Ove Sten-Knudsen

Biological Membranes

Theory of transport, potentials and electric impulses

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OVE STEN-KNUDSEN
Professor Emeritus of Biophysics
University of Copenhagen

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BIOLOGICAL MEMBRANES

This graduate text, suitable for students of physiology and biophysics, and medical students specializing in neurophysiology and related fields, provides a comprehensive discussion of biological mass transfer and bioelectrical phenomena. Emphasis has been given to the applicability of physics, physical chemistry and mathematics to the quantitative analysis of biological processes, with all the necessary mathematical grounding provided in Chapter 1.

The quantitative analysis is broken into four key stages:

- formulation of a biological/biophysical model,
- derivation of the associated mathematical description of the model,
- solution of the mathematical expression, and
- interpretation of the mathematical solution to a biological explanation.

This book guides the student through these stages, which are central to the understanding of cell membrane functions.

To
Nan-Marie
Helge, Nina
and
Henrik

Foreword

I was delighted when my friend Ove Sten-Knudsen asked if I would write a Foreword to this English translation of his book on biological membranes. I confess that I then had no idea of the immense scope and magisterial quality that I found when I saw the proofs. I wish that such a book had been available in the days when I was concerned with membranes and ion movements: I often had to struggle through the derivation of equations that are here worked through step by step. This will be invaluable not only to students but to the many biologists who work on membranes and use mathematics but are not themselves mathematicians in the full sense of the word. It will also be a major convenience to have the whole background collected in a single volume, instead of being scattered in numerous articles and books.

Another feature that gives me great pleasure is the biographical notes on the authors of classical papers in the field. Whenever one of those great men is mentioned for the first time, there is a footnote telling us his dates, where he worked and his main achievements. This is a welcome contrast to the usual practice of merely giving a name with no indication that it refers to an actual human being.

The book's title hardly does justice to its content: as well as dealing with the properties shared by all cell membranes, it includes very full accounts of the fundamentals of nerve conduction and of synaptic transmission. These were established half a century ago and nowadays they are too easily taken for granted while emphasis is put on the more modern studies of ion channels that followed from them.

This book will be a godsend to all who aim for a quantitative understanding of membrane phenomena.

Sir Andrew Huxley, OM, FRS
Cambridge
April 2002

Preface

I often say that when you can measure what you are speaking about, and express it in numbers, you know something about it; but if you cannot measure it, when you cannot express it in numbers, your knowledge is of a meager and unsatisfactory kind: It may be the beginning of knowledge, but you have scarcely in your thought advanced to the stage of science.

Lord Kelvin, 1883

The phenomena of mass transfer and electric activity across biological cell nembranes involve a variety of complex processes. To be able to understand and describe these basic mechanisms it is essential to have a thorough insight into the nature of mass transfer by migration, diffusion, and electrodiffusion, and of concepts and fundamental principles of physics and physical chemistry. It is difficult to understand and describe processes in a biological membrane without leaning on the knowledge of mechanisms that operate in simpler systems. In describing transport processes through a cell membrane, we use the concepts of simple passive transport theory. Command of these concepts is the basis on which one performs a quantitative analysis of processes that are observed experimentally.

The purpose of the present book is to give an overall account of diffusion, electrodiffusion, equilibrium potentials, diffusion potentials and membrane potentials, and, in this connection, to take relevant examples from membrane physiology/biophysics to illustrate the use of these tools in a quantitative analysis of the experimental results. It is hoped that the text may be of use to undergraduate studies in general physiology/biophysics and to some postgraduate researchers.

The mathematical background needed to read the book corresponds to the level of a college student graduating in science. These prerequisites for reading the book are presented in **Chapter 1**. They serve to refresh the memory of the reader, making frequent use of cross-reference in the following chapters. In the following chapters, the mathematical build-up is developed in detail without requiring an additional mathematical course. In this respect the book is self-contained. The presentation of the mathematics is deliberately written in a user-friendly manner, intended for readers who are not professional mathematicians or physicists. Therefore, the mathematical derivations are written out in detail, which may appear unnecessarily detailed to a reader who is skilled in handling mathematics. It is my experience that in this way most readers with no basic training in mathematics can be brought to understand – and later to apply – rather complicated mathematics. On the other hand I do not want to conceal the fact that at places the reader *is* confronted with problems that unavoidably are rather complicated to handle. But the reader will never meet the rather condescending phrase: 'it is easily seen that . . . '.

The theory of mass transfer by diffusion, migration, and by the superposition of these processes, is developed in **Chapter 2**. The chapter starts by introducing principles of migration flux and diffusion flux that define the associated parameters mobility and diffusion coefficient. This leads to the law of mass conservation (the diffusion equation). The exposition is based upon macroscopic considerations. Later these processes are reconsidered from the microscopic point of view of *Brownian motion* and *Boltzmann statistics*. I regard the introduction of these complementary aspects to be particularly useful to understand mass transfer across cell membranes. To solve the time-dependent diffusion equation no use is made of integral transforms, a mathematical technique that is beyond the scope of this book. Ludwig Boltzmann used an inspired transformation that by simple allowed him means to find a particular solution of the diffusion equation in terms of the Error function. The presentation in this book succeeded in using adaptations of this solution to solve both the new diffusion problems in **Chapter 2** and to handle problems in the remaining chapters.

Chapter 3 deals with the theory of transport of ions in aqueous solutions, as well as the origin of electric potential differences across cell membranes, i.e. membrane potentials. The basis for this is the theory of *electrodiffusion*: diffusion superimposed upon migration of ions with an electric field as driving force. The chapter starts by introducing the necessary concepts: electric potential and field, electric conductance of a single ion and of a mixture of ions. The Nernst–Planck equations, the equations of electrodiffusion most frequently occurring in electrophysiology, follow as a natural sequel of the general transport equation in Chapter 2. The condition of *electroneutrality* is assumed to hold almost throughout. The *equilibrium potential* across a membrane is introduced by applying the Nernst–Planck equation to the transport across an ion selective permeable membrane. The Donnan system is treated partly by making use of a thermodynamic argument and partly by using the Poisson–Boltzmann equation to determine the potential and concentration profiles. The treatment of the *diffusion potential* begins by considering the concentration differences of a single salt. This is followed by the descriptions of the general diffusion regimes of Planck and by Henderson which both relate to a membrane that is separated by mixtures of electrolytes of different composition. Membrane potentials in living biological cells will be described as complex diffusion potentials. Of common interest are three types of membrane whose properties are described in detail: (1) the anion/cation selective permeable membrane; (2) the constant field membrane (Goldman equation), and (3) the mosaic membrane, each type having its own merits. The chapter ends by comparing the membrane potentials obtained in experiments on a living single frog-muscle cell with those predicted from theory.

Most readers of this book are assumed to be biologists seeking an in-depth understanding of biological transport and bioelectrical phenomena. **Chapter 4** comprises a bridge between the theoretical treatment and some fundamental biological experiments performed in nerve (and muscle) fibre. Thus the chapter is essential for demonstrating the applicability of physics and physical chemistry to biology. Furthermore, it contains analyses not been treated in the previous chapters (e.g. cable analysis). The chapter starts by summarizing the basic properties of nerve excitability and impulse transmission. The emphasis is the meticulously planned and epoch-making work on the axon of the squid (*Loligo*) by A.L. Hodgkin & A.F. Huxley, with participation of B. Katz and R.D. Keynes. The experimental results were interpreted and followed by a quantitative analysis accounting for the origin of the action potential in the giant nerve of the squid. The lessons to be learned from this work extend far beyond its relation to nerve activity.

Chapter 5 presents the important investigations of Katz and co-workers on the processes involved in the neuromuscular transmission, where statistical arguments were used to account for their observations.

It should be emphasized that the aims of **Chapter 4** and **Chapter 5** are not to provide an up to date review of the field. The examples chosen only serve the didactic intentions of this book.

The basis of the present book is a similar text published in Danish in 1995* aimed at students of general physiology, biophysics and postgraduate researchers in neuromedicine. The present book is the result of many revisions and it has been supplemented with new sections.

I wish to thank my colleagues professor Rodney Cotterill, Dr phil & scient, Professor Erik Hviid Larsen, Dr scient, and Professor Ulrik V. Lassen, Dr med.,

* O. Sten-Knudsen (1995): *Stoftransport, membranpotentialer of elektriske impulser over biologiske membraner*. Akademisk Forlag, København.

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Finally, it gave me great pleasure that Sir Andrew Huxley, OM, FRS, kindly agreed to write the Foreword to the book. I also greatly appreciated the concomitant constructive comments to the text.

Ove Sten-Knudsen
Gentofte, May 2002

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