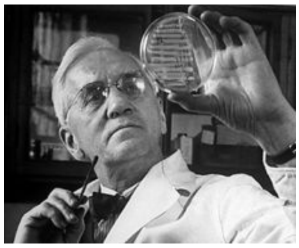
Curiosity-driven 'Blue Sky' Research: a threatened vital activity?

Sir John Cadogan

Inaugural President of the Learned Society of Wales



'One sometimes finds what one is not looking for.'

Alexander Fleming

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Although this is a paper commissioned by the Learned Society of Wales (Appendix 1), the threat addressed spans the entire UK scientific scene. In Wales, while Education is devolved, support of research through the Research Councils is not. This paper addresses funding in the latter category on the optimistic assumption that the vital QR (Quality-Related) funding from the University Funding Councils via the education budget line will be protected. Disaster would otherwise ensue. However, the same arguments apply to both categories of funding.

Important comments from 41 Fellows of the Royal Society (Appendix 2) and from Professor John Tucker, General Secretary of the Learned Society of Wales are gratefully acknowledged.

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A copy of this paper is available at:

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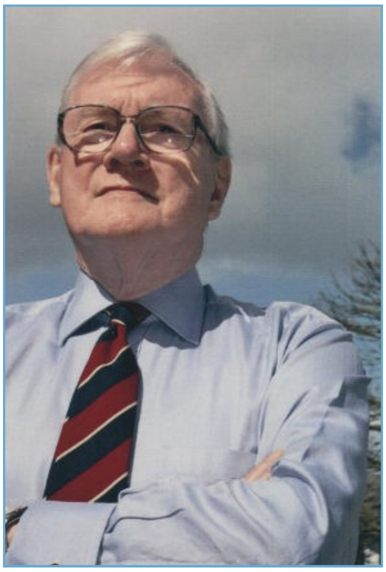

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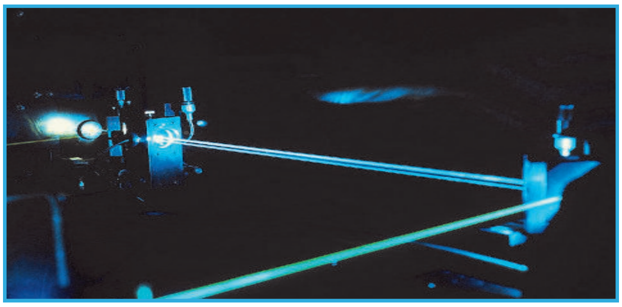
The Issue:

The word impact has become a favourite, indeed dangerously dominant, driver of our paymasters and their servants in relation to scientific research. Of course impact is an important factor but there is danger in deciding **in advance** the importance of a body of yet to be performed research. Emphasis on impact not only tempts scientists to go for the obvious in the light of fashionable targets of the moment, it may also stimulate the imaginations of our scientists— but in the wrong way, as Professor Dianne Edwards points out in Appendix 2, by imagining not new scientific ideas but dreaming up rationales to fit the demands of the programme managers. In most cases of the breakthroughs that have changed the world (Table) their impact was not seen at the time but realisation came many years later. Such demands for evidence of impact, in advance, displays convictions based on ignorance far beyond even a superficial understanding of the nature of scientific discovery. Heed should be taken of Nietzsche who asserted that 'Convictions are worse than lies'.

Industry and society depends on the university science base to make discoveries that no one knows need to be discovered.

The issue is the increasing imbalance in favour of directed research programmes relative to undirected, curiosity-driven research. The rationale of this paper is to attempt to redress the balance by reporting the impact of so-called 'blue sky' research. Much of the content of this paper has been underpinned by contributions from 41 Fellows of the Royal Society (including 7 Nobel Laureates, a Crafoord Laureate, a Dan David Prize winner and a Fields Medallist). These internationally distinguished researchers actually know the nature of discovery; they have done it and led it. Although this is a small sample it is significant. Their comments have great weight and are included with their permission in Appendix 2. Indeed, these are collectively so powerful they could well stand alone without the introduction provided by this paper.



We hear and see much about directed research programmes, and, of course, they have an important part to play, with the extent varying between research councils. Such programmes can and do lead to unexpected discoveries. Ole Petersen touches on this in Appendix 2 , commending the Medical Research Council's flexibility. Let no one deny these facts. Indeed the Medical Research Council (MRC) began as 'The Medical Research Committee and Advisory Council' in 1913 following concerns about tuberculosis. Time has modified the MRC's mission to accommodate, for example, the Laboratory of Molecular Biology which is an unsurpassed monument to, indeed beacon for, curiosity-driven research leading to immense and unforeseen practical outcomes, not to mention 13 Nobel Prizes, among the 30 which came after MRC support. This is as important as the vital service the MRC provides for the nation, for example, its continuous work in combating the ever-changing influenza virus.

It is easier for our paymasters to feel comfortable about proclaiming programmes related to Health, Energy, Materials, Climate Change, the Hydrogen Economy and so on rather than to announce, let alone trumpet, that money is available for scientists and engineers to follow their curiosity in their own disciplines .

However, some of the abundant directed programmes today smack of quasi-industrialism. But any knowledgeable industrialist will say that industry depends on the university science base to make discoveries that no one knows need to be discovered – discoveries outside the box, so-to-speak. As an aside, industrialists have an important part to play; they must have awareness 'in-house' in order to latch on as intelligent customers to discoveries made elsewhere. It is no good contracting-out research if there isn't the front line knowledge in-house to cherry-pick, and thus to know whether the outcome is of any value. Also, the process of contracting-out means that the crucial selection and management of operating personnel is not under in-house control. This can be disastrous. Sadly, UK industry no longer uniformly wants to be, or is good at such in-house capability. As the amount of research inside UK industry declines, so does research council support for vital curiosity-driven research in the universities. This describes not so much a vicious circle but a downward spiral, leading to the UK research deficit double whammy.

Socio-economic targets are not scientific disciplines. Without discoveries in and across disciplines populist targets become part of a meaningless and unattainable wish list.

Over the last 15 years the UK science budget has grown significantly, and successive Governments should be congratulated on this. But Government and research council direction has increased too. It is completely acceptable for Government to demand evidence that the taxpayers' money is being spent in ways which will return benefit to the nation. However, Government must also accept without challenge that the socioeconomic advancement of humankind has its roots in science and technology, and that much of that has been curiosity-driven. However, the nature of all politics and politicians means it is easier for our paymasters to feel comfortable about the proclaiming of programmes relating to Energy, Health, Materials, Climate Change, the Hydrogen Economy and so on, rather than to announce, let alone trumpet, that money is available for scientists to follow their curiosity in their own disciplines. Short-term populism is cemented into the way politicians work in order to gain or retain power. The result is that curiosity-driven research that may bear fruit after a long time is being squeezed. This is to

'Social media can make some people very rich but cannot save the planet. The latter requires new fundamental discoveries.' – Sir Andre Geim

deny not only the nature of scientific discovery, but the lessons of history.

That it has always been this way, to some extent, is no reason to just accept it. Sir John Meurig Thomas reminds us that Faraday, the unsurpassed genius of discovery and pioneer of curiosity-driven research, was once instructed by a joint committee of the Board of Longitude and the Royal Society, chaired by Humphry Davy, to investigate the properties of glass, and hence better telescopes for the Royal Navy. He didn't like this very much and said so in a letter of 13 May 1830 to Peter Roget, of Roget's Thesaurus, a secretary of the Royal Society:

> 'With reference to the request which the council of the Royal Society have done me the honour of making, namely, that I should continue the (glass) investigation, I should under circumstances of perfect freedom assent to it at once. But, obliged as I have been to devote the whole of my spare time to the experiments already described and consequently to resign the pursuit of such philosophical enquiries as suggested themselves to my own mind, I would wish, under present circumstances, to lay the glass aside for a while, that I may enjoy the pleasure of working out my own thoughts on other subjects.'

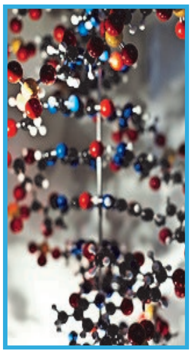
This was after Davy and Thomas Young of the committee had both died in 1829.The committee was subsequently dissolved and Faraday was free to return to exploring his own ideas. On 19 August 1831 he discovered electromagnetic induction.

The genesis of the problem is that the beloved socioeconomic targets of policy makers – as mentioned above – are not disciplines, unlike nuclear engineering, chemical and biological catalysis and synthesis, photobiology, studies of the solid state, genomics, molecular biology, immunology, electrochemistry, computer science, software engineering, optoelectronics and so on and on, which are. Without discoveries in and across these disciplines, the aforementioned populist targets become part of a meaningless and unattainable wish list. As Sir Andre Geim of graphene fame said 'Social media can make some people very rich but cannot save the planet. The latter requires new fundamental discoveries.'

Planned discovery is impossible.

Peter Doyle, former director of research for Astra Zeneca and Chairman of the Biotechnology and Biological Research Council (BBSRC), put it well when he said 'We don't much care what they [the scientists] do as long as they are first class, making discoveries working with and training excellent students and post-docs in areas of interest to us, such as chemistry, immunology, pharmacology, physiology and so on. Most of all we want to be close to such people. We don't look to them to find the drugs — we will do that, given a start.'

Scientific discovery is all about getting starts in races that were hitherto unknown. Nevertheless, it is highly desirable that scientists, whether following their curiosity or not, should develop peripheral vision, an awareness of what is going on elsewhere and of what is needed. Being constrained by the boundaries of a directed programme can be anticatalytic if not inhibiting. There is a tendency for such programmes to be based on proposals which are one step forward from what we know now. A discovery in one discipline often has application elsewhere. As Sir Colin Humphreys points out, 'the beauty and immense value of blue sky research lies in starting along a path but being free to branch out to follow where ever the science leads with no bureaucratic constraints. No one can say, "Don't do that because it wasn't in the original proposal."'



A good industrial example of a discovery coming from 'left field' relates to the production of ammonia by the Haber process, undoubtedly a world changing invention. Today the amount of ammonia needed to feed the world is immense. There are some 100 world-scale plants each producing up to 2000 tonnes a day. It is difficult to grasp what 2000 tonnes of ammonia looks like. The catalyst used is probably the most important catalyst ever discovered. But the essential catalytic systems have been largely unchanged over a century despite much research and suffer from the fact that the energy consumption needed for this vital component of world food production is very high. Scientists in the once great but now closed BP Sunbury Research Centre, were not interested in ammonia production, but, in looking for a better hydrocarbon reforming catalyst, discovered a ruthenium on carbon catalyst which one of their number, gifted with peripheral vision, sensed would fix nitrogen. Years of development in collaboration with the Kellogg Corporation led to a completely new low energy process (KAAP) based on a catalyst 20 times more active than the existing Haber catalysts. 7 world-scale plants are now in operation, no doubt with more to come.

The fact that planned discovery is impossible is surprisingly difficult to get across. Indeed it often leads to dismissive comments: 'So it is all a matter of luck then?' To constrain the genesis of new ideas within socioeconomic boxes is counter to the reality of discovery wherein ideas leading to really new starts come from the minds of scientists. Let us have some boxes but don't box everything. No Minister, civil servant administrator, committee, board of directors or even network has ever made a discovery. Discoveries are made in the laboratory and the library, while ideas can arise during walks in the fields. Some will come from directed programmes but so many have their genesis in curiosity-driven research. In the past, research councils have mainly responded positively to such proposals. The creeping emphasis in

Government and research council *dirigisme* is not favouring this approach. Sufficient support must also be available for our scientists to break new ground and make discoveries that we didn't know were there to be discovered and certainly those not dreamt of by the research council programme commanders.

It bears repeating that today, more and more funding is being directed to particular areas at the expense of curiosity-driven work out of which much discovery results, and from which directed programmes follow. There is evidence, rather than belief, that out of unplanned discoveries great and unexpected developments come. Indeed, Nobel Laureate George Porter's aphorism, 'There are two types of chemistry– applied and yet to be applied', fits most of science.

Recently our researchers reeled under a dangerous nonsensical command from the Engineering and Physical Sciences Research Council (EPSRC), only partly modified after outcry, that, from 15 November 2011 'applicants will have to clearly identify the national importance of their proposed research project over a 10-50 year time frame' – a remarkable instruction from a research council which should, in particular, be sponsoring research that could lead to unforeseen discoveries.

What are the lessons of history? Where have the great breakthroughs come from?

None of the great breakthroughs which have changed the world would have met the EPSRC's command. These discoveries were non-linear and not the result of taking the next obvious step from where we were before. They came from the unconstrained ideas and observations of scientists and not a programme chosen by a committee. This has been the case since Humphry Davy and Faraday. Just some examples, among hundreds, are given in the table.

Many more telling examples derived from our FRS contributors are described in Appendix 2. There is a monograph waiting to be written to give full weight to the gathered evidence, but the following examples are to the point:

The first computers were huge and were based on thermionic valves emitting immense quantities of heat. All work on improvement therefore focussed on better valves. 'There will be a need for four or five supercomputers in the world', said the head of IBM, 'and they will weigh no more than a ton.' Meanwhile, elsewhere, the transistor and microprocessor were being invented by people who did not have computers in mind at all at the outset. Even then the early work was directed at making transistors behave like thermionic valves as amplifiers, rather than capitalising on their properties as fast reliable switches – which led to the exponential changes in computer

Lasers
Haber process for the fixation of nitrogen
Optical fibres
All forms of spectroscopy from microwave to magnetic resonance imaging
X-Ray crystallography
X-rays and positron emission tomography
Nuclear fission
Penicillin and hence antibiotics
Dyestuffs
Photography
Liquid crystals
Small molecule therapeutics
Organic chemical synthesis in general
DNA and hence genomics
Monoclonal antibodies
Stem cells
Finite element analysis leading to countless applications including the Air Bus wing
Free radicals
Organic polymers and composites
3K and 'warm' superconductors
The transistor
Photovoltaics
Radio

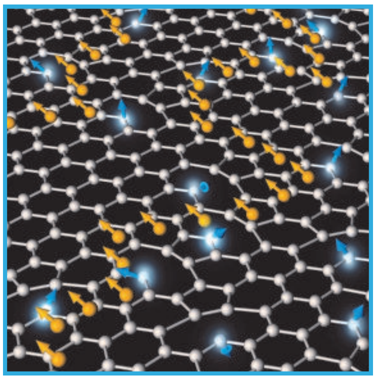
technology. In this case, as in countless others, scientists and engineers with peripheral vision often in 'intelligent' industry saw the opportunities for new technologies arising out of unforeseen discoveries.

Similarly, George Gray, the pioneer of the properties of liquid crystals, did not have flat screen TV in mind as he carried out what subsequently turned out to be seminal work. If, indeed, the paymasters of the day had had the nous to call for flat screen TV then it is likely that they would have taken a linear approach and funded attempts to design a narrower cathode ray tube. As an aside, it is interesting to note that Gray's proposal for exploratory research into liquid crystals was turned down flat by the then Chemistry Committee of the then Science Research Council (SRC) on the grounds of being dull. He was rescued by the foresight of the Ministry of Defence research group at Malvern. In the same vein Nobel Laureate Sir Harry Kroto's proposals relating to the fullerenes, foundered at the same committee. Afterwards a member of the committee said to the author 'He may well have a Nobel Prize but he can't write a decent research proposal.'

A really worrying downside of the emphasis on directed programmes is that the next generation of researchers will themselves become programmed to only have ideas which are user-oriented as seen today.

Again, when Nobel Laureate George Porter discovered the ClO free radical no one had the faintest idea that the ozone hole existed, let alone that this was the radical that caused it, and hence where the solution lay. Indeed the discovery of this radical led to the postulation that there might be a hole in the ozone layer, and later, to another Nobel prize.

When an ICI scientist discovered that his reaction 'went wrong ' and the unexpected slime in his reaction vessel subsequently turned out to be polyethylene, no one could then think of a use beyond non drip candles. Recognition of its myriad applications came later. The discovery of PTFE (Teflon) is a similar story.



When Sir Rex Richards had the idea that nuclear magnetic resonance, hitherto focussed on the quantum mechanics and physics of the process, could have seminal applications in chemistry he was at first denied by the experts. But he persevered. Realising that the future development of Nuclear Magnetic Resonance (NMR) lay in the strength of the magnets employed, and learning in 1963 that an American company had made a length of superconducting wire, Richards had a breakthrough idea. He and colleague Martin Wood bought a piece and wound it (in a garden shed) around a small magnet, cooled it in liquid helium, and achieved a field double the greatest field possible with an iron magnet. The Science Research Council responded at short notice to his curiosity-driven proposal and out of it came immense applications which transformed existing knowledge of chemistry, molecular biology and the solid state. The discovery led to the birth of Oxford Instruments and hence to a superconducting magnet leading to the enabling technology for the Large Hadron Collider (LHC) at CERN and to whole body magnetic resonance imaging (MRI), the word nuclear having been dropped lest it frightened patients.

As Sir Andre Geim points out:

> 'The silicon revolution would have been impossible without quantum physics. Abstract maths allows internet security and computers not to crash every second. Einstein's theory of relativity might seem irrelevant but your satellite navigation system would not work without it. The chain from discoveries to consumer products is long, obscure and slow, but destroy the basics and the whole chain will collapse. This logic

dictates that we invest in blue sky research to gain new knowledge. Without new knowledge only derivative technologies are possible.'

Lyn Evans, director of the great LHC experiment at CERN said in a lecture to the Learned Society of Wales: 'At the time, no one in CERN foresaw the subsequent impact of the World Wide Web.'

Sir Alec Jeffreys had a 'eureka' moment in his laboratory in Leicester after looking at the X-Ray film image of a DNA experiment which unexpectedly showed both similarities and differences between the DNA of different members of his technician's family. Within half an hour he realised the possibility of DNA 'Fingerprinting'. Its subsequent applications have been simply immense.

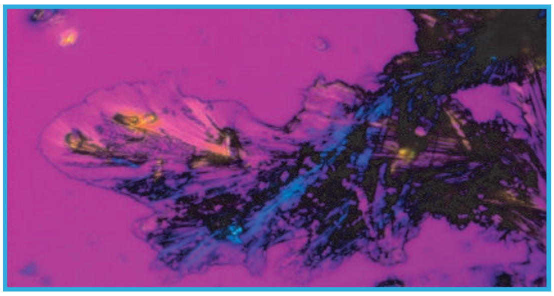
We should bear these lessons from history in mind, for example in the urgent problem of energy generation. It is not surprising that there is a call for bigger wind turbines but the prospect of a breakthrough in technology is minimal. Windmills have been around for ages – making things bigger is not a breakthrough, though great developments in engineering might well be needed. For now it appears we have to settle for this approach, but the prospect of a step change breakthrough here is as likely as that in the technology of the electric toaster. Meanwhile someone, somewhere, working at the frontier of solid state or photobiology might make an unheard of, unsought, discovery leading to a new fount of energy. Indeed someone else from another field might be the one to spot its significance. Maybe it will lie with graphene or with the finding of a usable material that will superconduct at room temperature. Who knows? This is the nature of discovery. There must be room for this.

What of the next generation of researchers?

An additional and very worrying downside of the emphasis on directed programmes is that the next generation of researchers will themselves become programmed to only have ideas which are user-oriented. When we built the canals no one foresaw the advent of steam or internal combustion engines. The time from discovery to applicable outcomes is well outside the attention span of politicians focussed on getting and retaining power within a five-year timetable. Who can blame our youngsters? They will be scared that, if their proposed research is not in response to direction by bureaucrats and politicians, not to mention the power wielders in the universities, they won't be able to get any support. This may be the worst and most insidious outcome of the present system. Professor Archie Howie notes in Appendix 2 that 'people simply get out of the habit of thinking blue skies.....more active, younger colleagues tend automatically to channel their thoughts along fashionable lines usually hyped with magic buzz words so seductive that they soon believe all of it themselves.'

None of the great breakouts that have changed the world have come from directed programmes.

The current emphasis on Doctoral Training Centres and Partnerships is another dangerous example of how the balance is being tipped the wrong way. The rationale here is that PhD programmes are all about training and not about discovery and education in how to think, work independently, identify worthwhile questions and conduct research to answer them. Worse, most of the centres operate in the directed-research mode, wherein all PhD topics must conform to areas designated by authority. Of course, training is an important component of postgraduate preparation but it must be said that many real steps forward in the past came via PhD students without any interference from the research councils on the topics studied. It was in these circumstances that much of our successful curiosity-driven research emerged. Nobel Laureate Brian Josephson's Junction is the pre-eminent example. These students actually made discoveries as well as being



supervised by young (importantly) as well as mature researchers. Now this really large source of blue sky discovery has largely gone. Thank goodness for the Royal Society's unfettered Research Fellowships (RSRF), charity support and related awards. The RSRF are funded by a direct grant from the science budget to the Royal Society. It is a mercy that previous calls for this budget to be passed to the research councils were resisted. It is a matter of opinion whether this money would have by now been shunted into directed programmes.

Sir John Enderby summed up nicely when he wrote, on becoming the Editor of the Journal of the Foundation for Science and Technology:

'The challenge facing those responsible for science policy is how to maintain an intellectual climate in which curiosity can flourish.'

Evidence from the short-lived ROPA (Realising Our Potential Awards) scheme:

Until the advent of the ROPA scheme, there had not been a thorough survey of the outcomes of curiosity-driven research in the UK. This was designed and controlled by the Office of Science and Technology to support Blue Sky research through modest start-up grants. They were intended to fund 'proof of concept' studies opening new research avenues outside the boundaries laid down by research council committees, and to demonstrate where there was a compelling case for follow up funding. The judgement on what should be researched was left entirely to the researchers themselves. Due to the councils' unease about this loss of control over what research would be carried out the scheme operated for five years only before it was killed off. But before its death, the output of the scheme over the first four years was assessed, and, in so doing provided a published systematic assessment of the value of curiosity-driven research. Despite the evidence now being sixteen years old, it is highly relevant to this paper.

The rationale of the ROPA scheme followed the justifiable fear that research council directed programmes and those undertaken in collaboration with industry were swallowing up support, making it difficult for researchers to get funding to follow their curiosity and attack targets of their own rather than those of a committee's or industrialist's choosing. The entry card to the scheme was limited to researchers who were in receipt of strategic research from industry, as opposed to those university researchers confined by contract work to solve particular industrial problems or make widgets for industry. In many cases industry just wanted to be close to established or potential research leaders, as Peter Doyle said above. The entry barrier was an industrial contribution of £25000 in cash, not in kind. So, a reward for working strategically with industry was a blue sky scoping grant for researchers to carry out work of their choosing, entirely independent of whether the research council approved of the topic of the proposal. The underlying assumption was that if industry thought the researcher was good enough to be supported then that was enough. This was not uniformly acceptable to the academic community or the research councils. There was an unjustified assumption by some who had not worked with industry that science so produced was of lower calibre. However, The Royal Society gave its general approval to the scheme.

'The challenge facing those responsible for science policy is how to maintain an intellectual climate in which curiosity can flourish.' – Sir John Enderby

The councils were required to certify that the proposals were 'original and technically feasible' and were truly blue sky in the sense that they were not merely extensions of the original industrial support. Furthermore, the sponsoring industry was to have nothing to do with the proposal. The councils were not to rank these in their normal terms of alpha, beta and so on.

The holders of all 974 ROPAs awarded during 1994-1997 (inclusive) were asked to complete a questionnaire to which 71% responded. During this period, 1209 awards (38.2% of applications) totalling £109 million were made. This was in the context of the then science budget of circa £1.3 billion.

The results were remarkably revealing, surprising even the scheme's most ardent supporters. First, they uncovered the fact that very substantial support from industry amounting to at least £207 million for strategic research (corresponding to the 38.2% success rate) was going into the university science base unbeknown to the research councils or, very importantly, the Treasury. The latter fact, subsequently, was key in countering the canard that university researchers were of little value in giving a return to the taxpayer. This realisation in part, led to the largest percentage increase in governmental departmental budget falling to the Science Base at the first and defining Comprehensive Spending Review. Although at the time of the survey's distribution only half of the projects had been completed, responses showed that ROPAs funding had helped win follow-up funding from:

- Research councils in 194 cases (20% of awards)
- Industry and commerce in 318 cases (33% of awards)
- EU and other bodies in 151 cases (15% of awards)

ROPAs funded blue sky research not aimed at direct commercial benefits and were forbidden to involve a commercial partner. Nevertheless, the outcomes were such that:

- in 386 cases a company expressed interest in the project
- in 145 cases a company agreed to fund further development
- in 73 cases new patents were applied for

ROPA holders were asked for comments on the scheme, the full list of which is given in Appendix 3. Here was evidence that unfettered curiosity-driven research produced many new starts. The early demise of ROPA was a decisive first strike against the support of curiosity-driven research.

When challenged recently the response from Government was:

'Over the last decade the landscape has changed in a way that makes the ROPA scheme approach less applicable now than at the time.'

Exactly… the landscape has indeed changed, but for the worse. It is reasonable to draw from this the conclusion that curiosity-driven research is now seen to be less important. What remains to be seen is how long the UK will be able to claim to be second only to the USA in terms of research achievements.

What next?

The conclusion of this paper is not that we should not have directed programmes but that the balance has swung too far in their favour. This reduces the probability of discovering new knowledge with the further downside that the next generation of scientists will become short-term practitioners driven solely by what are perceived to be user-needs of the day. All combining, this reduces the founts of 'new starts' and reservoirs of creative scientists that we need to nourish the general socio-medico-economic scene and creative industries other than Strictly Come Dancing and its ilk.

The UK Government's Chief Scientific Adviser and the Director General for Knowledge and Innovation should be charged with devising a funding programme, with its own budget line, to ensure ongoing support for blue sky research for its own sake, rather than tie it to some Grand Challenge or other. If this is too difficult then let the Royal Society do it. They owe this not only to the scientific community, but to the future of the Nation. Other countries will always beat the UK when it comes to low-cost, derivative manufacturing. We can only survive, let alone win, by being leaders in discovery and its subsequent application at the highest technological level. Not to strongly support curiosity-driven research is ridiculous.

APPENDIX 1: Call for contributions from Fellows of the Royal Society

The following letter was sent to 70 Fellows of the Royal Society. Written Replies were received from 45.Two of these declined on grounds of ill health, one could not through pressure of business and one over-modestly felt that his contribution was not significant.

Dear ……………………………………..

The need for "Blue Sky", curiosity driven research

I am preparing a paper for publication by the Learned Society of Wales on this subject and I write to ask for your help. The issue is the balance between directed research programmes and undirected, curiosity-driven research.

We hear and see much about directed research programmes and of course they have an important part to play, with the extent varying between research councils. But it is easier for our paymasters to feel comfortable about proclaiming programmes related to Energy, Health, Materials, Climate Change and so on rather than to announce, let alone trumpet, that money is available for scientists to follow their curiosity. The fact that planned discovery is impossible is difficult to get across. No Minister, civil servant, committee or board of directors has ever made a discovery. Discoveries are made in the laboratory and the library. Some will come from directed programmes but many have their genesis in curiosity-driven research where research councils respond to such proposals. We must ensure that sufficient support is available for our scientists to break new ground and make discoveries that we didn't know were there to be discovered.

More and more funding is being directed to particular areas at the expense of curiosity-driven work out of which much discovery results and directed programmes follow. We can all give many examples of the value of curiosity driven research such as the laser, once a solution looking for a problem but now is all pervasive. I already have a long and impressive list of these. Further suggestions would be welcome.

In addition it is my belief that some, maybe much, of the seminal work carried out by our best scientists — the FRS — did not arise from directed programmes but it would be most helpful and compelling to have specific examples of this. Can you help with this, please? Did what you consider to be your seminal results come in response to directed programmes? Would you have got a start under the present system?

It can also be said that many real steps forward came in the past via PhD students without any interference from the research councils on the topics studied. These students actually made discoveries as well as being trained by young as well as mature supervisors. The centres for doctoral training mostly operate in the directed research mode. Thank goodness for the Royal Society's Research Fellowships and related awards.

Happily, the extreme requirement by EPSRC that all applications for support should clearly state the benefits to the nation on a 10 to 50 year time scale has been modified, though not totally removed. Impact has become a favourite word of our paymasters. I hope the planned paper, with your help, will redress the balance by reporting the impact of undirected, curiosity-driven, 'blue sky' research.

I hope you will be able to find the time to contribute. You may find it easier to reply by e-mail, care of ………………………………..

Yours sincerely

John Cadogan

Sir John Cadogan

President

APPENDIX 2: Contributions from Fellows of the Royal Society

List of Contributors:

Professor Sir Andre Geim FRS, Nobel Laureate

Professor Sir John Gurdon FRS, Nobel Laureate

Professor Anthony Hewish FRS, Nobel Laureate

Professor Brian Josephson FRS, Nobel Laureate

Professor Sir Harold Kroto FRS, Nobel Laureate

Sir Paul Nurse PRS, Nobel Laureate

Professor Sir John Walker FRS, Nobel Laureate

Baron May of Oxford OM AC Kt FRS, Crafoord Laureate

Sir Michael Atiyah OM FRS, Fields Medallist

Professor Geoffrey Eglinton FRS, Dan David Prize winner

Dr Ray Baker CBE FRS

Professor Shankar Balasubramanian FRS

Professor Anthony Barrett FRS

Professor Sir Tom Blundell FRS

Professor Robin Clark CNZM FRS

Professor Dianne Edwards CBE FLSW FRS

Professor Sir John Enderby FRS

Professor Sir Anthony Epstein CBE FRS

Professor Jim Feast FRS

Professor Michael Hart CBE FRS

Professor Dame Julia Higgins DBE FRS

Professor Archie Howie CBE FRS

Sir Colin Humphreys CBE FRS

Professor Graham Hutchings FLSW FRS

Professor John H. Knox FRS

Baron Krebs of Wytham Kt FRS

Professor Steven Ley CBE FRS

Sir Ronald Mason KCB FLSW FRS

Professor Ken Packer FRS

Professor Gerald Pattenden FRS

Sir John Pendry FRS

Professor Ole Petersen CBE FLSW FRS

Sir Rex Richards FRS

Professor Wilson Sibbett FRS

Professor Tom Simpson FRS

Professor Malcolm Stevens FRS

Professor Charles Stirling FLSW FRS

Professor Sir Fraser Stoddart FRS

Sir John Meurig Thomas FLSW FRS

Professor Kenneth Walters FLSW FRS

Professor Robin Williams CBE FLSW FRS

Professor Sir Andre Geim FRS, Nobel Laureate

Dear Sir John,

Indeed, I do have a strong opinion about the importance of curiosity-driven research and expressed it vociferously on many occasions. Here are some opinion pieces in the *FT* and *Nature*, for your reference and, possibly, even enjoyment.

Available at:
http://www.condmat.physics.manchester.ac.uk/media/eps/condensedmatterphysicsgroup/people/academic/geim/Be-afraid,-very-afraid.pdf

Social media will not save us from a cosmic rock on course to hit Earth. "What are you doing here?" The software billionaire choked in astonishment when I told him I was a physicist. The reaction was informative: it was as if he had encountered a seasonal labourer at our meeting place, the World Economic Forum in Davos.

Between networking, self-promotion and all the other things politicians and financiers normally do (including skiing), the distinguished crowd at Davos last month discussed the poor health of the global economy. Heads of state saw the cure in better governance; central bankers, in better financial controls; investment bankers, in the markets. Economists offered new theories and Internet entrepreneurs put their trust in social media. The only thing they shared was a belief that a quick fix was available.

The advantage of ivory towers is that they allow a view beyond immediate problems. Where one sees banking crisis, debt crisis, currency crisis or some other crises, academics may see even more worrying developments. We are in the midst of a technology crisis. Disruptive technologies now appear less frequently than steady economic growth requires. Even bankers complain about a dearth of new technologies in which to invest.

Look back to the second half of the last century and it was packed with technological advances. The silicon revolution led to computers, microchips, mobile phones and the web. There was also Sputnik, lasers, the Moon race, the Global Positioning System. In the past two decades, apart from social media, it has been less about disruption, more about honing the same gadgets.

Many economists argue that the "low-hanging fruit" have been picked and we approach a prolonged period of stagnation. But since this has not yet led to a clear economic decline, people pay little attention. The fact that economists are well known for their eloquent explanations as to what went wrong with previous theories does not help.

My own ivory tower provides a view of basic science, where economists do not venture. I see a severe crisis in delivering new knowledge. It is not that discoveries no longer occur but that the rate has slowed. Without new knowledge, only derivative technologies are possible – and, however important, they are incapable of sustaining the sorts of economic growth rates the world has enjoyed since the coming of the industrial revolution.

For a lay person, blue-sky research can appear a waste of money as it does not immediately provide the modern equivalents of bread and circuses. Taking a longer view, however, there is no such thing as useless fundamental knowledge. The silicon revolution would have been impossible without quantum physics. Abstract maths allows internet security and computers not to crash every second. Einstein's theory of relativity might seem irrelevant but your satellite navigation system would not work without it. The chain from basic discoveries to consumer products is long, obscure and slow – but destroy the basics and the whole chain will collapse.

This logic dictates that we invest in blue-sky research to gain new knowledge. Everyone I spoke to at Davos was unequivocally in favour of increasing support for science. Unfortunately, humans are not logical animals. When I asked the same people whether their companies would pay a science-targeted tax, the answer was an equally unequivocal No. No to a personal tax, too. As if the money could come from somewhere else.

Until 40 years ago, the threat of hot and cold wars forced countries to look for long-term advantages over potential enemies. At the risk of being simplistic, let me say this threat fed back into investment in science, which allowed the industrial revolution to continue. Today, the threat from global warming, overpopulation and scarce natural resources seems insufficiently scary.

Western governments have been folding their blue-sky programmes in response to financial restraints and voters' negative view of academic research. Davos persuades me there is little hope of change. This would require a change in human nature. I fear economists might be right this time, and Japanese-style stagnation will look like a best-case scenario.

But I have a dream. The industrial revolution and economic growth continue. This is because astrophysicists find a huge cosmic rock on course to hit Earth in 50 years. This should be scary enough. The world can surely deflect this threat but will need to develop new knowledge and technologies. Finally, in my dream, humans realise social media can make some people very rich but cannot save the planet. The latter requires new fundamental discoveries.

Available at:

http://www.condmat.physics.manchester.ac.uk/media/eps/condensedmatterphysicsgroup/people/ academic/geim/Science-FT12.pdf

Amid more acute crises, chronic under-investment in science has gone unnoticed. My 10-year-old daughter no longer believes in fairies. Or so I thought until last month, when I asked her whether she still believed in Santa Claus. "Where do you think Christmas presents come from, Daddy?!" she replied.

I then experienced a distinct sense of déjà vu at the European Commission's first Innovation Convention in December. It was clear that everyone there loves science. José Manuel Barroso said both publicly and privately that he trusts science will in the end solve all our problems, from the current economic crisis to climate change. Science was unanimously referred to as the only reliable medicine for sorting out all our traumas and providing long-term growth. Such deep faith in science was remarkable, and my heart melted. But there was a catch. It was equally clear that policymakers perceive science as something abstract and remote, à la Santa.

The list of speakers at the forum implied that science has little to do with innovation. A couple of practising scientists were lost amid chief executives, entrepreneurs, heads of various councils, university presidents and science popularisers. The most entertaining speaker was Michael O'Leary, chief executive of Ryanair, who shared his personal vision of innovation: coin-operated toilets and taxing overweight passengers. His antics were at least fun, and the one-man-advertising-agency did not hide his intention to promote the airline among potential customers.

Sir Leszek Borysiewicz, Cambridge University vice-chancellor, was the most reassuring about our economic future. He reminded the audience several times that he represented an 800-year-old institution. According to Sir Leszek, innovation will be fine, so long as everyone follows the model of his 800-year-old institution. Everyone applauded his positive attitude at the time of crisis.

Don Tapscott, author of Wikinomics, was the advertised star of the show. He explained to the audience that Boeing's Dreamliner – 20 per cent more fuel efficient than earlier models – is possible due to a new business model of web networking. He did not bother with such details as better engines and aerodynamics, and the use of new composite materials. His message was so well received that, watching the enthusiastic applause given to him by officials, I imagined them issuing a mandate that all Commission staff join Twitter and carry a second Blackberry.

My own talk was a waste. I reminded the audience that without scientific discoveries there could be no new basic technologies and, without these, scope for innovation was limited. Eventually, we would end up in a great stagnation, if we are not there already. I also warned about the emerging technology crisis that stems from chronic underinvestment in basic sciences for the past 30 years. Amid other, more acute, crises this has gone unnoticed, because it takes decades for scientific discoveries to result in consumer products. Previously, science was high up governments' agenda because of external threats but, without them, calls for better funding are doomed to be ignored amid cries for lower taxes.

How far I was off the mark can be judged from the following anecdote. At a dinner table, European officials and science ministers were curious about my line of work. In 2010 I shared the Nobel Prize for physics for my work on graphene, an exciting new material with a wide range of potential applications. But graphene was no good as a reference.

So, I explained that I was at the start of a long economic chain leading to more powerful computers and gadgets, which require smaller and faster transistors. To my surprise, the listeners were well informed. I should not worry – one interjected – Moore's law, which says that the number of transistors on a microchip doubles every two years would take care of everything. I felt snubbed. I had no strength to explain that Moore's law is not a law of nature but an observation.

What is the moral of my journey? Karl Marx, who was a disastrous revolutionary but a good economist, once stated that every nation had the government it deserved. Judging from the Brussels convention, Europe has exactly the state of innovation that we deserve.

Kind regards,

Andre Geim

Professor Sir John Gurdon FRS, Nobel Laureate

Dear Sir John,

Thank you for your eminently reasonable view that too much emphasis is now placed on directed research and insufficient opportunity given for undirected discovery.

In the case of my own particular career, the work I did on nuclear transplantation many years ago might well not have had support at the present time. This is because, at that time, there was no indication that nuclear transfer could lead to the prospect of cell replacement in humans, as now seems a very likely outcome.

I believe that it is important that all non-directed research should have an aim of elucidating some important problem or question in how cells or organisms work. In my own case there was the question of whether all cells have, or did not have, the same set of genes. It turned out that they do, and this has opened up, some 50 years later, the prospect of cell replacement, especially in the human eye.

Thank you for your letter and I hope that this small example may be of some small value.

Yours sincerely,

John Gurdon

Professor Anthony Hewish FRS, Nobel Laureate

Dear Sir John,

In response to your request for examples of major discoveries resulting from curiosity-driven research I can mention a few from astrophysics which is certainly a blue-sky area!

The sky survey which I initiated at the Mullard Radio Astronomy Observatory, Cambridge, using a specially designed large phased array of dipole antennas to achieve high angular resolving power by means of interplanetary scintillation soon led to the totally unexpected discovery of pulsars in 1967. In addition to their astrophysical importance these rapidly rotating neutron stars provide time standards of high accuracy. In 1968, after announcing our discovery (and very tongue-in-cheek) I took out a patent for interstellar navigation using pulsars in much the same way as terrestrial satellite navigation!

During the sky survey for which the antenna was designed we also found that the day-to-day variations of interplanetary scintillation could be used to track major disturbances in the solar wind as they moved away from the Sun. Such space weather maps could be very useful in predicting the occurrence of geomagnetic storms and energetic particles which can damage spacecraft and disrupt electrical power lines on Earth.

Perhaps the most important observation in astrophysics over the past fifty years was the discovery of the cosmic microwave background radiation by Penzias and Wilson in 1965. This again was a lucky chance from curiosity-driven research.

Finally it is worth remembering that the first Nobel award in Physics was to Rontgen in 1901 for his discovery of X-rays. He was experimenting with cathode rays when he found that sensitive plates elsewhere became exposed.

I hope these few examples may help to demonstrate the importance of curiosity-driven research.

Yours sincerely,

Antony Hewish

Professor Brian Josephson FRS, Nobel Laureate

Dear Sir John,

My own research of the 1960s for which I was awarded a Nobel Prize (and which has a number of practical applications) was certainly curiosity-driven. My official PhD project involved superconductors, so I learned about them and was curious as to why this phenomenon occurred. My investigations led me to understand that the phase of the wave describing the superconducting state was crucial, and I wondered what more direct physical manifestations there might be of it. Studying this problem was what led me to my discovery.

I don't know much about the present system, though I hear complaints from my colleagues about the time spent in preparing grant applications, and this idiotic business of having to demonstrate that the research will benefit the economy. I have very occasionally applied for a grant but never been successful, but I do not require much funding as my work is theoretical, my college provides support for going to conferences, and in the 1960s a US foundation gave me a large award, half of which was in the form of research support, and which I draw upon occasionally, e.g. for equipment and short term funding of co-workers. Also, before my retirement I received an annual grant from the dept. as staff member.

Yours sincerely,

Brian Josephson

Professor Sir Harold Kroto FRS, Nobel Laureate

Dear John,

My story began with getting the money for my own microwave spectrometer (1974). These were the heady days of the dual support system when youngsters like me would receive a modest contribution to their research costs via a departmental allocation. The executive committee of the department had an incentive to make sure that young people that they had hired could do some research without having to spend inordinate amounts of time begging, cap-in-hand, for funding from faceless committees.

During the decade from 1979 onwards a revolution in astrophysical chemistry took place. It had its origins in the brilliant discoveries made by Charles Townes' group using radio astronomy which detected radio spectra from the interstellar molecules in the dark clouds in the space between stars. At this time we were measuring the radio frequency of polyynes. Following this and with Takeshi Oka we detected the first long carbon chain molecule to be found in space. I wondered whether the carbon chains were most likely produced in the atmospheres of red stars and subsequently expelled into the regions of the interstellar medium where we had detected them. The next step came in a visit to Rick Smalley and Bob Curl in Rice University, where Rick expounded the way in which his newly created cluster beam machine worked, using a laser to vaporise metals. During the demonstration I began to formulate a project to simulate in the laboratory the conditions I thought might occur in a red giant star and be responsible for the carbon chains we had detected by radio astronomy. Seventeen months later Bob called me to say that they were going to try the experiment and invited me to join. I paid my own intercontinental air ticket and during the 15 day visit in September 1985 carried out the research, with undergraduates Jim Heath, Sean O'Brien and Yuan Liu that resulted in the serendipitous discovery of the C_{60} fullerene molecule and to a new field of organic chemistry and on to carbon nanotubes.

None of the three key experiments in this story was part of any research proposal. There may be lessons here about how some fundamental breakthroughs occur and how strategic and applied science might fail. There also may be lessons about peer review and the impossibility of predicting the major discoveries themselves let alone the future impact of any discoveries. It is only when discoveries are made that possible applications become obvious and then almost invariably made by scientists in a totally different field. Excellent examples are the applications of lasers to eye surgery and bar code scanners at supermarkets, which I doubt were in the mind of Charles Townes who developed the microwave amplifier by simulated emission of radiation. I suspect, personally, that in general the mind-set of those who are successful at making fundamental breakthroughs in the sciences is fundamentally different from those of the entrepreneurs who are successful at applications – perhaps even orthogonal in many cases.

It is blindingly obvious that the really unexpected and unpredictable discoveries are invariably more important than those that are the result of targeted initiatives. However, my experience is that one can point out the obvious issues until one is blue in the face and no one with any influence on science funding ever takes a blind bit of notice! Good luck with your effort.

Harry

Sir Paul Nurse PRS, Nobel Laureate

Dear John,

As you are completely aware, I am a great supporter of non-directed programmes especially at the discovery end of research science. There is no doubt that my own work profited greatly from this so please pursue your agenda.

Best wishes,

Paul

Professor Sir John Walker FRS, Nobel Laureate

Dear Sir John,

I agree entirely with your concerns about the increase in directed research at the cost of curiosity-driven research.

Most of the major discoveries in molecular and structural biology from the 1960s onwards were curiosity-driven. Many of them had major scientific impact and brought extensive practical and economic benefit also. A few examples are: the Watson and Crick model of DNA, Perutz solving the phase problem by isomorphous replacement with heavy metals, thereby opening up protein structure analysis by X-ray crystallography; Milstein's discovery of monoclonal antibodies; Winter's work on humanising antibodies; Sanger's invention of methods for sequencing DNA; Gurdon's work on cloning frogs by nuclear transplantation.

My own work was entirely driven by my own curiosity (and encouraged by Sanger) to provide a molecular explanation of Peter Mitchell's chemiosmotic ideas about how ATP is made in mitochondria.

Yours sincerely,

John Walker

Baron May of Oxford OM AC Kt FRS, Crafoord Laureate

Dear John,

In reply to the question about 'curiosity driven research' in your letter, I can truthfully say that at no stage in my rather varied career – beginning as a member of the Division of Engineering and Applied Physics at Harvard, then theoretical physics generally (more specifically plasma physics) at Sydney University, next

Class of 1977 Professor of Biology (doing research on ecology actually) at Princeton, and most recently although a member of the Zoology Department at Oxford, for the past five years I have been working mainly on financial systems in collaboration (with people at the Bank of England) – has the work I have been doing been driven by any factor other than intellectual curiosity.

Work at Sydney University was supported by Research Council grants. During my roughly 16 years at Princeton University, I was consistently and generously funded by the National Science Foundation, and most of my research support in the earlier years at Oxford, when I held a Royal Society Research Professorship, was funded by those funds associated with the RS Chair. I emphasise this to indicate that although I have consistently received research funds, none of these funds were for 'directed research'.

I can see why Research Councils engage in this activity. I think there are two reasons. The first, for which one must have sympathy, is that ignorant politicians press them to tell people what they should be doing to benefit the economy. The second is less excusable, in that it is more fun for administrators in Research Councils to run directed programmes rather than simply do a good job of processing imaginative proposals; this was a particular problem at one stage in the USA, at the time when I was Vice-President for Research at Princeton University. But whatever the motives, they are misguided.

Best regards,

Bob

Sir Michael Atiyah OM FRS, Fields Medallist

John,

1. The best example from maths of a long period between fundamental research and applications is the work of Euclid on ellipses, eventually used for periodic orbits of planets.

2. If planetary motion is not sufficiently applied, Einstein's work on General Relativity came in useful after 100 years for GPS, where the precision in time signals needed required Einstein's improvement of Newtonian gravitation.

3. G. H. Hardy gloried in the purity of his maths and its uselessness (by which he meant it could not be used to kill people in war). However modern cryptology providing secure communications for banks and the military is based on prime numbers, Hardy's special 'useless' field. [You could get more information on such matters from Elmer Rees, retired Director of the Heilbronn Institute in Bristol, sponsored by GCH!]

4. The internet derived from the fundamental physics research carried out at CERN.

5. In a separate email you will find a recent video of 6 Nobel Laureates discussing this very issue of fundamental versus applied research - chaired by my friend Robbert Dijkgraaf, Director of the Institute for Advanced Study in Princeton.

6. Some years ago there was an influential government report on maths in the US (the David report: David being a leading industrialist).

I hope this is useful to you in your battle.

Michael

Professor Geoffrey Eglinton FRS, Dan David Prize winner

Dear John,

I am an ardent believer in the importance of curiosity-driven research in the discovery of new science and the much-desired 'great leaps forward'. I well remember the time in the Thatcher era when Sir George Porter was building a strong case at the Royal Society for government recognition and support for this theme: all was going well, with Mrs. Thatcher seemingly enthusiastic in support, when disaster struck in the shape of the Oxford University vote against her election to the University hierarchy!

The ways discoveries happen are diverse and often curious, though planning does play some part. This aspect has been put rather well; here is a quote from 'Your Inner Fish' by Neil Shubin:

> 'The paradoxical relationship between planning and chance is best described by Dwight D. Eisenhower's famous remark about warfare: "in preparing for battle, I have found that planning is essential, but plans are useless". This captures field palaentology in a nutshell. We make all kinds of plans to get us to promising fossil sites. Once we are there, the entire field plan maybe thrown out of the window. Facts on the ground can change our best laid plans.'

A general point that I hold strongly is that a key role for Research Councils etc., is to fund improved and novel enabling technologies, both at the large (e.g. Large Hadron Collider) and small scale (e.g. gas chromatographs) and then let the hounds of science – curiosity-driven scientists – loose to follow the most alluring scents.

But to address your main request, my personal experience (detail can be found in "Echoes of Life" by Gaines, Eglinton and Rullkotter, OUP, 2009). Of course, in my early days back in the 50s most University scientists did follow their own noses, with departmental funds being the main source of support, so I was already pre-conditioned to the curiosity-driven approach. Anyway, I broke away from my PhD acetylenic syntheses and set about exploring the molecular fate of biological organisms in the environment and the geological past. This was purely out of curiosity and the realization that newly emerging tools such as gas chromatography and mass spectrometry could be the keys with which to open up the world of complex mixtures of organic compounds present in Nature. We could at last 'see' the makeup of mixtures extracted from plants, sediments, fossils and petroleums. It was tantamount to entering a whole unexplored continent, with the delightful prospects of what would be fun to look at first and what basic questions could we ask, such as 'could we detect chemical signs of early life in the oldest sedimentary rocks'? One early topic we addressed at Glasgow was the composition of leaf cuticular waxes. (I attach a site which gives a 20 minute personal video on the startup of this work, which we made last year for the opening of the 26th International Meeting on Organic Geochemistry in the Canary Islands. Abstract attached).

The molecular distribution patterns we discovered have since become major tools for exploring the past climatic histories of land areas and indeed continental regions, as recorded in the geological sequences of lake and ocean sediments. Our work became of considerable interest to the oil companies and, for example, we had what were called 'Blue Skies' grants from them to do whatever we wanted – provided we told them of our findings! This whole field of molecular biogeochemistry is still growing at a phenomenal rate, with molecular distributions now being further characterized through compound-specific, isotopic information (deuterium and carbon 13 and 14). Most of this work both in our labs and worldwide has had a curiosity-driven basis which has enthused the research students and led to important commercial and environmental applications. We were able to fund much of our work at Bristol through partaking in community programmes, such as the Apollo Project, the International Ocean Drilling Project and the Ancient Biomolecule Initiative (NERC). Such programmes made a useful framework within which to work and to collaborate with other laboratories, both national and international.

Here is an abstract which may also be of interest to you:

In the autumn and winter of 1960, two organic chemists from the University of Glasgow, myself and Dick Hamilton teamed up with a resident natural product chemist Professor Don Antonio Gonzalez-Gonzalez of the University of La Laguna, to make the first chemotaxonomic survey of the leaf waxes of plants endemic to the island of Tenerife. Our aim was to look for evolutionary relationships within the carbon number distributions of n-alkanes of species of the succulent Crassulaceae family, which grow wild on roof tops and in remote canyons on this island. The recently developed gas chromatographic process had made this possible. Our principal analytical tool was considered cutting edge technology of the day – the 'Pye Argon Chromatograph', which we had smuggled into the University of La Laguna from Cambridge as our 'baggage'. The project was conceived as a somewhat naïve effort to emulate Darwin's seminal work on the finches of the Galapagos – but by using the distributions of n-alkane homologues instead of beak morphology. Our hypothesis was that the n-alkane patterns would reflect the evolutionary development of the Canary flora, following colonization from Africa a few million years ago and the subsequent radiative evolution into the diverse habitats of these mountainous and volcanic islands. The results for some 50 plant species obtained by the spring of 1961 were inevitably somewhat inconclusive, but none the less intriguing. Half a century later, such n-alkane analyses can be seen to have constituted one of the initial points of departure for the subsequent world-wide development of molecular markers as tools for exploring the natural world. Indeed, long chain n-alkanes epitomize the concept of a 'biological marker', a specific compound (or class of compound) that retains its original biochemical imprint through time and space as a distinctive molecular structure and isotopic composition. Such persistent imprints for these hydrocarbons result from their high chemical recalcitrance and valuable physical properties, notably crystallinity at ambient temperatures, extremely low water solubility and negligible UV absorption. Leaf wax biochemistry has since developed to include a range of proxy relationships with numerous and increasingly diverse applications in palaeontological studies.

I hope that some of the above thoughts may still prove useful in furthering the cause.

Yours sincerely,

Geoffrey Eglinton

Dr Ray Baker CBE FRS

Dear John,

It was good to hear from you and delighted that you have taken up the subject of curiosity-driven research and the move towards a greater concentration of funding into directed research. You have asked if I would have got a start under the present system. At that time I was working on mechanisms of organic reactions and much of the work was with my own hands. I gradually attracted graduate students to join me with Studentships from the Departmental Quota and, subsequently, on Case Awards. The latter was a real source of funds to add to the other Studentships and the existence of Case studentships encouraged me to make efforts to make contacts in industry.

I have enclosed a summary of my own work with some of the highlights and the justification and success of the programmes. I have not included the earlier mechanistic studies but it was all blue sky work with the results contributing to our knowledge on the way and the rate in which reactions proceeded. Needless to say, I doubt it would have been included in any directed programmes.

Insect chemistry:

This area of work was not directed but was an area that we developed in collaboration with biologists. It consisted of fundamental studies on the role of organic compounds in controlling insect behaviour and communication. It led into a study of insect pheromones and our work resulted in the identification of pheromones of over 30 insect species.

We were proud of our work with social insects ants and termites. For example, the weaver ant, Oecophylla longinoda, was shown to have a complex system of behaviour modifying chemicals for communicating alarm signals whilst under attack from predators. Different chemical agents with varying volatility signal a sequential behaviour pattern mediated by discrete chemical cues originating from the same mandibular gland secretion.

In other work, the defensive secretions of a number of species of ants and termites were characterised and shown, in some cases, to have insecticidal activity, some of these chemical agents were new and not previously characterised.

A range of other insects were studied and their sex pheromones defined. These included the Goosebury and larch sawfly and fruit flies such as the melon fly. The Mediterranean fruit fly, a serious pest in many parts of the world was shown to have a pheromone with the structure 3, 4-dihydro-2H pyrrole.

The most significant discovery was the isolation of the sex pheromone of the olive fruit fly (Dacus oleae) which is a major pest of olives and is widely distributed throughout the Mediterranean basin and parts of North Africa. It was known that the female produces a volatile pheromone that attracts males. We demonstrated that the major component was a spiroketal compound which was isolated and synthesised to confirm the nature of this new chemical entity. Tests with male olive flies in wind tunnel experiments confirmed that this was the sex pheromone. This compound is now used widely in monitoring traps to optimise the use of insecticides for aerial spraying control measures. The importance of this is that the number of sprays used in the season has been decreased substantially but with maximum effect. This discovery has, therefore, resulted in both commercial and environmental benefit.

A similar approach was taken with the pine beauty moth, Panolis flammea, a species associated with Scots pine and there have been severe outbreaks of the larvae of this moth this in Central Europe. Outbreaks have also occurred in Scotland and these have been controlled by aerial spraying. The sex attractant was shown to be a mixture of two long chain unsaturated acetates and this mixture was used to gain estimates of the population to determine optimum dates for control measures.

These studies of insect chemistry were undertaken by PhD students with funding from Research Councils without any direction. This funding was supplemented by some industrial support. The support received did enable the group to achieve a reputation as a leader in the world for insect and pheromone chemistry. None of it had funding from directed research programmes.

Synthetic Chemistry:

This area of work gained importance following the need to synthesise chemical entities in studies of insect chemistry. Considerable emphasis was placed on total synthesis of a range of targets, many with interesting biological activities. Syntheses were chosen for this reason but also to develop new reactions which could be then be used in synthesis of other target molecules. Examples of this was the use of organometallic reactions in syntheses of sarkomycin and pentalene and a number of stereoselective reactions have been employed in synthesis of paniculides B and C and ancistrofuran. In the latter study a stereospecific reduction of a hydroxyketone was suggested to originate from 'chelation control'. New synthetic methodology was developed for spiroacetals. This was utilised in an enantiospecific synthesis of a member of the milbemycin family. In subsequent work a general approach was established for the preparation of the series of insecticidal and anthelmintic milbemycins and avermectins. New approaches to the synthesis of the spiroacetal moities were discovered with stereochemical control of the various substituents. These studies were subsequently extended to novel syntheses of the bis-spiroacetal fragments of salinomycin and other antibiotic derivatives.

A total synthesis of (+) – Macbecin 1, a new antitumour antibiotic isolated from a fermentation broth was achieved. In this synthesis the route involved a novel cyclisation and stereospecific cuprate opening of a chiral epoxide.

None of this work was undertaken under any directed programme and the studies were directed towards the development of new methodology. In addition, all of the syntheses were carried out to produce compounds with interesting aspects of biological activity. The procedure employed could, in due course, be used to produce close analogues to study the basis of the activity and to determine structure/activity relations of these interesting compounds.

Kind regards

Ray

Professor Shankar Balasubramanian FRS

Dear Sir John,

I agreed with the sentiments expressed in your letter, and the need to recognise the true value of curiosity -driven research. Indeed, many 'useful' things are unintended outcomes of exploratory research. An example of this from our own laboratory is the creation of Solexa (now Illumina) sequencing technology, which now holds 80% of the global market in population scale clinical sequencing. This was an unintended outcome of 'Blue Sky' research funded by the BBSRC. I would be happy to provide more details on this example, if necessary.

With best wishes

Shankar

Professor Anthony Barrett FRS

Dear John,

As you know, I spent ten years as a professor in the USA from 1983 until 1993. During that time at

Northwestern University, I started a project with my good colleague and friend Brian Hoffman on the synthesis of a class of macrocyclic compounds, the porphyrazines. Whilst these compounds have been known since the early 20th century (R. P. Lindstead worked on them, whilst he was professor of organic chemistry at Imperial College from 1949 until 1955), we sought to synthesise porphyrazines with metal binding sites around the periphery. We speculated that we could make a range of porphyrazine metal complexes not only with a metal ion in the central cavity, which was well known, but also with additional metal ions bound around the periphery of the macrocycle. We had no particular goal in mind at the start save that the structures should be beautiful and may have some uses such as being novel molecular magnets.

The first PhD student, Chris Velazquez, charged to work on the project had many difficult months struggling with the synthetic chemistry but one day he was rewarded with dark green black crystals. The X -ray structure was solved and the compound proved to be pentametallic, as we hoped, but both Hoffman and I had incorrectly guessed the structure in that each tin was pentacoordinate in the S,S,meso-N-pocket not tetracoordinate. We additionally discovered that the UV-visible spectrum of the star-porphyrazine changed in the presence of anions and that led to molecules that were selective in the detection and distinguishing of chloride from fluoride.

Over the next few years we discovered how the nature of the peripheral metal and numbers of peripheral ligating groups could be controlled and this led to other multimetallic systems. I have attached a few reprints to my letter to better illustrate this than words. We synthesised Gemini-porphyrazines with two metals at the periphery, solitaire porphyrazines with one, fullerene-porphyrazine complexes (the structures of which were promptly copied by many porphyrin chemists across the world), metal linked porphyrazine dimers and porphyrazine-salen arrays. We discovered by accident the selective oxidative scission of one pyrrole ring in amino-porphyrazines gave seco-porphyrazines, compounds that were potent triplet sensitizers for the production of singlet oxygen. We discovered complexes with unusual magnetic, optical and electrochemical properties and we learnt how to tune the UV-visible spectrum photophysics of the compounds. In 2001, we published an invited chapter in Progress in Inorganic Chemistry, which consisted mostly of research from the Hoffman and Barrett team. As an organic chemist, I must tell you that I was surprised by this event.

Around early 2000, for no good reason at all, we decided to have about 250 assorted porphyrazine derivatives tested as possible anti-cancer agents. There was no expectation at all that there would be any selectivity in cellular uptake into cancer cells in the presence of healthy human cells, but there was. In short order we had 7 hit structures that showed high selectivity in uptake. Some of the compounds were effective imaging agents since they were strongly luminescent on uptake and we were able to carry out some optical imaging of cancer cells and even human xenografts in mice. We also accidentally found out that some porphyrazines were not only taken up selectively into cells but also were actively taken up and were not only imaging agents themselves but also were biological vectors. We have now used these porphyrazines as optical imaging vectors to facilitate the uptake of gadolinium MRI agents, which have poor pharmacokinetics alone, easily into cells by covalently attaching the Gd-complex to the porphyrazine. We are still examining biological applications of the porphyrazines. The work that started with no preordained list of benefits for the USA and UK, led to a rich lode of new chemistry and now some 25 years later to powerful biological tools and, if the latest experiments work out, new therapeutic agents for cancers. On the way we published some 76 papers and the list is attached to this letter. I would like to comment very briefly on events that led to my election as a Fellow of the Royal Society. Of course, I have no direct information as to the deliberations of Sectional Committee 3 in the year that I was elected, 1999. However, it is my understanding that inorganic members of the Committee at that time rather liked my work with Hoffman and that probably helped.

Finally, let me comment on my involvement with 'Blue Sky' research today. As a result of mistakes and mismanagement at the EPSRC, it is now extraordinarily difficult to continue and repeat the porphyrazine adventure. However, let me also send you a paper on spirodiamines, which promises to have most interesting organic and coordination inorganic chemistry. The first work was done by an exceptional Imperial College final year undergraduate. With the exception of two PhD students supported by the European Research Council and good undergraduates 'Blue Sky' research in my group is essentially extinct, at least in London.

Anthony G.M. Barrett

Professor Sir Tom Blundell FRS

Dear John,

Thank you for your letter about the need for 'Blue Sky' curiosity-driven research. It is very good to hear that you are preparing a report on this theme. Although we do need to show the Government and the general public that the very large sums of money spent on research will lead to improvements of health and wealth of the nation, I share your concerns about curiosity-driven 'Blue Sky' research.

In 1996, when I completed my time as Chief Executive of the BBSRC I continued to conduct an active research programme funded by the Wellcome Trust; I continue now – my H-fact is around 95 – and have over five hundred refereed papers, of which more than thirty are published in *Nature*. However, at the same time I have co-founded a further company called Astex, which began with two people in my laboratory and one in that of my colleague, Professor Chris Abell in Chemistry. We received an initial investment of half a million dollars from Abingworth. The preliminary experiments in the laboratory allowed us to move out within twelve months to raise over $20 million in venture capital. Since then we have had further investment and collaborations with $120 million from four large Pharma. Last October the company sold for $886 million.

Interestingly the research that led to this development was completely curiosity-driven: the observation of very small molecules, often of molecular weight less than 200 that had been soaked into crystals of large proteins. Our company thus developed structure-guided fragment-based drug discovery on the basis of 'Blue Sky' research. There are many other examples like this including the second-generation sequencing which came from a grant from the BBSRC in 1994 to Balasubramanian and Kleinerman for some fairly fundamental studies.

With kind regards,

Tom

Professor Robin Clark CNZM FRS

Dear John,

I am very sympathetic to curiosity-driven research, and always have been – even when just finishing a Masters Degree on diffusion-controlled reactions. I was interviewed then by Shell in NZ but, when learning of what work I could expect to undertake with them, decided (perhaps incorrectly) that this would be very unimaginative. I then embarked upon a PhD in high pressure chemistry, continuing at UCL on early transition metal chemistry. As a junior staff member my interests evolved into developing methods for structure determination, ligand field theory, IR , Raman, resonance Raman spectrocopy, spectroelectrochemistry, mixed valence-chemistry, metal-metal bonding, to the identification of pigments and dyes on artwork and archaeological artefacts by Raman microscopy. The last has now been developed into a highly sensitive and effective technique for the detection of forgeries in artwork, a procedure which is brilliant – see the programme (on a supposed Chagall) called 'Fake of Fortune' (Fiona Bruce) at 6pm last Sunday. The programme was made in my laboratory for demonstrating how to do this quickly and convincingly. In short, I was ever curiosity-driven in my chosen research areas and would always recommend it to someone with imagination…

You may recall that I gave the Thomas Graham Lecture at UCL in 1991 on the topic 'Thomas Graham – Would his Research be alpha-unfunded Today?' The start and especially the conclusion are all to do with my views on curiosity-driven research. They are unchanged today. See: Chem. Soc. Rev., 1991, 20, 405-424. I'll help further if I can.

Robin

Professor Dianne Edwards CBE FLSW FRS

Dear Sir John,

As you are aware the whole of my career (apart from the very rare contracts with geological surveys and oil companies) has involved curiosity-driven research and has been very well supported by the NERC and charities. With respect to the former my frustration now lies in having to complete the impact section on applications...A compendium of these, as submitted, would make very entertaining reading and at least demonstrate the very active imaginations of UK scientists although some Universities employ professional writers/authors for this. But seriously, we still have much to discover about planet Earth (– it is quite amazing that recent events have shown we know more about the surface of Mars than the floor of the Southern Indian Ocean –) and in my case its past history. I regard this as a form of scholarship as very effectively enunciated in the objectives of our Society and an essential part of our culture.

Best wishes,

Dianne

Professor Sir John Enderby FRS

Dear John,

Thank you for your letter. Like you I do believe in the importance of 'Blue Skies' research and I include my first editorial on this subject when I became Editor of the *FST* journal.

In my own case I became interested in exploiting isotopes in sorting out, via neutron scattering the structure of complex systems. At first I was on my own, but the power of the technique became accepted and is now one of the most widely used tools for the study of glasses, molten salts and aqueous solutions. One important application occurred when I was advising ICI on the use of ammonium nitrate gels for their civilian explosive division up in Scotland.

More recently, I have been involved with a Welsh Company (Melys), run by Dawood Parker in Whitland. Fundamental work on the IR spectra of Haemoglobin has led to a commercial product for critical care.

A very old paper (1967) on the optical properties of layered materials has helped Melys to solve a long standing problem in the use of Attenuated Total Reflection. Buried deep in this very mathematical paper was a clue on how to increase the depth of penetration of the evanescent wave without a loss of sensitivity...the accepted wisdom was that this could not be done. At present we are looking at possible applications.

I hope all this helps,

With my best wishes,

John Enderby

Professor Sir Anthony Epstein CBE FRS

Dear John,

Thank you for your timely letter about current modes of research funding; I agree strongly with your various points and wonder whether the following might be of help:

1. Several of George Porter's Anniversary Day PRS addresses dealt powerfully with this problem way back in the late 1980s.
2. At a personal level, all my contributions were made because I was left alone to do whatever I wanted with my own hands and one technician thanks to support from a distant British Empire Cancer Campaign (became Cancer Research Campaign in 1970 and today's Cancer Research UK in 2002).
3. Indeed, the most important contribution, the discovery of Epstein-Barr virus (the first human cancer virus) whose 50th Anniversary is being celebrated by a special lecture and an international meeting this year, exemplifies this. A Journal editorial 40 years after the discovery commented on how the gut feelings of a young investigator without supporting data was funded in 1961 unlike anything possible today and ended 'thank goodness that was the case 40 years ago'.

Best wishes for the success of your efforts. I hope all continues well and that you will let me know if there is anything further I can do to help.

Greetings!

Tony

Professor Jim Feast FRS

Dear John,

I agree with your position on this.

The move towards directed research programmes, while in part inevitable, is dangerous and poses a risk to the health of the academic research base in the UK. It appears to be part of a drift towards conformity, the enemy of originality. An antidote to these trends lies, in part, in the maintenance of multiple independent research funding streams with different assessment procedures. Also, referees and assessors have a role to play in counteracting 'bureaucratic correctness' by supporting originality; thus, the scientific community has some capacity to ameliorate the worst aspects of current trends, but only if their tendency towards 'tunnel-vision' and the 'not-invented-here syndrome' can be abandoned and some form of independent peer-review maintained.

Lessons from personal history:

My research was supported by multiple streams of funding. Appointment as a lecturer gave support from Durham University and the SRC Quota system for research studentships, my Head of Department introduced me to interaction with and support from industry (ICI Wilton and Imperial Smelters Avonmouth) and to government agencies, e.g. the MOD at RAE Farnborough. An independent studentship stream came via the Governments of Malaysia and Thailand and Japanese Company (NKK (Yokahama)) who sent very good students to work with me after selection from their own internal competitions. This all happened in the early years of my career and involved predominantly curiosity-driven research.

Subsequently funding arrived from ICI Paints at Slough, Unilever Port Sunlight, Smith and Nephew York, Ranier Cambridge, Camrex plc, BP International, Sunbury, Ciba-Geigy Ltd., Courtaulds Research, Exxon, Howmedica, International Paint, the European Research Office of the U.S. Army, the European Union Science Frameworks and BMFT (FRG). This totals 22 separate research funding sources, mostly allowing unfettered 'blue sky' research. During this period funding from UK Research Councils was a very small part of my research portfolio (essentially an occasional SRC Quota studentship); however, as an undergraduate

I had some excellent teachers and one, George Porter, talked about doing research and said something along the line 'in choosing your research topics you have to make best use of whatever resource is available or obtainable', in his case ex-MOD high capacity condensers allowing him to get big flashes of light. The lesson, albeit not the exact words, stuck in my head and I acted on it to the extent that by my late forties I had established sufficient reputation to be offered a Directorship in the Max Planck Society and Chairs in several overseas institutions.

At that point EPSRC set up competitions for Interdisciplinary Research Centres and I was encouraged to get involved, I was working in Mainz at the time and another of the Welsh Knights of Science who, like you, has influenced my career spent some of his valuable time extolling the possibilities inherent in this EPSRC move. I threw my hat in the ring and the process of choosing a place for the Polymer IRC was instructive in various ways. The feature which really amazed me was that in submitting our proposal we were not asked by the EPSRC managers to say what sort of research we would pursue if we won; statistical data (publications, kit available, plenary lectures, funding already received, space, etc) had to be provided but not what we wanted to do despite repeated questions from us.

In your letter you mention Doctoral Research Centres and it appears that not saying what problem you want to tackle and having it judged by your peers is still a modus operandi in RCs; I think that is wrong-headed. In the event about two weeks from the closing date for IRC applications we were asked to submit our research plans and management mechanisms; we had anticipated this so had prepared a case (maybe the competition were unprepared for what I presumed was a Pavlovian test) we won and received very generous funding which I believe was put to good and useful purposes, we deliberately encouraged interaction with other academics and industry and provided accessibility to our facilities as far as possible, the resource was well used.

However, there is a lesson in that managers in EPSRC instructed me that everything in our research portfolio in the IRC had to be new and that I should stop all work in the electroactive organic materials field, which accounted for a large part of my reputation at the time and was probably a component in the decision to give us the IRC. By this time I had a wide network of contacts largely established on the back of industrial support from BP Sunbury and several very good groups wanted to continue or initiate collaborations with our Durham group. This is where the multiplicity of funding streams came into play and we obtained funding via the EU Science Frameworks. Six or seven years later I was elected to the Royal Society; of course one never knows the deliberations of the Royal Society's Sectional Committee before your own election but I'm pretty sure that my involvement in the programme of collaborative work between Durham, Cambridge, Sussex and BP Sunbury will have been a significant, probably a major, component. That was based initially on our invention of the Durham route to polyacetylene, which resulted from 'blue sky' research conducted by a Senior Demonstrator who chose to work in my group.

Although the materials we worked on did not become part of a commercial technology I remain convinced that the programme of work was of high quality and laid the foundations for subsequent developments in the field worldwide.

I have some sympathy with leaders of Research Councils in their attempts to respond to pressure from their political masters to respond to the 'value for money' criteria and the short term nature of political horizons. Some measure of direction is not unreasonable but there has to be balance and some measure of freedom.

I am now retired, have stopped giving colloquia but still attend them and ask questions; I have seen several cycles of 'fashionability' in various areas of research of which I have knowledge. The latest fashion 'grapheme' and the current hype is something reminiscent of the polyacetylene 'who ha' of thirty years ago. One of the problems of the lack of understanding of the nature of research amongst politicians and managers (there are of course exceptions to this generalization – I think David Willetts understands and certainly Lord Sainsbury did) is that large pots of money are awarded to particular areas, academic staff under pressure to get research support plus overheads ask for a share of the money which either gets spread too thin to do any good or ends up in one pocket so denying others the chance to prosper. The sound bite inventors and plausible 'experts' crawl out of the wood work and general mayhem results; we see the phenomenon at present in all sorts and conditions of ignorance being elevated to expertise in hydrology, climate change and water management. In the physical sciences there is always the possibility that genuinely good science will be done some of which, but by no means all, will lead to useful exploitation. Unfortunately if money is only available to study blue widgets everybody will become experts on blue widgets and the subject will be distorted, damaged and possibly destroyed (although I'm not really that pessimistic).

To some extent this has always been the situation and one has to take one's chances but I believe that it is crucial to let young staff in Universities have the chance to develop by trying out their own ideas for a few years or so rather than being dragooned into specific areas at the whim of older and/or glibber people. Age and status doesn't lead to omniscience, and youth isn't always wrong, indeed graduate students have always played a role in invention; I did and members of my group did.

In my ideal world for academic research there would be:

1. A limit on the number of people one person was allowed to supervise.
2. A limit on the amount of funding in one group.
3. All new appointees should have enough resource to conduct research on their own ideas (i.e. blue sky stuff) for a few years although they might be associated with a larger team activity as well.
4. Essential services (spectroscopy, analysis, glass blowing, stores, etc) should be provided centrally by top slicing the incomes of the successful; this was what happened in my time in Durham, I think it was David Parker's idea and it worked well.
5. Effective and honest peer review should exist, an objective much more difficult to realize than is commonly believed.

I have worked in Belgium, Germany and The Netherlands and have some experience of various funding systems in other countries where I've acted as an assessor (admittedly from some years ago), their funding methods merit examination by the RCs. The Research Councils provided less than half the funding for academic research when I was a new boy, I don't know what the figure is now but I believe that the health of the system depends on multiple funding streams and a healthy user base (by which I mean industry and government agencies) for academic to interact with. Finally, we should acknowledge that not all academics will be excellent researchers but there are other important functions to be fulfilled, administration and particularly scholarship are important examples. A wise Head of Department will guide people to appropriate niches; I can say that because I was never a Head of Department but have seen the process work both efficiently and inefficiently.

Yours,

Jim Feast

Professor Michael Hart CBE FRS

My first post-doctoral position, in 1963, was funded, not by theme, but by 'Blue Sky' investment in the USA. ARPA (http://en.wikipedia.org/wiki/DARPA#History) funded a new centre for Materials Science at Cornell University. I regard 'Materials Science' within the ARPA remit as 'Blue Sky', not Committee targeted thematic funding. Within this definition, I have never received research funds which came from thematic funding sources.

Individual published works:

An X-ray interferometer
U Bonse and M Hart
Appl. Phys. Letts. 6 155-156 (1965)

This has since been developed into an x-ray interferometric spectrometer and is the basis of a major contribution to metrology, specifically, one of two approaches to replacing the artefact Standard kilogram by an atomic standard – known as the International Avogadro Project. In addition, the concept of a Bragg diffracting crystal interferometer has been applied to neutrons, enabling many different measurements and fundamental results in neutron physics and quantum mechanics.

Tailless X ray single crystal reflection curves obtained by multiple reflections
U Bonse and M Hart
Appl. Phys. Letts. 7 238-240 (1965)

This work forms the basis of many developments and applications of x-ray optical instruments, particularly in the world wide exploitation of synchrotron radiation facilities. For example, I designed and made several x-ray monochromators for the SRS at Daresbury during the 1980s and the crystal monochromator used on the Australian National Beamline in Tsukuba (Photon Factory, Japan). During it's 20 year lifetime the beamline produced about 1000 peer reviewed publications on EXAFS spectroscopy and powder diffraction in the first decade of operation. One review of the range of applications is given in;

X-ray optics for Synchrotron Radiation: Perfect Crystals, Mirrors and Multi-layers
M Hart and L.E. Berman
Acta. Cryst., A54, 850-858, (1998)

High precision lattice parameter measurements by multiple Bragg reflection diffractometry
M Hart
Proc. Roy. Soc. A309 281-296 (1969)
This permits the comparison of lattice parameters with a precision limited only by photon counting statistics – crucial in the Avogadro Project.

'Perfect crystals': a study of their structural defects
M Hart
Sci. Prog. (Oxford) 56 429-447 (1968)
Shows how to map crystal perfection at better than 1 in 10^8; important in the Avogadro Project.

An Ångstrom ruler
M Hart
Brit. J. Appl. Phys. (J. Phys. D) 1 1405-1408 (1968)
This shows how x-ray interferometers can be used to measure distances on the pm scale, on an absolute scale (when combined with optical interferometers). Combined x-ray and optical interferometry (COXI) has become an important measurement tool in the whole field of nano-technology, for the calibration and testing of transducers too.

Yours,

Michael

Professor Dame Julia Higgins DBE FRS

Dear John,

Your letter about the need for 'Blue Skies' research gave me opportunity to think a bit about my own career and its successes. As a consequence you have a small essay. I hope some of the thoughts may be useful to you. I have always said I was extraordinarily lucky to find myself with a new tool – neutron scattering – and an open field – polymer molecules – in which to play with it! The two came together when I joined Geoff Allen in Manchester as a post doc. Polymers as materials were of course well known and widely applied but the molecular understanding and hence control of structure and behaviour was as yet very incomplete. I was able to say frequently 'I wonder what would happen if…?' and then follow some blue skies idea as I wished. I do not believe any of my Research Council funding was part of a directed programme, and indeed, my industrial funding was also often extremely open ended. However I should say that there was a 'zeitgeist' that plastics were important and understanding them was crucial for further developments. It was the time of Sam Edwards developing reptation theory to understand the rheology of polymers and soon after came the development of new catalysts and new synthesis routes to control chemical structure. There was as I recall something called 'The Polymer Directorate' funded by SRC. So while my applications to SRC were not in any sense directed they obviously fell in an area where there was clearly both fundamental and industrial interest.

You asked about seminal results. Summarising, the answer for me is showing how neutron scattering can be applied to understanding organisation and structure of polymer molecules and the molecular dynamics of these in melt states. Much of my work was carried out at the UK's neutron facilities, in Grenoble (Institut Laue-Langevin shared with France and Germany) and at ISIS. Had UK research Councils not funded such facilities – pretty "blue skies" in terms of science to be investigated, none of that work would have been done. Although other countries subsequently built facilities, it was the example of what could be done at ILL which spurred them on, and in any case my access would have been very limited. I do not point to specific applications arising from this work, but the understanding of molecular behaviour has I believe been crucial. Henri Benoit – one of the leading French Polymer Chemists – said in the early days 'There will not be a polymer text book or an issue of a leading journal which does not have a report of work based on neutron scattering'. He was right – you only have to pick up any issue of the ACS leading polymer journal Macromolecules to see this. In a way I feel I led a charmed life. I certainly did respond to questions about polymers and their applications but I never had to work on anything where my own curiosity was not caught. Hope some of this is useful.

Best wishes

Julia

Professor Archie Howie CBE FRS

Dear Sir John,

Thank you for your letter with which you will not be too surprised to know I entirely agree.

The more directed research support policy can adversely affect the longer term future mostly because we may be deprived of many lucky surprises. One cannot of course specify these other than by reference to past examples – eg work of Max Perutz (frequently mentioned), the discovery of pulsars by Hewish and Bell-Burnell. Perutz had a long term aim that was thought by most people to be completely unrealistic but after 20 years produced the goods. Hewish was aiming at something quite different (the solar wind); however the radio telescope they built turned out to be very suitable for the unexpected discovery of pulsars.

Almost as significant and more easily observable is the insidious effect on attitudes at all levels of science. People simply get out of the habit of even thinking blue skies. Senior figures e.g. Heads of University

Departments are relieved of the burden (if it can be called that) of stimulating their younger colleagues to spark wild ideas in general discussion, and to take a chance themselves to fund some of these from the small pot that they used to hold. They rapidly sink into the much more mechanical discipline of reading research grant proposals and advising how these can be tweaked to match funders' objectives and University constraints. More active, younger colleagues tend automatically to channel their thoughts along fashionable lines usually hyped with magic buzz words so seductive that they soon believe all of it themselves.

Directed research projects with their short time scales invariably put increased pressure on rapid publication and must share some at least of the blame for the universal trend towards measuring everybody by their citations index.

A less significant but non-negligible effect is the increased bureaucracy and cost needed to process directed research work. The illusion that the future of a research project should be known leads inevitably to the request for far more details, including timetables and impact in the initial proposal, with similar detail at many reporting stages.

Of course what is blue sky to one researcher may be pedestrian or routine for another. This afternoon for instance I went to a lecture where particle physicists described their joint work with the local hospital over cancer therapy. This was not as I expected anything to do with novel irradiation e.g. use of anti-protons or even protons but hinged on their ability in fast processing of enormous data sets. Data from several thousand patients undergoing intensive radiation therapy will be followed working down to the level of ensuring that the patient is accurately placed on the couch each time!

There is a delicate balance here since the user (here the medicos) have to perceive the blue sky purveyor as exciting but still credible. It would be less easy for instance for the particle physicists to convince the upper echelons of the Health Service to make use of their processing expertise to fix some of the large scale debacles that have arisen over computerisation of patient records! Particle physics and astronomy are probably the main areas of physics where some blue skies work can be most easily supported. Each research group still of course has to jump over highly competitive hurdles to get funding for its project but the sums of money are usually so large that a modest amount can often be found to provide some initial support for a team member working on a line of their own. In radio astronomy (now astrophysics) in the Cavendish, David Mackay's early work on coding was supported in this way.

The closer any subject comes to having some useful applications the harder is it to carry on with basic developments. I am very familiar with that situation in electron microscopy. Although a lot of the initial development took place in physics departments they were increasingly seen by the Research Councils as not best qualified to pursue the growing applications they preferred to fund in materials science and chemistry. As funding for the subject in physics dried up, Physics Departments have largely abandoned it.

The biggest development in electron microscopy in the past 25 years has been the correction of lens aberrations. A route to doing this by replacing simple solenoidal magnetic lenses with multipolar lenses was well known, tried by a few pioneers but failed through difficulties in controlling the system. In the 1990s a German group as well as a team in Cambridge independently found solutions thanks to improvements in computer control. The Germans had a long continuous and major track record in electron optics. The Cambridge effort was smaller and led by Ondrej Krivanek, a former research student who had pursued a very successful career in EM instrumentation in the USA. Mick Brown failed to get support from the Research Council but got a grant from the Paul Instrument Fund to pay for equipment costs. The salaries of Krivanek and his associate were paid from Krivanek's own resources.

A successful working prototype was built (slightly ahead of the Germans) but once again the Research Councils declined support for further development. Krivanek then went back to the USA, set up his own company (NION) and now manufactures in small quantities (two or three a year) what is by many regarded as the best aberration corrected system in the world. The Germans have been much more successful commercially having licenced their rather different design to major manufacturers FEI and

JEOL. I believe that over 500 (maybe even more than 600) of these microscopes have now been sold costing between £3M and £5M each! This example with its strange mix of 'blue sky', application and business is perhaps characteristic of major advances in instrumentation.

Another example involving optical rather than electron microscopy is Roger Tsien's discovery of the green fluorescent dye that can be attached to a genetic key. Combined with various advances in super resolution fluorescent imaging, this has initiated a tremendous revolution in application of optical microscopy in biology and medicine. I know much less about the background to this but believe that it started when Tsien was a research student and postdoc in Cambridge. I don't know how it was supported or how much of the eventual applications were foreseen.

Best wishes,

Archie Howie

Sir Colin Humphreys CBE FRS

Dear John,

I very much believe that it is important to have 'blue skies' research with no milestones to be achieved at specific times. I also believe that we need strategic and applied research which does have such milestones. Basically, we need a mix of pure and strategic research, but when funding is tight there is always pressure to reduce the amount spent on 'blue skies' research. I believe it would be good if a certain amount of money to be spent on 'blue skies' research could be identified and agreed, and then for this amount of money to be ring-fenced. Let me now give two examples of 'blue skies' research in which I have been involved which totally unexpectedly resulted in considerable impact.

Let me first tell you how my highest impact paper, in terms of its total number of citations, so far over 1,750, came to be published. I believe this paper has had more citations than any other paper published in the Materials Department at Cambridge, even including the publications of John Meurig Thomas! Way back in 1993, I had put a huge amount of time into setting up a University Technology Centre with Rolls-Royce on Advanced Materials for Aerospace Engines. I founded this Centre and became its first Director (and still am its Director!). John, you may remember that you introduced ROPA Awards. These were awards given to scientists who had demonstrated success in working with industry, but who had a bright idea for some 'blue skies' research. I thought these Awards were a wonderful idea, and I was able to use the funding from Rolls-Royce as a ticket to apply for a 3-year ROPA Award, which was successful and started in 1994, and the topic was 'Understanding Bonding and Doping in Some Key Metallic Alloys'. At that time there was some controversy over what happened when one made an alloy such as NiAl, in particular was there any charge transfer between the two metal ions? I had the idea that if one did electron energy loss spectroscopy of such alloys, and looked at the fine structure, this might give some information to help us understand the bonding process in such metal alloys. This was a very much a curiosity-driven project with no obvious industrial applications.

The ROPA Award enabled me to hire a very bright post-doc called Gianluigi Botton from Canada. We looked at three different metallic alloys and used the latest and best density functional theory to interpret the results of the EELS spectra. The project was successful and a few good papers resulted. I presented these results at a conference, and while there heard a synchrotron radiation talk about the detailed atomic structure of NiO, in which a tiny distortion had been observed using the x-rays. The speaker said that only synchrotron radiation could detect such a distortion. I went back to Cambridge and wondered if electron diffraction could detect such a distortion, particularly convergent beam electron diffraction, which I knew was very sensitive to crystal symmetries and small distortions. I asked Gianluigi Botton if he could look into this, and because he was not constrained by a grant with milestones, etc, he had the time to do this, found that he could detect such a distortion and this resulted in a nice paper. However, since we now had some NiO, we thought we would do some EELS spectroscopy of this to see if we could detect the rather large charge transfer effects expected in this material. However, when we came to match the experimental EELS spectra with the best density functional theory calculations available, we could obtain no decent match at all whatever magnitude of charge transfer we put into the calculations! So we concluded that the best density functional theory available for some reason was not adequate to deal with NiO.

We needed more expert help, and I knew of an extremely good Russian theoretician working with Mike Whelan in the Materials Department in Oxford, so Gianluigi and myself went across to see him and explained to him the problem. He became really interested in this and we worked with him in an iterative manner, comparing his improved calculations with our experimental results. We found that we needed to take account of electron correlations in the 3d shell of the metal ions, we also needed to use spin density functional theory and use what is known as a Hubbard U correction. We then got excellent agreement with this new theory. We published this paper in Phys. Rev. B. in January 1998. At the time, we all thought that this paper was very obscure because it involved the EELS of NiO, in which very few people in the world had any interest! This proved to be true because the paper had no citations at all for the rest of 1998, four in 1999, three in 2000, two in 2001, and zero in 2002. Our paper had disappeared into obscurity!

I was asked to give an invited talk at a conference on our EELS work on metal alloys and at the end of the talk happened to mention the interesting work we had done on NiO and the new theory that had to be developed to explain the results. It so happened that in the audience there was a solid state physicist who had been working on some important physical properties of metal oxides, but his best density functional theory could not explain the results. It turned out that the theory that had been developed in our paper was just the theory he needed. So the theory that had been developed in our paper turned out to be of much wider interest than for the interpretation of EELS spectra. Since 2002, the number of citations per year for our paper has steadily increased from zero until in 2013 it was 366, and still rising. As I said earlier, the total number of citations of this paper is, so far, over 1,750. So this theory has been extremely useful in both explaining and predicting the properties of a variety of metal oxides, some of which have significant commercial importance today. All of this was made possible by a 'blue skies' ROPA Award in 1994. Had this been a standard EPSRC grant with milestones and deliverables, it would have been difficult to branch out from metals into oxides, which had not been mentioned at all in the grant proposal. However, with the ROPA Award we had the flexibility to do this and to follow wherever the science led with no constraints.

Let me give you a second example. Gallium nitride (GaN) is normally grown on sapphire or silicon carbide (SiC) substrates. In February 2003, I submitted what was called an Exploratory Grant Proposal to the EPSRC for three months funding to explore gallium nitride grown on silicon. My idea at the time was that this could be useful in optoelectronic devices, with the optoelectronics being performed in the GaN and the electronics being performed in Si, and linking the two together for a future optical computer. This was a 'blue skies' idea and we needed first to develop growth techniques. We did not know if we would be able to do this or not. As it turned out, we were able to grow GaN on Si, but this is now proving extremely useful for something I never dreamt of at the time, that is low-cost LEDs. LEDs for home and office lighting are relatively expensive because the GaN is grown on sapphire or SiC substrates, which are expensive. By growing such LEDs on 6-inch Si substrates the cost comes tumbling down.

We have continued to explore GaN growth on Si since 2003, filed a patent, set up two small companies, which were acquired by Plessey in 2012 and Plessey is now manufacturing LEDs based on our technology in Plymouth. This is the first manufacture of LEDs in the UK and the first GaN LEDs on Si to be available commercially in the world. All this applied work arose as a result of a 'blue skies' exploratory grant proposal to the EPSRC in 2003 and I had absolutely no idea at the time that this work might be useful in future low-cost LEDs for lighting. John, there are many other examples I could give but I hope these two are useful. I hope this helps and I very much support your campaign.

Colin Humphreys

Professor Graham Hutchings FRS

Dear John,

To some extent the whole field of catalysis by gold has come out of curiosity-driven research and this is now being commercialised. In the early 1980s when the key research was carried out it is doubtful that any funding agency would have funded research on gold catalysis since most would have perceived it to be inactive due to its non-reactive properties. Hence any research on this topic was true 'blue skies' work. For my part I was doing curiosity type research in industry in 1982 when it was still possible! I made the prediction that gold would be the best catalyst for acetylene hydrochlorination and based this on reading the literature i.e. a library discovery. Since then I found alloying gold with palladium has huge advance for redox catalysis and in particular for designing catalysts for the direct synthesis of hydrogen peroxide something that we are now advocating for water clean up which has huge potential. I hope this helps.

All best wishes,

Graham

Professor John H. Knox FRS

Dear John,

You ask for my comments in your fourth paragraph on how far my 'seminal results' arose from directed programmes or independently. My research was initially supported by the University of Edinburgh and the SRC. Later I had generous support from industry and particularly from the Wolfson Foundation. It is not really possible for me to say which of my 'discoveries' came from work supported by commercial sponsors or independently. In all cases I devised our grant applications myself as the principal investigator. I never felt under any pressure to carry out directed research. None of the sponsors put me under any pressure to carry out specific research projects and I would say that all my work was curiosity-driven. Of course, my grant applications to industrial sponsors were made with their interests and specific areas of business in mind. Some of our results may eventually have been useful to them. Research data relevant to any sponsor was mostly discussed at consultancy meetings. Regarding seminal results, I am not sure that any of my results were world shaking! Most were small advances dependent upon what was already published. Some of our more salient results are summarized below.

Hydrocarbon Combustion: My PhD with RGW Norrish at Cambridge was entitled the 'Cool Flame Oxidation or Propane'. Cool flames occur when a hydrocarbon is heated with a deficit of oxygen at around 300°C. In my PhD work, the cool flame (visible as a pale blue emission from electronically excited formaldehyde) was established in a conical tube, but could also be observed in a closed vessel. The products were trapped in a liquid air cooled vessel for later analysis. This used classical methods: low-temperature fractionation, combustion analysis, volumetricanalysis, and colourimetric analysis. Sadly with the high extents of reaction, these primitive methods were incapable of saying anything significant about the combustion mechanism. In reality, the key thing that Howard Pumell and I encountered in Norrish's lab – nothing to do with Norrish – was gas chromatography. We built our own GC and had a lot of fun. We astonished one of our colleagues by accurately determining the composition of a mixture of propane butane and isobutane which he had prepared. He claimed that we had surreptitiously seen his notebook! We wrote round to the oil and chemical companies to tell them all about it! But Shell and ICI were already well ahead. From then on GC became the key to our subsequent independent researches. Without GC we would have struggled and the whole course of our researches would have been totally different.

High Performance Liquid Chromatography: My interest in GC led me to apply my understanding to Liquid chromatography which, at the time, was a very primitive technique. The most sophisticated forms were the slow ion-exchange chromatography in amino-acid analysers, and paper chromatography, extensively used by Hirst et al for his work on the structure of carbohydrates by hydrolysis and methylation. The technique of GC was far ahead of these and indicated that the key to High Performance in Liquid Chromatography would be the use of very small particles of column packing material and high pressures across the length of the column. Accordingly, along with Jadwiga Jurand and Dick Wall, I applied in 1991 to the Wolfson Foundation for a grant as part of their scheme to 'Link Scientific Research with Industry'. £92,500 was awarded to cover a period of five years. The £18,500 per annum grant, which initiated the Wolfeon Liquid Chromatography Unit, funded capital equipment, a mechanical workshop technician, a laboratory technician and a postdoctoral fellow! Ten times that funding would now be required! The plan was to design and build a modern high pressure liquid chromatograph, to develop a range of micro particulate column packing materials (around 5 micron) and to develop new HPLC applications. This followed pioneering work by Jack Kirkland at Du Pont who had invented 50 micron surface layered packings for LC which he called Zipax. Before our application to the Wolfson Foundation I had carried out a comprehensive study of the performance of Zipax with John Done who had a PDF funded by Du Pont. Soon after, Kirkland developed a range of porous silica microspheres (5 micron in diameter) called Zorbax.

Andrew Pryde, our first Wolfson research fellow, first developed a new range of micro-particulate silica gels. Our silica gel was made by the simple process of emulsifying an acidified suspension of colloidal silica (Du Pont's Ludox) in hydrocarbon using a high-speed stirrer. This process did not infringe Du Pont's Zorbax patent. The microspheres were dried, and could then be derivatised to give octadecile ion-exchange and other derivative packings. After one unsuccessful start with a commercial partner, I interested Shandon Southern Scientific in commercializing our packing materials which they subsequently marketed under the name Hypersil. Unfortunately, we never convinced them that they should design and sell an HPLC. The Hypersil range sold very well and still does as one of the major microparticulate packing materials for HPLC.

Andrew moved to Switzerland and Dr Mary Gilbert took over his position. With her expertise we developed a method for making microparticlate porous graphite. Graphite has totally different adsorptive properties to silica. Production of this was added to Shandon's HPLC packing range as Hypercarb. The idea for Hypercarb came classically in the bath! A highly porous form of microparticulate silica gel was first prepared and submitted to hydrothermal treatment to produce a robust open porous silica micro-structure. The particles were then filled with a phenol-formaldehyde mixture and heated under nitrogen in a rotating oven to harden the polymer and then to pyrolise it to provide a porous carbon in the interstices of the silica spheres. The silica was dissolved out by alkali and the final porous carbon heated to some highly efficient HPLC columns as Hypersil. Hypercarb is now manufactured and marketed by Shandon and its successor Life Sciences International.

Finally, in 1996 at the request of my former research student Harry Ritchie who was MD of the Hypersil Division of Life Sciences Int. (the successor of Shandon), I developed a high purity microparticulate silica gel to match the products being marketed by Waters Associates. I realized that this could be achieved by the method of Stober and Fink to produce a pure silica sol via hydrolysis of Analar tetra ethyl silicate with readily controlled particle size. This overcame problems arising from the traces of metallic impurities in the original Ludox used to make Hypersil. This material is now marketed under the tradename Hypurity.

My final project has been to design a new high performance yacht anchor. This has presented its own problems, but, with my sons David, Andrew and Jonny, we now have a product which is on the market and performs better than any of the current 'New Generation' anchors. This is no longer research but the intellectual problems are very similar. It marks the final transition from pure research to product development!

Overall Assessment: I was lucky that I never had to justify my work or, perish the thought, 'state the benefits to the nation on a 10 to 50 year time scale'. I had no 'paymasters', only generous friends in industry and the invaluable support of the Wolfson Foundation. They evidently had confidence in my ability to produce something useful for the finance they invested in my work.

I am firmly of the opinion that purely commercial interests must not impinge and influence academic research, except marginally. But, on the other hand, without support from the real world there is a danger that research fails to get funding or loses its way. It seems to me that true 'blue sky' research is rare and the territory of only the greatest and most innovative of research workers who have enormous determination to plough ahead in the face of lack of interest from the majority. Only a few 'blue sky' ideas will make it in the end. For the majority we have to plough more fertile fields where the rewards are relatively short term. Science mostly advances in short steps. New blood takes over quickly and the work of forerunners is soon left behind. This is probably not the conclusion you want to hear. To get support it seems to me almost inevitable that the ideas which gain support will be the more mundane where a guarantee of useful results – a key criterion – somewhat sad but probably realistic. Forget the 10 to 50 year time scale unless you are in the genius category! As in all fields there is a continual graduation between the most mundane research (which may still be worth funding) and the blue sky stuff. It is most important that the work earned out by the Universities and Research Institutes comes in at the upper end of this spectrum.

Yours,

John H. Knox

Baron Krebs of Wytham Kt FRS

Dear John,

Of course I agree with you that there is a pressing need to allow people, especially young investigators, to do unconstrained, curiosity-driven research. The unpredictability of how research can be applied is beautifully illustrated by the recent sale of a company, Naturalmotion, started by a DPhil student (not mine I hasten to add) in Zoology at Oxford. He was doing a DPhil on the simulation of insect movements and developed algorithms that now power many games on smart phones and animation in blockbuster movies. His company was purchased for $500 million a few weeks ago.

In my own research career I have always pursued my interests in what I considered to be important problems that I found intellectually challenging, with no regard to their application.

As a by-product of one stream of my research, on modelling and experimental analysis of how birds respond to variability in their food supply (rather esoteric stuff), I have set up a successful business, Oxford Risk, that provides products and services to the financial sector. I have a problem to explain to people why a zoologist should have founded a company whose clients include HSBC, RBS, Standard Life, Brewin Dolphin etc. It is all about lateral connections that emerge in totally unexpected ways! Good luck with your project.

John

Professor Steven Ley CBE FRS

Dear John,

I share your concerns, especially now given that the EPSRC 'Shaping Capability' concept is with us; its consequences have already had a dramatic effect by reducing funds for organic synthesis in the UK. I am also very concerned that vast sums are being ploughed into the CDTs and into other student training activities as opposed to developing fundamentally new science that will eventually provide the opportunities for the future prosperity and well being of our nation. It also seems to me that those individuals who gang up into their clubs and cartels seem to raid the majority of funds to support hubs, centres and soft science initiatives.

Britain has always been at its best when individuals are allowed to be curious. This individuality extends to being creative and providing innovative solutions to complex questions that elude massive consortia. My best work has always come when I have had the freedom to explore ideas. While I can list a number of instances throughout my career, probably my best example arose through EPSRC funding of a large programme grant where I had the flexibility to try some new things. While we had not defined the area in the original proposal, we asked a simple question, 'Could we challenge the dogmas of the past that use too many inefficient, labour intensive, solvent wasteful and time-consuming batch processes to discover a new more sustainable approach using continuous flow chemistry?' This would require us to develop machine assisted protocols that harness all our modern hard and software, which include Wi-Fi, the Internet, tablets, ipads and all novel control algorithms and computer developments, such as the Raspberry Pi chip. It would require a complete rethink about how reagents and catalysts are delivered and immobilised. We invented a whole new set of devices and tools for downstream processing. We had to completely re-design our lab and recognise that we were proposing something that was more than a disruptive technology but was a massive change in the philosophy of synthesis.

This project is still ongoing; but since our early papers in the late 1990s and early 2000s there have now been over 6,000 publications and there are numerous start-up companies and specialist equipment makers in this area. It has opened our eyes and led us to many new opportunities with a greatly enhanced ability to make molecules more sustainably and with greater responsibility for our actions. We have discovered a lot of new science and I believe we still lead the world in this area. I repeat, none of this came by making a specific proposal in this area or responding to a particular initiative, but arose from a need and a curiosity to ask the right questions. I can now look back and be proud of what we have achieved in terms of its impact worldwide in industry and academia, none of which could have been fully predicted at the start.

Good luck with your campaign. It is such a shame for the country, and for the world in general, that we have to battle in this way rather than spend our time discovering and exploiting new science.

Steven Ley

Sir Ronald Mason KCB FLSW FRS

Dear John,

Blue Skies without a cloud is an apt description of the value of X-Ray crystallography. Dorothy Hodgkins's analyses in the 1950s and 60s –Vitamin B_{12}, Penicillin, and Insulin all changed the scope of biochemistry and the evolution of molecular biology culminating in the Watson-Crick note in *Nature*. In all cases, the need to know was simply to answer the question 'What is the structure?'

One short paper set the scene for the incredible growth of genomics and points to the eventual birth of personal medicine.

The discovery of cis-platin, of immense anticancer significance, came from curiosity-driven research. Barney Rosenberg had a NIH grant to support his study, with Leroy Augenstein, of the effects of electric fields on cell division. He chose E-coli in a field established by platinum electrodes.

Electrolysis generated a soluble platinum complex which inhibited binary fission of the bacterium, although cell growth continued producing filaments up to 300 times their normal length. I was associated with the team at the time and I was amazed to see the elongated form under the microscope, which was accompanied by pitting of the electrode.

It is noteworthy that the structure of cis-platin itself ($PtCl_2$ $(NH_3)_2$ was discovered by Werner in 1893.

Yours aye,

Ron

Professor Ken Packer FRS

Dear John,

The topic you address is one I have always been pushing.

Around 1960 I was a PhD student and, having synthesised only one new compound in a year and a half, I was excited that at least, the then quite unfamiliar NMR spectroscopy provided detailed information on its structure and led to two publications. I decided that NMR was for me; it was clearly more productive than the synthetic chemistry game! Being cautious, however, I asked those who knew about these matters (ie the experts – typical foresight panel members) for their views on the prospects for NMR as a research field. I was told *inter alia* that NMR was essentially fully understood and developed and, as such, offered not much more in the way of prospects for interesting research. NMR would clearly not have found favour in a 1960 foresight panel.

We now have Fourier transform NMR, noting that Ernst and Anderson's key paper on this was twice rejected, superconducting magnets, high resolution NMR in solids and MRI imaging. The development of imaging from curiosity-driven science to major wealth creation and social benefit has required inputs from many areas which thirty-five years ago would have been difficult to predict, such as whole body superconducting magnets, very fast array processors for high-speed multiple Fourier transformation, large scale fast access data storage devices, etc.

Planning, per se, is easy. Indeed, in some ways, it is so easy that it can become quite popular and take over as the apparent purpose of life. However the difficult thing to do is to have the confidence to then apply a light touch to the more detailed planning process and accept the risks of investing in a science base. It is then of vital importance to make sure there are mechanisms for capturing new things, supporting their development with a technically literate financial system and a technically aware, trained and energetic workforce. Funding of the science base has much in common with a day at the races. You can study form, prospects, the going, track records as much as you like but there is still a risk. However, there are always winners and if you don't invest you'll never back any of them!

Ken

Professor Gerald Pattenden FRS

Hello John,

I can state straightaway that *none* of the research I carried out in my heyday came from directed programs. These programs were less common in my day, but now they seem to be the norm, whether they are from our Research Councils or from European bodies. I doubt whether I would have gotten a chance under the present system. I was actually 'saved', as it were, by the sponsorship I received from pharma, agro, and other chemical industries. These industries seemed to like me and what we did and let me get on with it. They trusted me, both to deliver the new chemistry and to produce well-trained PhD students, and I believe we succeeded in both. Now that source of funding has all but evaporated.

I continue to have a small research presence in Nottingham, *i.e.* one post-doc, and visit and talk with young staff in Chemistry on a fairly regular basis. The younger staff I have spoken with in recent years seem pretty disillusioned and unsure where their future funding is going to come from. A fear they share is that some of our best universities might simply become applied research Institutes in the future! Many young staff are prostituting their research ideas and/or collaborating with the devil in order to keep going. I tell them that we all did a little of this in the past! It is certainly all about metrics now (how much funding and how many publications/ patents have you got? are you doing relevant research, creating wealth, looking out, forward looking etc?). Much less about following your nose and pursuing curiosity-driven research ideas. I have to say, however that I do tell some of my young colleagues to accept how it is and develop a get up and go attitude. They then come back with…it was all right in your day...what nonsense.

I do believe that Paul Nurse is banging on the door for more funding for and emphasis on curiosity-driven research and less metrics and auditing. I hope he succeeds, and I hope you do too with your publication.

Gerry

Sir John Pendry CBE FRS

Dear Sir John,

Thank you for your letter inviting me to comment on 'blue sky' curiosity driven research.

I have been very fortunate in my career to have had many opportunities to follow my own curiosity and I value these very much. Curiosity is not the only way forward in research of course but some of it is vital to the advancement of any field. In my early career I was greatly helped in establishing myself as an academic by the BP Venture Research initiative, more recently by an EPSRC Senior Research Fellowship, and currently by the Leverhulme award that my group received. None of these sources of funding imposed a program of research upon me.

To give a specific example, some time ago I proposed a new concept in electromagnetic materials in which the properties derived from their internal microstructure rather from their chemical composition. From this seemingly simplistic concept all sorts of new ideas have been enabled, including materials with the previously unheard of property of a negative refractive index, and designs for cloaks that can hide objects from electromagnetic radiation. For the first decade the interest was almost entirely academic, which I gather is not unusual for a new idea. Currently around 1500 scientific papers on metamaterials are published each year, attracting 24,000 citations in 2012, all from a baseline of zero in 1999. About 4 or 5 years ago serious commercialisation began. I cite in particular, Kymeta, a company that seeks to revolutionise the satellite communications market with a cheap satellite antenna based on metamaterials, now capitalised to around $50M with Bill Gates as an investor. Other companies are in the process of being floated. None of this could be foreseen when we were playing around with a tangle of wires 15 years ago.

John Pendry

Professor Ole Petersen CBE FLSW FRS

Dear John,

All my work has been consistently and continuously supported by the MRC since my arrival in the UK (1975); initially in the form of 3-year Project Grants and since 1988 in the form of Programme Grants successfully renewed at 5-year intervals (and since 1998 linked to an MRC Professorship award). The last renewal of the MRC Programme Grant and Professorship occurred in 2012 and will provide funding until May 2017. Without this continuous support this work would have been impossible.

While there were specific research programmes proposed in each grant application it was entirely possible to take up new lines or research during individual grant periods. Essentially the MRC – in my experience – have taken an admirably flexible approach to evaluation of what has been done. As long as good work has been done, they seem happy even if there has been some change of direction. In my own case that has been very important for the success of our work.

In general, I believe that it is also very important to support curiosity-driven research outside directed programmes.

Below, I attach a brief summary of how, after many years, my curiosity-driven research became clinically relevant.

Best wishes,

Ole

From basic studies of the function of pancreatic acinar cells to proof-of-principle for first rational treatment of acute pancreatitis (Ole Petersen CBE FRS FMedSci FLSW)

Studies of normal ion channel function and regulation in the enzyme-secreting pancreatic acinar cells in the 1980s (summarized in an ISI Citation Classic – Petersen & Maruyama, Nature 307, 693-696, 1984) together with studies of the regulating intracellular Ca2+ signal mechanisms in the 1990s (two of the key papers from the Petersen lab: Thorn et al Cell 74, 661-668, 1993; Mogami et al Cell 88, 49-55, 1997) led to a relatively complete understanding of the physiological regulation of secretion by the exocrine pancreas (finally reviewed: Petersen & Tepikin Annu Rev Physiol 70, 273-299, 2008).

On the basis of this knowledge, studies of the pathophysiology of the often fatal human disease acute pancreatitis, in which the pancreas digests itself, identified excessive Ca2+ signals evoked by bile acids or products of alcohol and fat as principal events initiating the disease process (two key papers from the Petersen lab: Raraty et al PNAS 97, 13126-13131, 2000; Gerasimenko et al PNAS 106, 10758-10763, 2009). Very recently, further developments have led to a study demonstrating proof-of-principle for the first rational treatment of Acute Pancreatitis by inhibiting specifically one type of Ca2+ entry channel responsible for the excessive Ca2+ signals initiating the disease (Gerasimenko et al PNAS 110, 13186-13191, 2013).

The journey from basic physiological studies to a clear mechanistic understanding of an important disease process and then towards a rational therapy is summarized in a recent review article (Gerasimenko et al J Physiol 592, 269-280, 2014) and presented in the video-recorded Keynote Lecture given by me at the last International Congress of Physiological Sciences (Birmingham 2013), which is freely accessible from The University of Oxford's 'Voices from Oxford':

http://www.voicesfromoxford.org/video/the-role-of-calcium-in-pancreatic-disease/397

Sir Rex Richards FRS

Dear John,

I agree with you that it is essential to retain some part of the science budget which can be used to support undirected curiosity-driven research. I would assume that judgements about what to support would have to be passed to a small group or groups of scientists who have shown themselves to be suitable. I think in some cases the initial grants need only be modest because it is often possible to show whether an idea has any mileage with simple homemade equipment. On the other hand this may not be possible and one must have sufficient funds to try out a very promising idea. My own experience illustrates this, if you forgive a personal note. I did my initial research with H W Thompson on infra-red spectroscopy. The instruments were largely homemade and quite primitive using galvanometer amplifiers and apparatus normally found in a physical chemistry laboratory. However there were two critical components; one was the detector to measure the heat from the radiation, and the other was an optically figured littrow mirror. I do not know where the funds for these came from. Those instruments did a lot of the exploratory work to show the value of I-r spectroscopy in organic chemistry, which was very important for some years.

I was appointed to a fellowship at Lincoln College in 1947 and kept a few graduate students busy with infra-red work; Tommy kindly allowed me to use the spectrometers for this purpose. However I naturally wanted to start something new myself and spent my first year reading the literature. I started some research into the physical properties of clathrate compounds using very sensitive calorimeters we design ourselves and this kept my research students busy while I was thinking of something new.

I found that NMR had been observed more or less simultaneously at Harvard and Stanford and all the focus in 1947 and 1948 was on the quantum mechanics and physics of the process. I later found that almost at the same time Bernard Rollin, in the Clarendon lab had observed NMR; his papers were on liquid and solid hydrogen, not the most obvious substances to spring to mind! I went over to see him and he was initially very discouraging and said that it could not possibly have any application to chemistry. However I had made up my mind to have a go, and when he realised that he could not have been more helpful. He directed me to 'the dump' where one could find great numbers of surplus electronics and purchase at next to nothing. I got lots of this and spent many evenings unsoldering components and putting them into labelled boxes. It was a hard time, but in 1948 (I think) I observed a signal. I needed a magnet and the laboratory allowed me £100 pounds to purchase one together with some lead acid batteries to drive it. John Smith was my first graduate student to work with the new instrument and we started to look at crystals containing hydrogen and found we could measure hydrogen-hydrogen distances and published a paper in January 1950. In the years that followed we were able to assign structures and distances to a variety of crystalline substances; it was not very exciting, but it was new. I remember giving seminars and being laughed at for 'using a steam-hammer to crack a nut!' However, I did have the last laugh, and you will know what an important phenomenon NMR has proved to be.

In 1963 or 1964 an American company announced that they had successfully made a length of superconducting wire using a hard conductor (one which will remain superconducting even in a strong magnetic field). My friend Martin Wood was in the States at that time, bought a long piece of this conductor, brought it back to Oxford, and in his garden shed he wound a small magnet with this wire. He took the magnet into the Clarendon, cooled it in liquid helium, attached it to a car battery, and achieved a field double the greatest field you can make with an iron magnet. This was a tremendous thrill, and I applied to the SRC, or was it SERC, and to their great credit, they appreciated the significance of this and gave me a grant to build, in collaboration with the Oxford Instrument Co., an initial design magnet and a working magnet. Of course the magnets were built by the splendid young engineers at O.I., but I had by now considerable experience of making magnetic fields homogeneous, and we had weekly meetings about the design. I do not need to tell you more except to say that one of those magnets is, I believe, still working, and that Oxford Instruments became the major manufacturer of magnets for NMR. They also designed a magnet for MRI with Peter Mansfield, and were for many years the major manufacturer of imaging magnets, until their whole design and manufacture was bought by a major global company.

Rex

Professor Wilson Sibbett FRS

Dear Sir John

I am pleased to relay to you my own research experience with regard to a key area that was seminal to my research at the University of St Andrews in the late 1980s and early 1990s.

1. Having moved to the University of St Andrews from Imperial College in 1985, I was very aware of the need to equip my laboratories in a manner that would both service the needs of my PhD research students and to ensure that my group could be competitive with the global front-runners in the field of ultrafast lasers and related science.

2. It was clear to me that the thinking within the then Council and Committee structures of the SERC (and later EPSRC) was that small groups as well as larger group configurations had the potential to undertake cutting-edge research.

3. In submitting a research proposal in which there was a request for funding to enable the purchase of a particular type of pump (argon-ion) laser, it was clear to me that the reviewers were persuaded that my research group, though still relatively small, had a potential to deliver to a 'blue-sky' agenda.

4. We wished to promote an idea where nonlinear optics could be combined with laser physics concepts to simplify the configuration of ultrashort-pulse lasers that could not only be tuned across the full gain spectrum of the laser crystal (titanium-sapphire) but where the peak power of the pulses could be enhanced to unprecedentedly high levels.

5. The technique that we developed, now called Kerr-lens modelocking, has had immense practical implications in sectors as diverse as fundamental physics (e.g. new attosecond physics!) through to eye surgery. BUT, at the outset, the research endeavour was purely speculative at the level of basic science and no-one could have predicted the full impact or range of the subsequent applications.

6. The associated post-deadline conference presentation (CLEO, May 1990) attracted an audience that overflowed the conference-room and the journal paper (Optics Letters, vol 16, pp 42-44, 1991) was considered to be one of the top breakthrough reports in optics for 1991. Without this work, it is unlikely that I would have gained Fellowship of the Royal Society nor would I have collected other accolades such as the Rank Prize for Opto-Electronics or the Charles Hard Townes Award from the Optical Society of America.

7. The justification of support for Directed Programmes within RCUK is often founded on existing programmes of ongoing research. If these are breaking new ground and maintaining originality in the research ideas, then this can be good for the UK research outputs. However, it must be recognised that some of the best and most novel ideas emerge from the efforts of individual researchers or small groups. In the case just cited for my experience in the late 1980s, I would in all likelihood have had an insufficiently strong platform of ongoing research at St Andrews to make a successful case to secure funding through a directed research programme. I was reliant on having access to funding through the channel of 'blue sky', curiosity-driven research. This therefore adds weight to the content of your recent communication on behalf of The Learned Society of Wales.

With best wishes,

W Sibbett

Professor Tom Simpson FRS

Dear Sir John,

I entirely support your initiative. While I agree that there is a need for a mix of directed research programmes and essentially curiosity-driven research, and note that the balance has veered wildly between the two over my research career, the current situation is without doubt unbalanced against the latter, especially in our own discipline which more than most others is driven by graduate students. BBSRC have very limited PhD support, and as you allude, the EPSRC is transferring the bulk of its graduate student support to CDTs which is OK if you can tap into them but a real problem if you cannot. A root problem is that EPSRC do not see provision of studentships as supporting 'research' but as support for 'training'. You may have seen David Parkers diatribe in 'Chemistry World' recently. Once that is accepted, their actions become entirely rational, from their perspective at least.

A major problem with CDTs is that they suffer from exactly the kind of top-down direction that we have suffered from for decades. Thus a large amount of resource is being allocated with little or no peer-review as we know it, to areas which are chosen by at best obscure processes. Thus they are often in areas that the high heid yins deem to be important, but which potential graduate students, an often surprisingly discerning group, do not actually want to work in. End result is that many CDTs do not attract particularly good students and so a lot of resource goes to not particularly exciting or high quality research. I can appreciate the problems the Research Council managements have in trying to persuade the Government to allocate the cash, but my perception is that they think they feel compelled tell the Treasury what they think the Ministers want to hear. That is of course much easier than saying that in the longer term the exciting and ultimately really important results come from undirected research.

In personal terms, I believe that I was fortunate to at least begin my career when there was essentially no top-down direction, at least that I was aware of. Studentships, the real life blood of research were freely available and young researchers and academics were free to pursue their own ideas via responsive mode. I would regard my major contributions to have been (i) application of stable isotope labelling to biosynthetic pathways which was essentially pre-FRS and largely supported via studentships and responsive mode, and (ii) applications of microbial molecular genetics to exploit these pathways – essentially post-FRS. These were achieved by a mixture of non-directed but also directed programme support and, to a large extent, overseas students. I sometimes say that I started off as an organic chemist, then I became successively a natural product chemist, a bioorganic chemist, a biochemist (God forbid), then deeply into molecular recognition, a chemical biologist and now finally a synthetic biologist (a directed programme that we are greatly benefitting from), but at the end of the day still an organic chemist. You change the title to pursue the funds for what you actually want to do.

A major problem with present day academic research is that there are simply too many of us trying (or maybe I should say feeling obliged) to do it. I look at major departments in e.g. Germany, Switzerland and North America and we have vastly higher numbers of Faculty. I would not often express too much sympathy for RCs but there is some truth in there being simply too many people chasing too little money. The total resource going into research in the UK is probably fairly comparable to other countries, but it is spread pretty damn thin. One of my best younger colleagues has just gone to a senior position in Hannover and visiting him a couple of weeks ago he was showing me round his floor – not his lab – his floor! A floor which he can populate without applying for a single grant! The numbers of academics that we 'need' is governed by the hugely inefficient way we teach – the malign legacy that Oxbridge has inflicted on the rest of the UK academic structure, especially small tutorial group 'teaching', too many 'spoon feeding' lectures, UG laboratories staffed by (senior) academics, paying PGs to demonstrate on top of their stipend rather than the demonstrating providing their stipends. Problem is that I do not see any easy way of changing the system!

Tom Simpson

Professor Malcolm Stevens FRS

Dear John,

What a surprise to get your letter. I wasn't aware that you were still campaigning on behalf of 'Blue Skies' research. The all-pervasive dominance of 'Impact' in the deliberations of the ongoing REF assessment is surely acting as an impediment to the recruitment of purely curiosity-driven staff who might ascend to a Fellowship later in their careers.

My own work on the discovery of the brain-tumour drug temozolomde is a perfect example of a curiosity-led project. In the discussions I had with Dr Ken Wooldridge of May & Baker (as was) in 1976 over the funding of a CASE studentship, he was interested in novel bicyclic heterocycles as part of their anti-allergy programme. In the end we resolved that my academic part would be just to 'make some interesting molecules' – inevitably containing lots of nitrogen atoms which I was quite good at. From that starting-point came a drug which eventually became a 'blockbuster' in 2008, some 30 years after its initial synthesis. The drug has now amassed sales of > $8.5 billion and that doesn't include the generics. I have become quite rich (for an academic) on my paltry share of the royalties! If you are interested in the finer personal details I wrote a full account of the discovery and development which has just been published in 'Cancer Drug Design and Discovery', 2nd Edition, Ed. S Neidle, Elevier, 2014, pp 145-164. The following chapter (pp. 165-175) details an account of the court case in the USA following a generic challenge where we successfully – eventually – won a defence of the validity of the US Patent.

In my early academic career I invented the slogan, 'Interesting chemistry begets interesting biology' mainly to antagonise my biological colleagues who were of the opposite opinion that only biology can drive drug innovation. I understand the quote has been used in university exam questions with the instruction: 'Discuss'. I would have hated to answer the question myself! Interestingly, the slogan has now been taken up by the 'Chemical Biology' research community along with the more emollient 'Chemistry teaches biology: biology teaches chemistry.'

Yours, with kind regards,

Malcolm Stevens

Professor Charles Stirling FLSW FRS

Dear Sir John,

In my own case, many years after my formal retirement, working at the bench and in collaboration with a young colleague, I was working on multiple low energy intermolecular interactions. I gave a populist lecture on this work in Cambridge which included a demonstration of a protein repulsive surface. In the audience was a silver-tongued entrepreneur who, on the basis of one of my slides set up a company that raised well over £1 million from adventure capital to use our chemistry for coating of biomedical inserts so as to preserve their function when placed in the body.

As it happens, the company will be hard-pressed to make any profits because of technical problems with insert coating but it does show what can be done.

Yours,

Charles J. M. Stirling

Professor Sir Fraser Stoddart FRS

Dear John,

Your letter says it all and I agree with the sentiments you express 100%. I would like to add two short comments.

1. I have found, during my time both in the UK and the US, that my research students (pre-and post-doctoral), the more so the very best of them, are drawn by instinct to the pursuit curiosity-driven research. Their creativity and passion are raised many-fold when they are left relatively free to explore the unknown and make discoveries.
2. The senior officers of the universities – at least here in the US – have aided and abetted the increasingly directed research programs supported by the government funding agencies by increasing their administrative officers tenfold in the past decade while the numbers of faculty and students has remained more or less constant. I recommend reading an essay in this February's *Nature Chemistry*, written by Bruce Gibb at Tulane University.

With best regards,

Fraser

Professor Sir John Meurig Thomas FLSW FRS

John,

'Research at the Institute is primarily curiosity-driven.' So wrote H-J. Freund, G. Meijer, M. Scheffler , R. Schiogl and M. Wolf to mark the centenary of the Fritz Haber Institute (FHI) of the Max Planck Society. These words were music to my ears. The philosophy that animates research at the FHI also prevailed in almost all universities of the United Kingdom in former times. But this is no longer so; indeed such has been the transformation in the attitudes of policy makers and funding bodies that it has prompted many leading academics to establish in this country a Council for the Defence of British Universities.

The freedom to pursue in an untrammelled fashion research prompted by curiosity is being increasingly restricted by the paladins of the research councils. Public bodies that fund academic research in the UK now tend to emphasize the perceived practical importance of the scientific research that they decide to support financially.

It is undoubtedly mutually beneficial for scientists at universities to interact and thereby help to foster work of national importance. But this must not be the only way forward. A very successful but short lived scheme in the UK that gave academics opportunities to indulge in blue sky research and to investigate natural phenomena out of curiosity was the ROPA (Realising Our Potential Awards) initiative. Nearly half of the 1000 or so ROPAs were so potentially interesting that industry was prompted to follow up the 'Blue Skies' investigation of the academics.

Here are a few examples form my own work, all of which came from 'Blue Sky' thinking. In 1974 I decided to investigate afresh the structural and intercalation properties of sheet silicates because I felt that techniques available to physical chemists were superior to those that clay mineralogists had been using. We soon discovered that interesting organic chemical reactions could take place in the interlamellar spaces of materials such as montmorillonite, hectorite and beidellite. These were thus new catalysts. With Howard Purnell and Jim Ballantine and your great help at BP we saw how easy it was to play tunes with interlamellar regions of clays leading for example to the one step formation of ethyl acetate from ethylene. As you know this was later developed by BP using a longer-lasting solid acid than our cation exchanged clays.

It was 'blue sky' thinking that prompted me, in 1998, to start playing compositional and structural tunes with microporous aluminophosphates and hence nanoporous single site acid catalysts as well as redox catalysts. They have now led to major advance in two important bulk chemical processes. First, the vapour and liquid phase Beckmann rearrangement of cyclohexanone oxime to give caprolactam and hence nylon. Second, we can readily and efficiently prepare cumene from iso propanol and benzene and then on to phenol.

Best wishes,

John

Professor Kenneth Walters FLSW FRS

Dear John,

Looking back over my own career, progress was made through a combination of money for research students (53 successful PhDs in all) from Aberystwyth University, EPSRC, CASE and private support, with PDRA support from EPSRC and EU sources, and direct funding from various industries, including Shell, BP, Unilever and ICI. It was not a case of either/or but both/and!

I feel very sorry for those who are just entering the scene, since all these 'rules and regulations' for current EPSRC funding, for example, seem obstacles rather than helps.

As a member of an EPSRC College, I am often frustrated by the rules as I referee new requests for funding.

Very best regards,

Ken

Professor Robin Williams CBE FLSW FRS

Dear John,

You ask some very interesting and important questions and, in general, I agree with your analysis. You ask about my own experience. I think I can best summarise the factors leading to my own research success as follows:

1. In my first job having funds to purchase new equipment which allowed me and my research student to carry out internationally competitive experiments based on my own ideas. This would be classed as QR funding and 'capital funding' today and provides the base for experimental research.
2. Having two or three outstanding technicians which enabled us to design and build apparatus for new experiments of the kind that nobody else at the time was able to do.
3. The emergence of synchrotron radiation as a Research Council central facility which enabled us to do new curiosity-driven experiments which were competitive on the world stage.
4. The availability of, and funding for, a string of excellent research students and research fellows which enabled my group to follow a number of original [undirected] ideas.
5. Once the base and the reputations were well established, industry and research establishments invited us to participate in joint directed programmes, many supported by the Research Councils and the EU. They wanted us in the programmes because our curiosity-driven research provided the base on which an understanding of issues of relevance to them could be developed.
6. Strong financial support from the Research Councils for curiosity-driven research and an appreciation of novel ideas and thinking, and an understanding that sometimes ambitious experiments might not succeed.

If I was starting today it would be a great deal more difficult to develop my own line of research. Lack of 'capital' funding and lack of support for research students, and in particular lack of quality time due to increased bureaucracy, is now much more of a problem. I am also totally opposed to the current fashion for doctoral training centres which operate in a 'directed research' mode. The Research Councils' emphasis on immediate impact has gone way too far which, in the long term, will make University research in the UK less useful for UK companies.

I should, perhaps, also mention the importance of central facilities such as Diamond, and such as Daresbury, in its day. My research students gained great experience and confidence using the SRS at Daresbury and made many excellent international contacts which have since led to highly productive international collaborations. New science often comes by bright young researchers from different disciplines talking together in the right environment, and I think some of the central facilities provided that environment.

Sincere regards,

Robin Williams

APPENDIX 3: Comments on the ROPA (Realising Our Potential Awards) scheme

'We intend to form a new company to exploit our various vectors in gene therapy procedures. The viruses made in the ROPA provide one proof that this would work.'

'The data from our studies are currently under analysis. We are hopeful that the results will provide a significant springboard for further funding.'

'This is a long term project which involves transgenic animal manipulation. The ROPA grant provided important seed corn funding to prove the concept. We have secured further development funding from the University of Leeds and await the outcome of further applications, we are confident of success.'

'Clinical trial planned.'

'Certainly advanced our knowledge with the development of a new method of assessing adults likely to become diabetic before detectable by GTT.'

'....we also found, through serendipity, some interesting additional findings which go beyond the original purpose of the grant...'

'ROPA provided the ideal means to investigate truly unknown hypothesis. Pharmasonics (a company) was very small at outset (private finance from two individuals). Raised $500,000 in spring 1997 from initial results; business plan to raise $5 million Jan/Feb 1998.'

'The ROPA has had an outstanding effect on the development of my group in many diverse ways...'

'This work has influenced the design of CTL-targeted vaccines or tuberculosis; currently of interest to several companies including UK based ones.'

'Project is still going. Could lead to development of synthetic elastomeric polymers based on fibrillin in the area of tissue engineering.'

'The MRC/ROPA scheme has been central to developing new technologies in our laboratory which have had direct benefits on a whole range of projects in the department...'

'Uptake of the test and further development of it by the forensic science service in Birmingham. It should be possible to introduce it routinely into forensic testing.'

'ROPA has given a world lead in the application of time resolved FTIR to metallo-proteins and related chemistry…'

'The ability to pursue "blue sky" ideas has generated a number of other leads which are being investigated. These will undoubtedly be the subject of further applications for funding to BBSRC/Industry. ROPA is essential in supporting fundamental research.'

'The research has proved to be highly significant to the area and has stimulated new directions of research during the project....'

'Several major pharmaceutical companies have expressed interest in the technology under development in the ROPA project...'

'The relevance of the work has become increasingly obvious during the period of the project but the work has not yet reached fruition.'

'The project on the prediction of pharmokinetic behaviour has helped in the establishment of a new academic centre in Manchester, The Centre for Applied Pharmokinetics, which is almost wholly supported by a consortium of pharmaceutical companies, from which other links with industry are likely to follow.'

'The ROPA award enabled my group to explore new collaborations with industry without the pressure of having to seek substantial amounts of funding for companies during the initiation of a new programme of work.'

'Work was first published in October J997 and has already won 3 international prizes for originality and innovation.'

'The work is part way through and results are now starting to emerge. I have high hopes of the remainder of this period leading to patents and new funding.'

'The substantiation of our research in this area due to the award of the ROPA has enabled stronger links with other commercial and non-commercial research groups. The links will, in the future, lead to formal collaborative projects in medical and veterinary bacteriology.'

'Several major pharmaceutical companies have expressed interest in the technology now under development in the ROPA project. The feasibility studies are progressing well and licensing deals will be sought when these are concluded.'

'The work carried out within this project so far has attracted the interest of a commercial organisation who have expressed an interest in patenting several of the genes isolated within it...'

'This project has done much to open new avenues. We have identified new molecular ligands that defy conventional thinking...'

'The project has led to collaborative partnerships with the universities of Keele and Bristol and has generated considerable interest from the process industries...'

'The EVA technique is now available in TRIPOS software.'

'A substantial collaboration emerged from this one year grant…'

'...It is anticipated that the technology developed will be of interest to pharmaceutical companies engaged in genomics research...'

'These ROPAs were tremendously important in taking the polyamino acid-catalysed asymmetric epoxidation protocol from a curious finding to a commercially exploitable process...'

'Likely to lead to new funding opportunities since systems under study have proved to be important and novel.'

'The research is looking incredibly promising. Dunlop have already sponsored 18 months research and we are currently organising a further contract They are hopeful of exploitation. An Italian group at Pisa University are just starting very similar work: it may be that we combine our efforts.'

'Work on the machine built in Durham has sparked off a lot more research, much collaboration and more grants.'

'The ROPA has led to the development of novel techniques and improved validation of a spark ignition engine simulation.'

'Excellent scheme.'

'Excellent kick-start for this work.'

'The company placed a schedule 2 contract with the department to provide 4 alpha test modules for evaluation in critical US sites.'

'ROPA led to the establishment of a new centre and a major new activity which has seen strong industrial interest.'

'Through our exploitation company we are in discussion with a major multinational company who have expressed serious interest.'

'The grants have enabled a valuable inroad to be made in important areas of combinatorial technology and immense pharmaceutical involvement.'

'The research base has allowed us to develop a skills base which we have used successfully to promote other projects, and this has enhanced out ability to attract EU funding through BRITE and Environment projects.'

'The materials developed are attracting interest widely: UK, Japan, and Sweden. Applications could come in catalytic sensors or in organic synthesis (clean technology).'

'The grant was very useful in initiating new areas of research and fostering links with other researchers. Industrial funded income is about 3 times the award so far, and more is to come.'

'The ROPA scheme has been extremely successful in this case in promoting new university/industrial research directions.'

'We have a major research programme on single electron devices with Hitachi. An aspect of this subject which is of great fundamental interest was addressed by the ROPA. The results give a fascinating insight and were part of the reason that our research was funded for a further 5 years.'

'The project was speculative and has provided the basis for further work. One section of the work has produced some novel data manipulation techniques, and with further minor modification a commercial product is quite possible.'

'The work was underpinning and generic and it has provided a scientific basis for developing our understanding of fatigue crack growth. Additionally, it has been applied directly to confirm the approach to material lifting at British Aerospace. '

'Enhances our industrial explosion hazard prediction capabilities bringing more funding from Shell, BP, BG and other companies.'

'This work now shows promise not only of huge academic development, but also of a wide range of industrially important applications in industries which include: oil; chemical engineering; food processing; pharmaceuticals.'

'Instrumentation and techniques devised under ROPA have been copied by two industrial firms for routine analytic purposes. Further funding is currently being used to extend the technology for use in other industries.'

'Results are producing continuing new interest from industrial research groups with whom we did not previously have contact.'

'A method developed as part of the ROPA has attracted funding from an industrial company for research in a related area.'

'The ROPA has allowed a close link to be forged between the final remnants of the UK dyestuff manufacturing Industry and academia where the opposite knowledge base is situated (UMIST).'

'The project played a key role in obtaining further research support from BP Chemicals.'

'The ROPA enabled a deeper theoretical analysis than would otherwise have been possible. In consequence, there are significantly wider follow on possibilities and new research lines opened up. I expect both commercially-oriented and fundamental projects to start in the near future. '

'Influential in attracting considerable consultancy work in forensic engineering.'

'The research has provided a fundamental understanding of statistical parallelism with industrial applications in neural network methods.'

'Yorkshire provided £70k to take the work from the proof of concept stage to a stage where fitness for purpose could be assessed. An additional £40k of field testing money was also provided.'

'Strong part of expanding research activity on supported catalysts.'

'This project was awarded the prestigious European Information Technology Prize last October; thus securing considerable visibility. Also, the prototype system was exhibited at Microwave 96 and Hanover 97 as well as Sampta 97. A real product has emerged.'

'A consortium of companies is funding further work including Unilever, Nestle, Chemagnetics, BNFL and others.'

'Without ROPA support, this project, being rather speculative, would not easily have attracted funds.'

'The work has led to the setting up of a new collaboration in interfacial chemistry.'

'Grant enabled me to enter a completely new area of research. The equipment which I purchased has helped to attract excellent research workers from abroad and has led to new collaborations within the EC and with industry. '

'ROPA is a good concept. It provides small but useful sums of money to try out new ideas. It has been of great benefit to us in developing oscillatory flow mimicry.'

'All three patents filed in UK, France, Germany, Japan and the USA.'

'The ROPA was very positive in starting not one but two new initiatives which have already attracted more than 100% of the EPSRC funding in industrial funding.'

'The ROPA has created a new facility which because it is virtually unique provides the UK with an enhanced research capability. The work is continuing with an industrial CASE award.'

'This research has been the basis of several collaborative projects with scientists at other academic institutions. These links will continue and be strengthened. '

'There has been very considerable interest in this process and its products.'

'Results obtained so far are extremely promising. Philips (with whom we have not had links before) are very interested in further development.'

'The new techniques developed on this ROPA have attracted world-wide interest and many invitations to give talks from around the world. We have pioneered a powerful new way of determining the bonding and charge transfer in key metallic alloys.'

'Research directly led to 3 EU contracts, and 1 RR contract, plus 1 other industry contract. Total value of contracts exceeds £250,000.'

'The research led to program code that is being incorporated in a major information extraction engine that almost certainly will be commercialised.'

'This project has attracted interest and support from the Environmental Agency and various industries to carry out further research/output.'

'We have developed links with the CBI, the British Chambers of Commerce, and the Construction Employers' Federation with a view to developing this research further.'

'Work on minimalisation of risk in the nursing profession has led to a grant from the Royal Society for the Prevention of Accidents.'

'ROPA helped to convert a germ of an idea into a major project. The oil companies were confident to sponsor bringing the idea to the market place since proof of concept had been realised. '

'ROPA has initiated on-going strong collaborations with the Universite de Nantes (named as co-inventors on patent) and CSIRO Division of Marine Research Australia. Each of these labs has contributed two species of algae which biosynthesise the bioactive chemicals which are the subject of the patent.'

'Development of a new technique for the direct dating of hydrocarbon source rocks with considerable potential for the direct dating of oil maturation events.'

'The work has stimulated interest in the European arena for the development of PROCLOUD a EUROTRACII (EUREKA) project. Development of ROPA work will be a major component of this.'

'ROPA contributed towards obtaining funds from the Department of Environment Transport and the Regions. Early indications of considerable interest from industry and regulators.'

'Our ROPA award was for the bluest of blue skies research potentially contributing to improved public safety and quality of life.'

Negative comments about ROPA scheme:

'For original, new research 12 months funding is not long enough in this area.'

'The MRC declined to fund a full application based on the exciting and novel findings. The funds would have enabled the 'pilot' ROPA grant to blossom into a programme that would have been attractive to industry. Indeed in the latest proposals for ROPA on 'neural research' the proposal was declined-despite attracting over £0.5 million in industrial funding. The policy of the ROPAs is confusing and needs more accountability in explaining the results of applications.'

'....However we do have anxieties about the ROPA approach, in general terms, as colleagues sitting on decision making boards have told us of ROPA proposals being funded which would not be funded via the normal route on science grounds alone. Also the cash crisis in the MRC a couple of years ago was, we are given to understand, largely caused by over exposure to ROPA commitments. The cash crisis led to many mid and even high alpha projects being unfunded. So although we won a ROPA grant and did, we believe, some good science with it, honesty dictates that we draw attention in your consultation to some of the downside of the ROPA scheme.'

'ROPA funding is a poor diversion away from mainstream funding by genuine peer review. It was a divisive and unhelpful scheme.'

(Not critical of ROPA itself)

'Work done under ROPA led to an offer of financial support from Wyeth which has not yet been established. An application for an MRC grant was alpha-rated but not funded, one referee commented that Wyeth should fund the work and other said that the MRC LINK scheme should fund but it has proved difficult to co-ordinate Wyeth and LINK. This is a bureaucratic nightmare. '

'Surely ROPAs were intended to allow groups with existing strong industrial support to pursue fundamental, yet strategically important, work. My view is that such work is most likely to produce new science rather than patentable technology and spin-off companies.'

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- to celebrate, recognise, preserve, protect and encourage excellence in all of the scholarly disciplines, and in the professions, industry and commerce, the arts and public service;
- to promote the advancement of learning and scholarship and the dissemination and application of the results of academic enquiry and research; and
- to act as a source of independent and expert scholarly advice and comment on matters affecting the wellbeing of Wales and its people and to advance public discussion and interaction on matters of national and international importance.

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