for optical trapping and fluorescence detection are separated by at least 13 μM, so there is no mutual interference."

They used their long tether approach to examine the effect of sub-picoNewton forces on the conformational properties of the Holliday junction, a cross-like DNA structure that forms during recombination of two DNA strands. Such a structure cannot be examined using a conventional optical trap and tether system.

They first labeled two arms of the Holliday junction with different fluorophores that would permit them to detect changes in the distance between the arms by fluorescence resonance energy transfer (FRET). They used the third arm to immobilize the molecule on a glass slide substrate and attached the fourth arm to a long DNA tether (bacteriophage λ DNA) whose other end was attached to an optically trapped bead (**Fig. 1**).

To apply a desired constant sub-picoNewton force to the Holliday junction while performing FRET measurements to look at changes in the structure, Ha and colleagues moved the microscope stage with the substrate toward or away from the stationary trapped bead. The separation of the trapping and imaging beams combined with the use of the vitamin E analog Trolox, to reduce bleaching and blinking, allowed measurements for as long as 250 seconds.

This method will be useful for many other studies that require the application of such small forces. "Our method is readily applicable to any of the nucleic acid structures and their interaction with protein," concludes Ha.

Daniel Evanko

RESEARCH PAPERS
Hohng, S. *et al.* Fluorescence-force spectroscopy maps two-dimensional reaction landscape of the Holliday junction. *Science* **318**, 279–283 (2007).

of its own inducible promoter so that the researchers could independently regulate the level of mRNA and sRNA. Measuring the reporter protein and mRNA levels at various degrees of sRNA expression, they confirmed the key properties of the sRNA-mediated regulation that they had predicted.

Hwa is optimistic that sRNA regulators will find use in developing gene circuits. He says: "Most people who work on bacterial gene circuits use the same small set of protein-based regulators. The feeling is that these tools are quite limited in terms of how you can induce them without causing other unintended changes to the cell. sRNA really gives us a whole new class of gadgets." Hwa also points out that new sRNA-mRNA pairs can be designed based on known templates and they can be made very specific to avoid cross-talk.

Of course, important challenges remain. A number of mRNAs are very short-lived, which does not give the sRNA enough time to find its target and necessitates the stabilization of the mRNA. Another requirement for this regulation to work is the presence of a chaperone, thought to mediate RNA degradation. If an sRNA-based gene circuit were to be established in an 'artificial' cell, this chaperone would have to be supplied.

Despite these challenges, bacterial noncoding RNAs deserve a chance to prove their worth in regulating gene circuits.

Nicole Rusk

RESEARCH PAPERS
Levine, E. *et al.* Quantitative characteristics of gene regulation by small RNA. *PLoS Biol.*, **9**, e229, 2007.

NEWS IN BRIEF

GENOMICS

HapMap version 2.0

Phase II of the human haplotype map (HapMap), characterizing more than 3.1 million single nucleotide polymorphisms (SNPs), has now been released. The data were collected from 270 individuals from diverse backgrounds, and the resulting HapMap has a density of about one SNP per kilobase. This valuable data resource should facilitate studies of human evolution as well as provide insights into the genetic basis of disease.

The International HapMap Consortium *Nature* **449**, 851–861 (2007).

PROTEIN BIOCHEMISTRY

Protein structures from scratch

With an all-atom rebuilding and refinement protocol, Qian and colleagues describe a computational method to improve protein models derived from NMR and X-ray crystallographic data without using any phasing information or homologous structures. Notably, they were also able to successfully predict the structure of a 112-residue protein without using any experimental information other than the protein sequence.

Qian, B. *et al. Nature* **450**, 259–264 (2007).

CHEMICAL BIOLOGY

Click chemistry without copper

The azide-alkyne reactions, the Staudinger ligation and the copper-catalyzed cycloaddition known as click chemistry are useful bioorthogonal labeling reactions. However, the Staudinger ligation is a rather slow process, and click chemistry requires the use of toxic copper. Baskin and colleagues now solve both problems with the development of a copper-free click chemistry reaction.

Baskin, J.M. *et al. Proc. Natl. Acad. Sci. USA* **104**, 16793–16797 (2007).

DRUG DISCOVERY

How drugs inhibit telomerases

Anticancer therapies using drugs that interfere with the maintenance of telomeres by binding to their single-stranded ends have shown good *in vivo* antitumor activity. These drugs were thought to inhibit the telomerase but De Cian and colleagues now show that the drugs inhibit the initial elongation step of the enzyme rather than its activity. This distinction is important when it comes to devising assays to measure the inhibitory potency of these drugs.

De Cian, A. *et. al. Proc. Natl. Acad. Sci. USA* **104**, 17347–17352 (2007).

RNA INTERFERENCE

Controlling pests through RNAi

New methods for controlling agricultural pests are urgently needed. Mao *et al.* and Baum *et al.* describe how to harness the power of RNA interference to control insect pests on crops. With transgenic crops expressing dsRNA specific for knocking down essential genes in insects these two groups independently showed that oral delivery of dsRNA caused lethality.

Mao, Y.B. *et al. Nat. Biotechnol.*, published online 4 November 2007.
Baum, J.A. *et al. Nat. Biotechnol.*, published online 4 November 2007.