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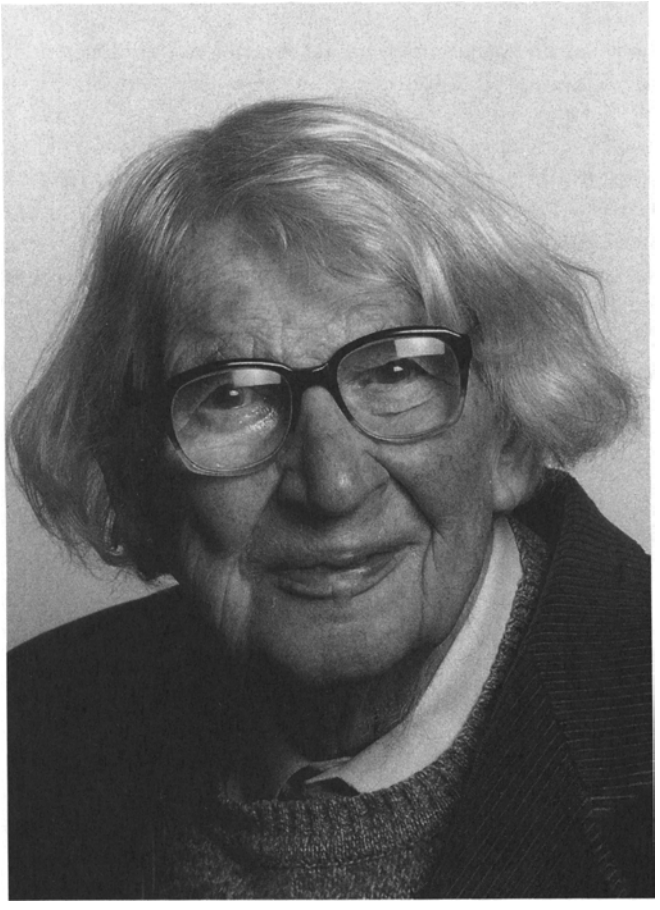

John Z. Young

BORN:

Bristol, England
March 18, 1907

EDUCATION:

Malborough College, Wiltshire, U.K.
Magdalen College, Oxford, M.A. (Zoology, 1928)

APPOINTMENTS:

Oxford University (1931)
Professor of Anatomy Emeritus, University College of London (1974)

HONORS AND AWARDS:

Fellow, Royal Society of London (1945)
Foreign Member, American Academy of Arts and Sciences (1957)
Royal Medal, Royal Society (1967)
Linnean Medal, Linnean Society (1973)
Member Lincei Soc., Accademia Nationale de Lincei (1973)
Honorary Fellow, British Academy (1986)
Foreign Member American Philosophical Society (1973)

John Z. Young carried out fundamental studies of invertebrate nervous systems. He discovered the squid giant axon and pioneered the use of the octopus for neurobiological studies. His work on octopus included studies of the radula, statocysts, eye muscles, visual behavior, and memory. His several books portray his broad interests in biology, zoology, brains, and minds.

John Z. Young

Ancestors and Relatives

If one can inherit scientific ability, I had a good start through both my parents. Dr. Thomas Young, F.R.S., was my great granduncle on my father's side. Thomas not only discovered the wave theory of light and the three-color process of vision, but was the founder of all modern neurophysiology by his claims that nerves carry information by their varying types. His is an everyday name through Young's module of elasticity. My maternal grandfather was John Eliot Howard, F.R.S. He was a chemist who discovered how to separate quinine from the toxic alkaloids in bark. His father, Luke Howard, F.R.S., was a meteorologist who studied the clouds and gave the names cumulus, nimbus, and cirrus. My second cousin, Henry Eliot Howard, F.Z.S., was a naturalist who established the function of song in territory in bird life.

Earliest Science

From childhood I was interested in how things change. At about age 10 I was given a chemistry set and became fascinated by the effects of heating, cooling, precipitation, and acids and alkalis. There were only simple inorganic chemicals in the set, but I began to supplement them by visits to the "chemist's." In those days, chemists were true pharmacists, who made up their own prescriptions. I used to go to these shops, past the huge flasks of water of various colors, which were the sign of the chemist. Inside the shops were rows of large drawers with label abbreviations such as Tinct. iod. I made friends with the chemists and tried to get them to sell me strong acids—which of course they would not do. Early on, I was interested in electrical communication. First, I learned about magnetism and made buzzers and bells all over the house. Then, it was telephones, and soon the wireless. In about 1920 I made a wireless receiver with a crystal set and coil and condenser, all homemade. This interest in wires and communication has stayed with me and is perhaps at the basis of my interest in nerves.

At my first school there was no science at all, but I developed some interest in history. During the first years at my secondary school, there was also little science. It was a public school—Marlborough—and I suf-

fered the usual hardships of boys who are no good at games. But I cannot say that I was really bullied or unhappy, and I loved the Wiltshire countryside, over which we were sent for long "runs" when the weather was bad. There was little science in the middle school, and I found that dull after my own experiments with chemicals and wires. I found no interest in chemistry until I came across the periodic table, which made some sense of it all. Organic chemistry seemed to me more systematic, with the families of acids and alcohols. Physics was deadly dull; I could not see the point in weighing bottles and knowing the difference between weight and mass; there was nothing about atoms or modern physics. Physics became interesting only when the instructors got to electricity and taught me more of what I had already found out for myself—how a current is produced and how it can be made to work motors, bells, and the wireless.

Introduction to Biology

I had not studied biology except when, at about seven years of age, I found fairy shrimps (*Chirocephalus*) in a pond near our house. When I reached the VIth form at the age of 16, I was taken on by a remarkable man, A.G. Lowndes. He realized that I was no good at chemistry and suggested that I study biology. I loved it from the first day, dissecting a rabbit before breakfast. Living tissues are wonderfully beautiful, whether fresh or seen under the microscope. Lowndes was a great teacher and had had a mixed career. From age 13 to 26, he had been in the merchant Navy. Then he went to Cambridge and took a double first class degree. Next he became a successful teacher and also did valuable research on Crustacea. He drove his pupils hard but gave them real opportunities to find fascination in living things and the possibilities of exact investigation of them. Several of his pupils became fellows of the Royal Society.

Oxford, 1925–1928

After one year under the guidance of Lowndes, I became a Demy (scholar) of Magdalen College, Oxford, and there studied zoology under E.S. Goodrich and Gavin de Beer. They were both able comparative anatomists (especially of the skull) but knew little of how to study function. From them I learned a great deal of comparative anatomy and later combined it with functional studies in *The Life of Vertebrates* (Young, 1950b). The third edition, issued in 1981, still sells more than a thousand copies a year in various languages 45 years after its initial publication. To it I tried to add functional knowledge to the comparative anatomy I learned from Goodrich and de Beer. But there is little in it about the nervous system. I find it curious that my name, for many people, is associated with that book rather than with my research, especially my work with the giant

nerve fibers. I often meet people who tell me that their introduction to biology was through *The Life of Vertebrates*.

Embryology and Evolution

Gavin de Beer had a great knowledge of the literature of experimental embryology. From him I learned of the experiments of Spemann and others on the induction of the sequence of processes of differentiation from the action of a limited region of the embryo, probably by diffusion of stimulants. Insight into the process of morphogenesis is essential if one is to understand how the effects of the genes unfold to produce an embryo. An idea of this is essential for an understanding of the whole process of evolution. With this background I have never had any difficulty believing Darwinian evolution. Understanding of the process of differentiation makes it possible to realize how change of genes may alter the gradient of concentration of morphogenetic molecules and so the shape, say, of a limb, giving selective advantage. I learned genetics early on through E.B. Ford, a disciple of R.A. Fisher. I found the genetical theory of natural selection provided a satisfactory account of how evolution proceeds. Throughout all the controversies of subsequent years, I have had no difficulty believing in the power of natural selection as the basic process in evolution.

Progress in Evolution

The problem of finding whether there is any direction in evolution is best attacked by considering the central fact of biology, namely that organisms maintain themselves distinct from the environment. I discussed the question of progress in a volume of essays presented to Goodrich in 1938. As I put it then, "Some organisms may be said to live in more difficult environments than others." I quoted C.S. Sherrington in his belief that "some organisms are higher than others in the sense that they dominate (the environment) more variously and extensively than do other organisms." I still believe that this concept of the varying difficulty of environments is useful though hard to quantify. Everyone must agree that there is some sense in which some complex organisms maintain themselves in situations that are inaccessible to those at a simpler level. As I put it in an article in 1938, "A marine protozoan is an aqueous salty system in an aqueous salty medium, but a man is an aqueous salty system in a medium in which there is but little water and most of that poor in salts." I used this conception of the colonization of more difficult habitats as a basis for discussion of the evolution of the nervous system. As I put it in 1938, "During the period since the Cambrian there has been a tendency for some of the organisms to become provided with more complex systems of self-maintenance by redistribution of energy than were possessed by their ancestors. This is especially clear from study of the nervous system." I went on to

show how the evolution of receptor and effector mechanisms and of the central nervous system shows this development of more complex systems.

Nerve Fibers and Synapses

My interest in the nervous system came through the school of C.S. Sherrington, who was professor of physiology in Oxford. He was a nice man, small in stature. When I told him about the fusion of the giant nerve fibers, he looked up at me and said, "Well, Young, if you say so I should believe it—but I find it difficult." He had, of course, been a champion with Santiago Ramón y Cajal of the independence of neurons and was against the reticular theory of Camillo Golgi. I went to visit Sherrington in 1945 when he was 88 years old and in a nursing home in Cambridge run by nuns. He greatly admired Goethe because of his nature worship: "How he admired the profligacy of nature. And why shouldn't nature be profligate, think of the spermatozoa, Young, millions of them," he said with a twinkle in his eye, deliciously innocent but naughty. I never went to his lectures but was greatly stimulated by his colleagues, especially Derek Denny-Brown and J.C. Eccles. Denny-Brown in particular taught me how to use the silver methods of Cajal to study nerve cells and their processes. I learned from these people about the problems of the brain and about the physiology of the nervous system, the study of which, then as now, was centered on the synapse.

I suggested to Eccles that the earthworm giant fibers would be interesting because they are interrupted by a series of membranes. He and I joined with Ragnar Granit, who was then working in Oxford. We showed that nerve impulses pass in either direction across these membranes. The paper by Eccles, Granit, and Young (1932) in *Procedings of the Physiology Society* must be an unusual example of cooperation in early work by later leaders.

I became fascinated by the question of the structure of nerve fibers and synapses. This subject has remained a central interest for me. All my thinking about how the nervous system works has been centered on the properties of nerve fibers and the connections between them. This has given me what I suppose could be called a rather mechanistic view of the brain and a reductionist attitude to the great problems of life and philosophy. I love diagrams of the patterns of organization of nerve fibers and the connections between them. This is evident in my later thoughts about memory as encoded in a series of matrices. With my early interest in electrical communication, I was naturally intrigued by the evidence that nervous conduction was an electrical process. I read about the work of Keith Lucas and Adrian but without understanding the details. I was fascinated by the fibrils within nerve fibers and found it difficult to understand that membrane properties were involved in nervous conduction. I was especially interested in the structure of synaptic junctions and fully accepted that there was no continuity at the synapse. I therefore readily received the evidence of chemical transmission at synaps-

es. I was fascinated by Dales experiments showing the chemical action of the vagus on the heart. Some of my earliest research was on the adrenal glands in dogfishes. This work led me to questions of chemical correlation. I published an article in which I suggested that we can recognize chemical action at three levels—vascular hormones, tissue hormones, and intracellular hormones (Young, 1934). Of tissue hormones I said that "some workers would go further and suggest that all transmission across synapses from one neuron to another is mediated by the liberation of a hormone." For this I quoted G.H. Parker, 1932, whose work in this context is often forgotten. For "intracellular hormones" I quoted the ideas of Goldschmidt that male and female sex determinants are produced by the chromosomes.

Naples, 1928–1929

Immediately after graduation I went to the Zoological Station in Naples, helped by a scholarship provided by Oxford. I went with the primary aim of studying the autonomic nervous system of fishes and was indeed fortunate to find satisfactory material in the fishes *Lophius* and *Uranoscopus*.

Autonomic Nerves

The sympathetic nervous system of the dogfish was the special subject for my degree in 1928, and I am still working on this subject in 1996. The general problem is to find out whether it is possible to recognize sympathetic and parasympathetic systems working in opposite directions in fishes as they do in mammals, according to the classical view of Langley. The answer is, briefly, "no." The visceral nerves are highly complex. I have given a detailed analysis of the anatomy of the nerves of the gut of dogfish and also of two teleostean angler fishes, *Lophius* and *Uranoscopus*. These species proved to be especially suitable because they are flattened and have no air bladder, and the sympathetic system can therefore be clearly displayed. I studied the effects of electrical stimulation and drugs on isolated pieces of the muscular coats of the viscera. The results showed no evidence for recognizing distinct sympathetic and parasympathetic systems. "The pharmacological reactions are almost uniform for the muscles here studied, acetylcholine causing contraction and adrenalin relaxation in every case" (Young, 1936). This conclusion refers not only to the muscles of the gut but also to those of the bladder and ovary (which in these animals is a hollow sac!). Later experiments showed many further complications, including the effect of ATP in the action of the vagus (Young, 1980a and 1980b).

An interesting complication appeared early with the observation that the iris muscle of these animals is controlled by sympathetic nerves producing constriction when stimulated and the third nerve producing dilation (Young, 1931). This is, of course, the direction of action opposite to that in mammals. Unfortunately, there has been no explanation of this curious contrast.

In the elasmobranch fishes—dogfish and rays—I found results quite different from those in teleosts (Young, 1980a). Stimulation of the vagus nerve has little effect on the muscles of the stomach, but stimulation of the sympathetic nerve produces inhibition followed by a large rebound after the stimulus ends. These actions are initiated by serotonin and by ATP; acetylcholine and adrenalin have only smaller effects. These fishes have a characteristic short spiral intestine, the muscles of which contract in response to electrical stimulation; and this reaction is imitated by adrenalin. The reactions of the rectum and urinary bladder are especially interesting because they receive a distinct pelvic nerve. These muscles showed spontaneous contractions that were inhibited by stimulation of the sympathetic nerve and by adrenalin or ATP but activated by 5 HT. These complex results show that it is not possible to recognize distinct sympathetic and parasympathetic systems in fishes on either morphological or pharmacological grounds. The viscera are controlled by different nerves using various combinations of transmitters to meet particular functional requirements.

I have been able in recent years, with the cooperation of Paul Andrews, to make satisfactory applications of these results to actual movements of the stomachs of freshly killed dogfish and skate. Electrical stimulation of the splanchnic sympathetic nerves of the dogfish produced contractions of the longitudinal muscles of the stomach, moving the contents forward even to the point of vomiting. Later there were contractions of the circular muscles, mixing the stomach contents. These movements were simulated by 5 HT, the effects of which were blocked by antagonists such as methysergide. These results thus support the evidence of the importance of 5 HT in these fishes. There are many complications such as the effect of peptides for which we also found evidence. The motor effects are so complicated that it is most unlikely that a single transmitter is involved. The general lesson that I have learned from this excursion over many years of physiology and pharmacology is that the nervous control of any process is complex. Even the fibers running in a single nerve may consist of several types producing varying effects, even on one organ.

The value of such work on little known animals like the fishes is to explore the different means by which homeostasis is ensured. These questions are summarized in the books by Nilsson (1983) and Nilsson and Holmgren (1994). They follow exactly the object of my work, and I am proud that the latter book is dedicated to me.

Cephalopods

The most important effect of my visit to Naples in 1928, however, was my introduction to the cephalopods. This came about through Enrico Sereni, who was professor of physiology at the Stazione Zoologica. He was an active physiologist but, unfortunately, had a short career. He and his

brother were communists and Enrico held meetings among workers at Castelamare, which was dangerous under the fascist regime. A year later he was found dead in his bath from causes never fully revealed. His brother became a prominent senator after the war.

The Epistellar Body: Photosensitive Vesicles

When I went to Naples, Enrico was studying various features of the physiology of *Octopus*, and with him I investigated the regeneration of their nerves. In the course of this, I found an undescribed organ—the epistellar body—attached to the stellate ganglion (Young, 1929). At the time I thought it was a gland, but 25 years later Alex Mauro showed that the processes in its center are rhabdoms, containing rhodopsin and responding to light. These extraocular photoreceptors, now known as photosensitive vesicles, have been seen in many squids where they may control counterillumination, turning the luminous organs on and off to match the wavelength and intensity of the down-welling light (R.E. Young, 1978).

Giant Nerve Fibers

It was while looking for the epistellar body in squids that I found the giant nerve fibers. There is no epistellar body at the hind end of the stellate ganglion in these animals, but there I saw a mass of small nerve cells, the processes of which fuse to form one giant fiber in each stellar nerve. At first I could hardly believe that these huge transparent strands were nerve fiber. They were more like veins. A simple experiment at the Marine Biological Laboratory in Woods Hole, Massachusetts then proved their action. You pinch the nerve close to the ganglion and a part of the mantle muscle contracts. Then you crush the fiber lower down and a pinch above this is no longer effective. Of course, we went on to show a sequence of action potentials after stimulating the fiber.

In the following years I worked out the detailed anatomy of the giant fiber system. It proved to be a curious mixture of conventional synapses and an unusual fusion of axons. The giant nerve cells in the brain had already been shown by Williams in 1909, but he supposed that their axons ran all the way to the stellar nerves. He gave no descriptions or illustrations of them. His work had not been referred to by anyone in the intervening years, so far as I can discover.

The two axons of the giant nerve cells in fact proceed only as far as the palliovisceral ganglion where they join, in *Loligo*, in a midline commissure. In other species of squids and in cuttlefish, the two axons do not fuse but make synaptic contacts with each other. This obviously ensures that the two sides of the mantle always contract together. This is an interesting demonstration that the law of neuron theory can be broken. Nerve fibers can fuse when they must always work together. This is "the exception that proves the rule" that discontinuity and synaptic action are necessary for

usual nerve functioning. The giant fibers in fact provide, in the stellate ganglion, synapses that are particularly useful for study. There it is possible to record electrically on both sides of the synapse. A further interesting feature of the system is the graded size of the giant fibers. R.J. Pumphrey and I were able to show that the smaller anterior fibers are slower and that the velocity of conduction follows the square root of the diameter. Alan Hodgkin helped us with these experiments and so began his great series of investigations of the giant axons. Of course the most valuable feature of the fibers for physiologists is their large size and accessibility. This feature allowed Alan Hodgkin and Andrew Huxley, and later many others, to increase greatly our understanding of the excitability of the nerve membrane and conduction of the nerve impulse. Indeed, the giant nerve fiber of the squid has become the classic material for the study of excitable membranes.

I made many other studies of the giant nerve fibers. With D.A. Webb I studied their content of potassium and sodium for correlation with the size of the action potential. With R.S. Bear and Frank Schmitt I made a thorough study of the sheath components of the fibers (Bear et al., 1937). This study was especially valuable to me as an introduction to the use of polarized light microscopy.

Chicago, 1936

My detailed study of synapses led to the next large change in my career, which was started by a Rockefeller Fellowship in 1936 and a visit to Chicago and Woods Hole. I crossed the Atlantic Ocean with my first wife, Phyllis, on the Queen Mary and we went at once to stay with John Fulton and his wife at Yale. He was an active physiologist and one of the first to examine the physiology of the frontal cortex in a modern way. He was also a keen historian and built up a library, which I believe is now owned by Yale University. After a happy Christmas with the Fultons, my wife and I went on to Chicago. We went by air, which the Rockefeller officials considered unwise, and indeed we became grounded by the weather in Cleveland and had to continue by rail.

In Chicago I worked in the anatomy department to meet C. Bartelmez who, as an embryologist, had developed special methods for preparing tissue for microscopy. I wanted to apply these methods to synapses, which were then studied mostly by silver methods, involving severe fixation and artifacts. Curiously enough, David Bodian came to Chicago at the same time for the same purpose, his material being Mauthner cells of fishes, which have large synapses. I got to know him well, and we played handball in the baseball building later used to make the atom bomb. While I was in Chicago I met many biologists. Paul Weiss was in the zoology department and Ralph Gerard in physiology. With Gerard, I studied the electrical activity of the brain of the frog, which is remarkable in that the waves continue after the brain is removed from the head (Gerard and

Young, 1936). Of the many other people I met there, perhaps the most interesting was H. Kluver, who made pioneer studies of how, after certain lesions of the brain, monkeys no longer show any fear of snakes.

From Chicago I went for a visit to St. Louis, where many people were working on the nervous system. Gasser and Erlanger were doing their classical studies on conduction in different sorts of nerve fibers. Gasser was a particularly nice man, tall and smiling with a high child's voice. I later stayed with him in New York. He was especially interested in the large and small fibers in a squid. Frank Schmitt, with whom I stayed in St. Louis, and his brother Otto, were making some of the first electronic recordings of electrical activities. I remember my surprise going into Schmitt's lab where a nerve was being stimulated—in absolute silence. I was used to labs in Sherrington's department that were an untidy maze of wires and where recording was done by a Matthews oscillograph after stimulation with a clanking Lucas pendulum.

Lorente de No came to my lecture and showed incredulity at the fusion of the giant fibers. He was an expert on the histology of the nervous system and did not like anyone else explaining the facts to him. Also there were George Bishop, always skeptical, and Peter Heinbacher. I went especially to see Kuntz but found that he was not very interested in the evolution of the autonomic nervous system of lower vertebrates. This visit to St. Louis was especially profitable because I arranged to join Frank Schmitt for work at Woods Hole the following summer.

Woods Hole, 1936

Before going to Woods Hole I went to a meeting at Cold Spring Harbor, where I lectured on the squid giant fibers and met K.C. Cole, who later made such good use of them. We tried to get squids from fishermen on Long Island, and we carried the squids back in large milk cans, but none survived. However, at Woods Hole squids are plentiful and we soon made the first studies of their action potentials. I tried to do this with Ralph Gerard, Det Bronk, and Keffer Hartline, but at first even these great men could not operate the stimulator and oscilloscope. So one day when Ralph and Det were out I suggested to Keffer that we put a crystal of oxalate on the cut end of the nerve, and out came a wonderful buzz and series of spikes—the first of many thousands of giant fiber impulses.

Oxford, 1937–1945

Lampreys and Cephalopods

During 1937 to 1945 as a Fellow of Magdalen and demonstrator (lecturer) in zoology, I taught many aspects of zoology under Goodrich. I continued work on the giant nerve fiber at Plymouth, largely with R.J. Pumphrey. It

was not easy to catch squids in good condition by trawling. The ship would make a special quick haul at the end of each day's work and come in at 4 o'clock. Meanwhile we had been bathing off the rocks below the lab. As soon as the ship arrived we started work and went on into the night.

At Oxford I worked mainly with lampreys. I had the idea to study one species of animal thoroughly—its behavior, its brain, and its possibilities for research. The lamprey seemed to be a good candidate because the larvae (*ammocoetes*) are abundant in the rivers at Oxford, and the adults are caught for food as they come up the river Severn. The lamprey proved to be an interesting animal. I was able to show for the first time that the pineal body is truly a photoreceptor; without it the animals do not change color at night. There are photoreceptors also in the tail, the impulses of which (unexpectedly) pass forward in the lateral line nerve. We also showed that the pituitary controls reproduction.

However, the brain of the lamprey was hard to investigate. There seemed to be little behavior that could be studied in the laboratory, so I thought that my plan should be transferred to the cephalopods. While looking for the giant fibers in squids I had seen the wonderful higher centers of the brain, hitherto little known. In particular, there are lobes that stimulate one another reciprocally. With F.K. Sanders I found that cutting such connections in the cuttlefish (*Sepia*) made the animals unable to follow a prawn that had disappeared out of sight. This finding led me to study the memory of cephalopods (discussed later).

Regeneration of Nerves

During World War II, I organized a group in Oxford to study the possibility of improving the results of surgery after injury to peripheral nerves. A special Center for Nerve Injuries was set up under the orthopedist Professor H.J. Seddon, and I collaborated with him in clinical and experimental studies. Many nerve injuries in wartime do not result in complete interruptions of nerves but cause damage by compression. The problem for surgeons is to know how long to wait for "spontaneous" recovery. The solution requires study of the rate of regeneration under various circumstances, and this we studied experimentally in rabbits. We also studied the clinical literature to find what results might be expected. The group involved no fewer than three people who later became fellows of the Royal Society, and one Nobel Prize winner—P.B. Medawar. The rate of regeneration of course includes not only the time for regrowth of the fibers but also for their maturation to a state fit to function. We found that the process of increase of diameter and myelination depends on both conditions at the lesion and connection with a suitable periphery. This work also led to study of the dependence of nerves on the connection with the cell body. I showed that after severance the central cut end swells more than the peripheral (Young, 1944).

This finding was evidence of axoplasmic transports found by Weiss at the same time.

A great problem for surgeons is the repair of gaps in damaged peripheral nerves. We experimented with various forms of grafting and showed that only nerves from the same individual were effective. This was Peter Medawar's first contact with grafts, and I believe it was the background for his discovery of the immune responses to foreign tissues.

Part of our work involved studying the atrophy of denervated muscle and means of delaying it. This was the field of Ludwig Guttmann, who joined us as a German refugee. Not allowed to do clinical work, he studied muscle atrophy in rabbits and went on to study rehabilitation in humans. This work led him to found the special clinic at Stoke Mandeville and ultimately led to the International Olympic Games for the Handicapped.

Another discovery we made during this work was that the length of internodes in nerves is a function of growth. We found that they are unusually long in eels, but short in nerves that have regenerated in adults. This finding has led to valuable diagnostic techniques for neurologists, which have been developed by P.K. Thomas, who worked with me on the eels. He is now a professor of neurology and has written a large work on the subject, to which I wrote a preface.

Professor of Anatomy, 1945–1974

University College of London was the first British medical school to appoint a zoologist as professor of anatomy. I insisted that all the staff do research and that the students take an extra year of biological work, for which we gave courses and awarded an honors degree, which has now become general practice. I happily meet old students who have become specialists in many aspects of medicine. A lot of postgraduate students and visitors came to University College and have become professors in many countries.

I tried to familiarize myself with human anatomy, but I was never able to teach the details. However, we devised methods of teaching anatomy as an experimental subject. These methods were published as a manual of anatomy that became widely used. The methods involved a system of studies in which students learned the action of bones and muscles by practical experiments on themselves or others. The emphasis was on discovery rather than demonstration by the teachers.

Perhaps my most useful contribution as professor of anatomy was a series of weekly lectures called "An Introduction to the Study of Man" (Young, 1971b). The lectures included discussions of many things such as philosophy, population numbers, and human evolution. These topics are often omitted by medical students who, at some colleges, do only two years of classes before becoming locked up in clinical work taught by dedicated but single-minded doctors.

The Flying Spot Microscope

One of my interests was to find ways to quantify microscopical data. It struck me as anomalous that one of our most powerful instruments yields only pictures. I therefore recruited an engineer, Frank Roberts, to apply scanning techniques to the microscope. With him and David Causley, I devised one of the first flying spot microscopes. We needed it especially to count the nerve fibers in normal and regenerating nerves. I was also interested in the subdivision of the cerebral cortex. The maps of cerebral areas by Brodmann were valuable but not quantitative. Exact delimitation of areas was obviously too difficult to do by eye and required automatic counts of numbers and sizes of nerve cells.

The microscope that we devised was technically successful and attracted wide attention, but it was not practically useful. The reason was that microanatomical preparations, even if well stained, do not define the edges of cells unambiguously. Successful counting was achieved only for simple black preparations such as those of dust particles. I gather that the problem of counting cells in brains is still only partly solved and essentially involves measurement of the size of each particle counted (Roberts and Young, 1951).

However, our engineering work changed course under W.K. Taylor into study of the recognition of patterns by machines. He devised, with D. Causley, a large machine that successfully recognized letters and faces, based essentially on the principles known a little later as a perceptron. This work was all in the 1940s and 1950s before the introduction of modern techniques. The instruments were large, involving hundreds of valves. Contacts with engineers gave me great help in understanding the problems of communication and vision.

Electron Microscopy

Being interested in the fine structure of tissues, I was naturally fascinated to hear of the possibilities of the electron microscope. My first direct contacts with it were with R.W.G. Wyckoff. He came to London as an official scientific representative and set up one of the earliest instruments within the American Embassy. On meeting him in 1953 and learning that he had no material to study, I prepared the spinal cord of a rabbit and we cut sections. The fixation in osmic acid was not good, but we made some of the first pictures of synapses with the electron microscope.

I was then able to recruit J. David Robertson in 1955 to set up an electron microscope department at University College where he continued his pioneer research on cell membranes and myelin sheaths of nerve fibers. We collaborated later on the brain of *Octopus* but I never learned the necessary techniques for myself. Dave remained with us for five years and we became great friends with him and his family. He became professor of anatomy at Duke University, and I often visited him there.

Anthropology

I became interested in primates and human history when working with Solly Zuckerman in Oxford. I made much further study of the fossil record of humans and of human diversity for my lectures to medical students, and for the book, *An Introduction to the Study of Man* (Young, 1971b). In this book I gave an account of the fossil evidence for human evolution and discussed the various theories of the climatic influences that were probably at work. I also tried to give an account of what is known about the origins of culture, language, and religion. I tried to connect these large subjects with what we know about the activities of the brain that are involved.

In this way I came to know many anthropologists in Britain and around the world. On a visit to Kenya as examiner in the university, I met Louis Leakey and his son Richard. On a later visit Richard flew me in his airplane to Olduvai Gorge. There Mrs. Mary Leakey showed me around the valley and what they called "the earliest human house." This was a wonderful visit, and it gave me insight into the practical problems of field anthropology. I was especially impressed by Mrs. Leakey's later discovery of the footprints of a family, presumably of *Homo erectus*. I was also impressed by the Leakeys' discoveries of fossil skulls, though somewhat skeptical of their early naming of the specimens. I was strongly in favor of Zuckerman's emphasis on the need to base human systematics on measurement.

With this background, I assisted in the joint organization by the British Academy and the Royal Society of a symposium on "The Emergence of Man" (1980). At this symposium I enjoyed meeting another group of anthropologists. I chaired a session and gave introductory remarks and tentative conclusions. I suppose it was useful to have a neurobiologist discussing these questions, but I never gave a really original contribution to the subject. I was therefore surprised when the British Academy offered me honorary membership. I suppose it was for my interest in anthropology, but I like to think that my other writings contributed as well. Randolph Quirk, president of the academy at that time, used various quotations from *The Life of Vertebrates* (1950b) as illustrations of the use of English. I should like to think that my contributions to current thought in the Reith Lectures and elsewhere played a part in my becoming F.B.A. as well as F.R.S.

The Radula of Cephalopods

In recent years I have spent a lot of time studying the radula—a toothed ribbon which moves in and out of the mouth of cephalopods during feeding. I first became interested in the radula because of a curious muscle involved in its movements, known as the "radula support" or "bolster" because of its shape. I saw in sections that the muscle fibers run across the bolster and are attached to the enclosing wall on one side but are free

at the other side where they are simply covered by a membrane. These muscle fibers are not attached to the radula ribbon and seem to have no function. In fact, like many muscles of mollusks, the action of the bolster is hydromuscular (Kier, 1982). Tightly enclosed in its sheath, the bolster must stiffen and change its shape when the muscles within it contract. The bolster is free at its front end, lying just beneath the point at which the ribbon moves out. By stimulating the bolster of *Octopus* electrically, I showed that the bolster does in fact elongate and push out the teeth.

An interesting complication is that in decapods, the bolster contains a mysterious structure known as the "rod." This rod contains large cells, which have been wrongly called cartilage. In fact, the bolster rod of cephalopods is a sac, with semiliquid contents. Enclosed in a membrane, the rod must change its shape when compressed. In fact, it elongates and in a cuttlefish actually protrudes from the bolster at the front end and pushes up the teeth of the radula. Bill Kier tells me that this is a unique case where a hydromuscular system transmits its force through a rod of this sort.

The question is of some general interest because bolsters with rods are found in the radula of many mollusks. I have examined them in many cephalopods. In *Nautilus* there is a large, watery rod attached to the front of the toothed ribbon. This may perhaps have been the original condition. The freeing of the front end allows more varied use of the teeth. In octopods, where there is no rod, the radula is used to bore holes in the shells of snails for the injection of poison. This highly sophisticated behavior involves recognition of a reward to be obtained later. Thus, there is a correlation between development of the radula and of a nervous system that is capable of a view of the future.

The Central Nervous System of Cephalopods

I have spent many years studying the anatomy and functions of the brain in cephalopods. This area was previously rather little studied, and I have tried to give a thorough account of it in *Octopus*, *Loligo*, *Sepia*, and *Nautilus*, and briefer accounts of a wide variety of other cephalopods. I have largely used light microscope sections stained by the method of Ramón y Cajal. This method works well, and I have made a large collection of sections of the brains of a great number of Cephalopod genera. The preparation of these sections has largely been the work of my technicians, especially James Armstrong, Pamela Stephens, and Tess Hogan. Such devoted attention to the preparation of long series of slides is essential for such work. We have also used Golgi methods, sometimes quite successfully.

In much of this anatomical work, I have been assisted by others. Brian Boycott was active from the start and is mostly responsible for the large book, *The Anatomy of the Brain of* Octopus vulgaris, to which he gave a

generous preface. Martin Wells contributed greatly to study of the tactile memory system. Others who have helped have been R. Lund, J.B. Messenger, J.S. Stanier, J.R. Pariss, M.F. Moody, V.G. Barber, G.F. Savage, J.S. Altmann, and M. Hobbs. Recently, I have had much help from B.U. Budelmann. Throughout, I have had continuous support from Dr. M. Nixon. She has an outstanding knowledge of cephalopods, which she has made available to me in many ways. Without her cooperation I could never have achieved so much.

The results of these investigations have been recorded in a series of papers and in a large book, *The Anatomy of the Nervous System of* Octopus vulgaris (Young, 1971a). The brain of *Loligo* has been described in similar detail across five papers in the *Transactions of the Royal Society*. The brain of *Sepia* was described by B. Boycott in 1961. Further detail will appear in the book by Dr. Nixon and I titled *The Brains and Lives of Cephalopods*. This book will give some information on the brain in every family of cephalopods. Altogether, therefore, we have tried to describe the anatomy of the nervous system throughout the group, and to note something of its functioning.

Many of the tracts in the octopus brain have been traced by degeneration methods. Some of the lobes have been examined by electron microscopy with the help of Dave Robertson and George Gray. Much work has also been done on the function of the various lobes, using electrical stimulation and study of the effects of removal and survival for both short and long periods.

The brain of cephalopods is divided into many lobes. It has been possible to recognize a clear-cut hierarchy of centers, but there is a special problem in that a large part of the nervous system lies outside the central ganglia. The centers in the arms contain 350 million nerve cells, the optic lobes contain 92 million, and the central brain only 42 million. Most of the final motor neurons and the reflex centers are therefore in the arm ganglia; the brain centers are mostly concerned with coordinated movements. We can recognize lower and higher centers. Their functions still are not fully understood, but some of them show striking similarity to centers in the vertebrate brain. For instance, the peduncle and anterior basal lobes contain many rows of fine fibers like those in the cerebellum. They may be concerned with the proper timing and succession of movements. Many studies have been made on the effects of electrical stimulation on these centers and of the defects that follow their removal. The parts of the brain occupying the regions above the higher motor centers give no response to electrical excitation and are concerned with memory and motivation, as will be discussed later.

Besides describing the connections of the cells of the brain, I have counted the cells and measured samples in the various genera of cephalopods. I have measured the volume of 30 of the lobes in 63 species. With the help of L. Maddock, I then compared these measurements using principal component analysis. The results provided the basis for the detailed description and discussions in the book to be published with M.

Nixon, *Brains and Lives of Cephalopods*. From this study I learned a great deal about the principles of organization that underlie the complex behavior of cephalopods. Comparison of *Nautilus* with the coleoids shows two conspicuous developments. First, new systems of motor control appeared in the higher motor centers—the peduncle and anterior basal lobes. Second, the higher supraoesophageal centers become developed for learning, memory, and motivation.

The modern coleoid brains are remarkably similar in their general organization, but their detailed differences are fascinating. The *Decabrachia* (squids) have especially well-developed visual systems and giant fibers for rapid movements and fins for steady movements. The *Octobrachia* have smaller optic lobes but specially developed centers for touch; the centers for the arms are greatly developed. The octopod brain shows great concentration and development of connection between the lobes, which are responsible for its highly integrated patterns of behavior.

These are only a few general characteristics. Within each group there are special developments correlated with the detailed habits of the species. For example, the deep-sea squid *Mastigoteuthis* has immensely long tentacles covered with minute suckers. Observations from submersibles have shown that this squid swims upside down, trailing its tentacles on the sea bottom to catch small crustacea. Our sections show that the tentacles and mantle both have connections directly with the magnocellular lobe, and this lobe has a complex internal structure and is larger than the vertical lobe. The magnocellular lobe has evidently become the main controlling agent for this special behavior. This and many other examples show the great capacity for evolutionary development involving quite wide departures from the general pattern. We hope that our descriptions of the nervous system of many little-known species will show similar correlations as their habits become known.

Statocysts of Cephalopods

I was attracted to the statocyst when I noticed that the crista of *Octopus* is a set of three ridges running in planes at right angles, like the semicircular canals of the vestibular systems of vertebrates (Young, 1960a). The ridges carry flaps, the cupulae, attached to sensory hairs, the movement of which registers the angular acceleration or velocity of turning in different planes. In cuttlefish and squids there is a series of projections. Some of these, which I called anticristae, partly enclose the crista. Others, called hamuli because they are hooked, limit the length of the cupulae. I suggested that the anticristae serve the same function as the vertebrate canals in limiting the flow of endolymph. In some squids the anticristae actually form a canal for part of the length of the crista. These restrictions by anticristae and hamuli reduce the flow of endolymph across the cupula flaps and alter the sensitivity to angular acceleration.

Measurements of the statocysts of *Loligo* and *Sepia* of different ages showed that the sacs are large at hatching and become relatively smaller with growth. The anticristae, however, are small or absent at first and grow faster than the body as a whole. These features limiting the endolymph are precisely similar to those imposed by the vertebrate canals. The cephalopods have evidently evolved a system functionally similar to that of vertebrates, using different materials. Measurements of the statocysts of a variety of cephalopods showed that they are large in 21 species of buoyant and deep sea forms, which move slowly and monitor slow turns by the large volume of fluid. These squids have small anticristae. Sixteen species of rapidly moving, nonbuoyant forms have small statocysts with large anticristae, which often form canals (Maddock and Young, 1984; Young, 1989).

I made a special study of the statocysts of cranchiid squids (Young, 1984). These squids have evolved a system of buoyancy by the use of their nitrogenous excretion to form ammonium chloride, which is lighter than sodium chloride. The liquid is stored in a special sac. Some species live in the deep sea and are transparent and slow moving. They have large statocysts, as would be expected, and they have few anticristae; one form, *Bathothauma*, is unique in having none at all. Conversely, some cranchiids move rapidly and have small statocysts with numerous anticristae. *Egea* has no fewer than 44 elongated rods. The significance of these extraordinary structures is still obscure. They show the great variety that has developed during cephalopod evolution, and they present great problems for future workers.

Eyes and Vision

I became interested in the details of the visual system of *Octopus* after observing that learning to make distinct reactions to visible shapes depends largely on the vertical and horizontal extents of the figures. Regularities in the retina and optic lobes provide clues to the mechanisms for coding in these two directions (Young, 1960b). The retinal receptors are the processes of the 107 million cells directed toward the lens, and each carries microvilli attached to opposite surfaces. These receptors are in pairs, one with villi in the horizontal and the other in the vertical plane. The retina thus has a strikingly regular pattern of squares. Each cell sends an axon into the optic nerves and so to the optic lobe. A strip of longer, thinner retinal cells runs horizontally along the equator. This presumably is a region of special importance, related to the presence of a horizontal pupil. Study of the adaptation of the retina to light and darkness shows that there is migration of pigment within and among the retinal cells. This migration occurs differently along the horizontal strip (Young, 1963).

The axons of the retinal cells enter the optic nerves, which make a striking chiasma that inverts the image dorso ventrally. I interpreted this

as attributable to the need for the visual system to work with the same orientation as the statocyst, involving gravity. This observation agrees with the finding that the dendrites of the second order neurons in the outer layer of the optic lobe are very long and are oriented largely, though not exclusively, in horizontal and vertical planes. Studies of form discrimination by N.S. Sutherland show that the animals can recognize rectangles in these two planes, but not when the rectangles are oblique. I therefore suspect that form recognition is accomplished by analysis of outlines, as suggested for mammals by David Hubel and Torsten Wiesel. Unfortunately, there has been no investigation of these cells (or any others) in the brain of *Octopus* using classical physiology. Attempts have been made by able researchers, but intracellular recordings had been impossible until done quite recently by B.U. Budelmann and T.H. Bullock. The reason for the difficulty is still not clear, but it may be the fragility of the finer blood vessels.

There are few suggestions for the functioning of the numerous large and small cells occupying the center of the optic lobes. In the outer part, the cells are arranged in columns, which are most marked in the species living in well-lit waters, and are reduced in those living deeper. Progressing inward in the optic lobes, there are more and more horizontal cells, presumably allowing for correlation between appearances in different parts of the field.

I have continued to be interested in the eyes of the various species of cephalopods, which show many variations. In some deep-sea forms, the *Bolitaenidae*, the eyes are elongated and transparent at one end but pigmented at the other. There thus seems to be an aphakic window allowing photosensitivity downward as well as laterally through the lens. A larger part of the retina is opposite the window, and the optic lobes are partly divided into two. In the deep sea, of course, the main light is bioluminescence. The eyes need to detect the direction of flashing prey; there is less need for form discrimination. Other visual simplifications are the absence of a lens in the cirrate octopod, *Cirrothauma*, and in *Nautilus*. In all these cases the optic lobes have few or no columns.

One of the most interesting questions about vision is the importance of visual search and movements on the retina. This question was emphasized for me by the importance of movement of the eyes in humans. I was impressed by the work of Yarbus (1967), who showed how eye movements pursue a search for items of interest. For example, when looking at a face, eye movements are mostly toward the eyes and mouth. I interpreted this finding in *Programs of the Brain* (Young, 1978). The direction of each eye movement depends on a forecast made by a program on the basis of information received as to what is likely to come next. Seeing in humans is thus not a matter of receiving a sort of photograph on the retina but is a dynamic process using a series of scans seeking answers to questions set by previous experience. The brain then constructs a hypothesis about what is there and produces appropriate action.

It would be most interesting to find whether vision in an octopus or squid consists of any such use of a program. Little information is available about any scanning process. An octopus bobs its head up and down when a new object appears. This movement would pass the image across the longitudinal strip at the center of the retina. Unfortunately, it is not possible to say any more yet about the process of vision in such animals, but I have been able to study the eye muscles with Ulli Budelmann, and they are certainly sufficiently developed to allow detailed scanning movements (Budelmann and Young, 1984, 1994).

Cephalopod Eye Muscles

In *Octopus* there are seven extraocular muscles, controlled by seven nerves. There are three recti muscles that produce linear movements and four oblique muscles, some of which pass halfway round the eyeball. We studied the movements of these muscles by stimulating the nerves and also recorded the constrictions and dilations of the pupil. By filling the nerves with cobalt we were able to identify the oculomotor center in the pedal suboesophageal lobe. Filling the nerves of the statocyst then showed that the static fibers run to many parts of the brain, including to the oculomotor center and to the higher motor centers of the basal and peduncle lobes. The statocyst-oculomotor system of *Octopus* thus shows two pathways from the receptors to the eye muscles, one direct and the other via higher motor centers where visual information is included with that from the statocysts. This system shows remarkable convergence with the vestibula-oculomotor system of vertebrates. Once again, we see how similar functional requirements have come to be met in similar ways despite differences in organization.

We went on to study the eye muscles of decapods and found a different situation (Budelmann and Young, 1993). There are 14 muscles in *Loligo* and 13 in *Sepia*. The extra muscles are all anterior and superior, and are concerned with the convergent eye movements used for binocular vision in fixating prey for capture by shooting out the tentacles. The muscles attached to the anterior face of the eye include two remarkable conjunctive muscles whose tendons cross the midline! Presumably the fibers on both sides contract together, moving both eyes at the same time during fixation. No such muscles are known in any other group of animals.

The other eye muscles of decapods are rather similar to those of octopods. The main actions of these muscles are linear, but three produce rotation. There are only four eye muscle nerves in decapods, and these nerves arise from an oculomotor center in the lateral anterior pedal lobe, as in octopods. An interesting feature of decapods is that the cell bodies for different nerves show different but overlapping distributions, which thus provides an opportunity to show that there are distinct motoneuron pools as in vertebrates.

Memory in Octopus

I first became interested in memory after seeing self re-exciting connections in the brain of cuttlefish, as discussed earlier. I then turned to the octopus, which has even more interesting memory centers than the cuttlefish and is much easier to work with. In *Octopus* the brain lies free in the cranium in a large cavity packed with jelly, and is accessible for operations. The animals are kept separately and their behavior can easily be studied. They are readily anesthetized, recover well from operations, and can be kept in the laboratory for months. I started experiments in Naples in 1947 with support from the Nuffield Foundation and also from the United States Air Force, which had shown interest in our work on the flying spot microscope. The Naples Zoological Station was ready to help with space and tanks. Octopuses are abundant in the Bay of Naples, and the fishermen of the station provided a constant supply.

Octopuses readily attack small crabs, and we fed them on these and dead sardines. Octopuses are ingenious at escaping through any small hole or crack, and we constantly suffered from escapes. Their arms can lift the lid of a tank, even if it is loaded with bricks. The octopus then forces its head and arms over the edge, drops the lid on itself, and dies. We found it necessary to design suitable tanks in which the octopus was given a home among bricks at one end and could be tested by showing it figures at the other end.

When an octopus is shown a strange moving object, it first watches it for a minute or more and then approaches it gradually, touches it with an arm, and takes it if it is eatable. Shown the same object again, it comes out more and more rapidly, finally attacking after only two or three seconds. This behavior shows a positive learning to attack. Conversely, if the octopus receives a shock, it remains at home. We tried various methods to automate this procedure, but the octopuses proved ingenious at removing anything attached to the tank. The problem was finally solved by Hector Maldonado with special tanks.

The training experiments used large sets of animals randomized between operations and controls. They were trained twice a day, and this involved many hours of work. I was helped in this by my wife, Raye, and daughter, Kate; also by students from University College, whom I brought out on my grants. This project gave the students some research experience and they enjoyed life with us in Naples.

The Two Sets of Memory Centers

In *Octopus* I soon found separate sets of centers for visual and tactile memory, with slight overlaps. Each set is composed of a sequence of four lobes that are similar in the two systems. Experiments have led me to give the following interpretation. The first lobe of each set receives fibers of taste from the lips and serves the positive learning to attack the object seen. This lobe sends fibers to the fourth lobe, which is a motor center. The sec-

ond lobe serves to assemble groups of signals, representing the input and passes them to the third lobe, which reassembles them with fibers that indicate pain. The axons from this lobe also pass to the fourth lobe, where they activate cells that produce retreat. The whole set thus constitutes an "unless" system, indicating taking the object seen or touched, unless pain supervenes. The presence of these two similar sets is striking evidence that their organization is an essential part of the learning system.

The Visual Memory Centers

This interpretation of the function of the paired lobes has been reached after a great many experiments over many years. In the visual system, the fibers of the optic tract carry signals already analyzed in the optic lobe. In the first of the paired centers, the signals meet taste signals from the lips. If this lateral superior frontal lobe has been removed, an octopus no longer makes attacks at a crab seen far away, even though it is not blind and will reach out an arm to take a crab placed near it.

In the second visual lobe, there are many interweaving bundles of branching visual fibers synapsing with the million cells of this superior frontal lobe. Each visual fiber thus meets many others on these cells, and vice versa. The axons of the cells carry signals representing the joint action of groups of photoreceptors. Granted appropriate modifications of synapses, this process ensures firing of these cells when the same group of receptors (or a part of it) is stimulated again. These axons pass to the third visual center, the vertical lobe, lying on the top of the brain. This lobe is characterized by 25 million minute cells, the amacrines, the axons of which do not extend beyond the lobe. In addition, there are about 70,000 quite large cells, with many branched dendrites and axons reaching to the subvertical lobe and so to motor centers. The fibers coming in from the superior frontal synapse with the amacrine cells, with the large cells, and also with fibers entering the lobe from below. These are believed to be pain fibers, arising all over the body and the skin. The function of this lobe is certainly inhibitory. Brian Boycott and I found early on that after removal of the vertical lobe, an octopus is uninhibited; it will persist in attacking at crabs even when given electric shocks. It can be trained only slowly to attack, say, at vertical rectangles but not to attack horizontal ones. The mistakes it makes are always to attack when it should retreat.

The large cells of the vertical lobes thus build up representations of visual features that should be avoided. Their axons proceed to the subvertical lobe and so to motor centers. Recursive fibers also pass back to the lateral superior frontal, allowing recurring stimulation, increasing appropriate synaptic learning changes. It remains uncertain how the many amacrine cells assist in the memory process. Their large nuclei suggest that a synthetic process is involved. Perhaps they consolidate synaptic changes taking place at the ends of their short trunks.

The Tactile Memory Centers

In the tactile system, there is a strikingly similar set of four centers. The first lobe receives the tactile signals from the arms and associates them with taste fibers. Its axons proceed to the fourth tactile lobe, the posterior buccal, which contains large cells; some of these cause the arms and suckers to reach out and take the object, other cells innervate circular muscles that push the arm away. The median inferior frontal system, constituting the second tactile lobe, is built exactly like the superior frontal lobe, with bundles of crisscrossing fibers. The cells of this lobe receive the fibers from the arms and thus carry representations of the actions of groups of touch cells. The axons carry signals to the third center, the subfrontal lobe. This lobe is precisely similar to the vertical lobe, with many millions of small amacrine cells and a few large ones with many dendrites. Like the vertical lobe, the subfrontal lobe receives pain fibers and it prevents the taking of unwanted objects. These four lobes perform for touch exactly as the other four do for vision. For example, Martin Wells and I showed that after removal of the subfrontal lobe, an octopus can no longer learn tactile discrimination. It continues to take objects from which it had received shocks.

The tactile system also makes use of some lobes of the visual system. Part of the tactile input from the arms passes to the superior frontal and so around the entire vertical system. Thus, eight matrices are involved in the tactile system, and removal of any one of them interferes with tactile learning (Young, 1983). This is indeed a striking demonstration that the memory is distributed between many parts of the brain.

The Origin of the Memory System

From detailed study of the anatomical relations, I have been able to produce a hypothesis as to how the vertical and subfrontal lobes have come to function as learning systems. Many small cells, similar to the amacrines, occur in the motor centers of the suboesophageal lobes, several small cells lying close to each large motoneuron. These small cells probably serve as inhibitors of the large cells when the latter are involved in reciprocal reflex actions. Such inhibition is needed even in the simplest reflex system. Small cells having this inhibitory function occur in the spinal cord of mammals. Sections show that the rows of cells of the subfrontal and vertical lobes are directly continuous with the inner rows of small cells of the superior buccal lobe. This lobe is a motor center that operates reflexes concerned with movements of the jaws. Its small cells presumably provide the inhibition of the large cells that produce these movements. The subfrontal and vertical lobes are thus specially developed parts of the eating system. The taste fibers they receive promote actions of attack at objects that have provided food. The inhibitory fibers of the subfrontal lobe promote the formation of representations that prevent the

intake of unsuitable materials. The functions of the vertical lobe, literally the highest part of the brain, have perhaps been extended to produce a balanced inhibition of the whole behavior. The memory system, as described, is simply an extension of the function of the buccal lobe in obtaining food. It remains to be seen whether it also extends to memories controlling other aspects of behavior.

Visual Discrimination

During the years 1955 to 1965, work in Naples was largely on the octopus' capacity for visual discrimination. This work was done mostly by observers showing the figures at one end of the tank and rewarding attacks with either shocks or food. This method has the obvious disadvantage that the octopus may take clues given consciously or not by the observer. We took great trouble to avoid such a danger and obtained consistent results with different observers. However, the "talking horse" danger was finally eliminated by Hector Maldonado, who devised an entirely automated procedure (1963, 1964, 1965). With this procedure, he was able to confirm the conclusions reached with open tanks and to measure exactly the times of the various phases of attack and the effect on these of removal of various lobes.

A thorough study of the extent of the capacity to recognize shapes was made by Stuart Sutherland, who devised a theory to explain his findings. Many variables of learning were studied, such as the capacity to reverse learned discriminations and to learn with a delayed reward. Partial removal of the vertical lobes decreased the capacity to learn in proportion to the amount removed.

Tactile Discrimination

This topic was first studied by Martin and Joyce Wells. They found that an octopus has great capacity to discriminate between objects with different degrees of roughness but has limited power to recognize shape. They attributed this finding to the absence of joints in the octopus' arms and the corresponding lack of proprioceptive determination of their position. I have made extensive further studies of the touch memory, some with M. Wells. We tested the animals with a series of plastic balls, each with a number of rings cut into it. The animal was given food for taking a certain ball, say three rings, and shocks for another, say nine rings. After a few trials, one ball was quickly taken under the web and the other ball was rejected. To avoid visual choice, the optic nerves were first cut; but in fact the octopus cannot make the distinction visually, and reliable results were obtained with intact animals.

After splitting the whole of the supraoesophageal lobe, we found that the two sides can be trained independently, even performing in opposite directions. Thus, it is possible to compare the effects of different lesions in

the same animal. I studied the effect on learning of removing each of the lobes involved, both separately and in combinations, using a final test of the degree of accuracy achieved. We found that removing each of the lobes reduced learning to a different extent. The tactile memory is therefore distributed between them, as is the visual memory (Young, 1983). This was a long series of experiments, spread over several years in Naples. Approximately 30 to 40 animals with each type of lesion were used and trained twice a day.

Interaction Between Visual and Tactile Learning

Dave Robertson established an octopus laboratory at the marine station of Duke University in Beaufort, North Carolina. He found fishermen able to collect live octopuses and bring them in good condition to the laboratory. With his electron microscope studies, he believed that he showed that fine filaments, the filopodia, became more numerous in the tactile centers after training one side of a bisected brain.

I used the facilities in Beaufort to study the possibility of interaction between visual and tactile senses in learning. This is a possibility because learning with both senses involves the vertical lobes. We found that a negative visual memory, not to attack white, for example, blocks the effect of a previously learned positive tactile memory, such as to take rough. But the effect is seen only in the period immediately after seeing the color. There is no long-term effect on the positive tactile memory. The only interaction between the two memories is the result of sharing common pathways to the arms. There is no evidence of second-order conditioning (Allen et al., 1986).

Learning in Squids

In Beaufort we were also able to show the learning capacity of the estuarine squid, *Lolliguncula*. This squid can readily be trained to feed when a horizontal rectangle is shown but to avoid feeding when attacks after showing a vertical rectangle were followed by shocks. The discrimination can be maintained for nine days without showing the figures again. The squid also learned to discriminate between black and white balls. The negative responses in these trials were definite; the squid often shot ink at the figure from which it had received shocks (Allen et al., 1985).

Theories of Memory

My ideas about memory in *Octopus* changed as I found out more about the conditions in the centers responsible for memory and their relation to the mechanisms suggested for other animals and humans. I was first attracted in the 1930s by the reverberatory connections of the vertical lobe as a possible basis for memory in *Sepia,* as recounted earlier. Then, as I came to know more of the details of the connections, I developed other theories. I

was perhaps unduly impressed by the finding of the long dendrites in the visual cells of the optic lobes and their orientation in vertical and horizontal directions. We were at the time mostly studying the process of learning to distinguish between orientation of rectangles, and I postulated that the visual classification was performed by these cells, rather like the findings of Hubel and Wiesel in mammals. I was also anxious to identify which cells or synapses are changed during learning. I emphasized that each classifying cell (one coding for "vertical," for example) must have the possibility of access to motor channels for attack and retreat. I suggested that this access was through memory cells. During learning, one of these pathways was closed as a result of signals, in the form of either food or pain. The circuits through the frontal and vertical lobes maintain the address of the relevant cells during the period of delay between the initial signals and the advent of the reward. I suggested that the classifying cells and memory cells constitute a unit of memory or mnemon. This theory was put forward (Young, 1965a) and developed in a Croonian Lecture (Young, 1965b).

The concept of mnemons was never very helpful and now seems simpleminded. The descriptions of the anatomy of the visual and tactile centers were all new and have proved accurate, but theory gave too much attention to unknown units and unsupported hypotheses about their excitability and closure. However, a great advantage was that the memory process was recognized as a development of the reflex responses of the cells of the buccal lobes in eating. This finding shows the way memory has evolved in octopuses. It remains to be seen whether other memory systems can be found to have evolved out of reflex systems in the same way. This process is unlikely for the complex systems of mammals.

A great defect of this way of thinking was that it did not emphasize the large numbers of cells in the nervous system. For a long time, I felt that these numbers might mean that there is a useful analogy among learning, natural selection, and selection of an immune response. Such selection between large numbers is nature's way of ensuring adaptation. I developed this theory in a lecture to the Australian Academy of Science (Young, 1973). The Australian immunologists Jerne and Burnet had already hinted at something similar. The idea was taken up by Edelman and developed in his book, *Neural Darwinism* (1987). He examines my treatment fully and I have been his guest in New York to discuss it. The question is, what are the units of selection and how are they generated? For me, these units are classifying cells produced during development. For Edelman, the units are groups of cells formed during development, and he stresses that this process gives great creativity to the system. Presumably this process is itself influenced by environmental events.

Matrices

In recent years I have realized that the *Octopus* systems can be understood as a series of matrices. I reached this conclusion by following work on the

hippocampus, such as Rolls (1990). We know enough of the structure and connectivity in octopuses to see that the system provides a series of matrices allowing, with appropriate synaptic change, for the interaction of groups of input fibers on the cells so that they represent external situations. The succession of lobes provides for association of groups of groups and so of representations of whole scenes or events. Recursive pathways increase the opportunity for consolidation of synaptic change, perhaps by a Hebb mechanism. The lobes concerned with both visual and tactile memories have the character of such matrices. Injury to any of the four lobes concerned with vision or the eight concerned with touch reduces the learning capacity in proportion to the amount removed or injured (Young, 1983).

These matrices are thus networks of the type defined by Hopfield (1982) as providing efficient storage and recovery of information. The matrices allow for recognition of part of an input and can survive degradation by loss of part of the system. In octopuses the matrices are developed to control reflex systems concerned with the acquisition of food. I have come to realize that the octopus system is analogous to that of many other centers that we know to be the seat of memory storage. The hippocampus has a series of such matrices, with recurrent connections, both within it and with the neocortex. The cerebellum is a classical example of such a matrix, known to be concerned with memories of conditional reflexes.

Brains and Minds

Throughout my work on the nervous system, I have been concerned to show how knowledge about the functions of the brain can help in everyday human affairs. In 1950 I gave the second series of Reith Lectures for the British Broadcasting Corporation (Young, 1950a). These lectures were intended to promote wide intellectual discussion. The first series had been given by Bertrand Russell. My lectures focused on the idea of "Man the Communicating Animal." I emphasized the human propensity to come together and worship at large meeting places, such as megaliths or cathedrals. The title of the lectures was "Doubt and Certainty in Science." I used the idea that we achieve the certainty of true beliefs by the experiments of "doubting," which establish a set of rules in the brain. I used the example of the demonstration by von Senden (1960) that a person born blind who later gained the use of his eyes had to learn to see. From various further examples I concluded that "the method I am going to suggest as a working basis is to organize all our talks about human powers and capacities around knowledge of what the brain does."

I have tried in later books to show that recent work on the brain has revealed how these "rules" are actually embodied in the activities of the nervous system. The Withering Lectures, given at Birmingham, developed the concept of "A Model of the Brain" (1964). In "An Introduction to the

Study of Man" (1971b) I included a discussion of the evolution of the powers of the human brain and of speech. Then, for the Gifford Lectures, "Programs of the Brain" (1978), I developed the theme, as Maudsley put it in 1867, that "we should treat mental phenomena from a physiological rather than a metaphysical point of view." One example I quoted was the evidence of Libet et al. (1983) showing that there are electrical activities in the brain half a second before a person makes a conscious decision to move a finger. This clearly shows that actions of the mind depend on the brain and that it is absurd to consider oneself as two separate entities.

I explored how the whole range of human capacities can be related to known cerebral activities. These activities include not only the familiar bodily actions but also matters usually considered to be mental, such as knowing and thinking, valuing and enjoying, loving and suffering, and believing, obeying, and worshipping. I was especially eager to show how artistic activities, whether creating or enjoying art, depend on the brain. I later treated this topic in detail as "Beauty and the Brain" (Young, 1981), a lecture that I gave at the Tate Gallery.

In describing how the human brain operates in so many ways, I was, of course, going far beyond my own immediate research or knowledge. Nevertheless, I consider that discussion of such wide cerebral activities is stimulating for any researcher of the nervous system. It is also necessary to emphasize such an approach to all those concerned with problems of human life and well-being. Such knowledge is certainly useful to every parent and to teachers at all levels. It should be valuable to politicians, to judges, to religious leaders, and to all those concerned with social welfare, and of course to those who deal with mental illness. Some understanding of the actions of the brain is indeed useful to each one of us as we face the problems of our lives. It helps to understand how entirely we depend on our brains.

In dealing with such large questions, I have become involved in many philosophical problems. I had been partly prepared for this involvement from my Oxford and London days, when I met and conversed with many philosophers. A.J. (Freddie) Ayer organized informal meetings of what we called "The Metalogical Club." I got to know Gilbert Ryle, Bertrand Russell, Karl Popper, Ted Honderich, and many others. I learned a lot from them but always suffered from not having studied classical philosophers from Aristotle and Plato to Immanuel Kant, John Locke, and David Hume. Philosophers depend on such knowledge for much of their discussion. However, I have always felt that it is difficult to take seriously the views even of such great thinkers when they did not have the advantage of the knowledge we now possess of science, and especially of the brain.

Philosophical discussion nearly always turns to looking inward; *cogito ergo sum* is the essential firm basis. I wonder whether "I think" is really our most fundamental experience. "I feel that I am alive" precedes thinking, if that is indeed a form of "knowledge." I have tried to discuss

this point of view in *Philosophy and the Brain* (1987). Philosophers of course do not like the book, but many people have said that they find it useful. The book has been translated into German and Japanese.

I do not regret these various diversions from conventional science. It is important for the practicing researcher to consider wider questions. Discussion of them is limited by lack of knowledge of the organization that produces "programs of the brain." Realizing this ignorance may help those who make detailed studies of neurons to be ambitious in trying to decipher the language in which the programs are written.

Summary

I do not feel that I have yet reached the point at which I can write "Conclusion." Indeed I have learned a lot from the difficulty of writing this scientific autobiography; however, I can make some sort of summary of my 88 years so far. I have discovered many previously unknown facts about fishes, lampreys, and especially cephalopods. These facts are recorded in books and papers, often with my own drawings. I have advanced knowledge of the operation of cephalopod brains and so helped toward the understanding of brains in general. I have shown that the two memory systems of octopuses consist of successions of matrices, and I have suggested how these have evolved from reflex operations of eating.

In addition to original discoveries, I have developed methods of teaching and research in anatomy and neurobiology. Many of my students have become successful doctors in general practice or research. I have helped to introduce many people to zoology through textbooks. I have emphasized the power of biological ideas in public lectures and books, which have been widely circulated in nine languages. In these books I have presented facts and ideas that I hope will help people to have richer and happier lives.

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I have had help from many marine laboratories, including the Marine Biological Association at Plymouth, U.K. from 1924 onward, and I finally

became its president (1975–1985). The Stazione Zoologica in Naples provided accommodation for my teams of assistants and a hundred or more octopuses for research on memory every summer from 1947 to 1975. In America I have enjoyed working at Woods Hole; the Duke University Marine Laboratory in Beaufort, North Carolina; the Marine Biomedical Institute in Galveston, Texas; and the Friday Harbor Laboratory in Washington. I am most grateful to them all.

When it comes to individuals, it is impossible to know which helpers to thank. I am thankful to all the scientists and technicians who have made my work possible. I shall only mention some of those who have helped recently and in the preparation of this autobiography. Dr. Marion Nixon has been a constant source of wisdom in all my work for 30 years. Miss P. Stephens was responsible for making most of the thousands of microscope sections that are at the center of my work. Recently Dr. P.L.R. Andrews helped me continue working on fishes, which age would no longer allow. Finally, in the preparation of this work, I have had secretarial help and much discussion with my wife, Raye. The typing of the final version and transferring to disk has been done by my daughter, Cordelia. I am deeply grateful to them all.

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