
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

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# Isis insights

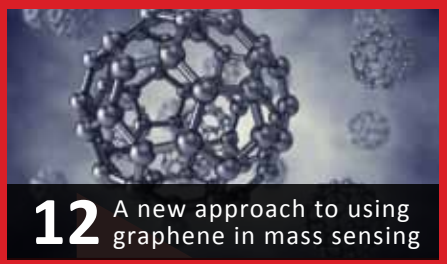
Issue 79 Spring 2015

## NANO SCALE TECHNOLOGIES

**Applications in lasers, medicine and materials**









The latest innovations, collaborations and technology transfer

UNIVERSITY OF OXFORD

ISIS INNOVATION

Issue 79
Spring 2015

# Nano Scale Technologies focus

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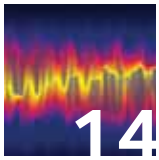


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Isis Innovation is the research and technology commercialisation company of the University of Oxford.

# NEWS

## REF ranks Oxford first for research

The results of the Research Excellence Framework 2014, a public review used to allocate almost £2 billion in research funding each year, has ranked the University of Oxford first for research.

"The University of Oxford's…submissions have the highest grade point average in 10 of the REF's 36 units of assessment." said Times Higher Education, and "Oxford is set to take the largest share of the block funding, after almost half of the research produced by its 2,400 academic staff was given the top four-star rating by panels of judges and experts in each subject." (The Guardian). Isis Innovation serves the University by transferring and commercialising its expertise and research for wider societal benefit.

## Type 1 diabetes could be diagnosed with simple breath test

Isis Innovation spin-out Oxford Medical Diagnostics is working on a hand-held diagnostic to identify children with diabetes before they become ill.

A study conducted in collaboration with Oxford University, published in IOP Publishing's Journal of Breath Research, link a sweet-smelling chemical marker in the breath with a build-up of potentially harmful chemicals in the blood that accumulates when insulin levels are low. It is hoped that these results will lead to a diagnostic device to identify children with new diabetes before the onset of diabetic ketoacidosis (DKA).

## Getting companies started

Record proof-of-concept funding of £2.6m supported 20 new Oxford technologies and ventures in 2014. The backing came from two seed funds managed by Isis Innovation, and the University of Oxford Isis Fund (UOIF) managed by Parkwalk Advisors.

Following the success of the first UOIF, which allows private investors to make tax efficient investments in a range of new Oxford technology companies, the second fund has recently closed.

As the number of spin-out companies grows, so does the need for suitable CEOs. We welcome approaches from experienced business leaders who are hungry for new challenges.

## Follow-on funding

Nightstar, spun out in 2014, has raised an additional £5m finance from its key investors to advance the company's clinical choroideremia programme, developing a retinal gene therapy for the condition. At formation the company raised £12 million from Syncona, the venture arm of the Wellcome Trust.

Summit Plc, spun out in 2003 has filed for a proposed offering on the NASDAQ Global Market in the United States. The company is developing therapies for Duchenne Muscular Dystrophy and C. difficile infection.

Genomics, a 2014 spin-out developing an analytical platform for genomic sequence data analysis, has completed a £10.3 million fundraising.

## Isis China Convention

The first Isis China Convention was held in Shenzhen in January. This brought together the Isis teams from Hong Kong, Japan, and Australia together with colleagues from Oxford and the four Isis Joint Venture companies in Changzhou, Liuzhou, Suzhou and Shenzhen. The event combined workshops and seminar presentations, and finished off with a friendly game of ping pong.

# Enterprising Consultancy

## News from Oxford University Consulting and Isis Enterprise

### Technology transfer support for St. George's, University of London

Isis Enterprise was approached by St. George's, University of London, the only University in the UK dedicated to medical and health sciences, to provide interim cover for three months, to the departing Head of Enterprise and Innovation in the Joint Research and Enterprise Office.

Isis currently provides the services of a Senior Consultant who has extensive technology transfer experience and the relevant credentials to manage a new team of Technology Transfer staff and Business Development Managers.

The guidelines cover a wide range of technology projects in the disciplines of Infection and Immunity, Cardiovascular and Cell Sciences and Population Health.

Project work currently being handled includes:

- Grants from public funding bodies;
- Internally funded Impact and Innovation Awards;
- The management of a patent portfolio covering many different commercially valuable projects;
- The management of a large funded project involving many collaborators, subcontractors and multiple funding bodies around a point-of-care diagnostic for sexually transmitted diseases;
- The formation of a new spin-out company around a diagnostic for Mycobacteria, allowing the identification of TB to be rapidly accelerated;
- The prospect of another spin-out around allergen delivery inhibitors for asthma, which represents a massive global market, and for which investment is currently being sought;
- The identification of early-stage funding for new inventions, clinical trials, prototypes, etc..

In addition to the current projects, Isis will look to streamline the internal systems, support the training for the new staff and promote a generally commercial approach to the work of the office.

### Indonesian religious education teachers visit to Oxford

In December, Oxford University Consulting arranged for thirty Islamic Religious Education teachers from Indonesia to come to Oxford for a teachers' training programme, focused on enriching their techniques and methodology in delivering Islamic religious education.

With the adoption of the new 2013 school curriculum in Indonesia, which emphasizes student-focused teaching, teachers are required to have the skills for interactive teaching, utilising resources outside of the classroom to engage students' creativity and critical thinking.

The Oxford training programme offers professional development for religious education teachers to enrich their delivery of Islamic religious education by encouraging creative and critical thinking among students, as well as promoting religious tolerance and peace within the context of a pluralistic environment. Created by a team from the MSc in Learning and Training (MLT) at the University's Department of Education, the training was delivered through classroom lectures, observation of religious education teachings in schools around Oxford, visits to places of worships and meetings with a range of organisations, including Ofsted and the Association for Muslim Schools UK.

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# The portfolio

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

## Exercise is more rewarding with Bounts

The social reinvention of exercise and fitness is largely driven by tracking apps and wearable devices. Most fitness apps offer a lot of features but don't always engage or improve retention. A start-up company based in Oxford has addressed the growing concerns surrounding personal health and fitness and created a unique app which rewards people for being active.


### Bounts is for everyone

Bounts is a fitness app which monitors activity completed using a fitness device or during a gym exercise class. Users create an account and connect the Bounts app to a preferred exercise app or device, to earn points which can be converted into high street vouchers and much more. The software is designed to track progress, motivate individuals and incentivise them for participating in physical activities.

Bounts has been working in partnership with a number of commercial and council run leisure centres to motivate their members and increase attendance. The centres can choose whether to integrate Bounts with their existing membership software and control what activities to reward and how often. Displaying Bounts scanning posters around venues is another way to incentivise users. The company also recognised the number of fitness tracking apps available to download and has links with a number of them including Fitbit, Garmin and Nike+ .

### Global appeal

The business was founded in 2011 by John Stuart whilst completing a postgraduate course at Oxford University. The company joined the Isis Innovation software incubator and attracted over £500,000 in seed funding from investors in the UK and overseas. Bounts has a Net Promoter Score of 69 and 50% of its 1 million members have been acquired through partners and organic referrals. Bounts is being used in 11 countries with specific reward options now available for the UK, Europe, USA and Australia.

Over the last two years, Bounts has been able to demonstrate that it not only works, but is proven to increase user engagement and keep people motivated.

During the next few months, Bounts will be focused on its business model and sustaining its low overhead costs to grow rapidly in the overseas markets. Bounts is well positioned for its Series A funding round later this year.

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# The Zeitgeist in the Machine

**TheySay**, an advanced text and sentiment analytics company, has developed a platform which analyses huge amounts of unstructured text in real time. **David Morgan** explains

**In September last year a pivotal moment in the history of the United Kingdom constitution had been determined by a huge turnout to vote YES or NO to Scottish independence. This caused emotions in the United Kingdom, and more specifically Scotland, to run wild.**

Gladiatorial televised debates between Alex Salmond and Alastair Darling resulted in minute scrutiny of the personalities, and issues on "currency" became pitched battle grounds. The strident rhetoric from both sides was also matched by vitriolic back-and-forth across social media. Instant emotion, discussion and opinion was being experienced on a huge scale. Social media, news, blogs and chat rooms were bulging with outrage, nervousness, despondency and joy.

Between the 2nd and 19th September 1.75m tweets were sent, with 1.225m from YES supporters and 0.525m from NO supporters.

A challenge then, for people and machines, to understand those emotions and opinions coursing through the data. No one could possibly read everything, let alone aggregate insights into how people are feeling, across all the multi-dimensional loyalties, biases and events expressed via thousands of messages an hour. But TheySay, a spin out from Oxford University founded by computational linguists, has built a sophisticated algorithm that analyses huge amounts of data in near real time. This involves over 68,000 rules being applied to the streaming data to determine the grammatical composition of the text. The machine effectively builds a picture of the relationships between the words in a phrase, sentence and document very similar to the way in which humans understand text. Then it extracts and assigns meaning and provides insights. These insights include sentiment (positive or negative), emotions (fear, anger, happiness and sadness), and sureness (certainty and confidence).

## Can we trust the machine to behave like a human?

In the Scottish referendum, there were peaks of activity around the televised debates, but the real activity started to ramp up in the seven days up to the day of the vote, and for hours after. TheySay analysed all of the Twitter traffic from the 2nd to the 19th, and in that last week, things really got hot. Early predictions suggested there would be euphoria from the NO voters when the result became a


*The TheySay 2015 General Election App*

foregone conclusion, matched by despair (with a smattering of anger) from the YES voters. TheySay's technology detected exactly that. It also showed that during the week before the vote, YES voters had high levels of certainty and confidence, extreme levels of anger, fear and happiness. With NO voters, there was less certainty and confidence (with noticeable drops and peaks in fearfulness), and flat readings for happiness and sadness. In contrast, in the early hours of the day after the vote, the YES voters descended into abject misery whereas the NO voters were bouncing with positivity.

## A vote of confidence

TheySay is repeating this exercise for the 2015 General Election. This time, the four party leaders, Cameron, Miliband, Clegg and Farage will be tracked against key issues like the economy, education and the NHS. Real-time graphical information will be displayed, including time slices of the day, last week and month. Social media scores and sentiment scores for each party leader in the aggregate, will also be included.

A lesson from the Scottish referendum indicated the number of people voting on social media is small and, analysis is restricted to a certain demographic. So whilst TheySay's analysis is not a prediction of outcome, the machine is nevertheless detecting aspects of the Zeitgeist influencing the result.

There is a public site (optimised for mobile) at ge2015.theysay.io

"Between the 2nd and 19th September 1.75m tweets were sent, with 1.225m from YES supporters and 0.525m from NO supporters."

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# The rise of the angel investor

**Dr Thomas Hellmann** of Oxford's Saïd Business School describes dramatic changes in entrepreneurial finance at the most recent Oxford Innovation Society meeting

**Over the last decade, the landscape of entrepreneurial finance has undergone dramatic changes. Venture capitalists used to be the dominant players in the financing of entrepreneurial start-ups, especially in high technology sectors, and especially in North America. Yet the hangover from the dotcom bubble changed the financial landscape. First the IPO market retrenched, depriving venture capitalists from one of their main exit channels. Then the truth about low returns to venture capital became apparent: the average returns to venture capital hardly matched returns in the stock market, not even accounting for risk; and only the top quartile was returning any money to their limited partners. As a consequence, many limited partners left the venture capital market.**

The decline of venture capital was gradual and slow because of the structure of venture capital funds, which have long lives and long lags between their fundraising and investment periods. Moreover, the decline of venture capital coincided with a boom in entrepreneurial activity. Entrepreneurs became more numerous in the last decade, because of the lack of corporate jobs, because of the lowering of the cost of starting a business (aided by Web 2.0 and cloud computing), and because many entrepreneurs learnt their lessons in the dotcom bust, and wanted to set the record straight.

With rising appetite for funding by entrepreneurs, and the decline of venture capital, a gap was created in the market for early stage funding. This was filled by three main players: accelerators, crowdfunding, and angels. Accelerators, such as the Y-Combinator, invented a new model for mentoring entrepreneurs, but the amounts of funding involved tended to be small. Crowdfunding pertained mostly to the pre-sale of products, such as on Kickstarter. Equity crowdfunding remained small, mainly because of legal difficulties. The most important development was therefore the rise of angel investors. One of the challenges with understanding this growing phenomenon is the dire lack of data: angel investors are private individuals that are typically under no reporting requirement, and frequently treasure their anonymity. As a consequence, the few studies about angel investors could only look at the tip of the iceberg, such as the more visible angel groups.

I have been involved in a research project for several years, together with Paul Schure (University of Victoria) and Dan Vo (University of British Columbia). The project leveraged unique data that allowed them to look 'below the surface'. The data was generously provided by the Investment Capital Branch of the Government of the Province of British Columbia, and is based on a unique tax credit program that gives a 30% tax refund for investments made in start-up companies. These tax credits are available not only to certain venture capitalists, but also to many angel investors that satisfy certain basic criteria, such as residency in BC.
The analysis of BC angels revealed several interesting insights. First, the data revealed a large diversity within the angel community. The analysis uses a three way classification,

## ‘The average returns to venture capital hardly matched returns in the stock market’

distinguishing between “individual angels” who invest directly as private individuals; “angel vehicles” which are investment entities that invest on behalf of an individual; and “angel funds” who are intermediaries in the angel market that aggregate the funds of several angels into one investment vehicle. Among other things, the analysis revealed that relative to angel funds, individual angels invest considerably smaller amounts, and are much less likely to write a second cheque to their company. Angel vehicles are somewhere in between those two extremes.

A second insight from the analysis concerns the performance of angel investments. Performance is always difficult to measure, but the analysis suggests some interesting patterns. Venture capitalists achieve a higher rate of exits (11% IPOs, 19% Acquisitions) than all angel categories (8% IPOs, 13% Acquisitions), and the three angel categories have remarkably similar performances. Moreover, imposing strong assumptions on limited data, our calculations suggest a 10% mean and 0% median return to angel investing.

### Parallel ecosystems

A third set of insights concern the relationship between angels and venture capitalists. A traditional argument suggests a “stepping stone logic”, where companies graduate from angel investors to venture capitalists. An alternative is to view angels and venture capitalists as “parallel ecosystems”, where companies that enter one type of financing stay with it, and rarely cross over to the other side. To analyse this, we performed a large variety of regression analyses that also control for a large number of other factors (such as firm location, industry, time of investment, amount of funding, etc..). We find that the evidence is broadly supportive of the “parallel ecosystems” hypothesis. For instance, the probability of obtaining a venture capital investment decreases when a company has prior angel financing; and vice versa.

The angel investment has several implications for academics, practitioners and policy makers. One is a simple recognition of the overall importance that angel investors have acquired over the last decade. Another is the need to appreciate the diversity within the angel community. Finally, analysis suggests that policy makers wanting to stimulate the market for early-stage financing must learn to appreciate the differences between traditional venture capitalists and angel investors, who seem to have parallel lives.

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# Converting entrepreneurial flair to commercial reality

What makes a business successful and what are the characteristics that distinguish the successful from the failures? **James Cowper Kreston** and **Blake Morgan** discussed this topic at the December 2014 Oxford Innovation Society meeting

**A company needs to have a core concept, commercial application and a sensible market opportunity. The management team need to have a focus on that market opportunity and drive the business to achieve its business plan objectives. They also need to be prepared to adapt their strategies in pursuit of those objectives - the successful businesses are those that adapt to market conditions. There are a number of companies that start out with a focus on one product or service only to change the focus at a later stage as another, better opportunity comes along or when it becomes clear that the original concept or technology has flaws or may be lacks sufficient market opportunity.**

There are a number of factors that could hinder an entrepreneur. For example, the company in receipt of an offer for its purchase for £12 million that ended up in liquidation with the deal undone; or the example of the company under investigation by HMRC for non-payment of payroll taxes. In both cases the key issue was a lack of understanding by the entrepreneurs of the importance of good business husbandry - keeping appropriate records of financial transactions; keeping personal expenditure and that of the company separate; and being disciplined in all business dealings.

## How is it possible to avoid these common pitfalls?

It is about taking the right advice at the right time from the right people.

## What is the right advice?

Consider professional advice from people used to advising a wide portfolio of companies in the early stages of their development. Unfortunately, advice from friends or family members or the internet can be fundamentally flawed when it is applied to your specific idea or circumstance. This can have pretty devastating effects which are difficult, expensive and in some cases, impossible to rectify. Not using a lawyer or an accountant, due to concerns over cost, can prove to be a very false economy. You could find that, unless drafted properly, just one or two lines in a document could prevent you qualifying for particular investor friendly tax reliefs or being unable to prevent business partners from leaving and setting up in competition whilst still owning a stake in your company.

## When is the right time?

It is never too early to take advice. Isis can provide guidance in relation to business planning and strategy for a particular idea or technology. Once a business plan has been written, it is sensible to run this past an accountant or lawyer for a sense check before you go further down the road. Taking advice before you form a company is important. There are so many things that need to be considered from the outset, such as how you regulate your relationship with fellow shareholders or how ownership is to be structured for optimum tax and

commercial effect. At this moment you should be putting in place a Shareholders Agreement (which is essentially a document governing the management and operation of the Company and acts a bit like a Pre Nuptial Agreement or a Will for a Company in the event that things don't pan out as planned.) Future investors will look at how you have set up your company and how you run it when making investment decisions. Putting good quality governance documentation in place (such as a Shareholders Agreement) and administrative and accounting practices all demonstrate a reassuring attention to detail and regard for the fundamental foundation blocks of your business.

## Who are the right team?

By having the right team around them the entrepreneur is enabled to be free to maximise their opportunities for the core product whilst ensuring that the routine management of a company is carried out. In December we likened this support team to the team around a key sportsman - Andy Murray, for example, has a whole team around him from the coach and manager to the nutritionist and physiotherapist. For a business the team will probably comprise the lawyer, the patent attorney and the accountancy and tax advisers. They are those with whom the entrepreneur can build a good relationship - they need to be able to work together well in times of adversity as well as good times! The right team has to comprise those who understand the company's needs and the nature of the business and who have genuine experience of working with companies at each stage as they scale from start up or spin out to sophisticated enterprises. Ideally they need to be a team who are used to working together to enable you to work efficiently and effectively to maximise opportunities and overcome any challenges you may face.

As you move from entrepreneurial flair to commercial reality James Cowper Kreston and Blake Morgan have the working relationship and depth and scope of expertise that can help you at every step of the way.

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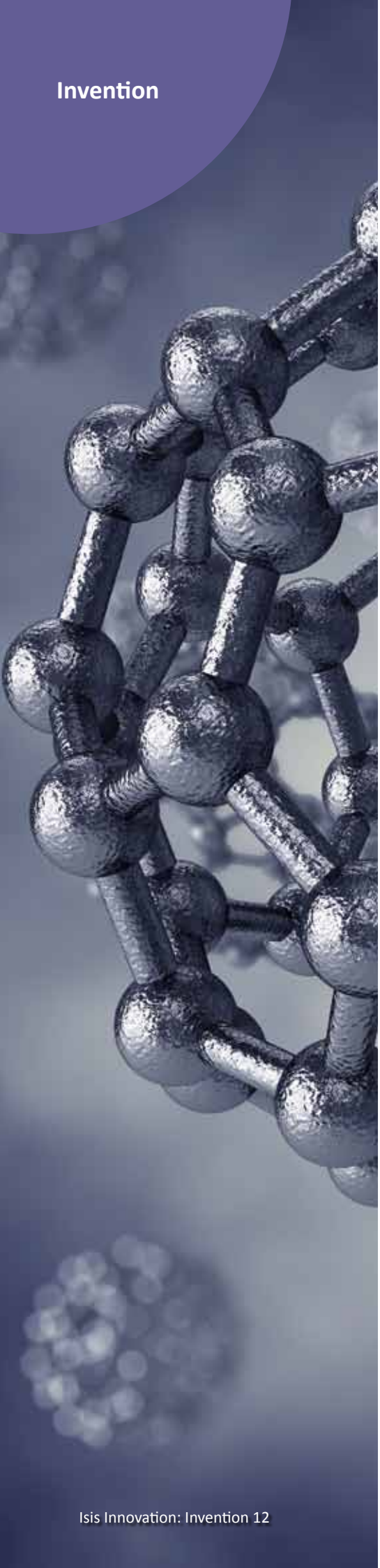

# Graphene mass sensor with protein molecule sensitivity

Researchers from the University of Oxford's Department of Materials have developed an ultrasensitive mass sensor using commercially available non-electronic grade graphene. **Lamin Ben-Hamdane** explains

## The use of graphene in mass sensing

**Graphene consists of a single layer of carbon atoms which display outstanding properties, such as, high rigidity, conductivity, as well as low mass density. This makes it an exceptional candidate for extremely small scale mass sensors (nano-electro-mechanical systems, NEMS), as any additional mass attaching to the system perturbs it significantly. Oscillating graphene, however, exhibits high damping at room temperature and this has hindered its application in mass sensors, as high damping results in low signal read out and resolution. Material scientists at Oxford have developed technology that circumvents this disadvantage by exploiting the piezoresistive properties of graphene and could be the basis for next generation mass sensors.**

## A new approach using the piezoresistive properties of graphene

When an atom attaches to a beam of graphene that oscillates at its resonance frequency, this additional tiny mass will significantly change the frequency and amplitude at which the beam oscillates. The change in oscillation alters mechanical stress inside the beam. Changes in mechanical stress in turn lead to changes in the electrical resistance of the graphene beam (the so called piezoresisitve effect). A corresponding change in the output signal, caused by the change in resistance, enables a convenient signal read-out via simple electronic circuitry.

By making use of use of graphene's intrinsic piezoresistivity, Oxford researchers have circumvented the problem of high damping and resulting low signal read out for graphene based sensors at room temperature, which has prevented the use of graphene in these devices so far. With this novel approach, the system functions at room temperature and reaches unprecedented mass resolution, using commercially available non-electronic grade graphene.

The minimum detectable mass is in the range of zeptograms, i.e. $10^{-21}$ grams – sufficient for single molecule detection. Such a technology could be scaled to reach hydrogen mass sensitivity, which

"The minimum detectable mass is in the range of zeptograms, i.e. $10^{-21}$ grams – sufficient for single molecule detection"

would lead to the most sensitive mass detectors, being able to sense single atoms.

## Commercial potential

Researchers at the Department of Materials have developed a system which works at room temperature using a circuit board and commercially available components. The graphene used is purchased as off-the-shelf wafers from commercial vendors, and can easily be upscaled for mass production.

Applications include various types of physical, biological, and chemical sensors, all expected to have sensitivities far exceeding those of competing technologies. Examples are gas sensors, which are used to detect combustible, flammable and toxic gases. The big challenge is to increase the sensitivity of these sensors to detect ever smaller quantities of substances e.g. the detection of pollutants in the air or the detection of small quantities of explosive substances for airport security. The development of the technology can lead to ultra-sensitive gas sensors in the future.

The sensor is small enough to fit into a mobile phone, and offers the potential to measure the quality of the air around you, how clean your hands really are, or how much you've had to drink, all at a tap of your smartphone.

## Commercialisation

A patent application has been filed to cover the sensor, applications and method of fabrication. Commercially available CVD graphene was used to demonstrate this concept, the electronic circuits needed are fairly simple. We can therefore expect to reach competitive cost targets when scaling up to mass production. Isis welcomes contact from parties interested in licensing this opportunity for the creation of highly advanced sensors.

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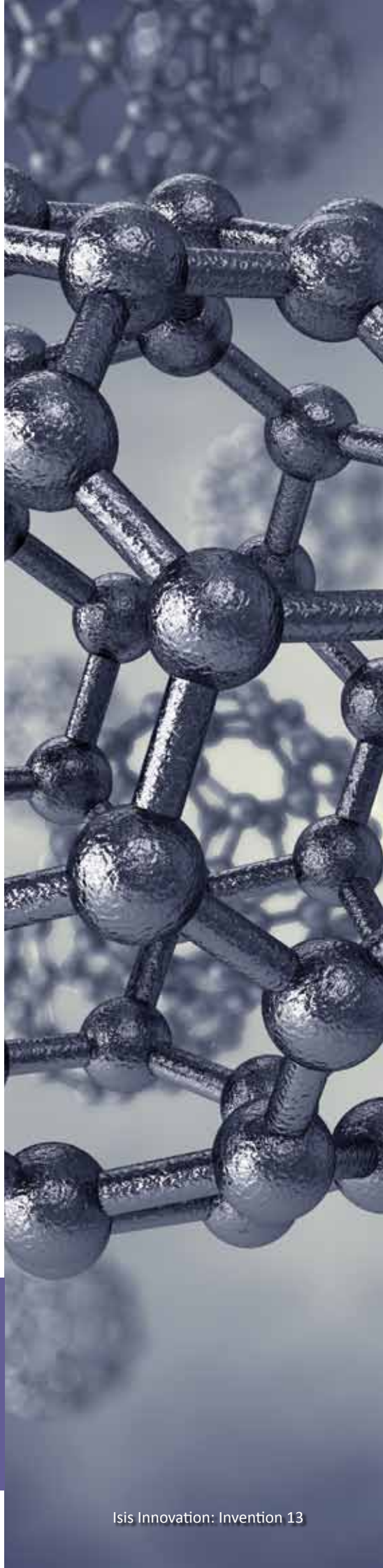


# Miniature tuneable dye laser

**Dr Jon Carr** explains how Oxford researchers have developed a miniature pumped dye laser based on manufactured micro-cavities

**"Laser" stands for light amplification by stimulated emission of radiation. True tuneable lasers use different organic dyes, capable of producing emission from the ultraviolet to near-infrared spectrum. They can operate in the visible spectrum with tuneable emissions of blue, green, yellow and red emissions at almost any wavelength. Common organic dye lasers are optically pumped and to obtain reliable operation, the dye flows through a cell using an argon ion laser as a pump, and a prism. Tuneable dye lasers are most used for scientific applications like high resolution spectroscopy.**

## Oxford Invention

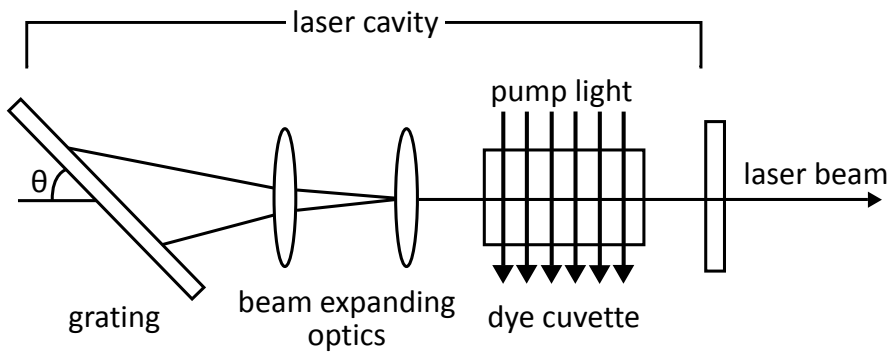
Over the last five years the University of Oxford Photonic Nanomaterials Group have developed a dye laser based on specialised optical micro-cavities. The technology is based around a microscopic resonator with a mode volume of 1-100 $\mu m^3$, which provides a spectral range large enough for single mode lasing with no need for additional mode selection or filtering. The resonator itself is a tuneable 'etalon', an optical device containing parallel mirrors used in laser, designed to delay light, into which the dye is placed. Novel fabrication techniques used to create the mirrors create an inexpensive, but flexible tuneable laser system.

With their current laboratory prototype, operation wavelengths spanning the visible and near infrared have been realised, with average output powers up to 30 nW, corresponding to 3pJ/pulse. The laser produces unpolarised beams and the intensity distribution and divergence can be engineered into the novel manufacturing process. Arrays for signal multiplexing and advanced spectroscopic applications have been envisaged by the team, as well as further significant increases in output power.

Due to the novel fabrication methods used the cavities are ultra-small and therefore the volume of dye required is small. This has the added advantage that the ambient diffusion of the dye molecules in solution is sufficient to enable recycling of the dye in the cavity. The rate at which the dye is used up is so small that a long lifetime stable laser could be made without any need for dye handling or replacement.

## Scientific applications

According to a Frost & Sullivan report ("Total Laser Systems Market" report




*Schematic of a simple dye laser cavity.*

#A292-10) 4 main types of laser make up an approximate $6.3 Billion market share (2009); Carbon-dioxide - 18.7%; Solid-state - 18.9%; Diode - 52.7%; and 'Other' - 9.7%. The main technology within 'Other' is Dye-lasers and this is seeing significant growth. Applications for lasers generally include cutting & welding, marking & engraving, semiconductor & micro processing, automotive industry, communication, excimer lithography, data storage, medical, defence, instrumentation & sensors, pumps & image recording, and research & development. Tuneable dye lasers are most used for scientific applications like high resolution spectroscopy.

## General advantages of Dye Lasers

- They are available in visible form (also in non-visible).
- A range of wavelengths can be produced by using dye lasers.
- Beam diameter is small.
- Beam divergence (0.8 milli radians to 2 milli radians) is also less than the beam divergence of many lasers.
- Construction of dye laser is not complex.
- High output power is also possible with dye lasers.

## Patent protection

This is now the subject of an international patent application and Isis would like to discuss with interested companies the licensing of the technology.

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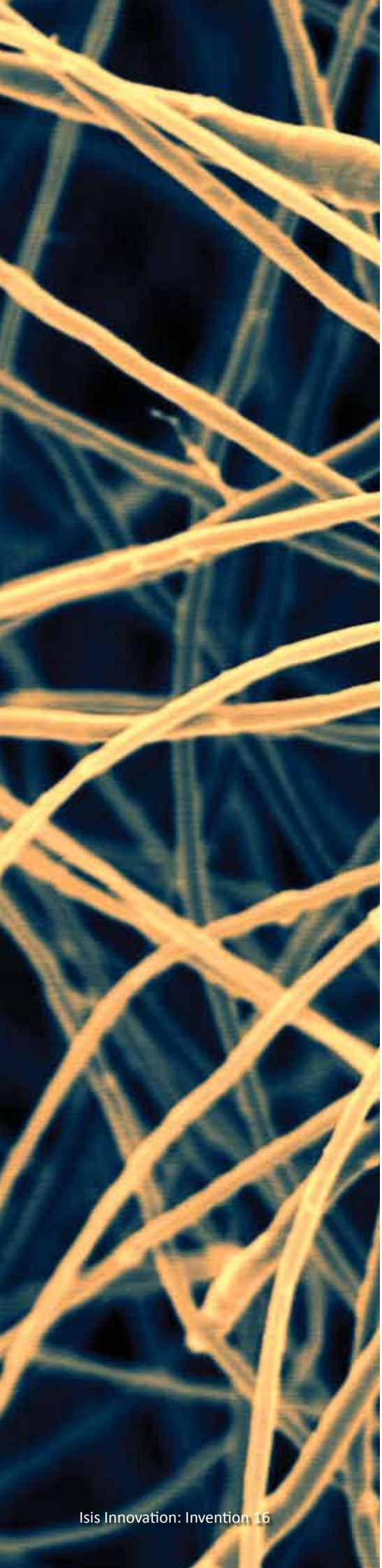


# Revolutionising medical sutures – The Oxford Bioyarn

**Nikolaos Chalkias** explores a novel method of manufacturing electrospun filaments that are biologically active and biocompatible

**Humans have used surgical sutures to hold body tissues together after injury for thousands of years. The earliest designs found in Egyptian mummies used plant materials such as flax or animal tissue such as catgut. Current sutures are made from synthetic polymers and are designed to be inert and simply act as a mechanical support to damaged tissue.**
**A team of Oxford researchers are looking to change the design and utility of modern sutures and have invented a nanofibrous suture which acts both as a suture and a biological scaffold.**

The Oxford Bioyarn actively helps tissue grow and therefore achieve better outcomes after surgery. Its unique properties are solely due to its physical structure and design. Bioyarn's innovative design was enabled by a new method of electrospinning long filaments with unique nano-scale properties. Electrospinning and electrospun materials have been known for decades, however, there is no methodology to generate continuous filaments in a robust and reliable manner. The Oxford team has developed an automated method and a custom-made device for the collection of continuous electrospun filaments made of micro and nano-scale fibres. The filaments are then processed with existing textile equipment into the final Bioyarn suture.

## New possibilities in medical textiles

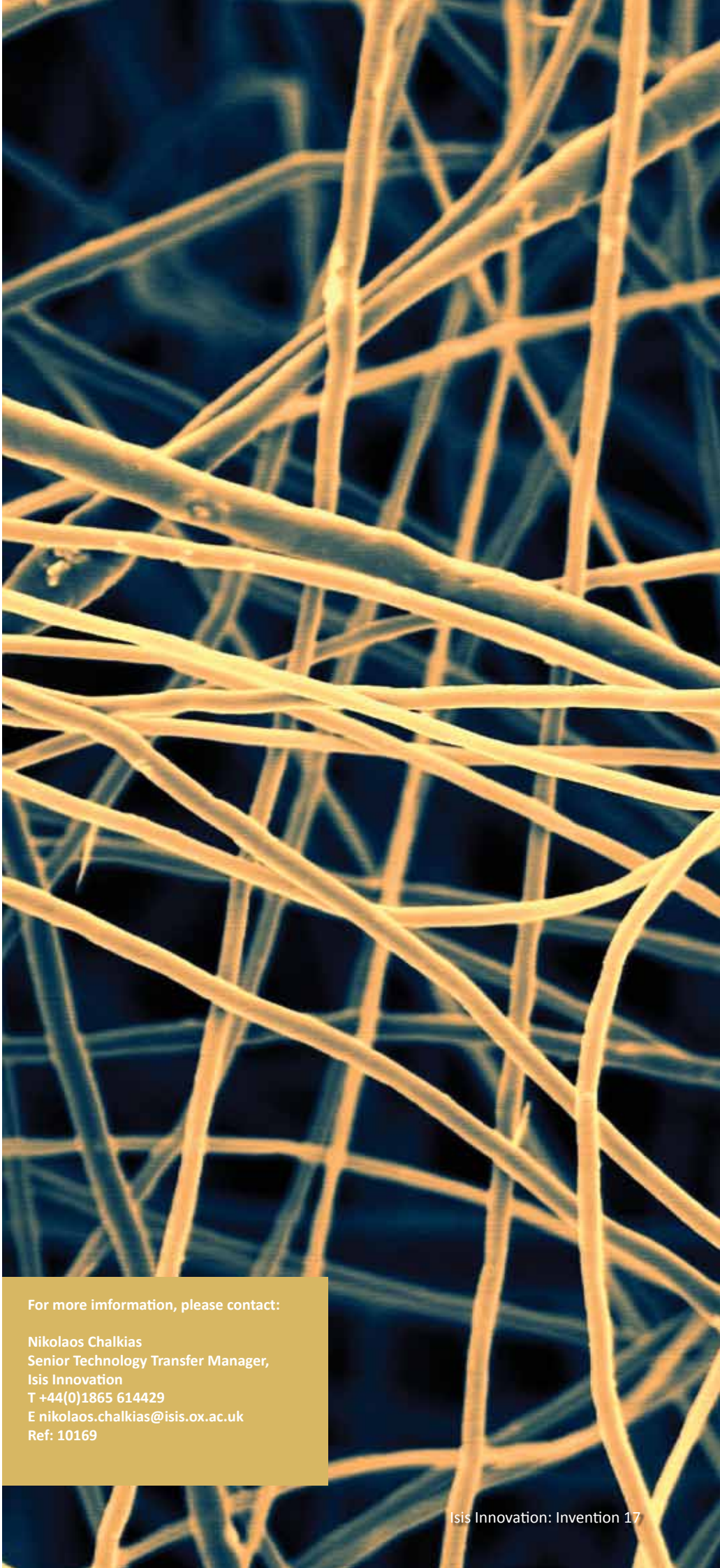
Nanoscale fibres have recently been identified as exceptional candidates for improved healing to damaged tissues and organs. Due to their extremely fine dimensions, nanofibrous materials possess a very high surface area to volume ratio and porosity. This means the material can rapidly absorb large volumes of fluids, display high exchange rates of gas and liquids; improve cell infiltration; carry and release drugs in a controlled way and contain biologically active agents. Due to their dimensions, they can also mimic the extracellular environment, making them excellent materials to support cell growth and new tissue formation. Replacing current medical fibres with nanofibrous threads has therefore a huge potential to improve the healing function of tissues and organs. Applications include:

- Surgical sutures
- Tissue scaffolds for tissue engineering
- Wound dressings
- Drug releasing devices
- Textiles
- Filtration

## Gearing up for the first clinical trial

The multidisciplinary team of clinicians and engineers are gearing up to get the Bioyarn into the clinic. The team has focussed on a common operation that will greatly benefit from the features of the Oxford Bioyarn. The randomised clinical trial's objective is to generate evidence that Bioyarn reduces significantly the current failure rate of rotator cuff repair surgery and improve patient outcomes.

A rotator cuff tear is a painful condition of the shoulder joint – common in contact sports and in an ageing population. Pain arising from a tear to these tendons can cause significant long term disability. Shoulder pain is the third commonest orthopaedic problem to present to General Practitioners. Currently 10,000 patients annually in England have torn tendons that require surgical repair and this number is increasing. Unfortunately around 40% of these surgical repairs fail which can result in long term disability. The team's first goal is to reduce the failure rate. However, the applications of the Oxford Bioyarn suture remain wide and diverse.



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# A marker for immune function and infection

Oxford researchers have developed a hand-held point-of-care style test which can assess the ability of the body to fight infection. **Andrew Bowen** explains

**Superoxide ($O_2^-$) is a free radical that is released as part of an immune response and can be used to diagnose the presence of infections in animals, such as mastitis in dairy cows. This common disease costs the U.S. dairy industry around $1.7 billion – $2 billion per year and is characterised by inflammation and an increase in immune system activity. A simple, early diagnostic tool could allow faster treatment with antibiotics and prevent milk deterioration and the spread of infection.**

Superoxide levels can be linked to the activity of the immune system. The detection of superoxide is also important in the diagnosis and monitoring of human conditions such as chronic granulomatous disorder (CGD). This disease is caused by a faulty bone marrow gene and means that neutrophils don't work effectively. The disease is life-threatening, life-limiting and affects about 1 in 200,000 people.

## Free radicals

Free radicals (atoms or molecules with unpaired electrons) such as superoxide are used by the immune system to kill dangerous microorganisms invading the body. Neutrophils engulf the microorganism and release reactive oxygen species including hydrogen peroxide ($H_2O_2$) and superoxide ($O_2^-$). These react within the phagolysosome to kill almost any microorganism.

## Current tests

The current test for superoxide is based on the ability of a phagocytic cell to induce a colour change in Nitro Blue Tetrazolium (NBT). This is only possible in the presence of superoxide radicals and is a measure of their occurrence. Unlike the Oxford test, the NBT test requires trained personnel for the interpretation of a patient's blood test results. This is also true of testing for bovine mastitis, which generally relies on an analysis of bacterial numbers and requires lab-based testing.

## The Oxford invention

Scientists at the University of Oxford have developed a hand-held point-of-care style test which can assess the presence of bacterial infections and the ability of the body to fight infection. The Oxford test is an electrochemical analogue of the standard Nitro Blue Tetrazolium test.
The Oxford electrochemical sensor:

- is easy to use and does not rely on trained personnel
- gives immediate quantitative results, as opposed to the traditional qualitative NBT test
- is a simple two-step process
- has a quick response time
- has high sensitivity
- has good reliability
- has a low detection limit
- has low cost implications
- can be miniaturised

The Oxford sensor overcomes previous problems with stability and dependence on temperature and pH.

The Oxford test uses a carbon paste electrode, which is immersed in an aqueous sample containing superoxide. The electrode is then immersed in a solution of Nitro Blue Tetrazolium Chloride (NBTC). The two solutions react within the carbon paste and NBTC is reduced to form diformazan, which produces a quantifiable peak that can be used to measure superoxide concentration.

A normal immune response to a known pathogen involves one-electron reduction of oxygen to form superoxide. This allows researchers to detect increased levels of the oxide during an infection.
This information could be used to assess the progress of an infection or the ability of white blood cells, such as neutrophils, to fight off infection.

## Superior results

The technology has been optimised in the laboratory to produce fast analysis times and could be integrated into a hand-held or desktop device. The sensor has a limit of detection of 0.059nM and can be used by people without any specific scientific training opening up the possibility of a fast, sensitive point-of-care diagnostic.

"The Oxford sensor overcomes previous problems with stability and dependence on temperature and pH"

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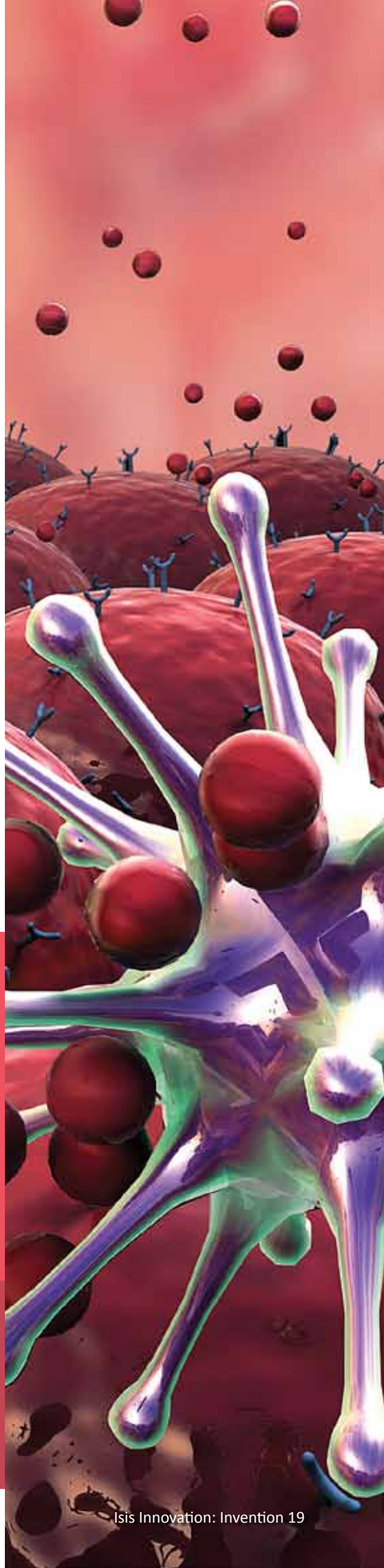

# Like water off a duck's back

A new surface modification method which can be used within a reel-to-reel process under vacuum. **Dr Andy Robertson** explains

**When drops of water are in contact with the feathers of a duck they simply roll off. The explanation is that complex microstructures and chemistry of the waterproof feather mean that the resulting surface energy prevents the spherical drop from spreading out on the feather's surface, ensuring that the still nearly spherical drop can simply roll away. One way to think about this is to consider the contact angle between the surface and the drop: an angle of 0° implying perfect wetting – the drop completely spreads across the surface. By modifying a surface, changing its surface energy and contact angle, we can influence its behaviour making it easier to wet, easier to glue to, or easier print on. One field in which these surface characteristics are critical to performance is that of polymer films.**

## Film features outstanding performance

Polymer films have a broad range of uses from packaging to electronics, automotive to building materials. Film manufacturers use multiple film layers and surface treatments to control surface energy, wetting, adhesion and a range of other parameters. Increasingly, complex structures including functional layers and devices containing organic thin-film layers are deposited onto polymer or other flexible substrates. In the case of creating organic thin film transistors, a particular problem is to modify the dielectric (insulator) layer to ensure that when the semiconductor layer is deposited on top, it performs well. Methods of doing this which are "solution-based" are known, but have proved difficult to use in large scale and at high yield. Yet these requirements are fundamental to the attraction of thin film, flexible, electronics. A new Oxford invention overcomes this problem by providing a surface modification method which can be used within the production environment i.e. in a reel-to-reel process under vacuum. The new process offers a number of benefits for film processors:

- Demonstrated ability to change surface energy within a high yield production process (images illustrate how processing increases the contact angle from 60° to 90°). This has broad application across a number of fields.

*(a) Original surface*

*(b) Modified surface*

- Improved transistor performance. Tests have demonstrated a factor of 3-5 times increase in hole mobility, e.g. from 0.08cm²/Vs for an untreated sample to 0.44cm²/Vs treated, with an improved threshold swing (1.0V/decade against 1.6V/decade) while maintaining the 100% production yield for these transistors.

- Reduced performance variability within a batch leading to better process capability for example compared to alternative processing techniques e.g. spin-coating.

The Oxford invention was aimed from the outset at high yield, high speed, production processes and although motivated by the challenges of producing organic thin film transistors, the invention has broad application.

## Patent status and commercial opportunities

The invention is the subject of UK patent application. Following successful spin coating trials, the method has been demonstrated on high yield production equipment with the substrate on a moving drum (simulating reel-to-reel behaviour). Funding is being sought to further develop the technique e.g. to understand the range of available materials and optimize processing parameters. This technology will be of interest to electronics companies and fast moving consumer goods companies, particularly those working in the field of organic thin film transistors, but also to others working in reel-to-reel film processing e.g. film converters and packaging manufacturers.

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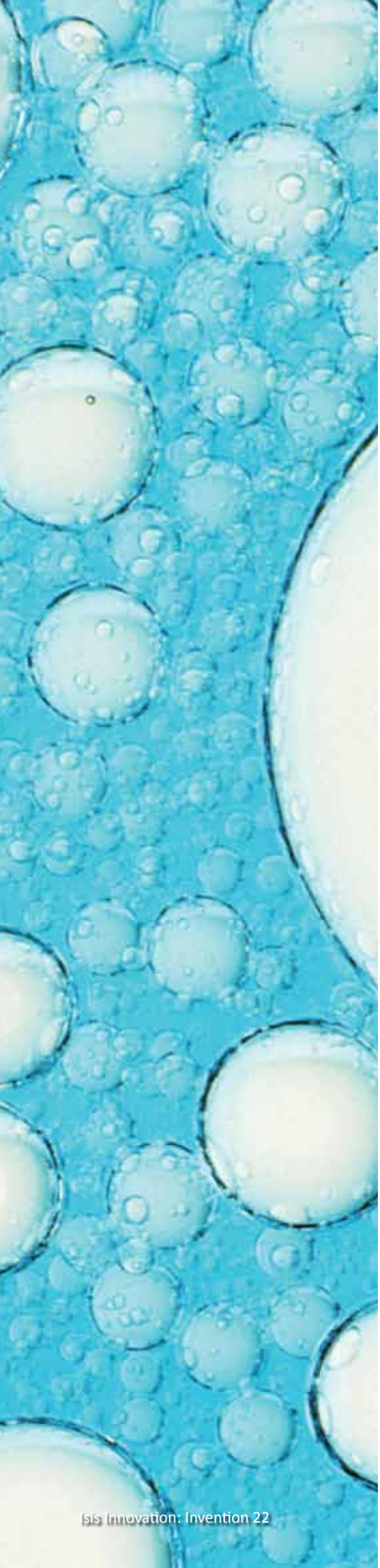

# Fluid analysis and monitoring

**Dr Gareth** Smith introduces a new sensor which offers the ability to conduct in-situ measurements of fluid samples with high sensitivity detection of contaminants

**With the increased reliance on automated technologies comes the need for sensors to monitor the operating conditions of systems. Highly sensitive and accurate monitoring of fluid quality and composition is a key requirement in many areas of technology as is the ability to conduct monitoring as a dynamic process.**

**Analysis of liquid samples has many applications. In-situ monitoring and sampling for analysis of fluids is key to industries ranging from healthcare to chemical engineering.**

## Cavity resonators as sensors

Microwave cavity resonators offer excellent sensitivity and have a range of potential applications in fluid monitoring through detection of change in the dielectric properties of samples entering them. This type of sensor offers the ability to conduct both static and dynamic in-line monitoring.

Scientists within the Department of Physics at the University of Oxford have developed a novel class of cavity sensor with a view to improving the study of liquid samples.

The device design incorporates a resonant microwave cavity weakly coupled to an amplifier with large gain. This is in turn coupled to a Robinson limiter, which is finally weakly coupled back to the resonant cavity to form a closed loop oscillator architecture.

## Commercial applications

### Aviation

Cold weather conditions during flights may lead to the formation of ice on critical aircraft components such as wings or jet inlets. Detection of ice formation can be achieved with the class of sensor described and offers the potential to reduce the use of fuel consuming heating systems and anti-icing fluids.

### Automotive

The range of fluids and the level of automation in cars and other road going vehicles means there are many applications requiring fluid sensors for monitoring purposes. A perfect example would be the detection of weak magnetic and non-magnetic contaminants as an indication of wear-and-tear in vehicle components. The Oxford sensor could also be used in dynamic monitoring of moisture build-up in brake fluid.

### Chemical Engineering

Monitoring of chemical reactions generally requires sampling for analysis offline. The Oxford sensor could be used to study chemical reactions through

changes in the dielectric constant of the composition. Additionally, the sensor could be adapted to work as an in-line detector for analytical chemistry systems.

### Medicine

The consistent and reproducible outputs from different detectors and the high sensitivity means that the Oxford sensor could be adapted to work as an in vitro diagnostic tool. For example it would be possible to detect cells specifically labelled with magnetic nanoparticles.

## Patent status and commercial opportunities

A granted patent exists in Europe and the USA. Isis would be keen to talk to companies interested in developing commercial opportunities for this technology. The technology readiness level is 2-3. Application engineering expertise is available to support the exploitation of the invention and to productise the technology with chosen industrial partners.

**Inventor Prof John Gregg described the sensor:**

*"The Robinson class of oscillators use innovative design to deliver precision engineering. Nonlinearity is "constructed" by the designer and implemented in a way that makes the oscillator performance independent of voltage, temperature and the individual devices used so that the product is both highly accurate and reproducible. A Robinson device operates to simultaneously produce two independent outputs that may be correlated with one another to deliver improved precision and reliability."*

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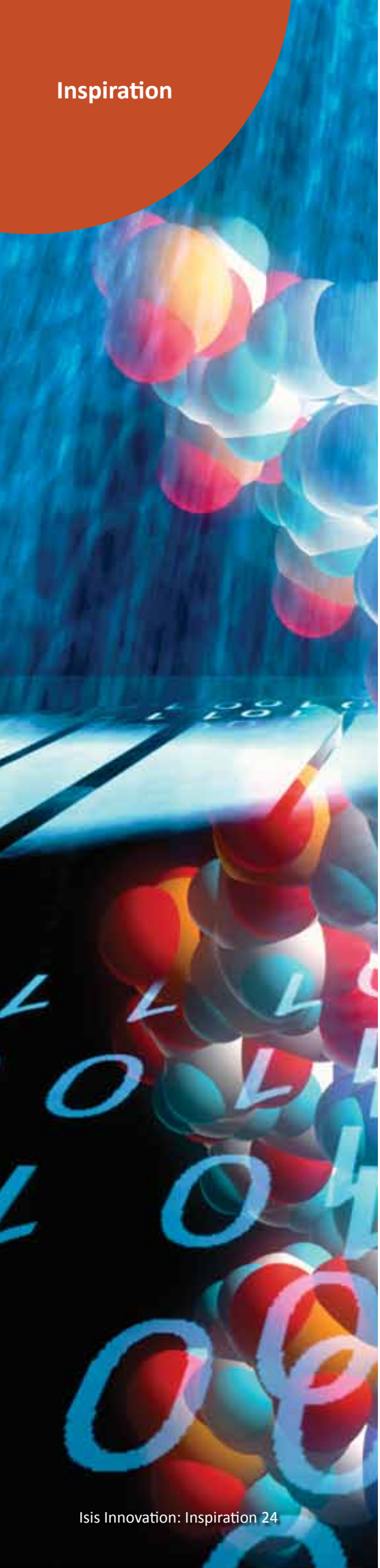

# Discovering new drug targets for rheumatoid arthritis

Persistent joint pain and swelling are common symptoms of rheumatoid arthritis (RA). PGXIS has been working with Professor Richard Williams to find new targets for drugs that will treat this significant disease. **Dr Josef Walker** explains

**Rheumatoid arthritis (RA) is a chronic condition that primarily involves painful, swollen joints and can have a debilitating effect on those individuals who develop it. Although the precise cause of the disease is not fully understood, the underlying mechanism is thought to be autoimmune in nature. The main methods for treating the symptoms include analgesics like paracetamol and anti-inflammatories like ibuprofen. These may be coupled with more potent disease modifying anti-rheumatic drugs (DMARDs) like methotrexate, corticosteroids and biological drugs including monoclonal antibodies that block tumour necrosis factor alpha (TNF-α) one of which is Humira®, the world's biggest selling drug in 2014.**

Although the current repertoire of therapies has made a significant impact on reducing the suffering of RA patients, a significant proportion of patients do not respond adequately, or develop tolerance to the treatments, which means that there is still a need for new treatments. With between 0.5% and 1% of adults in the developed world being affected by RA, this represents a significant unmet clinical need.

## Applying a different method

One company is seeking to break new ground in the search for novel RA therapies by taking a novel genomics approach, applying a unique computational method to a large set of genetic data generated from rheumatoid arthritis patients. PGXIS is a UK-based SME that has developed a novel technology called Taxonomy3®, a proprietary mathematical method that uses new algebra to identify and measure potential associations between different factors in highly complex datasets which might otherwise be undetectable.
The method can be applied in a range of settings including: predicting drug efficacy; predicting adverse events; and identifying and prioritising new drug targets. In the case of RA, PGXIS was seeking to identify interactions between different gene sequences, specific to RA, in order to find potential new drug targets in pathways of clinical relevance. To achieve this, PGXIS was able to use the excellent genetic dataset generated by the Wellcome Trust Case Control Consortium (www.wtccc.org), funded by the Wellcome Trust.

In April 2014, PGXIS was one of the few companies that was awarded a feasibility grant in a prior round of the Biomedical Catalyst fund from Innovate UK (previously the UK Technology Strategy Board (TSB)). The grant was available to UK academic institutions and SMEs seeking to move their research more quickly from discovery to commercialisation.

To maximise the chances of successfully identifying new drug targets, PGXIS

sought the help of Associate Professor Richard Williams, an expert in RA and the immunobiology of inflammation from the Kennedy Institute of Rheumatology at the University of Oxford. Professor Williams' research centres around the development of novel therapeutic strategies for treating RA, previously contributing to the successful development of anti-TNF-α therapies and now looking at TNF-α regulatory pathways and epigenetics with a view to combining treatment modalities to deliver long-term remission in RA patients.

## Discovery to commercialisation

A consultancy contract was put in place by Oxford University Consulting (OUC) to allow Professor Williams to work with the leadership team at PGIXS over a three-month period. The findings from the Taxonomy3® analysis of the RA genetic dataset provided an insight into the role that the genes, which they had identified as potential drug targets, might play in the context of the disease. Having successfully identified a number of suitable candidates and validated its method, PGXIS has spun-out its Taxonomy3® business into a new UK-based company, Adorial Ltd, which is in a strong position to seek additional funding to take this work to the next stage of development.

Reflecting on the project, Alun McCarthy, CEO of PGXIS said "We were delighted with the results of our collaboration with Prof Williams. His disease knowledge complemented our unique analysis technology excellently and we were able to identify a number of novel drug targets. We are looking forward to further collaboration with Prof Williams to progress these drug targets within Adorial Ltd".

Richard Williams added: "This consultancy has been extremely productive and has provided the foundation for a much longer-term collaboration. The Taxonomy3® analysis has identified novel therapeutic targets and our complementary skill-sets put us in an excellent position to validate these through further collaborative projects".

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# Argentinian training programme for technology managers

Isis Enterprise invited Argentinian technology innovation managers to learn about the Oxford commercialisation model. **Elena Andonova** explains

**Recently Isis Enterprise collaborated with GTec, the National Agency for the Promotion of Science and Technology in Argentina (Agencia Nacional de Promoción Científica y Tecnológica-ANPCyT), to develop a program on Technology Innovation Management. The programme focusses on the professional development of technology managers. It allows Argentinian universities to partner with the private sector in order to deliver a broad curriculum in innovation management to strengthen the technology transfer capabilities of their students. Since its inception in 2011, six programmes have run.**

In order to help the Agency achieve their goal, Isis Enterprise designed a six-week secondment programme for three Argentinian delegates in Oxford. The secondment was an effective way for the GTec delegates to gain hands-on technology transfer experience whilst learning about Intellectual Property protection and technology transfer project management, lessons from the market, licensing, spin-outs, and implementing successful internal marketing. It provided practical and detailed understanding of diverse aspects of technology transfer best practices, tailored to the delegates level of experience.

## Support and mentoring

During the first eight days, the delegates undertook intensive training, which helped them understand the strategy, operations and processes required to support technology transfer. Throughout the rest of the programme, Isis staff worked closely with the delegates to produce daily and weekly assignments based on real commercialisation projects from Oxford or other research organisations. Mentors were appointed to discuss, review and supervise the delegates progress on particular projects. The mentored assignments were tailored to the delegates specific individual desires and needs.

## Knowledge through interaction

Throughout the programme the three GTec delegates had opportunities to meet and interact with Isis technology transfer managers working on Oxford technologies, and senior managers of the business with the view to strengthen their understanding of working practices in technology transfer within Isis Innovation and Oxford, and visit centres of reference such as the Oxford Science Park. The GTec delegates were thereby exposed to Isis processes, procedures, and the Isis technology transfer culture as well as to the innovation and entrepreneurship ecosystems of Oxford and beyond.

## Appreciation and experience

Liza Peretti, one of the Argentinian delegates, commented “We had the opportunity to spend six weeks developing strategic capabilities, in order to bring back to our country some of the knowledge achieved by years of

## “The secondment programme has been a real inspiring and challenging experience for us”

experience and excellence in practice of technology transfer at Oxford. We expect to bring to our country the opportunity to capitalise on this experience in terms of enabling the enrichment of regional and national ecosystem.” Pablo Obreque and Iñaki Apezteguia found the interaction with the Oxford technology transfer professionals particularly useful, saying that, “The secondment programme has been a real inspiring and challenging experience for us.”

Isis Enterprise believes this secondment programme has indeed supported ANPCyT with its mission of promoting scientific and technological research and innovation, and hopes to continue its fruitful work with innovation stakeholders in Argentina, and expand its network and activities in the country as part of its continued development of a strong and lasting presence in Latin America.

Delegates who attended the six-week program were able to:

- Strengthen their understanding of the strategy and the operations required to promote and support technology transfer through interactions with Isis Enterprise project managers and the wider Isis staff;
- Improve their understanding of Intellectual Property, project analysis procedures, due diligence, and establishing the policies and systems needed to support technology transfer;
- Increase their knowledge, appreciation and experience of the day-to-day activities of a technology transfer office.

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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 17th September 2015
- Thursday 26th November 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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