Remembering Colin Blakemore (1944-2022), a giant of neuroscience, educator, mentor and colleague.

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Announcement of Colin's passing (date, place and age),

Professor Sir Colin Blakemore FRS, died after 18 months of suffering from motor neuron disease aged 78 on Monday 27th June surrounded by his daughters at Sobell House, Oxford.

Colin Blakemore was one of the giants of neuroscience of his time. An extraordinary scientist whose outstanding work evolved our knowledge of vision, of brain development, neuroplasticity, and neurodegeneration. Colin will be remembered as someone with unparalleled contributions to neuroscience, science administration and promoting science education and outstanding mentor. He made fundamental contributions in understanding how sensory systems work in our brain and how our brain changes with neuronal plasticity, the capacity of the nervous system to modify its own connections according to its needs. Colin was one of the first to show that manipulation of the sensory environment may exert a direct and profound influence on the growing nervous system. He demonstrated a direct link between the activation of nerve cells and their connections with the rest of the visual system and thereby set the scene for understanding that the computational functions of the brain are the outcome of adaptive processes. His interests ranged from very early development of forebrain through cerebral cortical specialisation to the functions of adult cerebral cortex. His expertise ranged from molecular and genetic mechanisms of neural and physiological function all the way across to psychology. His discoveries promoted changes in therapeutic practice and they are being exploited in clinical treatment of neurological conditions.

Colin's career/employment history.

Colin was born during the second world war at a military hospital in Stratford-upon-Avon, Warwickshire on 1 June 1944. He was the only child of Beryl Blakemore (née Smith) and Norman Blakemore. The family lived in a rented terrace house in the working-class district of Radford in Coventry. When Colin was five years old, his father left active army service and became a television repair engineer. Having a TV set enabled Colin to watch David Attenborough's Zoo Quest programmes. Colin developed a huge passion for natural history and science. He read Darwin's "On the Origin of Species" (1859) sitting in the local second-hand bookstore, because he

could not afford to purchase the book. Colin attended the local primary school but, when he performed well above the average for his age, his parents scraped together the funds to send him from the age of seven to the fee-paying junior section of King Henry VIII grammar school in Coventry. Passing the 11-plus exam entitled him to free secondary education in the senior school. Colin won a state scholarship to study medical sciences at Corpus Christi College, Cambridge. Illness prevented him from earning the expected first-class honours degree (1965). He was declared "aegrotat", deserved to receive honours, and took his MA (1969) in Medical Sciences. He was awarded a Harkness Fellowship that supported him for his PhD that he completed in 1965 under the supervision of Horace Barlow who was then Professor of Physiological Optics and Physiology at the University of California in Berkeley, USA. Colin had life-long admiration for Horace and they kept discussing science until Prof Barlow's death in 2020.

After his PhD, Colin returned immediately to Cambridge University for 11 years as a Demonstrator, Lecturer in Physiology, Director of Medical Studies (Downing College), and Royal Society Locke Research Fellow until 1979. He taught generations of medical and biomedical students. ~~One of his students at Cambridge was David Nutt.~~ He was appointed Waynflete Professor of Physiology at Oxford University in association with a Professorial Fellowship with Magdalen College in 1979. At 35 years old, he was the youngest ever to be appointed to the position. When he showed up for his first faculty meeting at Oxford, the chair told him that "student representatives are not required for these items". He held the Waynflete chair for 28 years until 2007, making him the longest standing Waynflete Professor of all times.

During his tenure at Oxford, he greatly enhanced the reputation of the University Laboratory of Physiology, attracting many eminent visitors to Oxford and established new areas of research for the university. He was Director of the Oxford McDonnell Centre for Cognitive Neuroscience at Oxford from 1996–2003, before becoming Chief Executive of the Medical Research Council from 2003 until 2007. He returned to Oxford to continue as Professor of Neuroscience and Supernumerary Fellow at Magdalen College until 2012. After this, Colin was appointed to a newly created Professorship of Neuroscience & Philosophy at the School of Advanced Study, University of London, where he directed the Centre for the Study of the Senses. Colin subsequently held other professorial positions, notably at the City University of Hong Kong, whilst maintaining links with Oxford, continuing both his own neuroscience research and his many other services to science and medical research. He remained a highly active member of our department as an Emeritus Professor at DPAG until his death.

~~Main contributions to neuroscience and their specific community (e.g. as a mentor and colleague).~~

Colin's research pursued the theme of visual, auditory and somatosensory perception, mechanisms of neural plasticity, investigating disorders of brain development that might lead to cognitive disorders such as autism and dyslexia. His research identified sensitive periods of early development when brain plasticity is enhanced and his work identified mechanisms by which devastating conditions can be delayed, such as brain pathology in Huntington's disease. Blakemore not only

pursued the consequence of this research into the clinical environment, translational research as it would be called today, but also realised that the new understanding of neuroscience would influence fields far outside science and medicine.

The initial influences were rooted in Cambridge of the 1960s where a fusion of different research traditions had been effected. Richard Gregory pursued the idea that perception was driven by internal models of the external world, an extension of Helmholtz's concept of unconscious inference in perception. At the same time, Kenneth Craik's writings on control systems and cognitive science and the achievements of Edgar (Lord) Adrian in sensory physiology promoted the view that brain mechanisms corresponding to these internal models were waiting to be discovered. It was into this territory, plus a healthy dose of cybernetics and information theory, that Colin stepped.

His initial encounter with Richard Gregory brought another strong influence. Colin relates that he posed a question on perception to Gregory and immediately received the suggestion of going to the lab to try something out experimentally. Blakemore was clearly hooked by this approach and thereafter transferred this to all his dealings with colleagues and students. Colin was generous with both his time and his resources to develop the work of others and passionately believed in the empirical approach to settling issues.

In 1965, Colin transferred to Horace Barlow's lab at the University of California Berkeley, supported by a Harkness Fellowship. He worked on a variety of aspects of binocular vision but the paper that is most celebrated from that time is the discovery of neurons in the primary visual cortex of the cat that are sensitive to binocular depth. This work was prompted by the arrival of Jack Pettigrew from Sydney, who had worked on binocular physiology in Peter Bishop's lab. The resulting collaborative paper [1] was a landmark step in understanding the physiology of 3D perception. Discovering neurons that could support perceptual function so early in cortical processing challenged much of the current thinking. The discovery went hand-in-hand with Bela Julesz's demonstrations of depth from random-dot stereogram figures, where depth emerges from local point to point matching of dots between left and right eyes. The BBP paper provided the physiological mechanism for this computational process.

On his return to Cambridge, Colin found that similar progress was being made with other aspects of early visual processing. This work coalesced into the proposal that early visual processing passes through a set of spatial and temporal filters that are selective for spatial frequency and orientation. One of the landmark papers was the selective adaptation of spatial frequency channels in human vision demonstrated by Colin with Fergus Campbell [2]. From this era of work, many of the modern developments of computer vision emerged. Colin rapidly established a visual neurophysiology lab in Cambridge and began a wide range of studies on the development and adult functions of the visual cortex.

~~Development of the brain depends on the visual environment~~

Closely related to Colin's fundamental research was the clinical observation that one out of ten persons have weak or non-existent binocular 3D vision. This is sometimes only exposed with specific tests where someone has to do tasks that require binocular depth vision. Colin's research sought to understand why some children acquire a squint during infancy. In this case, the inputs that the brain receives from each eye do not match; children then develop profoundly impaired vision in one eye, a condition known as amblyopia. His early animal experiments on the developing visual systems suggested that patching the eyes of affected children briefly during an early critical period of development could establish new visual pathways and improve their vision. These studies contributed to a growing understanding of neural plasticity – the idea that the brain retains the ability to rewire itself in response to changes in its environment – which has radically revised the traditional view that brain damage is irreversible. One of Colin's last publications was on a randomised clinical trial to establish treatment for amblyopia based on more recent understanding of the rules of synaptic plasticity. A large research consortium tested the hypothesis that asynchronous stimulation of the two eyes might induce synaptic plasticity and rebalance input. The study demonstrated that asynchronous binocular treatment alone is 50 times more efficient than the previously widely used patching only.

Colin was very interested in the fundamental question of how neuronal circuits get modified as they start to process sensory input and how they change by plasticity when there are changed environmental influences. Colin demonstrated that the visual cortex adjusts itself during maturation to the nature of its visual experience. In visual cortex the neurones are selective for the orientation of lines and edges in the visual field, and the preferred orientations of different cells are distributed all around the clock. Early visual experience can change this organization. Kittens were exposed to visual environments that entirely consisted of high contrast black and white stripes either horizontal or vertical. This intervention changed the distribution of the orientation sensitivity of the visual cortical neurons. These experiments were more recently reproduced with various imaging methods.

At later stages of Colin's career he extended his sensory work to rodent models, including the barrel field of the primary somatosensory cortex. This work helped to identify molecular pathways that are directly involved in the establishment of thalamocortical synapses and regulate their plasticity. Colin's most recent work identified some of the genes involved in enabling nerve cells to modify their connections in response to the flow of nerve impulses through them. Work from the laboratory started to correlate the area-specific thalamocortical innervation with cortical specialisation. This work extended the concept that the brain adjusts itself during maturation to the nature of its experience to the entire thalamocortical system. He also demonstrated that the visual cortex is 'taken over' by the other senses, especially touch, in people who have been blind since infancy.

In spite of Colin's very busy schedule, Colin performed most of his own experiments himself. He had exceptional manual skills and he was hugely efficient and precise. He led by example and taught generations of neurophysiologists. He was always a very active participant at scientific meetings, where he could spot contradictions immediately.

Colin's approach to understand the function of the nervous system was highly integrative. He viewed the nervous system as part of the whole body. His research used functional MRI imaging of human brains to study how sensory systems communicate with each other and with the rest of the brain and body in a highly dynamic fashion. His research was always guided by the function of the nervous system. In his view, the influence of the nervous system permeates the whole body and in reverse, the body constantly interacts with the brain, therefore it is impossible to understand them in isolation. For example, upon learning that some genetic mutations were linked to specific language functions and the media had identified these genes as "language genes", Colin emphasized the need to understand what the influence of that gene was on neurogenesis, migration of cells and formation of connections between cells. He stated, "Genes produce proteins at best": to understand in detail how a gene is influencing language, we need to understand how the underlying neuronal circuits are altered using the approaches of integrative neuroscience.

~~communication of science~~

Generations of medical and biomedical students grew up listening to his lectures and Universities of Cambridge and of Oxford. Colin consistently got the highest rating from medical students at Oxford for decades. He was well known for his passionate belief in the importance of public engagement with research and he was well known as science communicator. The Royal Society acknowledged him as 'one of Britain's most influential communicators of science'. He spoke about science with clarity, an easy elegance following tight and transparent logic. These exceptional qualities, evident from early stages of his career, made him much in demand in medical undergraduate and graduate teaching, in print and broadcast media. In 1976, Colin gave the BBC Radio 4 Reith Lectures "Mechanics of the Mind" and remains to date the youngest person ever to deliver these lectures, covering the neuroscience of sleep, language, consciousness and mental illness. He went on to present and contribut to hundreds of radio and television broadcasts. In 1988 Colin presented a 13-part TV series, The Mind Machine, on BBC Two accompanied with a popular book. Colin also wrote articles and opinion columns for national newspapers, and his books for the general public include Mechanics of the Mind (for which he won the Phi Beta Kappa Award in Science)*, Images and Understanding*, *Mindwaves*, *Gender and Society,* and *The Oxford Companion to the Body*. He received several awards for science communication, including the Royal Society's Michael Faraday prize.

Colin had huge impact on British science by engaging with the general public and with distinguished scientific organisations. He held several influential positions, including serving as President of the Biosciences Federation (now the Society of Biology), the British Neuroscience Association and The Physiological Society, and as President and Chairman of the British Association for the Advancement of Science (now the British Science Association). Colin worked for many medical charities and not-for-profit organisations and served in advisory roles for several UK government departments, agencies, foundations and government departments overseas. After his 'retirement' from Oxford, Colin continued to make. highly original and creative contributions to various fields. Colin received a knighthood in 2014 for services to scientific research, policy, and outreach.

~~**importance of animal research,**~~

Building on his integrative view of neuroscience, Colin defended animal use when there was no possibility to develop new alternative methods and when the benefits of the research really outweigh the moral cost of using animals. This became a costly activity with personal threats to him and his family. Without compromising his position, Colin sought to debate the ethics and practice of animal research with those who were publicly opposed to it. At the same time, Colin's laboratory was also an early adopter of alternative methods. His laboratory was amongst the first to use organotypic co-cultures of various tissues (e.g. thalamus and cortex) to study the cortical development with the influence of thalamic input. These preparations gave insight into fundamental cellular interactions within a controlled environment.

~~**other functions (MRC, science policy, charities).**~~

In 2003, Colin was appointed chief executive of the Medical Research Council, the government-funded body that operates medical research institutes and distributes grants. Colin immediately reinstated the research project grant, which had been abandoned as a mode of funding under his predecessor, as a means of stimulating and supporting innovation by individual research groups in the UK. Colin's tenure at the MRC was adversely affected by the controversy over the future of the National Institute for Medical Research (NIMR) at Mill Hill, which was only resolved in 2015 when NIMR fused with the new Crick institute in central London. Colin's expertise helped to shape public policy in many areas. Among his many government advisory roles, he was a member of the UK Drug Policy Commission. With Prof David Nutt and others, in 2007 he co-authored a controversial letter to the Lancet assessing the harms of legal and illegal substances, including alcohol and tobacco, and arguing that policy should be based on level of harm. In 2002, together with Richard Dawkins; Roger Penrose, Lewis Wolpert and dozens of other distinguished British scientists, Colin wrote a letter to Tony Blair urging for a statutory requirement that creationism should not be taught in the national curriculum "as anything other than religious myths" and advocated for the teaching of Darwinian evolution to be introduced in key stage 2. More recently, Colin played a major part, with Nicholas Wald and others, in the adoption of a new UK-wide policy to add folate to wheat flour to provide a baseline of protection against spina bifida in early pregnancies.

Mentor

Generations of neuroscientists have been inspired, influenced and trained by Colin's work. A brief chat with him made us feel energised and enthusiastic about our own work. Even after leaving his laboratory, he always showed great interest in our progress and encouraged is to develop further the ideas that we started together, being very proud if we made more advances. Many of the graduate students and postdoctoral fellows from his laboratory remained collaborators and friends for decades (https://neurotree.org/neurotree/tree.php?pid=205). Colin was extremely supportive especially to young researchers. He quickly understood the major goals of their research areas and gave many useful suggestions that were absolutely on point. He created a culture of collaboration at every scale and he put us in touch with the most qualified experts in the UK, Europe, Japan or US to pursue

collaborative work. These gestures of Colin will stay with us for the rest of our lives. Wo hope to pass this legacy down to our students and hope to their students' students. Colin will be dearly missed by all his many friends, generations of medical and biomedical students and the entire scientific community. He is survived by his three daughters Sarah-Jayne, Sophie and Jessica and four grandchildren. Colin's department in Oxford has renamed its Lecture Theatre to Blakemore Lecture Theatre in recognition of Colin's life and work.

(3084 words to this point here: but I think we should get rid of all the sub-headings)

~~**interests outside of science.**~~

~~Colin has excelled in sport from early ages. He was a superb long-distance runner who completed 18 marathons and maintained an enviable level of fitness until well into his 70s. His PB time was 2 hours 43 minutes. Colin was health fanatic and followed the newest developments in the recommendations in diet, nutrient supplements, exercise and vaccination. He was a wine enthusiast who could enjoy a bargain from Lidl or from Magdalen College Cellar. He had a unique collection of paintings and artworks, including some Miro, Picasso and …… He had superb eye for treasures during his foreign travels. He also put in great care to have some historic displays in the department to cultivate the legacy of Sir Charles Sherrington, Sir John Carew Eccles and many others who worked in our department.~~

~~Amend or abandon??~~

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