Ainsley Iggo, born in Napier, New Zealand on the 2nd of August 1924 died at his home in Edinburgh on the 25th of March 2012 aged 87. As an electrophysiologist Ainsley pioneered the study of sensory cutaneous receptors and afferents, the organisation of the dorsal horn and the physiology of the ascending tracts within the spinal cord. In particular he was amongst the first to classify C fibres and mechanoreceptors and discovered thermoreceptors in the skin. His most cited paper is a classic with Alan Muir, outlining the morphological and physiological characteristics for distinguishing a unique cutaneous receptor type from all others, in this case the Merkel receptor. Interestingly, his next most cited paper dates from 1955 describing his early work in Edinburgh which completed his studies for his PhD in the Rowett Research Institute in Aberdeen, on tension receptors in the stomach and urinary bladder. At this time he also established the mandatory requirements for the identification of action potentials recorded from a single fibre using the collision technique.

In his autobiography published in the series The History of Neuroscience in Autobiography on the Society of Neuroscience WEB site, Ainsley gives a fascinating and highly readable account of his life and career. He begins by describing his rather humble beginnings in an impoverished New Zealand; first in Greymouth on the west coast of the South Island and later in Invercargill where he attended secondary school at Southland Technology College. This was the start of a series of interlinked events orchestrated by a number of outstanding mentors, K. E. McKinnon in Invercargill, M. M. Burns in Lincoln College, Canterbury, J.C. Eccles in the University of Otago, A. T. Phillipson in the Rowett Research Institute in Aberdeen and David Whitteridge in Edinburgh. One of the many charms of the autobiography is the ease with which Ainsley highlights the contribution made by his mentors, colleagues and collaborators.

Ainsley’s first encounter with an electrophysiologist was when passing through Dunedin he phoned J. C. Eccles to ask for a temporary job. Ainsley had won a Travelling Scholarship while working for his masters degree in Canterbury Agricultural College which would only become available two years later and he needed an interim job. With the financial help of a cousin and later an assistant lectureship he was able to study physiology under Eccles, Archie McIntyre and others and take part in a research project recording extracellular potentials from excised superior cervical and the ciliary ganglia with Eccles' daughter, Rose Eccles. The project was a flop and Ainsley turned down the opportunity to work for a PhD in Otago. It is not clear why J.C.Eccles suggested isolating the ganglia. In his 1935 papers describing his work in Oxford Eccles emphasised the need to preserve the blood supply to the ganglion "care being taken not to endanger its blood supply". With the blessing of Eccles he set out for the UK and at the age of 26 began work for his PhD in the Rowett Research Institute in Aberdeen. The focus of his new mentor, Phillipson, was on the reflex regulation of ruminant gastric movements in sheep and Ainsley worked on the isolation of ciliated protozoa from the rumen of sheep while he tried to put an electrophysiology laboratory together using a manual published by C. J. Dickinson and the help of a local marine engineer. Although the quality of his electrophysiological recordings were a disappointment, over a two year period he developed a preparation for the analysis of the central control of the movement of the reticulum and rumen of sheep and this combination of viscera and recording from peripheral nerves was to dominate his early publications. This early need to build his own equipment was the stimulus for the superb, highly enviable, electronic and mechanical workshops he established in the Department of Veterinary Physiology on the Dick Vet campus at Summerhall.

In 1952 Ainsley joined David Whitteridge's Department of Physiology in Edinburgh and spent many months building an integrated electrophysiological recording unit under the supervision of Jock Austin. At Whitteridge's suggestion he began by recording from the pelvic visceral nerves as they entered the spinal cord and identifying tension receptors in the bladder and flow detectors in the wall of the urethra. Once he mastered this technique he returned to the stomach recording from identifiable single units of slowly conducting Aδ and C fibres of the vagus nerve. Not only did he find in-series tension receptors similar to those in the bladder but more superficially in the mucosa he isolated pH sensitive receptors.
Having mastered the technique of recording from single unmyelinated fibres Ainsley felt sufficient confidence to explore the role of C fibre afferents from the hairy skin of cats which were easily excited by innocuous stimuli. Contrary to the perceived wisdom based on work in man Ainsley showed several categories of C fibres could be activated by mechanical, thermal and chemical stimuli. Importantly, many C fibre mechanoreceptors were highly and specifically sensitive to innocuous tactile stimulation at thresholds only slightly higher than A\(\delta\) fibre receptors. As mentioned earlier he classified the receptors served by C fibres and assigned putative nociceptor roles to both A\(\delta\) and C fibres and drew attention to the similarity of the activation thresholds for both heat and pain receptors. Ainsley concluded that his results were consistent with the "specificity" concept of sensation rather than the more fashionable hypotheses developed by Weddell, Wall and others. Weddell argued that the anatomical arrangement of the nerve fibres in the nerve trunks was significant to the understanding of the mechanism of cutaneous sensibility. Wall was most insistent that sensation was critically dependent on the excitability of the second order neurones in the spinal cord and added insult to injury by writing "Of the unmyelinated C fibres, Iggo had reported [only] a few nociceptors (1960). It seemed possible, however, that these might have been damaged by his dissection method".

A visit to Hensel and Zotterman’s laboratory in Marburg, which was exceptionally well equipped, to test temperature sensitivity, allowed Ainsley to test his specificity hypothesis i.e., that skin thermoreceptors were specific and should be distinguishable from tactile receptors. The work was highly successful and identified cold receptors with a peak sensitivity of 25°C and warm receptors with a maximal sensitivity at 42°C. Importantly the temperature receptors were insensitive to mechanical stimuli.

In 1959 Ainsley departed on sabbatical leave to the Australian National University in Canberra where Eccles had built up an exceptionally well equipped and staffed laboratory. As others have done, Ainsley described the work required to obtain satisfactory results as long and gruelling. Although Ainsley describes the outcome as equivocal his attempt to quantify recurrent inhibition of motoneurones by firing impulses along the ventral roots while recording intracellularly from Renshaw cells would still be considered ambitious today.

When he returned to Edinburgh, Ainsley continued his pursuit of the controversy surrounding the modality specific hypothesis, now funded by a Locke Research Fellowship. This led to work in primates and the extension of his interests from viscera and skin to muscle systems. He also made an attempt to look at the ability of certain chemicals, chemalgogens such as acetylcholine, histamine and 5-hydroxytryptamine, to stimulate cutaneous afferents. Most importantly he identified mechanoreceptors innervated by myelinated fibres, by their adaption rate. The study on Merkel cells mentioned in the introduction was extended with Alan Brown to look at the effects of axon degeneration and regrowth. Critically the normal slow adapting response only reappeared when the regrowth of the axon was complete. Later in the 1990's on a visit to Monash University Ainsley, working with Uwe Proske, followed up the work on regenerating axons and suggested that substances transported down the axon and accumulated at the growing tip are required to give mechanical sensitivity. Only in the last two years has the role for one such protein, Piezo, been established. Touch spot afferents were subsequently classified into slowly adapting mechanoreceptors type I and II (SAI and SAII) and the idea that the cutaneous sensibility was served by a variety of distinctive receptors confirmed.

In 1962 Ainsley was appointed to the newly created Chair of Veterinary Physiology in the Edinburgh Veterinary College and moved into recently vacated space at Summerhall that allowed him to build state-of-the-art laboratories and workshops. Funding from the Agricultural Research Council prompted a return to work on ruminant digestion. By recordings from the afferent and efferent axons in the vagus Ainsley and Barry Leek showed that the pattern of discharge in the preganglionic afferents had a temporal relationship to the reticuloruminial contractions. Tonic afferent inflows from the in-series receptors during inactive phases of the digestive cycle initiate a reflex drive from the medullary gastric centers and the resultant muscle movement. This work was extended with David Cottrell to look at the duodenum. As in the stomach the sensory receptors adapted slowly to mechanical probing. Bolus injections of gastrointestinal polypeptides evoked contractions and activated tension receptors.
A new phase of work on somatosensory mechanisms began when Alan Brown rejoined the laboratory. The sensory innervation of the rabbit ear was shown to differ from the general body skin; Type D and G hair follicle units were present whereas SAI and SAII and type T hair units were absent. This went some way to explain the different approach of Graham Weddell and Simon Miller who had championed the temporospatial pattern hypothesis of sensation. With Alan Brown, Ainsley embarked on a rigorous sampling exercise using time-locked mechanical stimuli and established the characteristics of various classes of mechanoreceptors, hair follicle types T, G or D and SAI or SAII. In a parallel study with Margaret Chambers the nerve endings associated with SAII receptors were shown histologically to be spindle-shaped and orientated parallel to the surface of the skin i.e., typical Ruffini endings. A detailed study of whiskers and sinu hairs on the toes of cats with K-M Gottschaldt characterised receptors in terms of their rate of adaption.

An opportunity to look at the actions of the various types of cutaneous receptors on segmental spinal cells arose when Ainsley was invited to work with Manfred Zimmerman and Hermann Handwerker in Heidelberg. This led to the beginning of a classification of dorsal horn neurones as Class 1, driven by sensitive mechanoreceptors and Class 2 by noxious thermal and mechanical stimuli. Although prominent in spinal animals the Class 2 cells were often absent in intact preparations, suggestive evidence of potent supraspinal modulation of nociceptive cells. Class 3 cells excited only by noxious stimuli were recorded from lamina 1. These early studies of nociception were extended using ever more sophisticated techniques including electrical stimulation of the locus coeruleus and the raphe magnus nuclei. Both had inhibitory actions on dorsal horn neurones. In 1982, Sue Fleetwood-Walker joined the group and established that the major action of the descending catecholamine pathways was through alpha2-adrenergic receptors.

Following his trip to Heidelberg Ainsley's major interest switched to the neurones in the most superficial layer of the dorsal horn (Rexed's Lamina 1). With Fernando Cervero and Hisashi Ogawa, Ainsley was able to show that the large Waldeyer neurones in lamina 1 included nociceptive neurones sensitive to a number of different inputs. However, the zone included other cells driven by light tactile stimuli. Importantly the firing of these cells by light touch provoked a powerful inhibition of the nociceptive discharges in other cells. The inhibition remained when the spinal cord was cold blocked rostrally. Later working with Wilma Steedman and Vince Molony intracellular recordings were made from substantia gelatinosa neurones, some of which were shown, with some difficulty, to have short and long range projections in Lissauer's tract.

In an adjacent laboratory Alan Brown had shown the spinocervical tract to be an important pathway from hair follicle afferents. Ainsley with Vince Molony and others mentioned earlier confirmed that the centrally projecting spinocervical tract cells of lamina III could be affected by noxious inputs but were on only one occasion excited exclusively by a nociceptive input. Thus it was not possible to describe the tract as a nociceptive system. This work formed the basis of a series of reviews in Brain and symposia organised by the Royal Society and a NATO Advanced Science Institute.

With Hisahi Ogawa Ainsley continued to use a combination of electrophysiological and electron-microscopical techniques to explore cutaneous receptors in the cat's footpad. An attempt to resolve the role of Merkel cells failed. However, in 1991, Ainsley accepted an invitation to visit Okazaki in Japan and work with Haru Ohmori who had developed a technique for enzymatically isolating cochlear hair cells, with the hope that he could isolate Merkel cells. Although the intention to measure changes in calcium ion concentrations in the isolated cells failed, the work was continued in Edinburgh during a sabbatical by Masakazu Tazaki. Although the main objective again failed, since his return to Japan, Masakazu has succeeded in measuring the activity of calcium channels in Merkel cells.

Working first with Ulf Lindblom in Stockholm and Gisele Guilbaud in Paris and later with Danny McQueen and Blair Grubb in Edinburgh, Ainsley's interest turned to a rat model of rheumatoid arthritis and the action of aspirin. In inflamed joints the normally silent joint receptors discharge continuously and are excited by innocuous stimuli. The application of soluble aspirin or paracetamol reverses the enhanced excitability. This action was attributed to the prevention of the formation of prostaglandins. Prostaglandins were shown to enhance the ability of bradykinin to excite joint nociceptors. Specifically, PGI2 was shown to sensitise joint receptors in both normal
and arthritic rats suggesting that in arthritis it is the formation of PGI$_2$ that leads to the enhanced excitability of nociceptors.

In a final series of overseas visits to Monash University, Ainsley, working with Uwe Proske, identified unique electoreceptors concentrated on the tip of the bill of the platypus and the tip of the snout of the echidna or spiny anteater. Unlike the electroreceptor of fish the electoreceptors in these species is a structurally specialised afferent nerve ending rather than a separate cell.

In this account of his life I have focused on the details of Ainsley’s research and the contributions of his colleagues. Ainsley’s aspirations and work ethic were forged very early in his career before he left New Zealand. Likewise the central thread of his day to day research crystallised not long after he built his first electrophysiological rig and from then on he rarely departed far from his quest to prove his initial hypothesis that skin sensation including pain originated in an array of specific receptors associated with the afferent nerves and pathways. In Scotland he was fortunate to find equally dedicated colleagues with a similar vision.

Submitted by Professor J S Kelly

Professor Iggo served on the Council of the Royal Society of Edinburgh from 1990-96, including three years as Research Awards Convener from1993-96.