INNOVATION insights

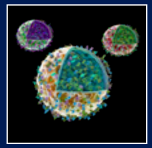
THE LATEST INNOVATIONS, COLLABORATIONS AND TECHNOLOGY TRANSFER FROM THE UNIVERSITY OF OXFORD

ISSUE 18 March 2022

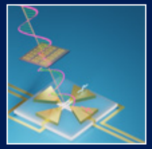
IN FOCUS: OXFORD NANOPORE

Sequencing pioneer comes of age with stellar IPO.

Other articles include:


Extracellular vesicle loading technology


Non-operative treatment of hand arthritis and fractures


3D-cross nanowire networks for terahertz detectors


Ultrafast analogue spatial light modulator

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Two momentous events

The end of an era, and a major milestone.

Since the last issue of Innovation Insights was published the death has been announced of Sir Martin Wood. 'Pioneer' and 'visionary' are overused words, often with little justification, but are entirely appropriate when reflecting on Sir Martin's enormous contribution to the Oxfordshire innovation ecosystem. From his research into specialist magnets he founded, with his wife Audrey, Oxford Instruments – Oxford's first spinout, and still one of the most successful. OI made use of superconducting magnets that eventually led to the development of MRI, which enables countless lives to be saved. Latterly Sir Martin's philanthropic endowments laid the foundations for Oxford's emergence as an innovation cluster. We are all indebted to his vision, dedication, and generosity.

Last September Oxford Nanopore successfully listed on the London Stock Exchange for £3.4bn. The company made a significant contribution to the UK's efforts in tackling the COVID-19 pandemic with its LamPORE tests used in NHS labs, and the flotation marked the culmination of a 15 year journey. Read more about the Nanopore story in the feature article in this issue.

With best wishes from everyone here at OUI, we welcome your feedback.

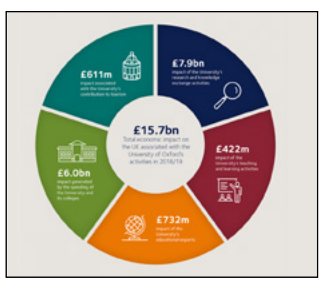
News

Oxford Nanopore Technologies Ltd

Oxford Nanopore launch IPO in London

DNA-sequencing company has held their IPO, valuing the company around £5bn, making it the most successful UK spinout IPO in history.

FULL ARTICLE ▶



Economic Impact

A new report - The Economic Impact of the University of Oxford - analysed the University's impact on the UK economy in 2018/19, concluding that it contributes around £15.7 billion to the UK economy, and supports more than 28,000 full time jobs. Research and knowledge transfer activities alone contribute £7.9 billion.

FULL ARTICLE ▶

NQCC

OQC and NQCC boost the UK's quantum capability

Oxford spinout, Oxford Quantum Circuits (OQC), has collaborated with the National Quantum Computing Centre (NQCC) to boost the UK's quantum-readiness.

FULL ARTICLE ▶

Nicola Blackwood appointed chair of OUI board

Baroness Blackwood, Chair of Genomics England, has been announced as the new Chair of Oxford University Innovation.

FULL ARTICLE ▶

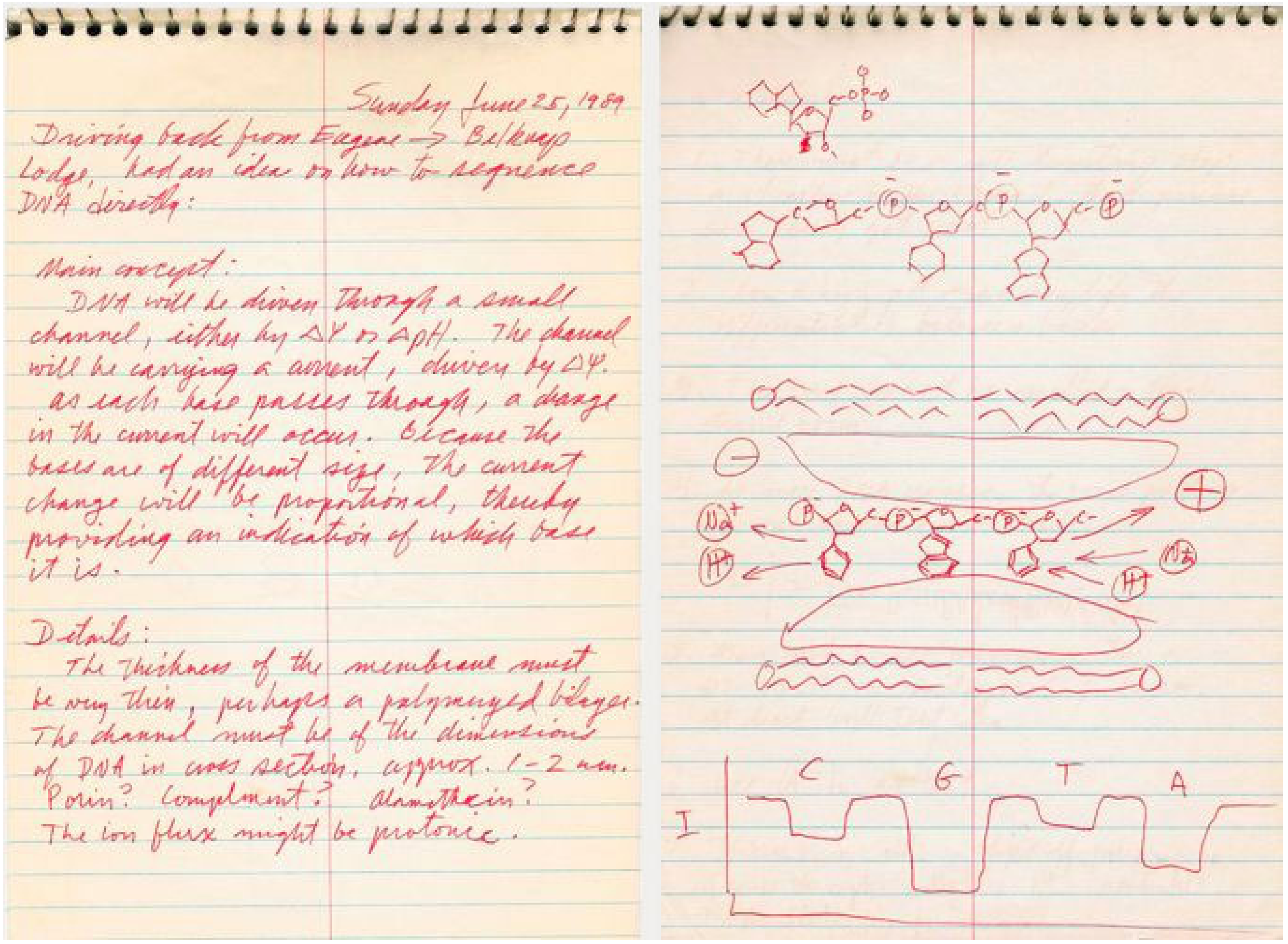
Spinout success

IP experts, GovGrant, have revealed the University of Oxford has generated some of the highest value spinout companies in the UK.

FULL ARTICLE ▶

In focus: Oxford Nanopore

In June of 1989, University of California Davis researcher David Deamer was out driving down the West Coast of the USA when a thought occurred to him. Pulling over to scribble down the concept in his notepad before continuing about his day, Professor Deamer didn't realise it at the time, but what he had jotted down would become a fundamental part of Oxford's innovation ecosystem: the Nanopore.



Professor Deamer's scribble theorised how to directly sequence DNA. The idea was that by passing electrically charged DNA particles through a small enough channel, he could ascertain what the particle was by the fluctuation in the channel's current. He then promptly closed his notepad, got back behind the wheel, and put aside the idea for two years.

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31 years later, Oxford Nanopore, an Oxford University spinout company which considers Professor Deamer's sketch as its equivalent to the Dead Sea Scrolls, held its flotation on the London Stock Exchange in one of the biggest UK biotech IPOs to date. Beyond its economic impacts, Oxford Nanopore's technology has been used to sequence DNA in space and deployed throughout the pandemic and its position in Oxford has helped grow the surrounding ecosystem from a small group of high-tech companies to a thriving cluster. Its backers have used Nanopore to catalyse new methods of accelerating companies just like it in Oxford and around the UK.

It all started with a sketch, and this is that sketch's story.

California Deaming

Pre-1989, Deamer's work focused on electron microscopy, which evolved into an interest in liposomes, which are artificially formed spherical vesicles with a lipid bilayer commonly used as drug delivery vehicles and are vital components of mRNA vaccines developed by Pfizer/BioNTech and Moderna for their COVID-19 vaccines. At the time of his idea, Deamer had also been working with Mark Akeson, a post-doctoral student, on bilayer research which would allow them to make pores.

Deamer would later describe the sketch as the result of a "click" in his head. While out driving again, Deamer realised that if you put a voltage across a suitably sized pore, you could pull an ion through the pore, and nucleotides passing through the pore would impact on the ionic current.

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Oxford's involvement in the sketch's story wouldn't begin until some 14 years after it was scribbled down, with the return of Professor Hagan Bayley from the US to the ecosystem in 2003. Bayley established a new, interdisciplinary group examining membrane proteins at the Department of Chemistry's new Chemistry Research Laboratory, located in the heart of the University's science area on South Parks Road. The group's focus was and remains both the basic science and the applications of biochemistry, and set about identifying protein engineering processes which could change the behaviour of proteins to get them to do what they wanted.

Drawing on his earlier work into the structure of the a-hemolysin pore in Staphylococcus, the same bacterium responsible for MRSA, Bayley's group began to look at ways of exploiting it. Crucially, the bacterium has a diameter of 2nm – about 1/50,000th of a human hair. Combined with an electric current about one billionth of what's used in a lightbulb – so slight it uses ions – the structure can be exploited to measure what was going through the pore. Essentially, using this process – stochastic sensing – the variations in the current combined with the incredibly small pore could tell a researcher what the molecule passing through the pore actually was.

Founding of Nanopore

When Bayley arrived in Oxford, he hit the ground running and wanted to use the University's innovation infrastructure to get a company spun out as soon as possible.

He came to see David Baghurst, Head of Physical Sciences at Oxford University Innovation at the time (then Isis Innovation), and the two began pulling together the intellectual property for Nanopore from the other universities while Bayley continued developing new IP at his Oxford lab.

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During this time, Gordon Sanghera was brought in to lead Nanopore. Sanghera came through the Oxford ecosystem, having previously worked on early Oxford spinout Medisense, which developed the glucose sensor used in the monitoring of diabetes (which sold to Abbott Laboratories for $800m – a record exit for Oxford which stood for two decades). Sanghera's role at Nanopore would prove pivotal for the company's success, leading the company through its early funding rounds through to the present day and its blockbuster IPO flotation.

Already having successfully made the jump from concept to research, the legacy of the sketch would become tangible as a fully-fledged company in 2005, when Nanopore launched as Oxford Nanolabs at the University-owned Begbroke Science Park.

The company was originally set up with the intention of furthering stochastic sensing. However, after a year in development, the company switched focus to DNA sequencing.

What Nanopore set out to do was audacious. Their stated mission was to sequence anything, anywhere. The work into sequencing the human genome had only been completed three years prior. The research took 10 years and cost $3bn. There are six billion bases in the human genome, which is approximately two meters in length. Even in 2007, sequencing a whole genome still cost $70m. What Nanopore set out to do is to not only make the process affordable and fast, but to do it on a device you could put in your pocket.

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Nanopore's Rise

Early work at Nanopore focused on combining the work of Professor Bayley with expertise and intellectual property from Professors Branton, Deamer and Akeson. In 2010, Nanopore brought innovations together from both Professor Bayley and Akeson's respective labs, both of which the company funded. Bayley's work had developed a mutated nanopore with the ability to discriminate necleotides, while Akeson's group had developed an enzyme motor which could control movement of DNA through the nanopore. When combined, this allowed for the first demonstration of DNA sequencing using a nanopore.

This led to the development of Nanopore's inaugural products, the GridION and MinION, a desktop and handheld DNA sequencer, respectively.

Nanopore's products have found a wide variety of uses. In a medical setting, Nanopore's technology is being utilised by the Seattle Children's Hospital (SCH) to rapidly identify genetic conditions. At present, this process can take months or even year. Even once complete, around 50% of children remain undiagnosed. SCH has been using Nanopore's tech to identify disease-causing variations in DNA not identified in regular testing. Practitioners at SCH believe that the technology will reduce the cost of testing, speed up the process, and produce much higher levels of accuracy.

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Veterinarians are also making use of the technology. Disease in animals tends to be the result of multiple pathogens, which makes diagnosis and treatment hard to pin down. In Belgium, Ghent University spinout PathoSense is using Nanopore's tech to help vets identify what pathogens are at play, giving them a clearer idea of what treatments to prescribe. The PathoSense team are also hoping that the work they are doing could have an impact on antimicrobial resistance, potentially offering research which can improve efficacy of antibiotics, and alert health authorities of potential outbreak risks.

The technology has even deployed by NASA on the International Space Station, where it conducted the first DNA sequencing tests in space using a MinION. The experiment demonstrated that DNA sequencing was perfectly possible in space, and could lead to Nanopore technology being utilised to safeguard and monitor astronauts on future missions.

While Nanopore's technology was opening up new ways to sequence DNA, the company boomed. From founding to pre-IPO, the company raised close to a £1bn from a wide range of domestic and international investors. It has held unicorn status since the mid-2010s. The company moved from Begbroke to the Oxford Science Park in 2010 and now employs over 600 people, many of whom are based in Oxfordshire, where it also opened a new high-tech manufacturing facility in 2019. It has also opened satellite offices in New York, Boston, Cambridge, San Francisco, and across Asia.

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In 2021, Nanopore held its long-awaited initial public offering. The company soared in its first day of trading by 45%, reaching a valuation of $6.8bn. It is one of the largest UK biotech flotations in history (3rd globally this year), the biggest IPO for any UK university spinout, and fifth largest for any university company worldwide – making David Deamer's sketch one of the most valuable in university innovation history.

Nanopore's Legacy

The sketch has a legacy beyond Nanopore itself, one that's now interwoven into the Oxford innovation ecosystem.

When he returned to Oxford in 2003, one of the attractions for Professor Bayley was the Chemistry Department's new Chemistry Research Laboratory, located in the heart of the University's research hub on South Parks Road.

The new building was made possible as the result of a ground-breaking deal in the university investment space between the University and the newly-formed IP Group, now an international university venture group. Under the terms of the deal, signed in 2000, IP Group provided the Chemistry Department £20m for the building in exchange to half of its equity in Chemistry department spinouts over the following 15 years. Five years later, that deal would include Oxford Nanopore.

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The deal with IP Group quickly turned the Chemistry Department into the most prolific generator of university spinouts in Oxford, with over 40 of the 270-plus spinouts to have passed through Oxford University Innovation tracing their roots back to the Department. Likewise, the deal spurred the rapid growth of IP Group, which first moved to back spinouts from across Oxford, then UK universities, and now also operates in the US and Australia. At present, IP Group is supporting over 60 spinouts across the world, many of which are from Oxford. Crucially, IPG's model has been duplicated numerous times, including by Oxford Science Enterprises. These funds provide patient capital – a critical model of funding for spinouts which looks to back spinouts from early stages through their many years of development until their IPOs.

Nanopore's growth, success and subsequent IPO has been a major validation for this model. It demonstrates to founders, entrepreneurs and investors that it is perfectly possible, given the right support and infrastructure, to take an academic concept and turn it into a major technology company. Particularly for investors, it also demonstrates that there are big returns to be made on backing university spinouts. Furthermore, it has been a validation of the UK's technology scene, with a homegrown company listing on the London Stock Exchange – historically averse to technology companies - over international counterparts and doing well as a result.

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Back in Oxford, Nanopore has acted as a rallying cry for the rest of the innovation ecosystem. In the innovation space, the three core resources needed are ideas, talent and investment. Thanks to the University and surrounding institutions, Oxford is awash with great ideas. In terms of talent though, we compete with global innovation hotspots such as Silicon Valley, Boston and Cambridge. To attract the leaders and thinkers required to transform our companies and secure the maximum impact for Oxford ideas, success stories like Nanopore are absolutely essential.

Nanopore also opened the door to the launch of Oxford Science Enterprises (OSE - originally Oxford Sciences Innovation) in 2015. An evolution of IP Group's deal, OSE received half of the University's equity in any spinout from the Medical Sciences Division and Mathematics, Physical and Life Sciences Division. In exchange, OSE have raised over £600m to invest into Oxford spinouts by offering investors a chance to be a part of the next Nanopore.

The result has been one of the largest surges in innovation stemming from a university worldwide in history. Nanopore itself was the 52nd spinout to have passed through Oxford University Innovation's doors since it opened in 1987. 10 years after Nanopore's incorporation, when OSE launched, the total had reached 119. At the turn of 2022, OUI welcomed its 280th company.

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Oxford is now a world leader in terms of spinout company creation, second only to ETH Zurich. This has been met with record levels of investment. In 2018, the UK received just shy of £1.5bn nationwide, with a third of that total coming to Oxford. Last year, Oxford University spinout companies alone received £1.5bn in investment. Funding and expertise that groups like OSE and OUI have brought in have certainly contributed to this growth. However, it is the companies themselves that are the main draw for investors, and out of the 280 stars we collectively have created, Nanopore's shines the brightest.

Autonomous robot navigation in a dynamic environment

Autonomous service robots are increasingly being deployed across many different industries. The robots must navigate complex and dynamic environments and often must collaborate with human co-workers. The formula often used to make navigation decisions in these sorts of human-populated environments is a Markov decision process (MDP). Although widely used, it can also be cumbersome and error prone.

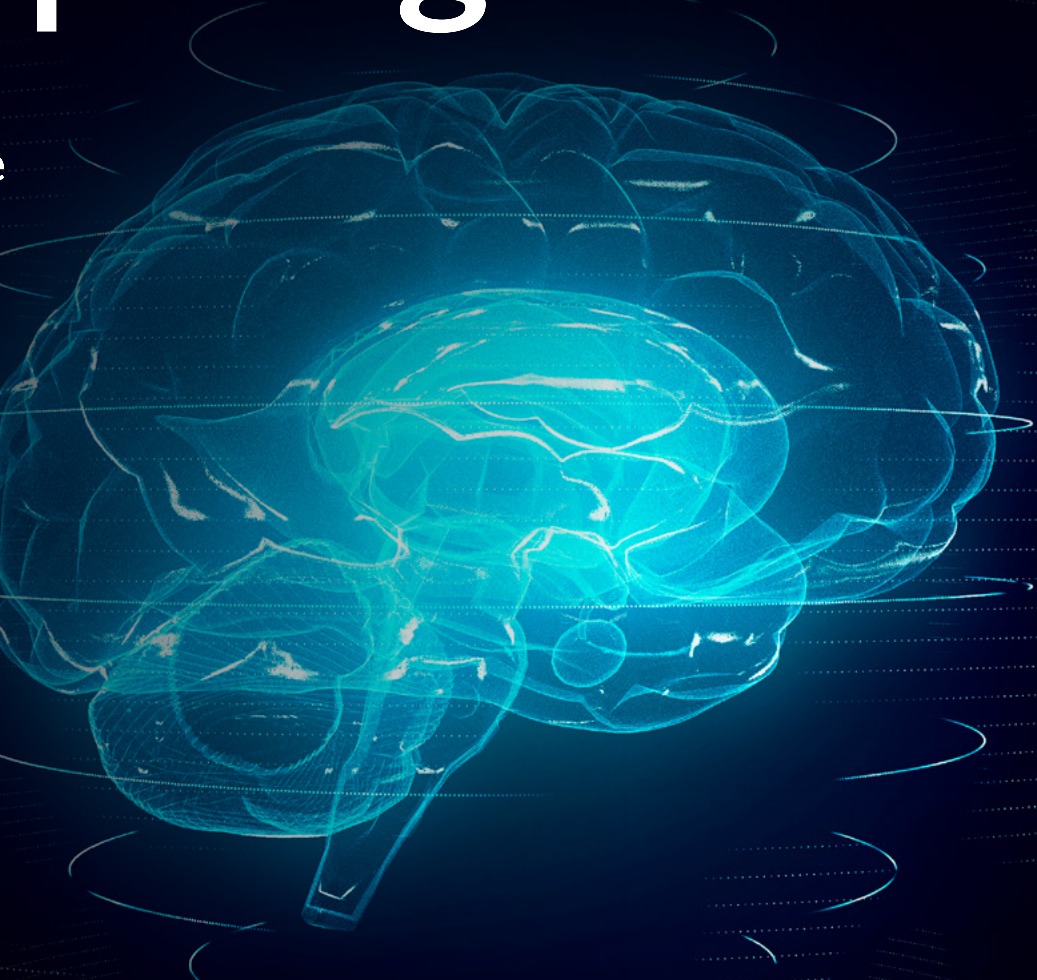
Academics at the University of Oxford have developed software using MDP models that allow a user to quickly assign a robot to a new task in a dynamic environment. The detailed planning of previous software is not required to the same extent. Multiple objectives can be handled, and probabilistic guarantees are created.

FULL WEB PROFILE ▶

Learning and recall algorithm for neuromorphic computing

Building on previous work focussed on developing an all-optical neuromorphic computer, researchers at the University of Oxford have devised an all-optical associative learning element. Such an element can be integrated with existing neuromorphic computing components to create circuitry which can receive inputs, capture associations, and output reactions analogous to Pavlov's dog experiment.

The optical design has two complementary optical 'sensor (input) neurons' which are embedded in two optical couplers. Light pulses from both couplers can be converged in an 'optical motor neurone' to determine when associations should be made. Simultaneous light pulses passing through each sensor neuron trigger a response in the 'motor neuron'. This leads to different output behaviour of the motor neuron to capture the fact that an association has been made previously.



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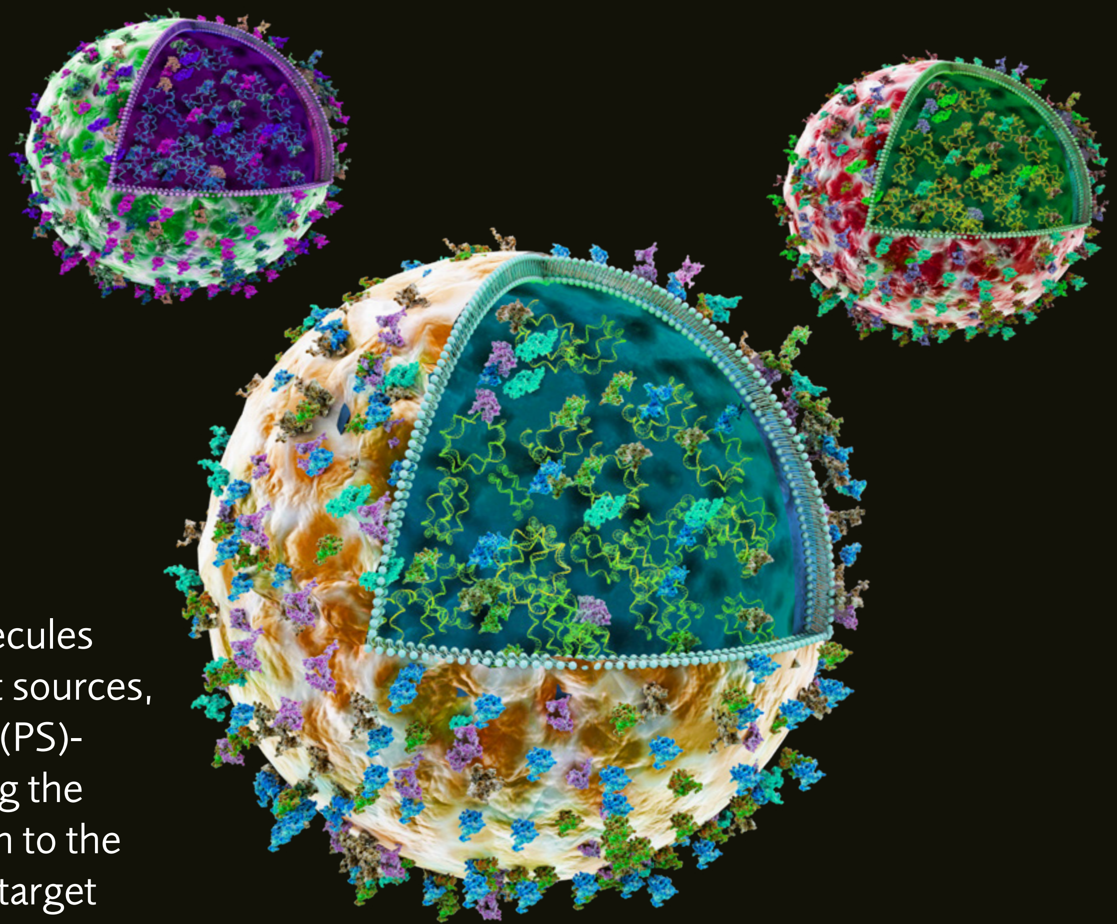
Extracellular vesicle loading technology

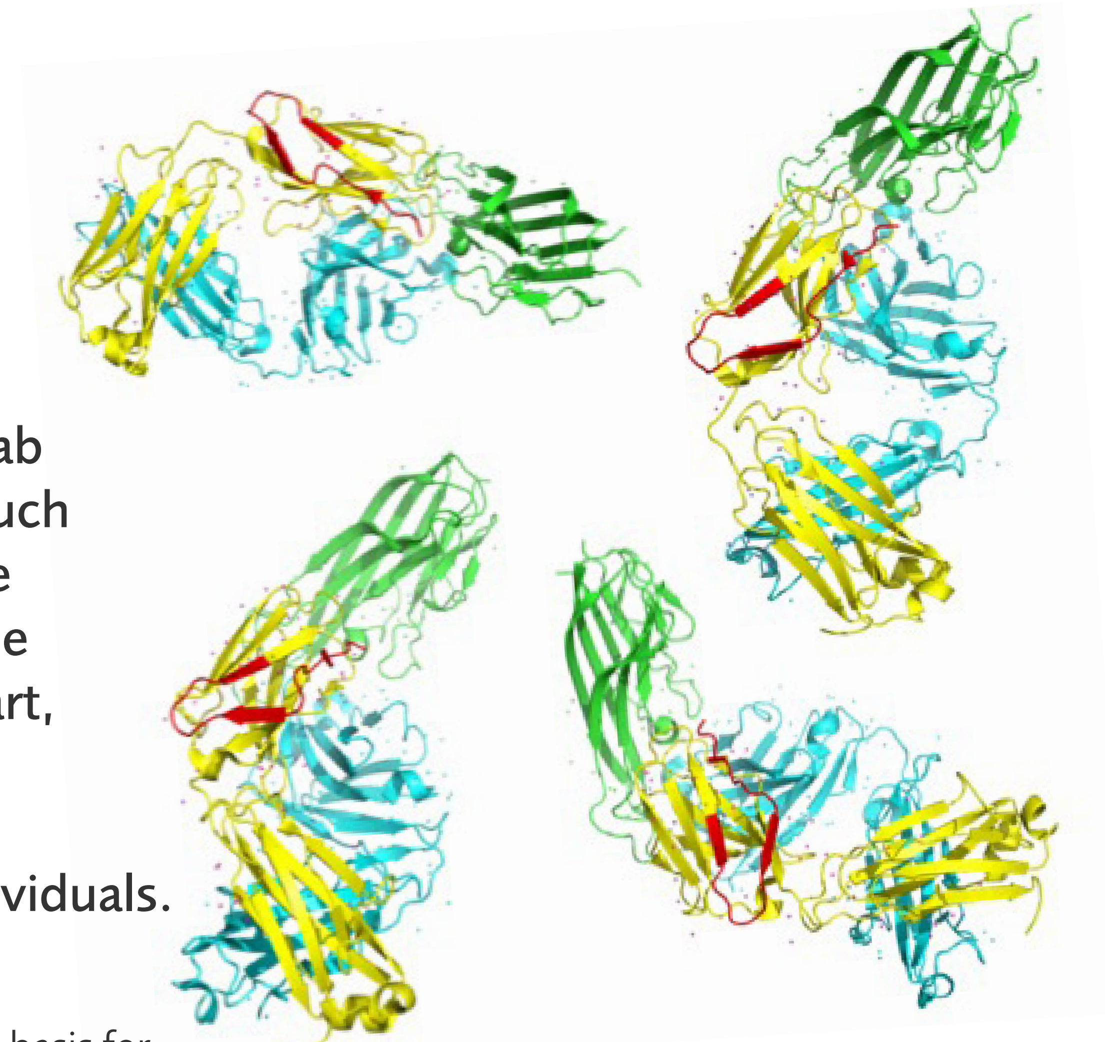


Extracellular Vesicles (EVs), such as exosomes, are natural lipid vesicle nanoparticles secreted by cells, with important roles in intercellular communication and pathophysiology. As cells can naturally take up EVs from their surroundings, EVs have great potential as therapeutic drug carriers and delivery vehicles to transport drugs into specific cells and tissues.

The University of Oxford has developed a technology for loading and delivering molecules including peptides, nucleic acids, and small molecules into EVs derived from different sources, including but not limited to exosomes. The EVs are coated with a Phosphatidylserine (PS)-binding protein which is linked to a second cargo-binding protein/peptide for carrying the aforementioned molecules. This technology allows loading of molecules of interest on to the surface of EV in a single step. It also allows efficient uptake of the molecules onto the target cells. Moreover, the technology can be used as a purification method for purifying EVs.

FULL WEB PROFILE ▶

Improved anti-TNF Antibodies



Anti-Tumour Necrosis Factor (Anti-TNF) drugs such as adalimumab and infliximab are currently used to treat autoimmune diseases such as Crohn's and ulcerative colitis. Whilst highly successful in some patients, adalimumab and infliximab are unfortunately found to be immunogenic in certain individuals. This immunogenicity is, in part, thought to be due to specific amino acid sequences at key points in the antibody structure which the individuals' immune systems target, rendering the therapy ineffective in those susceptible individuals.

Researchers at the University of Oxford have identified potential key regions of the infliximab structure that require modification to avoid immune stimulation, providing a basis for non-immunogenic anti-TNF therapy development. This discovery could significantly decrease the numbers of immunogenic non-responders currently observed with these treatments for a variety of diseases.

FULL WEB PROFILE ▶

Patient Flow Management System for Hospitals

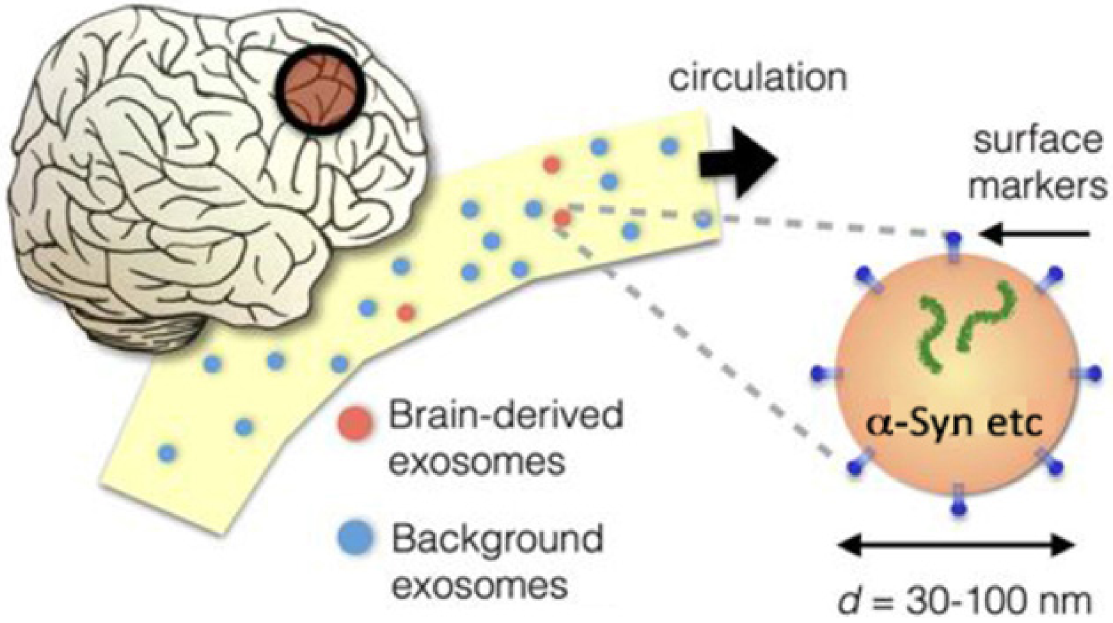
Scientists at the University of Oxford have developed a tool for optimising patient flow across a hospital's facilities: from forecasting hospital admissions via the emergency department, to identifying emergency department attendees at risk of not being treated within timely care targets, to predicting likely patient care pathways within the hospital, through to patient discharge prediction and prioritisation.

The technology is based on an integrated platform that provides an end-to-end solution for improving patient flow across the hospital, by predicting patient demands and care requirements ahead of time.

FULL WEB PROFILE ▶

A method to improve early Parkinson's diagnostic

Parkinson's Disease (PD) has devastating socioeconomic effects on patients, families, and society. The medical cost of PD in 2017 alone accounted for $25.4 billion in the USA. Currently there is no blood-test to objectively predict or diagnose Parkinson's disease, especially at the prodromal phase of the disease when patients are easily missed or misdiagnosed.

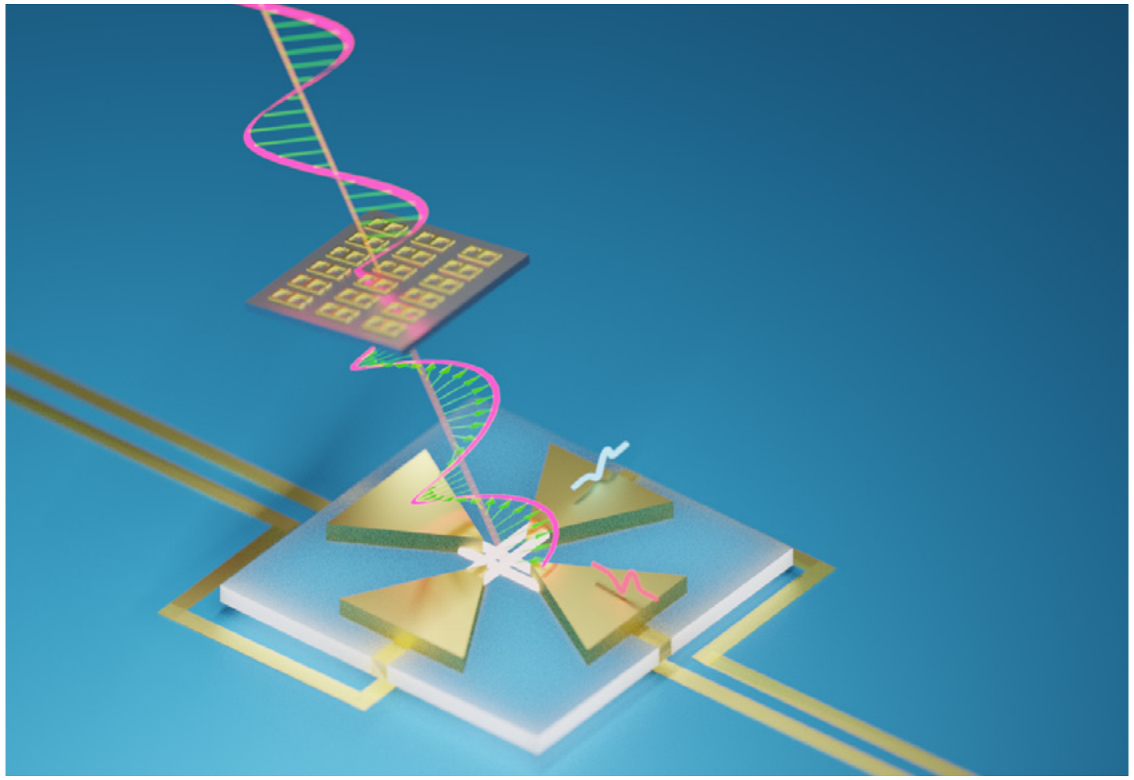


University of Oxford researchers and clinicians have developed a new immunocapture assay enabling highly efficient isolation and analysis of neuronally-derived microvesicles called exosomes that circulate in patients' blood. Using this new assay, they have shown that exosomal α-synuclein, in combination with other biomarkers, are effective in differentiating PD from closely related neurodegenerative diseases, offering a simple blood-based test for the identification and stratification of PD patients, especially at the prodromal phase of the disease.

FULL WEB PROFILE ▶

3D-cross nanowire networks for terahertz detectors

Terahertz radiation lies between the microwave and the infrared regions of the electromagnetic spectrum where electronics meets optics. This frequency band has many useful applications in wireless communication, spectroscopy, sensing and imaging. However, technical challenges remain in providing detectors of terahertz waves that are polarisation sensitive.



Starting from previous pioneering research, a team at the University of Oxford have devised a polarisation-sensitive terahertz detector that is simple, effective, and not susceptible to crosstalk (interference) between detection channels. The monolithic device allows simultaneous measurements of the orthogonal components of the terahertz electric field vector with high extension ratios (comparable to the state-of-the-art wire-grid polarizers).

FULL WEB PROFILE ▶

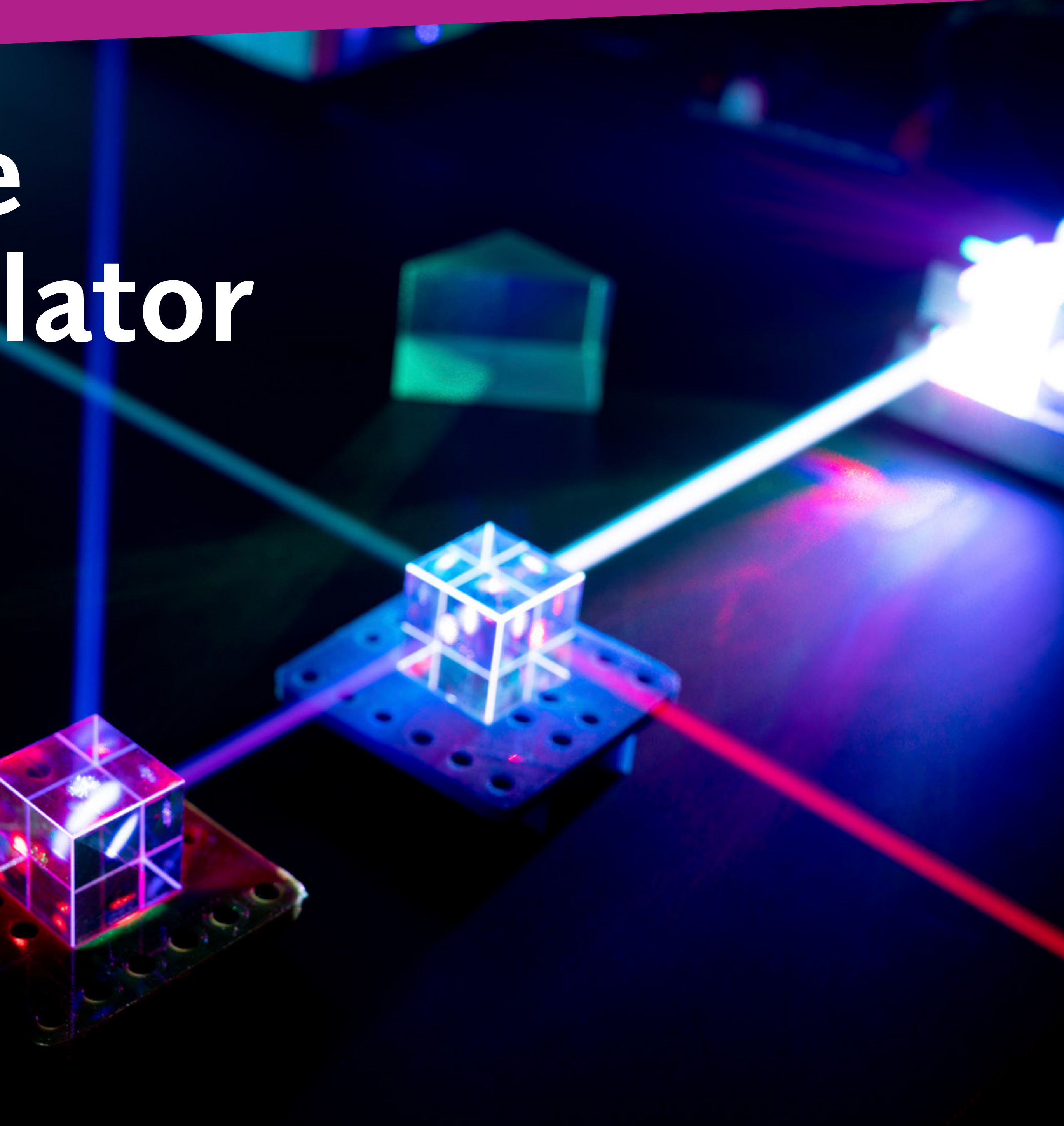
Non-operative treatment of hand arthritis and fractures

Osteoarthritis causes the breakdown of cartilage and bone of the joints. Joint distraction therapy can alleviate patient's symptoms and allows for repair of the joint tissues by mechanically separating (or stretching) the joint. Distraction mechanically "off-loads" the affected joint, returning the joint towards its normal position, and reducing the forces experienced by the joint tissues.

Researchers at the University of Oxford have developed a non-surgical device that sits at the base of a digit and attaches to the nail to apply a distraction force over a joint. This new non-surgical joint distraction orthosis has the potential to be the first disease-modifying treatment for osteoarthritis in the hand and foot.

FULL WEB PROFILE ▶

Ultrafast analogue spatial light modulator



Spatial light modulators (SLMs) have applications in a wide range of areas such as holography, biomedical imaging, laser micromachining and free-space optical communication, among others. Existing SLMs are limited to either analogue control with frame rates <100Hz or >1kHz frame rates with only binary modulation levels. The speed of current analogue SLMs is a limiting factor for many applications.

Researchers at Oxford have devised a technology capable both of frame rates at >1 kHz and full 2π phase modulation with analogue control, which enables the next generation of devices to be realised.

FULL WEB PROFILE ▶

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IMPORTANT NEWS
FOR OUR OIS MEMBERS

Oxford Innovation Society (OIS) meetings are currently suspended, and will resume as soon as feasible.

We invite OIS members to join online events until in-person events resume.

INNOVATION insights

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