Success stories

THE ROYAL SOCIETY

Contents

Quantum dots herald next generation TV Professor Paul O'Brien FRS	5
Fifty billion chips and counting Sophie Wilson FREng FRS	6
The next DNA revolution begins here Professor Shankar Balasubramanian FMedSci FRS and Professor David Klenerman FRS	9
Transforming lives by a new class of cancer drugs Professor Stephen Jackson FMedSci FRS	10
Smart software to 'understand' the world Dr Mike Lynch OBE FREng FRS	13
Green adsorbent nano-tubes to cut carbon emissions Dr Semali Perera	14
Blockbuster drugs: from fantasy to reality Sir Gregory Winter CBE FMedSci FRS	17
Sparking the plastic electronics revolution Professor Donal Bradley CBE FRS, Dr Jeremy Burroughes FREng FRS, Professor Sir Richard Friend FREng FRS	18
Success flows with green chemistry Professor Steven Ley CBE FMedSci FRS	21
Tiny molecules key to finding new therapies Sir Tom Blundell FMedSci FRS	22

Cover image

Dr Semali Perera, winner of the Royal Society's 2007 Brian Mercer Award for Innovation. $\hfill C$ Nic Delves-Broughton, University of Bath.

Foreword

The Royal Society is proud of the outstanding track record of research and development in the UK, including the contributions made by many of our Fellows.

As part of the Society's strategy to promote industrial science and translation, we are supporting activities that help scientists to commercialise innovative research. One approach we are taking is to identify the processes by which successful translation occurs between universities, businesses and the wider community.

In this booklet we present ten personal accounts, showcasing how the translation of scientific breakthroughs into commercial success has been achieved in the UK. These success stories have been selected from a range of academic disciplines and industry sectors, including ground-breaking scientific discoveries in nanotechnology, computing, biotechnology, chemical engineering, physics and material sciences. The leading scientists and entrepreneurs featured describe their different journeys from "lab to market", the economic impact of their discoveries and offer advice for aspiring scientific innovators. Together, the case studies demonstrate how excellent research in the UK has led to innovative new products and businesses, created jobs and income and improved people's health and well-being. They reinforce the need for increased investment in the UK science base.

S.F. Campbell

Sir Simon Campbell CBE FMedSci FRS Co-Chair, The Royal Society Science, Industry and Translation Committee

Dr Herman Hauser CBE FREng FRS Co-Chair, The Royal Society Science, Industry and Translation Committee

The biggest challenge was in the early stages in "raising the money to continue doing the work while still doing the day job".

Professor Paul O'Brien

Quantum dots herald next generation TV

Professor Paul O'Brien FRS

Better and sharper colour TVs with cheaper longerlasting displays is one thing that Professor Paul O'Brien believes work on quantum dots will lead to.

His research to more safely mass-produce nanocrystals called "quantum dots" led to a start-up company called Nanoco in 2002.

Quantum dots are small particles of semiconductors, which have unique properties due to their small size; they are composed of a few thousand atoms. Small alterations in size lead the dots to emit different colours of light. They are also highly efficient – emitting 80 to >90% of the light put into them.

Quantum dots are currently used as markers in biomedical diagnostic kits and some liquid crystal TV displays, but they may one day offer a revolution in flat screen technology and may also be used in solar cells and anti-counterfeiting markers.

Professor O'Brien, a Fellow of the Royal Society (FRS), had worked in inorganic chemistry since the 1980s. In 1996, whilst at Imperial College London, he and his student Tito Trindade discovered a simple method to make large quantities of quantum dots, which eliminated the need for hazardous chemicals. It also allowed dots of defined sizes to be made. "We thought that the method might actually have value", he says. Nanoco the company he founded with colleague Dr Nigel Pickett whilst at the University of Manchester, is now valued at approximately £250 million. The company has generated a revenue of £11 million in the last few years and has offices in the UK, USA and Japan, employing about 95 people.

Nanoco partnered with Dow Chemicals in 2013 and they are building the world's first large-scale plant to produce cadmium-free quantum dots in South Korea. Its first TVs using the technology may be produced by the end of 2015.

Nanoco's success was built on tenacity. The biggest challenge was in the early stages in "raising the money to continue doing the work while still doing the day job", says Professor O'Brien.

After two years, the funding started to flow, "and then the rest just kind of snowballed", he says.

Professor O'Brien says getting advice from trusted friends and experienced colleagues is critical in getting enterprises off the ground. "Because the biggest fault that scientists have, and academics in particular, is thinking that every idea they have is brilliant and worth millions and millions of pounds. And very, very few are".

Fifty billion chips and counting...

Sophie Wilson FREng FRS

What do three-quarters of people on this planet carry around in their smartphones, tablets, computers or WiFi devices? The answer is a small efficient microprocessor called an ARM.

Co-developed by Sophie Wilson, over fifty billion ARM powered integrated circuits have so far been shipped the world over.

The story of this ubiquitous technology goes back nearly four decades to a UK start-up company called Acorn, which built home computers.

Ms Wilson was recruited to Acorn in 1976 while still studying Computer Science at Cambridge University. In 1983, Acorn needed a processor for its next generation of computers and she and colleague Steve Furber set about designing one.

They developed the first ARM, which excelled in energy-efficiency thanks to its simplicity, needing fewer transistors than other designs – making it ideal for mobile devices. While international technology giants devoted plentiful staff and resources to similar designs, the creativity for Acorn's 32-bit RISC ARM processor chip rose from austerity.

Its success is credited by Acorn's co-founder Hermann Hauser, who gave the team two things that Intel, Motorola, National didn't give their engineers – no money and no resources. "So we had to keep it small, simple, understandable", says Ms Wilson.

Now ARM Ltd, which sells designs descended from the 1983 work, employs over 2,800 people. In 2013, it had 1,100 intellectual property licences with 300 partner companies, with a group revenue of £715 million.

Ms Wilson has been involved in many technological successes during her career. A generation of British schoolchildren grew up with computers in their classrooms – the BBC Microcomputer, which she helped design.

In 1999 she was one of 7 founders of a new start-up company in Cambridge based on her FirePath processor design. Acquired by Broadcom in 2000, now amongst the largest chip companies in the world, the FirePath processors drive much of the global DSL infrastructure.

Would-be entrepreneurs need tireless enthusiasm, advises Ms Wilson. When she wrote BBC Basic – the iconic programming language for the BBC Micro, she says: "I literally dreamt the code... the amount of dedication it takes is huge".

"I literally dreamt the code... the amount of dedication it takes is huge."

Sophie Wilson

Image By David Boughey. "The market for human genome sequencing in 1998 was zero. The market today is several billion dollars and growing."

Professor Shankar Balasubramanian

10.1

The next DNA revolution begins here

Professor Shankar Balasubramanian FMedSci FRS and Professor David Klenerman FRS

The idea that you could have your entire DNA make-up sequenced for just \$1000 – and in a matter of days, was once unthinkable.

But it was a vision of what the world might become that encouraged Professor Shankar Balasubramanian and Professor David Klenerman at the University of Cambridge to develop their work on DNA towards sequencing – at a time when there was no market for human genome sequencing.

It was the late 1990s, and the seminal Human Genome Project to map out human DNA was only part way through. But the pair realised their fundamental science research could be channelled towards decoding DNA.

"The sequencing was an application which was unanticipated, it just came from thinking about these types of [science] problems", says Professor Klenerman.

With initial funding from investment company Abingworth, they launched Solexa in 1998 to develop cheaper and faster ways of sequencing DNA than the method then available.

By 2006, Solexa launched its own commercial DNA sequencer. And in 2007, the company was bought for a formidable \$600 million by Ilumina Inc.

llumina is now approaching a value of \$30 billion.

The Solexa-Illumina approach harnessed "parallel sequencing" which allows fragments of DNA to be simultaneously analysed. This has slashed the costs and time needed to sequence genomes by a million-fold, says Professor Balasubramanian.

The technology is now widely used. For example, Britain's National Health Service (via Genomics England) is sequencing the genomes of 100,000 patients in a bid to understand disease.

Today it is "responsible for between 80 to 90% of all DNA and RNA sequenced on the planet" says Professor Balasubramanian.

But it took some convincing for investors to help a company with an end-product so far in the future. The first thing investment companies ask, he notes is "how big is the market?".

"The market for human genome sequencing in 1998 was zero. The market today is several billion dollars and growing", says Professor Balasubramanian.

He advises entrepreneurial scientists: "Have a vision for how the world might be several years ahead, along with a vision for how the world may be changed as a result of your invention".

Transforming lives by a new class of cancer drugs

Professor Stephen Jackson FMedSci FRS

The drug Lynparza (olaparib) by Astra Zeneca recently received approval in Europe and the USA, and has the potential to transform the lives of tens, possibly hundreds of thousands of patients.

But its origins go back to a small biotechnology start-up company launched by Professor Steve Jackson in 1997.

He founded KuDOS Pharmaceuticals on the back on a serendipitous observation he made in the early 1990s, just after setting up his lab at the University of Cambridge.

In a "sideline" experiment he noticed that a particular enzyme was switched on by the presence of broken DNA. "For me that was a Eureka moment", he says.

Professor Jackson realised that the molecule was involved in repairing damaged DNA, and could therefore potentially be a drug target. With backing from his university and "seed money" from Cancer Research Technology, he developed the idea, getting funding from venture capitalists in 1999. At its peak in 2006 KuDOS employed 75 people and was sold to Astra Zeneca for \$210 million. Astra Zeneca has taken three KuDOS drugs into clinical trials involving over 1,000 patients so far. The most advanced of these drugs, Lynparza, has just been approved for serious ovarian cancer, but ongoing trials could also lead to it being approved for several other cancer types. This drug is the first on the market that works by blocking the DNA repair enzyme "PARP", killing certain cancer cells but not the normal cells of the patient.

Professor Jackson launched another anti-cancer company, MISSION Therapeutics, in 2010, which has so far raised £27 million.

He advises entrepreneurial scientists to hire the best people and seek advice. He also emphasises how much hard work is involved in setting up a company and how the sheer amount of time needed was a big challenge for him.

But if scientists feel they have the energy to do this, he urges: "Then go for it because it can be an exciting and highly motivating experience... and hopefully will make the world a better place". In a "sideline" experiment he noticed that a particular enzyme was switched on by the presence of broken DNA. "For me that was a Eureka moment", he says.

Professor Stephen Jackson

"We have a saying: 'Always take a gun to a knife-fight'."

Dr Mike Lynch

Smart software to 'understand' the world

Dr Mike Lynch OBE FREng FRS

Wanting a synthesizer so much that he built one himself in the 1980s helped instill a passion in Dr Mike Lynch that later led to him founding a multi-billion dollar company called Autonomy.

Not being able to afford his coveted instrument, Dr Lynch designed his own and with that sealed his interest in the area of signal processing – technology harnessed for information transfer.

During his PhD in electrical science at Cambridge University, he realised that signal processing and pattern recognition could be applied to solving "high-value" commercial problems.

So he co-founded a small company called Cambridge Neurodynamics in 1992. By chance – at the suggestion of a policeman at a meeting – the company ended up developing fingerprint analysis machines.

"It took 30 skilled fingerprint operatives three weeks to search for a match", says Dr Lynch. "We made a machine that did it in about five minutes".

The company did well with a £4 million turnover but spun out of it came Dr Lynch's major triumph: Autonomy with its billion-dollar turnover.

Launched in 1996, Autonomy took pattern recognition technology to another level.

"The software allowed computers to 'understand' the world around them: to look at text or video or audio and get some idea of what was going on", says Dr Lynch.

It did this by "machine learning" where mathematical algorithms help computers to build on patterns rather than following rigid rules.

Today, this type of technology underscores everything from how online news articles are displayed, to which groceries shoppers are prompted to buy online, says Dr Lynch. One day it may even lead to autonomous vehicles.

Autonomy grew rapidly to become the UK's largest software company, entering the FTSE 100, and employing over 4,500 staff worldwide. In 2011, it was bought by Hewlett-Packard for \$11 billion.

Dr Lynch founded Invoke Capital in 2012, which invests in European technology companies.

For scientists hoping to go into business, he says: "It's very important when you are starting off to do something where you really can make quite a big difference from what's out there".

He adds: "We have a saying: 'Always take a gun to a knife-fight'".

Green adsorbent nano-tubes to cut carbon emissions

Dr Semali Perera

Winning the Royal Society's prestigious Brian Mercer Award for Innovation boosted Dr Semali Perera's efforts to spin-off a company to commercialise her research on environmentally-friendly fibres.

After scooping the £185,000 prize in 2007, she and colleagues at the University of Bath developed their technology for the marketplace, launching nano-porous solutions limited (n-psI) in July that year.

The Gateshead-based company, bought by the Norgren Group in October 2013, makes tubes harnessing AMT (Adsorbent Media Tubes) technology to filter air and gases.

The tubes consist of adsorbent crystals with tiny pores to trap molecules of a specific gas or vapour. Currently used in transport and healthcare, they have many other potential applications from aerospace to food and beverage industries.

One major application may be environmental: to remove pollutants like carbon dioxide from waste emissions, and then potentially recycle valuable resources back into the production process.

The design and heating system of the tubes means these novel fibres need half the energy of conventional filter systems. One estimate, in 2008, suggests the technology could save over four million tonnes of carbon dioxide from being emitted by the UK by 2050. Currently growing at a fast pace, the company hopes to increase its staff from 35 to 100 by 2018, and to achieve a turnover of \pounds 20 million.

After its initial huge boost from the Brian Mercer award, Dr Perera's enterprise received a further £2 million between 2007 and 2010 from backers including the Royal Society's Enterprise Fund which gave £500,000.

"Recognition by other scientists... really helped to boost the technology and n-psl", she says of the award. "The Enterprise Fund helped enormously as well to maintain the momentum of the company".

She advises that scientists wanting to commercialise their research must be at the right stage. "The research has to be mature enough, and you've got to understand your technology really well – otherwise there are a lot more hurdles to overcome".

She adds that one in ten spin-off companies do not succeed in gaining a market share. "There are many challenges: working alongside CEOs, talking to customers, selling your technology – you really have to be passionate and really want to do it otherwise you won't succeed".

"The research has to be mature enough, and you've got to understand your technology really well – otherwise there are a lot more hurdles to overcome."

Dr Semali Perera

Image © Nic Delves-Broughton, University of Bath.

"I guess they thought it was pretty hare-brained."

Sir Gregory Winter

Set of the set

Blockbuster drugs: from fantasy to reality

Sir Gregory Winter CBE FMedSci FRS

An entire new class of drugs was launched as a result of technology developed by Sir Gregory Winter. These drugs work by using antibodies to neutralise rogue human cells or molecules that cause disease – for example, cancer or autoimmune diseases. The great benefit of these therapies is that they are highly targeted.

However, their development has been a long story, initially requiring the immunisation of mice. "But in patients the mouse antibodies were recognised as foreign and attacked by the human immune system" says Sir Gregory.

He therefore tried to "humanise" the mouse antibodies using genetic engineering, this approach later giving rise to such blockbuster drugs as Herceptin and Avastin for cancer. He then developed a concept for making fully human antibodies directly – by creating a "vast repertoire" of human antibodies from human antibody genes and screening for the useful ones.

With limited money and lab space, Sir Gregory at the Medical Research Council (MRC) lab in Cambridge approached potential partners for funds – without success. It was considered too "pie-in-the-sky" by large pharmaceutical or venture capitalist companies. "I guess they thought it was pretty hare-brained", he says. "Besides there was no market for therapeutic antibodies at that time". In 2014, that market was worth \$68.9 billion globally. At the same time, another group in the US began working on a similar idea, so Sir Gregory knew he had to act. He managed to excite an Australian company in the concept, who in 1989 provided £750,000 as seed funds for a start-up company – other founders being David Chiswell from Amersham International and the MRC. "So the company was set up in some senses for the wrong reasons", says Sir Gregory. "It was set up to deal with scientific competition".

Cambridge Antibody Technology grew to 300 employees, and helped develop the first human therapeutic antibody. Humira for treatment of rheumatoid arthritis is now the world's best selling pharmaceutical drug. In 2006 it was purchased for £702 million by AstraZeneca. Sir Gregory has since launched two other companies: Domantis and Bicycle Therapies. He says the biggest barrier to setting up a company "amounts to people not being willing to think outside the box".

He advises: "You've got to find a way to sell your dream and fantasy to other people".

Sparking the plastic electronics revolution

Professor Donal Bradley CBE FRS, Dr Jeremy Burroughes FREng FRS and Professor Sir Richard Friend FREng FRS

It's a technology good enough for James Bond. But it wasn't picked out by fictional gadget master Q, rather it was co-developed by Philips and placed in Bond's hands in a clever product placement in Die Another Day.

The item was a shaver containing one of the first commercially developed polymer light-emitting diode (P-OLED) displays. And this is the product of a field called "plastic electronics" which didn't exist until three scientists at Cambridge University made a serendipitous discovery in 1989 that led to the founding of Cambridge Display Technology (CDT).

Professor Donal Bradley, Dr Jeremy Burroughes and Professor Sir Richard Friend had been testing an organic polymer called PPV for use in transistors when it transpired that on applying an electrical field, the polymer emitted light.

Though its efficiency was just 0.01%, the trio saw potential and filed a patent. At the time, no good blue LEDs had been invented. "The opportunity was a timely one in terms of what the other competing technologies were", says Professor Bradley, Vice-Provost of Research at Imperial College London.

They were joined by Cambridge chemists, Andrew Holmes and Paul Burn, and in 1990 published a seminal Nature paper which led to an explosion in plastic electronics research. The emerging industry – forecast to be worth \$300 billion globally by 2030 – uses carbon-based organic materials for electronics rather than traditional silicon and other inorganic semiconductors.

The advantages are that these are more easily processed at low temperature making them potentially cheaper and more environmentally friendly. They also have potential for superior performance in large area applications including flat screen displays, lighting and solar panels.

CDT was launched in 1992 once the scientists had reached their initial goal of 1% efficiency for their LEDs – it's much higher today. Funding came from various investors, including rock band Genesis members Phil Collins, Mike Rutherford and Tony Banks.

The company grew, with about 200 staff at its height and was sold to Sumitomo in 2007 for \$285 million. And some of its founding scientists have gone on to start up other companies.

One of the hardest challenges for commercialising this type of technology, says Professor Bradley, is timescale. "Many people we talked to wanted to see products in two or three years... you should be thinking on a 20-year timescale".

"Many people we talked to wanted to see products in two or three years... you should be thinking on a 20-year timescale."

Professor Donal Bradley

"As Professor Grubbs used to say, you don't have to work all the time, but you have to think all the time."

Professor Steven Ley

Vials

Glass Vials



PTFE

PFA Tubing

Biotage

Spares

Vacuum Spares

HALC

Success flows with green chemistry

Professor Steven Ley CBE FMedSci FRS

A pub conversation between three Pfizer employees led to the launch of a successful start-up that pioneered techniques in green chemistry.

Professor Steven Ley was approached by colleagues Dr Allan Marchington and Dr Ryszard Kobylecki about setting up a company to meet the growing demand for pharmaceutical compounds in the late 1990s.

The trio wanted to design compounds properly and so joined with an established company Oxford Molecular, headed by Allan's brother Tony, which had the software to do this. Together they launched Cambridge Discovery Chemistry in 1999.

One of the technologies they were working with meant they could make compounds without producing many of the waste products that would usually have to be removed using costly and energy-intensive methods, says Professor Ley, Director of Research at the Department of Chemistry at University of Cambridge.

Their technique used polymers to immobilise the reagents needed to make products, which meant that reactions could be filtered at the end of the process to "remove all the rubbish" and give pure compounds.

The company grew rapidly and at its peak had 130 staff and a turnover of \$15 million, with \$5 million profit. In 2000, it was bought for \$55 million by Millennium Pharmaceuticals. Though partnering with Oxford Molecular at the start was helpful in garnering financial support, Professor Ley said the need for continual cash injections to get the company established was the biggest challenge. But he urges scientists with good ideas not to be "inhibited by the grip of money in the process".

After the firm's success, Professor Ley launched another start-up in 2005 with Avecia Pharmaceuticals. Called Reaxa, this built on their green chemistry work particularly on "flow chemistry" techniques where the reagents are immobilised in tubes while chemicals flow past them. Reaxa has also since been sold.

In commercialising research, Professor Ley says good ideas are only the start of a process. "As Professor Grubbs used to say, you don't have to work all the time, but you have to think all the time", he says.

Tiny molecules key to finding new therapies

Sir Tom Blundell FMedSci FRS

He could have been a jazz musician, or a politician, but as a career Professor Sir Tom Blundell's love of basic science won out. And harnessing this passion led to an innovative therapeutics company developing potential cancer drugs.

In 1999, Professor Blundell co-founded Astex Technology to explore new approaches to drug discovery using fragments of larger molecules as starting points.

The idea came from his academic work studying the structures of biological molecules. Working with Nobel prizewinner, Dorothy Hodgkin, and colleagues, he was part of the first group to reveal the three-dimensional structure of vital hormone insulin in 1969.

At the same time he was a semi-professional musician and on the city council in Oxford. "Whilst I was re-organising the city plan of Oxford, I was also getting papers in Nature with Dorothy Hodgkin: being a scientist began to become much more attractive" says Professor Blundell.

Understanding the shape of biological molecules can help with drug discovery as compounds can be designed to fit specifically within well defined binding sites on different enzymes and receptors.

In the 1990s, many companies were creating huge libraries of complex molecules to test as potential drug candidates, but this was a massive undertaking which required millions of compounds to be screened, often with little success. "So how would you do better?" he and his colleagues asked. They came up with using tiny fragments of molecules instead – much simpler as fewer were needed to find leads to develop into potential drug candidates.

Professor Blundell, Dr Harren Jhoti, then at GlaxoSmithKline, and university colleague Professor Chris Abell set up Astex having secured an initial \$500,000 in 1999 from investment company Abingworth.

Getting money was the biggest challenge, says Professor Blundell. Over the years, Astex made 30 bids and gained support from venture capitalists, the university, and also received £120 million from pharmaceutical companies AstraZeneca, GSK, Janssen and Novartis.

The company grew and employed about 100 people in Cambridge, and in 2013 was sold to Otsuka Holdings for \$886 million. Crucially, Astex now has eight drugs in clinical trials.

Having a good business plan is vital in launching a company, says Professor Blundell. He also advises hiring entrepreneurial people who are "willing to come in and take a risk".

"Whilst I was re-organising the city plan of Oxford, I was also getting papers in Nature with Dorothy Hodgkin: being a scientist began to become much more attractive."

Professor Sir Tom Blundell



The Royal Society is a self-governing Fellowship of many of the world's most distinguished scientists drawn from all areas of science, engineering, and medicine. The Society's fundamental purpose, as it has been since its foundation in 1660, is to recognise, promote, and support excellence in science and to encourage the development and use of science for the benefit of humanity.

The Society's strategic priorities emphasise its commitment to the highest quality science, to curiosity-driven research, and to the development and use of science for the benefit of society. These priorities are:

- Promoting science and its benefits
- Recognising excellence in science
- Supporting outstanding science
- Providing scientific advice for policy
- Fostering international and global cooperation
- Education and public engagement

For further information

The Royal Society 6 – 9 Carlton House Terrace London SW1Y 5AG

- **T** +44 20 7451 2500
- E industry@royalsociety.org
- W royalsociety.org

Registered Charity No 207043 Issued: January 2015 DES3630