Joint RNA and ATAC analysis

Multiome scRNA-seq and scATAC-seq
downstream analysis with Seurat and Signac

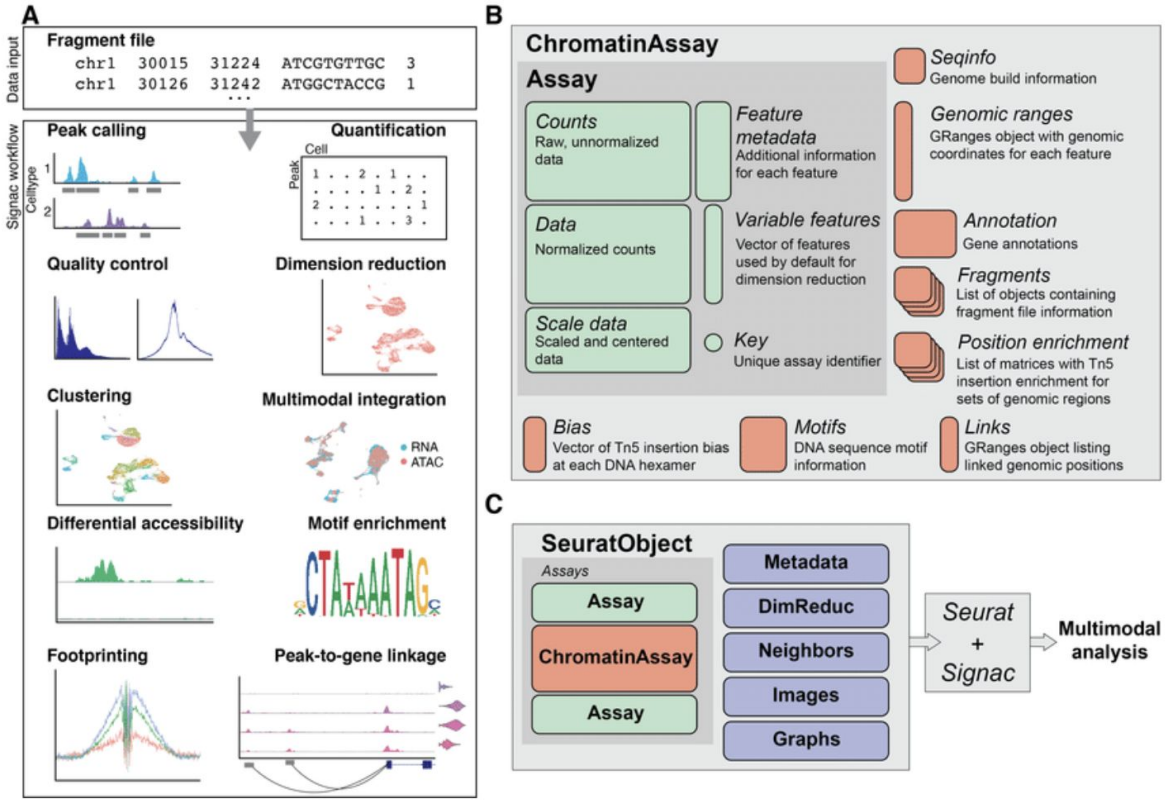
Session 3

Cynthia Cardinault

April 19th, 2024

Bi-modal integrative analysis of the RNA-ATAC scMultiome data

- R, RStudio
- Cell Ranger-ARC
- Seurat v5 (2022-11-18)
- Signac v1.9.0 (2022-12-08)



Single Cell Multiome Dataset

Flash-Frozen Human Healthy Brain Tissue (3k)	Single Cell Multiome ATAC + Gene Expression	v1	N/A	Cell Ranger ARC	v2.0.0	cellranger-arc count	Human

- Link to data:

  Flash-Frozen Human Healthy Brain Tissue (3k)

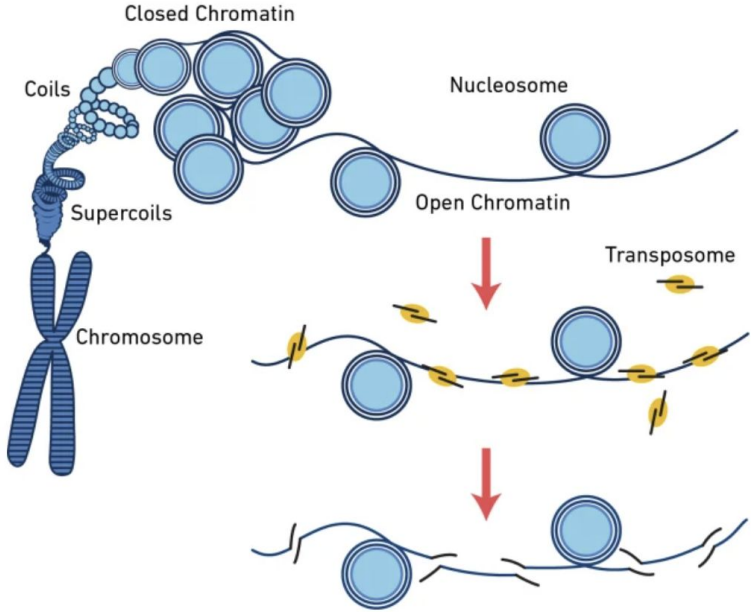
  https://www.10xgenomics.com/datasets/frozen-human-healthy-brain-tissue-3-k-1-standard-2-0-0

scRNA-seq and scATAC-se integration

This genomic features cannot be captured by scRNA-seq which only measures the transcriptome.

One difficulty when analyzing scATAC-seq data is to annotate different cell populations, as in most of the time, cell type/state is based on the expression or specific gene markers, which is not directly measured by scATAC-seq experiments.

Under the integration approach we have double the amount of analysis, and also jointly analyzing the two modalities together we increase the potential to get some more interesting insight.



Regions of open chromatin correlate with areas of active gene transcription. The assay for transposase-accessible chromatin (ATAC) works by generating short fragments of DNA specifically within open chromatin regions. Mapping these cut sites back to the genome provides a window into transcription factor motif binding, promoter and enhancer regions, and areas of euchromatin versus heterochromatin. CREDIT: 10x Genomics.

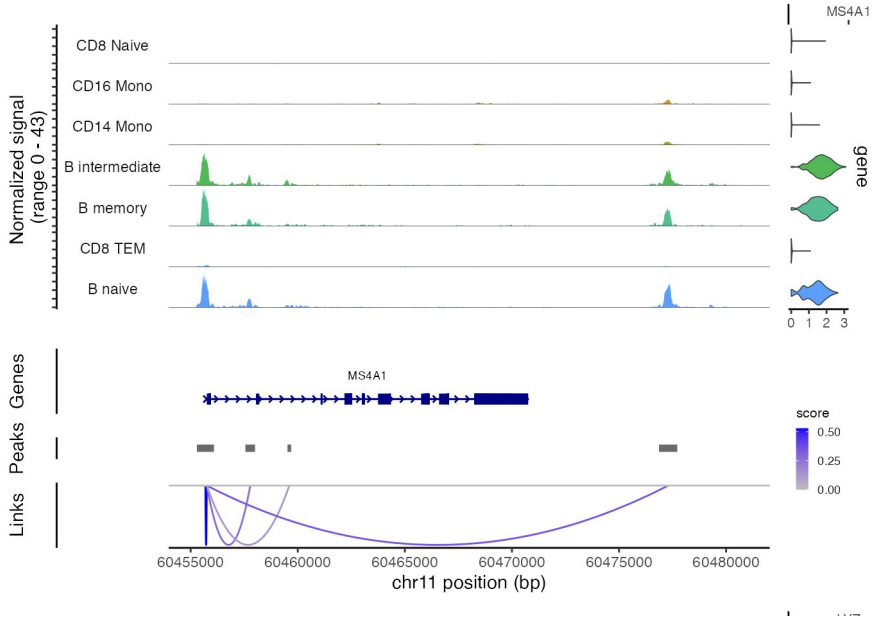
scRNA-seq and scATAC-se integration

Combining the RNA and ATAC information may allow us to look deeper into the transcriptional regulation.

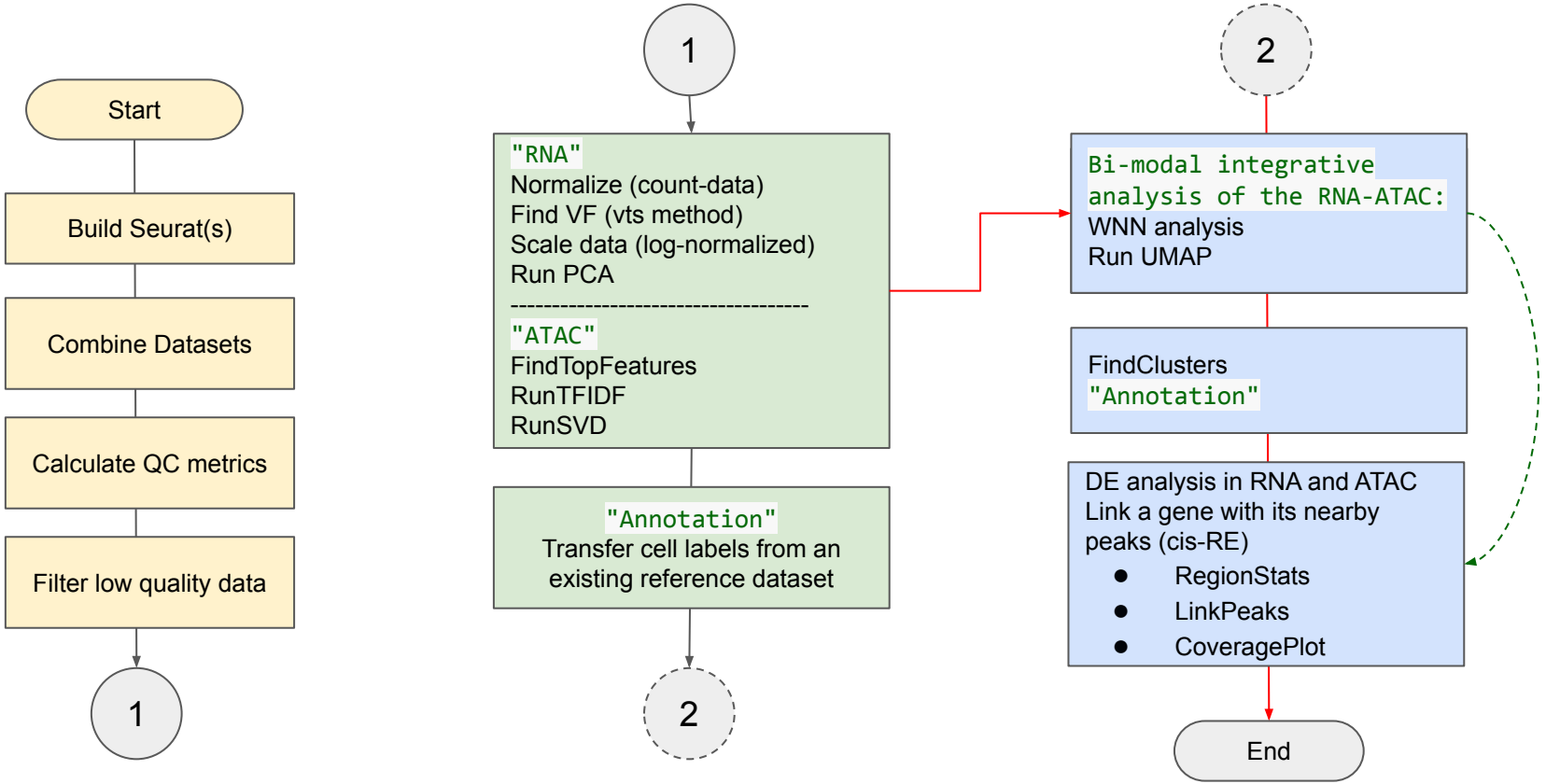
Weighted nearest neighbor analysis:

Generate a kNN network of cells based on the information of both modalities. It firstly calculates weights about how much each modality contribute in defining neighbors for each cell.

* Seurat methodology paper (Hao et al. 2021, Cell)



What strategy to use ?



Resources

Tutorials:

- https://stuartlab.org/signac/articles/pbmc_multiomic (*): transferring anchors strategy
- https://github.com/quadbio/scMultiome_analysis_vignette/blob/main/Tutorial.md
- https://stuartlab.org/signac/articles/snareseq
- https://satijalab.org/seurat/articles/seurat5_atacseq_integration_vignette
- https://stuartlab.org/signac/1.2.0/articles/pbmc_multiomic
- https://nbis-workshop-epigenomics.readthedocs.io/en/latest/content/tutorials/scAtacSeq/lab-sc_atac_seq.html

Paper:

- https://pubmed.ncbi.nlm.nih.gov/29608179/
- https://satijalab.org/seurat/reference/
- https://www.cell.com/cell/pdf/S0092-8674(21)00583-3.pdf
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9255697/

Github code:

- https://github.com/cyntsc/RStatClub_Seurat_Signac/tree/5e325042d76bbe6b56669ee8e8545e01c4122add/code

  10x Chromium dataset: Flash-Frozen Human Healthy Brain Tissue (3k)

Thanks