from natural spikes. By using light pulses as short as 10 ms, the authors showed they could precisely trigger fast and reproducible trains of spikes. They could also reliably produce subthreshold voltage transients, which are important in signaling but difficult to produce artificially.

Surprisingly the method worked without requiring application of retinal, which is used to form the light-absorbing chromophore in the protein. Presumably this is due to endogenous retinal or the presence of precursors in the culture medium. Deisseroth says, "Some tissues may need retinal supplementation and some may not. The jury is still out on that." The other surprise was the lack of toxicity seen even after expression for a week. "I think the reason for this is that ChR2 really is closed or mostly closed unless it is excited by light, and ambient light is about a thousand-fold too weak to excite it," remarks Deisseroth.

The great potential of the technique, however, will only be realized when it is demonstrated to work in acute brain slices and *in vivo*. It still isn't known whether it will be capable of functioning without the addition of retinal. Ease of use could also be improved with red-shifted variants that could be created by mutagenesis of ChR2. If this method does work well *in vivo*, the ability to express ChR2 in defined subsets of neurons should open up entire new avenues of research into neuronal signaling and functional integration.

Daniel Evanko

RESEARCH PAPERS

Nagel G. *et al.* Channelrhodopsin-2, a directly light-gated cation-selective membrane channel. *Proc. Natl. Acad. Sci. USA* **100**,13940–13945 (2003).

Boyden E.S. *et al.* Millisecond-timescale, genetically targeted optical control of neural activity. *Nat. Neurosci.* **8**, 1263–1268 (2005).

© 2005 Nature Publishing Group http://www.nature.com/naturemethods

algorithms to predict which sequence will make a good target for interference.

The usefulness of different silencing approaches is readily apparent in cases in which the phenotype after gene knockdown is more subtle. Corey reasons that if one sees the same phenotype regardless of whether DNA or RNA was targeted, the result is trustworthy and not an artifact of a specific method.

For Corey the excitement is not only in the efficiency of antigene RNAs to silence genes, but also in the underlying mechanism. "The bigger picture" he suggests, "is that in mammalian cells RNA is able to recognize DNA, and the importance of that is only beginning to be appreciated…the method works so well it is hard to believe that it isn't involved in natural regulation." Silencing genes by RNA recognition of transcription start sites may well be an application of a mechanism nature has been using all along, and it remains for us to explore this new type of cellular regulation.

Nicole Rusk

RESEARCH PAPERS

Janowski, B. *et al.* Inhibiting transcription of chromosomal DNA with antigene peptide nucleic acids. *Nat. Chem. Biol.* **1**, 210–215 (2005).

Janowski, B. *et al.* Inhibiting gene expression at transcription start sites in chromosomal DNA with antigene RNAs. *Nat. Chem. Biol.* **1**, 216–222 (2005).

NEWS IN BRIEF

BIOSENSORS

Direct molecular detection of nucleic acids by fluorescence signal amplification

PCR amplification is a typical component of most high-sensitivity DNA detection strategies, but Ho *et al.* present an alternative approach that relies on a specially designed optical polymer for fluorescence-based detection of target DNA sequences. This method is capable of detecting DNA at zeptomolar concentrations within five minutes without enzymatic amplification.

Ho, H.A. *et al. J. Am. Chem. Soc.*; published online 18 August 2005.

GENE REGULATION

Tuning genetic control through promoter engineering

Using error-prone PCR to introduce mutations into a constitutively active promoter, Alper *et al.* demonstrate an approach for the generation and analysis of libraries of promoters with varying transcriptional output levels. The authors suggest this method could be useful for more precise manipulation of gene expression or for studying sequence determinants of promoter activity.

Alper, H. *et al. Proc. Natl. Acad. Sci. USA* **102**, 12678–12683 (2005).

CHEMICAL BIOLOGY

Combinatorial polyketide biosynthesis by *de novo* design and rearrangement of modular polyketide synthase genes

Natural polyketide compounds perform a wide variety of biological functions, and the ability to synthesize novel polyketides could prove valuable. This process is complicated, however, and requires the coordinated action of multiple enzyme modules. Menzella *et al.* describe swappable enzymatic 'cassettes' that promise to simplify the combinatorial synthesis of new polyketides.

Menzella, H.G. *et al. Nat. Biotechnol.*; published online 14 August 2005.

PROTEOMICS

Large-scale identification of yeast integral membrane protein interactions

The difficulties of working with membrane proteins have limited the ability of researchers to study this segment of the interactome. Miller *et al.* performed a split-ubiquitin two-hybrid interaction screen and analyzed their data with a support vector machine 'learning algorithm' in an effort to more confidently assess the associations of integral membrane proteins in yeast.

Miller, J.P. *et al. Proc. Natl. Acad. Sci. USA* **102**, 12123–12128 (2005).

GENOMICS

The transcriptional landscape of the mammalian genome

Researchers from the FANTOM Consortium and RIKEN have collaborated in an extensive analysis of the mouse transcriptome, yielding the surprising finding that the mouse genome seems to contain many more genes than previously predicted: an estimated 181,047 transcripts generated from dense 'transcriptional forests' encompassing more than 60% of the genome.

The FANTOM Consortium *et al. Science* **309**, 1559–1563 (2005).