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ISSN 1359-7345 CODEN CHCOFS (1) 1–124 (2008)

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See Jonathan L. Sessler *et al.*, pp. 24–34.
Strapped and other topographically nonplanar calixpyrrole analogues display improved anion affinities and enhanced selectivities relative to unfunctionalized calix[4]pyrroles.
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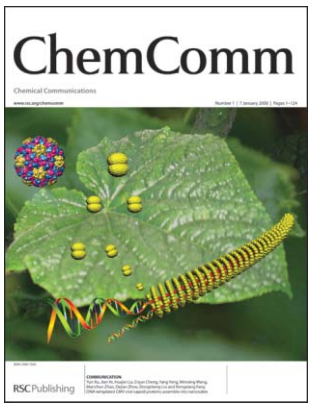

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See Dongsheng Liu *et al.*, pp. 49–51.
Protein nanotubes growing on DNA template.
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CHEMICAL BIOLOGY

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
January 2008/Volume 3/Issue 1
www.rsc.org/chembiology

EDITORIAL

ChemComm gets set for another high impact year

Welcome to the first issue of *ChemComm* for 2008. In this Editorial we take a glimpse at the exciting year ahead and welcome Professor Peter Kündig as the new Chair of the *ChemComm* Editorial Board.

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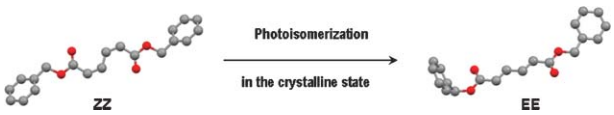
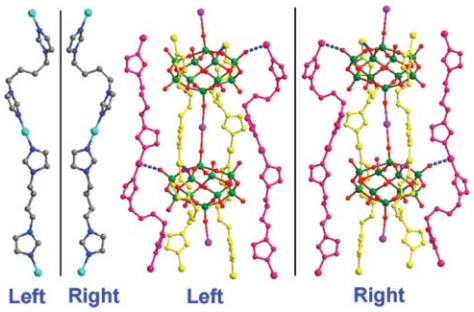
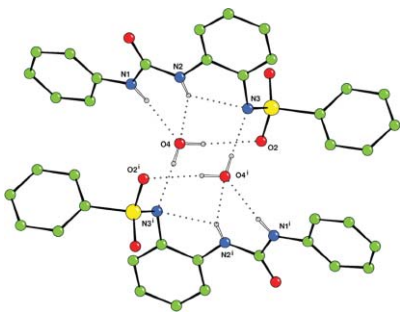
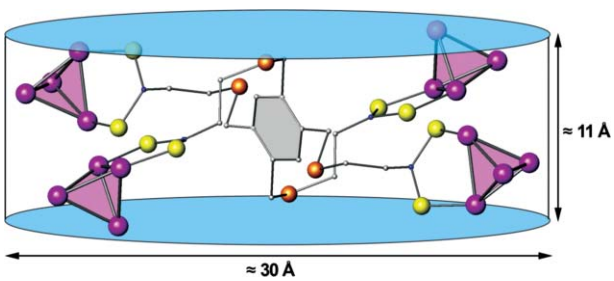
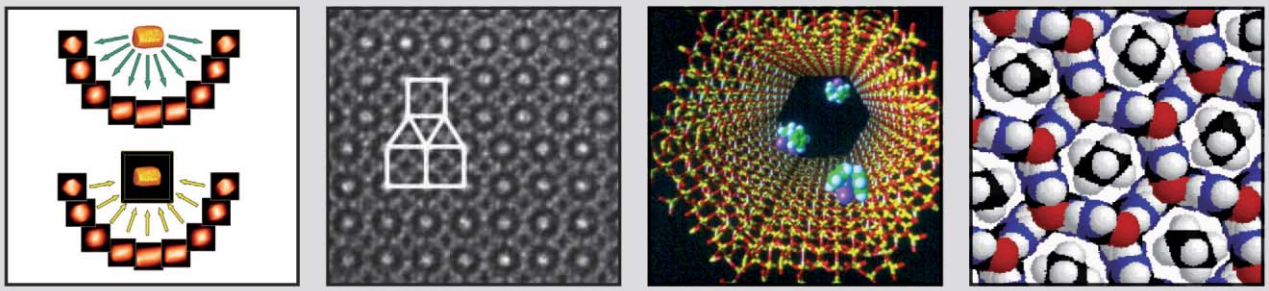




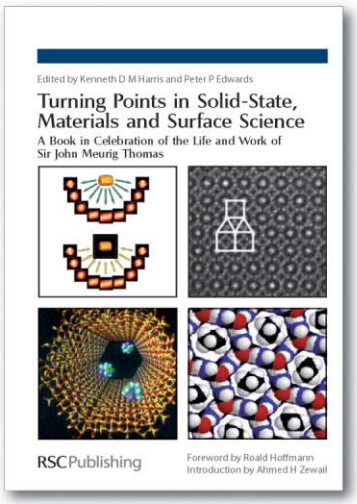




Turning Points in Solid-State, Materials and Surface Science



A Book in Celebration of the Life and Work of **Sir John Meurig Thomas**



Edited by: Kenneth D M Harris and Peter P Edwards
Foreword by: Roald Hoffmann
Introduction by: Ahmed H Zewail
Publication date: November 2007
Publisher: RSC Publishing
Book Type: Professional Reference
ISBN: 9780854041145
Price: £99.95

Turning Points in Solid-State, Materials and Surface Science provides a state-of-the-art survey of some of the most important recent developments across the spectrum of solid-state, materials and surface sciences, while at the same time reflecting on key turning points in the evolution of this scientific discipline and projecting into the directions for future research progress.

The book serves as a timely tribute to the life and work of Professor Sir John Meurig Thomas FRS, who has made monumental contributions to this field of science throughout his distinguished 50-year career in research, during which he has initiated, developed and exploited many important branches of this field. Indeed, the depth and breadth of his contributions towards the evolution and advancement of this scientific discipline, and his critical role in elevating this field to the important position that it now occupies within modern science, are demonstrated recurrently throughout the chapters of this book.

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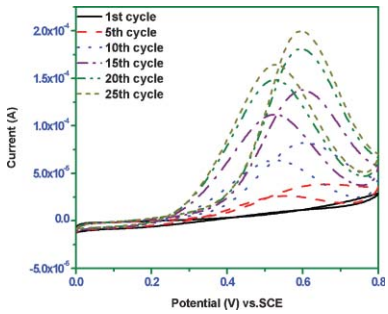
High performance platinized titanium nitride catalyst for methanol oxidation

O. T. Muhammed Musthafa and Srinivasan Sampath*

Pt–TiN: a highly efficient electrocatalyst for methanol oxidation.



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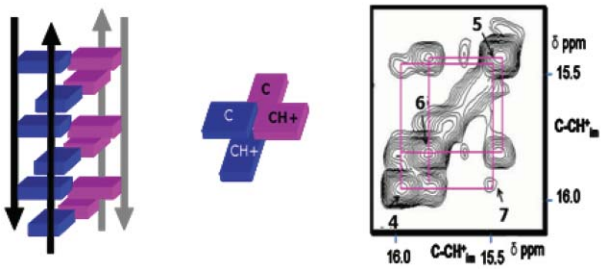
The RNA_2–PNA_2 hybrid i-motif—a novel RNA-based building block

Saikat Chakraborty, Souvik Modi and Yamuna Krishnan*

We report the formation of a hybrid RNA_2–PNA_2 i-motif comprised of two RNA and two PNA strands based on the sequence specific self assembly of RNA, with potential as a building block for structural RNA nanotechnology.



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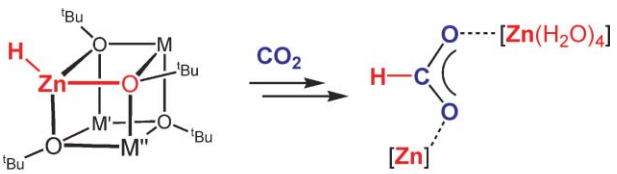
Lithium-promoted hydrogenation of carbon dioxide to formates by heterobimetallic hydridozinc alkoxide clusters

Klaus Merz, Mariluna Moreno, Elke Löffler, Lamy Khodeir, Andre Rittermeier, Karin Fink, Konstantinos Kotsis, Martin Muhler and Matthias Driess*

The hydridozinc hetero(bi)metallic alkoxides **1a–1d** represent the first molecular models for the Zn–H assisted and Li-promoted hydrogenation of carbon dioxide on zinc oxide supports to give formates selectively.



1a: M = M' = M'' = ZnH
1b: M = Li(thf), M' = M'' = ZnH
1c: M = M' = Li(thf), M'' = ZnH
1d: M = M' = M'' = Li(thf)

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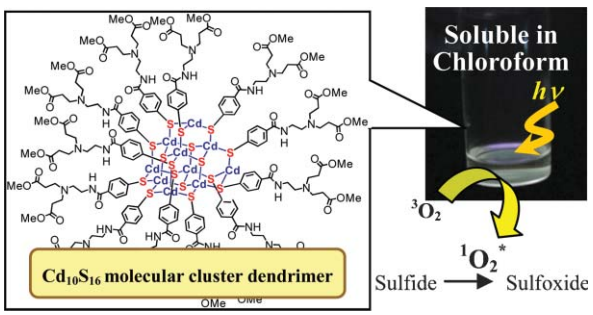
Preparation and photosensitizing property of novel $Cd_{10}S_{16}$ molecular cluster dendrimer

Takaaki Tsuboi, Yutaka Takaguchi* and Sadao Tsuboi

A successful photooxygenation reaction of sulfides to sulfoxides using a newly prepared $Cd_{10}S_{16}$ molecular cluster dendrimer.



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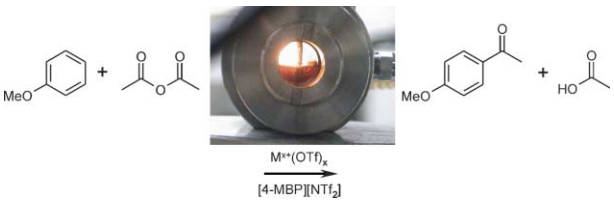
Continuous catalytic Friedel–Crafts acylation in the biphasic medium of an ionic liquid and supercritical carbon dioxide

Firas Zayed, Lasse Greiner, Peter S. Schulz, Alexei Lapkin and Walter Leitner*

Various metal triflates immobilised in an ionic liquid with supercritical CO_2 as the mobile phase are efficient continuous Friedel–Crafts acylation catalysts.



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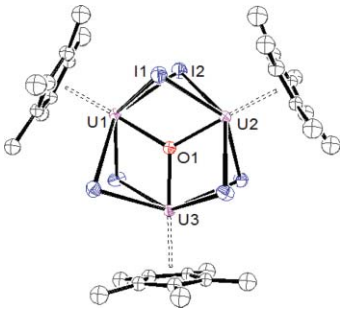
Activation and reduction of diethyl ether by low valent uranium: formation of the trimetallic, mixed valence uranium oxo species $[U(Cp^{RR'})(\mu\text{-}I)_2]_3(\mu^3\text{-}O)$ ($Cp^{RR'}$ = C_5Me_5, C_5Me_4H, $C_5H_4SiMe_3$)

Christopher P. Larch, F. Geoffrey N. Cloke* and Peter B. Hitchcock

The reaction of UI_3 and a range of potassium cyclopentadienyl reagents in diethyl ether results in novel two-electron reduction of the solvent, affording trimetallic, mixed valence uranium oxo species.



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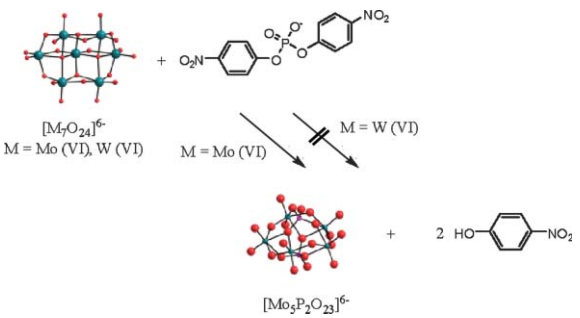
Questioning the paradigm of metal complex promoted phosphodiester hydrolysis: $[Mo_7O_{24}]^{6-}$ polyoxometalate cluster as an unlikely catalyst for the hydrolysis of a DNA model substrate

Els Cartuyvels, Gregory Absillis and Tatjana N. Parac-Vogt*

The first example of a phosphodiester bond cleavage promoted by a highly negatively charged polyoxometalate cluster has been discovered.



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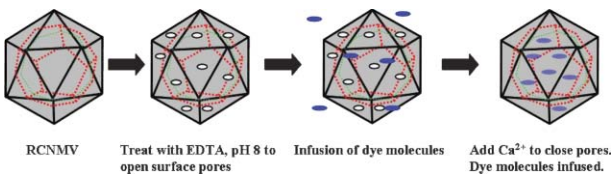
Infusion of dye molecules into *Red clover necrotic mosaic virus*

LiNa Loo, Richard H. Guenther, Steven A. Lommel and Stefan Franzen*

Encapsulation of fluorescent dyes and drugs inside a virus capsid is demonstrated using reversible opening and closing of pores.



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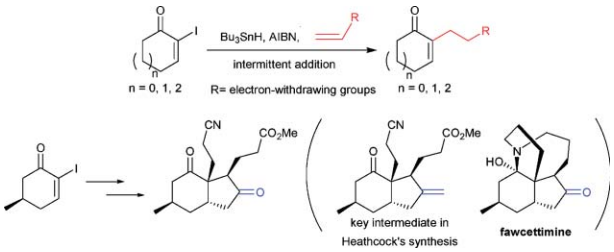

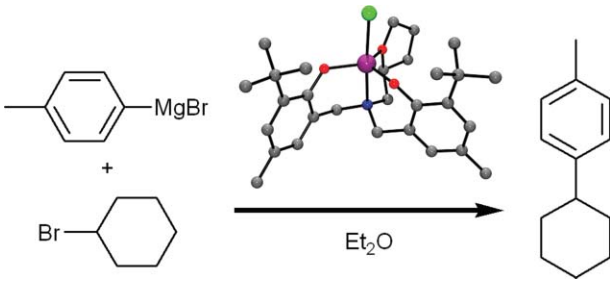

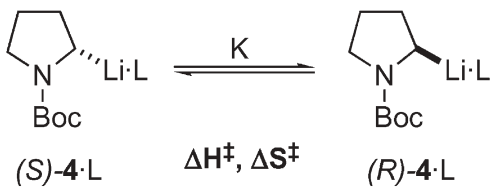

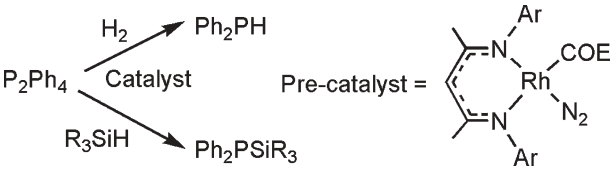

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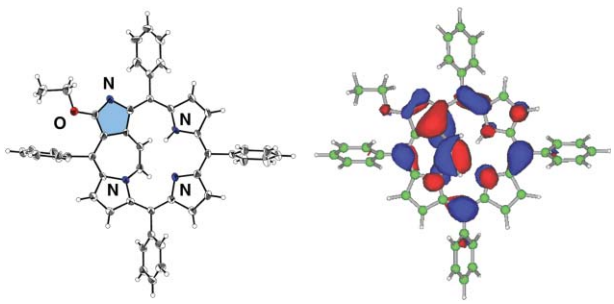

Endocyclic extension of porphyrin π-system in etheno-bridged N-confused tetraphenylporphyrin

Motoki Toganoh, Tomoyuki Kimura and Hiroyuki Furuta*

Etheno-bridged N-confused tetraphenylporphyrin was synthesized through flipping of the confused pyrrole ring and endocyclic extension of [18]annulenic π-conjugated system was exemplified by the absorption spectra as well as calculations.

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1,2-Addition of trialkylaluminium reagents to *N*-diphenylphosphinoylketimines in the absence of any additional reagents

Rüdiger Reingruber and Stefan Bräse*

Using reactive but environmentally benign trialkylaluminium reagents for the 1,2-addition on acetophenone- and benzophenone-derived ketimines, α-trisubstituted amines were obtained in excellent yields up to 99% under mild conditions.

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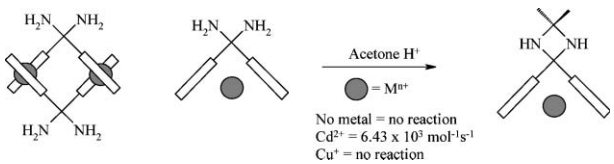

Metal-specific allosteric activation and deactivation of a diamine

Hayley J. Clayton, Lindsay P. Harding, John P. Irvine, John C. Jeffery, T. Riis-Johannessen, Andrew P. Laws, Craig R. Rice* and Martina Whitehead

The reaction of a potentially tetradentate bis(pyridyl–thiazole) ligand with acetone is allosterically activated upon complexation with Cd(II) but deactivated by reaction with Cu(I), demonstrating metal-specific allosteric controlled reactivity.

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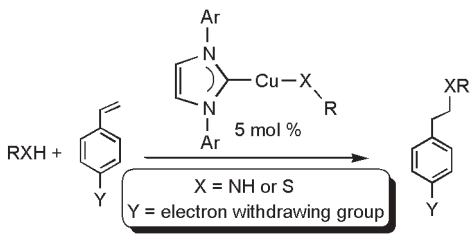

Anti-Markovnikov hydroamination and hydrothiolation of electron-deficient vinylarenes catalyzed by well-defined monomeric copper(I) amido and thiolate complexes

Colleen Munro-Leighton, Samuel A. Delp, Nikki M. Alsop, Elizabeth D. Blue and T. Brent Gunnoe*

Monomeric Cu(I) amido and thiolate complexes that are supported by the *N*-heterocyclic carbene ligand 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr) catalyze the hydroamination and hydrothiolation of electron-deficient vinylarenes.

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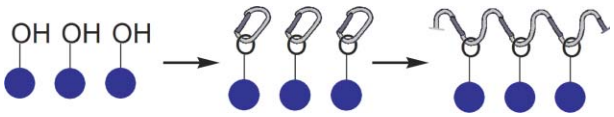
Tagging alcohols with cyclic carbonate: a versatile equivalent of (meth)acrylate for ring-opening polymerization

Russell C. Pratt, Fredrik Nederberg, Robert M. Waymouth and James L. Hedrick*

Coupling of alcohols to a biocompatible cyclic carbonate scaffold serves as a general method to introduce pendant functional groups into polycarbonates and block copolymers.



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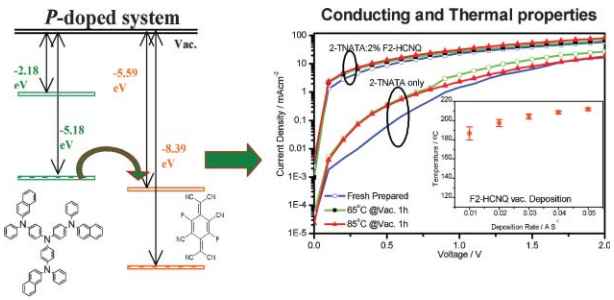
An organic *p*-type dopant with high thermal stability for an organic semiconductor

Zhi Qiang Gao, Bao Xiu Mi,* Gui Zhen Xu, Yi Qian Wan, Meng Lian Gong, Kok Wai Cheah and Chin H. Chen

To overcome the thermal instability of a *p*-doped organic hole transporting layer using the state-of-the-art *p*-type dopant, 2,3,5,6-tetrafluoro-7,7,8,8-tetracyanoquinodimethane, a potent electron accepter, 3,6-difluoro-2,5,7,7,8,8-hexacyanoquinodimethane, has been found to possess superior thermal stability and proved to be an excellent *p*-type dopant.



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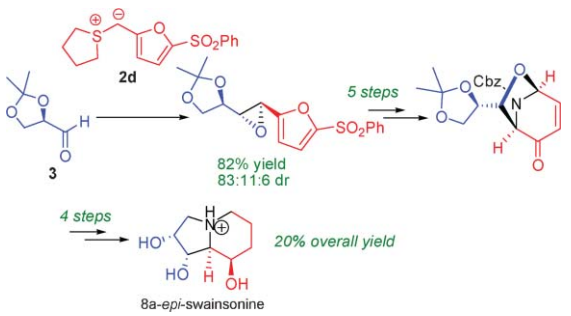
Application of furyl-stabilized sulfur ylides to a concise synthesis of 8a-*epi*-swainsonine

Jie Bi and Varinder K. Aggarwal*

A short synthesis of 8a-*epi*-swainsonine is presented which utilizes an epoxidation reaction between *R*-glyceraldehyde dimethylacetonide and the achiral furyl-substituted sulfonium ylide **2d** as one of the key steps.



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Chemical Biology

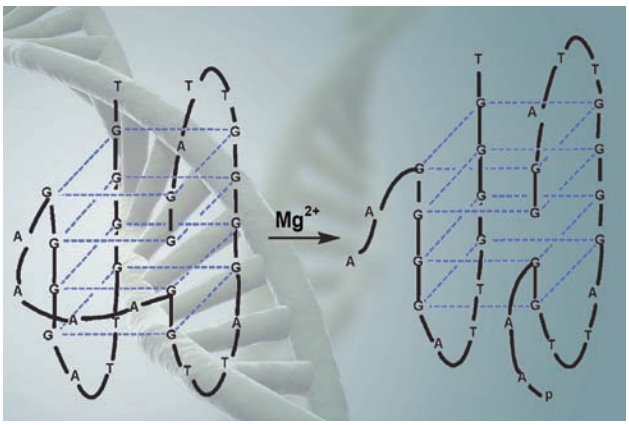
Serendipitous discovery could explain G-quadruplex function *in vivo*

Self-destructing DNA

Singaporean scientists have discovered a new type of catalytic DNA that can cut itself in two.

Tianhu Li and co-workers from the National University of Singapore have observed DNA perform hydrolytic self-cleavage at a specific site. The researchers found that structures called G-quadruplexes are core to these catalytic DNA molecules – DNAzymes – and the results could have important implications in understanding G-quadruplex function *in vivo*.

Found in nucleic acids, G-quadruplexes are stacks of two or more square planar arrays of guanine bases. They are thought to exist in a number of important regions of DNA *in vivo*, including those linked to defence against disease and to aging. The structures have attracted attention from scientists for their unusual spatial arrangement and many thousands of potential quadruplex formation sites have been identified in the human genome. But, while they appear to help control gene activity, their biological function is not yet completely understood.



The DNA folds into a G-quadruplex and cleaves itself in two

Now, in a serendipitous discovery, Li and co-workers have shown that DNA containing certain G-quadruplexes can self-cleave *in vitro*. The team stumbled onto this self-cleavage accidentally when attempting to design a transesterification reaction in a guanine-rich oligonucleotide.

'The discovery of self-cleavage activity in a short DNA molecule is a landmark finding made all the more interesting by the fact that it is mediated through a G-quadruplex motif,' said Jerry Davies, an expert on nucleic acid structure and function from Queen's University Belfast, UK. 'G-quadruplexes can adopt a wide variety of folding topologies and this raises the possibility that some may catalyse biologically important DNA cleavage reactions *in vivo*,' he said.

Li explained that this was a possibility, but added: 'We might need to further study whether this type of hydrolytic self-cleavage of DNA could be used by certain DNA-related cellular and viral processes *in vivo*.' The team said that it hopes the findings will inspire others to further explore the chemical and biological properties of G-quadruplexes.

Freya Mearns

Reference
X Liu *et al*, *Chem. Commun.*, 2008, DOI: 10.1039/b713445b

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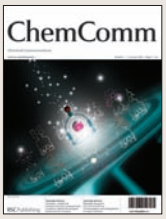
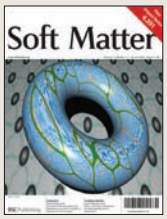




Research highlights

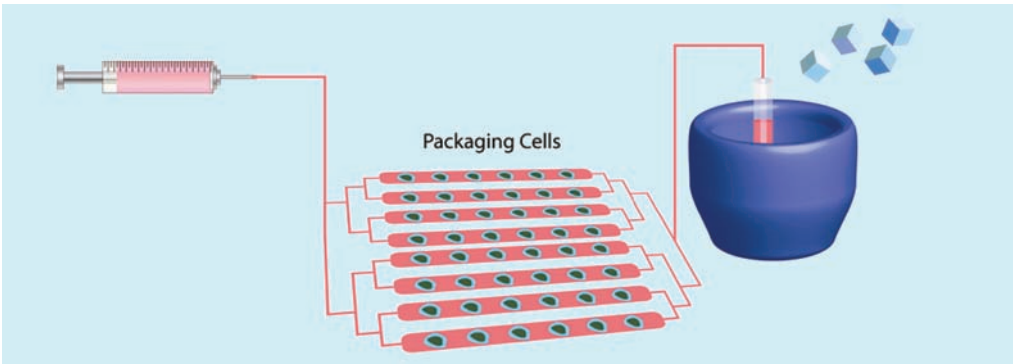
Microfactory supplies retrovirus for gene therapy applications

The viral production line

Not all viruses are bad news... Martin Yarmush and colleagues at the Massachusetts General Hospital in Boston, US, have designed a microfluidic bioreactor that can generate a continuous stream of freshly produced retrovirus ready for immediate use.

Having evolved over millions of years, viruses are nature's specialised gene delivery vehicles. Retroviruses in particular are able to introduce genetic material into target cell DNA, providing long-term gene expression. It is this ability that makes them ideal for use in gene therapy; by introducing genes modified to have a therapeutic effect they can be used to treat or even cure disease. However, their use in medicine is hindered because the viruses survive at body temperature for only a few hours so new ways of producing large amounts of virus are in demand.

In Yarmush's bioreactor, virus is produced by so-called packaging cells held in the channels of the device. When the researchers compared the bioreactor's virus output with conventional, static, tissue culture methods, they found a 1.4- to 3.7-fold increase over 5 days. This higher output was obtained only when the virus was exposed immediately to low temperatures to prevent its rapid degradation.



Packaging cells held in channels in a bioreactor can make a continual stream of retrovirus

Reference
H N Vu *et al*, *Lab Chip*, 2008, DOI: 10.1039/b711577f

John Yin, an expert in biomedical engineering at the University of Wisconsin-Madison, US, explained that the work demonstrates that microfluidic systems can be used to quantitatively characterise virus production and control culture conditions. 'It offers potential automation of an otherwise labour-intensive process,' he said.

By collecting and flowing virus supernatant (fluid) over target cells, the researchers confirmed that the bioreactor could be used to infect target cells with virus. Halong Vu, a member of the Boston team, described it as a first step toward developing more sophisticated devices to study viral targeting and infection dynamics for viruses in flowing liquids, such as the bloodstream, for gene therapy applications.

Janet Crombie

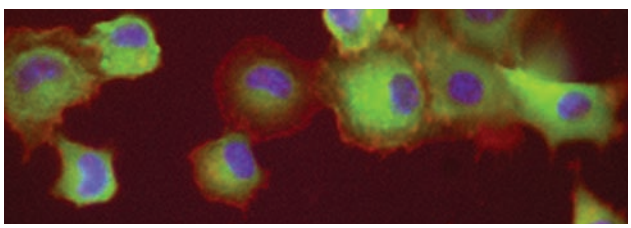
Polymers given the special treatment hold promise for medical implants

Selectively-sticky-back plastic

A simple and effective treatment can make plastics more biocompatible by altering their surface properties.

Jeffrey Schwartz and his group at Princeton University, US, work in the area of interfacial chemistry and noticed a persistent problem with polymers used in biomedical devices. When implanted in the body, the polymer comes in contact with bodily fluids and can be rejected as certain proteins and cells stick to its surface. 'The polymers' mechanical properties are great but surface issues are a stumbling block,' said Schwartz.

Schwartz and his colleague Joseph Dennes set about altering the surface of polyurethanes, a hugely versatile group of polymers used in applications as diverse as stretchy clothing to roller blade wheels. Polyurethanes are also used in medical devices such as artificial organs and synthetic vascular grafts.



Cells stick to a treated polyurethane surface

Reference
T J Dennes and J Schwartz, *Soft Matter*, 2008, **4**, 86 (DOI: 10.1039/b714947f)

The researchers reacted a polyurethane surface with zirconium tetra(*tert*-butoxide); the activated surface could then be used to attach various organic groups to the polymer, introducing properties for better biocompatibility. By attaching a cell-adhesive peptide to the zirconia group the scientists succeeded in encouraging fibroblast cells to grow on the polymer *in vitro*. Fibroblasts are known to help integrate such materials into the body. In a separate experiment, the researchers could also discourage unwanted cell growth by attaching a non-cell-adhesive group.

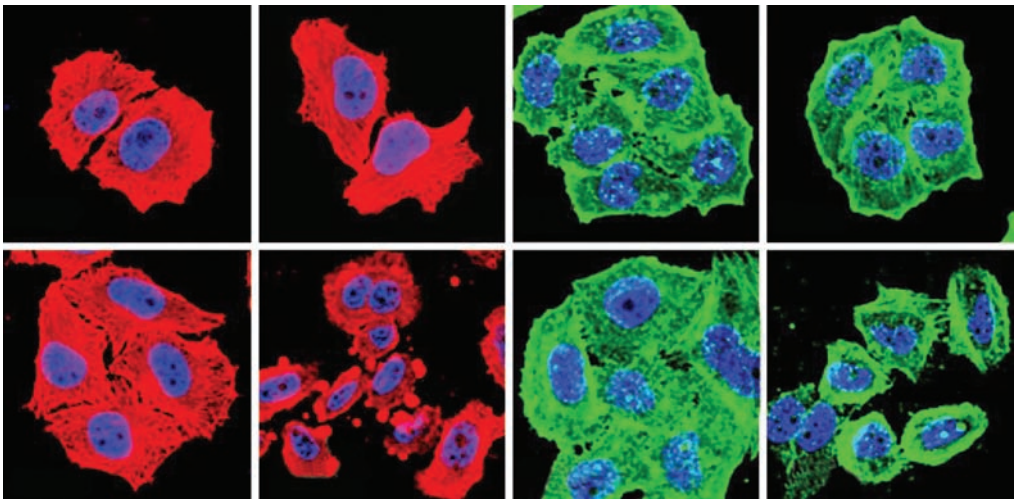
Kim Midwood, an expert on cell-adhesion, at Imperial College London, UK, described the work as elegant, and suggested that 'given the widespread use of polyurethane polymers in medical devices, the approach could have a significant impact on the way biomaterials are designed for medical use.'

The Schwartz group is now continuing its work in this field to control exactly where the cells adhere on the polymer surface.

Gavin Armstrong

Magnetic nanoparticles in action

Turning up the heat on cancer



Cells exposed to nanoparticles (second row) and a magnetic field (second and fourth columns) display disrupted cytoskeletons

Magnetic nanoparticles are being developed as a highly selective cancer treatment, heating tumour cells to death while leaving surrounding healthy tissue unscathed.

Iron oxide nanoparticles that heat up in response to an alternating magnetic field offer a promising approach to cancer therapy – scientists are already running clinical trials to combine the treatment, known as magnetic field hyperthermia (MFH), with traditional chemotherapy. Now chemists in Taiwan are looking to develop a new generation of more effective nanoparticles, while an Indian group has discovered just how MFH kills cells.

Yuh-Jiuan Lin at the Industrial Technology Research Institute (ITRI) in Hsinchu, Taiwan, and colleagues are investigating new nanoparticles that, when injected into a tumour, heat up faster in a magnetic field. Lin doped the iron oxide nanoparticles with gadolinium, an element already used in the magnetic resonance imaging (MRI) procedures used to look at tumours inside the body.

'The better the particles heat up the less you need to use,' said Philip Drake, a member of the ITRI team. 'We'd like to inject as little as possible to minimise any side effects. Magnetic nanoparticles have already been accepted for use in MRI, but for MFH we need to inject about 100 times the current FDA [Food and Drug Administration]-approved dose.'

Dhirendra Bahadur, of the Indian Institute of Technology Bombay in Mumbai, stressed the technique's inherent selectivity. 'Heat can be applied locally to cause fewer side effects,' he said. And oxygen-poor tumour cells are more heat-sensitive than healthy cells anyway, he added.

Bahadur's team has used immunofluorescence microscopy to examine cancer cells after MFH treatment, which showed the cells' underlying cytoskeleton had been 'significantly disrupted.' Until this study, the mechanism by which the method killed cells was unknown.

Both Drake and Bahadur see developing nanoparticles that specifically target cancer cells as the key challenge facing MFH. 'Our intention is to conjugate these nanoparticles with specific ligands or antibodies to make them site-specific,' said Bahadur.

'The use of basic hyperthermia combined with chemotherapy could happen very fast – maybe five years for certain cases,' said Drake. 'Hyperthermia as I'd like to see it, with particles that can actively seek out cancer cells, would be more like twenty-five years!'

James Mitchell Crow

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News in brief

Microfluidics prove in-gene-ious
Analysing genes in individual cells is now simpler, cheaper and more effective thanks to US researchers.

See **www.rsc.org/chembiology** *for a full version of this article.*

This month in *Chemical Science*

Yeast adopts a logical approach
Logic gates made from proteins could lead the way to yeast cells that can self regulate during fermentation, say US scientists.

Drug release watched by NMR
Controlled release of a β-blocker from its silica host has been investigated by solid state NMR spectroscopy.

Enzyme-powered delivery vehicles
Dutch scientists have made nanotubes move using enzyme-powered motors.

Changing climate for coral
As we enter the International Year of the Reef, Janice Lough wonders if the demise of the world's coral reefs may already be irreversible.

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

This month in *Chemical Technology*

Digital displays with better breeding
Mixing dyes with DNA could be the solution for bright, robust displays and digital paper.

Radioactive urine analysis
A system to detect plutonium in urine quickly in an emergency has been developed in Canada.

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

If you wish to receive an e-mail when the next issue of *Chemical Biology*, *Chemical Science* or *Chemical Technology* is published online, you can sign up to the RSC's e-mail alerting service. To sign up, go to www.rsc.org/ej_alert

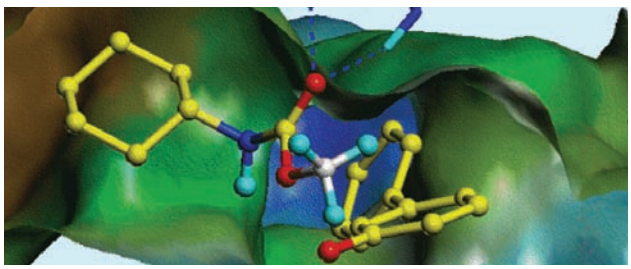
Following the mechanistic trail to find inhibitor binding orientation

A model solution to depression?

Scientists have finally calculated how to inhibit an enzyme linked to anxiety. Quantum and molecular mechanics are proving useful tools for drug design where other approaches fail, says the international team behind the research.

The quantum mechanics/molecular mechanics (QM/MM) approach has allowed Adrian Mulholland at the University of Bristol, UK, and colleagues in Italy and the US, to identify the correct binding orientation for an inhibitor of enzyme fatty acid amide hydrolase (FAAH). Knowledge of the mechanism will help the design of more potent inhibitors, say the researchers.

FAAH is a promising drug target for the treatment of anxiety, pain and depression and its inhibitors have shown analgesic and anti-depressant effects in rats. Carbamate inhibitors are known to bind to FAAH, resulting in covalent modification of catalytic residues and a corresponding loss of enzyme function, although the exact reaction mechanism has been unclear until now. Previously, conventional computational experiments revealed two possible binding orientations for FAAH inhibitors, but were unable to determine which of these leads to enzyme inhibition.



Which way round? Calculations resolve the mystery of inhibitor binding to the anxiety-linked enzyme FAAH

Using the QM/MM approach to model the inhibitor binding process for both orientations, Mulholland and his colleagues have finally solved the mystery. The QM/MM approach finds the intermediates and transition states on the reaction profiles for each binding orientation; the orientation that leads to inhibition has the lowest energy reaction pathway. 'The barrier for reaction was very high for one orientation,' said Mulholland. 'Only one orientation could feasibly produce the experimentally observed product.'

Hua Guo, an expert in modelling enzyme catalysis at the University of New Mexico, in Albuquerque, US, welcomed the research. 'This work showcases the power of the computational approach to understand enzyme binding and catalysis and underscores the importance of substrate binding orientation in enzyme catalysis,' said Guo. *Russell Johnson*

Reference
A Lodola *et al*, *Chem. Commun.*, 2008, DOI: 10.1039/b714136j

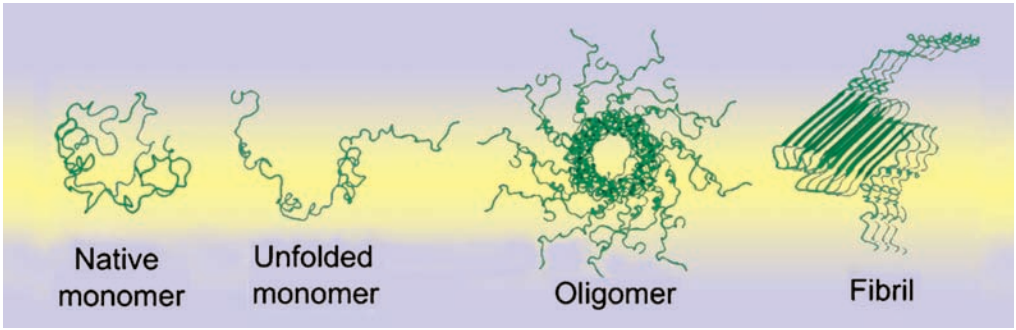
Electrochemical approach reveals self-assembly route of disease-linked protein

Solving the insoluble problem for Parkinson's

European scientists have developed a simple and cheap way to study protein aggregation in Parkinson's disease.

Parkinson's is a progressive disease that affects coordination of movement in sufferers. The condition results from a loss of dopamine-producing nerve cells in the brain. The reason behind the cell death is still unclear, but abnormal build-up of the protein α-synuclein (AS) in the brain is known to occur in patients with some neurodegenerative diseases, including Parkinson's. 'Uncovering why this build-up happens is important to increasing our understanding of Parkinson's and identifying targets for new treatments,' said Kieren Breen, director of research and development at the Parkinson's Disease Society of the UK.

Recently it has been proposed that intermediate forms of AS, as it converts from the soluble native form into insoluble fibrils, are the main pathogenic species. But these are hard to detect directly and the methods normally used to study fibril formation – circular dichroism and fluorescence – are not able to distinguish the early stages of the process. Now, Emil Paleček from the Academy of Sciences of the Czech Republic in Brno, and colleagues from the Czech Republic and Germany, have developed an electrochemical way of monitoring AS aggregation *in vitro*.



The intermediates formed as α-synuclein aggregates into fibrils have been proposed to be pathogenic

Paleček's method relies on AS adsorption at a mercury electrode. Proteins are known to catalyse hydrogen evolution at these electrodes and Paleček's team has used a method called constant current chronopotentiometric stripping to study this hydrogen evolution when catalysed by AS. The technique is remarkably sensitive to local and global changes in protein structure, say the researchers, and it can be used to detect proteins at subnanomolar concentrations.

The destabilisation of the native AS into unfolded monomer followed by aggregation into oligomer, protofibril and finally fibril can be monitored using the technique. 'Our electrochemical determinations reveal previously undetected changes in AS preceding the formation of protofilaments and fibrils,' said Paleček.

The team suggests its technique could allow a better understanding of intermediate formation in AS build-up. Paleček added that the team's results also offer simple methods for investigating various agents' abilities to affect AS aggregation *in vitro*. Such studies could lead to effective strategies for preventing and/or treating Parkinson's disease, he said.

Freya Mearns

Reference
E Paleček *et al*, *Analyst*, 2008, **133**, 76 (DOI: 10.1039/b712812f)

In the current issue of Research Articles...

Peptide ormosils as cellular substrates
Sabrina S Jedlicka *et al*, *J. Mater. Chem.*, 2007, **17**, 5058 (DOI: 10.1039/b705393b)

The chemistry of gliding bacteria
Markus Nett and Gabriele M. König, *Nat. Prod. Rep.*, 2007, **24**, 1245 (DOI: 10.1039/b612668p)

Asprich mollusk shell protein: *in vitro* experiments aimed at elucidating function in $CaCO_3$ crystallization
Yael Politi *et al*, *CrystEngComm*, 2007, **9**, 1171 (DOI: 10.1039/b709749b)

Rapid testing of infection and disease states: the faster the better
Karen M Black and Neeraj Vats, *Analyst*, 2007, **132**, 1183 (DOI: 10.1039/b712103m)

Carboranyl thymidine analogues for neutron capture therapy
Werner Tjarks *et al*, *Chem. Commun.*, 2007, 4978 (DOI: 10.1039/b707257k)

Polar stimulation and constrained cell migration in microfluidic channels
Daniel Irimia *et al*, *Lab Chip*, 2007, **7**, 1783 (DOI: 10.1039/b710524j)

Chemical properties of fatty acid derivatives as inhibitors of DNA polymerases
Ryoichi Nakamura *et al*, *Org. Biomol. Chem.*, 2007, **5**, 3912 (DOI: 10.1039/b710944j)

Milestones in the development of photodynamic therapy and fluorescence diagnosis
Asta Juzeniene *et al*, *Photochem. Photobiol. Sci.*, 2007, **6**, 1234 (DOI: 10.1039/b705461k)

Systems biology of antibiotic production by microorganisms
J Stefan Rokem *et al*, *Nat. Prod. Rep.*, 2007, **24**, 1262 (DOI: 10.1039/b617765b)

Read more at www.rsc.org/chembiology

Interview

Top marks for proteomics

Kathleen Too talks to Thomas Kodadek about Jacques Cousteau, biomarkers and diagnostic tools

Thomas Kodadek

Thomas Kodadek is based at the University of Texas Southwestern Medical Center where he is professor of internal medicine and molecular biology and also director of the division of translational research. His current research focuses on proteomics and the enzymology and regulation of eukaryotic gene expression. Tom is also the chairman of the *Molecular BioSystems* editorial board.

What inspired you to be a scientist?
I always found the idea of working in an area where I didn't already know the answer to be very attractive. I was influenced by science and nature TV when I was young. In particular, I remember the Jacques Cousteau series, which was terrific but did give one a bit of an odd idea about what scientists do. We don't just sail around the world!

What makes proteomics such a hot area of research?
Proteomics has the potential to have a huge impact on medicine. If you ask clinicians what they think would be the biggest breakthrough, it would be the facile discovery of biomarkers for a particular disease state or a response to a particular drug. They would desperately love to have a simple molecular test to help them design treatments. I think that proteomics is the answer.

What is the most exciting project you are working on?
We have developed a technology that we think will allow us to monitor immune system responses to almost any disease state. The method uses peptide-like compounds called peptoids spotted onto slides to form an array. When blood serum is reacted with the array, some of the antibodies in the serum bind to peptoids they recognise. These bound antibodies can be detected because they form a unique pattern of spots of light on the array. Because each person has a different combination of antibodies in their serum, they each have a slightly different pattern of spots.

When you get a disease, such as hepatitis C, the immune system amplifies antibodies associated with the disease. Our aim is to screen a set of people that we know have contracted hepatitis C. Although the background signature would be different for each patient, each would have a high level of hepatitis C antibodies and therefore the same spots would be very bright for all the patients. These peptoids would be a biomarker for hepatitis C. We haven't done that on humans yet; those experiments are ongoing. But we have demonstrated this in animal models.

As the chair of the *Molecular BioSystems'* editorial board, what have you found exciting in the launch and development of the journal?
I've enjoyed seeing the nuts and bolts of how one tries to launch a journal. In terms of a learning experience, it was eye-opening – there is certainly a lot more to it than simply the science. Scientifically, the most exciting thing is the interaction with the excellent board that we have. They are great people, from a number of different backgrounds, and it's been stimulating to interact with them and hear their ideas about the journal.

***Molecular BioSystems* has just gone solo. How do you foresee its growth?**
We are all going to work very hard to make sure that it's a sound, well-established journal that publishes good articles. It will certainly be a place where scientists will want to publish their work. Our review and highlight content is excellent and we are working towards attracting more and better primary content. The journal will become more successful as the areas covered by it become more active in the UK and Europe, combined with our efforts to reach out to emerging scientists in Asia.

What advice would you give to a young scientist wanting to pursue a career in molecular biology or biochemistry?
Focus on really important problems and differentiate yourself from what everybody else will do. People tend to focus on the same thing, and then it's just a question of who can do their experiments the fastest. That's a bad way to do science. Use your imagination, use your cleverness and give yourself some kind of an edge.

What is the most rewarding aspect of your career?
Dealing with my students and post-docs. I am very lucky to hang out with really smart people who are engaged and motivated and love to talk about ideas. I have a great group. They do all the real work. I haven't done an experiment in at least five years, so I owe everything to them. They're a lot of fun to work with.

Instant insight

Natural remedies

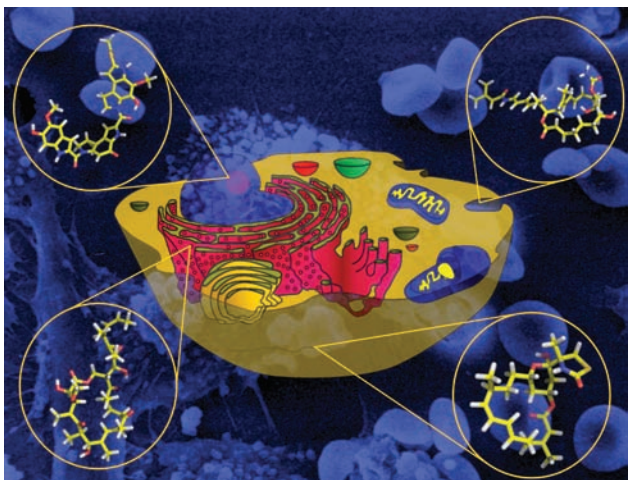
Jason Micklefield of the University of Manchester, UK, looks at how natural products hit the targets other molecules cannot reach

Natural products are an exceptional resource. These secondary metabolites are produced principally by bacteria, fungi, plants and marine organisms. Unlike primary metabolites they are not essential for the normal growth or development of an organism; some function in chemical defence, protecting the producer against invasion or infestation by other organisms, whilst others act as chemical signals, allowing communication and facilitating reproduction in certain species.

But the natural role of the majority of these compounds remains unknown. It is likely that many natural products function by binding with high affinity and selectivity to biological macromolecules including DNA, RNA and particularly proteins. Indeed, it has been suggested that these interactions have been selected for across the 3 billion years of biological evolution.

Natural products often have physiological effects that arise from their innate potential to bind to specific biological targets. These have been recognised for many years. For example, evidence dating back 4000 years refers to plant remedies for various illnesses and even Neanderthal man is suggested to have used medicinally active plants some 60 000 years ago.

Since then, many natural products have been isolated, from plants and other organisms, and shown to elicit potent physiological responses in humans. Not surprisingly, this has led the modern pharmaceutical companies to develop natural products as antibiotics, antifungal, anticancer and immunosuppressive agents as well as other medicines. But despite this, over the past decade, a number of major pharmaceutical companies have ceased to follow up natural products as leads, in favour of simpler synthetic compounds. Regardless of this trend, natural product research in academia and other sectors has advanced significantly during this period.



NEIL DIXON

Advances in structural biology have allowed many cell structures and their interactions with natural products to be characterised

The advent of chemical genetics and powerful high-throughput screening methodologies, has revealed a large number of new cellular targets with which natural products interact.[1] In chemical genomics small molecules, including natural products, are screened with the long term aim of identifying ligands that can modulate the function of all gene products in a cell. As a result many new natural product targets have been discovered that would not be explored in traditional pharmaceutical drug discovery programmes.

Also, with advances in structural biology we have seen a prodigious increase in the number of structures of key cellular targets characterised, including the ribosome, nucleosome and fatty acid synthases. As the sites with which natural products interact have begun to be resolved in detail, the modes of action of many natural products have been established.[1]

Notable advances have also been made in our understanding of natural product biosynthesis.[2] For example, improvements in DNA sequencing have allowed genes encoding biosynthetic pathways to be identified and exploited in so-called genome mining approaches. Many natural product producing organisms are difficult to cultivate in the laboratory and their biosynthetic gene clusters can often remain cryptic. To overcome this, metagenomics approaches, which use DNA recovered from environmental samples, and heterologous expression methods, which use DNA from several different species, have allowed the first glimpses of a vast array of unexplored natural products.

Also, developments in biosynthetic engineering have enabled scientists to reprogram the biosynthesis of several major classes of natural products, altering organisms to make new derivatives. Not only does this increase the number of product analogues for screening, but it also allows the physiochemical and biological properties of key lead compounds to be further optimised.

For more than 3 billion years nature has used natural products to modulate biomolecule function within the cell. Despite this, it has been chiefly only in the past few years, through advances in genomics, structural biology and related technologies, that we have begun to appreciate fully the immense and largely untapped resource that natural products provide.

Read Dixon, Wong, Geerlings and Micklefield's review 'Cellular targets of natural products' in Natural Product Reports.

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2 B Wilkinson and J Micklefield, *Nat. Chem. Biol.*, 2007, **3**, 379

Essential elements

A new journal for the new year

A new journal, *Energy & Environmental Science,* will be launched in summer 2008 by RSC Publishing. The announcement was made at the recent MRS Fall meeting in Boston, US, attended by RSC staff.

'The challenges relating to energy and environmental science that face the world today are complex,' said Robert Parker, managing director of RSC Publishing. 'From alternative fuels to environmental impacts, climate change to energy conversion and storage – research in the chemical sciences underpins all the work that is so important to the future of our world. RSC Publishing recognises the significance of this area by launching *Energy & Environmental Science*.'

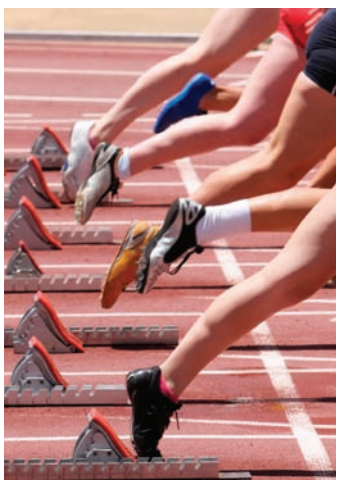
The journal will link all aspects of the chemical sciences by publishing research relating to energy conversion and storage, alternative fuel technologies, and environmental science. The monthly issues will contain topical reviews and original research as communications and full papers. Editor Philip Earis, announcing the appointment of Nathan Lewis of Caltech as editorial board chair, said: 'We're delighted to have such a prestigious scientist driving the journal forward.'

By recognising the complexity of issues and challenges relating to energy and environmental science, it is expected that the journal will provide a forum for work of an interdisciplinary nature across both the (bio)chemical sciences and chemical engineering disciplines.
www.rsc.org/ees

It's off and running!

Less than three years after the first ever publication in 2005 – *Molecular BioSystems* is now officially off and running as a solo publication.

Molecular BioSystems' editorial board chair, Thomas Kodadek, commented: 'Biologists interested in systems-level phenomena can benefit greatly from tools being developed by chemists to monitor and manipulate cellular processes. Likewise, chemists will increasingly turn to -omics approaches to understand mechanism of action and specificity of bioactive molecules. *Molecular BioSystems* provides a home for this rapidly developing interdisciplinary science.'



ISTOCKPHOTOS

Successes since launch include being indexed in MEDLINE, its first impact factor of 2.45*, rapid publication times of around 80 days from receipt to publication of papers, and extra online features such as enhanced HTML articles via RSC Prospect and 3D visualisation of complex molecules.

From January 2008, *Molecular BioSystems* is available with a subscription or as part of RSC Journals Package A/A+.
See www.molecularbiosystems.org

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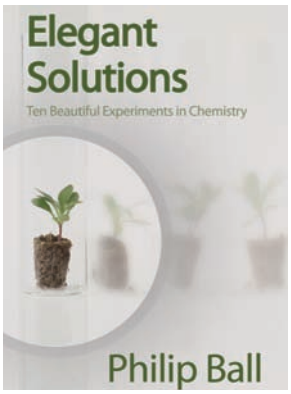

Elegant Solutions: Ten Beautiful Experiments in Chemistry by Philip Ball has been awarded the 2007 Dingle Prize. The Dingle Prize, presented by The British Society for the History of Science Outreach and Education Committee, acknowledges the best recent book that communicates the history of science, technology and/or medicine to a wide audience of non-specialists.

Published by RSC Publishing in 2005, *Elegant Solutions: Ten Beautiful Experiments in Chemistry* has received widespread critical acclaim. Philip Ball has won several awards himself, including the James T Grady–James H Stack Award for Interpreting Chemistry for the Public, awarded by the American Chemical Society in 2006. Philip is also a regular contributor to *Chemistry World*, with his column, '*The Crucible*'.

For more information on this award-winning book, and many other international best sellers, visit www.rsc.org/books

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