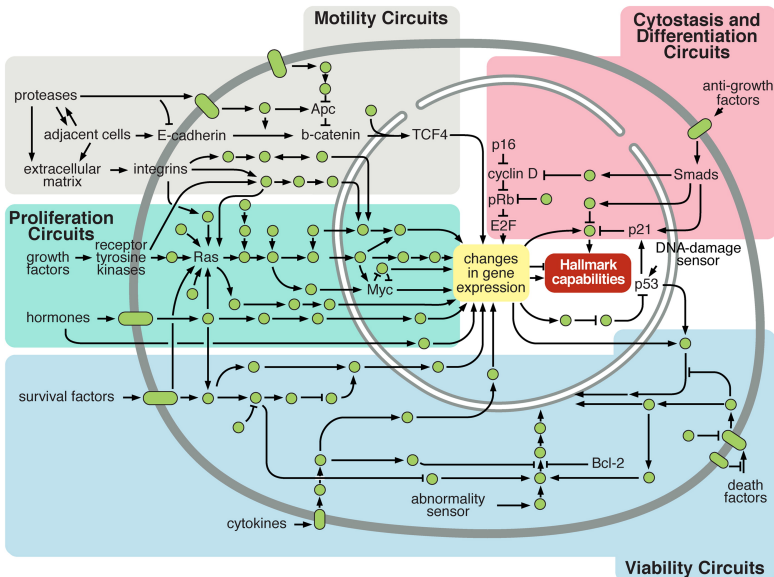


CS 5854: Single-Cell Gene Expression Analysis

T. M. Murali

To be scheduled, 2021

Signaling Pathways and Gene Expression



Gene Expression is a Dynamic Process

B

if (F = 1 or E = 1 or CD = 1) and (Z = 1) Repression functions of modules F, E, and DC mediated by Z site

$$\alpha = 1$$

else $\alpha = 0$

if (P = 1 and CG₁ = 1)

Both P and CG₁, needed for synergistic link with module B

$$\beta = 2$$

else $\beta = 0$

if (CG₂ = 1 and CG₃ = 1 and CG₄ = 1)

Final step up of system output

$$\gamma = 2$$

else $\gamma = 1$

$$\delta(t) = B(t) + G(t)$$

Positive input from modules B and G

$$\varepsilon(t) = \beta * \delta(t)$$

Synergistic amplification of module B output by CG₁-P subsystem

if ($\varepsilon(t) = 0$)

$$\xi(t) = Otx(t)$$

Switch determining whether Otx site in module A, or upstream modules (i.e., mainly module B), will control level of activity

else $\xi(t) = \varepsilon(t)$

if ($\alpha = 1$)

Repression function inoperative in endoderm but blocks activity elsewhere

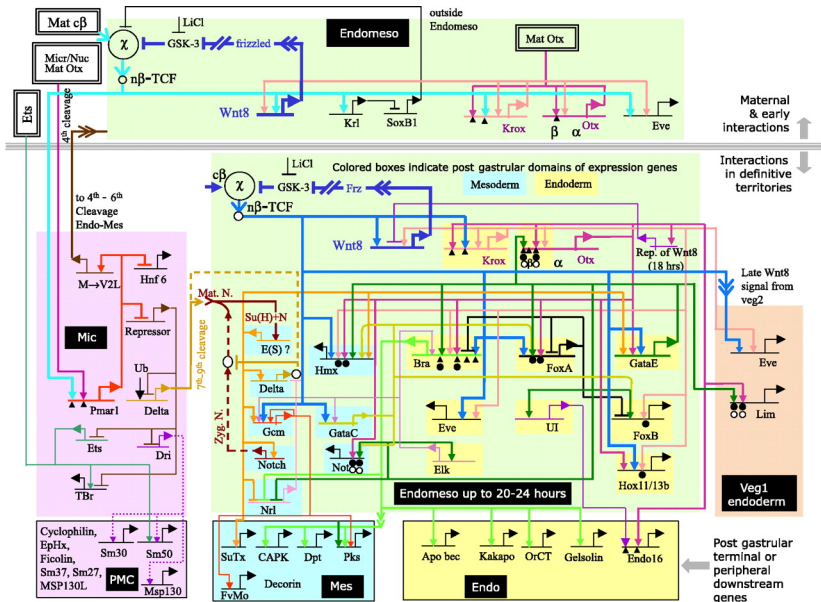
$$\eta(t) = 0$$

else $\eta(t) = \xi(t)$

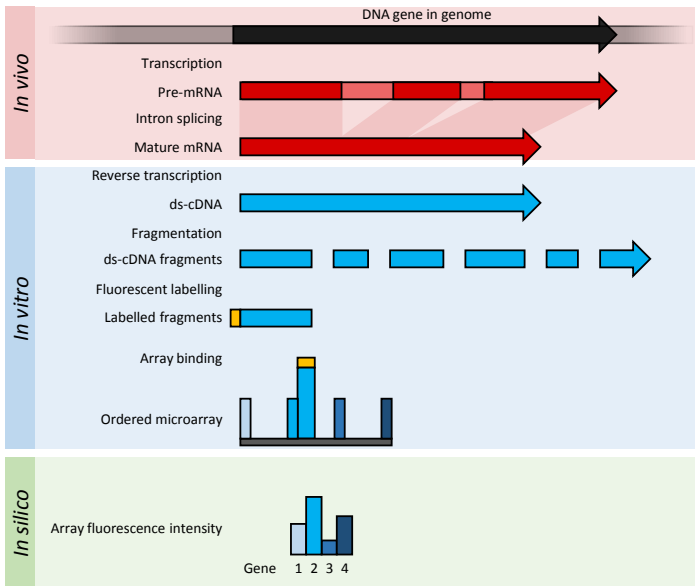
$$\Theta(t) = \gamma * \eta(t)$$

Final output communicated to BTA

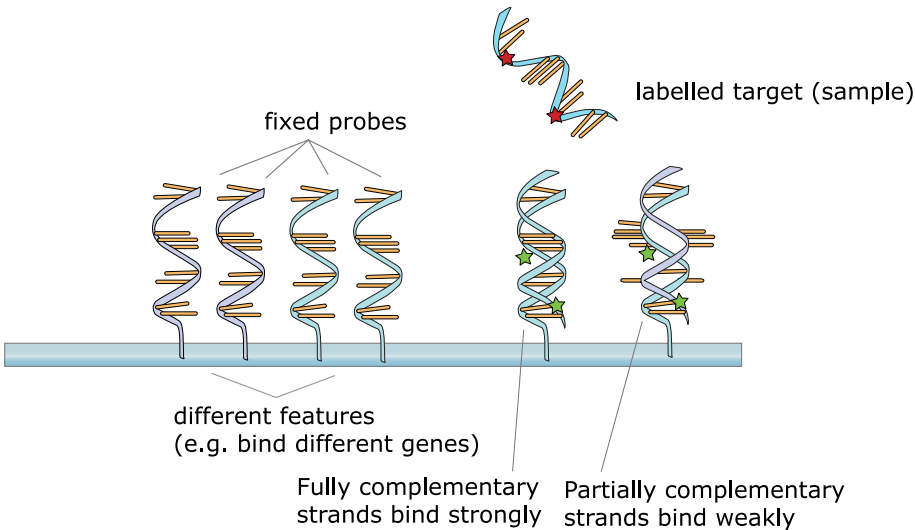
Gene Expression is a Dynamic Process



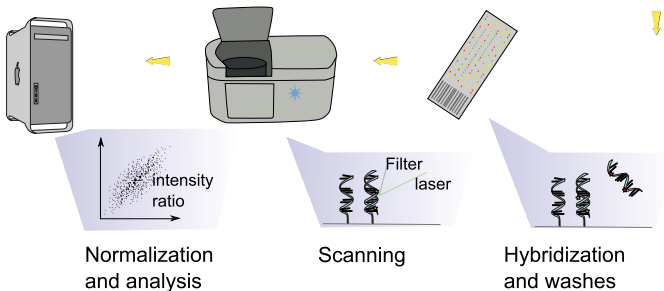
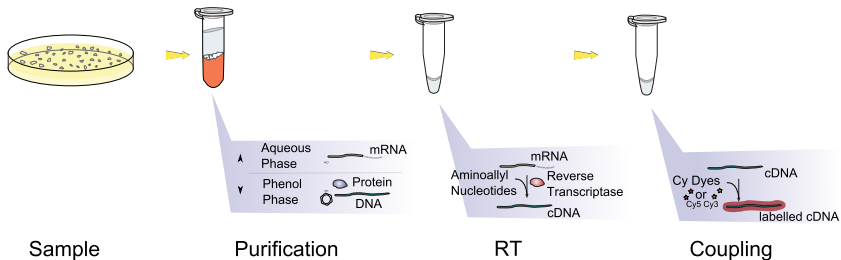
Measuring Genomewide Gene Expression: DNA Microarrays



Measuring Genomewide Gene Expression: DNA Microarrays



Measuring Genomewide Gene Expression: DNA Microarrays



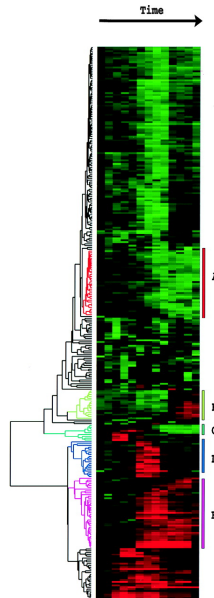
Applications of DNA Microarray Data

RESEARCH ARTICLE

Cluster analysis and display of genome-wide expression patterns

Michael B. Eisen, Paul T. Spellman, Patrick O. Brown, and David Botstein

PNAS December 8, 1998 95 (25) 14863-14868;



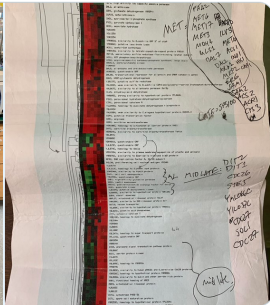
Applications of DNA Microarray Data



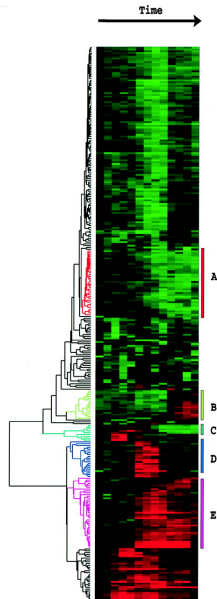
Michael Eisen ✓
@mbeisen

...

Inspired by @UCSDCooperLab's question about origins of the red/green color scheme in microarray clustering, I present THE FIRST dna microarray cluster analysis made by me in 1997 for ncbi.nlm.nih.gov/m/pubmed/97841... w/handwritten notes from Pat Brown and the late Ira Herskowitz.



6:27 PM · Jun 4, 2019 · Twitter for iPhone



Applications of DNA Microarray Data

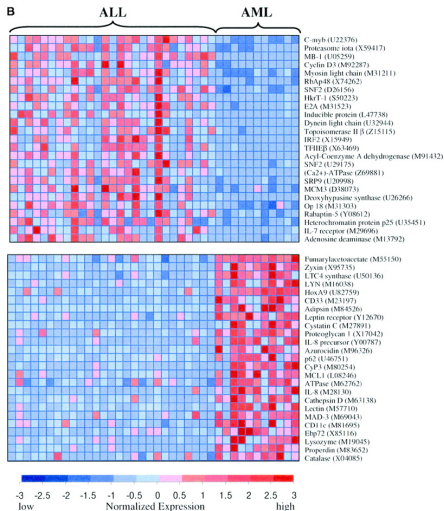
REPORT

Molecular Classification of Cancer: Class Discovery and Class Prediction by Gene Expression Monitoring

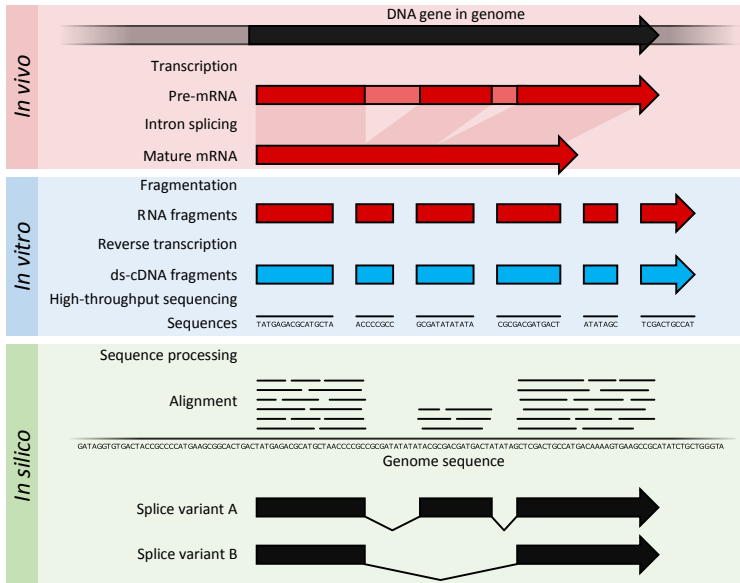
T. R. Golub^{1,2,3,4}, D. K. Slonim^{1,4}, P. Tamayo¹, C. Huard¹, M. Gaasenbeek¹, J. P. Mesirov¹, H. Collier¹, M. L. Loh², J. R. Downing¹

¹ See all authors and affiliations

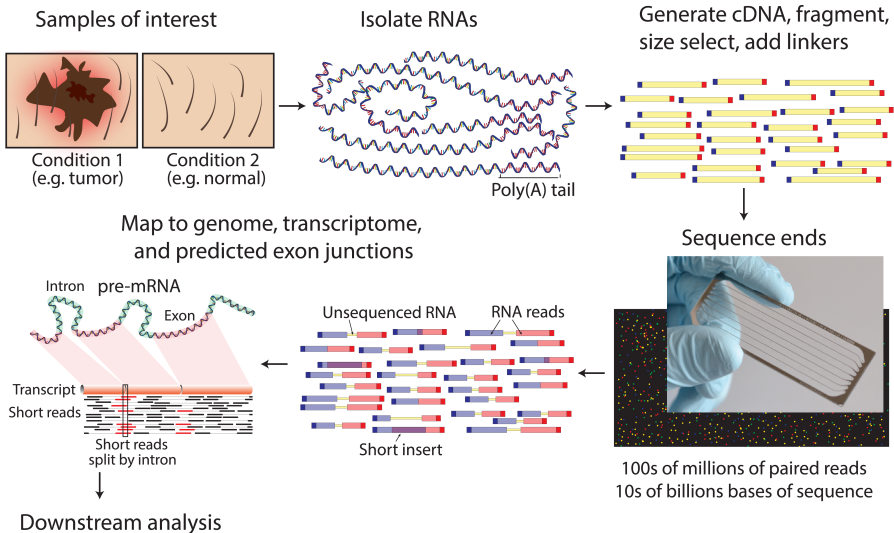
Science 15 Oct 1999;
Vol. 286, Issue 5439, pp. 531-537
DOI: 10.1126/science.286.5439.531



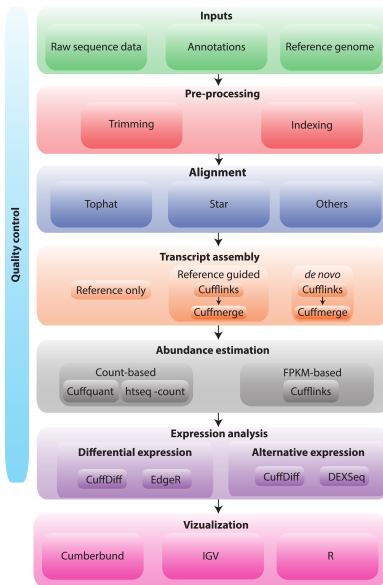
Measuring Genomewide Gene Expression: RNA-seq



Measuring Genomewide Gene Expression: RNA-seq

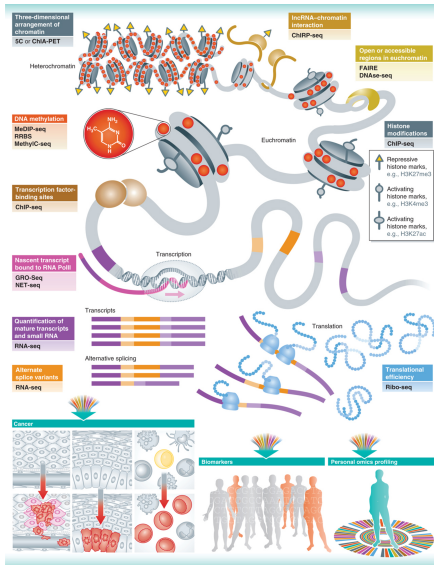


Measuring Genomewide Gene Expression: RNA-seq



Griffith et al., *Informatics for RNA Sequencing: A Web Resource for Analysis on the Cloud*. PLoS Comput Biol, 2015

*-Seq Techniques



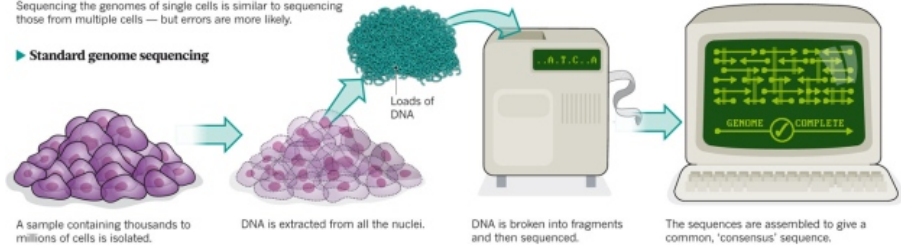
Soon, Hariharan, and Snyder. *High-throughput sequencing for biology and medicine*. Mol. Sys. Bio, 2013.

Single-Cell RNA-Seq

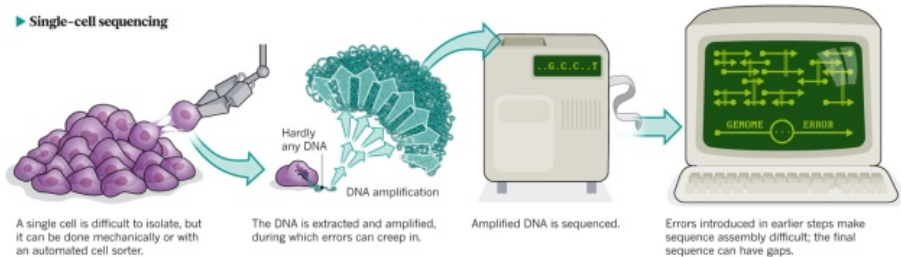
ONE GENOME FROM MANY

Sequencing the genomes of single cells is similar to sequencing those from multiple cells — but errors are more likely.

► Standard genome sequencing

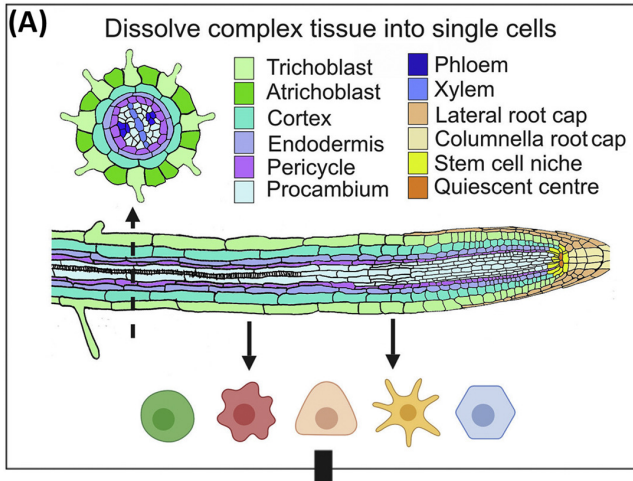


► Single-cell sequencing



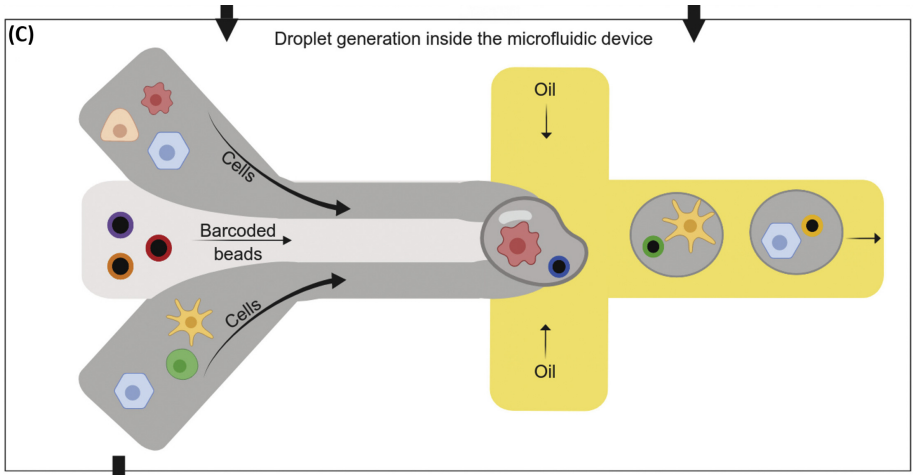
Owens, *Genomics: The single life*, Nature, 2012.

scRNA-seq Method



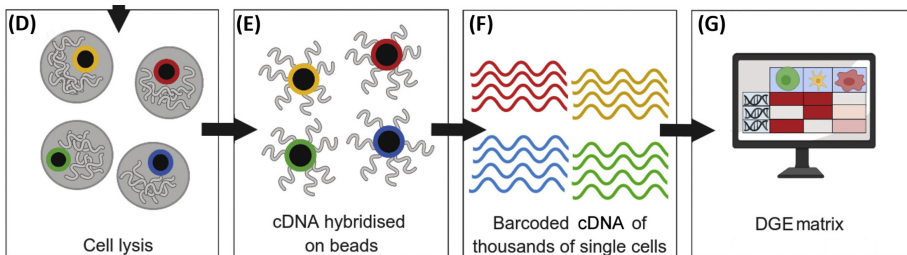
Single-Cell Transcriptomics: A High-Resolution Avenue for Plant Functional Genomics, Rich-Griffin et al., Trends in Plant Science, 2020

scRNA-seq Method



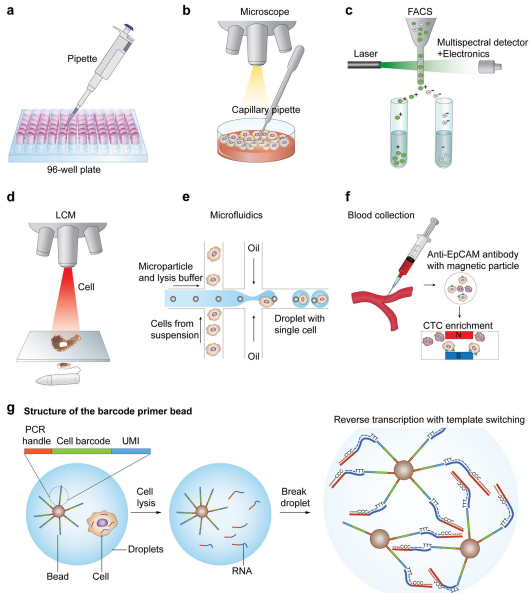
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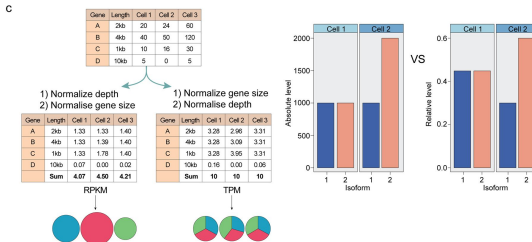
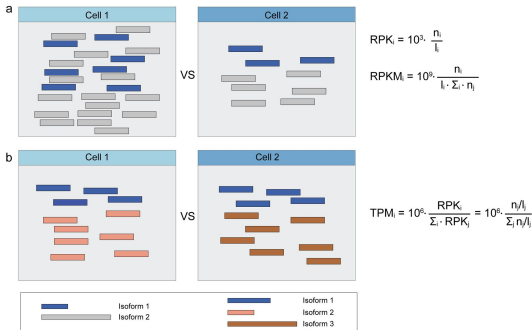
Single-Cell Transcriptomics: A High-Resolution Avenue for Plant Functional Genomics, Rich-Griffin et al., Trends in Plant Science, 2020

Cell Separation Methods

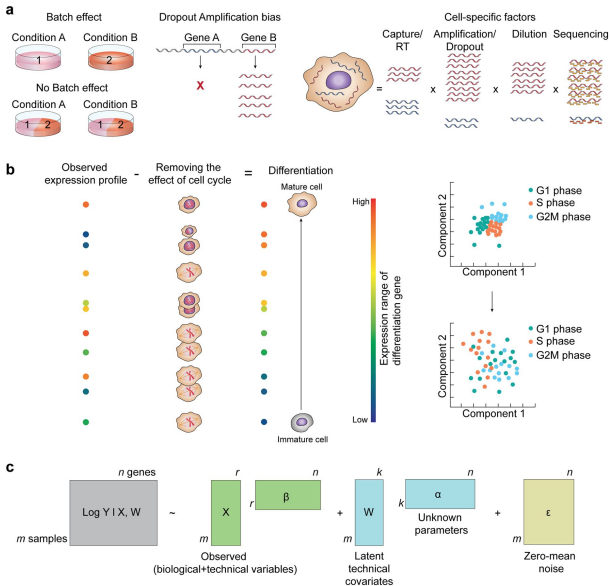


Hwang, Lee, and Bang, *Single-cell RNA sequencing technologies and bioinformatics pipelines*, *Exp. Mol. Med.*, 2018

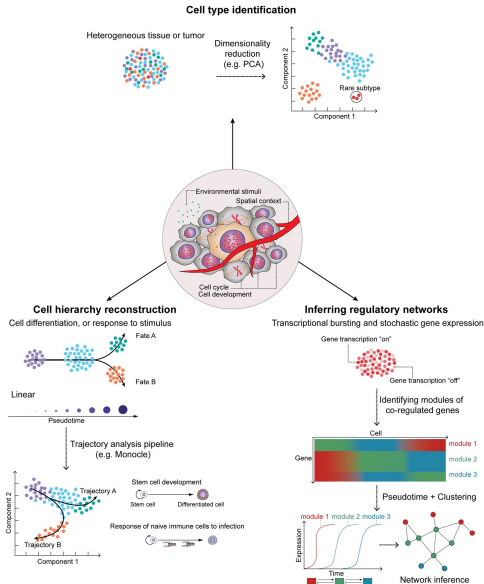
Quantification of scRNA-seq Data



Confounding Factors in scRNA-Seq Data



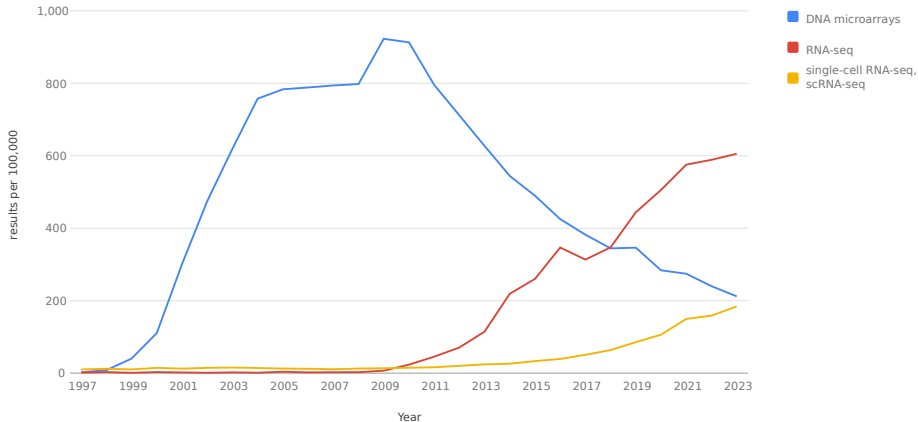
Applications of scRNA-seq Data



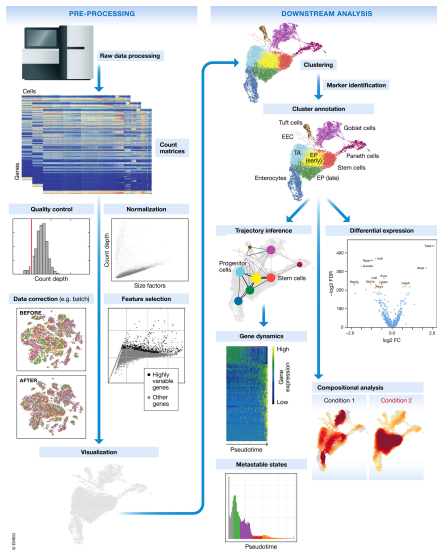
Hwang, Lee, and Bang, *Single-cell RNA sequencing technologies and bioinformatics pipelines*, Exp. Mol. Med., 2018

Technology Trends

Results per 100,000 citations in PubMed
proportion for each search by year, 1997 to 2023

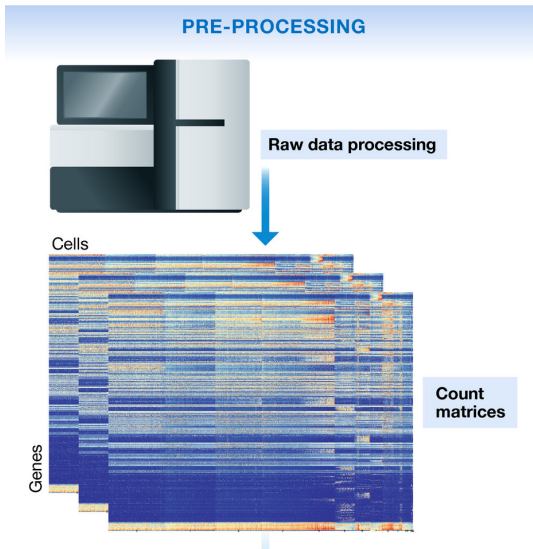


Typical scRNA-seq Analysis Workflow



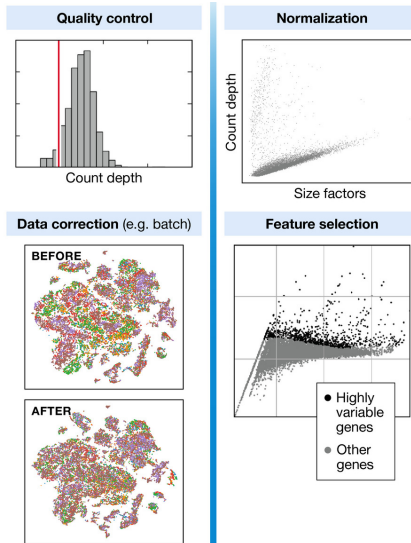
Leucken and Theis, *Current best practices in single-cell RNA-seq analysis: a tutorial*, *Mol. Sys. Bio.*, 2019, <https://doi.org/10.15252/msb.20188746>

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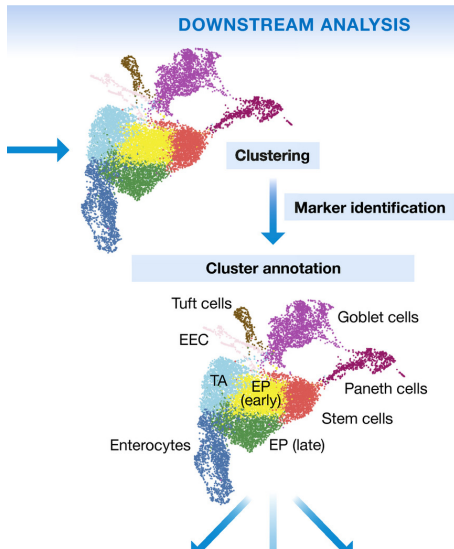
Typical scRNA-seq Analysis Workflow

Visualization



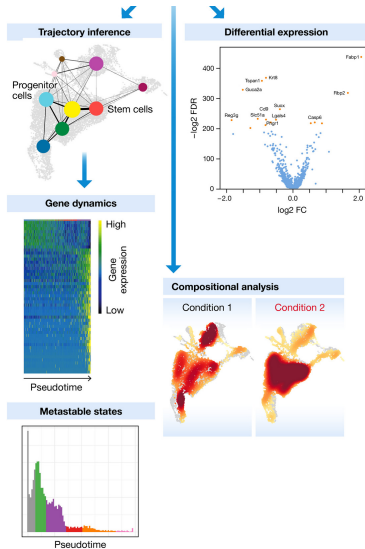
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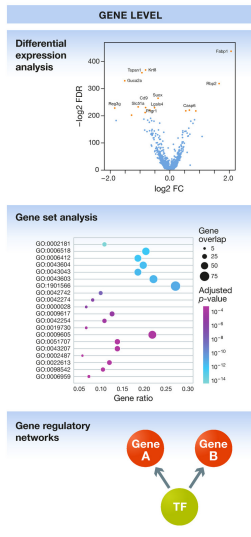
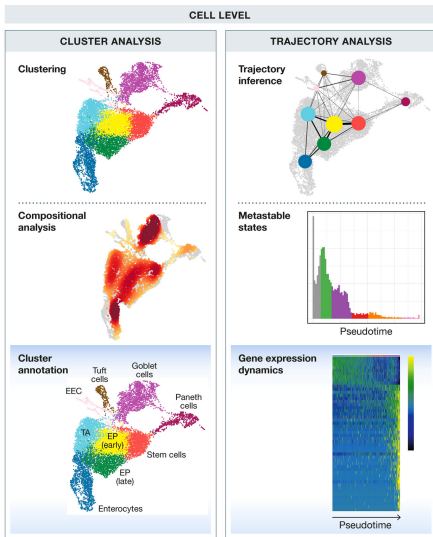
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Downstream Analysis Methods



Leucken and Theis, *Current best practices in single-cell RNA-seq analysis: a tutorial*, *Mol. Sys. Bio.*, 2019, <https://doi.org/10.15252/msb.20188746>

Pseudotime Inference in scRNA-Data

- Difficult to experimentally purify cells in intermediate states.
- A population of cells isolated at same time population of cells may correspond to multiple, distinct intermediate differentiation states.

Trapnell et al., The dynamics and regulators of cell fate decisions are revealed by pseudotemporal ordering of single cells, Nat. Biotech., 2014.

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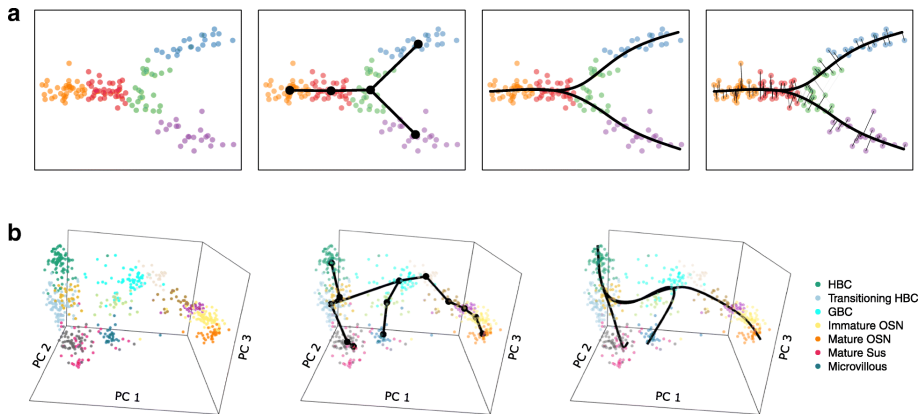
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Trapnell et al., The dynamics and regulators of cell fate decisions are revealed by pseudotemporal ordering of single cells, Nat. Biotech., 2014.

Pseudotime Trajectory Inference



By Kelly Street, Davide Risso, Russel B. Fletcher, Diya Das, John Ngai, Nir Yosef, Elizabeth Purdom, Sandrine Dudoit - <https://bmcbgenomics.biomedcentral.com/articles/10.1186/s12864-018-4772-0>, CC BY 4.0, <https://commons.wikimedia.org/w/index.php?curid=75075393>