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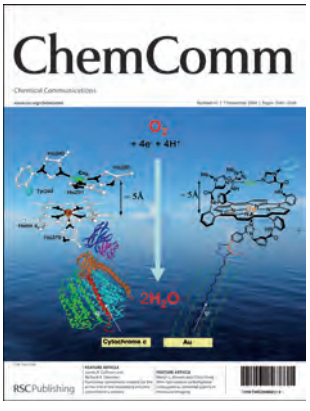
IN THIS ISSUE

ISSN 1359–7345 CODEN CHCOFS (41) 5041–5244 (2008)

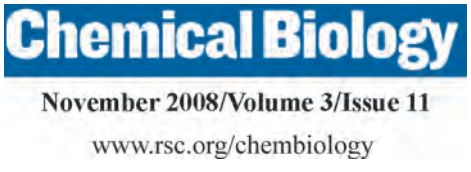


Cover
See James P. Collman and Richard A. Decréau, pp. 5065–5076.
The cover illustrates the catalytic reduction of oxygen to water by cytochrome c oxidase and by a functional biomimetic model of its active site.
Image reproduced by permission of James P. Collman and Richard A. Decréau from *Chem. Commun.*, 2008, 5066.

CHEMICAL BIOLOGY

B81

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.



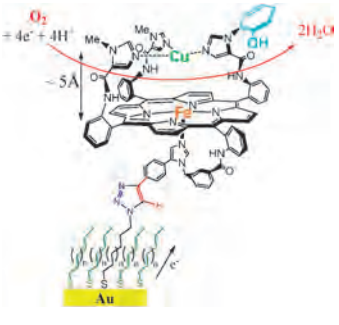
FEATURE ARTICLES

5065

Functional biomimetic models for the active site in the respiratory enzyme cytochrome c oxidase

James P. Collman* and Richard A. Decréau

A functional model of cytochrome c oxidase active site covalently attached to a liquid crystalline SAM film on an Au electrode continuously catalyzes the four-electron reduction of dioxygen under rate limiting electron flux.



Chemical Communications (print: ISSN 1359-7345; electronic: ISSN 1364-548X) is published 48 times a year by the Royal Society of Chemistry, Thomas Graham House, Science Park, Milton Road, Cambridge, UK CB4 0WF. All orders, with cheques made payable to the Royal Society of Chemistry, should be sent to RSC Distribution Services, c/o Portland Customer Services, Commerce Way, Colchester, Essex, UK CO2 8HP. Tel +44 (0)1206 226050; E-mail sales@rscdistribution.org

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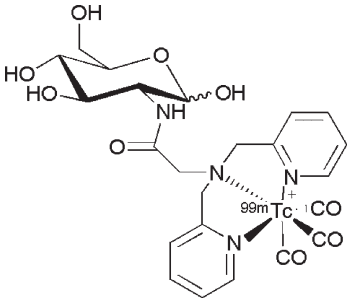
FEATURE ARTICLES

5077

99m-Technetium carbohydrate conjugates as potential agents in molecular imaging

Meryn L. Bowen and Chris Orvig*

This feature article discusses work towards the development of a ^{99m}Tc–carbohydrate based imaging agent for use in nuclear medicine.



COMMUNICATIONS

5092

Enantiomerically pure bicyclo[3.3.1]nona-2,6-diene as the sole source of enantioselectivity in BIPHEP-Rh asymmetric hydrogenation

Tharmalingam Punniyamurthy,* Monika Mayr, Alexander S. Dorofeev, Carole J. R. Bataille, Silvia Gosiewska, Bao Nguyen, Andrew R. Cowley and John M. Brown*

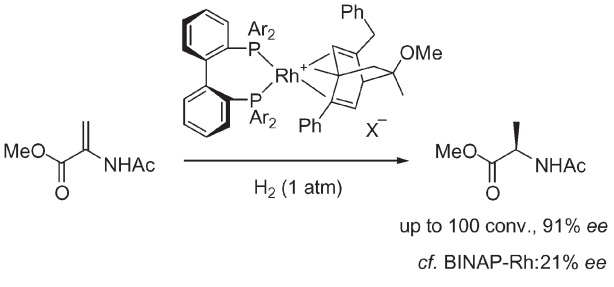
The cationic Rh complex of (*S*,*S*)-bicyclonona-2,6-diene acts as an *in situ* resolving agent for readily racemising ligands prior to catalysis; up to 95% ee in dehydroaminoester hydrogenation.

5095

Axial chirality control of *tropos* BIPHEP–Rh complexes by chiral dienes: synergy effect in catalytic asymmetric hydrogenation

Kohsuke Aikawa, Yūki Takabayashi, Susumu Kawauchi and Koichi Mikami*

Complete axial chirality control of *tropos* BIPHEP–Rh complexes was accomplished by chiral dienes rather than chiral amines to give the diastereopure Rh complexes. The Rh complexes bearing not only BIPHEP but also the chiral diene could be employed as highly enantioselective hydrogenation catalysts for an olefinic substrate.

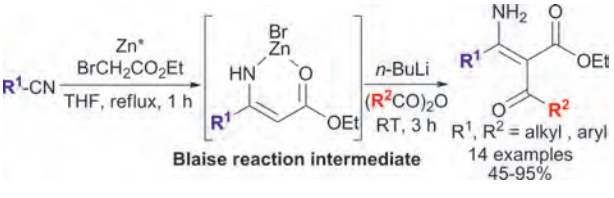


5098

The first chemoselective tandem acylation of the Blaise reaction intermediate: a novel method for the synthesis of α-acyl-β-enamino esters, key intermediate for pyrazoles

Yu Sung Chun, Ki Kon Lee, Young Ok Ko, Hyunik Shin* and Sang-gi Lee*

The Blaise reaction intermediate can be activated *in situ* by addition of a stoichiometric or catalytic amount of *n*-BuLi to allow chemoselective tandem C2-acylation providing α-acyl-β-enamino esters, which can easily be converted to pyrazoles.



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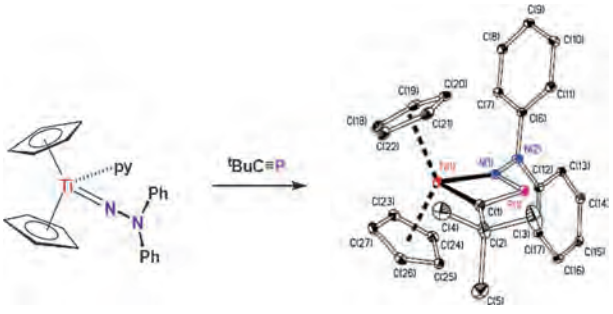
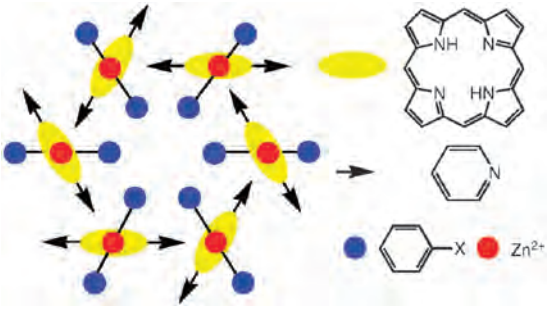


Cycloaddition reactions of transition metal hydrazides with alkynes and heteroalkynes: coupling of $Ti{=}NNPh_2$ with PhCCMe, PhCCH, MeCN and ^tBuCP

Jonathan D. Selby, Christian Schulten, Andrew D. Schwarz, Andreas Stasch, Eric Clot,* Cameron Jones* and Philip Mountford*

The first structurally authenticated [2 + 2] cycloaddition products of any transition metal hydrazide complexes are reported.

5104

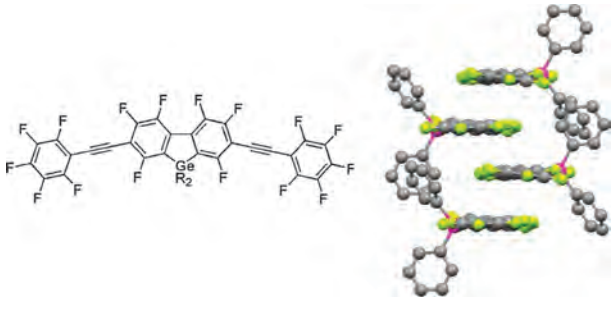


Molecular tectonics: control of pore size and polarity in 3-D hexagonal coordination networks based on porphyrins and a zinc cation

Elisabeth Kühn, Véronique Bulach* and Mir Wais Hosseini*

Both the size and polarity of channels in porous crystals may be tuned by the combination of Zn^{2+} with porphyrins bearing two 4-pyridyl and two 4-aryl substituted units as secondary coordination sites and decorating groups respectively.

5107

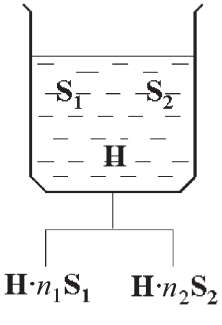


Synthesis and characterization of 2,7-bis(pentafluorophenylethynyl)hexafluoroheterofluorenes: new materials with high electron affinities

Katharine Geramita, Jennifer McBee, Yuefei Tao, Rachel A. Segalman and T. Don Tilley*

The synthesis, optical, electrochemical and physical characterization of 2,7-bis(pentafluorophenylethynyl)-hexafluoroheterofluorenes is described with preliminary photovoltaic performance.

5110



Concomitant formation of two different solvates of a hexa-host from a binary mixture of solvents

Dinabandhu Das and Leonard J. Barbour*

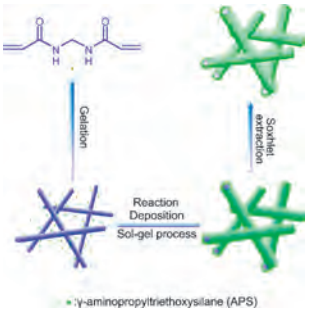
Crystallization of hexakis(4-cyanophenyloxy)benzene from a mixture of two different solvents produces two different solvates concomitantly, which were characterized by X-ray diffraction, thermal analysis and NMR spectroscopy.

5113

A facile approach to fabricate functional 3D macroscopic silica microtube networks using *N*,*N*′-methylenediacrylamide organogel as template

Yu Xia, Yu Wang, Kai Chen and Liming Tang*

A facile and versatile approach to fabricate functional silica microtube networks, which display large potential of future applications.

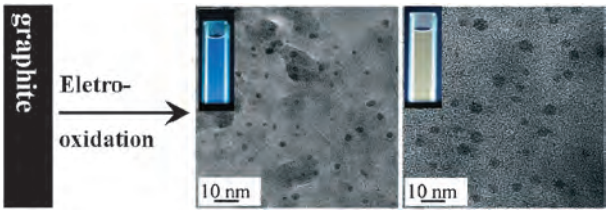


5116

Facile preparation of low cytotoxicity fluorescent carbon nanocrystals by electrooxidation of graphite

Qiao-Ling Zhao, Zhi-Ling Zhang, Bi-Hai Huang, Jun Peng, Min Zhang and Dai-Wen Pang*

A simple and facile method was developed to prepare fluorescent carbon nanocrystals (CNCs) with low cytotoxicity and no photobleaching by electrooxidation of graphite in aqueous solution. The CNCs were monodipserse and stable in solution with high ionic strength, which is promising for biological labeling and imaging *in vivo*.

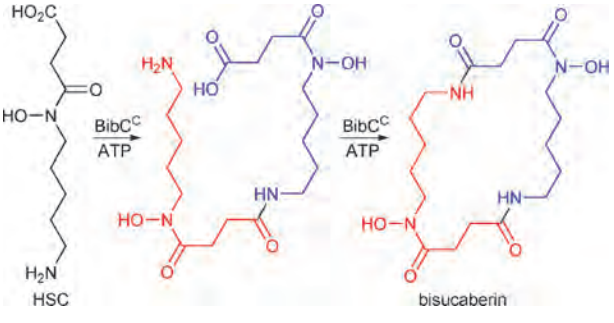


5119

Bisucaberin biosynthesis: an adenylating domain of the BibC multi-enzyme catalyzes cyclodimerization of *N*-hydroxy-*N*-succinylcadaverine

Nadia Kadi, Lijiang Song and Gregory L. Challis

The C-terminal adenylating domain of the BibC multienzyme encoded by the bisucaberin biosynthetic gene cluster identified in the draft genome sequence of *Vibrio salmonicida* catalyzes assembly of bisucaberin from two molecules of HSC *via* a free dimeric acyclic intermediate.

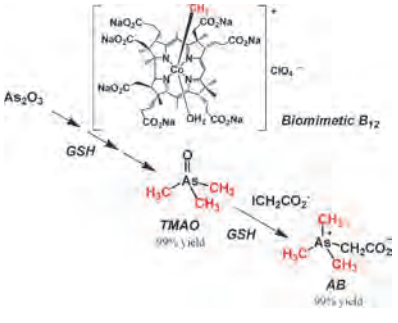


5122

Detoxification system for inorganic arsenic: transformation of As_2O_3 into TMAO by vitamin B_{12} derivatives and conversion of TMAO into arsenobetaine

Koichiro Nakamura,* Yoshio Hisaeda, Ling Pan and Hiroshi Yamauchi

A new two-step synthetic pathway developed for arsenobetaine involves treatment of As_2O_3 with native or biomimetic B_{12} to give TMAO; subsequent treatment of TMAO with iodoacetic acid gives arsenobetaine with a high conversion rate.



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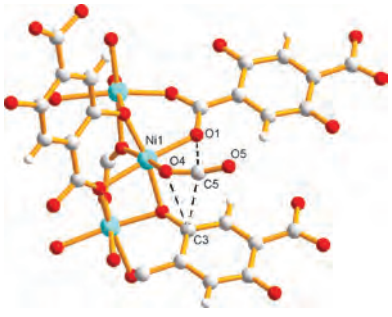
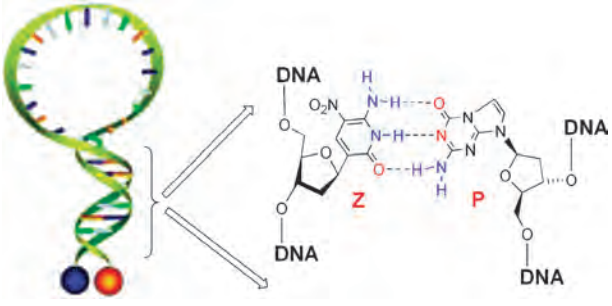


Adsorption properties and structure of CO_2 adsorbed on open coordination sites of metal–organic framework Ni_2(dhtp) from gas adsorption, IR spectroscopy and X-ray diffraction

Pascal D. C. Dietzel, Rune E. Johnsen, Helmer Fjellvåg, Silvia Bordiga, Elena Groppo, Sachin Chavan and Richard Blom*

Strong adsorption is achieved through direct end-on CO_2–nickel interaction.

5128

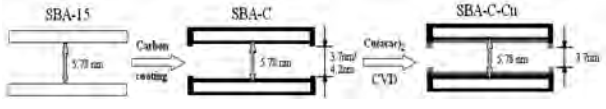


Design of a novel molecular beacon: modification of the stem with artificially genetic alphabet

Pinpin Sheng, Zunyi Yang,* Youngmi Kim, Yanrong Wu, Weihong Tan* and Steven A. Benner*

A molecular beacon that incorporates components of an artificially expanded genetic information system (AEGIS) in its stem is shown not to be opened by unwanted stem invasion by adventitious standard DNA. This should improve the "darkness" of the beacon in real-world applications.

5131

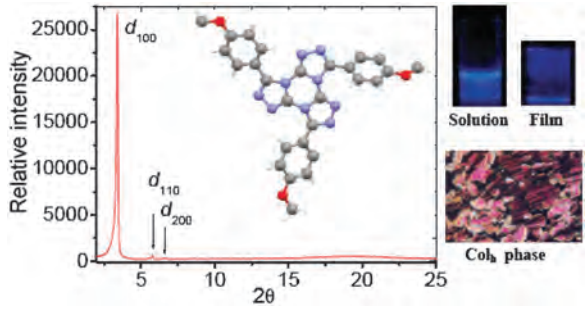


Formation of an ink-bottle-like pore structure in SBA-15 by MOCVD

Ying Zhang, Frank Leung-Yuk Lam, Xijun Hu* and Zifeng Yan

Metallorganic chemical vapor deposition is used as a simple pore-modifying method to fine tune the pore-opening size of SBA-15 materials without significant loss in pore volume and surface area.

5134



Tristriazolotriazines: a core for luminescent discotic liquid crystals

Rodrigo Cristiano, Hugo Gallardo,* Adailton J. Bortoluzzi, Ivan H. Bechtold, Carlos E. M. Campos and Ricardo L. Longo

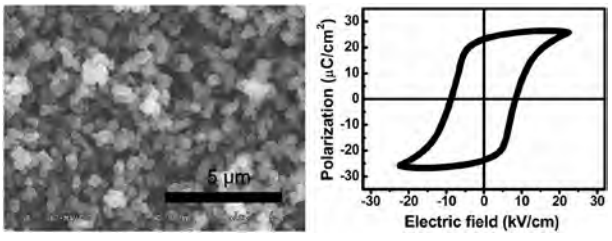
The synthesis and structural, thermal, optical and theoretical characterization of new tris[1,2,4]triazolo[1,3,5]triazines were performed to support their application as liquid crystals and advanced materials.

5137

Facile synthesis and high d_{33} of single-crystalline $KNbO_3$ nanocubes

Haiyan Ge, Yudong Hou,* Mankang Zhu, Hao Wang and Hui Yan

Single-crystalline $KNbO_3$ nanocubes with orthorhombic phase were prepared in a large scale by a simple one-step molten salt route without using any surfactant as template; the nanostructures exhibited high piezoelectric properties such as d_{33} = 105 pC/N and k_p = 0.34 as piezoelectric materials.



5140

Copper-catalyzed asymmetric allylic substitution with aryl and ethyl Grignard reagents

Khalid B. Selim, Ken-ichi Yamada and Kiyoshi Tomioka*

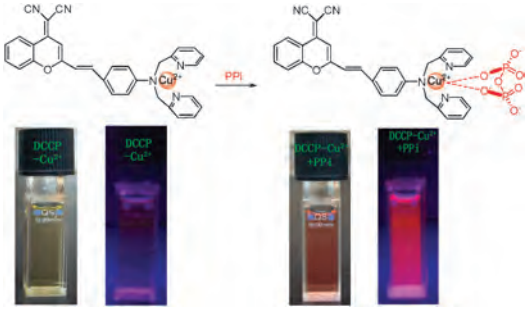
Chiral amidophosphane–copper(I) catalysts allow an unprecedently efficient asymmetric allylic arylation of aliphatic and difunctionalized brominated substrates with aryl Grignard reagents.

5143

A colorimetric and fluorescent turn-on sensor for pyrophosphate anion based on a dicyanomethylene-4*H*-chromene framework

Xiaomei Huang, Zhiqian Guo, Weihong Zhu,* Yongshu Xie and He Tian*

A new red fluorescent sensor DCCP–Cu^{2+} based on dicyanomethylene-4*H*-chromene shows turn-on fluorescent selectivity for pyrophosphate over other anions.

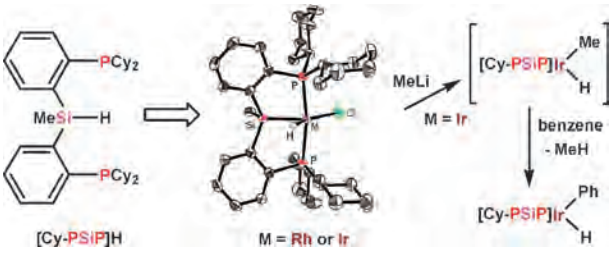


5146

Room temperature benzene C–H activation by a new [PSiP]Ir pincer complex

Darren F. MacLean, Robert McDonald, Michael J. Ferguson, Andrew J. Caddell and Laura Turculet*

Facile intermolecular arene C–H bond activation by a new coordinatively unsaturated bis(phosphino)silyl Ir pincer complex is reported.



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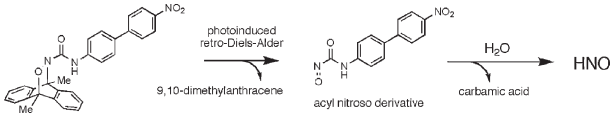
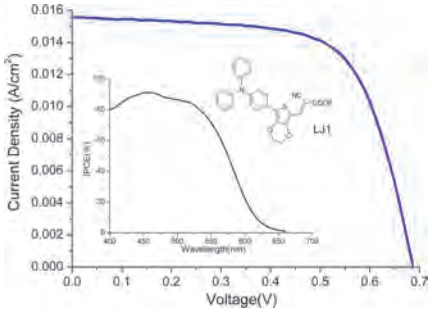


Photoactivatable HNO-releasing compounds using the retro-Diels–Alder reaction

Yusuke Adachi, Hidehiko Nakagawa,* Kazuya Matsuo, Takayoshi Suzuki and Naoki Miyata*

Several hetero-Diels–Alder cycloadducts were formed from acyl nitroso derivatives bearing a nitroaryl group and 9,10-dimethylanthracene, and it was found that a novel cycloadduct bearing a nitrobiphenyl moiety showed a photo-enhanced HNO-releasing property under UV-A irradiation.

5152

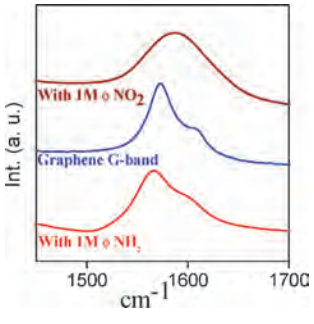


Simple organic molecules bearing a 3,4-ethylene-dioxythiophene linker for efficient dye-sensitized solar cells

Wei-Hsin Liu, I-Che Wu, Chin-Hung Lai, Cheng-Hsuan Lai, Pi-Tai Chou,* Yi-Tsung Li, Chao-Ling Chen, Yu-Yen Hsu and Yun Chi*

A series of simple organic molecules bearing a 3,4-ethylenedioxythiophene linker for dye-sensitized solar cells were synthesized, one of which achieved a solar-to-energy conversion efficiency of 7.3%.

5155

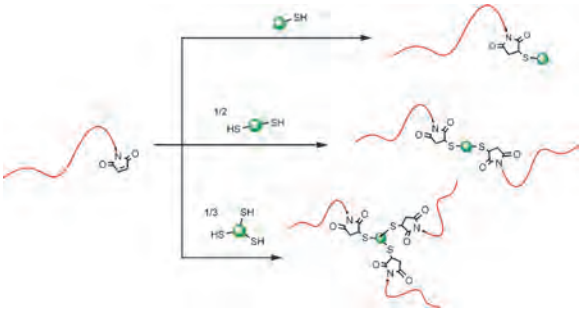


Changes in the electronic structure and properties of graphene induced by molecular charge-transfer

Barun Das, Rakesh Voggu, Chandra Sekhar Rout and C. N. R. Rao*

Raman spectra and electronic properties of graphene are markedly affected on interaction with electron-donor and -acceptor molecules.

5158



Metal free thiol–maleimide 'Click' reaction as a mild functionalisation strategy for degradable polymers

Ryan J. Pounder, Matthew J. Stanford, Paul Brooks, Stephen P. Richards and Andrew P. Dove*

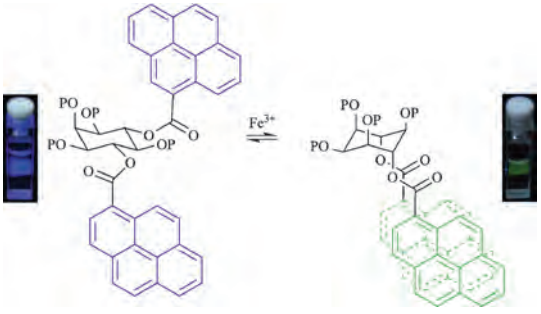
The stoichiometric reaction between thiols and maleimide-functional poly(ester)s is demonstrated to be a quantitative, tolerant, mild and efficient method for polymer modification.

5161

Fluorescent probe: complexation of Fe^{3+} with the *myo*-inositol 1,2,3-trisphosphate motif

David Mansell, Nicholas Rattray, Laura L. Etchells, Carl H. Schwalbe, Alexander J. Blake, Elena V. Bichenkova, Richard A. Bryce, Christopher J. Barker, Alvaro Díaz, Carlos Kremer and Sally Freeman*

The fluorescent probe mimic 4,6-bispyrenoyl-*myo*-inositol 1,2,3,5-tetrakisphosphate binds Fe^{3+} with pyrene excimer emission, supporting the penta-axial conformation of the Fe^{3+} complex.

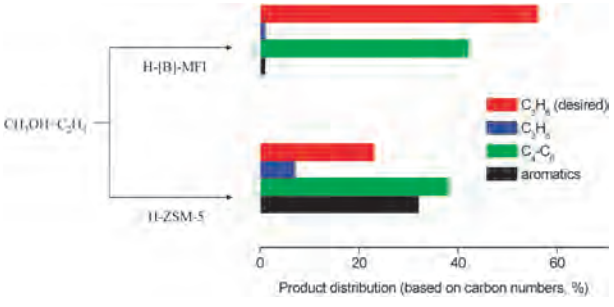


5164

Activation of hydrocarbons on acidic zeolites: superior selectivity of methylation of ethene with methanol to propene on weakly acidic catalysts

Qingjun Zhu, Junko N. Kondo, Tooru Setoyama, Masashi Yamaguchi, Kazunari Domen and Takashi Tatsumi*

H-[B]-MFI efficiently catalyzes the methylation of ethene with methanol to produce propene selectively, which is probably due to its weak acidity.

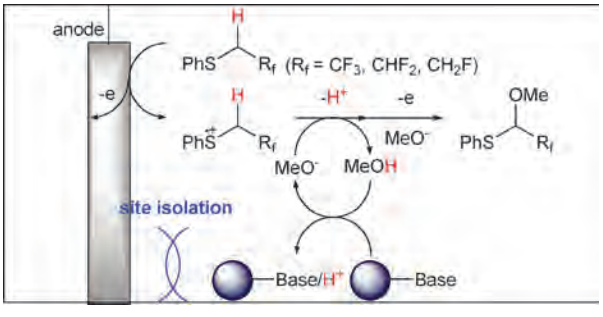


5167

Deprotonation in anodic methoxylation of fluoroethyl phenyl sulfides using site-isolated heterogeneous bases

Toshiki Tajima* and Hitoshi Kurihara

We have successfully demonstrated acceleration of the deprotonation step in anodic methoxylation of fluoroethyl phenyl sulfides using site-isolated heterogeneous bases.



5170

Defect chemistry of polyfluorenes: identification of the origin of "interface defects" in polyfluorene based light-emitting devices

Stefan Kappaun,* Horst Scheiber, Roman Trattnig, Egbert Zojer, Emil J. W. List and Christian Slugovc

Deprotonation of hydroxy terminated polyfluorenes results in a greenish emission also providing a rational explanation for so called "interface defects" in polymeric light-emitting devices (PLEDs).

Chemistry-Biology Interface

Chemistry-Biology Interface theme issue

This theme issue covers topical areas at the chemistry–biology interface from a chemical perspective. The biological consequences of specific molecular interactions have long been a part of scientific (and non-scientific) activities throughout human history. The last century witnessed a myriad of discoveries in the life sciences at molecular detail, and the associated growth of the pharmaceutical and biotech industries. This century has seen a further growth in the field with a resultant increase in publications and journals.

Reviews include:

Nucleic acid encoding to program self-assembly in chemical biology
Zbigniew L. Pianowski and Nicolas Winssinger

Chemical technologies for probing embryonic development
Ilya A. Shestopalov and James K. Chen

Interspecies and interkingdom communication mediated by bacterial quorum sensing
Colin A. Lowery, Tobin J. Dickerson and Kim D. Janda

Small molecule inhibition of microbial natural product biosynthesis—an emerging antibiotic strategy
Justin S. Cisar and Derek S. Tan

Identification of the cellular targets of bioactive small organic molecules using affinity reagents
Benjamin J. Leslie and Paul J. Hergenrother

Expanding dialogues: from natural autoinducers to non-natural analogues that modulate quorum sensing in Gram-negative bacteria
Grant D. Geske, Jennifer C. O Neill and Helen E. Blackwell

Guest editor:

David Spring
University of Cambridge, UK

"The interface with biology is a fertile scientific pursuit for chemists"

060833

See also:

Molecular BioSystems issue 6, 2008 – Emerging Investigators theme issue
For more details see www.molecularbiosystems.org/ei

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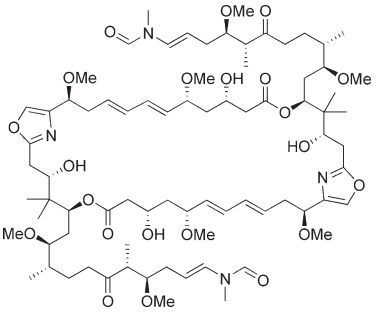
5173

Configurational assignment of rhizopodin, an actin-binding macrolide from the myxobacterium *Myxococcus stipitatus*

Nicole Horstmann and Dirk Menche*

The relative and absolute stereochemistry of the 38-membered myxobacterial polyketide rhizopodin, a potent actin-binding macrolide, was determined by *J*-based configurational analysis in combination with molecular modeling and chemical derivatization.

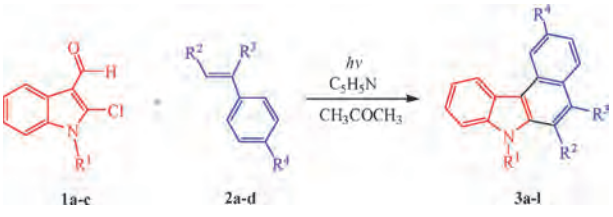


5176

One-pot synthesis of benzo[*c*]carbazoles by photochemical annulation of 2-chloroindole-3-carbaldehydes

Cailin Wang, Wei Zhang,* Shenci Lu, Jingfei Wu and Zongjun Shi

A novel and efficient procedure for the synthesis of benzo[*c*]carbazoles has been achieved in moderate to high yields by the one-pot photochemical annulation of 2-chloroindole-3-carbaldehydes by styrenes.

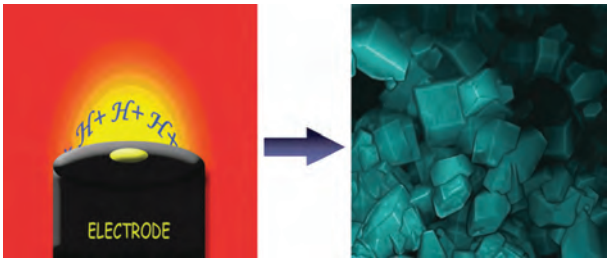


5179

Protein crystals make it big at electrode surfaces

Barry R. Silver* and Patrick R. Unwin*

Enhanced and rapid growth of lysozyme crystals at the surface of a platinum electrode, using an applied current and a simplified crystallizing solution, is reported.

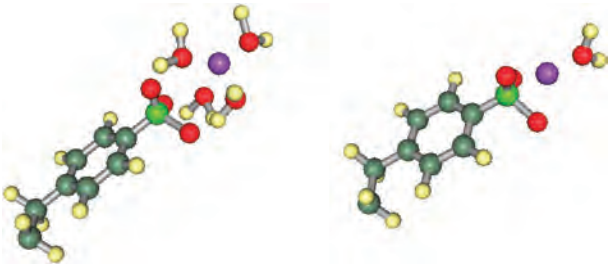


5182

Hydration of counterions in cation exchange resins studied by X-ray absorption fine structure

Makoto Harada and Tetsuo Okada*

Rb^+ (left) keeps its hydration shell on a cation-exchange resin, whereas K^+ (right) is partly dehydrated.



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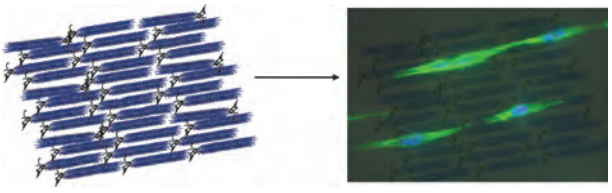
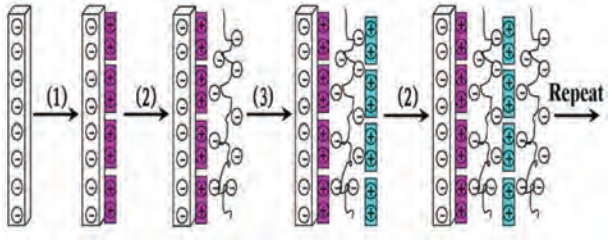


Oriented cell growth on self-assembled bacteriophage M13 thin films

Jianhua Rong, L. Andrew Lee, Kai Li, Brandon Harp, Charlene M. Mello, Zhongwei Niu* and Qian Wang*

Thin films with aligned nanogrooves were fabricated using RGD-grafted fibrillar M13 bacteriophages as building blocks, and were used to guide cell alignment and oriented growth along defined directions.

5188

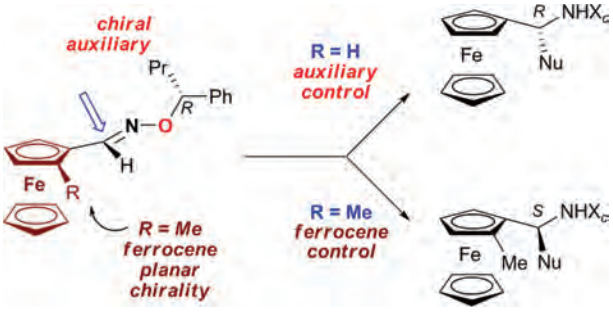


Heterogeneous ultrathin films fabricated by alternate assembly of exfoliated layered double hydroxides and polyanion

Jing Bin Han, Jun Lu, Min Wei,* Zhong Lin Wang* and Xue Duan

Schematic representation of the process for the fabrication of transparent heterogeneous ultrathin films of exfoliated layered double hydroxides (LDHs) nanosheets with polyanion.

5191

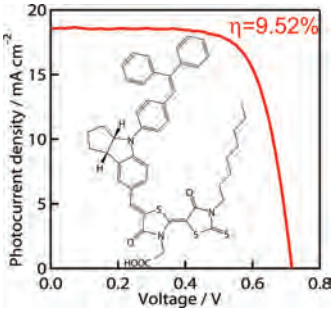


Competition between planar and central chiral control elements in nucleophilic addition to ferrocenyl imine derivatives

Kévin M. Joly, Claire Wilson, Alexander J. Blake, James H. R. Tucker and Christopher J. Moody*

Ferrocene dominates! Planar chirality associated with the ferrocene in FcCH=NR derivatives bearing chiral auxiliaries on N effectively competes with or overrides the normally excellent stereocontrol afforded by the auxiliary in determining the diastereoselectivity of addition to the C=N bond.

5194



High-conversion-efficiency organic dye-sensitized solar cells with a novel indoline dye

Seigo Ito,* Hidetoshi Miura, Satoshi Uchida, Masakazu Takata, Koichi Sumioka, Paul Liska, Pascal Comte, Peter Péchy and Michael Grätzel

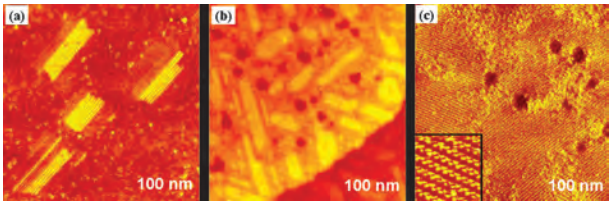
Solar cells sensitized by an organic dye (D205) on nanocrystalline-TiO_2 electrodes exhibited a high open-circuit photovoltage at 710 mV with the use of chenodeoxycholic acid; the resulting conversion efficiency was 9.52% under 1 sun irradiation.

5197

Two-dimensional ordering of benzenethiol self-assembled monolayers guided by displacement of cyclohexanethiols on Au(111)

Hungu Kang, Haiwon Lee, Youngjong Kang, Masahiko Hara and Jaegeun Noh*

Molecular-scale STM imaging reveals that the displacement of preadsorbed cyclohexanethiol self-assembled monolayers (SAMs) on Au(111) by benzenethiol (BT) can be a successful approach to obtain two-dimensional BT SAMs.

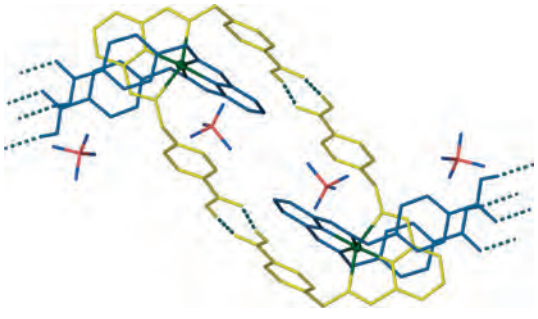


5200

A crystalline hydrogen-bonded network with a poly-catenate topology

A. Abibat Salaudeen, Colin A. Kilner and Malcolm A. Halcrow*

A polycatenate network, whose rings are formed from metal-templated hemispheres linked by hydrogen bonds, is reported.

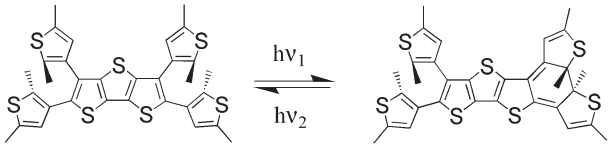


5203

Photochromic oligothienoacene derivatives with photo-switchable luminescene properties and computational studies

Chi-Chiu Ko, Wai Han Lam and Vivian Wing-Wah Yam*

Photochromic thieno[3,2-*b*]thiophenes and dithieno[3,2-*b*:2′,3′-*d*]thiophene with photo-switchable luminescence properties have been synthesized using a Suzuki cross-coupling reaction; their electronic structures, and photochromic and luminescence behaviour have also been studied.

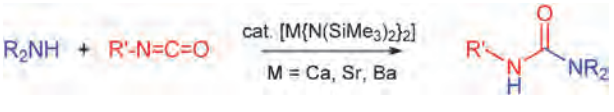


5206

Heavier group 2 element-catalysed hydroamination of isocyanates

Anthony G. M. Barrett,* Tanya C. Boorman, Mark R. Crimmin, Michael S. Hill,* Gabriele Kociok-Köhn and Panayiotis A. Procopiou

The heteroleptic calcium amides [{ArNC(Me)CHC(Me)NAr}Ca(NR_2)(THF)] (Ar = 2,6-di-*iso*-propylphenyl, R = $SiMe_3$, Ph) and the homoleptic heavier alkaline earth amides, [M{$N(SiMe_3)_2$}$_2$] (M = Ca, Sr and Ba) are reported as pre-catalysts for the hydroamination of isocyanates.



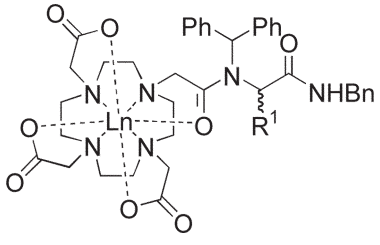
5209

Soft material with intense photoluminescence obtained by dissolving Eu_2O_3 and organic ligand into a task-specific ionic liquid

Huanrong Li,* Huifang Shao, Yige Wang,* Dashan Qin, Binyuan Liu, Wenjun Zhang and Weidong Yan

A soft material with intense photoluminescence has been obtained by directly dissolving Eu_2O_3, TTA (2-thenoyltrifluoroacetonate) and Phen (1,10-phenanthroline) into a task-specific ionic liquid.

5212

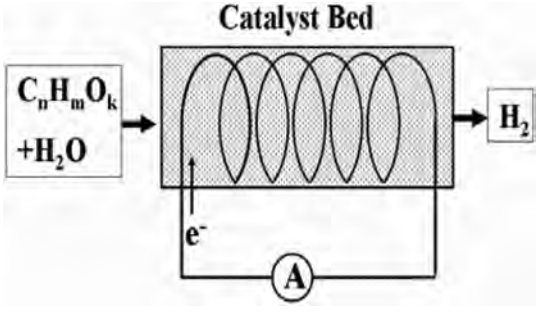


Using the Ugi multicomponent condensation reaction to prepare families of chromophore appended azamacrocycles and their complexes

Marcus Main, John S. Snaith,* Marco M. Meloni, Maite Jauregui, Daniel Sykes, Stephen Faulkner* and Alan M. Kenwright

The Ugi reaction offers an effective method for preparing chromophore-appended DOTA-monoamide ligands, which can readily be elaborated to their lanthanide complexes.

5215

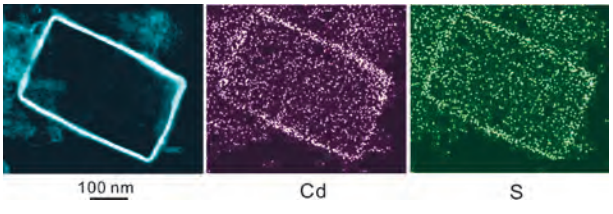


Electrochemical catalytic reforming of oxygenated-organic compounds: a highly efficient method for production of hydrogen from bio-oil

Lixia Yuan, Yaqiong Chen, Chongfu Song, Tongqi Ye, Qingxiang Guo, Qingshi Zhu, Youshifumi Torimoto and Quanxin Li*

A novel approach to produce hydrogen from bio-oil was obtained with high carbon conversion (>90%) and hydrogen yield (>90%) at $T < 500$ °C.

5218



One-step fabrication of well-defined hollow CdS nanoboxes

Mee Rahn Kim and Du-Jeon Jang*

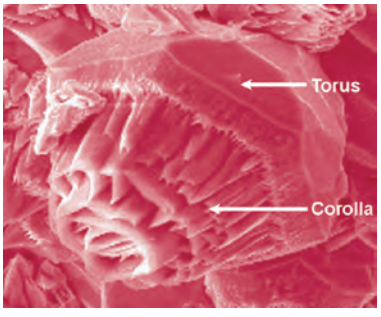
Hollow CdS nanoboxes, having paper-thin walls of well-defined facets, were synthesized at 170 °C *via* a simple reaction using Na_2SeO_3 for interior quasitemplates and ethylenediamine for exterior molecular templates.

5221

Three-dimensional AlN microroses and their enhanced photoluminescence properties

Weiwei Lei, Jian Zhang, Dan Liu, Pinwen Zhu, Qiliang Cui* and Guangtian Zou

Novel three-dimensional AlN microroses, for the first time, have been synthesized *via* direct reaction between Al and N_2 in arc plasma without any catalyst and template. The microrose has two parts: 'corolla' and 'torus'. The 'corolla' part is composed of vertically standing and smooth nanopetals, the 'torus' part has a pyramidal shape.

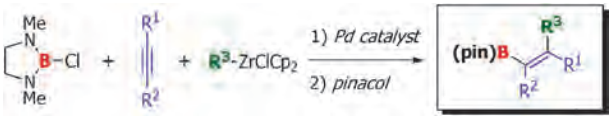


5224

Palladium-catalyzed carboboration of alkynes using chloroborane and organozirconium reagents

Masaki Daini and Michinori Suginome*

Boron and carbon substituents are added in a *cis*-fashion to the carbon–carbon triple bond of alkynes in the presence of a palladium catalyst, leading to the formation of stereo-defined alkenylboronic acid derivatives.

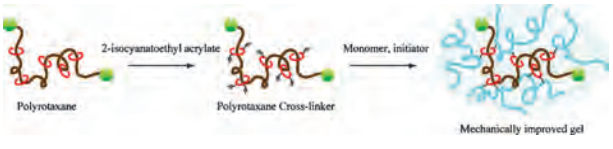


5227

Fabrication of mechanically improved hydrogels using a movable cross-linker based on vinyl modified polyrotaxane

Abu Bin Imran, Takahiro Seki, Toshiyuki Kataoka, Masatoshi Kidowaki, Kohzo Ito and Yukikazu Takeoka*

This manuscript describes the preparation of new slide-ring gels by using a polyrotaxane as a cross-linker.

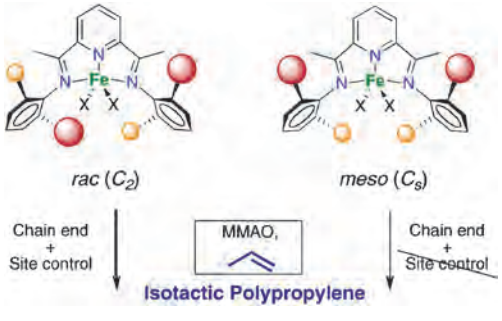


5230

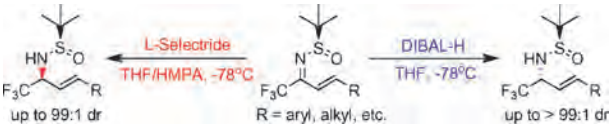
Separation of a diiminopyridine iron(II) complex into *rac*- and *meso*- diastereoisomers provides evidence for a dual stereoregulation mechanism in propene polymerization

Antonio Rodríguez-Delgado, Juan Cámpora,* A. Marcos Naz, Pilar Palma and Manuel L. Reyes

Enantiomorphic site control mechanism has been observed for the first time in the stereoregulation of propene polymerization with a late transition metal catalyst.



5233

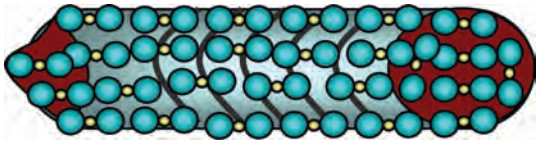


Asymmetric synthesis of either diastereomer of trifluoromethyated allylic amines by the selective reduction of trifluoromethyl α,β-unsaturated *N-tert*-butanesulfinyl ketoimines

Zhen-Jiang Liu and Jin-Tao Liu*

Regio- and diastereoselective reduction of chiral trifluoromethyl α,β-unsaturated *N-tert*-butanesulfinyl ketoimines was achieved by choosing appropriate reducing agent and either diastereomer of trifluoromethylated allylic amines was obtained with good yield and excellent diastereoselectivity (up to >99 : 1 dr) using DIBAL-H and L-Selectride as the reductant, respectively.

5236



Fast and reversible surface redox reduction in V_2O_5 dispersed on CN_x nanotubes

Wei-Chuan Fang* and Wei-Lee Fang

Well-dispersed V_2O_5 nanomaterials on N-doped carbon nanotubes exhibit significantly stable capacitive performance for promising energy-storage applications.

5239

An efficient heteropolyacid catalyzed acylation of pyruvate esters to α-acyloxyacrylate esters as potential candidate monomers for bio-based polymers

Wataru Ninomiya,* Masahiro Sadakane, Shinji Matsuoka, Hiroki Nakamura, Hiroyuki Naitou and Wataru Ueda*

α-Acyloxyacrylate esters, which are potential candidate monomers for bio-based polymers with high durability and transparency, are efficiently synthesized with Keggin type heteropolyacids as catalysts under mild conditions.

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Chemical Biology

Chip unifies cells' direction and separates the new from the old

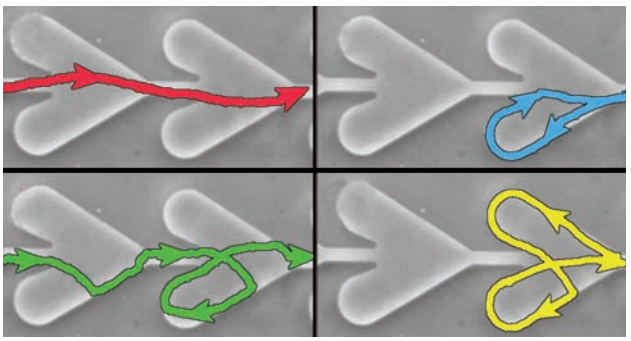
Sorting swimming cells

US scientists are making bacteria sort themselves by size.

Sorting cells is a key task in cell and systems biology. Although several sorting methods exist, they subject the cells to chemical or mechanical stresses to separate them. George Whitesides' group at Harvard University, Cambridge, has taken a different approach to the problem. The team takes advantage of *Escherichia coli* cells' motility to sort them by size in a microfluidic device.

In fluid, *E. coli* cells take random walks involving a period of swimming followed by tumbles that change their direction randomly. But without a chemical stimulus, the average displacement of a population of swimming cells is zero. To make the cells swim in one direction the team's device contains a series of ratchets. These arrowhead shaped channels redirect cells swimming in the 'wrong' direction, so that eventually most cells are swimming in one 'right' direction.

Once the cells have passed through the ratchets, the next part of the device, the bacterial sorter, sorts the cells by size. This exploits the fact that shorter cells follow a curved microchannel better than longer cells, allowing short cells to be separated from the population.



A series of ratchets encourages bacteria to travel in one direction

Group member Elizabeth Hulme explains the biological use for the technique: 'For *E. coli*, length is directly related to age: short cells are young, long cells are old. In separating out the short cells, we were selecting for cells that had recently divided, and isolating a population that was more synchronised with respect to age – that is, at a similar stage in the bacterial growth cycle.'

Damien Baigl from the Microfluidics, Chemical Organisation and Nanotechnology group at the École Normale Supérieure, Paris, France, calls the work 'conceptually beautiful'. He says that 'the methodology is efficient, robust and easy to implement,' adding that it is 'performed with minimised physical and chemical stresses on the cells. It promises to become a powerful tool to investigate challenging biological problems, such as phenotypic variability, in *E. coli* and other bacterial systems,' he says.

Hulme points out that this is just the beginning – the next challenge will be to develop other tools. 'What is needed is an expansion of the toolbox for manipulating and examining bacteria in lab-on-a-chip devices,' she says. *Edward Morgan*

Reference
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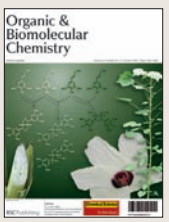
Quick on the uptake
Douglas Kell outlines his findings on drug uptake and the implications for drug discovery and development

Bacterial nanoinjectors
This month's Instant insight explains how some of the world's most deadly pathogens use needles to inject their prey



Research highlights

Protein's folded shape reconstructed from scattering data

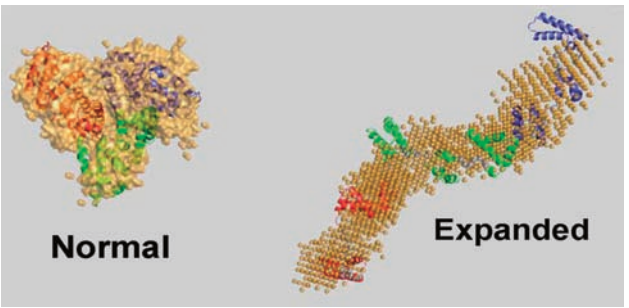
The solution to solve all solution structures?

The structures proteins adopt in solution are being unravelled by researchers in Italy.

Claudia Leggio and co-workers at Sapienza University of Rome have developed a method for determining the folded structures of proteins in solution, information they say is crucial for understanding protein function. They derive 3D models from small-angle x-ray scattering (SAXS) data and validate them with light scattering measurements.

The researchers' first goal was to reconstruct the solution form of human serum albumin (HSA). 'HSA's shape and dimensions at neutral pH has been a matter of controversy,' says Leggio, explaining the team's motivation. This is despite its being the most abundant protein in human plasma and involved in many physiological functions, including blood pH and pressure maintenance, she adds.

Early work indicated that HSA resembles a cigar-shaped ellipsoid, but recent studies have pointed to a heart-shaped structure in solution, similar to that obtained from x-ray crystallography. 'Our results show that in solution the defatted protein adopts a slightly more open heart-shaped structure than in the crystal,' says Leggio.



HSA adopts a heart-shaped structure (left) in solution rather than the cigar shape (right) originally thought

Reference
C Leggio, L Galantini and N V Pavel, *Phys. Chem. Chem. Phys.*, 2008, DOI: 10.1039/b808938h

William Heller, an expert in structural molecular biology at Oak Ridge National Laboratory in Tennessee, US, says that sophisticated methods such as Leggio's are a prerequisite for studying proteins in solution. 'Such systems are challenging to study structurally since high-resolution crystallography is often not possible,' he explains, 'because the systems do not adopt a single conformation that will produce high quality crystals.' SAXS, on the other hand, can be used for systems that adopt several conformations, making it suitable for proteins in solution. But, Leggio points out, what SAXS measures is an average over an ensemble of conformations. 'The challenge is to combine the technique with others to take the averaging into account,' she adds.

Leggio says that her methods could also be extended to study protein folding processes and mechanisms. Heller agrees, describing the work as 'pointing a way forward for other researchers in the field toward understanding the structures of proteins and the conformational changes that take place during the performance of their biological function.'

Colin Batchelor

Robust photoswitch offers potential to control protein function inside cells

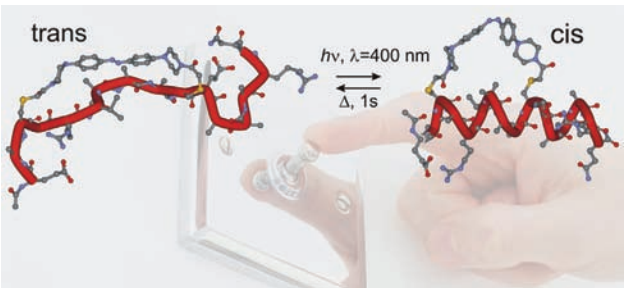
Protein changes at the flick of a switch

Photoswitches that make proteins change shape could eventually be used to test protein function in cells, say Canadian scientists.

Andrew Woolley and his group at the University of Toronto are interested in studying the structure and roles of various proteins. An important task, since defective protein interactions are implicated in a range of diseases.

The goal for Woolley has been altering protein structure reversibly, so that the protein can be switched on and off to discover its role in the cell. The group, and others, have managed to perform this trick in proteins outside cells, but the challenge has been to use the technology within cells, and now Woolley thinks he has the tools to do just that.

Woolley alters a protein's structure by introducing a small azo compound which binds between two side chains in the protein. Shining light onto the protein alters the orientation of the azo group, causing the protein to change its shape.



Light causes a change in structure in Woolley's photoswitch as the azo group converts from the *trans* to the *cis* form

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While other photoswitches have been used to control proteins on cell surfaces, the environment inside the cell has proved inhospitable to the azo groups that give the switches their shape changing property. However, Woolley's new photoswitch has an electron-rich structure that allows it to survive for hours under conditions similar to those found in cells.

Having proven that its new photoswitch can survive in these conditions, the group is now working on learning to control the switch inside cells. 'This photoswitch offers the possibility of turning off and on protein function using light, in an attempt to learn about protein functions in the cellular environment,' Woolley explains.

Ehud Isacoff of the University of California, Berkeley, US, uses light to investigate neural signalling. He says that the work makes Woolley 'a pioneer of methods for the reversible optical control of protein structure and function.'

Laura Howes

Liquid crystalline virus film imposes order on cell arrangement

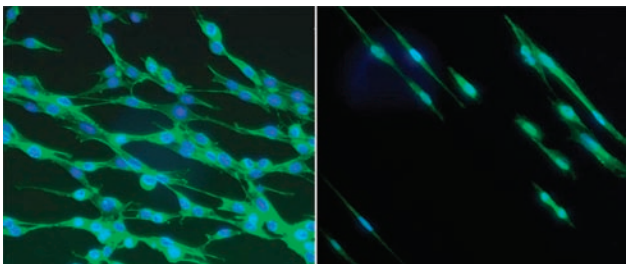
Cells take direction from virus

International scientists have made a simple cell scaffold from a virus.

Zhongwei Niu and Qian Wang at the University of South Carolina, and colleagues in the US and China, developed the viral film which can be used to grow oriented arrays of cells.

The team based its scaffold on bacteriophage M13, a virus with an innate ability to organise into liquid crystals. Their aim was to study how well-ordered M13 films would affect cell behaviour. As cell behaviour is controlled by interactions between the cell and its surroundings, explain the researchers, scaffold patterning can influence cell responses. They point out that understanding these interactions is important in designing scaffolds for tissue engineering.

To generate their scaffold, the researchers placed a suspension of M13 on a silane-coated glass slide. Slowly dragging the meniscus along the slide forced the virus to form a thin film exhibiting highly oriented M13 particles. The team then modified the film surface with tripeptides to enhance cell binding to the virus, and cultured mouse fibroblasts – cells typically found in connective tissue – on the film. They found that the cells were oriented and elongated along a single direction on the film.



Cells cultured on the bacteriophage film grew along a single direction

'Designing biocompatible surfaces for cells has been a hot topic for many scientists,' says Wang. 'Virus-based substrates confer certain unique advantages. One, the structure of the virus is well-defined, therefore we can determine the position of our chemical or genetic modification, and the distance between each functional group. Two, the viruses can be organised into one- or two-dimensional structures. And lastly, viruses are protein-based materials, just like collagen and many other natural cell matrices. We hope to continue with our virus-based materials and their variations to study many cellular behaviours, such as bone formation, neuron regeneration and blood vessel repair.'

Jeff Capadona of Case Western Reserve University, Cleveland, and the L. Stokes Cleveland VA Medical Center, US, who currently researches smart biomimetic polymer nanocomposites, looks forward to the results of these further studies. 'The simplicity and elegance of cell orientation through the alignment of bacteriophages into thin films promises to become an important tool in probing cell function and behaviour,' he says.

Vikki Chapman

Reference
J Rong *et al*, *Chem. Commun.*, 2008, DOI: 10.1039/b811039e

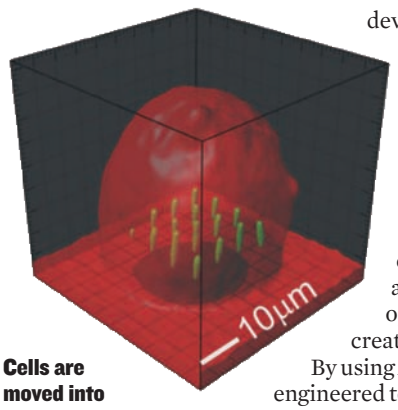
Cellular tiles made using optical tweezers in lab-on-a-chip device

Tiling yields model tissue

US scientists are creating tissue mimics by fixing together tiles of cells.

To create synthetic tissue researchers need to control where each cell is placed and which type of cell is used at each site. Holographic optical tweezers provide one method of manipulating cells in this way; however, this approach uses optical-trap lasers and prolonged exposure to these damages cells. 'The trouble with optical tweezers is that they kill things,' explains Gregory Timp of the University of Illinois at Urbana-Champaign, who led the team behind the research. 'We're looking for the gentlest possible way to position cells in a tissue.'

With this in mind, Timp and co-workers designed a microfluidic system to move cells that minimises their exposure to optical tweezers, limiting the photodamage. The device uses the tweezers to move cells before fixing them in position with a photopolymerisable hydrogel. Repeating this process allows the team to assemble microscopic tiles of cells which they can arrange – without optical tweezers – to create a larger structure.



Cells are moved into an array and fixed in place with a hydrogel – mimicking the extracellular matrix in real tissue

By using *Escherichia coli* cells engineered to produce fluorescent proteins the team could easily prove that the new structure was made of living cells.

Isaac Kuo-Kang Liu, an expert in biomedical engineering at Keele University, in Newcastle-under-Lyme, UK, suggests the new microfabrication technique could eventually allow scientists to prepare synthetic tissue for medical applications. 'Such a high throughput and cell-friendly method for making tissue constructs will create a new paradigm for tissue engineering and regenerative medicine applications,' he says.

Martin Gijs, an expert in microfabrication at the Swiss Federal Institute of Technology in Lausanne, points out that the technology could also allow scientists to analyse biological responses in biofilms – arrangements of single-celled organisms such as bacteria. He explains that it could be used to study chemical gradients across a biofilm or monitor how biofilms respond to antibiotics. 'The method brings the generation of artificial tissue samples that can be used for in vitro assays and in drug discovery one step closer,' says Gijs.

Russell Johnson

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Polymerase chain reaction followed using nanotube-coated electrode

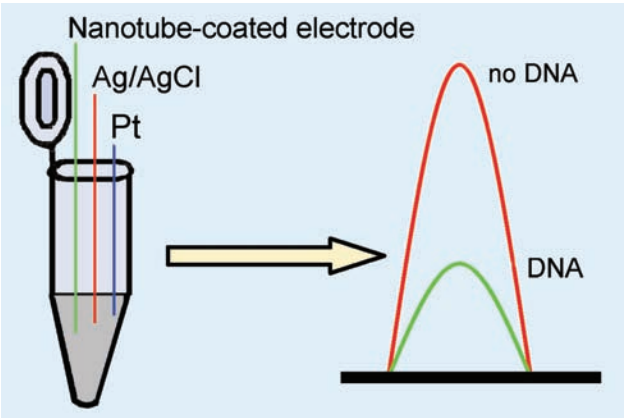
Dip-in DNA detective

Chinese scientists are monitoring the polymerase chain reaction (PCR), a process used by molecular biologists and forensic scientists across the world, using a new approach to DNA detection.

DNA sensors have many applications, including in disease diagnosis and environmental monitoring. The aim of the team led by Kui Jiao, at the Qingdao University of Science and Technology, was to develop a device for detecting genetically modified organisms. Their device combines an electrochemical sensor with PCR, a method which amplifies target DNA sequences by repeated copying.

While PCR is a very sensitive technique, methods of analysing the result are not perfect, often requiring toxic chemicals or extra steps, which increase the sample contamination risk and the time and cost of analysis. Jiao's new system detects successful amplification simply by dipping an electrode into the post-PCR sample.

Using an electrode coated with carbon nanotubes, the system determines the consumption of dGTP – one of DNA's building blocks – by the PCR. This is possible because the electrode can oxidise free dGTP, but is less able to oxidise dGTP when it is embedded in the DNA double helix. This results in a reduction in the system current proportional to the extent of the amplification reaction.



The nanotube-coated electrode records a reduced current in a successful polymerase chain reaction

Jiao says the team had previously looked to the electrochemical properties of the finished DNA for their detector. 'But the need for a sensor with super-sensitivity, made us consider the other side of the coin,' explains Jiao, monitoring the loss of starting material rather than the build up of product.

The DNA detection arises because a PCR is started by adding DNA fragments complementary to parts of a target sequence. Only if the target sequence is present will the added fragments initiate the copying process, and amplification and the current decrease be observed. Using this method, the team has successfully identified transgenic maize samples, obtaining results agreeing with a traditional PCR analysis method.

Edmond Magner, who researches bioelectrochemistry at the University of Limerick, Ireland, sees the technique's potential. He warns there are a number of hurdles which will need to be overcome, such as producing carbon nanotubes reliably and cheaply. But once these challenges are met 'it could provide a relatively fast and possibly cost effective means of monitoring PCRs if it could be applied on a wider scale,' says Magner. *Frances Galvin*

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X Zhang *et al*, *Analyst*, 2008, DOI: 10.1039/b808880b

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Read more at www.rsc.org/chembiology

Erratum: In the article **Boron implicated in the emergence of life** (*Chemical Biology*, September 2008) ribose is not a component of DNA but RNA.

Interview

Quick on the uptake

Douglas Kell tells Elinor Richards about his findings on drug uptake and the implications for drug discovery and development

Douglas Kell

Douglas Kell is director of the Manchester Centre for Integrative Systems Biology at the University of Manchester. His work focuses on systems biology, analytical science and computational biology. He is the recipient of numerous awards, including the RSC's Interdisciplinary Award, and is the current holder of the RSC Chemical Biology Award and the SAC/RSC Gold Medal. As of 1 October, he is the Chief Executive of the UK BBSRC.

Can you explain about your role and the aims of the Manchester Centre for Integrative Systems Biology?

We have a team of eight principal investigators who help manage the work of the centre, and I am the director. We are developing a pipeline that covers all areas of systems biology, including purifying (usually recombinant) biomolecules, assessing both qualitatively and quantitatively what they interact with and in effect doing quantitative enzyme kinetics with them.

Our 'set-piece' activity is to be the production of a genome-wide kinetic model of the yeast metabolic pathways that accounts for the bulk of the flux of substrates. If we can show that our methods work in yeast, we can then apply them to other systems, including humans.

What are you currently working on?

About 80% of my group is 'dry' and works on computational modelling and data analysis, with a lot of the 'wet' (experimental) work focused on the development of novel analytical methods for biomolecules. For instance, one major project, in collaboration with GlaxoSmithKline and AstraZeneca, is a mixed wet-and-dry project that concerns the analysis of human serum samples to understand their complement of metabolites. We have developed novel methods that can detect, and in many cases quantify, thousands of these metabolites, and these can be useful in diagnosing various diseases. We have recently published work on molecules diagnostic of heart failure and on pre-eclampsia, a major disease of pregnancy. The challenge is to integrate the measurements obtained with systems biology models.

What fascinated you about this area of research?

When I finished my DPhil in 1978, DNA sequencing had just been established, albeit at a rate of just three bases per day, and this was evidently going to usher in a new phase of the molecular biology agenda. I never felt that this would directly tell me how cells worked, and I went into other areas such as metabolic control analysis that subsequently morphed into systems biology. This happened in particular following the systematic genome sequencing programmes, where it was found that classical methods had missed the existence, let alone the function, of about half of the genes in even well-worked organisms such as baker's yeast and *Escherichia coli*. It was and is clear that to understand a system, one needed to understand, quantitatively, its internal interactions more than just the qualitative list of its components. Similarly, metabolism is the part of biology that is closest to the phenotype, and all the present concerns about diet and health are playing out on a background in which the genotype has not changed at all. So, just as many were attracted to chemistry through cookery, I always felt that small molecule metabolism, an obvious branch of physical organic chemistry, was where I would wish to focus.

Can you tell us about your work on drug uptake? How do your findings change the current understanding about drug uptake into cells?

We have a taste for iconoclastic areas of research, and this is one such area. According to a widespread assumption, the ease with which drugs diffuse ('leak') into cells across the cell membrane is a function of their lipophilicity, measured as the octanol : water partition coefficient log *P*. It is also recognised as an 'exception' that drugs may occasionally hitchhike on proteinaceous transporter molecules that normally move endogenous metabolites about. Actually, the evidence for the lipophilicity story is at best circumstantial, and we have adduced evidence that drug uptake into cells is almost certainly the rule and not the exception. The challenge then is to find out which drugs use which transporters; that changes this from a problem of biophysics (lipophilicity) to one of mechanistic systems biology.

What are the implications for drug discovery and development, and chemical genetics?

The implications are profound, because much of the design of libraries of candidate substances that become drugs has been predicated on estimates or measurements of log *P*. This is despite the fact that only about half the marketed drugs fulfil the stated criteria. By contrast, the systems biology approach offers the opportunity to understand, and to model precisely, the expected distributions of drugs based on the distributions of the transporter molecules for which they are the substrates. This will help to account for both the lack of efficacy and the toxicity that are the main reasons for drugs failing before (and in some cases after) they reach the market. The same holds true for the methods of chemical genetics.

Top tips for better chips

Chips & Tips is a new online resource from **Lab on a Chip**, discussing common problems encountered in the field of miniaturisation and microfabrication. Whether you want to learn the tricks of the trade or post your own tip, Chips & Tips is the place for you.

Some top tips so far…

In-line bubble trap for microfluidic devices
David T. Eddington

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Richard J. Holmes and Nicholas J. Goddard

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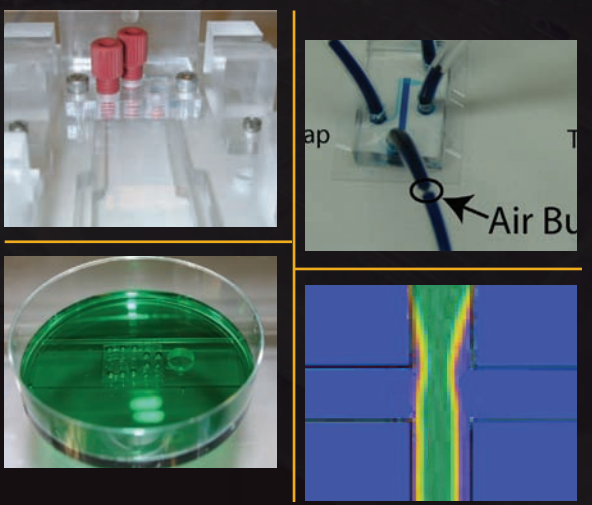

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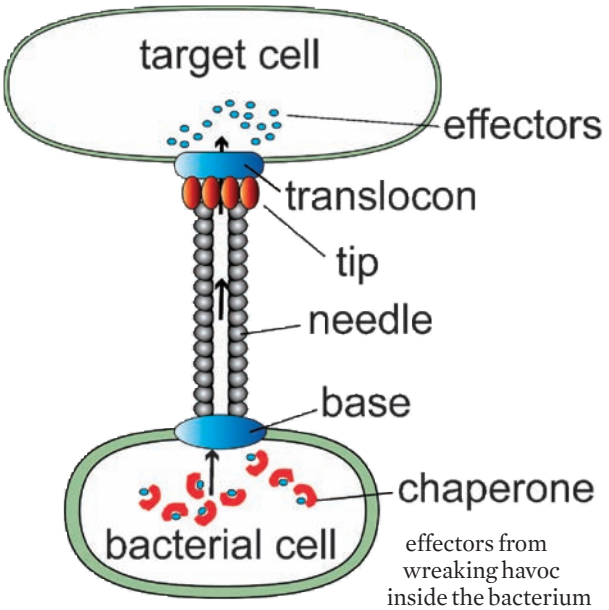
Instant insight

Bacterial nanoinjectors

Are you afraid of needles? Roberto De Guzman of the University of Kansas, US, reveals why these might also be a weak point for some of the world's most deadly pathogens

Many pathogenic bacteria use a complex protein assembly – a bacterial nanoinjector resembling a syringe with a needle – to inject virulence proteins into their target cells to initiate infections. Among these pathogens is *Salmonella typhimurium*, which this summer caused the largest food-borne outbreak in US history by sickening more than 1400 people. US authorities suspected tainted peppers and tomatoes, and American farmers lost an estimated US $250 million in sales. Other notable pathogens with nanoinjectors include *Yersinia pestis*, the cause of bubonic plague; *Pseudomonas aeruginosa*, which forms biofilms in lungs and is the leading cause of mortality among cystic fibrosis patients; *Escherichia coli* and *Shigella* species, responsible for many outbreaks of diarrhoeal diseases worldwide; and *Burkholderia pseudomallei*, a potential bioterrorism agent. No vaccines are currently approved for general use against any of these pathogens and, more alarmingly, many have developed multidrug resistance to current antibiotics. There is now a critical need to develop novel antibacterial therapies to counter the threat these bacteria pose to public health.

Delivering proteins across cell membranes is a major challenge in drug development. Bacterial nanoinjectors transport proteins across *three* membranes: the inner and outer bacterial membranes plus the host cell membrane. Nanoinjectors essentially connect the bacterial cell contents with the host cell's and form a conduit for delivering bacterial effector proteins into the host. Once inside, these proteins reprogram the host's cellular functions to promote survival, growth, and bacterial propagation. (To prevent effectors from wreaking havoc inside the bacterium itself, chaperone proteins sequester them in a non-functional state.) Together, the nanoinjector, effectors and chaperones are known as the type III secretion system.



The bacterial nanoinjector resembles a syringe with a needle and is used to inject virulence proteins into a target cell

Nanoinjectors are assembled from more than 20 different proteins, and many show sequence and structural conservation across species. The base spans the two bacterial membranes and is assembled from about 9 different proteins; many are membrane proteins, and others show ring-like structures. From the base is anchored the needle, which is formed by the polymerisation of a small α-helical protein. The needle sits outside the main cell structure and measures about 50nm in length with a ~7nm outside diameter and a 2–3nm channel diameter. On top of the needle a tip complex serves as a platform for the translocon, which punctures a hole in the host cell membrane, allowing effector proteins to pass into the host.

In the past few years the atomic structures of several nanoinjector proteins have been determined by crystallography and NMR spectroscopy. Electron microscopy and crystallography-derived models of the base and the needle itself have also become available. Nevertheless, major challenges remain in understanding how nanoinjectors are assembled. During assembly, proteins have to pass through the narrow needle channel and deposit on top of the growing structure. How proteins are moved across the needle remains unknown. Another enigma is what powers this protein movement. Although there is an energy-releasing ATPase enzyme at the base, this is believed to unfold effectors from their chaperones to allow delivery. Nanoinjectors lack a motor that would propel proteins across.

Awareness of these structures presents us with opportunities. Researchers have used nanoinjectors to deliver proteins into cells. Also, because nanoinjectors are surface-exposed and critical to virulence, disrupting this apparatus is an attractive target for developing anti-infectives – drugs that will prevent infection but not kill bacteria. Anti-infectives potentially could solve problems associated with current antibiotics; namely antibiotic-resistance (because the kill rate is not 100 per cent, bacteria that survive have a selective advantage and propagate), and the indiscriminate killing of other bacteria, including those beneficial to the host. First discovered by microbiologists, the potential therapeutic uses of bacterial nanoinjectors mean they will continue to fascinate as they begin to catch the eyes of chemical biologists.

Read more in Roberto De Guzman's highlight in issue 12, 2008, of Molecular BioSystems

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Essential elements

Good prospects for *Lab on a Chip*

Lab on a Chip, the miniaturisation journal for chemistry, biology and bioengineering is now taking miniaturisation science to the next level. With journal submissions steeply rising over the past years, 2009 will see the journal increase in frequency to 24 issues per year. The new year will also herald the arrival of George Whitesides as the new editorial board chair of *Lab on a Chip*. 'There is no one in the field who is better equipped than Professor Whitesides to help *Lab on a Chip* ascend to the next level in terms of quality, visibility and impact,' comments Harp Minhas, editor of *Lab on a Chip*.

Lab on a Chip has established itself at the heart of the miniaturisation community through various sponsorships for prizes and awards, which recognise and highlight the contributions of young and emerging scientists in the field, to online support via new initiatives such as 'Chips & Tips'- the quick-fix online forum providing useful advice on common practical problems for scientists in the miniaturisation world.

George Whitesides, the new editorial board chair of *Lab on a Chip*

More issues, more leading research and a new editorial board chair – 2009 promises to be an exciting year for the *Lab on a Chip* community.

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ChemComm in Korea

The Second *ChemComm* International Symposium on Supramolecular Chemistry will take place in Korea in November 2008 with one-day meetings in Seoul, Daejeon and Pohang. This follows a successful First *ChemComm* International Symposium on Polymers and Polymer Science in China in December 2007.

ChemComm, with an impact factor of 5.14, publishes some of the most significant work in the chemical sciences and is the fastest at publishing general chemistry communications. *ChemComm* Symposia aim to bring together scientists in an environment that fosters collaborations between the researchers and universities involved. All symposia are free to attend and each is devoted to a topical area of the chemical sciences, featuring an invited programme of international and locally-based expert speakers. In this second symposium, the programme is supplemented by a poster session, showcasing the work of local universities.

As the second symposium approaches fast and promises to be as successful as the first, plans for a third symposium next year in China are already well underway. The Third *ChemComm* International Symposium on the topic of Organic Chemistry will be held in February 2009, with meetings in Beijing, Shanghai and Chengdu.

For more details on *ChemComm* Symposia, and full programme schedules for the Second Symposium on Supramolecular Chemistry in Korea, visit www.rsc.org/chemcommsymposia.

Chemical Biology (ISSN: 1747-1605) 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*, *Organic & Biomolecular Chemistry*, *Molecular BioSystems*, *Natural Product Reports*, *Dalton Transactions* and *Photochemical & Photobiological Sciences*. *Chemical Biology* 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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