

Perturb Seq

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March 18, 2017

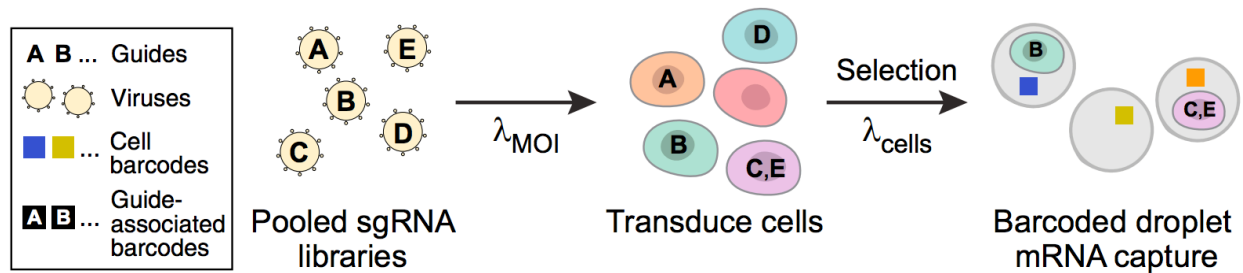


Figure 1: A graphical overview of the generalized linear model fit in Perturb-Seq analyses.

Introduction

In three recent papers published in the journal *Cell*, researchers at the Broad Institute, UCSF, and the Weizmann Institute described a new technology called Perturb-Seq, which integrates CRISPR-Cas9 genome editing and droplet-based single-cell RNA-Seq. **Figure 1** Additionally, a well-crafted Perturb-Seq experiment could enable the dissection gene regulation in the context of disease.

Basically they use CRISPRi to knockdown different genes in different cells, then examine the transcriptome outcome of the different knockdowns through single-cell RNA-seq. Very often after a genome-wide CRISPR screen, you often have many hits, so they can use CRISPRi to validate each hits and explore the mechanism of the KD effect. Although single-cell readout from Drop-Seq could be noisy, they sequence 500 cells per CRISPRi, so the average from the 500 should give a much more robust expression readout.

Where the stats are now

Links to the BST245 Course

Presentation Outline

- 0-6 minutes: discussion of CRISPR, scRNA-Seq, Drop-Seq, and requisite technological innovations as background
- 6-10 minutes: introduction of Perturb-Seq
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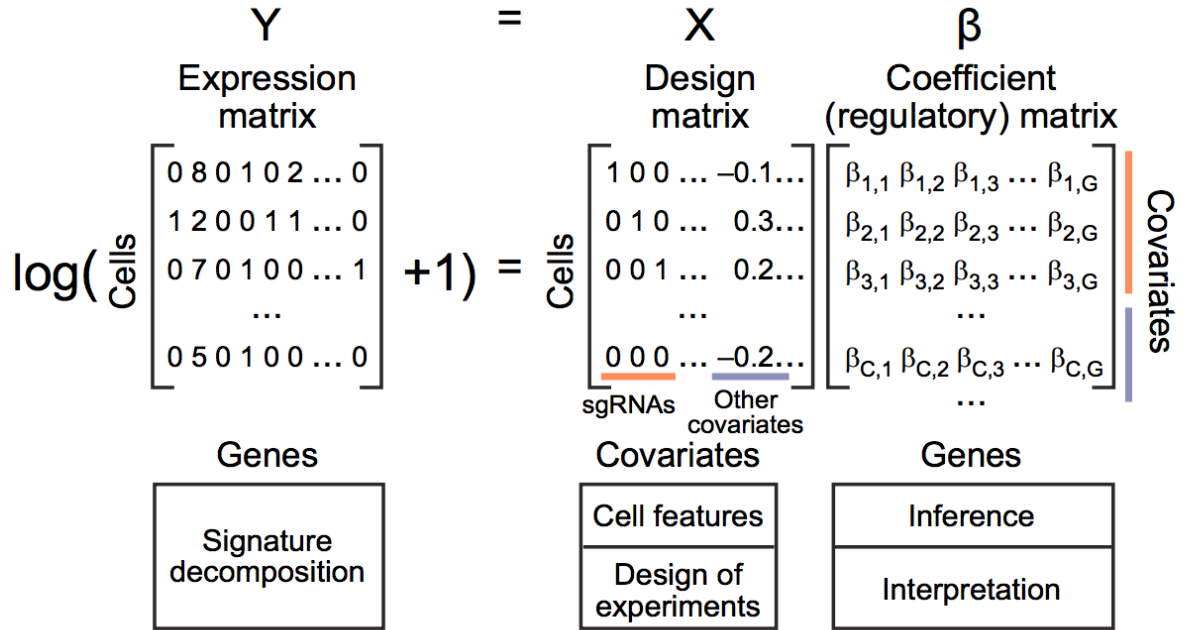


Figure 2: A graphical overview of the generalized linear model fit in Perturb-Seq analyses.

References

- Adamson, Britt, et al. "A multiplexed single-cell CRISPR screening platform enables systematic dissection of the unfolded protein response." *Cell* 167.7 (2016): 1867-1882.
- Dixit, Atray, et al. "Perturb-seq: dissecting molecular circuits with scalable single-cell RNA profiling of pooled genetic screens." *Cell* 167.7 (2016): 1853-1866.
- Jaitin, Diego Adhemar, et al. "Dissecting Immune Circuits by Linking CRISPR-Pooled Screens with Single-Cell RNA-Seq." *Cell* 167.7 (2016): 1883-1896.
- Wagner, Daniel E., and Allon M. Klein. "Genetic screening enters the single-cell era." *Nature Methods* 14.3 (2017): 237-238.