COMPUTER AND CONTROL ENGINEERING

DAUIN - Single-cell Multi-omics for Understanding Cellular Heterogeneity

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Context of the research activity	Single-cell multi-omics analysis integrates data from multiple molecular layers (e.g., transcriptomics, epigenomicsm, proteomics) within individual cells to provide a deeper understanding of cellular heterogeneity. This project will develop computational methods for integrating and analyzing single-cell sequencing data, supporting disease modeling and therapy optimization. The proposed algorithms will be applied to open datasets to uncover novel insights into cell identity and lineage evolution.
Objectives	Single-cell technologies have transformed biology by enabling the analysis of individual cells within heterogeneous populations. These methods allow researchers to study cellular diversity, track cell lineage, and identify molecular signatures underlying disease progression. However, most computational tools have been developed for analyzing individual omic layers, failing to leverage the full potential of multi-omics integration. This project aims to develop novel computational frameworks for integrating single-cell multi-omics data, improving our ability to interpret complex biological systems. Research Objectives - Cell Subtype Identification: Develop and refine algorithms that identify cellular subtypes within heterogeneous populations by leveraging multi-omic measurements. - Lineage Trajectory Reconstruction: Design computational approaches for tracing cell differentiation and evolution using integrated multi-omics data. - Inter-omic Relationship Discovery: Investigate regulatory interactions between different omic layers to understand cellular processes at a systems level. Work Plan: Year 1: Foundational Work - Acquire domain-specific knowledge through literature review and

Objectives	coursework. - Collect and preprocess publicly available single-cell multi-omics datasets. - Develop initial algorithms for cell subtype identification. Year 2: Algorithm Development - Design and implement trajectory reconstruction methods to study cell differentiation and disease progression. - Apply machine learning and probabilistic models to infer lineage relationships. - Use multi-omics data to investigate mutation-driven transitions, particularly in cancer. Year 3: Computational Framework Development - Integrate developed methods into an open-source computational library for the bioinformatics community. - Ensure compatibility with established frameworks such as Bioconductor (R) and Python-based bioinformatics tools. - Validate methods through extensive testing on disease-related datasets. Impact and Applications The proposed research will have broad applications in: Cancer Research: Identifying mutation-driven changes in cell identity. Developmental Biology: Tracing cell fate decisions during organismal growth. Personalized Medicine: Using multi-omics data to optimize therapeutic interventions.

Skills and competencies for the development of the activity	Required skills: Strong programming skills (Python, R) Ability to work with large-scale datasets and high-performance computing environments. Knowledge of machine learning models Nice-to-have skills: Background in bioinformatics, or computational biology Experience with statistical modeling and multi-omics data analysis Familiarity with single-cell sequencing techniques (scRNA-seq, scATAC-seq)