NOTES AND RECORDS

Notes Rec. (2016) **70**, 287–291
doi:10.1098/rsnr.2016.0015
Published online 6 April 2016

LECTURE

ADDRESS OF THE PRESIDENT, SIR PAUL NURSE, GIVEN AT THE ANNIVERSARY MEETING ON 30 NOVEMBER 2015

Ensuring a successful research endeavour

For my final Presidential Address I have decided to discuss the guidelines and principles used for 'Ensuring a successful research endeavour' that I recently presented to the government. My first question is: Why do we do research?

Research in the sciences, medicine, mathematics, technologies, the arts and the humanities produces knowledge that enhances our culture and civilization and can be used for the public good. It is aimed at generating knowledge of the natural world and of ourselves, knowledge that can be developed into useful applications, including driving innovation for sustainable economic growth, improving health, prosperity and the quality of life, and maintaining the environment. This has always been the case since the beginning of modern science in the seventeenth century, when Francis Bacon argued that science improved learning and knowledge, which 'leads to the relief of man's estate'. Today, for advanced nations such as the UK to prosper as knowledge economies, scientific research is essential—to produce both that knowledge and also the skills and people to use it. That is why science should occupy a central place in government thinking, if the UK is to thrive in our increasingly sophisticated scientific and technological age.

However, scientific research is not solely utilitarian. It generates knowledge that enhances humanity more generally. In the words of Robert Wilson, Director of the Fermilab particle accelerator: when asked by the US Congressional Joint Committee on Atomic Energy whether the accelerator in any way involved the security of the country, he replied, 'It has to do with the dignity of men, our love of culture … it has nothing to do directly with defending our country except to help make it worth defending.'

Research and development in the UK is funded by government, by private companies, and by charitable organizations. Government-funded research usually generates openly available knowledge, trains the scientific workforce and develops the skills necessary for the effective running of the country. It is also able to monitor research being carried out throughout the world. Research funded by private companies is most often aimed at developing knowledge into useful commercial applications, and is usually restricted in accessibility to maintain commercial advantage. Charitable organizations support research into specific objectives of interest to philanthropic organizations, often with an emphasis on biomedicine.

The research funded in these different ways often overlaps and is carried out in diverse sectors and in different research disciplines, forming a network of discovery science acquiring new knowledge, of translation of knowledge into innovation, and of developments for applications. It is a complex interactive system, with knowledge generated at different

places within the spectrum of activities, influencing both upstream in the creation of new discoveries, and downstream in the production of new inventions and applications. New discoveries enable new inventions, and new inventions enable new discoveries.

An effective research system for producing knowledge for the public good is characterized by freedom of action and movement—it needs to be permeable and fluid, allowing the ready transfer of ideas, skills and people in all directions between the different sectors, research disciplines, and various parts of the research endeavour. Throughout the system, research thrives on excellent scientists who are strongly motivated, most often by great curiosity and by the freedom to pursue their intellectual interests, and shares many values and common practices. It is built on a respect for reliable and reproducible data; a sceptical approach that challenges both orthodoxy and the researcher's own ideas; an abhorrence of the falsification or cherry-picking of data; and a commitment to the pursuit of truth. Science can only succeed when it is grounded in integrity and good practice. However, despite sharing many values and practices there are specific differences in the ways that research is carried out in different parts of the system.

Discovery research aims at acquiring new knowledge about the natural world and ourselves. It can work in various ways but most often proceeds through an iterative process of hypothesis generation and challenge. A researcher considers what is known about the subject of interest, and generates a hypothesis. This hypothesis is then challenged by investigating the predictions that it makes through experiment and observation. Should the new data obtained not support the hypothesis being tested, then it is either rejected or modified, and new hypotheses are tested by further observations and experiments. This approach is complemented by more exploratory ways of working aimed at accumulating sufficient knowledge to define a field of study and to generate hypotheses that can be tested. As a consequence, the ideas driving an investigation may well change during the course of an investigation. The original hypothesis can change, and even the phenomena under study may change. An important outcome is that although discovery research is efficient at producing knowledge, it is often difficult to predict where the research may go. Through this mechanism of challenge and modification, the scientific process is essentially self-correcting, and it is this characteristic that makes scientific research a reliable way to gather knowledge about the world.

Applied research is more goal-directed and aimed at achieving specific objectives and outcomes. For this to work successfully there are two necessary conditions. The objectives need to be well chosen, based on an understanding of customer needs, whether societal or commercial, to ensure that the applications being developed by the research are worthwhile. Also the knowledge base required for the application needs to be sufficiently well developed that effective development of the application is generally foreseeable. Its execution requires a directed approach and frequently uses a diverse, multi-disciplinary skill set.

Translational research aims at bridging discovery and application research, and can be considered as oriented discovery research. The objective is to expand the knowledge base in a certain area to a point at which more directed development work becomes possible that leads to desired applications. However, there is a danger with such activity that if more directed approaches are applied too early, the research may become less responsive to the self-corrective mechanisms crucial for the scientific process, whereby the researcher changes direction as a consequence of new data, ideas and hypotheses—wasting effort, to the ultimate detriment of the long-term objectives. If the ultimate driving force is to achieve a specific objective rather than to gain knowledge relevant for that objective, then the researcher may not respond effectively to the signals from new knowledge indicating

that the original aim may not be achievable in that manner. To rush into translation may result in becoming lost in translation. The aim of translational research should be to increase the knowledge base to determine what applications may be possible, whereupon more highly directed approaches can be taken. Therefore, it is usually more effective to identify research objectives in a broadly scoped manner, giving freedom for the individual researcher to propose a specific programme within that wider umbrella, and to pursue that research wherever it may lead.

Making good decisions about what research topics and which researchers should be supported is an integral part of the research process, and is crucial for a successful, cost-effective research endeavour. This requires proper investment in good-quality decision making, which should be seen not as an administrative burden but rather as an essential part of the research process ensuring that research funds are spent wisely.

Doing high-quality research is hard and there needs to be a clear focus on excellence along with a recognition that the actual outcomes achieved may not be what was originally planned. The highest standards need to be applied when judging whether research is indeed excellent. Three factors are particularly important for scientific research funding decisions: the researchers undertaking the research, the research programme itself, and the circumstances in which the research is to be pursued.

Research discoveries are often associated with talented individuals who combine a number of qualities: they need to have in-depth knowledge with a wider peripheral understanding of related work. They should possess the necessary skills, be creative, understand the values of research and how it is done, be motivated and be highly effective. Some research problems require a diverse body of researchers with different skills and approaches. Freedom of thought and action to pursue an investigation wherever it leads is essential. A researcher who is too strongly directed from above, or whose thoughts are restrained, is unlikely to be fully effective in research. Similarly, in my view, societies that do not encourage freedom will find it harder to excel in research.

The research programme should tackle an interesting problem and should demonstrate an approach that is both creative and practical. In the discovery part of the research continuum, the problem being proposed needs to have the potential for scholarly impact, which should be included as part of any judgement of impact of research activity. A similar approach should be used for most translational research that has the ultimate aim of improving the knowledge base relevant for an application of potential societal or commercial benefit. For research aimed at specific application a more directed approach is required. There needs to be an assessment of the needs for the customer and of the market in the research application.

The third issue that needs to be considered in research funding decisions is the location and circumstances in which the research is being carried out. Is there adequate infrastructure in place? Are the appropriate colleagues involved? Centres of research excellence can help here, but funding mechanisms should be flexible and inclusive, so that support is possible wherever quality research can take place. Sometimes novel approaches to problems can emerge more readily when carried out away from conventional centres of excellence, which sometimes become too dominated by current fashions and research leaders.

What are the best mechanisms for making funding decisions? Decisions, especially at the discovery levels of the research spectrum, should be driven mainly by peer-level scientists carrying out relevant research—they are the ones best placed to come to the best decisions. For translation research, review by peer-level scientists needs some input from those with the potential to apply the research, who in turn should take a more leading

role in decisions about applied research. A well-run response-mode funding system with effective peer review is a very successful way to deliver new scientific knowledge, because it uses those with the best understanding of the work being proposed.

How can science deliver for society? In discovery and translational research modes, the funder largely allows the body of knowledge and capability to grow wherever it may seem most fruitful to the researcher. What is then required are efficient mechanisms for the capture of that knowledge when it is useful for potential applications. An approach is required in which discovery and translational research are the major drivers for knowledge generation, and in which there is a culture that can efficiently capture that knowledge when it is relevant for application.

In the application mode the funder chooses to shape to some extent how that body of knowledge and capability develops. For example, a charitable funder might decide to invest to improve understanding of a specific disease; or the government might invest in such a way as to address perceived skills gaps for the economy or society.

Bringing about benefit for society from research introduces the issue of how much politicians should be involved in decision making about research funding. Important here is the Haldane Report of 1918. Haldane argued what is almost a truism, that decisions about the allocation of research funding are best taken by those who have the expertise and experience to know where it will be best spent. What has been termed the 'Haldane principle' is usually interpreted as meaning that researchers rather than politicians should decide how to spend funds. It must always be remembered that publicly funded research consumes significant financial resources that are ultimately the responsibility of democratically elected representatives. It is usually accepted that politicians, informed by external expert advice, should decide on the overall science budget and contribute to the high-level allocation of resources, for example identifying specific challenges and key infrastructures. These decisions are never fully technocratic, because they need also to reflect the desires of the society that provides that funding, including the views of society's representatives. However, it is crucial to get the mechanisms right that result in a good relationship between politicians across government and expert researchers, to ensure that the best decisions can be made. We need an effective dialogue and understanding in place between research scientists, politicians and the public. Without this engagement and societal endorsement, the research endeavour will ultimately stall or fail. Good policies and strategies developed by researchers who know how science operates, working together with policy makers and those responsible for societal and commercial interests, are essential for a successful research endeavour. This requires an effective way of working between these organizations and sectors, and a compact that bonds science and society which will both deliver excellent science and ensure that it is used for the public good. Without this in place, there is a risk of science becoming marginalized with limited influence in public policy making, resulting in reduced funding for research.

None of these principles and guidelines can be effective without sufficient funding. In delivering an effective research endeavour it is important to recognize that there are upper and lower bounds for optimal funding. If the boundary is set high with too much funding, there is a danger that the research supported will be of too low a quality; if the boundary is set too low with too little funding, then the research endeavour becomes dysfunctional. There is usually little danger of there being too much money for research! More common is below-optimal funding levels, which result in stress within the research endeavour, wasting time and resources and resulting in decision making becoming a lottery.

Similarly, with the balance between infrastructure spending and resource spending for operations, there is no precise optimum but there are upper and lower boundaries. If infrastructure is allowed to decay too much, then the delivery of research and the effective utilization of resource spending is damaged. If capital spending becomes restricted, beyond the very short term, research will suffer because it is mostly a venture that is highly dependent on the latest technologies, methodologies and infrastructures, which require capital spend. Equipment needs to be replaced, and laboratory and science infrastructure facilities need to be refreshed. In contrast, if the upper boundary is exceeded, then laboratories and facilities can be put in place that are under-utilized or absorb operational funds that put the rest of the research endeavour under strain. This can be best dealt with by ensuring that capital investment decisions are made contingent on sufficient resources being in place to ensure efficient operation of the new infrastructures or facilities, and that decisions are supported by good knowledge and a database of the UK research landscape and capability.

There are no hard and fast rules that can be applied as to the precise percentage of GDP that should be devoted to the public funding of research. Given the significance of research for driving productivity, economic growth, and societal good, there should be sufficient support in place to ensure that the UK has an effective knowledge-based economy. Comparisons of spend in other countries can provide a good starting point for discussions setting levels of support. The last five years of flat cash for science has resulted in 0.49% of the UK's GDP being invested by the government in research and development.

This level of investment is low compared with other similar nations. The top ten OECD countries on average invest 0.67% of GDP, ranging from 0.49% to 1.09%, and the Society has argued that by 2020 we should at least match the average of 0.67%. In the recent spending review it was announced by the Chancellor that, for the next five years, investment will remain constant in real terms rising with inflation, so the figure of 0.49% is unlikely to change very much during this period. It is crucial that investment be raised if science is to be adequately supported, and if science is to deliver all it is able to do for society.

This Address is my last formal duty as President of the Society. I want to thank my fellow Officers, the Executive Director, successive Councils, Fellows and Foreign Members of the Society, and all the Society's staff, for all their help and support during the last five years. It has been a privilege to serve the Society as President, and I want to wish my successor, Venki Ramakrishnan, the very best of luck for a highly successful and enjoyable Presidency.