Improving tools for synthetic biology

To rapidly and reliably engineer biological networks—one of the promises of synthetic biology—a larger repertoire of regulatory elements and better characterization of their performance are needed. Two groups now deliver on each of these aspects. Smolke and colleagues present a model to predict the expression of a target gene that is regulated by a microRNA and then extend the model to anticipate the behavior of genetic circuits that use protein-responsive microRNA switches to detect the concentration of a nuclear protein in mammalian cells. Fussenegger and colleagues create a library of protein-responsive ribozymes for translational control and then design a three-input AND gate in mammalian cells that combines transcriptional and translational control.
Articles p1147, p1154, News and Views p1105

A deeper look at proteogenomics

In a traditional shotgun mass spectrometry–based proteomics approach, experimental peptide mass spectra are identified by comparison to theoretical spectra generated from peptides present in reference protein databases. A limitation with this approach is that discovery of new peptides—including alternatively spliced forms, novel protein-coding loci and disease-related mutant peptides—is not possible. A relatively new way of identifying such peptides, known as proteogenomics, is thus gathering steam. In a proteogenomics approach, genomic or transcriptomic data are used to construct a customized protein database to aid in finding novel peptides not present in reference databases. Nesvizhskii discusses the fundamentals of proteogenomics technology and its applications in a Review, providing practical advice about the proper usage of statistical methods to avoid false positive results. In a Perspective, Boutros, Kislinger and colleagues make a strong case for applying a proteogenomics approach to study cancer biology.
Perspective p1107, Review p1114

Genomes from metagenomic data

Assembling microbial genomes from short sequenced DNA fragments is a challenge, but the difficulty multiplies when the sequence pool is a mixture of unknown microbial flora. A key step in reducing this complexity is to assign, or 'bin', sequence fragments according to the species or strain genome from which they originate. Here Quince, Andersson and colleagues develop CONCOCT, an open-source unsupervised software tool that bins genomic fragments that have first undergone limited preassembly into contigs. Their strategy uses a variational Bayesian approach combining sequence composition and correlated abundance across multiple samples to produce sequence assignments. CONCOCT bins genomes with high precision and recall in simulated and real data, providing higher coverage than can typically be reached by single-cell sequencing.
Brief Communication p1144

High-throughput single protein pulling

One of the main technical challenges in making single-molecule force spectroscopy measurements has been the method's low-throughput nature, which has precluded the screening of large protein-variant libraries. Nash and colleagues now describe a system that readily enables thousands of protein pulling measurements. They begin with a microspotted DNA array and synthesize proteins *in situ* with the aid of microfluidics-based cell-free expression technology. Each protein is labeled with a common dockerin tag, which then enables on-chip high-throughput single-molecule force spectroscopy measurements by pulling on individual, tagged proteins with a cohesin-modified cantilever. The method brings research in the single-molecule field one step closer to large-scale screening of protein nanomechanical properties.
Brief Communication p1127

Backpack recorders for zebra finches

Anyone who has tried to keep up a conversation in a noisy place can appreciate the difficulty of recording individual voices in a crowded social environment.

A. Victor

Vyssotski and colleagues now address the problem of distinguishing one voice among the flock with the development of recording devices that zebra finches can carry as backpacks. Each backpack weighs about 3 grams and contains a small microphone, an accelerator and electronic hardware. Whereas the microphone records all sound in the environment, the accelerator registers only the vibrations generated by the bird's own vocalizations. The researchers use the backpack song recorders to analyze vocal interactions in pairs of birds in the lab, but it should also be possible to use the recording devices in the wild.
Brief Communication p1135