News

Isis University of Oxford Innovation

Reviewing the latest innovations, collaborations
and technology transfer from Isis Innovation Limited
Edition 32 Winter 2001

New Look for Isis

Welcome to the winter edition of Isis Innovation News, which is the first public appearance of Isis Innovation's new visual identity. I am pleased to announce two new members of the Oxford Innovation Society: Samsung Advanced Institute of Technology and Hybaid.

The September meeting of the Oxford Innovation Society was held in the splendid new auditorium at Magdalen College followed by dinner in the rather more ancient, but no less splendid, College Hall. Several members have commented positively on the change of venue and we will continue to experiment from time to time with new locations.

At this meeting Professor Lionel Tarassenko's presentation on ***Neural networks in health monitoring: from jet engines to intensive care*** gave a fascinating insight of the applications of neural networks to simplify the interpretation of extremely complex data. Sir Peter Williams, Isis Chairman and Master of St Catherine's College described the challenges imposed by innovation and change and its impact on both University culture and University finances.

Isis Innovation continues to grow, there are now 20 of us including 10 Project Managers (and 10 Science doctorates). At the last count we were running 380 technology transfer projects so, as you can imagine, life at Isis is always exciting. I am pleased to announce that to help us we now have an in-house lawyer, Christine Beuermann. Christine benefits the Isis Project Managers, in that when they need advice on a licence or investment agreement they can now walk into her office rather than visiting the central Legal Services Office (LSO) and also benefits the LSO in that resources are freed for their many other duties.

Two new University owned enterprises, Business Liaison Unit and Oxford University Consulting Limited, have moved into Ewert House next door to Isis and are already referring new business links to us. A co-ordinated effort by the three units working closely with the University administration will provide a comprehensive support to both businesses and Oxford University researchers as they seek to work together for their mutual benefit.

I hope you enjoy this newsletter and look forward to receiving your comments.

Tim Cook

Dr Tim Cook
Managing Director, Isis Innovation

Neural Networks in Health Monitoring:
from Jet Engines to Intensive Care

Oxford Innovation Society Lecture – September 2000
Lionel Tarassenko, Professor of Electrical Engineering, University of Oxford

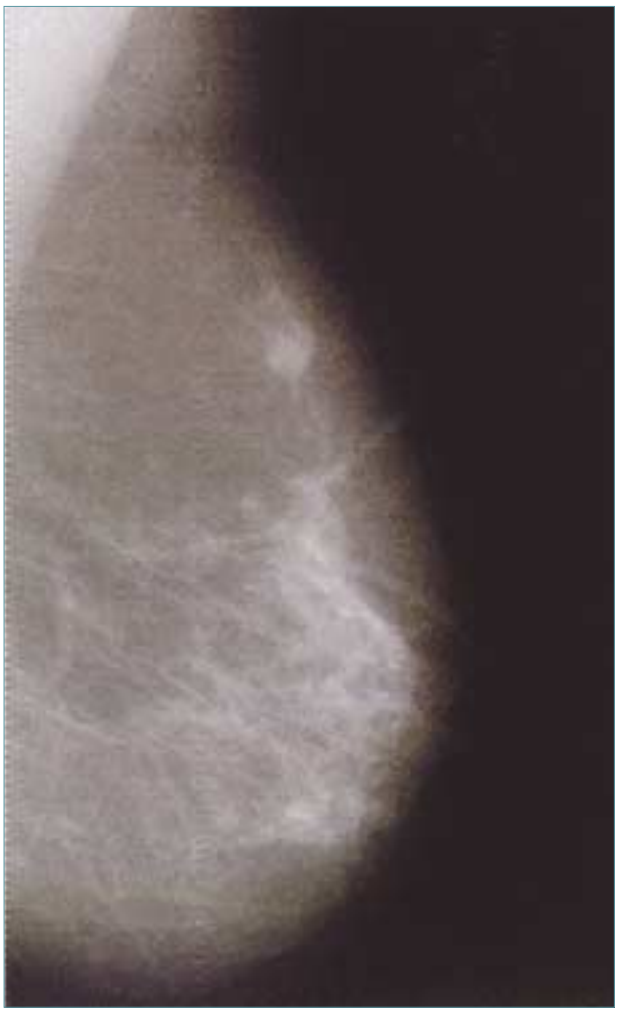
Introduction

Neural computing is a relatively new discipline which has arisen out of studies of how the brain processes information. Artificial neural networks consist of large numbers of small units ('neurons') with modifiable connections ('synapses'). With neural networks, the solution to a problem is learnt from a set of training examples using error correction to modify the synaptic weights. The most important property of neural networks is their ability to generalise, i.e. to generate the correct output response for an input pattern not previously seen.

The Signal Processing and Neural Networks Research Group in the Department of Engineering Science has been developing neural network techniques for health monitoring over the last decade. With high integrity systems such as jet engines or patients on a ward, conventional fault detection methods cannot be used for two main reasons: firstly, the most important examples (the abnormalities) are very rare; secondly, some of the 'fault conditions' may not have been seen before. We have therefore been pioneering a new approach whereby a description of normality is first of all learnt from a set of training examples displaying normal behaviour only and then new examples in the field are tested for novelty against this description. We have applied these novelty detection algorithms to a number of problems in the field of health monitoring, and three such examples will be described here: the detection of cancerous tumours in mammograms, the identification of abnormal vibration patterns during jet engine pass-off tests and the detection of abnormal beats in the electrocardiogram.

Mammography

Breast cancer is the major cause of death amongst women in the 35 to 55 age group. Early diagnosis greatly improves prognosis and so screening programmes have been instituted in many countries, including the USA and the UK. At the moment mammography remains the only viable imaging modality for screening large numbers of women. With the present screening policy, there are three million mammograms to be analysed each year in the UK; there is therefore a need for an automated analysis system which could highlight areas of interest. The aim is to develop a smart prompting system for use by a radiologist, not to try and replace him or her. The first step in novelty detection requires the extraction of a set of features which have some ability to discriminate between normal and abnormal tissue in the mammograms. These features have to be independent of the absolute pixel values in a given image as the images are not normalised against imaging conditions or breast thickness, remembering that a mammogram is a 2-D projection of a 3-D structure. The features fall into four main categories, which are related to the shape, texture, boundary and context of the bounded contours extracted from the images. Bounded contours are closed regions in the image which are of higher intensity than their neighbourhoods and could therefore correspond to tumours. The best description, in the statistical sense, of normality is the unconditional probability density function, $p(\mathbf{x})$, where $\mathbf{x}$ is a feature vector from normal data. If, subsequently a test vector $\mathbf{x}'$ from a new image belongs to a region of feature space for which $p(\mathbf{x}')$ is below a predetermined threshold, then that vector is deemed to be novel and the corresponding bounded contour will have a very high probability of representing abnormal tissue. There are a number of methods for obtaining probability density estimates, such as Gaussian mixture models and Parzen windows. The latter were used in our work because such a model requires fewer assumptions than the Gaussian mixture model. With the mammography data, however, the distribution of features, even for normal cases, is non-uniform and there are valid regions of feature space with low data density. If a global novelty threshold were used, feature vectors belonging to such regions would invariably be assessed as being novel, irrespective of how similar they might be to the training patterns in that region of feature space. The solution which was adopted was to make use of a local novelty threshold which depends on the data density in that region of feature space. This requires the feature space to be partitioned according to data density and for an estimate of the prob-



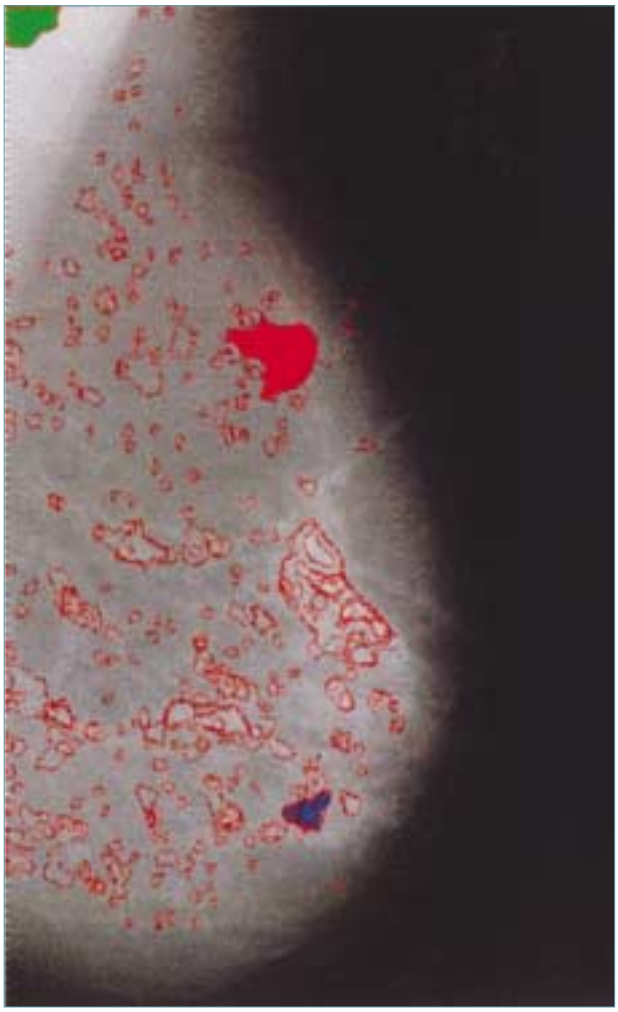


Figure 1: *Mammogram images 1a and 1b.*

ability density function to be calculated independently within each partition.

Approximately 120 images from a national database were analysed. Forty of these images contain a mass-like structure, subsequently confirmed as either benign or cancerous after biopsy. Twenty-four masses were chosen to analyse the discriminatory power of the features, the other sixteen being kept back to test the novelty detection model. The model was found to highlight correctly the regions of interest in each image which needed to be drawn to the attention of a human expert. All the masses investigated were identified as being novel (except for two failures of the bounded contour segmentation procedure). The level of false positives was reduced to just over one per image on average. A typical result is shown in Figure 1: Figure 1a shows the image of a breast in which a trained radiologist has identified a cancerous mass. Figure 1b shows all the bounded contours generated by the segmentation procedure, all of which are assessed as being normal except for the mass identified by the radiologist near the top of the breast which is classified as being highly novel by the algorithm (and hence shown in dark grey) and another, less novel, contour which may also be of interest to the radiologist.

There are three million mammograms to be analysed each year in the UK; there is therefore a need for an automated analysis system which could highlight areas of interest

Jet engine vibration analysis

Before a newly built jet engine is delivered to the customer, it is submitted to a number of pass-off tests, one of which records the vibration levels over the full range of operating speeds. The engine is mounted on a test bed and vibration gauges are attached to the casing of the engine, the speed of each shaft being measured by a tachometer. The engine is first accelerated from idle to full speed, and then decelerated back from full speed to idle. As the engine speed is changed, the tachometers are monitored continuously and measurements are recorded from the vibration gauges at consecutive engine speeds. Each set of vibration values is then transformed into an amplitude spectrum. The information contained in each of the three main vibration harmonics is encoded as a low-dimensional feature vector by calculating a weighted average over six equally spaced speed ranges, thereby creating an 18-dimensional shape vector describing the vibration signature of the engine. In our original work with Pegasus engines, there were only 52 healthy engines in the data base and hence any model of normality based on probability density estimation with 18 dimensional feature vectors would have far too many free parameters when there are only 52 training examples. Instead, we used a model of the distribution of the data in feature space with very few free parameters. The distribution of normal feature vectors was approximated by a small number of spherical clusters, the cluster centres being selected by applying a standard clustering algorithm. Each cluster radius is then calculated according to the data density within that cluster. The novelty of a test vector for a new engine is then given by its shortest normalised distance to a cluster centre, i.e. the distance to the nearest cluster centre is expressed as a multiple of the cluster radius in order to account for varying data densities in different regions of input space. If the test vector is sufficiently far from all the cluster centres, then it is in a region of input space in which there are very few training vectors and hence it is deemed to be novel. The novelty threshold is set so as just to accept all vectors in the training set. Figure 2 shows the results of applying our novelty detection algorithm to a Pegasus engine with an unusual peak in the vibration levels recorded from the high pressure shaft. The left-hand panel shows a pseudo 3-D vibration spectrogram, with grey level indicating the amplitude of vibration. The right-hand panel shows that the second peak in the vibration signature has been identified as novel, i.e. a normal vibration signature would not have such a peak at that engine speed.

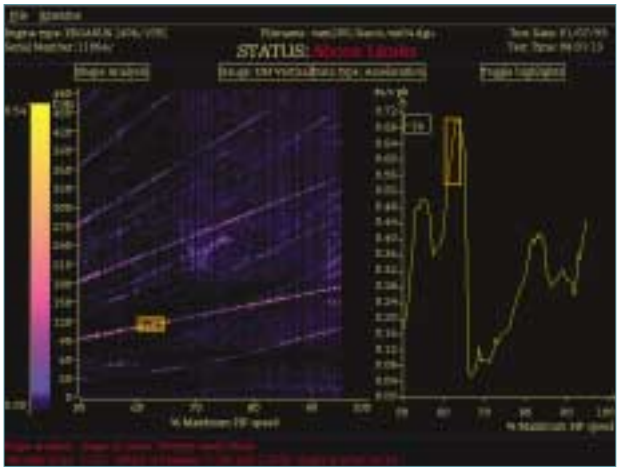


Figure 2: *Spectogram of Pegasus engine.*

Detection of abnormal heart beats

The electrocardiogram (ECG) is a characteristic waveform with a number of segments corresponding to the depolarisation and subsequent re-polarisation of various regions of the heart muscle. The dominant feature of the waveform is the high frequency spike known as the R wave in the middle of the QRS complex (see Figure 3a). The most common diagnostic use of the ECG is the identification of abnormal rhythms and heart rate computation is therefore a fundamental requirement of ECG analysis. Abnormal rhythms (arrhythmias) are often preceded by the occurrence of ectopic beats. These are beats which originate from a different region of the heart than that for normal beats. The most common type of ectopic beat is the ventricular ectopic beat (VEB), in which an ectopic beat in a ventricle gives rise an extra R wave, indicative of a premature ventricular contraction. It is important to try and detect these as reliably as possible, as they are often precursors of major arrhythmias. The shape of a VEB is usually that of a distorted QRS complex (see Figure 3b), but with an energy content sufficiently close to that of a normal beat that most VEBs trigger conventional QRS detectors. They are therefore mis-identified as normal beats and their presence in an ECG record is missed. We have shown that the output of an auto-associative neural network can be combined with that of a conventional QRS detection algorithm in order to identify VEBs correctly.

It is important to try and detect abnormal rhythms as reliably as possible

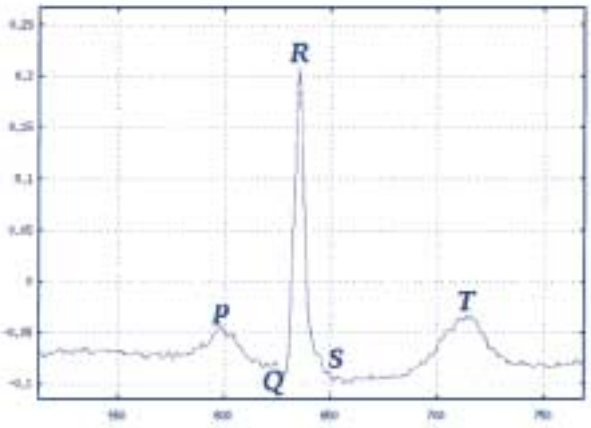


Figure 3a: *ECG waveform (with R wave peak).*

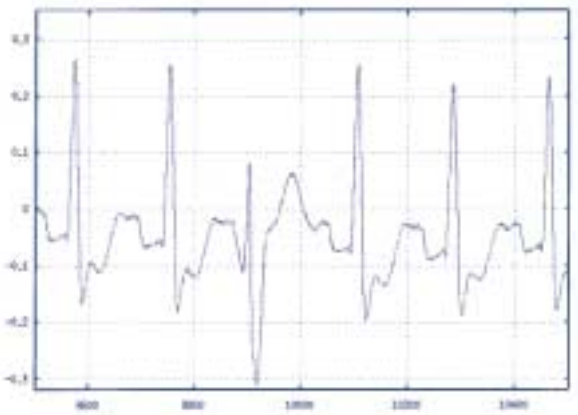


Figure 3b: *Distorted QRS complex (between 9800 and 10000).*

During learning, the auto-associative network is tuned to detect normal beats for the subject, so that the subtle abnormalities in shape of ectopic beats become clearly identifiable using the processed output of the trained network.

An auto-associative network is a neural network which learns to reproduce the input data at its output (in this case the ECG waveform centered on the R-peak). A multi-layer perceptron (MLP) configured as an auto-associative network can be trained to be a highly-tuned waveform matching system. As the auto-associative MLP is trained, it gradually learns the shape of a normal ECG waveform for that subject, including the allowable inter-beat variability. Once training is complete, all normal beats are reproduced at the output with a high degree of fidelity. When a distorted waveform caused by an ectopic beat is applied instead at the input of the trained MLP, the reconstructed waveform is very different from the input waveform. The difference between the input and output waveforms is quantified and used to identify ectopic beats. The auto-associative MLP can be trained on the first five minutes of ECG data, which makes it usable in clinical practice. With on-line learning, it is also possible for the MLP to adapt to the gradual changes in waveform morphology which can occur over several days of continuous monitoring.

Conclusion

In our current work on health monitoring, we are extending the concept of novelty detection so as to incorporate the fusion of multiple sources of data in order to produce more sensitive and robust indications of departure from normality. This research has been supported by Rolls-Royce and Oxford BioSignals (a University spin-off company set up in May 2000) in the context of two major projects. In the Rolls-Royce project, multiple sources of sensor data (performance parameters, vibration spectra and oil debris information) are being integrated in order to perform comprehensive whole-engine analysis and interpretation as part of a real-time in-flight monitoring system being developed for the Trent family of engines. In the project being funded by Oxford BioSignals, all the vital signs which can be recorded non-invasively (ECG, blood pressure, oxygen saturation, respiration and temperature) are being integrated in one instrument so that patient-adaptive models based on the fusion of these data can be developed. This will make it possible to track physiological instability and detect unexpected changes reliably, since robustness is increased as a result of using multiple sources of information. The first application of this work will be high-dependency care, which is aimed at patients who are generally considered too ill to be satisfactorily cared for on the wards but who fail to meet admission criteria for intensive care. Eventually the same novelty detection and data fusion techniques will be adapted for monitoring patients in their home environment.

Innovation and Change: Are we ready for it?

Oxford Innovation Society meeting – September 2000
Sir Peter Williams, Chairman of Isis Innovation, Master of St Catherine's College

Tim Cook has just described the recent developments at Isis Innovation and, although my own view is inevitably biased, there can be little doubt that progress over the last five years has been enormous. I will come back to this later.

Professor Lionel Tarassenko has just given us a great talk, for which many thanks. It is interesting to reflect that the last time he and I discussed the topic, I was an industrialist and he an academic. The situation is now nearer the other way round! The sleep monitor began life as a joint project between Lionel and Oxford Instruments of which I was then Chief Executive. I am pleased to say that Oxford Instruments now hold shares in Lionel's new spinout company in recognition for their contribution to the development.

Isis Innovation was actually founded in 1988 and those of us founder members who followed Peter Hirsch, Brian Smith, Martin Wood and David Cooksey well remember the beginning of the adventure. At the time it was all very new, different and exciting.

The Oxford Innovation Society, formed soon after, was very novel, and came well before the 1993 Government White Paper, but has provided a unique forum for the mixing of academia and industry with the objective of creating value, wealth (and fun).

Then in 1993 the Government White Paper raised suspicions (even from me on the industrial side of the fence) that over-concentration on wealth creation was a threat to pure science. Still today we constantly need to confirm the central theme of the importance of scholarship and research.

Since then important lessons have been learnt. Wealth creation and scholarship are not mutually exclusive, in fact they are complementary. Hence, I now look like Lionel Tarrasenko 10 years ago and he is more like a tycoon (only younger, life is so unfair!). The boundaries are now, rightly, becoming blurred.

The situation was not always so and Tim Cook's contribution over the last three years in helping the process has been significant. The agenda of synergy between Isis and the University is crucial and we need to work at it continuously.

Nevertheless, now might seem the moment to celebrate and party. Tim quoted some impressive statistics, £2 billion valuation of Oxford University spinouts. Oxford University owns £80 million of quoted shares in these, and we believe that other Universities have not created anywhere near this value. With creative thinking wealth can be generated from all corners of the University, from Old Norse to nano-technology. An important aspect of the wealth generated from spinouts is that it is money that is not earmarked so it greatly enhances the financial freedom of the University.

Innovation is a process of change but the process must be continuous and in the right direction

But Isis Innovation's style is not to dwell on temporary success, which is very ephemeral in any case. Innovation is a process of change – Isis was a fresh idea 10 years ago – but the process must be continuous and in the right direction. We have changed the nature of the debate on IPR exploitation in Oxford, but what next? Isis is continuing to evolve; the relocation in January, new staff, expansion of facilities, and ambitious future goals. Above all Isis is becoming central to the agenda of change in the University as a whole.

AD 2000 was not a good year for the home team here in Oxford with the access debate and so forth. This was a reminder that even a great institution like Oxford University cannot rest on its laurels any more than can Isis Innovation. But change is in the air for the University as a whole and for all the UK university system, particularly concerning the issues of finances and independence – freedoms and opportunities. The Russell Group is dis-

From left to right: *Lionel Tarassenko, Professor of Electrical Engineering; Sir Peter Williams, Chairman of Isis Innovation; Dr Tim Cook, Managing Director of Isis Innovation, at the September meeting of the OIS.*

cussing top up fees and independence from government in directing their destinies but how is this to be achieved?

One approach might be to wait for the 'Tory endowment'. Whilst an idea with some merits, I do not think it is the complete answer and in any case we can't wait. So where can we find financial independence? One approach would be a modified fee structure, but this is only a personal view and we shall see whether it is the answer. Alternatively we could step up fund raising, an activity increasingly central to all universities. The successors to the Campaign for Oxford continue.

I believe that in the long term Isis Innovation must be a key part of the answer. If the University can create £80 million in the last ten years what can we achieve with the 'new Isis' in the next ten? Another key part is the philosophy of the 'agenda of change' running through the University as a whole.

There is still an unsupportable press view of Oxford as elitist, isolated, arrogant and self-centred. The modern reality is that we strive to be excellent (not elitist), confident (not arrogant), self-aware (not self-centred) and integrated (not isolated). Isis and its spinouts foster links with the 'real world'. Increasingly universities, in partnership with outside bodies, are actually a strategic part of this 'real world'. The Oxford Innovation Society is an unique feature of this relationship – hence your presence here tonight.

So look at Lionel Tarassenko's work – abstruse maths with links to healthcare and aerospace. There is no compromise here on excellence or relevance. Oxford University is a great place 'to do business' and remains a great place to pursue scholarship and learning.

A Simplified Scheme for Quantum Computing

Researchers at the University of Oxford's Centre for Quantum Computation have brought Quantum Computing closer to reality with a simplified signal addressing system

Background

Information is a physical quantity, and the processing of information is ultimately governed by quantum mechanics. Conventional computers fail to take advantage of this 'physics of information'. For certain problems such as factorising large numbers (say >500 digits), an important task in code breaking, a quantum computer having just one megabyte of quantum bits, or 'qubits' could achieve what would be impossible with a conventional computer built from all the atoms in the Universe.

Problem

At present only quantum computers having a maximum of 5 qubits have been successfully built. The main challenge is that quantum computers are subject to 'decoherence', or the degradation of quantum information to regular information.

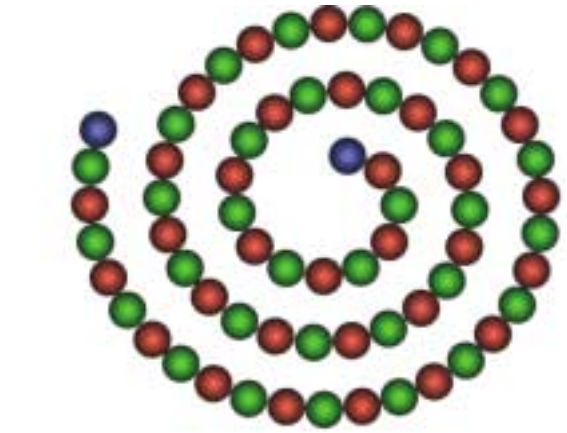
Manipulating individual qubits is a demanding task for many computer designs, whether they be solid state devices or, for example, molecular systems. The former are limited by the use of metallic contacts that may cause decoherence and the latter because the qubits cannot be addressed separately.

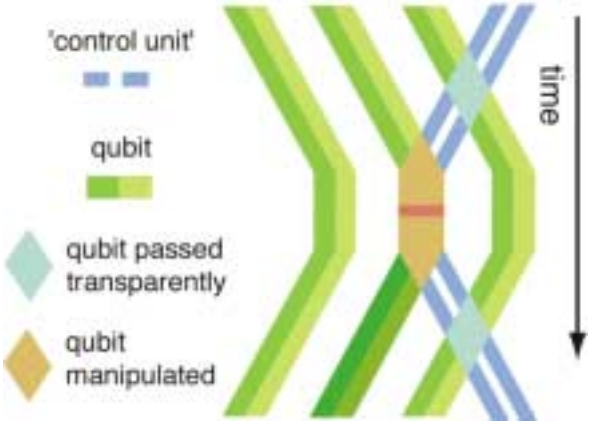
The Oxford Invention

The new Oxford scheme allows quantum computing to occur without the need to address qubits individually. A coiled linear array e.g. a linear molecule, as opposite, can address all qubits simultaneously. Special encoding of the stored information along with a sequence of global control signals, e.g. EM pulses, moves and manipulates the information as in the lower diagram.

The Oxford invention has an attractively simple overall array structure and allows different calculations to occur simultaneously at different places throughout the device; this is important for error correction.

Thus, global control is now a highly attractive and practical solution to the problems stated earlier.





the ultimate in process miniaturisation

Although aimed at making quantum computers more practical the invention could also be applied to processing conventional information on an atomic scale: the ultimate in process miniaturisation.

Commercialisation Opportunity

This invention is subject to a patent application, and companies interested in developing and utilising the work are invited to contact Isis Innovation for further discussion.

Fabrication of High Resolution Printed Circuit Boards

By precise control of the etching process Oxford inventors have made the reliable production of High Resolution Printed Circuit Boards (PCBs) with conductors down to 10 µm wide more of a cost effective reality

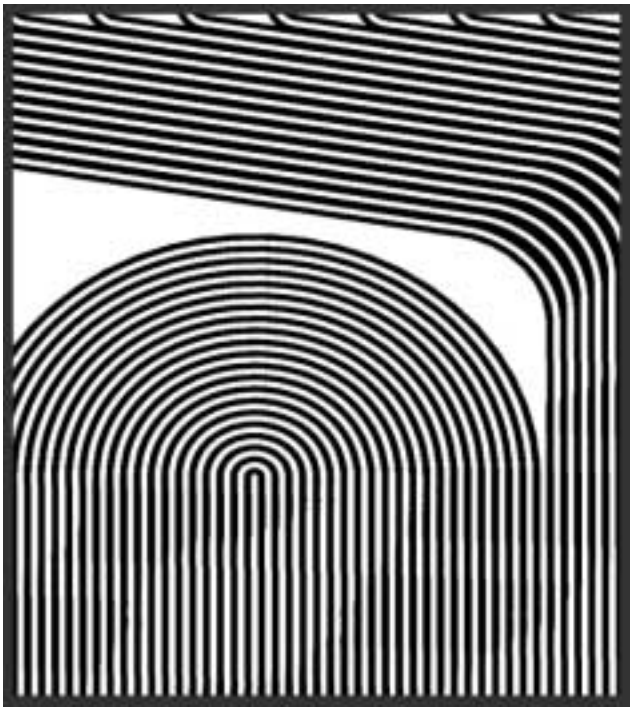
Introduction

With ever increasing demands for greater miniaturisation and the use of flexible circuitry the need for improved fabrication methods for high resolution printed circuit boards is becoming more important. PCBs currently include conductors as narrow as 150 µm, but there is now a requirement for conductors to be as narrow as 25 µm and even down to 10 µm. With current manufacturing techniques it is not possible to attain the required precision especially where the spacing between the conductors varies. The etching rate is highest where the conductors are furthest apart. This leads to over-etching and subsequent under-cutting of these very fine conductors in these areas. The resultant PCB has copper conductors of variable width, and its performance is, therefore, not optimum.

By controlling the etch conditions and the area to be etched the Oxford inventors have reduced the amount of over-etching to an acceptable level and under-cutting has been virtually eliminated

The Technology

By controlling the etch conditions and the area to be etched the Oxford inventors have reduced the amount of over-etching to an acceptable level and under-cutting has been virtually eliminated. The spaces between the conductors are now all of uniform width, but with more redundant copper remaining on the PCB; the etching has been confined to narrow tracks. In the magnified view of an actual PCB the white areas represent the exposed copper tracks, while the black show the intervening non-conducting substrate.



Benefits

This technology will benefit many of the applications that now demand PCBs with fine conductors or alternatively require flexible circuitry to facilitate yet further miniaturisation. Typically these include applications such as mobile phones, personal flip-top organisers and inkjet printers.

Commercialisation Opportunity

This invention is now the subject of a patent application and companies interested in developing this technology commercially are invited to contact Isis Innovation.

Surface Tension

This invention describes a novel method for the indirect measurement of surface tension by means of surface configuration assessment. The procedure is reliable, repeatable and quick to set-up and use. In addition it is contactless and non-destructive

Background

Surface tension measurement is an important tool in the characterisation of surface-active liquids and mixtures. There are currently a number of well-established techniques which are used commercially.

Problem

Although precise, the traditional measuring methods suffer from several problems. The volume of sample required may be many millilitres; sample recovery may be difficult or impossible. Furthermore, existing methods are usually time-consuming, manual, difficult to automate and unsuitable for hazardous samples.

The Oxford Invention

A research group at the University of Oxford has developed a novel method of measuring the surface tension of liquid utilising a multiwell plate reader. The invention is based upon the effect of variation of reflected or transmitted light intensity as a function of the angle of incidence of light on a sample's surface. This will provide a measurement of the surface configuration and hence surface tension.

Existing methods are usually time-consuming, manual, difficult to automate and unsuitable for hazardous samples.

The method improves on current techniques in several commercially relevant areas:

* Reduced sample size – microlitres vs. millilitres.
* Reduced measurement time – milliseconds vs. minutes per sample.

Inventors Dr David Vaux and Mr Matt Cottingham.

* High throughput for samples arrayed on 96 well microplates.
* Sensitivity – surface active detergent can be detected down to 1ppm.
* Facile automation leading to remote handling of toxic/infectious materials.
* Possible adaptation to incorporate atmospheric (pressure /gas) changes.

This technology will be potentially interesting to the multi-well plate reader business, manufacturers of surface tension measuring equipment and the surfactant/detergent industry. In addition, the standard usage of plate readers in the biotechnology industry may also be improved.

Commercialisation Opportunity

This discovery is subject to a patent application. Isis Innovation is interested in discussing suitable arrangements with companies able to utilise this technology.

Escherichia coli colonisation factors

Therapeutic areas: Enteric, urinary and systemic diseases caused by Escherichia coli and/or other enteric bacteria, neonatal meningitis and Gram-negative bacteraemia

Dr Angela Kukula, who has recently joined Isis Innovation, is the current Project Manager for this technology.

Background

Escherichia coli is by far the most common cause of a wide range of enteric and urinary diseases such as acute and persistent diarrhoea, urinary track infections and neonatal meningitis. For example, travellers' diarrhoea is typically caused by *E. coli*.

Colonisation of the host is a fundamental step to *E. coli* pathogenesis. It has been demonstrated that *E. coli* possesses a number of virulence factors (e.g. adhesion) that enhance its ability to cause infection. Identification of the genes involved in colonisation may provide important data for the development of novel antibacterial therapies and vaccine strategies.

The Oxford Invention

Research at the University of Oxford has identified *E. coli* gene sequences that are involved in colonisation during infection.

Identification of the genes involved in colonisation may provide important data for the development of novel antibacterial therapies and vaccine strategies

Applications

1) Manufacture of a medicament
The peptides encoded by any of the genes of the invention may have therapeutic use, particularly in the manufacture of medicaments or pharmaceuticals to treat bacterial infection.

2) Antibacterial vaccine
The invention may allow the development of attenuated vaccines by, for example, comprising a microorganism having a virulence gene deletion.

Commercialisation Opportunity

The patent application is available for licensing. Enquiries from potential partners wishing to commercially exploit this technology will be welcomed.

Novel Bacterial Polysaccharides

Application Areas: Modified celluloses for a wide range of industrial uses, e.g. food and cosmetic sectors (e.g. thickening agents and moisture retention), medical applications (wound dressings & artificial arteries), materials (filter membranes & special paper)

Background

Cellulose and modified celluloses are valuable industrial polymers. It is known that the precise structure of these products is important in determining their physical properties. Traditionally they are produced by chemical extraction methods applied to plants or by fermentation of *Acetobacter*, the only cellulose producing bacterium exploited by industry.

The Oxford Invention

Research has identified methods for identifying bacteria with latent abilities to produce cellulose-based polymers. In particular *Pseudomonas fluorescens* has been shown to contain genes coding for a substituted glucan polymer that are expressed in certain conditions. Knowledge of the genetic basis of polymer production allows 'designer' polymers to be synthesised and discovery of regulatory proteins allows polymer production to be controlled. *P. fluorescens* is easier to culture than *Acetobacter* and therefore not only provides a vehicle for an enhanced range of industrially useful polymers but also provides a superior production capability.

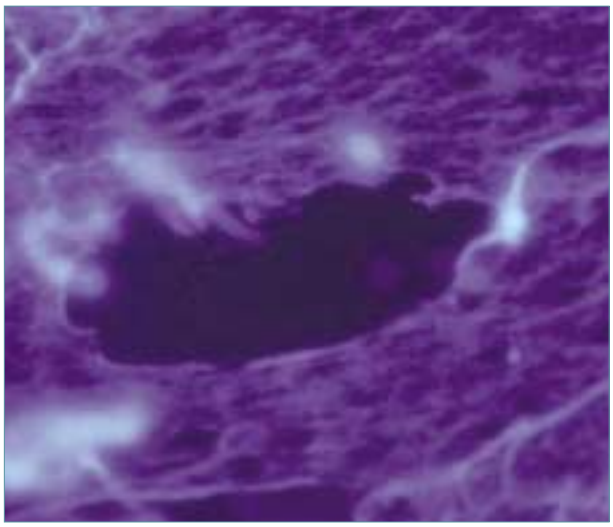
Applications

1) Isolation of polysaccharide-producing bacterial strains
The invention allows the development of a method for the isolation of bacterial strains (such as *Pseudomonas* and *E. coli*) capable of producing large amounts of a particular type of exopolysaccharide.

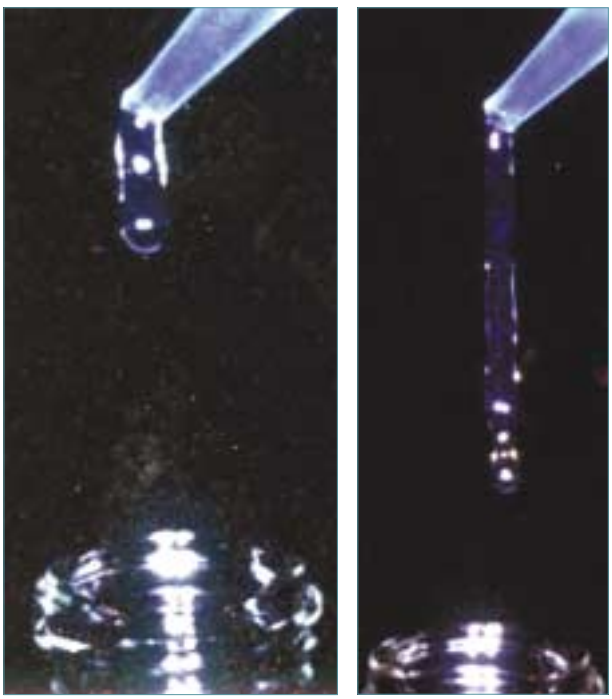
2) Biotechnological potential
The invention will enable production of modified celluloses of known specific structure. This opens up possibilities for new designer polymer products for different industrial sectors. In addition, by understanding the genetic control of exopolysaccharide synthesis this invention will enable regulation of the development of biofilms, this could, for example, alleviate problems in industrial plant in which biofouling occurs (e.g. paper making).

Commercialisation Opportunity

Patent applications are available for licensing and we are actively seeking partners for the commercial development of this technology.



An example of novel bacterial polysaccharides **above:** *stained with the cellulose-specific stain calcofluor (fluorescent microscopy) and* **below:** *a sample dripping from a pippette.*



Medical device for treatment of dislocated shoulders

Therapeutic Areas: Dislocated shoulders and associated injuries

Background

Shoulder dislocation is one of the most common sporting and general accident injuries.

Typical procedures used for relocating dislocated shoulders can involve a great deal of force and this in turn can further weaken the shoulder. For example, with young people (<20 years) there is an 80 – 90% chance of recurring dislocation and a permanent weakness developing.

A better procedure is needed to minimise the pain and damage done in relocating dislocated shoulders. Furthermore, with an improved procedure and customised relocating devices the need for analgesic drugs will be minimised or even negated and the hospital time per patient could be greatly reduced.

The Oxford Invention

Research led by Dr Philip Hormbrey, a consultant of the Accident and Emergency department of the John Radcliffe hospital, has resulted in the development of a novel device for the rapid and relatively painless treatment of dislocated shoulders. This innovative device greatly reduces the force required for relocating shoulders by using a combination of optimal positioning of the arm relative to the torso and using the patients' own body weight as a lever.

Trials have resulted in considerably reduced pain for the patient and therefore less need for analgesics. Also, the use of this novel medical device minimises any peripheral shoulder damage that can occur with traditional relocation practices.

Commercialisation Opportunity

Patent applications are available for licensing and we are actively seeking partners for commercial development of this technology opportunity.

This novel medical device minimises any peripheral shoulder damage that can occur with traditional relocation practices

Dr Mark Payton, who has recently joined Isis Innovation, is the current Project Manager for this technology.

An exciting year for Oxford Medical Image Analysis

Oxford University and Sir Martin and Lady Wood provided seed funding for Oxford Medical Image Analysis – OMIA – in December 1999. With this investment the business developed rapidly in 2000

We are now pleased to announce that OMIA and Isis Innovation have entered into licence agreements for separate developments by Professor Mike Brady and Dr Alison Noble of the University's Medical Vision Laboratory on the processing of medical image data. This and previous work provides support for OMIA's current and future product developments.

OMIA's first product, **Ridgex**®, is being integrated into the tumour diagnosis and treatment systems of three leading manufacturers of imaging and of radiotherapy equipment. **Ridgex**® is expected to go into clinical use during the first half of 2001, following clinical trials and then be made available under a quality system compliant with ISO 9001. **Ridgex**® attracted great interest at the meeting of the Radiological Society of North America in Chicago in December 2000.

Quamus®, OMIA's system for analysing and quantifying ultrasound images of the heart, moved into second stage clinical trials in March 2000. A new screen interface, with comprehensive facilities to present the quantification of the echocardiograms, has been well received by clinicians. The American Heart Association meeting in November 2000 once again confirmed that cardiologists want to use echocardiograms to quantify heart function. As a result, all the main echocardiograph equipment manufacturers are showing strong interest in **Quamus**®.

The next version of **Quamus**®, which is due to go to our clinical trial clinicians in March 2001, will offer substantially enhanced capabilities. The development of **Quamus**® is supported both by the European Commission and by the DTI under the SMART award programme.

The team at OMIA.

Having applied for a patent over the summer of 2000, OMIA developed a prototype of its **e-Mage**™ system. This enables the exchange and comparison of image analysis data over the Internet. This will be used first in the **Quamus**® clinical trials.

OMIA is currently in active negotiation in relation to the next round of funding.

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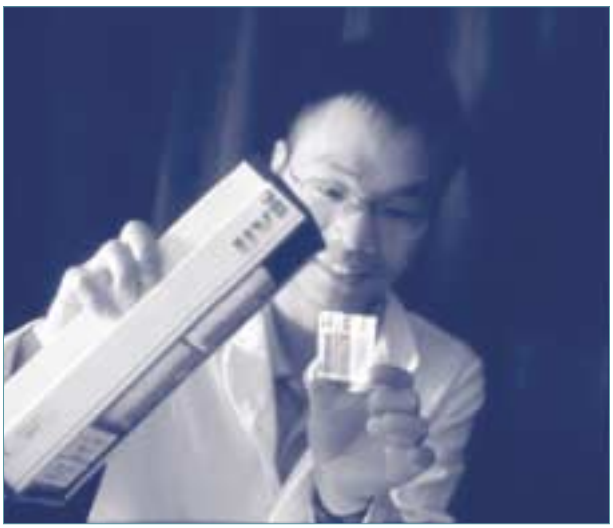
Opsys Limited

Three Licence Agreements On Electroluminescent Compounds



We are pleased to announce that Opsys Limited, the Oxford based displays technology company, has taken out a further three licences from Isis Innovation since July 2000. These licences cover recent developments made in two different areas of organic electroluminescent materials research: light emitting dendrimers and complexes of lanthanide metal ions. Following the completion of these licences, Opsys has sublicensed selected materials to H. W. Sands Corporation, a US speciality chemicals supplier to the displays industry.

This brings number of patents now licensed to Opsys to five. The rate at which licences are being concluded results from the significant level of research being funded directly by Opsys into organic electroluminescent compounds in several research groups, both in the Department of Chemistry and the Department of Materials at the University of Oxford and also at the School of Physics and Astronomy at the University of St Andrews.

Opsys Limited is a University of Oxford spin-out company, founded in October 1997 to develop and commercialise novel display technology based on new classes of light emitting materials and designs. Organic electroluminescent technology, also known as OLEDs (Organic Light Emitting Diodes), offers significant advantages over the LCDs commonly found in portable products such as mobile phones, personal organisers and laptop computers. OLEDs comprise a single light emitting layer, which combines uniform brightness and colour purity with a low operating voltage and high efficiency. Opsys' goal is to develop colour OLED displays which will be significantly lighter, thinner, and cheaper to produce than existing technologies, and which will be ideal not only for portable products such as laptop computers but, in the longer term, for larger screens such as televisions and desktop monitors.

The market for flat screen display technologies is expected to grow rapidly from its current estimated level of $13 billion to $70 billion by 2005.

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Oxford Biosensors

Fast, point of care diagnostics with a minimum of blood, sweat and tears

New technology pioneered by the University of Oxford is being exploited commercially by the latest spinout: Oxford Biosensors. The technology's combination of speed, small size and broad application will create new markets in life-science diagnostics.

Oxford Biosensors, after only six months of operation is now testing the first prototype instrument and by the summer of 2001 a dozen prototypes will be available for field-testing and proof of principle. The system will include a hand held instrument about the size of a mobile phone into which small, low cost and disposable test strips are inserted. Whereas today, on dry enzymatic test strips only one sensor can be placed, this technology will allow many different sensors to be placed, measuring groups of parameters. In clinical diagnostics this will enable medics or nurses to test for the presence and quantity of multiple substances in the tiniest drop of blood rather than drawing a vial of blood that then needs to be sent to the Pathology Laboratory.

Point of Care testing is already viewed as having clear benefits in eliminating unnecessary time and money and at the same time improving the patient information feedback, this technology will make the process more convenient and affordable with pocket sized units.

Although the company will not disclose its intended first application, it's interesting to consider potential uses. Imagine a test strip that can be used by paramedics transporting an overdose casualty to hospital, which can identify the presence of any of the top ten substances used in 90% of all over-doses. The results can be transmitted by mobile communi-cations to a medic who can prepare for treatment and save valuable time for the patient.

As well as delivering potential clinical solutions, this technology can also be applied to broader health care markets. With the convenience of small size and low weight athletes and serious gym enthusiasts may in future be able to measure not one but a number of parameters to determine if their exercise regime could be improved through the measurement of a number of parameters, this could be from a finger prick type blood test, or even a saliva/sweat test.

The core technology resulted from the integration of three equally important disciplines: Enzyme development, Electrochemistry and Micro-engineering within Oxford University's Departments of Engineering and Chemistry. Oxford is at the forefront of research in these fields; the University's pioneering work in electrochemical identification of glucose helped establish a diabetic control market that today turns over more than $2 billion, and improves quality of life for millions.

Imagine a test strip that can be used by paramedics transporting an overdose casualty to hospital, which can identify the presence of any of the top ten substances used in 90% of all overdoses

Oxford University academics Professor Allen Hill, Professor Peter Dobson, Dr Luet Wong and Dr Peter Leigh are Non-Executive Directors of the company. Professor Allen Hill commented, 'We have worked on this technology for a number of years and expect rapid progress to the initial prototypes. With the continuing progress in computer aided molecular modelling as well as genetic adaptation of chemical sensors the development time is accelerating, facilitating the rapid development of market specific test strips'.

Neil Butler, MD of the company said: 'The combination of a very strong technology base and a market that needs cost-effective and fast diagnoses makes our mission simple, adapting the technology to meet those market needs. We have world-class scientific knowledge in our field and there is no technology like this in the market today. The progress being made is excellent'.

Dr Tim Cook, Managing Director of Isis Innovation Ltd, the University of Oxford's technology transfer company said: 'This is the University's fourteenth spin out in the last three years and the third involving some level of funding from the University Challenge Seed Fund. We are delighted that we have succeeded in helping to form this Company which will bring advanced sensor technology to the market for the benefit of patients and industry, as well as the academics concerned and the University'.

Brian Pohl, Director of Arlington Group plc, a major investor in the business said: 'Investing in new Biotechnology businesses is viewed by many as a high risk investment due to the uncertainty of the technology and time frames. We found Oxford Biosensors attractive because of the strong Intellectual Property, and the tangible nature of the market. Also the participants have outstanding backgrounds and firmly believe in their abilities to commercialise the technology, as we do'.

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Nortran

Nortran Pharmaceuticals take option to Oxford heart therapeutic technology

A novel structural basis for class III anti-arrhythmia therapeutic molecules has been identified by research within Oxford University's Department of Pharmacology. Drs Terrar, Gill & Mamas have synthesised and tested molecules combining potassium and calcium channel blocking activity. The novel molecular structures have been shown to demonstrate anti-arrhythmic activity. Through careful modulation of their potassium and calcium ion blocking properties, via precise molecular composition, these new compounds have the promise of at least matching the best of the currently available class III drugs but with the added benefit of minimal, if any, pro-arrhythmic side effects.

Nortran Pharmaceuticals Inc. have taken an option to the Oxford technology. Nortran is a Canadian pharmaceutical company built around a proven approach to drug discovery, a low-risk business strategy, and a focus on major unmet medical needs through expertise in the area of ion channels. Current Nortran drugs in development target life-threatening arrhythmia of the heart and intractable cough. Nortran works in the cardiovascular, and respiratory areas with its lead programmes in the area of cardiac arrhythmia drugs and acute unproductive cough. In its programme to treat life-threatening cardiac arrhythmia, Nortran has developed drug candidates suitable for clinical testing as treatments for atrial arrhythmia.

Nortran's Sheila Grant says, 'We are very excited by the promise of the Oxford work. Nortran and Oxford will be working together in the next few months to validate the technology. It is hoped to enter a full licensing agreement once critical evaluation steps have been completed'.

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Other News: New Neighbours

The University's Business Liaison Unit moves in next door

Isis gained a new neighbour recently, when the University's Business Liaison Unit (BLU) moved in next door at Ewert House. The Unit was set up last year to boost Oxford University's links with the local business community, and became fully operational in October 2000 with the recruitment of two new Business Liaison Managers.

The Business Liaison Unit will be the University's Gateway for Business, forging new links between the University and businesses in the region – particularly small and medium-sized enterprises in the high-tech sector. In addition to promoting industrial contacts and raising the University's profile within the local business community, the team will be making sure that local businesses can benefit fully from the research, consultancy and support which the University can already offer, and will help advise on access to University resources.

So exactly how does the new Business Liaison Unit differ from Isis Innovation and the other University units which already have excellent links with industry? It might be useful at this point to look at the Unit's main aim: 'to create and develop new, sustainable and mutually beneficial relationships between the University of Oxford and the regional business community'.

You have only to look at the list of technologies licensed through Isis to know that there are already many successful academic / industrial partnerships with thriving offspring

The key words are new, regional and the University. 'New' because the Business Liaison Unit will be actively seeking out companies with no existing links with the University – or, where a link does exist, to see if that link might be extended into other areas of the University's activities. 'Regional' because the Unit's remit is to focus on businesses within the geographic area covering Oxfordshire and neighbouring counties. 'The University' because the Unit will be proactively helping companies to identify where their own needs might find a solution from the full range of University resources.

You have only to look at the list of technologies licensed through Isis, or the levels of research income now handled by the Research Services Office, to know that there are already many successful academic/industrial partnerships with thriving offspring. However, there are many potential partnerships that have not yet seen the light of day – and that's where the BLU comes in.

The range of resources offered by the University to business is extensive. It includes test facilities, expert help in the analysis or interpretation of results, consultancy and technologies across the spectrum – from those that are well-established to fledgling R&D needing substantial further development within the University. There are opportunities for student projects and graduate or student employment – through work placements, vacation or permanent employment. In staff development terms the University offers an extensive range of professional development and executive education opportunities, as well as staff secondment to or from companies and the chance to network through seminars and meetings.

The Unit is led by the University's Regional Liaison Director, Joe Barclay, supported by two Business Liaison Managers: Dr John Coyle for the physical sciences and Dr Mark Bowman for life sciences. Both John Coyle and Mark Bowman are themselves Oxford chemistry graduates, and John is already a familiar figure with local businesses from his previous role as Innovation and Technology Counsellor at Business Link Heart of England. Before Business Link, John was Deputy Director of Research and General Manager of the Cookson Technology Centre, based at the Begbroke site where the University has recently opened its new Business and Science Park.

Mark Bowman joins the Unit from the Western Arc BioScience Platform, a five-university consortium which

includes Cardiff, Bristol and Bath. The consortium successfully competed for pump-priming funds in 1997 through the DTI's Biotechnology Exploitation Platform to facilitate additional technology transfer activity in the area. Mark gained his Ph.D. from the Welsh School of Pharmacy and followed this with two years' industrially-funded medicinal chemistry research.

The BLU has ring-fenced government funding through the HEROBAC initiative (Higher Education Reach-out to Business and the Community), which allows it to operate as a dedicated business development resource for the whole of the University. It has received the support of many regional agencies, who endorse the view that the BLU has a key role to play as an engine of regional economic growth, and also in helping raise academic awareness of business needs.

Two further recent initiatives to help promote the University's links with business are the Faraday Partnerships and Oxford Entrepreneurs. Oxford University is a key player in two of the four new Faraday Partnerships, which aim to link universities and industry, ensuring a continuous flow of research, technologies and skilled personnel, building effective networks and increasing universities' awareness of industry's new technology requirements. The University's Saïd Business School is also to host a new Science Enterprise Centre (Oxford Entrepreneurs), which aims to stimulate scientific entrepreneurship and develop business expertise in science.

Joe Barclay, the University's Regional Liaison Director.

If you think the Business Liaison Unit might be able to help you, please contact us on (0)1865 280862 or e-mail nicola.shepard @admin.ox.ac.uk for further information.

Legal Services Offices

Appointment of Isis lawyer

Peter Webber, Frances Barnwell, Christine Beuermann, Carolyn McKee and Jonathan Anelay of the Legal Services Office.

Towards the end of September the University's Legal Services Office recruited Christine Beuermann from the London firm of Slaughter & May in order to handle the legal business of Isis. Christine is an Australian lawyer who is obtaining dual qualification in this country. She has degrees in law and commerce from Griffith University, Queensland, and a BCL first class honours from Oxford. She will be based in Ewert House, and will work with the Isis Project Managers on licensing deals and the negotiation of spin-outs.

Christine joins the other four lawyers in the Legal Services Office: Jonathan Anelay, Director of Legal Services; Frances Barnwell, Deputy Director; Carolyn McKee, an intellectual property lawyer whose main client is the Research Services Office; and Peter Webber, recently arrived from Boodle Hatfield, and working with the Land Agent on real property matters.

OION Joint Venture

In October Isis Innovation and The Oxfordshire Investment Opportunity Network held a joint Investment Meeting in the Martin Wood Lecture Theatre

The meeting turned out to be one of the busiest ever with over 90 attendees and six excellent investment presentations at the event. The meeting finished with a buffet which gave the participants the opportunity to network after witnessing some remarkable new business ideas.

Isis Innovation and The Oxfordshire Investment Opportunity Network brought six very interesting companies to the meeting and Dr Tim Cook entertained the audience with some interesting observations on the relative attributes of business angels and venture capitalists. As a result of this meeting a number of investment deals have already been closed and enquiries about these businesses are still coming in on a daily basis.

Due to the success of this meeting Isis Innovation and The Oxfordshire Investment Opportunity Network will be holding another joint Investment meeting next October. The Oxfordshire Investment Opportunity Network has seen the number of its investors double in the last year and presentation meetings have been increased to nine in the year 2000. Since the Network was founded six years ago, £7 million has been invested directly as a result of introductions through OION and it is estimated that well over 200 jobs have already been created in the 35 new businesses that have gained funding.

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Oxford University Consulting Ltd

Launched in 2001, a new wholly-owned subsidiary of the University of Oxford

Managing Director, Dr Mark Taylor.

The University has incorporated a new company, Oxford University Consulting Limited (OUCL), to help academics and departments market their services to local businesses and the wider world. They have appointed Professor Raymond A. Dwek, FRS as Chair of its Board, which also includes Tim Cook (Isis Innovation Ltd), Catherine Quinn (Research Services Office) and Joe Barclay (Business Liaison Unit).

The new company has appointed as its Managing Director Mark Taylor, formerly of Isis Innovation and 3i. The service, which was launched officially early this year, will identify consultancy and related opportunities with local, national and international companies for academics and departments throughout the University. OUCL will negotiate terms, conditions and payment. Mark said: 'We aim to offer a professional service to help staff and departments market their expertise and services. We believe we will not only save academics' time, but bring them greater financial rewards for their efforts'.

The new company is currently in the process of recruiting founder members.

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University Challenge Seed Fund

Over £1 million invested

The Oxford University Challenge Seed Fund has now invested over £1 million of its initial £4 million in a total of 19 investments ranging in size from £2,500 to £250,000. A further seven investments have been approved pending completion of formalities and another eight are currently under consideration. This is well in line with anticipated activity in the first 18 months of the Fund's operation.

The Fund has invested in the development of research within the laboratory; in commissioning external market and consultants reports; and into the start of spin-out companies. The Fund holds investments in three existing spin-out companies – Oxford Biosignals Ltd; Oxford Biosensors Ltd; Mindweavers Ltd. – and a number of other projects which it is expected will lead to new companies or licensing deals.

The Scheme's primary focus is the exploitation of science and engineering research outcomes

The background to the Fund is that during 1999 Oxford University was awarded one of 15 seed funds that have been established as part of the Government's University Challenge Seed Fund Scheme. The aim of the Scheme is to fill a funding gap in the UK in the provision of finance for bringing university research discoveries to a point where their commercial usefulness can be demonstrated and the first steps taken to ensure their utility. The Scheme's primary focus is the exploitation of science and engineering research outcomes. Oxford University has established a £4M Fund made up of contributions from the University (£1M) the Government (£1.4M) and the Wellcome Trust (£1.6M).

The Fund has identified five types of project activity on which its money may be invested: Initial proof of concept; Pre-patent research; Reduction to practice; Commercial demonstration; Spin-out company. The Fund may make investments into University Departments, into new spin-out companies and for the provision of external services (e.g. market research, business planning). The Fund may not invest in existing companies and its funds are not intended to be applied to projects that are eligible for research grant funding.

The key criteria for evaluating proposals are:

* Innovation of the science: How novel is the approach compared with other research in the field?
* Intellectual property: What does the backdrop of prior art look like?
* Background of the key people: Who are the key researchers, etc.?
* Commercial opportunity: Can the research be turned into a sustainable business?

In the case of spin-out proposals the criteria are as follows:

* Strong technology and IP base
* Products and / or services that offer a potential competitive advantage
* A strong business leader/entrepreneur
* Clear growth prospects

A researcher wishing to apply for funds should contact either the Project Manager at Isis Innovation with whom they are already working, or Tom Hockaday to be put in touch with the appropriate Project Manager. Isis has produced a booklet which explains the workings of the Fund in more detail. This can be found on the Isis web site at www.isis-innovation.com and copies are available from Isis.

University News

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Oxford University begins construction of £60 million Chemistry Laboratory

The University took the first steps towards a new era in Chemistry research when Councillor Maureen Christian, Lord Mayor of Oxford, performed the ground-breaking for a multimillion pound Chemistry Laboratory on the corner of South Parks Road and Mansfield Road on Thursday, 7 September 2000.

Top universities join e-alliance

Oxford, Princeton, Stanford and Yale Universities have become partners in a joint 'distance learning' venture which will provide on-line courses in the arts and sciences initially to their combined 500,000 alumni.

£5 million JIF grants for new virus facility

The University's Division of Structural Biology within Clinical Medicine has been awarded a Joint Infrastructure Fund Grant for over £5 million to build a top facility for the evaluation of infectious particles such as viruses.

New vaccine to combat AIDS epidemic

Evan Harris, MP for Oxford West and Abingdon, was the first volunteer to receive a new vaccine developed at the University's Weatherall Institute, designed to combat the AIDS pandemic currently devastating the population in Africa.

Begbroke home to Enterprise Hub

The University's Business and Science Park at Begbroke is to be home to one of the first five Enterprise Hubs to be launched by the South East England Development Agency (SEEDA).

New hope for sickle cell patients

Researchers from the Department of Physiology have teamed up with academics at St George's Hospital Medical School in Tooting to work on new treatments for sickle cell disease, following a grant of £90,000 from Action Research.

National asthma and eczema genetic database unveiled

Researchers at the Henry Wellcome Building of Genomic Medicine have teamed up with Great Ormond Street Children's Hospital to create the world's biggest database of genetic samples from patients who suffer from severe asthma and eczema.

New ways to learn

Researchers in the psychology departments of Oxford University and Oxford Brookes University will be co-operating in a large-scale project on how children should be taught to read, spell and do mathematics.

£1.7m for blood units

Funding of over £1.7 million from the Leukaemia Research Fund (LRF) will enable two specialist Units in the Department of Clinical Laboratory Sciences to build on their reputation as national centres of expertise in the study of leukaemias and lymphomas.

Oxford builds on meningitis knowledge

Researchers at the Departments of Paediatrics and Biochemistry have discovered the 'virulence genes' which affects the Meningitis B bacterium Neisseria meningitidis.

For more information about these articles

See *Oxford Blueprint*, The Newsletter of the University of Oxford

www.ox.ac.uk/blueprint

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The Life Sciences Group, **from back row:** *William Bartrip, Peter Hotten, David Phillips, and Mark Payton.* **Front row:** *Jo Fyson, Samantha Timmins, and Angela Kukula.*

The Physical Science Group, **from back row:** *Andy Goding, David Eastham, and Herb Askew.* **Front row:** *Robert Adams, Amanda Nolte, and Charles Harper.*

Meetings

Isis
University of Oxford
Innovation Society

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

Thursday 15th March 2001

Thursday 20th September 2001

Thursday 6th December 2001

All meetings will be held at 5:30 p.m. followed by a Reception and Dinner for members and invited guests at a University College.

For information about the OIS contact Jennifer Johnson, Marketing Administrator:
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