BENEDICT DELISLE BURNS
22 February 1915 — 6 September 2001
Ben Burns was a pioneer of operations research and of the statistical analysis of neuronal activity. During the war, Ben served in Solly Zuckermann’s operations research unit, which included a period of active service in the Mediterranean. After the war he worked with G. L. Brown at the National Institute for Medical Research (NIMR), where he investigated the effects of agents that affected neuromuscular transmission. In 1950 he moved to the Physiology Department of McGill University in Montreal, where he explored the properties of neural networks in neurologically isolated slabs of cerebral cortex and established the mechanisms responsible for maintaining rhythmic periods of excitation in isolated nerve networks. He subsequently provided evidence that self-re-exciting neural networks were implicated in establishing the respiratory rhythm. While at McGill, Ben initiated a number of highly original cross-disciplinary studies concerning the physiological bases of learning, memory and attention. He returned to NIMR in 1966 to head the Division of Physiology and Pharmacology, where he continued his investigations of visual perception. Ben was an ingenious experimenter and devised a number of mechanical and electronic devices for the statistical analysis of nerve cell activity at a time when digital computers were largely unavailable for biological work. In his 1968 book, *The uncertain nervous system*, he expressed his view that the interdisciplinary nature of central neurophysiology required of those who studied it a knowledge of classical physiology, experimental psychology, applied mathematics and electronic engineering. His broad view of the subject inspired a generation of students.
FAMILY AND EARLY LIFE

Benedict (always Ben) Delisle Burns came from a family of landowners on the Caribbean island of Saint Christopher, the larger of the two islands making up the Federation of Saint Christopher and Nevis. His grandfather, James Patrick Burns, was treasurer of the St Christopher-Nevis-Anguilla islands, which were then British colonies. James married Agnes Delisle, by whom he had five sons and one daughter. Ben’s father, Cecil Delisle Burns (1879–1942), was the eldest of James’s sons who survived to adulthood. Ben’s three uncles were remarkable men: one, Emile, was a committed communist, long-time secretary of the British Communist Party and journalist on the *Daily Worker*; the other two had distinguished careers in the Foreign Office, one of whom (Sir Alan Burns 1887–1980) served as governor of several colonies and was knighted for his service as Colonial Secretary of the Bahamas.

Ben’s father, Cecil, was educated at Christ’s College Cambridge and went to Rome to train as a Catholic priest, but around 1911 he lost his faith in traditional Catholic teachings and left the Catholic Church, becoming an atheist, social historian and secularist writer. In 1914 he married the artist Margaret Alice Arnold Hannay (1888–1974), by whom he had two sons: Ben, and his younger brother Dominic, who became an architect. In the course of his career, Cecil wrote over 20 books including *International politics*, *The world of states* and *The horizon of experience*.

Around 1920 the family moved to Keats Grove in Hampstead, where Ben was allowed a large amount of freedom. In a private memorandum for his family, Ben recalled being allowed to carry out chemical experiments in the basement of the family home, which was near to that of the Huxley family. Ben became close friends with the Huxley’s youngest son, Andrew (later Sir Andrew Huxley, 1917–2012 OM, FRS 1955, PRS 1980–1985).

EDUCATION

From 1922 to 1931 Ben attended University College School in Hampstead and when he was 15 or 16 years of age the school entered him for a scholarship to Cambridge University, but he was unsuccessful. His father was not surprised as he considered that Ben was too young; against the advice of the Foreign Office, he arranged for Ben to spend a year in Germany with the family of a professor of biochemistry at Tübingen University. This was 1931–1932, a very turbulent time in Germany with the rise of the National Socialist Party. While in Tübingen, Ben became fluent in German and registered to take lectures in physics and chemistry.

On his return to England in 1932, Ben was admitted to King’s College Cambridge, where he read for his degree in natural sciences. During this period, Ben was reunited with Andrew Huxley, who was reading natural sciences at Trinity College. In an unpublished memorandum, Huxley (2008) recalled that it was Ben who advised him to take physiology as his third subject. Huxley went on to become one of the most celebrated physiologists of his generation, sharing the Nobel Prize with Alan Hodgkin and John Eccles in 1963.

While undergraduates, Ben and Andrew investigated two psychophysical phenomena: the visual illusion known as the waterfall effect, and the means by which it is possible to determine whether a sound originates directly from the front or back of the head. These ambitious experiments required the construction of specific pieces of equipment, which was carried out in the attic of the Huxley’s house. While neither project was completed, they illustrate Ben’s
interests at the time and the enthusiasm which both he and Huxley demonstrated throughout their careers for designing and building the equipment necessary for resolving the problem at hand. They also give an early indication of Ben’s lifelong interest in the workings of the brain. Ben obtained his degree in natural sciences in 1936 and then read biology and anatomy for a further year to enable him to qualify for the clinical part of medical training. Before starting his clinical studies, he gave lectures for the Workers’ Education Association, and continued to do so during his first year at University College Hospital Medical School in London (1937–1939). He qualified in medicine just after the outbreak of the Second World War in 1939.

**WAR SERVICE**

In his personal recollections, Ben recalled fire watching on the roof of the Medical School with Peter Krohn (1916–2009, FRS 1963), who asked whether he would be interested in working on practical war-related issues with Solly Zuckerman (later Baron Zuckerman of Burnham Thorpe OM, 1904–1993, FRS 1943). Ben’s qualifications in medicine, physiology, chemistry, physics and mathematics were obvious advantages for this kind of work. No doubt influenced by his experiences of 1930s Germany, Ben duly joined Solly Zuckerman’s staff, which was engaged in what has since become known as operational research. During his time on Zuckerman’s staff, Ben wrote 10 secret reports, including an investigation of tissue damage inflicted by high-velocity objects that, untypically for usually classified work of this kind, he was able to publish (1). He was also involved in a survey of the casualties arising from the Dieppe raid of August 1942, and with analysing the effects of bombing on the town and harbour of Tripoli.

While working in Zuckerman’s team, Ben volunteered to fly to North Africa, aware that the previous flight had been shot down on its way to Algeria. On his arrival, he was instructed to join the operations of the US Air Force, based in the city of Constantine in the north east of Algeria. It was from here that the invasion of the Mediterranean island of Pantelleria (Operation Corkscrew) was planned as a precursor to the Allied invasion of Sicily in 1943.

Ben wrote of his experience of Operation Corkscrew:

Solly had arranged for me to go with the landing forces aimed at taking a small island called Pantelaria [sic] roughly half way between the coast of North Africa and Malta. I was put in a tank landing craft, which I presume carried either tanks or lorries, but my memory is of being in one of some fifty, or so, naval vessels which approached our destination through a veritable hail of bombs, released by dive bombers. All that I can remember is that none of them hit us, but the noise suggested that there were several near misses . . . I got ashore and was about to look for the AA unit I had been attached to when another wave of German Bombers attacked the harbour district. I can remember lying under a table in the ground floor, of a house with no roof, along with two kids about ten years old. When we reckoned that it was relatively safe to emerge, I found that the officer who was supposed to accompany me had not been so lucky . . . he had received a bullet through his head.

Ben’s task consisted of plotting the size and distribution of bomb craters around the town and harbour. Zuckerman hoped that the data would provide evidence for his view that a large number of small bombs was more effective than the same weight of large bombs. Ben strongly disagreed with Zuckerman’s interpretation of his data from Operation Corkscrew, pointing out in his memoir that no small bombs had been dropped. (It seems that Ben did not entertain the
possibility that Zuckerman had additional data.) Ben noted that, ‘The argument became so heated that Solly threatened to have me sent to the Far East unless I changed my attitude.’ It is ironic that later in his memorandum Ben wrote of his experience visiting the casualties in the base hospital:

I . . . managed to get some very interesting data. In particular it showed that, weight for weight, the 50 pound anti-personnel bomb is far superior to larger weights. I also became very interested in the psychological effects of modern warfare. In this case there was no relation between the size of bomb and its effect.

After further adventures flying around in North Africa, Ben returned to England.

The only trouble I had was on holding on to my notes during my journey home. The officer in charge of transport had never heard of the great Professor Zuckerman and said he would forward them for me. After a lot of saluting senior officers I ultimately persuaded them that I was a harmless boffin and they finally let me get on a transport plane with my notes . . . I am surprised that I got to Oxford without being arrested . . . My only clothes were dirty shorts and exceedingly worn desert boots, with a crumpled shirt bearing a couple of shoulder stripes. Something about my tired appearance must have convinced them that I was harmless.

NIMR 1945–1950

Ben’s scientific career began shortly after the end of the war. He was invited to join G. L. Brown (later Sir George Lindor Brown KB, 1903–1971, FRS 1946) at the National Institute for Medical Research as a member of the Division of Physiology and Pharmacology. Years later, Ben remarked to one of us (CDR) how grateful he was to Brown for offering him the opportunity of starting his career in basic scientific research and that it was a wonderful change from ‘counting how many shells were required to knock out a German Tank’.

In addition to his work at NIMR with Brown, Ben collaborated with a number of colleagues who either had made, or went on to make, major contributions to physiology and pharmacology, including W. D. M. Paton (later Sir William Paton CBE, 1917–1993, FRS 1956), Edith Bülbring (1903–1990, FRS 1958) and Wilhelm Feldberg CBE (1900–1993, FRS 1947). By 1949 Ben had begun to turn his attention to neurophysiological problems, beginning with his initial description of the isolated cerebral cortex—a preparation that occupied his attention for the next eight or nine years. One of his colleagues at NIMR was F. C. ‘Hank’ Macintosh (1909–1992, FRS 1954), who left the Institute in 1949 to head the Department of Physiology of McGill University in Montreal, intent on revitalizing its research. He persuaded Ben to join him, and in 1950 Ben emigrated to Canada with his young family (figures 1 and 2).

MONTREAL 1950–1966

The voyage to Montreal was not without incident as Ben’s son, Julian, developed measles. At the insistence of the ship’s doctor, who appears to have erroneously diagnosed scarlet fever, the family were relegated from their first class accommodation to a cabin at the stern of the ship from where Julian was to be delivered to an isolation hospital in Montreal. Ben recalled that, on arrival, ‘Hank Macintosh rescued us by meeting the ship at Montreal and playing the part of the big Professor of Medicine’.
The family rented a farmhouse outside the city. This they found too large for their needs, so Ben and his wife Angela invited a McGill colleague, Vernon Brooks, and his wife Nancy to share the house. Vernon later went on to make important contributions to the understanding of motor control and recalled that he and Ben drove to work together, often talking science—Vernon considered these sessions to be great tutorials (Brooks 2001). Ben’s marriage to Angela ended in 1953, and she and their four boys returned to the UK. Ben subsequently married Monica Kasputis in 1954. Their daughter, Ramune, was born in 1956.

McGill in the 1950s was a major centre for what has since become known as neuroscience—a term that did not become current until the founding of the Society for Neuroscience about 20 years later. Working in physiology was Ben, Arnold Burgen (later Sir Arnold Burgen, b. 1922, FRS 1964) and, later, Geoffrey Melvill Jones (FRS 1979), who, together with their younger colleagues, provided a lively forum for discussion. Hank
Macintosh invited a string of notable physiologists to visit the department including Edith Bülbring, Ragnar Granit (1900–1991, ForMemRS 1990), Alan Hodgkin (OM KBE, 1914–1998, FRS 1948, PRS 1970–1975) and Steven Kuffler (1913–1980; ForMemRS 1971). From 1957, biochemistry was led by the highly respected neurochemist K. A. C. Elliott (1903–1986). Donald Hebb was head of psychology and it was in Hebb’s department that James Olds and Peter Milner first described the basic reward systems of the subcortical structures of the brain. In a celebrated study, the neuropsychologist Brenda Milner (b.1918, FRS 1979) analysed the damaging effects on memory in patient HM, who had undergone bilateral hippocampal ablation to control severe epilepsy. The professor of neurology and neurosurgery at the Montreal Neurological Institute was Wilder Penfield (OM, 1891–1976, FRS 1943), who had described the topographical organization of the motor and sensory cortex of the human brain. Penfield worked closely with Herbert Jasper, who was professor of experimental neurology at the Institute and had made important contributions to the interpretation of the electroencephalogram.

Once he was firmly established at McGill, Ben collaborated with colleagues in physiology (10) as well as those in other departments, including Jerzy Olszewski, several members of the psychology department and with J. G. Robson (later Sir James Gordon Robson CBE, 1921–2007), who was then Wellcome Research Professor of Anaesthetics. They had two matters of interest to investigate. The first was to examine the effect of nitrous oxide on the process of learning in human subjects, which was undertaken to see what it might reveal about the nature of learning mechanisms at the cellular level (24). The second matter was of a more practical nature as it concerned the effectiveness of low concentrations of anaesthetics in producing amnesia and analgesia for the period of a surgical operation, when muscle relaxation was produced by muscle relaxants (paralysing agents) such as curare (25). Ben also collaborated with J. David DeJong of the Queen Mary Veterans Hospital Montreal on the assessment and treatment of Parkinson’s disease (26, 28, 35). At the time, the
symptoms of Parkinson’s were relieved by electrothermal destruction of the globus pallidus (pallidectomy), with limited success. Ben and his colleagues showed that the anticholinergic drug trihexyphenidyl (Artane) was effective in relieving the symptoms of Parkinson’s disease in some patients (32). However, the introduction of L-DOPA after 1960 subsequently provided a much more effective treatment.

Shortly before he had left for Canada, Ben had begun to explore the properties of isolated regions of the cat cerebral cortex as a route to understanding the physiological processes involved in memory. In particular he wanted to understand how cortical networks store and retrieve information and how connections between neurons can be permanently changed to alter pathways of transmission. Work on this problem continued in McGill and occupied Ben for much of the rest of his career. His first book, *The mammalian cerebral cortex* (17), was a distillation of his ideas at the time. Ben understood that the probabilistic nature of neuronal activity necessitated the use of computation to analyse trains of action potentials. This was at a time when digital computers were in their infancy and fearsomely expensive. The power of using a general purpose computer for such analysis was first shown by Gerstein and Kiang (1960) at MIT, but Ben had fewer resources and met this challenge by collaborating with colleagues to devise an interval analyser (23), an auto- and cross-correlator (31) and, later, a neurophysiological computer capable of compiling post-stimulus histograms of single unit responses in real time (34). At the time the only alternative was recording the raw data on film and painstakingly extracting the data by hand (29).

In 1954 a young physician, Gian Salmoiraghi, paid a short visit to McGill and joined Ben and his student, George Frank, who were examining the effects of focal application of veratrine on frog muscle (13). Inspired by this visit, Salmoiraghi returned to McGill to join the staff two years later, when Ben proposed that they investigate the central control of respiration. He considered it likely that the activity of individual respiratory neurons would reflect the intrinsic rhythmicity of breathing, as discussed below. By 1965 Ben and his colleagues had developed instruments that could analyse trains of action potentials by examining patterns of intervals between successive action potentials (‘interval analysis’) or by cross-correlation (23, 29, 31, 34) between a train of stimuli and the averaged response (‘post-stimulus time histograms’).

In 1963 Ben spent four months as a visiting scientist at the National Physical Laboratory (NPL), which was at that time a major centre of computer research. This was followed by a year’s sabbatical leave at the Autonomics Division at the NPL. Here, he collaborated with the pioneering computer scientist, mathematician and experimental psychologist Albert Uttley on the conductivity of pathways in the cerebral cortex.

Ben was a stimulating teacher and attracted a steady stream of graduate students during his time at McGill, among whom was Bernice Grafstein, who later served as the first female president of the Society for Neuroscience (Grafstein 2001), George Mandl, who went on to become chairman of the department at McGill, and one of us (TVPB). During his last year at McGill, Ben served as chairman of the physiology department before returning to England as head of the Division of Physiology and Pharmacology at NIMR.

**NIMR 1966–1976**

When he took over as head of division from Wilhelm Feldberg, Ben inherited a staff with varied physiological interests: Gordon Bisset (later professor of pharmacology at St Thomas’s
Biographical Memoirs

Figure 3. Ben with his mother Margaret in later life.

Medical School), who was interested in the neuroendocrine reflexes of the posterior pituitary gland; Otto Hutter (later regius professor of physiology in Glasgow), whose interests at that time lay in the biophysics of muscle membrane; David Sproull, who worked on the role of bioamines as neurotransmitters in the brain; and Richard Hellon, who was interested in the neural pathways that sense pain and temperature. However, within a short time Ben was able to recruit several young staff, including the authors of this biography. TVPB, who had been a PhD student of Ben’s in Montreal, joined the Division in 1967 as a junior member of staff. In 1968 Ben appointed a psychologist, Alison Webb, who became both his long-term collaborator and his partner. CDR joined the Division in April 1969 from Henry Mcllwain’s Department of Biochemistry at the Institute of Psychiatry in South London. During his time as head of division, Ben continued his collaborations with two of his former colleagues from Canada: George Mandl and Roy Pritchard.

Ben’s interest in the apparent random nature of action potential generation in the brain had led him to wonder how it extracted meaningful information from such apparently chaotic data. His conclusions were summarized in his second book, *The uncertain nervous system* (38), where he devoted an entire chapter to the problems of analysing the stochastic behaviour of the action potentials of cortical neurons, explaining the principles of autocorrelation, cross-correlation, interval analysis and post-stimulus time histograms. This clear exposition helped to popularize the use of these techniques as a means of summarizing neural activity.

Ben’s mother, Margaret, died in 1974, shortly before Ben retired from the Institute in 1976 (figure 3). He and Alison Webb moved to the University of Bristol as external members of Medical Research Council (MRC) staff. Ben was succeeded as head of division by Mike Keating (1940–1998), who renamed it as the Division of Neurophysiology and Neuropharmacology to reflect more precisely the focus on the nervous system that Ben had established.
BENEDICT DELISLE BURNS

BRISTOL AND NEWCASTLE

When Ben and Alison moved to Bristol, he was made honorary professor of anatomy. Here they continued to work on the effects of sleep and arousal on nerve cell activity in the cerebral cortex (43, 44). In 1980 Alison was recruited by Simon Miller to the anatomy department at Newcastle University so she and Ben moved to Newcastle, where they subsequently began a long collaboration with Philip Bradley on the response characteristics of neurons in thin slices of chick forebrain. They focused their attention on a region known as the intermediate medial hyperstriatum ventrale (IMHV), which plays an important role in a type of learning in birds known as imprinting. The in vitro slice preparation they developed allowed them to study this region under controlled conditions. Philip Bradley recalled that Ben constructed the slice chambers they used for their experiments. Moreover, Ben taught himself PASCAL and wrote several programs that they used for data analysis.

SCIENTIFIC WORK

After the war, G.L. Brown took over as head of the Division of Physiology and Pharmacology at NIMT and Ben was recruited as his assistant. At first, Ben collaborated with Brown, Edith Bülbring and Wilhelm Feldberg on the physiology and pharmacology of mammalian skeletal muscle (2, 3). In their final collaboration, he and Brown investigated the importance of neuromuscular block in reducing the tetanic tension in a fatigued muscle (4), and found that this did not account for the decline in tension, which therefore implied that the decline in tension represented fatigue of the tension-generating apparatus.

Although Ben had been recruited as Brown’s assistant, he was encouraged to develop his own interests. Ben recalled an occasion when Brown found him in the library and promptly sent him back to the laboratory, observing that ‘It is not your job to read the literature but to write it’. His first collaboration without Brown was with Bill Paton on the action of decamethonium on the motor end plate (8). They showed that decamethonium blocked neuromuscular transmission by causing a prolonged depolarization of the motor end plate, which thereby results in muscle paralysis. They coined the term ‘depolarisation block’ to describe its action and decamethonium was subsequently used for many years as an adjunct to general anaesthetics to induce muscle relaxation during surgery.

The neurologically isolated cerebral cortex

The most prominent features of the mammalian brain are the cerebral hemispheres and the overlying cerebral cortex—which is especially well-developed in man and the higher apes. This invites speculation on the role of the cerebral cortex in the activity of the central nervous system. Since the nineteenth century it had been known that stimulation of particular areas of the cerebral cortex of dogs gave rise to specific movements, and by the early 1940s the work of Penfield (Penfield & Boldrey 1937), Adrian (1941) and Woolsey et al. (1943) had revealed the topographical arrangement of the primary sensory and motor regions of mammals. However, it was not known how the cerebral cortex processed the information it received nor how this information was integrated. To quote Ben himself, ‘it is wise to admit that less is known about the functions of the normal cerebral cortex than any other organ in the body’ (17).
Confronted by the anatomical complexity of connections made by cortical neurons both within the cortex itself and with the rest of the nervous system, Ben developed a simplified ‘cortical slab’ preparation. In the late 1940s, he began to explore the functional properties of isolated slabs of the cerebral cortex in the hope that this would simplify the analysis of cortical neurons to electrical stimulation. To achieve this, he isolated a section of the suprasylvian gyrus of the cat brain by undercutting the subcortical connections and then reaming out the sides of the slab with a bent wire to just below the pial surface, leaving the blood supply to the isolated brain tissue intact. Brief electrical stimulation elicited responses that spread widely across the slab (5–7). Ben and his student, Bernice Grafstein, characterized the neural networks responsible for the observed activity (9, 11). By 1957, in collaboration with Jerzy Olszewski, Ben was able to identify the cells histologically and found that the largest have their cell bodies in layer V, although some were found in other cortical layers (16). Ben built an electronic model neuron to test his predictions (12) and concluded that ‘this network is the only system...’
Donald Hebb’s influential book, *The organization of behavior* (Hebb 1949), introduced the notion of what is now known as the Hebb synapse to account for information storage in the brain. Ben used the neurologically isolated preparation of cerebral cortex to simplify investigations of the cellular basis of learning. He reasoned that repeated stimulation should lead to changes in the ease with which specific synaptic contacts transmit information from one neuron to another (14). The persistent after-discharges he observed appeared to offer a simple explanation of the cellular basis of learning. However, a brief interruption of the blood supply extinguished the after-discharge (14), while memories are resistant to such insults. Nevertheless, Ben persisted with his investigations of the effects of stimulation on the long-term conductivity of specific neural paths. Indeed, when recruiting one of us (TVPB), Ben said: ‘There is one subject that interests me so intensely that I would want you to work on it if you do a PhD with me.’ The idea was to determine whether stimulation of local networks would provide evidence of long-term changes in synaptic connectivity. In these experiments, the stimulating electrodes were pushed into the grey matter of the cortex to provide the local stimulation. ‘Weightless’ recording microelectrodes (figure 4) devised by Ben and Gordon Robson (22) were used to minimize the effects of movements caused by the pulsations of the brain during the prolonged recordings necessary to assess the time course of any change in
Figure 6. The effect upon conductivity in a radial test pathway, $X_1$, of stimulation of a tangential pathway $X_2$ on the activity of a cortical cell ($Y$). The test stimulus was a short train of six stimuli at 50 per second repeated every five seconds. (a) Frequency of all discharges of the recorded cell, $Y$; (b) calculated conductivity along the radial pathway, $X_1$; (c) frequency of conditioning stimuli to $X_2$. The conditioning stimuli set up after-bursts which largely account for the rise in $Y$ following the conditioning period. (Figure 4 from (36).)

nerve cell connectivity. As the relationship between the conditioning period and any after-effect were completely unknown, conditioning periods varied widely from a few minutes to an hour. Relatively long-lasting changes in the conductivity of some cortical pathways were discovered, although such changes were no more likely to follow long periods of conditioning than short ones. The majority of pathways studied by Ben with Bliss and Uttley appeared to respond to the conditioning stimuli with a reduction in conductivity, as shown in figure 5, rather than an increase as might be expected if the activity of simple neural networks reflected a learnt connection. Nevertheless, a small number of their sample of neurons did show an increased conductivity (figure 6) and the authors concluded that the cerebral cortex had more than one type of modifiable (plastic) synapse (36). Later work has amply confirmed this view.

The central control of breathing
The regular cycle of breathing is perhaps the most prominent of all the automatic rhythms of the body. By the late nineteenth century it had been established that the respiratory
rhythm originated in the brainstem. The cause of the respiratory rhythm remained elusive—what initiated each cycle, was it a pacemaker system similar to that of the heart or was some other process involved? The evidence from Ben’s work on isolated slabs of cortex and on the after-discharge of spinal neurons (15) indicated that self re-exciting chains of neurons could play a role. To tackle this problem, Ben and Gian Salmoiraghi examined the role of respiratory neurons in the pons and medulla. Here they were handicapped by a surprising a lack of facilities for histology, so they had to rely on the accuracy of electrode placement with respect to anatomical features, the obex in particular, and on the depth at which individual active neurons were encountered. Consequently, they were unable to identify with any certainty which of the brainstem nuclei contained the respiratory neurons. They set out to answer three key points: (i) Where are those nerve-cells whose periodic activity is essential to rhythmic respiration located? (ii) How is each burst of activity among these respiratory neurons initiated? (iii) How is each burst of activity maintained for each phase of the cycle?

They defined inspiratory neurons as those most active just prior to and during inspiration and expiratory neurons as those active just prior to and during expiration, as exemplified by figure 7(a). They found that the basic rhythm of breathing was not causally related to the
activity of neurons in the pons, but rather was caused by activity of neurons in the medulla. They concluded that inspiratory and expiratory neurons were intermingled in this region of the brainstem (19) and, by means of a fine cut along the midline, Ben and Salmoiraghi showed that their axons cross over to the contralateral side in the lower brainstem. At the time, some investigators thought that respiration was driven by pacemaker cells in a similar manner to the cells of the heart. To test this notion, they investigated the effect of various surgical sections through the brainstem and cranial nerves. They showed that the periodic activity of respiratory neurons remained after cutting both the vagus nerves and the cranial nerves. Progressive isolation of the brainstem reduced the number of active neurons encountered in each electrode penetration, but short-lived bouts of periodic activity could be induced by brief stimulation of the caudal end of the medulla. From these experiments they concluded that there was no evidence for respiratory pacemaker cells (20) and proposed that the constant bombardment of the brain by sensory inputs kept up a steady background excitation analogous to the ‘central excitatory state’ proposed by Sherrington (1947, p. 433) for spinal reflexes and the ‘tonus cerebral’ introduced by Bremer (1949). Ben and Salmoiraghi proposed that
a network of self-exciting loops with reciprocal inhibitory connections between inspiratory and expiratory neurons could then provide a means of rhythmical self re-excitation (21). Ben summarized his views on the control of respiratory movements in a brief review a few years later (30) (figure 7b). Since these studies, the role of neural networks in generating the respiratory rhythm has been considerably elaborated, but a consensus is emerging that a group of neurons in the rostral part of the ventral medulla, a small region known as the pre-Bötzinger complex, may be responsible for the basic inspiratory rhythm (see Feldman et al. 2013); the elaborate respiratory neural networks then serve to shape the required motor output according to physiological demands.

**The visual system**

In the late 1950s Ben, with Roy Pritchard and Woody Heron, turned their attention to the responses of cortical neurons to visual stimulation at much the same time as David Hubel (1926–2013, ForMemRS 1982) and Torsten Weisel (b. 1924, ForMemRS 1982) had begun their celebrated work on the cat’s visual cortex (see Hubel & Wiesel 1959). Ben and his colleagues found that many cells responded preferentially to stimulation of one eye, so there was a dominant eye for many cells, but, in about a quarter of the cells they studied, the response to binocular stimulation was much greater than the sum of the responses for each eye separately (18). In their following paper (27) they described ‘ON’ and ‘OFF’ responses in cortical neurons similar to those previously reported for retinal ganglion cells (Kuffler 1953). They also noted that the most effective stimulation was achieved by mimicking the small oscillations of a physiological nystagmus. In a subsequent study (33), they investigated the responses of individual neurons to the movement of a light–dark boundary across their receptive field and found that the discharge frequency of individual neurons was higher when it represented the bright part of the field and so was likely to be implicated in the neural basis of contrast discrimination (figure 8). They went on to investigate the behaviour of neurons in the visual cortex that permitted binocular vision and concluded that binocular fusion was achieved by the visual system ‘hunting’ for the eye position that provided the greatest cortical response to the micro-saccadic movements of the eyes (37).

Ben and Roy Pritchard subsequently investigated the neural basis of optical illusions and found that the response to a single test line was altered by adding a test line at an angle of 30°, as in the Pogendorf illusion. They found that the second line displaced the position of maximal response in the receptive field and concluded that certain illusory percepts result from this distortion of visual information. Their paper (39) ended with the following provocative statement: ‘Illusions are seductive . . . However, if a particular illusory percept can be explained as a consequence of distorted sensory input then its importance in a continuing study of brain function becomes trivial.’

**Final years**

By the early 1970s Ben had begun to turn his attention to the behaviour of cortical neurons in various states of arousal. To do so he devised an ingenious means of recording from single units over a period of days (40). Working with John Stean and Alison Webb, he found that, in the intact brain, the firing rate of cortical cells was directly related to the level of arousal of the animal, but in recordings made in vivo from neurons in isolated slabs of cerebral cortex,
the firing rate was unaffected by changes in the level of arousal. This implies that subcortical structures determine the state of arousal, as measured by changes in the patterns of cortical neural discharges (41–44).

After moving to Newcastle, Ben’s interest in neural plasticity and memory was rekindled, and, as mentioned above, he and Alison began a fruitful collaboration with Philip Bradley on the neurophysiological correlates of imprinting in young chicks. They developed an in vitro slice preparation of the chick brain (45), characterized its local circuitry (46) and found that responses to electrical stimulation could be potentiated for many hours by two short periods of stimulation at 5 Hz (47). They went on to show that this potentiation depended on activation of N-methyl-d-aspartate (NMDA) receptors (51, 52), as in mammalian models of learning. The potentiation could be prevented by prior treatment with an inhibitor of protein kinase C (PKC), and initiated by activation of PKC (50). Moreover, the effect of activating PKC was correlated with an increase in the size and density of synapses on dendritic spines, providing good evidence that morphological changes contribute to the cellular basis of memory (48, 49).

Later in life, Ben had begun to suffer from severe back pain and underwent spinal surgery in 1996 to ameliorate his condition. Unfortunately, the surgery was not a success and left him wheelchair bound and in chronic pain for the rest of his life. Even so, he continued to work in the laboratory until 1999. He died on 6 September 2001.

Ben’s last paper with Philip Bradley and Alison was concerned with the role of GABA(B) receptors in synaptic plasticity and was published after his death (53).

**Epilogue**

Ben was an imaginative scientist who followed his own path, unmoved by the fashions of his day. Although a valued collaborator on topics that interested him and a loyal friend, he was not greatly interested in current trends in the wider field of neuroscience. For that reason, he was perhaps less successful as head of division of a major research institute than he might have been. But those of us who worked as young scientists in his division remember with gratitude the freedom and support he gave us to follow our own ideas.

As his record testifies, Ben brought great ingenuity both to the design of experiments and to the construction of the equipment that allowed them to be carried out. It is difficult at this remove to appreciate the technical challenges of analysing neuronal activity without the aid of computers. Ben met this challenge directly, devising dedicated analogue machines to allow on-line processing of neural activity. His work on respiratory control, the visual system and synaptic plasticity were ground-breaking at the time. In view of later developments, it would not be surprising if he felt a sense of disappointment that others had exploited some of the opportunities his own work had opened up. If so, he never showed it, focusing always on his current interests. Throughout his career Ben was fascinated by the problems of higher nervous function, especially that of learning and memory, and it is fitting that his last published contributions were directed towards an understanding of the cellular basis of synaptic plasticity.

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AUTHOR PROFILES

Chris Richards

Chris Richards is emeritus professor of experimental physiology at University College London (UCL). He read biological chemistry for his first degree at the University of Bristol and moved to the zoology department to work on ion transport in crab muscle in under the supervision of Peter Caldwell FRS. After completing his PhD studies, Chris joined Henry McIlwain’s biochemistry department at the Institute of Psychiatry, where he developed the use of slices of guinea-pig olfactory cortex for electrophysiological studies. In 1969 Ben Burns appointed him to the staff of the Division of Physiology and Pharmacology at NIMR, where he investigated the cellular and molecular mechanisms of anaesthetic action. In 1979 he left NIMR to join the physiology department of the Royal Free Hospital School of Medicine, where he continued to work on anaesthetic mechanisms, later developing an interest in pH regulation in mammalian neurons, before finally moving to the physiology department at UCL. After leaving NIMR, Chris remained in contact with Ben and Alison, visiting them in Bristol and Newcastle. He last saw them both in 1998 at a meeting in Cardiff, by which time Ben was in a wheelchair though still mentally vigorous.

Tim Bliss

Tim Bliss was head of the Division of Neurophysiology at the MRC National Institute for Medical Research, London, from 1988 to 2006. He began his research career as a PhD student with Ben Delisle Burns in the Department of Physiology at McGill University, receiving his PhD in 1967. He then rejoined Ben in the Division of Physiology and Pharmacology at NIMR. A year later he took leave of absence at the Neurophysiological Institute, University of Oslo, where he performed with Terje Lomo the experiments which established the phenomenon of long-term potentiation (LTP) as the primary model of synaptic plasticity in the mammalian brain. His subsequent work at NIMR concentrated on the cellular mechanisms of LTP and its relationship to learning and memory. In 2016 he was a recipient of the Brain Prize with Richard Morris FRS and Graham Collingridge FRS. He is currently an adjunct professor at the University of Toronto.
REFERENCES TO OTHER AUTHORS

Adrian, E. D. 1941 Afferent discharges to the cerebral cortex from peripheral sense organs. *J. Physiol.* **100**, 159–191. (doi:10.1113/jphysiol.1941.sp003932)

Bremer, F. 1949 Considérations sur l’origine et la nature des ‘ondes’ cérébrales. *Electroenceph clin Neurophysiol.* **1**, 177–193. (doi:10.1016/0013-4694(49)90021-8)

Brooks, V. B. 2001 Vernon B. Brooks. In *The history of neuroscience in autobiography* (ed. Larry R. Squire), vol. 3, pp. 76–116. San Diego: Academic Press.

Feldman, J. L., Del Negro, C. A. & Gray P. A. 2013 Understanding the rhythm of breathing: so near yet so far. *Ann. Rev. Physiol.* **75**, 423–452. (doi:10.1146/annurev-physiol-040510-130049)

Gerstein, G. L. & Kiang N. Y-S. 1960 An approach to the quantitative analysis of electrophysiological data from single neurons. *Biophys. J.* **1**, 15–28. (doi:10.1016/S0006-3495(60)86872-5)

Grafstein, B. 2001 Bernice Grafstein. In *The history of neuroscience in autobiography* (ed. Larry R. Squire), vol. 3, pp. 246–282. San Diego: Academic Press.

Hebb, D. O. 1949 *The organization of behavior*. London and New York: John Wiley.

Hubel, D. H. & Wiesel, T. N. 1959 Receptive fields of single neurons in the cat’s striate cortex. *J. Physiol.* **148**, 579–591. (doi:10.1113/jphysiol.1959.sp006308)

Huxley, A. F. 2008 *Memoir on B. D. Burns: family and boyhood* (unpublished memoir).

Kuffler, S. W. 1953 Discharge patterns and functional organization of mammalian retina. *J. Neurophysiol.* **16**, 37–68. (doi:10.1152/jn.1953.16.1.37)

Penfield, W. & Boldrey, E. 1937 Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. *Brain* **60**, 389–443. (doi:10.1093/brain/60.4.389)

Sherrington, C. S. 1947 *The integrative action of the nervous system*. New Haven and London: Yale University Press and Oxford University Press.

Woolsey, C. N., Marshall, W. H. & Bard, P. 1943 Note on the organization of the tactile sensory area of the cerebral cortex of the chimpanzee. *J. Neurophysiol.* **6**, 287–291. (doi:10.1152/jn.1943.6.4.287)

BIBLIOGRAPHY

The following publications are those referred to in the text. A full bibliography is available online at https://doi.org/10.6084/m9.figshare.c.4880148.

(1) 1941 (With A. N. Black & S. Zuckerman) An experimental study of the wounding mechanism of high-velocity missiles. *Br. Med. J.* **2** (4224), 872–874. (doi:10.1136/bmj.2.4224.872)

(2) 1948 (With G. L. Brown & E. Bülbbring) The action of adrenaline on mammalian skeletal muscle. *J. Physiol.* **107** (1), 115–128. (doi:10.1113/jphysiol.1948.sp004255)

(3) (With G. L. Brown & W. Feldberg) The effect of diisopropyl fluorophosphonate on neuromuscular transmission in cats. *J. Physiol.* **107** (3), 346–354. (doi:10.1113/jphysiol.1948.sp004279)

(4) 1949 (With G. L. Brown) Fatigue and neuromuscular block in mammalian skeletal muscle. *Proc. R. Soc. Lond. B* **136** (883), 182–195. (doi:10.1098/rspb.1949.0018)

(5) Some properties of the cat’s isolated cerebral cortex. *J. Physiol.* **110** (1/2), 9P. (doi:10.1113/jphysiol.1951.sp004652)

(6) 1950 Some properties of the cat’s isolated cerebral cortex. *J. Physiol.* **111** (1/2), 50–68.

(7) 1951 Some properties of isolated cerebral cortex in the unanesthetized cat. *J. Physiol.* **112** (1/2), 156–175.

(8) (With W. D. M. Paton) Depolarization of the motor end-plate by decamethonium and acetylcholine. *J. Physiol.* **115** (1), 41–73.

(9) 1952 (With B. Grafstein) The function and structure of some neurones in the cat’s cerebral cortex. *J. Physiol.* **118** (3), 412–433. (doi:10.1113/jphysiol.1952.sp004805)

(10) 1954 (With A. Bunzl, A. S. V. Burgen, N. Pedley & K. G. Terroux) Methods for studying the reflex activity of the frog’s spinal cord. *Br. J. Pharmacol. Chemother.* **9** (2), 229–235. (doi:10.1111/fj.1476-5381.1954.tb00846.x)
The production of after-bursts in isolated unanesthetized cerebral cortex. *J. Physiol.* **125** (3), 427–446. (doi:10.1113/jphysiol.1954.sp005170)

(12) 1955 The mechanism of after-bursts in cerebral cortex. *J. Physiol.* **28; 127** (1), 168–188. (doi:10.1113/jphysiol.1955.sp005247)

(13) (With G. B. Frank & G. Salmoiraghi) The mechanism of after-discharges caused by veratrine in frog’s skeletal muscles. *Br. J. Pharmacol. Chemother.* **10** (3), 363–370. (doi:10.1111/j.1476-5381.1955.tb00885.x)

(14) 1956 The electrophysiological approach to the problem of learning. *Can. J. Biochem. Physiol.* **34** (2), 380–389. (doi:10.1139/o56-040)

(15) The cause of reflex after-discharge in the frog’s spinal cord. *Can. J. Biochem. Physiol.* **34** (3), 456–465. (doi:10.1139/o56-047)

(16) 1957 (With B. Grafstein & J. Olszewski) Identification of neurones giving burst response in isolated cerebral cortex. *J. Neurophysiol.* **20** (2), 200–210. (doi:10.1152/jn.1957.20.2.200)

(17) 1958 *The mammalian cerebral cortex.* London: Edward Arnold. (doi:10.1113/jphysiol.1960.sp008951)

(18) 1960 (With W. Heron & B. Grafstein) Responses of cerebral cortex to diffuse monocular and binocular stimulation. *Am. J. Physiol.* **198**, 200–204. (doi:10.1152/ajplegacy.1960.198.1.200)

(19) (With G. C. Salmoiraghi) Localization and patterns of discharge of respiratory neurons in brain-stem of cat. *J. Neurophysiol.* **23**, 1–13. (doi:10.1152/jn.1960.23.1.1)

(20) (With G. C. Salmoiraghi) Notes on mechanism of rhythmic respiration. *J. Neurophysiol.* **23**, 14–26. (doi:10.1152/jn.1960.23.1.14)

(21) (With G. C. Salmoiraghi) Repetitive firing of respiratory neurons during their burst activity. *J. Neurophysiol.* **23**, 27–46. (doi:10.1152/jn.1960.23.1.27)

(22) (With J. G. Robson) ‘Weightless’ micro-electrodes for recording extracellular unit action potentials from the central nervous system. *Nature* **186**, 246–247. (doi:10.1038/186246a0)

(23) (With G. K. Smith) A biological interval analyser. *Nature* **187**, 512–513. (doi:10.1038/187512a0)

(24) (With J. G. Robson & P. J. Welt) The effect of inhaling dilute nitrous oxide upon recent memory and time estimation. *Can. Anaesth. Soc. J.* **7**, 399–410. (doi:10.1007/BF03021298)

(25) (With J. G. Robson & P. J. Welt) The effect of nitrous oxide upon sensory thresholds. *Can. Anaesth. Soc. J.* **7**, 411–422. (doi:10.1007/BF03021299)

(26) (With J. D. Dejong) A preliminary report on the measurement of Parkinson’s disease. *Neurology* **10**, 1096–1102. (doi:10.1212/WNL.10.7.1676)

(27) 1962 (With W. Heron & R. Pritchard) Physiological excitation of visual cortex in cat’s unanesthetized isolated forebrain. *J. Neurophysiol.* **25**, 165–181. (doi:10.1152/jn.1962.25.2.165)

(28) (With J. D. Dejong) An investigation of Parkinson’s disease. *Neurology* **12**, 402–409. (doi:10.1212/WNL.12.6.402)

(29) (With G. K. Smith) Transmission of information in the unanesthetized cat’s isolated forebrain. *J. Physiol.* **164**, 238–251. (doi:10.1113/jphysiol.1962.sp007017)

(30) 1963 The central control of respiratory movements. *Br. Med. Bull.* **19**, 7–9. (doi:10.1093/oxfordjournals.bmb.a070010)

(31) (With G. Mandl & G. K. Smith) An auto and cross-correlator for digital information. *Electronic Engng* **35**, 220–228. (doi:10.1113/jphysiol.1964.sp007526)

(32) (With J. D. Dejong & O. H. Solis-Quiróga) Effects of trihexyphenidyl hydrochloride (Artane) on Parkinson’s disease. *Neurology* **14**, 13–23. (doi:10.1212/WNL.14.1.13)

(33) (With R. Pritchard) Contrast discrimination by neurons in the cat’s visual cerebral cortex. *J. Physiol.* **175**, 445–463. (doi:10.1113/jphysiol.1964.sp007526)

(34) 1965 (With W. Ferch & G. Mandl) A neurophysiological computer. *Electronic Engng* **37**, 20–24. (doi:10.1113/jphysiol.1968.sp008462)

(35) 1967 (With J. D. Dejong) Parkinson’s disease: a random process. *Can. Med. Assoc. J.* **97**, 49–56.

(36) 1968 (With T. V. Bliss & A. M. Uttley) Factors affecting the conductivity of pathways in the cerebral cortex. *J. Physiol.* **195**, 339–367.

(37) (With R. Pritchard) Cortical conditions for fused binocular vision. *J. Physiol.* **197**, 149–171. (doi:10.1113/jphysiol.1968.sp008552)
(38) The uncertain nervous system. London: Edward Arnold. (doi:10.1113/jphysiol.1971.sp009403)

(39) 1971 (With R. Pritchard) Geometrical illusions and the response of neurons in the cat’s visual cortex to angle patterns. *J. Physiol.* 213, 599–616. (doi:10.1113/jphysiol.1971.sp009403)

(40) 1974 (With J. P. Stean & A. C. Webb) Recording for several days from single cortical neurons in completely unrestrained cats. *Electroencephalogr. Clin. Neurophysiol.* 36, 314–318. (doi:10.1016/0013-4694(74)90175-8)

(41) 1976 (With A. C. Webb) The spontaneous activity of neurons in the cat’s cerebral cortex. *Proc. R. Soc. Lond. B* 194, 211–223. (doi:10.1098/rspb.1976.0074)

(42) 1979 (With A. C. Webb) The correlation between discharge times of neighbouring neurons in isolated cerebral cortex. *Proc. R. Soc. Lond. B* 203, 347–360. (doi:10.1098/rspb.1979.0002)

(43) 1976 (With J. P. Stean & A. C. Webb) The effects of sleep on neurons in isolated cerebral cortex. *Proc. R. Soc. Lond. B* 206, 281–291. (doi:10.1098/rspb.1979.0105)

(44) 1982 (With A. C. Webb) Mechanisms governing the relation between activity in the cerebral cortex and level of arousal. *Proc. R. Soc. Lond. B* 214, 325. (doi:10.1098/rspb.1982.0014)

(45) 1988 (With P. M. Bradley & A. C. Webb) Response characteristics of neurons in chick forebrain slices. *Proc. R. Soc. Lond. B* 234, 145–157. (doi:10.1098/rspb.1988.0041)

(46) 1990 (With P. M. Bradley, P. F. Chinnery & A. C. Webb) Local circuitry in the IMHV of the domestic chick (*Gallus domesticus*). *Proc. R. Soc. Lond. B* 240, 479–492. (doi:10.1098/rspb.1990.0049)

(47) 1991 (With P. M. Bradley & A. C. Webb) Potentiation of synaptic responses in slices from the chick forebrain. *Proc. R. Soc. Lond. B* 243, 19–24. (doi:10.1098/rspb.1991.0004)

(48) 1992 (With P. M. Bradley, J. Titmuss & A. C. Webb) Morphological correlates of persistent potentiation in the chick brain slice. *Neuroreport* 2, 197–200. (doi:10.1097/00001756-199104000-00009)

(49) 1993 (With P. M. Bradley, J. Titmuss & A. C. Webb) Morphological correlates of protein kinase C induced potentiation in the chick brain slice. *Neuroreport* 3, 223–226. (doi:10.1097/00001756-199203000-00001)

(50) 2001 (With P. M. Bradley, J. Titmuss & A. C. Webb) Protein kinase activity and synaptic plasticity in a chick brain slice. *Neuroreport* 3, 227–230. (doi:10.1097/00001756-199203000-00002)

(51) 1993 (With P. M. Bradley, T. M. King & A. C. Webb) NMDA-receptors and potentiation in an area of avian brain essential for learning. *Neuroreport* 5, 313–316. (doi:10.1097/00001756-199312000-00034)

(52) 2004 (With P. M. Bradley & A. C. Webb) Low-threshold N-methyl-D-aspartate receptor function correlates negatively with learning. *Brain Res.* 900, 38–47. (doi:10.1016/S0006-8993(01)

(53) 2004 (With P. M. Bradley, C. J. Gowland & A. C. Webb) Post-synaptic GABA(B) receptors: possible controllers of coincidence detection? *Behav. Brain Res.* 155 (1), 27–35. (doi:10.1016/j.bbr.2004.03.032)