Universität Basel

Research Project

Inferring gene regulatory landscapes from single-cell omics data

Third-party funded project

Project title Inferring gene regulatory landscapes from single-cell omics data
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Organisation / Research unit
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Department
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In multi-cellular organisms such as animals and humans, a single genome sequence is expressed into a complex organization of hundreds of different cell types. Although it is well understood that this process is controlled by regulatory proteins that can switch genes on and off by binding to short sequences in the DNA, there is still an enormous gap in our understanding between experimentally determined lists of components on the one hand, and idealized mathematical models on the other hand.

In a major development, it has become possible over the last few years to experimentally quantitatively track the states of individual cells across tissues and embryos as they are developing, measuring how much each gene is expressed, the state of the DNA, which cells derived from the same ancestor cell, and so on. These methods promise to revolutionize our ability to understand the ways in which a single genome can be expressed into a complex organism.

However, there are many challenges on the way to realizing this promise. For example, single cell measurements are very noisy, with many missing values. Most importantly, it is currently unclear how the measured state of a single cell can be related to the actions of the regulatory proteins that guide the process. Therefore, novel computational methods are needed that allow bridging the gap between mathematical models and single-cell measurements.

The goals of the project are to develop new mathematical and computational methods for the analysis of genome-wide gene expression and DNA state measurements in single cells. In particular, we propose to develop new statistical models for carefully distinguishing true biological variability from measurement noise. Moreover, we propose to adapt a previously developed method for relating the measured state of a cell to the activities of regulatory proteins to be applied to single cells. The methods we propose should make it possible to precisely quantify the activities of regulatory proteins in single cells, and to map the landscapes that guide the states of cells.

The results of our work will consist of a suite of tools that can be used by researchers worldwide. Our project involves several collaborations with experimentalists at the forefront of developing these single cell measurements, and application of our methods to data generated in the labs will guide further refinement of our methods.

The methods we propose will make a major contribution to realizing the promise of single-cell methodologies for unraveling how a single genome is expressed into a complex multi-cellular organization. Understanding this will eventually have innumerable applications in human health and medicine.

Keywords single-cell RNA-seq, gene regulatory networks, computational systems biology
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Add publication

Published results

4619194, Breda, Jérémie; Zavolan, Mihaela; van Nimwegen, Erik, Bayesian inference of gene expression states from single-cell RNA-seq data, 1087-0156 ; 1546-1696, Nature Biotechnology, Publication: JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

4662521, de Groot, Daan H.; Tjalma, Age J.; Bruggeman, Frank J.; van Nimwegen, Erik, Effective bet-hedging through growth rate dependent stability, 0027-8424 ; 1091-6490, Proceedings of the National Academy of Sciences of the United States of America, Publication: JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

Add documents

Specify cooperation partners

ID	Kreditinhaber	Kooperationspartner	Institution	Laufzeit - von	Laufzeit - bis
2331193	van Nimwegen, Erik	Zavolan, Mihaela	Biozentrum, University of Basel	01.01.2000	31.12.2099
4663249	van Nimwegen, Erik	Rajewsky, Nikolaus	Max-Delbrueck center of molecular medicine	01.04.2019	31.12.2030
4663250	van Nimwegen, Erik	Schier, Alex	Biozentrum, University of Basel	01.04.2019	31.12.2030