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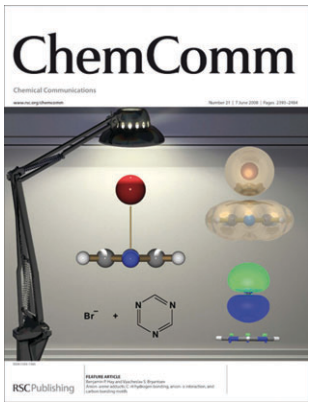
ISSN 1359–7345 CODEN CHCOFS (21) 2393–2484 (2008)

Cover

See J.-F. Nierengarten *et al.*, pp. 2450–2452. The sea urchin-shaped fullerene hexakis-adducts can be efficiently functionalized under click reaction conditions. The authors thank Jean-Claude Wollès for the background picture (see: http://subaqua.web.cern.ch/subaqua/bio/photos.html). Image reproduced by permission of J. Iehl, R. Pereira de Freitas, B. Delavaux-Nicot and J.-F. Nierengarten from *Chem. Commun.*, 2008, 2450.



Inside cover

See Benjamin P. Hay and Vyacheslav S. Bryantsev, pp. 2417–2428. Absence of covalent character in the anion–π interaction is visualized by graphical analysis of the wavefunction. Image reproduced by permission of Benjamin P. Hay and Vyacheslav S. Bryantsev from *Chem. Commun.*, 2008, 2417.

CHEMICAL BIOLOGY

B41

Drawing together research highlights and news from all RSC publications, *Chemical Biology* provides a 'snapshot' of the latest developments in chemical biology, showcasing newsworthy articles and significant scientific advances.

Chemical Biology

June 2008/Volume 3/Issue 6

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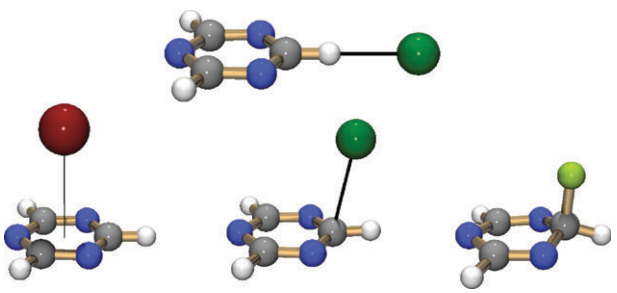
FEATURE ARTICLE

2417

Anion–arene adducts: C–H hydrogen bonding, anion–π interaction, and carbon bonding motifs

Benjamin P. Hay* and Vyacheslav S. Bryantsev

Experimental and theoretical evidence establishes the existence of four distinct binding modes for complexes of anions with charge-neutral arenes.



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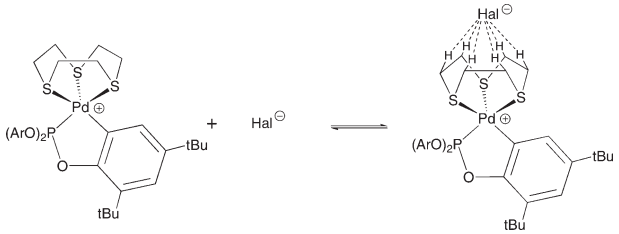

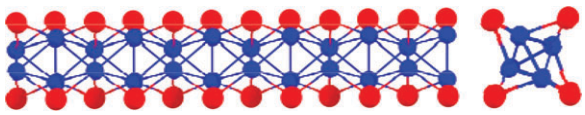

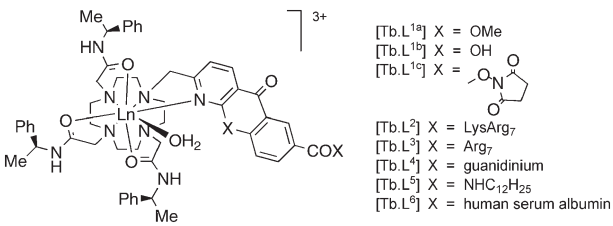

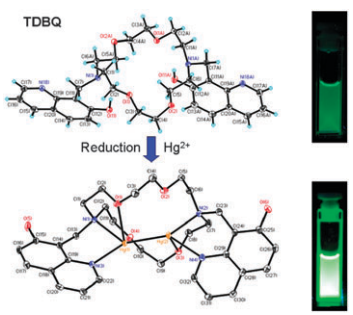

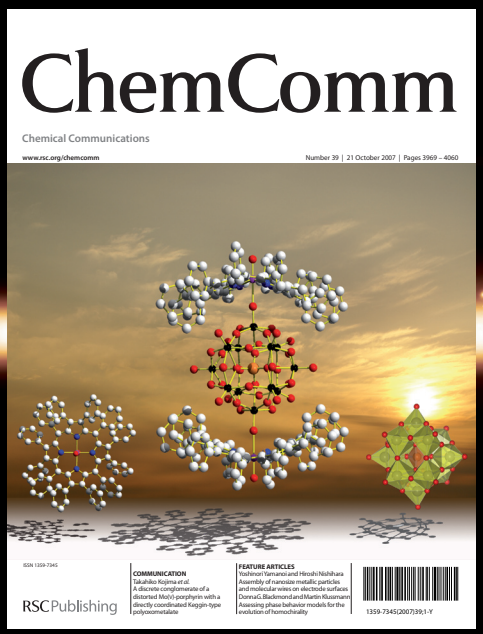

Make an impact

Introducing Professor Mike Doyle

Associate Editor for Organic Chemistry

Michael P. (Mike) Doyle is Professor and Chair of the Department of Chemistry and Biochemistry at the University of Maryland, College Park. He has been the recipient of numerous awards, including the George C. Pimentel Award for Chemical Education in 2002 and the Arthur C. Cope Scholar Award in 2006. He has written or coauthored ten books, including *Basic Organic Stereochemistry*, 20 book chapters, and he is the co-author of more than 270 journal publications. The inventor of chiral dirhodium carboxamidate catalysts known as "Doyle catalysts," his research is focused on applications with metal carbene transformations, Lewis acid catalyzed reactions, and selective catalytic oxidations.

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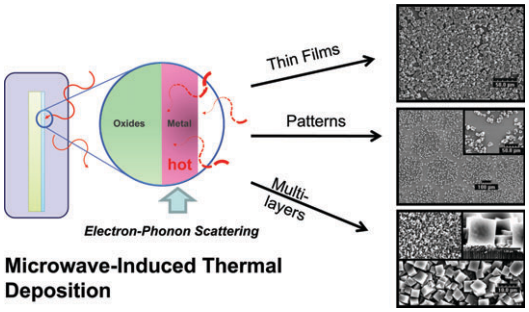

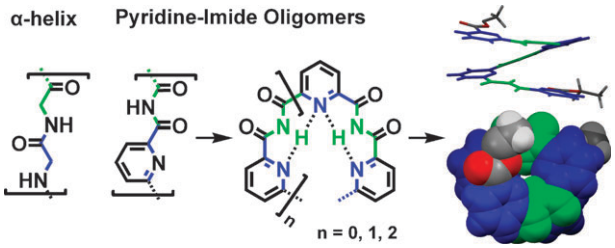

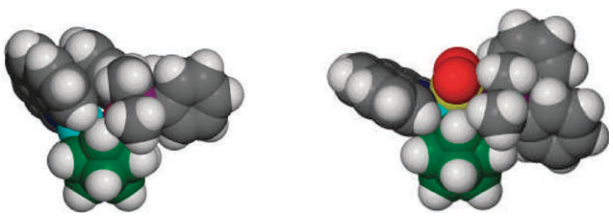

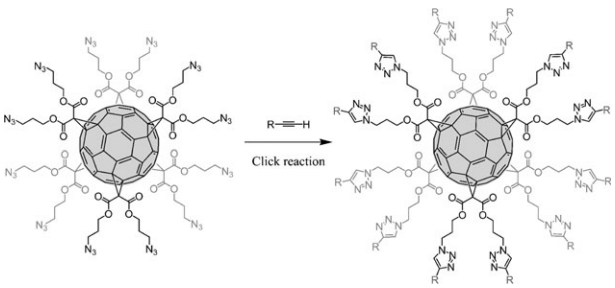

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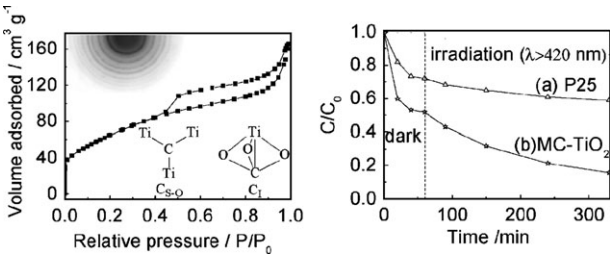

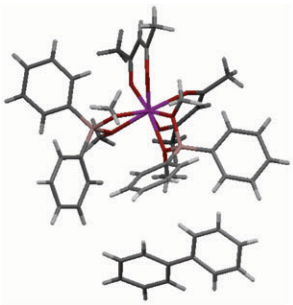

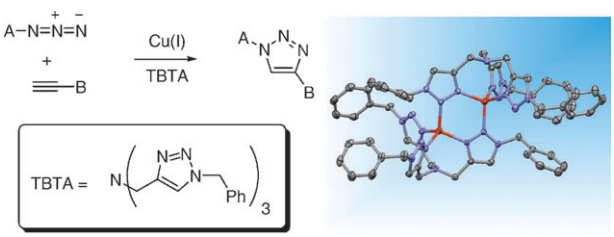

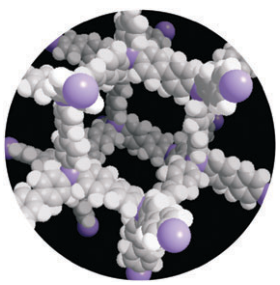

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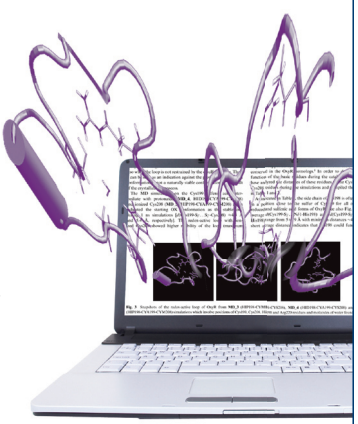

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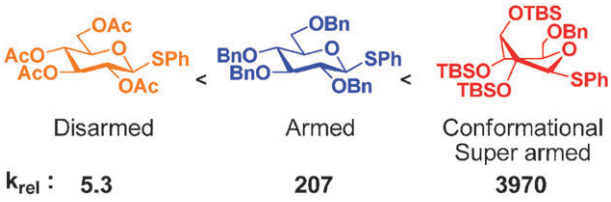
2465

Conformationally armed glycosyl donors: reactivity quantification, new donors and one pot reactions

Christian Marcus Pedersen, Lavinia G. Marinescu and Mikael Bols*

The relative reactivity of conformationally armed thioglycosides is quantified.



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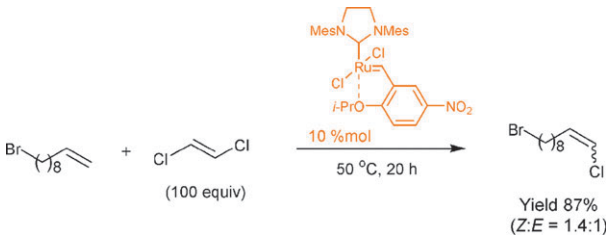
Olefin cross-metathesis with vinyl halides

Volodymyr Sashuk, Cezary Samojłowicz, Anna Szadkowska and Karol Grela*

The reaction of various terminal olefins with (*E*)-1,2-dichloroethylene promoted by 5–15 mol% of phosphine-free Ru catalysts led to formation of the expected products in good to moderate yields, showing that catalytic olefin cross-metathesis is a mild and selective method for the synthesis of chlorinated molecules.



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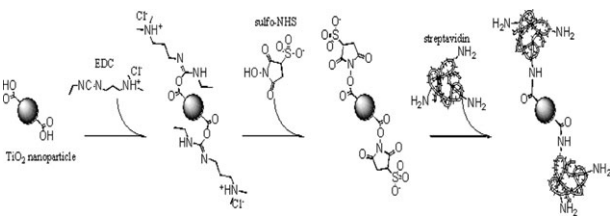
TiO_2 nanoparticles as a soft X-ray molecular probe

Jared M. Ashcroft, Weiwei Gu, Tierui Zhang, Steven M. Hughes, Keith B. Hartman, Cristina Hofmann, Antonios G. Kanaras, David A. Kilcoyne, Mark Le Gros, Yadong Yin, A. Paul Alivisatos and Carolyn A. Larabell*

The development of a TiO_2–streptavidin nanoconjugate as a new biological label for X-ray bio-imaging applications is reported.

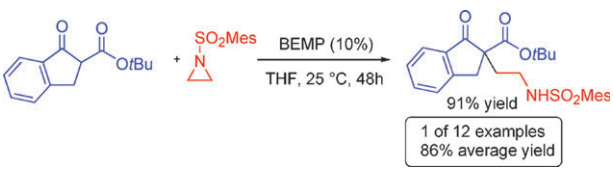


2474

Efficient base catalyzed alkylation reactions with aziridine electrophiles

Thomas A. Moss, Aurelie Alba, David Hepworth and Darren J. Dixon*

N-Mesitylene sulfonyl and *N*-tosyl aziridines have been identified as effective electrophiles in alkylation reactions of carbon acids catalyzed by the organic phosphorine base BEMP. Yields of up to 99% for a range of pro-nucleophiles under mild reaction conditions are reported.



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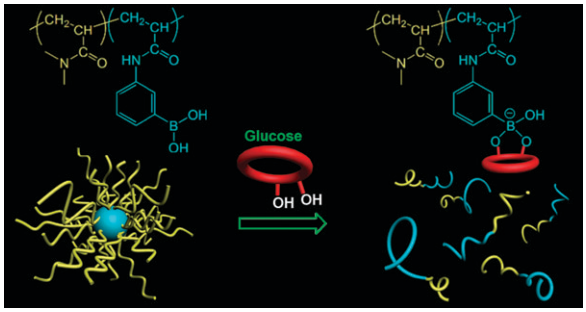

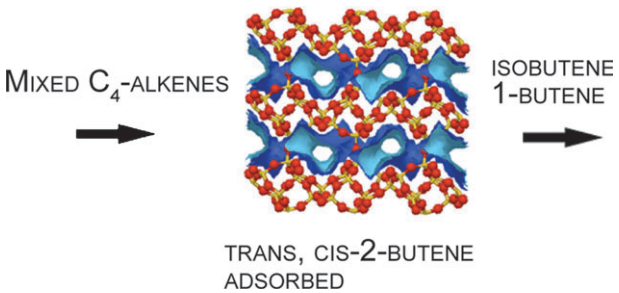

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Chemical Biology

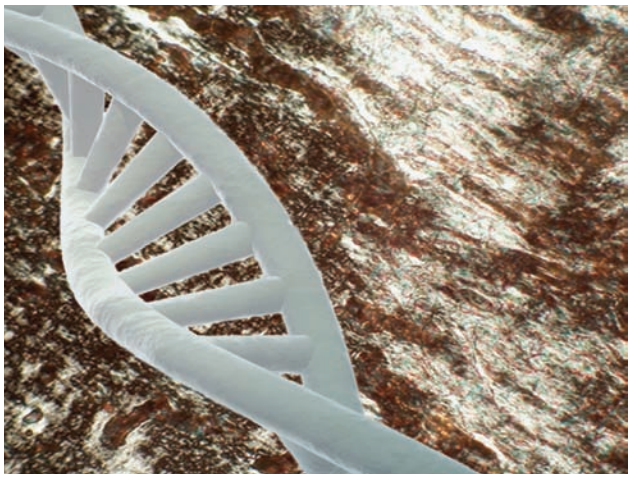
Potential phospholipid ordering in cell nuclei causes debate

Liquid crystals in all of us

European researchers have sparked debate by claiming that cell nuclei could contain liquid crystals. The hypothesis is supported by experiments revealing that DNA transcription is possible in such environments, says the team from the UK and Germany.

George Attard from the University of Southampton, UK, and colleagues have shown that DNA can be transcribed into RNA within a liquid crystalline phase formed by phospholipids. Moreover, they found that isolated cell nuclei exhibit an optical property known as birefringence that is characteristic of liquid crystals. The researchers say that together these results 'raise the possibility that lipids might form organised structures in the nucleus in vivo.'

Attard says his research is 'off the wall', and adds that mainstream researchers are reluctant to accept his views. Indeed, Roel van Driel, an expert in nuclear organisation from the University of Amsterdam, the Netherlands, is not convinced. He points out that Attard's group freeze-dried the studied nuclei, which will have caused major structural rearrangements. Therefore there is no evidence that living nuclei show birefringence, he says. Attard accepts this, but adds: 'We have x-ray data from non-freeze-dried nuclei which are consistent with long-range ordering.'



Birefringence suggests that phospholipids may form ordered structures inside the cell nucleus

Van Driel also says that for living nuclei to show birefringence, chromatin – a complex of DNA and proteins – would have to be ordered on the length scale of the nucleus, which it is not. Attard counters that chromatin could adopt any degree of structural ordering, or none at all, within a liquid crystalline phase, but that these phases would still cause birefringence.

Despite criticism, Attard says that it is 'likely' that nuclei are in a liquid crystalline state. Cell nuclei are rich in phospholipids and these molecules are known to self-organise into structures – for example membranes – he explains. Based on the intermolecular forces, 'you would be more surprised to find that nuclei are not liquid crystalline rather than the reverse,' says Attard.

Danièle Gibney

Reference

J Corsi *et al*, *Chem. Commun.*, 2008, 2307 (DOI: 10.1039/b801199k)

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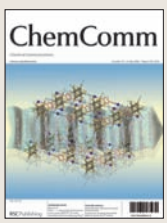

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Research highlights

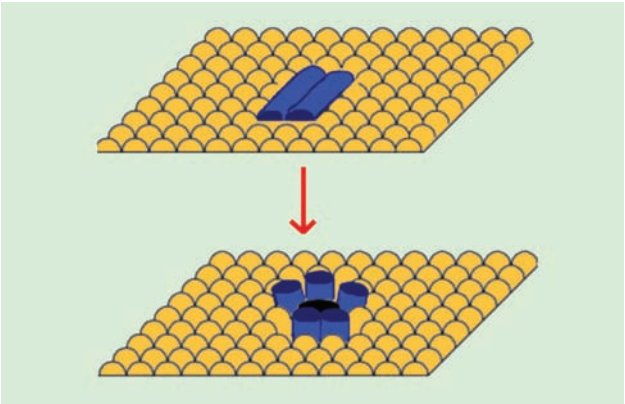
Break through study yields insights into viral mechanism

How does a virus bore a hole in a cell?

Chemists in the US studying how viruses enter cells say their results could help in the search for new antiviral medicines.

Stanford University chemists Richard Zare and Soonwoo Chah used cell and virus models to investigate an early stage in viral infection. Using lipid spheres called vesicles as cell mimics they studied the way the vesicles rupture after exposure to PEP1, a helix-shaped peptide that resembles a peptide found in the hepatitis C virus. Zare says that 'it is important to understand how viruses interact with and break up the cell membrane. Knowledge of the exact sequence and duration of these steps is crucial to developing possible strategies for combating disease.'

When a virus invades a cell in the body, it fuses with the cell membrane and releases its genetic material into the host cell, turning into a 'chemical factory' that produces more copies of the virus. It is known that there is an intermediate stage between the time a virus merges with the cell membrane and the time it delivers its genetic contents into the cell. 'During this period, the host cell's fate hangs in the balance,' Zare explains. Cell infection is often irreversible once a virus has penetrated the cell – so this stage 'may represent an opportunity for drug development,' suggests Zare.



Peptide PEP1 (blue) lies flat on a vesicle surface before rearranging to form a pore through the membrane

Zare and Chah investigated the intermediate stage more closely using surface plasmon resonance (SPR) microscopy to measure the lipids' optical properties. Since these properties are different for intact and ruptured vesicles, SPR allows the researchers to follow the rupture mechanism in real time. They found that, after introducing the peptide to the vesicles, the peptides first lie flat on the surface then switch to cross the membrane, forming pores. 'This attack causes the vesicles to transform into a lipid bilayer,' says Zare.

Richard Epand, a biochemist from McMaster University, Hamilton, Canada, is impressed. He says that although using a viral peptide and not the intact virus means there are some limitations, the work 'could contribute significantly to our understanding of viral fusion processes.'

Michael Spencelayh

Reference
S Chah and R N Zare, *Phys. Chem. Chem. Phys.*, 2008, DOI: 10.1039/b802632g

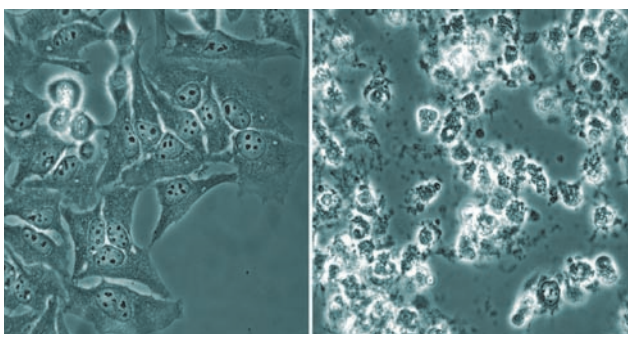
Nanostructures that puncture cell membranes prove selective

Peptides provide fatal blow for cancer cells

Peptide nanostructures that punch holes in cancer cells are 'the first step towards efficient nanochemotherapeutics,' say chemists in Canada. Normand Voyer and colleagues at the University of Laval in Quebec have designed a series of modified peptide nanostructures that can puncture cancer cell membranes, leading to the cells' death.

The team explains that in the past decade, cancer cell resistance to chemotherapeutic agents has led to increased cancer deaths. 'We believe that nanochemotherapeutics can overcome this problem due to the particular properties of nanometre-sized compounds,' says Voyer.

Basing their structures on a membrane-disrupting peptide they had made previously, the researchers engineered analogues that would be selective for cancer cells. The engineered peptides are inactive until they reach cancer cell surfaces where they convert into an active cell membrane disruption agent. Since the enzyme that activates the peptides is over-expressed in prostate cancer cells, normal cells do not activate the peptide to the same extent, leading to the peptides' selectivity.



When cancer cells (left) are treated with peptide nanostructures their cell membranes are destroyed (right)

Vincent Rotello, an expert in the supramolecular chemistry of biological and materials systems at the University of Massachusetts, Amherst, US, is enthusiastic about the findings. 'While enzymatic activation has been used before for therapeutics,' he says, 'this peptide-based scaffold has great promise due to the modular nature of its construction.' This is because the amino acid building blocks used to assemble the peptides can be readily varied, which provides 'incredible control over the structure and dynamics of the eventual therapeutics,' Rotello adds.

Voyer explains that the work 'illustrates chemists' abilities to design novel nanometre-sized molecular architectures from scratch to address highly challenging problems.' Future efforts will be geared towards 'determining the mechanism of action of this new class of antitumour agents,' he adds.

Kathleen Too

Reference
P L Boudreault *et al*, *Chem. Commun.*, 2008, 2118 (DOI: 10.1039/b800528a)

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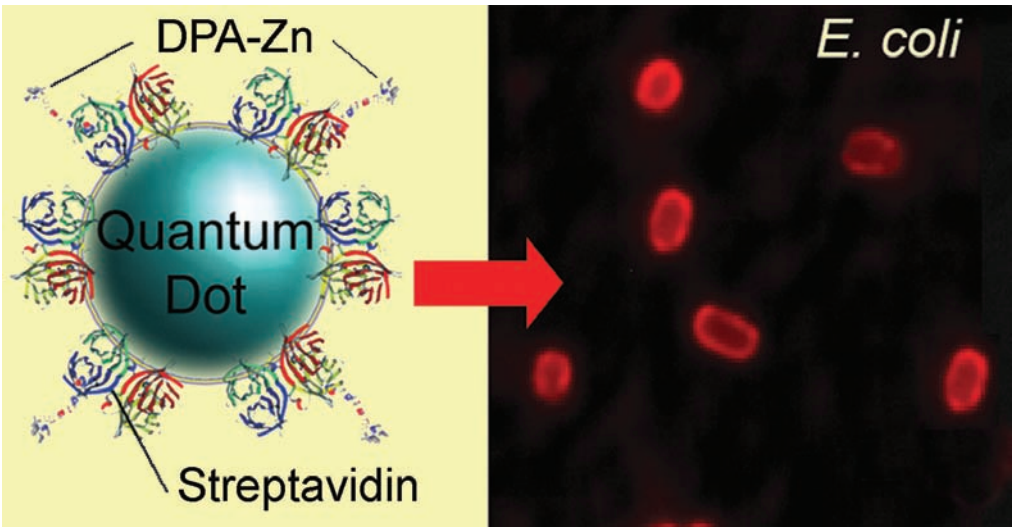
Nanoparticles target bacteria to illuminate infection in vivo

Probes spot the difference



Zinc(II) dipicolylamine coated quantum dots (left) are a selective stain for some bacteria such as a rough strain of *Escherichia coli* (right)

Fluorescent probes are shedding light on bacterial infection. Bradley Smith from the University of Notre Dame, US, and colleagues have made fluorescent probes that can distinguish between different mutants of the same bacterial species and can be used to observe the bacteria in vivo.

The team made the probes by attaching the bacteria-targeting ligand zinc(II) dipicolylamine (Zn-DPA) to a fluorescent nanoparticle called a quantum dot. Zn-DPA targets bacterial cells because it has a strong affinity for the phospholipids in their outer cell membranes. However, when attached to a relatively large quantum dot, it appears the ligand is unable to reach the phospholipids in some bacteria, leading to selective binding.

Smith's team showed that Zn-DPA–quantum dots can stain a rough strain of *Escherichia coli* intensely, but not smooth *E. coli* strains or Gram-positive bacteria – a group of bacteria that can be stained by crystal violet dye. They suggest this is because Gram-positive bacteria have thick cell walls with pores too small to allow the quantum dots to pass through. Similarly, the smooth *E. coli* strains are surrounded by a polysaccharide layer which prevents the Zn-DPA–quantum dots reaching the phospholipids in the membrane beneath.

The team says it should be possible to exploit the probes' selectivity in highly sensitive multicoloured staining schemes to identify bacterial species and mutant strains rapidly in contaminated samples.

The group also tested the feasibility of using the probes for in vivo imaging of bacterial infection in mice. They found the bacterial fluorescent signal to be 10-fold greater than the background autofluorescence. But, admit the scientists, it is only 1.5 times greater than when bacteria are labelled with Zn-DPA attached to an organic fluorophore rather than a quantum dot. The observed fluorescence is limited because maximum tissue penetration is achieved when a fluorophore's excitation and emission wavelengths are both between 650 and 900nm – these quantum dots emit at 800nm but excite below 500nm.

Smith plans to develop the optical imaging method so that it can be used to evaluate antibiotic therapy in animals. 'The challenge is to make very bright and highly selective near-infrared imaging probes that also exhibit favourable pharmacokinetics and low toxicity,' says Smith.

Freya Mearns

Reference
W M Leevy *et al*, *Chem. Commun.*, 2008, 2331 (DOI: 10.1039/b803590c)

News in brief

This month in *Chemical Science*

Swellable gels fix bad backs
This month's Instant insight sees Brian Saunders and Tony Freemont discuss a new approach for treating back pain using injectable microgel implants.

Carbon nanotubes wear coats to deliver drugs
Polymer coated carbon nanotubes could find a new use in drug delivery, claim Korean scientists.

Fungi wake up to new natural products
Re-awakening 'silent' metabolic pathways in fungi has revealed a new range of natural products to US scientists.

How mouldy is your house?
Concerns about mould growing in houses are on the increase, claim mycologists in France.

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

This month in *Chemical Technology*

People power
In this month's interview, Duncan Graham explains just how important people are for the future of science.

On-chip suction stops worm wiggling
US scientists have developed a microfluidic method for immobilising worms, allowing them to be used in high throughput studies of disease.

Making sense of DNAzymes
In this month's Instant insight, Itamar Willner and colleagues discuss the applications of DNA-based enzymes.

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Noise control as competitive RNA interferes with gene expression

Knowledge out of chaos

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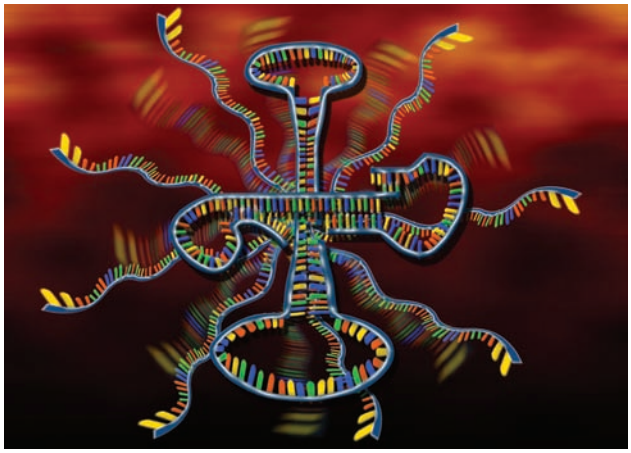
Scientists have upset gene expression to study its randomness and discover how the cell reduces this variability.

An organism's genetic code does not simply equate to a certain outcome. Noise in gene expression can result in physical differences in genetically identical populations. Synthetic biologists who want to construct and study gene networks need to understand this noise for their own experiments to be valid, and new work from America explores just that.

In gene expression, genes are read and translated into protein products using small RNA molecules overseen by a large complex called a ribosome. Because there are so many of these small RNAs in a cell, variations in their relative levels can affect protein production. Andrew Ellington, at the University of Texas at Austin, US, and colleagues decided to investigate this phenomenon further.



Variations in the amounts of different RNA molecules in cells can affect protein production

The group made small ribosome competing RNA (rcRNA) molecules that were designed to compete with cell RNA for the ribosome and affect gene expression. Their aim was to use the rcRNAs as a tool in gene expression noise studies to introduce noise controllably using different amounts and types of rcRNA.

When the researchers added the rcRNAs to *Escherichia coli* cells they found that their rcRNAs do generate noise, causing fluctuations in the production of a fluorescent protein by the bacteria. The team used its rcRNA approach to show that DNA sections called operons are highly effective at reducing noise as they eliminate the relative RNA fluctuations between genes.

Jim Collins, co-director of the Centre for BioDynamics at Boston University, US, is very impressed with the new tool. He describes the work as 'an excellent example of how synthetic biology techniques can be used to gain insight into fundamental biological principles.' *Laura Howes*

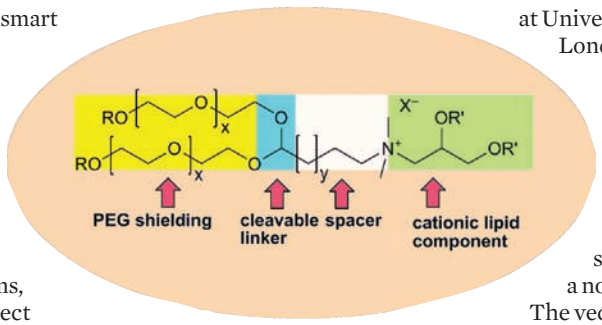
Reference
J J Tabor *et al, Mol. BioSyst.*, 2008, DOI: 10.1039/b801245h

Polymeric lipids ensure DNA vectors meet their targets

Plastic coats wrap up gene delivery

UK chemists have used smart polymers to deliver DNA into cells. Based on pH-sensitive poly(ethylene glycol) (PEG) lipids, the polymers can be used as a removable protective coat for gene delivery systems.

Gene delivery systems, or vectors, have to protect their DNA cargo from enzymes, cross cell membranes and yet still release a therapeutic dose of intact DNA inside the target cell. Viral vectors can deliver genes into cells, however, they can provoke an immune response which limits their therapeutic use. One of the problems often associated with non-viral gene delivery systems is that 'the efficiency is too low and that the vectors are not sufficiently stable, particularly in vivo,' says Helen Hailes a reader in chemical biology at University College London, UK.



The pH-sensitive coating shields the vector until the PEG region (yellow) is removed by hydrolysis at the linker (blue)

To overcome this problem, Hailes and her colleagues have developed acid-cleavable PEG lipids to shield the DNA in a non-viral vector. The vector consists of a targeting peptide and cargo DNA with the PEG lipids as covering. This coating stabilises the particles, protects the DNA from nuclease enzymes, provides water solubility and facilitates transport through the cell membrane. Once the vector is inside the cell, the lower pH triggers hydrolysis and shedding of the coating, releasing the cargo DNA. As different PEG lipid structures are hydrolysed at different pH, this offers a method of controlling the pH dependence of DNA release, suggests Hailes.

The team demonstrated the new system's effectiveness by using it to transfer DNA coding a bioluminescent enzyme into different cell types, and then measuring the enzyme's activity. 'The PEG lipids seem to provide cell specific properties,' comments Antonio Villaverde, an expert in non-viral gene therapy at the Autonomous University of Barcelona, Spain. 'This could be an interesting element to favour cell targeting in delivering such constructs.'

Looking to the future, Hailes says that the team hopes to 'design different tunable features into the lipids for a range of delivery applications.' She adds that this could include using the system to deliver small interfering RNA – short strands of RNA that can be used to interfere with gene expression. *Russell Johnson*

Reference
J B Wong *et al, Mol. BioSyst.*, 2008, DOI: 10.1039/b719782a

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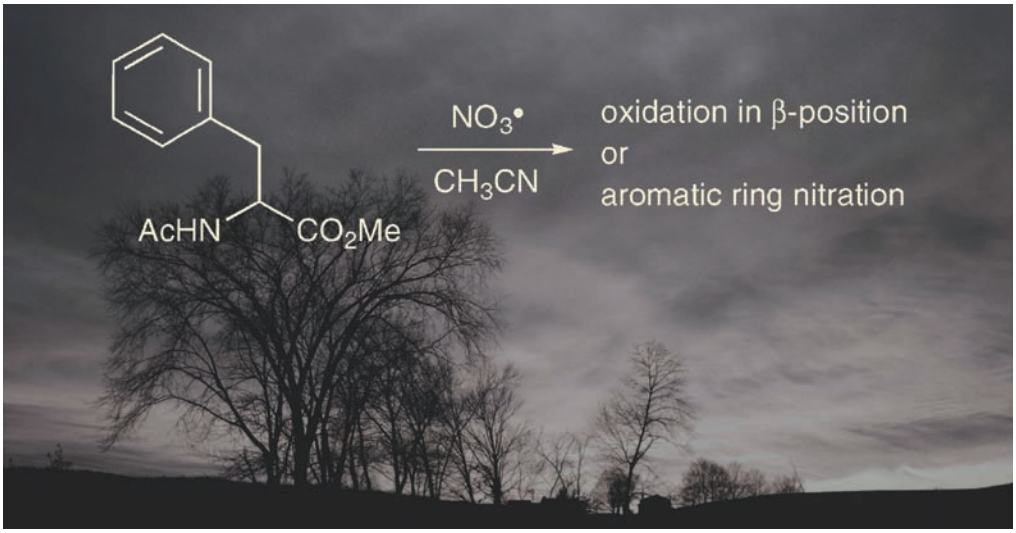
Reaction between atmospheric species could explain their role in airway disease

Radical proposal for nitrate link to asthma



Australian researchers have discovered that nitrate radicals irreversibly damage amino acids. This raises the possibility that the radicals play a role in respiratory disease, they claim.

Nitrogen dioxide and ozone have been linked to airway diseases such as asthma, although their exact role is not clear. In the atmosphere, these gases can react to form extremely reactive nitrate radicals, leading Uta Wille and Duanne Sigmund at the University of Melbourne, Victoria, to question whether there is a link between these radicals and respiratory illness.

As part of their research, the duo has found that nitrate radicals irreversibly damage aromatic amino acids, forming compounds including β-nitrate esters, β-carbonyl and aromatic nitro-compounds. 'The reaction forms oxidised products,' explains Wille, 'some of which have been found in polluted air and are associated with immune stimulation.' By analysing these products the researchers proposed a mechanism for the oxidation and nitration reactions.

Nitrate radicals will react with aromatic amino acids. The radicals form in the atmosphere and build up overnight

'The next step is to study the radicals' role in damage to proteins, peptides and carbohydrates – molecules that line the cells of the respiratory tract and so are in direct contact with the atmosphere,' says Wille. Ultimately the team wants to check whether the radicals can migrate through the cell membrane, 'where they could cause damage inside the cell,' Wille adds.

Malcolm Forbes, an expert in free radical chemistry at the University of North Carolina at Chapel Hill, US, welcomes the research, and says: 'The results will have a significant impact on research into oxidative damage to proteins, particularly in regard to respiratory illness. The challenge now is to correlate these results with in vivo studies to assess the real impact to society.'

Russell Johnson

Reference
D C E Sigmund and U Wille, *Chem. Commun.*, 2008, 2121 (DOI: 10.1039/b803456g)

In the current issue of Research Articles...

Fast-lysis cell traps for chemical cytometry
Paul J Marc *et al*, *Lab Chip*, 2008, **8**, 710 (DOI: 10.1039/b719301g)

Intracellular applications of analytical SERS spectroscopy and multispectral imaging
Igor Chourpa *et al*, *Chem. Soc. Rev.*, 2008, **37**, 993 (DOI: 10.1039/b714732p)

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Highly efficient quenching of excimer fluorescence by perylene diimide in DNA
Nicolas Bouquin *et al*, *Chem. Commun.*, 2008, 1974 (DOI: 10.1039/b802193g)

Measuring the simultaneous effects of hypoxia and deformation on ATP release from erythrocytes
Andrea Faris and Dana M Spence, *Analyst*, 2008, **133**, 678 (DOI: 10.1039/b719990b)

The importance of surfaces in single-molecule bioscience
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Quantitative SERRS for DNA sequence analysis
Duncan Graham and Karen Faulds, *Chem. Soc. Rev.*, 2008, **37**, 1042 (DOI: 10.1039/b707941a)

Porphyrin–bile acid conjugates: from saccharide recognition in the solution to the selective cancer cell fluorescence detection
Jarmila Králová *et al*, *Org. Biomol. Chem.*, 2008, **6**, 1548 (DOI: 10.1039/b717528k)

Read more at www.rsc.org/chembiology

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Interview

The protein detective

Kathryn Lilley tells Michael Smith how curry and beer could be the downfall of biomarkers

Kathryn Lilley

Kathryn Lilley is director of the Cambridge Centre for Proteomics, located in the Systems Biology Centre, Cambridge, UK. Her group is involved with several important collaborative proteomics projects, in particular involving the model organisms *Arabidopsis* and *Drosophila*.

What inspired you to become a scientist?
My grandfather was an amateur gardener and my mother picked up his love of plants. I think it was her love and enthusiasm for nature and plants that made me very interested in biology.

I always had a battle as to whether to become a musician, as that's my other great passion. I suppose I realised that you could be a professional scientist and an amateur musician but it would be very difficult to live your life the other way around!

Why did you choose to specialise in proteomics?
After my PhD, which involved a lot of protein sequencing, an opportunity came up to run a protein sequencing facility at the University of Leicester.

About that time, there were some major papers published on mass spectrometry of proteins, particularly from Mathias Mann's group at the European Molecular Biology Laboratory in Heidelberg. Although we purchased our own mass spectrometers in Leicester to support peptide and DNA synthesis, they were not the right type to carry out these new methods of protein identification. I was frustrated as I really wanted to carry out these wonderful new proteomics technologies.

Next, the opportunity came to move to Cambridge to set up a proteomics laboratory with funding from the BBSRC and with it, the idea that I could do all this wonderful scalable protein identification. After running a core facility for many years in Leicester, in Cambridge I got the opportunity to get back in touch with how to answer interesting biological questions.

What biological questions are you interested in?
In the early days of the facility, most projects centred around knowing the differences in protein abundances between mutant and wild types or treated and untreated states. If we can see which proteins are changing in their expression or post-translational state, it gives us an insight into what's going on inside a cell.

I got fed up with identifying the same sets of proteins and wanted to probe into the lower abundance fraction of proteins. I also wanted to get information on where they resided in a cell and who with!

What are you working on at the moment?
Organelle proteomics. The first stage of many proteomics experiments is to take the cells and mash them up. Usually you add a healthy dose of detergent. This means you lose all the spatial information about your proteins within a cell. I think this is a very important thing to study because where proteins are and what they associate with is going to give us a huge amount of information that we can't get from just looking at their abundance.

We are starting to look at components from signalling pathways – how they move around the cell upon signalling events and how this may change under different situations, including development and differentiation. We've spent a few years trying to fine tune the methodologies. We're not there yet but we've gone quite some way to be able to produce technology that is robust both in terms of identifying proteins associated with certain organelles and mapping onto that the position of protein complexes.

What do you think about biomarkers as an ultimate aim of proteomics?
Proteomics is a very attractive way of finding biomarkers but it is fraught with issues.

The main issue is the dynamic range of protein concentrations within plasma, which currently no techniques can cover.

Secondly, if you do find biomarkers in a certain set of proteins that are always up-regulated in someone who is suffering from a cold, how discriminatory is that? I can't see that there is going to be any one biomarker that will tell you which disease is present.

Finally, blood plasma is really a mirror of your general state of health and what you've been up to in the last day or two. There is a lot of person-in-person variability depending on your health and whether you've had a curry and several beers the night before! In a population set, I think it's going to be very difficult to find an abundance change that is disease-specific.

What advice would you give to someone considering a career in science?
Looking back on my own career, I became too specialised too soon. What I lost touch with very quickly, and I wish I hadn't, was maths. More and more in biology, we are making quantitative measurements. The way in which we deal with those measurements is controlled by statistical and mathematical tools. We need that know-how to be able to design our experiments properly and to see whether we believe the data that's coming out. My advice is to avoid losing touch with other scientific disciplines. Try and stay broadly focused.

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Instant insight

Communicating with nature

Bacteria have invented a potentially global language – quorum sensing. Kim Janda of the Scripps Research Institute in La Jolla, US, translates

NATIONAL SCIENCE FOUNDATION

Over the course of history, humans have developed countless ways to communicate with each other, and over 6800 languages have been catalogued. Despite these advances, our verbal relations with other species remain somewhat limited to gestures and shouts, as can be seen in the case of dogs and their owners. On a microscopic level, bacteria can communicate with one another through a different language, one based on small molecules, using a mechanism known as quorum sensing (QS). In contrast to humans' limited verbal communication capacities, QS allows communication and interaction with other bacterial species, and even other organisms such as mammals.

Bacterial language relies on the exchange of small chemical signals, called autoinducers. Through this exchange, bacteria monitor their density and regulate gene expression in a population-dependent manner. This allows them to coordinate their behavior and function, equipping the bacterial communities for competition or cooperation with multicellular organisms. A classic example is the symbiosis between the Hawaiian bobtail squid *Euprymna scolopes* and the luminescent bacterium *Vibrio fischeri*. In this relationship, the bacteria provide the squid with luminescence, allowing it to blend in with the moonlight while feeding, and so avoid casting shadows on the sea floor which would alert both predators and prey. At the same time, the bacteria also benefit, as they receive nutrients and safety.

QS has traditionally been referred to as a communication mechanism between bacteria within one species. However, research is emerging that implicates a role for QS in interspecies communication and competition, and such systems have been proposed to exist in a wide variety of bacteria. Particularly relevant to interspecies communication is the autoinducer 2 (AI-2)-based QS system, which has been suggested to function in over 50 bacterial species. Recently, it was shown that *Actinomyces naeslundii* and *Streptococcus oralis*, two bacteria responsible for oral plaque formation, require AI-2 production to initiate plaque development.

The Hawaiian bobtail squid has a symbiotic relationship with a luminescent bacterium

But communication amongst bacterial species is not always so cooperative; certain autoinducers and their by-products have been shown to have cytotoxic effects on other bacteria. *Pseudomonas aeruginosa* is especially adept at this intercellular competition, in that at least two autoinducer-derived molecules exhibit detrimental effects towards other bacteria, most notably *Staphylococcus aureus*. This activity may give *P. aeruginosa* a competitive advantage over *S. aureus* in the lungs of cystic fibrosis patients, a clinical setting plagued by infections due to these two pathogens.

In addition to helping bacteria organise their behaviour and functions, recent research suggests QS is a means for bacteria to interact with other organisms. Similar to bacterial interspecies relations, QS systems may mediate this interkingdom signalling either through host cell recognition of bacterial signals or through the unregulated action of an autoinducer on the host cell. Several studies have detailed the effects of AHL (*N*-acylhomoserine lactone)-based signalling molecules on human cells – the responses ranging from immuno-activation to cell death.

A potential communication language between humans and *Escherichia coli* has also been described. *E. coli* responds to two human-derived small molecule signals, adrenaline and noradrenaline, to regulate virulence expression. For this same purpose, *E. coli* also employs a small molecule of its own production, termed AI-3. Based on the role of *E. coli* in the gastrointestinal tract, and the overlap between bacterial recognition of AI-3 and adrenaline, AI-3 has been suggested to play a role in maintaining intestinal homeostasis.

Because QS can mediate so many relationships, it may represent a global language that spans every kingdom of life. Human interpretation may impart a deeper knowledge of bacterial lifestyles and provide the opportunity for an appropriate response, at least one of which would be developing pharmacological interventions for bacterial infection.

Read more in the tutorial review 'Interspecies and interkingdom communication mediated by bacterial quorum sensing' in issue 7, 2008 of Chemical Society Reviews.

Reference
C A Lowery, T J Dickerson, and K D Janda, *Chem. Soc. Rev.*, 2008, DOI: 10.1039/b702781h

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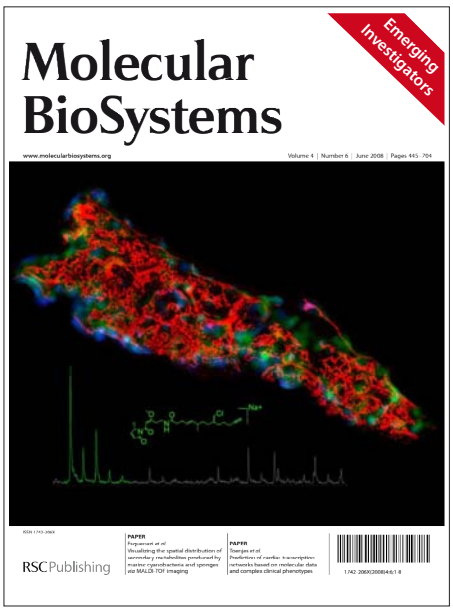
Essential elements

Emerging Investigators

Highlighting the brightest new researchers in the field, issue 6 of *Molecular BioSystems* (*MBS*) is not to be missed. The 20 full research papers, seven communications and two reviews are written by outstanding young scientists at the chemical- and systems-biology interfaces. The issue features novel methods to visualise and manipulate protein function in living cells, the development of chemical techniques to monitor specific protein post-translational modifications, new insights into metabolomics and much, much more.



All the contributors were personally recommended by *MBS* editorial or advisory board members as young scientists whose work has the potential to influence the future directions of these fields. All submissions were subjected to full peer review and the result is an issue showcasing work in some of the most fascinating and important areas of biology.

We intend to run future issues of this kind so watch this space. Finally, *MBS* extends a big thank-you to all the Emerging Investigators themselves for making this such an excellent collection of papers. We wish them every success in their future careers and – in the words of Tom Kodadek, the *MBS* editorial board chair – 'Clearly the future of this exciting area of biology is in good hands!'

Find out more at www.molecularbiosystems.org

And watch out for a related theme issue from *ChemSocRev* (*www.rsc.org/chemsocrev*) in July; issue 7 will be a thematic issue examining the interface of chemistry with biology.

Pioneers in Miniaturisation Prize

Leading the way in miniaturisation, *Lab on a Chip* has teamed up with Corning Incorporated to again host the Pioneers in Miniaturisation Prize. Spanning a variety of disciplines, this prize recognises outstanding achievements and significant contributions by a younger scientist to the understanding and advancement of micro- and nanoscale science.

As a leading-edge science and technology organisation, Corning Incorporated is keen to reward, recognise and encourage the development of miniaturisation in the chemical and biological sciences and promotes interdisciplinary research required for the most significant innovations in this area.

The recipient of the award will receive a US$5000 bursary to support their continued contribution to the field. A deadline for applications has been set for 31st August 2008. Following the final decision, which will be made by committee, a winner will be announced at the μTAS 2008 conference, in San Diego, CA, US.

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