image-analysis algorithms to yield 145 morphological features. Using neural networks and clustering techniques, the researchers separated cells with similar signatures into 'phenoclusters', which then allowed them to describe a signal network that regulates cell protrusion, adhesion and tension. "The computational and statistical approach that we've applied after data extraction was what led us to some good insights," notes Bakal.

One of the goals is to study more genes using this technique, so the group is trying to automate the process by using confocal microscopy to obtain images with less variability between them and thus eliminate the need for the manual correction. Bakal also envisions using this technique for small-molecule screening—generating a cell signature after treatment, and integrating it with signatures from RNAi studies to make predictions about the small molecule's targets.

This work also has potential application as a diagnostic tool. Just as scientists observe cells, pathologists examine cellular shape and features in clinical samples to determine the identity of a disease or what oncogene may be expressed. "Taking that a step further," hypothesizes Bakal, "we could make this quantitative in nature—take clinical samples, for example, assign a quantitative signature to their shape, and then by integrating that information with our database, match it up with cells overexpressing oncogenes or cells in which a tumor suppressor gene has been knocked out."

For now, CellSegmenter can be used on any image for which intensity thresholding can be used. "It's a very simple tool that allows a lot of user interface, so that simplicity allows you to do many different kinds of things with it" says Bakal.

Irene Kaganman

RESEARCH PAPERS
Bakal, C. *et al.* Quantitative morphological signatures define local signaling networks regulating cell morphology. *Science* **316**, 1753–1756 (2007).

to expand NetworKIN. They want to include common interaction motifs and make the algorithm available as a webserver. Linding predicts, "people will be able to upload their proteins with the phosphorylation sites and then get predictions."

The scientists emphasize that the algorithm yields most biological insight if applied in a data-driven approach. Rather than look at a whole phosphoproteome, Linding suggests focusing on sites that are dynamically regulated in response to a certain treatment. He forsees that "NetworKIN will be very powerful for modeling when applied to a specific system."

This algorithm has the potential to be of great use to the scientific community, plans for its expansion are in place, but what is not in place yet is the funding to guarantee NetworKIN's long-term survival.

Linding and Pawson comment wistfully that it is relatively easy to start a new database, but that its maintenance is more difficult. "It is also a question of political will," Linding says; "there is very little support to maintaining things, but when you want to do really good science, you need to maintain the databases and keep them current all the time."

Let us hope that those exercising the political will agree.

Nicole Rusk

RESEARCH PAPERS
Linding, R. *et al.* Systematic discovery of *in vivo* phosphorylation networks. *Cell* **129**, 1415–1426 (2007).

NEWS IN BRIEF

SPECTROSCOPY

Looking at fast kinetic events by NMR

Although NMR spectroscopy is a fantastic technology for obtaining detailed information about proteins at the atomic level, it has been limited to studying kinetic processes on the order of minutes to hours. Schanda *et al.* now introduce SOFAST NMR spectroscopy, which reduces the time resolution to a few seconds. They used the SOFAST method to observe folding of α-lactalbumin and unfolding of ubiquitin.

Schanda, P. *et al. Proc. Natl. Acad. Sci. USA* **104**, 11257–11262 (2007).

STEM CELLS

Large-scale human stem cell characterization

As a service to the community, the International Stem Cell Initiative has systematically characterized 59 independently derived human embryonic stem cell lines from 17 different laboratories. Remarkably, in testing the expression of 17 marker cell-surface antigens and 93 genes, they found common expression patterns in spite of the differences in genetic backgrounds and different protocols used.

The International Stem Cell Initiative, *Nat. Biotechnol.* **25**, 803–816 (2007).

IMAGING AND VISUALIZATION

Triplex molecular beacons

Molecular beacons are useful probes for analyzing nucleic acids. In their free state they form a quenched stem-loop structure, but upon binding a target sequence the stem-loop opens, restoring fluorescence. Grossman *et al.* describe the design of 'triplex' molecular beacons, which bind an additional stem-forming oligonucleotide sequence in their free state. Their modular assembly allows the introduction of other functionalities, such as an additional quencher.

Grossman, T.N. *et al. Angew. Chem. Int. Ed.* **46**, 5223–5225 (2007).

BIOPHYSICS

Making porous vesicles

The encapsulation of biomolecules inside lipid bilayer vesicles offers a way to observe molecular interactions for extended periods. Expanding the capabilities of the technique, Cisse *et al.* describe methods for introducing pores into vesicles, allowing exchange of buffer and chemical conditions in a controlled manner while keeping the local protein concentration constant. The system shows promise for use in single-molecule experiments.

Cisse, I. *et al. Proc. Natl. Acad. Sci. USA*; published online 11 June 2007.

CHEMICAL BIOLOGY

Testing peptide permeability

Tools for modulating protein activity, cyclic peptides are more proteolytically resistant than their linear counterparts, and their constrained conformation may provide more favorable binding characteristics and potentially increase cell-permeability. Kwon and Kodadek used a reporter gene assay to quantitatively compare cell permeability, and found that cyclic peptides are not generally more permeable than linear peptides.

Kwon, Y.U. & Kodadek, T. *Chem. Biol.* **14**, 671–677 (2007).