The Chinese University of Hong Kong
Department of Biomedical Engineering

Graduate Seminar – PhD Oral Defence

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Date	***:***	5 August 2025
Time	***:***	10:00 am
Venue	***:***	Room 1118, William M W Mong Engineering Building, CUHK

Title: Microfluidics-based High-Throughput Single-Cell Analysis

Cellular heterogeneity is prevalent even within isogenic populations due to genetic variations, phenotypic differences, and developmental discrepancies among cells. A wealth of evidence indicates that cellular heterogeneity commonly exists within isogenic or clonal populations. The analysis of cell-to-cell heterogeneity is recognized as crucial in biomedical research. Investigating chromatin open regions in different cells is a key method for determining whether proteins interact with DNA. Concurrently, the transcriptional regulation of these open regions plays a vital role in nearly all biological processes. Single-cell RNA sequencing (scRNA-seq) has emerged as an essential technique in molecular biology for studying genome function and disease progression. It is utilized for high-resolution analysis of differential gene expressions (DGE) and intra-population heterogeneity in tumor evolution. In recent years, single-cell analysis based on droplet microfluidics has rapidly advanced, revealing genetic differences at various developmental stages of organisms and heterogeneity in healthy and diseased tissues, thereby aiding in the exploration of the pathogenesis of various diseases. However, the currently proposed single-cell strategies based on microfluidics have not fully realized their advantages in terms of throughput, reaction efficiency, cost, and operability.

This thesis proposed a convenient method for synthesizing alginate microspheres based on molecularly loaded reverse micelles to synthesize alginate microspheres by transporting calcium chloride ($CaCl_2$) as cargo to fluorinated surfactant stabilized water-in-oil (W/O) droplets. A high-throughput single-cell platform was subsequently developed to perform single-cell ATAC-seq with high reaction efficiency and a low rate of doublets and multiplets. Lastly, high-throughput single cell full-length RNA-seq based on next-generation sequencing (NGS) platforms was made possible by an introduction of technical novelties on cDNA synthesis on polyacrylamide beads, Tn5 protein assembly in beads, barcode addition during droplet tagmentation. Taken together, the platforms developed in this thesis is expected to promote droplet microfluidics based single-cell analysis for different applications by improving the throughput, costs-effectiveness, and reaction efficiency.

***** ALL ARE WELCOME *****

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