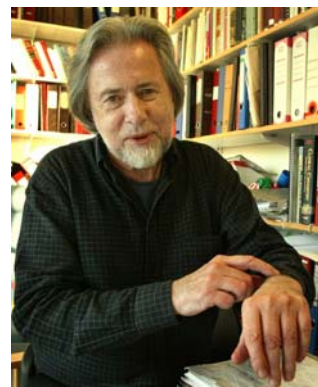


Professor Jóhann Axelsson
Founder of physiological research in Iceland

Prof. Johann Axelsson is the founder of the Department of Physiology at the University of Iceland, and despite his retirement as professor is still actively involved in research at the department. Most if not all Icelandic physiologists have studied physiology under his guidance at some point in their career, and/or worked under his leadership as mentor or department head. No Icelandic physiologist has been more frequently cited in peer-reviewed journals than prof. Jóhann Axelsson. His research areas have been varied, and include topics in neurophysiology, muscle physiology and pioneering work in research and teaching of physiology in Iceland.



Prof. Axelsson was born in Iceland in 1930, and received his MSc from the Pharmacological Institute, University of Oslo, in 1956. His work in Oslo involved studies on cholinergic mechanisms of neuromuscular transmission in skeletal muscles in a variety of species, with particular focus on the effect of cholinesterase inhibitors on tetanic contractions, and the effect of d-tubocurarine thereon (Axelsson, Gjone & Naess, 1957). In 1957 he spent a year working on the neurophysiology of cat cerebral cortex at the Centre Etude de Physiologie nerveuse et Electrophysiologie in Paris.

In 1960 Axelsson completed his Fil lic. degree from the Zoofysiologiska Institutionen, University of Lund, and then subsequently his Fil. Dr. degree from the same institution, working on the physiology of smooth and skeletal muscle with prof. Stephen Thesleff. Their collaboration led to a number of fundamental discoveries of muscle physiology. At that time it was assumed that the contractile state of muscle cells was dependent primarily on electrical phenomena, related to the membrane potential of these cells. In a paper published in *Acta Physiologica Scandinavica* in 1958, however, Axelsson and Thesleff showed that contracture can be induced chemically (by caffeine) in frog striate muscle cells, without any change in membrane potential; the same effect of caffeine on tension was observed when muscle was immersed in isotonic KCl solution. Thus a change in membrane potential of muscle cells is not “necessary or in themselves sufficient causes of contraction”, as he put it in his thesis (Axelsson, 1962). The paper by Axelsson and Thesleff in *Acta* in 1958 had great influence on thinking in muscle physiology and is still being cited in the literature, both in relation to cellular mechanisms in muscle cells, and related areas as caffeine use in sports and pharmacokinetics in man. To this day the paper has been cited over 250 times.

Another paper by Axelsson and Thesleff, published in the *Journal of Physiology*, London, in 1959, has had even greater impact not only in the field of muscle physiology, but also in areas such as plasticity in the nervous system, up-regulation of receptors, supersensitivity and neuronal development (Axelsson & Thesleff, 1959). At that time it was known that denervation of organs of motor nerves increase sensitivity to neurotransmitters, and was referred to as “denervation supersensitivity”, but the underlying mechanisms were largely unknown. Axelsson and Thesleff recorded the membrane potential of a single fibre of mammalian skeletal muscle with an intracellular microelectrode, whilst applying iontophoretically acetylcholine locally on the membrane. They found that before denervation only acetylcholine application on the end-plate evoked membrane depolarisation of the muscle fibre. But after about 14 days of denervation the entire membrane of the muscle fibre

will be as sensitive to acetylcholine application locally (by iontophoresis) as the end-plate of the muscle. This suggested that there was a fairly fast increase in the area on the membrane containing Ach receptors after denervation, and thus supersensitivity involves an increase in the distribution and number of acetylcholine receptors on the muscle membrane. So far this paper has been cited over 660 times.

In 1959 prof. Axelsson was offered the Riker Fellowship for Europe, and to work with prof. Edith Bülbring in Oxford, England, as Riker Research Fellow in Pharmacology. In 1964 he received his DPhil degree in pharmacology from the University of Oxford. In Oxford Axelsson's work with prof. Bülbring focused, among others, on the contractile mechanisms of spontaneously active smooth muscle, and the role of calcium ions therein.. They showed that in smooth muscle cells extracellular calcium ions are essential for contraction. The method used in these studies to measure the membrane potential was the sucrose gap method introduced by Stampfli in 1955, as modified for muscle cells by Burnstock and Straub in 1958. Axelsson and his collaborators at Oxford found that with the removal of glucose from the bathing medium the electrical activity in the muscle cells persisted whilst the muscle tension was abolished; metabolic inhibitors had a similar effect of dissociating electrical and mechanical activity in muscle under these experimental conditions (Axelsson, & Bülbring, 1961). Further experiments showed that by removing calcium ions from the bathing medium (and thus from the extracellular compartment) the contractile force in the muscle was totally abolished, whilst action potentials remained (Axelsson, 1961). Axelsson's work at Oxford thus shed important light on the processes involved in "electro-mechanical coupling" in muscle, and played a critical role in establishing that contraction in vascular smooth muscle can be activated by either chemical or electrical events.

In 1962 prof. Axelsson was called to be professor of Physiology at Gothenburg University in Sweden for one year, and subsequently served as associate professor and research associate professor in Physiology at the same institute until 1965. At Gothenburg Axelsson's research interests were centred on functions in vascular and intestinal smooth muscle, in particular the role of ions, ATP, glucose and catecholamines (e.g. Åberg, & Axelsson, 1965; Axelsson et. Al., 1965ab).

In 1965 prof. Axelsson was appointed professor of Physiology at the Faculty of Medicine of the University of Iceland, and served in that capacity until retirement in 2000. In Reykjavik from the very start his working hours were divided between a variety of tasks, most of them centred on the founding of the Department of Physiology and build-up of the needed facilities there. At his arrival at the medical faculty, he soon discovered that he was in fact the first (and the only, at the beginning) full-time faculty member in Physiology. So everything had to be done from scratch; the development of lectures and practica, acquisition of laboratory facilities and equipment for teaching and research, administrative duties, and the recruitment of additional faculty in Physiology. All this required considerable time and effort, aside from his scientific work. In addition, he served as dean of the faculty of medicine between 1974-78, at a time of great expansion of the faculty and planning of the construction of a new building for the entire faculty. At the time of writing there are 8 full time academic faculty members at the Physiology department in addition to other staff and graduate students, which demonstrates the expansion that has occurred since Axelsson's return to Iceland.

Still, several research projects were initiated and carried out under prof. Axelsson's leadership and initiative in Reykjavik at this time. Work on muscle physiology continued, but in addition Axelsson moved into other areas of research, based on the opportunities that presented themselves in Iceland. One of the earlier ones, and which still continues, was the

issue of genetic and environmental factors in cardiovascular physiology. To this end, prof. Axelsson initiated a research project in collaboration with colleagues in Reykjavik and Manitoba, Canada, which compared two separate but genetically comparable populations, in Iceland and descendants of Icelandic immigrants in Manitoba. This work demonstrated that environmental factors play a vital role. For instance it was found that residents of Manitoba of purely Icelandic descent had a significantly higher mortality rates for ischemic heart disease than a rural population from Northeastern Iceland (Axelsson et al, 1981). Furthermore, the native Icelanders exhibited significantly higher levels of total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol, but lower triglyceride levels. Their plasma phospholipids contained significantly lower levels of saturated fatty acids (SFA), monounsaturated fatty acids, and n-6 polyunsaturated fatty acids (PUFA). In contrast, their n-3 PUFA levels were three times as high as those of the Canadians of Icelandic descent (Skúladóttir et al., 1995). This and other evidence obtained in his studies performed in Canada and Iceland suggested that dietary factors are of critical importance in risk of cardiovascular diseases. It was found in a study of cross-sectional samples of Canadians of Icelandic descent and Icelanders in rural areas that these genetically comparable but geographically separate populations showed marked differences in cardiovascular physiology. The Canadians of 'pure' Icelandic descent had a higher prevalence of exaggerated exercise systolic blood pressure (ESBP), left atrial enlargement (LAE) and left ventricular hypertrophy (LVH) than native Icelanders, presumably due to environmental factors (Naimark et al., 1992). Axelsson and his collaborators therefore examined in particular the cardiovascular physiology of a cross-sectional sample of Canadians of Icelandic descent in Manitoba, living in rural or urban areas (e.g. Naimark et al., 1991, 1996; Bartfay et al, 1995). There were differences between these groups, but not in LVH or ESBP, suggesting a complex relationship between factors like exercise activity and work environment, and diet and cardiovascular physiology (Naimark et al., 1996).

At this time it was found that the prevalence of seasonal affective disorder (SAD) was surprisingly low in Iceland (Magnusson & Stefansson, 1993), given the "latitude hypothesis" which assumes that the prevalence of SAD is related to higher latitudes. It assumes further that there is a aetiological element, i.e. there is less ambient light with higher latitudes and that this may be a causal factor. In fact the prevalence in Iceland was found to be significantly lower than previously found in the southern parts of the United States. Axelsson therefore instigated a research project to address this issue, first by examining the prevalence of SAD among Canadians of Icelandic descent in the Interlake district of Manitoba. It was found to be very low, and in fact about the same as among Floridians, which contradicts the "latitude hypothesis" (Magnusson & Axelsson, 1993). This suggests that there may be a genetic factor in the aetiology of SAD, and to address this issue a study of Canadians of Icelandic and non-Icelandic descent was carried out in Manitoba. It was found that the prevalence of SAD was markedly lower in those of Icelandic descent (Axelsson et al., 2002). The reasons for this may be either genetic factors and/or unknown environmental factors unrelated to ambient light levels in the environment.

In addition to the projects that have been discussed here Axelsson has been engaged in a variety of other research projects that will be mentioned only briefly. He has always had a keen interest in exercise and cold physiology, and the treatment of hypothermia (e.g. Axelsson et al, 1985; Keatinge et al., 1986; Naimark et al., 1991). All his research work has been characterized by intellectual rigor and burning curiosity, which still remains after retirement. Jóhann Axelsson retired as head of the Physiology department of the University of Iceland in 2000, but as professor emeritus (and thus free from the burden of administration) is still actively involved in research at the department, and is likely to remain so for many years to come.

Thor Eysteinnsson, Associate Professor
Sighvatur S. Arnason, Associate Professor
Dept. of Physiology
University of Iceland, Reykjavik, Iceland.

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