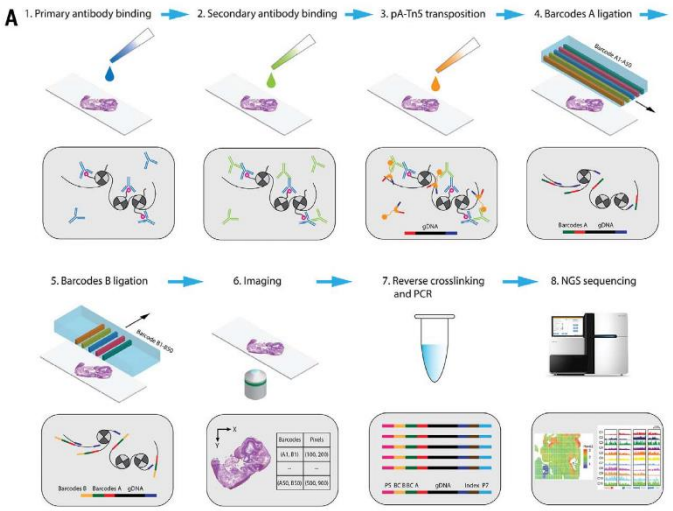
Single Cell Transcriptomics

Newsletter March 2022

Paper 1

Deng, Y *et al*. Spatial-CUT&Tag: Spatially resolved chromatin modification profiling at the cellular level *Science, 2022 Feb.*

Here the authors present spatial-CUT&Tag (cleavage under targets and tagmentation), a spatially resolved profiling of histone modifications (20-µm pixel size), by combining in situ CUT&Tag chemistry, microfluidic deterministic barcoding, and next-generation sequencing. The workflow is depicted in Fig A. They applied the technique to embryonic mouse brain and could identify cell types and spatial distinct patterns that agreed with the tissue histology. They calculate for example gene activity scores, transcription factor motif enrichments and analyzed Gene Ontology pathways. They were able to integrate their special CUT&Tag data with scRNA-seq data to retrieve more information about cell-types. They claim that a spatial multiomics approach is feasible by combining reagents for DBiT-seq and spatial-CUT&Tag.



Paper 2

Lotfollahi, M *et al.* Biologically informed deep learning to infer gene program activity in single cells *bioRxiv, 2022 Feb.*

Advances in experimental and computational single-cell genomic tools leads to large-scale atlases with million of cells. These serve as references for newly generated data sets that need to be integrate thereby facilitating their analysis and intrepretation. This integration known as referenc mapping is a computational challenge and in this paper a new tool called *expiMap (“explainable programmable mapper”)* is presented which makes the reference mapping more biological interpretable. *expiMap* uses known or newly learned gene programs (GPs) to answer questions as for example which GPs are disturbed in a disease query data compared to the healthy reference or which biological programs explain a novel cell-type in the query data. They applied the new tool to for example data of severe COVID-19 patients and could unreveal the role of annexins in the cellular communication between lymphoid and myeloid compartments for explaining patient response to the applied drugs.

Paper 3

Mitchel, J *et al.* Tensor decomposition reveals coordinated multicellular patterns of transcriptional variation that distinguish and stratify disease individuals *bioRxiv, 2022 Feb.*

Recent advances in sample multiplexing allow us to collect population-scale scRNAseq data sets of tens to hundreds of samples. Here it would be interesting to look at co-variation of cell states across samples, because biological processes at tissue- and organism-level often involve coordinated action of multiple distinct cell types. Here the authors introduce a computational approach called single-cell Interpretable Tensor Decomposition (scITD). This method extracts "multicellular transcriptional patterns" that vary across different biological samples and can be used to stratify disease individuals (Fig 2). scITD uses an unsupervised technique - the Tucker tensor decomposition (similar to PCA but for an n-dimensional array). They applied the computational approach on PBMC dataset of 83 COVID-19 samples and 20 controls and could identified reproducible multicellular patterns that stratify patients by disease severity.

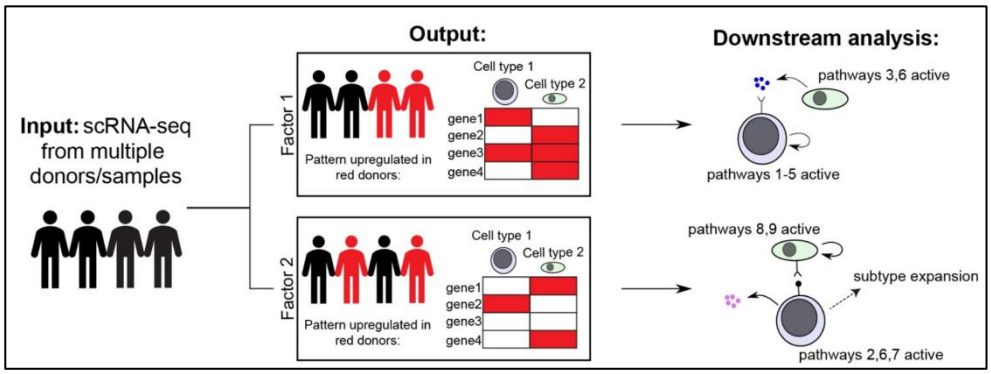


Figure 2) The tool takes clustered and annotated scRNA-seq data from multiple samples/donors as input. scITD then identifies multicellular patterns of gene expression that vary across the samples. These patterns can be further analyzed to reveal biological processes that are jointly active in multiple cell types.

Paper 4

Qiu, X *et al.* Mapping transcriptomic vector fields of single cells Cell, *2022 Feb*

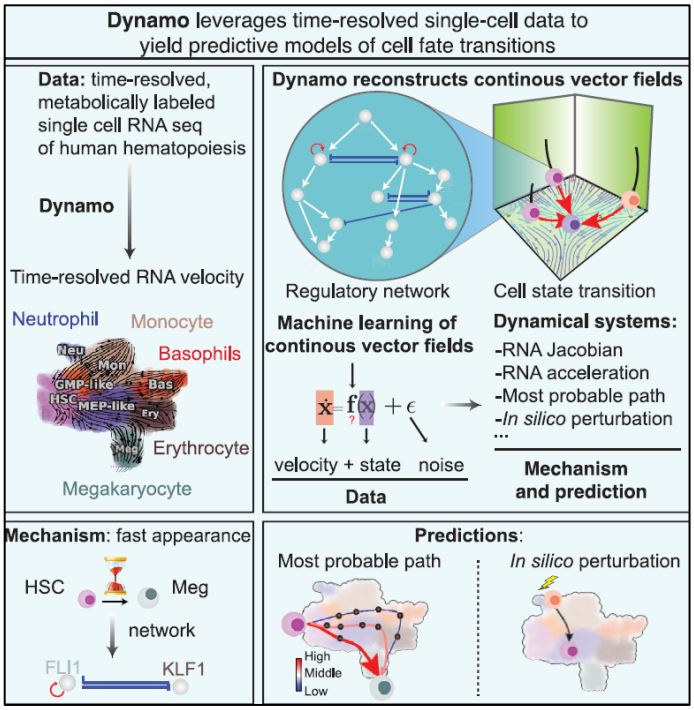


Figure 1) Summary overview.

The authors of this paper introduce the analytical framework *dynamo*. It uses scRNAseq data, together with RNA velocity and metabolic labeling to reveal cellular states and transitions. It consists of four steps: first they estimate RNA velocity vectors using the scRNAseq data set. Next, they use RNA abundance and velocity vectors to reconstruct the vector fields. They then apply differential geometry analyses made possible by the analytical vector field, thereby obtaining biological insights. Finally, they apply the LAP (least action paths) method and *in silico* perturbation to predict the optimal paths of cellular-state transitions and outcomes of genetic perturbations. They highlight dynamo's power to overcome fundamental limitations of conventional splicing-based RNA velocity analyses to enable accurate velocity estimations on a metabolically labeled human hematopoiesis scRNA-seq dataset.

Next Single Cell Seminar

Next seminar will take place by Jeffrey Moffitt, Harvard Medical School on 24th March 2022.
Details will be announced via Email.

If you would like to announce anything single cell related, being it job announcement, event, your published paper, technology development etc, please contact us.

Contact: laura.wolbeck@bric.ku.dk