~ MCB 5243 ~

Single-Cell Analysis of Animal Development and Cancer

Molecular biology reads the notes in the score. but systems biology plays the music.
After: Woese CR. A new biology for a new century. Microbiol Mol Biol Rev. 2004;68: 173–186.

This course is meant to provide an introduction to single-cell gene expression analysis of development and cancer, and to provide a grounding in the basic concepts, methods, and data analysis tools required for the analysis of gene expression at the single-cell level. New findings, experiments and data from single-cell studies will be analyzed and discussed with emphasis on a systems biology and gene regulatory network perspective. The course is designed to be accessible to anyone with a serious interest in single-cell analysis, regardless of background, but a working knowledge of molecular biology, development, and statistics will be very helpful to the student. Students from Biology, Computer Science, Statistics, Mathematics and related disciplines are all welcome. This Fall the course will be taught remotely. The course will be divided into two intertwined parts: conceptual and applied. For the conceptual work we will be using a selection of papers from the recent single-cell literature, online videos, and (as needed) portions of books from Oxford's "Very Short Introduction" series (inexpensive). In the applied portion we will be working with real gene expression data using the software platforms Cytoscape and JMP. Cytoscape is freeware, and a student version of JMP can be purchased for $15. All of the texts and software required for the course are estimated to total well under $100, and all are readily available online or from Amazon. Students will be graded based upon regular quizzes given at the beginning of class, a series of homework assignments and class participation. See following pages for a draft schedule for Fall 2020 and a selection of material (links, videos, articles, etc…) from previous offerings of the course.

MCB5243 Sample Materials

Tools:

- JMP
- Cytoscape
- ToppCluster

Sample Concepts in data analysis:

- Graphing
- Basic Analysis
- Clustering
- Differential Gene Expression
- Gene Set Enrichment Analysis
- Network Visualization in Cytoscape

Sample Videos:

How one cell gives rise to an entire body
https://www.youtube.com/watch?time_continue=32&v=3mCgHK-X6lE

Multiple Hypothesis Testing
FDR and the Benjamini-Hochberg Method clearly explained
https://www.youtube.com/watch?v=K8LQSvtjcEo

Dimension reduction with tSNE:
https://www.youtube.com/watch?v=wvsE8jm1GzE

PCA:
https://www.youtube.com/watch?v=FgakZw6K1QQ
https://www.youtube.com/watch?v=_UVHneBUBW0

tSNE:
https://www.youtube.com/watch?v=NEaUSP4YerM&t=3s

tSNE, Laurens van der Maaten, Visualizing Data Using Embeddings
https://www.youtube.com/watch?v=EMD106bB2vY&t=853s

Sample Books:

Holland J. **Hidden Order: How Adaptation Builds Complexity** (Helix Books). Basic Books; 1996.

Caldarelli G, Catanzaro M. **Networks: A Very Short Introduction** (Very Short

Introductions). 1 edition. Oxford University Press; 2012.

Holland JH. **Complexity: A Very Short Introduction** (Very Short Introductions). 1 edition. Oxford University Press; 2014.

Charlesworth B, Charlesworth D. **Evolution: A Very Short Introduction** (Very Short Introductions). 2 edition. Oxford University Press; 2017.

Sample Papers:

Chong KH, Zhang X, Zheng J. Dynamical analysis of cellular ageing by modeling of gene regulatory network based attractor landscape. PLoS One. journals.plos.org; 2018;13: e0197838.

Liu X, Long F, Peng H, Aerni SJ, Jiang M, Sánchez-Blanco A, et al. Analysis of cell fate from single-cell gene expression profiles in C. elegans. Cell. 2009;139: 623–633.

Packer JS, Zhu Q, Huynh C, Sivaramakrishnan P, Preston E, Dueck H, et al. A lineage-resolved molecular atlas of C. elegans embryogenesis at single-cell resolution. Science. 2019;365. doi:10.1126/science.aax1971

Davie K, Janssens J, Koldere D, De Waegeneer M, Pech U, Kreft Ł, et al. A Single-Cell Transcriptome Atlas of the Aging Drosophila Brain. Cell. 2018;174: 982–998.e20.

Wagner DE, Klein AM. Lineage tracing meets single-cell omics: opportunities and challenges. Nat Rev Genet. 2020. doi:10.1038/s41576-020-0223-2

Cao J, Packer JS, Ramani V, Cusanovich DA, Huynh C, Daza R, et al. Comprehensive single-cell transcriptional profiling of a multicellular organism. Science. 2017;357: 661–667.

Cusanovich DA, Reddington JP, Garfield DA, Daza RM, Aghamirzaie D, Marco-Ferreres R, et al. The cis-regulatory dynamics of embryonic development at single-cell resolution. Nature. 2018;555: 538–542.

Raj B, Wagner DE, McKenna A, Pandey S, Klein AM, Shendure J, et al. Simultaneous single-cell profiling of lineages and cell types in the vertebrate brain. Nat Biotechnol. 2018;36: 442–450.

Cusanovich DA, Reddington JP, Garfield DA, Daza RM, Aghamirzaie D, Marco-Ferreres R, et al. The cis-regulatory dynamics of embryonic development at single-cell resolution. Nature. 2018;555: 538–542.

Qin T, Fan C-M, Wang T-Z, Yang L, Shen W-L, Sun H, et al. Single-Cell RNA-Seq Reveals Novel Mitochondria-related Musculoskeletal Cell Populations during Adult Axolotl Limb Regeneration Process. bioRxiv. 2019. p. 704841. doi:10.1101/704841

Zilionis R, Engblom C, Pfirschke C, Savova V, Zemmour D, Saatcioglu HD, et al. Single-Cell Transcriptomics of Human and Mouse Lung Cancers Reveals Conserved Myeloid Populations across Individuals and Species. Immunity. 2019;50: 1317–1334.e10.

de Soysa TY, Ranade SS, Okawa S, Ravichandran S, Huang Y, Salunga HT, et al. Single-cell analysis of cardiogenesis reveals basis for organ-level developmental defects. Nature. 2019;572: 120–124.

Barkas N, Petukhov V, Nikolaeva D, Lozinsky Y, Demharter S, Khodosevich K, et al. Joint analysis of heterogeneous single-cell RNA-seq dataset collections. Nat Methods. 2019;16: 695–698.

Welch JD, Kozareva V, Ferreira A, Vanderburg C, Martin C, Macosko EZ. Single-Cell Multi-omic Integration Compares and Contrasts Features of Brain Cell Identity. Cell. 2019;177: 1873–1887.e17.

MCB 5243, Fall 2020, Draft Schedule

Week	Class #	Date	Lecture	Lecture Prep	Reading and Other Material	
1	1	Tuesday, September 1	Introduction to single-cell gene expression analysis	-		
1	2	Thursday, September 3	C elegans Development	Ce dev section from Gilbert		
2	3	Tuesday, September 8	C elegans Development, Single-Cell	Ce single-cell paper	A lineage-resolved molecular atlas of C. elegans embryogenesis at single-cell resolution. Science. 2019;365. doi:10.1126 /science.aax1971	
2	4	Thursday, September 10	Drosophila Development	Dm dev section from Gilbert		
3	5	Tuesday, September 15	Drosophila Embryogenesis, Single-Cell	Dm Embryogenesis Single-Cell Paper		
3	6	Thursday, September 17	The Aging Drosophila Brain Single-Cell	Dm Aging Brain Single-Cell Paper	A Single-Cell Transcriptome Atlas of the Aging Drosophila Brain. Cell. 2018;174: 982–998.e20.	
		Tuesday, September 22	Thanksgiving			
		Thursday, September 24				
		Tuesday, September 29				
4	7	Thursday, October 1	Data Analysis 1 - Dimension Reduction			
4	8	Tuesday, October 6	Introduction to JMP	Install JMP - Open Sample Data		
5	9	Thursday, October 8	Data Analysis 2 - Clustering			
5	10	Tuesday, October 13	Clustering in JMP			
6	11	Thursday, October 15	Data Analysis 3 - Differential Gene Expression			
6	12	Tuesday, October 20	DGE - Methods and Application			
7	13	Thursday, October 22	Data Analysis 4 - Gene Set Enrichment Analysis			
7	14	Tuesday, October 27	ToppGene etc...			
8	15	Thursday, October 29	Data Analysis 5 - Network Visualization and Analysis			
8	16	Tuesday, November 3	Cytoscape	Install Cytoscape - Open Sample Network		
9	17	Thursday, November 5	Gene Regulatory and Coexpression Networks			
9	18	Tuesday, November 10	Single Cell Data Analysis Pipelines - Seurat	Seurat paper		
10	19	Thursday, November 12	Mouse Development	Mm dev section from Gilbert		
10	20	Tuesday, November 17	Mouse single-cell	Mouse single-cell Organognesis paper		
11	21	Thursday, November 19	Combining Single-Cell Transriptomics with Other Omics Data		Comprehensive single-cell transcriptional profiling of a multicellular organism. Science. 2017;357: 661–667.	The cis-regulatory dynamics of embryonic development at single-cell resolution. Nature. 2018;555: 538–542.
11	22	Tuesday, November 24	Cancer 1 -			
12	23	Thursday, November 26	Cancer 2 -			
12	24	Tuesday, December 1	Cancer 3 -			
13	25	Thursday, December 3	Cancer 4 -			