# Workshop Introduction: Advances of AI Methods in Single Cell Spatial Omics

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The workshop "Advances of AI Methods in Single Cell Spatial Omics" will highlight recent developments in applying AI and machine learning to spatial transcriptomics, proteomics, and metabolomics. Featuring invited speakers and contributed talks, the program will cover methods for data integration, modeling cell–cell interactions, and translational applications to disease and precision medicine.

## 1. Background

Spatial omics technologies, including spatial transcriptomics, spatial proteomics, and spatial metabolomics, are rapidly redefining how we study biology at cellular resolution. By capturing both molecular information and spatial context, these technologies provide unprecedented opportunities to uncover the cellular architecture of tissues, the dynamics of cell–cell communication, and the molecular underpinnings of development and disease. In just a few years, spatial omics has expanded from pioneering proof-of-concept studies to large-scale applications across neuroscience, cancer biology, immunology, and precision medicine.

Despite this progress, the complexity of spatial omics data presents major challenges. Datasets are often high-dimensional, multimodal, and heterogeneous, with experimental protocols and spatial resolutions varying widely across platforms. Most technologies capture 2D tissue slices, leaving open the computational problem of reconstructing 3D tissue architecture. Moreover, extracting meaningful biological knowledge requires methods that can integrate spatial omics data with other modalities such as histology, imaging, and single-cell RNA-seq, while also ensuring reproducibility and interpretability. These challenges have created a unique opportunity for artificial intelligence

(AI) and machine learning (ML) methods, which are particularly well-suited for handling large-scale, complex, and noisy datasets.

## 2. Goal of workshop

The goal of this workshop is to bring together computational scientists, experimentalists, and biomedical researchers working at the intersection of AI and spatial omics. Through invited and contributed talks, the workshop will highlight recent methodological advances, explore open problems, and encourage discussion of future directions. Key themes include:

- AI-driven frameworks for integrating diverse spatial omics modalities and temporal data.
- Deep learning and generative modeling approaches for uncovering regulatory dynamics and reconstructing tissue-level organization.
- Methods to model and predict cell–cell interactions and signaling within tissue microenvironments.
- Development of scalable, generalizable, and interpretable foundation models for spatial omics.
- Translational applications, including biomarker discovery, drug repurposing, and the creation of clinically relevant tissue atlases.

## 3. Plan of workshop

This year's program features world-renowned invited speakers as well as eight contributed short talks, which together represent the breadth and depth of current innovation in this field.

The invited speakers are:

- Ben Raphael, Professor of Computer Science, Princeton University

  Ben Raphael is a leading researcher in computational genomics and cancer genomics, with a strong focus on spatial transcriptomics and tumor heterogeneity. His work has pioneered algorithmic methods for analyzing single-cell and spatial omics data, particularly in understanding cellular organization in cancer. His research has led to widely used computational tools for inferring spatial domains, tumor evolution, and network/pathway analysis of genetic variants.

- Theodore Alexandrov, Assistant Professor at the Department of Pharmacology, UCSD

  Theodore Alexandrov is a global expert in spatial metabolomics and computational mass spectrometry. He has developed machine learning methods to analyze spatial omics data, particularly for metabolite localization and tissue microenvironment profiling, with applications in drug discovery & therapy development.

- Xuegong Zhang, Professor, Tsinghua University

Xuegong Zhang is a pioneering researcher in computational biology and bioinformatics. His work focuses on developing AI-driven algorithms including foundation models to improve the analysis and interpretation of single cell multiomics data and spatially resolved gene expression data. His contributions have significantly advanced cell type identification, spatial domain detection, and embedding learning of cells. Xuegong currently serves as the vice-president of the International Society for Computational Biology (ISCB).

The selected contributed presentations address both core computational advances and real-world applications:

- *Learning mechanistic models of gene regulatory dynamics from spatial multi-omic datasets*
- *DeepCell at 10 years – AI for spatial biology*
- *STDrug: a computational method to use spatial transcriptomics to aid personalized drug-reposition recommendation*
- *A scalable human brain cell atlas foundation model dissects the cellular immune codes and cognitive resilience*
- *Mapping lineage-resolved scRNA-seq data with spatial transcriptomics using TemSOMap*
- *CELLestial: an end-to-end spatial proteomics framework for rapid cell type annotation and interactive visualization at scale for foundation model fine-tuning and large-scale clinical trial analyses*
- *Inferring cell migration, differentiation, and signaling from spatial transcriptomics*
- *STHD: probabilistic cell typing of single spots in whole transcriptome spatial data with high definition*

By combining technical innovation with biological applications, these talks reflect the transformative potential of AI in unlocking new insights from spatial omics. We expect lively discussions on how to tackle existing challenges, best practices for reproducibility, and the future of spatially resolved single-cell analysis.

## 4. Conclusions

In sum, this workshop is particularly timely given the rapid evolution of spatial omics technologies and the accelerating adoption of AI in biomedical research. It will provide a dedicated forum for advancing computational methodology, fostering interdisciplinary collaboration, and inspiring the next generation of scientific discoveries at the interface of spatial biology and AI.