# Seminar Report

Date: October 4, 2024

Speaker: Dr. Lin Xu, PhD

- Assistant Professor, Department of Health Data Sciences and Biostatistics, SPH

- Department of Paediatrics, Medical School

- Member, Quantitative Biomedical Research Centre, Harold C. Simmons Cancer Centre

- UT Southwestern Medical Centre

His Previous Research Focus:

Dr. Lin Xu's work spans the intersection of machine learning, genomics, and Bayesian modeling, with a particular focus on integrating high-dimensional datasets. His contributions have been recognized with 27 research grants from institutions such as the NIH, CPRIT, and DoD.

Seminar Topic:

3D Reconstruction of Spatial Transcriptomics with Spatial Pattern Enhanced Graph Convolutional Neural Network

Dr. Xu's talk centred on the limitations of current methods for analysing spatially resolved transcriptomics (SRT) data, which predominantly rely on 2D spatial coordinates. He introduced “Spa3D”, an innovative algorithm leveraging graph convolutional neural networks (GCNN) and anti-leakage Fourier transforms to reconstruct 3D spatial patterns from 2D SRT data.

Motivation:

The growing field of biology, particularly transcriptomics, has made significant strides with technological advances, such as:

- 2020: Visium Spatial Gene Expression

- 2020: Spatially Resolved Transcriptomics

However, traditional methods, like “SpaGCN”, focus on 2D profiling, limiting the analysis of full 3D spatial information. The challenge arises in integrating multiple 2D slides to capture 3D spatial data.

Existing Challenges:

- Current models like “PASTE” align 2D slides but fail to provide true 3D reconstructions.

- Most integration methods require similarity between individual slides.

Spa3D Algorithm:

Dr. Xu’s “Spa3D” addresses these limitations by utilizing full 3D spatial coordinates. It enhances spatial patterns, constructing a GCNN-based model to achieve accurate 3D reconstruction. The approach ensures better performance in:

- Elucidating 3D spatial domains

- Mapping cell-cell communication

- Understanding organ-level tempo-spatial development patterns

- Identifying 3D spatial trajectories, particularly those missed by 2D models.

Key Applications:

1. Spatial Domains & Clustering:

Spa3D outperforms state-of-the-art methods in identifying spatial domains, crucial for understanding cellular behaviour in tissue sections.

2. 3D Spatial Trajectory:

Applied to datasets such as the \*\*mouse hypothalamus\*\* (MERFISH), Spa3D showed superior clustering accuracy over methods like PASTE.

3. Cell-Cell Communication:

In highly complex biological systems, understanding how cells interact in 3D space has been a limitation. Spa3D provides deeper insights into cell-cell signalling that traditional models could not capture.

Example Case Studies:

1. Brain Omics Dataset:

Spa3D revealed overlapping spatially variable genes in the DLPFC layer, correlating well with known DLPFC genes. Using tools like edgeR and the Seurat package, the model improved gene expression analysis.

2. Human Embryonic Heart Dataset:

This dataset demonstrated Spa3D's ability to map cellular organization against temporal spatial development patterns, highlighting its application in developmental biology.

3. Mouse Hypothalamus Dataset:

By analysing the 3D spatial trajectory, Spa3D surpassed PASTE in clustering accuracy, illustrating its advantage in more complex datasets.

Conclusion:

Dr. Lin Xu’s “Spa3D” offers a groundbreaking approach to transcriptomics, extending beyond the limitations of 2D-based methods. By fully incorporating 3D spatial information, Spa3D enhances the understanding of spatial biology, cell communication, and developmental processes. Its application to a wide range of SRT technologies, including Visium, Slide-seq, and STARmapPLUS, demonstrates its versatility and potential to revolutionize the analysis of spatially resolved datasets.

This seminar provided a comprehensive overview of the challenges and opportunities in spatial transcriptomics, with Spa3D representing a significant leap forward in reconstructing biological structures in three dimensions.