Biophysical Reviews (2024) 16:11–12
https://doi.org/10.1007/s12551-024-01180-y

EDITORIAL

Special Mini-Issue: Quantitative methods to decipher cellular heterogeneity – from single-cell to spatial omic methods

Xi Chen[1] · **Angela Ruohao Wu**[2,3]

Received: 11 December 2023 / Accepted: 18 January 2024 / Published online: 30 January 2024
© International Union for Pure and Applied Biophysics (IUPAB) and Springer-Verlag GmbH Germany, part of Springer Nature 2024

Abstract
In this mini-issue, we have a collection of eight reviews that discuss various advanced topics on the investigation of cellular heterogeneity. These reviews highlight the latest developments in technologies that capture and assess biology at single cell resolution, as well as approaches for cellular measurements with spatial information. Challenges and opportunities to develop future innovations and approaches are also presented.

This collection on quantitative methods for studying cellular heterogeneity covers a broad range of research interests and biological application areas. Wang et al. provided an overview of the development of single-cell multimodal omics methods and discussed key examples of applications of those methods in recent years (Wang et al. 2023). Pan and Zhang focused on the temporal aspect of the single-cell data and discussed in great details regarding various types of temporal single-cell data, including trajectory analysis, lineage tracing and gene regulatory network inference (Pan and Zhang 2023). Mihai et al. offered fresh perspectives beyond the standard routines in the single-cell analysis workflow and described some interesting ways for the representation and analysis from the high-dimensional data generated by single-cell methods (Mihai et al. 2023). Kuang and Goh bring us a review from the cutting edge of chemical biology, discussing the additional layers of rich cellular heterogeneity that manifest through chemical modifications of cellular RNA; such epigenomic-level variation between individual cells is now recognized as a key factor in regulating cell function, and a new frontier of single cell and single molecule methodology is emerging to uncover these additional cellular mechanisms (Kuang and Goh 2023).

In addition to reviews focusing on specific technology developments, we also have reviews that spotlight specific biological questions and domains. Yu and colleagues discuss experimental and computational methods that have emerged for characterizing tumour cell heterogeneity that arises through tumour evolution, which leverage spatial analysis and barcoding based lineage tracing (Yu et al. 2023). Neuroscience has been an area where cellular heterogeneity is recognized to be extremely important, but where obtaining such measurements of hetereogeneity at scale is challenging in practice. Camuñas-Soler's review on integrating single-cell transcriptomic data with electrophysiology and imaging data tackles this subject, and highlights recent developments in methodology as well as challenges ahead (Camuñas-Soler 2023). Two complementary reviews discuss the implementation of novel sequencing and imaging-based approaches for understanding microbial heterogeneity and community compositions (Hosokawa and Nishikawa 2023; Liao 2023). Hosokawa and Nishikawa's review focuses on the advances in next-generation sequencing and single-cell techniques that help to dive deeper into microbial genomes and identities of microbes within a community, enabling higher resolution metagenomic studies, which is especially important in the context of unculturable microbes (Hosokawa and Nishikawa 2023). Liao's review, on the other hand, captures the latest developments in imaging and sequencing based analysis of microbes that allow analysis of function in addition to identity, sometimes while even preserving spatial information (Liao 2023).

✉ Angela Ruohao Wu
angelawu@ust.hk

[1] Department of Systems Biology, School of Life Sciences, Southern University of Science and Technology, Shenzhen, China

[2] Division of Life Science, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong S.A.R, China

[3] Department of Chemical and Biological Engineering, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong S.A.R, China

We hope that this diverse set of reviews in this special issue can serve as a guidebook for readers who are venturing into the investigation of single cell heterogeneity.

Acknowledgements AW acknowledges support from the State Key Laboratory of Molecular Neuroscience at The Hong Kong University of Science and Technology [ITCPD/17-9], and a special research fund from the HS Chau Foundation. XC acknowledges support from National Natural Science Foundation of China (32322019).

Author contributions AW and XC together wrote the editorial summary for the special issue. AW and XC also managed reviews and submissions to the issue as invited editors.

Declarations

Conflict of interest XC declares no conflict of interests. AW is the co-founder and shareholder of Z-omics Limited, and is an inventor on patent applications submitted by The Hong Kong University of Science and Technology that cover methods for performing multi-omics single-cell sequencing. No human or animal was harmed in the writing of this editorial.

References

Camunas-Soler J (2023) Integrating single-cell transcriptomics with cellular phenotypes: cell morphology, Ca2+ imaging and electrophysiology. Biophys Rev. https://doi.org/10.1007/s12551-023-01174-2

Goh WSS, Kuang Y (2023) Heterogeneity of chemical modifications on RNA. Biophys Rev. https://doi.org/10.1007/s12551-023-01128-8

Hosokawa M, Nishikawa Y (2023) Tools for microbial single-cell genomics for obtaining uncultured microbial genomes. Biophys Rev. https://doi.org/10.1007/s12551-023-01124-y

Liao Y (2024) Emerging tools for uncovering genetic and transcriptomic heterogeneities in bacteria. Biophys Rev. https://doi.org/10.1007/s12551-023-01178-y

Mihai IS, Chafle S, Henriksson J (2023) Representing and extracting knowledge from single-cell data. Biophys Rev. https://doi.org/10.1007/s12551-023-01091-4

Pan X, Zhang X (2023) Studying temporal dynamics of single cells: expression, lineage and regulatory networks. Biophys Rev. https://doi.org/10.1007/s12551-023-01090-5

Wang X, Wu X, Hong N et al (2023) Progress in single-cell multimodal sequencing and multi-omics data integration. Biophys Rev. https://doi.org/10.1007/s12551-023-01092-3

Xue Y, Su Z, Lin X, Ho MK, Yu KHO (2023) Single cell lineage tracing with endogenous markers

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.