METHODS IN BRIEF

SYNTHETIC BIOLOGY

Reprogramming cells to perform desired tasks or computations is a long-standing goal in synthetic biology. Although tools are being developed at a fast pace, engineering biocomputation circuits with multiple inputs and outputs in mammalian cells remains technically challenging. Weinberg *et al.* sought to address this challenge by developing Boolean logic and arithmetic through DNA excision (BLADE). BLADE is a general framework that uses site-specific recombinases for engineering complex logic circuits. These recombinases are powerful because they can function simultaneously as transcriptional activators and repressors. The researchers designed and tested over 100 different circuits and found that 96.5% functioned as intended without any additional optimization. The circuits represent a broad range of designs and can control CRISPR–Cas9 to regulate endogenous gene expression.

Weinberg, B.H. *et al. Nat. Biotechnol.* **35**, 453–462 (2017).

IMAGING

Track first and identify later

Imaging is a powerful tool for studying chromosome dynamics, but labeling and imaging multiple loci in live cells is technically challenging. To tackle this challenge, Takei *et al.* developed the 'track first and identify later' strategy for multiplexed chromosome imaging. This approach uses CRISPR–Cas9 to label multiple loci with the green fluorescent protein for live-cell imaging of their dynamics. Following single-color live-cell imaging, cells are fixed, and loci are barcoded using DNA sequential fluorescence *in situ* hybridization. Thus, the precise identity of each imaged loci, while unknown during imaging, is revealed. A potential caveat is that the loci must remain distinguishable throughout imaging. The researchers demonstrated the method by imaging twelve telomeric loci and recording their distinct dynamic properties.

Takei, Y. *et al. Biophys. J.* http://dx.doi.org/10.1016/j.bpj.2017.03.024 (2017).

SEQUENCING

Demand for single-cell genome sequences is on the rise, especially in areas such as cancer analysis, but whole-genome amplification remains challenging. Chen *et al.* develop linear amplification via transposon insertion (LIANTI), which uses Tn5 transposition to insert T7 promoters across the genome for *in vitro* transcription (IVT) followed by cDNA generation, sequencing and digital fragment counting. Amplification by IVT is linear and avoids the exaggerated quantification biases and errors that arise from nonspecific priming and exponential amplification in other protocols. LIANTI provides 97% genome coverage and even amplification, thus enabling accurate detection of copy number variants at 100-kb resolution. In human fibroblasts, the researchers resolve active replication origins and demonstrate low false-positive single-nucleotide-variant detection error. They also characterize UV-induced mutations and trace high C-to-T variant frequencies to cytosine deamination upon cell lysis.

Chen, C. *et al. Science* **356**, 189–194 (2017).

MICROSCOPY

Chip-based nanoscopy

Super-resolution microscopy methods typically require sophisticated optical setups, which can be a barrier to their use. Diekmann *et al.* develop a chip-based approach that uses a standard microscope in combination with a specialized waveguide chip for single-molecule localization microscopy. The waveguide is used for sample excitation and therefore removes the need for an excitation light path on the microscope; this allows for miniaturization of the entire setup. An added benefit of this method is that properly designed waveguides can offer excitation over large fields of view. An innovation in this work was the use of materials with high refractive index contrast to build the chip, as these materials allow for tighter confinement of light within the waveguide. The researchers demonstrated entropy-based super-resolution imaging as well as direct stochastic optical reconstruction microscopy over a large 0.5 mm × 0.5 mm field of view.

Diekmann, R. *et al. Nat. Photonics* **11**, 322–328 (2017).