

# Advanced topics in single cell analysis

Day 3 - Spatial Transcriptomics

Giovanni Palla, Basel, 28th April 2022



# **Table of content**

- Brief introduction to experimental techniques for spatial molecular measurements.
- Overview of analysis tools and methods for spatial omics analysis.
- Description of datasets and tasks for the day.

# The landscape of spatial transcriptomics technologies

**1982**

smFISH (on RN)

seqFISH

vizgen

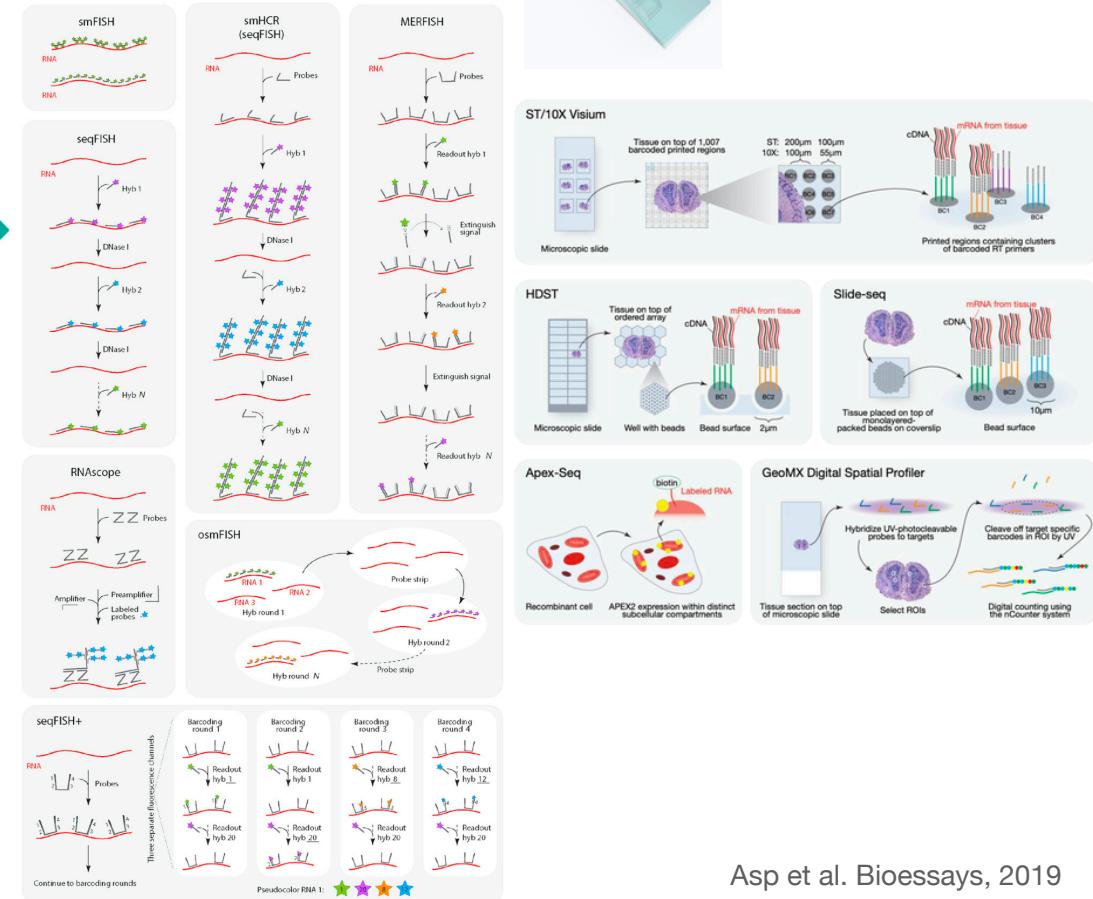
merscope

10X GENOMICS

FIND MORE DETAILS

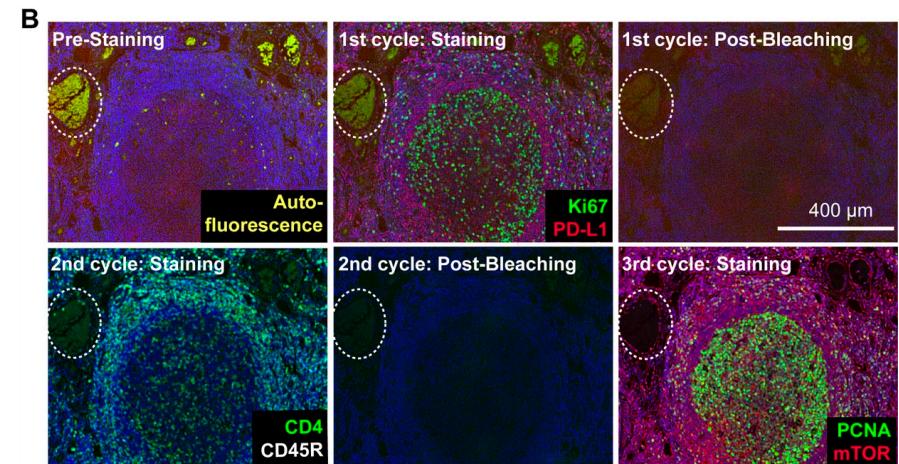
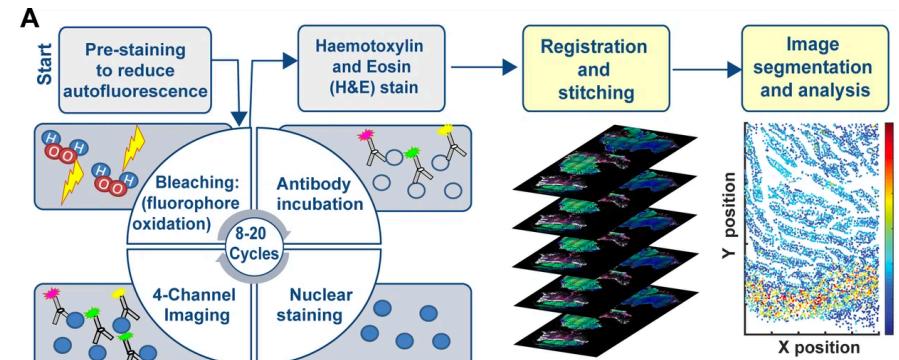
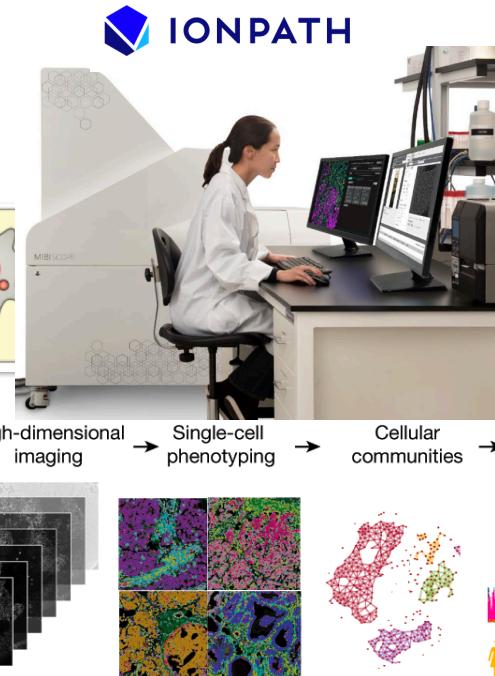
## GeoMx® Digital Spatial Profiler

The GeoMx Digital Spatial Profiler combines high-plex and high-throughput spatial analysis of RNA and protein expression data.



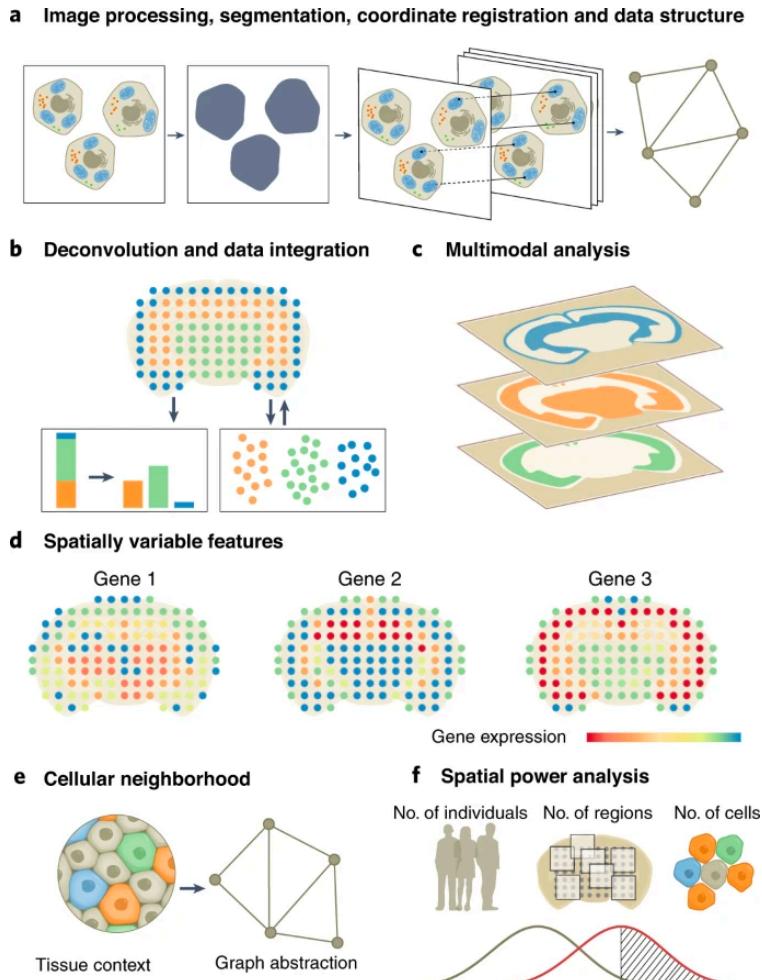
# Spatial proteomics

## Imaging Mass Cytometry and Multiplexed Immuno Histochemistry



Lin et al. Elife 2018  
Jackson et al. Nature 2020

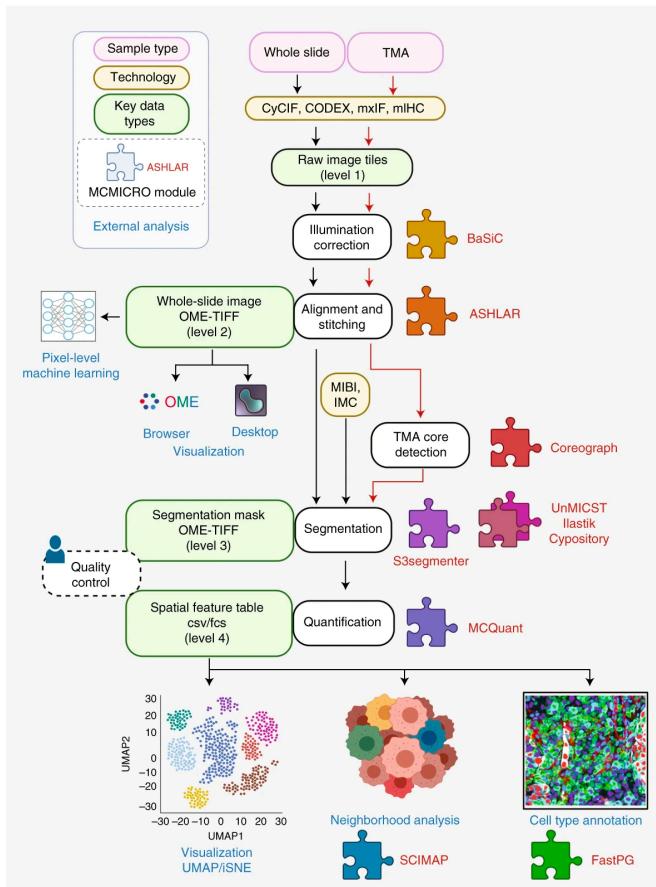
# Spatial molecular data processing and analysis



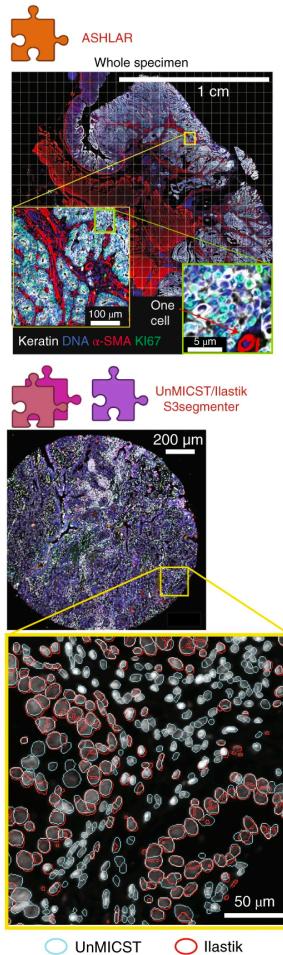
<b>Image processing, segmentation, registration and data structures</b>
Cell entity identification via segmentation
Cell entity identification via segmentation-free methods
Image processing
Image registration and alignment
Toolkit for spatial molecular data analysis
<b>Deconvolution and multimodal integration</b>
Cellular-interaction inference
Data integration and deconvolution
Gene-expression mapping and imputation
Spatial mapping of gene-expression profiles
<b>Multimodal integration</b>
<b>Spatially variable features, spatial communities and spatial power analysis</b>
Spatially variable genes
Spatial decomposition and clustering
Spatial power analysis

# Image processing, segmentation, registration and data structures

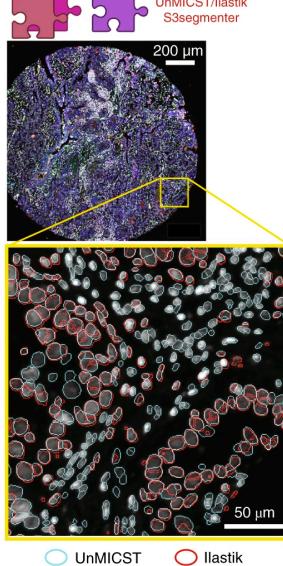
a



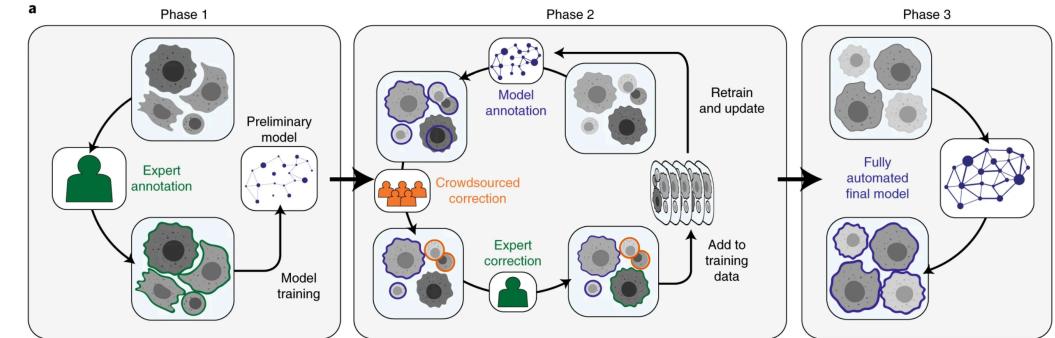
b



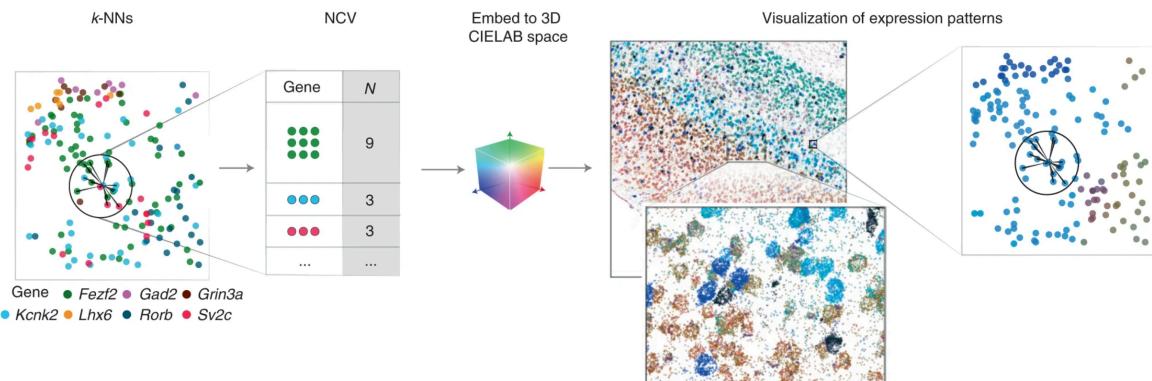
c



## Segmentation based methods and pipelines



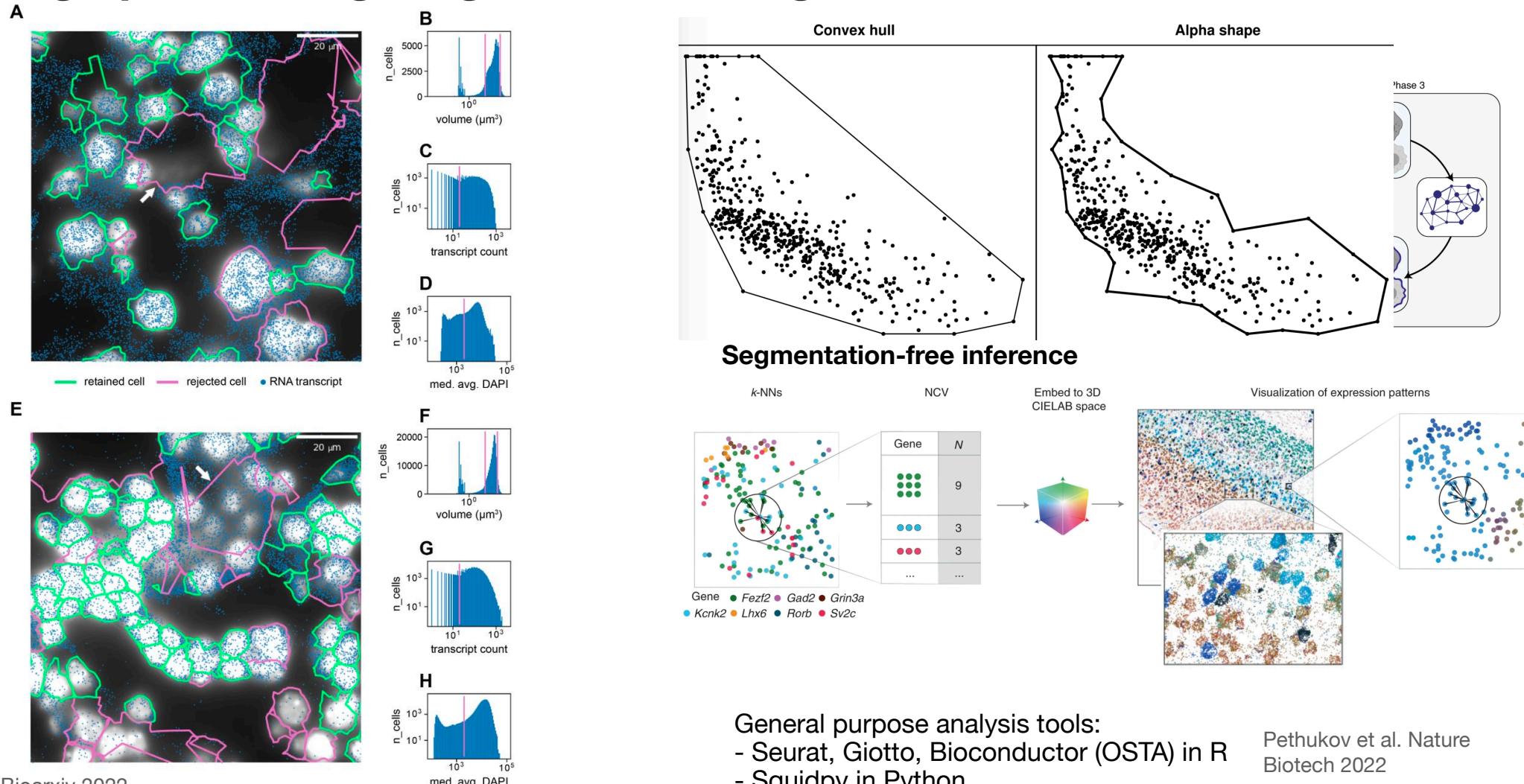
## Segmentation-free inference



## General purpose analysis tools:

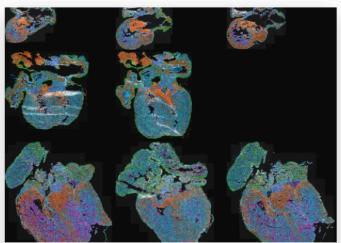
- Seurat, Giotto, Bioconductor (OSTA) in R
- Squidpy in Python

# Image processing, segmentation, registration and data structures



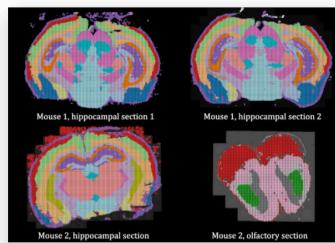
# Interactive visualization of spatial omics data

## TissUUmaps



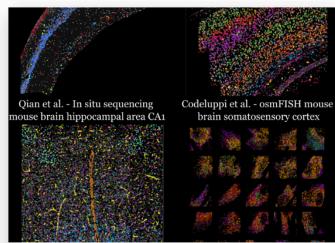
Modelling of cell-type signatures in the developmental human heart

▼ Read more ▼



Automated identification of the mouse brain's spatial compartments from in situ sequencing data

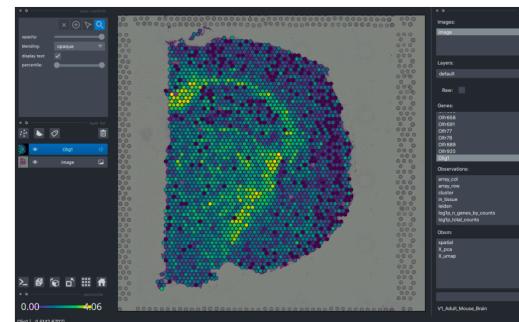
▼ Read more ▼



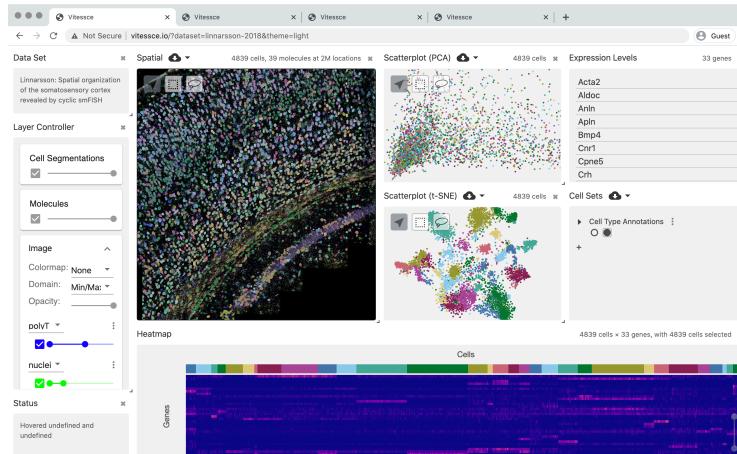
Spage2vec: Unsupervised representation of localized spatial gene expression signatures

▼ Read more ▼

## Napari



## Vitessce

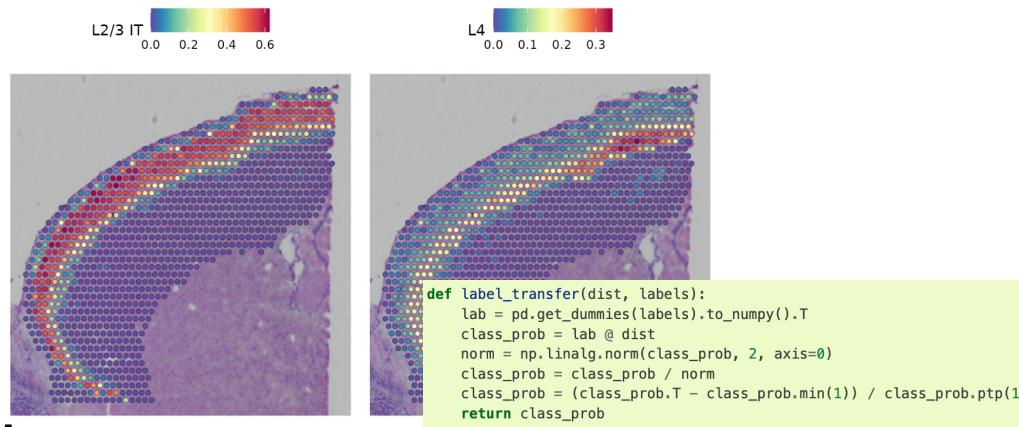


Pielawski et al. Bioarxiv 2022  
Snyder et al. Nature 2019

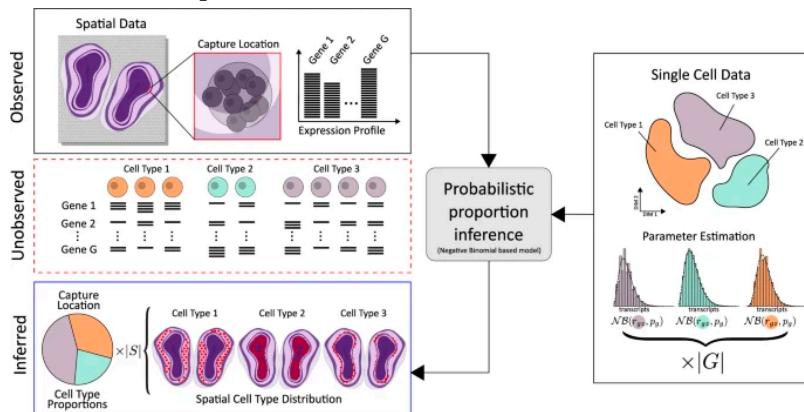
Palla, Spitzer et al. Nature Methods 2022

# From data integration to reference-based deconvolution

Seurat, Scanpy, others

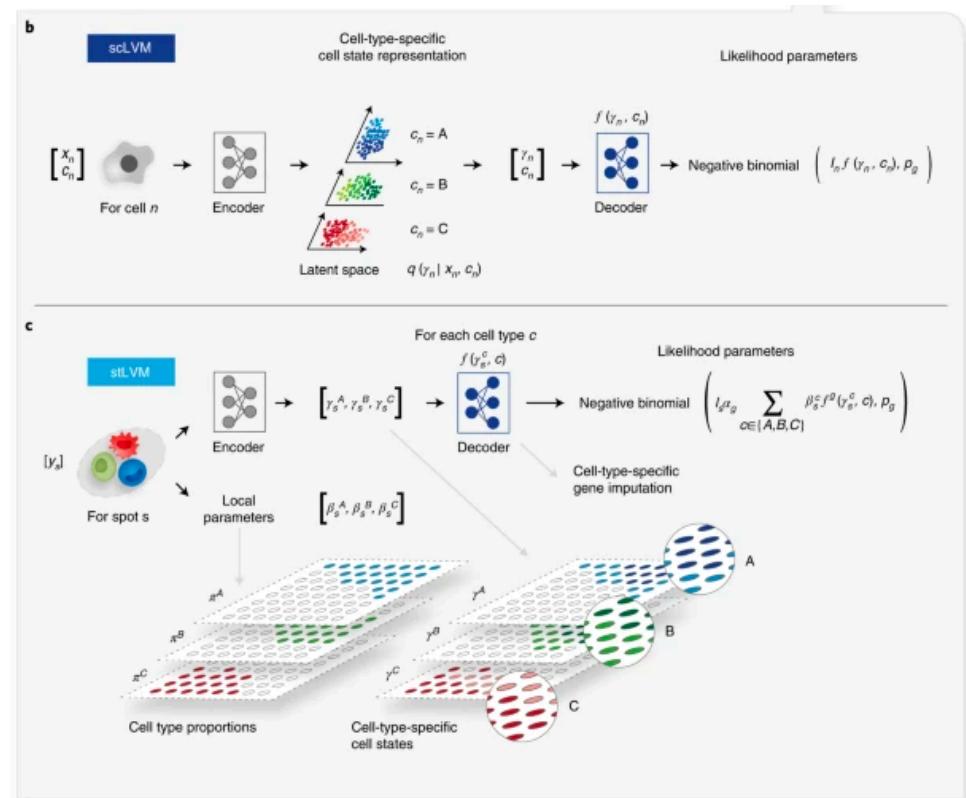


**Stereoscope**



Seurat vignette  
Andersson et al. Comm Bio. 2020

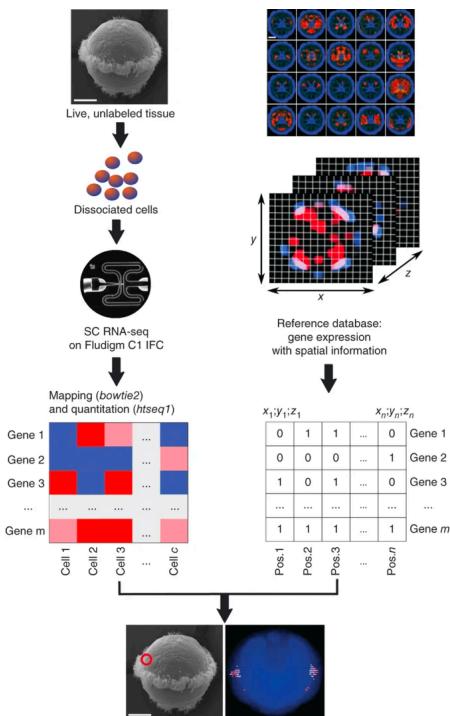
DestVI



Lopez et al. Nature Biotech 2022

# Gene expression imputation and cell type mapping

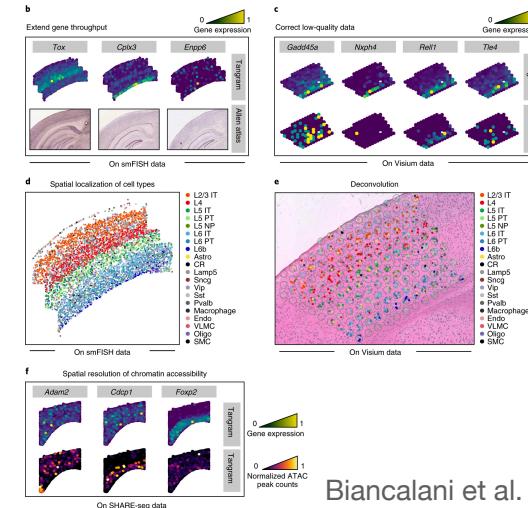
## Early work on single cell + spatial mapping



Afaik first mention of Seurat in literature 😊

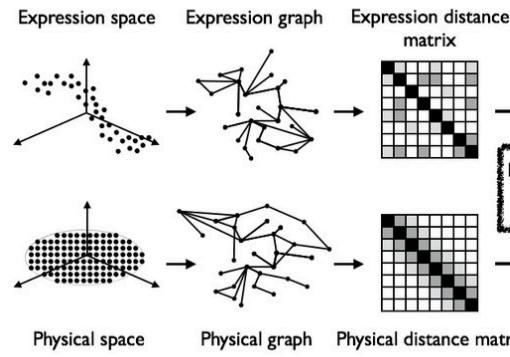
Achim et al. Nature Biotech 2015  
Satija et al. Nature Biotech 2015

## Tangram



Biancalani et al. Nature Methods 2021

## NovospaRC



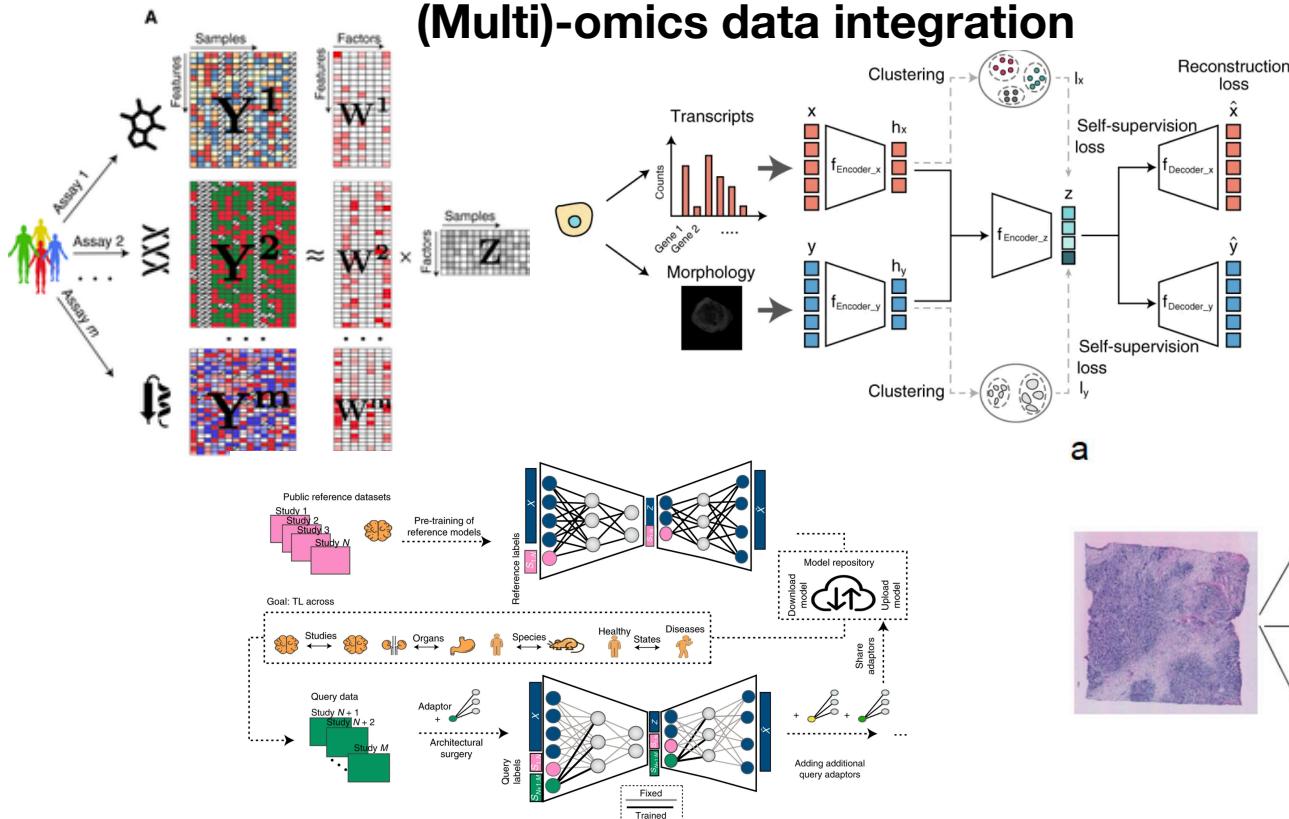
Optional:  
partial expression  
reference atlas

Nitzan et al. Nature 2021

# From multi-modal data integration to modality alignment

## From joint to aligned data representations

### (Multi)-omics data integration

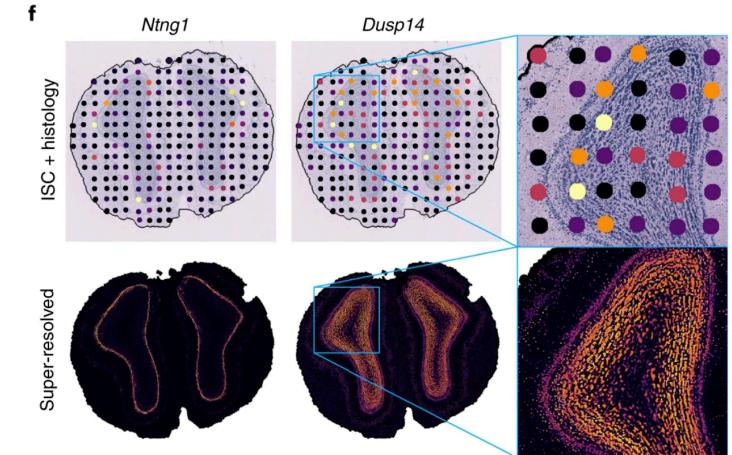


Argelaguet et al. Mol. Sys. Bio. 2018

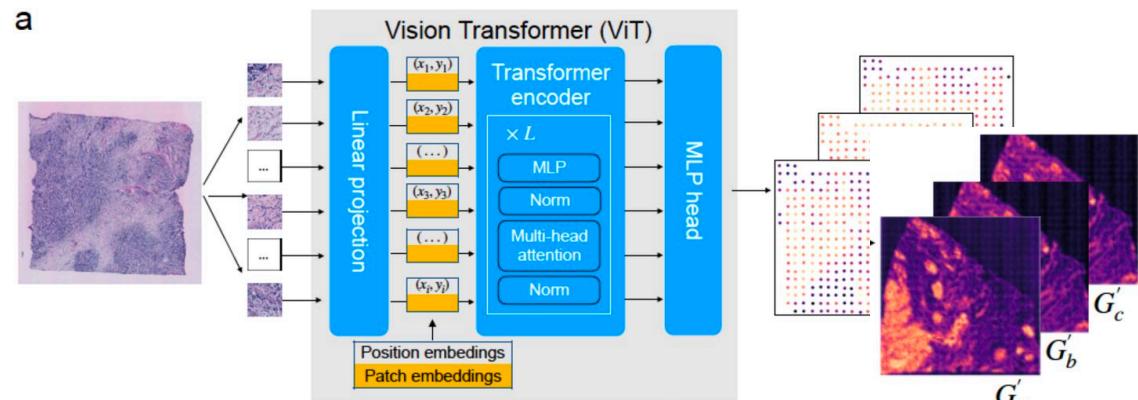
Bao et al. Nature Biotech 2022

Lotfollahi et al. Nature Biotech 2022

## Gene expression prediction



a



Berngestrahle et al. Nature Biotech 2022

Pang et al. Bioarxiv 2022

# From multi-modal data integration to modality alignment

## From joint to aligned data representations

Text prompt:

An astronaut riding a horse  
in the style of Andy Warhol

Image output:



Teddy bears shopping for  
groceries in the style of ukiyo-e



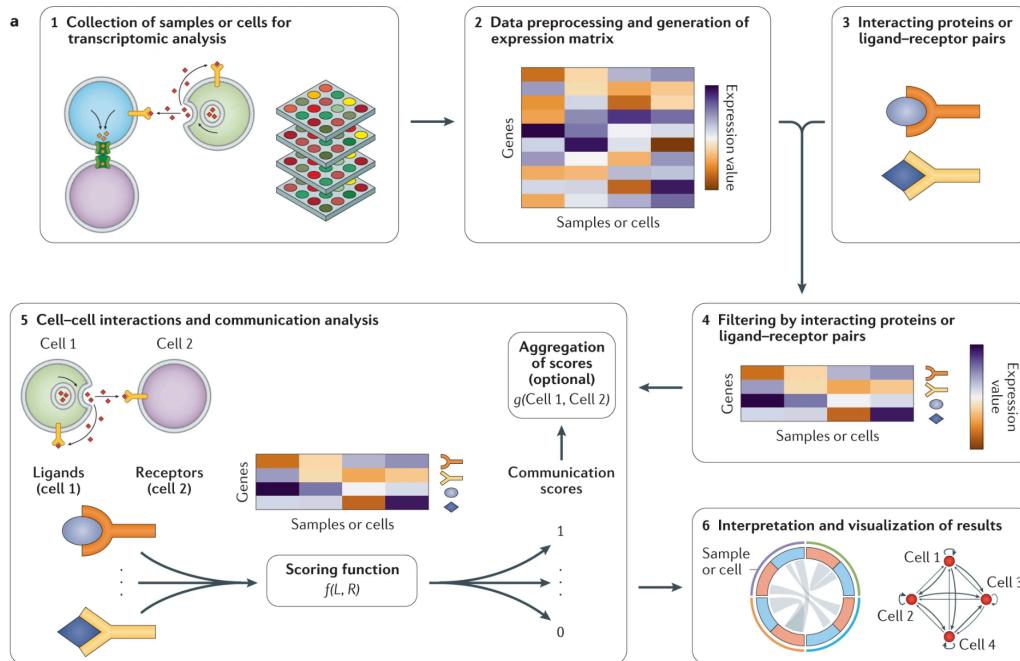
In ML/CV several efforts in recent years showed how representations learnt from large-scale experiments (data+compute) have great OOD and sampling capabilities.

OpenAI Dalle-2

# Cellular communication inference

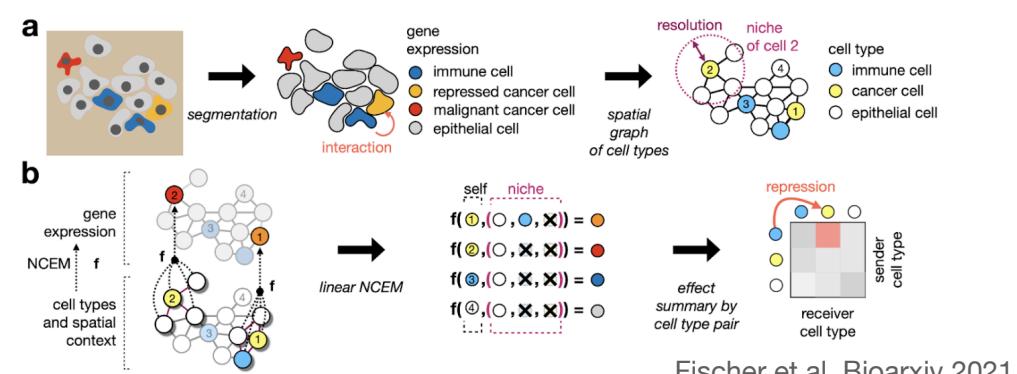
## From receptor-ligand interaction test to spatial variance component analysis

Cellchat, cellphonedb etc.



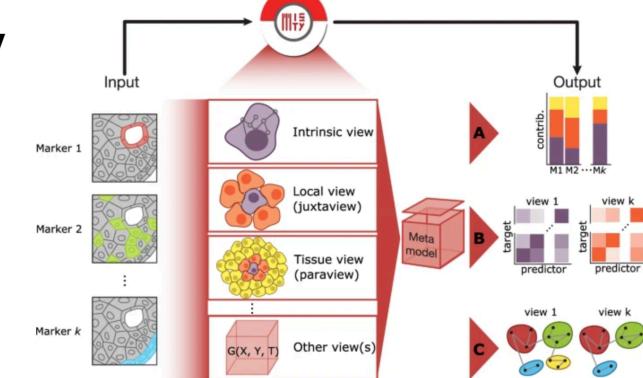
Armingol et al. Nature review genetics 2021

## Node-centric expression models



Fischer et al. Bioarxiv 2021

## MISTy

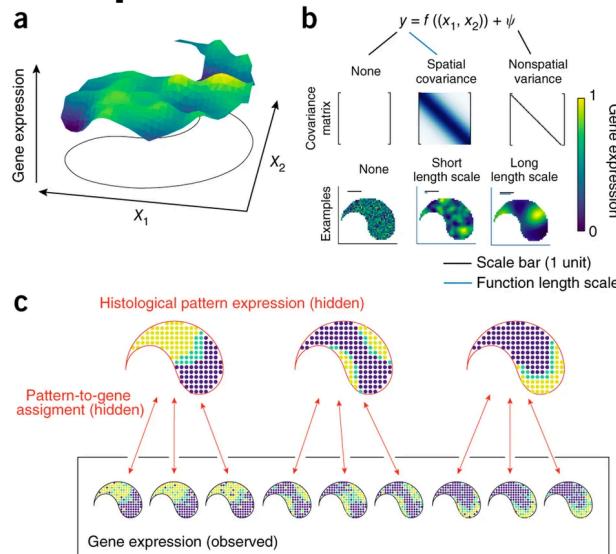


Tanevski et al. Genome Biology 2022

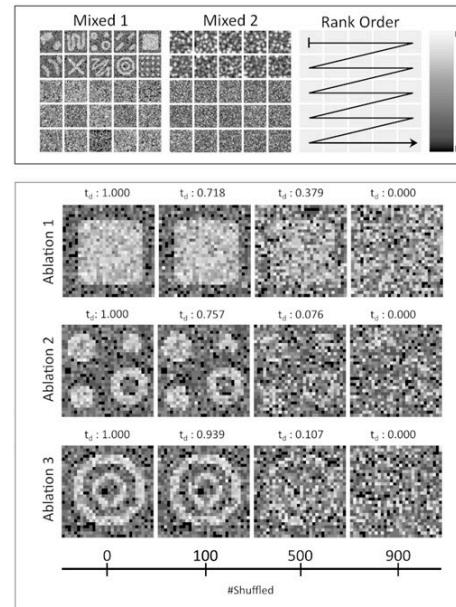
# Spatially variable genes and identification of tissue module

## Identifying spatial patterns in tissues.

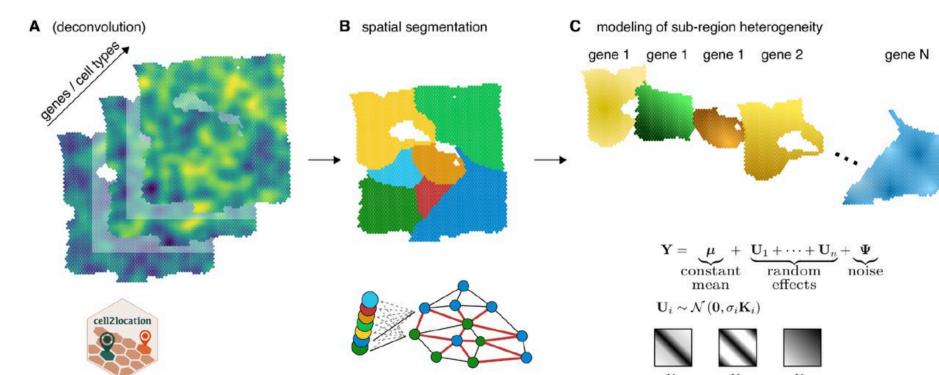
### SpatialDE



### Sepal

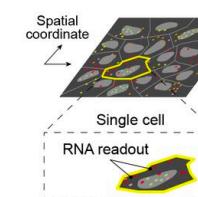


### SpatialDE2

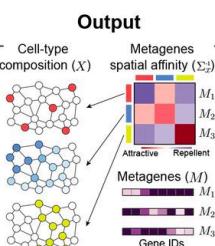
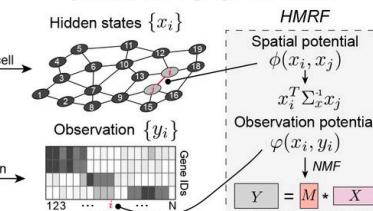


### SpiceMix

Spatial transcriptomics data  
(e.g. seqFISH+, STARmap, Visium)



SpiceMix: NMF-HMRF probabilistic graphical model

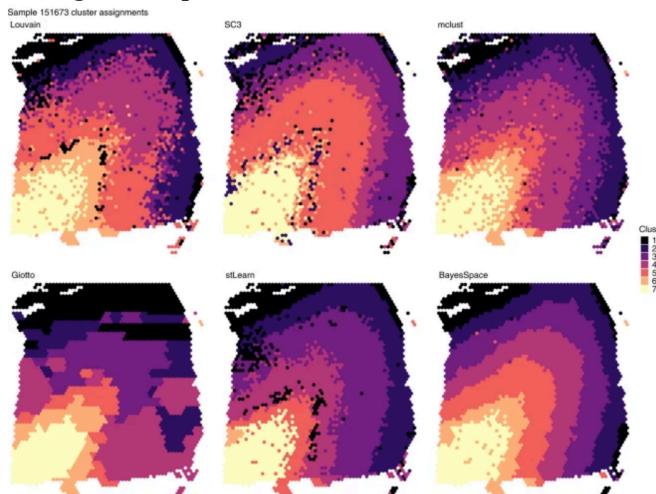


Svennsson et al. Nature Methods 2018  
Andersson et al. Bioinformatics 2021

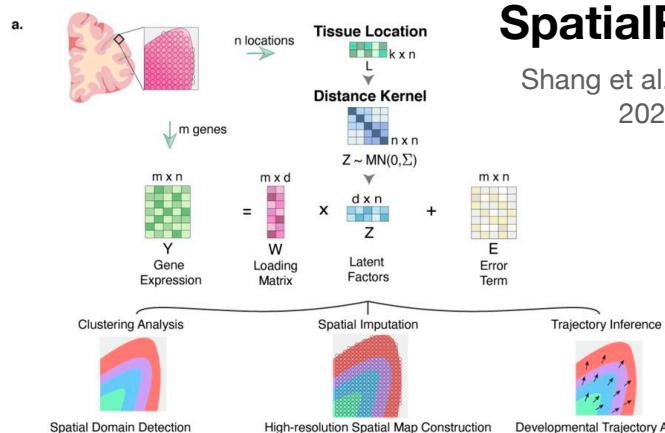
Kats et al. Bioarxiv 2021  
Chidester et al. Bioarxiv 2022

# Spatial clusters and spatially-aware dimensionality reduction

## BayesSpace



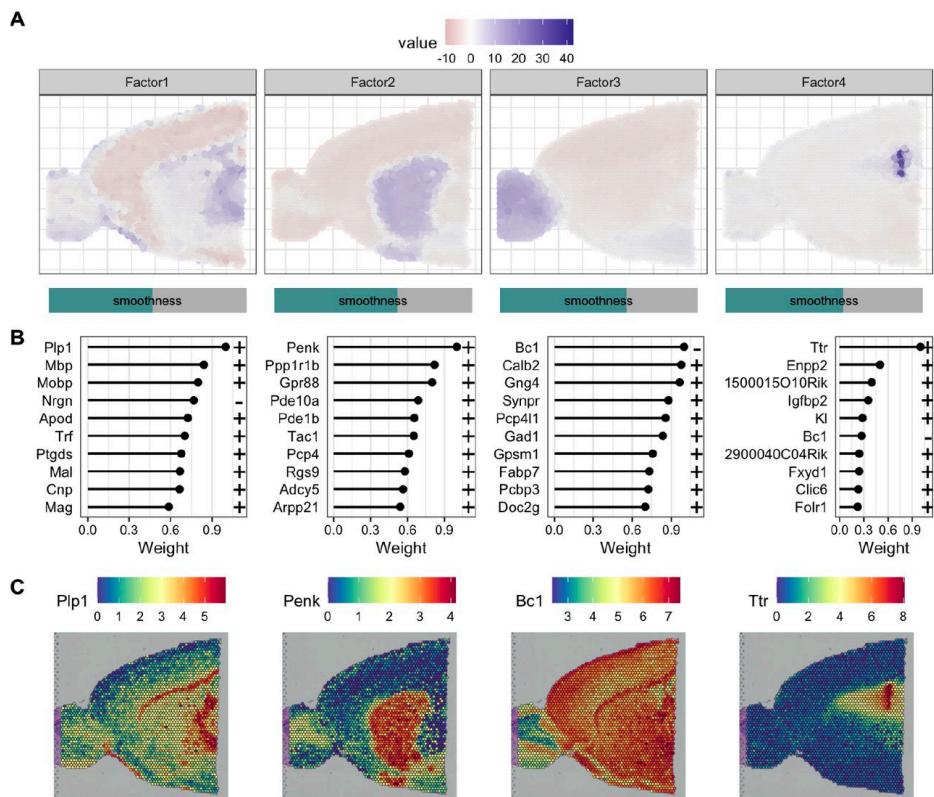
Zhao et al. Nature Biotech 2022



## SpatialPCA

Shang et al. Bioarxiv 2022

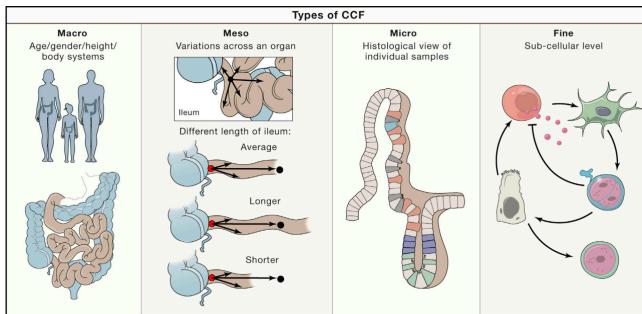
## Mefisto



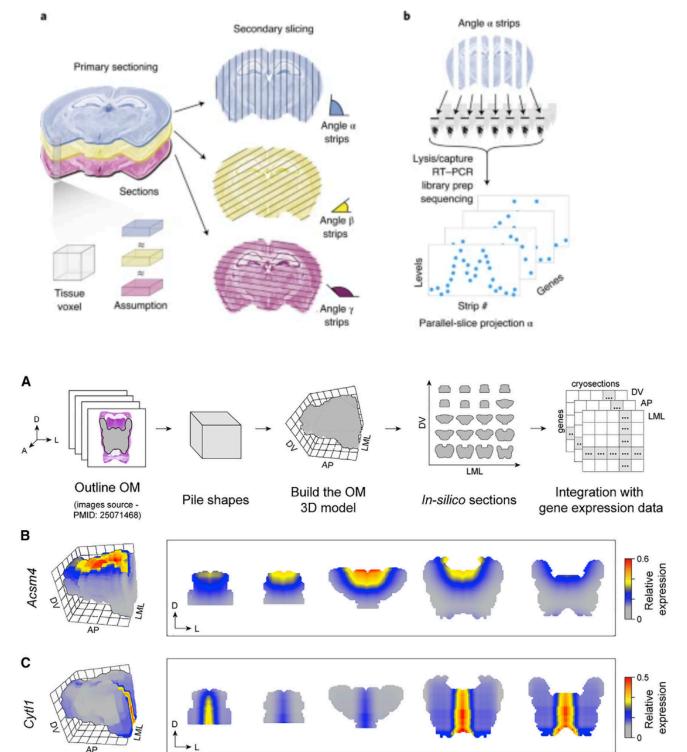
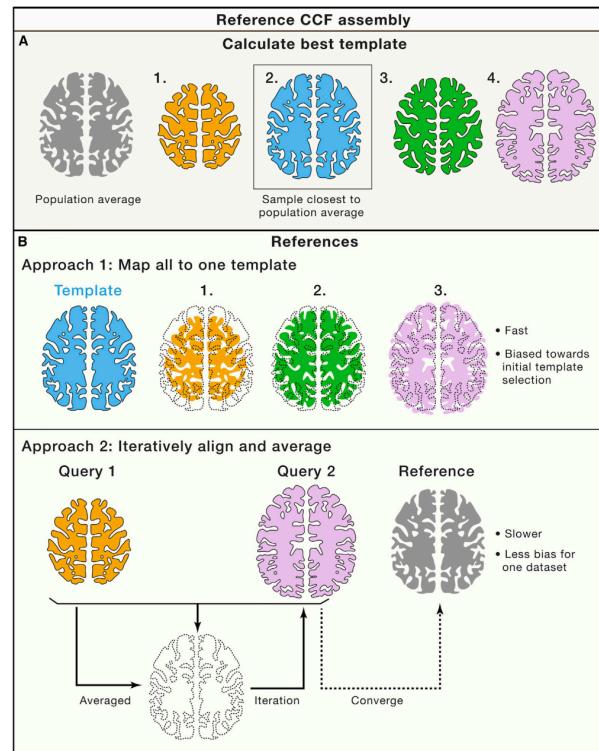
Velten et al. Nature Methods 2022

# Registration and alignment of spatial coordinates

## Towards building a Common Coordinate Framework of tissue and organs



Rood et al.  
Cell 2019



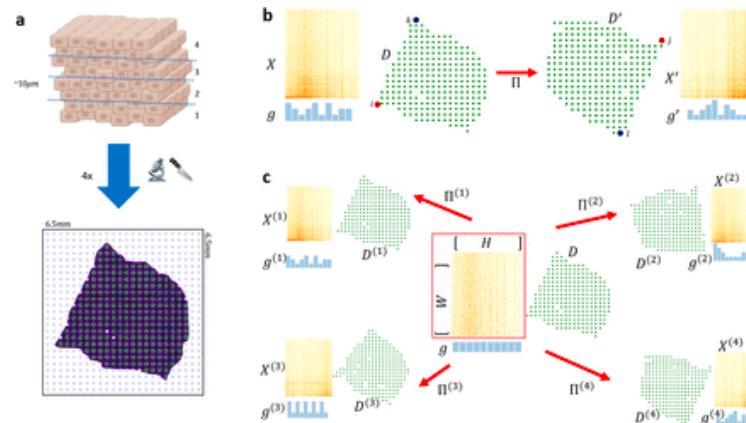
Schede et al Nature Biotech 2022  
Ruiz Teyada et al. Cell Reports 2022

# Registration and alignment of spatial coordinates

## Towards building a Common Coordinate Framework of tissue and organs

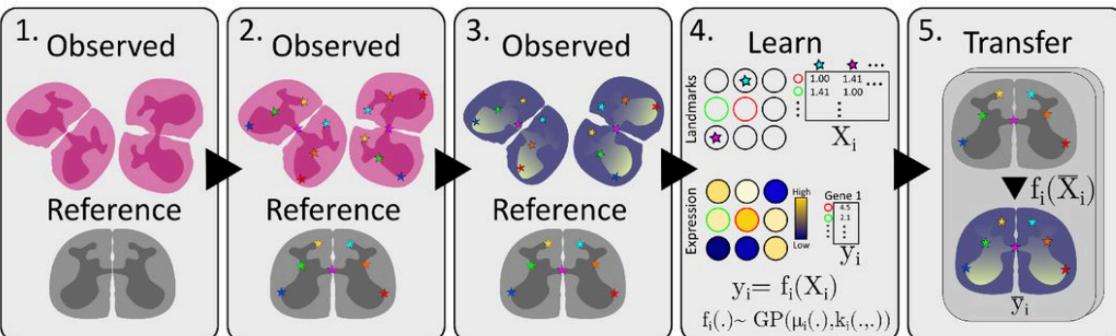
### Paste

Vieira et al.  
Bioarxiv 2022

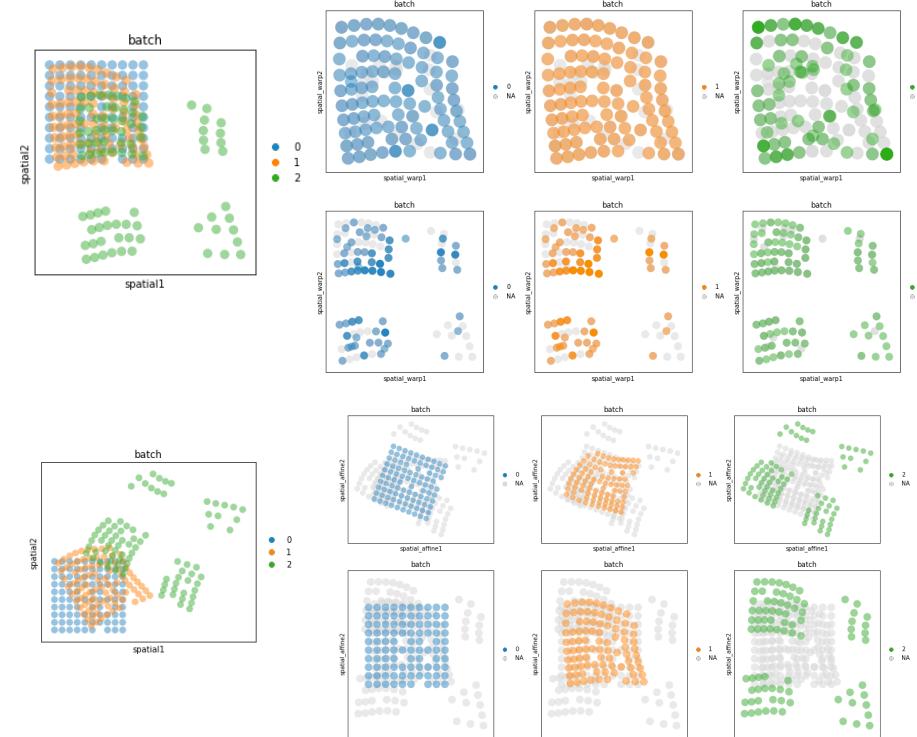


### Eggplant

Andersson et al.  
Bioarxiv 2022



### Moscot



Klein, Palla et al.  
in preparation

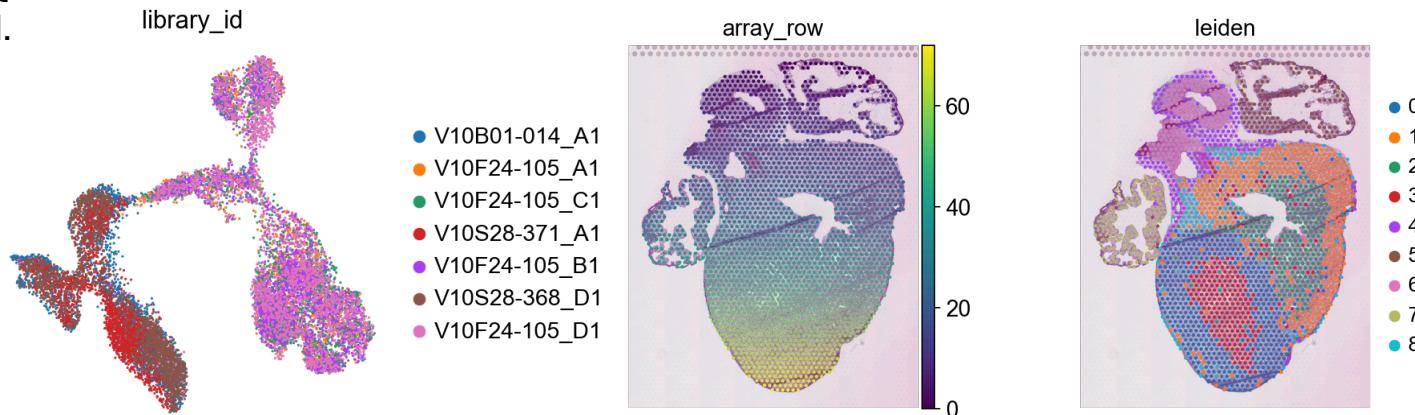
# Datasets

## Human Developmental Heart

### Spatial dataset

Andersson et al.  
Bioarxiv 2022

- 7 Visium slides:
- ~15k cells
- ~7k genes

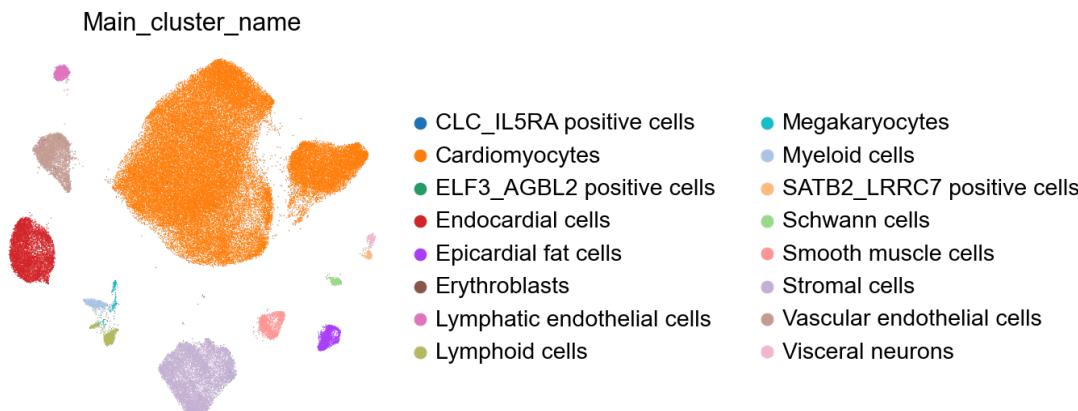


**Alma Andersson**  
PhD @ KTH Sweden

### Single-cell dataset

Cao et al. Science 2021

- ~ 96k cells
- ~30k genes



**Carlos Talavera Lopez**  
PI @ Helmholtz Munich

# Methods and notebooks

## Python

### Infrastructure, analysis and visualization

#### squidpy

Palla, Spitzer et al.  
Nat. Methods 2022

### Deconvolution

#### stereoscope

Andersson et al.  
Comm. Bio. 2021

### Registration

#### eggplant

Andersson et al.  
Comm. Bio. 2021

## R

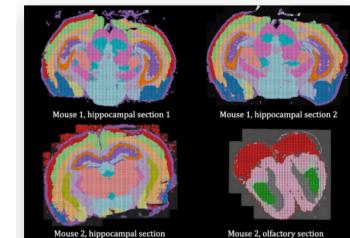
### spatial-experiment + bioconductor

Righelli, Weber et al.

## Browser

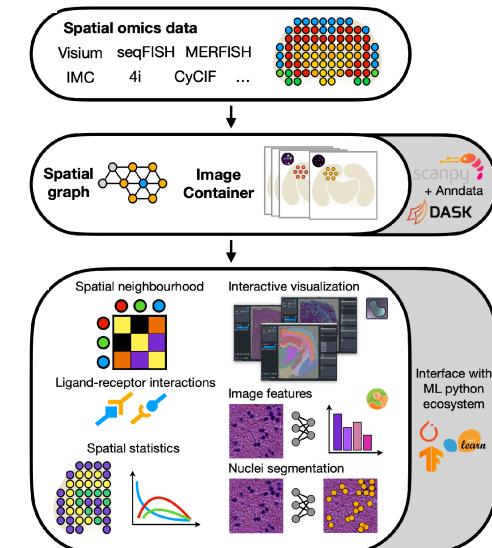
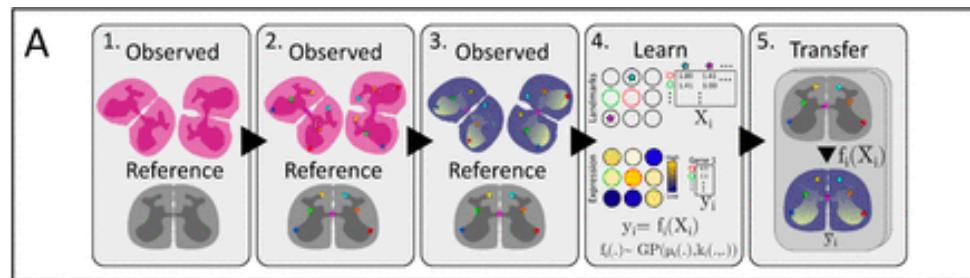
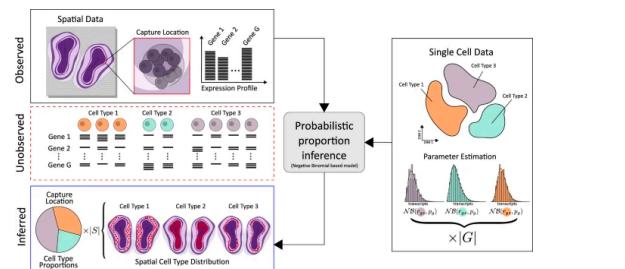
### tissuumap

Solorzano et al. 2020



Automated identification of  
the mouse brain's spatial  
compartments from in situ  
sequencing data

▼ Read more ▼



# Thank you for the attention!

The graphic features a central teal circle containing event details, surrounded by logos for various bioinformatics tools: squidpy, cell2location, egplant, and ncem.

**SCOG**  
Virtual Workshop:

**Spatial transcriptomics  
data analysis in Python**

**May 23 - 24, 2022**  
(1 - 5pm, CEST)

**REGISTER NOW**

**@singlecelomics**

**singlecell.de**

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DLR