involving the generation of animal radiotracer biodistribution data. As such, it represents a unique resource both for those contemplating entering this field and for those who wish to update and expand their skills and knowledge.

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BIOLOGICAL TRANSPORT OF RADIOTRACERS. L. G. Colombetti, Ed. Boca Raton, Florida, CRC Press, 1982, 329 pp, $94.00

The scientific study of biological transport began in the middle of the last century with the qualitative descriptions by Naegely and Cramer on plant-cell membrane permeabilities and with the quantitative studies and mathematical studies of Fick on diffusive transport. While these and the subsequent early results were elegant and insightful, the prodigious growth of our knowledge of biological transport to its present breadth began with the introduction to radioisotopic methodology following the pioneering work of von Hevesy in the 1920s. The delicate sensitivity and ease of measurement offered by the new technique have made it the basis for much of the information on biokinetic phenomena we now possess.

Biological Transport of Radiotracers is an extensive collection of review articles by 19 well-qualified scientists addressing the large topic of mass transport in living entities, with emphasis on, but by no means limited to, the use of radiolabeled tracers and indicators. This book is part of a still larger undertaking, the publication of the CRC Series in radiotracers in biology and medicine, which at the present time comprises eight other related volumes of comparable scope.

As is frequently the case with books of multiple authorship, each contribution stands isolated from the others, and in this book, except for a brief preface by the editor, no very effective attempt at unification has been made. This makes a holistic description and evaluation of it difficult to accomplish. Accordingly, this review proceeds chapter by chapter, with groupings that reflect perceived similarities of content.

The first two chapters "Biological Transport: An Historial View," and "Solute Translocations" are introductory. The first reviews briefly the development of the study of biological transport, dividing the subject in the same fashion as is done in the rest of the book by treating separately transport into cells and transport in body fluids. The second is a concise and lucid summary of present understanding of the mechanisms of transmembrane transport. The author considers it to be "a list of topics to be considered before embarking on an investigation requiring solute translocation across a biological membrane."

The next three chapters "Dynamic Aspects of Cell Membrane Structure," "Transmembrane Transport as a Rate-Limiting Phenomenon in the Distribution of Pharmacological Agents," and "Membrane Transport," cite the evidence for mobility of membrane constituents in the plane of the membrane and describe the influence of this lateral mobility on transmembrane transport. Additionally, a review is provided of the experimental conditions and criteria that must be applied to differentiate true transmembrane transport from binding unrelated to transport that experimentally would be falsely interpreted as "uptake." A detailed review of the various modes of transmembrane transport is given, expanding on the more summarized exposition of Chapter 2.

Chapter 6, "Thermodynamic Aspects of Radiotracer Flow," reviews the concepts that lead to the use of radiotracer flows to define the driving forces in coupled transport processes. The ideas of nonequilibrium thermodynamics are used as the basis for the descriptions given. The author shows that ratios of unidirectional fluxes, which in the unperturbed state can be measured only through the use of radiotracers, are a measure of the total Gibbs' free energy involved in the tracer transport process.

The chapter, "Kinetics of Blood To Cell Uptake of Radiotracers," in addition to being the most extensive is, at least from the point of view of the in vivo experimentalist investigating whole-organ or whole-body mass transport, one of the most fundamental. It seeks to provide answers to his question: "Given my observed laboratory or clinical data in the form of a temporal record of radiotracer response to a given radiotracer stimulus, how can I infer the parameters of biochemical or physiological importance that gave rise to my data?" The immediate answer is, of course, "By the judicious devising and use of mathematical models." The authors have provided a clearly written summary of much of the accomplishments in this difficult field since the early work of G. N. Stewart at the close of the last century. They point out that the techniques for obtaining information with relatively little disturbance in patients and animals has received great impetus in the last three decades with the advent of cardiac catheterization, and in the past few years, with the ever-increasing use of radionuclide-imaging techniques.

Included among the topics treated are descriptions of the general experimental and data-analysis methodologies that have evolved: single- and multicapillary distributed models, methods of accounting for blood-flow heterogeneities, estimation of flow by outflow- and residue-detection, and the delineation of conditions for the valid application of lumped-parameter or compartmental models. The chapter concludes with a brief review of whole-body kinetics of tracers taken up into cells.

Chapter 8, "Effect of Solute Structure on Transport of Radiotracers," and Chapter 9, "Effect of Transport on Distribution of Radioions and Radiometabolites," both by Y. Yano, are mutually complementary. One describes the pathways and binding sites of some of the radiopharmaceuticals commonly used in nuclear medicine, as influenced by the various mechanisms that bring about their transport and the other treats the inverse problem of designing radiopharmaceuticals to trace predetermined pathways and to bind to specific desired sites. From this viewpoint, it would seem reasonable to inquire why the two chapters were not combined into one. Chapter 8 gives some general principles of the relations between solute structure and transport. Effects such as lipid solubility, facilitated diffusion, and other structure-specific consequences are described. The possibility of designing radiotracers to predetermine their transport and binding behavior is considered and examples of successful efforts of this kind are described. Among these are the use of radiofluorinated deoxyglucose to effect "metabolic trapping" in brain and the use of similarly labeled fatty acids to study regional metabolism in the heart. No mention is made of the inherent limitations of analogs to study transport of endogenous substrates due to differences in kinetic behavior, especially in disease states. (This issue, however, is discussed fully in a general way in Chapter 13.) Chapter 9 reviews the effects of transport mechanisms on the spatial distribution of radiotracers used routinely in current clinical practice. Among the various labels discussed are those incorporating technetium-99m, iodine-123, -125, and -131, thallium-201, fluorine-18, xenon-127 and -133, krypton-81m, gallium-67, and indium-111 and -113m. Consideration is given to the interaction of the various radiolabels with plasma proteins and blood cells and to their mechanisms of uptake by cell-membrane permeation or by binding at specific sites. A short discussion is given on current developments in the use of the positron emitters carbon-11, nitrogen-13, and oxygen-15 to label biochemical compounds and blood-flow tracers for use in computer-aided, positron-emission tomography.

Chapter 10, "Transport of Protein-Bound Radiotracers into Tissues," and Chapter 12, "Transport of Radiolabeled Antibodies," includes an extensive review of kinetic factors, such as debinding rates, membrane permeabilities, and capillary transit

times, that must be taken into account for valid mathematical modeling of rates of plasma-protein-ligand debinding and ligand transport from capillary blood to tissue. Conditions under which equilibrium measurements of concentrations in vitro can be assumed to be valid for the dynamic nonequilibrium conditions prevailing in vivo during transit within the capillary are analyzed. The analysis is then applied to a wide variety of protein-bound ligands, viz., tryptophan, thyroid hormones, steroid hormones, propranolol, free fatty acids and cholesterol, vitamins, electrolytes, and bilirubin. A similar discussion is presented for binding by cytoplasmic proteins. Chapter 11, "Transport of Radiolabeled Enzymes," explains that in comparison with the wide variety of radiolabeled proteins, such as hormones, fibrinogen, and gamma globulin used for in vivo studies in man, the use of radiolabeled enzymes is not yet very extensive. Given their high specificity and the sensitivity of radioanalytical techniques used in their examination, however, enzymes are strong candidates for radiolabeling applications in the near future. Fundamentals are described concerning structure and radiolabeling of enzymes, such as direct labeling and indirect labeling by using radiolabeled antibiotics and alkaloids that bind strongly to some of them. A discussion is presented of the results and problems encountered in enzyme radiolabeling, such as lack of specificity, radiolysis, and the risk of denaturing. A short review of the physiochemical and biological factors influencing transport of radiolabeled enzymes concludes the chapter. Chapter 12, "Transport of Radiolabeled Antibodies," discusses the administration of radiolabeled antibodies in cancer therapy. The purpose of this use is to achieve simultaneously tumor localization by external detection of the emitted radiation and a synergistic coupling of antibody and ionizing-radiation effects that together cause in situ destruction of tumor cells. Transport to the tumor site is by way of intravenous or lymphatic injection. A diagrammatic depiction of the transport of radiolabeled antibodies is shown. A history of the development of radiolabeled antibodies is given, followed by a discussion of their characteristics and of the advantages and disadvantages of their use. Suggestions are made for further developments. The authors emphasize that to date the use of radiolabeled antibodies in tumor therapy cannot be considered alone, but rather as an adjunctive modality to surgery, chemotherapy, and conventional radiotherapy.

Chapter 13, "Clinical Considerations in Radiotracer Biodistribution Studies," calls attention to the potential for altered distribution of radiotracers due to the presence of pharmacologic agents. Accordingly, the author points out that in a clinical situation it is important to be aware of drug effects on the transport of diagnostic tracers if any unusual behavior of the tracer is to be construed as due to disease-induced effects. It is emphasized that the increasing use of short-lived, cyclotron-produced radiopharmaceuticals, given their attendant high costs, makes imperative a heightened awareness of all variables that can influence or even invalidate test results. This, of course, echoes the call for better understanding of the transport mechanisms for radiotracers, which is the underlying theme sounded in other chapters of the book.

Chapter 14, "The Measurement of Transport In-Vivo Using Radiotracers," and Chapter 15, "In Vitro Techniques to Study the Transport of Radiotracers," the concluding two chapters of the book, describe two complementary modalities in the study of biological mass transport: in vivo and in vitro techniques. Comparisons and contrasts between the two approaches are not very sharply drawn in either chapter. (On page 100 of Chapter 10, there is a brief but clear discussion of the supposed dichotomy.) In Chapter 14, the author begins by stating "The primary challenge in attempting to measure transport across a particular cell membrane from the circulating fluid is in the design of a suitable radiotracer. This design problem has been largely circumvented by using naturally occurring substrates of known endogenous biomolecules." He then points out that to achieve labeling in such a way as to avoid altering biochemical properties, one has had to rely on the use of radioisotopes of the principal constituent atoms of biochemical compounds, i.e., carbon, oxygen, and nitrogen. (By implication, the author seems to have in mind external detection exclusively.) He continues by implying that the high cost of producing these radionuclides motivates the design of the new radiotracers that mimic endogenous biomolecules in their transport and localization properties but that use more widely available radionuclides. As examples of such tracers, he cites the use of selenium-75 diamines for the measurement of regional intracellular pH, krypton-81m for regional brain blood flow, and flourine-18 to label glucose and dopamine analogs. In Chapter 15, the authors remark that the in vivo study of transport is hindered by action of many uncontrolled variables, such as vascular inhomogeneity, and in pathological states, by necrosis and phagocytosis. In contrast, by using in vitro techniques, the factors that regulate transport can be tested individually. They illustrate in vitro radiotracer-transport studies by making special reference to their own research in which they use cultured chick embryo fibroblasts and thyroid carcinoma cells. Additionally, they review the results of other workers who have used these same preparations for in vitro studies of radiotracer uptake. The authors give plots of the time histories of the uptake of gallium-67 citrate and of thallium-201 chloride in these cultures. They conclude by reviewing briefly some in vitro studies of the cellular uptake of radiolabeled glucose and its analogs.

The sequence of topics is logical, beginning at the relatively basic level of biological organization represented by the cell and its membrane, continuing through a development of multicapillary and organ models, and proceeding to clinical considerations. As would be expected in such a compilation of individual contributions, there is considerable uneveness of quality and breadth, together with some inevitable redundancies. The latter may after all be felicitous, for there is perhaps advantage in having discussions of the same topic from different perspectives. The quality of production is excellent, but no more than would be expected given the price of the book. There are some typographical errors, most of which are mathematical, and the context usually suggests the missing symbols. An annoying recurrence is the use of different fonts for the same symbol in the equations and in the text. Each chapter, except for three, has its individual table of contents, and the index is adequate. One of the most appealing features of this book is that it is exceedingly well referenced.

The scope of the book is reflected in the wide range of specialties of the various authors, and probably no single scientist (and certainly not this reviewer) could feel equally at home with the lot. For this reason, the book could most profitably serve as a reference text in a university interdepartmental library. There is much to recommend the book in this capacity.

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GENERAL PROCESSES OF RADIOTRACER LOCALIZATION, VOLUME I. L. J. Anghileri, Ed. Boca Raton, Florida, CRC Press, 1982, 257 pp, $78.00, US; $88.00, outside US

The use of radiotracers in biology and medicine is expanding at a tremendous rate. Radioisotopes are used to probe the metabolic pathways of organs and cells, and, with increasing specificity, are being used to differentiate diseased tissues from normal. *General Processes of Radiotracer Localization* is in two volumes, the most recent in a series of books concerning radiotracers in biology and medicine. Leopold J. Anghileri has endeavored to produce an in-depth reference on the science of tracer localization. Volume I is primarily concerned with the numerous factors related to the mechanism of localization of radiotracers by biological substrate. Each chapter has a general discussion on the basic cel-