postdoc Chris Harvey used whole-cell electrophysiological recordings to monitor the activity of hippocampal place cells as the mice navigated through a virtual linear track. The group could monitor place cells firing at specific locations in the trajectory and identified critical signatures in their activity patterns. As Tank explains, "the natural progression was then to put imaging and virtual reality together," which the group now shows (Dombeck *et al.*, 2010).

Given that the hippocampus is located deep in the brain, this was not a trivial task. Postdoc Dan Dombeck adapted a surgical procedure to expose a portion of the hippocampus and create a chronic hippocampal 'window'. To facilitate imaging the same neurons over several weeks, they monitored their activity using the genetically encoded calcium sensor GCaMP3.

Combining virtual reality and high-resolution functional imaging allowed the team to investigate novel aspects of circuit dynamics during navigation. "An important extension for the future is that with imaging we can link neuronal activity to the detailed wiring diagram of synaptic connectivity, which is more difficult to do with electrodes," says Tank. As a first step, the group optically identified place cells as the cells fired, and studied the correlations between the stimuli the cells responded to and the cells' anatomical location in the local circuit. Maybe one day virtual worlds will become routine in neuroscience labs as they can bring us closer to our brains' reality.

Erika Pastrana

RESEARCH PAPERS
Dombeck, D.A. *et al.* Functional imaging of hippocampal place cells at cellular resolution during virtual navigation. *Nat. Neurosci.* **13**, 1433–1440 (2010).
Harvey, C.D. *et al.* Intracellular dynamics of hippocampal place cells during virtual navigation. *Nature* **461**, 941–946 (2009).

from so many different lines, different labs, different passage numbers, different types of reprogramming." What is more, once a chromosomal region has been identified as aberrant in this way, one already has some information about functional expression changes that may result.

This is not to say that the approach does not have disadvantages as well. It is not as high-resolution as some of the more direct approaches: the smallest change the researchers detected so far was of about ten megabases. Furthermore, it could be confounded by epigenetic effects on gene expression, and it is likely to be less successful than other approaches on heterogenous samples.

Nevertheless, Mayshar, together with Uri Ben-David and their colleagues, identified abnormalities in about a fifth of the 66 hiPSC lines tested. The data at this stage are probably too limited in scale to suggest that particular reprogramming methods are more or less prone to problems—the analyzed dataset included lines generated using retroviral integration, protein-based reprogramming and episomal vectors—but it remains to be seen with future work on larger numbers of lines whether such patterns emerge.

Natalie de Souza

RESEARCH PAPERS
Mayshar, Y. *et al*. Identification and classification of chromosomal aberrations in human induced pluripotent stem cells. *Cell Stem Cell* **7**, 521–531 (2010).

NEWS IN BRIEF

SEQUENCING

RNA fitness landscapes

Pitt and Ferré-D'Amaré describe an approach to generate fitness landscapes for catalytic RNAs. They incubated a pool of ribozymes with a substrate RNA immobilized on beads; after allowing the RNAs to react, they isolated and deep-sequenced the ribozymes that bound the beads, identifying the fittest variants. The resulting high-resolution map, which yields insights into the fittest genotypes for a particular phenotype, contains 10^7 unique RNA genotypes.

Pitt, J.N. & Ferré-D'Amaré, A.R. *Science* **330**, 376–379 (2010).

CHEMISTRY

Capturing G-quadruplexes

G-quadruplex motifs are four-stranded nucleic acid structures found in genomic DNA that are thought to be associated with telomere maintenance and gene expression, though much remains to be discovered about G-quadruplex function. Müller *et al.* designed a small molecule that selectively binds G-quadruplexes in human cells, so that they can be isolated for further analysis. The small molecule contains a biotin moiety that serves as a handle for capturing G-quadruplexes on streptavidin-coated beads.

Müller, S. *et al. Nat. Chem.* advance online publication 10 October 2010.

SENSORS AND PROBES

Dual-color protein interaction probes

Protein-protein interactions can be detected via protein fragment complementation, whereby two pieces of a split fluorescent or bioluminescent protein are reunited and produce a signal when their fusion partners bind. Villalobos *et al.* describe several pairs of reversible, dual-color complementation fragments based on firefly and click beetle luciferases that use a single substrate, D-luciferin, to produce a bioluminescent signal, allowing dynamic analysis of multiple protein interactions in living cells.

Villalobos, V. *et al. Chem. Biol.* **17**, 1018–1029 (2010).

NEUROSCIENCE

Mapping microcircuitry in the fly brain

The complex patterns of synaptic connections in the brain, known as microcircuitry, form the basis of behavior. Mapping microcircuits across whole brains has been a technical challenge because it requires analyzing complete series of thin sections by transmission electron microscopy (TEM). Cardona *et al.* applied a software package called TrakEM2 to comprehensively reconstruct the neuronal microcircuitry from serial TEM sections of the larval brain of the fly *Drosophila melanogaster*.

Cardona, A. *et al. PLoS Biol.* **8**, e1000502 (2010).

BIOCHEMISTRY

Microscale thermophoresis

The term thermophoresis refers to the directed motion of molecules in solution as a result of temperature gradients; thermophoretic behavior depends on properties such as mass, size and charge. Wienken *et al.* exploited this phenomenon to develop a method to detect protein-protein and protein–small molecule interactions *in vitro* without immobilization. An infrared laser locally heats a solution containing a fluorescently labeled protein of interest; the thermophoretic behavior of the protein changes upon binding, as monitored by fluorescence.

Wienken, C.J. *et al. Nat. Commun.* advance online publication 19 October 2010.

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