TOOLS IN BRIEF

MICROSCOPY

Speeding up connectome analysis

The reconstruction of neural circuits from electron microscopy data sets is a notoriously slow and labor-intensive process. Berning *et al.* developed SegEM to speed up the segmentation of volumetric images. As a machine learning–based software tool, SegEM depends on a segmented training data set, which can either be generated manually or be reused from previous studies. In addition, SegEM requires a skeleton reconstruction of the data set to be segmented. Both prerequisites can be achieved with manageable manual input. Using SegEM, Berning *et al.* reconstructed mouse retina and cortex data sets 10–100-fold faster than with other methods, with high accuracy.

Berning, M. *et al. Neuron* **87**, 1193–1206 (2015).

STEM CELLS

Keeping score of stem cells

It is not easy to determine exactly how pluripotent stem cells, which can be derived from nearly any cell source or genetic background under a variety of conditions, compare in a given population with respect to their differentiation potential. Tsankov *et al*. provide an update of their ScoreCard assay for characterizing the potential of human pluripotent stem cells on the basis of gene expression signatures. The commercially available assay now relies on quantitative PCR rather than NanoString technology to measure gene expression, uses a revised set of 96 genes to better discriminate functional potential, and beefs up the statistical analysis to improve the power and accuracy of predictions of differentiation efficiency. The assay is a rapid and standardized way of assessing stem cells that may remove the need for the more involved and less quantitative teratoma-formation assay in mice.

Tsankov, A.M. *et al. Nat. Biotechnol.* **33**, 1182–1192 (2015).

BIOINFORMATICS

User-friendly software for analyzing MD simulations

Molecular dynamics (MD) simulations are a powerful way to study protein structure and dynamics *in silico*. As more biologists become interested in using MD simulations to supplement wet lab studies, there is a growing need for the development of broadly accessible tools for analyzing MD trajectories. McGibbon *et al.* present MDTraj: fast, lightweight, user-friendly Python-based software for analyzing MD simulations. MDTraj accepts trajectory data from a wide range of MD file formats and is interoperable with existing Python-based statistical analysis and visualization tools. MDTraj enables a number of different MD trajectory analyses, including root-mean-square deviation calculations, extraction of order parameters and secondary-structure assignments. It also includes an interactive three-dimensional-structure viewer.

McGibbon, R.T. *et al. Biophys. J.* **109**, 1528–1532 (2015).

GENOMICS

Tuning Cas9 function with guide RNA length

Researchers use the nuclease activity of Cas9 for genome editing and a nuclease-dead Cas9 mutant for gene activation and repression. Two groups now independently show that shorter guide RNAs (gRNAs) of 14 nucleotides (nt), while still targeting Cas9, fail to activate its nuclease domain. Kiani *et al*. used gRNAs of both lengths to target wild-type Cas9 fused to a transcriptional activator and to construct kill switches; 14-nt gRNAs activated gene expression of a reporter gene, and inducible 20-nt gRNAs 'killed' the activity of the shorter guides by cleaving the promoter of the reporter. Dahlman *et al*. observed robust gene activation but no nuclease activity when wild-type Cas9 was targeted by 14-nt gRNA fused to MS2 binding loops, which recruit MS2 protein fused to a transcriptional activator.

Kiani, S. *et al. Nat. Methods* **12**, 1051–1054 (2015).

Dahlman, J.E. *et al. Nat. Biotechnol.* **33**, 1159–1161 (2015).