METHODS IN BRIEF

GENE EXPRESSION

Quantifying protein synthesis rates, absolutely

Dividing cells expend a great deal of energy in protein synthesis, making it important to understand how the dynamics of the process have been optimized by evolution. Li *et al.* used ribosomal profiling to make absolute measurements of synthesis rates for more than 96% of cellular proteins produced by *Escherichia coli*. The method consists of digesting RNA and sequencing the fragments that are protected by bound ribosomes; protein synthesis rates can be derived from the density of bound ribosomes. Using the approach, the researchers found that steady-state levels of stable proteins are controlled to a large extent at the level of protein synthesis rather than degradation. The analysis revealed many cases of optimized translation in the bacterium. For example, individual components of protein complexes are synthesized in stoichiometric ratios.

Li, G.-W. *et al. Cell* **157**, 624–635 (2014).

IMAGING

Watching dopamine at work

Dopamine is an important neurotransmitter in the brain, but a detailed understanding of the role that dopamine signaling plays in motivation and addiction, as well as in disease, requires methods for detecting stimulus-evoked dopamine release at high spatial and temporal resolution. Lee *et al.* combined magnetic resonance imaging (MRI) with a specific dopamine sensor to identify brain regions that respond to microstimulation in the lateral hypothalamus, a region that has been implicated in addiction. The dopamine sensor is a paramagnetic heme protein called BM3h-9D7, which has been evolved for sensitivity to dopamine and can be used as a contrast agent for functional MRI. The researchers used the technique to construct a quantitative map of dopamine release in the nucleus accumbens upon stimulation in the lateral hypothalamus.

Lee, T. *et al. Science* **344**, 533–535 (2014).

GENOMICS

Using single-cell genomics to understand malaria

In geographic regions with a high occurrence of malaria, it is common to see infections with several malarial species; these multiple-genotype infections drive the spread of drug resistance. To determine malarial genotypes, Nair *et al.* developed a single-cell approach in which they isolated single infected red blood cells, amplified the parasitic genome and then genotyped and sequenced it. Their approach had high accuracy on artificial mixtures of *Plasmodium falciparum* and *Plasmodium vivax*. In real patient samples, the researchers determined the relatedness of haplotypes and the presence of drug-resistant alleles. The work has implications for treating malaria: the presence of multiple drug-resistance genes on the same haplotype would make treatment with these drugs ineffective, whereas occurrence of resistance genes on different haplotypes indicates that drug treatment is warranted.

Nair, S. *et al. Genome Res.* **24**, 1028–1038 (2014).

NEUROSCIENCE

Towards a molecular connectivity map

The neuroanatomical description of circuitry in the mouse brain has advanced at a fast pace. However, the corresponding molecular characterization of these circuits is lagging behind. Ekstrand *et al.* now describe a method for profiling neurons presynaptic to a region of interest. The researchers created a mouse line that expresses a ribosomal protein fused to a GFP-specific camelid nanobody in all neurons. Then they injected a retrograde tracing virus into the region of interest. The virus encoded GFP, thereby delivering the nanobody epitope to presynaptic sites. Immunoprecipitation of the GFP-associated ribosomes, and subsequent RNA sequencing, uncovered mRNAs that are specifically enriched in neurons presynaptic to the injected brain region. With this method, marker genes for neurons projecting to regions of interest can be identified.

Ekstrand, M.I. *et al. Cell* **157**, 1230–1242 (2014).