

Preface

In 2007, we published the first textbook on glial neurobiology, *Glial Neurobiology: A Textbook*. The aim of our first book was to provide an introduction to glial cells, aimed at undergraduates and postgraduates in neuroscience. However, it has become clear to us that there is also the need for a more detailed and comprehensively referenced account of glial neurobiology for researchers and clinicians. This is the aim of our new book, *Glial Physiology and Pathophysiology*. We have deliberately shaped this to be a textbook that is readily accessible to those who want to get a systematic view on neuroglial function in physiology and pathophysiology.

This is meant to be a learning resource, not a reference book. The glial field has a weighty reference book, *Neuroglia*, written by several dozen experts in the different aspects of glial cell biology under the auspices of H. Kettenmann and B. Ransom. However, a substantial gap exists between the reference book *Neuroglia* and our first book *Glial Neurobiology: A Textbook*, both in the scientific content and complexity. The aim of our new book *Glial Physiology and Pathophysiology* is to fill this gap and to provide an account of glial cell biology that, hopefully, is written in a style that is enjoyable and interesting to read.

Our purpose has been to write a comprehensive, yet concise and readable, account of neuroglia – the class of cells that provide for the housekeeping and defence of the nervous system. Neuroglial functions in health and disease are generally overlooked in contemporary curricula for medics and biologists. Indeed, neuroglia are mentioned only superficially in the absolute majority of university courses. This neglect has been developed over the course of the last century or so, mainly after the discovery of electrical excitability in neurones, the principal signalling cells in the nervous system. The discovery of action potentials and synaptic transmission provided us with a fundamental understanding of nervous system functioning; neuronal networks can be relatively easily reduced to logical units communicating in binary fashion, and electronic summation provides a simple tool to predict how the excitation/inhibition of a given neurone defines output. This has had a mesmerising effect upon the minds of neurophysiologists. We can see the most powerful computers in the world employed to model the brain,

based on an assumption of the primary role for action potential-mediated binary encoded signalling between logical elements that can exist in a limited (excited/resting/inhibited) number of states.

Nature, of course, is far more complex than our most ingenious engineering. The nervous system is not a computer, with an output that can be precisely calculated. There are many ways of signalling between neural cells that involve diffusion of many different molecules, each with their own targets, weaving an intricately interconnected canvas for information processing.

This book is not about processing in neural networks, but rather about overall homeostasis in the nervous system. Homeostasis is fundamental for the life of organisms, organs, tissues and cells. The nervous system is not an exception. In the course of the evolution of the nervous system that appeared in the most primitive multicellular organisms, neural cells have divided into the executive branch, represented by neurones (which control reception of sensory input and effect an output to control peripheral organs) and the housekeeping branch, represented by neuroglia. Perfection of fast signalling in neuronal networks required a division of labour, and neurones lost their ability to maintain their own survival adequately; these functions went to neuroglia.

This, then, was our endeavour – to relate the evolutionary history of neuroglia and to demonstrate how these cells assume every conceivable function aimed at maintaining nervous system homeostasis. Indeed, neuroglia oversee the birth and development of neurones, the establishment of inter-neuronal connections (the 'connectome'), the maintenance and removal of these inter-neuronal connections, wiring of the nervous system components, adult neurogenesis, the energetics of nervous tissue, metabolism of neurotransmitters, regulation of ion composition of the interstitial space and many, many more homeostatic functions.

In this book, we start with the history of neuroscience, trying to show the development of ideas and concepts of nervous system organisation. In particular, we emphasise that, from the very beginning of cellular neuroscience, little distinction was made between neural cell types and the great minds of neuroscience regarded glia as an indispensable element of the neural architecture. By doing this, we hope to prime the reader towards the notion that nervous tissue is not divided into 'more important' and 'less important' cells. The nervous tissue functions because of the coherent and concerted action of many different cell types, each contributing to an ultimate output. This reaches its zenith in humans, with the creation of thoughts, underlying acquisition of knowledge, its analysis and synthesis, and contemplating the Universe and our place in it.

Also, we contemplate the role of neuroglia in pathology. All diseases are, fundamentally, failures of the homeostasis that makes organs and organisms incompatible with life. The neurological diseases are, *ipso facto*, failures of homeostasis in the nervous tissue and are, in essence, failures of the homeostatic cells – neuroglia. Indeed, progression and outcome of all neurological diseases are

defined by neuroglia, which defends the brain. When this defence system crumbles, the nervous tissue dies.

This book has been shaped by many years of work and discussions with our friends and colleagues, to whom we extend our heartfelt thanks. Also, in writing this book we have relied on many authoritative papers and review articles written by those who are more expert than ourselves in particular aspects of glial cell biology. We hope that we have done a good job in representing their findings. We apologise for any inaccuracies and for any important omissions, which we trust are few.

Alexei Verkhratsky

Arthur Butt

June 20, 2012

Alexei Verkhratsky



Professor Alexei Verkhratsky, MD, PhD, D.Sc., Member of Academia Europaea, Member of Real Academia Nacional de Farmacia, was born in 1961 in Staroslov, Galicia, Western Ukraine. He graduated from Kiev Medical Institute in 1983 and received his PhD (1986) and D.Sc. (1993) in Physiology from Bogomoletz Institute of Physiology, Kiev, the Ukraine. From 1990 to 1995, he was Head of the Laboratory of Cellular Signalling in Bogomoletz Institute of Physiology.

In the period between 1989 and 1995, Professor Verkhratsky was visiting scientist in Heidelberg and Göttingen, and between 1995 and 1999 he was a research scientist at Max Delbrück Centre of Molecular Medicine in Berlin. He joined the Division of Neuroscience, School of Biological Sciences in Manchester in September 1999, became a Professor of Neurophysiology in 2002 and served as head of the said division from 2002 to 2004. From 2007 to 2010, he was appointed as Visiting Professor/Head of Department of Cellular and Molecular Neurophysiology at the Institute of Experimental Medicine, Academy of Sciences of Czech Republic. In 2010, he was appointed as a Research Professor of the Institutique (Basque Research Council) and in 2011 as a Visitor Professor at Kyushu University, Fukuoka, Japan.

Professor Verkhratsky was elected to membership of Academia Europaea in 2004 and since 2006 he has been Chairman of the Physiology and Medicine section. In 2011, he was elected a foreign member of Real Academia Nacional de Farmacia, Spain. He is editor-in-chief of *Cell Calcium* (2000) and *Membrane Transport & Signalling – Wiley Interdisciplinary Reviews* (2009), Reviewing Editor (neuroscience) of *Cell Death & Disease* (2009) and a member of the editorial boards of *Pflügers Archiv-European Journal of Physiology*, *Journal of Molecular & Cellular Medicine*, *Acta Physiologica* (Oxford), *Acta Pharmacologica Sinica* (2005), *GLA* (2008), *Frontiers in Neuropharmacology*, *Frontiers in Aging Neuroscience* (2009), *Paracrine Signalling*, *ASN Neuro* (2010), *Neuroscience Bulletin* (2011). He has delivered more than 450 international invited lectures and seminars.