Editorial

Year in review 2023

Check for updates

As we begin a new year, we reflect on some of our favorites among the papers published in 2023 in *Nature Methods*.

The start of a new year is always a good time to reflect on the past 12 months. 2023 was a busy and productive year for our editorial team, and we were thrilled by the many impactful methods and tool developments that we had the privilege to publish. Though we are proud of all the papers we published and found it difficult to choose, here we highlight a small selection of our favorites from 2023.

As in 2022, single-cell 'omics analysis continued to be an area in which we saw important methodological advances[1]. A deep learning-based approach for modeling and removing background noise from droplet-based single-cell RNA sequencing (RNA-seq) data, called CellBender[2], helps to improve the quality of such data. Multimodal single-cell data integration is also an important area of method development, exemplified by the MultiVI tool[3], which enables joint modeling of the transcriptome and chromatin accessibility, as well as surface protein expression. And the SCENIC+ tool[4] infers enhancer-driven regulatory relationships and gene regulatory networks from multimodal gene expression and chromatin accessibility data.

Single-cell proteomics is also a rapidly growing field. In case you missed it, we recommend you check out our Focus on single cell proteomics, which includes a number of pieces, both technical and opinion-driven, regarding the current state of the field and what may be in store for the future. This Focus included a standout news piece[5] covering this fast-moving area of research, featuring new developments from both academia and commercial companies. We also published two exciting research papers[6,7] describing substantial steps forward for nanopore-based protein sequencing that enable unambiguous discrimination of the 20 proteinogenic amino acids. Nanopore technology, though at a nascent stage of development, may one day enable single-cell proteome sequencing at the single-molecule level.

Spatial 'omics is a field that has continued to make strong advances. The MISAR-seq method[8] enables co-profiling of gene expression and chromatin accessibility while preserving spatial information, providing insights into tissue organization and regulatory mechanisms, for example, during mouse brain development. TEMPOmap[9], which combines pulse-chase metabolic labeling with highly multiplexed, 3D in situ sequencing, enables the temporal assessment of subcellular RNA profiles in a spatially resolved manner. And GPSA[10], a method that uses deep Gaussian processes for aligning spatial 'omics data, should prove to be a useful analysis tool.

We continued to see important advances in cryo-electron microscopy (cryo-EM) and tomography (cryo-ET). One standout paper described a generative neural network model that maps continuous molecular heterogeneity in flexible macromolecules from cryo-EM data, called 3DFlex[11]. Another interesting paper reported TomoTwin[12], a deep learning-based tool for the challenging task of particle picking in tomograms, without need for annotated training data or retraining a picking model for each protein of interest.

2023 was a strong year for chemical biology. Three tools in particular stood out as important developments that enable precise control or visualization of subcellular protein behavior. Bidirectional, cyanobacteriochrome-based light-inducible dimers (BICYCLs)[13] allow reversible control of protein–protein interactions with red and green light, and can be multiplexed with other tools that respond to blue light. The CATCHFIRE system[14] introduces new probes for chemically induced dimerization, enabling visualization of controlled dimerization in real time. And adaptable maturation (ATOM) biosensors[15] consist of circularly permuted monobodies or nanobodies inserted into loops of fluorescent proteins, for target-binding induced fluorescence. These sensors should prove useful in applications where tagging a target protein is undesirable.

Immunology is a field in which we continued to publish an increasing number of strong papers. The TRAPS-seq method[16] enables the secretomes of single cells to be assessed in a time-dependent manner. This method should find particular use for studying highly dynamic immune cells. And the sciCSR tool[17] provides a computational approach for deducing B cell dynamics and class switch recombination events from single-cell RNA-seq data.

In neuroscience, we published LIONESS[18], an adaptation of STED microscopy for imaging brain tissue at super resolution with limited phototoxicity. This approach enables 3D reconstruction of neuronal networks at the synapse level, allowing changes in network architecture to be monitored in living tissue. In the animal behavior field, we published a pair of papers reporting three-photon miniature microscopes[19,20]. These fiber-based, lightweight miniscopes allow calcium activity to be imaged throughout the cortex and below in freely moving mice, going beyond the range previously accessible with two-photon miniscopes.

Finally, we highlight three papers describing in vitro systems to study tissue and organ function. One reported the crystal ribcage[21] for studying the intact mouse lung from the organ to the single-cell level, including processes such as the mechanics of breathing, immune cell infiltration, and carcinogenesis. Another paper described an advanced organoid model of mammary gland development[22], used to study the early stages of oncogenesis. The final paper describes MISCOs[23] — assembloids that model the human dopamine system, providing a highly versatile model for studying neural circuits.

These papers represent just a small slice of our areas of interest; we encourage you to check out our website for a description of all the fields we cover. We extend a huge thank you to all of our authors who chose to submit and publish their work with *Nature Methods*. We also thank our peer reviewers, who provide us with rigorous and detailed technical advice and help make the quality of papers we publish the best they can be. And finally, we thank you, our readers, for your continued support. Happy new year!

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Editorial

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