Single Cell RNA-seq Analysis

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BioSB Statistics for Omics – 28 June 2019

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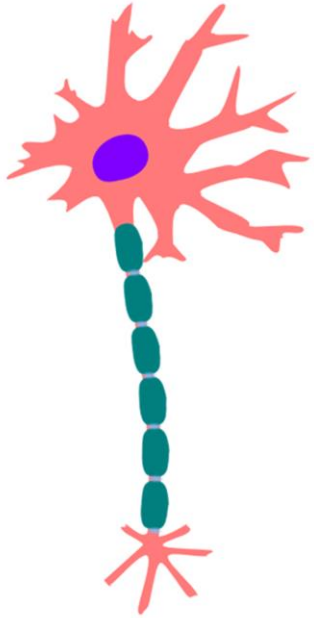
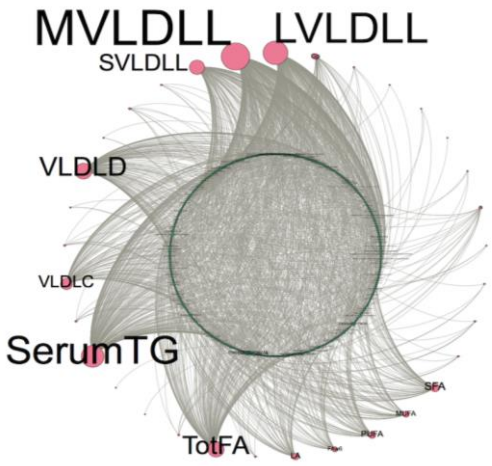
Spatio-Temporal Omics

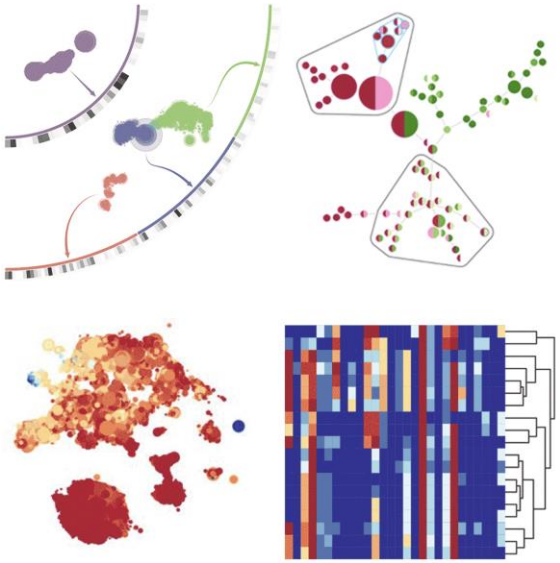
Singe Cell Omics



Multi-Omics Integration

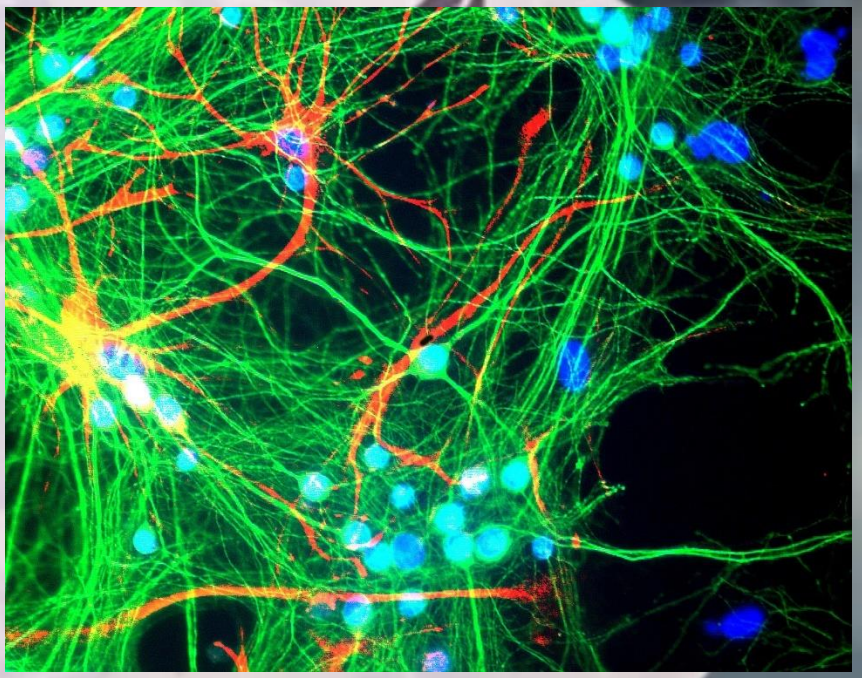


Visualization & Visual Analytics

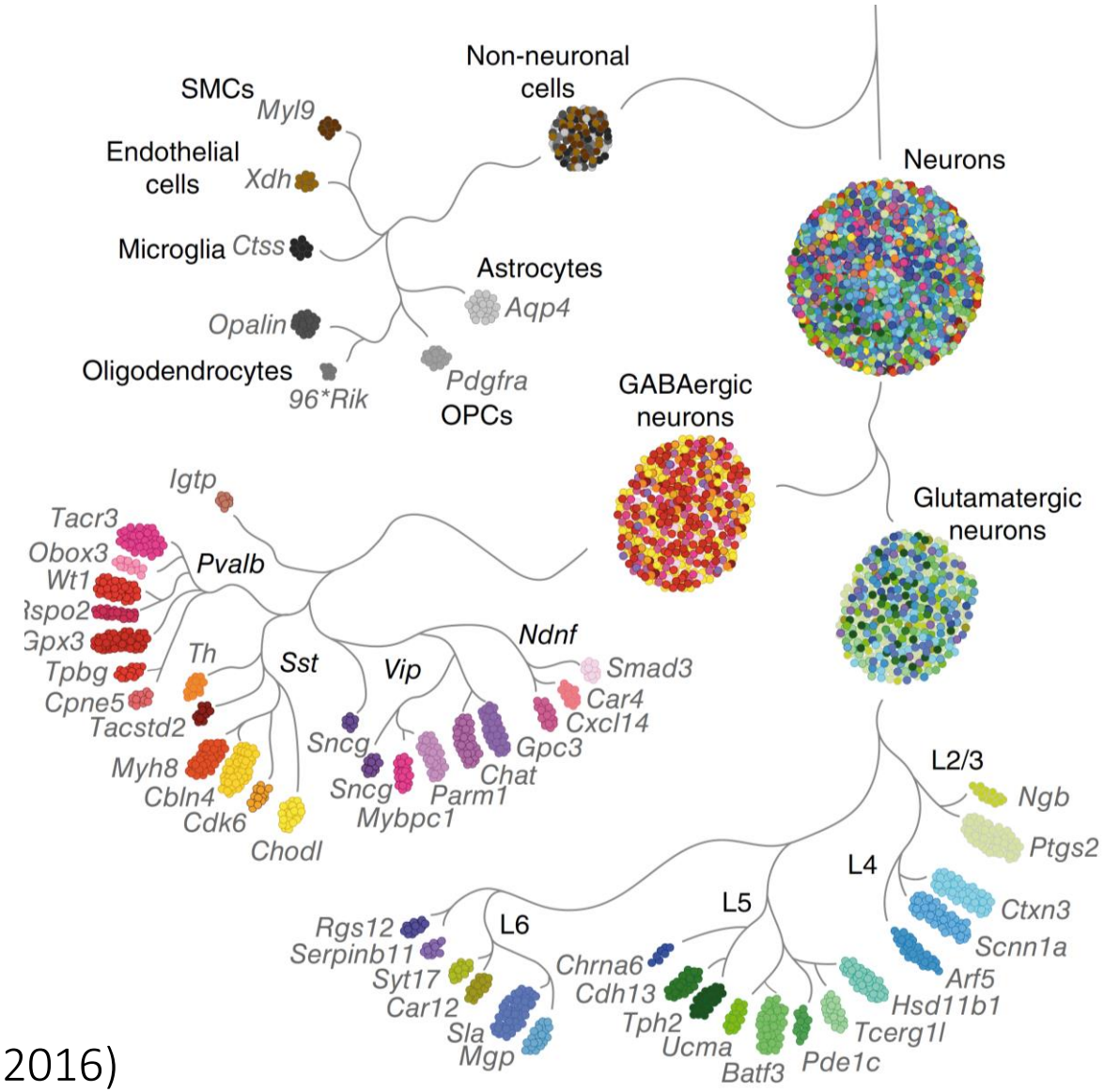


Session materials

https://github.com/ahmedmahfouz/BioSB-Statistics-for-Omics-2019



Cell types in the brain

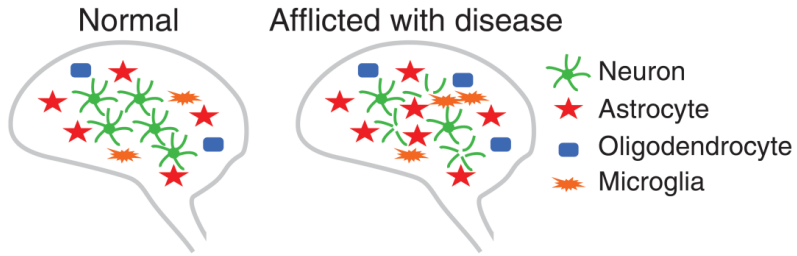


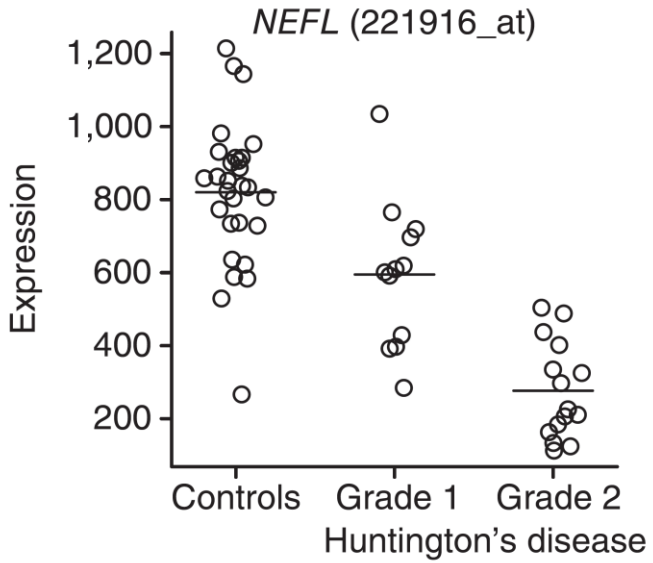
Tasic et al. (Nat. Neuroscience 2016)

Cellular heterogeneity in the brain

Human Molecular Genetics, 2006, Vol. 15, No. 6 **965–977**
doi:10.1093/hmg/ddl013
Advance Access published on February 8, 2006

Regional and cellular gene expression changes in human Huntington's disease brain





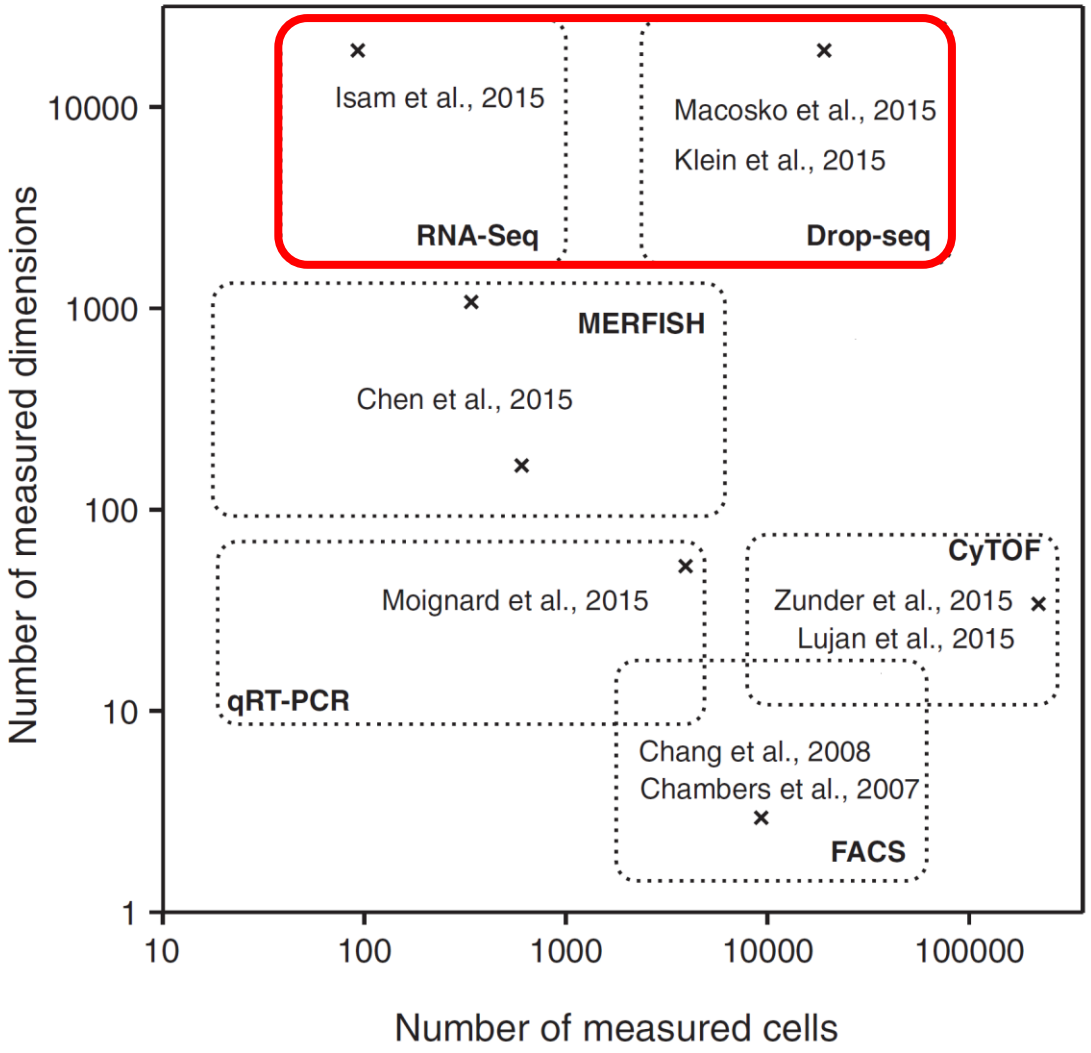
1) Decreased number of neurons?

2) Decreased expression?

3) Both?

Hodges et al. (Human Mol Genet 2006); Kuhn et al. (Nat Methods 2011)

How can we study single cells?



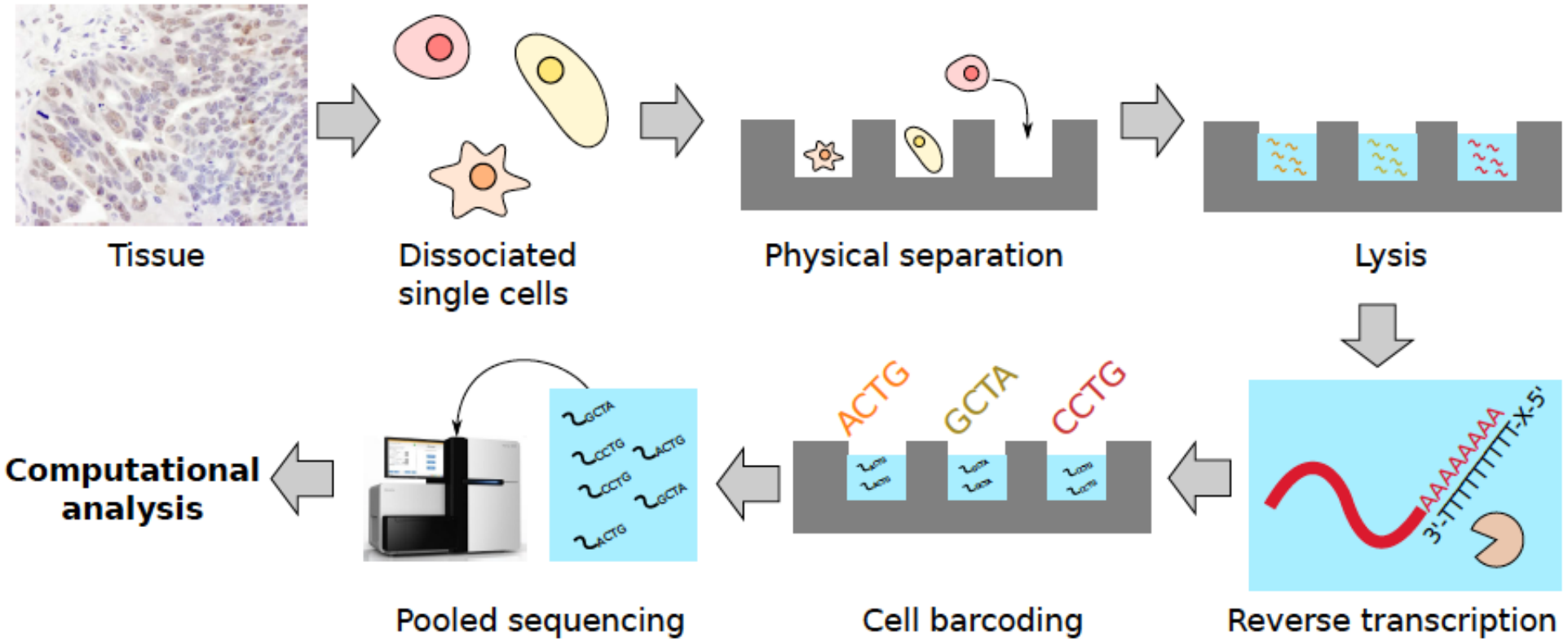
Every method has it's pros and cons.

Marr et al. *Curr Op Biotech* 2016

Goals of today

- Introduce single cell RNA-sequencing (scRNA-seq)
- Outline analysis workflow
- Go through (some) steps and discuss best practices

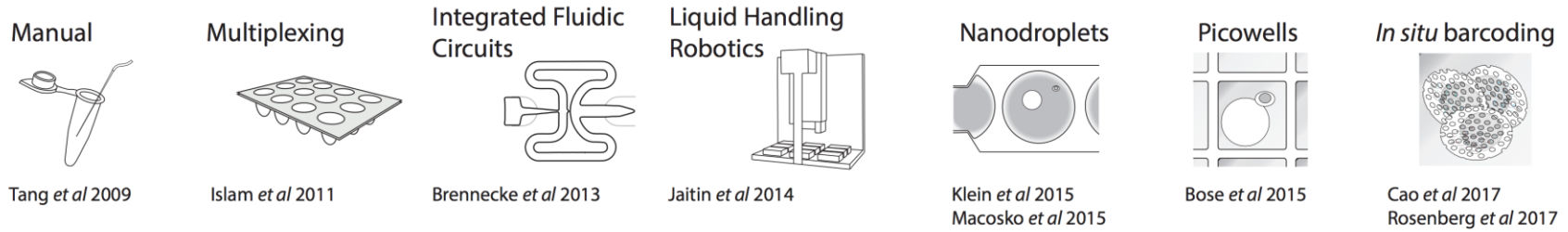
Single cell RNA-sequencing (scRNA-seq)

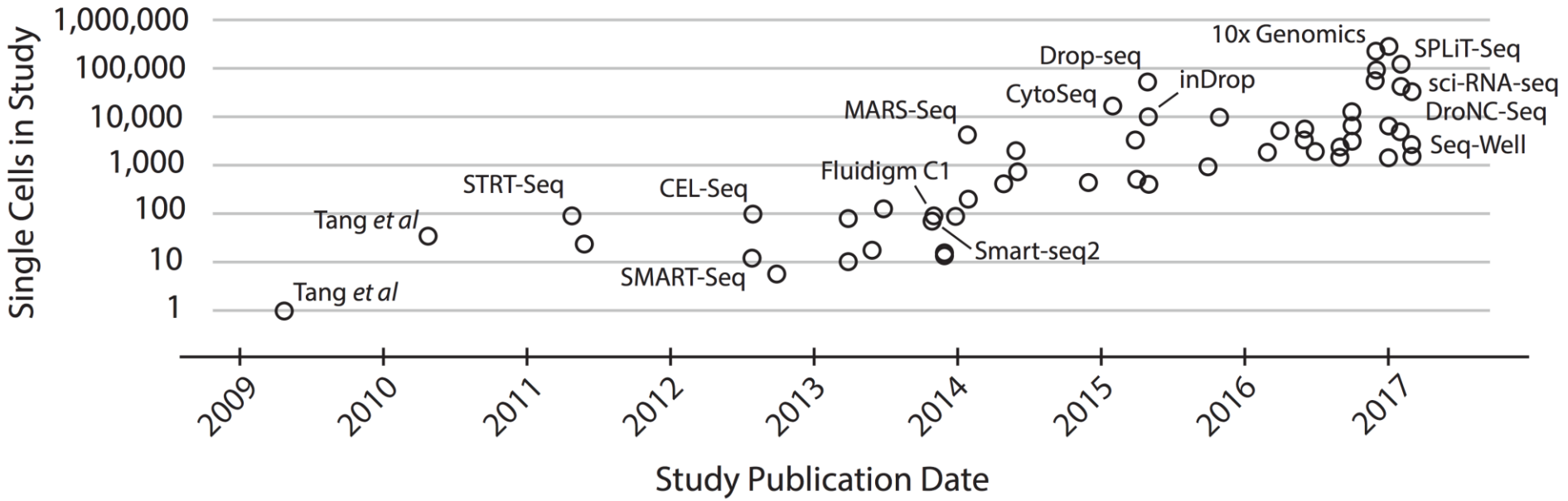


Aaron Lun (Marioni Group, EMBL-EBI)

scRNA-seq Protocols

Number of cells

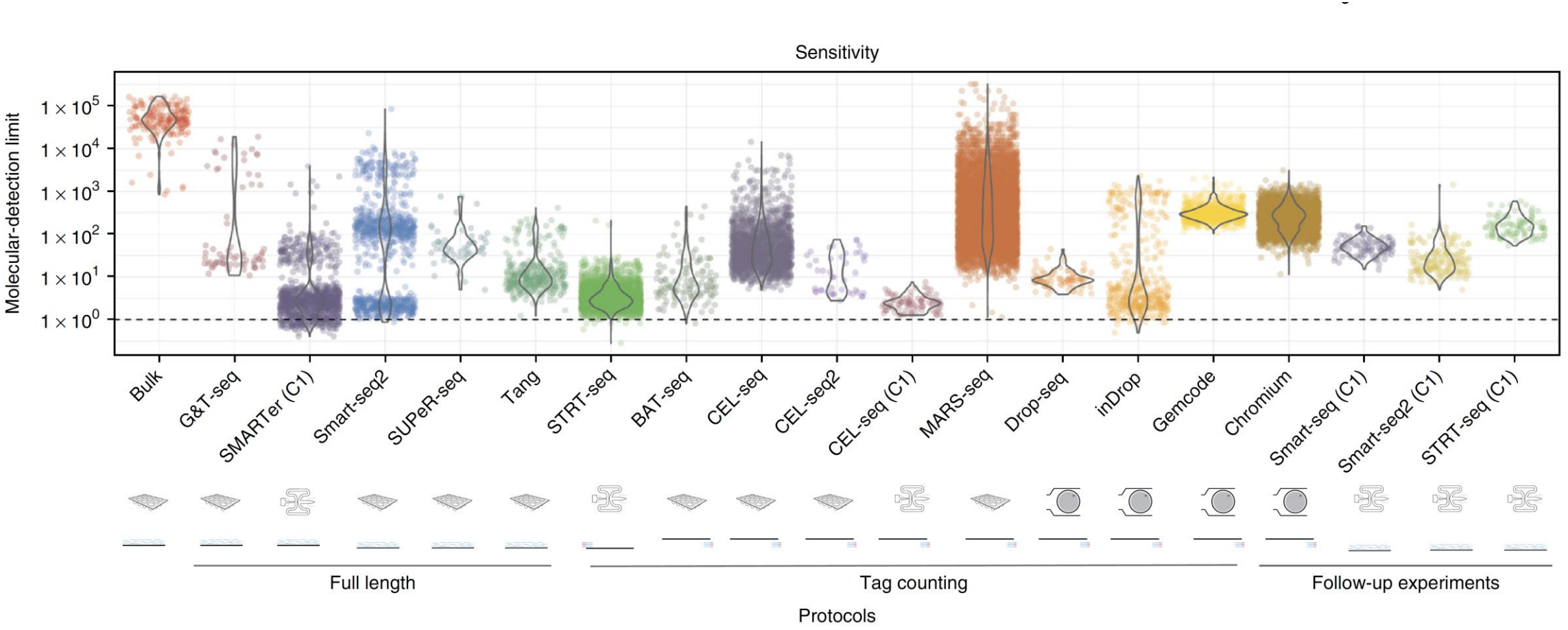




Svensson et al. Nature Methods 2017

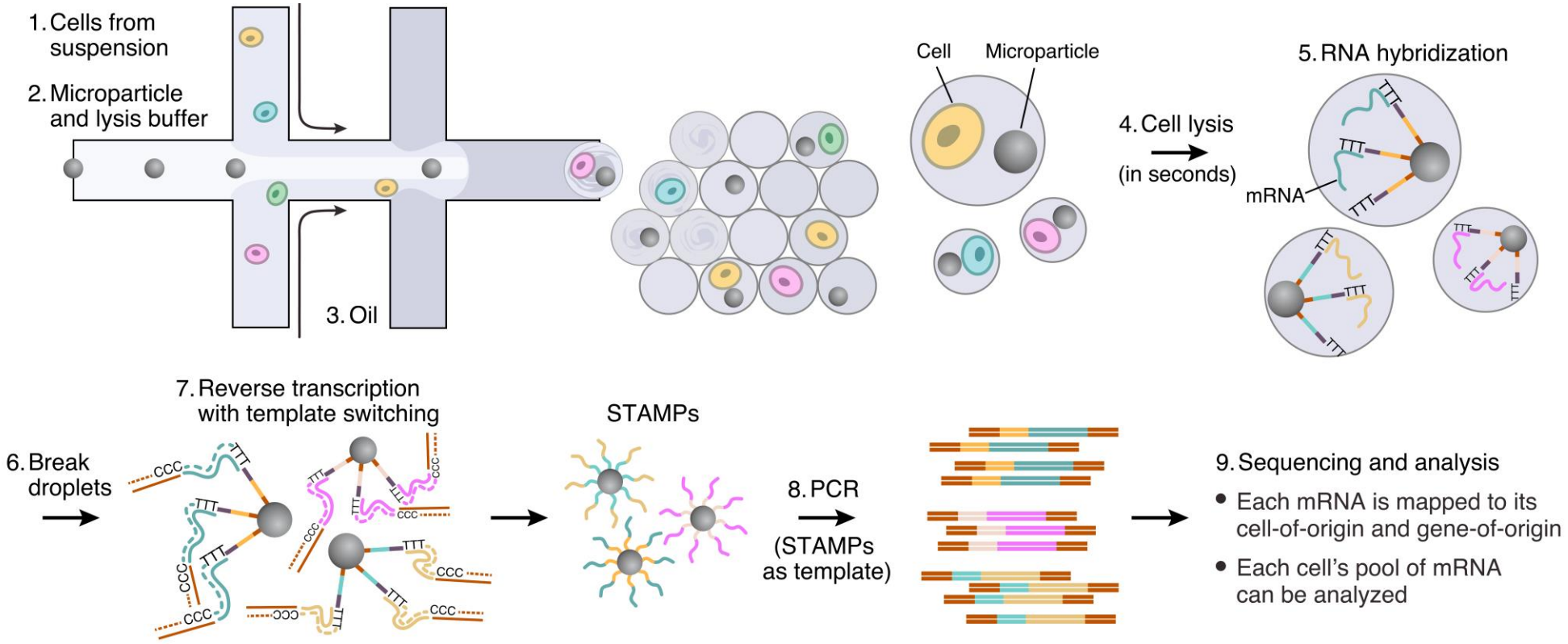
scRNA-seq Protocols

Sensitivity

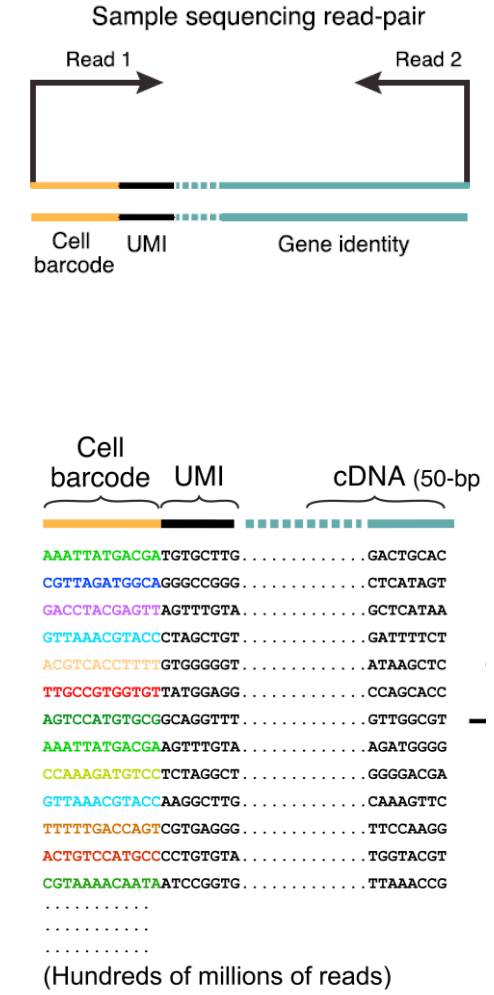


Svensson et al. Nature Methods 2017

Drop-seq



STAMPs: Single-cell transcriptomes attached to microparticles

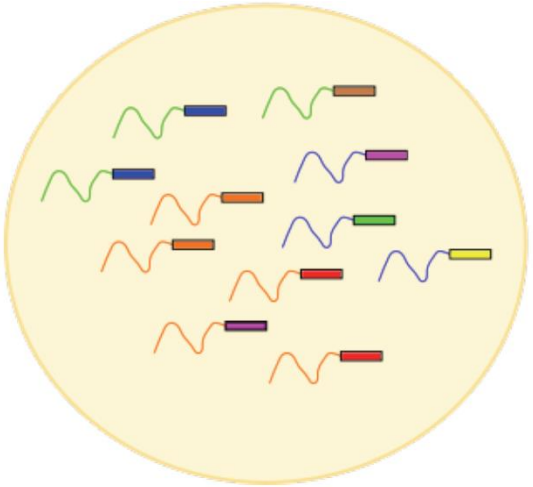


Macosko et al., Cell 2015

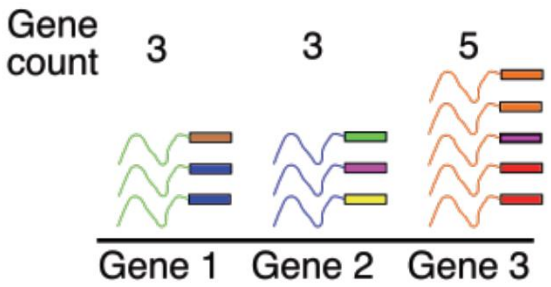
Unique Molecular Identifiers (UMIs)

- Unique molecular identifiers give (almost) exact molecule counts in sequencing experiments.
- They reduce the amplification noise by allowing (almost) complete de-duplication of sequenced fragments.

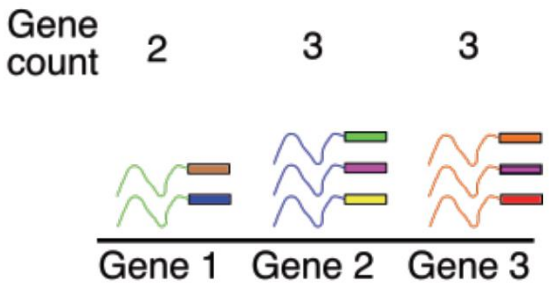
Sequenced fragments from an individual cell



Pre de-duplication



Post de-duplication



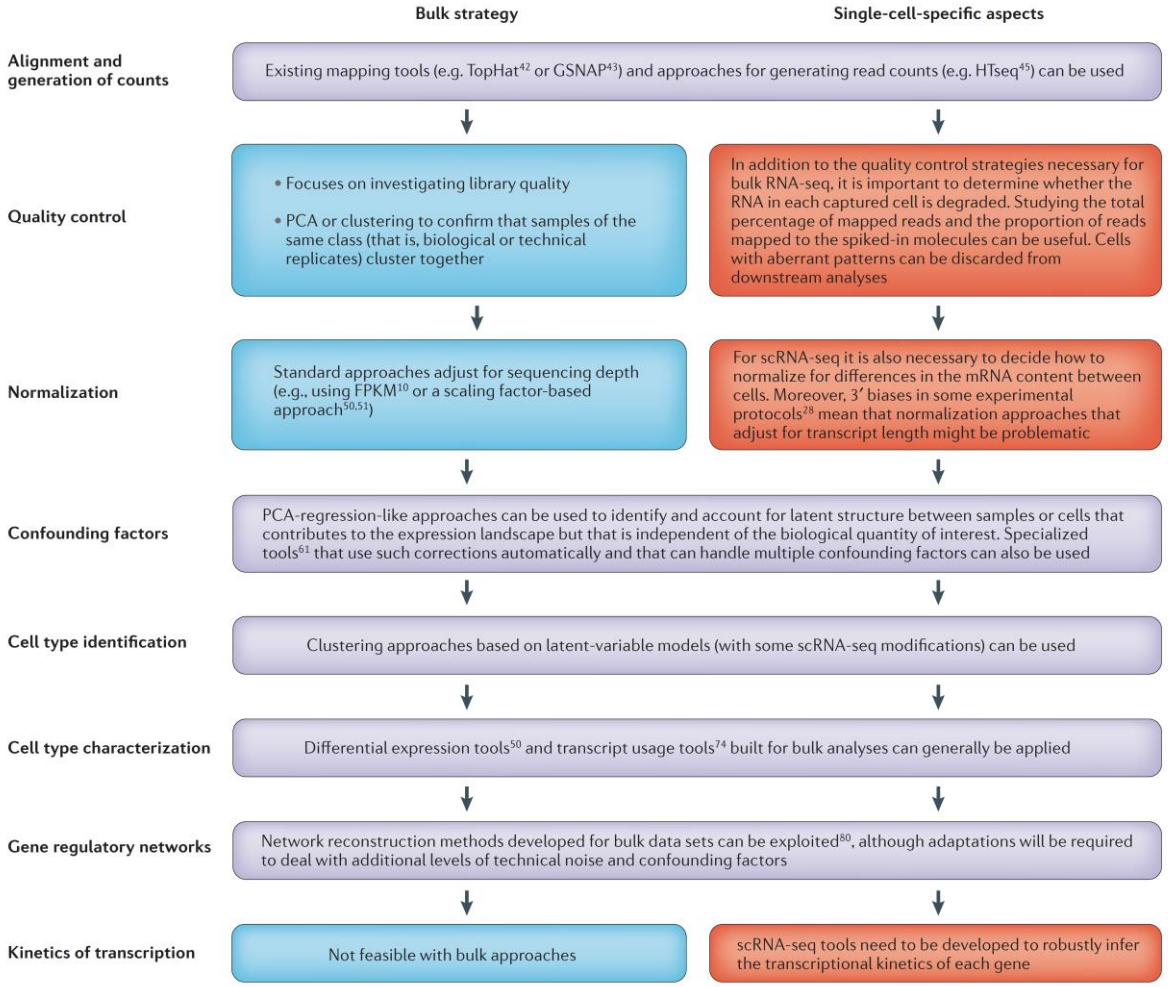
scRNA-seq Data Analysis

Our goal is to derive/extract real biology from technically noisy data

What is different from bulk?

- The main sources of discrepancy between the libraries are:
  - ➢ Amplification (up to 1 million fold)
  - ➢ Gene ‘dropouts’

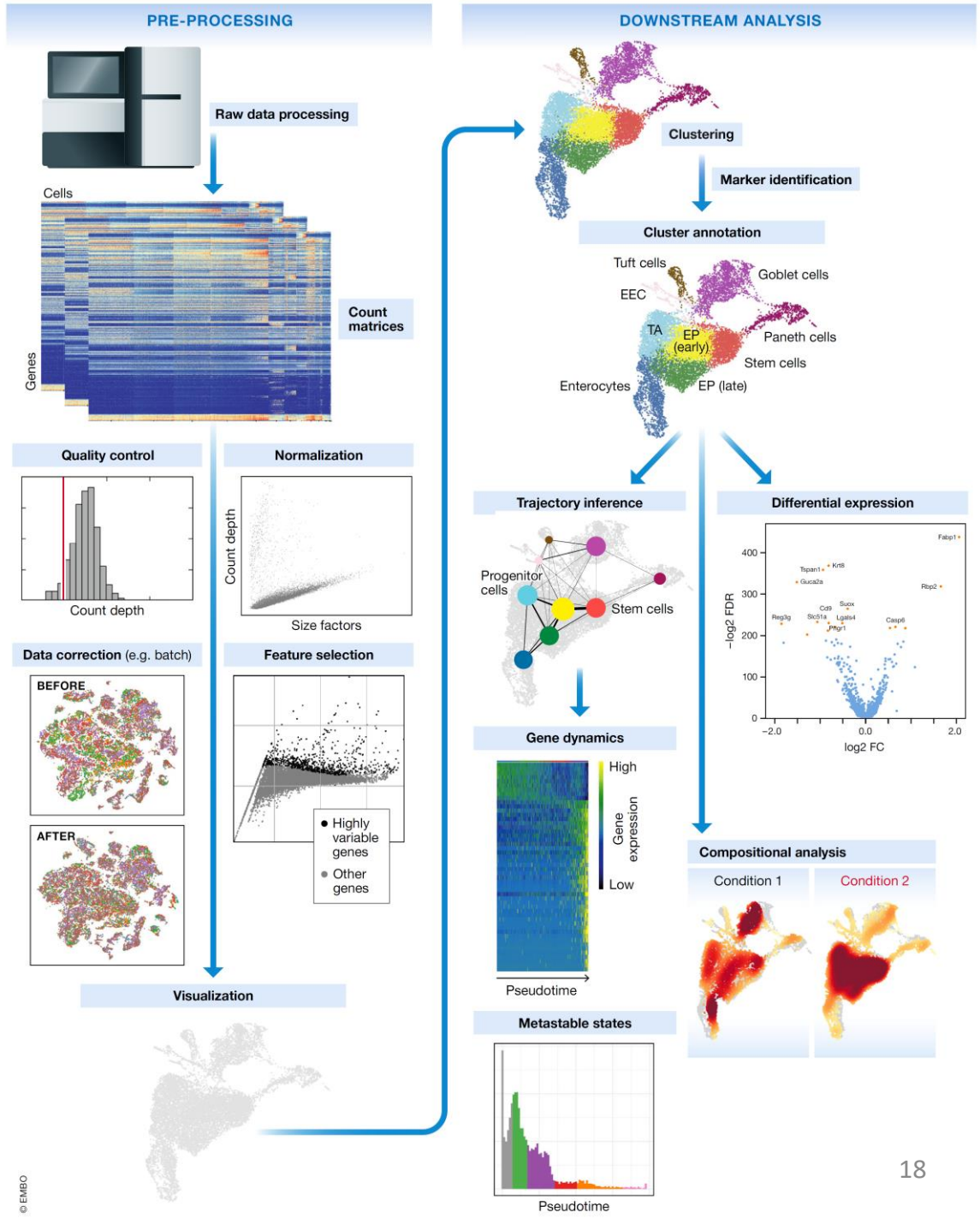
- Due to low starting amounts of transcripts since the RNA comes from one cell only.



Stegle, Teichmann, Marioni (Nat Rev Genetics 2015)

scRNA-seq Data Analysis

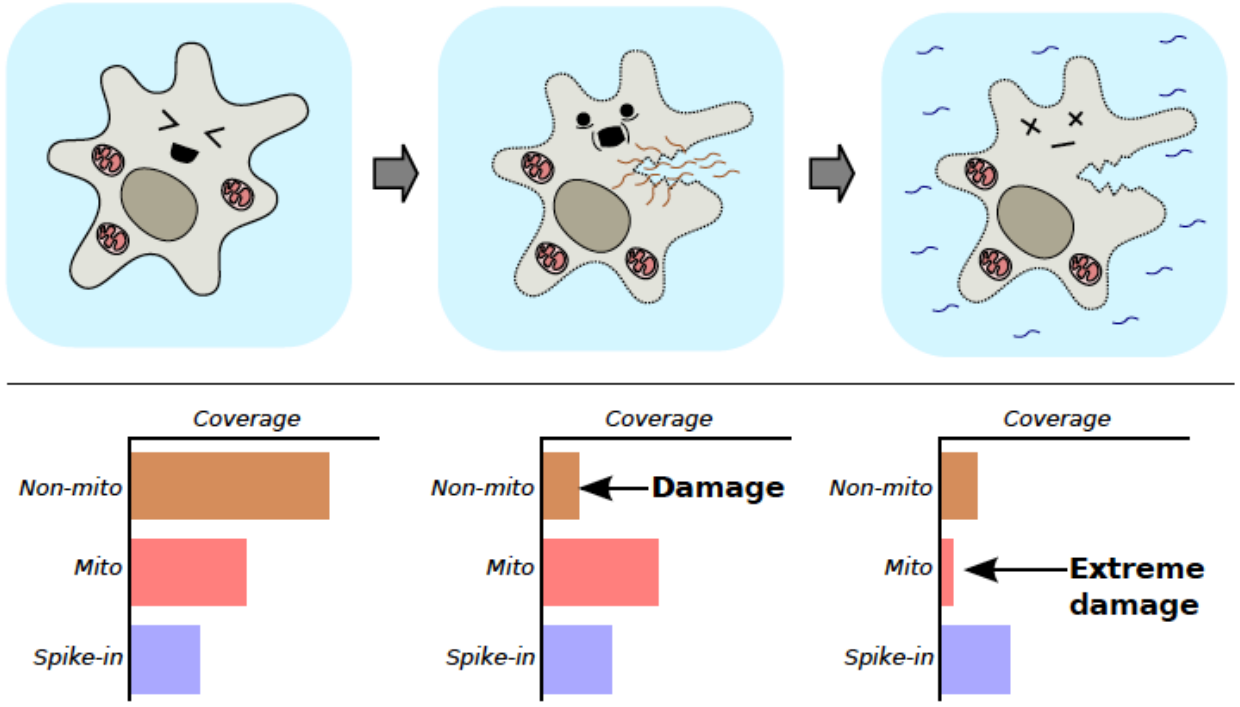
- Preprocessing:
  - Reads to count matrix
  - Quality control (QC)
  - Normalization
  - Batch correction
  - Feature selection
- Downstream
  - Cell type identification (clustering/classification)
  - Trajectory inference
  - Differential expression
  - Compositional analysis
  - Co-expression network analysis



Luecken and Theis (MSB 2019)

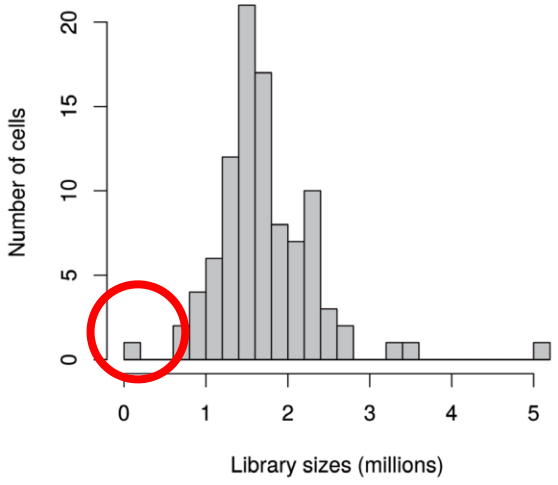
Quality control of cells (1)

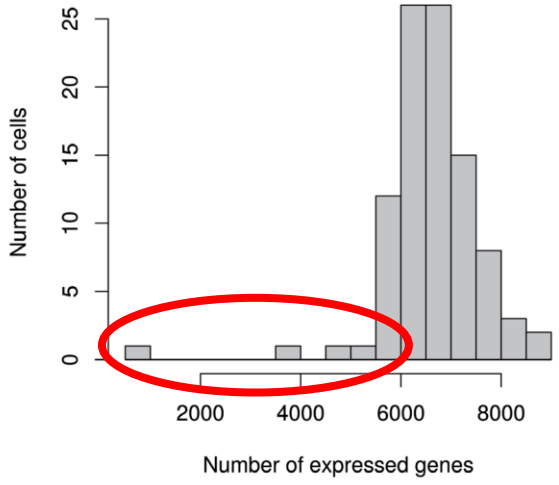
- Low sequencing depth
- Low numbers of expressed genes (i.e. any nonzero count)
- High spike-in (if present) or mitochondrial content



Quality control of cells (2)

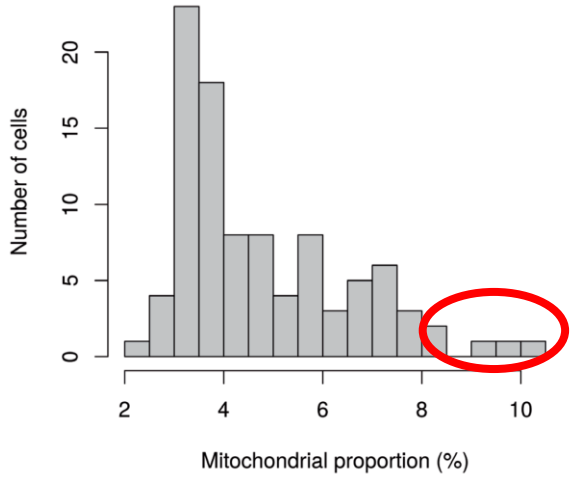
RNA has not been efficiently captured during library preparation

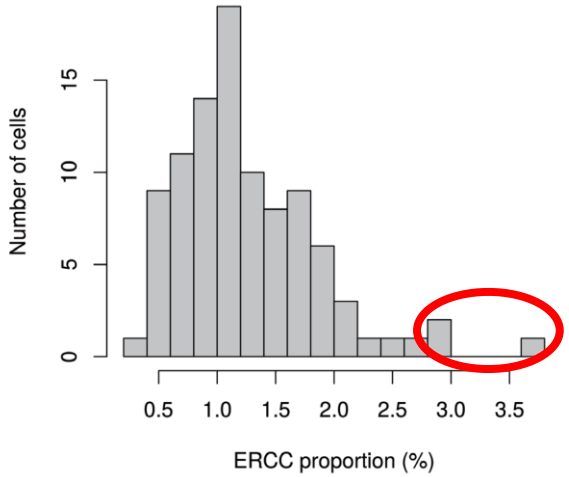




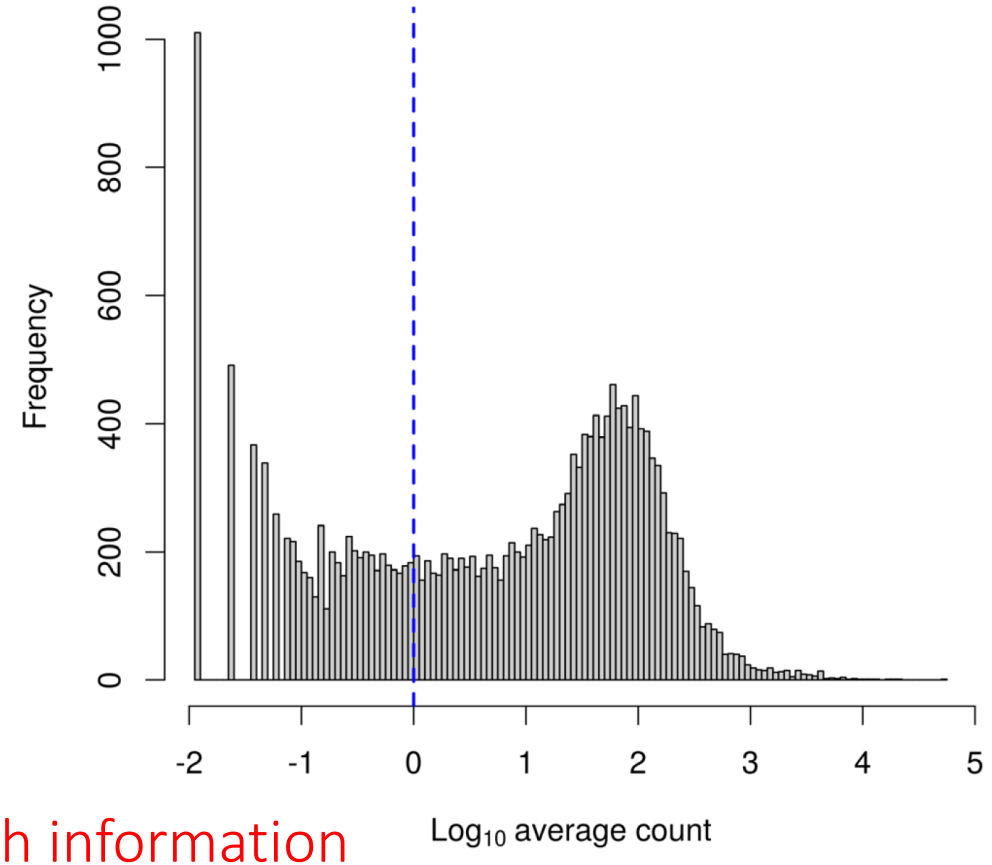
Diverse transcript population not captured

Possibly because of increased apoptosis and/or loss of cytoplasmic RNA from lysed cells

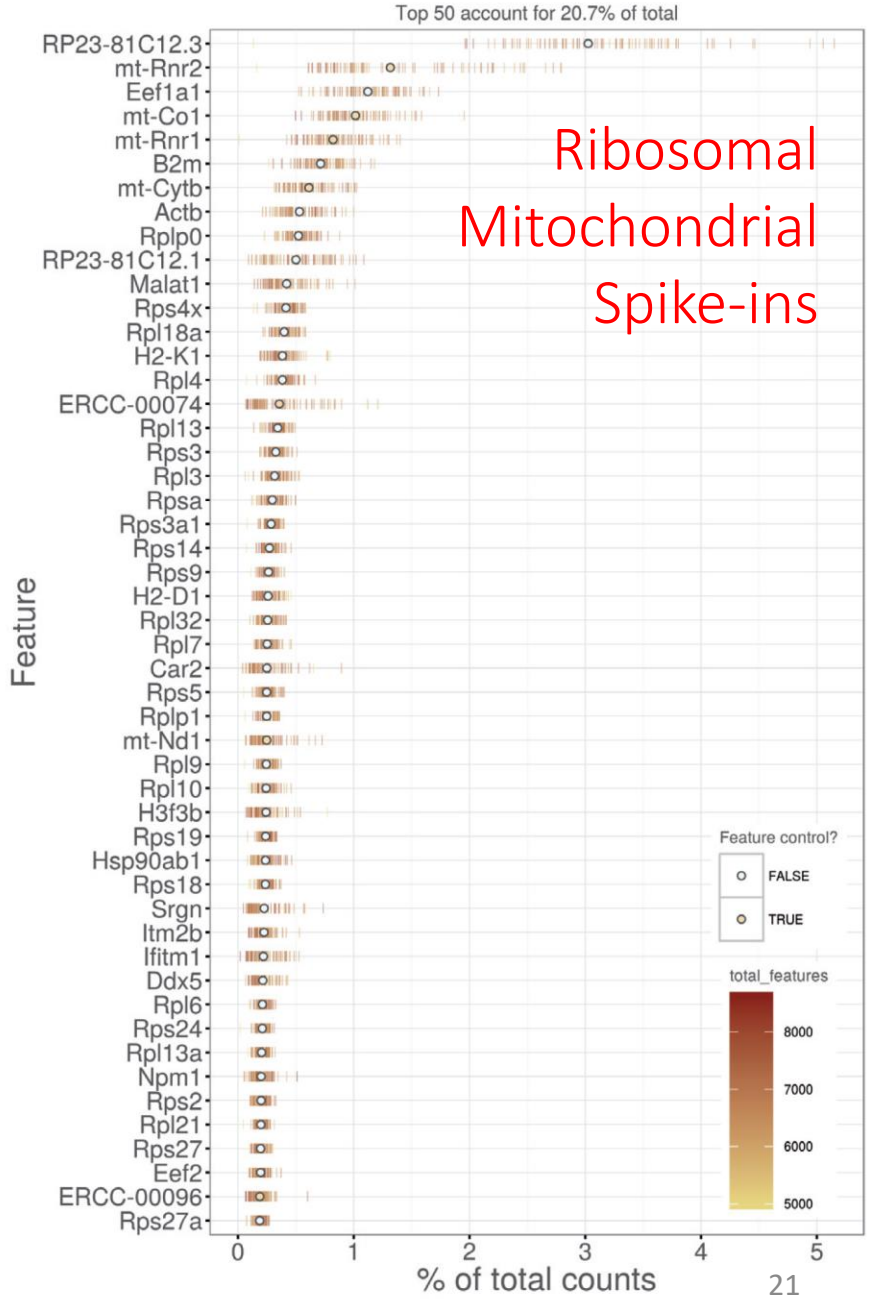




Quality control of genes



Not enough information for reliable statistical inference



Ribosomal
Mitochondrial
Spike-ins

QC (pitfalls and recommendations)

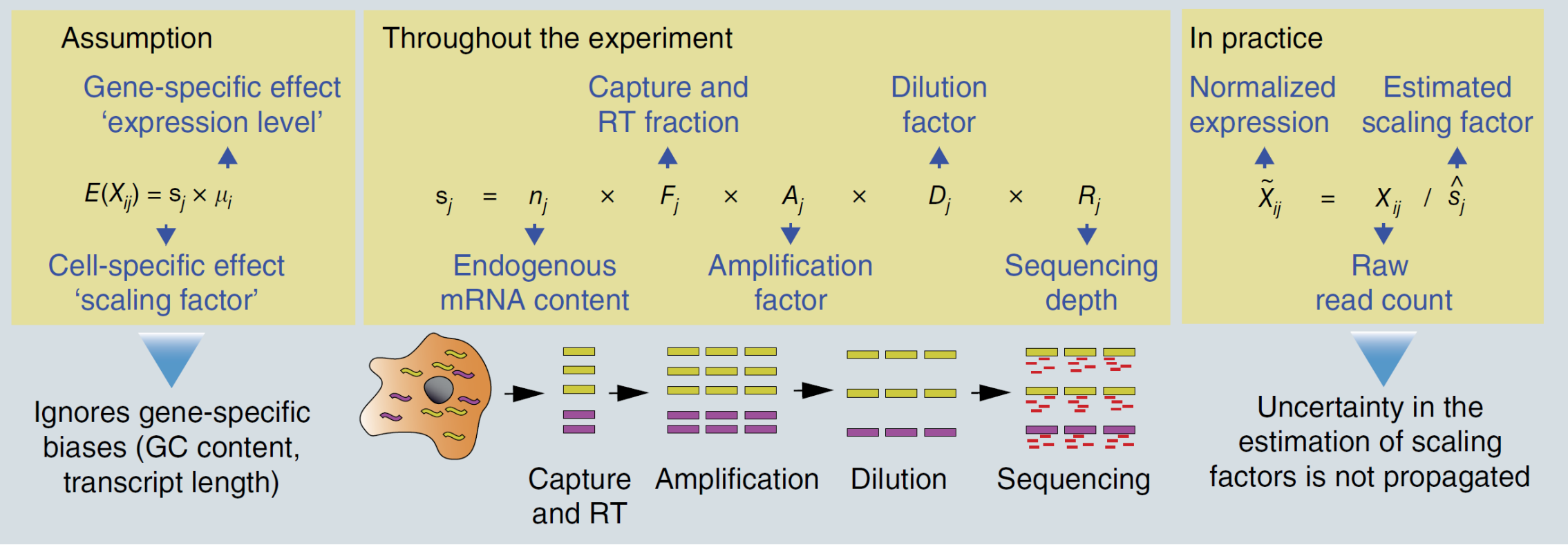
- Perform QC by finding outlier peaks in the number of genes, the count depth and the fraction of mitochondrial reads. Consider these covariates jointly instead of separately.

- Be as permissive of QC thresholding as possible, and revisit QC if downstream clustering cannot be interpreted.

- If the distribution of QC covariates differ between samples, QC thresholds should be determined separately for each sample to account for sample quality differences as in Plasschaert et al (2018).

Luecken and Theis (MSB 2019)

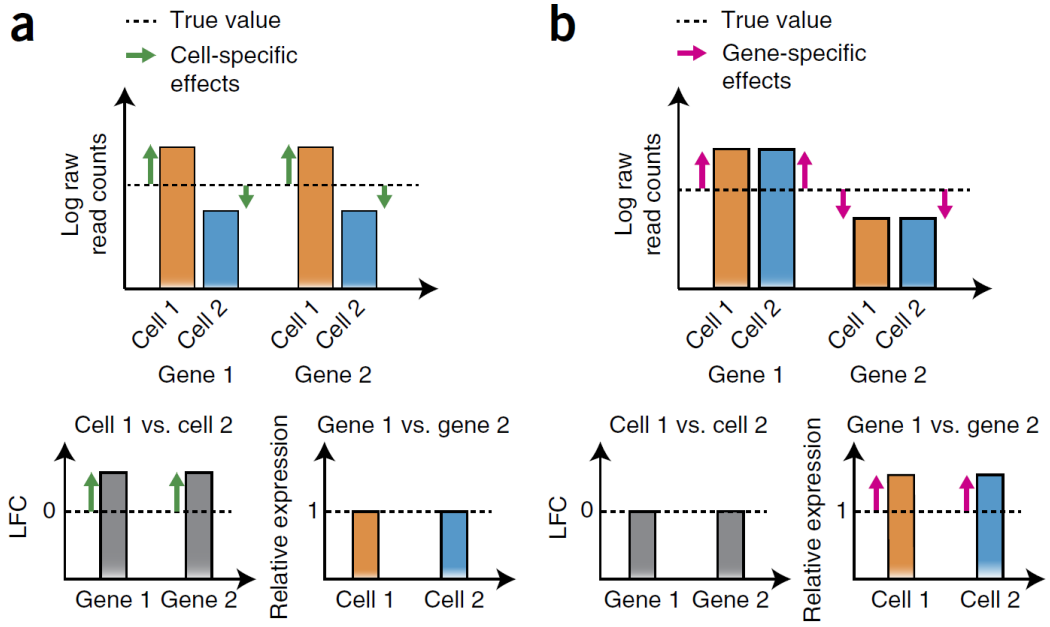
Normalization (1)



Vallejos et al. (Nat Methods 2017)

Normalization (2)

- The aim is bring all cells onto the same distribution to remove biases
- We want to preserve biological variability, not introduce new technical variation
- Primary source of bias is sequencing depth – scale down counts accordingly
- Need a method that is robust to sparsity and composition bias
  - TMM & DESeq size factors are not!



c

	Cell-specific effects	Gene-specific effects	Not removed by UMIs
Sequencing depth	✓		✓
Amplification	✓	✓	
Capture and RT efficiency	✓	✓	✓
Gene length		✓	
GC content	✓	✓	✓
mRNA content	✓		✓

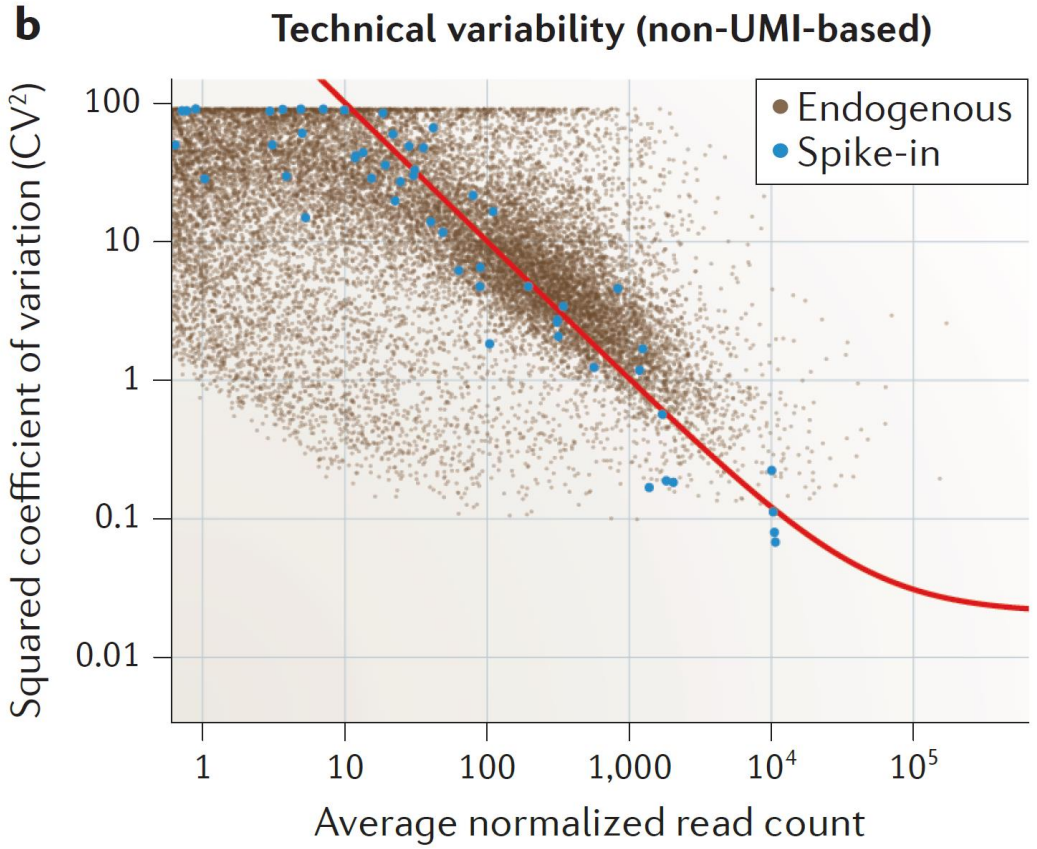
Vallejos et al. (Nat Methods 2017)

Normalization (3)

Using spike-ins

Caveats:

- The same quantity of spike-in RNA may not be consistently added to each sample
- Synthetic spike-in transcripts may not behave in the same manner as endogenous transcripts
- Not easily incorporated in all scRNA-seq protocols (not in droplet-based)

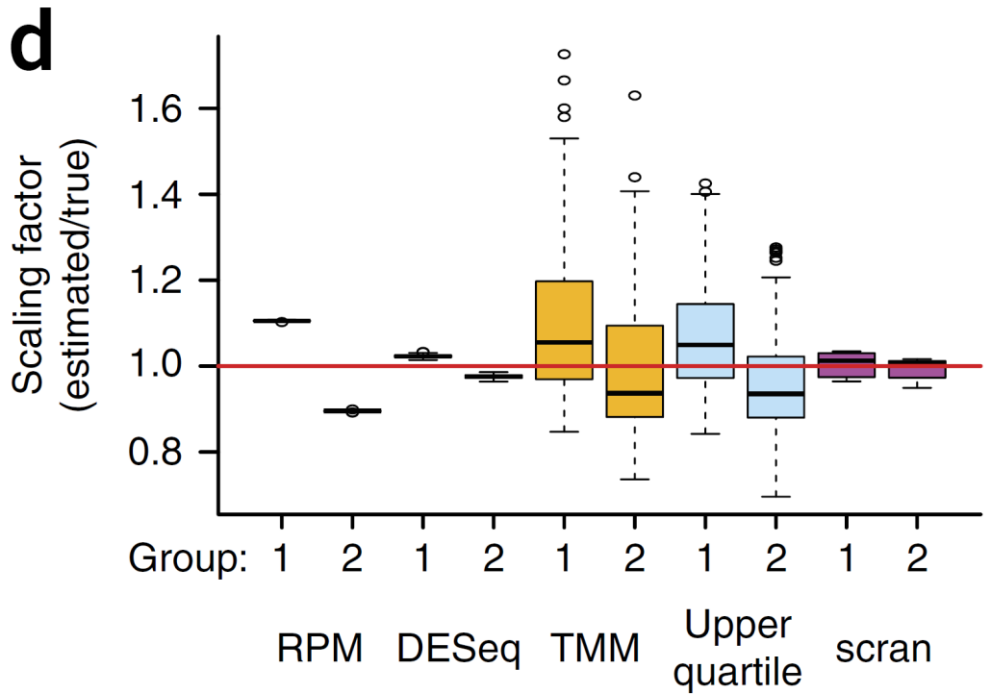


Brennecke et al. (Nat Methods 2013)

Normalization (5)

- Bulk RNA-based methods: FPKM, CPM, TPM, upperquartile *(NOT APPROPRIATE)*
- Log normalization (Seurat)
- Negative binomial (Monocole)
- Zero-inflated negative binomial (ZINB) models
- …

- Main approaches
  1. Size factors
  2. Probabilistic methods



Performance Assessment and Selection of Normalization Procedures for Single-Cell RNA-Seq
Cole et al, Cell Systems 2019

Vallejos et al. (Nat Methods 2017)

Normalization (pitfalls and recommendations)

- We recommend scran for normalization of non-full-length datasets. An alternative is to evaluate normalization approaches via scone especially for plate-based datasets. Full-length scRNA-seq protocols can be corrected for gene length using bulk methods.

- There is no consensus on scaling genes to 0 mean and unit variance. We prefer not to scale gene expression.

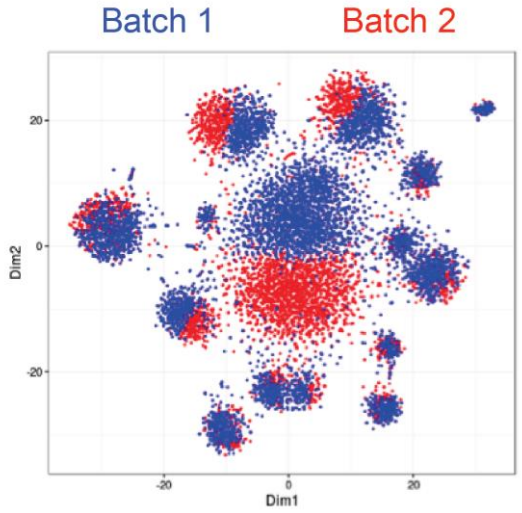
- Normalized data should be log(x+1)-transformed for use with downstream analysis methods that assume data are normally distributed.

Luecken and Theis (MSB 2019)

Confounders and batch effects (1)

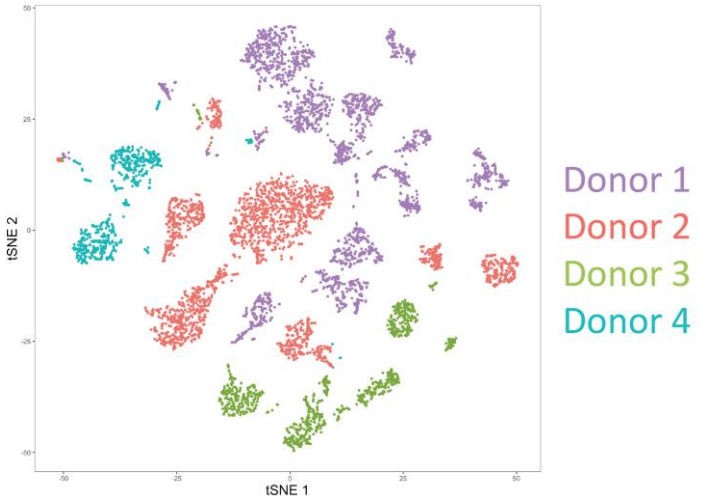
1. Technical variability
   - Changes in sample quality/processing
   - Library prep or sequencing technology
   - ‘Experimental reality’

Technical ‘batch effects’ confound downstream analysis



2. Biological variability
   - Patient differences
   - Environmental/genetic perturbation
   - Evolution! (cross-species analysis)

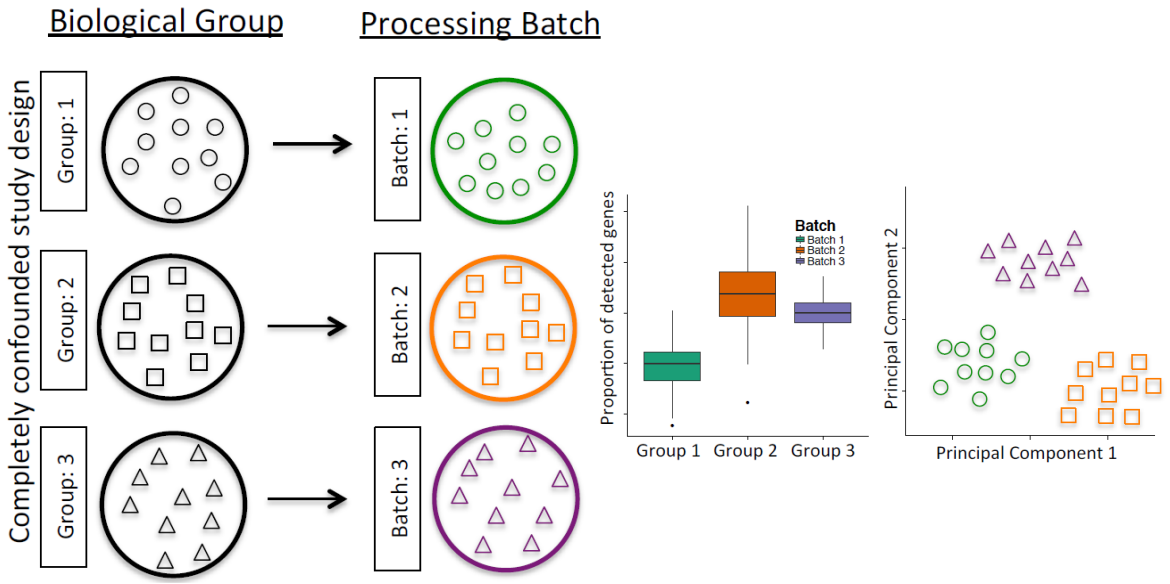
Biological ‘batch effects’ confound comparisons of scRNA-seq data



Shaham et al. (Bioinformatics 2017)

Confounders and batch effects (2)

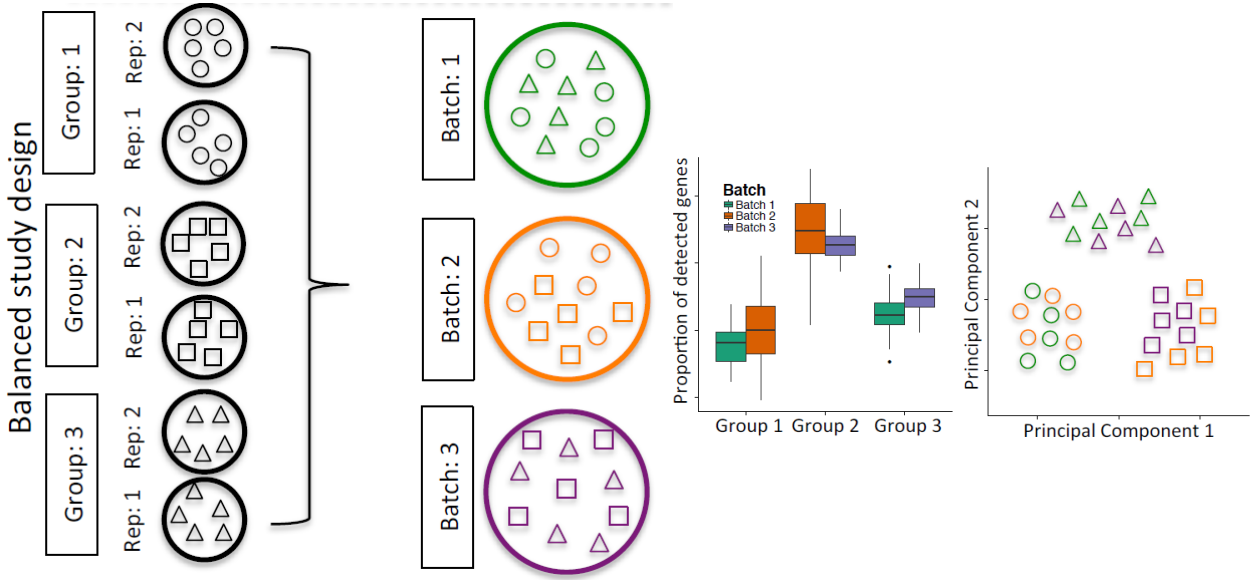
Confounded design



Don’t design your experiment like this!!!

Hicks et al. (bioRxiv 2015)

Not confounded design



Good experimental design *does not remove batch effects*, it prevents them from biasing your results.

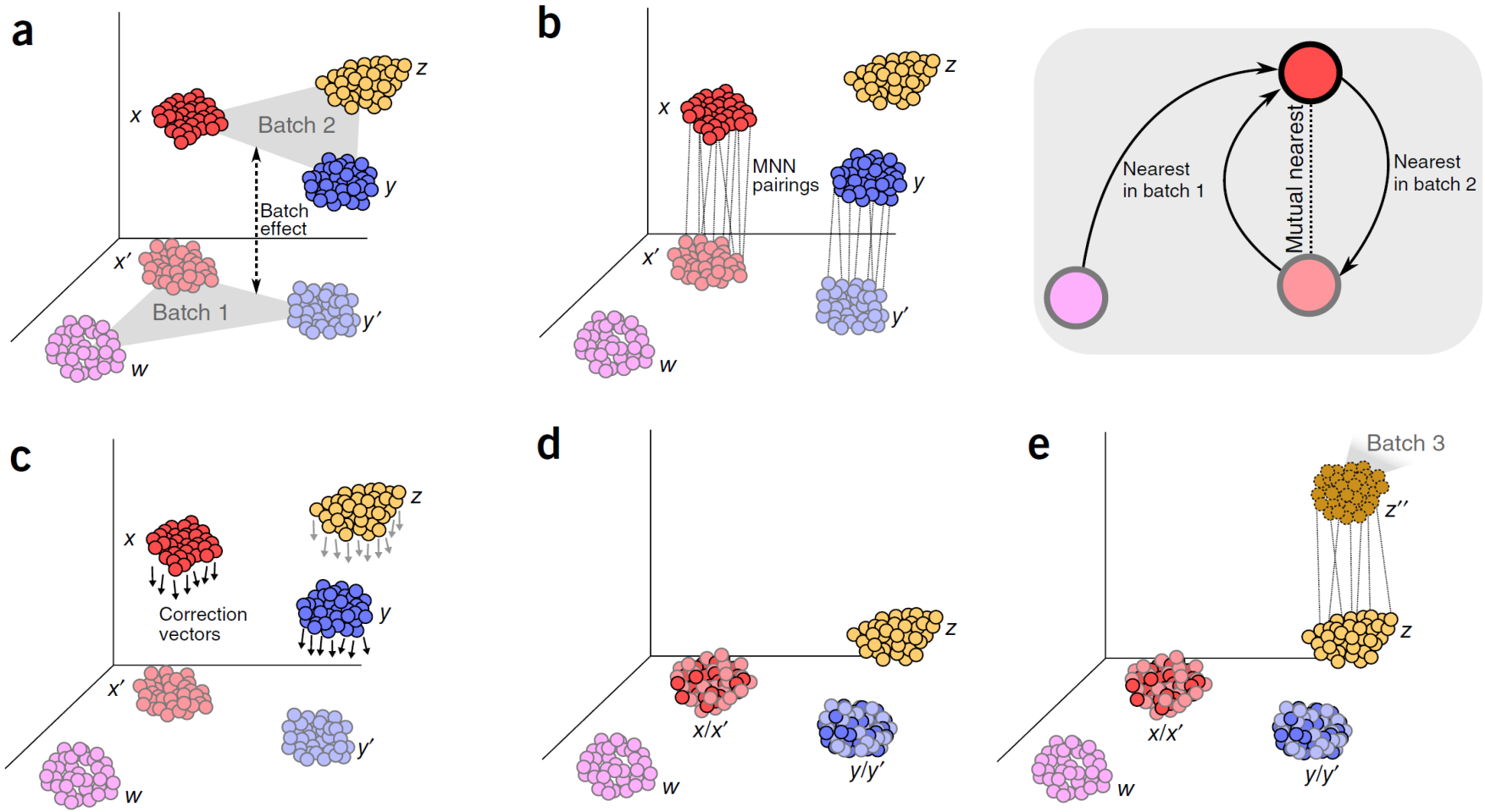
Batch correction methods

- MNNcorrect (https://doi.org/10.1038/nbt.4091)
- CCA + anchors (Seurat v3) (https://doi.org/10.1101/460147)
- CCA + dynamic time warping (Seurat v2) (https://doi.org/10.1038/nbt.4096)
- LIGER (https://doi.org/10.1101/459891)
- Harmony (https://doi.org/10.1101/461954)
- Conos (https://doi.org/10.1101/460246)
- Scanorama (https://doi.org/10.1101/371179)
- scMerge (https://doi.org/10.1073/pnas.1820006116)
- …

Two broad strategies:

- Joint dimension reduction
- Graph-based joint clustering

Mutual Nearest Neighbors (MNN)



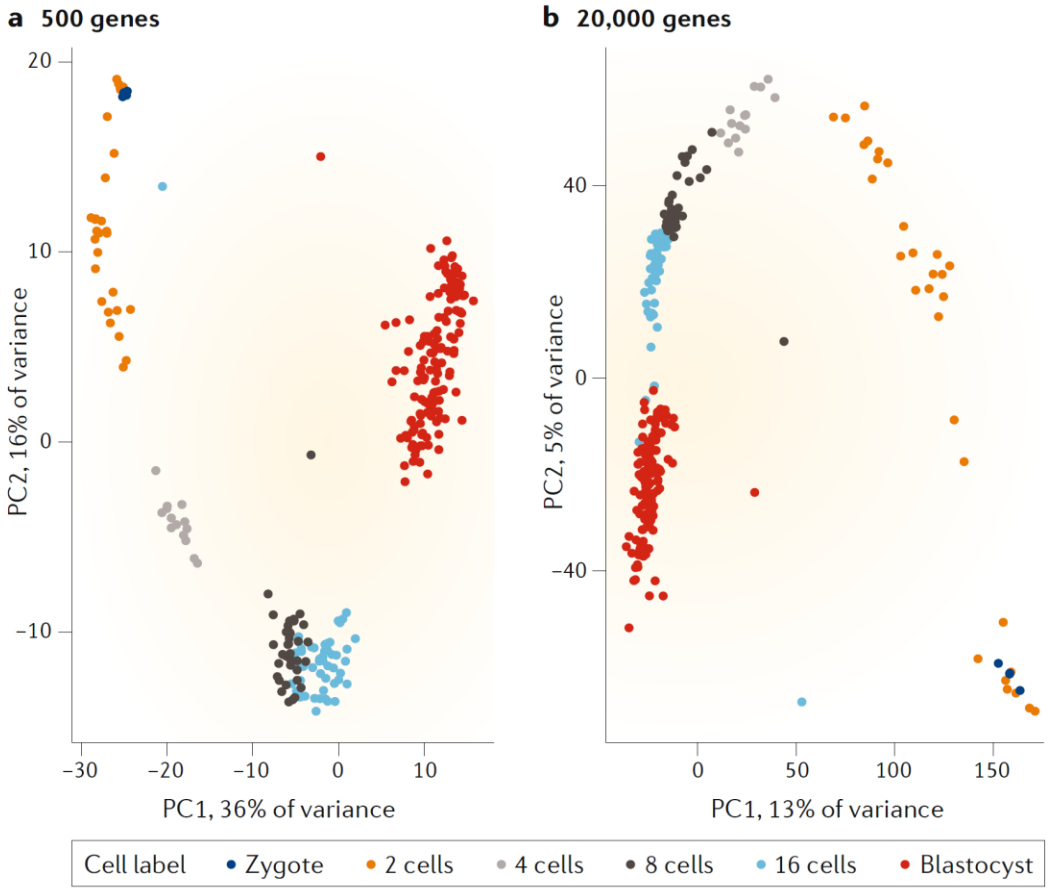
Haghverdi et al., (Nature Biotech 2017)

Feature selection

- Curse of dimensionality:

More features (genes) -> smaller distances between samples (cells)

- Remove genes which only exhibit technical noise
  - Increase the signal:noise ratio
  - Reduce the computational complexity



Kiselev et al. (https://doi.org/10.1038/s41576-018-0088-9)

Feature selection

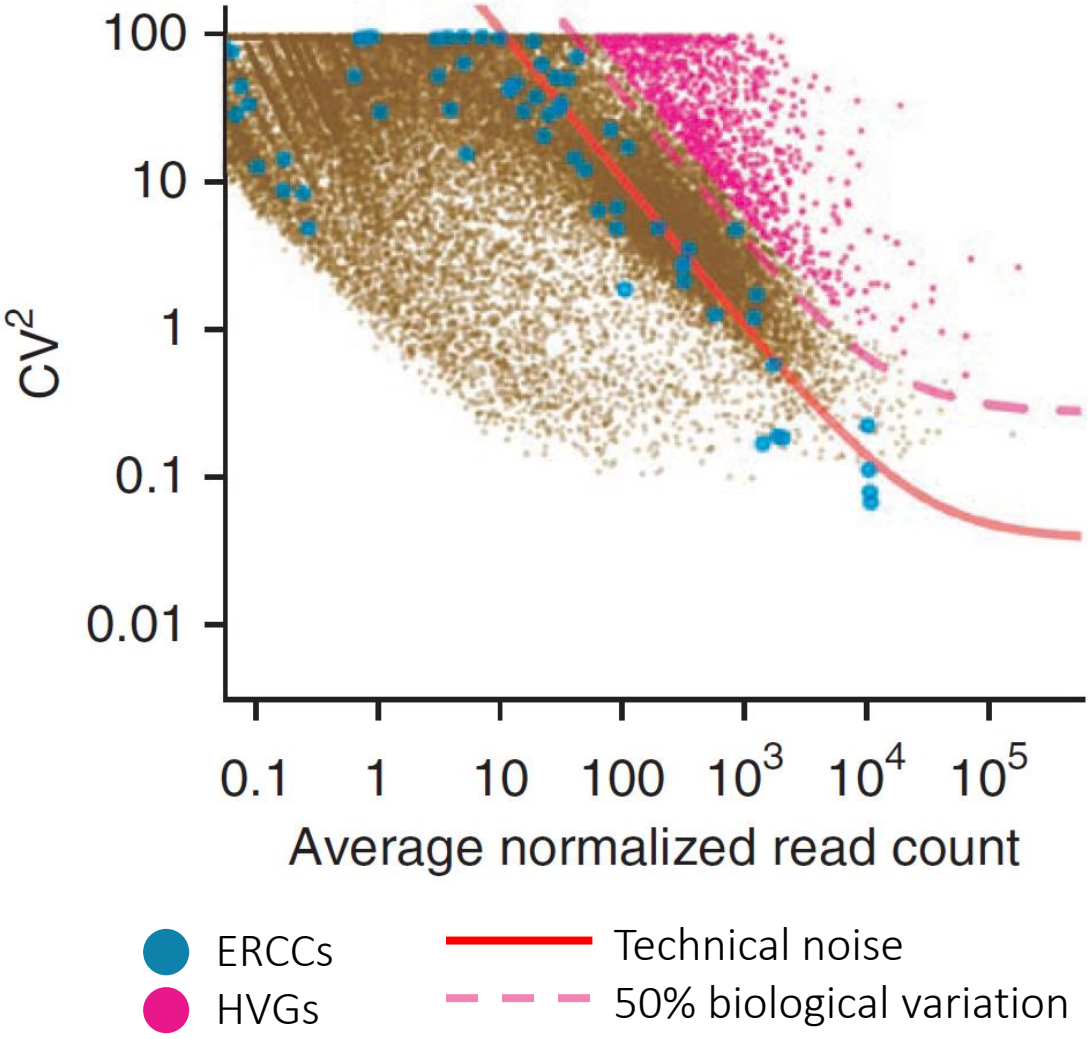
Highly Variable Genes (HVG)

- $CV = \frac{var}{mean} = \frac{\sigma}{\mu}$

- Fit a gamma generalized linear model

- No ERCCs?

  -> estimate technical noise based on all genes



Brennecke et al. (https://doi.org/10.1038/nmeth.2645)

Feature selection

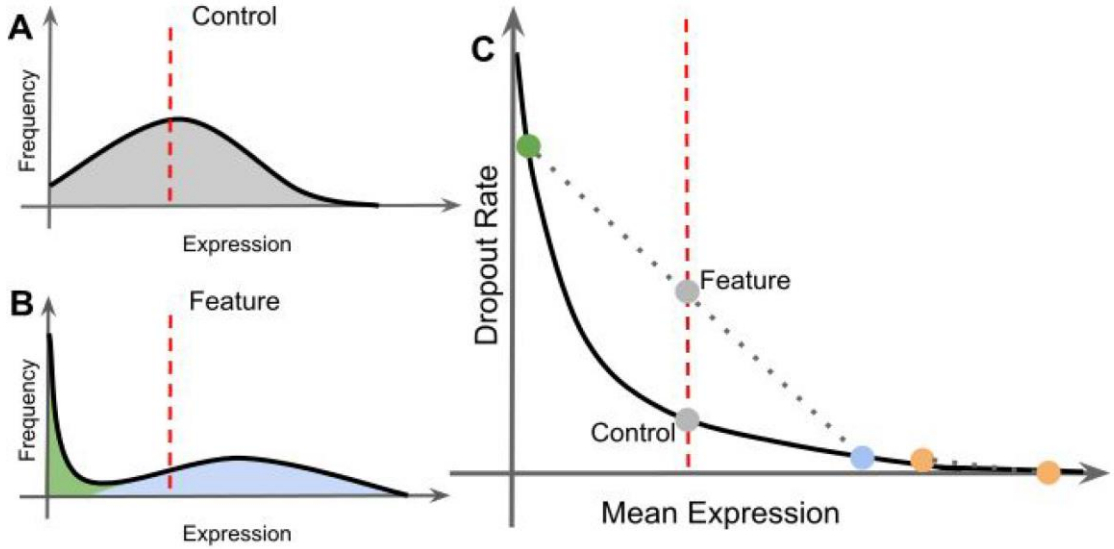
M3Drop: Dropout-based feature selection

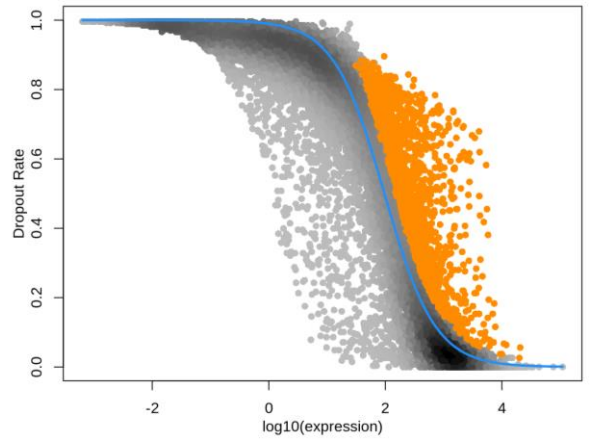
- Reverse transcription is an enzyme reaction thus can be modelled using the Michaelis-Menten equation:

$$P_{dropout} = 1 - \frac{S}{K_M + S}$$

S: average expression

K_M: Michaelis-Menten constant





Brennecke et al. (https://doi.org/10.1038/nmeth.2645)

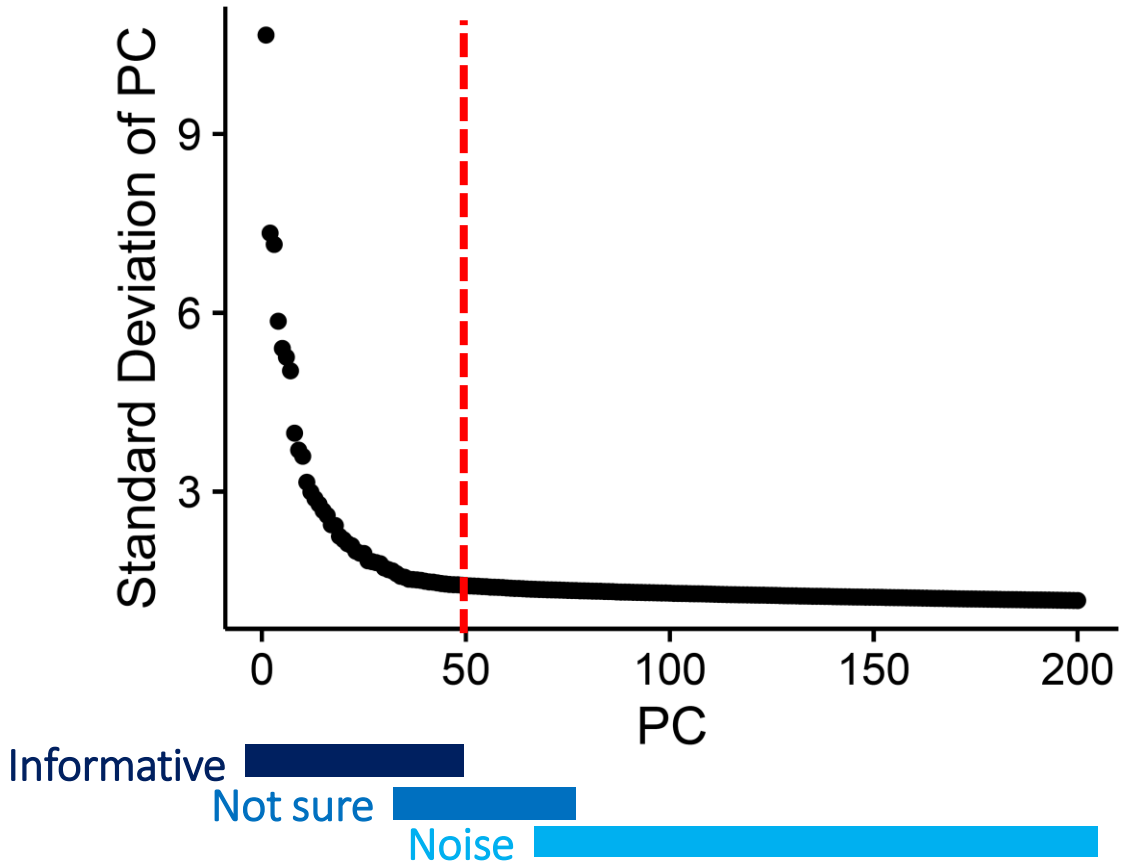
Feature selection

Selecting principal components

- To overcome the extensive technical noise in scRNA-seq data, it is common to cluster cells based on their PCA scores

- Each PC represents a ‘metagene’ that (linearly) combines information across a correlated gene set

Scree/elbow plot



Feature Selection (pitfalls and recommendations)

- We recommend selecting between 1,000 and 5,000 highly variable genes depending on dataset complexity.

- Feature selection methods that use gene expression means and variances cannot be used when gene expression values have been normalized to zero mean and unit variance, or when residuals from model fitting are used as normalized expression values. Thus, one must consider what pre-processing to perform before selecting HVGs.

Luecken and Theis (MSB 2019)

Dimensionality reduction (1)

Matrix factorization

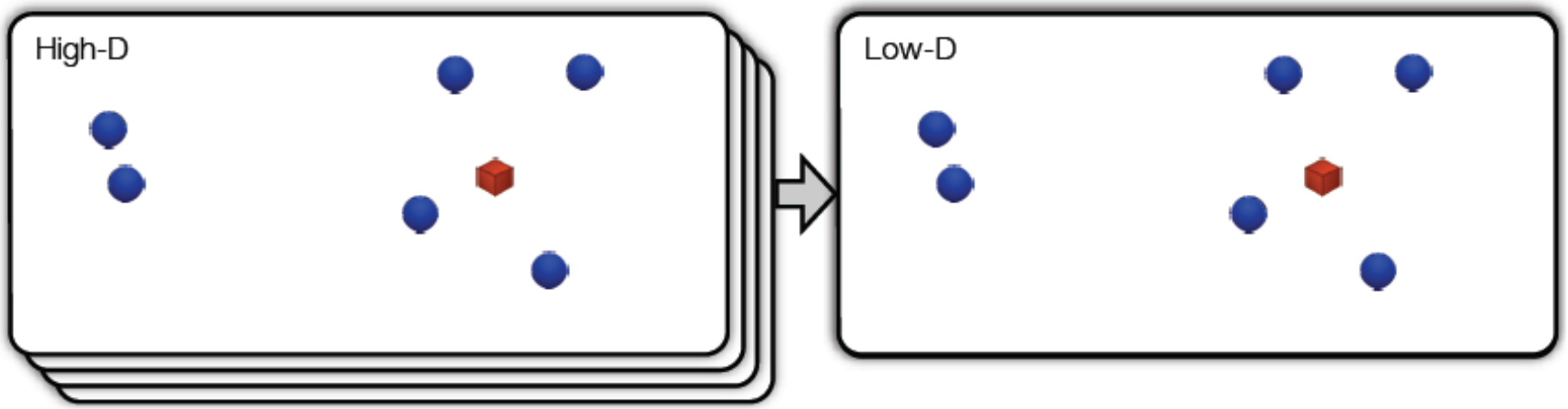
Graph-based

Auto-encoders

PCA	linear		
ICA	linear		
MDS	non-linear		
Sparce NNMF	non-linear	2010	https://pdfs.semanticscholar.org/664d/40258f12ad28ed0b7d4 c272935ad72a150db.pdf
cPCA	non-linear	2018	https://doi.org/10.1038/s41467-018-04608-8
ZIFA	non-linear	2015	https://doi.org/10.1186/s13059-015-0805-z
ZINB-WaVE	non-linear	2018	https://doi.org/10.1038/s41467-017-02554-5
Diffusion maps	non-linear	2005	https://doi.org/10.1073/pnas.0500334102
Isomap	non-linear	2000	10.1126/science.290.5500.2319
t-SNE	non-linear	2008	https://lvdmaaten.github.io/publications/papers/JMLR_2008.pdf
- BH t-SNE	non-linear	2014	https://lvdmaaten.github.io/publications/papers/JMLR_2014.pdf
- Flt-SNE	non-linear	2017	arXiv:1712.09005
LargeVis	non-linear	2018	arXiv:1602.00370
UMAP	non-linear	2018	arXiv:1802.03426
PHATE	non-linear	2017	https://www.biorxiv.org/content/biorxiv/early/2018/06/28/120378.full.pdf
scvis	non-linear	2018	https://doi.org/10.1038/s41467-018-04368-5
VASC	non-linear	2018	https://doi.org/10.1016/j.gpb.2018.08.003

Dimensionality Reduction (2)

- t-SNE: t-distributed stochastic neighborhood embedding



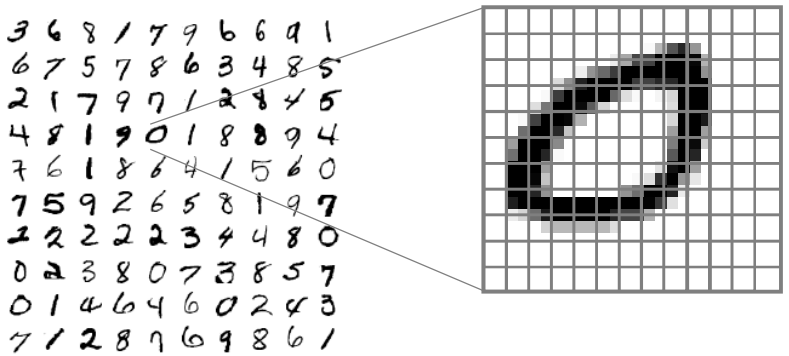
$$p_{ij} = \frac{\exp(-||\boldsymbol{x}_i - \boldsymbol{x}_j||^2/2\sigma^2)}{\sum_{k \neq l} \exp(-||\boldsymbol{x}_k - \boldsymbol{x}_l||^2/2\sigma^2)}$$

$$q_{ij} = \frac{(1 + ||\boldsymbol{y}_i - \boldsymbol{y}_j||^2)^{-1}}{\sum_{k \neq l}(1 + ||\boldsymbol{y}_k - \boldsymbol{y}_l||^2)^{-1}}$$

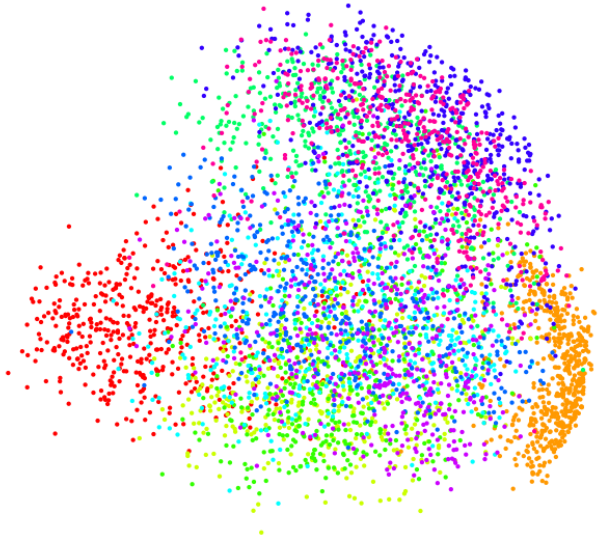
$$KL(P||Q) = \sum_{i \neq j} p_{ij} \log \frac{p_{ij}}{q_{ij}}$$

van der Maaten and Hinton, Journal of Machine Learning Research (2008)

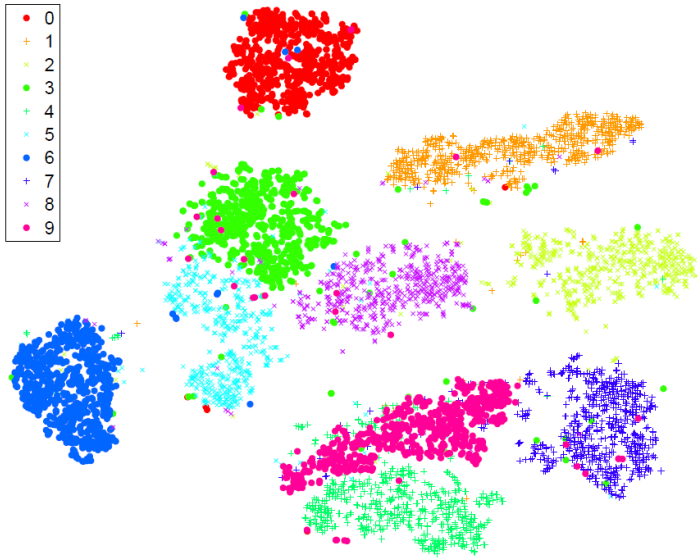
Dimensionality Reduction (3)



PCA



t-SNE

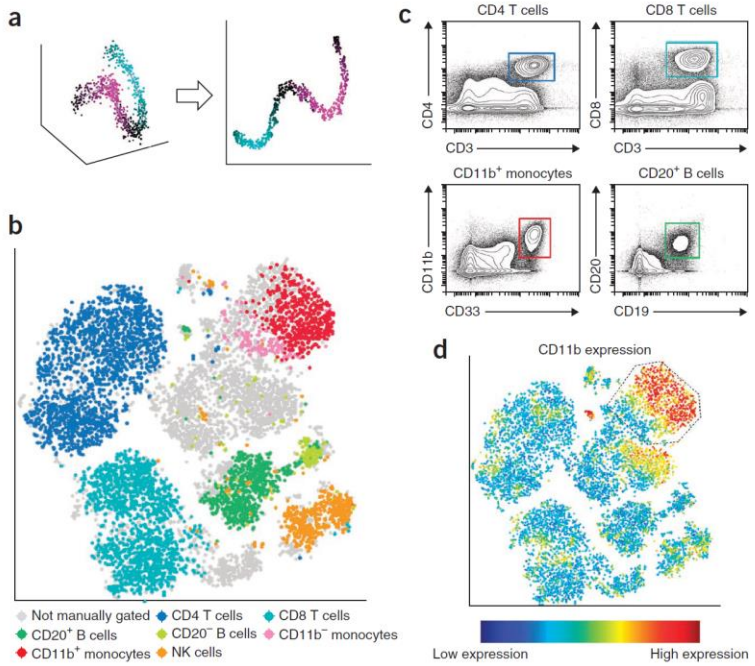


van der Maaten and Hinton, Journal of Machine Learning Research (2008)

Dimensionality Reduction (4)

viSNE enables visualization of high dimensional single-cell data and reveals phenotypic heterogeneity of leukemia

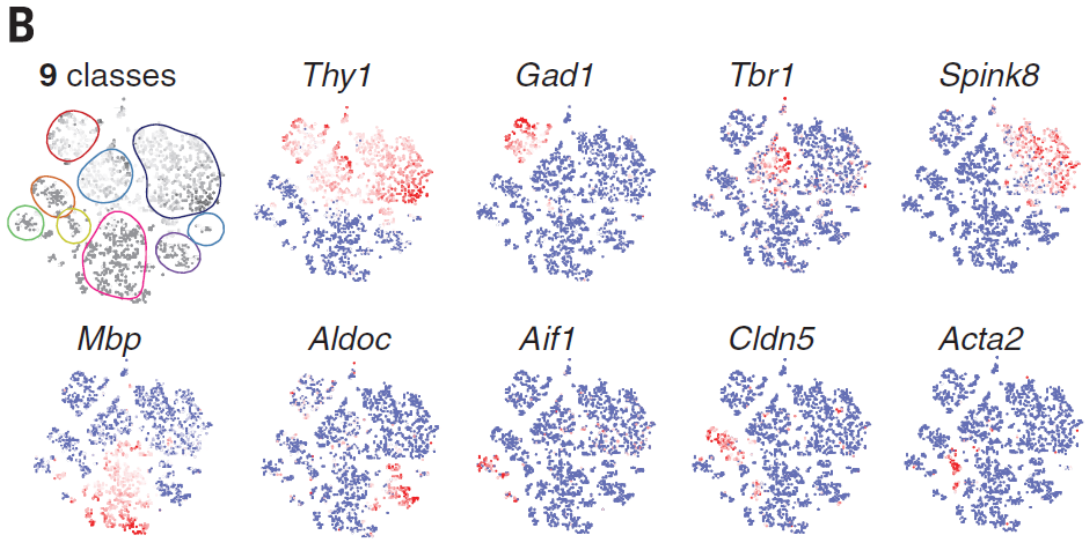
El-ad David Amir[1], Kara L Davis[2,3], Michelle D Tadmor[1,3], Erin F Simonds[2,3], Jacob H Levine[1,3], Sean C Bendall[2,3], Daniel K Shenfeld[1,3], Smita Krishnaswamy[1], Garry P Nolan[2,4] & Dana Pe'er[1,4]



Amir et al., Nature Biotechnology 2013

Cell types in the mouse cortex and hippocampus revealed by single-cell RNA-seq

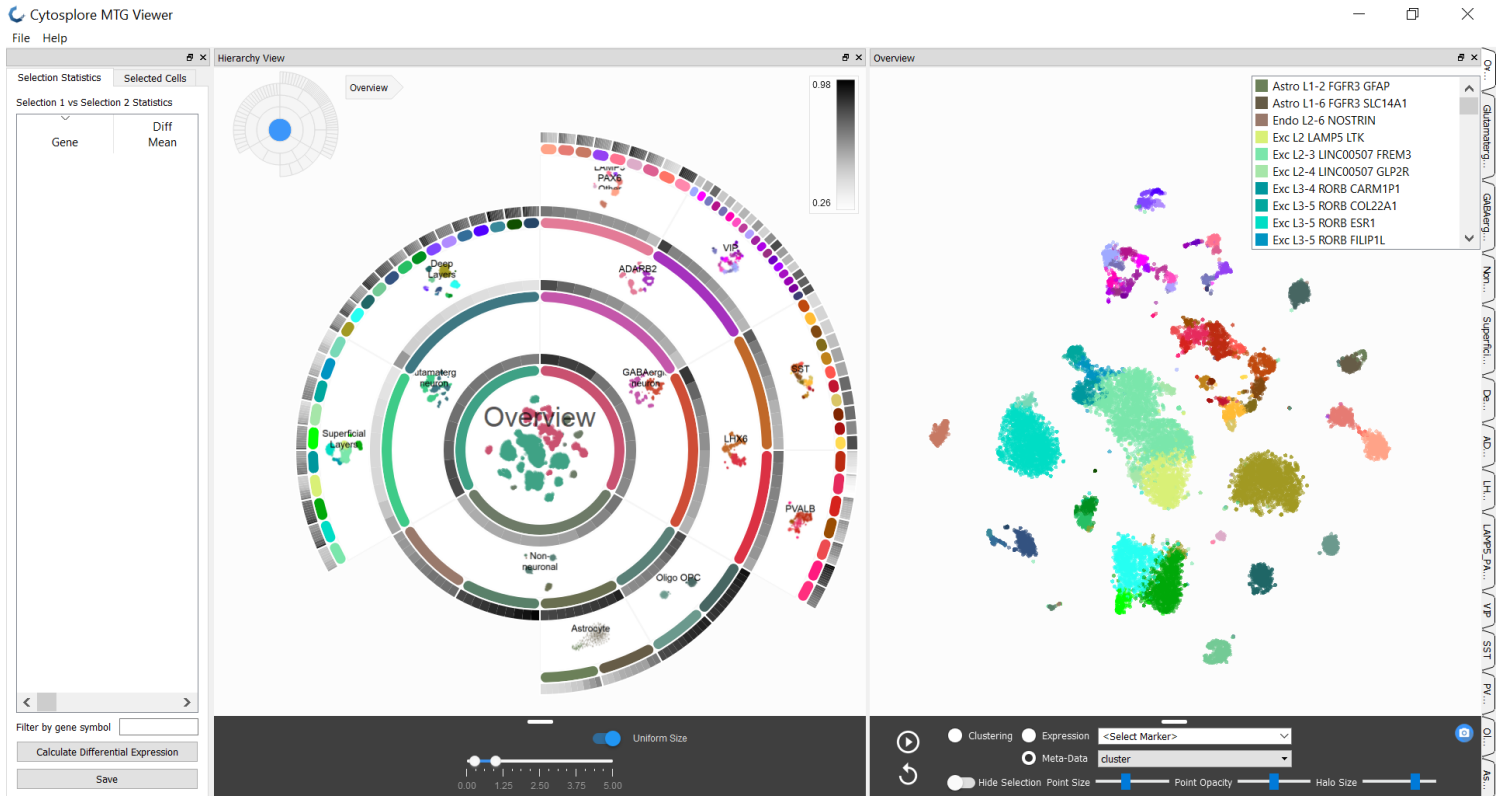
Amit Zeisel,[1*] Ana B. Muñoz-Manchado,[1*] Simone Codeluppi,[1] Peter Lönnerberg,[1] Gioele La Manno,[1] Anna Juréus,[1] Sueli Marques,[1] Hermany Munguba,[1] Liqun He,[2] Christer Betsholtz,[2,3] Charlotte Rolny,[4] Gonçalo Castelo-Branco,[1] Jens Hjerling-Leffler,[1†] Sten Linnarsson[1†]



Zeisel et al., Nature Biotechnology 2013

Dimensionality Reduction (5)

- CytoSplore: high performance single cell transcriptome visualizations https://viewer.cytosplore.org



Hodge et al. BioRxiv (2018)

Real-time tSNE

https://ai.googleblog.com/2018/06/realtime-tsne-visualizations-with.html

Google AI Blog

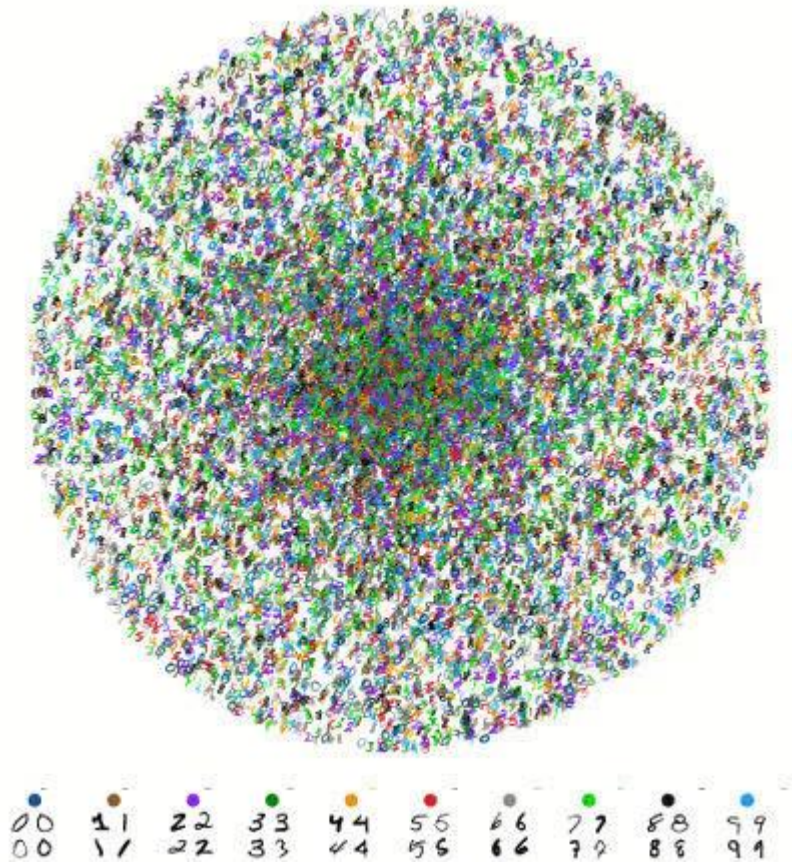
The latest news from Google AI

Realtime tSNE Visualizations with TensorFlow.js

Thursday, June 7, 2018

Posted by Nicola Pezzotti, Software Engineering Intern, Google Zürich

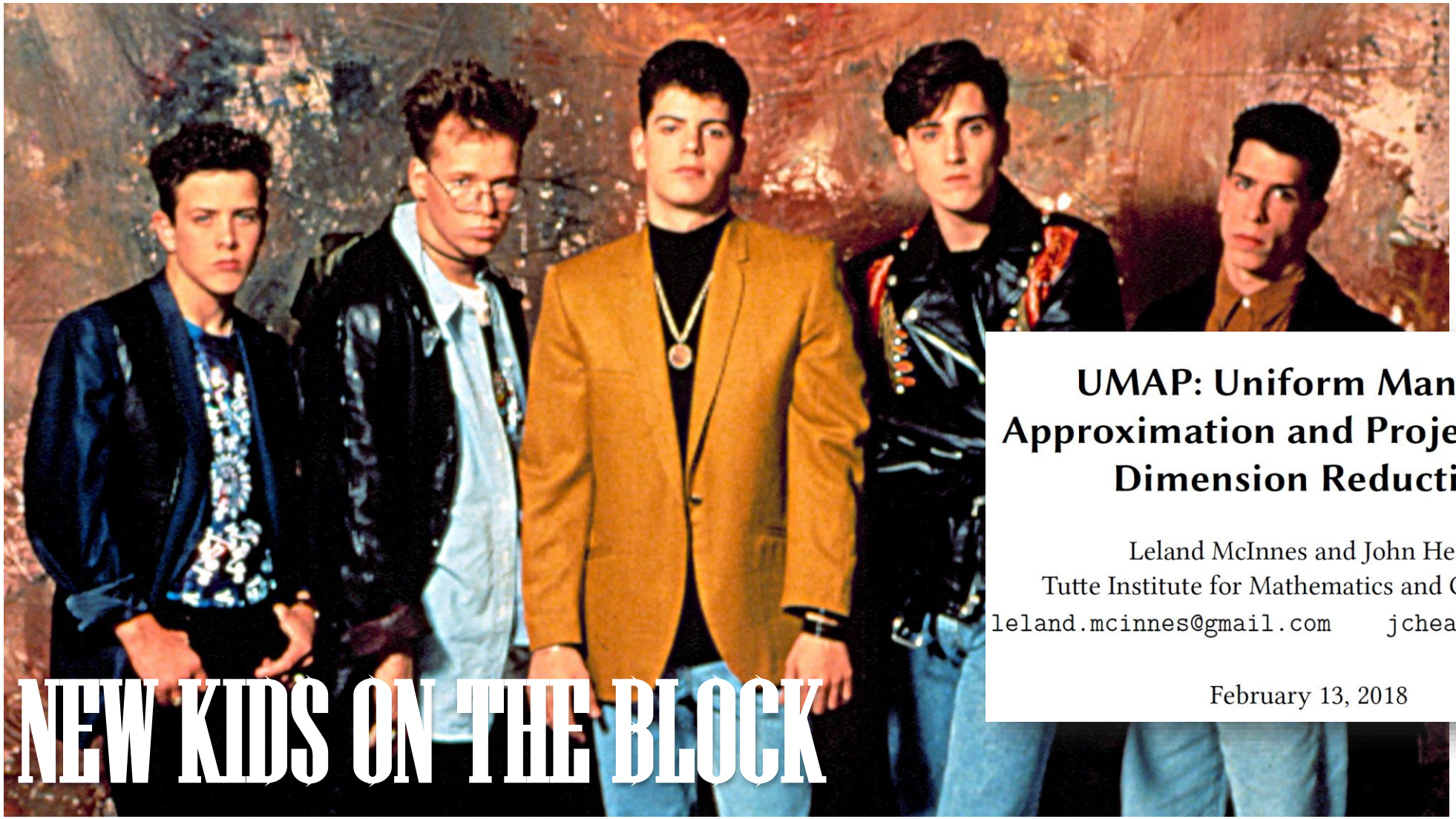
In recent years, the t-distributed Stochastic Neighbor Embedding (tSNE) algorithm has become one of the most used and insightful techniques for exploratory data analysis of high-dimensional data. Used to interpret deep neural network outputs in tools such as the TensorFlow Embedding Projector and TensorBoard, a powerful feature of tSNE is that it reveals clusters of high-dimensional data points at different scales while requiring only minimal tuning of its parameters. Despite these advantages, the computational complexity of the tSNE algorithm limits its application to relatively small datasets. While several evolutions of tSNE have been developed to address this issue (mainly focusing on the scalability of the similarity computations between data points), they have so far not been enough to provide a truly interactive experience when visualizing the evolution of the tSNE embedding for large datasets.



https://nicola17.github.io/tfjs-tsne-demo/

Pezzotti et al. arXiv 2018

Dimensionality Reduction (5)

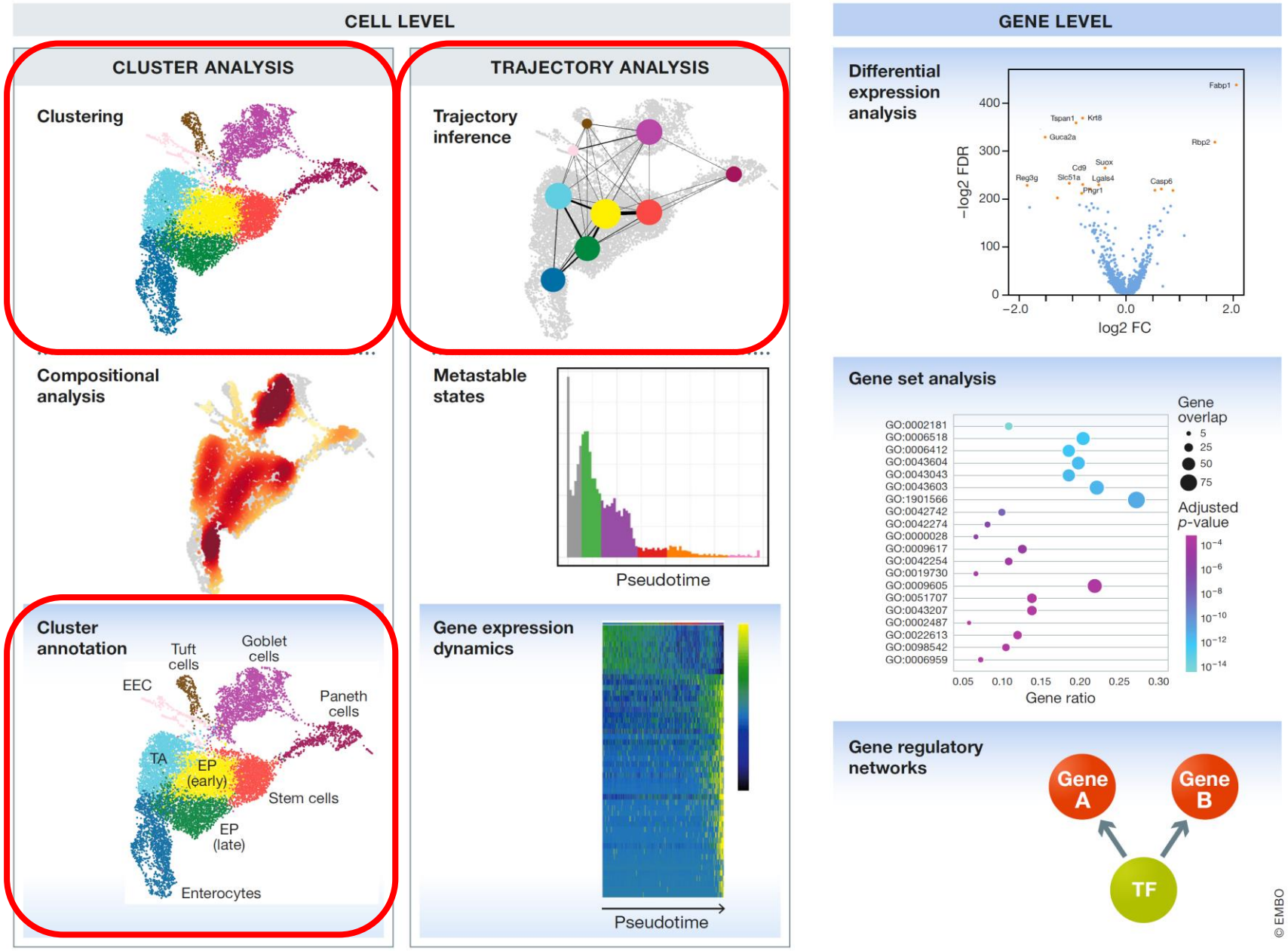


UMAP: Uniform Manifold Approximation and Projection for Dimension Reduction

Leland McInnes and John Healy
Tutte Institute for Mathematics and Computing
leland.mcinnes@gmail.com jchealy@gmail.com

February 13, 2018

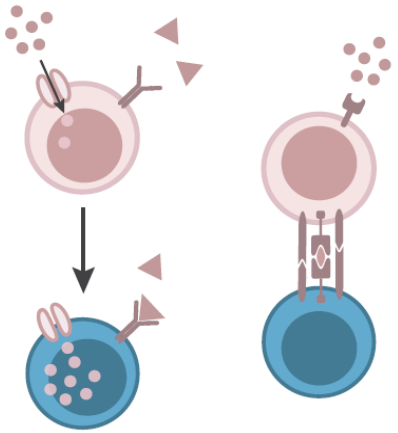
scRNA-seq Downstream Analysis



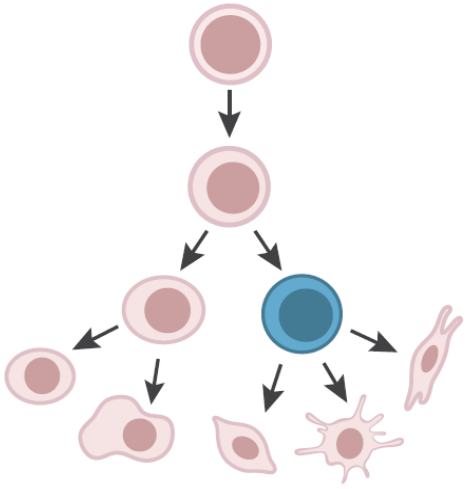
Luecken and Theis (MSB 2019)

Cell Identity

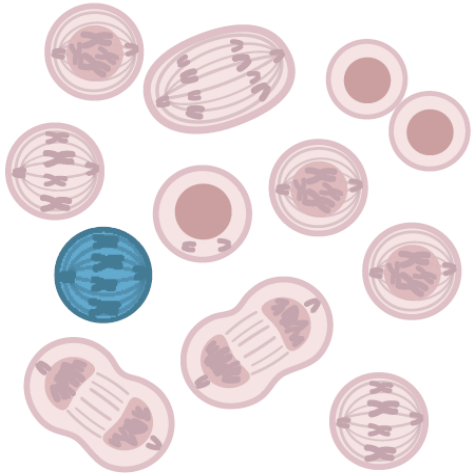
Environmental stimuli



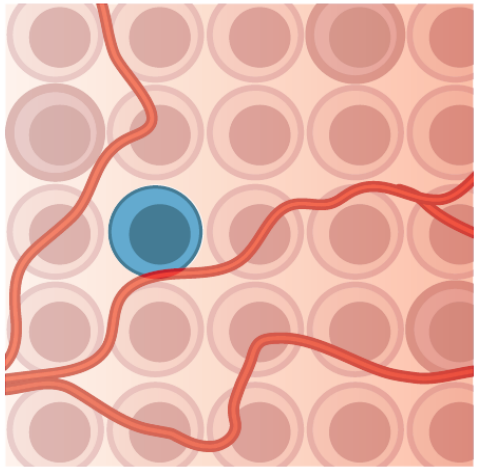
Cell development



Cell cycle

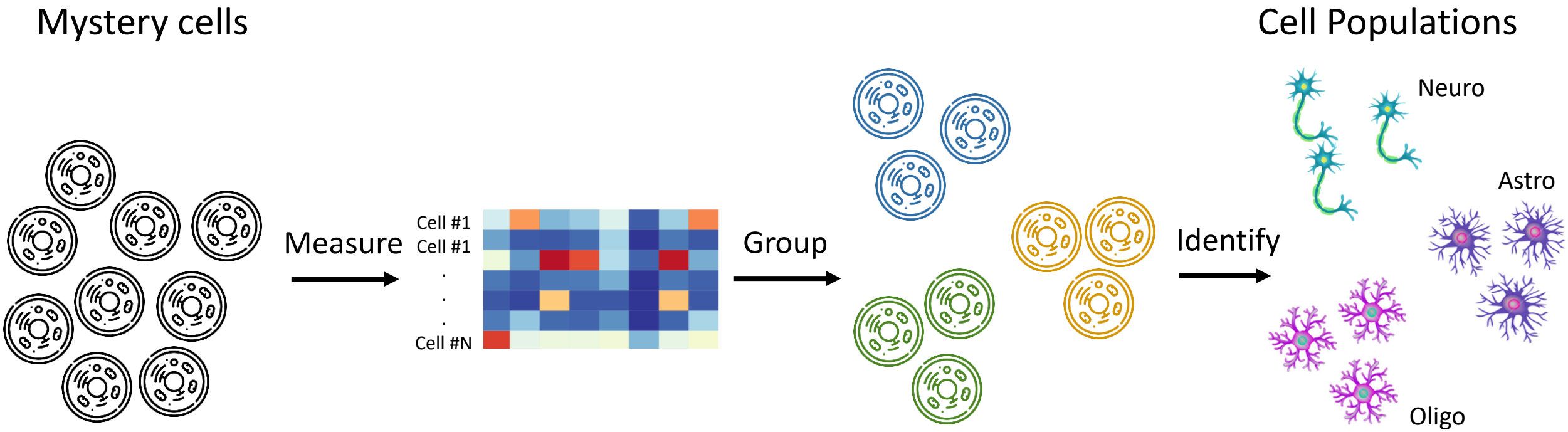


Spatial context

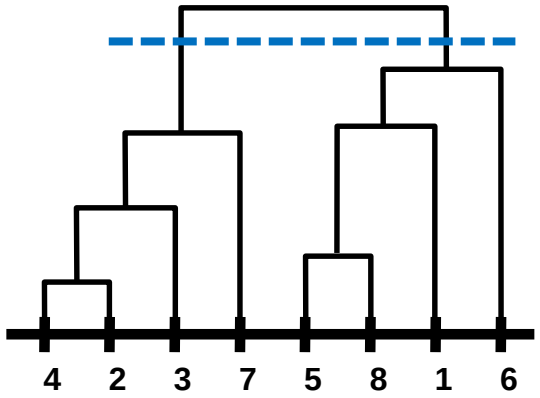


Wagner et al. (https://doi.org/10.1038/nbt.3711)

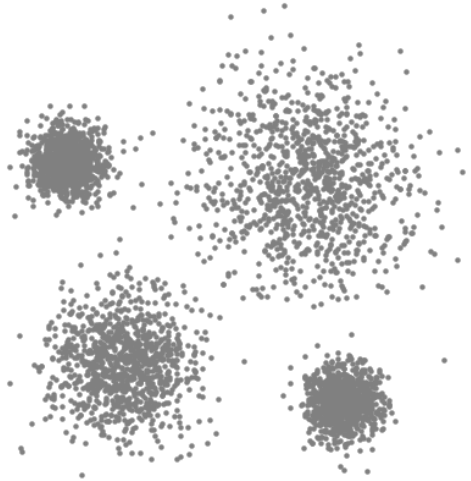
How can we identify cell populations?



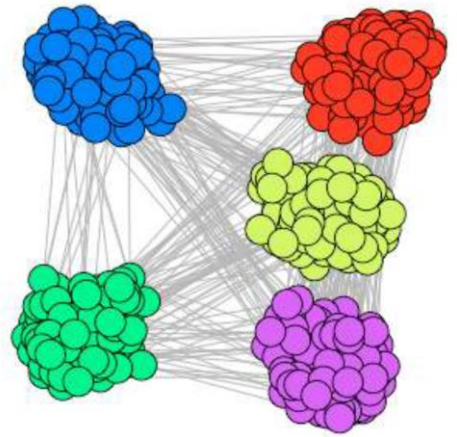
Many clustering approaches



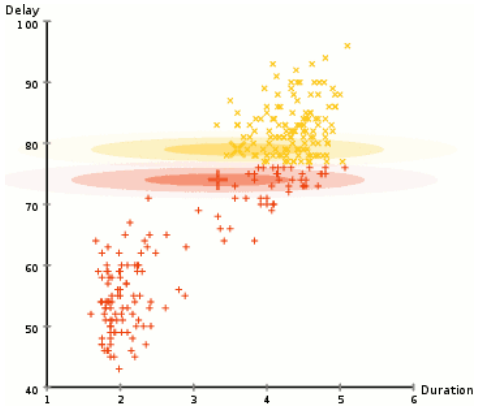
Hierarchical Clustering



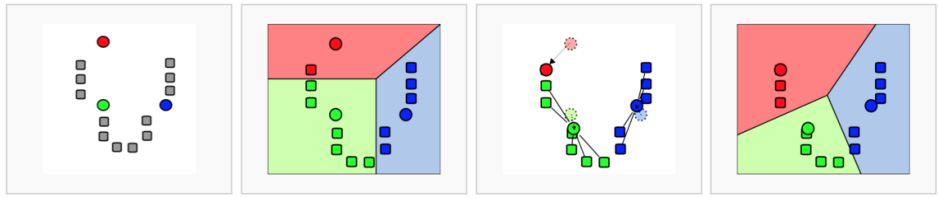
Mean shift clustering



Graph-based clustering



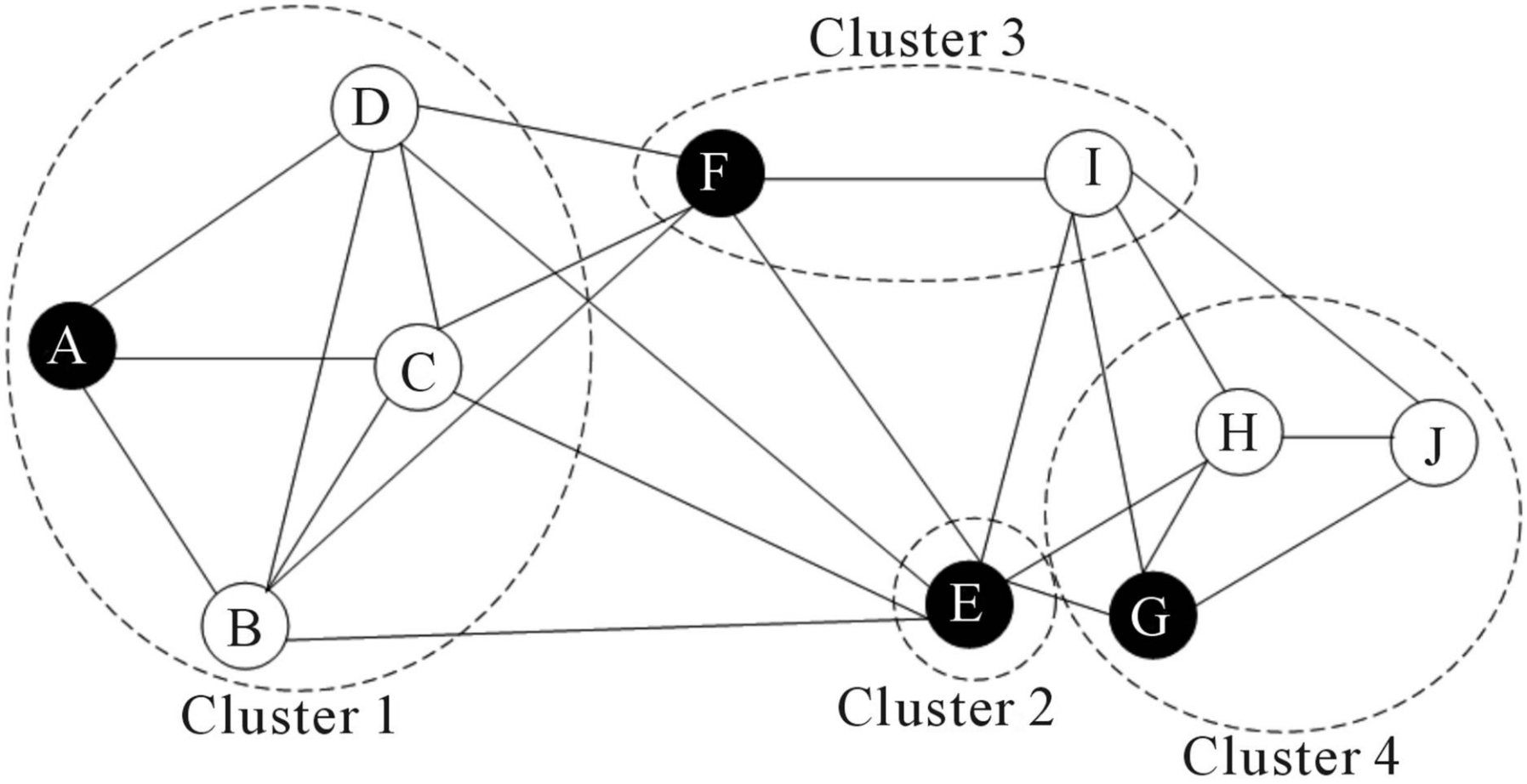
Gaussian mixture modeling



k-means clustering

Graph-based clustering

Nodes -> cells
Edges -> similarity



Graph Types

- **k-Nearest Neighbor (kNN) graph**

A graph in which two vertices *p* and *q* are connected by an edge, if the distance between *p* and *q* is among the *k*-th smallest distances from *p* to other objects from *P.*

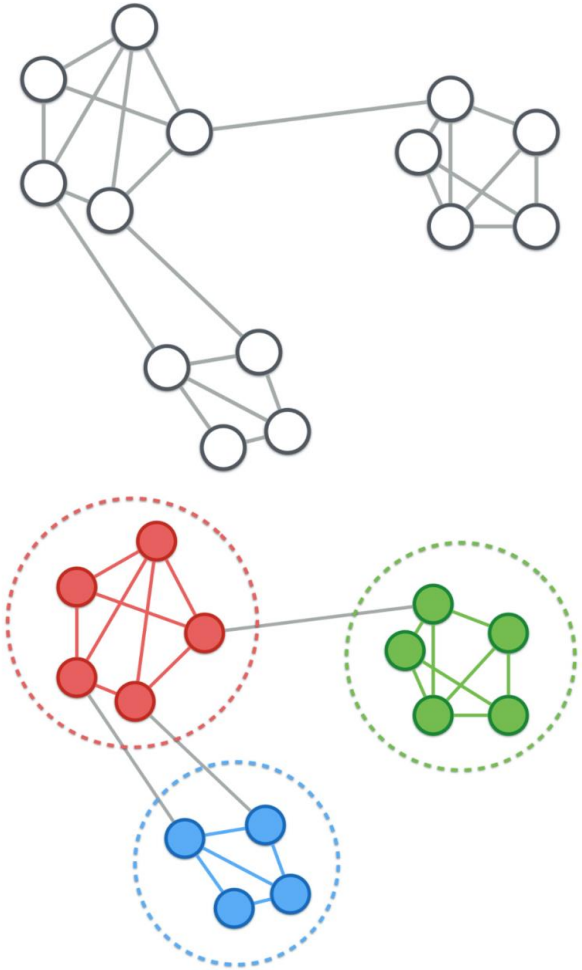
- **Shared Nearest Neighbor (SNN) graph**

A graph in which weights define proximity, or similarity between two nodes in terms of the number of neighbors (i.e., directly connected nodes) they have in common.

Graph clustering (Community detection)

- **Community detection:** find a group (community) of nodes with more edges inside the group than edges linking nodes of the group with the rest of the graph.

- Algorithms for community detection:
  - Spectral clustering
  - Louvain
  - Markov clustering
  - …



scRNA-seq clustering methods

Name	Year	Method type	Strengths	Limitations
scanpy[4]	2018	PCA + graph-based	Very scalable	May not be accurate for small data sets
Seurat (latest)[3]	2016			
PhenoGraph[32]	2015			
SC3 (REF.[22])	2017	PCA + *k*-means	High accuracy through consensus, provides estimation of *k*	High complexity, not scalable
SIMLR[24]	2017	Data-driven dimensionality reduction + *k*-means	Concurrent training of the distance metric improves sensitivity in noisy data sets	Adjusting the distance metric to make cells fit the clusters may artificially inflate quality measures
CIDR[25]	2017	PCA + hierarchical	Implicitly imputes dropouts when calculating distances	
GiniClust[75]	2016	DBSCAN	Sensitive to rare cell types	Not effective for the detection of large clusters
pcaReduce[27]	2016	PCA + *k*-means + hierarchical	Provides hierarchy of solutions	Very stochastic, does not provide a stable result
Tasic et al.[28]	2016	PCA + hierarchical	Cross validation used to perform fuzzy clustering	High complexity, no software package available
TSCAN[41]	2016	PCA + Gaussian mixture model	Combines clustering and pseudotime analysis	Assumes clusters follow multivariate normal distribution
mpath[45]	2016	Hierarchical	Combines clustering and pseudotime analysis	Uses empirically defined thresholds and a priori knowledge
BackSPIN[26]	2015	Biclustering (hierarchical)	Multiple rounds of feature selection improve clustering resolution	Tends to over-partition the data
RaceID[23], RaceID2 (REF.[115]), RaceID3	2015	*k*-Means	Detects rare cell types, provides estimation of *k*	Performs poorly when there are no rare cell types
SINCERA[5]	2015	Hierarchical	Method is intuitively easy to understand	Simple hierarchical clustering is used, may not be appropriate for very noisy data
SNN-Cliq[80]	2015	Graph-based	Provides estimation of *k*	High complexity, not scalable

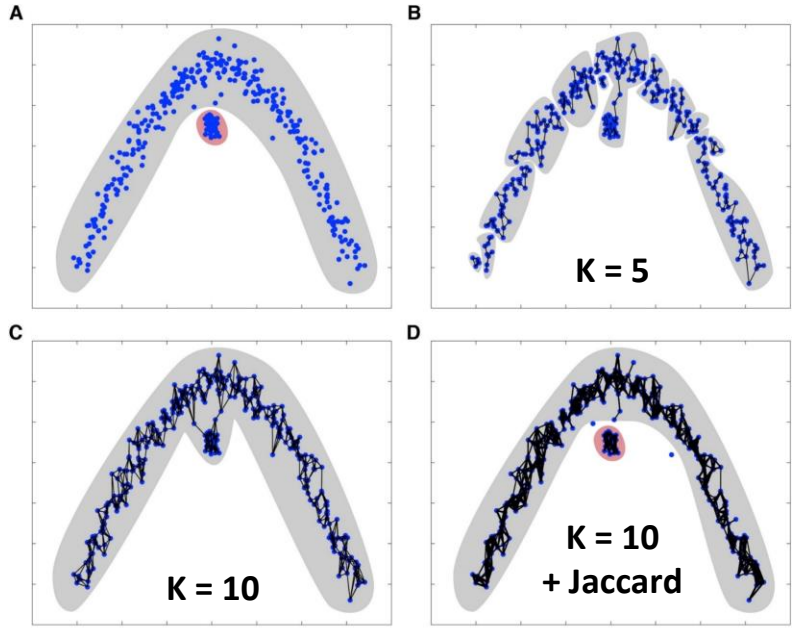
Kiselev et al. (https://doi.org/10.1038/s41576-018-0088-9)

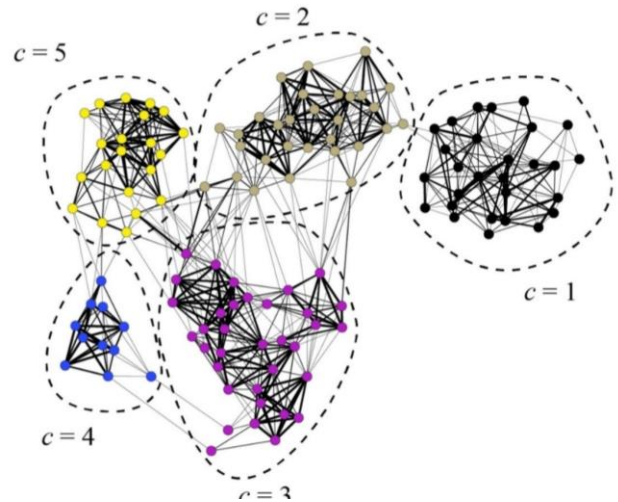
Seurat

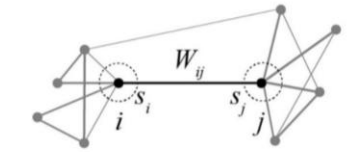
1) Construct KNN (k-nearest neighbor) graph based on the Euclidean distance in PCA space.

2) Refine the edge weights between any two cells based on the shared overlap in their local neighborhoods (Jaccard distance).

3) Cluster cells by optimizing for modularity (Louvain algorithm)



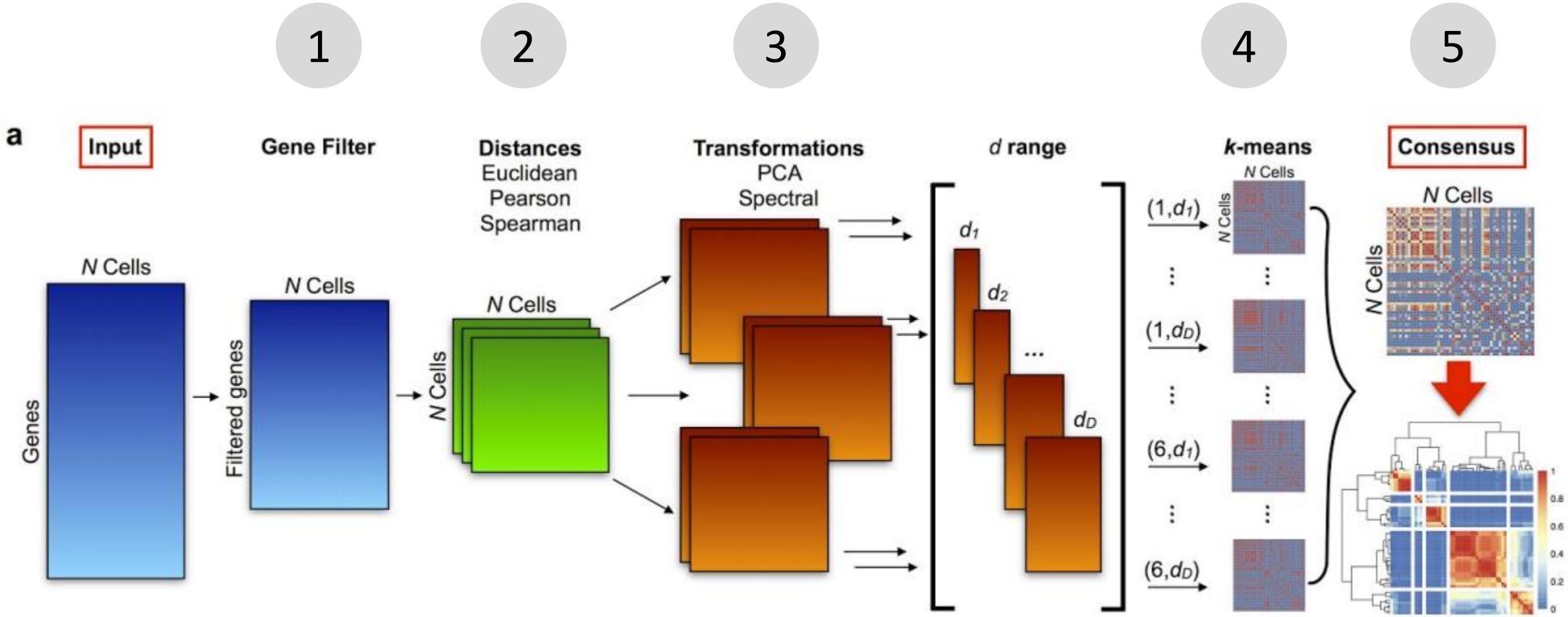




$$Q = \frac{1}{2m}\sum_{i,j}\left[W_{ij} - \frac{s_i s_j}{2m}\right]\delta(c_i, c_j)$$

Xu and Su (https://doi.org/10.1093/bioinformatics/btv088)
Levine et al. (https://doi.org/10.1016/j.cell.2015.05.047)

Single Cell Consensus Clustering – SC3



Kiselev et al. (https://doi.org/10.1038/nmeth.4236)

Single Cell Consensus Clustering – SC3

1) Gene filtering – rare and ubiquitous genes

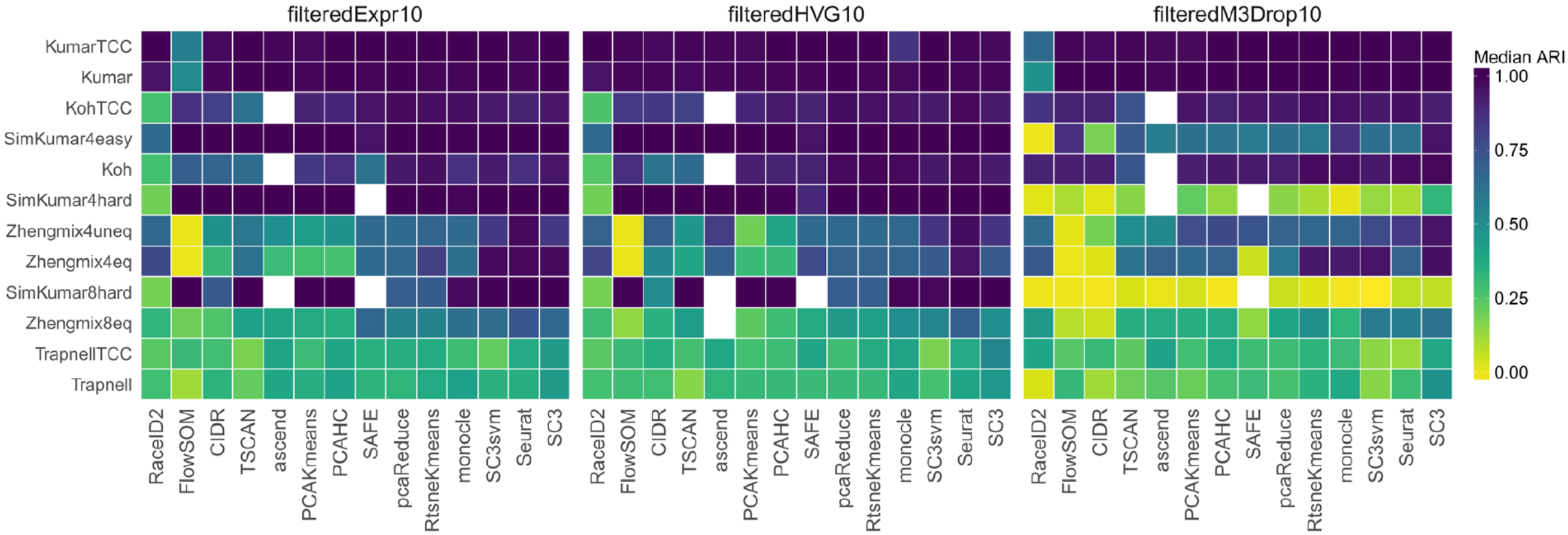
2) Distance matrices (DM) – Euclidean, Spearman, Pearson

3) Transformation of DM with PCA or Laplacian

4) K-means clustering with first *d* eigenvectors

5) Consensus clustering – distance 1/0 for cells in same/different clusters -> hierarchical clustering on average distances.

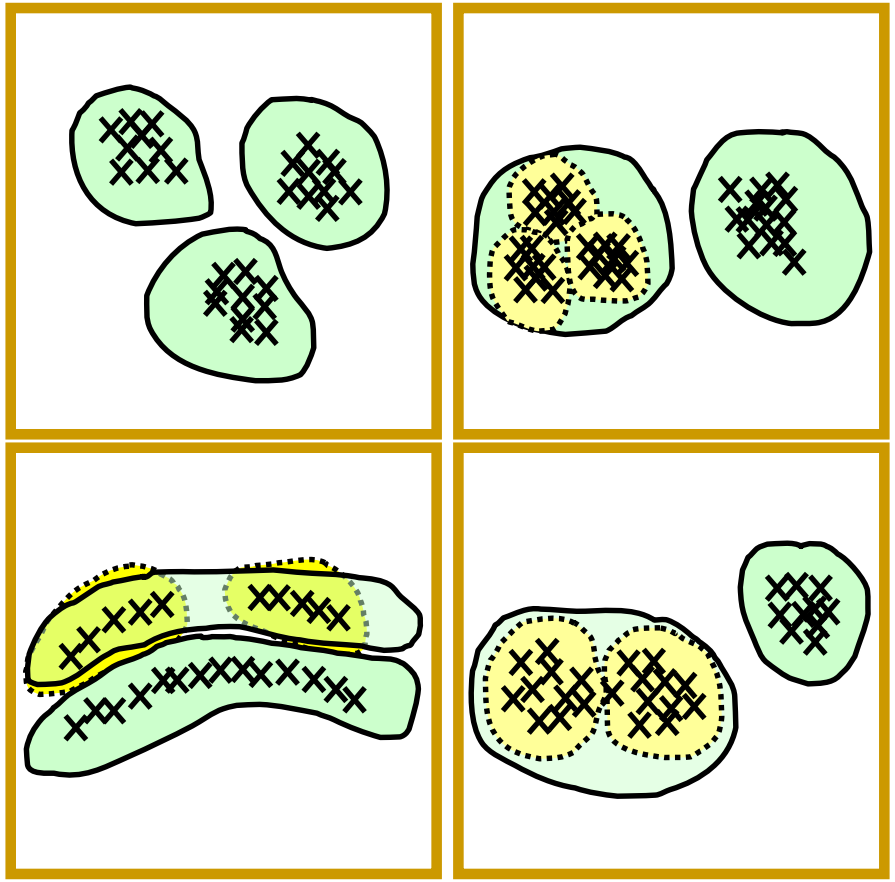
Benchmarking scRNA-seq clustering methods



Duò et al. (https://doi.org/10.12688/f1000research.15666.2)

Clustering is subjective!

- Principle choices
  - Similarity measure
  - Algorithm
- Different choice leads to different results
  - Subjectivity becomes reality
- Cluster process
  - Validate, interpret (generate hypothesis), repeat steps



How many clusters do you really have?

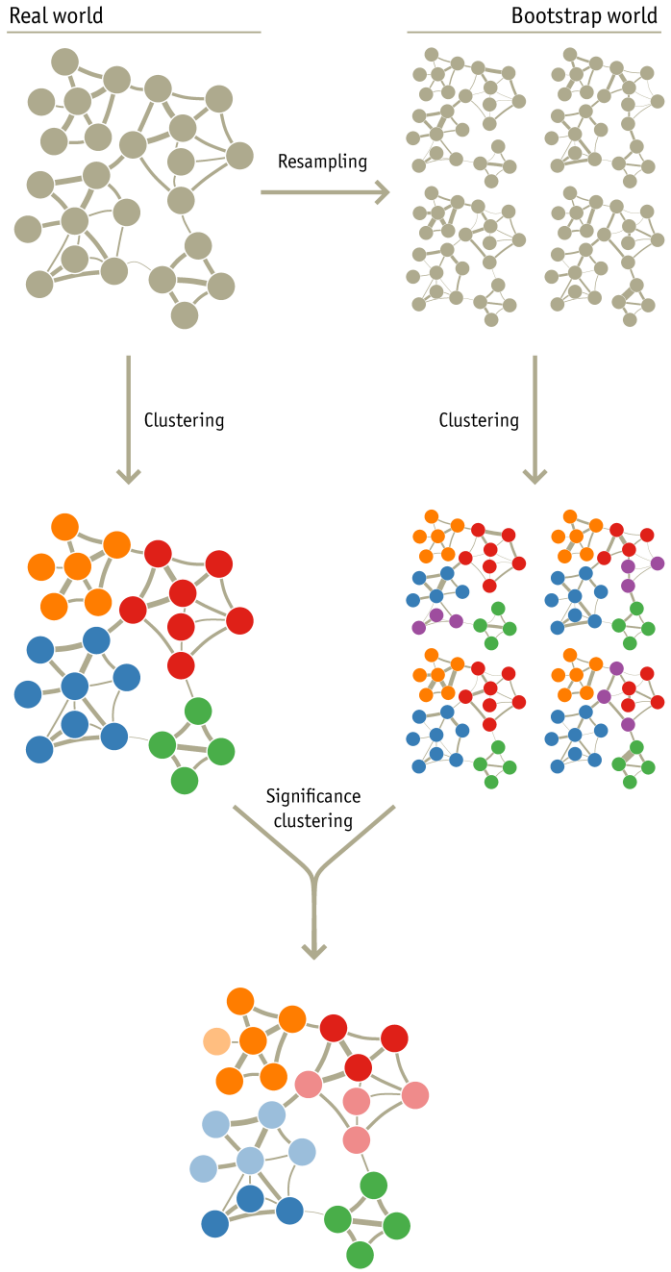
- It is hard to know when to stop clustering – you can always split the cells more times.

- Can use:
  - Do you get any/many significant DE genes from the next split?
  - Some tools have automated predictions for number of clusters – may not always be biologically relevant

Bootstrapping

- How confident can you be that the clusters you see are real?

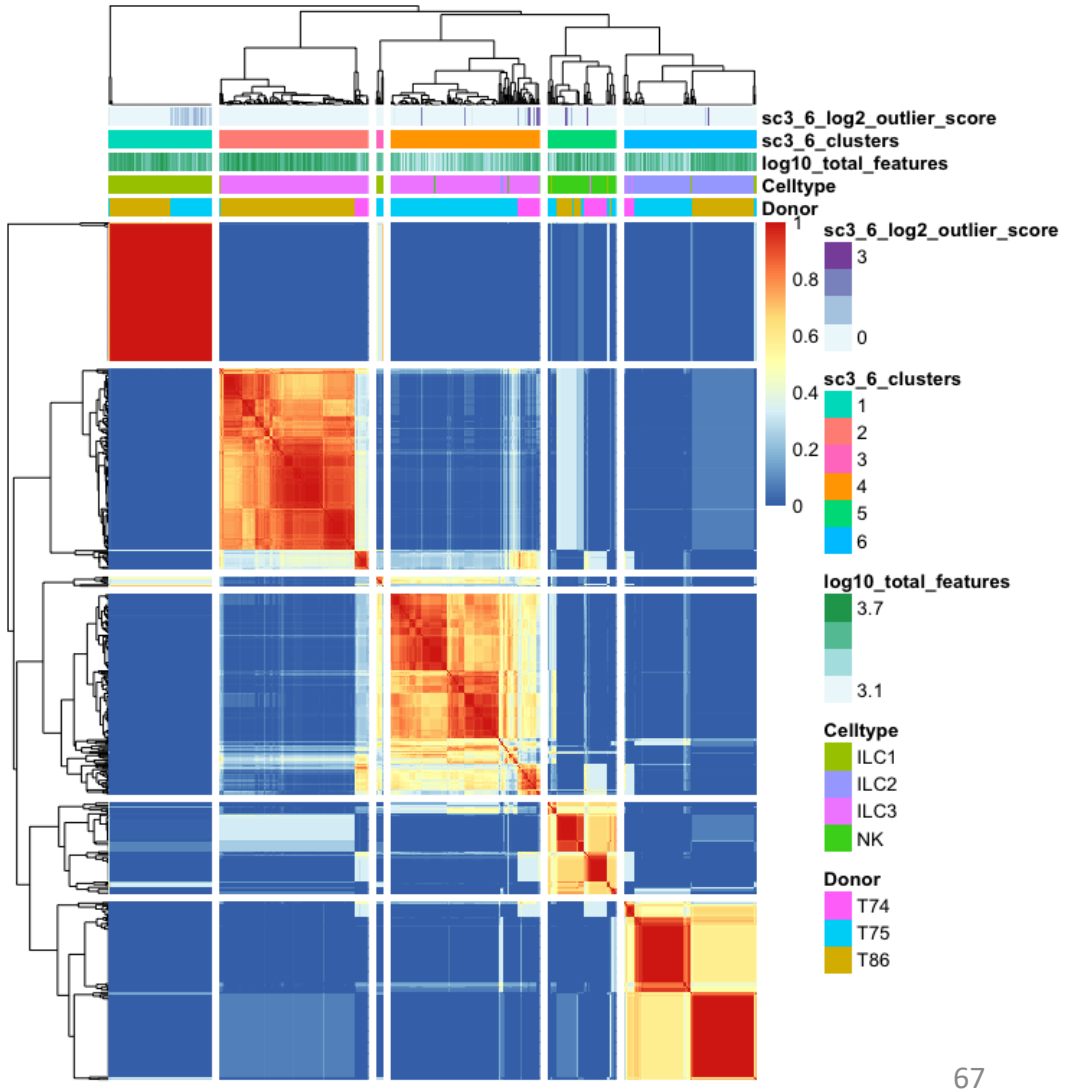
- You can always take a random set of cells from the same cell type and manage to split them into clusters.



Rosvall and Bergstrom (https://doi.org/10.1371/journal.pone.0008694)

Always check QC data

- Is what your splitting mainly related to batches, qc-measures (especially detected genes)?



From clusters to cell identities

- Using lists of DE genes and prior knowledge of the biology

- Using lists of DE genes and comparing to other scRNAseq data or sorted cell populations

Databases with celltype gene signatures

- PanglaoDB (https://panglaodb.se/)
  - Human: 295 samples, 72 tissues, 1.1 M cells
  - Mouse: 976 samples, 173 tissues, 4 M cells
  - Franzén et al (https://doi.org/10.1093/database/baz046)

- CellMarker (http://biocc.hrbmu.edu.cn/CellMarker/)
  - Human: 13,605 cell markers of 467cell types in 158 tissues
  - Mouse: 9,148 cell makers of 389 cell types in 81 tissues
  - Zhang et al. (https://doi.org/10.1093/nar/gky900)

Challenges in clustering

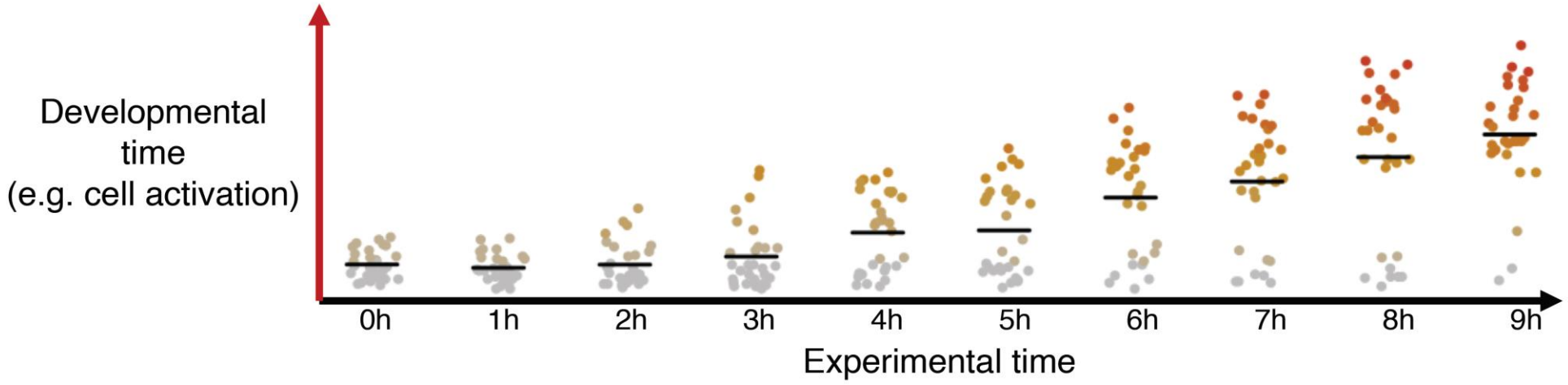
- What is a cell type?
- What is the number of clusters *k*?
- **Scalability**: in the last few years the number of cells in scRNA-seq experiments has grown by several orders of magnitude from ~10^2 to ~10^6

What is trajectory inference / pseudotime?

- Cells that differentiate display a continuous spectrum of states

- Individual cells will differentiate in an unsynchronized manner

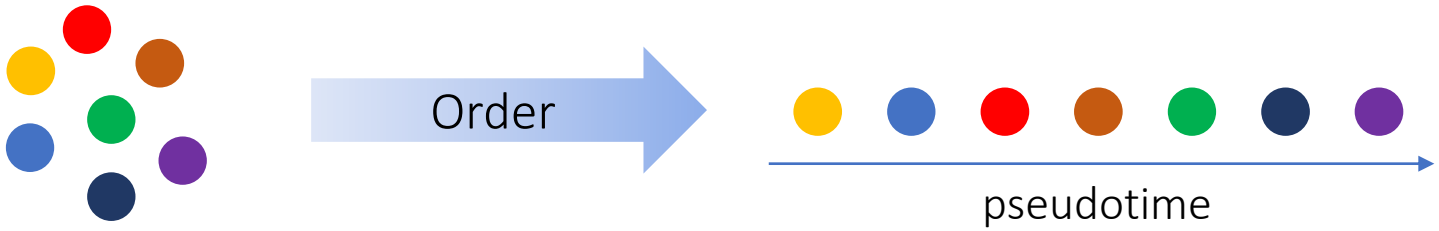
  -> Each cell is a snapshot of differentiation time



Trajectory Inference

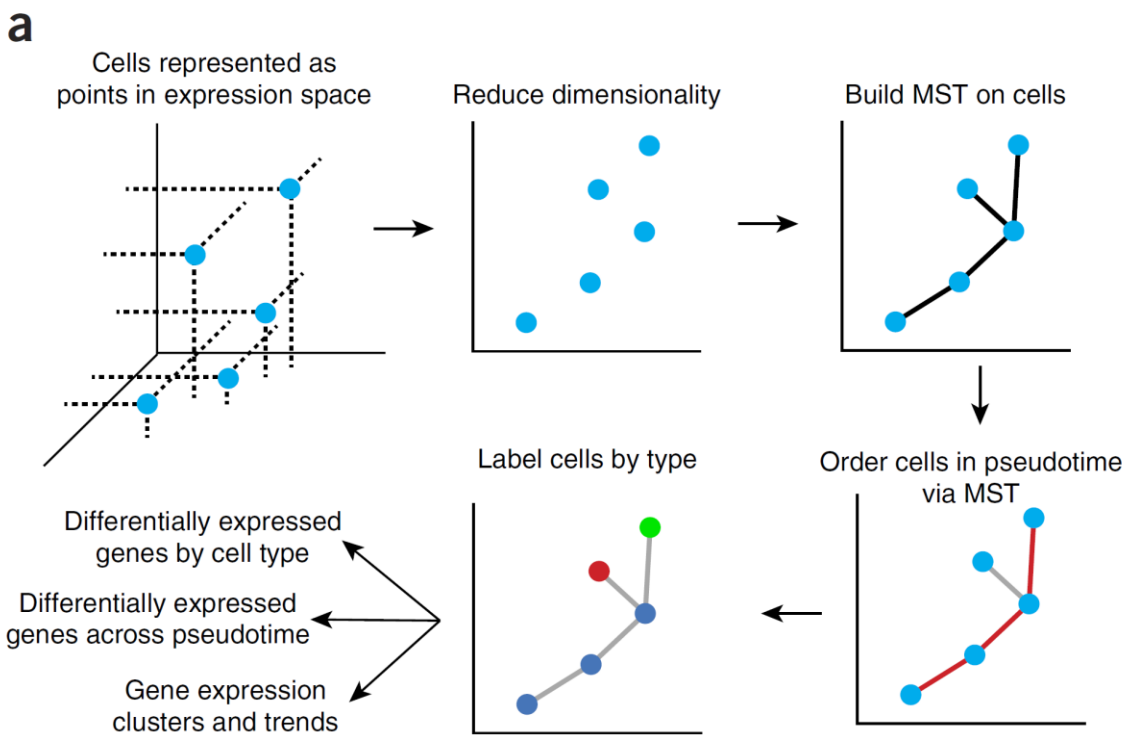
- Pseudotime: artificial measure of a cell's progression through some process (e.g. differentiation) from scRNA-seq snapshot data

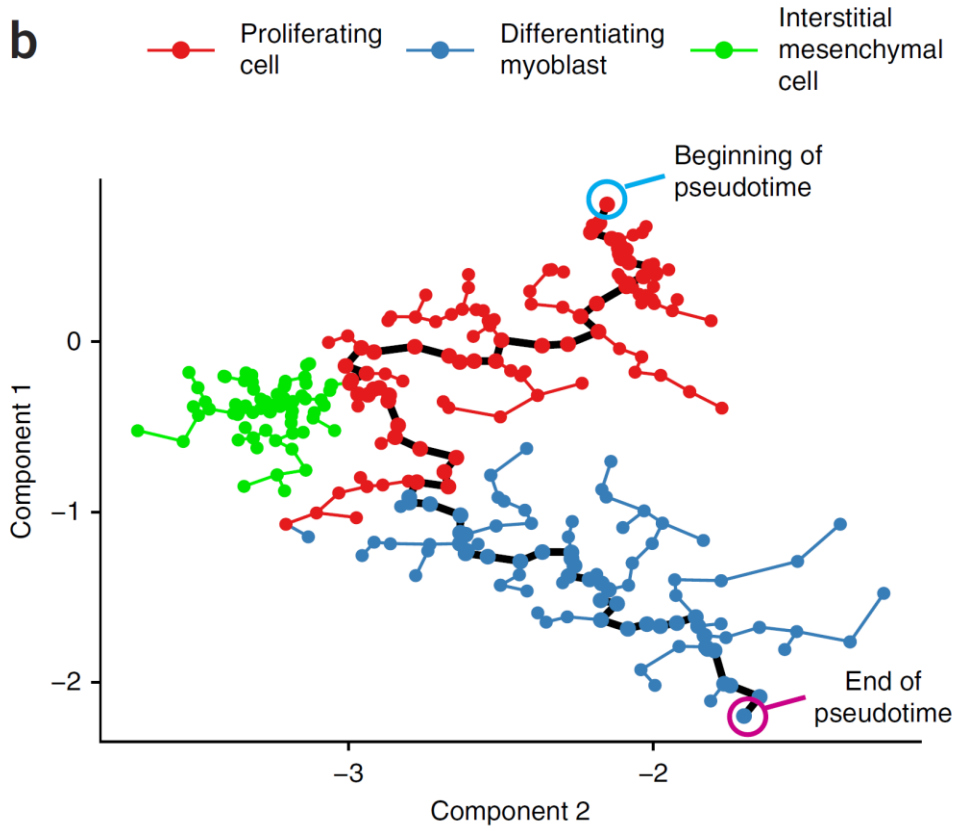
- Key assumptions:
  - continuity of transcriptome changes
  - presence of all intermediate cell stages



Monocole

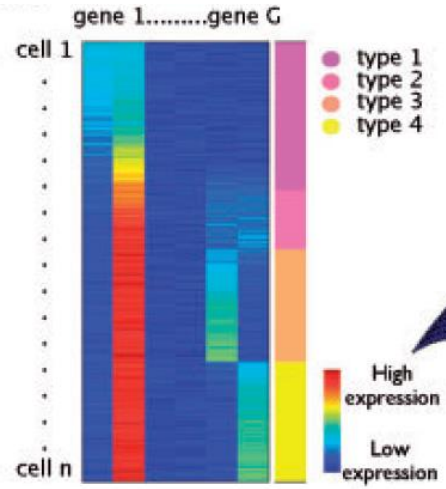
(v1 based on minimum spanning trees)



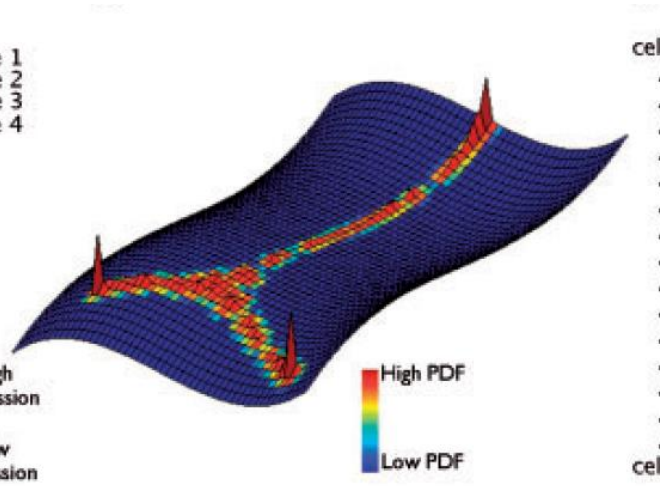


Trapnell et al., Nature Biotech 2014

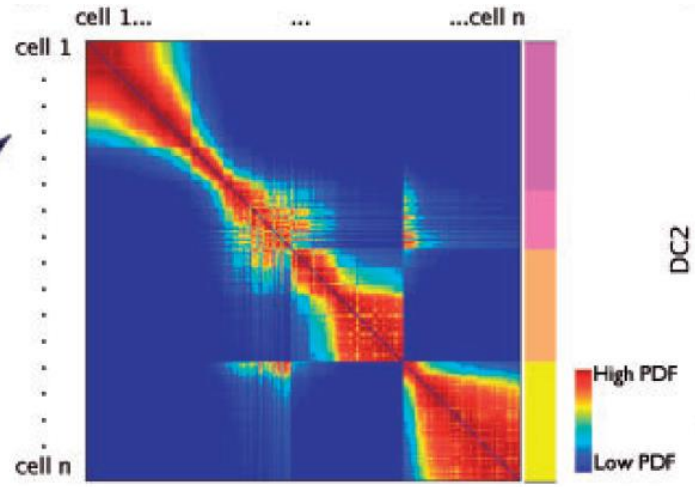
Diffusion Maps



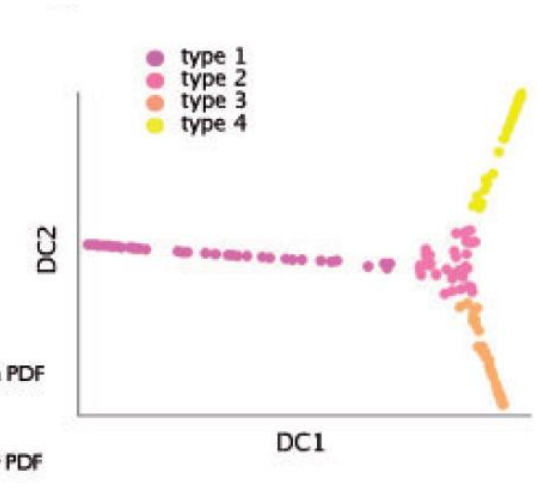
Cell X Gene matrix



Representation of each cell by a Gaussian in the G-dimensional gene space



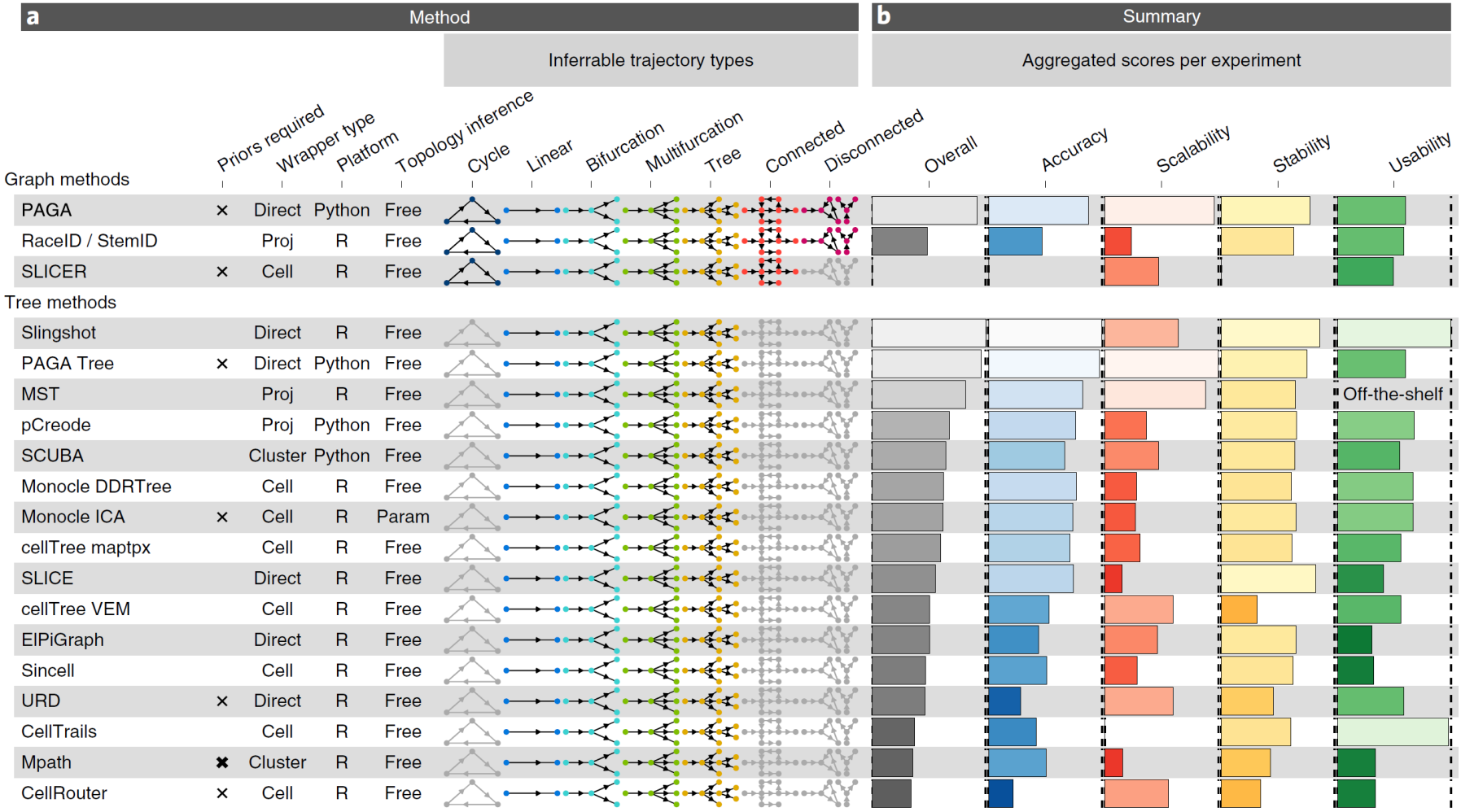
Cell X Cell Markovian transition probability matrix



Data embedding on the first two eigenvectors of the Markovian transition matrix

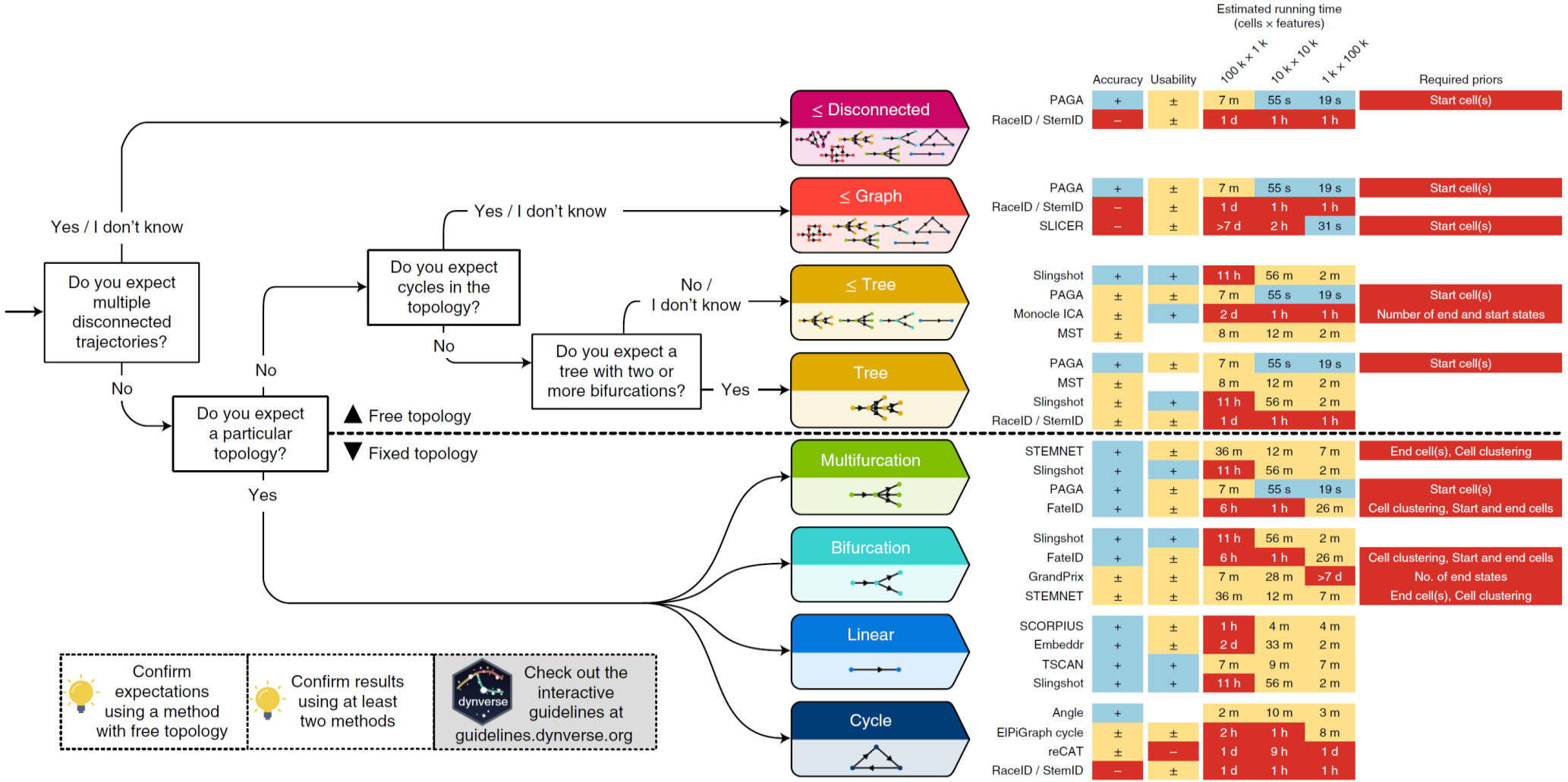
Haghverdi et al., Bioinformatics 2015

Trajectory inference methods



Saelens et al (2019) Nat Biotechnology; http://guidelines.dynverse.org

Trajectory inference methods



Saelens et al (2019) Nat Biotechnology; http://guidelines.dynverse.org

Summary

- Brief introduction to single cell RNA-sequencing

- Analysis workflow:
  - Quality control
  - Normalization
  - Feature selection
  - Dimensionality reduction
  - Clustering
  - Trajectory inference

There is more to it…

- Constructing the cell x gene matrix
- Batch correction methods
- Automatic cell type identification (classification methods)
- Single cell regulatory networks
- Imputation
- Single cell multi-omics
- Sample multiplexing
- Single cell isoform sequencing
- Cell lineage + scRNA-seq
- Spatial transcriptomics
- …

Useful Resources

- Best practices in single cell RNA-seq analysis (Luecken & Theis, MSB 2019)

https://www.embopress.org/doi/pdf/10.15252/msb.20188746

- Orchestrating Single-Cell Analysis with Bioconductor

https://osca.bioconductor.org/

- Single Cell Course (Martin Hemberg Lab, Welcome Trust Sanger):

http://hemberg-lab.github.io/scRNA.seq.course

- Aaron Lun's single cell workflow (very detailed):

https://www.bioconductor.org/packages/release/workflows/html/simpleSingleCell.html

- GitHub: Awesome Single Cell

https://github.com/seandavi/awesome-single-cell

- Recent developments in single cell genomics

https://www.dropbox.com/s/woya6ffgq8a3pkw/SingleCellGenomcisDay18_References.pdf?dl=1

Practical session

https://github.com/ahmedmahfouz/BioSB-Statistics-for-Omics-2019

Part A

- Quality control
- Normalization
- Feature selection

Part B:

- Dimensionality reduction
- Clustering

Thank You

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ANNOUNCEMENT

MGC course ' **Single Cell analysis** '
Date: **14 – 18 October, 2019**
Location: Erasmus MC
Registration: https://forms.lumc.nl/lumc2/RegistrationSingleCell
More information