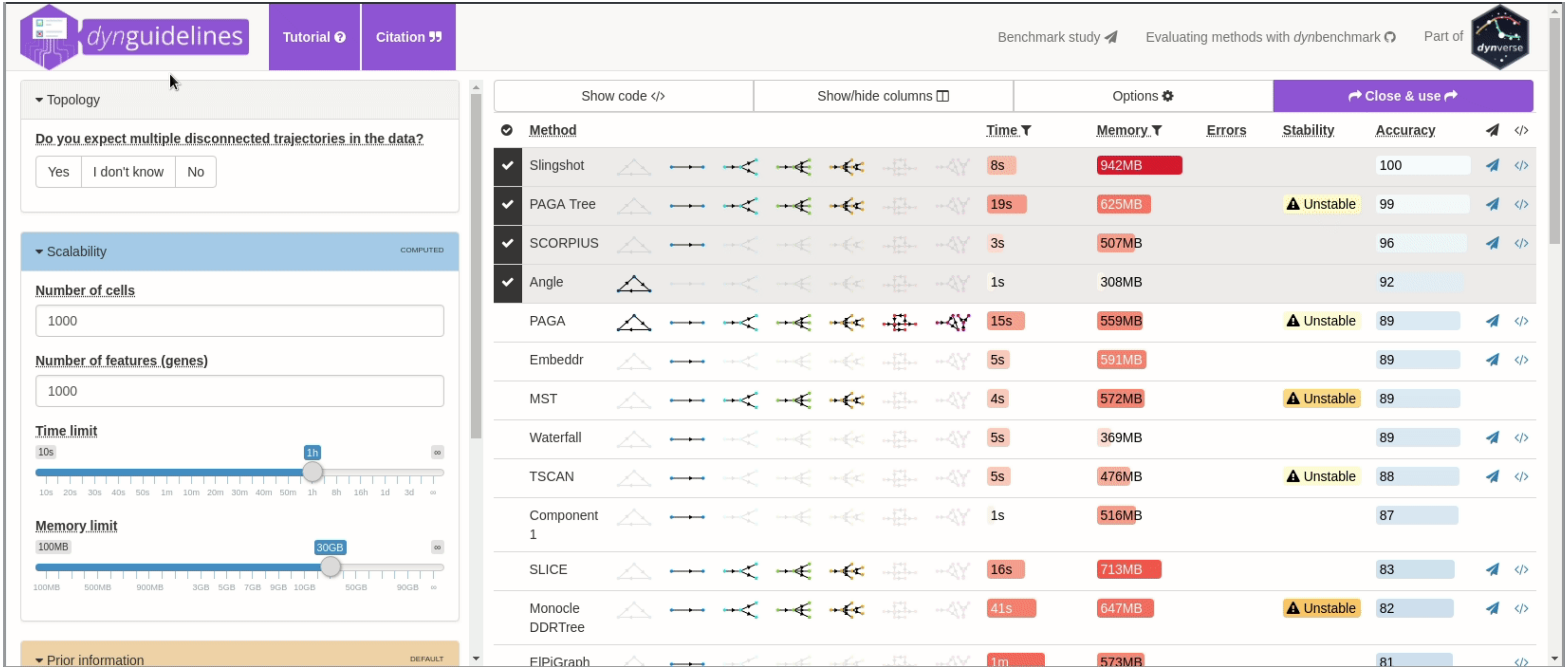
- TRABAJO

	Language	Platform	Input data	Approach
scVIA	Python	scanpy	*h5ad/ann data	trajectory
Monocle	R	seurat	*rds; *h5ad	trajectory
Monocle3	R	seurat	*rds;*h5ad	trajectory
Slingshot	R	SCE	*h5ad; *rds	trajectory
Diffusion map	R	SCE	*h5ad; *rds	trajectory
CAPITAL	Python	scanpy	*h5ad/ann data	alignment/trajectory

Each method is sensitive (exception DPT) to dimensionality reduction utilized to infer the trajectory!

dynverse/dynguidelines



dynguidelines

Tutorial ❓ Citation ❞

Benchmark study Evaluating methods with *dyn*benchmark Part of dynverse

▾ Topology

Do you expect multiple disconnected trajectories in the data?

Yes I don't know No

▾ Scalability COMPUTED

Number of cells

1000

Number of features (genes)

1000

Time limit

10s — 1h — ∞

10s 20s 30s 40s 50s 1m 10m 20m 30m 40m 50m 1h 8h 16h 1d 3d ∞

Memory limit

100MB — 30GB — ∞

100MB 500MB 900MB 3GB 5GB 7GB 9GB 10GB 50GB 90GB ∞

▾ Prior information DEFAULT

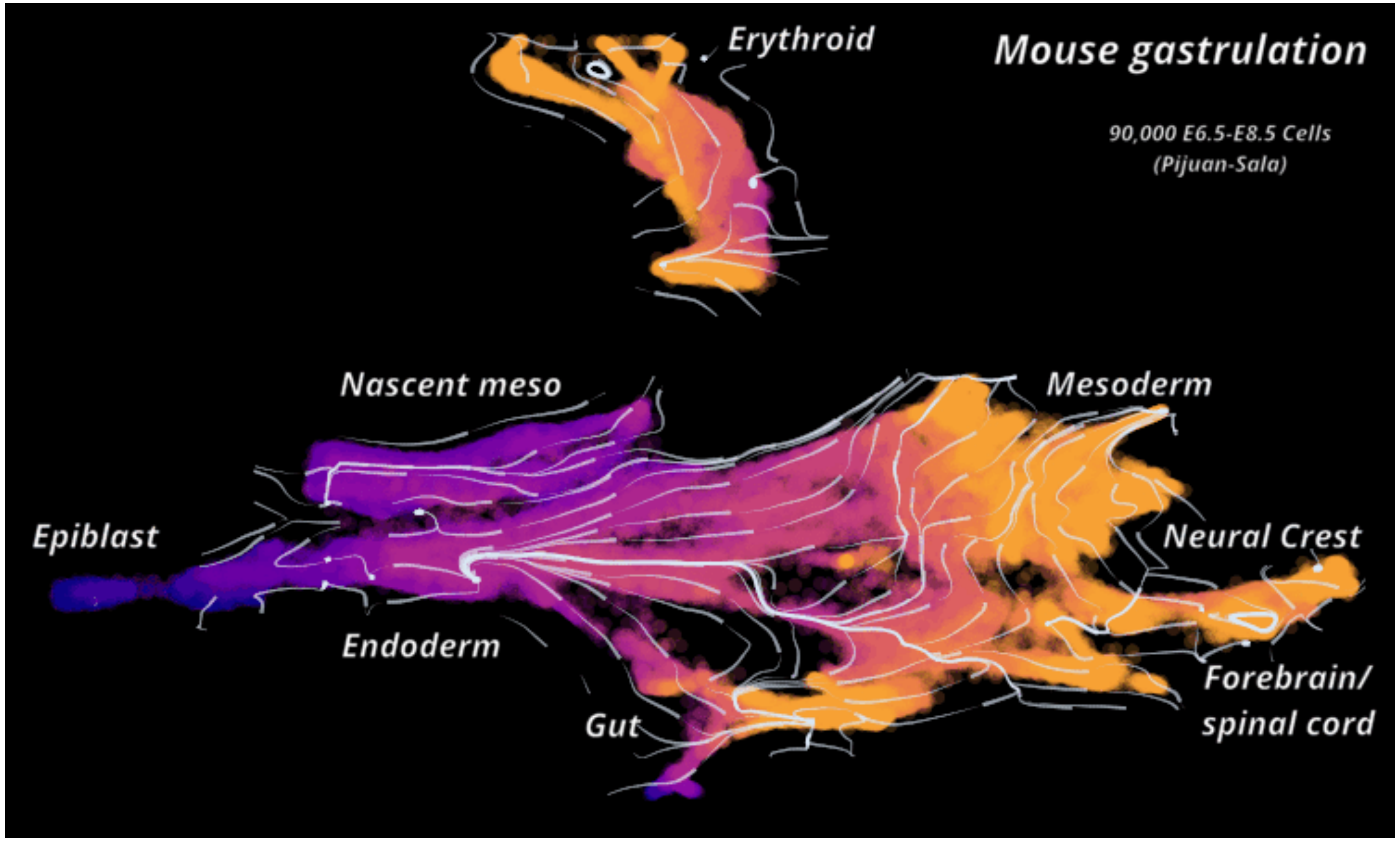
Show code </> Show/hide columns Options ⚙ Close & use

	Method	Time	Memory	Errors	Stability	Accuracy
✓	Slingshot	8s	942MB			100
✓	PAGA Tree	19s	625MB		⚠ Unstable	99
✓	SCORPIUS	3s	507MB			96
✓	Angle	1s	308MB			92
	PAGA	15s	559MB		⚠ Unstable	89
	Embeddr	5s	591MB			89
	MST	4s	572MB		⚠ Unstable	89
	Waterfall	5s	369MB			89
	TSCAN	5s	476MB		⚠ Unstable	88
	Component 1	1s	516MB			87
	SLICE	16s	713MB			83
	Monocle DDRTree	41s	647MB		⚠ Unstable	82
	ElPiGraph	1m	573MB			81

- scVIA

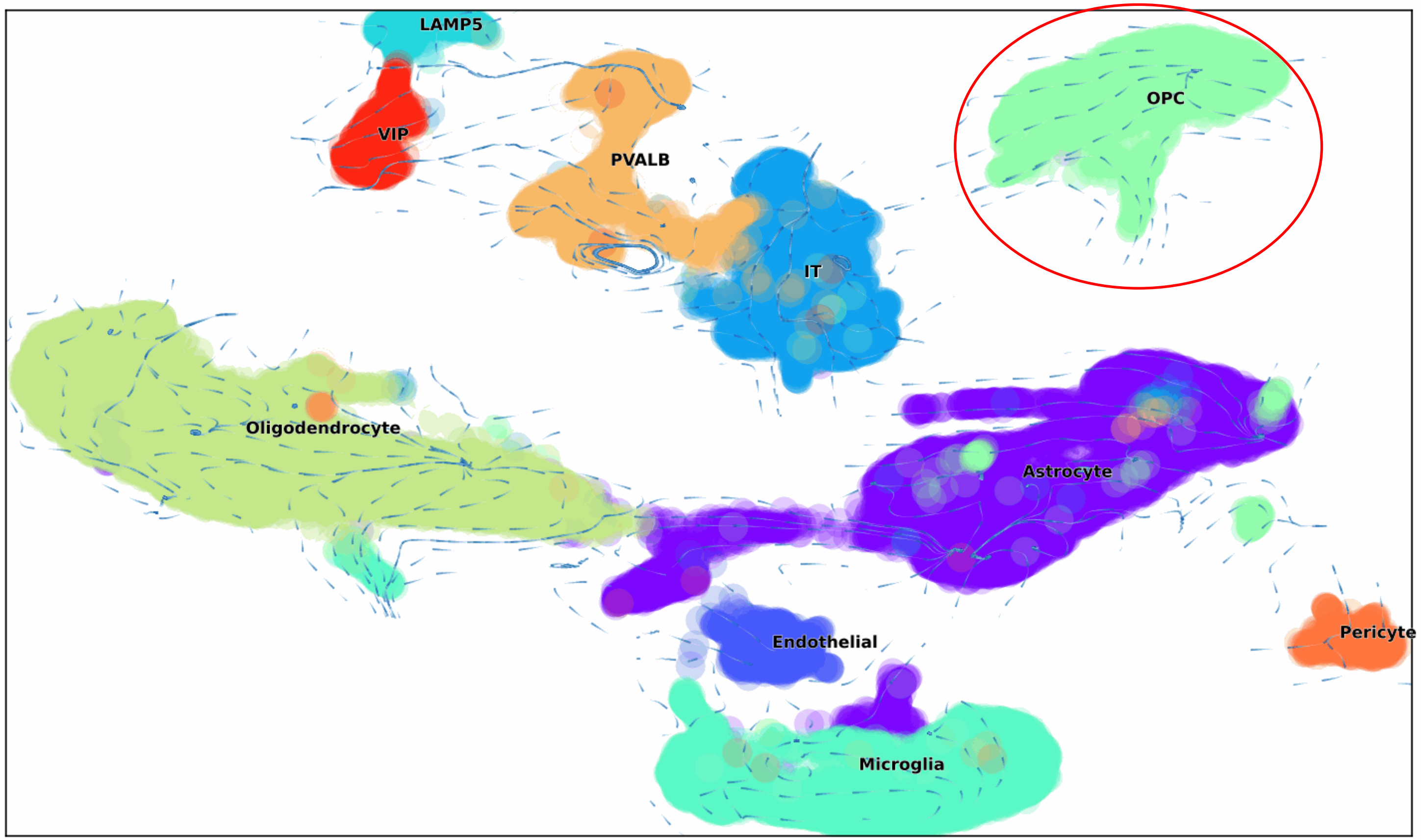
- VIA combines lazy-teleporting random walks and Monte-Carlo Markov Chain simulations to overcome common challenges such as

1) accurate terminal state and lineage inference
2) ability to capture combination of cyclic, disconnected and tree-like structures
3) scalability in feature and sample space
4) generalizability to multi-omic analysis



- scVIA

Potential temporal interactions between different cell types



Scanpy preprocessing
(or ann data with
pre-calculated UMAP)

Graph tree with
genes of potential interest

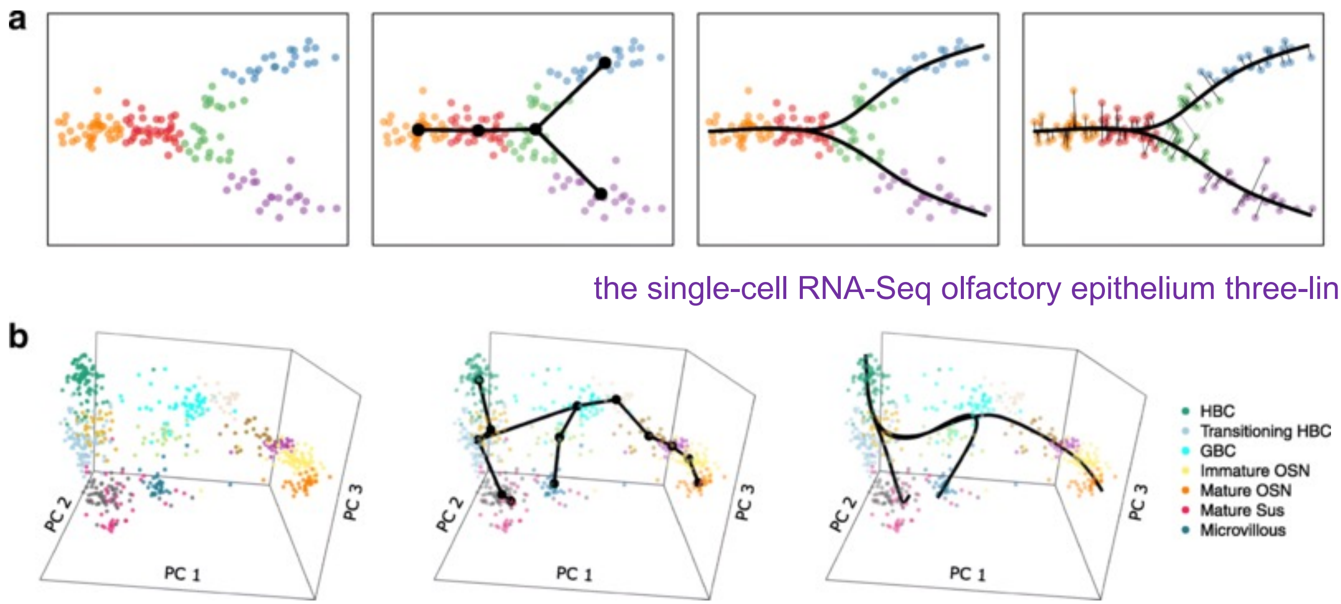
ACC brain-region
(3DG multiome, RNA-seq)

- Slingshot

use clusters of cells to uncover global structure and convert this structure into smooth lineages represented by one-dimensional variables, called “pseudotime”

2D

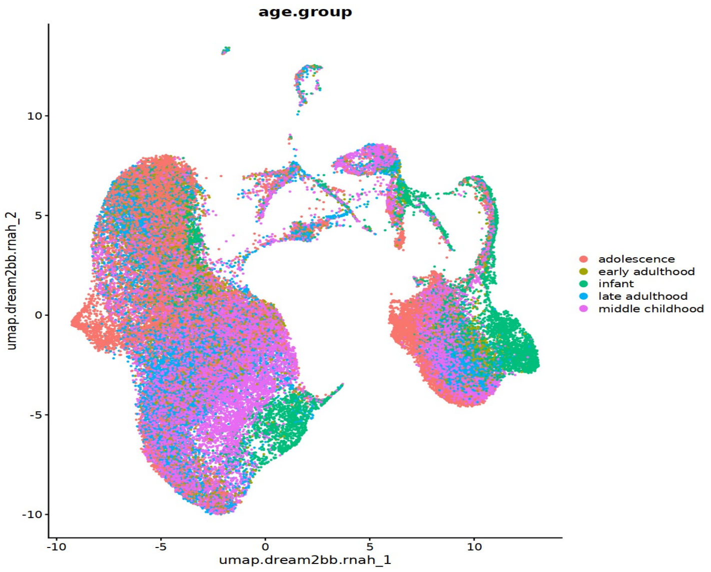
3D



the single-cell RNA-Seq olfactory epithelium three-lineage dataset

Step 1: A minimum spanning tree is constructed on the clusters to determine the number and rough shape of lineages.
Step 2: Simultaneous principal curves are used to obtain smooth representations of each lineage.
Step 3: Pseudotime values are obtained by orthogonal projection onto the curves

- Slingshot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● infant
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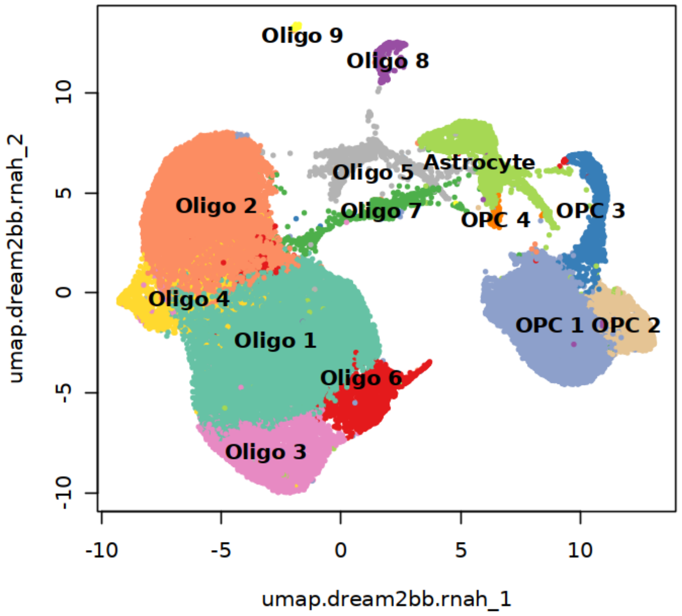
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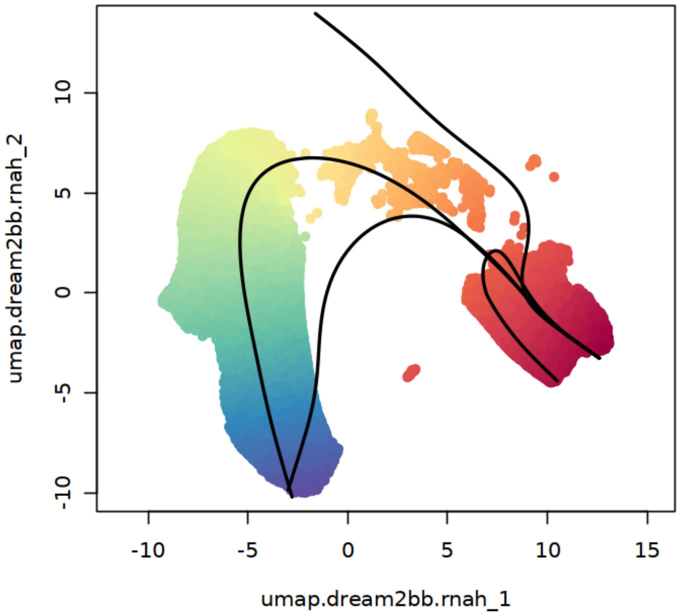
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Monocle3 vs Monocle/2

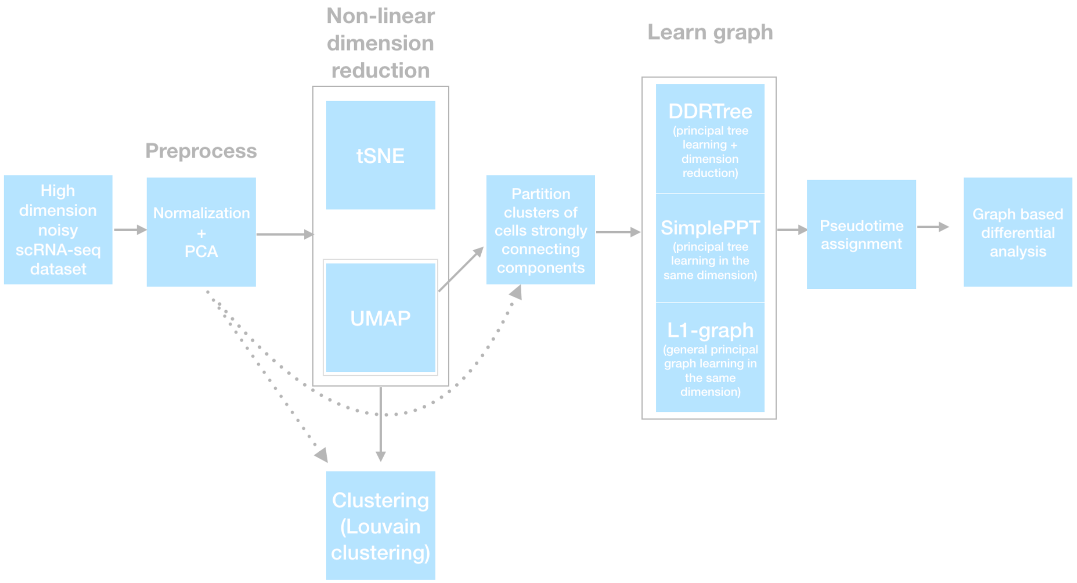
- Clustering, classifying, and counting cells.
- Constructing single-cell trajectories.
- Differential expression analysis.

Monocle3

(beta phase of development)

Improvement

- Support for the UMAP algorithm to initialize trajectory inference.
- Support for trajectories with multiple roots.
- Ways to learn trajectories that have loops or points of convergence.
- Algorithms that automatically partition cells to learn disjoint or parallel trajectories using ideas from "approximate graph abstraction".



High dimension noisy scRNA-seq dataset

Preprocess

Normalization + PCA

Non-linear dimension reduction

tSNE

UMAP

Clustering (Louvain clustering)

Partition clusters of cells strongly connecting components

Learn graph

DDRTree (principal tree learning + dimension reduction)

SimplePPT (principal tree learning in the same dimension)

L1-graph (general principal graph learning in the same dimension)

Pseudotime assignment

Graph based differential analysis

Monocle/2

ordering single cells in **pseudotime**

- placing them along a trajectory corresponding to a biological process
- by taking advantage of individual cell's asynchronous progression of those processes

- orders cells by learning an explicit principal graph from the scRNA data with advanced machine learning techniques (Reversed Graph Embedding)

The Ordering Workflow

Step 1: choosing genes that define progress (dpFeature: Selecting features from dense cell clusters)
Step 2: reducing the dimensionality of the data (Reverse Graph Embedding)
Step 3: ordering the cells in pseudotime

- assumes that the trajectory has a tree structure, with one end of it the "root", and the others the "leaves”
- Monocle's job is to fit the best tree it can to the data >> manifold learning

Monocle3 vs Monocle

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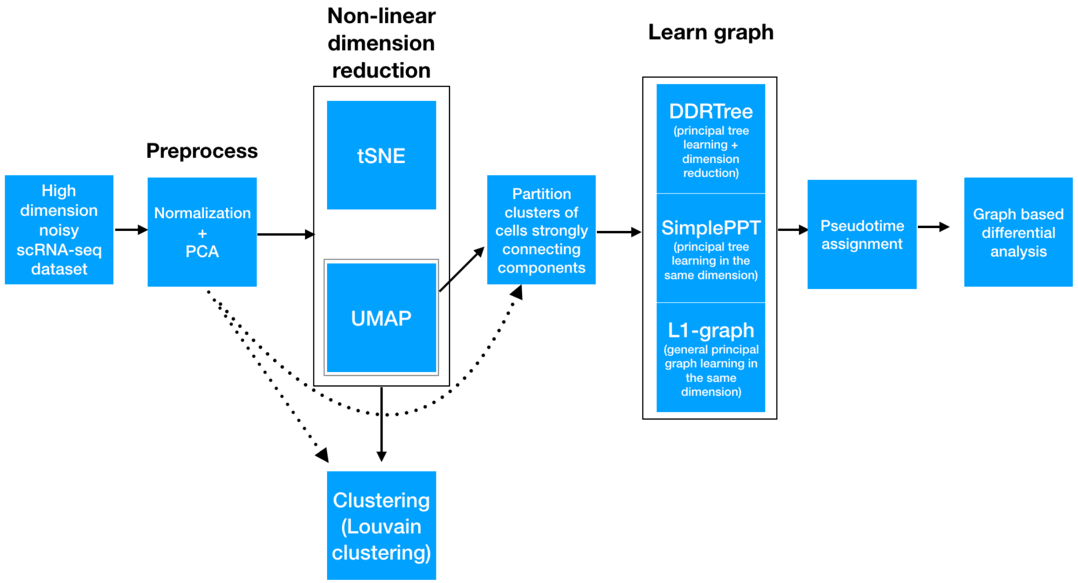

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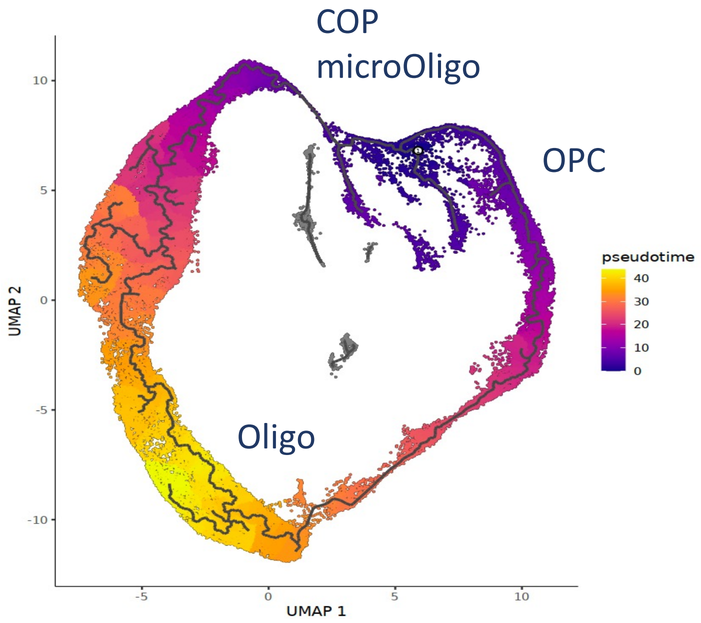
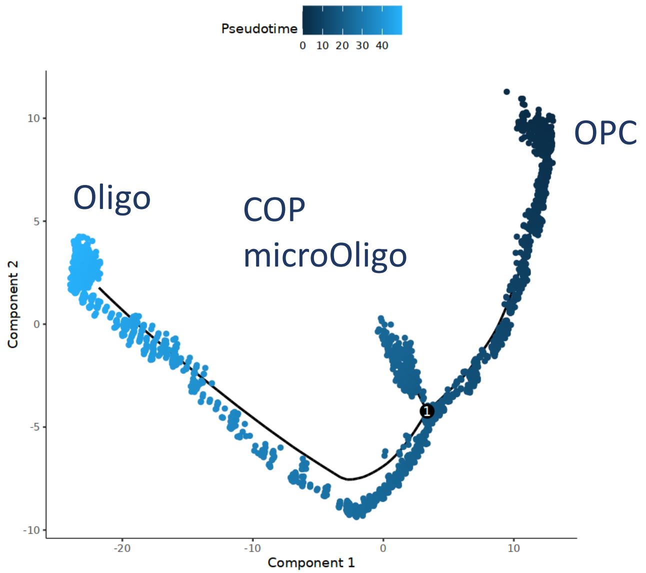
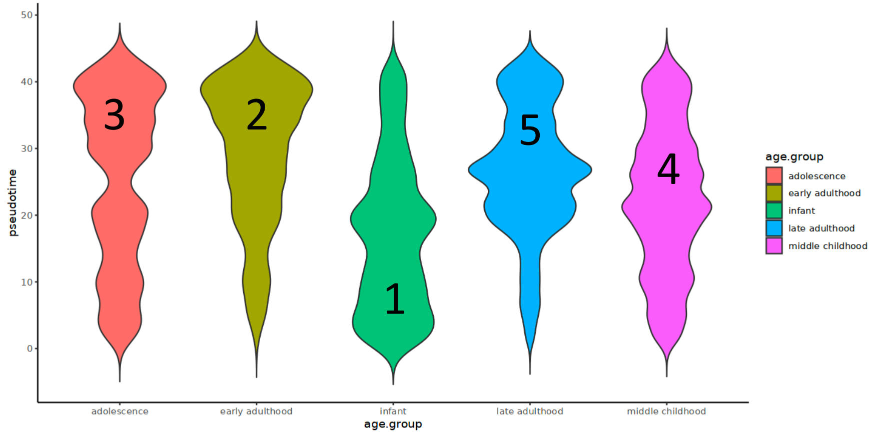
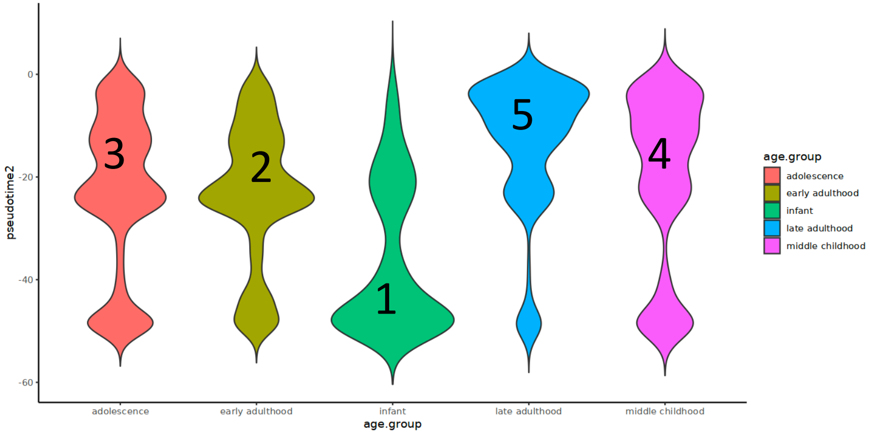
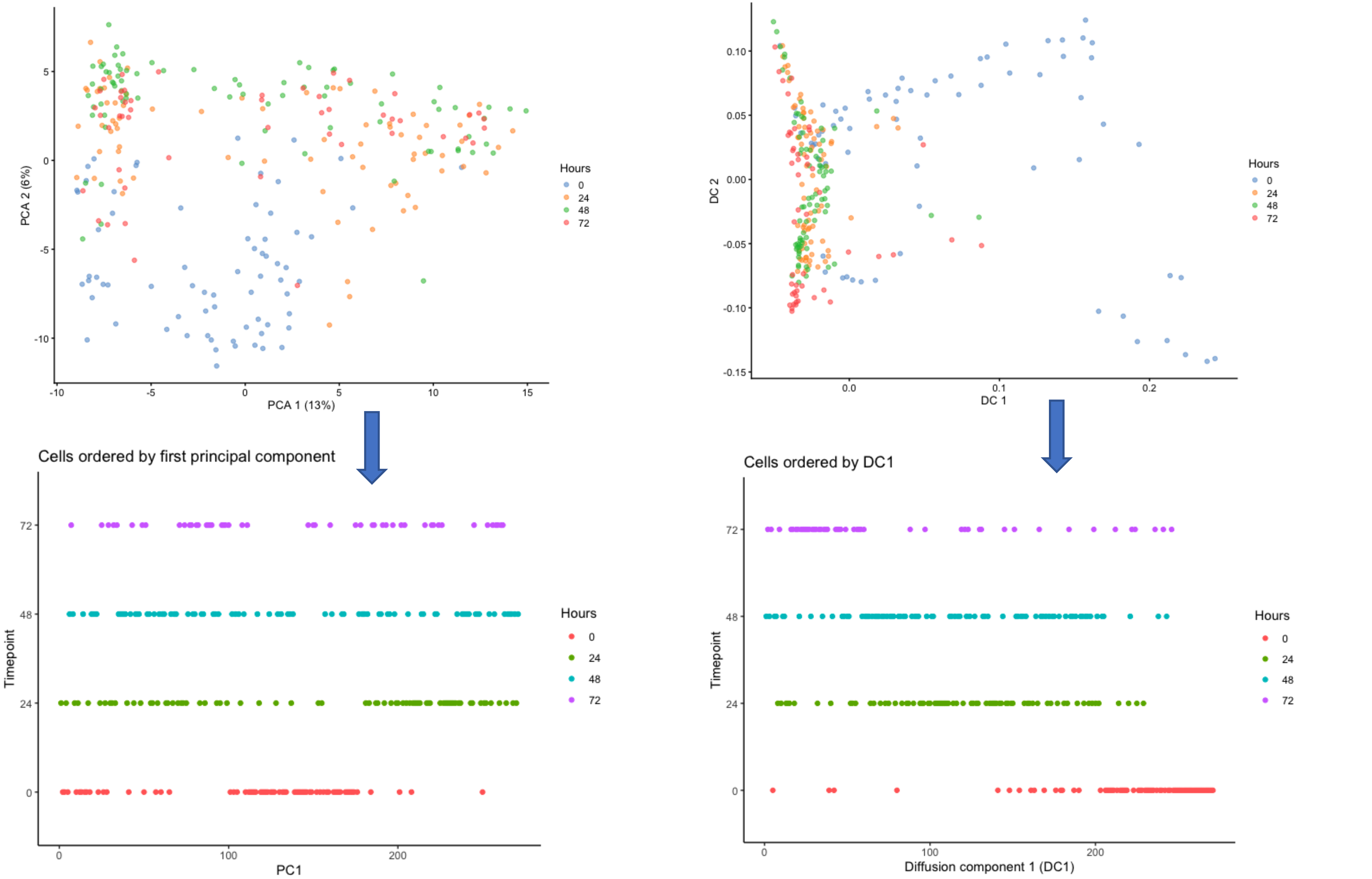








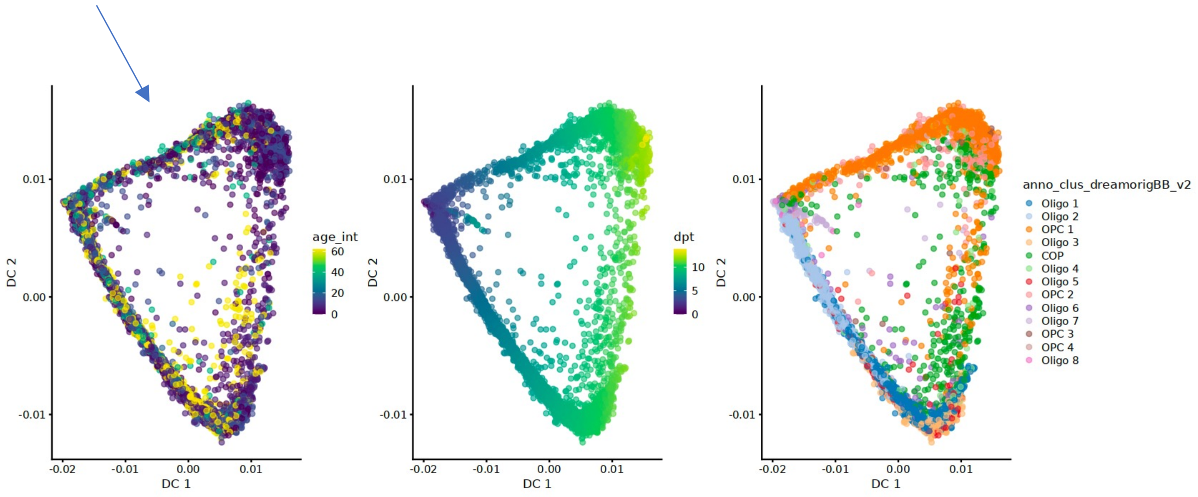
Diffusion map… how it should work

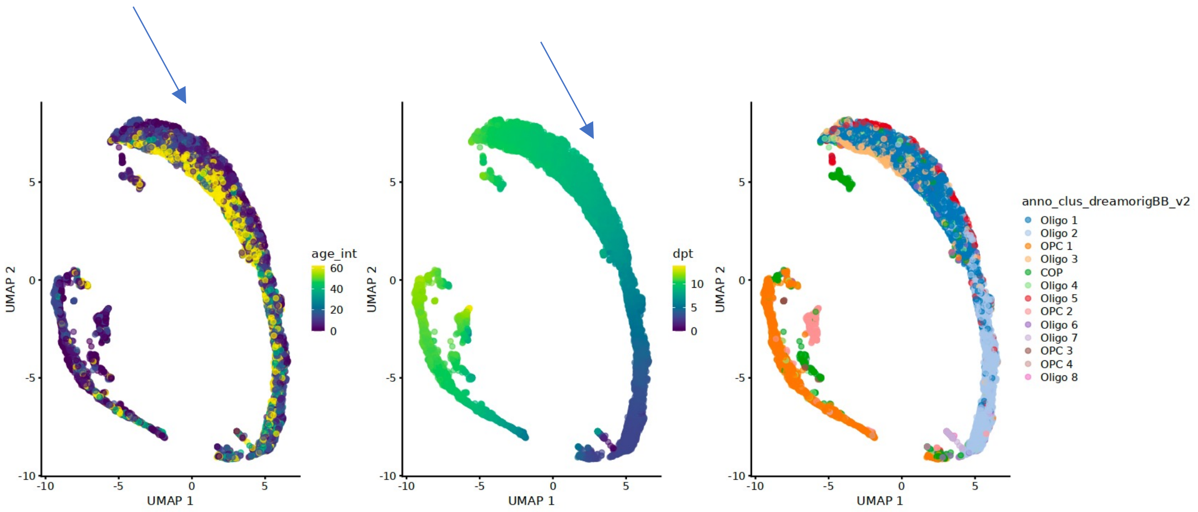


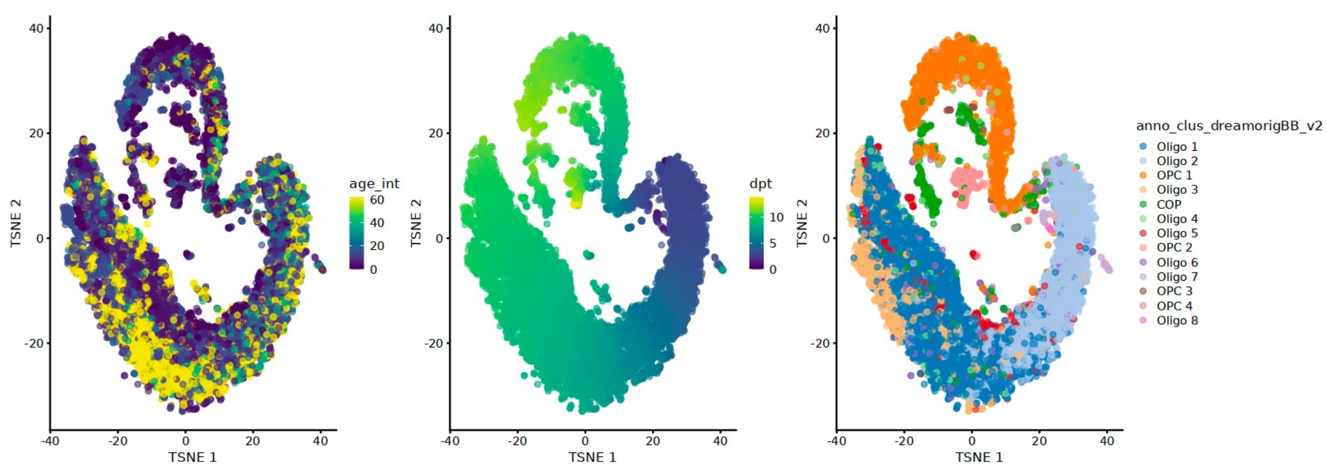
DC map

- the underlying idea is **to assume that the data are samples from a diffusion process**

Diffusion map… how it doesn't work

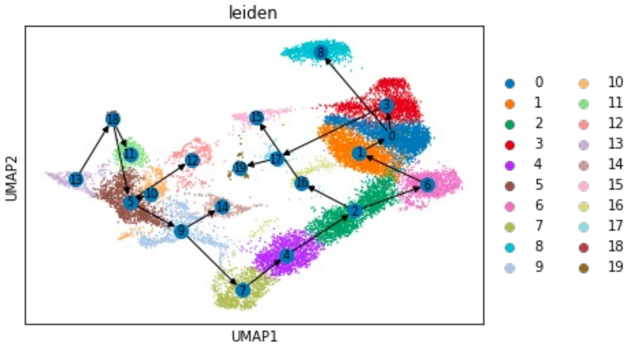






….and UMAP or tSNE is a better way to go

CAPITAL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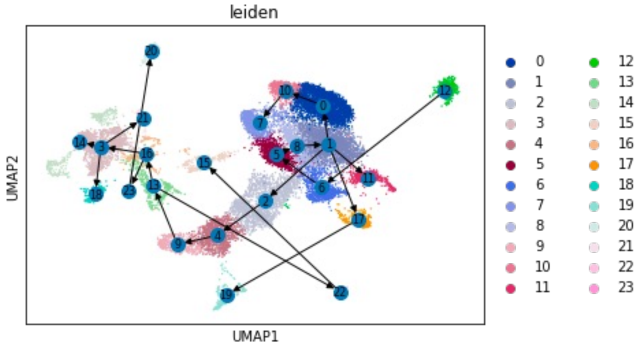
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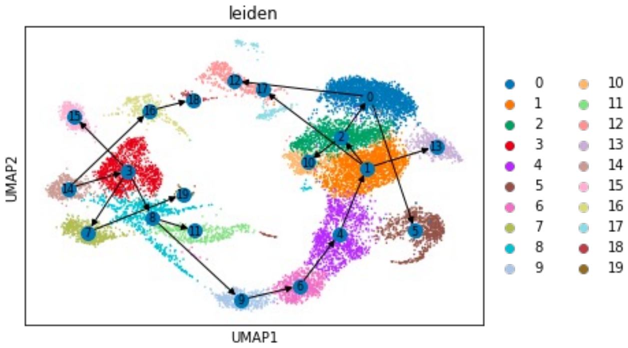
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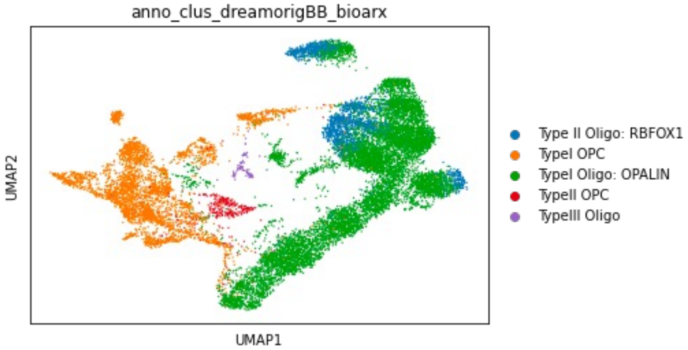
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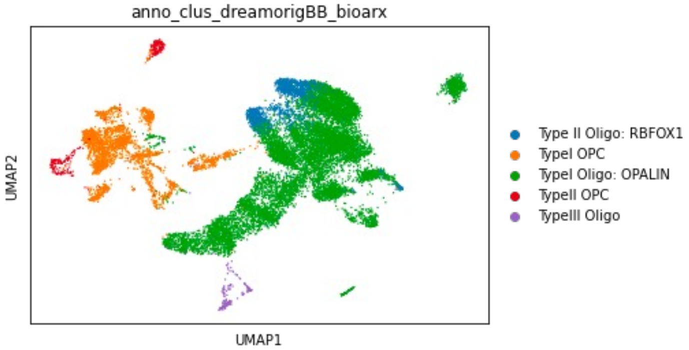
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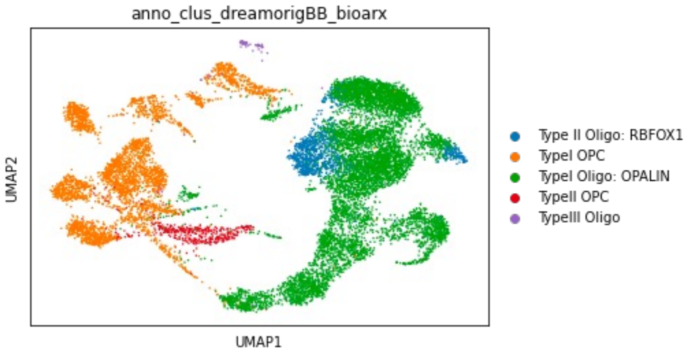
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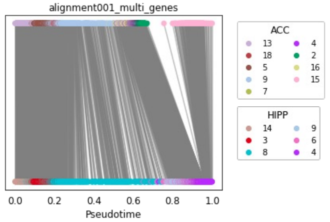
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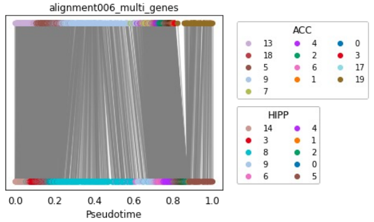
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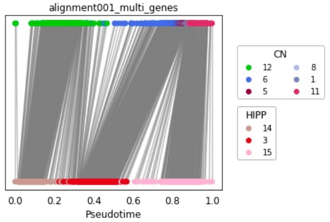
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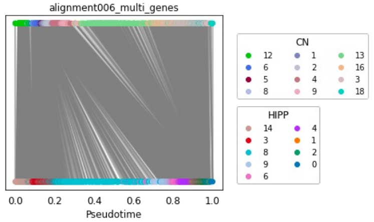
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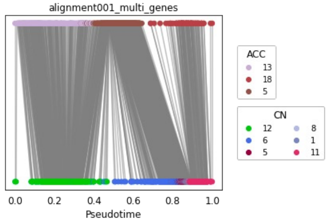
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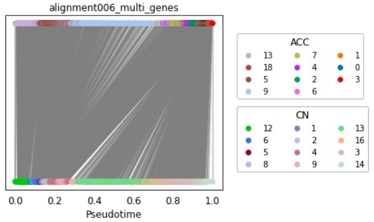
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