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MEETING REPORT

Quantitative Biology 2019: Dynamic Signaling in Cells and Embryos

Feng Liu[1,†,*], Yihan Lin[1,†,*], Chunmei Li[1], Miaomiao Tian[2]

[1] Center of Quantitative Biology, Peking University, Beijing 100084, China
[2] Editorial Office of Quantitative Biology, Beijing 100084, China
* Correspondence: liufeng-phy@pku.edu.cn, yihan.lin@pku.edu.cn

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The International Conference on "Quantitative Biology 2019: Dynamic Signaling in Cells and Embryos" was successfully held at Dongshan Hotel, Yantai, China, from June 22nd to 24th. The conference was co-sponsored by the Center for Quantitative Biology (CQB) of Peking University and Yantai University and was organized by Prof. Chao Tang, Prof. Feng Liu, and Prof. Yihan Lin from Peking University, China, Prof. Michael B. Elowitz from Caltech, USA, and Prof. Yibao Chen and Prof. Xuran Wu from Yantai University, China. Totally 26 experts in the field of quantitative biology were invited to deliver talks from Canada, China, France, Germany, Israel, Japan, Singapore, South Korea, Spain, and United States. A total of 267 researchers worldwide attended the conference, and participated in diverse conference activities, including invited and contributed talks, flash talks, poster presentations, and panel discussions.

The main theme of the meeting is based on two emerging questions in quantitative biology: (1) How do cells and embryos make decisions with dynamics-based strategies? (2) How can we achieve a systems-level understanding of cellular and embryo dynamics by integrating advanced imaging/omics tools and new theories? With the emergence of new quantitative measurement techniques, the frontier of quantitative biology is expanding from single-celled model organisms to more complex multicellular systems such as embryos. Quantitative imaging techniques enable the visualization of signaling dynamics at high spatiotemporal resolutions, while single-cell omics techniques provide a systems-level characterization of the dynamic signaling systems in cells and embryos. Increasing evidence from both types of techniques reveals that many signaling systems implement dynamic strategies to respond to stimuli and control key biological processes, from immune responses, to developmental pattern formation, and disease progression. Meanwhile, new mathematical models and theoretical methods have been developed for decoding the mechanisms and functional roles of signaling dynamics in cells and embryos and are expanding from pure gene network models to more complex interactions such as the coupling between metabolites and gene regulation, and the coupling between cellular mechanics and intracellular signals.

As Prof. Michael B. Elowitz concluded in the closing remark, most talks in the conference reflected three central themes in quantitative biology. The first theme is about the influence of engineering in quantitative biology. Using engineering tools, we can design protein communicators to look inside cells, measure cells with single molecular accuracy in the context of embryos, and even study different species in genome scales. Firstly, one of the powerful engineering tools is synthetic biology. In his own talk, Prof. Michael B. Elowitz introduced the emerging design paradigms of natural and synthetic protein circuits in mammalian cells. He demonstrated that some important intercellular pathways such as BMP and Notch pathways use multiple promiscuously interacting ligands and receptors to enable specificity. This learned principle can help design versatile synthetic protein-level circuits to engineer cells. Prof. Ping Wei from Peking University, China, presented a synthetic biology approach to reconstitute the NF-κB system in *S. cerevisiae*, which was instrumental for systematically studying complex

† These authors contributed equally to this article.

signaling behaviors. Secondly, one of the rapid developing engineering tools is imaging. Several talks presented exciting advances in employing imaging approaches to quantitatively study biology. Prof. Long Cai from California Institute of Technology, USA, introduced the advantages and applications of seqFISH+ in single cell genomic researches. Prof. Daniel R. Larson from National Cancer Institute, USA, demonstrated the dynamic imaging of nascent RNAs, which could reveal general principles of transcription dynamics and widespread recursive splicing. Prof. Seung Joong Kim from Korea Advanced Institute of Science and Technology, Korea, presented the integrative structure and functional anatomy of a Nuclear Pore Complex (NPC). Prof. Masahiro Ueda from RIKEN Quantitative Biology Center, Japan, introduced their automated single-molecule imaging apparatus to analyze live-cell and discussed its application in intracellular self-organization of signaling system for gradient sensing and directed cell migration in *Dictyostelium* cells. Prof. Robert E. Campbell from University of Alberta, Canada, showed engineering genetically-encoded fluorescent indicators to study the dynamic visualization of cell signaling and metabolism. Prof. Yi Yang from East China University of Science and Technology, China, described the development of Peppers, a series of stable fluorescent RNA mimics (FRs) with a broad range of emission maxima spanning from cyan to red and how to use them in studying mRNA dynamics and stochastic translation in live cells. Dr. Sheng-Yi Wu from University of Alberta, Canada, described the improvement of GINKO1 (green indicator for potassium (K^+) ion optical imaging) with more sensitive, selective and cellular trafficking to investigate roles of K^+ in biology. Prof. Wenlei Xiao from Beihang University, China, introduced how to reconstruct cell lineages from large-scale living imaging data. Thirdly, more tools are developing to investigate cellular mechanics. Prof. Glenn S. Edwards from Duke University, USA, demonstrated the experimental and quantitative results about tissue dynamics during *Drosophila* morphogenesis through mechano-chemical regulation. Prof. Konstantin Doubrovinski from the University of Texas Southwestern Medical Center, USA, introduced the physical model of *Drosophila* gastrulation morphogenesis. Dr. Kuan Tao from Peking University, China, contributed his work about mathematical models on cell polarity and migration with coupled mechano-chemical factors.

The second theme is about cell fate decision. Cells decided the differentiation fate through selecting specific pathways in different systems. Prof. Yan Song from Peking University showed that SEC (super elongation complex) mediated previously uncharacterized phosphorylation to keep epigenetic memory and thereby ensures timeliness and robustness in NSC (neuron stem cell) fate lock-in. Prof. Jianhua Xing from University of Pittsburgh, USA, talked about the work of studying cell phenotypic transition quantitatively by combining single cell imaging and theoretical/computational analysis. Prof. Joo-Yeon Yoo from Pohang University of Science and Technology, Republic of Korea, showed stochastic cell-ECM adhesion might be responsible to observe population heterogeneity, which directly influences the basal infectivity of cell population. Prof. Nan Hao from University of California San Diego, USA, presented the Waddington's landscape of cell aging. Prof. Manu from University of North Dakota, USA, introduced how to use top-down and bottom-up modeling approaches to understand hematopoietic cell-fate specification. Prof. Luhua Lai from Peking University, China, focused on tuning TNF receptor signaling output by adjusting TNF binding. Prof. Robert P. Zinzen from Max Delbrück Center in Germany presented how to use RNA-seq data to acquire the neurogenic identities in embryonic development. Prof. Roy Kishony from Technion-Israel Institute of Technology, Israel, gave a talk about the theory and experiment of the drug resistance of bacteria.

The third theme is about noise. Noise plays functional roles in systems, which helps cells perform different functions. Prof. Jordi Garcia-Ojalvo from University Pompeu Fabra, Spain, talked about the metabolic consequences of ion-flux dynamics in bacteria. Prof. Hao Yuan Kueh from University of Washington, USA, introduced the temporal scalability in developmental gene circuits. Prof. Yihan Lin from Peking University, China, showed the functional roles of stochastic pulsing in evolution. Prof. Hsu Ian from University of Toronto, Canada, introduced the stochastic dynamics of Crz1 and their evolution. On the other hand, noise challenges the precise and reproducible patterning in embryos. Prof. Nathalie Dostatni from Sorbonne University, France, described the new approach combining fluorescent labeling of nascent mRNA with live-cell imaging to research cell identity, which regulated by the Bicoid (Bcd) morphogen system along the antero-posterior (AP) axis of the fruit fly embryo. Prof. Huy Tran from Institute Curie, France, talked about their recent progress on data driven modeling to understand patterning. Prof. Timothy Sanders from National University of Singapore, Singapore, presented the timing and scaling of Bicoid gradients. Prof. Feng Liu from Peking University, China, gave a presentation about illuminating precise developmental patterning to reveal the biological noise in *Drosophila* embryos. Jingxiang Shen from Peking University, China, contributed his work about a deep neural network model in reversed engineering biological regulation network.

In addition, Prof. Xiaojun Tian from Arizona State University, USA, explained about restoring the memory

of gene circuit by uncoupling growth-mediated feedback. Dr. Tianmin Wang from Tsinghua University, China, introduced his massively parallel profiling method to precisely study the coordinating transcription-translation dynamics of bacterial indole signaling. Dr. Shujuan Wang from Beijing Institute of Lifeomics, China, showed the dynamic analysis on ERBB complex assembly, which might provide mechanistic insight on drug sensitivity. Dr. Shouwen Wang from Harvard University, USA, gave a talk about the emergence of collective oscillations in adaptive cells.

The poster committee selected Zhe Yang and Jianhan Zhang as the "Best Poster Awards", Annan Guo, Xiaoxuan Wu, Hongcun Zhu, Yiming Dong, Shanshan Qin, Xiaochan Xu, Wen Huang, Jiayin Hong, Wei Yang and Wenjie Shi as the "Excellent Poster Awards" from totally 50 posters from Peking University, Dalian University of Technology, Ocean University of China, and Chinese Academy of Sciences, etc.

In the end of this conference, the organization committee also interviews with several invited speakers to discuss about the development of Quantitative Biology. Here are the questions and answers.

How would you define quantitative biology (QB)?

Prof. Glenn S. Edwards (Glenn): QB is biological physics added the power of the fundamental formalisms of physics, chemistry, and mathematics to quantify the (dynamical) mechanisms underlying biological description. He advocated for any definition of quantitative biology to include the attributes of biological physics.

Prof. Robert P. Zinzen (Robert): QB attempts to develop statistical and mathematical frameworks with which to understand living systems (from single cells to whole tissues and organisms). As such, QB aims to identify the "rules" by which biological systems make decisions (*i.e.,* transcriptional, metabolic, physiological, etc.). The aim was not only to describe the natural world in terms of quantitative models about fitting the available data, but to use this understanding as a basis to test parameters and predict outcomes; to see where our models fail and where our understanding is incomplete and to dig deeper.

What was about the exciting development in QB and what's the future in the field of QB?

Glenn: I was quite impressed with the realization of engineering cell behaviors. In the near future, I would focus on how differential gene expression during development connects to the biomechanics of pattern formation to realize biology's body plan.

Robert: The exciting development in quantitative biology is that the research has began moving from the single cell level to the systems level. Animals and plants are more than the sum of their parts—they are assemblages of communicating, interacting, reacting, compensating cells that needed to be studied in concert.

What are your suggestions for students planning to study quantitative biology?

Glenn: Younger researchers should think about their career goals and how to be well trained to succeed after graduation and after any postdoctoral fellowships. If the goal was to become a Professor, the training should prepare them to perform successfully in a department setting. If the goal is to work as an industrial scientist, the training should prepare them to succeed in that setting, etc.

Robert: Biologists should learn to appreciate Math, Statistics, Physics. Because all three courses make for crucial tools to understand biological principles, know what is possible, and help them to stop thinking of our systems as boolean decision makers.

