European Review, Vol. 30, No. 5, 591–626 © The Author(s), 2022. Published by Cambridge University Press on behalf of Academia Europaea. This is an Open Access article, distributed under the terms of the Creative Commons Attribution licence (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted re-use, distribution, and reproduction in any medium, provided the original work is properly cited.

doi:10.1017/S1062798722000084

# GOLD MEDAL LECTURE HELD AT THE ACADEMIA EUROPAEA BUILDING BRIDGES CONFERENCE 2021

## Ups and Downs of Science during a Tumultuous Period of History: A Personal Perspective

OLE H. PETERSEN

School of Biosciences, Cardiff University, Sir Martin Evans Building, Museum Avenue, Cardiff, Wales CF10 3AX, UK. Email: PetersenOH@cardiff.ac.uk

Science has undergone remarkable changes both in scale, organization and influence over the last half century. It has changed the way we live and is more essential than ever before. Although the scientific effort today is more international than it was 50 years ago, only a small part of the world is fully engaged in this process. It is of course impossible in a single article to provide an overall balanced account of these developments and this is not an attempt to do so. Instead, certain trends are illustrated here, based solely on the personal experiences of an individual who – during a long career in the Life Sciences, and through work in many international science organizations – has been a witness and played a role in some of the changes that have occurred, often influenced by major political events.

### Introduction

When the President of Academia Europaea (AE), Sierd Cloetingh, announced at a Board dinner in Barcelona late in 2019 that I was to be awarded the Academy's 2020 Gold Medal, it was a great, and of course delightful, surprise. I was lucky enough to have been selected in 1988, by our Inaugural President, Arnold Burgen, as one of the Academy's Founding Members and have since then had the privilege of serving the Academy in different roles. Because of COVID-19, the Academy's 2020 Annual

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press


**Figure 1.** Ole Petersen receives AE's Gold Medal from President Sierd Cloetingh.

Conference was cancelled and I received the award, and gave the award lecture, at the 2021 Conference in Barcelona (Figure 1). In my lecture I took the opportunity to reflect on the dramatic changes in the scientific landscape and its organization that have occurred over the last 50 years, based on my personal experiences.

Since this article presents a personal perspective, it may be helpful to give a brief background to my life as a European scientist. I went to School in Denmark, Norway and Germany and graduated in Medicine from the University of Copenhagen. I was Lecturer and then Senior Lecturer in Physiology in Copenhagen until my appointment, at the age of 32, to the Symers Chair of Physiology and Head of the Physiology Department at the University of Dundee in Scotland. Six years later, I was appointed George Holt Professor of Physiology at the University of Liverpool. I held this chair for 28 years until I succeeded the Nobel laureate Martin Evans as Director of the School of Biosciences at Cardiff University in Wales. Although by far the major part of my work has been carried out in the UK, I have been closely involved in science evaluation in Germany, particularly as a member of scientific advisory boards of the Max Planck Society. I also have strong personal relations with Eastern Europe. My Mother, Elisabeth Klein, who was a classical pianist, grew up in Budapest, studied at the Liszt Academy, and had piano lessons with Bela Bartok, before coming to Denmark just before the outbreak of the Second World War. My wife, Nina Burdakova, grew up in the Soviet Union, graduated from Moscow's Linguistic University and worked in Ukraine as a translator and administrator at the Bogomoletz Institute for Physiology in Kyiv, before coming to the UK in 1994.

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

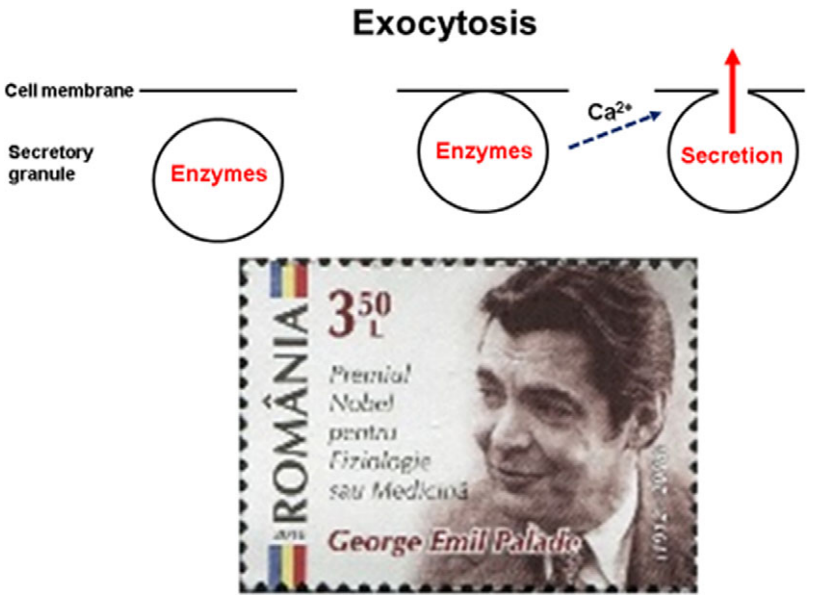


**Figure 2.** Top: simplified diagrammatic sketch of the process of exocytosis. Bottom: a Romanian stamp commemorating Palade's Nobel Prize is shown.

### George Palade's Foundational Work on the Mechanism of Secretion

In the early part of the twentieth century, Germany was by far the strongest science country in the world, as can be seen by the fact that this country had the largest share of science Nobel Prizes. Typically for that time, my grandfather, Julius Petersen, who was Professor of Chemistry at the University of Copenhagen (1907–1931) and introduced electrochemistry to Denmark, had learnt about the latest developments in his field during several study periods at the University of Göttingen. He and his Danish contemporaries knew German much better than English and frequently published in German. The situation began to change in 1933 with the exodus of Jewish university professors, primarily to the US and the UK. This problem not only affected Germany, but also other countries in Central Europe under the influence of Nazi/fascist policies. The Second World War, devastating most of continental Europe, caused a further dramatic decline in scientific activity, so that by the end of the war European science was in a disastrously bad state. Inevitably, this led to a further brain drain from all over continental Europe, mostly to the US. In my own field, the physiology of glandular secretion, this is exemplified by the fate of George Emil Palade. Born in Iasi, Romania, he graduated in Medicine in 1940 and was a member of the Faculty at the Carol Davila University in Bucharest until he went to the US in 1946. Palade became phenomenally successful in the US, working at the Rockefeller Institute and later at Yale University, and is universally recognized as one of the founding fathers of modern Cell Biology. One of his great achievements was the description in the 1960s of the secretory pathway in the acinar cells of the exocrine

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

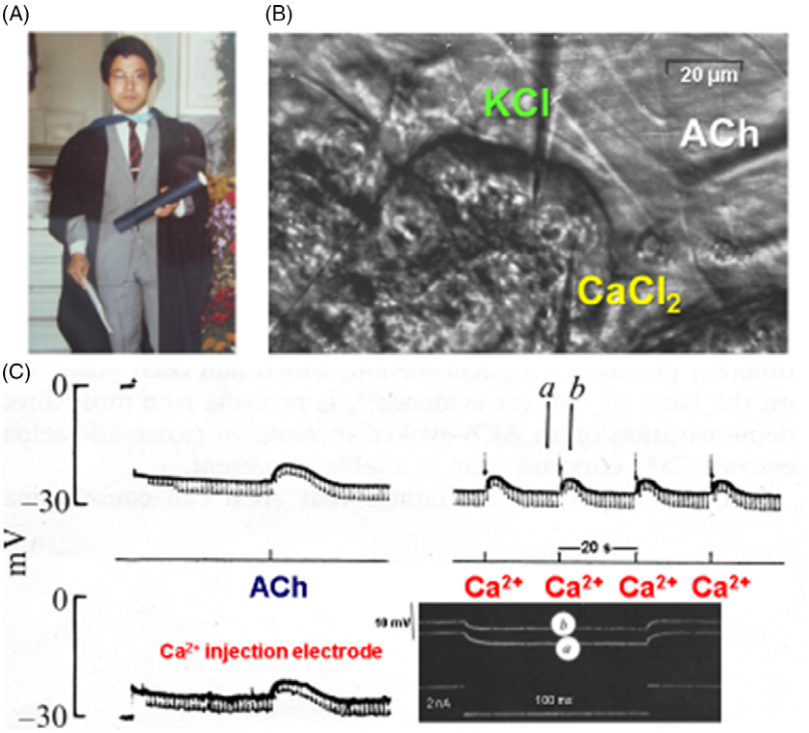


**Figure 3.** (A) Noriyuki Iwatsuki. (B) View of living pancreatic acinar unit with electrodes inserted into two neighbouring cells and an extracellular acetylcholine (ACh) pipette delivering the neurotransmitter. (C) External ACh application is mimicked by intracellular $Ca^{2+}$ injections. Adapted from Iwatsuki and Petersen (1977).

pancreas and the discovery of the process of exocytosis by which macromolecules, such as the digestive enzymes produced by the pancreatic acinar cells, can be exported without endangering the integrity of the cell membrane (Figure 2). This is beautifully described in Palade's Nobel Prize lecture (Palade, 1975).

Palade was a cell biologist and did not primarily work on the mechanism by which secretion is controlled, but he understood that the pancreas should not secrete continuously, as this would be wasteful of energy. Secretion should only be switched on when the pancreatic enzymes were required to digest food taken in. Classical physiological work had shown that secretion from the exocrine pancreas is controlled by parasympathetic nerves via the neurotransmitter acetylcholine (ACh) or by the hormone cholecystokinin (CCK). In his Nobel Prize lecture, Palade referred to a paper I had published in the *Journal of Physiology* (*J Physiol*) in 1973 (reference no. 79 in Palade 1975) in which I had shown that both ACh and CCK elicit a depolarization (reduction of the electrical membrane potential) of the pancreatic acinar cell membrane (Figure 3) and provided some evidence indicating that this was associated with a rise in the calcium ion ($Ca^{2+}$) concentration inside the cell (Matthews & Petersen

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

1973). Thus, the concept of $Ca^{2+}$-mediated exocytosis of pancreatic digestive enzymes was born (Figures 2 and 3).

The electrophysiological work reported in my 1973 paper (Matthews and Petersen 1973), which was carried out during a sabbatical stay (1971–1972) in the Pharmacology Department at the University of Cambridge, was – by today's standard – primitive. These were still the days of what we now call organ physiology. We isolated a small piece of the pancreas from a mouse, placed it in a small acrylic-glass bath and poked a fine glass micro-electrode into the pancreatic tissue. We knew from the histology of the gland that the vast majority of the cells were the enzyme-producing acinar cells and therefore assumed that our electrical recordings were derived from these cells. In retrospect, this was a rather bold assumption but, amazingly, it turned out to be true. Nevertheless, it was a big step forward when, after my move to the University of Dundee in Scotland in 1975, I had the opportunity to acquire a phase-contrast microscope with a long working distance, enabling simultaneous micro-electrode recordings from two cells inside an acinar unit under direct visual control (Figure 3).

## The Japanese Connection

We seemed to have more time in the 1970s than now and during my sabbatical year at the University of Cambridge I mostly spent a whole afternoon per week in the excellent library of the Physiological Laboratory, browsing through all kinds of journals. One day, I found a short abstract in the *Japanese Journal of Physiology* of a presentation at a meeting in Japan by the author Akinori Nishiyama. The abstract caught my attention because it dealt with an electrophysiological study of salivary glands. I wrote a letter to Akinori asking a number of questions and after several months a detailed reply arrived. This started a valuable correspondence between us and, after my return to Copenhagen, I had the opportunity to invite Akinori to come to my laboratory for a one-year stay. Akinori, who later became Professor of Physiology at Tohoku University in Sendai, was a very professional electrophysiologist from whom I learnt a great deal. Being largely self-taught (I never had a supervisor, but started research work independently as an undergraduate medical student), I benefited enormously from working daily and closely with a very experienced scientist. Akinori and I published a number of substantial papers in *J Physiol*, which made the field of glandular electrophysiology respectable. Furthermore, this initiated a period lasting for almost 20 years in which my laboratory and its output were dominated by a series of outstandingly talented and effective Japanese research fellows. Akinori was not only a superb electrophysiologist, but also a very wise man. With regard to evaluating potential collaborators, the first and most critical point for him was the person's character. When recommending someone to join my laboratory, he did not start out by mentioning how clever or practical or diligent a particular candidate was, but always started describing his/her character. A good character was for him alpha and omega, and he was an

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

excellent judge. Every single person he sent to my laboratory was not only technically excellent and extremely diligent, but also 100% honest and reliable. I was lucky to have encountered Akinori early in my career and to have learnt this important lesson.

Noriyuki Iwatsuki, a young surgeon from Sendai, arrived in Dundee shortly after I had taken up the Symers Chair of Physiology at the University. He became my first PhD student (Figure 3(A)) and a close friend. Noriyuki was the most confident experimenter I have ever met. His manual skills, including the ability to manipulate micro-electrodes at a microscopic scale with great precision, were unique. As seen in Figure 3(B), this enabled us to record electrical signals simultaneously from neighbouring cells within a pancreatic acinar unit, inject substances into one cell and record the reaction from its neighbour.

At that time, live demonstrations at meetings of the UK's Physiological Society were regarded as crucially important. However, complicated experiments often did not work when many visitors were present, as the experimenter became nervous and also disturbed by not only having to carry out a delicate procedure but at the same time having to explain to others what was happening. However, Noriyuki's experiments always worked, impressing all those attending the first Physiological Society meeting I hosted in Dundee in 1978. Sadly, such live demonstrations are no longer part of the Society's meetings. This is a great loss for the physiological community in general and specifically for assessing the reproducibility of scientific results. One of Noriyuki's most important results was the demonstration that intracellular injection of $Ca^{2+}$ could mimic the action following application outside the cells of the neurotransmitter ACh (Figure 3(C)). This paved the way for the important concept of intracellular $Ca^{2+}$ signals acting as intracellular messengers in the process of signal transduction (Iwatsuki and Petersen 1977). A few years later, at the start of my many years at the University of Liverpool, Yoshio Maruyama did pioneering work by recording the first single-channel currents in epithelial cells (Maruyama and Petersen 1982) and later, in the 1990s, Makoto Wakui and thereafter Hideo Mogami solved important general problems in the rapidly developing $Ca^{2+}$ signalling field (see references in Petersen *et al.* 2021).

In 1979, I visited Japan for the first time on a comprehensive one-month lecture tour from Asahikawa and Sapporo on the northern island of Hokkaido to Fukuoka on the southern island of Kyushu, with most of the time spent on Honshu, giving lectures at Tohoku University in Sendai, Tokyo University and Kyoto University. I also lectured at a symposium held at the National Institute for Physiological Sciences in Okazaki, the first of many such visits to this excellent research institute. In 1979, few scientists in Japan, outside the great scientific centres in Tokyo and Kyoto, were able to understand a lecture given in English and in most places my lectures therefore had to be translated to Japanese. Happily, this situation changed dramatically for the better in the following years. In 1993, I gave a lecture at a conference held at the National Institute of Physiological Sciences in Okazaki, honouring the late Setsuro Ebashi on his 70th birthday (Hama *et al.* 1993). Setsuro had discovered the mechanism by which the heart relaxes after a heart beat by rapidly

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

re-accumulating into organelles $Ca^{2+}$ that had been released into the cytosol (Ebashi 1993). Later, I had the privilege of delivering the plenary lecture at the 2005 annual meeting of the Japanese Physiological Society in Sendai. In my period as Secretary General of the International Union of Physiological Sciences (IUPS), I co-chaired the International Scientific Programme Committee for the 2009 International Physiology Congress in Kyoto, one of the largest IUPS congresses ever held (Petersen 2009).

## The Patch Clamp Revolution 1976–1984

In the field of physiology, by far the most dramatic development in my lifetime was the patch clamp revolution. Our understanding of electrophysiology was transformed, and the equipment we used, as well as the way we did our experiments, radically changed. At the heart of this revolution were two outstanding scientists working at the Max Planck Institute for Biophysical Chemistry in Göttingen, Erwin Neher and Bert Sakmann.

In 1976, Erwin and Bert published a paper in *Nature* (Neher and Sakmann, 1976) with the title 'Single-channel currents recorded from membrane of denervated frog muscle fibres'. In this article they showed the first recordings of the tiny currents, a few pico-amperes (pA), that flow through single protein molecules (ion channels) spanning the cell membrane. Before the discovery of these single-channel currents, electrophysiologists simply inserted a sharp microelectrode into the cell they were investigating and recorded the electrical potential difference between the inside of the cell and a reference electrode outside the cell. Stimulation with neurotransmitters or hormones could then be observed to change the membrane potential (Figure 3). By clamping the membrane potential at a constant value, one could also record the currents flowing across the whole of the cell membrane in response to a stimulus. This classical approach had in many ways been very successful and, for example, resulted in a convincing account of the transmembrane currents associated with the nerve action potential, for which Alan Hodgkin and Andrew Huxley had received the 1963 Nobel Prize. However, the recording of the macroscopic currents flowing across the whole of the cell membrane was incapable of giving information about the underlying microscopic events. The problem that had to be overcome was that the background electrical noise was of the order of at least 100 pA, whereas the current flowing through single channels was expected to be only a small fraction of this. In other words, the single-channel currents were buried in electrical noise. The intrinsic electrical noise decreases with decreasing membrane area. Erwin and Bert therefore solved this problem by isolating a small patch of cell membrane. An external micropipette tip was pressed onto the outer cell surface, thereby allowing them to record from an area small enough to contain just one or a few channel molecules. In this way it became possible to directly observe the current flowing through a single channel when it opened.

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

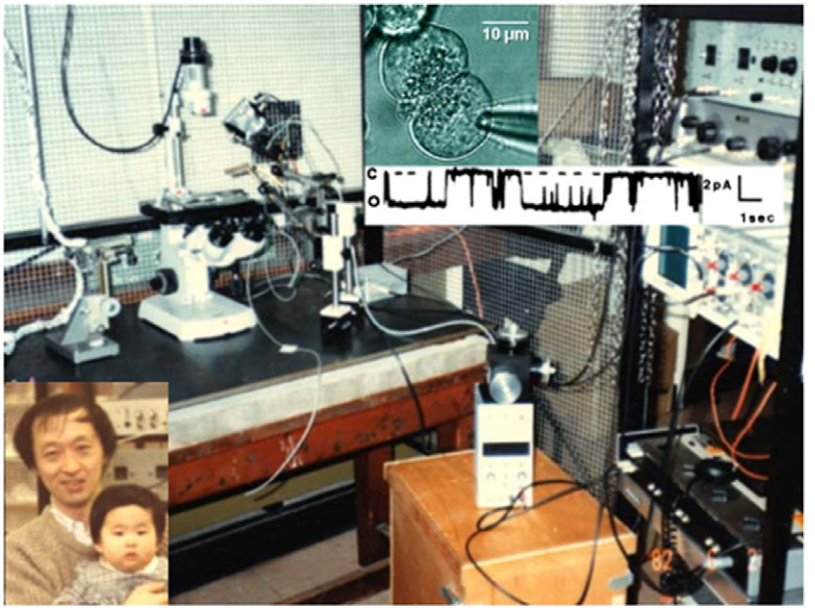


**Figure 4.** The first patch clamp set-up in the UK (Liverpool University, 1981). The upper inset shows a phase contrast image of a living pancreatic acinar doublet with a cell-attached patch pipette and, below, a single channel current trace. c denotes a closed state, and o an open state. Yoshio Maruyama and his baby daughter are shown, in a photo from that time, in the lower inset.

As seen in Figure 4, the channels work by frequently opening and closing. Importantly, it became clear that the channels always open to the same level, i.e. the current flowing through a particular channel type is always the same whenever it opens. Conceptually, the results of the 1976 *Nature* paper (Neher and Sakmann 1976) were extremely important, but the patch clamp method had not yet reached its final stage and was far from perfect. The electrical patch isolation was incomplete with an electrical seal resistance of only about 50 MΩ. The noise level was therefore still relatively high. The patch-clamp method, although much admired, did not at that point in time, 1976, lead other laboratories to change their methods.

The real breakthrough came in 1980, when Erwin Neher (Sigworth and Neher 1980) discovered the so-called giga-ohm seal, i.e. an electrical patch isolation with a very high seal resistance of many GΩ. The trick was to use a completely clean glass microelectrode (micropipette), which had not previously been in contact with any cell surface and, after making contact with the cell to be investigated, apply a bit of negative pressure to the pipette interior, thereby sucking a small patch of membrane into the pipette tip. The giga-seal paper was published in *Nature* on 2 October 1980. It was my great luck to visit Erwin's and Bert's laboratory in Göttingen shortly thereafter, early in December 1980. Erwin had invited me to give a seminar at the Max Planck Institute, which I of course accepted, as I was interested to see for myself this great new development in electrophysiology. I was not disappointed. Erwin and Bert

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

had not been wasting their time since the summer of that year when Erwin had discovered the giga-seal. It turned out that the seal between the glass micropipette and the cell membrane was mechanically very strong and that therefore it was possible, simply by withdrawing the patch pipette from the cell, to excise the bit of membrane covered by the pipette. Thus, an experimental situation was created in which currents flowing through a single or a few ion channels could be recorded under conditions with complete control of the electrical potential across the membrane and with known ionic compositions of the fluid on each side of the membrane. This was a dream come true for all electrophysiologists! Before my arrival in Göttingen, I had thought that the patch clamp technique was something that I might want to use in my own work at some point in the future, but as soon as I had seen with my own eyes what could be done with this amazing technique, I immediately understood that the time was now. Erwin and Bert were completely open about the technical aspects of their method and provided me with the blueprint of the electrical amplifier needed to record the tiny pA currents flowing through single channels, as well as showing me all details of their setups. They did this with all the many visitors who arrived in Göttingen at that time and later. Many scientists, having created a new and powerful method, would have wanted to keep some critical details for themselves in order to fully exploit the new way of doing things, before giving other colleagues the chance to compete. This was not Erwin's and Bert's style. In 1981, they also published a detailed description of the method. This paper (Hamill *et al*. 1981) is one of the most highly cited in all of the biological literature (cited $>$ 20,000 times). As a result, the new technique spread rapidly across the globe and remains to this day the state-of-the-art technique for all electrophysiologists.

Erwin and Bert are neuroscientists and they were naturally focused on investigating the properties of ion channels in nerve and muscle cells. It had been clear for many years that the electrical potential changes that occur during the firing of action potentials in neurons and muscle cells must be due to the opening and closing of various ion channels and therefore that these channels are the key molecules involved in, for example, the function of our brain. The cells I was interested in were epithelial cells, transporting ions, fluid and macromolecules – completely different functions from those of nerve and muscle cells. These epithelial cells do not conduct action potentials, i.e. they are – in contrast to nerve and muscle cells – not electrically excitable, and it was therefore by no means given that ion channels of the type found in the excitable tissues would also be expressed in epithelia.

Upon my return to Dundee I immediately wrote a grant application to the UK's Medical Research Council (MRC) to obtain funding for patch clamp investigations of the ion channels I hoped to identify in the exocrine pancreatic cells as well as in other exocrine glands. Happily, I did receive the grant from the MRC in the middle of 1981 and could therefore start buying the new equipment required for the work, but the key patch-clamp amplifier was not commercially available. Nobody in my laboratory had any experience in electronics, but a new research fellow, Yoshio Maruyama (who later became Professor of Physiology at Tohoku University in Sendai, succeeding Akinori Nishiyama), had just arrived in Dundee. Yoshio was

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

a recent medical graduate, who had been recommended to me by Akinori, as a person of extremely good character, but without any actual experience of doing experimental work. It fell to him to be first person to record single-channel currents from epithelial cells. There was, however, a delay in getting started. Early in 1981, even before I had received the critical grant from the MRC, I had accepted the position as George Holt Professor and Head of Physiology at the University of Liverpool and had agreed to take up this new job on 1 October 1981. In August/September 1981 my whole research group with five post-doctoral fellows moved to Liverpool and began setting up the new laboratories. Yoshio was very effective. He taught himself, by reading the necessary textbooks and asking for advice from colleagues in the neighbouring Electrical Engineering Department, what was necessary to build the patch clamp amplifier according to the general design that Erwin and Bert had given me. Having blown a few operational amplifiers and learned from these failures, he produced a simple prototype that actually worked and served us well for more than two years until a commercial product from a German company, recommended by the Göttingen scientists, became available. We recorded our first single-channel currents from an epithelial cell, a mouse pancreatic acinar cell, early in 1982 (Figure 4) and submitted our first patch-clamp paper to *Nature* in May 1982 (Maruyama and Petersen 1982). It was published in that journal on 9 September 1982. It demonstrated directly, and for the first time, that ion channels of the type identified in nerve and muscle cells existed in epithelial cells. Meanwhile, Bert and Erwin had arranged an advanced course (sponsored by the European Molecular Biology Organization) on single-channel recording in Erice, Sicily, which took place in May 1982. The proceedings were published in a book the following year (Sakmann & Neher 1983). It was a privilege for me to be able to speak at that meeting and contribute to the book.

In July 1982, Yoshio and I were able to submit a second paper to *Nature*, which was conceptually more important than the first one. We used a combination of recording single-channel currents from intact pancreatic acinar cells, and thereafter from the excised patch, to show $Ca^{2+}$-mediated activation of ion channels for the first time. The following year we published two further papers in *Nature*, demonstrating the surprising existence of voltage-activated ion channels in epithelial cells. We also combined single-channel and whole-cell current recording and thereby were able to count the number of ion channels in a single cell (see references in Petersen and Maruyama 1984). In 1983, I was invited to write a review article for *Nature* on calcium-activated potassium channels and their role in secretion, summarizing and commenting on our original patch clamp work. This review article, which also described a new hypothesis for the mechanism by which exocrine glands control fluid secretion, was published in *Nature* in February 1984 (Petersen and Maruyama 1984) and very quickly became highly cited. In ISI's (Institute of Scientific Information, now Web of Science) 29 November 1993 issue of *Current Contents*, our 1984 *Nature* article was signposted as 'This Week's Citation Classic'. It remains my most highly cited scientific paper to this day.

Following the publication of our five *Nature* papers on single-channel currents in epithelial cells (1982–1984), many scientists from all over the world came to visit my

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

laboratory to learn the new technique. One of them was Christine Bear from the Hospital for Sick Children in Toronto. Christine recorded $Ca^{2+}$-activated $K^+$ currents through single channels in liver cells and we published a paper about this in 1987. A few years later, after her return to Toronto, Christine caused a sensation by reporting the first results of recording single-channel currents through the Cystic Fibrosis (CF) Transmembrane Conductance Regulator (CFTR), proving that this protein, which is mutated in CF, is a Cl- channel (Bear *et al*. 1992). This paved the way for our current understanding of Cystic Fibrosis and, most importantly, led to effective therapies (Bear 2020). With regard to actual patient benefit from research using single-channel recording, this is probably the most important achievement so far.

Many years later, in 2006, I organized – as Chair of Academia Europaea's Physiology and Medicine Section, as it then was – a conference at the Klaus Tschira Foundation in Heidelberg celebrating the 25th anniversary of the publication of the detailed description of the patch clamp methods by Bert, Erwin and their collaborators (Hamill *et al*. 1981). This was a festive celebration of a most remarkable revolution in electrophysiology, which gave rise to an explosive development of the subject, and which had already been recognized at the highest level by the 1991 Nobel Prize for Physiology or Medicine to Erwin and Bert.

The new electrophysiological technique required a new kind of quantitative data analysis, which was very time-consuming to do manually and really demanded the use of computers. However, in the early 1980s my laboratory did not possess a computer and, in any case, nobody in my group was capable of using such an instrument. All quantitative analysis in our initial patch clamp papers was therefore done manually, although both Yoshio and I realized that this was not a sustainable way of doing things. Luckily, help was at hand. In 1983, I privately bought an early model of a microcomputer produced by Acorn and marketed by the British Broadcasting Corporation for my younger son Carl, who was 12 at that time (he is now Professor of Neuroscience at the Ecole Polytechnique Fédérale Lausanne in Switzerland and Director of its Brain Mind Institute). I asked him to create a program that would allow analysis of single-channel current traces and, impressively, he taught himself to do so. He also created a very neat teaching program that could analyse artificially generated single-channel current traces and personally demonstrated this and several other programs to a meeting of the UK's Physiological Society in Liverpool in April 1984. We used Carl's programs with the BBC computer for several years until, inevitably, more powerful computers and analysis programs became commercially available.

## The Ukrainian Connection

In 1988, Oleg Krishtal from the Bogomoletz Institute of Physiology in Kyiv, Ukraine, came to Liverpool to give a seminar. I did not know Oleg well, although we had been together at a Gordon Research Conference on ion channels in New

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

Hampshire in the early 1980s. I was not his host but, as Head of the Liverpool Physiology Department, I was invited to the dinner in his honour and was seated next to him. Oleg was amazed to learn that I had never been to what was still at that time the Soviet Union and told me that with all the excitement about Gorbachev's 'glasnost' and 'perestroika' now was the time to visit his country. Shortly after Oleg's visit, I received an invitation from the Bogomoletz Institute to give a lecture in Kyiv as well as invitations to give additional lectures at other Academy of Science Institutes in Moscow and Leningrad. It was agreed that my visit would occur in May 1989. There was at that time an agreement between the Soviet Academy of Sciences and the UK's Royal Society (RS) about the funding of academic visits between the two countries. In a case such as mine, all expenses in the Soviet Union would be covered by the Soviet Academy, but travel expenses between the UK and the Soviet Union would be covered by the RS.

Many months later, in April (1989), I received a letter from the RS informing me that my trip to the Soviet Union in May 1989 had to be cancelled, because there was no hotel accommodation available in Moscow. The arrangement between the RS and the Soviet Academy was such that an academic visitor from the UK should come to Moscow first and only thereafter visit other cities. Furthermore, I had not heard anything from Oleg for a long time, so I naturally cancelled my airline tickets and was just about to throw my visa to the Soviet Union in the bin but, for some reason, decided to put it into one of my desk drawers. I rearranged my calendar and did not think any further about the trip to the Soviet Union. However, a few days before I, according to the original travel plan, should have left for Moscow, I received a phone call from Oleg in Kyiv. He told me that they were eagerly looking forward to my arrival! I told him that my trip had been cancelled by the RS because of lack of hotel rooms in Moscow and since I also had not heard from him for a very long time, I thought that the whole plan had collapsed. Oleg then told me that there was no reason to go to Moscow first and that I should just go directly to Kyiv. He was so enthusiastic about the prospects of my visit, and all the plans they had for me, that my irritation about not having had any communication from him for a very long time evaporated and he finally persuaded me to reinstate the plans for the visit. Luckily, I still had the valid visa. I then flew to Kyiv on 18 May 1989, with the inaugural direct Sabena flight from Brussels to Kyiv. This trip, which had been so very close to not happening, changed both my private and professional life.

It is important here to understand that under the leadership of Academicians Platon Kostyuk and Oleg Krishtal, the Bogomoletz Institute had a worldwide reputation for excellence in the electrophysiology of the nervous system and was by far the most respected Physiological Institute in Eastern Europe and the Soviet Union. Nevertheless, even in that institute at that time, only a relatively small number of the leading scientists were fluent in English and could write English properly. Oleg had therefore hired Nina Burdakova, who had a Master's degree in English from the distinguished Linguistic University in Moscow, to be his private assistant and also translator and editor of scientific papers. Furthermore, it was also Nina's role to take care of foreign visitors to the Institute.

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

Oleg met me at the airport and took me to my hotel. Upon entering the hotel lobby, he quickly introduced me to Nina, who demanded my passport and then disappeared. I later understood that she had to arrange local visas for me to be allowed to visit Moscow and Leningrad. Oleg took me to dinner at a restaurant near the Dnieper river that night and I noticed that a bribe had to be paid to the doorman in order for us to get in. When seated at the table, Oleg saw that I was looking for a napkin and said "they disappeared in 1917". The next morning in Oleg's office, he introduced me to one of his collaborators, Yuri Osipchuk, who – he said – would come to my laboratory to work later that same month. There had actually been a very short letter, back in 1988, from Oleg mentioning that Yuri would like to come to my laboratory and I had replied that this would be possible, but that Yuri should contact me with his details and inform me about when he would like to come and for how long. I never received any reply to this request, so the news that a person I had never corresponded with was coming to my laboratory was rather surprising. Nevertheless, sitting in Oleg's office after having seen some excellent work in the Institute, I intuitively felt that Yuri would be a valuable collaborator and pretended that I was not in the least perturbed. I told Yuri and Oleg that everything would be arranged, including funding for his stay! Nothing had of course been arranged and I had a hectic time, upon my return to the UK, to get things sorted out but, miraculously, managed to do so. It turned out that my intuition had been spot on. Yuri was excellent.

Yuri did arrive in Liverpool about two weeks after my return, and stayed for seven months, during which he initiated a major methodological breakthrough in my laboratory by combining patch clamp whole-cell recording with fluorimetric $Ca^{2+}$ measurements (Osipchuk *et al*. 1990). Yuri was the first of a wave of brilliant investigators from the Bogomoletz Institute to my laboratory, including Alexei Tepikin, Alexei Verkhratsky, Oleg and Julia Gerasimenko (both still collaborating with me, having permanent faculty positions at Cardiff University), Pavel Belan and, most recently, Oleksiy Gryshchenko. Yuri's work marked the start of an entirely new approach in my laboratory with a primary focus on intracellular $Ca^{2+}$ signalling. In the following many years, the achievements of the Ukrainian diaspora, first in Liverpool and then in Cardiff, included the discovery of a releasable $Ca^{2+}$ pool in the nucleus of cells, as well as in secretory granules, published in *Cell* in 1995 and 1996, respectively, and later the first direct biophysical characterization of the $Ca^{2+}$ Release Activated $Ca^{2+}$ (CRAC) channels in the exocrine pancreas (Gerasimenko *et al*. 2013). I had the opportunity to discuss these discoveries, within a more general context, when I gave the American Physiological Society's Walter B Cannon Memorial Award lecture at Experimental Biology in San Diego in 2018 (Petersen *et al*. 2021).

In Kyiv in May 1989, it turned out that Oleg had planned for Nina to accompany me, first to Leningrad and then to Moscow. This was immensely helpful since I did not speak Russian and relatively few spoke English. During a week of travel, Nina and I naturally talked a lot and this paved the way for Nina's decisive move to Liverpool in 1994. By that time, I had become the UK Physiological Society's

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press


The Physiological Society Magazine

Winter 1994
No 17

WHY DOES THE SOCIETY SUPPORT A CENTRE OF EXCELLENCE IN UKRAINE?

*Nina Burdakova interviews Alexei Verkhratsky*

The first of several Physiological Society support schemes for centres of excellence in Eastern Europe and the Third World was established towards the end of 1993. The Bogomoletz Institute of Physiology of the Ukrainian Academy of Sciences was the first choice because of (a) its recognised scientific excellence, (b) the very serious economic problems in Ukraine and (c) the very favourable exchange rate between UK and Ukrainian currencies, allowing a relatively high impact of a small grant.

Committee News

***What is special about the Bogomoletz Institute of Physiology?***

"Fortunately, the Bogomoletz Institute of Physiology has a strong international reputation. The Institute was the leading organisation in neuroscience research in the whole of the USSR and therefore the majority of the international meetings in the USSR in the field of neuroscience or membrane physiology were held in our Institute. The scientists working in the Institute (Kostyuk, Krishtal, Shuba, Skok and many others) have the best international citation record among former Soviet physiologists."

*Nina Burdakova*

**Figure 5.** Excerpts from Nina Burdakova's report to members of the Physiological Society about the support scheme for centres of excellence in the former Soviet Union and Eastern Europe.

Foreign Secretary and engaged Nina to take charge of the Society's support programme for Centres of Excellence in Eastern Europe and the former Soviet Union (Figure 5). Nina administered this programme with great success for four years until my period as Foreign Secretary came to an end. In 1995, Nina and I married.

## Physiology Moves towards Pathophysiology

In an interview published in *Pancreatology* in relation to a keynote lecture I gave at Digestive Disease Week in Chicago in 2009, I said, 'Now we have to use the skills we have developed in cell physiological studies to attack the most crucial problems in pancreatic pathology' (Fernandez-Zapico 2009). The most important acute disease of the exocrine pancreas is acute pancreatitis, an often fatal inflammatory condition in which the pancreas digests itself and its surroundings. The disease is mainly caused by gallstone complications or excessive intake of alcohol and is a precursor of chronic pancreatitis, which again is a precursor of pancreatic cancer. In the following years, our research led to the discovery of a potential cure for the disease.

All agents inducing acute pancreatitis elicit large global and sustained intracellular $Ca^{2+}$ signals, in contrast to the physiological $Ca^{2+}$ signals evoking normal secretion, which are characterized by a pattern of repetitive small transient rises in the local $Ca^{2+}$ concentration, confined to the apical granular area of the acinar cells (Thorn *et al.* 1993). The excessive pathological inflow of $Ca^{2+}$ ions in acute

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

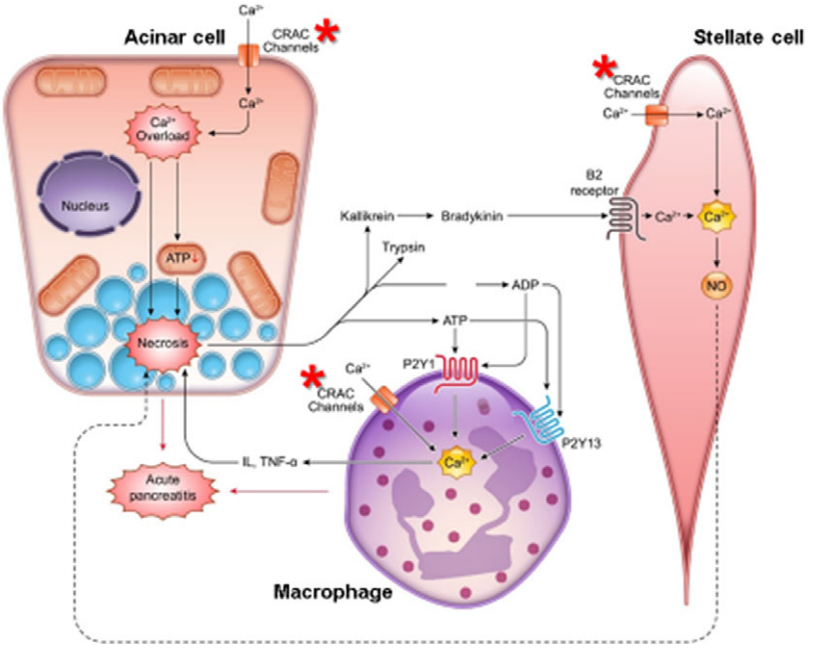


**Figure 6.** Current model for the initiation of the disease acute pancreatitis. Adapted from Petersen *et al.* (2021).

pancreatitis occurs through a special type of calcium channel in the cell membrane, namely the already mentioned CRAC channel. We established that pharmacological inhibition of the opening of this channel could markedly reduce $Ca^{2+}$ inflow and all its deleterious consequences (Gerasimenko *et al.* 2013). This work was reproduced by several other groups and in a further development we discovered that, contrary to general belief, not only the acinar cells participated in the disease process. Other adjacent cell types, which we were able to identify directly in the living tissue by advanced microscopy, also played important roles. It would now appear that the disease process is driven by excessive $Ca^{2+}$ inflow through CRAC channels (labelled with an asterisk in Figure 6) in three different neighbouring cell types. The $Ca^{2+}$ inflow in all these cells can be inhibited by one and the same pharmacological agent, named Auxora (Petersen *et al.* 2021). Clinical trials are now in progress in the US and we have high hopes that we may, in the not-too-distant future and for the first time, have a rational therapy for acute pancreatitis (Bruen *et al.* 2021).

The trend from physiology to pathophysiology is a general one. When I chaired the European Research Council's (ERC) Starting Grant Panel for Physiology, Pathophysiology and Endocrinology (2011–2013), I noticed that the vast majority of the proposals we were asked to evaluate were concerned with pathophysiology rather than basic physiology. This is typical of research in the large peripheral body systems, such as, for example, the cardio-vascular, respiratory, gastro-intestinal and endocrine systems. The situation is different in the neurosciences, where the state of

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

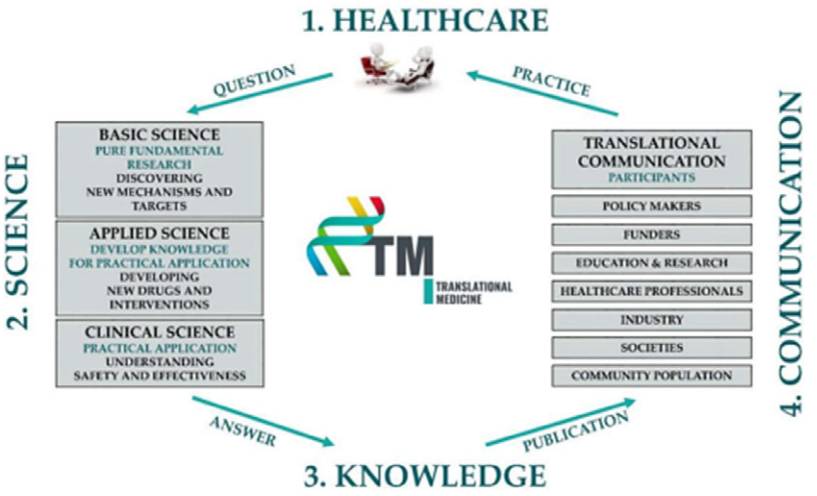


**Figure 7.** The translational medicine cycle (Hegyi *et al*. 2020).

our knowledge in the immensely complicated brain is less complete and where much basic research is still needed to acquire a sound basis for pathophysiological investigations.

Ultimately, the aim of biomedical research must be to provide real benefit for patients and, indeed, the whole population. It is increasingly recognized that it is insufficient just to create and publish new knowledge. New knowledge has to be applied (translated) into healthcare practice. In 2019, Peter Hegyi convened a meeting, supported by AE, at the Hungarian Academy of Sciences to discuss the issue of deriving more benefit from already existing scientific knowledge. Our discussions and conclusions were described in a paper published the following year in *Journal of Clinical Medicine* (Hegyi *et al*. 2020) that included the graphical representation of what we named the translational medicine cycle (Figure 7). In 2021, Peter and his Hungarian collaborators published a further article in *Nature Medicine* about accelerating the cycle (Hegyi *et al*. 2021). Later that year, it was a pleasure for me to speak at the excellent Semmelweis Symposium on Translational Medicine, organized by Peter in Budapest. Thanks to Peter's energetic leadership in this field, AE has been positioned centrally in what will continue for many years to be a critical issue for all nations.

### Politics Matter a Great Deal for Science

Although the Physiological Society's support scheme for centres of excellence in Eastern Europe and the former Soviet Union (Figure 5) kept a number of talented young physiologists in science at a time when they would otherwise have had to leave for jobs that provided proper salaries, we could not ultimately save what had been our primary concern, namely Ukrainian Physiology. Government investment in

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

science was simply insufficient to maintain a proper scientific infrastructure. Inevitably, a large number of excellent scientists, including many physiologists from the Bogomoletz Institute, emigrated to other countries (mainly the US, UK and Germany) that could provide them with decent salaries and the tools that would allow them to pursue their scientific work. I agreed to serve on various Ukrainian funding bodies and advisory committees and also met on several occasions with science ministers of the Ukrainian government, who all pledged more support for science, but were unable to deliver. Sadly, the inevitable consequence has been the sharp decline of the Bogomoletz Institute – not helped by very recent internal strife – which during the Soviet period had been a real international powerhouse and had made important contributions to our knowledge of the function of the nervous system. From this perspective, the demise of the Soviet Union, and particularly the chaotic manner in which it happened, was a disaster. Contrary to our intention of supporting Ukrainian scientists in Ukraine to be able to work in their own country, the poor nation, concentrating its resources on the defence against criminal Russian aggression, became a donor of highly educated scientists to the rich western world.

Bad politics have of course always impacted science and continue to do so. The most dramatic example, as already mentioned in a previous section, is probably what happened during the Nazi era in Germany. It is an extreme example of how a really bad, and indeed evil, government can deliberately destroy one of its strongest assets. German science was of course revived after the Second World War, when proper governance was established and, after many years of massive support, is now again in a good state. Since 1980, when I was first invited to become a member of the scientific advisory board at the Max Planck Institute for Biophysics in Frankfurt and subsequently had the pleasure of serving on other Max Planck Society and German Research Council (DFG) committees, I have been able to follow the remarkable progress of German science, based on a combination of stable funding and a rigorous assessment system. However, even so, German science has never recovered the top position it had in the first half of the twentieth century. Partly as a consequence of this, European science as a whole is also no longer in the world-leading position it enjoyed before the Second World War.

Sadly, I have been a witness to scientific efforts being undermined by incompetent and misguided governments in several countries. In 1989, a couple of months before my first trip to Ukraine and Russia, I visited the Venezuelan capital, Caracas, lecturing together with many leading US colleagues at an international advanced course on epithelial transport physiology held at Instituto Venezolano de Investigaciones Cientificas (IVIC). IVIC was at that time recognized as one of the strongest research institutions in South America, probably *the* strongest, and had superb facilities spread over a large and beautiful campus, with attractive residences for staff, visitors and students. Venezuela was relatively rich at that time, but there were clouds on the horizon. On 27 February, the second day of our advanced course, a popular revolt broke out in Caracas, and indeed many other cities in Venezuela, as a response to substantial price rises. The revolt was very violent, particularly in Caracas, lasted five days during which there was a complete curfew and many hundreds, possibly

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

thousands, of mostly very poor residents in the city lost their lives at the hands of brutal security forces and the military. The event is known as the Venezuelan *Caracazo* of 1989 (Lopez Maya 2003). Fortunately for me and my colleagues, the IVIC campus was outside the city area and we could move freely inside the campus but, because of the curfew, were unable to leave it. As the campus was sitting high up above the city, we could watch the many fires in the city and, in the evenings, we all watched the extensive TV coverage of the shooting, stoning of shops and widespread looting. It was impossible to call home and I vividly recall one frightened colleague from the US, who told the organizers of the course, 'I want to go home *now*!'. It was of course impossible, because of the curfew and the closure of the international airport. In the circumstances, the advanced course actually became particularly valuable because of the close contact outside the timetabled lectures and demonstrations, dictated by the reality that nobody could leave the campus. We all got together every night for social occasions kindly hosted by those members of IVIC staff who lived on campus. The riots were quelled before the end of the course, the airport re-opened and we were all able to leave Venezuela as originally planned. Although I never returned to Venezuela, I naturally kept in touch with colleagues there and have followed with great interest the very sad and indeed disastrous developments in the following years in that beautiful country, including, inevitably, the sharp decline in scientific activity due to a lack of resources and to emigration.

Rich, western countries are also capable of acting against their own best interests. Bad political developments have hit science in the UK in recent years. A populistic campaign for leaving the EU, largely propagated by lies, was successful. The Brexit referendum in the UK took place on 23 June 2016 and the result (51.89% in favour of leaving the EU and 48.11% in favour of remaining in the EU) became known on 24 June, just two days before the start of AE's Annual Conference, which took place in Cardiff that year. Both personally, and as host of the meeting, I was unhappy about the outcome, which inevitably became a major talking point during all coffee and tea breaks. To make matters even worse, the post-exit UK government decided to go for as 'hard' a Brexit as possible. The scientific communities in both the UK and in the EU countries were naturally alarmed and many of us did our best to engage in activities aimed at mitigating the many negative consequences of Brexit for European science. One of the principal aims was to persuade politicians, both in London and Brussels, that it was vitally important for European Science that the UK should continue to be associated with all major European funding programmes and co-operation schemes. One of our more visible activities was the public meeting held in London on 8 May 2017, organized by a cooperation between AE, EuroScience and the Royal Institution. It was a privilege for me to be a member of the panel of speakers on that occasion, which included Janet Thornton (ERC Council), Mark Ferguson (Chief Scientific Advisor Ireland) and Alex Halliday (Vice-President, RS). One of the key points made was the great benefit for all countries of free movement of researchers. This was clearly at risk following Brexit. At the meeting, I proposed that the UK Government, as a gesture of good will, but also in its own interest, should immediately guarantee that all scientists with EU

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

citizenship would continue to have unrestricted permission to work, and live with their families, in the UK after Brexit. This remark drew strong applause from the capacity audience, but was of course never implemented by the government. I also spoke at an event organized by the RS and the Wellcome Trust in January 2018, which was held at the Royal Society's International Centre at Chicheley Hall, just outside London, co-chaired by the then President of the RS, Venki Ramakrishnan and the Chair of the Wellcome Trust at that time, Baroness Manningham-Buller.

All efforts to persuade civil servants and politicians of the importance and benefit of continued post-Brexit scientific cooperation between the EU and the UK seemed finally to have borne some fruit, when the specific details of the so-called Trade and Co-Operation Agreement, which was signed by both parties on 30 December 2020, became known. One of the very positive aspects was that the UK would continue to be associated with the crucially important Horizon Europe programme. We were, however, disappointed that the UK would withdraw from participation in the very valuable Erasmus Programme. Nevertheless, with expectations quite low, there was a degree of relief in the scientific communities that our collective efforts had not been completely in vain. However, the relief was short-lasting. Continued disagreements between the UK and the EU concerning the so-called Northern-Ireland protocol constitute a threat to the UK's association with Horizon Europe and, at the time of writing this article, it is still not clear whether there will be a good outcome. In any case, it is abundantly clear that real and substantial damage has already been done to the pre-Brexit, well-functioning cooperation in science and education between the UK and continental Europe. Many EU scientists working in the UK have already left and recruitment of scientists from EU countries to the UK has become much more difficult and will, inevitably, hurt the quality of UK science over time. Given also the relatively low level of Research and Development spending in the UK, as compared to, for example, Germany, I am not convinced that the long-term prospects for UK science are as promising as we would all have hoped for.

Taking a global view, it becomes clear that scientific work is not being pursued with equal intensity in all countries. Scientific work at a meaningful scale is largely an activity confined to the US, the Pacific Rim of Asia and Western Europe. Large parts of the globe, including Africa, South America and major parts of Asia only play minor roles. Even within the EU there are enormous differences in government allocations for R&D, with the top countries (Luxembourg, Denmark and Germany) spending ~15 times more on this activity per capita than the bottom countries (Romania, Bulgaria, Hungary) (Eurostat 2022). As always, one should be careful not to take such figures as an indication of what happens in all scientific branches. There are always exceptions, as I have personally witnessed in relation to Hungarian science. Partly because of my personal links to Hungary, I have visited Hungarian institutions repeatedly over many years, have been a frequent speaker at scientific events in Budapest and Szeged and am also an Honorary Member of the Hungarian Academy of Sciences. In my own field of pancreatic research, for example, Hungary has a world-leading group directed by Peter Hegyi at Semmelweis University in Budapest.

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

The disparity in science funding between countries in Europe is holding back the whole of Europe as we are unable to fully utilize all the great talents in this part of the world. When I was the inaugural chair of the ERC's Starting Grant panel for physiology, pathophysiology and endocrinology, the panel observed that truly original ideas often came from what could be regarded as 'unusual' places in Eastern Europe. However, these proposals were often underdeveloped, partly due to inexperience, but also due to lack of even the most basic resources. Given the elitist approach of the ERC – and the unfortunate tendency of many leading scientific colleagues, who have been able to publish their own research in top journals, to disregard any contributions published in less visible outlets – applicants from 'unusual' places generally have little chance of succeeding in the tough competition for ERC grants. To their credit, the Young Academy of Europe is doing something about this problem and it was a pleasure for me to take part in a recent (2021) virtual ERC Starting Grant mentoring event specifically aimed at young researchers from Eastern Europe.

The EU is, unfortunately, by no means the world leader when it comes to R&D investment. The US, Japan, South Korea, Taiwan and Israel do considerably better, whereas some large countries, including India and Russia are much worse. China's total R&D spending is rapidly increasing, but still below that of the US, according to OECD figures for 2019. China may well by now have overtaken the US, although it would still be well below the US if expressed per capita. Because of its enormous size and ability to focus science investments strategically, China's share of papers in top journals has been rapidly increasing since 2015 and is now higher than that of the US in chemistry and close to that of the US in physics. In both cases, China's share of papers in top journals is much higher than traditional high performers such as Germany and the UK. The situation in the Life Sciences is significantly different. The US retains a very commanding lead and China has only just managed to squeeze past the UK and Germany (*Nature* Index 2022). With regard to publishing scientific papers in the life sciences, where descriptive skills in English are more critical than in the exact sciences, Chinese scientists still face significant challenges and those who have been successful are generally colleagues who have spent lengthy periods doing research in leading western laboratories, particularly in the US and the UK. Like many others, I have been speaking at conferences and visited laboratories in China over the last many years. In 2011, I was appointed Honorary Professor at Jinan University in Guangzhou and now have an active collaboration with a research group there, led by Shuang Peng, who did his PhD in my laboratory in Cardiff. When visiting Jinan University again in 2019, I could see enormous progress had been made. I had the pleasure of lecturing to undergraduate and postgraduate students in Guangzhou and was able to conduct extensive discussions with them in English without any difficulty. There is a new generation growing up, whose linguistic skills are much better than those of their teachers. The main threat to Chinese Science comes from an over-controlling government that is mistrustful of western influence. If the country continues to be largely closed down, as it has been, and still is, during the Covid pandemic, and in the future perhaps because of political

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

considerations, progress in the life sciences may well stall in spite of considerable new investments.

At the other end of the scale, there is the fate of small countries that previously belonged to larger federations. Armenia is such a case. In October 2018, I was lucky enough to have the opportunity to visit the very attractive Armenian capital, Yerevan, on the occasion of the celebrations to mark the 75th anniversary of the National Academy of Sciences of the Republic of Armenia. The event attracted presidents and vice-presidents of academies from many countries around the world, including the president of the Chinese Academy of Sciences at that time, Chunli Bai. We had the opportunity to interact directly with the Prime Minister, Nikol Pashinyan, during a 2-hour session. Pashinyan had become prime minister only a few months before the meeting, after a remarkably peaceful revolution in May 2018. It was an interesting time to visit Armenia, a beautiful country with a most remarkable cultural heritage, as there was great optimism after the revolution. It was clear that Pashinyan understood the importance of scientific investment and was eager to get good international advice. However, as so often in unstable regions of the world, he subsequently had to shift his attention to the increasingly worsening conflict with Azerbaijan over the Nagorna-Karabakh problem which, sadly, led to the disastrous 2020 war, ending badly for Armenia with significant losses of life and territory. I fear that just now science may not be a top priority in Armenia, which in spite of the relative wealth on display in Yerevan, is a very poor country.

## The Role of Academies

My first involvement in the work of an academy occurred in 1972, when I returned to Copenhagen after my sabbatical stay in Cambridge. The Alfred Benzon Foundation, which held a prestigious scientific symposium annually, had decided that the theme and title of its 1973 symposium should be 'Secretory Mechanisms of Exocrine Glands' and I was asked to join the three-member organizing committee. As the by far youngest member of the committee, it fell to me to do most of the work, but this gave me the opportunity to decide on the list of speakers to be invited. Given the very generous funding of the symposium, which allowed first class travel and a stay in one of Copenhagen's best hotels, it was easy to recruit top speakers from around the world. The symposium, held at the Royal Danish Academy of Sciences and Letters in September 1973, became an excellent networking opportunity. Many years later (1988) I was elected member of this academy, which in 1897 had awarded its Gold Medal to my grandfather, the chemist Julius Petersen. Although I was grateful for this recognition of my scientific work in my country of birth, I have inevitably not been able to participate very much in the local activities of the academy but, in 1994, I was privileged to receive the NOVO Nordisk Foundation's Jacobaeus Prize and presented the Award Lecture at the Academy's elegant building in central Copenhagen.

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

In 1988, I was also invited by the founder of AE, Arnold Burgen, to become one of the hundred foundation members of this unique Europe-wide academy and was able to participate in the foundation meeting, held in Cambridge. In contrast to my rather passive membership of the Royal Danish Academy, I have been, and continue to be, actively involved in working for AE. In the early years, I had no official position, but Arnold relied upon me to suggest colleagues for election to membership in the physiological sciences. In 1995, after a re-structuring of the Academy's sections and the creation of a section named Physiology & Medicine, I was asked to become its chair and compose the first section committee. We had an outstanding inaugural committee, including Harald Reuter from Bern, Theo Godfraind from Brussels, Klaus Thurau from Munich, Andras Spät from Budapest and Oleg Krishtal from Kyiv. AE's resources to fund meetings were at that time very limited, so Nina became the unpaid secretary of the committee. The enthusiasm for the work of the Section Committee was such that members decided to pay for all their own expenses when attending the annual meeting, which we held at the charming Hotel Spielweg, located in the beautiful Münstertal in Schwarzwald, Germany. After several years of productive meetings, resulting in a major expansion of the membership of the section, our self-funded efforts bore fruit and we managed to persuade the billionaire Klaus Tschira (winner of AE's Gold Medal in 2004) to fully fund an annual scientific symposium at the Tschira Foundation's wonderfully located state-of-the-art conference centre in Heidelberg. For many years, we met there annually, with all costs paid by the Tschira Foundation, and enjoyed superb science and great friendship.

After a competitive election process at AE's annual conference in Basel in 1998, I became a member of the Academy's Council, which at that time was the decisive body directing the organization. This was during the presidency of Stig Strömholm, who had previously been rector (president, vice-chancellor) of Uppsala University. Stig is a man with the greatest academic credentials, a superb and very witty orator and he was in every respect a remarkable president of AE. His predecessor, the distinguished former French Science Minister, Hubert Curien, had – in my opinion – not done too much for the academy and Stig took on the important task of actually leading the Academy forward with great energy. I became a member of several working groups, mostly meeting in Stockholm and chaired personally by Stig, which mapped the route ahead for the Academy both with regard to membership elections and activities.

For all academies, but particularly for a new academy that needs to grow to a reasonable size in order to be representative of the best of current scientific and scholarly activities, the process of electing new members is one of the most important tasks because the real strength of any academy is its membership. Given the limited resources of AE, it was impossible for the academy to use the elaborate membership election procedures employed by, for example, the RS with the involvement of large numbers of referees and several physical meetings of sectional committees. From the early days of AE's life, there was one Nominations Committee, which was chaired by Peter Swinnerton-Dyer, a brilliant Cambridge mathematician who

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

became well-known in the UK as the inventor and initiator of this country's now well-established and regular governmental Research Assessment Exercises (now called Research Excellence Frameworks).

Peter and his small committee received all the annual nominations from the whole of the AE membership and effectively decided on each case. Peter was an extremely shy individual and it was therefore very difficult to communicate directly with him. Following an annual election round, he would write very short letters to section chairs, in which he would concisely explain the reasons for having rejected some of the proposed candidates. In 2004, Peter decided to step down from his role as Chair of the Nominations Committee and I was asked to take over this rather onerous job. I then chaired this committee, which I quickly expanded to include all section chairs, for the next 10 years.

The direct involvement of the section chairs improved accountability and gave a stronger voice to the sections, but I nevertheless gradually came to the conclusion that our election system was unsatisfactory and required reform. Early in 2014, the AE Board asked me to chair a small working group charged with coming up with proposals for a better system. Within that same year, Donald Dingwell, Svend-Erik Larsen, Björn Wittrock, Gispert Wüstholz and I produced a report that also proposed a radical restructuring of the Academy into four broad classes, namely Humanities, Social and Related Sciences, Exact Sciences and Life Sciences, each with a class chair and a class committee comprised of all the section chairs within the class. The election of new members would effectively be devolved to the class committees. The four class chairs became ex-officio members of the AE Board. The proposal was accepted by the Board and the new structure implemented in 2014. It remains intact to this day. As a consequence of the new structure, I became the inaugural chair of the Life Sciences class and had to think about how to implement the new working arrangements.

During the presidency of Lars Walløe (2009–2014), AE embarked on a new path, establishing a series of knowledge hubs across Europe. The first opened in 2011 in Wroclaw, the second in Barcelona in 2013 and the third in Bergen, in early 2014. It occurred to me that it might be a good idea to establish a fourth hub at Cardiff University and I explored this possibility in talks with senior university colleagues. Fortunately, there was interest in this development and, after the election of Sierd Cloetingh to become the sixth President of AE in the autumn of 2014 – starting what has so far been the Academy's most successful period – I invited Sierd to come to Cardiff to reach an agreement with the president and vice-chancellor of Cardiff University (CU), Colin Riordan, about the establishment of a hub in Cardiff. Sierd, who at that time was also vice-president of the ERC, came to Cardiff in January 2015 and gave a superb lecture on European science policy to a capacity audience. We had a constructive meeting with Colin and it was decided to go ahead with the plan for a CU–AE Knowledge Hub, fully funded by CU. I was at that time nearing the end of my 5-year term as head of CU's School of Biosciences. As both I and my excellent personal assistant, Judith Lockett, were keen to continue working together, it was decided that she would be the initial administrator of the hub, which

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

started functioning in the autumn of 2015. My original thought was that the hub, like the already well-functioning hubs in Wroclaw and Barcelona, would have a regional role, arranging various scientific events and also take care of the Life Sciences class, specifically organizing the annual process of electing new members in the biomedical fields and this did indeed happen.

However, in September 2015, a surprising development occurred. At an AE-supported scientific symposium in Kyiv, Sierd asked me whether I would be prepared, as vice-president of AE, to take on the role of leading AE's work for a new consortium providing scientific advice for policy to the European Commission. The Juncker Commission that came into office in the autumn of 2014 had decided to change the scientific advice mechanism from reliance on one chief scientific advisor to a more broad-based and transparent system. It is to Sierd's eternal credit that he managed to secure a place for AE in this new mechanism that was to transform AE's influence and reputation. The architect of the new system was the Commission's then Director-General for Research, Robert-Jan Smits (AE Gold Medal 2018) (Figure 8).

The new Scientific Advice Mechanism (SAM) would consist of two branches: a small group of directly appointed advisors (originally known as the High-Level-Group, now called the Group of Chief Scientific Advisors) and a consortium of pan-European academic networks (which became known as SAPEA – Science Advice for Policy by European Academies). A SAM unit was established at the Commission in Brussels, coordinating the overall mechanism. I saw this as a great opportunity for AE and indeed also for the new Cardiff hub, but also realized that it was a considerable challenge. I participated in early planning and discussion meetings at the RS in London in November 2015 and at EMBO in Heidelberg in January 2016 as well as at the crucial meeting at the Royal Netherlands Academy of Arts and Sciences in Amsterdam in February 2016, where Sierd's presence was decisive. SAPEA, consisting of five networks (AE, All European Academies [ALLEA], European Academies Science Advisory Council [EASAC], Euro-Case [federation of European engineering academies] and FEAM [federation of European medical academies]) then came into operation in the autumn of 2016, funded by a grant from the European Commission. I represented AE at the first meeting of SAPEA leaders with Carlos Moedas, then Commissioner for Research & Innovation, at Berlaymont in Brussels, on 30 January 2017. After the great disappointment we had all experienced with regard to the UK's decision to pull out of the EU, it was heartening to hear Carlos Moedas state that he just wanted the best possible scientific advice and did not care about whether it came from inside or outside the EU. I also vividly remember Paul Nurse telling me on that occasion that now it was more important than ever for UK scientists to be visible in Brussels.

The additional resources that came to the CU–AE hub from the Commission enabled me to expand the hub staff and, most importantly, to engage a hub manager with considerable European experience. Louise Edwards turned out to be an excellent choice and very quickly became a major driving force in our SAPEA work. The first important task for SAPEA was the project on 'Food from the Oceans'. At an early meeting of the SAPEA Board, I indicated that AE would be prepared to take

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

**Figure 8.** Some of the key participants in the celebration, held at the Royal Society in London in 2018, of AE's 30th Anniversary. Front row from left: Lars Walløe, Arnold Burgen, Eva Kondorosi, Robert-Jan Smits (with the Gold Medal), Richard Catlow, Jürgen Mittelstrass and Sierd Cloetingh; Second row: Nicole Grobert, Johannes Klumpers and Ole Petersen. Back row: David Coates and Ortwin Renn.

on this task as the lead academy. It became the first major task for the Cardiff hub in SAPEA. We were asked to provide a substantial evidence review report in relation to the initial question from the Commission: 'Is it possible to increase the amount of food from the ocean? If so, by how much, by when and what does it depend on? If not, why not?' This was eventually changed to 'How can more food and biomass be obtained from the oceans in a way that does not deprive future generations of their benefits?' We quickly established two international expert working groups, one dealing with the biological aspects, chaired by Dag Aksnes from Bergen, and another, dealing with social science aspects, chaired by Poul Holm from Dublin. The substantial report (160 pages) was finished on time at the end of 2017. As with all subsequent SAPEA reports it was published and is freely available (SAPEA 2017). Throughout the process of assembling the evidence, discussing the findings at many working group meetings and finalizing the written report, we kept in touch with what was still at that time called the High-Level-Group, represented by one of its members, Carina Keskitalo. This was useful because it was her job to write the scientific opinion, based on SAPEA's evidence review report. The aim was to publish the two reports simultaneously and it would then be up to the Commission to decide on potential actions. All this proceeded surprisingly smoothly, to a large extent due to the excellent overall administration of the project by Louise Edwards and the hard

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

work by the two working groups. It set both the standard and the pattern for all subsequent SAPEA projects.

The principal conclusion of the SAPEA report was that 'the only way to obtain significantly more food and biomass sustainably from the ocean is to harvest seafood that on average is from a lower trophic level than we currently harvest'. If this was going to be successful, it would require substantial changes to our habits of seafood consumption, and outreach to the general population was therefore essential. We arranged a number of public events in various places involving discussions of the report as well as demonstrations and tasting events. In this context, I spoke (in German), together with the then chair of the High-Level-Group, Rolf-Dieter Heuer, at a public event in Hamburg in October 2017, organized by the Union of German Academies of Sciences and the Hamburg Academy of Sciences. Many other events followed.

Up to now, the Cardiff Hub has led the production of three SAPEA evidence review reports in the first SAPEA funding period (until the end of April 2022) and it will no doubt continue to be involved in further reports over the next funding period starting May 2022. During the Covid pandemic, we have of course not been able to organize physical outreach events, but have managed a substantial number of webinars with good international attendance. One of the most important, in relation to our latest evidence review on 'Biodegradability of plastics in the open environment', was held in the summer of 2021 in cooperation with the European Parliament. It was a pleasure for me to chair this event, at which we had talks from three MEPs, many high-level officials and scientific experts in the field.

Although SAPEA undoubtedly has taken most of the Cardiff hub's time and energy, we have also arranged many other events. The Academy's 2016 annual conference took place at Cardiff University and, in 2018, we organized a celebration of the Academy's 30th Anniversary in collaboration with the RS, which was held at the Society's Kohn Centre in London (Figure 8), hosted by the President of the RS, Venki Ramakrishnan.

Europe is fortunate in having a substantial number of well-established national academies. Many of these have a long and distinguished history as well as being housed in grand and often very elegant buildings. The two most influential such academies also have the longest continuous history, namely the RS and the Leopoldina. The RS was established in 1660 and created the first scientific journal published in English, rather than Latin, namely the *Philosophical Transactions of the RS*, which is still actively published today. The RS's tremendous reputation is based on the awesome achievements of many of its famous fellows going all the way back to Isaac Newton, one of its early presidents.

My first encounter with the RS happened in 1970 when, as a young and newly appointed lecturer at the University of Copenhagen, I was invited to speak at a discussion meeting (the name used by the RS for scientific symposia) in London on 'Active Transport of Salts and Water in Living Tissues' (Petersen 1971). The invitation increased my reputation in Copenhagen considerably and was also useful in establishing early contacts with leading British and international scientists in the

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

field. The excellent symposium happened very soon after Alan Hodgkin had become President of the RS. I have pleasant memories of the elegant dinner for the international speakers at the symposium, held at the president's apartment at the top of the RS building, where I had the surprising honour of being seated next to Lady Hodgkin.

To be elected a Fellow of the RS (FRS) is the dream of every scientist in the UK, as vividly described in C.P. Snow's famous novel *The Masters*. The competition to be elected (only a fixed number can be elected each year) is intense and many are inevitably frustrated. In 2000, I was elected and in keeping with the (very good) system operated by the RS, I was already the next year asked to join the sectional committee dealing with elections in the fields of anatomy, physiology and neuroscience. In 2002 I became chair of this committee. One of the strengths of the RS's election system is the rapid rotation of the membership of its committees, so that every member only serves for a continuous period of three years (but can come back again later after a suitable interval). Chairs only serve for a period of two years. This ensures that no single person or small group controls election to the RS for any length of time, allowing each candidate, who can be assessed annually for up to seven years, to be evaluated by different groups of fellows. Furthermore, there is extensive use of referees (at least five for each candidate and frequently many more) as well as detailed discussion of each candidate at two rounds of annual meetings of the sectional committees. It is probably the fairest and most rigorous evaluation system for academy elections in the world and is at the heart of the RS's continuing reputation for excellence. My experience as chair of an RS sectional committee informed my approach to elections to AE, although the more limited resources of the AE did not allow the same detailed scrutiny.

Elections to the RS Council are competitive, but I allowed my name to go forward after my period as sectional committee chair had come to an end, and in 2004 I was elected to serve on the Council. In my last period (2005–2006), Lord Martin Rees, then President, asked me to become vice-president in order to deal specifically with the Society's input to the UK government's review of health research funding. Gordon Brown, who was at that time chancellor of the exchequer (finance minister – later, prime minister) had asked the venture capitalist David Cooksey to make recommendations with regard to how health research funding could be improved by ring-fencing the government's healthcare R&D commitment into a single fund. It became a period of intensive meetings with many stakeholders and particularly with the Medical Research Council's (MRC's) then chief executive, Colin Blakemore, a distinguished neurophysiologist I had known for many years. There was a great fear at the time that Cooksey might recommend that the MRC should be replaced by a new Health Research Council and that thereby basic biomedical research could be undermined. In the event, our efforts to save the MRC were successful and Cooksey's final recommendation was a typical British compromise whereby there would be an overarching body, the Office for Strategic Coordination of Health Research, that would provide a degree of coordination of the MRC and the National Institute

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

of Health Research (NIHR) and specifically deal with the distribution of the research budgets between the two organizations.

After this relative success, I was given many other tasks by Martin, chairing various RS working groups and, on several occasions, standing in for him when he was too busy with other matters. I learnt a lot from Martin, whom I consider the most effective RS President I have known. He was extremely fast and precise, immediately grasping the essence of any issue, and at the same time seemingly unhurried.

One of my most important tasks, which actually happened in May 2007 after I had finished my official term as vice-president of the RS, was to give evidence on behalf of the RS to the UK Parliament's House of Commons Select Committee on Education and Skills. The hearing in Parliament's Portcullis House in London was directly transmitted to the general public by radio and the exact wording of what was said during the interchange between me and the parliamentarians was published (UK Parliament's House of Commons Education and Skills Committee 2007). I was particularly keen to emphasize the need for an increase in governmental research funding, making the point that it should, in my opinion, be doubled in order to make us fully competitive internationally. This did not happen, of course, although some additional funding was made available. I did, however, receive a reward for my work. In the autumn of 2007, I received a letter signed by Gordon Brown, who in the summer of 2007 had become prime minister of the UK, asking whether I would be prepared to accept the honour of being appointed Commander of the Order of the British Empire. I accepted of course and my name was duly published, together with those of many others to be honoured, in the Queen's New Year Honours List on 1 January 2008. I received the medal from Queen Elizabeth II personally, at a grand ceremony held at Buckingham Palace in May 2008. Having witnessed the sad decline of the quality of British governments since then, I am happy that I received this award upon the recommendation of Gordon Brown who, in my opinion, was the last UK Prime Minister with integrity and a high international standing.

Although I had been active in serving on research advisory boards in Germany over many years, my election to membership of the German National Academy of Sciences Leopoldina occurred relatively late, in 2010, but was nevertheless very welcome. The Leopoldina is the oldest European academy in continuous existence, having been established in 1652. It has, however, had a more difficult history than the RS, due to the tumultuous fate of Germany, and only became the national German academy of sciences in 2008. Due to its history, it has – in contrast to virtually all other national academies – its headquarters in a provincial city, Halle, rather than in the capital, Berlin. In 2012, it moved into its current premises, a magnificent palace and I had the honour, on the eve of the festivities in connection with the opening of the beautifully restored palace (a gift from the German federal government), to deliver the Leopoldina lecture (in German) in the academy's grand hall on the topic of alcohol-related acute pancreatitis. This was regarded as an appropriate theme, as the Leopoldina has a traditional medical orientation and has a much larger clinical membership than, for example, the RS. This also explains why Germany, in contrast to the UK and the US, does not have a separate medical academy. The election

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

process is perhaps less onerous than is the case for the RS, but the Leopoldina has a younger membership and a much better geographical distribution of its membership within the nation than is the case for the RS, with its heavy concentration of the fellowship in the so-called golden triangle (Cambridge, London and Oxford). During the Covid pandemic the Leopoldina has consistently provided detailed and evidence-based concrete advice that has been visible and influential. I also approve of the Leopoldina's international orientation. All materials, and its website, are available both in English and German. Overall, I think that the Leopoldina, in spite of its long history, reflects a modern well-governed nation that in many respects should be a model for many other European countries.

## Scientific Publishing

Early in my career, I was invited to join the editorial board of the oldest extant physiological journal *Pflügers Archiv der Gesammelten Physiologie* (later *Pflügers Archiv – European Journal of Physiology*). It became an extraordinarily long association that lasted from 1977 to 2020, and from 1998 I was one of the executive editors. *Pflügers Archiv* was, and is, a commercial journal published by Springer, now part of the very large Springer/Nature group of journals. *Pflügers Archiv* was and is a solid journal rooted in the great achievements of German physiology in the late nineteenth and early twentieth century but, in our time, it has lost out in the competition with the more successful *J Physiol* as well as the many now very trendy organ-specific journals dealing with, for example, the cardio-vascular system, the neurosciences and the gastro-intestinal tract. Much later in my career, I became involved in the work of *J Physiol*, as consulting and then executive editor (2013–2019).

Both *J Physiol* and *Pflügers Archiv* operate excellent peer-review systems, as good as or perhaps even better than many of the new and very successful organ-specific journals, which have higher impact. However, my experiences with both these basic physiology journals indicate that although rigorous peer-review can help to get rid of poor-quality submissions, it does not in itself attract authors to submit their best papers. The advent of 'metrics', particularly the attention paid to the number of times an article is cited in other papers has, in many ways, distorted the whole publication process as well as the assessment of individual academic merit.

During my time as vice-president of the RS, I chaired a RS working group that was charged with responding to the UK government Department for Education and Science's consultation on 'The Reform of Higher Education Research Assessment and Funding'. We warned against using citation data as a quality measure, particularly for individuals, as they are merely an indication of the interests in particular branches of science, which again depend heavily on the number of people active in a particular field. If, for example, you work in a research field with few research groups worldwide, you cannot expect large citation numbers for your published articles. Recently, during the Covid pandemic, we have seen that even minor contributions in that field attract enormous numbers of citations as compared with even

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

heavy-weight articles in other areas, further calling into question the use of citation numbers in evaluation processes. Our work at the RS was undoubtedly helpful in ensuring that the official UK Research Assessment Exercises, and now the Research Excellence Frameworks, make only very limited use of citation data and puts the main emphasis on traditional methods of peer-review assessment, depending on critical reading and evaluation of published articles. This is of course time-consuming and therefore costly, but there is no other reliable way.

There has been much talk about a 'Reproducibility Crisis'. Although the extent of this problem may have been somewhat exaggerated (Fanelli 2018), it is indisputable that many published findings resulting from biomedical research have turned out to be irreproducible. There are many aspects of this problem, but one element has been the frequent issue of finding out, from published articles, exactly what was done and how. Reproducible science requires transparent reporting and it would seem advisable to have a set of clear guidelines that could be adopted by all serious journals. Such guidelines would necessarily differ between different types of research, but might be particularly important for animal research, which mostly is an essential precursor for drug development. In 2018, I agreed to become a member of an international committee, chaired by Stephen Holgate from the University of Southampton, to formulate guidelines for the type of information that was required to fully document results obtained from animal experiments. The aim was to ensure that researchers, reviewers, and journal editors would become better equipped to improve the rigour and transparency of the scientific process and thus reproducibility. We published the new guidelines in the journal *PLoS* (Public Library of Science) *Biology* (Percie du Sert *et al*. 2020). This article has already been cited more than 1000 times in the scientific literature and is likely to have a positive influence on the quality of reporting data obtained from research involving work on animals.

Because of the enormous and continuing increase in the number of published papers, which makes it difficult for even the most diligent researchers to keep up with the literature in their field, review articles have become more and more important. In the physiological sciences, the most respected review journal has always been, and continues to be, the American Physiological Society's *Physiological Reviews* (*Physiol Rev*), which in 2021 celebrated its 100th anniversary. I was therefore delighted when, in 1999, I was asked to join its European editorial committee. In 2003, after competitive interviews, I was appointed chair of the committee with independent executive responsibility for dealing with all papers coming from Europe, Africa and India. We naturally cooperated with the US editorial board and my editorial assistant (Nina) and I attended the annual US board meeting, which was reciprocated by the chair of the US board, who was formally the editor-in-chief of the journal. This was probably my most enjoyable experience as scientific editor (2003–2011) as we had an outstanding European committee composed of the best physiologists in Europe and were dealing with invited submissions from highly selected top colleagues in the physiological sciences. Even so, the peer review process was helpful in improving the invited contributions.

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

Scientists, like all human beings, have a very strong sense of their own contributions and are prone to overlooking those made by others and particularly by their competitors. For authoritative review articles in a journal such as *Physiol Rev*, I felt it was very important to ensure that no important contributions to a particular topic were excluded and I often had to remind authors that it was ultimately in their own best long-term interest to be seen to be fair and inclusive.

The issue of attributing credit fairly remains a critical point in science. Human nature being what it is, there are unfortunately many examples of original discoveries that have been 'forgotten' (not cited) by those who should have known and perhaps in many cases have known. In my most recent and current editorial job, as editor-in-chief of the American Physiological Society's new open access journal *Function*, I wrote an editorial entitled 'When a discovery is a rediscovery: do we know the history of our own subject?' (Petersen 2021). It has been downloaded more than any other editorial in the journal, elicited an avalanche of messages from all over the world giving examples of such cases and resulted in several submissions to *Function* of opinion pieces presenting additional examples. Clearly my editorial hit a 'raw nerve' and exposed a serious problem in contemporary science.

It is also a serious problem, particularly for biology, that we are 'drowning' in masses of data that do not generate new ideas and are often published without proper context. Therefore, they do not contribute to real useful knowledge (Nurse 2021). As editor of *Function*, I see it as my job to select a relatively small number of outstanding papers, rooted in physiology or pathophysiology, and provide context by publishing a perspective (commentary) article in relation to every single original research article (Petersen 2020). *Function* is still very new, but it is my hope that this approach will be helpful by providing a focus for new ideas that will take the field forward.

Another important issue I have been concerned with relates to the financial aspects of scientific publishing and how it affects access to the published scientific and scholarly record. When I started publishing scientific papers in the 1960s, there were no publication fees. University libraries subscribed to the important journals and we all physically went to the reading rooms in our respective libraries to study the essential papers we needed to know about, and made notes of the key points in these articles. We would photocopy a few crucially important articles, but this was both expensive and time-consuming. There were of course no search engines and we basically relied on a small number of journals in our respective specialties. For those of us working in reasonably well-funded institutions with good libraries, the situation was satisfactory, but many colleagues in poorer countries would not have access to even the most important international journals in their field and had to rely on friends in more affluent institutions sending them copies of relevant papers. Inevitably, they would often not be fully informed about even important developments.

The subscription model for scientific journals continues to be important, but few scientists physically go to their libraries these days. Electronic access to literature has essentially replaced this activity and well-resourced institutions maintain subscriptions to a large number of journals, allowing individual scientists to download

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

relevant articles from their office or home whenever needed. A number of open-access journals have been created in recent years and, as already mentioned, I edit one of these, *Function*. Open-access journals allow anyone anywhere, and without payment, to download any of their articles immediately after publication. However, in order to publish in these journals, a publication fee has to be paid. Increasingly, traditional journals also allow authors to make their papers open access, but then require a fee to be paid. Many funding bodies now demand that articles reporting work they have supported must be made freely accessible and allow authors to pay publication fees from their grants. It is clear that we are gradually moving away from the classical model, in which university libraries pay journal subscriptions, to a situation in which authors pay for the publication of their articles via their research grants. Although many articles are still today behind paywalls, we may soon reach a state in which everyone can have free access to the whole of scientific literature. However, this has created a new problem. Whereas scientists working in, for example, a third world country can read most of the papers relevant for their work, they may not be able to afford paying the publication fees needed in order for them to report the results of their own work. We discussed many of these problems and possible solutions at a well-attended meeting organized by Juliet Davies from the AE Cardiff hub, but held at KU Leuven in 2019, chaired by the former editor of *European Review*, Theo d'Haen. There is still today no entirely satisfactory solution to this problem, which is not only causing difficulties for colleagues working in poor countries, but also for many people in the western world, who are not supported by large grants. If, for example, you are funded to conduct expensive experimental or clinical research, publication fees will only constitute a very minor part of your grant expenditure, whereas if you do theoretical work, not requiring much funding, the situation is completely different. Part of the problem is the excessive profit made by many commercial publishers. Surprisingly, many colleagues continue to primarily support commercial for-profit journals, by submitting their best papers to them, rather than support non-profit journals published by their own scientific societies. The power to change the situation lies in the hands of individual researchers and the large funding bodies.

## Conclusion

During a long working life, I have been a witness to remarkable changes in the way science in my own field, physiology, is conducted. Much more powerful techniques have been developed, enabling great progress in our understanding of how the body works. Increasingly, we are also beginning to acquire an in-depth insight into the mechanisms underlying important disease processes and are now thinking systematically about translating these insights into real benefits for patients and society. Given the crucial role science plays in our daily lives, the role of scientific advice for policy has also become more central and new ways of doing this, particularly within the European Union, have evolved. Nevertheless, the traditional roles of

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

academies, including the relatively young Academia Europaea, and scientific journals remain critical to high-quality science and scholarship. Sadly, many poor countries have become even poorer in this period, whereas rich countries have become even richer. Scientific activity has therefore become increasingly concentrated in a relatively small part of the world. This is a serious problem in search of a solution.

## Acknowledgements

Work in my laboratory has been supported by grants from the UK's Medical Research Council. I thank Nina Burdakova for critical reading of this article.

## References

**Bear CE** (2020) A therapy for most with Cystic Fibrosis. *Cell* **180**(2), 211. https://doi.org/10.1016/j.cell.2019.12.032

**Bear CE, Li CH, Kartner N, Bridges RJ, Jensen TJ, Ramjeesingh M and Riordan JR** (1992) Purification and functional reconstitution of the cystic fibrosis transmembrane conductance regulator (CFTR). *Cell* **68**(4), 809–818. https://doi.org/10.1016/0092-8674(92)90155-6

**Bruen C, Miller J, Wilburn J, Mackey C, Bollen TL, Stauderman K and Hebbar S** (2021) Auxora for the treatment of patients with acute pancreatitis and accompanying systemic inflammatory response syndrome: Clinical development of a Calcium Release-Activated Calcium channel Inhibitor. *Pancreas* **50**(4), 537–543. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8104014/

**Ebashi S** (1993) From the relaxing factor to troponin. *Biomedical Research* **14**(suppl. 2), 1–7.

**Eurostat** (2022) https://ec.europa.eu/eurostat/statistics-explained/index.php?title=R%26D_expenditure&oldid=551070#Gross_domestic_expenditure_on_R.26D (accessed 24 January 2022).

**Fanelli D** (2018) Opinion: Is science really facing a reproducibility crisis, and do we need it to? *Proceedings of the National Academy of Science USA* **115**(11), 2628–2631. https://doi.org/10.1073/pnas.1708272114

**Fernandez-Zapico ME** (2009) 'Now we have to use the skills we have developed in cell physiological studies to attack the most crucial problems in pancreatic pathology': an interview with Ole H. Petersen, Medical Research Council Professor of Physiology, University of Liverpool, UK. *Pancreatology* **9**(4), 323–326. https://doi.org/10.1159/000213711

**Gerasimenko JV, Gryshchenko O, Ferdek PE, Stapleton E, Hébert TO, Bychkova S, Peng S, Begg M, Gerasimenko OV and Petersen OH** (2013) Ca2+ release-activated Ca2+ channel blockade as a potential tool in antipancreatitis therapy. *Proceedings of the National Academy of Science USA* **110**(32), 13186–13191. https://doi.org/10.1073/pnas.1300910110

**Hama K, Kanno T, Obata K and Yamagishi S** (eds) (1993) Calcium regulated cellular activities. Proceedings of the eighteenth SEIRIKEN conference dedicated to Professor Setsuro Ebashi on the occasion of his 70th anniversary. Tokyo: Biomedical Research Foundation.

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

**Hamill OP, Marty A, Neher E, Sakmann B and Sigworth FJ** (1981) Improved patch-clamp techniques for high-resolution current recording from cells and cell-free membrane patches. *Pflügers Archiv* **391**(2), 85–100. https://doi.org/10.1007/BF00656997.

**Hegyi P, Petersen OH, Holgate S, Erőss B, Garami A, Szakács Z, Dobszai D, Balaskó M, Kemény L, Peng S, Monteiro J, Varró A, Lamont T, Laurence J, Gray Z, Pickles A, FitzGerald GA, Griffiths CEM, Jassem J, Rusakov DA, Verkhratsky A and Szentesi A** (2020) Academia Europaea position paper on translational medicine: The cycle model for translating scientific results into community benefits. *Journal of Clinical Medicine* **9**(5), 1532. https://doi.org/10.3390/jcm9051532

**Hegyi P, Erőss B, Izbéki F and Szentesi A** (2021) Accelerating the translational medicine cycle: the Academia Europaea pilot. *Nature Medicine* **27**, 1317–1319. https://doi.org/10.1038/s41591-021-01458-8

**Iwatsuki N and Petersen OH** (1977) Acetylcholine-like effects of intracellular calcium application in pancreatic acinar cells. *Nature* **268**(5616), 147–149. https://doi.org/10.1038/268147a0

**Lopez Maya M** (2003) The Venezuelan 'Caracazo' of 1989: popular protest and institutional weakness. *Journal of Latin American Studies* **35**(1), 117–137. https://www.jstor.org/stable/3875580

**Maruyama Y and Petersen OH** (1982) Single-channel currents in isolated patches of plasma membrane from basal surface of pancreatic acini. *Nature* **299**(5879), 159–161. https://doi.org/10.1038/299159a0

**Matthews EK and Petersen OH** (1973) Pancreatic acinar cells: ionic dependence of the membrane potential and acetycholine-induced depolarization. *Journal of Physiology* **231**(2), 283–295. https://doi.org/10.1113/jphysiol.1973.sp010233

**Nature Index** (2022) Share of papers in top journals: https://www.natureindex.com/annual-tables/2020/country/all/all (accessed 24 January 2022).

**Neher E and Sakmann B** (1976) Single-channel currents recorded from membrane of denervated frog muscle fibres. *Nature* **260**(5554), 799–802. https://doi.org/10.1038/260799a0

**Nurse P** (2021) Biology must generate ideas as well as data. *Nature* **597**(7876), 305. https://www.nature.com/articles/d41586-021-02480-z

**Osipchuk YV, Wakui M, Yule DI, Gallacher DV and Petersen OH** (1990) Cytoplasmic Ca2+ oscillations evoked by receptor stimulation, G-protein activation, internal application of inositol trisphosphate or Ca2+: simultaneous microfluorimetry and Ca2+ dependent Cl- current recording in single pancreatic acinar cells. *EMBO Journal* **9**(3), 697–704. https://doi.org/10.1002/j.1460-2075.1990.tb08162.x

**Palade G** (1975) Intracellular aspects of the process of protein synthesis. *Science* **189**(4200), 347–358. https://www.science.org/doi/10.1126/science.1096303

**Percie du Sert N, Hurst V, Ahluwalia A, Alam S, Avey MT, Baker M, Browne WJ, Clark A, Cuthill IC, Dirnagl U, Emerson M, Garner P, Holgate ST, Howells DW, Karp NA, Lazic SE, Lidster K, MacCallum CJ, Macleod M, Pearl EJ, Petersen OH, Rawle F, Reynolds P, Rooney K, Sena ES, Silberberg SD, Steckler T and Würbel H** (2020) The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. *PLoS Biology* **18**(7), e3000410. https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.3000410

**Petersen OH** (1971) Initiation of salt and water transport in mammalian salivary glands by acetylcholine. *Philosophical Transactions of the Royal Society B* **262**(842), 307–314. https://doi.org/10.1098/rstb.1971.0096

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

**Petersen OH** (2009) The International Union of Physiological Sciences. IUPS editorial VIII. *Physiology* **24**, 320–321. https://doi.org/10.1152/physiol.00035.2009

**Petersen OH** (2020) *FUNCTION* is now functional, *Function* 1(1), zqaa001. https://doi.org/10.1093/function/zqaa001

**Petersen OH** (2021) When a discovery is a rediscovery: do we know the history of our own subject? *Function* 2(4), zqab030, https://doi.org/10.1093/function/zqab030

**Petersen OH, Gerasimenko JV, Gerasimenko OV, Gryshchenko O and Peng S** (2021) The roles of calcium and ATP in the physiology and pathology of the exocrine pancreas. *Physiological Reviews* **101**(4), 1691–1744. https://doi.org/10.1152/physrev.00003.2021

**Petersen OH and Maruyama Y** (1984) Calcium-activated potassium channels and their role in secretion. *Nature* **307**(5953), 693–696. https://doi.org/10.1038/307693a0

**Sakmann B, Neher E** (eds) (1983) *Single-Channel Recording*. New York: Plenum Press.

**SAPEA** (2017) Evidence Review Report No. 1. https://www.sapea.info/wp-content/uploads/FFOFINALREPORT.pdf (accessed 24 January 2022).

**Sigworth FJ and Neher E** (1980) Single Na+ channel currents observed in cultured rat muscle cells. *Nature* **287**(5781), 447–449. https://doi.org/10.1038/287447a0

**Thorn P, Lawrie AM, Smith PM, Gallacher DV and Petersen OH** (1993) Local and global cytosolic Ca2+ oscillations in exocrine cells evoked by agonists and inositol trisphosphate. *Cell* **74**(4), 661–668. https://doi.org/10.1016/0092-8674(93)90513-P

**UK Parliament's House of Commons Education and Skills Committee** (2007) Eighth Report of Session 2006-07, 16 May 2007, vol. II, HC 285-II, Ev 227–245: https://publications.parliament.uk/pa/cm200607/cmselect/cmeduski/285/285ii.pdf (accessed 24 January 2022).

## About the Author

**Ole H Petersen**, CBE MAE ML FRS, is currently Professor of Physiology in the School of Biosciences at Cardiff University, Wales, UK, Vice-President of Academia Europaea and Director of the Academy's Knowledge Hub at Cardiff University. He graduated in Medicine from the University of Copenhagen and obtained his Dr Med (MD) degree from the same University. He has previously held professorial positions at the Universities of Dundee in Scotland and Liverpool in England. He is currently a member of the Board of SAPEA (Science Advice for Policy by European Academies) as the Alternate for the President of Academia Europaea. He is Editor-in-Chief of the American Physiological Society's new Open Access journal *Function* and was previously Chair of the European Editorial Committee of *Physiological Reviews*. He is a former Vice-President of the Royal Society, President of the Physiological Society (UK) and Secretary General of the International Union of Physiological Sciences. He has chaired the European Research Council's Starting Grant Panel for Physiology, Pathophysiology and Endocrinology and been Chair of the Biological Sciences

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press

Panel for the UK Government's Research Excellence Framework 2014. He has received many prizes for his scientific and organizational work, including the American Physiological Society's Cannon Award, the NOVO Nordisk Foundation's Jacobaeus Prize, the Czech Academy of Sciences Purkyne Medal and the award of Commander of the Order of the British Empire from Queen Elizabeth II. Most recently, 2021, he received Academia Europaea's Gold Medal.

https://doi.org/10.1017/S1062798722000084 Published online by Cambridge University Press