https://doi.org/10.1038/s41592-024-02591-1

Year in review 2024

We highlight several standout papers published in *Nature Methods* in 2024.

2024 was a big year for *Nature Methods*: we celebrated our 20th anniversary in October with a special issue. In the Editorial[1] we highlighted how *Nature Methods* has stayed true to its original vision to champion a broad range of innovative research methods for basic research across diverse disciplines in the life sciences. Here we highlight a few of our editorial team's favorites from 2024.

In the single-cell sequencing space, LiMCA[2] provides a multi-omics assay for simultaneously profiling 3D genome structure and the transcriptome, demonstrating exceptional sensitivity in capturing chromatin contacts per cell. The authors successfully integrated LiMCA with single-cell ATAC-seq to study the 'one neuron–one receptor' selection process in developing olfactory sensory neurons.

In genome editing, TnpBmax[3] offers a codon- and nuclear localization sequence-optimized version of ISDra2 TnpB, delivering enhanced activity with a compact genome editor. To support in vivo editing, machine learning models can predict guide RNA efficiencies, with TnpBmax achieving up to 75% editing efficiency in mice.

Spatial transcriptomics technology continued to advance rapidly, driven by a surge of both experimental methods and computational tools. A comparative analysis of 11 sequencing-based spatial transcriptomics protocols[4] using a set of reference tissues offers readers practical guidance for tool selection and serves as a foundation for future benchmarking efforts and tool development.

In August, we published a Focus issue on advanced AI in biology, highlighting the transformative impact that computational methods such as generative AI and large language models are having on diverse fields. One such area where AI has already made strong inroads is in single-cell biology: scGPT[5] and scFoundation[6] are foundation models that were pretrained on massive-scale single-cell genomics datasets. Both models enable diverse types of downstream analyses and can be adapted for solving specific tasks. These papers represented some of the earliest applications of foundation models in biology, which are now being developed to support data analysis in many different fields of research.

Computational methods are also powering new biological advances in structural biology. As methods journal editors, we believe that method transparency and usability is paramount, which is why we are happy to have published OpenFold[7], a faster, trainable, fully open-access reimplementation of AlphaFold2. In intrinsically disordered protein region (IDR) research, ALBATROSS[8] offers a deep learning model for predicting ensemble dimensions of IDRs. IDRs are defined as lacking a folded state, but they are not 'unstructured'. While experimental methods such as fluorescence resonance energy transfer (FRET), nuclear magnetic resonance (NMR) and small-angle X-ray scattering (SAXS) can measure properties like radius of gyration, end-to-end distances and asphericity, there are few computational methods that can predict these properties.

We also continued to see strong methodological advances in the exciting technology of cryo-electron tomography (cryo-ET). We published TomoDRGN[9] and cryoDRGN-ET[10], methods that enable the analysis of structural heterogeneity from cryo-ET datasets. Both methods extend the cryoDRGN framework based on deep reconstructing generative networks, originally developed for analyzing structural heterogeneity from cryo-electron microscopy data.

2024 was a strong year for imaging techniques at *Nature Methods*, with advances ranging from methods for improved single-particle tracking to advanced microscopes for deep tissue imaging in animals. Two papers stand out for their transformative potential: those describing monomeric derivatives of the extremely photostable green fluorescent protein StayGold. mStayGold[11] and mBaoJin[12] are bright and photostable monomeric tags that should usher in a new era of extended time-lapse observations of cellular activity.

In neuroscience, miniscopes have served an important role in studying behavior in freely moving rodents. However, miniaturization typically comes with trade-offs. The development of a 'cranial exoskeleton'[13], a robotic device that can move a headstage for imaging or electrophysiology with the animal, enables the study naturalistic behavior. Another approach for studying behavior in rodents involves virtual reality setups in which animals explore a virtual environment while walking on a treadmill or similar device. Two papers describing virtual reality displays, named MouseGoggles[14] and Moculus[15], offer improved virtual environments for rodents that are similar to virtual reality goggles for humans.

In immunology, we published several strong papers in 2024. While there are several methods for identifying $CD8^+$ T cell antigens, comparable methods for $CD4^+$ T cells have been limited. SABR-IIs[16] are bifunctional receptors encoding MHC class II molecules for $CD4^+$ T cell antigen discovery.

Last but not least, in the field of stem cell biology, we published a complex, induced pluripotent stem cell-derived bone marrow organoid model[17] that can accurately recapitulate critical functional properties of the bone marrow and serves as a physiological in vitro model to study hematopoietic development.

As we begin a new year, we look forward to seeing many more exciting methodological advances in these areas and in other areas of interest to *Nature Methods*. We thank all of our authors, peer reviewers and readers for your continued support. Happy New Year!

Published online: 13 January 2025

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