in the picomolar range, and requires very small quantities of material. The researchers hope in the future to extend the dynamic range to span all known biological interactions.

"Being able to do this in free solution is really the big deal," says Bornhop. "People have forever complained about surface plasmon resonance being tough in terms of needing to do the surface chemistry, and also needing to have a priori information. The nice thing for us is that we don't need to know much about the proteins we're studying." Thus the method has potential exciting applications in screening for as-yet unknown binding partners of orphan receptors.

The technology may be applicable to diagnostics and therapeutic monitoring as well. "You could do this (relatively cheaply) with a diode laser, a little plastic chip, and a simple detector or bar-code scanner," says Bornhop. The researchers are developing interferometry for benchtop point-of-care analysis, which would allow patients to receive diagnostic and treatment information within minutes, eliminating the need for repeated clinic visits. In the future, given sufficient investment and effort, it is possible that the method could even be harnessed for extremely low-tech field applications.

In the meantime, Bornhop envisions that free-solution interferometry will be useful for studying intramolecular changes such as solubilization and folding as well as binding. "If the molecular dipole changes enough to produce a refractive index change, we should be able to see it," he says. And because of the universal nature of the signal, this will apply not only to proteins, but to other macromolecules as well.

Natalie de Souza

RESEARCH PAPERS

Bornhop, D.J. *et al.* Free-solution, label-free molecular interactions studied by back-scattering interferometry. *Science* **317**, 1732–1736 (2007).

able to reliably detect the change in potential that occurred. The magnitude of the potential change for the protein-protein interaction was dependent on the ionic properties of the protein, but DNA hybridization gave a reliable twofold signal change.

Sinensky and Belcher showed that the technique is compatible with fast scanning speeds that should allow analyses similar in speed to what is achievable with fluorescent microarray systems but without the requirement for labeling. The limitation at this time is the slow speed of conventional DPN to manufacture the arrays. Once this is overcome, the high-density and label-free nature of KPFM should provide advantages over fluorescence-based arrays.

AFM is expanding quickly into new areas as the nanoscale resolution of the device finds new applications that are quite different from what AFM was developed for. Although it is unlikely that AFM-based devices will ever be as common as light-based microscopes in biology laboratories, the technology seems poised for rapid expansion.

Daniel Evanko

RESEARCH PAPERS

Dague, E. *et al.* Chemical force microscopy of single live cells. *Nano Lett.* **7**, 3026–3030 (2007).

Sinensky, A.K. & Blecher, A.M. Label-free and high-resolution protein/DNA nanoarray analysis using Kelvin probe force microscopy. *Nature Nano.* **2**, 653–659 (2007).

NEWS IN BRIEF

CHROMATIN TECHNIQUES

Assessing histone biology with SILAC

There is great interest in understanding how histone post-translational modifications regulate biological processes. Vermeulen *et al.* now use a combination of SILAC (stable isotope labeling by amino acids in cell culture), high accuracy mass spectrometry, and a new statistical procedure to monitor differences in transcription factor binding to methylated or nonmethylated histone H3 peptides.

Vermeulen, M. *et al. Cell* **131**, 58–69 (2007).

RNA INTERFERENCE

MicroRNAs need accessible targets

It is still not fully understood how microRNAs recognize their mRNA targets. Sequence complementarity at key positions is an important feature, and Kertesz *et al.* now show that accessibility of the binding site on the mRNA is equally crucial. They demonstrate that the total energy balance between unwinding an mRNA and binding the microRNA is an important feature in determining the overall silencing efficacy of the microRNA.

Kertesz, M. *et al. Nat. Genet.* **39**, 1278–1284 (2007).

CHEMICAL BIOLOGY

Promiscuous glycosyltransferases

The synthesis of glycosylated natural products would be made easier with glycosyltransferase enzymes that accept diverse sugar substrates. Williams *et al.* describe a fluorescence-based assay to screen for increased glycosyltransferase catalytic efficiency and substrate promiscuity via directed evolution. They evolved a 'universal' glycosyltransferase with broad activity.

Williams, G.J. *et al. Nat. Chem. Biol.* **3**, 657–662 (2007).

IMAGING AND VISUALIZATION

Imaging nitrogen fixation

Using a technique called multi-isotope imaging mass spectrometry (MIMS), Lechene *et al.* monitored nitrogen fixation by symbiotic bacteria in the gills of marine shipworms. They followed the incorporation of ^{15}N from nitrogen gas fixed by the bacterium *Teredinibacter turnerae* by bombarding shipworm gill tissue with a primary cesium ion beam to produce secondary cyanide ions, thus mapping the distribution of ^{15}N and the normal isotope ^{14}N. The technique may be useful in other microbial ecology studies.

Lechene, C.P. *et al. Science* **317**, 1563–1566 (2007).

GENE REGULATION

Assessing genomic ultraconservation

Sequences with 100% identity between human, mouse and rat (>200 nt), so-called ultraconserved elements, are thought to represent genomic regions of great functional relevance. Ahituv *et al.* now show that deletion of four such elements in mouse had no discernible effects on the animals. Although alternative explanations are possible, the observation suggests that not all ultraconserved elements are indispensable in mammals.

Ahituv, N. *et al. PLoS Biol.* **5**, e234 (2007).