



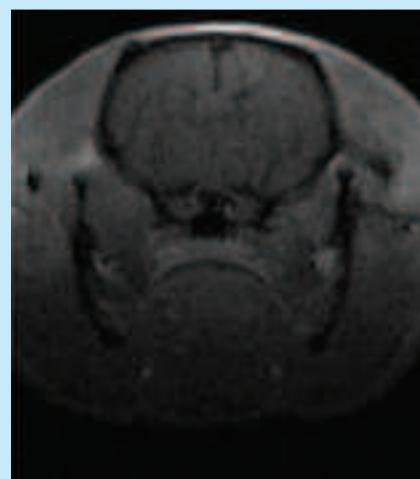
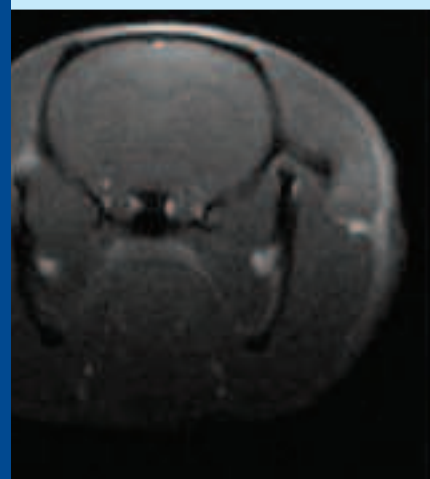
The Institute
of
Chemistry of Ireland

IrishChemicalNews

JOURNAL OF THE INSTITUTE OF CHEMISTRY OF IRELAND

FEATURE :

New MRI Contrast Agents Based on One-Dimensional Assemblies of Magnetic Nanoparticles



ALSO FEATURED IN THIS ISSUE:

- Young Chemist Profile
- Meeting Reports
- Congress Lectures
- Heavy Metal Su Doku
- Feature Article
- Literature Focus
- The ICN Crossword
- Department Profile: Chemistry at DIT

BLAUBRAND®
Volumetric Instruments

USP certificates!

Are you looking for volumetric instruments with USP tolerances?

Lennox offer the following BLAUBRAND® Volumetric Instruments:

- Volumetric flasks
- Graduated pipettes
- Bulb pipettes
- Graduated cylinders
- Burettes

with individual USP certificates.

BLAUBRAND® volumetric flasks, USP, class A are also available with batch certificates.

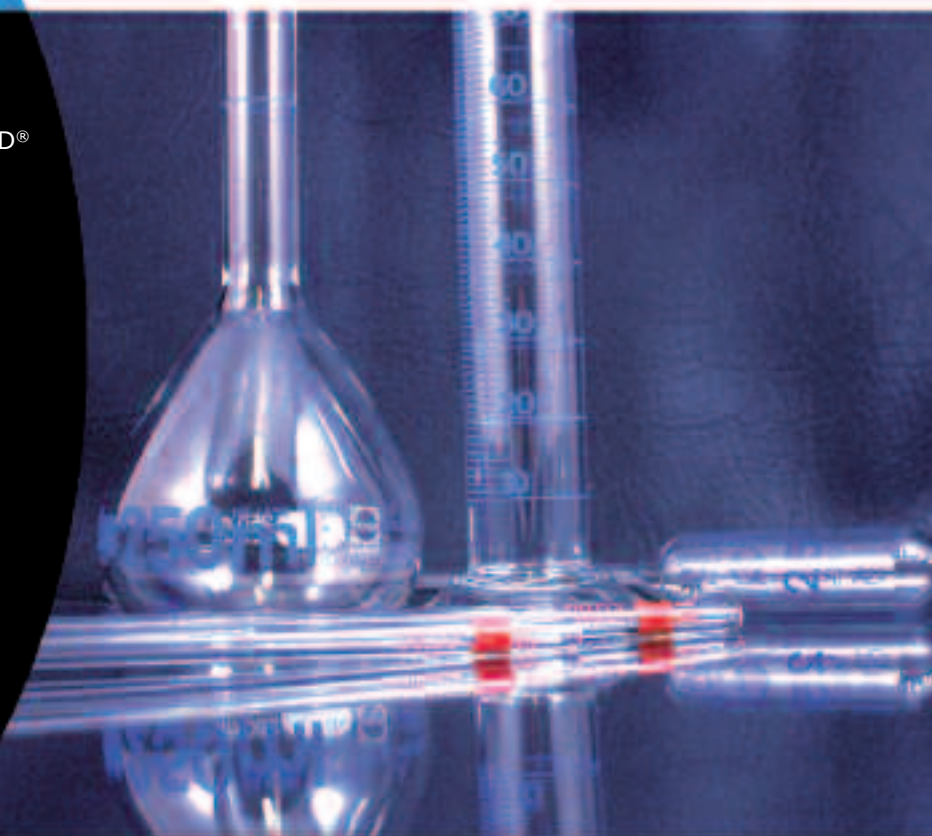


Lennox Laboratory Supplies Ltd.

Tel. 01 455 2201

Email. sales@lennox.ie

www.lennox.ie



ROMIL

When it's pure chemistry, it's ROMIL

ROMIL-SpS™ Super Purity Solvents
high purity solvents for instrumental analysis

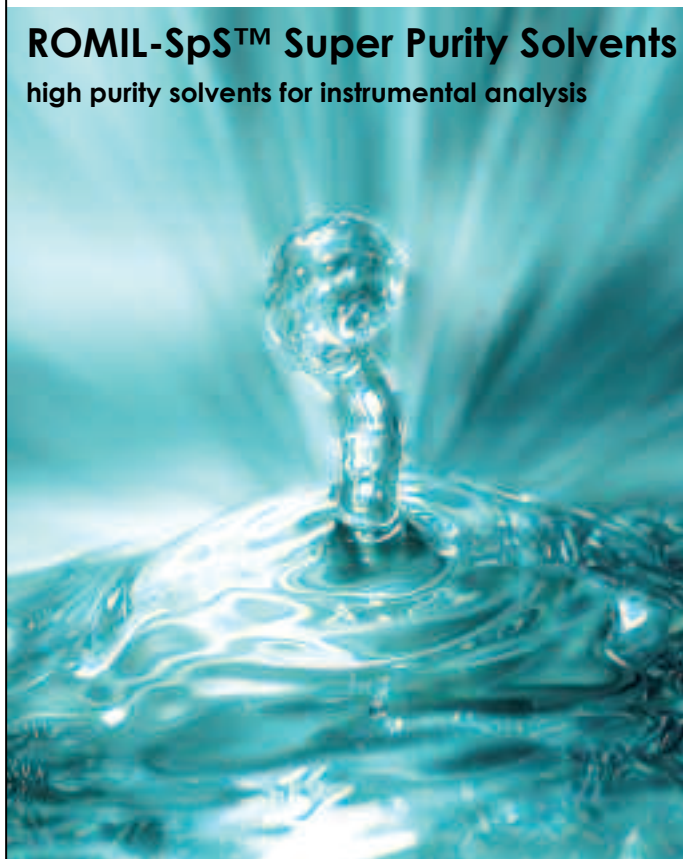
With the increasing importance of quality in the analytical laboratory and with trace level determinations now regarded as part of the routine, it takes a special reagent manufacturer just to keep up. A manufacturer like ROMIL, that has been dedicated to achieving the highest standards of chemical purity for more than two decades.

ROMIL-SpS™ Super Purity Solvents such as **Acetonitrile, Methanol and Water** are high purity solvents suitable for a wide range of applications. Since one grade only need be stocked for a variety of methods, ROMIL-SpS™ products also have the benefit of assisting laboratories, not only in their compliance with health, safety and environmental legislation, but also in their quality system accreditation to international standards such as ISO 9000 and ISO 17025.

For further details on how the range of ROMIL-SpS™ Super Purity Solvents can benefit your laboratory please contact our dedicated chemical sales team on 01 455 2201 or email sales@lennox.ie



Lennox Laboratory Supplies Ltd.
John F. Kennedy Drive,
Naas Road, Dublin 12.
www.lennox.ie



Editorial

There is something for everyone in this issue - a mix of regular items and contributions from members and ICN congress speakers. Our feature article comes from TCD, where **Prof. Yuri Gun'ko** and co-workers have been developing exciting and highly versatile new technologies based on the use of magnetic nanoparticles which have been receiving considerable attention in the field. **Dr Colm Campbell** and **Prof. Dermot Diamond** have supplied their very interesting congress presentations on the use of powder diffraction techniques to monitor crystallisation and the latest developments in novel sensor design in article form respectively. **Dr. Sarah Rawe** has provided a profile of School of Chemical and Pharmaceutical Sciences, in DIT and we have included a new feature where a young chemist shares his experiences working in industry in Ireland. **Margaret Franklin** has also been kind enough to submit a précis of the very-well received **Institute of Chemistry of Ireland Annual Eva Philbin Award Lecture** given by **Dr. Mary Archer** which dealt with the very important topic of the contributions that chemistry can make towards meeting the challenges associated with providing the planet with sufficient supplies of renewable energy.

We welcome comments and suggestions on the balance and direction of the ICN - members are also strongly encouraged to submit essays, articles and correspondence on any issues/developments affecting chemistry, either globally or in Ireland. This is your institute and magazine after all – as always we need to hear from you!

Dr. Stephen Connon

School of Chemistry, TCD
connon@tcd.ie

Contents

Editorial	1
Meeting Reports	2
Department Profile	8
Feature Article	13
Literature Focus	16
Contributions from ICI Congress Speakers	24
Young Chemist Profile	29
The ICN Crossword	30
Heavy Metal Sudoku	31

Meeting Report: The European Young Chemists Network Delegate Assembly

Leticia Albert and Colin Martin

During the EYCN 3rd Delegate assembly on the 19th-21st of March the ICI was represented by two delegates, Leticia Albert and Colin Martin. Below is a synopsis of the key points raised in the meeting and our opinions of them as they relate to young chemists in Ireland. (Note - as of yet minutes for the Madrid meeting are not yet available, they will be forwarded to the ICI as soon as possible)

- One of the most noticeable things from the discussions with representatives of other national societies is size of some of the organisations for young chemists throughout Europe. The EYCN have defined a “young chemist” as a person at the beginning of their chemistry career who is under the age of 35. Currently the Institute of Chemistry of Ireland, unlike the majority of chemical societies in Europe, has no specific section pertaining to this group. As such it was not possible for us as delegates to present any concrete information on the number of members of the society that we were representing at the meeting.
- Knowing the current number of ICI members under the age of 35, a strategy, based on “best practice” from other European societies could be implemented in order to increase the number of members who fall under the young chemist category.
- It is also worth noting that the scale of some of the societies (for example both the German JCF and the British RSC/YMD have in excess of 8000 members). In the future a young chemist division to the ICI may be something to consider but the lack of concrete information regarding numbers of relevant chemists in Ireland at the moment leads us to believe

this situation is not tenable in the short term. However it may be beneficial in attracting younger members to appoint an official delegate who is responsible for representing the ICI in EYCN business in the future.

- One of the decisions reached during the meeting was to hold an international student congress some time in 2009. This will be run in conjunction with one of the existing national student congresses (date/venue t.b.c.) similar to the Irish Universities chemistry colloquium. Again it would be beneficial to chemistry in Ireland if a suitable speaker was present at the meeting.
- At the moment the majority of ICI members know very little (or nothing at all) about the EYCN, in our opinion in order to increase knowledge of the network a number of possibilities exist.
- Information about the meeting and the relevant Irish representatives could be made available on the ICI website.
- An article giving out information about the Madrid meeting and the EYCN could be prepared and published in a future issue of the Irish Chemical News.
- Relevant representation (possibly through internal college chemical societies) should be sought from universities and institutes of technology along with some industrial input, in order to allow for contact between the EYCN and young chemists throughout Ireland.

We would like to take this opportunity to thank the Institute for its assistance in allowing us to attend the Madrid meeting and if anyone requires further information on the EYCN feel free to contact us at leti8383@hotmail.com (Leticia) or martincj@tcd.ie

Meeting Report: UCD Chemical Society Inaugural Lecture

Elaine O'Reilly, *Secretary, UCD Chemical Society*

The 63rd Annual Chemical Societies Inaugural event was held on the 11th of April 2008 at University College Dublin. The event was kindly sponsored by the Institute of Chemistry of Ireland. Following tradition, the evening was opened with a talk from an invited lecturer. This was followed by a wine reception in the school. This year, the Chemical Society was privileged to invite Professor John Sutherland from the University of Manchester to deliver the Inaugural Lecture, entitled “Prebiotic Chemistry in the Origins of Life”. Professor Sutherland received his B.A. Honours degree in Chemistry at Oxford. He subsequently worked with Professor Jack Baldwin at the University of Oxford. He currently holds the position of Professor of Biological Chemistry at the University of Manchester.

Professor Sutherland's research into Prebiotic Chemistry focuses on the evolution of nucleic acids and genetically-coded proteins. He has described Prebiotic Chemistry as the chemistry needed to “kick-start” the complex biological systems which exist today. Many challenges exist in this area of research, which strives to rationalise how DNA and RNA were derived from simple prebiotic molecules.

This Chemical Society event was attended by over 100 academic staff, postgraduate and undergraduate students from the university. Professor Sutherland's research proved to be a very refreshing topic for discussion, as it is not often the case that such complex, challenging research is geared towards curiosity rather than application.

Create a parallel process reactor...

Six heated & stirred reactions
from 5ml to 250ml...

A system includes:

- **Tornado™** - Powerful overhead stirring of up to 6 flasks
- **Carousel 6™** - Accepts round bottom flasks from 5ml to 250ml
- **Storm™** - Controlled heating & cooling from -65°C to +200°C

For more information contact:
e: sales@labplan.ie
t: (045) 870 560



Tenth Year of Eurachem Analytical Measurement Competition in Ireland

Marie Walsh, Dept. of Applied Science, Limerick Institute of Technology

The Eurachem Analytical Measurement Competition (EAMC) was initiated by Dr Sean Cawley of IT Carlow in 1999. It is promoted by Eurachem Ireland, the Heads of School of Science and Council of Directors of the Institutes of Technology. Industry, academic and state laboratories constitute the Reference Committee. The EAMC is designed to raise awareness among student analysts of uncertainty in measurement and the requirement for excellence in analytical skills. The EAMC Competition is open to teams of two full-time third-level registered students studying laboratory sciences in Universities or Institutes of Technology anywhere in Ireland and who have not yet entered the third year of their course. Competitors are chosen by their own Institution, for their practical laboratory skills. Each Institution may submit a first team (and one reserve team), for the National Final EAMC.

The imperative of science is to closely scrutinise everything in the world about us and give an unambiguous account of what is observed. Science fosters skill in deductive and inductive reasoning and helps us cope with an ever changing social and material environment. Accurate and reliable measurement is the keystone to the experimental process. In education, systematic processing and reliable reporting are not ends in themselves but processes which develop rigorous, integrated and logical thinking, thereby developing a systematic, analytical and reliable mind in the emerging graduate.

The competition aims to focus attention on improving these skills. At a time when all third-level colleges have suffered a downturn in numbers studying science, the competition has been instrumental in generating links between the competing colleges and renewing collegiality among the educators. Student participation is a valuable addition on the graduate Curriculum Vitae and is viewed by employers as such.

In 2008 we celebrated the tenth year of competition before the event in Dublin Institute of Technology. This year's competition involved comparative titrimetric analysis of bottled water samples and as in all previous years was a rigorous test of the students' skills. The competition promotes critical, analytical and observational skills, and raises awareness among student analysts of uncertainty in measurement and the skills needed in reducing and reporting it. While the judges deliberated over the laboratory performance and mathematical computation of results by the teams, the participants and their mentors attended an excellent and informative presentation by Dr. Sheila Willis, Director of the Forensic Science Laboratory. The winning team was from Dublin Institute of Technology and the runners-up from Letterkenny Institute of Technology and Galway-Mayo Institute of Technology. The winners, their Alma Mater and the runners up are awarded a replica of the 'Newgrange' art piece.



Irish Pewtermill, Timolin, Co. Kildare, designed the trophy artwork, sponsored by An Chomairle Oidhreachta. It is based on the Newgrange National Monument 'light box', illustrating a precision and reliability dating to 3200 BC. The monument incorporates an awesome six metre high chamber, built with a twenty one metre entrance corridor; it predates the Pyramids, Stonehenge and the Minoan Temples. The corbelling technology used is probably indigenous to Ireland. The archaeologist, O'Kelly demonstrated that an orifice located over the entrance, was so positioned above floor level and of such width and height that as the sun rose on the winter solstice, its light shone on a recessed 'cremation' bowl. Accurate positioning of the huge structure provided for fine adjustment of the orifice.

The importance of analytical science in third level education is evidenced by the promotion and support of this competition. The major sponsors of the competition are Eurachem Ireland, Mason Technology, the Association of Heads of School of Science, the Environmental Protection Agency, the Institute of Chemistry of Ireland, Discover Science and Engineering and Pharmaceutical Ireland.

For Further Information Contact: EAMC Secretariat, c/o Marie Walsh, Limerick Institute of Technology. Marie.Walsh@lit.ie

Science Week 2007: ISTA Quiz Report



1st place: Scoil Mhuire



2nd place: Scoil Mhuire



3rd place: St. Mel's College

The Annual Midland Regional Science Quiz was hosted by the Department of Life and Physical Sciences last Thursday 15th November. The venue was the Nursing and Health Sciences Building at AIT. This was the Midlands round of the National Science Table Quiz for Secondary School students of Science Subjects Biology, Chemistry and Physics. Seventeen teams competed from across the Midlands. The top three teams will be competing in the National finals in TCD on Saturday 24th November. The following Athlone schools were represented: Athlone Community School, Our Lady's Bower, and Summerhill College. Other schools who entered teams included: Moate Community School, Ballymahon Vocational School, St Mel's College, Longford, Sacred Heart Convent, Tullamore, Scoil Mhuire, Longford, Scoil Mhuire, Strokestown and Ard Scoil Mhuire, Ballinasloe

The winning team was from Scoil Mhuire, Strokestown and included Caroline Kelly, Ciaran Moran and Niall Cumpton, with a score of 39 points.

Scoil Mhuire, Strokestown also supplied the team placed second, on 37 points which included Aisling O'Gary, Catriona O'Rourke and Rory Molloy. Third place went to St Mel's who beat Our Lady's Bower in a tie breaker. St Mel's team included Colin McQuade, Paul Malony and Shaun Hughes. Our Lady's Bower team was represented by Caroline Monaghan, Iseult Flynn and Orla Hughes. The organisers would like to thank our two kind sponsors who sponsored the prize money yet again - the Athlone based Pharmaceutical company Arran Chemicals Limited, Monksland Industrial Estate, Athlone and the Institute of Chemistry of Ireland, the professional body for the promotion of Chemistry in Ireland.

The other Athlone teams included (Our Lady's Bower) Noreen Fleming, Eva Hamilton and Rebecca Higgins : (Community College) Katie Egan, Kaylie Duffy, and Aoife Tully and (Summerhill College): Roisin Connaughton, Maire Walshe, Bernie Tobin, Brid Curley, Deirdre Corbett and Orlaith Mannion.

Institute of Chemistry of Ireland Annual Eva Philbin Award Lecture 2007

Report on a lecture given by Mary Archer entitled 'Chemistry for the Good Life'

Margaret Franklin, *School of Science, Athlone Institute of Technology*



L. to R. Dave Birkett, (Institute of Chemistry of Ireland) Grainne O'Malley, (Head of Department of Life & Physical Sciences, AIT) Dr. Joe Ryan, (Academic Registrar AIT) Dr. Mary Archer (Eva Philbin Award recipient) Doreen Geraghty (Representative of Elan, sponsor of the wine reception) Pearse Murphy, Head of Department of Nursing & Health Sciences, AIT) Margaret Franklin (Senior Lecturer in Chemistry, AIT and Registrar, Institute of Chemistry of Ireland).

Athlone Institute of Technology was one of the venues for the Eva Philbin Annual Award Lecture series for 2007. The award, inaugurated by the Institute of chemistry of Ireland in 2005, is named for the Late Eva Philbin, who was a Professor of Chemistry in UCD for many years. It is presented annually to a distinguished chemist with an international reputation, who is also able to relate



(Left to right)
Margaret Franklin
(Senior Lecturer in
Chemistry, AIT and
Registrar, Institute of
Chemistry of
Ireland), Dr. Mary
Archer (Eva Philbin
Award recipient)

and communicate the importance of chemistry and chemical research to everyday life. This year's award recipient was Dr. Mary Archer, Baroness Archer of Weston -super-Mare, an eminent British chemist, who has specialised in the use of chemistry for solar energy conversion and is an expert in the development of biofuels.

Dr. Archer began her lecture by listing the many benefits that chemistry has brought to society. These include, for example, life-saving and health-giving medicines, fertilisers & pesticides so important to agriculture, construction materials such as cement, paints & other surface coatings, plastics and textiles, dyes and inks and of course biofuels. Given these benefits, one may ask why chemistry is not a more popular subject choice for 3rd level students?

The speaker suggested that this may have something to do with developments in mathematics teaching, where students are allowed to use calculators, rather than being encouraged to do mental arithmetic. This has led to a decline in numeracy among school pupils and so the calculations involved in solving chemistry problems may seem rather daunting to some. Dr. Archer conceded that chemistry has been given a bad image by some high-profile accidents, such as the explosion in Bhopal in India in the 1980s, which released a cloud of toxic fumes, resulting in many fatalities and casualties. Two decades earlier, another negative image had been portrayed by the publication of Rachel Carson's book 'Silent Spring', which raised public awareness of the harmful environmental effects of the indiscriminate use of pesticides, in particular DDT.

Solar Energy Conversion

Dr. Archer then launched into her principal theme, which dealt with the use of chemistry in solar energy conversion. Photosynthesis by green plants is of course the primary natural mechanism for harnessing the sun's energy, using the green chlorophyll pigments to trap the energy and use it to convert carbon dioxide and water, first into sugars, then more complex carbohydrates, which are in turn converted into all the chemicals of which biological organisms are made. Fossil fuels yield up that energy when they are burned, but in so doing, they release carbon dioxide into the atmosphere at a much faster rate than it was consumed in the first place, leading to increased levels of this gas in the atmosphere, contributing to global warming. The advantage of the new biofuels is that they are 'carbon neutral'. This is because they use crops that are grown at the present time (in contrast to fossil fuels which required millions of years to be formed) and the rate at which the carbon dioxide is returned to the atmosphere during combustion, is, to a large extent, offset by the rate at which it is removed by photosynthesis while the crop was growing..

Bio-ethanol

Comparing various plant sources of biofuels, Dr. Archer said that cane sugar was the most energy efficient crop. It is easy to grow and has an energy ratio of 8:1. The sugar is extracted from the cane and is fermented with yeast to yield ethanol, which can be burned as a fuel. In the United States of America, corn starch is being used as a source of bioethanol, to ensure security of energy supply, even though its energy ratio is not as good as that of cane sugar. Another possibility is to use cellulose, but this substance is more difficult to break down, as specialised enzymes are required. The US Government has put 250 million dollars into developing methods of obtaining bio-ethanol from cellulose. The great advantage of this is that cellulose forms such a large proportion of the mass of a plant crop. However, ethanol is not an ideal fuel, as it is too volatile and so evaporates rapidly. It is also rather corrosive, especially when it picks up water, with which it mixes well. Butanol, on the other hand, is a higher molecular weight alcohol and so is less volatile. It is immiscible with water and is less corrosive than ethanol. In addition, having more carbon atoms (four in butanol compared to two in ethanol) it is more energy dense. So it would be a preferred fuel. Unfortunately, it is more difficult to make than ethanol. However, experiments are under way in the UK to use beet sugar as a source of bio-butanol.

Biodiesel

This is a type of biofuel that can be made from plants that produce oily seeds and is highly suitable for use in motor engines. Mary Archer told the gathering that in fact the first diesel engine, invented by Diesel himself, ran on peanut oil. Rapeseed oil is suitable for conversion to fuel and the oilseed rape plant is now being grown extensively in many European countries for this

purpose. To make biodiesel, the oil, which is a triglyceride of fatty acids, is transesterified with methanol. This yields glycerol as a by-product (which can be sold to the cosmetics industry) while the biofuel product is a mixture of methyl esters. The esters contain oxygen as well as carbon and hydrogen, and so do not belong to the same class of chemicals as the hydrocarbons found in petroleum. However, they have similar molecular weights and combustion characteristics as diesel oil and so are referred to as bio-diesel.

Chlorophyll Mimics

The speaker told the audience of a very fine piece of chemical research, reported by D.M. Guldi et al. in 2002, in which a molecule has been synthesised which can mimic the way in which chlorophyll traps solar energy. This has a very interesting structure. The molecule has a 'Buckyball' at one end (similar in structure, though on a molecular scale, to the geodesic domes designed by the architect, Buckminster Fuller, consisting of a sphere formed by interlinked hexagons and pentagons, like a football) and a Ferrocene structure at the other (Ferrocene was first reported by Kealy and Pauson in 1951 and was the first of the 'sandwich' complexes to be synthesised, in which a metal atom, in this case iron, is sandwiched between two five-membered carbon ring structures). In between these two very interesting structures there are porphyrin rings (similar to the one in the chlorophyll molecule) which can facilitate electron transfer. This molecule has the potential to trap solar energy and it has been found that 1.1 eV (electron volts) of energy can be stored in this molecule for a 0.38 seconds. Obviously, it will take time to develop this process to the point where a steady electric current can be delivered, however it looks promising.

Solar Furnace

Dr. Archer also talked about physical, rather than chemical methods of harnessing solar energy. In Spain, a huge array of mirrors is used to focus the sun's rays in a solar furnace, which can produce very high temperatures of a few thousand degrees Celsius. This could be used for such processes as cement production, or for metal smelting. Solar energy harnessed in this way can also be used to detoxify water supplies and for reforming of hydrocarbons.

Photovoltaic Cells

The ability of silicon-based semiconductors to generate a voltage on exposure to light was an effect discovered in the 1940s in Bell Laboratories in the U.S. Silicon cells were first used in space and terrestrial applications have been slow to develop. Silicon cells are the first generation of photovoltaic cells. The next generation of such cells will most likely use an organic block co-polymer, but research is in the early stages as yet. The silicon cell has an energy efficiency of 15–20% while the co-polymer cells that have been developed so far are only about 5% efficient.

Hybrid Motor Engines

Hybrid cars have come on the market in recent years. They have a petrol engine, which is needed for acceleration and when driving at higher speeds, supplemented by a battery, which drives the wheels at low speeds and helps the engine when required. The energy efficiency of the design is due to the fact that the petrol engine also drives an electric motor, which re-charges the battery and in addition, when decelerating and braking, the energy is recovered and transferred *via* the electric motor to charge the battery. The battery itself is a nickel/metal hydride electrochemical device. This does not use solar energy, but these cars are very energy-efficient and of course have much lower carbon emissions than conventional petrol engines.

Chemistry and Health

Dr. Archer finally spoke about the contribution made by chemistry to health care. It is estimated that 40% of the population would not be alive today if it were not for the availability of modern medicines, designed by chemists. Time did not permit more extensive treatment of this topic, but the speaker also gave some fascinating insights into the way in which modern methods of chemical analysis have been applied to medical diagnostic techniques. One example is the use of nuclear magnetic resonance (NMR). In the chemistry laboratory, NMR uses the magnetic effect produced by the spin of protons in a magnetic field to identify particular substances. In medicine, the technique is referred to as magnetic resonance imaging (MRI) or MRS (magnetic resonance scanning) because of the negative connotations of the word 'nuclear'. Another technique is Positron Emission Tomography (PET). The patient is injected with a solution of glucose, which has been 'labelled' with an artificially produced radioisotope of fluorine. This does not emit harmful radiation, instead, it decays with the emission of a positron. A positron is the 'anti-particle' of an electron; it

has the same mass, but carries a positive charge, whereas an electron is negatively charged. As soon as the positron is emitted, it immediately encounters an electron, resulting in mutual annihilation and the production of a pair of photons with the same mass-energy as the electron-positron pair. The photons thus produced, form images on a computer screen, which result in bright spots where there is a high rate of glucose metabolism. The speaker showed two contrasting PET images of the human brain. One was of the brain of a normal person, who was asked to think about something which required some brain activity, while the other showed the brain of a cocaine addict, who had been given the same task. The normal subject's brain had many bright spots, showing plenty of activity, while that of the cocaine addict was dark almost everywhere.

The lecture was very well attended and Dr. Archer held her audience enthralled, by the clarity of her explanations and the fluency of her language, as well as by the beautiful slides which illustrated the lecture. It was a rare treat for the midlands to hear such an eminent scientist give such a fascinating lecture.

Annual Congress 2008

Margaret Franklin, *School of Science, Athlone Institute of Technology*

The Annual Congress of the Institute of Chemistry of Ireland, on the theme of 'Nanotechnology', was held at Athlone Institute of Technology on Friday, May 16th. The principal sponsor was the Athlone-based company, Elan Drug Technologies.

Nanotechnology, which deals with molecular assemblies having dimensions of only a few hundred nanometers and smaller, is an emerging interdisciplinary field, with many and diverse applications. This was reflected in the wide variety of topics dealt with by the speakers on the day. The meeting began with a brief welcoming address from Dr. Joseph Ryan, Academic Registrar of AIT, after which, the proceedings were formally opened by Dr. Donal Coveney, President of the Institute of Chemistry of Ireland. The Sessions were chaired by Dr. Paul Tomkins, Head of School of Science at AIT, Mr. Jim Roche, Lecturer, Department of Life & Physical Sciences at AIT and Dr. Clem Higginbotham, Director of the Centre for Nanotechnology & Materials Research (CNMR) at AIT.

The opening presentation, given by Professor Dermot Diamond from the National Centre for Sensor Research (NCSR) at DCU, gave an amazing insight into the use of adaptive materials. These are, in effect, molecular 'switches' whose properties (e.g. surface charge/polarity, colour, porosity or permeability,) can change, depending on the application of specific stimuli (e.g. chemical, electrical or exposure to light) and which may be used as sensors for environmental monitoring or clinical diagnosis, or which could have potential applications in separation science and drug delivery.

The second speaker was Professor Michael Morris, who is based in UCC and also works with the Centre for Research on Adaptive Nanostructures and Nanodevices (CRANN) at TCD. His presentation, entitled 'Future Scaling in the Microelectronics Industry: Engineering meets Chemistry', explained how the further miniaturisation of electronics circuitry may be achieved using a so-called 'bottom-up' approach. This involves self-organisation in polymer systems to produce highly regular nanopatterns, based around phase separation in block co-polymer systems.

The final speaker in the first session was Dr. Maria Davoren, a Toxicology graduate of AIT, who is now involved with a major research project in the FOCAS institute at DIT. Her presentation gave an account of her research group's investigation into the possible toxicity of nanoparticles, both to humans and the environment, including the development and validation of new methods of evaluating the toxicity of such engineered materials.

After a break for coffee and a visit to the trade exhibition, the second session got under way. This session was devoted to industrial applications of nanotechnology and it included presentations by Rick Bastin (Associate Director R&D, Elan), Dr. David Corr (CEO of NTERA) and Paul Blackie, of the Polymer Department and the CNMR at AIT. They dealt, respectively, with Elan's NanoCrystal technology in drug formulation, NTERA's use of nanomaterials in photochromic display technology for hand-held devices and the use of nanoclays to improve the properties of plastics.

After lunch, the afternoon session was devoted to research being conducted at the Centre for Nanotechnology and Materials Research (CNMR) at AIT, which is located in the former Polymer Development Centre, a facility originally established by Materials Ireland and located in the IDA Business and Technology Park, close to Athlone Institute of Technology. Each of the three presentations described a different medical application of nanotechnology. Dr. James Kennedy described the development of a special polymer coating for drug-eluting stents; Dr. John Lyons showed how the incorporation of nanoclay fillers in a polymer matrix material improved the controlled release of active pharmaceutical ingredients and Dr. Luke Geever showed how the use of temperature-sensitive hydrogels have potential for use in biomedical drug delivery devices.

Following this session, the participants were brought on a tour of the facilities at the CNMR. The CNMR building also provided the venue for the presentation of prizes to the winners of the Schools Essay Competition. Following the prize-giving, the recipients and their families joined members of the Institute for the tour. Finally, at the close of the congress, some light refreshments were enjoyed by everyone.

School Profile: The School of Chemical and Pharmaceutical Sciences, DIT

Dr. Sarah Rawe

School of Chemical and Pharmaceutical Sciences, DIT, Kevin St, Dublin

DIT in its current form was constituted by the 1992 Dublin Institute of Technology Act from the six further education colleges of the City of Dublin Vocational Education Committee (CDVEC). Having established a rich tradition for the provision of all levels of higher and further education, the newly established Institute was given authority to award undergraduate degrees in its own right and this was followed in 1997 by the powers to award Doctoral degrees. Prior to the 1992 Dublin Institute of Technology Act degrees were delivered and awarded in partnership with other HE Institutes, including the University of Dublin and professional bodies such as the Royal Society of Chemistry. Similar arrangements permitted research activities. Many of these partnerships and collaborations still exist to this day.

The School of Chemical and Pharmaceutical Sciences is located in the Faculty of Science on Kevin Street, Dublin 8. It can trace its origins to the first College of Technology established on the site in 1887, although the current building dates from 1968; courses in theoretical and practical chemistry were among the first delivered. By 1896, the College offered courses in 5 discipline areas: science, art, technology, commerce and women's work and included organic and inorganic chemistry reflecting developments within the field at that time.¹

The School has 22 academic members of staff who are ably supported by 8 technical staff and a School Administrator. Dr. Declan McCormack is the current Head of School following the retirement of Dr. Noel Russell in 2005. He will guide the School through a period of transformation as DIT moves to a new, single campus in Grangegorman; planning for the new campus is underway with relocation scheduled for 2012.

The College of Technology was established to provide technical and vocational training and a ladder of opportunity for all. Accordingly, the School remains committed to excellence in teaching, delivering innovative and adaptable programmes that are specifically designed to meet the needs of the market place; industrially relevant modules are a significant component of all courses. Taught programmes are offered at NQAI levels 6 to 9 (Certificates and Ordinary, Honours and Masters degrees) and successful graduates at each stage have the opportunity to progress to the next level. Rapidly expanding research activities are recognised as vital to underpinning the undergraduate provision; a new research facility situated across the road from the back gate of the main building (the Focas Institute, Camden Row) houses many of the School's researchers.



Figure 1. Faculty of Science, Kevin St (Front and Courtyard) and the Focas Institute, Camden Row

Teaching

The School offers five undergraduate and four taught Masters programmes designed to equip students with the knowledge and skills required to work in Ireland's chemical, pharmaceutical and related industries. A substantial teaching commitment and small student to staff ratio ensures average class sizes of 15-35 and considerable contact time with students. Teaching laboratories are equipped with state of the art spectroscopic facilities and instrumentation and all programmes are supported by a virtual learning environment

The 3-year level 7 (Ordinary) degree in Medicinal Chemistry and Pharmaceutical Sciences was updated in 2007 in response to the growth of Ireland's thriving pharmaceutical sector and the interests of the incoming cohorts of students. A strong emphasis on practical work and hands-on training as well as modules in drug design & development, quality assurance, regulation, chemical and pharmaceutical technology and validation ensure the course is directly relevant to future employment in the industry. Successful graduates may decide to continue their education by progressing to a 1.5 year 'add on' Honours degree in Chemical Sciences with Medicinal Chemistry.

An 'add on' level 8 (Honours) degree in Chemical Sciences evolved from the Graduateship of the Royal Society of Chemistry (Part II) which ran for over 20 years until replaced by the current course in 1999. Modules in core chemistry subjects and analytical techniques are complemented by modules in industrial chemistry, exposing students to the realities of chemical processes and the requirements of scale. A 3 month research project is carried out within a company or in the School, which has a dedicated project laboratory.



Figure 2. Undergraduate Laboratories (Analytical and Physical)

The level 8 (Honours) degree in Forensic & Environmental Analysis provides students with a strong foundation in the chemical sciences as applied to these specialist fields, with an emphasis on analytical techniques. This 4-year programme was the first of its kind in Ireland and is still unique in providing an insight into both forensic and environmental science through focused modules and case studies.

With a long standing tradition of providing interdisciplinary programmes, the level 8 (Honours) degree in Science with Nanotechnology was developed with the School of Physics in response to rapid progress in the field of materials science and an identified skills shortage. The programme was introduced in 2006, replacing the degree in Chemistry and Physics and is co-taught until year 3 when the students can choose to specialise in either chemistry or physics. A 6 month work placement in the 3rd year is a compulsory element of both 4-year Honours degree programmes; students have found positions in chemical and pharmaceutical companies as well as the Marine Institute, the Environmental Protection Agency and the State Laboratory. The placement provides them with invaluable experience and increasing awareness of the career paths and opportunities open to them.

A large number of the School's programmes are designed to upskill personnel currently or recently employed in the pharmaceutical sector: A level 7 (Ordinary) degree in Validation of Medicinal Products (developed and delivered jointly with DPS Engineering) and four taught Masters programmes: Quality Assurance (& Biotechnology or Regulation), Pharmaceutical & Chemical Process Technology (with the School of Control and Engineering Systems) and Pharmaceutical Validation Technology. These full and part time programmes aim to bridge the gap between undergraduate qualifications in science and engineering and the specific requirements of the pharmaceutical industry. Short courses (approximately one week) offering additional training to employees of the sector include Chemical Risk Assessment & Risk Management Training and Noise Risk Assessment.

Research

Early on in the Institute's development a significant number of its academic staff, many from the Faculty of Science, recognised the importance of research in underpinning and informing the development of the undergraduate provision. These individuals nurtured a growing research culture in the Institute and were successful in attracting significant external funding and developing links and collaborations with world class researchers from Ireland and around the world; their efforts ultimately culminated in a new research facility, the Focas Institute.

The Focas Institute (Facility for Optical Characterisation and Spectroscopy) was funded through PRTL Cycle 1, opening its doors in 2004. United by the need for core spectroscopic facilities, researchers from a number of scientific backgrounds are housed within Focas; thus it represents a truly interdisciplinary environment, exposing staff and students alike to a broad range of scientific enquiry. Built around the core facilities, specialist laboratories including Materials Synthesis and Applications (MSA), Biomedical and Environmental Sensing and the Radiation and Environmental Science Centre (RESC) provide accommodation for 18 of the School's 36 postgraduate students (MPhil and PhD) and 4 full time researchers and

postdoctoral fellows. Currently Focas is operating at its full capacity and recent success in PRTL Cycle 4 will allow significant expansion.

Reflecting the applied nature of much of the ongoing research in DIT, the School also has a significant number of postgraduates based in industry, the Marine Institute, the State Laboratory or undertaking industrial placements during of their studies. Many have the opportunity to spend time in other HE Institutes in Ireland and abroad, including TCD, UCD, DCU and NUI Maynooth. Three postgraduate students have been successful in the FÁS Science Challenge; in 2007/8 two postgraduates spent a year in Rice University, Texas under the supervision of Prof. Michael Wong and a third is taking part in the scheme this year, also heading for Rice to work with Prof. Kenton Whitmire.

Dr. Declan McCormack is Head of School and Academic Director of CREST (*vide infra*). His interests include the investigation of nanoparticulate ZnO and its electronic applications, sol-gel preparation of nanoparticulate materials, inhibition coatings to prevent build-up of biofilm (Figure 3) and the environmental & toxicological impact of nanoparticles.² He is member of the IMPART European Co-ordination Action Programme (IMPART - Improving understanding of impact of nanoparticles in human health and the environment).

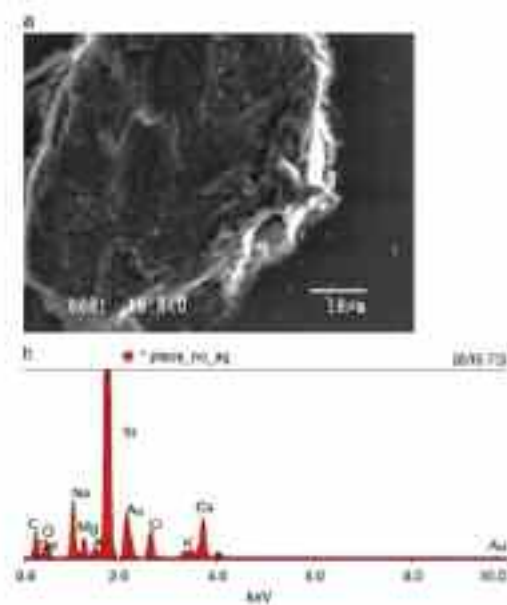


Figure 3. SEM image of (a) *Staph. epidermidis* biofilm on PhTEOS-coated glass and (b) elemental analysis of biofilm structure

Dr. Michael Seery has research interests in the photophysics of metal oxides and in particular the study of electron transfer in metal oxide systems (Figure 4).³ Current projects are concerned with the development of novel visible light activated metal oxide materials for photocatalysis applications and the study of the mechanism of enhancement of photocatalysis. The group works closely with Dr. Suresh Pillai (CREST) with a view to incorporating these materials into coatings to afford durable surfaces with self-cleaning and antibacterial properties, resistant to wear, oxidation and chemical abrasion. Dr. Seery is also a member of the School's Chemical Education Research Team (*vide infra*).

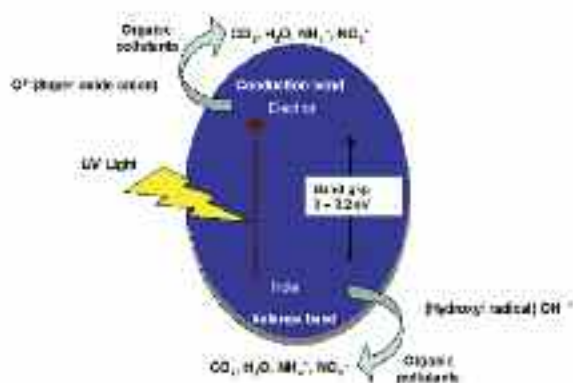


Figure 4. Mechanism of photocatalysis

Dr. John Cassidy is investigating thin electroactive films as sensing layers using covalently attached porphyrin films for electrochemical catalysis and mediation, specifically for analysis in flowing streams. The group uses reflectance spectroelectrochemistry for the study of processes at electrode surfaces with a view to developing gas sensors and studying the photoelectrochemical destruction of trace organic molecules in wastewaters (Figure 5) and recovery of precious metals.⁴

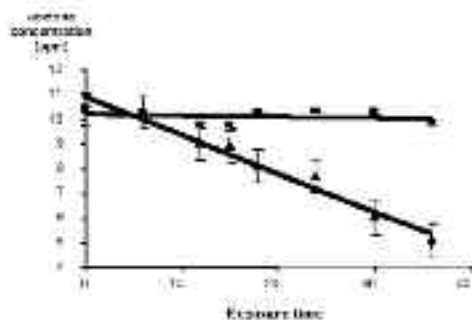


Figure 5. Photoelectrochemical degradation of acetone in aqueous solution

Dr. Barry Foley and **Dr. Patrice Behan** perform their research in collaboration with the Marine Institute and the State Laboratory and their work focuses on food safety and environmental issues mainly relating to the marine resource, including analysis of naturally occurring toxins in seafood such as shellfish. As one of twelve partners of the European BIOTOX project, the group are involved in the development, validation and standardisation of suitable analytical methods for the identification and quantification of lipophilic marine biotoxins (Figure 6). Projects also include the development of passive samplers as a tool for water quality monitoring and development of biological tests for the ecotoxicological assessment of marine sediments (in collaboration with the RESC).

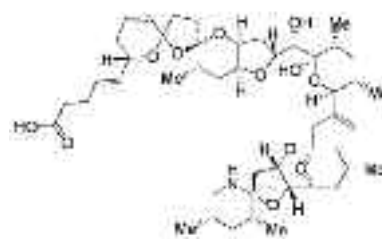


Figure 6. Chemical Structure of azaspiracid which causes diarrhetic shellfish poisoning

Dr. Mary McNamara and her group are involved in the preparation and spectroscopic characterisation of metallo derivatives of cyclodextrins with potential applications for the selective encapsulation and detection of chiral drugs. She works closely with a number of groups in the Focas institute and in collaboration with Dr. Hugh Byrne and the POMM group (Physics of Molecular Materials) has recently reported a systematic study of the effects of naphthalene and anthracene substitution on the properties of PPV derivative conjugated polymers. These polymers exhibit a strong electroluminescence and have applications in OLEDs (Figure 7).⁵ Other projects include spectroscopic investigation of the interactions of saccharides with carbon nanotubes with a view to developing biocompatible composites⁶ and development of new analytical techniques to investigate the radiation-induced bystander factor in cell conditioned media.



Figure 7. Appearance of the series of PPV derivative polymers under UV light

Dr. Claire Mc Donnell collaborates with Prof. Rory More O'Ferrall (UCD) to investigate the applications of biotechnology to oxidative biotransformations of aromatic substrates. The aims of this research programme are to; (i) examine the scope for processing of fermentation products to form pharmacologically and industrially useful materials and (ii) enhance understanding of the mutagenicity of polycyclic aromatic hydrocarbons. The research that is being undertaken in DIT involves developing a synthetic route, using iron tricarbonyl complexes, to convert arene *cis*-dihydrodiols formed by biotransformations to their *trans*-isomers, which are useful chiral building blocks.

This development work is being informed by mechanistic and stability studies on the intermediate iron tricarbonyl complexes (Figure 8).

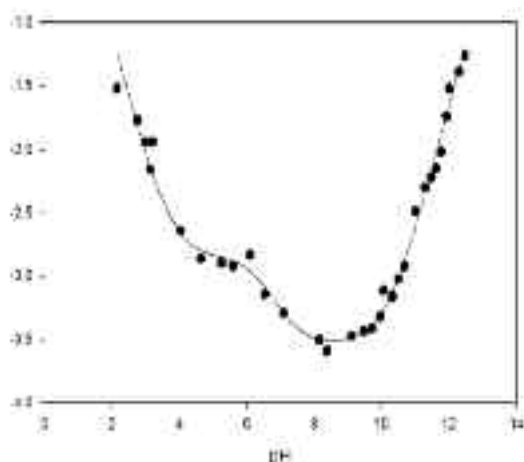


Figure 8. pH Profile ($\log k_{\text{obs}}$ against pH) for the hydrolysis of an iron tricarbonyl cyclohexadienyl intermediate

Dr. Christine O'Connor is interested in the design of targeted drug delivery vehicles and of suitable photosensitisers as chemotherapeutics. Work involving the synthesis and evaluation of novel cyclodextrin-folic acid conjugates as carrier molecules for PDT (Photodynamic Therapy) agents is in progress (Figure 9). FR- α is over-expressed in several human cancers including ovarian, breast and renal carcinomas and this property has been utilised to develop tumour-selective anti-neoplastic drugs. The photosensitisers and folic acid will both be covalently bound to the cyclodextrin. The rationale is that the cell-penetrating property of folic acid will be utilized to deliver the photosensitiser to the target tumour. In parallel, a series of metallic complexes of Ru(II) have been prepared and will shortly undergo evaluation in tumour and non-tumour cell lines for light and dark toxicity; due to their photochemical properties the complexes are suitable for photoactivation. Simple ruthenium complexes are unusually effective in suppressing the immune response by inhibiting T cell proliferation which warrants additional study of ruthenium complexes as anticancer drugs.



Figure 9. Encapsulated drug targeted to FR- α receptors

Dr. Anne Greene has research interests in the area of validation and quality assurance in the pharmaceutical industry. Dr. Greene and her student Kevin O'Donnell were awarded the prestigious *Article of the Year* award by the Institute of Validation Technology in the United States for a research paper they wrote on Quality Risk Management published in the *Journal of Validation Technology* in February 2007.⁷ The research was co-sponsored by the Dublin Institute of Technology and the Irish Medicines Board.

Dr. Jack Treacy has been carrying out research in the field of atmospheric chemistry for over 20 years, developing considerable expertise in areas of stratospheric and tropospheric chemistry. He has performed an investigation of Dublin's air quality using an OPSIS long path UV system based on the principle of differential optical absorption spectroscopy (DOAS). Priority pollutants monitored include sulfur dioxide, nitrogen dioxide, ozone, benzene and toluene.

Dr. Hassan Ali works with Dr. Steve Jerrams and the Centre for Elastomer Research (CER) and his work involves the testing of biomaterials (soft tissue and soft tissue mimics). He is also an advisor on other ongoing projects including an investigation into the swelling phenomenon in elastomers subjected to fatigue.

Dr. Sarah Rawe and her group are interested in the design, synthesis and biological evaluation of antitumour trioxane-containing hybrid drugs. In recent years, the use and investigation of combination therapies have had demonstrable success in treating cancer with two or more drugs targeting different and sometimes unrelated pathways to induce tumour cell death. It has been shown that cytotoxicity of antitumour agents can be maximised by delivering the drugs to the target simultaneously. Therefore, by covalently linking two compounds we hope to optimise the antitumour activity and create a hybrid that will be resilient to development of drug resistance. Trioxanes, such as Artemisinin (**1**, Figure 10) and its analogues have demonstrable antitumour, antiproliferative and antiangiogenic activity.

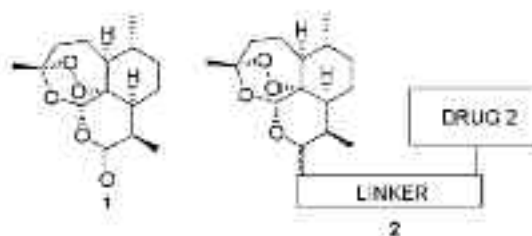


Figure 10. Artemisinin (**1**) and Hybrid (**2**)

CREST (The Centre for Research in Engineering and Surface Technology) is a leader in surface coating and corrosion control and is housed in the Focas Institute. This Centre is a platform for applied research in surface science that contributes to academic and industrial growth on this island. It is the premier surface coating consultancy service in Ireland and a national approval laboratory that has been used by many Irish government agencies (e.g. An Post, Luas, NRA) to give advice on public and private projects, typically dealing with 80-100 clients per year. DIT has become the first institution to receive the highest rating of '1' under the Applied Research Enhancement Programme (AREP) for establishing CREST as a 'centre of excellence'. CREST has assembled a team of highly trained scientists to focus on academic research and on helping companies in Ireland research and develop exciting new materials. 12 Research programs are ongoing of which a number are joint research projects with researchers from the School of Chemical and Pharmaceutical Sciences including development of a novel photoelectrochemical fuel cell, research into the applications of nanocrystalline photoactive materials such as TiO_2 and ZnO . CREST is a member of the EU consortium (COST 540 – Phonasum).

Dr. Suresh Pillai is acting Centre Director and a Senior R&D Manager in CREST and oversees all ongoing projects and consultations. He was recently successful in obtaining funding from FP6-MNT ERA-NET with Dr. Seery. The project "Visible Light Induced Photo-degradation of Organic Matter Using Semiconductor Nanoparticles for Hygiene Applications" aims to develop self-sterilising fabrics and surfaces for use in hospitals.²⁻³

Dr. Brendan Duffy (Senior R&D Manager in CREST) and his research group have developed a range of functionalised sol-gel coatings for corrosion and hygiene applications. In collaboration with researchers in the National Centre for Sensor Research (DCU), the group have developed a coating that has been proved to be a potential replacement for hexavalent chromium pre-treatments of aerospace aluminium.⁸ The novel coating could lead to a reduction in the overall weight of paint on aircraft leading to potential saving of fuel in excess of US \$50,000 over the lifetime of a typical commercial jet (Figure 11).



Figure 11. Anti-corrosion Sol-Gel Coating as Hexavalent Chromium Alternative

Using silver salts the group has also developed inhibition coatings, which can be used to reduce the occurrence of build-up of biofilm on indwelling devices.⁹ The group has also collaborated with researchers in TCD and ITTD to develop antimicrobial paints, which have proven to reduce the colony

forming ability of MRSA and *C. difficile*. The potential market for these paints is the healthcare sector where there is an increasing threat of such potentially lethal bacteria to vulnerable patients.

The Chemistry Education Research Team (CERT) was established in 2005 with the aim of incorporating emerging ideas from education research into the day-to-day teaching in the School. Areas of interest include the development of project-based learning laboratories; the contextualisation of laboratory and lecture material; development of a virtual learning environment as a support platform for lecture delivery; the development of e-learning materials to facilitate online and distance learning and the development and implementation of community based learning group projects.¹⁰

References

1. "The Story of the Dublin Institute of Technology", T. Duff, J. Hegarty and M. Hussey, **2000**, Blackhall Publishers, Dublin
2. (a) S. C. Pillai, J. M. Kelly, D. E. McCormack and R. Ramesh, *J. Mat. Chem.* **2008**, accepted. (b) G. M. Duffy, S. C. Pillai and D. E. McCormack, *Smart Mater. Struct.* **2007**, *16*, 1379. (c) S. C. Pillai, J. M. Kelly, D. E. McCormack and R. Ramesh, *Advances in Applied Ceramics* **2006**, *105*, 3.
3. (a) M. K. Seery, N. Fay, T. McCormack, E. Dempsey, R. J. Forster and T. E. Keyes, *Phys. Chem. Chem. Phys.* **2005**, *19*, 3426. (b) M. K. Seery, R. George, P. Floris and S. C. Pillai, *J. Photochem. Photobiol. A*, **2007**, *189*, 258. (c) S. C. Pillai, P. Periyat, R. George, D. E. McCormack, M. K. Seery, H. Hayden, J. Colreavy, D. Corr and S. J. Hinder, *J. Phys. Chem. C*, **2007**, *111*, 1605. (d) R. Georgekutti, M. K. Seery, and S. C. Pillai, *J. Phys. Chem. C*, **2008**, accepted.
4. (a) K. Crowley and J. Cassidy, *J. Electroanalytical Chemistry*, **2003**, *547*, 75. (b) E. F. Duffy, F. Touati, S. C. Kehoe, O. A. McLoughlin, L. W. Gill, W. Gernjak, I. Oller, M. I. Maldonado, S. Malato, J. Cassidy, R. H. Reed and K. G. McGuigan, *Solar Energy*, **2004**, *77*, 649. (c) J. A. Morales, S. J. O'Sullivan, J. F. Cassidy, *Sensors and Actuators*, **2005**, *195*, 266.
5. (a) L. O'Neill, P. Lynch, M. McNamara and H. J. Byrne, *J. Phys. Chem. A*, **2007**, *111*, 299. (b) P. J. Lynch, L. O'Neill, D. Bradley, H. J. Byrne and M. McNamara, *Macromolecules*, **2007**, *40*, 7895.
6. G. Chambers, C. Carroll, G. F. Farrell, A. B. Dalton, M. McNamara, M. Panhuis and H. J. Byrne, *Nano Lett.*, **2003**, *3*, 843.
7. K. O'Donnell and A. Greene, *Journal of Validation Technology*, **2007**, *13*
8. US Patent Application 60/996,565
9. N. Stobie, B. Duffy, J. Colreavy, M. Hidalgo, P. McHale and S. J. Hinder, *Biomaterials*, **2008**, *29*, 963.
10. (a) T. Cunningham, C. Mc Donnell, B. Mc Intyre and T. McKenna, A Reflection on Teachers' Experience as e- Learners, In *Applied e-Learning and e-Teaching in Higher Education*, Donnelly, R. and Mc Sweeney, F., Eds., IGI Global, Philadelphia, **2008**, 78. (b) C. M. O'Connor and H. Hayden, *Chem. Educ. Res. Pract.*, **2008**, *9*, 35. (c) C. Mc Donnell, C. O'Connor and M. K. Seery, *Chem. Educ. Res. Pract.*, **2007**, *8*, 130. (d) M. K. Seery, L. Clarke and S. C. Pillai, *Chem. Educator*, **2006**, *11*, 1.

Feature Article

New MRI contrast agents based on one dimensional assemblies of magnetic nanoparticles

Prof. Yurii K. Gun'ko

*School of Chemistry, University of Dublin, Trinity College, Dublin 2, Ireland***Abstract.**

Collaborative work between the School of Chemistry, Institute of Neuroscience in TCD and School of Chemical Sciences in DCU resulted in the development of new contrast agents for magnetic resonance imaging based on one dimensional linear assemblies of magnetic nanoparticles. The researchers have demonstrated the potential use of these materials as contrast agents by measuring their MR response in live rats. The new magnetic fluids have shown good biocompatibility and potential for in vivo MRI diagnostics.

Magnetic materials have an enormous impact to the modern science, technology and every day life. In particular, magnetic nanoparticles have been envisaged for many biomedical applications.¹ For example magnetic particles can be utilised as drug delivery agents which can be localised in the body at a site of interest using an external magnetic field. When exposed to an alternating magnetic field, magnetic nanoparticles can serve as powerful heat sources destroying tumor cells; this allows the use of these nanomaterials in cancer hyperthermia therapy. Magnetic fluids based on aqueous dispersions of small size superparamagnetic nanoparticles have also been utilised as contrast agents for Magnetic Resonance Imaging (MRI). MRI is proven to be one of the best and most advanced modern techniques in diagnostic and biomedical research. MRI has a number of advantages over other instrumental diagnostic methods. First of all, MRI can provide excellent, detailed images of soft tissue in vivo. Most imaging techniques provide a single contrast mechanism, for instance based on the differences in tissue density and atomic number (X-ray techniques), or acoustic impedance (ultrasound). However, MRI contrast is based on a range of parameters related to the water environment in the tissues; and is thus sensitive to water binding, to the concentration of macromolecules in the tissue, the concentration of iron containing or other paramagnetic species in the tissue. Secondly, MRI is a functional imaging modality, similar to nuclear medicine techniques. For instance, MRI can be used to measure blood flow in vessels or tissue perfusion as well as changes in blood oxygenation. Thirdly, MRI is a dynamic imaging modality. As it is apparently safe, images can be acquired continuously. This allows dynamic studies to be performed, for instance imaging of the beating of the heart, the transportation in vascular system, the movement of joints, or the central nervous system response to external stimuli.

The enormous versatility and flexibility of MRI, its relative safety and non-invasive nature, has led to a huge increase in



demand for clinical scans over the last decade. MRI contrast agents act to improve image quality by altering the magnetic resonance relaxation times of water in the tissues surrounding the agent, and hence causes an increase (or sometimes decrease) in the intensity of the water signal in these tissues. High relaxivities are important both to maximise the contrast and to minimise the dose of the agent that is required. Most of the existing MRI imaging techniques utilise gadolinium complexes as contrast agents. However, compared with gadolinium chelates such as diethylenetriaminopentaacetic acid (Gd-DTPA), magnetic nanoparticles are much more efficient as relaxation promoters, and their effect on the relaxivities of water is measurable even at nanomolar concentrations.² Gadolinium chelates also tend to be non-specific and accumulate rapidly in the liver. In addition, important biological properties of magnetic nanoparticles such as their biocompatibility, selective uptake, targeted delivery and removal from the body can be relatively easily tuned by changing the size and the nature of the surface coating of nanoparticles.

To date, most applications of magnetic nanoparticles in MRI have been focused on spherical (quasi 0-dimensional) primary nanoparticles with aspect ratios close to one, while the use of magnetic nanowires and linear assemblies of magnetic nanoparticles is still very limited. Initially, in 2004 Professors Gun'ko and Kelly with their co-workers from the Chemistry Department in TCD in collaboration with Dr. D. Brougham from the School of Chemical Sciences in DCU demonstrated that reaction between a mixture of ferrous and ferric chlorides (2:1 molar ratio respectively) with ammonia in a degassed water solution containing heat-induced denatured (substantially single-stranded) herring-sperm DNA leads to the chemical assembly of small (~9 nm) magnetite nanoparticles into long flexible many micron long wire-like structures (Figure 1).³ In these nanowires, magnetite nanoparticles are strongly chemically bonded to each other *via* a phosphate backbone of the single stranded DNA. These nanowire-like magnetite–DNA composites have extremely high solubility and stability in water and can demonstrate low field relaxivity over an order of magnitude higher than the currently used commercial MRI agents.

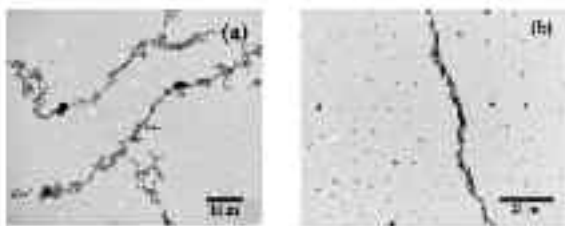
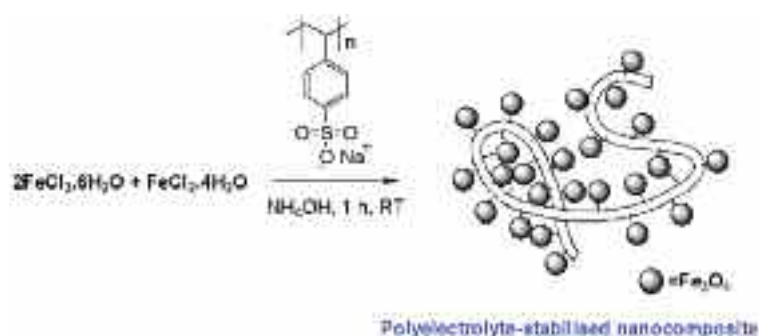


Figure 1. TEM images of (a) denatured hs-DNA-magnetite nanowires, (b) denatured hs-DNA-magnetite nanowires aligned in a 7T magnetic field. ³

This discovery has stimulated further research on magnetic nanoparticles-polyelectrolyte composites. Recently, Prof. Gun'ko co-workers developed a new magnetic fluid, which is based on flexible linear (quasi one dimensional) assemblies of magnetite nanoparticles.⁴ This nanomaterial was synthesised by co-precipitation of ferrous and ferric chlorides in the presence of polysodium-4-styrene sulfonate (PSSS) polyelectrolyte with ammonia in water (Scheme 1). In this case the negatively charged polyelectrolyte acts as both a stabiliser, where the positively charged iron ions can accumulate before particle precipitation, and as a template for nanowire formation once the particles are formed. When dried in an external magnetic field, the nanocomposites appear aligned showing parallel linear arrays or “nanowires” where neighboring particles are cross-linked by polyelectrolyte molecules into chains (Figure 2). The primary particle size (from 7 ± 1 to 11 ± 1 nm) and the nanowire width were found to change depending on iron/polyelectrolyte ratio. Therefore, the parameters and properties (including relaxivities and MRI sensitivity) of corresponding magnetic fluids can be controlled by simply changing the ratios of iron salts and polyelectrolyte during the synthetic procedure.



Scheme 1. Schematic presentation of the preparation of polysodium-4-styrene sulfonate-stabilised magnetite nanoparticles.

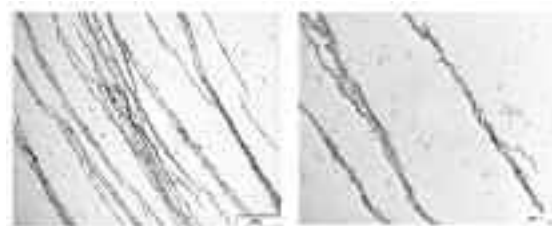


Figure 2. TEM images of polyelectrolyte stabilised-magnetite linear assemblies aligned into parallel arrays by 1.5 T external magnetic field.

Follow on research involved biological testing of new magnetic nanocomposites. In collaboration with the Institute of Neuroscience in TCD the researchers from the School of Chemistry demonstrated for the first time the utilisation of the new linear one-dimensional assemblies of magnetic nanoparticle as in MRI contrast agents in live animals. New magnetic fluids have been injected into live rats in order to study the effect of these contrast agents on the brain, specifically the hippocampus and brain vasculature.

Echo planar image images of the brain after injection have shown a significant darkening as the bolus has reached the brain (Figure 3a and 3b). Also in the FLASH scan (Figures 3c and 3d), of the coronal slice a significant darkening of the brain and a great contrast was noticed. In particularly the occlusion of the superior sinus sagittalis vein (SSS) can be clearly seen. No visible signs of any adverse reaction were noted after monitoring the rats for twenty-four hours. This research proved both the biocompatibility of these materials and that the contrast effect is retained in live rats, *i.e.* that the fluids remain effective, in this case in the brain, over the timescale of the imaging process. Of course, while initial results indicate this contrast agent is quickly cleared from the central nervous system, further studies are required to determine localisation in tissues over long periods of time.

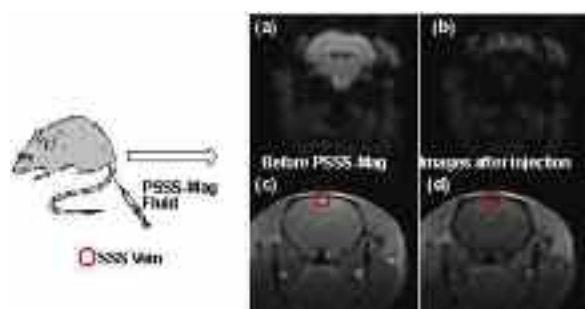


Figure 3. Echo planar image (EPI) of mouse brain (a) before and (b) as PSSS-Mag₁ passes through; Fast Low Angle Shot (FLASH) image of mouse brain (c) before and (d) as PSSS-Mag₁ passes through.⁴

These new one-dimensional magnetic nanoparticle assemblies have the potential to open up new aspects in biology and medicine, as their high aspect ratio results in a much larger dipole moment allowing magnetic resonance imaging using lower fields and lower concentrations of contrast agents. In addition one-dimensional morphology of nanocomposites should facilitate their easy passage through the circulatory system. Therefore these magnetic fluids are expected to be of particular importance for MR imaging of the cardiovascular system and blood vessels. These new nanomaterials have a combination of unique properties such as the sensitivity in the nanomolar range, high flexibility, an ability to penetrate the most unreachable, remote parts of the tissue and they can be manipulated by an external magnetic field. This could open the door not only for advanced MRI but also to other biomedical applications such as cancer hyperthermia therapy, imaging and treatment of micro-strokes, detection and cleaning of blocked blood vessels, micro- and even nano-surgery. All these aspects could be of great value in the further development of nanomedicine overall.

In conclusion it is important to notice that the area of one dimensional flexible nanomaterials is still underestimated and therefore very poorly developed. However, these nanocomposite materials have great potential and should play an important role in several biomedical fields in the near future. The above approach, developed by Irish research groups, could be expanded and utilised in other nanosystems (not necessarily magnetic nanoparticles), enabling the preparation of similar linear 1-D assemblies for a range of various small size particles, which could find a number of important potential applications in chemistry, physics, biology and medicine.

This research was supported by the SFI RFP scheme.

References

1. Q. A. Pankhurst, J. Connolly, S. K. Jones and J. Dobson, *J. Phys. D: Appl. Phys.* **2003**, *36*, R167.
2. L. LaConte, N. Nitin, G. Bao, *Materials Today* **2005**, *8*, 32.
3. S. J. Byrne, S. A. Corr, Y. K. Gun'ko, J. M. Kelly, D. F. Brougham, S. Ghosh, *Chem. Commun.* **2004**, 2560.
4. S. A. Corr, S. J. Byrne, R. Tekoriute, C. J. Meledandri, D. F. Brougham, M. Lynch, C. Kerskens, L. O'Dwyer and Y. K. Gun'ko, *J. Am. Chem. Soc.* **2008**, *130*, 4214.

Literature Focus

Anna Przbyl, Anne Horan, Michele Byrne, Padraic Nagle, Ian McKeogh and Paraic Keane
School of Chemistry, University of Dublin, Trinity College, Dublin 2, Ireland

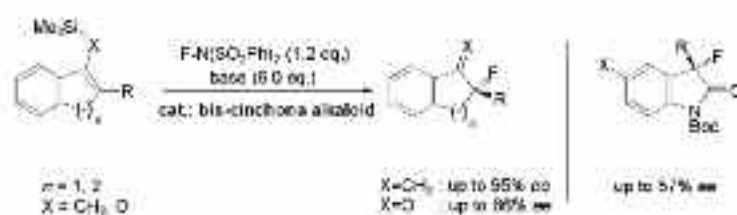
Literature focus is a new feature consisting of short abstracts highlighting recent developments of interest in the literature selected by postgraduate researchers.

Edited by Anne Horan and Michele Byrne

Fluorinating Reagents

Cinchona Alkaloid Catalyzed Enantioselective Fluorination of Allyl Silanes, Silyl Enol Ethers, and Oxindoles

T. Ishimaru, N. Shibata, T. Horikawa, N. Yasuda, S. Nakamura, T. Toru and M. Shiro, *Angew. Chem. Int. Ed.* **2008**, *47*, 4157

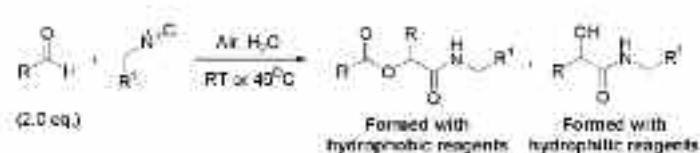


Combinations of bis-cinchona alkaloids, N-fluorobenzenesulfonimide (NFSI), and base were used as highly enantioselective fluorinating reagents in the reactions with allyl silanes and silyl enol ethers. **36 examples: Yield 31-99%.**

“Green” Organic Synthesis

Highly Efficient Organic Reactions “on Water”, “in Water”, and Both

N. Shapiro and A. Vigalok, *Angew. Chem. Int. Ed.* **2008**, *47*, 2849

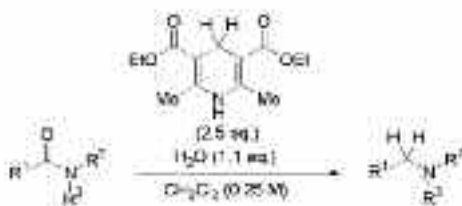


Shapiro and Vigalok have reported an environmentally friendly aerobic aldehyde oxidation/Passerini reaction in aqueous suspensions.

Reduction of Amides

Highly Chemoselective Metal-Free Reduction of Tertiary Amides

G. Barbe and A. B. Charette, *J. Am. Chem. Soc.* **2008**, *130*, 18

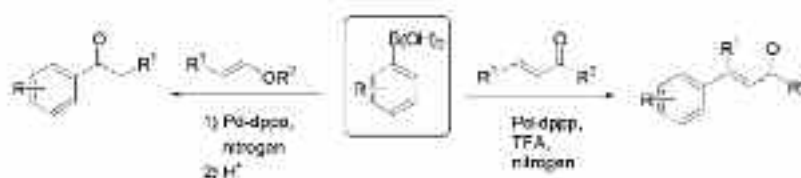


Barbe and Charette have reported the synthesis of tertiary amines via a chemoselective metal-free reduction of the corresponding amides. The described method was used in the synthesis of donepezil. **22 examples: Yield 5-91%.**

Heck Coupling

Oxygen and Base-Free Oxidative Heck Reactions of Arylboronic Acids with Olefins

J. Ruan, X. Li, O. Saidi and J. Xiao, *J. Am. Chem. Soc.* **2008**, *130*, 2424

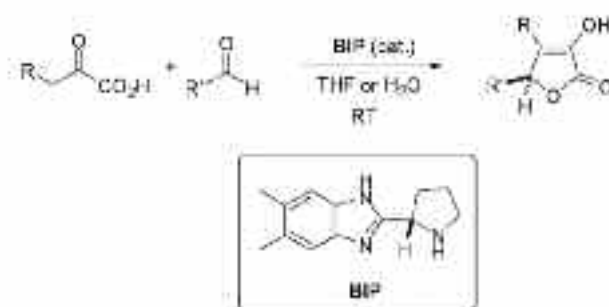


Xiao and co-workers have described the palladium-catalyzed oxidative Heck coupling of arylboronic acids with olefins (both electron rich and electron deficient), which does not require a base, oxygen, or any other external oxidants. **49 examples: Yield 34-94%.**

Aldol Reaction

A Consise Organocatalytic and Enantioselective Synthesis of Isotetronic Acids

J. -M. Vincent, C. Margottin, M. Berlande, D. Cavagnat, T. Buffeteau and Y. Landais, *Chem. Commun.* **2007**, *45*, 4782

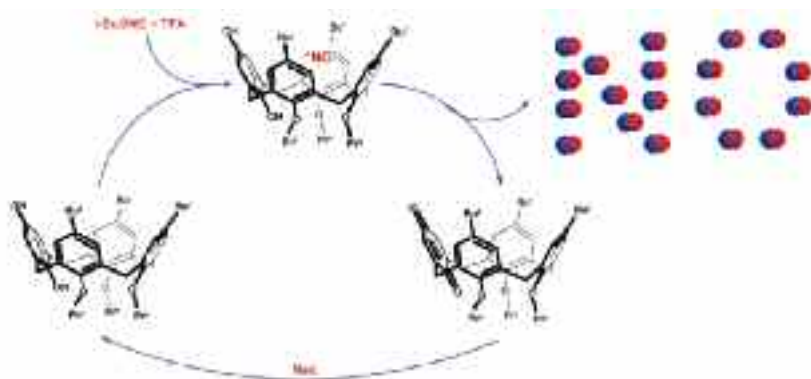


Vincent and co-workers have reported the synthesis of isotetronic acids using an organocatalyzed aldol reaction between α -keto acids and a series of aldehydes leading to moderate to good yields of the desired compounds with a good level of enantioselectivity. **18 examples**

Supramolecular System for NO Generation

Nitric Oxide Release Mediated by Calix[4]hydroquinones

E. Wanigasekara, C. Gaeta, P. Neri and D. M. Rudkevich, *Org. Lett.* **2008**, *10*, 1263

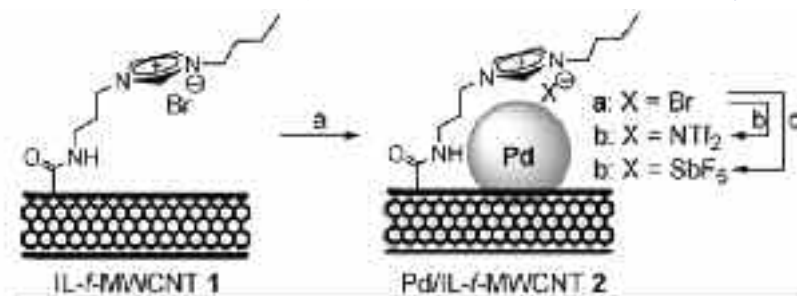


Wanigasekara and co-workers have reported a new calixarene-based supramolecular system endowed with an internal hydroquinone reducing moiety and therefore able to release NO without the addition of external agents.

Ionic Liquid-based Catalytic System

Palladium Nanoparticles Supported onto Ionic Carbon Nanotubes as Robust Recyclable Catalysts in an Ionic Liquid

Y. S. Chun, J. Y. Shin, C. E. Song and S. G. Lee, *Chem. Commun.* **2008**, *8*, 942

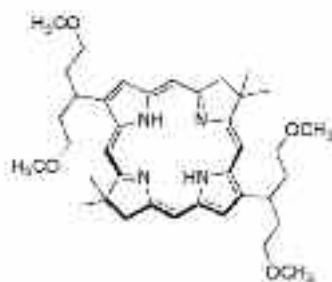


Palladium nanoparticles have been deposited onto imidazolium bromide-functionalised ionic MWCNTs through the reduction of Na_2PdCl_4 in water and combined with an ionic liquid to create a new recyclable ionic liquid-based catalytic system.

Near-Infrared Absorber

Swallowtail Bacteriochlorins. Lipophilic Absorbers for the Near-Infrared

K. E. Borbas, C. Ruzié and J. S. Lindsey, *Org. Lett.* **2008**, *10*, 1931

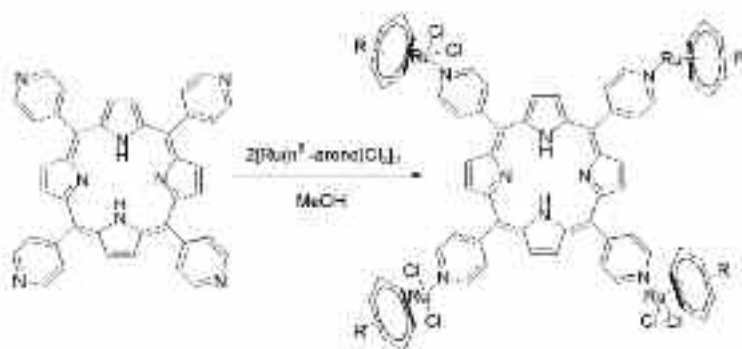


A de nova route has been exploited to prepare synthetic bacteriochlorins that bear a geminal dimethyl group in each pyrroline ring and a symmetrically branched 1,5-dimethoxypentyl group attached to each pyrrole ring, desirable for use in optical imaging and PDT.

Porphyrins in Cancer Therapy

Ruthenium Porphyrin Compounds for the Photodynamic Therapy of Cancer

F. Schmitt, P. Govindaswamy, G. Suss-Fink, W. Han Ang, P. Dyson, L. Juillerat-Jeanneret and B. Therrien, *J. Med. Chem.* **2008**, *51*, 1811

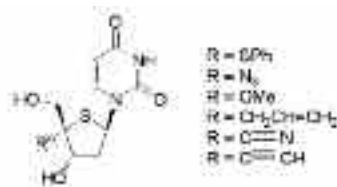


Schmitt and co-workers have reported the synthesis of a series of porphyrin derivatives that were characterized as potential photosensitising chemotherapeutic agents. The biological effects of these derivatives were assessed on human melanoma tumour cells, and their cellular uptake and intracellular localisation were determined.

Anti HIV Drugs

Conversion of α,β -Unsaturated Aldehydes into Saturated Esters: An Umpolung Reaction Catalyzed by Nucleophilic Carbenes

K. Haraguchi, H. Shimada, H. Tanaka, T. Hamasaki, M. Baba, E. Gullen, G. Dutschman and Y. Cheng, *J. Med. Chem.* **2008**, *51*, 1885

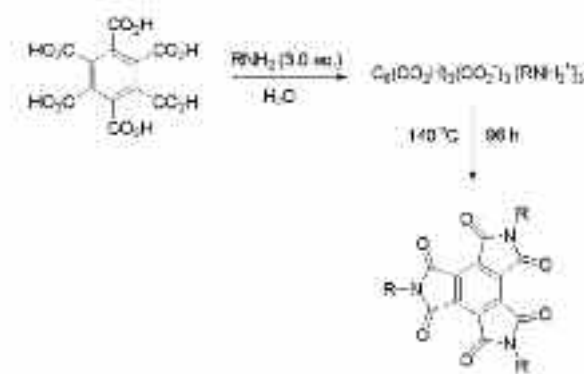


The preparation of 4'-phenylthio, 4'-azido, 4'-methoxy and 4'-allyl analogues of 4'-thiothymidine are reported using nucleophilic substitution with silicon reagents. Among these, the 4'-azido, 4'-cyano, 4'-ethynyl derivatives were seen to show potent inhibitory activity against HIV-1 and HIV-2

Preparation of Triimides

An Expedient Synthesis of Mellitic Triimides

K. Rose, D. Jaber, C. Gondo and D. Hamilton, *J. Org. Chem.* **2008**, *73*, 3950

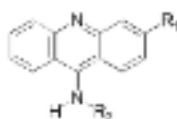


Rose et al. have reported an improved synthesis of triimides through the formation of a triammonium salt of metallic acid, followed by solid-state thermal dehydration to the triimide. **13 examples: Yield 22-55%.**

Acridines in Anti-Cancer Chemistry

Acridine-Based Agents with Topoisomerase II Activity Inhibit Pancreatic Cancer Cell Proliferation and Induce Apoptosis

J. Goodell, A. Ougolkov, H. Hiasa, H. Kaur, R. Rimmel, D. Billadeau and D. Ferguson, *J. Med. Chem.* **2008**, *51*, 2



Goodell et al. have evaluated on a series of 9-aminoacridines for antiproliferative activity towards pancreatic cancer cells. Results have indicated that these compounds inhibit cell proliferation by inducing a G1-S phase arrest.

Surfactant Interaction

Morphology Control of CNT-TiO₂ Hybrid Materials and Rutile Nanotubes

D. Eder and A. H. Windle, *J. Mater. Chem.* **2008**, *18*, 2036

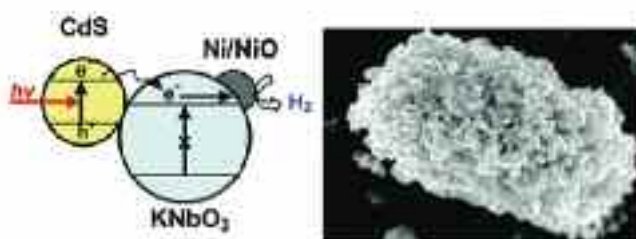


Using benzyl alcohol as a surfactant, TiO₂ was able to interact with the hydrophobic surface of pristine carbon nanotubes without the need for covalent functionalisation. These new materials can be used in photochemical and catalytic applications.

Photocatalytic Reduction

Photocatalytic Production of Hydrogen on Ni/NiO/KNbO₃/CdS Nanocomposites using Visible Light

J. Choi, S. Y. Ryu, W. Balcerski, T. K. Lee and M. R. Hoffmann, *J. Mater. Chem.* **2008**, *18*, 2371

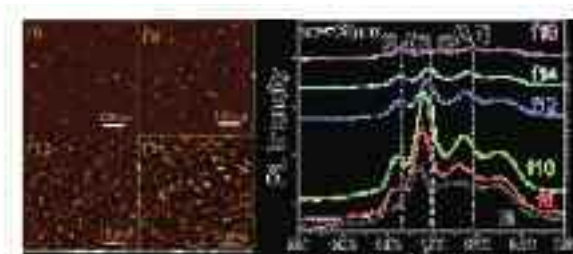


Using Ni/NiO/KNbO₃/CdS nanocomposites, hydrogen gas was produced from water by using visible light irradiation in the presence of isopropanol. Using nanosized CdS combined with Ni coated KNbO₃ instead of bulk CdS increased the photocatalytic properties.

Optical Properties of Nanotubes

Optical Properties of Ultrashort Semiconducting Single-Walled Carbon Capsules Down to Sub-10 nm

X. Sun, S. Zaric, D. Daranciang, K. Welscher, Y. Lu, X. Li and H. Dai, *J. Am. Chem. Soc.* **2008**, *130*, 6651



Dai et al. separated nanotubes smaller than 10 nm from long nanotubes via ultracentrifugation. Quantum confinement effects along the length of the short nanotubes blue-shift the absorbance and photoluminescence peaks. The short nanotubes essentially correspond to SWNT quantum dots.

Colour Tuning

Upconversion Multicolor Fine-Tuning: Visible to Near-Infrared Emission from Lanthanide-Doped NaYF₄ Nanoparticles

F. Wang and X. Liu, *J. Am. Chem. Soc.* **2008**, *130*, 5642

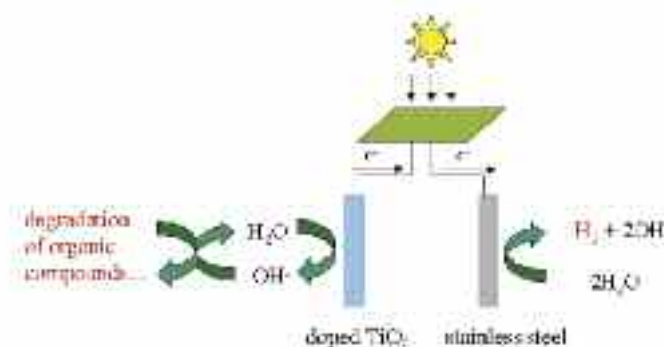


Liu and Wang described a general approach to tune emission colours of nanoparticles. By using different host-activator systems and dopant concentrations of Yb³⁺, Tm³⁺ and Er³⁺ the luminescence emission can be precisely controlled.

Electrochemical Water-Splitting

Solar-Powered Production of Molecular Hydrogen from Water

H. Park, C. D. Vecitis, W. Choi, O. Weres and M. R. Hoffmann, *J. Phys. Chem. C* **2008**, *112*, 885

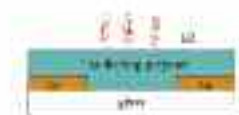


A solar-powered electrochemical cell oxidises organic pollutants at the TiO₂ anode, while hydrogen is extracted from water at the cathode.

Conducting Polymers

Conducting Polymers as Antennas for Probing Biophysical Activities

N. Arun and K. S. Narayan, *J. Phys. Chem. B* **2008**, *112*, 1564

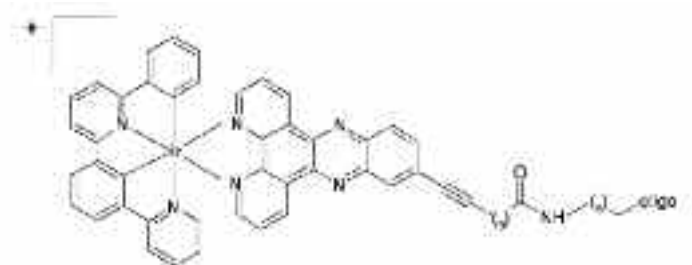


The bacteriorhodopsin (bR) protein is oriented on the surface of a conducting-polymer substrate, and light-driven processes in bR are monitored via photoelectric signals from the polymer.

Charge Transport in DNA

Charge Migration Along the DNA Duplex: Hole Versus Electron Transport

B. Elias, F. Shao and J. K. Barton, *J. Am. Chem. Soc.* **2008**, *130*, 1152

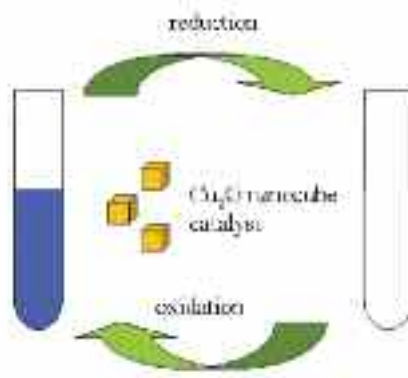


An intercalating iridium complex can probe the distance-dependence of both electron and hole transport through the bases in DNA, due to the ability of the complex to act as either a photo-oxidant or photoreductant.

A 'Clock' Reaction

Nanoparticle-Catalyzed Clock Reaction

S. Pande, S. Jana, S. Basu, A. K. Sinha, A. Datta and T. Pal, *J. Phys. Chem. C* **2008**, *112*, 3619

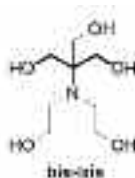


Cu₂O nanocubes act as a catalyst in the reduction of methylene blue by hydrazine, causing an oscillating redox reaction to occur.

High Nuclearity Complex

Linking Iron(III) Carboxylates into High Nuclearity Complexes by using Bis-Tris

A. Fergusson, J. McGregor, A. Parkin and M. Murrie, *J. Chem. Soc. Dalton Trans* **2008**, *6*, 731



Murrie *et al.* have developed two decanuclear iron(III) complexes with novel structures using the bis-tris ligand. These high nuclearity complexes have the potential to be used as nanoscale magnetic materials.

Crystal to Crystal Transformation upon Dehydration

Mixed Ligand Coordination Polymers from 1,2-bis(1,2,4-triazol-4-yl)ethane and Benzene-1,3,5 tricarboxylate: Trinuclear Nickel or Zinc Secondary Building Units for Three Dimensional Networks with Crystal to Crystal Transformation upon Dehydration

H. A. Habib, J. Sanchiz and C. Janiak, *J. Chem. Soc. Dalton Trans.* **2008**, 13, 1734

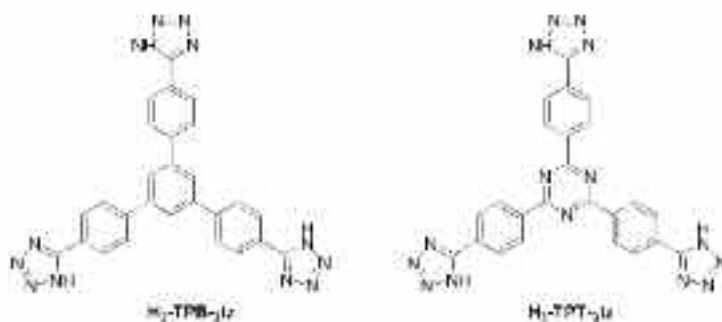


Janiak *et al.* have developed mixed ligand coordination polymers hydrothermally. Incorporated crystallisation water and aqua ligands can be removed from these polymers giving the dehydrated product via a solid state single-crystal to single crystal transformation.

Metal-Organic Frameworks

Expanded Sodalite -Type Metal-Organic Frameworks: Increased Stability and H₂ Adsorption through Ligand Directed Catenation

M. Dincă, A. Dailly, C. Tsay and J. R. Long, *Inorg. Chem.* **2008**, 47, 11

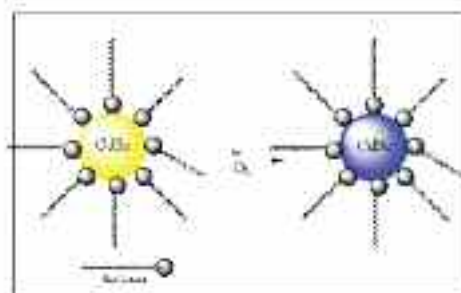


Long et al. found that the strain present between the central benzene ring and the outer aromatic ring in their ligand H₃ TPB-3tz causes a non-catenated framework to form. The lack of such strain in their ligand H₃ TPT-3tz forms a catenated structure. This allows for the stabilisation of porous metal-organic frameworks to enhance the ability of such a network to store H₂ gas.

CdSe Quantum Dots

An Effective Oxidation Route to Blue Emission Quantum Dots

L. Liu, Q. Peng, and Y. Li, *Inorg. Chem.* **2008**, 47, 3182



Nearly monodispersed blue-emitting quantum dots were synthesised via an oxidative process. This method takes quantum dots with yellow emission and oxidises them using a photooxidative process resulting in the formation of blue emission quantum dots.

Development of Crystallisation Processes, Supported by Powder Characterisation Techniques

Dr. Colm Campbell

Process Implementation Manager, Helsinn Chemicals Ireland, Damastown, Mulhuddart (cca@helsinn.com)

Abstract

The subtleties of crystallisation understanding have historically suffered neglect in many pharma processes, often leading to ineffective isolations and sub-optimal drug performance. While it is reasonable to claim that many organisations are now paying more attention to these important considerations, it is also true that material and bulk properties have yet to be explored, during process development. This article reviews these issues and expounds the innovative approach practiced at Helsinn, set against the back drop of two case studies.

Introduction

The *Crystallisation and Powder Characterisation* sub-group at Helsinn Chemicals Ireland, which acts within the Process Development function, solves crystallisation and bulk problems throughout the Helsinn group and recently, for third party customers.^{1,2} A widely held view of the recent paradigms in crystallisation understanding, as applied to process chemistry specialists in the API development units of the pharmaceuticals industry, is summarised below.

1990's: Addressing of Polymorph/Form issues: Driven by a need to recognise drugs in the context of the supramolecular framework

2000's: Beginning to address poorly performing crystallisation processes: Efforts at ensuring new processes have better crystallisations

Not Yet: Recognition of Active Substances as materials: not molecules (or even crystals). Bulk powders contain liquid (water, residual solvent) and gas (air) components, in addition to the solid (usually crystalline) phase.

The notional crystallisation/powder technology skill set of the process chemist is shown in Figure 1, which clearly shows that this facet of the industry has yet to fully embrace the fundamentals of this area.

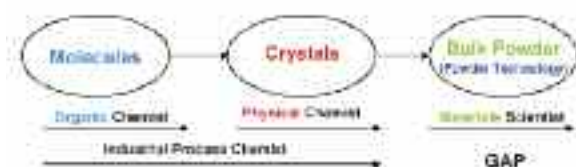


Figure 1. Notional crystallisation and powder technology skill sets for a notional process chemist

At Helsinn, we fully recognise and manipulate to our advantage, the fact that solid chemical entities can be viewed on 3 interdependent levels, progressing from nanometre to multi-tonne scale

- Molecular (spectroscopic)
- Crystal (polymorph/pseudo-polymorphs/solvates/clathrates)
- Bulk (properties of large mass of powder)

In this context, we define powder technology as the 'measurement and manipulation of bulk properties to give processing advantages. Two case studies, drawn from our experience of crystallisation and powder technology, are set-out below.

Case study 1: Dramatic improvements to isolation performance in a mature product

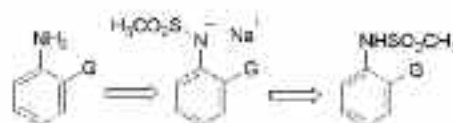


Figure 2. Generalised reaction scheme pertaining to Case Study 1

The key chemical transformations, for the process under discussion, are illustrated in Figure 2. Following sulphonylation of the aniline nitrogen, the work-up involves formation and extraction of the sodamide salt into a hot alkaline solution. Cooling triggers the onset of precipitation of this salt, prior to the addition of concentrated HCl, which ultimately affords the sulphonanilide product.

By changing the crystallisation method, to ensure the adulterant sodamide salt is in solution throughout free sulphonanilide liberation, granular material is now possible leading to enhanced bulk powder properties. The old process was run at lower temperatures, with the result that simultaneous crystallisation of the sodamide salt prevented formation of well-defined crystals. Figure 3 shows the particle distribution and microscope images, taken from old and new material. The contrast is striking, with the new process furnishing material with a more macro-crystalline habit, along with a significantly bigger particle size.

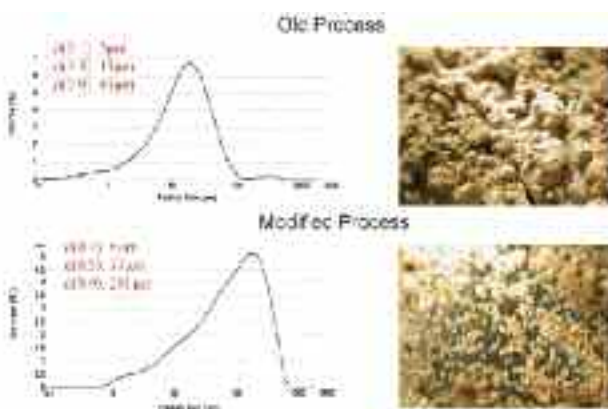


Figure 3. Contrasting particle size distributions and physical habit

This operationally trivial change, has lead to many advantages for this step of the process, the majority of which are summarised as follows:

1. LOD (loss on drying) of all batches ~10% after centrifuging (previously up to 25%)
 - Batches dry in 6 hours (vs. 18 hours in the old process), due to lower solvent content and better flow properties
2. Higher bulk density (0.60 g/mL, instead of ~0.45g/mL)
 - Fit more material into dryer and drums
 - Scope to centrifuge the batch in 4 loads instead of 5
3. Faster filtration: no longer need to spin out each load for ~45 minutes (the 10 minute loading is sufficient for effective de-liquoring)
4. Higher purity (typically we see slightly lower amounts of process related impurities in the granular material)
5. Much better flow properties
 - Comes out of centrifuge bag very easily
 - More easily transferred to and from dryer
6. Less dusty
7. Physical properties less dependant on purity of crystallisation mixture
 - Similar physical properties for batches run with fresh and re-used solvent
 - Dryer product from centrifuge - do we need to dry this intermediate at all?
 - Scope for possibly removing the drying step?

Case study 2: crystallisation development of a pre-commercial intermediate

Non-classical behaviour during crystallisations, where all the normal rules are broken, sometimes needs additional hardware to solve the problems. Crystallisation studies, supported by Lasentec FBRM (this technique, which involves *in situ* measurements on a crystal slurry, using a particular focussed beam reflectance probe, is widely used throughout the industry), conventional kit for studying crystal slurry build-up, showed that we appeared to get larger, easier to filter crystals when we

- Cooled to below the metastable zone and aged!
- Added anti-solvent quickly!
- Cooled quickly to isolation temperature!

There was a very obvious reason for this apparently odd behaviour, although it took Lasentec PVM analysis to understand this. This technique, which involves *in situ* particle visualisation measurements, is very useful for observing real time images throughout crystallisation. Rather than growing large single crystals, we found that growing fines, gave agglomerates and ultimately flocculates, which were easier to filter (Figure 4). So, fundamentally the conditions outlined above were, in fact, affording very fine crystals as expected, but the

finer the crystals the more they organised into macro-flocculates, presumably by electrostatic or other surface interactions. Thus the bulk properties were ultimately the determinant of ease of filtration rather than unaggregated particle size.

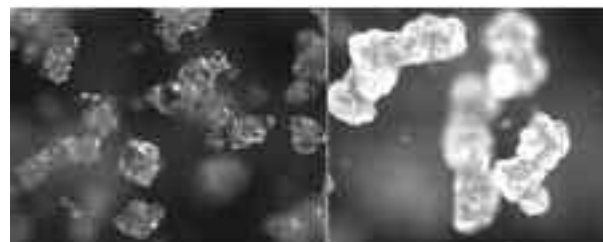


Figure 4. PVM images from Lasentec PVM study

Figure 5 shows comparative particle size distributions, measured on a Sympatec laser diffraction instrument, for classically grown crystals and non-classically grown flocculates. Of course, not all systems have the propensity to form these very hard agglomerates, which effectively have the filtration properties of very large, single crystals. However, use of this *in situ* imaging technique helped us to understand apparently odd behaviour and develop a crystallisation, based around an interesting phenomenon.

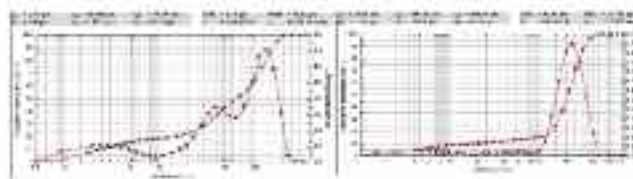


Figure 5. Particle size distributions of material grown under classical and non-classical conditions, respectively

Conclusions

Many old pharma crystallisation processes are manifestly inefficient, although case study 1 shows that there may be some benefit in re-visiting, seemingly good-functioning systems, which were developed without due-consideration of fundamental crystallisation theory. Other examples, published elsewhere, illustrate the importance of coupling powder characterisation techniques, especially rheology, particle size and surface area, with crystallisation expertise, to gain a better understanding of powder systems.^{1,2} At Helsinn Chemicals Ireland, we can trouble-shoot, re-design and provide analytical measurements for problematic materials, both for API processing and drug product formulations, using our knowledge of molecular, crystal and bulk properties. In addition, linking this expertise with our core competencies in process development and scale-up, provides very effective solutions for contract manufacturing, from 1kg to multi-tonne scale, in a cGMP environment.

Colm Campbell was a speaker at the 2007 ICI congress.

References

1. C. Campbell and D. Keenan, *Speciality Chemicals*, June 2005, 20-21
2. C. Campbell, *Speciality Chemicals*, November 2006, page number to be confirmed

Delinquent Sensors & Schizophrenic Materials: Using Molecular Switches to Make Materials with multiple personalities

Robert Byrne, Siliva Scaramagnai, Fernando Benito-Lopez, Alek Radu and Prof. Dermot Diamond
Adaptive Sensors Group, National Centre for Sensor Research School of Chemical Sciences, Dublin City University

Introduction

Chemical sensors and biosensors are devices that provide information about binding events happening at the interface between a sensitive film/membrane and a sample phase. The function of the sensitive film/membrane is to ensure that the binding at this interface is as selective as possible and hence the film/membrane usually contains entrapped or covalently bound sites (e.g. ligands, enzymes, antibodies) to impart the selectivity. The binding event is further coupled with a transduction mechanism of some kind; and in optical sensing, this usually involves a change in the colour or fluorescence of the film/membrane.

Clearly, these materials are 'active' in that they must interact with the sample, and binding processes must occur that lead to signal transduction for them to be of any analytical use. However, it is self-evident that these sensitive interfaces will change over time, for example due to non-specific binding in real samples that can lead to surface poisoning, or leaching of active components into the sample phase. Consequently, the response characteristics of chemical sensors and biosensors tend to change over time, and there tends to be a gradual decrease in sensitivity, loss of selectivity and drifting of the baseline signal. These effects are well-known to those experienced in using these devices, and in practice, they may be overcome by regular calibration, until the device deterioration reaches some limiting level.

Currently, there is very significant interest in the deployment of sensor networks, and many important applications require the involvement of chemical sensors and biosensors. However, for this to happen in large scale, there needs to be a revolution in the way chemical sensors/biosensors are employed, as conventional calibration is inappropriate for large-scale deployments due to the cost of ownership (particularly maintenance) of these rather complex devices.¹⁻³

In this article, we consider the use of 'adaptive' materials (*i.e.* materials that can be switched reversibly between two or more different forms with radically different characteristics). This may open the way to the development of materials that can exist in a passive form (non-binding) until a measurement is required, at which point the material is switched to an 'active' form. Binding then occurs and a signal is generated, and the material subsequently switched back to the 'passive' form. We have demonstrated that binding of metal ions and amino acids at spiropyran modified surfaces can be controlled photonicly using LEDs.³⁻⁵ It is possible that this may provide a route to more sophisticated materials whose host-guest binding behaviour and signal generation can be activated or deactivated on demand. This effect has important potential applications in sensors, purification resins, separation science and drug delivery. In this article we report progress on the modification of several materials with spiropyran and their incorporation within microfluidic devices.

Spiropyran- Photoswitchable ligands

Upon irradiation with UV light, spiropyran (SP) undergoes a heterolytic cleavage of the C-O bond switching from an acoplanar uncharged, colourless isomer to a planar zwitterionic, highly coloured merocyanine (MC) isomer.⁶⁻⁸ The MC isomer possesses an electron-rich phenolate oxygen atom capable of serving as a binding site for certain metal ions (Figure 1).^{7, 9} Conversely, irradiation with visible (green) light causes the ejection of bound metal ions from the MC-complex and regeneration of the passive SP form. This very interesting behaviour stimulated us to investigate whether SP could be used to make intelligent surfaces that exhibit photo-reversible ion-binding behaviour.

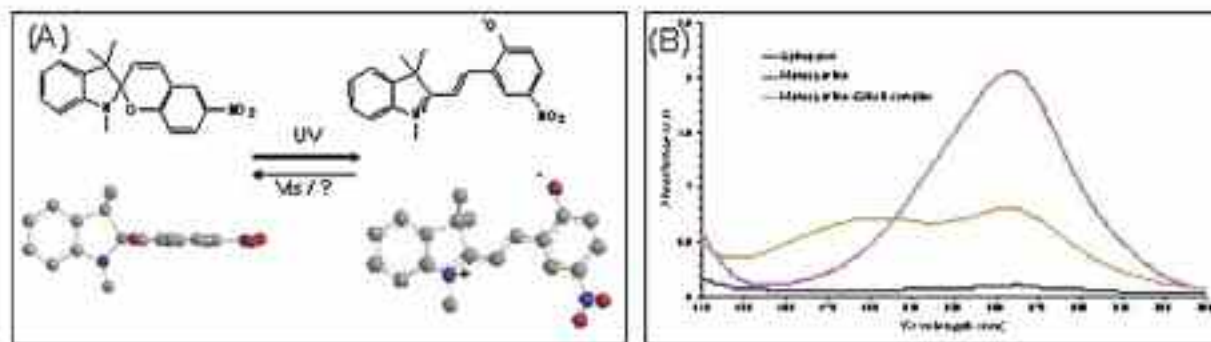


Figure 1. A: Molecular structures of nitro-benzospiropyran (left) and its photo-isomer merocyanine (right). Chem 3D structures included to emphasize the dramatic change in the molecular geometry when irradiated with UV or visible light. **B:** UV-vis spectra of 10^{-3} M spiropyran in acetonitrile, irradiated with 60 seconds UV light, and treated with CoCl_2 .

Attachment of SP to a polymer matrix or surface is a useful way to overcome the limited aqueous solubility of SP.^{10, 11} Coupled with the increasing spectral coverage and power output of LEDs, surface immobilised photoswitchable ligands offer exciting opportunities for new ways to control and mediate binding processes occurring at solution-surface interfaces. Recently, we have been using clusters of LEDs for triggering events and monitoring the resultant colour changes for colorimetric analysis.⁵ Previously, we produced a polymethyl methacrylate-based polymer which was SP-modified via a carboxylic handle and an 8-carbon linker. By solvent casting this onto a polymethyl methacrylate (PMMA) sheet we were able to form SP-modified films on the substrate that were approximately 130 μm thick.¹² We also demonstrated that the binding of metal ions such as Co^{2+} could be photonically controlled on these modified surfaces. It was found that an 8-carbon spacer from the polymer backbone was the minimum length needed to provide the necessary flexibility for effective formation of the 2:1 SP:metal ion sandwich complexes.¹³

Spiropyran functionalised microbeads

Microbeads are small spherical units that can be suspended in different solvents according to the nature of the beads matrix and whose diameter, on the microscale range (10^{-6} m), allows the development of relatively high surface areas when compared to flat film surfaces. The use of micro and nanobeads for different applications in life sciences, medicine and drug delivery has been widely reported in the literature,¹⁴⁻¹⁶ as they provide extensive surface areas upon which a molecule can be immobilised (solid-like behaviour), yet they are easily transported (liquid-like behaviour), and easily separated from the solution medium.

Photoswitchable silica and polystyrene microbeads with different diameters have been prepared by covalently functionalising with a spiropyran derivative. The spiropyran on the microbead surface can be switched using LEDs (Figure 2) between a passive SP state which exhibits no ion-binding behaviour, and an active MC state which forms complexes with certain metal ions, especially transition metals, such as Cu^{2+} , Co^{2+} and Zn^{2+} . Upon formation of the merocyanine-metal ion complex, the microbeads undergo a further ion-dependent spectral and colour change (see Figure 1). Exposure of these beads to a white LED causes the guest metal ion to be expelled and reformation of the passive MC form. The process to photocontrolled ion loading and release from the SP modified beads is fully reversible and can be recycled.

Microfluidic systems have emerged as novel analytical tools in many areas of science and industry. Their inherent qualities include low power requirements, small sample and reagent consumption, rapid analysis times, and these, coupled with autonomous operation provide unique opportunities to create novel and more powerful devices with a myriad of applications.¹⁷ Although highly desirable, examples of on-chip liquid chromatography microfluidic platforms (unlike electrophoresis) are relatively rare, partly because the integration of LC columns without external packing remains a difficult challenge.¹⁸

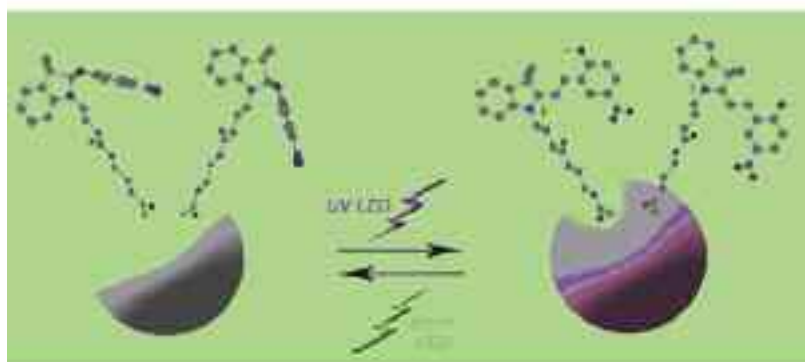
However, the spiropyran functionalised microbeads mentioned previously can be incorporated into microfluidic flow systems, such as capillary separation columns, whose binding behaviour can be externally modulated using LEDs. By utilizing the photoswitchable ion-binding properties of the microbeads, it is possible to spatially control certain areas of the column, switching on ion-binding, and inducing release of bound species using light. Figure 3 presents a simple chip device fabricated using soft lithography techniques. It consists of two independent 360 μm internal diameter quasi-circular channels fabricated in polydimethylsiloxane (PDMS)/glass, Figure 3A, with the chip channels connected to the macro-world by 50 μm internal diameter (I.D.) silica fibres.



Figure 3. A: hybrid PDMS-glass chip with two 360 μm I.D. channels. B: PDMS channels packed with 5 μm diameter SP-modified beads



Figure 2. Molecular and macroscopic colour change on the microbead surface; irradiation with a UV LED causes SP modified microbeads to convert to the ion-binding active, purple MC form, while exposure to white LED regenerates the inactive, colourless SP form. In contrast to the inactive SP form, the MC form will bind certain metal ions, and this process is fully reversible using a white or green LED



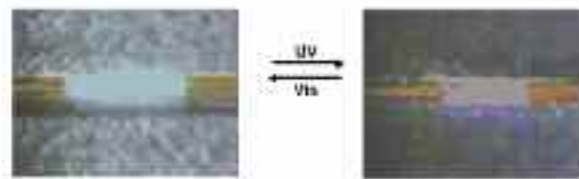


Figure 4. Polystyrene beads packed in a 360 μm PDMS channel chip. Photochromic switching of microbead column between the SP isomer (left) and the MC isomer (right) using LEDs.

5 μm diameter polystyrene microbeads functionalized with spiropyran were packed into the PDMS channels to form microbead columns. These were obtained by placing a filter at the channel outlet and introducing a suspension of functionalized microbeads into the channel (flow rate 5 $\mu\text{L min}^{-1}$). The microbead columns generated in the PDMS channels were approximately 2 cm in length, and could be successfully switched between the SP and MC isomers, using a 375 nm UV LED (for the SP \rightarrow MC conversion), and a white 430–760 nm LED (for the MC \rightarrow SP conversion), see Figure 4. In principle, this system could be used to preconcentrate certain metal ions from samples, and subsequently release them entirely under photonic control. In addition, the system is inherently self-indicating, in terms of which isomer is present (SP-inactive, MC-active) and whether the guest ion is bound or not.

Furthermore, as beads can be mobile, they can be used to pick up a chemical payload in one location, and transport it to another location where it can be released, again under photonic control. In addition, as MC interacts also with more complex guests like amino acids, it may be possible to use this concept to pick up and release a much wider range of molecular payloads.

Conclusion

In conclusion, we are beginning to witness the emergence of new, sophisticated functionalized materials with binding properties that can be turned on and off using light. They are inherently self-indicating in terms of whether the active or passive form is present, and whether a guest is bound. This can happen in solution, or on planar functionalized polymer surfaces, on beads, or within channels. The user can decide when and where binding will occur, and for how long the guest remains bound, using light, and the entire process is fully reversible. We regard these preliminary results presented in this paper point the way towards even more sophisticated materials capable of switching reversibly between active and passive forms, and simultaneously providing a number of transduction modes for gathering information about the molecular environment in the immediate vicinity of the binding site when in the active mode. We are witnessing the emergence of new, switchable materials, capable of binding molecular guests,

transporting them to remote locations and releasing them, and telling us what is happening at the same time. Clearly, fundamental materials science, and particularly the chemistry of these materials, is going to be an exciting area to work in for the foreseeable future.

Acknowledgements

We would like to acknowledge financial support from Science Foundation Ireland for RB under the Adaptive Information Cluster Initiative (SFI 03/IN.3/1361) and SS under the research Frontiers program (07/RFP/MASF812), Enterprise Ireland ‘MASTRA’ award for AR (CFTD/06/341), and an IRCSET postdoctoral fellowship for FB-L.

Prof. Dermot Diamond was a speaker at the 2008 ICI congress.

References

1. D. Diamond, *Anal. Chem.* **2004**, *76*, 278A–286A.
2. D. Diamond, *NATO Security through Science, Series A: Chemistry and Biology* **2006**, *2*, 121–146.
3. R. Byrne, D. Diamond, *Nature Materials* **2006**, *5*, 421–424.
4. S. Stitzel, R. Byrne, D. Diamond, *J. Mater. Sci.* **2006**, *41*, 5841–5844.
5. A. Radu, S. Scarmagnani, R. Byrne, C. Slater, K. T. Lau, D. Diamond, *D. J. Phys. D* **2007**, *40*, 7238–7244.
6. R. C. Bertelson, *Organic Photochromic and Thermochromic Compounds* **1999**, 11–83.
7. H. Gomer, A. K. Chibisov, *J. Chem. Soc. Faraday Trans.* **1998**, *94*, 2557–2564.
8. H. Gomer, *Phys. Chem. Chem. Phys.* **2001**, *3*, 416–423.
9. A. K. Chibisov, H. Gomer, *Chem. Phys.* **1998**, *237*, 425–442.
10. L. Evans, G. E. Collins, R. E. Shaffer, V. Michelet, J. D. Winkler, *Anal. Chem.* **1999**, *71*, 5322–5327.
11. J. D. Winkler, C. M. Bowen, V. Michelet, *J. Am. Chem. Soc.* **1998**, *120*, 3237–3242.
12. R. J. Byrne, S. E. Stitzel, D. Diamond, *J. Mat. Chem.* **2006**, *16*, 1332–1337.
13. D. Diamond, R. Byrne, S. Stitzel, (Invent DCU Ltd., Ire.) WO, 2007, pp 23pp.
14. F. L. Yap, Y. Zhang, *Biosensors and Bioelectronics* **2007**, *22*, 775–788.
15. D. Maysinger, *Org. Biomol. Chem.* **2007**, *5*, 2335–2342.
16. U. Bilati, E. Allemann, E. Doelker, *Drug Delivery Technology* **2005**, *5*, 40–47.
17. M. Brivio, W. Verboom, D. N. Reinhoudt, *Lab on a Chip* **2007**, *6*, 329–344.
18. J. Park, D. Lee, W. S. Kim, S. Lee, C. H. Ahn, *Anal. Chem.* **2007**, *79*, 3214–3219.

Corrections

In the last issue we published an appreciation of the late Prof. Wesley Cocker. In this article Prof. Brian McMurry’s name was spelt incorrectly and the time of Prof. Cocker’s passing (January 30th 2007) was inaccurately reported.

Young Chemist Profile Dr. Daire Osborne, *Development Chemist, Merck Sharp & Dohme*



My interest in chemistry developed while I studied for a degree in Applied Chemistry at the National University of Ireland, Galway. I was particularly fascinated by the complexity and creativity of organic synthesis. Following the completion of my degree I moved to Dr. Paul Stevenson's research group at Queen's University Belfast to pursue my doctoral studies. Our research focused mainly on natural product synthesis and methodology development. This research enabled me to consider a process development position within the pharmaceutical industry. Shortly after the completion of my PhD I joined the Process Development and Commercialisation department at Merck Sharp & Dohme near Clonmel, Tipperary. Merck Sharp & Dohme is a global research-driven pharmaceutical company with over 60,000 employees. Our Clonmel facility fulfils an important role within Merck. Firstly we are a supply site. We synthesise complex active pharmaceutical ingredients for many of the companies' most successful products. For example we produce the active ingredients for important products such as Singulair, Fosamax and Isentress. Production volume varies in scale from kilogram to multi-ton depending on the demand for the product. The second feature of the Clonmel site is that we are a 'Commercialisation' site. As a Commercialisation site we have substantial input into the development of new medicines and in addition we provide the pharmaceutical ingredients for Clinical Trial studies. The vast majority of Merck's new products pass through our site. My interest in chemistry developed while I studied for a degree in Applied Chemistry at the National University of Ireland, Galway. I was particularly fascinated by the complexity and creativity of organic synthesis. Following the completion of my degree I moved to Dr. Paul Stevenson's research group at Queen's University Belfast to pursue my doctoral studies. Our research focused mainly on natural product synthesis and methodology development. This research enabled me to consider a process development position within the pharmaceutical industry. Shortly after the completion of my PhD I joined the Process Development and Commercialisation department at Merck Sharp & Dohme near Clonmel, Tipperary. Merck Sharp & Dohme

is a global research-driven pharmaceutical company with over 60,000 employees. Our Clonmel facility fulfils an important role within Merck. Firstly we are a supply site. We synthesise complex active pharmaceutical ingredients for many of the companies' most successful products. For example we produce the active ingredients for important products such as Singulair, Fosamax and Isentress. Production volume varies in scale from kilogram to multi-ton depending on the demand for the product. The second feature of the Clonmel site is that we are a 'Commercialisation' site. As a Commercialisation site we have substantial input into the development of new medicines and in addition we provide the pharmaceutical ingredients for Clinical Trial studies. The vast majority of Merck's new products pass through our site.

I have worked within the Process Development and Commercialisation department at Merck for the last five years. It has been a highly enjoyable and challenging experience. Our department is the nerve centre for the development of our pharmaceutical products. We provide three key services to the plant:

- We provide technical support to enable the manufacture of commercial Merck products.
- We provide expertise during the 'Technology Transfer' of products to and from our site.
- We scale-up and develop commercially viable manufacturing routes for developmental medicines.

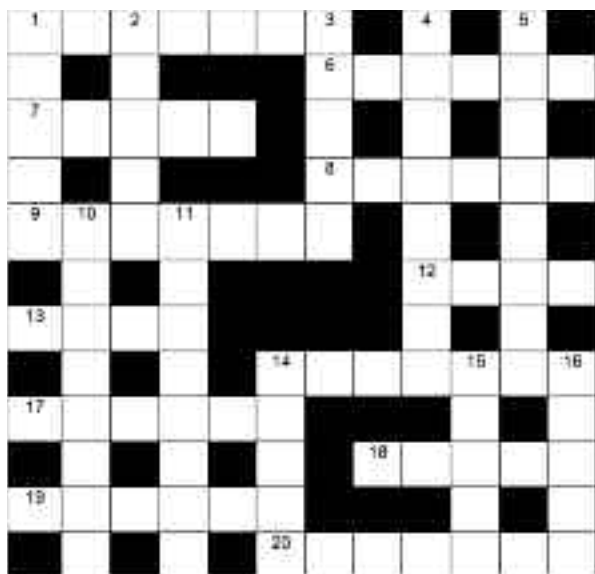
There are many career development opportunities as well as personal development opportunities within the company. We are encouraged to improve our technical ability by attending various international conferences, workshops and symposia. Development outside of one's functional area is strongly encouraged. For example I have developed skills in statistics, chemical engineering, Process Analytical Technology and project management. There are also many career opportunities available. Assignment to manufacturing operations, Quality Assurance and Process Engineering departments are frequent. One may also travel internationally within the company as we have sites in many diverse locations such as Puerto Rico, Singapore and South Africa. Rotational assignment to early Research and Development is also encouraged. For example I have recently completed a four month assignment at our New Jersey R&D facility. Later this year I will travel to India to perform a product Technology Transfer.

Overall, working at Merck is an enjoyable experience. A very strong community atmosphere exists and the age profile of the staff is relatively young. There are many diverse career opportunities and the work is highly challenging. New opportunities arise almost daily. We are currently constructing a new Pharmaceutical Formulation R&D plant on site and a new vaccine facility was recently announced in Carlow. These are truly exciting days at Merck Ireland.

The ICN Crossword

Dr. Donal Coveney FICl,

TopChem Laboratories Limited, 70 Western Parkway Business Park, Ballymount Drive, Dublin 12, Ireland



Across

- 1 Too hot to touch - lift with this hand tool (5)
- 2 Painful in any form but perforated! (5)
- 3 Avoid this canine like the plague (5)
- 4 Metal revealed from sad cumin? (7)
- 5 Curly moon? (8)
- 10 Fragrant and meets the $4n+2$ rule (8)
- 11 Cap music for chilli plant (8)
- 14 Small silvery fish (5)
- 15 Apportion (5)
- 16 Explosive salt to fill your airbag (5)

Down

- 1 Red hunt combine to deafen (7)
- 6 Jumble your Japanese car doc! (6)
- 7 Little corner of the market (5)
- 8 Remove electron (or add one?) (6)
- 9 Oi! Add to linked letters to generate a granuloma (7)
- 12 Individual article (4)
- 13 Cleansing salt (4)
- 14 Epidermal pores (7)
- 17 Metallic meal to reveal internal image (6)
- 18 Tiny intestinal fronds (5)
- 19 A sum of habitual actions (6)
- 20 House of drama (7)

Last Issue Solution

Across.

1. Molar 4. Acetic 7. Fillings. 8. Rhodium 9. Into 11. Bar

13. TNT 16. mbar 18. Heptane 20. Helmsman 21. Chiral 22. Smell

Down.

1. Mushroom 2. Liquor 3. Ruffian 4. Aplomb 5. Elixir 6. Ingot

10 Oriental 12. Appends 13. Trimer 14. Thymol 15. Saline 17. Beech

Heavy Metal Su Doku

Dr. David Birkett

Henkel Ireland Ltd., Tallaght Business Park, Whitestown, Dublin 24, Ireland

				Tl	Au			
			Ir	Os		Bi		
	Ir	Au	Pt			Hg		
Ir						Cd	Bi	
Hg	Bi			Ir			Os	Au
	Os	Cd						Hg
		Bi			Ir	Au	Pb	
		Ir		Cd	Hg			
			Os	Pb				

Solution previous Elemental Su Doku

Be	F	H	He	Li	N	B	O	C
He	N	C	F	H	O	Li	Li	Be
B	O	Li	Be	C	H	F	He	N
N	H	Be	O	He	F	Li	C	H
O	Li	He	N	H	C	Be	B	F
C	H	F	Li	Be	B	O	Li	He
H	C	N	H	O	He	He	F	Li
F	He	O	H	N	Li	C	Be	B
Li	Be	B	C	F	He	N	H	O

Notes



The Institute
of
Chemistry of Ireland

IrishChemicalNews
JOURNAL OF THE INSTITUTE OF CHEMISTRY OF IRELAND