Data Science in Systems Biology
TUM School of Life Sciences
Technical University of Munich

Hands-on: Single-cell to Spatial Mapping with Tangram

MOPITAS autumn school 2025

Instructors:

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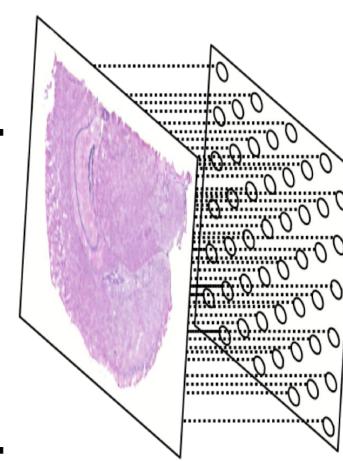
Garching, 14th Nov.

Single-Cell to Spatial Mapping

- **Spatially resolved single-cell transcriptomics** data is essential, but current technologies are limited

- Computational tools bridge gap by integrating spatial transcriptomics with scRNA-seq
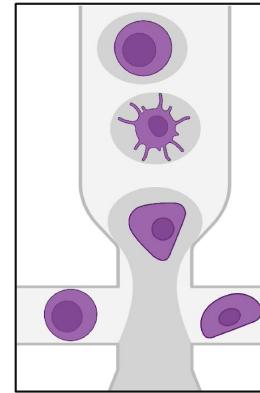
scRNA-seq

No spatial information

Spatial transcriptomics

Resolution & depth limits
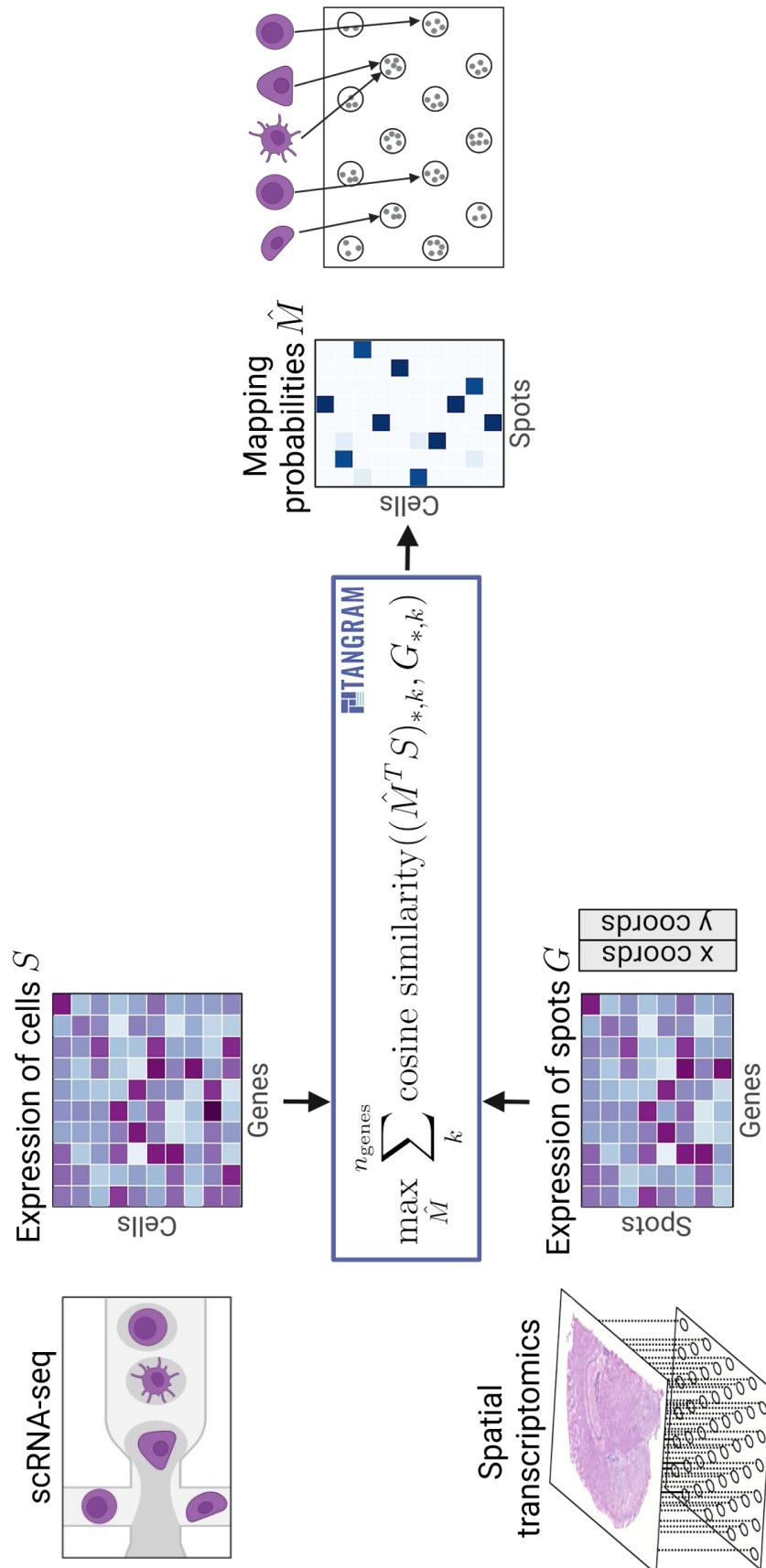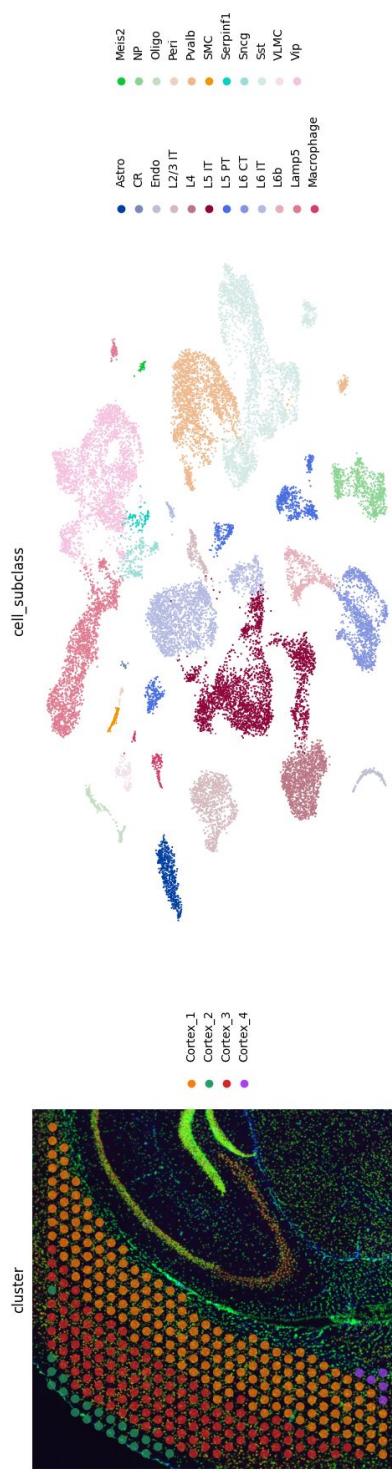
Tangram: Single-Cell to Spatial Mapping

scRNA-seq

Expression of cells S

Spatial transcriptomics

Expression of spots G

x coords

y coords

$$\max_{\hat{M}} \sum_{k}^{n_{\text{genes}}} \text{cosine similarity}((\hat{M}^{T} S)_{*,k}, G_{*,k})$$

TANGRAM

Mapping probabilities $\hat{M}$

Cells

Spots
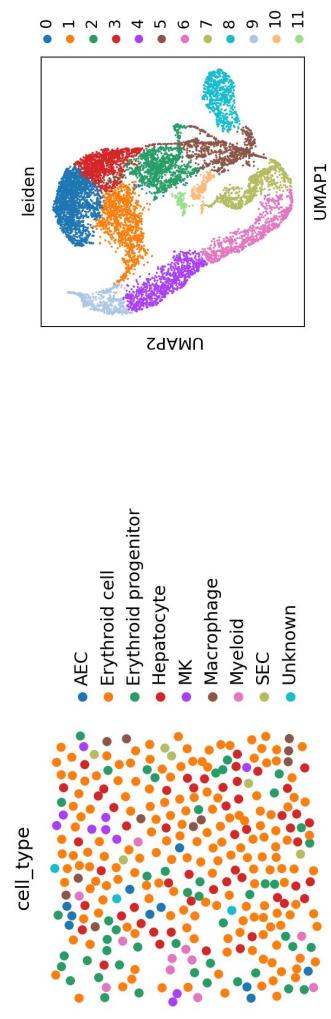
Agenda

Task 1: **Deconvolution** of mouse brain Visium data
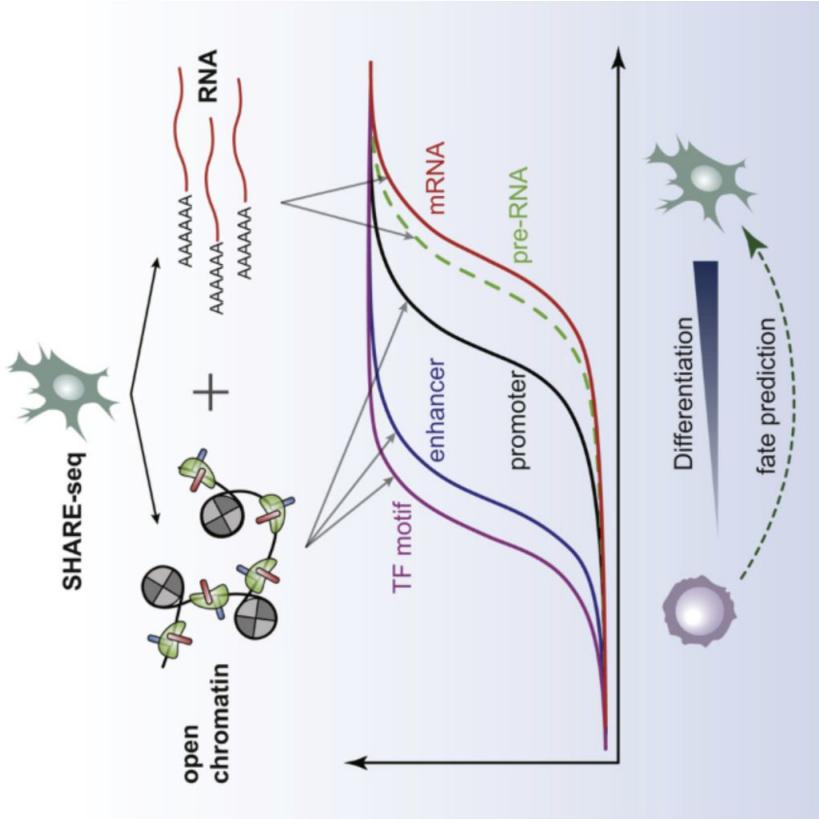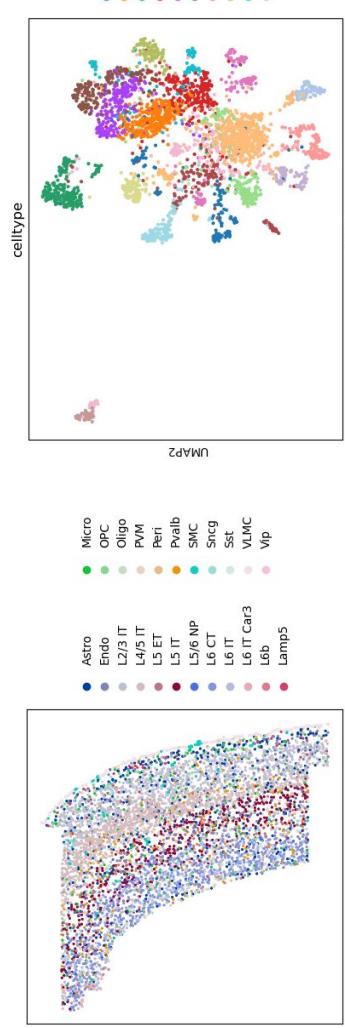
## Task 2: **Imputation** on mouse fetal liver MERFISH data

Agenda

Task 3: **Spatial chromatin accessibility** in mouse brain

SHARE-seq jointly profiles **chromatin accessibility (ATAC-seq)** and **RNA-seq** from the same single cell

→ Map cell to spot by aligning SHARE-seq's RNA expression with spatial expression

→ Transfer ATAC profile to assigned spot

Group Work

Now – Work in groups

- Start with Task 1

14:30 – Present your assigned section (~5 min):

- Explain the code

- Interpret the results

- How could you improve or extend the code and analysis?

▶ Task 1: Mapping of mouse brain Visium data

- Setting up
- Loading datasets
- Preprocessing
- Mapping cells into space
- Exploring training gene scores
  - ▶ Improving spatial data by projecting single-cell gene expres...
    - Inspecting training genes with low mapping scores
    - Predicting genes not measured in spatial data
    - Exploring testing gene scores
    - Projecting cell types into space

▶ Task 2: Imputation on mouse fetal liver MERFISH data

- Setting up
- Common gene set between reference and spatial dataset
- Computing the map from single-cells to spatial voxels
- Imputing genes and mapping cell-types to space
- Plotting genes that were not part of the training data

▶ Task 3: Mapping of Chromatin Accessibility in the Mouse Brain

- Introduction and Background
- Setup, data loading and preprocessing
- PCA and UMAP plotting
- Running Tangram
- Projecting celltype annotations to space
- Using Tangram's mapping to extend gene throughput of spatial...
- Transfering Tangram mapping to scATAC data to project peaks ....
- Spatial autocorrelation analysis on ATAC data
- Spatial autocorrelation analysis on RNA data

JupyterHub Hints

- Shut down unused kernels

- You can collaborate! Simply change the username in the url:
https://exbio.wzw.tum.de/jupyterHub/user/**exampleuser/**
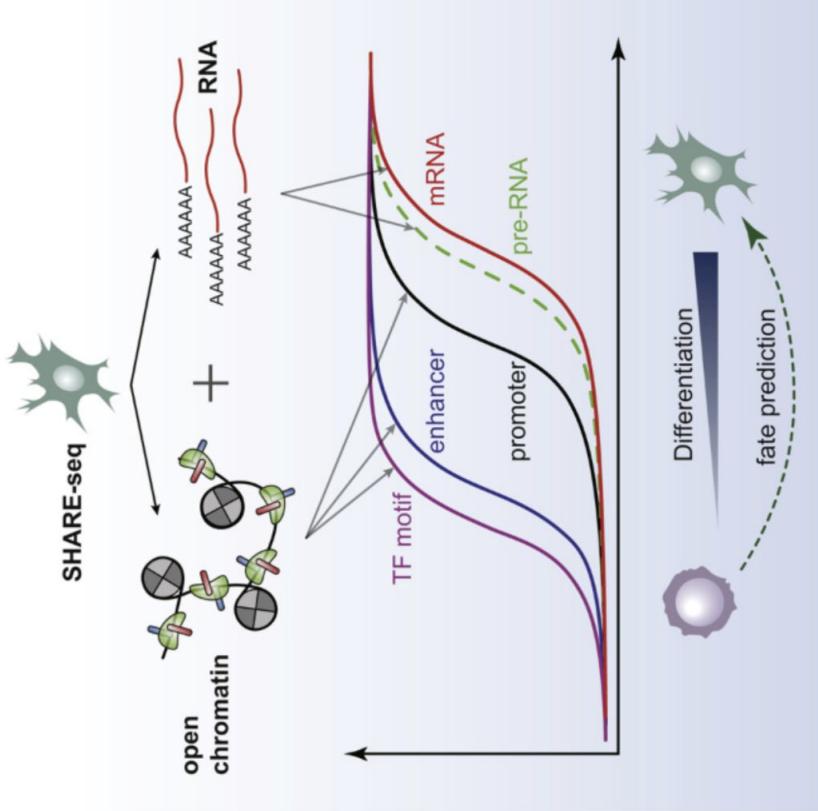
Mapping Chromatin Accessibility

SHARE-seq:

Jointly profiles chromatin accessibility (ATAC-seq) and RNA-seq from the same single cells

→ Map cells to spots by aligning SHARE-seqs RNA expression with spatial expression

→ Transfer ATAC profiles to assigned spot
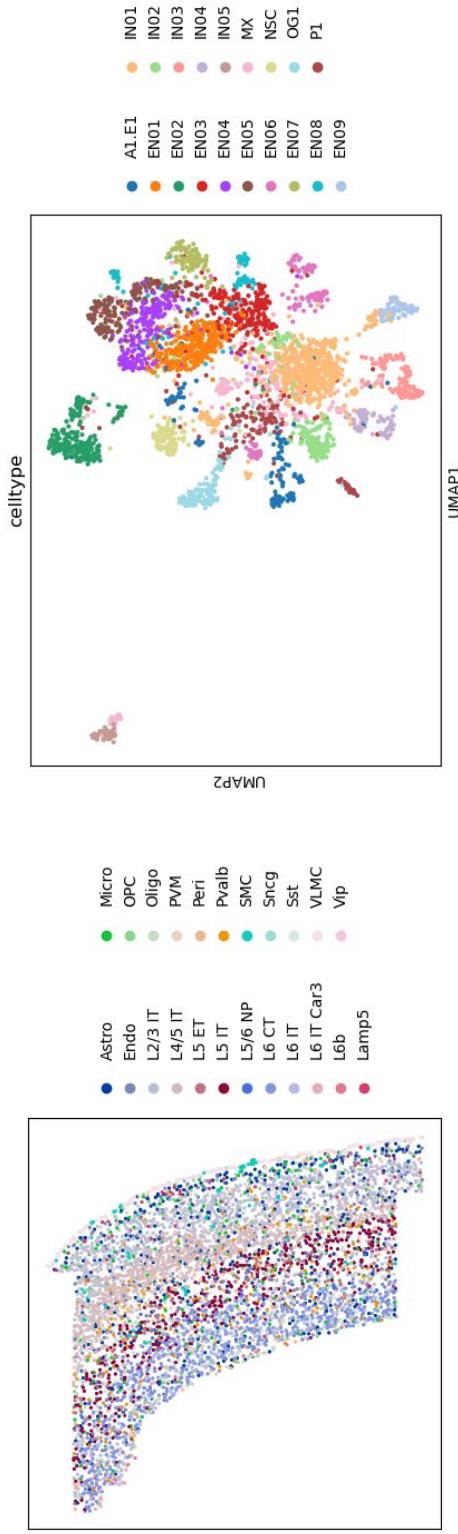
Agenda

**Task 3**: Spatial chromatin accessibility in the mouse brain
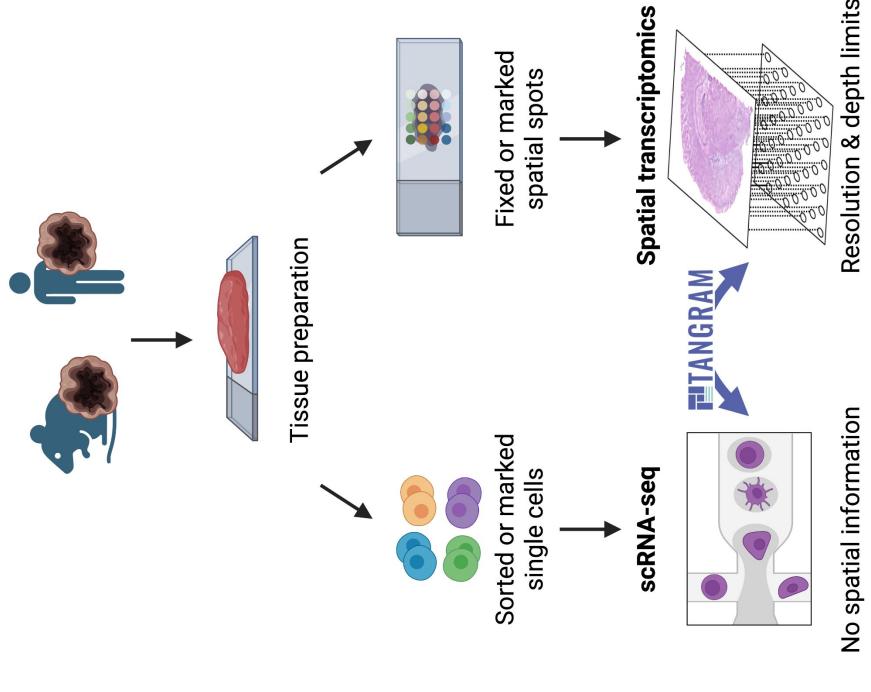
Single-Cell versus Spatial Transcriptomics

Single-cell RNA sequencing

- Profiles gene expression at the **single-cell level**, revealing cellular heterogeneity within tissues.

- Requires **cell dissociation**, losing spatial context but enabling deep molecular characterization.

- Enables **clustering, trajectory inference, and identification of cell types or states** based on transcriptomic profiles.

Spatial RNA-seq

- Measures **gene expression directly in tissue sections**, preserving the **spatial organization** of cells.

- Combines imaging and sequencing to map where genes are expressed within **tissue architecture**.

- Facilitates studies of **cell-cell interactions, microenvironments, and spatial gene regulation**.

Tissue preparation

Fixed or marked spatial spots

Spatial transcriptomics

Resolution & depth limits

Sorted or marked single cells

scRNA-seq

No spatial information

TANGRAM
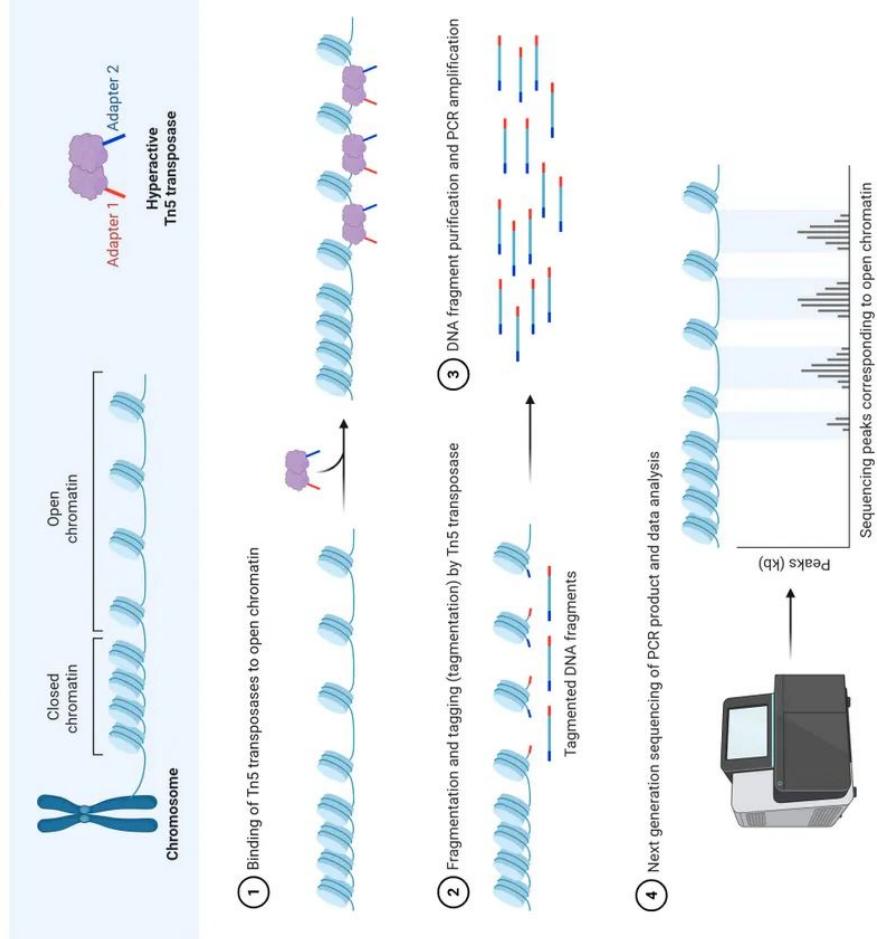
Measuring Chromatin Accessibility

Steps of ATAC Sequencing

① Binding of Tn5 transposases to open chromatin

Closed chromatin | Open chromatin

Chromosome

Adapter 1 | Adapter 2

Hyperactive Tn5 transposase

② Fragmentation and tagging (tagmentation) by Tn5 transposase

Tagmented DNA fragments

③ DNA fragment purification and PCR amplification

④ Next generation sequencing of PCR product and data analysis

Peaks (kb)

Sequencing peaks corresponding to open chromatin

https://microbenotes.com/atac-seq/

ATAC-seq (Assay for Transposase-Accessible Chromatin using sequencing)

- Profiles **chromatin accessibility** genome-wide to identify open regulatory regions.
- Reveals **potential active enhancers, promoters, and transcription factor binding sites.**
- Helps infer **gene regulatory mechanisms and cell-type–specific epigenetic landscapes.**

SHARE-seq (Simultaneous High-throughput ATAC and RNA Expression sequencing):

- **Jointly profiles chromatin accessibility (ATAC-seq) and gene expression (RNA-seq)** from the same single cells.
- Enables linking **regulatory elements to their target genes** by correlating open chromatin regions with transcriptional output.
- Provides insights into **gene regulatory dynamics and epigenetic control** during processes like differentiation or disease progression.