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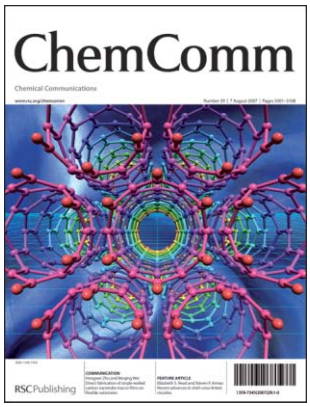
ISSN 1359-7345 CODEN CHCOFS (29) 3001–3108 (2007)



Cover

See Hongwei Zhu and Binqing Wei, page 3042. Single-walled carbon nanotube macro-films are directly fabricated on flexible substrates from metallic foils to polymer films utilizing chemical vapor deposition technique. Image reproduced by permission of Hongwei Zhu and Binqing Wei, from *Chem. Commun.*, 2007, 3042.

CHEMICAL BIOLOGY

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

August 2007/Volume 2/Issue 8

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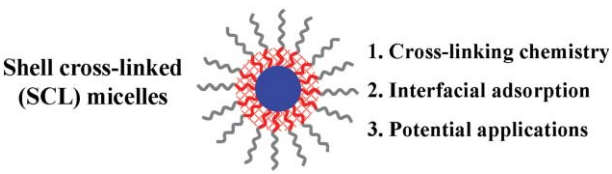
FEATURE ARTICLE

Recent advances in shell cross-linked micelles

Elizabeth S. Read and Steven P. Armes*

The field of shell cross-linked (SCL) micelles is briefly reviewed: important recent advances are emphasized, potential applications are discussed and current technical problems are highlighted; particular attention is paid to (i) development of new cross-linking chemistries and (ii) interfacial adsorption of SCL micelles.



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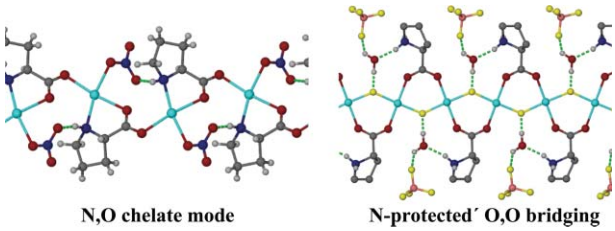

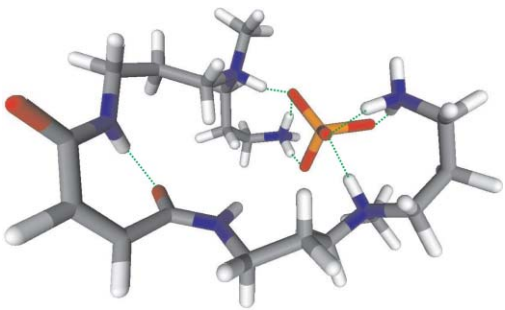

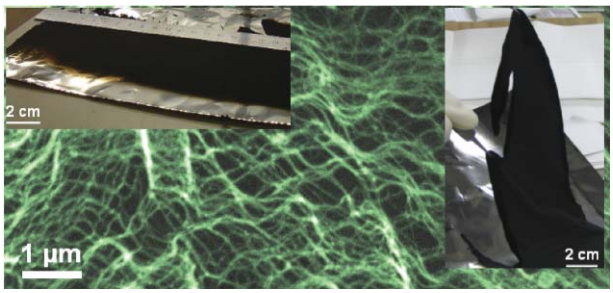

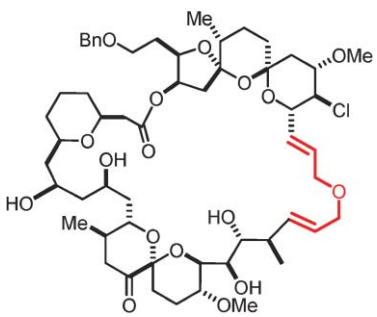

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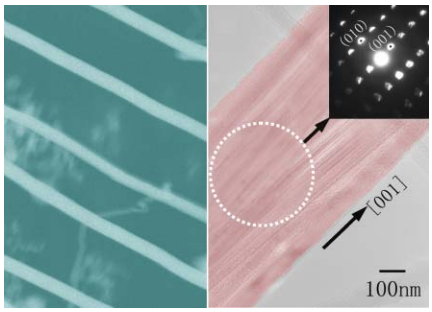

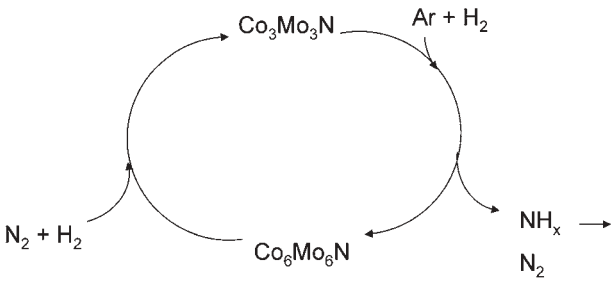

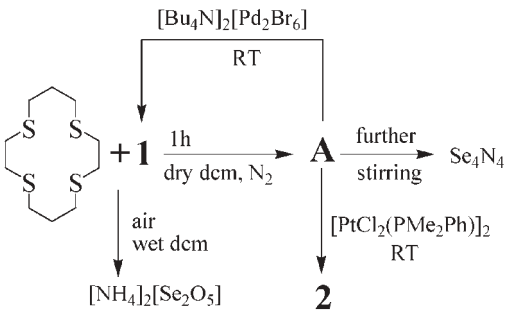

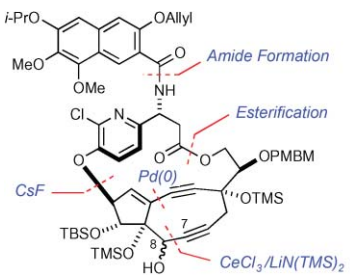

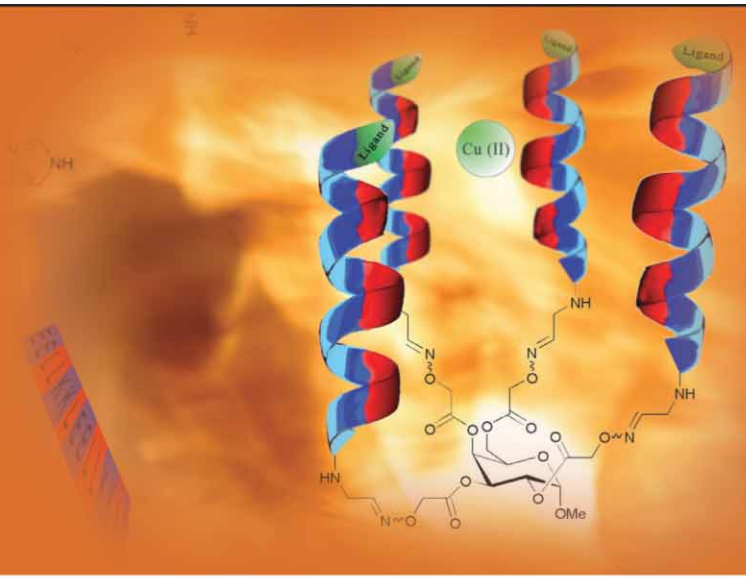

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Functional molecules in electronic circuits

Marcel Mayor, Switzerland

Emerging Area

Nanoparticles and cells: good companions and doomed partnerships

Dusica Maysinger, Canada

Articles

Coumarin-derived discodermolide analogues possessing equivalent antiproliferative activity as the natural product – a further simplification of the lactone region.

Simon Shaw & Amos B Smith III, USA

A strategy for the synthesis of 2,3-disubstituted indoles starting from *N*-(*o*-halophenyl)allenamides

Haruhiko Fuwa, Japan

LNA (locked nucleic acid) and analogs as triplex-forming oligonucleotides

Jesper Wengel, Denmark

Transport of chloride and carboxyfluorescein through phospholipid vesicle membranes by heptapeptide amphiphiles

George W. Gokel, USA

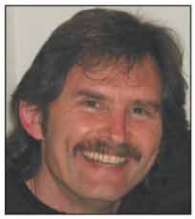
Chemical and chemoenzymatic synthesis of glycosyl-amino acids and glycopeptides related to Trypanosoma cruzi mucins

Rob Field, UK

A sequential enantioselective, organocatalytic route to chiral 1,2-oxazines and chiral pyridazines

Steven V Ley, UK

To discuss your submission, contact:



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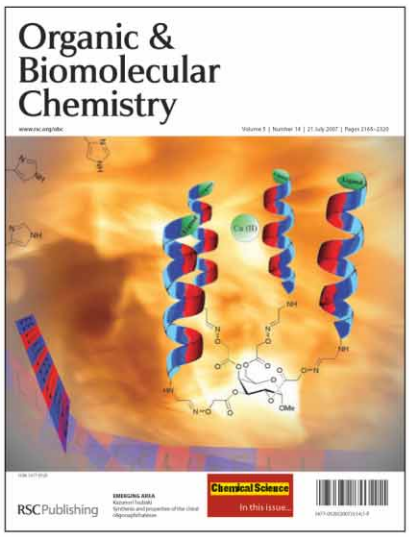

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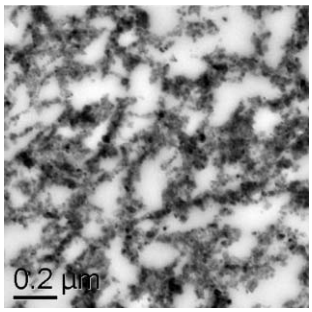
3060

Effective gel for gold nanoparticle formation, support and metal oxide templating

Xingdong Wang, Caroline E. Egan, Meifang Zhou, Kathryn Prince, David R. G. Mitchell and Rachel A. Caruso*

Gold nanoparticles supported on agarose gels were synthesised using three methods. The gold nanoparticles are well distributed in the organic support, which can then be used as a template for the formation of porous Au/TiO_2 nano-hybrids.

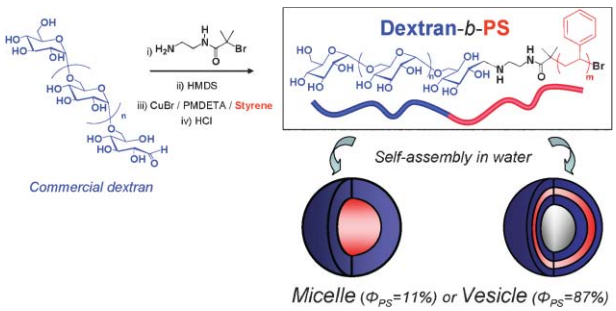


3063

Synthesis of ATRP-induced dextran-*b*-polystyrene diblock copolymers and preliminary investigation of their self-assembly in water

Clément Houga, Jean-François Le Meins, Redouane Borsali, Daniel Taton and Yves Gnanou

Dextran-*b*-polystyrene diblock copolymers forming spherical micelles or vesicles by self-assembly in water were obtained by chemical modification of the anomeric extremity of a commercial dextran followed by atom transfer radical polymerisation of styrene.



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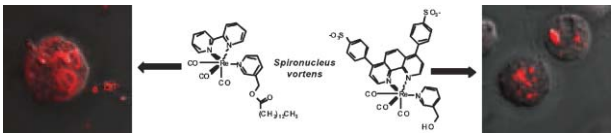
Rhenium *fac* tricarbonyl bisimine complexes: biologically useful fluorochromes for cell imaging applications

Angelo J. Amoroso, Michael P. Coogan,* Jennifer E. Dunne, Vanesa Fernández-Moreira, Jacob B. Hess, Anthony J. Hayes, David Lloyd, Coralie Millet, Simon J. A. Pope and Craig Williams

A series of lipophilic and hydrophilic *fac* tricarbonyl rhenium bisimine complexes are reported along with the first application of MLCT-fluorescent rhenium complexes in cell imaging with fluorescence microscopy.

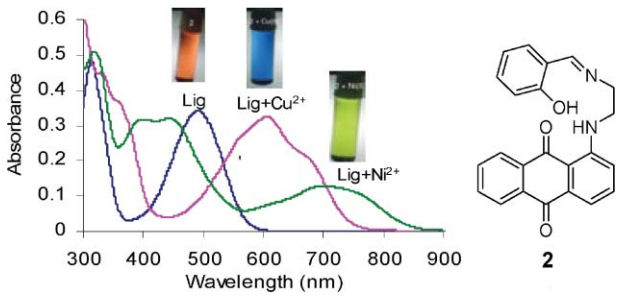


3069

Single molecular colorimetric probe for simultaneous estimation of Cu^{2+} and Ni^{2+}

Navneet Kaur and Subodh Kumar*

The different optical responses in chromogenic sensor **2** stimulated by addition of Cu^{2+} (red to blue) and Ni^{2+} (red to green) allow simultaneous estimation of Cu^{2+} and Ni^{2+}.



3071

Catalytic effect of a second H_3PO_2 in the mechanism of stabilisation of the unstable pyramidal tautomer of H_3PO_2 coordinated at $[Mo_3S_4M']$ clusters (M′ = Ni, Pd)

Andrés G. Algarra, Manuel G. Basallote,* María J. Fernández-Trujillo, Rita Hernández-Molina* and Vicent S. Safont

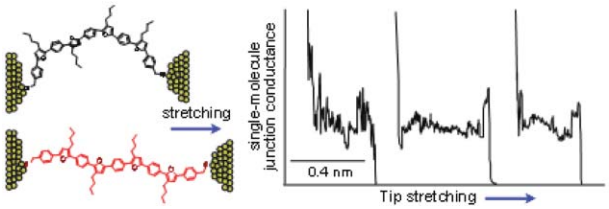
Kinetic and DFT studies indicate that the stabilization of a single pyramidal H_3PO_2 molecule at the M′ site of $[Mo_3S_4M']$ clusters requires the participation of two tetrahedral H_3PO_2 molecules, the second one assisting tautomerization.

3074

The effect of molecular conformation on single molecule conductance: measurements of π-conjugated oligoaryls by STM break junction

I-Wen Peter Chen, Ming-Dung Fu, Wei-Hsiang Tseng, Chun-hsien Chen,* Chih-Ming Chou and Tien-Yau Luh*

A strong correlation between the single-molecule conductance and the conformation of π-conjugated molecules is manifested by molecular break junction measurements of tailored oligoaryls with 6–18 conjugated double bonds.

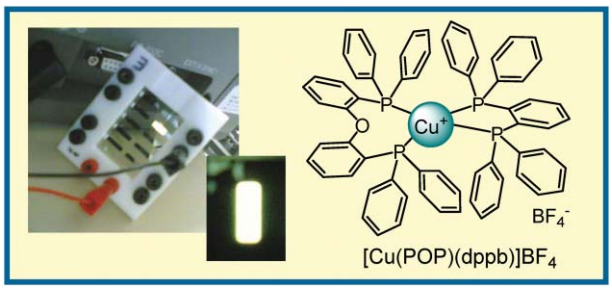


3077

Electrophosphorescent homo- and heteroleptic copper(I) complexes prepared from various bis-phosphine ligands

Omar Moudam, Adrien Kaeser, Béatrice Delavaux-Nicot, Carine Duhayon, Michel Holler, Gianluca Accorsi, Nicola Armaroli,* Isabelle Séguy, Jose Navarro, Pierre Destruel* and Jean-François Nierengarten*

Homo- and heteroleptic copper(I) complexes obtained from various chelating bis-phosphine ligands and $Cu(CH_3CN)_4BF_4$ have been used for the preparation of light emitting devices.

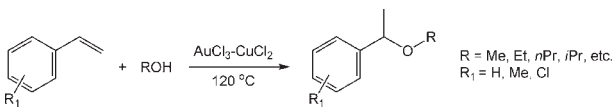


3080

Effective Au(III)–$CuCl_2$-catalyzed addition of alcohols to alkenes

Xin Zhang and Avelino Corma*

Effective addition of various alcohols to alkenes was realized by employing new gold(III)–$CuCl_2$ catalysts, in which copper(II) chloride greatly stabilizes the cationic gold(III) salt.



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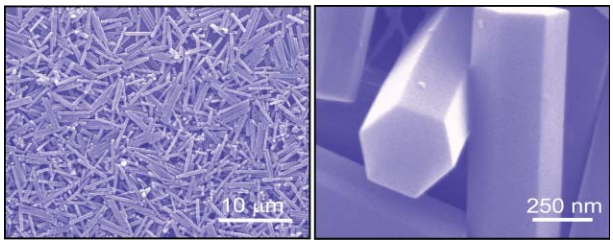
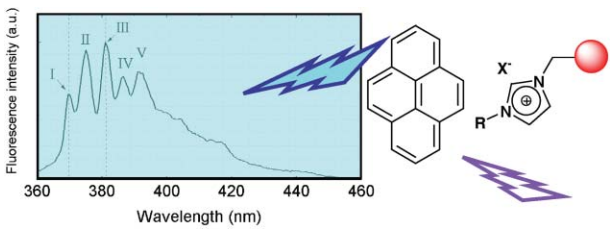


Facile solution synthesis of hexagonal Alq_3 nanorods and their field emission properties

Jin-Song Hu, Heng-Xing Ji, An-Min Cao, Zheng-Xi Huang, Yang Zhang, Li-Jun Wan,* An-Dong Xia, Da-Peng Yu, Xiang-Min Meng and Shuit-Tong Lee*

Hexagonal tris(8-hydroxyquinoline)aluminium (Alq_3) nanorods have been synthesized for the first time by a facile self-assembly growth route in solution. Their field-emission characteristics exhibit a very low turn-on field and a high field-enhancement factor.

3086

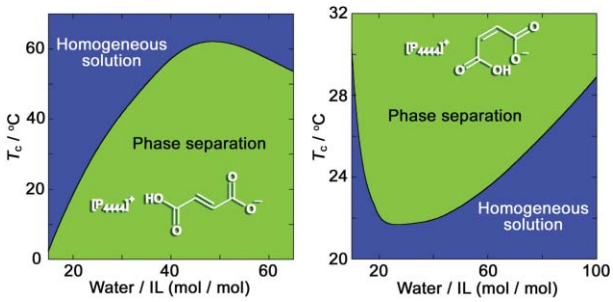


Polymer supported ionic liquid phases (SILPs) *versus* ionic liquids (ILs): How much do they look alike

M. Isabel Burguete, Francisco Galindo,* Eduardo García-Verdugo,* Naima Karbass and Santiago V. Luis*

The fluorescence of pyrene has been used for the first time to measure the static dielectric constant of a series of supported ionic liquids phases (SILPs) based on polymeric polystyrene networks.

3089

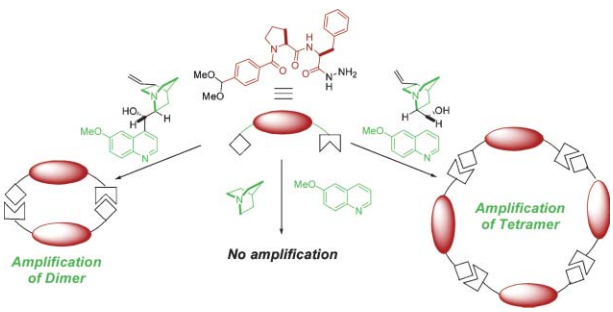


Miscibility and phase behavior of water–dicarboxylic acid type ionic liquid mixed systems

Yukinobu Fukaya, Kenta Sekikawa, Kenichi Murata, Nobuhumi Nakamura and Hiroyuki Ohno*

Tetra-*n*-butylphosphonium type ionic liquids with fumarate anion and maleate anion exhibit different physico-chemical properties and different solubility to water in their *cis* and *trans* conformations.

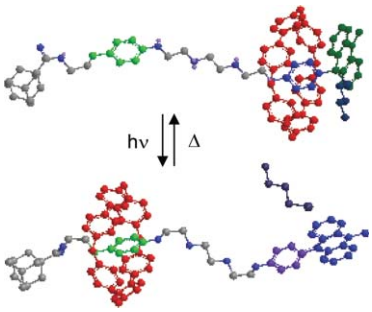
3092

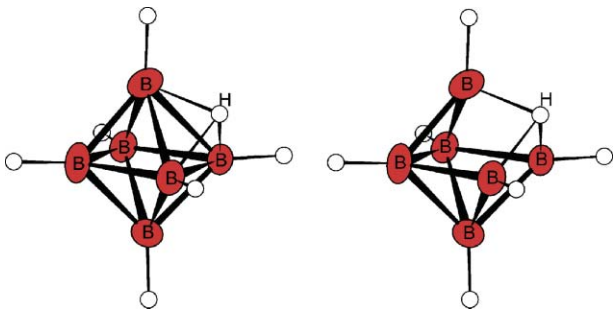


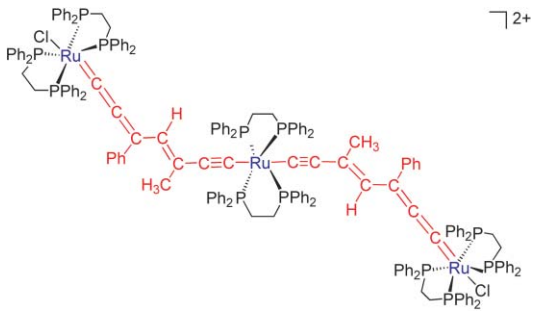
Molecular amplification of two different receptors using diastereomeric templates

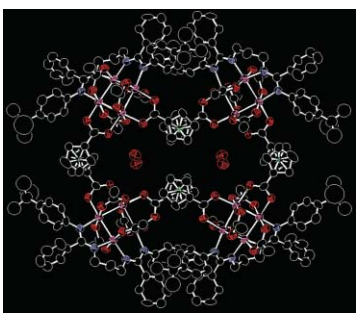
Fernando Bulos, Sarah L. Roberts, Ricardo L. E. Furlan* and Jeremy K. M. Sanders*

Two different macrocyclic members of a pseudo-peptide hydrazone dynamic combinatorial library were amplified using the diastereomeric templates quinine and quinidine.









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Constantinos J. Milios, Ross Inglis, Alina Vinslava, Alessandro Prescimone, Simon Parsons, Spyros P. Perlepes, George Christou and Euan K. Brechin

Turning up the spin, turning on single-molecule magnetism: from $S = 1$ to $S = 7$ in a $[Mn_8]$ cluster *via* ligand induced structural distortion

Haruhiko Fuwa and Makoto Sasaki

A new method for the generation of indole-2,3-quinodimethanes and 2-(*N*-alkoxycarbonylamino)-1,3-dienes. Intramolecular Heck/Diels–Alder cycloaddition cascade starting from acyclic α-phosphono enecarbamates

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Event description

Join us in Vancouver, British Columbia, Canada from Sunday, October 7 to Wednesday, October 10, 2007 for the International Symposium On Photochromism. This three-day event will highlight recent advances in the design, synthesis and performance of photoresponsive molecules, materials and devices. Through the combination of oral and poster presentations, participants will get a fresh look at photochromic organic and inorganic systems, and their applications from an international group of leading researchers.

Thematic sessions will include

- the development of novel photochromic platforms and new synthetic methods
- fundamental photochemistry of photochromic systems
- the integration of photochromic systems with solid-state platforms
- optical information storage and processing systems
- inorganic and hybrid photochromic systems
- photochromic systems for use in biological and medical applications.

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Frank van Veggel – University of Victoria
Wayne Wang – Carleton University
Vance Williams – Simon Fraser University
Mike Wolf – University of British Columbia
Yue Zhao – Université de Sherbrooke

For more information

More information on abstract submission will be posted on the web at www.isop07.org when it is available. If you have any questions, please contact Neil Branda or Vance Williams at info@isop07.org

Opening lecture

Barry Van Gemert – PPG Industries, Chemical Technical Center (USA)

Confirmed invited speakers

Sergey Aldoshin – Institute of Problem of Chemical Physics (Russia)
Yi Chen – Chinese Acadamy of Sciences (China)
Luisa De Cola – Universität Münster (Germany)
Stéphanie Delbaere – Université de Lille 2 (France)
Richard Evans – University of New South Wales (Australia)
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Chemical Biology

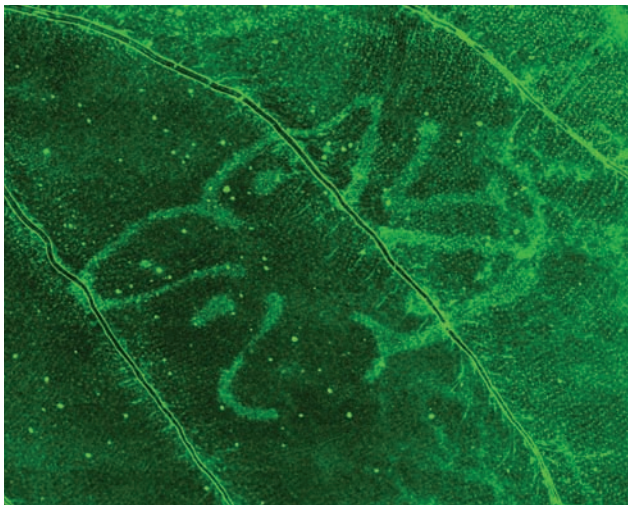
Manipulating the insect dress code as butterflies wear new genes

Genetic display for butterflies

Does the beauty of butterfly wings hold the key to understanding evolution?

Understanding how the genetic information of an organism (its genotype) relates to its physical characteristics (its phenotype) and how these characteristics evolved, is an ongoing challenge in biological science. According to Antónia Monteiro and Diane Ramos of the University at Buffalo in the US, Lepidoptera – the order of insects that includes butterflies and moths – are very useful for these sorts of studies as their diversity and two-dimensional nature make them very amenable to experimentation and mathematical modelling.

Recently, several new tools have allowed the US researchers and their peers to manipulate gene expression in Lepidoptera during the larval or pupal stages. These include a way to control gene expression using heat shock: introducing gene promoters and using lasers to activate them. The methods have enabled evolutionary biologists to test gene functions in wing pattern creation.



Genetic manipulation can reproduce a stencil image on a pupal wing

Wing pattern development in butterflies and moths can provide crucial insights, said Monteiro. 'The patterns are ultimately produced by activating different biochemical pigmentation pathways in different parts of the wing,' she explained. 'The challenge has been to identify the genes and developmental mechanisms that recruit these pigment pathways to their particular location. Several diffusible proteins and regulatory genes have been identified as possible candidates in playing that recruitment role but, until now, we lacked the tools to actually test their function.'

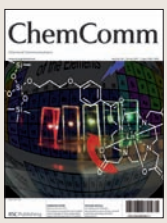
Further challenges lie ahead – in particular in the logistics of breeding the butterflies, said Monteiro. But she hopes the rich variety of Lepidopteran wing patterns will help reveal whether novel characteristics are created through adaptation of existing genetic interactions or built from scratch.

Edward Morgan

Reference

D M Ramos and A Monteiro, *Mol. BioSyst.*, 2007, **3**, 530 (DOI: 10.1039/b701965n)

In this issue



Research highlights

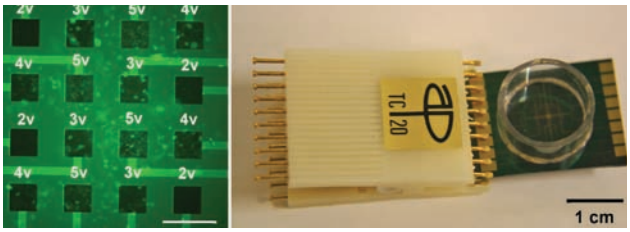
Microelectrode pulses control transfection into cell cultures

Delivering RNA with pinpoint precision

A microchip that allows controlled delivery of genetic material to cell cultures will be a major advance for the life sciences, say US bioengineers.

The chip, a microelectrode array developed by Tilak Jain and Jit Muthuswamy of the Arizona State University in Tempe, delivers electronic pulses to specific areas of a cell culture grown on top. The cell membranes in those areas become porous and the cells absorb any genetic material present in the surrounding medium.

Delivering genetic material to cells, known as transfection, is an important process in understanding gene function and drug discovery. The transfected material is designed to either overexpress or silence genes in target cells and the effect of the change in gene activity on the cells is then studied.



Cells exposed to higher voltage pulses from the microchip (right) show higher uptakes of genetic material and show up green (left)

Muthuswamy explained that a big advantage of his array is that multiple types of genetic material can be transfected sequentially and in different areas of the cell culture. In this way, combinations of overexpressed or silenced genes can be studied. Doing this in one culture is important: 'inter-culture variabilities are eliminated,' said Muthuswamy. 'Also, you can assess interactions between transfected cells and control cells.'

'This method is easier to use and quicker than previous methods,' Muthuswamy said. But, a drawback is that different RNAs or DNAs to be transfected would have to be sequentially applied to the cells and washed off again following transfection – a time-consuming process. To make the array more suitable for high-throughput studies, Muthuswamy plans to include a microfluidic system to deliver the genetic material to the cell culture.

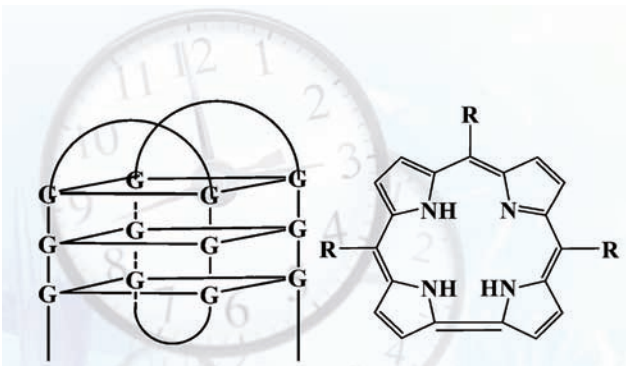
Muthuswamy intends to use his technology in his own research area of brain injury. 'We can test the role of specific genes in repair of damaged neurons,' he said. He is currently taking the first step, applying his method to transfect neuron cells.

Danièle Gibney

Reference
T Jain and J Muthuswamy, *Lab Chip*, 2007, DOI: 10.1039/b707479d

Electrostatic attraction helps give telomeres some structure

Is the clock ticking for cancer cells?



Corroles (right) induce G-quadruplexes (left) to form and could interfere with cancer cell division

Scientists in China have found a way to reset cancer cells' biological clock that could lead to new anticancer agents.

Cancer cells are distinguished from healthy cells by their ability to divide indefinitely. During normal cell division, telomeres, repeat DNA sequences at the end of chromosomes, shorten until they become too short for the cell to remain viable. But, in cancer cells, this shortening is reversed by the enzyme telomerase, which is found in 80–90 per cent of all cancers. Now, Xiang Zhou, at Wuhan University, and colleagues have synthesised two new corrole derivatives that interfere with telomerase action.

Telomeres are predominantly linear, but overhangs at the ends fold into structures called G-quadruplexes that block the action of telomerase. Zhou suggests that the group's corroles work by stabilising G-quadruplexes, as the corroles' positively charged planar ring structures bind to the negatively charged sugar-phosphate backbone of the telomere DNA.

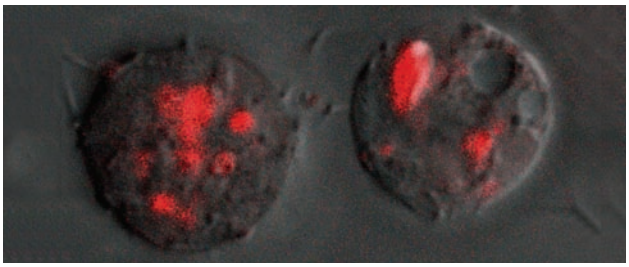
Zhou also found that the corroles could induce G-quadruplex formation in the absence of the usual complement of cations found in cells. This has physiological implications because salt concentrations fluctuate in living cells. Corroles could therefore have a use in cancer treatment by inducing G-quadruplex formation under physiological conditions and so interfering with telomerase activity and cancer cell division.

Steven Rokita, a specialist in the therapeutic aspects of DNA modification at the University of Maryland, US, explained: 'Telomerase and telomeres are extremely attractive targets for anticancer chemotherapy since they control the life and death of individual cells. While there are a number of strategies to exploit these targets, stabilising G-quadruplexes is particularly attractive. The corrole system provides a very interesting new platform for this purpose and these cationic corrole derivatives have already exceeded the performance of the standard in the field, TMPyP4.'

Janet Crombie

Reference
B Fu *et al*, *Chem. Commun.*, 2007, DOI: 10.1039/b704599a

Dye-namic transitions



Rhenium dyes can be used in cell imaging

Fluorescent dyes incorporating transition metals offer significant advantages over existing dyes in cell imaging, say UK scientists. Mike Coogan, at Cardiff University, and his colleagues have prepared a series of rhenium bipyridine dyes and demonstrated their potential in fluorescence microscopy cell imaging.

Fluorescence microscopy is commonly used for imaging biological systems pre-loaded with dyes. However, most current dyes are organic molecules, similar to those found in the biological samples. This can make it difficult to distinguish light produced by a dye from the background fluorescence of the biological material. Coogan's dyes avoid this problem because transition metal complexes fluoresce by a different mechanism – metal to ligand charge transfer (MLCT). Their different emission properties mean a clear image is obtained as dye emission is easily differentiated from the background.

According to Coogan, 'there has always been reluctance to apply transition metals in cell imaging due to worries about heavy metal toxicity, and the traditional feeling that organometallics are incompatible with water and oxygen. This study indicates a bright future for transition metals in fluorescence imaging.'

But there are still challenges to overcome, said Coogan. Ultraviolet radiation, often used to excite MLCT, is damaging to cells and the blue end of the visible spectrum has poor tissue penetration. If researchers can shift the dye photochemistry to lower energy, Coogan explained, the procedure will be less damaging and allow greater penetration. *Kathryn Lees*

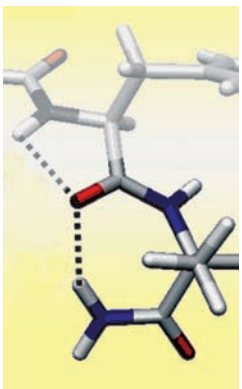
Reference
A J Amoroso *et al*, *Chem. Commun.*, 2007, 3066 (DOI: 10.1039/b706657k)

One good turn...

French researchers have been using spectroscopy to tell their left from their right.

Researchers at the CEA Saclay (Atomic Energy Research Centre), near Paris, have been investigating how amino acid chirality affects a peptide's secondary structure, that is, how the peptide chain folds up. Michel Mons and colleagues examine short lengths of peptide chain in the gas phase with ultraviolet and infrared laser spectroscopy. 'This allows us to examine precisely the interactions stabilising the structure, in particular the hydrogen-bonding network,' said Mons.

The group has started its study with a small motif called a γ-turn. This fold in a peptide chain is a seven-membered ring held together by a hydrogen bond. The researchers made the smallest system that contained a γ-turn: two peptide residues and an acetyl group. One of the residues was selected to be right-handed, left-handed or achiral, and its effect on the spectrum of the other peptide, phenylalanine, measured. From this, and careful theoretical calculations, the team can determine the turn's overall shape.



γ-Turns are 7-membered rings held together by an NH•••O hydrogen bond

The University of Paris XI's Anne Zehnacker, who pioneered the study of chiral recognition in the gas phase, is impressed by the work's quality and originality: 'The chirality of the amino acids influences the sense of the γ-turn of the peptides. This observation at the molecular level is important for subjects of biological relevance.'

The team plans to look at longer peptide chains, which can form bigger secondary structures. Mons added: 'An interesting experiment would be to measure the relative energy of two diastereomeric forms, because the energy difference is much smaller than the precision expected from quantum chemistry calculations.' *Colin Batchelor*

Reference
E Gloaguen *et al*, *Phys. Chem. Chem. Phys.*, 2007, DOI: 10.1039/b704573e

News in brief

Summing up how oxygen adds to heme
Spanish scientists have used computational chemistry to follow oxygen's journey to the iron centre of hemes. By calculating the different electronic states of O_2 and heme iron, the duo has found the most favourable, lowest energy route for oxygen–heme binding.

Nature's cancer treatments
Chemists working in China have used the protein apoferritin to deliver anticancer medicines to tumour cells. The cisplatin carrier decreases cell viability and the approach could be developed for targeted delivery of other drugs.

No more pumping iron?
A series of potential drugs for patients suffering from iron-overload disorders show unusual iron-binding properties. The new ligands bind to iron(II), as opposed to the iron(III) absorbed by most other iron-binding drugs.

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Sending peptides round the twist
Nanoparticles with flexible side chains cause peptides to adopt a helical form.

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Clearing a path to cancer detection
Improved imaging of prostate cancer proteins in single cells is possible thanks to UK scientists.

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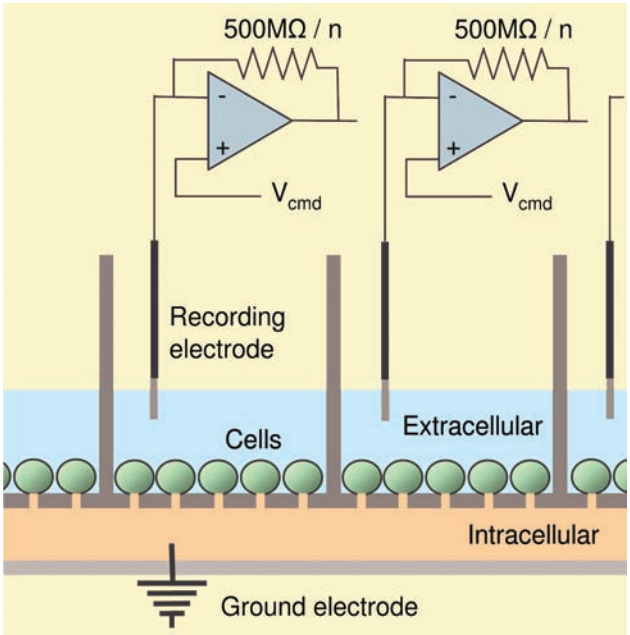
Population approach provides high throughput drug analysis

Current affairs of the cell

New bioassays could cut drug screening times. Researchers at GlaxoSmithKline in the UK and US have demonstrated how a technique called population patch clamp (PPC) electrophysiology can be used to probe multiple drug targets simultaneously.

Ion channels are pores that transport ions across cell membranes and are the molecular target of a number of drugs. Electrophysiology involves recording electrical currents across a cell membrane and, since these change when an ion channel responds to a drug, the method can be successful in drug screening.

Single-cell patch clamp electrophysiology is seen as the gold standard for monitoring these drug–ion channel interactions as it provides highly reliable information; however, it is too slow to be used as a primary screening method. The PPC approach measures the current across several cells in a single well, with multiple wells being analysed at the same time. This generates lower quality data but in a high-throughput format, allowing rapid screening of candidate drug libraries.



PPC method averages currents of several cells

Now, Derek Trezise at GlaxoSmithKline's site in Harlow, UK, and co-workers have used the PPC method in assay duplexing, where two different assays are run at the same time. This allows, for instance, one drug to be tested against two different cellular targets. The approach further increases the rate at which potential drugs can be analysed, cutting screening times and costs. 'Potentially there is scope for even higher throughput,' said Derek Trezise, adding that, on the technical side, 'the challenge is to improve the fluidics.'

The team was also able to measure modulator assays. These record a drug's effect on ion channels that require an activator, such as an additional ion. Being able to use PPC in this way extends the scope of the method.

'Population patch clamp provides a new approach with real promise to improve the efficiency of generating high-information-content activity data for ion channel targets,' said Jesús González, an expert in ion channel drug discovery from Vertex Pharmaceuticals, San Diego, US. 'Assaying simultaneously from a population of cells should improve *in vitro* pharmacological analysis and profiling of some challenging ion channel targets,' he added.

Russell Johnson

Reference
T J Dale *et al*, *Mol. BioSyst.*, 2007, DOI: 10.1039/b706152h

In the current issue of Research Articles...

Studies of structure and phosphorylation of tau protein using high resolution mass spectrometry
J Susanne Becker and Michael Przybylski, *J. Anal. At. Spectrom.*, 2007, **22**, 761 (DOI: 10.1039/b701440f)

Consecutive GC base pairs determine the energy barrier of DNA duplex formation under molecularly crowded conditions
Xiao-Bo Gu, Shu-ichi Nakano and Naoki Sugimoto, *Chem. Commun.*, 2007, 2750 (DOI: 10.1039/b702865b)

Electric field isolator (EFI) for isolated and electrophoretic manipulation of charged biomolecules
Jae Young Yun *et al*, *Lab Chip*, 2007, **7**, 916 (DOI: 10.1039/b618099j)

Speciation and toxicological relevance of manganese in humans
Bernhard Michalke, Stefan Halbach and Volker Nischwitz, *J. Environ. Monit.*, 2007, **9**, 650 (DOI: 10.1039/b704173j)

An introduction to electrochemical DNA biosensors
Katherine J Odenthal and J Justin Gooding, *Analyst*, 2007, **132**, 603 (DOI: 10.1039/b701816a)

The relationships between oxidase and synthase activities of flavin dependent thymidylate synthase (FDTS)
Anatoly Chernyshev *et al*, *Chem. Commun.*, 2007, 2861 (DOI: 10.1039/b700977a)

Supramolecular nanocarriers integrated with dendrimers encapsulating photosensitizers for effective photodynamic therapy and photochemical gene delivery
Nobuhiro Nishiyama, Woo-Dong Jang and Kazunori Kataoka, *New J. Chem.*, 2007, **31**, 1074 (DOI: 10.1039/b616050f)

Click multivalent neoglycoconjugates as synthetic activators in cell adhesion and stimulation of monocyte/machrophage cell lines
Mariano Ortega-Muñoz *et al*, *Org. Biomol. Chem.*, 2007, **5**, 2291 (DOI: 10.1039/b706331h)

Fungal photoreceptors: sensory molecules for fungal development and behaviour
Luis M. Corrochano, *Photochem. Photobiol. Sci.*, 2007, **6**, 725 (DOI: 10.1039/b702155k)

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Interview

Happiness on a chip

Yoshinobu Baba tells Celia Clarke how nanotechnology could measure our health and happiness

Yoshinobu Baba

Yoshinobu Baba is a professor of chemistry at Nagoya University and a director for nanobiotechnology research at the National Institute of Advanced Industrial Science and Technology in Japan. He is also a member of the steering committee for the International Symposium on Micro Total Analysis Systems (μTAS). His research focuses on using nanobiotechnology to solve biological problems in areas from genomics to personalised medicine.

Why did you choose to work in chemical biology?

I was an enthusiastic chemist who became interested in biology. Even during my PhD in inorganic analytical chemistry, I started working in biological areas.

After this, I became involved in genomic research based on analytical technologies. I was doing capillary electrophoresis for the separation of DNA molecules. Also, I was interested in and became involved in the genomic project in Japan.

What is the focus of your current research?

Our work is mainly in nanotechnology or nanoscience. We develop new nanomaterials and nanostructures using semiconductor, nanofabrication and chemical technologies. We aim to make new structures with bio- and medical applications. To achieve this we must select the appropriate nanostructures for DNA, protein or cell analysis.

For several years we have been applying nanotechnology to disease diagnosis, especially the detection of biomarkers, SNP [single nucleotide polymorphism] analysis and DNA sequencing. Now, we work with medical groups to develop very-early-stage cancer detection based on single cell or biomolecule analysis.

Also, I am collaborating with systems biologists who would like to analyse expression profiles of genes from yeast. For this we need to develop chip structures for analysing 6000 genes in a single run, in parallel. At the moment, the scale of analysis of genetic materials is still small – even a 1000 samples is large for the field. Yet humans have 20 000 genes and maybe 100 000 proteins.

Why is nanotechnology important for biology?

In situ, *in vivo* real time single molecule analysis is an important goal. The very small number of expressed proteins can be a key issue for cancer and other diseases. To look at interactions between small numbers of molecules, very small volumes are necessary but conventional technologies use large volumes. Using large volumes it is easy to detect single molecules, for example single molecule DNA or single molecule proteins. But if we want to detect interactions between proteins, proteins and DNA or molecules and cells, we need to make very small volumes or very small structures because biological reactions occur at micro- to nanomolar concentrations. Chip technology means we can use very small volumes, making nanotechnology key for this kind of work.

How far are we away from personalised and predictive medicine?

Personalised medicine has a wide variety of goals. For example, we can already use the detection of SNPs to predict side reactions of drugs. But SNPs are only a small part of personalised medicine. The real personalised medicine will take 10–20 years to reach. At present, we have no systems biology. We need an expression profile of all genes and all expressed proteins, all modifications of proteins and all other reactions in the cell. We need many technologies to do that.

You are a member of the steering committee for μTAS. What are the aims of μTAS?

μTAS is interdisciplinary so we encourage interaction between different disciplines, including the semiconductor, electronics, chemistry, biology, medicine and electrophysics fields. We organise μTAS meetings to bring together different people to meet the same research target.

We think the microchip is key for targeting the biological or medical fields so we encourage μTAS researchers towards these goals. Also, the technology is branching out and is applicable to synthesis, environmental and food analysis, to name a few. Computer chips are now in all electronic devices, including cars. Hopefully, μTAS will be such a basic kind of technology. Recently electronics and pharmaceutical companies have been involved in μTAS meetings. We'd like to expand to include people in industrial fields including the car and metal industries.

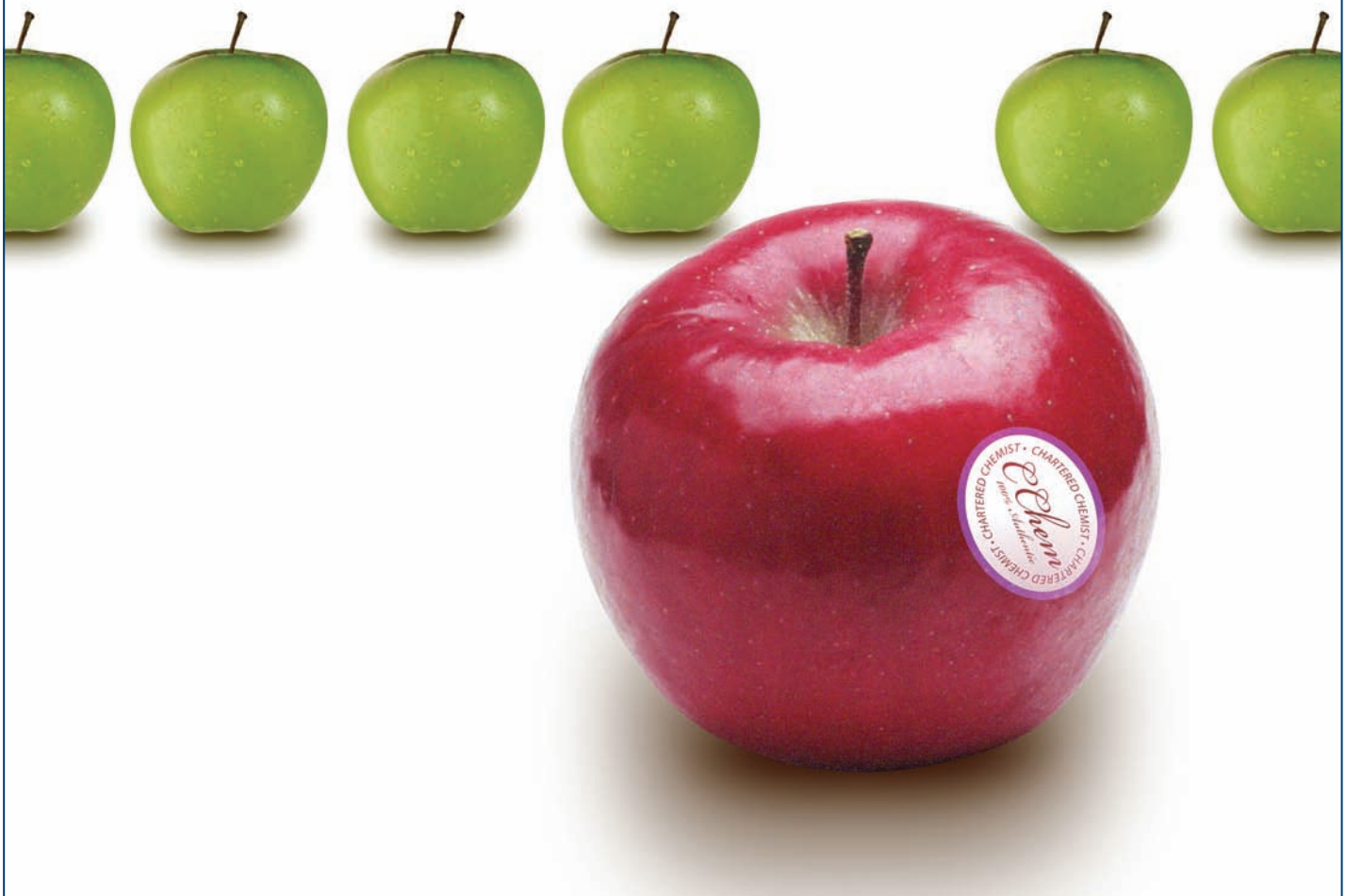
What's the next step for nanobiotechnology?

Nanobiotechnology could be used as a measure of happiness, stress levels and health. We can measure the stages of cancer or diabetes, since genomic research tells us which genes are related to which diseases. But we need to analyse proteomics and glycomics in more detail. The next stage is to measure the function of the brain, looking at happiness and stress.

The aging population is increasing. Eight years from now 26% of the Japanese population will be over 65. So we need to make older people feel happier. The control of disease means happiness for some people and we can develop measurements of health and control the disease. But we have no technology to measure the happiness. And the definition of happiness is different for each of us so we need a personalised happiness measurement. That is an important target.

Chartered Chemist

Pick of the crop



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Instant insight

Revealing the hidden depths

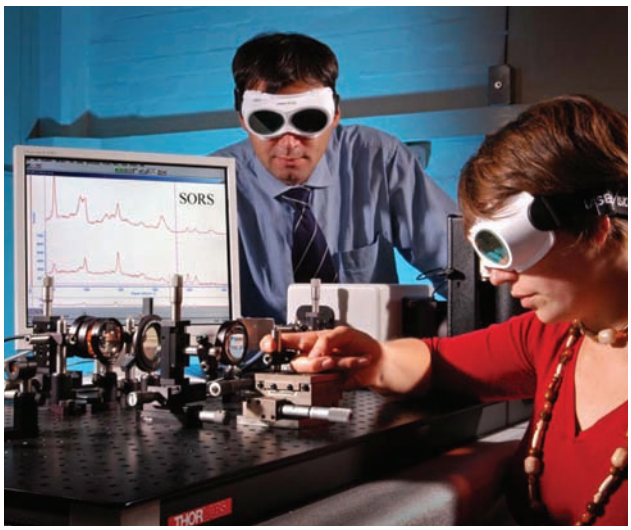
Pavel Matousek, at the Rutherford Appleton Laboratory, UK, describes emerging spectroscopic techniques that promise to change cancer and bone disease diagnosis.

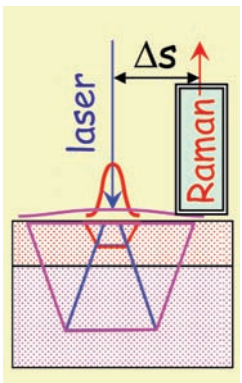
Over the past two years we have witnessed the emergence of chemically specific analytical tools that could revolutionise the way various diseases are diagnosed. The same tools could also have a profound impact on how pharmaceutical product quality is assessed and hidden drugs and explosives are detected. The methods are based on Raman spectroscopy – a powerful vibrational spectroscopy technique.

Raman spectroscopy provides detailed chemical information from the inelastic scattering of photons as they hit molecules in a sample. The scattered photons red shift from their original colour and the pattern of the red shifts can be used to identify the sample's chemical composition. Yet, until recently, Raman spectroscopy could be applied to only shallow depths in tissue; access to deeper layers has been prevented by their strong diffuse photon scattering.

Recently, several new methods have been developed that have allowed the penetration depth to be extended substantially. A technique holding a particular promise, because of its efficacy and simplicity, is spatially offset Raman spectroscopy (SORS). Unlike conventional methods, which rely on sharp image formation from the probed object to provide depth resolution, the SORS approach uses the diffuse component of light.

The concept is based on collecting Raman spectra from regions away from the illumination point on the sample surface. Each laterally-offset Raman spectrum contains different relative contributions from sample layers at different depths. This difference is brought about by a wider lateral diffusion of photons emerging from greater depths – these photons have to travel larger distances and on their way they diffuse sideways to a greater extent than the photons originating from shallower layers. For a two-layer system, a simple scaled subtraction of two spectra obtained at different spatial offsets can be used to produce pure Raman spectra of individual layers. If there are more than two layers, as is often the case with biological samples, then multivariate data analysis of a more extensive data set is needed.





Above: Scientists use SORS to probe deep inside samples
Below: Spectra are collected away from the point of illumination

Reference
P Matousek, *Chem. Soc. Rev.*, 2007, **36**, 1292 (DOI: 10.1039/b614777c)

Since its first demonstration, the SORS concept has been used in various areas, for example in biomedical applications. Several groups have shown that the technique has a potential for non-invasive diagnosis of a range of bone conditions, such as brittle bone disease or osteoporosis. In contrast with the conventional x-ray analysis, SORS enables both the mineral and protein components to be characterised, offering substantially richer information on the condition of the analysed bones.

Variants of SORS have also shown potential in the non-invasive detection and chemical composition analysis of calcifications buried deeply within breast tissue. As different types of calcifications apparently associate with different types of cancer lesions, benign and malignant, the techniques could potentially enhance the diagnostic potential of conventional mammography and help reduce the number of biopsies. Since reports suggest that 70–90% of needle biopsies uncover benign lesions, many of these invasive procedures could be avoided.

Examples of other applications include the quality control of pharmaceutical products, the non-invasive probing of counterfeit drugs through white plastic bottles and blister packs and the detection of powder explosives inside envelopes or plastic containers.

These exciting developments come at a time when Raman spectroscopy is completing its transformation from laboratory technique to practical analytical tool; a journey driven by recent advances in laser and detection technologies. Further developments of many of these new applications promise to exert a profound influence over our daily lives in the not too distant future.

Read Pavel Matousek's review 'Deep non-invasive Raman spectroscopy of living tissue and powders' in the August issue of Chemical Society Reviews.

Essential elements

RSC journals – even more impact!

RSC Publishing is celebrating the continued success of its journals following the release of the 2006 impact factors calculated by ISI®. Journals from across the collection have recorded significant rises, while new interdisciplinary titles have received their first official ranking of the internationally recognised publishing industry metric.

Among the headline success stories, *Green Chemistry*, the only journal publishing both primary and secondary research in the field, sees a staggering 29% rise in impact factor to 4.19. The already impressive impact factor for *Lab on a Chip* has increased by a further 10% to 5.82, ensuring it remains one of the leading journals in micro and nano-research.

The RSC materials science journals further strengthen and grow. For the second year running, weekly *Journal of Materials Chemistry*'s impact factor rose significantly, to 4.29. Meanwhile, new interdisciplinary journal *Soft Matter* (launched June 2005) received an impressive first (partial) impact factor of 4.39, positioning it ahead of its competitors and achieving the journal's aim of bringing together interdisciplinary research in this field.

RSC journals at the interface with biology have also been bolstered by increasing impact factors, with *Organic & Biomolecular Chemistry*

and *Natural Product Reports* achieving 2.87 and 8.89 (rises of 13% and 21%) respectively. Newcomer *Molecular BioSystems* (launched May 2005) celebrates its first (partial) impact factor of 2.45.

These successes come after a year of innovative developments to the presentation and linking of research in RSC Journals, particularly those containing biological content, through the industry-leading Project Prospect.

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Footnote: The annual ISI® impact factors provide an indication of the average number of citations per paper. The impact factor for 2006 is calculated from the total number of citations given in 2006 to citeable articles published in 2004 and 2005, divided by the number of citeable articles published in 2004 and 2005.

The immediacy index measures how topical and urgent the papers published in a journal are. The 2006 immediacy index is the total number of citations given in 2006 to citeable articles published in 2006 divided by the number of citeable articles published in 2006.

Data based on 2006 impact factors, calculated by ISI®, released June 2007.

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