

单细胞测序数据介绍

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专 业： 22级 数学

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提 纲

- 单细胞单组学
- 单细胞多组学
- 空间转录组学
- 空间多组学

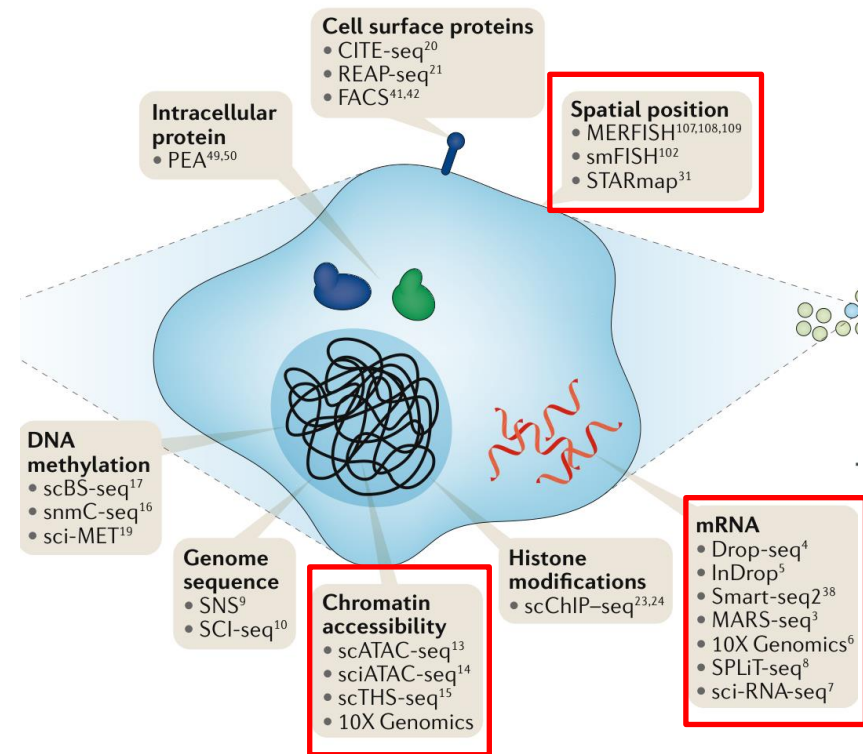
单细胞单组学

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- 单细胞多组学
- 空间转录组学
- 空间多组学

单细胞单组学 *single cell sequencing*

Single-cell sequencing (SCS) technology allows researchers to study *cell heterogeneity* at different levels of gene regulation.

- Single cell RNA-seq
- Single cell DNA-seq
- Single cell epigenomics
- Single cell multi-omics
- Single cell omics integrated with spatial transcriptomics



Stuart T. et al. *Nat. Rev. Genet.* (2019)

单细胞单组学 *scRNA-seq and scATAC-seq*

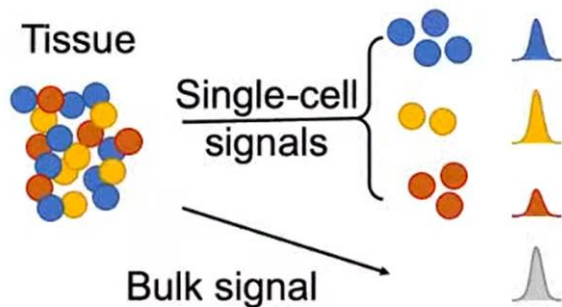
- **Single cell expression**(Compared with bulk-seq).

- Single cell RNA sequencing(scRNA-seq),

$$\mathbf{X} = (x_{ij})_{m \times n} \in \mathbb{N}^{m \times n}.$$

- Single cell ATAC sequencing(scATAC-seq),

$$\mathbf{X} = (x_{ij})_{m \times n} \in \{0, 1\}^{m \times n}.$$



	gene 1	gene 2	...	gene n
cell 1	3	0	...	0
cell 2	0	0	...	14
⋮	⋮	⋮	⋱	⋮
cell m	0	1	...	13

	peak 1	peak 2	...	peak n
cell 1	1	0	...	0
cell 2	0	0	...	1
⋮	⋮	⋮	⋱	⋮
cell m	0	1	...	0

单细胞单组学 *features of single cell omic data*

■ Challenges

- ❑ High dimensional data (e.g. thousands of genes).
- ❑ High missing data. (e.g. specific expression in each cell).
- ❑ Strong noisy data. (e.g. high amplification bias).
- ❑ Dropout events.

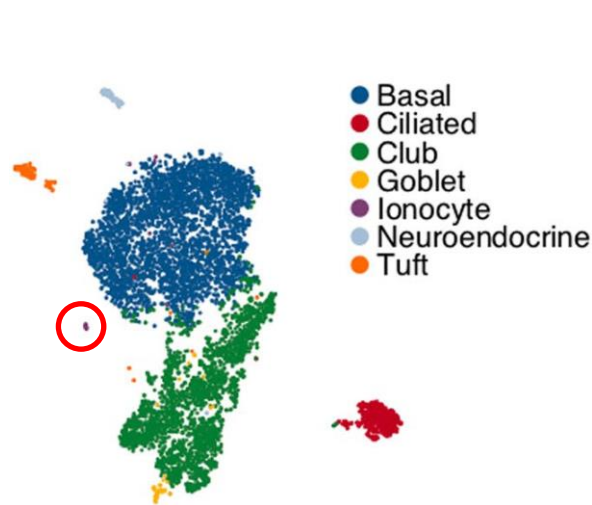
dataset	organ	platform	cell types	cells	zero percentage
Adam	Kidney	Drop-seq	8	3660	92.33%
Bach	Gammmary Gland	10x	8	23184	88.04%
Chen	Brain	Drop-seq	46	12089	93.74%
Klein	Embryonic Stem Cell	inDrop	4	2717	65.58%

Chen L. et al. *NAR Genom. Bioinform.* (2020)

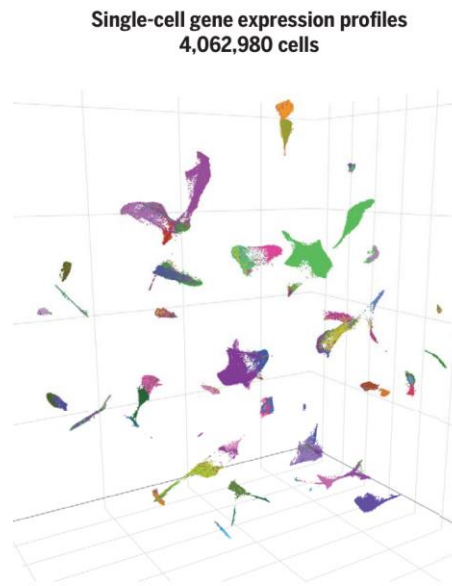


单细胞单组学 *pros of SCS*

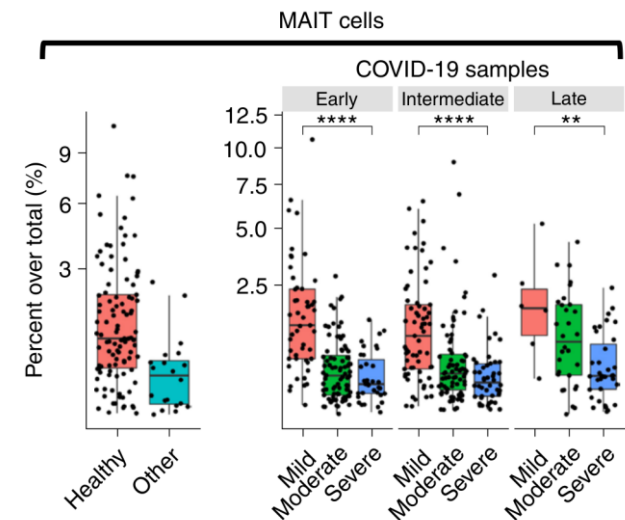
- Discovery of rare cell type,
- Cellular atlas construction,
- Understanding of pathological immunity.



Montoro D. et al. *Nature* (2018)



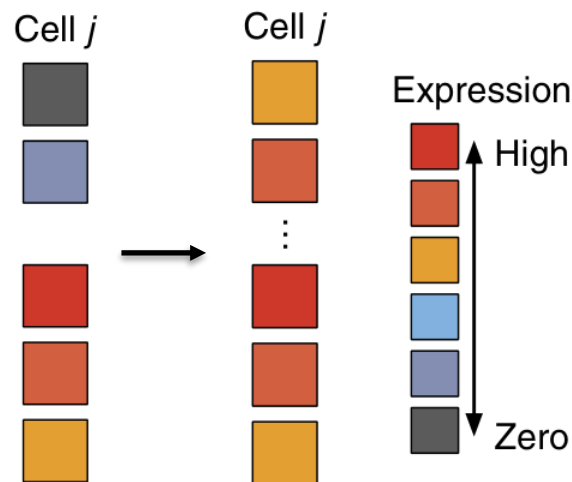
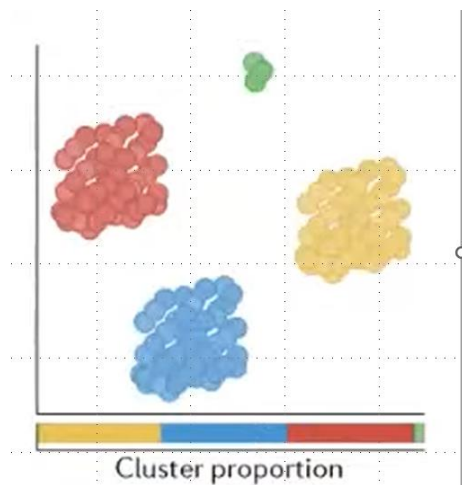
Cao J. et al. *Science* (2020)



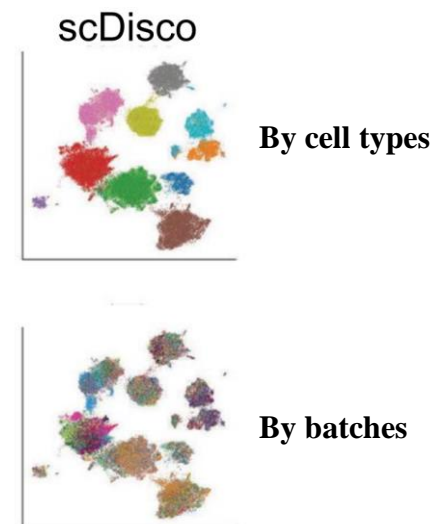
Tian Y. et al. *Nat. Biotechnol.* (2021)

单细胞单组学 *problems in scRNA-seq(scATAC-seq)*

- **Clustering**, separate cells to different clusters.
- **Imputation**, decline dropout events.
- **Integration**, correct batch effects.
- **Annotation**, labeling clusters to cell types.



Li W. et al. *Nat. Commun.* (2018)



Liu R. et al. *BMC Bioinformatics* (2024)

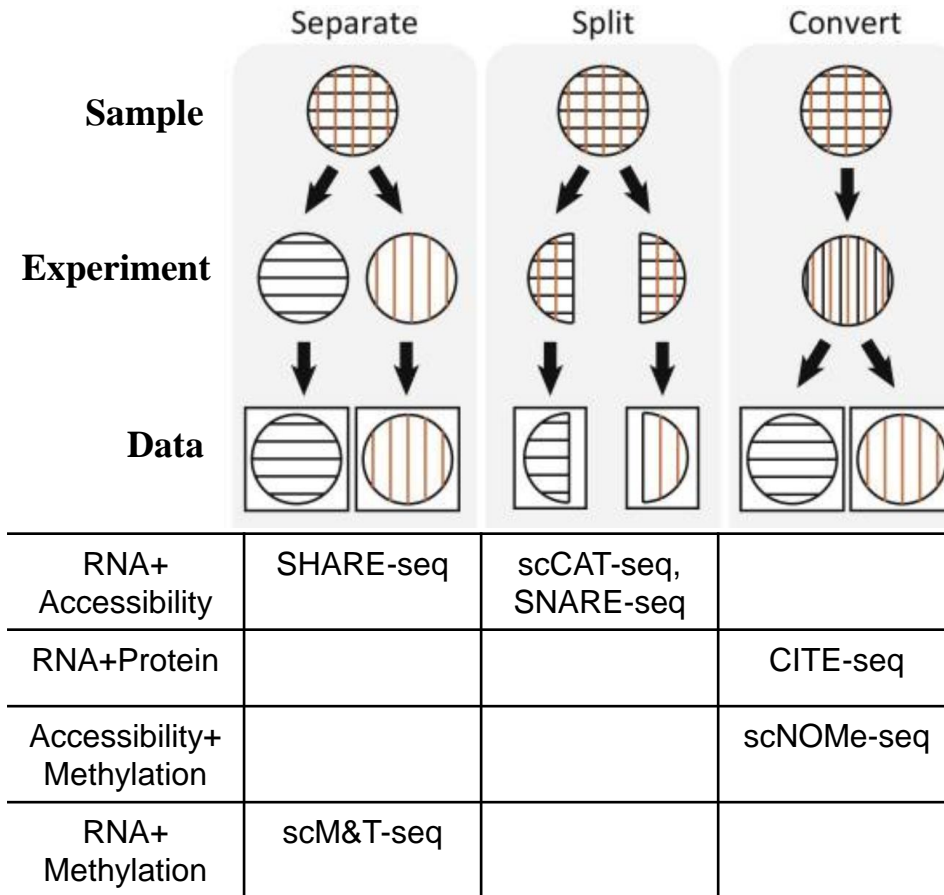
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单细胞多组学 *single cell **multimodal** omics*

Simultaneously obtain multimodal data (*aka* paired data).



■ Pros:

- More information.
- Deeper insights.

■ Cons:

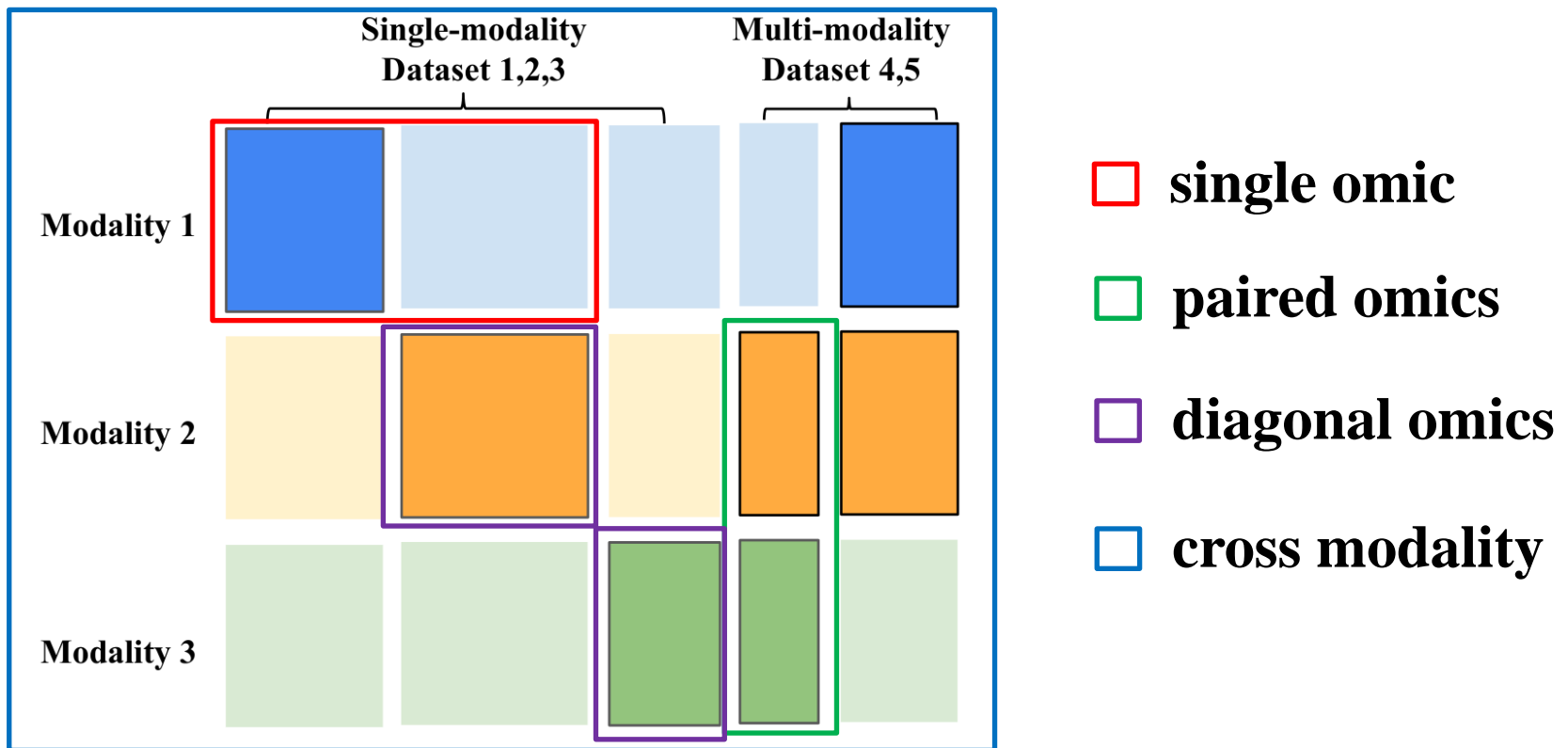
- More complicated.
- *More noise and lower quality.*

modality	technology	Avg. counts	Non-zeros
Multi-modal	sci-CAR	1600	2.19%
scRNA-seq	10X RNA	7589	9.65%
scATAC-seq	10X ATAC	15902	6.81%

Bock C. et al. *Trends Biotechnol.* (2016)

单细胞多组学 *integration task*

- Single omic integration: batch effect.
- Multiple omics integration: different feature spaces + different distributions



Tu X. et al. *NeuralIPS*. (2022)

空间转录组学

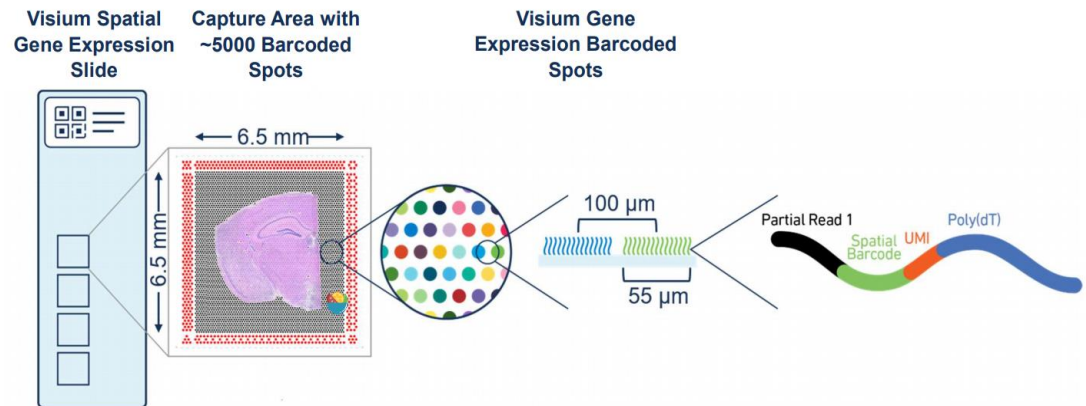
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空间转录组学 *spatial transcriptomics*

Spatial Transcriptomics (ST) profiles gene expression while retaining *spatial information*.

- Image based: high resolution, low depth;
- Sequencing based: high throughput, (low) resolution.
 - Slide-seq (v1, 2019; v2, 2021)
 - 10x Visium (2019)
 - HDST (2019)
 - Stereo-seq (2022)



<https://www.10xgenomics.com/>

空间转录组学 *comparing with scRNA-seq*



Bulk RNA-seq

Avg. expr. of cells



scRNA-seq

expr. of single cell

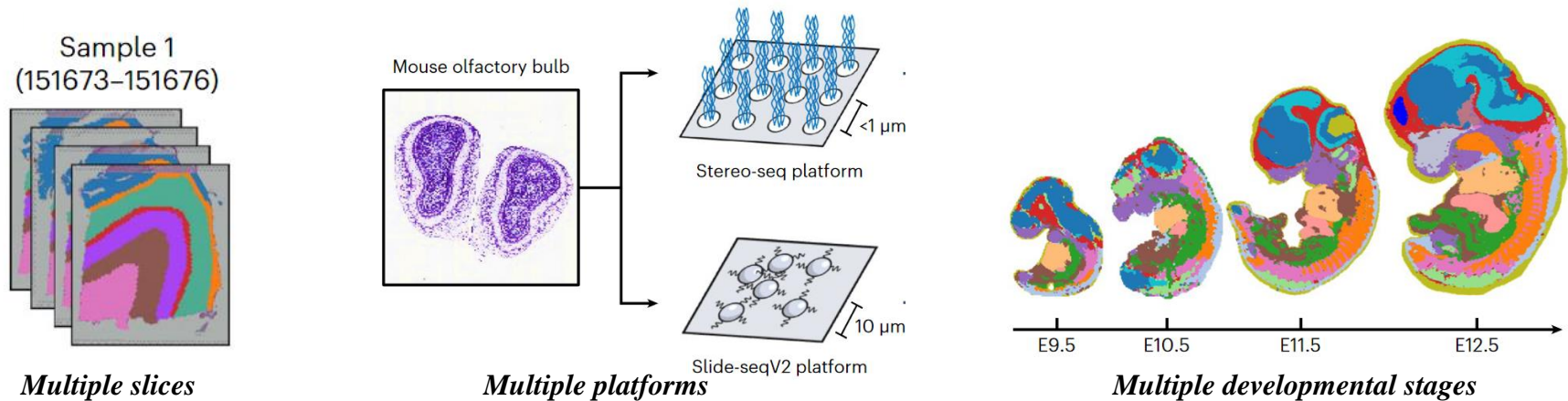


ST

Spot expression
+locations+(histology)

空间转录组学 *integration of ST data*

- **Clustering.** Identify different spatial domains.
- **Integration.** Integrate multiple samples.
- **Deconvolution.** Decipher cell type proportions in each spot.
- **Highly variable gene (HVG) detection.** Detect HVGs of specific domain.



Zhou X. et al. *Nat. Comput. Sci.* (2023)

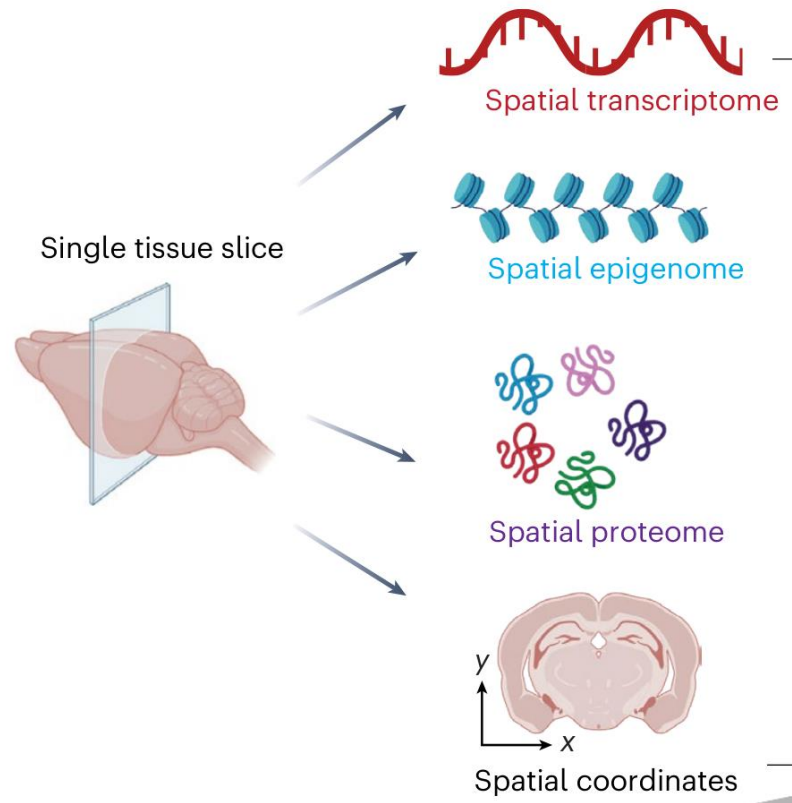
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空间多组学 *spatial multi-omics*

■ *Spatial locations + multi-omics data.*



Long Y. et al. *Nat. Methods* (2024)

Video links

See these videos for more details:

- Jin W. <https://www.youtube.com/watch?v=1SfRob9Y-4g>
- Cao Z. https://www.youtube.com/watch?v=cJ_I1_UzXbc&t=4579s
- Li R. <https://www.youtube.com/watch?v=7O26mRoJbMQ&t=127s>
- Li Y. <https://www.youtube.com/watch?v=CE-T-L1EX5I&t=4298s>
- Jin S. <https://www.youtube.com/watch?v=GNU0SwVr948&t=1032s>
- Tian Y. <https://www.youtube.com/watch?v=4b4lrY7DJIo>

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