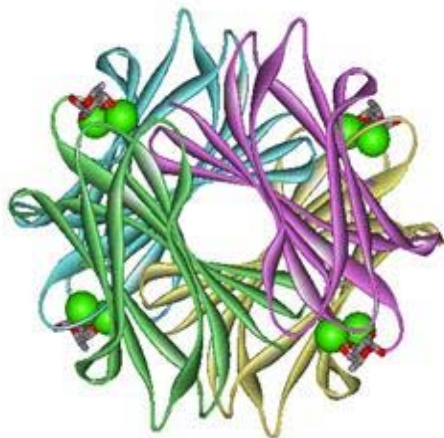


illuminations

Issue 11

Using DPI to Unravel Glycobiology



Glycobiology has emerged as an important area of biology, greatly facilitated by advances in biophysical measurement and characterisation of glycan structures. The field is made more complex as carbohydrate biochemistry is epigenetic with an infinite variety of structures that retain a specificity of action or regulatory function.

The advent of MALDI-TOF has made it possible to derive high resolution information from glycan structures. However, such data is derived from static measurements at equilibrium, rather than from a dynamic measurement of the mode of interaction of that structure with any of its biologically relevant molecular partners. Dynamic mass-based measurements have been conducted via such biosensor technologies as surface plasmon resonance (SPR). These studies have been hindered by the relatively low affinity of sugar-based interactions and the practical issues

of working at high sugar concentrations where prominent bulk refractive index effects interfere with the basic measurement principle.

The Solution: Dual Polarisation Interferometry (DPI) is increasingly being deployed in glycobiology as it's inherent sensitivity and large dynamic range allow the user to work with high sugar concentrations. Additionally, a more complete biophysical characterisation is possible with quantitative measurements being determined in molecular size, density, birefringence and mass and in real time. With DPI it is now possible to measure the mechanisms underlying the biomolecular interactions involving sugars together with the reaction rates and affinities of interaction. More information on page 4.

Developing a BioSensor Toolbox for Parkinson's Disease

Farfield Joins the Neurasyn Network

Parkinson's disease (PD) is the second most common neurodegenerative disorder. It is characterized pathologically by the accumulation of aggregated conformations of the presynaptic protein alpha-synuclein. A network of European partners will examine, using state of the art in vitro assays, structural biology and diverse cellular and animal models, alpha-synuclein conformations, regulation, and mechanisms of toxicity for the study of alpha-synuclein related to PD. Through this work, biomarkers and experimental therapeutics targeting alpha-synuclein will be tested. This Network will create the opportunity for training a number of early stage researchers in the diverse fields of protein chemistry, biochemistry, cell biology, neurobiology, and animal modelling of nervous system diseases, within an interdisciplinary setting, while exposing them to both academic and industrial environments.

The Network is pleased to be able to fund 11 positions for every facet of the project. Farfield's Project is the development of a biosensor toolbox for the structural characterisation of alpha-synuclein monomer, oligomer and membrane interactions. All interested applicants may contact Farfield's CSO, Dr. Marcus Swann, mswann@farfield-group.com.

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From our CEO

Note from our CEO - Dr. Gerry Ronan

Welcome to our latest issue of 'Illuminations'. 2009 has seen some super publications from our **AnaLight®** users around the world. In this issue we will be looking at one area, the study of glycans and, in particular, heparin. The introduction of a glycan kit for our **AnaLight®** instruments further extends the wide range of applications available for our award winning dual polarisation interferometer.

Details of these surfaces have been published in **J.F. Popplewell, M.J. Swann, Y. Ahmed, J.E. Turnbull and D.G. Fernig**. Fabrication of carbohydrate surfaces using non-derivatized oligosaccharides, and their application to measuring the assembly of sugar-protein complexes. **ChemBioChem, 2009 May 4;10(7):1218-26**.

This is such a large, cross disciplinary field that I am sure as we move from genomics through proteomics to glycomics, the potential of these surfaces to unlock previously un-studied areas of glycobiology will be vast. We are delighted to be able to offer this well characterised, mimetic surface and look forward to hearing of your ideas for its application in your research.



Farfield Around the World

AnaLight® 4D Product Launch in Germany



Farfield has now launched the **AnaLight® 4D** in German and Austrian territories where up to now Dual Polarisation Interferometry has had little exposure. However, with the help of Dr. Mario Noyer Weidner, Farfield has made tremendous progress recently with a number of leading academic and industrial research laboratories.

Dr. Noyer Weidner's background in academia, scientific publishing and industry make him an ideal partner for Farfield. Prior to working with Farfield, Mario led a research group at the Max-Planck Institute of Molecular Genetics in Berlin for many years. He later directed the Natural Science departments of a major German scientific publisher, and subsequently held global responsibility for the R&D of a US genetic screening instrumentation company. Mario is a member of the faculty of Biology, Chemistry and Pharmacy of the Free University of Berlin since 1989 and currently is also teaching as a visiting professor at various other European Universities. We are looking forward to expanding our opportunities in the German speaking market with the support of Mario. He can be contacted on: m.noyer-weidner@gmx.de

World Class Biomolecular Research in Taiwan



Professor Ho (Annie), pictured left, of the National Tsing Hue University (NTHU) in Taiwan is currently using a Farfield **AnaLight® 4D** system as an important tool in her research studying tethered lipid bi-layers together with one of her PhD students Ting-Yang Kuo. NTHU is one of the premier Universities in Taiwan known for its long and proud history. Students and faculty members have performed exceptionally well and are frequently being recognized for the quality works they have accomplished. They are one of a few universities in Taiwan selected by the Ministry of Education to receive special funds for a period of five years starting in 2006 to upgrade their teaching, research and, thus pave the way to move Tsing Hua into the rank of world-class universities.

Prof Ho (Annie) heads a research group with a focus on lipid membrane interactions and liposome-based biosensors. She gained her PhD in the USA in Cornell University (Ithaca, NY) and returned to Taiwan to take up a position at NCNU in Puli, Nantou. She then moved to NTHU where she has been at the Department of Chemistry for the past 4 years.

Learn more about Dr. Ho's research at the 'Hot Liposome' website - <http://hotliposome.chem.nthu.edu.tw/Home>

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Farfield Upgrades Waveguide Sensor Manufacture

On the back of strong sales worldwide in 2008/2009, Farfield has expanded its sensor manufacturing capability by bringing designs online in a 6" wafer process at INEX, Newcastle, UK. The wafer designs include radically new manufacturing processes which enable higher yield, better reproducibility and ultimately higher performance for our customers. Moving from 4" to 6" process has also increased output by a factor of four.

Farfield CEO, Dr Gerry Ronan commented that the collaboration has been a tremendous success. "We've also co-located our sensor functionalisation capability within the INEX laboratories, reducing handling, and improving overall product quality." Further product improvements are planned throughout 2009 and 2010 which will bring additional performance benefits to our existing users.



Free Software Upgrade To Version 1.5.4 For All AnaLight® Users

Farfield have always adopted a policy of providing low cost hardware and software upgrade plans to all of our **AnaLight®** users to ensure they can take advantage of our continuous development program. To celebrate our successes in our 12th year of trading, Farfield are pleased to offer all our users a free upgrade to the latest version of Farfield's **Explorer** software which automatically resolves the thickness, density and mass of molecular layers at world class resolution. The **Explorer** software also has the ability to automatically resolve the order and disorder within lipid bilayers this was launched with the **AnaLight® 4D** in 2008. This latest functionality, which is compatible with both Windows™ XP and Vista, is now available to all our users.

To discuss hardware compatibility and get your free copy, contact support@farfield-group.com

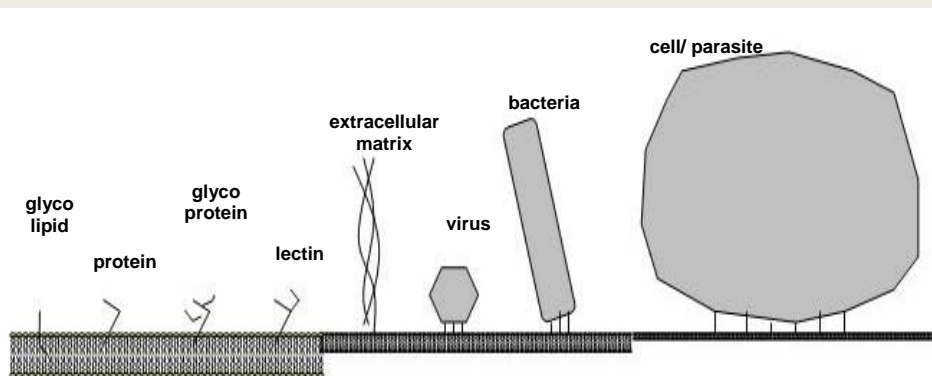
Farfield Extends its Wide Range of Chip Surfaces

AnaChip™Plus	Application	Surface
Unmodified AnaChip™ Plus	proteins from low to high molecular weight, peptides, nucleic acids, carbohydrates, lipids, and liposomes	silicon oxynitride giving hydroxyl surface chemistry carrying negative charge
Amine AnaChip™Plus	proteins from low to high molecular weight, peptides, nucleic acids, carbohydrates, lipids, and liposomes	surface via -NH ₂ , -CHO or -SH groups on target biomolecule, using one of a range of linker chemistries
His Tag AnaChip™Plus *NEW	high signal-to-noise levels and additionally is amenable to regeneration making it ideal for automated studies, for protein and small molecule interactions.	the M ²⁺ His-tag surface is a highly oriented capture surface showing extremely low levels of non specific binding (nsb).
Thiol AnaChip™ Plus	study of DNA, RNA, proteins from low to high molecular weight, peptides.	surface via -NH ₂ or -SH groups on target biomolecule, with or without linker chemistry
C18 AnaChip™Plus	adsorption of hydrophobic proteins and peptides and forming lipid-based mimics for membrane protein studies	surface for adsorption of hydrophobic biomolecules, usually those associated with membrane environments
Cellulose AnaChip™Plus	fabric care cleaning and conditioning formulation development, paper technology and ink formulation studies	Cellulose mimetic surface
GlycanSurface Kit * NEW	The surface is created for the capture of biomolecules such as lectins for glycobiology studies	Kit is assembled to allow user preparation of a quantitative heparin surface.

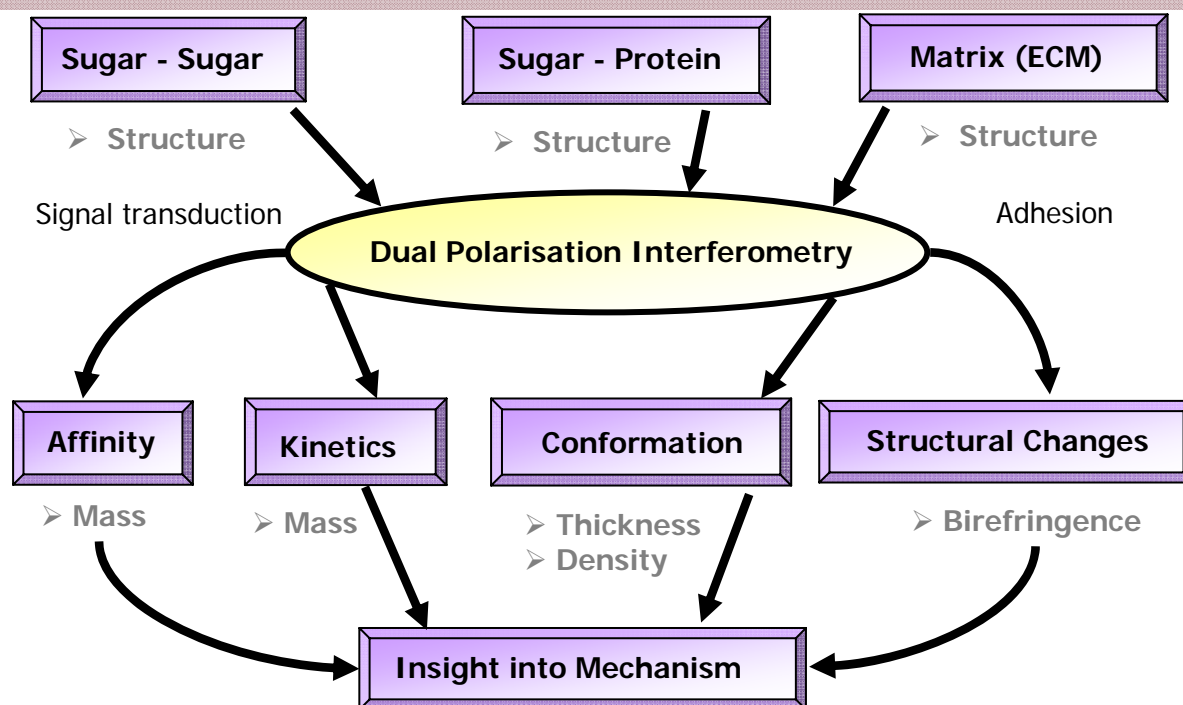
Spotlight on Glycan Surfaces

Glycan components are found in different forms, serving several important functions in cellular interactions and signalling including cell-parasite interactions.

Glycosylation is one of the most common post-translational protein modifications in mammalian systems.



DPI Provides Insight Into Glycan Surfaces

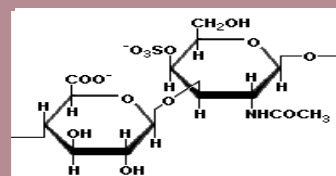


Criteria for DPI glycan surfaces:

- Planar rather than 3D sensor surface
- Use of well-defined and natural sugar components
 - does not contain synthetic modification or covalent attachment
- Quantified mass and orientation of captured oligosaccharide
- Free from non-specific binding
- Excellent regenerability, robust and prolonged shelf life
- Delivers structural data on carbohydrate-protein interactions
- Easily extendable to any naturally occurring oligosaccharide

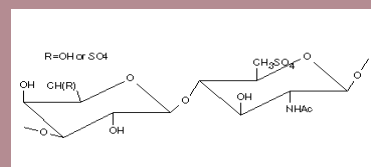
Chip 1: Chondroitin sulphate

Species: bovine
Tissue: Trachea
4-sulphonation level: 65%
6-sulphonation level: 35%
Chain length; 20 disaccharides



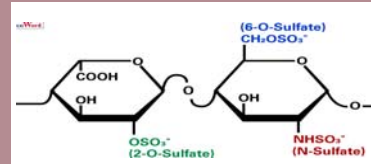
Chip 2: Keratan sulphate

Species: bovine
Tissue: Trachea
Galactose sulphonation 60-70%
Chain length; 14 disaccharides



Chip 3: Heparin

Species: Pig
Tissue: Mucosal
Chain lengths available; (dp) 4-20



Continuing Glycan Research...

DPI has unravelled the complex analysis of the carbohydrate-protein binding system of heparin–HepV, which has been shown to be difficult to measure using other optical techniques. The complex non-kinetic mass binding events observed by surface plasmon resonance (SPR) [Figure A] can be resolved by discriminating between bound mass and conformational changes via DPI in a way that could not be visualised via SPR [Figures B and C].

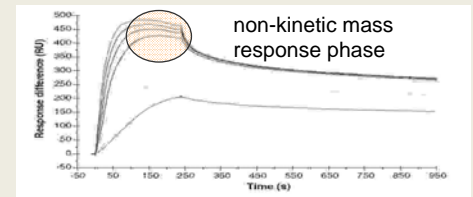
DPI is hence a very powerful technique to characterise underlying biomolecular interactions based upon biophysical interpretation of binding events rather than via an implied kinetic measurement.

[Ricard-Blum et al. Anal Biochem, 2006 352(2):252-259]

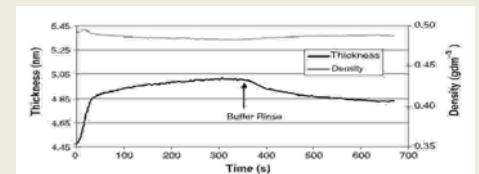
Technical challenges of working with glycan structures:

- Bulk effects
- High Refractive Index
- Immobilisation effects
- Low affinity
- Structural effects

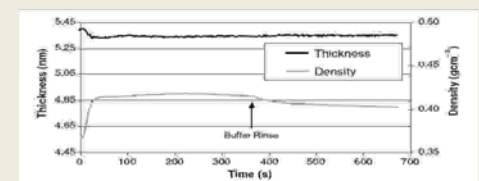
A: SPR binding of HepV to heparin surface



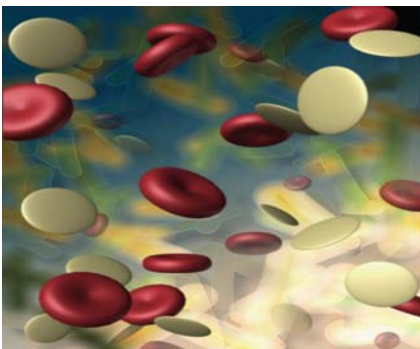
B: DPI binding of HepV to heparin surface



C: DPI binding of HepV to control surface



What Does Heparin Do?



Heparan sulfates (HS): are glycans (complex sugars) found on all cell surfaces. They act by binding selectively to a variety of proteins and pathogens and are critically relevant to many disease processes (eg. inflammation, neurodegeneration, angiogenesis, wound healing, cardiovascular disorders, cancer and infection). Many of these activities have been detected using heparin, which is a subclass of the HS family of glycans and the world's largest selling pharmaceutical by weight.

Heparin-based Pharmaceuticals: The use of heparin and its derivatives in the clinic illustrates the importance of the HS family of glycans and their potential as therapeutics: over 60 years as anticoagulants (preventing blood clotting) in the treatment of cardiovascular disease (responsible for 1 million deaths in the US alone in 2001) with a market of \$2 billion. It has also been known for many years that **heparin has a wide range of biological activities** including effects on tumour growth, microbial infectivity, inflammation and wound healing.

- heparin reduces tumour spread and prevents invasion in animal models, and there is anecdotal evidence for promise in the treatment of human cancer.
- heparin can prevent numerous bacteria (eg. Chlamydia, Staphylococcus aureus, N. gonorrhoea) and viruses (eg. Herpes simplex, HIV) binding and infecting human cells.
- heparin binds and regulates many proteins associated with inflammation (the process underlying diseases such as Asthma and Arthritis) and also many involved in tissue maintenance and repair.
- HS has been linked to neurodegenerative diseases such as Alzheimer's and Prion disease and has been shown to bind protein targets for these diseases.

Heparin-based glycans influence a huge variety of cellular events associated with major disease groups and represent drug targets of increasing importance. Farfield's Glycan kit provides a convenient and data rich platform to study many of these processes.

Farfield source all of our heparin from world renowned experts in the manufacture of natural glycans, Intellihep Ltd (www.intellihep.com) who will be delighted to discuss your analytical needs.

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Spotlight on Innovation Support

Farfield Receives Growth and Innovation Awards



The High Growth Programme

On the back of exceptional performance in 2008 and 2009, Farfield Group Ltd has been accepted as one of the few companies that will be supported by the UK's North West Regional High Growth Programme. The

Northwest Regional Development Agency (NWDA) and the NW European Regional Development Fund have launched this new High Growth business support programme designed to help businesses in the region capitalize on high growth performance (defined as experiencing greater than 30% growth year on year).

The program delivers a range of support services which underpin growth and build on the successes within the region and also provides coaching for High Growth that will support and grow the North West economy.

For further details of the High Growth Programme see: <http://www.highgrowthprogramme.co.uk/>



INVESTING IN
englandsnorthwest

EUROPEAN REGIONAL DEVELOPMENT FUND

Earlier this year Farfield secured an Innovation Voucher to enable it to access specialist skills within the region. The Innovation Voucher helped to partner with Manchester University to use a newly developed biosensor chip design to dynamically measure ex-situ and in-situ deposited thin films (named Multiple Path Length DPI or "MPL-DPI"). The project demonstrate the feasibility of measurements based

on the principle of an absolute interferometer and assessed the potential for the technique based around the existing DPI instrument.

The work produced a report that demonstrated the methodology for a specific real world application, showing that an ex-situ layer of acrylic polymer can be measured dynamically and an ad-layer of fibrinogen can also be measured above the ex-situ coated polymer layer.

Details of the work have also recently been published, **Paul D. Coffey, Marcus J. Swann, Thomas A. Waigh, Fred Schedin and Jian R. Lu**, Multiple Path Length Dual Polarization Interferometry Measurements of Refractive Index and Thickness of Ultrathin Films in Real Time *Optical Express*, Vol. 17, Iss. 13, pp. 10959–10969 (2009) and can be accessed by following the link below:

http://www.opticsinfobase.org/DirectPDFAccess/EA4343BC-BDB9-137E-C71198E5E651F364_180722.pdf?da=1&id=180722&seq=0&CFID=51856130&CFTOKEN=17919821

ISO9001:2008 — Farfield Leads The Way



FS 75229

Farfield Group is please to announce that it has successfully transferred our quality management registration to the latest **ISO9001:2008** quality standard and have been recertified for the coming 3 years. As **ISO9001:2008** was only released at the end of 2008, Farfield were one of the very first companies to be operating to this latest standard.

Farfield takes quality control in each step of our processes as underpinning our success. It is an essential part of the quality and reliable in our products and support services.

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Spotlight on Farfield Partners

Farfield Develop Membrane Protein Assays for ASMEMA Project



Farfield's Chief Scientific Officer, Dr Marcus Swann being joined by the rest of the ASMEMA consortium.

Farfield is a proud partner in the European FP7 programme ASMENA, which held its first annual project review meeting recently in Budapest. The consortium consisting of 15 partners in 7 countries.

The project will run over three years, and aims to develop new platforms for drug screening and analytical profiling based on in-vitro measurements of functional and conformational change in membrane proteins.

Current drug screening assays targeting membrane proteins rely to a large extent on fluorescence based techniques that can be problematic, relying on an unnatural attachment/component of the target protein in question, which in the worst case can lead to false readouts. Thus there is an increasing interest in label free. Building

on this, the core aim of the project is to develop functional based assays based on electrical and optical measurement techniques.

The partners of the consortium are world leading experts on surface functionalization, membrane self-assembly, biosensing, membrane protein functional measurements and technology commercialization. Under this project their complementary competences can be put together on the European level to create a timely breakthrough in the area.

Farfield's contribution to the project is focussing on developing membrane protein assays based on the ability of the Dual Polarisation Interferometry (DPI) technique to probe conformational changes in molecules. Together with the technologies developed with the other partners, Farfield believes such tools will allow a shortened time and cost in drug lead development by increased predictability as well as contribute to fundamental understanding of structure-function relationship of membrane proteins.

More information can be obtained from the ASMENA website at: <http://www.asmena.ethz.ch/>

Together with Farfield, the partners include ETHZ, Paul Scherrer Institut, SuSoS AG, Leister Process Technologies and F. Hoffmann - La Roche Ltd. From Switzerland, Chalmers University of Technology, Layerlab AB and Hydrogene AB From Sweden, Max Planck Institute from Germany, University of Bordeaux from France, University of Twente (ELTE) from the Netherlands, Eötvös Lorand University and MicroVacuum Ltd. From Hungary

Partnership On Glycan Chemistry

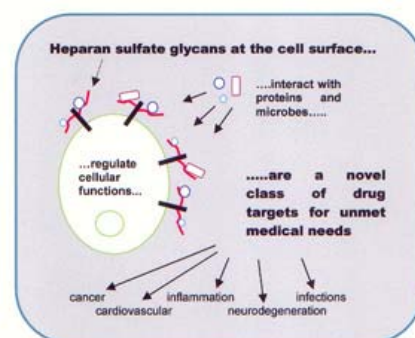


intellihep

creating heparin-based drugs

Intellihep is using innovative technologies to deliver new heparin-based glycans and novel drug leads in disease specific applications. Farfield is pleased to announce a collaboration with Intellihep for the supply of a range of high quality quantified natural glycan surfaces. The collaboration will enable Farfield to develop a broad range of surfaces for glycan related research. Contact Farfield (support@farfield-group.com) or Intellihep (info@intellihep.com) with details of your analytical needs.

You can learn more about these glycan surfaces on page 4-5 and about the other glycan research activities at Intellihep's website: www.intellihep.com



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Distributor News



Those pictured Sandra Wollschlaeger (Frankfurt), Rosemary Parslow (University of Birmingham), Usha Devi (Farfield), Christin Bissig (Geneva), Dr Mark Jeeves (University of Birmingham), Michal Grzybek (Max Plank Institute), Walis Jones (Farfield), Uenal Coskun (Max Plank Institute), Dr Timothy Knowles (University of Birmingham), Yu-Pin Lin (University of Birmingham)

Focus on Europe

News from Germany: - As part of Farfield's focus on the German speaking market, we were asked to join the European PRISM meeting in Dresden in Germany in August. PRISM is a European specific targeted research project network for lipid binding research. It includes representatives from academic groups in Germany, UK, Switzerland and The Netherlands. This meeting, which took the form of a workshop, took place at the Max-Planck Centre for Molecular Cell Biology and Genetics in Dresden (Germany). Farfield demonstrated an **AnaLight® 4D** at the meeting with Dr Usha Devi and Dr Walis Jones discussing how the instrument could be used to benefit the projects of the partner groups in PRISM.

Further detail of the PRISM network can be found at: www.lipidprism.org



Particular Sciences

Farfield are pleased to announce that they have established an Agency Agreement with Particular Sciences Ltd to cover Ireland. Particular Sciences (www.particular.ie), based in West Dublin, was founded twenty years ago to provide technical support in material characterisation for chemists, biologists, researchers and industrialists. The company has steadily grown with the market in Ireland and now services over 200 companies in pharma, minerals, food, pigments and increasingly in research with nanotechnology and biotech.

Farfield's CEO, Gerry Ronan, commented, "This is a fantastic opportunity to strengthen Farfield's presence in Ireland. Particular Sciences' reputation for excellence in customer service is exactly what we are looking for and I'm delighted that they are going to help accelerate our progress in 2009 and beyond".

Farfield Group

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INVESTOR IN PEOPLE



FS 75229

Farfield Group is now hiring, talented and multidisciplinary team members with experience and expertise across a wide range of disciplines. The development and commercialisation of Farfield's innovative technology base requires a team of flexible and self motivated individuals.

Farfield Group offers its employees the opportunity to both realize and further develop their potential. The company aims to offer its employees a comprehensive, performance-related benefits package.

Farfield Group is an Equal Opportunities employer and has achieved the Investors in People Standard.

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