template allows them to do so, two 5C primers bind in close proximity and are ligated to each other; then the product is amplified by PCR (**Fig. 1**). The resulting 5C library can be further amplified and analyzed using a high-throughput readout such as microarray or 454 sequencing.

The new method can be used in several configurations. One can ask how a single or a handful of 'fixed' elements interact with the neighboring chromatin, which the authors demonstrated on a 400-kb region containing the well-characterized β-globin locus. Alternatively, 5C is amenable to mapping a network of interactions between two large sets of elements. Dekker's group performed a proof-of-principle experiment examining a 100-kb conserved gene desert region, and they now plan to establish such maps for the ENCODE regions.

This is where the readout by sequencing comes in handy. Even if considering a single small chromosome, the number of possible interactions between the genes and regulatory elements present on this chromosome can easily reach several million. "By sequencing," explains Dekker, "you will only detect those interactions that are actually occurring, but with a microarray you would have to represent each possible combination." Capitalizing on the new sequencing technologies such as 454, which works optimally on short reads, Dekker's group specifically designed the 5C method so that short reads would be sufficient.

"With sequencing methods allowing you to read 100,000 or even 1 million sequences," explains Dekker, "this really opens up the possibility to map this network of interactions that we believe occur in the genome... linking things that are far apart on a chromosome, but actually are functionally related and physically associated."

Veronique Kiermer

RESEARCH PAPERS

Dostie, J. *et al.* Chromosome conformation capture carbon copy (5C): a massively parallel solution for mapping interactions between genomic elements. *Genome Res.* **16**, 1299–1309 (2006).

surface proteins using a CoA-based method, the inability to get the CoA analog inside the cell limited this technique to use only for membrane-protein modification. In addition to bringing this methodology inside the cell, the researchers plan to extend this technology to species other than *E. coli*. They also would like to improve the detection limit to allow work with native protein levels instead of relying on overexpression of the carrier protein fusion and PPTase, as they did in this study.

As they continue to develop this CoA-directing technology, Burkart notes that other researchers can now use their own fusions to study protein function inside the cell. "I think what will be exciting in this area now is to see others use their carrier protein fusions inside the cell with our CoA delivery technique to figure out what happens to proteins in the cellular context," he adds.

Irene Kaganman

RESEARCH PAPERS

Clarke, K.M., *et al. In vivo* reporter labeling of proteins via metabolic delivery of coenzyme A analogues. *J. Am. Chem. Soc.* **127**, 11234–11235 (2005).

Meier, J.L. *et al.* Synthesis and evaluation of bioorthogonal pantetheine analogues for *in vivo* protein modification. *J. Am. Chem. Soc.* **128**, 12174–12184 (2006).

NEWS IN BRIEF

PROTEOMICS

Automating phosphoproteomics

One of the most powerful applications of mass spectrometry–based proteomics is the ability to identify and map post-translational modifications. As data sets grow larger, however, the manual validation of such sites becomes nearly impossible. Beausoleil *et al.* have devised an automated scoring tool they call 'Ascore' that, using the intensities of site-determining ions from tandem mass spectrometry data, measures the probability of correct phosphorylation site localization.

Beausoleil, S.A. *et al. Nat. Biotechnol.* **24**, 1285–1292 (2006).

CELL BIOLOGY

Visualizing disulfide reduction

Yang *et al.* present a FRET-based strategy to image disulfide-bond cleavage in live cells. Using the folate receptor as an example to probe the endocytic pathway, they created a FRET reporter consisting of folate, rhodamine and BODIPY. When the disulfide bond between folate and rhodamine is cleaved, the fluorescence switches from red to green, providing a visual readout of cellular location.

Yang, J. *et al. Proc. Natl. Acad. Sci. USA* **103**, 13872–13877 (2006).

CHEMICAL BIOLOGY

Reversing reactions to make new sugars

Sugar-based natural products with therapeutic activities are notoriously difficult to make using organic synthesis alone. With the discovery that several glycosyltransferase enzymes can catalyze reversible reactions, Zhang *et al.* describe a powerful tool to synthesize exotic natural product variants and to incorporate chemical handles onto sugar scaffolds.

Zhang, C. *et al. Science* **313**, 1291–1294 (2006).

MICROBIOLOGY

Identification of parasite genes silenced to evade host immunity

A *Vibrio cholerae* strain expressing a Tet repressor–sensitive GFP and a transposon carrying the repressor permits the identification of genes that are silenced as the parasite adapts from the surface-water environment to its mammalian host. Transposon-containing bacteria clones turn green only when adapting from *in vitro* culture to the infection of infant mice, allowing identification of genes that are silenced to escape host immunity.

Hsiao, A. *et al. Proc. Natl. Acad. Sci. USA* **103**, 14542–14547 (2006).

IMAGING AND VISUALIZATION

Improving FlAsH

The fluorogenic, membrane-permeable biarsenical dye called FlAsH has been indispensable for the chemical labeling of proteins in cells, requiring only that the protein be engineered with a tetracysteine motif. Spagnuolo *et al.* have developed a new biarsenical dye they name F2FlAsH, which exhibits higher absorbance, quantum yield and photostability, with a reduced dependence on pH as compared to the original FlAsH.

Spagnuolo, C.C. *et al. J. Am. Chem. Soc.* **128**, 12040–12041 (2006).