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. Winner of the Best Annual Paper Award of Neuron journal.

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: Git, PyTorch, Scikit-Learn, NumPy, Matplotlib, Scanpy, Seurat, MACS3, STAR, etc.

WORK EXPERIENCE

Virginia Tech

Cupertino, CA, USA

Postdoctoral 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.

- Project 1: GO-BERT, Cell Type Annotation for scRNA-seq Data Using Large Language Model (LLM)
 - Data: 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
- Project 2: CMC, 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
- o 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)
- o Developed user-friendly R packages on different OS (Windows, Linux, iOS), and shared them via GitHub
- Project 3: Therapy Data Analysis for Non-Small Cell Lung Cancer Patients
 - Data: clinical data (medical record, RNA-seq, spatial transcriptomics), TCGA;
 Language: 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 Graduate Research Assistant

Arlington, VA, USA Aug. 2015 – Dec. 2022

Developed innovative AI/ML and statistical tools for omics data analysis, including 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 and clinicians from leading institutions such as Stanford University, Cincinnati Children's Hospital Medical Center, and the Salk Institute.

• Project 1: scRNA-seq Data Analysis to Uncover Microglial Heterogeneity During Development

- o <u>Data</u>: scRNA-seq data; <u>Language</u>: R
- Designed and implemented scRNA-seq data analysis pipeline, including sequence alignment (STAR, etc.), scRNA-seq normalization, clustering (graph-based), data visualization (tSNE), DEG analysis (rank-sum test), pathway enrichment analysis (Fisher's exact test), pseudotime analysis (monocle3), etc.
- 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

• Project 2: Driving Transcription Factor Prediction & Glial Progenitor Development Study

- o <u>Data</u>: scRNA-seq, ChIP-seq (Unibind DB), DNase-seq (CistromeDB DB), Motif (JASPAR DB); <u>Language</u>: R
- 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

Project 3: Full-length scRNA-seq Data Normalization

- o <u>Data</u>: scRNA-seq; <u>Language</u>: 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)

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

PUBLICATIONS

TOTAL PUBLICATIONS: 13; TOTAL CITATIONS: 1400 +

- Li Q*, Cheng Z* (co-first author), Zhou L, ... & Tony Wyss-Coray, Ben A Barres. Developmental heterogeneity of microglia and brain myeloid cells revealed by deep single-cell RNA sequencing. *Neuron*. 2019; 101(2)
- 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.
- 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.
- 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; 9(6):300-10.

AWARDS

• Best papers 2018-2019 published in Neuron