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

Issue 65 Autumn 11

Isis insights

The latest innovations, collaborations and technology transfer

Engineering advances

The physical possibilities...

ISIS INNOVATION

Ii Contents

Issue 65

Engineering advances

The physical possibilities...

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www.isis-innovation.com

Cover image: Laser printing (p12)

Newsflash

Isis Innovation Ltd is a growing and profitable business owned by the University of Oxford.

Isis income up 12.5% to £8.4m

The Isis 2011 Annual Report was published this September. The Report describes our activities transferring technologies and expertise from universities to the wider community to benefit society and create opportunities for sustainable economic growth. The year to March 2011 shows our income up 12.5% to over £8.4m, reflecting a very successful year in challenging circumstances. We are working with more academics and researchers, in Oxford and around the world, protecting more IP, signing more IP deals, setting up new companies and helping universities and business to work more closely together around the world. Please contact Isis if you would like a copy: innovation@isis.ox.ac.uk

Technology Transfer for Oxford – Proof-of-Concept Funds

Proof-of-Concept funds enable early stage research outputs to be converted into recognisable business development and investment opportunities for industry, leading to new products and services. The Oxford Invention Fund is managed by Isis and bridges the innovation gap, supporting University of Oxford inventors in proof of concept and prototyping work. In June the OIF reached its first close of £500,000 and made its first investment in a new class of antibiotics discovered in a natural product library at the University of Oxford's Department of Chemistry. The OIF is also being enhanced by a further £500,000 contribution from the University's Higher Education Innovation Fund (HEIF) allocation from central government over two years. All University researchers are encouraged to apply for support from the OIF for commercialisation projects.

Oxford University Consulting – No More Needles

Lein Applied Diagnostics, a medical technology company based in Reading, is using its proprietary confocal optical technologies to develop a non-invasive monitoring system that diabetics can use to take a snap-shot of their blood glucose levels. OUC worked closely with Lein and Oxford researchers to put in place a consulting agreement to explore how neural networks and machine learning could be applied to some of Lein's complex datasets in order to understand and elucidate the relationship between the data collected from the patient's eye and their blood glucose level. OUC has facilitated interactions through consultancy agreements for a number of companies seeking to gain an edge in the development of new medical technologies, including stents, MRI and vaccine delivery, exemplifying the range and depth of expertise at the University of Oxford. (For full story see p24.)

Isis Enterprise in China

We held the first meeting and dinner of the Oxford Innovation Society outside of the UK in Hong Kong in July. The event attracted sixty leading names from the fields of technology, innovation and finance to hear presentations from two Oxford academic researchers, Professor Zhanfeng Cui and Dr Tiancun Xiao, followed by dinner. Regional representatives from global organisations such as China Wireless, Panasonic and the Korean Intellectual Property Office were amongst those who attended. Senior figures from InvestHK and UK Trade & Investment, a department of the UK Government, were also present. In Hong Kong we are connecting world-class research from Oxford and its global partners with business, government and industry worldwide, and creating business opportunities between technology providers and technology seekers.

The latest insights from **Oxford University Consulting** and **Isis Enterprise**

The Loop

Beyond Consulting – Commercial Service Contracts

Oxford University Consulting (OUC) has built its reputation on organising successful academic consultancy projects for its clients, drawing upon the full depth and breadth of expertise found in the University of Oxford.

Last year, around a quarter of OUC's business came from clients wishing to access not only consultancy expertise but also equipment or facilities based in University departments.

The University boasts an outstanding array of technical facilities across its departments and although such facilities primarily support research and teaching activities, external organisations can make also use of them through departmental service agreements managed by OUC.

One recent example of a service contract managed by OUC was for a global pharmaceutical company who needed access to the University's biophysical instrument facility. This provided them with equipment and expertise not possessed internally, all in a highly cost-effective and flexible manner.

The Central Proteomics Facility (CPF) at the Sir William Dunn School for Pathology is another University resource used by clients in the biotech/pharma sector. The CPF provides a comprehensive advanced mass spectrometry and proteomics service, enabling sophisticated protein identification and quantitation.

Examples of recent projects include: characterisation of therapeutic antibody targets; characterisation of the effects of small molecule inhibitors on protein expression and phosphorylation dynamics; identification of protein binding partners and the identification of macrophage cell-surface markers.

Last year, around a quarter of OUC's business came from clients wishing to access not only consultancy expertise but also equipment or facilities based in University departments.

Whatever a client's requirements, OUC seeks not only to identify the right facility and equipment, but also the appropriate academic experts, technicians, and other services to provide an integrated solution.

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IE/Aston partnership aids glaucoma treatment development

Isis Enterprise (IE) has formed a short-term technology transfer partnership with Aston University to complement Aston's efforts towards Intellectual Property (IP) commercialisation. During this partnership, IE has recognised several promising technologies, one of which is a novel drug delivery system to treat glaucoma.

Glaucoma is an eye disorder in which changes of pressure in the eye's aqueous fluid, known as intraocular pressure, causes damage to the optic nerve. This damages vision and results in irreversible blindness. Intraocular pressure is a major risk factor for most glaucomas, and is the focus of attention during treatment.

The Aston innovation involves an ocular insert that is placed underneath the eyelids of a glaucoma patient overnight. The device releases two drugs of choice at pre-specified and varying rates. This novel controlled-release mechanism (protected by a granted European patent) stabilises ocular pressure throughout the night and especially in the early hours of the morning when sudden pressure 'spikes' are most likely to occur. Aston has attracted proof-of-concept funding to further develop the technology. The system is currently undergoing pre-clinical trials in preparation for commercialising the technology via a licence agreement. A US patent is pending.

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

The Portfolio

Prospective Oxford spin-out targets first-in-class allergy treatment

Oxford scientists are set to identify new, more effective drugs for clinical intervention in allergic disease. The new compounds will target the Calcium Release Activated Calcium (CRAC) channel for which there are currently no clinically effective inhibitors available. Abnormal CRAC channel activity has been linked to a growing number of diseases including allergy, autoimmunity and polyposis, Severe Combined Immunodeficiency disorders, inflammatory bowel disease and certain cancers.

The researchers from the Department of Physiology, Anatomy and Genetics, led by Professor Anant Parekh, were the first to identify the critical role that CRAC channels play in mast cell activation. Mast cells are key components of the innate immune system, where they help to orchestrate immune and inflammatory responses along with other cells types. Located at the environment-host interface, aberrant mast cell activation is linked to a variety of allergic diseases including rhinitis (hay fever), asthma, eczema and nasal polyposis.

Traditional therapies for allergic disease include anti-histamines, corticosteroid based drugs such as beclomethasone, and leukotriene receptor antagonists such as montelukast. However, current treatments – such as long-term use of steroids – can be linked to adverse side-effects, which may not be adequately outweighed by therapeutic benefit.

Investing in innovation

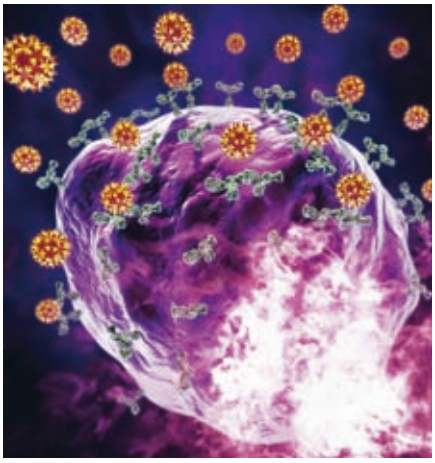
The market potential of a new therapeutic targeting CRAC channels is considerable. Estimates put the number of people being treated for allergic rhinitis in the United States alone at 8–20 million, and worldwide sales of therapeutic products have reached $6 billion per year. The number of asthma patients worldwide is expected to reach 400 – 450 million by 2025.

As a result, the global asthma market is predicted to reach the $20 billion mark by 2020. It will remain one of the fastest growing healthcare markets owing to the increasing number of patients. However, innovation in treatments for allergic disease is slow and there are very few new therapies in the development pipeline.

Future plans

Professor Parekh's vision is to identify a potent and selective CRAC channel inhibitor which could be used for clinical intervention in patients suffering from allergies and other immune disorders such as rheumatoid arthritis and multiple sclerosis. In order to identify these new compounds the research team intend to develop a high throughput assay for CRAC channel activity.

Potential hits will subsequently be validated using established electrophysiology methods. Despite the very early stage of development, this ambition has attracted the attention of local investors who share the belief that CRAC channel inhibitors hold the key to new therapies for allergy and other debilitating and life-threatening diseases. It is anticipated that a new company will be spun out from the University to begin the drug discovery process.



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Technology Steps Forward

DNA sequencing deal

Oxford Nanopore Technologies Ltd has signed two further worldwide exclusive licenses with Isis for intellectual property related to DNA sequencing through a protein nanopore, adding to a range of existing licenses in the field of nanopore sensing.

The first of the technologies licensed relates to modifying the protein pore to improve the accuracy of DNA base identification. The second revolves around modifying the protein to increase the efficiency of threading a DNA strand through the pore, allowing the DNA to be sequenced more quickly.

The capacity of scientific researchers to perform large studies on the links between genome and disease has increased in recent years in line with improvements in DNA sequencing technologies. There is a hunger for faster, cheaper DNA analysis techniques that Oxford Nanopore is addressing with its nanopore-based technology.

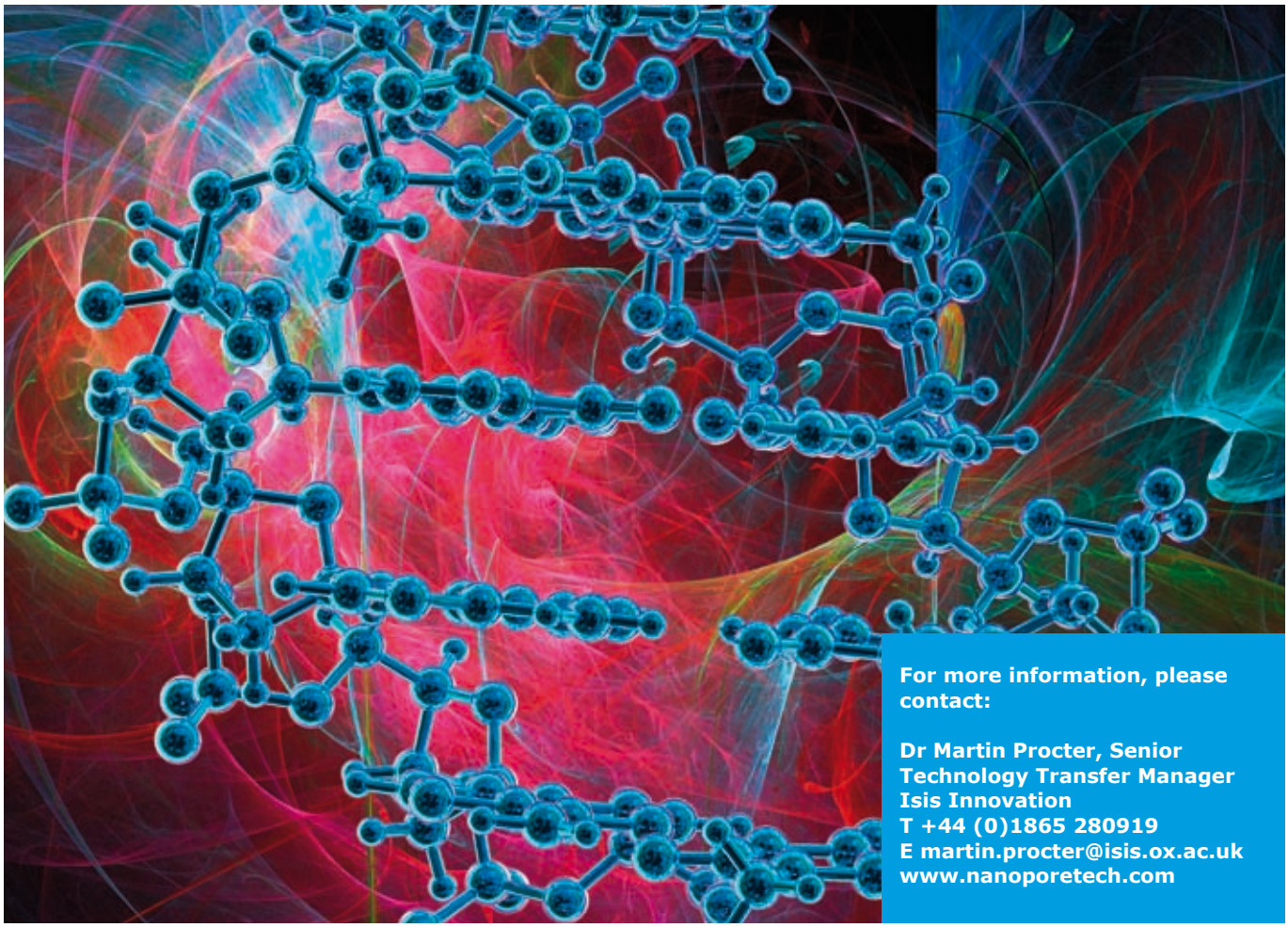
Against this backdrop, Oxford Nanopore Technologies Ltd is developing a new generation of DNA sequencing technology that is based on electronics combined with nanopores; small holes created by proteins that allow stochastic sensing of single molecules.

Nanopore sensing is a very sensitive and specific technique that measures single molecule binding events using an electrical signal. Different molecules that pass through the nanopore leave unique 'fingerprints' on a current. This removes the need for optical technologies and amplification of the original sample, paving the way for a new generation of faster and simpler technology.

Oxford Nanopore Technologies Ltd was spun-out of the University of Oxford in 2005 and is developing a novel technology for direct, electronic detection and analysis of single molecules using nanopores. Their lead application is DNA sequencing and they are also developing new techniques for the electronic analysis of proteins, with applications in biomarker development.

Weblink

www.nanoporetech.com



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Isis Outcomes and Symfo aid drug developers

Isis Outcomes and Symfo are offering a unique service that will help drug developers assess and choose the right patient reported outcome (PRO) measure and ensure that the study meets regulatory authority requirements.

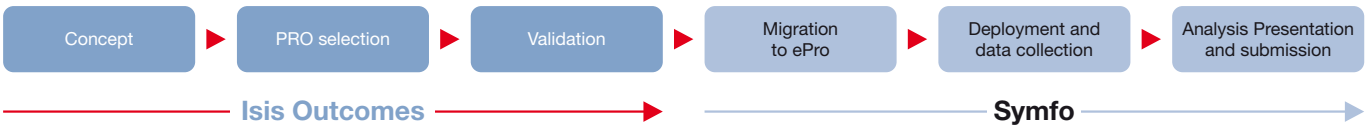
After a PRO has been designed, tested and validated it must be deployed correctly to collect the required information. Traditionally, PROs have been completed and collected on paper but there is a growing trend to use electronic systems (ePROs) to collect better and more reliable data.

Now, using ePRO technology, Symfo and Isis Outcomes deliver the whole PRO cycle.

PROs are increasingly used during the drug and medical device development process to prove effectiveness. Indeed, most Primary and Secondary endpoints in clinical trials use PRO instruments to measure efficacy.

Symfo, a privately owned, global electronic patient reported outcomes (ePRO) provider, specialise in creating patient-oriented, cost effective, robust and reliable ePRO and data collection solutions.

Isis Outcomes is an activity within Technology Transfer at Isis Innovation Ltd, dedicated to the provision and support of the highest quality PROs for healthcare providers and the pharmaceutical industry. It manages a large library of over 100 translated versions of the Oxford PROs, commissions user support materials, such as manuals, and arranges consultancy advice to customers from PRO experts in Oxford



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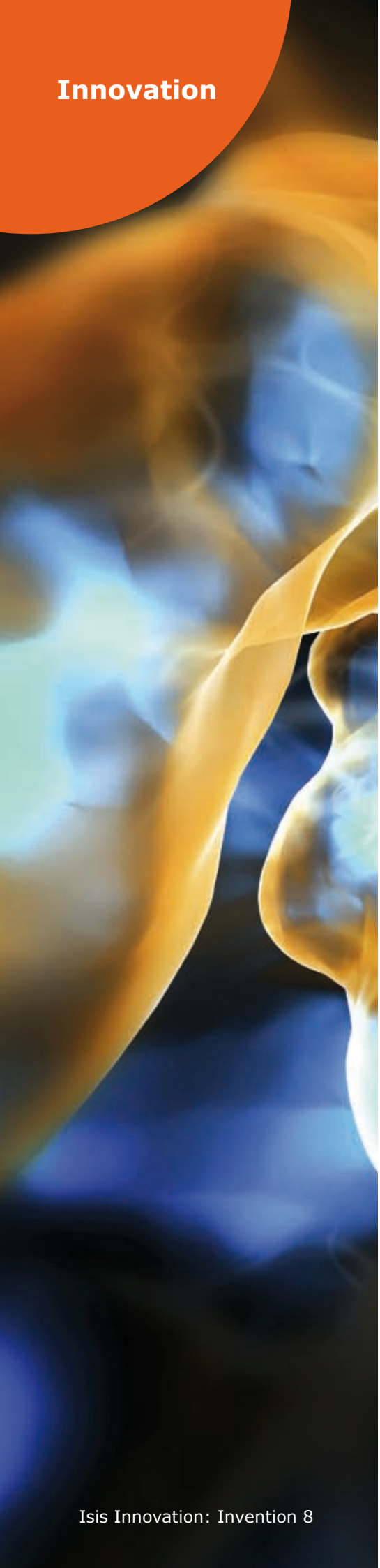

Biotech Transfer

The Oxford Biotechnology Roundtable's **Marvin Lee** – DPhil student in Biochemistry – introduces the new forum serving the campus community and beyond.

A knowledge-based economy led by the transfer of scientific and technological developments has been recognised as a major driver for long-term economic progress in many advanced economies. Great science and innovation have never been in short supply at Oxford, and with the recent inception of the Oxford Biotechnology Roundtable (OBR) a one-stop-shop for anyone at the University interested in the intersection between science and commerce has been established.

Asked about the objectives and vision behind this brainchild, Daniel Perez – founder of OBR and currently pursuing a doctorate on carbohydrate vaccine and antibody design in Dr Chris Scanlan's group at the Oxford Glycobiology Institute – described a "three-pronged approach" towards serving the campus community. Firstly, by promoting learning opportunities with a *Leaders of Biotech* seminar series, OBR aspires to foster an intimate and interactive environment between members and distinguished speakers. Secondly, an *Industry Immersion* programme will also provide Oxford students and postdoc members with real-world experience and relevant transferrable skills to pivot seamlessly between academia and management roles in biotech and pharma. The third prong comprises regularly updated interdisciplinary communications in the form of newsletters and blog posts, with discussions about biotech, pharma, entrepreneurship and Oxford innovations, as well as the stories and people behind those innovations.

Boasting, at the time of writing, a fast growing and diverse membership of over 350 students, postdocs, faculty and industry professionals, and a seemingly inexhaustible influx of applications from across disciplines after just four events, the inaugural launch event of OBR would not have been possible without the incredible work of the OBR team. The founding members consist of highly dynamic and creative students and postdocs from the life sciences, physical sciences, and business school.

Initially, this summer was meant to act as a pilot before Michaelmas term, to simply start a conversation and facilitate networking sessions between like-minded Oxonians and industry professionals. However, OBR has been overwhelmed with the positive response from students, faculty members and industry professionals.

Provocative questions were thrown at speakers during the first *Leaders in Biotech* seminar series, with a heavy emphasis on challenges facing start-ups, the transition between academia and bio-business, long-term career development and prospects for biotech entrepreneurs. James

The founding members consist of highly dynamic and creative students and postdocs from the life sciences, physical sciences, and business school.

Clough, vice president of clinical and genomic solutions, Oxford Gene Technology (OGT) Ltd – a successful 1995 spin-out from the University – took the opportunity to update the OBR on the history of OGT and their future directions. He highlighted the value in the University fostering relationships with local companies in order to take the lead in creating a biotechnology hub of global standing, where companies thrive and wealth is created for both the local and regional economy.

OBR is striving to create an interactive platform, bringing together scientific expertise, enterprising entities, key industrial players and highflying biotech-entrepreneurs. Simultaneously, it will play a pivotal role in serving the campus community as a learning resource, a provider of opportunities, and a conduit for members to enter the biotech and healthcare fields.

OBR has a lot more planned, including a packed schedule for Michaelmas term. If you are interested in learning more about OBR or the perks of sponsoring future events please get in touch with the OBR team.

Since this article was written, OBR has expanded its remit and can now be contacted through oxbridgebiotech.com.

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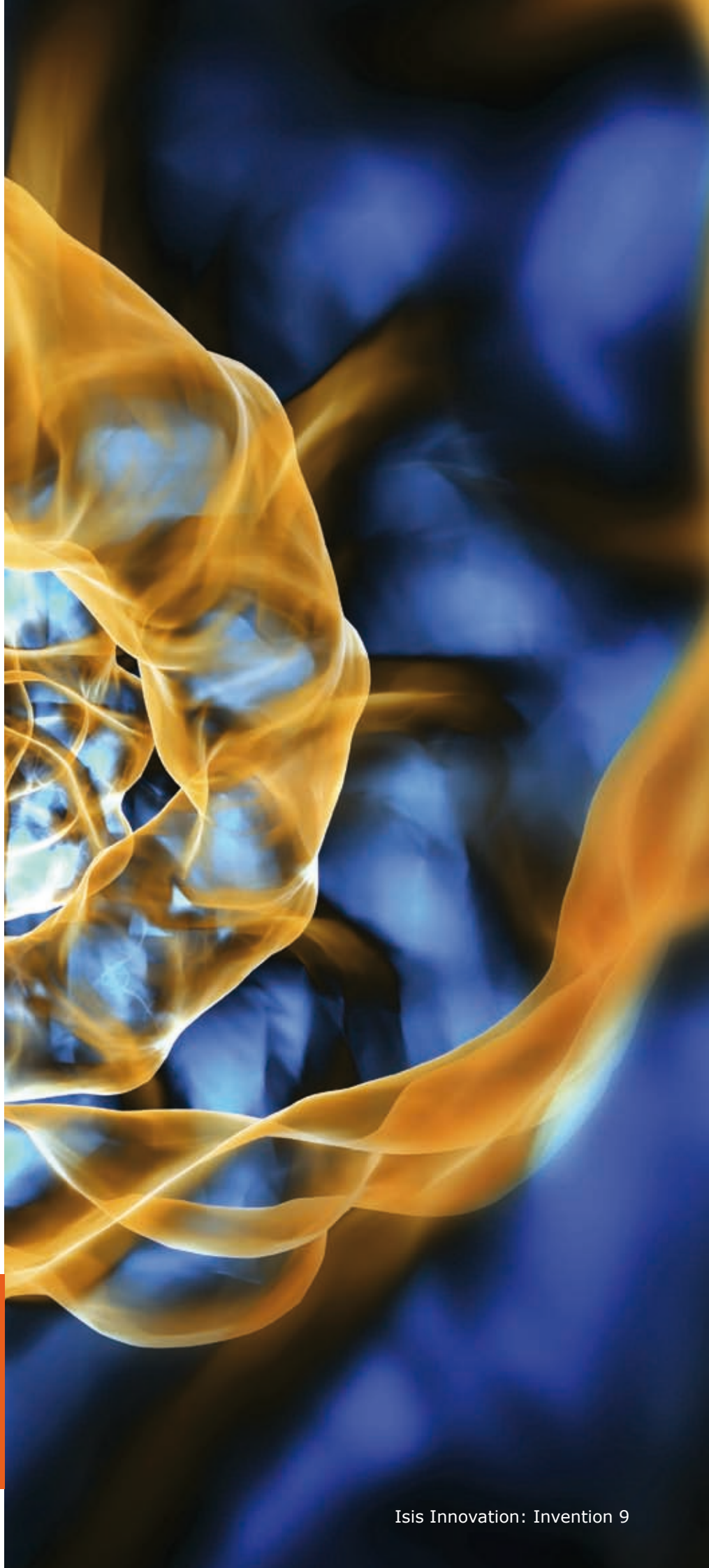

Japanese Open Innovation

Mitsui's **Tatsuya Kato** looks at the recent history of technology transfer in Japan and the Japanese version of the open innovation concept.

Tatsuya Kato spent six months with Isis on an internship from Mitsui earlier this year.

A decade of change

Over ten years have passed since the Japanese government passed technology transfer office legislation with the aim of creating a collaborative business-academia based eco-system. There are now around 50 technology transfer offices (TTOs) in Japan.

Whilst many patents were initially applied for, many of these same offices are now rather hesitant to file as the amount of licensing income received has not increased as much as was previously expected.

There is also a climate of austerity since the historic victory of the Democratic Party of Japan at the last general election in 2009. Some TTOs are now focusing on collaborative research with industries rather than licensing their technologies to them, in contrast to the self-sufficient model that has enjoyed some success in the UK and US.

Japanese industry attitudes

The Government's policy to reduce financial subsidies to TTOs, even though the offices do not generate enough income to be managed on a self-sufficient basis from licensing or spin-outs, of course acts as a motivation to look for other sources of income.

However, the unique attitude of Japanese industries is another major factor behind the most common TT business model in the country. Unfortunately, the Western open innovation concept does not seem to work in Japan. Japanese companies, in general, prefer to just buy ideas or immature technologies, rather than licensing in well developed products or acquiring spin-out companies.

Naturally this depends on the industry with which you are engaged. In the pharmaceutical sector, there is a rather different story, as pharma companies in

Japanese companies prefer to buy ideas or immature technologies, rather than licensing in well developed products or acquiring spin-out companies.

Japan are interested in and do acquire mature technologies and established companies as well. However, Japanese companies generally believe that there is great value in developing technologies themselves, or collaboratively with external research groups.

Japanese open innovation

Due to the prevailing industrial culture in Japan, it has proved necessary for not only Japanese industries but also for universities and research institutions to lean towards a "Japanese type" of open innovation, whereby companies, universities and research institutions collaboratively research and develop very immature ideas and technologies from start to end.

This can be considered similar to Japanese personnel systems, which typically favour recruiting new graduates over mid-career workers, preferring a blank canvas on which to draw the picture they want.

There has been a lot of trial and error with tech transfer in Japan to date, and it will be interesting to see how it evolves over the next decade. Let there be no doubt, it takes a long time to develop an ecosystem for technology transfer.

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Laser precision

Evert Geurtsen introduces a fast, flexible and accurate method of laser printing and machining from Isis.

Laser machining is widely applied industrially and scientifically to process a range of materials. In its simplest implementation, a powerful laser is used to cut materials such as steel to a high level of accuracy, leaving an edge with a good quality surface finish.

Laser machining is also applied to more delicate procedures, such as direct laser printing. By using tight focusing optics and short pulsed lasers, micron-scale feature sizes can be achieved, in addition to three dimensional resolution.

These capabilities can be used, for example, to fabricate structures with unusual and useful optical properties. Users of just such three-dimensional micro-fabrication will be interested in new technology developed by the researchers at Oxford University's Engineering Science Department.

With their new system, the researchers have developed a method for the adaptive control of multiple focal spot laser illumination. It combines holographic beam shaping (using an adaptive optical element) with multiple focal spot generation (using a micro-lens array).

Both micro-lens arrays and holographic methods are used to create arrays of independently controllable focal spots. This allows for the arbitrary control of large numbers of foci and will result in considerable increases in the versatility and speed of laser machining and fabrication.

The core innovation of this new method is the hybrid use of adaptive holographic diffractive elements and micro-lens arrays.

Also new are the holographic addressing schemes used to manipulate the individual spots. In combination these two innovations provide new capabilities such as periodic arrays of spots and the ability to switch foci from individual lenslets on or off, which in turn presents the possibility of inkjet style printing for fabrication.

The device will also make possible: focus shaping and control; compensation of non-uniform individual foci; adaptive optical aberration correction; reduction of chromatic aberration. Together these improvements will allow the laser manufacturing systems to maintain a greater number of practically applicable fabrication spots, thus adding to the machining precision, flexibility and speed.

Existing processes

Most laser fabrication systems use a single focused laser beam to machine or fabricate material in a sequential fashion. However, the process can be slow and time matters in manufacturing.

The speed can be increased by using parallelised fabrication, with hundreds of spots using micro-lens arrays that create a multitude of focal spots or foci from a single beam. However, this has the

The core innovation of this new method is the hybrid use of adaptive holographic diffractive elements and micro-lens arrays.

Both micro-lens arrays and holographic methods are used to create arrays of independently controllable focal spots.

disadvantage that the array of foci is fixed and cannot be controlled independently.

Another method currently used involves holographic patterns created by diffractive optical elements that can split the laser beam into many foci.

This approach can be more versatile if adaptive diffractive elements, such as spatial light modulators, are used. The downside of this approach is that the foci suffer from wavelength dependence and chromatic aberration (i.e. a failure to focus the entire spectrum of the beam on the same point). This, along with other device limitations, restricts the number of focal spots that can be created and practically used in parallel.

In other application fields holographic projection for the generation of multiple fabrication foci has been demonstrated, but until now these two techniques have not been combined for laser fabrication.

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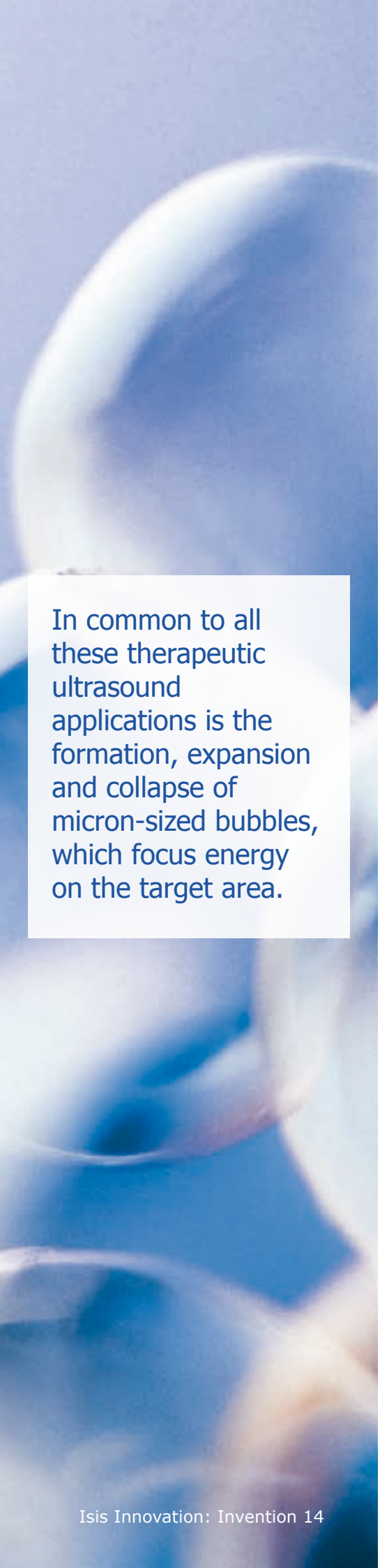
The technology

The new invention consists of an adaptive optical element coupled to a micro-lens array. This is further combined with a laser-based fabrication system to create a controllable array of fabrication focal spots, including addressing schemes, to control the pattern of foci.



Ultrasound, ultra-versatile

Ultrasound is now being used to non-invasively kill cancer tissues and deliver drugs. **Andy Self** explains three related technologies and looks at the therapeutic areas being targeted by Oxford researchers.

In common to all these therapeutic ultrasound applications is the formation, expansion and collapse of micron-sized bubbles, which focus energy on the target area.

Traditionally used in medical imaging, ultrasound is rapidly emerging as a tool for therapy and drug delivery. At energies far greater than those used for imaging, ultrasound can be focused to great depths within the body where it can be used to either kill or liquefy tissue non-invasively, or to release drugs from carriers that release their payload in response to sound, without causing damage to surrounding areas.

In common to all these therapeutic ultrasound applications is the formation, expansion and collapse of micron-sized bubbles, which focus energy on the target area. This phenomenon is known as cavitation and the core of the Oxford inventions is the mapping, control and use of cavitation activity to improve treatment delivery and treatment monitoring.

Technology trio

Oxford researchers have developed three new cavitation related technologies:

1 Passive acoustic mapping

Current systems for delivering therapeutic ultrasound under diagnostic ultrasound guidance are only capable of detecting damage to tissue after the therapeutic beam is switched off. The Oxford invention enables detection of cavitation and other parameters relevant to therapy during therapeutic ultrasound exposure, permitting real-time mapping in 3D of the tissue volume being treated or over which a drug is being released.

2 Cavitation-based sensing of temperature and rheological properties

The signals produced by cavitating bubbles can be used to sense changes in temperature, which can an important parameter for drug release and patient safety. Any change in tissue elasticity, which is a direct indicator of successful ablation, can also be detected. The Oxford IP exploits this to provide non-invasive and accurate measurements of localised changes in temperature, tissue viscosity or tissue elasticity.

3 Maximising and maintaining cavitation

Cavitation is an unstable phenomenon, typically lasting just a few seconds. Oxford inventors have developed an adaptive feedback controller which allows cavitation to be tightly localized and maintained for prolonged periods of time, enabling greatly enhanced energy deposition in tissue.

Cancer treatment

Oxford inventors have applied these technologies to a number of therapeutic areas, with cancer treatment being one of the most significant. High Intensity Focused Ultrasound (HIFU) is being utilised as a promising non-invasive cancer therapy. However, HIFU therapy is currently limited by the lack of real-time treatment monitoring. It can take more than five hours to treat a 10 cm tumour with HIFU. During this process only 30 minutes is spent actually treating the tumour, the remaining time being

The Oxford cavitation inventions allow HIFU treatment and monitoring to be performed simultaneously, drastically decreasing treatment times.

spent on treatment monitoring. The Oxford inventions allow HIFU treatment and monitoring to be performed simultaneously, drastically decreasing treatment times. Moreover, they are characterised by non-destructive localisation of the HIFU focus.

A reduction in the energies required to ablate tissue or deliver drugs prevents overheating and damage to surrounding areas. The invention also offers improved measures for non-invasive assessment of successful tissue ablation or drug release.

Passive acoustic mapping is currently in clinical trials at the clinical HIFU unit in Oxford for improved real-time monitoring during ablation of kidney tumours.

Destroying fat tissue

Liposuction is an invasive procedure where fat is removed from the body under suction. HIFU treatment is a non-invasive alternative where high intensity ultrasound is used to destroy fat tissue. Because the tissue being treated is close to the skin surface, it is essential to avoid excessive heating above the fat layer and to ensure continuous contact between the skin and ultrasound applicator.

The Oxford technology makes both of these possible, by providing the user with real-time information of the location of the HIFU focus, the ability to monitor focal and prefocal temperatures as well as a real-time indicator of successful coupling between the transducer and the skin.

Oxford researchers have generated proof of concept data that fat tissue can be accurately and effectively destroyed and monitored in real-time using the Oxford technologies.

Drug delivery and spinal repair

The Oxford cavitation technologies have a broad range of other potential applications. Two further areas currently being investigated in Oxford involve utilizing cavitation to monitor both drug release and drug delivery in the first low-cost system of its kind. The technology can be further used to treat degenerate spinal discs responsible for chronic back pain.

Market readiness

The Oxford technologies represent a major improvement over the current status quo and have the major advantage that they can be readily integrated within the ultrasound guidance technology being used by current therapeutic delivery systems.

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Gene switch-off

Martin Procter explains how an Oxford method for regulating gene activity will advance our understanding of how genes affect disease.

Tackling out-of-control genes

The presence of too much gene activity is found in many human diseases, from cancer to HIV. Gene-silencing, a form of repressing such activity, was thought to be a unique feature of plants as recently as a decade ago, but today is known to play an essential role in maintaining healthy cells across species.

Researchers from the University of Oxford's Dunn School of Pathology have now established a simple method to produce gene silencing that will have a large impact on genetic research and potentially future therapies.

Research tool

Gene silencing has become an important scientific tool and is intensively used in both academia and industry to help researchers understand the role of a particular gene's activity on cells' normal growth, function, and the development of many diseases. The findings from Oxford provide a new, exciting approach for long-lasting, specific control of gene silencing.

A unique feature of the Oxford invention is that it has the advantage of restricting the gene silencing to the nucleus of a cell.

This means that the gene silencing can be tuned very specifically to the activity of a single gene, whereas current techniques can suffer from accidental interference with other genes, leading to detrimental effects.

Current methods for gene silencing involve capturing the RNA in the cytoplasm after it has left the nucleus, but this has a number of drawbacks.

The Oxford team has shown that by controlling the way a gene is transcribed from DNA to RNA in a new way, known as convergent gene silencing, the process can be stopped much earlier.

Treatment

Gene silencing is not only used as a technique to study diseases, it is also being extensively pursued as a new method to treat certain diseases. One of the limitations of current techniques in this field is that the body is very adaptable in sensing foreign interference.

Interferon is an essential molecule produced by our immune systems and helps protect us from infection.

Current gene silencing methods can alert the immune system, leading to an interferon response which effectively neutralises the potential therapy. Restricting the gene silencing to the nucleus of the cell effectively masks the gene silencing, thus avoiding the interferon response.

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Relevant markets

This new method will be of interest to a range of companies from those engaged in the supply of laboratory reagents to companies in the pharmaceutical research and development sector.

Market readiness

The Oxford method has been shown to work in both yeast and mammalian cell lines and is the subject of a patent application. Isis is seeking commercial partners in a broad range of applications.

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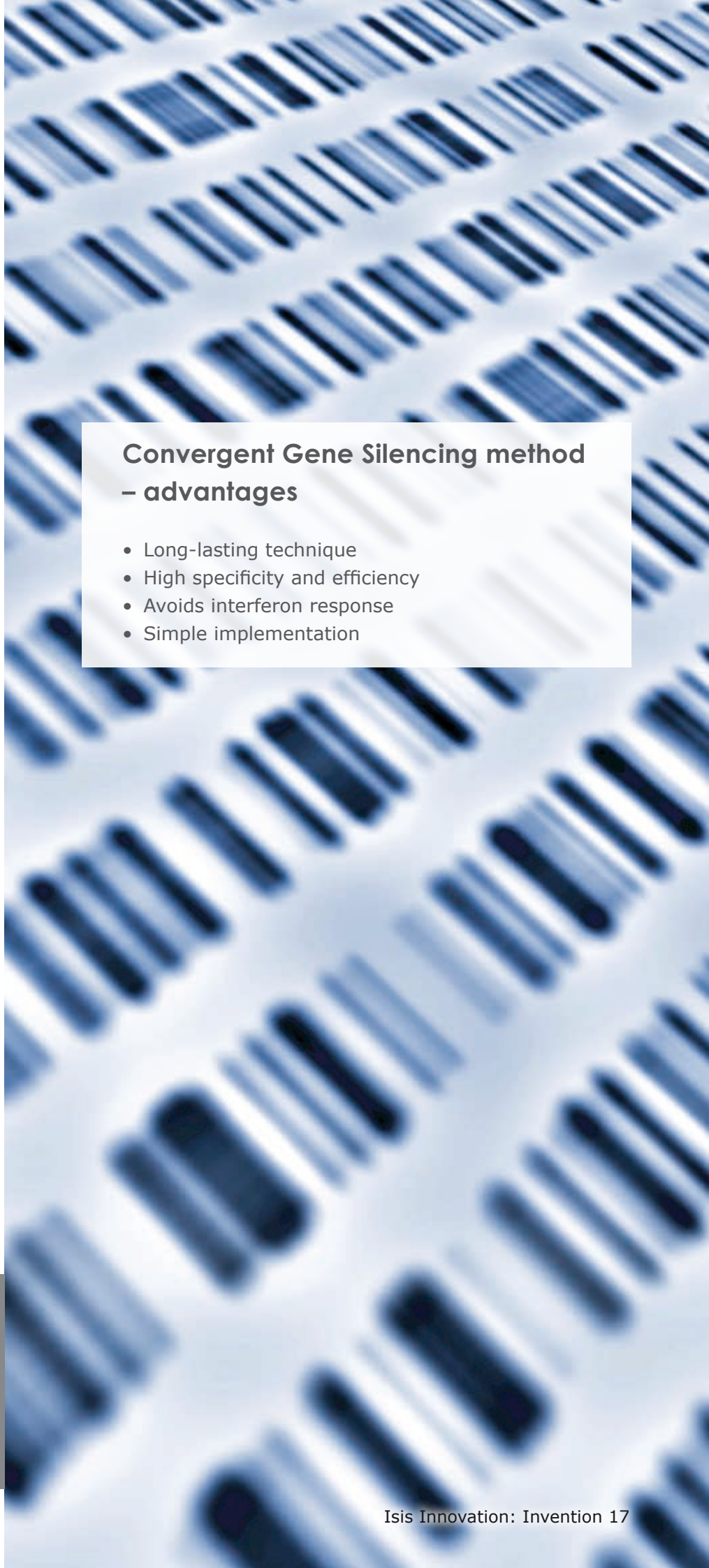
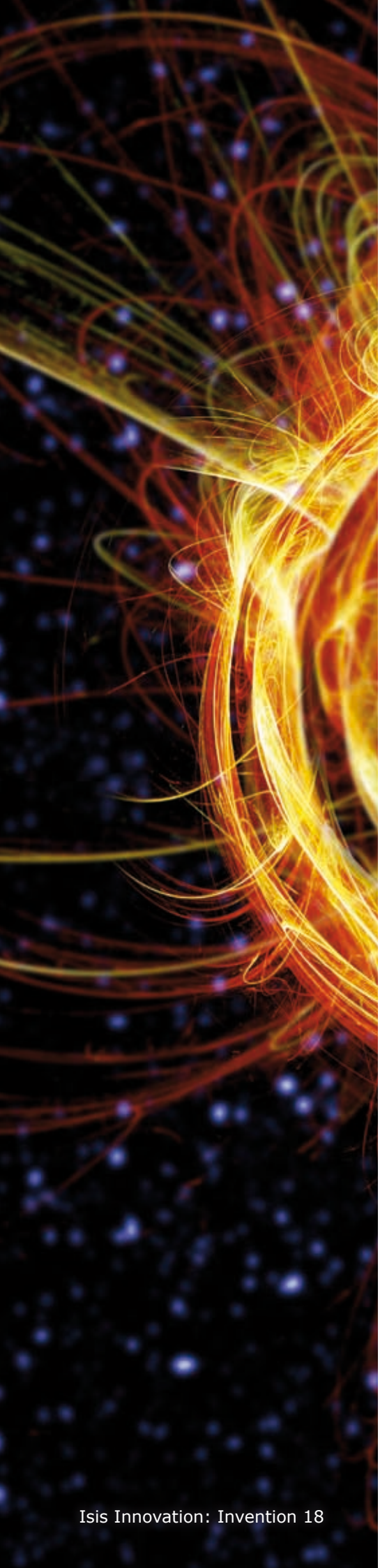


Convergent Gene Silencing method – advantages

- Long-lasting technique
- High specificity and efficiency
- Avoids interferon response
- Simple implementation



Smart navigation

Brendan Spillane discusses a method of localising mobile devices and smartphones, without the need for additional hardware.

Smartphones and other mobile consumer devices generally retrieve localisation data from Global Positioning System (GPS) satellites. However, GPS positioning can be unreliable in some situations, particularly when the user is underground, indoors or under cover of foliage. In these environments obtaining a satellite fix can be difficult or even impossible, leading to situations where the user has little or no location information available to them.

Now, an invention from Oxford researchers offers an alternative to GPS. Using the digital magnetic compasses (magnetometers) that are built into modern smartphones, the Oxford invention measures the magnitude and direction of magnetic fields to enable the device to identify its location.

Coded magnetic fields

It is possible to generate digitally coded magnetic fields using electrically powered coils, effectively 'barcoding' the magnetic fields. The coils that produce the magnetic fields can be small, and can be incorporated into electrical plugs or other similarly sized objects. With knowledge of the locations of the sources of these unique fields, the position of the device can be established within a 3D space. By installing the bar coded coils in a shopping mall, for example, the smartphone app can provide location and route instructions even without a GPS signal.

There are considerable potential uses for the Oxford invention in specialist scenarios also, such as mining, with fixed or temporary coils providing 3D locations.

GPS vs the Oxford app

In order to retrieve a location fix using GPS a significant amount of energy is needed, which is another limitation of the satellite location

Smartphones

The functionality of mobile phones has increased dramatically over recent years, due to a certain extent to advances in the field of solid state (small, self-contained, electronic) technology. This has led to the development of devices usually referred to as smartphones, which offer many enhanced features such as GPS tracking for location finding, accelerometers for motion sensing and compasses in the form of magnetometers for direction finding.

method. This is a particular issue for mobile telephones, in which it is important to keep energy usage as low as possible in order to preserve battery life. Another big advantage of the Oxford system is that once the coils are installed, no additional user equipment is required, other than an application which utilises the magnetometer.

Location based services are increasingly popular, with apps on phones providing information on the location of nearby shops, restaurants, or services. Usually the location app will then show a route on a map or give directions. However, these apps do not function where there is no GPS signal. There are considerable potential uses for the Oxford invention in specialist scenarios also, such as mining, with fixed or temporary coils providing 3D locations.

Market readiness

A patent has been applied for and Isis welcomes interest from companies interested in licensing the technology.

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Cultural pursuit

Bioreactors – engineered devices to support biologically active environments – play a key role in the development and screening of drugs. **Bharti Ranavaya** introduces an Oxford invention that facilitates automated cell culturing and ensures constant environmental conditions are maintained.

Cell culture, the process by which cells are grown under controlled conditions, is of fundamental importance in cellular and molecular biology as it enables the normal physiology and biochemistry of cells to be studied. Providing an excellent model system for analysing the effect of toxic compounds and drugs on a cell, the manufacture of biological compounds including vaccines and therapeutic proteins on a large scale is made possible by cell culture. Therefore the ability of cells within culture to mimic the organ and tissue behaviour of living cells *(in-vivo)* is of paramount importance.

Scientists at the University of Oxford have invented a bioreactor that provides a desktop solution for more *in vivo*-like cell culturing methods. An integrated air-driven pneumatic micropump facilitates automated cell culturing and also ensures that constant environmental conditions are maintained. Both space and cost have been minimised by eliminating the need for pumps, usually located externally to the bioreactor. Additionally, the size of the bioreactors have been adapted for 96 well plate apparatus, making the system compatible with current analysis equipment.

This novel bioreactor is completely sealed to prevent contamination and is gas permeable to enable control of the gas environment. Easier handling is facilitated by a relatively limited number of external tube connections. The bioreactor is capable of handling, in parallel, a variety of cell types each within their own defined environmental conditions. Cells can be grown in

suspension, monolayers (2D) or scaffolds (3D). The bioreactor can be operated without the need for a CO_2 incubator and hence greatly reduces the cost for cell culture facilities.

Demand

The manner in which variables and contamination are introduced through manual cell culturing techniques and the limited applications of monolayer cell culture are driving changes in the status quo for cell culture apparatus. There is a requirement for small cell culture systems which bear close resemblance to cells in *in vivo* conditions, but that do not suffer from the operational problems associated with lab-on-a-chip systems.

Market readiness

This automated bioreactor presents a step towards more realistic *in vivo* approaches which can be used in both general research and drug testing facilities. A prototype has been assembled and has been demonstrated to be effective at culturing mammalian cells in both monolayer (2D) and 3D.

The ability to study cell-cell and cell-matrix interaction on a small scale reduces the reliance on often expensive materials as well as the culturing time associated with large cell numbers. Channels and culture wells can be designed for specific needs depending on the desired field of research. Biosensors can also be inserted to monitor pH levels, glucose levels, electrical fields and more.

The underlying technology has been protected by a UK patent application.

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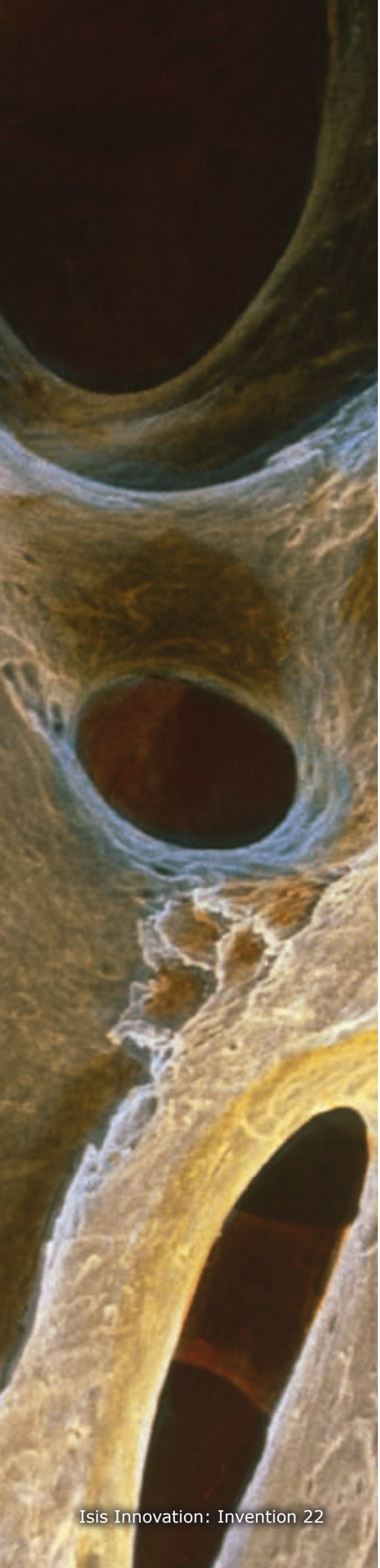


Bone disorder breakthrough

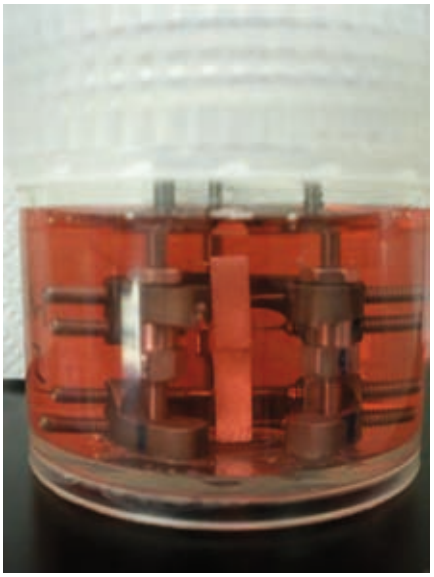
Dr Weng Sie Wong explains how a bone tissue model developed at Oxford will aid research into musculoskeletal engineering and regenerative medicine.

Oxford researchers have developed a working prototype and methods to enable detailed research into a surgical technique used to lengthen the long bones of the body or correct deformities in the bone.

The device was developed by the Oxford researchers due to a lack of availability of any satisfactory *in vitro* models and will be relevant to researchers interested in bone tissue formation and manufacturers of devices for the research environment.

Osteogenesis

Formation of new bone or "osteogenesis" is an important process in normal musculoskeletal development, as well as in bone tissue regeneration and repair following breakage. When osteogenesis occurs abnormally it can cause skeletal deformities when fractured or broken bone fails to heal properly or congenital diseases that lead to shortened height. It can also lead to conditions such as osteoporosis, which affects millions of people worldwide ever year.



Both therapeutic and surgical techniques – including regenerative approaches in the field of tissue engineering – are used to correct, treat or prevent the results of abnormal osteogenesis.

Tissue engineering is a relatively new method for regenerating injured, diseased or lost tissues by reproducing the native biological components of those tissues.

This method combines cells, extracellular structures that hold the cells in place such as collagen proteins, and biochemical and physical factors, to replace tissues that cannot be healed normally. Whilst treatments are available, there is still plenty of scope for improvement on what is currently on offer.

Research

With such a large potential market, research and funding into the musculoskeletal and tissue engineering field has grown rapidly in recent years. However, existing research models are either solely *in vivo* (i.e. require the use of experimental animals) or have an *in vivo* component.

This has limited the progression of research and development because of the high cost and ethical considerations associated with animal studies. In fact, there is increasing emphasis through EU initiatives and the US Multi-Agency Tissue Engineering Science (MATES) Interagency Working Group, for the reduction of animal testing. This is

driving the demand for more *in vitro* (outside a living organism) models.

Bone tissue model advantages

The Oxford invention addresses the need for a simple, fully *in vitro* model that mimics the naturally healing or regenerating bone.

- 3-dimensional and mimics *in vivo* bone tissue environment
- fully *in vitro* method – no need to use experimental animals
- single-sample device can be adapted for multiple samples
- allows application of static tension (stretching or compression) to the cells

Commercial opportunity

The devices and *in vitro* methods are the subject of an international PCT patent application. Isis would like to talk to both potential commercial partners (to whom the IPR could be licensed) and also to likely end users of the bone tissue model for information on the level of interest.

For further information please contact the Isis Technology Transfer Manager.

Weblink

http://www.tissueengineering.gov/welcome.htm

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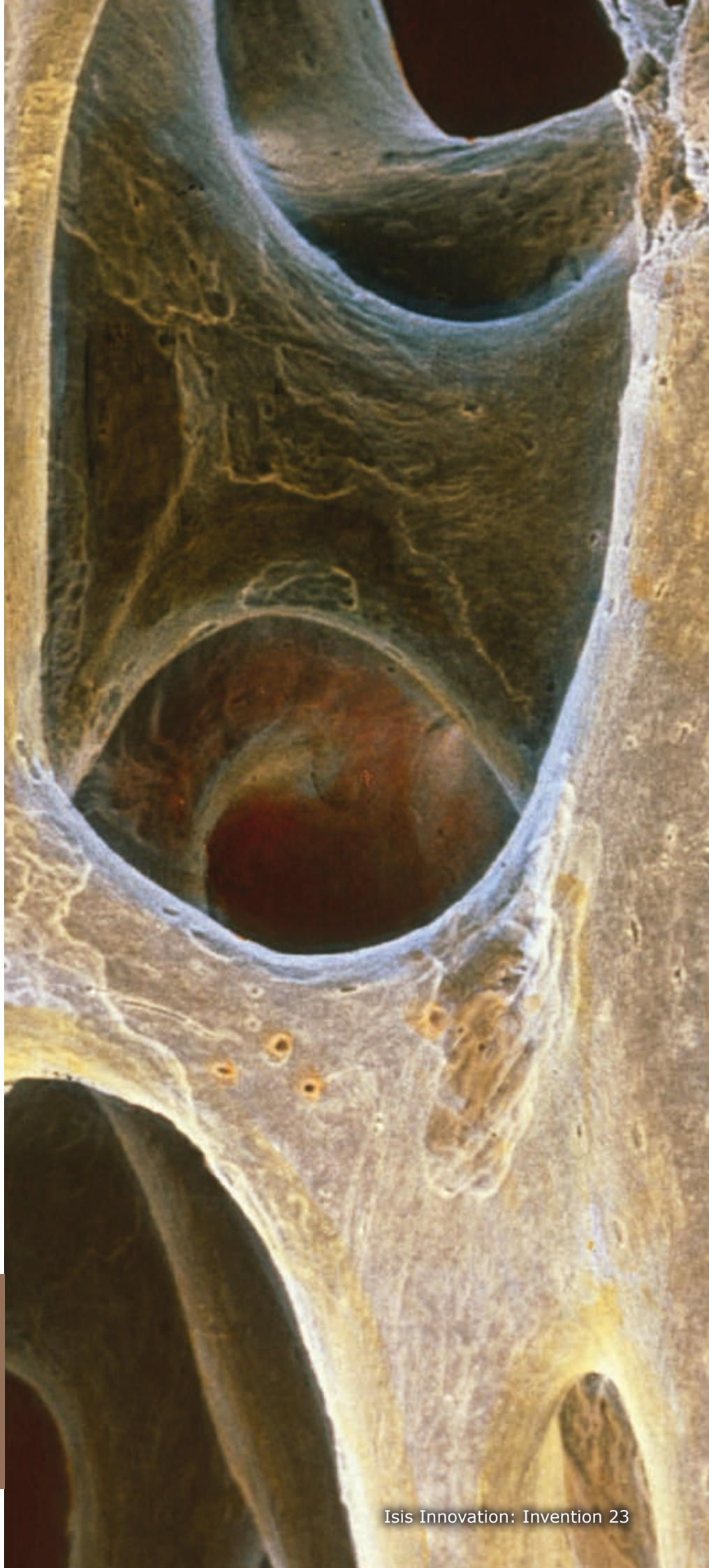


No more needles

Oxford University Consulting's **Josef Walker** showcases an alternative method for diabetics to measure blood glucose levels.

Monitoring blood glucose levels is critical in the clinical management of diabetes. It helps patients and clinicians tailor the correct dosage of medication (particularly the self-administration of injected insulin) and avoid hypoglycaemic events that are so detrimental to patient wellbeing.

Monitoring is currently performed using invasive needle-based devices that are painful to use and carry the risk of infection, which can mean patients do not test themselves with sufficient frequency to detect minor but significant changes in their blood glucose levels. This can, over time, lead to ineffectual control and diabetic complications. Alternative strategies are therefore being explored to circumvent this problem and improve monitoring compliance and patient quality of life.

Non-invasive system

One innovative company that has taken on this challenge is Lein Applied Diagnostics, a medical technology company based in Reading, England. Lein are using their proprietary confocal optical technologies to develop a non-invasive monitoring system that patients can use by simply holding a mobile-phone sized device in front of their eye and literally taking a snap-shot of their blood glucose levels.

To support the ongoing development of their system, Lein approached Dr Gari Clifford, University Lecturer in Biomedical Engineering based at the Institute of Biomedical Engineering at the University of Oxford, to explore how neural networks and machine learning could be applied to some of Lein's complex datasets in order to understand and elucidate the relationship between the data collected from the patient's eye and their blood glucose level.

Working under Gari's direction, Alistair Johnson, a DPhil student studying under the Healthcare Innovation programme at the Centre for Doctoral Training (a joint initiative between the Research Councils UK and the Department for Engineering Science at the University of Oxford), applied a series of regression analyses to the eye data. A neural network was created to identify the glucose association, robustly demonstrating the correlation between the changes in the eye measured by Lein and the changes in the blood glucose level.

Dr Clifford said, "The major advantage of using machine learning techniques like neural networks to explore complex datasets is that you do not have to assume a particular model or rely on a rigid, pre-defined hypothesis. You can also create extremely complex data-driven models and automatically determine the relevant parameters. By keeping things open and flexible, you can identify subtle but significant associations between data that you may not have expected and reveal additional insights beyond those attainable through the application of other methodologies."

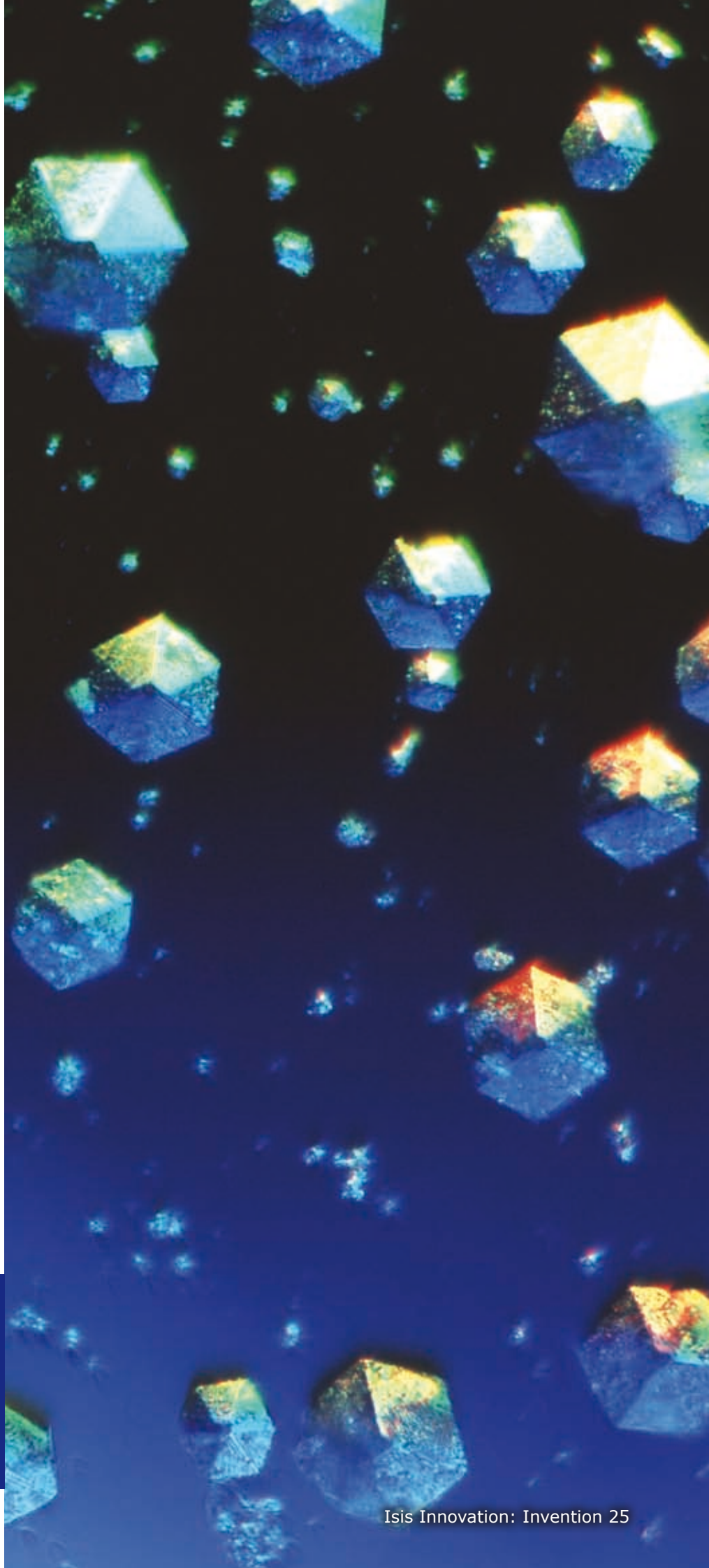
By adopting this cross-disciplinary approach and accessing complementary expertise from Gari, whose main research focuses on Signal Processing Data Fusion and Machine Learning in the field of Intelligent Patient Monitoring systems, Lein has been able to get a different perspective on their data to help inform and refine their ongoing development plans.

Patients can simply hold a mobile-phone sized device in front of their eye.

According to Dr Dan Daly, Founder Director of Lein, "Working with Gari and Alistair has made a real difference to our programme and made perfect sense from a strategic perspective. We have been able to benefit from Gari and Alistair's scientific insight as well as the practical application of their technical expertise, both of which complemented Lein's own in-house capabilities." Lein is now exploring its device in the clinical setting as well as the application of its optical technology in other areas of ophthalmic diagnosis and biometry.

The contract for Gari and Alastair's consultancy with Lein was arranged through Oxford University Consulting which worked closely with both parties to ensure that all needs were accommodated and a tailor-made solution was provided. For a number of companies seeking to gain an edge in the development of new medical technologies, including stents, MRI and vaccine delivery, the range and depth of expertise at the University of Oxford have provided invaluable support and insight, and OUC has facilitated such interactions through consultancy agreements.

Image: Polarised light micrograph (PLM) of insulin crystals



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Making the most of your intellectual property

Robert Swerdlow describes how Isis Enterprise's consultants can help you realise the potential of your IP.

Research institutes and companies with a strong research and development emphasis can generate intellectual property (IP) portfolios that create significant drains on their finances. Yet these can also represent untapped sources of potential income. Isis Enterprise (IE) works with such organisations to review and exploit their dormant technology and intellectual property assets, thereby reducing costs and generating licensing income.

IE provides two complementary services to organisations wishing to get the most from their IP portfolios: Portfolio Reviews and Commercialisation Support.

Portfolio Reviews

IP Portfolio Assessment: The act of patenting and, in particular, maintaining patents is a costly business. Companies and research institutions can incur substantial costs if they fail to keep a close eye on their IP assets. IE works with client organisations to assess:

- Patent family status and prioritisation based upon applications approaching PCT or National Phase deadlines
- Categorisation and grouping of patents based on project areas, inventors, and relevance to current research activities
- Costs associated with maintaining the entire non-core patent portfolio, and a breakdown for each patent family

In carrying out portfolio reviews, IE can reduce the IP management costs client organisations incur from their IP portfolios, while helping clients to also identify and realise new streams of income.

Commercial Potential of Patents – IE assesses the commercial potential of the IP through:

- Evaluating the strength of the patent relative to other competitive patents and the freedom to operate in target markets
- Measuring potential market value of the innovation in the target markets
- Providing recommendations as to whether patents should be maintained or dropped, or if further R&D is required

Exploitation Plan Development – Once IE establishes which patents and/or patent families have the greatest commercial potential it develops an IP exploitation plan for each, such plans include:

- Market overviews including recent developments, drivers and trends
- Competitive landscapes

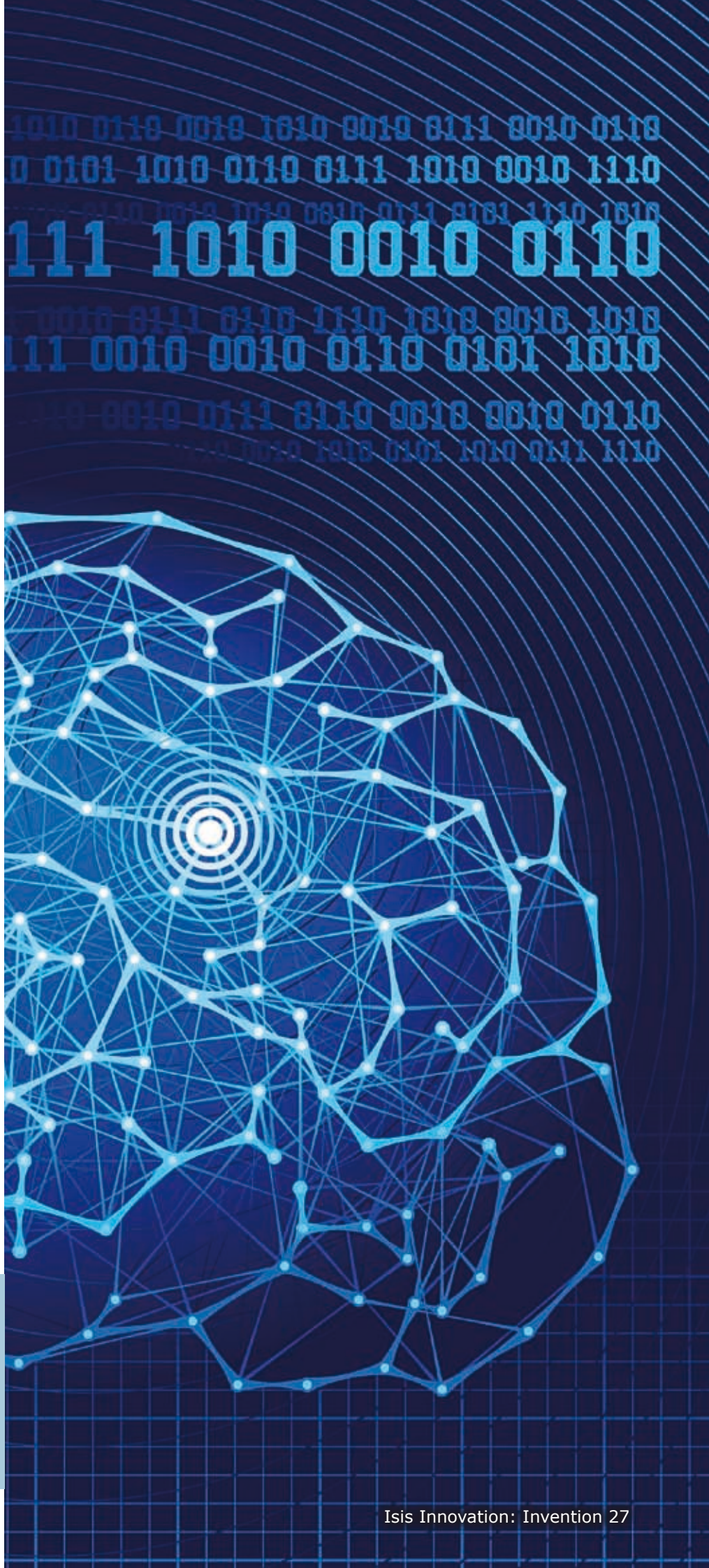
In carrying out portfolio reviews, Isis Enterprise can reduce the IP management costs client organisations incur from their IP portfolios, while helping clients to also identify and realise new streams of income.

- Unique Selling Points (USPs) and competitive advantages of the invention
- Potential licensees
- Recommended next steps for commercialisation and exploitation

Commercialisation Support

Having conducted an in-depth commercial assessment of the clients IP portfolio, and developed plans to realise value, IE selects promising projects and assists the client in the execution phase. Typically, this involves developing project marketing literature, approaching potential licensees and engaging in licensing discussions on behalf of the client. This results, for example, in commercial licensing agreements and royalty income for the client, or the creation of new commercial ventures, or spin-out companies.

IE is actively engaged with a number of companies and research institutions in the UK and abroad, assisting them with the management and commercialisation of their intellectual property portfolios. IE would be pleased to talk to institutions and companies interested in exploring opportunities in this area further.



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Oxford Innovation Society

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

- Thursday 22 September 2011
- Thursday 8 December 2011
- Thursday 22 March 2012

Meetings are held in Oxford for OIS members and invited guests, and are followed by a formal reception and dinner in an Oxford college hall.

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