MICROSCOPY

## Monitoring molecular jumps

Eilers, Y. et al. *Proc. Natl Acad. Sci. USA* **115**, 6117–6122 (2018).

The recently described MINFLUX nanoscopy method allows for high-resolution monitoring of single molecules with a small fraction of the photons needed for conventional super-resolution microscopy. Although the method was shown to work well for high-resolution imaging of DNA origami structures and for single-particle tracking with high spatiotemporal resolution, its benefits for the investigation of single-particle movements were not fully explored. Eilers et al. now show that MINFLUX can be used to monitor molecular movements of a few nanometers at rates that far surpass the spatiotemporal resolution of conventional approaches. They demonstrated their approach by studying the thermal fluctuation of fluorophore-labeled DNA strands, and achieved ~2-nanometer localization precision with measurements as short as 400 microseconds. These results highlight the power of this approach for studying the dynamics of single molecules. *RS*

https://doi.org/10.1038/s41592-018-0091-2

GENOMICS

## SPRITE maps the 3D genome

Quinodoz, S. A. et al. *Cell* https://doi.org/10.1016/j.cell.2018.05.024 (2018)

Great strides in understanding how eukaryotic genomes fold have been made with molecular methods based on cross-linking and ligation of genomic regions in close 3D proximity. But the need for ligation has also limited resolution and precluded regions that lie outside the ligation range from being incorporated into the overall structure. Quinodoz et al. have now found a way to profile higher-order interaction by using a method that does not rely on ligation. Their 'split-pool recognition of interactions by tag extension' (SPRITE) approach still requires cross-linking and fragmenting of chromatin. But instead of then ligating the ends, it splits the content in 96-well plates and barcodes molecules in each well. This process of pooling, splitting and barcoding is repeated several times, and eventually the string of barcodes for each fragment is read by sequencing. The barcode signature allows clustering of complexes that were part of a higher-order chromatin structure. SPRITE is not limited to pairwise interactions, and the researchers observed that active DNA regions in various A compartments interact and form higher-order complexes. *NR*

https://doi.org/10.1038/s41592-018-0092-1

BIOINFORMATICS

## Contrasting PCA across datasets

Abid, A. et al. *Nat. Commun.* **9**, 2134 (2018).

Principal component analysis (PCA) is a popular method for transforming high-dimensional data into a smaller set of orthogonal variables or components that capture most of the variation in the full dataset. PCA is often applied to multiple datasets, and the resulting two- or three-dimensional plots are visually compared to assess differences. Abid et al. have now developed contrastive PCA (cPCA), an unsupervised method that provides systematic rather than subjective comparisons. cPCA finds subspaces that capture a large amount of variation in one dataset but little variation in a background dataset used for comparison. With careful selection of control data, the approach allows researchers to look for the enriched components with the greatest biological relevance. The authors demonstrate cPCA as a contrastive tool to discriminate patterns in protein expression, single-cell RNA-seq and genetic polymorphism data. *TN*

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MICROBIOLOGY

## A model gut microbiome

Venturelli, O. S. et al. *Mol. Syst. Biol.* **14**, e8157 (2018).

The human gut harbors hundreds of species of microorganisms, thought to play a role in metabolism and disease. Interactions between species are likely to influence the functional properties of the microbiome, but are difficult to study. Venturelli et al. examined a synthetic 12-species, 4-phylum community of anaerobic microorganisms modeling those in the human gut. The researchers grew organisms in monospecies, dual-species, or more complex cultures and monitored them over time, using 16S RNA profiling to determine composition. They observed several outcomes: single-species dominance, stable coexistence, and historical dependence where the order of inoculation influenced outcome. They modeled the dynamics of these cultures, identifying positive and negative interactions. They further predicted the behavior of 11-member cultures with a model trained on dual-species data, indicating that pairwise interactions are a major driver of multi-species dynamics. *NDS*

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