**Single-cell gene expression with less noise**

Measuring the small quantities of transcript in single cells introduces a lot of technical noise, making it difficult or impossible to accurately characterize gene expression. van Oudenaarden and colleagues estimate technical noise in mouse embryonic stem cells by sequencing known amounts of spike-in RNA added to each cell and to single-cell equivalents of bulk-cel RNA and then fitting models that explain technical variation. They find that whereas genes with low expression are affected mainly by sampling noise, at higher expression levels, tube-to-tube variability in sequencing efficiency dominates. The estimates of technical noise can be subtracted to reveal biological variability in the absolute numbers of mRNA molecules, which the authors show depends on culture conditions of embryonic stem cells.

**Brief Communication p637**

**Bone marrow–on–a–chip**

Bone marrow is a complex structure responsible for regulating hematopoietic stem cells, which divide their time between self-renewal and differentiation into all mature blood cells. Ingber and colleagues recreate the bone marrow microenvironment on a chip and culture a complete, functional hematopoietic niche *in vitro* for a week. Their engineered bone marrow (eBM) is generated by implanting a chip into mice and letting bone marrow form in it; the device is then explanted and cultured *in vitro*. eBM shows the same response to radiation and drugs as *in vivo* bone marrow and will allow *in vitro* studies of hematopoiesis and hematological diseases.

**Article p677**

**A reporter for protein interaction dynamics**

The irreversibility of existing fluorescent protein complementation assays (PCAs) makes it challenging to image interaction dynamics within cells with this general approach. Michnick and colleagues describe a reversible PCA based on the previously reported infrared fluorescent protein IFP1.4 and use it to image the interaction dynamics of several protein pairs *in vitro*, in yeast and in mammalian cells. The dissociation rates of the regulatory and catalytic subunits of yeast and mammalian protein kinase A reported by this PCA were consistent (in their respective cell types) with rates reported by other methods. The experiments in yeast, moreover, demonstrate that expression level affects *in vivo* interaction dynamics.

**Brief Communication p661**

**Single-molecule imaging in live embryos**

The study of molecular processes during development is enabled by quantitative imaging. Munro and colleagues describe a collection of methods for single-molecule imaging at the surface of *Caenorhabditis elegans* embryos. Using near–total-internal-reflection fluorescence imaging, fluorescent reporter levels tuned with a combination of anti-GFP RNA interference and photobleaching, and simple image analysis, the researchers could reliably detect and track single molecules in several existing transgenic strains. They also describe a method, which does not require tracking, to monitor protein mobility and turnover at the cell surface, and they apply these approaches to study the spatiotemporal dynamics of actin and the polarity protein PAR-6 in early embryos.

**Article p663**

**Lights on for protein knockdown**

Heo and colleagues expand the optogenetic toolkit with genetically encoded tools for knocking down protein function quickly and reversibly in living mammalian cells. Their light-activated reversible inhibition by assembled trap (LARIAT) relies on two protein components that associate in the presence of light: one is fused to a protein of interest, and the other to a large multimeric protein. Upon light stimulation, the components come together to form large complexes that sequester and inactivate the protein of interest. The authors apply LARIAT to proteins involved in cytoskeleton modification, lipid signaling and the cell cycle. They also show that a nanobody can be coupled to one of the protein dimerizing components to target essentially any GFP fusion protein for conditional knockdown at high spatiotemporal resolution.

**Brief Communication p633**