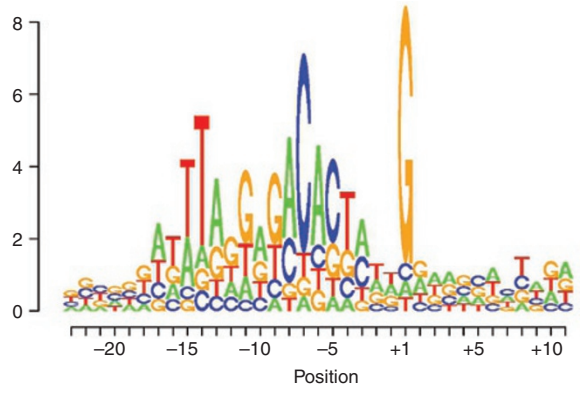

Activity logo for a particular promoter. Reprinted from *Nature Biotechnology*.

variations, Shendure also foresees that saturation mutagenesis will benefit the field of synthetic biology. "Groups that focus on synthetic circuits," he says, "are largely borrowing from nature's tool box. Less has been done to engineer them from the ground up, fine-tune, optimize or modulate those existing parts." This type of mutagenesis strategy would allow engineers to predetermine promoters with very specific properties, build an oligonucleotide library and characterize which mutants fit the requirements.

Genome biology and synthetic biology can share the same tool kit, one to understand nature's variation, the other to mimic and improve upon it.

Nicole Rusk

RESEARCH PAPERS

Patwardhan, R.P. *et al*. High-resolution analysis of DNA regulatory elements by synthetic saturation mutagenesis. *Nat. Biotechnol.* **27**, 1173–1175 (2009).

genetic and functional evidence, the researchers observed that less than 10% of their negative pairs were functionally associated by STRING. However, because STRING is not just limited to physical interactions, functional associations are likely to yield false positive hits. The Negatome also certainly includes false "negative" information; it is surely possible that some of the negative interactions can indeed occur under some biological context.

In addition to training protein-protein interaction prediction algorithms, the Negatome could also be used to judge the quality of high-throughput interactome screens such as two-hybrid methods, which have been criticized for being subject to a high false positive rate. "If you think about these famous 'hairballs,' these huge networks of interactions, use of the Negatome would be a way to erase some of the edges, if a particular edge is stated as being false," notes Frishman.

The Negatome currently contains data mostly for mammalian proteins, but Frishman and his colleagues have longer-term plans to continue adding new literature evidence and structure-based data from the PDB, which will continually improve the resource. Perhaps the larger scientific community will see the value of the Negatome and thus be encouraged to make negative results, in many different fields, more widely available.

Allison Doerr

RESEARCH PAPERS

Smialowski, P. *et al.* The Negatome database: a reference set of non-interacting protein pairs. *Nucleic Acids Res.* published online 17 November 2009.

NEWS IN BRIEF

GENOMICS

Complete genomes

Despite advances in high-throughput sequencing, the number of completely sequenced human genomes is still small. A new technique and business model by the company Complete Genomics promises to change that. Their technology involves the assembly of fragmented DNA into nanoballs that are arrayed and sequenced using combinatorial probe-anchor ligation chemistry. The low cost of consumables and efficient parallelization allow Complete Genomics to project that their company will sequence hundreds of individuals in the near future.

Drmanac, R. *et al. Science* advance online publication 5 November 2009.

PROTEOMICS

The human protein-DNA interactome

Although the DNA targets of key transcription factors have been intensively studied, the targets of the broader set of DNA-binding proteins are largely unknown. Hu *et al.* used a bioinformatics approach to predict human proteins likely to interact with a set of 460 diverse DNA motifs. They then used a protein microarray containing the 4,191 known and predicted DNA binding proteins to characterize the human protein-DNA 'interactome'; they identified a large number of known and previously unknown protein-DNA interactions.

Hu, S. *et al. Cell* **139**, 610–622 (2009).

BIOINFORMATICS

Correcting gene function annotations

Homology-based methods to annotate gene function are subject to misannotations that can propagate through databases; thus, they are very important to correct. Hsiao *et al.* describe an algorithm for policing gene annotations. The algorithm looks for genes with poor genomic correlations with their network neighbors, which are likely to represent errors. Hsiao *et al.* applied their approach to identify misannotations in *Bacillus subtilis*.

Hsiao, T.-L. *et al. Nat. Chem. Biol.* **6**, 34–40 (2010).

STEM CELLS

The fate of stem cells

There is high interest in understanding what happens, on a systems level, to stem cells upon perturbation. Lu *et al.* follow changes in histone acetylation, chromatin-bound RNA polymerase II, mRNA and nuclear protein levels in mouse embryonic stem cells after downregulation of the pluripotency factor Nanog. They find that this single perturbation has widespread repercussions across the epigenetic, transcriptional and translational systems.

Lu, R. *et al. Nature* **462**, 358–362 (2009).

GENOMICS

Dancing in the rain

When looking for variation in the human genome, researchers are often interested in just a specific subsection. But how best to enrich for such a region? Scientists from the company RainDance Technologies present a microdroplet-based technology in which each target region is amplified in a singleplex reaction within the confines of a microdroplet. This allows efficient amplification of target regions with uniform coverage, high accuracy and reproducibility.

Tewhey, R. *et al. Nat. Biotechnol.* **27**, 1025–1031 (2009).