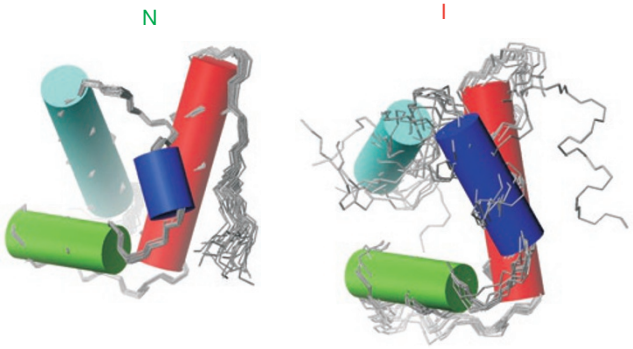

FF domain structures. The secondary and tertiary structures of the native state (N) differ from the structure of the folding intermediate (I), which is also more disordered. Reprinted with permission from the American Association for the Advancement of Science.

lack of experimental methods to simply detect intermediates, let alone solve their structures. Kay notes that the method could also be used to gain insights into many other interesting questions in biology, ranging from understanding protein misfolding, to molecular recognition, to enzyme catalysis and to how macromolecular machines function.

The future applications of this approach are no doubt 'exciting', but Kay stresses that these are still early days. "There will have to be development of NMR methodologies to keep pace with the biochemical questions that we want to answer," he notes.

Allison Doerr

RESEARCH PAPERS

Korzhnev, D.M. *et al.* A transient and low-populated protein-folding intermediate at atomic resolution. *Science* **329**, 1312–1316 (2010).

Shen, Y. *et al.* Consistent blind protein structure generation from NMR chemical shift data. *Proc. Natl. Acad. Sci. USA* **105**, 4685–4690 (2008).

Simpson and her colleagues systematically tested about 100 MiniPs for their ability to drive gene expression in the adult mouse brain. A substantial fraction of these constructs, about one-third, yielded interesting patterns. Some constructs apparently recapitulated endogenous expression of the gene from which they were derived, others could drive reporters in only a subset of the endogenously expressing cell types, and still others showed entirely new patterns, but all of them yielded reporter expression in restricted regions of the brain.

Undoubtedly, there is still much to be learned from these tools. "Even with a team like this, and it's obviously not small, we simply couldn't characterize these constructs in the kind of detail that a real biologist wants," says Simpson. But they are making all of the plasmids, embryonic stem cell lines and mice available to other researchers, she emphasizes, and hope that this will allow interested scientists to use them in their own work.

Together with the information available from the bioinformatics analysis, these resources should provide a finer set of tweezers both for probing gene regulation and for a multitude of functional studies in the brain and potentially other tissues.

Natalie de Souza

RESEARCH PAPERS

Portales-Casamar, E. *et al.* A regulatory toolbox of MiniPromoters to drive selective expression in the brain. *Proc. Natl. Acad. Sci. USA* **107**, 16589–16594 (2010).

NEWS IN BRIEF

MOLECULAR ENGINEERING

Monoclonal antibodies without screening

In developing a pipeline for rapid monoclonal antibody production, Reddy *et al.* describe a strategy that bypasses the need for extensive screening of immortalized B cells or recombinant antibody libraries. Instead, they used high-throughput DNA sequencing to identify the variable region gene repertoires produced by bone marrow plasma cells of immunized mice. They paired the most abundant variable region heavy and light chain genes, reconstructed them using automated gene synthesis and recombinantly expressed the monoclonal antibodies.

Reddy, S.T. *et al. Nat. Biotechnol.* **28**, 965–969 (2010).

IMAGING

Imaging mRNA transport

It is challenging to clearly observe mRNA export from nuclear pores. Grünwald and Singer now describe a super-registration approach for fluorescence microscopy that facilitates measuring distances between different fluorophores with very high time and spatial precision. This technique allowed them to observe the kinetics of β-actin mRNA transport in mammalian cells with an order of magnitude greater precision than previously possible. The method should be useful for imaging other transient cellular processes.

Grünwald, D. & Singer, R.H. *Nature* **467**, 604–607 (2010).

EPIGENETICS

Mapping the histone methyl lysine interactome

Vermeulen *et al.* report an integrated approach to understand how histone methyl lysine modifications regulate gene expression. First, they used quantitative mass spectrometry to identify proteins that bound to trimethyl lysine marks on histones H3 and H4. Then they fluoroscently tagged the identified proteins and performed pulldowns to identify physical interactions. Finally, using chromatin immunoprecipitation and DNA sequencing, they identified the genomic binding sites of the proteins. The resulting dataset is a rich resource for chromatin researchers.

Vermeulen, M. *et al. Cell* **142**, 967–980 (2010).

BIOINFORMATICS

Enzyme discovery without evolution

Before embarking on extensive direct evolution experiments to create enzymes with new activities, it is worth checking first whether such tools already exist in nature. Höhne *et al.* show that enzymes can be discovered by using rational design principles to predict key amino acids that perform the desired activity and then searching protein sequence databases to find proteins that already have these sequences. Applying this approach, they identified 17 (*R*)-enantioselective amine transaminases.

Höhne, M. *et al. Nat. Chem. Biol.* **6**, 807–813 (2010).

BIOPHYSICS

Monitoring membrane protein interactions

Casuso *et al.* show that high-speed atomic force microscopy (HS-AFM) can be used to experimentally monitor bacteriorhodopsin dynamics in native purple membranes from *Halobacterium salinarum*. Whereas AFM has a typical image scanning speed of about one minute, HS-AFM can record an image in about 187 milliseconds, allowing them to observe the movement of ATP-synthase c-rings, undetectable by other methods.

Casuso, I. *et al. Biophys. J.* **99**, L47–L49 (2010).