TOOLS IN BRIEF

SENSORS AND PROBES

Retinoic acid: now you see it

Early embryos owe much of their patterning to morphogens: signaling molecules with a graded distribution that direct cells to assume different identities according to molecule concentration. Retinoic acid, a morphogen that patterns posterior tissues in chordates, is believed to act by forming diffusion gradients, but scientists have been able to infer its distribution only indirectly. Shimozono *et al.* enable a more direct look by engineering three genetically encoded probes for retinoic acid. The probes consist of retinoic acid–receptor ligand-binding domains of different affinities flanked by cyan fluorescent protein and yellow fluorescent protein, which produce a Förster resonance energy transfer signal in the presence of the ligand. Imaging and perturbation studies confirmed a disputed two-tailed linear gradient of retinoic acid in the early zebrafish embryo hindbrain.

Shimozono, S. *et al. Nature* **496**, 363–366 (2013).

NEUROSCIENCE

Wireless, multifunctional optogenetic devices

Optogenetic experiments in neuroscience often involve penetrating the brain with devices that can deliver and detect light and record the electrical activity of neurons, ideally with 'all-in-one' functionality. It is also desirable that these devices be small and as nondisruptive to the animal's physiology and behavior as possible. Kim *et al.* describe a flexible, wireless, ultrathin optoelectronic system that offers several functionalities. The device incorporates several inorganic microemitting diodes for spatially confined, cellular-scale delivery of photons, a microscale inorganic photodetector and a temperature sensor. It also contains microelectrodes that measure extracellular voltage signals in the direct vicinity of the sensor and that can be used for electrical stimulation. The researchers demonstrate how these devices can be used for optogenetic experiments in behaving mice.

Kim, T.-i. *et al. Science* **340**, 211–216 (2013).

CELL BIOLOGY

Measuring cell deformability

Cells that move through the body must squeeze through tight spaces, and the metastatic potential of cancer cells may depend on their deformability. Several methods are used to monitor cellular mechanical properties; Byun *et al.* now describe a sensitive and high-throughput option. By introducing a constriction in the microchannel of a suspended microchannel resonator, the researchers monitor a cell's buoyant mass, its entry velocity into the constriction and its transit velocity through the constriction, at a rate of 10^5 cells per hour. For many cell types, overall passage time depends on cell mass, but this is not the only important parameter. Cell deformability predominantly affects entry velocity, cell friction mainly affects transit velocity, and both of these properties can contribute to the shorter passage time of cells with higher metastatic potential.

Byun, S. *et al. Proc. Natl. Acad. Sci. USA* **110**, 7580–7585 (2013).

GENOMICS

Finding function

Although cataloging all genes in model organisms is no longer a bottleneck, assigning function to genes still is. Despite the availability of several good gene-targeting tools, a large number of the 22,000 genes in mouse and of the 26,000 in zebrafish remain uncharacterized. Replacing the current gene-by-gene approach with an effort to phenotype disruptive mutations exome wide, Kettleborough *et al.* combined chemical mutagenesis with high-throughput sequencing. Aided by the latest well-annotated zebrafish genome (from the work of Howe *et al.*), the researchers designed exome-wide baits and used them to enrich exomes of the F_1 generation of a chemically mutagenized parent for sequencing. From 808 sequenced exomes, they found mutations in 75% of protein-coding genes. For rapid phenotypic analysis of the mutant alleles, the researchers examined the frequency of homozygous mutations in F_3 embryos of incrossed F_2 individuals.

Kettleborough, R.N.W. *et al. Nature* **496**, 494–497 (2013).
Howe, K. *et al. Nature* **496**, 498–503 (2013).