METHODS IN BRIEF

GENE EXPRESSION

Multiplexed single-cell protein and RNA measurements

Methods that characterize RNA and DNA at the single-cell level have attracted a great deal of attention recently, yet protein measurements also provide important information about cell state and function. Darmanis *et al*. describe a method for measuring both RNA and protein in multiplex from single cells. Cells are sorted into microwell plates, and the lysate is split in two; one fraction undergoes quantitative RT-PCR, and the other undergoes a proximity extension assay (PEA). PEA uses two different oligonucleotide-linked antibodies to bind a given protein target, forming a bridge that allows a PCR-based readout; the need for two antibodies lends high specificity. The authors developed 75 PEAs for proteins relevant to glioblastoma and profiled RNA and protein to assess the effects of BMP4 treatment on early-passage patient-derived glioblastoma cells.

Darmanis, S. *et al*. *Cell Rep*. **14**, 380–389 (2016).

SENSORS AND PROBES

Sensors destabilized by design

Genetically encoded sensors for small molecules are useful for studying numerous biological processes, but general strategies for developing such sensors are lacking. Feng *et al*. now describe such an approach, based on protein destabilization. Their strategy begins with a protein that binds a target ligand. Mutations are introduced into this protein that destabilize the unbound form but not the ligand-bound form; thus, the protein accumulates only in the presence of ligand. This destabilized protein is then fused to a reporter such as a fluorescent protein or a transcription factor for readout. The team used their strategy to make sensors for digoxin and progesterone and showed that they work in multiple systems. They also demonstrated that their destabilized proteins can be used for ligand-dependent regulation of Cas9 genome editing activity.

Feng, J. *et al*. *eLife* doi:10.7554/eLife.10606 (29 December 2015).

NEUROSCIENCE

Adapting to aberrations in brain imaging

Imaging fine details in deep regions of the mouse brain is challenging because of light scatter due to the differences in refractive indices within brain tissue and between the tissue and its environment. Sun *et al*. use adaptive optics to adjust for aberrations when imaging the activity of neurons in the mouse visual system. Although commonly used for correcting atmospheric aberrations in astronomy, adaptive optics technologies are slowly finding their way into basic biological research. Sun *et al*. show that this approach improves optical access to synapses or cell bodies of neurons in deep layers of the visual cortex and allows characterization of the orientation selectivity of these neurons in response to directional stimuli.

Sun, W. *et al*. *Nat. Neurosci*. **19**, 308–315 (2016).

SINGLE MOLECULE

Mapping active translation of single mRNAs

Methods that enable single-particle tracking of mRNAs have improved our understanding of how mRNA localization affects cellular function. However, these methods were previously unable to show whether an mRNA was undergoing translation. To address this question, Katz *et al*. tracked single β-actin transcripts labeled with the MS2-GFP system and fluorescent protein–labeled ribosomes in mammalian cells and studied the colocalization of the labeled mRNAs and ribosomes. They found that mRNAs diffused much more slowly when they colocalized with ribosomes, indicating that they were being actively translated in polysomes. The researchers also found that mRNAs were actively translated near focal adhesions, highlighting the power of their technique for studying local translation.

Katz, Z.B. *et al*. *eLife* doi:10.7554/eLife.10415 (13 January 2016).