NEUROSCIENCE

Speedy optogenetics in red

Mager, T. et al. *Nat. Commun.* **9**, 1750 (2018).

Optogenetic tools come in a variety of flavors: they can be activated by blue light or red light, and they can be slow or fast. Chrimson is activated by red light, which makes it particularly suitable for in vivo applications, as red light is less phototoxic than blue light. However, Chrimson's slow channel-closing kinetics are not ideal for applications that require high stimulation rates. Mager et al. report two Chrimson variants, f-Chrimson and vf-Chrimson, that have closing kinetics five to ten times faster than those of the original protein, potentially allowing neuronal stimulation at up to 600 Hz. This increase in speed is achieved through the mutation of residues in Chrimson's helix F, which moves during the transition from the open to the closed state of the channel. The researchers demonstrate the utility of the fast Chrimson variants in the auditory system of mice. Upon expression of f-Chrimson in spiral ganglion neurons (SGNs), the researchers were able to record responses in the auditory brainstem while illuminating the SGNs. *NV*

https://doi.org/10.1038/s41592-018-0065-4

BIOPHYSICS

DNA molecular forceps

Wang, J. L. et al. *Nat. Struct. Mol. Biol.* **6**, 482–487 (2018).

Repair of DNA double-strand breaks by nonhomologous end joining (NHEJ) is a complex process involving multiple proteins. Although the mechanism is generally understood, crucial insights into the kinetics of NHEJ complex assembly and disassembly have been lacking. Wang et al. devised a single-molecule method to analyze the process with finer detail. Their approach, which they call 'DNA molecular forceps', utilizes a construct that consists of two dsDNA segments connected by a third, bridging dsDNA segment. The construct is anchored to a surface at one end and attached to a magnetic bead at the other end; a magnet generates an extension force on the construct. When NHEJ protein components bind to the construct, the free ends of the two dsDNA segments are joined together, resulting in a reduction in overall construct length. The system allowed Wang et al. to carefully dissect the NHEJ process and propose a detailed model for DNA double-strand break repair by NHEJ. *AD*

https://doi.org/10.1038/s41592-018-0066-3

CANCER

Metastasis in a dish

Tian, X. et al. *Nat. Biomed. Eng.* **2**, 443–452 (2018).

The greatest damage from cancer usually results from its spread to other sites in the body. Metastases behave differently than primary tumors because of local cues from their new environment. Most in vitro methods lack this organ specificity, but Tian et al. have developed a culture system that uses decellularized tissue to model the metastatic niche. The researchers borrowed a perfusion-based method to chemically remove cells from rodent tissue, leaving behind nearly all of the extracellular matrix components. They found that four human colorectal cancer cell lines cultured on decellularized rat lung and liver scaffolds, representing the most common sites of metastases, formed large three-dimensional colonies. Compared with cells grown on plastic, collagen or Matrigel, scaffold-grown colonies exhibited growth and histology more similar to those of in vivo metastases. They also grew better when transplanted to the corresponding organ in a living mouse, and displayed organ-specific responses to chemotherapy and radiotherapy. *TN*

https://doi.org/10.1038/s41592-018-0067-2

MOLECULAR BIOLOGY

Clocking translation in live cells

Volkov, I. L. et al. *Nat. Chem. Biol.* **14**, 618–626 (2018).

The rate of protein synthesis is well characterized in vitro but is technically challenging to study in living cells. Volkov et al. addressed this challenge by tracking labeled tRNA molecules in *Escherichia coli*. They injected fluorescently labeled Phe-[Cy5]tRNA^{Phe} molecules into *E. coli* and then carried out single-particle tracking. They analyzed trajectories with hidden Markov modeling to assign parts of the trajectories with varying diffusion constants to different bound and unbound states of the tRNA. To determine the translation elongation rate, they measured the dwell time of the tRNA in the ribosome-bound state, and obtained codon resolution translation rates that are consistent with previous observations. This work highlights the power of single-molecule tracking for mechanistic analysis and will be useful for further investigation of translation as it occurs in cells. *RS*

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