

Trieste, 25 July 2023

SISSA mourns the loss of Professor John Nicholls – neuroscientist, colleague, mentor, advisor, and friend – who passed away on July 13, 2023. He leaves two sons, Julian and Stephen, two grandchildren, and his partner, Bettina von Hacke.

John Nicholls came to SISSA in 1998, having already earned recognition for a series of fundamental research lines in neurobiology, and gave our university over 20 years of scientific expertise, teaching, wisdom, and friendship.

John Graham Nicholls was born in 1929 in London. His parents had settled there after fleeing the hardships and persecutions of eastern Europe. His father, Nicolai, was a medical doctor and his mother, Lottie, was active in many aspects of classical music, principally in organizing and guiding the careers of young musicians. His youth was influenced by music and by the trauma of the Second World War, which required him to move to a school outside of the city.

Nicholls studied medicine in the 1950s at King's College, earned his degree at Charing Cross Hospital, and practiced clinical medicine for two years. In the light-hearted recounting of some of his life's most meaningful and outrageous experiences (*Pioneers of Neurobiology: My Brilliant Eccentric Heroes*, Sinauer, 2014), Nicholls depicts the episode in which he realized that treating patients was not to be his life's work. But, thanks to a first-class degree and the medical faculty's Physiology Prize, he was offered a PhD fellowship of £250 per year for two years. Bernard Katz (Nobel Prize in Physiology or Medicine, 1970), head of the Biophysics unit at University College London, accepted Nicholls into the laboratory. Under the supervision of Katz, Nicholls was awarded the PhD degree in 1955 for studies on the electrical properties of denervated skeletal muscle. It was in this period that elements of Nicholls' life-long academic credo began to take shape, including the choice never to put his name on a paper unless he had done the experiments with his own hands. One formative episode was Nicholls' rehearsal of his first-ever talk – from Katz's sharp critique, Nicholls learned how to prepare a succinct communication within the time limit. And luckily so: at the Physiological Society the next day, Lord Adrian, Henry Dale, Alan Hodgkin, and Andrew Huxley – all Nobel laureates – attended Nicholls' talk. For the next 70 years, Nicholls' students benefited from his firm, yet patient and humorous, tutorship on how to give an effective 10-minute talk.



On many occasions Nicholls spoke and wrote about the awe and trepidation of working under the exacting standards of Bernard Katz. Yet, years later, Nicholls and his parents became good friends of Katz and his wife, Rita, united by shared interests, including the love of Beethoven.

Nicholls did postdoctoral work at University College London and Oxford. He then went to Harvard (1962-65) to join the laboratory of Stephen Kuffler, where they showed that ions and small molecules move from blood to neurons by diffusion through extracellular space, not by transport through glial cells. They also discovered the long lasting hyperpolarization of glial cells after activity of nearby neurons and demonstrated that glial cells take up potassium at sites of activity and secrete it elsewhere, a function now known as spatial buffering.

His first faculty position, taken in 1965, was in the Physiology Department at Yale University, but in 1968 he returned to Harvard as associate professor. In 1966 Kuffler had begun to recruit to Harvard a faculty team that included David Hubel and Torsten Wiesel (winners, together, of the Nobel Prize in Physiology or Medicine, 1983) and several other brilliant young scientists. At that time, the practice was to segment brain research into the separate departments of anatomy, physiology, neurology, pharmacology, and so on. By contrast, Kuffler's idea was to build a single discipline based on investigating the nervous system as an integrative organ. Kuffler thus established from this core group a new research field, neurobiology, and the world's first Department of Neurobiology. Nicholls leapt at the opportunity to be part of it.

With his first Harvard graduate student, Denis Baylor, Nicholls began a new research line to investigate patterns of regeneration between individual nerve cells in the central nervous system of the leech. All the while, the collaboration and friendship with Kuffler deepened. While doing summertime research together at the Woods Hole Marine Biological Laboratory, they began the project of writing a textbook about the nervous system. They wished to propagate the idea of neurobiology as a cross-disciplinary research effort and set out to do so by presenting the actual experiments that ultimately led to the creation of new understanding. The book was not meant to be encyclopedic but to provide a glimpse, through selected problems treated in depth, into how (and why) brain research is done. And it was meant to be fun. The first edition of *From Neuron to Brain* (Sinauer) was published in 1976 and this popular textbook has been updated through the sixth edition (2021).

Nicholls moved from Harvard to Stanford in 1973, attracted by the prospect of starting a new neurobiology department. Collaborating closely with students and postdocs, he continued to work out the functional circuitry of the leech nervous

system. But his renown for discoveries in that system now began to work against him: he wanted to chase new problems and worried that US funding agencies would expect him to keep doing exactly what he already knew how to do. The Biozentrum of Basel University offered to support novel research lines, so he moved there in 1983. There, Nicholls established research projects concerning the origin of the respiratory rhythm in the brain stem as well as the regeneration of neurons after spinal cord injury. For the latter problem, he investigated opossum pups; they are born immature, and the spinal cord can regenerate if lesioned at the age of 6 days. If lesioned at the age of 9 days, regeneration no longer occurs. How does it regenerate, and what process inhibits regeneration in the older pup? For these and many other contributions, Nicholls was elected Fellow of the Royal Society in 1988 and received numerous prestigious honors, prizes, and medals.

Nicholls was passionate about teaching, and his efforts were never limited to his home institution. In 1994 the secretary of the International Brain Research Organization (IBRO) invited him to direct the Visiting Lecturer Program. The program aimed to bring neuroscience to regions that lacked infrastructure and education, and Nicholls was fully invested in the mission, once writing "Do those students not have the right to become interested in the nervous system?" Under the format developed by Nicholls, a group of five neurobiologists, all leading researchers, would give five lectures and also hold small group meetings, every day for 10 days. The small meetings would be devoted to teaching the students how to give a 10-minute talk, which they would present on the last day. In Asuncion, Paraguay, at the end of the course, the students went to the Dean of the Medical School and asked for a laboratory and materials to begin research. By the time Nicholls passed the program to the next director in 2002, it had reached over 1000 students through 21 courses held in 18 different countries. In 2003 IBRO named a fellowship in his honour.

As obligatory retirement from Basel University loomed at the age of 70, contacts with Andrea Nistri and other SISSA faculty brought Nicholls to Trieste in 1998. The long tenure at SISSA, however, was anything but a quiet rest. Nicholls set up a new lab and opossum colony. With Miranda Mladinic and others, he continued the experiments on spinal cord regeneration in the immature opossum, documenting developmental changes of gene expression after spinal cord injury in neonatal opossums.

In parallel, Nicholls established at SISSA an introductory doctoral course in neurobiology. The classroom meetings were treasured by the students as Nicholls, with every phrase rehearsed to perfection, taught the experiments of the pioneers (Katz, Hodgkin, Huxley, Kuffler, Hubel & Wiesel, and others), grasping

the original reprint in his fist as he sketched experimental designs on the blackboard. He also held smaller, free-form meetings, where students discussed their ongoing doctoral research and learned how to give a 10-minute talk, and how to write. At the end of every teaching cycle, Nicholls and his partner, Bettina, hosted the students for dinner at his home or at a Trieste restaurant. While the students felt immeasurable gratitude, it was Nicholls who would thank them profusely, and sincerely, for allowing him to be a part of their lives.

When declining vision no longer permitted him to run the experiments himself, around 2010, he closed his research activity. Without laboratory responsibilities, Nicholls redoubled his teaching and tutoring activities at SISSA, and devoted time to another book, *The Mindless Brain*. Written (with Alasdair Gibb and David Brown, of University College London) for non-experts, this book (to be published) explores the nervous system's control over functions we are not even aware of – breathing, balance, digesting.

SISSA joins countless collaborators, former students, and friends distributed across every continent in honoring the memory of John Graham Nicholls.