IN BRIEF

SEQUENCING

Sequencing BCR–antigen interactions

Setliff, I. et al. *Cell* **179**, 1636–1646 (2019).

B-cell receptor (BCR) sequencing offers an important approach for examining immune responses to infection. Antigen-specific BCRs are often sequenced following single-cell sorting with antigen baits. However, this strategy is low throughput. Setliff et al. developed LIBRA-seq for linking BCR sequences to antigen specificity via next-generation sequencing. Single B cells are mixed with a set of DNA-barcoded antigens that are used to sort antigen-positive B cells. Then the sorted B cells are encapsulated with oligonucleotide-labeled beads for indexing both BCR transcripts and antigen barcodes, which allows sequencing both the antigen barcodes and BCR sequences, thus providing a direct readout of BCR–antigen binding interactions. This transformation to sequencing readouts allows high-throughput mapping of BCR sequences to antigen specificity. The researchers applied LIBRA-seq to peripheral blood mononuclear cells collected from two people infected with HIV and identified HIV- and influenza-specific antibodies. *LT*

https://doi.org/10.1038/s41592-020-0749-4

NEUROSCIENCE

A brain observatory

De Vries, S. E. J. et al. *Nat. Neurosci.* **23**, 138–151 (2020).

Numerous studies have reported recordings from neurons in the visual cortex, but such studies have typically been limited in the number of neurons being recorded and have used a variety of different stimuli. De Vries et al. have acquired a large dataset under standardized experimental conditions to address this limitation. The researchers performed calcium imaging using two-photon microscopy in awake, behaving mice. They imaged activity in about 60,000 excitatory and inhibitory neurons in the visual cortex while the mice were presented with a battery of visual stimuli ranging from drifting gratings to natural movies. The researchers could classify many neurons into several functional response classes and model their responses by combining linear filters and nonlinearities. Nevertheless, many of the recorded neurons could not be modeled, and these may be driven by highly specific stimuli not represented in the battery of stimuli presented here or by non-visual features of the mouse behavior. The dataset is available at http://observatory.brain-map.org/visualcoding. *NV*

https://doi.org/10.1038/s41592-020-0751-x

BIOINFORMATICS

High-dimensional data visualization

Moon, K. R. et al. *Nat. Biotechnol.* **37**, 1482–1492 (2019).

High-dimensional biological data conveys rich information but presents major challenges for analysis and visualization. Mapping such data to lower-dimensional spaces for visualization is often accompanied by information loss. Vast sizes of datasets and omnipresent noise further complicate the task. Moon et al. developed a new method, PHATE (Potential of Heat Diffusion for Affinity-based Transition Embedding), for visualizing high-dimensional data. The main idea is to first encode local data structure and then use a potential distance to measure global relationships. Finally, multidimensional scaling (MDS) is performed to embed the data in a lower-dimensional space. By this strategy, both local and global structures of the original data are accounted for. PHATE not only enables better data visualization than existing methods, but also helps identify interesting patterns such as branching or end points. It is robust to noise, has good scalability and can be used for analyzing different data types, such as mass spectrometry, scRNA-seq, Hi-C and gut microbiota data. *LT**

https://doi.org/10.1038/s41592-020-0750-y

PROTEOMICS

MS3-based cross-link search platform

Yugandhar, K. et al. *Mol. Cell. Proteomics* https://doi.org/10.1074/mcp.TIR119.001847 (2019).

Determining the 3D structure of proteins and the structural basis of protein–protein interactions requires determining the spatial constraints between interacting partners. One method to capture these interactions is cross-linking mass spectrometry (XL-MS), and efficient MS-cleavable chemical cross-linkers have allowed the approach to be expanded to the proteome scale. Yugandhar et al. have developed MaxLinker, an MS3-centric cross-link search approach that the authors demonstrate to have a significantly lower misidentification rate than the standard MS2-only approach. MaxLinker starts with MS3-level cross-link candidates and discards the ones without reliable sequence information for at least one of the two cross-linked peptides. This is followed by an MS2-based rescue step that looks at discarded peptides that may have partial sequence information at this level. The authors demonstrate the search strategy on a human proteome-wide XL-MS experiment using K562 cells. More than 9,000 unique cross-links were identified at a 1% false discovery rate. The software is freely available for download from the lab website. *AS*

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