Unravelling cell fate decisions through single cell methods and mathematical models

Mircea, M.

Propositions

accompanying the thesis

Unravelling Cell Fate Decisions through Single Cell Methods and Mathematical models

1. Cell types should be defined by the cell's RNA or protein composition and not by morphology or function alone. Not all RNA molecules or proteins are relevant for the definition of a cell type.

[Chapter 2 of this thesis.]

2. Endothelial cells remain plastic during development and actively change their transcriptional profile based on environmental cues.

[Chapter 4 of this thesis.]

3. Well-processed single-cell atlases of development assist with the classification of cell types in new data sets and help to bridge the gap between *in vivo* and *in vitro* studies.

[Chapter 5 of this thesis.]

4. Data-driven machine learning techniques alone cannot infer fundamental and causal relationships between genes. Mathematical equations have to be combined with machine learning techniques to obtain causal relationships of gene regulatory networks from data.

[Chapter 6 of this thesis.]

5. Mittnenzweig et al. suggest that during development, cell types arise through the combinatorial expression of transcription factors which lead to multi-furcations. This view aligns with the many genes necessary in single-cell RNA-seq data to distinguish a cell type. It is important to consider equally the up-regulated genes as well as the down-regulated genes.

[M. Mittnenzweig et al., "A single-embryo, single-cell time-resolved model for mouse gastrulation," Cell, vol. 184, pp. 1–18, Apr. 2021.]

6. Xia et al. suggest to sort cell types into a periodic table with distingued categories. However, continous transitions during development and small differences between cell types make it difficult to find discrete categories.

[B. Xia and I. Yanai, Dev., vol. 146, no. 12, Jun. 2019.]

7. Stanoev et al. present a two-gene network that can differentiate robustly into two cell types. However, this holds only for a very narrow parameter regime suggesting that biological processes must include more variables to ensure robustness.

[A. Stanoev et al., "Robustness and timing of cellular differentiation through population-based symmetry breaking," Development, vol. 148, no. 3, Feb. 2021.]

8. Tarazi et al. were able to generate nearly entire embryos *in vitro* and *ex-utero*. This research raises ethical concerns that should be considered already in animal studies before starting experiments in human.

[S. Tarazi et al., Cell, vol. 185, pp. 1–17, Aug. 2022.]

9. The publication pressure put on researchers decreases the value of individual papers. Having more time to work out a research question will increase the quality of research.

10. A large amount of available information forces researchers to find a very narrow niche for science. Nevertheless, there is common ground between fields that should be explored in collaborations and not ignored.

11. Creativity is a crucial skill in science that can be learned and should be promoted early in the research career.

Maria Mircea
Leiden, October 10, 2022