

PHYSIOLOGY AND MAINTENANCE

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Summary

Humans, animals, and plants with long lifespans have well-functioning regulatory systems. Their metabolism requires the inflow and outflow of molecules in large quantities. Oxygen is essential for life but especially in heavy metabolic conditions, 1–3 percent of the oxygen used ends up with its reactive metabolites. They tend to damage the genomes, enzymes, and membranes as also do many pollutants caused by humans. Reactive oxygen metabolites in physiological concentrations also regulate signaling cascades of cellular functions. A multitude of nutrient and enzymatic antioxidants, and other mechanisms, continuously act to limit and carry out repairs in parallel for energy metabolism, nucleic acid and protein synthesis, detoxification, and many other metabolic functions. The service activities, such as respiration, circulation, digestion, and excretion, run year after year, perhaps for 100 years in humans. The replication of many cells, such as in skin and mucous membranes, as well as in bone marrow, also continues indefinitely throughout life. Although humans tend to gain weight in affluent societies, the human body maintains its shape if physical activity is continuing, as happens in animals. The capacity of regulatory mechanisms is also enough to permit remarkable sports performances and survival through terrible famines and diseases.

Our knowledge is still very limited despite intensive research, and the clarification of the human genome opens many more questions: what are the functions of the “junk DNA,” and what enzymes and other proteins are present at any given moment in response to internal and external stimuli while the 10^{15} cells (micro-organisms included) in the human body are going about their functions? Changing situations are always posing more questions than we can answer at the present. The neurons, which to a great extent control the integrity of the body, have so many interconnections that one cannot calculate their number.

Research in physiology is a most fascinating area. Every researcher has in principle as many approach possibilities as he/she has neurons.

1. Introduction and Background

Physiology studies the functions of the healthy organisms and their regulation. In some countries the word normal physiology is used. In Chinese the word physiology means the study of the logic of life. If we take into account the huge number of cells in numerous organs and the fact that they can successfully collaborate, possibly for 100 years, the quality and effectiveness of the regulatory systems of the human body are superior to those of any machine made by humans. Perhaps every molecule and their atoms have been replaced numerous times during a single lifetime, even in the most passive tissues.

Human physiology devotes its interests to humans, animal physiology to the comparative studies (see “General Comparative Physiology,” EOLSS on-line, 2002), plant physiology studies the functions and regulatory mechanisms in plants, and

microbial physiology works on the problems of bacteria and viruses. Quantum physiology approaches the responses under the influence of small electromagnetic effectors. Sports physiology specializes on the problems of physical activity in sports, work physiology on occupational loads, and aviation physiology on the problems in flying. Pathophysiology studies the genesis of health problems and diseases. In medicine clinical physiology is responsible for the services of functional diagnostics in hospital and other laboratories, as is also clinical neurophysiology. Both these special branches also develop new methods and contribute to the clinical research. Psychology is closely related to physiology, because many phenomena can be clarified by using physiological approaches. Psychophysiology is an area that especially contributes to the understanding of psychological reactions. Biochemistry covers the metabolic aspects of physiology, and physiological principles are applied in pharmacology in the development of drug therapies.

Living organisms share many common characteristics as far as the main metabolic functions and their regulation are concerned. Therefore by studying simple life forms like bacteria or cultivated cells, we can obtain significant new knowledge on higher life forms. One can also study cultured human cells and their responses (e.g. their membrane receptors and ion pumps (cell physiology)), and learn how they interact and find explanations for what happens in the whole organism. Although we can obtain valuable knowledge from research using individual cells, the understanding of the functioning of an animal or plant clearly requires studies of whole specimens of the species in question.

The different regulatory mechanisms at cellular, tissue, and organism level oscillate with time. They tend to maintain the oxygen level, the availability of energy sources and other nutrients, as well as the level of waste products, at about the same more-or-less constant level, with the aid of different mechanisms. The term homeostasis, or the balance of internal milieu, has been used, but homeodynamics (see “Homeodynamics,” EOLSS on-line, 2002) would better describe the situation, as there is continuously fluctuation within certain limits, depending on the functional stage of the organism.

One of the most common questions put forward to a physiologist is: “what is normal?” The individual variability among different species, humans included, is high. The variability usually follows a bell-shaped curve. If different parameters are measured from a group of people, and the fate of the individuals are plotted, the place of one individual varies greatly and finally one may have difficulty in understanding what actually is normal. Usually the distribution range of any parameter, which covers 95 percent of the people, is considered normal, but even outside of this range normally responding individuals are found.

Multicellular organisms have several regulatory systems to guarantee the homeodynamics in the body. The neural system is acting fast, and the humoral system usually works a bit slower. Also the neural system uses chemical transmitters (see “Neurotransmitters and modulators,” EOLSS on-line, 2002). Most probably there are also other systems that are poorly understood at present because some phenomena take place so fast that the traditional thinking has difficulties providing explanations. One of the less understood systems is what Chinese traditional medicine calls meridians. These

meridians can be visualized with electric methods, but the morphological substrate is not yet understood, if it exists.

Different life forms have always existed and functioned in communities, as discussed in 1859 by Charles Darwin in his *On the Origin of Species*. Thus interaction between the species is also an important area of study in physiology (ecosystem physiology). For instance, even healthy human beings host a huge number of different microbial species both in the skin and on all mucous membranes, and especially in the gastro-intestinal tract. The internal tissues may be sterile. Even healthy human cells can still host microorganisms, which are in a dormant stage. The number of microbes, their metabolic profiles, and the number of species varies in the gut of the same animal (or human) depending on the diet the individual is consuming.

The genome of some species—sixty or more already—have now been clarified. Also the human genome is almost completely known. The human genome size is about 3,000 megabases and about 30,000–35,000 genes. Humans have only about 300 genes that are not found in mice. The genome of common yeast, *Saccharomyces cerevisiae* is 12.1 megabases, and it contains 6,034 genes. The genome size of the fruit fly *Drosophila melanogaster* is 180 megabases, and it contains 13,061 genes. The size of the genome in mammals is much higher than would be expected from the number of genes. Thus the chromosome structure of humans and other vertebrates is more complicated than in other organisms. The architecture of the human chromosome structure apparently permits many more functional possibilities than in other models. When the human genome has been studied in different continents, it has been found that the gene pool in Africa contains more variation than in other parts of the world. This favors the conclusion that humans have their roots in Africa. All humans are thus actually Africans, although they may now live in distant territories.

The activation of individual genes or gene sets can now rather easily be studied with the aid of DNA chips and automated micro-arrays. These are helpful in understanding what happens at the genomic level, when the test organism is exposed to a new situation (e.g. a new chemical or physical environment). But of even greater significance will be methods, which hopefully will soon make it possible to clarify the proteomics of the cells (i.e. what proteins are found in which quantities through time, in cells at given conditions in response to internal and external stimuli). Technically the DNA arrays are simple compared to the techniques required for the analysis of physiological, i.e. dynamic, proteomics.

The major key component studied in physiology has been oxygen and its use. It is needed for respiration and energy production among many other roles in practically all biomolecules (see “*Respiration*,” EOLSS on-line, 2002). Many enzymes handle oxygen metabolism. Axel Theorell made discoveries on the nature and mode of action of oxidation enzymes (see Table 1). Oxygen in certain circumstances is, however, also potentially toxic due to its reactivity (see “*Metabolism of oxygen*” and “*Protection against oxidative stress*,” EOLSS on-line, 2002). Reactive oxygen species are at present considered to have a role in senescence and most diseases. The new technologies with the DNA array sets will probably soon provide a lot of new information on the effects of oxygen and oxygen-derived radicals, as well as on the effects of oxygen deficiency in

different organ systems and cells, both healthy and diseased. Wounds and tissue regeneration are interesting models in research, in addition to clinical medicine, because of disturbance in oxygen supply and its repair (see “Wound healing and regeneration,” EOLSS on-line, 2002).

Year	Area of achievement	Nobel Laureates
2001	Key regulators of the cell cycle	Leland H. Hartwell, R. Timothy (Tim) Hunt, and Sir Paul M. Nurse
2000	Signal transduction in the nervous system	Arvid Carlsson, Paul Greengard, and Eric Kandel
1999	Proteins have intrinsic signals that govern their transport and localization in the cell	Günter Blobel
1998	The nitric oxide as a signaling molecule in the cardiovascular system	Robert F. Furchgott, Louis J. Ignarro, and Ferid Murad
1997	Prions: a new biological principle of infection	Stanley B. Prusiner
1996	The specificity of the cell mediated immune defense	Peter C. Doherty and Rolf M. Zinkernagel
1995	The genetic control of early embryonic development	Edward B. Lewis, Christiane Nüsslein-Volhard, and Eric Wieschaus
1994	G-proteins and the role of these proteins in signal transduction in cells	Alfred G. Gilman and Martin Rodbell
1993	Split genes	Richard J. Roberts and Phillip A. Sharp
1992	Reversible protein phosphorylation as a biological regulatory mechanism	Edmond H. Fischer and Edwin G. Krebs
1991	The function of single ion channels in cells	Erwin Neher and Bert Sakmann
1990	Organ and cell transplantation in the treatment of human disease	Joseph E. Murray and E. Donnall Thomas
1989	The cellular origin of retroviral oncogenes	J. Michael Bishop and Harold E. Varmus
1988	For their discoveries of important principles for drug treatment	Sir James W. Black, Gertrude B. Elion, and George H. Hitchings
1987	The genetic principle for generation of antibody diversity	Susumu Tonegawa
1986	Growth factors	Stanley Cohen, Rita Levi-Montalcini
1985	The regulation of cholesterol metabolism	Michael S. Brown and Joseph L. Goldstein
1984	Theories concerning the specificity in development and control of the immune system and the discovery of the principle for production of monoclonal antibodies	Niels K. Jerne, Georges J. F. Köhler, and César Milstein
1983	Mobile genetic elements	Barbara McClintock
1982	Prostaglandins and related biologically active substances	Sune K. Bergström, Bengt I. Samuelsson, and John R. Vane
1981	• The functional specialization of the	Roger W. Sperry

	cerebral hemispheres • Information processing in the visual system	David H. Hubel and Torsten N. Wiesel
1980	Genetically determined structures on the cell surface that regulate immunological reactions	Baruj Benacerraf, Jean Dausset, and George D. Snell Jackson
1979	Development of computer assisted tomography	Allan M. Cormack and Godfrey N. Hounsfield
1978	Restriction enzymes and their application to problems of molecular genetics	Werner Arber, Daniel Nathans Hamilton, and O. Smith
1977	The peptide hormone production of the brain and for the development of radio-immunoassays of peptide hormones	Roger Guillemin, Andrew V. Schally, and Rosalyn Yalow
1976	New mechanisms for the origin and dissemination of infectious diseases	Baruch S. Blumberg and D. Carleton Gajdusek
1975	Interaction between tumor viruses and the genetic material of the cell	David Baltimore, Renato Dulbecco, and Howard Martin Temin
1974	The structural and functional organization of the cell	Albert Claude, Christian de Duve, and George E. Palade
1973	Organization and elicitation of individual and social behavior patterns	Karl von Frisch, Konrad Lorenz, and Nikolaas Tinbergen
1972	The chemical structure of antibodies	Gerald M. Edelman and Rodney R. Porter
1971	Mechanisms of the action of hormones	Earl W. Sutherland, Jr.
1970	The humoral transmitters in the nerve terminals and the mechanism for their storage, release and inactivation	Sir Bernard Katz, Ulf von Euler, and Julius Axelrod
1969	The replication mechanism and the genetic structure of viruses	Max Delbrück, Alfred D. Hershey, and Salvador E. Luria
1968	For their interpretation of the genetic code and its function in protein synthesis	Robert W. Holley, Har Gobind Khorana, and Marshall W. Nirenberg
1967	Primary physiological and chemical visual processes in the eye	Ragnar Granit, Haldan Keffer Hartline, and George Wald
1966	Tumor-inducing viruses and for discoveries concerning hormonal treatment of prostatic cancer	Peyton Rous, Charles Brenton, and Huggins Ben
1965	Genetic control of enzyme and virus synthesis	François Jacob, André Lwoff, and Jacques Monod
1964	The mechanism and regulation of the cholesterol and fatty acid metabolism	Konrad Bloch and Feodor Lynen
1963	The ionic mechanisms involved in excitation and inhibition in the peripheral and central portions of the nerve cell membrane	Sir John Carew Eccles, Alan Lloyd Hodgkin, and Andrew Fielding Huxley
1962	The molecular structure of nucleic acids and its significance for information transfer in living material	Francis Harry Compton Crick, James Dewey Watson, and Maurice Hugh Frederick Wilkins
1961	Physical mechanism of stimulation within the cochlea	Georg von Békésy

1960	Acquired immunological tolerance	Sir Frank Macfarlane Burnet and Peter Brian Medawar
1959	The mechanisms in the biological synthesis of ribonucleic acid and deoxyribonucleic acid	Severo Ochoa and Arthur Kornberg
1958	<ul style="list-style-type: none"> • For their discovery that genes act by regulating definite chemical events • Genetic recombination and the organization of the genetic material of bacteria 	George Wells and Edward Lawrie Tatum Joshua Lederberg
1957	For his discoveries relating to synthetic compounds that inhibit the action of certain body substances, and especially their action on the vascular system and the skeletal muscles	Daniel Bovet
1956	Heart catheterization and pathological changes in the circulatory system	André Frédéric Cournand, Werner Forssmann, and Dickinson W. Richards
1955	Nature and mode of action of oxidation enzymes	Axel Hugo Theodor Theorell
1954	The ability of poliomyelitis viruses to grow in cultures of various types of tissue	John Franklin Enders, Thomas Huckle Weller, and Frederick Chapman Robbins
1953	The citric acid cycle and co-enzyme A and its importance for intermediary metabolism	Hans Adolf Krebs and Fritz Albert Lipmann
1952	Streptomycin, the first antibiotic effective against tuberculosis	Selman Abraham Waksman
1951	Yellow fever and how to combat it	Max Theiler
1950	Hormones of the adrenal cortex, their structure and biological effects	Edward Calvin Kendall, Tadeus Reichstein, and Philip Showalter Hench
1949	The functional organization of the interbrain as a co-ordinator of the activities of the internal organs and the therapeutic value of leucotomy in certain psychoses	Walter Rudolf Hess Moniz and Antonio Caetano de Abreu Freire Egas
1948	The high efficiency of DDT as a contact poison against several arthropods	Paul Hermann Müller
1947	The course of the catalytic conversion of glycogen and the part played by the hormone of the anterior pituitary lobe in the metabolism of sugar	Carl Ferdinand Cori, Gerty Theresa Cori née Radnitz, and Bernardo Alberto
1946	Production of mutations by means of X-ray irradiation	Hermann Joseph Muller
1945	Penicillin and its curative effect in various infectious diseases	Sir Alexander Fleming, Ernst Boris Chain, and Sir Howard Walter Florey
1944	The highly differentiated functions of single nerve fibers	Joseph Erlanger and Herbert Spencer Gasser

1943	<ul style="list-style-type: none"> • Vitamin K • The chemical nature of vitamin K 	Henrik Carl Peter Dam Edward Adelbert Doisy
1940–2	One-third of the prize money was allocated to the Main Fund and two-thirds to the Special Fund of this prize section	
1939	For the discovery of the antibacterial effects of prontosil	Gerhard Domagk
1938	The role played by the sinus and aortic mechanisms in the regulation of respiration	Corneille Jean François Heymans
1937	The biological combustion processes, with special reference to vitamin C and the catalysis of fumaric acid	Albert von Szent-Györgyi Nagyrapolt
1936	Chemical transmission of nerve impulses	Sir Henry Hallett and Dale Otto Loewi Graz
1935	The organizer effect in embryonic development	Hans Spemann
1934	Liver therapy in cases of anaemia	George Hoyt Whipple, George Richards Minot, and William Parry Murphy
1933	The role played by the chromosome in heredity	Thomas Hunt Morgan
1932	Functions of neurons	Sir Charles Scott Sherrington and Edgar Douglas Adrian
1931	The nature and mode of action of the respiratory enzyme	Otto Heinrich Warburg
1930	Human blood groups	Karl Landsteiner
1929	<ul style="list-style-type: none"> • The antineuritic vitamin • The growth-stimulating vitamins 	Christiaan Eijkman Sir Frederick Gowland
1928	For his work on typhus	Charles Jules Henri Nicolle
1927	The therapeutic value of malaria inoculation in the treatment of dementia paralytica	Julius Wagner-Jauregg
1926	The Spiroptera carcinoma	Johannes Andreas Grib Fibiger
1925	The prize money was allocated to the Special Fund of this prize section	
1924	The mechanism of the electrocardiogram	Willem Einthoven
1923	For the discovery of insulin	Frederick Grant Banting and John James Richard Macleod
1922	<ul style="list-style-type: none"> • Production of heat in the muscle • The fixed relationship between the consumption of oxygen and the metabolism of lactic acid in the muscle 	Archibald Vivian Hill Otto Fritz Meyerhof
1921	The prize money was allocated to the Special Fund of this prize section	
1920	The capillary motor regulating mechanism	Schack August Steenberg Krogh
1919	For his discoveries relating to immunity	Jules Bordet

1915–18	The prize money was allocated to the Special Fund of this prize section	
1914	For his work on the physiology and pathology of the vestibular apparatus	Robert Bárány
1913	In recognition of his work on anaphylaxis	Charles Robert Richet
1912	Vascular suture and the transplantation of blood vessels and organs	Alexis Carrel
1911	For his work on the dioptrics of the eye	Allvar Gullstrand
1910	In recognition of the contributions to our knowledge of cell chemistry made through his work on proteins, including the nucleic substances	Albrecht Kossel
1909	For his work on the physiology, pathology, and surgery of the thyroid gland	Emil Theodor Kocher
1908	In recognition of their work on immunity	Ilya Ilyich Mechnikov and Paul Ehrlich
1907	Protozoa in causing diseases	Charles Louis Alphonse Laveran
1906	Structure of the nervous system	Camillo Golgi and Santiago Ramón y Cajal
1905	For his investigations and discoveries in relation to tuberculosis	Robert Koch
1904	Physiology of digestion, through which knowledge on vital aspects of the subject has been transformed and enlarged	Ivan Petrovich Pavlov
1903	In recognition of his contribution to the treatment of diseases, especially lupus vulgaris, with concentrated light radiation, whereby he has opened a new avenue for medical science	Niels Ryberg Finsen
1902	For his work on malaria, by which he has shown how it enters the organism and thereby has laid the foundation for successful research on this disease and methods of combating it	Ronald Ross
1901	For his work on serum therapy, especially its application against diphtheria, by which he has opened a new road in the domain of medical science and thereby placed in the hands of the physician a victorious weapon against illness and deaths	Emil Adolf von Behring

Note: Prizes have now been awarded for 100 years. Physiologist Robert Tigerstedt, as a friend of the great inventor and industrialist Alfred Nobel (1833–1896), helped him to formulate the regulations of the prizes.

Source: www.nobel.se.

Table 1. Nobel prizes in Physiology or Medicine

The present theme overview has been compiled with the aim of answering questions people commonly have in their minds. The article will not replace any textbooks of physiology. The topics selected cover some hot spots of research and then areas that one can meet in everyday life, and the reader may want to learn more. At the end the reader will be able to find electronic addresses that can be used for finding further information.

We start with Table 1, listing the Nobel Prize winners in Physiology or Medicine over the last 100 years. This list is not only a compilation of many great discoveries, but it also indicates the appreciation of the prize awarding committee at the time of decision. It is impossible to give such a prize to all great discoveries in physiology. Therefore traditional physiology is poorly represented in the list. For example, although the physiology and pathophysiology of the mouth is one of the most interesting and active areas of research, as well as the site of many diseases and the cause of diseases all around the body, no prizes have ever been awarded in this area. On the other hand one should also note that some important discoveries in physiology have received Nobel prizes in Chemistry and Physics.

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Darwin, C. 1859/2000. *On the Origin of Species*. Trans. from the English into Finnish by A. R. Koskimies. 4th edn. Hämeenlinna, Karisto Oy. 684 pp. [Comprehensive discussion on the interactions between the species, as well as on the mechanisms of species' success at different levels; one of the key texts in biology.]

De La Fuente-Fernandez, R.; Ruth, T. J.; Sossi, X.; Schulzer, M.; Calne, D. B.; Stoessl, A. J. 2001. Expectation and Dopamine Release: Mechanism of the Placebo Effect in Parkinson's Disease. *Science*, No. 293, pp. 1164–6. [Demonstration that the expectation of benefit has a therapeutically significant effect, and the effect can be visualized and measure in positron emission tomography.]

Hari, R.; Forss, N. 1999. Magnetoencephalography in the Study of Human Somatosensory Cortical Processing. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.*, Vol. 354, No. 1387, pp. 1145–54. [The possibilities of recording the handling of sensory information in the brain with sensors outside of the body are reviewed.]

Science. 2001. The Human Genome. *Science*, No. 291, pp. 1145–434. [Compilation of present knowledge by several authors on the human genome, and the presentation of the structure and presentation of the research challenges.]

Science. 2001. Epigenetics. *Science*, No. 292, pp. 1001–208. [Several authors describe and discuss the epigenetic control of genome by chromatin proteins and methylation of DNA.]

Science. 2001. Sleep, Dreams and Memory. *Science*, No. 294, pp. 945–1228. [A set of articles by several authors that cover most of the key topics in neurophysiology.]

Sen, C. K.; Packer, L.; Hänninen, O. (eds.) 2000. *Handbook of Oxidants and Antioxidants in Exercise*. Amsterdam, Elsevier. 1207 pp. [Comprehensive set of articles on oxygen metabolism, metabolites, and defense mechanisms that help to control the side effects of radicals in health and disease.]

Toivanen, H.; Helin, P.; Hänninen, O. 1993. Impact of Regular Relaxation Training and Psychosocial Working Factors on Neck–Shoulder Tension and Absenteeism in Hospital Cleaners. *Journal of Occupational Medicine*. Vol. 35, No. 11, pp. 1123–30. [Learning to relax with the aid of respiration exercises, practiced in 15-minute sessions during daytime breaks, decreased muscle tension levels and also work absenteeism.]

Wentworth, Jr., P.; Jones, L. H.; Wentworth, A. D.; Zhu, X.; Larsen, N. A.; Wilson, I. A.; Xu, X.; Goddard III, W. A.; Janda, K. D.; Eschenmoser, A.; Lerner, R. A. 2001. Antibody Catalysis of the Oxidation of Water. *Science*, No. 293, pp. 1806–11. [Demonstration that immunoglobulins catalyze the synthesis of hydrogen peroxide.]

A selection of Electronic Information Sources in Physiology

Basic research, the lifeline of medicine:

<http://www.nobel.se/medicine/articles/index.html>

<http://journals.bmn.com/> (BioMedNet)

<http://physiology.cup.cam.ac.uk/> (Physiology on-line)

<http://links.bmn.com/>

<http://www.nlm.nih.gov/medlineplus/>

<http://www.journals.uchicago.edu/PBZ/journal/index.html> (Physiological and biochemical zoology)

<http://server.physiol.arizona.edu/Physiology/Main.html>

<http://physiology.uthscsa.edu/>

http://www.ninds.nih.gov/health_and_medical/disorders/chronic_pain.htm

<http://bioinformatics.weizmann.ac.il/mb/db/enzymes.html> (Enzyme, metabolic, and signaling pathways databases)

<http://www.nal.usda.gov/fnic/> (Food and Nutrition Information Center)

<http://www.ursa.kcom.edu/Department/LectureNotes/NotesMaster.htm>

<http://cardiovascular.cx/>

<http://www.ursa.kcom.edu/Department/LectureNotes/NotesMaster.htm>

Brain briefings:

<http://www.sfn.org/briefings/>

Neuroscience gateway:

<http://reviews.bmn.com/?subject=neuroscience>

Plant physiology:

<http://www.plantphysiology.com/>.

<http://www.usu.edu/cpl/celss.htm> (Crop Physiology Lab)

<http://www.keil.ukans.edu/delta/angio/> (The families of flowering plants)

Biographical Sketch

Dr Osmo Otto Päiviö Hänninen, DMS, Ph.D., Professor of Physiology, Chairman of the Department, University of Kuopio, Finland was born in 1939, in Lahti, Finland. He studied at the University of Helsinki and the University of Turku, Finland, where he received his Master of Sciences (Biochemistry) in 1962, Licentiate of Medicine (MD) in 1964, Doctor of Medical Sciences (DMS) in 1966, and passed his dissertation in biochemistry for his Ph.D. in 1968. He has also studied genetics. He has been a specialist in sports medicine since 1986. He served as the Research Assistant of Professor K. Hartiala, 1962–4; Assistant of Physiology, 1964–5; Laborator of Physiology, 1966–7; Docent of Physiology, from 1967, and Associate Professor of Biochemistry, 1969–71, at the University of Turku; Acting Professor in the Planning Office, 1971–2; and from 1972, Professor of Physiology and Chairman of the Department of Physiology, University of Kuopio; Vice-President of the University of Kuopio, 1972–9; and President, University of Kuopio, 1981–4. Furthermore, he served as Visiting Professor of Physiology at Shanghai Medical University, China, 1991–2, and at Sun Yat Sen Medical University, Guangzhou, China, 1998–9; as Foreign Member of the Russian Academy of Natural Sciences, from 1994; and as Secretary General, International Council for Laboratory Animal Science, 1988–95. He was the President of *Societas Physiologica Finlandiae*, 1990–9, and has been President of the International Society for Pathophysiology and a Member of the Executive Committee since 1994, and the Treasurer of the International Union of Biological Sciences since 1997.

His special interests in research are biotransformation and adaptation to chemical loading, biomonitoring of toxicants, and comparative biochemical toxicology; muscle metabolism and function; and ergonomics.

He has contributed 266 papers in refereed journals and seventy-two in proceedings, and written fifty-five reviews, and thirty books or book chapters. He serves on the editorial board of four international journals and is at present the European Journal Editor of *Pathophysiology*.

Of his post-graduate students (thirty-two in biotransformation, twenty-seven in muscle metabolism and physiology, and five others), twelve serve as professors in China, Finland, Greece, Sweden, and the United States.