pH AND BRAIN FUNCTION.
By Kai Kaila and Bruce R. Ransom.

Over the last two decades, considerable information has been generated with regard to the regulation of brain pH and how neural cells respond to pH changes. Until now most of this information has been disseminated in various scientific journals. Thus, one of the aims of the editors of this book was to create a book that would render such information accessible to an audience that has no special training in this field. The editors largely achieve their aim with this book, and the reader will certainly feel like an expert in the field by the last page.

The book itself is comprised of 33 chapters, which have been grouped logically into seven sections. Section 1 (5 chapters) is entitled ‘Introduction to pH’. This section covers a wide range of topics that would not immediately spring to mind from the title. There is an introductory chapter that discusses the concept of pH and the role of H+ ions in physiology and pathophysiology. There is reference to an intriguing piece of work from a reputable group suggesting a link between brain cell pH and IQ. Other chapters of this section adequately cover pH buffering, the carbonic anhydrases, ion diffusion and cerebral energy metabolism. Complicated equations are generally kept to a minimum throughout the section; however, for those readers who enjoy such things, the appendices of Chapter 4 will be appreciated.
The four chapters of Section 2 consider the various possibilities of studying pH in vitro and in vivo. Consequently, ion-sensitive microelectrodes, absorbance pH indicators, fluorescence indicators and determination of brain pH by nuclear magnetic resonance (NMR) are covered. These chapters cover in fair detail the background and application of these various techniques. For those readers inspired to actually perform experiments, detailed protocols are not provided. However, each chapter contains a comprehensive list of references that should point interested parties in the right direction.

With the basics and techniques available for studying pH dealt with, the reader should feel reasonably well equipped to deal with the subsequent sections of the book, which directly relate to pH and brain function. The cellular mechanisms available for pH regulation are covered by Section 3. Consequently, there are chapters on the thermodynamics of pH regulation, regulation of pH by neuronal and glial cells (mammalian and invertebrate), and the effect of perturbations of calcium metabolism upon cellular pH.

As a result of cellular activity, considerable changes in both intracellular and extracellular pH can occur. These changes and the consequences of such alterations in pH are covered by the fourth section of the book. The first chapter of this section concentrates on the effect of neuronal activity upon the intracellular milieu of both neurons and glial cells. Of particular note is the pH sensitivity of the glycolytic enzyme, phosphofructokinase. It is proposed that the increase in glial cell pH that accompanies neuronal activity leads to increased glycolytic flux and lactate generation. This lactate may then be exported and utilized to sustain the energy requirements of the active neurons. Other chapters in this section consider the effect of various pathological states upon extracellular pH, e.g., in an experimental model of multiple sclerosis it appears that there is an increase in extracellular pH around the spinal cord which may be attributed to glial cell dysfunction. The final chapter of this section concentrates on the pH changes associated with glutamate uptake. Thus the various mechanisms for the uptake of this neurotransmitter and the associated changes in intra- and extracellular pH are discussed.

The first chapter of Section 5 commences with an interesting historical prelude that reviews early experiments involving the use of carbon dioxide (CO₂) as an anaesthetic. The chapter then goes on to discuss the effects of CO₂ and H⁺ in experimental animals, peripheral nerve preparations and cultured neurons. The important point is made that some observed effects may not be due to pH changes but arise as a direct effect of cellular interactions with CO₂. Generally, neurons decrease their activity in response to CO₂ exposure. However, for certain neurons in the brainstem the opposite appears to be the case, i.e. such cells may play a critical role in controlling respiration. The theme of pH modulation of neuronal activity continues in the next two chapters that concentrate in more detail on the interaction of H⁺ with voltage gated and ligand gated ion channels. The penultimate chapter of this section considers the possible mechanisms whereby alterations in the intracellular H⁺ and/or calcium concentration influence the opening of the gap junctions. Within the brain glial cells, as a result of gap junction interconnections, form interconnections that may extend throughout the brain. This synctium may function, under normal conditions, to provide buffering of potassium ions, neurotransmitters and their metabolites. Loss of this buffering capacity may therefore occur in certain pathological states that alter cellular H⁺ and calcium homeostasis. The section concludes with a chapter that considers the relationship between pH and the activity of the cell types to be found in the vertebrate retina. Extracellular pH changes of 0.2 units are reported to occur as a result of light stimulation. Furthermore, retinal activity is modulated by changes to the extracellular pH. This chapter also raises the important point that the experimental system utilized to study retinal cells, and presumably other cell types, can dramatically influence the result, i.e. particular attention should be paid to the buffering systems used and the initial pH of the system being studied.

The control of respiration is one of the functions of the mammalian central nervous system that is most sensitive to pH, i.e., one of the primary mechanisms of regulating acid–base balance is via respiration. Section 6 focuses on the probable cellular mechanisms, pH sensitivity and respiratory control. Thus the nature, location and mode of action of the putative central chemoreceptors are covered by the two chapters that make up this short section of the book.

The final section concerns itself with the pH changes associated with certain pathological conditions. The first two chapters cover ischaemia and the possible biochemical mechanisms involved in eliciting the cellular damage associated with this condition. Of particular note is the concluding comment of the first of these chapters, which points out that there can be major discrepancies between the results obtained with in vitro and in vivo models of ischaemia. The application of NMR for monitoring cerebral pH changes in various conditions is also covered in a chapter which builds upon the basic principles that were discussed in Section 2, Chapter 9. Until recently, alterations in cytoplasmic pH have not been considered to be an important factor in the pathogenesis of neuromuscular disorders. However, as a result of advances in techniques for measuring intracellular pH, abnormalities in cytoplasmic pH have been reported in a number of conditions known to affect nerve and muscle. Chapter 31 brings together data reporting pH changes and potential mechanisms for such changes in diabetic neuropathy and neuromuscular disorders such as the mitochondrial myopathies, and proposes that acidification of the cytoplasm may be an important factor in the muscle fatigue associated with such disorders. The final chapter of this book considers the control and disturbances of cerebrospinal fluid (CSF) pH. The chapter adequately covers the formation and chemistry of CSF before considering pH regulation and conditions that
may lead to perturbations of pH in the CSF, e.g. metabolic and respiratory acid–base disorders.

In conclusion, this is a comprehensive text that appears to cover every aspect of pH and its relationship to brain function. Whilst some of the chapters may be a little heavy going in places, this book would certainly be a worthwhile addition to the bookshelves of neuroscientists working on brain metabolism and disorders of the central nervous system.

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