

Chem Soc Rev

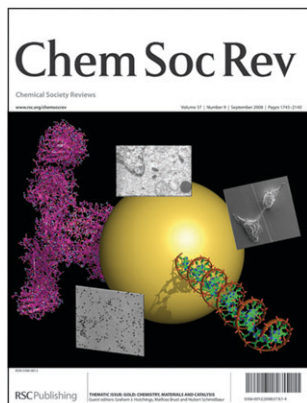
Chemical Society Reviews

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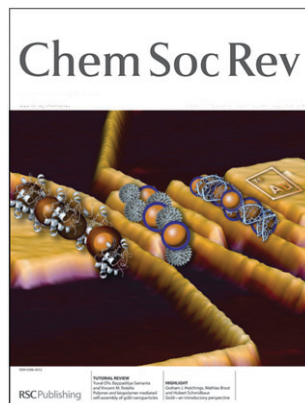
IN THIS ISSUE

ISSN 0306-0012 CODEN CSRVRB 37(9) 1745-2140 (2008)



Cover

Gold nanoparticles in biology: illustration of a gold nanoparticle conjugated with an antibody and a single strand of DNA. Electron microscopy images of cells, nanoparticles and nanoparticles inside cells. Image reproduced by permission of Ralph A. Sperling, Pilar Rivera Gil, Feng Zhang, Marco Zanella and Wolfgang J. Parak from *Chem. Soc. Rev.*, 2008, **37**, 1896.



Inside Cover

See V. M. Rotello *et al.*, page 1814. Assembly of gold nanoparticles using polymers and biopolymers provides access to new structures featuring unique properties and functions. Picture credit: Vincent Rotello and Yuval Ofir. Image reproduced by permission of Yuval Ofir, Bappaditya Samanta and Vincent M. Rotello from *Chem. Soc. Rev.*, 2008, **37**, 1814.

CHEMICAL SCIENCE

C65

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

Chemical Science

September 2008/Volume 5/Issue 9

www.rsc.org/chemicalscience

HIGHLIGHT

1759

Gold—an introductory perspective

Graham J. Hutchings, Mathias Brust and Hubert Schmidbaur

The reviews in this thematic issue of *Chemical Society Reviews* on gold chemistry are introduced and achievements in the field are reviewed.



Graham J. Hutchings



Mathias Brust



Hubert Schmidbaur

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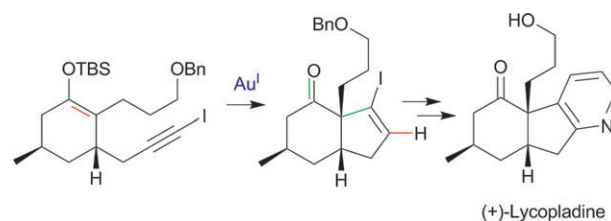
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1766

Gold catalysis in total synthesis

A. Stephen K. Hashmi* and Matthias Rudolph

Homogeneous gold catalysis of organic reactions is now no longer dominated by methodology studies dealing with simple test substrates. An increasing number of publications now demonstrate its use in key steps of efficient total syntheses of complex natural products.

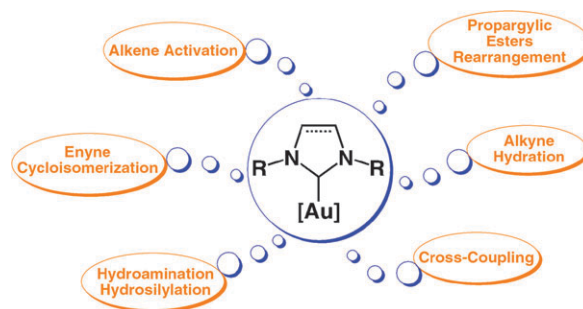


1776

N-Heterocyclic carbenes in gold catalysis

Nicolas Marion and Steven P. Nolan*

Hot date: N-heterocyclic carbene ligands meet gold for outstanding catalytic applications.

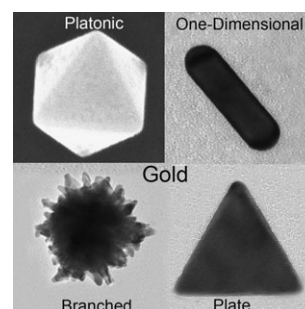


1783

Shape control in gold nanoparticle synthesis

Marek Grzelczak, Jorge Pérez-Juste,* Paul Mulvaney* and Luis M. Liz-Marzán*

This tutorial review summarises recent research into the controlled growth of gold nanoparticles of different morphologies and discusses the various chemical mechanisms that have been proposed to explain anisotropic growth.

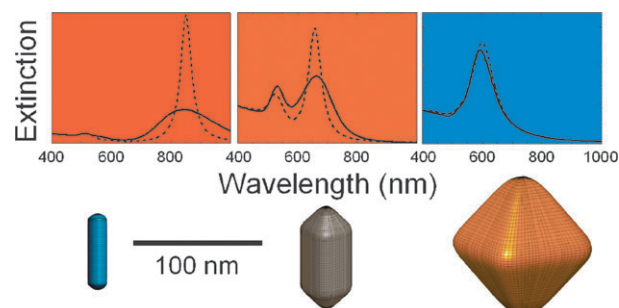


1792

Modelling the optical response of gold nanoparticles

Viktor Myroshnychenko, Jessica Rodríguez-Fernández, Isabel Pastoriza-Santos, Alison M. Funston, Carolina Novo, Paul Mulvaney, Luis M. Liz-Marzán and F. Javier García de Abajo*

Modern numerical methods provide a powerful tool for predicting and understanding the absorption and scattering response of gold nanoparticles.





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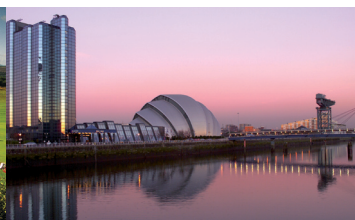
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- Analysis & Detection
- Chemistry for Health
- Communication & Education
- Energy & Environment
- Industry & Innovation
- Materials
- Synthesis & Mechanisms

Plenary speakers

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Chris Dobson, University of Cambridge
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Sir Harold Kroto, Florida State University
Klaus Müllen, Max-Planck Institute for Polymer Research
Sir J Fraser Stoddart, Northwestern University
Vivian W W Yam, The University of Hong Kong
Richard N Zare, Stanford University

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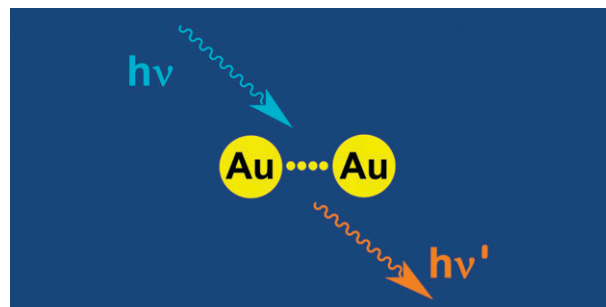
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1806

Highlights on the recent advances in gold chemistry—a photophysical perspective

Vivian Wing-Wah Yam* and Eddie Chung-Chin Cheng

Emissive gold—the chemistry and photophysics that make gold complexes luminescent.

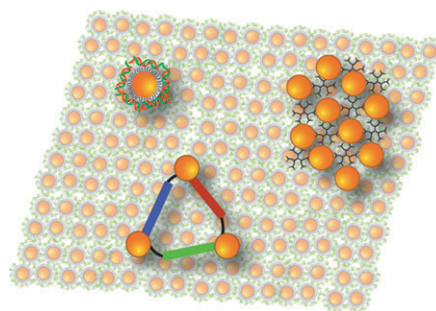


1814

Polymer and biopolymer mediated self-assembly of gold nanoparticles

Yuval Ofir, Bappaditya Samanta and Vincent M. Rotello*

Polymers and biopolymers provide useful tools for nanoparticle assembly, providing both structural and functional elements for nanocomposite construction.

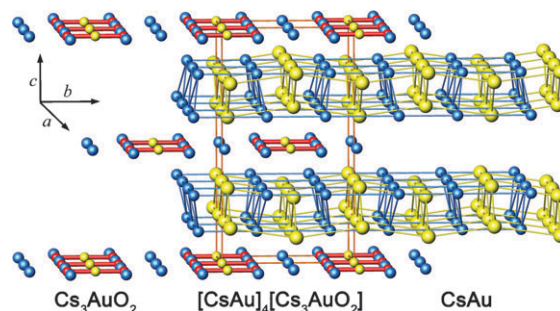


1826

The chemistry of gold as an anion

Martin Jansen

Gold can occur as an anion with the integral charge number of $1-$, e.g. in liquid electrolytes or during all-solid state interdiffusion experiments. This tutorial review addresses the chemistry of anionic gold, emphasizing some parallels to halide chemistry.

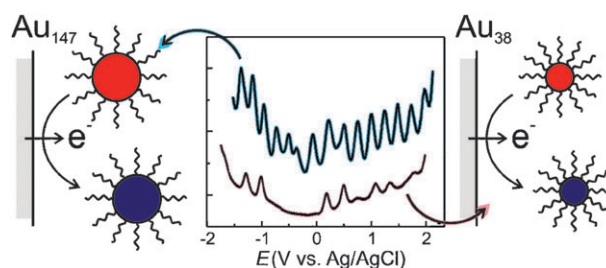


1836

Quantised charging of monolayer-protected nanoparticles

Timo Laaksonen, Virginia Ruiz, Peter Liljeroth and Bernadette M. Quinn*

Monolayer protected metal clusters (MPCs) can exhibit quantised charging at room temperature in simple electrochemical measurements.



Dynamic Stereochemistry of Chiral Compounds

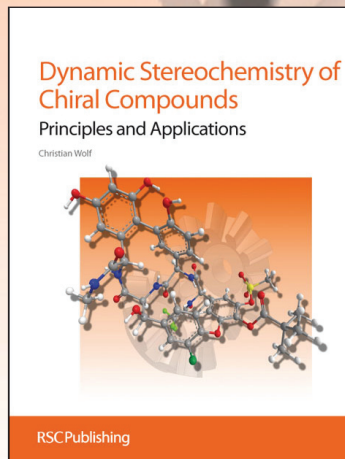
This book provides an overview of fundamental concepts of asymmetric synthesis highlighting the significance of stereochemical and stereodynamic reaction control. Topics include kinetic resolution (KR), dynamic kinetic resolution (DKR), dynamic kinetic asymmetric transformation (DYKAT), and dynamic thermodynamic resolution (DTR). In-depth discussions of asymmetric synthesis with chiral organolithium compounds, atropisomeric biaryl synthesis, self-regeneration of stereogenicity (SRS), chiral amplification with chiral relays and other commonly used strategies are also provided. Particular emphasis is given to selective introduction, interconversion and translocation of central, axial, planar, and helical chirality.

A systematic coverage of stereochemical principles and stereodynamic properties of chiral compounds guides the reader through the book and establishes a conceptual linkage to asymmetric synthesis, interconversion of stereoisomers, molecular devices that resemble the structure and stereomutations of propellers, bevel gears, switches and motors, and topologically chiral assemblies such as catenanes and rotaxanes. Racemization and diastereomerization reactions of numerous chiral compounds are discussed as well as the principles, scope and compatibility of commonly used analytical techniques.

- More than 550 figures, schemes and tables illustrating mechanisms of numerous asymmetric reactions and stereomutations of chiral compounds
- Technical drawings illustrating the conceptual linkage between macroscopic devices such as turnstiles, ratchets, brakes, bevel gears, propellers or knots and molecular analogs
- More than 3000 references to encourage further reading and facilitate additional literature research
- A comprehensive glossary with stereochemical definitions and terms which facilitate understanding and reinforce learning

This book will be of particular interest to advanced undergraduates, graduates and professionals working and researching in the fields of synthetic organic chemistry and stereochemistry.

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Author: Christian Wolf

Publication date: 14 December 2007

Publisher: RSC Publishing

Format: Hardback

ISBN: 9780854042463

Price: £49.90

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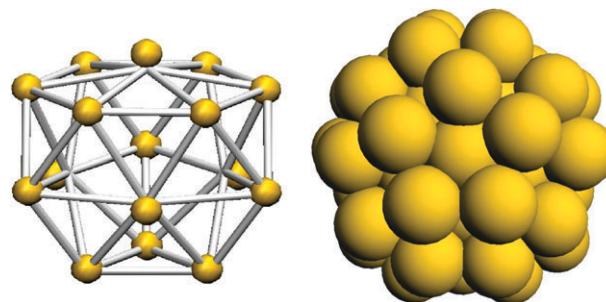
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1847

Atomic and electronic structure of gold clusters: understanding flakes, cages and superatoms from simple concepts

Hannu Häkkinen

The electronic-structure-derived stability of certain cage-like gold clusters and cores of ligand-protected gold clusters can be understood from simple physical concepts.



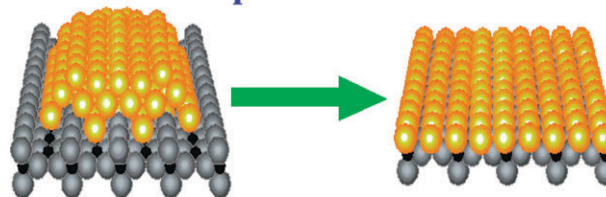
1860

Catalytically active gold on ordered titania supports

Mingshu Chen and D. Wayne Goodman*

The current understanding of the origin of the unique properties of titania-supported Au catalysts for carbon monoxide oxidation are summarised.

Golden Catalysts: From Nanoparticles to Nanofilms

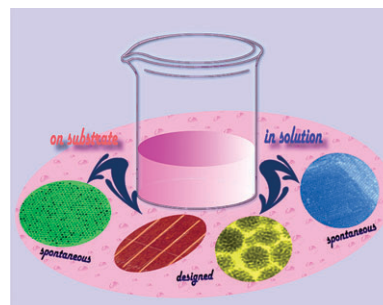


1871

Gold nanoparticle superlattices

B. L. V. Prasad,* C. M. Sorensen and Kenneth J. Klabunde

This tutorial review presents recent examples and advancement in the formation of nanoparticle superlattices—probably the biggest separating factor between current knowledge and enormous possible applications in the area of nanoparticle research.

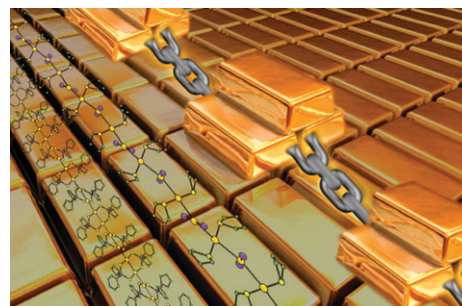


1884

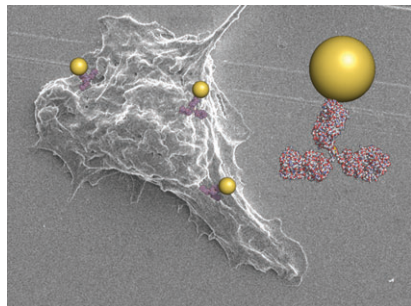
The use of aurophilic and other metal–metal interactions as crystal engineering design elements to increase structural dimensionality

Michael J. Katz, Ken Sakai and Daniel B. Leznoff*

Aurophilic interactions act as an intermolecular glue to generate high-dimensionality structures that have useful materials applications.



1896

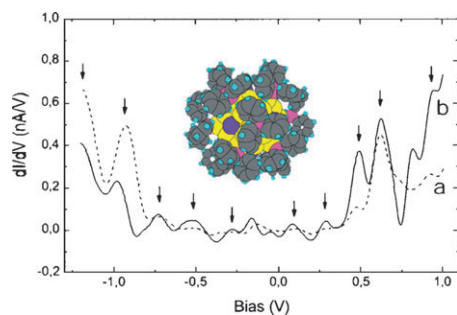


Biological applications of gold nanoparticles

Ralph A. Sperling, Pilar Rivera Gil, Feng Zhang, Marco Zanella and Wolfgang J. Parak*

A review of the widespread use of gold nanoparticles in biology. The authors have identified four classes of applications: labelling, delivering, heating, and sensing. For each of these applications the underlying mechanisms and concepts, the employed specific features of the gold nanoparticles, as well as several examples are described.

1909

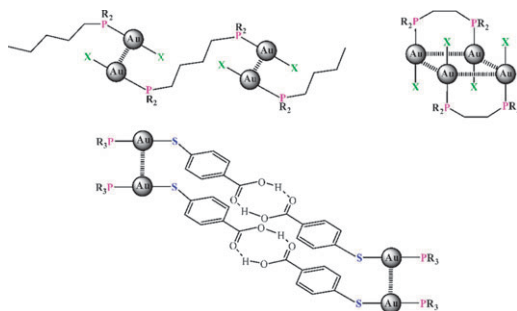


The relevance of shape and size of Au₅₅ clusters

Günter Schmid*

This review gives an overview on Au₅₅ clusters from their discovery in 1981 up to date. Syntheses, chemical and physical properties are discussed, ending with the surprising response of biological systems to the 1.4 nm gold clusters, characterizing them as extremely cell-toxic. Further the special electronic behaviour of ligand protected Au₅₅ clusters discriminates them from smaller or larger gold clusters. They behave as artificial big atoms and can be switched by single electrons.

1931

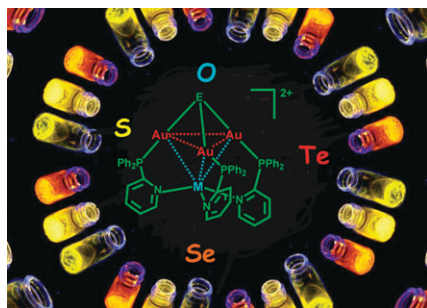


A briefing on aurophilicity

Hubert Schmidbaur and Annette Schier

An unforeseen type of chemical bonding: the experimental observations leading to the concept of "aurophilicity" are reviewed, the significance and relevance of the phenomenon is described, and the results of modern theoretical treatments are considered.

1952



Chalcogenide centred gold complexes

M. Concepción Gimeno and Antonio Laguna

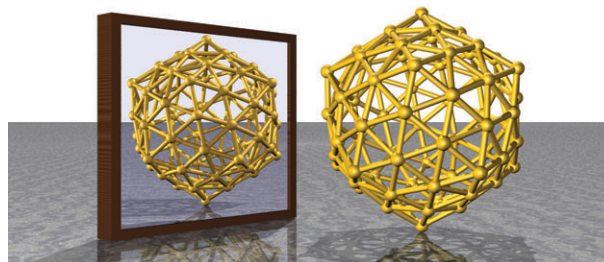
Chalcogenide-centred gold complexes are an important class of compounds from the structural and theoretical point of view and also present interesting properties such as luminescence.

1967

Theoretical chemistry of gold. III

Pekka Pyykkö*

From studies of small molecules to molecular dynamics simulations, including the aurophilic attraction and predictions for new species, theoretical chemistry of gold has come of age. The literature since mid-2005 is summarized and comprises about 500 further papers.

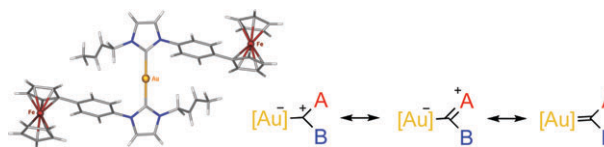


1998

Carbene complexes of gold: preparation, medical application and bonding

Helgard G. Raubenheimer* and Stephanie Cronje

The growth in the chemistry of gold carbene complexes is experiencing a bull phase. Important drivers are organometallic and organic synthesis, biological activity, and theoretical development.

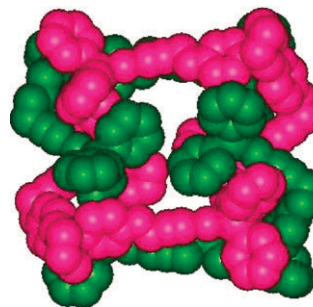


2012

Macrocycles, catenanes, oligomers and polymers in gold chemistry

R. J. Puddephatt*

All of the title compounds can be assembled easily by techniques such as dynamic ring-opening polymerization, including the doubly-braided catenane shown here.



2028

The use of gold nanoparticles in diagnostics and detection

Robert Wilson

This critical review describes how gold nanoparticles are being used in an ever-increasing variety of detection schemes, and predicts that because of their unique properties they will continue to play a leading role in the diagnostic devices of the future.



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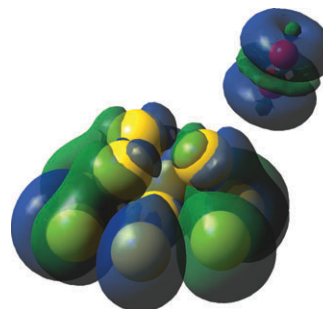
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2046

Theory and simulation in heterogeneous gold catalysis

Rudy Coquet, Kara L. Howard and David J. Willock*

We review applications of quantum chemistry to the structure and reactivity of Au catalyst nanoparticles, covering methods used, isolated and oxide supported clusters and the mechanism of CO oxidation.

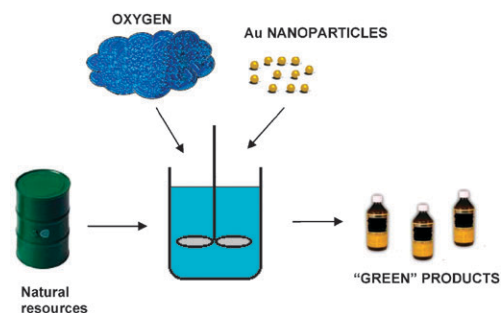


2077

Selective oxidation using gold

Cristina Della Pina, Ermelinda Falletta, Laura Prati and Michele Rossi*

The review surveys gold catalysis as a valid eco-friendly alternative to the traditional methods for the oxidation of organic substrates.

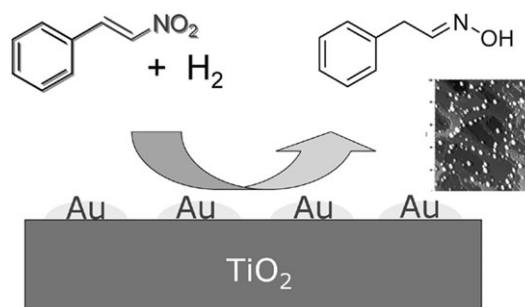


2096

Supported gold nanoparticles as catalysts for organic reactions

Avelino Corma* and Hermenegildo Garcia*

Gold at work: The small gold nanoparticles seen in the AFM image are unique catalysts able to promote unprecedented chemical transformations.

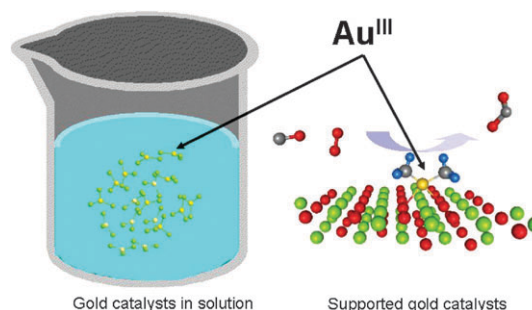


2127

Catalysis by gold dispersed on supports: the importance of cationic gold


Juan C. Fierro-Gonzalez and Bruce C. Gates*

The catalytic activity of supported gold has attracted wide attention because it was not expected, as gold is the least reactive metal. This paper is a review and a critical assessment of the evidence of cationic gold in supported gold catalysts for CO oxidation and ethylene hydrogenation.



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Chemical Science

Putting macrocycles that flex their muscles under the spotlight

Shining a light on molecular muscles

Australian researchers have developed a novel molecular muscle driven by light.

Biological machines, such as muscles, are commonly found in nature and are essential to many processes in the human body. Taking this as their inspiration, a team led by Christopher Easton at the University of Adelaide, Australia, developed a light-driven molecular muscle based on stilbene and α -cyclodextrin.

α -Cyclodextrin is a macrocyclic compound which forms host-guest complexes with hydrophobic guests of an appropriate size to be incorporated into α -cyclodextrin's central cavity. *trans*-Stilbenes can act as guests to α -cyclodextrin, but the *cis* isomer cannot as it is much less compact.

Easton and his team created rotaxane 'daisy chain' dimers, in which a stilbene bonded to an α -cyclodextrin molecule is threaded through another α -cyclodextrin bonded to a stilbene, and then the stilbenes are capped with bulky alkyl groups to prevent



the components separating. Initially both the stilbenes are in the *trans* conformation, and both stilbenes act as guests within the α -cyclodextrin. On irradiation with 350nm light, one or both of the stilbenes may isomerise, causing them to be released from the α -cyclodextrin and resulting in

The 'muscle' contracts and expands with light irradiation

Reference

R E Dawson, S F Lincoln and C J Easton, *Chem. Commun.*, 2008, DOI: 10.1039/b809014a

the extension of the rotaxane. This may be reversed by irradiation with 254nm light, causing the 'muscle' to contract or expand with light irradiation.

'Our molecular muscle switches between states but its particular feature of expanding and contracting as it changes states is of more interest in the development of so-called smart materials that respond to their environment,' says Easton. 'It is a relatively small step to envisage our muscle being incorporated into a polymer that shrinks and expands depending on its exposure to light.'

Jean-Pierre Sauvage of the Louis Pasteur University, Strasbourg, France, says the work is fascinating, saying 'Until now, molecular chemists had proposed to trigger related motions by chemical or electrochemical signals. The present system, based on photonic inputs only expands the field in a very significant fashion.'

Vikki Chapman

In this issue

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The wine fraud detective

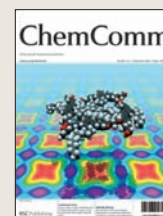
An electronic tongue with a taste for fine wine

Instant insight: Disease snapshots

Hye Jin Lee and Robert Corn look at the latest breakthroughs in the use of microarray technology for the fast detection and treatment of cancer

Interview: Medicinal reasons

Yixin Lu talks to Vikki Allen about dreams and the importance of medicinal chemistry



A snapshot of the latest developments from across the chemical sciences

Research highlights

Inorganic polymer-based microchips are resistant to solvent attack

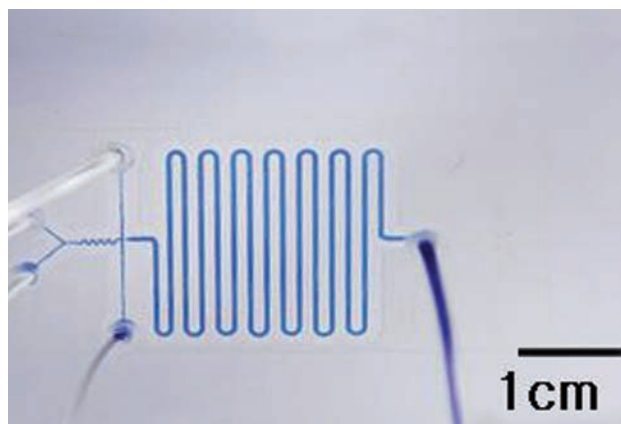
Prices of microreactors stamped down

Polymer-based microreactors turn inorganic to beat organic solvent attacks and reduce prices.

Dong-Pyo Kim from the Chungnam National University, Daejeon, Korea, and colleagues used inorganic polymers to make microreactors that are resistant to attack by organic solvents and should be cheap to manufacture.

Microreactors are miniaturised devices where reactions take place within a confined space typically in the form of microchannels on a chip. They have a number of advantages over conventional reaction systems including yield, energy efficiency, reaction control and safety.

A variety of materials have been used to make microreactors, including metal, silicon, glass and polymers. However, while metallic and silicon-based devices are durable they are expensive to make. Conversely, polymer reactors are cheap to manufacture but prone to attack by organic solvents limiting their use. Now Kim's team has developed inorganic polymer



microreactors which offer the best of both worlds.

The team made microreactors using two commercially available inorganic polymers – polyvinylsilazane and allylhydropolycarbosilane – and a well established microimprinting lithography technique. Kim believes this low cost method could be used for mass production. Tests showed the microreactors are resistant to attack by a variety of

Cycloaddition and condensation reactions have been carried out in a chip

Reference
T.-H. Yoon *et al.*, *Lab Chip*, 2008, DOI: 10.1039/b804726j

organic solvents.

To create the microreactor, Kim dropped liquid inorganic polymer onto a glass slide under a nitrogen atmosphere. He then placed a stamp – with the microchannel in relief on its surface – into the polymer and cured it using UV light. The polymer solidified, and the stamp was removed leaving the impression of the microchannel. The polymer was then heat cured before a second glass slide coated with the polymer was placed on top, enclosing the channel.

To demonstrate the performance of their new microreactors the team showed that they could be used to carry out three synthetic organic reactions – synthesis of 3,5-dimethylpyrazole, a Diels–Alder cycloaddition and a Knoevenagel condensation.

Kim is currently exploring ways to improve the fabrication process as well as looking at applying these microreactors in other fields such as biotechnology and biomedical engineering.

Nicola Burton

Selective recovery of valuable metals from industrial wastewater

Newspaper filters out gold

Ordinary newspaper can be used to recover precious metals from industrial wastewater, say researchers in Japan.

Katsutoshi Inoue, and co-workers from Saga University, formed an active gel by treating newspaper with *p*-aminobenzoic acid – a readily available compound used in sunscreen. Inoue shows that when water is passed through a column packed with this modified paper, gold, palladium and platinum are filtered out in preference to other metals.

Recovering valuable precious metals from industrial effluent is highly desirable, but not easy. Current methods suffer from incomplete metal removal, are expensive and have toxic



waste products. Inoue's method overcomes these problems, whilst also providing a use for old newspapers.

Jarek Drelich an expert in

Old newspapers prove to be useful absorbents

materials science at Michigan Technological University, Houghton, US, agrees saying that the route 'opens the prospect of mass producing waste biomass-based sorbents that could benefit not only the hydrometallurgical industry but also the paper recycling industry.'

Inoue showed that a column packed with the gel could be used repeatedly, a good sign for industrial applications. Future challenges for the Japanese workers include separation and purification of the recovered metals.

Roxane Owen

Reference
C R Adhikari *et al.*, *New J. Chem.*, 2008, DOI: 10.1039/b802946f

Nanoparticles offer a quick fix for decayed teeth

Pearly whites

Chinese scientists have found a new route to the perfect smile, using nanoparticles to repair tooth enamel.

Ruikang Tang at Zhejiang University and his team found that nanoparticles made from hydroxyapatite (HAP), a mineral which is the major component of dental enamel, adsorb very strongly onto the surface of the natural enamel – potentially enabling decayed teeth to be repaired and strengthened.

Tang explains that up to now dentists have found it hard to understand why synthetic hydroxyapatite has not been a good candidate for enamel repair, but they could now have the answer.

In contrast to previous studies, Tang's group have used much smaller particles, which they say are similar to the size of the building blocks of dental enamel. The features of these 20 nm sized



HAP nanoparticles may be more similar to the features of natural hydroxyapatite than those of the larger HAP particles that are usually used he explains.

George Nancollas, professor of chemistry at the University of Buffalo in the US, explains that the team's work with HAP nanoparticles has revealed

The nanoparticles absorb strongly onto the surface of natural tooth enamel

Reference
L Li *et al*, *J. Mater. Chem.*, 2008, DOI: 10.1039/b806090h

some exciting possibilities for the remineralisation of decayed enamel. 'The apparent restoration of enamel hardness using an in vitro method is particularly significant. The challenge will be to control the kinetics of the process and to achieve a degree of reproducibility.'

In order to confirm the effects seen with the HAP nanoparticles in vitro, Tang says they need to extend their work to in vivo studies. 'We are also interested in using these nanoparticles to repair other apatite hard tissue like bone,' he says.

Klaus Jandt, an expert in biomaterials research at Friedrich Schiller University of Jena in Germany, agrees: 'Enamel repair studies are important and of high relevance. In the future, it will be especially important to demonstrate the enamel repair potential in vivo and that the repaired enamel is mechanically stable.'

Katherine Davies

An electronic tongue with a taste for fine wine

The wine fraud detective

A portable electronic tongue that can 'taste' the grape varieties and vintages of wine has been created by Spanish scientists.

Cecilia Jiménez-Jorquera from the Barcelona Institute of Microelectronics, and colleagues, created a multisensor device and trained it to distinguish between different wines and grape juices.

When speaking with specialists of the wine industry, the need for a rapid route to obtain valuable information about product quality was noticed, explains Jiménez-Jorquera. It takes a long time to send samples to a centralised laboratory for analysis with complex equipment.

Jiménez-Jorquera's electronic tongue combines an array of six ion-sensitive field effect transistor-based chemical sensors, with cross-sensitivity to multiple ions in solution. The data are then analysed with an appropriate



The device is portable, meaning tests can be carried out on site

Reference
L M i Codinachs *et al*, *Analyst*, 2008, DOI: 10.1039/b801228h

chemometric method. 'This system enables the rapid and simultaneous measurement of different analytical parameters related to the quality control of wines and grape juices,' says Jiménez-Jorquera.

The electronic tongue is small and robust, Jiménez-Jorquera explains, and it is portable - which is essential for field measurements.

She adds that the device could be used to detect frauds committed regarding the vintage year of the wine, or the grape varieties used.

The advantage of this device is that it is 'fast, easy and relatively cheap' says Sue Ebeler from the University of California, Davis, US, who has studied wine flavour chemistry. 'One of the most interesting aspects', Ebeler adds, 'is the ability to predict sugar, acid and alcohol content using sensors that are not specifically sensitive to these components but respond to cations and heavy metals.'

The next step, says Jiménez-Jorquera, will be to extend the number of samples analysed to get more precise results, and give the best training for this electronic tongue. Other kinds of chemical sensors can then be incorporated to broaden the field of applications to other beverages and foods.

Rachel Cooper

News in brief

This month in Chemical Technology

Metal organic frameworks do the twist

Rotating solid-state crystals could outperform liquid crystals for optoelectronic applications, claim US scientists

Artificial cells seek out disease

Scientists in the US have made an artificial cell that can locate sites of disease, with potential uses for targeted drug delivery

Organic liquids capture CO₂

A new class of carbon dioxide-binding organic liquids could be used for capturing this greenhouse gas in coal power plants, say scientists in the US and Canada

The wonder of gold

Graham Hutchings, Mathias Brust and Hubert Schmidbaur introduce the newly discovered allure of gold for chemists

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

This month in Chemical Biology

Droplet traps for worms on chips

Watching how worms behave in droplets is the basis for a new assay that could find use in high-throughput drug screening

Putting the squeeze on cancer

Squashing and prodding suspect cells, then watching how they bulge and spring back into shape, can be used to tell cancer cells from healthy ones, say scientists from South Korea

New twist on protein binding

A fortuitous discovery by UK chemists has led to a new type of probe for protein interactions that could be used for cellular imaging

Medicines from the deep

In this month's interview, Mark Butler talks to Elinor Richards about Singapore, sponges and scuba diving

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

Knockout nanoparticles fight infections

Sterile nanoparticles



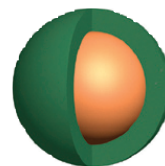
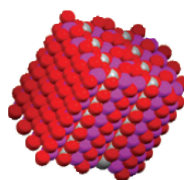
Septicaemia causing bacteria take a blow from two different types of antibacterial nanoparticles, made by scientists working independently in the UK and Korea.

With around 80 per cent of the infections that patients pick up in hospital associated with bacteria on the surface of medical devices and biomaterials, effective antibacterial agents are highly sought after. Nanoparticle-based agents, often applied as coatings, have shown recent promise in delivering improved sterility against a wide range of bacterial strains.

Free silver nanoparticles show good antimicrobial activity, exhibiting both size- and shape-dependent microbiological activity. But, these free nanoparticles are unsuitable for some applications like wound dressings because of their sensitivity to light and temperature. They also form aggregates, which reduce dissolution rates and efficacy.

Adam Lee and co-workers at the University of York, UK, provide an alternative method of stabilising silver particles using a porous alumina solid to support nanoparticles of silver carbonate.¹ Lee describes this material with its highly dispersed silver as 'alumina needles decorated with silver nanoparticles'. In this dispersed form the release rate of silver ions is maximised. And, the supported nanoparticles are 'easy to incorporate

Effective antibacterial coatings for wound dressings are highly sought after



Supported silver nanoparticles, top, and polymer coated nanoparticles, above, both show promise

into the foam or fabric dressing formats that are essential to confine active silver species within patients' wounds over several days,' explains Lee.

In tests using the bacteria *Staphylococcus aureus* – responsible for a range of illnesses from minor skin infections to septicaemia – the team found that their nanoparticles were better antibacterial agents than silver sulfadiazine, which is a widely used topical treatment for severe burns and ulcers. 'And', says Lee, 'unlike many other silver preparations these nanoparticles are: air- and light-stable, cheap to produce, non-toxic, non-allergenic and they don't stain clothing or skin during handling'.

Lee and his colleagues are now working with the medical products company Smith & Nephew to incorporate their nanoparticles into dressings suitable for patient trials in hospitals.

Korean scientists, Jyongsik Jang and Yura Kim at Seoul National University, are using an entirely different approach using antibacterial polymers, rather than silver, to create bioactive nanoparticles.²

Using chemical polymerisation techniques Jang coated silica-core nanoparticles with a thin layer of antibacterial polymer. He found that these encapsulated nanoparticles have excellent efficacy against *S. aureus* and also *Escherichia coli* – the bacteria that causes food poisoning.

By varying the diameter of the silica core Jang obtained uniformly-sized particles that crucially do not aggregate, an undesirable trait because it reduces the active surface area. 'Antibacterial nanostructures with high surface areas provide enhanced efficacy compared to their bulk counterparts,' says Jang.

He describes some of the challenges for his future research: 'Key issues involve the separation and recovery of the antimicrobial nanoparticles from a target solution.' But, he says, 'the introduction of antimicrobial nanoparticles with magnetic properties could prove to be a clever solution.' Janet Crombie

References

- 1 J Buckley *et al.*, *Chem. Commun.*, 2008, DOI:10.1039/b809086f
- 2 J Jang and Y Kim, *Chem. Commun.*, 2008, DOI:10.1039/b809137d

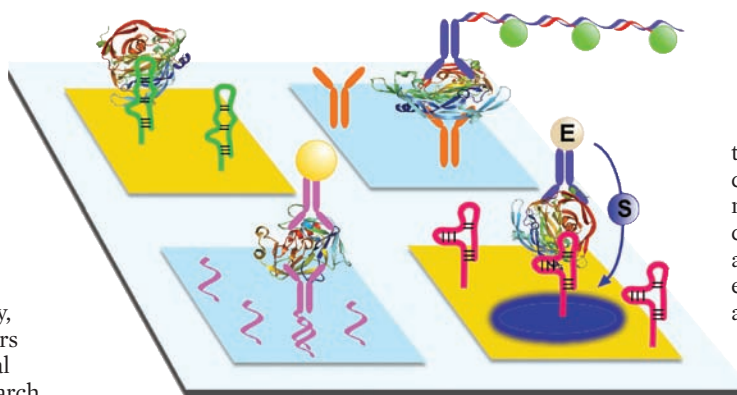
Disease snapshots

Hye Jin Lee, Alastair Wark and Robert Corn look at the latest breakthroughs in the use of microarray technology for the fast detection and treatment of cancer and other diseases

Detecting the presence of protein biomarkers in bodily fluids such as blood and urine offers a convenient route to critical information about the onset and progression of many types of diseases. Consequently, the discovery of new biomarkers is rapidly becoming an essential component of biomedical research with the goal of developing accurate tests that allow earlier detection and improve disease classification. With the end goal of developing a more targeted approach to patient therapy, and monitoring response to treatment.

However, the challenge of identifying and quantitatively measuring biomarkers, especially proteins, is a tough one. Many potential targets reside at concentrations several orders of magnitude lower than the most abundant proteins typically found in biological samples. Therefore, detection methods with both high sensitivity and specificity are needed. It is also becoming increasingly evident that complex diseases cannot be characterised through a single biomarker. Instead, large sets of proteins need to be screened simultaneously in an individual sample to reveal characteristic patterns where some proteins are over expressed and others strongly repressed compared to healthy patient samples. This will provide a more accurate assessment of the disease sub-type and the level of progression, where even small changes between different protein levels will be highly informative.

Underpinning the emergence of biomarker technology is the development of new proteomic tools alongside a concomitant effort by scientists to understand disease at the molecular level. The



most relied upon methods for protein diagnostics include gel-electrophoresis, western blotting and enzyme-linked immunosorbent assays (ELISA). Over the last decade the utility of mass spectrometry for protein mixture analysis has also improved dramatically. However, none of these techniques are well-suited for the multiplexed analysis of many targets within an individual sample and typically lack the sensitivity necessary for fully resolving proteins present in biological samples at very low concentrations.

Microarray-based techniques, consisting of large numbers of biomolecular capture probes immobilised on a single substrate surface, have become the leading technique for the high-throughput monitoring of biomolecular interactions. Each capture probe has a high binding affinity towards a particular target biomolecule present in the sample solution. However, despite the widespread use of DNA microarrays, the application of protein microarrays has proven to be considerably more challenging. This is due to both a limited availability of biomarker capture probes and the surface immobilisation of these probes without subsequent loss in bioactivity. Most efforts have focused on the successful development of antibody microarray

Microarrays are used to detect protein biomarkers in blood and urine

technology, but the issue of assay cross-reactivity especially as the number of probes and sample complexity increases still remains a fundamental hurdle. This has encouraged researchers to explore alternative biomolecular probes whose protein binding properties are similar to or better than those of antibodies. Examples include DNA and RNA aptamers, peptides and cell or tissue lysates that can be applied in an array format for protein biomarker measurements.

In addition to improving specificity, rapid advances are being made in the development of signal amplification methodologies for detecting interactions between molecular probes and their protein targets. It is essential that these new technologies can be readily applied in an array format without compromising the integrity of neighbouring array elements. Novel surface-based enzymatic amplification reactions such as rolling circle amplification have been used to further lower detection limits. Advances in nanotechnology have also enabled more sensitive detection by labelling protein probe molecules with different types of nanoparticles that open up a variety of new optical, electrical and magnetic techniques for biomarker detection.

Undoubtedly, as improvements in design and application continue, microarray technologies will play an increasingly important role in improving our understanding and treatment of disease.

Read Hye Jin Lee, Alastair Wark and Robert Corn's Highlight 'Microarray methods for protein biomarker detection' in issue 8, 2008 of The Analyst

Reference
H J Lee *et al.*, *Analyst*, 2008, **133**, 975 (DOI: 10.1039/b717527b)

A photograph of a woman in a white tennis shirt and sunglasses, captured in a dynamic pose as if hitting a tennis ball with a racket. The background is a clear blue sky and a green tennis court with a black net.

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Medicinal reasons

Yixin Lu talks to Vikki Allen about his dreams and the importance of medicinal chemistry



Yixin Lu

Yixin Lu is an assistant professor at the National University of Singapore. His main areas of interest are medicinal chemistry and asymmetric catalysis.

Who or what inspired you to become a scientist?

In my childhood, scientists were very highly regarded. In the past few decades, scientific and technological advances and inventions have transformed our world, and scientists are the heroes who made all these possible. It was a dream for me to become a scientist.

What motivated you to specialise in organic and medicinal chemistry?

Making completely new molecules with desired properties and functions is truly interesting and challenging. What is more, modern organic chemistry is very powerful; it also contributes enormously to developments in related fields, for example, biological sciences, materials science and medicinal chemistry. Developing efficient catalytic asymmetric synthetic methods is a major goal in our research.

Medicinal chemistry is a subject which is highly relevant to human health and I cannot think of anything more important than this. Medicinal chemistry relies so heavily on organic chemistry; the vast majority of synthetic molecules capable of interacting with biological systems are prepared by organic chemists. Being an organic chemist working in the areas related to medicinal chemistry means I can really do something with practical clinical applications – this is truly exciting.

Do you remember your first experiment?

The first organic experiment I carried out gave me many products. I still remember it took me almost a day to separate all those compounds, and I even had to miss going to the movies that night – it was a tough starting point!

What hot project are you working on at the moment?

We are currently looking at asymmetric organocatalysis and using substoichiometric amounts of small organic molecules to catalyse chemical reactions. One main focus is to develop novel enantioselective organic reactions which can be promoted by primary amino acid-derived organocatalysts. Ever since the renaissance of organocatalysis in 2000, proline has emerged as one of the most powerful and versatile organocatalysts. Surprisingly, the use of primary amino acids as

organocatalysts has been largely unexplored in the past few years. The potential of primary amino acids and their structural derivatives as privileged organocatalysts needs to be fully explored. Such research would greatly contribute to asymmetric organocatalysis.

What's going to be the next big thing in your field?

It is always a lot easier to look back into history and learn a lesson from the past than to predict what is going to happen in the future, even in your own field. I think that the development of organocatalytic systems that can truly mimic the enzymatic actions in nature will have a huge impact on asymmetric synthesis and catalysis.

You have trained and worked in a number of countries.

What made you choose to come to Singapore? In your experience, what are the benefits/disadvantages of working in Singapore compared to the other countries you have worked in?

I was born and raised in China, received my PhD in Canada, carried out postdoctoral work in Japan, worked briefly in the USA, and currently work in academia in Singapore. I have been exposed to both eastern and western cultures and I think a good mix of cultures is the best. This is why Singapore attracted me – it is a unique place with a blend of cultures, like a bridge linking the East and the West. The funding situation in Singapore is relatively good. Young faculty members are offered good research money and there are ample opportunities for interdisciplinary collaborations. However, as a city country, the chemical society in Singapore is really small. Chemists need to work hard to get connected to the outside world and be vigorously involved in the international activities.

What do you do when you aren't working?

I enjoy life as much as I can. I play with my daughter and spend wonderful time with my family. I also love sports and travelling. I try to play sport on a weekly basis to keep myself physically fit. My philosophy is to work hard and play hard.

If you weren't a scientist, what would you be?

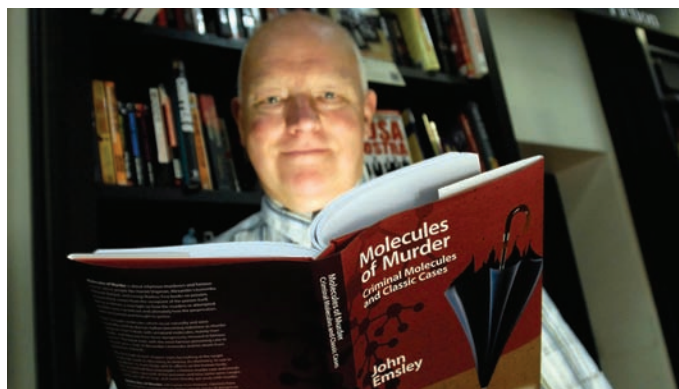
I really enjoy badminton so I probably would want to be a sports star.

Essential elements

Molecules of Murder book launch

On 30 July the RSC, with Waterstone's bookshop Gower Street London, were delighted to host the launch of John Emsley's highly anticipated book *Molecules of Murder: Criminal Molecules and Classic Cases*. John Emsley is a great science communicator, best known for his series of highly readable books about everyday chemistry. His latest book looks at 10 toxic molecules, discusses their chemistry and effects in humans, and re-examines their deliberate misuse in high profile murder cases.

At the book launch, guests were joined by two actors in Victorian costume, posing as the murderer and victim from Chapter 2 of the book: Hyoscine and the Murder of Belle Elmore (Mrs Crippen). The infamous Edwardian killer Dr Crippen poisoned his wife, Belle Elmore, then dissected and buried her under the cellar floor. The victim was a minor celebrity noted for her flamboyant clothing, and had appeared at



music halls around the country at that time. The two came to life in the basement of Waterstone's bookshop, and intrigued guests with spine chilling tales of poison and murder!

John Emsley signed copies of the book, described his reasons for embarking on the project and then read a piece of the work. Guests reading the book for the first time were interested to find out about other murder cases, such as the use of ricin in a rolled

umbrella to assassinate Georgi Markov 30 years ago, and most recently the murder of Alexander Litvinenko in London by polonium. *Molecules of Murder* is a gripping read with appeal to chemists and non-chemists alike. Anyone with an interest in popular science and crime will be enthralled by this exciting new book.

For more information please visit www.rsc.org/books

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Ascience feast in Philadelphia

It was an action-packed few days at the ACS Fall 2008 National Meeting in Philadelphia. The first print issue of *Energy & Environmental Science* generated a lot of interest, with its impressive range of articles on solar cells, hybrid fuel cells, hydrogen storage, biofuel production, sustainable energy, and more. *Integrative Biology* and *Metalomics*, the two new journals launching in 2009, were in the spotlight and grabbed

the attention of many visitors to the RSC booth. RSC Publishing staff were on hand as people signed up for journal e-alerts, hoping to win a solar-powered charger for mobile devices. The book sale proved popular, and authors John Emsley (*Molecules of Murder*) and Stephen Beckett (*The Science of Chocolate*) signed copies of their recent books for an appreciative audience. Other activities included stimulating

talks on science writing and chocolate – and the arrival of cookies, cakes and other goodies, gave everyone a chance to boost their energy levels!

The RSC Reception, held at a nearby Philadelphia hotel, gave assembled guests the opportunity to hear from RSC President Dave Garner about developments across the whole of the RSC, including how the RSC Roadmap will shape future RSC strategy.

Chemical Science (ISSN: 1478-6524) is published monthly by the Royal Society of Chemistry, Thomas Graham House, Science Park, Milton Road, Cambridge UK CB4 0WF. It is distributed free with *Chemical Communications*, *Dalton Transactions*, *Organic & Biomolecular Chemistry*, *Journal of Materials Chemistry*, *Physical Chemistry Chemical Physics*, *Chemical Society Reviews*, *New Journal of Chemistry*, and *Journal of Environmental Monitoring*. *Chemical Science* can also be purchased separately. 2008 annual subscription rate: £199; US \$396. All orders accompanied by payment should be sent to Sales and Customer Services, RSC (address above). Tel +44 (0) 1223 432360, Fax +44 (0) 1223 426017. Email: sales@rsc.org

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