# ZUOLIN CHENG

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#### **SUMMARY**

Highly skilled Ph.D. in Bioinformatics with 8+ years of experience in designing/implementing multi-omics data analysis pipelines & developing novel machine-learning/statistical models. Proficient in multiple programming languages, machine-learning/data-analysis libraries, and bioinformatics tools. Proven track record of successful data analysis enabling significant biological discoveries in cross-functional collaborative research.

### **CORE COMPETENCIES**

- Expertise: Bioinformatics, Machine Learning, Data Analysis, Statistical Modeling
- Programming languages: R, Python, MATLAB, C++, SQL
- Pipeline design: scRNA-seq, spatial transcriptomics, ATAC-seq, ChIP-seq, CUT&RUN, clinical data
- Tools: PyTorch, Scikit-Learn, NumPy, Matplotlib, Scanpy, Seurat, MACS3, STAR, etc.

## **EDUCATION**

Virginia Tech
PhD, Electrical Engineering
Arlington, VA, USA
Aug. 2015 – Dec. 2022

• Research areas: Bioinformatics; Machine Learning

Peking University Beijing, China

M.S., Electronic Science and Technology
• GPA: 3.87/4.0; Top Ranked: 1/30

### **WORK EXPERIENCE**

Virginia Tech
Cupertino, CA, USA
Research Associate
Feb. 2023 – Present

Lead omics data analysis in collaborative biological research studies, effectively facilitating scientific discoveries. Develop state-of-the-art Next Generation Sequencing (NGS) data analysis models and methods, providing user friendly tools to benefit a larger audience. Mentor and train junior graduate students in research practices.

#### GO-BERT, Cell Type Annotation for scRNA-seq Data Using Large Language Model (LLM)

<u>Data</u>: scRNA-seq data, Gene Ontology (GO);

- *Language*: Python, PyTorch
- Innovatively introduced GO knowledge into neural network architecture during supervised fine tuning,
   significantly enhancing cell type annotation performance, increasing F1-score to 0.76 (previously 0.69)
- o Reduced 31% parameters in fine tuning without loss of performance compared to the state-of-the-art
- Propose a domain-insight-based pretraining strategy for large-scale single-cell data, overcoming limitations of existing models (e.g. scBERT, scGPT, Geneformer) in capturing awareness of global context

## • A Machine Learning Model Unifying Various Omics Analysis Tasks

o Data: various types of omics/multi-omics data;

- *Language*: C++, R, MATLAB
- Unified various omics analysis tasks (e.g. scRNA-seq data normalization, cancer gene detection, single-cell
   GO term activity inference, etc.) by pinpointing the shared key mathematical problem behind them
- Developed a novel model of joint inference of multiple hidden factors by integrating sophisticated statistical/machine-learning techniques, enhancing confounding factor control in downstream analyses
- Proposed a highly efficient customized optimizer leveraging model structure & code optimization (C++),
   achieving scalability on large-scale real-world data (reduced running time: days to minutes)
- Developed user-friendly R packages on different OS (Windows, Linux, iOS), and shared them via GitHub

#### • Therapy Data Analysis for Non-Small Cell Lung Cancer Patients

- o <u>Data</u>: clinical data (medical record, RNA-seq, spatial transcriptomics), TCGA; <u>Language</u>: R, MATLAB
- o Design a pipeline of treatment effectiveness analysis for non-small cell lung cancer
- Successfully identified two patient clusters that both respond to "chemotherapy + immunotherapy" but have distinct highly active GO terms, revealing difference in underlying response mechanisms

# Virginia Tech, Computational Bioinformatics and Imaging Lab

Arlington, VA, USA

Graduate Research Assistant

Aug. 2015 - Dec. 2022

Developed innovative AI/ML and statistical tools for omics data analysis, including CMC, TySim, scRNA-seq normalization method, and algorithms for driving transcription factor inference. Designed and implemented pipelines for analyzing data in cross-functional projects, collaborating with biologists from leading institutions such as UT Southwestern Medical Center, Stanford University, and Cincinnati Children's Hospital Medical Center.

## • scRNA-seq Data Analysis to Uncover Microglial Heterogeneity During Development

o Data: scRNA-seg data;

*Language*: R

- Designed and implemented scRNA-seq data analysis pipeline, including sequence alignment (STAR, etc.), scRNA-seq normalization, clustering (graph-based), visualization (tSNE), DEG analysis (rank-sum test), pathway enrichment analysis (Fisher's exact test), pseudotime analysis (monocle3), etc.
- o Customized some modules in the pipeline, achieving best solutions to project-specific requests
- o Enabled biological discoveries, collaborating with Stanford University: revealed a novel microglia subset

## • Driving Transcription Factor Prediction

- Data: scRNA-seq, ChIP-seq (Unibind DB), DNase-seq (CistromeDB DB), Motif (JASPAR DB); Language: F
- Discovered a long-ignored key factor and integrated it into ML model, boosting the best record of disease driving TF detection based on large TF-gene binding database (38.8% to 49.0% on benchmark)
- o Identified and published a pivotal TF (Zfp36l1) in collaboration with Cincinnati Children's Hospital

#### Full-length scRNA-seq Data Normalization

o Data: scRNA-seq;

Language: R, C, C++

- Identified a key confounding factor (effective cDNA-length) ignored by previous analyses in scRNA-seq raw counts, by combining empirical data mining (high-throughput intermedia data of sequencing alignment) and theoretical reasoning (deep understanding of sequencing technologies)
- Proposed a ML algorithm to learn and address the factor during scRNA-seq data normalization, enhancing the accuracy of downstream differential expressed gene (DEG) detection (AUC: 0.886 to 0.938)

#### **PUBLICATIONS**

### TOTAL PUBLICATIONS: 13; TOTAL CITATIONS: 1415

- Li Q\*, Cheng Z\* (co-first author), ... & Ben A Barres. Developmental heterogeneity of microglia and brain myeloid cells revealed by deep single-cell RNA sequencing. Neuron. 2019 ("Best in Neuron 2018-2019")
- Weng Q, Wang J, Wang J, He D, **Cheng Z**, ... & Q Richard Lu. Single-cell transcriptomics uncovers glial progenitor diversity and cell fate determinants during development and gliomagenesis. *Cell stem cell*. 2019.
- Barclay K, Nora A, **Cheng Z**, Kim M, Zhou L, Yang J, Rustenhoven J, Mazzitelli J, et al. An inducible genetic tool for tracking and manipulating specific microglial states in development and disease. *Immunity*. 2024-05.
- Cheng Z, Wei S, Wang Y, Wang Y, Lu R, Wang Y, Yu G. An Efficient and Principled Model to Jointly Learn the Agnostic and Multifactorial Effect in Large-Scale Biological Data. *bioRxiv*. 2024:2024-04.
- Cheng Z, Wei S, Yu G. A Single-Cell-Resolution Quantitative Metric of Similarity to a Target Cell Type for scRNA-seq Data. *In 2022 IEEE International Conference on Bioinformatics and Biomedicine* (*BIBM*) 2022 Dec.
- Cheng Z, Cui X, Cui X, Lee CL. Self-heating burn-in pattern generation based on the genetic algorithm incorporated with a BACK-like procedure. *IET Computers & Digital Tech*. 2015 Nov;9(6):300-10.