

Motivation Letter

My name is Pengfei Yin, and I recently graduated with a Master's degree from Southern University of Science and Technology. My master's research focuses on using computational and theoretical methods to explore how 3D chromatin organization is structured and functions utilizing omics data. With a background in molecular biology and computational biology, complemented by physics, mathematical modelling, and research experience in 3D genomics, I am excited about the opportunity to further study how lncRNAs play roles in 3D genome plasticity, in your lab.

I completed my BSc at the Ocean University of China, where I became deeply fascinated with figuring out the mechanisms underlying molecular biology, largely due to the influence of "Molecular Biology of the Gene". This book not only provides a comprehensive and systematic introduction to the development of molecular biology but also inspires me to consider how I might approach and resolve cutting-edge biological problems if I were in the researcher's shoes. What particularly struck me in the book was Francis Crick's series of groundbreaking contributions, which inspired me to consider how I might develop such deep insights. Gradually, I realized that I could enhance myself in three aspects: scientific qualities, ways of thinking, and basic knowledge (For more details: https://astudentfromsustech.github.io/about/about_0/). Since then, I have been systematically enhancing my ability to decipher biological mechanisms. In addition to conducting experiments, I also learned mathematical modeling, machine learning, and core courses for Physics students (including the 3 volumes of the Feynman Lectures on Physics).

After graduation, I joined Meizhen Zheng's Lab at Southern University of Science and Technology to study 3D genomics. When I first learned about 3D genomics, I was surprised by the idea that DNA can interact with DNA to regulate gene expression. Then, I realized it is similar to the working mechanism of enhancers. Later, I came to understand that, just as transcription factors bind to DNA (protein-DNA) to regulate transcription, these interactions fundamentally involve interactions between macromolecules. Furthermore, could RNA, DNA, and proteins play roles in functional regulation through mutual interactions? Now, lncRNA-mediated chromatin interaction is a hot research topic.

My thesis project is to use computational and theoretical methods to explore how active and inactive regions are functionally changed in *Drosophila's* 3D chromatin architecture in response to heat stress (For more details: https://astudentfromsustech.github.io/projects/project_0/). As my research progresses, I have accumulated a lot of knowledge about how 3D chromatin organization is structured and functions. I have also realized that this mode of regulation is very common, so it is necessary to delve into specific mechanisms, say the potential role of lncRNA in 3D genome plasticity. Additionally, this field is highly interdisciplinary, allowing for the integration of various omics technologies, imaging techniques, and polymer physics. Different technologies provide different perspectives for us to explore the underlying mechanisms. Just like a detective, piece together disparate clues to solve the enigmas of nature. In these moments, I truly appreciate the charm of intellect. I believe when time goes by, my curiosity about the mysteries of nature endures. Therefore, I want to continue exploring this field during my PhD.

My core research interest is to figure out the mechanisms about how 3D chromatin organization is structured and functions. I've realized that scientists often notice specific mechanisms and study them through comparisons, either by comparing natural occurrences or by introducing perturbations. Comparisons can be made between different developmental stages, stages of the cell cycle, cell populations, and even species (over sufficiently large timescales, this relates to evolution). Examples of perturbations include some kind of treatment and genome editing. This explains why I am very interested in single-cell techniques, development, and evolution.

So, I think the PhD project highly matches my interests and pursuits. And I am also confident that I can handle this project. My background in genomics, combined with physics and mathematics, enhances my analytical capabilities and understanding of biological phenomena. At the same time, it also facilitates my ability to better comprehend different research directions and collaborate effectively with others in a multi-disciplinary team. Furthermore, I have experience using computational and theoretical methods to explore how the genome is organized into different layers and its impact on gene expression and regulation. So, I can quickly dive into the research. Additionally, I can also conduct routine experiments or experiments for validation with some training. I am hopeful for the opportunity to contribute to and grow within your distinguished research group.

Pengfei Yin

No.1088 Xueyuan Blvd • Shenzhen, Guangdong China | (+86) 15072757732 | 12133074@mail.sustech.edu.cn

EDUCATION

Southern University of Science and Technology (SUSTech), Master of Science in Biology Aug. 2021–Jun.2024

Major: Systems Biology; **GPA:** 3.68/4 (ranking 1/72)

Learned 3D genomics, deep learning, Python programming, Linux, data analysis in multi-omics.

Research field: 3D genomics | Advisor: Dr. Meizhen Zheng

Ocean University of China (OUC), Bachelor of Science in Agriculture

Aug. 2013–Jun. 2018

Major: Aquaculture, **GPA:** 3.67/4

Gained a strong foundation in molecular biology. Additionally, I learned physics and mathematical modelling which enhanced my understanding of life's intricate systems.

RESEARCH EXPERIENCE

Department of Systems of Biology, SUSTech | Advisor: Dr. Meizhen Zheng | Aug. 2021–Jun.2024

Thesis project: Dynamic 3D structure and gene regulation of *Drosophila* under heat stress

Contribution: Led the analysis of the project.

- Hi-C has been used to study how the 3D genome organization of *Drosophila* responds to heat stress (Li et al., Molecular Cell. 2015 and Ray et al., PNAS 2019). However, H3K27ac and H3K27me3 are mixed in Hi-C, here we apply *in situ* ChIA-PET to enrich H3K27ac and H3K27me3 separately to further explore how active and inactive regions are functionally changed in 3D chromatin architecture in response to heat stress. This study demonstrated the dynamic 3D structures at the levels of A/B compartments and TADs, along with their impacts on gene regulation, in response to heat stress. Furthermore, it proposes a model for the dynamic 3D structures at the levels of A/B compartments under heat stress. (For more details: https://astudentfromsustech.github.io/projects/project_0/)

Project 2: Topologically associating domains (TADs) recognition using Faster RCNN

Contribution: Prepared the datasets, adapted the Faster RCNN which is a convolutional neural network (CNN) in deep learning, and detect the TADs structure.

- I adapted the Faster RCNN to detect TADs, an important structure in 3D genome organization.

Participated project 1: MCI-frcnn: A deep learning method for topological micro-domain boundary detection

Contribution: Prepared the datasets and answered one reviewer's question

- We adapted the Faster RCNN to detect the micro-domain, a structure in 3D genome organization.

Participated project 2: p53 regulation network in 5-FU treated colon-cancer cell line HCT116.

Contribution: Provided data analysis on A/B compartment and TADs levels

- We uncovered the landscape of p53-associated chromatin interactions using 3D genome technique (ChIA-PET) and proposed regulatory networks for p53 involving promoter-dominant and enhancer-dominant types.

College of Fisheries, Ocean University of China (OUC)

Key Laboratory of Mariculture of OUC | Advisor: Dr. Jingjing Miao | Sep. 2016–Jan. 2018

Thesis project: Construction of recombinant yeast expressing estrogen-related receptor (ERR) of the *Ruditapes philippinarum* (rpERR)

Contribution: Participated in designing the project and did the molecular biology experiments

- We constructed the recombinant yeast expressing rpERR for further environmental toxicology research.

Key Laboratory of Mariculture of OUC | Advisor: Dr. Hongwei Shan | Nov. 2014–Nov. 2015

Project 2: Screening and identification of probiotics in shrimp intestines and environment

Contribution: Participated in designing the project and did the microbiology experiments; As the team leader of the SRDP (Student Research Developing Program).

- We screened several kinds of probiotics which can possibly be used to improve the production of aquatic products.

SKILLS & INTERSTS

Research skills:

- My solid background in genomics, combined with physics and mathematics, enhances my understanding and analytical capabilities in biological phenomena.
- Python, Linux, high-performance computing (HPC), docker/singularity. Run and construct pipelines using snakemake (like ChIA-PET, Hi-C, RNA-seq, ChIP-seq/ATAC-seq). Data analysis in multi-omics (advanced). (Some projects are in my github: <https://github.com/astudentfromsustech>)
- Modify algorithms (like Faster RCNN) according to our own needs. Mathematical modelling. Machine learning.

Language: English (fluent), Chinese (native).

Interests: Go, Chinese chess. Football (won the championship), badminton, table tennis.

ACADEMIC & EDUCATIONAL ACTIVITIES

- Gave oral presentation in Southern University of Science and Technology 4th Academic Star (Nov. 2023, Shenzhen)
- Guided undergraduates to win the Third Prize in the Guangdong Regional Competition of the National College Students' Life Science Competition. (Mar. 2022–Aug. 2023, Shenzhen)
- Served as the TA of biostatistics lectured by Dr. Xi Chen. (Feb. 2022–Jun. 2022, Shenzhen)
- Participated in Shenzhen Cup and Ocean University of China Mathematical Modeling Competition as team leader, and won the third Prize. (Jun. 2017, Qingdao)
- Participated in organization of Technology Camp for Qingdao No.2 middle school students, as member of Ocean University of China College Marine Life Science Association Science Technology (Jul. 2014–Aug. 2014, Qingdao)

AWARDS

- Nov. 2023, Excellence Award of Southern University of Science and Technology 4th Academic Star (15/college)
- Jun. 2017, Third Prize of Shenzhen Cup and Ocean University of China Mathematical Modeling Competition
- Jun. 2017, Championship of College of Fisheries Football Tournament
- Nov. 2016, Third-Class Scholarship for Academic Excellence (7/40)
- Nov. 2016, Outstanding Student
- Nov. 2015, Second-Class Scholarship for Academic Excellence (5/40)
- Nov. 2015, Nov. 2014, Self-powerful Student Award (2/college)
- Nov. 2014, Outstanding Student
- Nov. 2014, First-Class Scholarship for Academic Excellence (1/40)

PUBLICATIONS

- Tian SZ*, Yin P, Jing K, Yang Y, Xu Y, Huang G, Ning D, Fullwood MJ*, Zheng M*. MCI-frcnn: A deep learning method for topological micro-domain boundary detection. *Front Cell Dev Biol.* 2022 Nov 30;10:1050769. doi: 10.3389/fcell.2022.1050769.
- Tian SZ[†], Yang Y[†], Ning D[†], Fang K[†], Jing K, Huang G, Xu Y, Yin P, Huang H, Chen G, Deng Y, Zhang S, Zhang Z, Chen Z, Gao T, Chen W, Li G, Tian R, Ruan Y*, Li Y*, Zheng M*. 3D chromatin structures associated with ncRNA roX2 for hyperactivation and coactivation across the entire X chromosome. *Science Advances.* 2024 Jul 26;10(30). doi: 10.1126/sciadv.ado5716.
- Jing K, Xu Y, Yang Y, Yin P, Ning D, Huang G, Deng Y, Chen G, Li G, Tian SZ*, Zheng M*. ScSmOP: a universal computational pipeline for single-cell single-molecule multiomics data analysis. *Brief Bioinform.* 2023 Sep 22;24(6):bbad343. doi: 10.1093/bib/bbad343.
- Tian SZ*, Li G, Ning D, Jing K, Xu Y, Yang Y, Fullwood MJ, Yin P, Huang G, Plewczynski D, Zhai J, Dai Z, Chen W*, Zheng M*. MCIBox: a toolkit for single-molecule multi-way chromatin interaction visualization and micro-domains identification. *Brief Bioinform.* 2022 Nov 19;23(6):bbac380. doi: 10.1093/bib/bbac380.
- Liu P, Miao J*, Song Y, Pan L, Yin P. Effects of 2,2',4,4'-tetrabromodipheny ether (BDE-47) on gonadogenesis of the manila clam *Ruditapes philippinarum*. *Aquat Toxicol.* 2017 Dec; doi: 10.1016/j.aquatox.2017.10.022.

Contact information of referees

Dr. Zhengyu Liang (research field: 3D genomics)

Institution: Southern University of Science and Technology, Shenzhen, China

Academic Position: Assistant Professor

Tel number: +86 0755-88011109

Email: liangzy@sustech.edu.cn

Internet address of referee: <https://www.sustech.edu.cn/zh/faculties/zhengyuliang.html>

Address: No.1088 Xueyuan Blvd, Shenzhen City, China

Dr. Jingjing Miao (my undergraduate tutor)

Institution: Ocean University of China, Qingdao, China

Academic Position: Associate Professor

Tel number: +86 13589296553

Email: jmiao@ouc.edu.cn

Internet address of referee: <https://scxy.ouc.edu.cn/2011/0316/c20710a24197/page.htm>

Address: No.5 Yushan Road, Shinan District, Qingdao City, China

Dr. Xi Chen (research field: single-cell techniques)

Institution: Southern University of Science and Technology, Shenzhen, China

Academic Position: Associate Professor

Tel number: +86 0755-88018497

Email: chenx9@sustech.edu.cn

Internet address of referee: <https://www.sustech.edu.cn/zh/faculties/chenxi.html>

Address: No.1088 Xueyuan Blvd, Shenzhen City, China