IN BRIEF

GENOMICS

Comparing trajectory inference methods

Saelens, W. et al. *Nat. Biotechnol.* **37**, 547–554 (2019).

Single-cell transcriptomics data contain a wealth of information, not merely on the composition of a sample at the time it was taken, but also on the dynamic processes that gave rise to it. Over 70 computational methods have been developed that order cells along a pseudotime trajectory on the basis of similarities in their expression patterns. This myriad of tools can make the choice of a suitable one difficult. Saelens et al. have benchmarked 45 tools on 110 real and 229 synthetic datasets according to their accuracy, scalability of cells and features, stability after subsampling, and usability. Each method is also characterized by the type of trajectories it can infer, from a simple linear path to multifurcations and tree structures to more complex connected or disconnected graphs. The researchers evaluated whether the combination of any two methods yielded a model with a higher score. Their conclusion is that the choice of tool should be driven by the known or expected trajectories of the data. A practical user guide (https://benchmark.dynverse.org) will be helpful in guiding such choices. *NR*

https://doi.org/10.1038/s41592-019-0443-6

PROTEOMICS

Probes for protein prenylation

Storck, E. M. et al. *Nat. Chem.* https://doi.org/10.1038/s41557-019-0237-6 (2019).

Farnesyl transferase and geranylgeranyl transferase catalyze the attachment of a farnesyl or geranylgeranyl isoprenoid to a C-terminal cysteine motif in an irreversible post-translational process known as protein prenylation. Current approaches to study prenylation have had limited proteome coverage and poor selectivity. Storck et al. introduce a new approach to profile prenylation in cells by using chemical proteomics. They developed a pair of alkyne-containing probes named YnF and TnGG, which are metabolically incorporated into proteins; the alkyne tags allow such modified proteins to be affinity-purified via a click-chemistry reaction. Prenylated proteins can therefore be isolated and identified by liquid chromatography–mass spectrometry. In a human endothelial cell line, Storck et al. identified 80 prenylated proteins, many of which were previously unknown. They also applied the approach to study prenylation of Rab proteins in a mouse model of retinal disease (choroideremia). *AD*

https://doi.org/10.1038/s41592-019-0446-3

NEUROSCIENCE

Chromatic multiphoton imaging of the whole brain

Abdeladim, L. et al. *Nat. Commun.* **10**, 1662 (2019).

An efficient approach for visualizing fluorescently labeled neurons across the whole brain involves serial block-face imaging, in which the top layer of a tissue block is repeatedly imaged and then shaved off. Abdeladim et al. combine this approach with a strategy to image three different fluorescent proteins with two laser wavelengths. Blue and red chromophores are illuminated with the wavelengths appropriate for their two-photon excitation. Green chromophores, in contrast, can be excited by wavelength mixing, meaning that the chromophore requires concurrent illumination with shorter-wavelength and longer-wavelength light for two-photon excitation. An added benefit of this illumination strategy is that it facilitates registration of the different colors, as the green chromophore is visible only when the two laser beams are properly aligned. This chromatic multiphoton serial microscopy approach is particularly valuable for imaging Brainbow-labeled mouse brains in their entirety, which the researchers demonstrated. *NV*

https://doi.org/10.1038/s41592-019-0444-5

LAB-ON-A-CHIP

Forming coacervates inside liposomes

Deshpande, S. et al. *Nat. Commun.* **10**, 1800 (2019).

To understand the underlying mechanism of liquid–liquid phase separation (LLPS), researchers have developed in vitro models to reconstitute the process of LLPS. Yet, it is still a challenge to capture the dynamic process of coacervation—droplet formation via LLPS. Deshpande et al. have developed a microfluidic platform to generate liposomes that can be used as containers to control the formation of coacervates. The necessary components are initially loaded inside the liposomes, and the permeation of small molecules into liposomes can trigger phase separation. In addition to the diffusion-mediated coacervate formation, the researchers also demonstrate that the transport of substrate can catalyze an enzymatic reaction that in turn triggers the coacervate formation. The researchers applied the coacervate-in-liposome platform to demonstrate protein (FtsZ) sequestration and β-galactosidase metabolic reaction within coacervates inside liposomes. *LT*

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