It became quickly apparent that the specificity landscapes of several binders, including natural transcription factors, are rugged. Notably, this is true even of the innermost circle, which represents the binding motif. As the points on this circle represent the motif in the context of different flanking sequences, what this observation points to is the importance of contextual information in the binding of proteins to DNA. "When you look at a landscape like this, you see immediately that context matters," Ansari says, adding: "That sort of information gives us a much better way of annotating the genome than consensus motifs."

The specificity landscapes also allow an almost at-a-glance evaluation of the specificity of binding of a given factor because peaks in outer circles immediately indicate that the binder targets sequences other than the consensus motif. The researchers found that synthetic polyamide binders are in fact highly specific for their designed target sites, often more so than natural DNA-binding proteins. Gratifyingly, the *in vitro* binding data for one polyamide could explain discrepancies that have been observed in its regulation of target genes in living cells. Further study of how the *in vitro* data relate to binding within the cell will undoubtedly provide a more nuanced picture.

Ansari and colleagues hope to have a user interface available soon so that others can use this visualization tool. Exploration of the peaks and valleys of a specificity landscape will then be just a click and a drag away.

Natalie de Souza

RESEARCH PAPERS
Carlson, C.D. *et al.* Specificity landscapes of DNA binding molecules elucidate biological function. *Proc. Natl. Acad. Sci. USA* **107**, 4544–4549 (2010).

reported in *S. cerevisiae*, and there, poly(A+T) stretches had been shown to be crucial in keeping the DNA nucleosome free. However, in *S. pombe* such sequences are not enriched in NDRs. Apparently, *S. pombe* uses a different, yet to be determined, mechanism to keep NDRs free of nucleosomes. In general, the correlation between DNA sequence and nucleosome positioning was very different between both yeast, arguing against universally conserved DNA sequence rules.

Interestingly, promoter regions enriched for the histone variant H2A.Z, which is considered an epigenetic mark for silent chromatin, also had arrays upstream of the TSS, indicating that histone H2A.Z has a role in positioning as well, again in contrast to *S. cerevisiae*.

Although much remains to be done to elucidate mechanisms, the value of this map is obvious. As Korber describes it, "everyone can turn to this map and find out where in their gene of interest is an NDR or a regular array and how high the nucleosome occupancy is." And in addition every gene is annotated with a TSS and a TTS.

Elucidating the mechanism of positioning will give important clues as to the intricate interplay between chromatin packaging and all DNA-related processes such as transcription, replication or DNA repair.

Nicole Rusk

RESEARCH PAPERS
Lantermann, A.B. *et al. Schizosaccharomyces pombe* genome-wide nucleosome mapping reveals positioning mechanisms distinct from those of *Saccaromyces cerevisiae*. *Nat. Struct. Mol. Biol.* **17**, 251–257 (2010).

NEWS IN BRIEF

STEM CELLS

From fibroblasts to neurons

No biologist would be surprised these days if one cell type was converted to another by going through a pluripotent stage, nor if this reprogramming was done directly between two closely related cell lineages. But Vierbuchen *et al.* now demonstrate a way to directly convert fibroblasts into distantly related excitatory neurons. By introducing a specific combination of genes encoding transcription factors (*Ascl1*, *Brn2* and *Myt1l*) into mouse embryonic and postnatal fibroblasts, they made induced neuronal cells with characteristics and functional properties of mature neurons.

Vierbuchen, T. *et al. Nature* **463**, 1035–1041 (2010).

SYSTEMS BIOLOGY

Validating functional CRMs

Cis-regulatory modules (CRMs) control gene expression as parts of complex regulatory networks. To experimentally validate CRMs, which are often identified based on computational predictions, Nam *et al.* recently developed a high-throughput assay. The researchers barcoded each CRM that drove expression of a reporter gene, then injected the constructs into a sea urchin embryo and subsequently analyzed the isolated mRNA by quantitative PCR. This approach will be a valuable tool for regulatory systems biology.

Nam, J. *et al. Proc. Natl. Acad. Sci. USA* **107**, 3930–3935 (2010).

PROTEIN BIOCHEMISTRY

Routine NMR structures of large proteins

It is challenging to solve the structures of large proteins by nuclear magnetic resonance (NMR) spectroscopy without resorting to deuterium labeling. Raman *et al.* show that protein structures of up to 25 kilodaltons can be solved via NMR spectroscopy by using sparse information about backbone chemical shifts and residual dipolar couplings. The researchers used these data to guide Rosetta-based structural modeling of several proteins with known and novel structures.

Raman, S. *et al. Science* **327**, 1014–1018 (2010).

NEUROSCIENCE

Recording the flying brain

An ideal way to understand how the nervous system transforms sensory information into locomotor actions is by directly recording the activity of relevant neurons in animals that are receiving the stimulus while they are free to move. Maimon *et al.* developed a way to perform whole-cell patch-clamp recordings from genetically identified neurons in *Drosophila melanogaster* in flight, allowing them to study the activity of a class of visual neurons and monitor optomotor responses in the tethered, flying flies.

Maimon, G. *et al. Nat. Neurosci.* **13**, 393–399 (2010).

SYNTHETIC BIOLOGY

Designer promoters

The ability to tune the amounts of genes expressed in different cell types would permit more precise reverse genetic experiments. Schlabach *et al.* isolated strong synthetic enhancers by screening a library of 100-mer sequences consisting of tandem repeats of all possible 10-mers. Reporter expression varied in different cell lines and could be additionally modulated by screening for synergistic effects between enhancers.

Schlabach, M.R. *et al. Proc. Natl. Acad. Sci. USA* **107**, 2538–2543 (2010).