Q-BIO 2024 CONFERENCE

Shenzhen · China

July 26th - July 29th

CONTENTS

Introduction

Welcome to the 18th Annual Q-Bio Conference! The Q-Bio 2024 Conference will be held at Shenzhen, China from July 27 – July 29, 2024. It is jointly organized by Shenzhen Institute of Advanced Technology, Shenzhen Institute of Synthetic Biology and Peking University. The theme of this conference is "Predictive Modeling and Quantitative Principles in Complex Biological Systems".

The organizing committee has been working diligently to put together a very strong and comprehensive program, including three keynotes by James E. Ferrell from Stanford University, Jing-Dong Jackie Han from Peking University, Luonan Chen from Shanghai Institute of Biochemistry and Cell Biology, CAS. Our conference program also includes 20 invited talks, 13 contributed talks, poster sessions, and exciting social events that cover emerging challenges in fundamental theories and quantitative technologies of molecular and cellular biological systems.

With your full support, this conference attracts more than 230 researchers from all over the world. We hope that the conference will provide great opportunities for learning, networking, collaborations and recruiting. You will share the thoughts and ideas with conference guests, and receive inspirations from old research ideas and develop new ones. The local organizing committee and more than 15 student volunteers in SIAT have made a great effort to arrange the meeting logistics and social events in this conference. The social events include the cocktail dinner (Saturday, July 27 evening) and the banquet (Monday, July 29 evening). We believe this conference will be a memorable, interesting and enjoyable experience for all of you.

The city of Shenzhen enjoys a mild climate throughout the year, and is accessible from most cities across China. Shenzhen provides numerous opportunities for tour, shopping and lodging, etc. It is our sincere hope you have great opportunities to experience the wonderful activities during your stay in the beautiful city of Shenzhen.

Thanks again for coming to the Q-Bio 2024 Conference in Shenzhen!

Q-Bio 2024 Local Organizing Committee

Q-Bio 2024 Committee Members

Local organizers

Chenli Liu
Professor and Vice Precident
Shenzhen Institute of Advanced Technology, CAS

Xiongfei Fu
Professor
Director of Institute of Synthetic Biology,
Shenzhen Institue of Advanced Technology, CAS

Lei Dai
Professor
Center for Synthetic Microbiome
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Ping Wei
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Zheng Hu
Professor
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Shenzhen Institue of Advanced Technology, CAS

Zhiyuan Li
Assistant Professor
Peking University

Q-Bio organizing committee

- **Yi Jiang** *Georgia State University*
- **William S. Hlavacek** *Los Alamos National Laboratory*
- **Anne-Florence Bitbol** *Swiss Federal Institute of Technology in Lausanne*
- **Altan-Bonnet Gregoire** *Laboratory of Integrative Cancer Immunology NCI/CCR*
- **Minsu Kim** *Emory University*
- **Qiong Yang** *University of Michigan*
- **Prasad Ashok** *Colorado State University*
- **Shankar Mukherji** *Washington University in St. Louis*
- **Rosemary Braun** *Northwestern University*
- **Orna Resnekov**
- **Sahand Rahi** *Institute of Physics at EPFL*
- **Lei Dai** *Shenzhen Institute of Advanced Technology, CAS*
- **Ping Wei** *Shenzhen Institute of Advanced Technology, CAS*

Agenda

Friday, July 26, 2024

2:30-9:00 PM	**Registration and hotel check-in**	

Saturday, July 27, 2024

8:00-8:30 AM	**Sign-in**	
8:30-8:45 AM	**Moderator: Lei Dai**	
	Welcome speech	Chenli Liu *Shenzhen Institute of Advanced Technology, CAS*
8:45-9:30 AM	**Session 1** **Moderator: Chao Tang (*Westlake University*)**	
	Keynote talk: 'Switches and Waves in Biology'	James Ferrell *Stanford University*
9:30-10:00 AM	**Talk:** 'Understanding and engineering cell biology in space and time with programmable reaction-diffusion systems'	Scott M. Coyle *University of Wisconsin-Madison*
10:00-10:20 AM	**Talk:** 'Synthetic circuits for multicellular spatial patterning'	Sheng Wang *California Institute of Technology*
10:20-10:50 AM	**Break + Group Photo**	
10:50-11:20 AM	**Session 2** **Moderator: Leihan Tang (*Westlake University*)**	
	Talk: 'Nonreciprocity enables large-scale mechanical spiral wave in bacterial living matter'	Yilin Wu *Chinese University of Hong Kong*
11:20-11:50 AM	**Talk:** 'Acquisition and usage of sensory information in E. coli chemotaxis'	Keita Kamino *Academia Sinica*
11:50-12:10 PM	**Talk:** 'Rules of self-organisation in organoids: dynamics and morphology'	Linjie Lu *University of Strasbourg*
12:10-1:30 PM	**Lunch**	
1:30-2:00 PM	**Session 3** **Moderator: Zhuojun Dai (*Shenzhen Institute of Advanced Technology, CAS*)**	
	Talk: 'How do we discriminate a lethal, potentially pandemic-capable coronavirus from a 'common cold' coronavirus?'	Gerard Wong *The University of California, Los Angeles*
2:00-2:30 PM	**Talk:** 'From Cancer to Biofilms: Unveiling the Dance Between Cells and Materials'	Jinju (Vicky) Chen *Loughborough University*
2:30-3:00 PM	**Talk:** 'Activity, phase separation and nuclear architecture'	Gautam I. Menon *Ashoka University*
3:00-3:20 PM	**Talk:** 'Regulating biochemical dynamics through controlled phase-separated condensates'	Yuansheng Cao *Tsinghua University*
3:20-3:50 PM	**Break**	
3:50-4:20 PM	**Session 4** **Moderator: Xiao Yi (*Shenzhen Institute of Advanced Technology, CAS*)**	
	Talk: 'Models, Lies and Fluctuating Selection'	Antony M. Dean *University of Minnesota*
4:20-4:50 PM	**Talk:** 'Construction of Solution Landscapes of Complex Biological Systems'	Lei Zhang *Peking University*
4:50-5:20 PM	**Talk:** 'ACC-seq reveals chromatin condensate that stabilize intermediate expression levels'	Yingqing Li *Tsinghua University*
5:20-5:40 PM	**Talk:** 'The cyanobacterial circadian clock couples to pulsatile processes using pulse amplitude modulation'	Chao Ye *University of Warwick*
5:40-8:00 PM	**Cocktail + Poster session**	

Sunday, July 28, 2024

8:25-9:10 AM	**Session 5** **Moderator: Ping Wei (*Shenzhen Institute of Advanced Technology, CAS*)**	
	Keynote talk: 'Dynamical Systems Biology'	Luonan Chen *Shanghai Institute of Biochemistry and Cell Biology, CAS*

9:10-9:40 AM	**Talk:** 'Uncovering evolutionary and cellular dynamics from single-cell lineage trees'	Sahand Hormoz *Harvard Medical School*
9:40-10:10 AM	**Talk:** 'A theory of lineage-associated molecular similarity'	Allyson E. Sgro *Howard Hughes Medical Institute Janelia Campus*
10:10-10:30 AM	**Talk:** 'Enhanced Cellular Longevity Arising from Dynamic Perturbation'	Zhen Zhou *Interdisciplinary Research Center on Biology and Chemistry, CAS*
10:30-11:00 AM	**Break**	
11:00-11:30 AM	**Session 6** **Moderator: Lei Dai (*Shenzhen Institute of Advanced Technology, CAS*)**	
	Talk: 'Designing Flexible Protein Structures and Sampling Conformational Distributions with a Unified Model'	Haiyan Liu *University of Science and Technology of China*
11:30-12:00 PM	**Talk:** 'A synthetic protein-level neural network in mammalian cells'	Zibo Chen *Westlake University*
12:00-12:20 PM	**Talk:** 'Quantitative Framework for Synthetic Modular Transcription Units Across Biological Kingdoms'	Ye Chen *Shenzhen Institute of Advanced Technology, CAS*
12:20-1:30 PM	**Lunch**	
1:30-6:00 PM	**Half-day Excursion**	

Monday, July 29, 2024

8:25-9:10 AM	**Session 7** **Moderator: Zheng Hu (*Shenzhen Institute of Advanced Technology, CAS*)**	
	Keynote talk: 'AI and Aging'	Jing-Dong J. Han *Peking University*
9:10-9:40 AM	**Talk:** 'Statistical modelling of single cell transitions in RNA and DNA spaces'	Yuanhua Huang *Univeristy of Hong Kong*
9:40-10:00 AM	**Talk:** 'Exploring the noise filtering mechanism in early Drosophila embryogenesis'	Feng Liu *Hebei University of Technology*
10:00-10:20 AM	**Talk:** 'Learning Fate Choices and Cell Memory through Single-Cell Multi-Omic Lineage Tracing'	Shouwen Wang *Westlake University*
10:20-10:50 AM	**Break**	
10:50-11:20 AM	**Session 8** **Moderator: Wanze Chen (*Shenzhen Institute of Advanced Technology, CAS*)**	
	Talk: 'Decoding single cell replicational age in scATAC-seq data'	Yi Zhang *Euler Technology*
11:20-11:50 AM	**Talk:** 'Deciphering tumor origin and evolution with single-cell lineage tracing'	Zheng Hu *Shenzhen Institute of Advanced Technology, CAS*
11:50-12:10 PM	**Talk:** 'Geometric Quantification of Cell Phenotype Transition Manifolds with Information Geometry'	Miao Huang *Institute of Theoretical Physics, CAS*
12:10-1:30 PM	**Lunch**	
1:30-2:00 PM	**Session 9** **Moderator: Zhiyuan Li (*Peking University*)**	
	Talk: 'Spatiotemporal dynamics of bacterial chemotaxis'	Junhua Yuan *University of Science and Technology of China*
2:00-2:30 PM	**Talk:** 'Quantitative ecology of host-associated microbiomes'	Lei Dai *Shenzhen Institute of Advanced Technology, CAS*
2:30-2:50 PM	**Talk:** 'Emergent behaviors in complex microbial ecosystems'	Jiliang Hu *Massachusetts Institute of Technology*
2:50-3:10 PM	**Talk:** 'Ecological succession and the competition-colonization trade-off in microbial communities'	Juan E. Keymer *Shenzhen X-Institute*
3:10-3:30 PM	**Talk:** 'Predicting microbiome compositions and keystone species through deep learning'	Xu-Wen Wang *Harvard Medical School*
3:30-4:00 PM	**Break**	
4:00-4:30 PM	**Session 10** **Moderator: Tong Si (*Shenzhen Institute of Advanced Technology, CAS*)**	
	Talk: 'Impact of Transcription Factor Dosage on Reprogramming Heterogeneity via scTF-seq'	Wanze Chen *Shenzhen Institute of Advanced Technology, CAS*
4:30-5:00 PM	**Talk:** 'Synthetic bacterial orthogonal replication systems enable accelerated evolution'	Rongzhen Tian *MRC Laboratory of Molecular Biology*
5:00-5:20 PM	**Talk:** 'Inference and Verification of Time-varying Gene Regulatory Networks'	Haijun Gong *Saint Louis University*
6:00 PM	**Closing Banquet** **Banquet talk**	James Ferrell *Stanford University*

Introduction of Invited Speakers

James E. Ferrell, Jr.

Professor

Stanford University School of Medicine

Biography

Dr. James Ferrell was an undergraduate at Williams College, majoring in Physics, Mathematics, and Chemistry, and did graduate work at Stanford, receiving a Ph.D. in Chemistry and an M.D. degree. He was a postdoctoral fellow at UC Berkeley with G. Steven Martin. He has held faculty positions at the University of Wisconsin–Madison and Stanford University, where he is now a Professor of Chemical and Systems Biology and of Biochemistry. His lab is best known for their studies of cellular switches and oscillators, particularly in the area of cell cycle regulation.

Research field

Systems biology
Cell cycle regulation
Physical biology of the cytoplasm

Title

Switches and Waves in Biology

Abstract

Studies in Xenopus egg extracts have shown that the embryonic cell cycle is driven by an oscillator circuit built on positive feedback that makes the protein kinase Cdk1 turn on in an explosive fashion. This positive feedback also allows Cdk1 activity to spread via trigger waves, self-reinforcing fronts of Cdk1 activity that can propagate rapidly without ever slowing down or diminishing in amplitude. Trigger waves appear to be a recurring theme in long-range biological communication.
Our studies of trigger waves also led us to see that Xenopus cytoplasm can self-organize into cell-like structures, celluloids, which allow various aspects of cell biology to be perturbed and observed in powerful ways. Here we will present some of our recent work on signaling waves and the physical biology of the celluloid.

Jing-Dong J. Han

Professor

Peking University, College of Interdisciplinary Studies,
Center for Quantitative Biology

Biography

Prof. Jing-Dong Jackie Han obtained Ph.D. degree from Albert Einstein College of Medicine. She had her postdoctoral training at The Rockefeller University and Dana-Farber Cancer Institute. In 2004, she became an investigator/professor at the Institute of Genetics and Developmental Biology, Chinese Academy of Sciences. In 2010-2019, she was a director of the CAS-Max Planck Partner Institute for Computational Biology. In 2019, she became Boya professor at Peking University. Her research focuses on the structure and dynamic inference of molecular networks, using a combination of large-scale experiments and computational analysis to explore the design principles of the networks and to find how the complex phenotypes, in particular aging and stem cell development are regulated through molecular networks. She was awarded the NSFC Outstanding Young Scientist Award in 2006, and the Hundred Talent Plan Outstanding Achievement Award in 2009, selected as a Max Planck Follow in 2011 and a MaxNetAging Fellow in 2014, F1000 faculty in developmental biology in 2016.

Research field

1) Systems biology of development and aging
2) Computational inference of regulatory networks
3) Computational algorithm development for image analysis, data integration and network analysis

Title

AI and Aging

Abstract

Aging is a systems level process and needs systems level models to quantify. We have recently focused our attention on phenotypic images and single cell clocks using a combination of experimental and computational approaches, most recently artificial intelligence (AI). Our deep learning AI models trained on either chronological age or perceived age of the 3D facial images can precisely estimate individuals' aging status, and infer the molecular regulators mediating the impact of lifestyles (Xia et al., 2020). Further analysis of human aging related lncRNAs find that they are preferentially involved in senescence associated secretory phenotype and inflammation 1. We also found the highly abundant lncRNA KCNQ1OT1 through forming RNA-DNA Triplex targets and represses the evolutionarily young transposon elements in a sequence specific manner, thus guards the cells against genome instability and cellular senescence (Zhang et al., 2022). I will also discuss our recent results using AI to decipher aging and disease status (Zhu et al. 2023), and our recent Senescence Identification (SenCID) program for single cell senescence trajectory and perturbation analyses (Tao et al. 2024).

Luonan Chen

Professor

Shanghai Institute of Biochemistry and Cell Biology,
Chinese Academy of Sciences

Biography

Luonan Chen received BS degree in the Electrical Engineering from Huazhong University of Science and Technology, and the M.E. and Ph.D. degrees in the electrical engineering from Tohoku University, Sendai, Japan, respectively. From 1997, he was an associate professor of the Osaka Sangyo University, Osaka, Japan, and then a full Professor. Since 2010, he has been a professor and executive director at Key Laboratory of Systems Biology, Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences; Chair Professor of Hangzhou Institute for Advanced Study, University of Chinese Academy of Sciences. He was elected as the founding president of Computational Systems Biology Society of OR China, and Chair of Technical Committee of Systems Biology at IEEE SMC Society. In recent years, he published over 400 journal papers and four monographs (books) in the area of bioinformatics, nonlinear dynamics and machine learning.

Research field

Systems biology, bioinformatics, nonlinear dynamics, AI

Title

Dynamical Systems Biology

Abstract

I will present a new concept "Dynamical Systems Biology" for quantifying dynamical processes, disease progressions and various phenotypes, including dynamic network biomarkers (DNB) for early-warning signals of critical transitions, spatial-temporal information (STI) transformation for short-term time-series prediction, partial cross-mapping (PCM) for causal inference among variables, and further AI applications to medicine. These methods are all data-driven or model-free approaches but based on the theoretical frameworks of nonlinear dynamics. We show the principles and advantages of dynamical data-driven approaches for phenotype quantification as explicable, quantifiable, and generalizable. In particular, different from statistical data-science, dynamical data-science approaches exploit the essential features of dynamical systems in terms of data, e.g. strong fluctuations near a bifurcation point, low-dimensionality of a center manifold or an attractor, and phase-space reconstruction from a single variable by delay embedding theorem, and thus are able to provide different or additional information to the traditional approaches, i.e. statistics-based data science approaches. The dynamical data-science approaches for the quantifications of various phenotypes will further play an important role in the systematical research of various fields in biology and medicine.

Jinju (Vicky) Chen

Professor, Chair in Advanced Materials and Biointerfaces;
Research Director

Loughborough University

Biography

Jinju (vicky) Chen is a Professor and Chair in Advanced Materials and Biointerfaces at Loughborough University. Her passion lies in tackling fundamental scientific questions at the intersection of cells and materials. This knowledge is then translated into innovative materials designs, aiming to accelerate breakthroughs in human disease treatment and biofilm control. She has received over £9.3M from a wide range of funding agencies. Her research has garnered significant recognition, evidenced by her publication of 82 peer-reviewed journal papers and 83 invited talks. She is an elected Fellow of Royal Microscope Society and member of UKRI Talented Panel College. She is a Principal Editor of Journal of Materials Research, Editorial Board Member of Colloids and Surfaces B: Biointerfaces.

Research field

Biophysics of bacteria and biofilms using experimental and modelling approaches, biomechanics of mammalian cells, biointerfaces, bio-inspired materials.

Title

From Cancer to Biofilms: Unveiling the Dance Between Cells and Materials

Abstract

This talk delves into the fascinating world of cell mechanics and material interactions, exploring how cells sense and respond to their physical environment. I will begin by examining cell mechanics, focusing on how cancer or fibroblast cells interact with materials. This section will highlight how materials stiffness influence the behavior of cancer cells or fibroblast cells, which has potential for advancements in tissue regeneration, and the development of novel diagnosis strategies.

Next, I'll shift gears to explore bacteria-material interactions. I'll discuss how bacteria adhere to surfaces and form biofilms, which are complex communities of bacteria encased in a self-produced matrix. Understanding these interactions is crucial in combating bacterial infections associated with medical implants and devices.

Wanze Chen

Professor

Shenzhen Institute of Advanced Technology, CAS

Biography

Wanze Chen is a professor at Shenzhen Institute of Advanced Technology (SIAT), Chinese Academy of Sciences. Dr. Chen received his Ph.D. from Xiamen University, China. He then studied in the Laboratory of Systems Biology and Genetics as a postdoc at EPFL in Switzerland before establishing his lab at SIAT. The research focus of his lab is to understand and program the fate of stem cells. Driven by this primary interest, they actively develop and utilize multidisciplinary technologies, such as live cell RNA-seq, genome-wide genetics perturbation, miniaturized large-scale functional screening, etc. The current projects include stem cell in vitro expansion, single-cell RNA-seq-assisted cell programming, and microfluidic-based large-scale phenotyping.

Research field

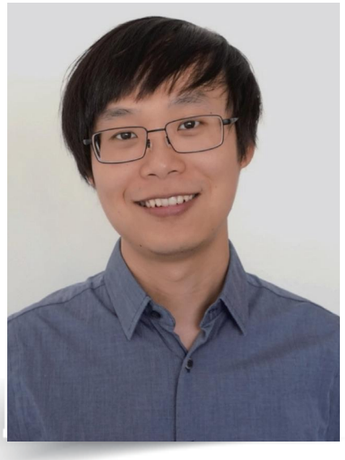
Single cell transcriptomics, Live-seq, Stem cell, Cell differentiation, Single cell analysis

Title

Impact of Transcription Factor Dosage on Reprogramming Heterogeneity via scTF-seq

Abstract

Reprogramming approaches often produce heterogeneous cell fates and the mechanisms behind this heterogeneity are not well-understood. To address this gap, we developed scTF-seq, a technique inducing single-cell barcoded and doxycycline-inducible TF overexpression while quantifying TF dose-dependent transcriptomic changes. Applied to mouse embryonic multipotent stromal cells (MSCs), scTF-seq produced a gain-of-function atlas for 384 murine TFs. This atlas offers a valuable resource for gene regulation and reprogramming research, identifying key TFs governing MSC lineage differentiation, cell cycle control, and their interplay. Leveraging the single-cell resolution, we dissected reprogramming heterogeneity along dose and pseudotime. We thereby revealed TF dose-dependent and stochastic cell fate branching, unveiling gene expression signatures that enhance our understanding and prediction of reprogramming efficiency. scTF-seq also allowed us to classify TFs into four sensitivity classes based on dose response and determining features. Finally, in combinatorial scTF-seq, we observed that the same TF can exhibit both synergistic and antagonistic effects on another TF depending on its dose. In summary, scTF-seq provides a powerful tool for gaining mechanistic insights into how TFs determine cell states, while offering novel perspectives for cellular engineering strategies.



Zibo Chen

Principal Investigator

Westlake University

Biography

Zibo Chen obtained his B.Sc. degree in Life Sciences with First Class Honours from National University of Singapore (2013). He received his Ph.D. degree in biochemistry with David Baker and Frank DiMaio at the University of Washington (2013-2018) and worked on synthetic biology with Michael Elowitz at Caltech as a Damon Runyon Fellow (2019-2022). He joined Westlake University in 2022 as an assistant professor.

Research field

The focus of the BioProgramming lab is to program biological behaviors by designing de novo proteins and protein circuits that encode information and collectively carry out user-defined computations in test tubes and living cells. Research projects in the lab span from fundamental questions to real-world applications, and can be broadly classified into the following directions:

1. Molecular Computing with Protein Circuits. We design protein-based circuits that programmably and robustly carry out computations both inside and outside of cells, enabling one to predictably control cell functions. Circuit components are proteins designed from scratch using Rosetta, which allows full customization of their functionalities at the single molecule level.

2. Programmable Self-assembly of Proteins. Proteins in nature self-assemble into cages, fibers, sheets, and crystals that are critical to cellular functions. In most cases, the algorithms governing such assemblies are embedded in local interactions between adjacent proteins, allowing complex structures to autonomously arise from simple building blocks. We design information-bearing proteins that programmably assemble into desired shapes, which can provide versatile supramolecular structure motifs to study and alter cellular functions.

Title

A synthetic protein-level neural network in mammalian cells

Abstract

Artificial neural networks provide a powerful paradigm for information processing that has transformed diverse fields. Within living cells, genetically encoded synthetic molecular networks could harness principles of neural computation to classify molecular signals. Here, we combine de novo designed protein heterodimers and engineered viral proteases to implement a synthetic protein circuit that performs winner-take-all neural network computation. This “perceptein” circuit includes modules that compute weighted sums of input protein concentrations through reversible binding interactions, and allow for self-activation and mutual inhibition of protein components using irreversible proteolytic cleavage reactions. Altogether, these interactions comprise a large network of chemical species and reactions involving diverse cleavage products of up to 10 co-expressed starting protein species. The complete system achieves multi-output signal classification with tunable decision boundaries in mammalian cells, and can be used to control cell death. These results demonstrate how engineered protein-based networks can enable programmable signal classification in living cells.

Scott Coyle

Assistant Professor

University of Wisconsin-Madison, Department of Biochemistry

Biography

Scott Coyle earned his Bachelor's degree in Biochemistry from the University of California, Berkeley. He went on to obtain his Ph.D in Biochemistry at UCSF in Wendell Lim's group, and commercialized technologies he developed as a student as a Founding Scientist at the immunotherapy startup CellDesignLabs. As a postdoc in Manu Prakash's lab at Stanford University, he defined how dynamic cell behaviors could arise from patterns of oscillating control signals. In his own group, Scott is using synthetic biology to develop biochemical programming interfaces that expand our ability to understand and engineer dynamic cell biology. A major focus of his group is to develop synthetic circuits that self-organize molecules in space and time within the cell, with novel applications for imaging, systems biology, and cell-engineering.

Research field

Synthetic biology, cell biology, systems biology, biochemistry

Title

Understanding and engineering cell biology in space and time with programmable reaction-diffusion systems.

Abstract

Cells self-organize molecules in space and time to generate complex behaviors, but we lack strategies for engineering spatiotemporal signaling. My group has developed programmable reaction-diffusion systems for the design of fast protein oscillations, patterns, and signaling circuits in mammalian cells, yeast, and multicellular systems. Our approach is based on repurposing bacteria-specific protein positioning systems of the SIMIBI NTPase super-family to act as orthogonal spatiotemporal signaling nodes inside cells. These systems are highly engineerable, allowing us to genetically encode specific protein dynamics or patterns, biochemically manipulate their behavior, and connect them to other nodes in cell biology using synthetic protein-protein or RNA-protein interactions. The resulting circuits can be used as "active probes" that amplify and encode endogenous cell dynamics in a barcoded frequency-domain data structure; or be used as "control signals" that synthetically pattern signaling activities or reorganize endogenous cellular components. By imposing additional spatiotemporal constraints on circuit components, patterns and oscillations can be confined to specific subcellular compartments and react to competing organizing mechanisms like nuclear/cytoplasmic shuttling or polarized membrane recruitment. Our work establishes a powerful suite of synthetic biology tools for visualizing, probing, and engineering cellular activities at length and timescales critical for biological function.

Lei Dai

Professor

Shenzhen Institute of Advanced Technology, CAS

Biography

Dr. Lei Dai is currently a Principal Investigator at the Shenzhen Institute of Advanced Technology (SIAT), Chinese Academy of Sciences. His research group at SIAT develops novel experimental and computational approaches to study the ecology of complex microbial communities and improve host health via precision microbiome engineering. His recent works have been published in Cell Host & Microbe, Nature Communications, ISME Journal, iMeta, etc. Dr. Dai received B.S. in Physics at University of Science and Technology of China and Ph.D. in Physics at Massachusetts Institute of Technology. He was a Jane Coffin Childs postdoctoral fellow at UCLA School of Medicine.

Research field

Microbiome; Ecology and Evolution; Synthetic Biology

Title

Quantitative ecology of host-associated microbiomes

Abstract

The realization that microbiomes, associated with virtually all multicellular organisms, have tremendous impact on their host health is considered as one of the most important scientific discoveries in the last decade. The host-associated microbiomes, composed of tens to hundreds of co-existing microbial species, are highly heterogenous at multiple scales (e.g. between different hosts and within a host). In this talk, I will share our recent works on understanding the heterogeneity of complex microbial communities, and how these conceptual and technological advances in microbial ecology pave the way for precision microbiome engineering to prevent and treat diseases.

Tony Dean

Professor

University of Minnesota

Biography

Tony obtained his PhD in 1987 from Washington University in St Louis, Prof. Daniel L. Hartl advisor, working on the metabolic basis of fitness in E. coli. He then completed further training as a postdoctoral fellow at UC Berkeley, Prof. Daniel E. Koshland Jr. advisor, working on protein phosphorylation. In 1991 he joined the Biochemistry Department at Chicago Medical School where he pursued studies in enzymology and protein engineering. In 1999 he moved to the BioTechnology Institute at the University of Minnesota where he has explored ancient enzyme adaptations, the evolution of catalytic mechanisms, adaptive landscapes, fluctuating selection and stopping evolution.

Research field

Microbial Evolution
Enzymology

Title

Models, Lies and Fluctuating Selection

Abstract

Models are conceptual simplifications that attempt to capture some essence of reality. They are used to explain observations and processes and they make testable predictions that can lead to new insights and unexpected discoveries. Models also ignore all manner of things, make hidden assumptions and sometimes include deliberate lies. As a consequence, a good model may sometimes deceive. I'll show how a classic model of fluctuating selection is deeply misleading and how a criterion identified as essential to correcting the flaw turns out to be irrelevant. I'll then present a simpler model of fluctuating selection, one that is both mechanistic and supported by experimental data. A slight modification to the new model recovers the classic model and in so doing exposes a hidden assumption in the classic theory of population genetics.

Sahand Hormoz

Associate Professor

Harvard Medical School / Dana-Farber Cancer Institute

Biography

Dr. Hormoz obtained his PhD in Applied Physics from Harvard University working with Michael Brenner. His postdoctoral studies were conducted jointly as a theorist at the Kavli Institute of Theoretical Physics (UCSB) with Boris Shraiman, and as an experimentalist in the lab of Michael Elowitz at Caltech. Dr. Hormoz is Associate Professor of Systems Biology at Harvard University. He is faculty of the department of Systems Biology at Harvard Medical School and the department of Data Science at the Dana-Farber Cancer Institute, associate member of the Broad Institute, and affiliated with the Harvard Stem Cell Institute and Harvard Cancer Center.

Research field

Systems Biology, Synthetic Biology, Cancer Biology

Title

Uncovering evolutionary and cellular dynamics from single-cell lineage trees

Abstract

In this talk, I will discuss two projects from my lab that involve lineage trees of cells (the branching diagram that represents the ancestry and division history of individual cells). In the first project, we reconstructed the lineage trees of individual cancer cells from the patterns of randomly occurring mutations in these cells. We then inferred the age at which the cancer mutation first occurred and the rate of expansion of the population of cancer cells within each patient. To our surprise, we discovered that the cancer mutation occurs decades before diagnosis. For the second project, we developed microfluidic 'mother machines' that allow us to observe mammalian cells dividing across tens of generations. Using our observations, we calculated the correlation between the duration of cell cycle phases in pairs of cells, as a function of their lineage distance. These correlations revealed many surprises that we are trying to understand using hidden Markov models on trees.

Zheng Hu

Professor

Shenzhen Institute of Advanced Technology, CAS

Biography

Dr. Zheng Hu is a Principal Investigator at Shenzhen Institute of Advanced Technology (SIAT), Chinese Academy of Sciences (CAS). He is also the Director of Center for Synthetic Biology and Evolution at SIAT. Dr. Hu received a B.S. in Biomedical Engineering from Huazhong University of Science and Technology in 2010. He received his Ph.D in Evolutionary Genetics from Beijing Institute of Genomics CAS in 2015. From 2015 to 2020, he was a postdoctoral fellow in Dr Christina Curtis's lab at Stanford University School of Medicine. Dr Hu's research interests span from cancer genomics, cancer evolution to computational modeling. His research on measuring cancer evolutionary dynamics has yielded novel insights into cancer formation and metastasis, facilitating biomarker discovery for risk prediction and treatment decision making.

Research field

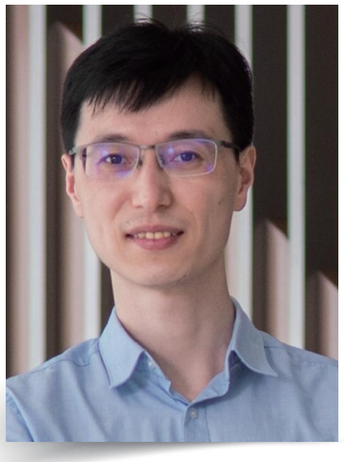
Cancer genomics, bioinformatics, lineage tracing, systems biology

Title

Deciphering tumor origin and evolution with single-cell lineage tracing

Abstract

High-resolution lineage tracing technology provides unprecedented opportunity for studying cell-fate decision and cancer evolution. The recent combination of single-cell omics and lineage tracing enables systematic mapping of cell fate trajectory and discovery of fate-determining mechanisms. In the first part of my talk, I will introduce a computational method we recently developed (named PhyloVelo) for inferring cell-state transitions by integrating single-cell RNA-seq and lineage tracing information. We demonstrated the high accuracy and robustness of PhyloVelo in inferring complex cell trajectories while outperforming RNA velocity, through applying it to different lineage-traced scRNA-seq datasets. In the second part, I will talk about the application of high-resolution lineage tracing to decipher the origin and evolution of early preneoplastic lesions in mouse model of colorectal cancers. Our systematic lineage mapping reveals polyclonal-to-monoclonal transition during early colorectal tumorigenesis.



Yuanhua Huang

Associate Professor

University of Hong Kong / School of Biomedical Sciences

Biography

Dr Huang received his PhD in informatics from the University of Edinburgh in 2017 and worked as an EBPOD research fellow at the University of Cambridge and the European Bioinformatics Institute (EMBL-EBI). Then, he joined the University of Hong Kong as an assistant professor in late 2019, between the School of Biomedical Sciences and the Department of Statistics and Actuarial Science. His research lies at the interface between machine learning, genomics, and biomedicine and has been supported by the NSFC Excellent Young Scientist Fund for single-cell data science.

Research field

Probabilistic machine learning
Bioinformatics
Single-cell genomics
Spatial data science
Somatic mutations and evolution

Title

Statistical modelling of single cell transitions in RNA and DNA spaces

Abstract

Single-cell sequencing technologies have become a powerful tool in dissecting cellular heterogeneity and disease progress. However, detecting cellular differentiation trajectories and identifying their regulations remain challenging from snapshots of cell populations. Here, we will first introduce our contributions to the RNA velocity methodology for cellular transition inference, followed by tailored dynamical systems in elucidating barcoded clonal differentiation bias in hematopoiesis. We will also show that an effective time predictor can identify cells with temporal displacement related to diseases. Last, we will present our recent work in modelling somatic mutations for tumor clonality and lineages, with impact to expression phenotypes and partly in a spatial context.

Keita Kamino

Assistant Research Fellow

Institute of Molecular Biology, Academia Sinica

Biography

Keita Kamino is an Assistant Research Fellow at the Institute of Molecular Biology (IMB) in Academia Sinica.His lab focuses on elucidating the fundamental principles underlying adaptive behaviors of cells using bacteria motility as a model. Before joining IMB in 2022, he studied physics at the University of Tokyo. In 2013, he earned his PhD in biophysics from the same institution, where he discovered a scale-invariant property in cell-to-cell signaling of the social amoeba, Dictyostelium. During his postdoctoral appointment at AMOLF in Amsterdam, the Netherlands, and Yale in the USA, he developed a single-cell FRET measurement system for studying the kinase-activity dynamics in single E. coli cells. Combining this system with mathematical modeling, he discovered, among other things, that E. coli acquire very little information from a chemical environment but use the information highly efficiently to navigate the environment.

Research field

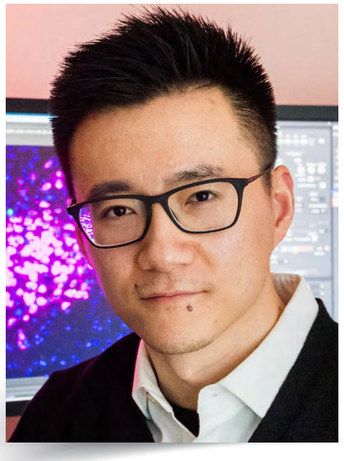
Bacterial motility, cellular information processing, live single-cell imaging, fluorescence microscopy, single-cell tracking, microfluidics, Bayesian inference, Machine learning, information theory, dynamical system modeling

Title

Acquisition and usage of sensory information in E. coli chemotaxis

Abstract

Organisms acquire and use sensory information to guide their behaviors. However, it is unclear whether and how this information constrains the ability of organisms to perform behavioral tasks. Using E. coli chemotaxis as a model system, we recently showed that the chemosensory information that a bacterium acquires sets an upper limit on its behavioral performance. In addition, through quantitative experiments, we quantified the rate at which E. coli cells acquire information during navigation and discovered that they use this information efficiently, operating near the theoretical limit for chemotaxis performance. More recently, we investigated what limits the amount of information a single E. coli cell can extract from a chemical environment. Cellular chemical sensing is inherently noisy due to the discrete nature of molecules. However, it remains unclear whether the limitation in information acquisition is primarily due to molecular-counting (external) noise or internal fluctuations in the chemical reaction networks that cells use to sense chemical signals. Our quantitative analyses revealed that, in E. coli chemotaxis, internal noise is much more dominant than external noise, significantly limiting the information acquisition and, consequently, their chemotaxis performance.



Yinqing Li

Associate Professor

Tsinghua University

Biography

Yinqing Li did Ph.D. in EECS from MIT and postdoc in the Broad Institute of MIT and Harvard, conducting research in genomics and neuroscience with Dr. Feng Zhang, Dr. Aviv Regev and Dr. Guoping Feng. He moved to Tsinghua in 2018 and became a faculty member in the School of Pharmaceutical Sciences and a principal investigator of IDG/McGovern Institute for Brain Research. His research builds new technologies for mapping, analyzing, and editing molecular programs, with the goal of ultimately understanding the maintenance and operational principle of neural systems. He has published in Cell, Nature, Science, and Nature portfolio journals with over 9,000 citations. His work has been recognized with awards such as Outstanding Young Professionals Beijing, Innovators Under 35 China, MIT Technology Review, Wenner-Gren Fellowship (2016), and McGovern Institute Fellowship.

Research field

Genome engineering, quantitative biology, single cell biology, gene regulation, epigenetics

Title

ACC-seq reveals chromatin condensate that stabilize intermediate expression levels

Abstract

Precise control of gene expression levels is essential for normal cell functions, yet how they are defined and tightly maintained, particularly at intermediate levels, remains elusive. Using ACC-seq, we uncover a class of transcription factors with dual roles as activators and repressors, referred to as condensate-forming level-regulating dual-action Transcription Factors (TFs). They reduce high expression but increase low expression to achieve stable intermediate levels. Dual-action TFs directly exert activating and repressing functions via condensate-forming domains that compartmentalize core transcriptional unit selectively. These selective nuclear spatial domains resist external disturbances, thereby stabilizing the transcriptional levels. These results collectively address a fundamental question in expression regulation and demonstrate the potential of level-regulating dual-action TFs as powerful effectors for engineering controlled expression levels. Moreover, further enhancement to ACC-seq incorporates additional modulations, such as longer-range fixative and ribonuclease, to map potential condensate occupancy linked to a wider range of regulatory elements across biological contexts.

Haiyan Liu

Professor

University of Science & Technology of China

Biography

Haiyan Liu received his BS degree in Biology from University of Science and Technology of China in 1990 and his PhD degree in Biochemistry and Molecular Biology from the same university in 1996. Since 2001, he has been a professor of Computational Biology at School of Life Sciences, USTC. His research interests include protein design, protein engineering, and computer simulation of protein structures and dynamics. He contributed to the development of a number of MD simulation techniques, including single step perturbation free energy calculation, QM/MM free energy surface calculation, and the amplified collective motion (ACM) simulation method. In recent years, his group have developed and experimentally tested data-driven methods for given-backbone amino acid sequence design (ABACUS and ABACUS-R) and for de novo protein backbone design (SCUBA and SCUBA-D). Haiyan Liu has (co)authored more than 100 papers.

Research field

computational biology, protein design, molecular simulation, deep learning

Title

Designing Flexible Protein Structures and Sampling Conformational Distributions with a Unified Model

Abstract

Protein structures are not static, with their dynamic changes being often critical for function. There are extensive and strong interest in developing deep learning models that can predict the conformational distributions of protein structures or design protein structures that can host rich conformational dynamics. Aiming for these needs, we developed a model named PVQD (Protein Vector Quantization Diffusion) that uses an auto-encoder regularized with vector quantization (VQ) to learn a latent space representation of protein backbone structures, and uses denoising diffusion in this latent space combined with the VQ-based decoder to model and sample protein structures. As a generator, PVQD can unconditionally sample designable protein backbones. By using a single amino acid sequence to condition the latent space diffusion, PVQD can predict structures and sample conformations. Using several benchmarks, we compared PVQD with state-of-the-art methods for tasks including protein backbone generation, structure prediction, and conformational sampling. We showed that PVQD achieves the generation of flexible backbone structures and the prediction of conformational distributions for natural proteins with a unified model.

Gautam I Menon

Professor

Ashoka University

Biography

Gautam I Menon is Dean (Research) and Professor of Physics and Biology at Ashoka University, Sonepat. Prior to this, he was a Professor in the Theoretical Physics and Computational Biology groups of IMSc, Chennai. He was an Adjunct Professor at the Department of Biological Sciences at TIFR, Mumbai (2019-2021) and a Visiting Professor at the Mechanobiology Institute of the National University of Singapore (2011-2013). He has been awarded the Swarnajayanti Fellowship of the DST, was named an Outstanding Research Investigator of the DAE-SRC and was named as an Outstanding Referee of the American Physical Society. He is an elected Fellow of the National Academy of Sciences (India) and was a member of the expert group that drafted the Science, Technology and Innovation Policy of India in 2020. He serves on scientific review committees of several national and international agencies, including the HFSP and the DBT-Wellcome India Alliance, as well as on the Editorial Board of PLoS Global Health.

Research field

Nuclear architecture, chromatin, molecular motors, axonal transport, epidemiology

Title

Activity, phase separation and nuclear architecture

Abstract

I will describe work in which we use computational descriptions of large-scale nuclear architecture to model the biophysics of chromatin organization and nucleolus assembly in eukaryotic cells. The model predicts the statistics of positional distributions, shapes, and overlaps of each chromosome. Simulations of the model reproduce common organizing principles underlying large-scale nuclear architecture across human cell nuclei in interphase. These include the differential positioning of euchromatin and heterochromatin, the territorial organization of chromosomes (including both gene-density-based and size-based chromosome radial positioning schemes), the nonrandom locations of chromosome territories, the shape statistics of individual chromosomes and the formation of the nucleolus. We propose that the biophysical consequences of the distribution of transcriptional activity across chromosomes should be central to any chromosome positioning code. These models combine relatively new concepts in the description of cell-scale biological structuring - activity and phase separation - illustrating how the overlap of physics, biology and computation can provide quantitative approaches to old problems.

Allyson Sgro

Group Leader

HHMI Janelia Research Campus

Biography

Dr. Allyson Sgro is a Group Leader in Computation and Theory and 4D Cellular Physiology at HHMI's Janelia Research Campus. She earned her B.A. in Chemistry and Pre-Medical Studies from Bard College at Simon's Rock, followed by a M.S. and Ph.D. in Chemistry from the University of Washington. At Princeton University as a postdoctoral fellow, she began working in quantitative biology and collective behavior. How cells encode information about the environment and each other to work together has been the focus of her independent career, first as an Assistant Professor of Biomedical Engineering at Boston University and now at Janelia.

Research field

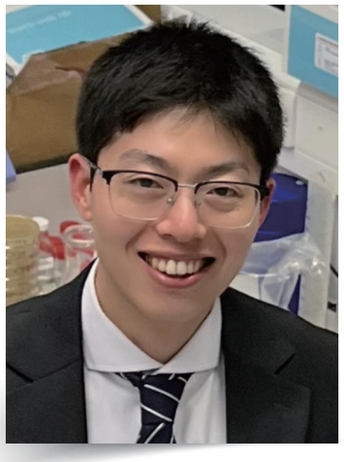
collective behavior, signaling dynamics, quantitative biology

Title

A theory of lineage-associated molecular similarity

Abstract

Multicellular systems often grow through proliferation, generating lineages of related cells where specific properties such as cell cycle time or fate are correlated with lineage. As many of these properties are controlled by the concentration of regulatory molecules, correlations in molecular concentration that persist over multiple generations confer similarity to related cells. The amount of any molecule in a cell is controlled by how the molecule is divided between child cells at each cell division as well as by the stochastic biochemical reactions that create, modify, and degrade the molecule. If and how these processes might create correlations in child cells that could persist for generations down a cell lineage is unknown. Here we introduce a conceptual and mathematical framework that identifies what properties of biochemical reactions create correlations, or similarity, between related cells. Lineage-associated molecular similarity exists when biochemical reactions create a larger variance in possible molecular concentration levels than is created by unequal molecular partitioning. Molecular similarity can have a multigenerational correlation time and the similarity conferred to a molecule by a specific biochemical reaction architecture is additive when these reactions are layered into signaling networks, with the length of similarity dependent on the molecular turnover rate. This mechanism explains a wide range of experimental observations, such as how inherited signaling levels can drive cell fate choices in metazoan development and how some bacterial traits persist for as many as 10 generations. Once a process's controlling molecules are identified, our framework provides a means to estimate multigenerational cellular similarity times that can drive both temporary functional specialization and differentiation.



Rongzhen Tian

Postdoctoral Fellow

Medical Research Council Laboratory
of Molecular Biology (MRC-LMB)

Biography

Rongzhen is currently a postdoctoral scientist in Jason Chin's lab at the Medical Research Council Laboratory of Molecular Biology (MRC-LMB). He is also a member of Trinity College Postdoctoral Society at University of Cambridge. He completed his undergraduate, master's, and PhD degrees at Jiangnan University from 2014 to 2022, where he was supervised by Professors Jian Chen, Guocheng Du and Yanfeng Liu in fermentation engineering. He dedicated himself to the research area of synthetic biology during his master's and PhD studies, specializing in the development of bacterial continuous evolution tools and expression regulation elements via diverse approaches. In November 2022, he joined Jason Chin's lab and is now focusing on continuous evolution, reprogramming translation and whole genome synthesis.

Research field

Synthetic biology
Directed evolution
Metabolic engineering

Title

Synthetic bacterial orthogonal replication systems enable accelerated evolution

Abstract

The evolution of new function in living organisms is the result of continuous genomic mutation and selection within a population. This process is slow, and the rate of evolution is fundamentally limited by the critical mutation rate. Directed evolution commonly sidesteps the limitation on in vivo mutation rate by generating genetic diversity in vitro, but this does not enable the continuous evolution of genes within an organism. The mutation rate of cells can be transiently increased, but high levels of untargeted mutation lead to a catastrophic mutational load on the genome and are unsustainable. Here, we established stable orthogonal replication systems in bacteria, including the Gram-negative bacterium Escherichia coli and the Gram-positive bacterium Bacillus thuringiensis. The orthogonal replicons can carry diverse DNA cargos and are not copied by host polymerases but are selectively copied by orthogonal DNA polymerases (O-DNAPs), which do not copy the genome. We engineered mutant O-DNAPs that selectively increase the mutation rate of the orthogonal replicons and demonstrated the utility of our system for accelerated continuous evolution by evolving improved cellular fluorescence, tigecycline resistance genes and the methanol assimilation pathway. This technology enables the rapid development of diverse research tools, biopharmaceutical leads, and strains for the production of industrial chemicals..

Gerard Chee Lai Wong

Professor

University of California, Los Angeles

Biography

Gerard C. L. Wong is a Professor in the Department of Bioengineering, Department of Chemistry & Biochemistry, Dept of Microbiology, Immunology, & Molecular Genetics, and the California NanoSystems Institute at UCLA. Wong received his BS and PhD in physics at Caltech and Berkeley, respectively. He was affiliated with the Materials Science & Engineering Department and Physics Department at the University of Illinois at Urbana-Champaign before moving to UCLA in 2009. His research recognition includes a Beckman Young Investigator Award and an Alfred P Sloan Fellowship. He is a Fellow of the American Physical Society, a Fellow of the American Academy of Microbiology, and a Fellow of the American Institute for Medical and Biological Engineering.
Group website: http://wonglab.seas.ucla.edu/

Research field

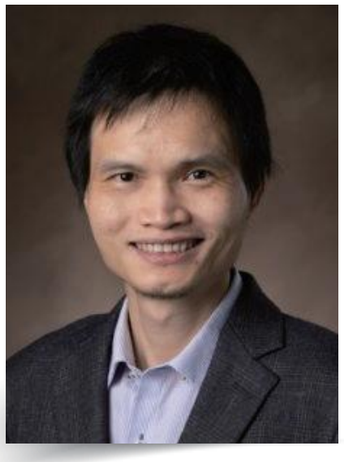
Immunology, autoimmune disorders, host-pathogen interactions, microbiology, bacterial biofilms, biophysics, soft condensed matter physics

Title

How do we discriminate a lethal, potentially pandemic-capable coronavirus from a ‘common cold’ coronavirus?

Abstract

At present, we can recognize genomic features in coronaviruses that promote human infection. However, this is a necessary rather than a sufficient condition for pandemic viruses, as 20-30% of common colds are caused by coronaviruses. It is unclear how SARS-CoV-2 infection in particular leads to the strong but ineffective inflammatory response that characterizes severe COVID-19. Proteolytic degradation of SARS-CoV-2 virions is one of the critical steps in host viral clearance, but the impact of viral peptide fragments from such processing at high viral loads is largely unknown. Using high-resolution mass spectrometry, we identify exposed SARS-CoV-2 peptide fragments with architectures cognate to host antimicrobial peptides (AMPs) in tracheal aspirates of critical COVID-19 patients. To assess effects of AMP-like viral fragments on host cells, we use machine learning to map out all sequence motifs in the SARS-CoV-2 proteome that mimic host cationic antimicrobial peptides (‘xenoAMPs’). Such xenoAMPs are strongly enriched in SARS-CoV-2 relative to low-pathogenicity coronaviruses. Moreover, xenoAMPs from SARS-CoV-2 but not low-pathogenicity homologs assemble dsRNA into nanocrystalline complexes with lattice constants commensurate with the steric size of Toll-like receptor TLR-3 and therefore capable of cooperative multivalent binding. Such complexes amplify cytokine secretion in diverse uninfected cell types in culture (epithelial cells, endothelial cells, monocytes, and macrophages). The induced transcriptome matches well with the global gene expression pattern in COVID-19, despite using <0.3% of the viral proteome. Delivery of these complexes to uninfected mice boosts plasma IL-6 and CXCL1 levels as observed in COVID-19 patients.



Yilin Wu

Professor

The Chinese University of Hong Kong

Biography

Yilin Wu obtained his B.S. in Physics from the University of Science and Technology of China in 2004 and Ph.D. in Physics from University of Notre Dame in 2009. After postdoctoral research at Rowland Institute of Harvard University (with Howard C. Berg), he joined the Department of Physics of the Chinese University of Hong Kong and currently holds the position of Professor. His research has substantially advanced the understanding on the collective motion and self-organization of primitive life forms and active matter. He is named as an RGC Research Fellow of Hong Kong SAR (2021-2025) and a recipient of The Xplorer Prize from New Cornerstone Science Foundation.

Research field

Physics of living matter, quantitative biology, active matter, biological collective motion, bacterial motility, self-organization

Title

Nonreciprocity enables large-scale mechanical spiral waves in bacterial living matter

Abstract

Propagating spiral waves have been discovered in various chemical, biological and physical systems. While spiral waves in multicellular organisms are often associated with essential living functions, evidence of spiral wave pattern has been lacking in the bacterial world. Here we report the discovery of a first instance of propagating spiral waves in dense bacterial populations. Specifically, we discovered that synchronization of type IV pilus activity in bacterial biofilms leads to large-scale spatiotemporal regulation of tension force in the form of propagating spiral waves. Theoretical modelling reveals that the spiral tension waves result from nonreciprocity in cell-cell interactions. Our findings reveal a novel collective behavior of type IV pilus motility and may shed light on the emergent mechanics of biofilms and microbiomes.

Junhua Yuan

Professor

University of Science and Technology of China

Biography

Dr. Yuan graduated from the Department of Modern Physics at USTC in 1998 with a bachelor's degree, obtained a Ph.D. in Physics from the California Institute of Technology in 2005, and conducted postdoctoral research at Harvard University from 2006 to 2012 with Howard Berg. He joined USTC in 2012 as a professor at the School of Physical Sciences and is currently engaged in interdisciplinary research in physical biology, focusing on microbial motility and signal transduction.

Research field

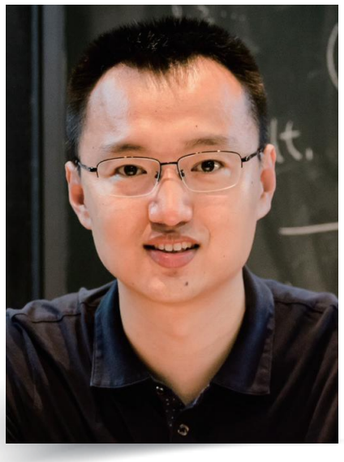
Microbial motility; Signal transduction

Title

Spatiotemporal dynamics of bacterial chemotaxis

Abstract

Bacterial chemotaxis exhibits rich spatiotemporal dynamics. Using Pseudomonas aeruginosa and Escherichia coli as examples, we will investigate the spatial integration of sensory input and motor output in P. aeruginosa chemotaxis, and the dynamics of potassium sensing in E. coli.



Lei Zhang

Professor

Peking University

Biography

Lei Zhang is Boya Distinguished Professor at Beijing International Center for Mathematical Research, Peking University. He is also a Principle Investigator at Center for Quantitative Biology, Center for Machine Learning Research. He obtained his Ph.D in Mathematics at Penn State University in 2009. His research is in the area of computational and applied mathematics and interdisciplinary science in biology, materials, and machine learning. He has published the papers in Phys. Rev. Lett., PNAS, Acta Numerica, Science journals, Cell journals, SIAM journals. He was awarded/funded by NSFC Innovation Research Group, NSFC Outstanding Youth Award, National Key Research and Development Program of China, NSFC Excellent Youth Award, Royal Society Newton Advanced Fellowship, etc. He serves as an Associate Editor for SIAM J. Appl. Math, Science China Mathematics, CSIAM Trans. Appl. Math, DCDS-B, The Innovation, and Mathematica Numerica Sinica.

Research field

Computational and applied mathematics;
Computational systems biology;
Quantitative biology

Title

Construction of Solution Landscapes of Complex Biological Systems

Abstract

Energy landscape has been widely applied to many physical and biological systems. A long standing problem in computational physics is how to search for the entire family tree of possible stationary states on the energy landscape without unwanted random guesses? Here we introduce a novel concept “Solution Landscape”, which is a pathway map consisting of all stationary points and their connections. We develop a generic and efficient saddle dynamics method to construct the solution landscape, which not only identifies all possible minima, but also advances our understanding of how a complex system moves on the energy landscape. As illustrations, we apply the solution landscape approach to study two problems: One is construction of the solution landscapes of gene regulatory networks in cell fate decisions, and the other one is to construct the solution landscape of reaction-diffusion systems, which reveals a nonlinear mechanism for pattern formation beyond Turing instability.

Yi Zhang

CTO

Euler Technology

Biography

Yi Zhang received his B.Sc. (2010) and Ph.D. (2018) in Biological Sciences from School of Life Sciences, Peking University. He serves as the CTO of Euler Technology, a company that develops liquid biopsy assays for disease diagnosis. His main research interest is to devise novel computational and experimental methods for tracking and timing important genetic and epigenetic events in disease-related biological processes such as cancer, pregnancy, development, and aging.

Research field

Bioinformatics; Epigenetics; Next-generation sequencing.

Title

Decoding single cell replicational age in scATAC-seq data

Abstract

Single-cell chromatin accessibility sequencing (scATAC-seq) reconstructs developmental trajectory by phenotypic similarity. However, inferring the exact developmental trajectory is challenging. If one could place a time stamp for each cell, it would give the static snapshot data a new reference axis of time. One candidate of such time marker is the replicational age of cell. We developed a computational method "EpiTrace" to perform single-cell replicational age inference from scATAC-seq data. To do this, EpiTrace counts the fraction of opened "clock-like loci" for each cell. It could be applied to data from different technical platforms, different cell lineages, and different animal species. EpiTrace inferred cell age shows concordance with known cell age and developmental hierarchies, correlates well with DNA methylation-based clocks, and is complementary with methods such as mutation-based lineage tracing, RNA velocity, and stemness predictions. Applying EpiTrace to scATAC-seq data reveals biological insights with clinically relevant implications, ranging from hematopoiesis, organ development, tumor biology and immunity to cortical gyrification.

Abstracts of Contributed Talks

Yuansheng Cao
Tsinghua University

Regulating biochemical dynamics through controlled phase-separated condensates

Phase-separated condensates are crucial for various biological processes, but their impact on biochemical dynamics remains unclear. By combining liquid-liquid phase separation theory with biochemical reaction kinetics, we found that condensates can induce unconventional dynamics not observed in homogeneous solutions. Firstly, by simply enriching reaction components, condensates can significantly enhance the amplitude of circadian rhythms while maintaining their period, provided the enrichment is finely controlled by the circadian network itself. Secondly, when multiple components are involved in the phase separation, differential enrichment can occur based on their interactions. Additionally, scaffold proteins within the condensate can further regulate reactions between enriched components. We present preliminary results showcasing the significant impact of phase-separated condensates on biochemical reactions and discuss potential implications for various biological functions.

Ye Chen
Center for Cell and Gene Circuit Design,
Institute of Synthetic Biology,
Shenzhen Institute of Advanced Technology, CAS

A Quantitative Framework for Synthetic Modular Transcription Units Across Biological Kingdoms

Cells respond to complex environmental signals through genetic networks regulated by promoters and transcription factors (TFs). Despite the development of numerous thermodynamic transcription models, the quantitative construction of synthetic transcription units remains underexplored. In this study, we introduce a modular design framework for dimerized transcription factors and their corresponding promoters across different biological kingdoms, enabling quantitative modeling. We modularize TFs into distinct structural and functional domains—DNA-binding domains (DBD), ligand-binding domains (LBD), and transcription activation domains (AD)—each with independent biophysical parameters. By manipulating DBDs and TF expression levels, we optimize the fold change and absolute expression strength of each TF. Using this approach, we engineered a Saccharomyces cerevisiae strain with 12 orthogonal biosensors, achieving an average 300-fold induction. This work provides an efficient TF optimization scheme and a general model for quantitative, signal-induced cooperative regulation of transcription.

Haijun Gong
Saint Louis University

Inference and Verification of Time-varying Gene Regulatory Networks

Modern genomic technologies have generated a large amount of data. One of the most challenging tasks in systems biology is how to correctly reconstruct the networks from the high-dimensional omics data. Different computational techniques, including the deterministic and statistical inference methods, have been developed to reconstruct networks. Most network inference methods assume the network structure does not change over time, i.e. it is stationary. Several studies have revealed that the structures of some cellular networks are non-stationary or time-varying under some circumstances. Understanding the structure of gene regulatory network, and how it changes over time will provide a key to discovering the mechanisms underlying important cellular processes and pathogenesis of diseases. No methods can correctly reconstruct and efficiently verify time-varying regulatory networks due to some severe drawbacks. Our work developed novel time-varying network inference and verification technique to investigate the structure changes of gene regulatory network.

Jiliang Hu
MIT

Emergent behaviors in complex microbial ecosystems

From tropical forests to gut microbiomes, ecological communities harbor diverse and abundant species. Understanding the complex emergent phenomena of diversity, stability, and invasibility in these communities within a unified framework has been a significant challenge. We address this knowledge gap by bridging experiment and theory showing that simple community-level features govern emergent behaviors. As the number of species or the strength of interactions increases, microbial ecosystems transition through three distinct dynamical phases: from stable coexistence to partial coexistence, to the emergence of persistent fluctuations and alternative stable states in species abundances. Notably, high biodiversity and dynamic fluctuations reinforce each other. Furthermore, we show that the interplay between dynamics, interaction strength, and diversity determines the invasion outcome in microbial communities. Communities with fluctuations in species abundance are both more invasible and more diverse than stable communities, leading to a positive diversity-invasibility relationship. Increasing interspecies interaction strength and species pool size leads to a decrease in invasion probability. We resolve the diversity-invasibility debate by showing a universal positive correspondence between invasibility and survival fraction of resident species. Communities composed of strongly interacting species can exhibit an emergent priority effect in which invader species are less likely to colonize than species in the original pool. Overall, my work uncovers predictable emergent patterns of diversity, dynamics, and invasibility in ecological communities, offering insights into a unified framework for microbial ecology.

Miao Huang
PhD student

Geometric Quantification of Cell Phenotype Transition Manifolds with Information Geometry

Cell phenotype transition (CPT) plays a pivotal role in various biological processes like development. Recent advancements in single-cell sequencing techniques have uncovered that cell transition dynamics during development are confined on low-dimensional manifolds. However, existing methods are inadequate for directly quantifying the manifolds from experimental data. Here we present SCIM (single cell information manifolds), a novel geometry-guided method to quantify the CPT manifolds using information geometry.

In particular, we convert single cells' high-dimensional gene vectors into probability distributions via Gaussian embedding. The Fisher metric is naturally defined in this embedding space. With the transformed Gaussian distributions, we calculate the coarse Ricci curvature of each single cell. Our analyses reveal that the cells with low curvature are associated with critical transitions. To further examine the invariant characteristics of the manifolds of CPT, we compute the information velocity of each single cell based on RNA velocity. Remarkably, the regions with high information velocity correspond with the low curvature regions, indicating that the geometry can guide the dynamics of single cells on the manifolds. The proposed method not only unveils the invariant characteristics of the CPT manifolds, but also establishes a generic approach for quantifying the intricate dynamics on the CPT manifolds.

Juan E. Keymer
Institute for Advanced Studies, Shenzhen X-Institute

Ecological succession and the competition-colonization trade-off in microbial communities

Background
During range expansion in spatially distributed habitats, organisms differ from one another in terms of their patterns of localization versus propagation. To exploit locations or explore the landscape? This is the competition-colonization trade-off, a dichotomy at the core of ecological succession. In bacterial communities, this trade-off is a fundamental mechanism towards understanding spatio-temporal fluxes in microbiome composition.

Results
Using microfluidics devices as structured bacterial habitats, we show that, in a synthetic two-species community of motile strains, Escherichia coli is a fugitive species, whereas Pseudomonas aeruginosa is a slower colonizer but superior competitor. We provide evidence highlighting the role of succession and the relevance of this trade-off in the community assembly of bacteria in spatially distributed patchy landscapes. Furthermore, aggregation-dependent priority effects enhance coexistence which is not possible in well-mixed environments.

Conclusions
Our findings underscore the interplay between micron-scale landscape structure and dispersal in shaping biodiversity patterns in microbial ecosystems. Understanding this interplay is key to unleash the technological revolution of microbiome applications.

Feng Liu
Hebei University of Technology

Exploring the noise filtering mechanism in early Drosophila embryogenesis

Using Drosophila embryos as our model system, we explore the noise filtering mechanism of the patterning gene regulatory networks (GRNs) through quantitative experiments and modeling. Experimentally, we develop novel tools to efficiently control the measurement errors in quantifying developmental patterns. We extend our research scope from transcriptional to translational regulation, employing the Suntag system to uncover mRNA- concentration-dependent translation regulation. Theoretically, we adopt a top-down approach rooted in the optimality theory to reveal information integration in early Drosophila embryos.

Linjie LU
University of Strasbourg

Rules of self-organisation in organoids: dynamics and morphology

Organoids are remarkable systems, generating organ-like structures from single cells. However, their dimensions and organisations are poorly reproducible. Our research focused on understanding their self-organisation.

(i) We compared lumen dynamics among three systems - MDCK cysts, epiblasts, and pancreatic spheres. All systems increased their numbers of lumens before eventually reaching a single lumen. Measurements compared to theory revealed consistent behavior across the systems with an increase in the number of lumens for increasing initial cell numbers. We then identified the driving forces yielding both phases and led by mechanisms for nucleation and by changes in pressure and tissue remodeling. The conclusions demonstrated novel, conserved, and differing mechanisms among systems1.

(ii) We investigated MDCK doublets spontaneous rotation and its physical mechanisms. A method was established to visualize dynamics of MDCK cell doublets, revealing their spontaneous rotations. We investigated rotation mechanisms by measuring rotation speeds, changes in direction, persistence, cell shapes, and polarity. We identified correlations between rotation speed and interface shape, as well as between cell shape and the localisation of adhesion/-force-generating motor myosin proteins illustrating the Curie principle. A generic active gel model was proposed, suggesting that polarised forces at the cell surface drive continuous rotation. Model predictions were tested successfully by experiments involving perturbations with Rho activation by optogenetics2.

Our interdisciplinary work demonstrates organoids robust self-organisation and paves the way for designing reproducible organoids with unprecedented reliability.

1. Linjie Lu, Kana Fuji et al, Generic rules of lumen nucleation and fusion in epithelial organoids. BioRxiv (2024).
2. Linjie Lu, Tristan Guyomar, Quentin Vagne et al, Polarity-driven three-dimensional spontaneous rotation of a cell doublet. Nat. Phys. (2024).

Sheng Wang
California Institute of Technology

Synthetic circuits for multicellular spatial patterning

During multicellular development, cells form spatially periodic patterns to generate repetitive structures like digits, vertebrae, and teeth. Turing patterns based on short-range self-activation and long-range inhibition have long provided a framework for understanding such processes. However, natural patterning processes are typically complex, involving many secreted factors and complex intracellular circuits. It has, therefore, remained unclear what minimal circuit designs are sufficient to implement Turing patterns among living cells. Here, to address this question, we designed, built, and analyzed modular synthetic reaction-diffusion circuits for self-organized spatial patterning. We compared two circuits composed of both natural and synthetic signaling systems with varying diffusion rates, and showed they allow spontaneous patterning on different length scales in mammalian cells. These circuits both implemented classic “local activation with long-range inhibition” regulation and dynamically adapt their active domains for regular patterns. Further, the resulting patterns are tunable via circuit parameters and can adapt to different boundary conditions, consistent with model predictions. Together, these results show that it is possible to engineer synthetic circuits that achieve spatial patterning in cell culture, and provide a foundation for constructing pattern-forming multicellular systems.

Shou-Wen Wang
Westlake University / Westlake Laboratory

Learning Fate Choice and Cell Memory through Single-Cell Multi-Omic Lineage Tracing

Cellular lineage histories and their molecular states encode fundamental principles of tissue development and homeostasis. Current lineage-recording mouse models have insufficient barcode diversity and single-cell lineage coverage for profiling tissues composed of millions of cells. Here, we developed DARLIN, an inducible Cas9 barcoding mouse line that utilizes terminal deoxynucleotidyl transferase (TdT) and 30 CRISPR target sites. DARLIN is inducible, generates massive lineage barcodes across tissues, and enables detection of edited barcodes in ~70% of profiled single cells. Using DARLIN, we examined fate bias within developing hematopoietic stem cells (HSCs) and revealed unique features of HSC migration. Additionally, we established a protocol for joint transcriptomic and epigenomic single-cell measurements with DARLIN and found that cellular clonal memory is associated with genome-wide DNA methylation rather than gene expression or chromatin accessibility. DARLIN will enable high-resolution study of lineage relationships and their molecular signatures in diverse tissues and physiological contexts.

Xu-Wen Wang
Harvard Medical School

Predicting microbiome compositions and keystone species through deep learning

Microbes form complex communities that perform critical functions in maintaining the integrity of their environment or their hosts' well-being. Rationally managing these microbial communities requires improving our ability to predict how different species assemblages affect the final species composition of the community. This prediction is challenging due to limited knowledge of the diverse physical, biochemical, and ecological processes governing microbial dynamics. To address this challenge, we present a deep learning framework that learns the mapping between species assemblages and community compositions from training data alone, enabling us to predict microbiome composition based on any species assemblage. Building on this, we propose a data-driven keystone species identification (DKI) framework. By training a deep-learning model with microbiome samples from a particular habitat, we implicitly learn the assembly rules of microbial communities. This well-trained model allows us to quantify the community-specific keystoneness of each species through thought experiments on species removal. Our approach demonstrates how deep learning can enhance the prediction and management of complex microbial communities, providing a powerful tool for community ecology.

Chao Ye
University of Warwick

The cyanobacterial circadian clock couples to pulsatile processes using pulse amplitude modulation

Cellular processes are often dynamic and oscillatory, yet their coordination is essential for the proper functioning of a cell. How distinct oscillatory processes couple within a single cell remain an open question. This study uses the cyanobacterial circadian clock as a model system to explore the coupling of oscillatory and pulsatile gene circuits. The cyanobacterial circadian clock generates 24-h oscillations in downstream targets in order to time processes across the day/night cycle. In part, this timing is mediated by clock's modulation of the activity of alternative sigma factors that direct RNA polymerase to specific promoters. Using single-cell time-lapse microscopy and modelling, we find that the clock modulates the amplitude of expression pulses of the sigma factor RpoD4, which occur only at cell division. This pulse amplitude modulation (PAM), analogous to AM regulation in radio transmission, allows the clock to generate a 24-h rhythm in rpoD4 expression despite rpoD4 pulses are not circadian in frequency. By altering cell division rates, we show that as predicted by our model, AM regulation produces a consistent 24-h period in rpoD4 pulse amplitude across various rpoD4 pulse frequencies. Furthermore, we demonstrate that rpoD4 expression levels affect cell size: deleting rpoD4 results in smaller cells, while increasing rpoD4 expression leads to larger cells in a dose-dependent manner. Thus, our work reveals a link between the cell cycle, circadian clock, and RpoD4 in cyanobacteria, and suggests that AM regulation can be a general mechanism that enables biological clocks to robustly modulate pulsatile downstream processes.

Zhen Zhou
IRCBC
(中国科学院生物与化学交叉研究中心)

Enhanced Cellular Longevity Arising from Dynamic Perturbation

Cellular longevity is regulated by both genetic and environmental factors. However, the interactions of these factors in the context of aging remain largely unclear. Here, we formulate a mathematical model for dynamic glucose modulation of a core gene circuit in yeast aging, which not only guided the design of pro-longevity interventions, but also revealed the theoretical principles underlying these interventions. We introduce the dynamical systems theory to capture two general means for promoting longevity - the creation of a stable fixed point in the "healthy" state of the cell and the dynamic stabilization of the system around this healthy state through environmental oscillations. Guided by the model, we investigate how both of these can be experimentally realized by dynamically modulating environmental glucose levels. The results establish a paradigm for theoretically analyzing the trajectories and perturbations of aging that can be generalized to aging processes in diverse cell types and organisms.

Abstracts of Poster Presentations

Jingyi Zhao
Institute of Biopharmaceutical and Health EngineeringTsinghua Shenzhen International Graduate School

Kinetics modeling of the translational regulation on the mitochondrial surface

Mitochondria are important organelles for cellular energy metabolism. The mRNAs tethered to mitochondria using the MS2-MCP system lead to higher protein expression. We hypothesized two possible mechanisms for protein production on the mitochondrial surface: increasing translation or stabilizing mRNA. Perturbing regulatory elements showed feedback mechanisms limiting gene expression. We then simulated the translation process with mRNA localization to the mitochondrial surface through mathematical modeling and computation. We compared these models with experimental results of different expression levels of mRNA and found that mitochondrial localization of mRNA increased mRNA stability rather than the translational rate, highlighting mitochondria's role in mRNA metabolism.

Lu Peng
Beijing Normal University, Zhuhai

Discovery of highly bioactive peptide through hierarchical structural information and molecular dynamics simulations

We developed PepHiRe, an innovative computa_x005f-tional framework that uses hierarchical structural information to design peptides with high bioactivity. Our method leverages the principles of Ladderpath Approach (which is under the umbrella of Algorithmic Information Theory) to generate novel peptides targeting Myeloid Cell Leukemia-1 (MCL-1), a protein crucial in various cancers. Using a limited dataset of eight wild type BH3 peptides, PepHiRe efficiently produces peptides with substantially improved binding affinities, achieving IC50 values between 28.13 and 167.42 nM. This study underscores the po tential of integrating advanced computational tools like multi conformational docking and molecular dynamics simulations in drug design, enhancing both the accuracy and efficiency of therapeutic peptide development.

Zishuo Zeng
Synceres Biosciences, Shenzhen

Contrastive Learning-based EC number prediction for enzymatic reactions

High throughput EC number prediction for chemical reactions can facilitate annotations during retrosynthe-sis planning, construction of metabolic models, and prediction of chemicals' metabolism. We developed an EC number predictor for enzymatic reactions based on pre-trained reaction representation, data augmentation, and contrastive learning framework. Results show that our predictor substantially outper-forms the state-of-the-art model. We also demonstrate the utility of our predictor in mapping reactions to their corresponding enzymes for a yeast metabolic model.

Yixuan Chen
Peking University

Characterizing cellular physiological states with 3D shape descriptors for cell membranes

The shape of a cell can be closely associated with its physiological state. In this study, 12 unique shape descriptors for a three-dimensional (3D) object were tested with a public dataset of ~400,000 independent 3D cell regions segmented based on fluorescent labeling of cell membranes in
Caenorhabditis elegans embryos. It's revealed that those shape descriptors could faithfully characterize cellular physiological states including cell division (cytokinesis), cell migration speed, differential cell lineage, and differential gene expression. The descriptors may be used for not only studying devel-opmental morphogenesis but also diagnosing human disease.

Tiancheng Xu
Nanjing University of Chinese Medicine

"Acupoint-Formula-Symptom" acupuncture knowledge graph: a new model for quantitative research in traditional Chinese medicine

Acupuncture, practiced worldwide, confronts challenges with Chinese-language documentation, hindering its integration into intelligent medical engineering. Our team utilized graph neural networks to classify entities from 82 medical texts, constructing an acupuncture knowledge graph with 54,593 entities. The graph includes 21 object-relationship mappings, 16,558 entities across seven categories, and 80,094 relationships in nine categories. Leveraging fractal theory, we digitized meridians and modeled 362 acupuncture points. Integrating complex networks with noninvasive diagnostic tools enabled innovative point diagnosis for syndrome differentiation. A clinical study with 426 patients assessed meridian diagnosis efficacy, marking a paradigm shift in evidence-based traditional medicine modernization.

Jingyu Zhang
Harvard Medical School

Cooperatively formed backbone facilitates chromosome structure folding

Increasing evidence underscores the critical role of three-dimensional (3D) chromosome structures in biological processes, yet the mechanisms of their formation remain elusive. This study focuses on the hierarchical compaction of 3D chromosome structures, particularly the impact of interactions between two genomic distant sites on the same chromosome in facilitating its folding. Using data analyses and experimental validation, we present the conservation and heterogeneity of long-range interactions. Moreover, we establish a data-driven mathematic model and show that the cooperatively formed hierarchal backbone helps fold chromosomes. Altogether, our approach provides insights into one basic aspect of 3D chromosome architecture.

Xuefang Gu
Institute of Biopharmaceutical and Health Engineering Tsinghua Shenzhen International Graduate School

Cell size modulates P-body formation by limiting molecular movement

Cells utilize intracellular structures like P_x005f bodies, formed through liquid-liquid phase separation, to regulate biological processes. The regulatory mechanisms and the influence of cell size on P-body formation are not fully understood and require further exploration. We postulate that cell size influences P-body formation and dynamics. Our initial observations suggest that smaller yeast cells tend to have larger but fewer P-bodies, while larger cells exhibit smaller P-bodies but in greater numbers. To investigate this further, we integrated a mathematical model to explore the relationship between yeast cell size and P-body formation. We surprisingly found that the model results aligned with the experimental data. By combining simulation and experimental results, we suggest that cellular structure might inhibit the movement of P-body components and modulate the size and number of granules.

Qinghe Wang
Institute of Biopharmaceutical and Health Engineering Tsinghua Shenzhen International Graduate School

ATP Synthase Component is Distinctively Distributed in Mitochondrial Network by Random Motion

ATP synthases, pivotal in cellular energy production, consist of F1 and F0 motors within mitochondria. While their structure is known, subunit transport and assembly processes remain to be understood. Utilizing network theory, we investigated ATP synthase component distribution. Microscopy assay revealed ATP3p, ATP4p, and ATP5p localized in specific mitochondrial regions, while ATP1p, ATP2p, and ATP7p were evenly spread through mitochondria. Computational reconstruction showed a distinctive pattern of ATP3p and ATP4p distribution in the mitochondrial network. Molecular dynamic simulations suggested random motion in the tubular structure could explain their distribution. This study advances understanding of ATP synthase structure and assembly process.

Yanfei Wu
Institute of Biopharmaceutical and Health Engineering Tsinghua Shenzhen International Graduate School

Integrated Simulation of RNA Motion Systems for Ground Truth Imaging

RNA localization within cells is crucial for understanding gene expression and cellular processes. However, traditional microscopy faces challenges in accurately capturing RNA dynamics due to motion artifacts. This study utilizes computational simulation to model RNA dynamics and motion artifacts in microscopy. By mimicking a camera's scanning plane and utilizing Gaussian functions, we simulated position of single molecule RNA. Simulated scanning lines replicate a CMOS camera's rolling shutter. Dynamic observation of simulated particles' positions provides insights into RNA motion and artifact mitigation. Addressing motion artifacts in live-cell microscopy through deep learning holds promise for advancing cellular biology and molecular imaging.

Rui Fang
Harvard Medical School, Westlake University

Weak interaction achieves a positive size selectivity in aggresome formation

Eukaryotic cells direct toxic and misfolded proteins to different protein quality control pathways including forming an “aggresome”, a perinuclear inclusion around the centrosome that sequestrates various species of protein aggregates. To understand how protein aggregates are identified and selectively targeted to the aggresome by the dynein motor, we reconstituted the aggresome formation process in Xenopus laevis egg extract using a chemically inducible aggregation-prone protein AgDD. We find a positive size selectivity (PSS) in aggregate transport, where the transport speed positively correlates with the aggregate’s size. Through high-resolution tracking experiments and mechanistic modeling, we postulate that the PSS appears specifically associated with the aggresome-specific dynein adaptors and emerges due to an avidity entropy mechanism that may bias larger aggregates towards the active transport state.

Zhenyi Zhang
Peking University

DECENT-niPGT: Advancing maternal contamination removal and CNV reconstruction in noninvasive preimplantation genetic testing through deep learning

Non-invasive preimplantation genetic testing for aneuploidy (niPGT-A) plays a crucial role in selecting embryos with high potential for healthy live births. However, maternal DNA contamination in spent embryo culture media (SECM) compromise the reliability of chromosome ploidy profiles, leading to false negative results particularly at high contamination levels. Here we present DECENT-niPGT, a deep learning method to mitigate maternal contamination in SECM and reconstruct embryonic CNVs from single-cell methylation sequencing of cell-free DNAs. Benchmarking study demonstrates DECENT’s robust ability to reconstruct CNVs in samples with varying contamination levels. Overall, DECENT contributes to substantially enhancing the effectiveness of SECM-based niPGT.

Nan Dong
Beijing Normal University, Zhuhai

Controlling individual nodes to restore the state of nodes in a complex network

Cellular regulatory systems, like protein expression, can be modeled as dynamical systems using differential equations on a complex network. Restoring a dysregulated system with simple methods is an intriguing problem. This paper presents a method to control individual nodes to restore the system. A node is randomly selected, and other nodes determine their layers based on the shortest path to it. Nodes in the same layer can be replaced by an average node. Results indicate that the system is more easily restored with greater control intensity and higher network average degree.

Haozheng Huang
South China University of Technology

Design and Apply An RNA-Protein Hybrid Gene Circuit for Robust Pulse-Like Gene Expression in Escherichia coli

Type 1 incoherent feed-forward loop (I1-FFL) can exhibit pulse-like expression under specific conditions. However, the use of multiple induction systems in I1-FFL and the metabolic burden of transcriptional factors on host cells limit its applications. In this study, we designed and proposed an RNA-protein hybrid I1-FFL gene circuit, incorporating a toehold switch[1] and CymR[2], to achieve pulse-like expression for target genes in Escherichia coli. We established a comprehensive mathematical model based on the cell growth, and gene expression at both RNA and protein levels for the I1-FFL. The agreement between experimental data and model predictions demonstrated the model's qualitative and quantitative accuracy under various conditions, including promoter strengths, toehold switch types, inducer concentrations, and host strains. We then constructed an acid-tolerant I1-FFL featuring an Hfq-DsrA module[3]. At pH 5.5 and pH 4.5, the acid-tolerant I1-FFL improved the cell growth of E. coli MG1655 by up to 23-29%. Our results validate that mathematical modeling aids in constructing complex gene circuits. The I1-FFL facilitated by model predictions has significant potential applications in microbial engineering.

Qianli Zhang
Peking University

Optimally efficient programming of intercellular signaling transduction for cell type diversification

Intercellular signaling via ligand-receptor binding is essential for cell diversification during embryogenesis and organogenesis, yet its overall design remains unclear. This study integrates data on Caenorhabditis elegans' embryonic cell_x005f cell contact maps, proposing a model that combines multicellular mechanics and cell differentiation. The model posits that specific signaling between contacting cells induces new cell types only if the target cell, not its sibling, contacts the signaling cell. Multiphase field simulations replicate embryonic structures up to the 12-cell stage. Enumerating possible signaling programs highlights C. elegans' efficiency in cell type diversification, providing insights for synthetic systems like synNotch.

Ye-Fan Hu
BayVax Biotech Limited,China

Antigenic Distance and Antigenic Field: A Novel Approach to Enhance COVID-19 Vaccination Against Emerging Variants of Concern

Current COVID-19 vaccines are effective against symptomatic disease, but repeated ancestral strain boosters offer limited extra protection against variants of concern (VOC). Our model based on "antigenic distance hypothesis" helps to select booster vaccine seed strains. Our model suggests that a SARS-CoV-1-based booster vaccine can cover a wider range of VOCs. The SARS-CoV-1-based booster vaccine performed better than other candidates. We introduce the concept of the "antigenic field" to illustrate the coverage and strength of protection induced by boosters. Our study proposes an "antigenic field" theory to quantify anti-viral responses, which could be valuable for designing vaccines and antigen-based immunotherapies.

Lu Wu
Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences

Data-driven prediction of colonization outcomes for complex microbial communities

Microbial interactions can lead to different colonization outcomes of exo_x005f genous species, be they pathogenic or beneficial in nature. Predicting the colonization of exogenous species in complex communities remains a fun damental challenge in microbial ecology, mainly due to our limited knowledge of the diverse mechanisms governing microbial dynamics. Here, we propose a data-driven approach independent of any dynamics model to predict coloni zation outcomes of exogenous species from the baseline compositions of microbial communities. We systematically validate this approach using syn thetic data, finding that machine learning models can predict not only the binary colonization outcome but also the post-invasion steady-state abun dance of the invading species. Then we conduct colonization experiments for commensal gut bacteria species Enterococcus faecium and Akkermansia muciniphila in hundreds of human stool-derived in vitro microbial communities, confirming that the data-driven approaches can predict the colonization outcomes in experiments. Furthermore, we find that while most resident species are predicted to have a weak negative impact on the colonization of exogenous species, strongly interacting species could significantly alter the colonization outcomes, e.g., Enterococcus faecalis inhibits the invasion of E. faecium invasion. The presented results suggest that the data-driven approaches are powerful tools to inform the ecology and management of microbial communities.

Yunxiao Dai
Shenzhen Institute of Advanced Technology, hinese Academy of Sciences

Generative design of protein interaction partner

Protein-protein interactions (PPIs) are crucial for biological functions and form the basis of modern protein detection methods. However, designing and generating new interacting partner proteins, such as antibodies, is both expensive and time-consuming. Recent advancements in deep learning have vastly improved PPI prediction, where protein sequences of both the target and the partner are given, with the partner sequence to be variable. Yet, exploring the extensive protein sequence space for the binding partner remains computationally expensive and challenging. This research aims to develop models that produce potential partners for a given protein using transformer-based models in a generative fashion. We will utilize data from STRING and PDB and validate the interactions using AlphaFold. Predictions will also be tested experimentally using a recombinant purified system and a yeast-cell-based system.

Huili Yuan
Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences

A dynamic metabolic model by integrating proteome allocation with flux balance analysis

Changes in the environment often generate global effects on bacterial gene expression, which are often accompanied by changes in the growth rate. Integrating non-metabolic cellular processes, such as gene expression and macromolecule synthesis, with modelling of metabolism remains a major challenge in systems biology, as there is a lack of mechanistic representation of gene expression regulation. Here, we introduce a new constraint-based modelling framework termed dynamic Constrained Allocation Flux Balance Analysis (dCAFBA), which unifies the modelling of metabolism, cellular resource allocation and gene regulation in a global manner. In the model, we adopted a quasi-steady-state assumption that the balance of reaction fluxes can be attained at each time step, as they adapt much faster than protein synthesis and growth dilution. This model allow us to predict the dynamics of reaction fluxes, and protein allocation required to achieve a cellular objective, such as optimising growth during the different growth shifts (carbon shifts, AA shift and exogenous gene expression shift), without involving molecular details on gene regulations. Our model provides a novel method for interpreting proteome allocation and cellular metabolism under complex and transient environments, and gives mechanistic guidance for metabolic engineering.

Xiaoting Xu
Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences

Experimental evolution of cytoplasmic density mutants

Many factors, including osmotic challenges and compression, can potentially change the cytoplasmic density of a cell. Cells must adapt to these changes, yet the specific cellular processes sensitive to these changes and the cell's coping mechanisms remain poorly understood. To investigate this, we performed experimental evolution to generate high-density and low-density yeast mutants, which were then used to study the effects of cytoplasmic concentration on cellular function.

Zhuo Mao
Westlake University

Synthetic Spatial Proofreading System for High-fidelity Intercellular Communication

At the single-molecule level, nature achieves high fidelity via kinetic proofreading. Inspired by the principles of classic kinetic proofreading and the mathematical simulation of gradient-based proofreading, we propose that designed spatial gradients could give rise to high-fidelity signal transduction at the bulk level by constructing a synthetic circuit for high-fidelity cell-cell communication.

Renyu Wang
Peking University

Compartmentalized Oscillating Translation Enhances Circadian Amplitude Rhythms

The experiment has revealed that oscillating translation is regulated by spatiotemporal condensation of two master regulators to achieve precise circadian rhythm in mammals. It has been identified mammalian ATXN2 and ATXN2L as cooperating master regulators of rhythmic translation, through oscillating phase separation in the suprachiasmatic nucleus along circadian cycles. The spatiotemporal oscillating condensates facilitate sequential initiation of multiple cycling processes, from mRNA processing to protein translation, for selective genes including core clock genes. Here, we characterize the effect of droplets on the oscillating system, based on Kim & Forger's interpretation of the circadian clock in mammals.

Qian Li
Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences

Genome-wide screening for mutants defective in biomass volume coordination

The coordination between cellular biomass and cell volume is crucial for biological functions, resulting in macromolecular concentration homeostasis. Disruption of biomass-cell volume coordination is correlated with senescence and aging. However, the mechanisms behind this coordination are poorly understood, and no specific regulators are known. Here, we use genome-wide screening in budding yeast to identify mutants with altered protein mass-volume balance. This screening will reveal factors involved in biomass-volume regulation and provide insights into how protein concentration homeostasis is achieved, as well as the causal relationship between macromolecular concentration homeostasis and cellular senescence.

Zhiyuan Li
Peking University

Forging the Iron-Net across the Microbial Kingdom

Iron is a critical yet limited nutrient for microbial growth. To scavenge iron, most microbes produce siderophores—diverse small molecules with high iron affinities. Different siderophores are specifically recognized and uptaken by corresponding recognizers, enabling targeted interventions and intriguing cheater-producer dynamics. We propose constructing a comprehensive iron interaction network, or "iron-net," across the microbial world. Such a network offers the potential for precise manipulation of the microbiota, with conceivable applications in medicine, agriculture, and industry, as well as advancing microbial ecology and evolution theories. Previously, our successful construction of an iron-net in the Pseudomonas genus demonstrated the feasibility of co-evolution-inspired digital siderophore typing. Enhanced by machine learning techniques and expanding sequencing data, forging such an iron-net calls for multidisciplinary collaborations, and holds significant promise in addressing critical challenges in microbial communities.

Abhilasha Batra
Indian Institute of Science Education and Research Bhopal

Deciphering the Adaptation Mechanism of Thermosensory Neurons to Temperature Signals in C. elegans

In animals, various sensory neurons perceive and transduce external stimuli through different signalling pathways, allowing them to adjust to shifts in their surroundings. Similarly, a type of thermosensory neurons (AFD) in small nematodes C. elegans is responsible for detecting external temperature changes. Our mathematical model of the AFD neurons aids in understanding the decoding mechanism of thermal stimuli by them, whereas through experiments we decipher the role of receptors specific to these neurons in the regulation of cellular processes in C. elegans. We explore through the model how the second messenger cGMP and calcium response of the neurons adapt to variations in stimuli in a growth conditions-dependent manner. We find that the receptors of the main signalling pathway in neurons decode the memory of growth temperature in worms. The model mainly reveals insights into the change in the dynamic responses of cGMP and calcium to external temperature perturbations. Along with this, the experiments on guanylyl (gcy's) receptor-based genes of AFD neurons show the influence of neuronal signalling on the ability of worms to cope with overall thermal stress.

Dianjie Li
Peking University

Dynamical modelling of viral infection and cooperative immune protection in COVID-19 patients

Upon encountering the SARS-CoV-2 virus, the human immune system launches a dynamic and complex response. Previous researches have primarily focused on individual aspects of the immune system, overlooking its tripartite compositions (innate, cellular and humoral immunity). Here, we present a mathematical model that captures virus-immunity dynamics during both primary infection and vaccine-induced protection. Our analysis reveals an integrated metric, combining cellular and humoral immunity, to quantify the overall immune response. This metric correlates strongly with disease severity and vaccine efficacy against different SARS-CoV-2 variants. Our findings offer a systematic framework for understanding virus-immune interactions and optimizing treatments and vaccine strategies.

Jianwei Li
Peking University

Reverse mitotic trigger wave in low ATP ADP region

Living organisms utilize external energy to convert into negative entropy and drive internal reactions to proceed orderly away from equilibrium states. On the level of molecular reactions, ATP and ADP play the crucial role. Focused on G2-M transition within the cell cycle, we explored different combinations of ATP and ADP level and showed how reaction rates and directions change under these combinations. Within certain region, even a reversed mitotic trigger wave can be achieved, that is, the propagation of interphase. Similar regulatory of ATP and ADP have also been observed in the MinCDE system. This reveals that ADP and ATP levels are two independent determinants that regulate energy-consuming biological reactions such as mitosis.

Jiayi Chen
Peking University

mRNA concentration-dependent translational regulation during Drosophila embryogenesis

The low correlation between the mRNA and protein notwithstanding external interferences suggest regulations beyond transcriptional regulation, particularly in a highly dynamic system. Quantitative deciphering of translational parameters reveals that the spatially and temporally heterogeneous mRNA translating proportion of hunchback (hb) and knirps (kni) genes during Drosophila embryogenesis, can be unified into the non-monotonical correlation with mRNA concentration, while the effective translational efficiency exhibiting an approximate negative correlation. A quantitative mathematical model successfully explains the observed data, which is experimentally supported in a hb-deficient mutant.

Zhijian Hu
University of Michigan

Spatial drug heterogeneity changes the bacteria dynamics in a deleterious diffusive environment

Diffusion and migration play a significant role in microbial communities'shaping, for example, colonization of new environments or the maintenance of spatial structure. In this work, we study the interplay of migration and spatial heterogeneity in an experimental meta-community of E. faecalis, a Gram-positive opportunistic pathogen. When the community is confined to a single habitat surrounded with deleterious boundaries, we find that population survival depends on a growth-rate dependent trade-off between intra-island migration rate and the physical size of the island--a phenomenon we explore by modulating antibiotic concentration within the island. When the island itself is heterogeneous--comprised of spatially patterned patches that support different levels of growth (e.g. different drug concentrations)--the fate of the population becomes dependent on the specific spatial arrangement of patches, even across populations that are identical at a mean-field level. These results are partially captured by simple analytical expressions which we derive using WKB-like approximations to reaction-diffusion models with explicit spatial dependence. Finally, we discuss our ongoing extensions of this approach to investigate increasingly complex, but tunable, experimental communities that can be quantitatively tracked on both ecological and evolutionary timescales.

Jingyu Dou
Fudan University

A method of reconstructing gene dynamic in multi-stable systems

Gene regulation dynamics are important for predicting cell fate and understanding transitions between cell states. This study introduces an approach using the enhanced Neural ODE to infer gene dynamics, focusing on core gene selection, network inference, and parameter estimation. Simulation results demonstrate the method's effectiveness in reconstructing gene networks and accurately estimating parameters. Our study offers methods to explore gene regulation mechanisms in complex biological systems.

Yi Zhang
Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences

Navigated range expansion promotes migratory culling

Motile organisms can expand into new territories and increase their fitness1–6, while nonmotile viruses usually depend on host migration to spread across long distances7–9. In general, faster host motility facilitates virus transmission10. However, recent ecological studies have also shown that animal host migration can reduce viral prevalence by removing infected individuals from the migratory group11. Here, we use a bacteria-bacteriophage co-propagation system to investigate how host motility affects viral spread during range expansion. We find that phage spread during chemotaxis-driven navigated range expansion decreases as bacterial migration speed increases. Theoretical and experimental analyses show that the navigated migration leads to a spatial sorting of infected and uninfected hosts in the co-propagating front of bacteria-bacteriophage, with implications for the number of cells left behind. The preferential loss of infected cells in the co-propagating front inhibits viral spread. Further increase in host migration speed leads to a phase transition that eliminates the phage completely. These results illustrate that navigated range expansion of the host can promote the migratory culling of infectious diseases in the migration group.

Jinchao Lv
Fudan University

Inferring model parameters from experimental data to reconstruct the landscape in gene regulatory networks

The Waddington landscape serves as an impor_x005f-tant tool for quantitatively describing the developmental and differentiation processes of cells. To reconstruct the landscape, researchers either manually specify model parameters or collect the joint statistics from the snapshot data. So far, it remains challenging to infer parameters in gene regulatory network (GRN) models by integrating experimental data. Here, we present a general framework that employs optimization methods to accurately estimate parameters in GRNs, including linear terms: each gene's basal production rate and maximum production rate, and nonlinear terms: the regulation threshold S. In silico data from a simplified two-dimensional mutual inhibition self-activation (MISA) model and a 52-dimensional Human Embryonic Stem Cell (HESC) model, our method demonstrates a strong capability to reconstruct system parameters. In vivo data from Type 2 Diabetes (T2D), our method reveals parameter differences between normal and diseased individuals, and provides strategies for identifying potential gene targets.

Xiaofang Zhong
Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences

Regulation of intracellular density in mammalian cells

Both cell mass and cell volume are regulated through complex mechanisms, yet intracellular density - defined as the ratio of cell mass to cell volume - remains remarkably constant. The mechanism governing the coordination between the growth laws of cell mass and cell volume is unknown. To investigate the genetic basis of density regulation in mammalian cells, we aimed to separate multipotent stem cells, each expressing one or a combination of over 500 transcription factors, into lighter or denser fractions from a Percoll gradient. Using the Next-Generation Sequencing (NGS), we will identify the transcription factors that influence the intracellular densities. Furthermore, we will conduct differentiation assays, both in vitro and in vivo, to assess the differentiation potential of cells with varying densities.

Pan Chu
Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences

Spatial pattern emerges from a toggle switch in bacterial colony

Microbial colony development depends on various factors, including mechanical, chemical, and environmental niches, shaping spatial patterns via gene regulatory networks. Here, we reveal the multi-stability of bacterial colony patterns with a simple bistable switch. We explore the deterministic process of a ring-like colony pattern formation from a single cell. This process is driven by bifurcation events programmed by the gene regulatory network and microenvironmental cues. Additionally, we observe a noise-induced process amplified by the founder effect, which leads to a symmetry-break pattern. The degrees of asymmetry are influenced by the initial conditions of the seed cell. These findings underscore how the process of range expansion enables a cell to exhibit emergent and self-organized behavior in a uniform environment.

Gang Xue
Peking University

A Logic-based Gene Regulatory Network Deciphers Principles in Cell Fate Decisions

To comprehensively understand the role of reg_x005f ulatory logic in cell fate decisions, we constructed a logic based gene regulatory network (GRN) and examined it under two driving forces. Under the noise-driven mode, we distilled the relationship among fate bias, regulatory logic, and noise. Under the signal-driven mode, we bridged regulatory logic and progression-accuracy trade-off. In addition, we characterized a special logic-dependent priming stage by the solution landscape during the differentiation process. Finally, we applied our findings to three biological instances: hematopoiesis, embryogenesis, and trans-differentiation. Our work presents a generalizable framework for top-down fate-decision studies and a practical approach to the taxonomy of cell fate decisions.

Hanyi Li
Tsinghua University

Concentration-Mediated Regulaiton Mechanism of Biomacromolecule Recruitment in Phase Separation

Liquid-Liquid Phase Separation (LLPS) can regulate various cellular processes, including biochemical reactions and gene expressions, by concentrating enzymes or regulatory factors [1,2,3]. Our study presents a quantitative model based on Flory-Huggins theory, describing the concentration of recruited components and relevant biological functions during LLPS.

The research focuses on phase separation behavior driven by a specific component (Driver, usually a macromolecule like protein capable of spontaneous phase separation) that recruits other components incapable of spontaneous phase separation (Passengers, can be enzymes, substrates or regulatory factors). On this basis, the study explores the physical mechanism by which phase separation affects the rate of biochemical reactions.

The results indicate that the recruitment of multiple Passenger components by Driver exhibits different patterns depending on the strength of components interactions and displays varying behaviors at different concentrations. In a two-Passenger system, the system exhibits either synchronous or asynchronous enrichment behaviors. Furthermore, for enzyme reactions facilitated by this phase separation (enzyme and substrate are passengers), the enzymatic activity can be up- or down-regulated by driver on a dose-dependent manner, and an optimal Driver concentration for the phase-separated droplets exists when enzyme and substrate are both sufficiently recruited. The model's reliability was verified by in vitrom experimental data of PRC2 (Passenger-1)-catalyzed methylation of MN (Mono-nucleosome, Passenger-2) with the recruitment by DDX18 (Driver).

This study establishes a comprehensive physical model for recruitment behavior during LLPS. Also, the study reveals the impact of components interactions on the phase separation process, indicating rich design flexibility of phase separation systems.

Xiaoyu Wu
Westlake University

Multivalency-enabled signal processing at the single protein level

Multivalency is common in nature and provides researchers with a strategy for incorporating a range of properties into their designs. Here we demonstrate with experiments and mathematical models that multivalency can give specificity and selectivity in cell discrimination. Our work offers researchers a general tool to design and optimize constructs with the magic of multivalency.

Luxuan Qu
Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences

Bacteria Treadmill: A powerful tool for providing stringent and extreme selection

Bacteria Treadmill, a machine custom-designed in our laboratory, can impose stringent and extreme selection pressure on the migration speed of E.coli MG1655. Both growth and chemotaxis contribute to the migration speed with previous research indicating a tradeoff between these two, though the underlying mechanisms are not well understood. We hypothesize that a cell's limited energy production capacity underlies this phenomenon as both growth and motility cost large amounts of energy. Over a 75-day period of tireless running on the treadmill, bacteria evolved a threefold increase in migration speed, coupled with a roughly 50% reduction in growth rate, illustrating a clear tradeoff. Genomic sequencing revealed mutations in genes associated with chemotaxis (FlhD, FliG, CheZ, Tsr), gene expression (InfC, RpoB), and cell shape (MreC, Lpp). All these mutations became fixed upon their appearance, confirming the extremely high selective pressure in of the Bacteria Treadmill, although the upper limit of growth-chemotaxis tradeoff remained unbroken. Future work will involve long-term operation of the Bacteria Treadmill and increased mutation rates to push hardeer on the limit of the tradeoff. Evolving a strain that breaks the tradeoff most likely by cranking up energy output would beg reconsideration of the evolutionof energetics:why higher energy producers can still evolve in the laboratory despite 4 billion years of optimization in nature ?Practically, bacteria with enhanced energy production could serve as superior chassis cells for the production of various bioproducts.

Guanyue Xiong
Peking University

A computational framework of BGC-receptor pairing

The synthesis of natural products relies on a series of biosynthetic genes and regulatory genes, typically clustered together in genomic regions known as biosynthetic gene clusters (BGCs). In many cases, BGCs evolve together with their cognate receptors, as the products synthesized need be recognized by corresponding receptors to function properly. Consequently, changes in synthetase genes are accompanied by changes in their cognate receptor genes, called the co-evolution. However, predicting the pairing relationships between BGCs and their cognate receptors directly from genome sequence remains challenging due to the complexity and variability in BGC synthesis and transport systems. Here, we propose a general computational framework to solve this problem based on the co-evolution between BGCs and receptors. We use the pyoverdine-TonB system to test our algorithm. Pyoverdine is a kind of siderophores, secreted by Pseudomonas for iron acquisition, with specific TonB-receptors responsible for their recycling. This algorithm enables unsupervised clustering of pyoverdine BGCs and TonB-receptors into functional groups based solely on genomic data, while pairing each pyoverdine group with its most compatible receptor group.

Yang Bai
Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences

Adaptive evolution of active navigation in disordered landscape

To navigate through disordered landscape filled with random traps, an organism needs to direct its motion to approach the destination while randomize its motion to overcome the disruption induced by traps. To understand how an organism balances the directness and randomness to achieve optimal navigation performance in disordered landscape, we studied the chemotactic range expansion of E. coli who bias its random run-tumble motions in agar gel. Using evolutionary assays and quantitative experiments, we show that bacterial chemotactic ability adapts to disordered landscape by optimizing its mean free runtime with the optimal mean free runtime increase with the mean free runtime between traps (negatively correlated to agar concentration). Based on detailed analysis of individual cell behavior in agar gel, we show that running of bacteria was randomly trapped while tumbled. we further developed a model that represents bacterial chemotaxis in a disordered landscape as a competitive stochastic process involving transitions between run-tumble and run-trap events. Increasing the free runtime enhances the cell's diffusivity, aiding bacterial navigation. However, it also increases the probability of run-trap events which has no contribution to the directness of the navigation. These opposing effects give rise to a non-monotonic relationship between chemotaxis ability and the mean free runtime with positively dependent to.In summary, our study demonstrates how bacterial chemotactic ability adapts to disorder landscape by optimizing its free runtime as an optimal strategy to balance the directness and randomness motions for effective navigation.

Lingling Wen
Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences

Strong segregation promotes self-destructive cooperation

Self-destructive cooperation (SDC), a phenomenon that individuals sacrifice themselves for the benefit of others, poses a significant personal cost yet is surprisingly prevalent in natural. However, the maintenance of SDC evolution Traditional evolutionary theories of group selection struggled to explain this behavior as the extreme cost of self-destruction overweighted its benefit to other SDC individuals. However, our theoretical analyses revealed that SDC can endure in highly segregated environments where populations are predominantly divided into homogeneous groups. In such contexts, the benefit derived from SDC acts are primarily confined within the SDC group, thus preserving the value of this altruistic sacrifice and ensuring its maintenance. These findings were further experimentally validated with synthetic SDC strains and developed automated experiments facilitated by biofoundry technology. This approach overcame the considerable challenge posed by the diverse growth behaviors of subgroups resulting from strong segregation. Furthermore, t elucidated that that high stress conditions is beneficial for SDC maintenance as it penetrates the yield of cheaters in heterogenous subgroups while keeping the yield of homogenous SDC subgroups. This study extends the group selection theory to encompass even the most extreme manifestations of altruism but also highlighted the potential of automation in advancing evolutionary studies.

Jianzhe Wei
Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences

Toggle switch, but not in Kramers' way

State switch is a crucial feature in various levels of biological systems, from genetic circuits to developing tissues, from immune systems to ecology systems. There have been intensive theoretical studies on this topic, including the construction of general frameworks and the investigations on specific models. In contrast, the experiment observation is rare. In this talk, we report a direct observation of switch process of a toggle switch circuit in bacteria. In the experiment, the states of over 1500 cells are tracked for 13 hours with the aid of the mother machine setup. The careful analysis on the trajectories suggests the switch does NOT happen in the small noise limit. The classical treatment since Kramers is hence invalid. Assuming the flat landscape limit, which is the verso of the small noise limit, the first-passage process of simple Ornstein-Uhlenbeck model can well explain the experiment observation. The distribution of the transition time is studied. The consequences of the observation are discussed.

Kang Xia
Peking University

Cysteine limitation and tumor immune evasion

Cysteine serves as the primary intracellular antioxidant provider. Depletion of cysteine triggers ferroptosis in cancer cells, rendering tumors more susceptible to diverse therapeutic interventions. In this study, we demonstrate that cysteine depletion amplifies the efficacy of immunotherapies in colorectal cancer. Employing a combination of quantitative metabolomics and single-cell transcriptomics, we observed that cysteine depletion rewires the metabolism of cancer cells and modifies the nutrient composition of the tumor microenvironment. This alteration impedes the activation and function of immune-suppressive regulatory T (Treg) cells, concurrently promoting the infiltration of cytotoxic CD8+ T cells.

Guang Shi
University of Texas at Austin

Predicting chromatin dynamics from structural information

Understanding the dynamic organization and packaging of the genome is crucial for addressing fundamental biological questions such as gene regulation and cell differentiation. Computational and theoretical modeling, utilizing existing experimental data, provides mechanistic insights into the physics of genome organization, underpinning much of our understanding in this area. We introduced a computational framework based on the maximum entropy principle, using pairwise distances between chromosomal loci as constraints, to generate a unique ensemble of 3D chromatin structures. This approach enabled us to quantitatively describe the distribution of pairwise distances, as well as three-body co-localizations and higher-order interactions, across both small and large chromosomal scales. Extending these methods, we now use static data sources, such as Hi-C and fixed-cell imaging, to predict the dynamic behavior of chromatin loci. Our model forecasts two-point mean square displacement and autocorrelation functions, revealing significant deviations from traditional polymer models like the Rouse model and the crumpled globule model. This indicates a more intricate interplay of interactions within chromatin. The model's predictions are validated against experimental data, demonstrating its potential to bridge the gap between static structural data and chromatin's spatiotemporal behaviors.

Venue

Guangming Tianan Cloud Park
(光明天安云谷)

Address:
No.98 Zhenyuan Road, GuangmingTianan Cloud Park, Guangming District, Shenzhen

Main venue:
International Conference Hall Third Floor
Lecture Hall Third Floor

Poster Session (evening of July 27th):
Conference Hall Third Floor

Transportation & Accommodation

Travel Information:

- **Airport:**
  The conference venue is approximately 1 hr by car from Shenzhen Bao'an International Airport.

- **Railway Station:**
  The conference venue conveniently located near Shenzhen North Railway Station.

Hotel Recommendations:

There are two locations for Room and Board.

1.EVEN Hotel Shenzhen Guangming Tianan Cloud Park 深圳光明天安云谷逸衡酒店
Address: No.98 Zhenyuan Road GuangmingTianan Cloud Park, Building B,Block 2, Guangming District, ShenZhen, Guangdong Province

地址： 广东省深圳市光明区新湖街道圳园路98号光明天安云谷产业园2栋B座

2.Holiday Inn Express Shenzhen Guangming Tianan Cloud Park 深圳光明天安云谷智选假日酒店
Address: No.98 Zhenyuan Road GuangmingTianan Cloud Park, Building B,Block 1, Guangming District, ShenZhen, Guangdong Province

地址： 广东省深圳市光明区新湖街道圳园路98号光明天安云谷产业园1栋B座

Banquet

Conference Banquet:

The conference banquet will be held on July 29th, 18:00-21:00 pm.
at International Conference Hall Third Floor. Meal and drinks will be served.

Meals and Tea Breaks:

In order to facilitate informal discussions among the participants, complimentary meals and tea breaks will be provided.

Three meals of July 27th

7:30-9:00am for breakfast served by the hotel of stay.
12:30-13:30pm for lunch at Holiday Inn Express Dinning Room Third Floor.
18:00-21:00pm the Poster Session will be held, appetizer and drinks at Hallway of International Conference Hall Third Floor.

Two meals of July 28th

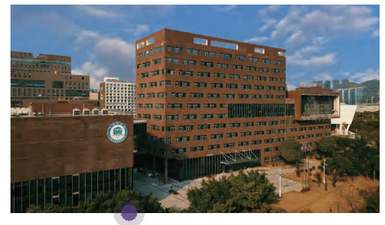
7:30-9:00am for breakfast served by the hotel of stay.
12:30-13:30pm for lunch at Holiday Inn Express Dinning Room Third Floor.

Three meals of July 29th

7:30-9:00am for breakfast served by the hotel of stay.
12:30-13:30pm for lunch at Holiday Inn Express Dinning Room Third Floor.
18:00-21:00pm the conference banquet will be held, meal and drinks will be served at International Conference Hall Third Floor.

Travel Guide

Science Park
（科学公园）


Shenzhen Institute of Advanced Technology, CAS
（中科院深圳先进技术研究院）


Urban Planning Exhibition Hall
（光明城市规划馆）


OCT-LOFT
（华侨城创意文化园）


Lianhuashan Park
（莲花山公园）


Fairy Lake Botanical Garden
（仙湖植物园）

Nantou Ancient Town
（南头古城）

Ping An International Finance Centre
（平安金融中心）


Shekou Sea World
（蛇口海上世界）

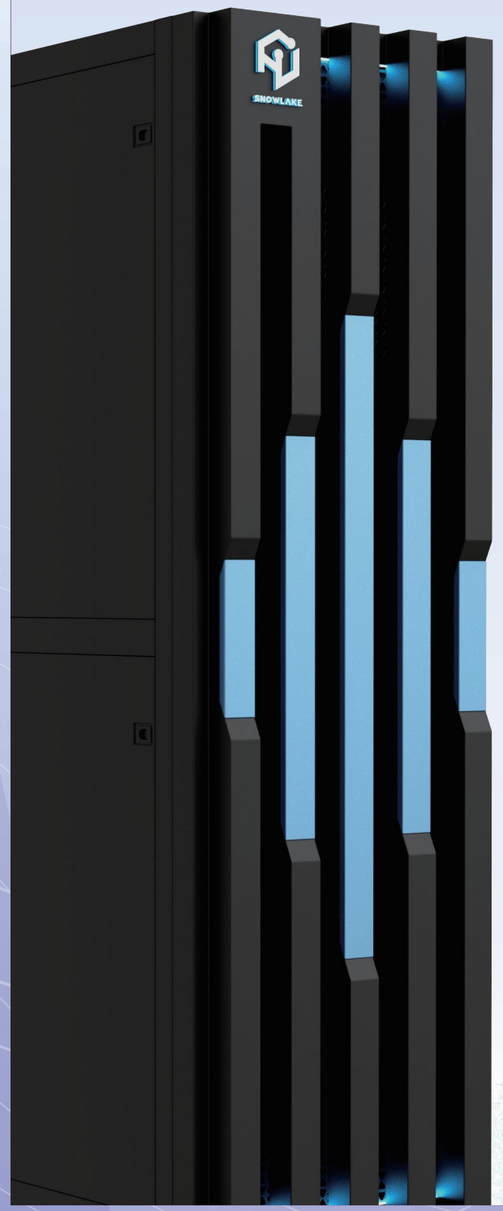

Shenzhen Bay Park
（深圳湾公园）


OCT Bay
（欢乐海岸）

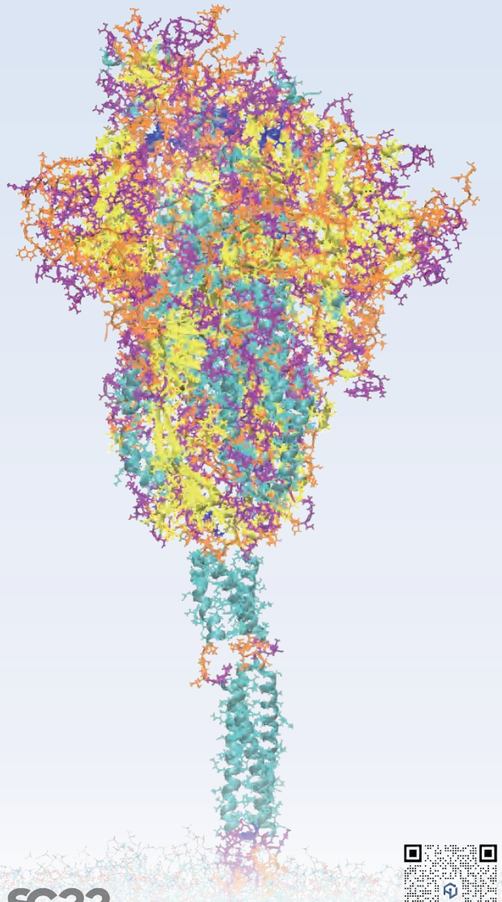
Splendid China Folk Culture Village
（锦绣中华民俗村）

雪湖科技
SNOWLAKE

SNOW LAKE SUPERCOMPUTING



Molecular dynamics simulations of
100,000,000 atoms



SC23
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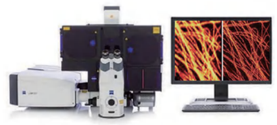
As the pioneer of science in optics, we continue to challenge the limits of our imagination. With our passion for excellence we create value and inspire the world to see things in new ways.

1864
Carl Zeiss
opened a workshop in Jena for precision engineering and optics

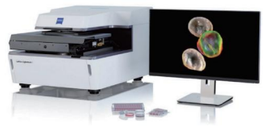
1866
Ernst Abbe
became part owner

1936
The first prototype of a phase-contrast microscope built by ZEISS in Jena (1936) based on Zernike's design

1982
ZEISS launched the first commercial laser scanning confocal microscopy named LSM 44



2013
The ZEISS Elyra system is based on the PALM Principle, developed by Eric Betzig and Harald Hess



2020
The ZEISS Lattice Lightsheet 7 system based on Betzig's Lattice Lightsheet principle

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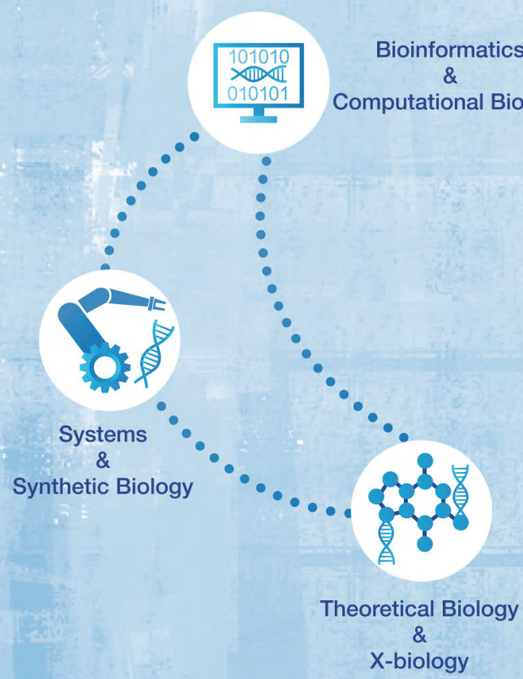
An X-disciplinary Journal Leading to Future Biology

Aims

Quantitative Biology is an interdisciplinary journal that focuses on cutting-edge progresses, in-depth reviews as well as future perspectives of research that uses all quantitative approaches to analyze, model and engineer biological systems, and to gain quantitative understanding of the mystery of life. The quarterly journal aims to provide a platform for sharing not only new methods, technologies and results, but also novel or even sometimes bold ideas, visions and perspectives. “All rivers run into sea.” The journal covers all disciplines related to experimental biology, theoretical biology, computational biology, systems biology, synthetic biology, digital and AI biology.

Scopes



Journal Metrics

Time for the first decision: 5 days
Time for peer-review decision: 10 days
Time from submission to accept: 90 days
Time for fast track papers: 7 days

Indexing Information

Emerging Sources Citation Index
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Email:
qbio2024@siat.ac.cn