probes allows them to be tracked within a cell, and can allow mechanistic studies of biological transformations. Such bioconjugation techniques usually rely on selective coupling reactions to the side chains of specific amino acid residues. The most common amino acid residues that are targeted are lysine and cysteine, but neither residue is ideal: lysines are too abundant and cysteines are rare and often linked in disulfide pairs.

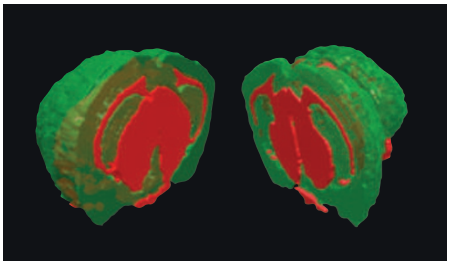
Now, Carlos Barbas and co-workers from the Scripps Research Institute in La Jolla, California, have developed a method of selectively functionalizing tyrosine residues under very mild aqueous conditions. In their method, the aromatic (phenolic) side chain of a tyrosine reacts with a cyclic diazodicarboxamide — a highly reactive electrophile that is also stable to the aqueous conditions desired. Tyrosine residues reacted selectively over other amino acids with aromatic side chains to form new C–N bonds that are stable to both strongly acidic and basic conditions even at high temperature.

A wide variety of molecules can be functionalized with the necessary cyclic diazocarboxamide group, including fluorescent dye reagents and other peptides. These include a bifunctional linker with both the diazo functionality and an azide, so the system is primed for the now widely used copper-catalysed [3+2] cycloaddition or 'click' reaction.

MASS SPECTROMETRY

## Brains in 3D

*Angew. Chem. Int. Ed.* **49,** 873–876 (2009)





Two-dimensional imaging mass-spectrometry has become a useful tool in biology for looking at the distribution of molecules such as lipids or drugs in cells and tissue. One of the benefits of using mass spectrometry for imaging is that it doesn't require the use of staining dyes or radioactive labelling. The technique identifies molecules on a surface and 3D images can be reconstructed from several sections.

Graham Cooks and colleagues from Purdue University have now developed a new technique that allows these sections to be quickly examined under ambient conditions, rather than the vacuum normally required. They used desorption electrospray ionization to liberate molecules from the samples, which then pass through the mass spectrometer. They optimized the conditions to provide the high-quality signal intensity and increased-quality two-dimensional images required to make up reliable three-dimensional models.

To test the technique, they looked at specific lipids in sections of mouse brain. Two characteristic lipids are distributed evenly in either the grey- or white-matter regions, so mapping only these rapidly built up a picture of the whole brain. Although this is only an approximation, the technique could be extended to look for other molecules and other organs. This could help build an 'atlas' that precisely correlates the presence of molecules to organ function.

ENZYME MODELLING

## $H_2S$ in hibernation

*Proc. Natl Acad. Sci. USA* **106,** 22090–22095 (2009)

Hydrogen sulfide ($H_2S$) is known by most chemists as a foul-smelling gas. It is toxic at concentrations of greater than 600 ppm, but is produced by enzymes in the body at lower concentrations and is known to produce effects similar to hibernation. Understanding these effects is important because they could be used, for example, to chemically preserve organs for transplant.

Now, James Collman and co-workers from Stanford University have found that the effects of $H_2S$ are probably due to a reversible inhibition of the enzyme cytochrome *c* oxidase (CcO). They used a model of the enzyme active site, which consists of a copper atom coordinated by several imidazole ligands that are in turn bound by a heme unit. The enzyme model catalysed the electrochemical reduction of oxygen — mimicking the reduction that occurs during respiration — and showed that it was reversibly inhibited by $H_2S$.

Collman and co-workers went on to perform a series of nuclear magnetic resonance, infrared and ultraviolet–visible spectroscopy and high-resolution mass spectrometry experiments to investigate how and where $H_2S$ binds to the enzyme active site. At moderate to high concentrations, $H_2S$ is thought to reversibly compete with oxygen binding to the iron in the heme unit. It also has an important role at lower concentrations (particularly in periods of hibernation), acting as a reductant for cytochrome *c*, a process that usually relies on energy from food metabolism.

The definitive versions of these Research Highlights first appeared on the *Nature Chemistry* website, along with other articles that will not appear in print. If citing these articles, please refer to the web version.

blogroll

## Lessons learnt

**Tips for prospective post-docs, Science Online 2010, and pipetting in 2154.**

Anyone looking for a post-doctoral position at the moment would do well to read Mitch's article at the Chemistry Blog (http://go.nature.com/xDgi3N). In his post "The Hidden World of the PostDoc Interview" he outlines some lessons that I suspect a lot of people would prefer to learn before their first interview. These include: have an hour-long talk ready to give to the whole department, be ready to last all day and wear a suit. Jared also offered useful advice in his comment: candidates shouldn't be afraid to ask the interviewers beforehand what to expect "and just try to relax. They're real-live human beings, too." After Mitch learnt lesson one the hard way, he seems to have got into his stride, because he thinks his "job hunting is over, thankfully it didn't last long."

What do you get it if you put a load of scientists, bloggers, journalists, web developers, publishers and programmers together for four days in North Carolina? The answer is Science Online 2010, a conference that aimed to "discuss, demonstrate and debate online strategies and tools for doing science, publishing science, teaching science and promoting the public understanding of science." You also get an awful lot of blog posts and tweets — just search for '#scio10' for a flavour. One place to start dipping your toe into the ocean of blog posts is at the official website's blog coverage page (http://go.nature.com/r24TSm), which links to all the blogposts and media reports generated by the conference.

And finally, in a galaxy far, far away Chemgeek of Homebrew and Chemistry (http://go.nature.com/DubT8V) wondered: "Avatar has made a billion dollars and counting. You would think they could have hired someone to teach Sigourney Weaver how to use an Eppendorf pipette." It seems Chemgeek wasn't alone in spotting this, because Weaver's poor pipette technique has already made Avatar's 'goof page' on the Internet Movie Database (http://go.nature.com/2kGPCP).