The research commercialisation office of the University of Oxford, previously called **Isis Innovation**, has been renamed **Oxford University Innovation**

All documents and other materials will be updated accordingly. In the meantime the remaining content of this Isis Innovation document is still valid.

URLs beginning www.isis-innovation.com/... are automatically redirected to our new domain, www.innovation.ox.ac.uk/...

Phone numbers and email addresses for individual members of staff are unchanged

Email : enquiries@innovation.ox.ac.uk

Isis insights

Issue 78 Winter 2014

MEDICAL TECHNOLOGIES

Healthcare advances with innovative technology

The latest innovations, collaborations and technology transfer

UNIVERSITY OF OXFORD

Isis INNOVATION

Issue 78
Winter 2014

Medical technologies focus

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www.isis-innovation.com

Isis is a research and technology commercialisation company owned by the University of Oxford.

NEWS

Isis Innovation wins Technology Transfer Unit of the Year

Global University Venturing, at its 2014 Summit, named Isis Innovation "Technology Transfer Unit of the Year". "Isis Innovation…has had a stellar year," said Global University Venturing editor Gregg Bayes-Brown in a news article. "The unit has raised a fund, seen one of the largest exits of any spin-out in the past academic year, been ranked the top TTO in Europe by Global University Venturing, and has been one of the most consistently active TTOs over the past year."

$15m returned from sale of Intellectual Property to Sequenom

US life sciences company Sequenom purchased non-invasive prenatal screening intellectual property from Isis Innovation for $15m. Sequenom now owns the global intellectual property for non-invasive prenatal genetic diagnostic testing on paternally inherited fetal nucleic acids derived from maternal plasma or serum, which it previously licensed. An article from Healthcare Royalty Partners, discussing the role of such royalty buyouts, is on page 6 of this issue.

News of our spin-outs and startups

A new spin-out from the University's renowned Mobile Robotics Group, Oxbotica, has been formed to commercialise technologies for robotics and autonomous systems. The new company, founded by Professor Ingmar Posner and Professor Paul Newman of the Department of Engineering Science, will apply expertise and IP to a wide range of applications.

Onfido, a startup incorporated from the Isis Software Incubator, has raised £500,000 in seed funding as its online real-time employee screening service is rolled out to help employers conduct vital background checks.

University of Oxford Isis Fund makes first investments

The £1.25 million University of Oxford Isis Fund, set up by Parkwalk Advisors and Isis Innovation in February, has made its first investments in medical device spin-out Oxtex and in Brainomix, a start up from the Isis Software Incubator which is developing software to improve stroke diagnosis. Events to present new investment opportunities to the Isis Angels Network, and to mark the opening of the 2nd UOIF Fund, took place in November.

Enterprising Consultancy

News from **Oxford University Consulting** and **Isis Enterprise**

Regional technology transfer partners in France

In May 2014, Isis Enterprise signed a contract with IDF Innov, one of the SATT (Les Sociétés d'Accélération du Transfert de Technologies) offices, which now act as the central technology transfer service for universities and research institutes on a regional basis in France. SATTs were set up in 2010 with a budget of €0.9bn as a component of the French government's 'Investments for the Future' programme. IDF Innov serves 19 universities and research institutes in the Paris region, covering more than 17,000 researchers, and represents the largest cluster of biomedical research in France.

Isis Enterprise is actively supporting IDF Innov in providing translational fund investment advice, benchmarking tech transfer activities, providing strategic advice, and licensing support. The initial phase of the relationship has proved successful for both parties and we are now working to establish closer links. Isis and IDF Innov expect to sign a new agreement by the end of 2014, and this will provide more opportunities for Isis and IDF Innov staff to work closely together on commercialisation of specific projects, and for IDF Innov to more effectively utilise the breadth of expertise and global industry networks within Isis for licensing work.

This is an exciting opportunity for both parties to combine Isis's expertise and experience in technology transfer with the rich and diverse academic research base in the Paris region.

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Medical policy advice

Tipik, a communications agency based in Brussels, has worked extensively with the EU for a number of years and has a framework agreement in place with CHAFEA, the EU's Consumer, Health and Food Executive Agency. Amongst other things, Tipik produces information sheets for the EU on key medical policy areas, including transplantation and organ donation, chronic diseases, HIV/AIDS and STI prevention, nutrition and healthy lifestyle, mental health and wellbeing, rare diseases, alcohol, patient safety, health security, and healthy ageing.

After successfully bidding for the project over the summer, OUC has been appointed by Tipik to identify and commission a number of academic consultants from Oxford's renowned Medical Sciences Division. The role of these academic consultants is to critically review the information sheets written by the agency's journalists and to provide them with advice through telephone interviews in order to ensure a proper understanding of the key issues.

This type of discrete, fast-turnaround consultancy project is appealing to busy academics as it plays to their strengths in peer-reviewing academic papers prior to publication and applies their academic expertise to topical health issues. Approximately half of the consultants commissioned are working through OUC for the first time, therefore helping OUC to expand its network of experts.

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The portfolio

The latest **spin-out** and **investment** news

Brain aneurysm treatment – Oxford Endovascular

Oxford Endovascular is a spin-out developing medical devices for the minimally-invasive treatment of neurovascular diseases. The company is seeking £2m start-up capital to commercialise its first product, Oxiflow, a flow-diverter for the treatment of brain aneurysms. Flow-diverters are a disruptive technology poised to dramatically change the landscape of the $1bn endovascular cerebral aneurysm repair market.

Clinical Need

Aneurysms occur at weak points in blood vessels where the pulsing blood pressure causes the vessel wall to balloon and potentially burst, bleeding into the space around the brain. 6 million people in the US suffer from brain aneurysms and one will rupture every 18 minutes leading to death or permanent neurological damage for the majority of patients.

Minimally invasive procedures have been available since the 1990's, enabling surgeons to treat aneurysms from within blood vessels and avoid open-brain surgery. The market leading treatment is endovascular coiling that involves filling the aneurysm with coiled metal wire. Coiling is a slow procedure that is poorly suited for treating many types of aneurysm and even successful procedures leave the aneurysm as a solid mass placing pressure on the surrounding brain.

Technology

Flow-diversion is a newly emerging treatment that uses a stent-like device made of low porosity tubular mesh that lines the blood vessel and shields the aneurysm from the pressure of blood flow, allowing it to shrink and heal naturally over the following weeks and months. The flow-diversion procedure appeals to surgeons because it is much faster to deploy than coiling and critically avoids the dangerous step of pushing a device into the fragile aneurysm.

In order for a surgeon to manage the tortuous navigation of blood vessels in the brain and access the aneurysm, flow-diverters must be very flexible while also possessing good radial strength. This is essential to ensure accurate deployment, good fit to vessel wall and to prevent movement of these permanently implanted devices. The first generation of flow-diverters have braided designs that achieve the required low porosity and high flexibility, however the inherent limitation of the braided design is poor radial strength, far weaker than the neurovascular stents used to support coiling.

Oxiflow is a next-generation flow-diverter developed over the past five years by a team at Oxford University Institute of Biomedical Engineering. Driven by their clinical experience using first-generation flow-diverters to treat patients, the team used engineering expertise to redesign the flow-diverter and create a device that combines high flexibility with a excellent radial strength. Oxiflow also has a number of additional competitive advantages including smaller diameter, variable porosity and an ergonomic delivery system. Oxiflow benefits from a strong IP position with family of patent applications covering the device and delivery system that will provide a defensive position for commercial exploitation in the world's major medical markets.

Oxford Endovascular is ideally positioned to capitalise on these rapidly growing markets and launch a next-generation product that can use a low cost regulatory pathway.

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Healthcare Royalty Financing: growing in use and demand

Louis Berneman and **Paul Hadden** of HealthCare Royalty Partners discuss means of raising funds from future royalty streams

HEALTHCARE ROYALTY PARTNERS™

The need for pharmaceutical companies to replenish and build their product pipelines has produced a proliferation of license agreements and a vast number of existing and future royalty streams. Estimated at $100 billion annually in 2009, these royalty streams are expected to grow at a rate in excess of the overall industry growth rate[1]. The abundance of royalty streams in healthcare products, combined with the pressing need for capital, has led to the rise of structured financings which provide a financing alternative to equity and debt using these future cash flows as security.

Historically, these royalty streams have been monetised through a traditional passive royalty investment in an existing license agreement, created when a licensor enters into an agreement with a licensee (such as a larger pharmaceutical company). Under these license agreements, the licensor is entitled to receive a stream of cash flow payments based on future sales of the product. Typically, these licensors have little or no ongoing role in product commercialisation, and therefore the future royalties are considered "passive" in regards to the product. In a traditional passive royalty investment, the royalty investor acquires all or part of the future cash flows. Passive royalties provide licensors with liquidity in the form of a lump sum payment and/or milestone payments. Since 2000, HealthCare Royalty Partners estimates that passive royalties have accounted for the majority of royalty investing activity, comprising more than 60% of publicly disclosed investment activity.

More recently, investments that imitate the cash flows of passive royalty investments have emerged as a means of providing non-dilutive capital to smaller healthcare companies that do not have the same access to low cost capital as the large pharmaceutical companies. This can be done in the form of a Synthetic Royalty® financing. In a Synthetic Royalty® investment, an investor creates a senior secured royalty contract with a healthcare company that owns the rights to one or more healthcare products. These companies are typically the principal developers and have retained rights to market and sell the products. This contract entitles the investor to receive a stream of cash flow payments that are principally secured by the future sales of the healthcare product, as well as by the underlying product assets. Synthetic Royalty® financings are typically treated as contingent debt for accounting purposes, and sometimes can be structured with a fixed interest component as well as a variable interest component based on product sales. This form of financing has become an attractive source of capital for smaller healthcare companies as it is designed with a high degree of flexibility at a cost that can be significantly less than equity, particularly in situations when a company believes their stock is undervalued.

While still a growing sector, the healthcare royalty space has seen significant growth in transaction volume over the past decade. HealthCare Royalty Partners estimates that there were more than $2.7 billion of transactions in 2013, and that the sector has experienced a 33% compounded annual growth rate since 2001. Royalty-generating license agreements have become an integral component of the pharmaceutical industry and valuable assets for healthcare companies. With the cost to bring a drug candidate from discovery to launch now estimated at $1.3 billion, smaller and mid-sized companies are continuously in need of growth capital to fund R&D projects, acquire and launch new products. Healthcare royalty financing can provide a cost-effective capital alternative for companies looking to raise much needed funds.

1. DechertOnPoint, "Securitization of Pharmaceutical Royalties: A Prescription for Market Growth" February 2011

"The volume of transactions consummated in the space between 2003 and 2013 has also increased by 14 times, from almost $200 million to over $2.7 billion"

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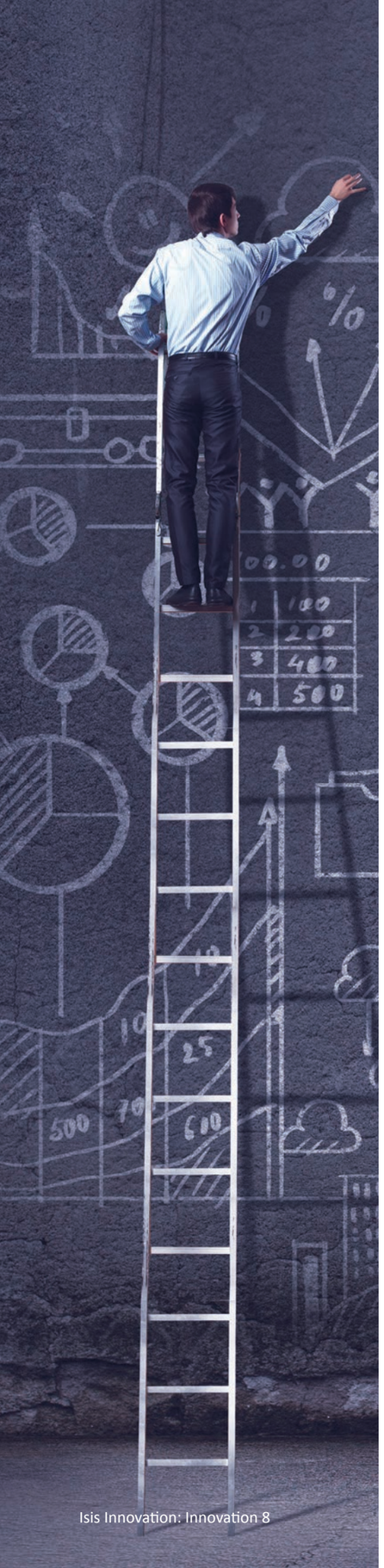

From the birth of an idea onwards, the right advice is vital

Blake Morgan, an OIS member, was recently formed by the merger of Oxford law firms Blake Lapthorn and Morgan Cole. **Nicola McConville** describes how the new firm supports entrepreneurial ventures.

BLAKE MORGAN

The brainwave is just the beginning but the commercial success of a venture is virtually impossible without good professional advice being in place from the start.

At Blake Morgan we understand the unique challenges and hurdles which young companies in the technology sector face from day one, and we have a long track record of working with spin-outs and start-ups to optimise their opportunities for successful commercialisation.

Blake Morgan, formed by the merger of leading Oxford law firms Blake Lapthorn and Morgan Cole in July, is now the largest law firm in Oxford and a leading force across Oxfordshire and the Thames Valley with further offices in Reading, London, Cardiff, Southampton and Portsmouth.

The coming together of the two firms enables us to supply a wide range of legal services for start-ups and spin-outs - now in even greater depth and breadth than ever before.

Our corporate, commercial and employment teams are at the heart of our offering, with a depth of knowledge of issues that are key to the technology sector – areas as diverse as structuring documents for investment rounds, immigration and employment law, intellectual property licensing and protection, and a wide variety of commercial contractual arrangements

The merger allows us to draw on the legacy firm Morgan Cole's long-standing record in working for local government and other public sector organisations, giving us a clear overview and deep understanding of the issues and requirements that are unique to technology companies which seek to find opportunities in this sector.

For those developing innovations that our relevant to the healthcare market, we are able to offer comprehensive understanding of medical technology and wide-ranging experience of working with healthcare providers, Primary Care Trusts and other public bodies, including regulatory bodies.

Our teams' experience working with a wide spectrum of universities is one of the areas where the merger has had an impact in bringing strength and depth to our offering – particularly with regard to expertise in the latest practices and thinking around technology transfer.

There are also several niche areas where Blake Morgan can now supply expertise such as competition law and, with the presence of an ex in house lawyer from the Financial Conduct Authority, we can provide companies with the advice they need in navigating the minefield of regulation when, for example, exploring crowdfunding options.

Blake Morgan is in the unique position of being a new, top 50 law firm with deep-seated roots in the Oxford region thanks to the long histories of its legacy firms.

This is a fact recently recognised by the prestigious directory the Legal 500 which noted that "Blake Morgan now has the strongest presence in the Thames Valley", referring to the firm as "a unique new challenger in the market".

Nicola McConville, corporate finance partner at Blake Morgan with particular expertise in working with start-ups and spin-outs, said: "Blake Morgan is immensely proud to be able to build on the heritage of its respective legacy firms. In particular, the merger gives us the exciting opportunity to further strengthen our work with technology companies at all stages of their development. Key to that is our highly valued relationship with Isis Innovation as a driver of innovation globally."

For more information about the legal services Blake Morgan supplies to the technology sector, see the contact details below.

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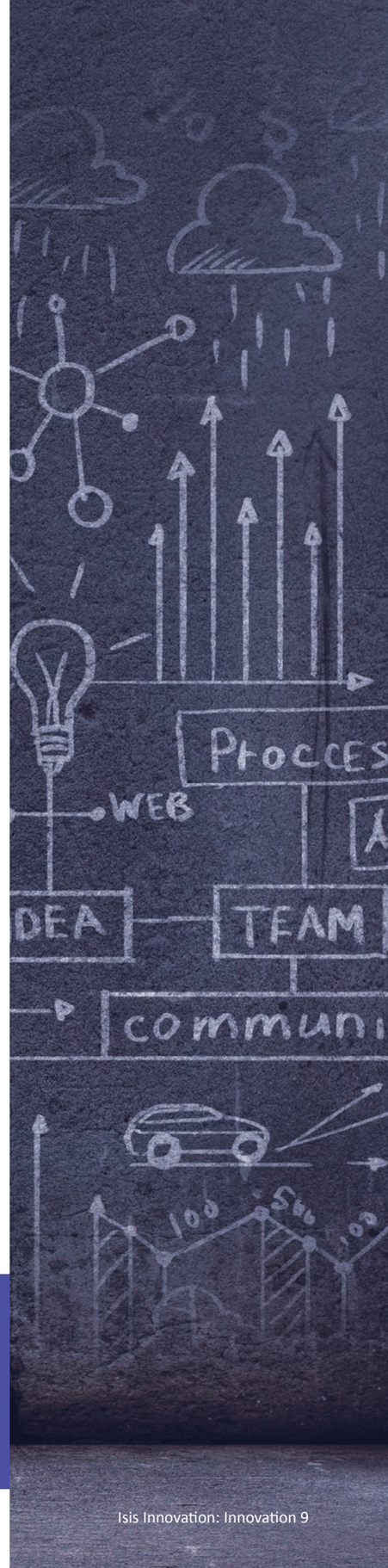


Isis Innovation: Innovation 10

Oxford Med-Tech, the Isis Innovation Technology Showcase 2014

Innovation with Impact – meet, see, learn, network, share ideas, try new things

Dr Fiona Story gives an overview of the second Isis Innovation Technology Showcase, a fantastic event where over 150 delegates heard about the best and brightest new medical technologies from Oxford and our partners

Med-tech is one of the biggest contributors to the vibrant Oxford bioscience community, which employs over 8,000 people. With the latest City Deal (expected to be worth over £1Bn when private funding is included), MedCity investment, and a double-digit growth rate, Oxford's bioscience cluster is a key part of the technology economy in the south-east region.

The University of Oxford and its spin-outs have contributed enormously to the cluster over the last two decades, with successes such as Oxford Nanopore, Oxford Immunotec, and Immunocore poised to become household names.

The Isis Med-tech showcase, held in September, was an opportunity for participants to get a glimpse of the newest technologies coming through the Oxford pipeline.

Professor Ian Walmsley FRS, Pro-Vice-Chancellor for Research, and Dr Penny Wilson from Innovate UK opened the event. Dr Wilson highlighted the support that Innovate UK gives to biotech, pharma and med-tech innovations. These investments are crucial for emerging new companies and technologies making the leap to the next phase of development.

Professor Alison Noble gave a guided tour through the hugely successful partnership between Oxford's Institute of Biomedical Engineering and Technikos, and the ten spin-outs formed under this alliance.

Delegates then heard about software projects with the potential to transform drug discovery and healthcare. Professor Blanca Rodriguez explained how VirtualAssay could help speed up drug safety testing with in silico modelling software. VirtualAssay has already been licensed to several leading pharmaceutical companies, and is featured on pages 12 & 13. Professor Steve Smith, from the Oxford Centre for the Functional Magnetic Resonance Imaging of the Brain (FMRIB), talked about the FMRIB Software Library (FSL), which has become the recognised standard in complex brain imaging data analysis. The latest version is used in around 1000 hospitals and university research labs.

Professor Mike English introduced a new way for healthcare professionals to learn emergency care through interactive gaming. Based in Kenya, Professor English has developed the first version of this platform for use in newborn resuscitation and emergency paediatric care in the developing world. This new way to learn is adaptable to many different subjects and different healthcare situations.

The Oxford e-Health Lab, which being established to provide a coordinating hub for e-health activity in Oxford, was presented by Dr Fred Kemp. The Lab will bring together Oxford academics, clinicians and private and public organisations across the region to accelerate innovations and aid their successful implementation.

Andy Self from Oxford spin-out OrganOx gave an update on the spectacular progress of the company and its liver preservation device, the OrganOx metra. Using this technology it is hoped that many more livers in better condition will be made available for transplantation. OrganOx are planning a European product launch during 2014.

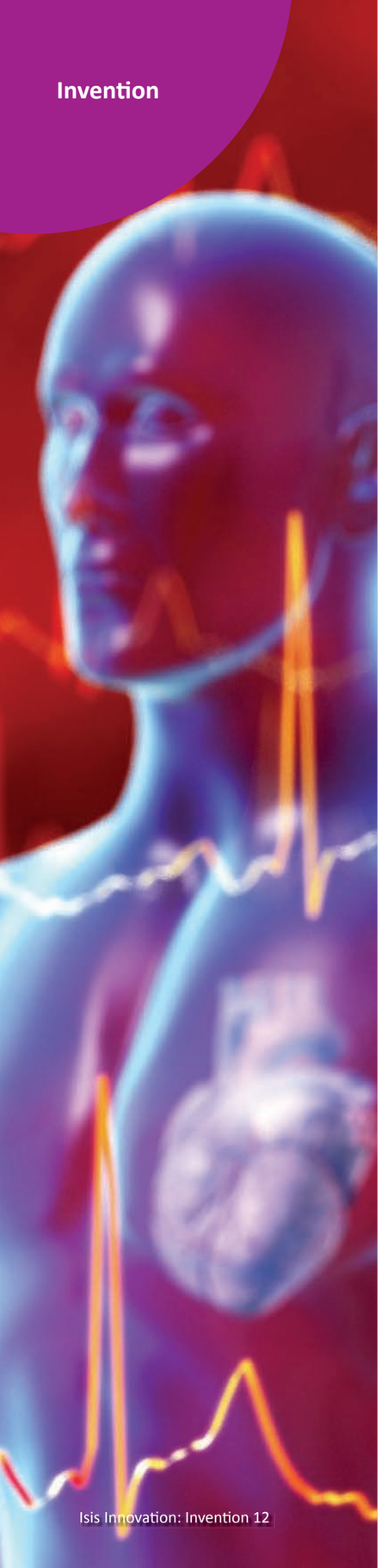
Concluding keynote speaker, Rosa Wilkinson from the UK Intellectual Property Office, spoke passionately about the process of commercialisation. She was emphatic about the importance of people who can communicate technical ideas and connect the right individuals to launch a project towards the right market, in the right way at the right time.

Many other Oxford technologies were on show at the Showcase Exhibition, including Isis Software Incubator startup Bounts, and True Colours, a platform for managing mental health conditions using text messages. The event ended with a canapés and drinks reception providing more of that all-important time and space to meet and share ideas.

To add your name to the mailing list for the 2015 Technology Showcase, please contact:

marketing@isis.ox.ac.uk

Isis Innovation: Innovation



Virtual Assay – easy to use drug screening software becomes a reality

Safer and more effective drugs, and reduced dependence on animal testing, are amongst the benefits of drug screening software, described by **Dr Fred Kemp**

Earlier this year, the US Food and Drug Administration (FDA) proposed a new regulatory paradigm that could revolutionise the drug testing process. For the first time they are proposing to specifically require computer modelling of cardiac electrophysiology to be carried out, alongside existing in vitro methods for pre-clinical screening. The announcement has highlighted the importance of an Isis drug screening software technology, Virtual Assay.

Modelling the heart

The FDA proposal has generated great interest in "in silico" modelling from both the academic community and the pharmaceutical industry bringing both together to define these new methodologies. A recent successful "Computational Technologies in Biomedicine and Pharmacology" workshop, held at Oxford University included more than 10 global pharmaceutical and CRO companies, alongside leading researchers from more than a dozen international universities. The event was organised by Professor Blanca Rodriguez, Professor of Computational Medicine and lead inventor for Virtual Assay. Prof Rodriguez leads a team with a diverse and interdisciplinary background to create computer modelling methods that look at healthy and diseased states in the human heart.

"It is exciting to feel that you are exploring a genuine frontier," said DPhil. Student, Oliver Britton, in a recent interview in the Guardian.

"No two individuals respond to a drug in exactly the same way. Due to sometimes subtle variability at a physiological level, what works for one person may not work for another, even before taking into account any additional complicating factors. This is one of the most significant challenges faced by the pharmaceutical industry; clearly it is neither practical nor desirable to test a new drug on the entire population to ensure it is both safe and effective."

Matching models to empirical data

"So we came up with this idea of using a population of varied models," says Britton, one the 2014 UK ICT Pioneers finalists. "This was the key step, as we can achieve more accurate results by first generating lots of different models of a human heart cell, then simulating how they would behave in control conditions and then discarding those that don't fit the range of experimental data we have available."

An additional benefit is the potential reduction in animal testing. Animal testing dates back to the 4th century BCE, and it has been a regulatory requirement for approval of new drugs since the 1938 Federal Food, Drug, and Cosmetic Act was introduced in response to the Elixir Sulfanilamide incident, where over 100 people died. From a safety and efficacy perspective, animal testing remains an inconsistent measure of how humans might react to the drug. Similarly, in vitro testing on human cell lines doesn't take into account potential systemic effects.

Computer modelling of physiological responses, has promised to revolutionise drug testing since the first mathematical model for transmission of nerve signals was published in 1952, but until now the regulatory agencies have been reluctant to make them a required part of testing procedures.

Avoiding unanticipated effects

With over half of the 40 drugs withdrawn from the market in the last 20 years being withdrawn for unanticipated cardiac effects such as drug-induced arrhythmia, or long QT, the FDA has understandably focussed on cardiac cell modelling. Virtual Assay was first developed for that purpose.

Virtual Assay would be applicable to a number of other cell, types, tissues and disease pathologies such as nerve cells, kidneys, liver, chronic pain and diabetes, etc. An easy to use, extensible version, developed over the past nine months with Oxford Computer Consultants, has been well received, and attracting the attention of the FDA. With FDA approval, it could usher in an era of safer and more effective drugs.

The development for Virtual Assay has been supported by the EPSRC Impact Acceleration Account awarded to the University of Oxford.

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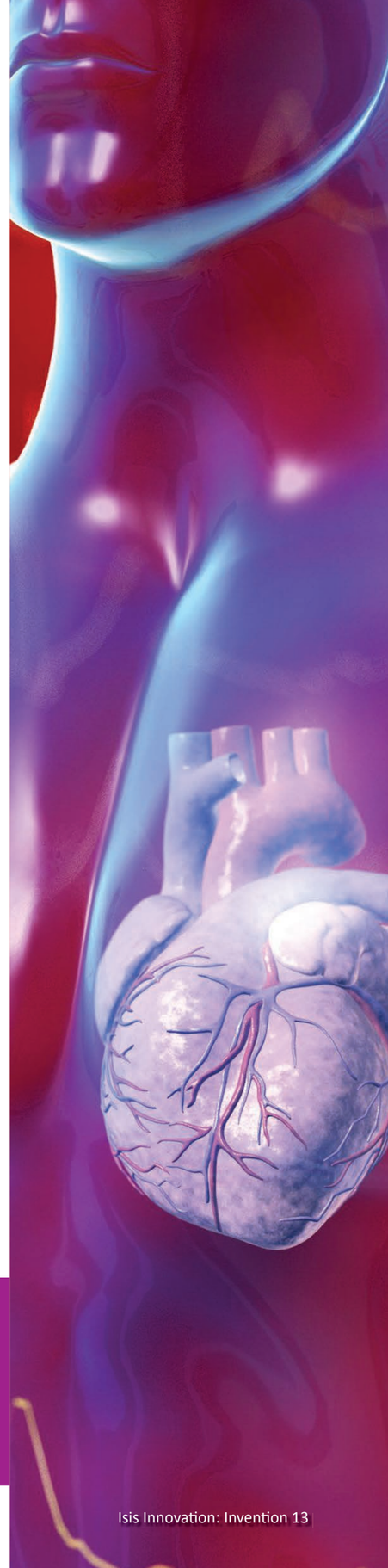


Molecules with a twist

Dr Andrew Bowen outlines a new method from researchers in Oxford's Department of Chemistry for synthesising chiral molecules

Researchers at Oxford University have developed an entirely new method to create left and right-handed "chiral" molecules used widely in the chemical and pharmaceutical industries.

The importance of chirality

Chiral molecules were discovered in 1848 by Louis Pasteur. He observed that crystals that formed on wine casks during fermentation contained equal amounts of left-handed and right-handed crystals of sodium ammonium tartrate. By painstakingly separating the two forms using a pair of tweezers he showed that they had different properties when he shone polarised light through them. One of them bent the light clockwise while the other bent it anti-clockwise.

Chiral molecules in nature and industry

More recently the role of chirality in pharmacology has been extensively investigated. It is now increasingly recognised that single-enantiomer drugs are more effective and have fewer side-effects than a racemic mix, to the extent that most regulatory bodies require that new drugs are single enantiomers. Flavour, fragrance and agrochemical industries are also taking advantage of chiral chemistry to improve the safety and efficacy of their products.

The current market

The market for chiral technologies is predicted to grow to $5.83 billion by 2017 (Transparency Market Research, 2014), with chiral synthesis making up the bulk of this figure. Despite the commercial interest, current methods of creating chiral carbon centres are largely limited to asymmetric hydrogenations, and organo- or palladium-catalysed reactions with soft nucleophiles. There is a real need to improve on these methods, which often require highly reactive organometallic nucleophiles and cryogenic temperatures, to increase the efficiency of chiral chemistry and the range of chiral centres that can be produced.

A new spin

The Oxford approach to carrying out asymmetric carbon-carbon bond formation to create chiral molecules improves on current methods by using readily-available alkenes as starting materials (nucleophiles) and:

- enables the use of hard nucleophiles in Tsuji - Trost alkylation
- allows the use of racemic starting materials in dynamic kinetic asymmetric transformations (DYKAT)
- is compatible with a wide range of solvents
- works at room temperature under mild reaction conditions
- enables completely new chemical transformations
- is compatible with a wide variety of functional groups

The method uses readily available copper catalysts and phosphoramidite ligands. A variety of new chiral phosphoramidite ligands have been developed in order to optimise specific processes and these show complementary and/or superior selectivity to widely used phosphoramidite ligands.

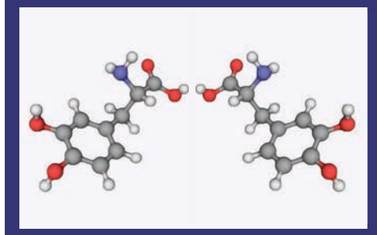
Ready to go

The technology has already been demonstrated on a variety of commercially applicable transformations and reactions have already been scaled up to over 5 gram scales with high levels of enantioselectivity (over 90% ee). Work is in progress that shows the method to be applicable to current drug intermediates, such as taxadiene (a precursor of taxol), and current drugs, such as latanoprost.

With an impressive and constantly growing evidence base, Isis Innovation is actively looking for partners interested in developing the technology to improve the efficiency and range of their chiral synthesis techniques.

Chiral Molecules

A molecule is chiral if it cannot be superimposed onto its mirror-image. Conversely an achiral system, such as a sphere, cannot be distinguished from its mirror image. The photo (below) shows the two different forms (enantiomers) of the DOPA molecule, which have very different activities. L-DOPA (levodopa) is one of the main drugs used to treat the symptoms of Parkinson's disease. The other form, D-DOPA, is biologically inactive.



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Bringing biodiversity to order

A data management system from Oxford's Department Of Plant Sciences is described by **Dr Brijesh Roy**

The Botanical Research and Herbarium Management System (BRAHMS) is widely used by herbaria, botanic gardens, seed banks and research botanists across the globe to assemble, edit, analyse and publish their botanical data. The software is intended to be simple enough for small research projects to use without the need for IT support, while providing the sophistication and powerful functionality required by the largest herbaria, botanic gardens and 'industrial scale' botanical surveys and biodiversity analyses.

Evolved data management

Botanists charged with capturing and storing specimen and biodiversity data are faced with a daunting task. Whether running an arboretum in Oxford, conducting field research in Antarctica or analysing diversity in the Amazonian region of Brazil, the scale and variety of data to be managed requires a system that is intuitive and flexible.

The idea for BRAHMS emerged in 1985, when researchers from the Department of Plant Sciences at the University of Oxford recognised the need to establish an effective data management system for the botanical sciences. Over the following three decades, the BRAHMS team worked to continually upgrade and improve the software, incorporating input from around the globe to develop, what is today, one of the most widely used botanical data management systems in the world.

Soon to launch its 8th iteration, BRAHMS has evolved to become an accessible and user-friendly software platform with the power to handle millions of specimens, the flexibility to store multiple media formats and the ability to empower curators and researchers to make the most of their own, and the world's, botanical data.

Globally accessible information

As well as providing comprehensive desktop data management services, BRAHMS WebConnect provides the tools to design websites and to upload selected data and images to any server where 'BRAHMS online' has been installed. This data can be searched, processed, analysed, mapped and visualised from any location in the world, while encouraging the sharing of information.

There is a regular stream of new institutions making the decision to switch their data management over to BRAHMS. The Morton Arboretum in the US, Bologna Botanical Garden in Italy and the South African National Biodiversity Institute are some of the most recent places to make the switch. You can see some of the most recent publications made using BRAHMS on the website, including "The taxonomic revision of the papaya family", "An atlas of the world's conifers", and "A checklist of Tasmanian higher plants."

Benefitting from BRAHMS

BRAHMS is proprietary software, and will be of interest to anyone engaged in managing botanical information and data, including research botanists, conservationists, herbarium and botanic garden curators.

For further information about BRAHMS, please visit the website (http://herbaria.plants.ox.ac.uk/bol/)

Highly evolved:
Three decades of constant development based on user feedback

Globally adopted:
Users registered in 60 countries across the world

Trusted:
Used by many of the world's most established herbaria and conservation projects

User friendly:
Enables desktop and online database creation without prior database experience

For institutional licensing enquiries please contact:

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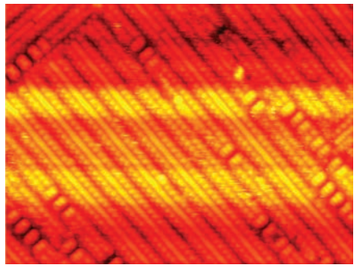
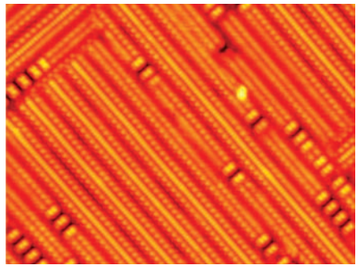
“Smart Align”– higher precision atomic resolution image analysis

Dr Manjari Chandran-Ramesh and **Dr Laura Droessler** present a quick and robust image registration software for scanned microscope images, precisely compensating image offsets and scanning distortions



Before: Typical single STM scan of $SrTiO_3$ (001) trilines with poor signal-noise ratio, scan-distortions and tip-height jumps (field of view = 40x40 nm).



After: Smart Align restored average frame, compensated for scan problems and tip-height errors. The periodicity along the ridge of the triline (≈2 Å spacing) is directly interpretable after restoration. Raw data courtesy: Matthew Marshall.

Photographing atoms requires microscopes of extraordinary power, precision and stability. When using magnifications to visualise on the atomic scale, the slightest disturbance can have a drastic impact on image quality. As microscope image data often forms the starting point for scientific investigations, resolving these data at the highest possible quality is of paramount importance.

‘Smart Align’ software delivers superior image performance, compensating for several of the most common imaging distortions and aiding quantification of both scanned-electron and scanned-probe microscope data. The software requires very little human intervention, using a weighted learning mode to guide the image offset correction. Built-in knowledge describing the scanning nature of the microscope’s serial acquisition further reduces the risk of artefact introduction. A mature demo version is available for assessment.

Automated registration

Both the scanning transmission electron microscopes (STEM) and scanning probe microscopes (SPM) acquire their images by rastering pixel by pixel over the sample. In modern labs these instruments routinely inspect materials at the atomic scale. This serial recording of data, however, can lead to acquisition times of minutes. At these acquisition times, stage and sample drift and low frequency distortions can perturb the image locally so that the stability of the sample stage, the microscope and even the room itself become a concern. In the STEM, there are several applications where recording a series of sequential images can be valuable including improving signal-noise ratios, optical-sectioning experiments or aberration studies, and to study dynamic processes like sample-damage. In the SPM, recording successive frames allows atomic-scale video of surface reactions to be observed.

Often the first step in any quantitative interpretation of microscope data is to correct for sample drifts and imaging distortions using so-called rigid and non-rigid registration respectively. The Oxford invention has improved tools that perform these registration steps automatically, customised for the challenges unique to STEM data.

Demonstration available

The improvements developed address the challenges of registering images which contain a large proportion of crystalline material with local features of interest such as crystallographic dislocations or edges. ‘Smart Align’ uses a new learning mode for rigid registration of images that are dominated by periodic (crystallographic) features and a ‘row-locking’ mode for artefact free non-rigid registration of serially acquired data. It includes novel options designed with electron microscopy image processing in mind but also options to correct tip-height errors in scanned probe data. The software has been rigorously tested and developed to a mature demonstration version.

While it is clearly not possible to improve resolution and signal-to-noise ratio beyond the performance of the microscope, Smart Align optimises the instrument’s performance, reducing corruption by scan-distortion and drift. The new algorithm facilitates higher precision automated analysis of atomic resolution STEM and SPM data.

Superior results

The Oxford invention enables processing and enhancement of microscopy images, delivering superior results and quantification compared with current methods. Through built-in knowledge and weighted learning filters this is achieved with very little human input. The technology has been specifically developed for the analysis of dark-field scanning transmission electron microscopy images, but can be used with bright-field data, conventional TEM, scanning tunnelling or atomic-force microscopes and in other image analysis applications.

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Where on earth...?

A revolutionary approach to GPS-free navigation that works reliably regardless of network connections is described by **Dr Fred Kemp**

There is increasing demand for smartphone applications and services that are location aware. Whilst many phones are GPS-capable, satellite reception is notoriously inconsistent in urban environments and frequently non-existent inside buildings.

To combat this, many phones and fitness trackers contain a range of other sensors, such as a compass, accelerometer and gyroscope, and use these, often in combination with WiFi-based systems, to provide position estimates. However, such "dead-reckoning" systems are particularly error-prone, and are thus ineffective without constraining the user's track within the context of an indoor map.

This leads to another problem. While indoor maps are becoming increasingly available, until now there has not been a practical and reliable indoor "map-matching" solution, which is also capable of running directly on a mobile device.

New standalone approach

To overcome this, the Sensor Networks Group in the University of Oxford's Department of Computer Science, have taken a revolutionary new approach to indoor positioning that is robust, reliable and requires no user input or infrastructure (such as WiFi or Bluetooth beacons).

Using pattern recognition and machine learning techniques which have been successful in the field of natural language processing, but have previously not been applied to GPS-free positioning, researchers from the Sensor Networks Group have created a flexible and lightweight method to combine data from mobile phone sensors with a digital map. The map then acts as a "sanity filter", thus avoiding "impossible" situations such as a user appearing to walk through a wall.

Dynamic map updating

MapCraft is a smartphone app combining this map-matching technique with a number of unique refinements to the sensor-based dead-reckoning process and, importantly, the ability for the system to learn. Not only, does MapCraft learn about the user (e.g. typical step length, gait, how they tend to carry the phone, etc), but also about the environments in which the user is navigating. Information about corrections derived from one user can be fed back into the metadata associated with the map, and thus improve navigational accuracy not just for the returning user, but also for new visitors, who would automatically benefit from this crowd-sourced data when they download a map.

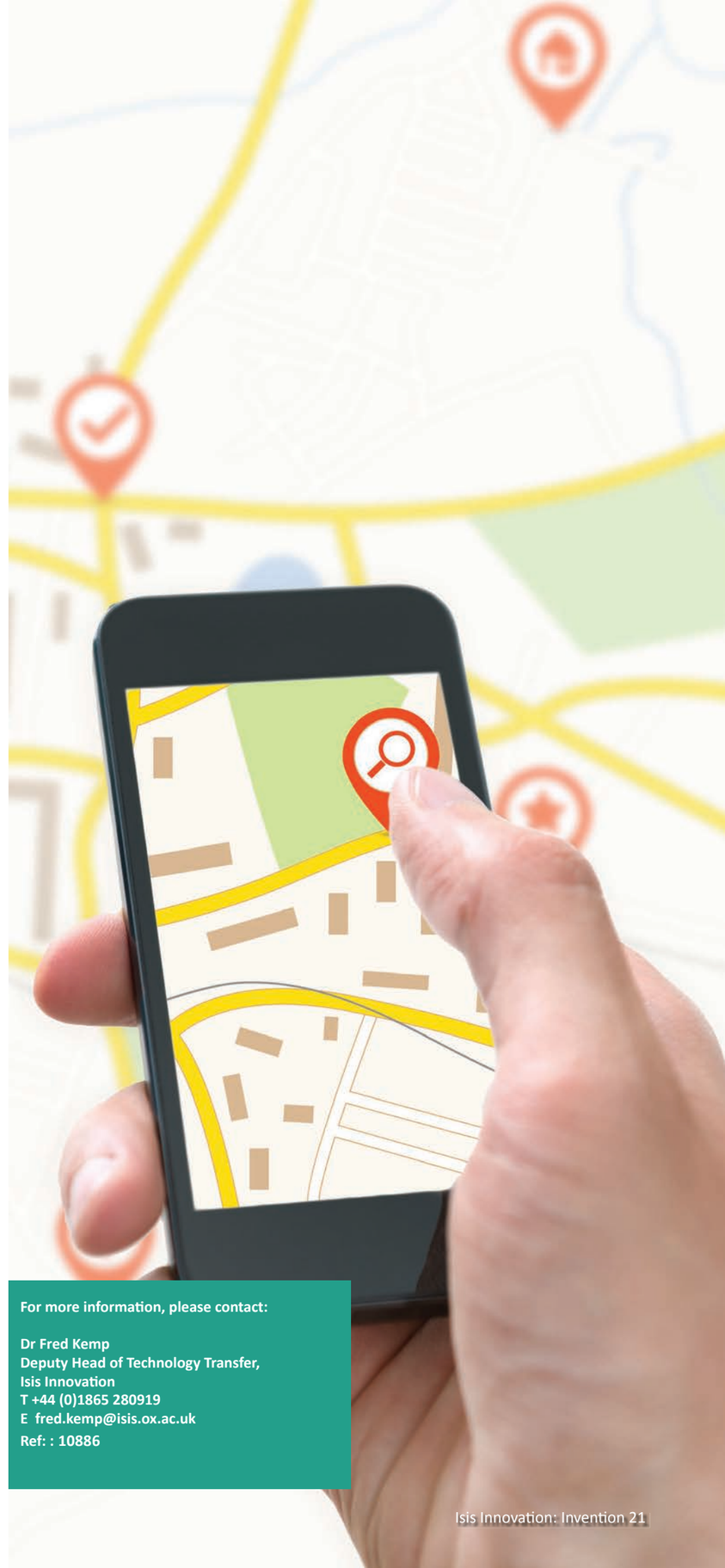
"Indoor localization through consumer mobile devices will revolutionize how people interact with their physical environments and with each other. Among more than a decade of research efforts in indoor localization, MapCraft is one of the most elegant solutions, especially for its low sensing and computation cost and high robustness. It has clear value proposition and the potential to be widely adopted."
Jie Liu,
Principal Research Manager, Microsoft.

Outstanding test results

The system has already been tested in a number of environments and outperforms all competing solutions, working reliably across different users, motion modes and devices. Consequently the system has received a lot of positive interest, winning awards at a number of conferences and attracting praise from industry leaders.

MapCraft could have significant impact throughout our daily lives. Imagine visiting a museum or exhibition centre, and being able to use your smartphone for turn-by-turn navigation; to receive notifications of other exhibits to see, based on where you have been so far; or in the shopping centre, to quickly locate the item you viewed online earlier (along with price matching of course!); or in a crowded bar, to order a drink without leaving your seat, and for the waiter to know exactly where to bring your order; or to know, as you enter the building, where exactly 'ward 37f' is, when visiting friends and family in hospital.

We might still take the same (small) steps through our urban spaces, but with Mapcraft's giant leap in GPS-free navigation, the journey can be easier and perhaps a little more interesting.



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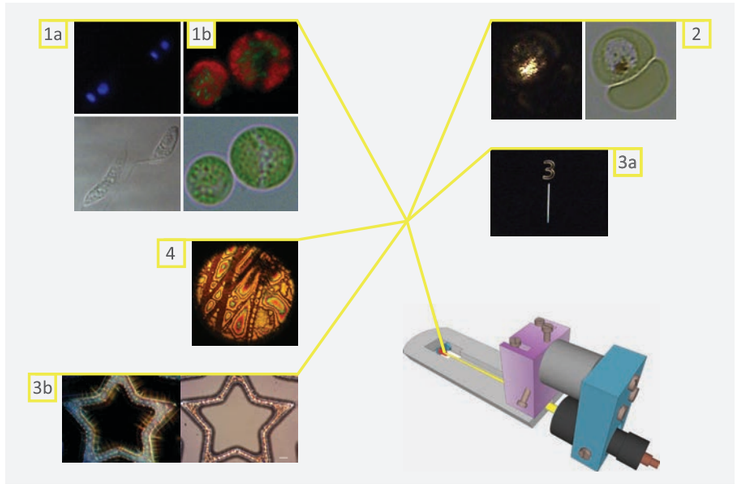
Transforming microscopes

Oxford researchers have invented a set of miniature modules that expand the capabilities of traditional bright-field optical microscopes at low cost. **Dr Weng Sie Wong** explains



Clever conversions

Oxford researchers in the Department of Physics have developed prototype miniature devices for bright-field light microscopes that fit into the slot reserved for DIC objective prisms – known as DIC slots. The Oxford devices can very simply and inexpensively transform standard light microscopes into instruments capable of far more complex microscopy including:

- epi-fluorescence
- backscattering dark field
- surface reflection
- interference reflection

Only one modular device is needed to add all these features to a standard microscope. It is also possible to develop individual devices for each technique.

Epi-fluorescence

Epi-fluorescence is a well-established and widely used technique, which has numerous life science and medical applications. It requires relatively expensive equipment including a special light source, an epi-illuminator and a set of filters.

Using the Oxford epi-fluorescence module, researchers can easily detect fluorescent objects using a filter-free setup or just a single emission filter. Samples that can be visualised include naturally fluorescent and fluorophore-labelled micro-organisms.

Backscattering dark field microscopy

Backscattering dark field microscopy is useful for detection of nanometre-sized objects below the diffraction limit, and is highly sought after in the nanotechnology sector. To date, research and development in this field has been limited as backscattering microscopes are not commercially available, and researchers tend to build them in-house. The instruments are bulky and expensive as a result.

Using the Oxford dark-field module, researchers are able to clearly view small objects of sub-micrometre size. Applications include stain-free detection of malaria-infected human red blood cells, which contain strongly scattering haem crystals, and observation of 50-100nm gold particles.

Surface reflection microscopy

Surface reflection microscopes are widely used in material science and the semiconductor industry to study surface features of specimens. They require special configuration of illuminating paths and cannot work without expensive purpose-made objectives. Used in surface-reflection mode, the Oxford device allows the result of photolithography or other surface modifying methods to be directly visualised.

Interference reflection microscopy

Interference reflection microscopy is used to monitor the thickness and quality of thin films. These microscopes usually require additional optical elements such as polarising prisms and special objectives. With the Oxford device, researchers can successfully monitor lipid bilayer formation and estimate how evenly a thin layer of material has been deposited on a surface of interest.

Isis Innovation has filed a patent on the technology and welcomes discussions with microscopy manufacturers interested in licensing it for commercial development.

Figure legend

Images obtained using the Oxford device:

Epi-fluorescent technique

1a - an image of Leishmania parasite labeled with DNA-staining blue fluorophore DAPI as seen with the Oxford device without any filters (top) and the same cells seen with a regular bright field microscope (bottom).

1b - red chlorophyll fluorescence of a photosynthetic green alga (top) detected with a single emission filter, and bright field image of the same sample (bottom).

Back Scattering Dark Field technique

2 - a bright-field image of a healthy and a malaria organism-infected human erythrocyte as seen with a regular light microscope (right) and a Back Scattering Dark Field image of the same cells with the Oxford device (left).

Surface Reflection technique of various surfaces

3a - a calibration scale on the surface of a special non-transparent graticule. Bright-field microscopy of such surfaces is otherwise impossible.

3b - a photo-lithography patterned surface of a transparent cover slip as seen with a bright-field microscope (right) and with the Oxford device (left).

Interference Reflection technique

4 - uneven varying thickness of a marker-drawn stripe on a glass surface seen as typical interference iridescent patches.

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Biobanking for spinal tumours

Dr Josef Walker explains how Oxford University Consulting supported AOSpine to engage expert advice and support from the University

"It is only through rigorous investigation and multi-centre collaborative efforts that we will be able to successfully develop new diagnostic, prognostic, and therapeutic methods for these patients. This model is allowing us to maximize our knowledge and is setting the stage to move prospectively, incorporating biobanking as a component"

Dr. Charles Fisher, Orthopaedic Spine Surgeon at the University of British Columbia, Vancouver, Canada and Chairman of the AOSpine Knowledge Forum Tumor Steering Committee.

AOSPINE

Biobanking of human tissue samples has been in the spotlight for a number of years and since the implementation of the Human Tissue Act of 2004, the activity has become highly regulated. Such regulation is vital for a number of reasons, not least to ensure human tissue donors are given the power of informed choice, and that their decision is respected.

Regulation is also required to ensure that the samples are used appropriately and ethically in high quality research. Such research is dependent on high-quality samples and this is only possible with a robust Quality Management System in place. Only by using quality-controlled Standard Operating Procedures (SOPs) can a consistent and standardised approach to the pre-analytical phase of human tissue research be ensured.

AOSpine is a professional medical association for the AO Foundation, a not for profit foundation based in Switzerland. An international community of spine surgeons generating, distributing, and exchanging knowledge, its mission is to advance science and the spine care profession through research, education, and community development to inspire lifelong learning and improve patients' lives.

The AOSpine Knowledge Forum Tumor, a clinical study group, has a keen interest in the management and prognosis of primary spinal column tumours, which are often aggressive and fatal and have various treatment approaches. Due to their rare occurrence and variable pathology, there is currently little evidence to guide their clinical management.

Spine tumour biobank

A key element of the Knowledge Forum Tumor is to develop an international spine tumour biobank to complement and enhance the 1,495 primary spinal column tumours and accompanying clinical data it has captured from a network of spine oncology centres for the purpose of research. This type of data collection will provide a valuable resource for clinicians to make important clinical observations and study the biological basis of primary spinal column tumours for which there are very little data currently available. The vision of the study is to create the largest multicenter, international collection of primary spinal column tumours in the world to improve research and overall management of spine neoplasms: the AOSpine Primary Spinal Tumor – Biobank Network (PST-BioNet).

The realisation of this vision requires specific expertise in biobanking, so AOSpine approached Ms. Karolina Kliskey, Manager of the Musculoskeletal BioBank in the Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences at the University of Oxford for help. Working through a consultancy arranged by Oxford University Consulting (OUC), Ms. Kliskey is advising AOSpine on the design and implementation of the biobank SOP's. According to Mrs. Niccole Germscheid, Research Project Manager at AOSpine:

"With her extensive experience and working knowledge, Karolina is providing invaluable advice, which we do not have internally, to develop the SOPs that are critical for the biobank to be successful at an international level. We very much enjoy working with Karolina and highly value her independent advice."

From Ms. Kliskey's perspective, working as a consultant on the project offers a number of interesting challenges.

"Not only are we implementing gold standard biobanking in each individual centre, but we are trying to achieve a high level of procedural consistency across all the centres involved in the project. This does pose some challenges as there are already a variety of established biobanking practices in place that need adjusting. This is where the importance of a robust system that can cope with site-to-site variation in procedure is of upmost importance, as these variables need to be recorded and considered in future research.

Implementing such a system has been made possible only by working with a highly proficient project manager at AOSpine who understands and effectively manages the needs of the different sites with both patience and diplomacy."

OUC works with individuals from across the University of Oxford to facilitate inter-disciplinarity through consultancy and enable its members to engage with external organisations and create broad impact beyond the boundaries of their current research.

Biobank

A biobank is a highly organised repository of physical biological material (usually human in origin) and associated information about the samples for the purposes of medical and scientific research.

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Aspects of Innovation

How Isis Enterprise is working with clients to build innovation capacity in the knowledge economy, by **Britta Wyatt** and **Dr Nathan Pike**

Innovation is commonly defined as the successful exploitation of new ideas. This simply refers to the process through which invention is guided toward commercialisation or other realisation in the real world.

When seeking to harness the innovation process, many institutions seek out Isis Enterprise in order to obtain advice and assistance with:

- creating and assisting with the implementation of intellectual property policies and procedures
- streamlining research services offices
- establishing and supporting technology transfer offices
- the provision of third-party advisory technology transfer support

To a large extent, these activities reflect a traditional approach to innovation – that is, one in which the focus remains on the production of intellectual property.

Expanding the scope

Recent years have seen a broadening in the perception of what activities should form part of a successful innovation process. This shift in what innovation means is reflected in the type of services Isis Enterprise now provides. In addition to the traditional models, clients are increasingly seeking higher-order services. These include:

- developing procedures and structures to facilitate Knowledge Transfer (including setting up Knowledge Transfer offices and partnerships)
- developing the human capital operating within the ecosystem by growing skills in entrepreneurship at all levels

Whereas traditional technology transfer focuses on producing and protecting goods, these higher-order services are often seen as 'innovation based predominantly on know-how' and are increasingly considered to be critical in rounding out an effective offering.

Case Study: a two-year programme for the University of Malta,funded by the European Social Fund.

- A Knowledge Transfer Office was established and a team including a Technology Transfer Manager, a Business Incubation Centre Manager, legal support staff, and administrative staff is now in place.
- Custom procedures, processes and template documents have been designed and implemented.
- University staff have received bespoke training that covered issues such as licencing, forming spin-outs and negotiating legal agreements.
- TAKEOFF, the University of Malta business incubator, was launched.
- An intensive training programme in Knowledge-Based Entrepreneurship (to Master's degree level) was developed and delivered.
- The relationship continues with support services relating to technology reviews and licencing assistance.

Case Study: Innovation strategy development for the University of Rijeka (Croatia), funded by the European Union Instrument for Pre-Accession Assistance.

- Isis Enterprise provided innovation strategy development and knowledge mapping for the University of Rijeka to capture and map the tacit and explicit knowledge within the university.
- Isis consultants worked with University staff to develop interview-based and questionnaire-based approaches, which were directed particularly at identifying the latent knowledge value in the humanities and social sciences faculties.
- Innovation strategies were developed and implemented. This work included interviews with the Senior Management of each University as well as presentations to all academic departments and faculties.

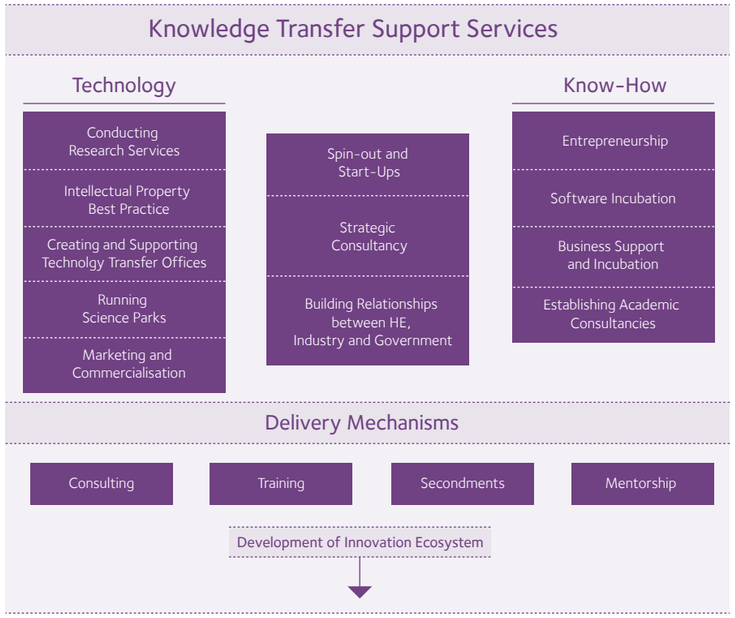

Figure 1: Some of the support services that Isis Enterprise offers across the innovation continuum from technology transfer through to supporting know-how and entrepreneurship.

Isis Enterprise assists clients to develop comprehensive innovation processes, all of which can be tailored to individual circumstances and requirements. These include:

Innovation Ecosystem Development

Develop and maintain effective innovation ecosystems both as standalone entities and within larger organisations. Collaboratively construct internal ecosystems that optimise innovation and collaboration, and provide ecosystem support, identify promising technologies and advising on the way forward.

Entrepreneurship Training

Develop practical skills and understanding of entrepreneurship for your students, academics and/or staff. Understand the institution's goals, and then provide training on entrepreneurship to achieve those goals through short intensive instruction (1-2 days), and longer training courses over a period of months.

Intrapreneurship, Mentoring & Collaboration

Identify opportunities within your organisation to advance via new innovations and to help develop a culture that nurtures entrepreneurship. Provide assistance establishing processes to improve internal innovation, and/or evaluation, advisory services on how to make your organisations products more viable and valuable, and utilising Isis Enterprise's expertise in identifying and evaluating opportunities for innovation.

Knowledge Transfer Support

Ensure the consulting services of experts within your institution are leveraged accurately and advantageously. This could involve setting up KT offices, working as a partner to deliver KT services, or assistance in setting up consulting units within an institution, and may involve provision of initial training with subsequent handover to a client's own staff.

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Oxford Innovation Society

Forthcoming meetings of the Oxford Innovation Society will be held on the following dates:

- Thursday 19th March 2015
- Thursday 15th September 2015
- Thursday 3rd December 2015

Meetings are held in Oxford for OIS members and invited guests, and are followed by a formal reception and dinner. Details on www.isis-innovation.com/ois.

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