

Recent developments in single-cell multi-omics and spatial transcriptomics sequencing

Qin Ma, PhD

Professor and Section Chief of Computational Biology and Bioinformatics
Department of Biomedical Informatics

Leader of the Immuno-Oncology Informatics Group
Pelotonia Institute for Immuno-Oncology



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What is scMulti-omics?

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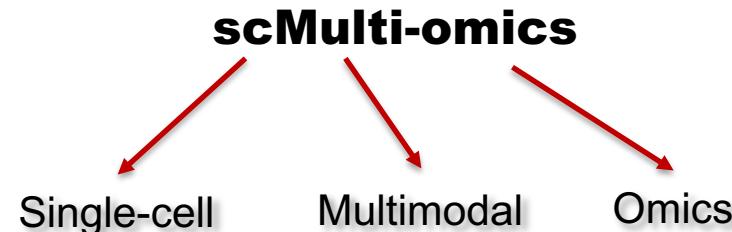
Method of the Year 2019: Single-cell multimodal omics

[Nature Methods](#) 17, 1 (2020) | [Cite this article](#)

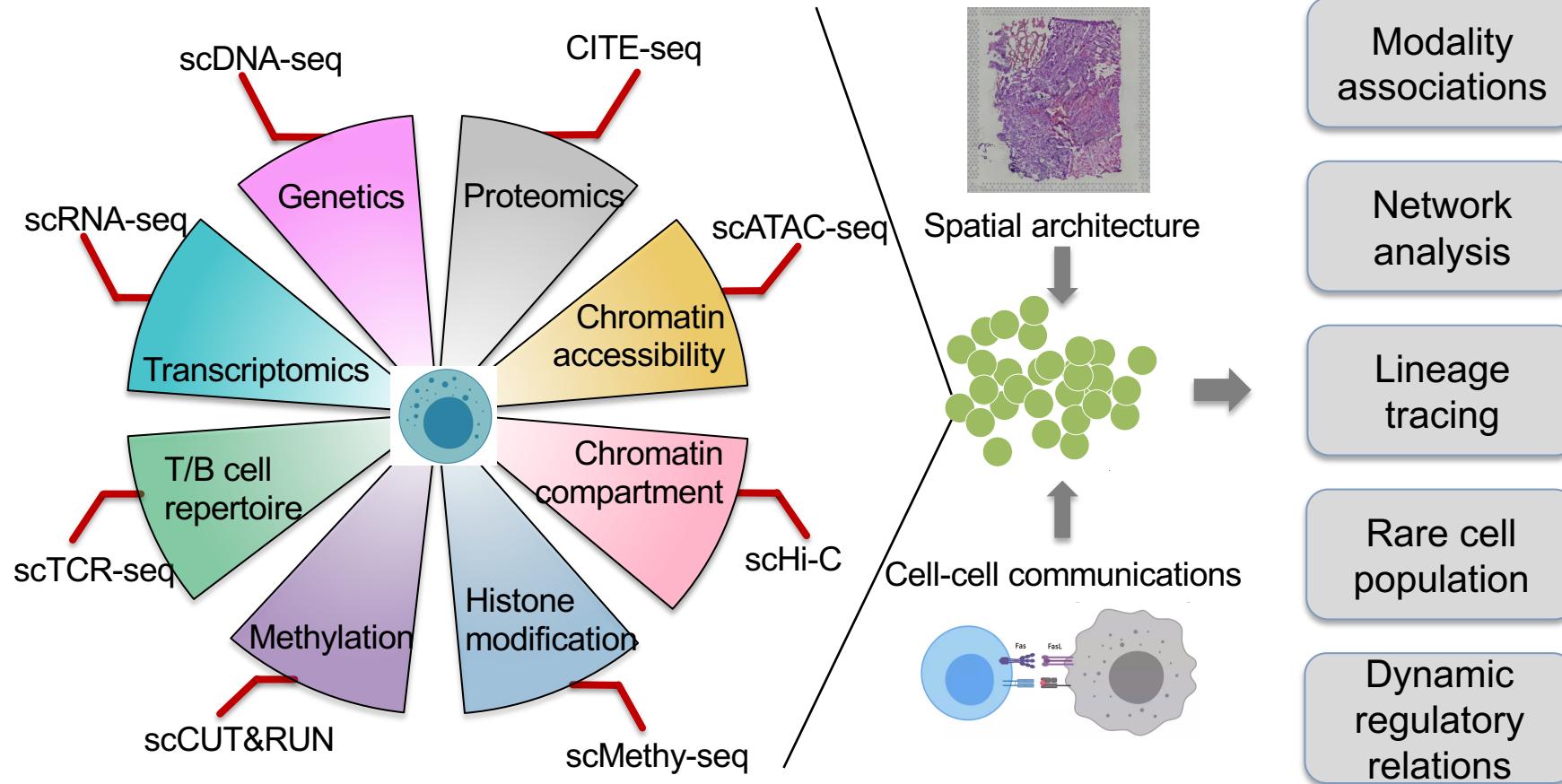
Single-cell data \neq scRNA-seq data

scRNA-seq is only one modality

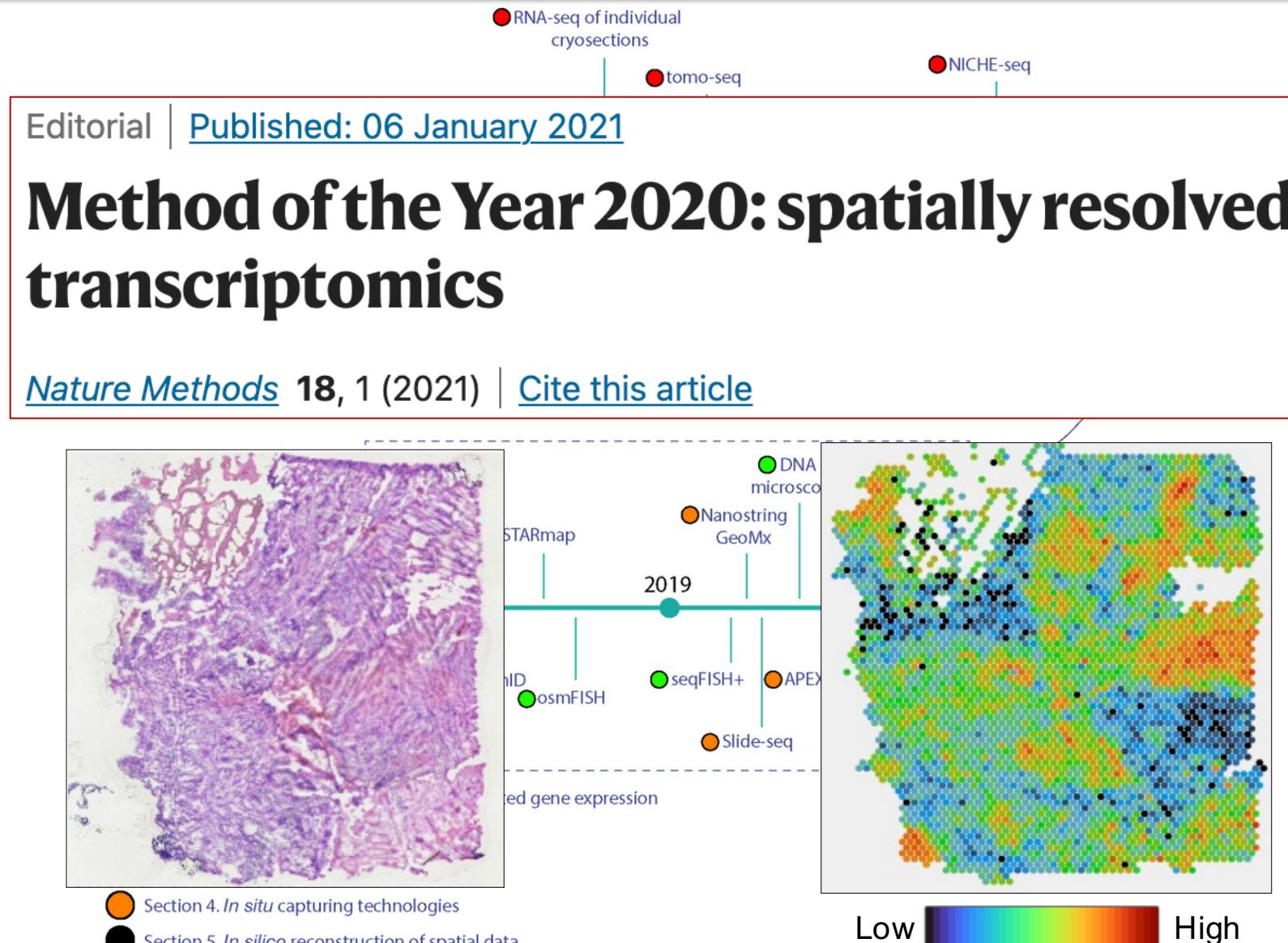
We have multiple modalities



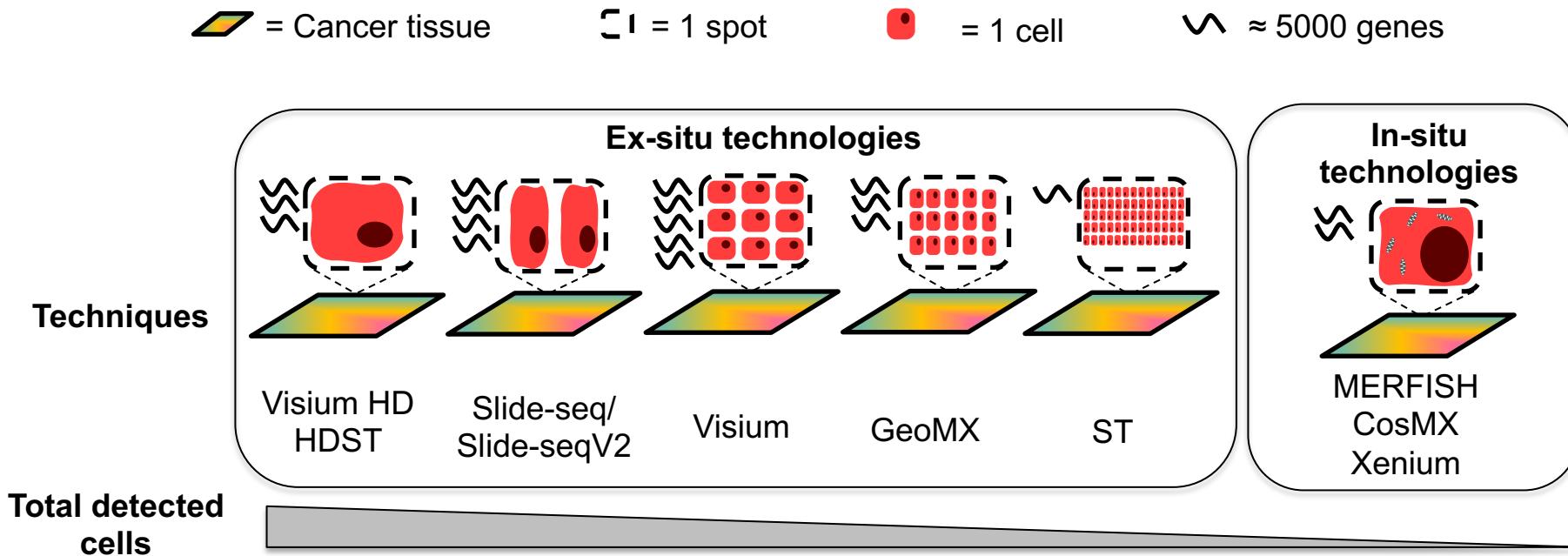
scMulti-omics enhance and enable various biological analyses



What is spatially resolved transcriptomics?



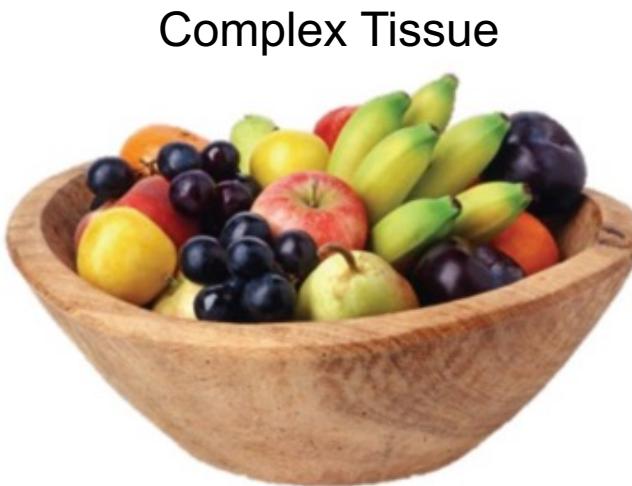
Spatial transcriptomics technologies



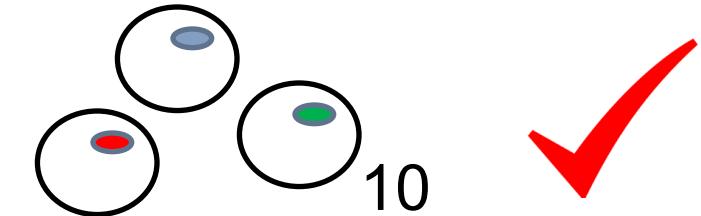
Take home message:

- In-situ technology (image-based) have a higher resolution.
- Ex-situ technology (sequencing-based) have a higher cell through and higher gene depth.

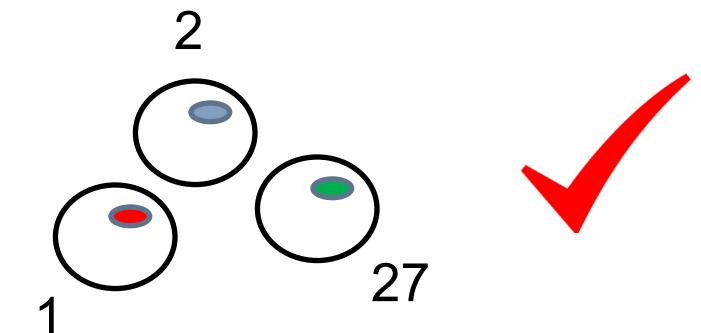
Understanding complexity using sequencing



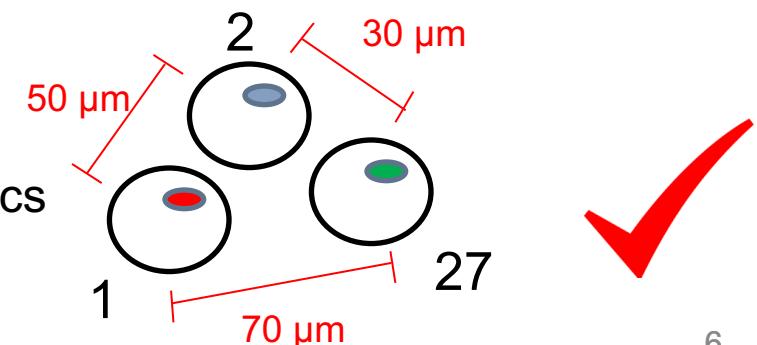
Bulk Genomics



Single Cell Genomics



Spatial Transcriptomics

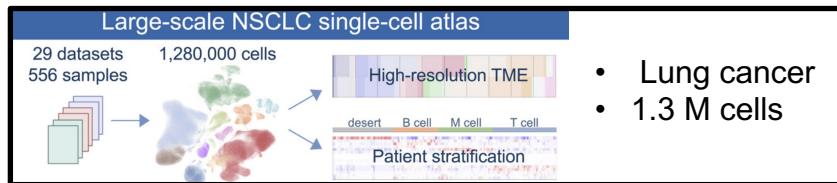


Big data in single-cell biology and spatial biology

Single-cell database



- Pan cancer
- 2.3 M cells



- Lung cancer
- 1.3 M cells



- Lung cells
- 2.4 M cells



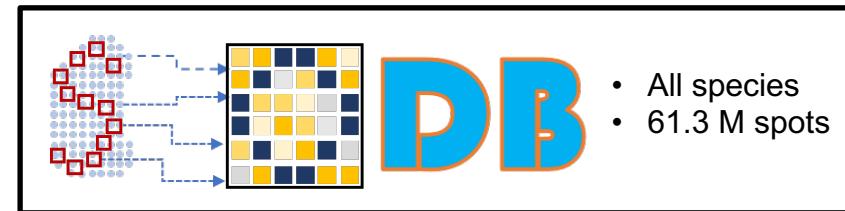
- Human cells
- 59.4 M



- Human cells
- 50.1 M



Spatial database database



- All species
- 61.3 M spots



- 128 tissues
- 221 datasets
- 17 species



- 2,785 samples
- 304 datasets
- 40 tissues



- 20k+ samples
- 20+ disease
- 200+ proteins



- 6.5K ROIs
- 15.7 M Spots
- 30 disease

Three “V” define big data:

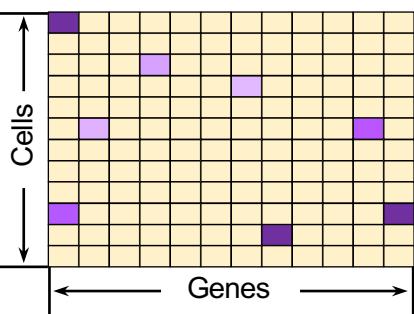
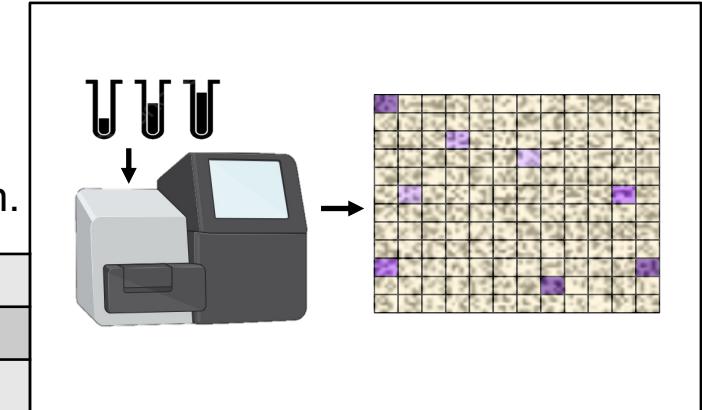
- High Volume
- High Velocity
- High Variety

Challenges in single-cell and spatial omics data

Technology noise

- Technology noise in single-cell and spatial omics data, such as amplification biases, batch effects, and droplet-based artefacts, can obscure true biological signals by introducing inconsistencies from sample preparation to data acquisition.

Single-cell data	Spatial data	
	Single-cell level	Bulk-level
✓	✓	✓



Data sparsity

- Data sparsity in single-cell and spatial omics refers to the phenomenon where many measurements (e.g., gene expression levels) contain a high proportion of zeros, indicating that no transcripts were detected for many genes in many cells.

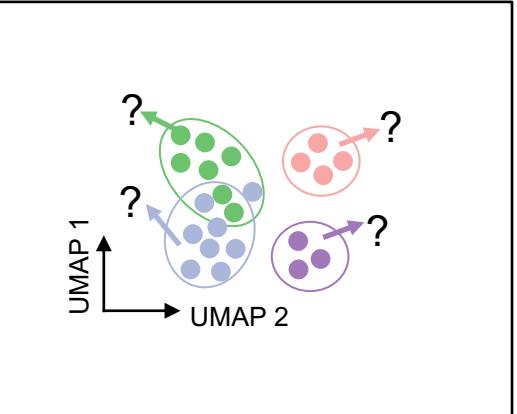
Single-cell data	Spatial data	
	Single-cell level	Bulk-level
✓	✓	

Challenges in single-cell and spatial omics data

Limited labeled data

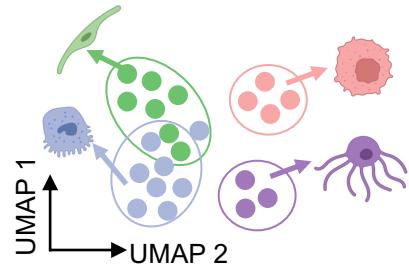
- Limited labeled data in the context of single-cell and spatial omics refers to the scarcity of annotated samples where specific cell types, states, or spatial features are identified and verified, typically through expert knowledge or additional experimental validation.

Single-cell data	Spatial data	
	Single-cell level	Bulk-level
✓	✓	✓



Heterogeneity

- Heterogeneity in single-cell and spatial omics data refers to the diverse and varied nature of biological samples at the cellular or subcellular level. This diversity can be due to differences in cell types, states, genetic expressions, or microenvironmental conditions within a tissue.



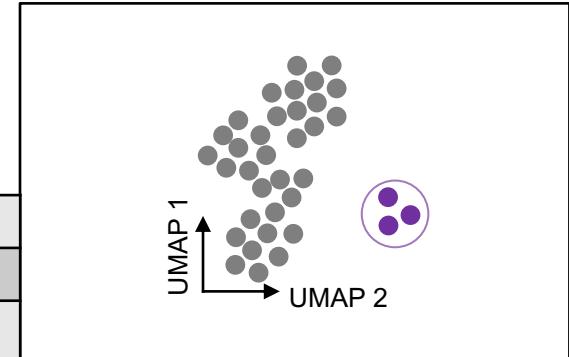
Single-cell data	Spatial data	
	Single-cell level	Bulk-level
✓	✓	✓

Challenges in single-cell and spatial omics data

Rare population

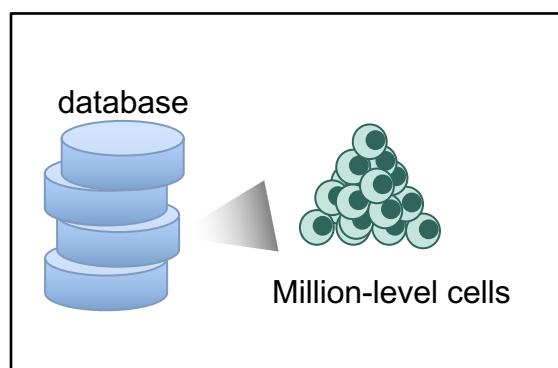
- Rare cell populations are infrequent yet crucial groups of cells within larger populations, significantly impacting biological processes and disease outcomes. Their identification and analysis offer profound insights into disease mechanisms and therapeutic targets.

Single-cell data	Spatial data	
	Single-cell level	Bulk-level
✓	✓	✓



Large scalability

- This scalability issue involves not only computational demands, such as storage, memory, and processing speed, but also analysis challenges in managing the high dimensionality and complexity of the data to extract meaningful biological insights.



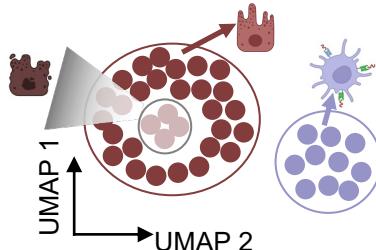
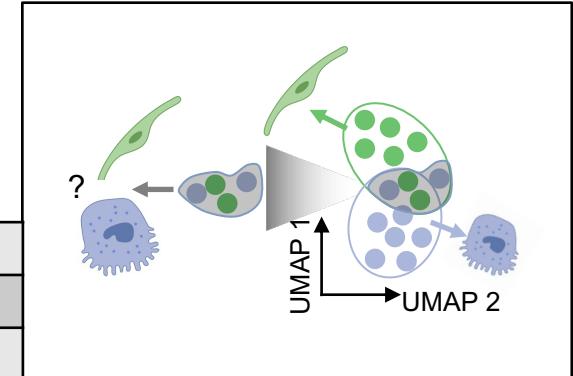
Single-cell data	Spatial data	
	Single-cell level	Bulk-level
✓	✓	✓

Challenges in single-cell and spatial omics data

Undistinguished cell ambiguity

- It refers to the difficulty in clearly identifying and differentiating between closely related or transitional cell states due to overlapping or subtle differences in their molecular profiles. This ambiguity can complicate analyses, such as cell type classification or the mapping of developmental trajectories

Single-cell data	Spatial data	
	Single-cell level	Bulk-level
✓	✓	



Hierarchical cell identification

- In hierarchical cell identification, ambiguity might arise when cells share properties with several categories within the hierarchy, making it unclear at which level they should diverge in the classification tree.

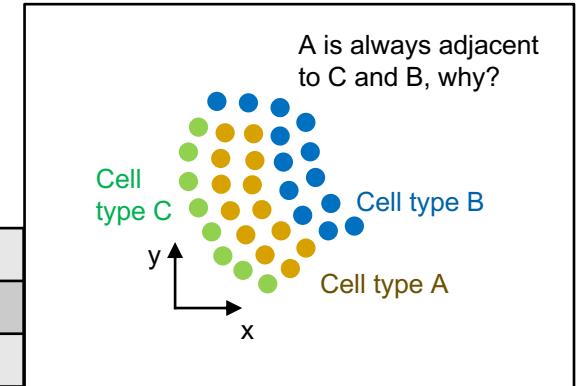
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	Single-cell level	Bulk-level
✓	✓	

Challenges in single-cell and spatial omics data

Uncertainty in spatial relationships

- Uncertainty in spatial relationships makes it difficult to provide accurate conclusions about cellular function and organization within the tissue context. For example, it would be hard to understand biological insights, like tissue functional units and cell-cell communication.

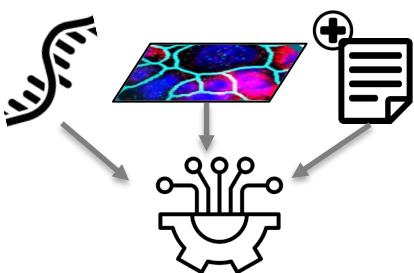
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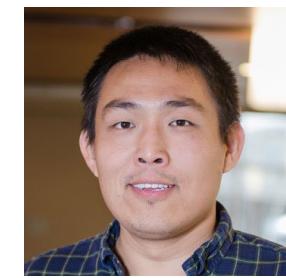
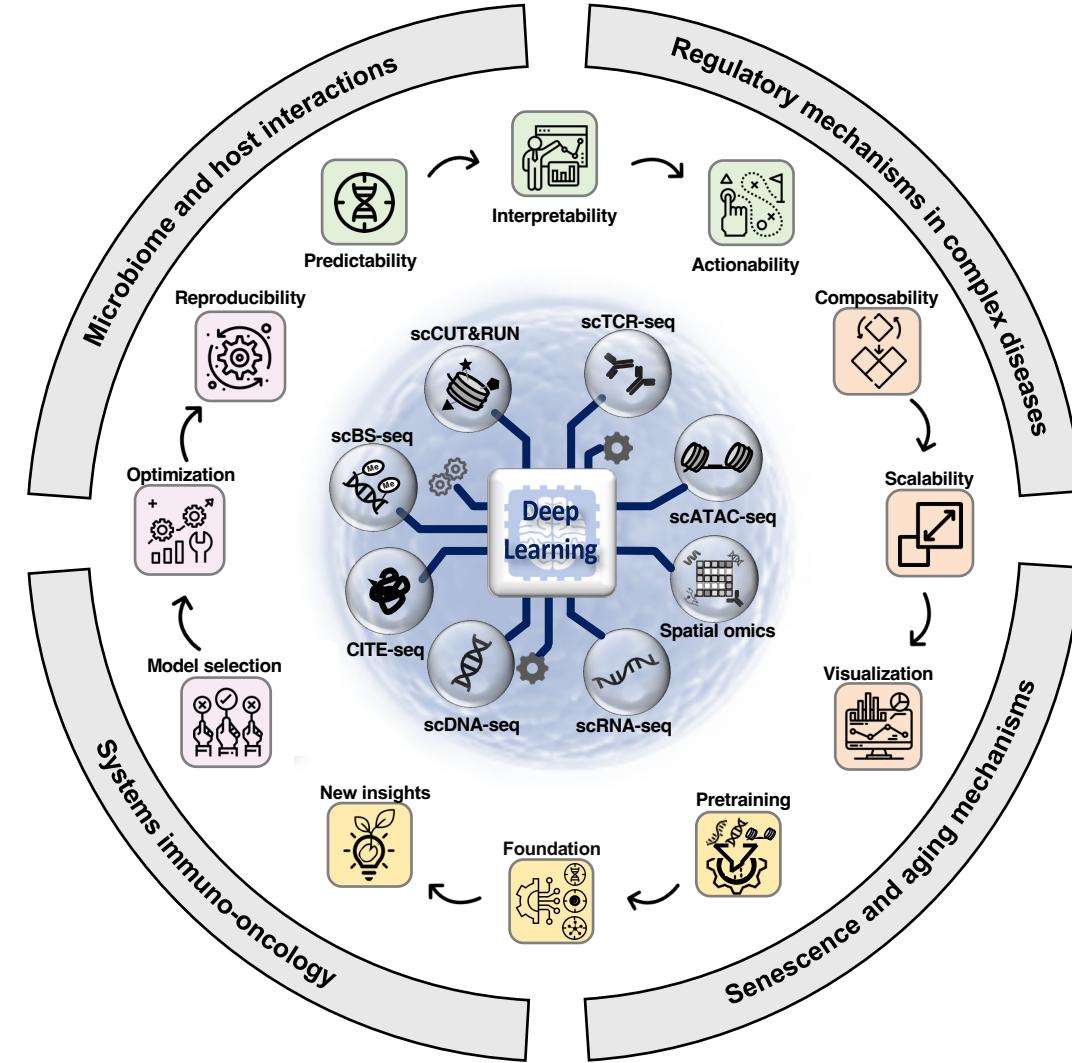


Integration gaps among complex multi-modalities

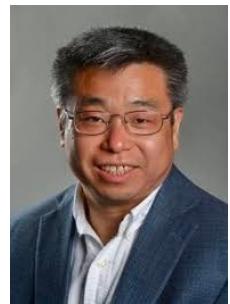
- It refers to the challenges in effectively combining data from different omics (like genomics, transcriptomics, and metabolomics) or from different technological platforms. These gaps can make it difficult to construct a comprehensive view of cellular function and organization.

Single-cell data	Spatial data	
	Single-cell level	Bulk-level
✓	✓	✓





Dr. Qin Ma
Professor, OSU

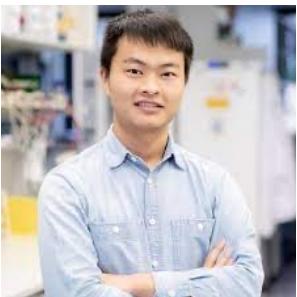
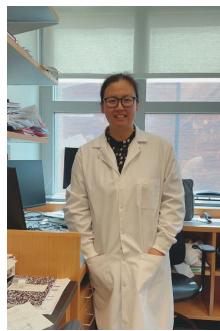


Dr. Dong Xu
Professor, MU

Ma, Q., et al. Deep learning shapes single-cell data analysis.
Nat Rev Mol Cell Biol (2022)

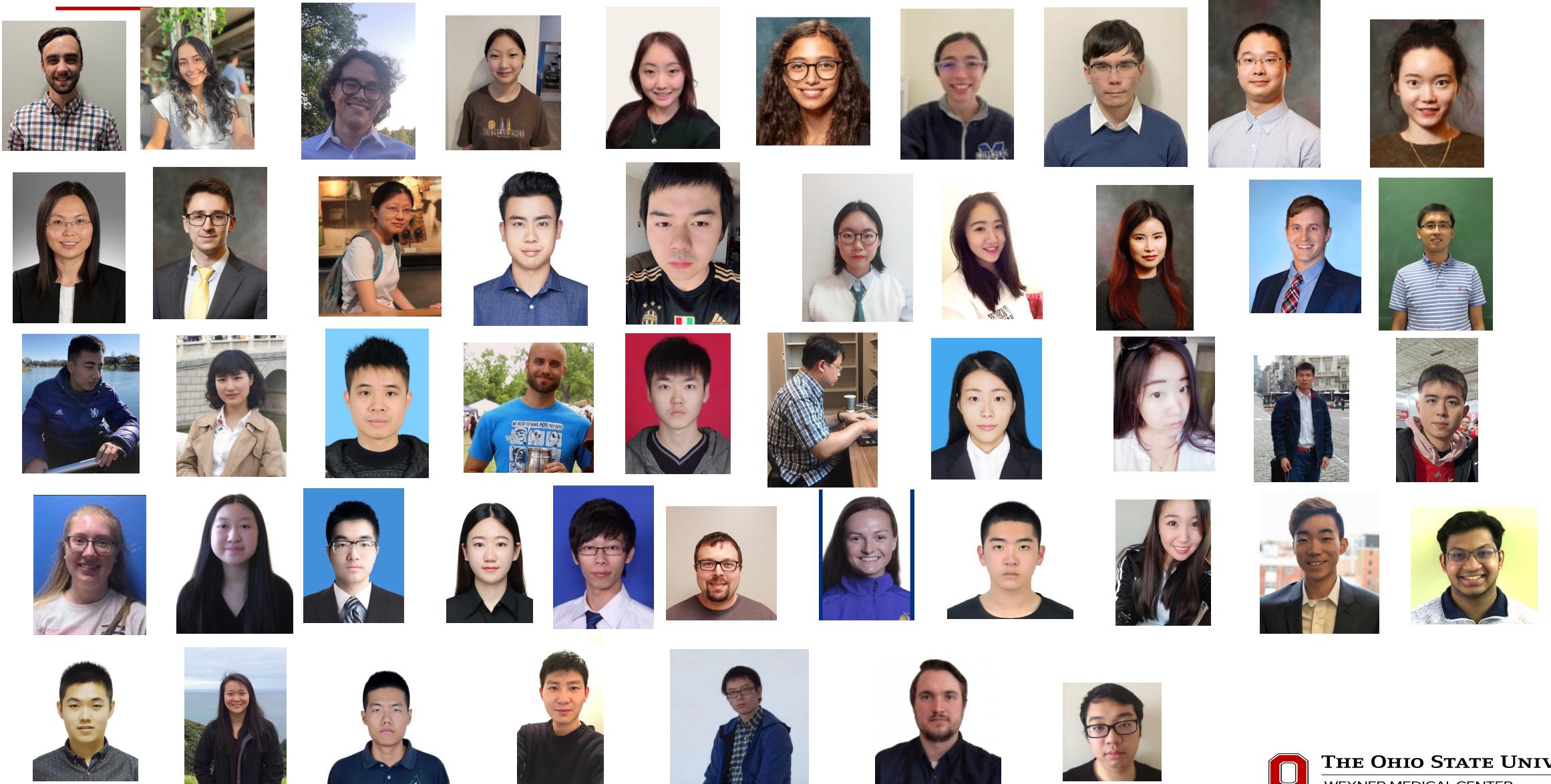
Ma, Q., et al. Harnessing the deep learning power of foundation models in single-cell omics. *Nat Rev Mol Cell Biol* (2024)

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Dr. Anru Zhang



<https://u.osu.edu/bmbl/>



@QinMaBMBL



Qin.Ma@osumc.edu

