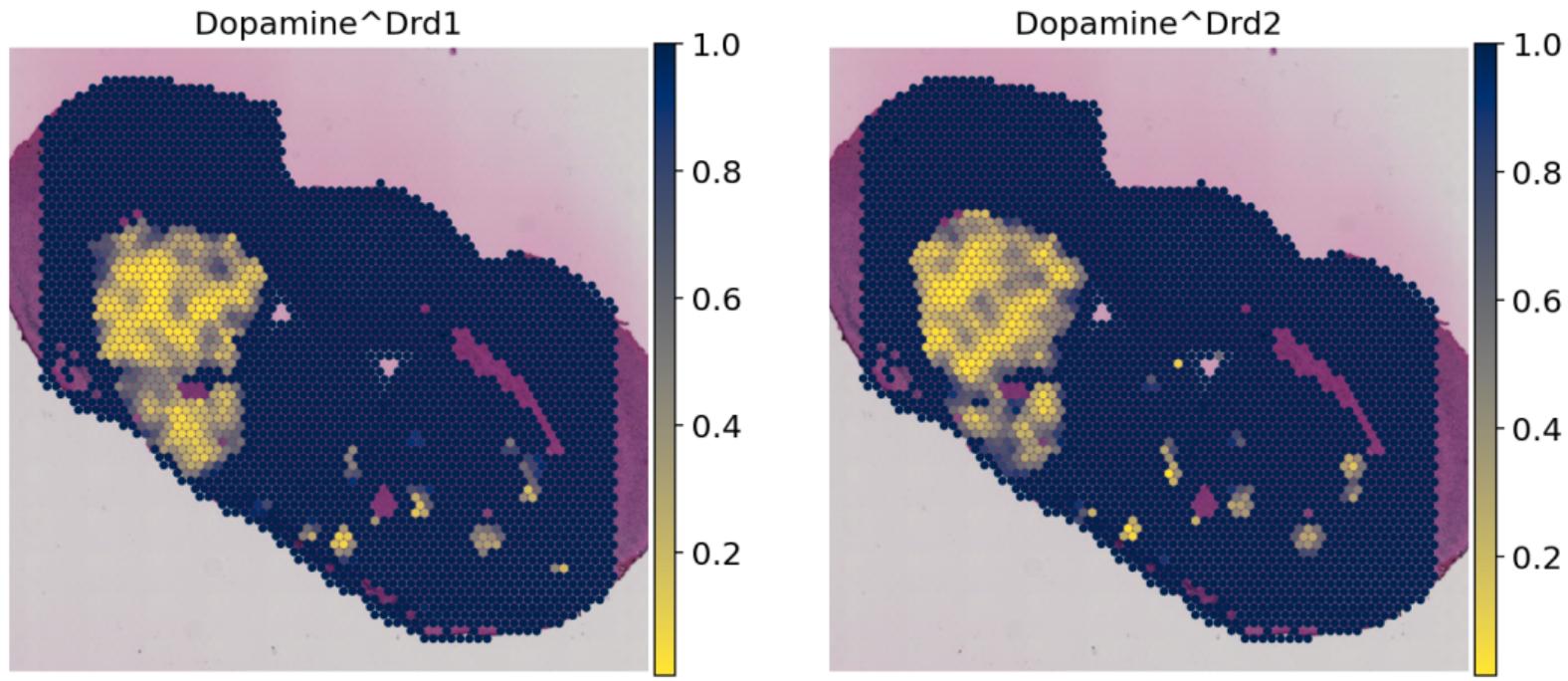


Figure: Dopamine Receptors ¹

¹<https://liana-py.readthedocs.io/en/latest/notebooks/sma.html>