

Chemical Biology

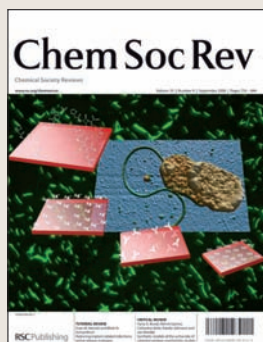
Mapping metalloproteins



The role of metals in biochemical processes is often not fully understood. Now analytical chemists are helping to address the problem, combining several techniques to study copper–protein interactions.

S Hann *et al*
J. Anal. At. Spectrom., 2006, DOI: 10.1039/b604974p

Anaesthetised brains under pressure



What happens if you get a frog drunk and then take him scuba diving? The answer could help explain how anaesthetics work, claim scientists in the UK.

A Wlodarczyk, P F McMillan and S A Greenfield
Chem. Soc. Rev., 2006, DOI: 10.1039/b517771p

Improving cell survival in chips



A way to monitor cell respiration in microchips could lead to better devices for fertility research. Using scanning electrochemical microscopy, the method can be used to measure oxygen uptake in single cells.

T Saito *et al*
Analyst, 2006, **131**, 1006

Spotting lipase fingerprints



Swiss scientists have revealed the fingerprints of lipase enzymes. The researchers have developed a microarray system that translates lipase activities into fluorescent patterns unique to each enzyme.

J Grognum and J-L Reymond
Mol. BioSyst., 2006, **2**, 492

 See www.rsc.org/chembiology/ for full versions of these articles

Research highlights

Mass spectrometry to demonstrate synthetic origins of nandrolone

Steroid cheats face testing times

A test for anabolic steroids that could help to crack down on drug cheats in sport has been developed by researchers in Germany and Canada.

Banned steroids such as nandrolone continue to be used by athletes to boost their muscle mass, and analysing urine samples for 19-norandrosterone, a metabolite of nandrolone, can uncover evidence of abuse. But traces of this chemical are also made naturally in the body, and current tests cannot determine whether the norandrosterone has a synthetic or physiological origin.

Moritz Hebestreit and colleagues from the German Sport University Cologne, in collaboration with a researcher from the Montreal Anti-doping Laboratory at the Institut Armand-Frappier, have now developed a technique that can distinguish between the two. This could help to resolve cases where athletes have elevated levels of



19-norandrosterone in their urine but insist that they have never taken steroids.

Hebestreit's test differentiates between synthetic and natural norandrosterone by analysing the ratio of ^{13}C to ^{12}C isotopes in urine samples using a technique called

Nandrolone is banned in competitive sport but can be made in the body

gas chromatography combustion isotope mass spectrometry. The synthetically produced compound has a lower concentration of the ^{13}C isotope because it is produced from a plant source with intrinsically less ^{13}C than that from normal dietary sources. The test is able to detect concentrations of 19-norandrosterone as low as 2ng per ml of urine – the level currently allowed by the World Anti-Doping Agency.

Tony Moffat, Head of the Centre for Pharmaceutical Analysis at the University of London, UK, said that the 'excellent' method was suitable for use in anti-doping programmes.

Hebestreit hopes to extend the technique to discover the origins of other drugs by studying different isotope ratios, such as D to H and ^{15}N to ^{14}N .

Nicola Burton

Reference

M Hebestreit et al, *Analyst*, 2006, **131**, 1021

Single-celled organisms swim to the infrared light to stave off hunger

Protozoan transformers

Infrared light can help hungry, water-dwelling protozoa adopt a sleeker, faster-swimming form, allowing them to disperse in search of new food sources. The tactic could be an evolutionary adaptation that helps populations of *Tetrahymena thermophila* to weather lean times, a team of Japanese and US scientists report.

The researchers spotted the behaviour while investigating the biological effects of infrared (IR) light. 'IR rays from sunlight permeate the Earth's atmosphere, yet little is known about their interactions with living organisms,' said Robert Shiurba of Waseda University. IR radiation has a wavelength between that of light and radio waves and, while its energy is too low to disrupt cell structures and molecules, it can interact with chemical bonds. 'The IR region is among the last to be



studied biologically,' said Shiurba.

To investigate how IR affects single cells, Shiurba and his colleagues studied the protozoan *T. thermophila*. In its freshwater environment it tends to swim upwards, gathering near the water surface in a teeming swarm where

Starving cells bathed in infrared light elongate into spindle shapes

there is more oxygen, edible debris – and sunlight.

Shiurba compared two cultures of *T. thermophila* in near-starvation conditions, one of which was bathed in IR radiation. The irradiated cultures grew normally, but major changes occurred in their cell physiology when the nutrients began to run out. The metabolic activity of the cells increased, and they elongated into spindle shapes.

These cells swam almost half as fast again as those in the control culture that was not exposed to IR light. They also followed much straighter trajectories. When competition for food reaches a maximum, transformation greatly increases a cell's odds of survival, suggested Shiurba. In future work, the group hopes to work out the molecular basis of this phenomenon.

Michael Spencelayh

Reference

R Shiurba et al, *Photochem. Photobiol. Sci.*, 2006, **5**, 799

Cleaning polluted water for farmed fish

A cheap and environmentally friendly system for cleaning polluted water should help keep farmed fish free of infections. Michela Magaraggia from the University of Padova, Italy, and colleagues have developed a technique to prevent fungal infections in trout farms.

Magaraggia's method combines visible light and porphyrin compounds to tackle diseases caused by the *Saprolegnia* species. When light shines on the porphyrins, they generate oxygen species with a short life span which can affect only their immediate surroundings. The oxygen species attack many cell constituents, ruling out the risk of selecting resistant microbial strains.

Concentrated fish populations, such as those found in fish farms, provide ideal conditions for fungal infections, said Magaraggia. 'Infections in fish eggs represent a heavy financial loss worldwide.'

The new method could remove an extensive range of pathogens and Magaraggia pointed out that the procedure is cheap and



Concentrated fish populations are prone to fungal infections

potentially safe. 'The accumulation of porphyrins in the environment is unlikely, owing to the gradual photodegradation induced by visible light,' she said.

It could also answer some wider issues for water sanitation, added Magaraggia. The procedure could be extended to the treatment of irrigation or drinking water – 'a major problem in developing countries for the prevention and limitation of diseases.'

Michele Zraggen

Reference
M Magaraggia *et al*, *J. Environ. Monit.*, 2006, **8**, 923

A switch for enzyme function

Researchers in Japan have changed the catalytic function of an enzyme by switching just one of its amino acids.

Hirofumi Ohta and colleagues at Keio University, Yokohama, Japan, prepared a mutated version of an enzyme called AMDase, different from the wild-type by just one cysteine amino acid in its core structure. They found that this single mutation gave the enzyme a new function – the enzyme now catalysed a racemase reaction, distinctly different from its normal decarboxylase reaction.

The group's first clue that this mutation might work came from the similarity of the two enzymes AMDase and glutamate racemase. Both enzymes contain a cysteine amino acid at the same position in their active sites, known to be important in controlling the intermediate step of their reactions. Also, both create an intermediate product called an enolate. However, an additional cysteine seems to be involved in glutamate racemase's mechanism. The AMDase mutant made by Ohta's team contains this additional cysteine residue in place of a glycine. This is the first report of a single mutation to change a decarboxylase to a racemase, said Ohta.

It is well established that enzymes can be used in organic synthesis, and redesigning them can improve their activity. Examining the common mechanistic points of apparently distinct enzymatic reactions is an important consideration for redesign, said Ohta.

Kurt Faber, an expert in biocatalysis from the University of Graz, Austria, sees enzyme design as an important way to develop new biocatalysts. 'The construction of a racemase from a decarboxylase by a single point mutation is a clever application of this concept,' said Faber.

Katherine Vickers

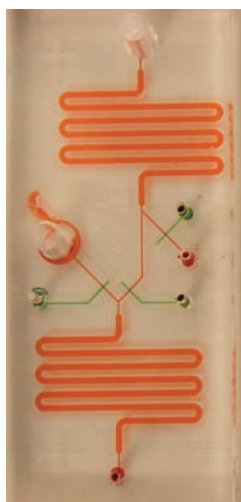
Reference
Y Terao, K Miyamoto and H Ohta, *Chem. Commun.*, 2006, 3600

Bio-barcodes scanned in cancer detection

A microchip that can detect tiny amounts of a protein associated with prostate and breast cancer could provide an early-warning detection system for the diseases.

Chang Liu, at the University of Illinois at Urbana-Champaign, US, led the team that produced the chip. 'Detecting protein biomarkers with high sensitivity and selectivity is critical for rapid disease diagnosis,' said Liu. Our microchip can detect the cancer indicator prostate specific antigen (PSA) at concentrations as low as 300 copies per microlitre of sample, 'a task akin to fishing out a needle out of a haystack.'

The detection process uses two types of particle: gold nanoparticles with hundreds of copies of a DNA 'barcode' attached, and magnetic beads. Both the nanoparticles and beads are attached to antibodies that can bind to PSA.



Reference
E D Goluch *et al*, *Lab Chip*, 2006, DOI: 10.1039/b606294f

When these particles meet PSA, they form a DNA-PSA-magnet complex resembling a sandwich. The complexes can be extracted from the sample using a magnet and, by measuring the total number of DNA barcodes, the sample's PSA level can be calculated. Because there are several hundred copies of DNA barcode for each copy of PSA, detecting tiny amounts of the antigen becomes much easier, said Liu.

The team's aim was to fit all the stages of this complex process onto a single microchip that could be used at the point of care, removing the need to send samples away for analysis, explained Liu. The group is currently working on microchips to detect proteins used to diagnose testicular cancer and Alzheimer's disease.

Clare Boothby

A warm reception across the globe And finally...

RSC members, authors, referees and readers met at three separate events on three continents in as many weeks, recently.

On 15 August, 120 delegates gathered at a reception in the Arabella Sheraton Grand Hotel in Cape Town at the 37th International Conference of Coordination Chemistry, to celebrate weekly publication of *Dalton Transactions*.

Following short welcoming speeches by Andrew Scott, RSC Membership Sales and Marketing Manager, and RSC Council Member, Professor Paul O'Brien, the Chairman of the *Dalton Transactions* Editorial Board, Professor Paul Walton, spoke about some of the journal's successes so far. '*Dalton Transactions* continues to go from strength to strength. It is now the highest ranked European journal for inorganic chemistry,' he explained, 'moving to weekly publication in January this year confirms its leading



position and we're delighted to have you celebrate this exciting development with us'.

A week later in Budapest, newly appointed RSC President, Professor Jim Feast, and RSC Chief Executive, Dr Richard Pike, hosted a joint reception with the GDCh at the 1st European Chemistry Congress in Budapest. Among the guests were representatives from the European Association for Chemical and Molecular Sciences (EuCheMS, formerly FECS) and international figures from the world of chemical sciences.

A popular annual event, the RSC Reception at the 232nd National Meeting & Exposition meeting took place on 10th September in the Grand Ballroom at the Hilton San Francisco. Addressing the ACS dignitaries, RSC members and other guests present, Professor Jim Feast introduced some new products in the RSCs portfolio and made an exclusive announcement regarding the RSC's policy on Open Access publishing.

Find out more in the next issue of *Essential Elements*.

From popular science books such as *Lust and Love: Is it more than chemistry?* to *Protein-Carbohydrate Interactions in Infectious Diseases* the RSC publishes books for all levels of readership and interest.

The new edition of *Nucleic Acids in Chemistry and Biology* has just been published. This popular undergraduate textbook has been thoroughly revised and updated, with expanded coverage on reactions and interactions with proteins and drugs. 'This book uniquely provides an introduction to both the chemistry and biology of nucleic acids, and thus will be of use to a very wide group of students and researchers. I can recommend it highly.' Stephen Neidle, Professor at the School of Pharmacy, University of London.

Another textbook recently published, *Chemistry and Medicines* provides an introduction to the subject of medicinal chemistry with additional sections on drugs to combat infectious diseases and cancers.

The RSC Biomolecular Sciences Series is a collection of research level books covering all areas of the biological sciences. Titles include: *Exploiting Chemical Diversity for Drug Discovery and Structural Biology of Membrane Proteins*. Other high level books include *Dendrimers in Medicine and Biotechnology and Metallochemistry of Neurodegeneration: Biological, Chemical and Genetic Aspects*.

Find out more about RSC books at www.rsc.org/books

Chinese medicine ... naturally

China is a hotbed for natural product related sciences, a fact demonstrated in the latest issue of *Natural Product Reports*. This special issue, guest edited by Professor R X Tan, Nanjing, focuses on 'Natural Product Chemistry in China' and brings together review articles from well established Chinese laboratories undertaking research in this vast field.

China is a country rich in plants and microbe species that cultivates a remarkable diversity of natural products; therefore it is no surprise that traditional Chinese medicine has used extracts from these plants to treat many diseases and that research into natural products remains important.

The comprehensive reviews in this special issue cover the

areas of phytochemicals; the bioactivity of the Liliaceae steroidal alkaloids; microorganisms as a source of biologically active natural products; mass production of important natural products and the development of plant tissue culture protocol for plant-derived medicines.

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