METHODS IN BRIEF

LAB-ON-A-CHIP

Following fitness after mutations in single cells

Mutations in DNA are crucial for adaptation and evolution. However, mutations and their effects are challenging to study directly, especially at the single-cell level. To address this challenge, Robert *et al.* developed an approach to study the effects of mutations as they arise in *Escherichia coli*. Their approach involves the use of a microfluidic device known as a 'mother machine' that enables imaging of single cells over multiple generations. In this device, they carried out time-lapse imaging of *E. coli* harboring a mismatch repair protein fused to a fluorescent protein reporter. This reporter formed fluorescent foci whenever a mutation occurred in a strain of *E. coli* that could not repair mutations. The researchers monitored ~20,000 mutation events in single cells over hundreds of generations, and found that 1% of mutations were lethal, whereas the vast majority were relatively neutral.

Robert, L. *et al. Science* **359**, 1283–1286 (2018).

NEUROSCIENCE

Chronic imaging of the fruit fly brain

Chronic window preparations allow longitudinal imaging of neuronal activity in rodent brains, but long-term imaging has so far not been possible in the fruit fly brain. Huang *et al.* combine laser microsurgery with a transparent epoxy window in the fly head cuticle. Flies prepared in this manner had a similar life span as untreated animals and were not affected in their behavior. The researchers used this preparation to visualize neuronal morphology by two-photon microscopy. They also conducted calcium imaging to investigate responses to odor stimulation and to perform voltage imaging upon mechanical stress. The flies could be released after each session and repeatedly imaged over the course of their life.

Huang, C. *et al. Nat. Commun.* **9**, 872 (2018).

IMAGING

Clearing the way for imaging of the human brain

Tissue-clearing methods have allowed imaging-based analysis of thick tissues and even whole organisms, with the rodent brain being a particularly common sample. However, clearing methods that perform well on rodent brains do not necessarily work as well on human brain samples, owing to challenges associated with the processing of postmortem tissue and inherent differences in tissue composition. To overcome this limitation, Lai *et al.* developed OPTIClear, a clearing method optimized for human brain tissue. The method is compatible with fluorescent dyes and works with both fresh and archival samples, including formalin-fixed paraffin-embedded tissues, opening the door to 3D visualization of many archived materials. Using their method along with cresyl violet staining, the team was able to study human dendritic spines in 3D.

Lai, H.M. *et al. Nat. Commun.* **9**, 1066 (2018).

NEUROSCIENCE

Extracting neuronal activity from microendoscopy videos

Several approaches enable the extraction of single-neuron activity from calcium imaging data. However, this task is particularly difficult in microendoscopic data sets because of the high background and signal overlap. Zhou *et al.* have optimized a constrained matrix factorization (CNMF) approach for enhanced performance on these difficult data sets that models the background more realistically than has been done in previous implementations. The researchers found that their CNMF-E approach accurately extracted neuronal activity, with better performance than that of, for example, a PCA/ICA approach. The team demonstrated the CNMF-E approach on data sets acquired in the mouse dorsal striatum, the prefrontal cortex, the ventral hippocampus and the bed nucleus of the stria terminalis.

Zhou, P. *et al. eLife* **7**, e28728 (2018).