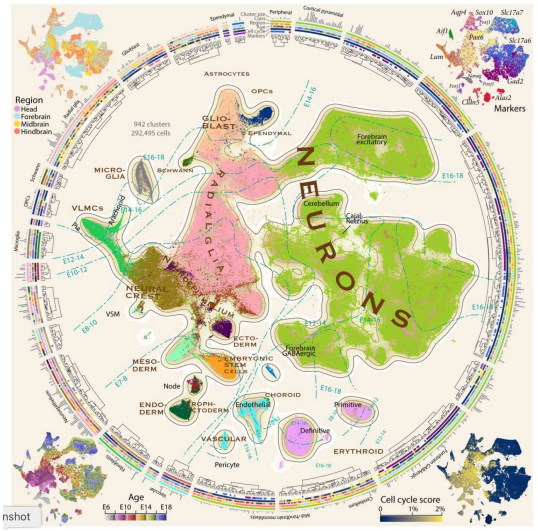
Single Cell Transcriptomics

Newsletter August 2020

Paper 1

La Manno G. et al. [Molecular architecture of the developing mouse brain](), *bioRxiv, 2020.*

In this preprint, Sten Linnarson's lab report a comprehensive single-cell transcriptome atlas of mouse brain development nervous system, spanning from gastrulation to birth. They collected embryonic brain tissue from 43 pregnant CD-1 mice, sampling each day from E7 to E18 resulting in almost 300.000 cells with an average over 5000 genes per cell.



They revealed almost a thousand different cell types, however, in the tSNE plot they show that cells were organized primarily by gestational age, branching to show the major lineages originating from the neuroepithelium. A large connected component — representing the neural tube and its derivatives — was surrounded by disconnected islets of microglia, erythrocytes, and vascular cells, none of which are derived from the neuroepithelium. They also resolve lineage-specific gene expression programs, using a pseudolineage algorithm that provides a tool to investigate gene expression along putative lineage trajectories leading to specific end states.

The wealth of information on time-, lineage-, and region-specific gene expression provides powerful tools for genetic targeting, and for understanding genes involved in neurodevelopmental disorders.

Don's miss the interactive version of figure 1: **http://mousebrain.org/development/**

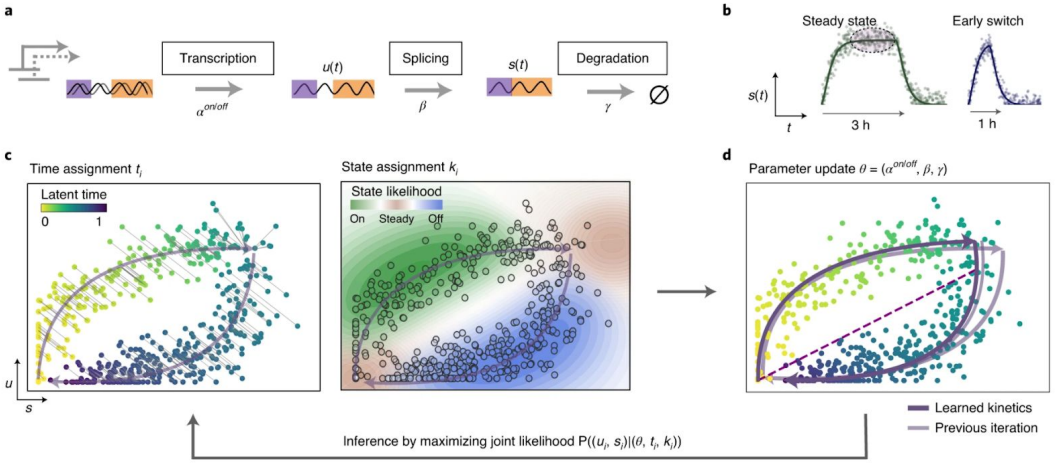
Paper 2

Bergen V. et al. [Generalizing RNA velocity to transient cell states through dynamical modeling.]() *Nat Biotechnol, 2020.*

RNA velocity is a powerful tool to study cellular differentiation as it describes the rate of gene expression change for an individual gene at a given time point based on the ratio of its spliced and unspliced mRNA. Positive RNA velocity indicates that a gene is upregulated, which occurs for cells that show higher abundance of unspliced mRNA for that gene than expected in steady state. Conversely, negative velocity indicates that a gene is downregulated. The combination of velocities across genes can then be used to estimate the future state of an individual cell.

The original model, published in 2018 by La Manno et al. estimates velocities under the assumption that (1) on the gene level, the full splicing dynamics with transcriptional induction, repression and steady-state mRNA levels are captured; and (2), on the cellular level, all genes share a common splicing rate and it has been shown that this is not the case when a population comprises multiple heterogeneous subpopulations with different kinetics.

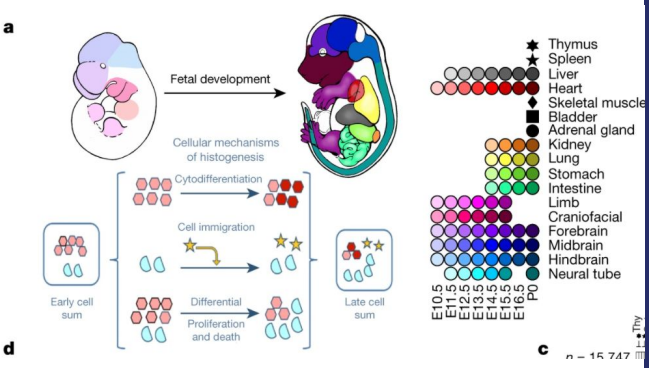
In this study, Theis lab developed scVelo, an excellent improvement on algorithms for estimating RNA velocity of single cells, including several new features such as differential kinetics and a user-friendly software package. They applied this dynamical model on various cell lineages in hippocampal dentate gyrus neurogenesis and pancreatic endocrinogenesis.



Paper 3

He P. et al [.The changing mouse embryo transcriptome at whole tissue and single-cell resolution.]() *Nature*, *2020*.

To study mammalian embryogenesis and as part of the ENCODE Consortium mouse embryo project, (which provides companion genome-wide microRNA, DNA methylation, histone mark, and chromatin accessibility datasets for the same sample matrix), researchers from the California Institute of Technology systematically quantified mouse polyA-RNA from day 10.5 of embryonic development to birth, sampling 17 tissues and organs.



The resulting developmental transcriptome is globally structured by dynamic cytodifferentiation, body-axis and cell-proliferation gene sets that were further characterized by the transcription factor motif codes of their promoters.

They found that neurogenesis and haematopoiesis dominate at both the gene and cellular levels, jointly accounting for one-third of differential gene expression and more than 40% of identified cell types. Moreover, using different bioinformatic tools they identify cluster-specific regulatory mechanisms, cis- and trans- acting cell type TF networks and lineage progression.

Paper 4

Bernstein N. et al. [Solo: Doublet Identification in Single-Cell RNA-Seq via Semi-Supervised Deep Learning]()
Cell systems, 2020.

In single-cell RNA sequencing experiments, doublets are artifactual libraries generated from two cells. They typically arise due to errors in cell sorting or capture, especially in droplet-based protocols involving thousands of cells. Doublets can incorrectly suggest the existence of intermediate populations or transitory states that not actually exist so their elimination from the data set is crucial.

Here, Bernstein and collaborators describe Solo, a semi-supervised deep learning approach that identifies doublets with greater accuracy than existing methods. Solo embeds cells unsupervised using a variational autoencoder and then appends a feed-forward neural network layer to the encoder to form a supervised classifier.

Upcoming online events

Webinar: Simultaneous profiling of the transcriptome and epigenome at single cell resolution

20 August, 2020, 6 pm CET
Organized by 10x genomics

Workshop: Temporal Single Cell Analysis
15 September 2020, 2-6pm (CEST)
Organized by Single Cell Omics Germany

Next Single Cell Seminar

Single Cell Seminars will start again soon, in an online format.
Date to be announced.

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: andrea.asenjo@bric.ku.dk