

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

GeoMx[®] Digital Spatial Profiler

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

[FIND MORE DETAILS](#)

1982

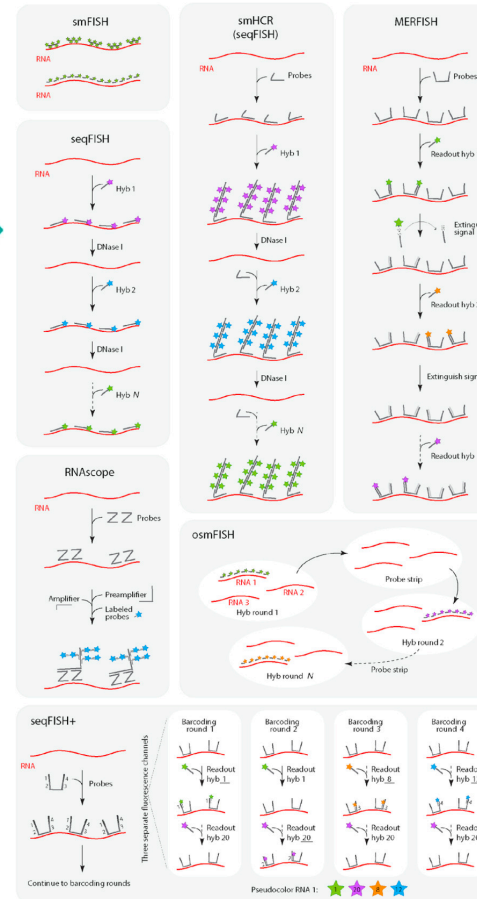
smFISH
(on RNA)

seqFISH

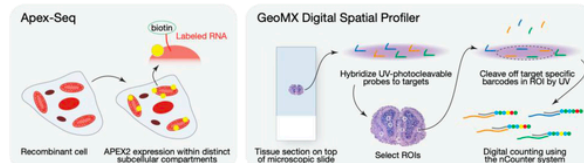
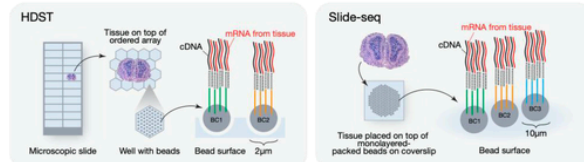
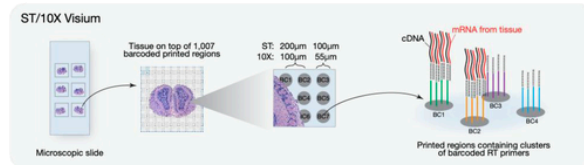
DNA
mic
Nanostring
GeoMx
10X GENOMICS



Section 5. *In silico* reconstruction of spatial data



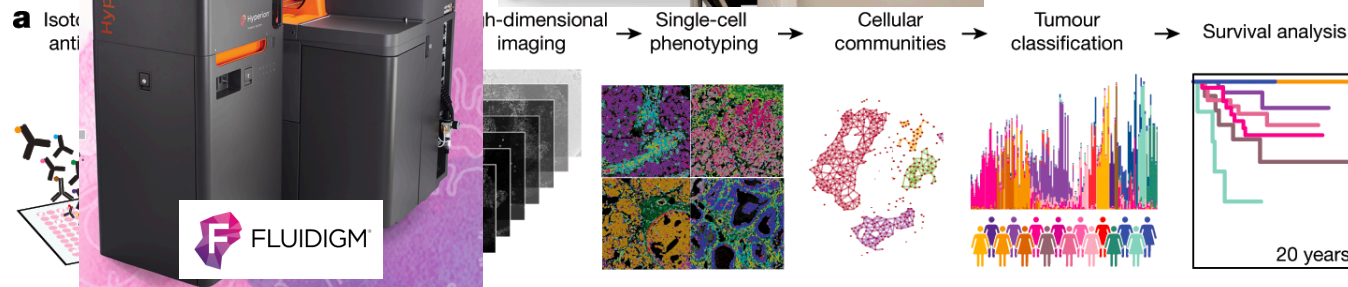
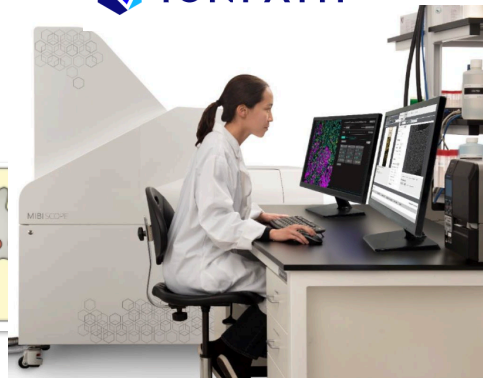
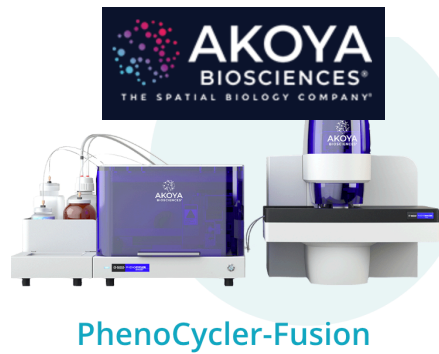
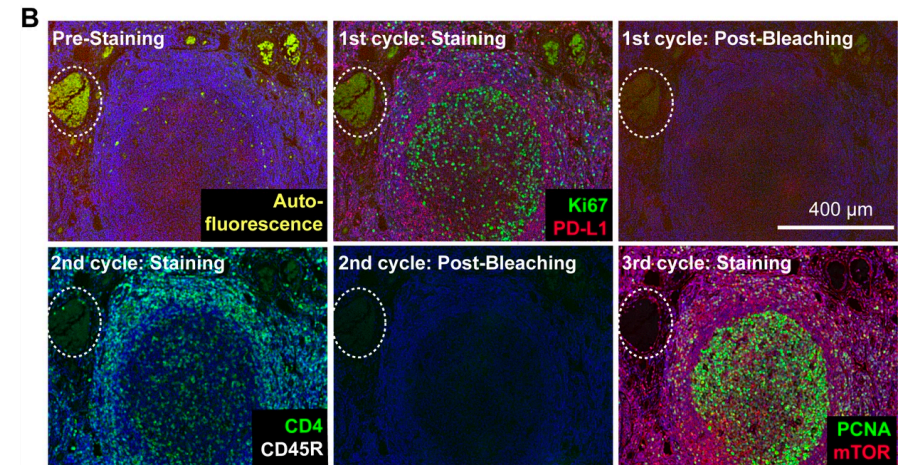
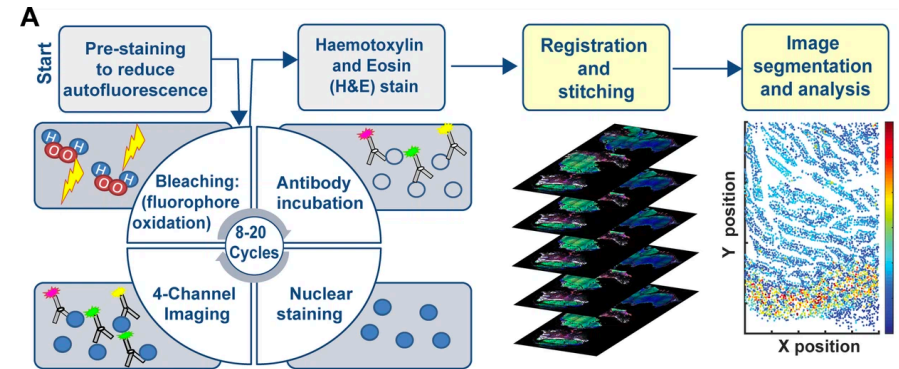
10X GENOMICS technologies



Asp et al. Bioessays, 2019

Spatial proteomics

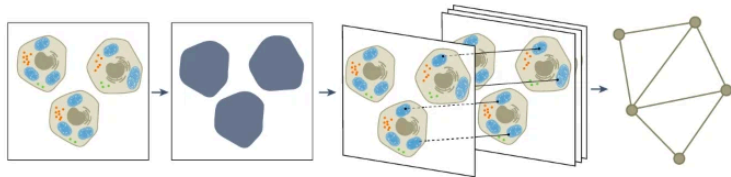
Imaging Mass Cytometry and Multiplexed Immuno Histochemistry



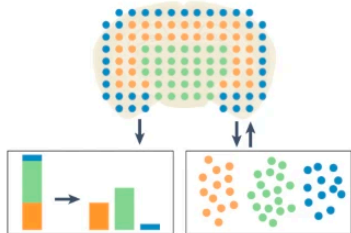
Lin et al. Elife 2018
Jackson et al. Nature 2020

Spatial molecular data processing and analysis

a Image processing, segmentation, coordinate registration and data structure



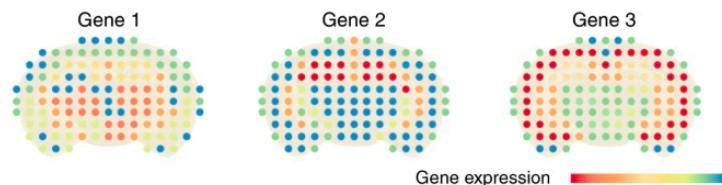
b Deconvolution and data integration



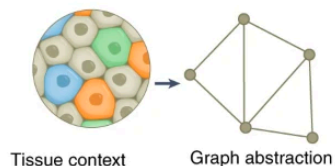
c Multimodal analysis



d Spatially variable features



e Cellular neighborhood



f Spatial power analysis

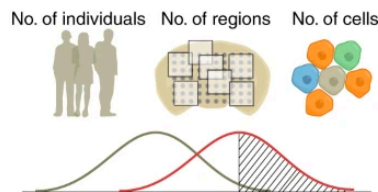


Image processing, segmentation, registration and data structures

Cell entity identification via segmentation

Cell entity identification via segmentation-free methods

Image processing

Image registration and alignment

Toolkit for spatial molecular data analysis

Deconvolution and multimodal integration

Cellular-interaction inference

Data integration and deconvolution

Gene-expression mapping and imputation

Spatial mapping of gene-expression profiles

Multimodal integration

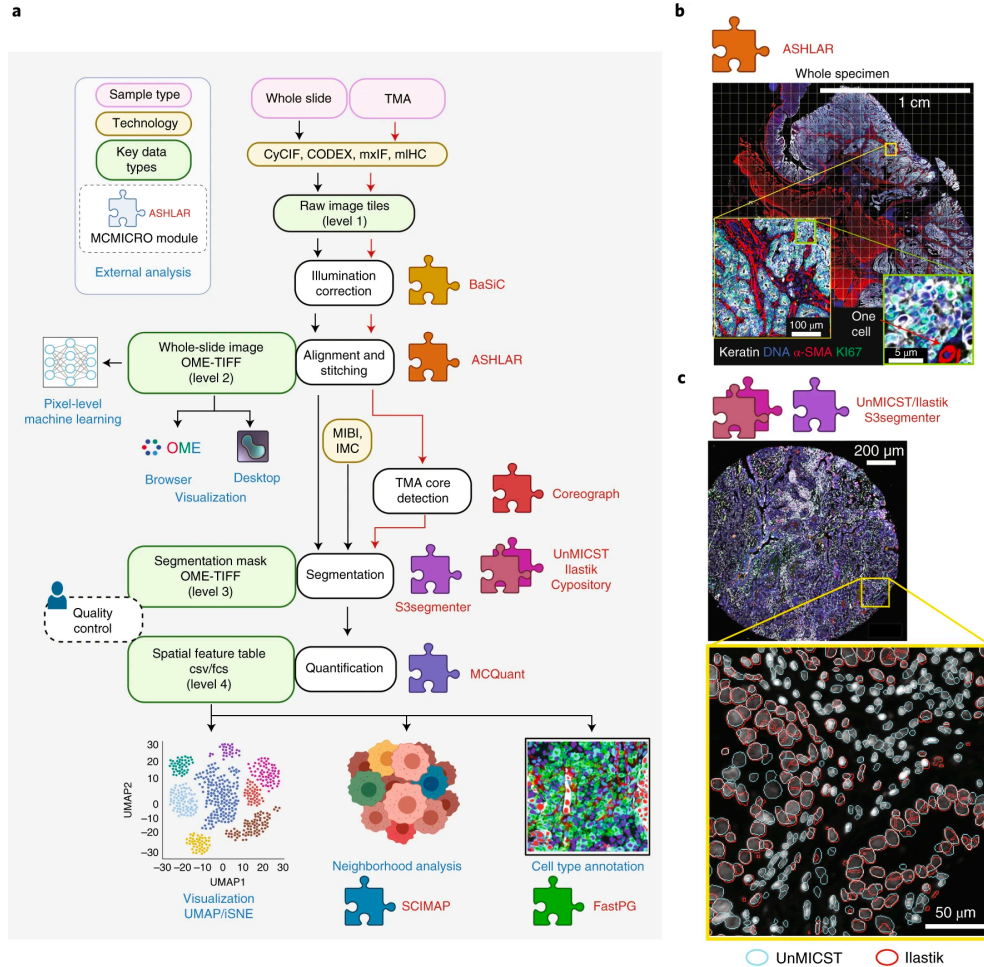
Spatially variable features, spatial communities and spatial power analysis

Spatially variable genes

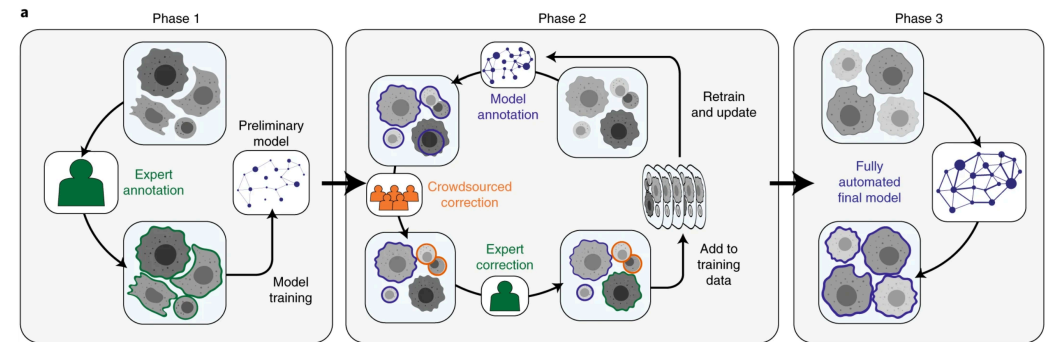
Spatial decomposition and clustering

Spatial power analysis

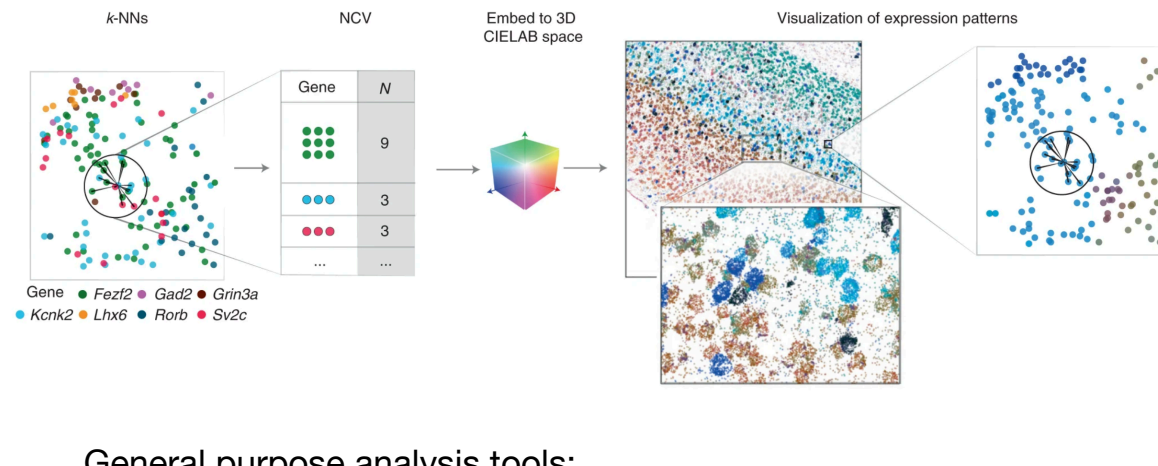
Image processing, segmentation, registration and data structures



Segmentation based methods and pipelines



Segmentation-free inference

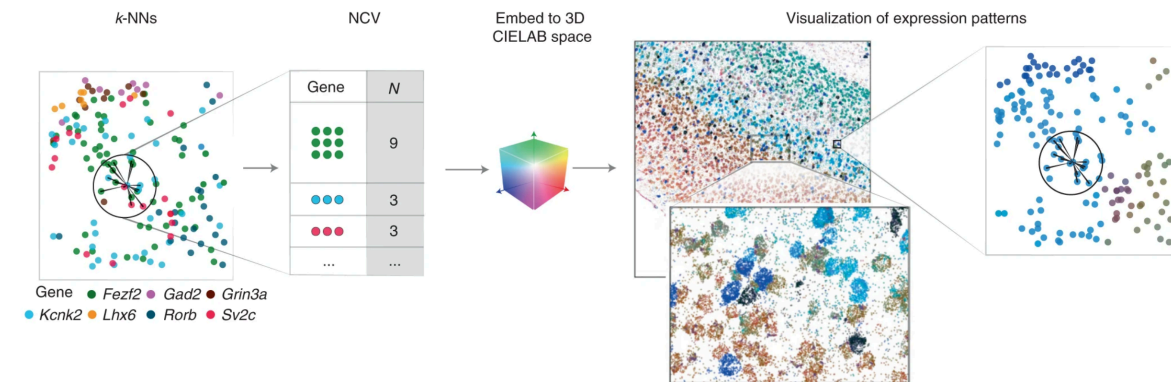
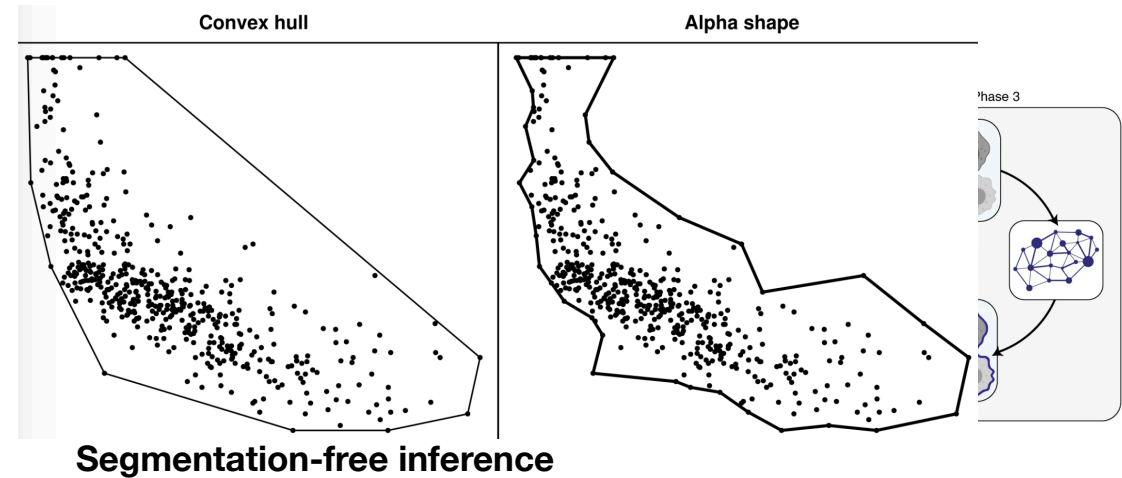
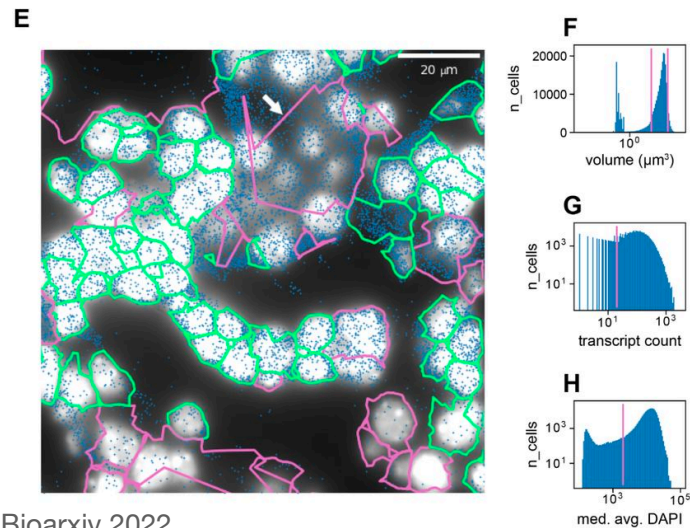
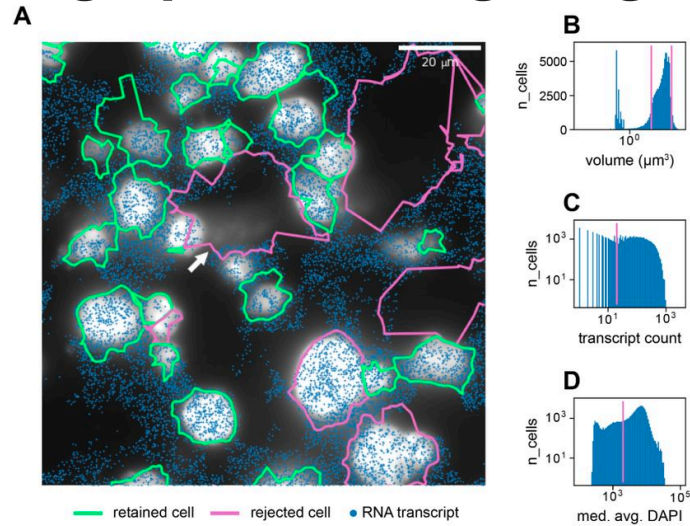


MCMICRO, Schapiro et al. Nature Methods 2022

General purpose analysis tools:
 - Seurat, Giotto, Bioconductor (OSTA) in R
 - Squidpy in Python

Pethukov et al. Nature Biotech 2022

Image processing, segmentation, registration and data structures



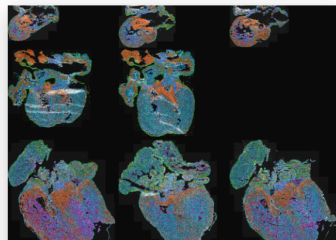
General purpose analysis tools:

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

Pethukov et al. Nature Biotech 2022

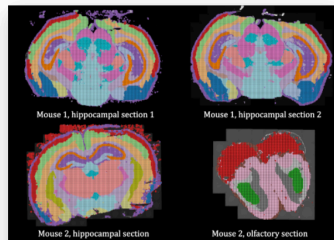
Interactive visualization of spatial omics data

TissUMaps



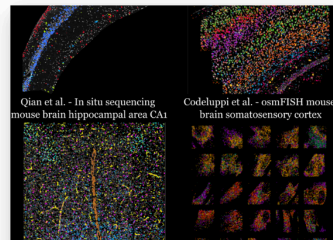
Modelling of cell-type signatures in the developmental human heart

▼ Read more ▼



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

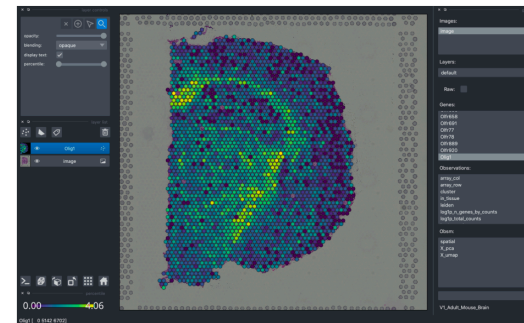
▼ Read more ▼



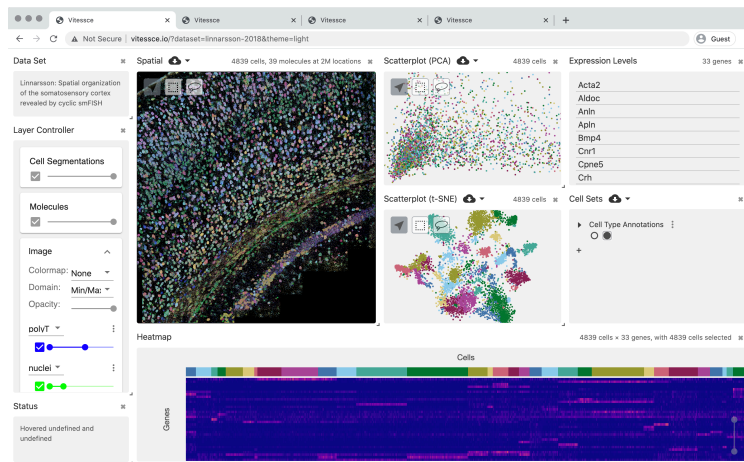
Spag2vec: Unsupervised representation of localized spatial gene expression signatures

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Napari



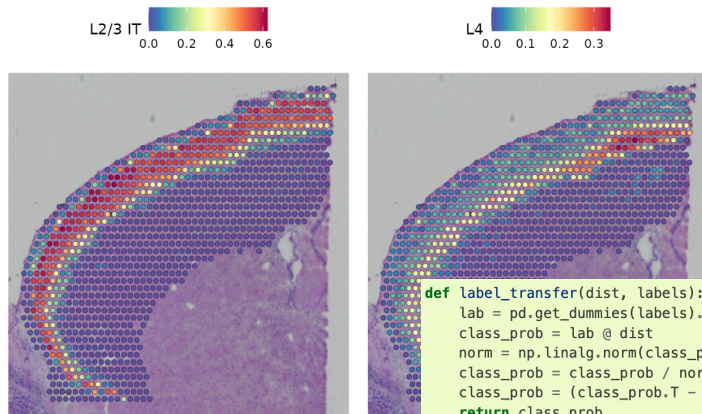
Vitessce



Pielawski et al. Bioarxiv 2022
Snyder et al. Nature 2019
Palla, Spitzer et al. Nature Methods 2022

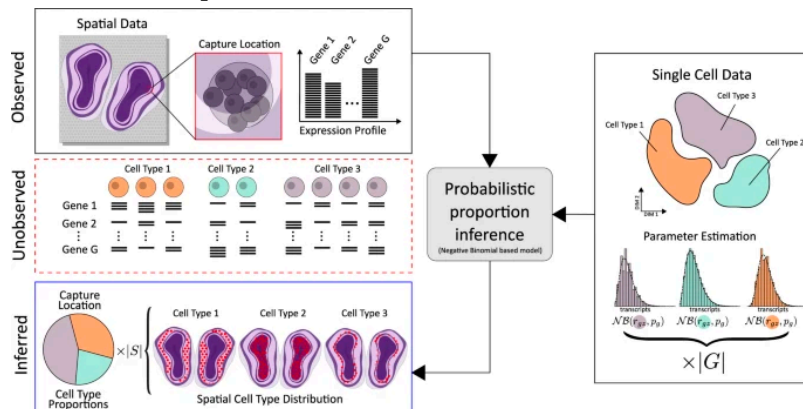
From data integration to reference-based deconvolution

Seurat, Scanpy, others



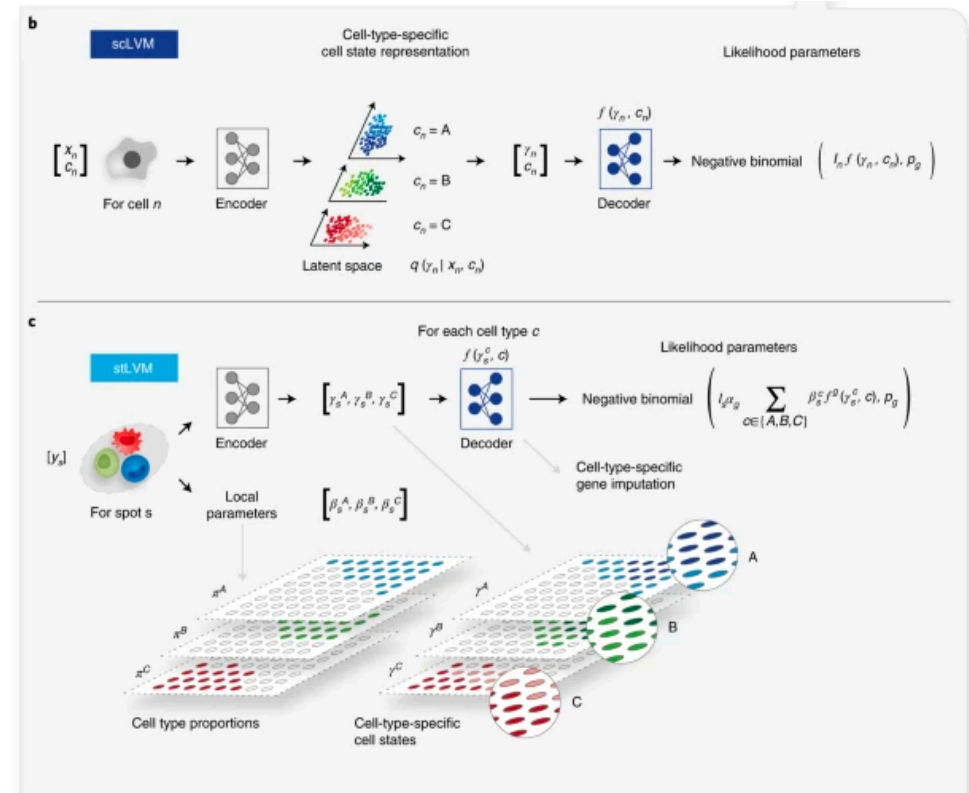
```
def label_transfer(dist, labels):
    lab = pd.get_dummies(labels).to_numpy().T
    class_prob = lab @ dist
    norm = np.linalg.norm(class_prob, 2, axis=0)
    class_prob = class_prob / norm
    class_prob = (class_prob.T - class_prob.min(1)) / class_prob.ptp(1)
    return class_prob
```

Stereoscope



Seurat vignette
Andersson et al. Comm Bio. 2020

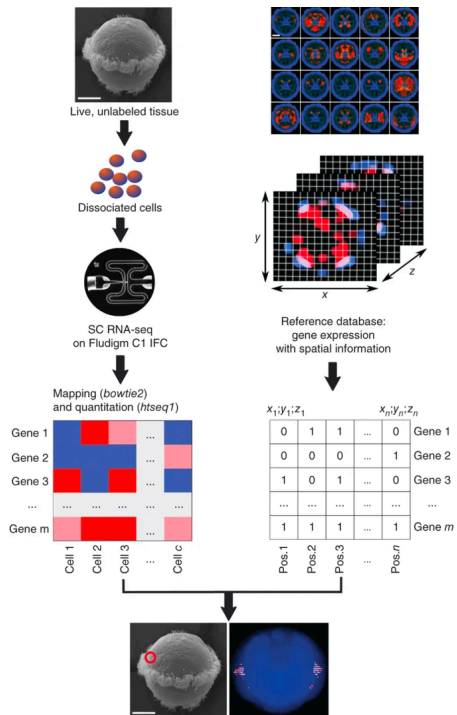
DestVI



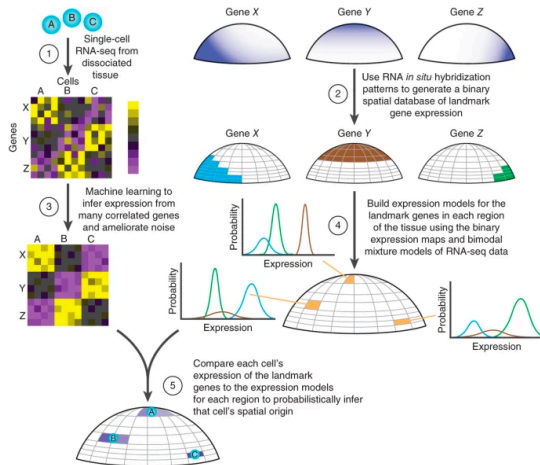
Lopez et al. Nature
Biotech 2022

Gene expression imputation and cell type mapping

Early work on single cell + spatial mapping

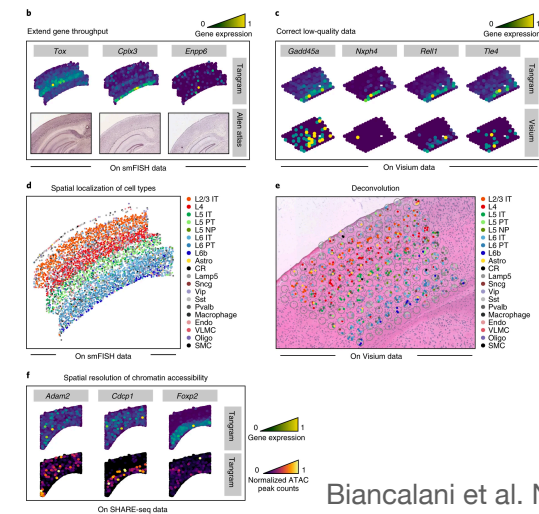


Achim et al. Nature Biotech 2015
Satija et al. Nature Biotech 2015

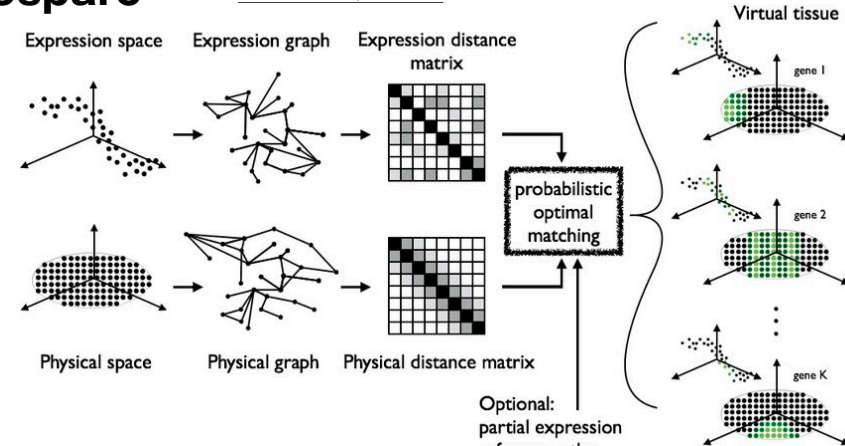


Afaik first mention of Seurat in literature 😊

Tangram

Biancalani et al. *Nature Methods* 2021

Novosparc

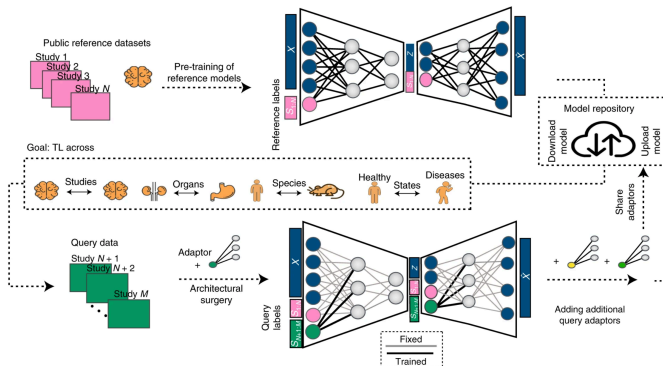
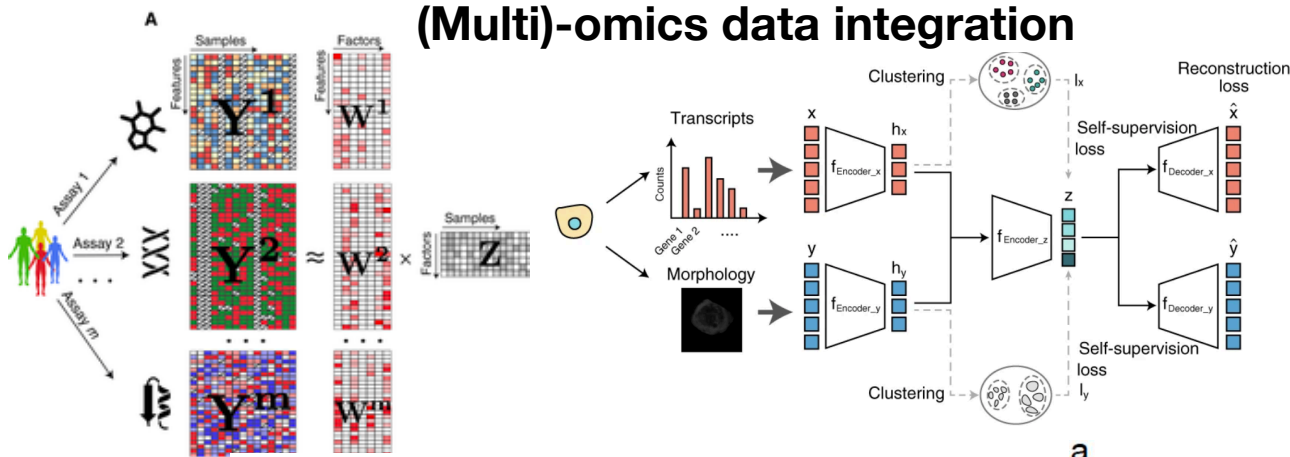


Nitzan et al. Nature 2021

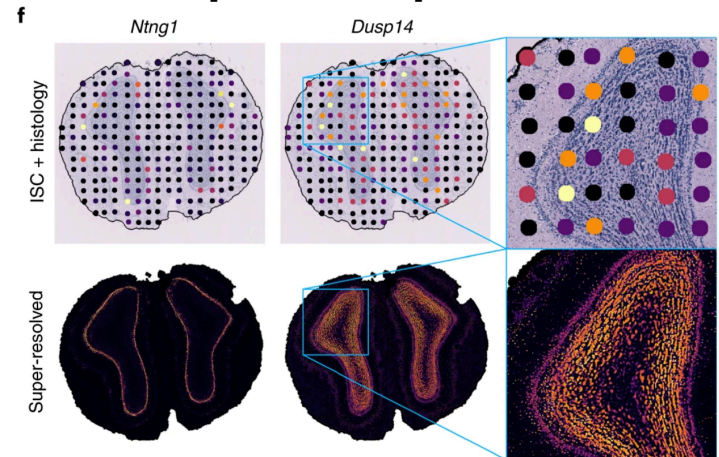
From multi-modal data integration to modality alignment

From joint to aligned data representations

(Multi)-omics data integration



Gene expression prediction



Argelaguet et al. Mol. Sys. Bio. 2018

Bao et al. Nature Biotech 2022

Lotfollahi et al. Nature Biotech 2022

Berngestrahle et al. Nature Biotech 2022

Pang et al. Bioarxiv 2022

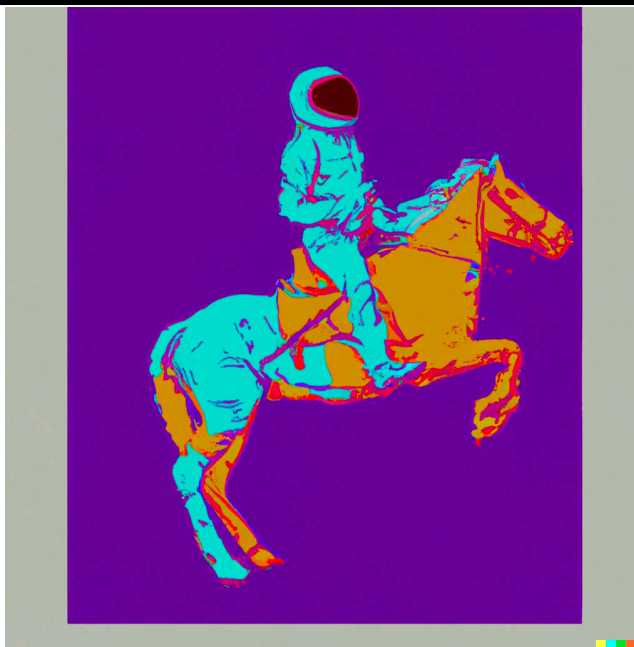
From multi-modal data integration to modality alignment

From joint to aligned data representations

Text prompt: An astronaut riding a horse in the style of Andy Warhol

Image output:

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



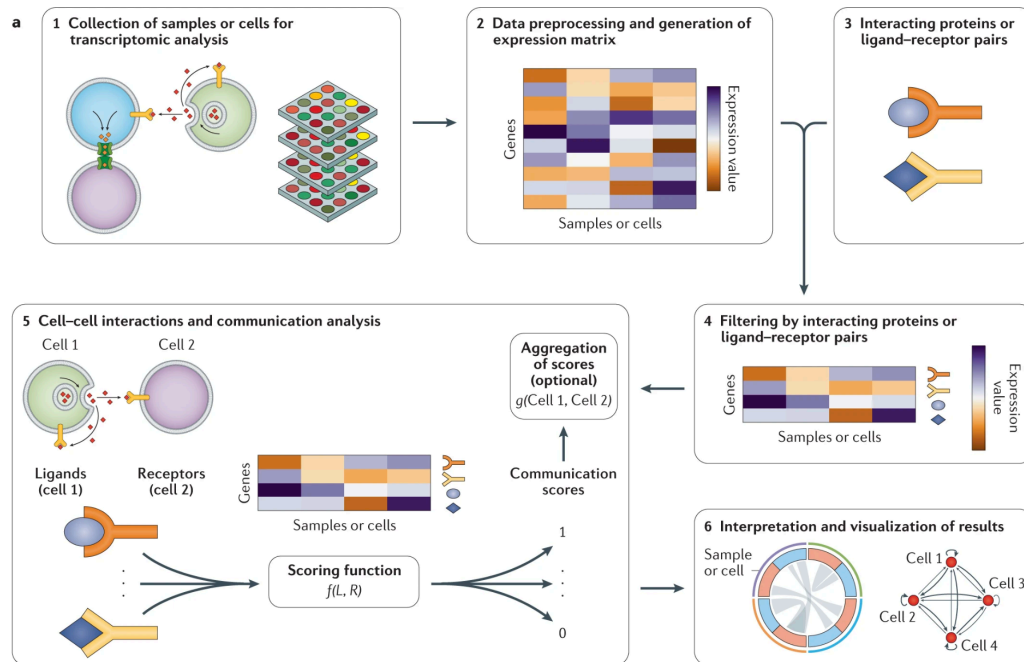
Teddy bears shopping for groceries in the style of ukiyo-e



Cellular communication inference

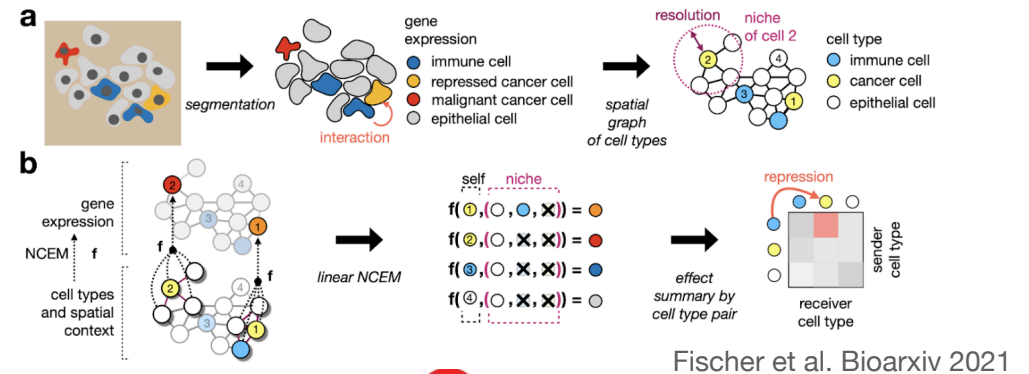
From receptor-ligand interaction test to spatial variance component analysis

Cellchat, cellphonedb etc.

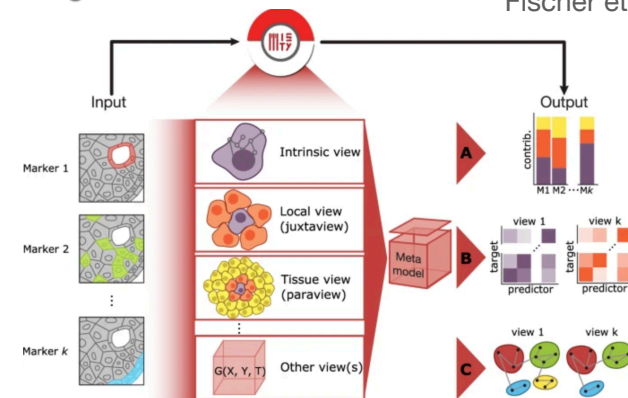


Armingol et al. Nature review genetics 2021

Node-centric expression models



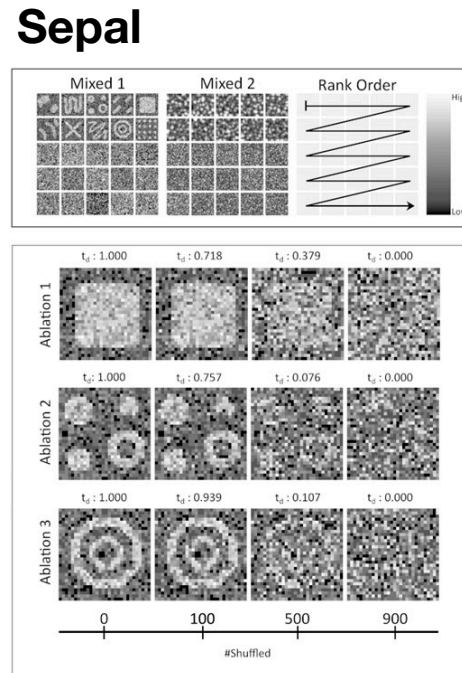
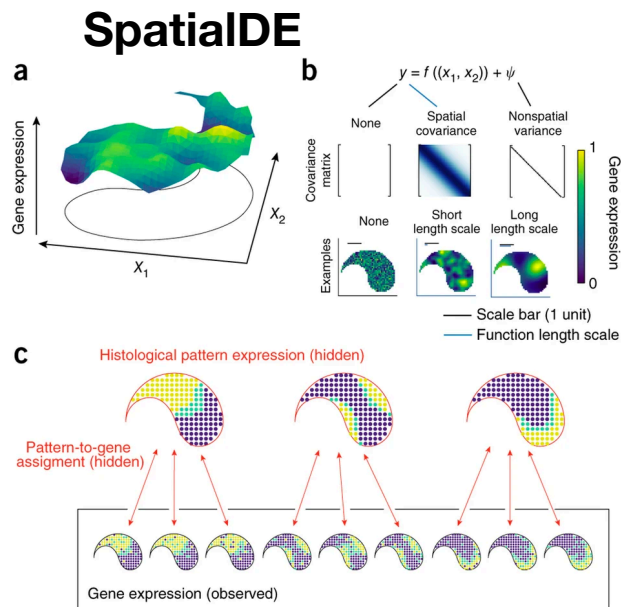
MISTy



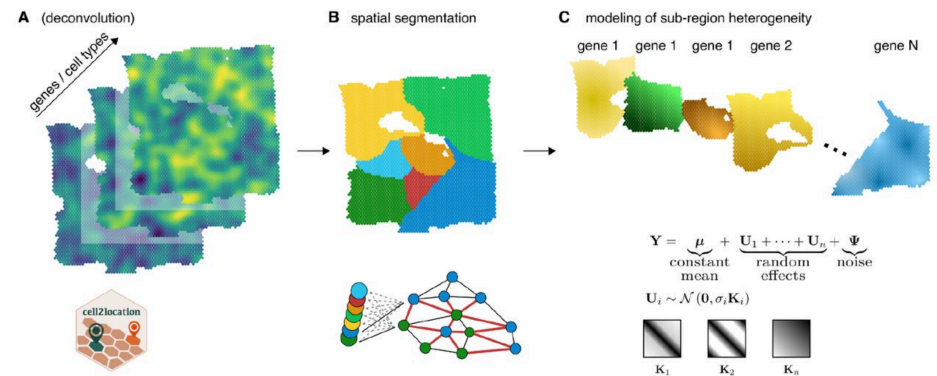
Tanevski et al. Genome Biology 2022

Spatially variable genes and identification of tissue module

Identifying spatial patterns in tissues.

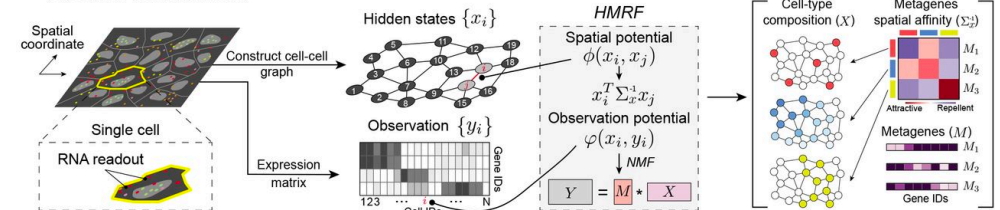


SpatialDE2



SpiceMix

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

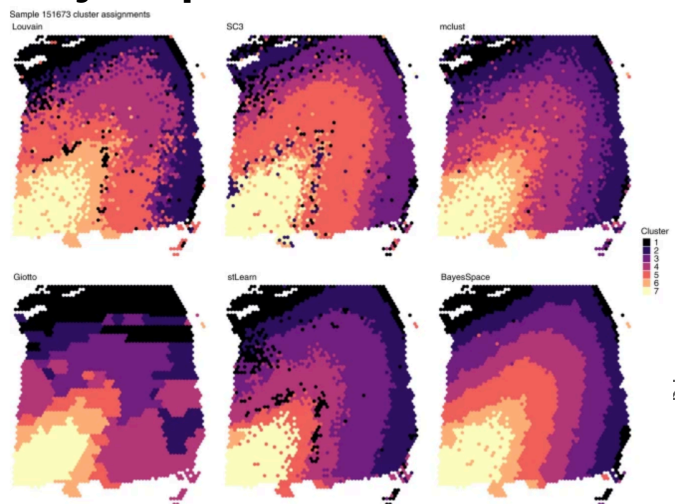


Svennson et al. Nature Methods 2018
Andersson et al. Bioinformatics 2021

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

Spatial clusters and spatially-aware dimensionality reduction

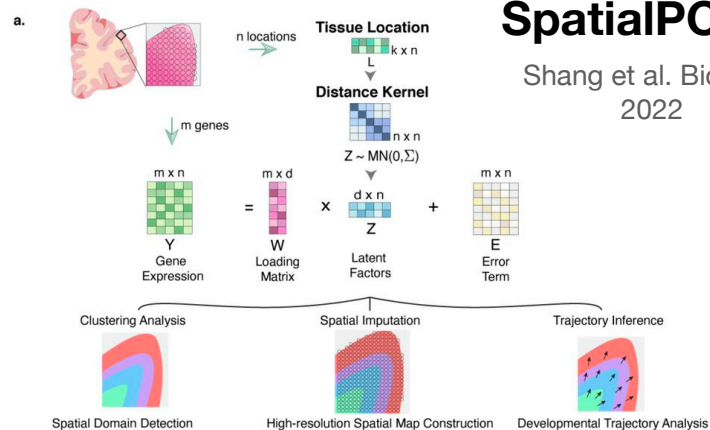
BayesSpace



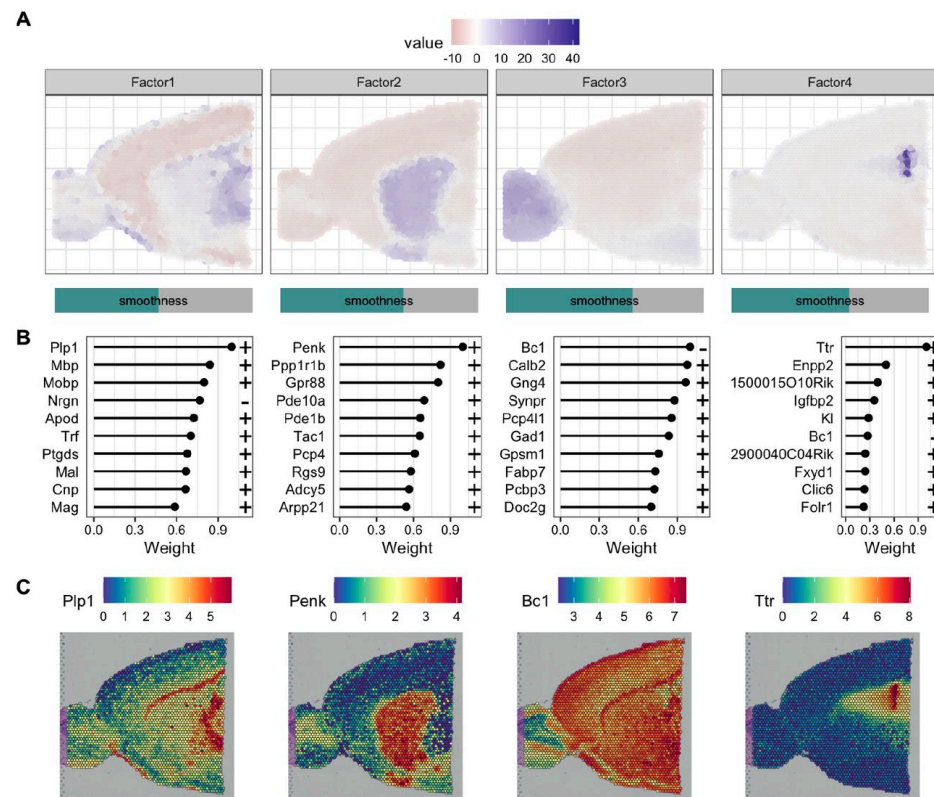
Zhao et al. Nature
Biotech 2022

SpatialPCA

Shang et al. Bioarxiv
2022



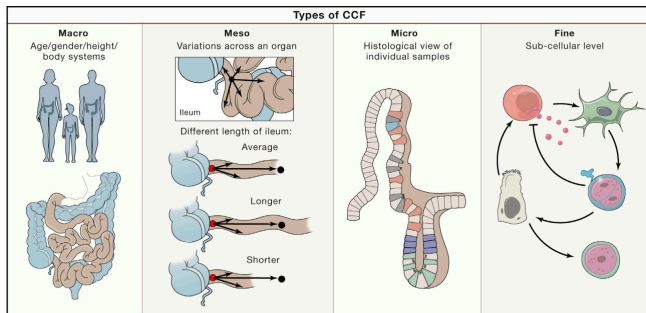
Mefisto



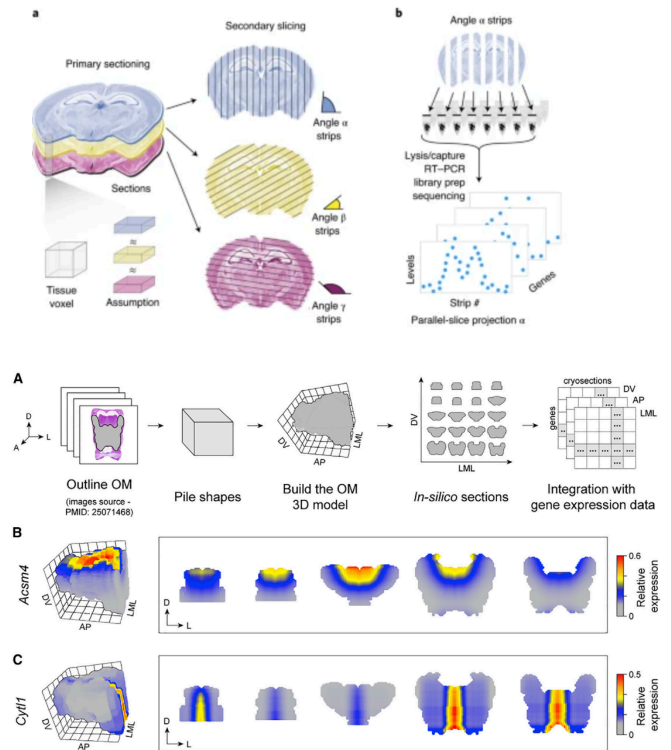
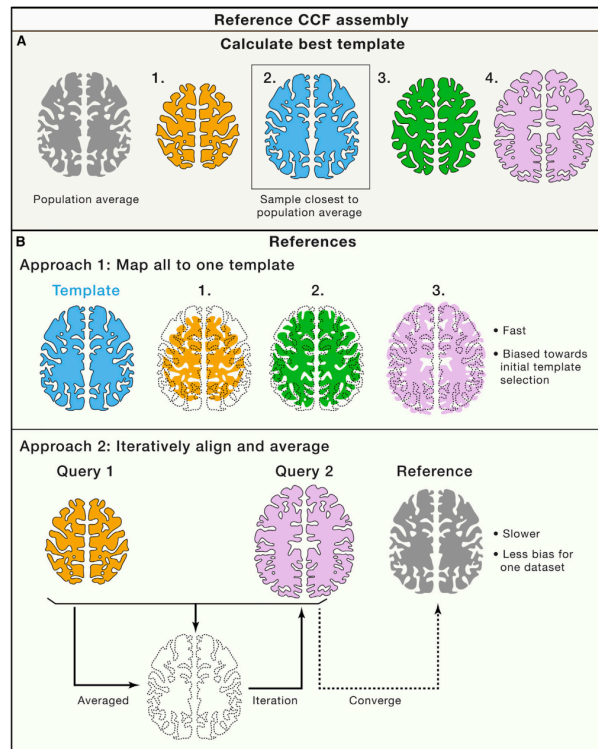
Velten et al. Nature Methods 2022

Registration and alignment of spatial coordinates

Towards building a Common Coordinate Framework of tissue and organs



Rood et al.
Cell 2019



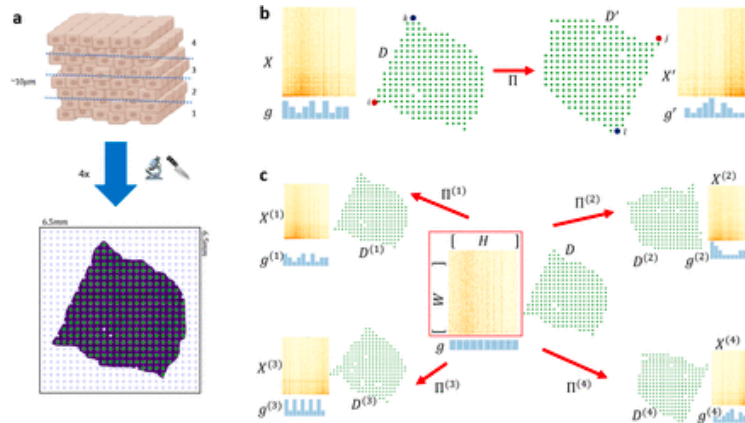
Schede et al Nature Biotech 2022
Ruiz Teyada et al. Cell Reports 2022

Registration and alignment of spatial coordinates

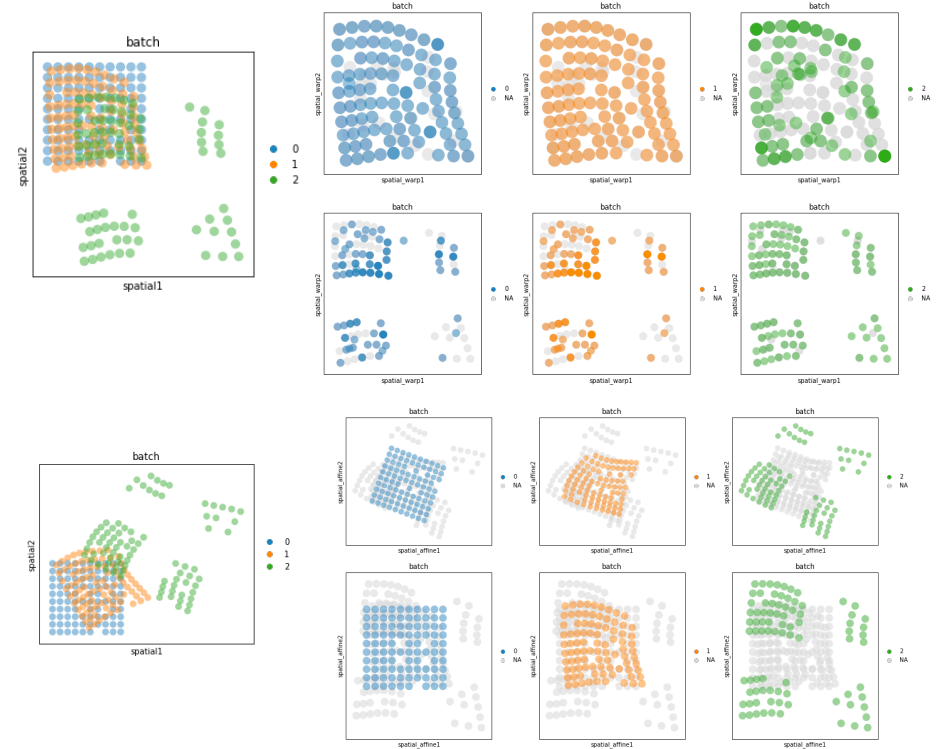
Towards building a Common Coordinate Framework of tissue and organs

Paste

Vieira et al.
Bioarxiv 2022

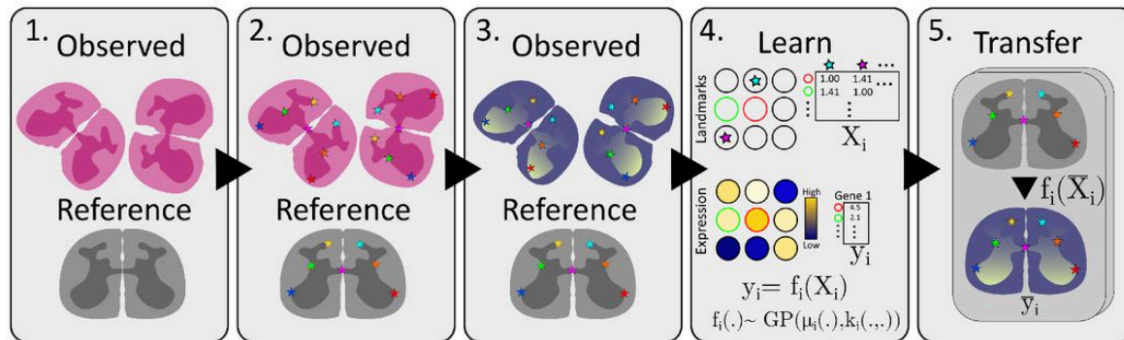


Moscot



Eggplant

Andersson et al.
Bioarxiv 2022



Klein, Palla et al.
in preparation

Datasets

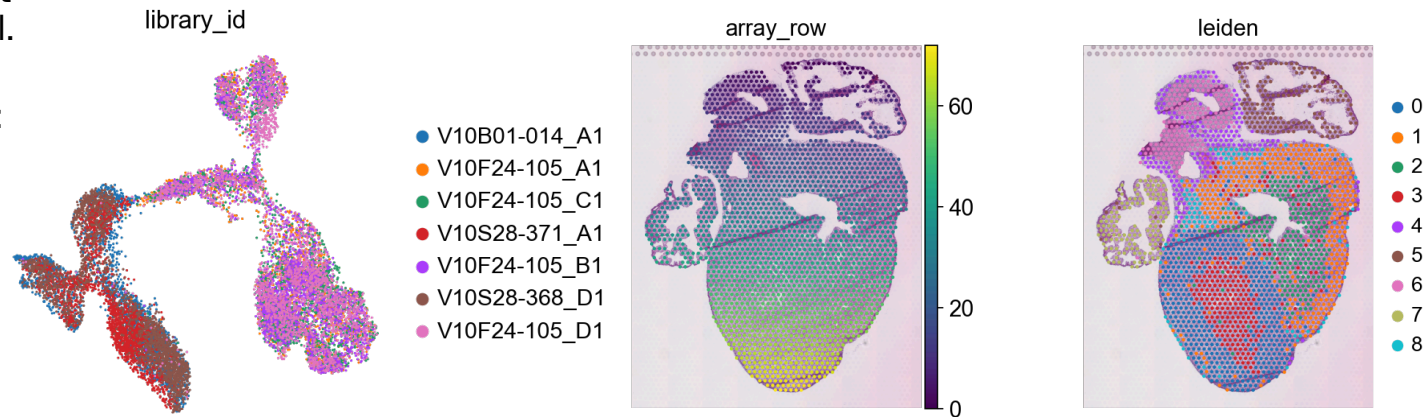
Human Developmental Heart

Spatial dataset

Andersson et al.
Bioarxiv 2022

7 Visium slides:

- ~15k cells
- ~7k genes

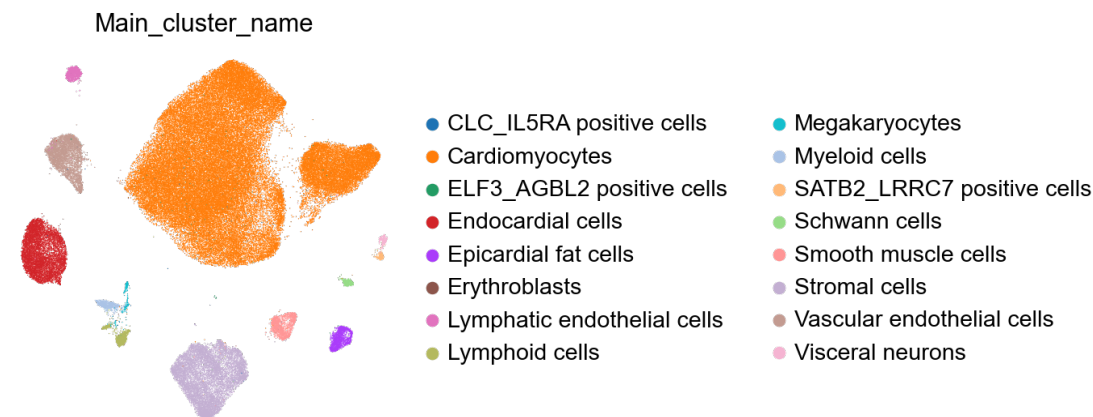


Alma Andersson
PhD @ KTH Sweden

Single-cell dataset

Cao et al. Science 2021

- ~ 96k cells
- ~30k genes



Carlos Talavera Lopez
PI @ Helmholtz Munich

Methods and notebooks

Python

R

Browser

Infrastructure, analysis and visualization

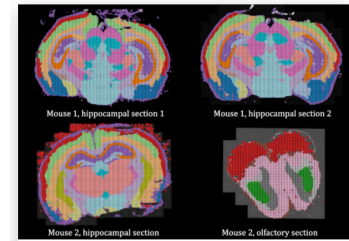
squidpy

Palla, Spitzer et al.
Nat. Methods 2022

**spatial-experiment +
bioconductor**
Righelli, Weber et al.

tissuemap

Solorzano et al. 2020



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

▼ Read more ▼

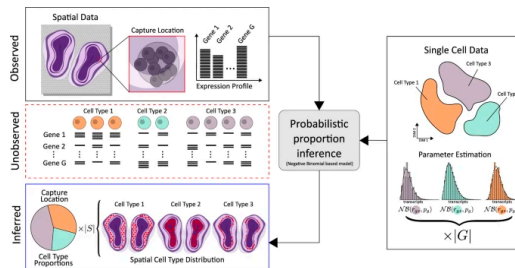
Deconvolution

stereoscope

Andersson et al.
Comm. Bio. 2021

scvi-tools

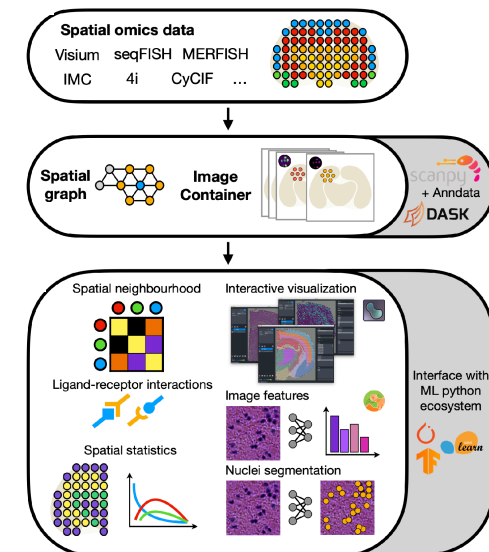
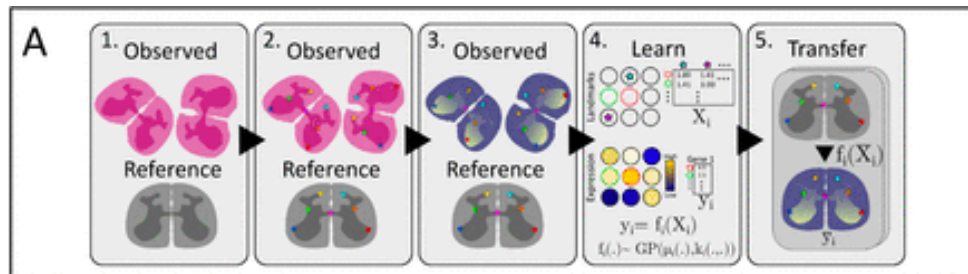
Gayoso, Lopez et al.
Nat. Biotech. 2022



Registration

eggplant

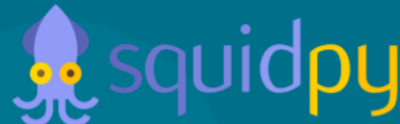
Andersson et al.
Comm. Bio. 2021



Thank you for the attention!



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